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Reactivity of Aryl Palladium Complexes with Amide Groups in Ortho Position. Synthesis of Five- to Nine-Membered Palladacycles and Heterocycles

Reactividad de complejos arílicos de paladio con grupos amida en posición orto. Síntesis de paladaciclos y heterociclos de 5 a 9 miembros

D. Roberto Frutos Pedreño

2013

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Memoria presentada por **D. Roberto Frutos Pedreño** para optar al grado de Doctor por la Universidad de Murcia

Debido a que la Tesis ha sido redactada en inglés, se incluye un resumen en castellano, con una extensión de más de 2000 palabras, encuadernado como parte de la Tesis, en cumplimiento del Artículo 18 del Reglamento de Doctorado de la Universidad de Murcia (Redacción de la tesis).

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D. JOSÉ J. VICENTE SOLER, Catedrático de Universidad, y D. PABLO GONZÁLEZ HERRERO, Profesor Titular de Universidad, ambos del Departamento de Química Inorgánica de la Universidad de Murcia, AUTORIZAN:

La presentación de la Tesis Doctoral titulada **"REACTIVIDAD DE COMPLEJOS ARÍLICOS DE PALADIO CON GRUPOS AMIDA EN POSICIÓN ORTO. SÍNTESIS DE PALADACICLOS Y HETEROCICLOS DE 5 A 9 MIEMBROS"**, realizada por D. ROBERTO FRUTOS PEDREÑO bajo su inmediata dirección y supervisión, y que presenta para la obtención del grado de Doctor por la Universidad de Murcia.

Murcia, 5 de septiembre de 2013

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Deseo expresar mi más sincero agradecimiento:

Al Prof. Dr. D. José Vicente Soler, director de esta tesis doctoral e investigador principal del Grupo de Química Organometálica, por darme la oportunidad de trabajar en este grupo de investigación, por transmitirme su entusiasmo por el trabajo bien hecho y por haber confiado en mí en la realización de esta tesis.

Al Dr. Pablo González Herrero, codirector de esta tesis, por guiar este trabajo, por su paciencia, ayuda y ánimo en todo momento.

A los Dres. Isabel Saura, María Teresa Chicote, Juan Gil, Aurelia Arcas y Eloisa Martínez por su ayuda, ánimo y sabios consejos.

A todos mis compañeros y por supuesto amigos del Grupo de Química Organometálica: Antonio, María José Oliva, Inma, María José Fernández, Verónica, Fabio y María, por hacer más fácil el trabajo en equipo, por su ayuda en todo momento y por crear un buen ambiente.

A mis ex compañeros y amigos doctores José Antonio, Rashmi, Antonio Jesús y Paco.

A Mari Carmen, Paco Otón y José Berna del departamento de Química Orgánica.

A Silvia Díez-González por aceptarme en su grupo de investigación durante mi estancia de tres meses en el Imperial College London.

A mis amigas del grupo B, Luisa y Rocío, y por supuesto a mis amigos de siempre.

A Lilian por su ánimo y gran apoyo en estos últimos meses de tesis.

A mis padres y a mi hermano Pascual por haber confiado siempre en mí, por su gran apoyo, y a ellos quiero dedicar especialmente este trabajo.

A mis padres y hermano

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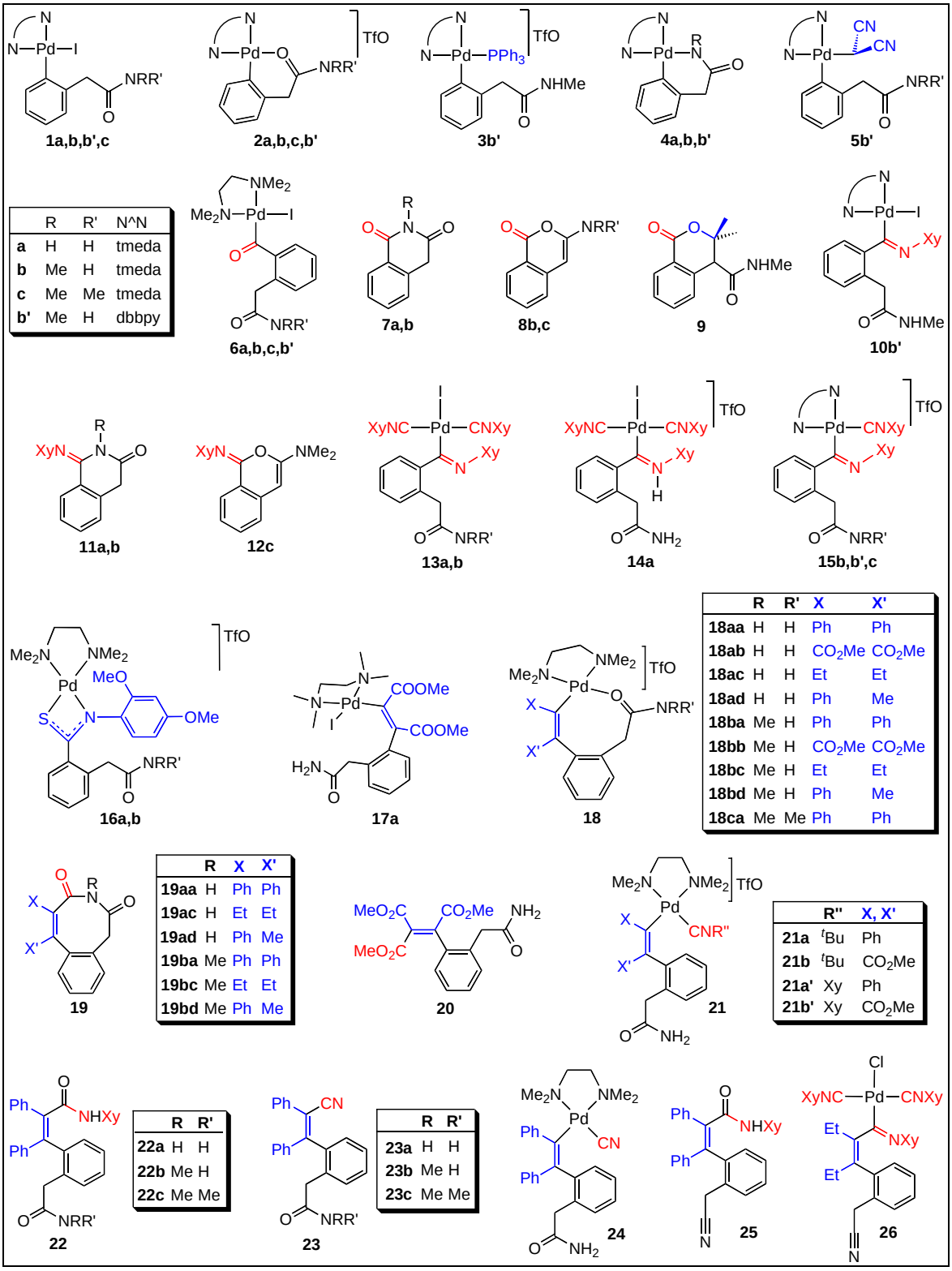
ABBREVIATIONS

APT	Attached Proton Test
Ar	aryl
br	broad
^{t}Bu	*tert*-butyl
calcd	calculated
d	doublet
dba	dibenzylideneacetone
dbbpy	4,4'-di-*tert*-butyl-2,2'-bipyridyl
dd	doublet of doublets
dec	decompose
equiv	equivalent
ESI	ElectroSpray Ionization
Et	ethyl
HMBC	Heteronuclear Multiple Bond Correlation
HMQC	Heteronuclear Multiple-Quantum Correlation
HRMS	High Resolution Mass Spectrum
IR	infrared
L	litre
m	multiplet
m/z	mass/charge ratio
Me	methyl
Mp	Melting point
MS	Mass Spectrum
NMR	Nuclear Magnetic Resonance
Ph	phenyl
ppm	parts per million
q	quartet
rt	room temperature
s	singlet
t	triplet
td	triplet of doublets
TfO	triflate (trifluoromethanesulfonate)
THF	tetrahydrofurane
tmeda	*N,N,N′,N′*-tetramethylethylenediamine
TMS	tetramethylsilane
Xy	xylyl (2,6-dimethylphenyl)
XyNC^c	coordinated xylyl isocyanide
XyNC^i	inserted xylyl isocyanide



	R	R'	N^N
a	H	H	tmeda
b	Me	H	tmeda
c	Me	Me	tmeda
b'	Me	H	dbbpy

	R	R'	X	X'
18aa	H	H	Ph	Ph
18ab	H	H	CO_2Me	CO_2Me
18ac	H	H	Et	Et
18ad	H	H	Ph	Me
18ba	Me	H	Ph	Ph
18bb	Me	H	CO_2Me	CO_2Me
18bc	Me	H	Et	Et
18bd	Me	H	Ph	Me
18ca	Me	Me	Ph	Ph

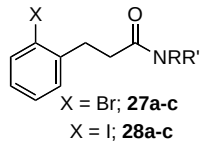
	R	X	X'
19aa	H	Ph	Ph
19ac	H	Et	Et
19ad	H	Ph	Me
19ba	Me	Ph	Ph
19bc	Me	Et	Et
19bd	Me	Ph	Me

	R''	X, X'
21a	^{t}Bu	Ph
21b	^{t}Bu	CO_2Me
21a'	Xy	Ph
21b'	Xy	CO_2Me

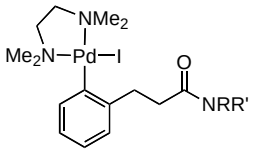
	R	R'
22a	H	H
22b	Me	H
22c	Me	Me

	R	R'
23a	H	H
23b	Me	H
23c	Me	Me

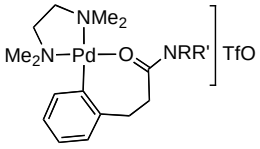
	R	R'
a	H	H
b	Me	H
c	Me	Me



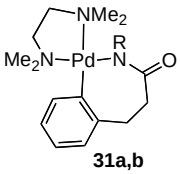
X = Br; **27a-c**
X = I; **28a-c**



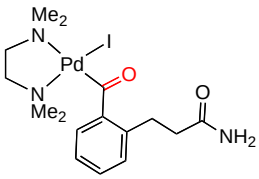
29a-c



30a-c



31a,b



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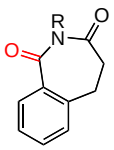

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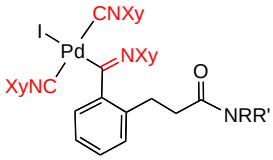
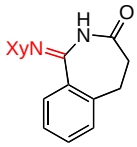
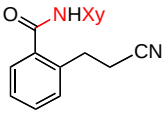


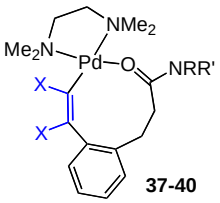
34a-c



35a

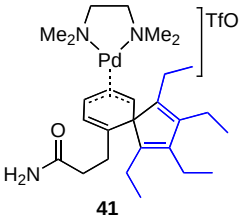


36a



37-40

	R	R'	X
37a	H	H	Ph
37b	Me	H	Ph
37c	Me	Me	Ph
38a	H	H	$C_6H_4{}^nBu$-4
39a	H	H	C_6H_4Br-4
40a	H	H	CO_2Me



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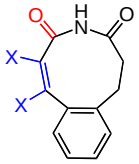
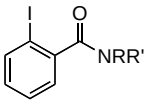
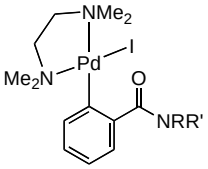


42-44

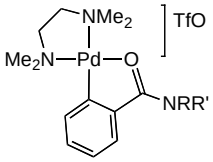
	X
42	Ph
43	$C_6H_4{}^nBu$-4
44	C_6H_4Br-4



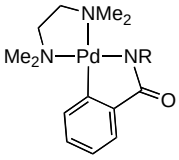
45b,c



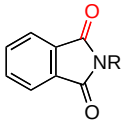
46a–c



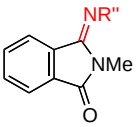
47a-c



48a,b

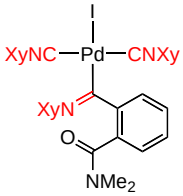


49a,b



50b,b'

	R''
50b	Xy
50b'	^{t}Bu



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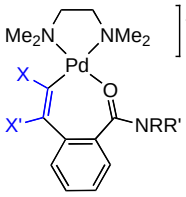
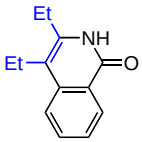


52-57

	R	R'	X	X'
52a	H	H	Ph	Me
52b	Me	H	Ph	Me
53b	Me	H	Ph	Ph
53c	Me	Me	Ph	Ph
54b	Me	H	Et	Et
54c	Me	Me	Et	Et
55b	Me	H	CO_2Me	CO_2Me
56b	Me	H	CO_2Me	Ph
57b	Me	H	CO_2Et	Ph



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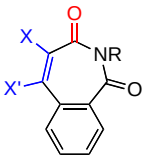
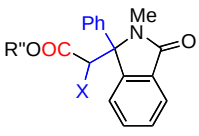


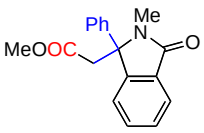
59a-d

	R	X	X'
59a	H	Ph	Me
59b	Me	Ph	Me
59c	Me	Ph	Ph
59d	Me	Et	Et



60a-d

	X	R''
60a	CO_2Me	H
60b	CO_2Me	Me
60c	CO_2Me	Et
60d	CO_2Et	Et



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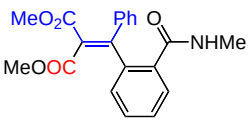

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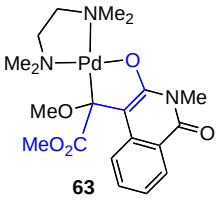

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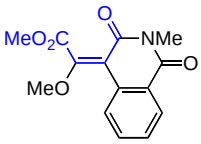

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GENERAL INTRODUCTION

Aryl Palladium Complexes

Palladium-mediated processes are of extraordinary relevance in modern organic synthesis. A wide range of methodologies employ this metal, either in catalytic or stoichiometric transformations. Among them, C–C and C–heteroatom bond-forming reactions have become essential tools for the synthesis of natural products, polymers, pharmaceuticals and other compounds with diverse applications. The advantageous use of palladium is mainly associated with its ability to catalyze many types of transformations and its tolerance to functional groups and the presence of moisture and molecular oxygen. Furthermore, palladium shows a low toxicity level.

The three oxidation states that predominate in the chemistry of palladium complexes are 0, +II, and +IV, although both the +I and +III states are known. The 0 and +II states are stable and readily interconvertible. In fact, many of the most important palladium-mediated transformations involve oxidative additions to Pd(0) and/or reductive eliminations from Pd(II) complexes.

Aryl palladium complexes participate as intermediates in many palladium-mediated organic reactions. The metal in these intermediates is usually in the +II oxidation state, although recent studies have provided evidences of the participation of Pd(IV) complexes as key intermediates in certain catalytic processes.[1, 2] Aryl complexes of Pd(II) exhibit an extraordinarily rich chemistry, mainly as a consequence of the relative lability of the Pd–C bond. Over the course of last decades, numerous studies have focused on how these complexes take part in diverse processes, including oxidative additions, reductive eliminations, β-hydride eliminations, carbometalations, migratory insertions or nucleophilic substitutions, which are common steps in many C–C and C–heteroatom bond-forming reactions. Migratory insertions of unsaturated molecules into the Pd–C bond are of particular importance because they allow the formation of new C–C bonds and the resulting complexes may undergo subsequent attack by internal o external nucleophiles, opening a wide range of possibilities for the synthesis of organic compounds, including carbocycles and heterocycles of biological relevance.

Palladium-Mediated Processes Involving Aryl Palladium Complexes

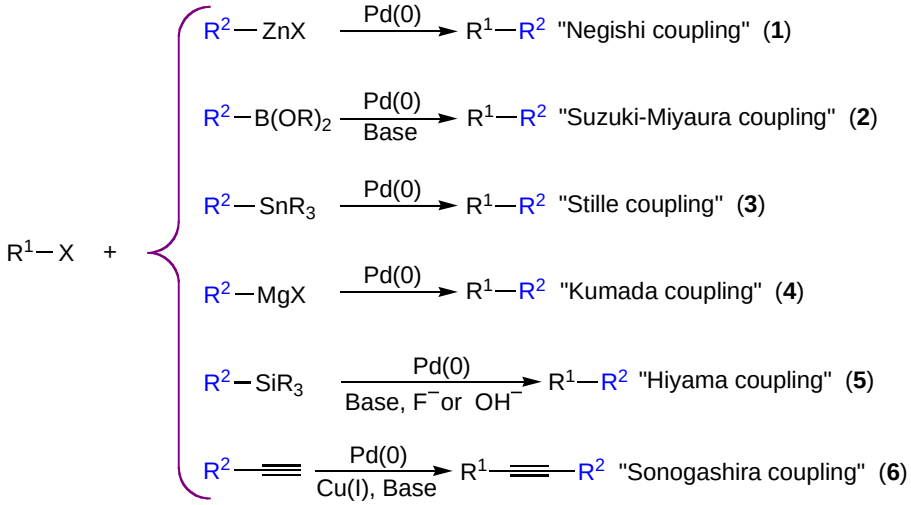
The most important palladium-mediated processes involving aryl palladium complexes are compiled in the following sections. They can be grouped into three main categories: (**1**) C–C bond formation through cross-coupling reactions, (**2**) C–N or C–O bond formation through cross-coupling reactions (Buchwald-Hartwig), and (**3**) insertion of unsaturated molecules into the Pd–C bond.

C–C Bond Formation Through Cross-Coupling Reactions

Cross-coupling Reactions with Organometallic Reagents Catalyzed by Palladium

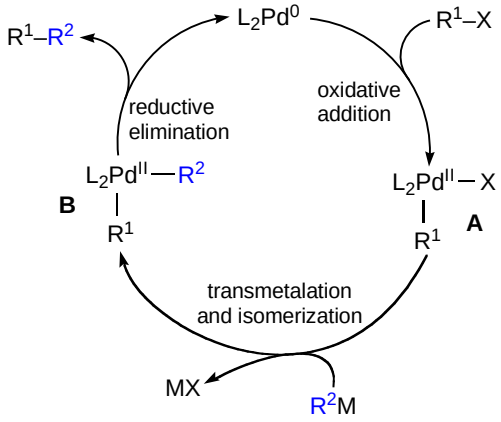
The reactions within this category are summarized in Scheme 1. All of them involve the coupling between organohalides or organotriflates with organometallic reagents catalyzed by Pd(0):[3] (1) the Negishi coupling,[4] employs organozinc species as the organometallic reagent, which may be obtained by oxidative addition of an organohalide to Zn(0) or be generated *in situ* by transmetalation of Grignard or organolithium reagents with $ZnCl_2$. (2) The Suzuki-Miyaura coupling,[5] is similar to the Negishi coupling, but it uses organoboron instead of organozinc reagents; an advantage over the Negishi reaction is that organoboron reagents are non-toxic. (3) The Stille coupling[6] employs organostannanes as organometallic reagents, its major drawback being the toxicity of these compounds; as an advantage, the Stille reaction is compatible with many functional groups. (4) The Kumada coupling,[7] is the cross-coupling between a Grignard reagent and an organohalide or triflate. A disadvantage is the poor functional-group tolerance of the Grignard reagents. However, the use of Grignard reagents may be advantageous because many of them are commercially available, or are easily synthesized. (5) The Hiyama coupling[8] is the cross-coupling reaction of organosilanes with organic halides or triflates, in the presence of a nucleophile such as F^- or OH^- to increase the polarization of the C–Si bond. Known advantages are the tolerance to many functional groups and their void toxicity. (6) The Sonogashira coupling[9] is based on the cross-coupling between a terminal alkyne and a vinyl or aryl halide using as cocatalyst a Cu(I) species that activates 1-alkynes through the formation of Cu(I) acetylides. In general, this reaction takes place under mild conditions and is compatible with a wide range of functional groups.

Scheme 1



These couplings follow a general mechanistic cycle (Scheme 2). The oxidative addition of the organohalide or -triflate to a Pd(0) complex to give an organopalladium(II) species (**A**) is the first step of the process. The organic group R^2 is then transferred to the palladium center by the organometallic reagent in a transmetalation process. The resulting intermediate (**B**) undergoes reductive elimination to give the coupling product R^1–R^2, regenerating the palladium catalyst $L_2Pd(0)$.

Scheme 2

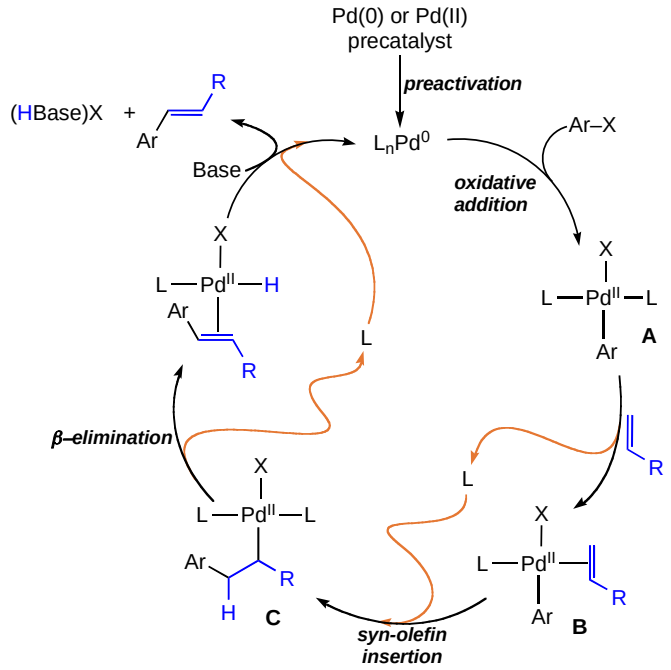


The Heck reaction

The Heck reaction, also called the Mizoroki-Heck reaction, is the palladium-catalyzed olefination of aryl or alkenyl halides or triflates in the presence of a base. It has proved to be of paramount importance because it allows to obtain highly functionalized alkenes through C–C coupling. This catalytic reaction was first reported by the Mizoroki[10] and Heck[11] groups in the early 1970s. The intramolecular version of the Heck reaction is extremely fruitful for the

synthesis of carbocycles and heterocycles.[12] The first step of the generally accepted mechanism (Scheme 3) is the oxidative addition of the aryl or alkenyl halide or triflate to the Pd(0) catalyst to give an organopalladium(II) complex (**A**). The next step is the coordination of the olefin to the palladium center (**B**). Then the olefin inserts into Pd–C in a *syn* fashion leading to an alkyl species (**C**) containing a *β*-hydrogen, which quickly decomposes through a *β*-hydride elimination process[13] that occurs by a cisoid metal/C–H(*β*). Finally, the desired (*E*)-product (thermodynamically controlled conditions) is liberated and the catalytically active Pd(0) species is regenerated by a base-assisted hydrogen halide or triflate elimination. Currently, mechanisms involving a Pd(II)/Pd(IV) cycle that employ a Pd(II) precatalyst are under debate.[14] There are even some evidences of the participation of Pd(IV) species, reported by our research group.[2,15]

Scheme 3

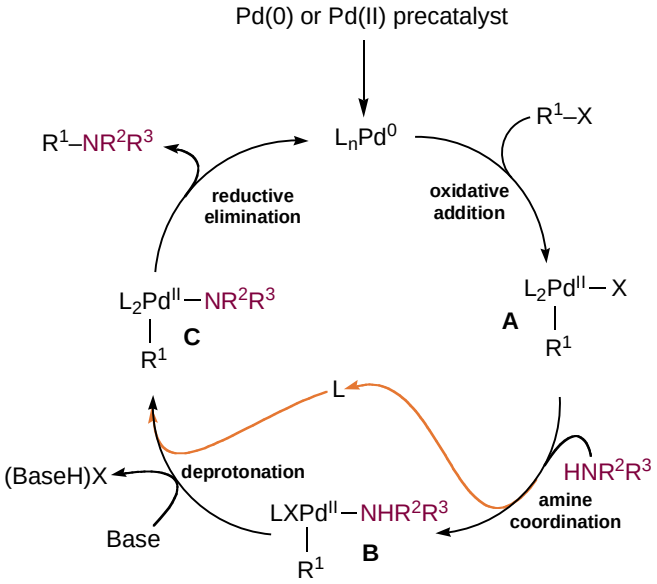


C–N and C–O Bond Formation Through Cross-Coupling Reactions (Buchwald–Hartwig)

Buchwald[16] and Hartwig[17] independently reported a method for the synthesis of arylamines based on the palladium-catalyzed C–N coupling reaction of aryl halides with amines in presence of a base. This reaction was extended to C–N couplings of aryl or vinylic halides with amines or amides. In addition, variations of the Buchwald–Hartwig method may be used for etherification of aryl halides.[18]

The mechanism (Scheme 4) of this reaction is similar to those known for C–C coupling reactions above mentioned, which includes the oxidative addition of the aryl or vinyl halide to a palladium(0) species to give the palladium(II) intermediate **A**. The coordination of the amine gives the intermediate **B**. The presence of a base causes the deprotonation of the coordinated amine to yield the intermediate amido complex **C**, which undergoes reductive elimination to give the arylic or vinylic amine or amide with the regeneration of the palladium(0) catalyst.

Scheme 4



Insertion of Unsaturated Molecules Into the Pd–C Bond

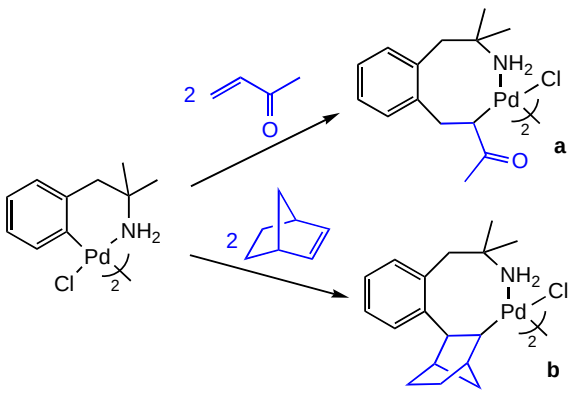
The study of the reactivity of organopalladium complexes towards unsaturated molecules is very useful to understand the mechanisms of palladium-catalyzed organic transformations or for developing new routes for the synthesis of organic compounds. The term "insertion" may be defined as the migration of a ligand from the palladium center to the adjacent coordinated unsaturated molecule, resulting in the formation of a new complex. If there is an internal nucleophile in the inserted molecule, a subsequent reductive elimination process may occur to give interesting carbocycles or heterocycles. The insertion of alkenes, alkynes, dienes and allenes into the Pd–C bond is often termed **carbopalladation**, because it is formally the *syn* addition of a C–Pd bond to a C–C multiple bond. These insertions are assumed to be key steps in many important palladium-catalyzed reactions and many efforts have been devoted to the isolation of intermediate species in order to get insight into their

mechanism. This can be done through the study of stoichiometric insertions of unsaturated molecules into the Pd–C bond.

Insertion of Alkenes

As previously noted, the insertion of alkenes into the Pd–C bond of aryl palladium complexes is a key step in the catalytic cycle of the Heck reaction. The alkyl intermediates cannot usually be isolated because they rapidly undergo a β-hydride elimination. Only a few examples of isolated alkyl palladium complexes resulting from the insertion of alkenes into the Pd–C bond are known, which have been reported by our research group.[19-22] For instance, the insertions of alkenes of the type CH_2=CHC(O)R (R = Me, OEt) or 2-norbornene into the Pd–C bond of ortho-palladated primary amines give stable alkyl complexes[22] (Scheme 5) that are assumed to be intermediates in the catalytic olefination of *N,N*-disubstituted arylalkylamines.[23] Although these complexes contain β-hydrogens, it is likely that the *syn* arrangement required for the β-hydride elimination is not possible, because of the existence of an intramolecular hydrogen bond (example a, Scheme 5). In the case of the complex arising from the insertion of 2-norbornene (example b, Scheme 5), its stability can be justified because the palladium atom and the β-hydrogen do not adopt the needed cisoid conformation for the β-hydride elimination.

Scheme 5



Complexes resulting from alkene insertions into a Pd–acyl bond are also known,[24, 25] which are considered key intermediates in the palladium-catalyzed alternating copolymerization of alkenes and carbon monoxide.[26]

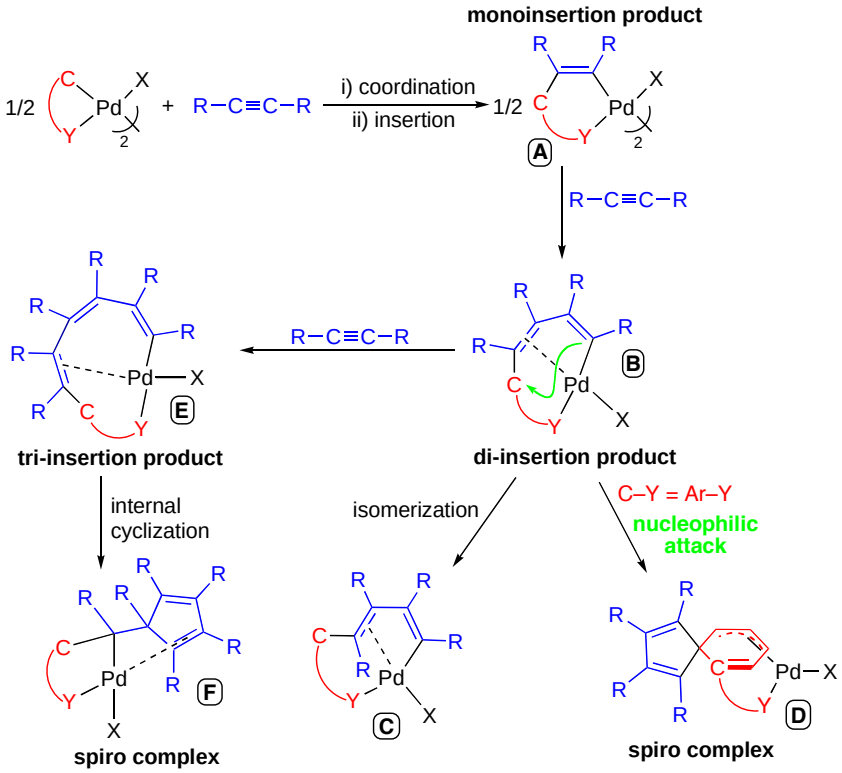
Insertion of Alkynes

The insertion of one alkyne molecule into the Pd–C bond of aryl palladium complexes usually results in the formation of vinylpalladium complexes.[19, 27-48] The insertion of two and even three alkyne molecules may also take place. These reactions have most often been reported for palladacycles (ortho-palladated arenes).[29, 31, 32, 35, 36, 39, 45, 49-56]

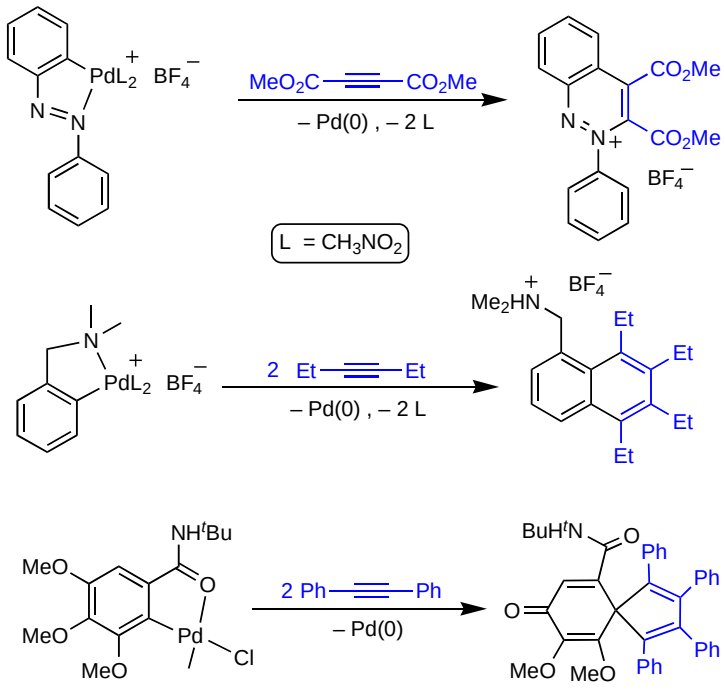
Polyinsertions of alkynes occur in a sequential manner (Scheme 6),[31, 39, 51] the rate-determining step being the formation of the monoinsertion complex.[55] The reaction starts with the coordination of the alkyne to the metal in a η^2-coordination mode,[49] followed by the migration of the aryl group to the coordinated alkyne to give a vinyl-palladated complex (**A**).[29, 45, 55, 56] A second insertion gives a *cis,cis*-butadienyl complex (**B**), which can either undergo an isomerization process to afford a more favorable conformation for the η^2-coordination of the first inserted vinyl group to the palladium center and/or possibly to relieve the strain between the substituents (**C**),[35] or a nucleophilic attack of the metalated carbon to an aromatic carbon to give a spiro ligand, which is coordinated to palladium through a η^3-allylic bond (**D**).[34, 36, 40, 51, 57] The insertion of a third molecule of alkyne may take place to give a hexatrienyl complex (**E**) that undergoes an internal cyclization to give a spiro complex with a η^2-bonded cyclopentadienyl fragment (**F**).[35, 50] The outcome of the reaction of an arylpalladium complex with an alkyne depends on the relative rates of the different steps,[35, 50, 52] which are in turn influenced by steric and electronic factors in both the complex and the alkyne, the temperature, the nature of the ancillary ligands on the metal or the way of mixing the reactants.[30, 31, 33, 43, 45, 50, 51, 58] Thus, the monoinsertion product cannot be isolated if the rate of the second insertion is faster than the first one, and the tri-insertion product cannot be trapped if the isomerization of the di-insertion intermediate **B** is faster than the third insertion. The insertion steps have been shown to be faster as the nucleophilicity of the metalated arylic carbon increases and when alkynes bearing smaller substituents or of a higher electron-withdrawing character are employed.[55]

Alkyne-insertion reactions are considered of great importance because of the possibilities they offer in organic synthesis. In particular, enlarged palladacycles obtained from the insertion of one, two or three molecules of alkyne may lead to the formation of interesting carbocyclic or heterocyclic compounds upon depalladation (examples, Scheme 7).[19, 28, 30-37, 39, 40, 42, 44, 52, 53, 59-61]

Scheme 6



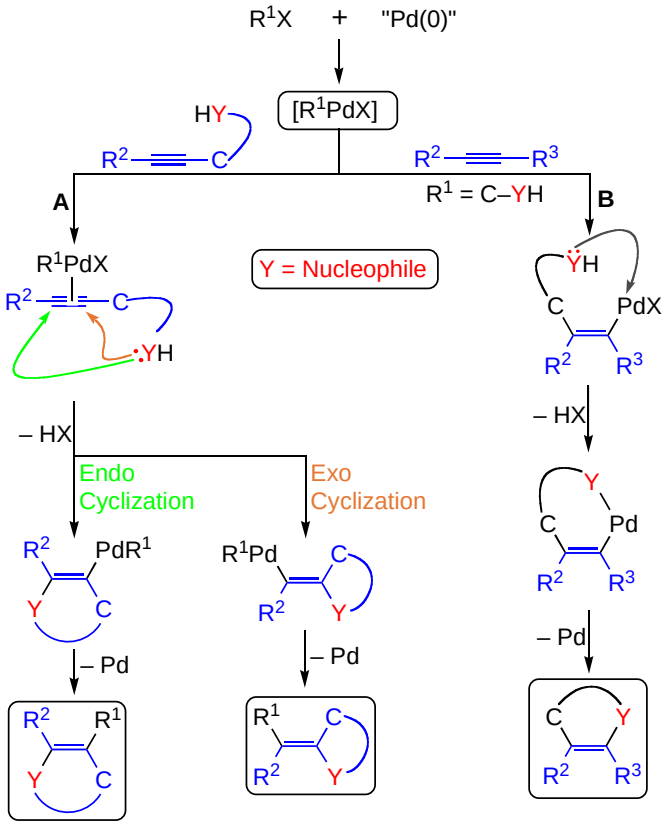
Scheme 7



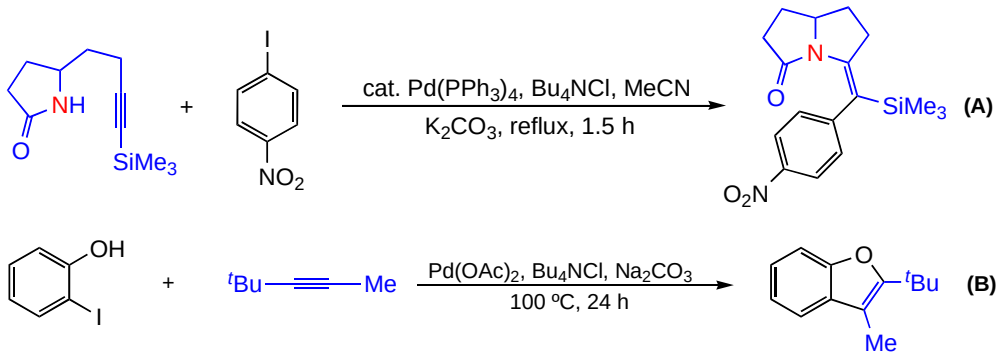
In addition, the insertion of alkynes into the Pd–C bond of aryl-palladium complexes is a key step in palladium-catalyzed cyclizations of aryl or vinyl halides with alkynes, which are very useful in carbocyclic and heterocyclic synthesis.[62-64] The catalytic process can take place

through two different reaction pathways (Scheme 8) depending on whether the alkyne contains an internal nucleophile (**A**) or the nucleophile comes from the aryl or vinyl halide (**B**). Two examples (**A**,[65] **B**[62]) are illustrated in Scheme 9.

Scheme 8



Scheme 9

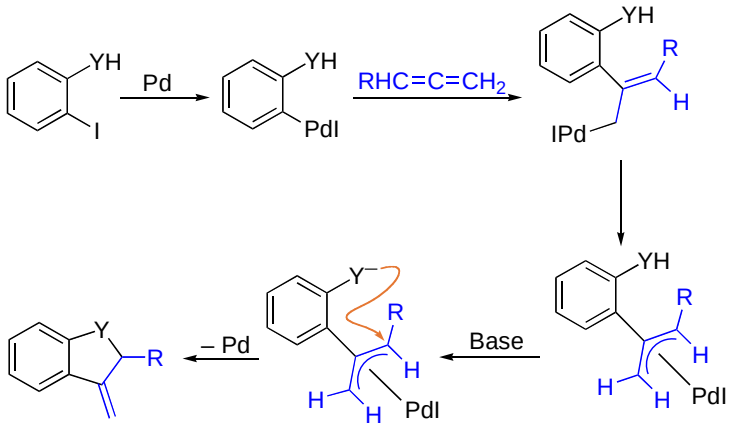


Insertion of Dienes and Cumulenes

The insertion of dienes into the Pd–C bond of organopalladium complexes may lead to the formation of: (a) η^1-η^2-enylpalladium[66,67] complexes, when non-conjugated dienes are used, which are intermediates in the formation of the thermodynamically more stable η^3-allyl

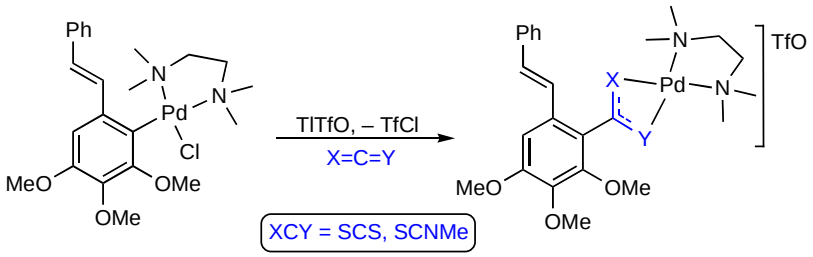
derivatives through a Pd-migration process[67] and (b) η^3-allylpalladium complexes when conjugated dienes[68] or allenes[20, 38, 69] are used. η^3-Allylpalladium complexes participate as intermediates in palladium-catalyzed reactions of aryl halides with allenes,[70, 71], which allow the synthesis of a wide number of heterocycles.[64, 71-73] In general terms, the oxidative addition of the aryl halide to Pd(0) is the first step of the process (Scheme 10).[72] The resulting arylpalladium intermediate undergoes insertion of the 1,2-diene affording a η^3-allylpalladium complex, which finally leads to the formation of the heterocycle through an intramolecular nucleophilic substitution.

Scheme 10



Heterocumulenes such as isothiocyanates or CS_2 also insert into the Pd–C bond of arylpalladium complexes,[38, 74, 75] giving thioamidate or dithiocarboxylate complexes, respectively, bonded to the metal in a $\kappa^2(X,S)$ fashion (X = S, N) (Scheme 11).

Scheme 11

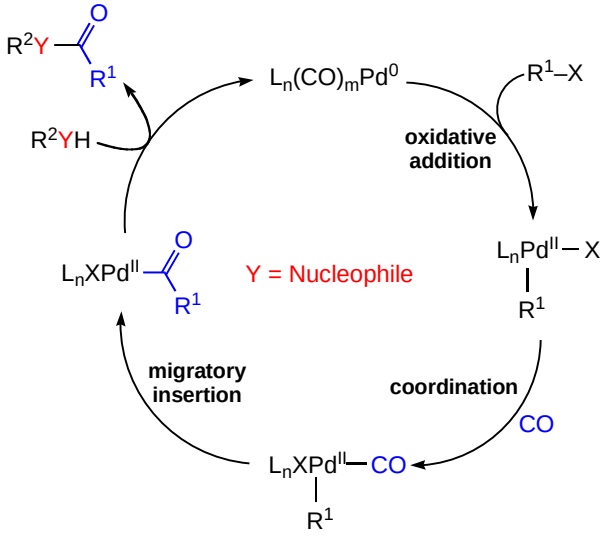


Insertion of CO. Carbonylation Reactions

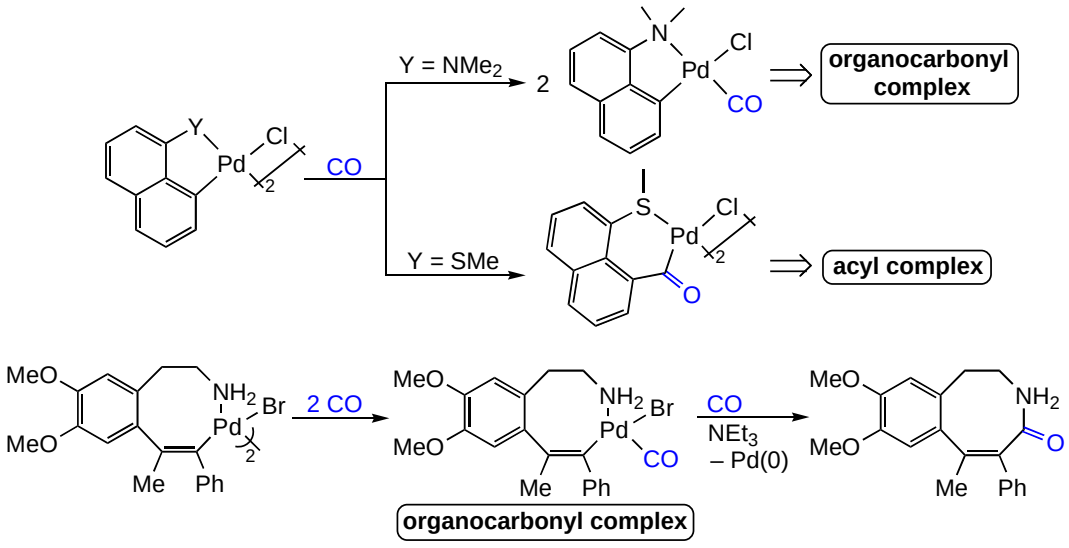
Aryl palladium complexes react with CO to give acyl complexes.[19, 44, 46, 47, 75-82] These reactions have been broadly studied because they constitute a key step in palladium-catalyzed carbonylations.[83, 84] A simplified mechanism of both stoichiometric and catalytic reactions (Scheme 12) includes the coordination of a molecule of CO to the metal to give an

organo(carbonyl)palladium complex,[25, 48, 77, 85] which is generally difficult to isolate because it readily undergoes migratory insertion to give an acyl derivative (Scheme 13); the latter may further react with an internal or external nucleophile to afford a carbonyl-containing organic product upon depalladation.

Scheme 12



Scheme 13

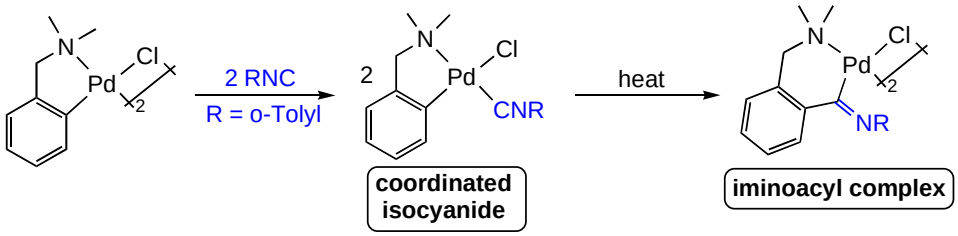


Palladium-catalyzed carbonylations of aryl halides are useful for the synthesis of aldehydes, carboxylic acids, esters, amides, etc.[86] In addition, they constitute an excellent method for the synthesis of heterocycles.[83]

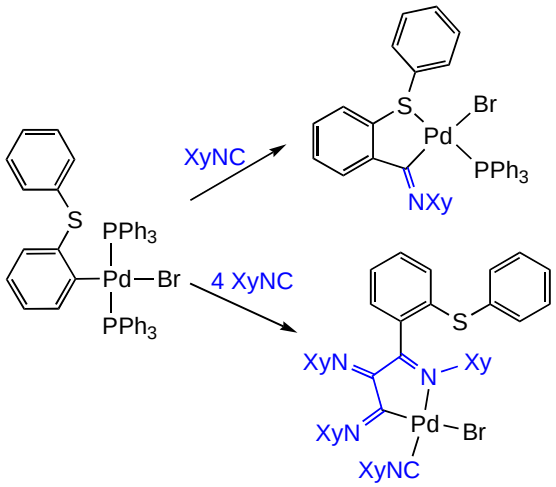
Insertion of Isocyanides

The insertion of isocyanides began to be studied to get insight into the mechanism of palladium-mediated carbonylation reactions because these ligands are isoelectronic with CO.[87] The main difference is that isocyanides are stronger σ donors and weaker π acceptors.[88] These characteristics are reflected by the ν(C≡N) stretching frequency, which is generally higher for coordinated isocyanides as compared to the free ligands, whereas the ν(CO) frequency decreases for coordinated CO. This happens as result of a donation of electron density from the antibonding HOMO of the ligand to the metal with a low or void π-back-donation into the carbon p_z orbital,[89] finally causing an increase in the C–N bond order. Isocyanides may readily undergo migratory insertion into the Pd–C bond after coordination to the Pd center, giving iminoacyl complexes (example in Scheme 14).[19, 37, 44, 47, 75, 77, 79-82, 90-101] In some cases, multiple insertions may take place (example in Scheme 15).[37, 81, 93, 95, 96, 102]

Scheme 14

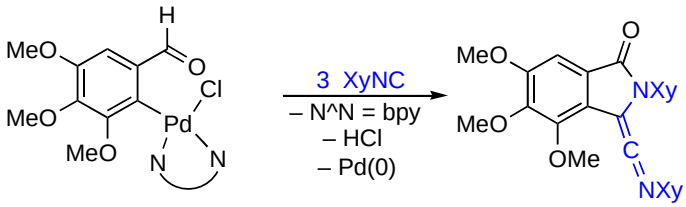


Scheme 15

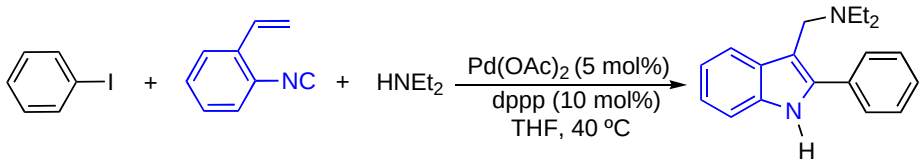


Isocyanide insertions into the Pd–C bond have been the subject of considerable interest because of their involvement in many stoichiometric[19, 37, 44, 75, 80, 92, 97, 103] (example in Scheme 16) and catalytic (example in Scheme 17)[104, 105] syntheses of organic compounds.

Scheme 16



Scheme 17

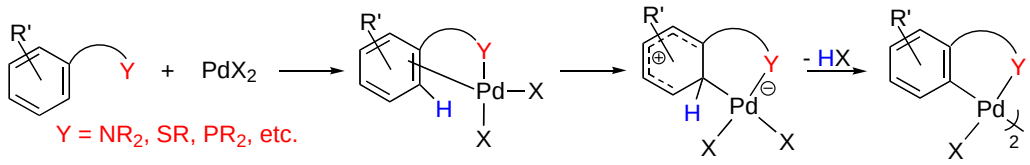


Synthesis of Aryl Palladium Complexes

C–H Bond Activation

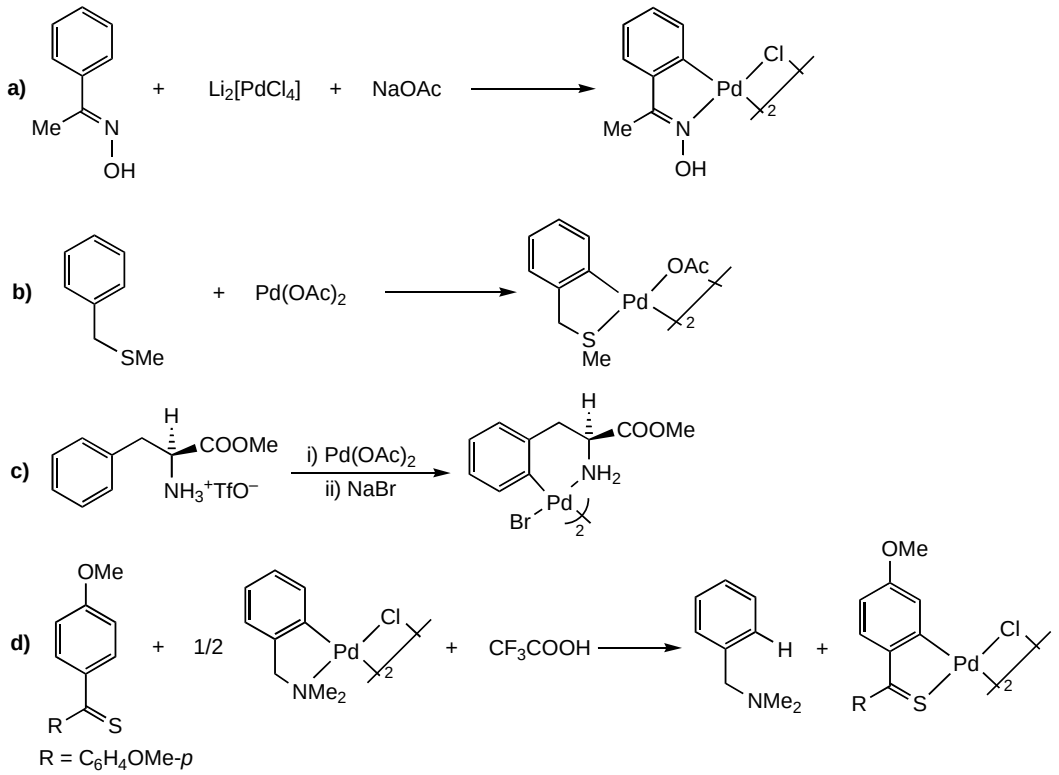
Direct C–H bond activations of aromatic derivatives most commonly involve the coordination of a substituent in *ortho* position to Pd(II) and subsequent electrophilic aromatic substitution (Scheme 18).[106] This type of reaction is often referred to as orthopalladation,[80, 82, 106, 107] an usually leads to the formation of palladacyles.

Scheme 18



Among the typical orthopalladation procedures (examples in Scheme 19) are the reaction of arenes with tetrachloropalladate salts in the presence of a base (example **a**)[108] or with palladium acetate (example **b**),[30] the reactions of ammonium salts of arenes bearing amino substituents with palladium acetate (example **c**),[82] or the reaction of the arene with a palladacycle to give a different palladacycle, which is known as transcyclopalladation[109] (example **d**).[110]

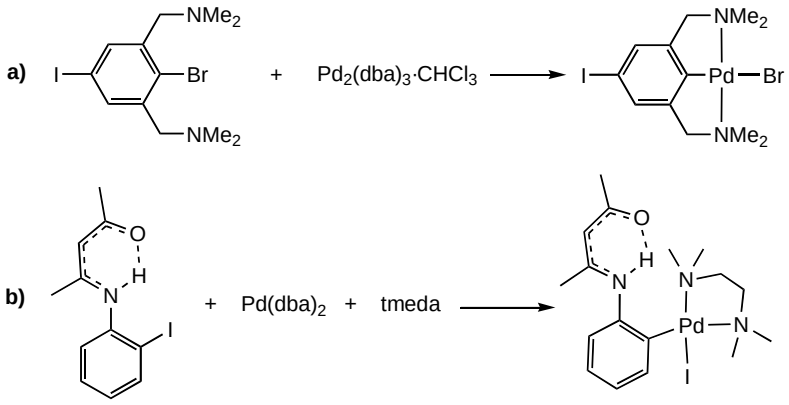
Scheme 19



Oxidative Addition

The oxidative addition of aryl halides to palladium(0) complexes leads to the formation of aryl(halo)palladium(II) complexes (examples **a**[111] and **b**[100] in Scheme 20). This method can be employed to introduce aryl ligands when the C–H bond activation method is not suitable. In some cases it is necessary to use ancillary ligands in order to stabilize the resulting complex. The rates of oxidative addition reactions depend on the halide, decreasing in the sequence C–I > C–Br >> C–Cl >> C–F. Several mechanisms have been postulated to explain the oxidative addition.[112]

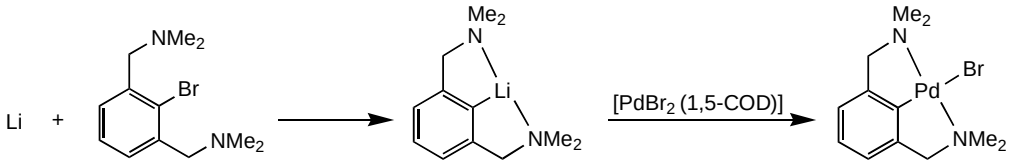
Scheme 20



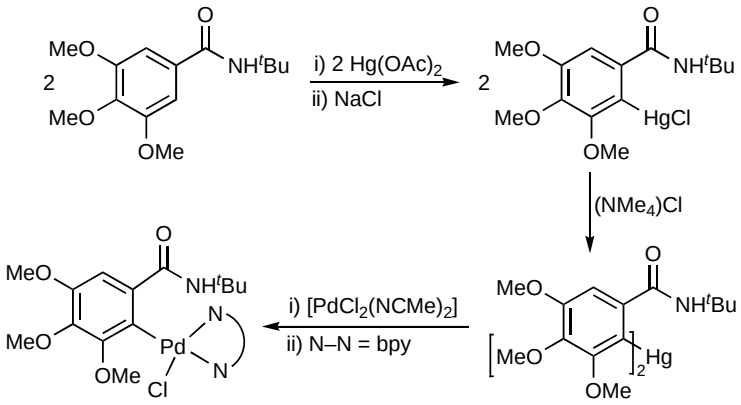
Transmetalation

This method is based on the transfer of the aryl ligand from one metal to another. Widely employed transmetalating agents are organolithiums (example in Scheme 21)[113, 114] and organomercurials (example in Scheme 22).[37,42,99,115-117]

Scheme 21



Scheme 22



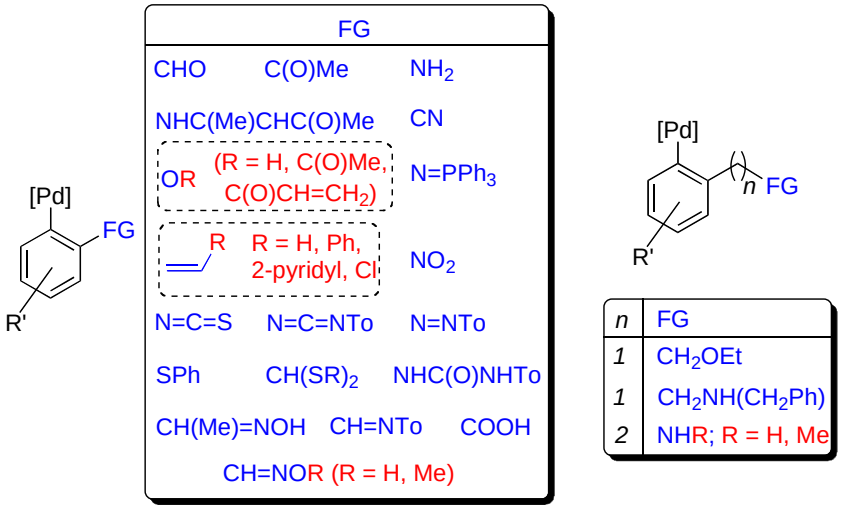
Ortho-Functionalized Aryl Palladium Complexes

One of the most important research lines of our research group is dedicated to the synthesis and study of the reactivity of ortho-functionalized aryl palladium complexes, with the main objective of discovering new type of processes and exploring its applicability in organic synthesis. These complexes react with unsaturated species (CO, isocyanides, alkenes, alkynes, cumulenes, etc.) to give insertion products. The proximity of the functional group to the metal exerts a great influence on the reactivity toward unsaturated molecules, which, in many cases may trigger additional processes involving the participation of such group, giving new complexes or interesting organic compounds, including heterocycles.

To date, our research group has prepared and studied the reactivity of palladium complexes with aryl ligands bearing a wide variety of groups in *ortho* position, including functional groups directly bound to the aryl ring or connected through an alkyl chain (Scheme 23). The first category includes carbonyl,[37,38,40,41,57,60,61,95,118] amino,[78,96,100] hydroxy,[19,94] alkene,[38, 61, 95, 119] cyano,[61, 95] iminophosphorane,[98] nitro,[115, 120] isothiocyanate,[121]

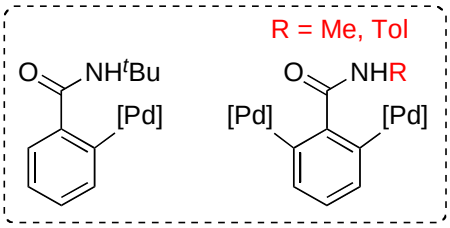
carbodiimide,[121] azo,[122] thioether,[81, 123] dithioacetal,[99] urea[44] imine,[117] carboxy,[117] and oxime,[101, 117] functionalities. The second category includes benzylethers,[42] benzylamines,[79, 97, 124] and phenethylamines.[45, 46, 75, 80, 82, 125]

Scheme 23



In addition, a few examples of aryl palladium complexes bearing an amide function in ortho have been studied by our research group, but are limited to ortho-palladated[37] and ortho-dipalladated benzamides[47] (Scheme 24).

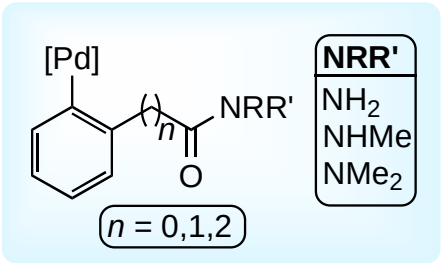
Scheme 24



Objectives

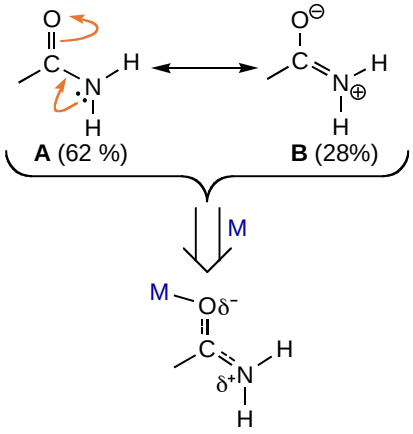
The precedents exposed above motivated us to extend the study of the reactivity toward unsaturated molecules (mainly CO, isocyanides and alkynes) of aryl palladium complexes containing an amide group in *ortho* position. In this work, we employ aryl ligands with the amide function directly bonded to the aryl ring (ortho-palladated benzamides) or connected through one or two methylene groups (ortho-palladated phenylacetamides or 3-phenylpropanamides) (Scheme 25). This study has allowed the synthesis of a series of new palladacycles and heterocycles of different ring sizes (5, 6, 7, 8 or 9 members).

Scheme 25



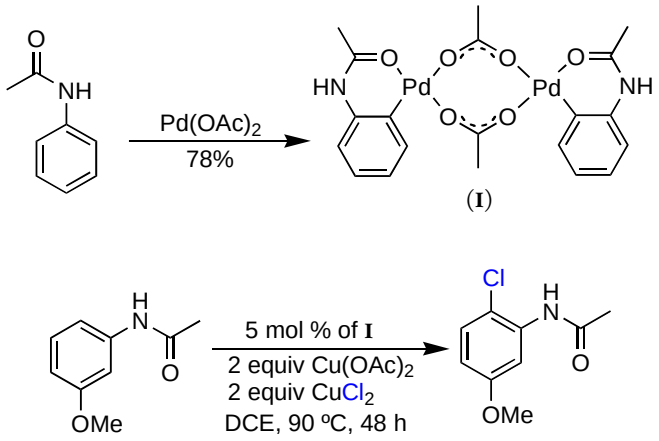
In terms of their properties as functional group, it is worth noting that in amides there is a delocalization of the lone pair on the nitrogen atom toward the oxygen atom leading to the formation of a partial double bond between the nitrogen and the carbonyl carbon. In a deeper analysis, computational studies have allowed to estimate the contributions of the resonance structures **A** (62%) and by **B** (28%) of acetamide (Scheme 26).[126]

Scheme 26



This delocalization allows the amide function to coordinate to the palladium center through the oxygen atom, which enables it to act as a directing group in palladium-catalyzed C–H functionalization reactions.[127] An example of this is the ortho-chlorination of acetanilides in presence of copper(II) chloride (Scheme 27).[128] Palladacycle **I**, resulting from the ortho-palladation of acetanilide,[129] can act as an active species in the catalytic cycle. This complex is a clear example of the *O*-coordination of amides to the palladium atom.

Scheme 27



Organization and Summary

This thesis is organized into four chapters. Each of them contains its own specific introduction, results and discussion section, experimental part and literature references. The chapters are ordered according to the chronological sequence in which they were completed. The general conclusions are summarized in one additional section. A *Supplementary Material* CD is attached to the end of this book, which collects the IR spectra, ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra for all the compounds and the crystallographic data in CIF format for the crystal structures.

A brief summary of each chapter is given in the following paragraphs.

Chapter I. Synthesis and Reactivity of Ortho-Palladated Phenylacetamides. Intramolecular C–N vs C–O Reductive Coupling after CO or XyNC Insertion into the Pd–C Bond. Synthesis of Isoquinoline- and Isocoumarin-based Heterocycles.

This chapter presents the synthesis of ortho-palladated phenylacetamides of the type $[Pd\{C_6H_4CH_2C(O)NRR'\text{-}2\}I(tmeda)]$ (NRR' = NH_2, NHMe, NMe_2), their corresponding cationic C,O- or neutral C,N-cyclopalladated derivatives. A systematic study of the reactions of these aryl complexes with CO and XyNC (Xy = 2,6-dimethylphenyl) has been carried out. These insertion reactions lead to isoquinoline- or isocoumarin-based heterocycles resulting from intramolecular C–N or C–O couplings that involve the deprotonation of the NH_2 or NHMe groups (C–N couplings) or the alpha CH_2 group (C–O couplings) and subsequent reductive elimination. The palladium-mediated C–O couplings included in this section are the first involving an amide function.

Chapter II. Sequential Insertion of Alkynes and CO or Isocyanides into the Pd–C Bond of Cyclopalladated Phenylacetamides. Synthesis of Eight-Membered Palladacycles, Benzo[*d*]azocine-2,4(1*H*,3*H*)-diones and Acyclic Acrylonitrile and Acrylamide Derivatives.

In this chapter, we describe the synthesis and reactivity towards CO and isocyanides of a series of eight-membered palladacycles of the type [Pd{κ^2*C*,*O*-C(X)=C(X')C$_6$H$_4$CH$_2$C(O)NRR'-2}(tmeda)]TfO, obtained from alkyne monoinsertions into the Pd–C bond of cationic cyclopalladated phenylacetamides [Pd{κ^2*C*,*O*-C$_6$H$_4$CH$_2$C(O)NRR'-2}(tmeda)]TfO, which were described in Chapter I. A set of unprecedented benzo[*d*]azocine-2,4(1*H*,3*H*)-diones were obtained from the NH$_2$ and NHMe derivatives after treatment with CO, resulting from the insertion of CO into the Pd–C bond and a subsequent C–N reductive coupling. In contrast, the reactions with isocyanides led to the isolation of complexes resulting from isocyanide coordination at room temperature. The formation of eight-membered heterocycles was not successful and instead, acyclic acrylamide or acrylonitrile derivatives were obtained, depending on the reaction conditions and the isocyanide.

Chapter III. Synthesis and Reactivity of Ortho-Palladated 3-Phenylpropanamides. Insertion of CO, XyNC and Alkynes into the Pd–C Bond. Synthesis of Seven- and Nine-Membered Palladacycles and Benzazepine- and Benzazonine-Based Heterocycles.

With the main objective of exploring the limits of the methodology described in Chapters I and II for the synthesis of palladacycles and heterocycles of a larger size, we describe the synthesis of arylpalladium complexes bearing a propanamide group in *ortho* position. Ortho-palladated 3-phenylpropanamides [Pd{C$_6$H$_4$CH$_2$CH$_2$C(O)NRR'-2}I(tmeda)], obtained by oxidative addition, are suitable precursors for the synthesis of their corresponding seven-membered cationic palladacycles via iodide abstraction, or neutral amidate palladacycles upon deprotonation of the amide function. The reactions of diarylalkynes or dimethylacetylenedicarboxylate with the cationic derivatives allowed the isolation of a series of nine-membered palladacycles, which, to our knowledge, are the first of that size obtained from alkyne monoinsertions. In contrast, by using 3-hexyne, a di-insertion product is obtained, which contains a spirocyclic ligand coordinated through a η^3-allylic bond.

In addition, a series of seven- or nine-membered cyclic imides and one iminobenzazepinone have been obtained from CO or XyNC insertion/C–N reductive coupling sequences.

Chapter IV. Reactivity of Ortho-Palladated Benzamides Toward CO, Isocyanides, and Alkynes. Synthesis of functionalized Isoindolin-1-ones- and 4,5-Disubstituted Benzo[*c*]azepine-1,3-diones.

This chapter is focused on the synthesis of a family of ortho-palladated benzamides [Pd{$C_6H_4C(O)NRR'$-2}I(tmeda)] and their cationic *C,O*- and neutral *C,N*-palladacyclic derivatives, and the study of their reactivity toward unsaturated species, with the main objective of exploring the feasibility of heterocycle formation from these systems. Most significantly, seven-membered palladacycles, resulting from the insertion of the alkyne into the Pd–C bond of *C,O*-cyclopalladated benzamides, may give rise to two different types of heterocyclic compounds after reacting with CO, depending on the nature of the inserted alkyne. Thus, the complexes containing inserted 1-phenylpropyne, diphenylacetylene or 3-hexyne (NH_2 or NHMe derivatives) lead to 4,5-disubstituted benzo[*c*]azepine-1,3-diones, resulting from the CO insertion into the Pd–C bond followed by a C–N reductive coupling. However, in the cases of the complexes with inserted methyl or ethyl phenylpropiolate (NHMe derivatives), an aza-Michael addition of the NHMe moiety to the vinyl group takes place after the insertion of CO, finally leading to the formation of isoindolin-1-one derivatives.

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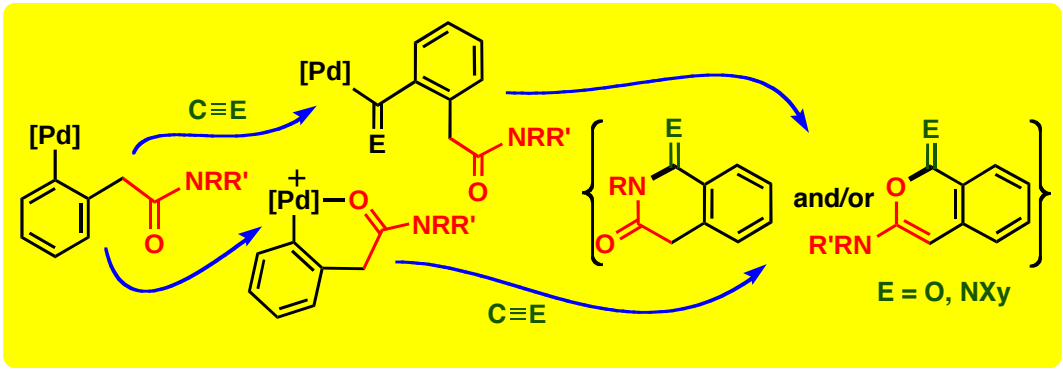
CHAPTER I

Synthesis and Reactivity of Ortho-Palladated Phenylacetamides. Intramolecular C–N vs C–O Reductive Coupling after CO or XyNC Insertion into the Pd–C Bond. Synthesis of Isoquinoline- and Isocoumarin-based Heterocycles



The results of this chapter have been published in:

J. Vicente, P. González-Herrero, R. Frutos-Pedreño, M. T. Chicote, P. G. Jones, D. Bautista, *Organometallics* **2011**, *30*, 1079–1093.

Abstract

Aryl palladium complexes [Pd{$C_6H_4CH_2C(O)NRR'$-2}I(N^N)] (N^N = *N,N,N′,N′*-tetramethylethylenediamine = tmeda, NRR' = NH_2 (**1a**), NHMe (**1b**), NMe_2 (**1c**); N^N = 4,4'-di-*tert*-butyl-2,2'-bipyridyl (dbbpy), NRR' = NHMe (**1b'**)) are prepared by oxidative addition of the corresponding 2-(2-iodophenyl)acetamide to "Pd(dba)$_2$" ([$Pd_2(dba)_3$]·dba; dba = dibenzylideneacetone) in the presence of the N^N chelating ligand. Cationic cyclometalated derivatives [Pd{κ^2*C,O*-$C_6H_4CH_2C(O)NRR'$-2}(N^N)]TfO (N^N = tmeda, NRR' = NH_2 (**2a**), NHMe (**2b**), NMe_2 (**2c**); N^N = dbbpy, R = NHMe (**2b'**)) are obtained by reacting the appropriate complex **1** with AgTfO. The reaction of **2b'** with PPh_3 affords [Pd{$C_6H_4CH_2C(O)NHMe$-2}(dbbpy)(PPh_3)]TfO (**3b'**). Neutral amidate complexes of the type [Pd{κ^2*C,N*-$C_6H_4CH_2C(O)NR$-2}(N^N)] (N^N = tmeda, R = H (**4a**), Me (**4b**); N^N = dbbpy, R = Me (**4b'**)), are obtained upon deprotonation of the corresponding complex **1** with KO^{t}Bu. The complex [Pd{$C_6H_4CH_2C(O)NHMe$-2}{$CH(CN)_2$}(dbbpy)] (**5b'**) has been prepared by reacting **4b'** with malononitrile. Acyl derivatives [Pd{$C(O)C_6H_4CH_2C(O)NRR'$-2}I(N^N)] (N^N = tmeda, NRR' = NH_2 (**6a**), NHMe (**6b**), NMe_2 (**6c**); N^N = dbbpy, NRR' = NHMe (**6b'**)) have been prepared by reacting the corresponding complex **1** with CO at low temperature; when N^N = tmeda, prolonged reaction times and high temperatures lead to Pd(0) and isoquinoline-1,3(2*H*,4*H*)-dione (**7a**), a 1:2 mixture of 2-methylisoquinoline-1,3(2*H*,4*H*)-dione (**7b**) and 3-(dimethylamino)-1*H*-2-benzopyran-1-one (**8b**) or 3-(methylamino)-1*H*-2-benzopyran-1-one (**8c**), respectively. Similar results are obtained from the reactions of **2a-c** with CO under much milder conditions, while **2b'** reacts with CO in acetone to give the isochroman-1-one derivative *N*,3,3-trimethyl-1-oxo-3,4-dihydro-1*H*-2-benzopyrane-4-carboxamide (**9**). While the reaction of **1b'** with one equiv of XyNC (Xy = 2,6-dimethylphenyl) gives the iminoacyl complex [Pd{$C(=NXy)C_6H_4CH_2C(O)NHMe$-2}I(dbbpy)] (**10b'**), the homologous products from the tmeda derivative **1a**, **1b** or **1c** decompose giving Pd(0) and 1-(2,6-dimethylphenylimino)-1,2-dihydroisoquinolin-3(4*H*)-one (**11a**), 1-(2,6-dimethylphenylimino)-2-methyl-1,2-dihydroisoquinolin-3(4*H*)-one (**11b**) or 1-(2,6-dimethylphenylimino)-3-(*N,N*-dimethylamino)-1*H*-2-benzopyrane (**12c**), respectively. The reaction of **1a** or **1b'** with three equiv XyNC affords *trans*-[Pd{$C(=NXy)C_6H_4CH_2C(O)NHR$-2}I($CNXy)_2$] (R = H (**13a**), Me (**13b**)); the protonation of **13b** with HTfO leads to [Pd{$C(=NHXy)C_6H_4CH_2C(O)NH_2$-2}I($CNXy)_2$]TfO (**14a**). Complexes [Pd{$C(=NXy)C_6H_4CH_2C(O)NRR'$-2}($CNXy$)(N^N)]TfO (N^N = tmeda,

NRR' = NHMe (**15b**), NMe_2 (**15c**); N^N = dbbpy, NRR' = NHMe (**15b'**)) are obtained by reacting the appropriate complex **2** with two equiv of XyNC.

Introduction

Amides are commonly employed as substrates or reagents in a variety of important palladium-mediated syntheses. Based on its ability to coordinate through the oxygen atom, the amide unit can act as a directing group in palladium-catalyzed C–H functionalization reactions,[1] which may lead to C–C[2] or C–O[3] coupling products. The palladium-catalyzed amidations of aryl halides[4-6] are among the most significant examples of the amide function participating directly in the bond formation process. These reactions have been shown to proceed through aryl(amidate)palladium complexes that undergo C–N reductive coupling.[6-8] In addition, a number of related Pd(II)-catalyzed amidations of C–H bonds have been reported, for which the participation of amidate complexes has also been proposed.[9]

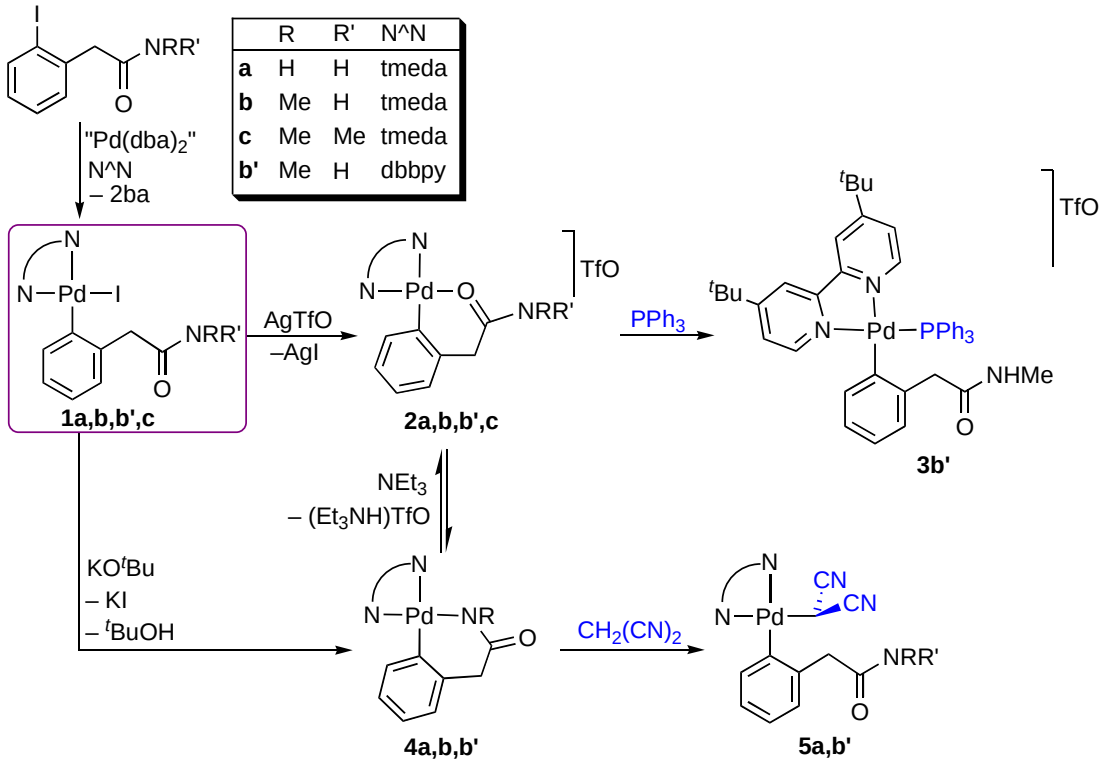
In this chapter, we describe the synthesis of aryl palladium complexes bearing an ortho-acetamide group and of several cyclometallated derivatives, including neutral amidate complexes. We report also a systematic study of the reactions of these aryl complexes with CO and XyNC (Xy = 2,6-dimethylphenyl). Depending on the substituents on the amidic nitrogen, these insertion reactions lead to isoquinoline- or isocoumarin-based heterocycles resulting from intramolecular C–N or C–O couplings. Both types of heterocyclic structures are present in numerous natural products and biologically active molecules, and both the development of suitable synthetic strategies and the study of their pharmacological activity are the subjects of intensive research.[10]

Results and Discussion

Synthesis of Ortho-Palladated Phenylacetamides and Cyclometallated Derivatives

Aryl derivatives of the type [Pd{$C_6H_4CH_2C(O)NRR'$-2}I(N^N)] [N^N = tmeda, NRR' = NH_2 (**1a**), NHMe (**1b**), NMe_2 (**1c**); N^N = dbbpy, NRR' = NHMe (**1b'**); Scheme I.1] were synthesized by oxidative addition of the corresponding 2-(2-iodophenyl)acetamides to "$Pd(dba)_2$" ($[Pd_2(dba)_3]$·dba; dba = dibenzylideneacetone) in the presence of tmeda or dbbpy. The reactions took place at room temperature in toluene, THF or CH_2Cl_2 and the products were isolated in yields over 60%.

Scheme I.1



The reactions of complexes **1** with one equiv of AgTfO led to the precipitation of AgI and the formation of the corresponding cationic cyclopalladated derivatives [Pd{κ^2*C,O*-$C_6H_4CH_2C(O)NRR'$-2}(N^N)]TfO (N^N = tmeda, NRR' = NH_2 (**2a**), NHMe (**2b**), NMe_2 (**2c**); N^N =dbbpy, NRR' = NHMe (**2b'**)), which were isolated in high yields. In these complexes, the amide function is coordinated to the metal through the oxygen atom, as revealed by the IR and NMR spectra and the crystal structure of **2b'** (see below). The reaction of **2b'** with one equiv of PPh_3 led to the splitting of the Pd–O bond to give the phosphino complex [Pd{$C_6H_4CH_2C(O)$NHMe-2}(dbbpy)(PPh_3)]TfO (**3b'**) in 69% yield.

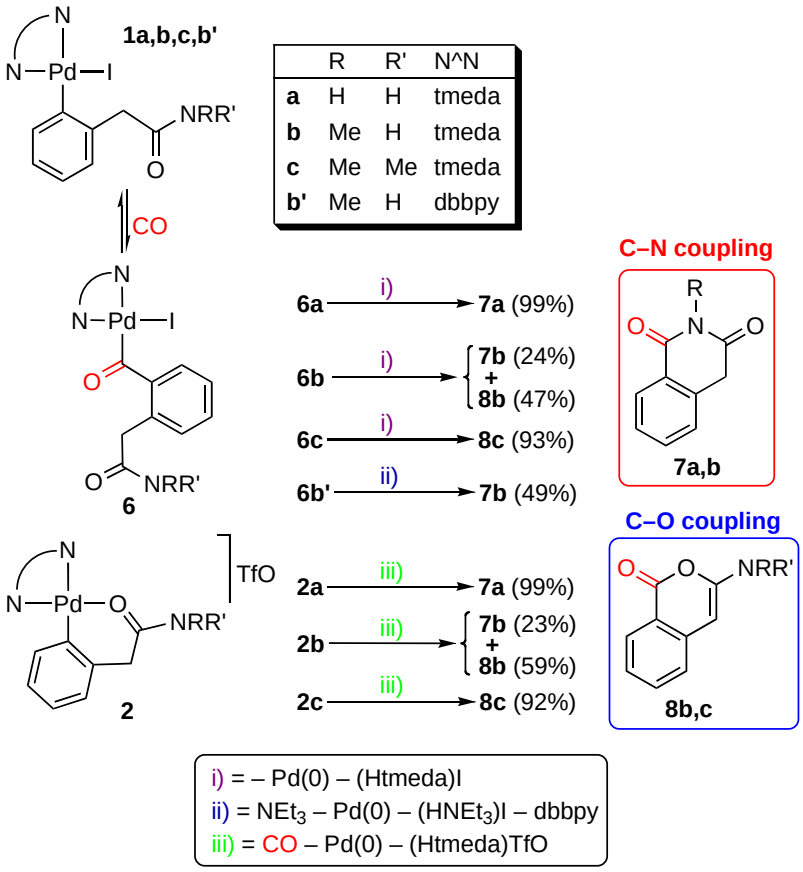
Deprotonation of the amide function in complex **1a**, **1b** or **1b'** with KO^{t}Bu in HO^{t}Bu led to the neutral cyclopalladated derivatives [Pd{κ^2*C,N*-$C_6H_4CH_2C(O)$NR-2}(N^N)] (N^N = tmeda, R = H (**4a**), Me (**4b**); N^N = dbbpy, R = Me (**4b'**)), which result from the displacement of the iodo ligand by the nitrogen of the anionic amidate group and were isolated in moderate to good yields. When NEt_3 was used instead, deprotonation of the amide occurred only to a small extent, as detected by NMR. A significantly higher amount of the amidate complexes **4** (around 33%) was detected by NMR after treatment of the cationic complexes **2a**, **2b** or **2b'** with excess NEt_3 in acetone.

In order to explore their basic character and usefulness for the preparation of other derivatives, we studied the reactivity of **4a** and **4b'** toward the methylene-active compounds malononitrile, acetylacetone, methyl cyanoacetate and dimethyl malonate. However, only the most acidic of these reagents, malononitrile,[11] reacted to give the expected derivatives [Pd{$C_6H_4CH_2C(O)NHR$-2}{$CH(CN)_2$}(N^N)] (N^N = tmeda, R = H (**5a**); N^N = dbbpy and R = Me (**5b'**)); whereas **5b'** was obtained using one equiv of malononitrile, the formation of **5a** required an excess of this reagent and the complex could not be isolated in pure form, probably because of the lower basicity of the C(O)NH group as compared to C(O)NMe.

Reactions with CO and Decomposition of the Resulting Acyl Complexes

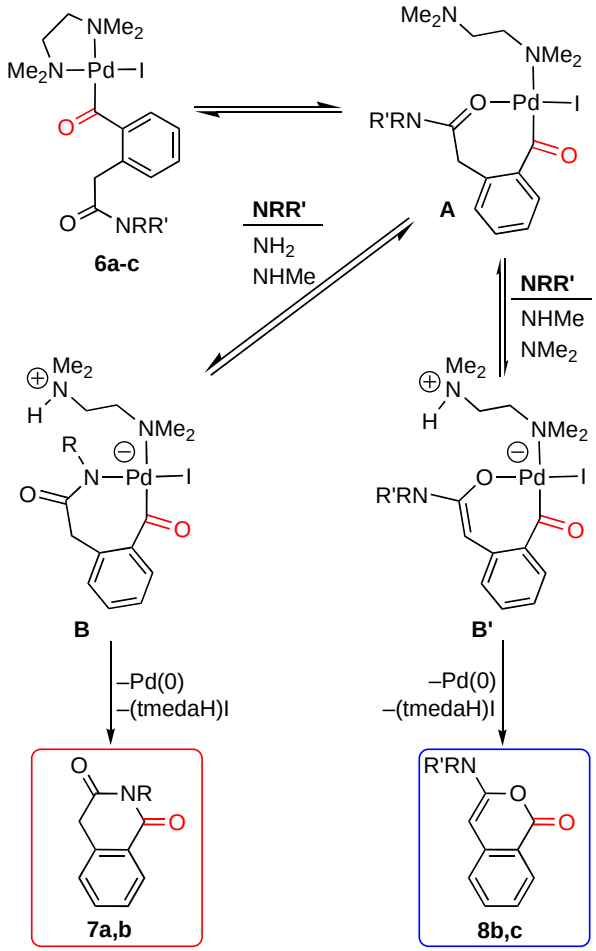
The reactions of complexes **1** with CO in CH_2Cl_2 at –17 °C afforded the insertion products [Pd{$C(O)C_6H_4CH_2C(O)NRR'$-2}I(N^N)] (N^N = tmeda, NRR' = NH_2 (**6a**), NHMe (**6b**), NMe_2 (**6c**); N^N = dbbpy, NRR' = NHMe (**6b'**)), which were isolated in high yields (Scheme I.2). The isolation of these compounds in pure form required low temperature because they slowly lose CO in solution at room temperature to give the parent arylpalladium compounds. Moreover, the tmeda complexes **6a-c** gradually decomposed when kept in solution under CO at room or higher temperatures (Scheme I.2). Complete decomposition of **6a** was observed after 30 h of reaction of **1a** with CO (1.4 bar) at 50 °C in $CDCl_3$ to give quantitatively colloidal palladium, (tmedaH)I[12] and isoquinoline-1,3(2*H*,4*H*)-dione (**7a**) (homophthalimide),[13-15] resulting from the reductive C–N coupling. Decomposition of **6b**, formed *in situ* from **1b** under CO, was considerably slower and reached only 71% after 3d (1.4 bar, 50 °C), giving an approximately 1:2 mixture of 2-methylisoquinoline-1,3(2*H*,4*H*)-dione[16] (**7b**) and the new isocoumarin derivative 3-(methylamino)-1*H*-2-benzopyran-1-one (**8b**), resulting from C–N and C–O couplings, respectively. Complex **6c** also decomposed under CO (1.4 bar, 3 d, 50 °C) giving via a C–O coupling exclusively the new compound 3-(dimethylamino)-1*H*-2-benzopyran-1-one (**8c**), which was isolated in 93% yield.

Scheme I.2



A possible reaction pathway for the C–N and/or C–O coupling processes from the tmeda derivatives **6a-c** is outlined in Scheme I.3. We assume that an equilibrium is established between **6** and the intermediate complex **A**, in which the tmeda ligand is monocoordinated and the acetamide group is O-coordinated, increasing the acidities of both the NH (if present) and CH_2 protons. The non-bonded tmeda nitrogen might reasonably be responsible for the deprotonation of the NH and/or CH_2 groups, either intra- or intermolecularly.

Scheme I.3



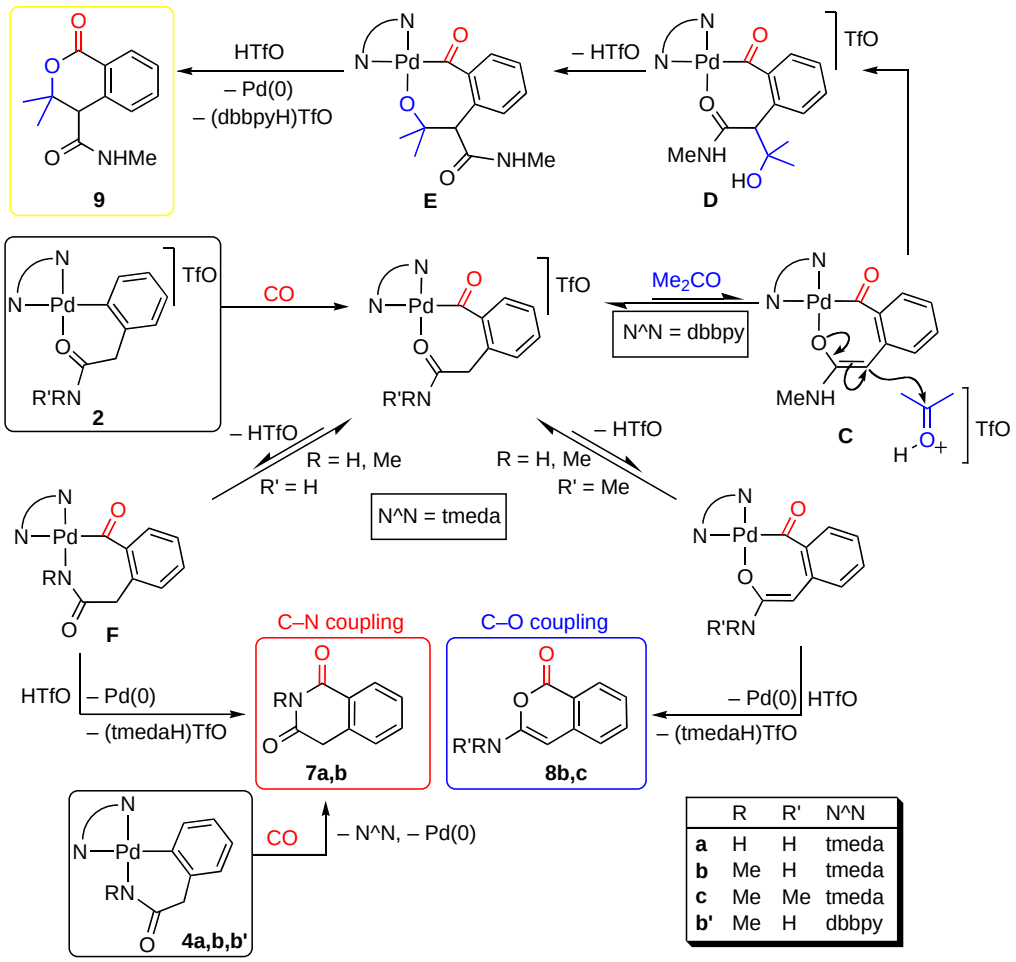
The different nature of the proton involved determines in turn the nature of the corresponding deprotonated complex, an amidato **B**, similar to **4**, or an aminoenolato **B'**, which could then undergo a C–N or C–O reductive coupling, respectively. While for **6c** only the C–O coupling can take place, for **6a** and **6b** both the C–N and C–O coupling products are possible and the relative proportions in which they are obtained are expected to be determined by the relative concentrations of intermediates **B** and **B'**, largely dictated by the relative acidities of NH and CH_2 protons, as well as by the rates of the reductive coupling steps. According to literature data,[11, 17] NH protons are somewhat more acidic than α-CH protons in amides, but in the case of the NHMe derivative, the difference between the acidities of these two types of protons will be diminished because of the electron-donating methyl group. Therefore, in the case of **6a**, the deprotonation and coupling steps leads to **7a** because of the higher concentration of the corresponding amidate **B** and/or the more rapid C–N coupling compared to the C–O coupling. For **6b**, the deprotonation of the methylene group competes with that of the NHMe group giving a 1:2 mixture of **7b** and **8b**, perhaps because the

steric repulsion of the methyl substituent makes the C–N coupling slower than the C–O coupling. Correspondingly, the slower decomposition of **6b** than of **6a** (see above) can be caused by the slower C–N coupling in the amidate **B** corresponding to **6b** than that in the unsubstituted analogue **6a**. We note that a similar reasoning has been used to explain the general observation that palladium-catalyzed intermolecular amidations of aryl halides are much slower when acyclic secondary amides are used instead of primary amides.[5]

In contrast to the tmeda derivative **6b**, the dbbpy complex **6b'** gave only traces of **7b** and **8b** after 30 h under CO (1.4 bar) at 50 °C. The stability of **6b'** can be attributed to the better coordination ability and lower basicity of the dbbpy ligand, which hinders its participation as a base in the process. When the reaction of **1b'** with CO was carried out in the presence of NEt_3, the reductive coupling did take place to an appreciable extent, although it was rather slow (49% after 48 h at 50 °C) and gave exclusively the isoquinolinedione **7b**; as mentioned above, NEt_3 deprotonates complex **1b'** to give, to a small extent, only amidate complex **4b'**, which would react with CO to give solely the C–N coupling product.

The reaction of the cationic cyclometallated tmeda complex **2a**, **2b** or **2c** with CO (1.4 bar, 3 h at room temperature in acetone) led to the formation of colloidal Pd and solutions containing **7a** (100% yield), **7b** + **8b** (82% total yield; 0.4:1 molar ratio) or **8c** (92% yield), respectively, at a much faster rate than their parent iodocomplexes **1a-c** (Scheme I.2). This is a new example of a well-known behavior: the rates of migratory insertions or catalytic reactions involving some such processes are enhanced when they implicate cationic species and a coordination position is easily accessible to the molecule to be inserted.[18] At a preparative scale, compound **7a** was isolated in 51% yield, while by extracting an Et_2O solution of the mixture of **7b** and **8b** with aqueous K_2CO_3, compound **8b** was isolated in 59% yield. In order to avoid the formation of **8b** and thus isolate **7b**, we carried out the reaction of **2b** with CO in the presence of NEt_3, which gave exclusively **7b** (67% yield); as previously noted for the reaction of **1b'** with CO, this result is explained by the formation of the amidate **4b**, which then reacts with CO to give the C–N coupling product. The formation of the organic products from the reactions of **2a-c** with CO must involve amidate and aminoenolate intermediates similar to those proposed for the reactions of the iodocomplexes **1a-c** with CO. However, given the higher acidity of the acetamide protons in the cationic complexes **2a-c** and the strengthening of the Pd–N bonds relative to **1a-c**, it is likely that the deprotonation step does not involve the participation of the tmeda ligand and is carried out by the acetone used as solvent (Scheme I.4).

Scheme I.4



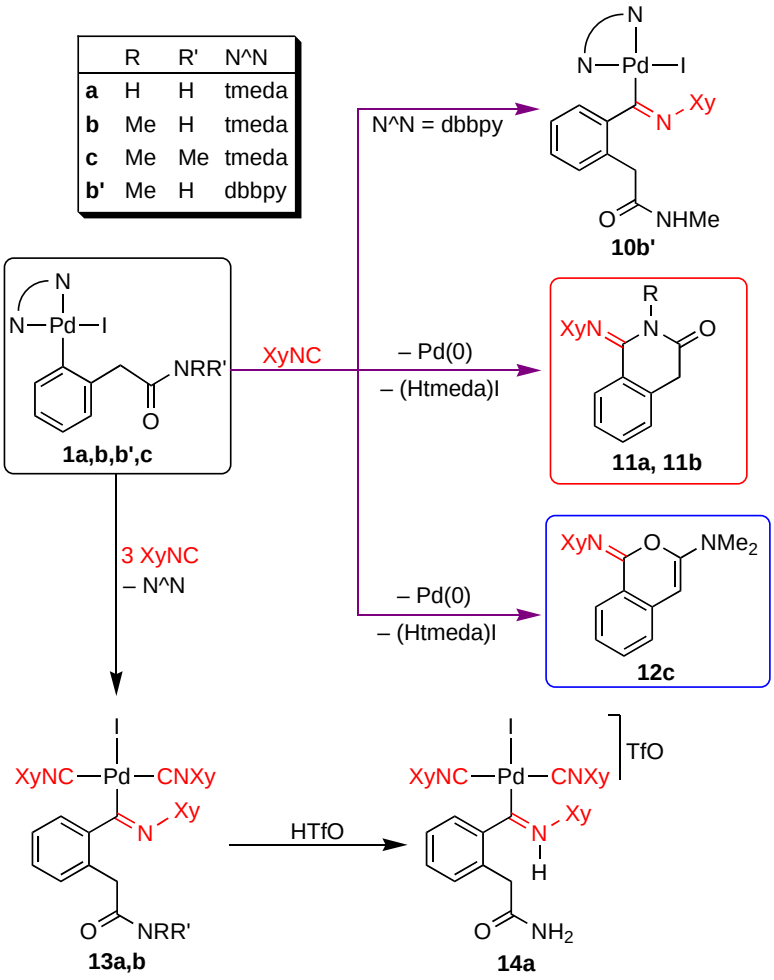
We have found that the dbbpy complex **2b'** shows a different behavior towards CO than do **2a**–**c**. Thus, **2b'** reacted with CO (1.4 bar) in acetone at room temperature to give the isochroman-1-one derivative *N*,3,3-trimethyl-1-oxo-3,4-dihydro-1*H*-2-benzopyrane-4-carboxamide (**9**), along with colloidal palladium and (dbbpyH)TfO, in a process that involves the participation of the solvent. A possible reaction pathway for the formation of **9** is outlined in Scheme I.4. The better coordination ability of dbbpy relative to tmeda may stabilize the aminoenolate intermediate **C**, making the reductive C–O coupling more difficult and favoring the reaction with a protonated acetone molecule to give **D**. This step is related to the previously reported reactions of *N*,*N*-disubstituted 3-amino-1*H*-2-benzopyran-1-ones with aldehydes to give 3,4-dihydro-1*H*-2-benzopyrane-4-carboxamides analogous to **9**,[19] although these require more energetic conditions, such as refluxing of the reagents in acetic acid, ethanol or acetonitrile. Next, the deprotonation of **D** would afford the alcoholato complex **E** and, finally, compound **9** would result from a C–O reductive coupling.

The neutral amidate complexes **4a** and **4b** or **4b'** also reacted rapidly with CO at room temperature in acetone to give Pd(0) and high yields of **7a** and **7b**, respectively, which result from a C–N coupling, probably occurring through an intermediate such as **F** (Scheme I.4). This fact additionally suggests that, in solution, the amidates are not in equilibrium, at least to an appreciable extent, with their isomeric aminoenolates.

Reactions with XyNC

The reaction of the dbbpy complex **1b'** with one equiv of XyNC (Xy = 2,6-dimethylphenyl) gave the insertion product [Pd{C(=NXy)$C_6H_4CH_2$C(O)NHMe-2}I(dbbpy)] (**10b'**) (Scheme I.5). However, the analogous iminoacyl derivatives could not be isolated when starting from the tmeda derivatives **1a** and **1b** because they immediately started to decompose, even at low temperature, giving colloidal Pd, (tmedaH)I, and the C–N coupling products 1-(2,6-dimethylphenylimino)-1,2-dihydroisoquinolin-3(4*H*)-one (**11a**) and 1-(2,6-dimethylphenylimino)-2-methyl-1,2-dihydroisoquinolin-3(4*H*)-one (**11b**), respectively. As observed for the previous C–N couplings, the decomposition is much faster for the unsubstituted derivative **1a** (30 min at room temperature) than for its methyl-substituted analogue **1b**, the latter requiring harsher reaction conditions (3 h at 61 °C). Compounds **11** are new members of the small family of imino derivatives of isoquinoline-1,3(2*H*,4*H*)-dione.[13,20] The reaction of **1c** with one equiv of XyNC gave a mixture containing a new organometallic derivative, probably the expected insertion product, and unreacted starting material, which could not be separated. However, heating this mixture at 60 °C for 24 h led to its gradual decomposition to give colloidal Pd, (tmedaH)I, and an almost quantitative yield of the new iminoisocoumarin derivative 1-(2,6-dimethylphenylimino)-3-(*N*,*N*-dimethylamino)-1*H*-2-benzopyran (**12c**), resulting from a C–O coupling. Although the formation of these organic products probably takes place through reaction pathways analogous to that proposed for the reactions of **1a-c** with CO, the experimental data clearly show that, for **1a** and **1b**, the C–N couplings are much faster than in the reactions with CO, and also than the C–O couplings. This would explain the isolation of only one iminoacyl complex and the absence of C–O coupling products in these reactions with XyNC.

Scheme I.5

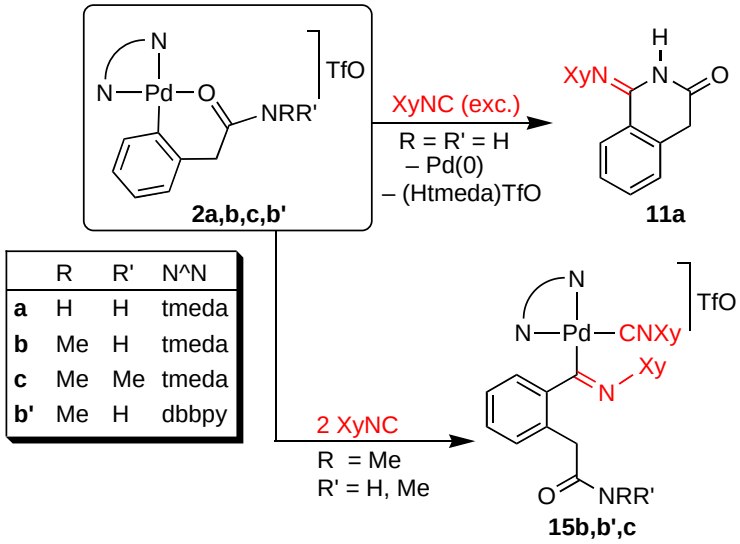


The reactions of **1a** or **1b'** with three equiv of XyNC gave *trans*-[Pd{C(=NXy)C$_6$H$_4$CH$_2$C(O)NHR-2}I(CNXy)$_2$] (R = H (**13a**), Me (**13b**)), which result from the displacement of the chelating ligands by two of the isocyanide molecules and the insertion of a third isocyanide into the Pd–C bond. The occupancy of both positions cis to the iminoacyl ligand prevents the coordination of the acetamide group and consequently rules out any coupling process such as that observed in the equimolecular reaction (see above and Scheme I.5). The reaction of **13a** with 1 equiv of triflic acid led to the protonation of the iminoacyl nitrogen to give *trans*-[Pd{C(=NHXy)C$_6$H$_4$CH$_2$C(O)NH$_2$-2}I(CNXy)$_2$]TfO (**14a**), formally containing an *N*-stabilized carbene ligand.

The reactions of the cationic complexes **2** with XyNC were attempted in order to explore the possible formation of coupling products (Scheme I.6). In the case of the NH$_2$ derivative **2a**, the 1:1 reaction led to the formation of a new complex that could not be conveniently characterized because of its instability, while the 1:2 reaction led to the

formation of the C–N coupling product **11a** almost quantitatively. Probably, the unstable compound from the 1:1 reaction is an insertion product and the second equiv of XyNC favors the C–N coupling by displacing one of the N atoms of the tmeda ligand, which can then act as a base. In contrast, the reactions of the NHMe and NMe_2 derivatives **2b**, **2c** and **2b'** with two equiv of XyNC produced the insertion of one XyNC into the Pd–C bond and the displacement of the *O*-coordinated amide group by a second XyNC (Scheme I.6) to give $[Pd\{C(=NXy)C_6H_4CH_2C(O)NRR'\text{-}2\}(CNXy)(N\text{^}N)]TfO$ (N^N = tmeda, NRR' = NHMe (**15b**), NMe_2 (**15c**); N^N = dbbpy, NRR' = NHMe (**15b'**)). The use of only one equiv of isocyanide led to the same compounds, but half of the unreacted starting materials were recovered. The formation of organic products is probably hindered because the C–N and/or C–O coupling processes are more difficult than the C–N coupling from the primary acetamide in **2a**, and thus the reaction sequence ends with the formation of the stable compounds **15b**, **15b'** or **15c**.

Scheme I.6



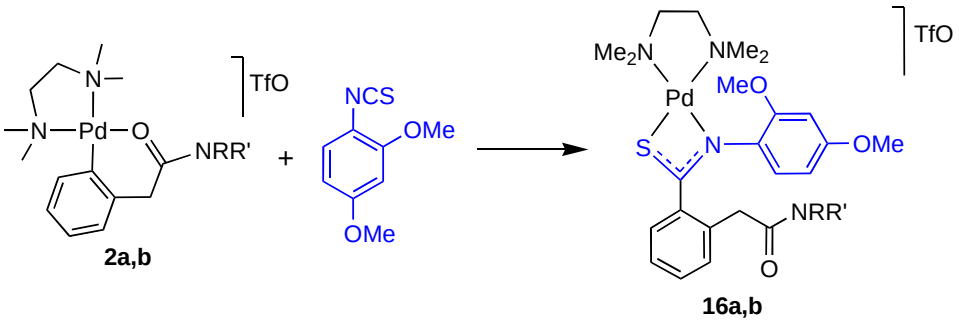
The amidate complexes **4a**, **4b** and **4b'** reacted only sluggishly with XyNC. In all the three cases, the main product was the C–N coupling compound **11a** or **11b**, but the reactions required heating at 60 °C in $CHCl_3$ for 16–48 h and the organic compounds were obtained contaminated by decomposition products.

Reactivity toward 2,4-dimethoxyphenyl isothiocyanate

Our research group has reported some examples of reactivity of arylpalladium complexes toward isothiocyanates, which have allowed the synthesis of heterocycles through

the insertion of the isothiocyanate into the Pd–C bond followed by the formation of PdS.[21] The reactions of the cyclopalladated complexes **2a,b** with excess 2,4-dimethoxyphenyl isothiocyanate in CH_2Cl_2 at room temperature afforded high yields of the stable thioamidato complexes $Pd\{\kappa^2N,S\text{-}SC(NC_6H_3(OMe)_2\text{-}2,4)(C_6H_4(CH_2C(O)NRR')\text{-}2)\}(tmeda)]TfO$ [NRR' = NH_2 (**16a**), NHMe (**16b**)] arising from the insertion of one molecule of 2,4-dimethoxyphenyl isothiocyanate into the Pd–C bond (Scheme I.7). Other examples of this type of insertion reactions giving thioamidato complexes have been previously reported.[22-24]

Scheme I.7



Spectroscopic Features

The methylenic protons are observed in the room temperature ^1H NMR spectra of the aryl complexes **1** and **3b'** as an AB system because the aryl ligand does not lie in the coordination plane and its rotation around the Pd–C bond must be restricted. In the iminoacyl complex **10b'** such restriction is only observed at low temperatures (Figure I.1) while the room-temperature spectrum shows the methylenic protons as a broad singlet.

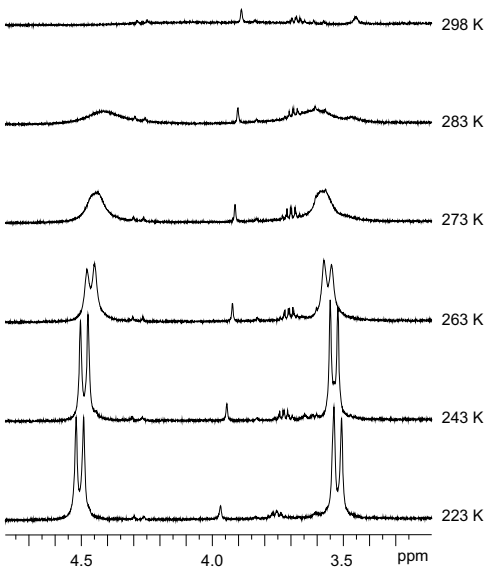


Figure I.1. Variable-temperature ^1H NMR spectra of **10b'** in CD_2Cl_2 (methylenic resonances).

The singlet observed for the CH_2 protons in the spectra of complexes **2** and **6** must be attributed, respectively, to a fast ring flipping process that makes them equivalent and to the lower steric demand of the O atom with respect to the NXy group present in **10b'**. In the cyclic amidate complexes **4** the methylenic protons generate, at room temperature, a broad singlet (**4a**), an AB system (**4b**) or a very broad resonance (**4b'**). The latter resolves as an AB system at 233 K (Figure I.2). Therefore, the rate of the ring flipping process follows the order **2** > **4a** > **4b'** > **4b**. The mutual repulsion between the H6 of dbbpy or the Me group of tmeda with the R group of the amidate in complexes **4** and the absence of such repulsions in complexes **2** could account for the above-mentioned differences.

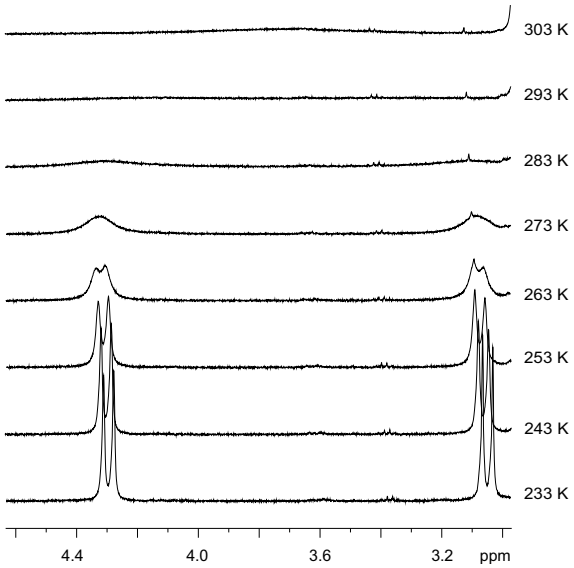


Figure I.2. Variable-temperature ^{1}H NMR spectra of **4b'** in CD_2Cl_2 (methylenic resonances).

The solid-state IR spectra of the Pd complexes that contain the free acetamide group show the ν(C=O) band in the range 1636-1687 cm^{-1}, that is, at frequencies similar to or slightly higher than those corresponding to 2-(2-iodophenyl)acetamides [$C_6H_4ICH_2CONRR'$-2, with NRR' = NH_2 (1659 cm^{-1}), NHMe (1641 cm^{-1}), NMe_2 (1642 cm^{-1})]. The cationic cyclopalladated derivatives **2** show lower energies for this band (~1615 cm^{-1}) because of the coordination of the amide function through the O atom, which must cause a slight decrease in the C–O bond order. The even lower energy of the ν(C=O) band found in the amidate complexes **4** (~1580 cm^{-1}) is typical of metal complexes with this kind of ligands[8,25] and can be ascribed to the delocalization of the negative charge over the N–C=O group, which significantly decreases the C–O bond order.

Crystal Structures

The crystal structures of complexes **1b'** (Figure I.3), **2b'**·Me_2CO (Figure I.6), **3b'** (Figure I.5), **4b'**·0.5CH_2Cl_2 (Figure I.8), **5b'** (Figure I.9), **6b'** (Figure I.10), **8b** (Figure I.12), **9** (Figures I.14), **10b'** (Figure I.16), **11b** (Figures I.17), **13b**·CH_2Cl_2 (Figure I.19), **14a** (Figure I.21), **15c** (Figure I.23), and **16**·0.5$CDCl_3$ (Figure I.24) were determined by means of X-ray diffraction studies. All the Pd complexes exhibit slightly distorted square planar environments around the metal. The greatest distortions are caused by the small bite of the dbbpy ligand (angles N–Pd–N around 78°) and the four-membered cycle in **16a** [angle N(2)–Pd–S(1): 69.52(9)°].

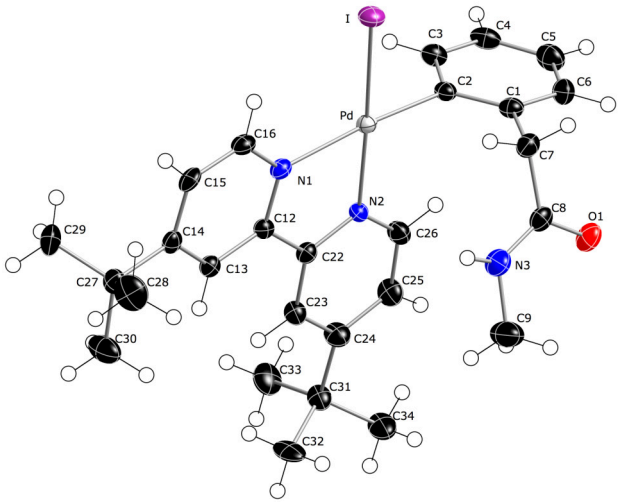


Figure I.3. Thermal ellipsoid plot (50% probability) and crystal packing of complex **1b'**. Selected bond distances (Å) and angles (deg): Pd(1)–C(2) 1.986(3), Pd(1)–N(1) 2.128(2), Pd(1)–N(2) 2.0735(19), Pd(1)–I(1) 2.5671(2); C(2)–Pd(1)–N(2) 94.02(9); C(2)–Pd(1)–N(1) 172.50(9), N(2)–Pd(1)–N(1) 78.63(8), C(2)–Pd(1)–I(1) 88.66(8), N(2)–Pd(1)–I(1) 177.33(6), N(1)–Pd(1)–I(1) 98.69(6), C(1)–C(2)–Pd(1) 123.40(19), C(3)–C(2)–Pd(1) 118.16(19).

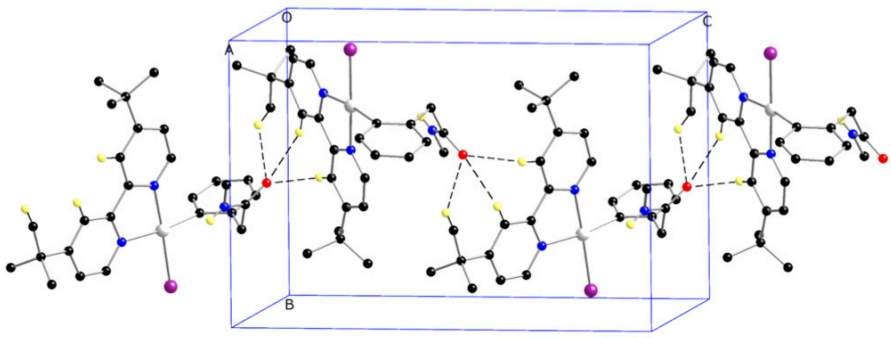


Figure I.4. Crystal packing of complex **1b'**.

The aromatic ring of the aryl ligand in complexes **1b'** and **3b'** (Figures I.3 and I.5, respectively) is almost perpendicular to the Pd coordination mean plane, as is commonly found in ortho-substituted arylpalladium derivatives and attributed to the steric demand of the *ortho* substituent.[8, 26, 27] This is in agreement with the NMR data mentioned above. The Pd–C bond distances are normal for this type of derivatives. The molecules in **1b'** are connected through three non-classical hydrogen bond C–H···O giving chains along *c* axis (Figure I.4). The triflate anion in **3b'** is connected to the cation through one N–H···O hydrogen bond involving the acetamide moiety (Figure I.5).

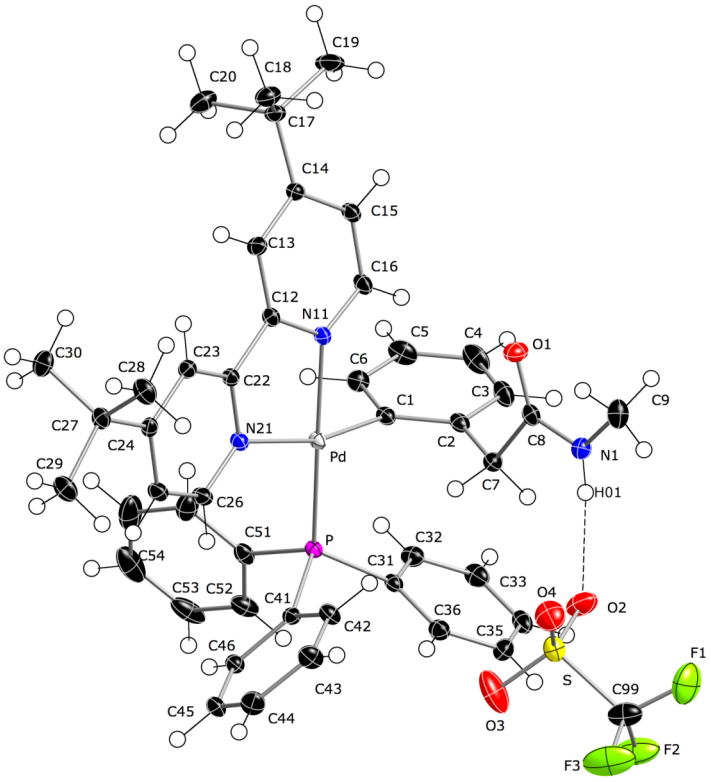


Figure I.5. Thermal ellipsoid plot (50% probability) of complex **3b'**. Selected bond distances (Å) and angles (deg): Pd–C(1) 1.9906(14), Pd–N(11) 2.1070(11), Pd–N(21) 2.1749(12), Pd–P 2.2643(4), C(1)–C(2) 1.399(2), C(1)–C(6) 140.1(2); C(1)–Pd–N(11) 90.68(5), C(1)–Pd–N(21) 166.96(5), N(11)–Pd–N(21) 77.00(4), C(1)–Pd–P 85.01(4), N(11)–Pd–P 174.92(3), N(21)–Pd–P 107.07(3), C(2)–C(1)–Pd 122.99(11), C(6)–C(1)–Pd 166.4(11).

The structure of **2b'** (Figure I.6) was solved as an acetone monosolvate. The acetamide group is coordinated to the Pd atom through the oxygen, forming a six-membered ring with a pseudo-boat conformation. The Pd(1)–O(1) bond distance of 2.031(2) Å is similar to that found for the *ortho*-palladated arylurea [Pd{κ^2C,O-$C_6H_4NHC(O)NHTo$-2}(tmeda)]TfO[28] and several *O*-coordinated amides.[29] The C(8)–O(1) bond distance of

1.263(4) Å is slightly longer than the corresponding distance in the free acetamide group of complex **1b'** (1.227(3) Å), because of the coordination to palladium through the oxygen atom. Consequently, the C(8)–N(3) bond distance of 1.317(4) Å is shorter than that found for **1b'** (1.333(4) Å). The triflate anion in **2b'** is connected to the cation through one N–H···O hydrogen bond giving double chains parallel to the *b* axis (Figure I.7).

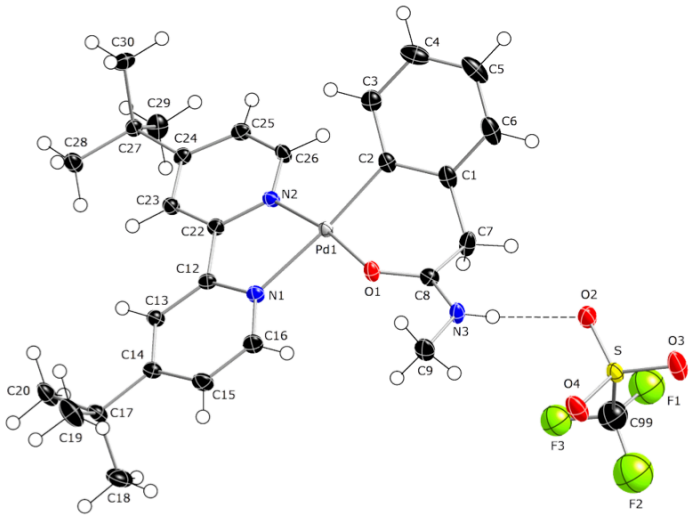


Figure I.6. Thermal ellipsoid plot (50% probability) of complex **2b'**. Selected bond distances (Å) and angles (deg): Pd(1)–C(2) 1.991(4), Pd(1)–N(2) 2.023(3), Pd(1)–O(1) 2.031(2), Pd(1)–N(1) 2.089(3), O(1)–C(8) 1.263(4), C(8)–N(3) 1.317(4), N(3)–C(9) 1.453(4); C(2)–Pd(1)–N(2) 100.15(13), C(2)–Pd(1)–O(1) 88.74(12), N(2)–Pd(1)–N(1) 79.23(11), O(1)–Pd(1)–N(1) 91.97(10), C(8)–O(1)–Pd(1) 121.1(2), C(8)–C(7)–C(1) 110.7(3), O(1)–C(8)–N(3) 120.0(3), O(1)–C(8)–C(7) 121.7(3), N(3)–C(8)–C(7) 118.3(3), C(8)–N(3)–C(9) 123.1(3).

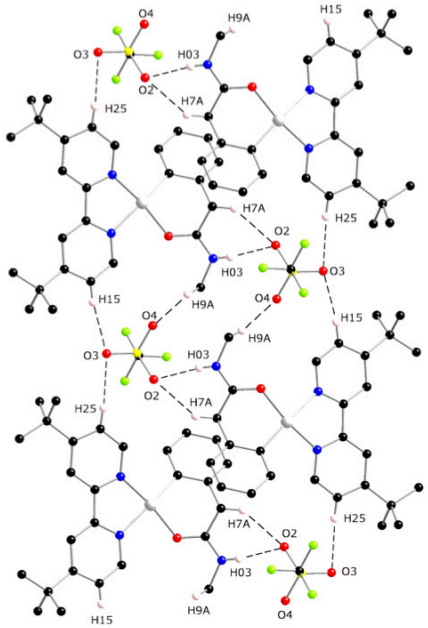


Figure I.7. Hydrogen bonds of complex **2b'**.

Compound **4b'** (Figure I.8) crystallized with two formula units and one CH_2Cl_2 molecule in the asymmetric unit. The amidate group is coordinated to the Pd atom through the nitrogen, forming a six-membered ring with a pseudo-boat conformation. The Pd–N(3) bond distance of 2.012(3) or 2.009(3) Å is typical of palladium amidate complexes.[30] The C(8)–O(1) bond length of 1.264(5) or 1.257(5) Å is slightly longer than the corresponding distance in the free acetamide group of complex **1b'**, consistent with a significant delocalization of the negative charge over the N–C=O group.

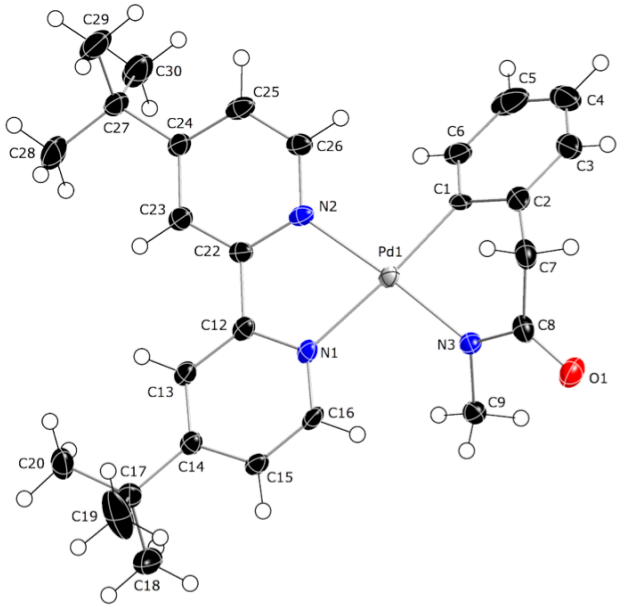


Figure I.8. Thermal ellipsoid plot (50% probability) of one of the two independent molecules of the structure of complex **4b'**. Selected bond distances (Å) and angles (deg): Pd(1)–C(1) 1.983(4), Pd(1)–N(3) 2.012(3), Pd(1)–N(2) 2.049(3), Pd(1)–N(1) 2.111(3), N(3)–C(8) 1.319(5), N(3)–C(9) 1.465(5), C(8)–O(1) 1.264(5); C(1)–Pd(1)–N(3) 86.02(14), C(1)–Pd(1)–N(2) 98.02(14), N(3)–Pd(1)–N(1) 98.19(12), N(2)–Pd(1)–N(1) 77.74(12), C(8)–N(3)–C(9) 114.8(3), C(8)–N(3)–Pd(1) 123.7(3), C(9)–N(3)–Pd(1) 121.5(2), O(1)–C(8)–N(3) 124.9(4), O(1)–C(8)–C(7) 119.0(3), N(3)–C(8)–C(7) 116.1(3).

The structure of **5b'** shows the malononitrilato ligand bonded to the Pd atom through the central carbon (Figure I.9). Prior to this work, only two crystal structures of Pd complexes containing this ligand had been reported, namely $[Pd(C_6F_5)\{CH(CN)_2\}(tmeda)]$[31] and $[\{Pd(C_6F_5)_2\{\mu\text{-}CH(CN)_2\}\}_2]^{2-}$.[32] As observed for **1b'** and **3b'**, the aromatic ring of the aryl ligand in **5b'** is practically perpendicular to the Pd coordination mean plane. The acetamide group is connected through an N–H···N hydrogen bond to one of the CN groups of a neighboring molecule, forming inversion-symmetric dimers.

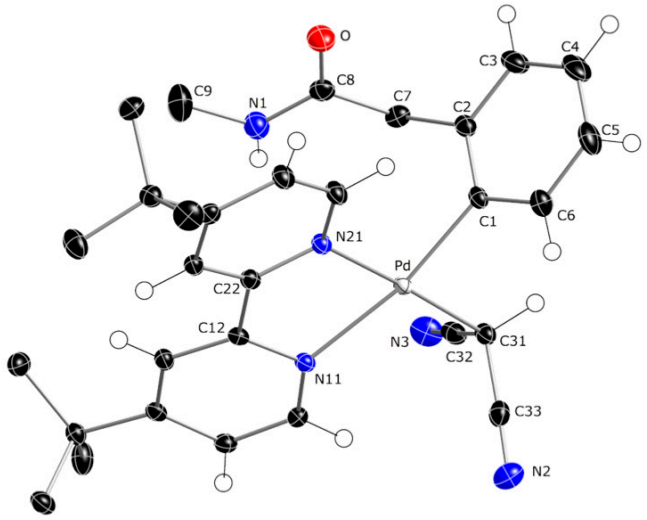


Figure I.9. Thermal ellipsoid plot (50% probability) of complex **5b'**. Selected bond distances (Å) and angles (deg): Pd–C(1) 1.9925(13), Pd–N(21) 2.0793(11), Pd–C(31) 2.0903(13), Pd–N(11) 2.1402(11), O–C(8) 1.2243(17), C(8)–N(1) 1.3406(19), C(9)–N(1) 1.449(2); C(1)–Pd–N(21) 94.59(5), C(1)–Pd–C(31) 87.06(5), N(21)–Pd–C(31) 175.99(5), C(1)–Pd–N(11) 169.10(5), N(21)–Pd–N(11) 78.33(4), C(31)–Pd–N(11) 100.55(5), C(32)–C(31)–C(33) 111.95(12).

The benzoyl ligand in complex **6b'** (Figure I.10) is practically planar (mean deviation 0.024 Å, excluding the acetamide group) and its mean plane forms an angle of 91.8° with the mean plane of atoms Pd-I-N(11)-N(21)-C(1) (mean deviation 0.085 Å). The Pd–C bond distance is normal for this type of compounds.[27, 33, 34] The acetamide groups of adjacent molecules are connected through N–H···O=C hydrogen bonds, thus forming infinite chains (Figure I.11).

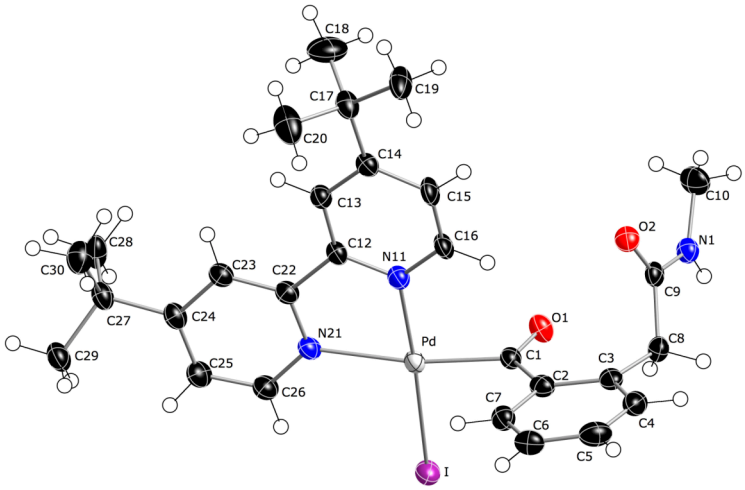


Figure I.10. Thermal ellipsoid plot (50% probability) of complex **6b'**. Selected bond distances (Å) and angles (deg): Pd–C(1) 1.970(4), Pd–N(11) 2.085(3), Pd–N(21) 2.168(3), Pd–I

2.5820(4), O(1)–C(1) 1.211(5), C(2)–C(3) 1.431(6), C(2)–C(7) 1.396(6); C(1)–Pd–N(11) 94.52(15), C(1)–Pd–N(21) 170.39(14), N(11)–Pd–N(21) 77.57(13), C(1)–Pd–I 88.33(11), N(11)–Pd–I 174.29(9), N(21)–Pd–I 100.04(9), O(1)–C(1)–Pd 118.3(3), O(1)–C(1)–C(2) 122.6(3), C(2)–C(1)–Pd 118.8(3).

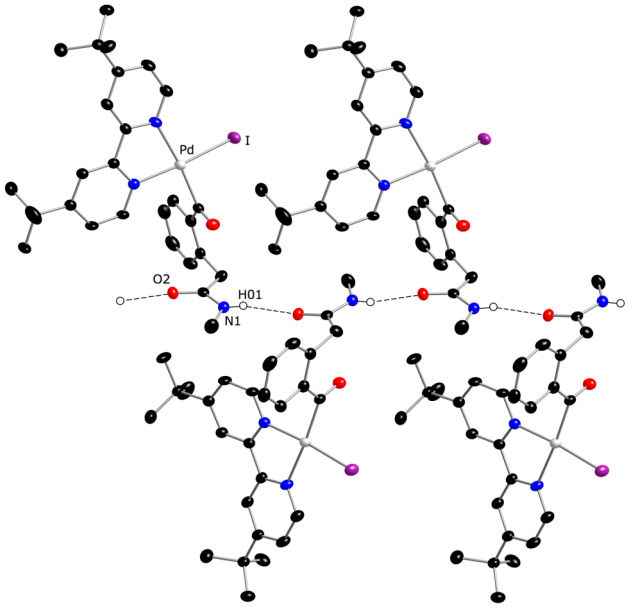


Figure I.11. Crystal packing of complex **6b'**.

Compound **8b** crystallized with two independent molecules in the asymmetric unit (Figure I.12). Both exhibit very similar bond lengths and angles and are practically planar; a least-squares fit of both molecules gave an r.m.s. deviation of 0.03 Å. Each independent molecule forms an inversion-symmetric dimer (Figure I.13) through intermolecular hydrogen bonds of the form C=O···H–N.

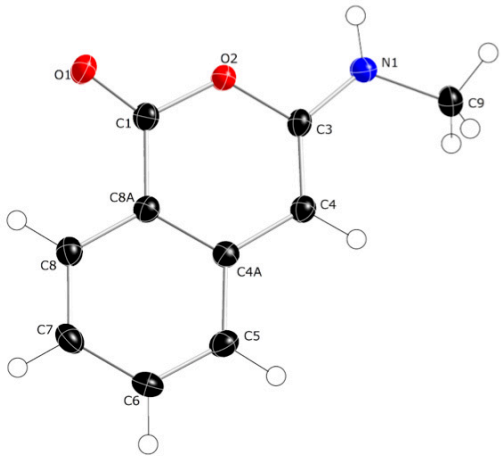


Figure I.12. Thermal ellipsoid plot (50% probability), showing one of the two independent molecules of compound **8b**. Selected bond distances (Å) and angles (deg): O(1)–C(1)

1.2147(11), C(1)–O(2) 1.3749(11), C(1)–C(8A) 1.4496(13), O(2)–C(3) 1.3750(10), C(3)–N(1) 1.3443(12), C(3)–C(4) 1.3546(13), C(4)–C(4A) 1.4286(12), C(4A)–C(8A) 1.4113(12), N(1)–C(9) 1.4451(12), O(1')–C(1') 1.2162(11), C(1')–O(2') 1.3784(11), C(1')–C(8A') 1.4506(12), O(2')–C(3') 1.3746(10), C(3')–N(1') 1.3521(11), C(3')–C(4') 1.3533(12), C(4')–C(4A') 1.4290(12), C(4A')–C(8A') 1.4068(12), N(1')–C(9') 1.4498(12), O(1)–C(1)–O(2) 116.07(8), O(1)–C(1)–C(8A) 126.48(9), O(2)–C(1)–C(8A) 117.44(8), C(1)–O(2)–C(3) 122.77(7), N(1)–C(3)–C(4) 128.56(9), N(1)–C(3)–O(2) 109.87(8), C(4)–C(3)–O(2) 121.56(8), C(3)–C(4)–C(4A) 119.20(8), C(3)–N(1)–C(9) 121.12(8), O(1')–C(1')–O(2') 115.88(8), O(1')–C(1')–C(8A') 126.95(8), O(2')–C(1')–C(8A') 117.18(8), C(3')–O(2')–C(1') 122.82(7), N(1')–C(3')–C(4') 128.42(8), N(1')–C(3')–O(2') 110.01(7), C(4')–C(3')–O(2') 121.51(8), C(3')–C(4')–C(4A') 119.29(8), C(3')–N(1')–C(9') 119.46(8).

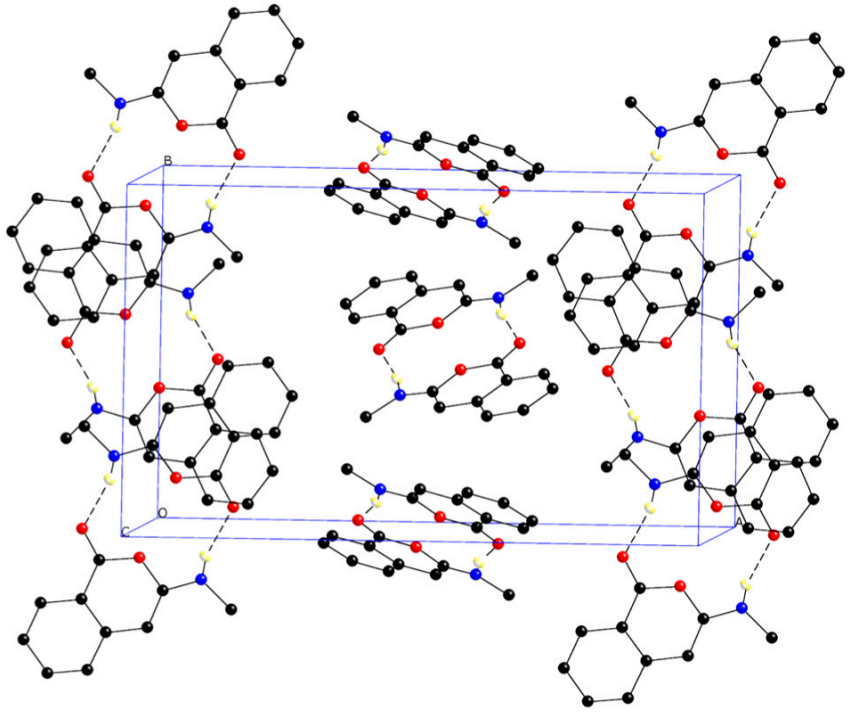


Figure I.13. Crystal packing of compound **8b.**

The crystal structure of **9** is shown in Figure I.14. The fused lactone ring displays a half-chair conformation. Neighboring molecules are connected through bifurcated hydrogen bond systems between the oxygen of the carbonyl group and both the NH group and the methynic hydrogen of the lactone ring (Figure I.15), resulting in infinite chains.

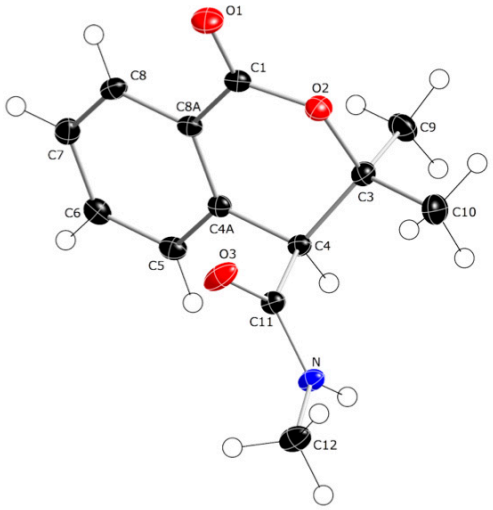


Figure I.14. Thermal ellipsoid plot (50% probability) of compound **9**. Selected bond distances (Å) and angles (deg): C(1)–O(1) 1.2128(17), C(1)–O(2) 1.3459(16), C(1)–C(8A) 1.4880(17), O(2)–C(3) 1.4720(15), C(3)–C(9) 1.5228(18), C(3)–C(10) 1.5237(19), C(3)–C(4) 1.5400(17), C(4A)–C(8A) 1.3933(15), C(4A)–C(4) 1.5012(16), C(4)–C(11) 1.5296(16), C(11)–O(3) 1.2362(14), C(11)–N 1.3319(15), C(12)–N 1.4542(16), O(1)–C(1)–O(2) 118.32(11), O(1)–C(1)–C(8A) 123.23(12), O(2)–C(1)–C(8A) 118.45(10), C(1)–O(2)–C(3) 121.27(9), O(2)–C(3)–C(9) 107.97(10), O(2)–C(3)–C(10) 104.45(11), C(9)–C(3)–C(10) 110.82(11), O(2)–C(3)–C(4) 110.36(10), C(9)–C(3)–C(4) 110.87(11), C(10)–C(3)–C(4) 112.10(10), C(8A)–C(4A)–C(4) 118.55(10), C(5)–C(4A)–C(4) 122.01(10), C(4A)–C(4)–C(11) 109.49(9), C(4A)–C(4)–C(3) 110.71(10), C(11)–C(4)–C(3) 110.73(10), C(4A)–C(8A)–C(1) 120.33(11), O(3)–C(11)–N 122.67(11), O(3)–C(11)–C(4) 121.38(10), N–C(11)–C(4) 115.94(10), C(11)–N–C(12) 121.30(10).

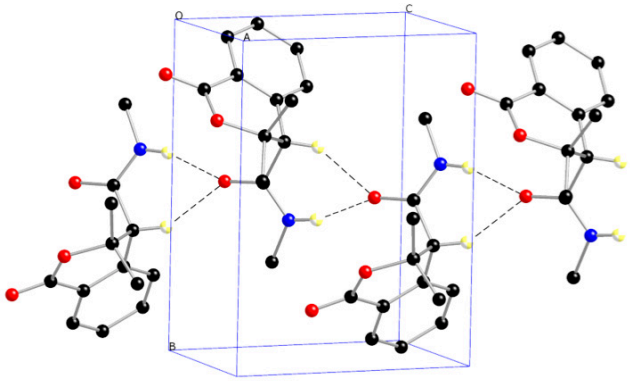


Figure I.15. Crystal packing of compound **9.**

Unlike the benzoyl group in **6b'**, the iminoacyl group in **10b'** (excluding the acetamide group) is not planar (Figure I.16). Thus, the mean plane of the aromatic ring (atoms C(1-6), mean deviation 0.016 Å) is rotated by 46.2° with respect to the C2-C10-N3 plane. In turn, the

latter subtends an angle of 72.2° to the mean Pd coordination plane (Pd-I-N(1)-N(2)-C(10), mean deviation, 0.191 Å). The particular conformation of the iminoacyl ligand appears to originate from the formation of an intramolecular hydrogen bond between the NH group and the iminoacyl N atom. The Pd(1)–C(10) bond distance of 1.995(2) Å and the arrangement of the iminoacyl ligand are similar to those found in [Pd{C(=NXy)C_6H_4OC(O)Me-2}I(bpy)].[34]

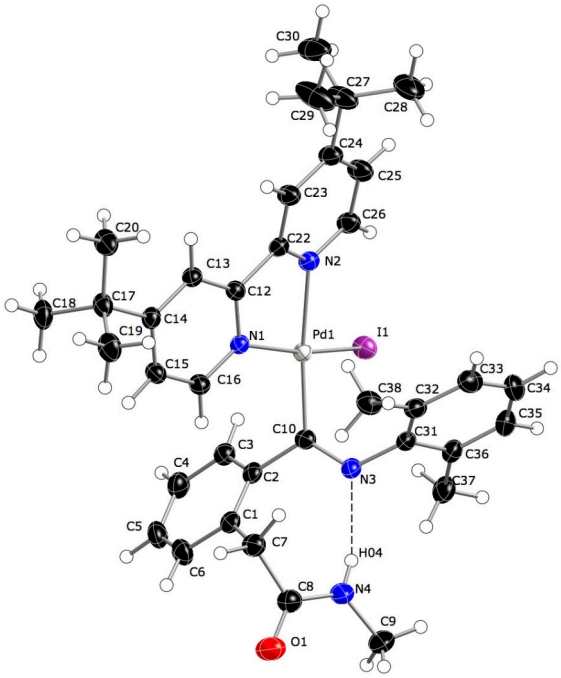


Figure I.16. Thermal ellipsoid plot (50% probability) of complex **10b'**. Selected bond distances (Å) and angles (deg): Pd(1)–C(10) 1.995(2), Pd(1)–N(1) 2.0928(17), Pd(1)–N(2) 2.1557(17), Pd(1)–I(1) 2.5753(2), N(3)–C(10) 1.285(3), N(4)–C(8) 1.330(3), O(1)–C(8) 1.226(3); C(10)–Pd(1)–N(1) 97.37(7), N(1)–Pd(1)–N(2) 78.10(6), C(10)–Pd(1)–I(1) 90.25(6), N(2)–Pd(1)–I(1) 96.52(5), C(10)–N(3)–C(31) 122.77(17), C(8)–N(4)–C(9) 122.1(2), O(1)–C(8)–N(4) 123.1(2), O(1)–C(8)–C(7) 121.9(2), N(4)–C(8)–C(7) 114.9(2), N(3)–C(10)–C(2) 117.88(18), N(3)–C(10)–Pd(1) 122.49(15), C(2)–C(10)–Pd(1) 119.61(14).

The crystal structure of **11b** (Figure I.17) revealed an *E* configuration for the C=N bond. Non-classical hydrogen bonds are established between the oxygen atom and one of the methylenic hydrogens of an adjacent molecule related by an inversion center (Figure I.18), resulting in a pairing of molecules.

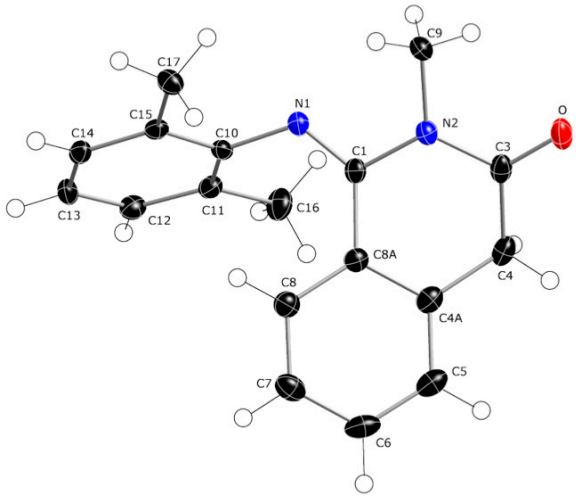


Figure I.17. Thermal ellipsoid plot (50% probability) of compound **11b**. Selected bond distances (Å) and angles (deg): N(1)–C(1) 1.276(2), N(1)–C(10) 1.410(2), N(2)–C(3) 1.379(2), N(2)–C(1) 1.412(2), O(1)–C(3) 1.221(2); C(1)–N(1)–C(10) 124.40(14), C(3)–N(2)–C(1) 123.23(14).

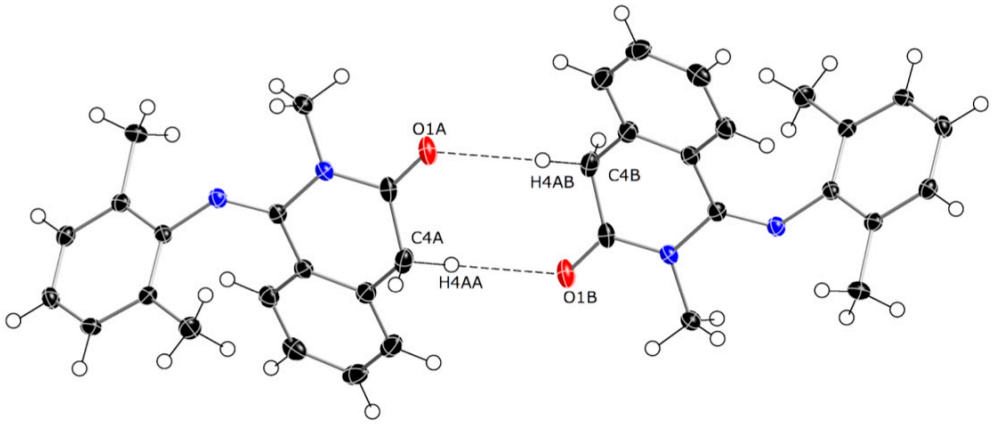


Figure I.18. Hydrogen bonds of compound **11b**.

The structure of complex **13b** (Figure I.19) was solved as a CH_2Cl_2 monosolvate. The arrangement and conformation of the iminoacyl ligand are very similar to those found in **10b'**, including the intramolecular N–H···N hydrogen bond. The Pd(1)–C(21) bond distance of 2.051(2) Å is similar to that found for $[Pd\{C(=NXy)C_6H_4OC(O)Me\text{-}2\}I(CNXy)_2]$.[34] The molecules are connected through non-classical hydrogen bonds C-H···O giving dimers (Figure I.20).

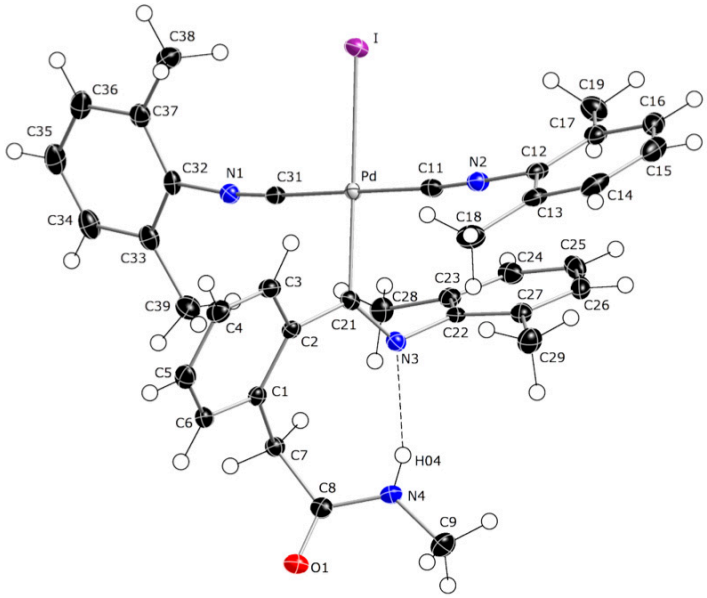


Figure I.19. Thermal ellipsoid plot (50% probability) of complex **13b**. Selected bond distances (Å) and angles (deg): Pd(1)–C(11) 1.971(2), Pd(1)–C(31) 1.978(2), Pd(1)–C(21) 2.051(2), Pd(1)–I(1) 2.7037(2), C(1)–C(2) 1.417(3), C(2)–C(3) 1.402(3), C(21)–N(3) 1.270(3), C(31)–N(1) 1.150(3), C(11)–N(2) 1.148(3), C(2)–C(21) 1.495(3); C(11)–Pd(1)–C(31) 179.05(9), C(11)–Pd(1)–C(21) 90.04(8), C(31)–Pd(1)–C(21) 89.93(8), C(11)–Pd(1)–I(1) 88.52(6), C(31)–Pd(1)–I(1) 91.55(6), C(21)–Pd(1)–I(1) 177.44(6), N(2)–C(11)–Pd(11) 175.91(19), N(3)–C(21)–Pd(1) 123.52(16), C(2)–C(21)–Pd(1) 115.62(15), N(1)–C(31)–Pd(1) 176.49(19).

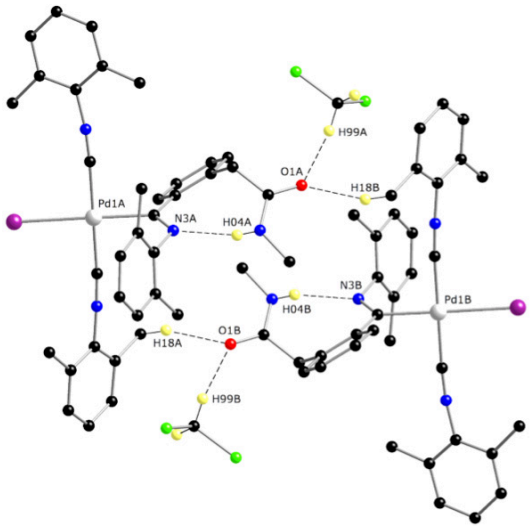


Figure I.20. Hydrogen bonds of complex **13b**.

The coordination environment around the palladium atom in complex **14a** (Figure I.21) is identical to that found in **13b**. The conformation and arrangement of the protonated iminoacyl ligand resemble those found for the iminoacyl ligand in **10b'** and **13b**, except that

the hydrogen bond is now formed between the NH group of the protonated iminoacyl and the oxygen of the acetamide group. The two H atoms of the NH_2 group are involved in hydrogen bonds with two oxygen atoms of different triflate anions, one within the asymmetric unit and one related by inversion (Figure I.22). The protonation of the iminoacyl N atom causes a slight lengthening of the C–N bond distance (1.303(3) Å) as compared to **13b** (1.270(3) Å), which reflects a decrease in the C–N bond order, while the Pd(1)–C(20) bond distance of 2.025(2) Å is slightly shorter than that found for **13b** (2.051(2) Å). These data suggest some degree of carbene character for the Pd–C bond.

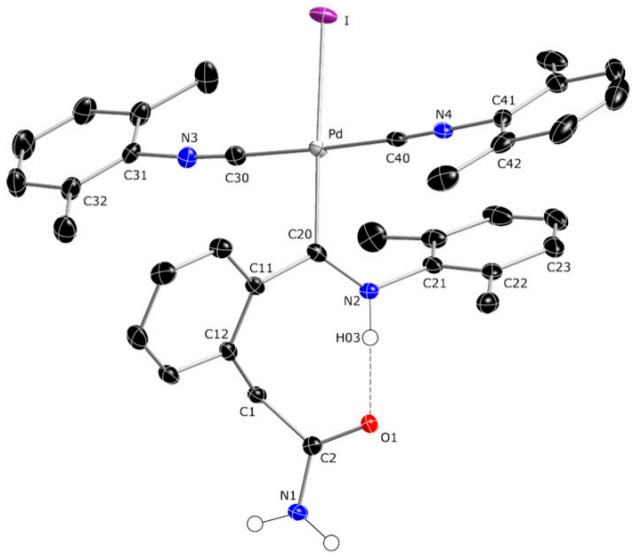


Figure I.21. Thermal ellipsoid plot (50% probability) and hydrogen bonding of complex **14a**. Selected bond distances (Å) and angles (deg): Pd–C(40) 1.964(2), Pd–C(30) 1.971(2), Pd–C(20) 2.025(2), Pd–I 2.6250(2), O(1)–C(2) 1.249(3), N(1)–C(2) 1.315(3), N(2)–C(20) 1.303(3), N(2)–C(21) 1.441(3), N(3)–C(30) 1.145(3), N(3)–C(31) 1.397(3), N(4)–C(40) 1.147(3), N(4)–C(41) 1.405(3); C(40)–Pd–C(20) 91.82(8), C(30)–Pd–C(20) 89.87(9), C(40)–Pd–I 89.00(6), C(30)–Pd–I 89.48(6), C(20)–N(2)–C(21) 125.47(18), C(30)–N(3)–C(31) 174.1(2), C(40)–N(4)–C(41) 176.2(2), O(1)–C(2)–N(1) 122.4(2), O(1)–C(2)–C(1) 119.96(19), N(1)–C(2)–C(1) 117.64(19), N(2)–C(20)–C(11) 119.94(19), N(3)–C(30)–Pd 177.7(2), N(4)–C(40)–Pd 177.24(18).

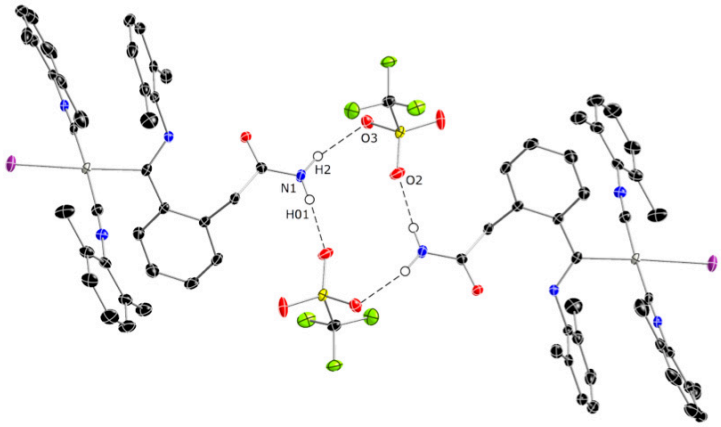


Figure I.22. Hydrogen bonding of complex **14a**.

The arrangement of the iminoacyl ligand in **15c** (Figure I.23) is similar to that found for **10b'** and **13b**, except that there is no intramolecular hydrogen bonding. Analogous structures have been found for [Pd{C(=NXy)C_6H_4OH-2}(CNXy)(bpy)]TfO·Et_2O[34] and [Pd{C(=NXy)$C_6H_4NH_2$-2}(CNXy)(bpy)]TfO.[35]

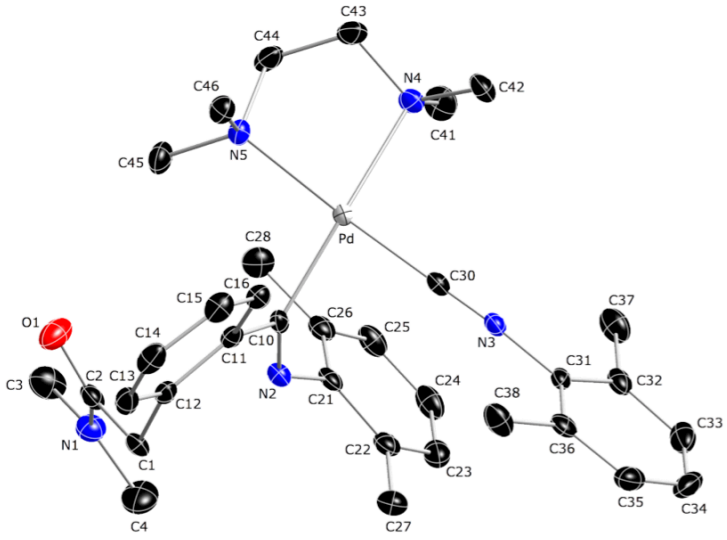


Figure I.23. Thermal ellipsoid plot (50% probability) of complex **15c**. Selected bond distances (Å) and angles (deg): Pd–C(30) 1.9253(18), Pd–C(10) 2.0327(16), Pd–N(5) 2.1625(14), Pd–N(4) 2.2029(13), O(1)–C(2) 1.225(2), N(1)–C(2) 1.352(2), N(2)–C(10) 1.266(2), N(3)–C(30) 1.154(2); C(30)–Pd–C(10) 84.73(7), C(10)–Pd–N(5) 97.61(6), C(30)–Pd–N(4) 95.17(6), N(5)–Pd–N(4) 83.10(5), N(3)–C(30)–Pd 177.73(15), N(2)–C(10)–C(11) 119.42(14), C(10)–N(2)–C(21) 127.90(14).

The crystal structure of **16a** is shown in Figure I.24. The asymmetric unit contains one molecule of the complex and half of $CDCl_3$. The triflate anion is connected to the cation

through an N–H···O hydrogen bond. The coordination environment around the Pd center is distorted square planar because of the small bite of the chelating tmeda ligand, leading to a N(3)–Pd–N(4) angle of 85.59(14)°, and the four-membered cycle, leading to a N(2)–Pd–S(1) angle of 69.52(9)°. The observed C(10)–S(1) and C(10)–N(2) bond distances of 1.731(4) and 1.287(5) Å respectively are between single and double bonds values.[36] However, the observed C(10)–N(2) bond distance is close to the double bond value of 1.26 Å, this indicates that C–N π bonding is slightly stronger than π C–S bonding. In addition, the Pd–S(1) and Pd–N(2) bond distances of 2.3103(9) and 2.041(3) Å respectively, are similar[24] or shorter,[23] than those of other thioamidato complexes. As far as we are aware, this is the first crystal structure of an alkyl or aryl thioamidato group chelated to a palladium atom resulting from the insertion reaction of an alkyl or aryl isothiocyanate into the Pd–C bond.

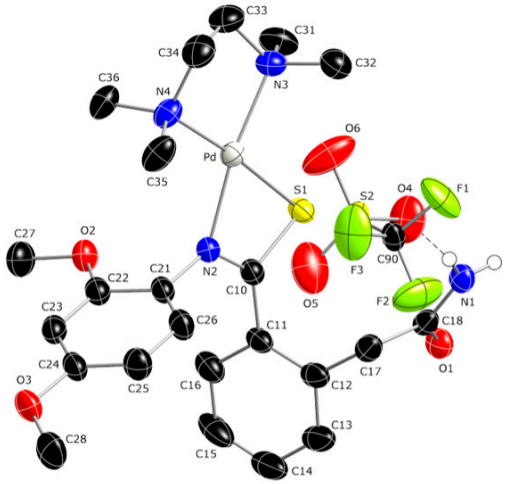


Figure I.24. Thermal ellipsoid plot (50% probability) of complex **16a**. Selected bond distances (Å) and angles (deg): Pd–N(2) 2.041(3), Pd–N(3) 2.063(3), Pd–N(4) 2.099(3), Pd–S(1) 2.3103(9), C(10)–N(2) 1.287(5), C(10)–S(1) 1.731(4); N(2)–Pd–N(3) 169.51(13), N(2)–Pd–N(4) 104.83(14), N(3)–Pd–N(4) 85.59(14), N(2)–Pd–S(1) 69.52(9), N(3)–Pd–S(1) 100.02(10), N(4)–Pd–S(1) 173.92(10), C(10)–N(2)–Pd 100.9(2), C(10)–S(1)–Pd 79.09(13).

Experimental Section

General Considerations, Materials and Instrumentation

Unless otherwise noted, all preparations were carried out at room temperature under atmospheric conditions. Synthesis grade solvents were obtained from commercial sources. Toluene, CH_2Cl_2 and THF were degassed and dried using a Pure Solv MD-5 solvent purification system from Innovative Technology, Inc. The compounds $[Pd_2(dba)_3]\cdot dba$,[37] 2-(2-iodophenyl)acetamide,[38] 2-(2-iodophenyl)-*N*-methylacetamide,[39] and

2-(2-iodophenyl)-*N,N*-dimethylacetamide[40] were prepared according to published procedures. All other reagents were obtained from commercial sources and used without further purification. NMR spectra were recorded on Bruker Avance 200, 300 or 400 spectrometers usually at 298 K, unless otherwise indicated. Chemical shifts are referred to internal TMS (^{1}H and $^{13}C\{^{1}H\}$) or external 85% H_3PO_4 ($^{31}P\{^{1}H\}$). The assignments of the ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were made with the help of HMBC and HMQC experiments. Inserted and coordinated XyNC are denoted by $XyNC^{i}$ and $XyNC^{c}$, respectively, and the C_6H_4 aryl group by Ar. Melting points were determined on a Reichert apparatus and are uncorrected. Elemental analyses were carried out with a Carlo Erba 1106 microanalyzer. Infrared spectra were recorded in the range 4000–200 cm^{-1} on a Perkin-Elmer Spectrum 100 spectrophotometer using Nujol mulls between polyethylene sheets. High-resolution ESI mass spectra were recorded on an Agilent 6220 Accurate-Mass TOF LC/MS.

X-Ray Structure Determinations

Crystals suitable for X-ray diffraction studies were obtained by liquid-liquid diffusion from CH_2Cl_2/*n*-hexane: **1b'**, **3b'**, **4b'**·0.5CH_2Cl_2; CH_2Cl_2/*n*-pentane: **6b'**, **10b'**, **13b**·CH_2Cl_2, **14a**; acetone/Et_2O: **2b'**·Me_2CO; $CDCl_3$/*n*-pentane: **5b'**; $CDCl_3$/Et_2O: **16a**·0.5$CDCl_3$; CH_2Cl_2/Et_2O: **9**, **15c**, or by sublimation at low pressure: **8b**, **11b**. Numerical details are presented in Tables I.1, I.2 and I.3. The data for **1b'**, **2b'**, **4b'**, **10b'**, **11b**, and **13b'** were collected on a Bruker Smart APEX CCD diffractometer using monochromated Mo-*K*α radiation in *ω*-scan mode. The data for **6b'** and **16a** were collected on an Oxford Diffraction Nova O diffractometer using mirror-focused Cu-*K*α radiation in *ω*-scan mode. The data for **3b'**, **5b'**, **8b**, **9**, **14a**, and **15c** were collected on an Oxford Diffraction Xcalibur S diffractometer using monochromated Mo-*K*α radiation in *ω*-scan mode. The structures were solved by direct methods and refined anisotropically on F^2 using the program SHELXL-97 (G. M. Sheldrick, University of Göttingen).[41] Restraints to local aromatic ring symmetry or light-atom displacement factor components were applied in some cases. Treatment of hydrogen atoms is as follows: NH free except for **1b'**, **2b'**, **6b'**, **10b'** (free with DFIX), and **14a** (free with SADI); ordered methyl groups, rigid; all others, riding. *Special features of refinement:* **1b'**: The Flack parameter is 0.001(14). One ^{t}Bu group is disordered over two positions. **2b'**: The triflate anion is disordered over two positions. An ill-defined region of residual electron density was tentatively interpreted as a disordered acetone. Its hydrogen atoms were not included in the refinement. **4b'**: One ^{t}Bu group is disordered over two positions. **9**: In the absence of

significant anomalous scattering, Friedel opposite reflections were merged and the Flack parameter is thus meaningless. **10b'**: A region of residual electron density could not be interpreted in terms of realistic solvent molecules, even allowing for possible disorder. For this reason the program SQUEEZE (Prof. A. L. Spek, University of Utrecht, Netherlands) was employed to remove mathematically the effects of the solvent. Standard deviations of refined parameters should be interpreted with caution. The void volume per cell was 1021 Å^3, with a void electron count per cell of 240. This solvent was not taken into account when calculating derived parameters such as the formula weight, because the nature of the solvent was uncertain. **16a:** The triflate is disordered over two positions with relative occupancy 83:17; the chloroform is disordered over an inversion centre.

Table I.1. Crystallographic Data for **1b'**, **2b'**·Me_2CO, **3b'**, **4b'**·0.5CH_2Cl_2.

Compound	**1b'**	**2b'**·Me_2CO	**3b'**	**4b'**·0.5CH_2Cl_2
formula	$C_{27}H_{34}IN_3OPd$	$C_{31}H_{40}F_3N_3O_5PdS$	$C_{46}H_{49}F_3N_3O_4PPdS$	$C_{27.5}H_{34}ClN_3OPd$
fw	649.87	730.12	934.31	564.43
T (K)	100(2)	100(2)	100(2)	100(2)
λ (Å)	0.71073	0.71073	0.71073	0.71073
cryst syst	orthorhombic	triclinic	triclinic	triclinic
space group	$Pna2_1$	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$
a (Å)	13.4414(6)	10.2621(5)	12.2756(5)	12.1373(5)
b (Å)	11.7373(5)	13.5328(7)	13.6966(5)	13.4080(6)
c (Å)	17.4652(8)	14.1804(7)	14.0469(5)	16.7547(7)
α (deg)	90	63.950(2)	70.198(4)	95.000(2)
β (deg)	90	71.051(2)	82.776(4)	99.522(2)
γ (deg)	90	72.364(2)	76.276(4)	105.510(2)
V (Å^3)	2755.4(2)	1643.30(14)	2156.00(14)	2566.23(19)
Z	4	2	2	4
ρ_{calcd} (Mg m^{-3})	1.567	1.476	1.439	1.461
μ (mm^{-1})	1.817	0.688	0.576	0.852
R1[a]	0.0203	0.0484	0.0291	0.0532
wR2[b]	0.0473	0.1189	0.0703	0.1082

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

Table I.2. Crystallographic Data for **5b'**, **6b'**, **8b**, **9** and **10b'**.

Compound	**5b'**	**6b'**	**8b**	**9**	**10b'**
formula	$C_{30}H_{35}N_5OPd$	$C_{28}H_{34}IN_3O_2Pd$	$C_{10}H_9NO_2$	$C_{13}H_{15}NO_3$	$C_{36}H_{43}IN_4OPd$
fw	588.03	677.88	175.18	233.26	781.04
T (K)	100(2)	103(2)	110(2)	100(2)	100(2)

λ (Å)	0.71073	1.54184	0.71073	0.71073	0.71073
cryst syst	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic
space group	$P2_1/c$	$P2_1/c$	$P2_1/c$	Pn	$C2/c$
a (Å)	10.6664(2)	19.8663(6)	19.5562(5)	7.8580(2)	31.3723(16)
b (Å)	26.7297(3)	10.1395(3)	11.9837(3)	9.7895(2)	12.4240(6)
c (Å)	10.2585(2)	14.4269(5)	7.2383(2)	8.1530(2)	21.9332(11)
α (deg)	90	90	90	90	90
β (deg)	108.641(3)	109.676(4)	100.198(4)	108.008(3)	118.671(2)
γ (deg)	90	90	90	90	90
V (Å^3)	2771.36(8)	2736.39(15)	1669.55(8)	596.45(2)	7500.7(6)
Z	4	4	8	2	8
ρ_{calcd} (Mg m^{-3})	1.409	1.645	1.394	1.299	1.383
μ (mm^{-1})	0.701	14.554	0.098	0.093	1.348
R1[a]	0.0224	0.0342	0.0342	0.0266	0.0268
wR2[b]	0.0533	0.0921	0.0852	0.0711	0.0701

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

Table I.3. Crystallographic Data for **11b**, **13b**·CH_2Cl_2, **14a**, **15c** and **16**·0.5$CDCl_3$

Compound	**11b**	**13b**·CH_2Cl_2	**14a**	**15c**	**16**·0.5$CDCl_3$
formula	$C_{18}H_{18}N_2O$	$C_{37}H_{39}Cl_2IN_4OPd$	$C_{36}H_{36}F_3IN_4O_4PdS$	$C_{35}H_{46}F_3N_5O_4PdS$	$C_{24.5}H_{33}D_{0.5}Cl_{1.5}F_3N_4O_6PdS_2$
fw	278.34	859.92	911.05	796.23	761.25
T (K)	100(2)	100(2)	100(2)	100(2)	100(2)
λ (Å)	0.71073	0.71073	0.71073	0.71073	1.54184
cryst syst	monoclinic	monoclinic	triclinic	monoclinic	monoclinic
space group	$P2_1/n$	$P2_1/c$	$P\bar{1}$	$P2_1/c$	$P2_1/c$
a (Å)	13.0014(12)	19.2766(8)	8.3013(3)	10.6738(2)	12.0319(6)
b (Å)	7.8134(7)	8.5432(6)	14.7697(4)	14.8048(3)	13.2242(6)
c (Å)	15.2139(14)	23.3527(9)	16.4066(4)	22.7526(4)	20.9260(12)
α (deg)	90	90	87.250(3)	90	90
β (deg)	111.926(2)	110.859(2)	75.566(4)	92.482(3)	105.195(6)
γ (deg)	90	90	76.134(4)	90	90
V (Å^3)	1433.7(2)	3593.8(3)	1891.16(10)	3592.07(12)	3213.2(3)
Z	4	4	2	4	4
ρ_{calcd} (Mg m^{-3})	1.290	1.589	1.600	1.472	1.574
μ (mm^{-1})	0.081	1.559	1.419	0.635	7.561
R1[a]	0.0599	0.0266	0.0278	0.0239	0.0405
wR2[b]	0.1265	0.0633	0.0728	0.0454	0.1037

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

Synthesis

[Pd{$C_6H_4CH_2C(O)NH_2$-2}I(tmeda)] (1a). To a suspension of $Pd(dba)_2$ (641 mg, 1.11 mmol) in CH_2Cl_2 (20 mL) was added tmeda (0.25 mL, 1.67 mmol) and the mixture was stirred for 10 min under an N_2 atmosphere. 2-(2-Iodophenyl)-acetamide (310 mg, 1.19 mmol) was then added and the stirring was continued for 1 h. The resulting suspension was filtered through Celite and the solution was concentrated (8 mL). Addition of Et_2O (25 mL) led to the precipitation of an orange solid, which was filtered off, washed with Et_2O (3 × 5 mL) and vacuum-dried to give **1a**. Yield: 339 mg, 63%. Anal. Calcd for $C_{14}H_{24}IN_3OPd$: C, 34.77; H, 5.00; N, 8.69. Found: C, 34.69; H, 5.09; N, 8.57. Mp: 170 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3372, 3175; ν(CO), 1672. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.30 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.06 (dd, $^4J_{HH}$ = 2.0 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.90 (td, $^4J_{HH}$ = 2.0 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.85 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.26 (br, 1 H, NH), 5.26 (br, 1 H, NH), 4.76, 3.77 (AB system, $^2J_{HH}$ = 14.4 Hz, 2 H, CH_2, acetamide), 2.89-2.83 (m, 1 H, CH_2, tmeda), 2.73 (s, 3 H, Me, tmeda), 2.70 (s, 3 H, Me, tmeda), 2.72-2.62 (m, 2 H, CH_2, tmeda), 2.58-2.50 (m, 1 H, CH_2, tmeda), 2.43 (s, 3 H, Me, tmeda), 2.18 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 175.6 (CO), 145.1 (C, Ar), 140.0 (C, aryl), 137.2 (CH, Ar), 128.1 (CH, Ar), 125.9 (CH, Ar), 124.1 (CH, Ar), 62.6 (CH_2, tmeda), 58.7 (CH_2, tmeda), 50.9 (Me, tmeda), 50.8 (Me, tmeda), 49.6 (Me, tmeda), 49.4 (Me, tmeda), 48.2 (CH_2, acetamide).

[Pd{$C_6H_4CH_2C(O)NHMe$-2}I(tmeda)] (1b). To a suspension of $Pd(dba)_2$ (662 mg, 1.15 mmol) in THF (20 mL) was added tmeda (0.2 mL, 1.33 mmol) and the mixture was stirred for 10 min under an N_2 atmosphere. 2-(2-Iodophenyl)-*N*-methylacetamide (400 mg, 1.45 mmol) was then added and the stirring was continued for 2 h. The solvent was removed under reduced pressure and the remaining residue was treated with CH_2Cl_2 (20 mL). The resulting suspension was filtered through Celite and the filtrate was concentrated to dryness. The residue was stirred in Et_2O for 15 min, whereupon a pale orange precipitate formed, which was filtered off, washed with Et_2O (3 × 5 mL) and vacuum-dried to give **1b**. Yield: 360 mg, 63%. Anal. Calcd for $C_{15}H_{26}IN_3OPd$: C, 36.20; H, 5.27; N, 8.44. Found: C, 36.33; H, 5.50; N, 8.44. Mp: 155-159 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3329; ν(CO), 1675. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.29 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.01 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.89 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 6.84 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 6.15 (br, 1 H, NH), 4.71, 3.77 (AB system, $^2J_{HH}$ = 14.8 Hz, 2 H, CH_2, acetamide), 2.89-2.80 (m, 1 H, CH_2, tmeda), 2.72 (s, 3 H, Me, tmeda), 2.70 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NMe), 2.69-2.60 (m, 2 H, CH_2, tmeda), 2.68 (s, 3 H, Me, tmeda), 2.55-2.48 (m, 1 H, CH_2,

tmeda), 2.42 (s, 3 H, Me, tmeda), 2.17 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ 173.2 (CO), 145.0 (C, Ar), 139.7 (C, Ar), 136.8 (CH, Ar), 128.0 (CH, Ar), 125.3 (CH, Ar), 123.6 (CH, Ar), 62.2 (CH_2, tmeda), 58.3 (CH_2, tmeda), 50.4 (Me, tmeda), 50.3 (Me, tmeda), 49.2 (Me, tmeda), 49.0 (Me, tmeda), 47.8 (CH_2, acetamide), 26.1 (NMe).

[Pd{$C_6H_4CH_2C(O)NMe_2$-2}I(tmeda)] (1c). This yellow complex was prepared as described for **1a**, from $Pd(dba)_2$ (851 mg, 1.48 mmol), tmeda (0.30 mL, 2.00 mmol) and 2-(2-iodophenyl)-*N,N*-dimethylacetamide (445 mg, 1.49 mmol). Yield: 403 mg, 53%. Anal. Calcd for $C_{16}H_{28}IN_3OPd$: C, 37.55; H, 5.52; N, 8.21. Found: C, 37.85; H, 6.01; N, 8.14. Mp: 92-93 °C. IR (Nujol, cm^{-1}): ν(CO), 1632. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.28 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.85 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 6.80 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 6.74 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 4.57, 4.06 (AB system, $^2J_{HH}$ = 16.0 Hz, 2 H, CH_2, acetamide), 3.02 (s, 3 H, Me, acetamide), 2.99 (s, 3 H, Me, acetamide), 2.93-2.87 (m, 1 H, CH_2, tmeda), 2.71 (s, 3 H, Me, tmeda), 2.67 (s, 3 H, Me, tmeda), 2.70-2.62 (m, 1 H, CH_2, tmeda), 2.58-2.53 (m, 1 H, CH_2, tmeda), 2.47 (s, 3 H, Me, tmeda), 2.51-2.44 (m, 1 H, CH_2, tmeda), 2.18 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 172.9 (CO), 144.8 (C, Ar), 139.5 (C, Ar), 135.7 (CH, Ar), 125.7 (CH, Ar), 124.8 (CH, Ar), 123.4 (CH, Ar), 62.1, 58.3 (CH_2, tmeda), 50.7, 50.3, 48.65, 48.60 (Me, tmeda), 47.0 (CH_2, acetamide), 39.04, 35.4 (Me, acetamide).

[Pd{$C_6H_4CH_2C(O)NHMe$-2}I(dbbpy)] (1b'). A solid mixture of $Pd(dba)_2$ (330 mg, 0.57 mmol) and dbbpy (170 mg, 0.63 mmol) was suspended in toluene (20 mL) under an N_2 atmosphere and stirred for 10 min. 2-(2-Iodophenyl)-*N*-methylacetamide (174 mg, 0.63 mmol) was then added and the mixture was stirred for 1 h. The solvent was removed under reduced pressure, CH_2Cl_2 (20 mL) was added, and the suspension was filtered through anhydrous $MgSO_4$. The filtrate was concentrated to *ca.* 1 mL and treated with *n*-hexane (20 mL) to give a precipitate, which was collected by filtration, washed with hot *n*-hexane (5 × 5 mL) and vacuum-dried to give **1b'** as a pale orange solid. Yield: 229 mg, 62%. Anal. Calcd for $C_{27}H_{34}IN_3OPd$: C, 49.90; H, 5.27; N, 6.47. Found: C, 49.61; H, 5.39; N, 6.39. Mp: 264-267 °C. IR (Nujol, cm^{-1}): ν(NH), 3418; ν(CO), 1660. ^1H NMR (400.9 MHz, $CDCl_3$): δ 9.46 (d, $^3J_{HH}$ = 5.6 Hz, 1 H, H6, dbbpy), 7.96 (d, $^4J_{HH}$ = 1.2 Hz, 1 H, H3, dbbpy), 7.56 (m, 1 H, Ar), 7.53 (dd, $^4J_{HH}$ = 2.0 Hz, $^3J_{HH}$ = 6 Hz, 1 H, H5, dbbpy), 7.35 (d, $^3J_{HH}$ = 5.6 Hz, 1 H, H6, dbbpy), 7.31 (dd, $^4J_{HH}$ = 2 Hz, $^3J_{HH}$ = 6.0 Hz, 1 H, H5, dbbpy), 7.13 (m, 1 H, Ar), 6.95 (m, 2 H, Ar), 6.18 (br c, $^3J_{HH}$ = 4.4 Hz, 1 H, NH), 4.31, 3.63 (AB system, $^2J_{AB}$ = 14.8 Hz, 2 H, CH_2), 2.65 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NMe), 1.44 (s, 9 H , ^{t}Bu), 1.39 (s, 9 H, ^{t}Bu). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 172.9

(CO), 163.5, 163.4 (C4, dbbpy), 156.0, 153.8 (C2, dbbpy), 152.4, 149.2 (C6, dbbpy), 147.6 (C, Ar), 139.1 (C, Ar), 138.2 (CH, Ar), 129.7 (CH, Ar), 125.4 (CH, Ar), 124.03, 123.99 (C5, dbbpy and CH, Ar), 123.8 (C5, dbbpy), 118.5, 118.0 (C3, dbbpy), 47.2 (CH_2), 35.54, 35.49 (CMe_3), 30.4, 30.2 (CMe_3), 26.0 (NMe).

[Pd{κ^2*C,O*-$C_6H_4CH_2C(O)NRR'$-2}(N^N)]TfO (N^N = tmeda, NRR' = NH_2 (2a), NHMe (2b), NMe_2 (2c); N^N =dbbpy, NRR' = NHMe (2b')). To a solution of **1** (**1a,** 82 mg, 0.17 mmol; **1b**, 293 mg, 0.59 mmol; **1c**, 60 mg, 0.12 mmol; **1b'**, 165 mg, 0.25 mmol) in acetone (20 mL) was added AgTfO (for **2a**: 52 mg, 0.20 mmol; for **2b**: 166 mg, 0.65 mmol; for **2c**: 42 mg, 0.16 mmol; for **2b'**: 72 mg, 0.28 mmol). The resulting suspension was stirred for 1 h and filtered through Celite. Partial evaporation of the filtrate (1 mL) and addition of Et_2O (20 mL) led to the precipitation of a solid, which was collected by filtration, washed with Et_2O (3 × 3 mL) and vacuum-dried to give **2a,b,c,b'**.

2a: Colorless solid. Yield: 74 mg, 86%. Anal. Calcd for $C_{15}H_{24}F_3N_3O_4PdS$: C, 35.62; H, 4.78; N, 8.31; S, 6.34. Found: C, 35.78; H, 4.73; N, 8.29; S, 6.01. Mp: 190-192 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3400, 3330, 3202; ν(CO), 1654. ^{1}H NMR (400.9 MHz, $(CD_3)_2CO$): δ 8.70 (br, 1 H, NH), 8.20 (br, 1 H, NH), 7.32 (m, 1 H, Ar), 7.01-6.93 (m, 3 H, Ar), 4.22 (s, 2 H, CH_2, acetamide), 3.10 (m, 2 H, CH_2, tmeda), 2.87 (m, 2 H, CH_2, tmeda), 2.84 (s, 6 H, Me, tmeda), 2.67 (s, 6 H, Me, tmeda). $^{13}C\{^1H\}$ NMR (75.5 MHz, $(CD_3)_2CO$): δ 181.6 (CO), 148.3 (C, Ar), 135.5 (C, Ar), 133.3 (CH, Ar), 127.2 (CH, Ar), 126.4 (CH, Ar), 125.4 (CH, Ar), 65.5 (CH_2, tmeda), 57.8 (CH_2, tmeda), 51.9 (Me, tmeda), 48.4 (CH_2, acetamide), 47.5 (Me, tmeda).

2b: Pale yellow solid. Yield: 275 mg, 90%. Anal. Calcd for $C_{16}H_{26}F_3N_3O_4PdS$: C, 36.97; H, 5.04; N, 8.08; S, 6.17. Found: C, 37.09; H, 5.23; N, 8.02; S, 5.95. Mp: 170-173 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3380; ν(CO), 1610. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.88 (br c, $^3J_{HH}$ = 3.9 Hz, 1 H, NH), 7.16 (m, 1 H, Ar), 7.05-6.93 (m, 3 H, Ar), 4.08 (s, 2 H, CH_2, acetamide), 2.94 (m, 2 H, CH_2, tmeda), 2.78 (d, $^3J_{HH}$ = 5.1 Hz, 3 H, NMe), 2.76 (s, 6 H, Me, tmeda), 2.78-2.71 (m, 2 H, CH_2, tmeda), 2.61 (s, 6 H, Me, tmeda). $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ 177.1 (CO), 145.9 (C, Ar), 134.3 (C, Ar), 131.6 (CH, Ar), 127.2 (CH, Ar), 125.9 (CH, Ar), 125.2 (CH, Ar), 64.9 (CH_2, tmeda), 57.2 (CH_2, tmeda), 51.7 (Me, tmeda), 48.2 (CH_2, acetamide), 47.5 (Me, tmeda), 27.4 (NMe).

2c: Pale yellow solid. Yield: 51 mg, 80%. Anal. Calcd for $C_{17}H_{28}F_3N_3O_4PdS$: C, 38.24; H, 5.29; N, 7.87; S, 6.01. Found: C, 38.38; H, 5.39; N, 7.86; S, 5.68. Mp: 170-173 °C (dec). IR

(Nujol, cm^{-1}): ν(CO), 1601. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.22–7.11 (m, 1 H, Ar), 7.04-6.97 (m, 2 H, Ar), 6.95-6.90 (m, 1 H, Ar), 4.32 (s, 2 H, CH_2, acetamide), 3.35 (s, 3 H, NMe), 3.04 (s, 3 H, NMe), 2.99 (m, 2 H, CH_2, tmeda), 2.78 (s, 6 H, Me, tmeda), 2.72 (m, 2 H, CH_2, tmeda), 2.65 (s, 6 H, Me, tmeda). $^{13}C\{^{1}H\}$ NMR (100.8 MHz, $CDCl_3$): δ 176.7 (CO), 146.2 (C, Ar), 134.3 (C, Ar), 131.8 (CH, Ar), 127.0 (CH, Ar), 126.1 (CH, Ar), 125.1 (CH, Ar), 64.8 (CH_2, tmeda), 57.3 (CH_2, tmeda), 51.8 (Me, tmeda), 47.8 (Me, tmeda), 44.6 (CH_2, acetamide), 40.2 (NMe), 37.4 (NMe).

2b'·H_2O: Pale yellow solid. Yield: 149 mg, 87%. Anal. Calcd for $C_{28}H_{36}F_3N_3O_5PdS$: C, 48.73; H, 5.26; N, 6.09; S, 4.65. Found: C, 48.98; H, 5.02; N, 5.99; S, 4.65. Mp: 216-220 °C. IR (Nujol, cm^{-1}): ν(NH), 3294; ν(CO), 1615. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 9.32 (br c, $^{3}J_{HH}$ = 4.4 Hz, 1 H, NH), 8.62 (d, $^{3}J_{HH}$ = 6.0 Hz, 1 H, H6, dbbpy), 8.54 (d, $^{3}J_{HH}$ = 5.6 Hz, 1 H, H6, dbbpy), 8.09 (d, $^{4}J_{HH}$ = 1.2 Hz, 1 H, H3, dbbpy), 8.08 (d, $^{4}J_{HH}$ = 2.0 Hz, 1 H, H3, dbbpy), 7.71 (dd, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 5.6 Hz, 1 H, H5, dbbpy), 7.51 (dd, $^{4}J_{HH}$ = 2.0 Hz, $^{3}J_{HH}$ = 6.0 Hz, 1 H, H5, dbbpy), 7.20 (m, 1 H, Ar), 7.10 (m, 3 H, Ar), 4.16 (s, 2 H, CH_2), 2.98 (d, $^{3}J_{HH}$ = 4.8 Hz, 3 H, NMe), 1.49 (s, 9 H, ^{t}Bu), 1.46 (s, 9 H, ^{t}Bu), 1.59 (s, 2 H, H_2O). $^{13}C\{^{1}H\}$ NMR (100.8 MHz, $CDCl_3$): δ 177.1 (CO), 165.2, 164.8 (C4, dbbpy), 156.5, (C2, dbbpy), 153.1 (C6, dbbpy), 152.9 (C, Ar), 150.1 (C2, dbbpy), 147.6 (C6, dbbpy), 134.8 (C, Ar), 133.9 (CH, Ar), 127.0 (CH, Ar), 126.7 (CH, Ar), 125.6 (CH, Ar), 124.3, 124.2 (C5, dbbpy), 119.4, 118.6 (C3, dbbpy), 47.6 (CH_2), 35.84, 35.75 (*C*Me$_3$), 30.4, 30.2 (C*Me*$_3$), 27.7 (NMe).

[Pd{$C_6H_4CH_2C(O)NHMe$-2}(dbbpy)(PPh_3)]TfO (3b'). To a solution of **2b'** (91 mg, 0.14 mmol) in CH_2Cl_2 (10 mL) was added PPh_3 (36 mg, 0.14 mmol). The resulting solution was stirred for 1 h, filtered through anhydrous $MgSO_4$, and concentrated (1 mL). *N*-hexane (20 mL) was added to precipitate a white solid, which was collected by filtration, washed with *n*-hexane (3 × 3 mL) and vacuum-dried to give **3b'**. Yield: 88 mg, 69%. Anal. Calcd for $C_{46}H_{49}F_3N_3O_4PPdS$: C, 59.13; H, 5.29; N, 4.50; S, 3.43. Found: C, 58.82; H, 5.25; N, 4.38; S, 3.27. Mp: 156-159 °C. IR (Nujol, cm^{-1}): ν(NH), 3340; ν(CO), 1670. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.13 (br s, 2 H, H3, dbbpy), 7.56 (m, 6 H, *o*-H, Ph), 7.46 (m, 3 H, *p*-H, Ph), 7.36 (m, 6 H, *m*-H, Ph), 7.30 (m, 2 H, H5, dbbpy), 7.21 (d, $^{3}J_{HH}$ = 6.0 Hz, 1 H, H6, dbbpy), 7.18 (ddd, $^{5}J_{HH}$ = 1.2 Hz, $^{4}J_{HH}$ = 3.2 Hz, $^{3}J_{HH}$ = 8 Hz, 1 H, Ar), 7.10 (d, $^{3}J_{HH}$ = 7.6 Hz, 1 H, H6, dbbpy), 7.05 (br c, 1 H, NH), 6.92 (m, 2 H, Ar), 6.72 (td, $^{4}J_{HH}$ = 1.2 Hz, $^{3}J_{HH}$ = 7.2 Hz, 1 H, Ar), 3.65, 3.01 (AB system, $^{2}J_{AB}$ = 14.8 Hz, 2 H, CH_2), 2.23 (d, $^{3}J_{HH}$ = 4.8 Hz, 3 H, N*Me*), 1.38 (s, 9 H, ^{t}Bu), 1.37 (s, 9 H, ^{t}Bu). $^{13}C\{^{1}H\}$ NMR (100.8 MHz, $CDCl_3$): δ 171.1 (CO), 164.5, 164.3 (C4, dbbpy), 155.7, 155.6 (C2, dbbpy), 155.4 (d, $^{2}J_{CP}$ = 11.0 Hz, C-Pd), 150.3, 149.9 (C6, dbbpy),

138.7 (d, $^{3}J_{CP}$ = 2.6 Hz, C, Ar), 134.6 (d, $^{2}J_{CP}$ = 12.1 Hz, *o*-C, Ph), 133.3 (d, $^{2}J_{CP}$ = 5.0 Hz, CH, Ar), 132.3 (CH, Ar), 131.4 (d, $^{4}J_{CP}$ = 2.1 Hz, *p*-C, Ph), 129.0 (d, $^{1}J_{CP}$ = 51.9 Hz, *i*-C, Ph), 128.9 (d, $^{3}J_{CP}$ = 11.0 Hz, *m*-C, Ph), 126.1 (CH, Ar), 125.0 (CH, Ar), 123.4, 122.9 (C5, dbbpy), 119.9, 119.1 (C3, dbbpy), 46.5 (CH_2), 35.5, 35.4 (*C*Me_3), 30.2, 30.1 (C*Me*$_3$), 25.8 (N*Me*).

[Pd{κ²*C*,*N*-$C_6H_4CH_2C(O)NH$-2}(tmeda)] (4a). To a solution of **1a** (107 mg, 0.22 mmol) in HO^{t}Bu (10 mL) were added KO^{t}Bu (50 mg, 0.45 mmol) and CH_2Cl_2 (2 mL) and the mixture was stirred for 2 h. The resulting suspension was filtered through Celite and the solvent was removed under reduced pressure. The residue was extracted with CH_2Cl_2 (20 mL) and filtered through Celite. Partial evaporation of the filtrate (1 mL) and slow addition of *n*-pentane (15 mL) led to the formation of a colorless precipitate, which was filtered off, washed with *n*-pentane (3 × 3 mL) and vacuum-dried to give **4a**·H_2O. Yield: 58 mg, 74%. Anal. Calcd for $C_{14}H_{25}N_3O_2Pd$: C, 44.99; H, 6.74; N, 11.24. Found: C, 44.95; H, 6.87; N, 11.17. Mp: 185-190 °C. IR (Nujol, cm^{-1}): ν(NH), 3385, 3269; ν(CO), 1577. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.23-7.19 (m, 1H, Ar), 6.96-6.92 (m, 1 H, Ar), 6.92-6.86 (m, 2 H, Ar), 3.85 (br, 1 H, NH), 3.72 (s, 2 H, CH_2, acetamide), 2.79-2.74 (m, 2 H, CH_2, tmeda), 2.66 (s, 6 H, Me, tmeda), 2.60 (m, 2 H, CH_2, tmeda), 2.56 (s, 6 H, Me, tmeda), 1.83 (s, 2 H, H_2O). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$): δ 179.0 (CO), 148.5 (C, Ar), 143.2 (C, Ar), 132.2 (CH, Ar), 126.0 (CH, Ar), 124.3 (CH, Ar), 123.7 (CH, Ar), 63.1 (CH_2, tmeda), 58.0 (CH_2, tmeda), 50.5 (Me, tmeda), 50.2 (CH_2, acetamide), 48.0 (Me, tmeda).

[Pd{κ²*C*,*N*-$C_6H_4CH_2C(O)NMe$-2}(N^N)] [(N^N = tmeda (4b), dbbpy (4b'))]. To a suspension of complex **1** (**1b**, 286 mg, 0.57 mmol; **1b'**, 81 mg, 0.12 mmol) in HO^{t}Bu (5 mL) was added KO^{t}Bu (97 mg, 0.86 mmol; 23 mg, 0.20 mmol, respectively) and the mixture was stirred for 1 h. The solvent was removed under reduced pressure and the residue was treated with CH_2Cl_2 (15 mL). The suspension was filtered through Celite and the filtrate was concentrated (1 mL). The addition of *n*-hexane (20 mL) led to a suspension, which was filtrated and the solid washed with *n*-hexane (3 × 3 mL) and vacuum-dried to give **4b**·$0.5H_2O$ or **4b'**·$0.5CH_2Cl_2$.

4b·$0.5H_2O$. Pale yellow solid. Yield: 146 mg, 69%. Anal. Calcd for $C_{15}H_{26}N_3O_{1.5}Pd$: C, 47.56; H, 6.92; N, 11.09. Found: C, 47.54; H, 7.09; N, 10.84. Mp: 170-180 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1580. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.15 (dd, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 6.8 Hz, 1 H, Ar), 6.94 (m, 1 H, Ar), 6.89-6.80 (m, 2 H, Ar), 4.39, 3.25 (AB system, $^{2}J_{HH}$ = 14.0 Hz, 2 H, CH_2), 2.80 (s, 3 H, NMe), 2.74 (s, 3 H, Me, tmeda), 2.78-2.69 (m, 1 H, CH_2, tmeda), 2.64 (s, 3

H, Me, tmeda), 2.62 (s, 3 H, Me, tmeda), 2.68-2.52 (m, 3 H, CH_2, tmeda), 2.31 (s, 3 H, Me, tmeda), 2.0 (s, 2 H, H_2O). $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ 176.5 (CO), 150.6 (C, Ar), 143.9 (C, Ar), 132.1 (CH, Ar), 125.6 (CH, Ar), 123.7 (CH, Ar), 123.4 (CH, Ar), 62.4 (CH_2, tmeda), 58.5 (CH_2, tmeda), 51.80 (Me, tmeda), 51.75 (CH_2), 49.3 (Me, tmeda), 49.1 (Me, tmeda), 48.5 (Me, tmeda), 36.9 (NMe).

4b'·0.5CH_2Cl_2. Bright yellow solid. Yield: 56 mg, 87%. Anal. Calcd for $C_{27.5}H_{34}ClN_3OPd$: C, 58.52; H, 6.07; N, 7.44. Found: C, 58.29; H, 6.30; N, 7.49. Mp: 240-250 °C. IR (Nujol, cm^{-1}): ν(CO), 1578. ^1H NMR (300.1 MHz, $CDCl_3$): δ 8.72 (d, $^3J_{HH}$ = 5.7 Hz, 1 H, H6, dbbpy), 8.71 (d, $^3J_{HH}$ = 6.0 Hz, 1 H, H6, dbbpy), 8.03 (d, $^4J_{HH}$ = 1.5 Hz, 1 H, H3, dbbpy), 8.01 (d, $^4J_{HH}$ = 1.5 Hz, 1 H, H3, dbbpy), 7.57 (dd, $^4J_{HH}$ = 1.5 Hz, $^3J_{HH}$ = 5.7 Hz, 1 H, H5, dbbpy), 7.42 (dd, $^4J_{HH}$ = 1.5 Hz, $^3J_{HH}$ = 6.0 Hz, 1 H, H5, dbbpy), 7.24 (m, 1 H, Ar), 7.00 (m, 3 H, Ar), 5.30 (s, 1 H, CH_2Cl_2), 3.90 (br s, 2 H, CH_2), 3.08 (s, 3 H, NMe), 1.46 (s, 9 H, ^{t}Bu), 1.43 (s, 9 H, ^{t}Bu). $^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ 177.6 (CO), 163.9, 163.4 (C4, dbbpy), 156.0 (C2, dbbpy), 154.6 (C, Ar), 153.7 (C2, dbbpy), 151.6, 150.1 (C6, dbbpy), 145.1 (C, Ar), 134.4 (CH, Ar), 125.2 (CH, Ar), 124.7 (CH, Ar), 123.55 (C5, dbbpy + CH, Ar), 123.36 (C5, dbbpy), 118.5, 118.0 (C3, dbbpy), 53.4 (CH_2Cl_2), 51.1 (CH_2), 37.9 (NMe), 35.54, 35.46 (*C*Me_3), 30.37, 30.26 (C*Me*$_3$).

[Pd{$C_6H_4CH_2C(O)NHMe$-2}{$CH(CN)_2$}(dbbpy)] (5b'). To a solution of **4b'** (95.6 mg, 0.183 mmol) in CH_2Cl_2 (10 mL) was added malononitrile (12.2 mg, 0.185 mmol) and the mixture was stirred for 1 h. The resulting colorless solution was concentrated (1 mL) and *n*-pentane (30 mL) was slowly added, whereupon a colorless solid precipitated, which was filtered off, washed with *n*-pentane (3 × 5 mL) and vacuum-dried to give **5b'**·0.25H_2O. Yield: 87 mg, 81%. Anal. Calcd for $C_{30}H_{35.5}N_5O_{1.25}Pd$: C, 60.81; H, 6.04; N, 11.82. Found: C, 60.67; H, 6.19; N, 11.93. Mp: 169-172 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3371; ν(CN), 2213, 2206; ν(CO), 1674. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.89 (d, $^3J_{HH}$ = 5.6 Hz, 1 H, H6, dbbpy), 8.03 (d, $^4J_{HH}$ = 1.6 Hz, 1 H, H3, dbbpy), 7.98 (d, $^4J_{HH}$ = 1.6 Hz, 1 H, H3, dbbpy), 7.68 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 5.6 Hz, 1 H, H5, dbbpy), 7.53 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.46 (d, $^3J_{HH}$ = 5.6 Hz, 1 H, H6, dbbpy), 7.27 (m, 1 H, H5, dbbpy), 7.23 (dd, $^4J_{HH}$ = 2 Hz, $^3J_{HH}$ = 6.8 Hz, 1 H, Ar), 7.07 (m, 2 H, Ar), 5.96 (br c, $^3J_{HH}$ = 4.4 Hz, 1 H, NH), 4.03, 3.74 (AB system, $^2J_{AB}$ = 15.2 Hz, 2 H, CH_2), 2.71 (s, 1 H, $CH(CN)_2$), 2.55 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NMe), 1.64 (s, 0.5 H, H_2O), 1.46 (s, 9 H, ^{t}Bu), 1.38 (s, 9 H, ^{t}Bu). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 172.4 (CO), 164.2, 163.9 (C4, dbbpy), 155.9 (C, Ar), 155.3, 154.4 (C2, dbbpy), 150.5, 149.4 (C6, dbbpy), 139.2 (C, Ar), 135.4 (CH, Ar), 129.9 (CH, Ar), 126.3 (CH, Ar),

124.5 (CH, Ar), 124.3, 123.8 (C5, dbbpy), 121.1, 120.6 (CN), 118.5, 118.4 (C3, dbbpy), 47.1 (CH_2), 35.6, 35.5 (CMe_3), 30.3, 30.2 (CMe_3), 26.1 (NMe) ($CH(CN)_2$ not observed).

[Pd{C(O)C$_6$H$_4$CH$_2$C(O)NH$_2$-2}I(tmeda)] (6a). CO was bubbled through a stirred solution of **1a** (105 mg, 0.18 mmol) in CH_2Cl_2 (10 mL) at –17 °C for 30 min and the resulting solution was filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (1 mL) and addition of Et_2O (20 mL) led to the precipitation of a yellow solid, which was collected by filtration, washed with Et_2O (3 × 3 mL) and vacuum-dried to give **6a**. Yield: 80 mg, 72%. Anal. Calcd for $C_{15}H_{24}IN_3O_2Pd$: C, 35.21; H, 4.73; N, 8.21. Found: C, 35.08; H, 4.73; N, 7.83. Mp: 165 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3396, 3187; ν(CO), 1671, 1635. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 9.14 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.51 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.38 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.23 (dd, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H3, Ar), 6.34 (s, 1 H, NH), 5.19 (s, 1 H, NH), 3.76 (s, 2 H, CH_2, acetamide), 2.73 (m, 2 H, CH_2, tmeda), 2.60 (s, 3 H, Me, tmeda), 2.55 (m, 2 H, CH_2, tmeda), 2.47 (s, 3 H, Me, tmeda). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$): δ 173.3 (CO), 139.7 (CH, Ar), 138.4 (C, Ar), 131.4 (CH, Ar), 131.2 (CH, Ar), 130.7 (C, Ar), 127.0 (CH, Ar), 61.9 (CH_2, tmeda), 57.7 (CH_2, tmeda), 50.4 (Me, tmeda), 49.0 (Me, tmeda), 41.6 (CH_2) (Pd*C* not observed).

[Pd{C(O)C$_6$H$_4$CH$_2$C(O)NRR'-2}I(N^N)] (NRR' = NHMe, N^N = tmeda (6b), dbbpy (6b'); NRR' = NMe$_2$, N^N = tmeda (6c)]. CO was bubbled through a stirred solution of the appropriate complex **1** (**1b**,153 mg, 0.31 mmol; **1b'**, 119 mg, 0.18 mmol; **1c**, 81 mg, 0.16 mmol) in CH_2Cl_2 (5 mL) at –17 °C for 30 min. The addition of *n*-pentane (25 mL) led to the precipitation of a solid, which was collected by filtration, washed with *n*-pentane (5 × 3 mL) and vacuum-dried to give **6b**, **6b'**·0.25CH_2Cl_2 or **6c**.

6b: Yellow solid. Yield: 128 mg, 79%. Anal. Calcd for $C_{16}H_{26}IN_3O_2Pd$: C, 36.55; H, 4.99; N, 7.99. Found: C, 36.24; H, 4.74; N, 8.08. Mp: 110-115 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3327; ν(CO), 1638. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 9.12 (d, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.50 (t, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.37 (t, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.23 (d, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 6.33 (br, 1 H, NH), 3.77 (s, 2 H, CH_2, acetamide), 2.80-2.65 (m, 2 H, CH_2, tmeda), 2.70 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, acetamide), 2.60 (s, 6 H, Me, tmeda), 2.57-2.53 (m, 2 H, CH_2, tmeda), 2.47 (s, 6 H, Me, tmeda). ^{13}C{^{1}H} APT NMR (50.3 MHz, $CDCl_3$): δ 171.3 (CO), 139.6 (CH, Ar), 138.4 (C, Ar), 131.4 (CH, Ar), 131.1 (CH, Ar), 131.0 (C, Ar), 126.9 (CH, Ar), 61.9 (CH_2,

tmeda), 57.6 (CH_2, tmeda), 50.4 (Me, tmeda), 48.9 (Me, tmeda), 41.8 (CH_2, acetamide), 26.3 (Me, acetamide).

6b'·0.25CH_2Cl_2: Yellow solid. Yield: 149 mg, 87%. Anal. Calcd for $C_{28.25}H_{34.5}Cl_{0.5}IN_3O_2Pd$: C, 48.53; H, 4.97; N, 6.01. Found: C, 48.50; H, 5.03; N, 6.14. Mp: 175-179 °C. IR (Nujol, cm^{-1}): ν(NH), 3347; ν(CO), 1655. ^1H NMR (200 MHz, $CDCl_3$): δ 9.23 (d, $^3J_{HH}$ = 5.8 Hz, 1 H, H6, dbbpy), 8.84 (m, 1 H, Ar), 8.07 (d, $^3J_{HH}$ = 6.0 Hz, 1 H, H6, dbbpy), 8.02 (d, $^4J_{HH}$ = 1.8 Hz, 1 H, H3, dbbpy), 7.97 (d, $^4J_{HH}$ = 1.6 Hz, 1 H, H3, dbbpy), 7.49 (dd, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 5.8 Hz, 1 H, H5, dbbpy), 7.43 (dd, $^4J_{HH}$ = 2.0 Hz, $^3J_{HH}$ = 6.0 Hz, 1 H, H5, dbbpy), 7.35 (m, 3 H, Ar), 6.54 (br c, $^3J_{HH}$ = 5 Hz, 1 H, NH), 5.30 (s, 0.5 H, CH_2Cl_2), 3.89 (s, 2 H, CH_2), 2.75 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NMe), 1.42 (s, 9 H, ^{t}Bu), 1.41 (s, 9 H, ^{t}Bu). $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ 171.7 (CO), 163.8, 163.5 (C4, dbbpy), 155.1, 152.9 (C2, dbbpy), 152.0, 150.2 (C6, dbbpy), 141.1 (C, Ar), 136.8 (CH, Ar), 131.2 (CH, Ar), 130.9 (CH + C, Ar), 126.8 (CH, Ar), 124.1, 123.7 (C5, dbbpy), 118.7, 117.9 (C3, dbbpy), 41.6 (CH_2), 35.6, 35.4 (CMe_3), 30.4, 30.2 (CMe_3), 26.3 (NMe) (PdC and CH_2Cl_2 not observed).

6c: Yellow solid. Yield: 70 mg, 82%. Anal. Calcd for $C_{17}H_{28}IN_3O_2Pd$: C, 37.83; H, 5.23; N, 7.79. Found: C, 37.92; H, 5.21; N, 7.97. Mp: 110-115 °C. IR (Nujol, cm^{-1}): ν(CO), 1654, 1643. ^1H NMR (300.1 MHz, $CDCl_3$): δ 9.34 (d, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.50 (t, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.35 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.01 (d, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 3.90 (br s, 2 H, CH_2, acetamide), 3.15 (s, 3 H, Me, acetamide), 2.92 (s, 3 H, Me, acetamide), 2.69-2.65 (m, 2 H, CH_2, tmeda), 2.57 (s, 6 H, Me, tmeda), 2.54-2.48 (m, 2 H, CH_2, tmeda), 2.45 (s, 6 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (50.3 MHz, $CDCl_3$): δ 171.3 (CO), 141.0 (CH, Ar), 136.6 (C, Ar), 132.6 (C, Ar), 131.4 (CH, Ar), 130.9 (CH, Ar), 126.5 (CH, Ar), 62.1 (CH_2, tmeda), 57.7 (CH_2, tmeda), 50.5 (Me, tmeda), 48.7 (Me, tmeda), 39.5 (CH_2, acetamide), 37.7 (Me, acetamide), 35.4 (Me, acetamide).

Isoquinoline-1,3(*2H*,*4H*)-dione (7a). A solution of **2a** (105 mg, 0.21 mmol) in acetone (15 mL) was stirred under a CO atmosphere (1.4 bar) at room temperature for 3 h. A black precipitate of Pd gradually formed. The solvent was evaporated under vacuum, the residue was extracted with CH_2Cl_2 (6 × 5 mL), and the extracts were filtered through anhydrous $MgSO_4$. The filtrate was evaporated to dryness; the yellow residue was stirred in water (15 mL), collected by filtration and washed with water (5 × 3 mL). The crude product was recrystallized from ethanol to give **7a** as a pale yellow microcrystalline solid. Yield: 17 mg,

51%. Mp: 224-236 °C (lit 217,[14] 233-235 °C[15]). The ^{1}H NMR data are in agreement with those reported in the literature.[14,15]

2-Methylisoquinoline-1,3(*2H,4H*)-dione (7b). A solution of **2b** (111 mg, 0.21 mmol) and NEt_3 (80 μL, 0.57 mmol) in acetone (15 mL) was stirred under a CO atmosphere (1.4 bar) at room temperature for 3 h. A black precipitate of Pd gradually formed. The solvent was evaporated under vacuum, the residue was extracted with CH_2Cl_2 (6 × 5 mL); the extracts were filtered through anhydrous $MgSO_4$. The yellow filtrate was evaporated to dryness and the residue was extracted with hexane (20 + 6 × 5 mL) and the extracts were filtered through anhydrous $MgSO_4$. The solvent was then removed under reduced pressure to give **7b** as a colorless solid. Yield: 25 mg, 67%. Mp: 120-122 °C (lit[16] 120-121 °C). The ^{1}H NMR data are in agreement with those reported in the literature.[16]

3-(Methylamino)-1*H*-2-benzopyran-1-one (8b). A solution of **2b** (81 mg, 0.16 mmol) in acetone (15 mL) was stirred under a CO atmosphere (1.4 bar) for 2.5 h. A black precipitate of Pd gradually formed. The solvent was evaporated under vacuum, the residue was extracted with Et_2O (6 × 5 mL), and the combined extracts were filtered through Celite. The filtrate was washed with a saturated aqueous solution of K_2CO_3 (3 × 5 mL), dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to give **8b** as a bright yellow solid. Yield: 16 mg, 59%. Mp: 116-119 °C. IR (Nujol, cm^{-1}): ν(NH), 3303; ν(COO), 1719, 1651. HRMS (ESI+, m/z): exact mass calcd for $C_{10}H_{10}NO_2$ $[M+H]^+$ requires 176.0706, found: 176.0711, error = 3.01 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.07 (ddd, $^5J_{HH}$ = 0.8 Hz, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 8.0 Hz, 1 H, H8), 7.51 (ddd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 8.0 Hz, 1 H, H6), 7.18 (br d, $^3J_{HH}$ = 8.0 Hz, 1 H, H5), 7.12 (ddd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 8.0 Hz, 1 H, H7), 5.19 (s, 1 H, H4), 4.24 (br s, 1 H, NH), 2.86 (d, $^3J_{HH}$ = 5.2 Hz, 3 H, Me). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$): δ 161.9 (CO), 156.8 (C3), 141.8 (C4a), 134.9 (C6), 129.6 (C8), 123.4 (C5), 123.2 (C7), 115.4 (C8a), 76.0 (C4), 28.8 (Me).

3-(Dimethylamino)-1*H*-2-benzopyran-1-one (8c). A solution of **1c** (61 mg, 0.12 mmol) in $CHCl_3$ (20 mL) was stirred under a CO atmosphere (1.4 bar) at 50 °C for 3 d. A black precipitate of Pd gradually formed. The solvent was evaporated under vacuum, the residue was extracted with Et_2O (6 × 5 mL), and the extracts were filtered through Celite. Compound **8c** was obtained as a bright yellow solid after evaporation of the solvent under vacuum. Yield: 23 mg, 93%. Mp: 67-71 °C. IR (Nujol, cm^{-1}): ν(COO), 1752, 1734. HRMS (ESI+, m/z): exact mass calcd for $C_{11}H_{12}NO_2$ $[M+H]^+$ requires 190.0863, found 190.0874,

error = 5.99 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.06 (m, 1 H, H8), 7.47 (ddd, $^{4}J_{HH}$ = 1.2 Hz, $^{3}J_{HH}$ = 7.2 Hz, $^{3}J_{HH}$ = 8.4 Hz, 1 H, H6), 7.14 (br d, $^{3}J_{HH}$ = 8.4 Hz, 1 H, H5), 7.08 (ddd, $^{4}J_{HH}$ = 1.2 Hz, $^{3}J_{HH}$ = 7.2 Hz, $^{3}J_{HH}$ = 8.4 Hz, 1 H, H7), 5.21 (s, 1 H, H4), 2.99 (s, 6 H, Me). $^{13}C\{^{1}H\}$ NMR (100.8 MHz, $CDCl_3$): δ 161.9 (CO), 157.0 (C3), 142.1 (C4a), 134.7 (C6), 129.6 (C8), 123.4 (C5), 122.9 (C7), 114.5 (C8a), 77.8 (C4), 37.7 (Me).

***N*,3,3-Trimethyl-1-oxo-3,4-dihydro-1*H*-2-benzopyrane-4-carboxamide (9).** A solution of **2b'** (103 mg, 0.15 mmol) in acetone (15 mL) was stirred under a CO atmosphere (1.4 bar) for 90 min. The resulting black suspension was filtered through Celite and the filtrate was concentrated to dryness. The residue was dissolved in CH_2Cl_2 (15 mL), Et_3N (42 μL, 0.30 mmol) was added and the solution was stirred for 1 h. Partial evaporation of the solvent (2 mL) and addition of Et_2O (20 mL) led to the precipitation of a colorless solid, which was filtered off, washed with Et_2O (3 × 3 mL) and vacuum-dried to give **9**. Yield: 24 mg, 67%. Mp: 243-244 °C. IR (Nujol, cm^{-1}): ν(NH), 3306; ν(CO), 1710, 1642. HRMS (ESI+, m/z): exact mass calcd for $C_{13}H_{16}NO_3$ $[M+H]^+$ requires 234.1125, found 234.1126, error = 0.54 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.17 (d, $^{3}J_{HH}$ = 7.6 Hz, 1 H, H8), 7.61 (t, $^{3}J_{HH}$ = 7.6 Hz, 1 H, H6), 7.48 (t, $^{3}J_{HH}$ = 7.6 Hz, 1 H, H7), 7.33 (d, $^{3}J_{HH}$ = 7.6 Hz, 1 H, H5), 5.56 (br s, 1 H, NH), 3.72 (s, 1 H, H4), 2.79 (d, $^{3}J_{HH}$ = 4.8 Hz, 3 H, NMe), 1.60 (s, 3 H, Me_2C), 1.44 (s, 3 H, Me_2C). $^{13}C\{^{1}H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 169.4 (CO, acetamide), 164.3 (C1), 136.9 (C4a), 134.5 (C6), 130.6 (C8), 128.8 (C7), 128.2 (C5), 124.2 (C8a), 81.5 (C3), 55.5 (C4), 28.0 (*Me*$_2$C), 26.7 (NMe), 25.8 (*Me*$_2$C).

[Pd{C(=NXy)C$_6$H$_4$CH$_2$C(O)NHMe-2}I(dbbpy)] (10b'). To a solution of **1b'** (114 mg, 0.18 mmol) in CH_2Cl_2 (7 mL) was added XyNC (23 mg, 0.18 mmol); the mixture was stirred for 1 h and concentrated under reduced pressure (2 mL). *n*-Pentane (30 mL) was then added to precipitate a yellow solid, which was collected by filtration, washed with *n*-pentane (3 × 3 mL) and vacuum-dried to give **10b'**·0.25CH_2Cl_2. Yield: 110 mg, 78%. Anal. Calcd for $C_{36.25}H_{43.5}Cl_{0.5}IN_4OPd$: C, 54.27; H, 5.47; N, 6.98. Found: C, 54.01; H, 5.18; N, 7.17. Mp: 155-158 °C. IR (Nujol, cm^{-1}): ν(C=N), 1567; ν(CO), 1665. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 9.34 (d, $^{3}J_{HH}$ = 6.0 Hz, 1 H, H6, dbbpy), 9.00 (dd, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.96 (d, $^{3}J_{HH}$ = 6.0 Hz, 1 H, H6, dbbpy), 7.93 (overlapped broad signal, 1 H, NH), 7.91 (d, $^{4}J_{HH}$ = 1.6 Hz, 1 H, H3, dbbpy), 7.87 (d, $^{4}J_{HH}$ = 1.6 Hz, 1 H, H3, dbbpy), 7.46 (dd, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.40 (dd, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 5.6 Hz, 1 H, H5, dbbpy), 7.31-7.38 (m, 3 H, H5 dbbpy + Ar), 6.99-6.90 (m, 3 H, Xy), 5.30 (s, 0.5 H, CH_2Cl_2), 4.00 (br, 2 H, CH_2), 2.60 (d, $^{3}J_{HH}$ = 4.8 Hz, 3 H, NMe), 2.23 (s, 6 H, Me, Xy), 1.38, 1.37 (both s, 9 H each, ^{t}Bu). $^{13}C\{^{1}H\}$ NMR (100.8

MHz, $CDCl_3$): δ 184.0 (C=N), 172.2 (CO), 163.6, 163.2 (C4, dbbpy), 155.4, 152.9 (C2, dbbpy), 152.9 (C6, dbbpy), 149.7 (*i*-C, Xy), 149.6 (C6, dbbpy), 140.0 (C, Ar), 136.7 (CH, Ar), 131.8 (C, Ar), 130.2 (CH, Ar), 128.5 (CH, Ar), 128.0 (CH, Xy), 126.5 (CH, Ar), 123.8, 123.5 (C5, dbbpy), 123.3 (CH, Xy), 118.6, 117.8 (C3, dbbpy), 41.7 (CH_2), 35.5, 35.4 (*C*Me_3), 30.3, 30.2 (C*Me*$_3$), 26.0 (N*Me*), 20.7 (Me, Xy) (*o*-C of Xy and CH_2Cl_2 not observed).

1-(2,6-Dimethylphenylimino)-1,2-dihydroisoquinolin-3(4*H*)-one (11a). To a solution of **1a** (183 mg, 0.38 mmol) in CH_2Cl_2 (25 mL) was added XyNC (49.6 mg, 0.38 mmol). The mixture was stirred for 30 min, concentrated under reduced pressure (10 mL) and then stirred for 24 h, whereupon a black suspension formed. The solvent was removed under vacuum, the residue was extracted with Et_2O (10 × 5 mL), and the combined extracts were filtered through anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure led to the precipitation of **11a** as a colorless solid. Yield: 59 mg, 58%. Mp: 149-151 °C. IR (Nujol, cm^{-1}): ν(N-H), 3360; ν(CO), 1694; ν(C=N), 1645. HRMS (ESI+, m/z): exact mass calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$ requires 265.1335, found 265.1333, error = 0.75 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.52 (dd, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H8), 7.63 (br, 1 H, NH), 7.55 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.46 (br t, $^3J_{HH}$ = 7.6 Hz, 1 H, H7), 7.28 (br d, $^3J_{HH}$ = 7.6 Hz, 1 H, H5), 7.09 (br d, $^3J_{HH}$ = 7.6 Hz, 2 H, *m*-H, Xy), 6.97 (br t, $^3J_{HH}$ = 7.6 Hz, 1 H, *p*-H, Xy), 3.97 (s, 2 H, H4), 2.08 (s, 6 H, Me, Xy). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$): δ 168.4 (CO), 145.0 (C=N), 143.6 (*i*-C, Xy), 133.0 (C4a), 132.0 (C6), 128.6 (*m*-C, Xy), 127.7 (*o*-C, Xy), 127.65 (C5), 127.60 (C7), 127.1 (C8), 125.8 (C8a), 124.2 (*p*-C, Xy), 35.8 (C4), 17.9 (Me, Xy).

1-(2,6-Dimethylphenylimino)-2-methyl-1,2-dihydroisoquinolin-3(4*H*)-one (11b). To a solution of **1b** (198 mg, 0.40 mmol) in $CHCl_3$ (20 mL) was added XyNC (52 mg, 0.40 mmol); the mixture was refluxed for 3 h and then stirred at room temperature for 60 h. The resulting black suspension was worked up as described for **11a** to give **11b** as a pale yellow solid. Yield: 89 mg, 80 %. Mp: 108-112 °C. IR (Nujol, cm^{-1}): ν(CO), 1697; ν(C=N), 1644. HRMS (ESI+, m/z): exact mass calcd for $C_{18}H_{19}NO_2$ $[M+H]^+$ requires 279.1492, found 279.1487, error = 1.79 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.35 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.23 (br d, $^3J_{HH}$ = 7.6 Hz, 1 H, H5), 7.17 (br, 1 H, H8), 7.05 (br d, $^3J_{HH}$ = 7.6 Hz, 2 H, *m*-H, Xy), 6.99 (br t, $^3J_{HH}$ = 4.8 Hz, H7), 6.90 (br t, $^3J_{HH}$ = 7.6 Hz, 1 H, *p*-H, Xy), 3.93 (s, 2 H, H4), 3.50 (s, 3 H, NMe), 2.00 (s, 6 H, Me, Xy). ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ 169.0 (CO), 147.8 (C=N), 146.2 (*i*-C, Xy), 132.2 (C4a) 131.1 (C6), 128.4 (*m*-C, Xy), 127.7

(C5), 127.0 (C7), 126.7 (C8), 126.2 (br, C8a), 125.2 (*o*-C, Xy), 122.6 (*p*-C, Xy), 37.4 (C4), 29.6 (NMe), 18.2 (Me, Xy).

1-(2,6-Dimethylphenylimino)-3-(*N*,*N*-dimethylamino)-1*H*-2-benzopyran (12c). To a solution of **1c** (91 mg, 0.17 mmol) in $CHCl_3$ (15 mL) was added XyNC (23 mg, 0.17 mmol) and the mixture was stirred at 60 °C for 24 h. Gradual formation of colloidal Pd was observed. The solvent was removed under vacuum, the residue was extracted with Et_2O (6 × 5 mL), and the combined extracts were filtered through anhydrous $MgSO_4$. Compound **12c** was isolated as a yellow oil after evaporation of the solvent under reduced pressure. Yield: 51 mg, 98%. IR (Nujol, cm^{-1}): ν(C=N), 1673, 1623. HRMS (ESI+, m/z): exact mass calcd for $C_{19}H_{21}N_2O$ $[M+H]^+$ requires 293.1648, found 293.1652, error = 1.09 ppm.^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.26 (d, $^3J_{HH}$ = 7.6 Hz, 1 H, H8), 7.38 (ddd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.10-7.06 (m, 2 H, H7 + H5), 7.03 (br d, $^3J_{HH}$ = 7.6 Hz, 2 H, *m*-H, Xy), 6.87 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, *p*-H, Xy), 4.94 (s, 1 H, H4), 2.60 (s, 6 H, NMe_2), 2.14 (s, 6 H, Me, Xy). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 155.6 (C3), 148.8 (C=N), 145.4 (*i*-C, Xy), 138.2 (C4a), 132.4 (C6), 128.1 (*o*-C, Xy), 127.4 (*m*-C, Xy), 127.3 (C8), 123.1 (C7), 122.9 (C5), 122.4 (*p*-C, Xy), 117.8 (C8a), 76.0 (C4), 37.1 (NMe_2), 18.2 (Me, Xy).

***trans*-[Pd{C(=NXy)C$_6$H$_4$CH$_2$C(O)NH$_2$-2}I(CNXy)$_2$] (13a).** To a solution of **1a** (93 mg, 0.19 mmol) in CH_2Cl_2 (20 mL) was added XyNC (78 mg, 0.59 mmol). The mixture was stirred at room temperature for 30 min and concentrated under reduced pressure (3 mL). The addition of *n*-pentane (15 mL) led to the precipitation of a yellow solid, which was filtered off, washed with *n*-pentane (3 × 3 mL) and vacuum-dried to give **13a**·H_2O. Yield: 134 mg, 92%. Anal. Calcd for $C_{35}H_{37}IN_4O_2Pd$: C, 53.96; H, 4.79; N, 7.19. Found: C, 53.84; H, 4.59; N, 7.25. Mp: 122-127 °C (dec). IR (Nujol, cm^{-1}): ν(C≡N), 2180; ν(CO), 1687; ν(C=N), 1586. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.24 (d, $^3J_{HH}$ = 8.0 Hz, 1 H, Ar), 7.72 (br, 1 H, NH), 7.46 (m, 2 H, Ar), 7.35 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.23 (t, $^3J_{HH}$ = 7.6 Hz, 2 H, *p*-H, XyNC^c), 7.08 (d, $^3J_{HH}$ = 7.6 Hz, 4 H, *m*-H, XyNC^c), 6.96 (s, 3 H, XyNC^i), 5.07 (br, 1 H, NH), 3.88 (s, 2 H, CH_2), 2.22 (s, 12 H, Me, XyNC^c), 2.21 (s, 6 H, Me, XyNC^i), 1.66 (br s, 2 H, H_2O). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 183.6 (*C*=N), 173.7 (CO), 149.3 (*i*-C, XyNC^i), 144.6 (C, Ar), 135.7 (*o*-C, XyNC^c), 132.7 (CH, Ar), 130.7 (CH, Ar), 130.2 (CH, XyNC^c), 130.0 (C, Ar), 129.0 (CH, Ar), 128.4 (CH, XyNC^i), 128.1 (CH, XyNC^c), 127.3 (*o*-C, XyNC^i), 127.1 (CH, Ar), 124.2 (CH, XyNC^i), 41.6 (CH_2), 19.2 (Me, XyNC^i), 18.7 (Me, XyNC^c); C≡N and *i*-C of XyNC^c not observed.

***trans*-[Pd{C(=NXy)C$_6$H$_4$CH$_2$C(O)NHMe-2}I(CNXy)$_2$] (13b).** To a solution of **1b'** (82 mg, 0.13 mmol) in CH_2Cl_2 (2 mL) was added XyNC (67 mg, 0.51 mmol) and the mixture was stirred at –17 °C for 30 min. *N*-hexane (30 mL) was then added to precipitate a yellow solid, which was collected by filtration, washed with *n*-hexane (3 × 3 mL) and vacuum-dried to give **13b**·H_2O. Yield: 93 mg, 95%. Anal. Calcd for $C_{36}H_{39}IN_4O_2Pd$: C, 54.52; H, 4.96; N, 7.06. Found: C, 54.31; H, 4.65; N, 7.01. Mp: 128-129 °C. IR (Nujol, cm^{-1}): ν(C≡N), 2180; ν(CO), 1661; ν(C=N), 1584. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.27 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.74 (br c, 1 H, NH), 7.49 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 8.0 Hz, 1 H, Ar), 7.44 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.34 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.23 (t, $^3J_{HH}$ = 7.6 Hz, 2 H, *p*-H, XyNC^c), 7.07 (d, $^3J_{HH}$ = 7.6 Hz, 4 H, *m*-H, XyNC^c), 6.97 (s, 3 H, XyNC^i), 3.88 (s, 2 H, CH_2), 2.59 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NMe), 2.22 (s, 18 H, Me, Xy), 1.58 (br s, 2 H, H_2O). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$): δ 183.5 (*C*=N), 172.0 (CO), 149.3 (*i*-C, XyNC^i), 144.5 (C, Ar), 135.7 (*o*-C, XyNC^c), 132.9 (CH, Ar), 130.7 (CH, Ar), 130.6 (C, Ar), 130.2 (CH, XyNC^c), 129.0 (CH, Ar), 128.4 (CH, XyNC^i), 128.1 (CH, XyNC^c), 127.4 (*o*-C, XyNC^i), 126.9 (CH, Ar), 124.2 (CH, XyNC^i), 41.6 (CH_2), 26.0 (NMe), 19.2 (Me, XyNC^i), 18.7 (Me, XyNC^c); *C*≡N and *i*-C of XyNC^c not observed.

***trans*-[Pd{C(=NHXy)C$_6$H$_4$CH$_2$C(O)NH$_2$)-2}I(CNXy)$_2$]TfO (14a).** To a solution of **13a** (159.2 mg, 0.21 mmol) in CH_2Cl_2 (15 mL) was added HTfO (18.3 μL, 0.21 mmol) and the mixture was stirred for 1 h. The resulting solution was concentrated under reduced pressure (1 mL) and Et_2O (30 mL) was added to precipitate a yellow solid, which was filtered off, washed with Et_2O (3 × 3 mL) and vacuum-dried to give **14a**. Yield: 173.0 mg, 91%. Anal. Calcd for $C_{36}H_{36}F_3IN_4O_4PdS$: C, 47.46; H, 3.98; N, 6.15; S, 3.52. Found: C, 47.73; H, 3.82; N, 6.18; S, 3.48. Mp: 143-145 °C (dec). IR (Nujol, cm^{-1}): ν(C≡N), 2199; ν(CO), 1650; ν(C=N), 1588. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 16.36 (br, 1 H, NH, iminium), 9.03 (br, 1 H, NH, acetamide), 8.36 (dd, $^4J_{HH}$ = 2.1 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.95 (dd, $^4J_{HH}$ = 2.1 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.65 (m, 2 H, Ar), 7.31 (t, $^3J_{HH}$ = 7.5 Hz, 3 H, *p*-H, Xy), 7.13 (d, $^3J_{HH}$ = 7.5 Hz, 6 H, *m*-H, Xy), 6.04 (br, NH, acetamide), 4.06 (s, 2 H, CH_2), 2.35 (s, 6 H, Me, Xy, iminium), 2.19 (s, 12 H, Me, XyNC^c). ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ 176.5 (CO), 142.1 (C, Ar), 139.7 (*i*-C, Xy, iminium), 136.0 (*o*-C, XyNC^c), 134.5 (CH, Ar), 133.9 (CH, Ar), 133.1 (CH, Ar), 132.8 (*o*-C, Xy, iminium), 131.3 (CH, XyNC^c), 130.0 (C, Ar), 129.7 (CH, Ar), 129.4 (CH, Xy, iminium), 128.5 (CH, XyNC^c), 39.2 (CH_2), 18.9 (Me, Xy, iminium), 18.6 (Me, XyNC^c); *C*=N, C≡N and *i*-C of XyNC^c not observed.

[Pd{C(=NXy)C$_6$H$_4$CH$_2$C(O)NRR'-2}(CNXy)(tmeda)]TfO [NRR' = NHMe (15b), NMe$_2$ (15c). To a solution of the appropriate complex **2** (**2b**, 125 mg, 0.24 mmol; **2c**, 105 mg, 0.20 mmol) in CH_2Cl_2 (15 mL) was added XyNC (for **15b**, 63 mg, 0.48 mmol; for **15c**, 51 mg, 0.39 mmol) and the resulting yellow solution was stirred for 2.5 h, filtered through Celite and concentrated under reduced pressure (2 mL). The addition of Et_2O (25 mL) led to the precipitation of a solid, which was filtered off, washed with Et_2O (5 × 3 mL) and vacuum-dried to give **15b**·0.5H_2O or **15c**.

15b·0.5H_2O: Yellow solid. Yield: 126 mg, 66%. Anal. Calcd for $C_{34}H_{45}F_3N_5O_{4.5}PdS$: C, 51.61; H, 5.73; N, 8.85; S, 4.05. Found: C, 51.51; H, 5.76; N, 8.86; S, 3.85. Mp: 103-104 °C . IR (Nujol, cm^{-1}): ν(NH), 3327; ν(C≡N), 2182; ν(CO), 1662; ν(C=N), 1583. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 8.20 (d, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.59-7.39 (m, 4 H, Ar + NH), 7.32 (t, $^3J_{HH}$ = 7.5 Hz, 1 H, *p*-H, XyNC^c), 7.14 (d, $^3J_{HH}$ = 7.5 Hz, 1 H, *m*-H, XyNC^c), 7.04-6.90 (m, 3 H, XyNC^i), 3.81 (br, 2 H, CH_2, acetamide), 2.80 (br, 4 H, CH_2, tmeda), 2.59 (d, $^3J_{HH}$ = 4.5 Hz, 3 H, NMe, acetamide), 2.42 (br s, 12 H, Me, tmeda), 2.17 (br s, 12 H, Me, XyNC), 1.84 (br s, 1 H, H_2O). ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ 180.4 (C=N), 171.3 (CO), 149.5 (*i*-C, XyNC^i), 138.2 (C, Ar), 135.3 (*o*-C, XyNC^c), 132.2 (CH, Ar), 131.9 (C, Ar), 131.0 (CH, Ar), 130.9 (CH, XyNC^c), 130.0 (CH, Ar), 128.5 (CH, XyNC^{c+i}), 127.5 (CH, Ar), 124.5 (CH, XyNC^i), 60.9 (CH_2, tmeda), 49.5 (Me, tmeda), 41.4 (CH_2, acetamide), 26.1 (NMe, acetamide), 19.8 (Me, XyNC^i), 18.6 (Me, XyNC^c); *C*≡N and *i*-C of XyNC^c and *o*-C of XyNC^i not observed.

15c: Yellow solid. Yield: 137 mg, 88%. Anal. Calcd for $C_{35}H_{46}F_3N_5O_4PdS$: C, 52.79; H, 5.82; N, 8.80; S, 4.03. Found: C, 52.58; H, 5.61; N, 8.54; S, 3.53. Mp: 128 °C (dec). IR (Nujol, cm^{-1}): ν(C≡N), 2188; ν(CO), 1636; ν(C=N), 1585. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 8.43 (d, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.58 (t, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.41 (t, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.31-7.25 (m, 2 H, Ar + *p*-H, XyNC^c), 7.10 (d, $^3J_{HH}$ = 7.5 Hz, 1 H, *m*-H, XyNC^c), 6.95 (br, 3 H, XyNC^i), 4.12 (br, 2 H, CH_2, acetamide), 2.90 (s, 3 H, NMe_2, acetamide), 2.85 (s, 3 H, NMe_2, acetamide), 2.80 (br, 4 H, Me, tmeda), 2.47 (br, 12 H, Me, tmeda), 2.14, 2.11 (partly overlapped br s, 12 H, Me, XyNC^{c+i}). ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ 176.1 (*C*=N), 171.0 (CO), 148.7 (*i*-C, XyNC^i), 137.7 (C, Ar), 135.3 (*o*-C, XyNC^c), 133.6 (CH, Ar), 132.5 (C, Ar), 131.4 (CH, Ar), 130.6 (CH, XyNC^c), 129.5 (CH, Ar), 128.3 (CH, XyNC^c), 128.2 (CH, XyNC^i), 127.4 (CH, Ar), 126.2 (*o*-C, XyNC^i), 123.8 (CH, XyNC^i), 50.2 (Me, tmeda), 38.4 (CH_2, acetamide), 37.4 (NMe, acetamide), 35.3 (NMe, acetamide), 19.8 (Me, XyNC^i), 18.5 (Me, XyNC^c); CH_2 of tmeda and C≡N and *i*-C of XyNC^c not observed.

[Pd{C(=NXy)C$_6$H$_4$CH$_2$C(O)NHMe-2}(CNXy)(dbbpy)]TfO (15b'). To a solution of **2b'** (77 mg, 0.11 mmol) in CH_2Cl_2 (20 mL) was added XyNC (30 mg, 0.23 mmol) and the resulting solution was stirred for 2.5 h, filtered through Celite and concentrated (2 mL). The addition of *n*-pentane (25 mL) led to the precipitation of a yellow solid, which was filtered off, washed with *n*-pentane (5 × 3 mL) and vacuum-dried to give **15b'**·0.5H_2O. Yield: 91 mg, 85%. Anal. Calcd for $C_{46}H_{53}F_3N_5O_{4.5}PdS$: C, 58.56; H, 5.66; N, 7.42; S, 3.40. Found: C, 58.64; H, 5.91; N, 7.51; S, 3.29. Mp: 138 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3331; ν(C≡N), 2184; ν(CO), 1665; ν(C=N), 1585. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.77 (m, 1 H, Ar), 8.37 (br s, 1 H, dbbpy), 8.20 (d, $^4J_{HH}$ = 1.6 Hz, 2 H, H3, dbbpy), 8.12 (br s, 1 H, dbbpy) 7.72 (br s, 1 H, dbbpy), 7.50-7.46 (m, 1 H, Ar), 7.44-7.39 (m, 2 H, 1 H dbbpy + 2 H Ar), 7.34 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, *p*-H, XyNC^c), 7.17 (d, $^3J_{HH}$ = 7.6 Hz, 2 H, *m*-H, XyCN^c), 6.98-6.87 (m 4 H, XyNC^i + 1 H NH), 4.19 (br s, 2 H, CH_2), 2.67 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NMe), 2.25 (s, 6 H, Me, XyNC^c), 2.17-1.72 (br, 6 H, Me, XyNC^i), 1.67 (s, 1 H, H_2O), 1.42 (s, 18 H, ^{t}Bu). ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ 179.2 (*C*=N), 171.7 (CO), 166.3 (C4, dbbpy), 150.8 (C6, dbbpy), 149.2 (*i*-C, XyNC^i), 138.6 (C, Ar), 135.6 (*o*-C, XyNC^c), 134.7 (CH, Ar), 134.0 (C, Ar), 132.0 (CH, Ar), 130.8 (CH, Ar), 130.2 (CH, Ar), 128.4 (CH, XyNC^{c+i}), 127.4 (C5, dbbpy), 124.1 (CH, XyNC^i), 120.0 (C3, dbbpy), 41.9 (CH_2), 35.9 (*C*Me$_3$), 30.2 (C*Me*$_3$), 26.2 (NMe), 19.0 (br, Me, XyNC^i), 18.7 (Me, XyNC^c); C2 of dbbpy, *C*≡N and *i*-C of XyNC^c, and *o*-C of XyNC^i not observed.

Pd{κ^2*N*,*S*–SC(NC$_6$H$_3$(OMe)$_2$-1,4)(C$_6$H$_4$(CH$_2$C(O)NH$_2$)-2)}(tmeda)]TfO (16a). A mixture of the complex **2a** (72 mg, 0.14 mmol) and 2,4-dimethoxyphenyl isothiocyanate (92 mg, 0.45 mmol) in CH_2Cl_2 (25 ml) was stirred at room temperature for 9 hours and then filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (2 mL) and addition of Et_2O (15 mL) led to the precipitation of the complex **16a** as a yellow solid, which was filtered off, washed with Et_2O (3 × 3 mL) and vacuum-dried. Yield: 75 mg, 75%. Anal. Calcd for $C_{24}H_{33}F_3N_4O_6PdS_2$: C, 41.12; H, 4.74; N, 7.99; S, 9.15. Found: C, 40.95; H, 4.66; N, 7.91; S, 8.86. Mp: 150–151 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3393, 3177; ν(CO), 1683. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.38 (d, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.29 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.08 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.99 [m, 2 H, Ph], 6.86 (br s, 1 H, NH), 6.34-6.30 [m, 2 H, Ar + Ph], 5.43 (br s, 1 H, NH), 3.83 (s, 3 H, OMe), 3.82, 3.78 (AB system, $^2J_{HH}$ = 16.0 Hz, 2 H, CH_2), 3.70 (s, 3 H, OMe), 3.00–2.90 (m, 1 H, CH_2, tmeda), 2.93 (s, 3 H, Me, tmeda), 2.90–2.73 (m, 3 H, CH_2, tmeda), 2.81 (s, 3 H, Me, tmeda), 2.45 (s, 3 H, Me, tmeda), 2.44 (s, 3 H, Me, tmeda). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 202.4 (NCS),

172.4 (CO), 160.2 (*C*–OMe), 152.7 (*C*–OMe), 139.4 (C, Ar), 131.65 (CH, Ar), 131.61 (C, Ar), 130.4 (CH, Ar), 126.5 (CH, Ar), 126.0 (CH, Ph), 125.5 (CH, Ar), 120.7 (*C*–NCS), 104.6 (CH, Ph), 99.4 (CH, Ph), 62.0 (CH_2, tmeda), 61.4 (CH_2, tmeda), 55.44, 55.40 (OMe), 52.05, 51.90, 49.9, 49.2 (Me, tmeda), 39.1 (CH_2, acetamide).

Pd{κ^2*N*,*S*–SC(NC_6H_3(OMe)$_2$-1,4)(C_6H_4(CH_2C(O)NHMe)-2)}(tmeda)]TfO (16b). To a solution of **2b** (113 mg, 0.22 mmol) in CH_2Cl_2 (10 ml) was added 2,4-dimethoxyphenyl isothiocyanate (90 mg, 0.44 mmol) and the mixture was stirred at room temperature for 9 hours and then filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (1 mL) and addition of Et_2O (15 mL) led to the precipitation of the complex **16b**·0.5H_2O as a yellow solid, which was filtered off, washed with Et_2O (5 × 3 mL) and vacuum-dried. Yield: 133 mg, 86%. Anal. Calcd for $C_{25}H_{35}F_3N_4O_6PdS_2(H_2O)_{0.5}$: C, 41.47; H, 5.01; N, 7.74; S, 8.86. Found: C, 41.21; H, 4.93; N, 7.73; S, 9.01. Mp: 152–156 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3352; ν(CO), 1650. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 7.41 (d, $^3J_{HH}$ = 8.0 Hz, 1 H, Ar), 7.29-7.27 (m, 1 H, Ar), 7.10 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.04 (dd, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.95 (d, $^3J_{HH}$ = 8.8 Hz, 1 H, Ph), 6.71 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 6.34-6.29 (m, 2 H, Ph), 3.81 (s, 3 H, OMe), 3.72, 3.65 (AB system, $^2J_{HH}$ = 15.6 Hz, 2 H, CH_2), 3.70 (s, 3 H, OMe), 2.92 (br s, 4 H, CH_2, tmeda), 2.81 (s, 6 H, Me, tmeda), 2.80 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, acetamide), 2.45 (s, 6 H, Me, tmeda). ^{13}C{^{1}H} APT NMR (75.5 MHz, $CDCl_3$): δ 202.5 (NCS), 170.6 (CO), 160.2 (*C*–OMe), 152.5 (*C*–OMe), 139.5 (C, Ar), 131.7 (C, Ar), 131.3 (CH, Ar), 130.4 (CH, Ar), 126.5 (CH, Ar), 125.9 (CH, Ph), 125.7 (CH, Ar), 120.6 (*C*–NCS), 104.6 (CH, Ph), 99.3 (CH, Ph), 62.0 (CH_2, tmeda), 61.4 (CH_2, tmeda), 55.42 (OMe), 55.38 (OMe), 52.0 (Me, tmeda), 51.8 (Me, tmeda), 49.9 (Me, tmeda), 49.2 (Me, tmeda), 39.7 (CH_2, acetamide), 26.4 (Me, acetamide).

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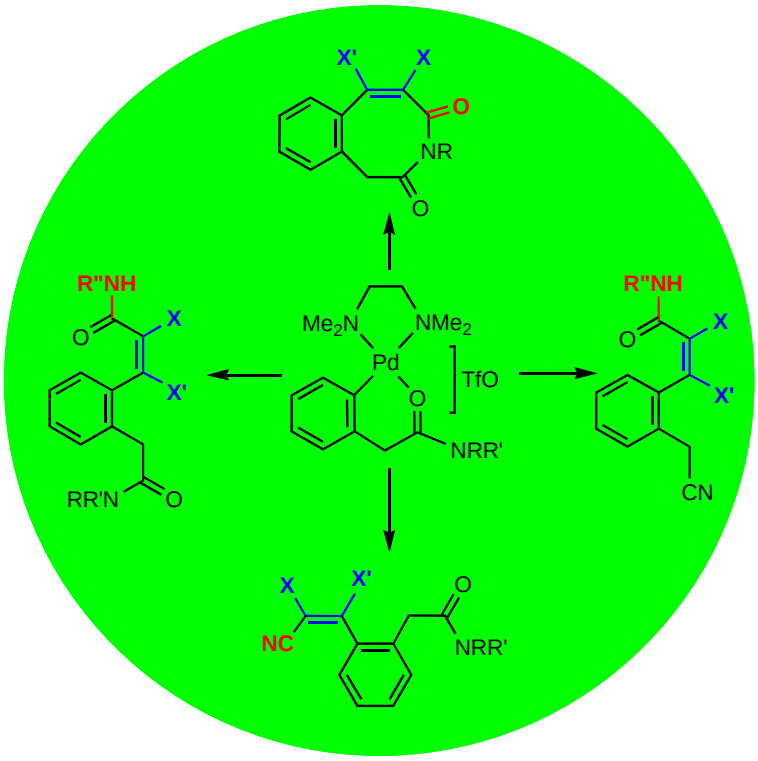
CHAPTER II

Sequential Insertion of Alkynes and CO or Isocyanides into the Pd–C Bond of Cyclopalladated Phenylacetamides. Synthesis of Eight-Membered Palladacycles, Benzo[*d*]azocine-2,4(1*H*,3*H*)-diones and Highly Functionalized Acrylonitrile and Acrylamide Derivatives



The results of this chapter have been published in:

R. Frutos-Pedreño, P. González-Herrero, J. Vicente, P. G. Jones, *Organometallics* **2012**, *31*, 3361–3372.

Abstract

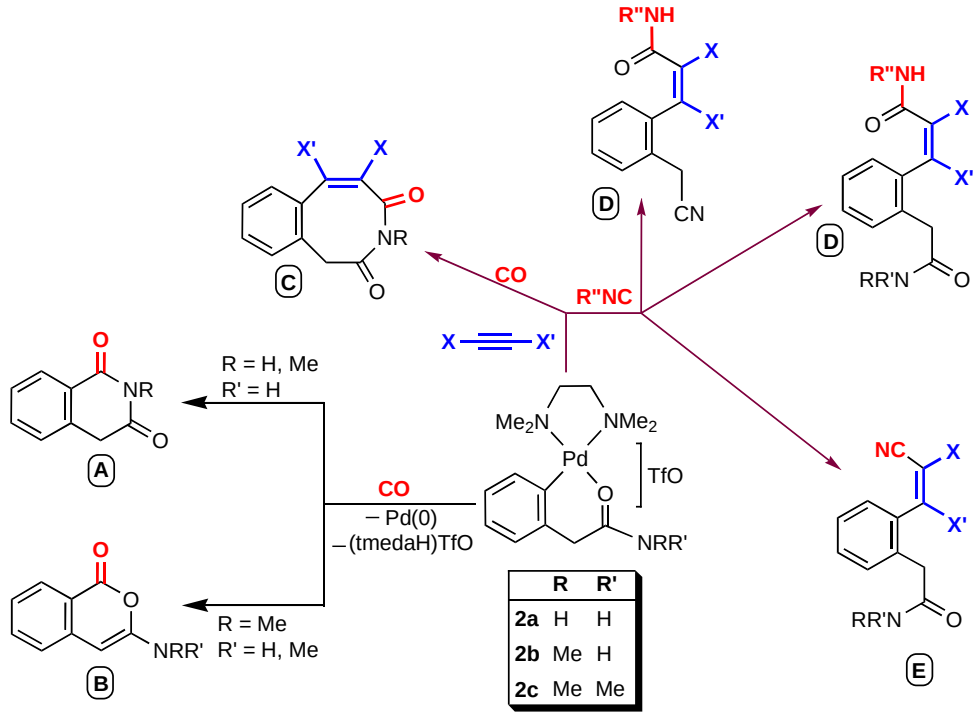
The cyclopalladated complexes [Pd{κ^2*C,O*-$C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO [R = R' = H (**2a**), R = Me, R' = H (**2b**), R = R' = Me (**2c**)] react with alkynes XC≡CX' in 1:3 molar ratio to give the eight-membered palladacycles [Pd{κ^2*C,O*-$C(X)=C(X')C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO [R = R' = H and X = X' = Ph (**18aa**), CO_2Me (**18ab**), Et (**18ac**) or X = Ph, X' = Me (**18ad**); R = Me, R' = H and X = X' = Ph (**18ba**), CO_2Me (**18bb**), Et (**18bc**) or X = Ph, X' = Me (**18bd**); R = R' = Me and X = X' = Ph (**18ca**)]. The treatment of complexes **18aa**, **18ac**, **18ad**, **18ba**, **18bc** and **18bd** with CO at 50 °C afford the corresponding benzo[*d*]azocine-2,4(1*H*,3*H*)-diones (**19**) that result from the insertion of a molecule of CO into the Pd–C bond and subsequent C–N reductive coupling and formation of (tmedaH)TfO. The reaction of **18ab** with CO in MeOH gives $(MeO_2C)_2C=C(CO_2Me)C_6H_4CH_2C(O)NH_2$-2 (**20**). Complexes **18aa** and **18ab** react with one equiv of R''NC 1:1 to give [Pd{$C(X)=C(X')C_6H_4CH_2C(O)NH_2$-2}(CNR'')(tmeda)]TfO [R'' = ^{t}Bu, X = X' = Ph (**21a**), CO_2Me (**21b**); R'' = Xy, X = X' = Ph (**21a'**), CO_2Me (**21b'**)]. While **18aa** reacts with one equiv of R''NC in refluxing $CHCl_3$ to give a low yield of the compound $XyHNC(O)C(Ph)=C(Ph)C_6H_4CH_2C(O)NH_2$-2 (**22a**) when R'' = Xy, the complex **18aa**, **18ba** or **18ca** affords the acrylonitrile derivative $NCC(Ph)=C(Ph)C_6H_4CH_2C(O)NRR'$-2 [R = R' = H (**23a**), R = Me, R' = H (**23b**), R = R' = Me (**23c**)] when R'' = ^{t}Bu; alternatively, the latter derivatives can be obtained by refluxing *in situ* generated solutions of the corresponding cyano-complexes [Pd{$C(Ph)=C(Ph)C_6H_4CH_2C(O)NRR'$-2}(CN)(tmeda)] in $CHCl_3$. The intermediate cyano-complex with R = R' = H (**24**) has been isolated and characterized. The reactions of **18aa**, **18ba**, **18ca** and **18ac** with four equiv of XyNC give $[Pd_3(CNXy)_6]$ and mixtures from which the compounds $XyNHC(O)C(Ph)=C(Ph)C_6H_4CH_2CN$-2 (**25**, from **18aa**), $XyNHC(O)C(Ph)=C(Ph)C_6H_4CH_2C(O)NRR'$-2 [R = Me, R' = H (**22b**), R = R' = Me (**22c**), from **18ba** or **18ca**, respectively] or [Pd{$C(=NXy)C(Et)=C(Et)C_6H_4CH_2CN$-2}$Cl(CNXy)_2$] (**26**, from **18ac**) can be isolated. The crystal structures of **18aa**·$2Et_2O$, **19aa**, **19ac**, **24**, **25** and **26** have been determined.

Introduction

Palladacycles constitute an extraordinarily important class of organometallic compounds because of their participation in numerous palladium-mediated organic transformations.[1] The Pd–C bond in these compounds shows a rich reactivity toward unsaturated molecules that has been widely exploited for both stoichiometric and catalytic syntheses. In particular, the insertion of alkynes has been used for the synthesis of enlarged palladacycles, which, in many cases, lead to the formation of interesting carbocycles and heterocycles after depalladation.[2-5] This reaction sequence is the basis of palladium-catalyzed cyclizations of aryl or vinyl halides with alkynes, which are very useful in heterocyclic synthesis.[6]

Medium-size heterocycles (8- to 11-membered) are found in numerous compounds of great biological or medicinal relevance.[7] These rings are difficult to prepare because of adverse enthalpic and entropic factors,[8] and therefore the development of efficient methods for their synthesis remains an active research area.[9] Our research group has reported the synthesis of a series of eight-membered palladacycles derived from the insertion of olefins into the Pd–C bond of *ortho*-palladated phenethylamines, which can be employed for the synthesis of eight-membered cyclic amidines via the insertion of isonitriles and subsequent depalladation.[10] We have also shown (Chapter I) that the six-membered cationic palladacycles [Pd{κ^2C,O-$C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO [R = R' = H (**2a**), R = Me, R' = H (**2b**), R = R' = Me (**2c**)] undergo C–N and/or C–O reductive couplings after the insertion of CO into the Pd–C bond, leading to isoquinoline (**A**) and/or isocoumarin (**B**) derivatives (Scheme II.1).[11] The fact that these couplings take place under very mild conditions prompted us to examine their suitability for the synthesis of heterocycles of a larger size. For this purpose, ring enlargement through the insertion of alkynes prior to the treatment with CO appeared to be a promising option. In this chapter, we describe the synthesis of a series of eight-membered palladacycles derived from alkyne monoinsertions into the Pd–C bond of **2a-c** and a systematic study of their reactivity toward CO or isocyanides, which afforded benzo[*d*]azocine-2,4(1*H*,3*H*)-diones (**C**), belonging to a new family of the small group of eight-membered cyclic imides[12, 13] or, respectively, highly functionalized acrylamides (**D**) or acrylonitriles (**E**).

Scheme II.1

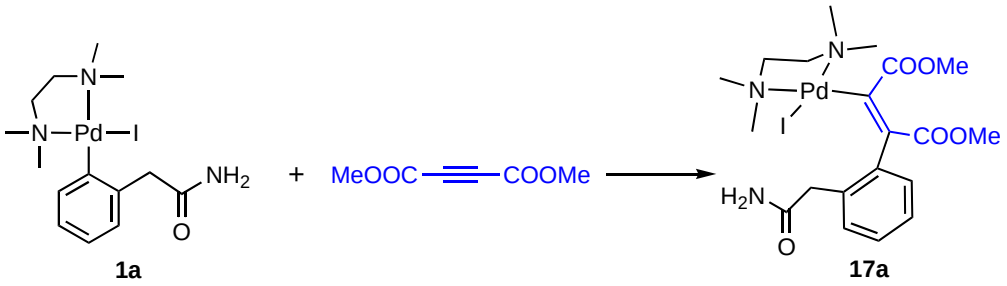


Results and Discussion

Alkyne Monoinsertion Reactions. Synthesis of Eight-Membered Palladacycles

We initially attempted the synthesis of vinyl palladium complexes by reacting the iodo(aryl) derivatives [Pd{$C_6H_4CH_2C(O)NRR'$-2}I(tmeda)] [NRR' = NH_2 (**1a**), NHMe (**1b**), NMe_2 (**1c**)] with diphenylacetylene at room temperature. However, the starting materials were recovered unreacted, even when an excess of the alkyne was employed. The NH_2 derivative **1a** did undergo the insertion of the more reactive dimethylacetylenedicarboxylate (DMAD) into the Pd–C bond to give the vinyl complex [Pd{$C(COOMe)=C(COOMe)C_6H_4CH_2C(O)NH_2$-2}I(tmeda)] (**17a**) (Scheme II.2), although this reaction required a 10-fold excess of the alkyne and heating at 45 °C for 12 h.

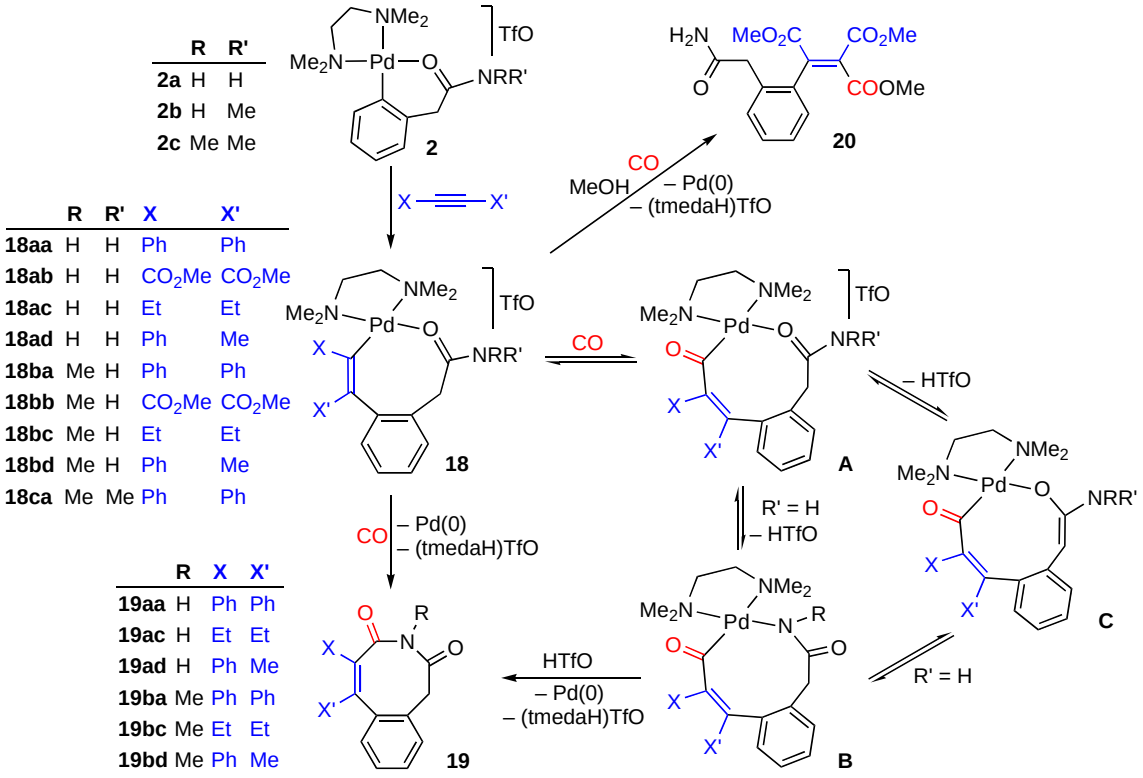
Scheme II.2



The cationic cyclopalladated complexes [Pd{κ^2C,O-$C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO [NRR' = NH_2 (**2a**), NHMe (**2b**), NMe_2 (**2c**)] were expected to react more easily with alkynes because their cationic nature and the lability of the Pd–O bond should facilitate the necessary alkyne coordination step. Their reactions with various alkynes XC≡CX' in 1:3 molar ratio at room temperature afforded high yields of the eight-membered palladacycles [Pd{κ^2C,O-$C(X)=C(X')C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO [R = R' = H and X = X' = Ph (**18aa**), CO_2Me (**18ab**), Et (**18ac**) or X = Ph, X' = Me (**18ad**); R = Me, R' = H and X = X' = Ph (**18ba**), CO_2Me (**18bb**), Et (**18bc**) or X = Ph, X' = Me (**18bd**); R = R' = Me and X = X' = Ph (**18ca**)], resulting from the insertion of one molecule of the alkyne into the Pd–C bond (Scheme II.3). We formulate these complexes assuming that the alkyne substituents are mutually cis because this is the geometry in all similar complexes[3, 4, 14] and was confirmed by the X-ray crystal structure of **18aa**·$2Et_2O$. Multiple-insertion products were not observed in any of the cases, which is surprising if we consider that the large size of palladacycles **18** should render them more reactive. Compounds **18ad** and **18bd** are the expected major regioisomers resulting from the insertion of 1-phenylpropyne, in agreement with the observed reaction pattern for the insertions of dissymmetric internal alkynes, which favors the isomer with the more sterically demanding substituent on the carbon atom next to the metal;[15] the regiochemistry of this insertion was confirmed by means of $^1H/^{13}C$ heteronuclear multiple bond correlation (HMBC) experiments.

The IR spectra of the cyclopalladated complexes **18** show the ν(C=O) band arising from the amide function at around 1660 (**18aa-d**), 1615 (**18ba-d**) or 1590 (**18ca**) cm^{-1}, which approximately match the frequencies observed for the corresponding precursors **2a-c**.[11] This indicates that in all cases the amide remains coordinated through the oxygen atom. The room temperature ^1H NMR spectra show the resonances of the methylenic protons as an AB system, which indicates that, at this temperature, there are no conformational equilibria making them equivalent; this is attributable to the restrictions imposed by the planar vinyl, amide and arylene groups.

Scheme II.3



Reactions with CO. Synthesis of Benzo[*d*]azocine-2,4(1*H*,3*H*)-diones

The derivatives **18aa**, **18ac**, **18ad**, **18ba**, **18bc** and **18bd** reacted with CO (1.4 bar) at 50 °C in $CHCl_3$ to give colloidal Pd, (tmedaH)TfO and the corresponding benzo[*d*]azocine-2,4(1*H*,3*H*)-diones **19** (Scheme II.3), which result from an insertion/C–N reductive coupling sequence. The NH_2 derivatives required shorter reaction times (5 h) and led to higher yields (78-94%) than the NHMe derivatives (24 h, 57-71%). No C–O coupling products were detected in any of the cases. The NMe_2 derivative **18ca** was recovered unreacted after 70 h under the same reaction conditions. As observed for complexes **18**, the ^{1}H NMR data of compounds **19** indicate that the methylenic protons do not interconvert at room temperature.

Possible intermediates in the formation of compounds **19** are depicted in Scheme II.3. The insertion of CO into the Pd–C bond of complexes **18** could give the nine-membered palladacycle **A**, in equilibrium with the amidate **B**. The latter could undergo a C–N reductive coupling to give compounds **19** and the displaced tmeda ligand should be taken up by the HTfO formed in the **A** ⇆ **B** equilibrium. The fact that the NHMe derivatives require longer

reaction times and lead to lower yields can be explained on the basis of the steric repulsion of the methyl substituent, which makes the C–N coupling slower. This is in agreement with our previous results on the C–N coupling processes that take place after insertion of CO into the Pd–C bond of the iodo(aryl) complexes [Pd{$C_6H_4CH_2C(O)NRR'$-2}I(tmeda)] (R = H, Me; R' = H)[11] and also with the general observation that palladium-catalyzed intermolecular amidations of aryl halides that proceed through amidate intermediates are considerably slower when acyclic secondary amides are used instead of primary amides.[16] The fact that no C–O reductive couplings are observed suggests that the required nine-membered aminoenolate intermediate **C** is either formed in minute amounts, because it transforms quickly into **B**, or is not formed at all.

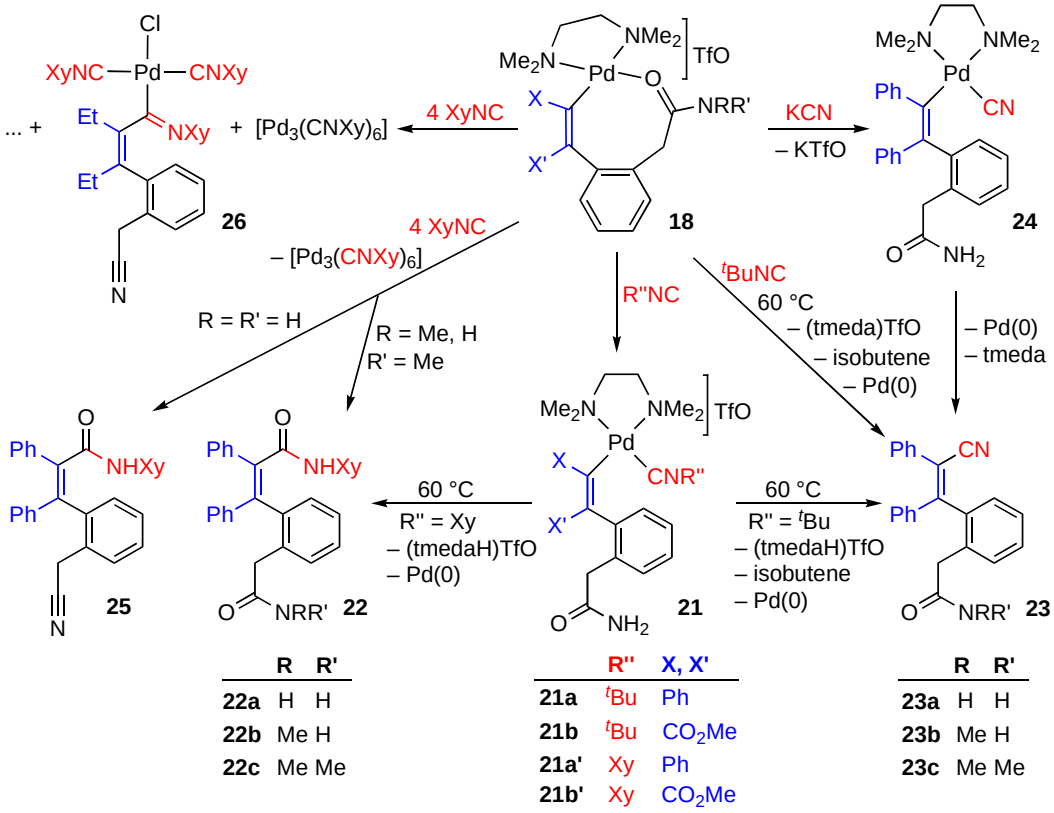
The complexes with inserted dimethyl acetylene dicarboxylate (DMAD) **18ab** and **18bb** reacted with CO in $CHCl_3$ at room temperature but gave mixtures of compounds in which the corresponding benzazocines **19** could not be identified, which means that the required C–N reductive coupling is hindered for the DMAD derivatives. When the reaction of **18ab** with CO was carried out in MeOH, the product $(MeO_2C)_2C=C(CO_2Me)C_6H_4CH_2C(O)NH_2$-2 (**20**), resulting from the methanolysis of the acyl palladium intermediate (Scheme II.3), was obtained as the sole product although it could only be isolated with a moderate yield (42%).

Reactions with Isonitriles

The reactions of complexes **18aa** or **18ab** with XyNC or ^{t}BuNC in molar ratio 1:1 at room temperature in $CHCl_3$ led to the formation of [Pd{$C(X)=C(X')C_6H_4CH_2C(O)NH_2$-2}(CNR'')(tmeda)]TfO [R'' = ^{t}Bu and X = X' = Ph (**21a**), CO_2Me (**21b**); R'' = Xy and X = X' = Ph (**21a'**), CO_2Me (**21b'**)], which result from the displacement of the coordinated oxygen atom by the isonitrile (Scheme II.4). Complexes **21a**, **21b** and **21b'** are sufficiently stable not to undergo subsequent reactions at room temperature. However, complex **21a'** was obtained along with decomposition products and could not be purified. The 1:1 reaction of **18aa** with XyNC at reflux temperature in $CHCl_3$ gave a precipitate of Pd metal and a mixture containing the acrylamide derivative $XyHNC(O)C(Ph)=C(Ph)C_6H_4CH_2C(O)NH_2$-2 (**22a**), which could be isolated in 24% yield. This result indicates that, although the insertion of the isocyanide takes place, the formation of an amidate intermediate analogous to **A** (Scheme II.3) and/or the subsequent C–N reductive coupling are not favored and that the hydrolysis of the iminoacyl ligand by residual water takes place instead. Under the same reaction

conditions, **18aa**, **18ba** or **18ca** and ^{t}BuNC led to the precipitation of Pd(0) and the formation of the acrylonitrile derivatives NCC(Ph)=C(Ph)$C_6H_4CH_2$C(O)NRR'-2 [R = R' = H (**23a**); R = Me, R' = H (**23b**); R = R' = Me (**23c**)], with the concomitant formation of isobutene and (tmedaH)TfO (Scheme II.4). Several unidentified decomposition products also formed and only **23a** and **23c** could be isolated in pure form from these reactions (55 or 29% yield, respectively). Compounds **23** apparently resulted from the C–C reductive coupling of a cyano(vinyl) palladium complex that could have formed after the dealkylation of the coordinated ^{t}BuNC ligand in the corresponding complexes **21** (Scheme II.4). There are numerous examples of ^{t}BuNC ligand dealkylation reactions, which have been found to be

Scheme II.4



relatively easy if the complex is cationic or the metal ion is in a high oxidation state.[17] Although we have not found any precedent involving a Pd complex, the cationic nature of the intermediate complexes **21** may facilitate this process. On the other hand, the coupling of cyanide and vinyl ligands in the coordination sphere of Pd(II) has been proposed as the last step in the mechanism of the Pd-catalyzed arylcyanation of internal alkynes.[18] To further support this reaction path, we prepared the cyanocomplex [Pd{C(Ph)=C(Ph)$C_6H_4CH_2$C(O)NH_2-2}(CN)(tmeda)] (**24**) from **18aa** and KCN and

refluxed it in $CHCl_3$ solution for 15 h, which afforded a precipitate of Pd(0) and compound **23a** in 61% isolated yield. Similar yields of derivatives **23b** and **23c** were obtained by refluxing *in situ* generated solutions of the corresponding cyanocomplexes in $CHCl_3$.

When 1:4 molar ratios were employed, the reactions of **18aa**, **18ba** and **18ca** with XyNC at room temperature in CH_2Cl_2 or acetone afforded dark red solutions containing the Pd(0) complex $[Pd_3(CNXy)_6]$,[19] which was identified by its ^1H NMR spectrum. The other reaction products were (tmedaH)TfO and the acrylamide derivatives XyHNC(O)C(Ph)=C(Ph)$C_6H_4CH_2$CN-2 (**25**, from **18aa**) or XyHNC(O)C(Ph)=C(Ph)$C_6H_4CH_2$C(O)NRR'-2 [NRR' = NHMe (**22b**), NMe_2 (**22c**), from **18ba** or **18ca**, respectively]. These compounds result from the insertion of a XyNC molecule into the Pd–C bond and the subsequent hydrolysis of the resulting iminoacyl complex. In the case of **25**, the process is accompanied by the dehydration of the unsubstituted carbamoyl group to give a nitrile, which takes place even in the presence of added water. The dehydration of primary amides to give nitriles is a functional group transformation of great importance in organic synthesis. Conventional procedures employ powerful dehydration reagents under energetic reaction conditions.[20] However, several methods have been developed that make use of transition-metal compounds as catalysts under milder conditions.[21] Of particular relevance to our results is the finding that $PdCl_2$, $[PdCl_2(NCMe)_2]$ or $Pd(OAc)_2$ catalyze at room temperature the dehydration of a series of primary amides in aqueous acetonitrile.[22] The existence of this precedent and the mild conditions required for the formation of **25** suggest that the dehydration step leading to this compound is mediated by some Pd species whose nature cannot be precisely established at present. Notably, the reaction does not require the use of a water/acetonitrile mixture as the solvent. In order to gain insight into this process, we carried out the 1:4 reaction of complex **18ac** with XyNC in dry CH_2Cl_2, which also produced $[Pd_3(CNXy)_6]$ and (tmedaH)TfO. After separation of these two products, a mixture was obtained from which a small amount of a microcrystalline solid could be isolated. An X-ray diffraction study revealed that this compound is $[Pd\{C(=NXy)C(Et)=C(Et)C_6H_4CH_2CN\text{-}2\}Cl(CNXy)_2]$ (**26**), containing two mutually *trans* XyNC ligands, one chloro ligand and an iminoacyl ligand resulting from the insertion of a XyNC molecule and the dehydration of the carbamoyl group. Apart from the fact that the chloro ligand must have originated from the reaction of some intermediate Pd complex with the solvent, the formation of **26** showed that the dehydration of the carbamoyl group and the hydrolysis of the iminoacyl ligand can take place independently.

Crystal Structures

The crystal structure of the complex **17a** (Figure II.1) was solved as a dichloromethane hemisolvate. It shows that the alkyne has inserted in a *syn* fashion, as is usually the case for alkyne monoinsertions.[3, 4, 14] The coordination environment around the palladium center is distorted square planar, the main distortion arising from the small bite of the chelating tmeda ligand, leading to a N(1)–Pd–N(2) angle of 83.53 (7)°. The molecules of **17a** form inversion-related dimers through N–H···O hydrogen bonds involving the amide group.

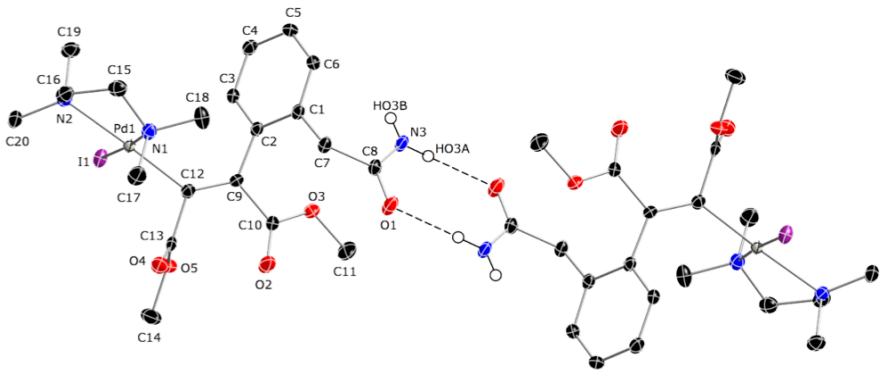


Figure II.1. Thermal ellipsoid plot (50% probability) of the cation of complex **17a**. Selected bond distances (Å) and angles (deg): Pd(1)–C(12) 2.014(2), Pd(1)–N(1) 2.126(2), Pd(1)–N(2) 2.1799(18), Pd(1)–I(1) 2.5902(2), C(2)–C(9) 1.494(3), C(9)–C(12) 1.341 (3); C(12)–Pd(1)–N(1) 94.69(8), C(12)–Pd(1)–N(2) 176.64(8), N(1)–Pd(1)–N(2) 83.53(7), C(12)–Pd(1)–I(1) 89.26(6), N(1)–Pd(1)–I(1) 176.01(5), N(2)–Pd(1)–I(1) 92.55(5), C(9)–C(12)–Pd(1) 130.89(17), C(12)–C(9)–C(2) 123.80(19).

The crystal structure of complex **18aa** (Figure II.2) was determined as a diethyl ether disolvate. It shows the diphenylacetylene molecule inserted in a *syn* fashion and confirms that the amide group remains coordinated to the Pd through the oxygen. The conformation of the resulting eight-membered ring is similar to that found in the urea derivative [Pd{κ^2*C*,*O*-C(Ph)=C(Ph)C$_6$H$_4$NHC(O)NHTo-2}(tmeda)]TfO[23] (To = *p*-tolyl) and can be approximately described as twist boat, although the usual designations of cyclooctane conformations[24] are not strictly applicable. The coordination environment around the Pd center is distorted square planar, the main distortions arising from the small bite of the tmeda ligand, leading to an N(2)–Pd–N(3) angle of 84.58(5)°, and the strain caused by the eight-membered cycle, leading to a C(4)–Pd–O(1) angle of 94.00(6)°. The Pd–C(4) bond distance of 1.9930(16) Å is typical of vinylpalladium complexes.[4, 5, 23, 25] The Pd–O(1) distance of 2.0682(11) Å is slightly longer than that found in the six-membered palladacycle

[Pd{κ^2C,O-$C_6H_4CH_2C(O)NHMe$-2}(dbbpy)]TfO (2.031 Å).[11] The NH_2 group forms two N–H···O hydrogen bonds, one of them to one of the diethyl ether molecules and the other to an oxygen atom of the triflate anion.

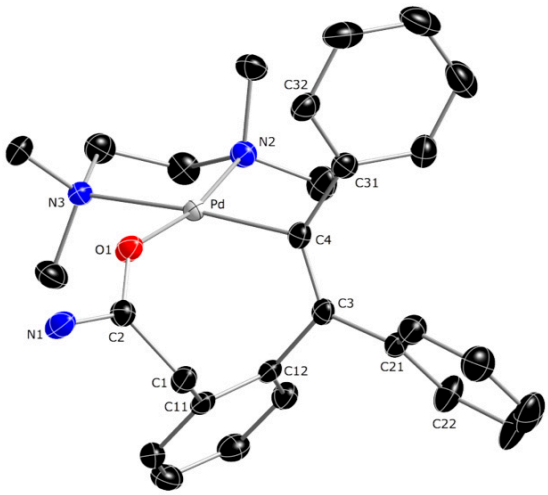


Figure II.2. Thermal ellipsoid plot (50% probability) of the cation of complex **18aa**. Selected bond distances (Å) and angles (deg): Pd–C(4) 1.9930(16), Pd–O(1) 2.0682(11), Pd–N(2) 2.0771(14), Pd–N(3) 2.1874(14), O(1)–C(2) 1.250(2), N(1)–C(2) 1.316(2), C(3)–C(4) 1.338(2), C(3)–C(12) 1.507(2); C(4)–Pd–O(1) 94.00(6), C(4)–Pd–N(2) 94.26(6), O(1)–Pd–N(3) 87.92(5), N(2)–Pd–N(3) 84.58(5), C(2)–O(1)–Pd 135.22(11), O(1)–C(2)–N(1) 119.42(16), O(1)–C(2)–C(1) 123.39(15), N(1)–C(2)–C(1) 117.19(15).

The X-ray diffraction analyses of **19aa** and **19ac** revealed very similar structures (Figures II.3 and II.4, respectively). The eight-membered ring exhibits a folded conformation imposed by the constraints of the planar imide, ethylene and benzene groups. The bond lengths and angles are normal except for the wide C(2)–N(3)–C(4) angle of 130.87(11)° (**19aa**) or 134.79(10)° (**19ac**), which may be associated with the ring strain. There is only one precedent of a crystal structure of an eight-membered cyclic imide, which shows a C–N–C angle of 135.13°.[12] A search of the Cambridge Database for the grouping C–CO–NH–CO–C in acyclic systems or rings with more than six atoms gave 56 hits and an average C–N–C angle of 128.4°. Both **19aa** and **19ac** form inversion-related dimers through hydrogen bonds N(3)–H(03)···O(1)#1 or N(3)–H(03)···O(2)#1, respectively.

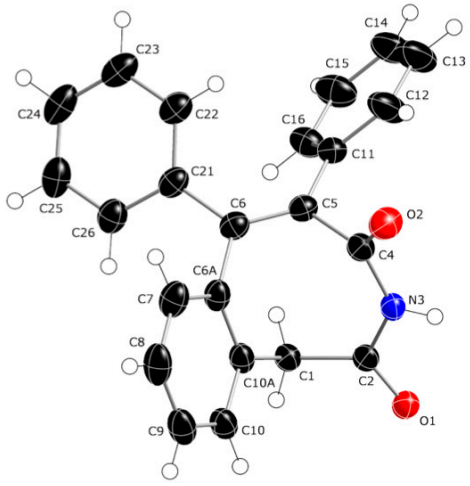


Figure II.3. Thermal ellipsoid plot (50% probability) of compound **19aa**. Selected bond distances (Å) and angles (deg): O(1)–C(2) 1.2260(15), O(2)–C(4) 1.2110(16), C(1)–C(2) 1.5097(17), C(1)–C(10A) 1.5184(17), C(2)–N(3) 1.3746(16), N(3)–C(4), 1.3976(16), C(4)–C(5) 1.5056(18), C(5)–C(6) 1.3463(19), C(6)–C(6A) 1.4935(17); C(2)–C(1)–C(10A) 111.59(10), O(1)–C(2)–N(3) 118.90(11), O(1)–C(2)–C(1) 121.45(11), N(3)–C(2)–C(1) 119.54(11), C(2)–N(3)–C(4) 130.87(11), O(2)–C(4)–N(3) 118.51(12), O(2)–C(4)–C(5) 120.92(11), N(3)–C(4)–C(5) 120.02(11), C(6)–C(5)–C(4) 120.01(11), C(5)–C(6)–C(6A) 118.87(11).

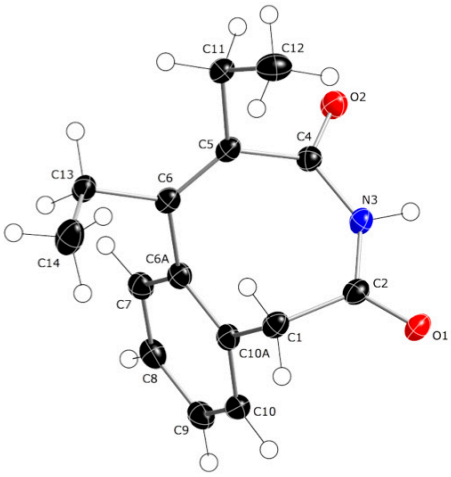


Figure II.4. Thermal ellipsoid plot (50% probability) of compound **19ac**. Selected bond distances (Å) and angles (deg): C(2)–O(1) 1.2161(13), C(2)–N(3) 1.3952(15), N(3)–C(4) 1.3835(14), C(4)–O(2) 1.2289(14), C(4)–C(5) 1.5042(15), C(5)–C(6) 1.3446(16); C(2)–C(1)–C(10A) 108.40(9), O(1)–C(2)–N(3) 117.82(10), O(1)–C(2)–C(1) 122.39(10), N(3)–C(2)–C(1) 119.61(9), C(4)–N(3)–C(2) 134.79(10), O(2)–C(4)–N(3) 117.18(10), O(2)–C(4)–C(5) 118.38(10), N(3)–C(4)–C(5) 124.20(10), C(6)–C(5)–C(4) 123.09(10), C(5)–C(6)–C(6A) 121.36(10).

The crystal structure of complex **24** (Figure II.5) shows a slightly distorted square planar coordination around the Pd atom (the donor atoms of the ligands lie alternatingly ±0.12 Å out of the mean plane). The vinyl moiety defines a planar group including the Pd and

the three connected C atoms from the aromatic rings (mean deviation from plane Pd-C(1)-C(11)-C(2)-C(21)-C(31), 0.02 Å), which forms an angle of 71.2° with the mean Pd coordination plane. The Pd–C(1) bond distance of 2.0092(11) Å is similar to the corresponding distance found in **18aa**. The two H atoms of the NH_2 group are involved in N–H···N hydrogen bonds with the cyano group, one of them intramolecular and the other with an inversion-related molecule, resulting in a pairing of molecules via a central ring $[(NH_2)_2\cdots(N_{cyano})_2]$ of graph set $R_4^2(8)$.

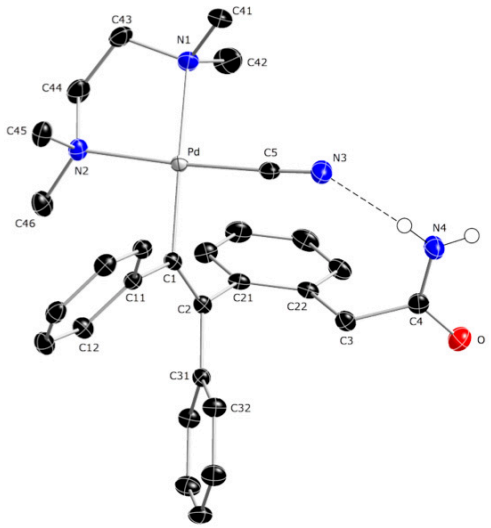


Figure II.5. Thermal ellipsoid plot (50% probability) of complex **24**. Selected bond distances (Å) and angles (deg): Pd–C(5) 1.9576(12), Pd–C(1) 2.0092(11), Pd–N(2) 2.1398(10), Pd–N(1) 2.1678(10), O–C(4) 1.2301(15), N(3)–C(5) 1.1513(16), N(4)–C(4) 1.3304(16), C(1)–C(2) 1.3499(16), C(3)–C(4) 1.5216(16); C(5)–Pd–C(1) 86.54(5), C(1)–Pd–N(2) 96.11(4), C(5)–Pd–N(1) 94.60(4), N(2)–Pd–N(1) 83.57(4), C(2)–C(1)–C(11) 124.34(10), C(1)–C(2)–C(21) 121.22(10), O–C(4)–N(4) 122.99(12), N(3)–C(5)–Pd 175.94(11).

The molecular structure of **25** is shown in Figure II.6. The conformation adopted by this compound in the crystal appears to be dictated by the formation of an intramolecular N–H···N hydrogen bond between the NHXy and cyano groups.

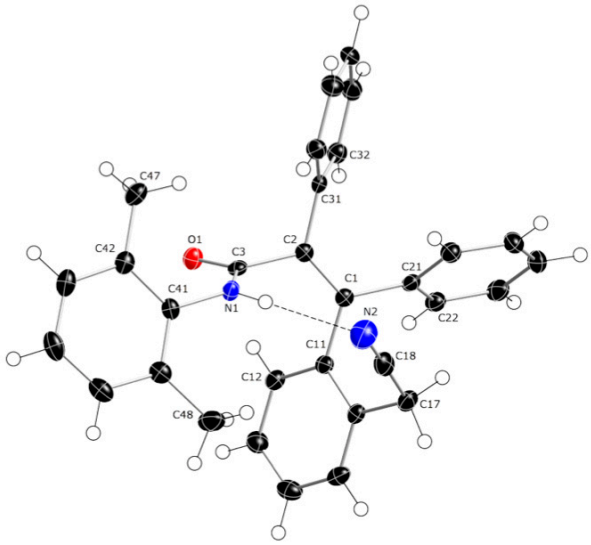


Figure II.6. Thermal ellipsoid plot (50% probability) of compound **25**. Selected bond distances (Å) and angles (deg): C(1)–C(2) 1.3416(15), C(2)–C(3) 1.5105(15), C(3)–O(1) 1.2251(13), C(3)–N(1) 1.3572(14), C(18)–N(2) 1.1391(15), C(41)–N(1) 1.4379(13); C(2)–C(1)–C(11) 122.19(9), C(1)–C(2)–C(3) 121.46(9), O(1)–C(3)–N(1) 123.18(10), O(1)–C(3)–C(2) 121.25(10), N(1)–C(3)–C(2) 115.53(9), N(2)–C(18)–C(17) 177.07(13), C(3)–N(1)–C(41) 122.50(9), O(1)–C(3)–N(1) 123.18(10).

The crystal structure of **26** (Figure II.7) shows an almost perfect square planar coordination around the Pd atom. The iminoacyl group is practically planar (mean deviation from plane C(1)–C(10)–N(1)–Pd, 0.01 Å) and forms an angle of 61.0° with the mean Pd coordination plane. The Pd–C(10) bond distance of 2.040(2) Å is similar to that found for other iminoacyl Pd complexes in an analogous coordination environment.[11,26]

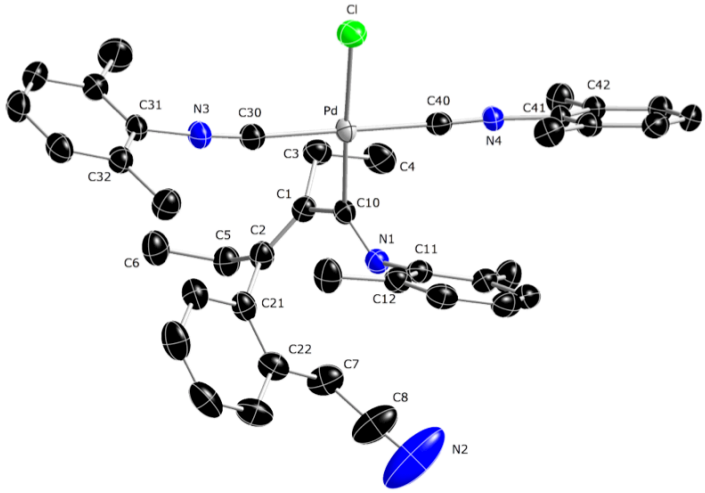


Figure II.7. Thermal ellipsoid plot (30% probability) of complex **26**. Selected bond distances (Å) and angles (deg): Pd–C(40) 1.976(2), Pd–C(30) 2.000(3), Pd–C(10) 2.040(2), Pd–Cl 2.4214(6), N(1)–C(10) 1.258(3), N(2)–C(8) 1.122(6), C(1)–C(2) 1.340(4), C(1)–C(10) 1.496(3), C(40)–Pd–C(10) 88.64(9), C(30)–Pd–C(10) 91.85(10), C(40)–Pd–Cl 89.32(7),

C(30)–Pd–Cl 90.17(8), N(1)–C(10)–C(1) 119.2(2), N(1)–C(10)–Pd 125.47(18), C(1)–C(10)–Pd 115.18(17), N(2)–C(8)–C(7) 178.0(6).

Experimental section

General Considerations, Materials and Instrumentation

Unless otherwise noted, all preparations were carried out at room temperature under atmospheric conditions. Synthesis grade solvents were obtained from commercial sources. All other reagents were obtained from commercial sources and used without further purification. NMR spectra were recorded on Bruker Avance 200, 300 or 400 spectrometers usually at 298 K, unless otherwise indicated. Chemical shifts are referred to internal TMS. The assignments of the ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were made with the help of HMQC and HMBC experiments. Inserted and coordinated XyNC are denoted by $XyNC^{i}$ and $XyNC^{c}$, respectively, and the 1,2-C_6H_4 arylene group by Ar. Melting points were determined on a Reichert apparatus and are uncorrected. Elemental analyses were carried out with a Carlo Erba 1106 microanalyzer. Infrared spectra were recorded in the range 4000–200 cm^{-1} on a Perkin-Elmer Spectrum 100 spectrophotometer using Nujol mulls between polyethylene sheets. High-resolution ESI mass spectra were recorded on an Agilent 6220 Accurate-Mass TOF LC/MS.

X-Ray Structure Determinations

Crystals suitable for X-ray diffraction studies were obtained by liquid-liquid diffusion from CH_2Cl_2/Et_2O (**17a**·0.5CH_2Cl_2), $CDCl_3/Et_2O$ (**18aa**·2Et_2O), $CDCl_3$/*n*-pentane (**19aa**), CH_2Cl_2/*n*-pentane (**24**, **25** and **26**) or by sublimation at low pressure (**19ac**). Numerical details are presented in Tables II.1 and II.2. The data for **17a** were collected on a Bruker Smart Apex CCD diffractometer using monochromated Mo-*K*α radiation in *ω*-scan mode. The data for **19aa**, **19ac** and **26** were collected on an Oxford Diffraction Nova diffractometer using mirror-focussed Cu-*K*α radiation in *ω*-scan mode. The data for **18aa**·2Et_2O, **24**, and **25** were collected on an Oxford Diffraction Xcalibur diffractometer using monochromated Mo-*K*α radiation in *ω*-scan mode. The measurement temperature was 100 K for all structures except **18aa**·2Et_2O and **26**, crystals of which shattered at 100 K (presumably because of a phase transition) and were therefore measured at 150 K. Absorption corrections were based on multi-scans except for **25**, for which no correction was applied. The structures were solved by direct methods and refined anisotropically on F^2 using the program SHELXL-97 (G. M. Sheldrick, University of Göttingen).[27] Treatment of hydrogen atoms is as follows: NH freely

refined (for **24** with N–H distance restraints), methyls as rigid groups allowed to rotated but not tip, other H using a riding model starting from calculated positions. *Special features of refinement:* The dichloromethane molecule in **17a** is disordered over an inversion center. The triflate group of **18aa** is slightly disordered (minor component ca. 8%); appropriate similarity restraints were employed to improve refinement stability, but dimensions of disordered groups should always be interpreted with caution.

Table II.1. Crystallographic Data for **17a**·0.5CH_2Cl_2, **18aa**·2Et_2O, **19aa**, and **19ac**.

	17a·0.5CH_2Cl_2	**18aa**·2Et_2O	**19aa**	**19ac**
formula	$C_{20.5}H_{31}ClIN_3O_5Pd$	$C_{37}H_{54}F_3N_3O_6PdS$	$C_{23}H_{17}NO_2$	$C_{15}H_{17}NO_2$
fw	668.23	832.29	339.38	243.30
T (K)	100(2)	150(2)	100(2)	100(2)
λ (Å)	0.71073	0.71073	1.54184	1.54184
cryst syst	monoclinic	triclinic	triclinic	monoclinic
space group	$P2_1/c$	$P\bar{1}$	$P\bar{1}$	$P2_1/n$
a (Å)	10.1691(4)	10.0071(3)	8.7948(11)	11.1524(4)
b (Å)	11.5598(4)	11.2824(3)	9.8117(10)	10.1077(4)
c (Å)	20.9544(8)	19.3538(6)	11.3509(13)	11.2671(4)
α (deg)	90	78.416(4)	104.998(10)	90
β (deg)	97.320(2)	82.150(4)	103.082(10)	91.129(4)
γ (deg)	90	72.009(4)	104.619(10)	90
V (Å^3)	2443.17(16)	2029.42(10)	869.78(17)	1269.84(8)
Z	4	2	2	4
ρ_{calcd} (Mg m^{-3})	1.817	1.362	1.296	1.273
μ (mm^{-1})	2.168	0.568	0.658	0.674
R1[a]	0.0235	0.0267	0.0398	0.0352
wR2[b]	0.0564	0.0676	0.1110	0.0909

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

Table II.2. Crystallographic Data for **24**, **25** and **26**.

	24	**25**	**26**
formula	$C_{29}H_{34}N_4OPd$	$C_{31}H_{26}N_2O$	$C_{41}H_{43}ClN_4Pd$
fw	561.00	442.54	733.64
T (K)	100(2)	100(2)	150(2)
λ (Å)	0.71073	0.71073	1.54184
cryst syst	triclinic	monoclinic	monoclinic
space group	$P\bar{1}$	$P2_1/c$	$P2_1/n$
a (Å)	8.3426(2)	15.4806(5)	11.2983(4)
b (Å)	9.7460(3)	8.6812(3)	8.6519(3)
c (Å)	17.8648(4)	18.5378(6)	37.1625(12)
α (deg)	81.605(3)	90	90
β (deg)	83.119(3)	106.395(4)	97.241(4)

γ (deg)	74.056(3)	90	90
V (Å^3)	1376.84(6)	2390.00(14)	3603.7(2)
Z	2	4	4
ρ_{calcd} (Mg m^{-3})	1.353	1.230	1.352
μ (mm^{-1})	0.701	0.074	5.089
R1[a]	0.0188	0.0368	0.0346
wR2[b]	0.0493	0.0867	0.0875

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

Synthesis

[Pd{C(COOMe)=C(COOMe)C$_6$H$_4$CH$_2$C(O)NH$_2$-2}I(tmeda)] (17a). To a solution of **1a** (100 mg, 0.21 mmol) in CH_2Cl_2 (15 mL) was added dimethylacetylenedicarboxylate (260 μL, 2.07 mmol) and the mixture was stirred at 45 °C for 12 h. The solvent was removed under reduced pressure and the residue was stirred in Et_2O for 1 h, whereupon a pale yellow precipitate formed, which was filtered off and washed with Et_2O (5 × 3 mL). The crude product was recrystallized from CH_2Cl_2/Et_2O and vacuum-dried to give **17a**. Yield: 97 mg, 75%. Anal. Calcd for $C_{20}H_{30}IN_3O_5Pd$: C, 38.39; H, 4.83; N, 6.71. Found: C, 38.20; H, 4.91; N, 6.38. Mp: 110-120 °C. IR (Nujol, cm^{-1}): ν(NH), 3397, 3191; ν(CO), 1695. ^{1}H NMR [300.1 MHz, $(CD_3)_2CO$]: δ 8.77 (br d, $^3J_{HH}$ = 6.6 Hz, 1 H, Ar), 7.37-7.24 (m, 3 H, Ar), 6.56 (br, 1 H, NH), 6.27 (br, 1 H, NH), 3.62 (s, 3 H, CO_2Me), 3.54 (s, 3 H, CO_2Me), 3.36, 3.25 (AB system, $^2J_{HH}$ = 15.6 Hz, 2 H, CH_2, acetamide), 2.80 (s, 3 H, Me, tmeda), 2.75-2.50 (m, 3H, CH_2, tmeda), 2.70 (s, 3 H, Me, tmeda), 2.53 (s, 3 H, Me, tmeda), 2.46-2.39 (m, 1 H, CH_2, tmeda), 2.15 (br s, 3 H, Me, tmeda). ^{13}C{^{1}H} APT NMR [75.5 MHz, $(CD_3)_2CO$]: δ 173.1 (CO_2Me), 172.5 (CO, acetamide), 165.2 (CO_2Me), 158.4 (CPd), 140.5, 136.6 (C, Ar), 134.0 (*C*–COOMe), 133.1, 130.0, 128.1, 126.3 (CH, Ar), 63.4, 59.3 (CH_2, tmeda), 51.7 (CO_2*Me*), 51.5, 51.4, 51.0, 50.4 (Me, tmeda), 40.5 (CH_2, acetamide).

[Pd{κ^2*C,O*-C(X)=C(X')C$_6$H$_4$CH$_2$C(O)NRR'-2}(tmeda)]TfO [R = R' = H and X = X' = Ph (18aa), CO_2Me (18ab), Et (18ac) or X = Ph, X' = Me (18ad); R = Me, R' = H and X = X' = Ph (18ba), CO_2Me (18bb), Et (18bc) or X = Ph, X' = Me (18bd); R = R' = Me and X = X' = Ph (18ca)]. A mixture of the appropriate complex **2** (0.15 mmol) and the alkyne (0.45 mmol) in CH_2Cl_2 (25 mL) was stirred for 9 h and then filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (1 mL) and addition of Et_2O (20 mL) led to the precipitation of the corresponding complex **18** as a yellow solid, which was filtered off, washed with Et_2O (3 × 3 mL) and vacuum-dried.

18aa. Yield: 91%. Anal. Calcd for $C_{29}H_{34}F_3N_3O_4PdS$: C, 50.92; H, 5.01; N, 6.14; S, 4.69. Found: C, 50.58; H, 5.21; N, 6.14; S, 4.48. Mp: 123–125 °C. IR (Nujol, cm^{-1}): ν(NH), 3345, 3193; ν(CO), 1667. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.06 (br s, 1 H, NH), 7.76 (d, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.57 (m, 1 H, Ar), 7.40–7.32 (m, 4 H, Ar + Ph), 7.23–7.19 (m, 3 H, Ph), 7.07–6.98 (m, 5 H, Ph), 6.96 (br s, 1 H, NH), 3.69, 3.58 (AB system, $^2J_{HH}$ = 16.0 Hz, 2 H, CH_2, acetamide), 2.63–2.56 (m, 1 H, CH_2, tmeda), 2.56 (s, 3 H, Me, tmeda), 2.47 (m, 1 H, CH_2, tmeda), 2.33 (s, 3 H, Me, tmeda), 2.22 (m, 1 H, CH_2, tmeda), 2.07 (m, 1 H, CH_2, tmeda), 1.96 (s, 3 H, Me, tmeda), 1.70 (s, 3 H, Me, tmeda). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 179.0 (CO), 147.9 (*C*Pd), 144.0 (C, Ar), 142.3 (C, Ph), 137.12 (PdC=*C*Ph), 137.07 (C, Ph), 132.7 (C, Ar), 131.1 (CH, Ar), 129.8 (CH, Ar), 128.67 (CH, Ph), 128,58 (CH, Ph), 128.1 (CH, Ph), 127.9 (CH, Ph), 127.56 (CH, Ar), 127.52 (CH, Ar), 126.2 (CH, Ph), 126.1 (CH, Ph), 64.0 (CH_2, tmeda), 56.9 (CH_2, tmeda), 53.2 (Me, tmeda), 49.3 (Me, tmeda), 48.8 (Me, tmeda), 45.0 (Me, tmeda), 38.3 (CH_2, acetamide).

18ab. Yield: 83%. Anal. Calcd for $C_{21}H_{30}F_3N_3O_8PdS$: C, 38.93; H, 4.67; N, 6.48; S, 4.95. Found: C, 39.07; H, 4.96; N, 6.57; S, 4.84. Mp: 197–200 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3408, 3319, 3248, 3150; ν(CO), 1708, 1660. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.43 (s, 1 H, NH), 7.52–7.40 (m, 4 H, Ar), 7.32 (s, 1 H, NH), 3.87 (A part of AB system, $^2J_{HH}$ = 16.0 Hz, 1 H, CH_2, acetamide), 3.84 (s, 3 H, CO_2Me), 3.65 (s, 3 H, CO_2Me), 3.51 (B part of AB system, 1 H, CH_2, acetamide), 2.82 (s, 3 H, Me, tmeda), 2.70 (m, 1 H, CH_2, tmeda), 2.60–2.53 (m, 4 H, CH_2 + Me, tmeda), 2.36 (s, 3 H, Me, tmeda), 2.27 (m, 1 H, CH_2, tmeda), 2.16 (m, 1 H, CH_2, tmeda), 1.75 (s, 3 H, Me, tmeda). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 179.3 ($CONH_2$), 171.6 (*C*O_2Me), 163.5 (*C*Pd), 161.0 (*C*O_2Me), 140.8 (C, Ar), 133.3 (C, Ar), 133.0 (PdC=*C*CO_2Me), 131.0 (CH, Ar), 129.1 (CH, Ar), 128.4 (CH, Ar), 127.7 (CH, Ar), 64.7 (CH_2, tmeda), 57.7 (CH_2, tmeda), 54.1 (Me, tmeda), 52.16 (CO_2*Me*), 52.07 (CO_2*Me*), 49.2 (Me, tmeda), 49.1 (Me, tmeda), 45.7 (Me, tmeda), 38.3 (CH_2, acetamide).

18ac. Yield: 82%. Anal. Calcd for $C_{21}H_{34}F_3N_3O_4PdS$: C, 42.90; H, 5.83; N, 7.15; S, 5.45. Found: C, 42.60; H, 5.90; N, 7.06; S, 5.35. Mp: 154–155 °C. IR (Nujol, cm^{-1}): ν(NH), 3350, 3197; ν(CO), 1664. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.35 (br s, 1 H, NH), 7.41–7.24 (m, 4 H, Ar), 6.58 (br s, 1 H, NH), 3.75, 3.63 (AB system, $^2J_{HH}$ = 15.2 Hz, 2 H, CH_2, acetamide), 2.68 (s, 3 H, Me, tmeda), 2.50–2.27 (m, 9 H, CH_2, Me, tmeda + C*H*$_2$CH$_3$), 2.14–2.06 (m, 1 H, CH_2, tmeda), 2.02, 1.89 (AB part of ABX_3 system, $^2J_{HH}$ = 14.6 Hz, $^3J_{HH}$ = 7.6 Hz, 2 H, C*H*$_2$CH$_3$), 1.68 (s, 3 H, Me, tmeda), 1.19 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$C*H*$_3$), 0.87 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$C*H*$_3$). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 179.8 (CO), 147.2 (C=C), 144.7 (C, Ar), 135.8

(C=C), 133.6 (C, Ar), 130.7 (CH, Ar), 128.4 (CH, Ar), 127.2 (CH, Ar), 126.6 (CH, Ar), 63.7 (CH_2, tmeda), 56.6 (CH_2, tmeda), 52.6 (Me, tmeda), 51.3 (Me, tmeda), 47.4 (Me, tmeda), 45.9 (Me, tmeda), 38.7 (CH_2, acetamide), 26.4, 26.3 (CH_2CH_3), 14.7, 13.4 (CH_2CH_3).

18ad. Yield: 74%. Anal. Calcd for $C_{24}H_{32}F_3N_3O_4PdS$: C, 46.34; H, 5.19; N, 6.76; S, 5.16. Found: C, 46.17; H, 5.44; N, 6,72; S, 4.87. Mp: 156–158 °C. IR (Nujol, cm^{-1}): ν(NH), 3365, 3198; ν(CO), 1661. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.28 (br s, 1 H, NH), 7.46–7.23 (m, 9 H, Ar + Ph), 6.83 (br s, 1 H, NH), 3.85, 3.54 (AB system, $^2J_{HH}$ = 15.6 Hz, 2 H, CH_2, acetamide), 2.54–2.39 (m, 5 H, CH_2 + Me, tmeda), 2.33 (s, 3 H, NMe), 2.25–2.18 (m, 1 H, CH_2, tmeda), 2.07 (m, 1 H, CH_2, tmeda), 2.03 (s, 3 H, CMe), 2.01 (s, 3 H, NMe), 1.72 (s, 3 H, NMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 179.3 (CO), 146.2 (C, Ar), 141.7 (C, Ph), 141.1 (*C*–Pd), 132.6 (PdC=*C*), 131.9 (C, Ar), 130.7 (CH, Ar), 128.4 (CH, Ph), 128.1 (CH, Ph), 128.0 (CH, Ar), 127.6 (CH, Ar), 127.0 (CH, Ar), 125.8 (CH, Ph), 63.8 (CH_2, tmeda), 56.8 (CH_2, tmeda), 52.8 (Me, tmeda), 49.6 (Me, tmeda), 48.4 (Me, tmeda), 45.1 (Me, tmeda), 38.3 (CH_2, acetamide), 20.1 (C*Me*).

18ba. Yield: 88%. Anal. Calcd for $C_{30}H_{36}F_3N_3O_4PdS$: C, 51.61; H, 5.20; N, 6.02; S, 4.59. Found: C, 51.63; H, 5.22; N, 6.11; S, 4.49. Mp: 207–209 °C. IR (Nujol, cm^{-1}): ν(NH), 3271; ν(CO), 1615. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.69 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.75 (d, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.56–7.51 (m, 1 H, Ar), 7.36–7.18 (m, 7 H, Ar + Ph), 7.06–6.95 (m, 5 H, Ph), 3.71, 3.55 (AB system, $^2J_{HH}$ = 16.0 Hz, 2 H, CH_2, acetamide), 2.92 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, acetamide), 2.63–2.58 (m, 1 H, CH_2, tmeda), 2.56 (s, 3 H, Me, tmeda), 2.54–2.44 (m, 1 H, CH_2, tmeda), 2.33 (s, 3 H, Me, tmeda), 2.24 (m, 1 H, CH_2, tmeda), 2.10 (m, 1 H, CH_2, tmeda), 1.97 (s, 3 H, Me, tmeda), 1.67 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.2 (CO), 147.5 (*C*Pd), 144.0 (C, Ar), 142.3 (C, Ph), 137.3 (PdC=*C*Ph), 137.1 (C, Ph), 133.0 (C, Ar), 131.1 (CH), 129.6 (CH), 128.62 (CH, Ph), 128.57 (CH, Ph), 128.1 (CH, Ph), 127.9 (CH, Ph), 127.46 (CH, Ar), 127.41 (CH, Ar), 126.2 (CH, Ph), 126.1 (CH, Ph), 63.8 (CH_2, tmeda), 56.9 (CH_2, tmeda), 53.1 (Me, tmeda), 49.3 (Me, tmeda), 48.4 (Me, tmeda), 45.0 (Me, tmeda), 38.5 (CH_2, acetamide), 27.5 (Me, acetamide).

18bb. Yield: 85%. Anal. Calcd for $C_{22}H_{32}F_3N_3O_8PdS$: C, 39.92; H, 4.87; N, 6.35; S, 4.84. Found: C, 39.77; H, 5.06; N, 6.38; S, 4.66. Mp: 182–184 °C. IR (Nujol, cm^{-1}): ν(NH), 3258; ν(CO), 1707, 1700, 1614. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.85 (br q, $^3J_{HH}$ = 4.4 Hz, 1 H, NH), 7.51–7.38 (m, 4 H, Ar), 3.85 (A part of AB system, $^2J_{HH}$ = 16.4 Hz, 1 H, CH_2, acetamide), 3.83 (s, 3 H, CO_2Me), 3.64 (s, 3 H, CO_2Me), 3.56 (B part of AB system, 1 H, CH_2, acetamide),

2.84 (s, 3 H, Me, tmeda), 2.82 (d, $^3J_{HH}$ = 4.4 Hz, 3 H, Me, acetamide), 2.80–2.70 (m, 1 H, CH_2, tmeda), 2.64–2.57 (m, 4 H, CH_2 + Me, tmeda), 2.37 (s, 3 H, Me, tmeda), 2.29 (s, 1 H, CH_2, tmeda), 2.21 (m, 1 H, CH_2, tmeda), 1.74 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.7 (CO, acetamide), 171.3 (CO_2Me), 163.7 (CPd), 160.9 (CO_2Me), 141.0 (C, Ar), 133.3 (C, Ar), 132.8 (PdC=*C*), 131.1 (CH, Ar), 128.9 (CH, Ar), 128.3 (CH, Ar), 127.7 (CH, Ar), 64.5 (CH_2, tmeda), 57.7 (CH_2, tmeda), 54.2 (Me, tmeda), 52.09 (CO_2*Me*), 51.95 (CO_2*Me*), 49.0 (Me, tmeda), 48.9 (Me, tmeda), 45.7 (Me, tmeda), 38.7 (CH_2, acetamide), 27.6 (Me, acetamide).

18bc. Yield: 76%. Anal. Calcd for $C_{22}H_{36}F_3N_3O_4PdS$: C, 43.89; H, 6.03; N, 6.98; S, 5.33. Found: C, 43.98; H, 6.15; N, 6.96; S, 5.23. Mp: 158–162 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3276; ν(CO), 1623. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.66 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.39–7.22 (m, 4 H, Ar), 3.70, 3.60 (AB system, $^2J_{HH}$ = 15.2 Hz, 2 H, CH_2, acetamide), 2.81 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NH*Me*), 2.68 (s, 3 H, Me, tmeda), 2.52–2.27 (m, 11 H, CH_2, Me, tmeda + CH_2CH_3), 2.18–2.11 (m, 1 H, CH_2, tmeda), 2.01, 1.89 (AB part of ABX_3 system, $^2J_{HH}$ = 14.6 Hz, $^3J_{HH}$ = 7.6 Hz, 2 H, CH_2CH_3), 1.64 (s, 3 H, Me, tmeda), 1.15 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3), 0.85 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.8 (CO), 147.3 (C=C), 144.8 (C, Ar), 135.6 (C=C), 133.9 (C, Ar), 130.6 (CH, Ar), 128.3 (CH, Ar), 127.1 (CH, Ar), 126.5 (CH, Ar), 63.6 (CH_2, tmeda), 56.6 (CH_2, tmeda), 52.5 (Me, tmeda), 51.2 (Me, tmeda), 47.1 (Me, tmeda), 45.9 (Me, tmeda), 39.0 (CH_2, acetamide), 27.2 (NHMe), 26.4, 26.2 (CH_2CH_3), 14.6, 13.4 (CH_2CH_3).

18bd. Yield: 88%. Anal. Calcd for $C_{25}H_{34}F_3N_3O_4PdS$: C, 47.21; H, 5.39; N, 6.61; S, 5.04. Found: C, 47.35; H, 5.21; N, 6.76; S, 4.80. Mp: 138–143 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3278; ν(CO), 1620. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.86 (br, 1 H, NH), 7.44–7.23 (m, 9 H, Ar + Ph), 3.88, 3.51 (AB system, $^2J_{HH}$ = 15.6 Hz, 2 H, CH_2, acetamide), 2.92 (d, $^3J_{HH}$ = 4.4 Hz, 3 H, Me, acetamide), 2.55–2.41 (m, 7 H, CH_2 + Me, tmeda), 2.34 (s, 3 H, Me, tmeda), 2.26–2.21 (m, 1 H, CH_2, tmeda), 2.12–2.06 (m, 1 H, CH_2, tmeda), 2.04 (s, 3 H, Me, tmeda), 2.02 (s, 3 H, CMe), 1.70 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (75.45 MHz, $CDCl_3$): δ 176.6 (CO), 146.2 (C, Ar), 141.7 (C, Ph), 140.8 (*C*–Pd), 132.9 (PdC=*C*), 132.3 (C, Ar), 130.9 (CH, Ar), 128.3 (CH, Ph), 128.0 (CH, Ph), 127.8 (CH, Ar), 127.4 (CH, Ar), 127.0 (CH, Ar), 125.8 (CH, Ph), 63.7 (CH_2, tmeda), 56.8 (CH_2, tmeda), 52.8 (Me, tmeda), 49.6 (Me, tmeda), 48.1 (Me, tmeda), 45.2 (Me, tmeda), 38.7 (CH_2, acetamide), 27.5 (Me, acetamide), 20.1 (C*Me*).

18ca. Yield: 95%. Anal. Calcd for $C_{31}H_{38}F_3N_3O_4PdS{\cdot}0.25H_2O$: C, 51.96; H, 5.41; N, 5.86; S, 4.47. Found: C, 51.67; H, 5.70; N, 5.91; S, 4.18. Mp: 162–163 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1590. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.79 (d, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.65 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.43 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.31 (m, 3 H, Ar + Ph), 7.24–7.18 (m, 3 H, Ph), 7.09–7.01 (m, 3 H, Ph), 6.98–6.93 (m, 2 H, Ph), 3.55, 3.41 (AB system, $^2J_{HH}$ = 17.2 Hz, 2 H, CH_2, acetamide), 3.27 (s, 3 H, Me, acetamide), 3.16 (s, 3 H, Me, acetamide), 2.72–2.57 (m, 2 H, CH_2, tmeda), 2.55 (s, 3 H, Me, tmeda), 2.38 (s, 3 H, Me, tmeda), 2.33 (m, 1 H, CH_2, tmeda), 2.18 (m, 1 H, CH_2, tmeda), 1.95 (s, 3 H, Me, tmeda), 1.79 (s, 3 H, Me, tmeda), 1.67 (s, 0.5 H, H_2O). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 177.3 (CO), 148.4 (*C*Pd), 144.0 (C, Ar), 142.1 (C, Ph), 137.3 (PdC=*C*), 137.2 (C, Ph), 132.0 (C, Ar), 131.8 (CH, Ar), 130.0 (CH, Ar), 128.8 (CH, Ph), 128.5 (CH, Ph), 128.1 (CH, Ph), 127.93 (CH, Ar), 127.89 (CH, Ph), 127.8 (CH, Ar), 126.2 (CH, Ph), 64.2 (CH_2, tmeda), 57.1 (CH_2, tmeda), 53.5 (Me, tmeda), 49.4 (Me, tmeda), 48.6 (Me, tmeda), 45.0 (Me, tmeda), 38.6 (Me, acetamide), 38.1 (CH_2, acetamide), 37.6 (Me, acetamide).

5,6-Substituted Benzo[*d*]azocine-2,4(1*H*,3*H*)-diones (19). A solution of the appropriate complex **18** (0.23 mmol) in $CHCl_3$ (10 mL) was stirred under a CO atmosphere (1.4 bar) at 50 °C for 5 h (NH_2 derivatives) or 24 h (NHMe derivatives), whereupon a black precipitate of Pd gradually formed. The suspension was filtered through anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel, using a 3:1 EtOAc/*n*-hexane mixture as eluent, except for **19bc**, which required a 1:2 mixture. The corresponding compound **19** was obtained as a colorless solid after evaporation of the solvents.

5,6-Diphenylbenzo[*d*]azocine-2,4(1*H*,3*H*)-dione (19aa). Yield: 78%. Mp: 238-240 °C. IR (Nujol, cm^{-1}): ν(C=O), 1702, 1681. HRMS (ESI+, m/z): exact mass calcd for $C_{23}H_{18}NO_2$ $[M+H]^+$ requires 340.1332, found 340.1337, error = 1.42 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.64 (br, 1H, NH), 7.44 (dd, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H10), 7.43–7.38 (m, 2 H, Ph), 7.35 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H9), 7.26 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H8), 7.24–7.09 (m, 7 H, Ph + H7), 6.96–6.93 (m, 2 H, Ph), 4.60 (d, $^2J_{HH}$ = 14.0 Hz, 1 H, CH_2), 3.93 (dd, $^4J_{HH}$ = 1.6 Hz, $^2J_{HH}$ = 14.0 Hz, 1 H, CH_2). ^{13}C{^{1}H} APT NMR (100.81 MHz, $CDCl_3$): δ 172.2 (C2), 169.6 (C4), 140.1 (C6a), 139.5 (C6), 139.2 (C, Ph), 135.6 (C5), 134.7 (C, Ph), 133.0 (C10a), 130.8 (CH, Ph), 130.6 (C7), 129.7 (CH, Ph), 129.4 (C9), 128.9 (C10), 128.52 (CH, Ph), 128.45 (CH, Ph), 128.37 (C8), 128.15 (CH, Ph), 128.08 (CH, Ph), 42.6 (C1).

5,6-Diethylbenzo[*d*]azocine-2,4(1*H*,3*H*)-dione (19ac). Yield: 84%. Mp: 159–162 °C. IR (Nujol, cm^{-1}): ν(CO), 1720, 1653. HRMS (ESI+, m/z): exact mass calcd for $C_{15}H_{18}NO_2$ $[M+H]^+$ 244.1332, found 244.1331, error = 0.53 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.71 (br s, 1 H, NH), 7.35–7.22 (m, 4 H, H7–10), 4.20, 3.68 (AB system, $^2J_{HH}$ = 13.6 Hz, 2 H, CH_2CO), 2.76 (A part of ABX_3 system, $^2J_{HH}$ = 13.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, C*H*$_2$CH$_3$), 2.60 (q, $^3J_{HH}$ = 7.6 Hz, 2 H, C*H*$_2$CH$_3$), 2.34 (B part of ABX_3 system, 1 H, C*H*$_2$CH$_3$), 1.21 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3), 0.90 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): 172.2 (C2), 171.0 (C4), 140.0 (C6), 139.4 (C6a), 135.4 (C5), 132.3 (C10a), 128.5, 128.4, 128.1, 127.9 (C7–10), 42.5 (C1), 27.8 (*C*H$_2$CH$_3$), 25.4 (*C*H$_2$CH$_3$), 14.0 (CH$_2$*C*H$_3$), 12.1 (CH$_2$*C*H$_3$).

6-Methyl-5-phenylbenzo[*d*]azocine-2,4(1*H*,3*H*)-dione (19ad). Yield: 94%. Mp: 217–222 °C. IR (Nujol, cm^{-1}): ν(C=O), 1697, 1672. HRMS (ESI+, m/z): exact mass calcd for $C_{18}H_{16}NO_2$ $[M+H]^+$ 278.1176, found 278.1171, error = 1.61 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.78 (br s, 1 H, NH), 7.50–7.46 (m, 2 H, aromatic), 7.44–7.30 (m, 7 H, aromatic), 4.42 (d, $^2J_{HH}$ = 14.0 Hz, 1 H, CH_2), 3.81 (dd, $^4J_{HH}$ = 1.6 Hz, $^2J_{HH}$ = 14.0 Hz, 1 H, CH_2), 2.05 (s, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 172.1 (C2), 169.2 (C4), 140.2 (C6a), 137.7 (C6), 136.3 (C, Ph), 135.4 (C5), 131.2 (C10a), 129.2 (CH, Ph) 129.1 (CH), 128.9 (CH), 128.7 (CH, Ph), 128.4 (CH), 128.3 (CH), 127.9 (CH), 42.5 (CH_2), 22.1 (Me).

3-Methyl-5,6-diphenylbenzo[*d*]azocine-2,4(1*H*,3*H*)-dione (19ba). Yield: 71%. Mp: 244–248 °C. IR (Nujol, cm^{-1}): ν(C=O), 1703, 1660. HRMS (ESI+, m/z): exact mass calcd for $C_{24}H_{20}NO_2$ $[M+H]^+$ requires 354.1489, found 354.1493, error = 1.27 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.40–7.11 (m, 12 H, H7–10 + Ph), 6.99 (m, 2 H, Ph), 4.68, 4.05 (AB system, $^2J_{HH}$ = 15.2 Hz, 2 H, CH_2), 3.10 (s, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 173.6 (C2), 172.3 (C4), 141.1 (C6a), 138.6 (C, Ph), 138.0, 137.7 (C5/C6), 134.5 (C, Ph), 133.7 (C10a), 130.9 (CH, Ph), 129.9 (C7), 129.3 (CH, Ph + C9/C10), 129.2 (C9/C10), 128.7 (CH, Ph), 128.5 (CH, Ph), 128.3 (C8), 128.2 (CH, Ph), 128.1 (CH, Ph), 44.3 (C1), 31.8 (Me).

5,6-Diethyl-3-methylbenzo[*d*]azocine-2,4(1*H*,3*H*)-dione (19bc). Yield: 70%. Mp: 72–82 °C. IR (Nujol, cm^{-1}): ν(CO), 1708, 1666. HRMS (ESI+, m/z): exact mass calcd for $C_{16}H_{20}NO_2$ $[M+H]^+$ 258.1489, found 258.1496, error = 2.94 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.32–7.22 (m, 4 H, H7–10), 4.33, 3.84 (AB system, $^2J_{HH}$ = 14.8 Hz, 2 H, CH_2CO), 3.10 (s, 3 H, NMe), 2.71 (A part of ABX_3 system, $^2J_{HH}$ = 13.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, C*H*$_2$CH$_3$),

2.62–2.46 (m, 2 H, C*H*$_2$CH$_3$), 2.36 (B part of ABX$_3$ system, 1 H, C*H*$_2$CH$_3$), 1.12 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$C*H*$_3$), 0.91 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$C*H*$_3$). ^{13}C{^{1}H} APT NMR (75.5 MHz, CDCl$_3$): 174.4 (C2), 173.9 (C4), 140.2 (C6a), 137.5 (C5), 137.3 (C6), 132.8 (C10a), 128.8, 128.2, 128.0, 127.1 (C7–10), 44.4 (C1), 31.1 (NMe), 26.3 (*C*H$_2$CH$_3$), 25.4 (*C*H$_2$CH$_3$), 13.5 (CH$_2$*C*H$_3$), 12.0 (CH$_2$*C*H$_3$).

3,6-Dimethyl-5-phenylbenzo[*d*]azocine-2,4(1*H*,3*H*)-dione (19bd). Yield: 57%. Mp: 183–188 °C. IR (Nujol, cm^{-1}): ν(C=O), 1704, 1662. HRMS (ESI+, m/z): exact mass calcd for $C_{19}H_{18}NO_2$ [M+H]$^+$ requires 292.1332, found 292.1335, error = 1.03 ppm. ^{1}H NMR (400.9 MHz, CDCl$_3$): δ 7.46–7.28 (m, 9 H, aromatic), 4.53, 3.95 (AB system, $^2J_{HH}$ = 15.2 Hz, 2 H, CH$_2$), 3.05 (s, 3 H, NMe), 2.08 (s, 3 H, CMe). ^{13}C{^{1}H} APT NMR (75.45 MHz, CDCl$_3$): δ 174.0 (C2), 172.2 (C4), 141.2 (C6a), 137.6 (C6), 135.7 (C, Ph), 135.2 (C5), 131.9 (C10a), 129.4 (CH) 128.83 (CH), 128.76 (CH), 128.73 (CH), 128.5 (CH), 128.2 (CH), 127.2 (CH), 44.4 (C1), 31.6 (NMe), 20.5 (C*Me*).

Trimethyl 2-(2-(carbamoylmethyl)phenyl)ethene-1,1,2-tricarboxylate (20). A solution of **18ab** (101 mg, 0.16 mmol) in MeOH (15 mL) was stirred under a CO atmosphere (1.4 bar) for 24 h. The gradual formation of colloidal Pd was observed. The solvent was removed under reduced pressure, the residue was extracted with Et$_2$O (6 × 5 mL) and the combined extracts were filtered through anhydrous MgSO$_4$. The solvent was evaporated to dryness and the residue was crystallized from CH$_2$Cl$_2$/*n*-hexane to give **20** as a colorless solid, which was filtered off, washed with *n*-hexane and vacuum-dried. Yield: 22 mg, 42%. Mp: 76–83 °C. IR (Nujol, cm^{-1}): ν(NH), 3405, 3194; ν(CO); 1731, 1720, 1658. HRMS (ESI+, m/z): exact mass calcd for $C_{16}H_{18}NO_7$ [M+H]$^+$ 336.1078, found 336.1083, error = 1.5 ppm. ^{1}H NMR (400.9 MHz, CDCl$_3$): δ 7.49 (br d, $^3J_{HH}$ = 7.6 Hz, 1 H, H3, C$_6$H$_4$), 7.39 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H4, C$_6$H$_4$), 7.29 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H5, C$_6$H$_4$), 7.19 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6, C$_6$H$_4$), 6.25 (br, 1 H, NH), 5.33 (br, 1 H, NH), 3.88 (s, 3 H, CO$_2$Me), 3.82 (s, 3 H, CO$_2$Me), 3.60 (s, 2 H, CH$_2$), 3.57 (s, 3 H, CO$_2$Me). ^{13}C NMR (100.8 MHz, CDCl$_3$): δ 172.8 (CONH$_2$), 166.7, 164.1, 163.0 (*C*O$_2$Me), 146.2 (C$_6$H$_4$*C*=C), 133.4 (C2, C$_6$H$_4$), 132.6 (C1, C$_6$H$_4$), 131.0 (C$_6$H$_4$C=*C*), 130.04 (C3, C$_6$H$_4$), 129.98 (C4, C$_6$H$_4$), 128.3 (C6, C$_6$H$_4$), 127.4 (C5, C$_6$H$_4$), 53.3, 53.2, 52.8 (CO$_2$*Me*), 40.5 (CH$_2$).

[Pd{C(Ph)=C(Ph)C$_6$H$_4$CH$_2$C(O)NH$_2$-2}(CN^{t}Bu)(tmeda)]TfO (21a). To a solution of **18aa** (194 mg, 0.28 mmol) in CH$_2$Cl$_2$ (10 mL) was added ^{t}BuNC (33 μL, 0.29 mmol) and the mixture was stirred for 1 h. The addition of *n*-pentane (10 mL) led to the

precipitation of a colorless solid, which was filtered off, washed with a 1:1 CH_2Cl_2/*n*-pentane mixture (5 × 3 mL) and vacuum-dried to give **21a**·0.5H_2O. Yield: 134 mg, 61%. Mp: 167–169 °C (dec). Anal. Calcd for $C_{34}H_{44}F_3N_4O_{4.5}PdS$: C, 52.61; H, 5.71; N, 7.22; S, 4.13. Found: C, 52.51; H, 5.99; N, 7.32; S, 3.85. IR (Nujol, cm^{-1}): ν(NH), 3601, 3408, 3188; ν(CN), 2206; ν(CO), 1691. ^{1}H NMR (400.9 MHz, CD_2Cl_2, 263 K): δ 7.87 (d, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.53 (m, 1 H, Ar), 7.42–7.37 (m, 2 H, Ar), 7.20–7.07 (m, 8 H, Ph), 6.91 (m, 2 H, Ph), 4.59 (br, 1 H, NH), 4.10 (br, 1 H, NH), 3.46, 3.20 (AB system, $^2J_{HH}$ = 14.8 Hz, 2 H, CH_2, acetamide), 3.16–3.13 (m, 1 H, CH_2, tmeda), 2.86–2.75 (m, 1 H, CH_2, tmeda), 2.64 (s, 3 H, Me, tmeda), 2.54 (s, 3 H, Me, tmeda), 2.49–2.37 (m, 2 H, CH_2, tmeda), 2.25 (s, 3 H, Me, tmeda), 1.74 (s, 3 H, Me, tmeda), 1.68 (s, 1 H, H_2O), 1.52 (s, 9 H, ^{t}Bu).

[Pd{C(CO$_2$Me)=C(CO$_2$Me)C$_6$H$_4$CH$_2$C(O)NH$_2$-2}(CN^{t}Bu)(tmeda)]TfO (21b). To a solution of **18ab** (102 mg, 0.16 mmol) in CH_2Cl_2 (10 mL) was added ^{t}BuNC (18 μL, 0.16 mmol). The mixture was stirred for 10 min and filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (1 mL) and addition of Et_2O (20 mL) led to the precipitation of a colorless solid, which was collected by filtration and recrystallized from CH_2Cl_2/Et_2O to give **21b**·H_2O. Yield: 78 mg, 65%. Anal. Calcd for $C_{26}H_{41}F_3N_4O_9PdS$: C, 41.69; H, 5.52; N, 7.48; S, 4.28. Found: C, 41.49; H, 5.25; N, 7.50; S, 4.18. Mp: 101–105 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3423, 3334, 3190; ν(CN), 2222; ν(CO), 1715, 1673. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.55 (m, 1 H, Ar), 7.44 (m, 3 H, Ar), 6.20 (br, 1 H, NH), 5.56 (br, 1 H, NH), 3.86 (s, 3 H, CO_2Me), 3.68 (s, 3 H, CO_2Me), 3.44 (s, 2 H, CH_2, acetamide), 2.95 (m, 1 H, CH_2, tmeda), 2.80 (s, 3 H, Me, tmeda), 2.74 (s, 3 H, Me, tmeda), 2.61 (m, 2 H, CH_2, tmeda), 2.48 (m, 4 H, CH_2, Me, tmeda), 2.23 (br, 3 H, Me, tmeda), 1.86 (br, 2 H, H_2O), 1.63 (s, 9 H, ^{t}Bu). ^{13}C{^{1}H} APT NMR (75.5 MHz, $CDCl_3$): δ 172.5 ($CONH_2$), 171.4 (CO_2Me), 163.5 (CO_2Me), 159.1 (PdC), 138.4 (C, Ar), 134.5 (C, Ar), 134.3 (Ar*C*=C), 130.5 (CH, Ar), 130.0 (CH, Ar), 129.1 (CH, Ar), 127.2 (CH, Ar), 63.1 (CH_2, tmeda), 60.5 (CMe_3), 59.1 (CH_2, tmeda), 52.4 (CO_2Me), 52.1 (Me, tmeda), 52.0 (CO_2Me), 51.2 (Me, tmeda), 49.5 (Me, tmeda), 49.1 (Me, tmeda), 40.4 (CH_2, acetamide), 29.7 (CMe_3). (C≡N not observed).

[Pd{C(CO$_2$Me)=C(CO$_2$Me)C$_6$H$_4$CH$_2$C(O)NH$_2$-2}(CNXy)(tmeda)]TfO (21b'). This pale yellow compound was obtained as a monohydrate as described for **21b**·H_2O, from **18ab** (139.4 mg, 0.22 mmol) and XyNC (28.3 mg, 0.22 mmol). Yield: 143 mg, 83%. Anal. Calcd for $C_{30}H_{41}F_3N_4O_9PdS$: C, 45.20; H, 5.18; N, 7.03; S, 4.02. Found: C, 45.19; H, 4.90; N, 7.01; S, 3.87. Mp: 89 °C. IR (Nujol, cm^{-1}): ν(NH), 3426, 3335, 3187; ν(CN), 2199; ν(CO), 1710, 1684. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.79 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar),

7.5 (br t, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.46 (td, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.37–7.33 (m, 2 H, Ar + *p*-H, Xy), 7.19 (d, $^{3}J_{HH}$ = 7.6 Hz, 2 H, *m*-H, Xy), 5.97 (br, 1 H, NH), 5.44 (br, 1 H, NH), 3.87 (s, 3 H, CO_2Me), 3.67 (s, 3 H, CO_2Me), 3.31 (d, $^{2}J_{HH}$ = 15.6 Hz, 1 H, CH_2, acetamide), 3.15–2.45 (m, 17 H, Me, CH_2, tmeda, CH_2, acetamide), 2.41 (br s, 6 H, Me, Xy), 1.80 (br, 2 H, H_2O). $^{13}C\{^{1}H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 172.0 ($CONH_2$), 171.0 (CO_2Me), 163.5 (CO_2Me), 136.0 (*o*-C, Xy), 135.4 (Ar*C*=C), 134.3 (C, Ar), 131.3 (CH, Ar), 130.7 (CH, Ar), 130.1 (CH, Ar), 129.3 (CH, Ar), 128.7 (*m*-C, Xy), 127.6 (*p*-C, Xy), 124.7 (br, *i*-C, Xy), 63.7 (CH_2, tmeda), 59.3 (CH_2, tmeda), 52.8 (Me, tmeda), 52.5 (CO_2Me), 52.2 (CO_2Me), 51.7 (Me, tmeda), 49.9 (Me, tmeda), 40.0 (CH_2, acetamide), 18.6 (Me, Xy).

(*Z*)-3-(2-(carbamoylmethyl)phenyl)-*N*-(2,6-dimethylphenyl)-2,3-diphenylacrylamide (22a). To a solution of **18aa** (202 mg, 0.30 mmol) in $CHCl_3$ (20 mL) was added XyNC (39 mg, 0.30 mmol) and the mixture was refluxed for 48 h. The resulting dark suspension was filtered through anhydrous $MgSO_4$, the solvent was removed under vacuum and the residue was chromatographed on silica gel, using a 2:1 CH_2Cl_2/*n*-hexane mixture as eluent. A colorless fraction with Rf = 0.65–0.8 was collected. Compound **22a** was obtained as a colorless solid after evaporation of the solvents. Yield: 32 mg, 24%. Mp: 275–278 °C. IR (Nujol, cm^{-1}): ν(CO), 1667, 1639. HRMS (ESI+, m/z): exact mass calcd for $C_{31}H_{29}N_2O_2$ $[M+H]^+$ requires 461.2224, found 461.2228, error = 0.98 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.61 (m, 1 H, C_6H_4), 7.58 (br s, 1 H, NH), 7.37–7.22 (m, 8 H, C_6H_4 + Ph), 7.17 (br s, 1 H, NH), 7.11–7.05 (m, 3 H, Ph), 7.02–6.91 (m, 5 H, Ph + *m*-H, *p*-H, Xy), 5.19 (br s, 1 H, NH), 3.32, 3.10 (AB system, $^{2}J_{HH}$ = 16.0 Hz, 2 H, CH_2), 1.94 (s, 6 H, Me, Xy). $^{13}C\{^{1}H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 174.0 ($CONH_2$), 168.0 (*C*ONXy), 145.5 (C_6H_4C=C), 141.6 (C1, C_6H_4), 139.3 (C, Ph), 137.9 (C, Ph), 137.8 (C_6H_4C=*C*), 135.3 (*o*-C, Xy), 133.9 (C2, C_6H_4), 133.4 (*i*-C, Xy), 131.2 (C3, C_6H_4), 130.6 (C6, C_6H_4), 130.36 (CH, Ph), 130.28 (CH, Ph), 128.8 (C4, C_6H_4), 128.75 (CH, Ph), 128.2 (*m*-C, Xy), 128.1 (CH, Ph), 127.9 (CH, Ph), 127.8 (CH, Ph), 127.5 (C5, C_6H_4), 127.3 (*p*-C, Xy), 40.9 (CH_2), 18.6 (Me, Xy).

(*Z*)-3-(2-(methylcarbamoylmethyl)phenyl)-*N*-(2,6-dimethylphenyl)-2,3-diphenylacrylamide (22b). To a solution of **18ba** (97 mg, 0.14 mmol) in acetone (25 mL) was added XyNC (70 mg, 0.53 mmol) and the mixture was stirred for 24 h, whereupon a red solution was obtained. The solvent was removed under vacuum and the residue was chromatographed on silica gel, using a 2:1 EtOAc/*n*-hexane mixture as eluent. A colorless fraction with Rf = 0.6 was collected. Compound **22b** was obtained as a colorless solid after evaporation of the solvents. Yield: 33 mg, 50%. Mp: 290–293 °C. IR (Nujol, cm^{-1}): ν(NH),

3261; ν(CO), 1655, 1629. HRMS (ESI+, m/z): exact mass calcd for $C_{32}H_{31}N_2O_2$ $[M+H]^+$ requires 475.2380, found 475.2390, error = 2.07 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.86 (br, 1 H, NH), 7.62 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, C_6H_4), 7.35–7.23 (m, 7 H, C_6H_4 + Ph), 7.17 (m, 1 H, C_6H_4), 7.12–7.04 (m, 3 H, Ph), 7.02–6.89 (m, 6 H, Ph + NH + *m*-H + *p*-H, Xy), 3.19, 3.10 (AB system, $^2J_{HH}$ = 16.0 Hz, 2 H, CH_2), 2.68 (d, $^3J_{HH}$ = 4.4 Hz, 3 H, Me), 1.97 (s, 6 H, Me, Xy). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 171.9 (*C*ONMe), 167.9 (*C*ONXy), 145.1 (C_6H_4C=C), 141.7 (C1, C_6H_4), 139.3 (C, Ph), 138.0 (C, Ph), 137.8 (C_6H_4C=*C*), 135.3 (*o*-C, Xy), 133.9 (C2, C_6H_4), 133.6 (*i*-C, Xy), 131.5 (C3, C_6H_4), 130.7 (C6, C_6H_4), 130.35 (CH, Ph), 130.29 (CH, Ph), 128.8 (C4, C_6H_4), 128.7 (CH, Ph), 128.1 (*m*-C, Xy), 127.9 (CH, Ph), 127.8 (CH, Ph), 127.7 (CH, Ph), 127.5 (C5, C_6H_4), 127.1 (*p*-C, Xy), 41.5 (CH_2), 26.4 (N*Me*), 18.5 (Me, Xy).

(*Z*)-3-(2-(dimethylcarbamoylmethyl)phenyl)-*N*-(2,6-dimethylphenyl)-2,3-diphenylacrylamide (22c). This colorless compound was obtained as described for **22b**, from **18ca** (116 mg, 0.16 mmol) and XyNC (85 mg, 0.66 mmol). Yield: 42 mg, 53%. Mp: 203–208 °C. IR (Nujol, cm^{-1}): ν(NH), 3204; ν(CO), 1666, 1634. HRMS (ESI+, m/z): exact mass calcd for $C_{33}H_{33}N_2O_2$ $[M+H]^+$ requires 489.2537, found 489.2539, error = 0.45 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 10.02 (s, 1 H, NH), 7.82 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, C_6H_4), 7.38 (br t, $^3J_{HH}$ = 7.6 Hz, 1 H, C_6H_4), 7.31 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, C_6H_4), 7.28–7.26 (m, 2 H, Ph), 7.22–7.16 (m, 3 H, Ph), 7.14–7.05 (m, 4 H, Ph + C_6H_4), 6.97–6.91 (m, 3 H, *m*-H, *p*-H, Xy), 6.84–6.82 (m, 2 H, Ph), 3.16, 2.99 (AB system, $^2J_{HH}$ = 17.2 Hz, 2 H, CH_2), 2.97 (s, 3 H, NMe), 2.68 (s, 3 H, NMe), 1.90 (br, 6 H, Me, Xy). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 171.2 (*C*ONMe), 168.0 (*C*ONXy), 141.9 (C1, C_6H_4), 140.4 (C_6H_4C=C), 139.7 (C, Ph), 139.5 (C_6H_4C=*C*), 138.8 (C, Ph), 135.3 (*o*-C, Xy), 134.6 (*i*-C, Xy), 134.2 (C2, C_6H_4), 132.1 (C6, C_6H_4), 132.0 (C3, C_6H_4), 130.3 (CH, Ph), 130.1 (CH, Ph), 128.4 (C4, C_6H_4), 128.1 (CH, Ph + C5, C_6H_4), 127.9 (*m*-C, Xy), 127.7 (CH, Ph), 127.14 (CH, Ph), 127.09 (CH, Ph), 126.2 (*p*-C, Xy), 39.2 (CH_2), 37.2 (NMe), 35.9 (NMe); Me of Xy not observed.

(Z)-2-(2-(2-Cyano-1,2-diphenylvinyl)phenyl)acetamide (23a). *Method A:* To a solution of **18aa** (147 mg, 0.21 mmol) in acetone (20 mL) was added KCN (15 mg, 0.23 mmol) and the mixture was stirred for 15 h. The solvent was removed under reduced pressure, $CHCl_3$ (20 mL) was added, and the resulting suspension was refluxed for 24 h, whereupon the gradual formation of colloidal Pd was observed. The solvent was evaporated to dryness, the residue was extracted with a 1:10 $CHCl_3/Et_2O$ mixture (20 + 5 × 3 mL) and the combined extracts were filtered through anhydrous $MgSO_4$. The filtrate was evaporated to dryness and

the residue was crystallized from CH_2Cl_2/*n*-hexane (10 mL) to give **23a** as a colorless solid, which was filtered off, washed with *n*-hexane (3 × 3 mL) and vacuum-dried. Yield: 44 mg, 61%. *Method B:* A solution of **18aa** (155 mg, 0.23 mmol) and ^{t}BuNC (26.2 mg, 0.23 mmol) in $CHCl_3$ (15 mL) was refluxed for 24 h, whereupon the gradual formation of colloidal Pd was observed. The reaction mixture was worked up as described for method A to give **23a**. Yield: 42 mg, 55%. Mp: 198–204 °C. IR (Nujol, cm^{-1}): ν(NH), 3398, 3203; ν(CN), 2210; ν(CO), 1655. HRMS (ESI+, m/z): exact mass calcd for $C_{23}H_{19}N_2O$ $[M+H]^+$ requires 339.1492, found 339.1491, error = 0.29 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.55–7.44 (m, 3 H, H3, H4, H5, C_6H_4), 7.43–7.37 (m, 1 H, H6, C_6H_4), 7.34–7.14 (m, 8 H, Ph), 7.03–7.00 (m, 2 H, Ph), 5.25 (br s, 1 H, NH), 5.21 (br s, 1 H, NH), 3.43, 3.37 (AB system, $^2J_{HH}$ = 15.6 Hz, 2 H, CH_2). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 172.2 (CO), 156.4 (*C*=CCN), 140.7 (C, C_6H_4), 137.0 (C, Ph), 133.4 (C, Ph), 133.1 (C, C_6H_4), 131.4 (C, C_6H_4), 130.8 (CH, C_6H_4), 130.17 (CH, Ph), 130.13 (CH, C_6H_4), 129.6 (CH, Ph), 129.5 (CH, Ph), 128.9 (CH, Ph), 128.7 (CH, Ph), 128.5 (CH, Ph), 128.2 (CH, C_6H_4), 119.4 (CN), 114.6 (C=*C*CN), 40.7 (CH_2).

(*Z*)-2-(2-(2-Cyano-1,2-dyphenylvinyl)phenyl)-*N*-methylacetamide (23b). This colorless compound was prepared as described for **23a** (method A), from **18ba** (83 mg, 0.12 mmol) and KCN (8 mg, 0.12 mmol). Yield: 28 mg, 67%. Mp: 170–173 °C. IR (Nujol, cm^{-1}): ν(NH), 3282; ν(CN), 2209; ν(CO), 1640. HRMS (ESI+, m/z): exact mass calcd for $C_{24}H_{21}N_2O$ $[M+H]^+$ requires 353.1648, found 353.1655, error = 1.81 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.57–7.53 (m, 1 H, H3, C_6H_4), 7.51–7.46 (m, 2 H, H4, H5, C_6H_4), 7.38–7.35 (m, 1 H, H6, C_6H_4), 7.30–7.24 (m, 5 H, Ph), 7.22 (m, 1 H, Ph), 7.18–7.14 (m, 2 H, Ph), 7.00 (m, 2 H, Ph), 5.18 (br, 1 H, NH), 3.39, 3.33 (AB system, $^2J_{HH}$ = 16.0 Hz, 2 H, CH_2), 2.69 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 170.4 (CO), 156.5 (*C*=CCN), 140.9 (C, C_6H_4), 136.9 (C, Ph), 133.3 (C, Ph), 133.2 (C, C_6H_4), 131.7 (CH, C_6H_4), 130.7 (CH, C_6H_4), 130.1 (CH, C_6H_4 + Ph), 129.6 (CH, Ph), 129.4 (CH, Ph), 128.9 (CH, Ph), 128.7 (CH, Ph), 128.4 (CH, Ph), 128.2 (CH, C_6H_4), 119.3 (CN), 114.6 (C=*C*CN), 41.3 (CH_2), 26.5 (Me).

(*Z*)-2-(2-(2-Cyano-1,2-dyphenylvinyl)phenyl)-*N*,*N*-dimethylacetamide (23c). This colorless compound was prepared as described for **23a** (method A), from **18ca** (116 mg, 0.16 mmol) and KCN (11 mg, 0.17 mmol). Yield: 37 mg, 62%. *Method B:* A solution of **18ca** (113 mg, 0.16 mmol) and ^{t}BuNC (18.4 μL, 0.16 mmol) in $CHCl_3$ (15 mL) was refluxed for 24 h, whereupon the gradual formation of colloidal Pd was observed. The reaction mixture was worked up as described for method A to give **23c**. Yield: 17 mg, 29%. Mp: 122-132 °C. IR

(Nujol, cm^{-1}): ν(CN), 2202; ν(CO), 1646. HRMS (ESI+, m/z): exact mass calcd for $C_{25}H_{23}N_2O$ $[M+H]^+$ requires 367.1805, found 367.1821, error = 4.37 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.46-7.39 (m, 3 H, H3, H4, H5 of C_6H_4), 7.34-7.26 (m, 6 H, H6 of C_6H_4 + Ph), 7.23-7.19 (m, 1 H, Ph), 7.16-7.13 (m, 2 H, Ph), 7.04-7.01 (m, 2 H, Ph), 3.58, 3.45 (br, 2 H, CH_2), 2.89 (s, 3 H, Me), 2.80 (s, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 170.2 (CO), 156.8 (*C*=CCN), 139.9 (C, C_6H_4), 137.2 (C, Ph), 133.9 (C, Ph), 133.6 (C, C_6H_4), 130.4 (CH, Ph), 130.3 (CH, C_6H_4), 129.9 (CH, C_6H_4), 129.8 (CH, C_6H_4), 129.6 (CH, Ph), 129.3 (CH, Ph), 128.72 (CH, Ph), 128.67 (CH, Ph), 128.2 (CH, Ph), 127.3 (CH, C_6H_4), 119.2 (*C*N), 113.6 (C=*C*CN), 38.6 (CH_2), 37.5 (Me), 35.5 (Me).

[Pd{C(Ph)=C(Ph)C$_6$H$_4$CH$_2$C(O)NH$_2$-2}(CN)(tmeda)] (24). To a solution of **17a** (150 mg, 0.22 mmol) in acetone (25 mL) was added KCN (14 mg, 0.22 mmol) and the mixture was stirred for 15 h. The solvent was removed under reduced pressure, the residue was extracted with CH_2Cl_2 (6 × 5 mL) and the combined extracts were filtered through Celite. Partial evaporation of the filtrate (3 mL) and addition of *n*-pentane (15 mL) led to the precipitation of a colorless solid, which was filtered off, washed with *n*-pentane (3 × 3 mL) and vacuum-dried to give **24**. The product was purified by recrystallization from CH_2Cl_2/*n*-pentane. Yield: 98 mg, 80%. Anal. Calcd for $C_{29}H_{34}N_4OPd$: C, 62.09; H, 6.11; N, 9.99. Found: C, 61.64; H, 6.03; N, 9.90. Mp: 180 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3311, ν(CN), 2120; ν(CO), 1680. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.74 (d, $^3J_{HH}$ = 6.0 Hz, 1 H, Ar), 7.61 (br s, 1 H, NH), 7.38-7.34 (m, 1 H, Ar), 7.33-7.27 (m, 4 H, Ar + Ph), 7.13 (t, $^3J_{HH}$ = 7.2 Hz, 2 H, Ph), 7.09-7.02 (m, 1 H, Ph), 6.99-6.91 (m, 3 H, Ph), 6.86-6.82 (m, 2 H, Ph), 5.12 (br s, 1 H, NH), 3.90 (d, $^2J_{HH}$ = 15.6 Hz, 1 H, CH_2, acetamide), 2.99 (td, $^3J_{HH}$ = 3.2 Hz; $^2J_{HH}$ = 12.8 Hz, 1 H, CH_2, tmeda), 2.69-2.58 (m, 8 H, CH_2, tmeda, acetamide + Me), 2.28 (s, 3 H, Me), 2.28-2.18 (m, 2 H, CH_2, tmeda), 1.77 (s, 3 H, Me). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 175.3 (CO), 148.7 (PdC), 147.8 (C, Ar), 144.8 (C, Ph), 141.3 (PdC=*C*), 140.8 (C, Ph), 135.4 (C, Ar), 131.2 (CN), 130.5 (CH, Ph), 130.4 (CH, Ar), 129.9 (CH, Ph), 127.8 (CH, Ar), 127.7 (CH, Ph), 127.3 (CH, Ph), 127.1 (CH, Ar), 125.3 (CH, Ph), 124.9 (CH, Ph), 124.6 (CH, Ar), 62.4 (CH_2, tmeda), 58.2 (CH_2, tmeda), 51.7 (Me), 51.2 (Me), 47.5 (Me), 46.9 (Me), 41.4 (CH_2, acetamide).

(*Z*)-3-(2-(Cyanomethyl)phenyl)-*N*-(2,6-dimethylphenyl)-2,3-diphenylacrylamide (25). To a solution of **18aa** (171 mg, 0.25 mmol) in CH_2Cl_2 (5 mL) was added XyNC (131 mg, 1.00 mmol) and the mixture was stirred for 15 h, whereupon a dark red solution was obtained. The solvent was removed under vacuum, the residue was extracted with a 1:5

CH_2Cl_2/*n*-pentane mixture (10 × 3 mL), and the combined extracts were filtered through Celite. Evaporation of the solvent under reduced pressure and addition of Et_2O (10 mL) and *n*-pentane (10 mL) led to the formation of a colorless solid, which was filtered off, washed with a 1:1 Et_2O/*n*-pentane mixture (5 × 3 mL) and vacuum-dried to give **25**. Yield: 63 mg, 57%. Mp: 217-221 °C. IR (Nujol, cm^{-1}): ν(NH), 3362; ν(CO), 1660. HRMS (ESI+, m/z): exact mass calcd for $C_{31}H_{27}N_2O$ $[M+H]^+$ requires 443.2118, found 443.2122, error = 0.83 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.71 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, C_6H_4), 7.43 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, C_6H_4), 7.40-7.36 (m, 4 H, aromatic + NH), 7.33 (br d, $^3J_{HH}$ = 7.2 Hz, 1 H, C_6H_4), 7.31-7.27 (m, 3 H, Ph), 7.15-7.09 (m, 3 H, Ph), 7.02-6.98 (m, 3 H, Ph + *p*-H, Xy), 6.93 (d, $^3J_{HH}$ = 7.2 Hz, 2 H, *m*-H, Xy), 3.55, 3.37 (AB system, $^2J_{HH}$ = 18.4 Hz, 2 H, CH_2), 1.82 (s, 6 H, Me, Xy). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 167.1 (CO), 140.7 (C1, C_6H_4), 140.6 (C_6H_4C=C), 139.5 (C_6H_4C=*C*), 138.1 (C, Ph), 137.0 (C, Ph), 135.3 (*o*-C, Xy), 133.1 (*i*-C, Xy), 131.4 (C6, C_6H_4), 130.2 (CH, Ph), 129.9 (CH, Ph), 129.6 (C3, C_6H_4), 129.0 (C4, C_6H_4), 128.9 (C2, C_6H_4), 128.6 (C5 of C_6H_4 + CH, Ph), 128.16 (CH, Ph), 128.13 (*m*-C, Xy), 128.0 (*p*-C, Xy), 127.9 (CH, Ph), 127.2 (CH, Ph), 118.9 (CN), 22.5 (CH_2), 18.3 (Me, Xy).

[Pd{C(=NXy)C(Et)=C(Et)$C_6H_4CH_2$CN-2}Cl(CNXy)$_2$] (26). To a solution of **18ac** (120 mg, 0.20 mmol) in dry CH_2Cl_2 (15 mL) was added XyNC (108 mg, 0.82 mmol) and the mixture was stirred for 15 h under an N_2 atmosphere, whereupon a dark red solution was obtained. Partial evaporation of the solvent (2 mL) and addition of *n*-pentane (15 mL) gave a red-orange oil, which was extracted with a 1:5 CH_2Cl_2/*n*-pentane mixture (10 × 3 mL) and the combined extracts were filtered through Celite. Evaporation of the filtrate under reduced pressure and addition of Et_2O (5 mL) and *n*-pentane (5 mL) led to the formation of a colorless solid, which was filtered off, washed with a 1:1 Et_2O/*n*-pentane mixture (5 × 3 mL) and vacuum-dried to give **26**. Yield: 17 mg, 12%. Mp: 162-164 °C (dec). Anal. Calcd for $C_{41}H_{43}ClN_4Pd$: C, 67.12; H, 5.91; N, 7.64. Found: C, 66.83; H, 6.33; N, 7.59. IR (Nujol, cm^{-1}): ν(C≡N), 2203; ν(C≡NXy), 2179; ν(C=N), 1628. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.38 (d, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.26 (t, $^3J_{HH}$ = 7.6 Hz, 2 H, *p*-H, XyNC^c), 7.20 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.11 (t, $^3J_{HH}$ = 7.6 Hz, 4 H, *m*-H, XyNC^c), 7.01 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.93 (d, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.79 (br d, $^3J_{HH}$ = 7.6 Hz, 1 H, *m*-H, XyNC^i), 6.72 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, *p*-H, XyNC^i), 6.63 (br d, $^3J_{HH}$ = 7.6 Hz, 1 H, *m*-H, XyNC^i), 4.08, 3.83 (AB system, $^2J_{HH}$ = 18.4 Hz, 2 H, CH_2), 3.26 (A part of ABX_3 system, $^2J_{HH}$ = 13.4 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, CH_2CH$_3$), 2.79 (B part of ABX_3 system, $^2J_{HH}$ = 13.4 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, CH_2CH$_3$), 2.49 (A part of ABX_3 system, $^2J_{HH}$ = 14.0

Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, CH_2CH$_3$), 2.41-2.32 (m, 13 H, B part of ABX$_3$ system + Me, XyNC^c), 1.99 (br s, 3 H, Me, XyNC^i), 1.65 (br s, 3 H, Me, XyNC^i), 1.39 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$CH_3), 0.99 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$CH_3). ^{13}C{^{1}H} APT NMR (75.45 MHz, CDCl$_3$): δ 149.3 (*i*-C, XyNC^i), 144.8 (ArC=C), 141.6 (C, Ar), 135.5 (*o*-C, XyNC^c), 133.8 (ArC=C), 130.6 (C, Ar), 130.1 (*p*-C, XyNC^c), 128.8 (CH, Ar), 128.4 (*m*-C, XyNC^i), 128.1 (CH, Ar + *m*-C, XyNC^c), 127.5 (CH, Ar), 127.4 (*m*-C, XyNC^i), 127.3 (CH, Ar), 126.8 (*o*-C, XyNC^i), 125.3 (br, *i*-C, XyNC^c), 123.1 (*p*-C, XyNC^i), 118.9 (CN), 27.7, 25.3 (CH$_2$CH$_3$), 22.2 (CH$_2$CN), 19.1 (Me, XyNC^i), 18.8 (Me, XyNC^c), 18.7 (Me, XyNC^i), 14.1, 12.6 (CH$_2$CH$_3$); C=N, one *o*-C of XyNC^i, and C≡N of XyNC^c not observed.

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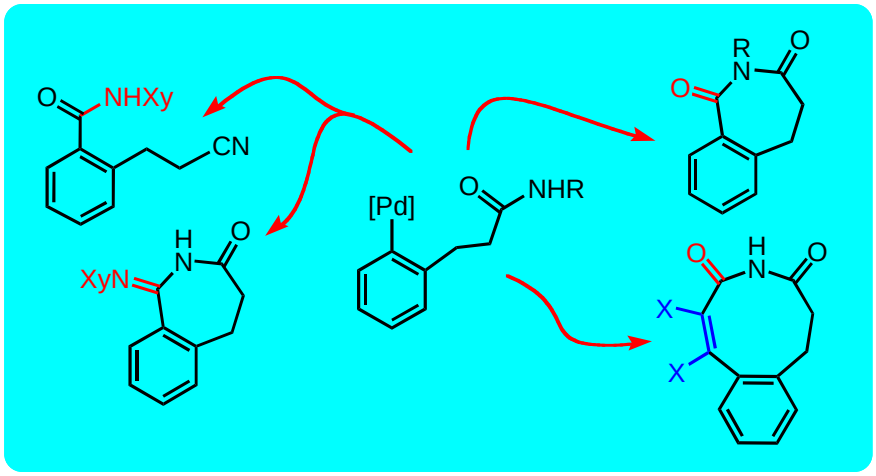
CHAPTER III

Synthesis and Reactivity of Ortho-Palladated 3-Phenylpropanamides. Insertion of CO, XyNC and Alkynes into the Pd–C Bond. Synthesis of Seven- and Nine-Membered Palladacycles and Benzazepine- and Benzazonine-Based Heterocycles



The results of this chapter have been published in:

R. Frutos-Pedreño, P. González-Herrero, J. Vicente, P. G. Jones, *Organometallics* **2013**, *32*, 1892–1904.

Abstract

Aryl palladium complexes [Pd{$C_6H_4(CH_2)_2C(O)NRR'$-2}I(tmeda)] [NRR' = NH_2 (**29a**), NHMe (**29b**), NMe_2 (**29c**); tmeda = *N,N,N′,N′*-tetramethylethylenediamine] are prepared by oxidative addition of the corresponding 3-(2-iodophenyl)propanamides (**28**) to "$Pd(dba)_2$" ([$Pd_2(dba)_3$]·dba; dba = dibenzylideneacetone) in the presence of tmeda. The cationic seven-membered palladacycles [Pd{κ^2C,O-$C_6H_4(CH_2)_2C(O)NRR'$-2}(tmeda)]TfO (**30a-c**) are obtained by reacting **29a-c** with AgTfO. Neutral amidate complexes of the type [Pd{κ^2C,N-$C_6H_4(CH_2)_2C(O)NR$-2}(tmeda)] [R = H (**31a**), Me (**31b**)] are obtained upon deprotonation of the amide function in **29a** or **29b** with KO^{t}Bu. The reaction of **29a** with CO at room temperature affords the stable acyl derivative [Pd{$C(O)C_6H_4(CH_2)_2C(O)NH_2$-2}I(tmeda)] (**32**), while **30a** gives Pd, (tmedaH)TfO, and 4,5-dihydro-2*H*-benzo[*c*]azepine-1,3-dione (**33a**). Compound **33a** can also be obtained in high yield by treating the amidate complex **31a** with CO, while a low yield of 2-methyl-4,5-dihydro-2*H*-benzo[*c*]azepine-1,3-dione (**33b**) was obtained from **31b** under the same conditions. Complexes **29a-c** react with 3 equiv of XyNC to give *trans*-[Pd{$C(=NXy)C_6H_4(CH_2)_2C(O)NRR'$-2}I$(CNXy)_2$] [NRR' = NH_2 (**34a**), NHMe (**34b**), NMe_2 (**34c**)]. By refluxing a $CHCl_3$ solution of **34a** or **29a** and XyNC in 1:1 molar ratio, mixtures of 1-(2,6-dimethylphenylimino)-1,2,4,5-tetrahydrobenzo[c]azepin-3-one (**35a**) and 2-(2-cyanoethyl)-*N*-(2,6-dimethylphenyl)benzamide (**36a**) are obtained. Complexes **30a-c** react with alkynes in 1:1 molar ratio to give nine-membered palladacycles of the type [Pd{κ^2C,O-$C(X)=C(X)C_6H_4(CH_2)_2C(O)NRR'$-2}(tmeda)]TfO [NRR' = NH_2, X = Ph (**37a**), $C_6H_4{}^n$Bu-4 (**38a**), C_6H_4Br-4 (**39a**), CO_2Me (**40a**); NRR' = NHMe, X = Ph (**37b**); NRR' = NMe_2, X = Ph (**37c**)]. The reaction of **30a** with an excess of 3-hexyne gives the complex [Pd{η^3-$C_6H_4(C_4Et_4)(CH_2)_2C(O)NH_2$}(tmeda)]TfO (**41**), containing a spirocyclic ligand coordinated to Pd through a η^3-allylic bond. The derivatives **37a**, **38a** and **39a** react with CO at 50 °C in $CHCl_3$ to give colloidal Pd, (tmedaH)TfO, and the corresponding 6,7-disubstituted 1,2-dihydro-4*H*-benzo[*e*]azonine-3,5-diones (**42, 43, 44**), which result from a CO insertion/C–N reductive coupling sequence.

Introduction

Palladacycles are key intermediates in palladium-mediated cyclization reactions,[1-3] which have become one of the most valuable tools for the synthesis of carbo- and heterocycles.[4] The use of these reactions for the synthesis of medium-size rings through C–C or C–heteroatom coupling is of particular importance, because they form the basic structural motif in many compounds of biological or pharmacological significance[5] and are difficult to prepare by other methods.[6] However, the ring size of the majority of the isolated palladacycles described to date (five or six members)[3, 7] is not appropriate for this purpose because the organic ring generally has one fewer member. Palladacycles larger than six members are relatively uncommon and have been considered difficult to prepare because they tend to be unstable.[1, 8] However, methods for the enlargement of palladacycles are of utility, even when the product can not be isolated, because in many cases the desired organic ring is among the products of decomposition (see below).

Insertion reactions into the Pd–C bond are the best-known method to enlarge the ring size of palladacycles. Thus, alkyne monoinsertion reactions lead to a two-atom enlargement and have allowed the synthesis of seven-[9-15] or, less frequently, eight-membered[11-13, 16-20] palladacycles. Alkyne di-insertions may lead to the expansion of the cyclopalladated ligand through the incorporation of a butadienyl fragment, giving nine-[9, 13, 15, 21, 22] or ten-membered[13] palladacycles that are generally stabilized by the π-coordination of one internal double bond. Similarly, palladacycle enlargements from six to eight members has been achieved by insertion of olefins into the Pd–C bond,[23, 24] while insertion of CO or isocyanides has allowed conversions from six to seven members.[25, 26] In addition, sequential insertion of one or two molecules of alkyne and CO or isocyanides have allowed conversions from six to nine[20] or five to ten[22] members. Some of these enlarged palladacycles undergo depalladation reactions under certain conditions[23,25] or are not isolable and decompose spontaneously[20,24,25,27] to give heterocyclic compounds.

We have previously shown that ortho-palladated phenylacetamides of the type [Pd{$C_6H_4CH_2C(O)NRR'$-2}I(tmeda)] and their cyclopalladated derivatives [Pd{κ^2C,O-$C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO (NRR' = NH_2, NHMe, NMe_2) undergo C–N and/or C–O reductive couplings after the insertion of CO or XyNC into the Pd–C bond, leading to isoquinoline and/or isocoumarin derivatives under relatively mild conditions.[28] These reactions involve the deprotonation of NH_2 or NHMe groups (C–N couplings) or the α-CH_2

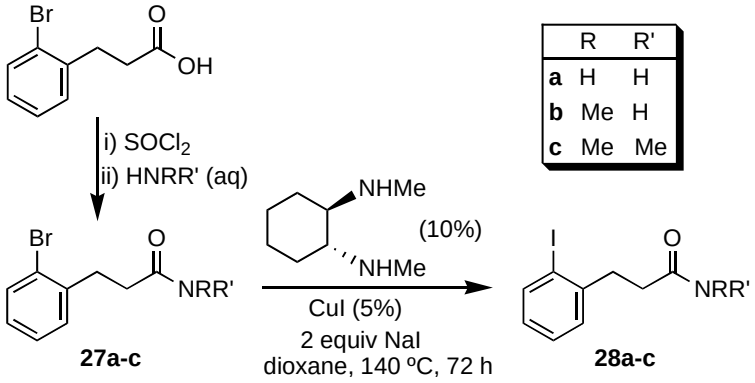
group (C–O couplings), which is effected by the tmeda ligand. In a subsequent study, we described the synthesis of a series of eight-membered palladacycles of the type [Pd{κ^2*C,O*-C(X)=C(X')$C_6H_4CH_2$C(O)NRR'-2}(tmeda)]TfO (NRR' = NH_2, NHMe), obtained from alkyne monoinsertion reactions.[20] The enlarged palladacycles also reacted with CO to give 3-benzazocine-2,4(1*H*,3*H*)-diones, resulting from an analogous CO insertion/C–N reductive coupling sequence. With the main objective of exploring the limits of this methodology for the synthesis of heterocycles of a larger size, the present chapter extends our reactivity studies to ortho-palladated 3-phenylpropanamides, from which seven-membered palladacycles can be obtained that, in turn, can be enlarged through the insertion of alkynes into the Pd–C bond to give nine-membered derivatives. Only a few examples of isolated nine-membered palladacycles have been previously reported that are not stabilized by the coordination of an internal double bond,[22, 29] and none of them were obtained from alkyne monoinsertion reactions. A systematic study of the reactivity of the new complexes toward CO or XyNC has allowed the synthesis of seven- and nine-membered heterocycles.

Results and Discussion

Synthesis of 3-(2-Bromophenyl)propanamides and 3-(2-Iodophenyl)propanamides

The compounds 3-(2-bromophenyl)propanamide (**27a**), 3-(2-bromophenyl)-*N*-methylpropanamide (**27b**), and 3-(2-iodophenyl)-*N,N*-dimethylpropanamide (**27c**) were obtained by reacting 3-(2-bromophenyl)propanoic acid with $SOCl_2$ in dry CH_2Cl_2 at 50 °C for 6 h under an N_2 atmosphere and subsequent addition of an aqueous solution of the corresponding amine NHRR' [R = R' = H (**a**); R = H, R' = Me (**b**); R = R' = Me (**c**)] (56–79% yield) (Scheme III.1). The compounds 3-(2-iodophenyl)propanamide (**28a**), 3-(2-iodophenyl)-*N*-methylpropanamide (**28b**), and 3-(2-iodophenyl)-*N,N*-dimethylpropanamide (**28c**) were prepared in moderate to good yields (60–90%) via copper-catalyzed halogen exchange[30] from the corresponding compound **27** and excess NaI, in the presence of racemic *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine.

Scheme III.1

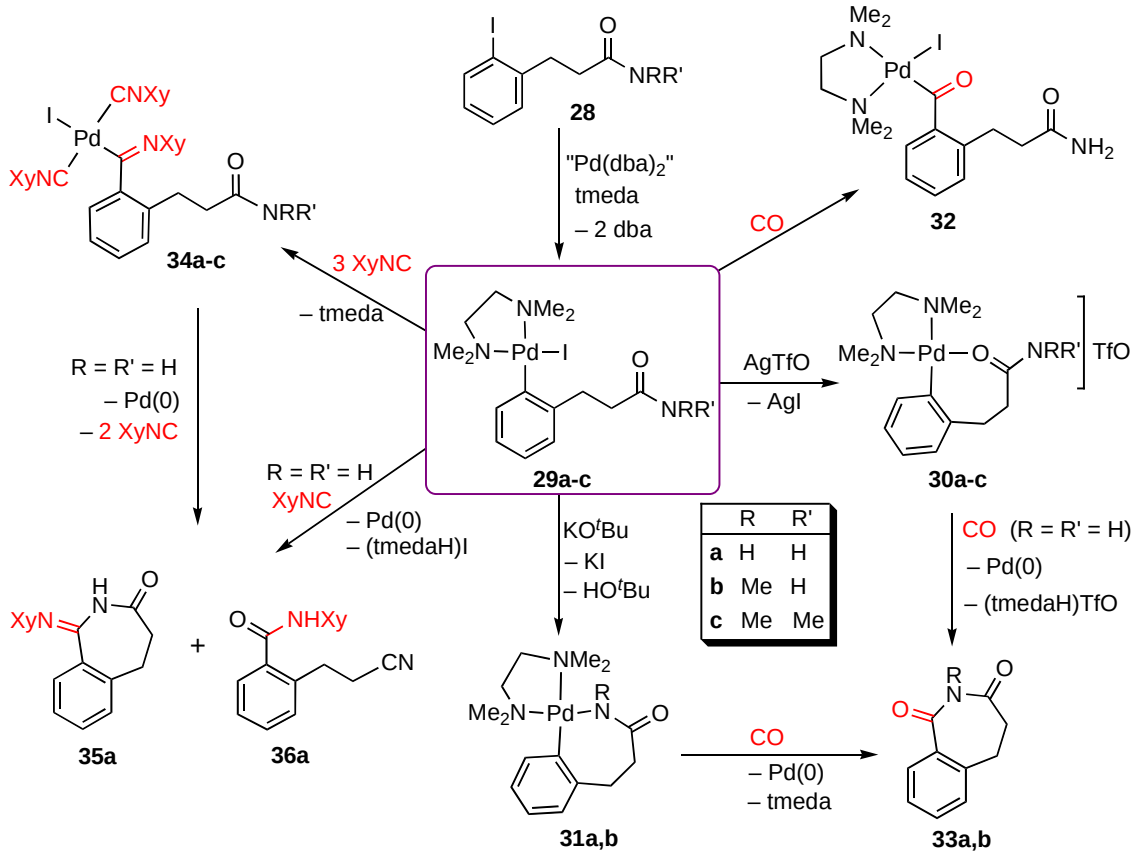


Synthesis of Ortho-Palladated 3-Phenylpropanamides and Cyclometalated Derivatives

The aryl derivatives [Pd{$C_6H_4(CH_2)_2C(O)NRR'$-2}I(tmeda)] [NRR' = NH_2 (**29a**), NHMe (**29b**), NMe_2 (**29c**); Scheme III.2] were obtained in moderate yields by oxidative addition of the corresponding 3-(2-iodophenyl)propanamides (**28**) to "$Pd(dba)_2$" in the presence of tmeda in CH_2Cl_2 at room temperature.

The reactions of complexes **29** with one equiv of AgTfO in acetone led to the precipitation of AgI and the formation of the corresponding cationic palladacycles [Pd{κ^2C,O-$C_6H_4(CH_2)_2C(O)NRR'$-2}(tmeda)]TfO (**30a-c**). These compounds turned out to be highly hygroscopic amorphous solids which could not be crystallized and were isolated by evaporating the solvent. Their IR spectra in CH_2Cl_2 solution show the ν(C=O) band at 1646 (**30a**), 1608 (**30b**) or 1591 (**30c**) cm^{-1}; these frequencies are appreciably lower than those of the corresponding free amides (range 1670-1635 cm^{-1}), which confirms that the amide function is coordinated to the metal through the oxygen atom. Complexes **30a** and **30c** could not be obtained in analytically pure form because reprecipitations from acetone/Et_2O or CH_2Cl_2/Et_2O led to partial decomposition. However, they can be employed for the synthesis of other products (see below).

Scheme III.2



Deprotonation of the amide function in complexes **29a** and **29b** with excess KO^{t}Bu in CH_2Cl_2 led in good yield to the neutral palladacycles [Pd{κ^2C,N-$C_6H_4(CH_2)_2C(O)NR$-2}(tmeda)] [R = H (**31a**), Me (**31b**)], which result from the displacement of the iodo ligand by the nitrogen of the anionic amidate group. Their solid-state IR spectra show the ν(C=O) band at 1551 (**31a**) or 1558 (**31b**) cm^{-1}, which is typical of *N*-coordinated amidato complexes.[31, 32] The attempts to deprotonate the α-CH_2 in the NMe_2 derivative **29c** with KO^{t}Bu were unsuccessful.

Reactions with CO

Treatment of complex **29a** with CO in CH_2Cl_2 at room temperature afforded the expected insertion product [Pd{$C(O)C_6H_4(CH_2)_2C(O)NH_2$-2}I(tmeda)] (**32**) in good yield (Scheme III.2). In contrast to its homolog with *ortho*-palladated phenylacetamide,[28] complex **32** is remarkably stable and we did not observe any decomposition to Pd(0) in solution under CO at room temperature, which implies that the possible C–N reductive coupling is much less favored. We then carried out the reactions of in situ generated solutions

of palladacycles **30a-c** in CH_2Cl_2 with CO (1.4 bar) at room temperature, in the expectation that their cationic nature and cyclic structure would facilitate the insertion/reductive coupling sequence. When starting from the NH_2 derivative **30a**, colloidal Pd, (tmedaH)TfO, and 4,5-dihydro-2*H*-benzo[*c*]azepine-1,3-dione[33] (**33a**; 42% isolated yield) were obtained. However, the NHMe and NMe_2 derivatives (**30b** and **30c**, respectively) were recovered unreacted. With hindsight, it is reasonable to assume that CO inserts reversibly into the Pd–C bond of **30b** and **30c**, but a subsequent C–N or C–O reductive coupling does not occur. The C–N coupling process may be difficult for **30b** because of the lower acidity of the NH proton and the steric hindrance of the methyl group, while the anticipated C–O coupling processes from both **30b** and **30c** may not be possible because the α-CH_2 protons are not acidic enough and thus the necessary deprotonation step does not take place.

The amidate complexes **31a** and **31b** were also treated with CO (1.4 bar) in $CDCl_3$ to test the feasibility of the C–N coupling. Whereas **31a** reacted in 3 h at room temperature to give compound **33a** in 88% yield, derivative **31b** required heating at 60 °C for 24 h to produce a 30% yield of 2-methyl-4,5-dihydro-2*H*-benzo[*c*]azepine-1,3-dione (**33b**), which was identified by its NMR data.[34] The reaction mixture also contained several unidentified species that reverted to complex **31b** upon evaporation of the solvent, which suggests that they are CO insertion or coordination products. This result confirmed that the methyl substituent on the amide function is a major obstacle for the C–N coupling step, consistent with our previous findings that the C–N couplings of *ortho*-palladated phenylacetamides are generally much slower for NHMe derivatives than for their NH_2 homologs.[28]

The reactions of palladacycles **30** and **31** with CO are related to those of cyclopalladated arylalkylamines, which may afford esters[35] or lactams.[25-27, 36, 37] The lack of reactivity of the NMe_2 derivative **30c** contrasts with the ability of classical cyclopalladated *N,N*-dialkylbenzylamines to give C–N reductive coupling products after the insertion of CO into the Pd–C bond by losing one of the alkyl groups.[36]

Reactions with XyNC

The reactions of **29a-c** with three equiv of XyNC (Xy = 2,6-dimethylphenyl) at room temperature gave the iminoacyl complexes *trans*-[Pd{C(=NXy)C_6H_4(CH_2)$_2$C(O)NRR'-2}I(CNXy)$_2$] [NRR' = NH_2 (**34a**), NHMe (**34b**), NMe_2 (**34c**)], which result from the displacement of the tmeda ligand by two of the isocyanide molecules and the insertion of a third isocyanide into the Pd–C bond. Complexes **34a-c** were also obtained when using only

one equiv of isocyanide at room temperature, leaving two-thirds of the starting complex unreacted. The behavior of **29a-c** toward XyNC is quite usual for arylpalladium derivatives[18, 38] but differs from that of the analogous *ortho*-palladated phenylacetamides [Pd{$C_6H_4CH_2C(O)NRR'$-2}I(tmeda)], which react with one equiv of the isocyanide to give iminoisoquinoline or iminoisocoumarin derivatives resulting from an insertion/C–N or C–O reductive coupling sequence.[28] This is a clear indication that the C–N or C–O couplings are much more difficult for the phenylpropanamide derivatives, in agreement with the behavior of acyl complex **32**.

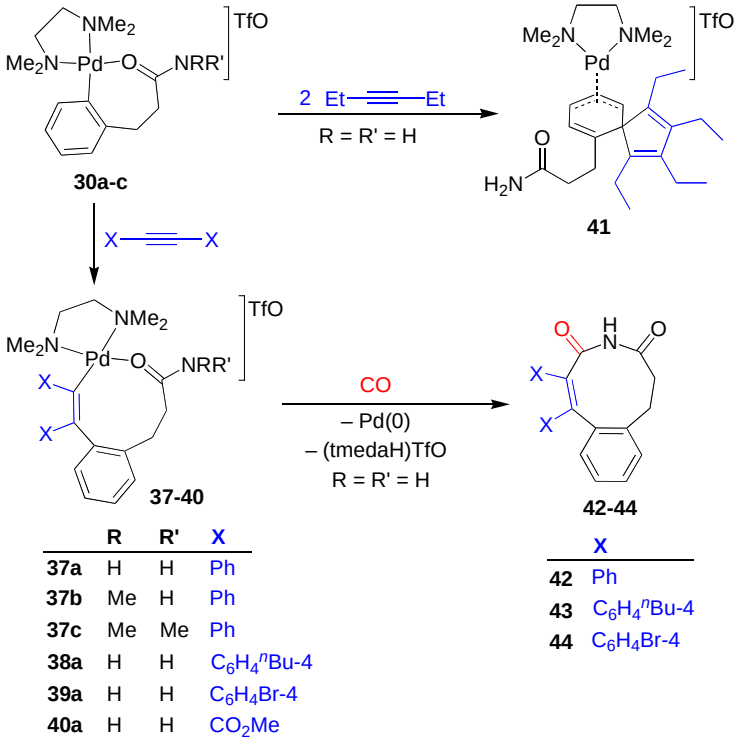
We then attempted the 1:1 reaction of **29a** with XyNC in $CHCl_3$ at reflux temperature, which gave a precipitate of Pd metal, (tmedaH)I, and an approximately 1:0.85 mixture of 1-[(2,6-dimethylphenyl)imino]-1,2,4,5-tetrahydro-3*H*-2-benzazepin-3-one (**35a**) and 2-(2-cyanoethyl)-*N*-(2,6-dimethylphenyl)benzamide (**36a**). A similar mixture, but with a higher proportion of **36a** (0.45:1), was obtained when complex **34a** was stirred at reflux temperature in $CHCl_3$. Thus, two competing transformations of iminoacyl intermediates take place: (i) an intramolecular C–N reductive coupling leading to compound **35a**, and (ii) the hydrolysis of the iminoacyl ligand, which is accompanied by the dehydration of the unsubstituted carbamoyl group to give **36a**. We have previously shown in the previous chapter that a similar hydrolysis/dehydration sequence takes place when the eight-membered palladacycle [Pd{κ^2C,O-$C(Ph)=C(Ph)C_6H_4CH_2C(O)NH_2$-2}(tmeda)]TfO (**18aa**) reacts with 4 equiv of XyNC.[20] The reactions of complexes **29b** or **29c** with XyNC in 1:1 molar ratio in $CHCl_3$ at reflux temperature gave mixtures of products that could not be identified.

Reactions with Alkynes

The reactions of in situ generated solutions of complexes **30** in acetone with various alkynes at room temperature afforded high yields of the nine-membered palladacycles [Pd{κ^2C,O-$C(X)=C(X)C_6H_4(CH_2)_2C(O)NRR'$-2}(tmeda)]TfO [NRR' = NH_2, X = Ph (**37a**), $C_6H_4{}^n$Bu-4 (**38a**), C_6H_4Br-4 (**39a**), CO_2Me (**40a**); NRR' = NHMe, X = Ph (**37b**); NRR' = NMe_2, X = Ph (**37c**)], resulting from the insertion of one molecule of the alkyne into the Pd–C bond (Scheme III.3). These reactions required the use of strictly 1 equiv of the alkyne and were complete in less than 3 h, except for the case of **39a**, which required 20 h. The use of an excess of alkyne led to complex mixtures, probably as a result of polyinsertion reactions. These monoinsertions are thus, in general, considerably faster than those from the six-membered palladacycles [Pd{κ^2C,O-$C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO, previously

depicted by us,[20] which require an excess of the alkyne and longer reaction times. Presumably, the larger size of palladacycles **30** facilitates the ring opening and the alkyne coordination step. The IR spectra of complexes **37**-**40** show the ν(C=O) band in the range 1651-1592 cm^{-1}, indicating that the amide function remains coordinated to the metal through the oxygen atom, which was confirmed by the crystal structure of **37a** (see below).

Scheme III.3



	R	R'	X
37a	H	H	Ph
37b	Me	H	Ph
37c	Me	Me	Ph
38a	H	H	$C_6H_4{}^nBu$-4
39a	H	H	C_6H_4Br-4
40a	H	H	CO_2Me

	X
42	Ph
43	$C_6H_4{}^nBu$-4
44	C_6H_4Br-4

The reaction of **30a** with 3-hexyne gave the complex [Pd{η^3-$C_6H_4(C_4Et_4)(CH_2)_2C(O)NH_2$}(tmeda)]TfO (**41**), which contains a spirocyclic ligand coordinated to Pd through a η^3-allylic bond (Scheme III.3). This type of ligand has been previously reported to arise from the insertion of two molecules of the alkyne and a subsequent cyclization of the resulting butadienyl fragment.[16, 17, 39] Complex **41** was obtained in high yield by using an excess of 3-hexyne, but it is also formed when only one equivalent of this alkyne is employed and the reaction is carried out at low temperatures, and therefore a monoinsertion product analogous to complexes **37**-**40** could not be isolated. The proclivity of 3-hexyne to give polyinsertion products is typical of electron-rich alkynes, for which it is often impossible to isolate the monoinsertion product.[40]

Reactions of Alkyne-Monoinsertion Products with CO. Synthesis of 1,2-Dihydro-4*H*-benzo[*e*]azonine-3,5-diones

Treatment of palladacycles **37a**, **38a** and **39a** with CO (1.4 bar) at 50 °C in $CHCl_3$ for 15 h gave colloidal Pd, (tmedaH)TfO, and the corresponding 6,7-disubstituted 1,2-dihydro-4*H*-benzo[*e*]azonine-3,5-diones (**42, 43, 44**), which were isolated in moderate to good yields (Scheme III.3). These heterocycles are the expected products from a CO insertion/C–N reductive coupling sequence. Only a few nine-membered cyclic imides have been previously reported, which were synthesized via ring expansion reactions[41] or oxidation of nine-membered lactams.[42] Under the same reaction conditions, complex **40a**, containing inserted dimethylacetylenedicarboxylate (DMAD), was recovered unreacted, probably because the low nucleophilicity of the vinylic carbon bonded to palladium hampers the CO insertion step.

The reactions of NHMe and NMe_2 derivatives (**37b** and **37c**, respectively) gave mixtures of unidentified compounds. As previously noted for the seven-membered precursors, the failure to give C–N or C–O coupling products can be ascribed to the steric hindrance of the methyl substituent in **37b** and/or the lower acidity of the NH and α-CH_2 protons in both cases.

Crystal Structures

The crystal structure of complex **29b** is shown in Figure III.1. As usually observed for ortho-substituted arylpalladium derivatives, the aromatic ring of the aryl ligand is almost perpendicular to the Pd coordination mean plane, which can be attributed to the steric demand of the ortho substituent. The coordination environment and bond distances and angles around the Pd center are similar to those found in analogous derivatives.[28, 32, 43] Molecules are linked via hydrogen bonds N–H···I to form zigzag chains parallel to the *c* axis (Figure III.2).

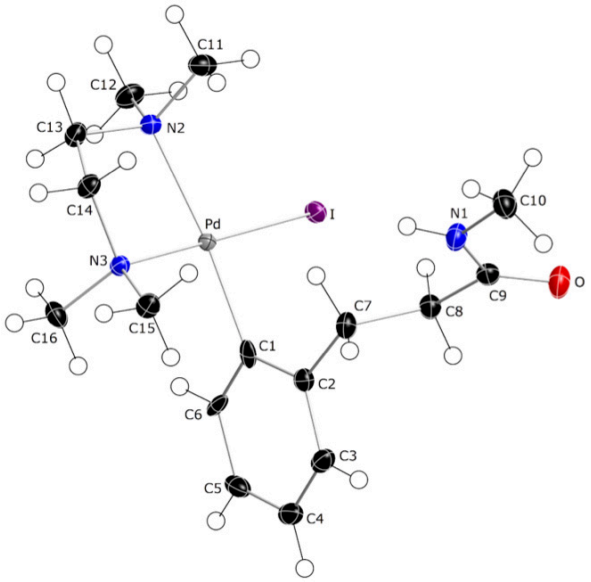


Figure III.1. Thermal ellipsoid plot (50% probability) of complex **29b**. Selected bond distances (Å) and angles (deg): Pd–C(1) 2.015(2), Pd–N(2) 2.2052(16), Pd–N(3) 2.1240(15), Pd–I 2.5827(2); C(1)–Pd–N(3) 92.23(6), N(3)–Pd–N(2) 83.92(6), C(1)–Pd–I 87.83(5), N(2)–Pd–I 96.14(4), C(6)–C(1)–Pd 117.17(14), C(2)–C(1)–Pd 123.40(15).

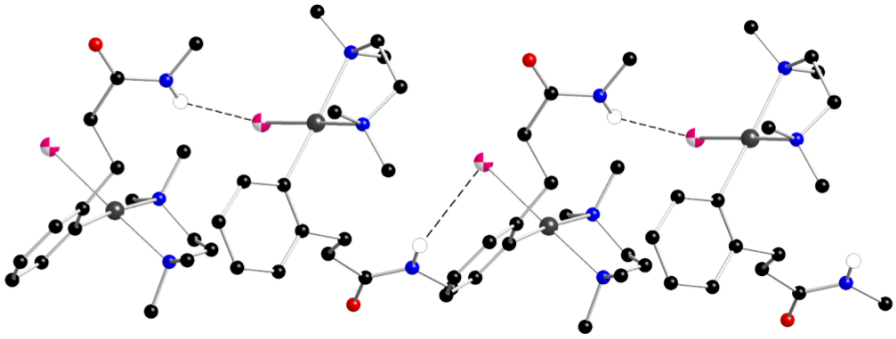


Figure III.2. Association of molecules of **29b** via the *c* glide plane. Hydrogen bonds are indicated by dashed lines.

The amidate group of complex **31a** is coordinated to the Pd atom through the nitrogen, forming a seven-membered ring with a folded conformation (Figure III.3). The Pd–N(1) bond distance of 2.0165(11) Å is similar to that found in the six-membered cyclic amidate [Pd{κ^2*C*,*N*-$C_6H_4CH_2C(O)NMe$-2}(dbbpy)] [2.012(3), 2.009(3) Å][28] and is typical of palladium amidate complexes.[44] The C(9)–O(1) bond length of 1.2566(16) Å is longer than the corresponding distance in the free propanamide group of **29b** [1.223(2) Å], which can be ascribed to a significant delocalization of the negative charge over the N–C=O group. The molecules are linked into loose inversion-symmetric dimers by weak contacts N–H···Pd and C–H_{methyl}···O (Figure III.4).

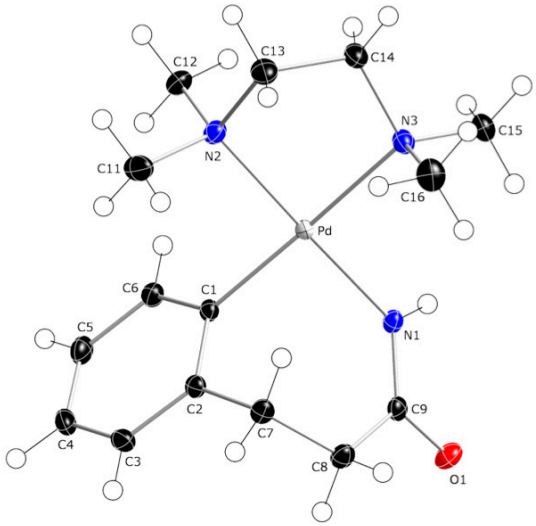


Figure III.3. Thermal ellipsoid plot (50% probability) of complex **31a**. Selected bond distances (Å) and angles (deg): Pd–C(1) 1.9875(12), Pd–N(1) 2.0165(11), Pd–N(2) 2.1058(11), Pd–N(3) 2.1882(11), C(9)–O(1) 1.2566(16), C(9)–N(1) 1.3337(17); C(1)–Pd–N(1) 88.66(5), C(1)–Pd–N(2) 92.80(5), N(1)–Pd–N(3) 94.28(4), N(2)–Pd–N(3) 84.28(4), C(2)–C(7)–C(8) 111.28(11), C(9)–C(8)–C(7) 120.52(11), O(1)–C(9)–N(1) 123.43(12), O(1)–C(9)–C(8) 116.18(12), N(1)–C(9)–C(8) 120.32(12), C(9)–N(1)–Pd 134.03(9).

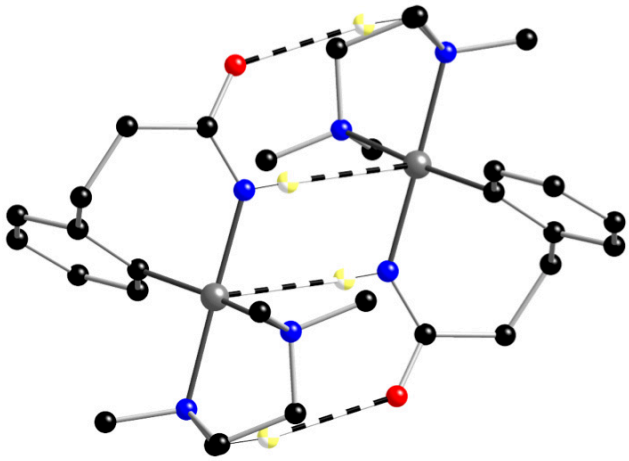


Figure III.4. A loose dimer of **31a**, with weak hydrogen bonds N–H···Pd (2.94 Å) and C–H_{methyl}···O (2.49 Å) indicated as dashed lines.

The crystal structure of compound **36a** is shown in Figure III.5. The asymmetric unit contains two pairs of independent molecules; each pair participates in an infinite chain parallel to the *a* axis, whereby the molecules are linked through N–H···O=C hydrogen bonds between the amide groups.

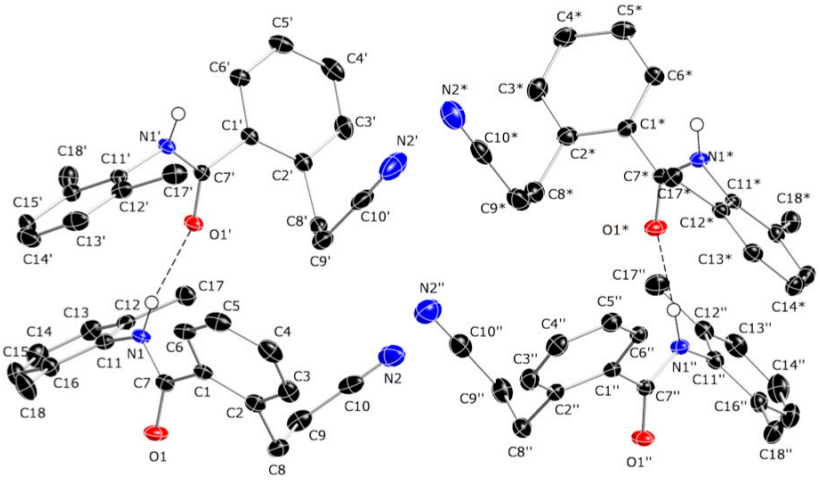


Figure III.5. Thermal ellipsoid plot (50% probability), hydrogen bonds and crystal packing of compound **36a**. Selected bond distances (Å) and angles (deg) of one of the four independent molecules: C(1)–C(7) 1.497(3), C(7)–O(1) 1.238(2), C(7)–N(1) 1.345(3), C(11)–N(1) 1.435(3), C(10)–N(2) 1.143(3); O(1)–C(7)–N(1) 122.0(2), O(1)–C(7)–C(1) 121.2(2), N(1)–C(7)–C(1) 116.77(18), C(7)–N(1)–C(11) 121.02(17), N(2)–C(10)–C(9) 179.5(3).

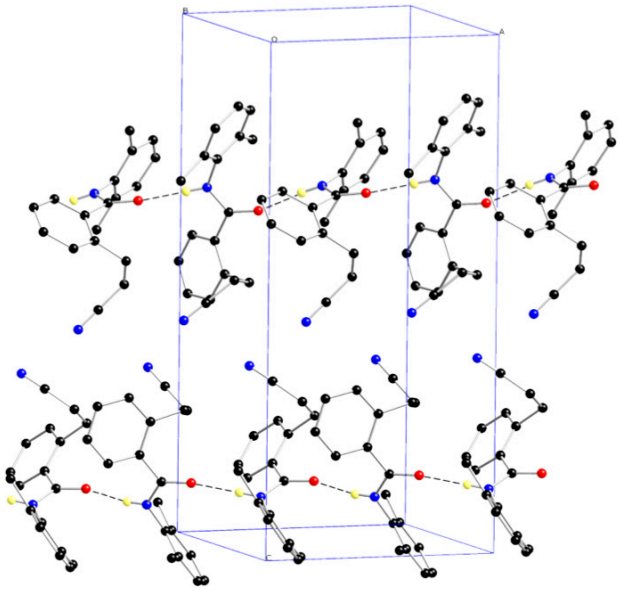


Figure III.6. Packing diagram of **36a**, showing chains of molecules linked by hydrogen bonds (dashed lines). The upper chain consists of molecules 3, 4, 3, 4 ... and the lower chain of 2, 1, 2, 1 ..., in each case starting from the left.

The crystal structure of complex **37a** (Figure III.7) shows that the diphenylacetylene molecule has inserted in a *syn* fashion, as usual for alkyne monoinsertions, while the amide group remains coordinated to the Pd through the oxygen. The conformation of the resulting *C,O*-palladacycle can be approximately described as boat-chair. The square-planar

coordination environment around the Pd center is slightly distorted, mainly because of the small bite of the tmeda ligand [angle N(2)-Pd-N(3): 85.59(4)°], while the nine-membered ring does not seem to cause any strain, as deduced from the C(1)–Pd–O(1) angle of 90.47(4)°. The Pd–C(1) bond distance of 2.0039(11) Å is typical of vinylpalladium complexes.[12, 14-16, 18, 45] The Pd–O(1) distance of 2.0498(9), is slightly shorter than that found in the eight-membered palladacycle [Pd{κ^2C,O-C(Ph)=C(Ph)$C_6H_4CH_2C(O)NH_2$-2}(tmeda)]TfO [2.0682(11) Å].[20] The two H atoms of the NH_2 group are each involved in a hydrogen bond with one oxygen atom of different triflate anions.

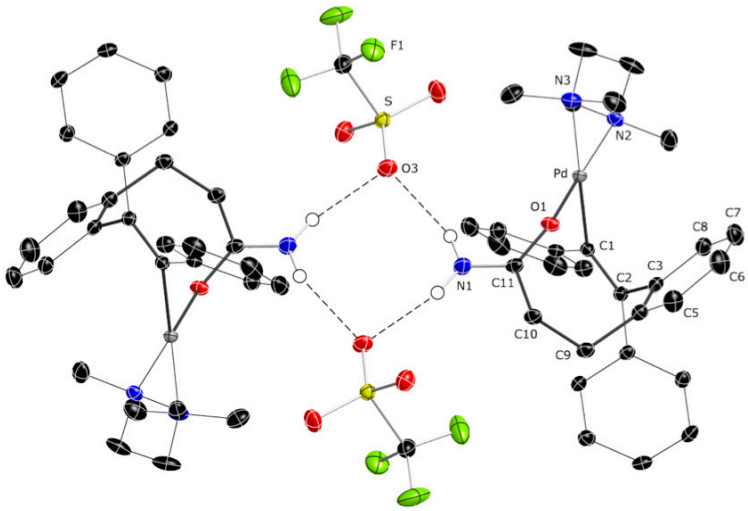


Figure III.7. Thermal ellipsoid plot (50% probability) and hydrogen bonds (dashed lines) in an inversion-symmetric dimer of complex **37a**. Selected bond distances (Å) and angles (deg): Pd–C(1) 2.0039(11), Pd–O(1) 2.0498(9), Pd–N(2) 2.0889(10), Pd–N(3) 2.1524(11), O(1)–C(11) 1.2547(15), N(1)–C(11) 1.3199(17), C(1)–C(2) 1.3534(16), C(2)–C(3) 1.5015(16); C(1)–Pd–O(1) 90.47(4), C(1)–Pd–N(2) 96.38(4), O(1)–Pd–N(3) 87.44(4), N(2)–Pd–N(3) 85.59(4), C(11)–O(1)–Pd 134.38(8), C(2)–C(1)–Pd 118.42(9), C(1)–C(2)–C(3) 119.94(10), C(4)–C(9)–C(10) 112.69(10), C(11)–C(10)–C(9) 111.75(10), O(1)–C(11)–N(1) 123.21(12), O(1)–C(11)–C(10) 117.48(11), N(1)–C(11)–C(10) 119.31(11).

The structure of complex **41** (Figure III.8) was solved as a CH_2Cl_2 monosolvate. The spirocyclic ligand is coordinated to palladium via η^3-allylic interaction through the atoms C6, C7, and C8. The coordination environment around the metal is similar to that found in analogous [Pd(η^3-allyl)(tmeda)]$^+$ derivatives.[46] The cations are linked by hydrogen bonds N–H···O across inversion centers; the triflate anion is connected to the amide moiety and to the CH_2Cl_2 molecule through one N–H···O and two short C–H···O hydrogen bonds. The extended structure consists of inversion-symmetric dimers (Figure III.9).

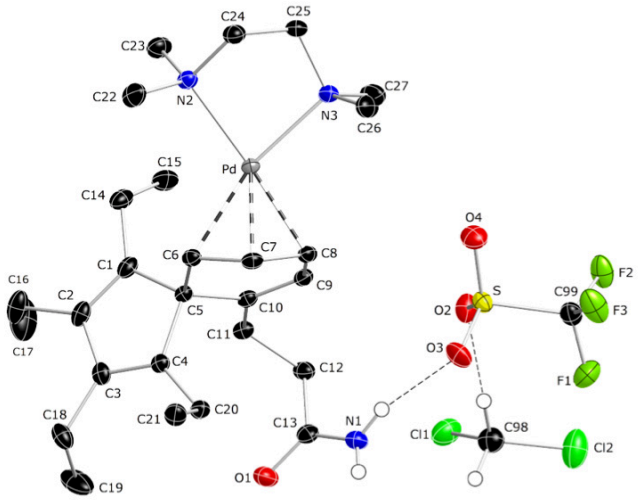


Figure III.8. Thermal ellipsoid plot (50% probability) of complex **41**. Selected bond distances (Å) and angles (deg): Pd–C(6) 2.2193(12), Pd–C(7) 2.0828(12), Pd–C(8) 2.1385(12), Pd–N(2) 2.2027(11), Pd–N(3) 2.1708(11), O(1)–C(13) 1.2361(17), N(1)–C(13) 1.3359(19), C(1)–C(2) 1.3484(19), C(1)–C(5) 1.5218(17), C(2)–C(3) 1.480(2), C(3)–C(4) 1.3491(17), C(3)–C(18) 1.5030(18), C(4)–C(5) 1.5336(17), C(5)–C(10) 1.5231(17), C(5)–C(6) 1.5255(17), C(6)–C(7) 1.4076(17), C(7)–C(8) 1.4186(18), C(8)–C(9) 1.4662(17), C(9)–C(10) 1.3425(17); N(3)–Pd–N(2) 83.19(4), C(7)–Pd–N(2) 134.17(5), C(8)–Pd–N(2) 172.91(5), C(7)–Pd–N(3) 127.03(5), C(8)–Pd–N(3) 99.94(4), C(7)–Pd–C(8) 39.25(5), C(7)–Pd–C(6) 38.03(5), C(8)–Pd–C(6) 65.85(5), N(3)–Pd–C(6) 164.72(4), N(2)–Pd–C(6) 110.31(4), C(7)–C(6)–C(5) 118.87(11), C(6)–C(7)–C(8) 113.96(11), C(7)–C(8)–C(9) 119.70(11), O(1)–C(13)–N(1) 122.72(13), O(1)–C(13)–C(12) 119.71(13), N(1)–C(13)–C(12) 117.57(12).

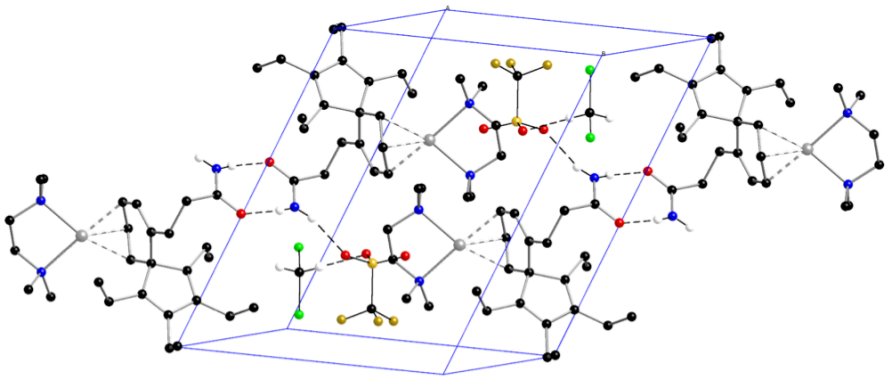


Figure III.9. Packing diagram of **41**.

The crystal structure of compound **42** is shown in Figure III.10. The nine-membered ring exhibits a boat-like conformation. The ring strain is revealed by the C(3)–N(4)–C(5) angle of 134.31(8)°, which is appreciably wider than the average value of 125.2° found for acyclic imides in the Cambridge Structural Database. There are no reported structures of

cyclic imides of this size available for comparison, and the only three eight-membered examples display similar C–N–C angles.[20, 47] The molecules of **42** form inversion-related dimers through hydrogen bonds N(4)–H(04)···O(3)#1 (Figure III.11).

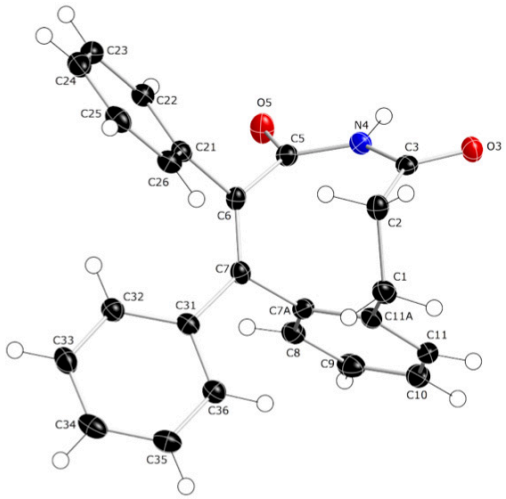


Figure III.10. Thermal ellipsoid plot (50% probability) of compound **42**. Selected bond distances (Å) and angles (deg): C(1)–C(2) 1.5566(14), C(2)–C(3) 1.5060(13), C(3)–O(3) 1.2232(12), C(3)–N(4) 1.3865(13), N(4)–C(5) 1.3911(13), C(5)–O(5) 1.2165(12), C(5)–C(6) 1.5150(13), C(6)–C(7) 1.3466(14); C(11A)–C(1)–C(2) 115.88(8), C(3)–C(2)–C(1) 110.73(8), O(3)–C(3)–N(4) 117.94(9), O(3)–C(3)–C(2) 120.96(9), N(4)–C(3)–C(2) 121.09(8), C(3)–N(4)–C(5) 134.31(8), O(5)–C(5)–N(4) 117.94(9), O(5)–C(5)–C(6) 119.33(9), N(4)–C(5)–C(6) 122.69(8), C(7)–C(6)–C(5) 118.94(9), C(6)–C(7)–C(7A) 118.26(8).

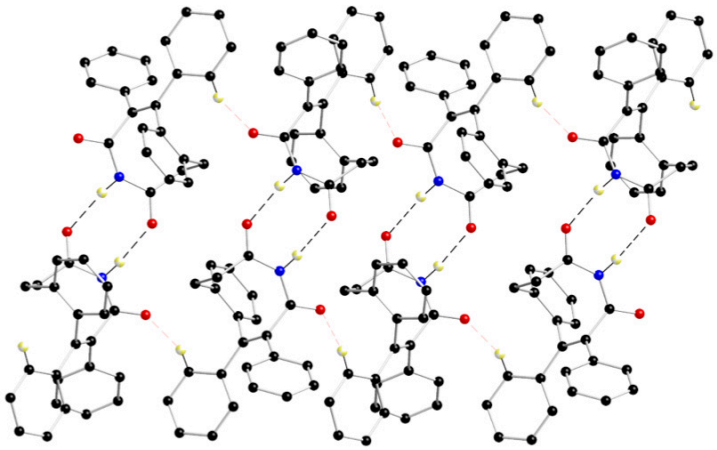


Figure III.11. Packing diagram of **42**.

Experimental section

General Considerations, Materials and Instrumentation

Unless otherwise noted, all preparations were carried out at room temperature under atmospheric conditions. Synthesis grade solvents were obtained from commercial sources. CH_2Cl_2 was degassed and dried using a Pure Solv MD-5 solvent purification system from Innovative Technology, Inc. $[Pd_2(dba)_3]\cdot dba$ was prepared following the reported procedure.[48] All other reagents were obtained from commercial sources and used without further purification. NMR spectra were recorded on Bruker Avance 200, 300 or 400 spectrometers at 298 K. Chemical shifts are referred to internal TMS. The assignments of the ^1H and $^{13}C\{^1H\}$ NMR spectra were made with the help of HMQC and HMBC experiments. Inserted and coordinated XyNC are denoted by $XyNC^i$ and $XyNC^c$, respectively, and the 1,2-C_6H_4 arylene group is denoted by Ar. Melting points were determined on a Reichert apparatus and are uncorrected. Elemental analyses were carried out with Carlo Erba 1106 and LECO CHNS-932 microanalyzers. Infrared spectra were recorded in the range 4000–200 cm^{-1} on a Perkin-Elmer Spectrum 100 spectrophotometer using Nujol mulls between polyethylene sheets or CH_2Cl_2 solutions. High-resolution ESI mass spectra were recorded on an Agilent 6220 Accurate-Mass TOF LC/MS.

X-Ray Structure Determinations

Crystals suitable for X-ray diffraction studies were obtained by liquid-liquid diffusion from CH_2Cl_2/Et_2O (**29b**), CH_2Cl_2/*n*-pentane (**31a**), $CDCl_3$/*n*-pentane (**36a**), $CDCl_3/Et_2O$ (**37a**), CH_2Cl_2/*n*-pentane (**41**·CH_2Cl_2), Et_2O/*n*-hexane (**42**). Numerical details are given in the Tables III.1 and III.2. The data for **29b**, **31a**, **36a**, **37a**, and **41**·CH_2Cl_2 were collected on an Oxford Diffraction Xcalibur diffractometer using monochromated Mo-*K*α radiation in *ω*-scan mode. The data for **42** were collected on an Oxford Diffraction Nova diffractometer using mirror-focussed Cu-*K*α radiation in *ω*-scan mode. Absorption corrections were based on multi-scans. The structures were solved by direct methods and refined anisotropically on F^2 using the program SHELXL-97 (G. M. Sheldrick, University of Göttingen).[49] Treatment of hydrogen atoms was as follows: NH hydrogens were refined freely, methyl hydrogens incorporated into idealized rigid groups allowed to rotate but not tip, other H using a riding model starting from calculated positions. *Exceptions and special features*: For **29b**, the two largest difference peaks lay near C2. These could not be interpreted and may be caused by unidentified twinning or disorder phenomena. For **31a**, the TMEDA group is slightly

disordered, with the minor position being occupied to the extent of 7%. For **36a**, no absorption correction was applied. This compound crystallizes by chance in a Sohncke space group; in the absence of significant anomalous dispersion, Friedel opposite reflections were merged and the absolute structure is thus indeterminate. For **41**·CH_2Cl_2, H atoms at coordinated C atoms were refined freely, but all freely refined hydrogens were subjected to NH or CH distance restraints.

Table III.1. Crystallographic Data for **29b**, **31a** and **36a**.

	29b	**31a**	**36a**
formula	$C_{16}H_{28}IN_3OPd$	$C_{15}H_{25}N_3OPd$	$C_{18}H_{18}N_2O$
fw	511.71	369.78	278.34
T (K)	103(2)	100(2)	100(2)
λ (Å)	0.71073	0.71073	0.71073
cryst syst	monoclinic	monoclinic	monoclinic
space group	$P2_1/c$	$P2_1/n$	$P2_1$
a (Å)	13.8170(4)	11.9985(3)	9.4029(2)
b (Å)	11.4064(4)	8.5100(2)	15.6438(4)
c (Å)	12.3040(4)	15.4033(4)	20.8748(5)
α (deg)	90	90	90
β (deg)	108.468(4)	102.645(3)	91.508(2)
γ (deg)	90	90	90
V (Å^3)	1839.27(10)	1534.63(7)	3069.56(13)
Z	4	4	8
ρ_{calcd} (Mg m^{-3})	1.848	1.600	1.205
μ (mm^{-1})	2.693	1.209	0.076
R1[a]	0.0195	0.0192	0.0459
wR2[b]	0.0445	0.0428	0.0903

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

Table III.2. Crystallographic Data for **37a**, **41**·CH_2Cl_2 and **42**.

	37a	**41**·CH_2Cl_2	**42**
formula	$C_{30}H_{36}F_3N_3O_4PdS$	$C_{29}H_{48}Cl_2F_3N_3O_4PdS$	$C_{24}H_{19}NO_2$
fw	698.08	769.06	353.40
T (K)	100(2)	100(2)	100(2)
λ (Å)	0.71073	0.71073	1.54184
cryst syst	monoclinic	triclinic	monoclinic
space group	$C2/c$	$P\bar{1}$	$C2/c$
a (Å)	25.0366(5)	10.4168(3)	36.899(2)
b (Å)	9.8044(2)	12.4158(4)	7.9959(5)
c (Å)	25.8625(5)	14.5218(4)	12.4947(8)
α (deg)	90	112.399(4)	90
β (deg)	97.947(2)	96.100(3)	104.559(7)

γ (deg)	90	94.524(3)	90
V (Å^3)	6287.5(2)	1711.99(9)	3568.0(4)
Z	8	2	8
ρ_{calcd} (Mg m^{-3})	1.475	1.492	1.316
μ (mm^{-1})	0.713	0.812	0.662
R1[a]	0.0220	0.0236	0.0341
wR2[b]	0.0536	0.0555	0.0861

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

Synthesis

3-(2-Bromophenyl)propanamide (27a). To a solution of 3-(2-bromophenyl)propanoic acid (5.00 g, 21.8 mmol) in anhydrous CH_2Cl_2 (60 mL) was added $SOCl_2$ (10 mL, 136.5 mmol) and the mixture was stirred at 50 °C for 6 h under an N_2 atmosphere. The solvent was evaporated under reduced pressure and the remaining oily residue was dissolved in ethyl acetate (4 mL). Aqueous ammonia (20%, 100 mL) was then added dropwise while keeping the solution at 0 °C in an ice bath. The resulting suspension was stirred at 0 °C for 1 h and then concentrated to ca. 40 mL. The white precipitate was filtered off, washed with H_2O (3 × 5 mL) and vacuum-dried at 60 °C. Yield: 2.8 g, 56%. Anal. Calcd for $C_9H_{10}BrNO$: C, 47.39; H, 4.42; N, 6.14. Found: C, 47.70; H, 4.10; N, 6.05. Mp: 108°C. IR (Nujol, cm^{-1}): ν(NH), 3336, 3166; ν(CO); 1670. HRMS (ESI+, m/z): exact mass calcd for $C_9H_{11}BrNO$ $[M+H]^+$ requires 228.0019, found 228.0019. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.53 (d, $^3J_{HH}$ = 8.0 Hz, 1 H, C_6H_4), 7.29-7.21 (m, 2 H, C_6H_4), 7.08 (m, 1 H, C_6H_4), 5.65 (br, 1 H, NH), 5.45 (br, 1 H, NH), 3.09 (t, $^3J_{HH}$ = 7.6 Hz, 2 H, CH_2), 2.54 (t, $^3J_{HH}$ = 7.6 Hz, 2 H, CH_2). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 174.6 (CO), 139.8 (C, C_6H_4), 132.7 (CH, C_6H_4), 130.5 (CH, C_6H_4), 128.0 (CH, C_6H_4), 127.6 (CH, C_6H_4), 124.2 (C, C_6H_4), 35.5 (CH_2), 31.8 (CH_2).

3-(2-Bromophenyl)-*N*-methylpropanamide (27b). To a solution of 3-(2-bromophenyl)propanoic acid (5.00 g, 21.8 mmol) in anhydrous CH_2Cl_2 (60 mL) was added $SOCl_2$ (10 mL, 136.5 mmol) and the mixture was stirred at 50 °C for 6 h under an N_2 atmosphere. The solvent was evaporated under reduced pressure and the remaining oily residue was dissolved in ethyl acetate (4 mL). Aqueous $MeNH_2$ (40%, 80 mL) was then added dropwise while keeping the solution at 0 °C in an ice-bath. The resulting mixture was stirred at 0 °C for 1 h, treated with a saturated solution of K_2CO_3 in H_2O (100 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$,

filtered and evaporated to dryness to give the product as a colorless solid. Yield: 4.00 g, 76%. Anal. Calcd for $C_{10}H_{12}BrNO$: C, 49.61; H, 5.00; N, 5.79. Found: C, 49.23; H, 5.18; N, 5.71. Mp: 52-57 °C. IR (Nujol, cm^{-1}): ν(NH), 3289; ν(CO); 1635. HRMS (ESI+, m/z): exact mass calcd for $C_{10}H_{13}BrNO$ $[M+H]^+$ requires 242.0175, found 242.0181, error = 2.06 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.52 (m, 1 H, C_6H_4), 7.28-7.20 (m, 2 H, C_6H_4), 7.06 (td, $^4J_{HH}$ = 2.0 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H4), 5.72 (br, 1 H, NH), 3.07 (m, 2 H, CH_2), 2.77 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me), 2.48 (m, 2 H, CH_2). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 172.4 (CO), 140.0 (C, C_6H_4), 132.7 (CH, C_6H_4), 130.5 (CH, C_6H_4), 127.9 (CH, C_6H_4), 127.5 (CH, C_6H_4), 124.1 (C, C_6H_4), 36.2 (CH_2), 32.1 (CH_2), 26.2 (Me).

3-(2-Bromophenyl)-*N,N*-dimethylpropanamide (27c). This compound was obtained as a colorless oil following the procedure described for 3-(2-bromophenyl)-*N*-methylpropanamide from 3-(2-bromophenyl)propanoic acid (2.57 g, 11.2 mmol), $SOCl_2$ (6 mL, 81.9 mmol), and aqueous Me_2NH (40%, 40 mL). Yield: 2.27 g, 79%. Anal. Calcd for $C_{11}H_{14}BrNO$: C, 51.58; H, 5.51; N, 5.47. Found: C, 51.44; H, 5.42; N, 5.33. IR (Nujol, cm^{-1}): ν(CO); 1665. HRMS (ESI+, m/z): exact mass calcd for $C_{11}H_{15}BrNO$ $[M+H]^+$ requires 256.0332, found 256.0338, error = 2.59 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.53 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, C_6H_4), 7.30 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, C_6H_4), 7.23 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, C_6H_4), 7.07 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, C_6H_4), 3.09 (m, 2 H, CH_2), 2.95 (s, 6 H, NMe), 2.63 (m, 2 H, CH_2). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 171.9 (CO), 140.6 (C, C_6H_4), 132.7 (CH, C_6H_4), 130.8 (CH, C_6H_4), 127.9 (CH, C_6H_4), 127.6 (CH, C_6H_4), 124.2 (C, C_6H_4), 37.2 (Me), 35.4 (Me), 33.3 (CH_2), 31.9 (CH_2).

3-(2-Iodophenyl)propanamide (28a). A Carius tube was charged with CuI (87.0 mg, 0.46 mmol), 3-(2-bromophenyl)propanamide (2.07 g, 9.08 mmol), NaI (2.72 g, 18.15 mmol), racemic *trans-N,N'*-dimethyl-1,2-cyclohexanediamine (143 μL, 0.91 mmol), and deaerated dioxane (10 mL), and the mixture was stirred at 140 °C for 72 h under an N_2 atmosphere. After cooling down to room temperature, dichloromethane (50 mL) was added and the mixture was stirred for 10 min and filtered. The dark filtrate was washed with 20% aqueous ammonia (3 × 30 mL) and evaporated to dryness to give a brown oil, which was redissolved in dichloromethane (30 mL). The solution was dried over anhydrous $MgSO_4$ and concentrated (10 mL). Slow addition of *n*-pentane (30 mL) led to the precipitation of a colorless solid, which was collected by filtration, washed with a 1:3 CH_2Cl_2/*n*-pentane mixture (4 × 5 mL), recrystallized from CH_2Cl_2/*n*-pentane and vacuum-dried to give **28a**. Yield: 1.51 g, 60%. Anal. Calcd for $C_9H_{10}INO$: C, 39.30; H, 3.66; N, 5.09. Found: C, 39.20; H, 3.54; N, 5.15. Mp: 109-

110 °C. IR (Nujol, cm^{-1}): ν(NH), 3364, 3189; ν(CO); 1662. HRMS (ESI+, m/z): exact mass calcd for $C_9H_{11}INO$ $[M+H]^+$ requires 275.9880, found 275.9882, error = 0.84 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.81 (m, 1 H, C_6H_4), 7.29-7.26 (m, 2 H, C_6H_4), 6.94-6.88 (m, 1 H, C_6H_4), 5.74 (br, 1 H, NH), 5.49 (br, 1 H, NH), 3.09-3.05 (m, 2 H, CH_2), 2.54-2.50 (m, 2 H, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 173.9 (CO), 143.1 (C, C_6H_4), 139.5 (CH, C_6H_4), 129.7 (CH, C_6H_4), 128.6 (CH, C_6H_4), 128.2 (CH, C_6H_4), 100.2 (C, C_6H_4), 36.4 (CH_2), 36.0 (CH_2).

3-(2-Iodophenyl)-*N*-methylpropanamide (28b). This colorless compound was obtained following the procedure described for 3-(2-iodophenyl)propanamide, from 3-(2-bromophenyl)-*N*-methylpropanamide (2.00 g, 8.26 mmol), CuI (79.0 mg, 0.41 mmol), NaI (2.50 g, 16.68 mmol), and racemic *trans-N,N'*-dimethyl-1,2-cyclohexanediamine (134 μL, 0.85 mmol). The crude product was purified by flash chromatography on silica gel, using a 1:2 ethyl acetate/Et_2O mixture as eluent. Yield: 1.77 g, 74%. Anal. Calcd for $C_{10}H_{12}INO$: C, 41.54; H, 4.18; N, 4.84. Found: C, 41.46; H, 4.01; N, 4.94. Mp: 68 °C. IR (Nujol, cm^{-1}): ν(NH), 3295; ν(CO); 1640. HRMS (ESI+, m/z): exact mass calcd for $C_{10}H_{13}INO$ $[M+H]^+$ requires 290.0036, found 290.0041, error = 1.52 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.81 (d, $^3J_{HH}$ = 8.0 Hz, 1 H, C_6H_4), 7.29-7.26 (m, 2 H, C_6H_4), 6.93-6.87 (m, 1 H, C_6H_4), 5.38 (br, 1 H, NH), 3.07 (m, 2 H, CH_2), 2.79 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me), 2.45 (m, 2 H, CH_2). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 172.2 (CO), 143.3 (C, C_6H_4), 139.4 (CH, C_6H_4), 129.7 (CH, C_6H_4), 128.5 (CH, C_6H_4), 128.1 (CH, C_6H_4), 100.2 (C, C_6H_4), 36.7 (CH_2), 26.2 (Me).

3-(2-Iodophenyl)-*N,N*-dimethylpropanamide (28c). This compound was obtained as a brown oil following the procedure described for 3-(2-iodophenyl)propanamide, from 3-(2-bromophenyl)-*N,N*-dimethylpropanamide (2.60 g, 10.15 mmol), CuI (97.0 mg, 0.51 mmol), NaI (3.10 g, 20.68 mmol), and racemic *trans-N,N'*-dimethyl-1,2-cyclohexanediamine (165 μL, 1.02 mmol). Yield: 2.78 g, 90%. Anal. Calcd for $C_{11}H_{14}INO$: C, 43.58; H, 4.66; N, 4.62. Found: C, 43.58; H, 4.53; N, 4.68. IR (Nujol, cm^{-1}): ν(CO); 1664. HRMS (ESI+, m/z): exact mass calcd for $C_{11}H_{15}INO$ $[M+H]^+$ requires 304.0193, found 304.0199, error = 1.98 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.81 (m, 1 H, C_6H_4), 7.31-7.25 (m, 2 H, C_6H_4), 6.90 (ddd, $^4J_{HH}$ = 2.4 Hz, $^3J_{HH}$ = 6.4 Hz, $^3J_{HH}$ = 8.0 Hz, 1 H, C_6H_4), 3.08 (m, 2 H, CH_2), 2.95 (s, 6 H, Me), 2.60 (m, 2 H, CH_2). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 171.7 (CO), 144.0 (C, C_6H_4), 139.5 (CH, C_6H_4), 129.9 (CH, C_6H_4), 128.5 (CH, C_6H_4), 128.1 (CH, C_6H_4), 100.2 (C, C_6H_4), 37.2 (Me), 36.4 (CH_2), 35.5 (Me), 33.6 (CH_2).

[Pd{$C_6H_4(CH_2)_2C(O)NRR'$-2}I(tmeda)] [NRR' = NH_2 (29a), NHMe (29b), NMe_2 (29c)]. To a suspension of $Pd(dba)_2$ (903 mg, 1.57 mmol) in CH_2Cl_2 (20 mL) were added tmeda (0.3 mL, 2.00 mmol) and 3-(2-iodophenyl)propanamide (**28a**), 3-(2-iodophenyl)-*N*-methylpropanamide (**28b**), or 3-(2-iodophenyl)-*N,N*-dimethylpropanamide (**28c**) (1.57 mmol), and the mixture was stirred for 1 h under an N_2 atmosphere. The resulting black suspension was filtered through anhydrous $MgSO_4$ and the clear orange filtrate was concentrated (1 mL). The addition of Et_2O (20 mL) led to the precipitation of a pale orange solid, which was filtered off, washed with Et_2O (5 × 3 mL), recrystallized from CH_2Cl_2/Et_2O and vacuum-dried to give the corresponding complex **29**.

29a. Yield: 68%. Anal. Calcd for $C_{15}H_{26}IN_3OPd$: C, 36.20; H, 5.27; N, 8.44. Found: C, 35.82; H, 5.22; N, 8.20. Mp: 147-152 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3370, 3156; ν(CO), 1652. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.27-7.23 (m, 1 H, Ar), 6.89-6.86 (m, 1 H, Ar), 6.85-6.77 (m, 2 H, Ar), 6.03 (br, 1 H, NH), 5.30 (br, 1 H, NH), 3.84, 3.23 (AB part of ABXY system, $^2J_{AB}$ = 12.8 Hz, $^3J_{AX} = {}^3J_{BY}$ = 10.4 Hz, $^3J_{AY}$ = 4.4 Hz, $^3J_{BX}$ = 7.2 Hz, 2 H, CH_2, propanamide), 2.95-2.83 (m, 2 H, CH_2, tmeda + propanamide), 2.71 (s, 3 H, Me), 2.66 (s, 3 H, Me), 2.69-2.49 (m, 4 H, CH_2, tmeda + propanamide), 2.43 (s, 3 H, Me), 2.15 (s, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.2 (CO), 143.72, 143.66 (C, Ar), 135.9, 127.1, 124.6, 123.2 (CH, Ar), 62.1, 58.2 (CH_2, tmeda), 50.4, 50.2, 49.1, 48.7 (Me), 36.7, 35.9 (CH_2, propanamide).

29b. Yield: 67%. Anal. Calcd for $C_{16}H_{28}IN_3OPd$: C, 37.55; H, 5.51; N, 8.21. Found: C, 37.31; H, 5.50; N, 7.83. Mp: 142-145 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3384; ν(CO), 1656. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.24 (m, 1 H, Ar), 6.87-6.76 (m, 3 H, Ar), 6.01 (br c, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 3.78, 3.24 (AB part of ABXY system, $^2J_{AB}$ = 12.8 Hz, $^3J_{AX} = {}^3J_{BY}$ = 10.0 Hz, $^3J_{AY}$ = 4.4 Hz, $^3J_{BX}$ = 7.6 Hz, 2 H, CH_2, propanamide), 2.89-2.76 (m, 2 H, CH_2, tmeda + propanamide), 2.73 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NH*Me*), 2.71 (s, 3 H, Me, tmeda), 2.66 (s, 3 H, Me, tmeda), 2.69-2.48 (m, 4 H, CH_2, tmeda + propanamide), 2.43 (s, 3 H, Me, tmeda), 2.15 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 174.3 (CO), 143.8, 143.6 (C, Ar), 135.9, 127.1, 124.5, 123.2 (CH, Ar), 62.1, 58.2 (CH_2, tmeda), 50.3, 50.2, 49.2, 48.7 (Me, tmeda), 37.2, 36.0 (CH_2, propanamide), 26.0 (NHMe).

29c. Yield: 55%. Anal. Calcd for $C_{17}H_{30}IN_3OPd$: C, 38.84; H, 5.75; N, 7.99. Found: C, 38.48; H, 5.81; N, 7.88. Mp: 170 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1639. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.26-7.22 (m, 1 H, Ar), 6.88-6.85 (m, 1 H, Ar), 6.82-6.77 (m, 2 H, Ar), 3.83-3.74 (m, 1 H, CH_2, propanamide), 3.29-3.16 (m, 2 H, CH_2, tmeda + propanamide), 3.00 (s, 3

H, Me, propanamide), 2.96 (s, 3 H, Me, propanamide), 2.88-2.82 (m, 1 H, CH_2, tmeda), 2.69 (s, 3 H, Me, tmeda), 2.65 (s, 3 H, Me, tmeda), 2.69-2.42 (m, 4 H, CH_2, tmeda + propanamide), 2.40 (s, 3 H, Me, tmeda), 2.19 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 173.6 (CO), 144.6, 143.8 (C, Ar), 136.1, 127.1, 124.2, 123.0 (CH, Ar), 62.0, 58.2 (CH_2, tmeda), 50.3, 50.2, 49.2, 48.8 (Me, tmeda), 37.6, 35.3 (Me, propanamide), 34.9, 34.3 (CH_2, propanamide).

[Pd{κ^2*C,O*-$C_6H_4(CH_2)_2C(O)NRR'$-2}(tmeda)]TfO [NRR' = NH_2 (30a), NHMe (30b), NMe_2 (30c)]. To a solution of the appropriate complex **29** (0.25 mmol) in acetone (20 mL) was added AgTfO (63 mg, 0.25 mmol) and the mixture was stirred for 30 min. The solvent was removed under reduced pressure, the residue was extracted with CH_2Cl_2 (6 × 5 mL), and the combined extracts were filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (1 mL) and addition of Et_2O (20 mL) led to the precipitation of an oily solid. The mother liquor was decanted and the precipitate was thoroughly dried under a vacuum to give the corresponding complex **30** as a pale yellow solid. Reprecipitations from acetone/Et_2O or CH_2Cl_2/Et_2O did not improve the purity of the products and acceptable elemental analyses were obtained only for **30b**.

30a. Yield: 84%. IR (CH_2Cl_2, cm^{-1}): ν(CO), 1646. HRMS (ESI+, m/z): exact mass calcd for $C_{15}H_{26}N_3OPd$ $[M]^+$ requires 370.1111, found 370.1103, error = 2.16 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9532, error = 4.03 ppm. ^1H NMR (300.1 MHz, $CDCl_3$): δ 7.84 (br, 1 H, NH), 7.06-7.02 (m, 1 H, Ar), 6.96-6.92 (m, 2 H, Ar), 6.86-6.81 (m, 1 H, Ar), 6.42 (br, 1 H, NH), 4.41 (m, 1 H, CH_2 propanamide), 3.05-2.95 (m, 2 H, CH_2, tmeda + propanamide), 2.81 (s, 3 H, Me), 2.79-2.62 (m, 5 H, CH_2, tmeda + propanamide), 2.58 (s, 3 H, Me), 2.50 (s, 3 H, Me), 2.46 (s, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 181.0 (CO), 145.5, 143.0 (C, Ar), 132.0, 126.6, 126.0, 125.1 (CH, Ar), 64.3, 57.2 (CH_2, tmeda), 53.7, 50.3, 47.9, 46.7 (Me), 34.1, 30.7 (CH_2, propanamide).

30b. Yield: 91%. Anal. Calcd for $C_{17}H_{28}F_3N_3O_4PdS$: C, 38.24; H, 5.29; N, 7.87; S, 6.01. Found: C, 38.17; H, 5.26; N, 7.86; S, 6.31. Mp: 60-65 °C (dec). IR (CH_2Cl_2, cm^{-1}): ν(CO), 1608. HRMS (ESI+, m/z): exact mass calcd for $C_{16}H_{28}N_3OPd$ $[M]^+$ requires 384.1267, found 384.1274, error = 1.82 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9529, error = 2.26 ppm. ^1H NMR (300.1 MHz, $CDCl_3$): δ 8.17 (br c, $^3J_{HH}$= 4.8 Hz, NH), 7.06-7.02 (m, 1 H, Ar), 6.96-6.89 (m, 2 H, Ar), 6.83-6.79 (m, 1 H, Ar), 4.44

(m, 1 H, CH_2 propanamide), 3.15-2.88 (m, 3 H, CH_2, tmeda + propanamide), 2.86-2.58 (m, 4 H, CH_2, tmeda + propanamide), 2.82 (s, 3 H, Me, tmeda), 2.65 (s, 3 H, Me, tmeda), 2.63 (d, $^3J_{HH}$= 4.8 Hz, NH*Me*), 2.53 (s, 3 H, Me, tmeda), 2.44 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 178.0 (CO), 145.4, 142.9 (C, Ar), 131.9, 126.6, 125.8, 125.0 (CH, Ar), 64.3, 57.2 (CH_2, tmeda), 53.9, 50.0, 48.1, 46.5 (Me, tmeda), 34.6, 30.9 (CH_2, propanamide), 26.8 (NHMe).

30c. Yield: 58%. IR (CH_2Cl_2, cm^{-1}): ν(CO), 1591. HRMS (ESI+, m/z): exact mass calcd for $C_{17}H_{30}N_3OPd$ $[M]^+$ requires 398.1424, found 398.1437, error = 3.27 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9530, error = 3.20 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.08-7.04 (m, 1 H, Ar), 6.98-6.91 (m, 2 H, Ar), 6.85-6.82 (m, 1 H, Ar), 4.66 (td, $^3J_{HH}$ = 3.2 Hz, $^2J_{HH}$ = 13.6 Hz, 1 H, CH_2 propanamide), 3.19-3.09 (m, 2 H, CH_2, tmeda + propanamide), 3.00 (s, 3 H, Me, propanamide), 2.97-2.94 (m, 1 H, CH_2), 2.89 (s, 3 H, Me, propanamide), 2.82 (s, 3 H, Me, tmeda), 2.82-2.67 (m, 3 H, CH_2), 2.64 (s, 3 H, Me, tmeda), 2.62 (s, 3 H, Me, tmeda), 2.57-2.47 (1 H, CH_2), 2.48 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.0 (CO), 145.6, 143.4 (C, Ar), 132.0, 126.2, 125.9, 124.9 (CH, Ar), 64.4, 57.2 (CH_2, tmeda), 54.0, 50.1, 48.1, 46.7 (Me, tmeda), 38.0, 37.0 (Me, propanamide), 34.1, 31.1 (CH_2, propanamide).

[Pd{*κ*²*C,N*-$C_6H_4(CH_2)_2C(O)NR$-2}(tmeda)] [R = H (31a), Me (31b)]. To solution of **29a** or **29b** (0.46 mmol) in CH_2Cl_2 (25 mL) was added KO^{t}Bu (414 mg, 3.69 mmol) and the resulting suspension was stirred for 4 h and then filtered through Celite. Partial evaporation of the pale yellow filtrate (3 mL) and slow addition of *n*-pentane (20 mL) led to the precipitation of a colorless solid, which was filtered off, recrystallized from CH_2Cl_2/*n*-pentane and vacuum-dried to give the corresponding complex **31**.

31a. Yield: 83%. Anal. Calcd for $C_{15}H_{25}N_3OPd$: C, 48.72; H, 6.81; N, 11.36. Found: C, 48.54; H, 7.21; N, 11.21. Mp: 140-143 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1551. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.19-7.14 (m, 1 H, Ar), 6.90-6.84 (m, 3 H, Ar), 4.16 (m, 1 H, CH_2, propanamide), 4.09 (br, 1 H, NH), 2.92 (td, $^3J_{HH}$ = 4.0 Hz, $^2J_{HH}$ = 12.8 Hz, 1 H, CH_2, propanamide), 2.85-2.79 (m, 1 H, CH_2, tmeda), 2.68 (s, 3 H, Me, tmeda), 2.72-2.67 (m, 1 H, CH_2, propanamide), 2.55 (s, 3 H, Me, tmeda), 2.66-2.47 (m, 3 H, CH_2, tmeda), 2.44 (s, 3 H, Me, tmeda), 2.31-2.27 (m, 1 H, CH_2, propanamide), 2.27 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (50.3 MHz, $CDCl_3$): δ 178.4 (CO), 151.4, 145.8 (C, Ar), 132.6, 125.6, 124.5, 123.4

(CH, Ar), 62.4, 58.0 (CH_2, tmeda), 51.9, 48.9, 47.9, 47.2 (Me, tmeda), 37.8, 36.8 (CH_2, propanamide).

31b. This complex was obtained as an hydrate. Yield: 79%. Anal. Calcd for $C_{16}H_{29.4}N_3O_{2.2}Pd$: C, 47.40; H, 7.31; N, 10.36. Found: C, 47.33; H, 7.55; N, 10.33. Mp: 108-109 °C. IR (Nujol, cm^{-1}): ν(CO), 1558. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.27-7.22 (m, 1 H, Ar), 6.85-6.80 (m, 3 H, Ar), 3.86-3.70 (m, 2 H, CH_2, propanamide), 3.12-3.05 (m, 1 H, CH_2, propanamide), 2.79-2.72 (m, 1 H, CH_2, tmeda), 2.72 (s, 3 H, Me, propanamide), 2.68-2.60 (m, 13 H, Me, CH_2, tmeda + CH_2, propanamide), 2.28 (s, 3 H, Me, tmeda), 1.96 (s, 2 H, H_2O). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.1 (CO), 149.1, 144.0 (C2, Ar), 132.7, 127.5, 123.9, 122.9 (CH, Ar), 62.1, 58.3 (CH_2, tmeda), 51.5, 49.3, 48.8, 48.2 (Me, tmeda), 38.6 (CH_2, propanamide), 36.4 (Me, propanamide), 33.8 (CH_2, propanamide).

[Pd{C(O)C$_6$H$_4$(CH$_2$)$_2$C(O)NH$_2$-2}I(tmeda)] (32). CO was bubbled through a stirred solution of **29a** (103 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) for 30 min, and the resulting solution was filtered through Celite. Partial evaporation of the filtrate (5 mL) and addition of *n*-pentane (20 mL) led to the precipitation of a yellow solid, which was collected by filtration, washed with CH_2Cl_2/*n*-pentane (5 × 5 mL) and vacuum-dried to give **32**·0.5CH_2Cl_2. Yield: 101 mg, 86%. Anal. Calcd for $C_{16.5}H_{27}ClIN_3O_2Pd$: C, 34.88; H, 4.79; N, 7.40. Found: C, 34.58; H, 5.06; N, 7.24. Mp: 91-94 °C. IR (Nujol, cm^{-1}): ν(NH), 3385, 3144; ν(CO), 1677, 1640. ^1H NMR (400.9 MHz, $CDCl_3$): δ 9.09 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.45 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.31 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.11 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.07 (s, 1 H, NH), 5.30 (s, 1 H, CH_2Cl_2), 5.13 (s, 1 H, NH), 3.17 (m, 2 H, CH_2, propanamide), 2.76 (m, 2 H, CH_2, tmeda), 2.59 (s, 6 H, Me, tmeda), 2.55 (m, 2 H, CH_2, tmeda), 2.52 (s, 6 H, Me, tmeda), 2.49 (m, 2 H, CH_2, propanamide). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 175.3 ($CONH_2$), 139.6 (CH, Ar), 138.4, 136.8 (C, Ar), 130.9, 130.6, 126.2 (CH, Ar), 61.8, 57.6 (CH_2, tmeda), 50.4, 48.9 (Me, tmeda), 37.4, 31.2 (CH_2, propanamide); Pd*C* not observed.

4,5-dihydro-2*H*-benzo[*c*]azepine-1,3-dione (33a). To a solution of **29a** (134 mg, 0.27 mmol) in acetone (15 mL) was added AgTfO (70 mg, 0.27 mmol) and the resulting suspension was stirred for 15 min. The solvent was removed under vacuum, the residue was extracted with CH_2Cl_2 (6 × 5 mL), and the combined extracts were filtered through Celite. The filtrate was stirred under a CO atmosphere (1.4 bar) for 6 h, whereupon a black precipitate of Pd gradually formed. The solvent was removed under vacuum, the residue was

extracted with a 1:10 CH_2Cl_2/*n*-hexane mixture (6 × 5 mL), and the combined extracts were filtered through Celite. Evaporation of the solvents under reduced pressure gave **33a** as a colorless solid. Yield: 20 mg, 42%. Mp: 115-118 °C. IR (Nujol, cm^{-1}): ν(CO), 1668, 1662. HRMS (ESI+, m/z): exact mass calcd for $C_{10}H_{10}NO_2$ $[M+H]^+$ requires 176.0706, found 176.0709, error = 1.71 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.36 (br, 1 H, NH), 8.12 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H9), 7.52 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H7), 7.42 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H8), 7.23 (m, 1 H, H6), 3.13-3.10 (m, 2 H, H5), 2.91-2.89 (m, 2 H, H4). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 173.3 (C3), 166.2 (C1), 140.5 (C5a), 133.6 (C7), 133.1 (C9), 129.9 (C9a), 128.8 (C6), 127.6 (C8), 36.8 (C4), 29.1 (C5).

***trans*-[Pd{C(=NXy)C$_6$H$_4$(CH$_2$)$_2$C(O)NRR'-2}I(CNXy)$_2$] [NRR' = NH$_2$ (34a), NHMe (34b), NMe$_2$ (34c)].** A mixture of the appropriate complex **29** (0.16 mmol) and XyNC (66 mg, 0.50 mmol) in CH_2Cl_2 (20 mL) was stirred for 15 min and filtered through Celite. Partial evaporation of the yellow filtrate (2 mL) and addition of *n*-pentane (30 mL) led to the precipitation of a yellow solid, which was filtered off, recrystallized from CH_2Cl_2/*n*-pentane and vacuum-dried to give the corresponding complex **34**.

34a. Yield: 77%. Anal. Calcd for $C_{36}H_{37}IN_4OPd$: C, 55.79; H, 4.81; N, 7.23. Found: C, 55.63; H, 4.61; N, 7.45. Mp: 138-140 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3440; ν(C≡N), 2180; ν(CO), 1677; ν(C=N), 1584. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 7.86 (m, 1 H, Ar), 7.33-7.20 (m, 5 H, Ar + *p*-H, XyNC^c), 7.07 (d, $^3J_{HH}$ = 7.8 Hz, 4 H, *m*-H, XyNC^c), 6.90 (s, 3 H, XyNC^i), 6.24 (br, 1 H, NH), 5.20 (br, 1 H, NH), 3.43-3.71 (m, 2 H, CH_2, propanamide), 2.99-2.94 (m, 2 H, CH_2, propanamide), 2.22 (s, 6 H, Me, XyNC^i), 2.20 (s, 12 H, Me, XyNC^c). ^{13}C{^{1}H} APT NMR (75.5 MHz, $CDCl_3$): δ 178.8 (*C*=N), 174.6 (CO), 149.9 (*i*-C, XyNC^i), 145.1 (C, Ar), 143.0 (br, *i*-C, XyNC^c), 136.7 (C, Ar), 135.6 (*o*-C, XyNC^c), 130.1 (CH, Ar + XyNC^c), 129.6, 128.8 (CH, Ar), 128.2 (CH, XyNC^i), 128.0 (CH, XyNC^c), 127.0 (*o*-C, XyNC^i), 126.6 (CH, Ar), 123.7 (CH, XyNC^i), 39.4, 30.4 (CH_2), 19.1 (Me, XyNC^i), 18.7 (Me, XyNC^c); *C*≡N of XyNC^c not observed.

34b. Yield: 74%. Anal. Calcd for $C_{37}H_{39}IN_4OPd$: C, 56.32; H, 4.98; N, 7.10. Found: C, 56.50; H, 5.27; N, 7.10. Mp: 131-133 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3347; ν(C≡N), 2178; ν(CO), 1673; ν(C=N), 1586. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.76 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.34-7.28 (m, 2 H, Ar), 7.27-7.21 (m, 3 H, Ar + *p*-H, XyNC^c), 7.07 (d, $^3J_{HH}$ = 7.2 Hz, 4 H, *m*-H, XyNC^c), 6.91 (s, 3 H, XyNC^i), 6.33 (br c, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 3.40-3.35 (m, 2 H, CH_2, propanamide), 2.96-2.92 (m, 2 H, CH_2, propanamide), 2.57 (d, $^3J_{HH}$ = 4.8

Hz, 3 H, NMe), 2.22 (s, 6 H, Me, XyNC^{i}), 2.20 (s, 12 H, Me, XyNC^{c}). $^{13}C\{^{1}H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 178.6 (*C*=N), 172.8 (CO), 149.9 (*i*-C, XyNC^{i}), 145.3 (C, Ar), 143.0 (br, *i*-C, XyNC^{c}), 137.1 (C, Ar), 135.6 (*o*-C, XyNC^{c}), 130.2 (CH, Ar), 130.1 (CH, XyNC^{c}), 128.8 (CH, Ar), 128.2 (CH, XyNC^{i}), 128.0 (CH, XyNC^{c}), 127.0 (*o*-C, XyNC^{i}), 126.6 (CH, Ar), 123.7 (CH, XyNC^{i}), 40.3, 30.9 (CH_2), 25.8 (NMe), 19.1 (Me, XyNC^{i}), 18.7 (Me, XyNC^{c}); *C*≡N of XyNC^{c} not observed.

34c. Yield: 79%. Anal. Calcd for $C_{38}H_{41}IN_4OPd$: C, 56.83; H, 5.15; N, 6.98. Found: C, 56.94; H, 5.34; N, 6.93. Mp: 139-140 °C (dec). IR (Nujol, cm^{-1}): ν(C≡N), 2174; ν(CO), 1649; ν(C=N), 1590. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 8.08 (d, $^{3}J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.34-7.19 (m, 5 H, Ar + *p*-H, XyNC^{c}), 7.06 (d, $^{3}J_{HH}$ = 7.5 Hz, 4 H, *m*-H, XyNC^{c}), 6.90 (s, 3 H, XyNC^{i}), 3.33-3.28 (m, 2 H, CH_2, propanamide), 2.89-2.84 (m, 2 H, CH_2, propanamide), 2.85 (s, 3 H, NMe), 2.77 (s, 3 H, NMe), 2.21 (s, 18 H, Me, XyNC^{i} + XyNC^{c}). $^{13}C\{^{1}H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 177.8 (*C*=N), 172.4 (CO), 149.8 (*i*-C, XyNC^{i}), 145.1, 136.8 (C, Ar), 135.6 (*o*-C, XyNC^{c}), 131.3, 130.6 (CH, Ar), 129.9 (CH, XyNC^{c}), 128.4 (CH, Ar), 128.0 (CH, XyNC^{i}), 127.9 (CH, XyNC^{c}), 126.9 (*o*-C, XyNC^{i}), 126.2 (CH, Ar), 123.4 (CH, XyNC^{i}), 37.1 (NMe), 36.5 (CH_2), 35.2 (NMe), 30.3 (CH_2), 19.2 (Me, XyNC^{i}), 18.7 (Me, XyNC^{c}); *i*-C and *C*≡N of XyNC^{c} not observed.

Synthesis of 1-(2,6-Dimethylphenylimino)-1,2,4,5-tetrahydrobenzo[*c*]azepin-3-one (35a) and 2-(2-Cyanoethyl)-*N*-(2,6-dimethylphenyl)benzamide (36a). To a solution of **29a** (217 mg, 0.44 mmol) in $CHCl_3$ (15 mL) was added XyNC (57.2 mg, 0.44 mmol) and the mixture was refluxed for 24 h. A black precipitate of Pd gradually formed. The solvent was removed under vacuum, the residue was extracted with Et_2O (6 × 5 mL) and the extracts were filtered through Celite. Partial evaporation of the solvents (3 mL) and slow addition of *n*-pentane (30 mL) led to the precipitation of a colorless solid, which was filtered off, washed with *n*-pentane (5 × 3 mL) and vacuum-dried to give **36a**. The filtrate was evaporated to dryness, the residue was stirred in *n*-pentane (30 mL) for 1 h and the resulting suspension was filtered through Celite. Compound **35a** was obtained as a yellow oil after evaporation the solvent.

35a. Yield: 57 mg, 47 %. IR (Nujol, cm^{-1}): ν(NH), 3325; ν(CO), 1707; ν(C=N), 1633. HRMS (ESI+, m/z): exact mass calcd for $C_{18}H_{19}N_2O$ $[M+H]^+$ requires 279.1492, found 279.1496, error = 1.55 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.19 (dd, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, H9), 7.47 (td, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, H7), 7.44 (overlapped broad

signal, 1 H, NH), 7.42 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H8), 7.23 (m, 1 H, H6), 7.10 (m, 2 H, *m*-H, Xy), 6.97 (m, 1 H, *p*-H, Xy), 3.08-3.05 (m, 2 H, H5), 2.88-2.86 (m, 2 H, H4), 2.14 (s, 6 H, Me). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 172.8 (C3), 147.7 (C1), 143.5 (*i*-C, Xy), 139.6 (C5a), 132.5 (C9a), 131.4 (C7), 131.2 (C9), 128.7 (*m*-C, Xy), 128.0 (C6), 127.5 (C8), 124.3 (*p*-C, Xy), 38.0 (C4), 29.4 (C5), 17.9 (Me); *o*-C of Xy not observed.

36a. Yield: 22 mg, 18%. Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.70; H, 6.70; N, 10.10. Mp: 120-122 °C. IR (Nujol, cm^{-1}): ν(NH), 3243; ν(CN), 2245; ν(CO), 1643. HRMS (ESI+, m/z): exact mass calcd for $C_{18}H_{19}N_2O$ $[M+H]^+$ requires 279.1492, found 279.1496, error = 1.6 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.69 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6, Ar), 7.52 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H4, Ar), 7.44 (m, 1 H, H3, Ar), 7.41 (m, 1 H, H5, Ar), 7.20-7.13 (m, 4 H, NH + Xy), 3.14 (t, $^3J_{HH}$ = 7.2 Hz, 2 H, CH_2CH_2CN), 2.86 (t, $^3J_{HH}$ = 7.2 Hz, 2 H, CH_2CH_2CN), 2.34 (s, 6 H, Me). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 167.7 (CO), 137.8 (C2, Ar), 135.5 (C1, Ar), 135.4 (*o*-C, Xy), 133.3 (*i*-C, Xy), 131.4 (C3, Ar), 131.1 (C4, Ar), 128.4 (*m*-C, Xy), 127.8 (*p*-C, Xy), 127.6 (C5, Ar), 127.1 (C6, Ar), 119.4 (CN), 30.0 (CH_2CH_2CN), 19.6 (CH_2CH_2CN), 18.6 (Me).

[Pd{κ^2*C*,*O*-C(X)=C(X)C$_6$H$_4$(CH$_2$)$_2$C(O)NRR'-2}(tmeda)]TfO [NRR' = NH$_2$, X = Ph (37a), C$_6$H$_4$^{n}Bu-4 (38a), C$_6$H$_4$Br-4 (39a), CO$_2$Me (40a); NRR' = NHMe, X = Ph (37b); NRR' = NMe$_2$, X = Ph (37c)]. A mixture of the appropriate complex **29** (0.27 mmol) and AgTfO (74 mg, 0.29 mmol) in acetone (15 mL) was stirred for 30 min. The solvent was removed under vacuum, the residue was extracted with CH_2Cl_2 (6 × 5 mL), and the combined extracts were filtered through anhydrous $MgSO_4$. The alkyne (0.27 mmol) was then added to the filtrate and the solution was stirred at room temperature for 3 h (except for the synthesis of **39a**, which required 20 h) and then filtered through anhydrous $MgSO_4$. The filtrate was evaporated to dryness and the residue was crystallized from CH_2Cl_2/Et_2O (**37a-c**, **40a**), Et_2O/*n*-pentane (**38a**), or acetone/*n*-pentane (**39a**). Analytically pure samples of the products were obtained by successive recrystallizations.

37a. Yield: 77%. Anal. Calcd for $C_{30}H_{36}F_3N_3O_4PdS$: C, 51.61; H, 5.20; N, 6.02; S, 4.59. Found: C, 51.49; H, 5.26; N, 6.01; S, 4.32. Mp: 163-164 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3395, 3218; ν(CO), 1651. HRMS (ESI+, m/z): exact mass calcd for $C_{29}H_{36}N_3OPd$ $[M]^+$ requires 548.1893, found 548.1901, error = 1.46 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9530, error = 3.20 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.76 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.74 (overlapped broad signal, 1 H,

NH), 7.53 (br, 1 H, NH), 7.50-7.44 (m, 3 H, Ph + Ar), 7.29 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.20-7.16 (m, 2 H, Ph), 7.13-7.10 (m, 2 H, Ar + Ph), 7.00-6.94 (m, 3 H, Ph), 6.81-6.78 (m, 2 H, Ph), 3.03 (td, $^3J_{HH}$ = 3.2 Hz, $^2J_{HH}$ = 12.8 Hz, 1 H, CH_2, tmeda), 2.89-2.83 (m, 1 H, CH_2, propanamide), 2.68 (td, $^3J_{HH}$ = 3.2 Hz, $^2J_{HH}$ = 14.0 Hz, 1 H, CH_2, tmeda), 2.56 (s, 3 H, Me), 2.53-2.40 (m, 2 H, CH_2, propanamide), 2.36 (s, 3 H, Me), 2.38-2.31 (m, 1 H, CH_2, propanamide), 2.27-2.24 (m, 1 H, CH_2, tmeda), 2.15-2.11 (m, 1 H, CH_2, tmeda), 1.97 (s, 3 H, Me), 1.88 (s, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 184.2 (CO), 145.1 (C, Ar), 143.8 (CPd), 142.6 (C, Ph), 140.34 (PdC=*C*), 140.28 (C, Ph), 139.8 (C, Ar), 130.6, 130.02 (CH, Ar), 129.96, 129.5 , 128.3, 127.40 (CH, Ph), 127.35 (CH, Ar), 125.8 (CH, Ph), 125.7 (CH, Ar), 125.5 (CH, Ph), 65.0, 56.6 (CH_2, tmeda), 53.3, 49.1, 48.9, 44.7 (Me), 37.7, 30.3 (CH_2, propanamide).

37b. Yield: 75%. Anal. Calcd for $C_{31}H_{38}F_3N_3O_4PdS$: C, 52.28; H, 5.38; N, 5.90; S, 4.50. Found: C, 52.28; H, 5.42; N, 5.93; S, 4.37. Mp: 153-155 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3278; ν(CO), 1614. HRMS (ESI+, m/z): exact mass calcd for $C_{30}H_{38}N_3OPd$ $[M]^+$ requires 562.2050, found 562.2059, error = 1.60 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9529, error = 2.18 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.48 (br c, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.75 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.48 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.40-7.37 (m, 2 H, Ph), 7.25 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.22-7.19 (m, 3 H, Ph), 7.09 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.03-6.99 (m, 3 H, Ph), 6.87-6.85 (m, 2 H, Ph), 3.29-3.22 (m, 1 H, CH_2, propanamide), 2.98 (td, $^3J_{HH}$ = 3.2 Hz, $^2J_{HH}$ = 12.8 Hz, 1 H, CH_2, tmeda), 2.69 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, propanamide), 2.68-2.52 (m, 4 H, CH_2, propanamide + tmeda), 2.58 (s, 3 H, Me, tmeda), 2.39-2.35 (m, 1 H, CH_2, tmeda), 2.36 (s, 3 H, Me, tmeda), 2.26-2.21 (m, 1 H, CH_2, tmeda), 1.94 (s, 3 H, Me, tmeda), 1.91 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 180.2 (CO), 144.1 (C, Ar), 143.2 (CPd), 142.3 (C, Ph), 139.0 (PdC=*C*), 138.42, 138.39 (C, Ph, Ar), 131.2, 129.8 (CH, Ar), 128.8, 128.7, 128.5, 127.7 (CH, Ph), 127.5, 126.18 (CH, Ar), 126.15, 126.0 (CH, Ph), 64.5, 56.8 (CH_2, tmeda), 52.8, 49.4, 48.6, 45.1 (Me, tmeda), 34.5, 31.4 (CH_2, propanamide), 27.6 (Me, propanamide).

37c. Yield: 62%. Anal. Calcd for $C_{32}H_{40}F_3N_3O_4PdS$: C, 52.93; H, 5.55; N, 5.79; S, 4.42. Found: C, 52.96; H, 5.71; N, 5.79; S, 4.90. Mp: 153-154 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1592. HRMS (ESI+, m/z): exact mass calcd for $C_{31}H_{40}N_3OPd$ $[M]^+$ requires 576.2206, found 576.2217, error = 1.81 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9525, error = 0.22 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): 7.69 (dd, $^4J_{HH}$ =

1.6 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.50 (td, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.44-7.40 (m, 2 H, Ph), 7.33 (td, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.22-7.19 (m, 3 H, Ph), 7.11 (dd, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.06-6.99 (m, 3 H, Ph), 6.86-6.83 (m, 2 H, Ph), 3.59-3.51 (m, 1 H, CH_2, propanamide), 3.23 (s, 3 H, Me, propanamide), 2.95 (s, 3 H, Me, propanamide), 2.95-2.87 (m, 2H, CH_2, propanamide + tmeda), 2.74-2.54 (m, 4 H, CH_2, propanamide + tmeda), 2.51 (s, 3 H, Me, tmeda), 2.44 (s, 3 H, Me, tmeda), 2.41-2.35 (m, 1 H, CH_2, tmeda), 2.08 (s, 3 H, Me, tmeda), 2.06 (s, 3 H, Me, tmeda). $^{13}C\{^{1}H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 178.6 (CO), 145.2 (CPd), 143.8 (C, Ar), 142.6, 139.3 (C, Ph), 138.9 (PdC=*C*), 138.0 (C, Ar), 130.6, 130.3 (CH, Ar), 128.95, 128.91, 128.4 (CH, Ph), 127.7 (CH, Ar), 127.6 (CH, Ph), 126.7 (CH, Ar), 126.1, 125.9 (CH, Ph), 64.7, 56.9 (CH_2, tmeda), 52.4, 50.1, 48.5, 45.9 (Me, tmeda), 39.4, 37.4 (Me, propanamide), 33.5, 29.4 (CH_2, propanamide).

38a. Yield: 60%. Anal. Calcd for $C_{38}H_{52}F_3N_3O_4PdS$: C, 56.33; H, 6.47; N, 5.19; S, 3.96. Found: C, 56.48; H, 6.77; N, 5.08; S, 4.20. Mp: 104-105 °C. IR (Nujol, cm^{-1}): ν(NH), 3335, 3191; ν(CO), 1649. HRMS (ESI+, m/z): exact mass calcd for $C_{37}H_{52}N_3OPd$ $[M]^+$ requires 660.3145, found 660.3154, error = 1.36 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9529, error = 1.97 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.74 (br, 1 H, NH), 7.73 (m, 1 H, Ar), 7.45-7.40 (m, 3 H, Ph + Ar), 7.29 (m, 1 H, Ar), 7.25 (br, 1 H, NH), 7.13 (m, 1 H, Ar), 7.01 (d, $^{3}J_{HH}$ = 8.0 Hz, 2 H, Ph), 6.77 (d, $^{3}J_{HH}$ = 8.0 Hz, 2 H, Ph), 6.66 (d, $^{3}J_{HH}$ = 8.0 Hz, 2 H, Ph), 3.01 (td, $^{3}J_{HH}$ = 3.2 Hz, $^{2}J_{HH}$ = 12.8 Hz, 1 H, CH_2, tmeda), 2.80-2.75 (m, 1 H, CH_2, propanamide), 2.69 (td, $^{3}J_{HH}$ = 2.8 Hz, $^{2}J_{HH}$ = 13.6 Hz, 1 H, CH_2, tmeda), 2.56 (s, 3 H, Me, tmeda), 2.53-2.43 (m, 6 H, CH_2, ^{n}Bu + propanamide), 2.38 (s, 3 H, Me, tmeda), 2.37-2.31 (m, 1 H, CH_2, propanamide), 2.23-2.20 (m, 1 H, CH_2, tmeda), 2.12-2.08 (m, 1 H, CH_2, tmeda), 1.98 (s, 3 H, Me, tmeda), 1.90 (s, 3 H, Me, tmeda), 1.58-1.44 (m, 4 H, CH_2, ^{n}Bu), 1.35-1.21 (m, 4 H, CH_2, ^{n}Bu), 0.91 (t, $^{3}J_{HH}$ = 7.2 Hz, 3 H, Me), 0.87 (t, $^{3}J_{HH}$ = 7.2 Hz, 3 H, Me). $^{13}C\{^{1}H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 183.8 (CO), 145.1 (C, Ar), 142.9 (CPd), 140.6 (C, $C_6H_4{}^{n}$Bu-4), 140.0 (C, Ph), 139.7 (C, $C_6H_4{}^{n}$Bu-4), 139.4 (C, Ar), 139.3 (PdC=*C*), 137.3 (C, $C_6H_4{}^{n}$Bu-4), 130.5, 130.2 (CH, Ar), 129.6, 129.1, 128.4, 127.4 (CH, $C_6H_4{}^{n}$Bu-4), 127.2, 125.7 (CH, Ar), 64.8, 56.6 (CH_2, tmeda), 53.2, 48.9, 48.8, 44.6 (Me, tmeda), 37.1 (CH_2, propanamide), 35.3, 35.1, 33.3, 33.2 (CH_2, ^{n}Bu), 30.5 (CH_2, propanamide), 22.2, 22.1 (CH_2, ^{n}Bu), 13.92, 13.88 (Me, ^{n}Bu).

39a. Yield: 72%. Anal. Calcd for $C_{30}H_{34}Br_2F_3N_3O_4PdS$: C, 42.10; H, 4.00; N, 4.91; S, 3.75. Found: C, 42.33; H, 4.14; N, 4.86; S, 3.66. Mp: 172-173 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3378, 3199; ν(CO), 1646. HRMS (ESI+, m/z): exact mass calcd for $C_{29}H_{34}N_3OPd$

$[M]^+$ requires 706.0093, found 706.0093, error = 0 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9526, error = 0 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.19 (br, 1 H, NH), 7.70 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.53 (br, 1 H, NH), 7.45-7.41 (m, 3 H, C_6H_4Br-4 + Ar), 7.35-7.30 (m, 3 H, C_6H_4Br-4 + Ar), 7.16 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.11-7.08 (m, 2 H, C_6H_4Br-4), 6.64-6.61 (m, 2 H, C_6H_4Br-4), 3.02 (td, $^3J_{HH}$ = 3.2 Hz, $^2J_{HH}$ = 13.2 Hz, 1 H, CH_2, tmeda), 2.82-2.70 (m, 2 H, CH_2, propanamide + tmeda), 2.53 (s, 3 H, Me), 2.46-2.44 (m, 2 H, CH_2, propanamide), 2.40 (s, 3 H, Me), 2.35-2.31 (m, 1 H, CH_2, propanamide), 2.27-2.23 (m, 1 H, CH_2, tmeda), 2.12-2.08 (m, 1 H, CH_2, tmeda), 2.01 (s, 3 H, Me), 2.00 (s, 3 H, Me). ^{13}C{^{1}H} APT NMR (75.5 MHz, $CDCl_3$): δ 184.7 (CO), 145.0 (C, Ar), 143.6 (CPd), 141.6 (C, C_6H_4Br-4), 140.41 (C, Ar), 140.36 (PdC=*C*), 139.6 (C, C_6H_4Br-4), 131.9, 131.6, 131.4, 130.7 (CH, C_6H_4Br-4), 130.5, 129.7, 127.6, 125.6 (CH, Ar), 120.1, 119.5 (CBr), 65.2, 56.7 (CH_2, tmeda), 53.5, 49.4, 49.0, 44.8 (Me), 38.7, 29.9 (CH_2, propanamide).

40a. Yield: 85%. Anal. Calcd for $C_{22}H_{32}F_3N_3O_8PdS$: C, 39.92; H, 4.87; N, 6.35; S, 4.84. Found: C, 40.13; H, 5.11; N, 6.37; S, 4.67. Mp: 144-146 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3385, 3263, 3226; ν(CO), 1712, 1683, 1669. HRMS (ESI+, m/z): exact mass calcd for $C_{21}H_{32}N_3O_5Pd$ $[M]^+$ requires 512.1377, found 512.1385, error = 1.56 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9528, error = 1.62 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.84 (s, 1 H, NH), 7.79 (s, 1 H, NH), 7.46 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.38 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.33 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.21 (m, 1 H, Ar), 3.89 (s, 3 H, CO_2Me), 3.61 (s, 3 H, CO_2Me), 3.07-2.78 (m, 4 H, CH_2, tmeda + propanamide), 2.90 (s, 3 H, Me, tmeda), 2.86 (s, 3 H, Me, tmeda), 2.55-2.48 (m, 1 H, CH_2, propanamide), 2.34 (s, 3 H, Me, tmeda), 2.35-2.23 (m, 2 H, CH_2, tmeda + propanamide), 2.20-2.17 (m, 1 H, CH_2, tmeda), 2.03 (s, 3 H, Me, tmeda). ^{13}C{^{1}H} APT NMR (75.5 MHz, $CDCl_3$): δ 184.2 ($CONH_2$), 172.9, 162.3 (*C*O_2Me), 159.6 (CPd), 140.6, 139.9 (C, Ar), 135.2 (PdC=*C*), 129.7, 128.9, 128.1, 126.3 (CH, Ar), 65.5, 57.7 (CH_2, tmeda), 55.0 (Me, tmeda), 52.11, 52.04 (CO_2*Me*), 49.2, 48.6, 45.0 (Me, tmeda), 39.3, 31.1 (CH_2, propanamide).

[Pd{η^3-$C_6H_4(C_4Et_4)(CH_2)_2C(O)NH_2$}(tmeda)]TfO (41). To a solution of **29a** (262 mg, 0.53 mmol) in acetone (15 mL) was added AgTfO (136 mg, 0.53 mmol) and the resulting suspension was stirred for 30 min. The solvent was removed under a vacuum, the residue was extracted with CH_2Cl_2 (6 × 5 mL), and the combined extracts were filtered through anhydrous $MgSO_4$. 3-Hexyne (180 μL, 1.57 mmol) was then added to the filtrate and

the mixture was stirred for 15 h and filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (5 mL) and addition of *n*-pentane (30 mL) gave a yellowish orange precipitate, which was collected by filtration and recrystallized from CH_2Cl_2/Et_2O to give **41** as a yellow solid. Yield: 291 mg, 81%. Anal. Calcd for $C_{28}H_{46}F_3N_3O_4PdS$: C, 49.16; H, 6.78; N, 6.14; S, 4.69. Found: C, 48.71; H, 6.79; N, 6.05; S, 4.50. Mp: 122-123 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3353, 3160; ν(CO), 1684. HRMS (ESI+, m/z): exact mass calcd for $C_{27}H_{46}N_3OPd$ $[M]^+$ requires 534.2676, found 534.2697, error = 3.93 ppm. HRMS (ESI–, m/z): exact mass calcd for CF_3O_3S $[M]^-$ requires 148.9526, found 148.9529, error = 2.05 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 6.70 (br, 1 H, NH), 6.10 (d, $^3J_{HH}$ = 6.0 Hz, H9), 6.01 (dd, $^3J_{HH}$ = 6.4 Hz, $^3J_{HH}$ = 6.8 Hz, H7), 5.24 (br, 1 H, NH), 4.69-4.64 (m, 2 H, H6, H8), 2.91-2.63 (m, 8 H, CH_2CH_3 + CH_2, tmeda), 2.78 (s, 12 H, Me, tmeda), 2.39-2.23 (m, 6 H, CH_2CH_3 + CH_2, propanamide), 2.01-1.79 (m, 1 H, CH_2CH_3), 1.78-1.62 (m, 2 H, CH_2CH_3 + CH_2, propanamide), 1.56-1.47 (m, 1 H, CH_2, propanamide), 1.16 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3), 1.11-1.06 (m, 6 H, CH_2CH_3), 0.98 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 174.5 (CO), 147.6, 146.3, 139.8, 138.2 (C1–4), 129.4 (C10), 114.2 (C9), 107.8 (C7), 103.1 (C6), 70.7 (C5), 64.6 (C8), 60.2 (CH_2, tmeda), 51.0 (br, Me, tmeda), 31.7, 25.2 (CH_2, propanamide), 22.4, 19.12, 19.09, 18.3 (CH_2CH_3), 15.3, 15.1, 14.9, 14.5 (CH_2CH_3).

Synthesis of (*Z*)-6,7-diphenyl-1,2-dihydro-4*H*-benzo[*e*]azonine-3,5-dione (42), (*Z*)-6,7-Bis(4-butylphenyl)-1,2-dihydro-4*H*-benzo[*e*]azonine-3,5-dione (43), and (*Z*)-6,7-Bis(4-bromophenyl)-1,2-dihydro-4*H*-benzo[*e*]azonine-3,5-dione (44). A solution of the corresponding complex **37a**, **38a**, or **39a** (0.30 mmol) in $CHCl_3$ (15 mL) was stirred under a CO atmosphere (1.4 bar) at 50 °C for 15 h, whereupon a black precipitate of Pd gradually formed. The suspension was filtered through anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel, using a 3:1 EtOAc/*n*-hexane mixture as eluent [Rf = 0.8-0.9 (**42**), 0.7-0.8 (**43**), 0.8 (**44**)]). The compounds were isolated as colorless solids (**42** and **44**) or as a yellow oil (**43**) after evaporation of the solvents.

42. Yield: 52%. Mp: 202-203 °C. IR (Nujol, cm^{-1}): ν(NH), 3224; ν(C=O), 1685. HRMS (ESI+, m/z): exact mass calcd for $C_{24}H_{20}NO_2$ $[M+H]^+$ requires 354.1489, found 354.1493, error = 1.19 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.68 (br, 1 H, NH), 7.36-7.08 (m, 14 H, H8–11 + Ph), 3.99-3.91 (m, 1 H, H2), 3.25-3.19 (m, 1 H, H1), 3.07-2.99 (m, 1 H, H1), 2.87-2.82 (m, 1 H, H2). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 172.4 (C3), 169.6 (C5), 141.7 (C7), 140.1 (C7a), 137.0 (C, Ph), 135.6 (C11a), 134.6 (C, Ph), 134.1 (C6),

131.2 (C11), 129.8 (CH, Ph), 129.4 (CH, Ph + C8), 128.9 (CH, Ph), 128.8 (C10), 128.6 (CH, Ph), 128.32 (CH, Ph), 128.28 (CH, Ph), 127.7 (C9), 34.4 (C2), 31.2 (C1).

43. Yield: 46%. IR (CH_2Cl_2, cm^{-1}): ν(C=O), 1701, 1681. HRMS (ESI+, m/z): exact mass calcd for $C_{32}H_{36}NO_2$ $[M+H]^+$ requires 466.2741, found 466.2746, error = 1.15 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.59 (br, 1 H, NH), 7.31-7.21 (m, 5 H, H8–10 + H2 and H6 of $C_6H_4{}^nBu$-4), 7.15-7.13 (m, 1 H, H11), 7.11-7.07 (m, 2 H, H3 and H5 of $C_6H_4{}^nBu$-4), 7.01-6.98 (m, 2 H, H2 and H6 of $C_6H_4{}^nBu$-4), 6.96-6.94 (m, 2 H, H3 and H5 of $C_6H_4{}^nBu$-4), 3.97-3.91 (m, 1 H, H2), 3.23-3.17 (m, 1 H, H1), 3.04-2.96 (m, 1 H, H1), 2.83-2.78 (m, 1 H, H2), 2.59 (t, $^3J_{HH}$ = 8.0 Hz, 2 H, CH_2, ^{n}Bu), 2.52 (t, $^3J_{HH}$ = 8.0 Hz, 2 H, CH_2, ^{n}Bu), 1.59-1.49 (m, 4 H, CH_2, ^{n}Bu), 1.39-1.25 (m, 4 H, CH_2, ^{n}Bu), 0.92 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, Me), 0.89 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 172.6 (C3), 170.0 (C5), 143.4, 143.3 (C, $C_6H_4{}^nBu$-4), 141.0 (C7), 140.5 (C7a), 135.7 (C11a), 134.3 (C, $C_6H_4{}^nBu$-4), 133.4 (C6), 131.9 (C, $C_6H_4{}^nBu$-4), 131.1 (C11), 129.7 (CH, $C_6H_4{}^nBu$-4), 129.5 (C8), 129.2, 128.9 (CH, $C_6H_4{}^nBu$-4), 128.7 (C10), 128.2 (CH, $C_6H_4{}^nBu$-4), 127.7 (C9), 35.4, 35.3 (CH_2, ^{n}Bu), 34.4 (C2), 33.3, 33.2 (CH_2, ^{n}Bu), 31.2 (C1), 22.3 (CH_2, ^{n}Bu), 13.91, 13.89 (Me).

44. Yield: 72%. Anal. Calcd for $C_{24}H_{17}Br_2NO_2$: C, 56.39; H, 3.35; N, 2.74. Found: C, 56.31; H, 3.38; N, 2.82. Mp: 155-157 °C. IR (Nujol, cm^{-1}): ν(NH), 3200; ν(C=O), 1702, 1682. HRMS (ESI+, m/z): exact mass calcd for $C_{24}H_{18}Br_2NO_2$ $[M+H]^+$ requires 511.968, found 511.969, error = 2.01 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.64 (br, 1 H, NH), 7.47-7.43 (m, 2 H, C_6H_4Br-4), 7.34-7.28 (m, 4 H, H9, H10 + C_6H_4Br-4), 7.24-7.21 (m, 2 H, C_6H_4Br-4), 7.20-7.16 (m, 2 H, H8, H11), 6.97-6.93 (m, 2 H, C_6H_4Br-4), 3.81-3.73 (m, 1 H, H2), 3.21-3.15 (m, 1 H, H1), 3.09-3.01 (m, 1 H, H1), 2.87-2.82 (m, 1 H, H2). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 172.0 (C3), 168.8 (C5), 141.1 (C7), 139.4 (C7a), 135.7 (C, C_6H_4Br-4), 135.4 (C11a), 133.6 (C6), 133.1 (C, C_6H_4Br-4), 132.4, 131.8 (CH, C_6H_4Br-4), 131.4 (C11), 131.3, 130.9 (CH, C_6H_4Br-4), 129.3 (C8), 129.2 (C10), 128.0 (C9), 123.2, 123.0 (CBr), 34.5 (C2), 31.1 (C1).

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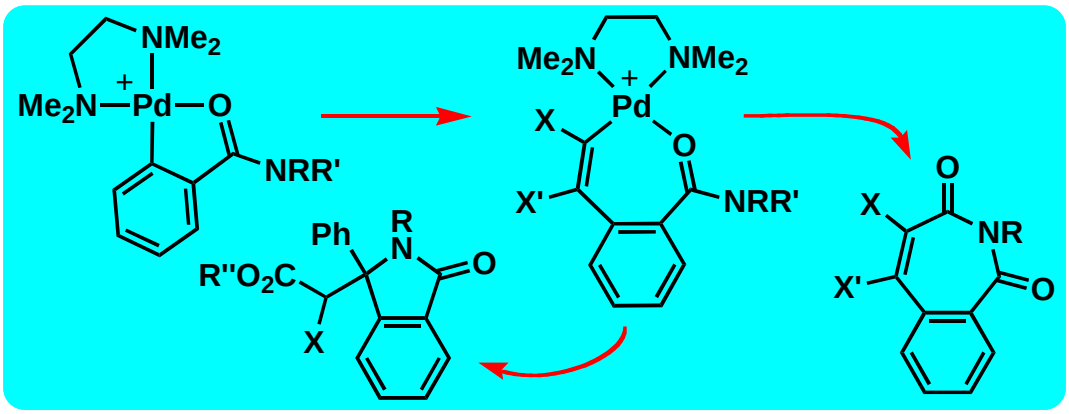
CHAPTER IV

Reactivity of Ortho-Palladated Benzamides Toward CO, Isocyanides, and Alkynes. Synthesis of Functionalized Isoindolin-1-ones and 4,5-Disubstituted Benzo[*c*]azepine-1,3-diones



The results of this chapter have been published in:

R. Frutos-Pedreño, P. González-Herrero, J. Vicente, P. G. Jones, *Organometallics* **2013**, *32*, 4664–4676.

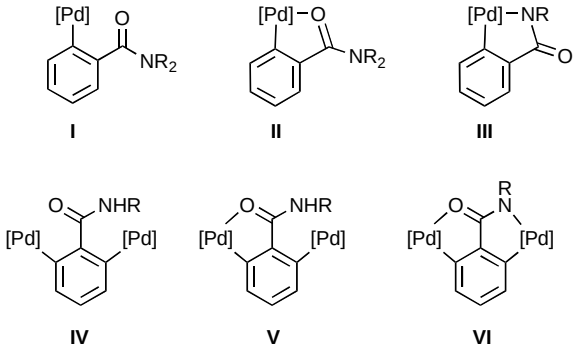
Abstract

Aryl palladium complexes [Pd{$C_6H_4C(O)NRR'$-2}I(tmeda)] [NRR' = NH_2 (**46a**), NHMe (**46b**), NMe_2 (**46c**); tmeda = *N,N,N′,N′*-tetramethylethylenediamine] are prepared by oxidative addition of the corresponding 2-iodophenylbenzamides (**45a-c**) to "$Pd(dba)_2$" ([$Pd_2(dba)_3$]·dba; dba = dibenzylideneacetone) in the presence of tmeda. Cationic cyclometalated derivatives [Pd{κ^2C,O-$C_6H_4C(O)NRR'$-2}(tmeda)]TfO (**47a–c**) are obtained by iodide abstraction from the appropriate complex **46** with AgTfO, while the deprotonation of the amide function of **46a** or **46b** with KO^{t}Bu gives the neutral amidate complexes [Pd{κ^2C,N-$C_6H_4C(O)NR$-2}(tmeda)] [R = H (**48a**), Me (**48b**)]. Complexes **47a,b** and **48a,b** react with CO under mild conditions to yield phthalimide (**49a**) or *N*-methylphthalimide (**49b**), whereas the reactions of derivatives **46c** and **47c** with CO are very slow and give N^1,N^1,N^2,N^2-tetramethylphthalamide and phthalic anhydride. The reaction of **46b** with 1 equiv of XyNC (Xy = 2,6-dimethylphenyl) or ^{t}BuNC affords Pd(0), (tmedaH)I and 3-(2,6-dimethylphenyimino)-2-methylisoindolin-1-one (**50b**) or 3-(*tert*-butylimino)-2-methylisoindolin-1-one (**50b'**), respectively, while complex **46c** reacts with 3 equiv XyNC to give *trans*-[Pd{$C(=NXy)C_6H_4C(O)NMe_2$-2}I$(CNXy)_2$] (**51**). The seven-membered palladacycles [Pd{κ^2C,O-$C(X)=C(X')C_6H_4C(O)NRR'$-2}(tmeda)]TfO [NRR' = NH_2 and X = Ph, X' = Me (**52a**); NRR' = NHMe and X = Ph, X' = Me (**52b**), X = X' = Ph (**53b**), Et (**54b**), CO_2Me (**55b**), X = CO_2Me, X' = Ph (**56b**), X = CO_2Et, X' = Ph (**57b**); NRR' = NMe_2 and X = X' = Ph (**53c**), Et (**54c**)] are obtained from the reactions of **47a–c** with alkynes. Treatment of complexes **52a**, **52b**, **53b** and **54b** with CO at room temperature gives the corresponding 2*H*-benzo[*c*]azepine-1,3-diones (**59**), resulting from the insertion of a molecule of CO into the Pd–C bond followed by a C–N reductive coupling. In contrast, the reactions of **56b** or **57b** with CO in the presence of residual water or 2 equiv of ROH (R = Me, Et) lead to 2-methyl-3-phenylisoindolin-1-one derivatives (**60**), resulting from a CO insertion followed by an intramolecular aza-Michael addition of the NHMe moiety to the activated vinyl group and subsequent hydrolysis or alcoholysis of the acyl–Pd bond. The neutral complex [Pd(κ^2C,O-$C_{14}H_{13}O_5$)(tmeda)] (**63**) was synthesized by reacting the cationic derivative **55b** with NaOMe in MeOH. Depalladation of **63** gives (*E*)-4-[methoxy(methoxycarbonyl)methylene]-2-methylisoquinoline-1,3(2*H*,4*H*)-dione (**64**).

Introduction

Ortho-palladated benzamides are involved as intermediates in certain palladium-catalyzed C–C and C–heteroatom cross-coupling processes, including methodologies for the arylation,[1] trifluoromethylation[2] and alkenylation[3] of benzamides and the preparation of diverse heterocyclic systems.[4-7] Most often, they are produced by oxidative addition of 2-halobenzamides to Pd(0) or amide-directed C–H activations by Pd(II). Despite their important role, only a few of these complexes have been isolated and structurally characterized, and studies of their reactivity are very limited. Examples of isolated ortho-palladated benzamides include acyclic complexes of the type **I**[5, 8] (Chart IV.1) and five-membered *C,O*- (**II**).[6, 8] Deprotonation of the amide function can lead to *C,N*-palladacyclic amidates (**III**).[2, 7] To our knowledge, there are no examples of *C,N*-cyclopalladated arylamides; the coordination of an amide through the nitrogen is highly unfavorable because the nitrogen lone pair is conjugated with the carbonyl group, and therefore amides usually coordinate through the oxygen atom. Several pincer-type complexes containing a *C,N*-cyclopalladated benzamide fragment are also known.[9] Our research group has recently reported the synthesis of ortho-dipalladated benzamides, as well as *C,O*-cyclopalladated and *C,O*/*C,N*-dicyclopalladated ("akimbo") derivatives (**IV** – **VI**).[10]

Chart IV.1



As part of our ongoing research on the reactivity of ortho-functionalized arylpalladium complexes, we have recently shown that ortho-palladated phenylacetamides[11] and 3-phenylpropanamides[12] undergo C–N reductive coupling after the insertion of CO or isocyanides into the Pd–C bond, leading to six- or seven-membered heterocycles under mild conditions. Eight- and nine-membered heterocycles were also obtained via sequential insertion of alkynes and CO into the Pd–C bond followed by reductive C–N coupling.[12, 13] In this chapter, we report the synthesis of a family of ortho-palladated benzamides and their *C,O*-

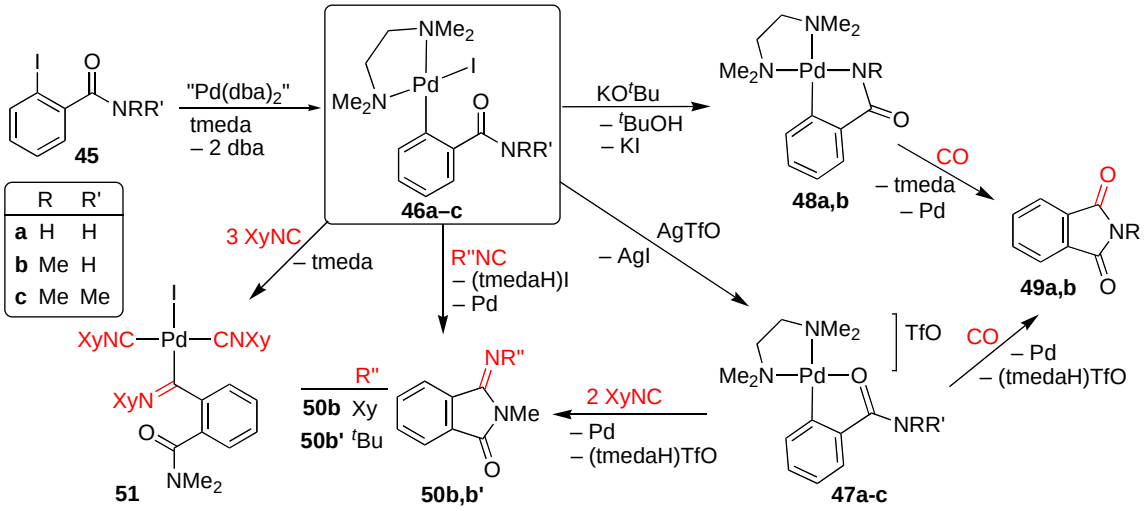
and *C,N*-palladacyclic derivatives and the study of their reactivity toward CO, isocyanides, and alkynes, with the main objective of exploring the feasibility of heterocycle formation from these systems. A series of new functionalized isoindoline-1-ones and 4,5-disubstituted benzazepine-1,3-diones have been obtained. Both of these heterocyclic frameworks are of great importance because they are found in a variety of bioactive compounds displaying a wide range of therapeutic activities.[14] Benzazepine-1,3-diones are particularly scarce,[15] and, to the best of our knowledge, there are no precedents for 4,5-disubstituted derivatives.

Results and Discussion

Synthesis of Ortho-Palladated Benzamides and Cyclometalated Derivatives. Reactions with CO and Isocyanides

The aryl palladium complexes [Pd{$C_6H_4C(O)NRR'$-2}I(tmeda)] [NRR' = NH_2 (**46a**), NHMe (**46b**), NMe_2 (**46c**); Scheme IV.1] were obtained in moderate yields by oxidative addition of the corresponding 2-iodobenzamides (**45a-c**) to "$Pd(dba)_2$" in the presence of tmeda in CH_2Cl_2 at room temperature.

Scheme IV.1



The cationic derivatives [Pd{κ^2C,O-$C_6H_4C(O)NRR'$-2}(tmeda)]TfO (**47a–c**) were obtained in high yields from **46a–c** via iodide abstraction with AgTfO. In these complexes, the amide function is coordinated through the oxygen atom, as usually observed for amide complexes,[8,10-13,16] thus forming five-membered palladacycles.

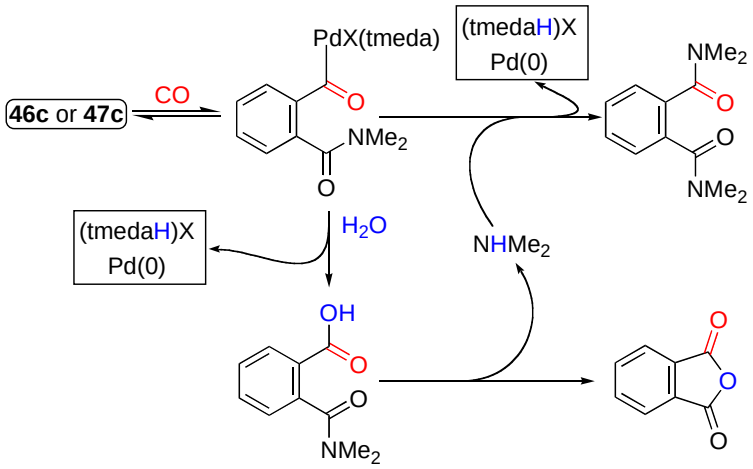
Treatment of complexes **46a** or **46b** with KO^{t}Bu in MeOH led to the deprotonation of the amide function and the formation of the neutral palladacyclic derivatives [Pd{κ^2C,N-

$C_6H_4C(O)NR$-2}(tmeda)] [R = H (**48a**), Me (**48b**)]. These complexes result from the displacement of the iodo ligand by the nitrogen of the amidate group and can be isolated in moderate to good yields. Attempts to deprotonate the methyl group in the NMe_2 derivative **46c** with KO^{t}Bu were unsuccessful.

Complexes **47a,b** and **48a,b** were treated with CO (1.4 bar) in order to verify the possible CO insertion/C–N reductive coupling process. The reactions were complete in about 3 h at room temperature in acetone-D_6 (**47a,b**) or $CDCl_3$ (**48a,b**), quantitatively giving colloidal Pd, (tmedaH)TfO or free tmeda, and phthalimide (**49a**, from **47a** or **48a**) or *N*-methylphthalimide (**49b**, from **47b** or **48b**). At a preparative scale, these organic compounds were isolated in *ca.* 80% yield from **47a** or **47b**, respectively.

The reactions of the NMe_2 derivatives **46c** or **47c** with CO were also carried out to check the possible activation of the methyl groups, which has been shown to be catalyzed by Pd(0) for a series of 2-bromo-*N*-alkyl-*N*-methylbenzamides.[5] However, complete decomposition of these complexes to Pd(0) required 3 days under CO (1.4 bar) at 68 °C in $CHCl_3$ and resulted in the formation of a mixture of (tmedaH)X (X = I^- or TfO^-), phthalic anhydride[17] and N^1,N^1,N^2,N^2-tetramethylphthalamide,[18] which were identified by their NMR data. In addition to these products, the ESI(+) mass spectrum of the crude reaction mixture showed a small amount of *N,N*-dimethylphthalamic acid. It is reasonable that this compound arises from the hydrolysis of an acyl complex by residual water, after which it undergoes internal *O*-cyclization to give phthalic anhydride and dimethylamine (Scheme IV.2).[19] Further molecules of the acyl complex can then undergo aminolysis by dimethylamine to give N^1,N^1,N^2,N^2-tetramethylphthalamide.

Scheme IV.2



The reaction of **46b** with one equiv of XyNC or ^{t}BuNC at room temperature gave colloidal Pd, (tmedaH)I, and 3-(2,6-dimethylphenyimino)-2-methylisoindolin-1-one (**50b**) or 3-(*tert*-butylimino)-2-methylisoindolin-1-one (**50b'**), respectively (Scheme IV.1), which resulted from the insertion of a molecule of isocyanide into the Pd–C bond and a subsequent intramolecular C–N coupling. The intermediate iminoacyl complex could not be isolated because it rapidly decomposed to give the organic product. Compound **50b** was also obtained from **47b** and XyNC, but in this case 2 equiv of the isocyanide were required. In contrast, the reaction of the NH_2 derivative **46a** or **47a** with 1 or 2 equiv, respectively, of XyNC gave mixtures of two products that could not be separated, while the NMe_2 derivative **46c** reacted with 3 equiv of XyNC to give *trans*-[Pd{C(=NXy)C_6H_4C(O)NMe_2-2}I$(CNXy)_2$] (**51**), resulting from the displacement of the tmeda ligand by two of the isocyanide molecules and the insertion of a third isocyanide into the Pd–C bond. Complex **51** was also obtained when only one equiv of isocyanide was employed, leaving part of the starting complex unreacted.

Insertion of Alkynes

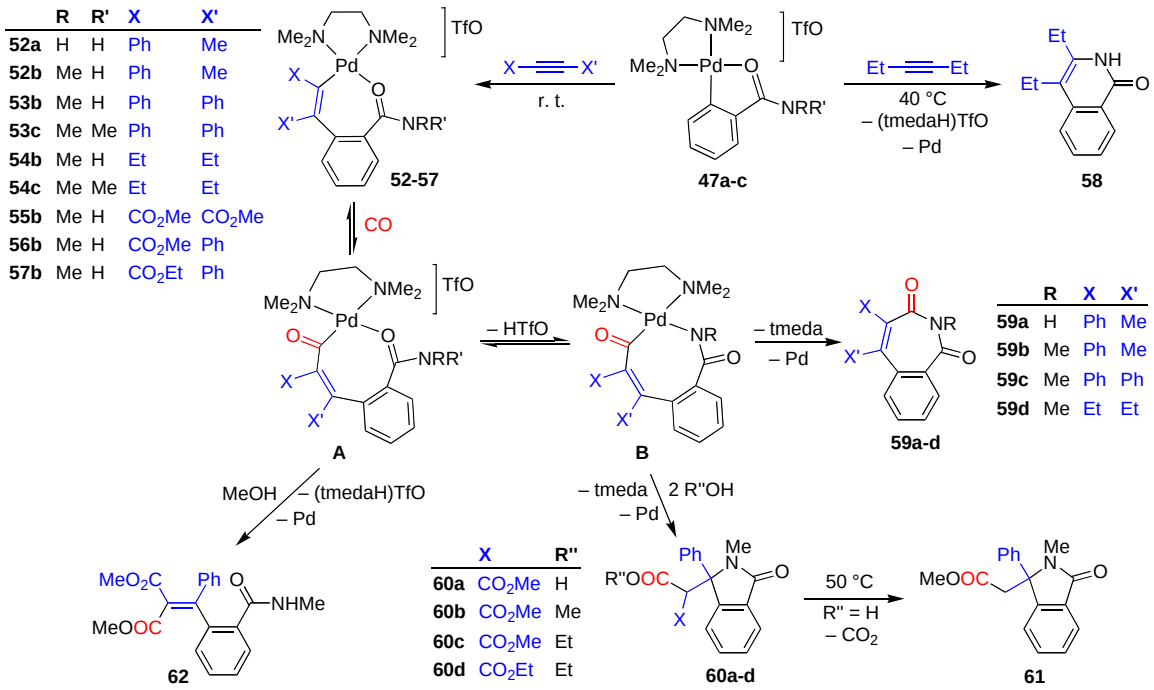
The reactions of palladacycles **47a–c** with a series of internal alkynes XC≡CX' at room temperature afforded good yields of the seven-membered palladacycles [Pd{κ^2*C,O*-C(X)=C(X')C_6H_4C(O)NRR'-2}(tmeda)]TfO [NRR' = NH_2, X = Ph, X' = Me (**52a**); NRR' = NHMe, X = Ph, X' = Me (**52b**), X = X' = Ph (**53b**), Et (**54b**), CO_2Me (**55b**), X = CO_2Me, X' = Ph (**56b**), X = CO_2Et, X' = Ph (**57b**); NRR' = NMe_2, X = X' = Ph (**53c**), Et (**54c**)], resulting from the insertion of one molecule of the alkyne into the Pd–C bond (Scheme IV.3). These reactions required an excess of the alkyne and reaction times in the range 1–5 days to complete, and were thus considerably slower than those of the six- and seven-membered palladacycles [Pd{κ^2*C,O*-$C_6H_4(CH_2)_n$C(O)NRR'-2}(tmeda)]TfO (n = 1,[13] 2[12]). The insertion of alkynes into the Pd–C bond of aryl complexes requires the coordination of the alkyne and the migration of the aryl group to the coordinated alkyne. This process has been shown to be faster as the nucleophilicity of the metalated arylic carbon increases and when alkynes bearing smaller substituents or of a higher electron-withdrawing character are employed.[20] The slower alkyne-monoinsertion reactions of **47a–c** can be ascribed to the higher stability of the five-membered palladacycle, which makes the alkyne coordination step more difficult, and the lower nucleophilicity of the metalated arylic carbon caused by the electron-withdrawing amide function directly bonded to the aryl ring. The required reaction conditions for each case (Table IV.1) clearly reflect the effects of the NRR' group and the

alkyne. For example, the NMe_2 derivative **47c** required a lower excess of the alkyne (five-fold) and a shorter reaction time (1 day) than did the NHMe derivative **47b** for the insertion of diphenylacetylene (ten-fold excess, 5 days), while in the case of the NH_2 derivative **47a** no reaction was observed with a ten-fold excess of this alkyne at room temperature. The attempts to obtain the monoinsertion products by reacting **47a** or **47b** with diphenylacetylene at higher temperatures led to partial decomposition to metallic Pd and complex mixtures. The increasing reactivity toward the insertion of alkynes in the order **47a** < **47b** < **47c** can thus be associated with an increasing nucleophilicity of the metalated arylic carbon as the number of methyl substituents of the amide function increases. The effect of the alkyne is also in line with previously observed trends,[20] as the reactions of more electrophilic or less sterically demanding alkynes with **47a** or **47b** were faster. Thus, the insertion of 1-phenylpropyne into the Pd–C bond of **47a** was feasible at room temperature and the reaction times required in the case of **47b** decreased in the sequence diphenylacetylene > methyl phenylpropiolate ~ ethyl phenylpropiolate > 1-phenylpropyne ~ 3-hexyne ~ dimethylacetylenedicarboxylate. Compound **47a** also reacted with 3-hexyne at room temperature, although the resulting monoinsertion product is unstable and could not be obtained in pure form; when the reaction mixture was heated at 40 °C for 24 h, a partial decomposition to colloidal Pd, (tmedaH)TfO and 3,4-diethylisoquinolin-1(2*H*)-one[21] (**58**) was observed.

Table IV.1. Molar Ratios, Reaction Times and Yields of the Alkyne-Monoinsertion Reactions.

starting complex	alkyne	molar ratio	reaction time (h)	product	yield (%)
47a	1-phenylpropyne	1:10	64	**52a**	65
47b	1-phenylpropyne	1:10	24	**52b**	76
	diphenylacetylene	1:10	120	**53b**	74
	3-hexyne	1:10	24	**54b**	53
	dimethylacetylenedicarboxylate	1:10	24	**55b**	96
	methyl phenylpropiolate	1:10	48	**56b**	71
	ethyl phenylpropiolate	1:10	48	**57b**	67
47c	diphenylacetylene	1:5	24	**53c**	88
	3-hexyne	1:5	24	**54c**	87

Scheme IV.3



Di- or tri-insertion products were not observed in any of the cases, which is striking considering the presence of an excess of alkyne and the larger size of palladacycles **52–57**, which should facilitate the ring opening and the coordination of additional alkyne molecules. This is possibly associated with the relatively low nucleophilicity of the vinylic carbon bonded to Pd, because of the electron-withdrawing effect of the amide carbonyl group.

The regiochemistry of the insertions of the unsymmetrical alkynes 1-phenylpropyne, methyl phenylpropiolate and ethyl phenylpropiolate was established by means of $^{1}H/^{13}C$ heteronuclear multiple-bond correlation (HMBC) experiments and confirmed by the crystal structures of **52a** and **56b** (see below). We have reviewed the regiochemistry of the insertion of alkynes into the Pd–C bond of aryl palladium complexes.[22] The insertion of 1-phenylpropyne led to only the regioisomer with the most sterically demanding substituent in the α-position with respect to the metal (**52a,b**), which is the usual pattern observed for the insertion of unsymmetrical alkynes.[23, 24] However, methyl and ethyl phenylpropiolate led to an approximately 1:0.2 mixture of regioisomers, the major one with the ester group in the α-position, and only this regioisomer was isolated after work-up (**56b**, **57b**). The insertion of phenylpropiolate derivatives into the Pd–C bond of five-membered palladacycles has previously been shown to give preferentially the regioisomer with the ester group in the β-

position.[25] We have recently shown this also to be the case for six-membered palladacycles.[24] Nevertheless, this pattern can be reversed for palladacycles with weakly chelating aryl ligands,[22,26,27] such as **47a–c**, or a highly electron-deficient character.[27,28]

Reactions of Alkyne-Monoinsertion Products with CO

Palladacycles **52a**, **52b**, **53b**, and **54b** reacted with CO (1.4 bar) at room temperature in $CHCl_3$ to give colloidal Pd, (tmedaH)TfO and the corresponding 4,5-disubstituted benzo[*c*]azepine-1,3-diones **59** (Scheme IV.3), resulting from a CO insertion/C–N reductive coupling sequence. The formation of these derivatives probably involves an eight-membered cyclic acyl intermediate **A**, in equilibrium with the amidate **B**, resulting from the deprotonation of the amide function. The latter would ultimately undergo the C–N reductive coupling. In line with our previous observations,[11-13] the NHMe derivatives **52–54b** required a longer reaction time (24 h) than did the NH_2 derivative **52a** (3 h), because the steric repulsion of the methyl substituent makes the C–N coupling slower. The reactions of the NMe_2 derivatives **53c** and **54c** with CO in $CHCl_3$ at 50 °C gave mixtures of decomposition products. The complex with inserted DMAD **55b** also reacted with CO in $CHCl_3$ at room temperature, but gave a mixture of at least three compounds that could not be properly identified.

The palladacycles containing inserted phenylpropiolate derivatives showed a different behavior. Thus, the room-temperature reaction of **56b** with CO (1.4 bar) in CH_2Cl_2 gave colloidal Pd, (tmedaH)TfO and 3-[carboxy(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (**60a**). The NMR data of this compound showed two sets of signals in approximately 1:1 ratio corresponding to the two possible diastereomeric pairs of enantiomers. The cyclization to give the isoindolinone ring is formally the result of an aza-Michael addition of the NHMe moiety to the vinyl group originating from the alkyne. This process probably takes place from the amidate intermediate **B** (Scheme IV.3) and is certainly favored because the vinyl group is highly activated toward conjugated additions. Similar intramolecular aza-Michael additions of an amine or amide function to an α,β-unsaturated ester, ketone or aldehyde moiety are a key step in several methodologies employed for the synthesis of isoindolines or isoindolinones.[29] Finally, the depalladation step takes place through the hydrolysis of the acyl–Pd bond by residual water. Our attempts to isolate compound **60a** from the reaction mixture were unsuccessful because decarboxylation easily occurred to give 3-(methoxycarbonylmethyl)-2-methyl-3-phenylisoindolin-1-one (**61**);

indeed, the latter compound was obtained in pure form after refluxing the reaction mixture in CH_2Cl_2 for 24 h. The facile decarboxylation of phenylmalonic diacids and hemiesters is well known.[30]

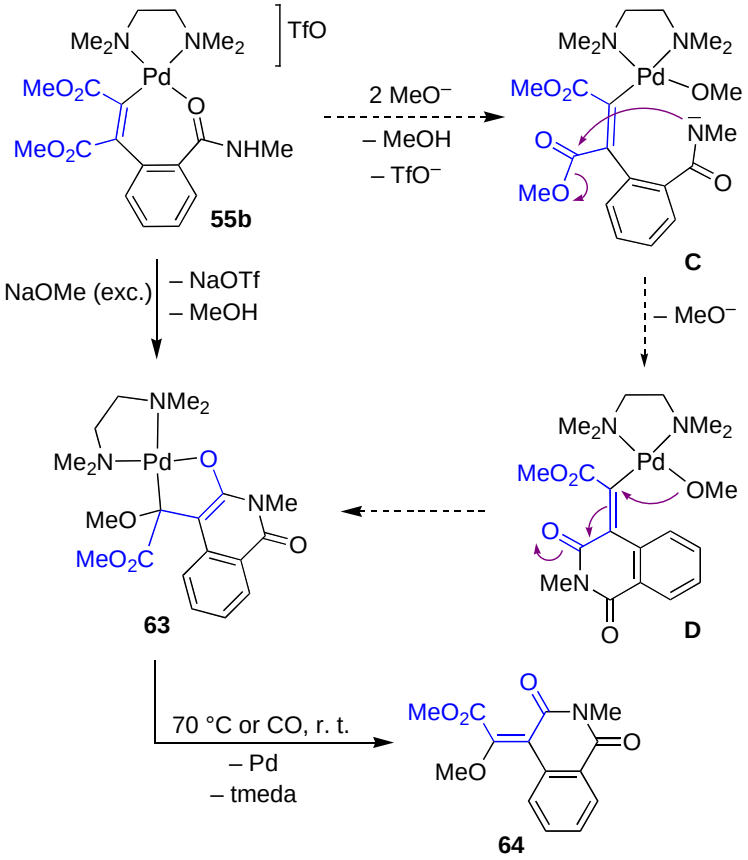
When the reaction of **56b** with CO was carried out in the presence of 2 equiv MeOH or EtOH, the same process took place, but in these cases the depalladation step is an alcoholysis leading to the diesters 3-[di(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (**60b**) or 3-[ethoxycarbonyl(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (**60c**), respectively. Analogously, the reactions of **57b** with CO in the presence of 2 equiv MeOH or EtOH gave **60c** or 3-[di(ethoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (**60d**), respectively.

The use of MeOH as solvent for the reaction of **56b** and CO led to the formation of dimethyl 2-((2-(methylcarbamoyl)phenyl)(phenyl)methylene)malonate (**62**), resulting from the methanolysis of the intermediate acyl complex **A**, and only trace quantities of the heterocyclic compound **60b** were detected in the reaction mixture. Logically, in the presence of a large excess of MeOH, the methanolysis of **A** is much faster than the cyclization. The attempt to cyclize **62** by heating a $CDCl_3$ solution at 70 °C for 24 h in the presence of an excess of tmeda was unsuccessful, suggesting that the aza-Michael addition leading to **60a–d** is assisted by the Pd(II) center, which is consistent with the participation of an amidate intermediate.

Formation and Depalladation of a Neutral Alkyl-Alcoholate Complex

The deprotonation of the amide function in complex **55b** with NaOMe was attempted in order to obtain a seven-membered cyclic amidate and use it as a precursor for the preparation of an additional benzo[*c*]azepine-1,3-dione derivative. However, the reaction of this complex with excess NaOMe in MeOH led to the formation of the unexpected neutral complex [Pd(κ^2*C*,*O*-$C_{14}H_{13}O_5$)(tmeda)] (**63**), which contains a chelating alkyl-alcoholate ligand based on the isoquinoline-1,3-dione scaffold (Scheme IV.4). The formation of this ligand must involve the nucleophilic attack of an amidate group (intermediate **C**) to the ester group in β with respect to the metal to generate a six-membered cyclic imide (**D**). Subsequently a methoxide anion would attack the metalated carbon atom.

Scheme IV.4



The depalladation of complex **63** was achieved by refluxing it in $CHCl_3$ for 2 d and led to the organic compound (*E*)-4-[methoxy(methoxycarbonyl)methylene]-2-methylisoquinoline-1,3(2*H*,4*H*)-dione (**64**). The same product was observed by ^{1}H NMR after reacting complex **63** with CO (1.4 bar) in $CDCl_3$ for 6 h at room temperature (93%). In this case the insertion of CO into the Pd–C bond did not take place, but probably the excess CO assisted the reduction process.

Crystal Structures

The structure of **47a** is shown in Figure IV.1. The amide group is coordinated to the Pd atom through the oxygen, forming a practically planar five-membered *C,O*-palladacycle [mean deviation from plane Pd–C1–C2–C7–O1: 0.03 Å]. The square-planar coordination environment around the Pd center is slightly distorted, because of the small bite of both the chelating benzamide unit [angle C(1)–Pd–O(1): 82.38(6)°] and the tmeda ligand [angle N(2)–Pd–N(3): 85.43(7)°]. The Pd–O(1) bond distance of 2.0220(12) Å is similar to that found for the ortho-palladated benzamide derivative [Pd{κ^2*C,O*-C_6H_4{C(O)NH^{t}Bu}-6-(OMe)$_3$-2,3,4}(bpy)]TfO [2.009(2) Å].[8] The two H atoms of the NH_2 group are involved in

hydrogen bonds with two oxygen atoms of different triflate anions forming infinite chains parallel to [110] (Figure IV.2).

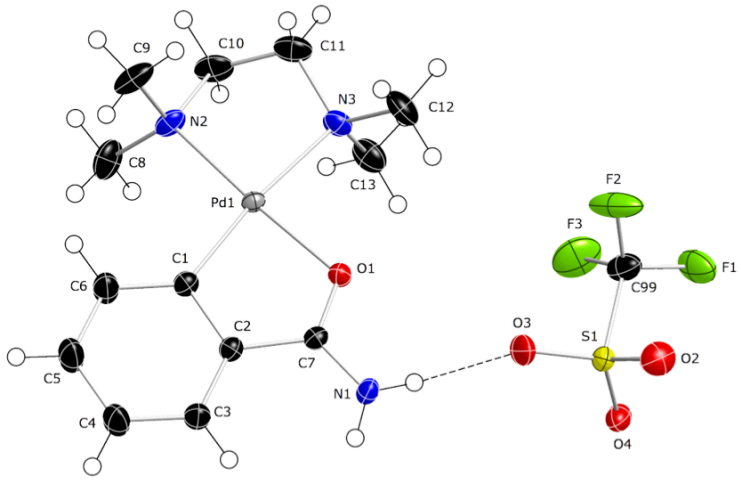


Figure IV.1. Thermal ellipsoid plot (50% probability) of complex **47a**. Selected bond distances (Å) and angles (deg): Pd–C(1) 2.0025(18), Pd–O(1) 2.0220(12), Pd–N(2) 2.0728(15), Pd–N(3) 2.1494(16), O(1)–C(7) 1.272(2), N(1)–C(7) 1.318(2); C(1)–Pd–O(1) 82.38(6), N(2)–Pd–N(3) 85.43(7), C(7)–O(1)–Pd 114.03(11), O(1)–C(7)–C(2) 118.02(15), N(1)–C(7)–C(2) 123.10(16).

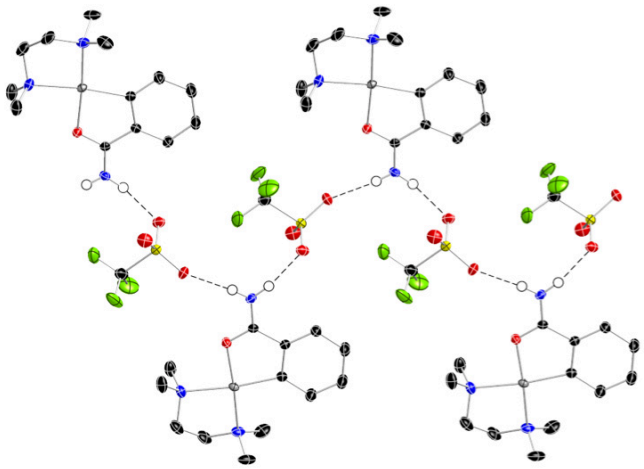


Figure IV.2. Chain of residues connected by hydrogen bonds (dashed bonds).

The amidate group of **48a** is coordinated to the Pd atom through the nitrogen atom, forming an almost planar (mean deviation: 0.05 Å) five-membered ring (Figure IV.3). The Pd–N(1) bond distance of 1.9943(16) Å is similar to or slightly shorter than that found for previously reported five-,[10, 31] six-,[11, 32] or seven-membered[12] cyclic palladium amidate complexes. The O(1)–C(7) bond distance of 1.252(2) Å is longer than the average C–O

distance found in amides (1.234 Å),[33] as expected because of the delocalization of the negative charge over the N–C=O group. The molecules are connected to form inversion-symmetric dimers by a hydrogen bond N1–H01···O1.

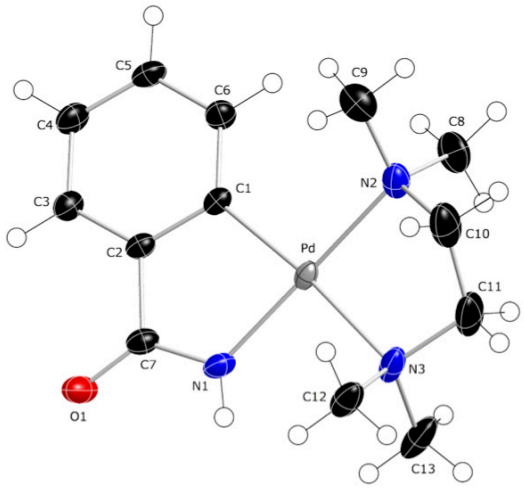


Figure IV.3. Thermal ellipsoid plot (50% probability) of complex **48a**. Selected bond distances (Å) and angles (deg): Pd–N(1) 1.9943(16), Pd–C(1) 2.0058(15), Pd–N(2) 2.1228(16), Pd–N(3) 2.1575(14), O(1)–C(7) 1.252(2), N(1)–C(7) 1.328(2); N(1)–Pd–C(1) 80.56(6), N(2)–Pd–N(3) 84.15(6), C(7)–N(1)–Pd(1) 119.03(12), O(1)–C(7)–C(2) 122.59(15), N(1)–C(7)–C(2) 110.83(15).

The crystal structures of complexes **52a** (Figure IV.4) and **56b** (Figure IV.6) show that the 1-phenylpropyne or methyl phenylpropiolate molecule, respectively, has inserted in a *syn* fashion and the amide function remains coordinated to the metal through the oxygen. The resulting ring shows a folded conformation dictated by the constraints of the planar vinyl, benzene and amide groups; the atoms C1, C2, C9 and O1 are essentially coplanar, with the atoms Pd, C3, C4 lying *ca.* 1.2, 0.9, 0.9 Å to the same side of the plane. The Pd atom is in a square planar environment, slightly distorted by the small bite of the tmeda ligand and the strain of the seven-membered ring. The latter leads to a C(1)–Pd–O(1) angle of 86.17(7)° (**52a**) or 85.50(6)° (**56b**), which is appreciably narrower than the corresponding angle in the larger palladacycles [Pd{κ^2C,O-C(Ph)=C(Ph)C_6H_4(CH_2)$_n$C(O)NH_2-2}(tmeda)]TfO (n = 1, 94.00°;[13] n = 2, 90.47°[12]). In **52a**, the H atoms of the NH_2 group are involved in hydrogen bonds with one oxygen atom of a triflate anion and another oxygen atom of an adjacent molecule, forming inversion-symmetric dimers (Figure IV.5). In **56b**, the NHMe group is connected to the triflate anion through a hydrogen bond.

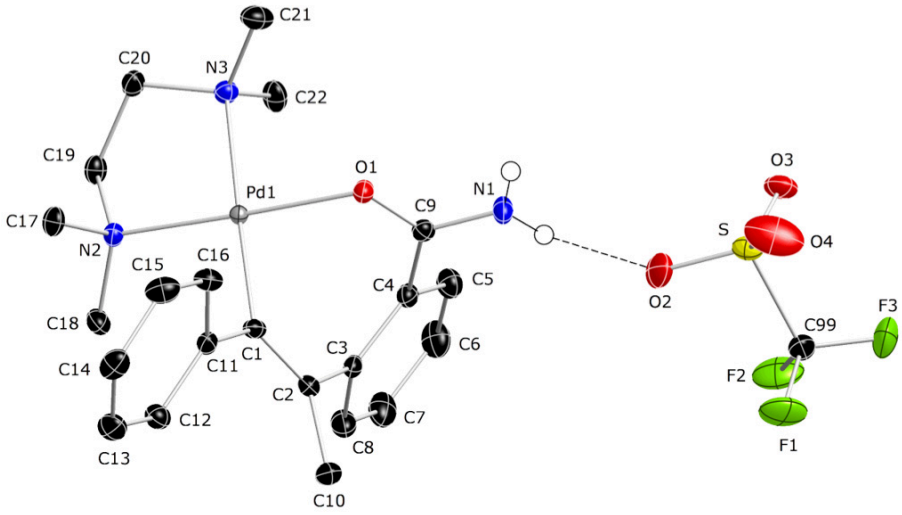


Figure IV.4. Thermal ellipsoid plot (50% probability) of complex **52a**. Selected bond distances (Å) and angles (deg): Pd–C(1) 1.9936(19), Pd–O(1) 2.0525(13), Pd–N(2) 2.0672(16), Pd–N(3) 2.1715(17), O(1)–C(9) 1.266(2), N(1)–C(9) 1.317(3), C(1)–C(2) 1.344(3); C(1)–Pd–O(1) 86.17(7), N(2)–Pd–N(3) 85.37(6), C(9)–O(1)–Pd 120.42(13), C(2)–C(1)–Pd 118.94(15), C(1)–C(2)–C(3) 120.85(18), O(1)–C(9)–C(4) 122.54(17), N(1)–C(9)–C(4) 118.43(18).

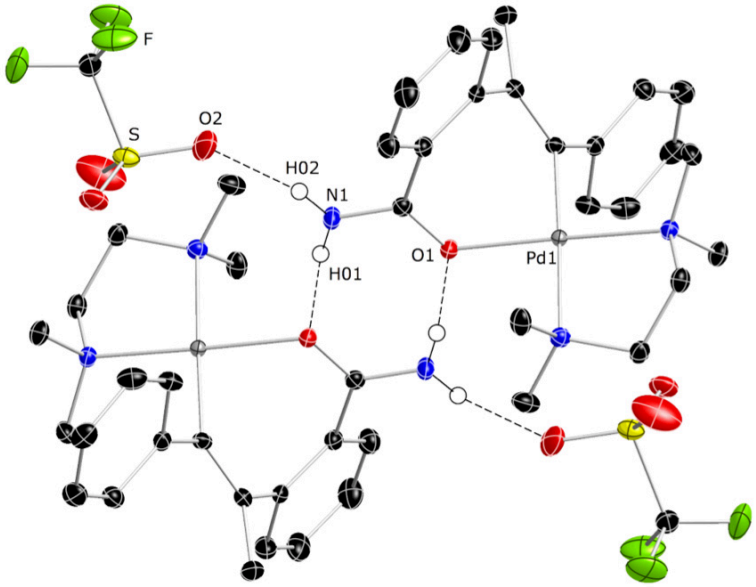


Figure IV.5. Inversion-symmetric dimer of **52a** connected by hydrogen bonds (dashed lines).

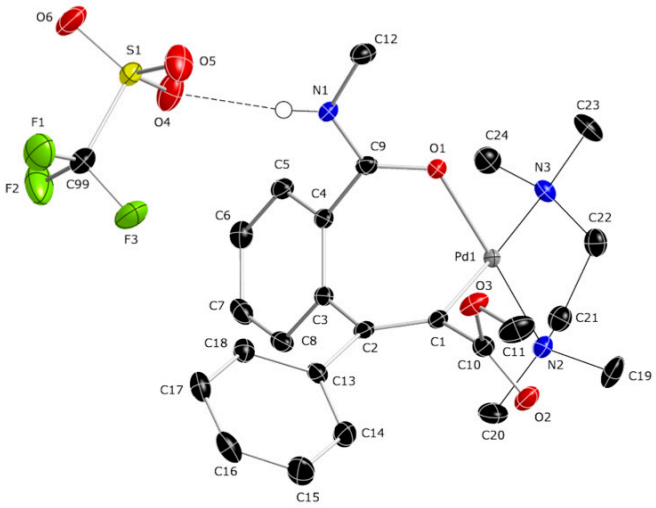


Figure IV.6. Thermal ellipsoid plot (50% probability) of complex **56b**. Selected bond distances (Å) and angles (deg): Pd–C(1) 1.9962(18), Pd–O(1) 2.0580(12), Pd–N(2) 2.0628(15), Pd–N(3) 2.1474(15), C(1)–C(2) 1.345(3), C(9)–O(1) 1.265(2); C(1)–Pd–O(1) 85.50(6), N(2)–Pd–N(3) 85.14(6), C(2)–C(1)–C(10) 124.58(17), C(2)–C(1)–Pd 119.59(14), C(9)–O(1)–Pd 117.92(12), C(1)–C(2)–C(3) 119.39(17), O(1)–C(9)–N(1) 120.28(17), O(1)–C(9)–C(4) 123.27(16).

The crystal structure of compound **59b** is shown in Figure IV.7. The seven-membered ring shows a twisted conformation (N2, C3, C4 lie 0.7, 1.4, 0.65 Å to the same side of the plane C1–C9A–C5A–C5) involving a non-planar imide group (angle of 48° between the C(9A)–C(1)–O(1)–N(2) and C(4)–C(3)–O(2)–N(2) mean planes). Only a few structures of cyclic imides of this size have been reported to date, and these display a similar conformation.[34]

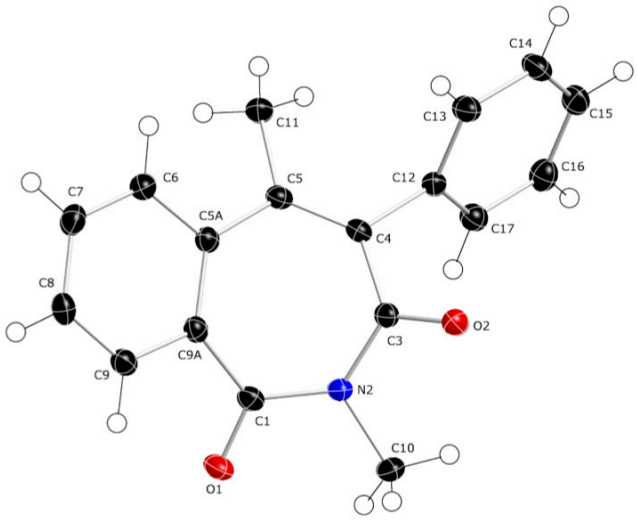


Figure IV.7. Thermal ellipsoid plot (50% probability) of compound **59b**. Selected bond distances (Å) and angles (deg): C(1)–O(1) 1.2194(12), C(1)–N(2) 1.3901(13), C(1)–C(9A) 1.4982(14), N(2)–C(3) 1.4036(13), C(3)–O(2) 1.2164(12), C(3)–C(4) 1.4941(13), C(4)–C(5) 1.3458(14); O(1)–C(1)–N(2) 119.25(9), O(1)–C(1)–C(9A) 120.27(9), N(2)–C(1)–C(9A)

120.06(8), C(1)–N(2)–C(3) 126.46(8), O(2)–C(3)–N(2) 119.37(9), O(2)–C(3)–C(4) 120.86(9), N(2)–C(3)–C(4) 118.85(8), C(5)–C(4)–C(3) 125.71(9), C(4)–C(5)–C(5A) 123.11(9).

Compound **60b** crystallized with two independent molecules in the asymmetric unit (Figure IV.8), for which a least-squares fit gave a r.m.s. deviation of 0.28 Å. The bond distances and angles within the isoindoline fragment are comparable to those found in analogous compounds.[35]

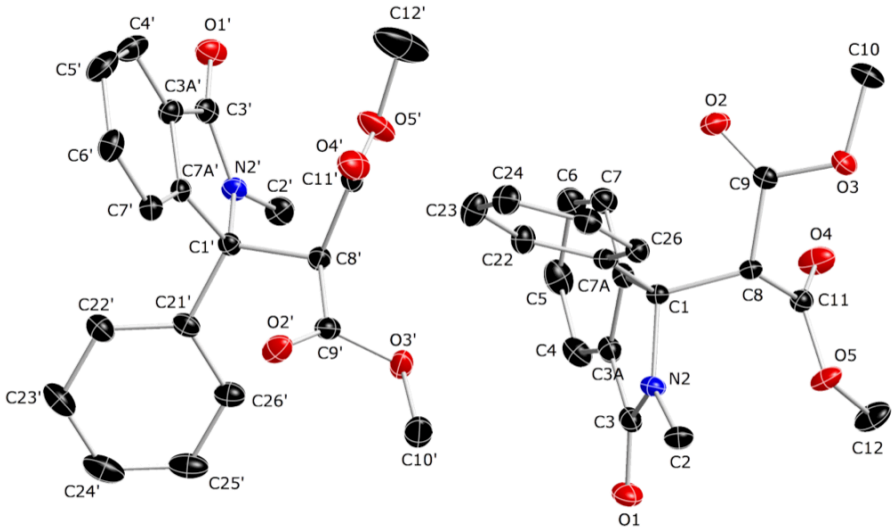


Figure IV.8. Thermal ellipsoid plot (50% probability) of compound **60b**. Selected bond distances (Å) and angles (deg): O(1)–C(3) 1.2290(15), C(1)–N(2) 1.4877(15), C(1)–C(7A) 1.5303(17), N(2)–C(3) 1.3591(16), C(3)–C(3A) 1.4763(18), C(3A)–C(7A) 1.3883(17); N(2)–C(1)–C(7A) 100.41(9), N(2)–C(1)–C(21) 109.52(9), C(7A)–C(1)–C(21) 113.89(10), N(2)–C(1)–C(8) 107.48(9), C(7A)–C(1)–C(8) 112.89(10), C(21)–C(1)–C(8) 111.81(10), C(3)–N(2)–C(2) 121.38(10), C(3)–N(2)–C(1) 113.92(10), C(2)–N(2)–C(1) 124.33(10), O(1)–C(3)–N(2) 125.31(12), O(1)–C(3)–C(3A) 128.18(12), N(2)–C(3)–C(3A) 106.50(10).

The structure of complex **63** (Figure IV.9) proved to be a CH_2Cl_2 monosolvate. It shows the isoquinoline-1,3-dione–based ligand coordinated through one of the oxygen atoms and the deprotonated methoxy(methoxycarbonyl)methyl group, forming a nearly planar five-membered palladacycle (mean deviation 0.04 Å). The Pd–O(1) distance of 2.0267(11) is comparable to that found in some Pd(II) phenolato complexes.[36]

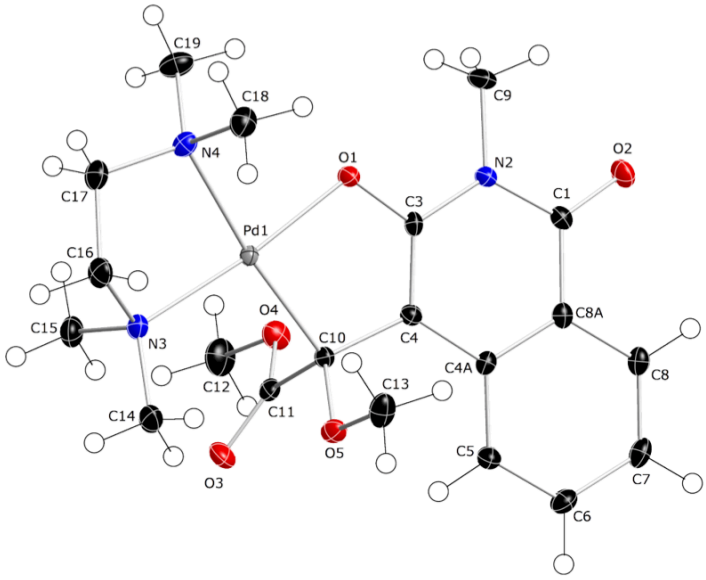


Figure IV.9. Thermal ellipsoid plot (50% probability) of complex **63**. Selected bond distances (Å) and angles (deg): Pd–O(1) 2.0267(11), Pd–C(10) 2.0635(14), Pd–N(3) 2.1058(12), Pd–N(4) 2.1783(12), C(1)–O(2) 1.2422(19), C(1)–N(2) 1.388(2), N(2)–C(3) 1.3967(19), C(3)–O(1) 1.3075(18), C(3)–C(4) 1.368(2), C(4)–C(10) 1.507(2); O(1)–Pd–C(10) 84.38(5), N(3)–Pd–N(4) 83.42(5), C(4)–C(10)–Pd(1) 105.48(9), C(3)–O(1)–Pd 110.72(10), C(1)–N(2)–C(3) 122.90(13), O(1)–C(3)–C(4) 122.66(15), O(1)–C(3)–N(2) 116.22(14), C(4)–C(3)–N(2) 121.10(15), C(3)–C(4)–C(10) 115.87(14), C(3)–C(4)–C(4A) 119.76(15).

The crystal structure of compound **64** (Figure IV.10) reveals that the C4–C9 double bond has an *E* configuration, which must be the most sterically favored.

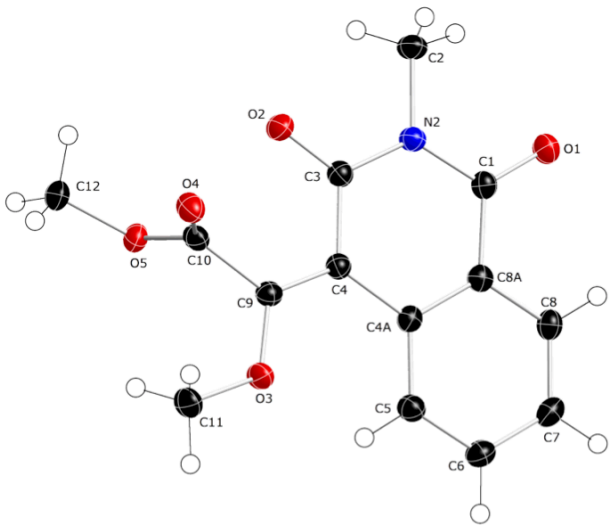


Figure IV.10. Thermal ellipsoid plot (50% probability) of compound **64**. Selected bond distances (Å) and angles (deg): O(1)–C(1) 1.2194(14), O(2)–C(3) 1.2285(14), C(1)–N(2) 1.3917(14), C(1)–C(8A) 1.4820(15), N(2)–C(3) 1.3823(14), C(3)–C(4) 1.4838(15), C(4)–C(9) 1.3573(16), C(4)–C(4A) 1.4707(15); O(1)–C(1)–N(2) 120.45(10), O(1)–C(1)–C(8A)

122.68(10), N(2)–C(1)–C(8A) 116.86(9), C(3)–N(2)–C(1) 125.01(9), C(3)–N(2)–C(2) 116.94(9), C(1)–N(2)–C(2) 118.03(9), O(2)–C(3)–N(2) 119.41(10), O(2)–C(3)–C(4) 122.24(10), N(2)–C(3)–C(4) 118.34(10), C(9)–C(4)–C(4A) 126.22(10), C(9)–C(4)–C(3) 114.69(10), C(4A)–C(4)–C(3) 119.08(10).

Experimental Section

General Considerations, Materials and Instrumentation

Unless otherwise noted, all preparations were carried out at room temperature under atmospheric conditions. Synthesis grade solvents were obtained from commercial sources. CH_2Cl_2 was degassed and dried using a Pure Solv MD-5 solvent purification system from Innovative Technology, Inc. The compound $[Pd_2(dba)_3]$·dba was prepared according to the published procedure.[37] The preparations of 2-iodo-*N*-methylbenzamide and 2-iodo-*N,N*-dimethylbenzamide are given in the Supporting Information. All other reagents were obtained from commercial sources and used without further purification. NMR spectra were recorded on Bruker Avance 200, 300 or 400 spectrometers at 298 K. Chemical shifts are referred to internal TMS. The assignments of the ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were made with the help of HMBC and HMQC experiments. Inserted and coordinated XyNC are denoted by $XyNC^{i}$ and $XyNC^{c}$, respectively, and the 1,2-C_6H_4 arylene group is denoted by Ar. Melting points were determined on a Reichert apparatus and are uncorrected. Elemental analyses were carried out with Carlo Erba 1106 and LECO CHNS-932 microanalyzers. Infrared spectra were recorded in the range 4000-200 cm^{-1} on a Perkin-Elmer Spectrum 100 spectrophotometer using Nujol mulls between polyethylene sheets or CH_2Cl_2 solutions. High-resolution ESI mass spectra were recorded on an Agilent 6220 Accurate-Mass TOF LC/MS.

X–Ray Structure Determinations

Crystals suitable for X–ray diffraction studies were obtained by liquid-liquid diffusion from acetone/Et_2O (**47a**), CH_2Cl_2/Et_2O (**48a**), CH_2Cl_2/Et_2O (**52a**), $CDCl_3$/Et_2O (**56b**), $CDCl_3$/*n*-hexane (**60b**) or CH_2Cl_2/*n*-hexane (**63**·CH_2Cl_2), or by sublimation at low pressure (**59b** and **64**). Numerical details are given in the Supporting Information (Tables IV.2 and IV.3). The data for **48a**, **52a**, **56b**, **60b**, and **63**·CH_2Cl_2 were collected on an Oxford Diffraction Xcalibur E diffractometer using monochromated Mo-*K*α radiation in *ω*-scan mode. The data for **47a**, **59b**, and **64** were collected on an Oxford Diffraction Nova A diffractometer using mirror-focused Cu-*K*α radiation in *ω*-scan mode. Absorption corrections were based on

multi-scans. The structures were solved by direct methods and refined anisotropically on F^2 using the program SHELXL-97 (G. M. Sheldrick, University of Göttingen).[38] Treatment of hydrogen atoms was as follows: NH (where present) freely refined, methyls as idealized rigid groups allowed to rotate but not tip, other H using a riding model starting from calculated positions. *Exceptions and special features*: The Flack parameter refined to –0.019(4) for **47a** and –0.025(12) for **63**. For **60b**, no absorption correction was applied. For **48a**, a significant isolated difference peak near the twofold axis was tentatively refined as a water oxygen, but no water hydrogens were located.

Table IV.2. Crystallographic Data for **47a**, **48a**, **52a**, and **56b**.

	47a	**48a**·1.17H_2O	**52a**	**56b**
formula	$C_{14}H_{22}F_3N_3O_4PdS$	$C_{13}H_{21.34}N_3O_{1.17}Pd$	$C_{23}H_{30}F_3N_3O_4PdS$	$C_{25}H_{32}F_3N_3O_6PdS$
fw	491.81	344.84	607.96	666.00
T (K)	100	100	100	100
λ (Å)	1.54148	0.71073	0.71073	0.71073
cryst syst	trigonal	monoclinic	orthorhombic	orthorhombic
space group	$P3_221$	$C2/c$	$Pbcn$	$Pbca$
a (Å)	11.60504(8)	17.7877(7)	28.1406(8)	17.8564(4)
b (Å)	11.60504(8)	12.4571(3)	9.4389(3)	16.0031(4)
c (Å)	24.7296(2)	15.6840(6)	19.7762(6)	19.9027(4)
α (deg)	90	90	90	90
β (deg)	90	124.139(6)	90	90
γ (deg)	120	90	90	90
V (Å^3)	2884.31(4)	2876.42(17)	5252.9(3)	5687.3(2)
Z	6	8	8	8
ρ_{calcd} (Mg m^{-3})	1.699	1.593	1.538	1.556
μ (mm^{-1})	9.3	1.3	0.8	0.8
R1[a]	0.0144	0.0223	0.0306	0.0290
wR2[b]	0.0374	0.0531	0.0673	0.0656

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

Table IV.3. Crystallographic Data for **59b**, **60b**, **63** and **64**.

	59b	**60b**	**63**·CH_2Cl_2	**64**
formula	$C_{18}H_{15}NO_2$	$C_{20}H_{19}NO_5$	$C_{21}H_{31}Cl_2N_3O_5Pd$	$C_{14}H_{13}NO_5$
fw	277.31	353.36	582.79	275.25
T (K)	100	100	100	100
λ (Å)	1.54148	0.71073	0.71073	1.54148
cryst syst	triclinic	triclinic	orthorhombic	monoclinic
space group	$P\bar{1}$	$P\bar{1}$	$Pca2_1$	$P2_1/n$
a (Å)	8.8386(10)	8.5887(2)	18.1799(2)	10.2315(6)
b (Å)	9.2130(10)	13.2148(4)	8.36643(10)	6.8252(4)

c (Å)	10.0650(10)	15.8792(4)	15.7760(2)	18.2358(11)
α (deg)	115.140(10)	99.440(2)	90	90
β (deg)	105.462(10)	96.959(2)	90	104.125(6)
γ (deg)	98.329(10)	96.003(2)	90	90
V (Å^3)	683.09(13)	1750.45(8)	2399.54(5)	1234.93(13)
Z	2	4	4	4
ρ_{calcd} (Mg m^{-3})	1.348	1.341	1.613	1.480
μ (mm^{-1})	0.7	0.1	1.0	1.0
R1[a]	0.0318	0.0443	0.0167	0.0320
wR2[b]	0.0812	0.1085	0.0404	0.0903

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

Synthesis

2-Iodo-*N*-methylbenzamide (45b). To a solution of 2-iodobenzoic acid (5 g, 20.16 mmol) in dry CH_2Cl_2 (80 mL) was added $SOCl_2$ (10 mL, 137.85 mmol) and the mixture was stirred at 50 °C for 6 h under an N_2 atmosphere. The solvent was evaporated under reduced pressure to give an oil. Aqueous $MeNH_2$ (40%, 100 mL) was then added dropwise while keeping the solution at 0 °C in an ice-bath. The resulting suspension was stirred at 0 °C for 1 h and then concentrated to ca. 50 mL. The colorless precipitate was collected by filtration, washed with H_2O (5 × 5 mL) and vacuum-dried at 50 °C for 16 h. Yield: 4.64 g, 88%. HRMS (ESI+, m/z): exact mass calcd for C_8H_9INO $[M+H]^+$ requires 261.9723, found 261.9729, error = 2.33 ppm. Mp: 153 °C (lit 145-147 °C[39]). The ^1H NMR data are in agreement with those reported in the literature.[39]

2-Iodo-*N*,*N*-dimethylbenzamide (45c). To a solution of 2-iodobenzoic acid (5.00 g, 20.16 mmol) in dry CH_2Cl_2 (80 mL) was added $SOCl_2$ (10 mL, 137.85 mmol) and the mixture was stirred at 50 °C for 6 h under an N_2 atmosphere. The solvent was evaporated under reduced pressure to give an oil. Aqueous Me_2NH (40%, 40 mL) was then added dropwise while keeping the solution at 0 °C in an ice-bath. The mixture was stirred at 0 °C for 30 min, treated with a saturated solution of K_2CO_3 in H_2O (100 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The solvent was then evaporated under reduced pressure and the residue was vacuum-dried at 60 °C for 16 h to give the product as a viscous oil. Yield: 5.30 g, 96%. HRMS (ESI+, m/z): exact mass calcd for $C_9H_{11}INO$ $[M+H]^+$ requires 275.988, found 275.9891, error = 3.96 ppm. The ^1H NMR data are in agreement with those reported in the literature.[40]

[Pd{$C_6H_4C(O)NRR'$-2}I(tmeda)] [NRR' = NH_2 (46a), NHMe (46b), NMe_2 (46c)]. To a suspension of $Pd(dba)_2$ (1234 mg, 2.15 mmol) in CH_2Cl_2 (20 mL) were added tmeda (0.4 mL, 2.66 mmol) and 2-iodobenzamide, 2-iodo-*N*-methylbenzamide, or 2-iodo-*N,N*-dimethylbenzamide (2.15 mmol), and the mixture was stirred for 90 min under an N_2 atmosphere. The resulting black suspension was filtered through anhydrous $MgSO_4$ and the clear orange filtrate was concentrated (1 mL). The addition of Et_2O (20 mL) led to the formation of a precipitate, which was filtered off, washed with a 1:2 MeOH/Et_2O mixture (3 × 5 mL) (**46a**) or Et_2O (3 × 5 mL) (**46b,c**) and vacuum-dried to give the corresponding complex **46**.

46a. Yellow solid. Yield: 53%. Anal. Calcd for $C_{13}H_{22}IN_3OPd$: C, 33.25; H, 4.72; N, 8.95. Found: C, 33.34; H, 4.80; N, 8.60. Mp: 130-132 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3307; ν(CO), 1647. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.26 (br s, 1 H, NH), 7.63 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.55 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.03 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.93 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.02 (br s, 1 H, NH), 2.73 (br s, 6 H, Me), 2.82-2.59 (m, 4 H, CH_2), 2.27 (br s, 6 H, Me). $^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ 172.7 (CO), 144.0, 140.1 (C, Ar), 137.6, 129.3, 128.7, 123.4 (CH, Ar), 62.2, 58.5 (CH_2), 50.0 (br, Me).

46b. Yellow solid. Yield: 62%. Anal. Calcd for $C_{14}H_{24}IN_3OPd$: C, 34.76; H, 5.00; N, 8.69. Found: C, 34.77; H, 4.68; N, 8.66. Mp: 158-161 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3321; ν(CO), 1650. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.22 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.56 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.50 (dd, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.99 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.91 (td, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 3.08 (d, $^3J_{HH}$ = 4.8 Hz 1 H, NH*Me*), 2.72 (br s, 6 H, Me, tmeda), 2.72-2.58 (m, 4 H, CH_2, tmeda), 2.22 (br s, 6 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 171.0 (CO), 142.6, 140.9 (C, Ar), 137.4, 128.9, 128.2, 123.3 (CH, Ar), 62.2, 58.4 (CH_2), 50.1 (br, Me, tmeda), 26.3 (NHMe).

46c. Pale orange solid. Yield: 51%. Anal. Calcd for $C_{15}H_{26}IN_3OPd$: C, 36.20; H, 5.27; N, 8.44. Found: C, 36.25; H, 5.18; N, 8.40. Mp: 165-168 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1612. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.27 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 6.96 (m, 1 H, Ar), 6.86 (m, 1 H, Ar), 6.80 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 3.27-3.20 (m, 1 H, CH_2), 3.08 (s, 3 H, Me, benzamide), 2.93 (s, 3 H, Me, benzamide), 2.77 (m, 1 H, CH_2), 2.71 (s, 3 H, Me, tmeda), 2.68 (s, 3 H, Me, tmeda), 2.61 (s, 3 H, Me, tmeda), 2.37-2.30 (m, 2 H,

CH_2), 2.19 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 175.0 (CO), 144.3, 143.1 (C, Ar), 135.4, 127.0, 125.0, 121.8 (CH, Ar), 61.5, 58.4 (CH_2), 51.4, 51.2, 48.3, 47.7 (Me, tmeda), 40.4, 35.4 (Me, benzamide).

[Pd{κ^2*C,O*-$C_6H_4C(O)NRR'$-2}(tmeda)]TfO [NRR' = NH_2 (47a), NHMe (47b), NMe_2 (47c)]. To a suspension of the appropriate complex **46** (1.02 mmol) in acetone (15 mL) was added AgTfO (1.02 mmol). The mixture was stirred for 30 min and filtered through Celite. Partial evaporation of the filtrate (2 mL) and addition of Et_2O (20 mL) led to the precipitation of a colorless solid, which was collected by filtration, washed with Et_2O (5 × 3 mL) and vacuum-dried to give **47**.

47a. Yield: 94%. Anal. Calcd for $C_{14}H_{22}F_3N_3O_4PdS$: C, 34.19; H, 4.51; N, 8.54; S, 6.52. Found: C, 34.10; H, 4.77; N, 8.42; S, 6.08. Mp: 179-181 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3334, 3215, 3180; ν(CO), 1663. ^1H NMR (400.9 MHz, $(CD_3)_2CO$): δ 8.76 (br, 1 H, NH), 8.34 (br, 1 H, NH), 7.66 (m, 1 H, Ar), 7.40-7.35 (m, 2 H, Ar), 7.22-7.18 (m, 1 H, Ar), 3.13-3.10 (m, 2 H, CH_2), 3.06 (s, 6 H, Me), 2.92–2.89 (m, 2 H, CH_2), 2.75 (s, 6 H, Me). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $(CD_3)_2CO$): δ 183.8 (CO), 153.8, 142.0 (C, Ar), 133.2, 133.0, 127.8, 125.9 (CH, Ar), 65.9, 58.2 (CH_2), 52.1, 47.8 (Me).

47b. Yield: 91%. Anal. Calcd for $C_{15}H_{24}F_3N_3O_4PdS$: C, 35.62; H, 4.78; N, 8.31; S, 6.34. Found: C, 35.65; H, 4.87; N, 8.31; S, 6.12. Mp: 209-210 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3283; ν(CO), 1615. ^1H NMR (400.9 MHz, $(CD_3)_2CO$): δ 9.04 (br, 1 H, NH), 7.57 (m, 1 H, Ar), 7.36-7.31 (m, 2 H, Ar), 7.21-7.14 (m, 1 H, Ar), 3.14-3.11 (m, 2 H, CH_2), 3.07 (s, 6 H, Me, tmeda), 3.06 (d, $^3J_{HH}$ = 4.4 Hz, 3 H, NH*Me*), 2.94-2.91 (m, 2 H, CH_2), 2.82 (s, 6 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $(CD_3)_2CO$): δ 180.7 (CO), 152.6, 142.3 (C, Ar), 132.9 , 132.7, 126.5, 125.9 (CH, Ar), 66.0, 58.1 (CH_2), 52.1, 48.0 (Me, tmeda), 27.1 (NHMe).

47c. Yield: 91%. Anal. Calcd for $C_{16}H_{26}F_3N_3O_4PdS$: C, 36.97; H, 5.04; N, 8.08; S, 6.17. Found: C, 36.90; H, 4.75; N, 8.09; S, 6.54. Mp: 132-133 °C. IR (Nujol, cm^{-1}): ν(CO), 1586. ^1H NMR (400.9 MHz, $(CD_3)_2CO$): δ 7.64 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.39 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.33 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.19 (ddd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 3.63 (s, 3 H, Me, benzamide), 3.30 (s, 3 H, Me, benzamide), 3.14-3.11 (m, 2 H, CH_2), 3.05 (s, 6 H, Me, tmeda), 2.91-2.88 (m, 2 H, CH_2), 2.79 (s, 6 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $(CD_3)_2CO$): δ 180.6 (CO), 153.7, 141.9 (C, Ar), 133.1, 132.0, 130.1, 125.4 (CH, Ar), 66.0, 58.0 (CH_2), 52.0, 48.1 (Me, tmeda), 41.9, 39.1 (Me, benzamide).

[Pd{κ^2*C,N*-$C_6H_4C(O)NR$-2}(tmeda)] [R = H (48a), Me (48b)]. To a solution of the appropriate complex **46** (0.40 mmol) in MeOH (20 mL) was added KO^{t}Bu (0.45 mmol) and the mixture was stirred for 1 h. The solvent was removed under reduced pressure and the residue was extracted with CH_2Cl_2 (6 × 5 mL); the combined extracts were filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (2 mL) and slow addition of *n*-pentane (20 mL) led to the formation of a pale yellow precipitate, which was filtered off, washed with *n*-pentane (3 × 3 mL) and vacuum-dried to give the corresponding complex **48**.

48a. Yield: 88%. Anal. Calcd for $C_{13}H_{21}N_3OPd$: C, 45.69; H, 6.19; N, 12.30. Found: C, 45.55; H, 6.25; N, 12.17. Mp: 183-184 °C. IR (Nujol, cm^{-1}): ν(NH), 3252; ν(CO), 1608. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 7.48-7.42 (m, 1 H, Ar), 7.18-7.12 (m, 1 H, Ar), 7.10-7.04 (m, 2 H, Ar), 4.36 (br, 1 H, NH), 2.95 (s, 6 H, Me), 2.77-2.74 (m, 2 H, CH_2), 2.63 (s, 6 H, Me), 2.63-2.61 (m, 2 H, CH_2). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 181.8 (CO), 146.4, 144.4 (C, Ar), 129.7, 128.7, 127.4, 124.3 (CH, Ar), 63.5, 58.5 (CH_2), 51.0, 48.8 (Me).

48b·H_2O. Yield: 57%. Anal. Calcd for $C_{14}H_{25}N_3O_2Pd$: C, 44.99; H, 6.74; N, 11.24. Found: C, 45.02; H, 6.60; N, 11.25. Mp: 92-93 °C (dec). IR (Nujol, cm^{-1}): ν(OH), 3399; ν(CO), 1589. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 7.48 (dd, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 6.9 Hz, 1 H, Ar), 7.12 (m, 1 H, Ar), 7.07-6.96 (m, 2 H, Ar), 3.02 (s, 3 H, Me, benzamide), 2.92 (s, 6 H, Me, tmeda), 2.72 (m, 8 H, CH_2 + Me, tmeda), 2.61 (br, 2 H, CH_2, tmeda), 2.15 (s, 2 H, H_2O). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 180.2 (CO), 146.0, 145.1 (C, Ar), 129.0, 127.6, 127.0, 124.4 (CH, Ar), 63.7, 60.3 (CH_2), 51.1, 48.8 (Me, tmeda), 34.8 (Me, benzamide).

Isoindoline-1,3-dione (Phthalimide) (49a). A solution of **47a** (130 mg, 0.26 mmol) in acetone (15 mL) was stirred under a CO atmosphere (1.4 bar) for 3 h. A black precipitate of Pd gradually formed. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel, using a 2:1 EtOAc/Et_2O mixture as the eluent. Compound **49a** was obtained as a colorless solid after evaporation of the solvents. Yield: 32 mg, 82%. Mp: 235 °C (lit 237-238 °C[41]). The ^{1}H NMR data are in agreement with those reported in the literature.[42]

2-Methylisoindoline-1,3-dione (*N*-Methylphthalimide) (49b). A solution of **47b** (139 mg, 0.27 mmol) in acetone (15 mL) was stirred under a CO atmosphere (1.4 bar) for 3 h. A black precipitate of Pd gradually formed. The solvent was evaporated under reduced pressure and the residue was extracted with Et_2O (6 × 5 mL). The combined extracts were filtered through anhydrous $MgSO_4$ and the filtrate was evaporated to dryness to give **49b** as a

colorless solid. Yield: 35 mg, 79%. Mp: 134 °C (lit 134 °C[43]). The ^{1}H NMR data are in agreement with those reported in the literature.[43,44]

3-(2,6-Dimethylphenylimino)-2-methylisoindolin-1-one (50b). *Method A.* To a solution of **46b** (100 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) was added XyNC (27.1 mg, 0.21 mmol) and the mixture was stirred for 6 h. A black suspension was obtained. The solvent was removed under vacuum, the residue was extracted with *n*-hexane (8 × 5 mL), and the combined extracts were filtered through anhydrous $MgSO_4$. Compound **50b** was obtained as a yellow solid after evaporation of the solvent. Yield: 46 mg, 84%. *Method B.* To a solution of **47b** (127 mg, 0.25 mmol) in acetone (15 mL) was added XyNC (66 mg, 0.50 mmol). The mixture was stirred for 6 h and the solvent was removed under vacuum. Compound **50b** was isolated as described for method A. Yield: 60 mg, 90%. Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 76.92; H, 5.92; N, 10.51. Mp: 92-94 °C. IR (Nujol, cm^{-1}): ν(CO), 1743; ν(C=N), 1669. HRMS (ESI+, m/z): exact mass calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$ requires 265.1335, found 265.1344, error = 3.08 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.84 (m, 1 H, H7), 7.52 (td, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.31 (td, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, H5), 7.11 (br d, $^3J_{HH}$ = 7.6 Hz, 2 H, *m*-H, Xy), 7.03-6.98 (m, 1 H, *p*-H, Xy), 6.50 (d, $^3J_{HH}$ = 7.6 Hz, 1 H, H4), 3.43 (s, 3 H, NMe), 2.04 (s, 6 H, Me, Xy). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 167.8 (CO), 151.3 (C=N), 146.0 (*i*-C, Xy), 133.2 (C5), 132.2 (C7a), 132.0 (C7), 130.1 (C3a), 128.3 (*m*-C, Xy), 126.7 (*o*-C, Xy), 123.8 (C4), 123.7 (*p*-C, Xy), 123.1 (C7), 25.2 (NMe), 18.1 (Me, Xy).

3-(*tert*-Butylimino)-2-methylisoindolin-1-one (50b'). This compound was obtained as a colorless solid using the procedure described for **50b** (Method A), from **46b** (148 mg, 0.31 mmol) and ^{t}BuNC (35 μL, 0.31 mmol). Yield: 50 mg, 76%. Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.11; H, 7.29; N, 12.92. Mp: 133-135 °C. IR (Nujol, cm^{-1}): ν(CO), 1728; ν(C=N), 1650. HRMS (ESI+, m/z): exact mass calcd for $C_{13}H_{17}N_2O$ $[M+H]^+$ requires 217.1335, found 217.1335, error = 0.03 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.99 (br d, $^3J_{HH}$ = 7.6 Hz, 1 H, H7), 7.89 (m, 1 H, H4), 7.62 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.58 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H5), 3.18 (s, 3 H, NMe), 1.55 (s, 9 H, ^{t}Bu). ^{13}C{^{1}H} APT NMR (75.5 MHz, $CDCl_3$): δ 167.5 (CO), 147.3 (C=N), 134.4 (C3a), 131.8 (C6), 130.9 (C5), 129.0 (C7a), 127.0 (C7), 123.1 (C4), 53.6 (CMe_3), 30.8 (CMe_3), 25.2 (NMe).

***trans*-[Pd{C(=NXy)C$_6$H$_4$C(O)NMe$_2$-2}I(CNXy)$_2$] (51).** To a solution of **46c** (132 mg, 0.27 mmol) in CH_2Cl_2 (10 mL) was added XyNC (105 mg, 0.80 mmol) and the mixture was stirred for 30 min. Partial evaporation of the solvent (3 mL) and addition of *n*-pentane (15 mL) led to the precipitation of a yellow solid, which was filtered off, washed with *n*-pentane (5 × 3 mL) and vacuum-dried to give **51**. Yield: 173 mg, 84 %. Anal. Calcd for $C_{36}H_{37}IN_4OPd$: C, 55.79; H, 4.81; N, 7.23. Found: C, 55.89; H, 4.70; N, 7.21. Mp: 154-155 °C (dec). IR (Nujol, cm^{-1}): ν(C≡N), 2184; ν(CO), 1623; ν(C=N), 1584. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.07 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.45 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.37 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.26 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.20 (t, $^3J_{HH}$ = 7.6 Hz, 2 H, *p*-H, XyNC^c), 7.04 (m, 4 H, *m*-H, XyNC^c), 6.85 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, *p*-H, XyNC^i), 6.90-6.60 (br, 2 H, *m*-H, XyNC^i), 3.08 (s, 3 H, Me, benzamide), 3.075 (s, 3 H, Me, benzamide), 2.24 (s, 12 H, Me, XyNC^c), 2.40-2.00 (br, 6 H, Me, XyNC^i). ^{13}C{^{1}H} APT NMR (75.5 MHz, $CDCl_3$): δ 175.8 (*C*=N), 171.2 (CO), 150.2 (*i*-C, XyNC^i), 143.9 (C, Ar), 136.0 (C, Ar + *o*-C, XyNC^c), 129.85 (CH, XyNC^c), 129.76, 128.4, 128.3 (CH, Ar), 128.2 (CH, XyNC^i), 127.9 (CH, XyNC^c), 127.1 (*o*-C, XyNC^i), 126.1 (CH, Ar), 123.3 (CH, XyNC^i), 39.7, 34.6 (NMe), 18.8 (Me, XyNC); *C*≡N and *i*-C of XyNC^c not observed.

[Pd{κ^2*C*,*O*-C(X)=C(X')C$_6$H$_4$C(O)NRR'-2}(tmeda)]TfO [NRR' = NH$_2$ and X = Ph, X' = Me (52a); NRR' = NHMe and X = Ph, X' = Me (52b), X = X' = Ph (53b), Et (54b), CO$_2$Me (55b), X = CO$_2$Me, X' = Ph (56b), X = CO$_2$Et, X' = Ph (57b); NRR' = NMe$_2$ and X = X' = Ph (53c), Et (54c)]. A solution of the appropriate complex **47** (0.47 mmol) and the alkyne (4.70 mmol for NH_2 and NHMe derivatives; 2,35 mmol for NMe_2 derivatives) in a 1:2 acetone/CH_2Cl_2 mixture (15 mL) (**52a**) or CH_2Cl_2 (10 mL) (other complexes) was stirred for 64 h (**52a**), 24 h (**52b**, **54b**, **55b**, **53c**, **54c**), 48 h (**56b**, **57b**), or 5 d (**53b**). The mixture was filtered through anhydrous $MgSO_4$ and the filtrate was concentrated to *ca.* 4 mL (**56b**, **57b**) or 1 mL (other complexes). The addition of Et_2O (20 mL) led to the precipitation of a yellow solid, which was filtered off, washed with Et_2O (3 × 3 mL), recrystallized from CH_2Cl_2/Et_2O and vacuum-dried to give the corresponding complex **52–57**.

52a. Yield: 65%. Anal. Calcd for $C_{23}H_{30}F_3N_3O_4PdS$: C, 45.44; H, 4.97; N, 6.91; S, 5.27. Found: C, 45.37; H, 4.89; N, 6,79; S, 5.27. Mp: 146-147 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3330, 3197; ν(CO), 1662. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.89 (br s, 1 H, NH), 7.66 (m, 1 H, Ar), 7.58 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.51-7.47 (m, 3 H, Ar + Ph), 7.39-7.33 (m, 3 H, Ar + Ph), 7.26-7.23 (m, 2 H, NH + Ph), 2.65-2.50 (m, 5 H, CH_2 + NMe), 2.34 (s, 3 H,

NMe), 2.27-2.18 (m, 2 H, CH_2), 2.10 (s, 3 H, NMe), 2.08 (s, 3 H, CMe), 1.83 (s, 3 H, NMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 178.8 (CO), 144.8 (PdC), 143.4 (C, Ar), 142.5 (C, Ph), 133.3 (C, Ar), 131.7, 129.2 (CH, Ar), 128.5 (*C*Me), 128.4, 128.3 (CH, Ph), 127.2, 126.4 (CH, Ar), 125.9 (CH, Ph), 63.7, 57.1 (CH_2), 52.8, 48.9, 48.8, 45.9 (NMe), 20.7 (C*Me*).

52b. Yield: 76%. Anal. Calcd for $C_{24}H_{32}F_3N_3O_4PdS$: C, 46.34; H, 5.19; N, 6.76; S, 5.16. Found: C, 46.10; H, 5.27; N, 6.71; S, 5.10. Mp: 80-82 °C. IR (Nujol, cm^{-1}): ν(NH), 3280; ν(CO), 1600. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.50 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.60 (dd, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.53 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.48-7.44 (m, 3 H, Ar + Ph), 7.36-7.31 (m, 3 H, Ar + Ph), 7.27-7.23 (m, 1 H, Ph), 3.00 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.62-2.51 (m, 5 H, CH_2 + Me, tmeda), 2.34 (s, 3 H, Me, tmeda), 2.29-2.21 (m, 2 H, CH_2), 2.07 (s, 3 H, Me, tmeda), 2.06 (s, 3 H, CMe), 1.84 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.4 (CO), 144.5 (PdC), 143.3 (C, Ar), 142.7 (C, Ph), 134.1 (C, Ar), 131.2, 128.8 (CH, Ar), 128.7 (*C*Me), 128.3, 128.2 (CH, Ph), 127.5, 126.4 (CH, Ar), 125.8 (CH, Ph), 63.6, 57.1 (CH_2), 52.7, 48.9, 48.8, 46.0 (Me, tmeda), 28.1 (Me, benzamide), 20.6 (C*Me*).

53b·H_2O. Yield: 74%. Anal. Calcd for $C_{29}H_{36}F_3N_3O_5PdS$: C, 49.61; H, 5.17; N, 5.98; S, 4.57. Found: C, 49.21; H, 5.13; N, 6.14; S, 4.73. Mp: 178-180 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3273; ν(CO), 1600. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.51 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.64 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.53 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.48 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.35-7.30 (m, 3 H, Ar + Ph), 7.18-7.07 (m, 5 H, Ph), 7.04-6.98 (m, 3 H, Ph), 3.07 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.64-2.53 (m, 2 H, CH_2), 2.53 (s, 3 H, Me, tmeda), 2.50 (s, 3 H, Me, tmeda), 2.34-2.21 (m, 2 H, CH_2), 2.07 (s, 3 H, Me, tmeda), 2.00 (s, 3 H, Me, tmeda), 1.68 (s, 2 H, H_2O). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 176.6 (CO), 151.6 (PdC), 142.6 (C, Ph), 141.6 (C, Ar), 140.5 (C, Ph), 135.4 (PdC=*C*), 135.3 (C, Ar), 131.2, 130.0 (CH, Ar), 129.4, 128.1, 128.0, 127.9 (CH, Ph), 127.3, 126.7 (CH, Ar), 126.2, 125.8 (CH, Ph), 63.7, 57.2 (CH_2), 53.0, 49.01, 48.95, 46.2 (Me, tmeda), 28.2 (Me, benzamide).

53c. Yield: 88%. Anal. Calcd for $C_{30}H_{36}F_3N_3O_4PdS$: C, 51.61; H, 5.20; N, 6.02; S, 4.59. Found: C, 51.52; H, 5.19; N, 5.93; S, 5.06. Mp: 210-212 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1587. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.73 (m, 1 H, Ar), 7.61 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.49-7.41 (m, 2 H, Ar), 7.34-7.32 (m, 2 H, Ph), 7.18-7.05 (m, 6 H, Ph), 7.00-6.98 (m, 2 H, Ph), 3.29 (s, 3 H, Me, benzamide), 2.93 (s, 3 H, Me, benzamide), 2.76-2.62 (m, 2 H, CH_2),

2.59 (s, 3 H, Me, tmeda), 2.48 (s, 3 H, Me, tmeda), 2.42-2.32 (m, 2 H, CH_2), 2.14 (s, 3 H, Me, tmeda), 1.95 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.6 (CO), 152.9 (PdC), 142.5 (C, Ph), 142.3 (C, Ar), 140.3 (C, Ph), 135.2 (C, Ar), 135.1 (PdC=*C*), 130.8, 129.7 (CH, Ar), 128.8, 128.2, 128.1, 128.0 (CH, Ph), 126.6 (CH, Ar), 126.3, 125.9 (CH, Ph), 125.7 (CH, Ar), 64.0, 57.4 (CH_2), 53.1, 49.1, 49.0, 46.2 (Me, tmeda), 41.5, 36.6 (Me, benzamide).

54b. Yield: 53%. Anal. Calcd for $C_{21}H_{34}F_3N_3O_4PdS$: C, 42.90; H, 5.83; N, 7.15; S, 5.45. Found: C, 42.57; H, 5.81; N, 7.04; S, 5.39. Mp: 127-129 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3237; ν(CO), 1608. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.34 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.50 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.47 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.34 (m, 1 H, Ar), 7.28 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 2.93 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NH*Me*), 2.62 (s, 3 H, Me, tmeda), 2.50 (s, 3 H, Me, tmeda), 2.64-2.45 (m, 4 H, CH_2, tmeda), 2.34 (s, 3 H, Me, tmeda), 2.30-2.17 (m, 2 H, C*H*$_2$CH$_3$), 2.13-2.04 (m, 1 H, C*H*$_2$CH$_3$), 2.04 (s, 3 H, Me, tmeda), 2.02-1.88 (m, 1 H, C*H*$_2$CH$_3$), 1.29 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$C*H*$_3$), 0.70 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$C*H*$_3$). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.7 (CO), 150.2 (PdC), 141.9, 136.7 (C, Ar), 133.5 (PdC=*C*), 130.8, 128.3, 126.6, 126.0 (CH, Ar), 63.4, 56.8 (CH_2), 52.2, 51.2, 47.5, 47.0 (Me, tmeda), 27.9 (NHMe), 26.5, 26.3 (*C*H$_2$CH$_3$), 15.5, 14.4 (CH$_2$*C*H$_3$).

54c. Yield: 87%. Anal. Calcd for $C_{22}H_{36}F_3N_3O_4PdS$: C, 43.89; H, 6.03; N, 6.98; S, 5.33. Found: C, 43.83; H, 6.06; N, 6.99; S, 5.34. Mp: 137-138 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1587. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.53 (m, 1 H, Ar), 7.42 (m, 1 H, Ar), 7.36 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.31 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 3.13 (s, 3 H, Me, benzamide), 3.00 (s, 3 H, Me, benzamide), 2.73-2.64 (m, 1 H, C*H*$_2$CH$_3$), 2.63-2.61 (m, 1 H, CH_2, tmeda), 2.61 (s, 3 H, Me, tmeda), 2.51 (s, 3 H, Me, tmeda), 2.58-2.48 (m, 2 H, CH_2, tmeda), 2.31 (s, 3 H, Me, tmeda), 2.34-2.21 (m, 2 H, CH_2, tmeda, + C*H*$_2$CH$_3$), 2.14-2.04 (m, 1 H, C*H*$_2$CH$_3$), 2.04 (s, 3 H, Me, tmeda), 1.96-1.87 (m, 1 H, C*H*$_2$CH$_3$), 1.25 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$C*H*$_3$), 0.73 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH$_2$C*H*$_3$). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.4 (CO), 152.0 (PdC), 142.7, 135.8 (C, Ar), 133.4 (PdC=*C*), 130.5, 128.6, 125.9, 125.5 (CH, Ar), 63.6, 56.9 (CH_2, tmeda), 52.2, 51.2, 47.5, 47.1 (Me, tmeda), 41.3, 36.3 (Me, benzamide), 26.4, 25.7 (*C*H$_2$CH$_3$), 15.6, 14.7 (CH$_2$*C*H$_3$).

55b. Yield: 96%. Anal. Calcd for $C_{21}H_{30}F_3N_3O_8PdS$: C, 38.93; H, 4.67; N, 6.48; S, 4.95. Found: C, 39.09; H, 4.94; N, 6.34; S, 4.54. Mp: 149-151 °C. IR (Nujol, cm^{-1}): ν(NH), 3333;

ν(COO), 1695; ν(CO), 1618. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.65 (br q, $^{3}J_{HH}$ = 4.8 Hz, 1 H, NH), 7.70 (m, 1 H, Ar), 7.59 (td, $^{4}J_{HH}$ = 1.2 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.50-7.45 (m, 2 H, Ar), 3.87 (s, 3 H, CO_2Me), 3.65 (s, 3 H, CO_2Me), 2.99 (d, $^{3}J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.75 (s, 3 H, Me, tmeda), 2.81-2.73 (m, 2 H, CH_2, tmeda), 2.553 (s, 3 H, Me, tmeda), 2.549 (s, 3 H, Me, tmeda), 2.37-2.30 (m, 2 H, CH_2), 2.13 (s, 3 H, Me, tmeda). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 175.7 (*C*ONHMe), 171.4 (*C*O_2Me), 164.0 (PdC), 161.5 (*C*O_2Me), 136.1, 134.4 (C, Ar), 131.3, 131.1 (CH, Ar), 129.3 (PdC=*C*), 127.94, 127.91 (CH, Ar), 64.6, 58.1 (CH_2), 54.4 (Me, tmeda), 52.2, 52.0 (CO_2*Me*), 49.7, 48.2, 46.4 (Me, tmeda), 28.3 (NHMe).

56b. Yield: 71%. Anal. Calcd for $C_{25}H_{32}F_3N_3O_6PdS$: C, 45.08; H, 4.84; N, 6.31; S, 4.81. Found: C, 44.67; H, 4.66; N, 6.22; S, 4.51. Mp: 175-177 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3233; ν(COO), 1693; ν(CO), 1600. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 9.04 (br q, $^{3}J_{HH}$ = 4.8 Hz, 1 H, NH), 7.72 (m, 1 H, Ar), 7.48-7.40 (m, 2 H, Ar), 7.25-7.14 (m, 4 H, Ar + Ph), 7.03-7.00 (m, 2 H, Ph), 3.49 (CO_2Me), 3.03 (d, $^{3}J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.88 (s, 3 H, Me, tmeda), 2.81-2.79 (m, 2 H, CH_2), 2.70 (s, 3 H, Me, tmeda), 2.58 (s, 3 H, Me, tmeda), 2.35-2.29 (m, 2 H, CH_2), 2.16 (s, 3 H, Me, tmeda). ^{13}C{^{1}H} APT NMR (75.5 MHz, $CDCl_3$): δ 176.3 (*C*ONHMe), 171.5 (*C*O_2Me), 141.6 (C, Ar), 140.6 (C, Ph), 140.4 (PdC=*C*), 138.2 (PdC), 134.6 (C, Ar), 131.4, 130.9 (CH, Ar), 128.5, 128.1 (CH, Ph), 127.7, 127.6 (CH, Ar), 127.3 (CH, Ph), 64.5, 57.9 (CH_2), 54.4 (Me, tmeda), 51.8 (CO_2*Me*), 49.9, 48.2, 46.6, 28.4 (NHMe).

57b. Yield: 67%. Anal. Calcd for $C_{26}H_{34}F_3N_3O_6PdS$: C, 45.92; H, 5.04; N, 6.18; S, 4.72. Found: C, 45.93; H, 5.15; N, 6.18; S, 4.63. Mp: 199-200 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3240; ν(COO), 1690; ν(CO), 1604. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 9.01 (br q, $^{3}J_{HH}$ = 4.8 Hz, 1 H, NH), 7.63 (dd, $^{4}J_{HH}$ = 1.2 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.44 (td, $^{4}J_{HH}$ = 1.2 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.38 (dd, $^{4}J_{HH}$ = 1.2 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.22-7.14 (m, 4 H, Ar + Ph), 7.02-6.99 (m, 2 H, Ph), 4.06, 3.89 (AB part of ABX_3 system, $^{2}J_{HH}$ = 10.8 Hz, $^{3}J_{HH}$ = 6.8 Hz, 2 H, CH_2CH_3), 3.00 (d, $^{3}J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.88 (s, 3 H, Me, tmeda), 2.81-2.78 (m, 2 H, CH_2, tmeda), 2.68 (s, 3 H, Me, tmeda), 2.56 (s, 3 H, Me, tmeda), 2.38-2.30 (m, 2 H, CH_2, tmeda), 2.13 (s, 3 H, Me, tmeda), 0.89 (t, $^{3}J_{HH}$ = 6.8 Hz, 3 H, CH_2CH_3). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 176.4 (*C*ONHMe), 171.0 (*C*O_2Et), 141.6 (C, Ar), 140.5 (PdC=*C* + C, Ph), 138.9 (PdC), 134.5 (C, Ar), 131.3, 130.9 (CH, Ar), 128.7, 127.9 (CH, Ph), 127.6, 127.5 (CH, Ar), 127.2 (CH, Ph), 64.5 (CH_2, tmeda), 60.4 (CH_2CH_3), 57.9 (CH_2, tmeda), 54.4, 49.8, 48.2, 46.5 (Me, tmeda), 28.3 (NHMe), 13.7 (CH_2CH_3).

3,4-Diethylisoquinolin-1(2*H*)-one (58). A mixture of **47a** (122 mg, 0.25 mmol) and 3-hexyne (285 μL, 2.50 mmol) in acetone (20 mL) was stirred at 40 °C for 24 h. The solvent was evaporated under vacuum, the residue was extracted with Et_2O (6 × 5 mL), and the combined extracts were filtered through anhydrous $MgSO_4$. The pale yellow filtrate was evaporated to dryness and the residue was stirred in *n*-pentane (10 mL) for 16 h, whereupon a colorless precipitate formed, which was filtered off and vacuum-dried to give **58**. Yield: 15 mg, 30%. HRMS (ESI+, m/z): exact mass calcd for $C_{13}H_{16}NO$ $[M+H]^+$ requires 202.1226, found 202.1233, error = 3.41 ppm. Mp: 180 °C (lit 173-175 °C[21]). The ^1H NMR data are in agreement with those reported in the literature.[21]

(*Z*)-5-Methyl-4-phenyl-2*H*-benzo[*c*]azepine-1,3-dione (59a), (*Z*)-2,5-Dimethyl-4-phenyl-2*H*-benzo[*c*]azepine-1,3-dione (59b), (*Z*)-2-Methyl-4,5-diphenyl-2*H*-benzo[*c*]azepine-1,3-dione (59c), and (*Z*)-4,5-Diethyl-2-methyl-2*H*-benzo[*c*]azepine-1,3-dione (59d). A solution of complex **52a**, **52b**, **53b**, or **54b** (0.45 mmol) in $CHCl_3$ (15 mL) was stirred under a CO atmosphere (1.4 bar) for 3 h (**52a**) or 24 h (**52–54b**), whereupon a black precipitate of Pd gradually formed. The suspension was filtered through anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel, using as the eluent Et_2O [Rf = 0.8-0.9 (**59a**), 0.9 (**59d**)], a 1:1 EtOAc/*n*-hexane mixture [Rf = 0.8-0.9 (**59b**)], or a 2:1 Et_2O/*n*-hexane mixture [Rf = 0.7-0.8 (**59c**)]. The compounds were isolated as colorless solids (**59a–c**) or as a yellow oil (**59d**) after evaporation of the solvents.

59a. Yield: 81%. Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.64; H, 4.90; N, 5.34. Mp: 200-202 °C. IR (Nujol, cm^{-1}): ν(CO), 1688, 1655. HRMS (ESI+, m/z): exact mass calcd for $C_{17}H_{14}NO_2$ $[M+H]^+$ requires 264.1019, found 264.1025, error = 2.29 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.64 (br,1 H, H2), 8.20 (m, 1 H, H9), 7.72 (m, 1 H, H6), 7.67 (m, 1 H, H7), 7.55 (m, 1 H, H8), 7.46-7.41 (m, 2 H, Ph), 7.39-7.35 (m, 1 H, Ph), 7.25-7.22 (m, 2 H, Ph), 2.18 (s, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 166.7 (C1), 166.5 (C3), 142.4 (C5), 139.1 (C, Ph), 136.7 (C5a), 136.6 (C4), 132.8 (C7), 131.7 (C9), 131.3 (C9a), 129.4 (C8), 129.0 (CH, Ph), 128.7 (C6), 128.6, 127.9 (CH, Ph), 23.7 (Me).

59b. Yield: 83%. Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.03; H, 5.57; N, 4.98. Mp: 98-99 °C. IR (Nujol, cm^{-1}): ν(CO), 1687, 1649. HRMS (ESI+, m/z): exact mass calcd for $C_{18}H_{16}NO_2$ $[M+H]^+$ requires 278.1176, found 278.1184, error =

2.89 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.91 (m, 1 H, H9), 7.59 (m, 2 H, H7 + H6), 7.50-7.46 (m, 1 H, H8), 7.44-7.34 (m, 3 H, Ph), 7.28-7.26 (m, 2 H, Ph), 3.44 (s, 3 H, NMe), 2.10 (s, 3 H, CMe). ^{13}C{^{1}H} APT NMR (100.8 MHz, $CDCl_3$): δ 170.9 (C1), 170.7 (C3), 139.2 (C4), 138.0 (C5), 137.4 (C, Ph), 136.0 (C5a), 134.1 (C9a), 131.6 (C7), 131.0 (C9), 129.1 (CH, Ph), 128.9 (C8), 128.5, 127.8 (CH, Ph), 127.1 (C6), 33.6 (NMe), 21.2 (C*Me*).

59c. Yield: 76%. Anal. Calcd for $C_{23}H_{17}NO_2$: C, 81.40; H, 5.05; N, 4.13. Found: C, 81.25; H, 4.81; N, 4.19. Mp: 151-153 °C. IR (Nujol, cm^{-1}): ν(CO), 1689, 1645. HRMS (ESI+, m/z): exact mass calcd for $C_{23}H_{18}NO_2$ $[M+H]^+$ requires 340.1332, found 340.1338, error = 1.74 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.96 (m, 1 H, H9), 7.45 (td, $^{4}J_{HH}$ = 1.2 Hz, $^{3}J_{HH}$ = 7.2 Hz, 1 H, H8), 7.37 (td, $^{4}J_{HH}$ = 1.6 Hz, $^{3}J_{HH}$ = 7.2 Hz, 1 H, H7), 7.29-7.27 (m, 2 H, Ph), 7.15-7.11 (m, 6 H, Ph), 6.97-6.94 (m, 3 H, Ph + H6), 3.44 (s, 3 H, Me). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$): δ 170.86, 170.84 (CO), 142.5 (C5), 139.6, 137.2 (C, Ph), 136.3 (C4), 135.7 (C5a), 134.7 (C9a), 131.1 (C7), 130.8 (C9), 130.6 (CH, Ph + C6), 129.2 (C8), 127.9, 127.50, 127.45, 127.3 (CH, Ph), 33.9 (Me).

59d·0.25H_2O. Yield: 79%. Anal. Calcd for $C_{15}H_{17.5}NO_{2.25}$: C, 72.70; H, 7.12; N, 5.65. Found: C, 72.84; H, 6.92; N, 5.49. IR (Nujol, cm^{-1}): ν(CO), 1700, 1662. HRMS (ESI+, m/z): exact mass calcd for $C_{15}H_{18}NO_2$ $[M+H]^+$ requires 244.1332, found 244.1341, error = 3.71 ppm. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.81-7.79 (m, 1 H, H9), 7.53-7.50 (m, 2 H, H6, H7), 7.43-7.37 (m, 1 H, H8), 3.41 (NMe), 2.70 (q, $^{3}J_{HH}$ = 7.6 Hz, 2 H, CH_2), 2.63 (q, $^{3}J_{HH}$ = 7.6 Hz, 2 H, CH_2), 1.62 (br, 0.5 H, H_2O), 1.12 (t, $^{3}J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3), 1.05 (t, $^{3}J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3). ^{13}C{^{1}H} APT NMR (75.5 MHz, $CDCl_3$): δ 173.0 (C3), 171.1 (C1), 140.3 (C5), 137.9 (C4), 135.5 (C5a), 134.9 (C9a), 131.3 (C7), 130.7 (C9), 128.1 (C8), 126.4 (C6), 33.0 (NMe), 26.5, 25.6 (CH_2CH_3), 14.0, 13.9 (CH_2CH_3).

^{1}H NMR of the mixture of 3-[carboxy(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (60a) and (tmedaH)TfO. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 9.60 (br, 2 H), 8.09 (d, $^{3}J_{HH}$ = 7.6 Hz, 1 H), 7.73 (m, 2 H), 7.56 (m, 2 H), 7.47 (m, 2 H), 7.39 (td, $^{4}J_{HH}$ = 1.2 Hz, $^{3}J_{HH}$ = 7.2 Hz, 1 H), 7.33-7.23 (m, 6 H), 7.13 (m, 2 H), 7.00 (m, 2 H), 4.82 (s, 1 H), 4.72 (s, 1 H), 3.69 (s, 3 H), 3.59 (s, 3 H), 3.17 (s, 6 H, CH_2, tmedaH$^+$), 2.87 (s, 3 H), 2.59 (s, 3 H, 12 H, Me, tmedaH$^+$).

3-[Di(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (60b). To a solution of **56b** (137 mg, 0.21 mmol) in $CHCl_3$ (15 mL) was added MeOH (17 μL, 0.42 mmol) and the mixture was stirred under a CO atmosphere (1.4 bar) for 6 h, whereupon a

black precipitate of Pd gradually formed. The suspension was filtered through anhydrous $MgSO_4$, the filtrate was evaporated to dryness and the residue was purified by column chromatography on silica gel, using Et_2O as the eluent (Rf = 0.50). Compound **60b** was isolated as a colorless solid after evaporation of the solvent. Yield: 60 mg, 83%. Mp: 120-121 °C. Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.87; H, 5.34; N, 4.23. IR (Nujol, cm^{-1}): ν(CO), 1759, 1739, 1687. HRMS (ESI+, m/z): exact mass calcd for $C_{20}H_{20}NO_5$ $[M+H]^+$ requires 354.1336, found 354.1343, error = 2.07 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.85 (m, 1 H, H7), 7.79 (m, 1 H, H4), 7.55 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, H5), 7.49 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.33-7.29 (m, 3 H, Ph), 7.06-7.03 (m, 2 H, Ph), 4.86 (s, 1 H, C*H*CO_2Me), 3.64 (s, 3 H, CO_2Me), 3.48 (s, 3 H, CO_2Me), 2.97 (s, 3 H, NMe). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 168.0 (C1), 166.6, 166.3 (CO_2Me), 146.6 (C3a), 138.0 (C, Ph), 131.9 (C5), 131.8 (C7a), 128.92 (C6), 128.87 (CH, Ph), 128.4, 125.9 (CH, Ph), 125.0 (C4), 123.1 (C7), 70.4 (C3), 55.6 (*C*HCO$_2$Me), 52.79, 52.77 (CO$_2$*Me*), 25.6 (NMe).

3-[Ethoxycarbonyl(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (**60c**). This compound was obtained as a colorless oil using the method described for **60b**, either from **56b** (160 mg, 0.24 mmol) and EtOH (29 μL, 0.50 mmol) or from **57b** (161 mg, 0.24 mmol) and MeOH (20 μL, 0.49 mmol), and purified by column chromatography using Et_2O as the eluent (Rf = 0.60–0.70). An approximately 1:1 mixture of the two diastereomeric pairs of enantiomers was obtained. Yield: 97%. Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.43; H, 5.76; N, 3.74. IR (CH_2Cl_2, cm^{-1}): ν(CO), 1760, 1736, 1696. HRMS (ESI+, m/z): exact mass calcd for $C_{21}H_{22}NO_5$ $[M+H]^+$ requires 368.1492, found 368.1506, error = 3.74 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.86-7.83 (m, 3 H, H4, H7), 7.74 (m, 1 H, H4), 7.55-7.47 (m, 4 H, H5, H6), 7.32-7.28 (m, 6 H, Ph), 7.08-7.02 (m, 4 H, Ph), 4.85 (s, 1 H, CHCOO), 4.84 (s, 1 H, CHCOO), 4.08-4.05 (m, 2 H, C*H*$_2$CH$_3$), 3.95-3.89 (m, 2 H, C*H*$_2$CH$_3$), 3.65 (s, 3 H, CO_2Me), 3.50 (s, 3 H, CO_2Me), 3.02 (s, 3 H, NMe), 2.95 (s, 3 H, NMe), 1.08 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, CH$_2$C*H*$_3$), 0.98 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, CH$_2$C*H*$_3$). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 168.2, 167.9 (C1), 166.8, 166.5 (*C*O$_2$Me), 166.1, 165.8 (*C*O$_2$Et), 147.0, 146.5 (C3a), 138.2, 138.0 (C, Ph), 132.1 (C7a), 131.9 (C5), 131.6 (C7a), 128.93 (C6), 128.90 (CH, Ph), 128.81 (C6), 128.80, 128.4, 128.3, 126.0, 125.7 (CH, Ph), 125.3, 124.6 (C4), 123.2, 123.1 (C7), 70.5, 70.4 (C3), 62.0, 61.9 (*C*H$_2$CH$_3$), 56.2, 55.6 (*C*HCOO), 52.72, 52.71 (CO$_2$*Me*), 26.0, 25.4 (NMe), 13.7, 13.6 (CH$_2$CH$_3$).

3-[Di(ethoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (60d). This compound was obtained as a colorless oil using the method described for **60b**, from **57b** (192 mg, 0.28 mmol) and EtOH (33 μL, 0.56 mmol), and purified by column chromatography using Et_2O as the eluent (Rf = 0.70). Yield: 107 mg, 99%. Anal. Calcd for $C_{22}H_{23}NO_5$: C, 69.28; H, 6.08; N, 3.67. Found: C, 69.13; H, 5.94; N, 3.78. IR (CH_2Cl_2, cm^{-1}): ν(CO), 1757, 1733, 1696. HRMS (ESI+, m/z): exact mass calcd for $C_{22}H_{24}NO_5$ $[M+H]^+$ requires 382.1649, found 382.1661, error = 3.2 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.85 (m, 1 H, H7), 7.82 (m, 1 H, H4), 7.54 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H5), 7.48 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.33-7.28 (m, 3 H, Ph), 7.07-7.04 (m, 2 H, Ph), 4.83 (s, 1 H, C*H*COO), 4.09 (m, 2 H, C*H*$_2$CH$_3$), 3.94 (m, 2 H, C*H*$_2$CH$_3$), 3.00 (s, 3 H, NMe), 1.11 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, CH$_2$C*H*$_3$), 1.00 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, CH$_2$C*H*$_3$). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 168.0 (C1), 166.2, 165.9 (*C*O$_2$Et), 146.8 (C3a), 138.3 (C, Ph), 131.92 (C7a), 131.86 (C5), 128.8 (C6 + CH, Ph), 128.3, 125.9 (CH, Ph), 125.0 (C4), 123.1 (C7), 70.4 (C3), 61.85, 61.77 (*C*H$_2$CH$_3$), 56.1 (*C*HCO$_2$Et), 25.7 (NMe), 13.8, 13.6 (CH$_2$*C*H$_3$).

3-(Methoxycarbonylmethyl)-2-methyl-3-phenylisoindolin-1-one (61). A solution of **56b** (118 mg, 0.18 mmol) in $CHCl_3$ (15 mL) was stirred under a CO atmosphere (1.4 bar) at room temperature for 6 h and then at 50 °C for 24 h. The resulting black suspension was filtered through anhydrous $MgSO_4$ and the filtrate was concentrated to dryness. The residue was chromatographed on silica gel, using Et_2O as the eluent [Rf = 0.4-0.5]. Compound **61** was isolated as a colorless solid after evaporation of the solvent. Yield: 51 mg, 98%. Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.22; H, 5.93; N, 4.67. Mp: 98-100 °C. IR (Nujol, cm^{-1}): ν(CO), 1732, 1686. HRMS (ESI+, m/z): exact mass calcd for $C_{18}H_{18}NO_3$ $[M+H]^+$ requires 296.1281, found 296.1288, error = 2.35 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.87 (m, 1 H, H7), 7.48 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, H5), 7.44 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, H6), 7.37-7.28 (m, 3 H, Ph), 7.24 (m, 1 H, H4), 7.15-7.12 (m, 2 H, Ph), 3.57, 3.37 (AB system, $^2J_{HH}$ = 14.0 Hz, 2 H, CH$_2$), 3.39 (s, 3 H, CO$_2$Me), 2.91 (s, 3 H, NMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 168.9 (*C*O$_2$Me), 168.5 (C1), 148.7 (C3a), 138.9 (C, Ph), 131.8 (C5), 131.1 (C7a), 129.1 (CH, Ph), 128.5 (C6), 128.3, 125.8 (CH, Ph), 123.4 (C7), 122.3 (C4), 68.2 (C3), 51.9 (CO$_2$*Me*), 39.1 (CH$_2$), 25.0 (NMe).

Dimethyl 2-((2-(Methylcarbamoyl)phenyl)(phenyl)methylene)malonate (62). A solution of **56b** (154 mg, 0.23 mmol) in MeOH (15 mL) was stirred under a CO atmosphere (1.4 bar) for 3 h, whereupon a black precipitate of Pd gradually formed. The suspension was filtered through Celite and the filtrate was concentrated to dryness. The residue was

chromatographed on silica gel, using Et_2O as the eluent [Rf = 0.35]. Compound **62** was isolated as a colorless solid after evaporation of the solvent. Yield: 47 mg, 58%. Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.65; H, 5.57; N, 4.04. Mp: 152-154 °C. IR (Nujol, cm^{-1}): ν(NH), 3250; ν(CO), 1729, 1632. HRMS (ESI+, m/z): exact mass calcd for $C_{20}H_{20}NO_5$ $[M+H]^+$ requires 354.1336, found 354.1340, error = 1.05 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.64-7.61 (m, 1 H, Ar), 7.48-7.43 (m, 2 H, Ar), 7.35-7.25 (m, 4 H, Ar + Ph), 7.03-7.00 (m, 2 H, Ph), 6.81 (br q, $^3J_{HH}$ = 5.2 Hz, 1 H, NH), 3.67 (s, 3 H, CO_2Me), 3.65 (s, 3 H, CO_2Me), 2.80 (d, $^3J_{HH}$ = 5.2 Hz, 1 H, NMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 168.8 (CONH), 167.0, 166.1 (CO_2Me), 157.6 (C=CCO_2Me), 137.9 (C, Ar), 137.8 (C, Ph), 136.1 (C, Ar), 130.2 (CH, Ph), 130.1, 129.5, 129.0 (CH, Ar), 128.6 (CH, Ph), 128.33 (CH, Ar), 128.29 (CH, Ph), 125.5 (C=$C$$CO_2Me$), 52.8, 52.5 ($CO_2Me$), 26.7 (NHMe).

[Pd(κ²*C,O*-$C_{14}H_{13}O_5$)(tmeda)] (63). To a solution of **55b** (110 mg, 0.17 mmol) in MeOH (15 mL) was added NaOMe (92 mg, 1.70 mmol) and the mixture was stirred for 15 h. The solvent was removed under reduced pressure and the remaining residue was extracted with CH_2Cl_2 (6 × 5 mL). The combined extracts were filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (4 mL) and slow addition of *n*-hexane (30 mL) led to the formation of an orange precipitate, which was filtered off, washed with *n*-hexane (3 × 3 mL) and vacuum-dried to give **63**·CH_2Cl_2. Yield: 95 mg, 96%. Anal. Calcd for $C_{21}H_{31}Cl_2N_3O_5Pd$: C, 43.28; H, 5.36; N, 7.21. Found: C, 42.88; H, 4.96; N, 7.10. Mp: 167-168 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1688, 1632. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.19 (m, 1 H, H8), 7.33 (m, 1 H, H6), 7.25 (m, 1 H, H5), 6.98 (m, 1 H, H7), 5.30 (s, 2 H, CH_2Cl_2), 3.61 (s, 3 H, CO_2Me), 3.51 (s, 3 H, COMe), 3.49 (s, 3 H, NMe), 3.05-2.98 (m, 1 H, CH_2, tmeda), 2.80-2.74 (m, 1 H, CH_2, tmeda), 2.74 (s, 3 H, Me, tmeda), 2.72 (s, 3 H, Me, tmeda), 2.69 (s, 3 H, Me, tmeda), 2.66 (s, 3 H, Me, tmeda), 2.49-2.40 (m, 2 H, CH_2, tmeda). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 177.1 (CO_2Me), 164.2 (CONMe), 137.5 (C4a), 131.7 (C6), 128.2 (C8), 119.71, 119.70 (C7, C5), 117.9 (C8a), 93.9 (C4), 79.4 (PdC), 64.5, 57.1 (CH_2, tmeda), 54.1 (OMe), 51.8 (CO_2Me), 50.7, 49.7, 48.1, 46.1 (Me, tmeda), 26.7 (NMe) (C3 not observed).

(*E*)-4-[Methoxy(methoxycarbonyl)methylene]-2-methylisoquinoline-1,3(2*H*,4*H*)-dione (64). A solution of **63**·CH_2Cl_2 (127 mg, 0.22 mmol) in $CHCl_3$ (15 mL) was stirred at 70 °C for 2 d, whereupon a black precipitate of Pd gradually formed. The solvent was evaporated to dryness and the residue was extracted with Et_2O (8 × 5 mL). The combined extracts were filtered through anhydrous $MgSO_4$ and the resulting pale orange filtrate was evaporated to dryness. The residue was purified by column chromatography on silica gel, using

Et_2O as the eluent [Rf = 0.8]. Compound **64** was isolated as a colorless solid after evaporation of the solvent. Yield: 25 mg, 42%. Anal. Calcd for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 61.01; H, 4.42; N, 5.19. Mp: 116-119 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1734, 1696, 1657. HRMS (ESI+, m/z): exact mass calcd for $C_{14}H_{14}NO_5$ $[M+H]^+$ requires 276.0866, found 276.0874, error = 2.90 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.36 (m, 1 H, H5), 8.31 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H8), 7.62 (ddd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.43 (m, 1 H, H7), 4.09 (s, 3 H, COMe), 4.03 (s, 3 H, CO_2Me), 3.39 (s, 3 H, NMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 165.4 (C3), 164.1 (C1), 163.1 (CO_2Me), 161.7 (MeO*C*=C), 133.4 (C6), 131.3 (C4a), 129.1 (C8), 127.6 (C7), 126.6 (C5), 123.8 (C8a), 104.7 (C4), 58.4 (COMe), 53.0 (CO_2*Me*), 27.0 (NMe).

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CONCLUSIONS

1. Ortho-palladated benzamides, phenylacetamides and 3-phenylpropanamides of the type [Pd{$C_6H_4(CH_2)_nC(O)NRR'$-2}I(N^N)] [n = 0, 1, 2; NRR' = NH_2, NHMe, NMe_2; N^N = tmeda or dbbpy] have been synthesized by oxidative addition of their corresponding 2-iodobenzamides, 2-iodophenylacetamides or 3-(2-iodophenyl)propanamides, respectively, to "$Pd(dba)_2$" in the presence of tmeda or dbbpy.

2. Cationic five-, six-, and seven-membered *C,O*-palladacycles [Pd{κ^2*C,O*-$C_6H_4(CH_2)_nC(O)NRR'$-2}(N^N)]TfO have been obtained via iodide abstraction with AgTfO.

3. Neutral five-, six-, and seven-membered *C,N*-palladacyclic amidates of the type [Pd{κ^2*C,N*-$C_6H_4(CH_2)_nC(O)NR$-2}(N^N)] [R = H , Me] have been obtained upon deprotonation of the amide function from the corresponding iodo(aryl) complexes (NH_2 or NHMe derivatives) with KO^{t}Bu.

4. The reactivity of the iodo(aryl) complexes and their palladacyclic derivatives toward CO and isocyanides has been studied. The results depend on the type of amide and the substituents on the amidic nitrogen:

4.1. The insertion of CO or isocyanides into the Pd–C bond of ortho-palladated benzamides triggers the rapid C–N reductive coupling under mild conditions (NH_2 or NHMe derivatives), leading to the formation of isoindoline-1,3-diones (phthalimides) or 3-iminoisoindolin-1-ones. These reactions involve the deprotonation of NH_2 or NHMe groups.

4.2. In the case of ortho-palladated phenylacetamides, intramolecular C–N and/or C–O reductive couplings can take place under relatively mild conditions after the insertion of CO or XyNC into the Pd–C bond, depending on the substituents on the amidic nitrogen. Thus, NH_2 derivatives lead only to the C–N coupling product, the NHMe derivatives to a mixture of C–N and C–O coupling products, and the NMe_2 derivatives to the C–O coupling product. The C–O couplings involve the deprotonation of the α-CH_2 group and, as far as we are aware, they are the first reported palladium-mediated C–O couplings involving an amide function. The resulting organic products are isoquinoline-1,3(2*H*,4*H*)-diones or their imino

derivatives (C–N couplings), or isocoumarins or their imino derivatives (C–O couplings).

4.3. The reactions cyclometalated 3-phenylpropanamides with CO or XyNC have allowed the synthesis of seven-membered cyclic imides and one iminobenzazepinone resulting from insertion/C–N reductive coupling sequences. When compared to analogous cyclopalladated phenylacetamides, the cyclizations via C–N couplings proved to be more difficult because of the larger ring size of the starting palladacycles, and were only satisfactory from the palladacyclic derivatives with the unsubstituted amide function; in the cases of NHMe derivatives, the C–N couplings are hampered because of the steric hindrance of the methyl substituent and the lower acidity of the NH proton. Reductive C–O coupling processes do not take place, probably because the α-CH_2 protons are not acidic enough and thus the necessary deprotonation step does not take place. The C–N couplings are generally slower for NHMe derivatives than for their NH_2 homologs.

5. The reactions of the cationic *C,O*-cyclopalladated complexes with internal alkynes have allowed the isolation of seven-, eight- and nine-membered palladacycles of the type $[Pd\{\kappa^2C,O\text{-}C(X)=C(X')C_6H_4(CH_2)_nC(O)NRR'\text{-}2\}(tmeda)]TfO$ (n = 0, 1, 2), which result from the insertion of the alkyne into the Pd–C bond; to the best of our knowledge, the nine-membered palladacycles are the first of that size obtained from alkyne monoinsertions. These insertions are faster for larger ring sizes, the required reaction times decreasing in the sequence benzamides > phenylacetamides > 3-phenylpropanamides. The much slower alkyne monoinsertion reactions of cyclopalladated benzamides can be ascribed to the higher stability of the five-membered palladacyclic precursors and the lower nucleophilicity of the metalated carbon caused by the electron-withdrawing amide function directly bonded to the aryl ring; in addition, the substitution degree of the amidic nitrogen clearly affects the rate of the insertion reaction, which increases significantly with the number of methyl substituents.

6. The reactions of the enlarged palladacycles resulting from alkyne monoinsertions with CO may give 4,5-disubstituted benzo[*c*]azepine-1,3-diones, 5,6-disubstituted benzo[*d*]azocine-2,4(1*H*,3*H*)-diones, or 6,7-disubstituted 1,2-dihydro-4*H*-benzo[*e*]azonine-3,5-diones, which are the result of CO insertion/C–N reductive coupling sequences. These cyclizations are generally more favored for derivatives with the

unsubstituted amide function, while for NHMe derivatives, they can be slower or, as in the case of 3-phenylpropanamide derivatives, hampered because of the steric hindrance of the methyl substituent and the lower acidity of the NH proton. In addition, the reactions of the benzamide palladacycles containing inserted methyl or ethyl phenylpropiolate (NHMe derivatives) with CO result in an aza-Michael addition of the NHMe moiety to the vinyl group after the insertion of CO, finally leading to the formation of isoindolin-1-one derivatives.

7. The reactions of palladacycles resulting from alkyne monoinsertions with isocyanides were tested only for the phenylacetamide derivatives. In contrast to the analogous reactions with CO, eight-membered heterocycles were not obtained, but a series of diverse acyclic products whose nature depends on the reaction conditions and the isocyanide. Thus, the 1:1 reactions with XyNC or ^{t}BuNC at room temperature led to the isocyanide coordination products [Pd{C(X)=C(X')$C_6H_4CH_2$C(O)NH_2-2}(CNR)(tmeda)]TfO, which at higher temperatures may undergo insertion of the isocyanide ligand into the Pd–C bond and subsequent hydrolysis to give acyclic acrylamide derivatives (R = Xy), or the dealkylation of the isocyanide (R = ^{t}Bu) and the C–C reductive coupling of a cyano(vinyl) palladium intermediate to give acrylonitrile derivatives. The 1:4 reactions with XyNC at room temperature gave [Pd_3(CNXy)$_6$] and moderate yields of acyclic *N*-xylyl acrylamides resulting from the insertion of a XyNC molecule into the Pd–C bond and the subsequent hydrolysis of an iminoacyl intermediate; in addition, the dehydration of the unsubstituted carbamoyl group takes place, which constitutes a rare example of primary amide dehydration under exceptionally mild conditions.

RESUMEN EN CASTELLANO

Los derivados arílicos de paladio constituyen un tipo muy importante de compuestos organometálicos debido a su participación en numerosas reacciones mediadas por paladio, tanto estequiométricas como catalíticas, algunas de las cuales se han convertido en métodos imprescindibles en síntesis orgánica. Entre estas reacciones se encuentran diversos procesos de acoplamiento C–C (reacciones de Heck, Stille o Suzuki) o C–heteroátomo (Buchwald-Hartwig).

El enlace Pd–C de los complejos arílicos de Pd(II) presenta una reactividad extraordinariamente rica, debido, en parte, a su relativa labilidad. Durante las últimas décadas, numerosos estudios se han dedicado a estudiar cómo estos complejos participan en diversos tipos de procesos, incluyendo reacciones de adición oxidante y eliminación reductora, inserciones migratorias, carbometalaciones, o sustituciones nucleofílicas, las cuales constituyen etapas habituales en las reacciones catalíticas mediadas por paladio.

Una de las líneas de investigación más importantes del grupo de *Química Organometálica* de la Universidad de Murcia está dedicada a la síntesis y el estudio de la reactividad de complejos arílicos de paladio que contienen un grupo funcional en posición *orto*, con objeto de descubrir nuevos tipos de procesos y explorar su aplicabilidad en síntesis orgánica. Estos complejos reaccionan con moléculas insaturadas (CO, isocianuros, alquenos, alquinos, etc.) para dar productos de inserción en el enlace Pd–C. Dependiendo de la naturaleza del grupo funcional en *orto*, pueden ocurrir procesos adicionales en los que intervenga este grupo, dando lugar a nuevos complejos o compuestos orgánicos, incluyendo heterociclos.

Esta tesis doctoral se centra en la síntesis de complejos arílicos de paladio que contienen un grupo amida en posición *orto* y el estudio de su reactividad frente a moléculas insaturadas (CO, isocianuros y alquinos, principalmente). Este grupo puede estar directamente unido al ligando arilo (benzamidas ortopaladiadas) o separado por uno o dos grupos metileno (fenilacetamidas o 3-fenilpropanamidas ortopaladiadas, respectivamente). Este estudio ha permitido la síntesis de una serie de nuevos paladaciclos y heterociclos de 5, 6, 7, 8 y 9 miembros.

La memoria está organizada en cuatro capítulos, cuyo resumen se expone en las siguientes secciones. No se incluyen referencias bibliográficas, ya que aparecen en la memoria completa escrita en inglés.

La mayor parte del trabajo recogido en esta memoria ha sido publicado en los siguientes artículos:

1. J. Vicente, P. González-Herrero, R. Frutos-Pedreño, M. T. Chicote, P. G. Jones, D. Bautista, *Organometallics* **2011**, *30*, 1079–1093.
2. R. Frutos-Pedreño, P. González-Herrero, J. Vicente, P. G. Jones, *Organometallics* **2012**, *31*, 3361–3372.
3. R. Frutos-Pedreño, P. González-Herrero, J. Vicente, P. G. Jones, *Organometallics* **2013**, *32*, 1892–1904.
4. R. Frutos-Pedreño, P. González-Herrero, J. Vicente, P. G. Jones, *Organometallics* **2013**, *32*, 4664–4676.

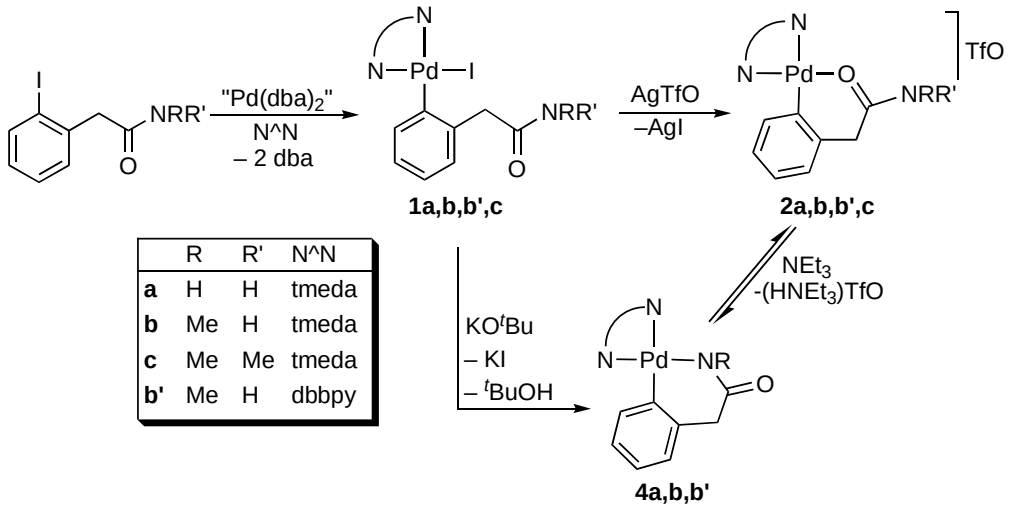
Capítulo I. Síntesis y reactividad de fenilacetamidas ortopaladiadas. Inserción de CO o XyNC en el enlace Pd–C. Síntesis de heterociclos mediante acoplamientos intramoleculares C–N ó C–O.

En este capítulo se describe la síntesis de complejos arílicos de paladio(II) conteniendo un grupo acetamida en posición *orto* y de varios derivados ciclometalados catiónicos y amidato-complejos neutros. También se lleva a cabo un estudio sistemático de la reactividad de estos complejos frente a CO y XyNC (Xy = xililo = 2,6-dimetilfenilo). Dependiendo del grado de sustitución del átomo de nitrógeno de la función amida, la inserción de estas moléculas en el enlace Pd–C pueden conducir a la formación de heterociclos derivados de la isoquinolina o de la isocumarina, que resultan de acoplamientos C–N ó C–O, respectivamente. Ambos tipos de estructuras heterocíclicas están presentes en numerosos productos naturales y moléculas biológicamente activas. Hasta la fecha, no se habían observado acoplamientos C–O mediados por paladio en los que estuviera implicada una función amida.

Síntesis de fenilacetamidas ortopaladiadas y derivados ciclometalados. Los complejos [Pd{$C_6H_4CH_2C(O)NRR'$-2}I(N^N)] [N^N = tmeda, NRR' = NH_2 (**1a**), NHMe

(**1b**), NMe_2 (**1c**); N^N = dbbpy, NRR' = NHMe (**1b'**)] se obtuvieron por adición oxidante de 2-iodofenilacetamida, o sus derivados *N*-metil o *N,N*-dimetil-sustituidos, a $[Pd_2(dba)_3]$·dba (dba = dibencilidenacetona) en presencia del ligando auxiliar N^N (Esquema 1). Los correspondientes derivados cíclicos catiónicos [Pd{κ^2*C,O*-$C_6H_4CH_2C(O)NRR'$-2}(N^N)]TfO (**2**) se obtuvieron por reacción de los complejos **1** con AgTfO, mientras que la desprotonación del grupo NH_2 (**1a**) o NHMe (**1b,b'**) con KO^{t}Bu permitió obtener amidatos neutros del tipo [Pd{κ^2*C,N*-$C_6H_4CH_2C(O)NR$-2}(N^N)] (**4**). La desprotonación de **1a**, **1b** y **1b'** ocurre también cuando se emplea NEt_3 como base, aunque sólo en una pequeña cantidad; una proporción significativamente mayor de los amidatos **4** (33%) se forma cuando se tratan los complejos catiónicos **2a**, **2b** y **2b'** con exceso de NEt_3 en acetona, debido a que los protones NH del grupo amida coordinado tienen una acidez mayor.

Esquema 1



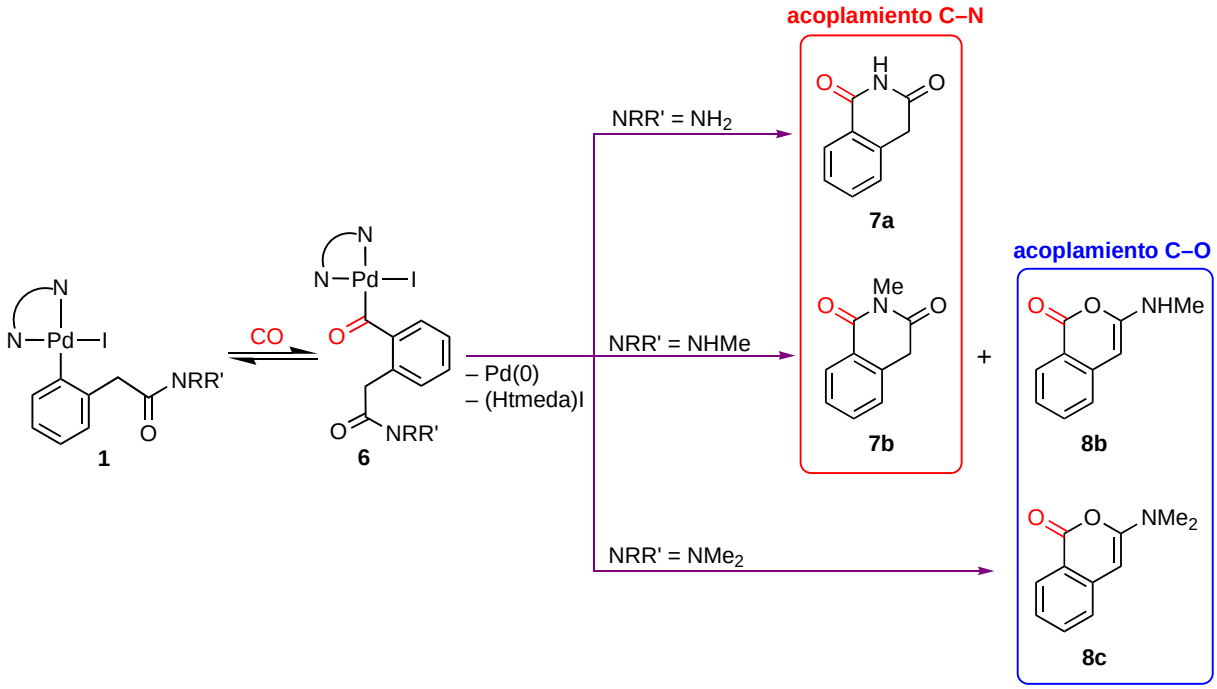
	R	R'	N^N
a	H	H	tmeda
b	Me	H	tmeda
c	Me	Me	tmeda
b'	Me	H	dbbpy

En los paladaciclos catiónicos **2** la coordinación del grupo amida al paladio se produce a través del átomo de oxígeno, mientras que en los complejos **4** el resto amidato se coordina al centro metálico a través del átomo de nitrógeno.

Reacciones con CO. Las reacciones de los complejos arílicos **1** con CO a –17 °C dan lugar a los correspondientes acil-derivados [Pd{$C(O)C_6H_4CH_2C(O)NRR'$-2}I(N^N)] (**6**), que resultan de la inserción de una molécula de CO en el enlace Pd–C. Cuando el ligando auxiliar N^N es tmeda, estos complejos se descomponen gradualmente para dar Pd(0), (tmedaH)I y compuestos heterocíclicos resultantes de acoplamientos C–N ó C–O. Los heterociclos obtenidos y las condiciones necesarias para la descomposición dependen del grado de sustitución del nitrógeno amídico (Esquema 2). Así, el derivado no sustituido da el producto de acoplamiento C–N isoquinolina-1,3(2*H*,4*H*)-diona (**7a**), el derivado *N*-metil-

sustituido da una mezcla de los productos de acoplamiento C–N 2-metilisoquinolina-1,3(2*H*,4*H*)-diona (**7b**) y C–O 3-(metilamino)-1*H*-2-benzopiran-1-ona (**8b**), y el derivado *N*,*N*-dimetil-sustituido da el producto de acoplamiento C–O 3-(dimetilamino)-1*H*-2-benzopiran-1-ona (**8c**).

Esquema 2

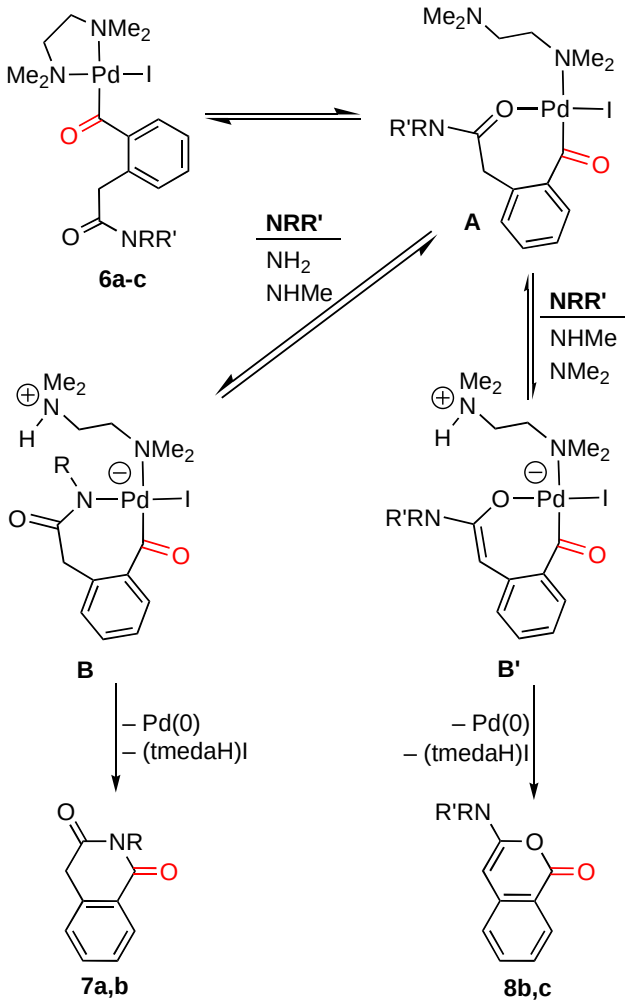


	NRR'	Condiciones de reacción	Resultados. Rendimiento (%)
6a	NH_2	CO, $CHCl_3$, 30 h, 50 °C	**7a** (99%)
6b	NHMe	CO, $CHCl_3$, 72 h, 50 °C	**7b** (24%) + **8b** (47%)
6c	NMe_2	CO, $CHCl_3$, 72 h, 50 °C	**8c** (93%)

El mecanismo que proponemos para la formación de estos heterociclos (Esquema 3) implica la desprotonación del nitrógeno amídico (si contiene algún átomo de hidrógeno) o del grupo metileno, que darían lugar, respectivamente, a un intermedio amidato (**B**), que sufriría un acoplamiento C–N, o a un intermedio aminoenolato (**B'**), que sufriría un acoplamiento C–O. La concentración relativa de estos dos intermedios debe depender de la acidez de los protones NH y CH_2, así como de la velocidad de la etapa de acoplamiento reductor. Cuando el nitrógeno amídico no está sustituido (**6a**), la formación de amidato **B** está favorecida porque los protones del grupo NH_2 tienen un mayor carácter ácido en

comparación con los del grupo CH_2, de modo que solo se obtiene el producto de acoplamiento C–N. En el caso del derivado *N*-metil-sustituido (**6b**), se produce una competencia entre los productos de acoplamiento C–N y C–O porque el protón NH es menos ácido que en el caso anterior y, además, el acoplamiento C–N está dificultado por la repulsión estérica del grupo metilo, lo que se refleja en las condiciones más enérgicas que se requieren para la descomposición de **6b** en comparación con **6a**. El derivado *N,N*-dimetil-sustituido únicamente puede dar el producto de acoplamiento C–O.

Esquema 3

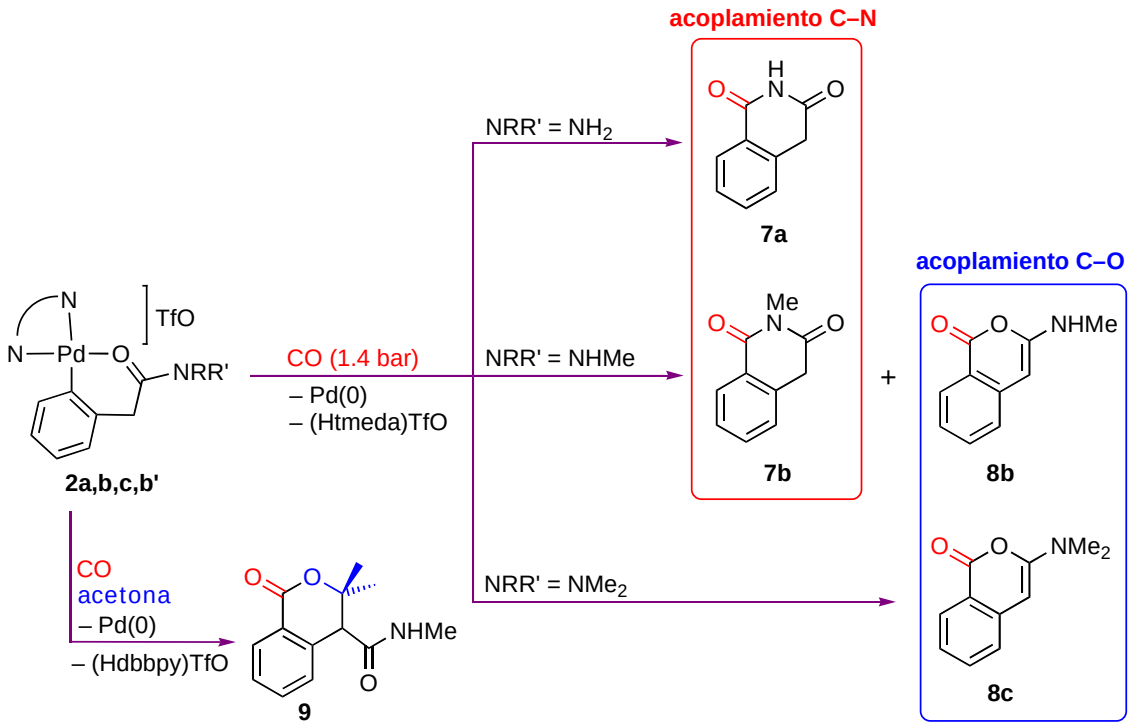


La reacción del complejo **6b'**, que contiene el ligando auxiliar dbbpy, con CO produjo sólo trazas de **7b** y **8b**. La estabilidad de **6b'** puede atribuirse a la mejor capacidad coordinante del ligando dbbpy y su menor basicidad, que dificultan su participación como una base en el proceso.

Las reacciones de los derivados catiónicos **2a–c** con CO dieron resultados comparables a los obtenidos a partir de los complejos **1a–c** (Esquema 4), si bien son mucho

más rápidas. Esto se debe a que la velocidad de las inserciones migratorias aumenta cuando especies catiónicas están implicadas y una posición de coordinación es fácilmente accesible a la molécula que se va a insertar.

Esquema 4



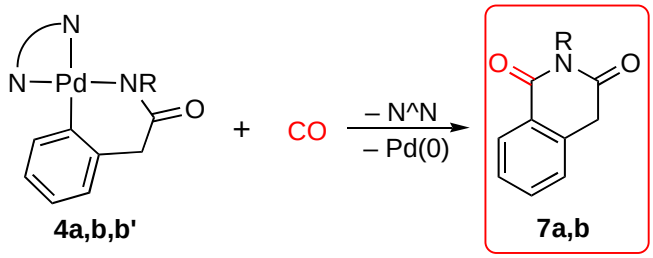
	NRR'	Condiciones de reacción	Resultados. Rendimiento (%)
2a	NH_2	CO, acetona, 3 h, r.t.	**7a** (99%)
2b	NHMe	CO, acetona, 3 h, r.t.	**7b** (23%) + **8b** (59%)
2c	NMe_2	CO, acetona, 3 h, r.t	**8c** (92%)

El complejo **2b'**, que contiene el ligando auxiliar dbbpy, se comporta de forma diferente a **2a–c** (Esquema 4). Así, su reacción con CO en acetona a temperatura ambiente da lugar a la formación de *N*,3,3-trimetil-1-oxo-3,4-dihidro-1*H*-2-benzopirano-4-carboxamida (**9**), junto con paladio coloidal y (dbbpyH)TfO, en un proceso que implica la participación del disolvente.

Los amidatos **4a**, **4b** y **4b'** también reaccionan con CO a temperatura ambiente en acetona, dando Pd(0) y rendimientos altos de **7a** ó **7b**, que resultan de la inserción de una

molécula de CO en el enlace Pd–C seguida de un acoplamiento C–N (Esquema 5). Este hecho sugiere que, en disolución, los amidatos no están en equilibrio con sus isómeros aminoenolato.

Esquema 5



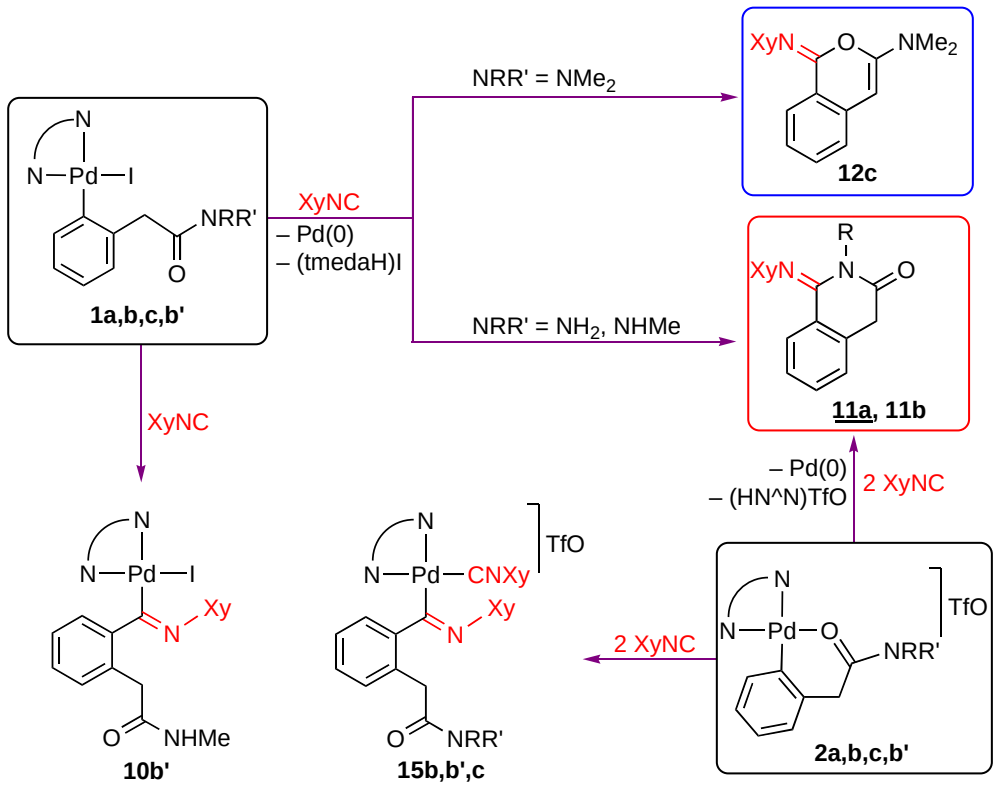
	R	Condiciones de reacción	Resultados. Rendimiento (%)
4a	H	CO, acetona, 3 h, r.t.	**7a** (74%)
4b	Me	CO, acetona, 3 h, r.t.	**7b** (87%)
4b'	Me	CO, acetona, 3 h, r.t	**7b** (95%)

Reacciones con XyNC. La reacción del complejo **1b'** con un equivalente de XyNC (Xy = xililo = 2,6-dimetilfenilo) conduce al producto de inserción [Pd{C(=NXy)C$_6$H$_4$CH$_2$C(O)NHMe-2}I(dbbpy)] (**10b'**). En cambio, los iminoacilos análogos no se pudieron aislar a partir de las reacciones de los derivados de tmeda **1a** y **1b** con XyNC, ya que se descomponen para dar Pd(0), (tmedaH)I y los productos de acoplamiento C–N 1-(2,6-dimetilfenilimino)-1,2-dihidroisoquinolin-3(4*H*)-ona (**11a**) ó 1-(2,6-dimetilfenilimino)-2-metil-1,2-dihidroisoquinolin-3(4*H*)-ona (**11b**), respectivamente. A partir de la reacción de **1c** con un equivalente de XyNC a 60 °C durante 24 h se forma la nueva iminoisocumarina 1-(2,6-dimetilfenilimino)-3-(*N*,*N*-dimetilamino)-1*H*-2-benzopirano (**12c**), que resulta de un acoplamiento C–O (Esquema 6).

La reacción de **2a** con XyNC también conduce a la formación del producto de acoplamiento C–N **11a**, aunque se necesitan 2 equivalentes del isocianuro. Sin embargo, las reacciones de los derivados *N*-metil ó *N*,*N*-dimetil-sustituidos **2b**, **2b'** ó **2c** con XyNC en relación molar 1:2 condujeron a la inserción de una molécula de XyNC en el enlace Pd–C y el desplazamiento del oxígeno coordinado de la amida por una segunda molécula de XyNC para dar los complejos [Pd{C(=NXy)C$_6$H$_4$CH$_2$C(O)NHMe-2}(CNXy)(N^N)] (**15b**, **15b'**, **15c**); probablemente, la formación de los productos orgánicos a partir de estos complejos no se

produce porque las etapas de acoplamiento C–N ó C–O son más difíciles que el acoplamiento C–N a partir de la acetamida primaria **2a**, de modo que la reacción concluye con la formación de los complejos estables **15**.

Esquema 6



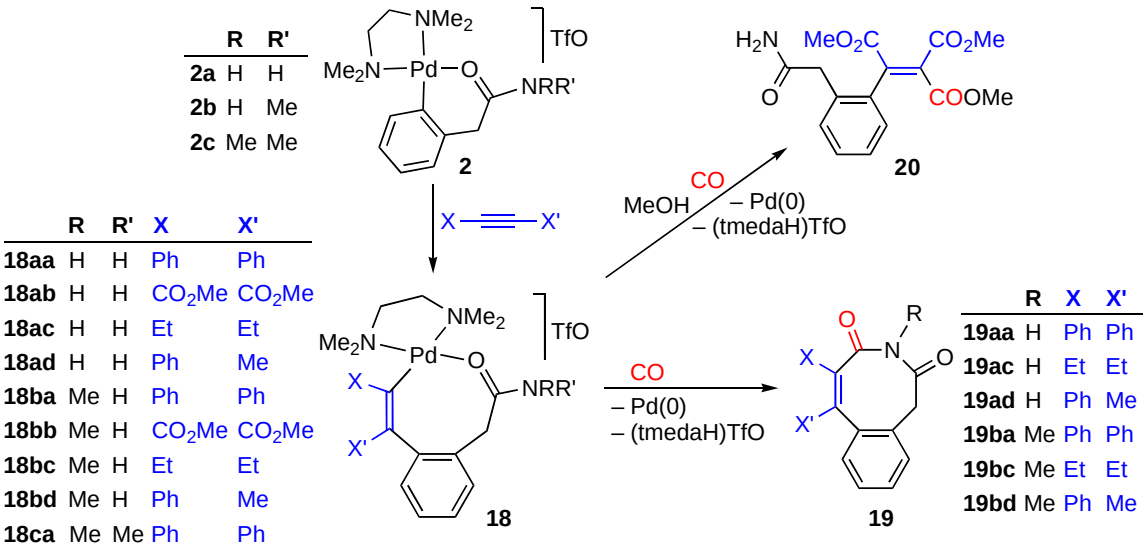
Capítulo II. Inserción secuencial de alquinos y CO o isocianuros en el enlace Pd–C de fenilacetamidas ciclopaladiadas. Síntesis de paladaciclos de 8 miembros, benzazocino-2,4(1*H*,3*H*)-dionas, y derivados de acrilonitrilo y acrilamida altamente funcionalizados.

En este capítulo se describe la síntesis de paladaciclos de 8 miembros mediante reacciones de monoinserción de alquinos en el enlace Pd–C de los derivados catiónicos [Pd{κ^2*C*,*O*-$C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO descritos en el capítulo I, y el estudio de su reactividad frente a CO e isocianuros. El objetivo principal de este estudio es explorar la posibilidad de que se produzcan procesos de inserción/acoplamiento reductor similares a los descritos en el capítulo I, pero a partir de paladaciclos de mayor tamaño, que en este caso darían lugar a compuestos heterocíclicos de 8 miembros. Los heterociclos de entre 8 y 11

miembros, considerados de tamaño medio, constituyen la base estructural de numerosos compuestos de gran relevancia biológica y/o farmacéutica. Sin embargo, su síntesis presenta dificultades asociadas a factores entálpicos y entrópicos desfavorables, por lo que el desarrollo de nuevas metodologías continúa siendo objeto de numerosas investigaciones. Hemos conseguido obtener una serie de benzo[*d*]azocino-2,4(1*H*,3*H*)-dionas mediante la inserción de CO, que son nuevos miembros de la escasa familia existente de imidas cíclicas de 8 miembros, mientras que la inserción de isocianuros produjo derivados acíclicos de acrilamidas o acrilonitrilo.

Reacciones de monoinserción de alquinos. Síntesis de paladaciclos de 8 miembros. Las reacciones de los complejos catiónicos [Pd{κ^2C,O-$C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO [NRR' = NH_2 (**2a**), NHMe (**2b**), NMe_2 (**2c**)] con diversos alquinos XC≡CX' en relación molar 1:3 a temperatura ambiente conducen a la formación de paladaciclos de 8 miembros del tipo [Pd{κ^2C,O-$C(X)=C(X')C_6H_4CH_2C(O)NRR'$-2}(tmeda)]TfO [NRR' = NH_2 y X = X' = Ph (**18aa**), CO_2Me (**18ab**), Et (**18ac**) ó X = Ph, X' = Me (**18ad**); NRR' = NHMe y X = X' = Ph (**18ba**), CO_2Me (**18bb**), Et (**18bc**) ó X = Ph, X' = Me (**18bd**); NRR' = NMe_2 y X = X' = Ph (**18ca**)] (Esquema 7) con altos rendimientos. Estos complejos son el resultado de la inserción de una molécula de alquino en el enlace Pd–C, que tiene lugar en condiciones muy suaves debido a la naturaleza catiónica de los precursores **2a–c** y la labilidad del enlace Pd–O, que debe facilitar la etapa previa de coordinación del alquino. En ningún caso se observaron inserciones múltiples.

Esquema 7



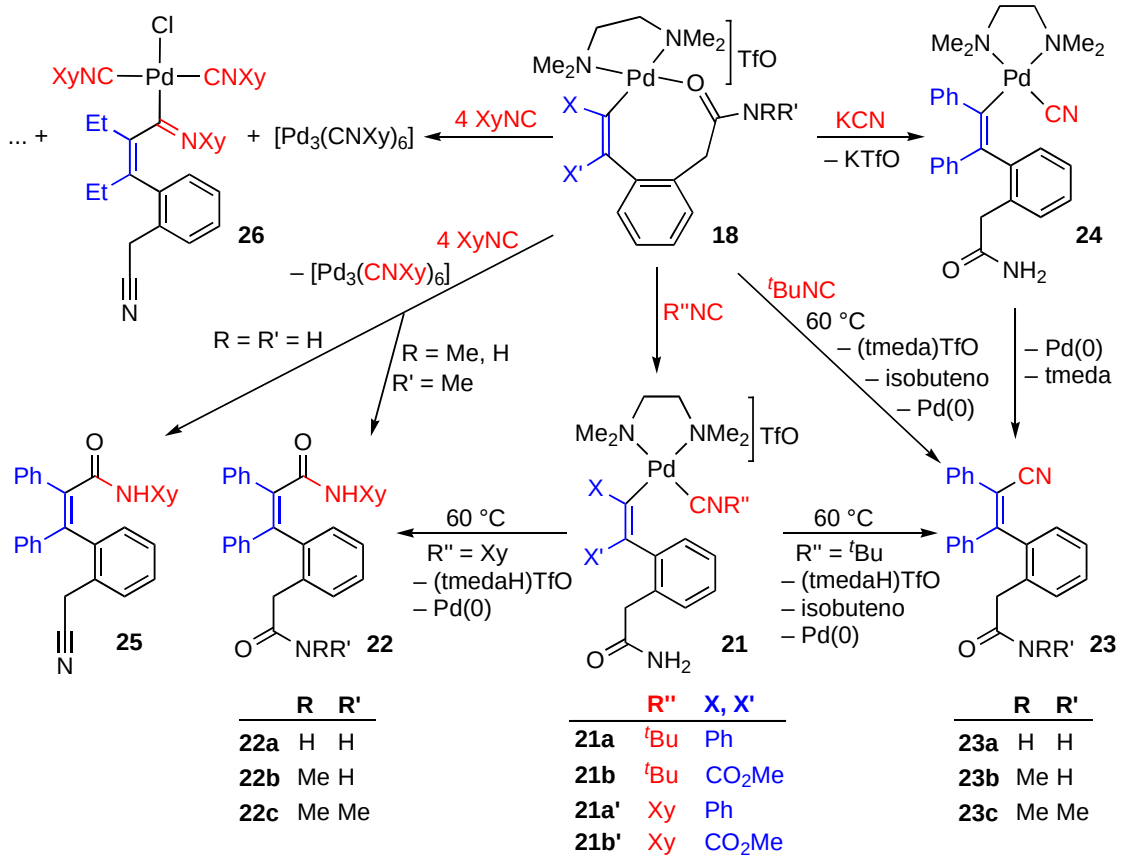
Reacciones con CO. Síntesis de benzo[*d*]azocino-2,4(1*H*,3*H*)-dionas. Algunos de los paladaciclos de 8 miembros del apartado anterior (**18aa**, **18ac**, **18ad**, **18ba**, **18bc** y **18bd**) reaccionan con CO (1.4 bar) a 50 °C en $CHCl_3$ para dar Pd(0), (tmedaH)TfO y las correspondientes benzo[*d*]azocino-2,4(1*H*,3*H*)-dionas **19** (Esquema 7), que resultan de la inserción de CO en el enlace Pd–C y el posterior acoplamiento reductor C–N. Tal y como se observó en el capítulo I, los complejos con el grupo amida no sustituido requirieron tiempos de reacción más cortos para la descomposición (5 h) y condujeron a mejores rendimientos de los compuestos heterocíclicos (78-84%) que los complejos *N*-metil-sustituidos (24 h, 57-71%). Sin embargo, en ningún caso se obtuvo el producto de acoplamiento C–O. El derivado *N,N*-dimetil-sustituido **18ca** se recuperó intacto después de tratarlo con CO durante 70 h en las mismas condiciones de reacción.

Las reacciones de los complejos con el alquino dimetilacetilenodicarboxilato (DMAD) insertado (**18ab**, **18bb**) con CO no produjeron los productos esperados de acoplamiento C–N. La reacción de **18ab** con CO en MeOH da lugar a la formación del compuesto $(MeO_2C)_2C{=}C(CO_2Me)C_6H_4CH_2C(O)NH_2$-2 (**20**) (Esquema 7), que resulta de la metanolisis de un acil-complejo intermedio.

Reacciones con isocianuros. Las reacciones de los complejos **18aa** ó **18ab** con XyNC ó ^{t}BuNC en relación molar 1:1 a temperatura ambiente dan lugar a los complejos [Pd{C(X)=C(X')$C_6H_4CH_2C(O)NH_2$-2}(CNR'')(tmeda)]TfO [R'' = ^{t}Bu y X = X' = Ph (**21a**), CO_2Me (**21b**); R'' = Xy y X = X' = Ph (**21a'**), CO_2Me (**21b'**)] (Esquema 8), que resultan del desplazamiento del oxígeno coordinado por el ligando isocianuro. Los complejos **21a**, **21b** y **21b'** son estables a temperatura ambiente. Sin embargo, el complejo **21a'** se obtiene contaminado con productos de descomposición; con objeto de identificar estos productos, se llevó a cabo la reacción de **18aa** con XyNC (1:1) a reflujo en $CHCl_3$, que produjo Pd(0) y una mezcla que contiene la acrilamida XyHNC(O)C(Ph)=C(Ph)$C_6H_4CH_2C(O)NH_2$-2 (**22a**, 24%), que resulta de la inserción de isonitrilo y posterior hidrólisis del ligando iminoacilo por agua residual. Este resultado indica que, aunque tiene lugar la inserción del isocianuro, la etapa de acoplamiento reductor C–N no está favorecida, a diferencia de lo que ocurre con las reacciones de inserción de CO. Cuando se hacen reaccionar los complejos **18aa**, **18ba** ó **18ca** con ^{t}BuNC en las mismas condiciones, se obtiene Pd(0), isobuteno, (tmedaH)TfO y el derivado del acrilonitrilo NCC(Ph)=C(Ph)$C_6H_4CH_2C(O)NRR'$-2 [NRR' = NH_2 (**23a**), NHMe (**23b**), NMe_2 (**23c**)]. Los derivados **23a–c** deben proceder del acoplamiento reductor C–C de un ciano(vinil) complejo de paladio, que puede haberse formado después de un

proceso de des-alquilación del ligando ^{t}BuNC coordinado en los correspondientes complejos **21**. Para apoyar este camino de reacción, se sintetizó el cianocomplejo [Pd{C(Ph)=C(Ph)C$_6$H$_4$CH$_2$C(O)NH$_2$-2}(CN)(tmeda)] (**24**) a partir de **18aa** y KCN y se agitó a reflujo en $CHCl_3$, obteniéndose el compuesto esperado **23a**. Los compuestos **23b** y **23c** también se pueden obtener al refluir disoluciones de los correspondientes cianocomplejos en $CHCl_3$ generadas *in situ* (Esquema 8).

Esquema 8



Las reacciones de **18aa**, **18ba** y **18ca** con 4 equivalentes de XyNC a temperatura ambiente en CH_2Cl_2 o acetona dan lugar a disoluciones conteniendo el complejo de Pd(0) [Pd$_3$(CNXy)$_6$]. Los demás productos de la reacción son (tmedaH)TfO y los derivados de acrilamida XyHNC(O)C(Ph)=C(Ph)C$_6$H$_4$CH$_2$CN-2 (**25**, a partir de **18aa**) o XyHNC(O)C(Ph)=C(Ph)C$_6$H$_4$CH$_2$C(O)NRR'-2 [NRR' = NHMe (**22b**), NMe_2 (**22c**), a partir de **18ba** ó **18ca**, respectivamente]. Estos compuestos resultan de la inserción de una molécula de XyNC en el enlace Pd–C y la posterior hidrólisis del iminoacilo resultante. En el caso de **25**, ocurre además la deshidratación del grupo carbamoilo para dar un grupo nitrilo, incluso en presencia de agua añadida en el medio. La reacción del complejo **18ac** con 4 equivalentes de XyNC en CH_2Cl_2 seco da una mezcla de productos, entre ellos [Pd$_3$(CNXy)$_6$],

(tmedaH)TfO y se aísla una pequeña cantidad de un complejo microcristalino. Un estudio de difracción de rayos X reveló que se trataba del complejo [Pd{C(=NXy)C(Et)=C(Et)$C_6H_4CH_2$CN-2}Cl$(CNXy)_2$] (**26**), que contiene dos ligandos XyNC mutuamente *trans*, un ligando cloro y un ligando iminoacilo que resulta de inserción de una molécula de XyNC y la deshidratación del grupo carbamoilo. Aparte de que el ligando cloro debe proceder de una reacción con el disolvente, la formación del complejo **26** demuestra que la deshidratación del grupo carbamoilo y la hidrólisis del ligando iminoacilo pueden ocurrir de forma independiente.

Capítulo III. Síntesis y reactividad de 3-fenilpropanamidas ortopaladiadas. Inserción de CO, XyNC y alquinos en el enlace Pd–C. Síntesis de paladaciclos de 7 y 9 miembros y heterociclos derivados de benzazepinas y benzazoninas.

En este capítulo se aborda la síntesis de una serie de 3-fenilpropanamidas ortopaladiadas y derivados paladacíclicos, así como el estudio de su reactividad frente a CO, XyNC y alquinos. El objetivo principal de este estudio es explorar los límites de aplicación de la metodología empleada en los capítulos I y II para obtener paladaciclos y heterociclos de mayor tamaño. A partir de 3-fenilpropanamidas pueden obtenerse paladaciclos de 7 miembros que, a su vez, pueden agrandarse mediante la inserción de alquinos en el enlace Pd–C para dar paladaciclos de 9 miembros. Se han aislado muy pocos ejemplos de paladaciclos de este tamaño que no se encuentren estabilizados por la coordinación de un doble enlace interno, y ninguno de ellos se ha obtenido mediante inserción de alquinos. El estudio sistemático de la reactividad de los nuevos complejos frente CO o XyNC ha permitido la síntesis de imidas cíclicas de 7 y 9 miembros y una iminobenzazepinona.

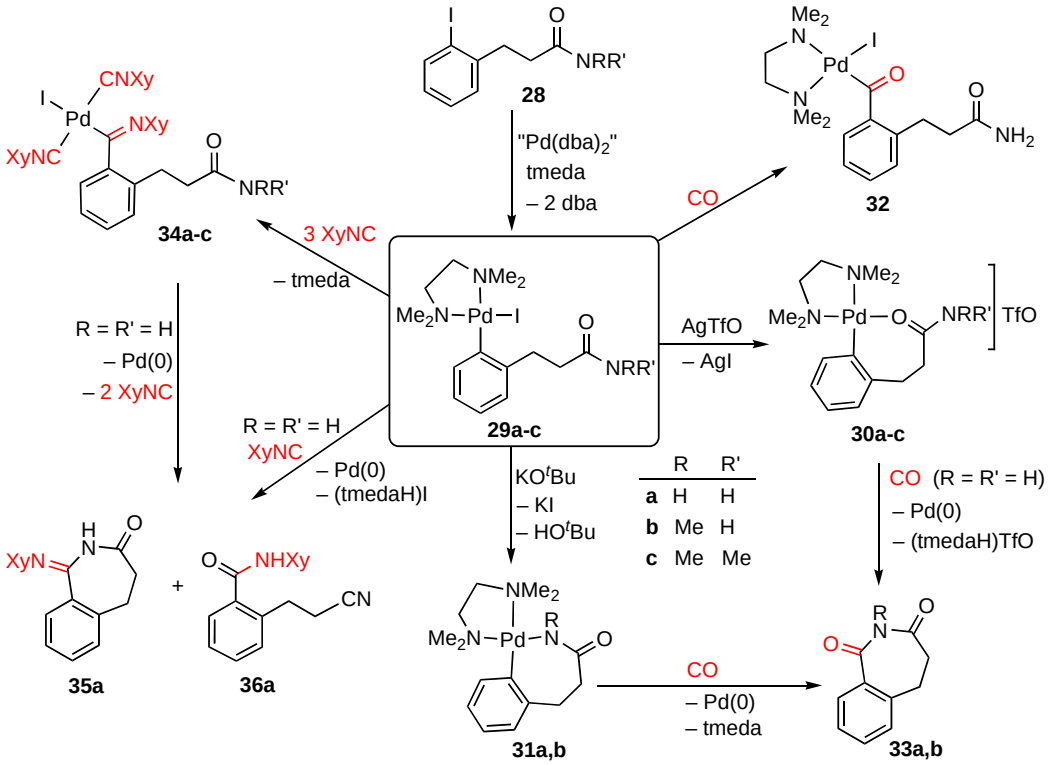
Síntesis de 3-fenilpropanamidas ortopaladiadas y derivados ciclometalados. Los complejos [Pd{$C_6H_4(CH_2)_2$C(O)NRR'-2}I(tmeda)] [NRR' = NH_2 (**29a**), NHMe (**29b**), NMe_2 (**29c**)] se obtuvieron con rendimientos moderados por adición oxidante de las correspondientes 3-(2-iodofenil)propanamidas (**28**) a $Pd(dba)_2$ en presencia de tmeda a temperatura ambiente. Los correspondientes paladaciclos catiónicos de 7 miembros [Pd{κ^2C,O-$C_6H_4(CH_2)_2$C(O)NRR'-2}(tmeda)]TfO (**30a–c**) se obtuvieron por reacción de **29a–c** con un equivalente de AgTfO, mientras que los amidatos [Pd{κ^2C,N-

$C_6H_4(CH_2)_2C(O)NR\text{-}2\}(tmeda)]$ [R = H (**31a**), Me (**31b**)] se forman por desprotonación de la amida en **29a** ó **29b** con un exceso de KO^{t}Bu (Esquema 9).

Reacciones con CO. El complejo **29a** reacciona con CO en CH_2Cl_2 a temperatura ambiente para dar el producto de inserción esperado $[Pd\{C(O)C_6H_4(CH_2)_2C(O)NH_2\text{-}2\}I(tmeda)]$ (**32**). A diferencia de su homólogo con fenilacetamida, el complejo **32** es estable y no se descompone en disolución en atmósfera de CO, lo que implica que el posible proceso de acoplamiento C–N está mucho menos favorecido. Por ello, intentamos las reacciones de los complejos **30a–c** con CO (1.4 bar) en CH_2Cl_2 a temperatura ambiente, con la expectativa de que la naturaleza catiónica de estos complejos y su estructura cíclica favoreciera el proceso de inserción/acoplamiento reductor. Cuando se parte del complejo con la amida no sustituida **30a**, se obtienen Pd(0), (tmedaH)TfO y 4,5-dihidro-2*H*-benzo[*c*]azepina-1,3-diona (**33a**; 42% de rendimiento). Sin embargo, los derivados *N*-metil- y *N,N*-dimetil-sustituidos **30b** y **30c** se recuperaron intactos. Es razonable suponer que el CO se inserta de forma reversible en el enlace Pd–C de **30b** y **30c**, pero la etapa de acoplamiento reductor C–N o C–O no se produce. El acoplamiento C–N debe ser difícil para **30b** debido a la menor acidez del protón NH y la repulsión estérica del grupo metilo, mientras que el proceso de acoplamiento C–O que podría esperarse a partir de **30b** ó **30c** no es posible debido a que los protones del grupo metileno en α a la amida no son suficientemente ácidos y el paso de desprotonación no se produce.

Los amidatos **31a** y **31b** también se trataron con CO (1.4 bar) en $CDCl_3$. Mientras que **31a** reaccionó en 3 h a temperatura ambiente para dar el compuesto **33a** con rendimiento del 88%, el derivado **31b** requirió 60 °C durante 24 h para dar un rendimiento del 30% del 2-metil-4,5-dihidro-2*H*-benzo[*c*]azepina-1,3-diona (**33b**). Este resultado confirma que el sustituyente metilo dificulta en gran medida el proceso de acoplamiento C–N.

Esquema 9



Reacciones con XyNC. Las reacciones de **29a–c** con tres equivalentes de XyNC a temperatura ambiente dan lugar a los iminoacil-complejos [Pd{C(=NXy)C_6H_4(CH_2)$_2$C(O)NRR'-2}I(CNXy)$_2$] [NRR' = NH_2 (**34a**), NHMe (**34b**), NMe_2 (**34c**)] (Esquema 9). Estos complejos se obtuvieron también cuando se empleó un solo equivalente del isocianuro, lo que contrasta con el comportamiento de los derivados con fenilacetamida ortopaladiada, que dan los heterociclos resultantes del proceso de inserción/acoplamiento reductor. Esto indica que los acoplamientos C–N o C–O son mucho más difíciles para los derivados de 3-fenilpropanamida, de acuerdo con lo mencionado en el apartado anterior.

La reacción 1:1 de **29a** con XyNC en $CHCl_3$ a reflujo produjo un precipitado de Pd(0), (tmedaH)I, y una mezcla 1:0.85 de 1-[(2,6-dimetilfenil)imino]-1,2,4,5-tetrahidro-3*H*-2-benzazepin-3-ona (**35a**) y 2-(2-cianoetil)-*N*-(2,6-dimetilfenil)benzamida (**36a**). Una mezcla similar, pero con una mayor proporción de **36a** (0.45:1), se obtuvo cuando el complejo **34a** se refluyó en $CHCl_3$. Según estos resultados, compiten dos posibles transformaciones de intermedios iminoacilo: (i) un acoplamiento reductor C–N intramolecular que da el compuesto **35a**, y (ii) la hidrólisis del ligando iminoacilo, acompañada por la deshidratación del grupo carbamoilo, para dar **36a**.

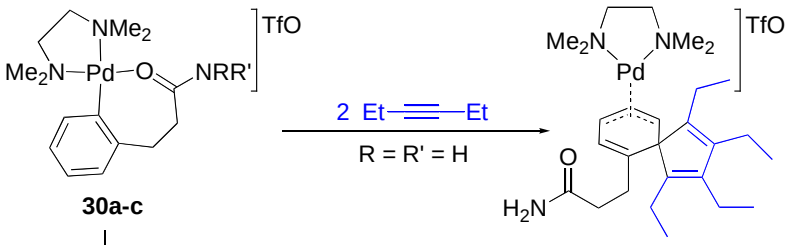
Inserción de alquinos. Los complejos **30a–c** reaccionan con alquinos para dar rendimientos altos de los paladaciclos de 9 miembros [Pd{κ^2*C,O*-C(X)=C(X)C$_6$H$_4$(CH$_2$)$_2$C(O)NRR'-2}(tmeda)]TfO [NRR' = NH$_2$, X = Ph (**37a**), C$_6$H$_4$^{n}Bu-4 (**38a**), C$_6$H$_4$Br-4 (**39a**), CO$_2$Me (**40a**); NRR' = NHMe, X = Ph (**37b**); NRR' = NMe$_2$, X = Ph (**37c**)], que resultan de la inserción de una molécula del alquino en el enlace Pd–C (Esquema 10). Estas reacciones requieren el uso de un solo equivalente del alquino y en la mayoría de los casos se completan en menos de 3 horas a temperatura ambiente. El uso de un exceso de alquino conduce generalmente a mezclas complejas, probablemente como resultado de reacciones de poliinserción. Por tanto, estas reacciones de monoinserción son mucho más rápidas que las que tienen lugar a partir de los paladaciclos de 6 miembros [Pd{κ^2*C,O*-C$_6$H$_4$CH$_2$C(O)NRR'-2}(tmeda)]TfO descritas en el capítulo II, probablemente porque el mayor tamaño de los paladaciclos **30a–c** facilita la apertura del anillo y la coordinación del alquino.

La reacción de **30a** con 3-hexino da lugar al complejo [Pd{η^3-C$_6$H$_4$(C$_4$Et$_4$)(CH$_2$)$_2$C(O)NH$_2$}(tmeda)]TfO (**41**), que contiene un ligando espirocíclico coordinado a través de un enlace η^3-alílico. Este compuesto resulta de la inserción de dos moléculas del alquino en el enlace Pd–C.

Reacciones de los productos de monoinserción de alquinos con CO. Síntesis de 1,2-dihidro-4*H*-benzo[*e*]azonina-3,5-dionas. El tratamiento de los paladaciclos **37a**, **38a** y **39a** con CO (1.4 bar) a 50 °C en CHCl$_3$ durante 15 h dio Pd(0), (tmedaH)TfO, y las correspondientes 1,2-dihidro-4*H*-benzo[*e*]azonina-3,5-dionas 6,7-disustituidas (**42**, **43**, **44**) (Esquema 10). Estos heterociclos son los que se esperan de un proceso secuencial de inserción de CO y acoplamiento reductor C–N.

Las reacciones de los complejos *N*-metil- y *N,N*-dimetil-sustituidos **37b** y **37c** dieron mezclas de compuestos que no se pudieron identificar. Tal y como se ha comentado para los paladaciclos precursores de 7 miembros, la dificultad para obtener los productos de acoplamiento C–N ó C–O puede justificarse por la repulsión estérica del grupo metilo en **37b** y/o la baja acidez de los protones NH y α-CH$_2$ en ambos casos.

Esquema 10



	R	R'	X
37a	H	H	Ph
37b	Me	H	Ph
37c	Me	Me	Ph
38a	H	H	$C_6H_4{}^nBu$-4
39a	H	H	C_6H_4Br-4
40a	H	H	CO_2Me

	X
42	Ph
43	$C_6H_4{}^nBu$-4
44	C_6H_4Br-4

Capítulo IV. Reactividad de benzamidas ortopaladiadas frente a CO, isocianuros y alquinos. Síntesis de isoindolin-1-onas funcionalizadas y benzo[*c*]azepin-1,3-dionas 4,5-disustituidas.

En este capítulo se aborda la síntesis de una familia de benzamidas ortopaladiadas, incluyendo derivados ciclopaladiados, y el estudio de la reactividad frente a CO, isocianuros y alquinos, con el principal objetivo de explorar la formación de heterociclos. Se han obtenido una serie de isoindolin-1-onas funcionalizadas y benzazepin-1,3-dionas 4,5-disustituidas. Estos sistemas heterocíclicos son de gran importancia porque se encuentran en diversos tipos de compuestos que presentan actividad farmacológica. Las benzazepin-1,3-dionas son relativamente escasas y, hasta la realización del presente trabajo, no se han descrito derivados 4,5-disustituidos.

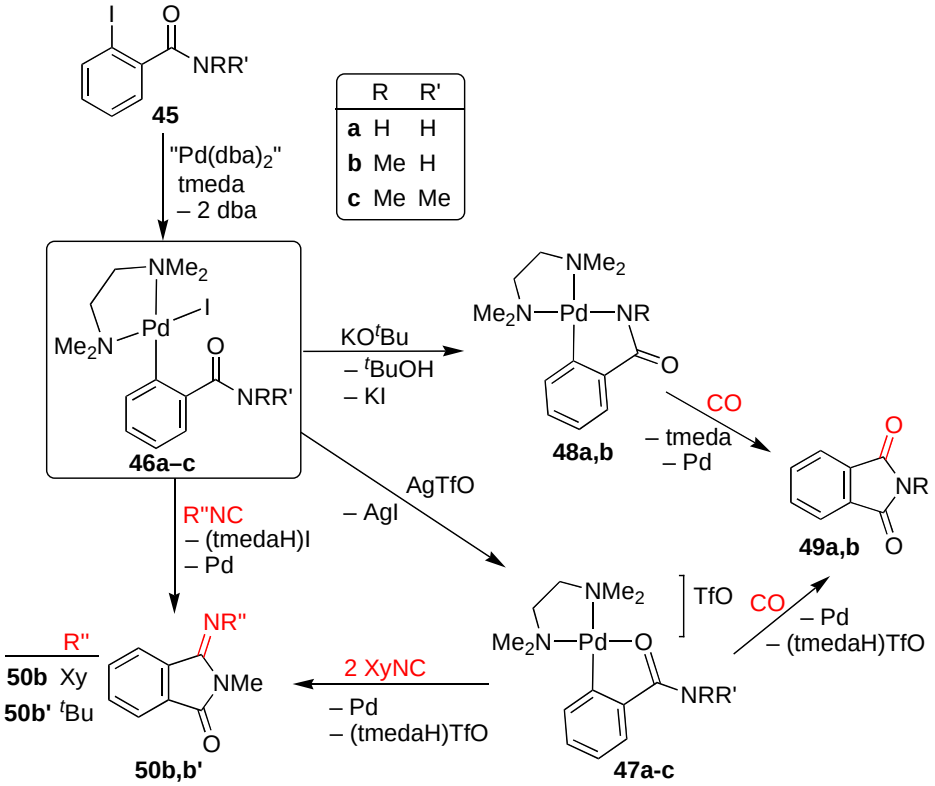
Síntesis de benzamidas ortopaladiadas y derivados ciclometalados. Reacciones con CO e isocianuros. Las benzamidas ortopaladiadas [Pd{$C_6H_4C(O)NRR'$-2}I(tmeda)] [NRR' = NH_2 (**46a**), NHMe (**46b**), NMe_2 (**46c**); Esquema 11] se obtuvieron por adición oxidante

de sus 2-iodobenzamidas correspondientes (**45**) a $Pd(dba)_2$ en presencia del ligando auxiliar tmeda con rendimientos moderados. Los derivados catiónicos [Pd{κ^2C,O-$C_6H_4C(O)NRR'$-2}(tmeda)]TfO (**47a–c**) se sintetizaron en altos rendimientos a partir de las reacciones de **46a–c** con AgTfO, mientras que los amidatos neutros [Pd{κ^2C,N-$C_6H_4C(O)NR$-2}(tmeda)] [R = H (**48a**), Me (**48b**)] se prepararon por desprotonación del grupo amida en **46a** ó **46b** con KO^{t}Bu.

Las reacciones de los complejos **47a,b** o **48a,b** con CO (1.4 bar) a temperatura ambiente producen Pd(0), (tmedaH)TfO o tmeda libre, y ftalimida (**49a**, a partir de **47a** ó **48a**) o *N*-metilftalimida (**49b**, a partir de **47b** ó **48b**)

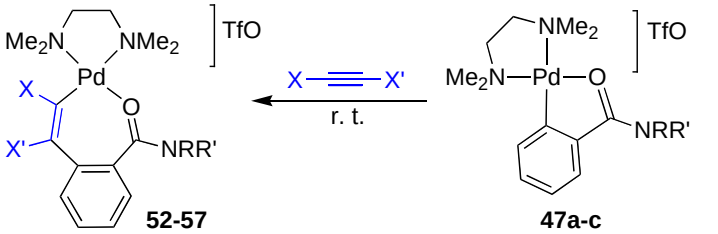
La reacción de **46b** con XyNC o ^{t}BuNC (1:1) a temperatura ambiente condujo a la formación de Pd(0), (tmedaH)I, y 3-(2,6-dimetilfenilimino)-2-metilisoindolin-1-ona (**50b**) o 3-(*terc*-butilimino)-2-metilisoindolin-1-ona (**50b'**), respectivamente (Esquema 11), que resultan de la inserción de una molécula de isocianuro en el enlace Pd–C seguida de un acoplamiento reductor C–N. Los iminoacil-complejos intermedios no se pudieron aislar porque se descomponen rápidamente para dar los productos orgánicos. El compuesto **50b** puede obtenerse también mediante la reacción de **47b** con XyNC, pero en éste caso se requieren 2 equivalentes del isocianuro.

Esquema 11

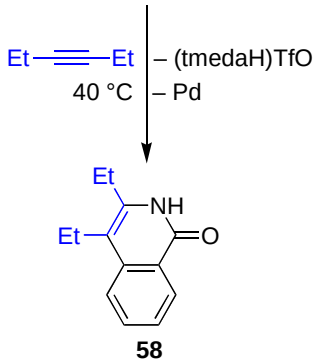


Inserción de alquinos. Los paladaciclos **47a–c** reaccionan con una serie de alquinos internos XC≡CX' a temperatura ambiente para dar buenos rendimientos de paladaciclos de 7 miembros [Pd{κ^2C,O-C(X)=C(X')C_6H_4C(O)NRR'-2}(tmeda)]TfO [NRR' = NH_2 y X = Ph, X' = Me (**52a**); NRR' = NHMe y X = Ph, X' = Me (**52b**), X = X' = Ph (**53b**), Et (**54b**), CO_2Me (**55b**), X = CO_2Me, X' = Ph (**56b**), X = CO_2Et, X' = Ph (**57b**); NRR' = NMe_2 y X = X' = Ph (**53c**), Et (**54c**)], que resultan de la inserción de una molécula de alquino en el enlace Pd–C (Esquema 12). Estas reacciones requieren un exceso de alquino y tiempos de reacción de entre 1 y 5 días, siendo considerablemente más lentas que las reacciones análogas de los paladaciclos catiónicos de 6 y 7 miembros [Pd{κ^2C,O-$C_6H_4(CH_2)_n$C(O)NRR'-2}(tmeda)]TfO (n = 1, 2) mencionados en capítulos anteriores. La mayor lentitud de las reacciones de monoinserción de alquinos de **47a–c** puede ser atribuida a la alta estabilidad de los paladaciclos de 5 miembros, que puede dificultar la etapa de coordinación del alquino, y el menor carácter nucleofílico del carbono arílico metalado, debido al carácter electroaceptor del grupo amida directamente unido al anillo aromático. Las condiciones requeridas para cada caso reflejan claramente los efectos de los grupos NRR' y el alquino. Por ejemplo, el derivado *N,N*-dimetil-sustituido **47c** requirió un exceso menor de alquino (5 equivalentes) y un tiempo de reacción menor (1 día) que el derivado *N*-metil-sustituido **47b** para la inserción de difenilacetileno (10 equivalentes de alquino y 5 días), mientras que en el caso del derivado no sustituido **47a** no se observó reacción con un exceso de 10 equivalentes de este alquino a temperatura ambiente. El aumento de la reactividad frente a la inserción de alquinos en el orden **47a** < **47b** < **47c** se puede asociar con el incremento de la nucleofilia del carbono arílico metalado debido al aumento de número de sustituyentes metilo en el grupo amida. Los alquinos con sustituyentes de menor tamaño o de mayor carácter electrofílico reaccionaron más fácilmente. Así, la inserción de 1-fenilpropino en el enlace Pd–C de **47a** fue posible a temperatura ambiente y los tiempos de reacción que se necesitaron en el caso de **47b** decrecen en la secuencia difenilacetileno > fenilpropiolato de metilo ~ fenilpropiolato de etilo > 1-fenilpropino ~ 3-hexino ~ dimetilacetilenodicarboxilato. El compuesto **47a** reaccionó con 3-hexino a 40 °C observándose descomposición a paladio coloidal, (tmedaH)TfO y la formación de 3,4-dietilisoquinolin-1(2*H*)-ona (**58**) en 24 horas.

Esquema 12

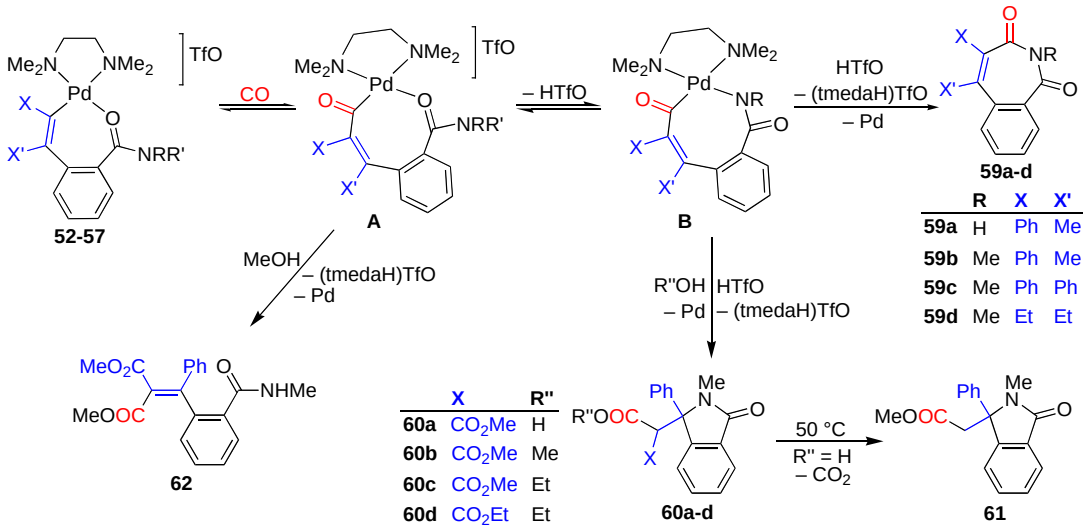


	R	R'	X	X'
52a	H	H	Ph	Me
52b	Me	H	Ph	Me
53b	Me	H	Ph	Ph
53c	Me	Me	Ph	Ph
54b	Me	H	Et	Et
54c	Me	Me	Et	Et
55b	Me	H	CO_2Me	CO_2Me
56b	Me	H	CO_2Me	Ph
57b	Me	H	CO_2Et	Ph



Reacciones de los productos de monoinserción de alquinos con CO. Los paladaciclos **52a**, **52b**, **53b**, y **54b** reaccionaron con CO (1.4 bar) a temperatura ambiente en $CHCl_3$ para dar Pd(0), (tmedaH)TfO y las correspondientes benzo[*c*]azepino-1,3-dionas 4,5-disustituidas **59** (Esquema 13), que resultan de un proceso secuencial de inserción de CO/acoplamiento reductor C–N. La formación de estos compuestos debe implicar la participación de un acil-complejo intermedio cíclico de 8 miembros **A**, que puede estar en equilibrio con el amidato **B**, resultante de la desprotonación de la amida. Este último sufriría el acoplamiento reductor C–N. De acuerdo con los resultados mencionados en los capítulos anteriores, los derivados *N*-metil-sustituidos **52–57b** requirieron tiempos de reacción más largos (24 h) que el derivado no sustituido **52a** (3 h), debido a que la repulsión estérica del grupo metilo dificulta el acoplamiento C–N.

Esquema 13



Los paladaciclos que contienen derivados de fenilpropiolato mostraron un comportamiento diferente. Así, la reacción de **56b** con CO (1.4 bar) en CH_2Cl_2 a temperatura ambiente produjo Pd(0), (tmedaH)TfO y 3-[carboxi(metoxicarbonil)metil]-2-metil-3-fenilisoindolin-1-ona (**60a**). La ciclación para dar el anillo de isoindolinona es formalmente el resultado de una adición aza-Michael del grupo NHMe al grupo vinilo que procede del alquino. Este proceso puede desencadenarse a partir del intermedio **B** y está favorecido porque el grupo vinilo está muy activado para sufrir adiciones conjugadas. La etapa final de esta reacción debe ser la hidrólisis del enlace acil–paladio por agua residual. Nuestros intentos para aislar el compuesto **60a** de la mezcla de reacción fueron infructuosos, ya que ocurre fácilmente un proceso de descarboxilación para dar 3-(metoxicarbonilmetil)-2-metil-3-fenilisoindolin-1-ona (**61**) (Esquema 13).

Cuando la reacción de **56b** con CO se realizó en presencia de 2 equivalentes de MeOH o EtOH, tuvo lugar el mismo proceso, pero en estos casos la etapa de despaladación es una alcoholisis que conduce a los diésteres 3-[di(metoxicarbonil)metil]-2-metil-3-fenilisoindolin-1-ona (**60b**) ó 3-[etoxicarbonil(methoxicarbonil)metil]-2-metil-3-fenilisoindolin-1-ona (**60c**), respectivamente. Análogamente, las reacciones de **57b** con CO en presencia de 2 equivalentes de MeOH o EtOH condujeron a la formación de **60c** ó 3-[di(etoxicarbonil)metil]-2-metil-3-fenilisoindolin-1-ona (**60d**), respectivamente.

El uso de MeOH como disolvente para la reacción de **56b** con CO condujo a la formación de dimetil 2-((2-(metilcarbamoil)fenil)(fenil)metilen)malonato (**62**), resultando de la metanolisis del acil-complejo intermedio A. Razonablemente, en presencia de un gran

exceso de MeOH, la metanolisis es mucho mas rápida que la ciclación. El intento de producir la ciclación por calentamiento de una disolución de **62** en $CDCl_3$ a 70 °C durante 24 h en presencia de un exceso de tmeda no tuvo éxito, lo que sugiere que la adicción aza-Michael para dar **60b–d** es asistida por el centro de Pd(II), lo que es consistente con la participación de un intermedio amidato.

Formación y despaladación de un alquil-alcoholato complejo. La desprotonación del grupo amida en el complejo **55b** con exceso de NaOMe en MeOH se intentó con objeto de obtener un amidato cíclico de 7 miembros para utilizarlo como precursor para la síntesis de una benzo[*c*]azepin-1,3-diona adicional. Sin embargo, se obtuvo inesperadamente el complejo neutro [Pd(κ^2C,O-$C_{14}H_{13}O_5$)(tmeda)] (**63**), que contiene un ligando alquil-alcoholato derivado de la isoquinolina-1,3-diona (Esquema 14). La despaladación del complejo **63** se logró a reflujo en $CHCl_3$ durante 2 horas y condujo al compuesto (*E*)-4-[metoxi(metoxicarbonil)metileno]-2-metilisoquinolina-1,3(2*H*,4*H*)-diona (**64**). El mismo producto se detectó mediante RMN de ^{1}H después de hacer reaccionar el complejo **63** con CO (1.4 bar) in $CDCl_3$ durante 6 h a temperatura ambiente (93%); en este caso la inserción de CO en el enlace Pd–C no tuvo lugar, pero probablemente el exceso de CO contribuyó al proceso de reducción.

Esquema 14