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ORIGINAL ARTICLE

Unlocking the synthetic potential of aziridine and cyclopropane-fused quinolin-2-ones by regioselective fragmentation of its three-membered rings

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KEYWORDS

Aziridino[2,3-*c*]quinolin-2-ones;
Cyclopropa[*c*]quinolin-2-ones;
3-aminoquinolin-2-ones;
Benzazepin-2-ones;
6π-electrocyclic ring opening;
[1,5]-H shift

Abstract The cyclization of *cis*-2-(2-azidophenyl)-1-benzyl-3-ethoxycarbonylaziridines and *trans*-2-(2-azidophenyl)-3-nitrocyclopropane-1,1-dicarboxylates yielded the respective aziridino[2,3-*c*]quinolin-2-ones and cyclopropa[*c*]quinolin-2-ones. Ring-opening of the aziridine-fused species under silica gel catalysis provided 3-aminoquinolin-2-ones whereas the ring-expansion of the cyclopropane-fused derivatives by the action of sodium hydride gave 1-benzazepin-2-ones, in both cases in a regioselective manner. A computational study using DFT methods revealed that the mechanism for the transformation of cyclopropa[*c*]quinolin-2-ones into 1-benzazepin-2-ones involves the initial deprotonation step of its amide function followed by two pericyclic events: a 6π-electrocyclic ring opening and a subsequent [1,5]-H shift.

1. Introduction

The presence of an aziridine ring into the skeleton of organic compounds is often responsible for the pharmaceutical and biological behaviour of such molecules (Degennaro et al., 2014; Sweeney, 2002). Mitosanes **1**, antitumor agents exhibiting antibiotic activity (Kasai and Kono, 1992; Remers and Dorr, 1988; Remers, 1979), are probably the best-known class of naturally occurring products bearing the aziridine ring (Fig. 1). Compounds **2** derived from the aziridino[2,3-*c*]quinoline ring

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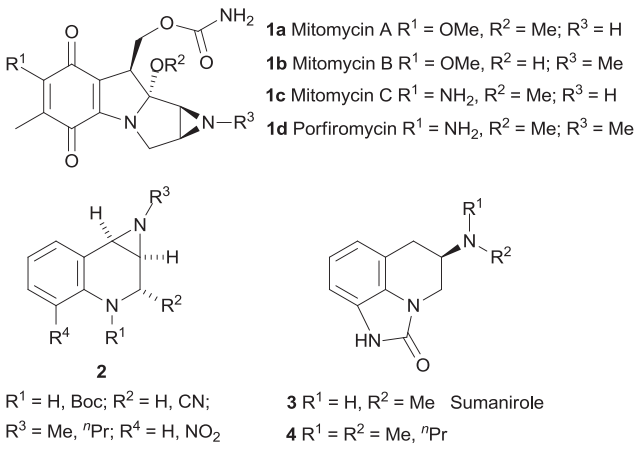


Fig. 1 Mitosanes, examples of aziridino[2,3-*c*]quinolines and Sumanirole.

system have been scarcely reported in the chemical literature (Hao et al., 2017; Jean-Gérard et al., 2012; Heier et al., 1997; Heier et al., 1996; Moon et al., 1993; Walser et al., 1973; Greibrokk, 1972), in most cases as valuable intermediates en route towards the synthesis of Sumanirole **3** (Jean-Gérard et al., 2012; Heier et al., 1996), a highly selective D2 receptor agonist which was developed for the treatment of Parkinson disease, or analogues **4** (Fig. 1) (Heier et al., 1997; Moon et al., 1993).

The cyclopropane ring is also a key structural motif found in a great number of natural products and drugs with a broad range of relevant biological activities, frequently in conjunction with a nitrogen atom in a proximal position (Talele, 2016). Representative examples of compounds sharing this arrangement are shown in Fig. 2. Cyclopropane-containing drugs have found application in a variety of therapeutic areas such as cancer, HIV and bacterial infections, inflamations, cardiovascular diseases, bone disorders, etc. Trovafloxacin, from the antimicrobial quinolone group, shows a broad-spectrum

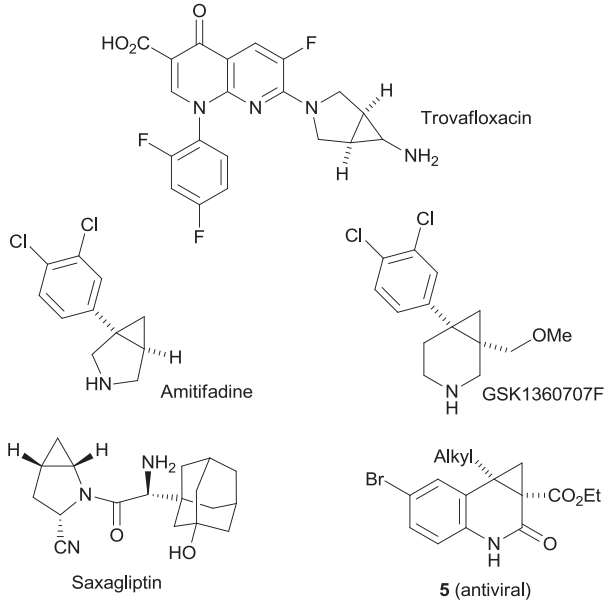


Fig. 2 Selected examples of biologically active compounds and drugs having an annulated cyclopropane ring.

bactericidal action resulting from inhibition of the enzymes DNA gyrase and topoisomerase IV (Aldred et al., 2014; Hooper, 1999; Gootz et al., 1996). Amitifadine and GSK1360707F are potent and selective triple reuptake inhibitors developed for the treatment of major depressive disorders (Sharma et al., 2015; Micheli et al., 2010). Saxagliptin is an oral hypoglycemic drug of the dipeptidyl peptidase inhibitor class (Savage et al., 2009), and cyclopropa[*c*]quinolones of general structure **5** were discovered as antiviral drugs acting as HIV-1 non-nucleoside reverse transcriptase inhibitors (Luo et al., 2015; Pedroni et al., 2015; Truong et al., 2013; Saget and Cramer, 2012; Yong et al., 2007; Ellis et al., 2006; Bates et al., 1987).

Furthermore, as highly strained three-membered rings, aziridines and cyclopropanes are very active species for ring-opening and ring-expansion reactions (Tummanapalli et al., 2014; Stankovic et al., 2012; Tang and Qin, 2012; Li et al., 2011; Ye and Yu, 2011; De Simone and Waser, 2009; Xu et al., 2008; Singh et al., 2007; Coldham and Hufton, 2005; Rotzoll et al., 2005; Kim et al., 2004; Reissig and Zimmer, 2003), thus providing access to a wide variety of multifunctional compounds.

Our long standing interest in developing synthetic strategies for fused heterocyclic compounds (Marin-Luna et al., 2015; Alajarin et al., 2012; Alajarin et al., 2007; Alajarin et al., 2005; Molina et al., 1992a,b; Molina et al., 1991; Molina et al., 1990; Molina et al., 1989a,b; Molina et al., 1988) focused our attention to the tricyclic scaffolding present in the aziridino[2,3-*c*]quinolines **2** and the antiviral cyclopropa[*c*]quinolones **5**. To facilitate synthetic access to this type of aziridine and cyclopropane-fused quinolines we envisioned an unprecedented protocol based on materials with a preformed aziridine or cyclopropane ring (Fig. 3). Here we also disclose the application of ring-opening and ring-expansion processes to

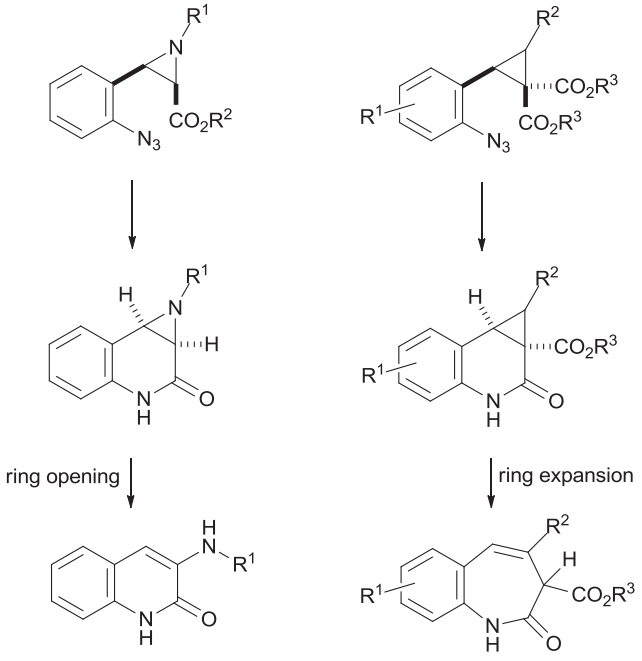
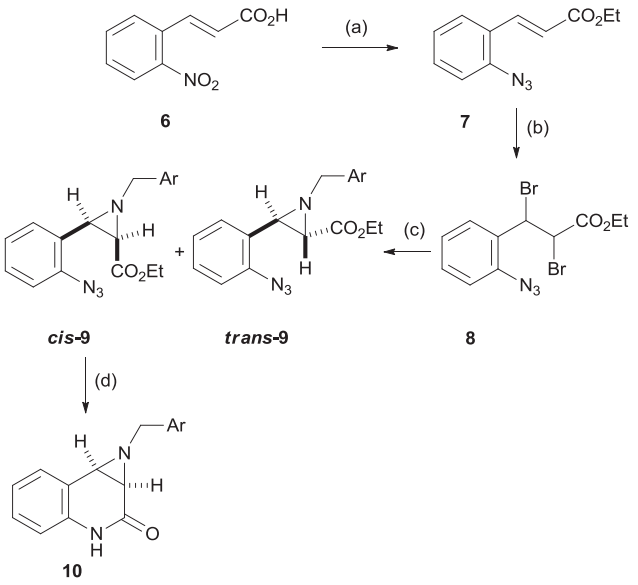


Fig. 3 Synthetic strategies designed to access to aziridino[2,3-*c*]quinolin-2-ones and cyclopropa[*c*]quinolin-2-ones as well as to their ring opening/expansion products.



Scheme 1 Synthesis of aziridino[2,3-*c*]quinolin-2-ones with diverse benzyl substituents at the N atom of the aziridine ring. Reagents and conditions: (a) 3 steps: 1. EtOH, cat. H_2SO_4, reflux, 48 h (99%); 2. Fe, AcOH/EtOH, reflux, 5 h (92%); 3. $NaNO_2$, AcOH/HCl, 0 °C, 1 h and then NaN_3, AcOH/HCl, 0 °C, 4 h (95%). (b) Br_2, chloroform, 0 °C, 24 h (75%). (c) $ArCH_2NH_2$, EtOH, r.t., 4.5 days. (d) 1. PMe_3, toluene (anh.), r.t., 30 min; 2. Silica gel column chromatography.

aziridino[2,3-*c*]quinolin-2-ones and cyclopropa[*c*]quinolin-2-ones for giving access to other heterocyclic ring systems as quinolin-2-ones substituted with an amino group at the C3 position and to polysubstituted 1-benzazepin-2-ones (Fig. 3).

2. Results and dicussion

2.1. Synthesis of aziridinoquinolin-2-ones and 3-amino-1H-quinolin-2-ones

The commercially available (*E*)-3-(2-nitrophenyl)propenoic acid **6** following a lineal sequence of three reported experimental steps (see supplementary material), Fischer esterification, reduction and diazotation/azidation, was transformed into ethyl (*E*)-3-(2-azidophenyl)propenoate **7**. The addition of bromine to the exocyclic C = C bond of the propenoate **7**, in chloroform solution at 0 °C, provided the 2,3-dibromopropanoate **8**. Further treatment of **8**, in ethanol at room temperature, with a series of benzyl amines afforded mixtures of the *cis* and *trans* isomers of the 2-(2-azidophenyl)-3-ethoxycarbonyla ziridines **9**, in total yields of 64–91%, with *cis*/*trans* ratios ranging from 3.9 to 1.2 being the *cis* isomer the major one. These mixtures of aziridines ***cis*-9** and ***trans*-9** were resolved into the pure isomers by column chromatography. The relative spacial relationship between the adjacent aryl and etoxycarbonyl groups was determined from the vicinal coupling constants between *H*-C2 and *H*-C3, $J_{2\text{-}3}$ = 6.4–6.9 Hz in the *cis* isomer and $J_{2\text{-}3}$ = 2.4–2.8 Hz in the *trans* isomer.

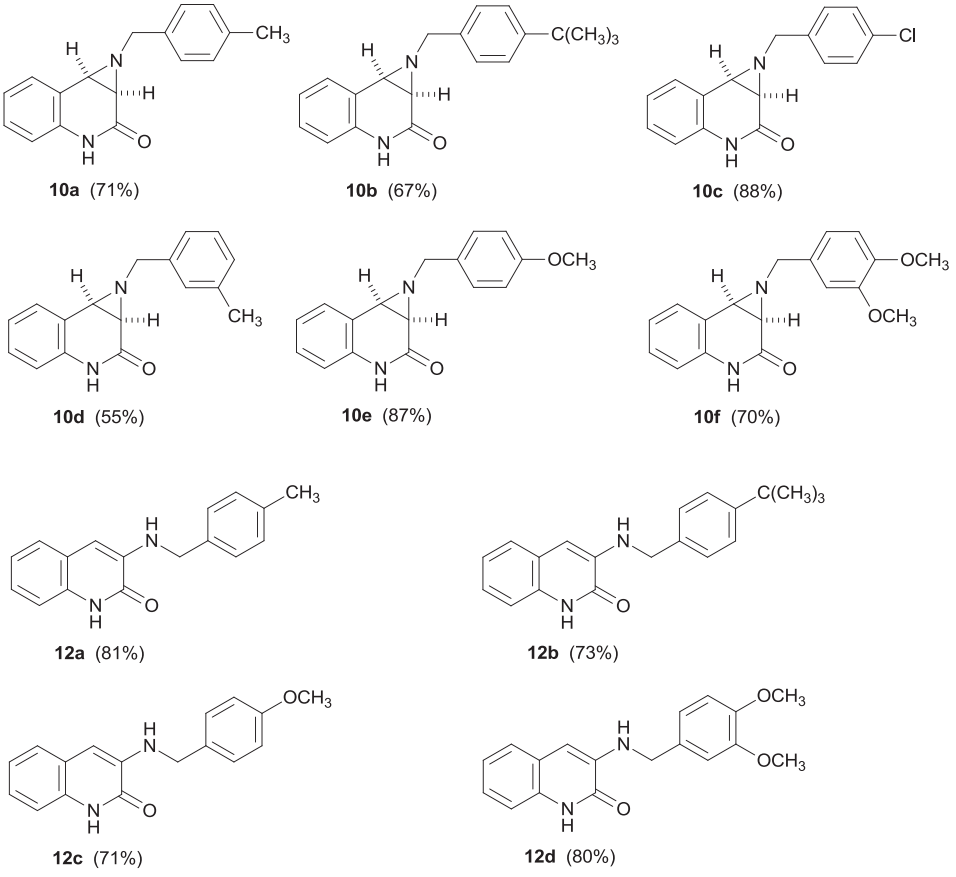


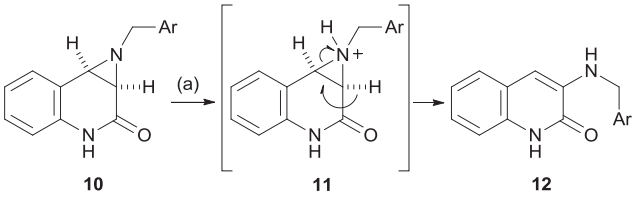
Fig. 4 Aziridino[2,3-*c*]quinolin-2-ones **10** and 3-benzylamino-1*H*-quinolin-2-ones **12.**

Subsequent treatment with trimethylphosphine of azides ***cis*-9**, in toluene at room temperature, followed by chromatographic purification led to the isolation of the aziridinoquinolin-2-ones **10** as the reaction products in moderate to good yields (Scheme 1, Fig. 4).

When solutions of aziridinoquinolones **10** in dichloromethane were stirred at room temperature for two days in the presence of silica gel cleanly converted into 3-benzylamino-1*H*-quinolin-2-ones **12** (Scheme 2, Fig. 4).

The conversion **10** → **12** could be considered as an isomerization of the aziridine core into an enamino function involving a simultaneous 1,2 hydrogen migration from carbon to nitrogen (Scheme 2). This unprecedented transformation might be tentatively explained as a sequence of two simple chemical events: the protonation of the nitrogen atom of the aziridine ring by the weakly acidic silica gel followed by removal of the acidic *H*-C1a hydrogen atom, which promotes the regioselective ring opening of the aziridine ring by fragmentation of the distal C7b-N bond. Release of strain and the generation of aromaticity at the pyridine ring of compounds **12** positively contribute to the occurrence of these transformations.

X-Ray crystallographic analysis of a monocrystal of quinolone **12a** (Ar = 4-CH_3-C_6H_4) confirmed that products **12** bear



Scheme 2 Synthesis of 3-benzylamino-1*H*-quinolin-2-ones. Reagents and conditions: (a) Wet silica gel, dichloromethane, r. t., 48 h.

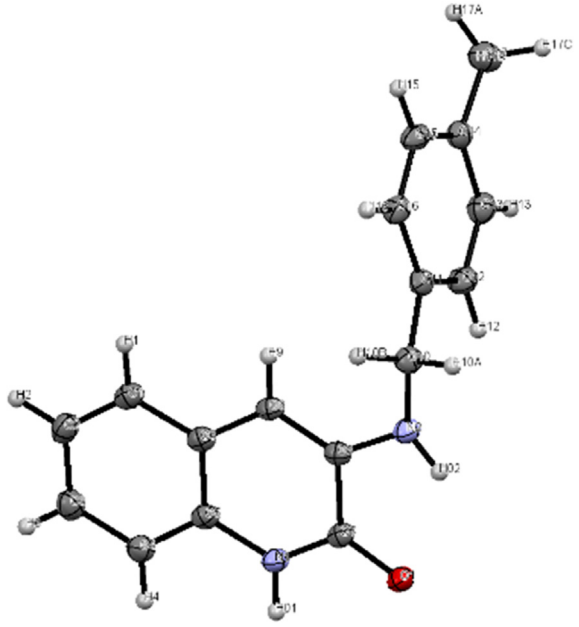
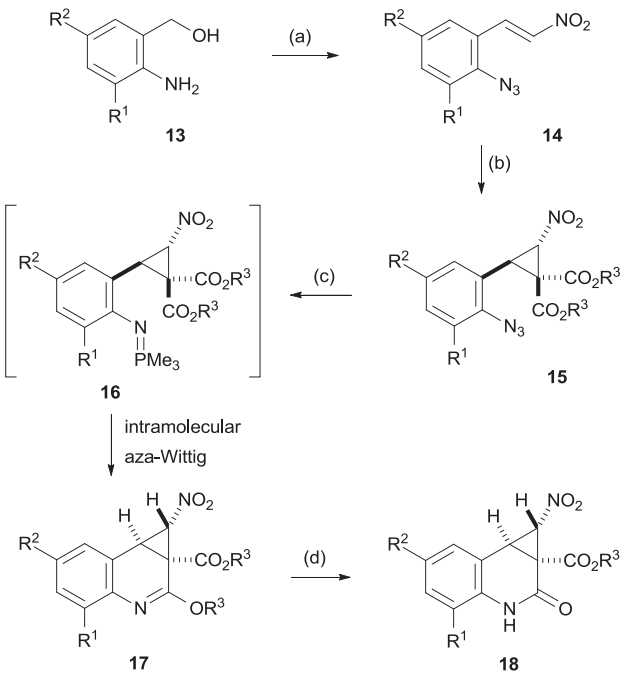


Fig. 5 Solid-state molecular structure of **12a**. Thermal ellipsoids are drawn at the 50% probability level.

the benzylamino substituent at the C3 position of the quinolin-2-one skeleton (Fig. 5).

2.2. Synthesis of cyclopropa[c]quinolin-2-ones and 1-benzazepin-2-ones

The synthesis of cyclopropa[*c*]quinolones was undertaken selecting 2-(2-azidophenyl)-3-nitrocyclopropane-1,1-dicarboxylates **15** as key precursors. First, three different substituted 2-azido-β-nitrostyrenes **14** were obtained starting from readily available 2-aminobenzyl alcohols **13**, through a sequence of four steps comprising diazotation/azidation, oxidation, Henry condensation and subsequent dehydration (see supplementary material). The one-pot Michael addition, promoted by triethylamine, of dialkyl bromomalonates to the 2-azido-β-nitrostyrenes **14** and further ring closure of the resulting adducts provided *trans*-2-(2-azidophenyl)-3-nitrocyclopropane-1,1-dicarboxylates **15** in 56–99% yields. The treatment of azides **15** with trimethylphosphine in toluene solution at room temperature led to, somewhat unexpectedly, the 2-alkoxy cyclopropa[*c*]quinolines **17** as a result of an intramolecular aza-Wittig reaction occurring through phosphazenes **16** (Scheme 3). Under these conditions the cyclizations finished in 30 min and the resulting **17** were obtained in high yields (Scheme 3, Fig. 6). Subsequently we carried out the hydrolysis of the imino ethers **17** performing the reaction in a combination of TFA/H_2O/THF that afforded the desired cyclopropa[*c*]quinolin-2-ones **18** in excellent yields (Scheme 3, Fig. 6).



Scheme 3 Synthesis of cyclopropa[*c*]quinolin-2-ones with a nitro group at the cyclopropane ring. Reagents and conditions: (a) 4 steps: 1. $NaNO_2$, AcOH/HCl, 0 °C, 1 h and then NaN_3, AcOH/HCl, 0 °C, 16 h (70–90%); 2. PCC, dichloromethane, r.t., 4 h (78–81%); 3. CH_3NO_2, NaOH, EtOH/H_2O, r.t., 24 h (92–99%); 4. $(AcO)_2O$, pyridine, 24 h (57–81%). (b) $BrCH(CO_2R^3)_2$, Et_3N, dimethylformamide (anh.), r.t., 24 h (56–99%). (c) PMe_3, toluene (anh.), r.t., 30 min. (d) TFA/H_2O/THF, r.t., 3 h.

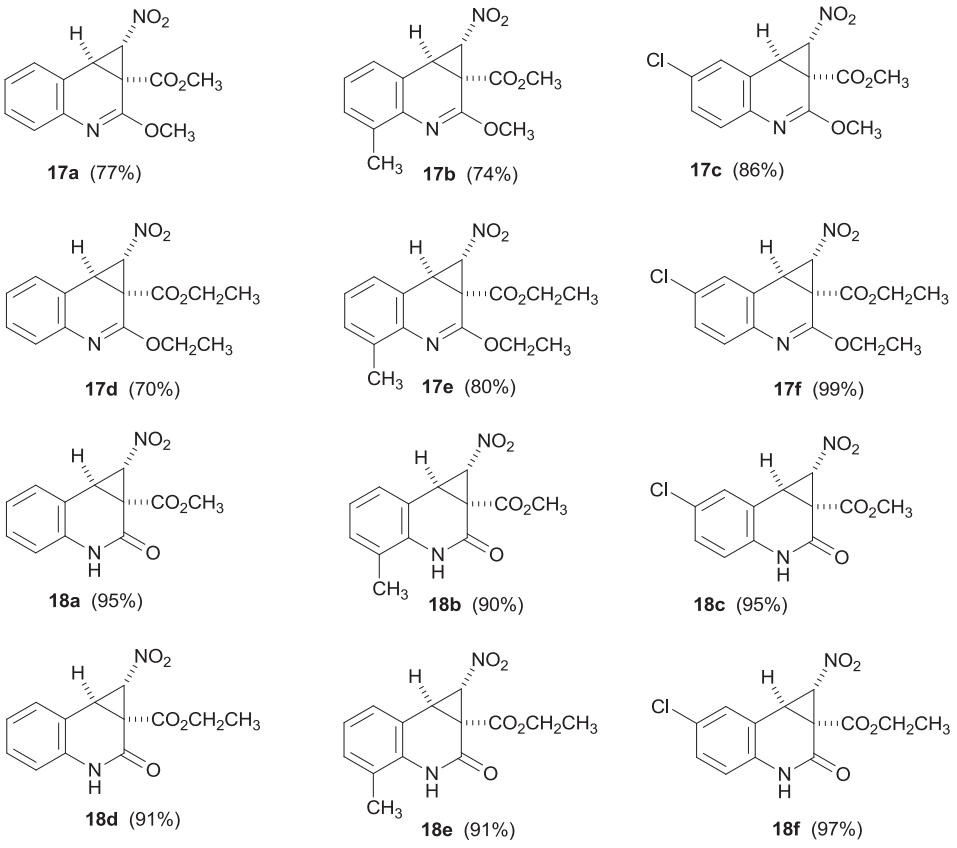


Fig. 6 Cyclopropa[*c*]quinolines **17** and cyclopropa[*c*]quinolin-2-ones **18.**

The crystal structure of the cyclopropa[*c*]quinoline **17a** (R^1 = R^2 = H; R^3 = CH_3) was determined by single-crystal X-ray diffraction analysis which displayed an essentially planar quinoline ring system (r.m.s. deviation = 0.0322 Å) (Fig. 7). The dihedral angle between the mean planes of the quinoline and cyclopropane rings is 76.3°.

We presumed that tricyclic compounds **18** might undergo ring opening of the cyclopropane ring via deprotonation under the action of bases. Pleasingly, the exposure of compounds **18** to sodium hydride in tetrahydrofuran at 0 °C resulted in their conversion into the respective 1-benzazepin-2-ones **19**, isolated in good yields (Scheme 4).

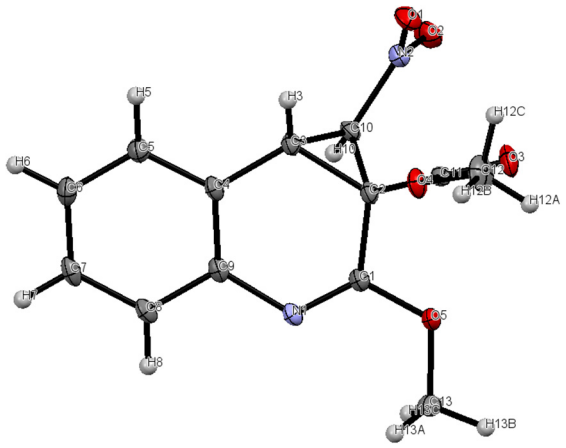


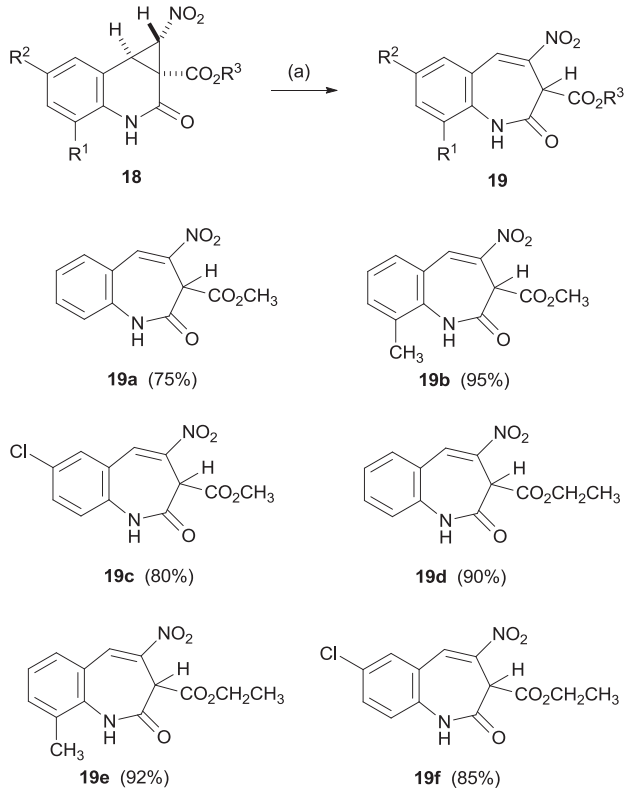
Fig. 7 Solid-state molecular structure of **17a**. Thermal ellipsoids are drawn at the 50% probability level.

The substituted benzazepin-2-ones **19** were identified by ^{1}H and ^{13}C NMR analysis, as well as by the X-ray crystal structure determination of **19f** (Fig. 8). The X-ray study showed that the seven-membered 2-azepinone ring present a chair conformation. In the crystal, molecules form dimers by means of two bifurcated hydrogen bonds C4-H4...O4...H6-C6.

To the best of our knowledge the ring expansion of compounds **18** into **19** does not have precedents in the chemical literature. We could not find previous reports on the fragmentation of analogous [*c*]-fused cyclopropane quinolin-2-ones, whereas a scarce number of related ring expansions of cyclopropa[c]quinolines to benzazepines are known. These latter processes are triggered by chemical events quite different to that used herein, such as hydrogenolysis (Saget and Cramer, 2012), deprotection of a silyl ether by the fluoride anion (Truong et al., 2013) or deprotonation of an exocyclic methyl group at C4 of a quinolinium cation (Luo et al., 2015).

2.3. Computational study

With the aim of elucidating the reaction mechanism corresponding to the conversion of cyclopropa[*c*]quinolin-2-ones **18** into benzazepin-2-ones **19** we have carried out a computationally study by means of DFT calculations at the M06/6-311 + G**//M06/6-311 + G** theoretical level. The effect of



Scheme 4 Synthesis of 1-benzazepin-2-ones. Reagents and conditions: (a) NaH, tetrahydrofuran, 0 °C, 3 h and then NH_4Cl/H_2O.

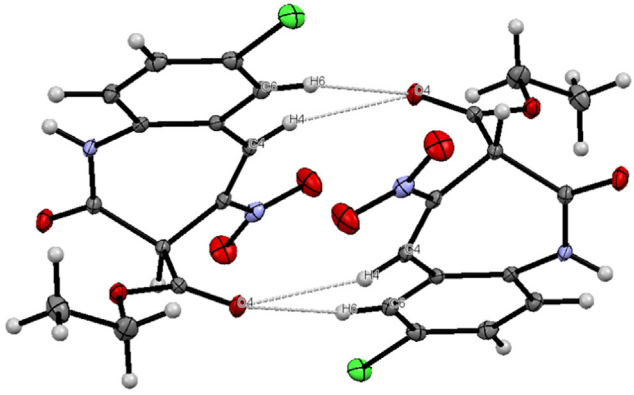


Fig. 8 Solid-state molecular structure of **19f**. Thermal ellipsoids are drawn at the 50% probability level.

the solvent has been taken into account through the polarizable continuum model SMD at the same level of theory.

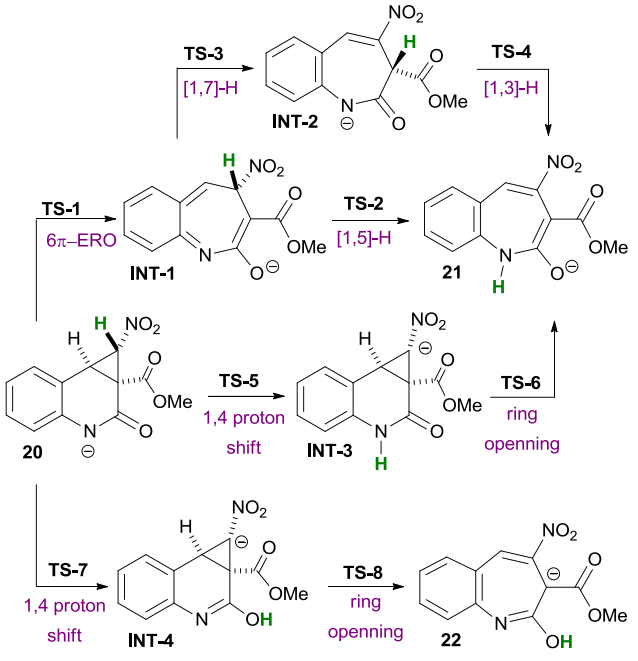
This computational research has been conducted by considering the transformation of the parent cyclopropa[*c*]quinolin-2-one **18a**, with no substituents at the benzene ring, into the 1*H*-benzazepin-2-one **19a**. We will comment on the results obtained in THF with the SMD model. Nonetheless, it is worth to mention there are not significant differences between the values of the Gibbs free energy barriers computed at the gas phase and in THF.

Previous computational studies have demonstrated that the alpha proton of nitrocyclopropanes exhibits very weak acidic character due to hybridization requirements (Bartmess et al., 1992). Taking into consideration this precedent, we reasoned that the lactamic proton of compounds **18** should be the most acidic one. Consequently, given that treatment of **18** with sodium hydride leads to benzazepines **19**, the abstraction of the lactamic proton from the prototypical **18a** affording the corresponding cyclopropa[*c*]quinolin-1-ide anion **20**, should trigger the series of chemical events resulting into a deprotonated form of the reaction product. The final protonation of this latter species during the work up of the reaction would finally lead to **19a**.

Furthermore, the conversions **18** → **19** involve not only the ring expansion of the cyclopropa[*c*]pyridine assembly, but also the migration of the hydrogen atom from the nitromethine group. Accordingly, we have intensively explored the potential energy surface associated to the cleavage of the C-C bond shared by the cyclopropane and the pyridine ring as well as shifts of the nitromethine proton which could jointly lead to the benzazepin-2-olate **21**, the 2-hydroxybenzazepin-3-ide **22**, or any other analogous species. In this way, we have found three mechanistic paths accounting for these transformations as shown in Scheme 5.

The first mechanistic route we addressed involves a tandem of two pericyclic events starting with a 6π electrocyclic ring opening through transition structure **TS-1** leading to intermediate **INT-1**. The energy barrier computed for this process is 30.6 kcal·mol^{-1}. **INT-1** is only 0.3 kcal·mol^{-1} lower in energy than **TS-1**, and can be transformed into **21** by a [1,5]-H shift via **TS-2**. The value of the energy barrier associated to this second step is only 15.5 kcal·mol^{-1}. This small value may be due to the recovering of aromaticity taking place when going from **INT-1** to **21**.

We also found an alternative route accounting for the conversion of **INT-1** into species **21** involving two consecutive H sigmatropic rearrangements: a [1,7]-H shift via **TS-3** leading



Scheme 5 Mechanistic paths found for the transformation of **20** into **21** and **22.**

Table 1 Gibbs free relative energies in gas phase G and in THF G_{THF} (in kcal·mol^{-1}) of the stationary points involved in the conversion of the cyclopropa[*c*]quinolin-1-ide **20** into the 1*H*-benzazepin-2-olate **21** and the 2-hydroxybenzazepin-3-ide **22** along with the Gibbs free energy barriers, ΔG and ΔG_{THF} (in kcal·mol^{-1}) computed at the M06/6-311 + G** theoretical level.

	G	G_{THF}	Mechanistic Step	ΔG	ΔG_{THF}
20	0.0	0.0	**20 → TS-1**	30.1	30.6
TS-1	30.1	30.6	**INT-1 → TS-2**	15.7	15.5
INT-1	29.7	30.3	**INT-1 → TS-3**	34.7	35.3
TS-2	45.4	45.8	**INT-2 → TS-4**	57.6	59.2
21	-6.2	-5.1	**20 → TS-5**	37.0	39.2
TS-3	64.4	65.6	**INT-3 → TS-6**	16.4	16.1
INT-2	-6.2	-4.5	**20 → TS-7**	50.1	52.4
TS-4	51.5	54.6	**INT-4 → TS-8**	13.0	13.5
TS-5	37.0	39.2			
INT-3	13.4	10.1			
TS-6	29.8	26.2			
TS-7	50.1	52.4			
INT-4	23.7	22.1			
TS8	36.7	35.5			
22	4.9	7.7			

to the benzazepin-1-ide **INT-2**, followed by a [1,3]-H shift through the transition structure **TS4**. Notwithstanding, this path cannot compete with the [1,5]-H shift which directly transforms **INT-1** into **21** because of the larger values of the energy barriers computed for both steps (35.3 and 59.2 kcal·mol^{-1} respectively) (see Table 1) when compared to those of the first path.

The second mechanistic path also consist of two steps. Interestingly, the first step, which takes place through **TS-5**, involves a [1,4] proton shift from the nitromethine carbon atom to the nitrogen atom of the pyridine ring leading to **INT-3**, which in a second step undergoes a ring opening with a simultaneous electric reorganization via **TS-6** leading to **21**. The computer energy barriers were 39.2 and 16.1 kcal·mol^{-1} respectively.

Finally, the third mechanistic route involving the transition structures **TS-7** and **TS-8** is very similar to the previous one. First, the hydrogen atom of the nitromethine group in **20** shifts to the oxygen atom of the deprotonated amide group leading to the hydroxy-imino intermediate **INT-4**, which in a second step undergoes ring expansion to finally give **22**. The value of the energy barrier computed for the first step is high, 52.4 kcal·mol^{-1}, while that of the second one is easily surmountable, 13.5 kcal·mol^{-1}.

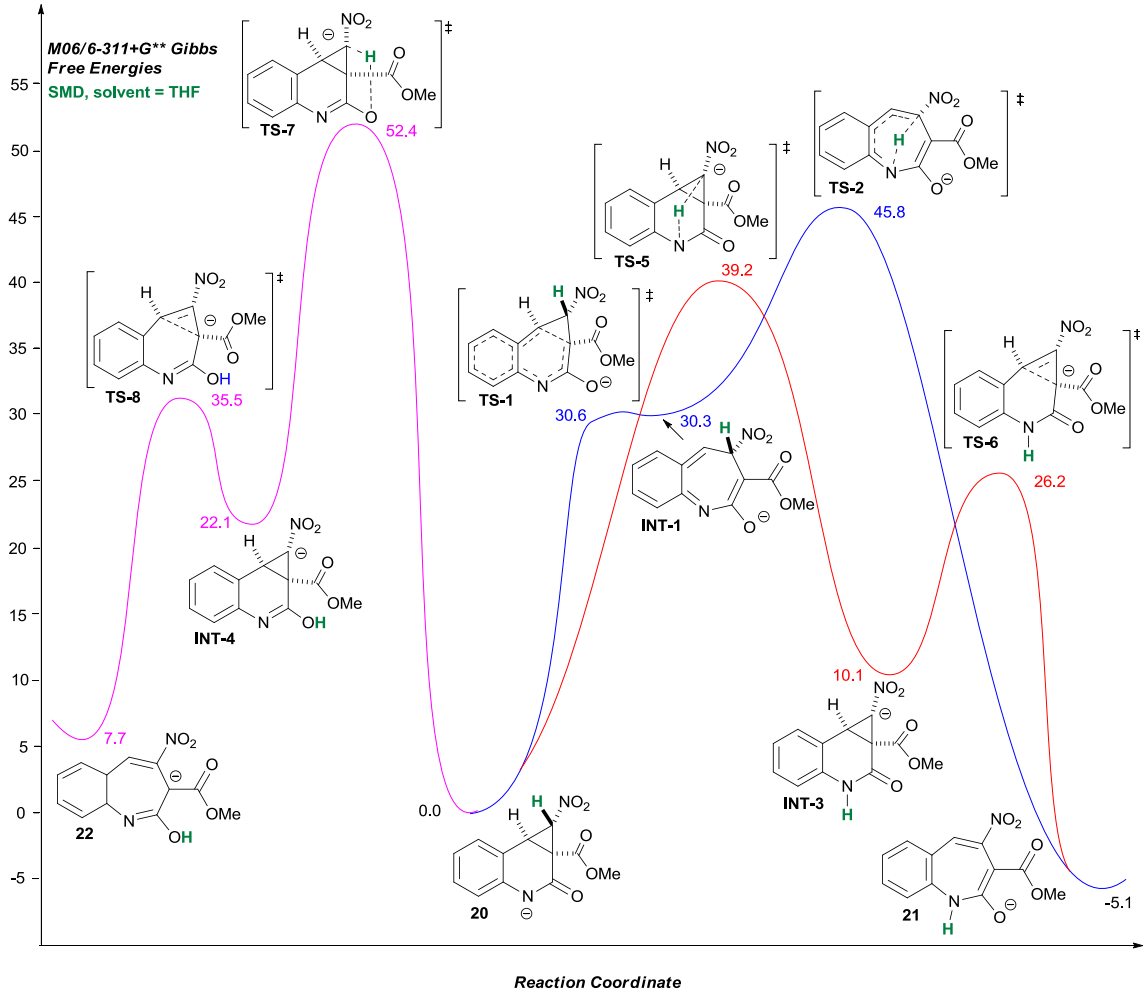


Fig. 9 Reaction profile found at the M06/6-311 + G** theoretical level for the conversion of **20** into **21** and **22**.

The qualitative reaction coordinates are depicted in Fig. 9, except the route passing through **INT-2**. On the basis of the computed energy barriers values of each mechanistic path, this study predicts that the tandem of two pericyclic reactions, 6π-electrocyclic ring opening/[1,5]-H shift taking place through the transition structures **TS-1** and **TS-2**, is clearly the preferred reaction path. None of the other two alternatives, initiated by the shift of the nitromethine proton, can compete with it because the energy values of the rate limiting steps of these paths (39.2 and 52.4 kcal·mol^{-1}) are quite higher than that of the favoured mechanistic path (30.6 kcal·mol^{-1}).

It is also worth to point out that **21** is 12.8 kcal·mol^{-1} lower in energy than its hydroxy-imino tautomer **22**. Taking this fact into account, and by considering the first mechanistic path as the preferred one, the 1*H*-benzazepin-2-olate **21** would be both the kinetically and thermodynamically controlled product.

3. Conclusions

In conclusion, we have developed a new synthetic approach to aziridine and cyclopropane-fused quinolones, based on the annulation of the quinoline core to adequately substituted aziridines and cyclopropanes. The resultant aziridino[2,3-*c*]quinolin-2-ones were isomerized into 3-aminoquinolin-2-ones by a silica gel promoted regioselective ring opening of the three membered heterocycle. Moreover, the synthesised cyclopropa[*c*]quinolin-2-ones transformed into benzo-fused azepinones via base triggered ring-enlargement of the cyclopropane fragment. The mechanism by which cyclopropa[*c*]quinolin-2-ones are transformed into 1-benzazepin-2-ones has been scrutinized by means of DFT computations. Several reaction paths were found all starting by the deprotonation of the lactam fragment of the cyclopropa[*c*]quinolin-2-ones. Based on the values of the computed energy barriers, the predicted mechanistic route consists of two successive pericyclic events, an initial 6π-electrocyclic ring opening at the cyclopropaquinoline nucleus yielding the seven-membered azepine ring, followed by a subsequent [1,5]-H sigmatropic shift.

4. Experimental

4.1. General remarks

All melting points are uncorrected. Infrarred (IR) spectra were recorded neat or as Nujol emulsions. ^{1}H NMR spectra were recorded at 300 or 400 MHz. ^{13}C NMR spectra were recorded at 75 or 100 MHz. The chemical shifts in the ^{1}H NMR spectra are expressed in ppm relative to Me_4Si at $\delta = 0.00$. The chemical shifts in the ^{13}C NMR spectra are reported relative to the resonance of $CDCl_3$ at $\delta = 77.10$ ppm. J values are given in Hz.

4.2. General procedure for the preparation of the 2H-aziridino[2,3-c]quinolin-2-ones **10**

To a solution, under nitrogen, of the *cis*-2-(2-azidophenyl)-3-ethoxycarbonylaziridine ***cis*-9** (0.6 mmol) in anhydrous toluene (10 mL) 1 M trimethylphosphine in toluene (0.63 mL, 0.63 mmol) was added. The reaction mixture was stirred at room temperature for 30 min. Then, the solvent was removed under reduced pressure. The resulting material was chromatographed on a silica gel column, using first as eluent hexanes/diethyl ether (7:3, v/v) and then ethyl acetate.

4.2.1. 2H-Aziridino[2,3-c]quinolin-2-one **10a** (Ar = 4-CH_3-C_6H_4)

(0.11 g, 71%); mp 151–152 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3199, 1692; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.24 (3H, s), 2.72 (1H, dd, *J* 5.6, 1.6), 2.98 (1H, d, *J* 5.6), 3.51 (1H, d, *J* 13.6), 3.86 (1H, d, *J* 13.6), 6.75–6.78 (1H, m), 6.93 (1H, td, *J* 7.6, 1.2), 7.04 (2H, d, *J* 8.0), 7.11–7.15 (3H, m), 7.26 (1H, dd, *J* 7.6, 1.2), 9.15 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 42.3, 44.0, 62.8, 116.1, 120.6 (s), 122.9, 127.7, 128.6, 128.7, 129.1, 134.4 (s), 136.0 (s), 136.9 (s), 168.4 (s); HRMS (ESI): *m*/*z* calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$ 265.1335, found 265.1341.

4.2.2. 2H-Aziridino[2,3-c]quinolin-2-one **10b** [Ar = 4-$(CH_3)_3$C-C_6H_4]

(0.12 g, 67%); mp 159–160 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3283, 1670; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (9H, s), 2.81 (1H, dd, *J* 6.0, 1.6), 3.09 (1H, d, *J* 6.0), 3.65 (1H, d, *J* 13.6), 3.94 (1H, d, *J* 13.6), 6.86 (1H, d, *J* 7.6), 7.03 (1H, td, *J* 7.6, 1.2), 7.23 (1H, td, *J* 7.6, 1.6), 7.24–7.28 (2H, m), 7.33–7.39 (3H, m), 9.20 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.3, 34.4 (s), 42.3, 44.1, 62.8, 116.0, 120.7 (s), 122.9, 125.4, 127.4, 128.7, 134.5 (s), 136.1 (s), 150.2 (s), 168.4 (s); HRMS (ESI): *m*/*z* calcd for $C_{20}H_{23}N_2O$ $[M+H]^+$ 307.1805, found 307.1793.

4.2.3. 2H-Aziridino[2,3-c]quinolin-2-one **10c** (Ar = 4-Cl-C_6H_4)

(0.15 g, 88%); mp 165–167 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3186, 1677; ^{1}H NMR (400 MHz, DMSO d_6): δ 2.78 (1H, dd, *J* 6.0, 2.0), 3.31 (1H, d, *J* 6.0), 3.66 (2H, s), 6.68 (1H, dd, *J* 8.0, 0.8), 6.93 (1H, td, *J* 7.2, 1.2), 7.18 (1H, td, *J* 7.6, 1.2), 7.33–7.38 (4H, m), 7.40 (1H, dd, *J* 7.6, 1.6), 10.18 (1H, s); ^{13}C NMR (100 MHz, DMSO d_6): δ 41.7, 43.2, 60.9, 115.2, 120.6 (s), 121.8, 128.2, 128.3, 128.7, 129.8, 131.7 (s), 137.0 (s), 137.7 (s), 166.8 (s); HRMS (ESI): *m*/*z* calcd for $C_{16}H_{14}ClN_2O$ $[M+H]^+$ 285.0789, found 285.0788.

4.2.4. 2H-Aziridino[2,3-c]quinolin-2-one **10d** (Ar = 3-CH_3-C_6H_4)

(0.087 g, 55%); mp 145–147 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3265, 1675; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (3H, s), 2.82 (1H, dd, *J* 5.7, 1.8), 3.07 (1H, d, *J* 5.7), 3.59 (1H, d, *J* 13.8), 3.97 (1H, d, *J* 13.8), 6.88 (1H, d, *J* 7.8), 7.02 (1H, td, *J* 7.5, 1.2), 7.06–7.15 (3H, m), 7.19–7.25 (2H, m), 7.35 (1H, dd, *J* 7.5, 1.2), 9.44 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.3, 42.4, 44.1, 63.1, 116.1, 120.6 (s), 122.9, 124.7, 128.0, 128.3, 128.5, 128.6, 128.7, 136.0 (s), 137.4 (s), 138.0 (s), 168.4 (s); HRMS (ESI): *m*/*z* calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$ 265.1335, found 265.1341.

4.2.5. 2H-Aziridino[2,3-c]quinolin-2-one **10e** (Ar = 4-CH_3O-C_6H_4)

(0.15 g, 87%); mp 177–179 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3203, 1683; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.74 (1H, dd, *J* 5.6, 1.6), 3.28 (1H, d, *J* 6.0), 3.58 (2H, s), 3.71 (3H, s), 6.85–6.87 (3H, m), 6.93 (1H, td, *J* 7.6, 1.2), 7.17 (1H, td, *J* 7.6, 1.2), 7.26 (2H, d, *J* 8.8), 7.39 (1H, dd, *J* 7.6, 1.2), 10.15 (1H,

s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 41.7, 43.2, 55.0, 61.5, 113.7, 115.2, 120.8 (s), 121.8, 128.2, 128.7, 129.4, 130.6 (s), 137.0 (s), 158.4 (s), 167.0 (s); HRMS (ESI): m/z calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$ 281.1285, found 281.1287.

4.2.6. 2H-Aziridino[2,3-c]quinolin-2-one ***10f*** *[Ar = 3,4-$(CH_3O)_2$-C_6H_3]*

(0.13 g, 70%); mp 238–240 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3184, 1673; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.76 (1H, dd, *J* 5.7, 1.5), 3.31 (1H, d, *J* 5.7), 3.58 (2H, s), 3.70 (3H, s), 3.71 (3H, s), 6.82–6.89 (3H, m), 6.91–6.96 (2H, m), 7.18 (1H, td, *J* 7.5, 1.5), 7.42 (1H, dd, *J* 7.5, 1.2), 10.17 (1H, s); ^{13}C NMR (75 MHz, DMSO-d_6): δ 41.7, 43.2, 55.3, 55.5, 61.6, 111.6, 111.8, 115.2, 120.1, 120.8 (s), 121.7, 128.2, 128.7, 131.1 (s), 137.0 (s), 147.9 (s), 148.5 (s), 167.0 (s); HRMS (ESI): m/z calcd for $C_{18}H_{19}N_2O_3$ $[M+H]^+$ 311.1390, found 311.1394.

4.3. General procedure for the preparation of the 3-benzylamino-1H-quinolin-2-ones ***12***

To a solution of the 2*H*-aziridino[2,3-*c*]quinolin-2-one **10** (0.25 mmol) in dichloromethane (20 mL) silica gel (5 g) and water (0.2 mL) were added. The reaction mixture was stirred at room temperature for 48 h. Then, the silica gel was separated by filtration and washed with dichloromethane (30 mL) and ethyl acetate (120 mL). The solvent was removed under reduced pressure. The resulting solid was precipitated with diethyl ether (5 mL), filtered and dried.

4.3.1. 1H-Quinolin-2-one ***12a*** *(Ar = 4-CH_3-C_6H_4)*

(0.053 g, 81%); mp 207–209 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3407, 1646; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.24 (3H,s), 4.33 (2H, d, *J* 6.0), 6.33 (1H, t, *J* 6.0), 6.40 (1H, s), 7.00 (1H, t, *J* 6.8), 7.07–7.11 (3H, m), 7.19 (1H, d, *J* 8.0), 7.24 (2H, d, *J* 8.0), 7.28 (1H, d, *J* 7.2), 11.88 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.7, 45.5, 103.3, 114.6, 121.8 (s), 122.0, 124.0, 124.5, 127.0, 129.0, 131.4 (s), 135.8 (s), 136.0 (s), 137.3 (s), 158.0 (s); HRMS (ESI): m/z calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$ 265.1335, found 265.1341.

CCDC-1816436 contains the supplementary crystallographic data of this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

4.3.2. 1H-Quinolin-2-one ***12b*** *[Ar = 4-$(CH_3)_3$C-C_6H_4]*

(0.056 g, 73%); mp 225–226 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3405, 1648; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.19 (9H, s), 4.30 (2H, d, *J* 6.3), 6.23 (1H, t, *J* 6.3), 6.41 (1H, s), 6.96 (1H, td, *J* 7.8, 1.5), 7.06 (1H, td, *J* 7.2, 1.5), 7.15 (1H, d, *J* 7.5), 7.22–7.30 (5H, m), 11.81 (1H, s); ^{13}C NMR (75 MHz, DMSO-d_6): δ 31.1, 34.1 (s), 45.3, 103.1, 114.5, 121.8 (s), 121.9, 123.9, 124.4, 125.1, 126.8, 131.4 (s), 136.0, 137.3 (s), 149.1 (s), 157.9 (s); HRMS (ESI): m/z calcd for $C_{20}H_{23}N_2O$ $[M+H]^+$ 307.1805, found 307.1816.

4.3.3. 1H-Quinolin-2-one ***12c*** *(Ar = 4-CH_3O-C_6H_4)*

(0.050 g, 71%); mp 225–228 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3395, 1658; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.70 (3H, s), 4.30 (2H, d, *J* 6.3), 6.26 (1H, t, *J* 6.3), 6.43 (1H, s), 6.87 (2H, d, *J* 8.4), 6.98–7.03 (1H, m), 7.07–7.13 (1H, m), 7.19 (1H, d, *J* 7.8), 7.20–7.31 (3H, m), 11.86 (1H, s); ^{13}C NMR (75 MHz, DMSO-d_6): δ 45.2, 55.0, 103.3, 113.8, 114.6, 121.8 (s), 122.0, 124.0, 124.4, 128.4, 130.8 (s), 131.4 (s), 137.2 (s), 158.0 (s), 158.2 (s); HRMS (ESI): m/z calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$ 281.1285, found 281.1284.

4.3.4. 1H-Quinolin-2-one ***12d*** *[Ar = 3,4-$(CH_3O)_2$-C_6H_3]*

(0.062 g, 80%); mp 242–244 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3404, 1653; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.70 (3H, s), 3.72 (3H, s), 4.29 (2H, d, *J* 6.3), 6.24 (1H, t, *J* 6.3), 6.46 (1H, s), 6.88 (2H, s), 6.98–7.01 (2H, m), 7.10 (1H, td, *J* 6.9, 1.2), 7.18 (1H, d, *J* 7.8), 7.31 (1H, dd, *J* 7.8, 0.9), 11.85 (1H, s); ^{13}C NMR (75 MHz, DMSO-d_6): δ 45.6, 55.4, 55.5, 103.4, 111.2, 111.7, 114.6, 119.2, 121.8 (s), 122.0, 124.0, 124.5, 131.3 (s), 131.4 (s), 137.3 (s), 147.7 (s), 148.7 (s), 158.0 (s); HRMS (ESI): m/z calcd for $C_{18}H_{19}N_3O_2$ $[M+H]^+$ 311.1390, found 311.1394.

4.4. General procedure for the preparation of the 2-alkoxy-1H-cyclopropa[c]quinolines ***17***

To a solution, under nitrogen, of the cyclopropane **15** (1.5 mmol) in anhydrous toluene (20 mL) 1 M trimethylphosphine in toluene (1.6 mL, 1.6 mmol) was added. The reaction mixture was stirred at room temperature for 30 min. Then, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on a silica gel column, using hexanes/diethyl ether (7:3, v/v) as eluent.

4.4.1. 1H-Cyclopropa[c]quinoline ***17a*** *(R^1 = R^2 = H, R^3 = CH_3)*

(0.32 g, 77%); mp 176–177 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 1744, 1629; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (3H, s), 3.96 (1H, d, *J* 3.6), 3.97 (3H, s), 4.10 (1H, d, *J* 3.6), 7.21 (1H, td, *J* 7.2, 1.6), 7.28 (1H, dd, *J* 8.0, 1.2), 7.34 (1H, td, *J* 8.0, 1.6), 7.42 (1H, dd, *J* 7.6, 1.6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.5, 38.9 (s), 53.6, 55.0, 61.9, 118.5 (s), 126.4, 127.1, 128.1, 129.4, 140.1 (s), 155.3 (s), 163.2 (s); HRMS (ESI): m/z calcd for $C_{13}H_{13}N_2O_5$ $[M+H]^+$ 277.0819, found 277.0828.

CCDC-1816437 contains the supplementary crystallographic data of this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

4.4.2. 1H-Cyclopropa[c]quinoline ***17b*** *(R^1 = CH_3, R^2 = H, R^3 = CH_3)*

(0.32 g, 74%); mp 133–134 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 1747, 1644; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (3H, s), 3.82 (3H, s), 3.94 (1H, d, *J* 3.6), 3.97 (3H, s), 4.09 (1H, d, *J* 3.6), 7.11 (1H, t, *J* 7.6), 7.20–7.23 (1H, m), 7.25–7.27 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.4, 35.1, 39.0 (s), 53.5, 54.8, 61.9, 118.2 (s), 125.7, 125.8, 130.7, 135.4 (s), 138.1 (s), 154.1 (s), 163.3 (s); HRMS (ESI): m/z calcd for $C_{14}H_{15}N_2O_5$ $[M+H]^+$ 291.0975, found 291.0977.

4.4.3. 1H-Cyclopropa[c]quinoline ***17c*** *(R^1 = H, R^2 = Cl, R^3 = CH_3)*

(0.40 g, 86%); mp 151–152 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 1743, 1628; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.81 (3H, s), 3.95 (3H, s), 3.96 (1H, d, *J* 3.6), 4.05 (1H, d, *J* 3.6), 7.21 (1H, d, *J*

8.7), 7.29 (1H, dd, *J* 8.7, 2.4), 7.42 (1H, d, *J* 2.4); ^{13}C NMR (75 MHz, $CDCl_3$): δ 33.8, 38.6 (s), 53.7, 55.2, 61.6, 119.9 (s), 128.0, 128.3, 129.5, 131.5 (s), 138.8 (s), 155.6 (s), 162.9 (s); HRMS (ESI): *m*/*z* calcd for $C_{13}H_{12}ClN_2O_5$ $[M+H]^+$ 311.0429, found 311.0427.

4.4.4. 1H-Cyclopropa[c]quinoline ***17d*** *($R^1 = R^2 = H$, $R^3 = CH_2CH_3$)*

(0.32 g, 70%); mp 108–109 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 1741, 1630; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.29 (3H, t, *J* 7.2), 1.37 (3H, t, *J* 7.2), 3.96 (1H, d, *J* 3.6), 4.09 (1H, d, *J* 3.6), 4.18–4.48 (4H, m), 7.19 (1H, td, *J* 7.2, 1.8), 7.25 (1H, dd, *J* 8.1, 1.5), 7.30–7.35 (1H, m), 7.41 (1H, dd, *J* 7.5, 1.5); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 13.9, 34.4, 39.2 (s), 62.0, 62.6, 63.7, 118.5 (s), 126.2, 127.0, 128.1, 129.3, 140.3 (s), 155.0 (s), 162.7 (s); HRMS (ESI): *m*/*z* calcd for $C_{15}H_{17}N_2O_5$ $[M+H]^+$ 305.1132, found 305.1141.

4.4.5. 1H-Cyclopropa[c]quinoline ***17e*** *($R^1 = CH_3$, $R^2 = H$, $R^3 = CH_2CH_3$)*

(0.38 g, 80%); mp 101–102 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 1743, 1636; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (3H, t, *J* 7.2), 1.39 (3H, t, *J* 7.2), 2.38 (3H, s), 3.93 (1H, d, *J* 3.6), 4.09 (1H, d, *J* 3.6), 4.20–4.48 (4H, m), 7.09 (1H, t, *J* 7.2), 7.19–7.22 (1H, m), 7.24–7.26 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 13.9, 17.4, 34.9, 39.3 (s), 62.0, 62.6, 63.6, 118.2 (s), 125.5, 125.7, 130.6, 135.3 (s), 138.3 (s), 153.8 (s), 162.8 (s); HRMS (ESI): *m*/*z* calcd for $C_{16}H_{19}N_2O_5$ $[M+H]^+$ 319.1288, found 319.1290.

4.4.6. 1H-Cyclopropa[c]quinoline ***17f*** *($R^1 = H$, $R^2 = Cl$, $R^3 = CH_2CH_3$)*

(0.50 g, 99%); mp 135–136 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 1747, 1628; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (3H, t, *J* 7.2), 1.36 (3H, t, *J* 7.2), 3.95 (1H, d, *J* 3.6), 4.04 (1H, d, *J* 3.6), 4.19–4.45 (4H, m), 7.17 (1H, d, *J* 8.4), 7.28 (1H, dd, *J* 8.4, 2.4), 7.41 (1H, d, *J* 2.4); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 13.9, 33.7, 38.9 (s), 61.7, 62.8, 64.0, 119.9 (s), 128.0, 128.2, 129.4, 131.2 (s), 139.0 (s), 155.3 (s), 162.4 (s); HRMS (ESI): *m*/*z* calcd for $C_{15}H_{16}ClN_2O_5$ $[M+H]^+$ 339.0742, found 339.0738.

4.5. General procedure for the preparation of the 2H-cyclopropa[c]quinolin-2-ones ***18***

The corresponding 1*H*-cyclopropa[*c*]quinoline **17** (0.6 mmol) was dissolved in 12 mL of a mixture of TFA:H_2O:THF (1:1:12.5), and the solution was stirred at room temperature during 3 h. Then, the reaction mixture was neutralized by dropwise addition of 5% $NaHCO_3$ (15 mL) and extracted with ethyl acetate (3 × 25 mL). The combined organic phase was washed with water (100 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the resulting material was purified by column chromatography on silica gel, using hexanes/ethyl acetate (3:2, v/v) as eluent.

4.5.1. 2H-Cyclopropa[c]quinolin-2-one ***18a*** *($R^1 = R^2 = H$, $R^3 = CH_3$)*

(0.15 g, 95%); mp 176–177 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3215, 1744, 1692; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.71 (3H, s), 4.21 (1H, d, *J* 3.6), 5.34 (1H, d, *J* 3.6), 6.95 (1H, d, *J* 8.0), 7.05 (1H, t, *J* 7.2), 7.27 (1H, t, *J* 7.2), 7.59 (1H, d, *J* 7.2), 10.92 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 32.8, 41.4 (s), 53.3, 62.6, 115.0 (s), 115.7, 123.0, 129.0, 129.2, 135.8 (s), 159.2 (s), 163.5 (s); HRMS (ESI): *m*/*z* calcd for $C_{12}H_{10}N_2NaO_5$ $[M+Na]^+$ 285.0482, found 285.0474.

4.5.2. 2H-Cyclopropa[c]quinolin-2-one ***18b*** *($R^1 = CH_3$, $R^2 = H$, $R^3 = CH_3$)*

(0.15 g, 90%); mp 228 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3209, 1744, 1682; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.22 (3H, s), 3.71 (3H, s), 4.20 (1H, d, *J* 3.6), 5.33 (1H, d, *J* 3.6), 6.97 (1H, t, *J* 7.6), 7.13 (1H, d, *J* 7.6), 7.45 (1H, d, *J* 6.8), 9.98 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 17.3, 33.1, 41.6 (s), 53.2, 62.5, 115.0 (s), 122.7, 124.0 (s), 127.0, 130.8, 133.8 (s), 159.9 (s), 163.4 (s); HRMS (ESI): *m*/*z* calcd for $C_{13}H_{12}N_2NaO_5$ $[M+Na]^+$ 299.0638, found 299.0639.

4.5.3. 2H-Cyclopropa[c]quinolin-2-one ***18c*** *($R^1 = H$, $R^2 = Cl$, $R^3 = CH_3$)*

(0.17 g, 95%); mp 214–216 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3193, 1748, 1682; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.71 (3H, s), 4.24 (1H, d, *J* 3.6), 5.38 (1H, d, *J* 3.6), 6.93 (1H, d, *J* 8.8), 7.33 (1H, dd, *J* 8.8, 2.4), 7.71 (1H, d, *J* 2.4), 11.03 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 32.2, 41.2 (s), 53.3, 62.4, 116.9 (s), 117.2, 126.6 (s), 128.8, 128.9, 134.8 (s), 159.1 (s), 163.2 (s); HRMS (ESI): *m*/*z* calcd for $C_{12}H_9ClN_2NaO_5$ $[M+Na]^+$ 319.0092, found 319.0088.

4.5.4. 2H-Cyclopropa[c]quinolin-2-one ***18d*** *($R^1 = R^2 = H$, $R^3 = CH_2CH_3$)*

(0.15 g, 91%); mp 156 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3197, 1736, 1682; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.18 (3H, t, *J* 7.2), 4.16 (2H, q, *J* 7.2), 4.19 (1H, d, *J* 3.6), 5.34 (1H, d, *J* 3.6), 6.94 (1H, d, *J* 8.0), 7.05 (1H, td, *J* 7.6, 0.8), 7.27 (1H, td, *J* 7.6, 1.2), 7.60 (1H, d, *J* 6.8), 10.91 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.7, 32.7, 41.5 (s), 62.1, 62.6, 115.0 (s), 115.6, 123.0, 129.0, 129.2, 135.8 (s), 159.3 (s), 162.9 (s); HRMS (ESI): *m*/*z* calcd for $C_{13}H_{12}N_2NaO_5$ $[M+Na]^+$ 299.0638, found 299.0647.

4.5.5. 2H-Cyclopropa[c]quinolin-2-one ***18e*** *($R^1 = CH_3$, $R^2 = H$, $R^3 = CH_2CH_3$)*

(0.16 g, 91%); mp 213–215 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3218, 1736, 1678; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.17 (3H, t, *J* 7.2), 2.23 (3H, s), 4.18 (2H, q, *J* 7.2), 4.20 (1H, d, *J* 3.6), 5.32 (1H, d, *J* 3.6), 6.95 (1H, t, *J* 7.6), 7.12 (1H, d, *J* 6.8), 7.45 (1H, d, *J* 6.8), 9.98 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.7, 17.4, 33.0, 41.7 (s), 62.2, 62.6, 115.1 (s), 122.7, 124.0 (s), 127.0, 130.8 (s), 160.0 (s), 162.9 (s); HRMS (ESI): *m*/*z* calcd for $C_{14}H_{14}N_2NaO_5$ $[M+Na]^+$ 313.0795, found 313.0799.

4.5.6. 2H-Cyclopropa[c]quinolin-2-one ***18f*** *($R^1 = H$, $R^2 = Cl$, $R^3 = CH_2CH_3$)*

(0.18 g, 97%); mp 210–212 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3197, 1740, 1687; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.17 (3H, t, *J* 7.2), 4.16 (2H, q, *J* 7.2), 4.22 (1H, d, *J* 3.6), 6.93 (1H, d, *J* 8.8), 5.36 (1H, d, *J* 3.6), 7.33 (1H, dd, *J* 8.8, 2.4), 7.71 (1H, d, *J* 2.8), 11.00 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.6,

32.0, 41.2 (s), 62.2, 62.4, 116.9 (s), 117.2, 126.5 (s), 128.8, 134.8 (s), 159.2 (s), 162.6 (s); HRMS (ESI): *m/z* calcd for $C_{13}H_{11}ClN_2NaO_5$ $[M+Na]^+$ 333.0249, found 333.0251.

4.6. General procedure for the preparation of the 1-benzazepin-2-ones **19**

To a solution of the cyclopropa[*c*]quinolin-2-one **18** (0.2 mmol) in anhydrous THF (10 mL), under nitrogen at 0 °C, sodium hydride [0.005 g (0.008 g 60% mineral oil), 0.2 mmol] was added. After stirring during 3 h the reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (15 mL), and extracted with ethyl acetate (3 × 15 mL). The combined organic phase was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure. The resulting solid was precipitated with diethyl ether (5 mL), filtered and dried.

4.6.1. 1-Benzazepin-2-one **19a** ($R^1 = R^2 = H$, $R^3 = CH_3$)

(0.039 g, 75%); mp 212 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3210, 1755, 1690; ^1H NMR (400 MHz, DMSO-d_6): δ 3.35 (3H, s), 5.52 (1H, t, *J* 1.6), 7.21 (1H, d, *J* 8.0), 7.25 (1H, td, *J* 7.2, 1.2), 7.53 (1H, td, *J* 8.4, 1.6), 7.71 (1H, dd, *J* 8.0, 1.2), 8.57 (1H, d, *J* 2.0), 11.06 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.5, 53.1, 121.6, 121.7 (s), 124.3, 132.6, 132.9, 135.0, 136.5 (s), 140.4 (s), 165.0 (s), 165.2 (s); HRMS (ESI): *m/z* calcd for $C_{12}H_{10}N_2NaO_5$ $[M+Na]^+$ 285.0482, found 285.0470.

4.6.2. 1-Benzazepin-2-one **19b** ($R^1 = CH_3$, $R^2 = H$, $R^3 = CH_3$)

(0.052 g, 95%); mp 218–219 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3210, 1752, 1680; ^1H NMR (400 MHz, DMSO-d_6): δ 2.33 (3H, s), 3.26 (3H, s), 5.49 (1H, s), 7.21 (1H, t, *J* 7.6), 7.42 (1H, d, *J* 7.6), 7.56 (1H, d, *J* 8.0), 8.58 (1H, d, *J* 2.0), 10.24 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 18.3, 51.4, 52.9, 124.5 (s), 125.0, 130.0, 131.4 (s), 133.8, 134.5 (s), 135.0, 141.8 (s), 165.0 (s), 165.5 (s); HRMS (ESI): *m/z* calcd for $C_{13}H_{12}N_2NaO_5$ $[M+Na]^+$ 299.0638, found 299.0645.

4.6.3. 1-Benzazepin-2-one **19c** ($R^1 = H$, $R^2 = Cl$, $R^3 = CH_3$)

(0.047 g, 80%); mp 225 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3197, 1747, 1681; ^1H NMR (400 MHz, DMSO-d_6): δ 3.39 (3H, s), 5.53 (1H, s), 7.22 (1H, d, *J* 8.8), 7.59 (1H, dd, *J* 8.8, 2.4), 7.87 (1H, d, *J* 2.4), 8.55 (1H, d, *J* 2.0), 11.16 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 51.6, 53.2, 123.3 (s), 123.5, 128.1 (s), 131.7, 132.3, 133.7, 135.4 (s), 141.2 (s), 164.7 (s), 165.0 (s); HRMS (ESI): *m/z* calcd for $C_{12}H_9ClN_2NaO_5$ $[M+Na]^+$ 319.0092, found 319.0078.

4.6.4. 1-Benzazepin-2-one **19d** ($R^1 = R^2 = H$, $R^3 = CH_2CH_3$)

(0.050 g, 90%); mp 201–202 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3201, 1734, 1678; ^1H NMR (400 MHz, DMSO-d_6): δ 0.72 (3H, t, *J* 7.2), 3.81–3.83 (2H, m), 5.48 (1H, s), 7.21 (1H, d, *J* 8.4), 7.26 (1H, d, *J* 7.6), 7.52 (1H, t, *J* 8.0), 7.71 (1H, d, *J* 8.0), 8.57 (1H, d, *J* 1.6), 11.04 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.4, 51.6, 61.8, 121.7, 121.9 (s), 124.3, 132.5, 132.8, 135.0, 136.6 (s), 140.7 (S), 164.7 (s), 165.3 (s); HRMS (ESI): *m/z* calcd for $C_{13}H_{12}N_2NaO_5$ $[M+Na]^+$ 299.0638, found 299.0644.

4.6.5. 1-Benzazepin-2-one **19e** ($R^1 = CH_3$, $R^2 = H$, $R^3 = CH_2CH_3$)

(0.053 g, 92%); mp 193–194 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3205, 1757, 1666; ^1H NMR (400 MHz, DMSO-d_6): δ 0.69 (3H, t, *J* 6.8), 2.34 (3H, s), 3.70–3.80 (2H, m), 5.46 (1H, t, *J* 1.6), 7.21 (1H, t, *J* 7.6), 7.42 (1H, d, *J* 7.2), 7.56 (1H, d, *J* 6.8), 8.58 (1H, d, *J* 1.6), 10.22 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.3, 18.3, 51.6, 61.8, 124.5 (s), 124.9, 130.1, 131.4 (s), 133.7, 134.5 (s), 135.0, 141.9 (s), 164.5 (s), 165.6 (s); HRMS (ESI): *m/z* calcd for $C_{14}H_{14}N_2NaO_5$ $[M+Na]^+$ 313.0795, found 313.0796.

4.6.6. 1-Benzazepin-2-one **19f** ($R^1 = H$, $R^2 = Cl$, $R^3 = CH_2CH_3$)

(0.053 g, 85%); mp 220 °C (from Et_2O); ν_{max} (Nujol)/cm^{-1} 3185, 1744, 1684; ^1H NMR (400 MHz, DMSO-d_6): δ 0.78 (3H, t, *J* 7.2), 3.82–3.90 (2H, m), 5.49 (1H, s), 7.23 (1H, d, *J* 8.8), 7.58 (1H, dd, *J* 8.8, 2.4), 7.86 (1H, d, *J* 2.4), 8.54 (1H, d, *J* 2.0), 11.13 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.4, 51.7, 62.0, 123.5 (s), 123.6, 128.1 (s), 131.5, 132.1, 133.6, 135.4 (s), 141.5 (s), 164.4 (s), 165.0 (s); HRMS (ESI): *m/z* calcd for $C_{13}H_{11}ClN_2NaO_5$ $[M+Na]^+$ 333.0249, found 333.0250.

CCDC-1816438 contains the supplementary crystallographic data of this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

5. Declaration of interest

None.

6. Contributors

MA and AV designed, coordinated the experimental part of this research and drafted the manuscript. PSA designed and performed the computational study. JD, DR, FJB and AV carried out the experiments and data analysis. RAO realized the x-ray structural determination. The authors read and approved the final manuscript.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.arabjc.2018.07.002.

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