Synthesis of Chiral C_2-Symmetric 1,10-Phenanthrolines from Naturally Occurring Monoterpenes

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Abstract: A convenient procedure for the preparation of chiral C_2-symmetric 1,10-phenanthrolines bearing a chiral framework in the form of a cycloalkeno-condensed substituent in the 2,3- and 8,9-positions of the heterocycle is reported. Starting from the 2-benzyloxycyclohexanone, four 1,10-phenanthrolines derived from (–)-β-pinene, (+)-α-pinene, (–)-isopinocampheol, and (+)-camphor were prepared according to a method based on a double Michael-aza-annulation-aromatization sequence.

Key words: nitrogen heterocycles, 1,10-phenanthrolines, nitrogen ligands, bidentate ligands, Michael additions

Since the design of chiral ligands plays a key role in the development of enantioselective reactions, many recent studies have addressed the development of novel chiral ligands for metal-catalyzed reactions.[1] In the context of nitrogen based ligands,[2] there has been considerable work involving the synthesis and application of chiral 1,10-phenanthrolines[3] (phens) in asymmetric catalysis. The studies were, however, limited to C_1-symmetric derivatives owing to the difficulties associated with the preparation of the C_2-symmetric counterpart.[3i,m,n] In fact, only one example of this kind of phens has been reported[3i] and used in asymmetric catalysis.[4]

In a recent communication, we have reported a new approach to the synthesis of chiral C_2-symmetric phens describing the preparation of the phen **1** in which the chiral starting material, (–)-β-pinene, is present in the form of a cycloalkeno-condensed substituent in the 2,3- and 8,9-positions of the heterocycle (Figure 1).[5] The preliminary results obtained with the Cu(I)-complex containing ligand **1**, indicate that this kind of phens are good catalysts in asymmetric catalyzed allylic oxidation of cycloalkenes.[5] The outcome of these experiments prompted us to determine the scope and limitations of the synthetic strategy used for the preparation of **1** in order to obtain an array of chiral C_2-symmetric phens.

Herein, we wish to report full experimental details for the synthesis **1** and the results obtained using this protocol for the synthesis of the C_2-symmetric phens **2**–**4** and their 5,6-dihydro derivatives from other monoterpenes, namely (+)-α-pinene, (–)-isopinocampheol and (+)-camphor.

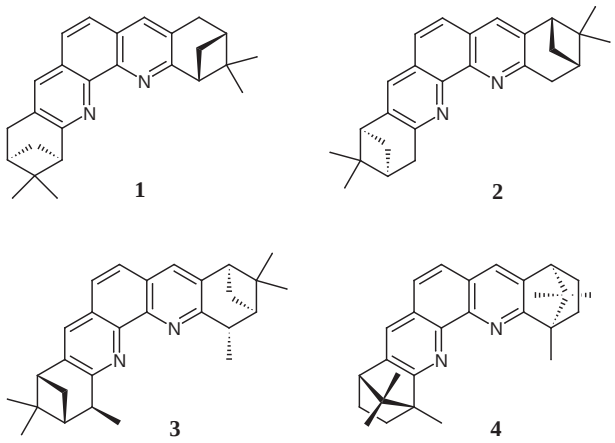

Figure 1 Structures of chiral C_2-symmetric phens **1**–**4**

We envisaged that the most direct approach to phens of type **1**–**4** could be based on the construction of the 5,6-dihydrophen skeleton by a double Michael addition of the dianion of cyclohexane-1,2-dione to an α-methylene ketone, followed by pyridoannulation of the corresponding 1,5-dicarbonyl intermediate, which was not isolated. Thus, cyclohexane-1,2-dione was treated with lithium diisopropylamide (LDA, two equivalents, –40 °C, 2 h) and then with the Michael acceptor (–)-pinocarvone (**8**), obtained from (+)-α-pinene.[6] The crude reaction mixture was then submitted to azaannulation with concomitant aromatization (NH_4OAc, AcOH, reflux, 2 h). However, this procedure afforded an untractable reaction mixture from which it was impossible to isolate the desired 5,6-dihydrophen.

Therefore, we decided to build the two pyridines rings in succession starting from a cyclohexanone derivative bearing a functional group in the α-position that could be easily converted into a carbonyl group after the construction of the first pyridine ring. To this purpose, the 1,4-dithiaspiro[4.5]decan-6-one (**5**)[7] was initially identified as a suitable substrate (Scheme 1). Thus, following the same method outlined above (Michael-azaannulation-aromatization sequence) the pyridine **6** was obtained in moderate yield (38%). However, the conversion of the dithiolane function into carbonyl group was proven to be very problematic. In fact, although many procedures were explored[8] in no case the yield of the desired ketone was >19% (NBS, acetone).[9]

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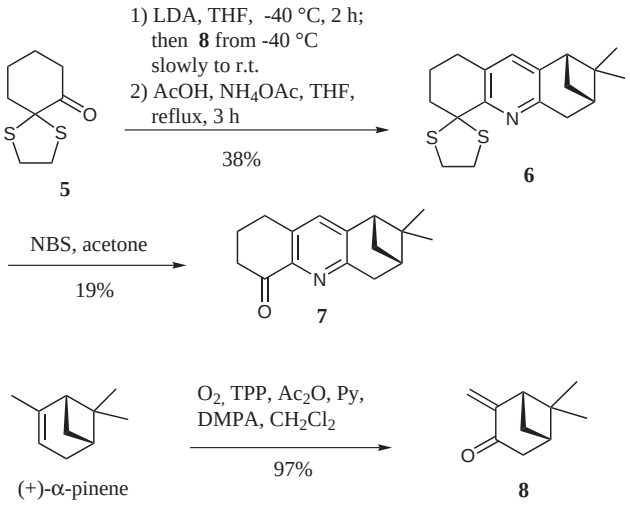
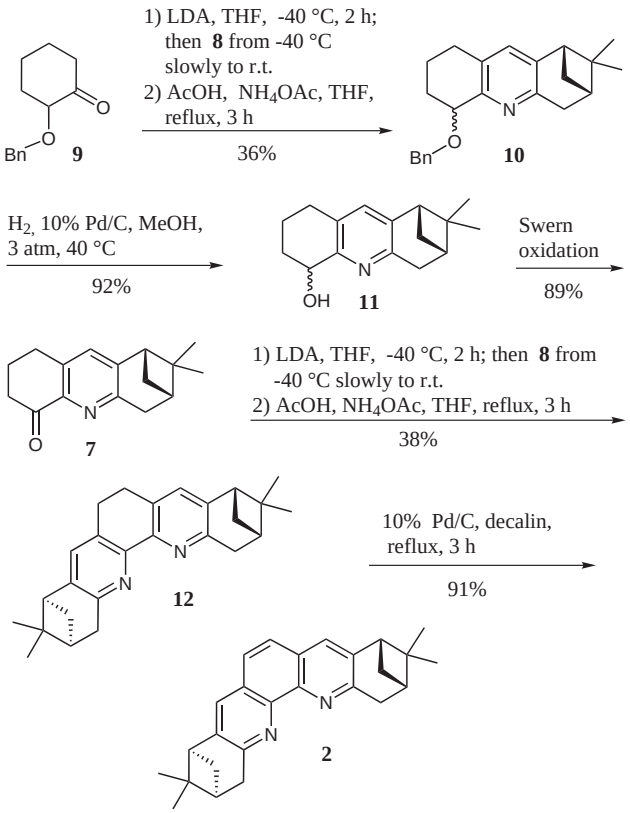


Scheme 1

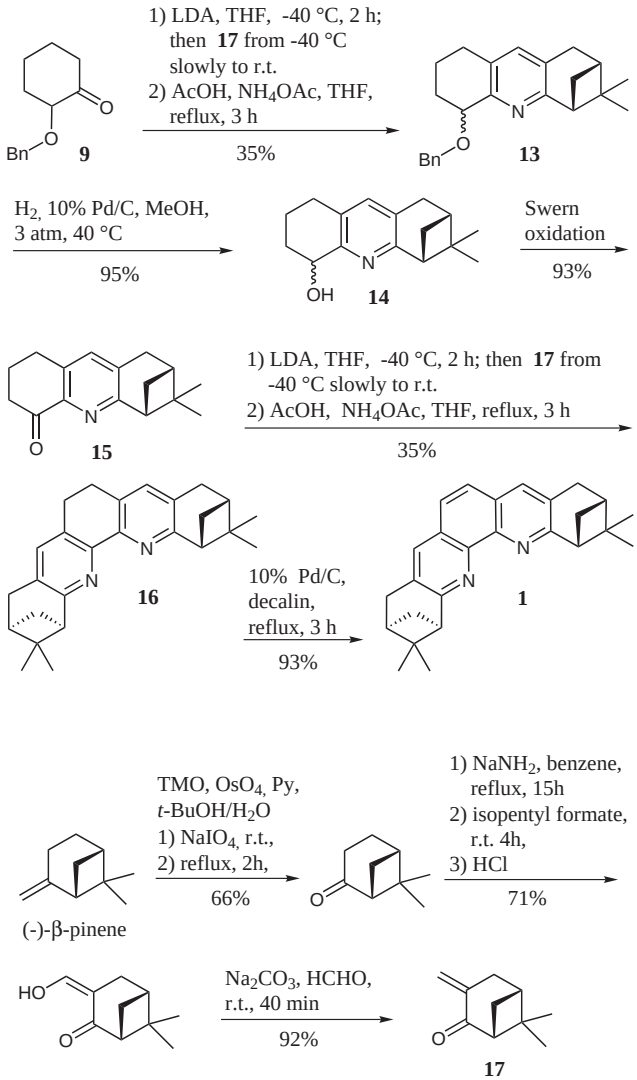
Then, we devoted our attention to racemic 2-benzyloxycyclohexanone (**9**) that is easily prepared from 2-hydroxycyclohexanone dimer[10] (Scheme 2). The lithium enolate of this ketone (LDA, one equivalent, THF, –40 °C, 2 h) was treated with (–)-pinocarvone (**8**) to give a 1,5-dicarbonyl intermediate by conjugate addition, which was not isolated. This intermediate underwent azaanulation-aromatization in the usual way to afford the pyridine **10** as a 52:48 mixture of epimers at C5 (36% overall yield). Catalytic hydrogenolysis (Pd/C at 3 atm) of this mixture of benzyloxy derivatives gave the corresponding mixture of the carbinol **11** (92%) that was oxidized under Swern conditions to ketone **7** (89%). Starting from this key intermediate, the 5,6-dihydrophen **12** was prepared by building up the second pyridine ring in a similar manner to that used to prepare **10** from **9** (38% overall yield). Dehydrogenation by using a catalytic amount of palladium on charcoal in refluxing decalin completes the synthesis of **2** (91%).



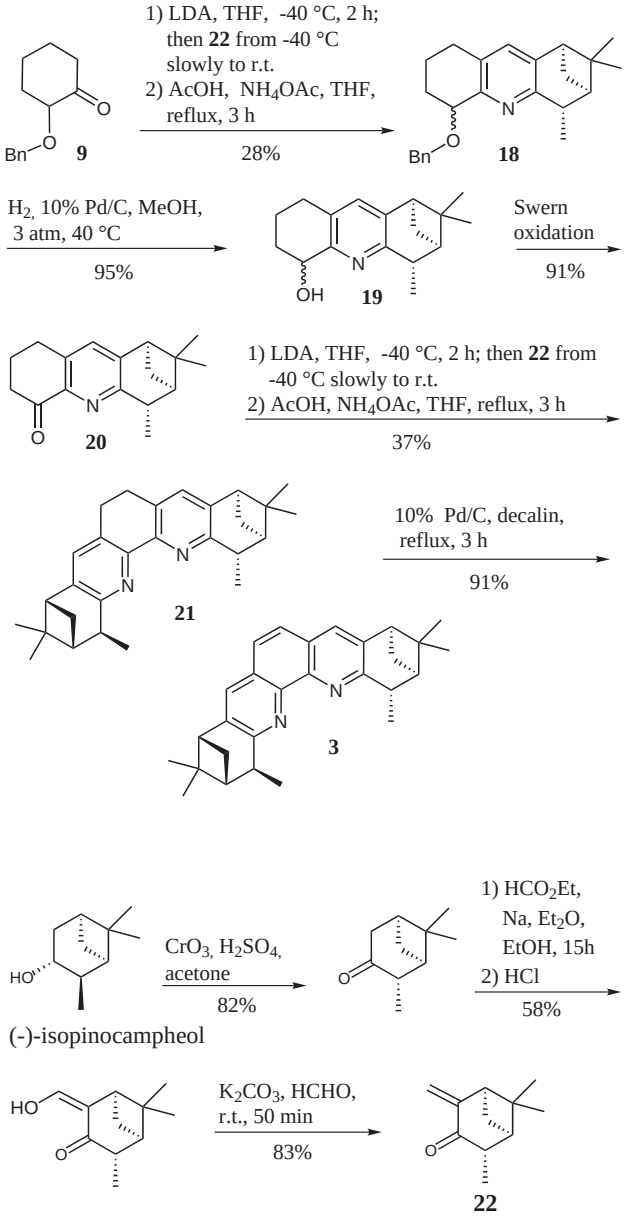
Scheme 2

Having obtained the desired phen **2**, in order to determine the scope and limitations of this protocol, more sterically hindered α-methylene ketones were submitted to this reaction sequence (Schemes 3–5). Thus, the ketones **17**, **22** and **27** obtained from (–)-β-pinene,[11] (–)-isopinocampheol[12] and (+)-camphor,[11] respectively, yielded the benzyloxypyridines **13**, **18** and **23** (35%, 28% and 14% yields, respectively).

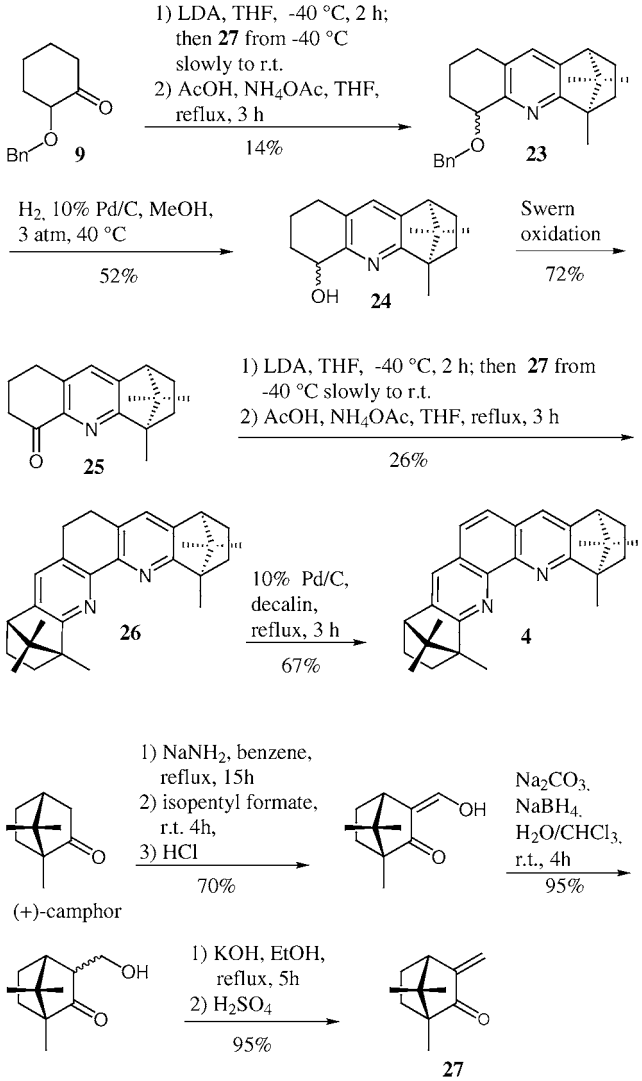
Cleavage of these benzyl ethers afforded the alcohols **14**, **19** and **24** (95%, 95% and 52% yields, respectively) that were transformed into the ketones **15**, **20** and **25** (93%, 91% and 72% yields, respectively). These ketones gave the corresponding dihydrophens **16**, **21** and **26** (35%, 37%



Scheme 3



Scheme 4



Scheme 5

and 26% yields, respectively) that were finally converted into the phens **1**, **3** and **4** (93%, 91% and 67% yields, respectively).

The overall yield of the process was comparable for all phens (10%) with the exception of phen **4**, derived from camphor. This ketone afforded a much lower overall yield (2%) which principally differs from that obtained with the other phens by the two Michael-azaannulation-aromatization steps in that the overall yield of the other three steps, conversion of the protected hydroxy group to ketone and final aromatization, is fairly good. This great difference can be attributed to the steric hindrance of camphor carbonyl group that reduces the ability of this ketone to undergo the azaannulation step.[3a,13]

All reagents and solvents were purchased from Aldrich and used as received. Low boiling petroleum ether was the fraction collected between 40 °C and 60 °C. THF was distilled from sodium-benzophenone ketyl and degassed thoroughly with dry N_2 directly before use.

Melting points were determined on a Büchi 510 capillary apparatus and are uncorrected. The NMR spectra were recorded on a Varian VXR-300 spectrometer at 300 for ^{1}H and 75.4 MHz for ^{13}C. Chemical shifts are reported in ppm downfield from internal Me_4Si in $CDCl_3$. Optical rotations were measured with a Perkin-Elmer 241 polarimeter in a 1 dm tube. Elemental analyses were performed on a Perkin-Elmer 240 B analyser.

(–)-Pinocarvone (**8**) was obtained by oxidation of (+)-α-pinene (98% pure, 91% ee by GC, Aldrich).[6] (1*R*,5*R*)-6,6-Dimethyl-3-methylenebicyclo[3.1.1]heptan-2-one (**17**), (1*R*,4*S*,5*R*)-4,6,6-trimethyl-2-methylenebicyclo[3.1.1] heptan-3-one (**22)** and (1*R*,4*S*)-1,7,7-trimethyl-3-methylenebicyclo[2.2.1] heptan-2-one (**27**) were prepared from (–)-β-pinene (99% pure, Aldrich),[11] (–)-isopinocampheol (98% pure, 95% ee by GC, Aldrich),[12] and (+)-camphor (98% pure, Aldrich),[11] respectively. 1,4-Dithiaspiro[4.5]decan-6-one (**5**)[7] and 2-benzyloxycyclohexanone (**9**)[10] were prepared according to reported procedures.

(6*S*,8*S*)-(+)-6,8-Methano-7,7-dimethyl-4-(1,4-dithiaspiro-cyclopentane)-2,3,5,6,7,8-hexahydro-1*H*-acridine (6)

A solution of 1,4-dithiaspiro[4.5]decan-6-one (**5**; 1.13 g, 6.0 mmol) in anhyd THF (5 mL) was added dropwise to a cooled (–78 °C) solution of LDA (6.0 mmol) in anhyd THF (30 mL). The resulting solution was stirred at –40 °C for 2 h and then a solution of (–)-pinocarvone (**8**; 901 mg, 6.00 mmol) in THF (5 mL) was added dropwise at –40 °C. After 15 min at –40 °C, the solution was allowed to reach slowly r.t. (overnight) and then poured into a mixture of NH_4OAc (9.24 g, 0.12 mol) and AcOH (30 mL). The flask was connected with a distillation head and the THF was distilled off over a 3 h period. Most part of the AcOH was removed under reduced pressure and the residue was taken up with H_2O (0.5 L) and extracted with Et_2O (3 × 100 mL). The combined organic phases were washed with a 5% NaOH solution (2 × 100 mL) and then dried (Na_2SO_4). The solvent was evaporated and the residue was purified by flash chromatography (petroleum ether–EtOAc, 8:2); yield: 725 mg (38%); mp 125 °C; $[\alpha]_D^{25}$ +40.0 (*c* = 3.12, $CHCl_3$).

^{1}H NMR: δ = 6.78 (s, 1 H), 3.90–3.78 (m, 2 H), 3.52–3.40 (m, 2 H), 3.06 (d, 2 H, *J* = 2.7 Hz), 2.76–2.65 (m, 4 H), 2.54–2.44 (m, 2 H), 2.38–2.28 (m, 1 H), 2.04–1.94 (m, 2 H), 1.37 (s, 3 H), 1.25 (d, 1 H, *J* = 9.3 Hz), 0.64 (s, 3 H).

Anal. Calcd for $C_{18}H_{23}NS_2$: C, 68.09; H, 7.30; N, 4.41. Found: C, 68.23; H, 7.33; N, 4.43.

(6*S*,8*S*)-(+)-6,8-Methano-7,7-dimethyl-2,3,5,6,7,8-hexahydro-1*H*-acridin-4-one (7)

A solution of **6** (2.68 g, 8.45 mmol) in acetone (30 mL) was added dropwise to a cooled (0 °C) solution of NBS (12.00 g, 67.42 mmol) in 90% aq acetone (100 mL). After stirring at r.t. for 20 min, the mixture was basified with a 4 N aq solution of NaOH (100 mL) and then treated with a sat. solution of Na_2SO_3 (100 mL). The mixture was extracted with Et_2O (3 × 100 mL) and the organic phase was washed with H_2O (2 × 100 mL) and then dried (Na_2SO_4). The solvent was evaporated and the residue was purified by flash chromatography (petroleum ether–EtOAc, 1:1); yield: 0.39 g (19%); mp 112–114 °C; $[\alpha]_D^{25}$ +63.8 (*c* = 1.24, $CHCl_3$).

^{1}H NMR: δ = 7.14 (s, 1 H), 3.21 (d, 2 H, *J* = 2.4 Hz), 2.95 (t, 2 H, *J* = 5.7 Hz), 2.86–2.64 (m, 4 H), 2.43–2.34 (m, 1 H), 2.20–2.10 (m, 2 H), 1.42 (s, 3 H), 1.26 (d, 1 H, *J* = 9.6 Hz), 0.65 (s, 3 H).

Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.88; H, 7.97; N, 5.83.

4-Benzyloxy-1,2,3,4,5,6,7,8-octahydroacridines 10, 13, 18, 23; General Procedure

A solution of 2-benzyloxycyclohexanone (**9**) (2.04 g, 10.00 mmol) in anhyd THF (5 mL) was added dropwise to a cooled (–78 °C) solution of lithium diisopropylamide (10.00 mmol) in anhyd THF (50 mL). The resulting solution was stirred at –40 °C for 2 h and then a solution of the α-methylene ketone **8** (or **17**, **22**, **27**) (10.00 mmol) in THF (5 mL) was added dropwise at –40 °C. After 15 min at –40 °C, the solution was allowed to reach slowly r.t. (overnight) and then poured into a mixture of NH_4OAc (7.71 g, 0.10 mol) and AcOH (50 mL). The flask was connected with a distillation head and the THF was distilled off over a 3 h period. Most of the AcOH was removed under reduced pressure and the residue was taken up with H_2O (500 mL) and extracted with Et_2O (3 × 150 mL). The organic phase was separated, washed with a 5% aq NaOH solution (3 × 50 mL) and then dried (Na_2SO_4). The solvent was evaporated and the residue was purified by flash chromatography (petroleum ether–EtOAc, 9:1) to give 4-benzyloxyoctahydroacridines as a mixture of diastereomers.

(4*R*,6*S*,8*S*)- and (4*S*,6*S*,8*S*)-4-Benzyloxy-6,8-methano-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroacridine (10)

Compound **10** was obtained as a 52:48 mixture of epimers at C4; yield: 1.20 g (36%); oil.

^{1}H NMR: δ = 7.44–7.36 (m, 2 H), 7.36–7.18 (m, 3 H), 6.94 (s, 1 H, major isomer), 6.92 (s, 1 H, minor isomer), 4.82 (AB, J_{AB} = 12.0 Hz, 2 H), 4.59–4.55 (m, 1 H), 3.10 (d, 2 H, *J* = 2.4 Hz), 2.84–2.58 (m, 4 H), 2.38–2.22 (m, 2 H), 2.18–2.02 (m, 1 H), 1.86–1.66 (m, 2 H), 1.38 (s, 3 H), 1.24 (d, 1 H, *J* = 9.3 Hz), 0.65 (s, 3 H, minor isomer), 0.63 (s, 3 H, major isomer),

Anal. Calcd for $C_{23}H_{27}NO$: C, 82.84; H, 8.16; N, 4.20. Found: C, 82.66; H, 8.15; N, 4.18.

(4*R*,5*R*,7*R*)- and (4*S*,5*R*,7*R*)-4-Benzyloxy-5,7-methano-6,6-dimethyl-1,2,3,4,5,6,7,8-octahydroacridine (13)

Compound **13** was obtained as a 55:45 mixture of epimers at C4; yield: 1.12 g (35%); oil.

^{1}H NMR: δ = 7.43–7.34 (m, 2 H), 7.32–7.20 (m, 3 H), 7.16 (s, 1 H, minor isomer), 7.14 (s, 1 H, major isomer), 4.80 (AB, J_{AB} = 12.0 Hz, 2 H), 4.55–4.53 (m, 1 H), 3.03–2.99 (m, 1 H), 2.89 (d, 2 H, *J* = 3.0 Hz), 2.79–2.62 (m, 3 H), 2.30–2.22 (m, 2 H), 2.15–2.02 (m, 1 H), 1.85–1.73 (m, 2 H), 1.42 (s, 3 H, minor isomer), 1.40 (s, 3 H, major isomer), 1.28–1.24 (m, 1 H), 0.66 (s, 3 H, major isomer), 0.65 (s, 3 H, minor isomer).

Anal. Calcd for $C_{23}H_{27}NO$: C, 82.84; H, 8.16; N, 4.20. Found: C, 82.93; H, 8.15; N, 4.19.

(4*R*,5*S*,6*R*,8*R*)- and (4*S*,5*S*,6*R*,8*R*)-4-Benzyloxy-6,8-methano-5,7,7-trimethyl-1,2,3,4,5,6,7,8-octahydroacridine (18)

Compound **18** was obtained as a 55:45 mixture of epimers at C4; yield: 0.96 g (28%); oil.

^{1}H NMR: δ = 7.55–7.40 (m, 2 H), 7.40–7.20 (m, 3 H), 6.91 (s, 1 H, minor isomer), 6.88 (s, 1 H, major isomer), 4.87 (s, 2 H, major isomer), 4.86 (s, 2 H, minor isomer), 4.54–4.48 (m, 1 H), 3.30–3.10 (m, 1 H), 2.81–2.57 (m, 3 H), 2.55–2.48 (m, 1 H), 2.29–1.98 (m, 3 H), 1.95–1.54 (m, 2 H), 1.48–1.35 (m, 6 H), 1.29 (d, 1 H, *J* = 10.5 Hz), 0.66 (s, 3 H, minor isomer), 0.65 (s, 3 H, major isomer).

Anal. Calcd for $C_{24}H_{29}NO$: C, 82.95; H, 8.41; N, 4.03. Found: C, 82.83; H, 8.46; N, 4.05.

(4*R*,5*R*,8*S*)- and (4*S*,5*R*,8*S*)-4-Benzyloxy-5,8-methano-5,9,9-trimethyl-1,2,3,4,5,6,7,8-octahydroacridine (23)

This compound was purified by flash chromatography using petroleum ether–EtOAc, 97:3. Yield: 0.48 g (14%); oil.

^{1}H NMR: δ = 7.43 (d, 2 H, *J* = 9.0 Hz), 7.33–7.23 (m, 3 H), 7.20 (s, 1 H), 4.84 (AB, J_{AB} = 13.8 Hz, 2 H), 4.60–4.52(m, 1 H), 2.80–2.62 (m, 3 H), 2.30–2.22 (m, 2 H), 2.12–2.05 (m, 1 H), 1.85–1.60 (m, 3 H), 1.42 (s, 3 H), 1.26–1.05 (m, 2 H), 0.97 (s, 3 H), 0.67 (s, 3 H).

Anal. Calcd for $C_{24}H_{29}NO$: C, 82.95; H, 8.41; N, 4.03. Found: C, 82.77; H, 8.45; N, 4.05.

1,2,3,4,5,6,7,8-Octahydroacridin-4-ols 11, 14, 19, 24; General Procedure

A mixture of benzyloxyoctahydroacridine **10** (or **13**, **18**, **23**) (10.00 mmol) and 10% Pd/C (0.80 g) in 95% EtOH (50 mL) was hydrogenated at 40 °C and 3 atm in a Parr apparatus. H_2 absorption ceased after the uptake of one equivalent. The mixture was filtered, the filtrate was evaporated at reduced pressure and the residue was purified by flash chromatography (petroleum ether–EtOAc, 9:1) to give 4-hydrooxyoctahydroacridines as a mixture of diastereomers.

(4*R*,6*S*,8*S*)- and (4*S*,6*S*,8*S*)-6,8-Methano-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroacridin-4-ol (11)

Compound **11** was obtained as a 53:47 mixture of epimers at C4; yield: 2.23 g (92%); oil.

^{1}H NMR: δ = 6.93 (s, 1 H), 4.77–4.68 (m, 1 H), 4.43 (br s, 1 H, exchangeable with H_2O), 3.03 (s, 2 H), 2.78–2.58 (m, 4 H), 2.38–2.28 (m, 1 H), 2.24–2.14 (m, 1 H), 2.04–1.92 (m, 1 H), 1.92–1.70 (m, 2

H), 1.38 (s, 3 H), 1.24 (d, 1 H, *J* = 9.3 Hz), 0.64 (s, 3 H, major isomer), 0.62 (s, 3 H, minor isomer).

Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.88; H, 8.72; N, 5.75.

(4*R*,5*R*,7*R*)- and (4*S*,5*R*,7*R*)-5,7-Methano-6,6-dimethyl-1,2,3,4,5,6,7,8-octahydroacridine-4-ol (14)
Compound **14** was obtained as a 60:40 mixture of epimers at C4; yield: 2.28 g (95%); oil.

^{1}H NMR: δ = 7.14 (s, 1 H), 4.72–4.63 (m, 1 H), 3.95 (br s, 1 H, exchangeable with H_2O), 2.94 (t, 1 H, *J* = 5.7 Hz), 2.89 (d, 2 H, *J* = 1.8 Hz), 2.74–2.65 (m, 3 H), 2.33–2.20 (m, 2 H), 2.03–1.92 (m, 1 H), 1.84–1.75 (m, 2 H), 1.41 (m, 3 H), 1.25 (d, 1 H, *J* = 10.5 Hz), 0.66 (s, 3 H, major isomer), 0.64 (s, 3 H, minor isomer).

Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.77; H, 8.69; N, 5.74.

(4*R*,5*S*,6*R*,8*R*)- and (4*S*,5*S*,6*R*,8*R*)-6,8-Methano-5,7,7-trimethyl-1,2,3,4,5,6,7,8-octahydroacridin-4-ol (19)
Compound **19** was obtained as a 1:1 mixture of epimers at C4; yield: 2.57 g (95%); mp 78–80 °C.

^{1}H NMR: δ = 7.12 (s, 1 H), 4.90–4.86 (m, 1 H), 4.88 (br s, 1 H, exchangeable with H_2O), 3.31–3.25 (m, 1 H), 2.79–2.45 (m, 4 H), 2.40–2.07 (m, 2 H), 2.07–1.60 (m, 3 H), 1.48 (d, 3 H, *J* = 1.8 Hz, one isomer), 1.46 (d, 3 H, *J* = 2.1 Hz, one isomer), 1.42 (m, 3 H), 1.29 (d, 1 H, *J* = 10.5 Hz), 0.64 (s, 3 H, one isomer), 0.63 (s, 3 H, one isomer).

Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44. Found: C, 79.15; H, 9.03; N, 5.47.

(4*R*,5*S*,8*R*)- and (4*S*,5*S*,8*R*)-5,8-Methano-5,9,9-trimethyl-1,2,3,4,5,6,7,8-octahydroacridin-4-ol (24)
Compound **24** was obtained as a 52:48 mixture of epimers at C4; yield: 1.32 (52%); oil.

^{1}H NMR: δ = 7.06 (s, 1 H), 4.74–4.67 (m, 1 H), 4.41 (br s, 1 H, exchangeable with H_2O), 2.79–2.64 (m, 3 H), 2.28–2.17 (m, 1 H), 2.12–2.05 (m, 1 H), 2.02–1.92 (m, 1 H), 1.88–1.70 (m, 3 H), 1.28 (s, 3 H, major isomer), 1.27 (s, 3 H, minor isomer), 1.23–1.04 (m, 2 H), 0.97 (s, 3 H), 0.54 (s, 3 H, major isomer), 0.53 (s, 3 H, minor isomer).

Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44. Found: C, 79.23; H, 9.02; N, 5.46.

2,3,5,6,7,8-Hexahydro-1*H*-acridin-4-ones 7, 15, 20, 25; General Procedure
A solution of DMSO (820 mg, 10.50 mmol) in anhyd CH_2Cl_2 (3 mL) was added dropwise to a cooled (–60 °C) solution of oxalyl chloride (672 mg, 5.30 mmol) in CH_2Cl_2 (13 mL). After stirring for 5 min, a solution of 4-hydroxyoctahydroacridine **11** (or **14**, **19**, **24**) (4.00 mmol) in CH_2Cl_2 (5 mL) was added. The cloudy mixture was stirred at –60 °C for 50 min and Et_3N (2.02 g, 20.00 mmol) was added dropwise. The resulting mixture was warmed to r.t. and stirred for 1 h. The mixture was poured into H_2O (50 mL) and extracted with CH_2Cl_2 (2 × 100 mL). The organic phase was dried (Na_2SO_4), the solvent was evaporated and the residue was purified by flash chromatography (petroleum ether–EtOAc, 1:1).

(6*S*,8*S*)-(+)-6,8-Methano-7,7-dimethyl-2,3,5,6,7,8-hexahydro-1*H*-acridin-4-one (7)
This compound was purified by flash chromatography using petroleum ether–EtOAc, 8:2, yield: 2.23 g (89%); mp 113–114 °C; $[\alpha]_D^{25}$ +64.4 (*c* = 1.32, $CHCl_3$). For spectral data, *vide supra*.

(5*R*,7*R*)-(–)- 5,7-Methano-6,6-dimethyl-2,3,5,6,7,8-hexahydro-1*H*-acridin-4-one (15)
Yield: 2.32 g (93%); mp 113–116 °C; $[\alpha]_D^{25}$ –11.3 (*c* = 1.65, $CHCl_3$).

^{1}H NMR: δ = 7.39 (s, 1 H), 3.24 (t, 1 H, *J* = 5.4 Hz), 3.02–2.94 (m, 4 H), 2.80–2.70 (m, 3 H), 2.36–2.28 (m, 1 H), 2.22–2.12 (m, 2 H), 1.41 (s, 3 H), 1.25 (d, 1 H, *J* = 10.2 Hz), 0.65 (s, 3 H).

Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.55; H, 7.93; N, 5.82.

(5*S*,6*R*,8*R*)-(–)-6,8-Methano- 5,7,7-trimethyl-2,3,5,6,7,8-hexahydro-1*H*-acridin-4-one (20)
Yield: 2.42 g (91%); mp 162–164 °C; $[\alpha]_D^{25}$ –0.6 (*c* = 1.08, $CHCl_3$).

^{1}H NMR: δ = 7.10 (s, 1 H), 3.35–3.28 (m, 1 H), 2.96–2.91 (m, 2 H), 2.82–2.73 (m, 3 H), 2.61–2.54 (m, 1 H), 2.19–2.11 (m, 3 H), 1.42 (s, 6 H), 1.30 (d, 1 H, *J* = 9.9 Hz), 0.64 (s, 3 H).

Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 79.85; H, 8.34; N, 5.47.

(5*R*,8*S*)-(–)-5,8-Methano-5,11,11-trimethyl-2,3,5,6,7,8-hexahydro-1*H*-acridin-4-one (25)
Yield: 1.89 g (72%); mp 176–177 °C; $[\alpha]_D^{25}$ –1.4 (*c* = 1.12, $CHCl_3$).

^{1}H NMR: δ = 7.26 (s, 1 H), 2.96 (t, 2 H, *J* = 6.3 Hz), 2.88 (d, 1 H, *J* = 4.2 Hz), 2.77–2.72 (m, 2 H), 2.19–2.11 (m, 3 H), 1.93–1.84 (m, 1 H), 1.41 (s, 3 H), 1.33–1.24 (m, 1 H), 1.17–1.09 (m, 1 H), 1.00 (s, 3 H), 0.54 (s, 3 H).

Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 79.79; H, 8.27; N, 5.51.

Dihydrophenanthrolines 12, 16, 21, 26; General Procedure
Starting from the 4-oxooctahydroacridine **7** (or **15**, **20**, **25**) (5.00 mmol), the procedure used for the preparation of 4-benzyloxyoctahydroacridines was followed. The crude mixture was purified by flash chromatography (petroleum ether–EtOAc, 8:2).

(2*S*,4*S*, 9*S*,11*S*)-(+)-2,4,9,11-Dimethano-3,3,10,10-tetramethyl-1,2,3,4,6,7,9,10,11,12-decahydrodibenzo[*b*,*j*][1,10]phenanthroline (12)
Yield: 0.70 g (38%); mp 62–64 °C; $[\alpha]_D^{25}$ +153.6 (*c* = 1.25, $CHCl_3$).

^{1}H NMR: δ = 7.05 (s, 2 H), 3.30 (m, 4 H), 2.92–2.84 (m, 4 H), 2.75 (t, 2 H, *J* = 5.7 Hz), 2.70–2.62 (m, 2 H), 2.42–2.33 (m, 2 H), 1.40 (s, 6 H), 1.27 (d, 2 H, *J* = 9.3 Hz), 0.69 (s, 6 H).

Anal. Calcd for $C_{26}H_{30}N_2$: C, 84.28; H, 8.16; N, 7.59. Found: C, 84.38; H, 8.15; N, 7.61.

(1*R*,3*R*,10*R*,12*R*)-(+)-1,3,10,12-Dimethano-2,2,11,11-tetramethyl-1,2,3,4,6,7,9,10,11,12-decahydrodibenzo-[*b*,*j*][1,10]phenanthroline (16)
Yield: 0.64 g (35%); mp 118–120 °C; $[\alpha]_D^{25}$ +111.5 (*c* = 1.04, $CHCl_3$).

^{1}H NMR: δ = 7.26 (s, 2 H), 3.29 (t, 2 H, *J* = 5.7 Hz), 3.00–279 (m, 8 H), 2.69 (m, 2 H), 2.29 (m, 2 H), 1.40 (s, 6 H), 1.30 (d, 2 H, *J* = 9.6 Hz), 0.69 (s, 6 H).

Anal. Calcd for $C_{26}H_{30}N_2$: C, 84.28; H, 8.16; N, 7.59. Found: C, 84.15; H, 8.14; N, 7.61.

(1*S*,2*S*,4*S*,9*S*,11*S*,12*S*)-(+)-2,4,9,11-Dimethano-1,3,3,10,10,12-hexamethyl-1,2,3,4,6,7,9,10,11,12-decahydrodibenzo-[*b*,*j*][1,10]phenanthroline (21)
Yield: 0.94 g (37%); mp 238–240 °C; $[\alpha]_D^{25}$ +111.3 (*c* = 1.12, $CHCl_3$).

^{1}H NMR: δ = 7.02 (s, 2 H), 3.32–3.25 (m, 2 H), 2.93–2.73 (m, 6 H), 2.58–2.51 (m, 2 H), 2.18–2.13 (m, 2 H), 1.57 (d, 6 H, *J* = 6.9 Hz), 1.41 (s, 6 H), 1.31 (d, 2 H, *J* = 9.6 Hz), 0.67 (s, 6 H).

Anal. Calcd for $C_{28}H_{34}N_2$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.25; H, 8.63; N, 7.04.

(1*R*,4*S*, 9*S*,12*R*)-(–)-1,4,9,12-Dimethano-1,12,13,13,14,14-hexamethyl-1,2,3,4,6,7,9,10,11,12-decahydrodibenzo-[*b*,*j*][1,10]phenanthroline (26)
Yield: 0.51 g (26%); mp 229–231; $[\alpha]_D^{25}$ –54.4 (*c* = 0.86, $CHCl_3$).

^{1}H NMR: δ = 7.21 (s, 2 H), 2.92–2.80 (m, 6 H), 2.17–2.07 (m, 2 H), 1.93 (dt, 2 H, *J* = 12.8, 3.8 Hz), 1.47 (s, 6 H), 1.47–1.40 (m, 2 H), 1.14–1.06 (m, 2 H), 1.00 (s, 6 H), 0.61 (s, 6 H).

Anal. Calcd for $C_{28}H_{34}N_2$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.18; H, 8.58; N, 7.05.

Phenanthrolines 1–4; General Procedure
A suspension of 10% Pd/C (100 mg) in decahydronaphtalene (10 mL) containing dihydrophenanthroline **12** (or **16**, **21**, **26**) (1.00 mmol) was refluxed for 3 h. After cooling, the suspension was filtered, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (petroleum ether–EtOAc, 8:2).

(1*R*,3*R*, 10*R*,12*R*)-(+)-1,3,10,12-Dimethano-2,2,11,11-tetramethyl-1,2,3,4,9,10,11,12-octahydrodibenzo[*b*,*j*][1,10]phenanthroline (1)
Yield: 344 mg (93%); mp 104–106 °C; $[\alpha]_D^{25}$ +68.2 (*c* = 1.13, $CHCl_3$).

^{1}H NMR: δ = 7.91 (s, 2 H), 7.63 (s, 2 H), 3.58 (t, 2 H, *J* = 5.7 Hz), 3.17 (m, 4 H), 2.80 (m, 2 H), 2.28 (m, 2 H), 1.46 (s, 6 H), 1.42 (d, 2 H, *J* = 9.9 Hz), 0.71 (s, 6 H).

^{13}C NMR: δ = 167.2, 142.9, 134.2, 130.3, 127.4, 124.9, 51.4, 39.8, 39.2, 31.4, 31.0, 26.1, 21.5.

Anal. Calcd for $C_{26}H_{28}N_2$: C, 84.74; H, 7.66; N, 7.60. Found: C, 84.55; H, 7.64; N, 7.58.

(2*S*,4*S*, 9*S*,11*S*)-(+)-2,4,9,11-Dimethano-3,3,10,10-tetramethyl-1,2,3,4,6,7,9,10,11,12-decahydrodibenzo[*b*,*j*][1,10]phenanthroline (2)
Yield: 336 mg (91%); mp 101–103 °C; $[\alpha]_D^{25}$ +117.1 (*c* = 0.74, $CHCl_3$).

^{1}H NMR: δ = 7.67 (s, 2 H), 7.63 (s, 2 H), 3.58–3.56 (m, 4 H), 3.50–3.46 (m, 2 H), 3.00 (t, 2 H, *J* = 5.7 Hz), 2.81–2.74 (m, 2 H), 2.52–2.42 (m, 2 H), 1.46 (s, 6 H), 1.37 (d, 2 H, *J* = 9.6 Hz), 0.84 (s, 6 H).

^{13}C NMR: δ = 158.8, 144.1, 141.3, 131.3, 126.3, 125.3, 46.9, 40.2, 39.7, 37.3, 32.1, 26.0, 21.5.

Anal. Calcd for $C_{26}H_{28}N_2$: C, 84.74; H, 7.66; N, 7.60. Found: C, 84.58; H, 7.68; N, 7.57.

(1*S*,2*S*,4*S*,9*S*,11*S*,12*S*)-(–)-2,4,9,11-Dimethano-1,3,3,10,10,12-hexamethyl-1,2,3,4,9,10,11,12-octahydrodibenzo-[*b*,*j*][1,10]phenanthroline (3)
This compound was purified by chromatography on neutral Al_2O_3 (petroleum ether–EtOAc, 95:5); yield: 345 mg (91%); mp 186–188 °C; $[\alpha]_D^{25}$ –6.7 (*c* = 0.63, $CHCl_3$).

^{1}H NMR: δ = 7.64 (s, 2 H), 7.62 (s, 2 H), 3.49 (ddd, 2 H, *J* = 6.9, 5.1, 1.8 Hz), 2.99 (t, 2 H, *J* = 5.7 Hz), 2.68 (m, 2 H), 2.26 (dt, 2 H, *J* = 5.7, 2.1 Hz), 1.73 (d, 6 H, *J* = 6.9 Hz), 1.46 (s, 6 H), 1.40 (d, 2 H, *J* = 9.9 Hz), 0.67 (s, 6 H).

^{13}C NMR: δ = 162.2, 144.3, 141.2, 130.9, 126.6, 125.4, 47.6, 47.0, 41.4, 39.8, 29.3, 26.5, 21.3, 18.5.

Anal. Calcd for $C_{28}H_{32}N_2$: C, 84.80; H, 8.13; N, 7.06. Found: C, 84.89; H, 8.11; N, 7.05.

(1*R*,4*S*, 9*S*,12*R*)-(–)-1,4,9,12-Dimethano-1,12,13,13,14,14-hexamethyl-1,2,3,4,9,10,11,12-octahydrodibenzo[*b*,*j*][1,10]-phenanthroline (4)
Yield: 266 mg (67%); mp 253–255 °C; $[\alpha]_D^{25}$ –72.8 (*c* = 0.85, $CHCl_3$).

^{1}H NMR: δ = 7.80 (s, 2 H), 7.66 (s, 2 H), 3.02 (d, 2 H, *J* = 3.9 Hz), 2.58–2.15 (m, 2 H), 1.95 (dt, 2 H, *J* = 12.6, 3.9 Hz), 1.62 (s, 6 H), 1.62–1.53 (m, 2 H), 1.25–1.17 (m, 2 H), 1.08 (s, 6 H), 0.59 (s, 6 H).

^{13}C NMR: δ = 171.2, 144.1, 140.9, 127.4, 126.7, 125.3, 56.2, 54.8, 51.3, 31.8, 26.3, 20.6, 19.2, 10.7.

Anal. Calcd for $C_{28}H_{32}N_2$: C, 84.80; H, 8.13; N, 7.06. Found: C, 84.76; H, 8.12; N, 7.15.

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