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Enantioselective syntheses of coronaridine and 18-methoxycoronaridine

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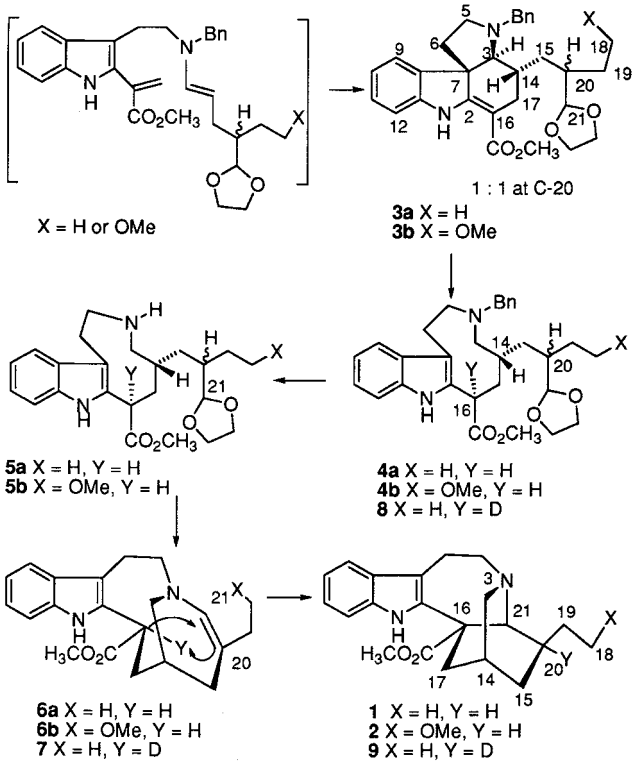
Abstract—Condensation of indoloazepines bearing the chiral N^b-substituents: 1-(*R*)-naphthyl-α-ethyl, [1-(*R*)-[(*S*)-2-(diphenylphospheno)-ferrocenyl]-ethyl], or 2,3-(*R*)-ferroceno-6,6-dimethyl-1-(*S*)-cyclohexyl, with 4-(1,3-dioxolan-2-yl)-hexanal, or with 4-(1,3-dioxolan-2-yl)-6-methoxyhexanal, gave diastereoselectively, through a secodine-type intramolecular Diels–Alder reaction, tetracyclic intermediates that could be carried to (−)-coronaridine or to the important anti-addictive (−)-18-methoxycoronaridine. The 2,3-(*R*)-ferroceno-6,6-dimethyl-1-(*S*)-cyclohexyl chiral auxiliary was most effective, providing >99% ee of a tetracyclic intermediate after removal of the chiral auxiliary group.

With the syntheses of racemic coronaridine (**1**),[1] and 18-methoxycoronaridine (**2**),[2] and especially because of the great potential of the latter as an anti-addictive agent,[3] enantioselective syntheses of coronaridine and its congeners became important. While a rather arduous resolution of racemic 18-methoxycoronaridine (**2**) has provided the enantiomers,[4] continuing studies of the suppression of demand for morphine, cocaine, nicotine, methamphetamine and alcohol by 18-methoxycoronaridine in conditioned rats,[3] and studies of its mechanism of action, with a search for corresponding drug receptors and binding proteins, call for an enantioselective version of the original synthesis.

Our synthesis of racemic coronaridine (**1**) was based on the generation of a D-*seco*-ψ-vincadifformine intermediate **3a** by an intramolecular, secodine-type, Diels–Alder reaction (Scheme 1). Reductive cleavage of this tetracyclic intermediate's central C-3 to C-7 bond (**4a**), N^b-debenzylation and hydrolysis of the tricyclic aminoacetal **5a**, with cyclization of a transient C-21 aminoaldehyde, provided an enamine **6a**. This tetracyclic enamine **6a** then underwent a remarkable, spontaneous, quantitative rearrangement to coronaridine (**1**).[1]

The rearrangement, which occurred slowly at room temperature (120 h), under vacuum, was first assumed to be initiated by acid catalysis, that could have been fortuitously introduced on isolation of the enamine **6a**. However, a subsequent study of the rearrangement revealed that it is not promoted by acid (or by base), but that it is accelerated by heating in toluene, suggesting that the rearrangement occurs by a stereospecific intramolecular hydrogen transfer from the C-16 methoxycarbonyl substituted carbon to the C-20 enamine terminus, with concomitant formation of a C-21 to C-16 bond.



Scheme 1.

Keywords: enantioselective syntheses; coronaridine; 18-methoxycoronaridine.

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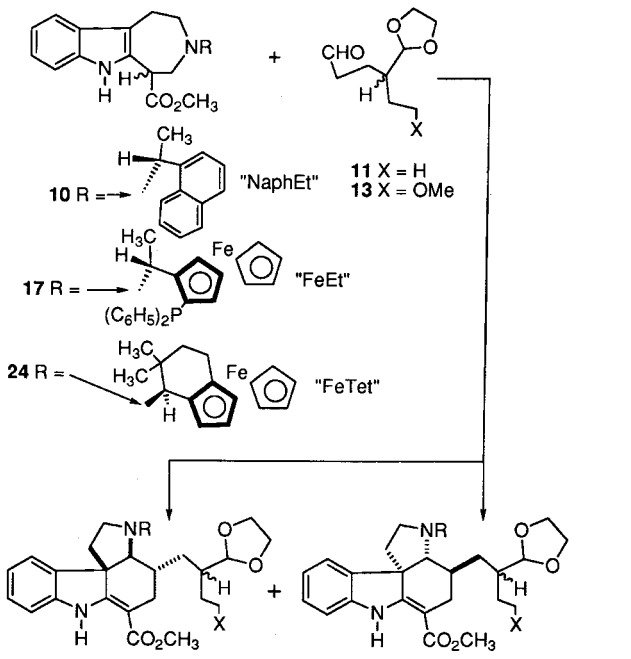


12a,b R = "NaphEt", X = H 89 : 11 **12c,d** R = "NaphEt", X = H

14a,b R = "NaphEt", X = OCH_3 89 : 11 **14c,d** R = "NaphEt", X = OCH_3

18a,b R = "FeEt", X = OCH_3 estimate 87 : 13 **18c,d** R = "FeEt", X = OCH_3

21a,b R = "FeEt", X =H prep.yld. 84 : 16 **21c,d** R = "FeEt", X =H

25a,b R = "FeTet", X = OCH_3 >99 : 1 **25c,d** R = "FeTet", X = OCH_3 not detected

Scheme 2.

To substantiate this mechanism, the C-16 deuterated enamine **7** was prepared by reductive cleavage of the tetracyclic amine **3a** with sodium borohydride in deuterioacetic acid, followed by debenzylation of the resulting tricyclic amine **8**, and hydrolysis of its acetal function. On heating the enamine **7** in toluene, C-20 deuterated coronaridine (**9**) was formed in 67% overall yield from its tricyclic acetal precursor **8**.

Spectroscopic data for intermediates **7** and **8** in the deuterated series mirrored those of the undeuterated compounds, except for the absence of the ^{1}H NMR C-16 hydrogen doublet of doublets in the cleavamines **4a** and **5a**. The ^{1}H NMR spectrum of the C-20 deuterated coronaridine (**9**) matched the spectrum of coronaridine (**1**), except for the absence of the C-20 hydrogen signal. A transfer of deuterium from C-16 to C-20 was also supported by a corresponding lack of splitting of the C-19 methylene hydrogen signals (δ 1.45, 1.55) by CH-20 and of the C-15 hydrogen signals (α:δ 1.73, β:δ 1.14) by a C-20 hydrogen, and by the lack of coupling of the C-21 hydrogen (δ 3.54). Signal assignments were substantiated by a 2D cosy spectrum. Also, the mass spectra of all deuterated compounds gave major ion fragments with one more atomic mass unit than their normal H counterparts.

For an extension of this synthesis of racemic coronaridine (**1**) to an enantioselective synthesis, it should be noted that the chirality established in the tetracyclic intermediate **3a** at C-3, C-7, and C-20 is lost in the enamine intermediate **6a** and needs to be preserved only at C-14, with the coronaridine (**1**) product chirality at C-16, C-20, and C-21 then arising from the now established intramolecular hydrogen transfer on rearrangement of the enamine **6a**.

We had found that for enantioselective syntheses of intermediates of type **3**, a chiral N^b-α-naphthylethyl substituent provided a 4:1 ratio of diastereomeric products in our vinblastine synthesis.[5] Subsequently, a chiral α-ferrocenylethyl N^b-substituent gave complete selectivity (>99% de) in this condensation reaction.[6] However, with other aldehyde precursors of the secodine-type intermediate, the selectivity was less favorable, resulting mostly in a 6:1 ratio of diastereomers (syntheses of vincadifformine, ψ-vincadifformine, ibophyllidine),[7] but dropping to a 1.2:1 ratio with acetoxyacetaldehyde (mossambine synthesis).[7] With our new chiral *N*-auxiliary for alkylation, (+)-(*R*)-1,2-(α-(*R*)-hydroxy-β-dimethyltetramethylene)-ferrocene,[8] the last synthesis could be raised to >99% de of intermediates and >99% ee of final product.

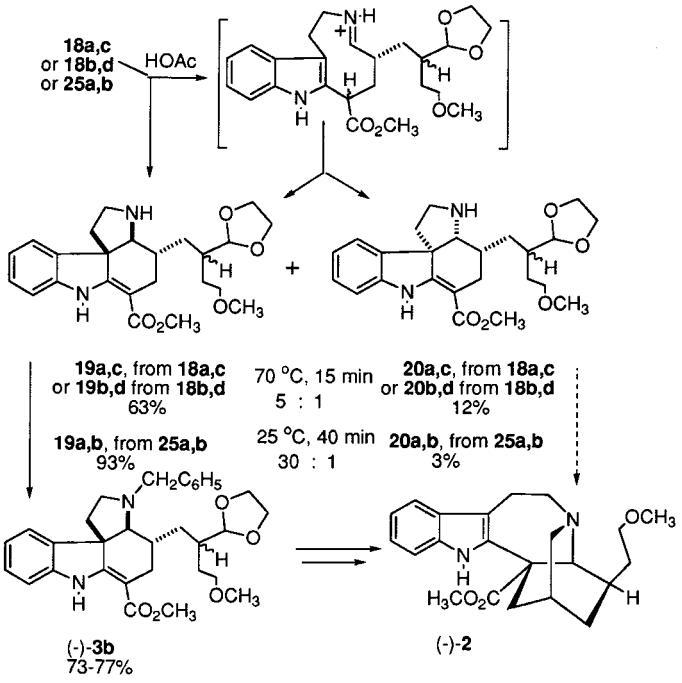
It was thus of interest to compare these chiral auxiliaries in the syntheses of coronaridine (**1**) and 18-methoxycoronaridine (**2**). Initially, our synthesis of coronaridine by condensation of the indoloazepines **10** bearing an α-naphthylethyl N^b-substituent with 4-(1,3-dioxalan-2-yl)-hexanal (**11**), through two C-20 epimeric tetracyclic intermediates **12a**,**b** (Scheme 2) seemed to result in complete selectivity, with formation of (−)-coronaridine ((−)-**1**) in >99% ee, as established by NMR Eu(hfc)$_3$ chiral shift studies of the indolic NH signals, using a comparison with the corresponding racemic coronaridine.[9]

However, later examination of the tetracyclic C-20 epimeric products **12** by NMR, focusing on the acetal hydrogen signal, and a chiral column HPLC analysis, indicated an 89:11 diastereomeric ratio within the C-20 epimeric intermediate products **12a**,**c** and **12b**,**d**.

Completion of the coronaridine synthesis with the chromatographically purified combined major diastereomers **12a** and **b**, through the N^b-naphthylethyl analogue of **4a** (**15a**,**b**) and intermediates (−)-**5a**, (−)-**6a** (Scheme 1), gave (−)-coronaridine ((−)-**1**) in >99% ee, while use of the initial crude mixture of isomers **12a**–**d** resulted in (−)-coronaridine ((−)-**1**) in 75% ee.

A synthesis of (−)-18-methoxycoronaridine ((−)-**2**) with the same indoloazepines **10** and 4-(1,3-dioxalan-2-yl)-6-methoxyhexanal (**13**) also gave an 89:11 ratio of diastereomeric tetracyclic intermediates **14a**,**b** and **14c**,**d** as determined by integration of the respective acetal hydrogen NMR signals. Here, chromatographic retentions of the major and minor diastereomers (**14a** vs. **14c** and **14b** vs. **14d**) were too close for separation to allow removal of the minor isomers.

The subsequent reductive ring cleavage of the tetracycles **14a**–**d**, with generation of the *N*-naphthylethyl analogue of **4b** (**16a**–**d**), and intermediates (−)-**5b**, and (−)-**6b**, provided (−)-18-methoxycoronaridine ((−)-**2**) in 74–76%



Scheme 3.

ee, as determined by NMR Eu(hfc)$_3$ chiral shift of the indolic NH signals, and by HPLC on a Chiralcel OD column. Separation of the major enantiomer (−)-18-methoxycoronaridine ((−)-**2**) could then be obtained by fractional crystallization of the racemic component of the mixture.

Condensation of the indoloazepines **17** bearing a chiral N^b-α-ferrocenylethyl substituent with 4-(1,3-dioxalan-2-yl)-6-methoxyhexanal (**13**) provided, 1:1, two separable, C-20 epimeric, series of diastereomers **18a**,**c** and **18b**,**d**. In contrast to the **12a**,**c** and **12b**,**d** or **14a**,**c** and **14b**,**d** series of compounds, their composition could not be determined by NMR analysis of the acetal H signal because of three ferrocenyl H signals obscuring the minor **18c**,**d** acetal doublets. While the two C-20 epimeric series (1:1) were chromatographically separated, the diastereomers **18a**,**c** and **18b**,**d** could not be separated. Each of these diastereomeric mixtures was subjected to cleavage of the ferrocenyl substituent with acetic acid at 70°C to provide the secondary amines **19a**,**c** and **19b**,**d.** in 63% yield (Scheme 3).

In addition, the C-3, C-7 epimeric products **20a**,**b** (containing minor isomers **20c**,**d**) were formed in 12% yield and separated by chromatography. We had previously observed an acid-catalyzed epimerization at C-3 and C-7 in analogous tetracyclic secondary amines,[6] and thus ascribe corresponding structures to the minor products **20a**,**b**. While these minor products were separated, it should be noted that their retention in the subsequent reactions would not affect the enantiomeric purity of the final product (−)-18-methoxycoronaridine ((−)-**2**).

N^b-benzylation of the major secondary amine products **19a**,**c** or **19b**,**d** provided enantiomerically enriched tertiary amines corresponding to our previous racemic intermediate **3b**. Following the steps of the racemic synthesis,[2] the enantiomerically enriched intermediates could be carried to (−)-18-methoxycoronaridine ((−)-**2**), which was obtained in 65% ee. On this basis, an 87:13 ratio of tetracyclic Diels–Alder products **18a**,**b** to **18c**,**d** was estimated, and found to correspond to previous results in analogous reactions.[7]

Starting from the ferrocenylethyl substituted indoloazepine **17**, a synthesis of (−)-coronaridine ((−)-**1**) could also be completed. Here, the tetracyclic intermediates **21a–d** could be chromatographically separated, resulting in a preparative 84:16 ratio of the major diastereomers **21a** and **21b** (1:1) to minor diastereomers **21c** and **21d**. Cleavage of the chiral auxiliary substituent from the major diastereomers **21a**,**b** with hot acetic acid provided the secondary amines (**22a**,**b** corresponding to **19a**,**b**) and some C-3, C-7 epimerization (**23a**,**b** corresponding to **20a**,**b**). Benzylation of the major secondary amine products **22a**,**b** then furnished the C-20 epimeric tetracyclic intermediates (−)-**3a**, which were then taken to (−)-coronaridine ((−)-**1**) by the sequence used in the synthesis of the racemic compound.

A satisfactory enantioselective synthesis of the key tetracyclic precursors (−)-**3b** of (−)-18-methoxycoronaridine ((−)-**2**) was finally obtained by condensation of 4-(1,3-dioxalan-2-yl)-6-methoxyhexanal (**13**) with the indoloazepines **24** bearing an N^b-(*R*)-1,2-(α-(*R*)-β-dimethyltetramethylene)-ferrocene substituent.[8] Only one (C-20-epimeric) product **25a**,**b** was detected by HPLC on a Chiralcel OD column. The chromatographically inseparable C-20 epimers were converted to the corresponding secondary amines **19a**,**b** by treatment with acetic acid at room temperature.

Under these relatively milder auxiliary group cleavage conditions (in contrast to those required above), less C-3,

C-7 epimerization was observed and two pairs of diastereomeric products **19a**,**b** and **20a**,**b** were formed in a 93:3 ratio, and separated by chromatography.

Benzylation of the major product pair **19a**,**b** provided the tetracyclic tertiary amines (−)-**3b**, which were compared with the corresponding racemate **3b**.[2] HPLC on a Chiralcel OD column showed baseline separation of enantiomers in the racemate and >99% ee for the product (−)-**3b**.

Completion of the synthesis of (−)-18-methoxycoronaridine from the enantiomerically pure intermediates (−)-**3b** could then follow the reaction steps described for the corresponding racemate.[2]

1. Experimental

1.1. Data for compounds

1.1.1. C-16 Deuterated cleavamines (8). A solution of 0.59 g (1.2 mmol) of the racemic *N*-benzyl tetracycles **3a** (0.59 g, 1.2 mmol) in CH_3CO_2D (25 mL) was heated at 90°C, and sodium borohydride (0.5 g, 13 mmol) was added over 5 min. The mixture was poured into ice, basified with concentrated ammonium hydroxide, extracted with dichloromethane, dried over magnesium sulfate and concentrated. Flash chromatography, eluting with 1:1 ether/hexane, afforded 0.443 g (75%) of the title product as a white foam. TLC R_f=0.48, 0.45 (1:1 ether/hexane, CAS green); UV (EtOH) λ_{max} 228, 284, 292 nm; IR (thin film) ν_{max} 3382, 2878, 2928, 1726, 1461, 1454, 1246, 1109, 954, 740 cm^{-1}; 270 MHz ^{1}H NMR ($CDCl_3$) δ 0.86 (t, *J*=7.5 Hz, 3H), 1.16–1.32 (m, 4H), 1.44 (m, 2H), 1.52–1.63 (m, 2H), 1.77–2.09 (m, 2H), 2.26 (brm, 3H), 2.62–2.85 (m, 3H), 3.33 (m, 1H), 3.67–3.92 (m, 7H, includes s, 3.74), 4.72 (d, *J*=4 Hz, 1H), 7.02–7.49 (m, 9H), 8.60 (s, 1H); 67.9 MHz ^{13}C NMR ($CDCl_3$) δ 11.3, 22.5, 26.2, 34.8, 35.8, 39.5, 40.0, 52.1, 52.1, 52.7, 60.5, 61.1, 64.7, 64.8, 64.9, 106.7, 110.7, 111.7, 118.1, 119.0, 121.6, 126.7, 127.9, 128.2, 128.6, 128.7, 134.1, 136.0, 140.5, 175.3; EIMS *m*/*z* (relative intensity) 492 (M^+, 24), 491 (61), 335 (27), 275 (22), 274 (85), 262 (17), 261 (28), 216 (45), 205 (16), 204 (18), 203 (54), 202 (15), 170 (16), 160 (16), 157 (16), 134 (26), 133 (44), 132 (22), 121 (16), 91 (100), 73 (31). HRMS, FAB^+ Calcd for $C_{30}H_{38}N_2O_4D$ (M^++H): 492.2972; Found: 492.2962.

1.1.2. C-20 Deuterated coronaridine (9). A solution of the C-16-D-aminoacetal **8** (0.123 g, 0.25 mmol) and 10% Pd/C (0.05 g) in acetic acid (5 mL) was subjected to hydrogenation at atmospheric pressure for 3 h. Filtration through a Celite plug was followed by basification with ammonium hydroxide, extraction with dichloromethane, drying over magnesium sulfate, and concentration. The crude secondary amine was immediately taken up in 1N HCl (15 mL) and the reaction mixture stirred until all starting material was consumed (TLC). The mixture was cooled to 0°C, basified with 10% ammonium hydroxide in saturated brine, and extracted with dichloromethane (3×25 mL). Concentration of the dried ($MgSO_4$) extracts under vacuum gave an oil (enamine **7**) that was taken up in dry toluene (20 mL), and heated to reflux for 48 h. Flash chromatography, eluting with 1:1 ether/hexane, gave 0.57 g (67%) of C-20-D-coronaridine (**9**). TLC (SiO_2, 1:1 ether/hexane) R_f=0.49 (CAS green). UV (EtOH) λ_{max} 216, 275, 284 nm; 500 MHz ^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J*=7.0 Hz, 3H), 1.14 (brd, *J*=12.5 Hz, 1H), 1.41–1.49 (m, 2H), 1.73 (brd, *J*=12.5 Hz, 1H), 1.89 (brd, 1H), 3.17–3.25 (m, 1H), 2.81 (d, 1H), 2.89–2.94 (m, 1H), 2.98–3.07 (m, 1H), 3.17–3.25 (m, 1H), 3.36–3.42 (m, 1H), 3.55 (s, 1H), 3.71 (s, 3H), 7.08 (t, *J*=7.5 Hz, 1H), 7.15 (t, *J*=8.0 Hz, 1H), 7.24–7.27 (m, 1H), 7.47 (d, *J*=7.5 Hz, 1H), 7.76 (brs, 1H); 67.9 MHz ^{13}C NMR ($CDCl_3$) δ 11.6, 22.2, 26.7, 26.8, 27.5, 32.0, 36.6, 51.7, 52.5, 53.2, 55.1, 57.4; 110.3, 118.5, 119.3, 122.0, 128.9, 129.7, 135.5, 136.7, 176.0; EIMS *m*/*z* (relative intensity) 340 (M^+, 25), 339 (70), 338 (20), 214 (26), 209 (19), 195 (13), 170 (15), 169 (15), 168 (17), 167 (19), 154 (32), 149 (22), 137 (25), 136 (100), 135 (34), 130 (20), 125 (48), 122 (25), 111 (15), 97 (25), 95 (15), 86 (31), 85 (19), 84 (47), 83 (20), 71 (26), 69 (25), 57 (42). HRMS, FAB^+ Calcd for $C_{21}H_{25}N_2O_2D$ (M^+): 340.2135. Found: 340.2121.

1.1.3. (3a*S*,4*R*,11b*R*)-Methyl 3-[1(*R*)-(1-naphthyl)-ethyl]-2,3,3a,4,5,7-hexahydro-4-[2-ξ-(1,3-dioxolan-2-yl)-1-butyl]-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylates (12a,b), minor diastereomers (12c,d) and enantiomers. A solution of 1.813 g (4.50 mmol) of methyl 3-[1(*R*)-(1-naphthyl)ethyl]-1,2,3,4,5,6-hexahydroazepino [4,5-*b*] indole-5-ξ-carboxylates (**10**,[5] 1.813 g, 4.50 mmol) and 4-(1,3-dioxolan-2-yl) hexanal (**11**,[1] 1.096 g, 7.30 mmol) were heated at reflux for 48 h in 40 mL of toluene, using a Dean–Stark water separator filled with 4 Å molecule sieves. Concentration under vacuum and chromatography, eluting with 3:2 ether/hexane, afforded 2.02 g of the condensation products as a yellow foam (80%). TLC showed two major products with R_f=0.36 and 0.19 (SiO_2, 3:2 ether/hexane, CAS blue), and two minor products with slightly greater and lower polarities than the main components. ^{1}H NMR spectra of the less polar fraction showed acetal hydrogen signals at δ 4.73 and 4.35 in a ratio of 92:7 and for the more polar fraction acetal signals at δ 4.65 and 4.49 in a ratio of 89:11. HPLC on a Chiralcel OD column, using 5% isopropanol in hexane at a flow rate of 0.9 mL min^{-1} for the more polar fraction, showed an 88:11 ratio of components with retention times of 10.5 and 14.9 min, respectively. Repeated column chromatography eliminated the minor acetal signals. For the less polar diastereomer **12a**: UV (EtOH) λ_{max} 222, 282, 292, 334 nm; IR (thin film) ν_{max} 3372, 2955, 2929, 2870, 1670, 1605, 1455, 1429, 1273, 1240, 1194, 1103, 797, 771, 738 cm^{-1}; 500 MHz ^{1}H NMR ($CDCl_3$) δ 9.01 (s, 1H), 8.65 (brs, 1H), 7.87 (d, *J*=8.0 Hz, 1H), 7.79 (d, *J*=8.2 Hz, 1H), 7.70 (d, *J*=6.9 Hz, 1H), 7.51 (m, 4H), 7.11 (t, *J*=8.5 Hz, 1H), 6.77 (d, *J*=7.4 Hz, 2H), 4.74 (d, *J*=3.6 Hz, 1H), [4.36 (d, *J*=3.3 Hz, 0.076H), minor C-3a,4,11b-epi diastereomer], 3.92 (d, *J*=5.9 Hz, 1H), 3.90–3,75 (m, 3H), 3.75 (s, 3H), 2.99 (s, 1H), 2.93 (m, 1H), 2.81 (d, *J*=12.5 Hz, 1H), 2.75 (m, 1H), 2.53 (d, *J*=12.6 Hz, 1H), 2.41 (m, 1H), 2.09 (m, 1H), 1.72 (d, *J*=6.8 Hz, 3H), 1.59 (m, 2H), 1.48 (m, 1H), 1.28 (m, 1H), 1.12–0.79 (m, 4H), 0.71 (t, *J*=7.5 Hz, 3H); 67.9 MHz ^{13}C NMR ($CDCl_3$) δ 169.2, 165.1, 143.0, 140.1, 138.1, 134.2, 131.7, 129.6, 128.8, 127.6, 127.5, 125.6, 125.4, 125.1, 124.2, 122.5, 120.5, 109.0, 106.8, 90.1, 71.6, 65.0, 64.6, 55.8, 50.7, 49.8, 41.1, 40.1, 38.7, 30.2, 27.8, 22.9, 22.2, 21.3, 11.7; EIMS *m*/*z* (relative intensity) 552 (M^+, 6), 397

(6), 339 (6), 338 (26), 241 (17), 184 (12), 167 (5), 156 (14), 155 (100), 154 (9), 153 (7), 149 (6), 127 (8), 73 (12). HRMS, FAB$^+$ Calcd for $C_{35}H_{41}N_2O_4$ (M^++1): 553.3066; Found: 553.3087.

For the more polar diastereomer **12b**: UV (EtOH) λ_{max} 223, 283, 292, 332 nm; IR (KBr) ν_{max} 3354 (m), 3293 (m), 2923 (s), 2869 (s) 1730 (s), 1669 (s), 1599 (s), 1453 (s), 1369 (m), 1284 (s), 1230 (s), 1192 (m), 1099 (m), 1038 (m), 938 (s), 799 (s), 768 (s), 730 (m), 560 (m) cm^{-1}; 500 MHz ^{1}H NMR ($CDCl_3$) δ 8.97 (s, 1H), 8.60 (brs, 1H), 7.87 (d, J=8.3 Hz, 1H), 7.78 (d, J=7.7 Hz, 1H), 7.71 (d, J=6.5 Hz, 1H), 7.50 (m, 4H), 7.11 (m, 1H), [6.95 (brm, 1H)], 6.79 (m, 2H), 4.75 (brm, 1H), 4.65 (d, J=4.1 Hz, 1H), [4.49 (d, J=4.2 Hz, 0.12H), minor C-3a,4,11b-epi diastereomer], 3.85–3.70 (m, 3H), 3.82 (s, 3H), 3.09 (s, 1H), 2.93 (m, 1H), 2.79 (m, 2H), 2.55 (m, 1H), 2.24 (m, 1H), 2.13 (m, 1H), 1.75 (d, J=6.9 Hz, 3H), 1.70–1.55 (m, 3H), 1.40 (m, 2H), 1.32 (m, 1H), 1.21 (m. 1H), 0.94 (t, J=12.5 Hz, 3H), 0.81 (m, 1H), [0.59 (t, J=12.5 Hz, 0.10H), minor C-3a,4,11b-epi diastereomer]. 67.9 MHz ^{13}C NMR ($CDCl_3$) δ 169.1, 164.8, 143.1, 140.5, 138.0, 134.1, 131.5, 128.8, 127.7, 127.5, 125.7, 125.5, 125.4, 125.1, 124.0, 122.5, 120.4, 109.1, 106.7, 90.1, 71.1, 64.8, 64.7, 55.9, 50.6, 40.0, 39.5, 38.5, 29.3, 22.3, 21.5, 21.3, 15.3, 11.4; ElMS: *m/z* (relative intensity) 552 (M^+, 1), 397 (1), 355 (1), 339 (1), 338 (5), 283 (1), 241 (6), 210 (15), 184 (9), 155 (100), 127 (9), 91 (25), 73 (8). HRMS, FAB$^+$ Calcd for $C_{35}H_{41}N_2O_4$ (M^++1): 553.3066; Found: 553.3063.

Starting from methyl 3-[1(*S*)-(1-naphthyl)ethyl]-1,2,3,4,5,6-hexahydroazepino [4,5-*b*] indole-5-ϵ-carboxylates, the enantiomer of **12a**, with HRMS, FAB$^+$ Calcd for $C_{35}H_{41}N_2O_4$ (M^++1): 553.3066; Found: 553.3040, and the enantiomer of **12b**, with HRMS, FAB$^+$ Calcd for $C_{35}H_{41}N_2O_4$ (M^++1): 553.3066; Found: 553.3069, were obtained, with otherwise equivalent spectroscopic data.

1.1.4. (5*R*,7*R*)-Methyl 3-[1(*R*)-(1-naphthyl)-ethyl]-1,2,3,4,5,6,7,8-octahydro-5-[2-ξ-(1,3-dioxolan-2-yl)-1-butyl]-azonino[6,7*b*]indole-7-carboxylates (15a,b) and enantiomers. A solution of the C-20 epimeric tetracyclic compounds **12a**,**b** (1.6 g, 2.9 mmol) in acetic acid (15 mL) was heated at 90°C and sodium borohydride (1.1 g, 29 mmol) was added in portions over 5 min. The mixture was poured into ice, basified with concentrated ammonium hydroxide, extracted with dichloromethane (3×100 mL), dried over magnesium sulfate and concentrated. Flash chromatography, eluting with 1:1 ether/hexane, gave the cleavamine diastereomers **15a**,**b** (1.32 g, 82%) as a white foam. TLC (SiO_2, ether/hexane 1:1) R_f=0.23 and 0.15, CAS green. For the less polar diastereomer: UV (ethanol) λ_{max} 222, 280, 294 nm; IR (film) ν_{max} 3380 (m), 3049 (w), 2920 (s), 1712 (s), 1455 (s), 1154 (s), 799 (m), 774 (s), 737 (s) cm^{-1}; 250 MHz ^{1}H NMR ($CDCl_3$) δ 0.69 (t, J=7.4 Hz, 3H), 0.92–1.40 (m, 6H), 1.54 (d, J=6.5 Hz, 3H), 1.71–1.80 (m, 1H), 1.83–2.09 (m, 3H), 2.19 (brt, J=14.3 Hz, 1H), 2.35–2.67 (m, 3H), 3.15–3.38 (m, 6H), 3.73 (s, 3H), 4.26 (d, J=4 Hz, 1H), 4.71 (q, J=6.6 Hz, 1H), 5.36 (dd, J=12, 5 Hz, 1H), 6.96–7.09 (m, 2H), 7.23 (d, J=8.4 Hz, 1H), 7.33 (d, J=7.5 Hz, 1H), 7.41–7.61 (m, 4H), 7.75 (d, J=8.0 Hz, 1H), 7.83 (d, J=8 Hz, 1H), 8.30 (1H), 8.56 (brs, 1H); 67.9 MHz ^{13}C NMR ($CDCl_3$) δ 176.0, 140.7, 136.1, 134.2, 132.4, 131.8, 129.0, 128.1, 127.8, 126.3, 125.4, 124.5, 124.0, 121.3, 118.9, 117.8, 114.8, 110.7, 106.4, 64.5, 64.4, 63.2, 59.7, 51.9, 51.6, 41.8, 40.2, 39.8, 33.6, 31.7, 25.8, 22.8, 15.5, 11.1; EIMS *m/z* (relative intensity) 554 (M^+, 5), 400 (6), 399 (35), 339 (6), 254 (5), 244 (9), 243 (41), 214 (5), 169 (8), 156 (16), 155 (100), 154 (17), 153 (18), 152 (5), 144 (9), 129 (9), 128 (9), 127 (14), 124 (7), 123 (6), 115 (7), 86 (9), 84 (12), 73 (38). HRMS, FAB$^+$ Calcd for $C_{35}H_{43}N_2O_4$ (M^++1): 555.3223; Found: 555.3223.

For the more polar diastereomer: UV (ethanol) λ_{max} 216, 224, 282, 292 nm; IR (film) ν_{max} 3436 (m), 3391 (m), 3371 (m), 3044 (w), 2922 (s), 2877 (m), 1714 (s), 1599 (w), 1458 (s), 1361 (m), 1335 (m), 1259 (m), 1201 (m), 1156 (s), 1104 (m), 1066 (m), 1015 (m), 950 (m), 796 (s), 777 (s), 732 (s) cm^{-1}; 270 MHz ^{1}H NMR ($CDCl_3$) δ 0.59 (t, J=7.4 Hz, 3H), 0.83–0.98 (m, 2H), 1.04–1.11 (m, 2H), 1.25 (s, 1H), 1.55 (d, J=6.6 Hz, 3H), 1.71–1.76 (m), 1.91 (d, J=12.3 Hz), 2.20 (t, J=11.1 Hz, 1H), 2.42 (t, J=11.2 Hz, 1H), 2.55–2.65 (m, 2H), 3.19 (m, 1H), 3.37–3.53 (m, 4H), 3.76 (s, 3H), 4.50 (d, J=3.6 Hz, 1H), 4.72 (q, J=6.6 Hz, 1H), 5.35 (dd, J=12, 5 Hz, 1H), 6.95–7.08 (m, 2H), 7.23 (d, J=8.4 Hz, 1H), 7.35 (d, J=7.5 Hz, 1H), 7.44–7.62 (m, 4H), 7.78 (d, J=8.0 Hz, 1H), 7.86 (d, J=7.8 Hz, 1H), 8.35 (d, J=8.2 Hz, 1H), 8.55 (s, 1H); 67.9 MHz ^{13}C NMR ($CDCl_3$) δ 175.7, 140.8, 136.1, 134.2, 132.4, 131.9, 128.9, 128.1, 127.6, 126.1, 125.3, 124.4, 123.9, 121.3, 118.9, 117.7, 114.8, 112.1, 110.6, 106.8, 64.8, 64.6, 64.5, 62.4, 59.8, 51.8, 51.7, 41.9, 40.3, 33.5, 31.7, 25.9, 23.0, 16.0, 11.2; EIMS, *m/z* (relative intensity) 554.7 (M^+, 4), 399 (13), 243 (29), 215 (7), 214 (8), 202 (3), 196 (4), 184 (5), 182 (4), 170 (4), 169 (6), 156 (14), 155 (100), 153 (8), 144 (10), 129 (6), 127 (8), 115 (4), 85 (5), 73 (20). HRMS, FAB$^+$ Calcd for $C_{35}H_{43}N_2O_4$ (M^++1): 555.3223; Found: 555.3228.

Starting from methyl (3a*R*,4*S*,11b*S*)-methyl 3-[1(*S*)-(1-naphthyl)-ethyl]-2,3,3a,4,5,7-hexahydro-4-[2-ξ-(1,3-dioxolan-2-yl)-1-butyl]-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylates (enantiomers of **12a.b**), the less polar product enantiomer, with HRMS, FAB$^+$ Calcd for $C_{35}H_{43}N_2O_4$ (M^++1): 555.3223; Found: 555.3206, and the more polar product enantiomer, with HRMS, FAB$^+$ Calcd for $C_{35}H_{43}N_2O_4$ (M^++1): 555.3223, Found: 555.3221 were obtained, with otherwise equivalent spectroscopic data to those given above.

1.1.5. (5*R*,7*R*)-Methyl 1,2,3,4,5,6,7,8-octahydro-5-[2-ξ-(1,3-dioxolan-2-yl)-1-butyl]azonino[6,7-*b*]indole-7-carboxylates ((−)-5a) and enantiomer ((+)-5a). A solution of the diastereomeric cleavamines **15a**,**b** (1.56 g, 2.81 mmol) in acetic acid (30 mL), and 10% Pd/C (0.70 g) were subjected to hydrogenation at atmospheric pressure for 4 h. Filtration through a plug of Celite and washing with acetic acid was followed by pouring over ice and basifying with concentrated ammonium hydroxide. Extraction with methylene chloride (3×100 mL), drying over magnesium sulfate, concentration, and flash chromatography, eluting with 5% methanol in methylene chloride, gave the secondary amine-acetal **5a** (1.01 g, 89%) as a mixture of inseparable diastereomers. TLC (SiO_2, 5% MeOH in CH_2Cl_2) R_f=0.10–0.28; UV (EtOH) λ_{max} 202, 225, 284, 292 nm;

IR (film) ν_{max} 3338 (m), 3382 (s), 2916 (s), 1721 (s), 1586 (m), 1458 (s), 1433 (s),1329 (s), 1255 (s), 1200 (s), 1157 (s), 1102 (s), 1010 (m), 943 (m), 728 (s), 636 (w), 581 (w) cm^{-1}; 270 MHz ^1H NMR ($CDCl_3$) δ 0.63 (t, J=7 Hz, 3H), 0.83–1.20 (m, 5H), 1.31–1.41 (m, 1H), 1.68–1.79 (m, 2H), 2.05 (q, J=2 Hz, 1H), 2.23 (t, J=12 Hz, 1H), 2.46 (t, J=12 Hz, 1H), 2.67 (dt, J=14, 3 Hz, 2H), 2.92 (dd, J=3, 14 Hz, 1H), 3.34–3.55 (m, 4H), 3.73 (s, 3H), 4.53 (d, J=4 Hz, 1H), 5.46 (dd, J=5, 12 Hz, 1H), 7.03–7.13 (m, 2H), 7.25–7.31 (m, 1H), 7.48 (d, J=7 Hz, 1H), 8.65 (s, 1H); 67.9 MHz ^{13}C NMR δ 11.3, 22.9, 27.6, 31.5, 33.3, 40.2, 41.9, 49.7, 57.3, 64.4, 64.6, 106.7, 110.6, 114.2, 117.8, 118.9, 121.3, 128.0, 132.1, 135.9, 175.9; EIMS, m/z (relative intensity) 400 (M^+, 13), 252 (6), 215 (6), 202 (7), 184 (6), 182 (5), 171 (6), 170 (9), 169 (8), 156 (7), 155 (5), 154 (7), 144 (6), 142 (4), 141 (7), 140 (4), 130 (7), 129 (4), 126 (12), 116 (4), 114 (6), 73 (100), 70 (5), 57 (7), 55 (10). HRMS, FAB^+ Calcd for $C_{23}H_{33}N_2O_4$ (M^++1): 401.2440; Found: 401.2442.

Starting from (5*S*,7*S*)-methyl 3-[1(*S*)-(1-naphthyl)-ethyl]-1,2,3,4,5,6,7,8-octahydro-5-[2-ξ-(1,3-dioxolan-2-yl)-1-butyl]-azonino[6,7-*b*]indole-7-carboxylates, the enantiomers of (−)-**5a**, with HRMS, FAB^+ Calcd for $C_{23}H_{33}N_2O_4$ (M^++1): 401.2440; Found: 401.2433, were obtained, with otherwise equivalent spectroscopic data.

1.1.6. (−)-Coronaridine ((−)-1) and (+)-coronaridine ((+)-1). *Method a:* To a solution of the aminoacetals (−)-**5a** (0.530 g, 1.32 mmol) in methanol (15 mL), rapidly stirred at room temperature, was added 1N aqueous HCl (15 mL). After 4 h the starting material had been consumed (TLC). The mixture was cooled to 0°C and basified with 10% ammonium hydroxide in saturated brine. The mixture was extracted with methylene chloride (3×25 mL), dried over magnesium sulfate, and concentrated to give an oil. The oily residue was taken up in chloroform (25 mL), and allowed to stand for 5 h at ambient temperature. Removal of the chloroform and placement under vacuum for one week converted the enamine **6a** to coronaridine (TLC monitoring). Flash chromatography, eluting with 1:1 ether/hexane, gave 0.35 g (68%) of (−)-coronaridine (**1**) as a white foam.

Method b: A solution of freshly generated enamine **6a** (0.135 g, 0.40 mmol) in dry toluene (25 mL) was heated at reflux for 18 h. Concentration and flash chromatography, eluting with 1:1 ether/hexane, gave (−)-coronaridine (**1**, 0.085 g, 63%). TLC (SiO_2, 1:1 ether/hexane) R_f=0.44 (CAS green); $[\alpha]_D$=−9 (HCl, c=0.244, CH_3OH; reported:[10] −9); circular dichroism in EtOH for free base and for HCl salt ellipticity λ_{max} 225, λ_{min} 278, matching natural (−)-coronaridine; UV (HCl EtOH) λ_{max} 224, 284, 292 nm; 270 MHz ^1H NMR ($CDCl_3$) δ 0.89 (t, J=7.2 Hz, 3H), 1.14 (m, 1H), 1.33 (brdt, 1H), 1.45 (dq, J=7 Hz, 1H), 1.55 (m, 1H), 1.73 (m, 1H), 1.91 (brd, 1H), 2.59 (brd, J=12 Hz, 1H), 2.80 (d, J=9 Hz, 1H), 2.90 (brd, J=9 Hz, 1H), 3.03 (m, 1H), 3.15 (m, 1H), 3.20 (m, 1H), 3.40 (m, 1H), 3.55 (m, 1H), 3.71 (s, 3H), 7.05–7.23 (m, 3H), 7.47 (d, J=7.7 Hz, 1H), 7.75 (brs, 1H); 67.9 MHz ^{13}C NMR δ 11.5, 22.3, 27.0, 27.8, 32.3, 36.8, 39.3, 52.0, 52.3, 53.3, 55.4, 57.5, 110.4, 110.6, 118.5, 119.4, 122.0, 129.1, 135.8, 136.9, 175.6; EIMS, m/z (relative intensity) 339 (M^+, 8), 338 (40), 323 (8), 253 (6), 215 (5), 214 (15), 208 (12), 195 (6), 182 (5), 180 (5), 169 (14), 168 (8), 167 (10), 165 (9), 155 (5), 154 (21), 148 (13), 144 (7), 143 (7), 139 (9), 137 (14), 136 (100), 135 (34), 131 (7), 130 (22), 128 (5), 127 (6), 125 (7), 124 (54), 123 (11), 122 (42), 121 (7), 110 (7), 109 (5), 108 (13), 98 (11), 96 (15), 95 (7), 94 (9), 86 (27), 84 (47), 82 (8), 81 (5), 77 (6), 69 (6), 68 (7), 67 (9), 57 (8), 55 (15). HRMS, FAB^+ Calcd for $C_{21}H_{27}N_2O_2$ (M^++1): 339.2073; Found: 339.2060.

Starting from the initial product mixture of intermediates **12a–d**, and following the above reaction procedures, (−)-coronaridine ((−)-**1**) was obtained in 75% ee, as determined by HPLC on a Chiralcel OD column eluted with 96:4 hexane/ethanol.

Starting from (5*S*,7*S*)-methyl 1,2,3,4,5,6,7,8-octahydro-5-[2-ξ-(1,3-dioxolan-2-yl)-1-butyl]azonino[6,7-*b*]indole-7-carboxylates((+)-**5**), (+)-coronaridine, with HRMS, FAB^+ Calcd for $C_{21}H_{27}N_2O_2$ (M^++1): 339.2073, Found: 339.2057, was obtained, with otherwise equivalent spectroscopic data to (−)-coronaridine; $[\alpha]_D$=+34.4 (free base, c=0.30, $CHCl_3$, natural coronaridine free base: −34.6).

1.1.7. (3a*S*,4*R*,11b*R*) Methyl 3-[1(*R*)-1-[(*S*)-2-(diphenylphospheno)-ferrocenyl]-ethyl-2,3,3a,4,5,7-hexahydro-4-[2-(1,3-dioxolan-2-yl)-1-butyl]-1*H*-pyrrolo-(2,3-*d*)carbazole-6-carboxylates (21a, 21b). A solution of the ferrocenyl indoloazepines (−)-**17** (2.00 g, 3.12 mmol) and aldehyde **11** (0.650 g, 3.75 mmol) in dry benzene (20 mL) was heated under reflux until TLC showed no remaining indoloazepines **17** (4 h). The benzene was removed under reduced pressure and the residue was chromatographed on silica gel (ether/hexane 1:1) to give the major less polar isomer **21a** (0.83 g) and the major more polar isomer **21b** (0.75, 30%). The respective 3a*R*,4*S*,11b*S* minor diastereomers **21c** and **d** preceded these products on elution. An 84:16 ratio of major to minor diastereomers was thus obtained preparatively. A small amount of contaminating minor isomer was readily eliminated by rechromatography of **21a** on flash silica, eluting with ether/hexane (1:1), to provide pure **21a** (0.79 g, 32%). For **21a**: $[\alpha]^{25}_D$=−378 (c=0.98, $CHCl_3$); mp 103–105°C (dec.); TLC R_f=0.36, (silica gel, hexane / ether, 1:1, CAS blue to purple); UV (EtOH) λ_{max} 214, 228, 302, 330 nm; IR (KBr) ν_{max} 3370, 3043, 2951, 2936, 2866, 1667, 1601, 1471, 1457, 1424, 1365, 1286, 1273, 1240, 1195, 1103, 1031, 926, 814, 729, 683 cm^{-1}; 270 MHz ^1H NMR ($CDCl_3$) δ 0.57 (t, J=7.2 Hz, 3H), 0.74–0.93 (m, 2H), 1.22–1.72 (m, 7H), 1.75 (d, J=6.9 Hz, 3H) 2.29 (d, J=15 Hz, 1H), 2.78–2.87 (m, 3H), 3.67 (s, 3H), 3.76–3.93 (m, including 5H singlet at δ 3.84, 9H), 4.15 (s, 1H), 4.37–4.93 (m, 4H), 6.72 (d, J=7.7 Hz, 1H), 6.78 (t, J=7.4 Hz, 1H), 6.83 (d, J=7.2 Hz, 1H), 7.02–7.14 (m, 4H), 7.25 (t, J=7.5 Hz, 2H), 7.35 (m, 3H), 7.63–7.70 (m, 2H), 8.90 (s, 1H); 67.9 MHz ^{13}C NMR ($CDCl_3$) δ 11.7, 17.8, 20.6, 22.0, 29.6, 37.8, 39.8, 40.1, 49.0, 50.6, 52.5, 52.6, 55.5, 64.7, 64.9, 67.4, 69.6 (5C), 71.2, 75.0, 90.0, 99.0, 99.2, 106.2, 108.8, 120.2, 122.7, 127.3, 127.5, 127.8, 127.9, 128.0, 129.0, 132.5, 132.6, 135.3, 135.5, 137.9, 139.0, 140.1, 142.9, 164.9, 169.1; CIMS, m/z (relative intensity) 795 (M^++1, 2.6), 794 (M^+, 11), 398 (10), 397 (49), 217 (12), 113 (18), 111 (28), 73 (100); Anal. Calcd for $C_{47}H_{51}N_2O_4PFe$: C, 71.03; H, 6.47; N,

3.52; P, 3.90; Fe, 7.03; Found: C, 70.85; H, 6.70; N, 3.38; P, 3.89; Fe, 6.85.

For **21b**: $[\alpha]^{25}_{D=}-431$ (c=1.46, $CHCl_3$); mp 103−105°C (decomp); TLC R_f=0.26, (silica gel/hexane ether, 1:1, CAS blue to purple); UV (EtOH) λ_{max} 214, 226, 302, 330 nm; IR (KBr) ν_{max} 3370, 3043, 2958, 2931, 2866, 1673, 1601, 1476, 1457, 1430, 1365, 1286, 1266, 1240, 1188, 1129, 1102, 1031, 939, 821, 721, 690 cm^{-1}; 270 MHz ^1H NMR ($CDCl_3$) δ 0.89 (t, J=7.4 Hz, 3H), 1.25–1.75 (m, 7H), 1.75 (d, J=6.9 Hz, 3H), 2.20 (d, J=19.0 Hz, 1H), 2.75–2.95 (m, 3H), 3.66–3.72 (m, including 3H singlet at δ 3.69, 7H), 3.86 (s, 5H), 4.18 (s, 1H), 4.38 (s, 1H), 4.39–4.52 (m, 2H), 6.72 (d, J=8.0 Hz, 1H), 6.79 (d, J=8.0 Hz, 1H), 6.85 (d, J=8.0 Hz, 1H), 7.05–7.20 (m, 4H), 7.26–7.40 (m, 5H, 7.60–7.75 (m, 2H), 8.87 (s, 1H); 67.9 MHz ^{13}C NMR ($CDCl_3$) δ 11.8, 17.3, 20.4, 21.1, 26.6, 28.7, 37.5, 39.3, 40.0, 45.7, 49.0, 50.6, 52.4, 52.6, 55.5, 64.5, 64.6, 67.1, 69.7 (5C), 71.2, 75.1, 90.1, 98.8, 99.2, 106.7, 108.9, 120.1, 122.6, 127.3, 127.6, 127.7, 127.8, 127.9, 128.0, 129.0, 132.4, 132.6, 135.2, 135.5, 137.8, 138.9, 139.9, 140.1, 143.0, 164.4, 169.0; CIMS, *m/z* (relative intensity) 796 (M^++2, 14), 795 (M^++1, 65), 794 (M^+, 50), 425 (20), 398 (23), 397 (100), 243 (91), 242 (43), 211 (21), 79 (19); Anal. Calcd for $C_{47}H_{51}N_2O_4PFe$: C, 71.03; H, 6.47; N, 3.52; P, 3.90; Fe, 7.03. Found: C, 71.21; H, 6.56; N, 3.34; P, 3.41; Fe, 6.90.

1.1.8. (3a*R*,4*R*,11b*R*)-Methyl 2,3,3a,4,5,7-hexahydro-4-[1-(2-(*S* or *R*)-(1,3-dioxolan-2-yl)-1-butyl]-1*H*-pyrrolo-[2.3-*d*]carbazole-6-carboxylates 22a,b and 3a,11b-epimers 23a,b. The tetracycle **21b** (0.75 g, 0.94 mmol) in glacial acetic acid (10 mL) was heated at 70°C for 15 min. The mixture was then poured into crushed ice and basified with 15% NH_4OH in brine (25 mL) to produce a yellow precipitate (a mixture of PPFOAc and secondary amines), which was extracted with ether (4×25 mL). The ether layer was extracted with 20% acetic acid (5×25 mL). The ether extract was dried over $MgSO_4$ and concentrated to give a yellow solid (0.408 g), which was rich in PPFOAc. The acid layer was basified with 15% NH_4OH in brine (25 mL) to produce a white precipitate, which was extracted with ether (4×25 mL). The extracts were dried over $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on silica gel, eluting with 5% methanol in CH_2Cl_2 to give the *trans* epimer **22b** (0.237 g, 63%), and the *cis* epimer **23b** (0.045 g, 12%). For **22b**: $[\alpha]^{25}_{D}=-331$ (c=0.4, $CHCl_3$); TLC R_f=0.28, (silica gel, 5% methanol in CH_2Cl_2, CAS blue to purple); UV (EtOH) λ_{max} 214, 226, 298, 328 nm; IR (KBr) ν_{max} 3369, 3042, 2951, 2872, 1673, 1601, 1456, 1424, 1378, 1273, 1234, 1188, 1096, 1030, 939, 873, 782, 729 cm^{-1}; 270 MHz ^1H NMR ($CDCl_3$) δ 0.75 (t, J=7.3 Hz, 3H), 0.83–0.92 (m, 2H), 1.04–1.53 (m, 5H), 1.86–2.05 (m, 2H), 2.28–2.35 (m, 1H), 3.10–3.25 (m, 2H), 3.50 (bs, 1H), 3.75–3.95 (m, including 3H singlet at δ 3.79, 7H), 4.64 (d, J=3.7 Hz, 1H), 6.81–6.96 (m, 2H), 6,68–6.70 (m, 2H) 6.81 (t, J=7.3Hz, 1H), 6.93 (t, J=7.1 Hz, 2H), 7.13 (t, J=7.6 Hz, 2H), 7.11–7.26 (m, 2H), 9.03 (s, 1H); EIMS, *m/z* (relative intensity) 398 (M^+, 17), 215 (45), 184 (100), 167 (12), 154 (15), 129 (17), 127 (21), 85 (15), 73 (45), 71 (20), 68 (22), 57 (40), 55 (27).

For **23b**: $[\alpha]^{25}_{D}=+343$ (c=0.57, $CHCl_3$); TLC R_f=0.28, (silica gel, 5% methanol in CH_2Cl_2, CAS blue); UV (EtOH) λ_{max} 214, 226, 298, 328 nm; IR (KBr) ν_{max} 3368, 3046, 2954, 2914, 2875, 1664, 1598, 1456, 1466, 1434, 1374, 1243, 1183, 1104, 1039, 947, 867, 802, 736, 690 cm^{-1}; 270 MHz ^1H NMR ($CDCl_3$) δ 0.92 (t, J=7.5 Hz, 3H), 1.25–2.52 (m, 10H), 3.05–3.14 (m, 2H), 3.05–3.14 (m, 2H), 3.75–4.05 (m, including 3H singlet at δ 3.76, 7H), 4.78 (d, J=3.9 Hz, 1H), 6.81–6.92 (m, 2H), 7.13–7.26 (m, 2H), 8.93 (s, 1H); EIMS, *m/z* (relative intensity) 398 (M^+, 16), 215 (43), 184 (100), 168 (11), 167 (11), 154 (13), 129 (16), 127 (19), 85 (13), 73 (46), 68 (20), 56 (13), 55 (12).

An analogous cleavage of **21a** produced *trans* and *cis* secondary amines **22a** and **23a** in similar yields with a similar ratio.

1.1.9. (−)-Coronaridine ((−)-1). Benzyl bromide (0.24 g, 1.38 mmol) was added to a stirred solution of N^b-*H* tetracycle **22a** (0.5 g, 1.25 mmol) and triethyl amine (0.35 mL, 2.5 mmol) in acetone (15 mL) and powdered anhydrous K_2CO_3 (1 g) was then added. The mixture was stirred at room temperature for 6 h, filtered and the solid was washed with CH_2Cl_2 (3×25 mL). The filtrate was concentrated and the crude product was purified by flash chromatography on silica gel, eluting with ether/hexane (1:1) to give the *N*-benzylated tetracycle (−)-**3a** (0.47 g, 77%) as a viscous oil; $[\alpha]^{25}_{D}=-362$ (c=1.68, $CHCl_3$). The debenzylated cleaveamine acetals (−)-**5a** were prepared according to the procedure described for the racemic compounds.[1] To a stirred solution of the aminoacetals (−)-**5a** (0.3 g, 0.75 mmol) in methanol (10 mL) was added 1N HCl (10 mL). After stirring for 4 h at room temperature under nitrogen the mixture was cooled to 0°C and basified with 15% NH_4OH in saturated brine. The mixture was extracted with CH_2Cl_2 (3×25 mL), dried over $MgSO_4$ and concentrated to an oil. The oily residue was dissolved in dry toluene (5 mL) and heated to reflux for 3 h. Concentration and flash chromatography on silica gel, eluting with ether, gave (−)-coronaridine (0.154 g, 60%) as a white foam. $[\alpha]^{25}_{D}=-9$ (HCl, c=0.2, CH_3OH).

1.1.10. (−)-18-Methoxycoronaridine ((−)-2). *Method a:* A solution of methyl 3-[1(*R*)-(1-naphthyl)ethyl]-2,3,3a,4,5,7-hexahydroazepino [4,5-*b*]indole-5-ξ-carboxylates (**10**, 313 mg, 0.785 mmol),[5] and 4-(1,3-dioxolan-2-yl)-6-methoxyhexanal (**13**, 189 mg, 0.916 mmol),[2] in dry toluene (8 mL), was heated at reflux for 12 h under nitrogen, using a Dean–Stark trap filled with 4 Å molecular sieves. The reaction mixture was cooled to room temperature and concentrated under vacuum. The crude product was dissolved in 5 mL of methanol and cooled to 0°C, and $NaBH_4$ (69 mg, 1.83 mmol) was added in portions to reduce excess aldehyde. After stirring for 15 min at 0°C, the reaction mixture was partitioned between water and dichloromethane, and the dried ($MgSO_4$) extract was concentrated under vacuum. The residue was flash chromatographed on silica gel, eluting with ether/hexane (1:1) to give the tetracyclic vinylogous urethane (3a*S*,4*R*,11b*R*) methyl 3-[1(*R*)-(1-naphthyl)ethyl]-2,3,3a,4,5,7-hexahydro-4-[1-[2-ξ-(1,3-dioxolan-2-yl)]-4-(methoxy)butyl]-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylates (**14a**,**b**), and the minor 3a,4,11b epimeric product **14c**,**d** (total 389 mg, 85%). TLC (SiO_2, ether/hexane 3:2): R_f= 0.16, CAS blue; UV (EtOH) λ_{max} 214, 226, 300, 330 nm;

IR (KBr) ν_{max} 3382, 2945, 2874, 1677, 1610, 1478, 1466, 1437, 1281, 1248, 1206, 1115, 1050, 949, 748, 701 cm^{-1}; 500 MHz ^1H NMR showed two major acetal doublets at δ 4.84 and 4.61 and two minor acetal doublets at δ 4.49 and 4.41 in a ratio of 10:1.2 for the two diastereomeric C-20 epimeric product pairs. HPLC on a Chiralcel OD column, eluted with 90% hexane-isopropanol at 0.8 mL min^{-1}, gave two equivalent peaks at 10.1 and 12.7 min for **14a**,**b**, with respective longer retention shoulders for the minor diastereomers **14c**,**d**. EIMS, *m*/*z* 582 (M^+), 440, 368, 155.

A solution of the mixture of isomers of the tetracyclic products **14a**–**d** (44 mg, 0.075 mmol) in glacial acetic acid (0.5 mL) was heated at 90°C in an oil bath and $NaBH_4$ (29 mg, 10 eq.) was added in small portions over a period of 5 min. Then the mixture was poured over crushed ice, made basic with NH_4OH, and extracted with dichloromethane. The organic phase was dried over $MgSO_4$ and concentrated. Flash chromatography on silica gel, eluting with 2:1 hexane/ether, gave a stereoisomeric mixture of tricyclic tertiary amines **16a**–**d** (33 mg, 74%). TLC R_f= 0.21 and 0.14 (silica gel, 2:3 hexane/ether, CAS green). For the less polar diastereomers: UV (EtOH) λ_{max} 226, 284 nm; IR (film) ν_{max} 3378, 3048, 2924, 1726, 1462, 1264, 1161, 1112, 1024, 945, 781, 740 cm^{-1}; EIMS *m*/*z* 584 (M^+), 429, 369, 325, 256, 243, 155. For the more polar diastereomers: UV (EtOH) λ_{max} 232, 282 nm; IR (film) ν_{max} 3387, 3048, 2925, 1729, 1462, 1435, 1164, 1113, 781, 742 cm^{-1} EIMS *m*/*z* 584 (M^+), 429, 369, 325, 256, 243, 155.

A solution of the diastereomeric cleavamines **16a**–**d** (316 mg, 0.54 mmol) in acetic acid (6 mL), and 10% Pd-C (142 mg) was subjected to hydrogenation at atmospheric pressure for 15 h. Filtration through a plug of Celite and washing with acetic acid was followed by pouring the solution over ice, and basifying with concentrated ammonium hydroxide. Extraction with methylene chloride, concentration of the dried extract ($MgSO_4$), and chromatography on silica gel, eluting with ether/hexane, 1:1, gave the enantiomerically enriched secondary amines **5b** (152 mg, 65%) as an unstable oil. EIMS *m*/*z* 430 (M^+), 398, 371, 358, 323, 281, 252, 215, 169, 156, 73.

To a solution of the enantiomerically enriched aminoacetal **5b** (125 mg, 0.29 mmol) in 2 mL of degassed CH_3CN, under protection of nitrogen and covered by aluminum foil, was added 10% HCl (2 mL). After stirring at rt for several hours the starting material had been consumed. The mixture was cooled to 0°C and basified with 15% ammonium hydroxide in saturated brine. The mixture was extracted with ether (4×10 mL), the extract dried ($MgSO_4$), and concentrated. The resulting oil was dissolved in 6 mL of dry toluene and heated at reflux overnight. Concentration and flash chromatography gave (−)-18-methoxycoronaridine ((−)-**2**, 65 mg, 61%) as a white solid. HPLC on a Chiralcel OD column, eluting with 9:1 hexane/ethanol indicated a 76% ee. NMR chiral shift studies of this product with $Eu(hfc)_3$ showed that the product was formed in 74% ee; $[\alpha]^{28}_D$=−31.4 (free base, *c*=0.26, $CHCl_3$), and −29.7 (HCl salt, *c*=0.75, $CHCl_3$); reported for (−)-18-methoxycoronaridine hydrochloride, obtained by resolution and our method of purification: $[\alpha]^{25}_D$=−42.4.[4] Circular dichroism in EtOH, for free base, ellipticity λ_{max} 227, λ_{min} 276, but for HCl salt ellipticity λ_{min} 223, λ_{max} 254, λ_{min} 275. These values matched those obtained with (−)-18-methoxycoronaridine derived from resolution of the racemic compound,[4] and they were inverted in the corresponding enantiomer, obtained by resolution.[4]

Enantiomerically further enriched (−)-18-methoxycoronaridine was obtained by fractional crystallization: The enantiomeric mixture of 18-methoxycoronaridine (0.625 g, 74% ee) was dissolved in a mixture of CH_2Cl_2 (5 mL), ether (25 mL) and hexane (25 mL). The solution was left in a freezer overnight and precipitated white crystals (0.14 g) were collected. The mother liquor was concentrated to give a pale yellow powder (0.465 g). NMR $Eu(hfc)_3$ chiral shift studies on the initial white crystals showed them to be essentially racemic 18-methoxycoronaridine, while the powder (mp 148°C) from the mother liquor was essentially (−)-18-methoxycoronaridine (>98% ee).

Spectroscopic data for intermediates matched those reported for the corresponding racemic intermediates.[2]

Method b: A solution of (−)-methyl 3[1(*R*)-[(*S*)-2-(diphenylphospheno)ferrocenyl]-ethyl]-1,2,3,4,5,6-hexahydroazepino[4,5-*b*]indole-5-ξ-carboxylates (**17**, 2.00 g, 3.12 mmol),[6] and 4-(1,3-dioxolan-2-yl)-6-methoxyhexanal (**13**, 0.77 g, 3.75 mmol),[2] in dry benzene (20 mL), was heated under reflux until TLC showed no remaining indoloazepines (4 h). The benzene was removed under reduced pressure and the residue was chromatographed on silica gel (ether/hexane 1:1) to give (3a*S*,4*R*,11b*R*)-methyl-3-[1(*R*)-[(*S*)-2-(diphenylphospheno) ferrocenyl] ethyl]-2,3,3a,4,5,7-hexahydro-4-[1-(2-(*S* and *R*)-(1,3-dioxolan-2-yl)-4-methoxybutyl]-1*H*-pyrrolo (2,3-*d*)carbazole]-6-carboxylates (**18a**,**b**) as the less polar 2-(*S*)-butyl isomer (0.93 g, 32%), and the more polar 2-(*R*)-butyl isomer 0.88 g, (30%), each containing its minor 3a*R*,4*S*,11b*S* epimer (**18c**,**d**).

A solution of either the 2-(*S*)-or the 2-(*R*)-methoxybutyl isomer of the (3a*S*,4*R*,11b*R*)-methyl-3-[1(*R*)-[(*S*)-2-(diphenylphospheno) ferrocenyl] ethyl]-2,3,3a,4,5,7-hexahydro-4-[1-(2-(*S* or *R*)-(1,3-dioxolan-2-yl)-4-methoxybutyl]-1*H*-pyrrolo(2,3-*d*)carbazole]-6-carboxylates (**18a** or **18b**, 0.83 g, 0.94 mmol) in glacial acetic acid (10 mL) was heated at 70°C for 15 min. The mixture was then poured into crushed ice and basified with 15% NH_4OH in brine (25 mL) to produce a yellow precipitate. Glacial acetic acid was slowly added until the solution became slightly acidic. The mixture was vigorously shaken in a separatory funnel. The undissolved yellow precipitate was filtered and the clear filtrate was basified with 15% NH_4OH in brine (25 mL) to produce a white precipitate, which was extracted with ether (3×25 mL). The dried ($MgSO_4$) extract was concentrated under vacuum. The residue was chromatographed on silica gel, eluting with 5% methanol in CH_2Cl_2, to give the (3a*S*,4*R*,11b*R*)-tetracyclic secondary amine epimer (**19a**, or **19b**, 0.26 g, 63%, each containing the minor epimers **19c** or **19d**), and the (3a*R*,4*S*,11b*S*)-tetracyclic secondary amine epimer (**20a** or **20b**, 0.049 g, 12%, with minor epimers **20c**,**d**).

Benzyl bromide (0.24 g, 1.38 mmol) was added to a stirred

solution of (3a*S*,4*R*,11b*R*)-tetracyclic secondary amine epimer (**19a**, 0.54 g, 1.25 mmol) and triethyl amine (0.35 mL, 2.5 mmol) in acetone (15 mL), and powdered anhydrous K_2CO_3 (1 g) was then added. The mixture was stirred at room temperature for 6 h, filtered and the solid was washed with acetone (2×25 mL). The filtrate was concentrated and the crude product purified by flash chromatography on silica gel, eluting with ether/hexane 1:1, to give the N^b-benzylated tetracycle ((−)-**3b**, 0.51 g, 77%) as a viscous oil. Its spectroscopic data matched those of the corresponding racemic compound.[2]

Following each step of the procedure given for the corresponding racemic tetracyclic amine,[2] the (3a*S*,4*R*,11b*R*)-tetracyclic N^b-benzyl amine was converted to (−)-18-methoxycoronaridine, $[\alpha]^{25}_D=-26.6$ (c=0.068, $CHCl_3$); mp 148°C.

1.1.11. (3a*S*,4*R*,11b*R*)-Methyl 3-(2,3-(*R*)-ferroceno-6,6-dimethyl-1(*S*)-cyclohexyl)-2,3,3a,4,5,7-hexahydro-4-[1-(2-(*S* and *R*)-(1,3-dioxolan-2-yl)-4-methoxybutyl]-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylates 25a,b. A solution of methyl 3-(2,3-(*R*)-ferroceno-6,6-dimethyl-1(*S*)-cyclohexyl-1,2,3,4,5,6-hexahydroazepino[4,5-*b*]indole-5-ξ-carboxylates (**24**, 20 mg, 0.038 mmol),[8] and 4-(1,3-dioxolan-3-yl)-6-methoxyhexanal (**13**, 37 mg, 0.180 mmol),[2] in dry benzene (1.5 mL) was heated at reflux for 22 h. The solvent was then evaporated under reduced pressure. The resulting residue was dissolved in dry MeOH (2.3 mL), and $NaBH_4$ (17 mg, 0.45 mmol) was added, with stirring at 0°C, to reduce excess aldehyde. After stirring at room temperature for an additional 15 min, some water was added at 0°C, while stirring the mixture for 5 min. The mixture was then stirred at room temperature for 10 more min. The MeOH was removed under reduced pressure and the aqueous mixture was extracted with Et_2O (3×10 mL). The combined ether layers were washed with brine (5 mL), and dried over sodium sulfate. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 8:1 to 5:1), to give an inseparable mixture of C-2′ epimers **25a**,**b** (23 mg, 87%,) as a yellow foam, with > 99% de, on the basis of HPLC on a Chiralcel OD column: TLC R_f=0.42 (silica gel, hexane/ethyl acetate, 5:3, yellow, CAS blue to purple); $[\alpha]^{25}_D=-36$ (c=0.23, $CHCl_3$); UV (EtOH) λ_{max} 210, 302, 330 nm; IR (KBr) ν_{max} 3381, 3089, 2923, 2868, 1677, 1610, 1477, 1466, 1437, 1294, 1275, 1242, 1201, 1152, 1113, 1105, 1047, 911, 733 cm^{-1}; 500 MHz ^1H NMR ($CDCl_3$) δ 9.08, 9.03 (2×s, 1H), 7.30 (d, J=7.4 Hz, 1H), 7.16 (m, 1H), 6.90 (q, J=7.9 Hz, 1H), 6.85 (dd, J=2.8, 7.7 Hz, 1H), 4.85–4.76 (m, 1H), 4.45 (d, J=1.7 Hz, 1H), 4.19 (s, 1H), 4.07, 4.06 (2×s, 5H), 3.97–3.83 (m, 4H), 3.81, 3.80 (2×s, 3H), 3.78 (m, 1H), 3.73–3.72 (m, 1H), 3.68, 3.63 (2×s, 1H), 3.32–3.27 (m, 2H), 3.15–3.00 (m, 4H), 2.83–2.35 (m, 5H), 2.05 (1H, m), 1.90–1.67 (m, 5H), 1.59–1.56 (m, 1H), 1.48–1.45 (m, 1H), 1.36–1.34 (m, 1H), 1.33, 1.32 (2×s, 3H), 1.15 (m, 1H), 1.10 (m, 1H), 0.99, 0.98 (2×s, 3H), 0.92 (m, 1H), 0.85 (m, 1H); 125 MHz ^{13}C NMR ($CDCl_3$, 51 peaks due to the C-20 (1:1) epimeric mixture) δ 169.0, 168.9, 166.0, 165.9, 143.1, 137.8, 137.7, 127.6, 127.6, 122.2, 120.6, 109.1, 109.1, 106.9, 106.3, 105.9, 104.6, 89.8, 89.3, 87.0, 85.0, 70.9, 70.5, 69.7, 69.6, 67.1, 65.1, 65.1, 64.9, 64.9, 64.7, 64.7, 62.0, 58.4, 58.2, 56.0, 50.8, 50.7, 41.3, 39.8, 39.74, 39.7, 35.9, 35.9, 31.2, 30.7, 30.6, 29.7, 29.6, 23.9, 21.9; CIMS (isobutane) m/z (relative intensity) 696 (M^+ +1, 0.6), 695 (M^+, 0.5), 247 (100), 203 (37), 147 (36), 141 (22), 89 (15), 73 (43); EI HRMS Calcd $C_{40}H_{50}N_2O_5Fe$ (M^+) 694.3069. Found 694.3015.

1.1.12. (3a*S*,4*R*,11b*R*)-Methyl 2,3,3a,4,5,7-hexahydro-4-[1-(2-(*S* and *R*)-(1,3-dioxolan-2-yl)-4-methoxybutyl]-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylates (19a,b) and 3a,11b-epimers (20a,b). The tetracycle intermediates **25a**,**b** (207 mg, 0.297 mmol), dissolved in acetic acid (1.5 mL), were stirred under nitrogen at room temperature for 40 min. The reaction mixture was cooled to 0°C and added to concentrated ammonium hydroxide (4 mL), and crushed ice. It was then extracted with CH_2Cl_2 (3× 15 mL). The organic layers were washed with brine (5 mL), dried over sodium sulfate, and concentrated under reduced pressure. The resulting residue was subjected to chromatography on silica gel (3% MeOH in CH_2Cl_2) to give the less polar product **20a**,**b** (4 mg, 3%) as a colorless oil, and the more polar product **19a**,**b** (118 mg, 93%) as a colorless oil (**20a**,**b** are epimeric with **19a**,**b** at position 3a,11b). For **20a**,**b**: TLC R_f=0.27 (silica gel, 10% MeOH in CH_2Cl_2, CAS blue); $[\alpha]^{25}_D=+144$ (c=0.06, $CHCl_3$); IR (KBr) ν_{max} 3368, 2957, 2928, 2872, 1681, 1610, 1482, 1468, 1440, 1383, 1284, 1206, 1114, 1043, 951, 752 cm^{-1}; CIMS (isobutane) m/z (relative intensity) 429 (M^++1, 15), 428 (M^+, 3), 298 (19), 267 (13), 215 (13), 189 (15), 171 (31), 163 (15), 141 (40), 115 (60), 101 (100), 84 (62), 79 (87). For **19a**,**b**: TLC R_f=0.17 (silica gel, 10% MeOH in CH_2Cl_2, CAS blue); $[\alpha]^{25}_D=-384$ (c=0.31, $CHCl_3$); UV (EtOH) λ_{max} 212, 228, 300, 328 nm; IR (KBr) ν_{max} 3361, 2946, 2927, 2876, 1676, 1609, 1479, 1466, 1437, 1388, 1304, 1284, 1247, 1204, 1109, 1044, 748 cm^{-1}; 500 MHz ^1H NMR ($CDCl_3$) δ 9.07, 9.04 (2×s, 1H), 7.24 (d, J=7.4 Hz, 1H), 7.15 (m, 1H), 6.88 (dd, J=7.2, 14.0 Hz 1H), 6.83 (dd, J=2.8, 7.8 Hz, 1H), 4.69, 4.65 (2×d, J=2.8, 3.5 Hz, 1H), 3.85–3.66 (m, including 3H, s, 7H), 3.50 (d, J=10.3 Hz, 1H), 3.26 (m, 2H), 3.21 (m, 1H), 3.14 (m, 3H), 2.68 (t, J=16.9 Hz, 1H), 2.52 (brs, 1H), 2.34, 2.31 (2×t, J=4.3, 4.5 Hz, 1H), 1.95 (m, 1H), 1.90 (m, 1H), 1.82 (m, 1H), 1.74–1.66 (m, 2H), 1.39 (m, 1H), 1.31 (m, 1H), 1.10 (m, 1H), 0.88 (m, 1H); 125 MHz ^{13}C NMR ($CDCl_3$, 42 peaks due to C-20 epimers) δ 169.0, 168.9, 165.6, 165.4, 143.2, 143.1, 137.8, 137.7, 127.8, 127.7, 121.9, 121.9, 120.7, 109.2, 109.1, 106.8, 106.1, 90.3, 90.1, 71.1, 70.8, 66.6, 64.9, 64.8, 64.8, 64.7, 58.4, 58.3, 55.7, 50.8, 45.3, 44.4, 39.1, 38.8, 35.9, 35.9, 31.7, 31.3, 29.9, 29.1, 22.6, 22.5; CIMS (isobutane) m/z (relative intensity) 430 (M^++2, 22), 429 (M^++1, 46), 428 (M^+, 13), 298 (21), 270 (13), 214 (12), 171 (11), 159 (22), 124 (14), 101 (24), 84 (100); EI HRMS Calcd $C_{24}H_{32}N_2O_5$ (M^++1) 429.2389, (M^+) 428.2311. Found 429.2345, 428.2318.

1.1.13. (3a*S*,4*R*,11b*R*)-Methyl 3-benzyl-2,3,3a,4,5,7-hexahydro-4-[1-(2-(*S*and *R*)-(1,3-dioxolan-2-yl)-4-methoxybutyl]-1*H*-pyrrolo[2.3-*d*]carbazole-6-carboxylates ((−)-3b). Benzyl bromide (35 μL, 0.29 mmol) was added to a stirred solution of the amines **19a**,**b** (114 mg, 0.267 mmol) and triethylamine (76 μL, 0.540 mmol) in acetone (4 mL), and powdered anhydrous K_2CO_3 (200 mg) was then added. The mixture was stirred at room temperature for 4.5 h and filtered. The solid was washed with CH_2Cl_2 (3×6 mL). The filtrate was dried over sodium sulfate, and concentrated

under reduced pressure. The crude product was purified by flash chromatography on silica gel, eluting with ether/hexane (1:2 and 1:1) to give the title product **(−)-3b** (102 mg, 73%) as an inseparable mixture of diastereomers, >99% ee, on the basis of HPLC on a Chiralcel OD column and comparison with the corresponding racemic compound, which showed base line separation of enantiomers: TLC R_f=0.33 (silica gel, ether/hexane, 2:1, CAS blue to yellow); $[\alpha]^{25}_D$=−368 (c=0.67, $CHCl_3$); UV (EtOH) λ_{max} 210, 226, 302, 330 nm; IR (KBr) ν_{max} 3378, 2924, 2870, 1677, 1610, 1478, 1466, 1437, 1294, 1280, 1249, 1205, 1125, 948, 747, 700 cm^{-1}; 500 MHz ^1H NMR ($CDCl_3$) δ 9.00, 8.96 (2×s, 1H), 7.40 (2×s, 2H), 7.36–7.33 (m, 2H), 7.29–7.27 (m, 1H), 7.12 (m, 1H), 7.01–6.96 (2×d, J=7.3, 7.2 Hz, 1H), 6.84–6.79 (m, 2H), 4.65–4.63 (2×d, J=2.7, 3.5 Hz, 1H), 4.15 (m, 1H), 3.83–3.61 (m, including 3H, 2×s, 7.5H), 3.26 (m, 1H), 3.22 (s, 1H), 3.17 (t, J=6.8 Hz, 1H), 3.11 (s, 1H), 2.99–2.95 (2×s, 1H), 2.90 (m, 1H), 2.66–2.56 (m, 3H), 2.04 (m, 2H), 1.73–1.65 (m, 3.5H), 1.43–1.30 (m, 1H), 1.09 (m, 1H), 0.98 (m, 1H), 0.80–0.65 (m, 1H); 125 MHz ^{13}C NMR ($CDCl_3$, 56 peaks due to C-20 epimers) δ 169.0, 169.0, 165.5, 165.1, 143.0, 142.9, 139.3, 139.1, 138.0, 137.9, 128.9, 128.8, 128.2, 128.2, 127.6, 127.5, 126.9, 126.9, 122.2, 122.2, 120.4, 120.4, 109.1, 109.0, 106.8, 106.3, 90.7, 90.6, 71.7, 71.6, 70.9, 70.9, 64.9, 64.8, 64.7, 64.6, 58.3, 58.3, 58.0, 57.9, 55.0, 55.0, 50.8, 50.5, 42.4, 42.2, 37.0, 36.6, 35.9, 35.8, 31.0, 30.6, 30.0, 29.1, 22.9, 22.7; CIMS (isobutane), m/z (rel intensity) 519 (M^++1, 42), 518 (M^+, 14), 221 (18), 171 (22), 117 (55), 102 (54), 83 (37), 69 (100).

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