

Supporting Information

Towards Diversity-Oriented, Stereoselective Syntheses of Biaryl- or Bis(aryl)metal-Containing Medium Rings

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Experimental Techniques and Apparatus

Except as otherwise indicated, reactions were carried out under argon with dry, freshly distilled solvents. Tetrahydrofuran was distilled from sodium/benzophenone ketyl. Anhydrous 2-methyltetrahydrofuran (Aldrich, racemic) was stored over activated molecular sieves. Dichloromethane was distilled from calcium hydride. *n*-BuLi in hexane (Aldrich) and *t*-BuLi in pentane (Aldrich) were titrated with 1,10-phenanthroline and anhydrous 2-butanol before use.¹ All other reagents were purified in accordance with the instructions in "Purification of Laboratory Chemicals"² or used as obtained from commercial sources.

Yields refer to chromatographically and spectroscopically pure compounds. All reactions were monitored by thin layer chromatography (TLC) using glass plates precoated with Merck silica gel 60 F₂₅₄ or aluminium oxide 60 F₂₅₄. Visualization was by the quenching of UV fluorescence (λ_{max} =254nm) or by staining with ceric ammonium molybdate or Dragendorff's reagent (0.08% w/v bismuth subnitrate and 2% w/v KI in 3M aq. AcOH). Retention factors (R_f) are quoted to 0.01. Melting points were obtained using a Mel-Temp II melting point apparatus and are uncorrected. Infrared spectra were recorded either as a thin film between NaCl plates or as a KBr disc on a Nicolet 5PC FT-IR spectrometer with internal referencing. Absorption maxima (ν_{max}) are reported in wavenumbers (cm⁻¹) and the following abbreviations are used: w, weak; m, medium; s, strong; br, broad. Proton magnetic resonance spectra were recorded on Varian Mercury400 (400MHz), Bruker Avance DMX500 (500MHz), and Varian Unity/Inova500 (500MHz) spectrometers.³ Proton assignments are supported by ¹H-¹H COSY, HMQC, NOESY and

¹ Watson, S. C.; Eastham, J. F. J. *Organometal. Chem.* **1967**, *9*, 165-168.

² Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals, Fourth Edition*; Butterworth-Heinemann: Oxford, 1997.

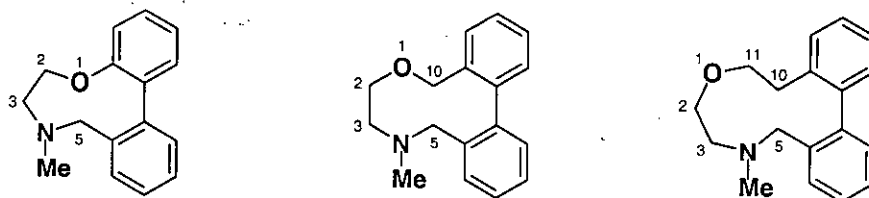
³ See: <http://nmrhc.harvard.edu:80/nimrlab/>

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GOESY spectra where necessary. Chemical shifts (δ_{H}) are quoted in ppm and are referenced to tetramethylsilane (internal). Coupling constants (J) are reported in Hertz to the nearest 0.5Hz. Data are reported as follows: chemical shift, integration, multiplicity [br, broad; s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; sept, septet; m, multiplet; or as a combination of these (*e.g.* dd, dt, *etc.*)], coupling constant(s) and assignment. Diastereotopic protons are assigned as X and X', where the ' indicates the lower field proton. Carbon magnetic resonance spectra were recorded on Varian Mercury400 (100MHz) and Varian Unity/Inova500 (125MHz) spectrometers. Carbon spectra assignments are supported by DEPT editing and where necessary ^{13}C - ^1H (HMQC) correlations. Chemical shifts (δ_{C}) are quoted in ppm to the nearest 0.01ppm, and are referenced to tetramethylsilane (internal). Fluorine magnetic resonance spectra (^{19}F) were recorded on a Varian Mercury300 (282MHz) spectrometer. Chemical shifts (δ_{F}) are quoted in ppm to the nearest 0.01ppm and are referenced to $\text{CF}_3\text{CH}_2\text{OH}$ (external).⁴ Low resolution mass spectra⁵ were obtained with JEOL AX-505H, SX-102A (CI/ED), Micromass Platform II and LCT (APCI/ES/LCMS) spectrometers. Only molecular ions, fractions from molecular ions and other major peaks are reported. High resolution mass spectra was obtained with a Micromass LCT (ES) spectrometer, and reported mass values are within the error limits of ± 5 ppm mass units.⁶ Microanalyses were performed by E&R Microanalytical Laboratory, Inc. (Parsippany, NJ) and Robertson Microlit Laboratories, Inc. (Madison, NJ),⁷ and are quoted to the nearest 0.1% for all elements except for hydrogen, which is quoted to the nearest 0.05%. Reported atomic percentages are within the error limits of $\pm 0.4\%$. X-ray crystallographic data were recorded on a SMART CCD single crystal diffractometer by Dr. Richard J. Staples (Harvard University).⁸

NMR Assignments

For clarity, the following numbering system has been used consistently for the biaryl ring systems:



⁴ Ribeiro, A.; Glen, M. J. *J. Magn. Reson., Ser. A* **1994**, *107*, 158-166.

⁵ See: http://paula.harvard.edu:80/mass/FACILITY_WEB_PAGE.HTM

⁶ By Dr. Andrew Tyler and Jennifer A. Lynch.

⁷ See: <http://www.robertson-microlit.com/>

⁸ See: <http://xriris2.harvard.edu/> Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (deposit@ccdc.cam.ac.uk). Also see: http://www-schreiber.chem.harvard.edu/home/research_results.html

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Experimental Procedures

General Procedure for Biaryl Synthesis. An oven-dried, three-necked round-bottomed flask containing the cyclization precursor and equipped with a magnetic stirring bar, a septum, a low temperature thermometer and a vacuum/gas inlet (greased joints) was evacuated and twice heated with a heat gun over 30 minutes. The flask was filled with argon and charged with anhydrous 2-methyltetrahydrofuran (2-MeTHF, 0.05-0.15M). The solution was cooled to -78°C and *t*-BuLi (4.0 equiv.)⁹ was added dropwise. After addition the reaction was stirred for 30 minutes to give a clear yellow solution of the dilithium intermediate. A freshly prepared 1M solution of CuCN·2LiBr in 2-MeTHF (1.0 equiv.)¹⁰ was added dropwise, then the mixture was stirred for 2 hours allowing the reaction temperature to slowly rise to -40°C . At this temperature a freshly prepared 1M solution of 1,3-dinitrobenzene in 2-MeTHF (4.0 equiv.)¹¹ was added to give a dark brown-black solution. The solution was allowed to warm to room temperature over 1-12 hours. The black solution was quenched with a 1M solution of HCl in MeOH to give a clear yellow-brown solution and was stirred for 30 minutes. A solution of 10% NH_4OH in saturated aqueous NH_4Cl was added and the resulting two-phase mixture was stirred for 30 minutes, then separated and the aqueous phase was extracted three times with Et_2O . The combined organic layers were washed (saturated aqueous NaCl), dried (K_2CO_3), filtered, concentrated *in vacuo* and chromatographed. In order to determine the thermodynamic diastereomeric ratio (dr) each diastereomer was heated neat under argon at 150°C for 24-48 hours; if the atropisomers were not separable then the mixture was heated until no change in ratio was observed.

(*P*,10*S*)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*P*)-3a. Colorless oil; yield: 88%; kinetic dr: 20:1 (*P*:*M*); R_f 0.30 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 97:2:1); $[\alpha]_D -13.8$ ($c=1.49$, CH_2Cl_2); ν_{max} (thin film)/ cm^{-1} 2922s, 2854s, 1475s, 1451s, 1094s, 1070s, 755s, 699s; δ_{H} (500MHz, CDCl_3) 2.32 (1H, dd, $J_{13.5}$, 7.5Hz, PhCHH'), 2.38 (3H, s, NCH_3), 2.39-2.44 (1H, m, C(3)H), 2.57 (1H, dd, $J_{13.5}$, 6.5Hz, PhCHH'), 3.22 (1H, dd, $J_{12.5}$, 3.5Hz, C(2)H), 3.39 (1H, dd, $J_{12.5}$, 10Hz, C(2)H'), 3.64 (1H, d, $J_{14.5}$ Hz, C(5)H), 3.88 (1H, d, $J_{14.5}$ Hz, C(5)H'), 4.10 (1H, d, $J_{12.5}$ Hz, C(10)H), 4.65 (1H, d, $J_{12.5}$ Hz, C(10)H'), 6.96 (1H, d, $J_{7.5}$ Hz, aryl CH), 7.17-7.44 (12H, m, aryl CH); δ_{C} (125MHz, CDCl_3) 35.09 (CH_3), 37.77 (Ph CH_2), 59.11 (C5), 64.71 (C3), 72.23 (C2), 73.65 (C10), 125.74, 126.42, 126.71, 127.33, 127.91, 128.04, 128.61, 128.91, 129.27, 129.65 & 130.58 (11 x CH), 138.32, 138.43, 140.03,

⁹ If more than four equivalents of *t*-BuLi are added and not quenched, then Ar-*t*-Bu adducts are preferentially formed.

¹⁰ Two equivalents of copper can be used without effecting the reaction yield or selectivity.

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141.22 & 143.03 (5 x quaternary); m/z (ES) 344 (MH^+ , 100%); HRMS found 344.2004, $C_{24}H_{26}NO$ (MH^+) requires 344.2014.

(M,10S)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-3a. Colorless crystals; thermodynamic dr: 1:6 (*P:M*); m.p. 134-135°C (MeOH); R_f 0.27 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 97:2:1); $[\alpha]_D$ -37.1 ($c=0.75$, CH_2Cl_2); ν_{max} (KBr disc)/ cm^{-1} 2943s, 2860s, 1444m, 1088s, 1063s, 757s, 700s; δ_H (500MHz, $CDCl_3$) 2.43 (1H, dd, $J_{13.5}$, 6Hz, $PhCHH'$), 2.55 (3H, s, NCH_3), 2.69-2.74 (1H, m, $PhCHH'$), 3.37 (1H, dd, $J_{12.5}$, 3.5Hz, C(2)H), 3.43 (1H, br s, C(3)H), 3.59 (1H, d, J_{12} Hz, C(5)H), 3.97 (1H, t, $J_{11.5}$ Hz, C(2)H), 4.12 (1H, d, $J_{12.5}$ Hz, C(5)H), 4.27 (1H, d, $J_{9.5}$ Hz, C(10)H), 4.36 (1H, d, $J_{9.5}$ Hz, C(10)H), 7.11-7.16 (4H, m, aryl CH), 7.22-7.37 (6H, m, aryl CH), 7.431-7.46 (2H, m, aryl CH), 7.51 (1H, d, J_7 Hz, aryl CH); δ_C (125MHz, $CDCl_3$) 35.46 (CH_3), 35.78 ($PhCH_2$), 53.89 (C3), 57.15 (C5), 68.23 (C10), 68.53 (C2), 125.91, 126.64, 127.62, 127.78, 128.04, 128.32, 129.34, 130.14, 130.24, 130.41 & 130.66 (11 x CH), 135.13, 138.48, 140.09, 141.00 & 142.04 (5 x quaternary); m/z (ES) 344 (MH^+ , 100%). Found: C, 83.7; H, 7.60; N, 4.3%. $C_{24}H_{25}NO$ requires C, 83.9; H, 7.35; N, 4.1%.

(P,10S)-10-Benzyl-16-fluoro-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-3b. Colorless oil; yield: 84%; kinetic dr: 13:1 (*P:M*); R_f 0.35 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 97:2:1); ν_{max} (thin film)/ cm^{-1} 2923s, 2856s, 1613s, 1584s, 1478s, 1453s, 1293m, 1195s, 1177s, 1103s, 898m, 751s, 699s; δ_H (500MHz, $CDCl_3$) 2.27 (1H, dd, $J_{13.5}$, 8.5Hz, $PhCHH'$), 2.31 (3H, s, NCH_3), 2.37-2.43 (1H, m, C(3)H), 2.56 (1H, dd, $J_{13.5}$, 6.5Hz, $PhCHH'$), 3.17 (1H, dd, $J_{12.5}$, 4Hz, C(2)H), 3.26 (1H, dd, $J_{12.5}$, 10Hz, C(2)H), 3.59 (1H, d, $J_{14.5}$ Hz, C(5)H), 3.82 (1H, d, $J_{14.5}$ Hz, C(5)H), 4.05 (1H, d, $J_{12.5}$ Hz, C(10)H), 4.46 (1H, d, $J_{12.5}$ Hz, C(10)H), 6.90-6.94 (3H, m, aryl CH), 7.01 (1H, td, J_9 , 3Hz, aryl CH), 7.08 (1H, dd, $J_{7.5}$, 1.5Hz, aryl CH), 7.12-7.17 (2H, m, aryl CH), 7.22 (2H, t, $J_{7.5}$ Hz, aryl CH), 7.27 (1H, td, $J_{7.5}$, 1.5Hz, aryl CH), 7.30-7.35 (2H, m, aryl CH); δ_C (100MHz, $CDCl_3$) 36.45 (CH_3), 37.94 ($PhCH_2$), 59.02 (C5), 65.45 (C3), 72.49 & 73.05 (C2 & C10), 113.96 (d, $J_{20.5}$ Hz, CH), 116.91 (d, $J_{21.5}$ Hz, CH), 126.00, 126.67, 127.32, 128.28, 128.61, 129.06 & 130.69 (7 x CH), 130.89 (d, $J_{8.5}$ Hz, CH), 134.56 (d, J_3 Hz, quaternary), 138.57 & 140.04 (2 x quaternary), 145.21 (d, $J_{8.5}$ Hz, quaternary), 162.17 (d, J_{247} Hz, quaternary); δ_F (282MHz, $CDCl_3$) -115.80; m/z (ES) 344 (MH^+ , 100%); HRMS found 362.1908, $C_{24}H_{25}FNO$ (MH^+) requires 362.1920.

¹¹ One equivalent could be used, but then the reaction was less clean and the yield of product lower.

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(M,10S)-10-Benzyl-16-fluoro-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-3b. Colorless crystals; thermodynamic dr: 1:10 (*P:M*); m.p. 106-108°C (EtOH); *R_f* 0.20 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); *v_{max}* (KBr disc)/cm⁻¹ 2923m, 2856m, 1612m, 1584s, 1478s, 1293m, 1177s, 1103s, 898m, 751s, 699s; δ_{H} (500MHz, CDCl₃) 2.33 (1H, dd, *J*13.5, 6Hz, PhCHH'), 2.46 (3H, s, NCH₃), 2.62 (1H, dd, *J*13.5, 8.5Hz, PhCHH'), 3.25-3.32 (2H, m, C(2)H & C(3)H), 3.50 (1H, d, *J*12.5Hz, C(5)H), 3.86 (1H, dd, *J*12, 10.5Hz, C(2)H'), 3.99 (1H, d, *J*12.5Hz, C(5)H'), 4.10 (1H, d, *J*10Hz, C(10)H), 4.24 (1H, d, *J*10Hz, C(10)H'), 6.86 (1H, dd, *J*9.5, 3Hz, aryl CH), 6.98 (1H, d, *J*8Hz, aryl CH), 7.03-7.07 (4H, m, aryl CH), 7.17 (1H, td, *J*7.5, 1.5Hz, aryl CH), 7.20-7.29 (4H, m, aryl CH), 7.38 (1H, dd, *J*9, 6.5Hz, aryl CH); δ_{C} (100MHz, CDCl₃) 35.70 (CH₃), 36.03 (PhCH₂), 54.04 (C3), 57.37 (C5), 67.60 & 68.74 (C2 & C10), 114.67 (d, *J*20.5Hz, CH), 117.54 (d, *J*21.5Hz, CH), 126.04, 126.84, 128.09, 128.14, 129.43, 130.06 & 130.32 (7 x CH), 131.34 (d, *J*3Hz, quaternary), 132.16 (d, *J*8.5Hz, CH), 137.44, 139.92 & 140.08 (3 x quaternary), 114.24 (d, *J*7.5Hz, quaternary), 162.33 (d, *J*247Hz, quaternary); δ_{F} (282MHz, CDCl₃) -115.29; *m/z* (ES) 344 (MH⁺, 100%); HRMS found 362.1935, C₂₄H₂₅FNO (MH⁺) requires 362.1920.

(P,10S)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[13.4.0.0^{2,7}]nonadeca-1(15),2,4,6,16,18-hexaene; (P)-3c. Colorless oil; yield: 85%; kinetic dr: 1.3:1 (*P:M*); *R_f* 0.29 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); *v_{max}* (thin film)/cm⁻¹ 2923s, 2856s, 1495s, 1473s, 1118s, 748s, 699s; δ_{H} (500MHz, CDCl₃) 2.38-2.45 (2H, m, PhCHH' and C(10)H), 2.48 (3H, s, NCH₃), 2.56-2.60 (1H, m, C(3)H), 2.82-2.90 (2H, m, PhCHH' and C(10)H'), 3.01 (1H, dd, *J*10, 2Hz, C(2)H), 3.07 (1H, dd, *J*10, 8Hz, C(2)H'), 3.31 (1H, d, *J*15Hz, C(5)H), 3.37 (1H, dt, *J*7, 4Hz, C(11)H), 3.73 (1H, td, *J*11, 3Hz, C(11)H'), 3.94 (1H, d, *J*15Hz, C(5)H'), 7.01-7.05 (2H, m, aryl CH), 7.10 (2H, d, *J*8Hz, aryl CH), 7.15-7.34 (8H, m, aryl CH), 7.68 (1H, d, *J*8Hz, aryl CH); δ_{C} (125MHz, CDCl₃) 32.68 (PhCH₂), 38.77 (C10), 43.99 (CH₃), 56.90 (C5), 68.14 (C3), 69.62 (C2), 71.76 (C11), 125.52, 125.56, 126.07, 126.93, 127.54, 128.34, 129.22, 129.49, 129.53, 129.63 & 129.95 (11 x CH), 138.41, 139.99, 140.43, 140.90 & 142.21 (5 x quaternary); *m/z* (ES) 358 (MH⁺, 100%); HRMS found 358.2166, C₂₅H₂₈NO (MH⁺) requires 358.2171.

(M,10S)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[13.4.0.0^{2,7}]nonadeca-1(15),2,4,6,16,18-hexaene; (M)-3c. Colorless oil; thermodynamic dr: 1:4 (*P:M*); *R_f* 0.22 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); *v_{max}* (thin film)/cm⁻¹ 2926s, 2854s, 1474, 1371m, 1132s, 1030m, 755s, 699s; δ_{H} (500MHz, CDCl₃) 2.18 (3H, s, NCH₃), 2.31 (1H, dd, *J*13.5, 8.5Hz, PhCHH'), 2.59 (1H, ddd, *J*14.5, 7.5, 4Hz, C(10)H), 2.72 (1H, dd, *J*13.5, 6.5Hz, PhCHH'), 2.87 (1H, ddd, *J*14.5, 7.5, 4Hz, C(10)H'), 3.00 (1H, dd, *J*11.5,

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3.5Hz, C(2)H), 3.12-3.14 (1H, m, C(3)H), 3.16 (1H, ddd, J_{11} , 7.5, 4Hz, C(11)H), 3.39 (1H, ddd, J_{11} , 7.5, 4Hz, C(11)H'), 3.44 (1H, d, $J_{13.5}$ Hz, C(5)H), 3.57 (1H, dd, $J_{11.5}$, 10Hz, C(2)H'), 3.77 (1H, d, $J_{13.5}$ Hz, C(5)H'), 7.02 (1H, d, $J_{7.5}$ Hz, aryl CH), 7.08-7.10 (2H, m, aryl CH), 7.18-7.30 (10H, m, aryl CH); δ_c (125MHz, CDCl₃) 35.18 (PhCH₂), 35.53 (C10), 36.52 (CH₃), 57.13 (C5), 57.34 (C3), 69.75 (C2 & C11), 125.65, 126.05, 126.27, 126.96, 127.25, 128.40, 129.12, 129.28, 129.40, 129.59 & 130.22 (11 x CH), 137.59, 138.39, 140.30, 141.68 & 142.36 (5 x quaternary); m/z (ES) 358 (MH⁺, 100%); HRMS found 358.2173, C₂₅H₂₈NO (MH⁺) requires 358.2171.

(P,10S)-10-Benzyl-9-methyl-12-oxa-9-azatetracyclo[12.8.0.0^{2,7}.0^{13,22}]docosa-1(14),2,4,6,15,17(22),18,20-octaene; (P)-3d. Colorless crystals; yield: 92%; kinetic dr: 1.5:1 (*P:M*); m.p. 142-144°C (*i*-PrOH); R_f 0.36 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 93:5:2); ν_{max} (KBr disc)/cm⁻¹ 2940s, 2866s, 1449s, 1340s, 1103s, 1090s, 1056s, 826s, 759s, 638s; δ_H (500MHz, CDCl₃) 2.25 (1H, dd, $J_{13.5}$, 8.5Hz, PhCHH'), 2.27 (3H, s, NCH₃), 2.33-2.39 (1H, m, C(3)H), 2.46 (1H, dd, $J_{13.5}$, 6Hz, PhCHH'), 3.21 (1H, dd, $J_{12.5}$, 4Hz, C(2)H), 3.35 (1H, dd, $J_{12.5}$, 10Hz, C(2)H'), 3.42 (1H, d, J_{15} Hz, C(5)H), 3.56 (1H, d, J_{15} Hz, C(5)H'), 4.19 (1H, d, $J_{12.5}$ Hz, C(10)H), 4.69 (1H, d, $J_{12.5}$ Hz, C(10)H'), 6.82 (2H, d, $J_{7.5}$ Hz, aryl CH), 7.09-7.16 (4H, m, aryl CH), 7.28-7.41 (6H, m, aryl CH), 7.46 (1H, t, $J_{7.5}$ Hz, aryl CH), 7.85 (1H, d, $J_{8.5}$ Hz, aryl CH), 7.90 (1H, d, J_{8} Hz, aryl CH); δ_c (100MHz, CDCl₃) 35.72 (CH₃), 38.22 (PhCH₂), 59.72 (C5), 64.96 (C3), 72.99 & 74.35 (C2 & C10), 125.93, 126.10, 126.27, 126.58, 127.22, 127.63, 127.74, 128.16, 128.24, 129.04, 129.55 & 130.89 (12 x CH), 132.83, 133.29, 135.89, 138.82, 139.74, 140.02 & 140.22 (7 x quaternary); m/z (ES) 394 (MH⁺, 100%). Found: C, 85.7; H, 7.05; N, 3.5%. C₂₈H₂₇NO requires C, 85.5; H, 6.90; N, 3.6%.

(M,10S)-10-Benzyl-9-methyl-12-oxa-9-azatetracyclo[12.8.0.0^{2,7}.0^{13,22}]docosa-1(14),2,4,6,15,17(22),18,20-octaene; (M)-3d. Colorless oil; thermodynamic dr: 1:2 (*P:M*); R_f 0.32 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 93:5:2); ν_{max} (thin film)/cm⁻¹ 2929s, 2853s, 1495s, 1454s, 1383s, 1088s, 1064s, 909s, 822s, 733s, 698s; δ_H (500MHz, CDCl₃) 2.32 (3H, s, NCH₃), 2.41 (1H, dd, $J_{13.5}$, 5.5Hz, PhCHH'), 2.64 (1H, dd, $J_{13.5}$, 8.5Hz, PhCHH'), 3.20-3.23 (1H, m, C(3)H), 3.23 (1H, dd, $J_{13.5}$, 9Hz, C(2)H), 3.44 (1H, d, J_{12} Hz, C(5)H), 3.67 (1H, d, J_{12} Hz, C(5)H'), 3.71 (1H, dd, $J_{13.5}$, 4Hz, C(2)H'), 4.35 (1H, d, $J_{10.5}$ Hz, C(10)H), 4.46 (1H, d, $J_{10.5}$ Hz, C(10)H'), 7.02-7.07 (2H, m, aryl CH), 7.15 (1H, dd, J_{7} , 2Hz, aryl CH), 7.21-7.33 (8H, m, aryl CH), 7.45 (1H, td, $J_{6.5}$, 1Hz, aryl CH), 7.57 (1H, d, $J_{8.5}$ Hz, aryl CH), 7.86 (1H, d, $J_{8.5}$ Hz, aryl CH), 7.89 (1H, d, $J_{8.5}$ Hz, aryl CH); δ_c (100MHz, CDCl₃) 36.03 (CH₃), 36.45 (PhCH₂), 54.34 (C3), 56.77 (C5), 67.04 & 68.38 (C2 & C10), 125.98, 126.02, 126.14, 126.69, 127.19, 127.86, 127.95, 128.03, 128.14,

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128.26, 129.33, 130.85 & 131.18 (13 x $\underline{\text{CH}}$), 132.59, 133.49, 138.26, 138.32, 138.90 & 140.20 (6 x quaternary); m/z (ES) 394 (MH^+ , 100%). Found: C, 85.6; H, 6.85; N, 3.7%. $\text{C}_{28}\text{H}_{27}\text{NO}$ requires C, 85.5; H, 6.90; N, 3.6%.

(S)-10-Benzyl-11-methyl-8-oxa-4-thia-11-azatricyclo[11.4.0.0^{2,7}]heptadeca-1(13),2,5,14,16-pentaene; 3e. Colorless crystals; yield: 86%; m.p. 151-152°C (MeOH); R_f 0.14 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 97:2:1); ν_{max} (KBr disc)/ cm^{-1} 2940s, 2860s, 1450s, 1090s, 1064s, 802s, 765s; δ_{H} (500MHz, CDCl_3) 2.31 (1H, dd, J 13.5, 6Hz, PhCHH'), 2.49 (3H, s, NCH_3), 2.60 (1H, dd, J 13.5, 8.5Hz, PhCHH'), 3.27 (1H, dd, J 12.5, 3.5Hz, $\text{C}(2)\text{H}$), 3.30-3.34 (1H, m, $\text{C}(3)\text{H}$), 3.47 (1H, d, J 12.5Hz, $\text{C}(5)\text{H}$), 3.91 (1H, dd, J 12.5, 10.5Hz, $\text{C}(2)\text{H}'$), 3.99 (1H, d, J 10.5Hz, $\text{C}(10)\text{H}$), 4.11 (1H, d, J 12.5Hz, $\text{C}(5)\text{H}'$), 4.37 (1H, d, J 10.5Hz, $\text{C}(10)\text{H}'$), 6.95 (1H, d, J 8Hz, aryl CH), 7.01-7.04 (3H, m, aryl CH), 7.09-7.27 (6H, m, aryl CH), 7.36 (1H, d, J 3.5Hz, aryl CH); δ_{C} (100MHz, CDCl_3) 35.90 (CH_3), 35.94 (PhCH_2), 54.42 (C3), 57.53, 63.58 & 69.36 (C2, C5 & C10), 124.04, 125.99, 126.02, 126.67, 128.16, 128.17, 129.50, 130.39 & 131.19 (9 x $\underline{\text{CH}}$), 136.53, 137.63, 138.44, 140.14 & 143.18 (5 x quaternary); m/z (ES) 344 (MH^+ , 100%). Found: C, 75.9; H, 6.70; N, 4.0; S, 9.5%. $\text{C}_{22}\text{H}_{23}\text{NOS}$ requires C, 75.6; H, 6.65; N, 4.0; S, 9.2%.

(S)-10-Benzyl-17-chloro-9-methyl-12-oxa-21-thia-9-azatetracyclo[12.7.0.0^{2,7}.0^{15,20}]uncosa-1(14),2,4,6,15,17,19-heptaene; 3f. Colorless crystals; yield: 73%; m.p. 126-128°C (*i*-PrOH); R_f 0.31 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 97:2:1); ν_{max} (KBr disc)/ cm^{-1} 2926s, 2854s, 1584m, 1438s, 1421s, 1114s, 1078s, 1039s, 744s, 699s; δ_{H} (500MHz, CDCl_3 , 40°C)¹² 2.25 (1H, dd, J 13.5, 7.5Hz, PhCHH'), 2.48 (3H, s, NCH_3), 2.77 (1H, dd, J 13.5, 6Hz, PhCHH'), 3.25 (1H, d, J 12.5Hz, $\text{C}(5)\text{H}$), 3.28-3.31 (2H, m, $\text{C}(2)\text{H}$ & $\text{C}(3)\text{H}$), 3.64 (1H, dd, J 13.5, 11Hz, $\text{C}(2)\text{H}'$), 4.05 (1H, d, J 12.5Hz, $\text{C}(5)\text{H}'$), 4.69 (1H, d, J 11.5 Hz, $\text{C}(10)\text{H}$), 4.96 (1H, br d, J 11.5Hz, $\text{C}(10)\text{H}'$), 7.04 (2H, d, J 7.5Hz, aryl CH), 7.14-7.34 (8H, m, aryl CH), 7.73 (1H, d, J 8.5Hz, aryl CH), 7.92 (1H, d, J 2Hz, aryl CH); δ_{C} (100MHz, CDCl_3) 33.91, 38.12, 54.39, 61.28, 62.80, 65.19, 122.78, 123.13, 125.26, 126.11, 127.06, 128.43, 128.95, 129.31, 129.71, 131.25, 131.49, 131.91, 133.19, 137.69, 138.07, 140.07, 141.08, 144.47; m/z (ES) 434 (MH^+ , ^{35}Cl , 100%), 436 (MH^+ , ^{37}Cl , 36%); HRMS found 434.1349, $\text{C}_{26}\text{H}_{25}\text{ClNOS}$ (MH^+) requires 434.1345.

(S)-11-Benzyl-12-methyl-9-oxa-3,12-diazatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; 3g. Colorless oil; yield: 70%; R_f 0.26 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 77:20:3); ν_{max} (thin film)/ cm^{-1} 2931s, 2853s, 1567s, 1431s, 1088s, 1062s, 759s, 699s; δ_{H} (500MHz, CDCl_3) 2.33 (1H, dd, J 13.5, 6Hz, PhCHH'), 2.42 (3H, s,

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NCH₃), 2.65 (1H, dd, *J*_{13.5}, 8.5Hz, PhCHH'), 3.29-3.34 (2H, m, C(2)H & C(3)H), 3.54 (1H, d, *J*_{12.5}Hz, C(5)H), 3.84 (1H, td, *J*₁₂, 2Hz, C(2)H'), 3.95 (1H, d, *J*_{12.5}Hz, C(5)H'), 4.24-4.30 (2H, ABq, *J*_{AB} 10.5Hz, C(10)H₂), 7.00 (1H, d, *J*₈Hz, aryl CH), 7.05 (2H, d, *J*_{8.5}Hz, aryl CH), 7.16-7.31 (7H, m, aryl CH), 7.73 (1H, dd, *J*₈, 2Hz, aryl CH), 8.63 (1H, dd, *J*₅, 2Hz, aryl CH); δ_c (100MHz, CDCl₃) 35.67 (CH₃), 35.73 (PhCH₂), 54.67 (C3), 57.27, 67.85 & 69.01 (C2, C5 & C10), 122.69, 126.08, 127.12, 128.18, 128.41, 129.40, 129.67 & 130.18 (8 x CH), 131.26 & 136.97 (2 x quaternary), 138.25 (CH), 139.98 & 140.20 (2 x quaternary), 149.34 (CH), 159.86 (quaternary); *m/z* (ES) 345 (MH⁺, 100%); HRMS found 345.1970, C₂₃H₂₅N₂O (MH⁺) requires 345.1967.

(*P*,10*S*,11*S*)-9,10-Dimethyl-11-phenyl-12-oxa-9-

azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*P*)-3h. Colorless crystals; yield: 88%; kinetic dr: 17:1 (*P*:*M*); m.p. 97-98°C (MeOH); *R_f* 0.38 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 98:1:1); [α]_D +25.8 (c=0.66, CH₂Cl₂); *v*_{max} (KBr disc)/cm⁻¹ 2933s, 1452s, 1071s, 758s, 701s; δ_H (500MHz, CDCl₃) 0.64 (3H, d, *J*_{6.5}Hz, C(3)CH₃), 2.29 (3H, s, NCH₃), 2.61-2.64 (1H, m, C(3)H), 3.50 (1H, d, *J*₁₄Hz, C(5)H), 3.53 (1H, d, *J*₉Hz, C(2)H), 3.95 (1H, d, *J*_{11.5}Hz, C(10)H), 4.06 (1H, d, *J*₁₄Hz, C(5)H'), 4.33 (1H, d, *J*_{11.5}Hz, C(10)H'), 7.05 (2H, d, *J*₇Hz, aryl CH), 7.10 (1H, d, *J*_{7.5}Hz, aryl CH), 7.22-7.38 (8H, m, aryl CH), 7.44 (1H, t, *J*_{7.5}Hz, aryl CH), 7.23 (1H, d, *J*_{7.5}Hz, aryl CH); δ_c (125MHz, CDCl₃) 15.36 (C(3)CH₃), 45.72 (NCH₃), 55.87 (C5), 64.21 (C3), 72.16 (C10), 87.55 (C2), 126.21, 127.23, 127.30, 127.43, 127.44, 127.58, 128.16, 128.76, 129.36, 129.88 & 129.93 (11 x CH), 137.90, 140.90, 140.94, 142.02 & 142.62 (5 x quaternary); *m/z* (ES) 344 (MH⁺, 100%). Found: C, 83.9; H, 7.40; N, 4.0%. C₂₄H₂₅NO requires C, 83.9; H, 7.35; N, 4.1%.

(*M*,10*S*,11*S*)-9,10-Dimethyl-11-phenyl-12-oxa-9-

azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*M*)-3h. Colorless oil; thermodynamic dr: 1:1.5 (*P*:*M*); *R_f* 0.30 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 98:1:1); [α]_D +55.3 (c=0.62, CH₂Cl₂); *v*_{max} (thin film)/cm⁻¹ 2928s, 2871s, 2790s, 1451s, 1364s, 1195s, 1084s, 1061s, 754s, 700s; δ_H (500MHz, CDCl₃) 0.67 (3H, d, *J*_{6.5}Hz, C(3)CH₃), 2.58 (3H, s, NCH₃), 3.20 (1H, d, *J*_{13.5}Hz, C(5)H), 3.26-3.30 (1H, m, C(3)H), 3.74 (1H, d, *J*_{13.5}Hz, C(5)H'), 4.16 (1H, d, *J*₁₀Hz, C(2)H), 4.24 (1H, d, *J*₁₂Hz, C(10)H), 5.09 (1H, d, *J*₁₂Hz, C(10)H'), 7.15-7.21 (2H, m, aryl CH), 7.27-7.44 (10H, m, aryl CH), 7.53 (1H, d, *J*_{7.5}Hz, aryl CH); δ_c (125MHz, CDCl₃) 10.37 (C(3)CH₃), 40.59 (NCH₃), 52.12 (C5), 61.62 (C3), 68.51 (C10), 78.54 (C2), 126.53, 127.10, 127.39, 127.59, 127.68, 128.06, 128.25, 129.44, 129.76, 129.90 & 130.55 (11 x CH), 136.04, 138.55, 140.49, 140.73 &

¹² At 25°C C(10)H' appears as a broad singlet.

Supporting Information

142.66 (5 x quaternary); m/z (ES) 344 (MH^+ , 100%). Found: C, 84.0; H, 7.40; N, 4.0%. $C_{24}H_{25}NO$ requires C, 83.9; H, 7.35; N, 4.1%.

(*P*,10*S*,11*S*)-5,16-Dichloro-9,10-dimethyl-11-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*P*)-3i. Colorless crystals; yield: 94%; kinetic dr: 6:1 (*P*:*M*); m.p. 169.5-170.5°C (MeOH); R_f 0.56 (base-washed SiO_2 ; Hexane); $[\alpha]_D +99.7$ ($c=1.70$, CH_2Cl_2); ν_{max} (KBr disc)/ cm^{-1} 2910s, 2783s, 2763s, 1589m, 1453s, 1224s, 1096s, 1084s, 821s, 767s, 703s; δ_H (500MHz, $CDCl_3$) 0.68 (3H, d, $J_{6,5}Hz$, C(3) \underline{CH}_3), 2.36 (3H, s, NCH_3), 2.65 (1H, dq, $J_{9,5}$, 6.5Hz, C(3) \underline{H}), 3.48 (1H, d, 14.5Hz, C(5) \underline{H}), 3.61 (1H, d, $J_{9,5}Hz$, C(2) \underline{H}), 3.83 (1H, d, $J_{11}Hz$, C(10) \underline{H}), 4.09 (1H, $J_{14.5}Hz$, C(5) \underline{H}'), 4.26 (1H, d, $J_{11}Hz$, C(10) \underline{H}'), 7.02 (1H, d, $J_{8}Hz$, aryl \underline{CH}), 7.12-7.15 (3H, m, aryl \underline{CH}), 7.29-7.39 (6H, m, aryl \underline{CH}), 7.82 (1H, d, $J_{2}Hz$, aryl \underline{CH}); δ_C (100MHz, $CDCl_3$) 16.22 (C(3) \underline{CH}_3), 45.62 (NCH_3), 55.58 (C5), 63.99 (C3), 71.26 (C10), 87.51 (C2), 126.19, 127.02, 127.48, 127.55, 128.12, 129.03, 129.65, 130.12 & 131.06 (9 x \underline{CH}), 132.95, 133.52, 137.28, 139.29, 139.54, 140.98 & 142.95 (7 x quaternary); m/z (ES) 412 (MH^+ , ^{35}Cl , 100%), 414 (MH^+ , ^{37}Cl , 62%). Found: C, 70.0; H, 5.70; Cl, 17.1; N, 3.4%. $C_{24}H_{23}Cl_2NO$ requires C, 69.9; H, 5.60; Cl, 17.2; N, 3.4%.

(*M*,10*S*,11*S*)-5,16-Dichloro-9,10-dimethyl-11-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*M*)-3i. Colorless oil; thermodynamic dr: 1:2 (*P*:*M*); R_f 0.28 (base-washed SiO_2 ; Hexane); $[\alpha]_D +28.5$ ($c=0.80$, CH_2Cl_2); ν_{max} (thin film)/ cm^{-1} 2928s, 2795s, 1591m, 1470s, 1193s, 1099s, 909s, 732s, 701s; δ_H (500MHz, $CDCl_3$) 0.65 (3H, d, $J_{7}Hz$, C(3) \underline{CH}_3), 2.49 (3H, s, NCH_3), 3.17 (1H, d, $J_{14}Hz$, C(5) \underline{H}), 3.16-3.19 (1H, m, C(3) \underline{H}), 3.60 (1H, d, $J_{14}Hz$, C(5) \underline{H}'), 4.00 (1H, d, $J_{10}Hz$, C(2) \underline{H}), 4.07 (1H, d, $J_{12}Hz$, C(10) \underline{H}), 4.87 (1H, d, $J_{12}Hz$, C(10) \underline{H}'), 7.02 (1H, d, $J_{8.5}Hz$, aryl \underline{CH}), 7.06 (1H, d, $J_{8.5}Hz$, aryl \underline{CH}), 7.25-7.39 (8H, m, aryl \underline{CH}), 7.49 (1H, d, $J_{2}Hz$, aryl \underline{CH}); δ_C (100MHz, $CDCl_3$) 10.73 (C(3) \underline{CH}_3), 40.43 (NCH_3), 52.38 (C5), 61.27 (C3), 68.17 (C10), 79.63 (C2), 126.64, 127.74, 127.76, 127.87, 128.30, 129.21, 129.64, 130.46 & 131.42 (9 x \underline{CH}), 132.95, 133.25, 137.93, 138.00, 139.68, 139.89 & 141.10 (7 x quaternary); m/z (ES) 412 (MH^+ , Cl^{35} , 100%), 414 (MH^+ , Cl^{37} , 60%). Found: C, 70.0; H, 5.75; Cl, 17.1; N, 3.4%. $C_{24}H_{23}Cl_2NO$ requires C, 69.9; H, 5.60; Cl, 17.2; N, 3.4%.

(*P*,10*S*)-10-Benzyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*P*)-3j. Colorless crystals; yield: 92%; kinetic dr: 16:1 (*P*:*M*); m.p. 143-144°C (MeOH); R_f 0.18 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 88:10:2); $[\alpha]_D +1.93$ ($c=1.50$, CH_2Cl_2); ν_{max} (KBr disc)/ cm^{-1} 2986s, 2919s, 1604m, 1509s, 1438s, 1245s, 1101s, 951s, 865s, 758s, 699s; δ_H (500MHz, $CDCl_3$)

Supporting Information

2.33 (1H, dd, J_{13} , 8.5Hz, PhCHH'), 2.40 (3H, s, NCH₃), 2.40-2.45 (1H, m, C(3)H), 2.60 (1H, dd, J_{13} , 5.5Hz, PhCHH'), 3.26-3.35 (2H, m, C(2)H₂), 3.51 (1H, d, $J_{14.5}$ Hz, C(5)H), 3.85 (1H, d, $J_{14.5}$ Hz, C(5)H'), 3.84' (3H, s, OCH₃), 3.96 (3H, s, OCH₃), 4.15 (1H, d, J_{12} Hz, C(10)H), 4.51 (1H, d, J_{12} Hz, C(10)H'), 6.65 (1H, s, aryl CH), 6.96-6.97 (3H, m, aryl CH), 7.17-7.28 (5H, m, aryl CH), 7.35-7.42 (2H, m, aryl CH); δ_c (125MHz, CDCl₃) 36.91 (NCH₃), 37.96 (PhCH₂), 55.80 & 55.82 (OCH₃), 58.32 (C5), 64.78 (C3), 72.27 (C2), 73.42 (C10), 111.81, 113.28, 125.67, 127.27, 127.88, 127.96, 128.83, 129.21 & 130.02 (9 x CH), 131.29, 132.73, 138.31, 139.81, 142.65, 146.84 & 147.30 (7 x quaternary); m/z (ES) 404 (MH⁺, 100%). Found: C, 77.0; H, 7.05; N, 3.4%. C₂₆H₂₉NO₃ requires C, 77.4; H, 7.25; N, 3.5%.

(*M*,10*S*)-10-Benzyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*M*)-3j. Colorless crystals; thermodynamic dr: 1:11 (*P*:*M*); m.p. 146-148°C (MeOH); R_f 0.26 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 87:10:3); $[\alpha]_D^{25} +10.4$ ($c=1.08$, CH₂Cl₂); ν_{max} (KBr disc)/cm⁻¹ 2936s, 2848s, 1512s, 1243s, 1206s, 1143s, 1090s, 755s, 699s; δ_H (500MHz, CDCl₃) 2.36 (1H, dd, $J_{13.5}$, 6Hz, PhCHH'), 2.51 (3H, s, NCH₃), 2.68 (1H, dd, $J_{13.5}$, 9Hz, PhCHH'), 3.30 (1H, dd, J_{12} , 4Hz, C(2)H), 3.43-3.48 (1H, m, C(3)H), 3.52 (1H, d, J_{12} Hz, C(5)H), 3.56 (3H, s, OCH₃), 3.83 (3H, s, OCH₃), 3.92 (1H, t, $J_{11.5}$ Hz, C(2)H'), 4.01 (1H, d, J_{12} Hz, C(5)H'), 4.22 (1H, d, $J_{9.5}$ Hz, C(10)H), 4.30 (1H, d, $J_{9.5}$ Hz, C(10)H'), 6.56 (1H, s, aryl CH), 6.68 (1H, s, aryl CH), 7.11-7.46 (9H, m, aryl CH); δ_c (100MHz, CDCl₃) 35.18, 35.82, 52.58, 55.71, 55.75, 57.24, 68.04, 68.66, 111.58, 112.51, 125.65, 127.49, 127.92, 128.10, 129.15, 129.36, 130.15, 130.63, 132.61, 134.95, 139.79, 141.55, 146.96, 148.26; m/z (ES) 404 (MH⁺, 100%). Found: C, 77.2; H, 7.35; N, 3.4%. C₂₆H₂₉NO₃ requires C, 77.4; H, 7.25; N, 3.5%.

(*M*,10*R*)-4,5-dimethoxy-9-methyl-10-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*M*)-3k. Colorless oil; yield: 84%; kinetic dr: 1:23 (*P*:*M*); R_f 0.18 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); ν_{max} (thin film)/cm⁻¹ 2907s, 2864s, 2788m, 1604m, 1512s, 1243s, 1206s, 1134s, 1102s, 758s, 732s, 702s; δ_H (500MHz, CDCl₃) 2.30 (3H, s, NCH₃), 3.21 (1H, t, J_{10} Hz, C(2)H), 3.36 (1H, d, $J_{14.5}$ Hz, C(5)H), 3.45 (1H, dd, J_{10} ; 2Hz, C(3)H), 3.55 (1H, dd, J_{10} ; 2Hz, C(2)H'), 3.83 (3H, s, OCH₃), 3.86 (1H, d, $J_{10.5}$ Hz, C(10)H), 4.07 (3H, s, OCH₃), 4.19 (1H, d, $J_{14.5}$ Hz, C(5)H'), 4.45 (1H, d, $J_{10.5}$ Hz, C(10)H'), 7.22 (1H, s, aryl CH), 7.23-7.39 (9H, m, aryl CH), 7.61 (1H, s, aryl CH); δ_c (125MHz, CDCl₃) 46.02 (NCH₃), 55.44 (C5), 56.19 & 56.23 (OCH₃), 70.58 (C3), 73.32 (C2), 76.21 (C10), 112.56, 112.95, 127.35, 127.77, 127.79, 128.41, 128.58, 129.14 & 130.54 (9 x CH), 131.34, 134.16, 137.68,

Supporting Information

142.82, 143.28, 146.90 & 148.58 (7 x quaternary); m/z (ES) 390 (MH^+ , 100%); HRMS found 390.2086, $C_{25}H_{28}NO_3$ (MH^+) requires 390.2069.

(*P*,10*R*)-4,5-dimethoxy-9-methyl-10-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*P*)-3k. Colorless crystals; thermodynamic dr: 2:1 (*P*:*M*); m.p. 197-199°C (EtOH); R_f 0.33 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 90:7:3); ν_{max} (KBr disc)/ cm^{-1} 2933m, 2846m, 1604m, 1514s, 1241s, 1207s, 1139s, 756s, 733s, 699s; δ_H (500MHz, $CDCl_3$) 2.32 (3H, s, NCH_3), 3.64 (1H, d, $J_{12}12$ Hz, C(5) H), 3.78 (1H, dd, $J_{11}1.5$, 3.5Hz, C(3) H), 3.85 (3H, s, OCH_3), 3.99 (3H, s, OCH_3), 4.12 (1H, d, $J_{12}12$ Hz, C(5) H), 4.31 (1H, dd, $J_{10}1.5$, 3.5Hz, C(2) H), 4.35 (1H, d, $J_{11}1.5$ Hz, C(2) H), 4.37-4.40 (2H, ABq, $J_{AB}7.5$ Hz, C(10) H_2), 6.62 (1H, s, aryl CH), 7.22-7.25 (2H, m, aryl CH), 7.29-7.34 (5H, m, aryl CH), 7.38-7.43 (2H, m, aryl CH), 7.48-7.50 (1H, m, aryl CH); δ_C (100MHz, $CDCl_3$) 36.12 (NCH_3), 53.38 (C3), 56.24 & 56.33 (OCH_3), 57.51 (C5), 66.60 & 68.39 (C2 & C10), 111.99, 113.22, 127.00, 127.84, 128.00, 128.34 & 128.55 (7 x CH), 130.29 (quaternary), 130.63 & 131.14 (2 x CH), 133.48, 135.37, 140.82, 142.03, 147.64 & 148.86 (6 x quaternary); m/z (ES) 390 (MH^+ , 100%); HRMS found 390.2055, $C_{25}H_{28}NO_3$ (MH^+) requires 390.2069.

(*P*,10*S*)-10-*tert*-Butyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*P*)-3l. Colorless oil; yield: 83%; kinetic dr: 4:1 (*P*:*M*); R_f 0.30 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 93:5:2); ν_{max} (thin film)/ cm^{-1} 2950s, 1515s, 1484s, 1464s, 1337s, 1236s, 1210s, 1109s; δ_H (500MHz, $CDCl_3$) 0.61 (9H, s, $C(CH_3)_3$), 1.52 (1H, dd, J_{11} , 4.5Hz, C(3) H), 2.28 (3H, s, NCH_3), 3.42 (1H, dd, J_{13} , 4.5Hz, C(2) H), 3.63-3.74 (2H, ABq, $J_{AB}14$ Hz, C(5) H_2), 3.70 (1H, dd, J_{13} , 11Hz, C(2) H), 3.82 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 4.08 (1H, d, $J_{12}12.5$ Hz, C(10) H), 4.89 (1H, d, $J_{12}12.5$ Hz, C(10) H), 6.69 (1H, s, aryl CH), 6.74 (1H, s, aryl CH), 7.20 (1H, d, $J_{7}7.5$ Hz, aryl CH), 7.31 (1H, t, $J_{7}7$ Hz, aryl CH), 7.34 (1H, d, $J_{6}6.5$ Hz, aryl CH), 7.39 (1H, t, $J_{7}7.5$ Hz, aryl CH); δ_C (100MHz, $CDCl_3$) 27.26, 34.70, 35.83, 55.76, 55.79, 61.95, 68.38, 69.74, 73.62, 111.44, 114.58, 126.92, 127.73, 129.23, 129.78, 130.21, 133.26, 138.82, 143.47, 146.33, 146.65; m/z (ES) 370 (MH^+ , 100%); HRMS found 370.2390, $C_{23}H_{32}NO_3$ (MH^+) requires 370.2382.

(*M*,10*S*)-10-*tert*-Butyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*M*)-3l. Colorless oil; thermodynamic dr: 1:2 (*P*:*M*); R_f 0.45 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 93:5:2); ν_{max} (thin film)/ cm^{-1} 2951s, 2847m, 1605m, 1513s, 1242s, 1207s, 1141s, 1090s, 755m; δ_H (500MHz, $CDCl_3$) 0.94 (9H, s, $C(CH_3)_3$), 2.42 (3H, s, NCH_3), 2.83 (1H, dd, $J_{10}1.5$, 3.5Hz,

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C(3)H), 3.52 (1H, dd, J_{12} , 3.5Hz, C(2)H), 3.54 (1H, d, J_{12} Hz, C(5)H), 3.85 (3H, s, OCH₃), 3.92 (1H, d, J_{12} Hz, C(5)H'), 3.94 (3H, s, OCH₃), 4.07 (1H, dd, J_{12} , 10.5Hz, C(2)H'), 4.19 (1H, d, $J_{9.5}$ Hz, C(10)H), 4.26 (1H, d, $J_{9.5}$ Hz, C(10)H'), 6.58 (1H, s, aryl CH), 7.15 (1H, s, aryl CH), 7.15-7.17 (1H, m, aryl CH), 7.36-7.38 (2H, m, aryl CH), 7.43-7.45 (1H, m, aryl CH); δ_c (100MHz, CDCl₃) 29.25, 33.78, 37.91, 55.67, 55.74, 57.12, 59.60, 65.00, 67.50, 112.52, 112.71, 127.48, 128.05, 130.15, 130.30, 130.89, 133.18, 135.02, 141.70, 147.30, 148.08; m/z (ES) 370 (MH⁺, 100%); HRMS found 370.2389, C₂₃H₃₂NO₃ (MH⁺) requires 370.2382.

(P,10S)-10-Cyclohexylmethyl-4,5-dimethoxy-9-methyl-12-oxa-9-

azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-3m. Colorless oil; yield: 88%; kinetic dr: 22:1 (*P:M*); R_f 0.28 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 90:7:3); ν_{max} (thin film)/cm⁻¹ 2920s, 2848s, 1605m, 1515s, 1485s, 1446s, 1344s, 1241s, 1212s, 1138s, 1109s, 1028s, 753s, 601s; δ_H (500MHz, CDCl₃) 0.58-0.63 (1H, m), 0.70-0.78 (2H, m), 0.99-1.18 (5H, m), 1.29 (1H, br d, J_{13} Hz), 1.49 (1H, br d, $J_{12.5}$ Hz), 1.57-1.62 (3H, m), 2.07-2.13 (1H, m, C(3)H), 2.23 (3H, s, NCH₃), 3.16 (1H, dd, $J_{12.5}$, 4.5Hz, C(2)H), 3.29 (1H, dd, $J_{12.5}$, 3.5Hz, C(2)H'), 3.55 (1H, d, $J_{14.5}$ Hz, C(5)H), 3.82 (3H, s, OCH₃), 3.84 (1H, d, $J_{14.5}$ Hz, C(5)H'), 3.93 (3H, s, OCH₃), 4.19 (1H, d, J_{12} Hz, C(10)H), 4.60 (1H, d, J_{12} Hz, C(10)H'), 6.65 (1H, s, aryl CH), 6.88 (1H, s, aryl CH), 7.21 (1H, d, J_{8} Hz, aryl CH), 7.32-7.38 (3H, m, aryl CH); δ_c (100MHz, CDCl₃) 26.46, 26.51, 26.88, 33.27, 34.03, 34.75, 35.40, 39.32, 56.13, 56.17, 59.14, 60.33, 73.91, 74.08, 112.27, 113.93, 127.62, 128.09, 129.61, 130.35, 131.36, 133.43, 138.93, 143.02, 147.26, 147.51; m/z (ES) 410 (MH⁺, 100%); HRMS found 410.2714, C₂₆H₃₆NO₃ (MH⁺) requires 410.2695.

(M,10S)-10-Cyclohexylmethyl-4,5-dimethoxy-9-methyl-12-oxa-9-

azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-3m Colorless crystals; thermodynamic dr: 1:11 (*P:M*); m.p. 167-169°C (EtOH); R_f 0.35 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 90:7:3); ν_{max} (KBr disc)/cm⁻¹ 2921s, 2847s, 1514s, 1242s, 1207s, 1142s, 1090s, 755s; δ_H (500MHz, CDCl₃) 0.69-0.76 (1H, m), 0.85-0.93 (2H, m), 1.06-1.29 (4H, m), 1.37-1.43 (1H, m), 1.56-1.69 (5H, m), 2.32 (3H, s, NCH₃), 3.15 (1H, dd, $J_{12.5}$, 8.5Hz, C(2)H), 3.19-3.22 (1H, m, C(3)H), 3.52 (1H, d, $J_{12.5}$ Hz, C(5)H), 3.76 (1H, dd, $J_{12.5}$, 10Hz, C(2)H'), 3.85 (3H, s, OCH₃), 3.96 (3H, s, OCH₃), 3.98 (1H, d, $J_{12.5}$ Hz, C(5)H'), 4.25-4.32 (2H, ABq, J_{AB} 10Hz, C(10)H₂), 6.58 (1H, s, aryl CH), 7.15 (1H, s, aryl CH), 7.18-7.20 (1H, m, aryl CH), 7.35-7.40 (2H, m, aryl CH), 7.44-7.45 (1H, m, aryl CH); δ_c (100MHz, CDCl₃) 26.71, 26.81, 27.01, 33.76, 34.45, 34.74, 35.60, 38.14, 48.02, 56.17, 56.24, 57.63, 68.11, 69.30, 112.08, 113.15, 127.90, 128.40, 130.22, 130.50, 131.04, 133.31,

Supporting Information

135.47, 142.02, 147.44, 148.68; m/z (ES) 410 (MH^+ , 100%); HRMS found 410.2714, $C_{26}H_{36}NO_3$ (MH^+) requires 410.2695.

(*P*,10*S*)-10-Isobutyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*P*)-3n. Colorless oil; yield: 97%; kinetic dr: 35:1 (*P*:*M*); R_f 0.40 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 87:10:3); ν_{max} (thin film)/ cm^{-1} 2952s, 2866s, 1605m, 1515s, 1485s, 1464s, 1239s, 1212s, 1138s, 1111s, 1096s, 1046s, 913s, 732s; δ_H (500MHz, $CDCl_3$) 0.60 (3H, d, $J_{6.5Hz}$, $CHCH_3$), 0.69-0.74 (1H, m, $CHH'CH(CH_3)_2$), 0.77 (3H, d, $J_{6.5Hz}$, $CHCH_3$), 1.02-1.08 (1H, m, $CHH'CH(CH_3)_2$), 1.44-1.52 (1H, m, $CH(CH_3)_2$), 2.05-2.10 (1H, m, C(3) H), 2.26 (3H, s, NCH_3), 3.16 (1H, dd, $J_{12.5}$, 4.5Hz, C(2) H), 3.34 (1H, dd, $J_{12.5}$, 10Hz, C(2) H'), 3.59 (1H, d, $J_{14.5Hz}$, C(5) H), 3.85 (3H, s, OCH_3), 3.88 (1H, d, $J_{14.5Hz}$, C(5) H'), 3.95 (3H, s, OCH_3), 4.20 (1H, d, J_{12Hz} , C(10) H), 4.68 (1H, d, J_{12Hz} , C(10) H'), 6.69 (1H, s, aryl CH), 6.89 (1H, s, aryl CH), 7.23 (1H, d, J_{7Hz} , aryl CH), 7.34-7.41 (3H, m, aryl CH); δ_C (100MHz, $CDCl_3$) 22.54 & 23.50 ($CH(CH_3)_2$), 25.29 ($CH(CH_3)_2$), 34.87 (NCH_3), 40.79 ($CH_2CH(CH_3)_2$), 56.16 & 56.22 (OCH_3), 59.46 (C5), 61.02 (C3), 74.01 (C2 & C10), 112.21, 113.99, 127.62, 128.06, 129.57 & 130.31 (6 x CH), 131.22, 133.46, 138.91, 143.00, 147.21 & 147.40 (6 x quaternary); m/z (ES) 370 (MH^+ , 100%); HRMS found 370.2368, $C_{23}H_{32}NO_3$ (MH^+) requires 370.2382.

(*M*,10*S*)-10-Isobutyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*M*)-3n Colorless crystals; thermodynamic dr: 1:10 (*P*:*M*); m.p. 146-147°C (EtOH); R_f 0.32 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 93:5:2); ν_{max} (KBr disc)/ cm^{-1} 2951s, 2847s, 1513s, 1242s, 1207s, 1141s, 1090s, 755s; δ_H (500MHz, $CDCl_3$) 0.76 (3H, d, $J_{6.5Hz}$, $CHCH_3$), 0.78-0.81 (1H, m, $CHH'CH(CH_3)_2$), 0.88 (3H, d, J_{7Hz} , $CHCH_3$), 1.25-1.31 (1H, m, $CHH'CH(CH_3)_2$), 1.75-1.80 (1H, m, $CH(CH_3)_2$), 2.34 (3H, s, NCH_3), 3.15 (1H, dd, $J_{13.5}$, 3.5Hz, C(2) H), 3.16-3.21 (1H, m, C(3) H), 3.53 (1H, d, $J_{12.5Hz}$, C(5) H), 3.79 (1H, dd, $J_{12.5}$, 10.5Hz, C(2) H'), 3.85 (3H, s, OCH_3), 3.93 (3H, s, OCH_3), 4.00 (1H, d, $J_{12.5Hz}$, C(5) H'), 4.29 (2H, ABq, J_{AB} 10Hz, C(10) H), 6.59 (1H, s, aryl CH), 7.16 (1H, s, aryl CH), 7.18-7.20 (1H, m, aryl CH), 7.35-7.40 (2H, m, aryl CH), 7.43-7.45 (1H, m, aryl CH); δ_C (100MHz, $CDCl_3$) 23.31 & 24.08 ($CH(CH_3)_2$), 25.11 ($CH(CH_3)_2$), 35.46 (NCH_3), 39.24 ($CH_2CH(CH_3)_2$), 48.61 (C3), 55.98 & 56.12 (OCH_3), 57.65 (C5), 68.14 & 69.44 (C2 & C10), 112.04, 113.11, 127.89 & 128.44 (4 x CH), 130.30 (quaternary), 130.57 & 131.10 (2 x CH), 133.29, 135.49, 142.01, 147.44 & 148.63 (5 x quaternary); m/z (ES) 370 (MH^+ , 100%). Found: C, 75.0; H, 8.55; N, 3.8%. $C_{23}H_{31}NO_3$ requires C, 74.8; H, 8.45; N, 3.8%.

Supporting Information

(M,10R)-10-Ethyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-3o. Colorless oil; yield: 91%; kinetic dr: 1:25 (*P:M*); R_f 0.30 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 90:7:3); ν_{max} (thin film)/cm⁻¹ 2932s, 1605m, 1515s, 1464s, 1244s, 1210s, 1138s, 1028s, 756m; δ_H (500MHz, CDCl₃) 0.73 (3H, t, J 7.5Hz, CH₂CH₃), 1.12-1.25 (2H, m, CH₂CH₃), 1.96-2.01 (1H, m, C(3)H), 2.28 (3H, s, NCH₃), 3.24 (1H, dd, J 12.5, 9.5Hz, C(2)H), 3.31 (1H, dd, J 12.5, 4Hz, C(2)H'), 3.49 (1H, d, J 14.5Hz, C(5)H), 3.81 (3H, s, OCH₃), 3.87 (1H, d, J 14.5Hz, C(5)H'), 3.93 (3H, s, OCH₃), 4.25 (1H, d, J 12Hz, C(10)H), 4.42 (1H, d, J 12Hz, C(10)H'), 6.61 (1H, s, aryl CH), 7.02 (1H, s, aryl CH), 7.19 (1H, dd, J 6.5, 2Hz, aryl CH), 7.29-7.37 (3H, m, aryl CH); δ_C (100MHz, CDCl₃) 11.05 (CH₂CH₃), 24.36 (CH₂CH₃), 38.12 (NCH₃), 56.08 & 56.13 (OCH₃), 58.48 (C5), 65.30 (C3), 73.75 (C2 & C10), 112.30, 113.65, 127.60, 128.12, 129.41 & 130.35 (6 x CH), 132.17, 132.91, 138.68, 142.94, 147.11 & 147.74 (6 x quaternary); m/z (ES) 342 (MH⁺, 100%); HRMS found 342.2085, C₂₁H₂₈NO₃ (MH⁺) requires 342.2069.

(P,10R)-10-Ethyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-3o Colorless crystals; thermodynamic dr: 9:1 (*P:M*); m.p. 136-138°C (EtOH); R_f 0.17 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 90:7:3); ν_{max} (KBr disc)/cm⁻¹ 2934s, 2845s, 1605m, 1513s, 1464s, 1241s, 1207s, 1141s, 1091s, 755s; δ_H (500MHz, CDCl₃) 0.95 (3H, t, J 7Hz, CH₂CH₃), 1.03-1.18 (1H, m, CHH'CH₃), 1.23-1.30 (1H, m, CHH'CH₃), 2.33 (3H, s, NCH₃), 3.03-3.08 (1H, m, C(3)H), 3.19 (1H, dd, J 12.5, 4Hz, C(2)H), 3.55 (1H, d, J 12.5Hz, C(5)H), 3.80 (1H, dd, J 12, 10.5Hz, C(2)H'), 3.85 (3H, s, OCH₃), 3.93 (3H, s, OCH₃), 4.03 (1H, d, J 12.5Hz, C(5)H'), 4.21-4.31 (2H, ABq, J_{AB} 9.5Hz, C(10)H₂), 6.59 (1H, s, aryl CH), 7.19 (1H, s, aryl CH), 7.20 (1H, dd, J 9, 5Hz, aryl CH), 7.35-7.39 (2H, m, aryl CH), 7.42-7.45 (1H, m, aryl CH); δ_C (100MHz, CDCl₃) 11.74, 22.00, 35.04, 51.85, 56.11, 56.17, 57.57, 68.27, 69.58, 112.07, 113.00, 127.87, 128.46, 130.41, 130.57, 131.04, 133.15, 135.43, 141.89, 147.36, 148.63; m/z (ES) 342 (MH⁺, 100%); HRMS found 342.2081, C₂₁H₂₈NO₃ (MH⁺) requires 342.2069.

(M,10R)-4,5-Dimethoxy-9,10-dimethyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-3p. Colorless oil; yield: 94%; kinetic dr: 1:32 (*P:M*); R_f 0.15 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 90:7:3); ν_{max} (thin film)/cm⁻¹ 2931s, 2847s, 1605m, 1514s, 1463s, 1247s, 1209s, 1138s, 1110s, 1028s, 758s, 733s; δ_H (500MHz, CDCl₃) 0.82 (3H, d, J 7Hz, C(3)CH₃), 2.27-2.31 (1H, m, C(3)H), 2.29 (3H, s, NCH₃), 3.17 (1H, dd, J 12, 9.5Hz, C(2)H), 3.28 (1H, dd, J 12, 3.5Hz, C(2)H'), 3.43 (1H, d, J 14.5Hz, C(5)H), 3.82 (3H, s, OCH₃), 3.89 (1H, d, J 14.5Hz,

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C(5)H'), 3.93 (3H, s, OCH₃), 4.28 (1H, d, *J*11.5Hz, C(10)H), 4.42 (1H, d, *J*11.5Hz, C(10)H'), 6.60 (1H, s, aryl CH), 7.01 (1H, s, aryl CH), 7.18-7.20 (1H, m, aryl CH), 7.32-7.36 (3H, m, aryl CH); δ_c (100MHz, CDCl₃) 17.49 (C(3)CH₃), 38.93 (NCH₃), 56.25 (OCH₃), 57.86 (C5), 59.38 (C3), 73.72 & 75.06 (C2 & C10), 112.39, 113.46, 127.59, 128.01, 129.31 & 130.19 (6 x CH), 131.76, 132.89, 138.48, 142.70, 147.05 & 147.67 (6 x quaternary); *m/z* (ES) 328 (MH⁺, 100%); HRMS found 328.1898, C₂₀H₂₆NO₃ (MH⁺) requires 328.1912.

(*P*,10*R*)-4,5-Dimethoxy-9,10-dimethyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (*P*)-3p. Colorless oil; thermodynamic dr: 6:1 (*P*:*M*); *R_f* 0.13 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 77:20:3); ν_{max} (thin film)/cm⁻¹ 2933s, 2845s, 1605m, 1513s, 1242s, 1208s, 1141s, 1092s, 1077s, 756s; δ_H (500MHz, CDCl₃) 0.89 (3H, d, *J*7Hz, C(3)CH₃), 2.39 (3H, s, NCH₃), 3.20 (1H, dd, *J*12.5, 4Hz, C(2)H), 3.34-3.38 (1H, m, C(3)H), 3.53 (1H, d, *J*12.5Hz, C(5)H), 3.78 (1H, dd, *J*12.5, 10.5Hz, C(2)H'), 3.85 (3H, s, OCH₃), 3.94 (3H, s, OCH₃), 3.97 (1H, d, *J*12.5Hz, C(5)H'), 4.24-4.32 (2H, ABq, *J_{AB}*9.5Hz, C(10)H₂), 6.59 (1H, s, aryl CH), 7.14 (1H, s, aryl CH), 7.19-7.21 (1H, m, aryl CH), 7.35-7.40 (2H, m, aryl CH), 7.43-7.45 (1H, m, aryl CH); δ_c (100MHz, CDCl₃) 15.91 (C(3)CH₃), 35.49 (NCH₃), 46.67 (C3), 56.18 & 56.43 (OCH₃), 57.67 (C5), 68.36 & 69.85 (C2 & C10), 111.60, 113.11, 127.90 & 128.44 (4 x CH), 130.19 (quaternary), 130.53 & 131.01 (2 x CH), 133.26, 135.49, 141.87, 147.45 & 148.86 (5 x quaternary); *m/z* (ES) 328 (MH⁺, 100%); HRMS found 328.1898, C₂₀H₂₆NO₃ (MH⁺) requires 328.1912.

(*P*,10*S*)-10-Benzyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[11.4.0.0^{2,7}]heptadeca-1(13),2,4,6,14,16-hexaene; (*P*)-3q. Colorless oil; yield: 97%; kinetic dr: 3:1 (*P*:*M*); *R_f* 0.22 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 77:20:3); ν_{max} (thin film)/cm⁻¹ 2935s, 2845s, 1600m, 1516s, 1488s, 1445s, 1259s, 1213s, 1141s, 1046s, 1025s, 732s, 700s; δ_H (500MHz, CDCl₃) 2.41 (3H, s, NCH₃), 2.52 (1H, dd, *J*13.5, 7.5Hz, PhCHH'), 2.69 (1H, dd, *J*14, 7.5Hz, PhCHH'), 3.18-3.23 (1H, m, C(3)H), 3.36 (1H, d, *J*14Hz, C(5)H), 3.85 (1H, d, *J*14Hz, C(5)H'), 3.86 (3H, s, OCH₃), 3.90 (3H, s, OCH₃), 4.03 (1H, dd, *J*11.5, 9.5Hz, C(2)H), 4.14 (1H, dd, *J*11.5, 2.5Hz, C(2)H'), 6.74 (1H, s, aryl CH), 6.90 (1H, s, aryl CH), 6.99 (1H, d, *J*8.5Hz, aryl CH), 7.08-7.31 (8H, m, aryl CH); δ_c (100MHz, CDCl₃) 35.21 (NCH₃), 37.53 (PhCH₂), 56.18 & 56.40 (OCH₃), 60.26 (C5), 65.72 (C3), 69.76 (C2), 112.95, 114.99, 118.17, 123.06, 126.11, 128.38, 128.96 & 129.08 (8 x CH), 129.92 (quaternary), 130.58 (CH), 131.72, 134.45, 140.19, 147.44, 148.09 & 155.96 (6 x quaternary); *m/z* (ES) 390 (MH⁺, 100%); HRMS found 390.2080, C₂₅H₂₈NO₃ (MH⁺) requires 390.2069.

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(M,10S)-10-Benzyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-3q. Colorless oil; R_f 0.22 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 77:20:3); δ_H (500MHz, CDCl₃) 2.11 (3H, s, NCH₃), 2.58 (1H, dd, J_{14} , 7.5Hz, PhCHH'), 2.75 (1H, dd, J_{14} , 9.5Hz, PhCHH'), 3.09 (1H, d, J_{13} Hz, C(5)H), 3.41-3.44 (1H, m, C(3)H), 3.42 (1H, d, J_{13} Hz, C(5)H), 3.86 (3H, s, OCH₃), 3.91 (3H, s, OCH₃), 3.95-4.05 (2H, m, C(2)H₂), 6.73 (1H, s, aryl CH), 6.81 (1H, s, aryl CH), 6.98 (1H, d, $J_{8.5}$ Hz, aryl CH), 7.08-7.31 (8H, m, aryl CH); δ_C (100MHz, CDCl₃) 36.02 (NCH₃), 36.59 (PhCH₂), 56.18 & 56.35 (OCH₃), 58.37 (C5), 61.71 (C3), 72.84 (C2), 112.58, 112.62, 120.20, 123.17, 126.33, 128.45, 129.08, 129.14 & 129.44 (9 x CH), 130.58, 132.40, 135.47, 139.72, 147.92, 148.09 & 158.80 (7 x quaternary); m/z (ES) 390 (MH⁺, 100%); HRMS found 390.2080, C₂₅H₂₈NO₃ (MH⁺) requires 390.2069.

(P,10S)-10-Isobutyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[11.4.0.0^{2,7}]heptadeca-1(13),2,4,6,14,16-hexaene; (P)-3r. Colorless oil; yield: 93%; kinetic dr: 2:1 (P:M); R_f 0.23 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 93:5:2); ν_{max} (thin film)/cm⁻¹ 2952s, 1599m, 1518s, 1488s, 1464s, 1265s, 1214s, 1138s, 1046s, 750m; δ_H (500MHz, CDCl₃) 0.80 (3H, d, $J_{6.5}$ Hz, CHCH₃), 0.86 (3H, d, $J_{6.5}$ Hz, CHCH₃), 0.88-0.93 (1H, m, C(3)CHH'), 1.25-1.31 (1H, m, C(3)CHH'), 1.67-1.75 (1H, m, CH(CH₃)₂), 2.30 (3H, s, NCH₃), 2.94-3.00 (1H, m, C(3)H), 3.41 (1H, d, $J_{14.5}$ Hz, C(5)H), 3.86 (3H, s, OCH₃), 3.89-3.94 (1H, m, C(2)H), 3.92 (3H, s, OCH₃), 3.94 (1H, d, $J_{14.5}$ Hz, C(5)H), 4.11 (1H, dd, J_{12} , 3Hz, C(2)H'), 6.74 (1H, s, aryl CH), 6.88 (1H, s, aryl CH), 7.09-7.36 (4H, m, aryl CH); δ_C (100MHz, CDCl₃) 22.47 & 23.66 (CH(CH₃)₂), 25.48 (CH(CH₃)₂), 33.22 (NCH₃), 39.26 (C(3)CH₂), 56.15 & 56.38 (OCH₃), 60.71 (C5), 61.56 (C3), 70.83 (C2), 113.00, 115.14, 117.86, 122.90 & 128.90 (5 x CH), 130.06 (quaternary), 130.57 (CH), 131.82, 134.43, 147.29, 148.01 & 155.88 (5 x quaternary); m/z (ES) 356 (MH⁺, 100%); HRMS found 356.2209, C₂₂H₃₀NO₃ (MH⁺) requires 356.2225.

(M,10S)-10-Isobutyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[11.4.0.0^{2,7}]heptadeca-1(13),2,4,6,14,16-hexaene; (M)-3r. Colorless oil; R_f 0.23 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 93:5:2); δ_H (500MHz, CDCl₃) 0.86 (3H, d, $J_{6.5}$ Hz, CHCH₃), 0.88 (3H, d, J_{7} Hz, CHCH₃), 0.90-1.03 (1H, m, C(3)CHH'), 1.36-1.42 (1H, m, C(3)CHH'), 1.67-1.75 (1H, m, CH(CH₃)₂), 2.04 (3H, s, NCH₃), 3.03-3.09 (1H, m, C(3)H), 3.05 (1H, d, $J_{12.5}$ Hz, C(5)H), 3.62 (1H, d, $J_{12.5}$ Hz, C(5)H), 3.87 (3H, s, OCH₃), 3.89-3.96 (2H, m, C(2)H₂), 3.91 (3H, s, OCH₃), 6.75 (1H, s, aryl CH), 7.00 (1H, d, J_{8} Hz, aryl CH), 7.09-7.36 (4H, m, aryl CH); δ_C (100MHz, CDCl₃) 22.04 & 23.88 (CH(CH₃)₂), 25.29 (CH(CH₃)₂), 35.96 (NCH₃), 39.87 (C(3)CH₂), 56.10 & 56.33 (OCH₃), 58.14 (C3),

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58.54 (C5), 74.13 (C2), 112.25, 112.45, 120.53, 123.28, 129.04 & 129.61 (6 x $\underline{\text{CH}}$), 129.62, 132.34, 135.40, 147.96, 148.24 & 158.66 (6 x quaternary); m/z (ES) 356 (MH^+ , 100%); HRMS found 356.2209, $\text{C}_{22}\text{H}_{30}\text{NO}_3$ (MH^+) requires 356.2225.

***rel*-(*P,4S,9S*)-3-Oxa-10-azatetracyclo[16.4.0.0^{4,9}.0^{12,17}]docosa-12,14,16,18,20,22-hexaene; 3s.** Colorless oil; yield: 77%; kinetic dr: 11:1 [*rel*-(*P,4S,9S*) : *rel*-(*M,4S,9S*)]; R_f 0.50 (SiO_2 ; Hexane:EtOAc; 1:1); ν_{max} (thin film)/ cm^{-1} 2929s, 2856s, 1448s, 1089s, 755s; δ_{H} (500MHz, CDCl_3) 0.93 (1H, m), 1.03-1.12 (2H, m), 1.23 (1H, m), 1.57 (1H, m), 1.63 (1H, m), 1.86 (1H, m), 1.98 (1H, m), 2.04 (1H, m, C(3) $\underline{\text{H}}$), 2.17 (3H, s, NCH_3), 2.54 (1H, m, C(2) $\underline{\text{H}}$), 3.48 (1H, d, J 14.5Hz, C(5) $\underline{\text{H}}$), 3.90 (1H, d, J 14.5Hz, C(5) $\underline{\text{H}}'$), 3.97 (1H, d, J 11.5Hz, C(10) $\underline{\text{H}}$), 4.58 (1H, d, J 11.5Hz, C(10) $\underline{\text{H}}'$), 7.09 (1H, dd, J 7.5, 1Hz, aryl $\underline{\text{CH}}$), 7.17 (1H, m, aryl $\underline{\text{CH}}$), 7.26-7.39 (5H, m, aryl $\underline{\text{CH}}$), 7.59 (1H, d, J 7.5Hz, aryl $\underline{\text{CH}}$); δ_{C} (125MHz, CDCl_3) 24.65, 25.19, 29.16, 33.83, 45.32 (NCH_3), 55.53 (C5), 67.64 (C3), 72.03 (C10), 82.93 (C2), 126.04, 127.18, 127.21, 127.40, 128.48, 129.21, 129.48, 129.84, 138.18, 140.59, 140.99, 142.52; m/z (ES) 308 (MH^+ , 100%); HRMS found 308.2027, $\text{C}_{21}\text{H}_{26}\text{NO}$ (MH^+) requires 308.2014.

***rel*-(*3S,8S*)-2-Oxa-9-azatetracyclo[15.4.0.0^{3,8}.0^{11,16}]uncosa-11,13,15,17,19,21-hexaene; 3t.** Colorless oil; yield: 96%; kinetic dr: >50:1 (*P:M*); R_f 0.37 (SiO_2 ; Hexane:EtOAc:Et₃N; 82:17:1); ν_{max} (thin film)/ cm^{-1} 2926s, 2786s, 1473s, 1242s, 1028s, 984s, 745s; δ_{H} (500MHz, C_6D_6) 0.46-0.68 (3H, m), 0.93 (1H, m), 1.00-1.11 (2H, m), 1.18 (1H, m), 1.45 (3H, s, NCH_3), 1.77 (1H, m), 2.36 (1H, m, C(3) $\underline{\text{H}}$), 3.16 (1H, d, J 14Hz, C(5) $\underline{\text{H}}$), 3.28 (1H, m, C(2) $\underline{\text{H}}$), 3.33 (1H, d, J 14Hz, C(5) $\underline{\text{H}}'$), 6.57 (1H, d, J 8Hz, aryl $\underline{\text{CH}}$), 6.63 (1H, m, aryl $\underline{\text{CH}}$), 6.77-6.97 (6H, m, aryl $\underline{\text{CH}}$); δ_{C} (125MHz, CDCl_3) 24.60, 24.97, 25.81, 32.65, 35.33 (NCH_3), 59.29 (C5), 63.06 (C3), 82.39 (C2), 118.15, 121.49, 126.89, 127.09, 127.78, 128.98, 129.53, 130.55, 136.09, 138.25, 140.95, 159.79; m/z (ES) 294 (MH^+ , 100%); HRMS found 294.1849, $\text{C}_{20}\text{H}_{24}\text{NO}$ (MH^+) requires 294.1858.

(*M,3S*)-17-Bromo-5-methyl-3-phenyl-2-oxa-5-azatricyclo[11.4.0.0^{7,12}]heptadeca-7,9,11,13,15,17-hexaene; (*M*)-3u. Colorless oil; yield: 81%; kinetic dr: 1:>50 (*P:M*); R_f 0.48 (SiO_2 ; Hexane:EtOAc:Et₃N; 90:9:1); ν_{max} (thin film)/ cm^{-1} 2926s, 2838s, 2788s, 1495s, 1430s, 1073s, 1012s, 755s, 699s; δ_{H} (500MHz, CDCl_3) 2.34 (3H, s, NCH_3), 2.53 (1H, d, J 15Hz, C(3) $\underline{\text{H}}$), 3.09 (1H, dd, J 15, 9Hz, C(3) $\underline{\text{H}}'$), 3.44 (1H, d, J 13Hz, C(5) $\underline{\text{H}}$), 3.53 (1H, d, J 13Hz, C(5) $\underline{\text{H}}'$), 5.24 (1H, d, J 9Hz, C(2) $\underline{\text{H}}$), 6.96 (1H, t, J 7.5Hz, aryl $\underline{\text{CH}}$), 7.06 (1H, dd, J 7.5, 2Hz, aryl $\underline{\text{CH}}$), 7.18-7.36 (9H, m, aryl $\underline{\text{CH}}$), 7.51 (1H, dd, J 8, 2Hz, aryl $\underline{\text{CH}}$); δ_{C} (125MHz, CDCl_3) 43.27 (NCH_3), 59.24 (C5), 61.84 (C3), 81.26 (C2), 115.20, 124.15, 125.86, 127.20, 127.35, 127.72, 128.13, 128.17, 129.66,

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130.05, 132.75, 136.57, 138.91, 139.88, 141.20, 154.77; m/z (ES) 394 (MH^+ , 100%); HRMS found 394.0815, $C_{22}H_{21}BrNO$ (MH^+) requires 394.0806.

(P,6S)-6-Phenyl-5-oxa-8-azatetracyclo[15.4.0.0^{4,16}.0^{10,15}]uncosa-1,3,10,12,14,16,18,20-octaene; (P)-3v. White solid; yield: 73%; kinetic dr: 1.5:1 (*P:M*); m.p. 60°C; R_f 0.50 (base-washed SiO_2 ; Hexane:EtOAc:Et₃N; 82:17:1); ν_{max} (KBr disc)/ cm^{-1} 2923s, 1458s, 1385s, 1209s, 1018s, 748s, 698s; δ_H (500MHz, $CDCl_3$) 2.36 (3H, s, NCH_3), 3.10 (1H, dd, J_{15} , 3.5Hz, C(3) H), 3.25 (1H, dd, J_{15} , 6.5Hz, C(3) H'), 3.52 (1H, d, $J_{13.5Hz}$, C(5) H), 3.62 (1H, d, $J_{13.5Hz}$, C(5) H'), 5.09 (1H, dd, $J_{6.5}$, 3.5Hz, C(2) H), 7.10 (1H, d, J_{9Hz} , aryl CH), 7.20 (1H, d, J_{8Hz} , aryl CH), 7.28-7.49 (11H, m, aryl CH), 7.52 (1H, d, J_{9Hz} , aryl CH), 7.83 (1H, d, J_{8Hz} , aryl CH); δ_C (100MHz, $CDCl_3$) 43.23 (NCH_3), 60.49, 63.19, 77.69 (C2), 122.91, 124.36, 125.23, 126.37, 126.51, 126.68, 127.83, 127.92, 128.05, 128.18, 128.68, 128.97, 130.19, 131.18, 131.56, 134.21, 136.40, 137.92, 142.40, 152.14; m/z (ES) 366 (MH^+ , 100%); HRMS found 366.1872, $C_{26}H_{24}NO$ (MH^+) requires 366.1858.

(M,6S)-6-Phenyl-5-oxa-8-azatetracyclo[15.4.0.0^{4,16}.0^{10,15}]uncosa-1,3,10,12,14,16,18,20-octaene; (M)-3v. White solid; R_f 0.38 (base-washed SiO_2 ; Hexane:EtOAc:Et₃N; 82:17:1); m.p. 141°C; ν_{max} (KBr disc)/ cm^{-1} 2939s, 2787s, 1448s, 1329s, 1232s, 1020s, 761s, 748s; δ_H (500MHz, $CDCl_3$) 2.48 (3H, s, NCH_3), 2.81 (1H, d, J_{15Hz} , C(3) H), 3.20 (1H, d, $J_{12.5Hz}$, C(5) H), 3.31 (1H, dd, J_{15} , 7Hz, C(3) H'), 3.64 (1H, d, $J_{12.5Hz}$, C(5) H'), 5.10 (1H, d, J_{7Hz} , C(2) H), 7.13 (1H, d, J_{9Hz} , aryl CH), 7.26-7.46 (10H, m, aryl CH), 7.62-7.65 (2H, m, aryl CH), 7.81-7.87 (2H, m, aryl CH); δ_C (125MHz, $CDCl_3$) 44.52 (NCH_3), 57.45 (C3), 63.17 (C5), 82.03 (C2), 120.14, 124.41, 125.54, 125.77, 126.31, 127.11, 127.31, 127.51, 128.13, 128.47, 128.52, 129.62, 130.38, 130.75, 131.12, 132.86, 136.93, 137.33, 142.23, 154.22; m/z (ES) 366 (MH^+ , 100%); HRMS found 366.1872, $C_{26}H_{24}NO$ (MH^+) requires 366.1858.

(M,3S,4R)-4,5-Dimethyl-3-phenyl-2-oxa-5-azatricyclo[11.4.0.0^{7,12}]heptadeca-7,9,11,13,15,17-hexaene; (M)-3w. Colorless oil; yield: 68%; kinetic dr: 1:10 (*P:M*); R_f 0.42 (base-washed SiO_2 ; Hexane:EtOAc:Et₃N; 82:17:1); ν_{max} (thin film)/ cm^{-1} 2935s, 2762s, 1480s, 1228s, 1011s, 740s, 700s; δ_H (500MHz, $CDCl_3$) 0.72 (3H, d, J_{7Hz} , C(3) HCH_3), 2.67 (3H, s, NCH_3), 3.01 (1H, q, J_{7Hz} , C(3) H), 3.38 (1H, d, $J_{13.5Hz}$, C(5) H), 3.67 (1H, d, $J_{13.5Hz}$, C(5) H'), 5.22 (1H, s, C(2) H), 6.80 (1H, m, aryl CH), 7.13-7.39 (11H, m, aryl CH), 7.68 (1H, m, aryl CH); δ_C (125MHz, $CDCl_3$) 14.14 (C(3) CH_3), 47.27 (NCH_3), 57.05 (C5), 69.27 (C3), 82.55 (C2), 118.77, 123.70, 125.61, 126.95, 127.09, 127.29, 128.32, 129.13,

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129.40, 129.88, 130.54, 134.02, 138.22, 138.26, 142.47, 156.85; m/z (ES) 330 (MH^+ , 100%); HRMS found 330.1872, $C_{23}H_{24}NO$ (MH^+) requires 330.1858.

Synthesis of (S)-12-Benzyl-17,18-dimethoxy-13-methyl-10-oxa-13-aza-2-mercura-tricyclo[13.4.0.0^{3,8}]nonadeca-1(15),3,5,7,16,18-hexaene; 4. The dilithium intermediate was prepared from [(S)-1-benzyl-2-(2'-bromobenzyloxy)ethyl]-(2''-bromo-3'',4''-dimethoxybenzyl)methylamine (**1j**) as described in the general procedure above. To the clear yellow solution a freshly prepared solution of dry $HgBr_2$ (1.0 equiv.) in anhydrous 2-MeTHF (ca. 2ml) was added dropwise, then the mixture was stirred for 12 hours allowing the reaction temperature to rise slowly to room temperature. Water and Et_2O was added and the resulting two-phase mixture was separated, and then the aqueous phase was extracted three times with Et_2O . The combined organic layers were dried ($MgSO_4$), filtered, concentrated *in vacuo* and recrystallized from EtOH to give **4** (65%) as colorless crystals; m.p. 156.5-157.5°C (EtOH); R_f 0.32 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 80:15:5); ν_{max} (KBr disc)/ cm^{-1} 2831s, 1498s, 1458s, 1248s, 1208s, 1158s, 1104s, 1048s, 1030s, 737s, 697s; δ_H (500MHz, $CDCl_3$) 2.26 (3H, s, NCH_3), 2.35 (1H, dd, J_{13} , 10.5Hz, $PhCHH'$), 3.10 (1H, br d, J_{12} Hz, $PhCHH'$), 3.36-3.42 (1H, m, C(3) H), 3.52 (1H, dd, J_{11} , 3.5Hz, C(2) H), 3.65-3.73 (2H, br m, C(2) H' & C(5) H), 3.90 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 3.94-4.00 (1H, br m, C(5) H'), 4.29 (1H, d, J_{11} Hz, C(10) H), 4.62 (1H, d, J_{11} Hz, C(10) H'), 6.85 (1H, s, aryl CH), 7.13 (1H, s, aryl CH), 7.15-7.33 (8H, m, aryl CH), 7.55 (1H, d, $J_{7.5}$ Hz, aryl CH); δ_C (100MHz, $CDCl_3$)¹³ 31.20, 56.11, 56.35, 64.75, 69.08, 74.51, 112.48, 121.53, 126.38, 127.18, 127.26, 127.61, 128.78, 129.14, 138.92, 139.79, 140.04, 145.72, 147.23, 148.08, 160.32; m/z (ES) 602 (MH^+ , ^{198}Hg , 14%), 603 (MH^+ , ^{199}Hg , 40%), 604 (MH^+ , ^{200}Hg , 72%), 605 (MH^+ , ^{201}Hg , 38%), 606 (MH^+ , ^{202}Hg , 100%), 607 (MH^+ , ^{202}Hg , ^{13}C , 10%), 608 (MH^+ , ^{204}Hg , 10%); HRMS found 606.1929, $C_{26}H_{30}HgNO_3$ (MH^+) requires 606.1932.

Synthesis of 5 & 6. The dilithium intermediate was prepared from [(S)-1-benzyl-2-(2'-bromobenzyloxy)ethyl]-(2''-bromo-3'',4''-dimethoxybenzyl)methylamine (**1j**) as described in the general procedure above. To the clear yellow solution a freshly prepared solution of Me_2SiCl_2 or Ph_2SiCl_2 (1.0 equiv.) in anhydrous 2-MeTHF (ca. 5ml) was added dropwise, then the mixture was stirred for 12 hours allowing the reaction temperature to slowly rise to room temperature. A solution of 10% NH_4OH in saturated aqueous NH_4Cl was added and the resulting two-phase mixture separated and the aqueous phase was extracted twice with CH_2Cl_2 . The combined organic layers were dried (K_2CO_3), filtered, concentrated *in vacuo* and chromatographed to give **4** (86%) or **5** (80%) as colorless oils.

¹³ The spectrum is complicated by dynamic effects and ^{199}Hg and ^{201}Hg coupling; the data is given as observed.

Supporting Information

(S)-12-Benzyl-17,18-dimethoxy-2,2,13-trimethyl-10-oxa-13-aza-2-sila-tricyclo[13.4.0.0^{3,8}]nonadeca-1(15),3,5,7,16,18-hexaene; 5. R_f 0.41 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 80:15:5); ν_{max} (thin film)/cm⁻¹ 2949s, 2854s, 1593s, 1505s, 1455s, 1248s, 1207s, 1063s, 838s, 734s, 699s; δ_H (500MHz, CDCl₃) 0.28 (3H, s, SiCH₃), 0.34 (3H, s, SiCH₃), 1.87 (3H, s, NCH₃), 1.99 (1H, dd, $J_{9.5}$, 4Hz, PhCHH'), 2.46-2.52 (2H, m, PhCHH' & C(3)H), 2.86 (1H, dd, $J_{11.5}$, 3Hz, C(2)H), 3.24 (1H, d, $J_{12.5}$ Hz, C(5)H), 3.28-3.33 (1H, m, C(2)H'), 3.48 (3H, s, OCH₃), 3.48 (1H, d, $J_{12.5}$ Hz, C(5)H'), 3.55 (3H, s, OCH₃), 3.95 (1H, d, $J_{10.5}$ Hz, C(10)H), 4.05 (1H, d, $J_{10.5}$ Hz, C(10)H'), 6.53 (1H, s, aryl CH), 6.74 (2H, d, $J_{7.5}$ Hz, aryl CH), 6.78 (1H, s, aryl CH), 6.83-6.98 (5H, m, aryl CH), 7.03 (1H, d, $J_{4.5}$ Hz, aryl CH), 7.29-7.31 (1H, m, aryl CH); δ_C (100MHz, CDCl₃) 0.00 & 0.35 (SiCH₃), 31.40 (PhCH₂), 33.41 (NCH₃), 53.23 & 53.45 (OCH₃), 57.62 (C5), 60.95 (C3), 65.26 & 70.91 (C2 & C10), 110.44, 115.24, 123.32, 124.64, 125.69, 126.42 & 126.64 (7 x CH), 126.83 (quaternary), 127.26 (CH), 130.27 (quaternary), 132.76 (CH), 135.99, 137.36, 140.51, 144.36 & 146.60 (5 x quaternary); m/z (ES) 462 (MH⁺, 100%); HRMS found 462.2455, C₂₈H₃₆NO₃Si (MH⁺) requires 462.2464.

(S)-11-Benzyl-5,6-dimethoxy-10-methyl-2,2-diphenyl-13-oxa-10-aza-2-sila-tricyclo[13.4.0.0^{3,8}]nonadeca-1(15),3,5,7,16,18-hexaene; 6. R_f 0.27 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 85:10:5); ν_{max} (thin film)/cm⁻¹ 2933s, 2845s, 1591s, 1505s, 1463s, 1428s, 1373s, 1244s, 1065s, 740s, 700s; δ_H (500MHz, CDCl₃) 2.30 (3H, s, NCH₃), 2.50 (1H, dd, $J_{13.5}$, 7.5Hz, PhCHH'), 2.81 (1H, dd, $J_{13.5}$, 6.5Hz, PhCHH'), 3.27-3.31 (2H, m, C(2)H & C(3)H), 3.33 (1H, d, J_{14} Hz, C(5)H), 3.59 (3H, s, OCH₃), 3.70(3H, s, OCH₃), 3.76-3.82 (1H, m, C(2)H'), 3.96 (1H, d, $J_{10.5}$ Hz, C(10)H), 4.03 (1H, d, J_{14} Hz, C(5)H'), 4.73 (1H, d, $J_{10.5}$ Hz, C(10)H'), 6.85 (1H, s, aryl CH), 7.16 (1H, s, aryl CH), 7.17-7.65 (19H, m, aryl CH); δ_C (100MHz, CDCl₃) 37.18, 37.81, 55.70, 56.02, 61.89, 63.77, 70.02, 72.00, 112.61, 120.40, 126.22, 127.11, 127.74, 127.85, 127.91, 128.39, 128.52, 128.55, 129.21, 129.47, 130.09, 131.35, 134.49, 135.49, 136.23, 136.51, 136.63, 137.97, 139.20, 140.04, 140.96, 145.29, 146.62, 150.24; m/z (ES) 586 (MH⁺, 100%); HRMS found 586.2781, C₃₈H₄₀NO₃Si (MH⁺) requires 586.2777.

Solid-phase synthesis of 3y. The cyclization precursor **1x** (0.56mequiv./g, 500-560 μ m polystyrene, 1-2% DVB) was azeotroped twice with benzene, then dried at 50°C *in vacuo* for 1 hour. An oven-dried, round-bottomed flask, equipped with a small magnetic stirring bar and septum, was charged with **1x**, argon and *n*-BuLi (2.5M, 100 equiv.), then evacuated and refilled with argon three times. The flask was then charged with anhydrous benzene (6ml) and rotated for 24 hours at room temperature to give orange-colored beads.

Supporting Information

The mixture was freeze-dried, cooled to -78°C and then 2-MeTHF (5ml) was added. To the slowly-stirred mixture was added a 1M solution of 1,2-bis-(2-bromobenzyloxy)-ethane in 2-MeTHF (50 equiv.). After addition the reaction was stirred for 30 minutes to give a clear yellow solution. A freshly prepared 1M solution of $\text{CuCN}\cdot 2\text{LiBr}$ in 2-MeTHF (50 equiv.) was added dropwise, then the mixture was stirred for 48 hours at -40°C . At this temperature a freshly prepared 1M solution of 1,3-dinitrobenzene in 2-MeTHF (200 equiv.) was added to give a dark brown-black solution. The solution was stirred at -10°C for 12 hours. The black solution was quenched with a 1:1 aqueous solution of NH_4OH (10% v/v) and THF, and filtered in a 2ml fritted polypropylene Bio-Spin[®] chromatography column. The dark-colored beads were washed with a 1:1 aqueous solution of NH_4OH (10% v/v) and THF (3 x 5 minutes each), 1M HCl in MeOH (2 x 1 minute each), pyridine (3 x 30 minutes each), *i*-PrOH (3 x 5 minutes each), THF (3 x 5 minutes each) and dried *in vacuo*. The resultant pale yellow beads were suspended in a solution of HF·pyridine in THF (5% v/v) and tumbled for 1 hour, then TMSOMe (to give a 1:1 v/v solution) was added and the mixture tumbled for a further hour. The solution was filtered and concentrated *in vacuo*. In order to obtain the thermodynamically more stable diastereomer, **3x** beads were heated under argon at 150°C for 48 hours before cleaving the substrate off the solid support with HF·pyridine.

5-((*P*,10*S*)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaen-9-yl)-pentan-1-ol; (*P*)-3y. Colorless oil; yield: 55%; kinetic dr: 6:1 (*P*:*M*); R_f 0.19 (SiO_2 ; Hexane: EtOAc; 7:3); ν_{max} (thin film)/ cm^{-1} 3333m, 2926s, 2856s, 1454s, 1366m, 1197m, 1093s, 757s, 699s; δ_{H} (500MHz, CDCl_3) 1.26-1.60 (6H, m, CH_2), 2.01 (1H, br s, OH), 2.29 (1H, dd, J 13.5, 8Hz, PhCHH'), 2.35-2.43 (1H, m, NCHH'), 2.49-2.63 (3H, m, NCHH', C(3)H & PhCHH'), 3.11 (1H, dd, J 12, 9.5Hz, C(2)H), 3.25 (1H, dd, J 12, 3.5Hz, C(2)H'), 3.63 (2H, t, J 6.5Hz, CH_2OH), 3.66-3.79 (2H, ABq, J_{AB} 15Hz, C(5)H₂), 4.17 (1H, d, J 12Hz, C(10)H), 4.40 (1H, d, J 12Hz, C(10)H'), 6.94 (1H, d, J 7Hz, aryl CH), 7.08-7.41 (12H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 23.55, 27.68, 32.82, 38.05, 49.52, 53.60, 62.97, 64.75, 72.29, 73.55, 125.60, 126.11, 126.84, 127.14, 127.68, 127.91, 128.89, 129.47, 129.93, 130.18, 130.47, 137.73, 139.43, 139.89, 141.01, 142.74; m/z (ES) 416 (MH^+ , 100%); HRMS found 416.2603, $\text{C}_{28}\text{H}_{34}\text{NO}_2$ (MH^+) requires 416.2589.

5-((*M*,10*S*)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaen-9-yl)-pentan-1-ol; (*M*)-3y. Colorless oil; thermodynamic dr: 1:7 (*P*:*M*); R_f 0.16 (SiO_2 ; Hexane: EtOAc; 7:3); ν_{max} (thin film)/ cm^{-1} 3385m, 2928s, 2858s, 1496s, 1455s, 1375s, 1085s, 755s, 698s; δ_{H} (500MHz, CDCl_3) 1.25-1.60 (7H, m, CH_2 & OH), 2.34 (1H, dd, J 13.5, 6.5Hz, PhCHH'), 2.48-2.54 (1H, m, NCHH'), 2.61 (1H, dd, J 13.5, 8Hz, PhCHH'), 2.77-2.83 (1H, m, NCHH'), 3.27 (1H, dd, J 12.5, 4Hz, C(2)H), 3.67-

Supporting Information

3.42 (1H, m, C(3)H), 3.63 (2H, t, J 7Hz, CH_2OH), 3.66 (1H, d, J 12Hz, C(5)H), 3.82 (1H, dd, J 12.5, 10.5Hz, C(2)H'), 3.84 (1H, d, J 12Hz, C(5)H''), 4.15 (1H, d, J 10Hz, C(10)H), 4.27 (1H, d, J 10Hz, C(10)H'), 7.00-7.42 (13H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 23.52, 27.85, 32.75, 36.29, 47.17, 53.08, 53.80, 62.95, 67.96, 69.05, 125.62, 126.25, 127.35, 127.55, 127.75, 128.02, 129.12, 129.69, 130.04, 130.15, 130.42, 134.87, 137.72, 139.87, 140.87, 141.94; m/z (ES) 416 (MH^+ , 100%); HRMS found 416.2605, $\text{C}_{28}\text{H}_{34}\text{NO}_2$ (MH^+) requires 416.2589.

Supporting Information

X-ray Data:

For detailed structural analysis of the biaryl medium rings, including crystal data and Chem3D files, see:

http://www-schreiber.chem.harvard.edu/home/research_results.html

Data were collected using a Bruker SMART CCD (charge coupled device) based diffractometer¹⁴ equipped with an LT-2 low-temperature apparatus operating at 213K. A suitable crystal was chosen and mounted on a glass fiber using grease. Data were measured using omega scans of 0.3° per frame for 30 seconds, such that a hemisphere was collected. A total of 1271 frames were collected with a maximum resolution of 0.75Å. The first 50 frames were recollected at the end of data collection to monitor for decay. Cell parameters were retrieved using SMART¹⁵ software and refined using SAINT on all observed reflections. Data reduction was performed using the SAINT software¹⁶ which corrects for Lp and decay. Absorption corrections were applied using SADABS¹⁷ supplied by George Sheldrick. The structures are solved by the direct method using the SHELXS-97¹⁸ program and refined by least squares method on F², SHELXL-97,¹⁹ incorporated in SHELXTL-PC V 5.10.²⁰ All non-hydrogen atoms are refined anisotropically. Hydrogens were calculated by geometrical methods and refined as a riding model. All drawings are done at 50% ellipsoids.

¹⁴ The CCD based x-ray diffractometer at Harvard University was purchased through NIH grant (1S10RR11937-01).

¹⁵ SMART V 5.050 (NT) *Software for the CCD Detector System*; Bruker Analytical X-ray Systems; Madison, WI (1998).

¹⁶ SAINT V 5.01 (NT) *Software for the CCD Detector System* Bruker Analytical X-ray Systems, Madison, WI (1998).

¹⁷ SADABS. *Program for absorption corrections using Siemens CCD based on the method of Robert Blessing*; Blessing, R.H. *Acta Cryst. A*51 (1995) 33-38.

¹⁸ Sheldrick, G. M. SHELXS-90, *Program for the Solution of Crystal Structure*, University of Göttingen, Germany, 1990.

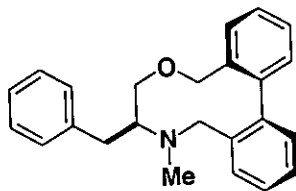
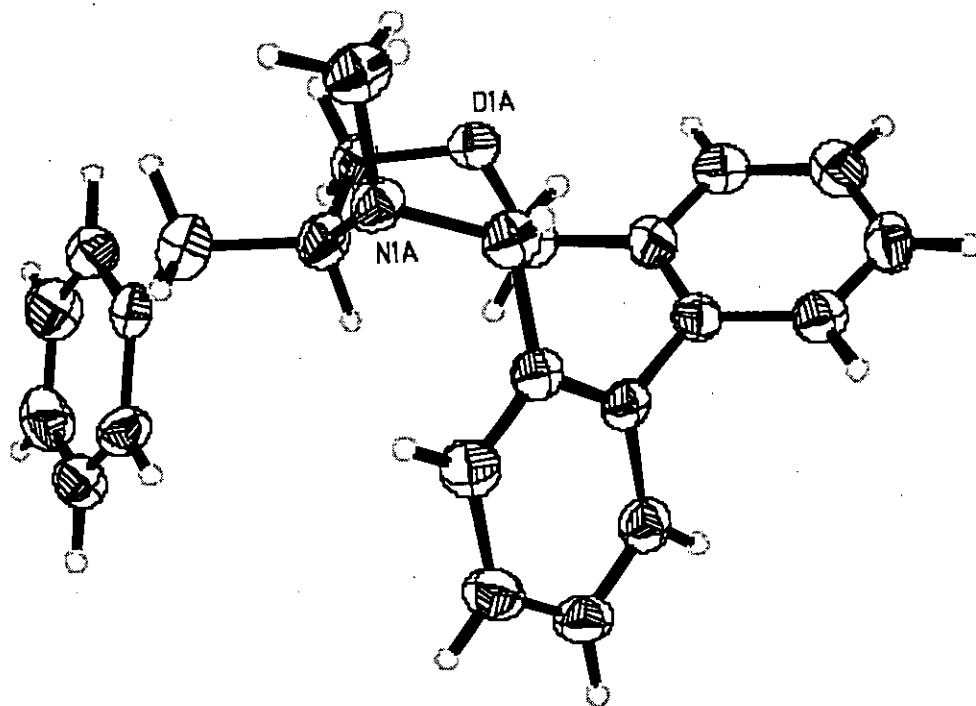
¹⁹ Sheldrick, G. M. SHELXL-97, *Program for the Refinement of Crystal Structure*, University of Göttingen, Germany, 1997.

²⁰ SHELXTL 5.10 (PC-Version), *Program library for Structure Solution and Molecular Graphics*; Bruker Analytical X-ray Systems, Madison, WI (1998).

Supporting Information

X-ray Crystal Structures

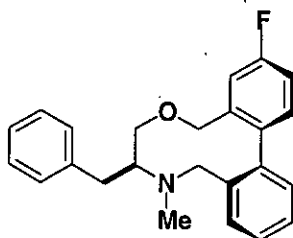
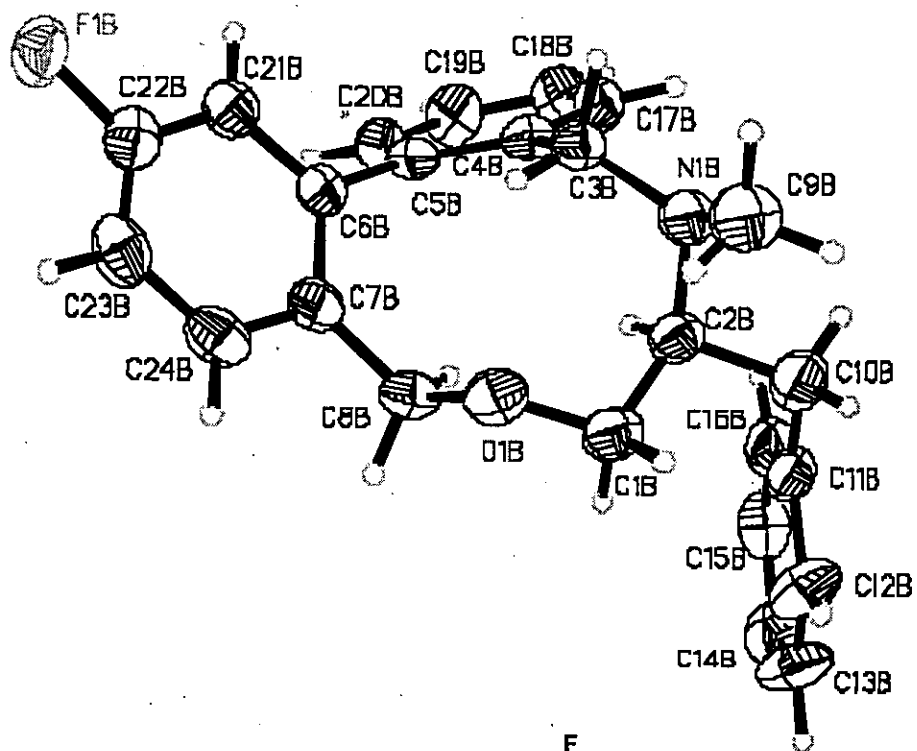
(*M*)-3a (10-membered ring; thermodynamic product):



$C_{24}H_{25}NO$
Mol. Wt.: 343.46

Supporting Information

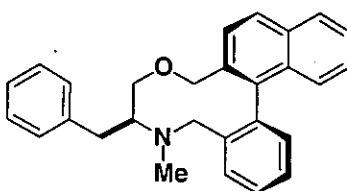
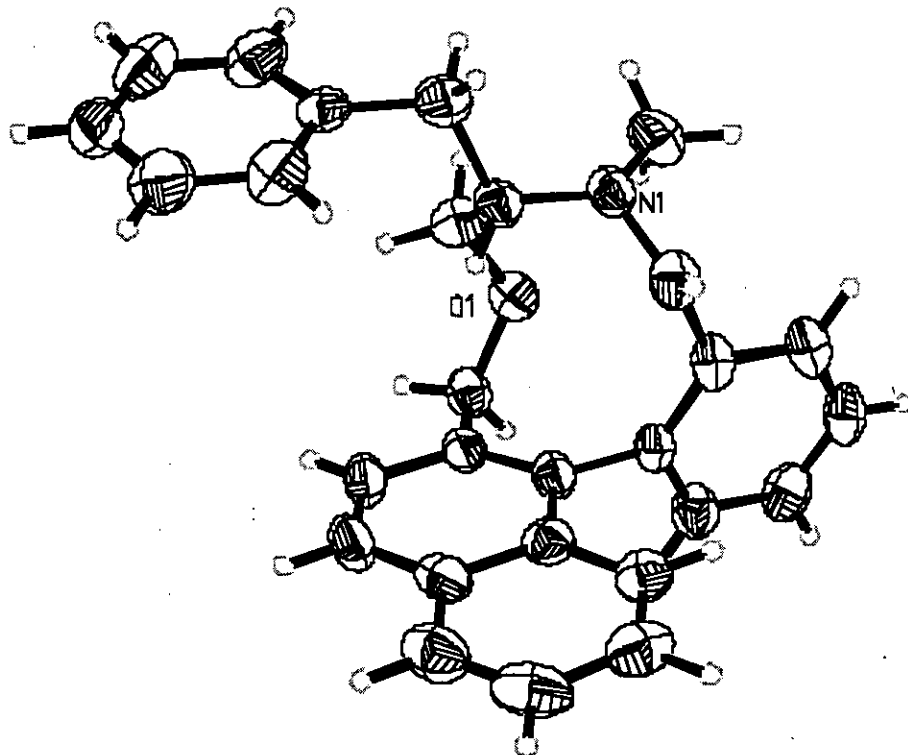
(*M*)-3b (10-membered ring; thermodynamic product):



$C_{24}H_{24}FNO$
Mol. Wt.: 361.45

Supporting Information

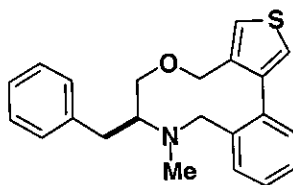
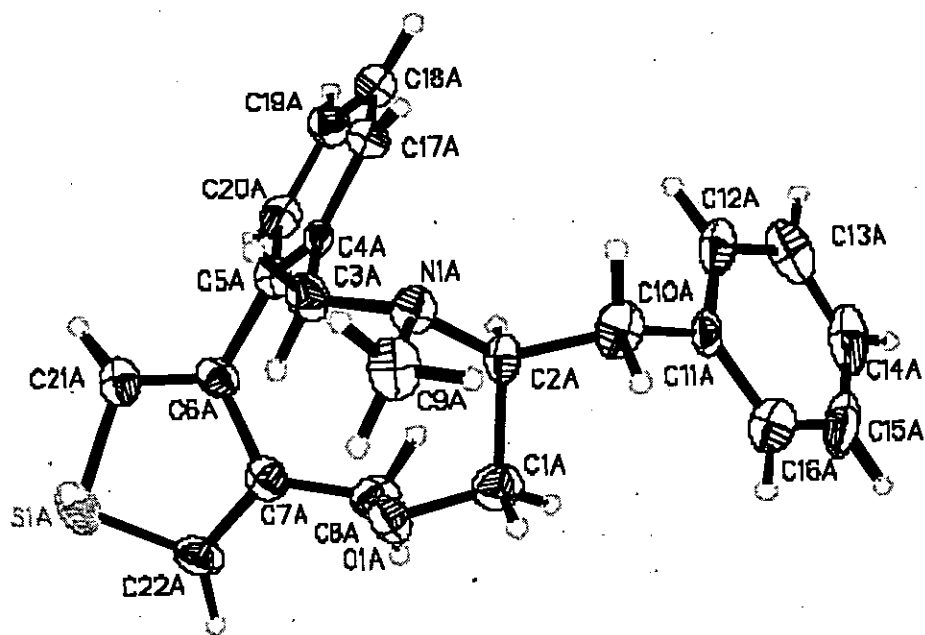
(*P*)-**3d** (10-membered ring; kinetic product):



$C_{28}H_{27}NO$
Mol. Wt.: 393.52

Supporting Information

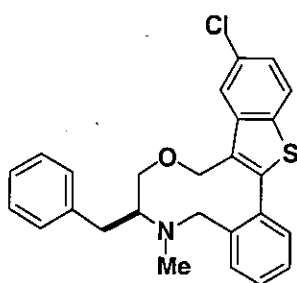
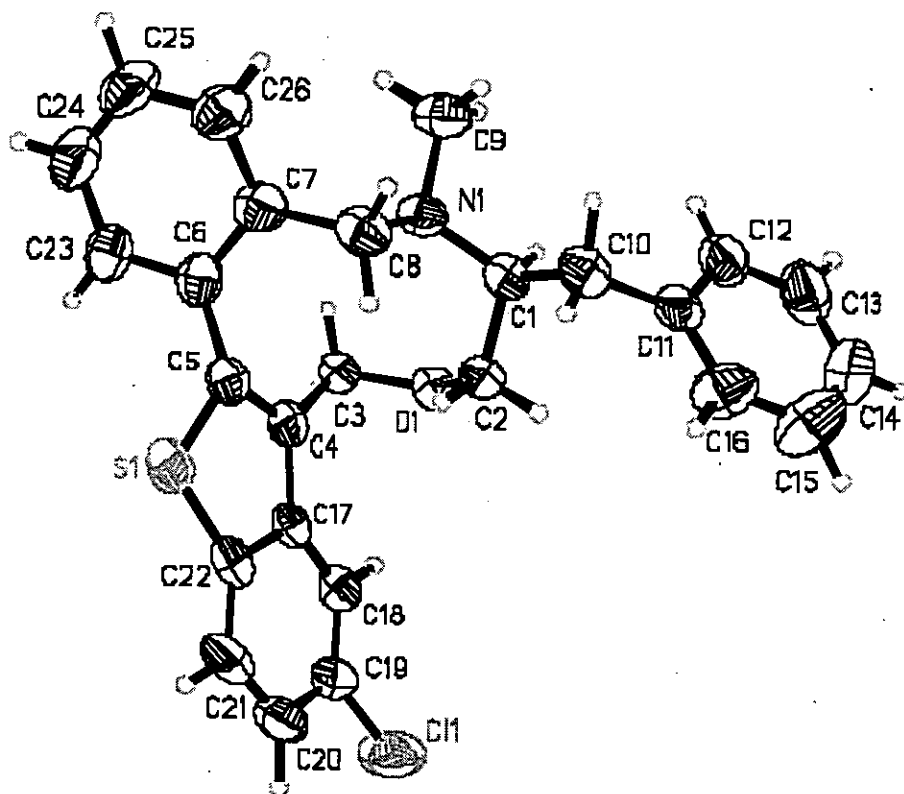
3e (10-membered ring):



$C_{22}H_{23}NOS$
Mol. Wt.: 349.49

Supporting Information

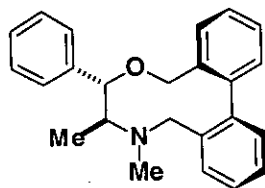
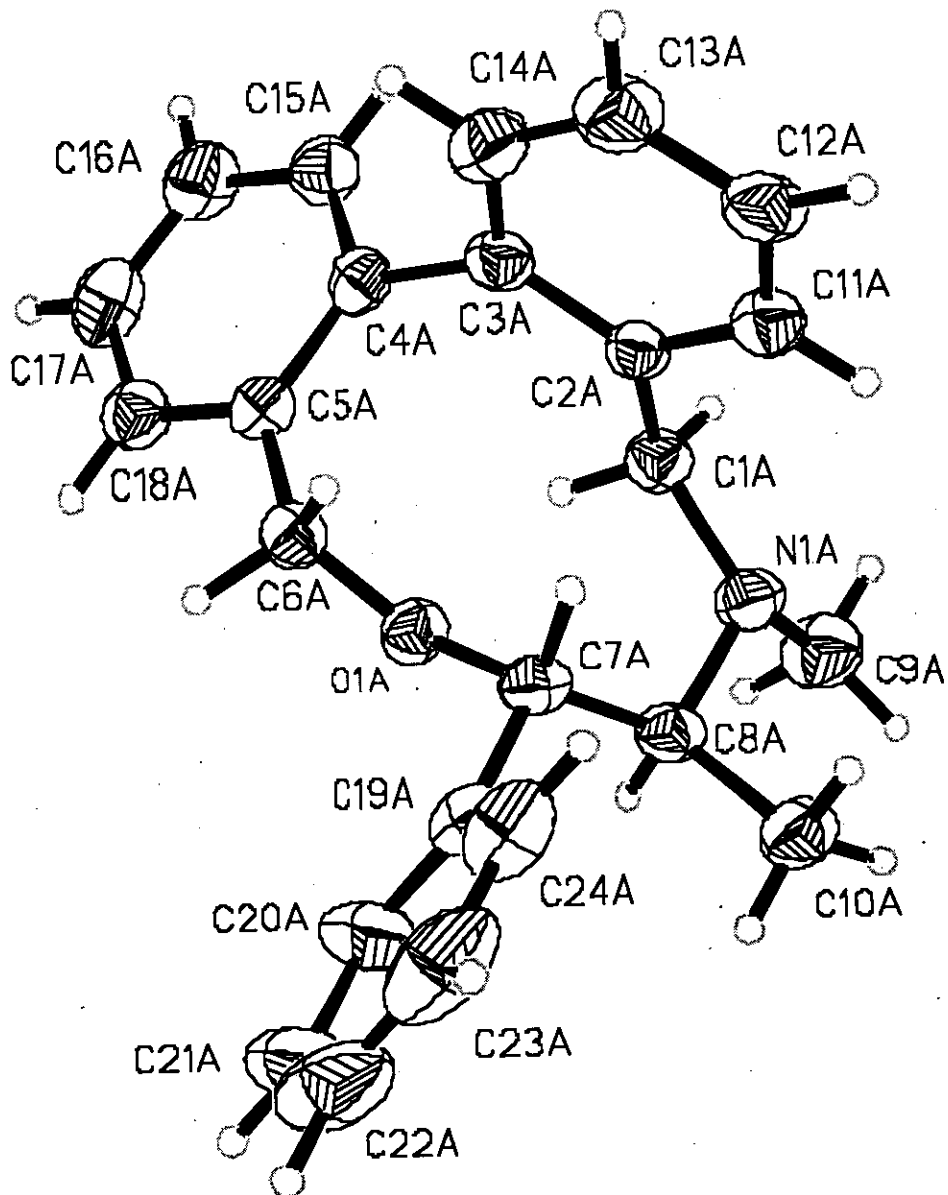
3f (10-membered ring):



C₂₆H₂₄ClNOS
Mol. Wt.: 433.99

Supporting Information

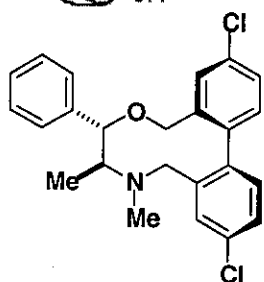
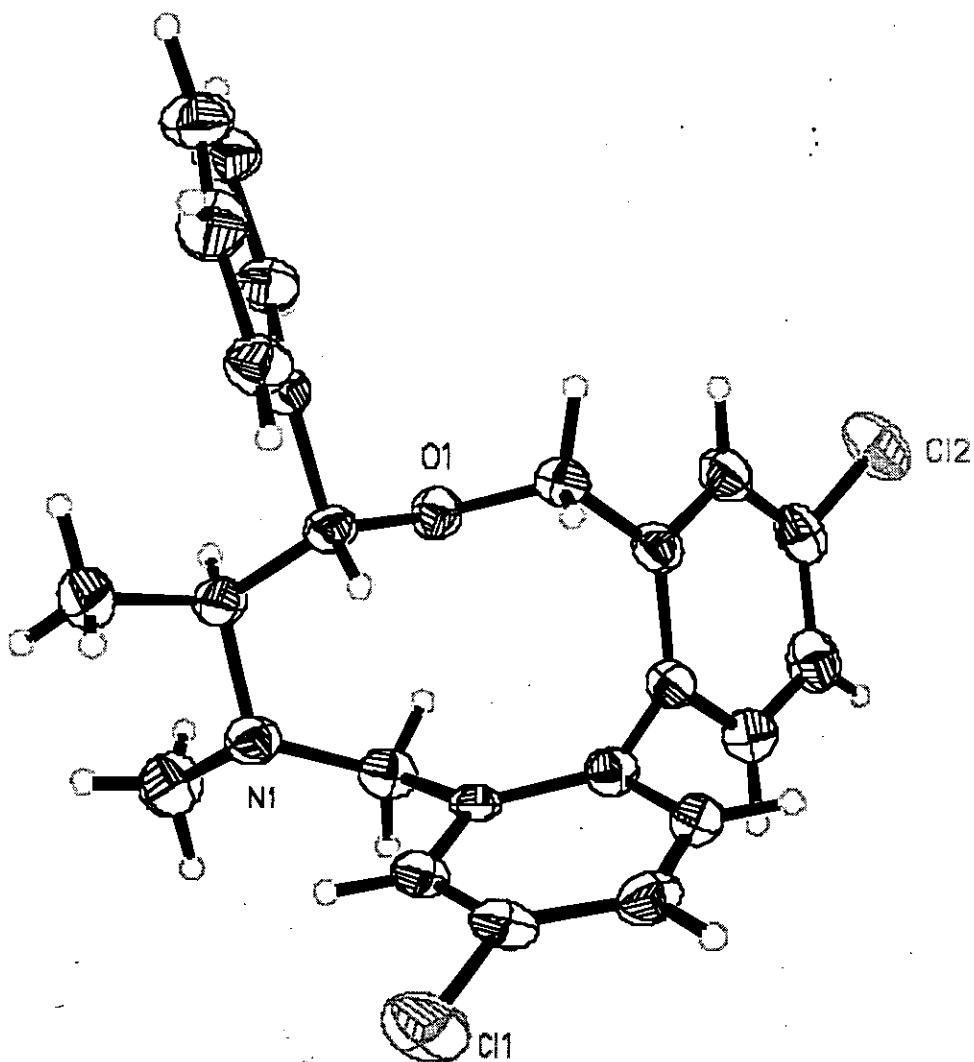
(P)-3h (10-membered ring; kinetic product):



$C_{24}H_{25}NO$
Mol. Wt.: 343.46

Supporting Information

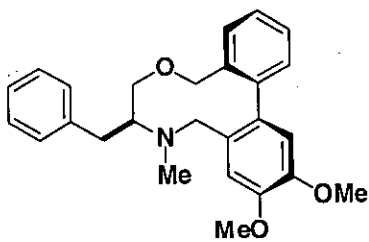
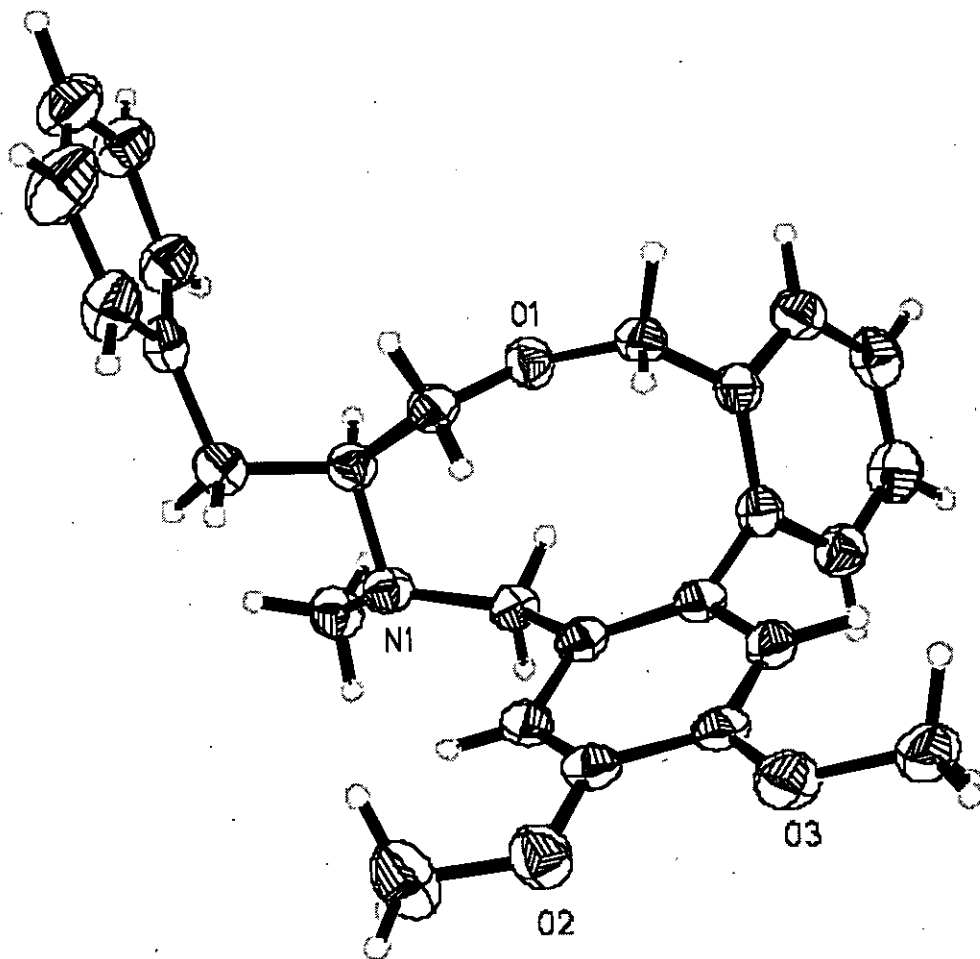
(*P*)-**3i** (10-membered ring; kinetic product):



$C_{24}H_{23}Cl_2NO$
Mol. Wt.: 412.35

Supporting Information:

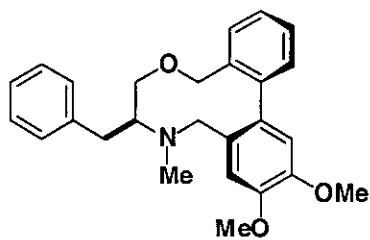
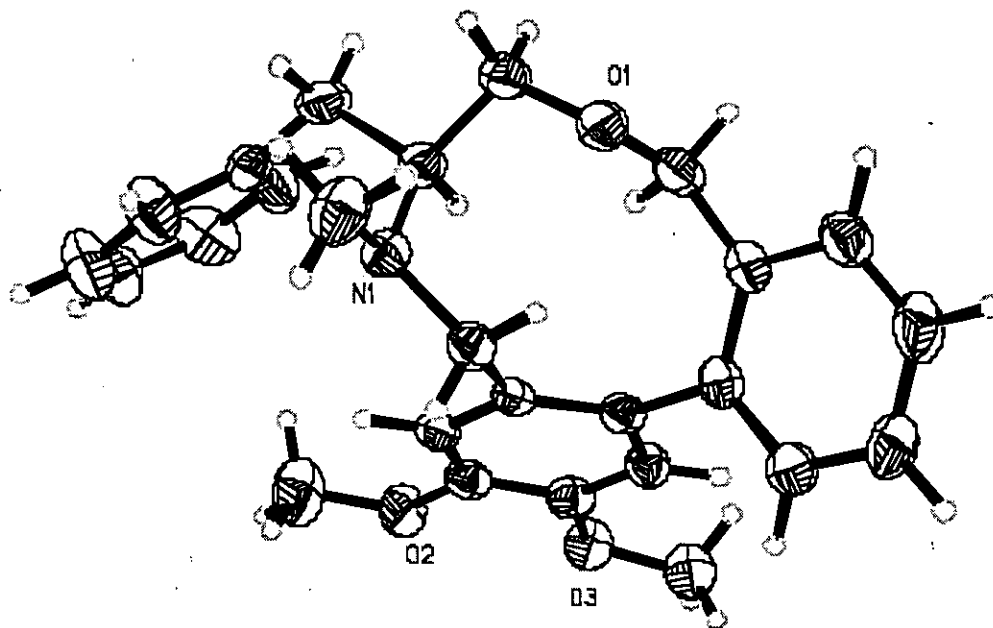
(*P*)-3j (10-membered ring; kinetic product):



$C_{26}H_{29}NO_3$
Mol. Wt.: 403.51

Supporting Information

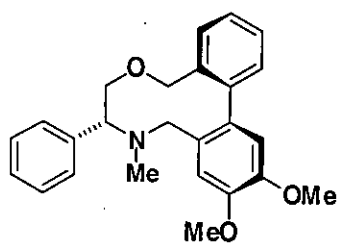
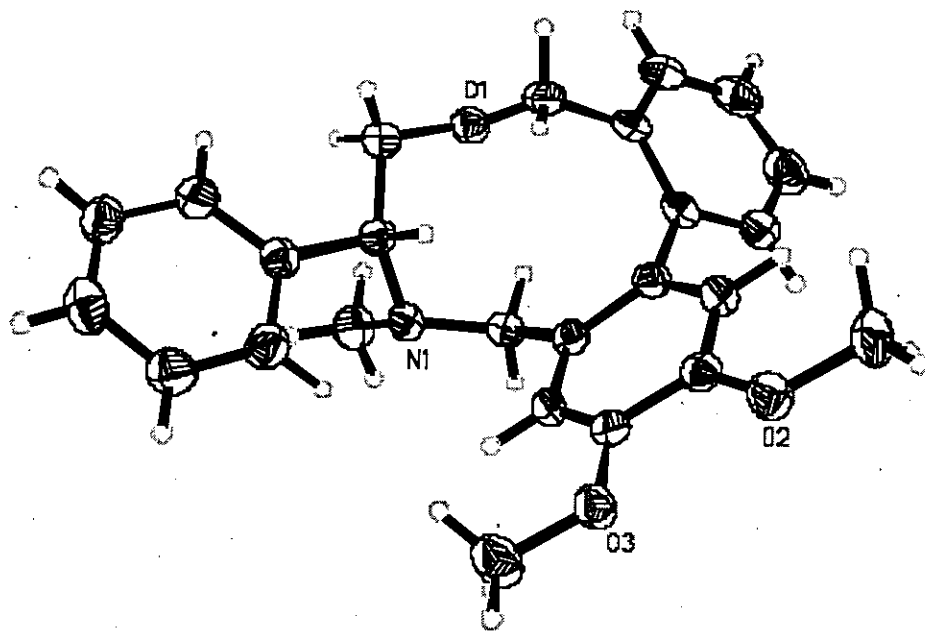
(*M*)-3j (10-membered ring; thermodynamic product):



$C_{26}H_{29}NO_3$
Mol. Wt.: 403.51

Supporting Information

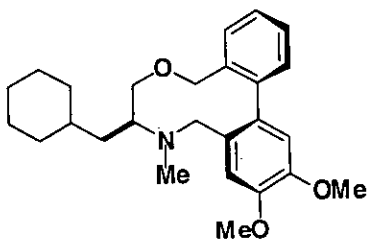
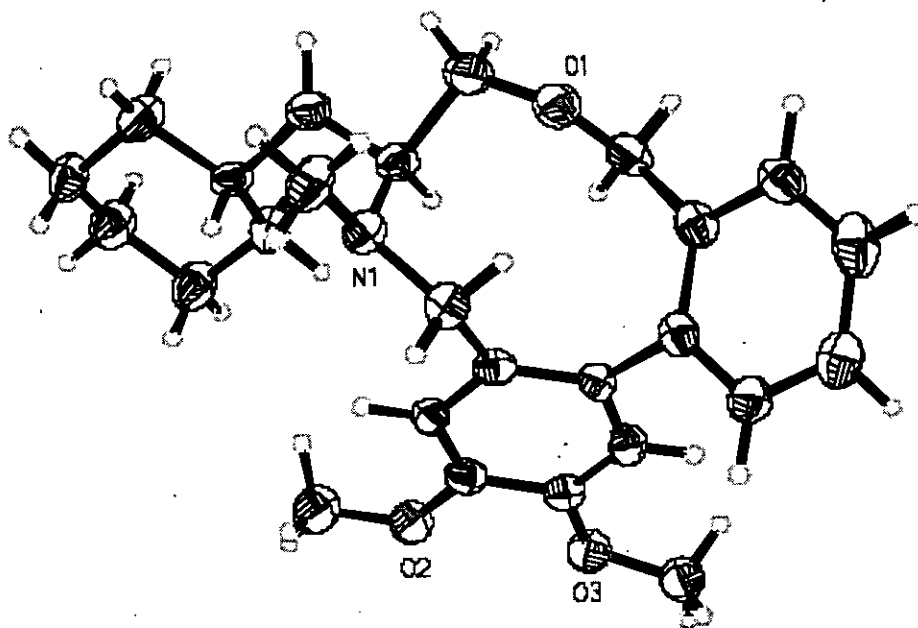
(*P*)-**3k** (10-membered ring; thermodynamic product):



$C_{25}H_{27}NO_3$
Mol. Wt.: 389.49

Supporting Information

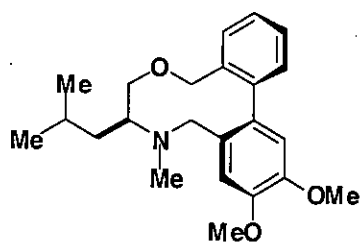
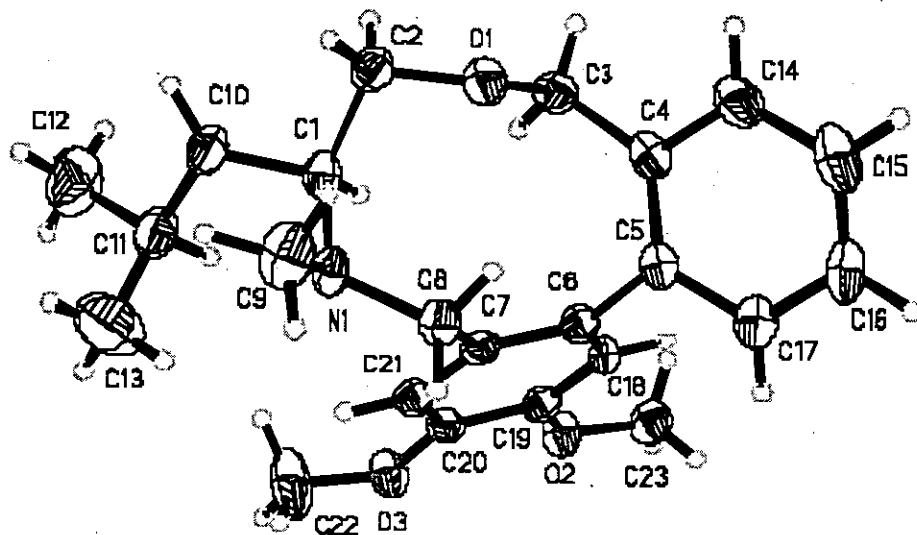
(*M*)-3m (10-membered ring; thermodynamic product):



$C_{26}H_{35}NO_3$
Mol. Wt.: 409.56

Supporting Information

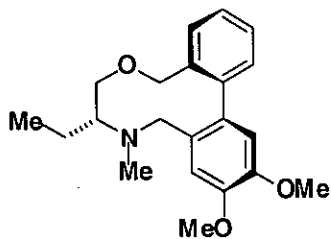
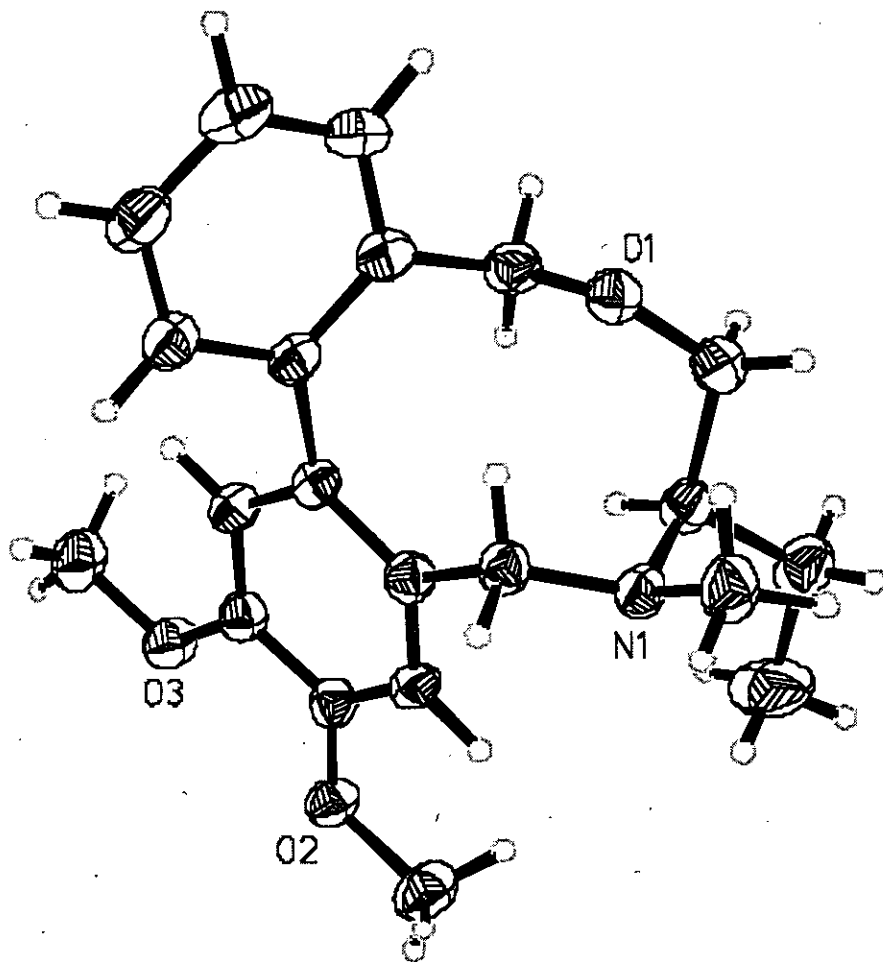
(*M*)-**3n** (10-membered ring; thermodynamic product):



$C_{23}H_{31}NO_3$
Mol. Wt.: 369.50

Supporting Information

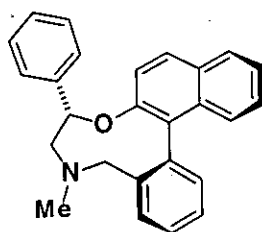
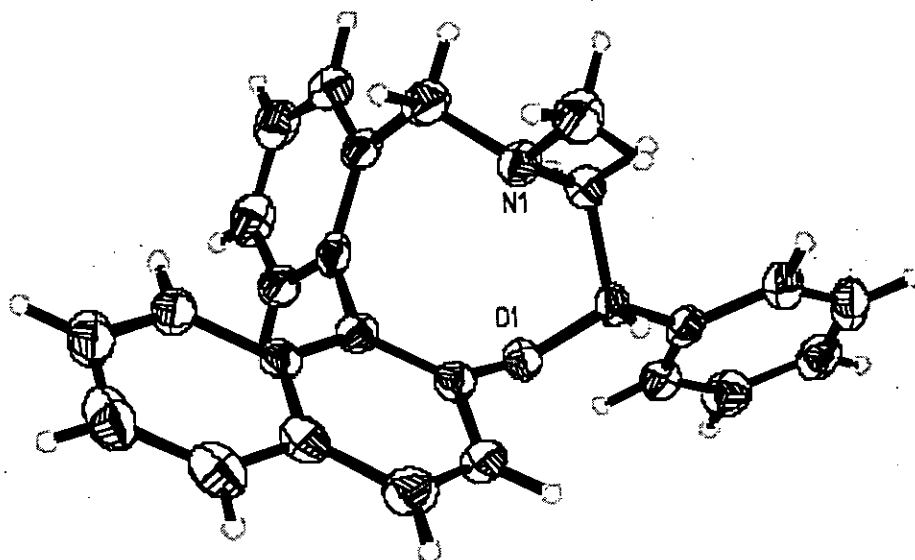
(*P*)-**3o** (10-membered ring; thermodynamic product):



$C_{21}H_{27}NO_3$
Mol. Wt.: 341.44

Supporting Information

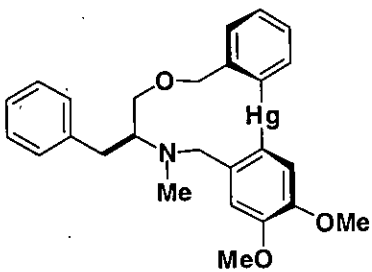
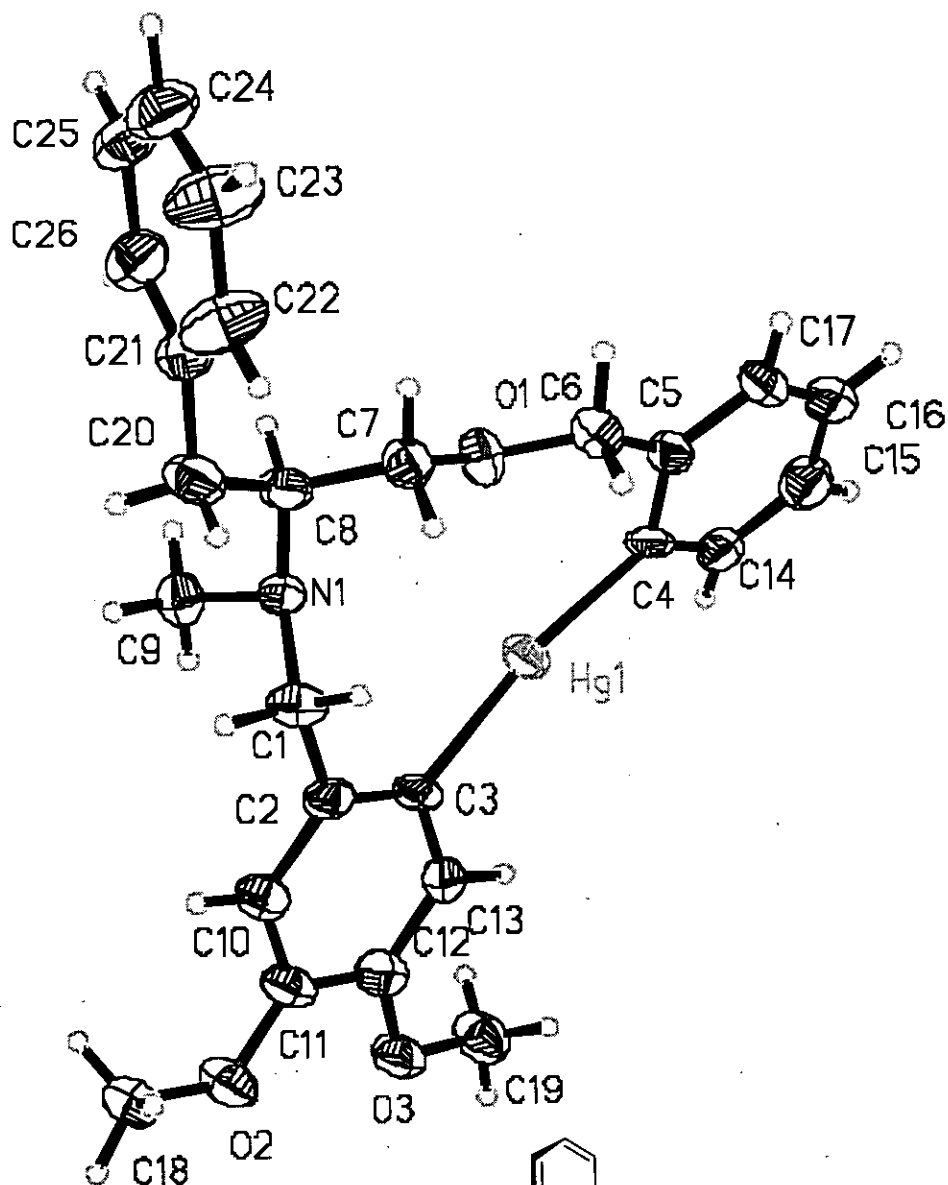
(*M*)-3v (9-membered ring):



$C_{26}H_{23}NO$
Mol. Wt.: 365.47

Supporting Information

4 (11-membered ring):



$C_{26}H_{29}HgNO_3$
Mol. Wt.: 604.10