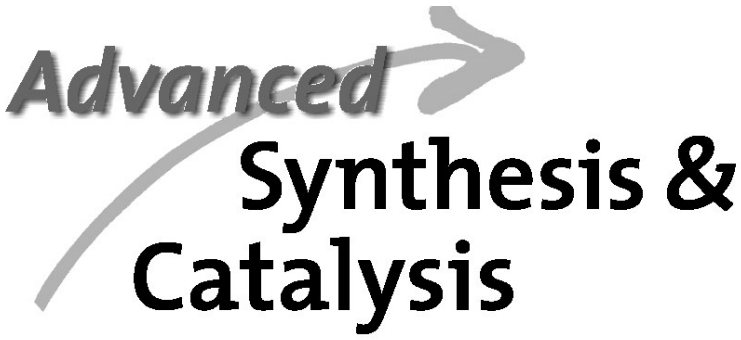

Supporting Information

Design of a Conformationally Rigid Hydrazide Organic Catalyst

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SUPPORTING INFORMATION

General. All solvents were used as obtained from commercial suppliers unless otherwise indicated. Standard inert atmosphere techniques were employed in handling air and moisture sensitive reagents. All starting materials were purchased and were used without purification unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) using commercial aluminum-backed silica gel sheets coated with silica gel 60 F_{254}. TLC spots were visualized under ultraviolet light or developed by heating after treatment with potassium permanganate. Room temperature corresponds to 22 °C. Excess solvents were removed *in vacuo* at pressures obtained by water or air aspirators connected to a rotary evaporator. Trace solvents were removed on a vacuum pump. Product purification by flash chromatography was performed with Silica Gel 60 (230-400 mesh). Infrared (IR) spectra were obtained as neat films on a sodium chloride cell. Chemical shifts are reported downfield from tetramethylsilane (δ scale) in ppm. Mass spectroscopy (MS), using either electron impact (EI) or chemical ionization (CI), was performed on a mass spectrometer with an electron beam energy of 70 eV (for EI). Electrospray analyses were run on a triple quad mass spectrometer VG QUATTRO. High resolution mass spectroscopy (HRMS) was performed on a mass spectrometer with an electron beam of 70 eV, or a double focusing magnetic sector mass spectrometer. GLC were performed on a gas chromatograph equipped with a split-mode capillary injection system and a flame ionization detector using CycloSil-B columns. Melting points were measured using a Melt Temp apparatus and are uncorrected. Non-commercial mono-substituted hydrazines were prepared by syringe pump addition of a methanolic solution of alkyl or benzyl halides to an excess of hydrazine monohydrate (10 eq) at 0 °C.[1]

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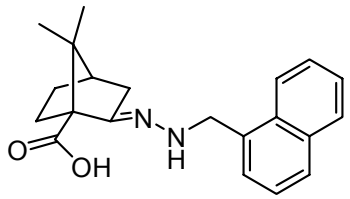
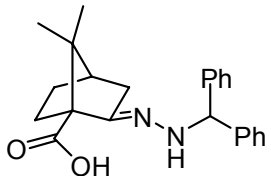
[1] J. Finneman, J. Fishbein *J. Am. Chem.* Soc. **1995**, 117, 4228-4239.



(*S*)-(+)-7,7-Dimethyl-2-(naphthalen-1-ylmethyl-hydrazono)-bicyclo [2.2.1]heptane-1-carboxylic acid. Acetic acid (0.12 mL, 2.16 mmol) was added drop wise to a solution of (*S*)-(+)-ketopinic acid[2] (1.97 g, 10.8 mmol) and naphtyl(1-methylhydrazine) (2.25 g, 13.0 mmol) in anhydrous dichloromethane (100 ml) at room temperature. The reaction mixture was stirred at that temperature until judged complete by TLC analysis (15 hours). Removal of solvent *in vacuo* and purification by silica gel chromatography (30% EtOAc/hex) provided the compound as a pale yellow oil in 86% yield (3.12 g, 9.29 mmol); IR (neat) 3278, 1724 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 1H), 7.88-7.77 (m, 2H), 7.57-7.39 (m, 4H), 4.82 (d, J = 13.0 Hz, 1H), 4.76 (d, J = 13.0 Hz, 1H), 2.39 (ddd, J = 12.3, 12.3, 4.5 Hz, 1H), 2.25 (ddd, J = 17.1, 3.7, 3.7 Hz, 1H), 2.08-1.88 (m, 2H), 1.74-1.63 (m, 2H), 1.27-1.22 (m, 1H), 1.20 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8 (C), 159.4 (C), 133.9 (C), 133.5 (C), 131.4 (C), 128.9 (CH), 128.6 (CH), 127.1 (CH), 126.4 (CH), 125.9 (CH), 125.4 (CH), 123.3 (CH), 59.6 (C), 52.9 (CH_2), 51.5 (C), 44.3 (CH), 32.6 (CH_2), 32.1 (CH_2), 28.2 (CH_2), 20.0 (CH_3), 19.6 (CH_3); MS (EI) 336.2 (M^+)**;** HRMS (EI) calcd. for $C_{21}H_{24}N_2O_2$ (M^+) 336.1838 found; 336.1822.



(*S*)-(+)-2-(Benzhydryl-hydrazono)-7,7-dimethyl-bicyclo[2.2.1]heptane-1-carboxylic acid. Prepared by a procedure similar to that described above from (*S*)-(+)-ketopinic acid[2] (2.78 g, 15.3 mmol) and benzhydrylhydrazine (3.64 g, 18.4 mmol). Purification by silica gel chromatography (30% EtOAc in hexanes) provided the compound as a pale yellow oil (4.16 g, 75 %); $[\alpha]_D$ +5.94° (*c* 1.00, $CHCl_3$); IR (neat) 3268, 2972, 1735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.31 (m, 8H), 7.29-7.24 (m, 2H), 5.53 (s, 1H), 2.46-2.36 (m, 2H), 2.11-2.03 (m, 1H), 2.01 (t, J = 4.3 Hz,

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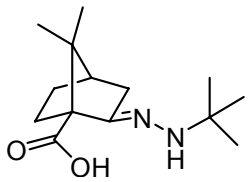
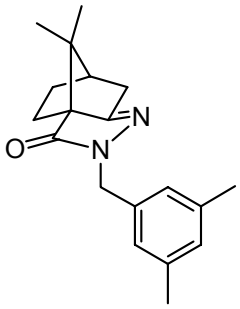
[2] P.P. Bartlett, L.H. Knox Organic Syntheses, Coll. Vol. 5, p.689; Vol. 45, p.55

1H), 1.88 (d, J = 17.2 Hz, 1H), 1.71-1.66 (m, 1H), 1.33-1.27 (m, 1H), 1.22 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6 (C), 141.4 (C), 141.1 (C), 128.7 (CH), 128.6 (CH), 127.7 (CH), 127.6 (CH), 127.4 (CH), 67.8 (CH), 59.6 (C), 51.5 (C), 44.4 (CH), 32.9 (CH_2), 28.2 (CH_2), 20.0 (CH_3), 19.6 (CH_3); MS (EI) *m/z* 362.2 (M+).

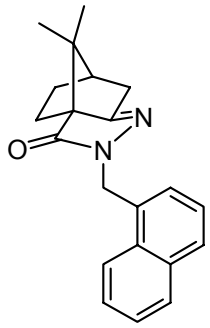


(*S*)-(+)-2-(tert-Butyl-hydrazono)-7,7-dimethyl-bicyclo[2.2.1]heptane-1-carboxylic acid. Acetic acid (0.16 mL, 3.29 mmol) was added drop wise to a solution of (*S*)-(+)-ketopinic acid[2] (3.00 g, 16.5 mmol), *tert*butyl-hydrazine monohydrochloride (2.75 g, 16.5 mmol) and sodium acetate (1.35g 16.5 mmol) in anhydrous dichloromethane (100 ml) at room temperature. The reaction mixture was stirred at that temperature until judged complete by TLC analysis (17 hours). Removal of solvent *in vacuo* and purification by silica gel chromatography (30% EtOAc/hex) provided the compound as a pale yellow oil in 79% yield (3.29 g, 13.0 mmol); mp 119-121°C; $[\alpha]_D$ +67.9° (*c* 1.03, $CHCl_3$); IR (neat) 1689, 2969, 3237 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.42-2.32 (m,2H), 2.09-1.97 (m, 2H), 1.80 (d, J = 17.1 Hz, 1H), 1.73 (ddd, J = 13.1, 9.4, 4.3 Hz, 1H), 1.34-1.27 (m, 1H), 1.21 (s, 3H), 1.16 (m, 9H), 0.84 (s, 3H); ^{13}C NMR δ (125 MHz, $CDCl_3$) 173.1 (C), 158.3 (C), 59.4 (C), 53.7 (C), 51.3 (C), 44.4 (CH), 32.3 (CH_2), 32.2 (CH_2), 28.3 (CH_3), 28.2 (CH_2), 20.0 (CH_3), 19.7 (CH_3); MS 252.2 (M^+); HRMS calcd for $C_{14}H_{24}N_2O_2$ 252.1838; found 252.1839.



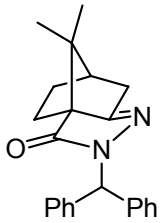
(*S*)-(+)-3-(3,5-Dimethylbenzyl)-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]dec-4-en-2-one. Acetic acid (0.16 mL, 3.33 mmol) was added drop wise to a solution of (*S*)-(+)-ketopinic acid[2] (3.70 g, 16.5 mmol) and (3,5-Dimethyl-benzyl)-hydrazine (2.50 g, 16.5 mmol) in anhydrous dichloromethane (100 ml) at room temperature. The reaction mixture was stirred at that temperature until judged complete by TLC analysis (17 hours), then passed through a short silica

plug and the solvent was removed *in vacuo*. The crude hydrazonocarboxylic acid was dissolved in mesitylene (90 mL) and was refluxed while water was removed in dean-stark apparatus. Reflux was continued until consumption of the starting material was complete as judged by TLC (36 hours). The cooled reaction mixture was directly loaded onto a silica column and was purified by flash chromatography (hexanes followed by 15 % EtOAc in hexanes) to provide the desired compound as a white solid (2.70 g, 55 %). mp 83.5-84.5^{o}C; $[\alpha]_D$ +27.8° (*c* 1.08, $CHCl_3$); IR (neat) 2963, 1696, 1610 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.89-6.86 (m, 3H), 4.73 (s, 2H), 2.59-2.52 (m, 1H), 2.32-2.21 (m, 8H), 2.16-2.08 (m, 2H), 1.66 (ddd, J = 13.5, 9.4, 4.4 Hz, 1H), 1.47 (ddd, J = 13.4, 9.4, 4.3 Hz, 1H), 1.21 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5 (C), 173.6 (C), 138.1 (C), 137.0 (C), 129.1 (CH), 125.6 (CH), 63.7 (C), 49.9 (CH), 49.2 (CH_2), 47.8 (C), 32.0 (CH_2), 27.0 (CH_2), 25.3 (CH_2), 21.2 (CH_3), 19.1 (CH_3), 18.6 (CH_3); MS 296.2 (M^+); HRMS calcd for $C_{19}H_{24}N_2O$ 296.1889; found 296.1900.



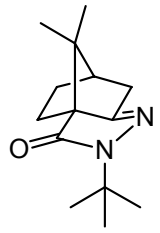
***S*)-(+)-10,10-Dimethyl-3-naphthalen-1-ylmethyl-3,4-diazatricyclo [5.2.1.0^{1,5}]dec-4-en-2-one.** A solution of (*S*)-(+)-7,7-Dimethyl-2-(naphthalen-1-ylmethyl-hydrazono)-bicyclo [2.2.1]heptane-1-carboxylic acid (2.51 g, 7.88 mmol) in mesitylene (110 mL) was refluxed while water was removed in dean-stark apparatus. Reflux was continued until consumption of the starting material was complete as judged by TLC. The cooled reaction mixture was directly loaded onto a silica column and was purified by flash chromatography (hexanes followed by 30 % EtOAc in hexanes) to provide the desired compound as a white solid (1.82 g, 72 %). mp 92-93^{o}C; $[\alpha]_D$ +57.5° (*c* 1.10, $CHCl_3$); IR (neat) 1690 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 (dd, J = 5.1, 0.3 Hz, 1H), 7.81 (dd, J = 14.4, 4.8 Hz, 2H), 7.51-7.41 (m, 4H), 5.33 (d, J = 9.0 Hz, 1H), 5.14 (d, J = 9.0 Hz, 1H), 2.52-2.47 (m, 1H), 2.28 (ddd, J = 7.2, 7.2, 2.7 Hz, 1H), 2.19 (dd, J = 2.4, 2.4 Hz, 1H), 2.12-2.02 (m, 1H), 2.04 (d, J = 10.5 Hz, 1H), 1.57 (ddd, J = 8.1, 5.7, 2.7 Hz, 1H), 1.41 (ddd, J = 7.8, 5.7, 2.7 Hz, 1H), 1.22 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6 (C), 173.1 (C), 133.7 (C), 132.5 (C), 131.2 (C), 128.5 (CH), 128.5 (CH), 127.4 (CH), 126.2 (CH), 125.7 (CH), 125.2 (CH),

123.7 (CH), 63.7 (C), 49.7 (C), 49.1 (CH), 46.1 (CH_2), 31.9 (CH_2), 26.8 (CH_2), 25.3 (CH_2), 19.1 (CH_3), 18.5 (CH_3); MS 318.1 (M^+); HRMS calcd. for $C_{21}H_{22}N_2O$ 318.1732; found 318.1737.



(*S*)-(+)-3-Benzhydryl-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]dec-4-en-2-one.

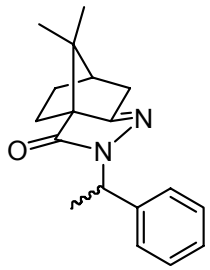
Prepared by a procedure similar to that described above for (*S*)-(+)-10,10-Dimethyl-3-naphthalen-1-ylmethyl-3,4-diazatricyclo [5.2.1.$0^{1,5}$]dec-4-en-2-one from (*S*)-(+)-2-(Benzhydryl-hydrazono)-7,7-dimethyl-bicyclo[2.2.1]heptane-1-carboxylic acid (502 mg, 1.39 mmol). Purification by silica gel chromatography (hexanes then 20% EtOAc in hexanes) provided the compound as a white solid (294 mg, 62 %). mp 156-158^{o}C; $[\alpha]_D$ +0.23° (*c* 1.00, $CHCl_3$); IR (neat) 1694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10H), 6.64 (s, 1H), 2.59 (m, 1H), 2.35-2.09 (m, 4H), 1.72-1.64 (m, 1H), 1.53-1.45 (m, 1H), 1.22 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2 (C), 173.6 (C), 140.0 (C), 139.5 (C), 128.5 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 127.4 (CH), 127.3 (CH), 63.5 (C), 59.8 (CH), 50.1 (C), 49.2 (CH), 32.2 (CH_2), 27.0 (CH_2), 25.3 (CH_2), 19.1 (CH_3), 18.6 (CH_3); MS (EI) 344.2 (M^+); HRMS calcd. for $C_{23}H_{24}N_2O$ 344.1890; found 344.1881.



(*S*)-(+)-3-tert-Butyl-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]dec-4-en-2-one.

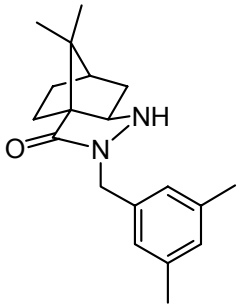
(*S*)-(+)-2-(tert-Butyl-hydrazono)-7,7-dimethyl-bicyclo[2.2.1]heptane-1-carboxylic acid (2.31 g, 9.15 mmol) and triethylamine (926 mg, 9.15 mmol) were dissolved in EtOAc (90 ml). $SOCl_2$ (0.86 ml, 11.9 mmol) was added drop wise and the reaction was brought to 60 °C for 6 hours and quenched with H_2O. The products were extracted with EtOAc, washed with brine and dried over sodium sulphate. The solvent was removed *in vacuo* and the product was purified by flash chromatography (20% EtOAc in hexanes) to afford the desired compound as pale yellow crystals (1.01 g, 47 %). mp 45-46 ^{o}C; $[\alpha]_D$ +38.3° (*c* 1.06, $CHCl_3$); IR (neat) 2965, 1637, 1694, 1290 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.56-2.50 (m, 1H), 2.21-2.15 (m, 2H), 2.11-2.03 (m, 2H), 1.66-1.59 (m, 1H), 1.47 (s, 9H), 1.46-1.41 (m, 1H), 1.15 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5 (C), 172.2 (C), 64.6 (C), 57.6 (C), 49.6 (C), 49.1 (CH), 32.0 (CH_2), 28.4 (CH_3), 27.0 (CH_2), 25.1 (CH_2), 18.8 (CH_3), 18.4 (CH_3); MS 234.2 (M^+); HRMS calcd for $C_{14}H_{22}N_2O$ 234.1732; found 234.1734.



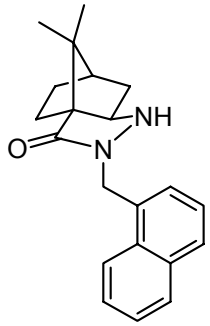
(*S*)-(+)-10,10-Dimethyl-3-(1-phenylethyl)-3,4-diaza-tricyclo[5.2.1.01,5]dec-4-en-2-one.

Prepared by a procedure similar to that described above for (*S*)-(+)-3-(3,5-Dimethylbenzyl)-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]dec-4-en-2-one from (*S*)-(+)-ketopinic acid (7.14 g, 39.2 mmol) and (1-Phenylethyl)-hydrazine (6.4 g, 47.0 mmol). Purification by silica gel chromatography (hexanes then 20% EtOAc in hexanes) provided an inseparable mixture of diastereoisomers as a clear oil (6.97 g, 63 %). IR (neat) 2962, 1693, 1633 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.17 (m, 5H), 5.56-5.39 (m, 1H), 2.60-2.48 (m, 1H), 2.30-2.02 (m, 4H), 1.69-1.38 (m, 5H), 1.19 (s, 1.5H major isomer), 1.15 (s, 1.5H minor isomer), 0.91 (s, 1.5H major isomer), 0.72 (s, 1.5H minor isomer); ^{13}C NMR (100 MHz, $CDCl_3$) δ major isomer: 174.0 (C), 173.1 (C), 141.3 (C), 128.3 (CH), 127.2 (CH), 126.8 (CH), 63.9 (CH), 51.6 (C), 49.7 (CH), 49.6 (CH), 32.0 (CH_2), 26.9 (CH_2), 24.9 (CH_2), 19.3 (CH_3), 18.8 (CH_3), 18.5 (CH_3); minor isomer: 174.0 (C), 173.2 (C), 141.8 (C), 128.2 (CH), 127.1 (CH), 126.6 (CH), 63.9 (CH), 51.7 (C), 49.9 (CH), 49.2 (CH), 31.9 (CH_2), 26.9 (CH_2), 25.1 (CH_2), 18.9 (CH_3), 18.8 (CH_3), 18.5 (CH_3); MS 282.2 (M^+); HRMS calcd for $C_{18}H_{22}N_2O$ 282.1732; found 282.1718.



(*S*)-(+)-3-(3,5-Dimethyl-benzyl)-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one.

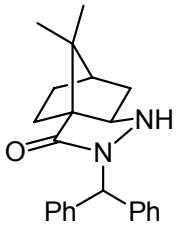
A solution of 10,10-Dimethyl-3,4-diazatricyclo[5.2.1.01,5]dec-4-en-2-one (300 mg, 1.01 mmol) in a 2:1 mixture of acetic acid and methanol (20 mL) was added sodium cyanoborohydride (636 mg, 10.1 mmol) in small portions over 1 h. The reaction mixture was then stirred at room temperature until TLC indicated that the reaction was complete (21 hours). Excess borohydride was quenched by the addition of 10 % HCl. The products were extracted using CH_2Cl_2 and the aqueous phase was made basic using sodium hydroxide pellets then further extracted with CH_2Cl_2. The organic extracts were combined, washed with brine and dried over sodium sulphate. The solvent was removed *in vacuo* and the product was purified by flash chromatography (30% EtOAc in hexanes) to afford the desired compound as a white solid (263 mg, 87 %). mp 84-85 ^oC; $[\alpha]_D$ +16.3° (*c* 1.18, $CHCl_3$); IR (neat) 3241, 1665 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.89-6.86 (m, 3H), 4.65 (d, J = 13.4 Hz, 1H), 4.31 (d, J = 13.4 Hz, 1H), 3.49 (dd, J = 8.2, 4.8 Hz, 1H), 2.25 (s, 6H), 2.15 (dt, J = 11.5, 4.6 Hz, 1H), 2.03-1.96 (m, 1H), 1.92-1.82 (m, 2H), 1.62 (dd, J = 13.1, 8.4 Hz, 1H), 1.32-1.25 (m, 1H), 1.24-1.17 (m, 1H), 1.11 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4 (C), 138.2 (C), 135.6 (C), 129.3 (CH), 126.1 (CH), 65.1 (CH), 58.4 (C), 51.2 (C), 47.7 (CH_2), 46.7 (CH), 36.3 (CH_2), 28.6 (CH_2), 26.6 (CH_2), 21.1 (CH_3), 20.9 (CH_3), 20.2 (CH_3); MS 298.2 (M^+); HRMS calcd for $C_{19}H_{26}N_2O$ 298.2045; found 298.2055.



(*S*)-(+)-10,10-Dimethyl-3-naphthalen-1-ylmethyl-3,4-diaza-tricyclo [5.2.1.0^{1,5}]decan-2-one (table 1, entry 5).

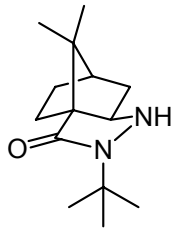
Prepared by a procedure similar to that described above for (*S*)-(+)-3-(3,5-Dimethyl-benzyl)-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one from (*S*)-(+)-10,10-Dimethyl-3-naphthalen-1-ylmethyl-3,4-diazatricyclo [5.2.1.0^{1,5}]dec-4-en-2-one (1.60 g, 5.02 mmol). Purification by silica gel chromatography (30% EtOAc in hexanes) provided the title compound as a white solid (1.43 g, 89 %). mp 144-145 ^oC; $[\alpha]_D$ +39.5 (*c* 1.00, $CHCl_3$); IR (neat) 3245, 1667 cm^{-1}; ^1H NMR (500 MHz,

$CDCl_3$) δ 8.27 (d, J = 4.8 Hz, 1H), 7.81 (dd, J = 10.2, 4.8 Hz, 2H), 7.56-7.37 (m, 4H), 5.26 (br, 1H), 4.78 (br, 1H), 3.88 (br, 1H), 3.43-3.40 (m, 1H), 2.17 (ddd, J = 7.2, 7.2, 3.0 Hz, 1H), 1.97-1.81 (m, 3H), 1.58 (dd, J = 7.5, 4.8 Hz, 1H), 1.28-1.15 (m, 2H), 1.08 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0 (C), 133.7 (C), 131.4 (C), 128.9 (CH), 128.4 (CH), 127.9 (CH), 126.6 (CH), 126.0 (CH), 125.0 (CH), 124.1 (CH), 64.9 (CH), 58.6 (C), 51.3 (C), 46.6 (CH), 46.2 (CH_2), 36.4 (CH_2), 28.5 (CH_2), 26.6 (CH_2), 20.8 (CH_3), 20.1 (CH_3); MS 320.2 (M^+); HRMS calcd for $C_{21}H_{24}N_2O$ 320.1889; found 320.1894.



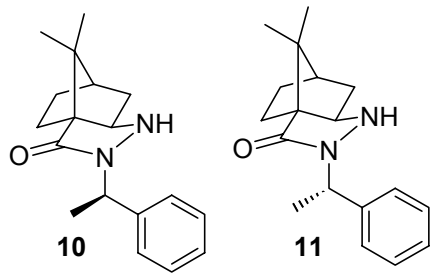
(*S*)-(+)-3-Benzhydryl-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one.

Prepared by a procedure similar to that described above for (*S*)-(+)-10,10-Dimethyl-3-naphthalen-1-ylmethyl-3,4-diaza-tricyclo [5.2.1.$0^{1,5}$]decan-2-one from (*S*)-(+)-3-Benzhydryl-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]dec-4-en-2-one (760 mg, 2.21 mmol). Purification by silica gel chromatography (20% EtOAc in hexanes) provided the title compound as a white solid (698 mg, 91 %). mp 178-179 ^oC; $[\alpha]_D$ -71.1° (*c* 1.00, $CHCl_3$); IR (neat) 1675, 3336 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.26 (m, 10H), 6.65 (s, 1H), 3.62 (dd, J = 4.7, 8.3 Hz, 1H), 2.24-2.15 (m, 1H), 2.00-1.87 (m, 3H), 1.71 (dd, J = 8.4, 13.1 Hz, 1H), 1.39-1.22 (m, 2H), 1.07 (s, 3H) 0.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4 (C), 138.6 (C), 138.4 (C), 129.5 (CH), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.6 (CH), 127.3 (CH), 66.0 (CH), 59.3 (CH), 58.0 (C), 51.0 (C), 47.0 (CH), 35.6 (CH_2), 28.9 (CH_2), 26.6 (CH_2), 21.2 (CH_3), 20.2 (CH_3); MS 346.2 (M^+); HRMS calcd for $C_{23}H_{26}N_2O$ 346.2047; found 346.2056.



(*S*)-(+)-3-tert-Butyl-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one

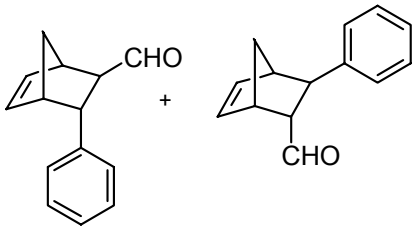
Prepared by a procedure similar to that described above for (*S*)-(+)-10,10-Dimethyl-3-naphthalen-1-ylmethyl-3,4-diaza-tricyclo [5.2.1.0^{1,5}]decan-2-one from (*S*)-(+)-3-tert-Butyl-10,10-dimethyl-3,4-diaza-tricyclo[5.2.1.01,5]dec-4-en-2-one (200 mg, 0.854 mmol). Purification by silica gel chromatography (30% EtOAc in hexanes) provided the title compound as a white solid (190 mg, 94 %). mp 103-106 ^{o}C; $[\alpha]_D$ +26.1° (*c* 1.10, $CHCl_3$); IR (neat) 3263, 2961, 1647 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.38 (dd, J= 8.3 Hz, 1H), 2.03-1.93 (m, 2H), 1.82-1.74 (m, 2H), 1.59 (dd, J = 13.2, 8.4 Hz, 1H), 1.34 (s, 9H), 1.21-1.08 (m, 2H), 1.16 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3 (C), 64.5 (CH), 59.3 (C), 55.9 (C), 50.5 (C), 46.8 (CH), 36.2 (CH_2), 28.9 (CH_2), 27.6 (CH_3), 26.4 (CH_2), 20.9 (CH_3), 20.5 (CH_3); MS 236.2 (M^+); HRMS calcd for $C_{14}H_{24}N_2O$ 236.1889; found 236.1864.



10 **11**

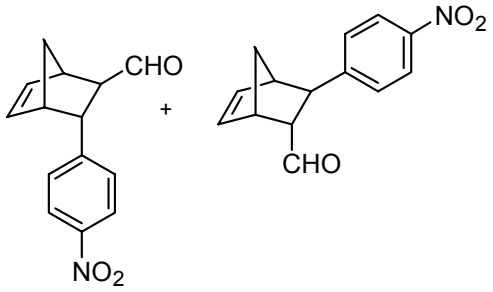
(*S*)-(+)-10,10-Dimethyl-3-(*R*-1-phenyl-ethyl)-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one (10) and (*S*)-(+)-10,10-Dimethyl-3-(*S*-1-phenyl-ethyl)-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one (11). Prepared by a procedure similar to that described above for (*S*)-(+)-10,10-Dimethyl-3-naphthalen-1-ylmethyl-3,4-diaza-tricyclo [5.2.1.0^{1,5}]decan-2-one from (*S*)-(+)-10,10-Dimethyl-3-(1-phenylethyl)-3,4-diaza-tricyclo[5.2.1.01,5]dec-4-en-2-one (300 mg, 1.06 mmol). The diastereoisomers were separated by silica gel chromatography (5% EtOAc in hexanes) to provide (*S*)-(+)-10,10-Dimethyl-3-(*R*-1-phenyl-ethyl)-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one **10** as a white solid (160 mg, 53 %). Crystals of **10** suitable for X-ray chrystallographic analysis were obtained by slow evaporation of the product from a minimum amount of THF at -20 °C. Mp 79-81^{o}C; $[\alpha]_D$ +62.1° (*c* 1.44, $CHCl_3$); IR (neat) 3249, 2958, 1662 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.35 (m, 4H), 7.26-7.22 (m, 1H), 5.50 (q, J = 7.0 Hz, 1H), 3.83 (br, 1H), 3.39 (dd, J = 8.3, 4.5 Hz, 1H), 2.19-2.11 (m, 1H), 2.07-2.01 (m, 1H), 1.90-1.81 (m, 2H), 1.58 (dd, J = 12.9, 8.3 Hz, 1H), 1.54 (d, J = 7.0 Hz, 3H), 1.28-1.23 (m, 2H), 1.22 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2 (C), 139.6 (C), 128.5 (CH), 127.6 (CH), 127.0 (CH), 64.9 (CH), 58.7 (C), 51.0 (C),

50.7 (CH), 46.8 (CH), 36.6 (CH_2), 28.7 (CH_2), 26.6 (CH_2), 20.8 (CH_3), 20.5 (CH_3), 16.3 (CH_3); MS 284.2 (M^+); HRMS calcd for $C_{18}H_{24}N_2O$ 284.1889; found 284.1888 and (*S*)-(+)-10,10-Dimethyl-3-(*S*-1-phenyl-ethyl)-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one **11** as a clear oil (102 mg, 34%). $[\alpha]_D$ -73.9° (*c* 1.03, $CHCl_3$); IR (neat) 3248, 2959, 1659 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.33 (m, 2H), 7.32-7.27 (m, 2H), 7.26-7.21 (m, 1H), 5.51 (q, J = 7.0 Hz, 1H), 3.45 (dd, J = 8.3, 4.5 Hz, 1H), 3.32 (br, 1H), 2.15-2.06 (m, 1H), 1.89-1.78 (m, 3H), 1.70-1.64 (m, 1H), 1.57 (d, J = 7.0 Hz, 3H), 1.28-1.17 (m, 2H), 1.02 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9 (C), 139.7 (C), 128.4 (CH), 127.6 (CH), 127.5 (CH), 66.5 (CH), 58.2 (C), 50.8 (C), 50.6 (CH), 46.9 (CH), 35.4 (CH_2), 28.6 (CH_2), 26.5 (CH_2), 21.3 (CH_3), 20.1 (CH_3), 16.3 (CH_3); MS 284.2 (M^+); HRMS calcd for $C_{18}H_{24}N_2O$ 284.1889; found 284.1917.

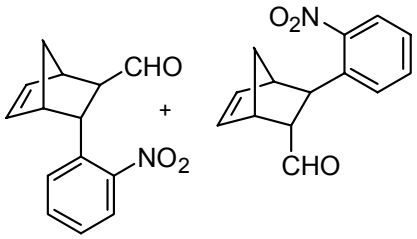


(1*R*, 2*R*, 3*R*, 4*S*)-3-phenylbicyclo[2.2.1]hept-5-ene-2-carboxaldehyde and (1*S*, 2*S*, 3*S*, 4*R*)-3-phenylbicyclo[2.2.1]hept-5-ene-2-carboxaldehyde (Table 2, entry 2). To a suspension of (*E*)-cinnamaldehyde (50 mg, 0.378 mmol) in distilled water (0.4 ml) was added (*S*)-(+)-10,10-Dimethyl-3-(*R*-1-phenyl-ethyl)-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one **10** (21.5 mg, 0.076 mmol) followed by CF_3SO_3H (6.7 μL, 0.07 mmol). After stirring for 1 to 2 minutes cyclopentadiene (75 mg, 1.13 mmol) was slowly added and the resulting mixture was stirred at room temperature until the reaction was judged to be complete by TLC analysis. The reaction mixture was extracted twice with ether and the combined organic extracts were washed successively with water and brine then dried over Na_2SO_4. Purification by silica gel chromatography (5% EtOAc in hexanes) provided the desired material as a 2.8:1 mixture of *exo* and *endo* isomers (colorless oil, 71 mg, 94 %). e*xo* ee 95%, *endo* ee 93%. Enantiomeric ratios were determined using chiral GLC analysis (Agilent/J&W CycloSil-B, 100 °C hold 3 min then 2 °C/min

gradient, flow=3.0 mL/min) *exo* isomers tr=42.7 min, 43.8 min, *endo* isomers tr=43.4 min, 44.3 min. ^{1}H NMR, ^{13}C NMR and IR data were identical to those previously reported.[3]



(1*R*, 2*R*, 3*R*, 4*S*)-3-(4-Nitrophenyl)-bicyclo[2.2.1]hept-5-ene-2-carboxaldehyde and (1*S*, 2*S*, 3*S*, 4*R*)-3-(4-Nitrophenyl)-bicyclo[2.2.1]hept-5-ene-2-carboxaldehyde (Table 2, entry 4). Prepared according to the general procedure described above from (*E*)-4-nitrocinnamaldehyde (50 mg, 0.28 mmol) and cyclopentadiene (56 mg, 0.85 mmol). Purification by silica gel chromatography (15% EtOAc in hexanes) provided the desired material as a 4:1 mixture of *exo* and *endo* isomers (pale yellow oil, 62 mg, 90 %). e*xo* ee 96 %, *endo* ee 93%. Enantiomeric ratios were determined by acetalization with (+)-(*R,R)*-hydrobenzoin and ^{1}H NMR analysis: (500 MHz, C_6D_6) *exo* isomers δ 5.48 (d, J = 5.2 Hz, CHO_2, major isomer), 5.46 (d, J = 6.0 Hz, CHO_2, minor isomer), *endo* isomers δ 5.14 (d, J=8.1 Hz, CHO_2, major isomer), 5.07 (d, J=8.2 Hz, CHO_2, minor isomer). ^{1}H NMR, ^{13}C NMR and IR data were identical to those previously reported.[3]



(1*R*, 2*R*, 3*R*, 4*S*)-3-(2-Nitrophenyl)-bicyclo[2.2.1]hept-5-ene-2-carboxaldehyde and (1*S*, 2*S*, 3*S*, 4*R*)-3-(2-Nitrophenyl)-bicyclo[2.2.1]hept-5-ene-2-carboxaldehyde (Table 2, entry 7). Prepared according to the general procedure described above from (*E*)-2-nitrocinnamaldehyde (100 mg 0.564 mmol) and cyclopentadiene (112 mg, 1.69 mmol). Purification by silica gel chromatography

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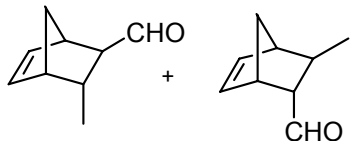
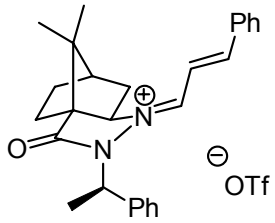
[3] a) M. Lemay, W.W. Ogilvie *Org. Lett.,* **2005**, *7,* 4141-4144; b) H. Fujioka, N. Kotoku, T. Fujita, R. Inoguchi, K. Murai, Y. Nagatomi, Y.; Sawama, Y.; Kita *Chirality*, **2003**, *15*, 60.

(15% EtOAc in hexanes) provided the desired material as a 3.3:1 mixture of *exo* and *endo* isomers (pale yellow oil, 122 mg, 89 %). *exo* ee 94%, *endo* ee 92%. Enantiomeric ratios were determined by acetalization with (+)-(*R,R)*-hydrobenzoin and ^{1}H NMR analysis: (500 MHz, C_6D_6) *exo* isomers δ 5.55 (d, J = 5.2 Hz, CHO_2, major isomer), 5.51 (d, J = 6.3 Hz, CHO_2, minor isomer), *endo* isomers δ 5.22 (d, J = 8.1 Hz, CHO_2, major isomer), 5.14 (d, J = 8.3 Hz, CHO_2, minor isomer). ^{1}H NMR, ^{13}C NMR and IR data were identical to those previously reported.[3]



(1*R*, 2*S*, 3*R*, 4*S*)-3-Methyl-bicyclo[2.2.1]hept-5-ene-2-carbaldehyde and (1*S*, 2*S*, 3*R*, 4*R*)-Methyl-bicyclo[2.2.1]hept-5-ene-2-carbaldehyde (Table 2, entry 9). Prepared according to the general procedure described above from (*E*)-crotonaldehyde (100 mg 1.42 mmol) and cyclopentadiene (282 mg, 4.28 mmol). Purification by silica gel chromatography (5% EtOAc in hexanes) provided the desired material as a 1.8:1 mixture of *exo* and *endo* isomers (clear oil, 151 mg, 78 %). e*xo* ee 82%, *endo* ee 80%. Enantiomeric ratios were determined by acetalization with (+)-(*R,R)*-hydrobenzoin and ^{1}H NMR analysis: (500 MHz, $CHCl_3$) *exo* isomers δ 5.53 (d, J = 6.2 Hz, CHO_2, major isomer), 5.52 (d, J = 6.2 Hz, CHO_2, minor isomer), *endo* isomers δ 5.17 (d, J=8.2 Hz, CHO_2, major isomer), 5.12 (d, J=8.2 Hz, CHO_2, minor isomer). ^{1}H NMR, ^{13}C NMR and IR data were identical to those previously reported.[3]



Imimium ion from (*S*)-(+)-10,10-Dimethyl-3-(*R*-1-phenyl-ethyl)-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one, (*E*)-cinnamaldehyde and triflic acid for X-ray Analysis (12): To a solution of (E)-cinnamaldehyde (46.0 mg, 0.352 mmol) and (*S*)-(+)-10,10-Dimethyl-3-(*R*-1-phenyl-ethyl)-3,4-diaza-tricyclo[5.2.1.01,5]decan-2-one **10** (100 mg, 0.352 mmol) in 19:1 CH_3NO_2 :H_2O (0.5 ml) was added CF_3SO_3H (31 μl, 0.352 mmol). After 4 hours the solvent was removed *in*

vacuo to afford a yellow oil which was dissolved in a minimum of THF. The solvent was then removed *in vacuo* and then the sample was redissolved in THF. This cycle was repeated several times until a pale yellow solid was obtained. This material was then dissolved in a minimum amount of THF and the mixture was allowed to stand at -20 °C to afford crystals of the iminium ion **12** that were of suitable quality for X-ray analysis.

Computational Methods:

Calculations for the dihedral driver experiment were carried out at the PM3 semi empirical level of theory using the Gaussian 98 suite of programs. To account for possible hysterysis in the dihedral driver experiment, the rotations about the C-N bond were performed from 0^o to 360^o and then back to 0^o. The values were averaged and converted to relative kcal/mol. The X-ray structure of **12** was compared to calculated structure **12 150°**. The average bond length error between the crystal structure **12** and **12 150°** was 0.021 Å and the average dihedral angle error was 1.45°, indicating a good correlation between the calculated structures (Figure 2 in article) and the actual iminium intermediate. One significant deviation was noted between these structures that involved the planarity of the "amide" nitrogen (N1 in Figure 4). In the calculated structure **12 150°** the improper torsion along C10-N1-N2-C11 was 136.1° whereas the same angle in the X-ray structure of **12** was almost 180 °. This discrepancy could be accounted for by the well known propensity of the PM3 basis set to pyramidalize amide nitrogens.

Iminium **3**

Dihedral Angle (°)	Hartree	Calculated Energy (kcal/mol)	Relative Energy (kcal/mol)
0	0.3475	218.059725	4.1603913
30	0.34725	217.9028475	4.0035138
60	0.34708	217.7961708	3.8968371
90	0.3461	217.181211	3.2818773
120	0.3419	214.545669	0.6463353
150	0.34148	214.2821148	0.3827811
180	0.34166	214.3950666	0.4957329
210	0.34439	216.1081689	2.2088352
240	0.34195	214.5770445	0.6777108
270	0.34087	213.8993337	0
300	0.3413	214.169163	0.2698293
330	0.34485	216.3968235	2.4974898
360	0.3475	218.059725	4.1603913

Iminium **12**

Dihedral Angle (°)	Hartree	Calculated Energy (kcal/mol)	Relative Energy (kcal/mol)
0	0.33969	213.1588719	4.4992467
30	0.34003	213.3722253	4.7126001
60	0.34278	215.0978778	6.4382526
90	0.34078	213.8428578	5.1832326
120	0.3364	211.094364	2.4347388
150	0.33252	208.6596252	0
180	0.33659	211.2135909	2.5539657
210	0.33893	212.6819643	4.0223391
240	0.34001	213.3596751	4.7000499
270	0.33828	212.2740828	3.6144576
300	0.33636	211.0692636	2.4096384
330	0.33853	212.4309603	3.7713351
360	0.33967	213.1463217	4.4866965

Iminium **13**

Dihedral Angle (°)	Hartree	Calculated Energy (kcal/mol)	Relative Energy (kcal/mol)
0	0.34141	214.2381891	5.2899093
30	0.33941	212.9831691	4.0348893
60	0.33652	211.1696652	2.2213854
90	0.33883	212.6192133	3.6709335
120	0.34191	214.5519441	5.6036643
150	0.34052	213.6797052	4.7314254
180	0.33577	210.6990327	1.7507529
210	0.3349	210.153099	1.2048192
240	0.33733	211.6779483	2.7296685
270	0.33298	208.9482798	0
300	0.33742	211.7344242	2.7861444
330	0.3453	216.679203	7.7309232
360	0.34141	214.2381891	5.2899093

X-Ray Structures:

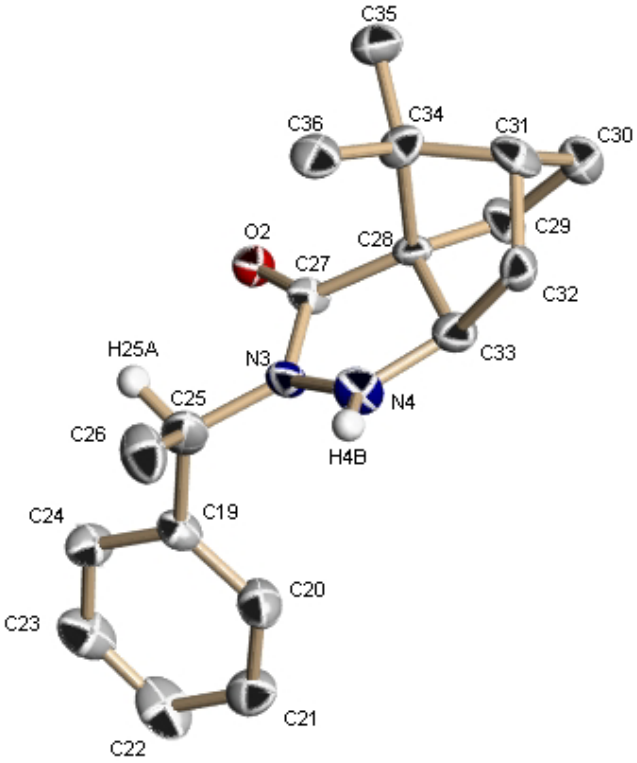


Figure 4

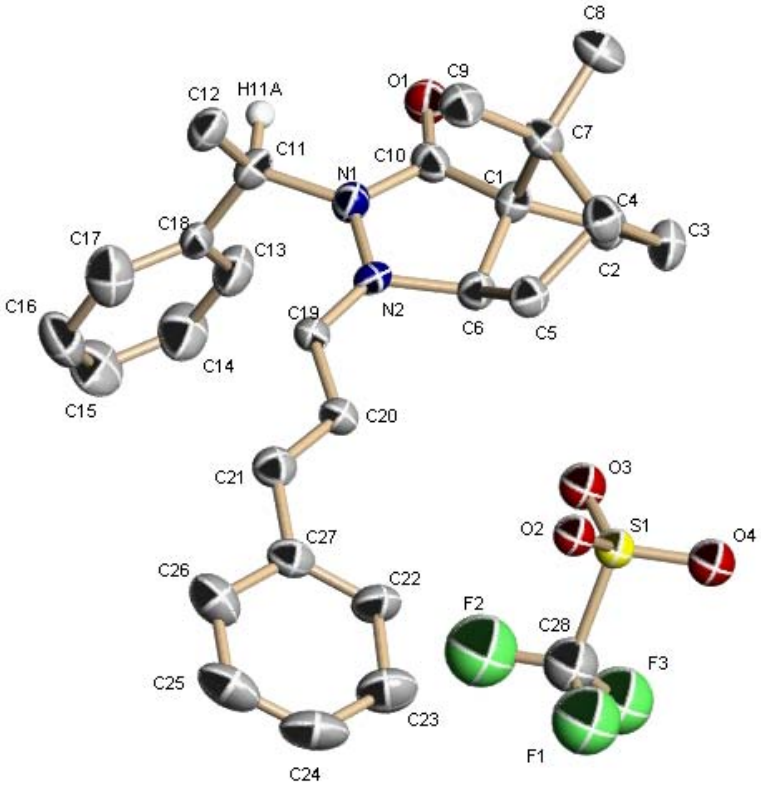


Figure 5