δ-Amino β-Ketoesters, A Designed Polyfunctionalized Chiral Building Block for Alkaloid Synthesis. Asymmetric Synthesis of (*R*)-(+)-2-Phenylpiperidine and (-)-SS20846A(1)

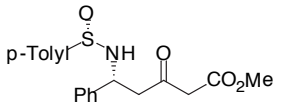
Franklin A. Davis*, Bin Chao, Tianan Fang and Joanna M. Szewczyk
Department of Chemistry, Temple University, Philadelphia, PA 19122

Supplemental Material

General procedure: Column chromatography was performed on silica gel, Merck grade 60 (230-400 mesh). Analytical and preparative thin layer chromatography was performed on precoated silica gel plates (250 and 400 mm) purchased from Analtech Inc. TLC plates were visualized by quenching of the UV fluorescence (λ_{max} 254nm), staining with iodine or staining with 0.5% ninhydin in ethanol. Melting points were recorded on a MelTemp apparatus and are uncorrected. Optical rotations were measured on a Perkin Elmer 341 polarimeter. IR spectra were recorded using NaCl plates or as KBr discs, on a Mattson 4020 FTIR spectrometer. ^{1}H and ^{13}C NMR were recorded on a General Electric Omega 500, operating at 500 and 125 M Hz respectively and the spectra were referenced to solvent residues as internal standards. HRMS were performed at the Department of Chemistry, Drexel University, Philadelphia, PA using a Fissions ZAB HF double focusing mass spectrometer. Elemental analyses were performed at the Department of Chemistry, University of Pennsylvania, Philadelphia, PA.

THF was freshly distilled under an inert atmosphere from a purple solution of sodium/benzophenone ketyl. Anhydrous CH_2Cl_2 was obtained by refluxing over calcium hydride followed by distillation under an inert atmosphere. $Zn(BH_4)_2$ was prepared according to a literature procedure.[1] All other reagents were obtained from commercial sources and used without further purifications. All reactions were performed under an inert atmosphere of argon unless otherwise stated and all glassware were vacuum or oven dried before use.

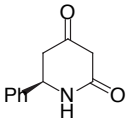
Methyl (*Ss,R*)-(+)-3-(*p*-toluenesulfinylamino)-3-phenyl-propanoate (**2**) was prepared as previously described.[2]



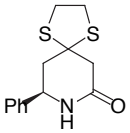
Methyl (*Ss,R*)-3-oxo-5-*N*-(*p*-toluenesulfinylamino)-5-phenyl-pentanoate (3) - (Two-step method). In a 25 mL one-necked round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed 4 mL (1.0 M solution in THF, 4 mmol) of NaHMDS in THF (6 mL). The solution was cooled to –78 ^{o}C and 0.19 mL (0.24 mmol, 4.0 equiv.) of anhydrous methyl acetate was slowly added via syringe. After stirring for 1 h at this temperature a solution of 0.191 (0.599 mmol) of (*Ss,R*)-(+)-**2**[2] in THF (4 mL) was added and the reaction mixture was quenched after 4 h with sat. NH_4Cl (1 mL) and H_2O (5 mL). The solution was extracted with EtOAc (2 x 25 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated. Flash chromatography gave 0.20 g (93%) of (*Ss,R*)-(+)-**3** as a colorless oil; $[\alpha]^{20}_{D}$ 73.60 (*c* 1.63, $CHCl_3$); IR (neat) 3194, 2361, 1748, 1718, 1319, 1260, 1090, 1059 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3 H), 3.08 (dd, J = 17.59, 5.5 , 1 H), 3.12 (dd, J = 17.59, 6.6, 1 H), 3.34 (s, 2 H), 3.63 (s, 3 H), 4.92 (dd, J = 5.86, 12.1, 1 H), 4.99 (d, J = 5.5, 1 H), 7.21-7.42 (m, 7 H), 7.57 (d, J = 8.3, 2 H); enol form (~10%) 2.19 (bs, 1 H), 2.39 (s, 3 H), 3.67 (s, 3 H), 4.88 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.2, 49.9, 50.5, 52.2, 54.0, 125.2,

127.2, 127.9, 128.6, 129.4, 140.3, 141.2, 142.0, 167.0, 200.4; enol form (43.8, 55.4, 51.1, 91.2); HRMS calcd. for $C_{19}H_{21}NO_4S$ (M+Na): 382.1089. Found: 382.1096.

One-step Method for the Preparation of 3. In a 500 mL of one-necked round-bottomed flask equipped with a magnetic stirring bar, rubber septum, and argon inlet was placed 148.2 mL (1.0 M solution in THF, 148.2 mmol, 6 equiv.) of NaHMDS in THF (100 mL), cooled to –78 °C and 7.85 mL (98.8 mmol) of anhydrous methyl acetate in THF (20 mL) was slowly added via syringe. After stirring for 1 h, anhydrous ether (100 mL) was added followed by the addition of 7.83 g (24.7 mmol) of sulfinimine (*S*)-(+)-**1** in THF (20 mL). The reaction mixture was stirred at –78 °C for 3.5 h (followed by TLC), and quenched at this temperature with sat. NH_4Cl (50 mL). The solution was extracted with ethyl acetate (3 x 150 mL) and the combined organic phases were dried (Na_2SO_4), and concentrated. Purification by flash chromatography (50% EtOAc/hexanes) to give 7.89 g (89%) of (*Ss,R*)-(+)-**3** and 0.86 g (11%) of (*Ss,R*)-(+)-**2**.

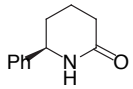


(*R*)-6-(+)-Phenylpiperidine-2,4-dione (4). In a 10 mL one-necked round-bottomed flask equipped with stirring bar and rubber septum was placed 1.0 g (2.785 mmol) of (*Ss, R*)-(+)-**3** in CH_2Cl_2 (20 mL) and MeOH (5 mL). To the reaction mixture at 0 °C was added 0.6 mL (7.78 mmol) of TFA. After stirring for 1 h, the solution was concentrated, the residue was loaded onto a short pad of silica gel and was washed with 30% EtOAc/hexanes (20-30 mL) until TLC indicated that the methyl *p*-toluenesulfinate by-produce had been removed. Elution with MeOH (20 mL) and concentrated gave a residue which was dissolved in CH_2Cl_2 (10 mL) and treated with sat. $NaHCO_3$ (5 mL). The reaction mixture was stirred for 1 h at rt and acidified to pH~3 with concentrated HCl . The organic phase was separated and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic phases were dried ($MgSO_4$) and concentrated to give 0.474 g (90%) of pure (*R*)-(+)-**4**; mp 166-168 °C [lit.[3] mp 167-169 °C for (±)-**4**]; $[\alpha]^{20}_D$ 124.3 (*c* 0.37, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.78 (dd, J = 16.13, 9.53, 1 H), 2.89 (dd, J=16.13,4.4, 1 H), 3.37 (s, 2 H), 4.81 (octet, J = 9.53, 4.47, 1.47, 1 H), 6.35 (br s, 1 H), 7.25-7.45 (m, 5 H).

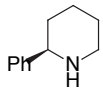


(*R*)-(-)-1-Aza-2-oxo-6-phenyl-1',3'-dithiaspiro[5,4]decane (5). In a 5 mL one-necked round-bottomed flask equipped with a magnetic stir bar, a rubber septum, and an argon balloon was placed 0.220 g (1.16 mmol, 1 equiv.) of (*R*)-(+)-**4** in CH_2Cl_2 (2 mL). To this solution was added dropwise, at rt, 0.97 mL (11.6 mmol, 10 equiv.) of ethanedithiol and 0.37 mL (2.92 mmol, 2.5 equiv.) of $BF_3{\cdot}OEt_2$ via syringe. The reaction mixture was stirred at rt for 8 h and 2 N NaOH (2 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic phases were washed with 10% NaOH (2 x 3 mL), brine (5 mL), dried (Na_2SO_4), and concentrated. Flash chromatography (10% EtOAc/hexanes) gave 0.26 g (85%) of (*R*)-**5** as a colorless oil; $[\alpha]^{20}_D$ -61.9 (*c* 0.42, $CHCl_3$); IR 3438.21, 3179.67, 3067.76, 1670.67, 1400.75, 1335.15, 1057.31 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.21 (dd, J =13.57, 11.00, 1 H), 2.45-2.50 (m, 2 H), 2.90-3.05 (m, 1 H), 3.32-3.45 (m, 4 H), 4.73 (dd, J = 11.0, 4.4, 1 H), 5.85

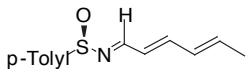
(bs, 1 H), 7.23-7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 40.00, 40.57, 48.22, 48.40, 57.81, 63.19, 126.88, 129.12, 129.73, 141.57, 170.08; HRMS calcd. for $C_{13}H_{15}NOS_2$(M+1): 266.0595; Found 266.0661.



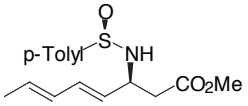
(*R*)-(+)-6-Phenylpiperidin-2-one (6): In a 50 mL one-necked round-bottomed flask equipped with a magnetic stir bar, a rubber septum, and an argon balloon was placed absolute ethanol (20 mL) and 0.26 g (0.99 mmol) of (*R*)-(+)-**5**. To this solution was added 1 g of W2 Raney nickel. The mixture was refluxed for 1 h (followed by TLC), and then cooled to rt. The suspension was filtered through a pad of Celite, concentrated and purified by flash chromatography (EtOAc/hexane/MeOH = 2.5:7:0.5) to afford 0.13 g (75%) of (*R*)-(+)-**6**; mp 119-120 °C; $[\alpha]^{20}_D$ 72.8 (*c* 1.2, $CHCl_3$); IR (KBr) 3420, 3055, 2243, 1597, 1444 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.66-1.93 (m, 3 H), 2.10-2.14 (m, 1 H), 2.42-2.48 (m, 2 H), 4.53-4.56 (m, 1 H), 5.96 (bs, 1 H), 7.27-7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 172.3, 142.5, 128.8, 128.0, 126.1, 57.8, 32.2, 31.3, 19.7; Anal. calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99; Found: C, 74.98; H 7.54; N, 7.79.



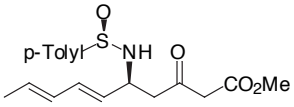
(*R*)-(+)-6-Phenylpiperidine (7). In a 10 mL one-necked round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon balloon was placed 0.033 g (0.19 mmol, 1 equiv.) of (*R*)-(+)-**6** and THF (1.2 mL). Lithium aluminum hydride (0.95 mL, 1.0 M solution in THF, 0.95 mmol) was added slowly via syringe and the reaction mixture was stirred at rt for 8 h. The solution was cooled to 0 °C, sat. Na_2SO_4 (0.17 mL) was added, stirred for 0.5 h at rt and the reaction mixture was filtered through Celite. The organic phases were concentrated and flash chromatography (7% MeOH/CH_2Cl_2) gave 0.025 g (82%) of (*R*)-(+)-**7** as volatile oil; $[\alpha]^{20}_D$ 50.0 (*c* 0.31, $CHCl_3$) [lit.[4] $[\alpha]^{20}_D$ 48.4 (*c* 0.31, $CHCl_3$) ; ^{1}H NMR ($CDCl_3$) δ 1.48-1.91 (m, 7 H), 2.80 (m, 1 H), 3.19 (d, J = 9.7 , 1 H), 3.59 (d, J =10.2 , 1 H), 7.20-7.39 (m, 5 H).



***E,E*-(*R*)-(-)-*N*-(2,4-hexadienalidene)-*p*-toluenesulfinamide (9)**. Prepared from 0.679 g (4.4 mmol) of (*R*)-(-)-*p*-toluenesulfinamide (**8**),[5] 0.48 mL (4.4 mmol) of sorbic aldehyde, 4.6 mL (22 mmol) of $Ti(OEt)_4$ at rt in CH_2Cl_2 (20 mL) as previously described[5] to give 0.974 g (95%) of (*R*)-(-)-**9** as a white solid; Rf 0.35 (20% EtOAc/hexanes). Since sorbic aldehyde (Aldrich) contains about 10% of the cis isomer approximately 10% of the cis-sulfinimine being formed. Two crystallization from hexanes improved the purity to >96% affording **9** in 50% yield; mp 89-90 °C; $[\alpha]^{20}_D$ -1009 (*c* 1.2, $CHCl_3$); IR (KBr) 1641, 1605, 1174, 1089, 1006 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.87 (dd, J = 0.7, 7.0, 3 H), 2.39 (s, 3 H), 6.11-6.17 (m, 1 H), 6.22-6.27 (m, 1 H), 6.37 (dd, J = 9.5, 15.0, 1 H), 6.86 (dd, J = 10.6, 15.4, 1 H), 7.29 (d, J = 8.4, 2 H), 7.56 (d, J = 8.4, 2 H), 8.36 (d, J = 9.5, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.4, 147.9, 142.8, 142.3, 139.9, 131.3, 130.5, 127.4, 125.3, 22.1, 19.4; Anal. calcd. for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48; N, 6.00; Found: C, 66.87; H, 6.51; N, 6.00.



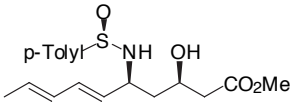
Methyl 4*E*,6*E*-(*Rs*,*S*)-(-)-3-*N*-(*p*-toluenesulfinylamino)-octa-4,6-dienoate (10): In a 100 mL two-necked round-bottomed flask equipped with a magnetic stir bar and argon-filled balloon was placed 1.95 mL (1.0 M solution in THF, 1.95 mmol) of NaHMDS in dry ether (30 mL). This solution was cooled to –78 °C and 0.15 mL (1.89 mmol) of anhydrous methyl acetate was added dropwise. After stirring for 30 min, 0.379 g (1.63 mmol) of sulfinimine (*R*)-(-)-**9** in Et_2O (30 mL) was added dropwise. After stirring for 5 h the reaction mixture was quenched at -78 °C with sat. NH_4Cl (2 mL), H_2O (2 mL) and the solution was warmed to rt. The reaction mixture was diluted with EtOAc (100 mL), washed with brine (30 mL), dried (Na_2SO_4) and concentrated to give crude product which was purified by flash chromatography (30% EtOAc/hexanes) to afford 0.425 g (85%) of the product as a single isomer (de > 97%); oil, Rf 0.30 (40% EtOAc/hexanes); $[\alpha]^{20}_D$ –133.9 (*c* 1.2, $CHCl_3$); IR (neat) 3189, 3020, 1739, 1437, 1176, 1091, 1061 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.74 (d, J = 6.6, 3 H), 2.39 (s, 3 H), 2.57 (dd, J = 6.6, 16.1, 1 H), 2.62 (dd, J = 5.7, 16.1, 1 H), 3.62 (s, 3 H), 4.24-4.29 (m, 1 H), 4.73 (d, J = 6.2, 1 H), 5.55 (dd, J = 7.3, 15.0, 1 H), 5.70-5.77 (m, 1 H), 6.01-6.06 (m, 1 H), 6.24 (dd, J = 10.4, 15.0, 1 H), 7.27(d, J = 8.2, 2 H), 7.57 (d, J = 8.2, 2 H); ^{13}C NMR ($CDCl_3$) δ 172.0, 142.9, 142.0, 133.8, 131.7, 131.1, 130.2, 129.8, 126.2, 53.6, 52.4. 41.4, 22.0, 18.8; Anal. calcd. for $C_{16}H_{21}NO_3S$: C, 62.51; H, 6.89; N, 4.56; Found: C, 62.52; H, 6.99, N, 4.38.



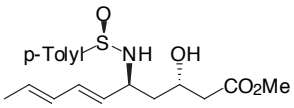
Methyl 6*E*,8*E*-(*Rs*,*S*)-(-)-3-oxo-5-*N*-(*p*-toluenesulfinylamino)-deca-6,8-dienoate (11) (one-step method). Following the one-step procedure described for the preparation of (*Ss,R*)-(+)-**3**, 0.489 g (2.1 mmol) of sulfinimine (*R*)-(-)-**9** was treated with 12.6 mL (1.0 M solution in THF, 12.6 mmol) of NaHMDS, and 0.67 mL (8.4 mmol) of anhydrous methyl acetate at –78 °C for 1.5 h. The solution was warmed to –20 °C, stirred for 8 h and quenched with sat. NH_4Cl (5 mL) and H_2O (5 mL). The solution was extracted with EtOAc (2 x 20 mL), the combined organic phases were dried (Na_2SO_4) an concentrated. Purification by flash chromatography (40% EtOAc:Hexanes) afforded 0.594 g (81%) of (*Rs*,*S*)-(-)-**11** as a colorless oil (de > 97%). Rf 0.13 (40% EtOAc/hexanes); $[\alpha]^{20}_D$ –78.9 (*c* 1.5, $CHCl_3$); IR (neat) 3191, 1750, 1718, 1089, 1058 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75 (d, J = 6.6, 3 H), 2.40 (s, 3 H), 2.88 (d, J = 5.9, 2 H), 3.40 (s, 2 H), 3.71 (s, 3 H), 4.30-4.33 (m, 1 H), 4.62 (d, J = 6.2, 1 H), 5.56 (dd, J = 7.3, 15.2, 1 H), 5.72-5.76 (m, 1 H), 6.03 (ddd, J = 1.5, 10.6, 15.2, 1 H), 6.24 (dd, J = 10.6, 15.2, 1 H), 7.28 (d, J = 8.0, 2 H), 7.56 (d, J = 8.0, 2 H); enol form (~10%): 1.96 (bs, 1 H), 3.72 (s, 3 H), 4.95 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 204.1, 167.8, 142.9, 142.0, 133.8, 131.8, 131.0, 130.2, 129.6, 126.1, 53.2, 53.1, 50.1. 49.6, 22.0, 18.8; enol form: 174.9, 134.0, 129.9, 91.9, 54.3, 51.9, 42.7; Anal. calcd. for $C_{18}H_{23}NO_4S$: C, 61.87; H, 6.63; N, 4.01; Found: C, 62.14; H, 6.74, N, 3.88.

(**Two-step procedure**): In a 25 mL two-necked round-bottomed flask equipped with a magnetic stir bar and argon-filled balloon was placed 2.9 mL (1.0 M in THF, 2.9 mmol) of NaHMDS in THF (3 mL), and cooled to –78 °C. Anhydrous methyl acetate 0.16 mL (2.0 mmol) was added dropwise at –78 °C and the solution was stirred for 30 min. A solution of 0.15 g (0.49 mmol) of methyl (*Rs*,*S*)-(-)-3-*N*-(*p*-toluenesulfinylamino)-octa-

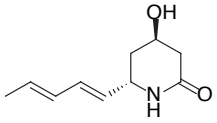
4,6-dienoate (**10**), prepared as described above, in THF (1 mL) was added dropwise and stirred for 0.5 h at –78 °C and at –20 °C for 8 h. The reaction mixture was quenched with sat. NH_4Cl (0.5 mL) and H_2O (0.5 mL) at –78 °C and warm to rt. The mixture was diluted with EtOAc (20 mL), washed with brine (5 mL), dried (Na_2SO_4) and concentrated to give the crude product which was purified by flash chromatography (40% EtOAc/CH_2Cl_2) to afford 0.13 g (76%) of (*Rs*,*S*)-(-)-**11** as a colorless oil; Rf 0.13 (40% EtOAc/hexanes); $[\alpha]^{20}_D$ –78.3 (*c* 1.6, $CHCl_3$).



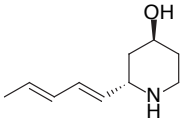
***syn* 6*E*,8*E*-Methyl (*Rs*,3*R*,5*S*)-(-)-3-hydroxy-5-*N*-(*p*-toluenesulfinylamino)-deca-6,8-dienoate (12)**. In a 5 mL of one-necked round-bottomed flask equipped with a magnetic stir bar and argon-filled balloon was placed 0.131 g (0.375 mmol) of (*Rs*, *S*)-(-)-**10**, in THF (10 mL). The solution was cooled to –78 °C and 2.9 mL (0.14 M in Et_2O, 0.41 mmol) of $Zn(BH_4)_2$[1] was added dropwise via syringe. The reaction mixture was stirred at –78 °C for 4 h , quenched with MeOH (2 mL) and sat. NH_4Cl (2 mL). After warming to rt, the mixture was extracted with ethyl acetate (3 x 10 mL) and the combined organic phases were washed with brine (10 mL), dried (Na_2SO_4) and concentrated to afford the product as a 76:24 mixture of diastereoisomers. Purification by prep. TLC (40% EtOAc/CH_2Cl_2) afforded 0.080 g (61%) of *syn*-(-)-**12** as a colorless oil; Rf 0.22 (40% EtOAc/CH_2Cl_2); $[\alpha]^{20}_D$ –57.7 (*c* 1.3, $CHCl_3$); IR (neat) 3372, 3267, 1738, 1437, 1168, 1088, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.63 (ddd, J = 2.6, 5.5, 13.9, 1 H), 1.73-1.76 (m, 1 H), 1.77 (dd, J = 1.3, 6.6, 3 H), 2.40 (s, 3 H), 2.41 (s, 1 H), 2.42 (d, J = 1.5, 1 H), 3.56 (d, J = 2.9, 1 H), 3.67 (s, 3 H), 4.15-4.19 (m, 2 H), 4.81 (d, J = 3.3, 1 H), 5.49 (dd, J = 7.8, 15.2, 1 H), 5.74-5.78 (m, 1 H), 6.07 (ddd, J = 1.3, 10.4, 15.2, 1 H), 6.30 (dd, J = 10.4, 15.2, 1 H), 7.28 (d, J = 8.1, 2 H), 7.58 (d, J = 8.1, 2 H); ^{13}C NMR ($CDCl_3$) δ 173.3, 143.3, 141.9, 133.7, 131.4, 131.2, 131.1, 130.2, 126.0, 67.6, 56.2, 52.4, 43.2. 42.3, 22.0, 18.8; HRMS calcd. for $C_{18}H_{25}NO_4S$ (M+Na): 374.1402; Found: 374.1391.



***anti* 6*E*,8*E*-Methyl (*Rs*,3*S*,5*S*)-(-)-3-hydroxy-5-(*p*-toluenesulfinylamino)-deca-6,8-dienoate (12)**: 0.010 g (8%); Rf 0.30 (40% EtOAc/CH_2Cl_2); $[\alpha]^{20}_D$ –69.5 (*c* 0.8, $CHCl_3$); IR (neat) 3375, 3268, 1736, 1437, 1168, 1087, 1048 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.64 (ddd, J = 3.3, 8.4, 14.3, 1 H), 1.77 (d, J = 6.6, 3 H), 1.82 (ddd, J = 4.4, 9.5, 14.3, 1 H) 2.41 (s, 3 H), 2.42 (dd, J = 4.0, 16.5, 1 H), 2.52 (dd, J = 8.8, 16.5, 1 H), 3.40 (bs, 1 H), 3.69 (s, 3 H), 4.18-4.23 (m, 2 H), 4.52 (d, J = 6.6, 1 H), 5.59 (dd, J = 6.6, 15.4, 1 H), 5.71-5.76 (m, 1 H), 6.07 (ddd, J = 1.6, 10.4, 15.4, 1 H), 6.25 (dd, J = 10.4, 15.4, 1 H), 7.30 (d, J = 8.2, 2 H), 7.61 (d, J = 8.2, 2 H); ^{13}C NMR ($CDCl_3$) δ 172.7, 142.1, 141.4, 131.7, 131.0, 130.5, 130.3, 129.5, 125.4, 64.7, 53.7, 51.7, 42.1. 41.1, 21.3, 18.1; HRMS calcd. for $C_{18}H_{25}NO_4S$ (M+Na): 374.1402; Found: 374.1391.



***Trans*-(4*R*,6*S*)-(+)-4-hydroxy-6-(1'*E*,3*E*'-penta-1',3'-dienyl)-2-piperidone (13)**. In a single necked round-bottomed flask equipped with a magnetic stirring bar and argon-filled balloon was placed 0.062 g (0.18 mmol) of (-)-**11** in MeOH (5 mL), and 0.069 mL (0.89 mmol) of TFA was added. After stirring at rt for 1 h (monitored by TLC, for the disappearance of the starting material), the solution was concentrated and the residue was loaded onto a short silica gel column and eluted with 40% EtOAc/hexanes (40-50 mL) until TLC into the removal of the methyl *p*-toluenesulfinate by-product. Further elution with methanol (50 mL) and concentration gave the amine triflate salt which was dissolved in THF (6 mL), and treated with sat. $NaHCO_3$ (2 mL). After stirring for 1 h, EtOAc (30 mL) was added, the organic layer was washed with brine (5 mL), dried (Na_2SO_4), and concentrated to afford 0.03 g (94%) of pure *trans*-(**+**)-**13** as a white gum; Rf 0.42 (10%, MeOH/CH_2Cl_2); $[\alpha]^{20}_D$ 90.9 (*c* 1.5, MeOH); IR (neat) 3362, 3266, 3180, 1646, 1475, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.69-1.74 (m, 2 H), 1.81 (dd, J = 1.5, 6.6, 3 H), 2.03-2.08 (m, 1 H), 2.46 (ddd, J = 1.8, 3.7, 18.0, 1 H), 2.63 (dd, J = 4.4, 18.0, 1 H), 4.28-4.32 (m, 1 H), 4.35-4.38 (m, 1 H), 5.49 (dd, J = 7.7, 15.0, 1 H), 5.73 (bs, 1 H), 5.75-5.82 (m, 1 H), 6.04-6.10 (m, 1 H), 6.21 (dd, J = 10.4, 15.2, 1 H); ^{13}C NMR (CD_3OD) δ 172.9, 132.2, 131.12, 131.09, 130.4, 62.9, 51.1, 39.4, 36.0, 17.4; Anal. Calcd. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73; Found: C, 65.74; H, 8.65, N, 7.56.



(2*S*,4*S*)-(-)-2-(Penta-1',3'-dienyl)piperidin-4-ol (14) (SS20846A). In a 25 mL single-necked round-bottomed flask equipped with a magnetic stir bar, rubber septum and argon-filled balloon was placed 0.070 g (0.39 mmol) of *trans*-(+)-**12** in THF (4 mL). The solution was cooled to –78 °C, and 1.93 mL (1.0 M solution in THF, 1.93 mmol) of lithium aluminum hydride was added slowly via syringe and the solution was stirred for 8 h at rt. The reaction mixture was cooled to 0 °C, and quenched with 2 N NaOH (1 mL). The aqueous phase was extracted with EtOAc (3 x 10 mL), the combined organic phases were washed with brine (5 mL), dried (Na_2SO_4) and concentrated. The residue was purified by prep. TLC (90:15:2, CH_2Cl_2/MeOH/28% NH_4OH) to afford 0.045 g (71%) of (-)-**14** as a colorless oil. $[\alpha]^{20}_D$ -15.7 (*c* 0.51, $CHCl_3$) [lit.[6] $[\alpha]^{24}_D$ -15.2 (*c* 0.53, $CHCl_3$), lit.[7] $[\alpha]^{25}_D$ -20 (*c* 1.4, $CHCl_3$)]. It had spectral properties identical with literature values[7].

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