# Supporting information

## Enantioselective Synthesis of $\alpha$-Hydroxy Acids Employing (1*S*)-(+)-*N*,*N*-Diisopropyl-10-camphorsulfonamide as Chiral Auxiliary

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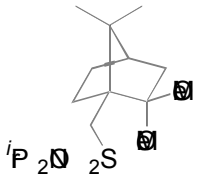
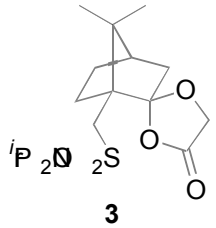


**2**

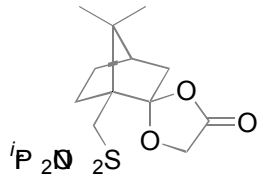
**(1*R*)-*N*,*N*-Diisopropyl-(2,2-dimethoxy-7,7-dimethylbicyclo[2.2.1]hept-1-yl) methanesulfonamide (2).** A mixture of 30g of **1**, 1g of *p*-TSA and 84 mL of $CH(OCH_3)_3$ in 150 mL of MeOH was stirred for 84 h at room temperature. The solution was quenched with 100 mL of saturated $NaHCO_{3(aq)}$, and MeOH was evaporated under reduced pressure. The residue was extracted with ethyl acetate (3_100mL). The combined organic phases were washed with brine, dried with $Na_2SO_{4(s)}$, evaporated *in vacuo*, and the residue was purified by column chromatography ($SiO_2$, hexane-EtOAc, 8:1, added 1~2% $NEt_3$) to give 3.40g (10.5%) of **1** and 31.46 g (85%) of **2** as white solid: mp = 73.8-74.6 _; $[\alpha]_D^{25}$ +16.54 (*c* 1.00, $CHCl_3$); IR (KBr) 2973, 2871, 2836, 1748, 1460, 1402, 1377, 1330, 1199, 1136 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz) δ 3.70 (hept, *J*=6.8 Hz, 2H), 3.46 (d, *J*=15.6 Hz, 1H), 3.30 (s, 3H), 3.13 (s, 3H), 2.72 (d, *J*=15.6 Hz), 2.29 (td, *J*=12.6, *J*=5.2 Hz, 1H), 2.16 (dt, *J*=13.2, *J*=3.6 Hz, 1H), 1.91 (ddd, *J*=7.7, *J*=7.7, *J*=3.6 Hz), 1.84-1.76 (m, 1H), 1.63 (t, *J*=4.8 Hz, 1H), 1.30 (d, *J*=6.8 Hz, 6H), 1.29 (d, *J*=6.8 Hz, 6H), 1.28-1.22 (m, 1H), 1.18 (d, *J*=13.2 Hz, 1H), 0.99 (s, 3H), 0.88 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 108.5, 53.3, 52.1, 51.1, 49.4, 48.2, 47.4, 43.0, 41.2, 27.0, 24.7, 22.4, 22.2, 21.5, 20.4; Anal. Calcd for $C_{18}H_{35}NO_4S$: C, 59.80; H, 9.76; N, 3.87; S, 8.87. Found: C, 60.07; H, 9.60; N, 4.22; S, 8.51.

**General procedure for Lewis acid catalyzed condensation of 2 with $\alpha$-hydroxy acid.** A solution of **2** (1 mmol) in $CH_2Cl_2$ (1mL) was added to the mixture of $\alpha$-hydroxy acid and $BF_3{\cdot}OEt_2$ (1.6 eq) in $Et_2O$ over 10 min at –50 $^oC$ under argon. After stirring about 30 to 60 min, the reaction was quenched with $Et_3N$ (0.6 mL). The solution was poured into 5 mL of iced water and extracted with $Et_2O$ (3_20mL). The combined organic phases were washed with brine, dried ($Na_2SO_4$), evaporated *in vacuo* and the residue was purified by column chromatography ($SiO_2$, hexane-EtOAc, 6:1) to give the condensation product.



**3**

**(1*R*,2*S*)-*N*,*N*-Diisopropyl-[2-spiro-2´-(1´-3´-dioxolane-4´-one)-7,7-dimethylbicyclo [2.2.1]hept-1-yl]methanesulfonamide (3).** Preparation from condensation with glycolic acid (2.2 eq), 74% yield: mp = 140.3-140.7 _; $[\alpha]_D^{25}$ –7.99 (*c* 1.00, $CHCl_3$); IR (KBr) $cm^{-1}$ 2974, 2879, 1806, 1468, 1394, 1281, 1258, 1338, 1258, 1243, 1198, 1154.; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 4.44 (d, *J*=14.2 Hz, 1H), 4.28 (d, *J*=14.2 Hz, 1H), 3.68

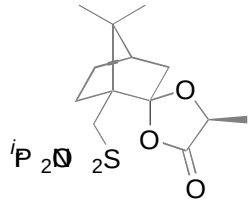


**4**

(hept, *J*=6.8 Hz, 2H), 3.30 (d, *J*=13.2 Hz, 1H), 2.56 (d, *J*=13.2 Hz, 1H), 2.38-2.26 (m, 2H), 1.80-1.90 (m, 3H), 1.76 (d, *J*=13.6 Hz, 1H), 1.39-1.38 (m, 1H), 1.28 (d, *J*=6.8 Hz, 3H), 1.27 (d, *J*=6.8, 3H), 0.99 (s, 3H), 0.87 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 171.0, 119.2, 64.7, 54.6, 52.4, 51.0, 48.3, 45.5, 44.0, 26.1, 26.6, 22.36, 22.2, 20.5, 20.1, Anal. Calcd for $C_{18}H_{31}NO_5S$: C, 57.88; H, 8.37; N, 3.75; S, 8.59. Found: C, 57.36; H, 8.34; N, 3.65; S, 8.61.

**(1*R*,2*R*)-*N*,*N*-Diisopropyl-[2-spiro-2´-(1´,3´-dioxolane-4´-one)-7,7-dimethylbicyclo [2.2.1]hept-1-yl]methanesulfonamide (4).** mp = 139.9-140.2 _; $[\alpha]_D^{25}$ –13.35 (*c* 1.00, $CHCl_3$); IR (KBr) 2997, 2968, 2934, 1800, 1458, 1333, 1270., 1240, 1199, 1174, 1136 $m^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz) δ 4.42 (d, *J*=14.6 Hz, 1H), 4.11, (d, *J*=14.6 Hz, 1H), 3.69 (hept, *J*=6.8 Hz, 2H), 3.17 (d, *J*=14 Hz, 1H), 2.59 (d, *J*=14 Hz, 1H), 2.50-2.40 (m, 1H), 2.26 (dt, *J*=13.2, 2.8 Hz, 1H), 1.84-1.72 (m, 3H), 1.69 (d, *J*=14 Hz, 1H), 1.38-1.30 (m, 1H), 1.27 (d, *J*=7.2 Hz, 12H), 1.00 (s, 3H), 0.88 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 172.2, 118.3, 62.9, 54.8, 52.3, 50.8, 48.3, 44.8, 44.2, 26.5, 25.2, 22.3, 22.2, 20.4, 20.1, Anal. Calcd for $C_{18}H_{31}NO_5S$: C, 57.88; H, 8.37; N, 3.75; S, 8.59. Found: C, 57.76; H, 8.24; N, 3.92; S, 8.24.

**(1*R*,2*S*,5´*S*)-*N*,*N*-Diisopropyl-[2-spiro-2´-(5´-methyl-1´,3´-dioxolane-4´-one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl]methanesulfonamide (7a).** Preparation from

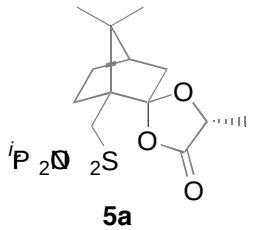


**7a**

condensation with *rac*-lactic acid (4.5eq), 77% yield: mp = 94.4-94.6 _; $[\alpha]_D^{25}$ +6.36 (*c* 1.00, $CHCl_3$); IR (neat) 2973, 2949, 2879, 1794, 1370, 1334, 1133, 976, 658 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 4.43 (q, *J* = 6.4 Hz, 1 H), 3.70 (hept, *J* = 6.4 Hz, 2 H), 3.30 (d, *J* = 13.2 Hz, 1 H), 2.56 (d, *J* = 13.2 Hz, 1 H), 2.39 (ddd, *J*=13.2, 9.6, 3.6 Hz, 1 H), 2.29 (dt, 1 H, *J* = 9.6, 3.6 Hz, 1 H), 1.92 (td, *J* = 13.2, 3.6 Hz, 1 H), 1.85-1.80 (m, 2 H), 1.71 (d, *J* = 13.2 Hz, 1 H), 1.53 (d, *J* = 6.4 Hz, 1 H), 1.38-1.22 (m, 1 H), 1.29 (d, *J* = 6.4 Hz, 6 H), 1.27 (d, *J* = 6.4 Hz, 6 H), 1.02 (s, 3 H), 0.90 (s, 3 H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 173.0,116.2, 70.6, 53.7, 52.1, 50.7, 48.2, 44.2, 43.9, 26.6, 26.1, 22.4, 22.2, 20.5, 20.2, 15.4; MS (EI) m/z (relative intensity) 387 ($M^+$, 0.1), 372 (3), 223 (21), 215 (7), 151 (100), 123 (47), 109 (56), 81 (35); HRMS calcd for $C_{19}H_{33}O_5NS$ ($M^+$ - Me) m/z 372.1842, found 372.1847; Anal. Calcd for $C_{19}H_{33}O_5NS$: C, 58.89; H, 8.58; N, 3.61; S, 8.27. Found: C, 58.79; H, 8.34; N, 3.64; S, 8.30.

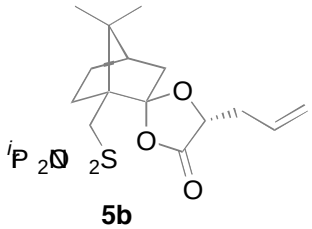
**(1*R*,2*S*,5′*S*)-*N*,*N*-Diisopropyl-[2-spiro-2′-(5′-phenyl-1′,3′-dioxolane-4′-one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl]methanesulfonamide (7b).** Preparation from condensation with *rac*-mandelic acid (2.2eq), 56% yield: Chromatography on silica gel (hexane-EtOAc, 6:1): mp = 112.3-112.6 _; $[\alpha]_D^{25}$ +2.29 (*c* 1.00, $CHCl_3$); IR (KBr) 3070, 2970, 2879, 1799, 1458, 1335, 1121, 977, 774 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.61-7.59 (m, 2 H), 7.36-7.32 (m, 3 H), 5.36 (s, 1 H), 3.43 (hept, *J* = 6.9 Hz, 1 H), 3.28 (d, *J* = 13.7 Hz, 1 H), 2.53 (d, *J* = 13.7 Hz, 1 H), 2.46 (dt, *J* = 13.4, 4.0 Hz, 1 H), 2.34-2.29 (m, 1 H), 2.09 (dt, *J* = 5.1, 13.4 Hz, 1 H), 1.90-1.80 (m, 4 H), 1.41-1.35 (m, 1 H), 1.16 (d, *J* = 6.9 Hz, 6 H), 1.22 (d, *J* = 6.9 Hz, 6 H), 1.07 (s, 3 H), 0.94 (s, 3 H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 170.2, 133.4, 128.6, 128.3, 127.3, 116.6, 75.0, 53.9, 51.7, 50.6, 48.0, 44.2, 44.0, 26.6, 25.7, 22.7, 21.6, 20.6, 20.2; MS (EI) m/z (relative intensity) 449 ($M^+$, 0.04), 434 (4), 284 (7), 257 (10), 151 (100), 123 (42), 109 (60), 93 (21), 81 (38), 67 (21); HRMS calcd for $C_{24}H_{35}O_5NS$ ($M^+$ - Me) m/z 434.1999, found 434.2003; Anal. Calcd for $C_{24}H_{35}O_5NS$: C, 64.11; H, 7.85; N, 3.12; S, 7.13 Found: C, 64.00; H, 7.64; N, 3.27; S, 7.16.

**General procedure for alkylations of 3, 7a, 7b.** A solution of LDA in THF (1.0 mL) was prepared under argon from diisopropylamine (0.14 mL, 1.0 mmol) and *n*-BuLi solution (2.2 M solution in hexane, 0.44 mL) at 0 °C. After stirring for 30 min, HMPA (1.2 eq) was added and cooling to –100 °C. A solution of dioxolanone (0.8 mmol) in THF (1.0 mL) was added over 20 min, and the mixture was allowed to stir for 30 min, then the alkyl halide (1.5 eq) was added. The mixture was allowed to warm to –78 °C, and stirred for 1 h. To the mixture was added 1% $H_2C_2O_{4(aq)}$ (1 mL) and warmed to 0°C and neutralized with 1% $H_2C_2O_{4(aq)}$ to pH=6~7. The solution was extracted with EtOAc, the combined organic phases were washed with brine, dried ($Na_2SO_4$), evaporated *in vacuo* and the residue was purified by column chromatography on silica gel to give the desired compound.



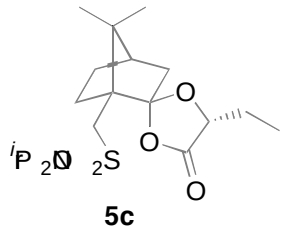
**5a**

**(1*R*,2*S*,5′*R*)-*N*,*N*-Diisopropyl-[2-spiro-2′-(5′-methyl-1′,3′-dioxolane-4′-one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl)methanesulfonamide (5a).** Chromatography on silica gel (hexane-EtOAc, 6:1): mp = 106.0-107.0 _; $[\alpha]_D^{25}$ –17.67 (*c* 1.00, $CHCl_3$); IR (KBr) 3002, 2973, 2886, 1801, 1457, 1413, 1375, 1328, 1283, 1257, 1240, 1200, 1154, 1117, 1034 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz) δ 4.60 (quat, *J*=6.8 Hz, 1H), 3.68 (hept, *J*=6.8 Hz, 2H), 3.28 (d, *J*=13.6 Hz, 1H), 2.55 (d, *J*=13.6 Hz, 1H), 2.37-2.24 (m, 2H), 1.90-1.76 (m, 4H), 1.43 (d, *J*=7.2 Hz 3H), 1.40-1.30 (m, 1H), 1.271 (d, *J*=6.8 Hz, 6H), 1.268 (d, *J*=6.8 Hz, 6H), 1.00 (s, 3H), 0.87 (s, 3H) ; $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 173.7, 117.5, 72.3, 54.8, 52.5, 51.2, 48.3, 47.2, 44.1, 26.6, 25.9, 22.5, 22.2, 20.6, 20.2, 19.0 ; Anal. Calcd for $C_{19}H_{33}O_5NS$: C, 58.89; H, 8.58; N, 3.61; S, 8.27; Found: C, 58.87; H, 8.50; N, 3.91; S, 8.65.



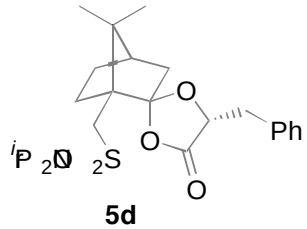
**5b**

**(1*R*,2*S*,5′*S*)-*N*,*N*-Diisopropyl-{2-spiro-2′-[5′-(prop-2′′-enyl)-1′,3′-dioxolane-4′-one]-7,7-dimethylbicyclo[2.2.1]hept-1-yl}methanesulfonamide (5b).** Chromatography on silica gel (hexane-EtOAc, 6:1): mp = 149.5-151.4 _; $[\alpha]_D^{25}$ –3.77 (*c* 1.00, $CHCl_3$); IR (KBr) 3007, 2973, 2881, 1798, 1332, 1283, 1240, 1201, 1153, 1136 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz) δ 5.74-5.85 (m, 1H), 5.20-5.13 (m, 2H), 4.62 (dd, *J*=6.8, *J*=4.8 Hz, 1H), 3.68 (hept, *J*=6.8 Hz, 2H), 3.29 (d, *J*=13.6 Hz, 1H), 2.64-2.50 (m, 1H), 2.56 (d, *J*=13.6, 1H), 2.62-2.54 (m, 1H), 2.48-2.23 (m, 2H), 1.90-1.73 (m, 4H), 1.38-1.30 (m, 1H), 1.28 (d, *J*=6.8 Hz, 6H), 1.27 (d, *J*=6.8 Hz, 6H), 0,99 (s, 3H), 0.86 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 172.3, 132.1, 118.9, 117.6, 75.8, 54.7, 52.3, 51.0, 48.2, 47.2, 43.8, 36.7, 26.4, 25.7, 22.4, 22.0, 20.4, 20.0 ; Anal. Calcd for $C_{21}H_{35}O_5NS$: C, 60.99; H, 8.53; N, 3.39; S, 7.75. Found: C, 60.65; H, 8.85; N, 3.27; S, 7.90.



**5c**

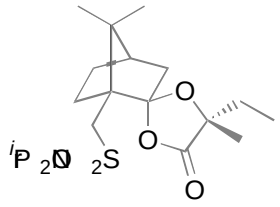
**(1*R*,2*S*,5′*R*)-*N*,*N*-Diisopropyl-[2-spiro-2′-(5′-ethyl-1′,3′-dioxolane-4′-one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl)methanesulfonamide (5c).** Chromatography on silica gel (hexane-EtOAc, 6:1): mp = 143.1-143.8 _; $[\alpha]_D^{25}$ –7.17 (*c* 1.00, $CHCl_3$); IR (KBr) 3002, 2968, 2949, 2891, 1800, 1328, 1238, 1155, 1136 $cm^{-1}$, $^1H$ NMR ($CDCl_3$, 400 MHz) δ 4.49 (dd, *J*=6.6, J=4.8 Hz, 1H), 3.69 (hept, *J*=6.8 Hz, 2H), 3.30 (d, *J*=13.6, 1H), 2.57 (d, *J*=13.6 Hz, 1H), 2.36-2.24 (m, 2H), 1.93-1.68 (m, 6H), 1.39-1.31 (m, 1H), 1.284 (d, *J*=6.8 Hz, 6H), 1.278 (d, *J*=13.6 Hz, 6H), 1.006 (s, 3H), 1.004 (t, *J*=7.2 Hz, 3H), 0.87 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 173.0, 117.5, 77.2, 54.8, 52.4, 51.1, 48.3, 47.0, 43.9, 26.5, 25.72, 25.68, 22.5, 22.1, 20.5, 20.1, 9.3 ; Anal. Calcd for $C_{20}H_{35}O_5NS$: C, 59.82; H, 8.79; N, 3.49; S, 7.99; Found: C, 59.82; H, 8.77; N, 3.77; S, 7.96.



**5d**

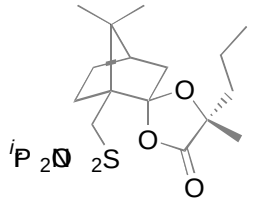
**(1*R*,2*S*,5′*R*)-*N*,*N*-Diisopropyl-[2-spiro-2′-(5′-phenylmethyl-1′,3′-dioxolane-4′-one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl)methanesulfonamide (5d).** Chromatography on silica gel (hexane-EtOAc, 6:1): mp = 160.3-161.0 _; $[\alpha]_D^{25}$ +1.78 (*c* 1.00, $CHCl_3$); IR (KBr) 2992, 2944, 2886, 1787, 1336, 1240, 1199, 1149, 1134 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.30-7.20 (m, 5H), 4.83 (t, *J*=5.2 Hz, 1H), 3.67 (hept, *J*=6.8 Hz, 2H), 3.25 (d, *J*=13.2 Hz, 1H), 3.25 (d, *J*=13.2 Hz, 1H), 3.08 (d, *J*=5.2 Hz, 2H), 2.51 (d, *J*=13.2 Hz, 1H), 2.42 (m, 1H), 1.82 (td, *J*=12.6 Hz, 1H), 1.76-1.60 (m, 3H), 1.26 (d, *J*=6.8 Hz, 12H), 1.30-1.18 (m, 1H), 1.16 (d, *J*=13.6 Hz, 1H), 0.91 (s, 3H), 0.80 (s, 3H) ; $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 172.5, 136.2, 129.8, 128.3, 126.9, 118.0, 77.4, 54.8, 52.4, 51.0, 48.3, 45.9, 43.7, 38.1, 26.4, 25.7, 22.5, 22.0, 20.4, 20.1 ; Anal. Calcd for $C_{25}H_{37}O_5NS$:

C, 64.76; H, 8.04; N, 3.02; S, 6.92; Found: C, 64.76; H, 8.00; N, 3.43; S, 7.11.



**8a**

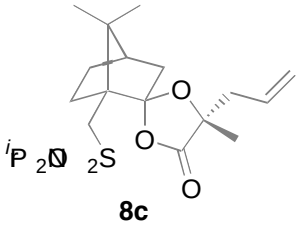
**(1*R*,2*S*,5′*R*)-*N*,*N*-Diisopropyl-[2-spiro-2′-(5′-ethyl-5′-mthyl-1′,3′-dioxolane-4′-one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl)methanesulfonamide (8a).** Alkylation without HMPA, chromatography on silica gel (hexane-ether, 4:1): mp = 185.4-185.5 _; $[\alpha]_D^{25}$ +9.52 (*c* 1.00, $CHCl_3$); IR (KBr) 3007, 2977, 1796, 1635, 1458, 1330, 1189, 1148, 1135, 1115, 983, 774 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 3.69 (hept, *J* = 6.4 Hz, 2 H), 3.28 (d, *J* = 13.2 Hz, 1 H), 2.58 (d, *J* = 13.2 Hz, 1 H), 2.35-2.24 (m, 2 H), 2.06-1.98 (m, 1 H), 1.84-1.68 (m, 5 H), 1.48 (s, 3 H), 1.38-1.21 (m, 1 H), 1.33 (d, *J* = 6.4 Hz, 6 H), 1.28 (d, *J* = 6.4 Hz, 6 H), 1.02 (s, 3 H), 1.0 (t, *J* = 8.0 Hz, 3 H), 0.91 (s, 3 H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 174.74, 115.1, 80.7, 54.1, 51.8, 50.4, 48.0, 46.5, 44.10, 30.36, 26.36, 25.6, 22.5, 21.7, 20.4, 20.0, 19.7, 7.2; MS (EI) m/z (relative intensity) 415 ($M^+$, 67), 267 (22), 251 (20), 171 (29), 151 (100), 109 (63), 86 (61), 55 (77); HRMS calcd for $C_{21}H_{37}O_5NS$ ($M^+$ - Me) m/z 400.2163, found 400.2154; Anal. Calcd for $C_{21}H_{37}O_5NS$: C, 60.69; H, 8.90; N, 3.37; S, 7.72. Found: C, 60.59; H, 8.71; N, 3.43; S, 7.78.



**8b**

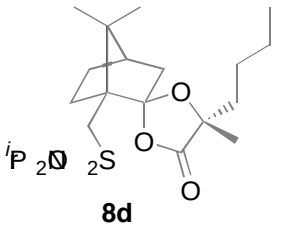
**(1*R*,2*S*,5′*R*)-*N*,*N*-Diisopropyl-[2-spiro-2′-(5′-methyl-5′-propyl-1′,3′-dioxolane-4′-one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl)methanesulfonamide (8b).** Alkylation without HMPA, chromatography on silica gel (hexane-ether, 4:1): mp = 191.6-191.8 _; $[\alpha]_D^{25}$ +2.17 (*c* 1.00, $CHCl_3$); IR (KBr) 2965, 2877, 1798, 1635, 1334, 1187, 1114, 1039, 982, 775, 660 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 3.69 (hept, *J* = 6.4 Hz, 2 H), 3.27 (d, *J* = 13.6 Hz, 1 H), 2.58 (d, *J* = 13.6 Hz, 1 H), 2.34-2.23 (m, 2 H), 2.06-1.99 (m,

1 H), 1.84-1.76 (m, 3 H), 1.71-1.21 (m, 5 H), 1.49 (s, 3 H), 1.29 (d, *J* = 6.4 Hz, 6 H), 1.27 (d, *J* = 6.4 Hz, 6 H), 1.01 (s, 3 H), 0.93 (t, *J* = 7.2 Hz, 3 H), 0.91 (s, 3 H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) δ 174.9, 115.3, 80.6, 54.3, 51.9, 50.4, 48.1, 46.5, 44.3, 39.8, 26.4, 25.7, 22.6, 21.8, 20.5, 20.5, 20.1, 16.4, 14.1; MS (EI) m/z (relative intensity) 429 ($M^+$, 0.2), 151 (32), 123 (15), 109 (25), 86 (75), 84 (100), 69 (9); HRMS calcd for $C_{22}H_{39}O_5NS$ ($M^+$ - Me) m/z 414.2349, found 414.2290; Anal. Calcd for $C_{22}H_{39}O_5NS$: C, 61.51; H, 9.15; N, 3.26; S, 7.46. Found: C, 61.60; H, 9.37; N, 3.34 S, 7.61.



**8c**

**(1*R*,2*S*,5′*R*)-*N*,*N*-Diisopropyl-{2-spiro-2′-[5′-methyl-5′-(prop-2′′-enyl)-1′,3′-dioxolane-4′-one]-7,7-dimethylbicyclo[2.2.1]hept-1-yl}methanesulfonamide (8c).** Alkylation without HMPA, chromatography on silica gel (hexane-Eether, 4:1): mp = 177.7-177.8 _; $[\alpha]_D^{25}$ +18.65 (*c* 1.00, $CHCl_3$); IR (KBr) 3007, 2971, 1798, 1645, 1332, 1247, 1185, 1146, 984, 919, 774, 660 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 5.87-5.76 (m, 1 H), 5.21-5.14 (m, 2 H), 3.69 (hept, *J* = 6.8 Hz, 2 H), 3.27 (d, *J* = 14.0 Hz, 1 H), 2.57 (d, *J* = 14.0 Hz, 1 H), 2.51-2.29 (m, 4 H), 2.06-1.98 (m, 1 H), 1.85-1.77 (m, 3 H), 1.55 (s, 3 H), 1.38-1.23 (m, 1 H), 1.28 (d, *J* = 6.8 Hz, 6 H), 1.27 (d, *J* = 6.8 Hz, 6 H), 1.01 (s, 3 H), 0.91 (s, 3 H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) δ 174.3, 131.1, 119.7, 115.5, 80.1, 54.3, 51.9, 50.5, 48.1, 46.6, 44.2, 41.9, 26.4, 25.7, 22.6, 21.8, 20.6, 20.5, 20.1; MS (EI) m/z (relative intensity) 427 ($M^+$, 0.13), 316 (3), 300 (2), 263 (16), 215

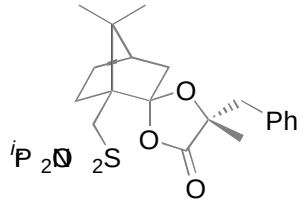


**8d**

(16), 151 (100), 123 (40), 109 (67), 81 (36), 67 (25); HRMS calcd for $C_{22}H_{37}O_5NS$ ($M^+$ - Me) m/z 412.2174, found 412.2147; Anal. Calcd for $C_{22}H_{37}O_5NS$: C, 61.80; H, 8.72; N, 3.28; S, 7.50 Found: C, 61.57; H, 8.52; N, 3.36; S, 7.51.

**(1*R*,2*S*,5′*R*)-*N*,*N*-Diisopropyl-[2-spiro-2′-(5′-methyl-5′-butyl-1′,3′-dioxolane-4′-**

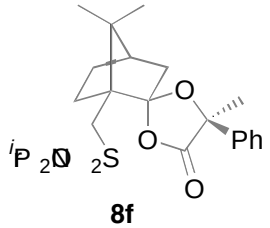
**one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl]methanesulfonamide (8d).** Alkylation without HMPA, chromatography on silica gel (hexane-ether, 4:1): mp = 148.3-148.5 _; $[\alpha]_D^{25}$ +5.13 (*c* 1.0, $CHCl_3$); IR (KBr) 2963, 2939, 2876, 1794, 1338, 1148, 1137, 978, 778, 661 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 3.69 (hept, *J* = 6.4 Hz, 2 H), 3.27 (d, *J* = 13.6 Hz, 1 H), 2.58 (d, *J* = 13.6 Hz, 1 H), 2.35-2.23 (m, 2 H), 2.06-1.99 (m, 1 H), 1.82-1.75 (m, 3 H), 1.71-1.64 (m, 2 H), 1.49 (s, 3 H), 1.39-1.27 (m, 3 H), 1.29 (d, *J* = 6.4 Hz, 6 H), 1.27 (d, *J* = 6.4 Hz, 6 H), 1.02 (s, 3 H), 0.92-0.88 (m, 5 H), 0.91 (s, 3 H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 175.0, 115.3, 80.6, 54.3, 52.0, 50.6, 48.2, 46.6, 44.3, 37.3, 26.5, 25.8, 25.1, 22.7, 22.6, 22.0, 20.6, 20.5, 20.2, 13.6; MS (EI) m/z (relative intensity) 443 ($M^+$, 0.3), 279 (12), 215 (14), 151 (100), 123 (42), 86 (46), 81 (35), 67 (20); HRMS calcd for $C_{23}H_{41}O_5NS$ ($M^+$ - Me) m/z 428.2464, found 428.2476; Anal. Calcd for $C_{23}H_{41}O_5NS$: C, 62.27; H, 9.32; N, 3.16. S, 7.23. Found: C, 62.15; H, 9.37; N, 3.34; S, 7.33.




**8e**

**(1*R*,2*S*,5′*R*)-*N*,*N*-Diisopropyl-[2-spiro-2′-(5′-methyl-5′-phenylmethyl-1′,3′-dioxolane-4′-one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl]methanesulfonamide (8e).** Alkylation without HMPA, chromatography on silica gel (hexane-ether, 4:1): mp = 130.4-130.6 _; $[\alpha]_D^{25}$ +32.33 (*c* 1.0, $CHCl_3$); IR (KBr) 3061, 3027, 2997, 2973, 2944, 2881, 1790, 1333, 1179, 1146, 1119, 979 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.32-7.22 (m, 5 H), 3.66 (hept, *J* = 6.8 Hz, 2 H), 3.22 (d, *J* = 14.0 Hz, 1 H), 3.14 (d, *J* = 14.8 Hz, 1 H), 2.88 (d, *J* = 14.8 Hz, 1 H), 2.60 (d, *J* = 14.0 Hz, 1 H), 2.28-2.20 (m, 2 H), 2.13-2.06 (m, 1 H), 1.83-1.76 (m, 2 H), 1.56 (d, *J* =13.2 Hz, 1 H), 1.44 (s, 3 H), 1.41-1.42 (m, 1 H), 1.26 (d, *J* = 6.8 Hz, 6 H), 1.25 (d, *J* = 6.8 Hz, 6 H), 1.02 (s, 3 H), 0.92 (s, 3 H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 174.6, 135.3, 130.4, 128.3, 127.1, 116.5, 81.4, 54.6, 51.9, 50.6, 48.2, 46.1, 44.4, 43.8, 26.4, 25.7, 22.9, 21.9, 21.6, 20.8, 20.2; MS (EI) m/z (relative intensity) 477 ($M^+$, 1.4), 313 (100), 300 (17), 215 (56), 151 (61), 123 (12), 109 (10); HRMS calcd for $C_{26}H_{39}O_5NS$ ($M^+$ - Me) m/z 477.2584, found 477.2517; Anal. Calcd for $C_{26}H_{39}O_5NS$: C, 65.38; H, 6.71; N, 2.93; S, 6.71. Found: C, 65.42; H,

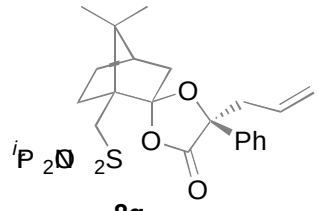
6.85; N, 3.03; S, 6.73.




**8f**

**(1*R*,2*S*,5′*S*)-*N*,*N*-Diisopropyl-[2-spiro-2′-(5′-methyl-5′-phenyl-1′,3′-dioxolane-4′-one)-7,7-dimethylbicyclo[2.2.1]hept-1-yl]methanesulfonamide (8f).** Alkylation without HMPA, chromatography on silica gel (hexane-ether, 4:1): mp = 142.2-142.4 _; $[\alpha]_D^{25}$ –18.55 (*c* 1.0, $CHCl_3$) IR (KBr) 3060, 2982, 2880, 1791, 1639, 1394 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.69–7.71(m, 2H), 7.35-7.23 (m,3H), 3.09 (d, *J*=14 Hz, 1H), 2.95 (b, 2H), 2.50-2.45 (m, 1H), 2.45 (d, *J*=14 Hz, 1H), 2.30-2.23 (m, 1H), 2.11-2.04 (m, 1H), 1.94-1.78 (m, 3H), 1.70 (m, 3H), 1.42-1.36 (m, 1H), 1.15 (s, 3H), 1.02 (d, *J*=6.4 Hz, 6H), 0.94 (d, *J*=6.4 Hz, 6H), 0.93 (s,3H) ; $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 172.7, 140.6, 128.0, 127.1, 124.1, 115.9, 79.8, 54.2, 51.2, 50.4, 47.5, 46.6, 44.2, 30.5, 26.5, 25.3, 22.8, 21.0, 20.5, 20.0; MS (EI) m/z (relative intensity) 464 ($M^+$+1, 1.08), 448 (11), 316 (27), 299 (46), 271 (28), 151 (100), 70 (50); HRMS calcd for $C_{25}H_{37}NO_5S$ ($M^+$) m/z 463.2392, found 463.2400; Anal. Calcd for $C_{25}H_{37}NO_5S$: C, 64.76; H, 8.04; N, 3.02; S, 6.92. Found: C, 64.76; H, 8.07; N, 3.03; S, 6.92.

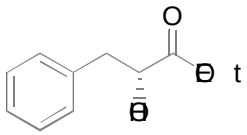
**(1*R*,2*S*,5′*S*)-*N*,*N*-Diisopropyl-{2-spiro-2′-[5′-phenyl-5′-(prop-2′′-enyl)-1′,3′-dioxolane-4′-one]-7,7-dimethyl-bicyclo[2.2.1]hept-1-yl}methanesulfonamide (8g).** Alkylation without HMPA, chromatography on silica gel (hexane-ether, 4:1): mp =




**8g**

147.5-147.7 _; $[\alpha]_D^{25}$ –19.64 (*c* 1.0, $CHCl_3$); IR (KBr) 2958, 2880, 1793, 1640, 1615, 1338, 1120, 977, 936, 702, 664 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.69-7.67 (m, 2H), 7.35-7.22 (m, 3H), 5.63-5.53 (m, 1H), 5.08-4.97 (m, 2H), 3.07 (d, *J*=13.2 Hz, 1H), 2.91

(b, 2H), 2.66 (d, *J*=7.2 Hz, 2H), 2.49-2.44 (m, 1H), 2.45 (d, *J*=13.2 Hz, 1H), 2.27-2.20 (m, 1H), 2.14-2.06 (m, 1H), 1.90-1.78 (m, 1H), 1.40-1.33 (m, 1H), 1.15 (s, 3H), 1.02 (d, *J*=6.4 Hz, 6H), 0.94 (d, *J*=6.4 Hz, 6H), 0.93 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) δ 171.0, 138.2, 130.1, 127.4, 126.7, 124.1, 119.4, 115.9, 81.6, 53.9, 51.0, 49.9, 46.9, 46.5, 46.4, 43.5, 26.0, 24.9, 22.4, 20.4, 20.0, 19.5; MS (EI) m/z (relative intensity) 490 ($m^+$+1,4.52), 420 (54), 316 (55), 215 (32), 151 (71), 105 (100), 77 (68), 43 (29); HRMS calcd for $C_{27}H_{39}NO_5S$ ($M^+$) m/z 489.2549, found 489.2556; Anal. Calcd for $C_{27}H_{39}NO_5S$: C, 66.23; H, 8.03; N, 2.82; S, 6.55. Found: C, 66.25; H, 8.08; N, 2.87; S, 6.53.

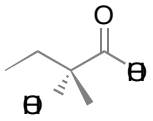



**6d**

**(2*R*)-Ethyl 2-hydroxy-3-phenylproponate (6d).** Anhydrous hydrogen chloride was bubbled through a solution of **5d** (464 mg, 1 mmol) in absolute ethanol (4 mL) for 10 min. After being refluxed for 6 hr, the solution was cooled, poured into the saturated $NaHCO_{3(aq)}$, and extracted twice with ether. The combined organic phases were washed with brine, dried ($MgSO_4$), and concentrated. The crude product was purified by column chromatography (SiO2, hexane-EtOAc, 6:1) to give 161 mg(83%) of **6d** and recover **1** (287mg, 91%): $[\alpha]_D^{25}$ +22.21 (*c* 3.85, $CHCl_3$); IR (neat) 3471(b), 3085, 3060, 3030, 2982, 2939, 1733, 1604, 1497, 1455, 1370, 1201, 1096, 1031 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 7.19-7.30(m, 5H), 4.42 (dd, *J*=6.4, *J*=4.4 Hz, 1H), 4.2 (quatet, *J*=7.2 Hz, 2H), 3.11 (dd, J=13.6, J=4.4 Hz, 1H), 2.95 (dd, *J*=13.6, J=6.4 Hz, 1H), 1.26 (t, *J*=7.2 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) δ 174.1, 136.3, 129.4, 128.2, 126.7, 71.1, 61.5, 40.4, 14.0.

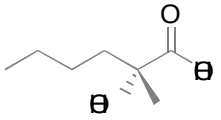
**General procedure for hydrolysis of 8a, 8d, and 8g.** A solution containing 1 g of **8** in 4 mL of MeOH and 1 mL of 1*N* $NaOH_{(aq)}$ was heated at 60 $^oC$ for 4h. After the solution was cooled, methanol was evaporated *in vacuo*. The residue was diluted with water (5 mL), and extracted with EtOAc (2_10mL). The organic phases were dried ($Na_2SO_4$) and concentrated to recover **1**. The pH value of aqueous layer was adjusted to 2 with concentrated $HCl_{(aq)}$, and then the solvent (water) was evaporated in reduced pressure.

The residue was dissolved in 10 mL of ether and filtered to remove salt (NaCl). The resulting solution was dried with $Na_2SO_{4(s)}$ and concentrated to give **9**.



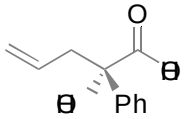
**9a**

**(2*R*)-2-hydroxy-2-methylbutanoic acid (9a).** 97% yield of **9a**, and 96% recovery yield of **1**: mp = 72.4-72.6 _; $[\alpha]_D^{24}$ –7.03 (*c* 1.4, 0.2N NaOH); IR (KBr) 3447, 3343, 2981-2583 (b), 1737 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.02 (b, 1H), 1.84-1.66 (m, 2H), 1.43 (s, 3H), 0.90 (t, J=7.3 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 181.8, 75.2, 32.9, 25.4, 7.8; MS (EI) m/z (relative intensity) 118 (M+, 2), 73 (100), 71 (14), 57 (42), 55 (90).



**9d**

**(2*R*)-2-hydroxy-2-methylhexanoic acid (9d).** 97% yield of **9d**, and 96% recovery yield of **1**: mp = 67.8-67.9 _; $[\alpha]_D^{23}$ –8.12 (*c* 0.85, $H_2O$); IR (neat) 3457, 3421, 2961-2578(b), 1735 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.10 (b, 1H), 1.78-1.62 (m, 2H), 1.43(s, 3H), 1.31-1.13 (m, 4H), 0.86 (t, *J*=6.96 Hz, 3H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ 161.8, 74.9, 39.7, 25.8, 25.7, 22.7, 13.8; MS (EI) m/z (relative intensity) 146 (M+, 39.51), 128 (44), 122 (42), 85 (59), 55 (100).



**9g**

**(2*S*)-2-hydroxy-2-phenyl-4-pentenoic acid (9g).** 94% yield of **9g**, and 93% recovery yield of **1**: mp = 132.1-132.3 _; $[\alpha]_D^{26}$ +29.54 (*c* 1.0, $CHCl_3$); IR (neat) 3423, 3080, 2915, 1725, 1640 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ 7.61-7.60(m, 2H), 7.37-7.24(m, 3H), 5.81-5.71(m, 2H), 5.25-5.81(m, 2H), 3.02(dd, *J*=14, *J*=7.2 Hz, 1H), 2.79 (dd,

*J*=14, *J*=7.2Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) δ178.5, 140.2, 131.7, 128.4, 128.2, 125.5, 120.4, 77.8, 44.1.