

**Asymmetric Aerobic Oxidation of α -Hydroxy Acid Derivatives by C_4 -Symmetric,
Vanadate-centered, Tetrakisvanadyl(V) Clusters Derived from
N-Salicylidene- α -aminocarboxylates**

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SUPPORTING INFORMATION

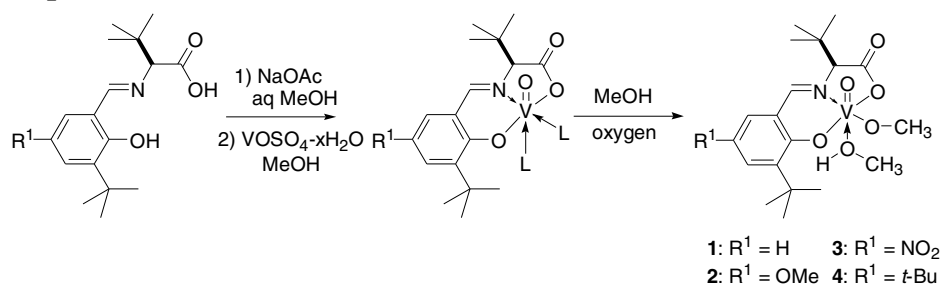
Representative experimental procedures, spectral data, X-ray data for **1'**, **4'**, and **5**, ¹H and ¹³C NMR spectra, and HPLC traces for racemic and resolved products (129 pages)

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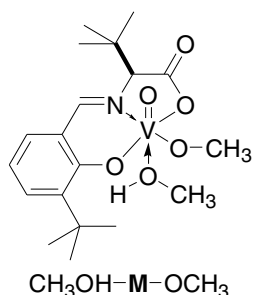
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General. ^1H NMR and ^{13}C NMR spectra were recorded on 400 MHz ^1H (100 MHz ^{13}C) spectrometers in deuteriochloroform with chloroform as an internal reference unless otherwise stated. Chemical shifts are reported in ppm (δ). Coupling constants, J , are reported in Hz. Infrared spectra were recorded on a FTIR spectrometer. Peaks are reported in units of cm^{-1} with the following relative intensities: br (broad), s (strong 67-100 %), m (medium 33-67 %), or w (weak 0-33 %). Mass spectra were recorded with an ionization voltage of 70 or 20 eV unless otherwise stated. Elemental analyses were obtained by the Northern Instrument Center of Taiwan. Fast atom bombardment (FAB) and electrospray ionization (ESI) mass spectra were recorded with data reported in the form m/e (intensity relative to base peak). Analytical TLC was performed on silica gel plates. Visualization was accomplished with UV light or with phosphomolybdic acid (PMA) and KMnO_4 staining agents. Column (flash) chromatography was performed using 32-63 μm silica gel. Analytical high pressure liquid chromatography (HPLC) was performed with a built-in photometric detector ($\lambda = 220 \text{ nm}$ or 254 nm) using a CHIRALPAK AD-H (0.46 cm \times 25cm) or CHIRALCEL AS (0.46 cm \times 25 cm) column. Solvents for HPLC analyses were of spectroscopic grade and filtered before use. All enantiomeric excess determinations for optically enriched products were correlated with the corresponding racemic samples by HPLC analyses on chiral columns. Solvents for extraction and chromatography were reagent grade. Optical rotations are reported as follows: $[\alpha]^T$ ($c = \text{g}/100\text{mL}$, solvent). THF and toluene were dried over benzophenone-ketyl intermediate under nitrogen atmosphere and distilled before use. MeOH was dried over magnesium turnings under nitrogen atmosphere and distilled before use. All reaction products were isolated as chromatographically pure materials.

Representative preparation procedure and analytical data for vanadyl(V) methoxide (or hydroxide) complexes 1-4



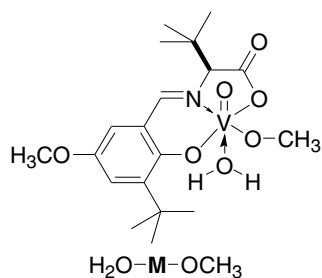
In a 50-mL, two-necked, round-bottomed flask was placed L-tert-leucine (5 mmol) and NaOAc·5H₂O (1.17 g, 10 mmol) in degassed water (10 mL). After having been stirred at 60 °C for 10 min to effect their complete dissolution, the reaction mixture was treated dropwise with a solution of respective 2-hydroxy-benzaldehyde derivatives (5 mmol) in degassed EtOH (12.5 mL). The reaction mixture became homogeneous by heating at 80 °C for 15 min and then gradually cooled to ambient temperature for 2 h. To the resultant Schiff base was added a solution of vanadyl(IV) sulfate trihydrate (1.08 g, 5 mmol) in degassed water (5 mL). Dark green complex started crashing out in 15 min. The reaction mixture was stirred for 2h and then concentrated to half of the original solvent volume. The crude vanadyl(IV) complex collected by filtration was washed sequentially with water (5 × 25 mL) and cold ether (5 × 25 mL) and then dried *in vacuo* to furnish pure vanadyl(IV) catalyst. The corresponding analytically pure vanadyl(V) methoxide (or hydroxide) complexes were obtained by re-crystallization from oxygen-saturated MeOH and were used for asymmetric aerobic oxidation experiments.



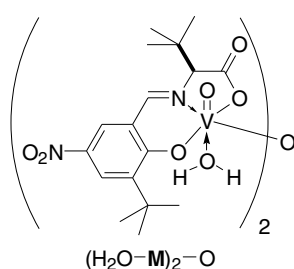
Data for complex **1**: M.W. (M: C₁₇H₂₃NO₄V) 356; MS (ESI) 752 (M₂O+H+Na⁺, 12), 1090 (M₃+Na⁺, 100); IR (KBr) ν 3114 (br, m), 2959 (m), 2915 (m), 2817 (m), 1690 (m), 1657 (m), 1617 (m, C=N), 1606, 1587 (m, COO), 1554 (m), 1425 (m), 1395 (m), 1362 (m), 1303 (m), 1285 (m), 1259 (m), 1196 (m), 1145 (m), 979 (m, V=O) cm⁻¹; $[\alpha]_D^{25}$ -28.5 (*c* 1.0, CH₂Cl₂);

TLC R_f 0.32 (MeOH/CH₂Cl₂, 1/8); Anal. Calcd. For [(CH₃OH)MOCH₃]: C, 54.41; H, 7.21; N, 3.34.

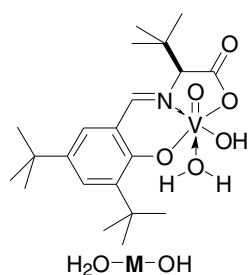
Found: C, 54.53; H, 7.05; N, 2.59.



Data for complex **2**: M.W. (**M**: $\text{C}_{18}\text{H}_{25}\text{NO}_5\text{V}$) 386; MS (ESI) 820 ($\text{M}_2\text{O}+\text{MeOH}^+$, 11), 819 ($\text{M}_2\text{O}+\text{OMe}^+$, 19), 405 ($\text{M}+\text{H}_2\text{O}+1^+$, 15), 404 ($\text{M}+\text{H}_2\text{O}^+$, 21), 402 ($\text{M}+\text{O}^+$, 100); IR (KBr) ν 3424 (br, m), 3070 (m), 2952 (s), 2908 (s), 2871 (s), 1687 (s), 1654 (s, C=N), 1598 (s, COO), 1555 (s), 1458 (s), 1425 (s), 1395 (s), 1351 (s), 1289(s), 1215 (s), 1196(s), 1148 (s), 1053 (s), 1027 (m), 979 (s, V=O) cm^{-1} ; $[\alpha]_{\text{D}}^{25}$ -33.5 (*c* 1.0, CH_2Cl_2); TLC R_f 0.25 (MeOH/ CH_2Cl_2 , 1/8); Anal. Calcd. For $[(\text{H}_2\text{O})\text{MOCH}_3]$: C, 52.41; H, 6.95; N, 3.22. Found: C, 52.67; H, 6.75; N, 2.98.

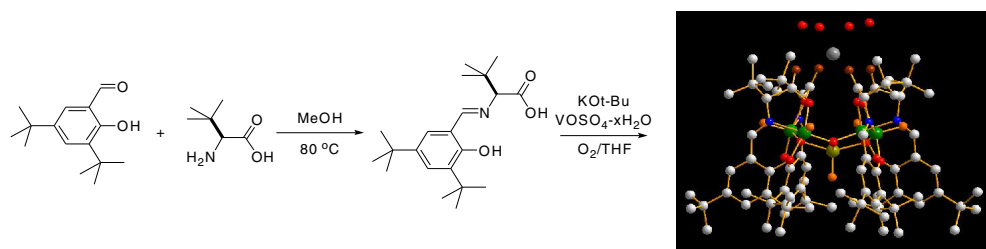


Data for complex **3**: M.W. (**M**: $\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}_6\text{V}$) 401; MS (ESI) 850 ($\text{M}_2\text{O}+\text{MeOH}^+$, 90), 420 ($\text{M}+\text{H}_2\text{O}+1^+$, 7), 419 ($\text{M}+\text{H}_2\text{O}^+$, 9), 417 ($\text{M}+\text{O}^+$, 100); IR (KBr) ν 3365 (br, w), 2967 (w), 2915 (w), 2817 (w), 1631 (m, C=N), 1598 (m, COO), 1569 (w), 1513 (w), 1484 (w), 1465 (w), 1425 (w), 1399 (w), 1373 (w), 1329 (m), 1226 (w), 1024 (w), 1182 (w), 1112 (w), 1034 (w), 990 (w), 927 (m, V=O) cm^{-1} ; $[\alpha]_{\text{D}}^{25}$ -14.1 (*c* 1.0, CH_2Cl_2); TLC R_f 0.30 (MeOH/ CH_2Cl_2 , 1/4); Anal. Calcd. For $[(\text{H}_2\text{O})\text{M}]_2\text{O}\cdot 2\text{H}_2\text{O}$: C, 45.85; H, 5.88; N, 6.29. Found: C, 45.57; H, 5.83; N, 6.15.



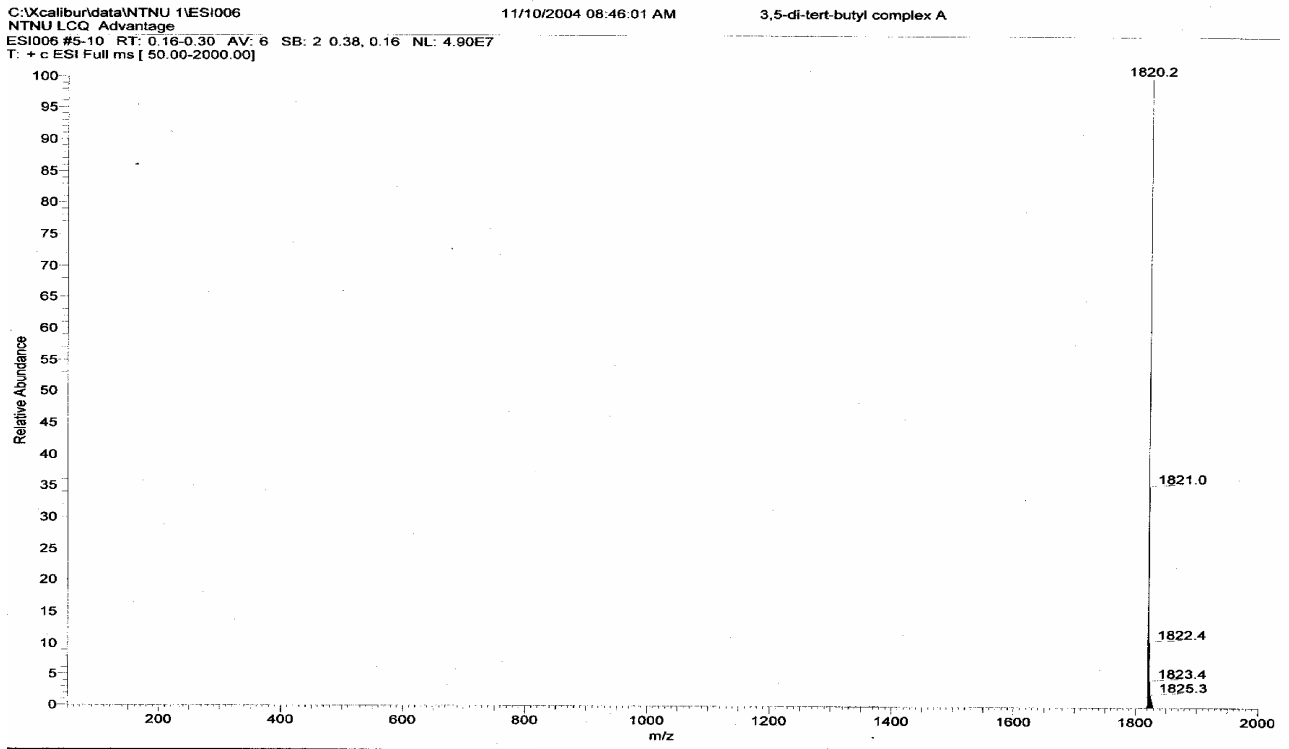
Data for complex **4**: M.W. (**M**: $\text{C}_{21}\text{H}_{31}\text{NO}_4\text{V}$) 412; MS (ESI) 881 ($\text{M}_2\text{O}+\text{H}_2\text{O}+\text{Na}^+$, 6), 460 ($\text{MOCH}_3+\text{H}_2\text{O}^+$, 77), 444 ($\text{M}+\text{CH}_3\text{OH}^+$, 13), 413 ($\text{M}+\text{H}^+$, 100); ^{51}V NMR (CDCl_3) δ -583.38; IR (KBr) ν 3322 (br, w), 2959 (m), 2908(w), 2871 (w), 1698 (m), 1613 (s, C=N), 1557 (w, COO), 1477 (w), 1462 (m), 1436 (w), 1414 (w), 1392 (w), 1362 (w), 1322 (w), 1300 (w), 1274 (w), 1252 (w), 1211 (w), 1182 (w), 1078 (w), 982 (w, V=O) cm^{-1} ; $[\alpha]_{\text{D}}^{25}$ +36.02 (*c* 1.0, CH_2Cl_2); TLC R_f 0.37 (MeOH/ CH_2Cl_2 , 1/8); Anal. Calcd. For $[(\text{H}_2\text{O})\text{MOH}]$: C, 56.37; H, 7.66; N, 3.13. Found: C, 55.72; H, 7.32; N, 2.71.

Procedure for the preparation of C_4 -symmetric penta-nuclear vanadyl(V) cluster-5

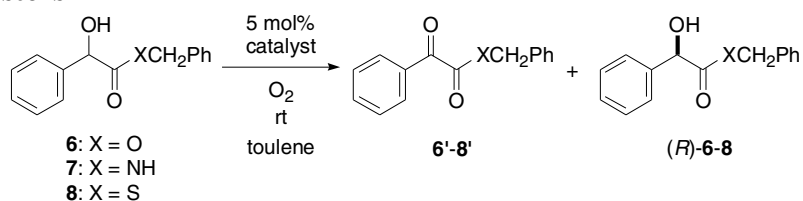


In a 50-mL, round-bottomed flask was placed *L-tert-leucine* (131 mg, 1.0 mmol) and 3,5-di-*tert*-butyl-salicylaldehyde (234 mg, 1.0 mmol) in anhydrous methanol (5 mL) under oxygen atmosphere. After having been refluxed at 80 °C for 12 hours, the reaction mixture led to complete formation of the resultant Schiff base. A solution of potassium *tert*-butoxide (258 mg, 2.3 mmol) in anhydrous THF (1 mL) was added dropwise to the Schiff base at ambient temperature. The reaction mixture was then stirred for 1 hour and a solution of $VOSO_4 \cdot xH_2O$ (203.8 mg, 1.25 mmol) in anhydrous THF (1 mL) was added gradually. A dark green species was formed immediately and precipitated out completely in 20 min. After having been stirred under oxygen atmosphere for additional 24 hours, the dark green reaction mixture was concentrated in vacuo to half of the original volume. The crude penta-nuclear cluster was collected by filtration and washed sequentially with water (5 × 25 mL) and cold diethyl ether (5 × 25 mL) and then dried under vacuum. The pure penta-nuclear cluster-**5** was obtained by recrystallization from wet MeOH with slow evaporation of MeOH and then used for asymmetric aerobic oxidation experiments. Single crystal suitable for X-ray crystallographic analysis was obtained by re-crystallization from MeOH to yield 742 mg (38%) of brown prism: 1H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.82 (d, $J = 2.0$, 1H), 7.50 (d, $J = 2.4$, 1H), 4.03 (s, 1H), 1.59 (s, 3H), 1.38 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 143.0, 138.1, 132.9, 128.4, 121.2, 86.9, 38.2, 35.2, 34.9, 31.7, 30.4, 30.3, 28.1; ^{51}V NMR ($CDCl_3$) δ -536.14, -609.59; MW MS (ESI) (**M**: $C_{84}H_{132}KN_4O_{25}V_5$, 1891.74) 1820 (**M**-4 H_2O , 100); IR (KBr) ν 3434 (br, w), 3188 (br, m), 2969 (w), 1619 (s, C=N), 1541 (m, COO), 1510 (m), 1455 (m), 1429 (m), 1390 (m), 1362 (m), 1340 (m), 1309 (m), 1250 (m), 1192 (m), 1164 (m), 1244 (m), 1004 (m, V=O), 979 (bs, V=O) cm^{-1} ; $[\alpha]_D^{25}$ +66.3 (c 1.0, CH_2Cl_2); Anal. Calcd. For **M**+2**MeOH** ($C_{86}H_{140}KN_4O_{27}V_5$): C, 52.81; H, 7.21; N, 2.86. Found: C, 52.37; H, 6.75; N, 2.97.; m.p.

260-262 °C.

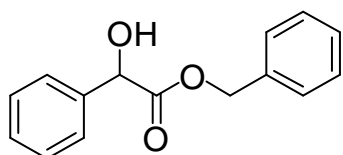


Representative procedure for the asymmetric aerobic oxidation of X-benzyl α -hydroxy-esters, amides, and thioesters



To a 50-mL, two-necked, round-bottomed flask was placed vanadyl(V) catalyst (0.05 mmol, 5 mol%) in oxygen-saturated toluene (3 mL) under oxygen atmosphere. The reaction flask was vacuum-evacuated at 15 torr for 20 sec and then filled with an O₂ balloon (150 mL). A solution of α -hydroxy-ester/amide/thioester (1 mmol) in oxygen-saturated toluene (2 mL) was added by cannula and the resulting dark brown mixture was stirred at ambient temperature. The reaction progress was monitored by ¹H NMR spectroscopy for percent conversion (142 mg; i.e. 1 mmol of 2-methyl-naphthalene was used as an internal standard). The enantiomeric excess of the kinetically resolved product was determined by chiral HPLC analysis after filtration of the reaction aliquot (100 μ L) over a short plug of silica gel (Et₂O or CH₂Cl₂ as eluent). Upon reaching optimal resolution of the asymmetric oxidation (50-53 % conversion), the reaction was quenched by addition of silica gel (150 mg) and the mixture was concentrated under reduced pressure. The resulting residue was loaded directly on top of an eluent-filled silica gel column and purified by flash column chromatography. The enantiomeric excess of the pure, resolved α -hydroxy-ester, amide, and thioester was analyzed again by chiral HPLC analysis.

Benzyl 2-hydroxy-2-phenyl-acetate¹ (6)

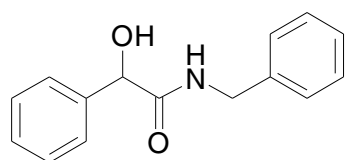


¹H NMR (400 MHz, CDCl₃) δ 7.43-7.30 (m, 7H), 7.21-7.19 (m, 2H), 5.24 (d, J = 12.0, 1H), 5.22 (d, J = 5.2, 1H), 5.14 (d, J = 12.0, 1H), 3.41 (d, J = 5.2, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 173.5, 138.2,

135.0, 128.6, 128.5, 128.5, 128.4, 127.9, 126.6, 73.0, 67.6; MS (EI, 70 eV) (C₁₅H₁₄O₃, 242) 242 (M⁺, 4), 226 (12), 107 (100), 92 (18), 90 (24), 80 (12), 79 (19), 77 (11); TLC R_f 0.34 (EtOAc/hexane, 1/5); HPLC t_R 19.1 min (*S*), 23.5 min (*R*) (Chiralpak AD-H, *i*-PrOH/hexane, 6/94, 1.0 ml/min, λ = 254 nm). After kinetic resolution: 19.1 min (*S*, minor, 0.8%), 23.5 min (*R*, major,

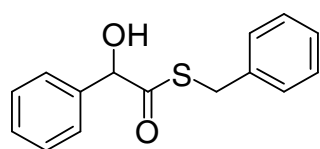
99.2%). $[\alpha]_{\text{D}}^{25}$ -53.9 (*c* 1.0, MeOH) for 98 %ee (lit. $[\alpha]_{\text{D}}^{25}$ -49.2 (*c* 1.51, MeOH) for (*R*)); m.p. 96-98 °C.

N-Benzyl-2-hydroxy-2-phenyl-acetamide² (7)



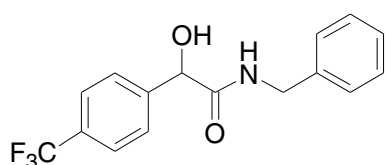
¹H NMR (400 MHz, CDCl₃) δ 7.42-7.35, 7.31-7.26 (m, 8H), 7.19-7.17 (m, 2H), 6.48 (bs, 1H, NH), 5.07 (s, 1H), 4.50-4.39 (m, 2H), 3.61 (bs, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 172.1, 139.4, 139.3, 137.7, 128.9, 128.7, 127.57, 127.55, 126.8, 74.2, 43.4; MS (ESI) (C₁₅H₁₅NO₂, 241) 505 (M₂+Na⁺, 100), 264 (M+Na⁺, 12); TLC R_f 0.28 (EtOAc/hexane, 1/2); HPLC t_R 18.1 min (*R*), 30.2 min (*S*) (Chiralpak AD-H, *i*-PrOH/hexane, 8/92, 1.0 mL/min, λ = 254 nm). After kinetic resolution: 18.4 min (*R*, major, > 99 %), $[\alpha]_{\text{D}}^{25}$ -82.4 (*c* 1.0, CHCl₃) for >99 % ee (lit. $[\alpha]_{\text{D}}^{23}$ -78.7 (*c* 1.09, CHCl₃) for (*R*)); m.p. 133-135 °C.

2-Hydroxy-2-phenyl-thioacetic acid *S*-benzyl ester³ (8d)



¹H NMR (400 MHz, CDCl₃) δ 7.43-7.37 (m, 5H), 7.30-7.27 (m, 5H), 5.21 (s, 1H), 4.16 (d, *J* = 13.6, 1H), 4.10 (d, *J* = 13.6, 1H), 3.57 (bs, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 201.4, 137.8, 136.7, 128.8, 128.79, 128.7, 128.6, 127.3, 127.0, 79.7, 33.2; MS (EI, 70 eV) (C₁₅H₁₄O₂S, 258.3) 259 (M+1⁺, 5), 213 (23), 124 (26), 107 (100), 91 (31), 79 (25), 77 (16); HRMS calcd for (C₁₅H₁₄O₂S) 258.0715, found 258.0782; TLC R_f 0.37 (EtOAc/hexane, 1/6); HPLC t_R 19.55 min (*S*), 23.66 min (*R*) (Chiralcel AD-H, *i*-PrOH/hexane, 6/94, 1.0 ml/min, λ = 254 nm). After kinetic resolution: 19.75 min (*S*, minor, 2.59%), 23.92 min (*R*, major, 97.41%). $[\alpha]_{\text{D}}^{28}$ -82.32 (*c* 1.0, CHCl₃) for 95% ee; $[\alpha]_{\text{D}}^{25}$ +141.9 (*c* 1.0, MeOH) for 78 % ee. The absolute configuration was deduced to be *R* according to the sign of optical rotation; m.p. 83-85 °C.

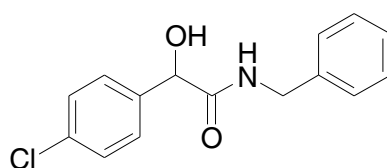
N-Benzyl-2-hydroxy-2-(4'-trifluoromethyl)acetamide (9)



$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.49 (d, $J = 8.4$, 2H), 7.34-7.27 (m, 5H), 7.18 (d, $J = 7.8$, 2H), 6.58 (brs, 1H, -NH), 5.03 (s, 1H), 4.43 (dd, $J = 15.2$, 6.0, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 171.1, 143.2,

137.4, 13.0.8 (q, $J = 32.2$ Hz), 128.8, 127.8, 127.6, 127.0, 126.6 (q, $J = 228.3$ Hz), 125.7 (q, $J = 3.0$ Hz), 73.6, 43.6; MS (ESI) ($\text{C}_{16}\text{H}_{14}\text{F}_3\text{NO}_2$, 309) 641 ($2\text{M}+\text{Na}^+$, 100), 332 ($\text{M}+\text{Na}^+$, 26); Anal. Calcd. For $\text{C}_{16}\text{H}_{14}\text{F}_3\text{NO}_2$: C, 62.13; H, 4.56. Found: C, 62.42; H, 4.47; TLC R_f 0.33 (EtOAc/hexane, 1/2); HPLC t_R 5.7 min (*S*), 10.7 min (*R*) (Chiralpak AD-H, *i*-PrOH/hexane, 12/88, 1.0 ml/min, $\lambda = 254$ nm). After kinetic resolution: 5.6 min (*S*, major, 1.7 %), 10.7 min (*R*, minor, 98.3%). $[\alpha]_D^{25}$ -56.6 (*c* 1.0, CHCl_3) for 96% ee; The absolute configuration was deduced to be *R* by analogy; m.p. 185-186 °C.

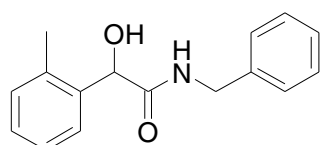
***N*-Benzyl-2-hydroxy-2-(4'-chlorophenyl)acetamide⁴ (10)**



$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.34-7.25 (m, 7H), 7.18 (d, $J = 7.2$, 2H), 6.53 (bs, 1H, NH), 5.05 (s, 1H), 4.48-4.38 (m, 2H), 3.75 (bs, 1H, OH); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 172.0, 138.0, 137.5, 134.3,

128.73, 128.69, 128.0, 127.6, 127.5, 73.4, 43.3; MS (ESI) ($\text{C}_{15}\text{H}_{14}\text{ClNO}_2$, 275) 573 (M_2+Na^+ , 100), 298 ($\text{M}+\text{Na}^+$, 6); TLC R_f 0.37 (EtOAc/hexane, 1/2); HPLC t_R 16.3 min (*R*), 36.6 min (*S*) (Chiralpak AD-H, *i*-PrOH/hexane, 8/92, 1.0 ml/min, $\lambda = 254$ nm). After kinetic resolution: 16.5 min (*R*, major, 98.3%), 36.7 min (*S*, minor, 1.7%). $[\alpha]_D^{25}$ -57.2 (*c* 1.0, CHCl_3) for 97 %ee (lit. $[\alpha]_D^{25}$ +64.0 (*c* 1.0, CHCl_3) for (*S*)); The absolute configuration was thus deduced to be *R*; m.p. 117-118 °C.

***N*-Benzyl-2-hydroxy-2-*o*-tolyl-acetamide (11)**

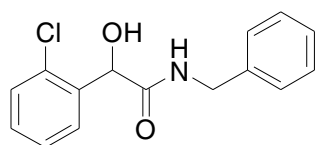


$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.34-7.15 (m, 9H), 6.61 (bs, 1H, -NH), 5.20 (s, 1H), 4.44 (dd, $J = 14.8$, 6.0, 1H), 4.38 (dd, $J = 14.8$, 6.0, 1H), 2.37 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 172.6, 137.7, 137.4, 136.8,

130.9, 128.6, 128.5, 127.53, 127.5, 127.4, 126.2, 71.9, 43.2, 19.2; MS ESI ($\text{C}_{16}\text{H}_{17}\text{NO}_2$, 255) 533

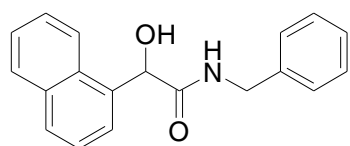
(M_2+Na^+ , 100), 279 ($M+Na+H^+$, 10); Anal. Calcd. For $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71. Found: C, 75.27; H, 7.05; TLC R_f 0.32 (EtOAc/hexane, 1/2); HPLC t_R 17.8 min (*R*), 26.9 min (*S*) (Chiralpak AD-H, *i*-PrOH/hexane, 8/92, 1.0 ml/min, $\lambda = 254$ nm); After kinetic resolution: 17.0 min (*R*, major, 96.8%), 26.0 min (*S*, minor, 3.2%); $[\alpha]_D^{25}$ -20.8 (c 1.0, $CHCl_3$) for 94 %ee; The absolute configuration was deduced to be *R* by analogy; m.p. 90-92 °C.

***N*-Benzyl-2-hydroxy-2-(2'-chlorophenyl)acetamide (12)**



1H NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, $J = 7.6, 1.6$, 1H), 7.38 (dd, $J = 7.6, 1.6$, 1H), 7.39-7.25 (m, 5H), 7.17 (dd, $J = 7.6, 1.2$, 2H), 6.55 (bs, 1H, NH), 5.55 (d, $J = 4.4$, 1H), 4.52 (dd, $J = 14.8, 6.0$, 1H), 4.42 (dd, $J = 14.8, 6.0$, 1H), 4.10 (d, $J = 4.4$, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 137.4, 137.2, 132.6, 129.7, 128.7, 128.6, 127.6, 127.4, 70.2, 43.8; MS (ESI) ($C_{15}H_{14}ClNO_2$, 275) 573 (M_2+Na^+ , 100), 299 ($M+Na+1^+$, 96); Anal. Calcd. For $C_{15}H_{14}ClNO_2$: C, 65.34; H, 5.12. Found: C, 65.14; H, 5.19; TLC R_f 0.38 (EtOAc/hexane, 1/2); HPLC t_R 18.0 min (*R*), 22.3 min (*S*) (Chiralpak AD-H, *i*-PrOH/hexane, 10/90, 1.0 ml/min, $\lambda = 254$ nm); After kinetic resolution: 18.0 min (*R*, major, 96.1%), 22.2 min (*S*, minor, 3.9%); $[\alpha]_D^{25}$ -72.8 (c 1.0, $CHCl_3$) for 92 %ee; The absolute configuration was deduced to be *R* by analogy; m.p. 111-113 °C.

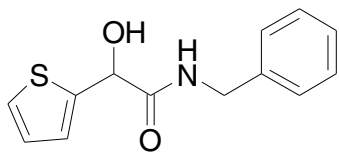
***N*-Benzyl-2-hydroxy-2-naphthalen-1-yl-acetamide (13)**



1H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, $J = 6.3$, 1H), 7.91-7.86 (m, 2H), 7.55-7.54 (m, 3H), 7.45 (t, $J = 7.6$, 1H), 7.29-7.26 (m, 2H), 7.11 (t, $J = 3.6$, 2H), 6.40 (bs, 1H, NH), 5.61 (s, 1H), 4.47 (dd, $J = 15.2, 6.4$, 1H), 4.39 (dd, $J = 15.2, 6.4$, 1H), 4.00 (bs, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 137.5, 134.4, 134.2, 131.0, 129.8, 128.9, 128.6, 127.52, 127.47, 127.1, 126.8, 126.1, 125.2, 123.9, 73.2, 43.6; MS ESI ($C_{19}H_{17}NO_2$, 291) 605 (M_2+Na^+ , 100), 315 ($M+Na+1^+$, 13); Anal. Calcd. For $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88. Found: C, 78.47; H, 5.52; TLC R_f 0.36 (EtOAc/hexane, 1/2); HPLC t_R 24.3 min (*R*), 36.1 min (*S*) (Chiralpak AD-H, *i*-PrOH/hexane, 10/90, 1.0 ml/min, $\lambda = 254$ nm);

After kinetic resolution: 24.9 min (*R*, major, 99.7%), $[\alpha]_{\text{D}}^{25}$ -38.8 (*c* 1.0, CHCl₃) for >99 %*ee*; The absolute configuration was deduced to be *R* by analogy; m.p. 196-197 °C.

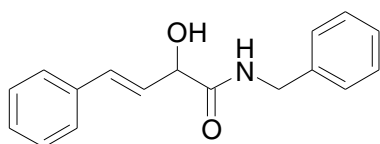
***N*-Benzyl-2-hydroxy-2-thiophen-2-yl-acetamide⁴ (14)**



¹H NMR (400 MHz, CDCl₃) δ 7.33-7.27 (m, 4H), 7.22-7.20 (m, 2H), 7.08 (d, *J* = 3.2, 1H), 6.95 (t, *J* = 4.4, 1H), 6.83 (bs, 1H, NH), 5.30 (bs, 1H), 4.50 (dd, *J* = 15.2, 6.0, 1H), 4.39 (dd, *J* = 15.2, 6.0, 1H); ¹³C NMR

(100 MHz, CDCl₃) δ 171.2, 142.3, 137.5, 128.7, 127.6, 126.9, 126.1, 126.0, 70.1, 43.5; MS (ESI) (C₁₃H₁₃NO₂S, 247) 485 (M₂+Na⁺, 100), 270 (M+Na⁺, 12); TLC R_f 0.29 (EtOAc/hexane, 1/2); HPLC *t*_R 20.1 min (*R*), 30.6 min (*S*) (Chiralpak AD-H, *i*-PrOH/hexane, 8/92, 1.0 ml/min, λ = 254 nm); After kinetic resolution: 20.1 min (*R*, major, 99.6%), 30.7 min (*S*, minor, 0.4%); $[\alpha]_{\text{D}}^{25}$ -15.1 (*c* 1.0, CHCl₃) for > 99 %*ee* (lit. $[\alpha]_{\text{D}}^{25}$ +27.4 (*c* 1.0, CHCl₃) for (*S*)); m.p. 93-95 °C.

***N*-Benzyl-2-hydroxy-4-phenyl-but-3-enoamide (15)**

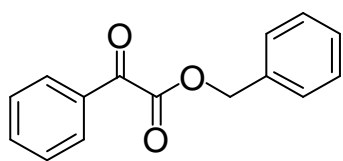


¹H NMR (400 MHz, CDCl₃) δ 7.37-7.16 (m, 10H), 6.85 (t, *J* = 5.2, 1H, NH), 6.73 (dd, *J* = 16.0, 0.9, 1H), 6.33 (dd, *J* = 16.0, 6.4, 1H), 4.76 (dd, *J* = 6.4, 1.2, 1H), 4.46 (dd, *J* = 14.8, 3.2, 1H), 4.41 (dd, *J* =

14.8, 3.2, 1H), 3.72 (bs, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ 172.3, 137.5, 135.9, 132.5, 128.6, 128.5, 127.9, 127.54, 127.48, 126.7, 126.6, 72.7, 43.3; MS (ESI) (C₁₇H₁₇NO₂, 267) 557 (M₂+Na⁺, 73), 289 (M+Na⁺, 100); Anal. Calcd. For C₁₇H₁₇NO₂: C, 76.38; H, 6.41. Found: C, 76.53; H, 6.29; TLC R_f 0.28 (EtOAc/hexane, 1/2); HPLC *t*_R 19.2 min (*S*), 28.6 min (*R*) (Chiralpak AD-H, *i*-PrOH/hexane, 8/92, 1.0 ml/min, λ = 254 nm); After kinetic resolution: 19.2 min (*R*, major, >99%). $[\alpha]_{\text{D}}^{25}$ -24.3 (*c* 1.0, CHCl₃) for > 99 %*ee*; The absolute configuration was deduced to be *R* by analogy; m.p. 127-128 °C.

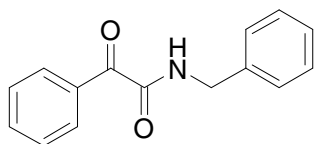
Analytical data for the α -keto-compounds 6'-8d' and 9'-15'

Benzyl Oxo-phenyl-acetate (6')⁵



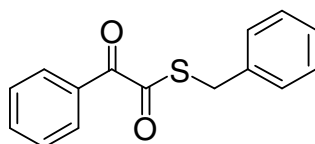
¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, J = 8.0, 1.0, 2H), 7.65 (t, J = 7.8, 1H), 7.51-7.37 (m, 7H), 5.42 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 185.9, 163.5, 134.7, 134.4, 132.2, 129.7, 128.7, 128.6, 128.5, 128.3, 67.5; MS (ESI) (C₁₅H₁₂O₃, 240) 504 (M₂+Na+1⁺, 72), 264 (M+Na+1⁺, 87); TLC R_f 0.32 (EtOAc/hexane, 1/25).

N-Benzyl-2-oxo-2-phenyl-acetamide (7')⁶



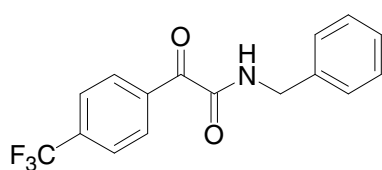
¹H NMR (400 MHz, CDCl₃) δ 8.36 (dd, J = 8.0, 0.8, 2H), 7.62 (t, J = 7.2, 1H), 7.47 (t, J = 8.0, 2H), 7.39-7.30 (m, 6H), 4.58 (d, J = 6.0, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 187.5, 161.5, 137.1, 134.4, 133.3, 131.2, 128.9, 128.5, 127.9, 127.8, 43.5; MS (ESI) (C₁₅H₁₃NO₂, 239) 501 (M₂+Na⁺, 100), 262 (M+Na⁺, 52); TLC R_f 0.42 (EtOAc/hexane, 1/8); m.p. 97-98 °C.

oxo-phenyl-thioacetic acid S-benzyl ester-(8d')



¹H NMR (400 MHz, CDCl₃) δ 8.14 (d, J = 8.0, 2H), 7.66 (td, J = 8.0, 0.8, 1H), 7.50 (t, J = 7.6, 2H), 7.38-7.28 (m, 5H), 4.28 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 192.1, 186.0, 136.4, 134.9, 131.6, 130.8, 129.0, 128.8, 128.75, 127.6, 33.3; MS (EI, 70 eV) (C₁₅H₁₂O₂S, 256) 256 (M⁺, 3), 228 (53), 105 (100), 91 (17), 77 (29); TLC R_f 0.39 (EtOAc/hexane, 1/28); Anal. Calcd. for C₁₅H₁₃O₃S: C, 70.29; H, 4.72. Found: C, 70.52; H, 4.48.

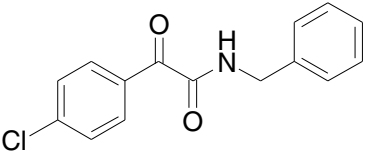
N-Benzyl-2-hydroxy-2-(4'-trifluoromethyl)acetamide (9')



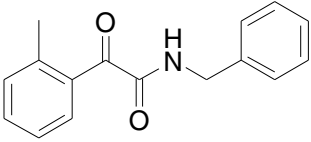
¹H NMR (400 MHz, CDCl₃) δ 8.484 (d, J = 8.1, 2H), 7.75 (d, J = 8.1, 2H), 7.47 (brs, 1H, -NH), 7.39-7.30 (m, 5H), 4.58 (d, J = 6.0, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 186.5, 160.7, 136.8, 136.0, 135.4 (q, J =

31.2 Hz), 131.6, 130.8, 128.9, 127.96, 127.90, 126.2 (q, $J = 271.6$ Hz), 125.4 (q, $J = 3.0$ Hz), 43.6; MS (ESI) ($C_{16}H_{12}F_3NO_2$, 307) 637 ($2M+Na^+$, 100), 330 ($M+Na^+$, 38); TLC R_f 0.41 (EtOAc/hexane, 1/8); Anal. Calcd. For $C_{16}H_{12}F_3NO_2$: C, 62.54; H, 3.94. Found: C, 62.81; H, 3.73.; m.p. 164-168 °C.

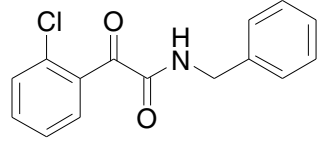
***N*-Benzyl-2-(4-chloro-phenyl)-2-oxo-acetamide⁴ (10')**

 1H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, $J = 6.7$, 2H), 7.46 (bs, 1H, NH), 7.45 (d, $J = 6.7$, 2H), 7.38-7.31 (m, 5H), 4.56 (d, $J = 6.1$, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.1, 161.1, 141.2, 136.9, 132.7, 131.6, 128.85, 128.83, 127.9, 43.5; TLC R_f 0.41 (EtOAc/hexane, 1/8); MS (ESI) ($C_{15}H_{12}ClNO_2$, 273) 569 (M_2+Na^+ , 100), 296 ($M+Na^+$, 35); m.p. 106-107 °C.

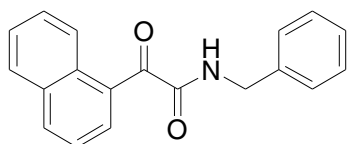
***N*-Benzyl-2-oxo-2-*o*-tolyl-acetamide (11')**

 1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, $J = 7.7$, 1H), 7.47-7.27 (m, 9H), 4.57 (d, $J = 6.0$, 2H), 2.50 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1, 161.8, 140.2, 137.1132.8, 132.7, 132.0, 131.7, 128.8, 127.9, 127.8, 125.4, 43.6, 20.9; MS (ESI) ($C_{16}H_{15}NO_2$, 253) 1036 (M_4+Na^+ , 27), 529 (M_2+Na^+ , 92), 277 ($M+Na+1^+$, 100); TLC R_f 0.44 (EtOAc/hexane, 1/8); Anal. Calcd. For $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97. Found: C, 76.19; H, 6.07; m.p. 71-72 °C.

***N*-Benzyl-2-(2-chloro-phenyl)-2-oxo-acetamide (12')**

 1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, $J = 1.4$, 1H), 7.49-7.43 (m, 2H), 7.40-7.29 (m, 7H), 4.56 (d, $J = 6.0$, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.0, 160.6, 136.9, 133.9, 133.1, 133.0, 131.2, 130.4, 128.8, 127.9, 127.8, 126.5, 43.7; TLC R_f 0.40 (EtOAc/hexane, 1/8); MS (ESI) ($C_{15}H_{12}ClNO_2$, 273) 569 (M_2+Na^+ , 74), 296 ($M+Na^+$, 12); Anal. Calcd. For $C_{15}H_{12}ClNO_2$: C, 65.82; H, 4.42. Found: C, 65.56; H, 4.17; m.p. 91-92 °C.

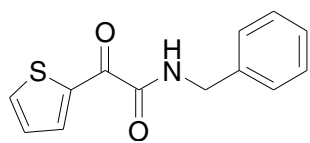
***N*-Benzyl-2-naphthalen-1-yl-2-oxo-acetamide⁷ (13')**



^1H NMR (400 MHz, CDCl_3) δ 8.60 (d, $J = 8.4$, 1H), 8.35 (d, $J = 7.2$, 1H), 8.08 (d, $J = 8.4$, 1H), 7.90 (d, $J = 8.4$, 1H), 7.64-7.54 (m, 4H), 7.41-7.32 (m, 5H), 4.62 (d, $J = 6.0$, 2H); ^{13}C NMR (100 MHz, CDCl_3)

δ 187.1, 161.85, 137.2, 136.2, 135.1, 132.4, 130.6, 130.4, 129.4, 128.9, 128.4, 128.0, 127.9, 127.8, 126.9, 125.3 43.6; MS (ESI) ($\text{C}_{19}\text{H}_{15}\text{NO}_2$, 289) 601 (M_2+Na^+ , 94), 312 ($\text{M}+\text{Na}^+$, 8); TLC R_f 0.37 (EtOAc/hexane, 1/8); m.p. 123-125 °C.

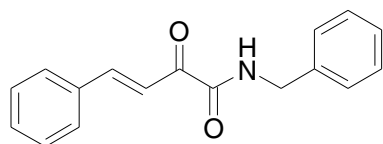
***N*-Benzyl-2-oxo-2-thiophen-2-yl-acetamide⁴ (14')**



^1H NMR (400 MHz, CDCl_3) δ 8.41 (dd, $J = 3.9$, 1.0, 1H), 7.82 (dd, $J = 5.0$, 1.1, 1H), 7.71 (bs, 1H, NH), 7.41-7.28 (m, 5H), 7.18 (dd, $J = 4.7$, 4.1, 1H), 4.56 (d, $J = 6.2$, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 178.2,

160.6, 138.6, 138.1, 136.9, 136.7, 128.7, 128.2, 127.8, 127.7, 43.4; MS (ESI) ($\text{C}_{13}\text{H}_{11}\text{NO}_2\text{S}$, 245) 513 (M_2+Na^+ , 100), 268 ($\text{M}+\text{Na}^+$, 86); TLC R_f 0.39 (EtOAc/hexane, 1/8); m.p. 93-95 °C.

***N*-Benzyl-4-phenyl-but-3-enoic acid-2-oxo-acetamide (15')**

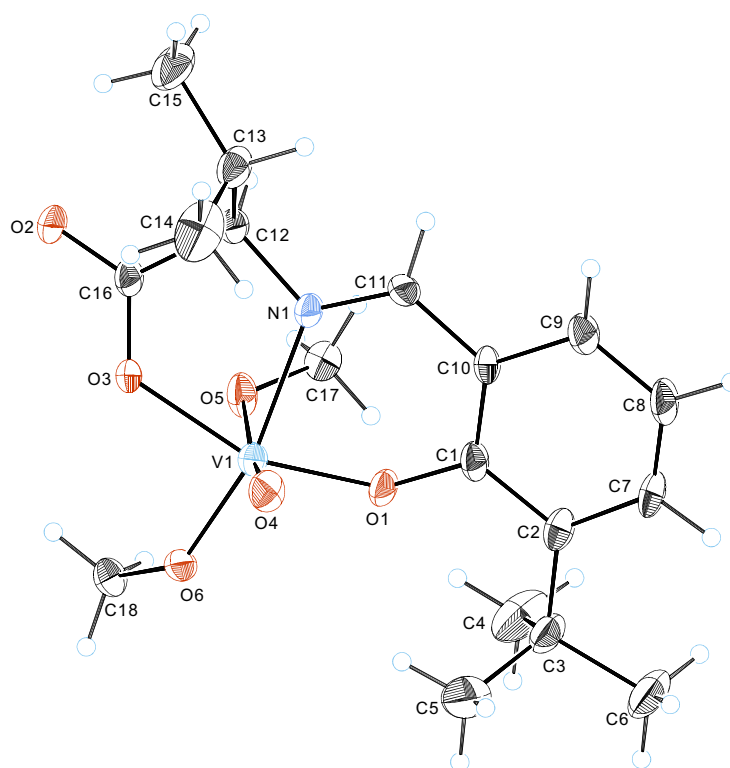


^1H NMR (400 MHz, CDCl_3) δ 7.96 (d, $J = 16.0$, 1H), 7.81 (d, $J = 16.0$, 1H), 7.67 (dd, $J = 8.0$, 2.0, 2H), 7.49-7.40 (m, 4H), 7.38-7.29 (m, 5H), 4.55 (d, $J = 6.4$, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ

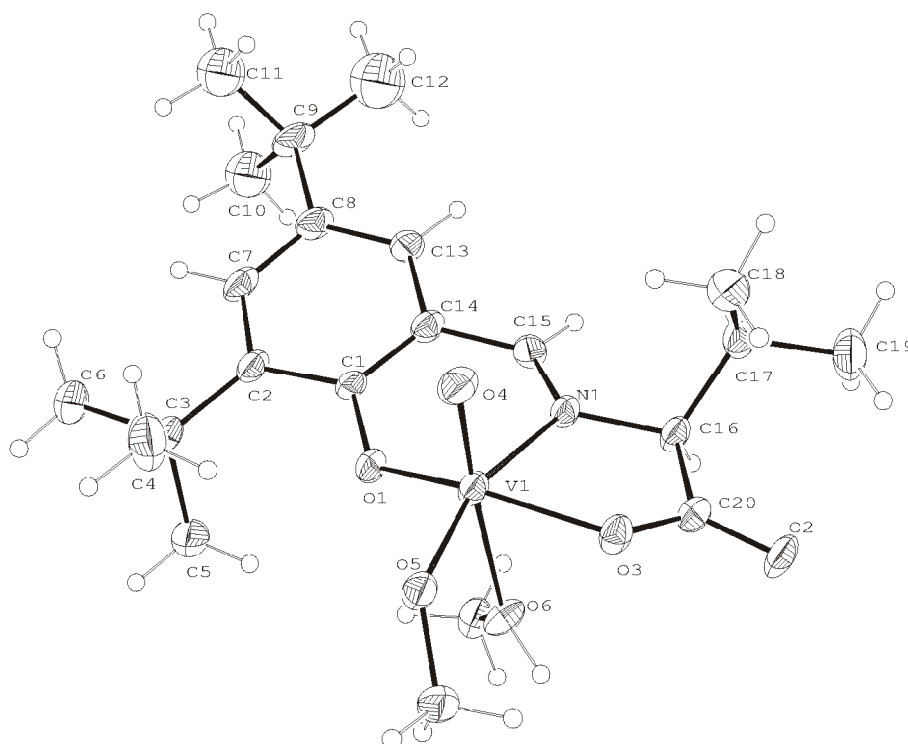
185.3, 161.2, 148.1, 137.1, 134.4, 131.5, 129.2, 129.0, 128.8, 127.9, 127.8, 118.6, 43.5; MS (ESI) ($\text{C}_{17}\text{H}_{15}\text{NO}_2$, 265) 553 (M_2+Na^+ , 73), 289 ($\text{M}+\text{Na}+1^+$, 100); TLC R_f 0.41 (EtOAc/hexane, 1/8); Anal. Calcd. For $\text{C}_{17}\text{H}_{15}\text{NO}_2$: C, 76.96; H, 5.70. Found: C, 76.69; H, 5.70; m.p. 127-128 °C.

Ortep drawings and selected crystal data for X-ray structures of 1', 4', and 5

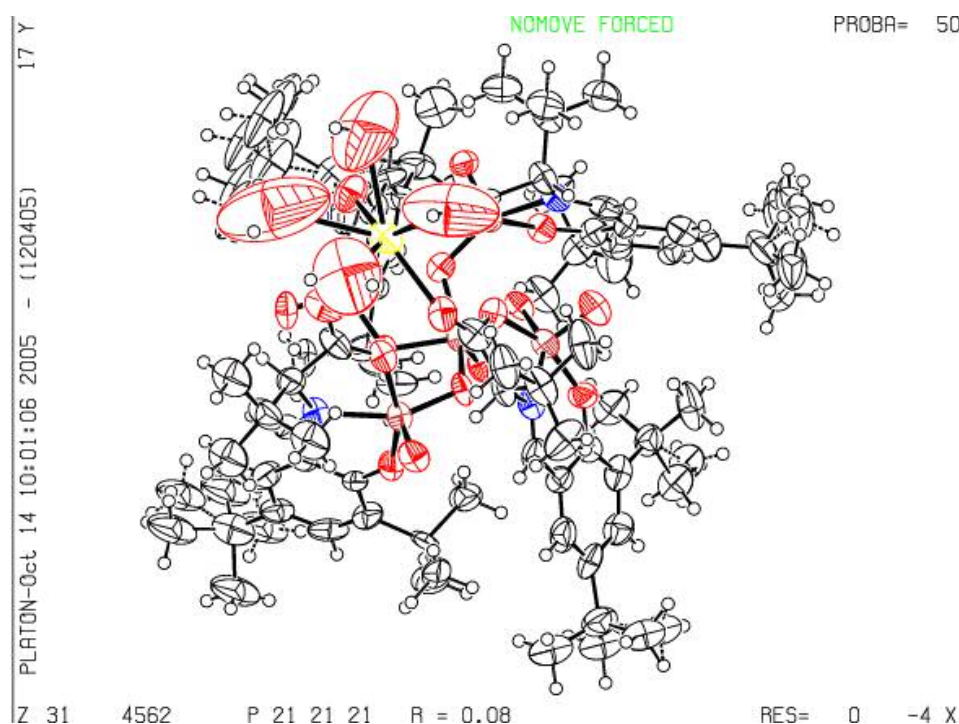
Crystal data for **1'**: $C_{18}H_{28}NO_6V$, $M_r = 405.36$, orthorhombic, space group $P212121$, $a = 26.568(9)$ Å, $b = 6.663(2)$ Å, $c = 12.383(5)$ Å, $V = 2093.6(13)$ Å³, $Z = 4$, $\rho_{\text{calcd}} = 1.283$ Mgm⁻³, $T = 200$, Nonius CAD-4 diffractometer, $Mo_{k\alpha}$ radiation ($\lambda = 0.70930$), $\mu = 0.504$ mm⁻¹. The structure was solved by NRCVAX Solver. All non-hydrogen atoms were refined anisotropically (NRCVAX LSTSQ). Final block-diagonal matrix least-square refinement on F2 with all 6906 reflections and 235 variables converged to $R1 (I > 2\sigma(I)) = 0.060$, $wR2$ (all data) = 0.074, and GOF = 1.061.



Crystal data for **4'**: $C_{22}H_{36}NO_6V$, $M_r = 461.46$, monoclinic, space group $C2$, $a = 32.0650(3) \text{ \AA}$, $b = 6.5700(5) \text{ \AA}$, $c = 12.4110(8) \text{ \AA}$, $V = 2526.6(3) \text{ \AA}^3$, $Z = 4$, $\rho_{\text{calcd}} = 1.213 \text{ gcm}^{-3}$, $T = 200$, Nonius CAD-4 diffractometer, $\text{MoK}\alpha$ radiation ($\lambda = 0.71073$), $\mu = 0.426 \text{ mm}^{-1}$. The structure was solved by NRCVAX Solver. All non-hydrogen atoms were refined anisotropically (NRCVAX LSTSQ). Final block-diagonal matrix least-square refinement on F2 with all 4592 reflections and 235 variables converged to $R1 (I > 2\sigma(I)) = 0.0664$, $wR2$ (all data) = 0.1804, and GOF = 1.012.



Crystal data for **5**: $C_{84}H_{132}KN_4O_{25}V_5$, $M_r = 1891.74$, monoclinic, space group $C2$, $a = 14.294(3) \text{ \AA}$, $b = 14.681(3) \text{ \AA}$, $c = 51.888(10) \text{ \AA}$, $V = 10889(4) \text{ \AA}^3$, $Z = 4$, $\rho_{\text{calcd}} = 1.154 \text{ Mgm}^{-3}$, $T = 200$, Nonius CAD-4 diffractometer, $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$), $\mu = 0.514 \text{ mm}^{-1}$. The structure was solved by NRCVAX Solver. All non-hydrogen atoms were refined anisotropically (NRCVAX LSTSQ). Final block-diagonal matrix least-square refinement on F2 with all 15003 reflections and 1042 variables converged to $R1 (I > 2\sigma(I)) = 0.085$, $wR2$ (all data) = 0.227, and GOF = 1.003.

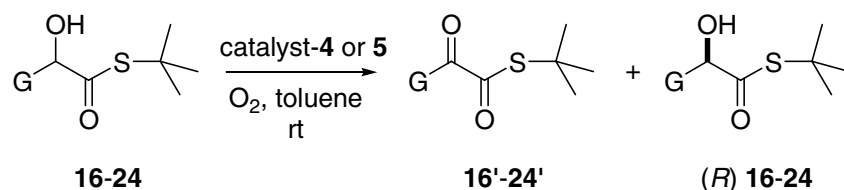


Because of a long axis of the unit cell for the C_4 -symmetric cluster **5**, the data collection was divided into three portions, and the sum of the integration for three portions of data collection did not completely replicate unique reflections. Solvent accessible voids of 727 \AA^3 in the unit cell are caused by squishing distorted solvent molecules except the water molecules coordinated on the potassium ion out of the unit cell.

Representative procedure for the preparation of *S*-*tert*-butyl- α -hydroxythioesters

To a solution of a methyl mandelate derivative⁹ (5 mmol) in CH₃CN (10 mL) was added VOCl₃ (0.09 mL, 0.5 mmol) under oxygen atmosphere. After having been stirred for several hours, the reaction mixture was concentrated under reduced pressure and the crude ketoester product was purified by column chromatography (eluent, hexane) on silica gel. The purified α -ketoester (2 mmol) was treated with aqueous KOH (4 mmol, 224 mg in 4 mL of H₂O) in EtOH (8 mL) to effect saponification. After acidification of the reaction mixture with 1N HCl (5 mL) at 0 °C, the crude acid mixture was then extracted with ether (3 \times 15 mL). The combined organic layers were concentrated, dried (MgSO₄), and evaporated. The resultant α -keto acid (2 mmol) was dissolved in CH₂Cl₂ (5 mL) and was then cooled to 0 °C. To this solution was added oxalyl chloride (2.5 mL, 2 mmol) under nitrogen. After having been stirred for 30 min, the reaction mixture was treated with a cooled mixture of anhydrous *tert*-butanethiol (1.8 mL, 2 mmol) and dry Et₃N (2.7 mL, 2 mmol) at 0 °C and then gradually warmed to ambient temperature. After completion of the reaction, the mixture was concentrated under reduced pressure and the crude thioester was taken up by ether (30 mL). The concentrated residue was purified by column chromatography (hexane/EtOAc, 9/1) on silica gel. The purified α -keto-thioesters (2 mmol) was dissolved in THF (2 mL) and then treated with NaBH₄ (18.9 mg, 0.5 mmol). After completion of the reaction, the reaction mixture was acidified with 1N HCl at 0 °C. Ether (15 mL) was added and the organic layer was collected. The aqueous layer was separated and extracted with ether (3 \times 10 mL). The combined organic layers were dried (MgSO₄), filtered, and evaporated. The crude α -hydroxy-thioester was purified by column chromatography (hexane/Et₂O, 8/2) on silica gel.

Representative procedure for the asymmetric aerobic oxidation of *S*-*tert*-butyl- α -hydroxythioesters

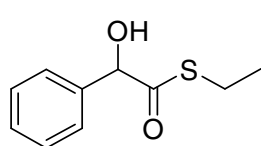


To a 50-mL, two-necked, round-bottomed flask was placed monomer catalyst-4 (0.05 mmol, 5

mol%) or cluster-5 (0.0125 mmol, 1.25 mol%) in oxygen-saturated toluene (3 mL) under oxygen atmosphere. The reaction flask was vacuum-evacuated at 15 torr for 20 sec and then filled with an oxygen balloon (150 mL). A solution of a α -hydroxythioester (1 mmol) in oxygen-saturated toluene (2 mL) was added by cannula and the resulting dark brown mixture was stirred at ambient temperature. The reaction progress was monitored by ^1H NMR spectroscopy to determine the extent of oxidative conversion. The enantiomeric excess of the kinetically resolved product was determined by chiral HPLC analysis after filtration of the reaction aliquot (100 μL) over a short plug of silica gel (Et_2O or CH_2Cl_2 as eluent). Upon reaching optimal resolution of the asymmetric oxidation (50-51% conversion), the reaction mixture was concentrated under reduced pressure. The resulting residue was loaded directly on top of an eluent-filled silica gel column and purified by flash column chromatography. The enantiomeric excess of the pure, resolved α -hydroxythioester was analyzed again by chiral HPLC analysis.

Analytical data for α -hydroxythioesters 8a-e

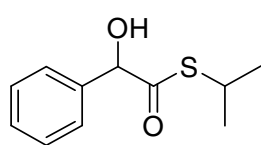
S-Ethyl Hydroxy-phenyl-thioacetate 8a^{8a,b}



^1H NMR (400 MHz, CDCl_3) δ 7.43-7.26 (m, 5H), 5.21 (d, $J = 4.4$, 1H), 3.54 (d, $J = 4.4$, 1H), 2.93-2.89 (m, 2H), 1.23 (t, $J = 4.4$, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 202.3, 137.8, 128.3, 128.2, 126.6, 79.3, 22.7, 13.9; MS (EI, 70 eV)

($\text{C}_{10}\text{H}_{12}\text{O}_2\text{S}$, 196.3) 196 (M^+ , 16), 107 (100), 79 (43), 77 (31), 51(10); High-Resolution MS calcd for ($\text{C}_{10}\text{H}_{12}\text{O}_2\text{S}$) 196.0558, found 196.0563; TLC R_f 0.36 ($\text{EtOAc}/\text{hexane}$, 2/8); HPLC t_R 19.7 min (*S*), 20.9 min (*R*) (Chiralpak AD-H, *i*-PrOH/hexane, 3/97, 1.0 ml/min, $\lambda = 254$ nm). After kinetic resolution: 17.0 min (minor, 0.88 %), 20.4 min (major, 99.12 %); $[\alpha]_D^{25} -126.7$ (c 1.0, MeOH) for 99 % ee.^{8c}

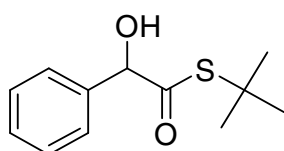
S-Isopropyl Hydroxy-phenyl-thioacetate 8b



^1H NMR (400 MHz, CDCl_3) δ 7.41-7.31 (m, 5H), 5.13 (s, 1H), 3.76 (s, 1H), 3.67-3.61 (m, 1H), 1.28 (d, $J = 6.8$, 3H), 1.27 (d, $J = 6.8$, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 201.9, 138.1, 128.5, 128.3, 127.1, 79.7, 34.7, 22.6; MS (EI,

70 eV) ($C_{11}H_{14}O_2S$, 210.3) 210 (M^+ , 9), 107 (100), 78 (39), 77 (28); High Resolution -MS calcd for ($C_{11}H_{14}O_2S$) 210.0715, found 210.0709; TLC R_f 0.35 (EtOAc/hexane, 2/8); HPLC t_R 46.4 (S) min, 50.1 min (R) (Chiralpak AD-H, *i*-PrOH/hexane, 1/99, 1.0 ml/min, λ = 254 nm). After kinetic resolution: 49.5 min (major, 99 %); $[\alpha]_D^{25}$ -23.8 (*c* 1.0, MeOH) for 99 % ee; m.p. 54-56 °C.

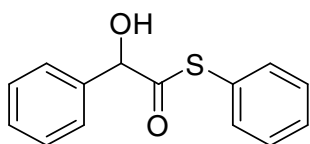
***S*-tert-Butyl Hydroxy-phenyl-thioacetate 8c⁹**



1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.35 (m, 5H), 5.10 (s, 1H), 3.54 (s, 1H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.91, 138.5, 128.6, 127.1, 79.9, 48.9, 29.8; MS (EI, 70 eV) ($C_{12}H_{16}O_2S$, 224.3) 224 (M^+ , 5), 107

(100), 79 (38), 57 (25); High Resolution-MS calcd for ($C_{12}H_{16}O_2S$) 224.0871, found 224.0944; TLC R_f 0.36 (EtOAc/hexane, 2/8); HPLC t_R 10.5 min (S), 12.1 min (R) (Chiralpak AD-H, *i*-PrOH/hexane, 6/94, 1.0 ml/min, λ = 254 nm). After kinetic resolution: 10.7 min (minor, 1.38 %), 12.2 (major, 98.62 %); $[\alpha]_D^{25}$ +48.38 (*c* 1.0, MeOH) for 98 % ee; m.p. 59-61 °C.

***S*-Phenyl Hydroxy-phenyl-thioacetate 8e¹⁰**

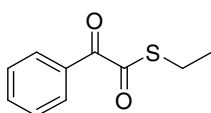


1H NMR (400 MHz, $CDCl_3$) δ 7.51-7.36 (m, 5H), 7.29-7.23 (m, 5H), 5.24 (d, J = 4.4, 1H), 3.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 137.8, 136.6, 128.8, 128.7, 128.6, 128.5, 127.3, 126.9, 79.9; MS (EI, 70

eV) ($C_{14}H_{12}O_2S$, 244.3) 244 (M^+ , 5), 107 (100), 77 (45), 53 (30), 42 (20); TLC R_f 0.31 (EtOAc/hexane, 2/8); HPLC t_R 10.5 min (S), 12.1 min (R) (Chiralpak AD-H, *i*-PrOH/hexane, 6/94, 1.0 ml/min, λ = 254 nm). After kinetic resolution: 9.70 min (minor, 26.41 %), 12.1 min (major, 73.59 %); $[\alpha]_D^{25}$ -122.7 (*c* 1.0, MeOH) for 47 % ee; m.p. 58-61 °C.

Analytical data for α -keto-thioesters

***S*-Ethyl Oxo-phenyl-thioacetate 8a¹¹**

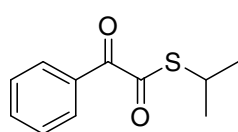


1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 7.2, 2H), 7.64 (t, J = 7.4, 1H), 7.49 (t, J = 7.6, 2H), 3.06 (q, J = 7.4, 1H), 1.37 (t, J = 7.4, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 193.0, 186.4, 134.8, 131.6, 130.7, 128.8, 23.3, 14.2; MS (EI, 70 eV) ($C_{10}H_{10}O_2S$, 194.3)

194 (M^+ , 5), 105 (100), 77 (56), 51 (20); TLC R_f 0.44 (EtOAc/hexane, 1/9).

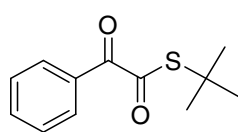
S-Isopropyl Oxo-phenyl-thioacetate 8b'



^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 7.1$, 2H), 7.65 (t, $J = 7.4$, 1H), 7.49 (t, $J = 7.6$, 2H), 3.79 (sept, $J = 6.9$, 1H), 1.42 (d, $J = 6.9$, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 192.9, 186.6, 134.7, 131.7, 130.7, 128.8, 35.0, 22.8; MS (EI,

70 eV) ($\text{C}_{11}\text{H}_{12}\text{O}_2\text{S}$, 208.3) 208 (M^+ , 2), 105 (100), 77 (40), 51 (15); High Resolution-MS calcd for ($\text{C}_{11}\text{H}_{12}\text{O}_2\text{S}$) 208.0558, found 208.0561; TLC R_f 0.45 (EtOAc/hexane, 1/9).

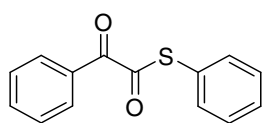
S-tert-Butyl Oxo-phenyl-thioacetate 8c'¹²



^1H NMR (400 MHz, CDCl_3) δ 8.05 (d, $J = 7.2$, 2H), 7.62 (t, $J = 7.4$, 1H), 7.49 (t, $J = 7.6$, 2H), 1.59 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 193.6, 187.1, 134.6, 131.6, 130.5, 128.7, 49.0, 29.6; MS (EI, 70 eV) ($\text{C}_{12}\text{H}_{14}\text{O}_2\text{S}$, 222.3)

222 (M^+ , 13), 105 (100), 219 (29), 77 (22), 57 (18); TLC R_f 0.45 (EtOAc/hexane, 1/9).

S-Phenyl Oxo-phenyl-thioacetate 8e'¹³



^1H NMR (400 MHz, CDCl_3) δ 8.13 (d, $J = 8.0$, 2H), 7.64 (t, $J = 7.6$, 1H), 7.50 (t, $J = 7.6$, 2H), 7.38-7.26 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 192.1, 185.9, 136.4, 134.9, 131.6, 130.8, 129.0, 128.83, 128.75, 127.6; MS (EI, 70

eV) ($\text{C}_{14}\text{H}_{10}\text{O}_2\text{S}$, 242.3) 242 (M^+ , 4), 105 (100), 92 (51), 71 (43), 38 (12); TLC R_f 0.42 (EtOAc/hexane, 1/9).

References

- (1) Peter, Y.; Bernard, S. *J. Org. Chem.* **1958**, *23*, 759.
- (2) Choi, D.; Stables, J. P.; Kohn, H. *Bioorg. Med. Chem.* **1996**, *12*, 2105.
- (3) Hall, S. S.; Doweiko, L. M.; Doweiko, A. M.; Zilenovski, J. S. R. *J. Med. Chem.* **1977**, *20*, 1239.
- (4) Carpentier, J.-F.; Mortreux, A. *Tetrahedron: Asymmetry* **1997**, *8*, 1083.
- (5) Domagala, J. M. *Tetrahedron Lett.* **1980**, *21*, 4997.
- (6) Kolasa, T.; Miller, M. J. *J. Org. Chem.* **1987**, *52*, 4978.
- (7) Chen, J. J.; Deshpande, S. V. *Tetrahedron Lett.* **2003**, *44*, 8873.
- (8) (a) Douglas, K. T.; Demircioglu, H. *J. Chem. Soc. Perkin Trans. 2* **1985**, 1951. (b) Creary, X.; Geiger, C. C. *J. Am. Chem. Soc.* **1982**, *104*, 4151. (c) Aggarwal, V. K.; Thomas, A.; Franklin, R. J. *J. Chem. Soc. Chem. Commun.* **1994**, *14*, 1653.
- (9) Hatch, R. P.; Weinreb, S. M. *J. Org. Chem.* **1977**, *42*, 3960.
- (10) (a) Hewkin, C. T.; Jackson, R. F. W.; Clegg, W. J. *J. Chem. Soc. Perkin Trans. 1* **1991**, *12*, 3091. (b) Gais, H.-J.; Lied, T. *Angew. Chem.* **1978**, *90*, 283.
- (11) Lapkin, E. A. *J. Org. Chem. USSR (Engl. Transl.)* **1977**, *13*, 915; *Zh. Org. Khim.* **1977**, *13*, 996.
- (12) Gassmann, J.; Guenther, H.; Osternack, K.; Sawluk, A.; Thimm, K.; Voss, J. *Magn. Reson. Chem.* **1994**, *32*, 624.
- (13) (a) Fortes, C. C.; Souto, C. R.O.; Okino, E. A. *Synth. Commun.* **1991**, *21*, 2045. (b) Kakimoto, M.-A.; Imai, Y. *Chem. Lett.* **1984**, 1831.