Me_2Zn Mediated, *tert*Butylhydroperoxide Promoted, Catalytic Enantioselective Reformatsky Reaction with Aldehydes.

Pier Giorgio Cozzi,* Fides Benfatti, Montse Guiteras Capdevila, and Alessandro Mignogna

Dipartimento di Chimica "G. Ciamician", Alma Mater Studiorum, Università di Bologna, Via Selmi 2, I-40126, Bologna, Italy

Email: piergiorgio.cozzi@unibo.it

1. General Information

General: ^{1}H NMR spectra were recorded on Varian 200 MHz or Varian 300 MHz spectrometers. Chemical Shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ 7.27 ppm). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian 50 MHz or Varian 75 MHz spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard (deuterochloroform: δ 77.0 ppm). Mass spectra were performed at an ionizing voltage of 70 eV. Chromatographic purification was done with 240-400 mesh silica gel. Analytical gas chromatography (GC) was performed on a Hewlett-Packard HP 6890 gas chromatograph with a flame ionization detector and split mode capillary injection system, using a Crosslinked 5% PH ME Siloxane (30 m) column or a Megadex5 chiral (25 m) column. Analytical high performance liquid chromatograph (HPLC) was performed on a HP 1090 liquid chromatograph equipped with a variable wavelength UV detector (deuterium lamp 190-600 nm), using a Daicel Chiralcel^{TM} OD column (0.46 cm I.D. x 25 cm) (Daicel Inc.) and AD. Column. HPLC grade isopropanol and hexane were used as the eluting solvents. All the reactions were carried out under a nitrogen atmosphere in flame-dried glassware using standard inert techniques for introducing reagents and solvents. Me_2Zn 2M in toluene was purchased by Fluka.. Anhydrous Et_2O, THF, and CH_2Cl_2 were purchased by Aldrich.

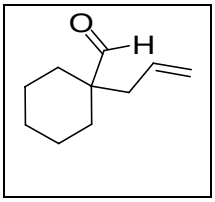
All aldehydes were carefully purified by crystallization of distillation before their use.

2-Methyl-2-phenyl propionaldehyde, 1-allyl-cyclohexane carbaldehyde, 2,2-dimethyl-3-phenylpropionaldehyde, 2,2-dimethyl-pent-4-enal, 2,2-dimethyl-3-oxo-butyraldehyde, 2,2-dimethyl-3-oxo-pentanal were obtained by synthetic methods reported in literature.[1]

[1] a) De Kimpe, N.; De Smaele, D.; Hofkens, A.; Dejaegher, Y.; Kesteleyn, B. *Tetrahedron* **1997**, *53*, 10803-10816. b) Noack, M.; Göttlich, R. *Eur. J. Org. Chem.* **2002**, 3171-3178; c) Artaud, I.; Torossian, G.; Viout, P. *Tetrahedron* **1985**, *41*, 5031-5037.

1-allylcyclohexanecarbaldehyde

De Kimpe, N.; De Smaele, D.; Hofkens, A.; Dejaegher, Y.; Kesteleyn, B. *Tetrahedron* **1997**, *53*, 10803-10816.

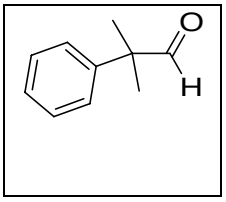


$C_{10}H_{16}O$ Fw = 152.23

Colorless oil.

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.10-1.40 (6H, m); 1.40-1.60 (2H, m); 1.75-1.90 (2H, m); 2.15 (2H, d, J = 7.2 Hz); 4.98 (2H, m); 5.47-5.80 (1H, m); 9.38 (s, 1H).

2-methyl-2-phenylpropanal



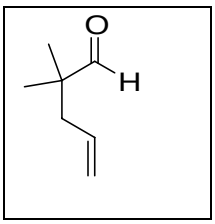
$C_{10}H_{12}O$ Fw = 148.2

Colourless oil.

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.46 (6H, s); 7.30-7.25 (3H, m); 7.40-7.35 (2H, m); 9.49 (1H, s).

2,2-dimethylpent-4-enal

Noack, M.; Göttlich, R. *Eur. J. Org. Chem.* **2002**, 3171-3178.



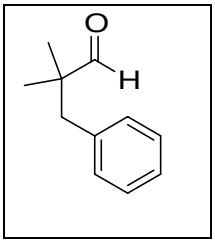
$C_7H_{12}O$ Fw = 112.17

Brown oil.

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.05 (6H, s); 2.23 (2H, dt, J = 7.4, 1.2 Hz); 5.06 (2H, m); 5.71 (1H, m); 9.48 (1H, s).

2,2-dimethyl-3-phenylpropanal

Artaud, I.; Torossian, G.; Viout, P. *Tetrahedron* **1985**, *41*, 5031-5037.



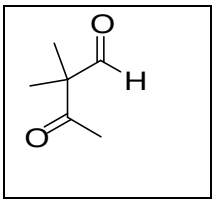
$C_{11}H_{14}O$ Fw = 162.23

Colourless oil.

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 0.95 (6H, s); 2.62 (2H, s); 7.10-7.5 (5H, m); 9.42 (s, 1H).

2,2-dimethyl-3-oxobutanal

Noack, M.; Göttlich, R. *Eur. J. Org. Chem.* **2002**, 3171-3178.



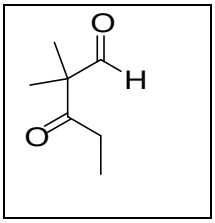
$C_6H_{10}O_2$ Fw = 114.14

Yellow oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.27 (6H, s); 2.18 (3H, s); 9.40 (s, 1H).

2,2-dimethyl-3-oxopentanal

Noack, M.; Göttlich, R. *Eur. J. Org. Chem.* **2002**, 3171-3178.



$C_7H_{12}O_2$ Fw = 128.17

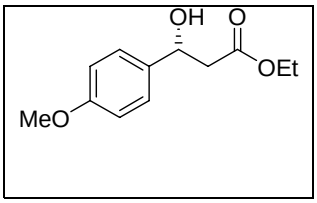
Yellow oil.

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.05 (3H, t, J = 7.2 Hz); 1.33 (6H, s); 2.49 (2H, q, J = 7.2 Hz); 9.60 (s, 1H).

Catalytic enantioselective Reformatsky reaction with aldehyde promoted by *t*BuOOH

A flame-dried, 25 mL, two necked round-bottom flask, equipped with magnetic stirring bar and nitrogen inlet is charged with Et_2O (3 mL), THF (2 mL), Me_2Zn (200 μL, 2 equiv.) and (1*R*, 2*S*)-1-phenyl-2-(1-pyrrolidinyl)-1-propanol (25% mol, 10.3 mg). The mixture is then cooled to –25 °C in a liquid N_2/acetone bath and aldehyde (0.2 mmol), ethyl iodoacetate (50 μL, 0.4 mmol, 2 equiv), Ph_3PO (20 mol %, 11.2 mg) are added in sequence. Finally, a 5.5 M solution of *t*BuOOH in decane (0.011mL) was added to the reaction. The homogeneous clear solution stirred at the same temperature for 100-140 hours, then quenched with HCl 1N and diluted with Et_2O. The phases are separated, and the aqueous phase is extracted with Et_2O. The organic phases were collected, dried over Na_2SO_4 and evaporated under reduced pressure to give an oil purified by chromatography (Cyclohexane:Et_2O 9:1 –7:3).

Ethyl-3-hydroxy-3(4-methoxyphenyl)-propanoate (1a).



$C_{12}H_{16}O_4$ Fw = 224.10

$[\alpha]_D$ = + 25.7 (c 1.4, $CHCl_3$).

Yellow oil.

IR (film): 3452, 2982, 2962, 2935, 2839, 1731, 1621, 1512, 1373, 1304, 1250, 1176, 1034, 833 cm^{-1}.

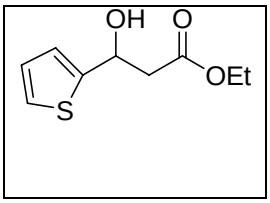
^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.27 (3H, t, J = 7 Hz); 2.72 (dd, 1H, J = 16.5, 4 Hz); 2.74 (dd, 1H, J = 16.5, 9 Hz); 3.19 (1H, brs); 3.81 (3H, s); 4.19 (2H, q, J = 7 Hz); 5.10 (1H, dd, J = 9, 4 Hz); 6.89 (2H, d, J = 9 Hz); 7.31 (2H, d, J = 9 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1; 43.3; 55.2; 60.8; 69.9; 113.8(2); 126.9(2); 134.7; 159.2; 172.4.

GC MS: 224(9); 206(28); 191(1); 178(4); 161(40); 137(100); 109(20); 94(12); 77(17).

HPLC analysis OJ: ramp, flow 0.5mL/min (hexane: *i*-PrOH) 99:1 to 90:10 in 30 min. TM: 50.6 min; tm: 52.9 min.

Ethyl-3-hydroxy-3-(2-thienyl)-propionate (1b).



$C_9H_{12}O_3S$ Fw = 200.25

$[\alpha]_D$ = +18 (c 2.8, $CHCl_3$).

Yellow oil.

IR (film): 3440, 3105, 2982, 2931, 1728, 1419, 1373, 1277, 1165, 1038, 852, 791, 737, 679 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.27 (3H, t, J = 7.2Hz); 2.78 (2H, AB; J = 6.9 Hz); 3.32 (1H, brs); 4.19 (2H, q, J = 7.2 Hz); 5.21 (1H, t, J = 6.3 Hz); 7.08 (1H, dd, J = 5, 1.5 Hz); 7.23-7.25 (1H, m); 7.31 (1H, dd; J = 3 Hz, J = 5.1 Hz).

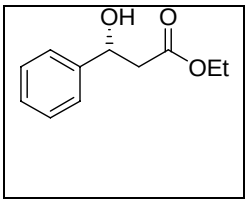
^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.08; 42.53; 60.83; 66.72; 120.90; 125.44; 126.21; 143.91; 172.22.

GC MS: 200(46); 184(14); 154(14); 137(31); 113(100); 97(10); 85(95); 65(13).

ESI-MS: rt: 4.4 min; *m/z*: 223.6 ($M+Na^+$); 239.1 ($M+K^+$).

HPLC analysis OD: isocratic, flow 0.5mL/min (hexane: *i*-PrOH) 86:14. tm: 13.5 min; TM: 31.9 min.

Ethyl-3-hydroxy-3 phenyl-propionate (1c).



$C_{11}H_{14}O_3$ Fw = 194.22

$[\alpha]_D$ = +38 (c 1, $CHCl_3$).

Colorless oil.

IR (film): 3444, 3086, 3063, 3032, 2982, 2920, 1724, 1493, 1454, 1396, 1373, 1296, 1269, 1195, 1161, 1038, 914, 871, 760, 737, 702, 604 cm^{-1}.

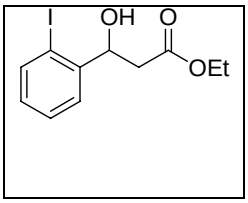
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.27 (3H, t, J = 7.3 Hz); 2.70 (1H, dd, J = 16.5, 4.5 Hz); 2.78 (1H, dd, J = 16.5, 8.4 Hz); 4.19 (2H, q, J = 7.3 Hz); 5.15 (1H, dd, J = 8.4, 4.5 Hz); 7.28-7.41 (5H, m).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1; 43.3; 60.8; 70.3; 125.6(2); 127.7; 128.5(2); 142.5; 172.4.

GC MS: 194(31); 176(5); 165(5); 147(10); 131(10); 120(19); 107(100); 88(17); 79(70); 60(11); 51(19).

HPLC analysis OD: isocratic, flow 0.5mL/min (hexane: *i*-PrOH) 90:10. tm:15 min; TM: 20 min.

Ethyl-3-hydroxy-3-(2-iodophenyl)-propionate (1d).



$C_{11}H_{13}IO_3$ Fw = 320.12

$[\alpha]_D$ = +28.7 (c 3, $CHCl_3$).

Pink oil.

IR (film): 3475, 3059, 2982, 2931, 1724, 1585, 1562, 1461, 1434, 1373, 1292, 1196, 1115, 1072, 1011, 867, 756, 652, 609 cm^{-1}.

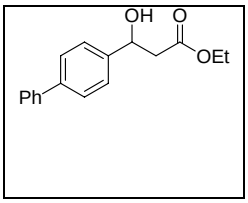
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.29 (3H, t, J = 7.2 Hz); 2.53 (1H, dd, J = 16.8, 10.2 Hz); 2.85 (1H, dd, J = 16.8, 2.4 Hz); 4.22 (2H, q, J = 7.5 Hz); 5.29 (1H, dd, J = 10.2, 2.4 Hz); 6.99 (1H, dt, J = 7.8, 1.8 Hz); 7.39 (1H, dt, J = 7.5, 1.2 Hz); 7.59 (1H, dd, J = 7.8, 1.8 Hz); 7.80 (1H, dd, J = 7.8, 1.2 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1; 41.6; 61.0; 73.7; 96.8; 127.0; 128.6; 129.4; 139.3; 144.2; 172.3.

GC MS: 320(1); 303(1); 275(3); 233(81); 193(100); 165(18); 147(56); 123(9); 105(56); 91(21); 78(56).

HPLC analysis OD: isocratic, flow 0.5mL/min (hexane: *i*-PrOH) 90:10. tm: 14.6 min; TM: 29.3 min.

Ethyl-3-hydroxy-3(4-phenylphenyl)-propionate (1e).



$C_{17}H_{18}O_3$ Fw = 270.32

$[\alpha]_D$ = +18.6 (c 2.8, $CHCl_3$).

White solid. m.p.:79-81 °C

IR (film): 3437, 3076, 3032, 2982, 2916, 1728, 1484, 1373, 1157, 1038, 833, 764, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.29 (3H, t, J = 7.2 Hz); 2.75 (1H, dd, J = 16.5, 4.5 Hz); 2.83 (1H, dd, J = 16.5, 8.4 Hz); 4.22 (2H, q, J = 7.2 Hz); 5.20 (1H, dd, J = 8.4, 4.5 Hz); 7.33-7.39 (1H, m); 7.42-7.50 (4H, m); 7.58-7.62 (4H, m).

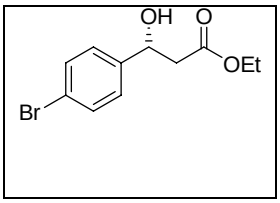
^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1; 43.2; 60.9; 70.0; 126.1(2); 127.0(2); 127.2(2); 127.3(2); 128.7(2); 140.7; 141.5; 72.4.

GC MS: 270(22); 252(43); 224(7); 207(28); 183(100); 165(16); 152(42); 77(5).

ESI-MS: rt: 9.0 min; *m/z:* 293.1 ($M+Na^+$); 563.0 ($2M+Na^+$).

HPLC analysis OJ: isocratic, flow 0.6mL/min (hexane: *i*-PrOH) 80:20. tm: 32.0 min; TM: 38.8 min.

Ethyl-3-hydroxy-3-(4-bromophenyl)-propanoate (1f).



$C_{11}H_{13}BrO_3$ Fw = 272.12

$[\alpha]_D$ = +16.7 (c 1.5, $CHCl_3$).

Yellow pale oil

IR (film):3460, 3063, 2981, 2931, 1728, 1597, 1570, 1473, 1373, 1296, 1192, 1095, 1074, 1037, 891,787, 694, 667 cm^{-1}.

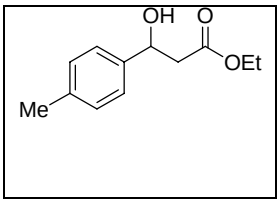
^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.28 (3H, t, J = 7.2 Hz); 2.71 (2H, d, J = 6.4 Hz); 4.20 (2H, q, J = 7.2 Hz); 5.10 (1H, t, J = 6.4 Hz); 7.27 (2H, d, J = 12.6 Hz); 7.50 (2H, d, J = 12.6 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1; 43.1; 61.0; 69.6; 121.6; 127.4(2); 131.6(2); 141.5; 172.2.

GC MS: 274(18) [M^+; ^{81}Br]; 272(18) [M^+; ^{79}Br]; 254(2); 227(8); 211(5); 198(6); 185(100); 157(20); 105(17); 88(40); 77(56).

HPLC analysis AD: isocratic, flow 0.5mL/min (hexane: *i*-PrOH) 95:5. tm: 31.3 min; TM: 34.4 min.

Ethyl-3-hydroxy-3-(4-methylphenyl)-propionate (1g).



$C_{12}H_{16}O_3$ Fw = 208.25

$[\alpha]_D$ = +9.4 (c 1.7, $CHCl_3$).

Colorless oil.

IR (film): 3460, 2982, 2924, 2874, 1731, 1516, 1446, 1373, 1265, 1196, 1161, 1038, 818 cm^{-1}.

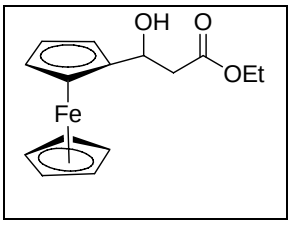
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.27 (3H, t, J = 7 Hz); 2.35 (3H, s); 2.68 (1H, dd, J = 16.5, 4.2 Hz); 2.77 (1H, dd, J = 16. 5, 9 Hz); 4.21 (2H, q, J = 7 Hz); 5.11 (1H, dd, J = 9, 4.2 Hz); 7.18 (2H, d, J = 8.1 Hz); 7.28 (2H, d, J = 8.1 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1; 21.1; 43.3; 60.8; 70.2; 125.6(2); 129.2(2); 137.5; 139.6; 172.4

GC MS: 208(20); 193(13); 163(4); 145(14); 134(6); 121(100); 105(11); 91(51); 77(21); 65(12).

HPLC analysis OF: isocratic, flow 0.7mL/min (hexane: *i*-PrOH) 83:17. TM: 13.2 min; tm: 14.5 min.

Ethyl-3-hydroxy-3 ferrocenyl-propionate (1h).



$C_{15}H_{18}O_3$ Fw = 302.06

$[\alpha]_D$ = +5 (c 1.2, $CHCl_3$).

Red oil.

IR (film):3460, 3093, 2982, 2927, 2854, 2360, 2341, 1732, 1627, 1373, 1273, 1196, 1161, 1026, 818 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.30 (3H, t, J = 6.9 Hz); 1.60 (1H, brs); 2.71-2.74 (2H, m); 4.17-4.27 (11H, m); 4.87 (1H, m).

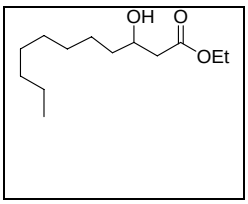
^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.2; 42.7; 60.7; 66.0; 66.4; 66.5; 68.0; 68.1; 68.5(5); 91.5; 172.0.

GC MS: 302(9); 284(100); 256(34); 239(8); 219(28); 191(16); 175(25); 147(17); 121(35); 89(13); 56(12).

ESI-MS**:** rt: 10.9 min, *m/z:* 284.0 (M-H_2O).

HPLC analysis OJ:ramp, flow 0.5mL/min (hexane: *i*-PrOH) from 95:5 to 80:20 in 30 min. TM: 25.3 min; tm: 27.6 min.

Ethyl-3-hydroxy-undecanoate (1i).



$C_{13}H_{26}O_3$ Fw = 230.34

Colorless oil.

IR (film): 3444, 2954, 2928, 2854, 1736, 1466, 1408, 1373, 1300, 1180, 1119, 1030, 721 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.87 (3H, t, J = 6.3 Hz); 1.25-1.51 (17H, m); 2.39 (1H, dd, J = 16.5, 8.7 Hz); 2.50 (1H, dd, J = 16.5, 3 Hz); 2.97 (1H, d, J = 3 Hz); 3.95-4.05 (1H, m); 4.17 (2H, q, J = 7.2 Hz).

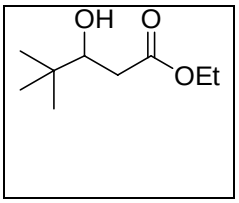
^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.0; 14.1; 25.5; 29.2(2); 29.5(2); 31.8; 36.5; 41.3; 60.62; 68.0; 173.1.

GC MS: 229(1); 212(1); 185(1); 141(7); 117(100); 89(18); 71(32); 55(14).

ESI-MS: rt: 11.1 min; *m/z*: 231.1 ($M+Na^+$); 478.7 ($2M+H_2O$).

Enantiomeric excess evaluated with chiral GC analysis. Ti = 130 °C for 20 min then ramp 1 °C/ min. to 160 °C. tm: 31.4 min. TM: 32.2 min.

Ethyl-3-hydroxy-4,4-dimethyl-pentanoate (1j).



$C_9H_{18}O_3$ Fw = 174.23

$[\alpha]_D$ = +20 (c 1.2, $CHCl_3$).

Colorless oil.

IR (film): 3491, 2958, 2876, 1724, 1465, 1369, 1304, 1261, 1165, 1030, 914, 802 cm^{-1}.

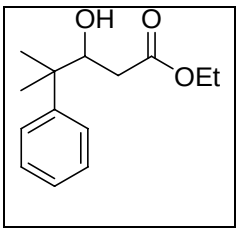
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.93 (9H, s); 1.29 (3H, t, J = 6.9 Hz); 2.35 (1H, dd, J = 16.2, 10.5 Hz); 2.53 (1H, dd, J = 16.2, 2.4 Hz); 2.87-2.90 (1H, m); 3.71 (1H, dd; J = 10.5, 2.4 Hz); 4.18 (2H, q, J = 6.9 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.2; 25.6(3); 34.3; 36.6; 60.7; 75.4; 173.9.

GC MS: 173(1); 155(1); 141(3); 129(6); 117(100); 111(24); 89(34); 83(9); 75(13); 71(81); 57(33).

Enantiomeric excess evaluated with chiral GC analysis. Ti = 50 °C for 2 min, then ramp 5 °C/ min to 180 °C. tm: 19.9 min. TM: 20.2 min.

Ethyl-3-hydroxy-4-methyl-4-phenyl-pentanoate (1k).



$C_{14}H_{20}O_3$ Fw = 236.30

$[\alpha]_D$ = -7 (c 0.7, $CHCl_3$).

Yellow oil

IR (film) : 3504, 3090, 3059, 2978, 2933, 1718, 1654, 1637, 1497, 1446, 1372, 1302, 1170, 1030 cm^{-1}.

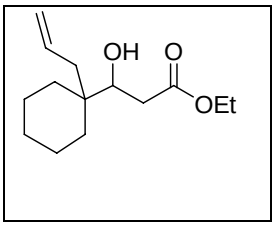
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.26 (3H, t, J = 6.9 Hz); 1.39 (3H, s); 1.42 (3H, s); 2.21-2.36 (2H, m); 2.81 (1H, bs); 4.10-4.29 (3H, m); 7.23-7.45 (5H, m).

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 14.1; 22.8; 25.2; 36.8; 41.8; 60.7; 75.3; 126.2; 126.5; 128.3; 146.3; 173.5.

GC MS: *m/z* 218(4); 173(13); 145(8); 117(93); 105(100); 91(77); 71(35); 65(5); 51(6).

HPLC analysis: OD flow 1.0mL/min (hexane: *i*-PrOH) ramp from 99:1 to 90:10 in 15 min. TM: 12.4min; tm: 9.0min.

Ethyl-3-(1-allyl-cyclohexyl)-3-hydroxy-propionate (1l).



$C_{14}H_{24}O_3$ Fw = 240.17

$[\alpha]_D$ = -15 (c 0.5, $CHCl_3$).

Yellow oil

IR (film) : 3523, 2977, 2927, 2861, 1721, 1457, 1400, 1373, 1305, 1170 cm^{-1}

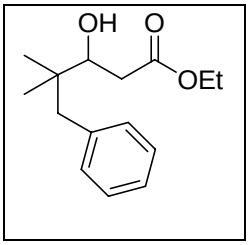
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.25 (3H, t, J = 6.9Hz); 1.18-1.54 (10H, m), 2.06 (1H, dd, J = 14.3, 6.6 Hz), 2.30 (1H, dd, J= 14.3, 7.8 Hz), 2.40 (1H, dd, J = 16.0, 10.2 Hz), 4.52 (1H, dd, J = 16.0, 2.4 Hz), 2.72 (1H, bs), 3.91 (1H, dd, J = 10.2, 2.4 Hz), 4.14 (2H, q, J = 6.9 Hz), 5.03 (1H, d, J = 10.5 Hz), 5.06 (1H, d, J = 8.1 Hz), 5.78-5.92 (1H, m);

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 14.1; 21.2; 21.3; 26.1; 30.5; 31.0; 35.9; 36.7; 39.4; 60.7; 72.6; 117.1; 135.2; 173.9.

GC MS: *m/z* 222(0.4); 199(5); 181(9); 153(6); 135(21); 118(19); 117(100); 111(23); 107(16); 93(15); 81(60); 67(29); 55(24).

Enantiomeric excess evaluated with chiral GC analysis. Ramp 3 °C/ min from Ti = 50 °C to 200°C. tm: 23.4min. TM: 23.9min.

Ethyl-3-hydroxy-4,4-dimethyl-5-phenyl-pentanoate (1m).



$C_{15}H_{22}O_3$ Fw = 250.33

$[\alpha]_D$ = -38 (c 1, $CHCl_3$).

Yellow oil

IR (film) : 3519, 3062, 3028, 2964, 2934, 2874, 1731, 1469, 1453, 1371, 1304, 1162, 1072, 1027 cm^{-1}.

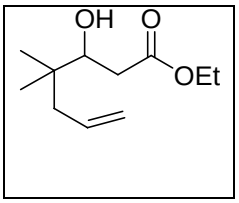
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.86 (3H, s); 0.95 (3H, s); 1.32 (3H, t, J=7.2 Hz); 2.46 (1H, dd, J = 16.5, 10.5 Hz), 2.54 (1H, d, J = 12.9 Hz), 2.58 (1H, dd, J = 2.4, 16.2 Hz), 2.85 (1H, d, J = 12.9 Hz), 3.18 (1H, d, J = 3.3 Hz), 3.78 (1H, dt, J = 10.5, 2.7 Hz), 4.21 (2H, q, J = 7.2 Hz), 7.20-7.38(5H, m);

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1, 22.0, 23.2, 36.2, 38.0, 44.4, 60.7, 73.3, 125.9, 127.7, 130.8, 138.5, 174.0;

GC MS: *m/z* 232(17), 186(7), 158(11), 145(17), 117(69), 91(100), 71(48), 55(6);

Enantiomeric excess evaluated by lanthanide induced shift (LIS) NMR measurement with (+) $Eu(hfc)_3$ ($CO_2CH_2\underline{CH_3}$ signals: δ_m=1.50ppm, δ_M=1.61ppm);

Ethyl-3-hydroxy-4,4-dimethyl-hept-6-enoate (1n).



$C_{11}H_{20}O_3$ Fw = 200.27

$[\alpha]_D$ = 8 (c 0.5, $CHCl_3$).

Yellow oil

IR (film) : 3477, 3075, 2962, 2927, 1731, 1468, 1372, 1306, 1261, 1158, 1026 cm^{-1}.

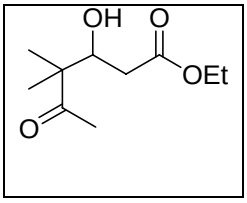
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.85 (3H, s); 0.88 (3H, s); 1.26 (3H, t, J = 6.9 Hz); 1.96 (1H, dd, J = 13.5, 7.5 Hz); 2.14 (1H, dd, J = 13.5, 7.2 Hz); 2.35 (1H, dd, J = 15.9, 10.5 Hz); 2.49 (1H, dd, J = 15.9, 2.4 Hz); 2.85 (1H, bs); 3.75 (1H, dd, J = 10.4, 2.4 Hz); 4.15 (2H, q, J = 6.9 Hz); 5.03 (1H, d, J = 14.7 Hz); 5.04 (1H, d, J = 11.4 Hz); 5.76-5.90 (1H, m);

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1; 22.3; 23.0; 36.3; 37.2; 43.4; 60.8; 73.9; 117.5; 135.0; 173.9.

GC MS: *m/z* 159(6); 137(8); 117(100); 113(19); 109(9); 95(14); 89(23); 71(80); 55(36).

Enantiomeric excess evaluated with chiral GC analysis. Ramp 4 °C/ min from Ti = 80 °C to 180°C. tm: 13.6min. TM: 13.8min.

Ethyl-3-hydroxy-4,4-dimethyl-5-oxo-hexanoate (1o)



$C_{10}H_{18}O_4$ Fw = 202.24

$[\alpha]_D$ = +58 (c=1, $CHCl_3$).

Yellow oil

IR (film): 3417, 2970, 2924, 2849, 1732, 1701, 1652, 1464, 1307, 1261, 1180, 1119 cm^{-1}.

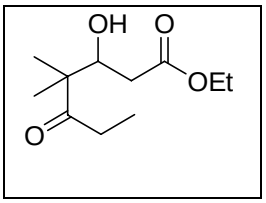
^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.11 (3H, s); 1.35 (3H, s); 1.25 (3H, t, J = 7.2 Hz); 2.17 (3H, s); 2.35 (2H, dd, J = 16.2, 9.9 Hz), 2.44 (1H, dd, J = 16.2, 3.0 Hz); 3.24 (1H, d, J = 4.2 Hz); 4.12-4.23 (3H, m).

^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1; 19.4; 21.5; 26.3; 36.6; 51.1; 60.9; 72.5; 173.0; 200.0.

GC MS: *m/z* 184(2); 142(18); 139(29); 117(12); 115(13); 111(13); 96(21); 86(65); 72(12); 71(100); 70(14); 69(56); 57(15); 53(5).

Enantiomeric excess evaluated by lanthanide induced shift (LIS) NMR measurement with (+) $Eu(hfc)_3$ ($CO\underline{CH_3}$ signals: δ_m=2.64ppm; δ_M=2.59ppm).

Ethyl-3-hydroxy-4,4-dimethyl-5-oxo-eptanoate (1p).



$C_{11}H_{20}O_4$ Fw = 216.27

$[\alpha]_D$ = -27.3(c 1, $CHCl_3$).

Yellow oil

IR (film): 3389, 2962, 2924, 2852, 1737, 1707, 1596, 1459, 1412, 1381, 1260, 1108, 1040 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.01 (3H, t, J = 7.2 Hz); 1.12 (3H, s); 1.15 (3H, s); 1.26 (3H, t, J = 7.2 Hz); 2.34 (1H, dd, J = 16.2, 9.0 Hz); 2.44 (1H, dd, J = 16.2, 2.4 Hz); 2.53 (2H, q, J = 7.2 Hz); 3.24 (1H, d, J = 3.0 Hz); 4.10-4.23 (3H, m).

^{13}C NMR ($CDCl_3$, 75 MHz) δ:7.8; 14.1; 19.6; 21.6; 31.4; 36.7; 50.8; 60.7; 72.8; 173.0; 198.0.

GC MS: *m/z*: 198(3); 169(139); 153(24); 142(34); 125(18); 117(13); 100(70); 96(36); 85(37); 72(19); 71(99); 70(24); 69(100); 57(96); 55(11).

Enantiomeric excess evaluated by lanthanide induced shift (LIS) NMR measurement with (+) $Eu(hfc)_3$ ($COCH_2\underline{CH_3}$ signals: δ_m=1.65ppm, δ_M=1.54ppm).