

# CeCl<sub>3</sub>·7H<sub>2</sub>O-NaI Catalyzed Hydrooxacyclization of Unsaturated 3-Hydroxy Esters

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## Supporting Information

**General:** <sup>1</sup>H NMR spectra were recorded at 300.00 or 200.00 MHz at 20°C with either tetramethylsilane (δ 0.00), chloroform (δ 7.25) as the internal standard. <sup>13</sup>C NMR spectra were recorded at 75.46 or 50.3 MHz at 20 °C with chloroform (δ 77.0) as the internal standard. Signal multiplicities were established by DEPT experiments. Melting points were determined through a Büchi instrument and are uncorrected. Mass spectra were recorded on a VG7070-E spectrometer by electron ionization. Specific optical rotations were determined at the sodium D line through a Perkin Elmer 341 polarimeter. Flash chromatographic separations were performed over Merck Silica gel 60 (230-400 mesh), TLC analyses were performed over Merck precoated TLC plates (Silica gel 60 GF<sub>254</sub> 0.25 mm). GC analyses were performed on HP 6890 instrument with a split/splitless injector, a FID detector, and a 5% phenyl methyl silicone column (30 m, i.d. 0.32 mm, film thickness 0.0025 mm). HPLC analyses were carried out on a HP1100 system. Detailed conditions are reported in footnotes below. Unless otherwise stated, ACS grade acetonitrile and other solvents and reagents were used as received.

**Hydroxy unsaturated compounds.** 3-Hydroxyalkenoic acid esters **1a-f**, and **1i** have been prepared by a Reformatsky reaction according to a known procedure (Rosini, G.; Confalonieri, G.; Marotta, E.; Rama, P.; Righi, P. *Org. Synth.* **1997**, *74*, 158) using as starting materials, respectively, 5-methyl-5-hexen-2-one, 3,3-dimethyl-4-pentenal, 6-methyl-5-hepten-2-one, 6-methyl-6-hepten-2-one, 5-hexenal, and (2-methyl-allyloxy)-acetaldehyde. The latter compound was prepared according to a known procedure recently utilized by Roos and Effenberger (*Tetrahedron: Asymmetry* **1999**, *10*, 2817), all the other unsaturated carbonyl compounds are commercially available. Hydroxy unsaturated compounds **1i** and **1j** have been prepared by reaction of 6-methyl-5-hepten-2-one with the Grignard reagent obtained from, respectively, benzyl bromide and (2-bromoethyl)-benzene. Commercial 6-methyl-5-hepten-2-one has been used as starting material for the preparation of dimethyl phosphonate **1k**. 3-Hydroxyalkenoic acid esters **1g** and **1h** have been prepared in two step sequence by the reaction of the dianion of methyl acetoacetate respectively with 3-chloro-2-methylpropene and with 1-chloro-3-methyl-2-butene to obtain the 3-oxoester intermediates followed by chemoselective reduction of them with NaBH<sub>4</sub> in methanol at 0 °C (Marotta, E.; Pagani, I.; Righi, P.; Rosini, G. *Tetrahedron* **1994**, *50*, 7645).

**3-Hydroxy-3,6-dimethyl-hept-6-enoic acid ethyl ester (1a):** as an oil from flash chromatography (PE : Et<sub>2</sub>O = 7:3); 81 % yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 4.70 (*m*, 2H); 4.18 (*q*, 2H, *J* = 7.1); 3.61 (*bs*, 1H); 2.52 (*d*, 1H, *J* = 15.4); 2.46 (*d*, 1H, *J* = 15.4); 2.09 (*m*, 2H); 1.73 (*s*, 3H); 1.66 (*m*, 2H); 1.28 (*t*, 3H, *J* = 7.1); 1.26 (*s*, 3H) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 173.48 (*s*); 146.26 (*s*); 110.30 (*t*); 71.39 (*s*); 61.18 (*t*); 48.54 (*t*); 40.50 (*t*); 32.58 (*t*); 27.17 (*q*); 23.12 (*q*); 14.73 (*q*) ppm. **IR** (film) *v*: 3468; 2974; 1734; 1653; 1458; 1373; 1189; 1030; 887 cm<sup>-1</sup>. **TLC:** R<sub>f</sub> 0.19 (PE : Et<sub>2</sub>O = 4:1). **GC:** 7.19 min (80 °C, 2 min then 15°C/min). Anal. Calcd for C<sub>11</sub>H<sub>20</sub>O<sub>3</sub>: C, 66.64; H, 9.15. Found: C, 66.53; H, 9.08.

**3-Hydroxy-3,7-dimethyl-oct-6-enoic acid benzyl ester (1b):** as an oil from flash chromatography (PE :Et<sub>2</sub>O = 7:3); 75% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.36 (*m*, 5H); 5.16 (*s*, 2H); 5.08 (*m*, 1H); 3.43 (*s*, 1H); 2.58 (*d*, 1H, *J* = 15.7); 2.50 (*d*, 1H, *J* = 15.7); 2.06 (*m*, 2H); 1.68 (*s*, 3H); 1.57 (*s*, 3H); 1.52 (*m*, 2H); 1.24 (*s*, 3H) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 172.71 (*s*); 135.47

(s); 131.77 (s); 128.59 (d); 128.38 (d); 128.30 (d); 123.97 (d); 71.00 (s); 66.42(t); 44.88 (t); 41.81 (t); 26.60(q); 25.63 (q); 22.62 (t); 17.56 (q) ppm. **IR** (film)  $\nu$ : 3477; 2965; 2922; 1733; 1719; 1376, 1171, 1085  $\text{cm}^{-1}$ . **MS** (m/z): 277 (M+1), 261 (4), 167 (9), 107 (7), 91 (15), 85 (50), 75 (26), 43 (100), 41 (49). **TLC**:  $R_f$  0.33 (PE: Et<sub>2</sub>O = 7:3). **GC**: 13.62 min (70 °C, 2 min then 15°C/min). Anal. Calcd for C<sub>17</sub>H<sub>24</sub>O<sub>3</sub>: C, 73.88; H, 8.75;. Found: C, 74.01; H, 8.73.

**3-Hydroxy-5,5-dimethyl-hept-6-enoic acid ethyl ester (1c)**: as an oil from flash chromatography (PE:Et<sub>2</sub>O = 7:3); 52 % yield. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>)  $\delta$  5.89 (*dd*, 1H,  $J$  = 17.6, 10.6); 5.00 (*dd*, 1H,  $J$  = 17.6, 1.3); 4.97 (*dd*, 1H,  $J$  = 10.6, 1.3); 4.16 (*q*, 2H,  $J$  = 7.2); 4.11 (*m*, 1H); 2.85 (*d*, 1H,  $J$  = 3.6); 2.42 (*d*, 2H,  $J$  = 6.5); 1.61 (*dd*, 1H,  $J$  = 14.3, 8.2); 1.40 (*dd*, 1H,  $J$  = 14.3, 2.8); 1.27 (*t*, 3H,  $J$  = 7.2); 1.17 (*bs*, 6H) ppm. **<sup>13</sup>C NMR** (CDCl<sub>3</sub>)  $\delta$  173.20 (*s*); 149.00 (*d*); 111.61 (*t*); 66.49 (*d*); 61.15 (*t*); 49.76 (*t*); 43.37 (*t*); 36.85 (*s*); 28.16 (*q*); 27.54 (*q*); 14.78 (*q*) ppm. **IR** (film)  $\nu$ : 3490; 2963; 1733; 1377; 1185; 1027, 910  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.26 (PE:Et<sub>2</sub>O = 7:3). **GC**: 7.28 min (80 °C, 2 min then 15°C/min). Anal. Calcd for C<sub>11</sub>H<sub>20</sub>O<sub>3</sub>: C, 66.64; H, 9.15. Found: C, 66.80; H, 9.17.

**3-Hydroxy-3,7-dimethyl-oct-6-enoic acid ethyl ester (1d)**: as an oil from flash chromatography (PE:Et<sub>2</sub>O = 7:3); 95% yield. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>)  $\delta$  5.10 (*m*, 1H); 4.18 (*q*, 2H,  $J$  = 7.2); 3.58 (*s*, 1H); 2.52 (*d*, 1H,  $J$  = 15.3); 2.44 (*d*, 1H,  $J$  = 15.3); 2.06 (*m*, 2H); 1.68 (*s*, 3H); 1.61 (*s*, 3H); 1.54 (*m*, 2H); 1.28 (*t*, 3H,  $J$  = 7.2); 1.25 (*s*, 3H) ppm. **<sup>13</sup>C NMR** (CDCl<sub>3</sub>)  $\delta$  173.47 (*s*); 132.17 (*s*); 124.69 (*d*); 71.43 (*s*); 61.09 (*t*); 45.46 (*t*); 42.42 (*t*); 27.18 (*q*); 26.18 (*q*); 23.22 (*t*); 18.11 (*q*); 14.71 (*q*) ppm. **IR** (film)  $\nu$ : 3509; 2976; 2922; 1735; 1716; 1376, 1202, 1026  $\text{cm}^{-1}$ . **MS** (m/z): 214 (M<sup>+</sup>, <1), 196 (25), 122 (33), 109 (87), 107 (40), 85 (28), 69 (47), 43 (100), 41 (59). **TLC**:  $R_f$  0.21 (PE: Et<sub>2</sub>O = 9:1). **GC**: 8.37 min (80 °C, 2 min then 15°C/min). Anal. Calcd for C<sub>12</sub>H<sub>22</sub>O<sub>3</sub>: C, 67.25; H, 10.35. Found: C, 67.45; H, 10.27.

**3-Hydroxy-3,7-dimethyl-oct-7-enoic acid ethyl ester (1e)**: as an oil from flash chromatography (PE:Et<sub>2</sub>O = 4:1); 65% yield. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>)  $\delta$  4.69 (*m*, 2H); 4.18 (*q*, 2H,  $J$  = 7.1); 3.59 (*s*, 1H); 2.51 (*d*, 1H,  $J$  = 15.5); 2.45 (*d*, 1H,  $J$  = 15.5); 2.01 (*m*, 2H); 1.71 (*s*, 3H); 1.50 (*m*, 4H); 1.28 (*t*, 3H,  $J$  = 7.1); 1.24 (*s*, 3H) ppm. **<sup>13</sup>C NMR** (CDCl<sub>3</sub>)  $\delta$  173.67 (*s*); 146.17 (*s*); 110.69 (*t*); 71.54 (*s*); 61.23 (*t*); 45.52 (*t*); 42.17 (*t*); 38.64 (*t*); 27.31 (*q*); 22.90 (*q*); 22.48 (*t*); 14.81 (*q*) ppm. **IR** (film)  $\nu$ : 3460; 2980; 1718; 1374; 1207; 1030, 887  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.29 (PE:Et<sub>2</sub>O = 85:15). **GC**: 10.26 min (50 °C, 2 min then 15°C/min). Anal. Calcd for C<sub>12</sub>H<sub>22</sub>O<sub>3</sub>: C, 67.25; H, 10.35. Found: C, 67.32; H, 10.30.

**3-Hydroxy-7-octenoic acid ethyl ester (1f)**: as an oil from flash chromatography (PE:Et<sub>2</sub>O = 7:3); 32% yield. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>)  $\delta$  5.81 (*ddt*, 1H,  $J$  = 6.6, 10.2, 16.8); 4.99 (*m*, 2H); 4.18 (*q*, 2H,  $J$  = 7.2); 4.02 (*m*, 1H); 3.06 (*d*, 1H,  $J$  = 4.2); 2.50 (*dd*, 1H,  $J$  = 16.4, 3.4); 2.42 (*dd*, 1H,  $J$  = 16.4, 8.8); 2.09 (*m*, 2H); 1.51 (*m*, 4H); 1.28 (*t*, 3H,  $J$  = 7.2) ppm. **<sup>13</sup>C NMR** (CDCl<sub>3</sub>)  $\delta$  173.61 (*s*); 139.10 (*d*); 115.30 (*t*); 68.44 (*d*); 61.26 (*t*); 41.98 (*t*); 36.49 (*t*); 34.13 (*t*); 25.31 (*t*); 14.76 (*q*) ppm. **IR** (film)  $\nu$ : 3449; 2980; 1734; 1373; 1186; 1029; 887  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.22 (PE:Et<sub>2</sub>O = 7:3). **GC**: 9.24 min (50 °C, 2 min then 15°C/min). Anal. Calcd for C<sub>10</sub>H<sub>18</sub>O<sub>3</sub>: C, 64.49; H, 9.74. Found: C, 64.38; H, 9.58.

**3-Hydroxy-6-methyl-hept-6-enoic acid methyl ester (1g)**: as an oil from flash chromatography (PE:Et<sub>2</sub>O = 7:3); 64% yield. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>)  $\delta$  4.96 (*s*, 1H); 4.94 (*s*, 1H); 4.25 (*m*, 1H); 3.95 (*s*, 3H); 3.27 (*d*, 1H,  $J$  = 4.0); 2.76 (*dd*, 1H,  $J$  = 16.2, 3.6); 2.68 (*dd*, 1H,  $J$  = 16.2, 8.5); 2.37 (*m*, 2H); 1.97 (*s*, 3H); 1.86 (*m*, 2H) ppm. **<sup>13</sup>C NMR** (CDCl<sub>3</sub>)  $\delta$  173.92 (*s*); 145.85 (*s*); 110.87 (*t*); 68.31 (*d*); 52.35 (*q*); 41.78 (*t*); 34.99 (*t*); 34.27 (*t*); 23.05 (*q*) ppm. **IR** (film)  $\nu$ : 3436; 2952; 1737; 1649; 1439; 1082  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.22 (PE:Et<sub>2</sub>O = 7:3). Anal. Calcd for C<sub>9</sub>H<sub>16</sub>O<sub>3</sub>: C, 62.72; H, 9.36. Found: C, 62.54; H, 9.39.

**3-Hydroxy-7-methyl-opt-6-enoic acid methyl ester (1h)**: as an oil from flash chromatography (PE:Et<sub>2</sub>O = 9:1); 54% yield. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>)  $\delta$  5.11 (*m*, 1H); 4.01 (*m*, 1H); 3.71 (*s*, 3H); 3.00 (*d*, 1H,  $J$  = 4.1); 2.51 (*dd*, 1H,  $J$  = 16.5, 3.6); 2.43 (*dd*, 1H,  $J$  = 16.5, 8.7); 2.11 (*m*, 2H); 1.69 (*s*, 3H); 1.62 (*s*, 3H); 1.56 (*m*, 2H) ppm. **<sup>13</sup>C NMR** (CDCl<sub>3</sub>)  $\delta$  173.98 (*s*); 132.90 (*s*); 124.26 (*d*); 68.23 (*d*); 52.31 (*q*); 41.83 (*t*); 37.14 (*t*); 26.30 (*q*); 24.68 (*t*); 18.27 (*q*) ppm. **IR** (film)  $\nu$ : 3439; 2922; 1735; 1437; 1295, 1170, 1067  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.25 (PE:Et<sub>2</sub>O = 9:1). **GC**: 8.00 min (80°C, 2 min then 15°C/min). Anal. Calcd for C<sub>12</sub>H<sub>22</sub>O<sub>3</sub>: C, 67.25; H, 10.35. Found: C, 67.32; H, 10.10.38.

**2,6-Dimethyl-1-phenyl-hept-5-en-2-ol (1i)**: as an oil from flash chromatography (PE:EtAc = 5:2); 75% yield. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>)  $\delta$  7.24 (*m*, 5H); 5.11 (*m*, 1H); 2.77 (*d*, 1H,  $J$  = 13.3); 2.72 (*d*, 1H,  $J$  = 13.3); 2.11 (*m*, 2H); 1.68 (*s*, 1H); 1.62 (*s*, 3H); 1.51 (*s*, 1H); 1.48 (*m*, 2H); 1.14 (*s*, 3H) ppm. **<sup>13</sup>C NMR** (CDCl<sub>3</sub>)  $\delta$  138.19 (*s*); 132.13 (*s*); 131.16 (*d*); 128.71 (*d*); 126.97 (*d*); 125.06 (*d*); 73.10 (*s*); 48.79 (*t*); 42.22 (*t*); 26.99 (*q*); 26.30 (*q*); 23.34 (*t*); 18.27 (*q*) ppm. **IR** (film)  $\nu$ : 3416; 2959; 2915; 1450; 1373; 1111; 698  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.24 (PE: EtAc = 9:1). **GC**: 10.6 min (80°C, 2 min then 15°C/min). Anal. Calcd for C<sub>15</sub>H<sub>22</sub>O: C, 82.51; H, 10.16. Found: C, 82.57; H, 10.22.

**3,7-Dimethyl-1-phenyl-oct-6-en-3-ol (1j)**: as an oil from flash chromatography (PE:EtAc = 5:1); 75% yield.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.20 (*m*, 5H); 5.14 (*m*, 1H); 2.67 (*m*, 2H); 2.06 (*m*, 2H); 1.76 (*m*, 2H); 1.69 (*s*, 3H); 1.68 (*bs*, 1H), 1.63 (*s*, 3H); 1.54 (*m*, 2H); 1.23 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  143.26 (*s*); 132.42 (*s*); 129.03 (*d*); 128.96 (*d*); 126.35 (*d*); 125.01 (*d*); 73.30 (*s*); 44.48 (*t*); 42.35 (*t*); 31.04 (*t*); 27.45 (*q*); 26.35 (*q*); 23.39 (*t*); 18.31 (*q*) ppm. **IR** (film)  $\nu$ : 3393; 2928; 1603; 1454; 1375; 1114; 931  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.24 (PE: EtAc = 5:1). **GC**: 11.36 min (80°C, 2 min then 15°C/min). Anal. Calcd C, 82.70; H, 10.41. Found: C, 82.71; H, 10.47.

**3-Hydroxy-4-(2-methyl-allyloxy)-butyric acid ethyl ester (1k)**: as an oil from flash chromatography (PE:Et<sub>2</sub>O = 1:1); 65% yield.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  4.93 (*m*, 2H); 4.21 (*m*, 1H); 4.17 (*q*, 2H,  $J = 7.2$ ); 3.93 (*s*, 2H); 3.44 (*dd*, 1H,  $J = 0.5, 3.3$ ); 3.42 (*dd*, 1H,  $J = 0.5, 4.4$ ); 3.07 (*bs*, 1H); 2.54 (*d*, 2H,  $J = 6.1$ ); 1.73 (*s*, 3H); 1.27 (*t*, 3H,  $J = 7.2$ ) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  172.72 (*s*); 142.46 (*s*); 113.05 (*t*); 75.87 (*t*); 73.49 (*t*); 67.78 (*d*); 61.28 (*t*); 38.92 (*t*); 19.96 (*q*); 14.76 (*q*) ppm. **IR** (film)  $\nu$ : 3451; 2981; 1736; 1373; 1177; 1096; 903  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.25 (PE:Et<sub>2</sub>O = 1:1). **GC**: 8.00 min (80°C, 2 min then 15°C/min). Anal. Calcd for C<sub>10</sub>H<sub>18</sub>O<sub>4</sub>: C, 62.25; H, 7.60. Found: C, 62.32; H, 7.75.

**(2-Hydroxy-2,6-dimethyl-hept-5-enyl)-phosphonic acid dimethyl ester (1l)**. The  $\beta$ -hydroxyalkylphosphonate **1l** was prepared according to the procedure developed by Kawashima et al. (*Bull. Chem. Soc. Jpn.* **1998**, *71*, 209) by sequential treatment of methylphosphonic acid dimethyl ester (3.25 mL, 30.0 mmol) in THF (55 mL) with *n*-BuLi (1.6M *n*-hexane solution, 33.0 mL) at -70°C under argon atmosphere. The solution was stirred for 15 min at -70°C and then a solution of commercial 6-methyl-5-hepten-2-one (4.88 mL, 33.0 mmol) in THF (10 mL) was slowly added. Stirring was continued for additional 5 min and the reaction was quenched with aqueous NH<sub>4</sub>Cl. The solvent was evaporated under reduced pressure. The residue was taken with the minimal amount of water and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2x200 mL). Combined extracts were dried over MgSO<sub>4</sub> and filtered. The removal of the solvent at reduced pressure gave a residue that was distilled with kugelrohr (190 °C/0.5 mmHg) to give compound **1l** as an oil (94% yield):  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  5.20 (*m*, 1H); 3.97 (*bs*, 1H); 3.85 (*d*, 6H,  $J_{\text{HP}} = 6.0$ ); 2.15 (*m*, 4H); 1.78 (*s*, 3H); 1.72 (*s*, 3H); 1.70 (*m*, 2H); 1.45 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  131.88 (*s*); 124.46 (*d*); 70.71 (*s*); 52.55 (*q*); 52.47 (*q*); 43.64 (*t*); 36.78 (*t*); 28.23 (*q*); 26.01 (*q*); 23.14 (*t*); 17.95 (*q*) ppm. **IR** (film)  $\nu$ : 3401; 2968; 2855; 1452; 1377, 1230, 1033, 854  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.15 (CH<sub>2</sub>Cl/MeOH = 99:1). Anal. Calcd for C<sub>11</sub>H<sub>23</sub>O<sub>4</sub>P: C, 52.79; H, 9.26. Found: C, 52.83; H, 9.35.

**General procedure for the hydrooxacyclization promoted by CeCl<sub>3</sub>·7H<sub>2</sub>O-NaI (0.1 eq) in refluxing acetonitrile.** Reactions were performed under magnetic stirring in a 25 mL three-necked flask equipped with a refrigerant, a CaCl<sub>2</sub> tube and a nitrogen inlet. To a solution of 3-hydroxyalkenoic acid ester (**1**, 18 mmol) in 10 mL of acetonitrile were added CeCl<sub>3</sub>·7H<sub>2</sub>O (0.67g, 1.8 mmol) and NaI (0.26 g, 1.8 mmol). The resulting mixture was stirred under reflux for the time reported in Table 1 and was monitored by TLC. The reaction mixture was cooled at room temperature, and acetonitrile was partially evaporated at reduced pressure. Then the residue was added with diethyl ether (75 mL), water (15 mL) and 1.0 N HCl (10 mL). The organic layer was separated and the aqueous phase was extracted again with diethyl ether (75 mL). The combined organic layers were consecutively washed with water (3x10 mL), 10% aqueous solution of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (3x10 mL), brine solution (2x10 mL) and then dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was then removed under reduced pressure, and the crude product was purified by flash chromatography to give the cyclic derivative **2** with the yield reported in Table 1.

**General procedure for the hydrooxacyclization promoted by CeCl<sub>3</sub>·7H<sub>2</sub>O-NaI (1.5 eq) in refluxing acetonitrile.** Reactions were performed by using the same reaction conditions, the same equipment and the same work-up already depicted. However, 3-hydroxyalkenoic acid esters (**1**, 5.0 mmol) dissolved in acetonitrile (12.5 mL) were treated with CeCl<sub>3</sub>·7H<sub>2</sub>O (2.79 g, 7.5 mmol) and NaI (1.12 g, 7.5 mmol). The yields of cyclic derivatives **2** are reported in Table 1.

**(2,5,5-Trimethyl-tetrahydro-furan-2-yl)-acetic acid ethyl ester (2a)**: yellow oil from flash chromatography;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  4.12 (*q*, 2H,  $J = 7.3$ ), 2.51 (*s*, 2H); 2.19 (*m*, 1H); 1.86 (*m*, 3H); 1.34 (*s*, 3H); 1.26 (*t*, 3H,  $J = 7.3$ ); 1.25 (*s*, 3H); 1.23 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  171.59 (*s*); 82.02 (*s*); 81.94 (*s*); 60.68 (*t*); 47.53 (*t*); 38.87 (*t*); 37.33 (*t*); 30.24 (*q*); 29.84 (*q*); 28.61 (*q*); 14.76 (*q*) ppm. **IR** (film)  $\nu$ : 2971; 1735; 1460; 1367; 1101; 1034; 982; 887  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.36 (PE: Et<sub>2</sub>O = 4:1). Anal. Calcd for C<sub>11</sub>H<sub>20</sub>O<sub>3</sub>: C, 66.64; H, 9.15. Found: C, 66.45; H, 9.07.

**(2,6,6-Trimethyl-tetrahydro-pyran-2-yl)-acetic acid benzyl ester (2b)**: yellow oil from flash chromatography;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.30 (*m*, 5H); 5.12 (*d*, 1H,  $J = 12.4$ ); 5.07 (*d*, 1H,  $J = 12.4$ ); 2.61 (*d*, 1H,  $J = 13.4$ ); 2.49 (*d*, 1H,  $J = 13.4$ ); 1.71 (*m*, 6H); 1.31 (*s*, 3H); 1.20 (*s*, 3H); 1.13 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  170.85 (*s*); 136.07 (*s*); 128.34 (*d*); 128.11 (*d*); 127.93 (*d*); 72.36 (*s*); 71.64 (*s*); 65.82 (*t*); 47.94 (*t*); 36.20 (*t*); 34.01 (*t*); 31.12 (*q*); 29.40 (*q*); 27.75 (*q*); 16.26 (*t*) ppm. **IR** (film)  $\nu$ : 2972; 2929; 1735; 1456; 1378; 1224; 1112; 1068; 825  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.52 (PE: Et<sub>2</sub>O = 8 : 2). Anal. Calcd for C<sub>17</sub>H<sub>24</sub>O<sub>3</sub>: C, 73.88; H, 8.75. Found: C, 73.81; H, 8.72.

**trans-(4,4,5-Trimethyl-tetrahydro-furan-2-yl)-acetic acid ethyl ester (2c):** yellow oil from flash chromatography;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  4.37 (*dddd*, 1H,  $J = 9.2, 7.3, 6.5, 6.5$ ); 4.10 (*q*, 2H,  $J = 7.2$ ); 3.59 (*q*, 1H,  $J = 6.5$ ); 2.57 (*dd*, 1H,  $J = 15.3, 7.3$ ); 2.37 (*dd*, 1H,  $J = 15.3, 6.5$ ); 1.90 (*dd*, 1H,  $J = 12.3, 6.5$ ); 1.46 (*dd*, 1H,  $J = 12.3, 9.2$ ); 1.21 (*t*, 3H,  $J = 7.2$ ); 1.01 (*d*, 3H,  $J = 6.5$ ); 0.94 (*s*, 3H); 0.86 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  171.91 (*s*); 82.57 (*d*); 71.37 (*d*); 60.93 (*t*); 48.22 (*t*); 42.31 (*t*); 42.04 (*s*); 25.34 (*q*); 21.46 (*q*); 14.80 (*q*); 14.73 (*q*) ppm. **IR** (film)  $\nu$ : 2964; 1739; 1458; 1368; 1188; 1091; 1028  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.40 (PE:  $\text{Et}_2\text{O} = 7:3$ ). Anal. Calcd for  $\text{C}_{11}\text{H}_{20}\text{O}_3$ : C, 66.64; H, 9.15. Found: C, 66.48; H, 9.10.

**(2,6,6-Trimethyl-tetrahydro-pyran-2-yl)-acetic acid ethyl ester (2d):** yellow oil from flash chromatography;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  4.09 (*q*, 2H,  $J = 7.1$ ); 2.53 (*d*, 1H,  $J = 13.7$ ); 2.40 (*d*, 1H,  $J = 13.7$ ); 1.71 (*m*, 4H); 1.41 (*m*, 2H); 1.29 (*s*, 3H); 1.23 (*t*, 3H,  $J = 7.1$ ); 1.19 (*s*, 3H), 1.14 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  171.75 (*s*); 73.02 (*s*); 72.33 (*s*); 60.57 (*t*); 48.66 (*t*); 39.96 (*t*); 34.53 (*t*); 31.89 (*q*); 30.11 (*q*); 28.48 (*q*); 16.96 (*t*); 14.88 (*q*) ppm. **IR** (film)  $\nu$ : 2975; 2936; 1732; 1368; 1223; 1113; 1037; 805  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.47 (PE:  $\text{Et}_2\text{O} = 4 : 1$ ). **GC**: 7.41 min (80 °C, 2 min then 15°C/min). Anal. Calcd for  $\text{C}_{12}\text{H}_{22}\text{O}_3$ : C, 67.25; H, 10.35. Found: C, 67.32; H, 10.18.

**cis-(6-Methyl-tetrahydro-pyran-2-yl)-acetic acid ethyl ester (2f):** oil from flash chromatography;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  4.14 (*q*, 2H,  $J = 7.1$ ); 3.77 (*m*, 1H); 3.46 (*m*, 1H); 2.53 (*dd*, 1H,  $J = 15.1, 7.4$ ); 2.37 (*dd*, 1H,  $J = 15.1, 5.9$ ); 1.81 (*m*, 1H); 1.55 (*m*, 3H); 1.25 (*t*, 3H,  $J = 7.1$ ); 1.19 (*m*, 2H); 1.14 (*d*, 3H,  $J = 6.2$ ) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  171.99 (*s*); 74.88 (*d*); 74.57 (*d*); 60.82 (*t*); 42.34 (*t*); 33.48 (*t*); 31.51 (*t*); 24.03 (*t*); 22.61 (*q*); 14.75 (*q*) ppm. **IR** (film)  $\nu$ : 2972; 2934; 1740; 1373; 1195; 1174; 1075; 1042  $\text{cm}^{-1}$ . **MS** ( $m/z$ ): 186 ( $\text{M}^+$ , 8), 144 (27), 143 (43), 130 (100), 99 (88), 81 (40), 71 (37), 69 (21), 55 (50), 45 (34), 43 (62), 42 (84), 41 (69). **TLC**:  $R_f$  0.40 (PE:  $\text{Et}_2\text{O} = 4:1$ ). **GC**: 6.95 min (80°C, 2 min then 15°C/min). Anal. Calcd for  $\text{C}_{10}\text{H}_{18}\text{O}_3$ : C, 64.49; H, 9.74. Found: C, 64.62; H, 9.68.

**(5,5-Dimethyl-tetrahydro-furan-2-yl)-acetic acid methyl ester (2g):** yellow oil from flash chromatography;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  4.35 (*qui*, 1H,  $J = 6.6$ ); 3.68 (*s*, 3H); 2.64 (*dd*, 1H,  $J = 15.2, 6.5$ ); 2.45 (*dd*, 1H,  $J = 15.2, 7.0$ ); 2.14 (*m*, 1H); 1.74 (*m*, 3H); 1.25 (*s*, 3H); 1.23 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  172.28 (*s*); 81.64 (*s*); 75.19 (*d*); 52.06 (*q*); 41.80 (*t*); 38.81 (*t*); 32.28 (*t*); 29.71 (*q*); 28.56 (*q*); ppm. **IR** (film)  $\nu$ : 2971; 1739; 1435; 1365; 1054  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.14 (PE:  $\text{Et}_2\text{O} = 9 : 1$ ). **GC**: 5.60 min (80°C, 2 min then 15°C/min). Anal. Calcd for  $\text{C}_9\text{H}_{16}\text{O}_3$ : C, 62.72; H, 9.36. Found: C, 62.84; H, 9.48.

**(6,6-Dimethyl-tetrahydro-pyran-2-yl)-acetic acid methyl ester (2h):** oil from flash chromatography;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  3.98 (*m*, 1H); 3.67 (*s*, 3H); 2.49 (*dd*, 1H,  $J = 15.1, 7.2$ ); 2.34 (*dd*, 1H,  $J = 15.1, 6.2$ ); 1.64, 1.43-1.08 (*2m*, 6H); 1.20 (*s*, 3H); 1.18 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  171.94 (*s*); 72.03 (*s*); 67.24 (*d*); 51.37 (*q*); 41.83 (*t*); 35.74 (*t*); 31.67 (*q*); 31.08 (*t*); 21.75 (*q*); 19.78 (*t*) ppm. **IR** (film)  $\nu$ : 2974; 2935; 1740; 1435; 1380; 1192  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.57 (PE:  $\text{Et}_2\text{O} = 7:3$ ). Anal. Calcd for  $\text{C}_{10}\text{H}_{18}\text{O}_3$ : C, 64.49; H, 9.74. Found: C, 64.52; H, 9.69.

**2-Benzyl-2,6,6-trimethyl-tetrahydro-pyran (2i):** yellow oil from flash chromatography;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.22 (*m*, 5H); 2.85 (*d*, 1H,  $J = 13.1$ ); 2.65 (*d*, 1H,  $J = 13.1$ ); 1.77-1.24 (*m*, 6H); 1.22 (*s*, 3H), 1.21 (*s*, 3H), 1.17 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  139.37 (*s*); 131.58 (*d*); 128.18 (*d*); 126.51 (*d*); 74.40 (*s*); 72.07 (*s*); 51.24 (*t*); 37.27 (*t*); 34.31 (*t*); 33.08 (*q*); 29.47 (*q*); 27.50 (*q*); 17.14 (*t*) ppm. **IR** (film)  $\nu$ : 2966; 2935; 1493; 1371; 1224; 1116; 1023; 986  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.74 (PE:  $\text{Et}_2\text{O} = 4:1$ ). **GC**: 9.15 min (80°C, 2 min then 15°C/min). Anal. Calcd for  $\text{C}_{15}\text{H}_{22}\text{O}$ : C, 82.51; H, 10.16. Found: C, 82.58; H, 10.22.

**2,2,6-Trimethyl-6-phenethyl-tetrahydro-pyran (2j):** oil from flash chromatography;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.18 (*m*, 5H); 2.67 (*m*, 2H); 1.89-1.30 (*m*, 8H); 1.23 (*s*, 6H); 1.22 (*s*, 3H) ppm.  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  144.03 (*s*); 129.04 (*d*); 128.92 (*d*); 126.11 (*d*); 73.46 (*s*); 71.89 (*s*); 46.07 (*t*); 37.55 (*t*); 35.52 (*t*); 31.87 (*q*); 30.93 (*t*); 30.51 (*q*); 28.40 (*q*); 17.22 (*t*) ppm. **IR** (film)  $\nu$ : 2974; 2934; 1454; 1371; 1223; 1118; 1000; 699  $\text{cm}^{-1}$ . **TLC**:  $R_f$  0.74 (PE:  $\text{Et}_2\text{O} = 4:1$ ). Anal. Calcd for  $\text{C}_{16}\text{H}_{24}\text{O}$ : C, 82.70; H, 10.41. Found: C, 82.78; H, 10.38.

**Reactions of 3-hydroxyalkenoic acid ester 1d with a variety of  $\text{CeX}_3$ .** Each reaction has been performed and worked-up according to the procedure already described and using 0.1 equivalents of reagents. All the reactions were kept at reflux under nitrogen for 21 h by using ACS grade acetonitrile or acetonitrile dried and distilled on A4 molecular sieves.  $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ , NaI,  $\text{CeCl}_3$ ,  $\text{CeBr}_3$ ,  $\text{CeI}_3$  were used as obtained from Aldrich. The results of the experiments are summarized in Table 2.

**(R)-(-)-3-Hydroxy-7-methyl-6-octenoic acid methyl ester (R1h).** The enantiopure **R1h** (ee >99%) has been prepared from 3-oxo-7-methyl-6-octenoic acid methyl ester in a 39 % overall yield following the procedure developed by Hiramata et al. (*J. Chem. Soc., Chem. Commun.* **1983**, 599; Reduction of Acyclic  $\beta$ -Keto Esters, 2:1.12 in *Preparative*

*Biotransformations*- Professor S. M. Roberts, Ed.-Wiley, Chichester, UK). A 1M solution of KOH in water (88 mL) was added in one portion to a stirred solution of 3-oxo-7-methyl-6-octenoic acid methyl ester (8.0 g, 43 mmol) in EtOH (130 mL) at 0°C. The mixture was stirred at room temperature until no more ester was detected by TLC (PE/Et<sub>2</sub>O 3:1). After 30 h the mixture was evaporated at reduced pressure using a cool water bath (< 30°C). The yellow residue (roughly 10 g) turned solid and was diluted with water (700 mL) and subdivided in four portions. Whilst the ethanol was evaporated bakers' yeast (*Saccharomyces cerevisiae*, Sigma, Type II, 56.0 g), D-glucose (62.00 g, 344.1 mmol), KH<sub>2</sub>PO<sub>4</sub> (0.39 g), MgSO<sub>4</sub> (0.20 g, 1.7 mmol) and water (180 mL) were added in four 1 L Erlenmeyer flasks, loosely stoppered with cotton wool, and were thoroughly mixed, then shaken at 30°C and 220 r.p.m. in an orbital shaker for 30 min to initiate the fermentation. Then a portion of the diluted solution of potassium salt obtained by alkaline hydrolysis of ester was added in each flask and the whole mixture was shaken for 58 h (TLC PE/ Et<sub>2</sub>O 3:2). Each flask was added with Celite (75 g) and then stirred for additional 30 min. Each reaction mixture was filtered through a Celite pad (25 g, 2.5 cm high) and the filter was washed with water (60 mL). The filtrate was acidified with 2M HCl until pH 3, saturated with solid NaCl and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4x250 mL). The organic extracts were collected, dried (MgSO<sub>4</sub>) and evaporated at reduced pressure to leave the β-hydroxyacid as a viscous brown oil. The four reaction mixtures gave 2.95 g (39.4 % yield) of product that was dissolved in diethyl ether (50 mL) and treated at 0°C with diazomethane in diethyl ether prepared from Diazald® and potassium hydroxyde. The excess of diazomethane was destroyed with acetic acid. The residue was concentrated at reduced pressure to give the corresponding ester in a 30 % overall yield from compound **R1h**. The spectroscopic data are in perfect agreement with those registered on the racemic compound and already reported to describe compound **1h**. **HPLC**: 8.42 min (*R* isomer>99.5%), and 10.66 min (*S* isomer, <0.5%) [Chiralcel OD-H 250 mm × 4.6 mm (*n*-hexane/*i*-PrOH 95:5), 0.7 mL/min, λ = 206 nm, 25°C]. [α]<sub>D</sub><sup>20</sup> -15.7 (*c* 1.04, CHCl<sub>3</sub>). Anal. Calcd for C<sub>10</sub>H<sub>18</sub>O<sub>3</sub>: C, 64.49; H, 9.74. Found: C, 64.55; H, 9.58.

**(-)-(6,6-Dimethyl-tetrahydro-pyran-2-yl)-acetic acid [(-)-3]**: *CeCl<sub>3</sub>·7H<sub>2</sub>O/NaI Cyclization*: The hydrooxacyclization of **R1h** was performed following the general procedure already reported and gave an oil purified by flash chromatography. Its spectral data agree with those described for racemic mixture. [α]<sub>D</sub><sup>20</sup> -30.6 (*c* 1.04, CHCl<sub>3</sub>). Anal. Calcd for C<sub>10</sub>H<sub>18</sub>O<sub>3</sub>: C, 64.49; H, 9.74. Found: C, 64.61; H, 9.78.

*Ester hydrolysis*: Methyl ester (2.85g, 15.4 mmol) was dissolved in a solution of KOH (1.68 g, 30.0 mmol) in methanol (15 mL) and the solution was maintained under magnetic stirring at room temperature until no more ester can be seen by TLC. After 21 h methanol was removed by evaporation under reduced pressure, using a cool water bath (< 30°C). The residue was diluted with water (100 mL) and extracted with diethyl ether (2x50 mL). The aqueous layer was acidified by adding 6 N HCl and then extracted with diethyl ether (3x50 mL). The combined organic layers were consecutively washed with water (3x10 mL), brine solution (2x10 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated at reduced pressure to give a pale yellow oil in an almost quantitative yield. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>) δ 10.15 (*bs*, 1H); 4.00 (*m*, 1H); 2.52 (*dd*, 1H, *J* = 15.7, 7.5); 2.45 (*dd*, 1H, *J* = 15.7, 5.4); 1.75-1.11(*m*, 6H); 1.23 (*bs*, 6H) ppm. **<sup>13</sup>C NMR** (CDCl<sub>3</sub>) δ 175.97 (*s*); 73.77 (*s*); 67.88 (*d*); 42.16 (*t*); 36.31 (*t*); 32.19 (*q*); 31.53 (*t*); 22.40 (*q*); 20.17 (*t*) ppm. **TLC**: R<sub>f</sub> 0.25 (Et<sub>2</sub>O). **IR** (film) ν: 3077; 2929; 2664; 1712; 1380; 1295; 1207; 1070; 1041; 978 cm<sup>-1</sup>. [α]<sub>D</sub><sup>20</sup> -51.2 (*c* 0.86, CHCl<sub>3</sub>). Anal. Calcd for C<sub>9</sub>H<sub>16</sub>O<sub>3</sub>: C, 62.76; H, 9.36. Found: C, 62.81; H, 9.51.

**Reaction of acid (-)-3 with (S)-Phenylethylamine**. To a stirred solution of acid (-)-**3** (1.03 g, 6.0 mmol) in THF (10 mL) was added triethylamine (0.84 mL, 6.0 mmol) and then cyanuric chloride (1.11 g, 6.0 mmol) dissolved in THF (5 mL). The addition is accompanied by the formation of a white solid. After 5 min under magnetic stirring (*S*)-phenylethylamine (2.32 mL, 18.0 mmol) in THF (5 mL) was added at once. An exothermic reaction was observed. The reaction was maintained under stirring at room temperature. After 1h the reaction mixture was quenched by the addition of water (20 mL) and dichloromethane (50 mL), whereupon it was transferred into a separatory funnel and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3x50 mL). The combined organic extracts were washed with brine and then dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and the solvent evaporated under reduced pressure to give a crude product that was purified by flash chromatography eluting with Et<sub>2</sub>O/CH<sub>2</sub>Cl<sub>2</sub> 3:1 to obtain compound **A** (1.21 g, 74% yield). Crystallization from isopropyl ether gave a white solid with mp 180-182°C; **<sup>1</sup>H NMR** (CDCl<sub>3</sub>) δ 7.24 (*m*, 6H); 5.08 (*m*, 1H); 3.88 (*m*, 1H); 2.31 (*d*, 2H, *J* = 5.8); 1.67-1.04 (*m*, 6H); 1.45 (*d*, 3H, *J* = 6.9); 1.20 (*s*, 3H); 1.14 (*s*, 3H) ppm. **<sup>13</sup>C NMR** (CDCl<sub>3</sub>) δ 171.15 (*s*); 144.24 (*s*); 129.17 (*d*); 127.75 (*d*); 126.72 (*d*); 73.31 (*s*); 68.54 (*d*); 49.06 (*d*); 44.00 (*t*); 36.33 (*t*); 32.35 (*q*); 31.52 (*t*); 22.90 (*q*); 22.59 (*q*); 20.28 (*t*) ppm. **IR** (KBr) ν: 3269; 2974; 2929; 2870; 1638; 1553; 1203; 1063; 868; 742 cm<sup>-1</sup>. **MS** (*m/z*): 275 (M<sup>+</sup>, 37), 205 (18), 120 (100), 106 (39), 105 (93), 104 (21), 95 (19), 43 (19), 41 (29). **TLC**: R<sub>f</sub> 0.58 (Et<sub>2</sub>O/CH<sub>2</sub>Cl<sub>2</sub> = 3:1). **GC**: 16.37 min (50°C, 2 min then 15°C/min). **HPLC**: 7.20 min [Chiralcel OD-H 250 mm × 4.6 mm (*n*-hexane/*i*-PrOH 90:10), 1.0 mL/min, λ = 220 nm, 25 °C]. [α]<sub>D</sub><sup>20</sup> -83.0 (*c* 1.01, CHCl<sub>3</sub>). Anal. Calcd for C<sub>17</sub>H<sub>25</sub>O<sub>2</sub>N: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.03; H, 9.08; N, 4.89. The

absolute configuration of compound **A** has been assigned by X-Ray diffraction analysis and resulted consistent with **2R-(6,6-dimethyl-tetrahydro-pyran-2-yl)-N-(1S)-(1-phenyl-ethyl)-acetamide**.

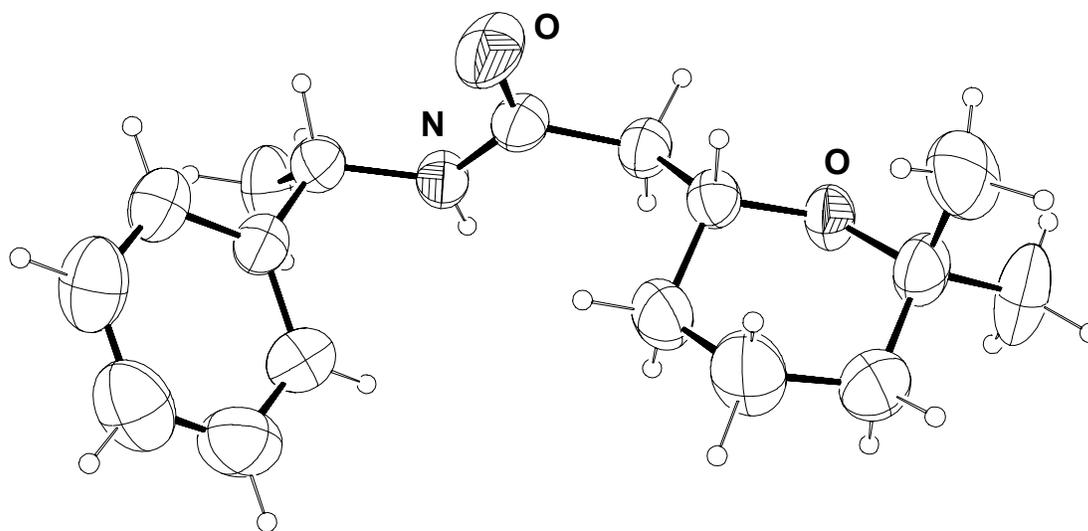
**Reaction of acid (-)-3 with (R)-Phenylethylamine.** The reaction of acid (-)-3 with (*R*)-phenylethylamine was performed according to the same protocol used for the reaction with the (*S*)-enantiomer. The diastereoisomeric amide **B** was obtained in a 85% yield as pure compound by crystallization from *n*-hexane: white solid; mp 90-92°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.25 (*m*, 6H); 5.08 (*m*, 1H); 3.85 (*m*, 1H); 2.35 (*dd*, 1H, *J* = 15.2, 8.1); 2.29 (*dd*, 1H, *J* = 15.2, 3.1); 1.69-0.85 (*m*, 6H); 1.48 (*d*, 3H, *J* = 6.9); 1.16 (*s*, 3H); 1.06 (*s*, 3H) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 171.67 (*s*); 144.28 (*s*); 129.13 (*d*); 127.73 (*d*); 126.69 (*d*); 73.27 (*s*); 68.53 (*d*); 49.13 (*d*); 44.16 (*t*); 36.49 (*t*); 32.35 (*q*); 31.82 (*t*); 22.72 (*q*); 22.30 (*q*); 20.28 (*t*) ppm. IR (KBr) ν: 3269; 2974; 2929; 2870; 1638, 1553, 1203, 1063, 868, 742 cm<sup>-1</sup>. MS (*m/z*): 275 (M<sup>+</sup>, 37), 205 (18), 120 (100), 106 (39), 105 (93), 104 (21), 95 (19), 43 (19), 41 (29). TLC: R<sub>f</sub> 0.48 (Et<sub>2</sub>O). GC: 16.37 min (50°C, 2 min then 15°C/min). HPLC: 13.35 min [Chiralcel OD-H 250 mm × 4.6 mm (*n*-hexane/*i*-PrOH 99:1), 1.0 mL/min, λ = 220 nm, 25 °C]. [α]<sub>D</sub><sup>20</sup> +18.5 (*c* 1.06, CHCl<sub>3</sub>). Anal. Calcd for C<sub>17</sub>H<sub>25</sub>O<sub>2</sub>N: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.97; H, 9.19; N, 4.93. The absolute configuration of compound **B** has been assigned by X-Ray diffraction analysis and resulted consistent with **2R-(6,6-dimethyl-tetrahydro-pyran-2-yl)-N-(1R)-(1-phenyl-ethyl)-acetamide**.

## X-ray Crystallography

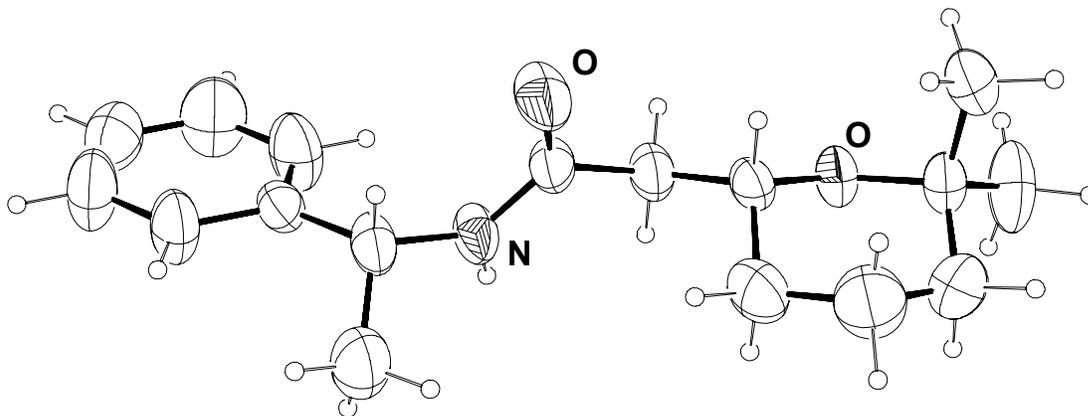
Crystals suitable for X-ray structure determination were mounted on a Bruker AXS SMART 2000 CCD diffractometer and irradiated with graphite monochromated Mo-K $\alpha$  radiation

( $\lambda = 0.71073 \text{ \AA}$ ) for data collection. The data were collected using  $0.3^\circ$  wide  $\omega$  scans, crystal-to-detector distance of 5.0 cm, and corrected for absorption empirically using the SADABS routine. Data collections nominally covered a full sphere of reciprocal space with 10 s exposure time per frame. The structure was solved by direct methods and refined on  $F^2$  by full matrix least squares calculations using the SHELXTL/PC package.<sup>a</sup>

Crystal data for **A**: orthorhombic system, space group  $P_{212121}$ ,  $a=9.4582(7) \text{ \AA}$ ,  $b=11.2046(9) \text{ \AA}$ ,  $c=15.389(1) \text{ \AA}$ ,  $V=1630.8(2) \text{ \AA}^3$ ,  $Z=4$ ,  $\rho_{\text{calc}}=1.122 \text{ Mg/m}^3$ ,  $R=0.0559$  ( $R_w=0.1142$ ) for 1813 observed reflections (170 parameters) with  $I > 2\sigma I$ . Goodness of fit = 0.975.



Crystal data for **B**: triclinic system, space group  $P1$ ,  $a=7.885(5)$  Å,  $b=9.159(6)$  Å,  $c=11.307(7)$  Å,  $\beta=72.20(2)^\circ$ ,  $V=700.5(8)$  Å<sup>3</sup>,  $Z=2$ ,  $\rho_{\text{calc}}=1.306$  Mg/m<sup>3</sup>,  $R=0.0731$  ( $R^2w=0.1657$ ) for 5401 observed reflections (362 parameters) with  $I > 2\sigma I$ . Goodness of fit = 1.009.



(a) Siemens *SHELXTLplus Version 5.1 (Windows NT version) Structure Determination Package*; Siemens Analytical X-Ray Instruments Inc.: Madison, W1, 1998.

(b) Farrugia, L. J. *J. Appl. Crystallogr.* 1997, 565. (Si riferisce al disegno ORTEP)