

## Supporting Information (Experimental Procedures and Spectra)

### ***trans*-2-(Trityl)cyclohexanol (TTC) as a Chiral Auxiliary in Permanganate-Mediated Oxidative Cyclization of 2-Methylenehept-5-enoates: Application to the Synthesis of *trans*-(+)-Linalool Oxide**

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#### Experimental details and characterization data

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## General Methods

All air/ moisture sensitive reactions were carried out under an inert atmosphere, in oven dried glassware. The solvents THF and Et<sub>2</sub>O (from Na/benzophenone) and CH<sub>2</sub>Cl<sub>2</sub> (from CaH<sub>2</sub>) were distilled before use, and where appropriate, other reagents and solvents were purified by standard techniques.<sup>1</sup> TLC was performed on aluminium-precoated plates coated with silica gel 60 with an F<sub>254</sub> indicator; visualised under UV light (254 nm) and/or by staining with KMnO<sub>4</sub> (10% aq.). Flash column chromatography was performed with Merck Kieselgel 60 silica gel.

Fourier-transform infrared (FT-IR) spectra are reported in wavenumbers (cm<sup>-1</sup>) and were recorded using a diamond ATR accessory, as solids or neat liquids.

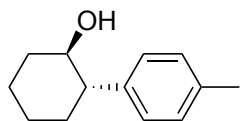
<sup>1</sup>H NMR (300, 400, 500 or 600 MHz), <sup>19</sup>F NMR (282 MHz) and <sup>13</sup>C NMR (75 or 100 MHz) spectra were recorded in CDCl<sub>3</sub> solutions. Chemical shifts are reported in δ units using CHCl<sub>3</sub> as an internal standard (δ 7.27 ppm <sup>1</sup>H, δ 77.0 ppm <sup>13</sup>C, respectively). Coupling constants (*J*) are recorded in Hz. The following abbreviations are employed for the multiplicity of the peaks: s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sept (septet), br (broad), and m (multiplet).

Melting points were obtained in an open capillary and are uncorrected. Electron impact and chemical ionisation mass spectra were obtained using a Fisons VG platform single quadropole mass spectrometer. Electrospray mass spectra were obtained using a Micromass platform mass analyser with an electrospray ion source.

Chiral HPLC analysis was carried out on Diacel Chiralcel® OJ, OD-H or Chiralpak® AD-H columns eluting with IPA/hexane in the specified ratio. Enantiomeric excess for (+)-linalool oxide were determined using a CP-Cyclodextrin-B-236-M-19 (50 m × 0.25 mm i.d.) column.

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<sup>1</sup> Armarego, W. L. F.; Perrin, D. D.; Perrin, D. R. *Purification of Laboratory Chemicals*; 4th ed.; Butterworth-Heinemann Ltd: Oxford,

**(1*R*\*,2*S*\*)-2-*p*-Tolylcyclohexanol ((±)-5a)**C<sub>13</sub>H<sub>18</sub>O

Mol. wt.: 190.28 g/mol

White powder

To stirring Mg turnings (1.00 g, 41.1 mmol) was added dropwise a solution of 4-bromotoluene (6.98 g, 40.8 mmol) in dry THF (7 mL) at a rate sufficient to maintain gentle reflux of the reaction mixture. After the addition of 4-bromotoluene was completed, and the reaction had ceased, dry THF (27 mL) was added. The solution was cooled to -30 °C (dry ice-acetone bath) and CuBr (0.258 g, 1.80 mmol) was added. The resulting mixture was stirred for 10 min then a solution of cyclohexene oxide (2.8 mL, 27.7 mmol) in dry THF (3 mL) was added dropwise. On completion, the reaction mixture was allowed to warm to 0 °C and stirred for 2 h, then quenched by adding sat. aq. (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (14 mL). The layers were separated and the organic layer was washed with sat. aq. (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (5 mL). The combined aqueous layers were extracted with ether (3x30 mL). The organic layers were combined, dried (MgSO<sub>4</sub>), filtered, and the solvent was removed *in vacuo*. The crude was recrystallized from pentane to give the title alcohol (±)-**5a** as a white powder (3.76 g, 19.8 mmol, 71%). Spectroscopic data are consistent with reported values.<sup>2</sup>

**mp** 66–68 °C; (lit. 70–72 °C).<sup>2</sup>

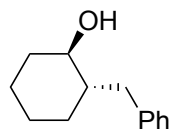
**FT-IR** (neat)  $\nu_{\text{max}}$  3450–3100, 2920, 2849, 1513, 1446, 1417 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  7.15 (4H, m), 3.64 (1H, m), 2.45 (1H, m), 2.35 (3H, s), 2.13 (1H, m), 1.94–1.72 (3H, m), 1.67–1.26 (5H, m) ppm.

**<sup>13</sup>C-NMR**  $\delta$  140.1, 136.3, 129.4, 127.7, 74.0, 52.8, 34.4, 33.4, 26.1, 25.1, 21.0 ppm.  
(75 MHz, CDCl<sub>3</sub>)

**LRMS** (ES<sup>+</sup>)  $m/z$  213 ([M+Na]<sup>+</sup>).

<sup>2</sup> Basaviah, D.; Rao, P. D. *Tetrahedron: Asymmetry*. **1994**, 5, 223–234.

**(1*R*\*,2*S*\*)-2-Benzylcyclohexanol ((±)-5b)**C<sub>13</sub>H<sub>18</sub>O

Mol. wt.: 190.28 g/mol

White powder

A solution of BnCl (1.16 mL, 10.1 mmol) in dry THF (8 mL) was added dropwise to stirred Mg turnings (1.01 g, 41.6 mmol) in dry THF (12 mL) followed by the addition of 5 drops of dibromoethane. The mixture was stirred at rt for 24 h. The resulting reddish-brown solution of BnMgCl was added dropwise to a stirred solution of cyclohexene oxide (0.7 mL, 6.92 mmol) in dry THF (15 mL) at  $-78^{\circ}\text{C}$ . Subsequently, the mixture was warmed to rt and stirred for 24 h. H<sub>2</sub>O (30 mL) was added and the reaction mixture was neutralized using aq. HCl (2M). The organic layer was separated and the aqueous layer was extracted with EtOAc ( $3 \times 20$  mL). The combined organic layers were dried (MgSO<sub>4</sub>), filtered and the solvent was removed *in vacuo*. The crude was recrystallized from *n*-pentane to afford cyclohexanol (±)-**5b** as a white powder (0.50 g, 2.63 mmol, 38%). Spectroscopic data are consistent with reported values.<sup>3</sup>

**mp** 69–71 °C; (lit. 74–75 °C).<sup>3</sup>

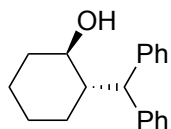
**FT-IR** (neat)  $\nu_{\text{max}}$  3349, 3025, 2923, 2854, 1603 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  7.35–7.14 (5H, m), 3.31 (1H, td,  $J = 9.8$  and 4.6 Hz), 3.18 (1H, dd,  $J = 4.0$  and 13.4 Hz), 2.37 (1H, dd,  $J = 9.2$  and 13.4 Hz), 1.98 (1H, m), 1.81–1.45 (5H, m), 1.37–1.18 (2H, m), 1.10 (1H, m), 0.92 (1H, m) ppm.

**<sup>13</sup>C-NMR**  $\delta$  140.7, 129.4, 128.1, 125.7, 74.5, 47.0, 39.0, 35.8, 30.0, 25.4, 24.9 ppm.  
(75 MHz, CDCl<sub>3</sub>)

**LRMS** (ES<sup>+</sup>)  $m/z$  213 ([M+Na]<sup>+</sup>)

<sup>3</sup> Wong, W. C.; Sun, W.; Cui, W.; Chen, Y.; Forray, C.; Vaysse, P. J. J.; Branchek, T. A.; Gluchowski, C. *J. Med. Chem.* **2000**, *43*, 1699–1704.

**(1*R*\*,2*S*\*)-2-Benzhydrylcyclohexanol ((±)-5c)**C<sub>19</sub>H<sub>22</sub>O

Mol. wt.: 266.38 g/mol

Pale yellow viscous oil

To a stirred solution of diphenylmethane (4.0 mL, 24.0 mmol) in dry THF (50 mL) at  $-78^{\circ}\text{C}$ , was added dropwise a solution of *n*-BuLi (9.7 mL of 2.45M in hexane, 23.7 mmol) producing an orange solution. The solution was warmed to rt and stirred for 4 h, then the resulting blood-red solution of diphenylmethyl anion was re-cooled to  $-78^{\circ}\text{C}$ . Cyclohexene oxide (6.1 mL, 60.3 mmol) was added dropwise and the reaction mixture was warmed to rt and stirred for 3 h. The reaction was quenched by addition of H<sub>2</sub>O (60 mL) and the aqueous layer was extracted with Et<sub>2</sub>O (3 × 50 mL). The organic layer was washed with brine (100 mL) and dried (Na<sub>2</sub>SO<sub>4</sub>). The crude was purified by column chromatography on SiO<sub>2</sub> (Et<sub>2</sub>O/hexane, 5→50%) to afford the cyclohexanol (±)-**5c** as a pale yellow viscous oil (5.38 g, 20.2 mmol, 84%). This compound was reported previously although no characterization data were provided.<sup>4</sup>

**FT-IR** (neat)  $\nu_{\text{max}}$  3334, 3025, 2929, 2856, 1599 cm<sup>-1</sup>.

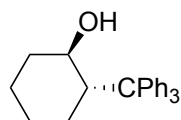
**<sup>1</sup>H-NMR**  $\delta$  7.34–7.13 (10H, m), 4.21 (1H, d,  $J = 7.9$  Hz), 3.44 (1H, td,  $J = 8.4$  and 4.0 Hz), 2.31 (1H, m), 1.90 (1H, m), 1.82–1.64 (2H, m), 1.58 (1H, m), 1.42–1.18 (3H, m), 1.39 (1H, d,  $J = 4.0$  Hz), 0.95 (1H, m) ppm.

**<sup>13</sup>C-NMR**  $\delta$  144.1, 143.1, 129.0, 128.6, 128.3, 128.1, 126.3, 126.1, 72.5, 53.5, 47.3, 34.2, 27.6, 24.6, 23.9 ppm.

**LRMS** (ES<sup>+</sup>)  $m/z$  289 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>)  $m/z$  For C<sub>38</sub>H<sub>45</sub>O<sub>2</sub><sup>+</sup> ([2M+H]<sup>+</sup>), calculated 533.3414, found: 533.3420.

<sup>4</sup> Whitesell, J. K.; Lawrence, R. M.; Chen, H. H., *J. Org. Chem.* **1986**, *51*, 4779–4784.

**(1*R*\*,2*S*\*)-2-Tritylcyclohexanol ((±)-5d)**C<sub>25</sub>H<sub>26</sub>O

Mol. wt.: 342.47 g/mol

White powder

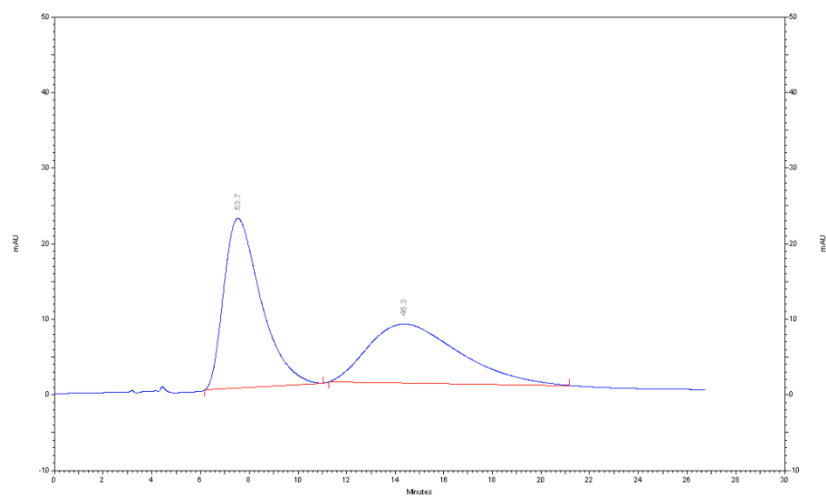
The reaction was performed using an adaptation of the procedure described by Peddle.<sup>5</sup> To a solution of triphenylmethane (45.18 g, 184.9 mmol)<sup>6</sup> in THF (200 mL) at  $-78\text{ }^{\circ}\text{C}$  under N<sub>2</sub> was added *n*-BuLi in (73.2 mL of a 2.5M solution in hexanes, 183.1 mmol) using a pressure equalizing dropping funnel over 30 min whilst maintaining an internal temperature below  $-70\text{ }^{\circ}\text{C}$ . The solution was stirred for 30 min, allowed to warm to rt and stirred for a further 1.5 h during which time the solution became dark red. The reaction mixture was cooled to  $0\text{ }^{\circ}\text{C}$  and cyclohexene oxide (47.2 mL, 457.7 mmol) was added using a pressure equalizing dropping funnel over 30 min. The reaction was then stirred for 16 h at rt turning yellow in color. The reaction was quenched with H<sub>2</sub>O (100 mL) and the phases were separated. The aqueous layer was extracted with EtOAc (3 × 80 mL). The organic layers were combined, dried (MgSO<sub>4</sub>) and concentrated *in vacuo* affording a viscous yellow oil. The oil was triturated from *n*-hexane (150 mL) precipitating the title compound as a white solid that was isolated by filtration under suction. The product was used without any further purification (35.02 g, 102.3 mmol, 56% yield). An analytical sample was obtained by recrystallization from EtOH. Physical and spectroscopic data were consistent with reported literature values. This compound exhibited broadening of some signals in its NMR spectra due to restricted rotation.

<b>mp</b>	171–178 °C (EtOH); (lit. 168–170 °C). <sup>5</sup>
<b>FT-IR</b> (neat) $\nu_{\text{max}}$	3054, 2940, 2919, 2846, 1594, 1491, 1446 cm <sup>-1</sup> .
<b><sup>1</sup>H-NMR</b> (400 MHz, CDCl <sub>3</sub> )	$\delta$ 7.87–6.74 (15H, m), 3.28 (1H, ddd, $J$ = 11.1, 9.9 and 2.0 Hz), 3.10 (1H, tt, $J$ = 9.9 and 4.1 Hz), 2.05 (1H, d, $J$ = 13.7 Hz), 1.93 (1H, m), 1.72 (1H, m), 1.68–1.50 (2H, m), 1.47 (1H, d, $J$ = 4.1 Hz), 1.41 (1H, qt, $J$ = 13.1 and 3.5 Hz), 1.09 (1H, qt, $J$ = 13.1, 4.1 Hz), 0.50 (1H, tdd, $J$ = 13.1, 11.1 and 3.1) ppm.
<b><sup>13</sup>C-NMR</b> (100 MHz, CDCl <sub>3</sub> )	$\delta$ 129.4 br, 127.6, 125.7, 73.6, 60.7, 48.8, 37.0, 28.9, 26.2, 25.3, (quaternary aromatic carbon signal was not observed) ppm.
<b>LRMS</b> (ES <sup>+</sup> ) $m/z$	365 ([M+Na] <sup>+</sup> ).
<b>HRMS</b> (ES <sup>+</sup> ) $m/z$	For C <sub>50</sub> H <sub>53</sub> O <sub>2</sub> <sup>+</sup> ([2M+H] <sup>+</sup> ), calculated 685.4040, found 685.4040.
<b>HPLC</b>	Daicel Chiralcel® OJ - ( <i>eluent</i> : IPA/ <i>n</i> -hexane 1:19) - 1 mL/min Retention times: 7.5 &

<sup>5</sup> Peddle, G. J. D., *J. Organometal. Chem.* **1968**, *14*, 115–121.

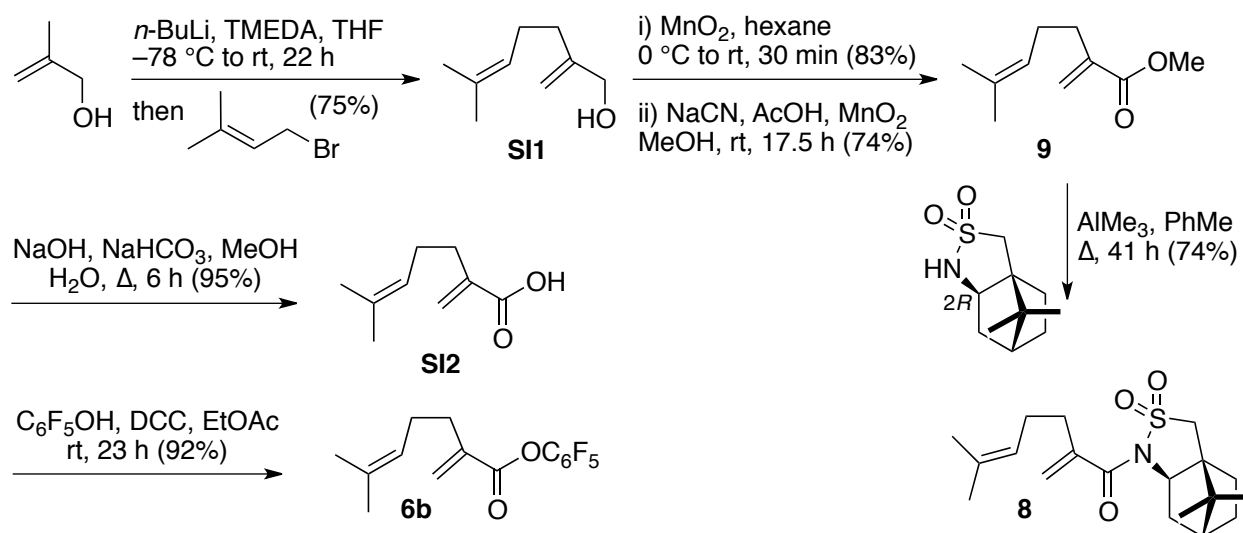
<sup>6</sup> Triphenylmethane was recrystallized from EtOH.

15.0 min.

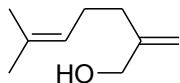


## Dienoate Synthesis

*N*-(6-Methyl-2-methylenehept-5-enoyl)-(2*R*)-camphor-10,2-sultam (**8**), 6-methyl-2-methylenehept-5-enoic acid, PFP ester **6b** and methyl 6-methyl-2-methylenehept-5-enoate (**9**) were synthesized following the route outlined in scheme SI 1.



**Scheme SI 1** Synthesis of 6-methyl-2-methylenehept-5-enoic acid derivatives

**6-Methyl-2-methylenehept-5-en-1-ol (SI1)**C<sub>9</sub>H<sub>16</sub>O

Mol. wt.: 140.22 g/mol

Pale yellow oil

Following the method reported by Taber *et al.*,<sup>7,8</sup> TMEDA (45.1 mL, 300.8 mmol) was added dropwise to a solution of *n*-BuLi (130 mL of 2.35M in hexane, 305.5 mmol) at  $-78^{\circ}\text{C}$  resulting in a white precipitate. After stirring for 20 min, methallyl alcohol (14.6 mL, 173.5 mmol) was added dropwise followed by Et<sub>2</sub>O (120 mL). The cooling bath was removed and stirring was continued for 22 h at rt. A dark orange mass was observed in the reaction mixture. Subsequently, the reaction mixture was chilled to  $-78^{\circ}\text{C}$  and 3,3-dimethylallyl bromide (8.5 mL, 73.6 mmol) in distilled Et<sub>2</sub>O (15 mL) was added. The cooling bath was removed and the resultant yellow mixture was allowed to warm to rt and stirred for 1 h. The reaction was chilled to  $0^{\circ}\text{C}$  and quenched with 10% aq. HCl (325 mL). The aqueous layer was extracted with Et<sub>2</sub>O (5×150 mL). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to afford a dark yellow oil (15.34 g). Purification by column chromatography on SiO<sub>2</sub> (ether/hexane, 5→20%) afforded the title alcohol as pale yellow oil (7.72 g, 55.1 mmol, 75%).

**FT-IR** (neat)  $\nu_{\text{max}}$  3600–3150, 2967, 2915, 2856 cm<sup>-1</sup>.

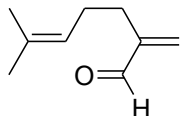
**<sup>1</sup>H-NMR**  $\delta$  5.14 (1H, t.septet,  $J = 6.7$  and  $1.5$  Hz), 5.04 (1H, m), 4.90 (1H, sextet,  $J = 1.3$  Hz), 4.09 (2H, d,  $J = 6.0$  Hz), 2.24–2.05 (4H, m) 1.7 (3H, d,  $J = 1.1$  Hz), 1.64 (3H, s), 1.39 (1H, t,  $J = 6.0$  Hz).

**<sup>13</sup>C-NMR**  $\delta$  149.0, 140.0, 123.9, 109.3, 66.0, 33.1, 26.5, 25.6, 17.7.  
(75 MHz, CDCl<sub>3</sub>)

**LRMS** (EI)  $m/z$  140 (5%, [M]<sup>+</sup>), 107 (10%), 79 (13%), 69 (74%).

<sup>7</sup> Taber, D. F.; Louey, J. P., *Tetrahedron* **1995**, *51*, 4495–4506.

<sup>8</sup> The synthesis of dienol **SI1** was reported previously, but without experimental details or characterization data: Takano, S.; Morimoto, M.; Satoh, S. Ogasawara, K., *Chem. Lett.* **1984**, *13*, 1261–1262.

**6-Methyl-2-methylenehept-5-enal**C<sub>9</sub>H<sub>14</sub>O

Mol. wt.: 138.21 g/mol

Colorless oil

A mixture of allylic alcohol **SI1** (6.0 g, 42.8 mmol) and activated MnO<sub>2</sub> (74.4 g, 728 mmol) in *n*-hexane (450 mL) at 0 °C, was stirred for 1 h. Then, the ice bath was removed and stirring was continued for a further 30 min at room temperature. Filtration through celite and concentration *in vacuo* afforded **6-methyl-2-methylenehept-5-enal** as a colourless oil (4.90 g, 35.4 mmol, 83%). The crude material was used in the next step without further purification. Physical and spectroscopic data were consistent with reported values.<sup>9</sup>

**FT-IR** (neat)  $\nu_{\max}$  2967, 2917, 2856, 1692 cm<sup>-1</sup>.

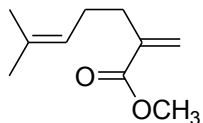
**<sup>1</sup>H-NMR**  $\delta$  9.55 (1H, s), 6.25 (1H, q,  $J = 1.3$  Hz), 5.99 (1H, d,  $J = 0.7$  Hz), 5.09 (300 MHz, CDCl<sub>3</sub>) (1H, t, septet,  $J = 7.0$  and 1.5 Hz), 2.29 (2H, t,  $J = 6.6$  Hz), 2.15 (2H, q,  $J = 7.5$  Hz), 1.69 (3H, d,  $J = 1.1$  Hz), 1.61 (3H, s).

**<sup>13</sup>C-NMR**  $\delta$  194.7, 149.9, 134.0, 132.5, 123.2, 28.0, 26.2, 25.6, 17.7.  
(75 MHz, CDCl<sub>3</sub>)

**LRMS** (EI)  $m/z$  138 ([M]<sup>+</sup>).

**HRMS** (EI)  $m/z$  For C<sub>9</sub>H<sub>14</sub>O<sup>+</sup> ([M]<sup>+</sup>), calculated 138.1045, found: 138.1042.

<sup>9</sup> Krügener, S.; Schaper, C.; Krings, U.; Berger, R. G., *Bioresource Technol.* **2009**, *100*, 2855–2860.

**Methyl 6-methyl-2-methylenehept-5-enoate (9)** $C_{10}H_{16}O_2$ 

Mol. wt.: 168.23 g/mol

Yellow oil (crude)

To a mixture prepared from powdered NaCN (2.98 g, 60.8 mmol)<sup>10</sup> and absolute AcOH (1.0 mL, 17.5 mmol) in dry MeOH (100 mL) at rt, was added 6-methyl-2-methylenehept-5-enal (1.55 g, 11.2 mmol) in dry MeOH (60 mL) over 30 min. After 60 min, activated MnO<sub>2</sub> powder (20.94 g, 240.9 mmol) was added, and the mixture stirred for 17.5 h. The solution was filtered through celite and MeOH was removed *in vacuo*. The organic material was extracted into ether (3x50 mL), washed with sat. aq. NaHCO<sub>3</sub> (50 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to afford the crude methyl ester **9** as a yellow oil (1.40 g, 8.32 mmol, 74%), which was used without further purification in subsequent reactions. Physical and spectroscopic data are consistent with reported values.<sup>11</sup>

**FT-IR** (neat)  $\nu_{\max}$  2950, 2923, 2858, 1721, 1631 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  6.14 (1H, s with fine coupling), 5.53 (1H, q,  $J = 1.5$  Hz), 5.12 (1H, (300 MHz, CDCl<sub>3</sub>) t.septet,  $J = 7.1$  and 1.3 Hz), 3.76 (3H, s), 2.33 (2H, t,  $J = 7.1$  Hz), 2.16 (2H, q,  $J = 7.1$  Hz), 1.69 (3H, d,  $J = 1.1$  Hz), 1.60 (3H, s).

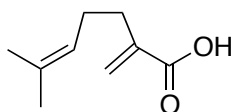
**<sup>13</sup>C-NMR**  $\delta$  167.8, 140.4, 132.3, 124.8, 123.3, 51.7, 32.1, 26.9, 25.6, 17.7. (75 MHz, CDCl<sub>3</sub>)

**LRMS** (EI)  $m/z$  168 (12%, [M]<sup>++</sup>), 69 (100%).

**HRMS** (EI)  $m/z$  For C<sub>10</sub>H<sub>16</sub>O<sub>2</sub><sup>++</sup> ([M]<sup>++</sup>), calculated 168.1150, found: 168.1147.

<sup>10</sup> Caution! Sodium cyanide is very toxic, and can liberate HCN upon exposure to acids.

<sup>11</sup> Gilbert, B. C.; Lindsay, C. I.; McGrail, P. T.; Parsons, A. F.; Whittaker, D. T.E., *Synth. Commun.*, **1999**, 29, 2711–2718.

**6-Methyl-2-methylenehept-5-enoic acid (SI2)**C<sub>9</sub>H<sub>14</sub>O<sub>2</sub>

Mol. wt.: 154.21 g/mol

Yellow oil (crude)

To a solution of methyl ester **9** (2.34 g, 13.9 mmol) in MeOH (30 mL) at rt, was added a solution of NaOH (3.62 mg, 90.4 mmol) and NaHCO<sub>3</sub> (619 mg, 7.37 mmol) in water (40 mL). The resulting mixture was heated a reflux for 9 h. The reaction was cooled to 0 °C, washed with hexane (30 mL) and carefully acidified with HCl aq. (30 mL of 2M), while maintaining the temperature at 0 °C. The organic phase was separated and the aqueous phase was extracted with Et<sub>2</sub>O (4 × 50 mL). The combined organic phases were dried (MgSO<sub>4</sub>) and concentrated *in vacuo* to afford the title dienoic acid **SI2** as a yellow oil (2.04 g, 13.2 mmol, 95%). The crude material was used in the next step without purification. Physical and spectroscopic data are consistent with reported values.<sup>12</sup>

**FT-IR** (neat)  $\nu_{\max}$  3500–2500, 2966, 2915, 2857, 1691, 1627, 1439, 1302, 1221, 946 cm<sup>-1</sup>.

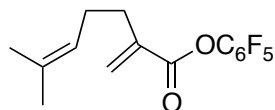
**<sup>1</sup>H-NMR**  $\delta$  6.30 (1H, d,  $J$  = 1.3 Hz), 5.65 (1H, q,  $J$  = 1.3 Hz), 5.12 (1H, tsept,  $J$  = 7.0, 1.0 Hz), (300 MHz, CDCl<sub>3</sub>) 2.36–2.31 (2H, m), 2.20 (2H, dt,  $J$  = 7.0, 7.0 Hz), 1.70 (3H, d,  $J$  = 1.0 Hz), 1.61 (3H, s) ppm.

**<sup>13</sup>C-NMR**  $\delta$  172.6, 139.8, 132.5, 127.1, 123.2, 31.6, 26.9, 25.6, 17.7 ppm. (75 MHz, CDCl<sub>3</sub>)

**LRMS** (ES<sup>-</sup>)  $m/z$  153 ([M–H]<sup>-</sup>).

**HRMS** (ES<sup>+</sup>)  $m/z$  For C<sub>9</sub>H<sub>13</sub>O<sub>2</sub><sup>-</sup> ([M–H]<sup>-</sup>), calculated 153.0921, found 153.0918.

<sup>12</sup> Yajima, A.; Urao, S.; Katsuta, R.; Nukada T., *Eur. J. Org. Chem.* **2014**, 731–738.

**Perfluorophenyl 6-methyl-2-methylenehept-5-enoate (6b)**C<sub>15</sub>H<sub>13</sub>F<sub>5</sub>O<sub>2</sub>

Mol. wt.: 320.25 g/mol

Pale yellow oil

To a solution of 6-methyl-2-methylenehept-5-enoic acid (**SI2**, 2.00 g, 13.0 mmol) and pentafluorophenol (2.77 g, 15.0 mmol) in EtOAc (60 mL) at rt, was slowly added a solution of DCC (3.07 g, 14.9 mmol) in EtOAc (90 mL). After stirring for 7.5 h, the mixture was diluted in hexane (50 mL) and white solids were removed by filtration. The organic layer was washed with sat. aq. NaHCO<sub>3</sub> (3 × 50 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* afforded a pale yellow oil (4.19 g). Purification by column chromatography on SiO<sub>2</sub> (hexane) afforded the title PFP ester **6b** as a pale yellow oil (3.84 g, 12.0 mmol, 92%).

**FT-IR** (neat)  $\nu_{\max}$  2967, 2928, 2857, 1758, 1516, 1072, 994 cm<sup>-1</sup>.

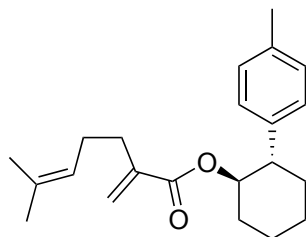
**<sup>1</sup>H-NMR**  $\delta$  6.48 (1H, s), 5.87 (1H, s), 5.13 (1H, t,  $J = 7.1$  Hz), 2.46 (2H, t,  $J = 7.1$  Hz), 2.26 (2H, q,  $J = 7.1$  Hz), 1.71 (3H, s), 1.62 (3H, s) ppm.

**<sup>13</sup>C-NMR**  $\delta$  162.96, 137.78, 133.08, 129.40, 122.62, 32.09, 26.79, 25.62, 17.65 ppm. (Aromatic carbon signals were not observed).

**<sup>19</sup>F NMR**  $\delta$  -152.94 (2F, d,  $J = 20.3$  Hz), -158.55 (1F, t,  $J = 21.4$  Hz), -162.80 (2F, dd,  $J = 21.4$ , 20.3 Hz) ppm.

**LRMS** (EI)  $m/z$  320 (5%, [M]<sup>++</sup>), 184 (40%), 137 (100%).

**HRMS** (EI)  $m/z$  For C<sub>15</sub>H<sub>13</sub>F<sub>5</sub>O<sub>2</sub><sup>++</sup> ([M]<sup>++</sup>), calculated 320.0836, found 320.0839.

**(1*R*\*,2*S*\*)-2-*p*-Tolylcyclohexyl 6-methyl-2-methylenehept-5-enoate ((±)-7a)**C<sub>22</sub>H<sub>30</sub>O<sub>2</sub>

Mol. wt.: 326.47 g/mol

Colorless oil

a) Preparation of **6-methyl-2-methylenehept-5-enoyl chloride (6a)**: To a stirred solution of 6-methyl-2-methylenehept-5-enoic acid (**SI2**, 160 mg, 1.04 mmol) and DMF (81  $\mu$ L, 1.05 mmol) in *n*-hexane (30 mL) at rt, was added dropwise oxalyl chloride (440  $\mu$ L, 5.13 mmol). A white precipitate formed immediately and the mixture was stirred at rt for 1 h. Then, the mixture was filtered and the solvent and excess oxalyl chloride were removed *in vacuo* to give the acid chloride **6a** as a yellow oil (179 mg, 1.04 mmol, 100%).

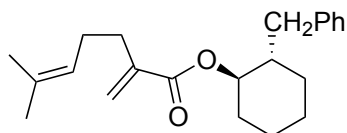
b) To a stirred solution of the cyclohexanol (±)-**5a** (210 mg, 1.10 mmol) in dry THF (16 mL) was added NaHMDS (1.2 mL of a 1.0 M solution in THF, 1.2 mmol) at −35 °C. The solution was allowed to warm to −25 °C over 30 min whereupon a solution of the acid chloride **6a** (179 mg, 1.04 mmol) in dry THF (11 mL) was added dropwise. The mixture was stirred for 3 h at rt, then the reaction was diluted with Et<sub>2</sub>O (35 mL) and quenched with sat. aq. NH<sub>4</sub>Cl (75 mL). The organic layer was separated and washed with sat. aq. NaHCO<sub>3</sub> (3  $\times$  25 mL). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and the solvent was removed *in vacuo*. The crude was purified by column chromatography on SiO<sub>2</sub> (Et<sub>2</sub>O/hexane, 5 $\rightarrow$ 10%) to afford the ester (±)-**7a** as a colorless oil (194 mg, 0.594 mmol, 57%).

**FT-IR** (neat)  $\nu_{\max}$  2929, 2857, 1710, 1631 cm<sup>−1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  7.13–7.06 (4H, m), 5.86 (1H, d, *J* = 1.5 Hz), 5.30 (1H, q, *J* = 1.5 Hz), 4.99 (2H, m), (300 MHz, CDCl<sub>3</sub>) 2.70 (1H, ddd, *J* = 14.5, 10.8, 3.7 Hz), 2.29 (3H, s), 2.21 (1H, m), 2.13 (2H, t, *J* = 7.5 Hz), 1.99–1.73 (4H, m), 1.67 (3H, d, *J* = 1.1 Hz), 1.69–1.28 (5H, m), 1.51 (3H, s) ppm.

**<sup>13</sup>C-NMR**  $\delta$  166.6, 140.7, 140.2, 135.7, 132.0, 129.0, 127.3, 124.0, 123.5, 76.5, 49.4, 34.0, 32.3, (75 MHz, CDCl<sub>3</sub>) 32.0, 26.8, 25.9, 25.6, 24.8, 21.0, 17.6 ppm.

**LRMS** (ES<sup>+</sup>) *m/z* 349 ([M+Na]<sup>+</sup>).

**(1*R*\*,2*S*\*)-2-Benzylcyclohexyl 6-methyl-2-methylenehept-5-enoate ((±)-7b)**C<sub>22</sub>H<sub>30</sub>O<sub>2</sub>

Mol. wt.: 326.47 g/mol

Colorless oil

Following the procedure for the preparation of diene (±)-**7a**, reaction of the freshly prepared acid chloride **6a** (112 mg, 0.649 mmol) with the cyclohexanol (±)-**5b** (129 mg, 0.678 mmol) in dry THF (15 mL) for 3.5 h afforded the title diene (±)-**7b** as a colorless oil (119 mg, 0.365 mmol, 56%).

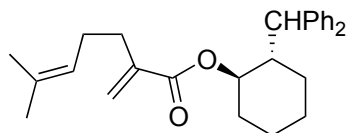
**FT-IR** (neat)  $\nu_{\text{max}}$  3930, 2857, 1711, 1630 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  7.28–7.05 (5H, m), 6.12 (1H, d,  $J$  = 1.5 Hz), 5.48 (1H, q,  $J$  = 1.5 Hz), 5.11 (1H, br t,  $J$  = 7.0 Hz), 4.62 (1H, td,  $J$  = 10.0, 4.4 Hz), 2.91 (1H, dd,  $J$  = 3.9, 13.5 Hz), 2.37–2.09 (5H, m), 2.05 (1H, m), 1.87–1.59 (5H, m), 1.67 (3H, s), 1.58 (3H, s), 1.43–1.25 (2H, m), 1.10 (1H, m) ppm.

**<sup>13</sup>C-NMR**  $\delta$  166.9, 140.8, 140.3, 132.3, 129.2, 128.2, 125.8, 124.5, 123.4, 76.9, 43.9, 38.8, 32.1, 31.7, 29.9, 27.1, 25.6, 25.0, 24.5, 17.7 ppm.

**LRMS** (ES<sup>+</sup>)  $m/z$  349 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>)  $m/z$  For C<sub>22</sub>H<sub>30</sub>O<sub>2</sub>Na<sup>+</sup> ([M+Na]<sup>+</sup>), calculated 349.2138, found 349.2143.

**(1*R*\*,2*S*\*)-2-Benzhydrylcyclohexyl 6-methyl-2-methylenehept-5-enoate ((±)-7c)**C<sub>28</sub>H<sub>34</sub>O<sub>2</sub>

Mol. wt.: 402.57 g/mol

Colorless viscous oil

Following the procedure for the preparation of diene (±)-**7a**, reaction of the freshly prepared acid chloride **6a** (143 mg, 0.828 mmol) with the cyclohexanol (±)-**5c** (460 mg, 1.72 mmol) in dry THF (27 mL) for 4 h afforded the title diene (±)-**7c** as a colorless, highly viscous oil (144 mg, 0.358 mmol, 43%).

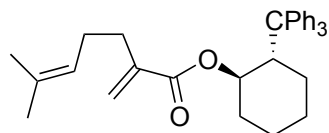
**FT-IR** (neat)  $\nu_{\text{max}}$  3026, 2933, 2860, 1710, 1630 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  7.38–7.15 (10H, m), 6.00 (1H, d,  $J$  = 0.9 Hz), 5.43 (1H, d,  $J$  = 0.9 Hz), 5.10 (1H, t,  $J$  = 6.8 Hz), 4.75 (1H, td,  $J$  = 7.1, 3.3 Hz), 4.15 (1H, d,  $J$  = 9.0 Hz), 2.78 (1H, m), 2.25 (2H, t,  $J$  = 7.7 Hz), 2.20–2.07 (2H, m), 1.95 (1H, m), 1.83–1.25 (6H, m), 1.70 (3H, s), 1.61 (3H, s), 1.12 (1H, m) ppm.

**<sup>13</sup>C-NMR**  $\delta$  166.4, 143.5, 143.1, 140.7, 132.1, 128.7, 128.5, 128.4, 128.0, 126.2, 126.1, 124.4, 123.0, 74.3, 52.2, 42.8, 31.9, 29.3, 27.0, 26.3, 25.7, 23.0, 22.9, 17.7 ppm.

**LRMS** (ES<sup>+</sup>)  $m/z$  425 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>)  $m/z$  For C<sub>28</sub>H<sub>34</sub>O<sub>2</sub><sup>+</sup> ([M+H]<sup>+</sup>), calculated 403.2632, found 403.2637.

**(1*R*\*,2*S*\*)-2-Tritylcyclohexyl 6-methyl-2-methylenehept-5-enoate ((±)-7d)**C<sub>34</sub>H<sub>38</sub>O<sub>2</sub>

Mol. wt.: 478.66 g/mol

Colorless viscous oil

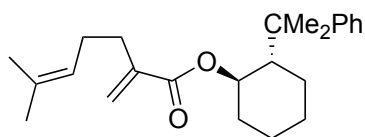
Following the procedure for the preparation of diene (±)-**7a**, reaction of the freshly prepared acid chloride **6a** (112 mg, 0.649 mmol) with the cyclohexanol (±)-**5d** (467 mg, 1.36 mmol) in dry THF (27 mL) for 1.5 h afforded the title diene (±)-**7d** as a colorless, highly viscous oil (93 mg, 0.194 mmol, 30%).

**FT-IR** (neat)  $\nu_{\text{max}}$  3032, 2925, 2857, 1708, 1630 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  7.70–6.90 (15H, m), 5.20 (1H, d,  $J$  = 1.3 Hz), 5.14 (1H, q,  $J$  = 1.3 Hz), 5.05 (1H, m), (300 MHz, CDCl<sub>3</sub>) 4.00 (1H, td,  $J$  = 10.0, 3.8 Hz), 3.60 (1H, td,  $J$  = 10.0, 2.3 Hz), 2.25–2.11 (2H, m), 2.10–1.90 (5H, m), 1.73 (3H, s), 1.85–1.34 (4H, m), 1.61 (3H, s), 0.88 (1H, m) ppm.

**<sup>13</sup>C-NMR**  $\delta$  166.4, 148.5, 140.4, 131.9, 128.9, 127.4, 125.1, 124.3, 123.6, 76.3, 60.7, 46.5, 33.3, (75 MHz, CDCl<sub>3</sub>) 31.9, 29.0, 26.9, 26.3, 25.7, 24.9, 17.7 ppm.

**LRMS** (ES<sup>+</sup>)  $m/z$  501 ([M+Na]<sup>+</sup>).

**(1*R*,2*S*)-2-(2-Phenylpropan-2-yl)cyclohexyl-6-methyl-2-methylenehept-5-enoate ((-)-7e)**

C<sub>24</sub>H<sub>34</sub>O<sub>2</sub>  
 Mol. wt.: 354.53 g/mol  
 Yellow oil

To a solution of (-)-TCC ((-)-**5e**, *ee*: 97%) (287 mg, 1.31 mmol) in dry THF (19 mL) at -20 °C, was added NaHMDS (1.4 mL, 1.0 M in THF, 1.40 mmol). The mixture was allowed to warm to -5 °C over 40 min, then a solution of the PFP ester **6b** (400 mg, 1.25 mmol) in dry THF (4 mL) was added dropwise at -5 °C and the mixture was stirred for 1.5 h, during which time the temperature rose to 5 °C. Et<sub>2</sub>O (10 mL). Sat. aq. NH<sub>4</sub>Cl (5 mL) and H<sub>2</sub>O (5 mL) were added to the mixture. The organic phase was separated, washed with NaHCO<sub>3</sub> (2x25 mL), dried (MgSO<sub>4</sub>) and concentrated in *vacuo* to afford a yellow oil. Purification by column chromatography on SiO<sub>2</sub> (EtOAc/petroleum ether, 5%→10%) afforded the title compound (-)-**7e** as a yellow oil (269 mg, 0.759 mmol, 58%).

[α]<sub>D</sub><sup>22</sup> -17.0 (*c* 1.64, CHCl<sub>3</sub>)

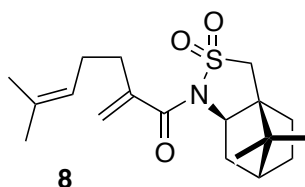
FT-IR (neat) ν<sub>max</sub> 2969, 2927, 2859, 1707 cm<sup>-1</sup>.

<sup>1</sup>H-NMR δ 7.30–7.22 (4H, m), 7.11 (1H, tt, *J* = 6.6, 2.2 Hz), 5.69 (1H, d, *J* = 1.6 Hz), 5.30 (1H, d, *J* = 1.6 Hz), 5.08 (1H, m), 4.89 (1H, td, *J* = 10.3, 4.4 Hz), 2.13–1.92 (6H, m), 1.70 (3H, s), 1.70–1.62 (4H, m), 1.61 (3H, s), 1.32 (3H, s), 1.23 (3H, s), 1.17–0.92 (2H, m) ppm.

<sup>13</sup>C-NMR δ 166.2, 151.4, 140.5, 132.0, 128.0, 125.4, 125.0, 124.4, 123.6, 75.0, 50.96, 40.0, 33.3, 31.6, 27.3, 26.9, 26.8, 26.4, 26.0, 25.7, 24.7, 17.7 ppm.

LRMS (ES<sup>+</sup>) *m/z* 377 ([M+Na]<sup>+</sup>).

HRMS (ES<sup>+</sup>) *m/z* For C<sub>24</sub>H<sub>34</sub>O<sub>2</sub>Na<sup>+</sup> ([M+Na]<sup>+</sup>), calculated 377.2451, found 377.2457.

***N*-(6-Methyl-2-methylene-hept-5-enoyl)-(2*R*)-camphor-10,2-sultam ((-)-8)**C<sub>19</sub>H<sub>29</sub>NO<sub>3</sub>S

Mol. wt.: 351.50 g/mol

White foam

To a solution of (2*R*)-10,2-camphorsultam (799 mg, 3.71 mmol) in freshly distilled toluene (18 mL) was added dropwise a solution of Me<sub>3</sub>Al (1.86 mL of 2.0M in hexane, 3.72 mmol) at rt. After stirring for 15 min, a solution of methyl ester **9** (500 mg, 2.97 mmol) in toluene (2 mL) was added and the resulting mixture was heated under reflux for 41 h. CH<sub>2</sub>Cl<sub>2</sub> (30 mL), H<sub>2</sub>O (10 mL) and sat. aq. Rochelle's salt (10 mL) were added and the mixture stirred for an additional 1 h. The organic phase was separated, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to afford a yellow oil (835 mg). Purification by column chromatography on SiO<sub>2</sub> (EtOAc/hexane, 10%) afforded the dienoyl sultam ((-)-**8**) as a white foam (774 mg, 2.20 mmol, 74%).

[α]<sub>D</sub><sup>23</sup> -39.2 (*c* 0.22, CHCl<sub>3</sub>).**FT-IR** (neat) ν<sub>max</sub> 2961, 2919, 2882, 1679, 1334, 1194, 1132, 1063, 976 cm<sup>-1</sup>.

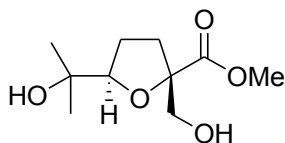
**<sup>1</sup>H-NMR** δ 5.75 (1H, s), 5.64 (1H, s), 5.14 (1H, t, *J* = 6.8 Hz), 4.05 (1H, dd, *J* = 7.5, 5.0 Hz), 3.51 (1H, d, *J* = 13.6 Hz), 3.40 (1H, d, *J* = 13.6 Hz), 2.38–2.31 (2H, m), 2.20 (2H, q, *J* = 7.0 Hz), 2.06–1.90 (5H, m), 1.68 (3H, s), 1.62 (3H, s), 1.47–1.33 (2H, m), 1.23 (3H, s), 1.00 (3H, s) ppm.

**<sup>13</sup>C-NMR** δ 171.1, 143.2, 132.2, 123.6, 123.4, 65.5, 53.6, 47.9, 47.7, 45.2, 38.4, 33.2, 32.6, 26.5, 26.3, 25.6, 21.2, 19.9, 17.6 ppm.

**LRMS** (ES<sup>+</sup>) *m/z* 374 ([M+Na]<sup>+</sup>).**HRMS** (ES<sup>+</sup>) *m/z* For C<sub>19</sub>H<sub>30</sub>NO<sub>3</sub>S<sup>+</sup> ([M+H]<sup>+</sup>), calculated 352.1941, found 352.1937.

## Permanganate-mediated oxidative cyclization

### (2*S*\*,5*R*\*)-Methyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate ((±)-10)



C<sub>10</sub>H<sub>18</sub>O<sub>5</sub>

Mol. wt.: 218.25 g/mol

Pale yellow oil

To a vigorously stirred mixture of diene ester **9** (1.20 g, 7.13 mmol) and phosphate buffer (14 mL) in acetone (120 mL) at  $-35\text{ }^{\circ}\text{C}$  was added a solution of NaMnO<sub>4</sub> (24.6 mL, 0.4 M aq., 9.84 mmol) containing AcOH (1.23 mL, 21.4 mmol). The purple mixture was stirred rapidly for 1 h, during which time the temperature of the acetone cooling bath increased to  $-5\text{ }^{\circ}\text{C}$  and the reaction mixture had turned dark brown. The reaction was quenched with sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>5</sub> (40 mL) to dissolve all of the precipitated manganese salt and then repeatedly extracted using CH<sub>2</sub>Cl<sub>2</sub> (4x60 mL). The organic extracts were combined, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to afford a yellow oil (1.55 g). Purification by column chromatography on SiO<sub>2</sub> (EtOAc/hexane, 20→60%) afforded the title racemic THF diol (±)-**10** as a pale yellow oil (1.43 g, 6.55 mmol, 92%).

**FT-IR**  $\nu_{\text{max}}$  (neat) 3383, 2971, 2877, 1728, 1452, 1103, 1051 cm<sup>-1</sup>.

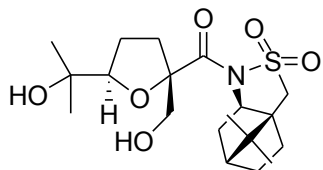
**<sup>1</sup>H NMR**  $\delta$  4.05 (1H, t,  $J = 7.3\text{ Hz}$ ), 3.87 (1H, d,  $J = 11.3\text{ Hz}$ ), 3.77 (1H, d,  $J = 11.3\text{ Hz}$ ), 3.75 (300 MHz, CDCl<sub>3</sub>) (3H, s), 2.97 (2H, br), 2.21–2.00 (2H, m), 1.99–1.86 (2H, m), 1.30 (3H, s), 1.14 (3H, s) ppm.

**<sup>13</sup>C NMR**  $\delta$  174.5, 87.6, 86.8, 71.5, 66.1, 52.3, 32.0, 27.4, 26.0, 25.0 ppm.  
(75 MHz, CDCl<sub>3</sub>)

**LRMS** (ES<sup>+</sup>)  $m/z$  241 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>)  $m/z$  For C<sub>10</sub>H<sub>18</sub>O<sub>5</sub>Na<sup>+</sup> ([M+Na]<sup>+</sup>), calculated: 241.1046, found: 241.1041.

***N*-[*(2S,5R)*-Tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furanoyl]-2-(*(2R)*-camphor-10,2-sultam (*(-)*-11)**



C<sub>19</sub>H<sub>31</sub>NO<sub>6</sub>S

Mol. wt.: 401.52 g/mol

White foam

To a vigorously stirred mixture of dienoate (*(-)*-**8** (250 mg, 0.71 mmol) with adogen 464 (200 mg) in Et<sub>2</sub>O (25 mL) at rt, was added a solution of KMnO<sub>4</sub> (3.55 mL, 0.4 M aq., 1.42 mmol) containing AcOH (0.46 mL, 2.84 mmol). The purple mixture was stirred rapidly for 30 min during which time the reaction mixture had turned dark brown. At this stage, the reaction was quenched with sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>5</sub> (30 mL) to dissolve all of the precipitated manganese salt and then repeatedly extracted using CH<sub>2</sub>Cl<sub>2</sub> (4x40 mL). The organic extracts were combined, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated *in vacuo* to give the yellow oily crude. <sup>1</sup>H NMR of the crude product showed that diol (*(-)*-**11** was present as a single isolated diastereoisomer. Purification by column chromatography on SiO<sub>2</sub> (EtOAc/hexane, 20→40%) afforded the title THF diol (*(-)*-**11** as a white foam (108 mg, 0.27 mmol, 38%).

[α]<sub>D</sub><sup>23</sup> -35.7 (*c* 1.05, CHCl<sub>3</sub>).

**FT-IR** ν<sub>max</sub> (neat) 3440, 2962, 2930, 2882, 1672, 1335, 1138, 909, 727 cm<sup>-1</sup>.

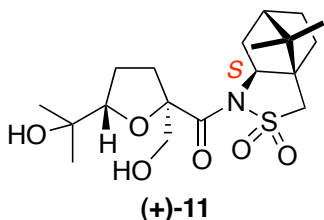
**<sup>1</sup>H NMR** δ 4.15 (1H, dd, *J* = 8.8, 6.5 Hz), 4.08 (1H, dd, *J* = 7.5, 4.5 Hz), 3.99 (1H, d, *J* = 11.0 Hz), 3.66 (1H, d, *J* = 11.0 Hz), 3.54 (1H, d, *J* = 13.4 Hz), 3.43 (1H, d, *J* = 13.4 Hz), 2.83 (2H, br), 2.33–2.03 (3H, m), 1.93–1.83 (6H, m), 1.43–1.25 (2H, m), 1.28 (3H, s), 1.21 (3H, s), 1.15 (3H, s), 0.99 (3H, s) ppm.

**<sup>13</sup>C NMR** δ 176.8, 89.2, 88.4, 71.5, 67.8, 67.0, 54.8, 47.7, 47.5, 45.45, 39.4, 35.0, 33.7, 27.5, 26.1, 26.0, 24.5, 21.8, 19.9 ppm.

**LRMS** (ES<sup>+</sup>) *m/z* 424 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>) *m/z* For C<sub>19</sub>H<sub>31</sub>NO<sub>6</sub>SNa<sup>+</sup> ([M+Na]<sup>+</sup>), calculated: 424.1764, found: 424.1764.

***N*-[*(2R,5S)*-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furanoyl]-2-(*(2S)*-camphor-10,2-sultam ((+)-11)**



$C_{19}H_{31}NO_6S$

Mol. wt.: 401.52 g/mol

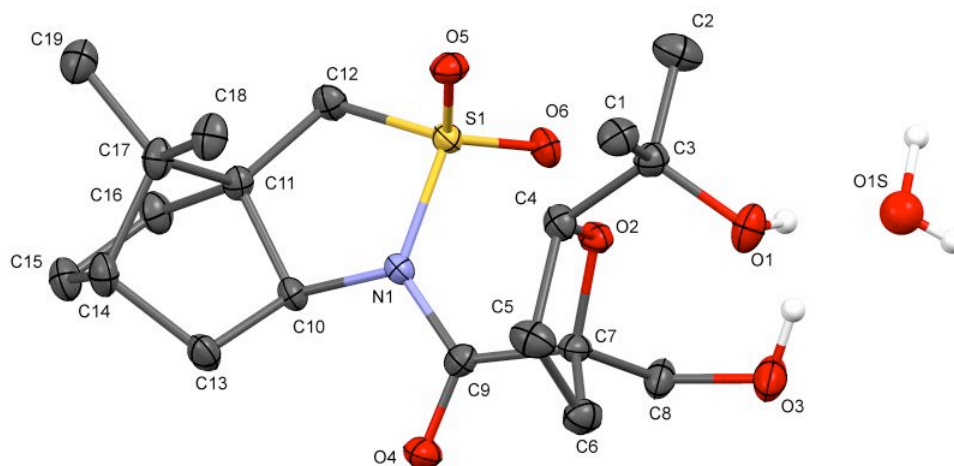
White slabs

The enantiomer *N*-[*(2R,5S)*-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furanoyl]-2-(*(2S)*-camphor-10,2-sultam ((+)-11) was synthesized in the same way from (+)-8. Spectroscopic data were consistent with that reported above for (–)-11. Crystallization from  $CH_2Cl_2$ /hexane gave colorless slabs that were suitable for X-ray structural determination (see below).

**mp** 49–54 °C (EtOAc/hexane)

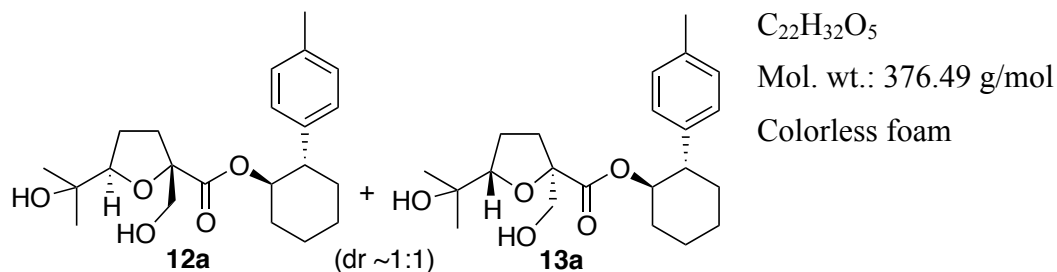
**$[\alpha]_D^{22}$**  +20.5 (*c* 0.4,  $CH_2Cl_2$ ).

**X-Ray structure of *N*-[*(2R,5S)*-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furanoyl]-2(*(2S)*-camphor-10,2-sultam ((+)-11).** Thermal ellipsoids drawn at the 50% probability level.<sup>13</sup>



<sup>13</sup> Bataille, C. J. R.; Brown, R. C.D.; Horton, P.N; Huth, S. L., **2014**, Private communication to the Cambridge Structural Database, deposition number CCDC 1014228.

**(1*R*\*,2*S*\*)-2-*p*-Tolylcyclohexyl (2*S*\*,5*R*\*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (12a) and (1*R*\*,2*S*\*)-2-*p*-Tolylcyclohexyl (2*R*\*,5*S*\*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (13a)**



To vigorously stirred mixture of diene ( $\pm$ )-**7a** (100 mg, 0.306 mmol) and phosphate buffer (pH  $\sim$ 7.4, 0.067M aq. sol. of both KH<sub>2</sub>PO<sub>4</sub> and NaH<sub>2</sub>PO<sub>4</sub> in volumetric ratio 8:2, 0.6 mL) in acetone (6.6 mL) at  $-35$  °C was added aq. NaMnO<sub>4</sub> (1.1 mL of 0.4 M, 0.44 mmol) containing AcOH (43.5  $\mu$ L, 0.761 mmol). The purple mixture was stirred rapidly for 1 h during which the temperature of acetone bath increased to  $-5$  °C, and the reaction mixture turned dark brown. The ice-cooled reaction mixture was quenched with sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>5</sub> (20 mL), adding sufficient H<sub>2</sub>O to dissolve the inorganic salts. The organic layer was separated, re-extracting the aqueous layer with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  60 mL). The combined organic solution was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and the solvent was removed *in vacuo*. The crude was purified by column chromatography on SiO<sub>2</sub> (EtOAc/hexane, 10 $\rightarrow$ 60 %) to afford the title THFdiol diastereoisomers **12a** and **13a** as a colorless foam (65 mg, 0.173 mmol, 57%). Spectroscopic data are reported for the inseparable mixture of diastereoisomers (1:1, estimated from NMR spectrum).

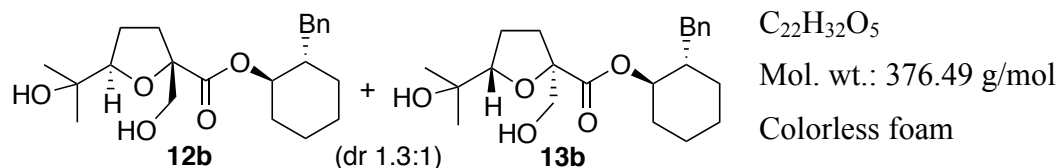
**FT-IR** (neat)  $\nu_{\max}$  3394, 2933, 2859, 1721 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR** (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.08 and 7.08 (4H, s), 5.00 (1H, td,  $J$  = 10.6 and 4.6 Hz), 3.77 and 3.66 (1H, t,  $J$  = 7.1 Hz), 3.65 and 3.52 (1H, d,  $J$  = 11.6 Hz), 3.53 and 3.45 (1H, d,  $J$  = 11.6 Hz), 2.65 (1H, m), 2.38 (1H, br), 2.29 (3H, s), 2.14 (1H, m), 1.97–1.30 (12H, m), 1.21 and 1.20 (3H, s), 1.06 and 1.05 (3H, s) ppm.

**<sup>13</sup>C-NMR** (75 MHz, CDCl<sub>3</sub>)  $\delta$  173.4 and 172.7, 140.1 and 139.9, 136.1 and 136.0, 129.1 and 128.9, 127.4 and 127.2, 87.1 and 86.9, 86.6, 77.7 and 77.0, 71.3, 65.8 and 65.7, 49.6 and 49.5, 34.3 and 33.9, 32.2 and 32.1, 31.8 and 31.1, 27.3, 25.8 and 25.7, 25.5 and 25.4, 24.8 and 24.7, 24.6, 20.9 ppm.

**LRMS** (ES<sup>+</sup>)  $m/z$  399 ([M+Na]<sup>+</sup>).

**(1*R*\*,2*S*\*)-2-Benzylcyclohexyl (2*S*\*,5*R*\*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (12b) and (1*R*\*,2*S*\*)-2-Benzylcyclohexyl (2*R*\*,5*S*\*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (13b)**



Following the procedure for permanganate-mediated oxidative cyclization of ( $\pm$ )-**7a**, diene ( $\pm$ )-**7b** (59 mg, 0.181 mmol) afforded the title THF diols **12b** and **13b** as a colorless foam (56 mg, 0.149 mmol, 82%). Spectroscopic data are reported for a mixture of diastereoisomers (1.3:1, HPLC). NMR signals are identified as maj and min where possible.<sup>14</sup>

**FT-IR** (neat)  $\nu_{\max}$  3403 (br), 2934 (m), 2859 (w), 1725 (s), 1604 (w) cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  7.30–7.08 (5H, m), 4.61 (1H, m), 4.08<sub>maj</sub> and 4.06<sub>min</sub> (1H, t,  $J$  = 7.1 Hz), 3.90<sub>min</sub> and 3.87<sub>maj</sub> (1H, d,  $J$  = 11.4 Hz), 3.77<sub>min</sub> and 3.75<sub>maj</sub> (1H, d,  $J$  = 11.4 Hz), 3.10 (1H, br), 2.91 (1H, m), 2.68 (1H, br), 2.30–1.52 (11H, m), 1.37–0.90 (3H, m), 1.30 (3H, s), 1.14 (3H, s) ppm.

**<sup>13</sup>C-NMR**  $\delta$  173.7<sub>maj</sub> and 173.6<sub>min</sub>, 140.0<sub>maj+min</sub>, 129.20<sub>maj+min</sub>, 128.20<sub>maj+min</sub>, 125.90<sub>maj+min</sub>, 87.6<sub>maj</sub> and 87.5<sub>min</sub>, 86.8<sub>min</sub> and 86.6<sub>maj</sub>, 77.6<sub>min</sub> and 77.4<sub>maj</sub>, 71.5<sub>min</sub> and 71.4<sub>maj</sub>, 66.2<sub>maj</sub> and 66.1<sub>min</sub>, 43.8<sub>maj</sub> and 43.7<sub>min</sub>, 38.5<sub>maj</sub> and 38.4<sub>min</sub>, 32.0<sub>maj</sub> and 31.9<sub>min</sub>, 31.5<sub>maj+min</sub>, 29.60<sub>maj+min</sub>, 27.5, 26.1<sub>maj</sub> and 26.0<sub>min</sub>, 25.1<sub>maj</sub> and 25.0<sub>min</sub>, 24.9<sub>maj</sub> and 24.8<sub>min</sub>, 24.30<sub>maj+min</sub> ppm.

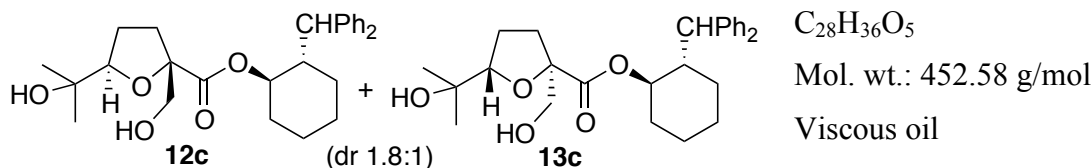
**LRMS** (ES<sup>+</sup>)  $m/z$  399 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>)  $m/z$  For C<sub>22</sub>H<sub>32</sub>O<sub>5</sub>Na<sup>+</sup> ([M+Na]<sup>+</sup>), calculated: 399.2142, found: 399.2147.

**HPLC** Agilent Zobax Sil C18 (5 $\mu$ m, 4.6  $\times$  250 mm) - (eluent: IPA/*n*-hexane 1:19) - 0.5 mL/min  
Retention times:  $t_{\text{maj}}$  = 40.5 min &  $t_{\text{min}}$  = 36.0 min.

<sup>14</sup> Relative configuration of the major stereoisomer **12b** tentatively assigned by analogy with **12d** and **12e**.

**(1*R*\*,2*S*\*)-2-Benzhydrylcyclohexyl (2*S*\*,5*R*\*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (12c) and (1*R*\*,2*S*\*)-2-Benzhydrylcyclohexyl (2*R*\*,5*S*\*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (13c)**



Following the procedure for permanganate-mediated oxidative cyclization of ( $\pm$ )-**7a**, diene ( $\pm$ )-**7c** (100 mg, 0.248 mmol) afforded a mixture of diastereoisomeric THF diols **12c** and **13c** as a thick viscous oil (111 mg, 0.245 mmol, 99%). Spectroscopic data are reported for a mixture of two diastereoisomers (1.8:1, HPLC).<sup>15</sup> NMR signals are identified as maj and min where possible.

**FT-IR** (neat)  $\nu_{\max}$  3402, 3036, 2936, 2863, 1724), 1598 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  7.39–7.13 (10H, m), 4.73 (1H, m), 4.15 (1H, d,  $J$  = 8.6 Hz), 4.06<sub>maj</sub> and 4.05<sub>min</sub> (1H, t,  $J$  = 7.1 Hz), 3.83<sub>min</sub> and 3.82<sub>maj</sub> (1H, d,  $J$  = 11.3 Hz), 3.72<sub>min</sub> and 3.71<sub>maj</sub> (1H, d,  $J$  = 11.3 Hz), 3.05 (1H, br), 2.72–2.53 (2H, br), 2.21–1.22 (11H, m), 1.31<sub>min</sub> and 1.30<sub>maj</sub> (3H, s), 1.15 (3H, s), 1.15 (1H, m) ppm.

**<sup>13</sup>C-NMR**  $\delta$  173.3<sub>maj</sub> and 173.1<sub>min</sub>, 143.1<sub>maj</sub> and 143.0<sub>min</sub>, 142.7<sub>min</sub> and 142.6<sub>maj</sub>, 128.8<sub>maj</sub> and 128.7<sub>min</sub>, 128.6<sub>min</sub> and 128.5<sub>maj</sub>, 128.4<sub>maj+min</sub>, 128.0<sub>maj+min</sub>, 126.4<sub>maj+min</sub>, 126.3<sub>min</sub> and 126.2<sub>maj</sub>, 87.6<sub>maj</sub> and 87.5<sub>min</sub>, 86.7<sub>min</sub> and 86.4<sub>maj</sub>, 74.8<sub>maj</sub> and 74.3<sub>min</sub>, 71.5<sub>min</sub> and 71.4<sub>maj</sub>, 66.2<sub>maj+min</sub>, 51.5<sub>maj</sub> and 51.2<sub>min</sub>, 42.3<sub>maj</sub> and 41.9<sub>min</sub>, 31.9<sub>maj+min</sub>, 28.5<sub>maj</sub> and 28.1<sub>min</sub>, 27.5<sub>maj</sub> and 27.4<sub>min</sub>, 26.1<sub>maj</sub> and 26.0<sub>min</sub>, 25.4<sub>maj+min</sub>, 25.1<sub>maj</sub> and 25.0<sub>min</sub>, 22.5<sub>maj+min</sub>, 22.2<sub>maj</sub> and 22.1<sub>min</sub> ppm.

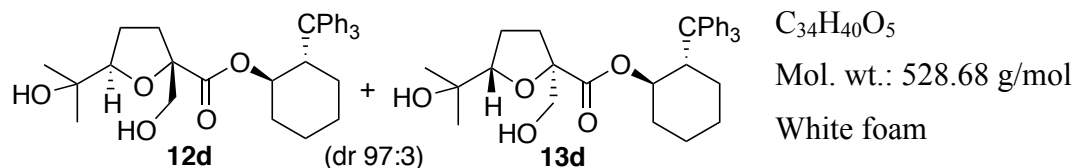
**LRMS** (ES<sup>+</sup>)  $m/z$  475 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>)  $m/z$  For C<sub>28</sub>H<sub>36</sub>O<sub>5</sub>Na<sup>+</sup> ([M+Na]<sup>+</sup>), calculated: 475.2455, found: 475.2460.

**HPLC** Agilent Zobax Sil C18 (5 $\mu$ m, 4.6  $\times$  250 mm) - (eluent: IPA/*n*-hexane 1:19) - 0.5 mL/min  
Retention times:  $t_{\text{maj}}$  = 36.2 min &  $t_{\text{min}}$  = 42.8 min.

<sup>15</sup> Relative configuration of the major stereoisomer **12c** tentatively assigned by analogy with **12d** and **12e**.

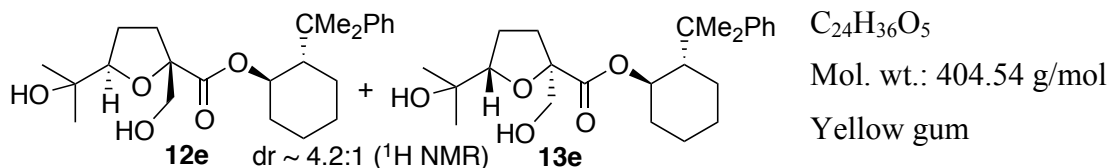
**(1*R*\*,2*S*\*)-2-Tritylcyclohexyl (2*S*\*,5*R*\*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxy propan-2-yl)furan-2-carboxylate (12d) and (1*R*\*,2*S*\*)-2-Tritylcyclohexyl (2*R*\*,5*S*\*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxy propan-2-yl)furan-2-carboxylate (13d)**



Following the procedure for permanganate-mediated oxidative cyclization of (±)-**7a**, diene (±)-**7d** (59 mg, 0.123 mmol) afforded a mixture of diastereoisomeric THF diols **12d** and **13d** as a white foam (40 mg, 0.076 mmol, 62%). Spectroscopic data are reported for a mixture of diastereoisomers (dr 97:3, HPLC). This compound exhibited broadening of some signals in its NMR spectra due to restricted rotation. Only signals for the major isomer (±)-**12d** were observed in the NMR spectra.

<b>mp</b>	61–65 °C
<b>FT-IR</b> (neat) $\nu_{\text{max}}$	3423 (br), 3056 (w), 2939 (m), 2860 (w), 1729 (s), 1595 (w) cm <sup>-1</sup> .
<b><sup>1</sup>H-NMR</b> (300 MHz, CDCl <sub>3</sub> )	$\delta$ 7.50–6.95 (15H, m), 4.08 (1H, td, $J$ = 13.8, 3.8 Hz), 3.81 (1H, t, $J$ = 7.2 Hz), 3.62 (1H, d, $J$ = 11.3 Hz) 3.59 (1H, td, $J$ = 12.1, 2.0 Hz), 3.43 (1H d, $J$ = 11.3 Hz), 2.35 (1H, br), 2.15 (1H, m), 1.97 (1H, m), 1.79–1.60 (5H, m), 1.52–1.30 (3H, m), 1.25 (3H, s), 1.14 (2H, m), 1.09 (3H, s), 0.82 (1H, m) ppm.
<b><sup>13</sup>C-NMR</b> (75 MHz, CDCl <sub>3</sub> )	$\delta$ 172.1, 131.4, 128.7, 127.5, 125.0, 86.8, 86.7, 77.2, 71.5, 66.1, 61.0, 45.6, 33.0, 30.3, 28.7, 27.3, 25.9, 25.7, 25.0, 24.6 ppm.
<b>LRMS</b> (ES <sup>+</sup> ) $m/z$	546 ([M+NH <sub>4</sub> ] <sup>+</sup> ).
<b>HRMS</b> (ES <sup>+</sup> ) $m/z$	For C <sub>34</sub> H <sub>44</sub> NO <sub>5</sub> <sup>+</sup> ([M+ NH <sub>4</sub> ] <sup>+</sup> ), calculated: 546.3214, found: 546.3219.

**(1*R*,2*S*)-2-(2-Phenylpropan-2-yl)cyclohexyl (2*S*,5*R*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (12e) and (1*R*,2*S*)-2-(2-Phenylpropan-2-yl) (2*R*,5*S*)-cyclohexyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (13e)**

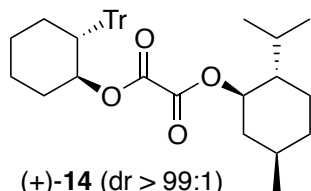


Following the procedure for permanganate-mediated oxidative cyclization of ( $\pm$ )-**7a**, dieneoate ( $-$ )-**7e** (56.0 mg, 0.158 mmol) afforded a mixture of diastereoisomeric THF diols **12e** and **13e** (dr  $\sim$  4.2:1, estimated by 600 MHz  $^1\text{H}$  NMR), as a yellow gum (60 mg, 0.148 mmol, 94%). Spectroscopic data are reported for the mixture of diastereoisomers, identified as maj and min where possible.

$[\alpha]^{25}_{\text{D}}$	+0.3 ( <i>c</i> 1.12, CHCl <sub>3</sub> ).
FT-IR $\nu_{\text{max}}$ (neat)	3390, 2911, 2929, 2860, 1721, 1447 cm <sup>-1</sup> .
$^1\text{H}$ NMR (600 MHz, CDCl <sub>3</sub> )	$\delta$ 7.29–7.23 (4H, m), 7.14 (1H, m), 4.86 <sub>min</sub> and 4.76 <sub>maj</sub> (1H, td, <i>J</i> = 10.7, 4.4 Hz), 4.01 <sub>maj</sub> and 3.90 <sub>min</sub> (1H, t, <i>J</i> = 7.1 Hz), 3.68 <sub>maj</sub> and 3.60 <sub>min</sub> (1H, d, <i>J</i> = 11.0 Hz), 3.53 <sub>maj</sub> and 3.49 <sub>min</sub> (1H, d, <i>J</i> = 11.0 Hz), 3.20 (1H, br), 2.60 (1H, br), 2.05–1.78 (6H, m), 1.64 (1H, m), 1.57 (1H, m), 1.44 (1H, m), 1.25–1.20 (2H, m), 1.34 <sub>maj</sub> (3H, s), 1.26 <sub>maj</sub> (3H, s), 1.25 <sub>maj</sub> (3H, s), 1.11 <sub>maj</sub> (3H, s), 1.08 (1H, m), 0.94 (1H, m) ppm.
$^{13}\text{C}$ NMR (100 MHz, CDCl <sub>3</sub> )	$\delta$ 173.5 <sub>maj</sub> and 173.1 <sub>min</sub> , 150.6 <sub>min</sub> and 150.4 <sub>maj</sub> , 128.2 <sub>min</sub> and 128.0 <sub>maj</sub> , 125.7 <sub>maj</sub> and 125.3 <sub>min</sub> , 125.34 <sub>maj+min</sub> , 87.6 <sub>maj</sub> and 87.3 <sub>min</sub> , 86.6 <sub>min</sub> and 86.2 <sub>maj</sub> , 76.5 <sub>maj</sub> and 76.4 <sub>min</sub> , 71.4 <sub>min</sub> and 71.30 <sub>maj</sub> , 65.9 <sub>maj</sub> and 65.4 <sub>min</sub> , 50.7 <sub>maj</sub> and 50.4 <sub>min</sub> , 40.3 <sub>maj+min</sub> , 31.9 <sub>maj</sub> and 31.3 <sub>min</sub> , 30.3 <sub>min</sub> and 29.7 <sub>maj</sub> , 28.7 <sub>maj</sub> and 28.4 <sub>min</sub> , 27.51 <sub>maj+min</sub> , 27.48 <sub>maj</sub> and 27.4 <sub>min</sub> , 26.1 <sub>maj+min</sub> , 25.8 <sub>maj</sub> and 25.7 <sub>min</sub> , 25.4 <sub>maj+min</sub> , 25.1 <sub>maj+min</sub> , 24.5 <sub>maj+min</sub> ppm.
LRMS (ES <sup>+</sup> ) <i>m/z</i>	427 ([M+Na] <sup>+</sup> ).
HRMS (ES <sup>+</sup> ) <i>m/z</i>	For C <sub>24</sub> H <sub>36</sub> O <sub>5</sub> Na <sup>+</sup> ([M+Na] <sup>+</sup> ), calculated: 427.2455, found: 427.2446.

## Resolution of TTC enantiomers

### (1*R*,2*S*,5*R*)-2-*iso*-Propyl-5-methylcyclohexyl (1*S*,2*R*)-2-tritylcyclohexyl oxalate ((+)-14)



$C_{37}H_{44}O_4$

Mol. wt.: 552.74 g/mol

White powder

To a solution of oxalyl chloride (22.2 mL, 258.6 mmol) in  $CH_2Cl_2$  (150 mL) at 0 °C under  $N_2$  was added a solution of (–)-menthol (15.59 g, 99.76 mmol) in  $CH_2Cl_2$  (150 mL) using a pressure equalising dropping funnel over 30 min. The mixture was stirred for 30 min at 0 °C, and then allowed to warm to rt. After 2 h TLC analysis indicated full consumption of (–)-menthol, and the reaction mixture was concentrated *in vacuo* giving crude (–)-menthylchloro(oxo)acetate as a colorless liquid which was used immediately without purification.

(±)-TTC (32.53 g, 94.99 mmol) was dissolved in anhydrous pyridine (20.2 mL, 250.8 mmol) and  $CH_2Cl_2$  (70 mL) and then added dropwise using a pressure equalising dropping funnel to a solution of (–)-menthylchloro(oxo)acetate (prepared above) in  $CH_2Cl_2$  (150 mL) at 0 °C under  $N_2$ . Upon completion (3 h), the reaction mixture was quenched with sat.  $NH_4Cl$  (150 mL), the phases were separated and the organic layer washed with 2N aq. HCl (3 × 70 mL), sat.  $NaHCO_3$  (100 mL) and sat. brine (70 mL). The organic phase was dried ( $MgSO_4$ ) and concentrated *in vacuo*. The residue was treated with MeOH (200 mL) and the resulting suspension stirred rapidly at 0 °C. The title compound was isolated by filtration under suction as an amorphous white solid (49.39 g, 89.35 mmol, 94% yield).

**HPLC** Daicel Chiralcel® OD-H - (*eluent*: IPA/*n*-hexane 1:99) - 0.5 mL/min. Retention times: 12.5 & 15.0 min.

The diastereomeric mixture of oxalate diesters (48.01 g, 86.86 mmol) was suspended in MeOH (300 mL) and heated at reflux for 30 min. The suspension was filtered through a hot sintered funnel under suction and the solids washed with hot MeOH (2 × 250 mL). This process was repeated three times, analysing the filter cake by TLC for diastereomeric purity. The solid was dried *in vacuo* affording (+)-14 as a white solid (15.84 g, 28.66 mmol, 33% yield, dr > 99:1). This compound exhibited broadening of some signals in its NMR spectra due to restricted rotation.

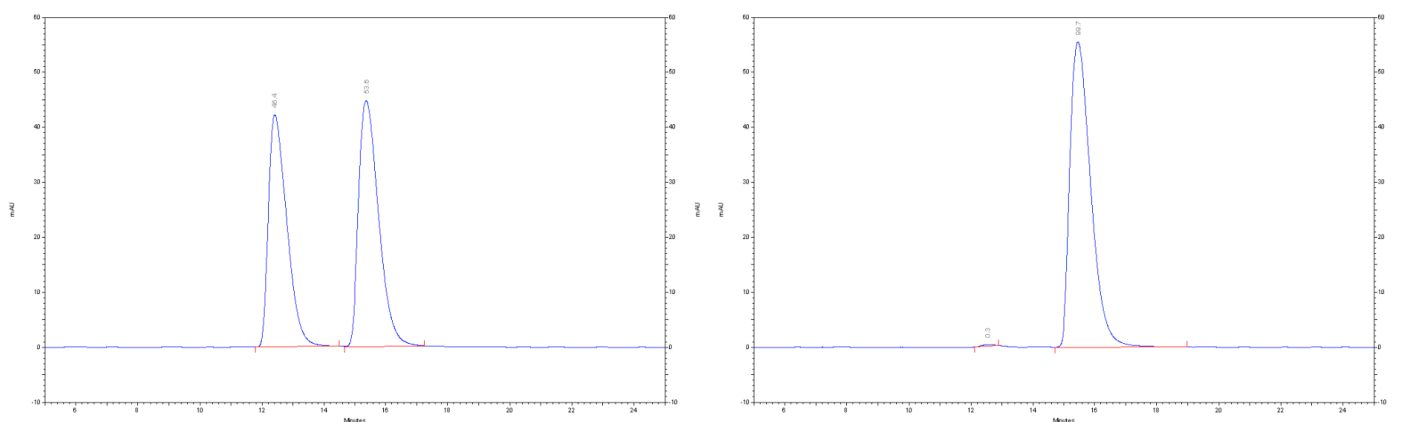
$[\alpha]_D^{26}$  +10.8 (*c* 1.16,  $CHCl_3$ ).

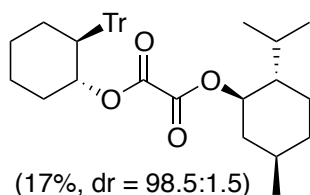
**mp** 191–194 °C (MeOH).

**FT-IR** (neat)  $\nu_{max}$  3080, 3051, 3031, 2944, 2866, 1758, 1733  $cm^{-1}$ .

<b><math>^1\text{H-NMR}</math></b>	$\delta$ 7.72–6.72 (15H, m), 4.64 (1H, td, $J = 10.9, 4.5$ Hz), 4.14 (1H, td, $J = 10.6, 3.9$ Hz), (400 MHz, $\text{CDCl}_3$ ) 3.60 (1H, td, $J = 10.6, 2.1$ Hz), 2.12 (1H, d, $J = 13.8$ Hz), 2.00 (1H, m), 1.87–1.58 (7H, m), 1.52–1.13 (4H, m), 1.12–0.78 (10H, m), 0.75 (3H, d) ppm.
<b><math>^{13}\text{C-NMR}</math></b>	$\delta$ 157.9, 157.7, 129.9 (br), 127.4, 125.7, 78.5, 77.0, 60.8, 46.3, 46.2, 40.0, 34.0, 32.7, (100 MHz, $\text{CDCl}_3$ ) 31.3, 28.9, 26.0, 25.9, 24.6, 23.2, 22.0, 20.6, 16.2 (quaternary aromatic carbon signal was not observed) ppm.
<b>LRMS (<math>\text{ES}^+</math>) <math>m/z</math></b>	616.3 ( $[\text{M}+\text{MeCN}+\text{Na}^+]^+$ ).
<b>HRMS (<math>\text{ES}^+</math>) <math>m/z</math></b>	For $\text{C}_{37}\text{H}_{44}\text{NaO}_4^+$ ( $[\text{M}+\text{Na}]^+$ ), calculated: 575.3132, found: 575.3137.
<b>HPLC</b>	Daicel Chiralcel® OD-H - (eluent: IPA/ <i>n</i> -hexane 1:99) - 0.5 mL/min. Retention times: $t_{\text{min}} = 12.5$ & $t_{(+)-14} = 15.0$ min.

### HPLC Chromatograms for the mixture of diastereoisomers and (+)-14



**(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl ((1*R*,2*S*)-2-tritylcyclohexyl) oxalate**

$C_{37}H_{44}O_4$   
 Mol. wt.: 552.74 g/mol  
 White crystals

The collected filtrates from the isolation of (+)-**14** were combined and concentrated *in vacuo* giving an amorphous white solid enriched in the (1*R*,2*S*) diastereoisomer. Serial recrystallization of this material from MeCN led to the isolation of the title diester as a white crystalline solid (8.16 g, 14.76 mmol, 17% yield, *de* 97%).

$[\alpha]_D^{26}$  −67.4 (*c* 1.15,  $CHCl_3$ ).

**mp** 138–140 °C (MeCN).

**FT-IR** (neat)  $\nu_{max}$  3086, 3059, 3032, 2949, 2926, 2863, 1751, 1730  $cm^{-1}$ .

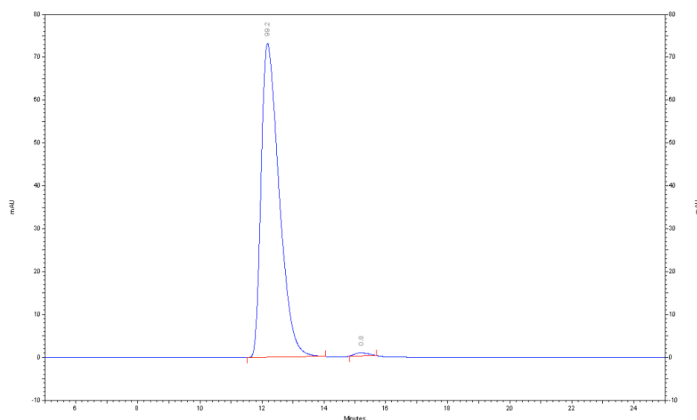
**$^1H$ -NMR**  $\delta$  7.61–6.85 (15H, m), 4.63 (1H, td,  $J$  = 10.9, 4.5 Hz), 4.15 (1H, td,  $J$  = 10.5, 3.8 Hz), 3.61 (1H, td,  $J$  = 10.5, 2.3 Hz), 2.13 (1H, d,  $J$  = 13.7 Hz), 1.96 (1H, m), 1.87 (1H, d,  $J$  = 11.8 Hz), 1.80–1.60 (6H, m), 1.53–1.34 (3H, m), 1.24 (1H, m), 1.12–0.81 (11H, m), 0.71 (3H, d,  $J$  = 7.0 Hz) ppm.

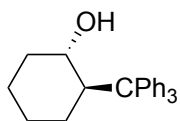
**$^{13}C$ -NMR**  $\delta$  157.3, 157.3, 129.4 (br), 127.4, 125.6, 78.6, 77.2, 60.8, 46.3, 40.0, 34.0, 32.6, 31.3, 28.9, 26.2, 25.9, 24.6, 23.4, 21.9, 20.6, 16.4 ppm.

**LRMS** ( $ES^+$ )  $m/z$  616.3 ( $[M+MeCN+Na]^+$ ).

**HRMS** ( $ES^+$ )  $m/z$  For  $C_{37}H_{44}NaO_4^+$  ( $[M+Na]^+$ ), calculated: 575.3132, found: 575.3133.

**HPLC** Daicel Chiralcel® OD-H - (*eluent*: IPA/*n*-hexane 1:99) - 0.5 mL/min. Retention times:  $t_{maj}$  = 12.5 min &  $t_{(+)-14}$  = 15.0 min.



**(-)-(1*S*,2*R*)-Triphenylmethyl cyclohexanol ((-)-5d)**C<sub>25</sub>H<sub>26</sub>O

Mol. wt.: 342.47 g/mol

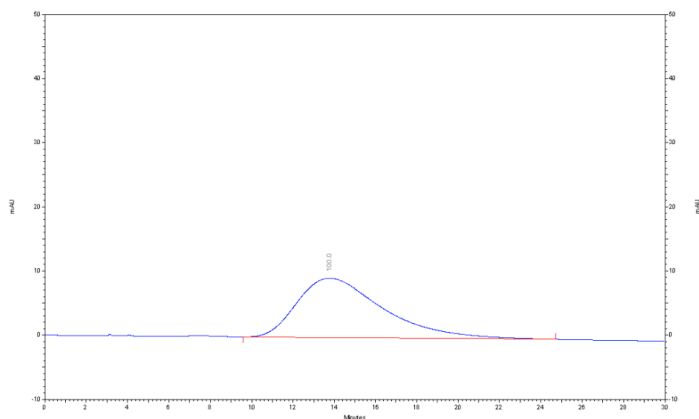
White powder

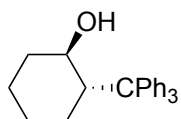
Oxalate diester **(+)-14** (15.01 g, 27.16 mmol) was suspended in MeOH/H<sub>2</sub>O (250 mL - 5:1) and KOH (3.53 g, 62.91 mmol) was added. The reaction mixture was heated under reflux for 16 h. The reaction was allowed to cool to rt and concentrated *in vacuo*. The residue was treated with H<sub>2</sub>O (100 mL) and extracted with EtOAc (5 × 100 mL). The organic layers were combined, dried (MgSO<sub>4</sub>) and concentrated *in vacuo*. The residue was triturated from *n*-hexane and filtered under vacuum. The solid residue was washed with cold *n*-hexane (3 × 100 mL) affording the title compound as a white solid (8.37 g, 24.44 mmol, 90%, > 99% *ee*). NMR, IR and MS data recorded for **(-)-5d** are consistent with those for **(±)-5d**.

[α]<sub>D</sub><sup>27</sup> -37.1 (c 1.03, CHCl<sub>3</sub>).

mp 190–192 °C.

**HPLC** Daicel Chiralcel® OJ - (*eluent*: IPA/*n*-hexane - 1:19) - 1 mL/min. Retention time: 14.0 min.



**(+)-(1*R*,2*S*)-Triphenylmethyl cyclohexanol ((+)-5d)**C<sub>25</sub>H<sub>26</sub>O

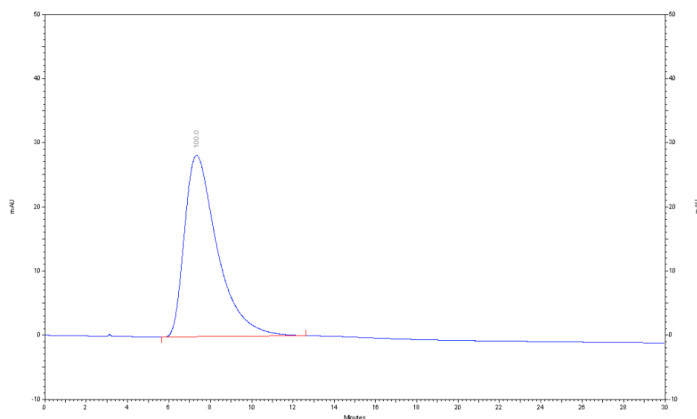
Mol. wt.: 342.47 g/mol

White powder

**(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl ((1*R*,2*S*)-2-tritylcyclohexyl) oxalate** (7.51 g, 13.59 mmol) was suspended in MeOH/H<sub>2</sub>O (125 mL - 5:1) and KOH (1.77 g, 33.95 mmol) was added. The reaction mixture heated under reflux for 16 h. The reaction was allowed to cool to rt and concentrated *in vacuo*. The residue was treated with H<sub>2</sub>O (50 mL) and extracted with EtOAc (5 × 50 mL). The organic layers were combined, dried (MgSO<sub>4</sub>) and concentrated *in vacuo*. The residue was triturated with *n*-hexane and filtered under vacuum. The solid residue was washed with cold *n*-hexane (3 × 100 mL) affording the title compound as a white solid (4.28 g, 12.50 mmol, 92% yield). Physical and spectroscopic data recorded are consistent with those for (±)-**5d**.

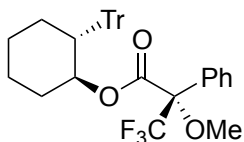
**[α]<sub>D</sub><sup>25</sup>** +32.8 (c 0.99, CHCl<sub>3</sub>).

**HPLC** Daicel Chiralcel® OJ - (*eluent*: IPA/*n*-hexane - 1:19) - 1 mL/min Retention time: 8.0 min.



## Determination of absolute stereochemistry for (–)-TTC

### (2*S*)-(1*S*,2*R*)-2-Tritylcyclohexyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate



$C_{35}H_{33}F_3O_3$

Mol. wt.: 558.63 g/mol

Colorless crystals

To a stirred solution of (–)-(1*S*,2*R*)-2-tritylcyclohexanol ((–)-**5d**, 27.3 mg, 0.08 mmol) in dry THF (2 mL), was added a solution of NaHMDS (0.12 mL of 1.0 M in THF, 0.12 mmol) at –35 °C. The solution was allowed to warm to –10 °C over 30 min, whereupon (*R*)- $\alpha$ -methoxy- $\alpha$ -trifluorophenyl acetic acid chloride (30  $\mu$ L, 0.16 mmol) was added dropwise. The reaction mixture was allowed to warm to rt and stirred for 1 h. The crude was purified by column chromatography on SiO<sub>2</sub> (ether/hexane, (5%→20 %)) to afford the title ester as a colorless solid which was recrystallized from EtOH to give a colorless crystalline solid (33 mg, 0.059 mmol, 74%).

$[\alpha]^{27}_D$  +16.4 (*c* 0.24, CHCl<sub>3</sub>).

mp 169–171 °C

FT-IR  $\nu_{max}$  (neat) 3057, 2944, 2862, 1737, 1595 cm<sup>–1</sup>.

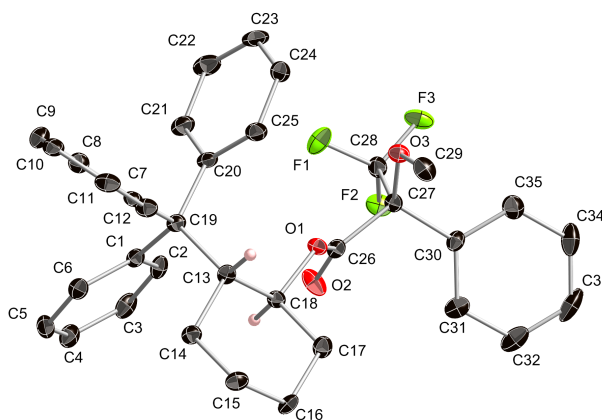
<sup>1</sup>H NMR ( $\delta$  7.52–7.00 (20H, m), 4.70 (1H, td, *J* = 7.0, 3.0 Hz), 3.61 (1H, m), 3.32 (3H, s), 2.05 (1H, m), 1.55–1.25 (5H, m), 1.20–1.01 (2H, m) ppm.

<sup>13</sup>C NMR ( $\delta$  165.6, 132.0, 129.3, 128.3, 127.5, 125.5, 78.6, 76.7, 61.2, 55.0, 44.2, 29.5, 26.5, 23.7, 21.9 ppm.

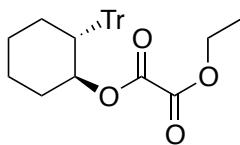
LRMS (ES<sup>+</sup>) *m/z* 581 ([M+Na]<sup>+</sup>).

HRMS (ES<sup>+</sup>) *m/z* For C<sub>35</sub>H<sub>33</sub>F<sub>3</sub>NaO<sub>3</sub><sup>+</sup> ([M+Na]<sup>+</sup>), calculated: 581.2274, found: 581.2279.

**X-Ray Structure.** Thermal ellipsoids drawn at the 35% probability level, only hydrogen atoms at chiral centres shown for clarity.<sup>16</sup>



<sup>16</sup> Al Hazami, A. M., Brown, R. C.D.; Light, M.E., **2014**, Private communication to the Cambridge Structural Database, deposition number CCDC 1014225.

**Ethyl ((1*S*,2*R*)-2-tritylcyclohexyl) oxalate**C<sub>29</sub>H<sub>30</sub>O<sub>4</sub>

Mol. wt.: 442.55 g/mol

White powder

Ethyl chloro oxoacetate (4.7 mL, 41.25 mmol) was added dropwise over 20 min to a stirred mixture of DMAP (6.79 g, 55 mmol) and (–)-(1*S*,2*R*)-triphenylmethylcyclohexanol ((–)-**5d**, 9.42 g, 27.5 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (80 mL). The mixture was stirred at rt for 1 h then, CH<sub>2</sub>Cl<sub>2</sub> was removed *in vacuo*. The mixture was dissolved in EtOAc (60 mL) and washed with 2N HCl aq. (60 mL). The organic layer was separated, dried (MgSO<sub>4</sub>), and EtOAc was removed *in vacuo*. *n*-Hexane (60 mL) was added to the crude product and removed *in vacuo* to give a white solid, which was washed with *n*-hexane to give corresponding oxalate as a white powder (10.5 g, 23.7 mmol, 86%). This compound exhibited broadening of the signals in its NMR spectra data due to restricted rotation.

**[α]<sup>23</sup><sub>D</sub>** +23.1 (*c* 0.915, CHCl<sub>3</sub>).

**mp** 124–127 °C.

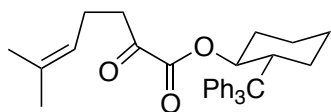
**FT-IR** (neat)  $\nu_{\text{max}}$  3056, 2939, 2861, 1760, 1733 cm<sup>–1</sup>.

**<sup>1</sup>H-NMR** δ 7.60–6.85 (15H, m), 4.30 (1H, dt, *J* = 4.0, 10.3 Hz), 4.07 (2H, q, *J* = 7.0 Hz), 3.60 (1H, m), 2.14 (1H, m), 1.80–1.58 (3H, m), 1.55–1.10 (3H, m), 1.24 (3H, t, *J* = 7.1 Hz), 0.78 (1H, m) ppm.

**<sup>13</sup>C-NMR** δ 157.8, 157.1, 129.6, 127.3, 125.3, 78.3, 62.4, 60.7, 46.2, 32.7, 28.9, 25.8, 24.6, 13.8, ppm. (quaternary aromatic carbon signal was not observed).

**LRMS** (ES<sup>+</sup>) *m/z* 907.6 ([2M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>) *m/z* For C<sub>29</sub>H<sub>34</sub>NO<sub>4</sub><sup>+</sup> ([M+NH<sub>4</sub>]<sup>+</sup>), calculated: 460.2482, found: 460.2475.

**(1*S*,2*R*)-2-Tritylcyclohexyl 6-methyl-2-oxohept-5-enoate (15)**C<sub>33</sub>H<sub>36</sub>O<sub>3</sub>

Mol. wt.: 480.64 g/mol

White powder

To a mixture of stirring Mg (2.55 g, 105 mmol) in dry THF (50 mL) was added a portion solution of a solution of 5-bromo-2-methylpent-2-ene (5.69 g, 34.91 mmol) in dry THF (10 mL). A few crystals of iodine were added to promote reaction, and the mixture was heated to reflux. The remainder of the alkyl bromide solution was added dropwise, and upon completion of addition, heating under reflux was continued for 45 min. The resulting Grignard solution was added dropwise through a cannula to a stirred solution of **Ethyl ((1*S*,2*R*)-2-tritylcyclohexyl) oxalate** (10.3 g, 23.27 mmol) in dry THF (60 mL) at  $-78^{\circ}\text{C}$ . The mixture was stirred at the same temperature for 2 h. The reaction was quenched with water (80 mL) and sat. aq. NH<sub>4</sub>Cl (40 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3x100 mL). The organic layer was dried (MgSO<sub>4</sub>) and the solvent was removed *in vacuo*. The crude mixture was purified by column chromatography on SiO<sub>2</sub> (CH<sub>2</sub>Cl<sub>2</sub>/hexane, 2→60%) to give the title dienoate **15** as a white powder (9.69 g, 20.16 mmol, 87%). This compound exhibited broadening of some signals in its NMR spectra due to restricted rotation.

**[ $\alpha$ ]<sub>D</sub><sup>25</sup>** +2.1 (*c* 0.8, CHCl<sub>3</sub>).

**mp** 162–165 °C.

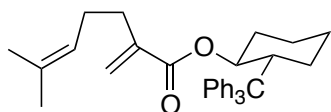
**FT-IR** (neat)  $\nu_{\text{max}}$  3056, 2935, 2859, 1719 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  7.50–7.00 (15H, m), 4.97 (1H, t with fine coupling, *J* = 7.0 Hz), 4.32 (1H, td, *J* = 10.2, 4.0 Hz), 3.60 (1H, m), 2.48–1.58 (6H, m), 1.80–1.10 (5H, m), 1.70 (3H, s), 1.62 (3H, s), 0.75 (1H, m) ppm.

**<sup>13</sup>C-NMR**  $\delta$  194.2, 160.5, 132.9, 129.6, 127.5, 125.6, 122.0, 77.6, 60.8, 46.2, 39.1, 33.0, 29.1, 25.8, 25.7, 24.7, 21.3, 17.6 ppm. (quaternary aromatic carbon signal was not observed).

**LRMS** (ES<sup>+</sup>) *m/z* 983 ([2M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>) *m/z* For C<sub>33</sub>H<sub>40</sub>NO<sub>3</sub><sup>+</sup> ([M+NH<sub>4</sub>]<sup>+</sup>), calculated: 498.3003, found: 498.3008.

**(1S,2R)-2-Tritylcyclohexyl 6-methyl-2-methylenehept-5-enoate ((-)-7d)**C<sub>34</sub>H<sub>38</sub>O<sub>2</sub>

Mol. wt.: 478.66 g/mol

Colorless viscous oil

DBU (3.49 mL, 22.86 mmol) was added dropwise at rt to a stirred solution of CH<sub>3</sub>Ph<sub>3</sub>PBr (5.56 g, 15.24 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (40 mL). The mixture was heated under reflux for 1 h. Then, ketoester **15** (2.45 g, 5.08 mmol) was added in dry CH<sub>2</sub>Cl<sub>2</sub> (30 mL), and heating under reflux was continued for 21 h. The solvent was removed *in vacuo* and the mixture was dissolved in EtOAc (40 mL) and washed with 2N HCl aq. (60 mL). The organic layer was dried (MgSO<sub>4</sub>) and the solvent was removed *in vacuo*. The crude mixture was purified by column chromatography on SiO<sub>2</sub> (CH<sub>2</sub>Cl<sub>2</sub>/hexane (2→20%)) to give the product **(-)-7d** as a colorless viscous oil (2.19 g, 4.58 mmol, 90%). This compound exhibited broadening of some signals in its NMR spectra due to restricted rotation.

**[α]<sub>D</sub><sup>25</sup>** +50.5 (*c* 0.86, CHCl<sub>3</sub>).

**FT-IR** (neat)  $\nu_{\max}$  3056, 2924, 2857, 1705 cm<sup>-1</sup>.

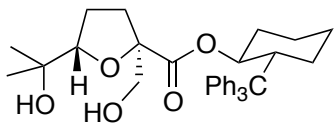
**<sup>1</sup>H-NMR** δ 7.60–6.85 (15H, m), 5.20 (1H, d, *J* = 1.5 Hz), 5.14 (1H, m), 5.05 (1H, m), 4.00 (1H, td, *J* = 10.3, 3.7 Hz), 3.60 (1H, m), 2.16 (1H, m), 2.10–1.89 (5H, m), 1.78–1.35 (4H, m), 1.71 (3H, s), 1.61 (3H, s), 1.25 (1H, m), 0.88 (1H, m) ppm.

**<sup>13</sup>C-NMR** δ 166.4, 148.5, 140.4, 131.9, 128.8, 127.4, 125.3, 124.3, 123.6, 76.3, 60.8, 46.6, 33.3, 31.9, 29.1, 26.9, 26.3, 25.7, 24.9, 17.7 ppm.

**LRMS** (ES<sup>+</sup>) *m/z* 501 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>) *m/z* For C<sub>34</sub>H<sub>39</sub>O<sub>2</sub><sup>+</sup> ([M+H]<sup>+</sup>), calculated: 479.2945, found: 479.2950.

**(1*S*,2*R*)-2-Tritylcyclohexyl (2*R*,5*S*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxy propan-2-yl)furan-2-carboxylate ((-)-12d)**



$C_{34}H_{40}O_5$

Mol. wt.: 528.68 g/mol

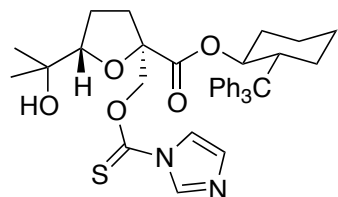
White foam

To a rapidly stirring solution of the diene **(-)-7d** (6.66 g, 13.9 mmol) in acetone (250 mL) and H<sub>2</sub>O (40 mL) at –40 °C was added a solution of NaMnO<sub>4</sub> (52.1 mL of 0.4 M aq., 20.84 mmol,) containing AcOH (2.76 mL, 48.1 mmol). The mixture was stirred for 1 h during which the color changed to dark brown and temperature rose to –5 °C. The reaction was quenched by adding sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>5</sub> (120 mL) with ice-cooling. The reaction mixture was concentrated *in vacuo*, to remove the acetone, then the residue was extracted with EtOAc (4x100 mL). The combined organic solution was dried (MgSO<sub>4</sub>), filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on SiO<sub>2</sub> (EtOAc/hexane, 2.5→50 %) to give the title THF diol **(-)-12d** as a white foam (5.35 g, 10.12 mmol, 73%). IR, NMR and MS data are consistent with those reported above for **(±)-12d**.

$[\alpha]^{24}_D$  –3.8 (c 0.52, CHCl<sub>3</sub>).

**HPLC** Agilent Zobax Sil C18 (5μm, 4.6 × 250 mm) - (*eluent*: IPA/*n*-hexane - 1:19) - 0.5 mL/min, elution times:  $t_{maj}$  = 43.85 min,  $t_{min}$  = 34.90 min, dr = 97:3.

**(1*S*,2*R*)-2-Tritylcyclohexyl (2*R*,5*S*)-tetrahydro-2-(*O*-methoxy-1*H*-imidazole-1-carbothioyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (**16**)**



$C_{38}H_{42}N_2O_5S$

Mol. wt.: 638.82 g/mol

Yellow foam

To a stirred solution of THF-diol (–)-**12d** (3.53 g, 6.68 mmol) in dry  $CH_2Cl_2$  (100 mL) was added DMAP (0.49 g, 4.01 mmol) and 1,1'-thiocabonyldiimidazole (3.76 g, 20.0 mmol). The mixture was stirred for 12 h at rt. Following removal of the solvent under reduced pressure, the crude product was purified directly by column chromatography on  $SiO_2$  (EtOAc/hexane, 0:1→1:1) to give the product **16** as a yellow foam (3.74 g, 5.85 mmol, 88%). This compound exhibited broadening of some signals in its NMR spectra due to restricted rotation.

$[\alpha]_D^{24}$  +10.0 (*c* 0.5,  $CHCl_3$ ).

**FT-IR** (neat)  $\nu_{max}$  3400, 2941, 2859, 1740  $cm^{-1}$ .

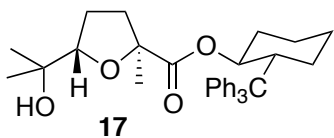
**$^1H$ -NMR**  $\delta$  8.36 (1H, s), 7.61 (1H, s), 7.55–7.00 (15H, m), 7.04 (1H, s), 4.82 (1H, d,  $J$  = 11.0 Hz), (400 MHz,  $CDCl_3$ ) 4.38 (1H, d,  $J$  = 11.0 Hz), 4.13 (1H, td,  $J$  = 10.2, 3.8 Hz), 4.07 (1H, t,  $J$  = 7.3 Hz), 3.56 (1H, m), 2.14 (1H, m), 2.04–1.00 (11H, m), 1.24 (3H, s), 1.11 (3H, s), 0.72 (1H, m) ppm.

**$^{13}C$ -NMR**  $\delta$  184.0, 170.2, 137.1, 131.5, 131.0, 128.6, 127.7, 125.2, 117.8, 87.7, 84.3, 77.5, 75.5, (100 MHz,  $CDCl_3$ ) 71.0, 61.0, 45.6, 33.0, 31.2, 28.8, 27.1, 25.8, 25.1, 24.9, 24.7 ppm.

**LRMS** ( $ES^+$ )  $m/z$  661 ( $[M+Na]^+$ ).

**HRMS** ( $ES^+$ )  $m/z$  For  $C_{38}H_{43}N_2O_5S^+$  ( $[M+H]^+$ ), calculated: 639.2887, found: 639.2893.

**(1*S*,2*R*)-2-Tritylcyclohexyl (2*S*,5*S*)-tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-carboxylate (17)**



$C_{34}H_{40}O_4$

Mol. wt.: 512.68 g/mol

Pale yellow foam

To a stirred solution of THF **16** (243 mg, 0.380 mmol) in dry toluene (19 mL) was added AIBN (28 mg, 0.17 mmol), followed by dropwise addition of TTMS (700  $\mu$ L, 2.21 mmol). The resultant solution was stirred at 85  $^{\circ}$ C for 20 min then diluted with EtOAc (20 mL). The mixture was washed with sat. aq.  $NaHCO_3$  (20 mL), dried ( $MgSO_4$ ) and the solvent was removed *in vacuo* to afford a pale yellow oil. Purification by column chromatography on  $SiO_2$  (EtOAc/hexane, 20 $\rightarrow$ 40%) afforded the title THF **17** as a pale yellow foam (130 mg, 0.254 mmol, 67%). This compound exhibited broadening of some signals in its NMR spectra due to restricted rotation.

$[\alpha]_D^{26}$  +1.6 (*c* 0.59,  $CHCl_3$ ).

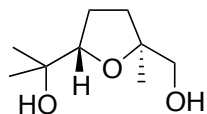
**FT-IR** (neat)  $\nu_{max}$  3468, 2937, 2860, 1728, 1595  $cm^{-1}$ .

**$^1H$ -NMR**  $\delta$  7.62–6.92 (15H, m), 4.06 (1H, td,  $J$  = 10.1 and 3.7 Hz), 3.82 (1H, t,  $J$  = 7.1 Hz), 3.61 (1H, m), 2.15 (1H, m), 2.04–1.90 (2H, m), 1.77–1.57 (4H, m), 1.55–1.35 (2H, m), 1.30–1.02 (3H, m), 1.23 (3H, s), 1.19 (3H, s), 1.10 (3H, s), 0.83 (1H, m) ppm.

**$^{13}C$ -NMR**  $\delta$  173.5, 131.4, 128.8, 127.4, 125.4, 86.1, 83.6, 76.4, 71.1, 61.0, 45.6, 35.1, 32.8, 28.6, 27.0, 25.9, 25.6, 24.6, 24.3, 23.7 ppm.

**LRMS** ( $ES^+$ )  $m/z$  535 ( $[M+Na]^+$ ).

**HRMS** ( $ES^+$ )  $m/z$  For  $C_{34}H_{44}NO_4^+$  ( $[M+NH_4]^+$ ), calculated: 530.3265, found: 530.3270.

**(2S,5S)-Tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-carbaldehyde ((2S,5S)-SI3)**C<sub>9</sub>H<sub>18</sub>O<sub>3</sub>

Mol. wt.: 174.23 g/mol

Colorless oil

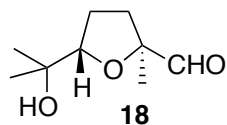
To a stirred solution of ester **17** (800 mg, 1.56 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (28 mL) at rt was added dropwise a solution of DIBAL-H (6.24 mL of 1.0 M in hexanes, 6.24 mmol). The mixture was heated under reflux for 1 h, before cooling to rt and quenching by successive addition of sat. aq. NH<sub>4</sub>Cl (24 mL) and a solution of Rochelle's salt (24 mL, sat. aq.). After vigorous stirring for 30 min, the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (4x30 mL) and Et<sub>2</sub>O (2x30 mL) (monitored by TLC to ensure complete extraction of the diol). The combined organic phases were dried (MgSO<sub>4</sub>), filtered and the solvent was removed under reduced pressure to give the crude diol as a yellow liquid. Purification by column chromatography on SiO<sub>2</sub> (Et<sub>2</sub>O/hexane, 1:1→1:0) afforded the alcohol **(2S,5S)-SI3** as a colorless oil (199 mg, 1.14 mmol, 73%) and (–)-TTC ((–)-**5d**, 448 mg, 1.31 mmol, 84%).

[α]<sub>D</sub><sup>23</sup> –19.8 (*c* 0.69, CHCl<sub>3</sub>).FT-IR (neat) ν<sub>max</sub> 3396, 2970, 2931, 1052 cm<sup>–1</sup>.

<sup>1</sup>H-NMR δ 3.79 (1H, t, *J* = 7.7 Hz), 3.45 (2H, d, *J* = 5.9 Hz), 2.33 (1H, t, *J* = 6.4 Hz), 2.88 (1H, s), (300 MHz, CDCl<sub>3</sub>) 2.02–1.78 (3H, m), 1.65 (1H, m), 1.20 (3H, s), 1.19 (3H, s), 1.13 (3H, s), ppm.

<sup>13</sup>C-NMR δ 86.9, 83.6, 70.8, 68.4, 33.6, 27.4, 26.6, 23.9, 23.8 ppm. (75 MHz, CDCl<sub>3</sub>)

LRMS (ES<sup>+</sup>) *m/z* 197.2 ([M+Na]<sup>+</sup>).HRMS (ES<sup>+</sup>) *m/z* For C<sub>9</sub>H<sub>18</sub>NaO<sub>3</sub><sup>+</sup> ([M+ Na]<sup>+</sup>), calculated: 197.1148, found: 197.1152.

**(2S,5S)-Tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-carbaldehyde (18)**C<sub>9</sub>H<sub>16</sub>O<sub>3</sub>

Mol. wt.: 172.22 g/mol

Colorless oil

To a stirred solution of alcohol **(2S,5S)-SI3** (199 mg, 1.14 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at rt was added Dess–Martin periodinane (620 mg, 1.42 mmol). After 1 h and the reaction mixture was diluted with Et<sub>2</sub>O (35 mL), then sat. aq. NaHCO<sub>3</sub> (35 mL) and sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>5</sub> (14 mL) were added. The mixture was stirred vigorously for 1 h, then the organic layer was separated and the aqueous layer was re-extracted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL), followed by Et<sub>2</sub>O (5x20 mL). The combined organic phases were dried (MgSO<sub>4</sub>), filtered and the solvent was removed under reduced pressure to give the title aldehyde as a colorless oil (197 mg, 1.14 mmol, 100%). The crude isolated aldehyde **18** was used in the subsequent reaction without further purification. <sup>1</sup>H and <sup>13</sup>C NMR data were consistent with reported values.<sup>17</sup>

**[α]<sub>D</sub><sup>24</sup>** +19.0 (*c* 0.46, CHCl<sub>3</sub>).

**FT-IR** (neat)  $\nu_{\max}$  3435, 2976, 2873, 1732 cm<sup>-1</sup>.

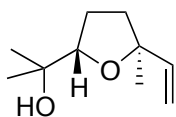
**<sup>1</sup>H-NMR** δ 9.58 (1H, s), 3.86 (1H, dd, *J* = 6.6, 8.4 Hz), 2.15 (1H, m), 1.97–1.82 (2H, m), 1.71 (1H, m), 1.32 (3H, s), 1.28 (3H, s), 1.16 (3H, s), (OH signal not observed) ppm.

**<sup>13</sup>C-NMR** δ 202.7, 87.5, 86.5, 70.7, 32.7, 27.3, 25.9, 24.3, 21.0 ppm.  
(75 MHz, CDCl<sub>3</sub>)

**LRMS** (ES<sup>+</sup>) *m/z* 195 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>) *m/z* For C<sub>9</sub>H<sub>16</sub>NaO<sub>3</sub><sup>+</sup> ([M+ Na]<sup>+</sup>), calculated: 195.0992, found: 195.0997.

<sup>17</sup> (a) Duan, S.; Moeller, K. D. *Org. Lett.* **2001**, 3, 2685–2688. (b) Liu, B.; Duan, S.; Sutterer, S. A. C.; Moeller, K. D., *J. Am. Chem. Soc.* **2002**, 124, 10101–10111.

**(2S,5S)-Tetrahydro-5-methyl-5-vinylfuran-2-yl)propan-2-ol (19) or (2S,5S)-linalool oxide 19**C<sub>10</sub>H<sub>18</sub>O<sub>2</sub>

Mol. wt.: 170.25 g/mol

Colorless oil

DBU (540  $\mu$ L, 3.58 mmol) was added dropwise at rt to a stirred solution of Ph<sub>3</sub>PCH<sub>3</sub>Br (700 mg, 1.92 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL). The mixture was heated to reflux for 45 min. A solution of aldehyde **18** (189 mg, 1.10 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL) was added and the reaction heated under reflux for 48 h. The solvent was removed under reduced pressure and the crude product partitioned between Et<sub>2</sub>O (30 mL) and H<sub>2</sub>O (30 mL). The organic layer was separated, re-extracting the aqueous layer with Et<sub>2</sub>O (3x30 mL). The combined organic phases were washed with sat. aq. NaHCO<sub>3</sub> (20 mL) then dried (MgSO<sub>4</sub>) and concentrated *in vacuo*. The crude product was purified by column chromatography on SiO<sub>2</sub> (Et<sub>2</sub>O/pentane, 0:1→3:7) to give linalool oxide **19** as a colorless oil (120 mg, 0.705 mmol, 64%, er = 97:3). The product was subjected to GC analysis (column: CP-Cyclodextrin-B-236-M-19 (50 m  $\times$  0.25 mm i.d., column temp., 100  $^{\circ}$ C (40-min hold)  $\rightarrow$  1  $^{\circ}$ C/min  $\rightarrow$  130  $^{\circ}$ C). Elution times:  $t_{(2R,5R)\text{-enantiomer}}$  (minor) 38.55,  $t_{(2S,5S)\text{-enantiomer}}$  (major) 40.39 min. The order of elution of the isomers is consistent with the major isomer possessing (2S,5S) absolute configuration.<sup>18</sup> Physical and spectroscopic data were consistent with reported values.<sup>17,19</sup>

**[ $\alpha$ ]<sup>22</sup><sub>D</sub>** +7.6 (*c* 0.6, CHCl<sub>3</sub>) [Lit. +8.33 *c* 0.6, CHCl<sub>3</sub>, 20  $^{\circ}$ C].<sup>17a</sup>

**FT-IR** (neat)  $\nu_{\text{max}}$  3448, 2973, 2873, 1641 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR**  $\delta$  5.88 (1H, dd, *J* = 17.2, 10.6 Hz), 5.19 (1H, dd, *J* = 17.2, 1.7 Hz), 4.99 (1H, dd, *J* = 10.6, 1.7 Hz), 3.80 (1H, t, *J* = 6.9 Hz), 2.16 (1H, s), 1.95–1.68 (4H, m), 1.32 (3H, s), 1.23 (3H, s), 1.14 (3H, s) ppm.

**<sup>13</sup>C-NMR**  $\delta$  143.7, 111.3, 85.5, 83.0, 71.1, 37.5, 27.2, 26.8, 26.3, 24.2 ppm.  
(75 MHz, CDCl<sub>3</sub>)

**LRMS** (ES<sup>+</sup>) *m/z* 193 ([M+Na]<sup>+</sup>).

**HRMS** (ES<sup>+</sup>) *m/z* For C<sub>10</sub>H<sub>18</sub>NaO<sub>2</sub><sup>+</sup> ([M+ Na]<sup>+</sup>), calculated: 193.1199, found: 193.1204.

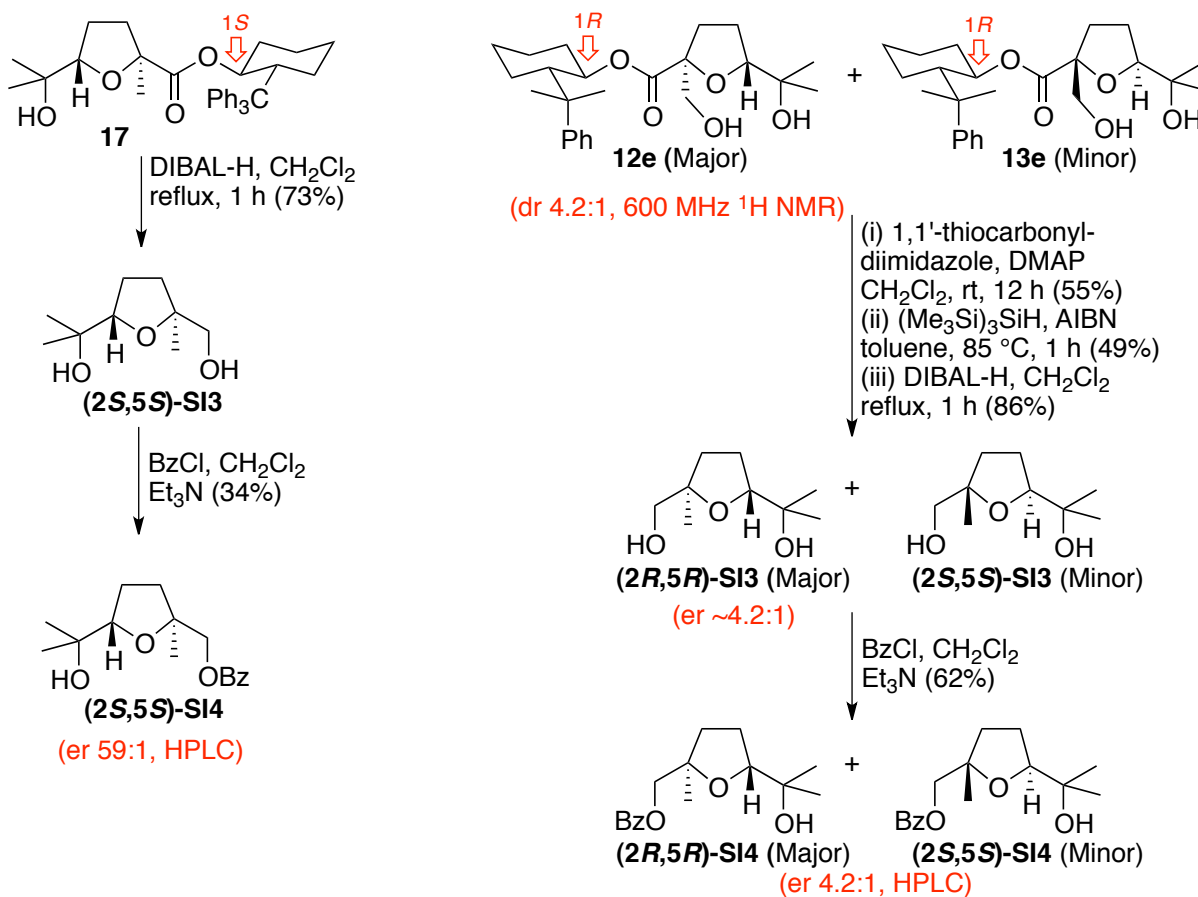
**GC** Column: CP-Cyclodextrin-B-236-M-19 (50 m  $\times$  0.25 mm i.d.) - (*programme*: 100  $^{\circ}$ C (40 min hold)  $\rightarrow$  1  $^{\circ}$ C/min  $\rightarrow$  130  $^{\circ}$ C). Retention times:  $t_{(2R,5R)\text{-enantiomer}}$  38.55,  $t_{(2S,5S)\text{-enantiomer}}$  40.39 min.

<sup>18</sup> Wang, D. M.; Ando, K.; Morita, K.; Kubota, K.; Kobayashi, A., *Biosci. Biotechnol. Biochem.* **1994**, 58, 2050–2053.

<sup>19</sup> (a) Howell, A. R.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2715–2720. (b) Wan, K. K.; Litz, J. P.; Vosburg, D. A., *Tetrahedron: Asymmetry* **2010**, 21, 2425–2428.

## Stereochemical Correlation for oxidative cyclization products from TCC and TTC esters

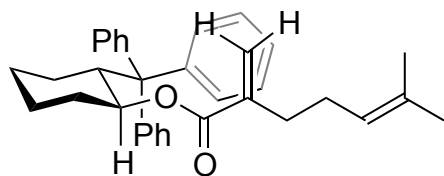
The stereochemistry of the major oxidative cyclization product (–)-**12d** obtained from diene (–)-**7d** ((1*S*,2*R*)-TTC auxiliary) was established through its conversion to (+)-(2*S*,5*S*)-linalool oxide (**19**) as described in the main paper. The sense of diastereoselection observed for the trityl-substituted auxiliary (TTC) was inconsistent with our earlier reported assignment for the oxidation of trienoate **1**, bearing the cumyl-substituted auxiliary (TCC).<sup>20</sup> It transpired that our original assignment of the major stereoisomer from triene oxidation, which was based on comparison of optical rotation data with a known compound, was in error. To unambiguously establish the sense of the diastereofacial selectivity for oxidative cyclization of (1*R*,2*S*)-TCC dienoate (–)-**7e**, the oxidative cyclization products of (1*S*,2*R*)-TTC dienoate (–)-**7d** and (1*R*,2*S*)-TCC dienoate (–)-**7e** were converted to a common intermediate and analyzed by chiral HPLC (Scheme SI2). It is worthy of note that the TTC and TCC auxiliaries possessing the same absolute configurations give rise to opposite signs of optical rotation.



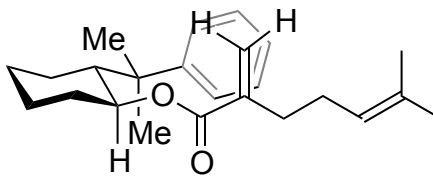
**Scheme SI2.** Conversion of the oxidative cyclization products from (1*S*,2*R*)-TTC and (1*R*,2*S*)-TCC to benzoate esters **(2*S*,5*S*)-SI4** and **(2*R*,5*R*)-SI4** for stereochemical correlation using chiral HPLC.

<sup>20</sup> Sheikh, N. S.; Bataille, C. J.; Luker, T. J.; Brown, R. C. D., *Org. Lett.* **2010**, 12, 2468–2471.

Thus, the diol obtained from reduction of (1*S*,2*R*)-TTC ester **17** was converted to the corresponding mono-benzoate derivative **(2*S*,5*S*)-SI4** (er 59:1, HPLC). The mixture of diastereomeric THF-diols **12e/13e** (from oxidative cyclization of the (1*R*,2*S*)-TCC dienoate **7e**) was taken through the same reaction sequence of radical deoxygenation of the primary alcohol, reductive cleavage of the auxiliary and conversion to the enantiomeric benzoates **(2*R*,5*R*)-SI4** and **(2*S*,5*S*)-SI4**. Chiral HPLC analysis indicated that the major product from the (1*S*,2*R*)-TTC dienoate had the same absolute configuration at the THF 2 and 5 positions as the minor product from the (1*R*,2*S*)-TCC dienoate, confirming that both cyclohexyl auxiliaries impart the same relative sense of diastereofacial selectivity as illustrated in the Figure below.

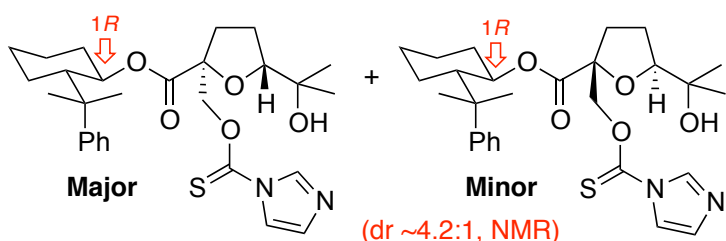


(1*S*,2*R*)-TTC dienoate



(1*S*,2*R*)-TCC dienoate

**(2*S*,5*R*)-(1*R*,2*S*)-2-(2-Phenylpropan-2-yl)cyclohexyl 2-(((1*H*-imidazole-1-carbonothioyl)oxy)methyl)-5-(2-hydroxypropan-2-yl)tetrahydrofuran-2-carboxylate (+ minor diastereoisomer)**



$C_{28}H_{38}N_2O_5S$

Mol. wt.: 514.68 g/mol

White solid

To a solution of THF diol diastereoisomers **12e/13e** (50.7 mg, 0.125 mmol) in  $CH_2Cl_2$  (1.9 mL) was added DMAP (9.0 mg, 0.0376 mmol) and thiocarbonyl diimidazole (67.0 mg, 0.373 mmol) under Ar. The resultant yellow solution was stirred at rt for 21 h. The reaction solution was concentrated in *vacuo* and the resulting crude product was purified by column chromatography on  $SiO_2$  (EtOAc/hexane, 30→50%) to afford the title compound as a white solid (35 mg, 0.068 mmol, 55%).

$[\alpha]_D^{27}$  −8.5 (*c* 0.6,  $CHCl_3$ ).

**FT-IR** (neat)  $\nu_{max}$  3356, 3000, 2972, 1725  $cm^{-1}$ .

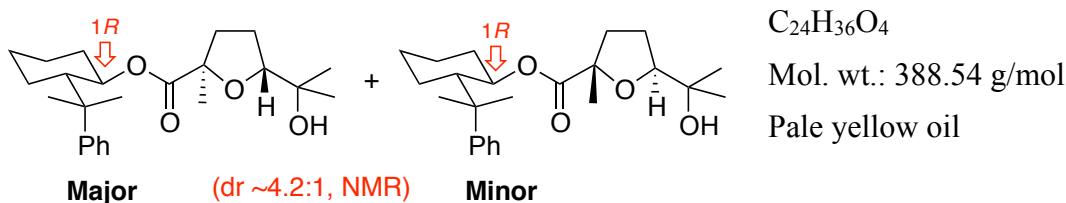
**$^1H$ -NMR**  $\delta$  8.32<sub>maj+min</sub> (1H, s), 7.60<sub>maj+min</sub> (1H, s), 7.30–7.10<sub>maj+min</sub> (5H, m), 7.01<sub>maj+min</sub> (1H, s), 4.90<sub>min</sub> and 4.84<sub>maj+min</sub> (1H, m), 4.70<sub>min</sub> and 4.62<sub>maj</sub> (1H, d, *J* = 11.3 Hz), 4.54<sub>maj</sub> and 4.53<sub>min</sub> (1H, d, *J* = 11.3 Hz), 4.12<sub>maj</sub> and 3.92<sub>min</sub> (1H, m), 2.25–1.85<sub>maj+min</sub> (7H, m), 1.71–1.45<sub>maj+min</sub> (5H, m), 1.34<sub>maj</sub> and 1.31<sub>min</sub> (3H, s,  $CH_3$ ), 1.24<sub>maj+min</sub> (3H, s,  $CH_3$ ), 1.22<sub>maj+min</sub> (3H, s,  $CH_3$ ), 1.12<sub>maj+min</sub> (3H, s,  $CH_3$ ), 1.08–0.90<sub>maj+min</sub> (2H, m) ppm.

**$^{13}C$ -NMR**  $\delta$  184.0<sub>maj</sub> and 183.8<sub>min</sub>, 171.6<sub>maj</sub> and 171.0<sub>min</sub>, 150.8<sub>maj</sub> and 150.5<sub>min</sub>, 137.1<sub>maj+min</sub>, 131.0<sub>min+maj</sub>, 128.2<sub>maj</sub> and 128.1<sub>min</sub>, 125.6<sub>min</sub> and 125.5<sub>maj</sub>, 125.4<sub>maj+min</sub>, 117.8<sub>maj+min</sub>, 88.4<sub>maj</sub> and 87.9<sub>min</sub>, 84.1<sub>maj</sub> and 84.0<sub>min</sub>, 77.2<sub>min</sub> and 77.1<sub>maj</sub>, 75.0<sub>maj</sub> and 74.6<sub>min</sub>, 70.7<sub>maj</sub> and 70.6<sub>min</sub>, 50.4<sub>maj</sub> and 50.3<sub>min</sub>, 40.3<sub>min</sub> and 40.2<sub>maj</sub>, 33.1<sub>maj</sub> and 33.0<sub>min</sub>, 32.98<sub>maj</sub> and 32.1<sub>min</sub>, 27.9<sub>maj</sub> and 27.6<sub>min</sub>, 27.50<sub>maj+min</sub>, 27.4<sub>maj+min</sub>, 26.20<sub>maj+min</sub>, 25.9<sub>min</sub> and 25.7<sub>maj</sub>, 25.6<sub>min</sub>, 24.8<sub>maj+min</sub>, 24.5<sub>maj+min</sub> ppm.

**LRMS** ( $ES^+$ ) *m/z* 515 ( $[M+H]^+$ ).

**HRMS** ( $ES^+$ ) *m/z* For  $C_{28}H_{39}N_2O_5S^+$  ( $[M+H]^+$ ), calculated: 515.2574, found: 515.2572.

**(2*R*,5*R*)-(1*R*,2*S*)-2-(2-Phenylpropan-2-yl)cyclohexyl tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-carboxylate (+ minor diastereoisomer)**



To a solution of the diastereoisomeric thiocarbonyl imidazole derivatives (35 mg, 0.068 mmol) in toluene (3.8 mL) was added AIBN (6 mg, 0.034 mmol), followed by dropwise addition of TMTSS (126  $\mu$ L, 0.409 mmol). The resultant solution was stirred at 85  $^{\circ}$ C for 2 h. The mixture was cooled to rt, and EtOAc (5 mL) was added. The solution was washed with aq.  $NaHCO_3$ , dried ( $MgSO_4$ ) and then concentrated in vacuo. Purification by column chromatography on  $SiO_2$  ( $CH_2Cl_2$ /hexane, 5 $\rightarrow$ 20%) afforded the title THF diastereoisomers as a pale yellow oil (13 mg, 0.033 mmol, 49%).

$[\alpha]_D^{26}$  +24.6 (*c* 0.75,  $CHCl_3$ ).

**FT-IR** (neat)  $\nu_{max}$  3458, 2949, 2927, 2858, 1725  $cm^{-1}$ .

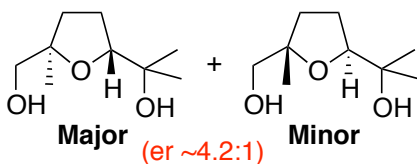
**$^1H$ -NMR**  $\delta$  7.33–7.28<sub>maj+min</sub> (4H, m), 7.16<sub>maj+min</sub> (1H, m), 4.86<sub>min</sub> and 4.79<sub>maj</sub> (1H, td, *J* = 10.0, 4.3 Hz), 3.97<sub>maj</sub> and 3.91<sub>min</sub> (1H, t, *J* = 7.0 Hz), 2.15–1.90<sub>maj+min</sub> (4H, m), 1.87–1.78<sub>maj+min</sub> (2H, m), 1.75–1.50<sub>maj+min</sub> (4H, m), 1.48–1.12<sub>maj+min</sub> (2H, m), 1.37<sub>maj</sub> (3H, s), 1.36<sub>maj</sub> (3H, s), 1.32<sub>min</sub> (3H, s), 1.28<sub>maj</sub> (3H, m), 1.25<sub>maj</sub> (3H, s), 1.14<sub>maj</sub> (3H, s), 1.13<sub>min</sub> (3H, s), 1.11<sub>maj</sub> (1H, m), 0.97<sub>maj</sub> (1H, m) ppm.

**$^{13}C$ -NMR**  $\delta$  174.6<sub>maj</sub> and 174.0<sub>min</sub>, 150.7<sub>min</sub> and 150.6<sub>maj</sub>, 128.3<sub>min</sub> and 128.0<sub>maj</sub>, 125.7<sub>maj+min</sub>, 125.3<sub>maj+min</sub>, 87.0<sub>maj</sub> and 86.9<sub>min</sub>, 83.7<sub>min</sub> and 83.6<sub>maj</sub>, 76.1<sub>maj+min</sub>, 70.9<sub>maj+min</sub>, 50.8<sub>maj</sub> and 50.6<sub>min</sub>, 40.5<sub>min</sub> and 40.4<sub>maj</sub>, 36.6<sub>maj</sub> and 36.0<sub>min</sub>, 33.13<sub>min</sub> and 33.08<sub>maj</sub>, 29.1<sub>maj+min</sub>, 27.6<sub>maj</sub> and 27.5<sub>min</sub>, 27.3<sub>min</sub> and 27.2<sub>maj</sub>, 25.9<sub>maj</sub> and 25.8<sub>min</sub>, 25.84<sub>maj</sub> and 25.77<sub>min</sub>, 25.0<sub>maj</sub> and 24.9<sub>min</sub>, 24.6<sub>maj+min</sub>, 24.4<sub>min</sub> and 24.3<sub>maj</sub>, 24.2<sub>maj</sub> and 24.0<sub>min</sub> ppm.

**LRMS** ( $ES^+$ ) *m/z* 406 ( $[M+NH_4]^+$ ).

**HRMS** ( $ES^+$ ) *m/z* For  $C_{24}H_{36}NaO_4^+$  ( $[M+Na]^+$ ), calculated: 411.2506, found: 411.2508.

**(2*R*,5*R*)-Tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-carbaldehyde ((2*R*,5*R*)-SI3) (+ minor enantiomer)**

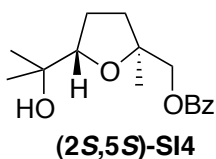


$C_9H_{18}O_3$

Mol. wt.: 174.23 g/mol

Colorless oil

Following the procedure described above for the reduction of **17**, the mixture of diastereoisomeric TCC esters (13 mg, 0.0335 mmol) gave a mixture of enantiomeric diols **(2*R*,5*R*)-SI3** and **(2*S*,5*S*)-SI3** (5 mg, 0.0287 mmol, 86%, er ~ 4.2:1, from  $^1H$  NMR analysis of **12e/13e**). Spectroscopic data were consistent with those reported above for **(2*S*,5*S*)-SI3**.

**((2*S*,5*S*)-5-(2-Hydroxypropan-2-yl)-2-methyltetrahydrofuran-2-yl)methyl benzoate ((2*S*,5*S*)-SI4)**C<sub>16</sub>H<sub>22</sub>O<sub>4</sub>

Mol. wt.: 278.34 g/mol

Pale yellow oil

To a solution of diol **((2*S*,5*S*)-SI3)** (12 mg, 0.0689 mmol), obtained from the (–)-TTC ester, in CH<sub>2</sub>Cl<sub>2</sub> (300 μL) and Et<sub>3</sub>N (48 μL, 0.344 mmol) was added PhCOCl (8 μL, 0.0689 mmol) at rt. After 23 h at rt, the solvent was removed under reduced pressure and Et<sub>2</sub>O (2 mL) was added. The mixture was washed with aq. K<sub>2</sub>CO<sub>3</sub> (2x1 mL of 10% w/v), then with brine (1 mL) and H<sub>2</sub>O (3 mL). The organic phase was dried (MgSO<sub>4</sub>), and the solvent was removed under reduced pressure to afford the crude ester. Purification by column chromatography on SiO<sub>2</sub> (EtOAc/hexane, 5%→30%) afforded the title benzoate **((2*S*,5*S*)-SI4)** as a pale yellow oil (6.5 mg, 0.0233 mmol, 34%), which was analyzed by chiral HPLC giving an enantiomeric ratio of 98.3:1.7.

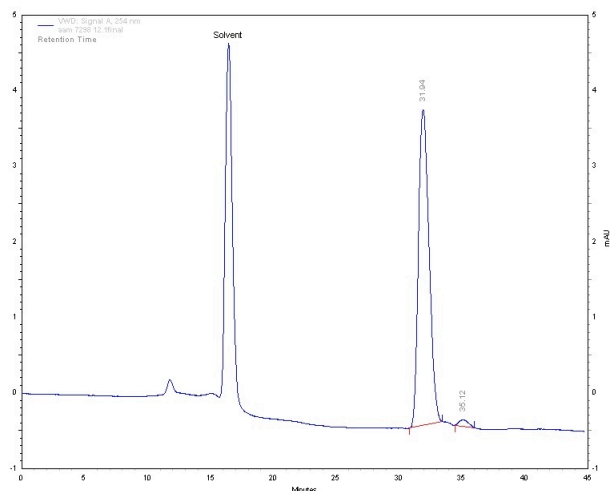
[α]<sub>D</sub><sup>21</sup> +10.0 (*c* 0.11, CHCl<sub>3</sub>).FT-IR (neat) ν<sub>max</sub> 3490, 2974, 2917, 2875, 1720, 1275 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ 8.07 (2H, d, *J* = 7.5 Hz), 7.59 (1H, t, *J* = 7.5 Hz), 7.47 (2H, t, *J* = 7.5 Hz), 4.29 (1H, d, *J* = 10.9 Hz), 4.24 (1H, d, *J* = 10.9 Hz), 3.88 (1H, t, *J* = 7.5 Hz), 2.10 (1H, br), 2.05 (1H, m), 1.96–1.89 (2H, m), 1.80 (1H, m), 1.36 (3H, s), 1.23 (3H, s), 1.15 (3H, s) ppm.

<sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ 166.4, 133.0, 130.2, 129.6, 128.4, 86.6, 81.7, 70.7, 69.9, 34.7, 27.5, 26.3, 24.6, 24.1 ppm.

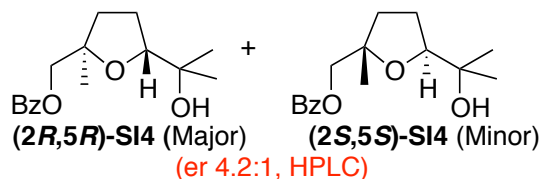
LRMS (ES<sup>+</sup>) *m/z* 301 ([M+Na]<sup>+</sup>).HRMS (ES<sup>+</sup>) *m/z* For C<sub>16</sub>H<sub>22</sub>NaO<sub>4</sub><sup>+</sup> ([M+Na]<sup>+</sup>), calculated: 301.1410, found: 301.1409.

HPLC Chiralpak® AD-H - (eluent: IPA/*n*-hexane 7.5:92.5) - 0.3 mL/min Retention times: *t*<sub>maj</sub> = 31.9 min & *t*<sub>min</sub> = 35.1 min.



Retention Time	Area	Area%
31.94	4110581	98.33
35.12	69933	1.67
Total	4180514	100.00

**((2*R*,5*R*)-5-(2-Hydroxypropan-2-yl)-2-methyltetrahydrofuran-2-yl)methyl benzoate ((2*R*,5*R*)-SI4) (+ minor enantiomer (2*S*,5*S*)-SI4)**



$C_{16}H_{22}O_4$

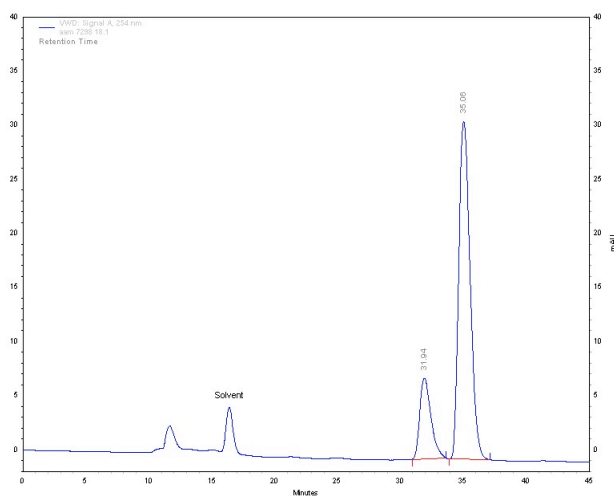
Mol. wt.: 278.34 g/mol

Pale yellow oil

Following the procedure for the benzylation of the (2*S*,5*S*)-diol (**(2*S*,5*S*)-SI3**), the mixture of enantiomeric diols (**(2*R*,5*R*)-SI3** and (**(2*S*,5*S*)-SI3** (5 mg, 0.029 mmol) was converted to the corresponding benzoates (**(2*R*,5*R*)-SI4** and (**(2*S*,5*S*)-SI4** (5 mg, 0.0179 mmol, 62%). Physical and spectroscopic data were consistent with that reported above. The sample was analyzed by chiral HPLC, which showed an enantiomeric ratio of 80.9:19.1 (~4.2:1).

**HPLC**

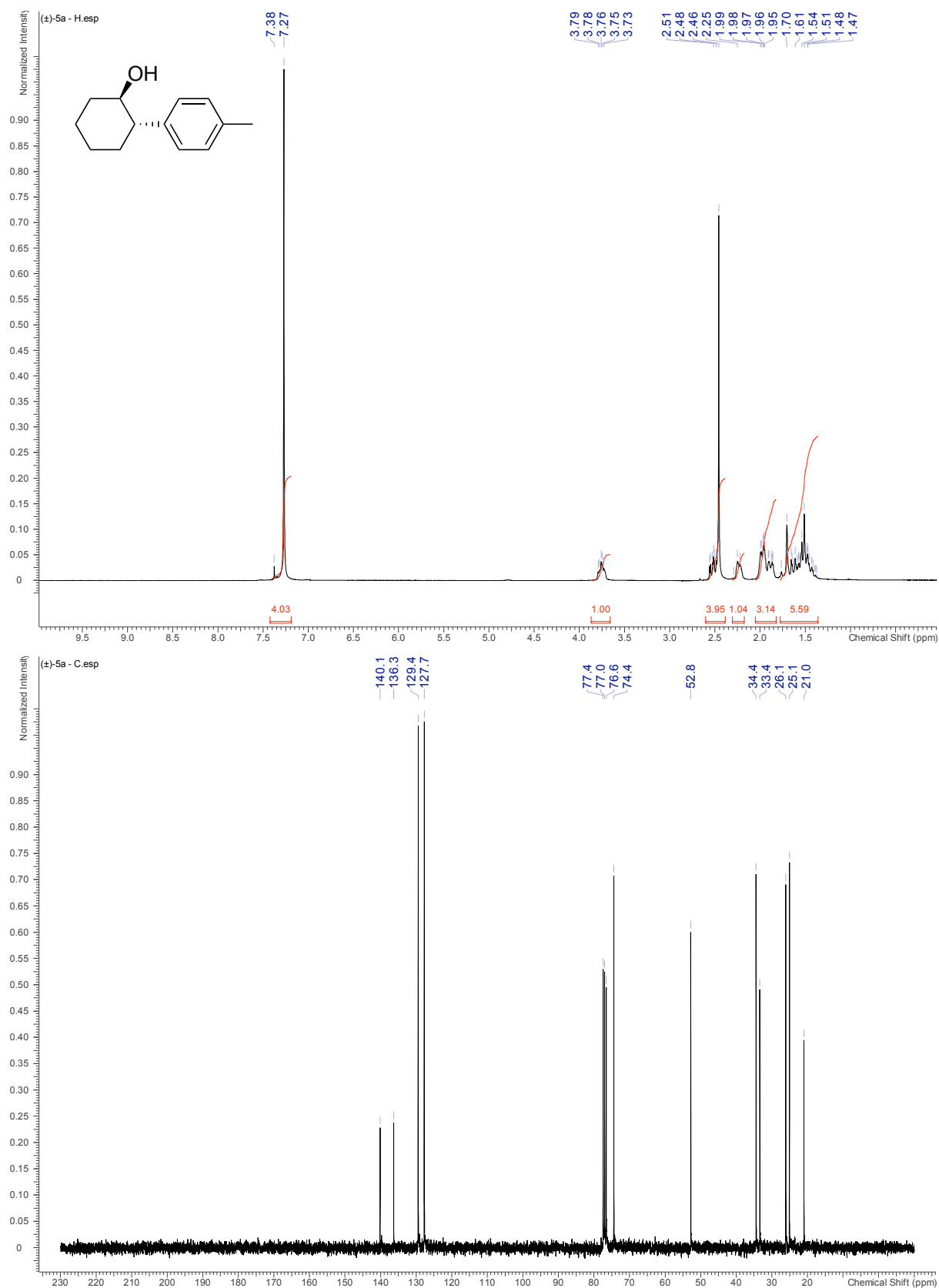
Chiralpak® AD-H - (eluent: IPA/*n*-hexane 7.5:92.5) - 0.3 mL/min Retention times:  $t_{\text{maj}}$  = 35.1 min &  $t_{\text{min}}$  = 31.9 min.

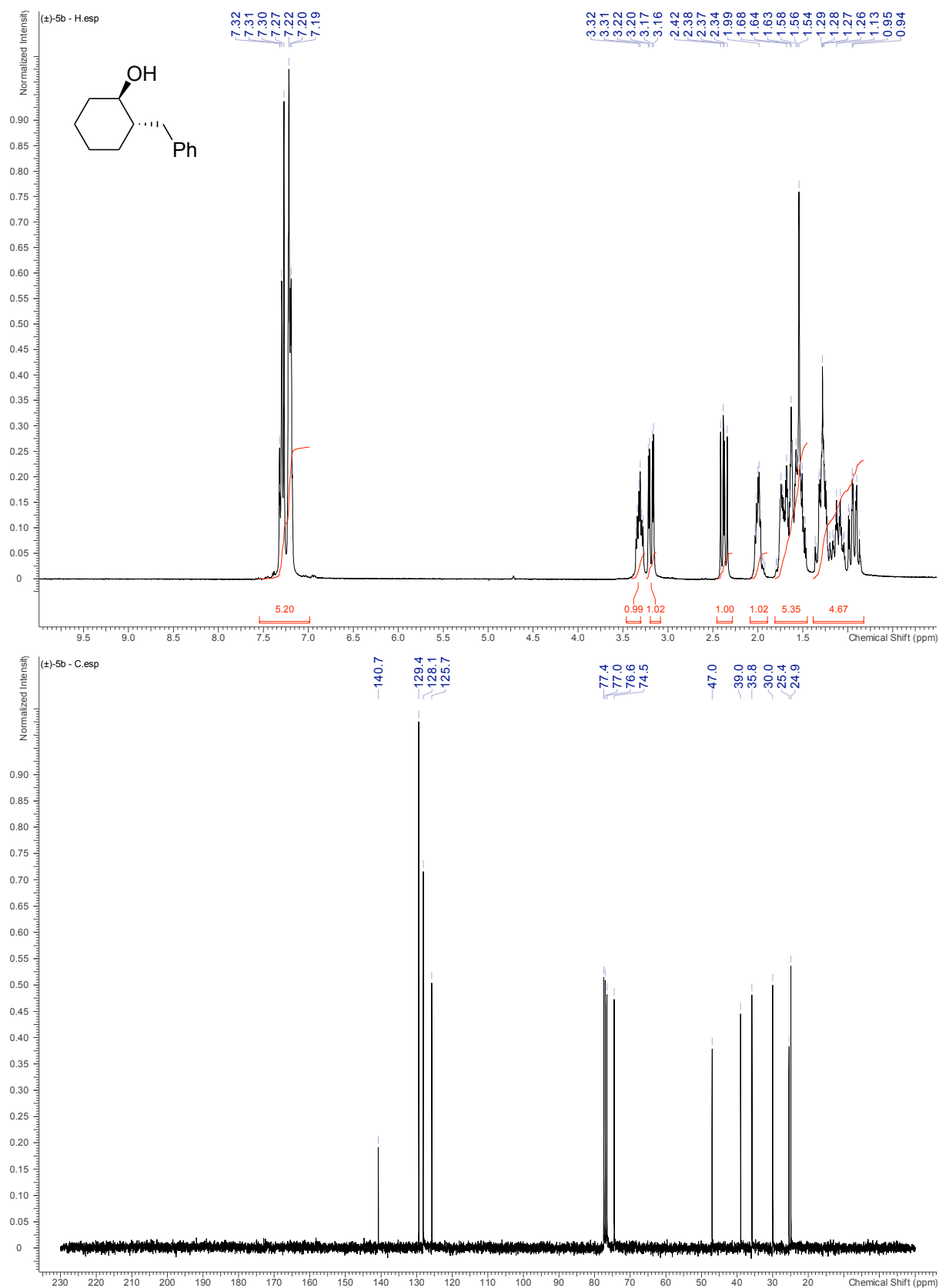


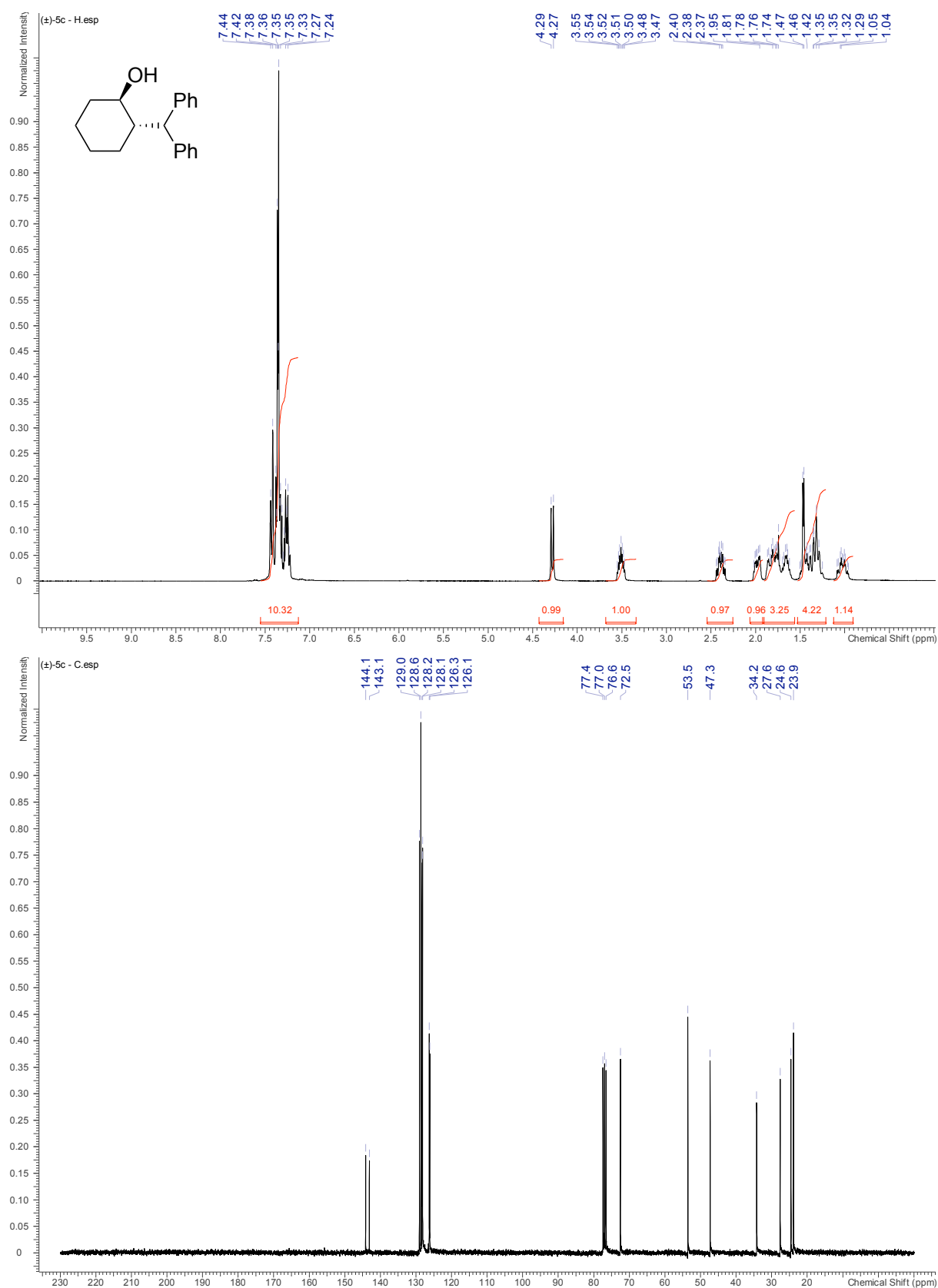
Retention Time	Area	Area%
31.94	7733851	19.12
35.06	32719419	80.88
Total	40453270	100.00

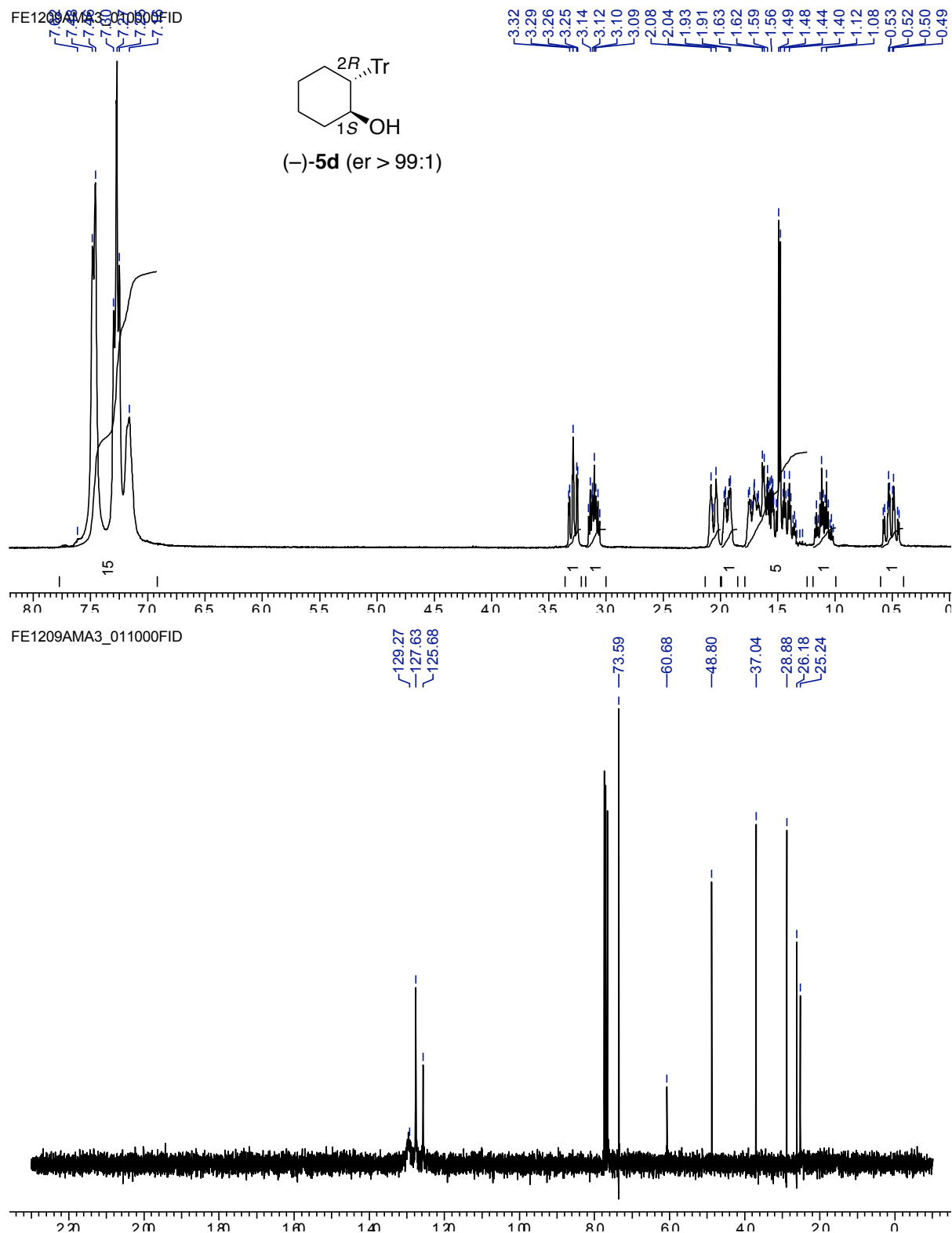
## Copies of NMR spectra

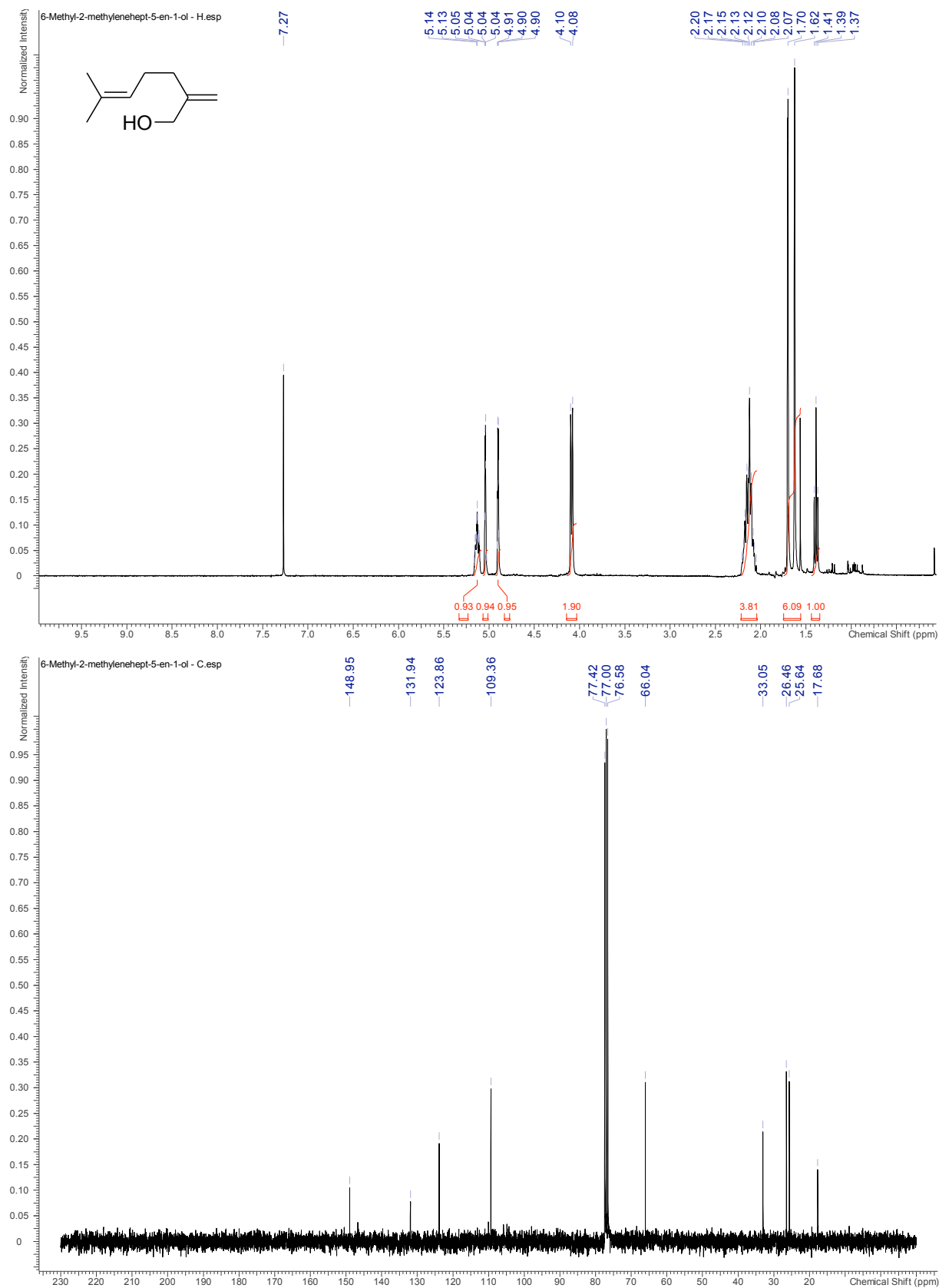
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S50	Index of spectra
S51	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound (±)- <b>5a</b>
S52	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound (±)- <b>5b</b>
S53	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound (±)- <b>5c</b>
S54	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound (–)- <b>5d</b>
S55	<sup>1</sup> H and <sup>13</sup> C NMR spectra for 6-Methyl-2-methylenehept-5-en-1-ol ( <b>SI1</b> )
S56	<sup>1</sup> H and <sup>13</sup> C NMR spectra for 6-methyl-2-methylenehept-5-enal
S57	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound <b>9</b>
S58	<sup>1</sup> H and <sup>13</sup> C NMR spectra for 6-methyl-2-methylenehept-5-enoic acid ( <b>SI2</b> )
S59	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound <b>6b</b>
S60	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound (±)- <b>7a</b>
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S69	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound <b>12c</b> and <b>13c</b>
S70	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound (–)- <b>12d</b>
S71	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound <b>12e</b> and <b>13e</b>
S72	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound (+)- <b>14</b>
S73	<sup>1</sup> H and <sup>13</sup> C NMR spectra for (1 <i>R</i> ,2 <i>S</i> ,5 <i>R</i> )-2-isopropyl-5-methylcyclohexyl ((1 <i>R</i> ,2 <i>S</i> )-2-tritylcyclohexyl) oxalate
S74	<sup>1</sup> H and <sup>13</sup> C NMR spectra for ethyl (1 <i>S</i> ,2 <i>R</i> )-2-tritylcyclohexyl oxalate
S75	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound <b>15</b>
S76	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound (–)- <b>12d</b>
S77	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound <b>16</b>
S78	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound <b>17</b>
S79	<sup>1</sup> H and <sup>13</sup> C NMR spectra for compound <b>18</b>
S80	<sup>1</sup> H and <sup>13</sup> C NMR spectra for (2 <i>S</i> ,5 <i>S</i> )-linalool oxide ( <b>19</b> )
S81	<sup>1</sup> H and <sup>13</sup> C NMR spectra for (2 <i>S</i> ,5 <i>R</i> )-(1 <i>R</i> ,2 <i>S</i> )-2-(2-phenylpropan-2-yl)cyclohexyl 2-(((1 <i>H</i> -imidazole-1-carbonothioyl)oxy)methyl)-5-(2-hydroxypropan-2-yl)tetrahydrofuran-2-carboxylate (+ minor diastereoisomer)
S82	<sup>1</sup> H and <sup>13</sup> C NMR spectra for (2 <i>R</i> ,5 <i>R</i> )-(1 <i>R</i> ,2 <i>S</i> )-2-(2-phenylpropan-2-yl)cyclohexyl tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-carboxylate (+ minor diastereoisomer)
S83	<sup>1</sup> H and <sup>13</sup> C NMR spectra for 2-((2 <i>S</i> ,5 <i>S</i> )-5-(Hydroxymethyl)-5-methyltetrahydrofuran-2-yl)propan-2-ol ( <b>(2<i>S</i>,5<i>S</i>)-SI3</b> ) (From reduction of TTC ester <b>17</b> )
S84	<sup>1</sup> H and <sup>13</sup> C NMR spectra for ((2 <i>S</i> ,5 <i>S</i> )-5-(2-hydroxypropan-2-yl)-2-methyltetrahydrofuran-2-yl)methyl benzoate ( <b>(2<i>S</i>,5<i>S</i>)-SI4</b> )

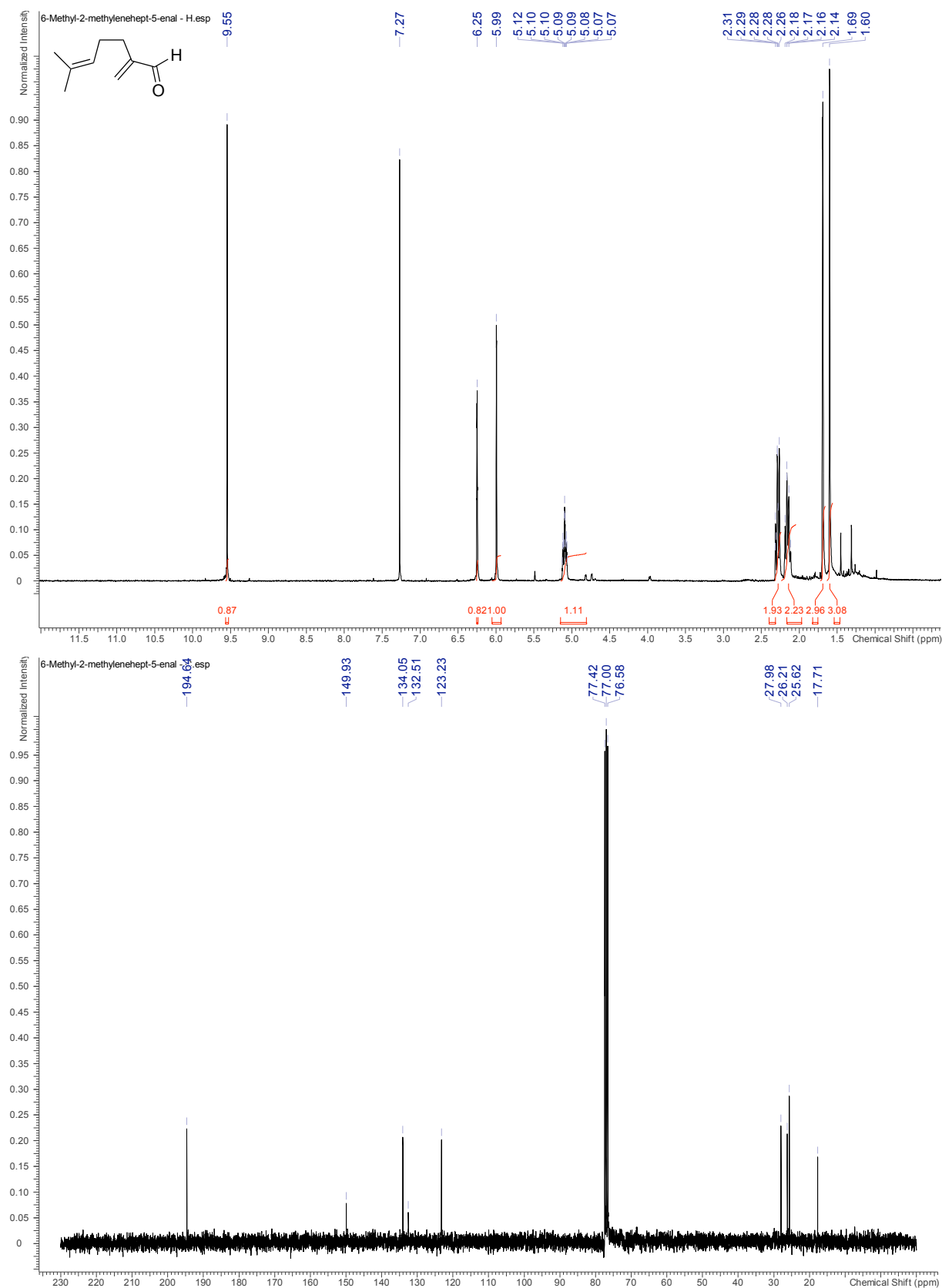
**(1*R*\*,2*S*\*)-2-*p*-Tolylcyclohexanol ((±)-5a)**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

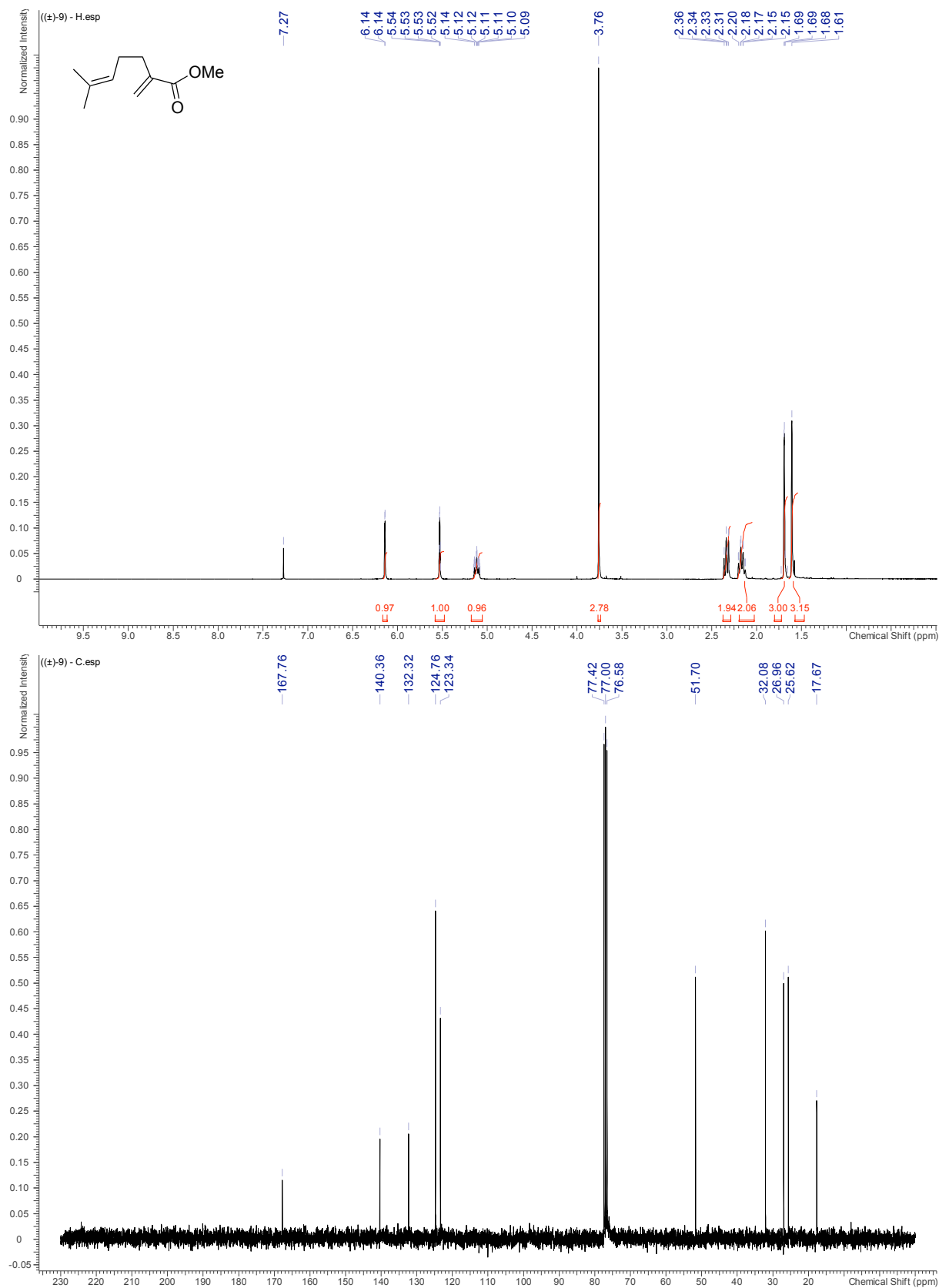
**(1*R*\*,2*S*\*)-2-Benzylcyclohexanol ((±)-5b)**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

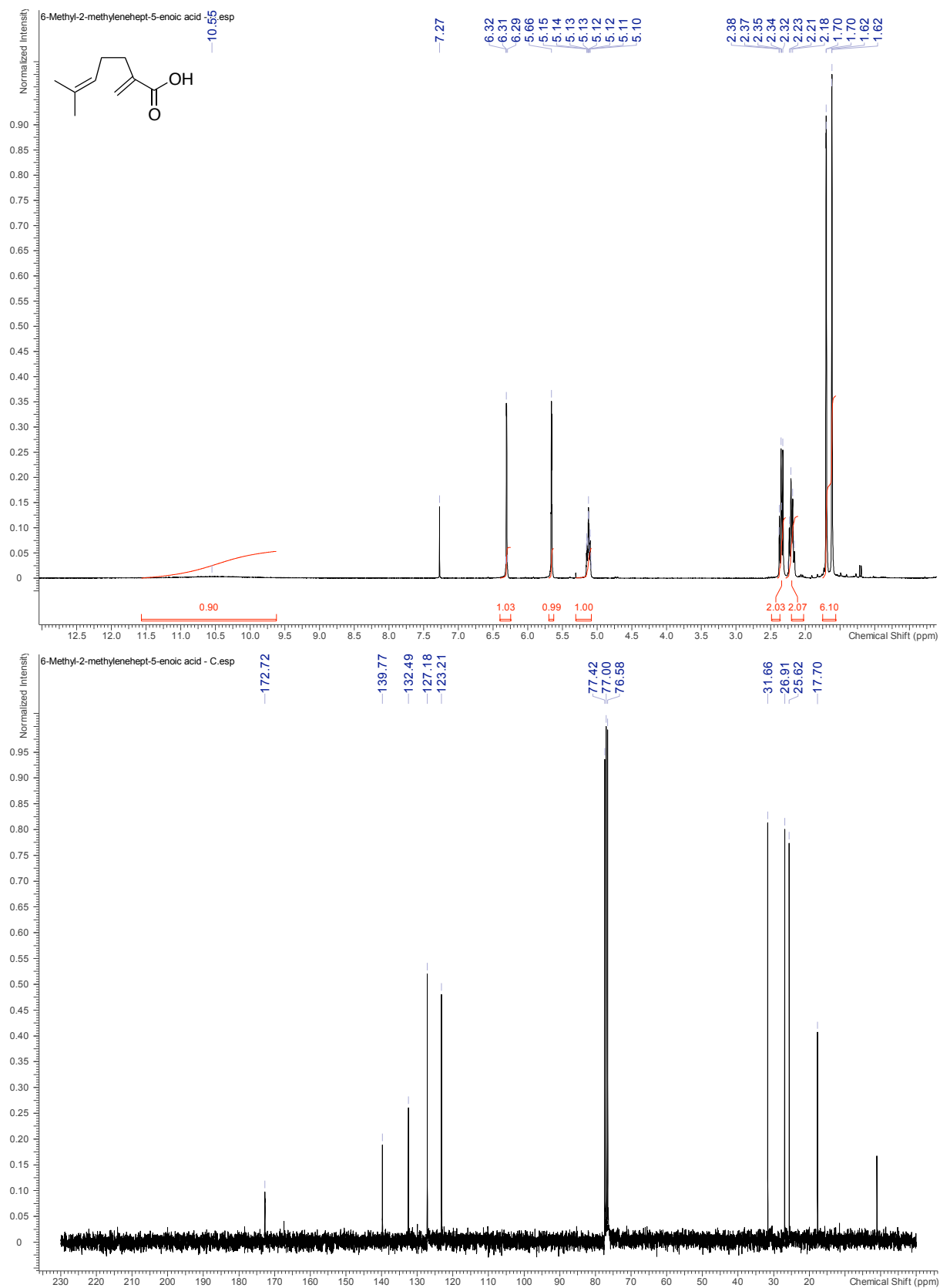
**(1*R*\*,2*S*\*)-2-Benzhydrylcyclohexanol ((±)-5c)**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

**(-)-(1*S*,2*R*)-Triphenylmethyl cyclohexanol ((-)-5d)**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)

**6-Methyl-2-methylenehept-5-en-1-ol (SI1)** $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

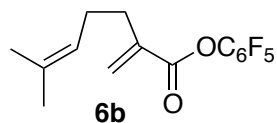
**6-Methyl-2-methylenehept-5-enal** $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

**Methyl 6-methyl-2-methylenehept-5-enoate (9)** $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

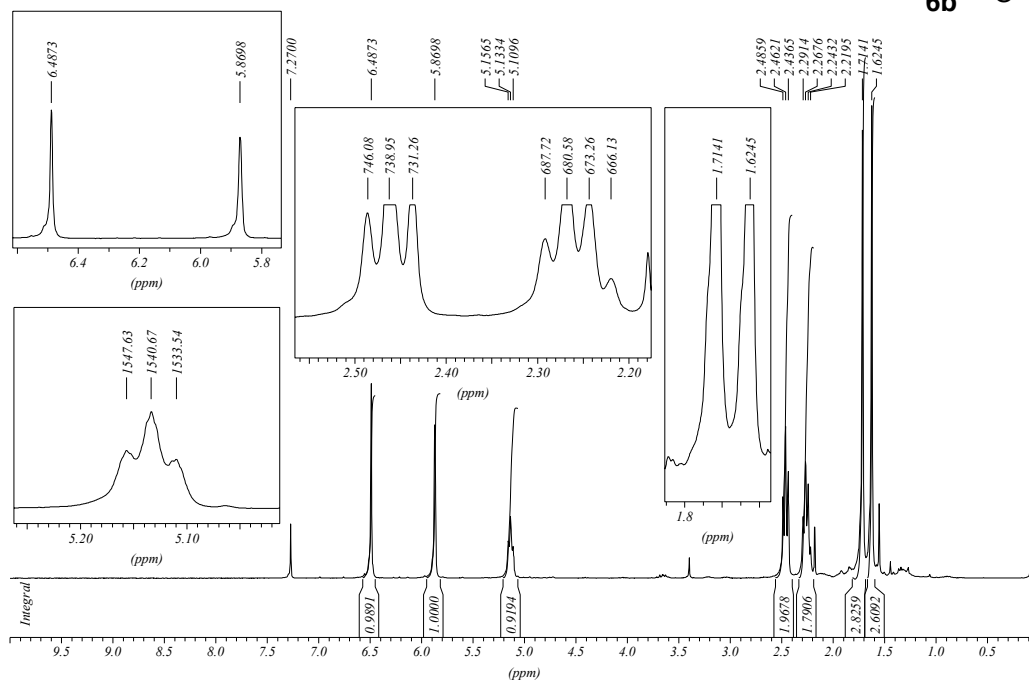
**6-Methyl-2-methylenehept-5-enoic acid (S12)** $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

# Perfluorophenyl 6-methyl-2-methylenehept-5-enoate (6b)

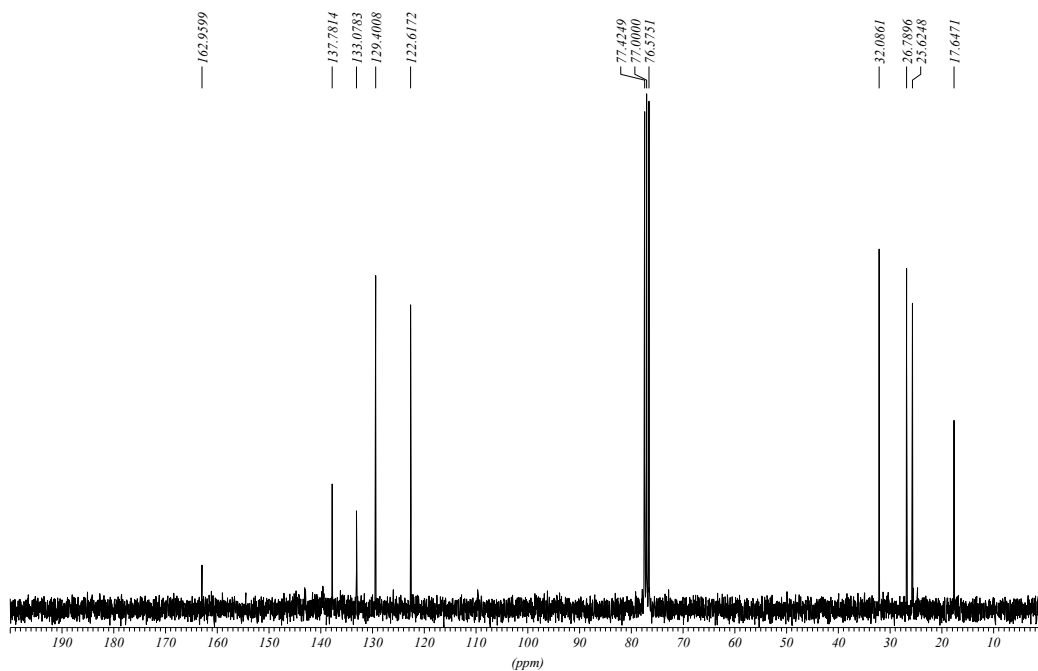
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

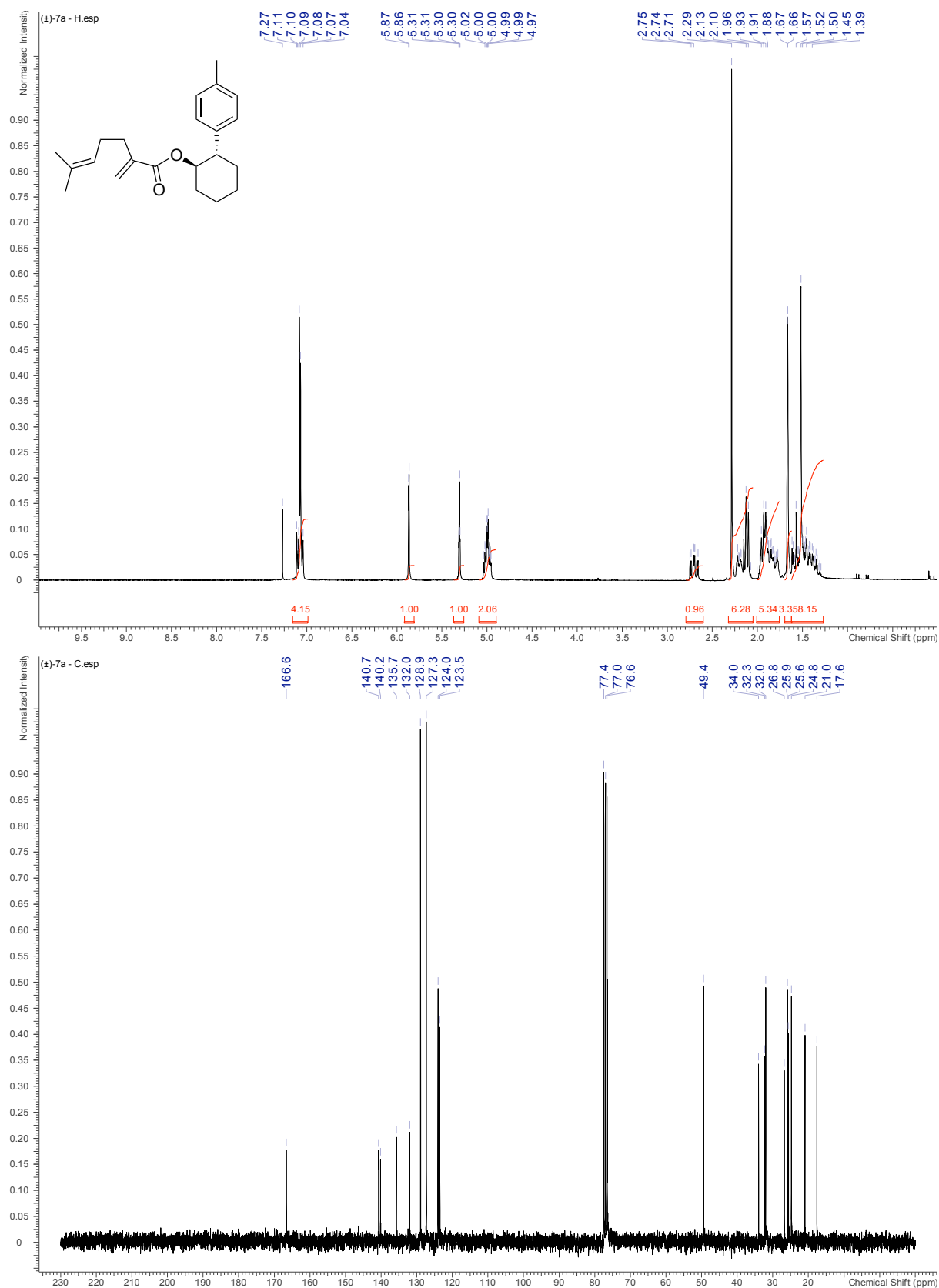


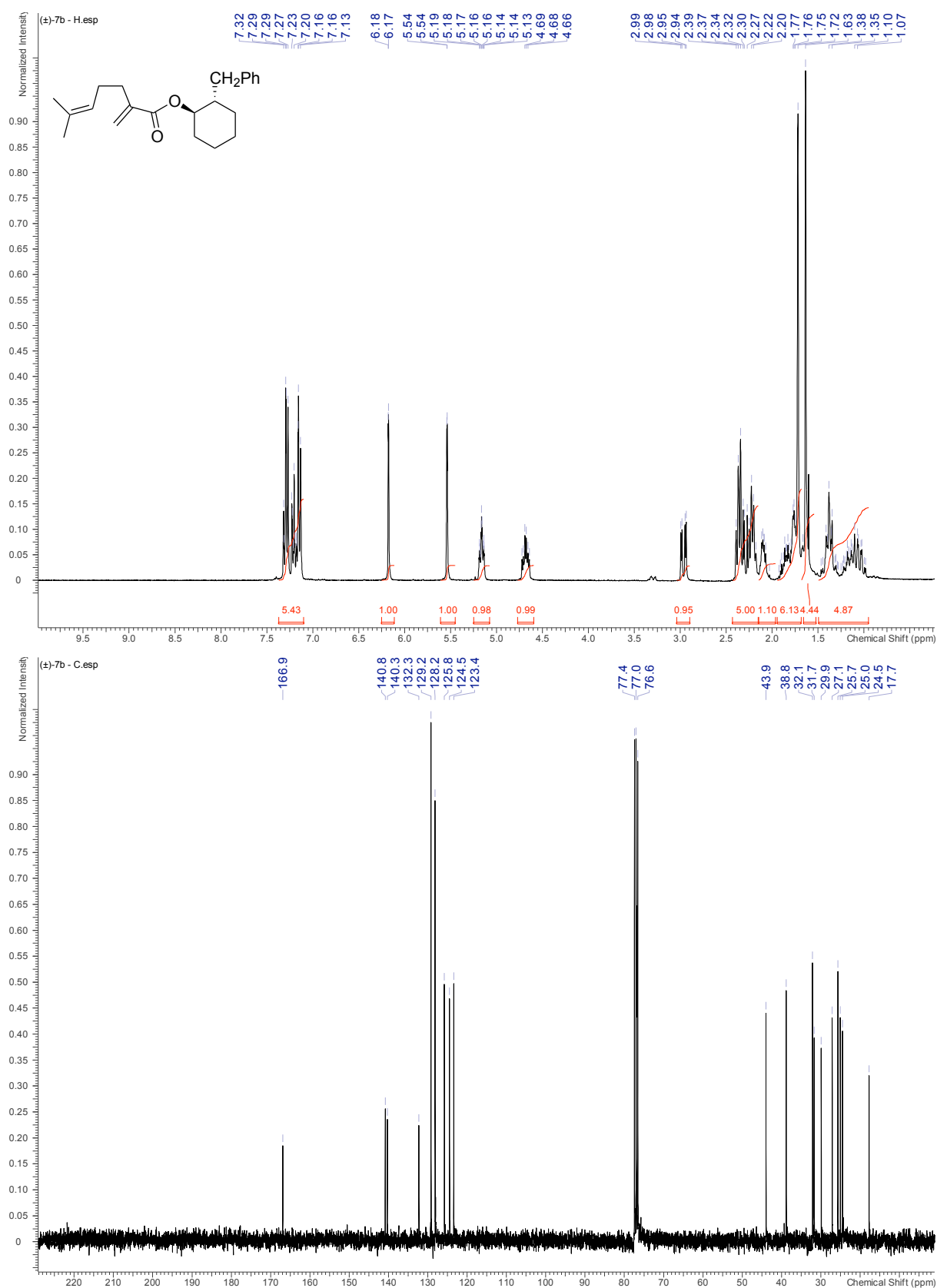
nss/419785 (Product)



nss/419785 (Product)

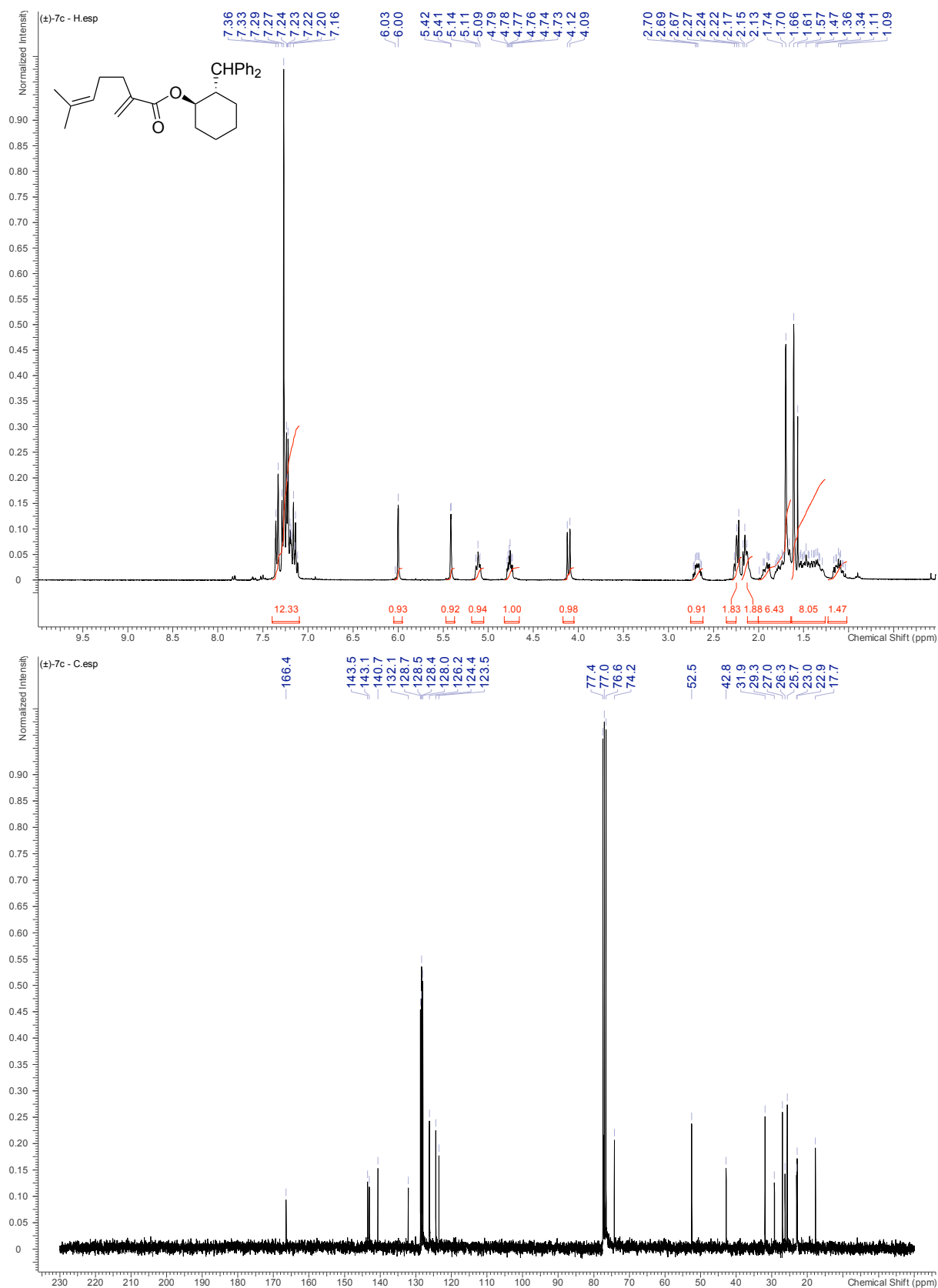


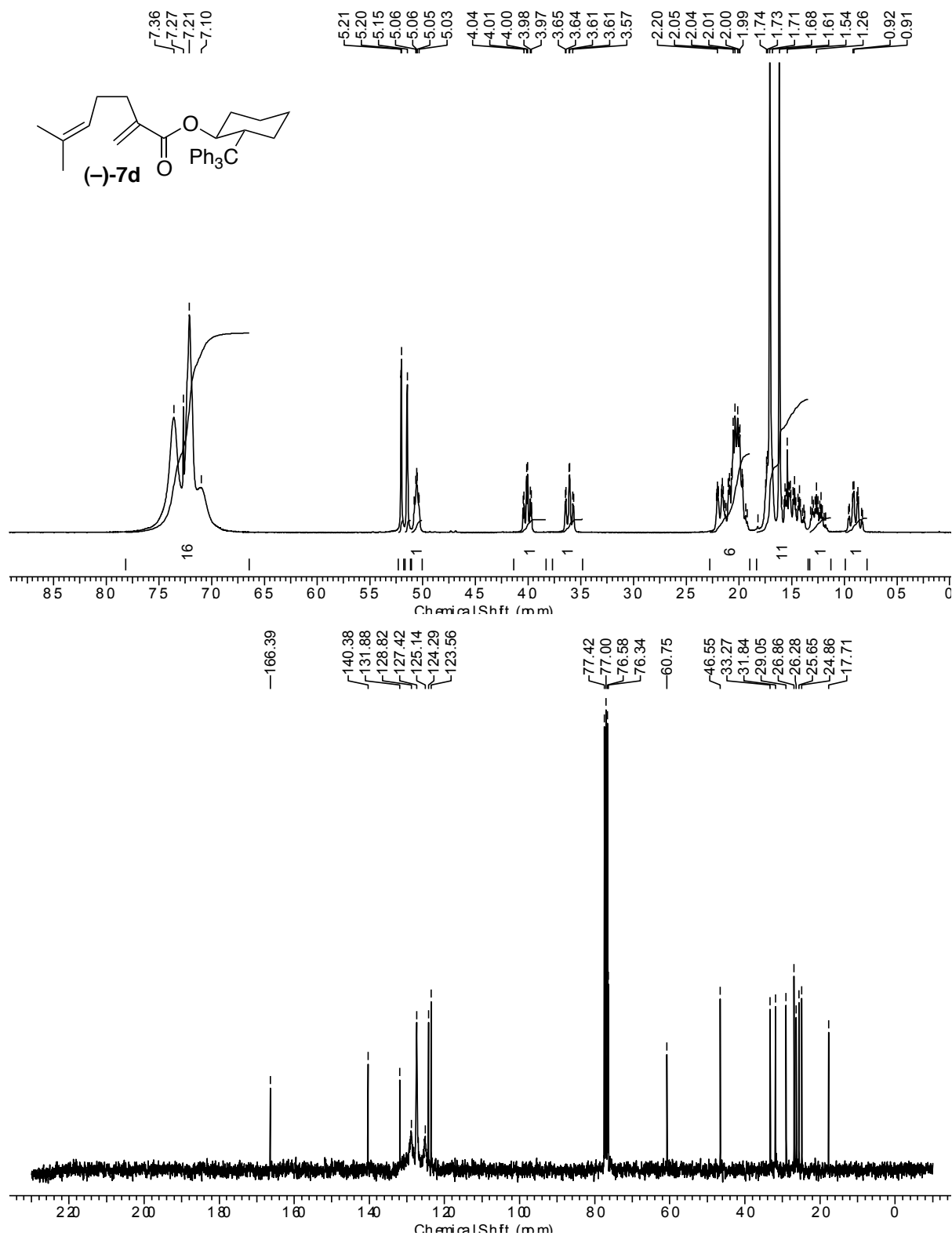
**(1*R*\*,2*S*\*)-2-*p*-Tolylcyclohexyl 6-methyl-2-methylenehept-5-enoate ((±)-7a)**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

**(1*R*\*,2*S*\*)-2-Benzylcyclohexyl 6-methyl-2-methylenehept-5-enoate ((±)-7b)**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

**(1*R*\*,2*S*\*)-2-Benzhydrylcyclohexyl 6-methyl-2-methylenehept-5-enoate ((±)-7c)**

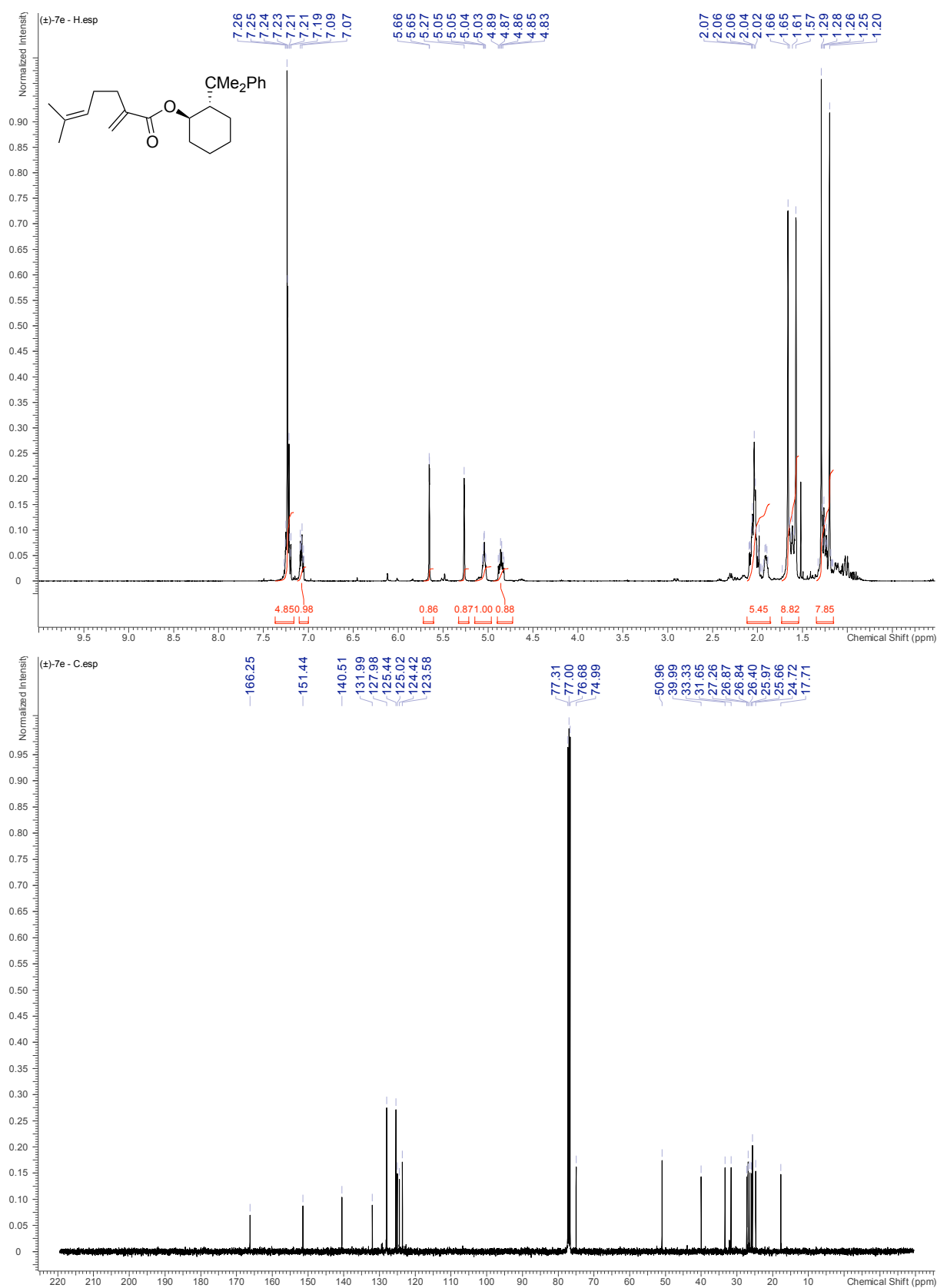
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



**(1*S*,2*R*)-2-Tritylcyclohexyl 6-methyl-2-methylenehept-5-enoate ((-)-7d)**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

**(1*R*,2*S*)-2-(2-Phenylpropan-2-yl)cyclohexyl-6-methyl-2-methylenehept-5-enoate ((-)-7e)**

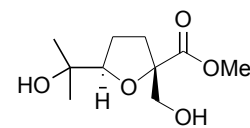
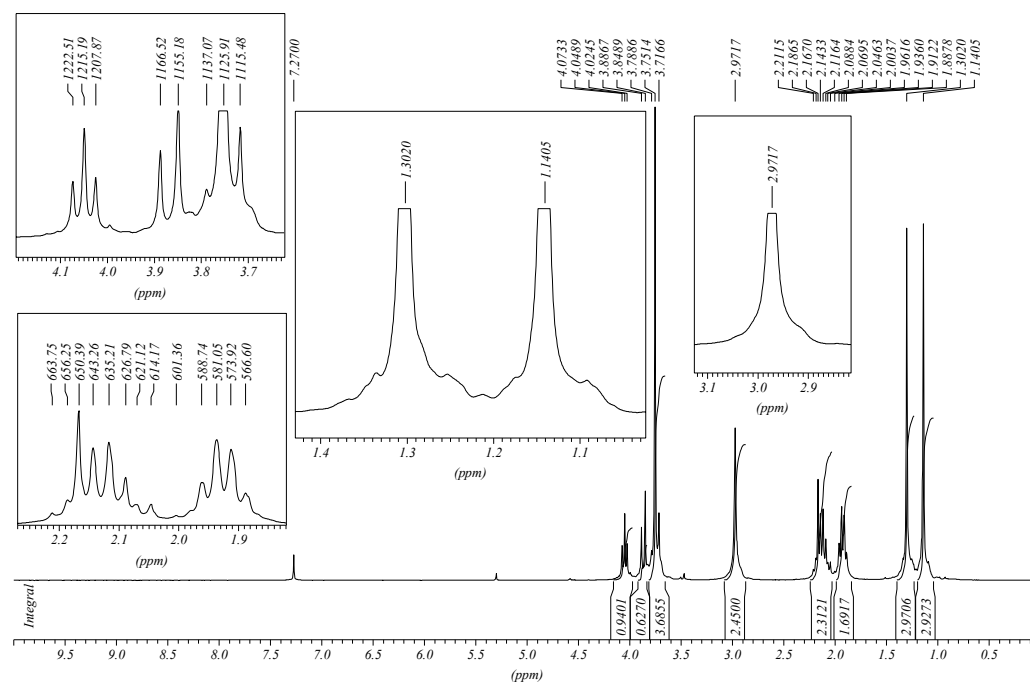
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



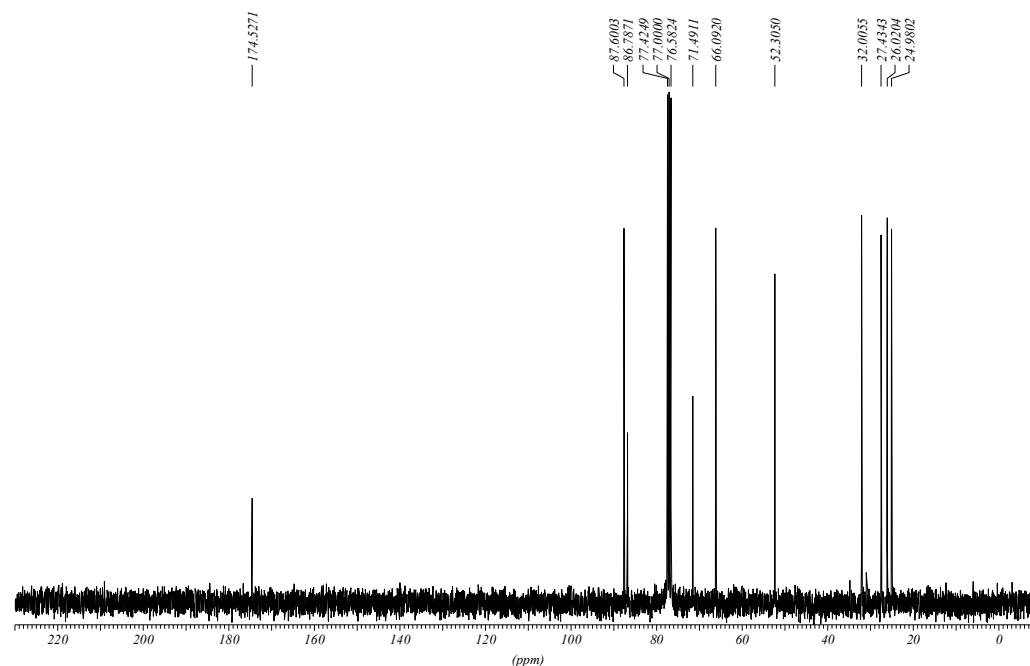
**(2*S*,5*R*)-Methyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate ((±)-10)**

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

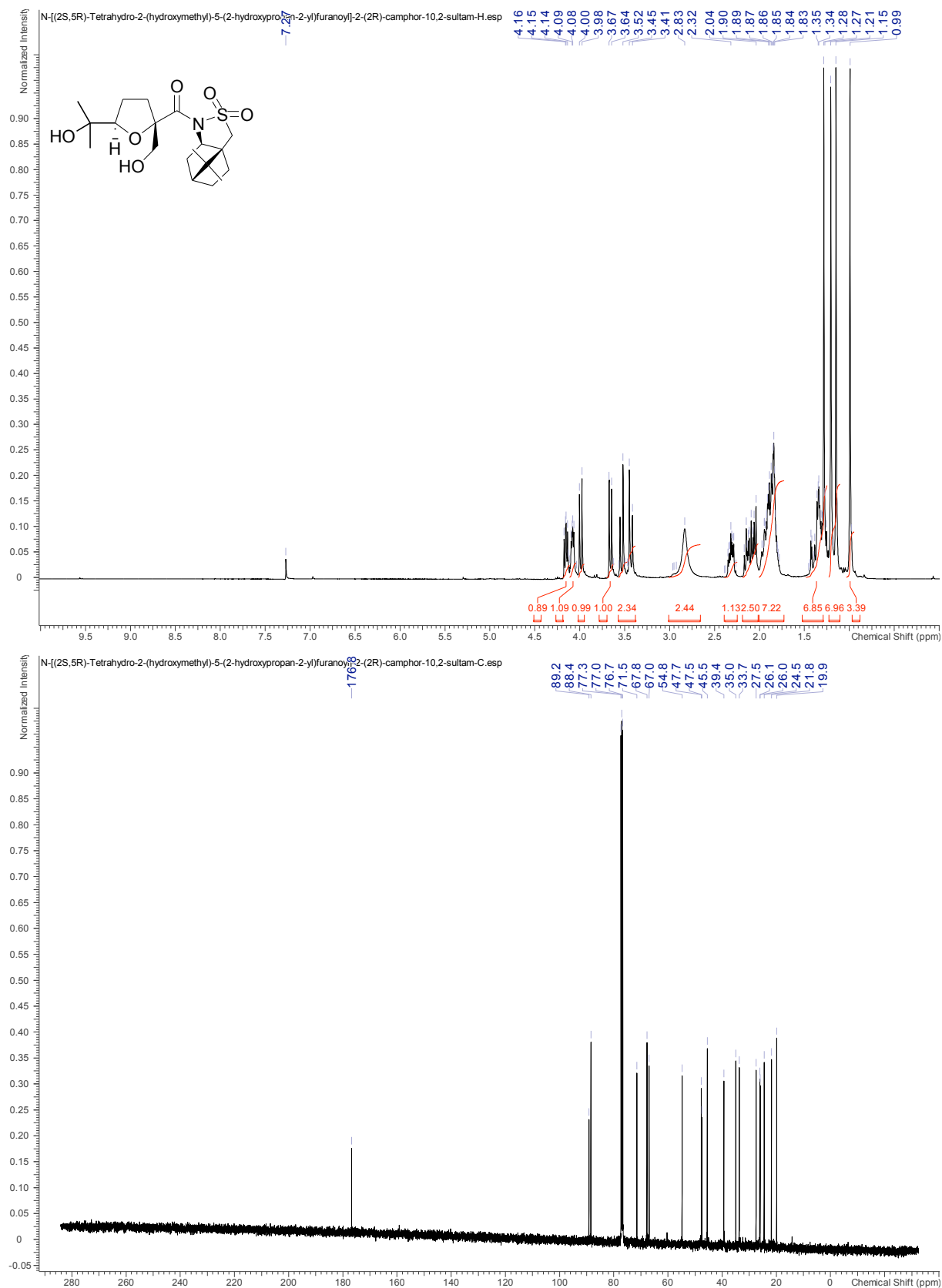
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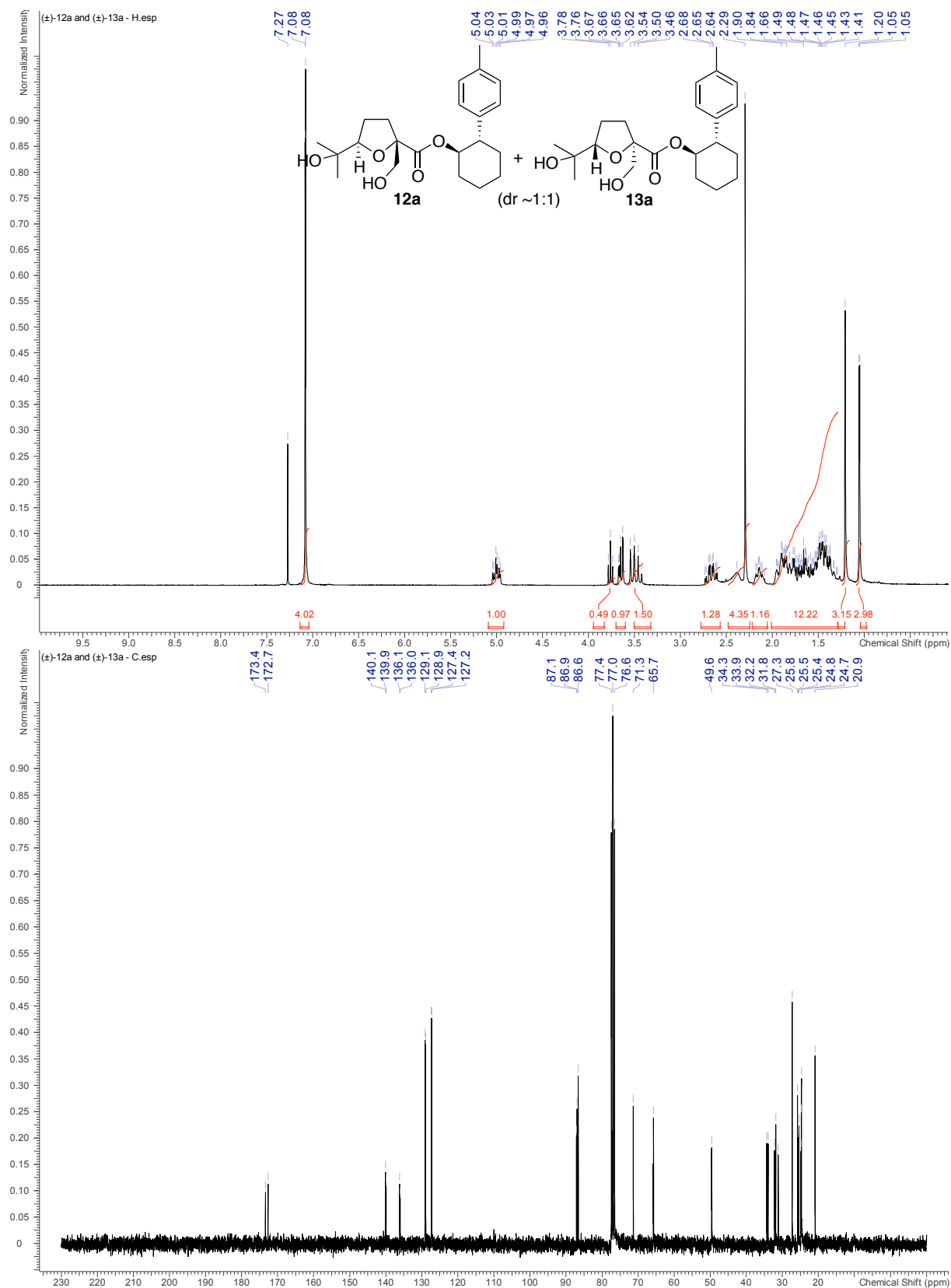
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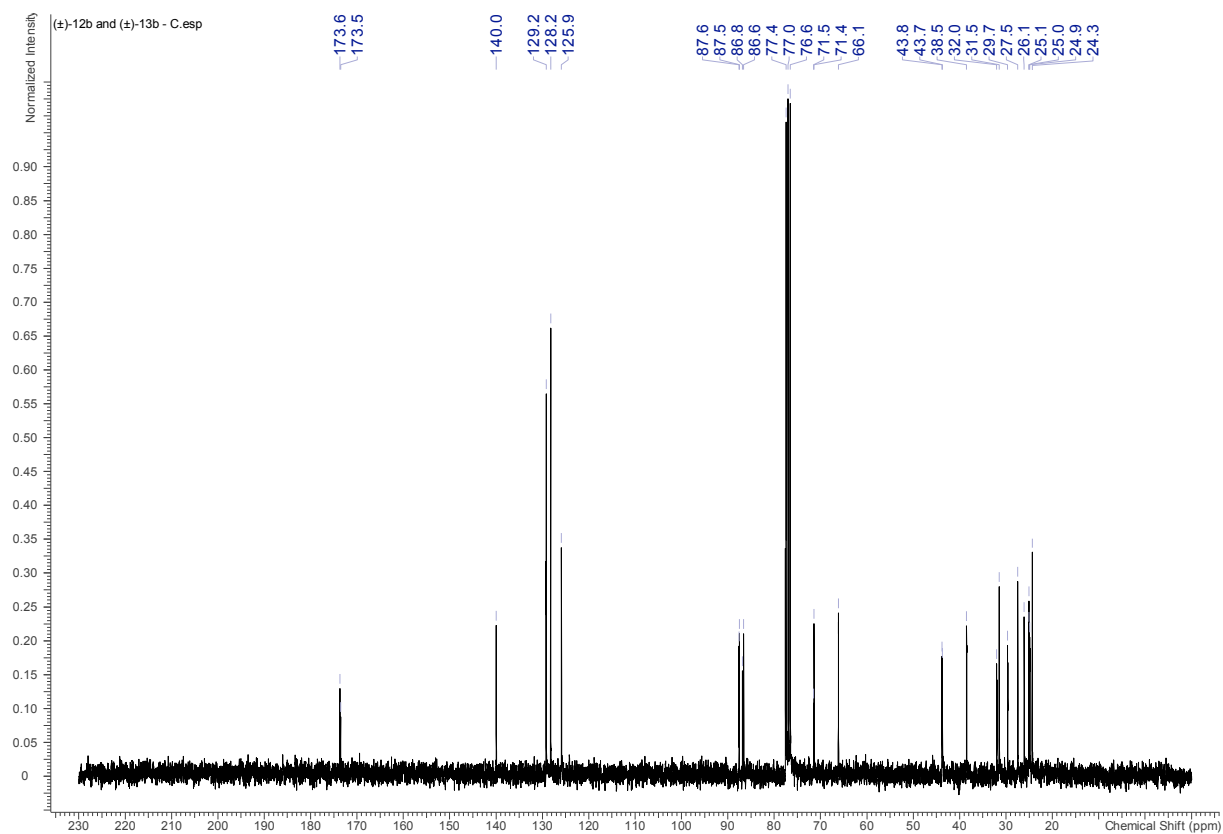
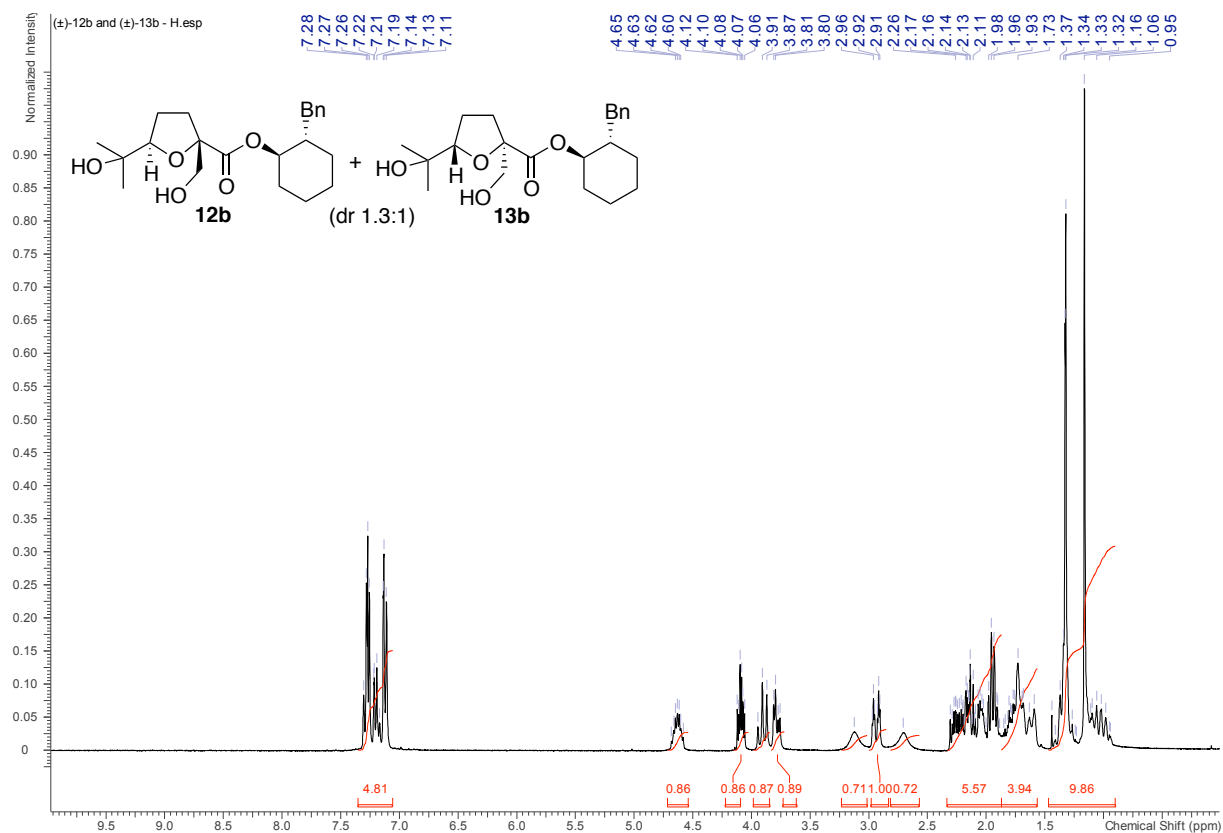
***N*-[(2*S*,5*R*)-Tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furanoyl]-2-(2*R*)-camphor-10,2-sultam ((-)-11)** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



**(2*S*\*,5*R*\*)-(1*S*\*,2*R*\*)- 2-*p*-Tolylcyclohexyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl) furan-2-carboxylate (12a) and (2*R*\*,5*S*\*)-(1*S*\*,2*R*\*)- 2-*p*-Tolylcyclohexyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (13a)** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

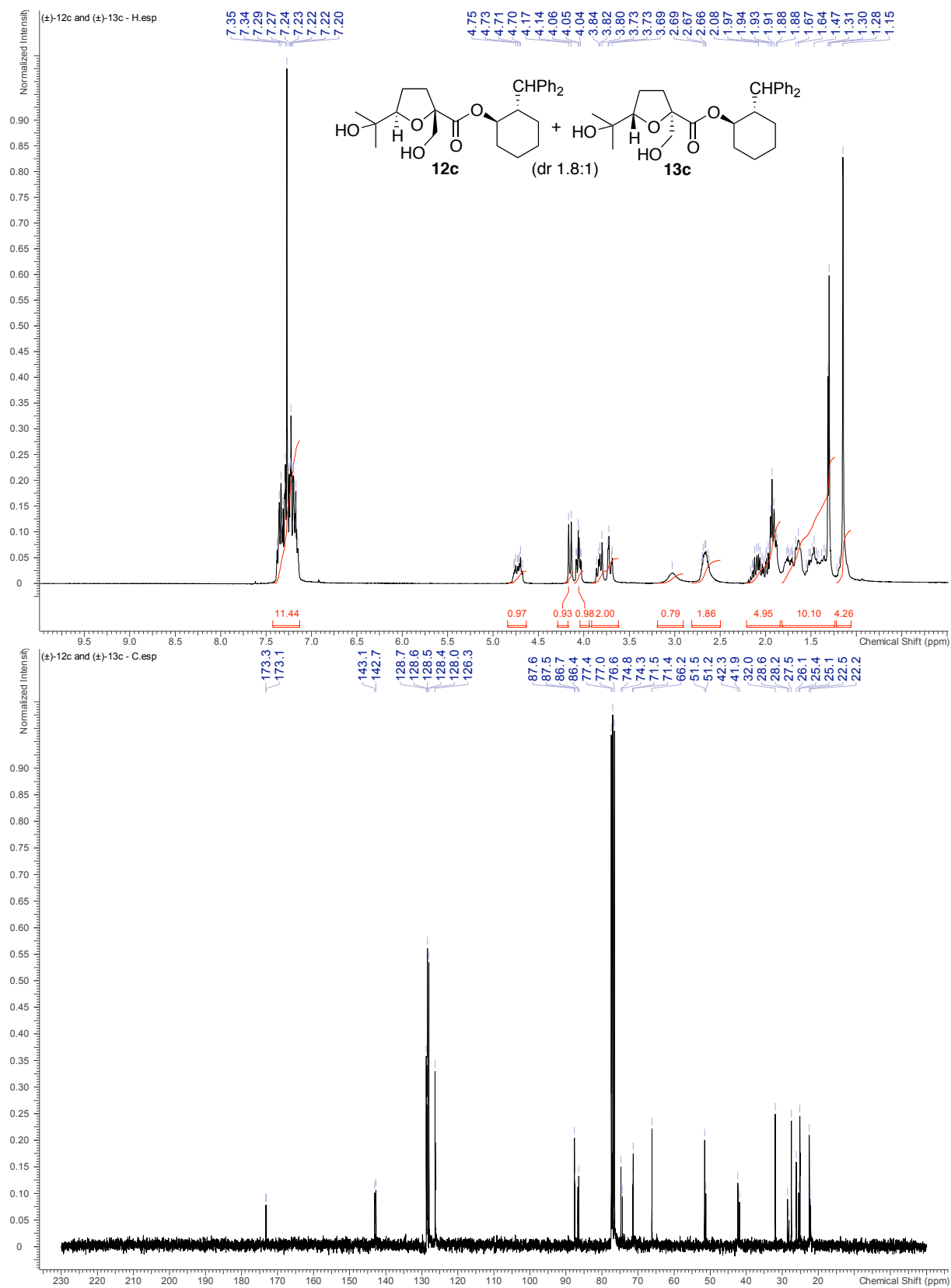


**(2*S*\*,5*R*\*)-(1*R*\*,2*S*\*)-2-Benzylcyclohexyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxy propan-2-yl) furan-2-carboxylate (12b) and (2*R*\*,5*S*\*)-(1*R*\*,2*S*\*)-2-Benzylcyclohexyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (13b)** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)



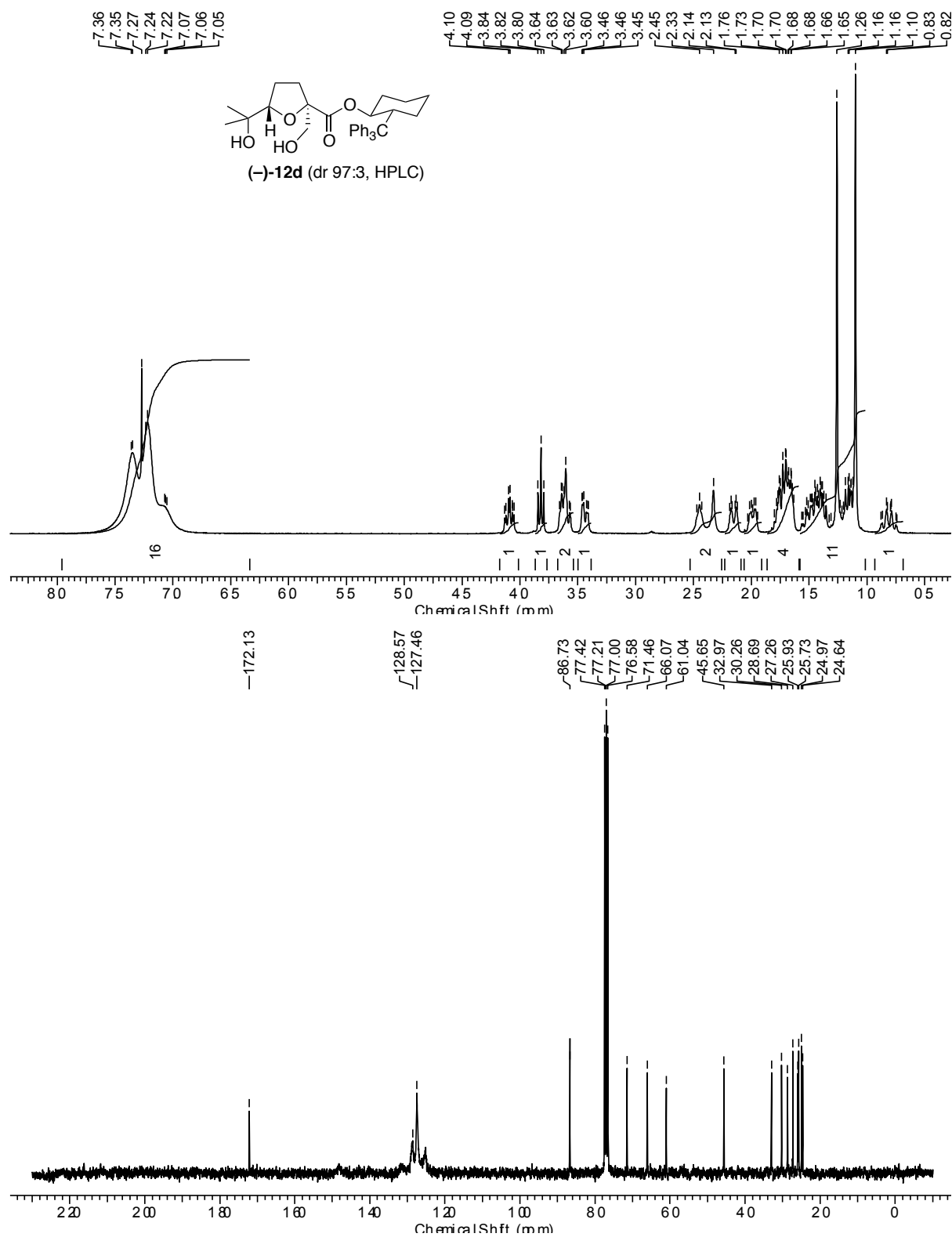
**(2*S*\*,5*R*\*)-(1*R*\*,2*S*\*)-2-Benzhydrylcyclohexyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl) furan-2-carboxylate (12c) and minor diastereoisomer (13c)**

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)



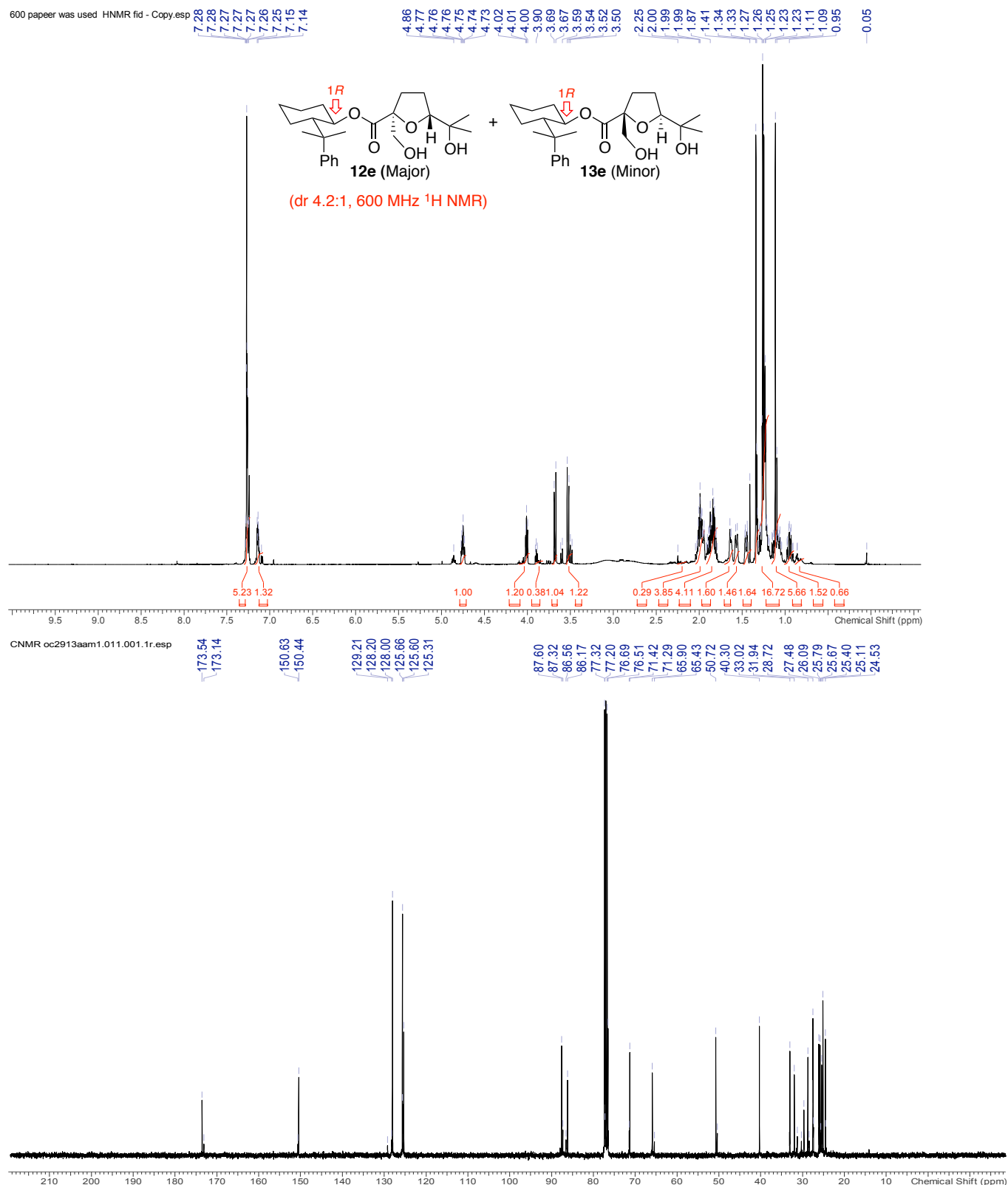
**(2*R*,5*S*)-(1*R*,2*S*)-2-Tritylcyclohexyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate ((-)-12d)**

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)



**(1*R*,2*S*)-2-(2-Phenylpropan-2-yl)cyclohexyl (2*S*,5*R*)-tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (12e) and (1*R*,2*S*)-2-(2-Phenylpropan-2-yl) (2*R*,5*S*)-cyclohexyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (13e)**

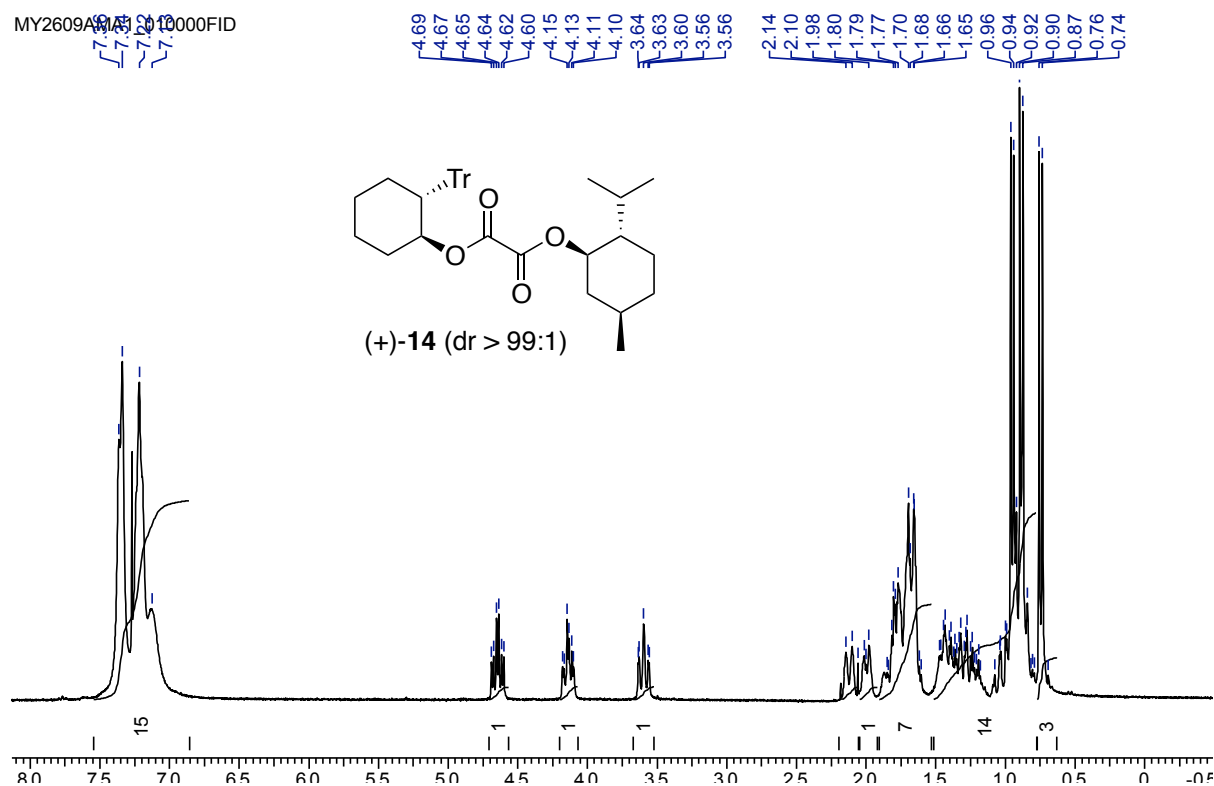
$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



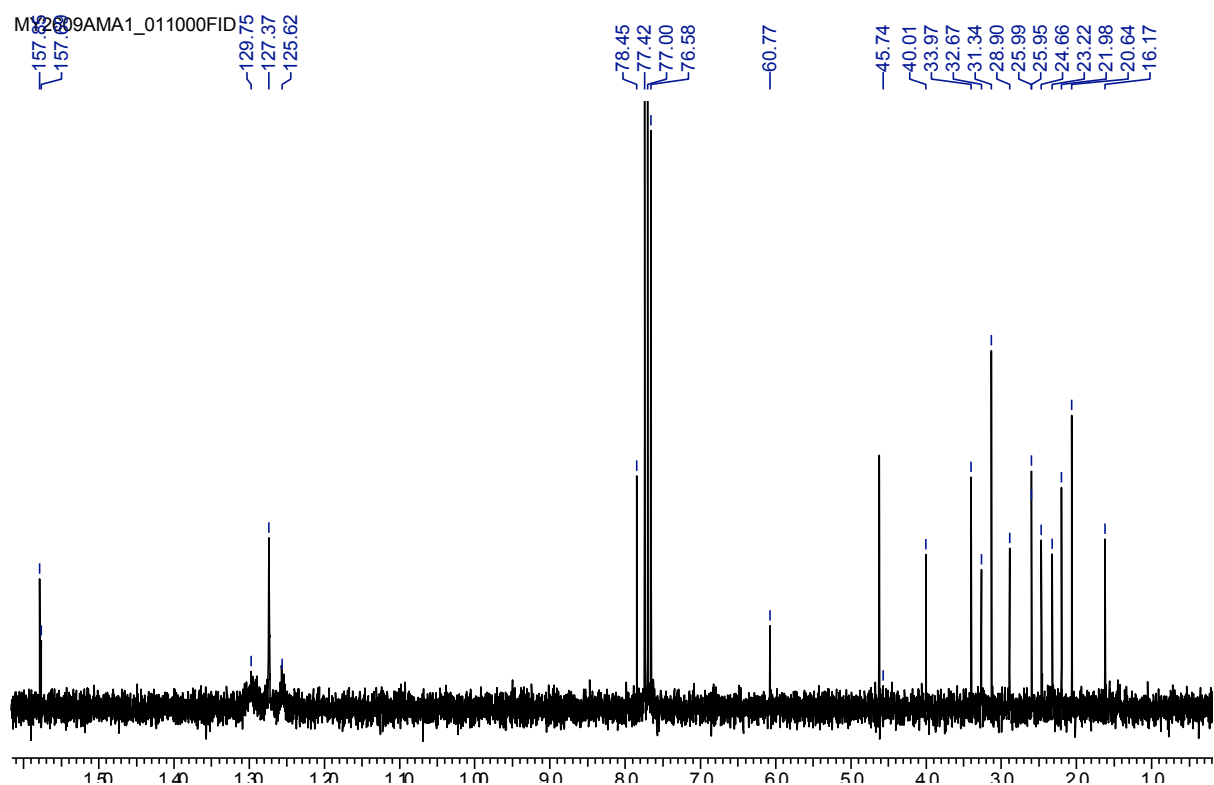
**(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl (1*S*,2*R*)-2-tritylcyclohexyl oxalate ((+)-14)**

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

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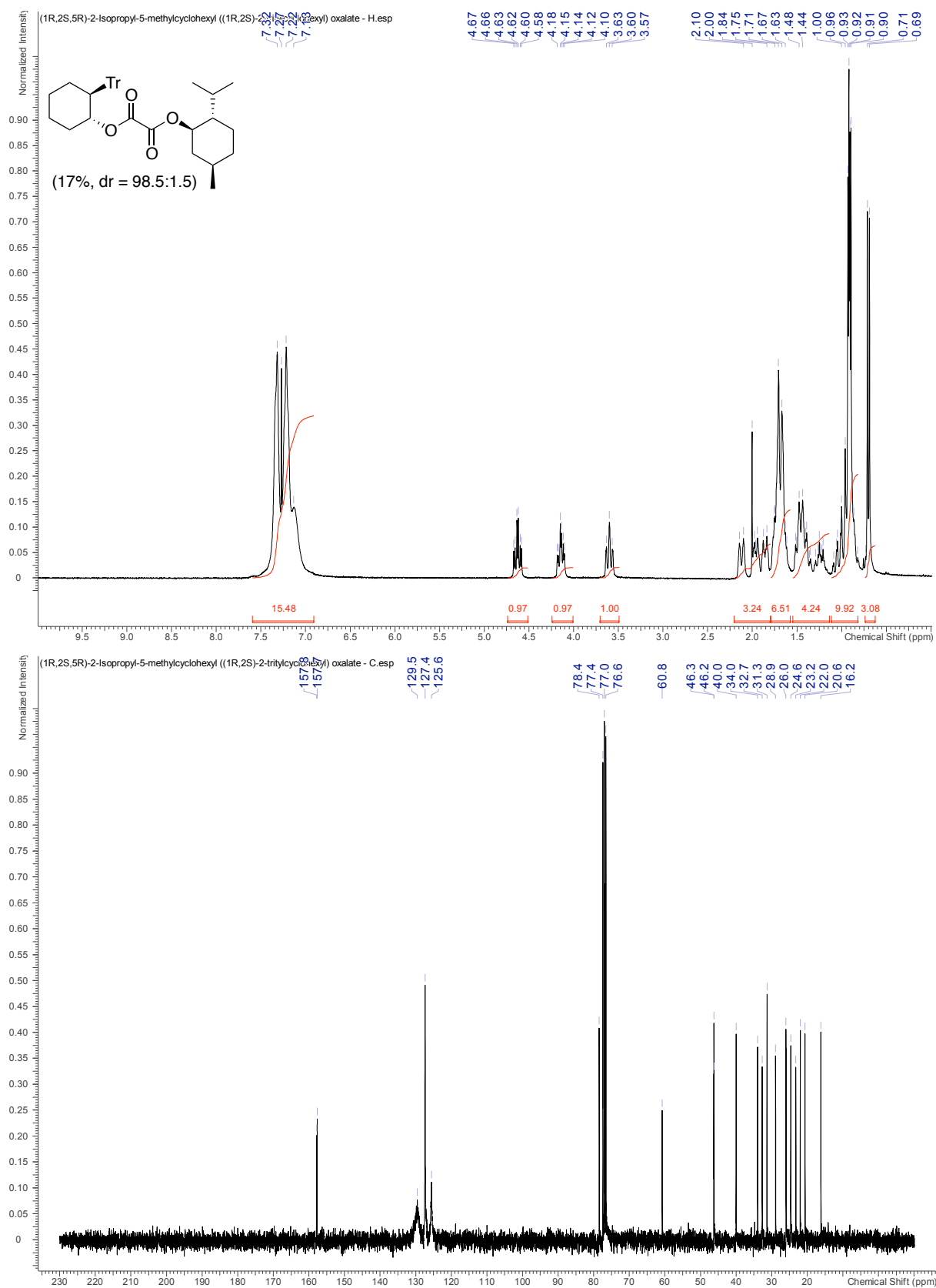


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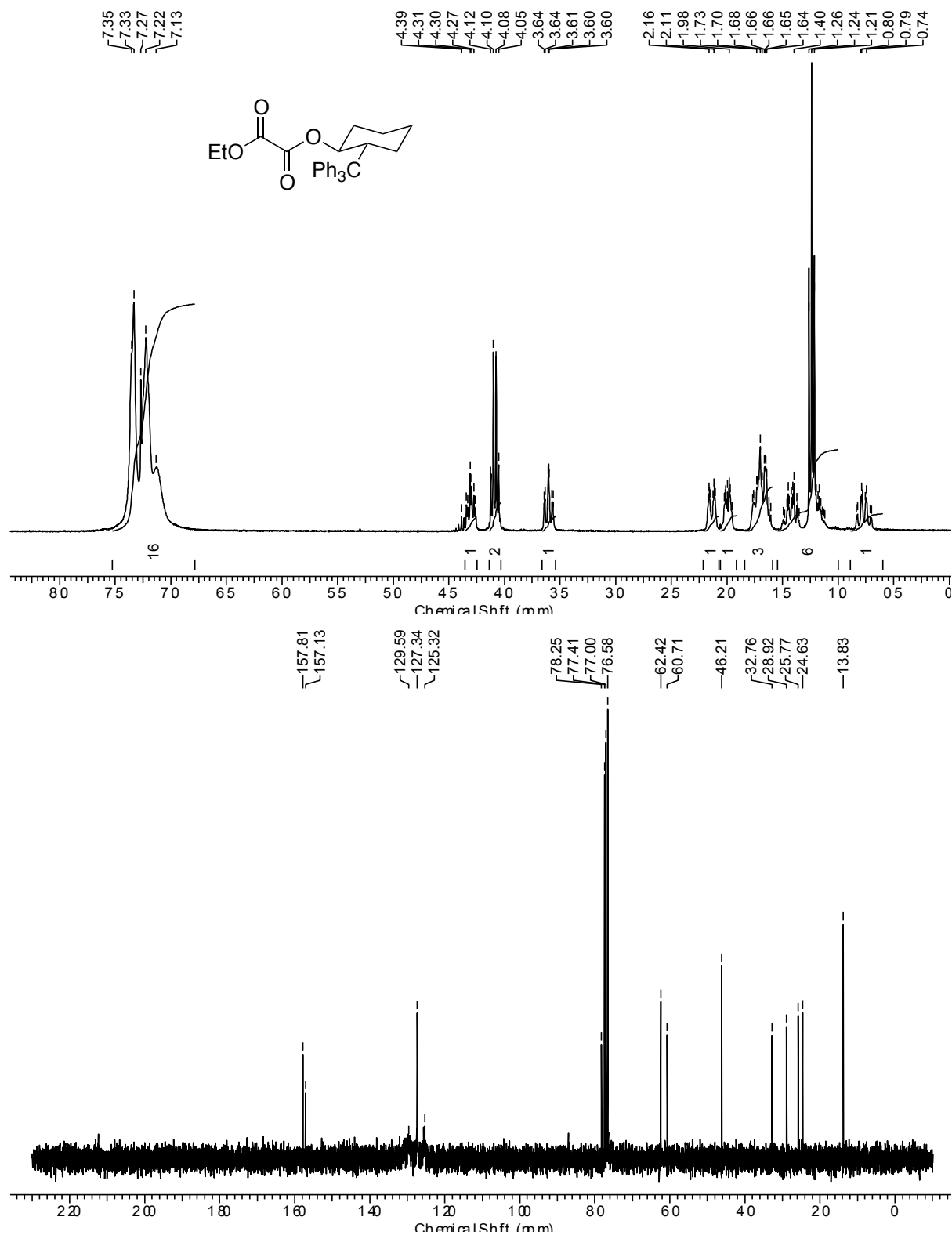
**(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl ((1*R*,2*S*)-2-tritylcyclohexyl) oxalate**

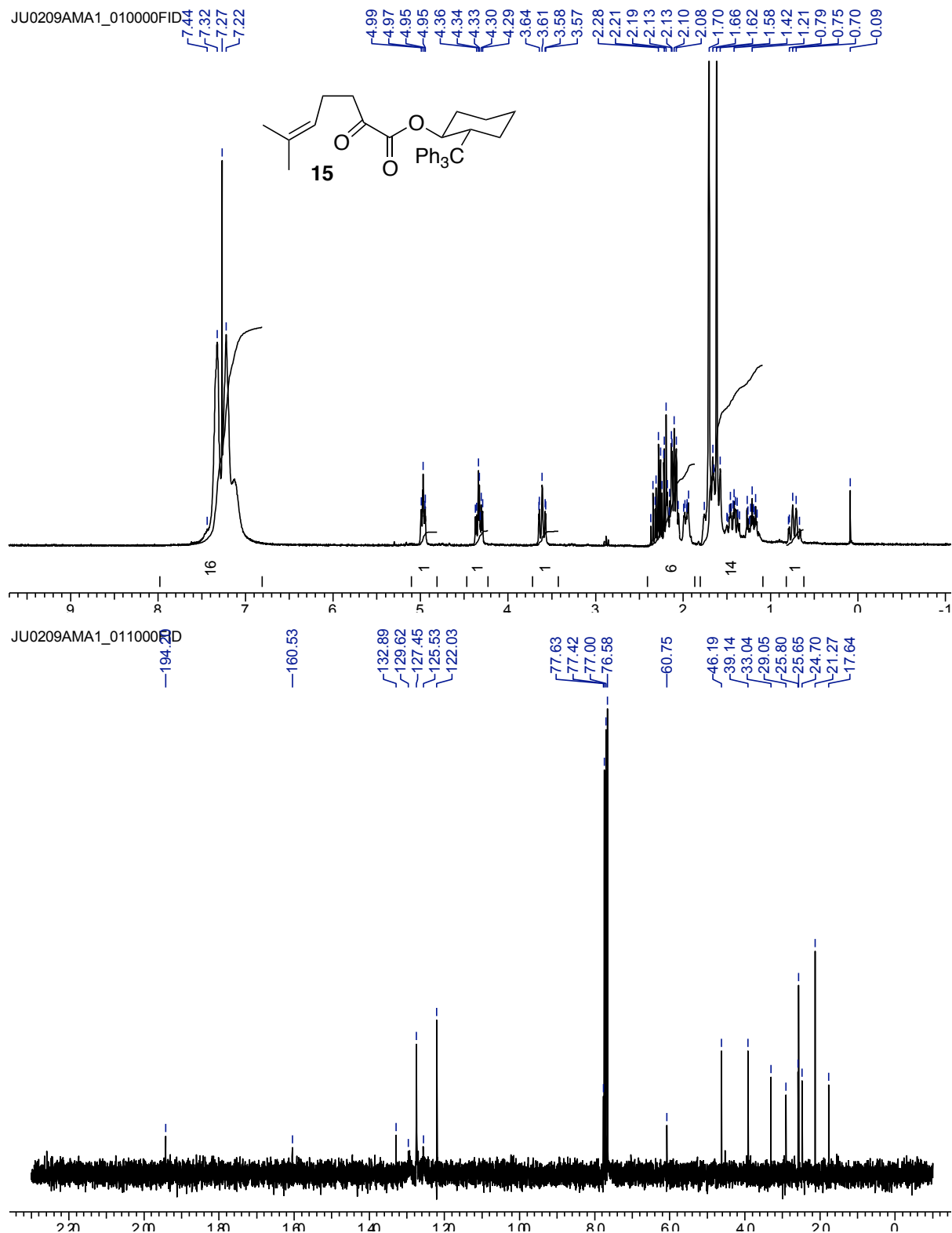
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



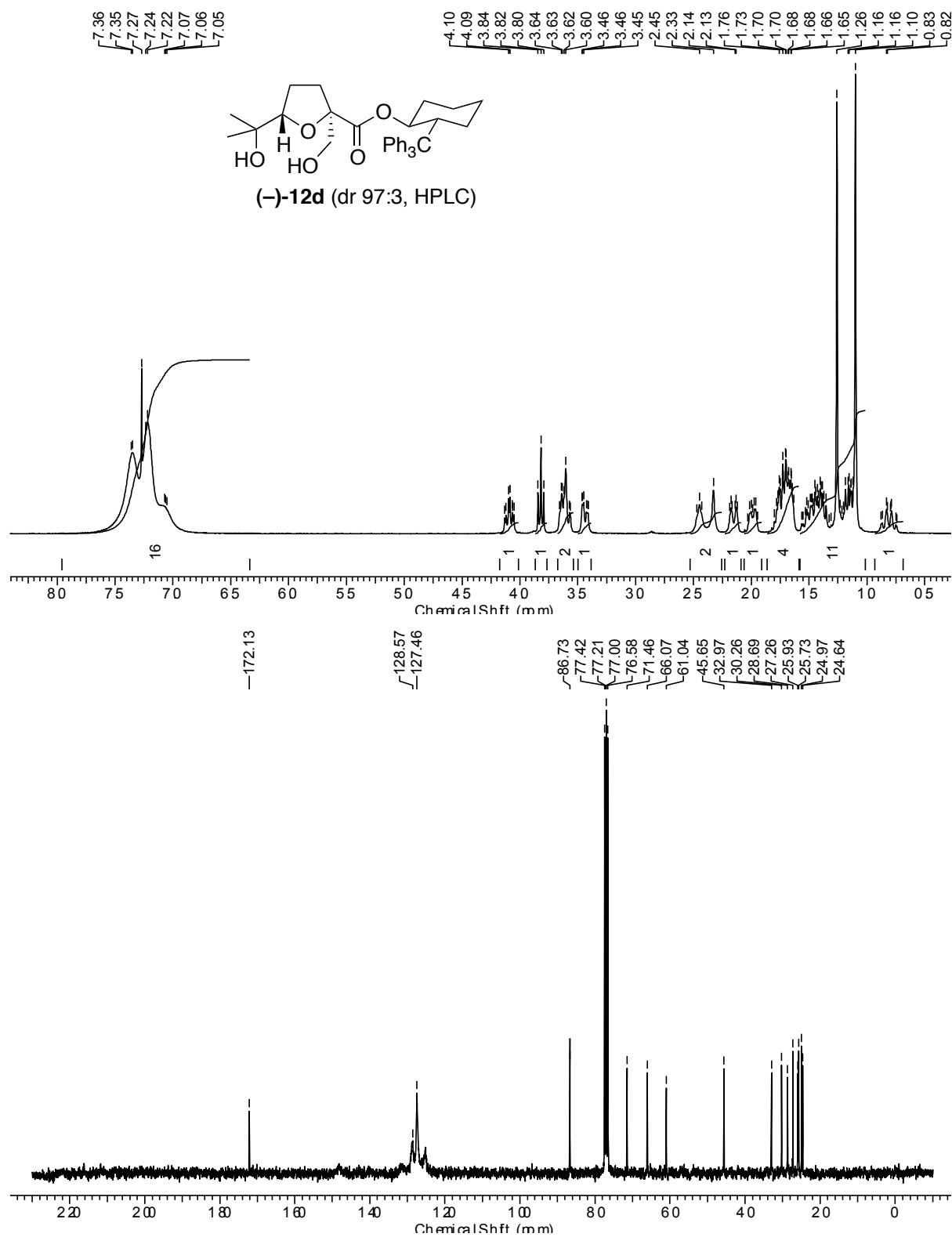
# Ethyl (1*S*,2*R*)-2-tritylcyclohexyl oxalate

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

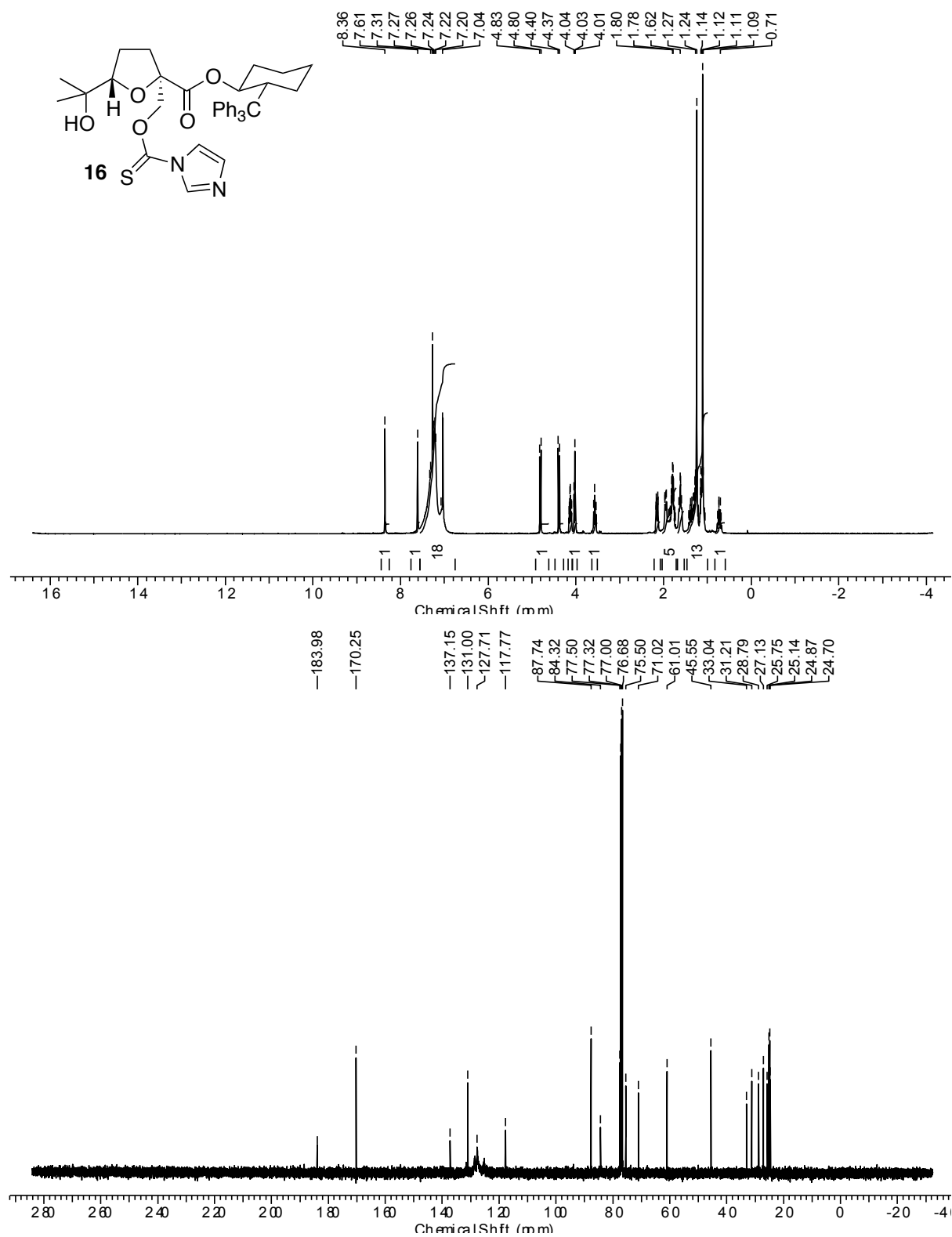


**(1*S*,2*R*)-2-Tritylcyclohexyl 6-methyl-2-oxohept-5-enoate (15)**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

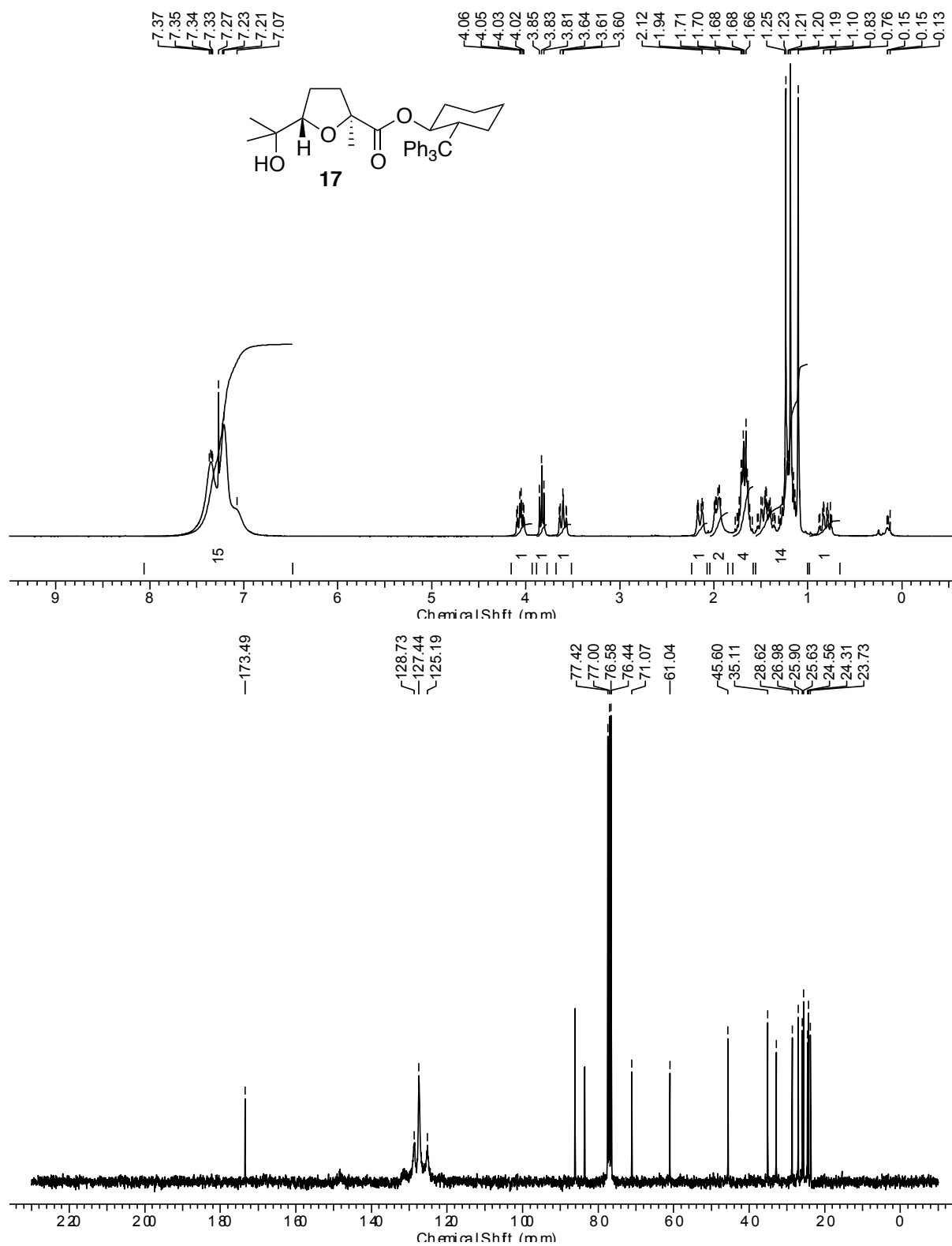
**(2*R*,5*S*)-(1*R*,2*S*)-2-Tritylcyclohexyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate ((-)-12d)** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

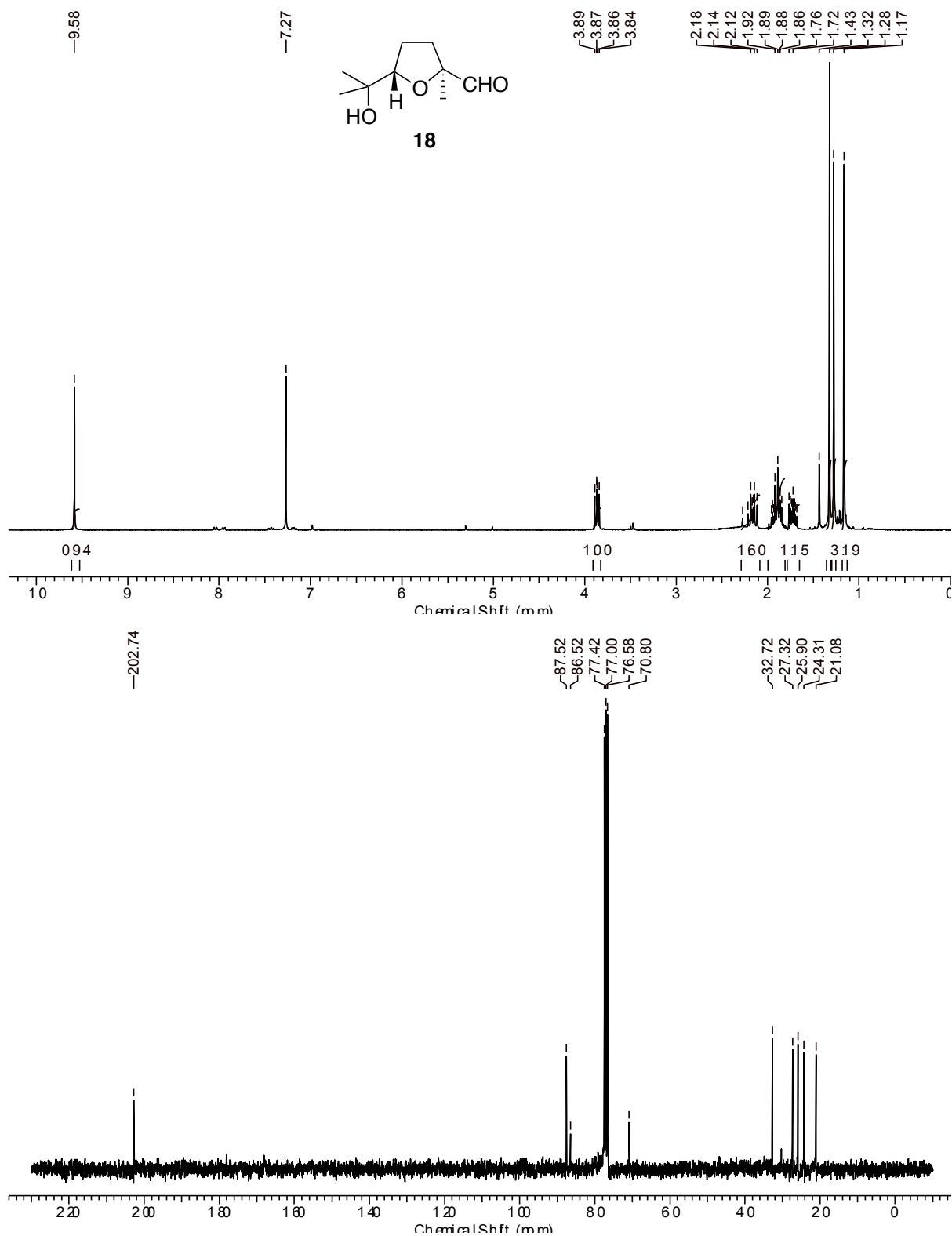


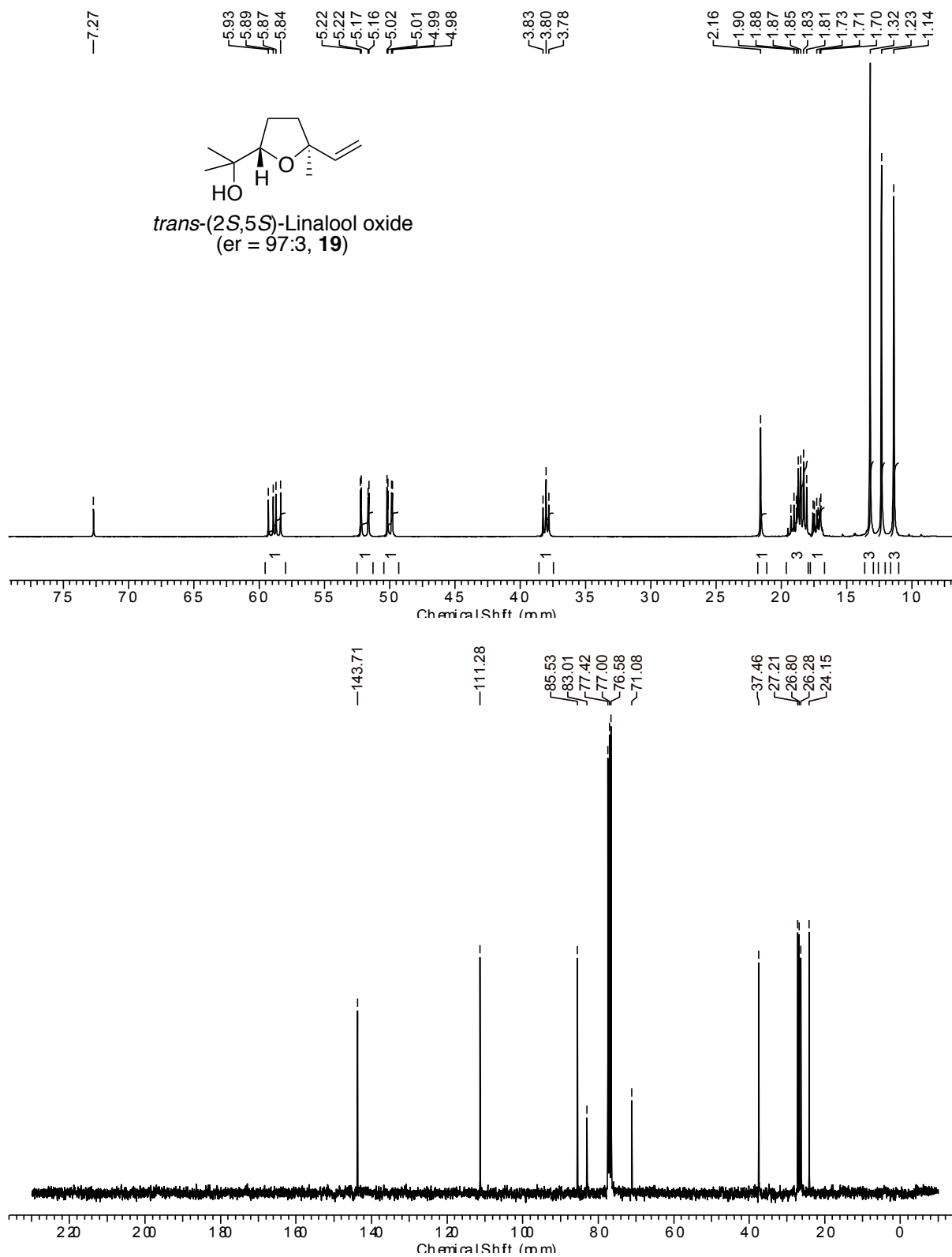
**(2*R*,5*S*)-(1*S*,2*R*)-2-Tritylcyclohexyl tetrahydro-2-(*O*-methoxy-1*H*-imidazole-1-carbothioyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (**16**)** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



**(2*S*,5*S*)-(1*S*,2*R*)-2-Tritylcyclohexyl tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-carboxylate**  
**(17)**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

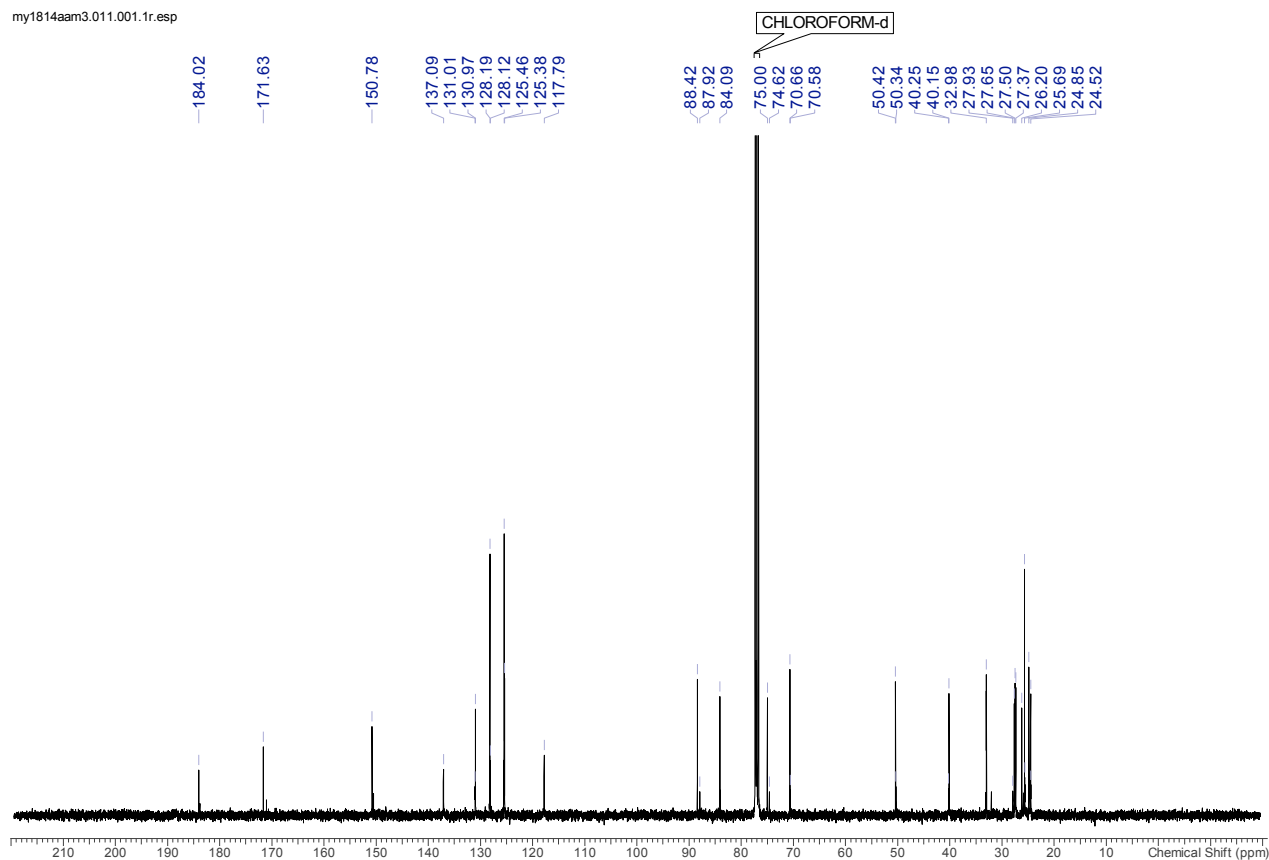
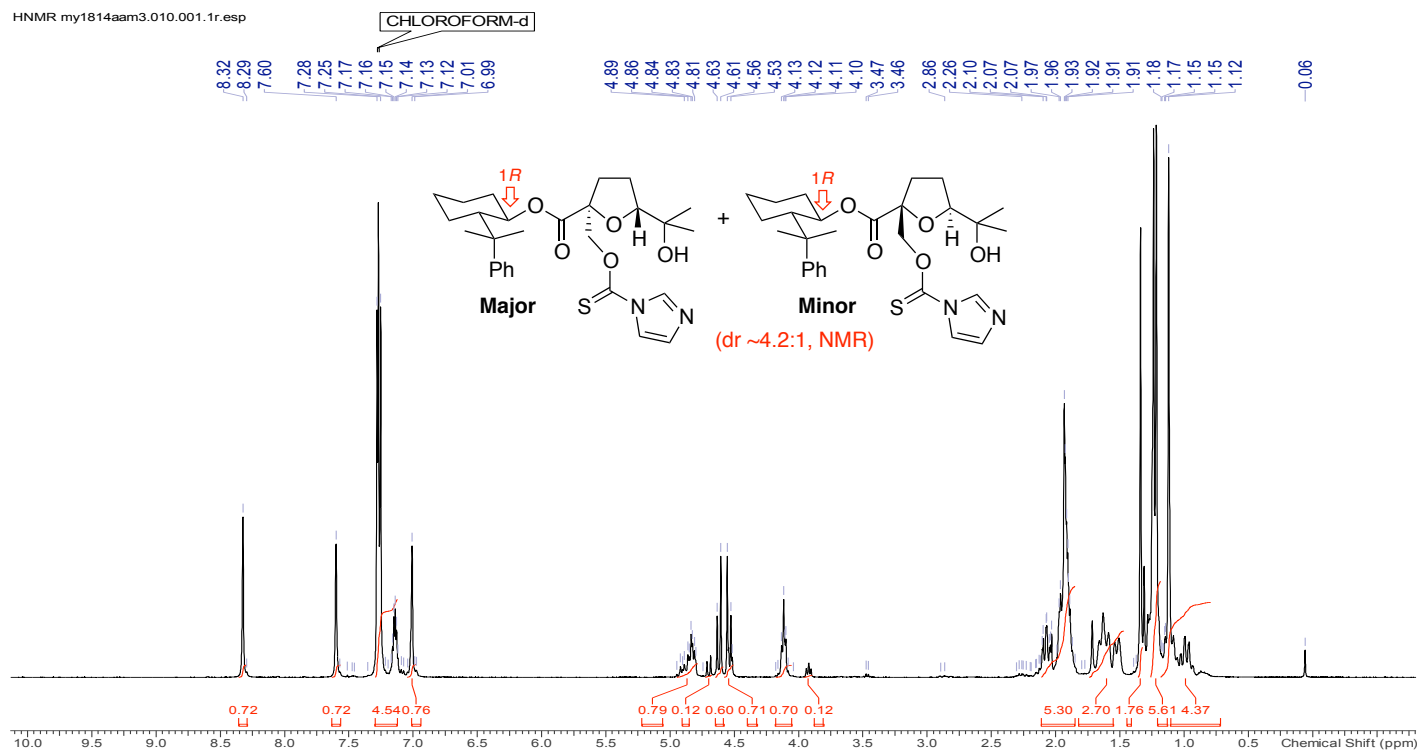


**(2S,5S)-Tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-carbaldehyde (18)**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

**(2S,5S)-Tetrahydro-5-methyl-5-vinylfuran-2-yl)propan-2-ol (19) or (2S,5S)-linalool oxide 19**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)

**(2*S*,5*R*)-(1*R*,2*S*)-2-(2-Phenylpropan-2-yl)cyclohexyl 2-(((1*H*-imidazole-1-carbonothioyl)oxy)methyl)-5-(2-hydroxypropan-2-yl)tetrahydrofuran-2-carboxylate (+ minor diastereoisomer)**

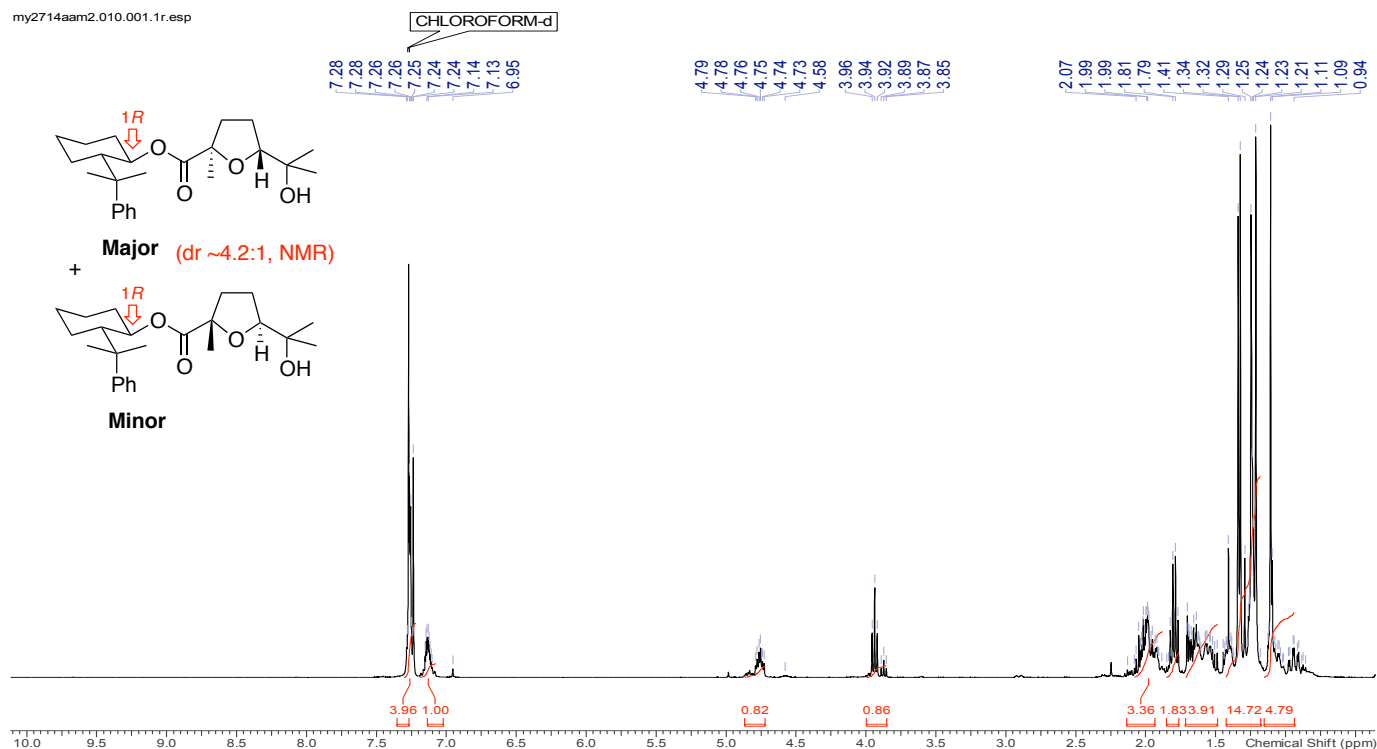
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



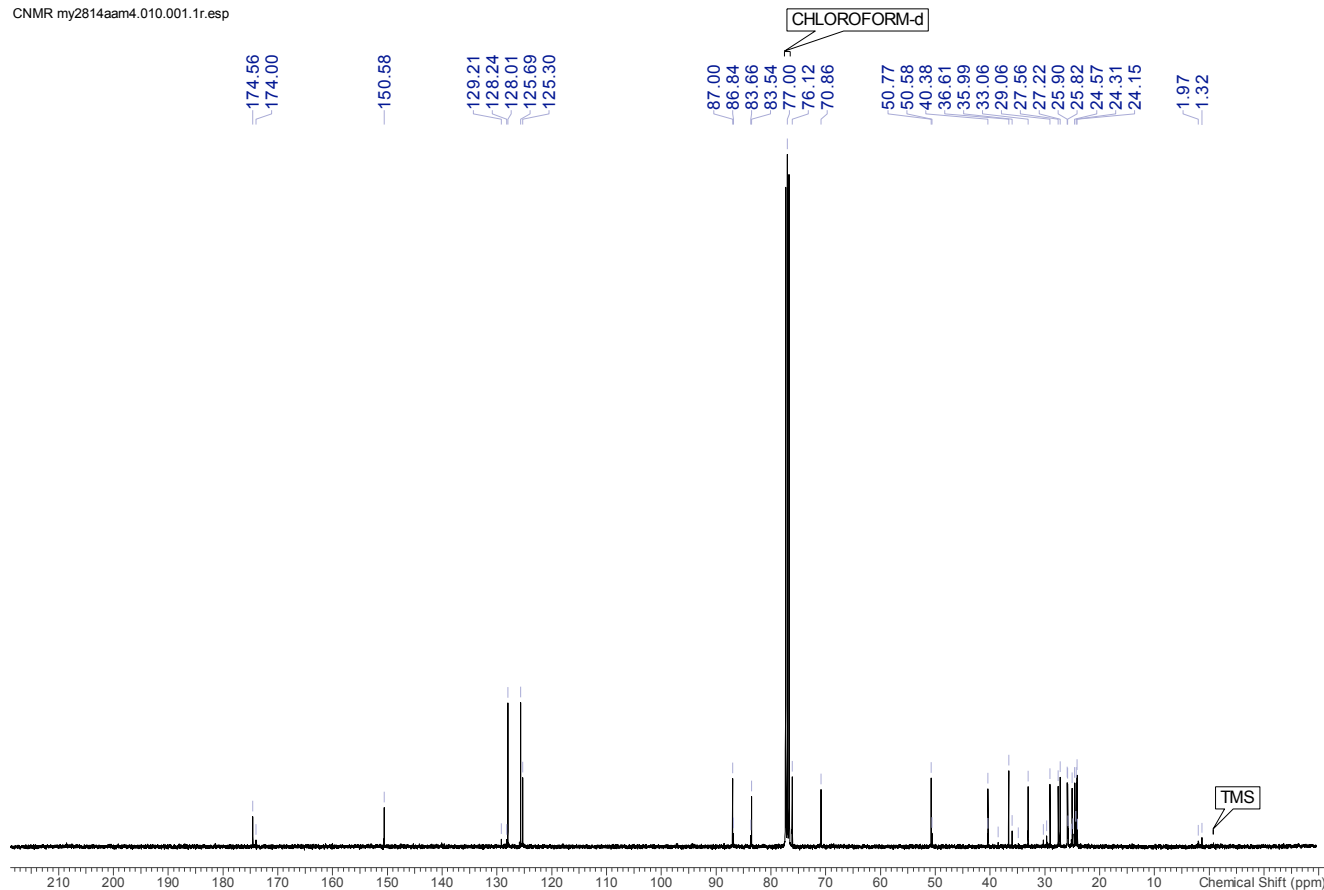
**(2*R*,5*R*)-(1*R*,2*S*)-2-(2-Phenylpropan-2-yl)cyclohexyl tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-carboxylate (+ minor diastereoisomer)**

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

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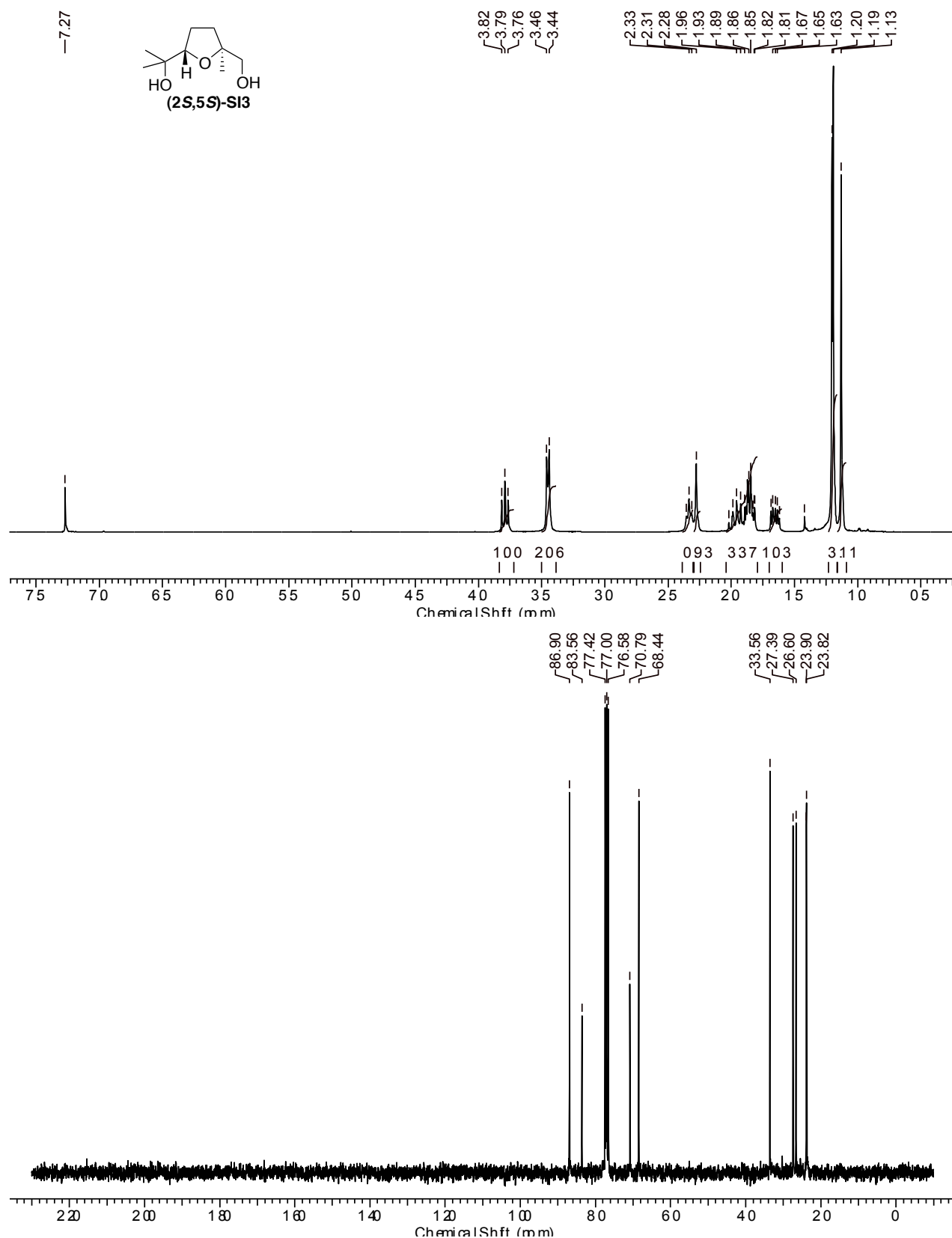


CNMR my2814aam4.010.001.1r.esp



Supporting Information

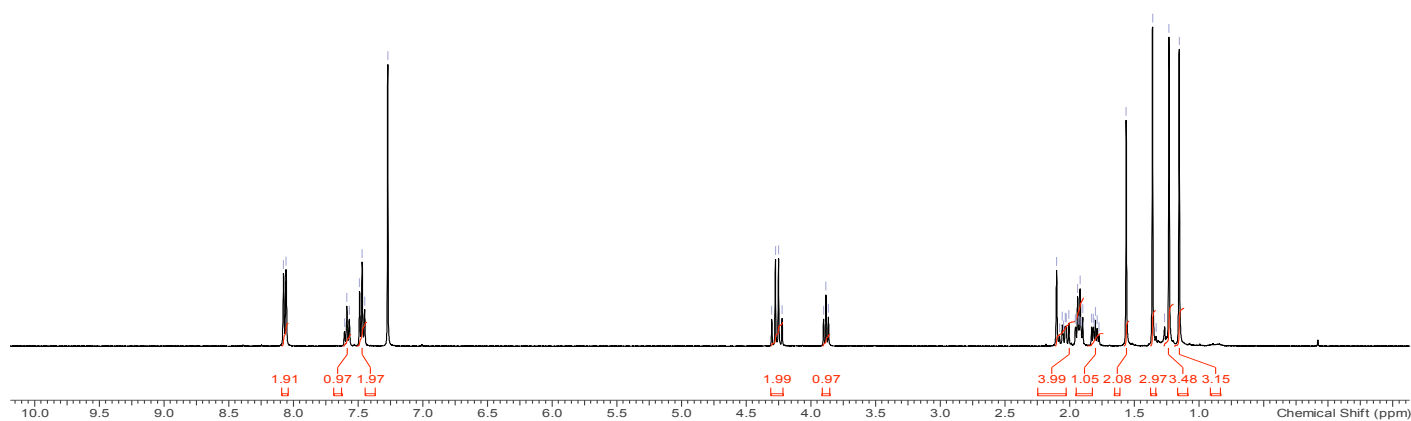
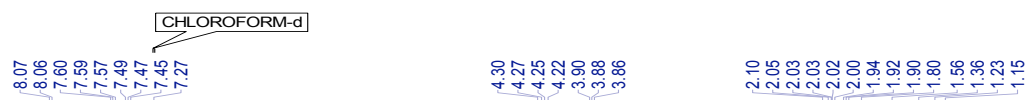
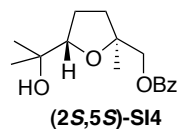
**2-((2*S*,5*S*)-5-(Hydroxymethyl)-5-methyltetrahydrofuran-2-yl)propan-2-ol ((2*S*,5*S*)-SI3) (From reduction of TTC ester 17)**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ) and  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



**((2*S*,5*S*)-5-(2-Hydroxypropan-2-yl)-2-methyltetrahydrofuran-2-yl)methyl benzoate ((2*S*,5*S*)-SI4)**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)

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cnmr my2914aam2.010.001.1r.esp

