
Supporting information

An enantioselective desymmetrisation approach to C9-substituted *trans*-hydrindene rings based on a diastereotopic group-selective intramolecular Diels-Alder reaction.

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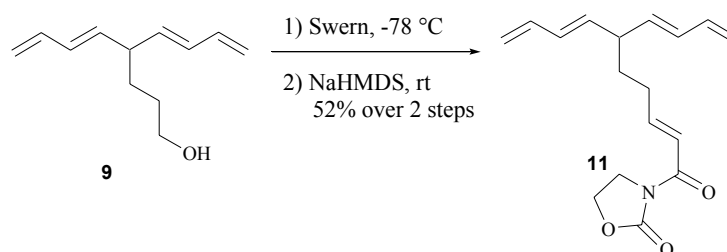
- Experimental procedure from **11**
- Characterisation data for **11**
- Copy of ¹H NMR and ¹³C NMR spectrum of **11**

B) The IMDA process

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A) Synthesis of 3-[(2E,7E)-6-((E)-buta-1,3-dienyl)-deca-2,7,9-trienoyl]-oxazolidin-2-one (11)



To a solution of oxalyl chloride (754 μL , 6.8 mmol) in CH_2Cl_2 (3.4 mL) at -78 °C was added DMSO (963 μL , 13.6 mmol). After 20 min, a solution of alcohol **9** (417 mg, 2.3 mmol) in CH_2Cl_2 (1 mL) was added. After 2.5 h, TEA (1.9 mL, 13.6 mmol) was added. The reaction mixture was warmed up to 0 °C. After 30 min at this temperature, the reaction mixture was concentrated *in vacuo*. The resulting residue was suspended in THF and filtered through a glass frit followed by rinsing with THF. The filtrate was concentrated *in vacuo* to afford an orange oil which was used in the next step without further purification.

To a solution of phosphonate **10** (1.4 g, 5.1 mmol) in THF (5 mL) at 0 °C was added NaHMDS (1 M in THF, 5.1 mL, 5.1 mmol). The bright yellow solution was stirred for 5 min at the same temperature and was warmed up to room temperature. A solution of crude aldehyde, as obtained above, in THF (1 mL) was added. The orange solution was stirred for 2 h. The reaction was quenched with phosphate buffer pH 7.2 (10 mL) and diluted with AcOEt (10 mL). The layers were separated and the aqueous layer was extracted with AcOEt (2 \times 10 mL). The combined organic layers were washed with 1 M aqueous NaHSO_4 (1 \times 10 mL), water (1 \times 10 mL), saturated aqueous NaHCO_3 (1 \times 10 mL), brine (1 \times 10 mL) and dried over anhydrous MgSO_4 . After removing the solvent *in vacuo*, the residue was purified by column chromatography (hexane/AcOEt 2:1) to afford **11** as a yellow oil (347 mg, 52% from **9**).

IR (film): ν_{max} 2923 (w), 1773 (s), 1681 (m), 1633 (m), 1603 (w), 1360 (s), 1219 (s), 1004 (s) cm^{-1} ;

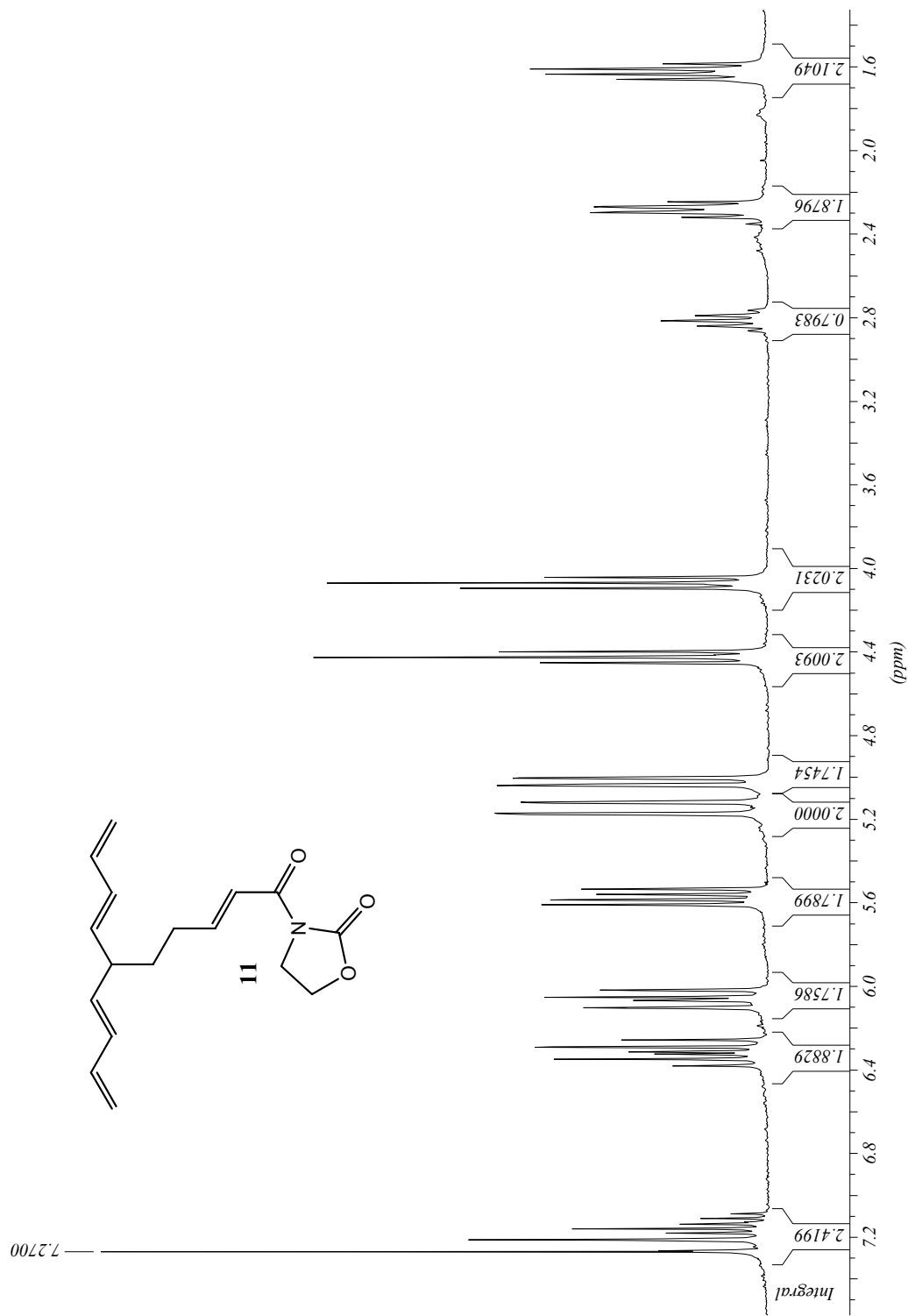
^1H NMR (300 MHz; CDCl_3): δ_{H} 7.24 (1 H, d, J 15.5, $\text{CH}=\text{CH}-\text{C}=\text{O}$), 7.12 (1 H, dt, J 15.5 and 6.4, $\text{CH}=\text{CH}-\text{C}=\text{O}$), 6.31 (2 H, dt, J 16.9 and 10.2, $2 \times \text{CH}_2=\text{CH}$), 6.05 (2 H,

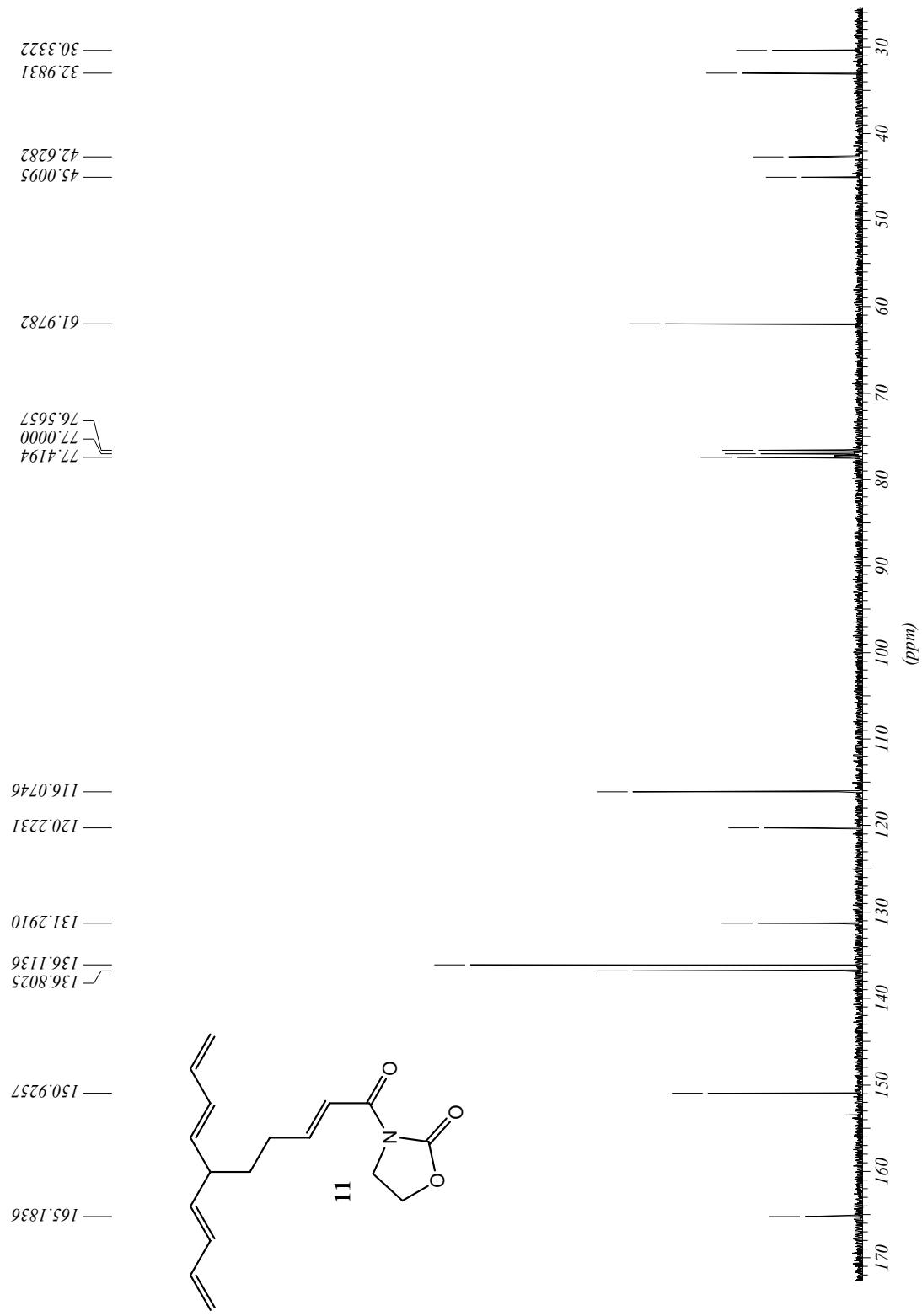
dd, J 15.3 and 10.3, $2 \times \text{CH}_2=\text{CH}-\text{CH}$), 5.57 (2 H, dd, J 15.3 and 7.7, $2 \times \text{CH}_2=\text{CH}-\text{CH}=\text{CH}$), 5.14 (2 H, dd, J 17.0 and 1.7, $2 \times \text{CH}=\text{CH}_{\text{cis}}\text{H}_{\text{trans}}$), 5.01 (2 H, dd, J 10.2 and 1.7, $2 \times \text{CH}=\text{CH}_{\text{cis}}\text{H}_{\text{trans}}$), 4.42 (2 H, t, J 8.0, CH_2-N), 4.06 (2 H, t, J 8.1, CH_2-O), 2.81 (1 H, quint, J 7.4, $\text{CH}-\text{CH}_2-\text{CH}_2$), 2.28 (2 H, q, J 7.3, $\text{CH}_2-\text{CH}=\text{CH}$) and 1.62 (2 H, q, J 7.5, $\text{CH}-\text{CH}_2-\text{CH}_2$) ppm;

^{13}C NMR (75 MHz; CDCl_3): δ_{C} 165.2 (1 \times s), 153.4 (1 \times s), 150.9 (1 \times d), 136.8 (2 \times d), 136.1 (2 \times d), 131.3 (2 \times d), 120.2 (1 \times d), 116.1 (2 \times t), 62.0 (1 \times t), 45.0 (1 \times d), 42.6 (1 \times t), 32.9 (1 \times t), 30.3 (1 \times t) ppm;

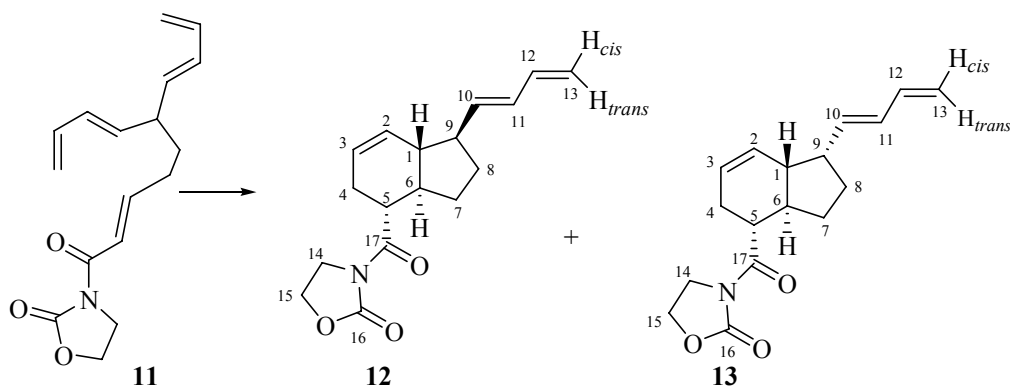
MS (CI) m/z 288 (($\text{M}+\text{H}$) $^+$, 26%), 201 (30), 172 (18), 146 (92), 91 (100);

HRMS (ES) for $\text{C}_{17}\text{H}_{21}\text{NO}_3\text{Na}$ ($\text{M}+\text{Na}$) $^+$ calcd 310.1413 found 310.1417.





B) The IMDA process



Under thermal conditions:

To a solution of **11** (284 mg, 0.99 mmol) in anhydrous toluene (20 mL) in a sealed tube was added BHT (2 mg, 0.01 mmol). The solution was degassed with a nitrogen stream. The reaction was heated at 150 °C for 24 h. The solvent was removed and the residue was purified by column chromatography (neat CH₂Cl₂) to afford the product as a white solid (227 mg, 80%) in a 70:30 ratio of **12/13**.

Under achiral Lewis-acid catalysed conditions:

To a solution of **11** (40 mg, 0.14 mmol) in anhydrous CH₂Cl₂ (4.6 mL) at -78 °C was added Me₃Al (2 M in hexane, 100 μL, 0.20 mmol). The bright yellow solution was immediately warmed up to -30 °C. After 4 h at this temperature, the reaction was diluted with Et₂O (5 mL) and quenched with saturated aqueous solution of Rochelle's salt (5 mL). After the phase separation, the aqueous phase was extracted with Et₂O (2 × 5 mL). The combined organic phases were washed with brine (1 × 5 mL) and dried over anhydrous MgSO₄. After removing the solvent *in vacuo*, the residue was purified by column chromatography (CH₂Cl₂/MeOH 99.5:0.5) to afford **12/13** as a white solid (24 mg, 59%) as a 78:22 ratio of **12/13**.

With the chiral bis(oxazoline) catalyst:

To a solution of **11** (60 mg, 0.21 mmol) in anhydrous CH₂Cl₂ (5.2 mL) was added a solution of [Cu(S,S)-bis(tert-butyloxazoline)](SbF₆)₂ (0.014 M in CH₂Cl₂, 1.5 mL, 0.02 mmol). The reaction was stirred at room temperature for 24 h. The solvent

was removed and the residue was purified by column chromatography (neat CH₂Cl₂) to afford **2** as a white solid (34 mg, 56%) in a 82:18 ratio of **12/13**.

The diastereoisomers were separated by reverse phase HPLC (X-Terra Prep RP₁₈ column 5 μm 19×100 mm, mobile phase 50-55% 1% aqueous NH₃ in CH₃CN and the detection was performed at 230 nm).

Data for the major isomer 12:

mp 94 °C;

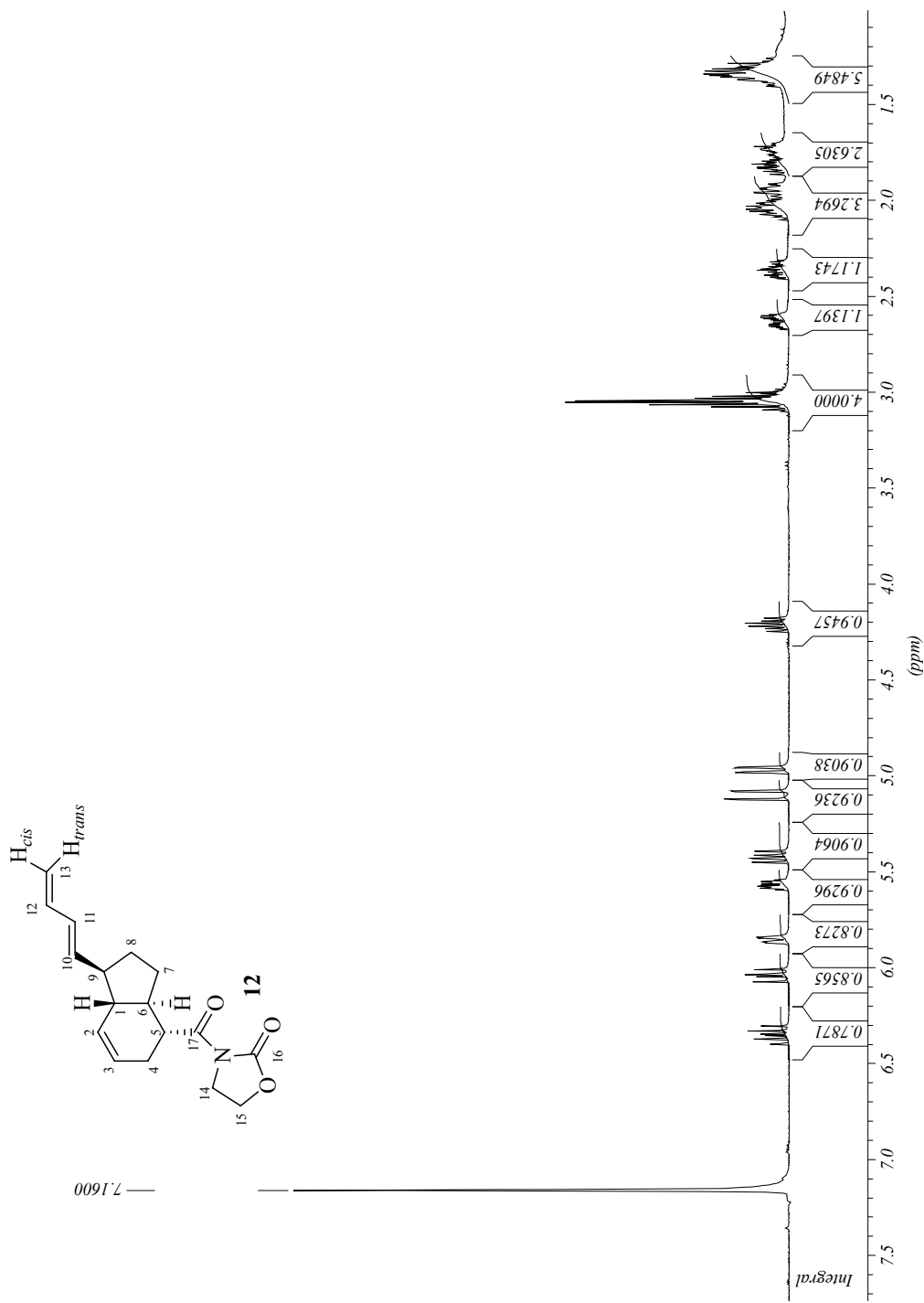
IR (film): ν_{\max} 2961 (w), 2911 (w), 2864 (w), 1784 (s), 1688 (s), 1650 (w), 1604 (w), 1385 (s), 1200 (s) cm⁻¹;

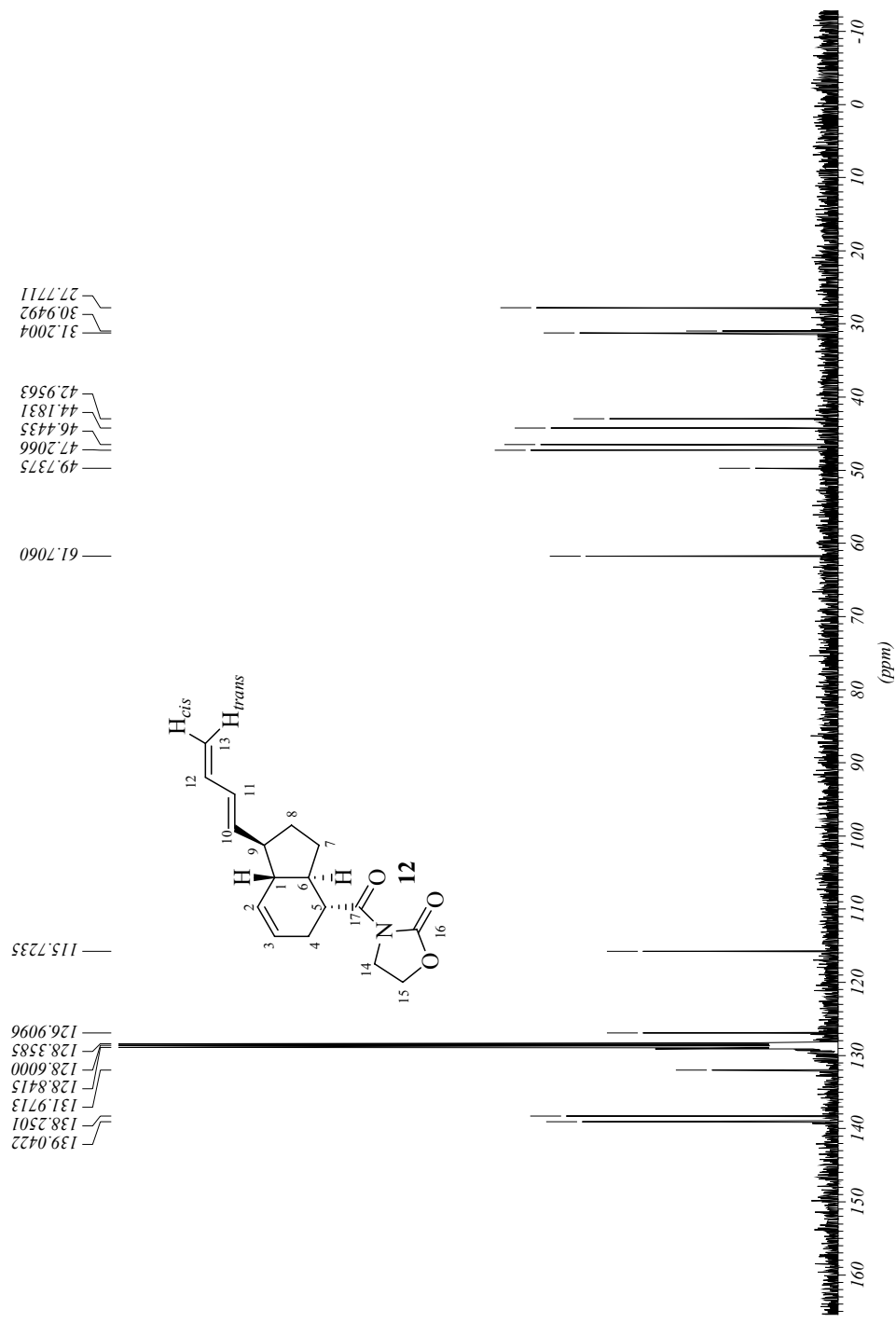
¹H NMR (400 MHz; C₆D₆): δ_{H} 6.33 (1 H, dt, *J* 17.1 and 10.0, H₁₂), 6.02 (1 H, dd, *J* 15.0 and 11.0, H₁₁), 5.84 (1 H, d, *J* 9.5 and 2.0, H₂), 5.55 (1 H, m, H₃), 5.41 (1 H, dd, *J* 15.0 and 8.5, H₁₀), 5.07 (1 H, dd, *J* 17.0 and 2.0, H_{13trans}), 4.95 (1 H, dd, *J* 10.0 and 2.0, H_{13cis}), 4.20 (1 H, td, *J* 10.6 and 6.0, H₅), 3.08-2.97 (4 H, m, H₁₄, H₁₅), 2.62 (1 H, m, H₄), 2.34 (1 H, m, H₄), 2.09-1.97 (2 H, m, H₉, H₆), 1.93 (1 H, m, H₈), 1.82 (2 H, m, H₁), 1.74 (1 H, m, H₇), 1.39-1.24 (2 H, m, H₇, H₈) ppm;

¹³C NMR (100 MHz; C₆D₆): δ_{C} 175.9 (1 × s, C₁₇), 154.2 (1 × s, C₁₆), 139.0 (1 × d, C₁₀), 138.2 (1 × d, C₁₂), 132.0 (1 × d, C₁₁), 128.9 (1 × d, C₂), 126.9 (1 × d, C₃), 115.7 (1 × t, C₁₃), 61.7 (1 × t, C₁₅), 49.7 (1 × d, C₆), 47.2 (1 × d, C₉), 46.4 (1 × d, C₁), 44.2 (1 × d, C₅), 42.9 (1 × t, C₁₄), 31.2 (1 × t, C₄), 30.9 (1 × t, C₇), 27.8 (1 × t, C₈) ppm;

ES (CI) *m/z* 288 ((M+H)⁺, 82), 201 (22), 173 (8), 91 (100);

HRMS (EI) for C₁₇H₂₁NO₃ (M)⁺ calcd 287.1521 found 287.1525.





Partial data for the minor isomer 13:

IR (film): ν_{\max} 2961 (w), 2911 (w), 2864 (w), 1784 (s), 1688 (s), 1650 (w), 1604 (w), 1385 (s), 1200 (s) cm^{-1} ;

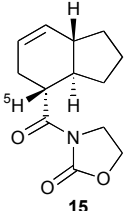
^1H NMR (400 MHz; C_6D_6): δ_{H} 6.36 (1 H, dt, J 17.1 and 10.2, H_{12}), 6.08 (1 H, dd, J 15.0 and 10.0, H_{11}), 5.87 (1 H, d, J 9.5, H_2); 5.17 (1 H, d, J 16.6, $\text{H}_{13\text{trans}}$), 5.01 (1 H, d, J 10.5 and 1.5, $\text{H}_{13\text{cis}}$) and 4.27 (1 H, td, J 9.5 and 6.5, H_5) ppm;

^{13}C NMR (100 MHz; C_6D_6): δ_{C} 175.9 (1 \times s, C_{17}), 154.2 (1 \times s, C_{16}), 138.8 (1 \times d, C_{10}), 138.2 (1 \times d, C_{12}), 129.3 (1 \times d, C_{11}), 128.9 (1 \times d, C_2), 126.9 (1 \times d, C_3), 115.7 (1 \times t, C_{13}), 61.7 (1 \times t, C_{15}); 48.1 (1 \times d, C_6), 44.4 (1 \times d, C_9), 43.9 (1 \times d, C_1), 43.2 (1 \times d, C_5), 42.9 (1 \times t, C_{14}), 31.3 (1 \times t, C_7); 31.2 (1 \times t, C_4) and 28.6 (1 \times t, C_8) ppm;

MS (CI) m/z 288 ($(\text{M}+\text{H})^+$, 82%), 201 (22), 173 (8), 91 (100);

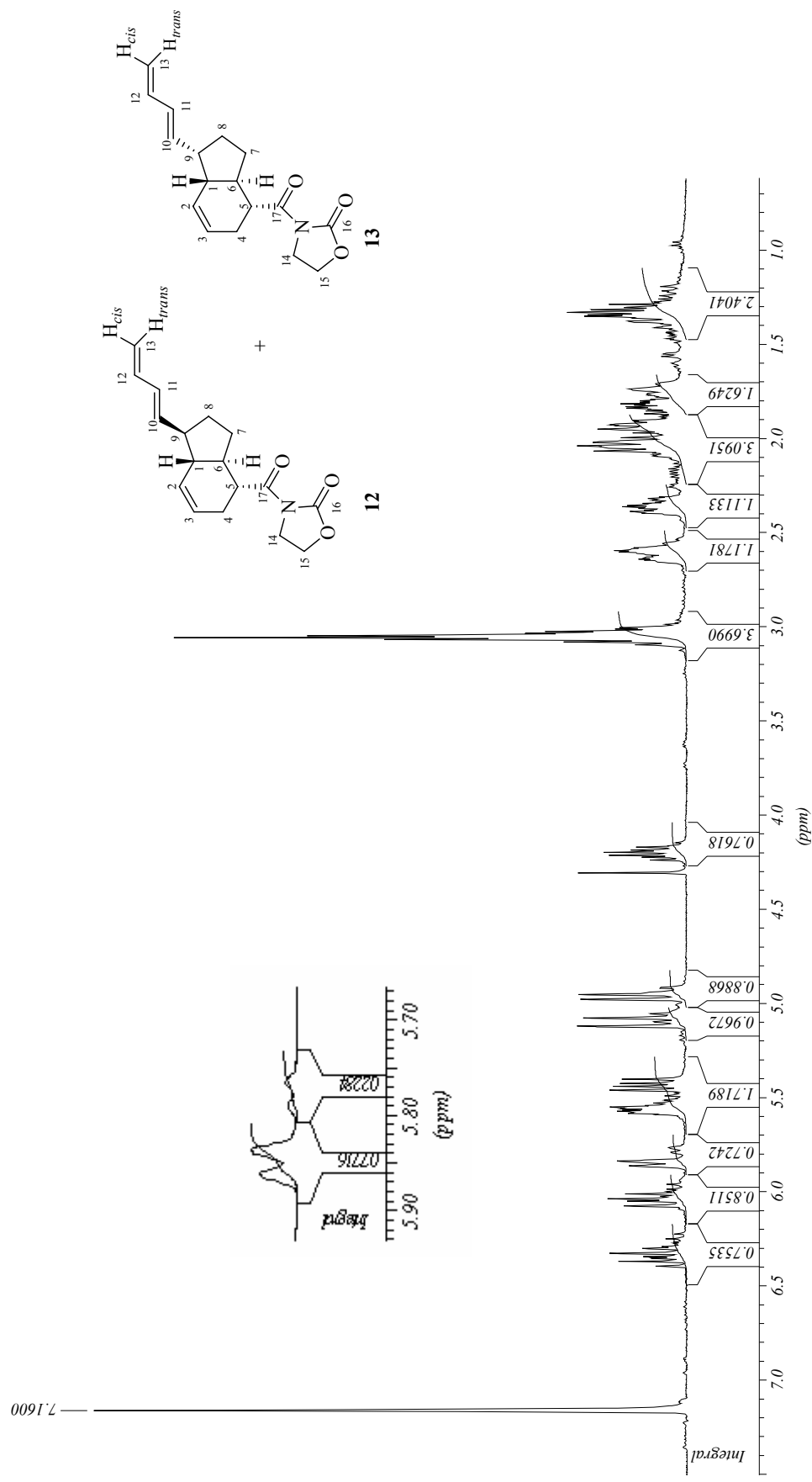
HRMS (EI) for $\text{C}_{17}\text{H}_{21}\text{NO}_3$ (M) $^+$ calcd 287.1521 found 287.1525.

Comparison with literature ^1H NMR data to establish the *trans* ring junction in the minor diastereoisomer

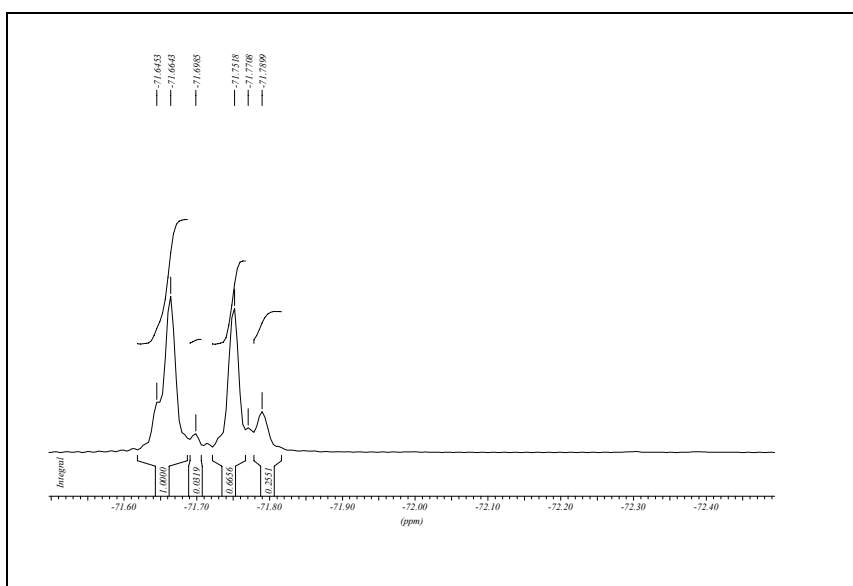
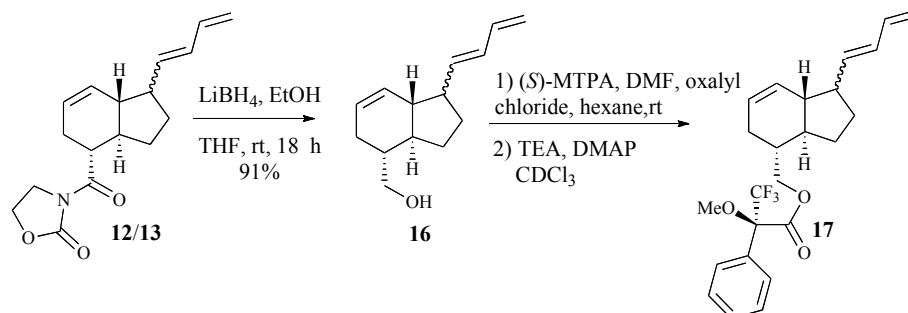
entry	cycloadduct	^1H NMR of H_5 in CDCl_3	
1	12	δ 3.92, td, $J = 10.2, 6.0$ Hz	
2	13	δ 3.91, td, $J = 10.6, 6.2$ Hz	
3	15	δ 3.91, td, $J = 10.8, 6.2$ Hz ^a	

^a D. A. Evans, D. M. Barnes, J. S. Johnson, T. Lectka, P. von Matt, S. J. Miller, J. A. Murry, R. D. Norcross, E. A. Shaughnessy, and K. R. Campos, *J. Am. Chem. Soc.*, 1999, **121**, 7582

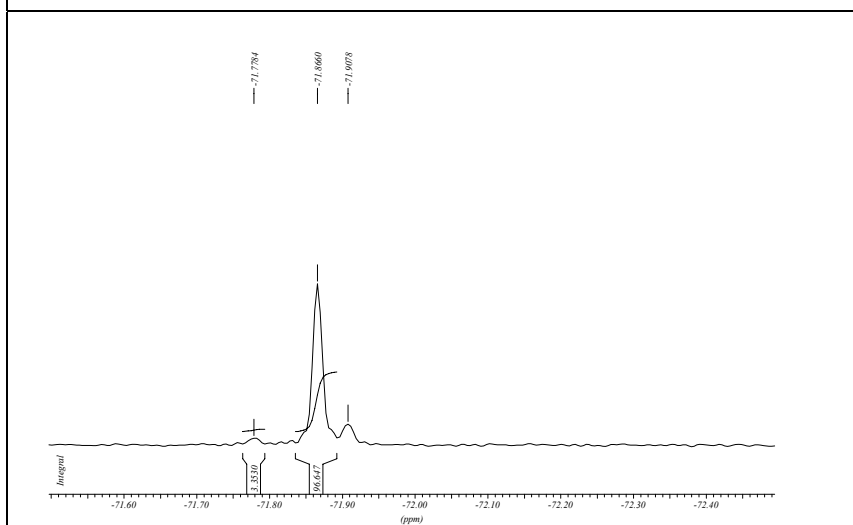
Mixture after IMDA reaction



C) Mosher's ester analysis



Racemic Mosher ester



Non racemic Mosher ester

