

Supporting information

Stereoarrayed 2,3-Disubstituted-1-indanols via Ruthenium(II)-Catalyzed Dynamic Kinetic Resolution-Asymmetric Transfer Hydrogenation

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1 Materials and methods

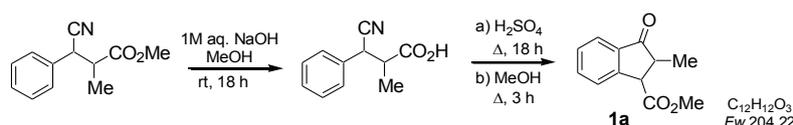
General. Reactions were conducted under an inert atmosphere using anhydrous solvents when required. Analytical thin layer chromatography (TLC) was performed on Silica Gel 60F₂₅₄ plates. Flash column chromatography was performed using Silica Gel 60 (40–63 μm). Melting points were determined on a Kofler apparatus and are uncorrected. The enantiomeric excess (ee) of reduced products was determined by HPLC (Knauer UV detector K-2501) using chiral columns. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. ¹H (299.9 MHz; internal Me₄Si) and ¹³C NMR (75.4 MHz; internal CDCl₃, δ 77.00) spectra were recorded for solutions in CDCl₃ if not stated otherwise. HRMS measurements were obtained on a Waters Micromass Q-TOF Premier instrument equipped with an orthogonal Z-spray ESI interface or on Agilent 6224 Accurate Mass TOF LC/MS System.

Catalysts. The active *ansa*-Ru(II) complexes **A** and **B** were prepared according to our published procedure starting from (*S,S*)- or (*R,R*)-DPEN.¹

Reagents. HCO₂H/Et₃N 3:2 was prepared by adding Et₃N (280 mL, 2 mol) to HCO₂H (113 mL, 3 mol) at 0 °C under nitrogen atmosphere and used as such.

2 Synthesis of indanones 1a–1n

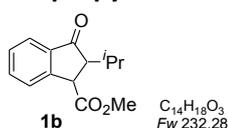
2-Methyl-3-methoxycarbonyl-1-indanone (1a)



STEP 1. Preparation of 3-cyano-2-methyl-3-phenylpropionic acid. To a solution of methyl 3-cyano-2-methyl-3-phenylpropionate^[2] (38.2 g, 188 mmol) in MeOH (375 mL) was added under stirring 1 M NaOH (225 mL) maintaining the internal temperature below 20 °C. The resulting solution was left to stir at rt for 18 h then concentrated to ca 250 mL, washed with Et₂O (2 × 150 mL), and the aqueous layer acidified to pH 4 with 37% HCl. Extraction with CH₂Cl₂ (4 × 250 mL), drying (Na₂SO₄), filtration and concentration afforded 3-cyano-2-methyl-3-phenylpropionic acid as a colorless oil (25.4 g, 71%); dr = 57:43 (by ¹H NMR). ¹H NMR (300 MHz, CDCl₃) δ 7.4 (m, 10H, major+minor), 7.33 (d, *J* = 6.8 Hz, 0.57H, major), 4.08 (d, *J* = 7.9 Hz, 0.43H, minor), 3.07 (m, 0.43H, minor), 2.95 (m, 0.57H, major), 1.42 (d, *J* = 7.2 Hz, 1.71H, major), 1.21 (d, *J* = 7.2 Hz, 1.29H, minor). NMR data is in accordance with the literature.²

STEP 2. Preparation of 1a. A suspension of 3-cyano-2-methyl-3-phenylpropionic acid (14.6 g, 77 mmol) in 98% H₂SO₄ was heated at 90 °C for 18 h, then cooled and poured onto cold (0 °C) MeOH. The resulting brown solution was refluxed for 3 h then poured onto ice-water (300 mL). The product was extracted with Et₂O, washed with satd. aq. NaHCO₃, dried (MgSO₄), and concentrated affording the title compound as a white solid (6.6 g, 42% yield); dr = 85:15 (by ¹H NMR). ¹H NMR (300 MHz, CDCl₃) δ 7.83–7.76 (m, 1H, major+minor), 7.69–7.61 (m, 2H, major+minor), 7.53–7.43 (m, 1H, major+minor), 4.41 (d, *J* = 8.1 Hz, 0.15H, minor), 3.86 (d, *J* = 4.6 Hz, 0.85H, major), 3.82 (s, 2.55H, major), 3.70 (s, 0.45H, minor), 3.12 (qd, *J* = 7.4 and 4.6 Hz, 0.85H, major), 3.00 (qd, *J* = 15.0 and 8.1 Hz, 0.15H, minor), 1.39 (d, *J* = 7.4 Hz, 2.55H, major), 1.28 (d, *J* = 7.4 Hz, 0.45H, minor). NMR data is in accordance with the literature.^[2]

2-Isopropyl-3-methoxycarbonyl-1-indanone (1b). The title compound was prepared following a similar reaction sequence as for **1d**, starting from isobutyraldehyde (4.33 g, 60.0 mmol) and phenylacetonitrile (7.03 g, 60.0 mmol). Characterization data for intermediate compounds and the reaction yields are as follows:



- (1) For the preparation of catalyst **A**, see: a) Kišić, A.; Stephan, M.; Mohar, B. *Adv. Synth. Catal.* **2015**, 357, 2540–2546. For the preparation of catalyst **B**, see: b) Cotman, A. E.; Cahard, D.; Mohar, B. *Angew. Chem. Int. Ed.* **2016**, 55, 5294–5298.
- (2) Coe, J.; O'Donnell, C. US2005/0020616.

STEP 1. Preparation of 3-isopropyl-2-phenylacrylonitrile.³ Orange syrup (9.89 g, 96.3% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.57–7.50 (m, 2H), 7.44–7.30 (m, 3H), 6.63 (d, *J* = 10.1 Hz, 1H), 3.16–2.98 (m, 1H), 1.17 (d, *J* = 6.6 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 153.4, 133.2, 128.9, 128.8, 125.6, 116.5, 113.6, 31.9, 22.1.

STEP 2a. Preparation of 3-isopropyl-2-phenylsuccinonitrile.⁴ Off-white solid after trituration with cold petroleum ether (8.57g, 74.8% yield); dr = 83:17 (by ¹H NMR). Major diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 7.49–7.38 (m, 5H), 3.96 (d, *J* = 10.6 Hz, 1H), 2.98 (dd, *J* = 10.6, 4.1 Hz, 1H), 2.38 (app sptd, *J* = 6.7, 4.1 Hz, 1H), 1.20 (d, *J* = 6.7 Hz, 3H), 1.20 (d, *J* = 6.8 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 132.1, 129.5, 128.0, 127.6, 117.6, 116.5, 45.8, 38.4, 28.9, 21.4, 17.2. Minor diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 7.61–7.32 (m, 5H), 4.09 (d, *J* = 6.4 Hz, 1H), 2.75 (app t, *J* = 6.8 Hz, 1H), 2.12–1.94 (m, 1H), 1.15 (d, *J* = 6.7 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 132.1, 129.6, 129.4, 127.6, 117.3, 117.1, 45.9, 38.2, 29.1, 20.8, 19.4.

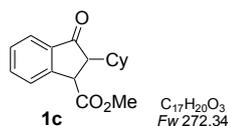
STEP 2b. Preparation of 3-isopropyl-2-phenylsuccinic acid. White powder (7.85 g, 80.3% yield); dr = 97:3 (by ¹H NMR); m.p. 199–201 °C (lit.⁵ 178 °C). Major diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 12.4 (br s, 2H), 7.45–7.26 (m, 5H), 3.94 (d, *J* = 12.0 Hz, 1H), 3.14 (dd, *J* = 12.0, 3.0 Hz, 1H), 1.59 (sptd, *J* = 7.1, 3.0 Hz, 1H), 0.99 (d, *J* = 7.0 Hz, 1H), 0.85 (d, *J* = 6.9 Hz, 1H).

STEP 3a. Preparation of 3-isopropyl-2-phenylsuccinic anhydride.⁶ Brown oil; dr = 55:45 (by ¹H NMR). Major diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 7.48–7.18 (m, 5H), 4.02 (d, *J* = 6.4 Hz, 1H), 3.27–3.13 (m, 1H), 2.47–2.27 (m, 1H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H). Minor diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 7.50–7.19 (m, 5H), 4.44 (d, *J* = 9.3 Hz, 1H), 3.26–3.11 (m, 1H), 1.88–1.66 (m, 1H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H).

STEP 3b. Preparation of 2-isopropyl-3-oxo-indan-1-carboxylic acid. Light brown solid (3.22g, 73.7% yield for steps 3a and 3b); dr = 52:48 (by ¹H NMR); m.p. 103–105 °C (lit.⁷ 103–104 °C). Major diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 10 (br s, 1H), 7.81–7.54 (m, 3H), 7.52–7.41 (m, 1H), 4.39 (d, *J* = 7.3 Hz, 1H), 2.69 (app t, *J* = 7.6 Hz, 1H), 2.41–2.22 (m, 1H), 1.14 (d, *J* = 6.6 Hz, 3H), 1.09 (m, 3H). Minor diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 10 (br s, 1H), 7.81–7.54 (m, 3H), 7.52–7.41 (m, 1H), 4.08 (d, *J* = 3.9 Hz, 1H), 3.13 (app t, *J* = 4.2 Hz, 1H), 2.57–2.40 (m, 1H), 1.07 (m, 3H), 0.82 (d, *J* = 6.8 Hz, 3H). Both diastereomers: ¹³C NMR (75 MHz, CDCl₃) δ 206.0, 204.3, 178.2, 177.3, 149.7, 148.4, 137.5, 136.7, 135.1, 134.5, 129.0, 126.3, 126.1, 124.0, 123.8, 58.4, 56.4, 48.7, 46.1, 29.1, 27.2, 22.1, 20.6, 20.5, 17.8.

STEP 4. Preparation of 1b. Light brown oil (2.09 g, 98% yield); dr >99 (by ¹H NMR). ¹H NMR (300 MHz, CDCl₃) δ 7.78–7.74 (m, 1H), 7.66–7.59 (m, 2H), 7.50–7.40 (m, 1H), 4.07 (d, *J* = 4.1 Hz, 1H), 3.80 (s, 3H), 3.15 (app t, *J* = 4.2 Hz, 1H), 2.48 (app sptd, *J* = 6.9, 4.3 Hz, 1H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 206.03, 172.8, 150.4, 136.7, 134.9, 128.7, 126.0, 123.8, 56.6, 52.6, 46.2, 28.9, 20.5, 17.7. HRMS (ESI): calculated for C₁₄H₁₇O₃ [M+H]⁺ 233.1178, found 233.1177.

2-Cyclohexy-3-methoxycarbonyl-1-indanone (1c). The title compound was prepared following a similar reaction sequence as for **1d**, starting from cyclohexanecarboxaldehyde (6.73 g, 60.0 mmol) and phenylacetonitrile (7.03 g, 60 mmol). Characterization data for intermediate compounds and the reaction yields are as follows:



STEP 1. Preparation of 3-cyclohexyl-2-phenylacrylonitrile.⁸ White crystals after trituration with petroleum ether at 0 °C (9.89 g, 78 % yield). ¹H NMR (300 MHz, CDCl₃) δ 7.61–7.46 (m, 2H), 7.50–7.28 (m, 3H), 6.65 (d, *J* = 10.0 Hz, 1H), 2.86–2.66 (m, 1H), 1.93–1.66 (m, 5H), 1.53–1.11 (m, 5H). ¹³C NMR (75 MHz, CDCl₃) δ 152.1, 133.3, 128.9, 128.7, 125.6, 116.7, 113.7, 41.4, 32.1, 25.6, 25.2.

STEP 2a. Preparation of 3-cyclohexyl-2-phenylsuccinonitrile. White solid; dr = 94:6 (by ¹H NMR). Major diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 7.58–7.36 (m, 5H), 4.01 (d, *J* = 10.5 Hz, 1H), 2.95 (dd, *J* = 10.5, 4.0 Hz, 1H), 2.11–1.67 (m, 6H), 1.48–1.13 (m, 5H). ¹³C NMR (76 MHz, CDCl₃) δ 132.2, 129.5, 129.5, 128.1, 117.7, 117.0, 45.0, 37.9, 37.7, 31.8, 27.9, 25.8, 25.6, 25.5. Minor diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 7.56–7.37 (m, 5H), 4.15 (d, *J* = 5.7 Hz, 1H), 2.73 (dd, *J* = 7.8, 5.9 Hz, 1H), 2.13–1.64 (m, 6H), 1.50–1.09 (m, 4H).

STEP 2b. Preparation of 3-cyclohexyl-2-phenylsuccinonic acid. White powder (12.0 g, 92.9% yield for steps 2a and 2b); dr = 99:1 (by ¹H NMR). Characteristic signal for minor diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 3.25

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(4) CAS [15297-74-2]; no characterization data available.

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(6) CAS [1352708-83-8]; no characterization data available.

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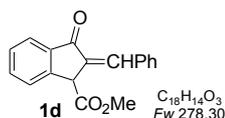
(dd, $J = 11.1, 5.2$ Hz, 1H). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 12.68 (br s, 2H), 7.52–7.25 (m, 5H), 3.98 (d, $J = 12.0$ Hz, 1H), 3.08 (dd, $J = 12.0, 2.7$ Hz, 1H), 1.89–0.78 (m, 11H). ^{13}C NMR (75 MHz, CDCl_3) δ 180.8, 180.3, 135.5, 129.1, 128.4, 128.2, 53.4, 51.2, 36.7, 32.1, 27.9, 26.6, 26.3, 26.0.

STEP 3a. Preparation of 3-cyclohexyl-2-phenylsuccinonic anhydride.⁹ White powder after trituration with Et_2O at -20 °C (6.51 g, 84% yield); dr = 60:40 (by ^1H NMR). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.53–7.15 (m, 5H), 4.44 (d, $J = 9.3$ Hz, 1H), 3.20–3.14 (m, 1H), 2.13–0.82 (m, 11H). Minor diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.53–7.15 (m, 5H), 4.06 (d, $J = 6.2$ Hz, 1H), 3.20–3.14 (m, 1H), 2.13–0.82 (m, 11H). Both diastereomers: ^{13}C NMR (75 MHz, CDCl_3) δ 171.8, 171.4, 171.2, 170.7, 135.5, 131.0, 129.5, 129.1, 128.6, 128.5, 127.5, 54.9, 51.7, 50.1, 49.9, 39.2, 35.8, 31.2, 30.0, 29.2, 29.2, 26.0, 25.9, 25.9, 25.7, 25.6, 25.4 (the signal of 1 aromatic carbon is not observed due to overlapping).

STEP 3b. Preparation of 2-cyclohexyl-3-oxo-indan-1-carboxylic acid. Beige solid (6.51 g, 100% yield); dr = 53:47 (by ^1H NMR); m.p. 145–147 °C (lit.¹⁰ 149 °C). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.76 (d, $J = 7.6$ Hz, 1H), 7.74–7.53 (m, 2H), 7.54–7.39 (m, 1H), 4.37 (d, $J = 7.3$ Hz, 1H), 2.76 (app t, $J = 7.4$ Hz, 1H), 2.36–0.85 (m, 11H). Minor diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.76 (d, $J = 7.6$ Hz, 1H), 7.74–7.53 (m, 2H), 7.54–7.39 (m, 1H), 4.14 (d, $J = 3.8$ Hz, 1H), 3.12 (app t, $J = 4.1$ Hz, 1H), 2.36–0.85 (m, 1H). Both diastereomers: ^{13}C NMR (75 MHz, CDCl_3) δ 206.2, 204.6, 178.0, 177.1, 149.8, 148.5, 137.5, 136.8, 135.1, 134.4, 128.94, 128.92, 126.3, 126.0, 123.9, 123.7, 57.4, 56.2, 48.3, 46.8, 39.3, 36.9, 31.9, 31.0, 30.8, 28.2, 26.4, 26.3, 26.2, 26.09, 26.06, 25.9.

STEP 4. Preparation of 1c. White solid after trituration with petroleum ether (1.65 g, 89% yield), dr >99 (by ^1H NMR); m.p. 89 °C (lit.¹¹ 88 °C). ^1H NMR (300 MHz, CDCl_3) δ 7.75 (d, $J = 7.6$ Hz, 1H), 7.65–7.58 (m, 2H), 7.49–7.39 (m, 1H), 4.12 (d, $J = 3.9$ Hz, 1H), 3.79 (s, 3H), 3.12 (t, $J = 4.2$ Hz, 1H), 2.20–2.05 (m, 1H), 1.84–1.59 (m, 4H), 1.49–0.97 (m, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 206.2, 172.8, 150.5, 136.8, 134.9, 128.7, 126.0, 123.7, 56.4, 52.6, 47.0, 39.2, 30.9, 28.2, 26.4, 26.10, 26.07.

2-Benzylidene-3-methoxycarbonyl-1-indanone (1d). **STEP 1. Preparation of 2-benzal-3-oxoindancarboxylic acid.**¹² To a solution of NaOMe [prepared from Na (36 mg, 1.6 mmol) and dry MeOH (16 mL)] was added benzaldehyde (585 mg, 5.52 mmol). To this solution cooled to 0 °C was added dropwise a solution of methyl 3-oxoindancarboxylate (1.00 g, 5.26 mmol) then

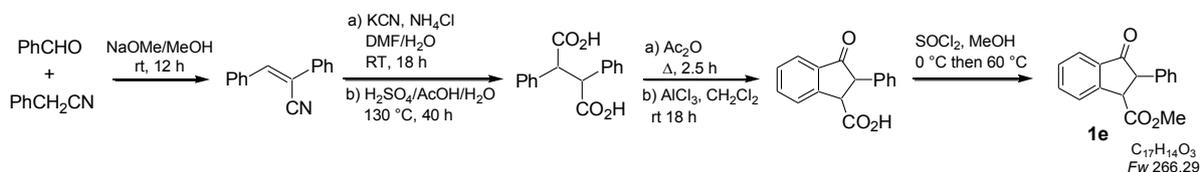


allowed to warm to rt overnight. The reaction mixture was poured onto satd. aq. NH_4Cl

(20 mL), pH adjusted to 2 with 2N HCl and the product extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude product was triturated with hexane/EtOAc to obtain a light yellow powder (1.13 g, 81% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.94 (d, $J = 7.6$ Hz, 1H), 7.81 (d, $J = 1.8$ Hz, 1H), 7.70 (d, $J = 7.6$ Hz, 1H), 7.68–7.62 (m, 1H), 7.61–7.55 (m, 2H), 7.51 (t, $J = 7.3$ Hz, 1H), 7.44–7.32 (m, 3H), 5.12 (d, $J = 1$ Hz, 1H).

STEP 2. To a solution of the above acid (600 mg, 2.27 mmol) in MeOH (12 mL) was added dropwise SOCl_2 (250 μL , 1.5 eq). The resulting solution was refluxed overnight, then concentrated to 5 mL and cooled to 0 °C. The white precipitate was filtered and washed with cold MeOH yielding the title compound as white crystals (470 mg, 74% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.96 (d, $J = 7.6$ Hz, 1H), 7.81 (d, $J = 1.8$ Hz, 1H), 7.73–7.37 (m, 8H), 5.17 (d, $J = 1.3$ Hz, 1H), 3.56 (s, 3H). NMR data are in accordance with the literature.¹²

3-Methoxycarbonyl-2-phenyl-1-indanone (1e)



STEP 1. Preparation of (Z)-2,3-diphenylacrylonitrile. A solution of NaOMe in MeOH [prepared from Na (2.76 g, 120 mmol, 1.2 eq) and dry MeOH (40 mL)] was added to a solution of benzaldehyde (10.6 g, 100 mmol) and phenylacetonitrile (11.7 g, 100 mmol) in dry MeOH (160 mL). The reaction mixture was stirred at rt for 12 h, concentrated to 100 mL and cooled to 0 °C. The white precipitate was filtered and washed with cold MeOH

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(11) Fieser, L. F.; Bader, A. R. *J. Am. Chem. Soc.* **1951**, *73*, 681–684.

(12) Murray, R. J.; Cromwell, N. H. *J. Org. Chem.* **1976**, *41*, 3540–3545.

(19.6 g, 95.3 %). ^1H NMR (300 MHz, CDCl_3) δ 7.94–7.86 (m, 2H), 7.74–7.64 (m, 2H), 7.54 (s, 1H), 7.52–7.35 (m, 6H).¹³

STEP 2a. Preparation of 2,3-diphenylsuccinonitrile. To a suspension of KCN (8.07 g, 124 mmol, 1.3 eq) and (Z)-2,3-diphenylacrylonitrile (19.6 g, 95.3 mmol) in DMF (390 mL) was carefully added an aqueous solution of NH_4Cl (prepared from 5.62 g (105 mmol, 1.1 eq) NH_4Cl and 143 mL H_2O) keeping the internal temperature below 50 °C. After stirring at rt for 18 h, the reaction mixture was poured onto water (1.0 L), and the precipitate filtered and washed with water (3×100 mL). This was dried by suction on the frit for 4 h and was used as such in the next step. For its analysis, a small sample was further dried under high vacuum. ^1H NMR (300 MHz, CDCl_3) δ 7.46–7.34 (m, 6H), 7.29–7.19 (m, 4H), 4.25 (s, 2H). NMR data is in accordance with the literature.¹⁴

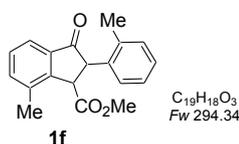
STEP 2b: Preparation of 2,3-diphenylsuccinic acid. To a suspension of the above succinonitrile in AcOH (80 mL) and water (80 mL) was added at 0 °C portionwise 98% H_2SO_4 (80 mL). The reaction mixture was refluxed for 30 h. When hydrolysis was completed (followed by ^1H NMR), the white slurry was cooled, poured onto ice (1.3 L), the solid collected and washed with water (3×100 mL). The product was dried on frit with suction for 4 h, then in vacuum over P_2O_5 for 12 h to yield the title compound as a white powder (22.1 g, 85.9 % for steps 2a and 2b); dr = 75:25. ^1H NMR (300 MHz, acetone- d_6) δ 11.86–9.93 (br s, 2H), 7.61–7.53 (m, 3H), 7.50–7.23 (m, 4H), 7.24–7.03 (m, 3H), 4.40 (s, 1.5H, major diastereomer), 4.30 (s, 0.5H, minor diastereomer).

STEP 3a: Preparation of 2,3-diphenylsuccinic anhydride. A suspension of 2,3-diphenylsuccinic acid (8.12 g, 30.0 mmol) in acetic anhydride (45 mL) was heated at 110 °C for 1.5 h. The resulting brown solution was concentrated under reduced pressure and triturated with Et_2O to get the title compound as white powder; dr = 94:6 (by ^1H NMR). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.20–7.06 (m, 6H), 6.93–6.79 (m, 4H), 4.72 (s, 2H).

STEP 3b: Preparation of 3-oxo-2-phenylindan-1-carboxylic acid. To a solution of the above anhydride in CH_2Cl_2 (60 mL) at 0 °C was added portionwise AlCl_3 (8.0 g, 60 mmol, 2 eq) and the reaction mixture stirred at 25 °C for 18 h. The resulting brown solution was poured onto ice-water (300 mL)/10% HCl (15 mL) and extracted with CH_2Cl_2 (200 mL then 50 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated to get beige crispy foam (7.10 g, 93.8% yield for steps 3a and 3b); *trans/cis* = 94:6 (by ^1H NMR). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.85 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 7.7 Hz, 1H), 7.71 (app t, J = 7.5 Hz, 1H), 7.53 (app t, J = 7.4 Hz, 1H), 7.37–7.27 (m, 3H), 7.23–7.15 (m, 2H), 4.39 (d, J = 4.4 Hz, 1H), 4.36 (d, J = 4.4 Hz, 1H). NMR data is in accordance with the literature.¹⁵

STEP 4: Preparation of 1e. To a cooled suspension of 3-oxo-2-phenylindan-1-carboxylic acid (6.50 g, 25.8 mmol) in dry MeOH (130 mL) was added dropwise SOCl_2 (3.8 mL, 51.5 mmol). The resulting solution was refluxed for 3 h then poured onto ice-cold satd. aq. NaHCO_3 (150 mL). After partial concentration, the product was extracted with EtOAc (150 mL), the organic layer washed with brine, dried (Na_2SO_4), and concentrated. Trituration with cyclohexane gave the title compound as a white solid (6.18 g, 90% yield); *trans/cis* = 97:3 (by ^1H NMR). ^1H NMR (300 MHz, CDCl_3) δ 7.85 (d, J = 7.7 Hz, 1H), 7.77–7.66 (m, 2H), 7.55–7.49 (m, 1H), 7.38–7.27 (m, 3H), 7.21–7.16 (m, 2H), 4.39 (d, J = 4.6 Hz, 1H), 4.37 (d, J = 4.6 Hz, 1H), 3.82 (s, 3H). NMR data is in accordance with the literature.¹⁶

3-Methoxycarbonyl-4-methyl-2-*o*-tolyl-1-indanone (1f). The title compound was prepared following a similar reaction sequence as for **1e**, starting from *o*-tolualdehyde (7.21 g, 60 mmol) and *o*-tolylacetonitrile (7.87 g, 60 mmol). Characterization data for intermediate compounds and the reaction yields are as follows:



STEP 1. Preparation of (Z)-2,3-di-*o*-tolylacrylonitrile. The reaction mixture was heated at 50 °C overnight. White solid (12.2 g, 86.9% yield). ^1H NMR (300 MHz, CDCl_3) δ 8.10–7.93 (m, 1H), 7.49–7.14 (m, 8H), 2.50 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 145.8, 137.2, 136.1, 135.2, 132.8, 130.8, 130.4, 130.2, 129.4, 129.1, 127.8, 126.4, 126.3, 117.6, 113.3, 20.1, 19.9.

STEP 2a. Preparation of 2,3-di-*o*-tolylsuccinonitrile. White solid; dr = 78:22 (by ^1H NMR). ^1H NMR (300 MHz, CDCl_3) δ 7.77–7.64 (m, 1H), 7.41–7.24 (m, 5H), 7.23–7.10 (m, 2H), 4.53 (s, 0.22H, minor diastereomer), 4.38 (s,

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0.78H, major diastereomer), 2.21 (s, 6H). ^{13}C NMR (76 MHz, CDCl_3) δ 136.1, 135.2, 131.2, 131.2, 129.9, 129.6, 129.4 (2C), 129.1, 128.7, 127.3, 127.1, 117.6, 117.6, 39.1, 38.3, 19.2, 19.0.

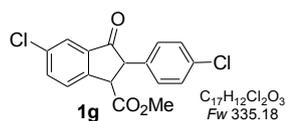
STEP 2b. Preparation of 2,3-di-*o*-tolylsuccinic acid. White solid (14.1 g, 90.2% yield for steps 2a and 2b); dr = 96:4 (by ^1H NMR). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 12.24 (br s, 2H), 7.43 (dd, $J = 7.6, 1.2$ Hz, 2H), 7.08 (td, $J = 7.5, 1.5$ Hz, 2H), 7.02 (td, $J = 7.4, 1.5$ Hz, 2H), 6.94 (dd, $J = 7.5, 0.9$ Hz, 2H), 4.72 (s, 2H), 2.15 (s, 6H). Characteristic signals for minor diastereomer: δ 4.32 (s, 2H), 2.03 (s, 6H).¹⁷

STEP 3a: Preparation of 2,3-di-*o*-tolylsuccinic anhydride. White solid (4.71 g, 84% yield); dr = 95:5 (by ^1H NMR). ^1H NMR (300 MHz, CDCl_3) δ 7.32–7.21 (m, 4H), 7.21–7.11 (m, 4H), 4.93 (s, 0.10H, minor diastereomer), 4.54 (s, 1.9H, major diastereomer), 2.13 (s, 0.3H, minor diastereomer), 2.01 (s, 5.7H, major diastereomer).

STEP 3b: Preparation of 7-methyl-2-(*o*-tolyl)-3-oxoindan-1-carboxylic acid. Beige solid. Used in the next step without purification.

STEP 4: Preparation of 1f. Colorless oil (1.5 g, 30% yield for steps 3b and 4) after column chromatography, eluting with petroleum ether/ CH_2Cl_2 (1:1 then 1:2; $R_f = 0.27$); dr = 87:13 (by ^1H NMR). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.73 (d, $J = 7.1$ Hz, 1H), 7.54–7.41 (m, 2H), 7.25–7.05 (m, 3H), 6.81 (d, $J = 7.5$ Hz, 1H), 4.34 (d, $J = 3.6$ Hz, 1H), 4.22 (d, $J = 3.6$ Hz, 1H), 3.77 (s, 3H), 2.37 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 204.6 (C = O), 173.1 (CO_2Me), 149.1, 136.5 (ArCH), 130.8 (ArCH), 129.3 (ArCH), 127.5 (ArCH), 127.2 (ArCH), 126.5 (ArCH), 122.1 (ArCH), 55.7 (ArCH), 52.8, 52.6, 20.0, 18.1. Characteristic peaks for the minor diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 4.74 (d, $J = 8.7$ Hz, 1H), 4.43 (d, $J = 8.7$ Hz, 1H), 3.13 (s, 3H), 2.45 (s, 3H), 2.33 (s, 3H). HRMS (ESI): calculated for $\text{C}_{19}\text{H}_{19}\text{O}_3$ $[\text{M}+\text{H}]^+$ 295.1334, found 295.1332.

6-Chloro-3-methoxycarbonyl-2-(*p*-chlorophenyl)-1-indanone (1g). The title compound was prepared following



a similar reaction sequence as for **1e**, starting from *p*-chlorobenzaldehyde (8.43 g, 60.0 mmol) and *p*-chlorophenylacetonitrile (9.10 g, 60.0 mmol). Characterization data for intermediate compounds and the reaction yields are as follows:

STEP 1: Preparation of (Z)-2,3-di-*p*-chlorophenylacrylonitrile. White solid (15.2 g, 92.5% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.82 (d, $J = 8.6$ Hz, 2H), 7.60 (d, $J = 8.5$ Hz, 2H), 7.50–7.38 (m, 5H). NMR data is in accordance with the literature.¹⁸

STEP 2a: Preparation of 2,3-di-*p*-chlorophenylsuccinonitrile. White solid; dr = 94:6 (by ^1H NMR); m.p. 210–214 °C (lit.¹⁹ 234–236 °C). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.38 (d, $J = 8.3$ Hz, 4H), 7.15 (d, $J = 8.4$ Hz, 4H), 4.23 (s, 2H). Characteristic signal for the minor diastereomer is at 4.26 (s, 2H).

STEP 2b: Preparation of 2,3-di-*p*-chlorophenylsuccinic acid.²⁰ White solid (17.2 g, 99.6% yield for steps 2a and 2b), dr \approx 1:1 (by ^1H NMR). ^1H NMR (300 MHz, CDCl_3) δ 10.52 (br s, 2H), 7.17 (d, $J = 8.3$ Hz, 4H), 7.03 (d, $J = 8.4$ Hz, 4H), 4.21 (s, 2H). ^{13}C NMR (mixture of diastereomers) (75 MHz, $\text{DMSO}-d_6$) δ 173.6, 172.0, 136.2, 135.5, 132.4, 131.9, 130.3, 130.2, 128.5, 128.4, 53.7, 52.8.

STEP 3a: Preparation of 2,3-di-*p*-chlorophenylsuccinic anhydride. White solid; dr = 71:29 (by ^1H NMR). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.39 (d, $J = 8.4$ Hz, 4H), 7.14 (d, $J = 8.4$ Hz, 4H), 4.33 (s, 2H). Minor diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.17 (d, $J = 8.4$ Hz, 4H), 6.82 (d, $J = 8.4$ Hz, 4H), 4.70 (s, 2H).

STEP 3b: Preparation of 5-chloro-2-(*p*-chlorophenyl)-3-oxoindan-1-carboxylic acid. Off-white crispy foam, dr = 60:40 (by ^1H NMR). The product was used in the next step without further purification. Characteristic peaks: ^1H NMR (300 MHz, CDCl_3) δ 4.67 (d, $J = 8.4$ Hz, 0.4H, minor), 4.35 (d, $J = 4.7$ Hz, 0.6H, major).

STEP 4: Preparation of 1g. White solid (1.3 g, 35% yield for steps 3 and 4); dr > 99 (by ^1H NMR) after trituration with petroleum ether 40-60/ CH_2Cl_2 . ^1H NMR (300 MHz, CDCl_3) δ 7.79 (d, $J = 1.7$ Hz, 1H), 7.70 (app dt, $J = 8.2, 0.8$ Hz, 1H), 7.65 (dd, $J = 8.3, 1.9$ Hz, 1H), 7.31 (d, $J = 8.4$ Hz, 2H), 7.12 (d, $J = 8.4$ Hz, 3H), 4.38 (d, $J = 4.7$ Hz, 1H), 4.27 (d, $J = 4.7$ Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 201.6, 171.1, 147.4, 136.8, 135.9, 135.9, 135.5, 133.6, 129.5, 129.2, 127.6, 124.4, 56.3, 53.0, 52.5. HRMS (ESI): calculated for $\text{C}_{17}\text{H}_{13}\text{Cl}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 335.0236, found 335.0231.

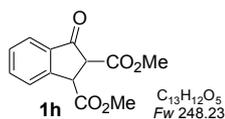
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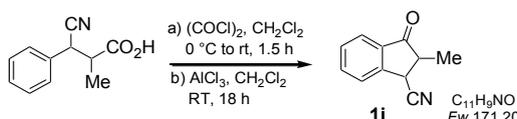
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2,3-Di(methoxycarbonyl)-1-indanone (1h). To a mixture of NaH (379 mg, 15.8 mmol) and dimethyl carbonate (3.08 g, 34.2 mmol) in benzene (0.5 mL) was added dropwise at 60 °C a solution of 3-oxo-1-indancarboxylic acid methyl ester (1.00 g, 5.26 mmol) in benzene (6.5 mL) over 2 h. The reaction mixture was stirred at 60 °C for 30 min then cooled to 0 °C, quenched with acetic acid (1.3 mL), and partitioned between water (30 mL) and toluene (3 × 20 mL). The combined organic layers were washed with satd. aq. NaHCO₃ and brine, dried (MgSO₄) and concentrated. After purification by column chromatography (hexane/EtOAc = 4:1), the title compound was obtained as light brown oil (1.11 g, 85% yield); dr = 80:20 (by ¹H NMR). Major diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 7.82–7.76 (m, 2H), 7.72–7.65 (m, 1H), 7.52–7.46 (m, 1H), 4.78 (d, *J* = 4.3 Hz, 1H), 4.25 (d, *J* = 4.3 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H). Characteristic signals for the minor diastereomer are 3.85 (s, 3H) and 3.71 (s, 3H).

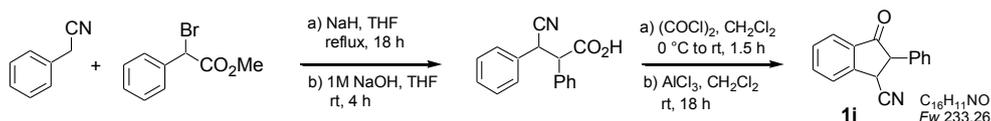


2-Methyl-3-cyano-1-indanone (1i)



To a cold (0 °C) solution of 3-cyano-2-methyl-3-phenylpropionic acid (for its preparation, see in procedure for **1a**) (10.0 g, 52.9 mmol) in dry CH₂Cl₂ (100 mL) was added under stirring oxalyl chloride (5.9 mL, 68.7 mmol) followed by a catalytic amount of DMF (100 μL). The resulting mixture was left to stir at rt for 1.5 h then concentrated. The brown oily residue was taken in dry CH₂Cl₂ (50 mL), cooled to 0 °C and AlCl₃ (14.1 g, 106 mmol) was added portionwise. After stirring at rt for 18 h, the reaction mixture was poured onto ice-water (200 mL), and the layers separated. The aqueous layer was extracted with CH₂Cl₂ (100 mL), and the combined organic layers washed with aq. NaHCO₃ and brine, dried (Na₂SO₄), filtered through a plug of silica gel and concentrated. The resulting brown solid was triturated with cold *i*Pr₂O to afford the title compound as a white solid (4.81 g, 53% yield); dr = 98:2 (by ¹H NMR). ¹H NMR (300 MHz, CDCl₃) δ 7.82 (d, *J* = 7.7 Hz, 1H), 7.79–7.69 (m, 2H), 7.59–7.52 (m, 1H), 3.93 (d, *J* = 5.7 Hz, 1H), 3.05 (qd, *J* = 7.3, 5.7 Hz, 1H), 1.49 (d, *J* = 7.3 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 202.5, 146.0, 135.9, 135.0, 129.9, 125.9, 124.6, 119.1, 48.1, 36.5, 14.4. HRMS (ESI): calculated for C₁₁H₁₀NO [M+H]⁺ 172.0762, found 172.07.

3-Cyano-2-phenyl-1-indanone (1j)



STEP 1a: preparation of methyl 3-cyano-2,3-diphenylpropanoate. A mixture of benzyl cyanide (15.2 mL, 132 mmol), NaH (3.80 g, 158 mmol), and methyl 2-bromo-2-phenylacetate (30 g, 132 mmol) in dry THF (150 mL) was refluxed for 18 h. The reaction mixture was cooled to rt and partitioned between satd. aq. NH₄Cl (250 mL) and CH₂Cl₂ (EtOAc, 250 mL), washed with brine, dried (Na₂SO₄), filtered and concentrated to get an oil containing some unreacted starting material, and the product with *anti/syn* = 57:43 (by ¹H NMR). After crystallization from MeOH at –20 °C, the pure *anti* product was isolated as white crystals (5.72 g, 16% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.43–7.30 (m, 10H), 4.57 (d, *J* = 9.9 Hz, 1H), 4.00 (d, *J* = 9.9 Hz, 1H), 3.55 (s, 3H). NMR data is in accordance with the literature.²¹

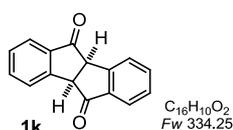
STEP 1b: preparation of 3-cyano-2,3-diphenylpropanoic acid.²² A mixture of the above ester (5.72 g, 21.5 mmol), THF (40 mL) and 1M NaOH (26 mL) was vigorously stirred at rt for 4 h. THF was partially removed under reduced pressure, CH₂Cl₂ (50 mL) was added and the layers separated. The water layer was acidified to pH 2 using 37% HCl. The product was extracted with CH₂Cl₂ (3 × 50 mL), the combined organic layers dried (Na₂SO₄) and concentrated. After trituration with hexane, the product was obtained as a white powder (5.19 g, 96%

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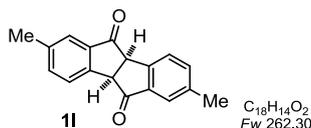
yield), dr = 55:45 (by ^1H NMR). ^1H NMR (300 MHz, CDCl_3) δ 7.42–7.18 (m, 8H), 7.10–7.02 (m, 2H), 4.55 (d, J = 9.5 Hz, 0.55H), 4.28 (d, J = 10.0 Hz, 0.45H), 4.04 (d, J = 10.0 Hz, 0.45H), 4.03 (d, J = 9.5 Hz, 0.55H).

STEP 2: preparation of 1j. To a suspension of the above acid (5.00 g, 19.9 mmol) in CH_2Cl_2 (40 mL) was added at rt oxalyl chloride (1.8 mL, 20.9 mmol) followed by catalytic amount of DMF (50 μL). The reaction mixture was stirred for 2 h, then AlCl_3 (7.94 g, 59.7 mmol) was added portionwise and the resulting suspension refluxed overnight. The reaction mixture was poured onto ice-water (200 mL) and extracted with CH_2Cl_2 (200 mL). The organic layer was washed with brine, dried (Na_2SO_4), filtered and concentrated to get brown oil. After column chromatography eluting with hexane/ CH_2Cl_2 3:2 then CH_2Cl_2 , pure **1j** was obtained as colorless thick oil which solidified upon standing (2.00 g, 43% yield); dr = 84:16 (by ^1H NMR). ^1H NMR (300 MHz, CDCl_3) δ 7.94–7.88 (m, 1H), 7.86–7.74 (m, 2H), 7.68–7.58 (m, 1H), 7.45–7.31 (m, 3H), 7.25–7.18 (m, 1.7H, major), 7.17–7.09 (m, 0.3H, minor), 4.86 (d, J = 8.4 Hz, 0.15H, minor), 4.39 (d, J = 5.7 Hz, 0.85H, major), 4.24 (d, J = 8.4 Hz, 0.15H, minor), 4.18 (d, J = 5.7 Hz, 0.85H, major). If exposed to air, the compound converts partially to 3-cyano-2-phenylindene as indicated in the literature.²²

cis-Indeno[2,1-a]indene-5,10(4bH,9bH)-dione (1k). Prepared according to the literature procedure.²³ Thus, 2,3-diphenylsuccinic acid (12.0 g, 44.4 mmol) was added at 25 °C to 97% H_2SO_4 (78 mL) under stirring. The reaction mixture was stirred at 110 °C for 1.5 h then poured onto ice (400 mL). The white precipitate was collected, washed with water (3 \times 70 mL) and dried under high vacuum to get the title compound as a white powder (4.34 g, 41.7% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.93 (d, J = 7.7 Hz, 2H), 7.79–7.62 (m, 4H), 7.44 (app td, J = 7.6, 0.8 Hz, 2H), 4.41 (s, 2H).



cis-2,7-Dimethylindeno[2,1-a]indene-5,10(4bH,9bH)-dione (1l). First, 2,3-di-*p*-tolylsuccinic acid was prepared following a similar reaction sequence as for **1e**, starting from *p*-tolualdehyde (7.21 g, 60.0 mmol) and *p*-xylylcyanide (7.87 g, 60.0 mmol). Characterization data for intermediate compounds and the reaction yields are as follows:



STEP 1. Preparation of 2,3-di-*p*-tolylacrylonitrile. The reaction mixture was heated at 50 °C overnight. White solid (13.5 g, 97% yield); dr = 75:25 (by ^1H NMR). ^1H NMR (300 MHz, CDCl_3) δ 7.78 (d, J = 8.2 Hz, 1.5H), 7.55 (d, J = 8.2 Hz, 1.5H), 7.46 (s, 0.75H), 7.32–7.20 (m, 4H), 7.15 (d, J = 7.9 Hz, 0.5H), 7.07 (d, J = 8.3 Hz, 0.5H), 7.02 (d, J = 8.3 Hz, 0.5H), 2.40 (s, 2.25H), 2.39 (s, 2.25H), 2.37 (s, 0.75H), 2.31 (s, 0.75H). NMR data is in accordance with the literature.²⁴

STEP 2a. Preparation of 2,3-di-*p*-tolylsuccinonitrile. The reaction mixture was heated at 60 °C overnight. White powder; dr = 94:6 (by ^1H NMR). Major diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.21–7.16 (m, 4H), 7.15–7.10 (m, 4H), 4.18 (s, 2H), 2.37 (s, 6H). Characteristic peak for the minor diastereomer is 4.20 ppm (s, 2H). NMR data is in accordance with the literature.²⁵

STEP 2b. Preparation of 2,3-di-*p*-tolylsuccinic acid.^{26a} White powder (15.9 g, 96.8% yield for 2 steps). ^1H NMR (300 MHz, CDCl_3) δ 7.01 (d, J = 8.5 Hz, 1H), 6.96 (d, J = 8.5 Hz, 1H), 4.22 (s, 1H), 2.21 (s, 2H).

STEP 3. Preparation of 1l. A mixture of the above diarylsuccinic acid (2.0 g, 6.70 mmol) and polyphosphoric acid (20 g) was stirred at 150 °C for 48 h. The resulting black liquid was poured onto ice (150 mL), the precipitate filtered, air-dried and recrystallized from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to get the title compound as grey powder (390 mg, 22% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.78 (d, J = 8.6 Hz, 2H), 7.52–7.44 (m, 4H), 4.34 (s, 2H), 2.37 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 201.8, 147.3, 139.2, 136.9, 134.9, 126.1, 124.6, 52.6, 21.1. HRMS (ESI): calculated for $\text{C}_{18}\text{H}_{15}\text{O}_2$ $[\text{M}+\text{H}]^+$ 263.1072, found 263.1078.

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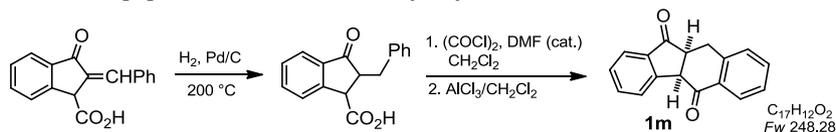
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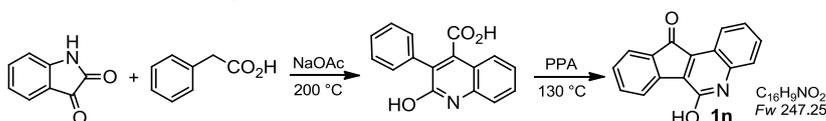
cis-10,10a-Dihydro-4*b*H-benzo[*b*]fluorene-5,11-dione (**1m**)



STEP 1. 2-Benzyl-3-oxo-1-indancarboxylic acid was prepared according to the literature procedure^{26b} by hydrogenation of 2-benzylidene-3-oxo-1-indancarboxylic acid (1.80 g, 6.81 mmol) at 20–30 psig H₂ using 10% Pd/C (180 mg) in EtOAc (34 mL). Light yellow crystals (1.81 g, 100% yield); dr = 70:30 (by ¹H NMR). ¹H NMR (300 MHz, CDCl₃) δ 7.85 (d, *J* = 7.6 Hz, 0.3H, minor), 7.79 (d, *J* = 7.6 Hz, 0.7H, major), 7.67–7.42 (m, 3H), 7.32–7.12 (m, 5H), 4.26 (d, *J* = 7.2 Hz, 0.3H, minor), 3.97 (d, *J* = 4.4 Hz, 0.7H, major), 3.58–3.42 (m, 1H), 3.33 (dd, *J* = 14.1, 5.1 Hz, 0.7H, major), 3.27–3.18 (m, 0.3H, minor), 2.96 (dd, *J* = 14.1, 8.5 Hz, 0.7H, major), 2.94 (dd, *J* = 14.8, 10.2 Hz, 0.3H, minor).

STEP 2. Preparation of 1m. To a solution of the above carboxylic acid (1.33 g, 5 mmol) in CH₂Cl₂ (10 mL) was added oxalyl chloride (0.55 mL, 6.5 mmol, 1.3 eq), followed by catalytic amount of DMF (50 μL). The reaction mixture was stirred at rt for 1.5 h then it was concentrated. The resulting crude acyl chloride [dr = 84:16 by ¹H NMR; characteristic signals: ¹H NMR (300 MHz, CDCl₃) δ 4.36 (d, *J* = 4.2 Hz, 1H, major), 4.00 (d, *J* = 4.6 Hz, 1H, minor)] was dissolved in CH₂Cl₂ (10 mL) and AlCl₃ (1.33 g, 10 mmol, 2 eq) was added portionwise. The reaction mixture was stirred at rt overnight then poured onto ice (150 mL). The product was extracted with CH₂Cl₂ (5 × 150 mL), dried (Na₂SO₄), filtered through a short plug of silica gel and concentrated to obtain a yellow solid (917 mg, 74% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.92 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.77–7.68 (m, 2H), 7.65 (td, *J* = 7.6, 1.2 Hz, 1H), 7.51–7.36 (m, 2H), 7.35–7.20 (m, 2H), 4.51 (d, *J* = 7.4 Hz, 1H), 3.53 (dd, *J* = 15.6, 2.7 Hz, 1H), 3.38 (dd, *J* = 7.4, 2.7 Hz, 1H), 3.28 (dd, *J* = 15.6, 7.2 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 205.6, 196.2, 151.0, 141.1, 136.2, 135.4, 134.1, 132.4, 128.8, 128.6, 127.6, 127.3, 127.1, 123.8, 50.4, 45.5, 27.1. HRMS (ESI): calculated for C₁₇H₁₃O₂ [M+H]⁺ 249.0916, found 249.0923.

6-Hydroxy-11*H*-indeno[1,2-*c*]quinolin-11-one (**1n**).



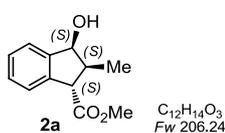
STEP 1. The Pfitzinger product of isatin and phenylacetic acid was prepared according to the literature procedure.²⁷

STEP 2. Preparation of 1n. A mixture of the above 2-hydroxy-3-phenyl-4-quinolinecarboxylic acid (7.41g, 27.9 mmol) and polyphosphoric acid (91 g) was heated at 130 °C for 2 h, then it was poured onto ice-water (300 mL) and the precipitate filtered. The crude product was dissolved in boiling EtOH, cooled to 5 °C and the brick-red fine powder collected on the frit No. 4 (4.32 g, 63% yield). ¹H NMR (300 MHz, DMSO-*d*₆) δ 12.36 (s, 1H), 8.40 (d, *J* = 7.9 Hz, 1H), 7.95 (d, *J* = 7.0 Hz, 1H), 7.62–7.51 (m, 3H), 7.46–7.23 (m, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 195.4, 158.8, 141.7, 140.5, 136.8, 135.2, 134.9, 131.1, 130.8, 129.3, 123.9 (2C), 123.3, 123.2, 115.8, 114.7. HRMS (ESI): calculated for C₁₆H₁₀NO₂ [M+H]⁺ 248.0712, found 248.0716.

3 ATH of indanones **1a–1n**

Racemic alcohols as standards: The HPLC analysis reference racemic alcohols were prepared by mixing the corresponding ATH products derived from runs with (*S,S*)- and (*R,R*)-DPEN-based Ru(II) catalysts **A** or **B**.

(1*S*,2*S*,3*S*)-2-Methyl-3-methoxycarbonyl-1-indanol (**2a**).



To a solution of active Ru(II) catalyst **B** (2.00 μmol) prepared from the corresponding (*S,S*)-DPEN-based μ-chlorido Ru(II) dimer (1.40 mg) in HCO₂H/Et₃N 3:2 (1 mL), was added **1a** (204 mg, 1.00 mmol), and stirred at 60 °C for 1 h with continuous mild N₂ sweeping. ¹H NMR analysis of the crude reaction mixture showed 90% conversion and dr = 43:50:7:0.

(27) Tseng, C.-H.; Chen, Y.-L.; Lu, P.-J.; Yang, C.-N.; Tzeng, C.-C. *Bioorg. Med. Chem.* **2008**, *16*, 3153–3162.

The stirring was continued at 60 °C without N₂ sweeping, monitoring the diastereomeric ratio by ¹H NMR: dr = 44:50:6:0 (2 h, 100% conversion), dr = 59:35:6:0 (24 h), dr = 76:17:7:0 (48 h), dr = 86:8:6:0 (170 h). Thus, after 170 h, the reaction mixture was partitioned between EtOAc (10 mL) and H₂O (10 mL), the organic layer was washed with brine (10 mL), filtered through a short plug of silica gel/Na₂SO₄, and concentrated. The title compound was obtained as light brown oil (195 mg, 95% yield). Dr = 86:8:6:0 by ¹H NMR (300 MHz, CDCl₃); diagnostic signals (CHOH): δ 5.15 (d, *J* = 6.0 Hz; *cis,trans*-**2a**), 4.82 (d, *J* = 5.8 Hz; *cis,cis*-**2a**), 4.69 (d, *J* = 4.6 Hz *trans,trans*-**2a**). >99.9% ee (major) by HPLC. Silica gel chromatography eluting with hexane/EtOAc (7:1) afforded the major diastereomer as a colorless thick oil (153 mg, 74% yield); dr = 95:0:5:0. ¹H NMR (300 MHz, CDCl₃) δ 7.48–7.40 (m, 1H), 7.37–7.27 (m, 3H), 5.15 (d, *J* = 5.9 Hz, 1H), 3.84 (d, *J* = 7.5 Hz, 1H), 3.77 (s, 3H), 2.85 (app dd, *J* = 7.1, 6.0 Hz, 1H), 1.23 (d, *J* = 7.1 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 173.7, 144.5, 140.6, 128.9, 128.1, 125.0, 124.9, 76.6, 55.1, 52.1, 43.4, 12.9. Anal. calcd. for C₁₂H₁₄O₃: C, 69.88; H, 6.84. Found: C, 70.01; H, 7.12.

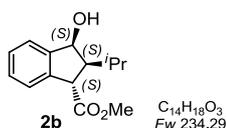
Enantiomeric excess was determined by HPLC analysis on Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, λ = 220 nm, *t_R*: 12.3 min (minor), 14.0 min (major).

The absolute configuration was attributed on the basis of the obtained enantioselectivity for **2f** and **2h**.

2-g scale DKR-ATH of **1a** with S/C = 10 000:

To a solution of active Ru(II) catalyst **B** (2.00 μmol) prepared from the corresponding (*S,S*)-DPEN-based μ-chlorido Ru(II) dimer (0.700 mg) in HCO₂H/Et₃N 3:2 (10.0 mL), was added **1a** (2.04 g, 10.0 mmol), and stirred at 60 °C for 7 days with continuous mild N₂ sweeping. ¹H NMR analysis of the crude reaction mixture showed full conversion and dr = 87:7:6:0. The reaction mixture was partitioned between EtOAc (100 mL) and H₂O (100 mL), the organic layer washed with brine, dried (Na₂SO₄), filtered through a short pad of silica gel and concentrated. After drying in high vacuum overnight, the title compound was obtained as a colorless oil (2.04 g, 99% yield).

(1*S*,2*S*,3*S*)-2-Isopropyl-3-methoxycarbonyl-1-indanol (2b**).** To a solution of active Ru(II) catalyst **B** (2.00 μmol)



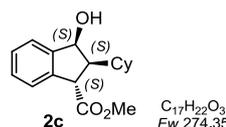
prepared from the corresponding (*S,S*)-DPEN-based μ-chlorido Ru(II) dimer (1.40 mg) in HCO₂H/Et₃N 3:2 (1 mL), was added **1b** (232 mg, 1.00 mmol), and stirred at 60 °C for 24 h with continuous mild N₂ sweeping. The reaction mixture was partitioned between EtOAc (10 mL) and H₂O (10 mL), the organic layer was washed with brine (10 mL), filtered through a plug of silica gel/Na₂SO₄, and concentrated. The title compound was obtained as

a thick oil (234 mg, 100% yield); dr = 95:5:0:0 by ¹H NMR (CHOH)*; 99.8% ee (major) by HPLC. The major diastereomer was isolated by recrystallization from cyclohexane at ca. 8 °C as white crystals (198 mg, 85% yield). Dr >99 by ¹H NMR (300 MHz, CDCl₃); diagnostic signals (CHOH): δ 5.19 (d, *J* = 5.6 Hz, *cis,trans*-**2b**), 4.96–4.91 (m, *cis,cis*-**2b**). >99.9% ee. ¹H NMR (300 MHz, CDCl₃) δ 7.47–7.38 (m, 1H), 7.35–7.25 (m, 2H), 7.25–7.16 (m, 1H), 5.19 (d, *J* = 5.6 Hz, 1H), 3.98 (d, *J* = 9.0 Hz, 1H), 3.79 (s, 3H), 2.56–2.48 (m, 1H), 2.19–2.00 (m, 1H), 1.51 (br s, 1H), 1.15 (d, *J* = 6.4 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 174.6, 144.7, 142.0, 129.3, 128.2, 125.0, 123.9, 75.5, 55.7, 52.8, 52.2, 27.7, 21.8, 21.1. HRMS (ESI): calculated for C₁₄H₁₈O₃Na [M+Na]⁺ 257.1154, found 257.1159.

Enantiomeric excess was determined by HPLC analysis on Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, λ = 220 nm, *t_R*: 12.5 (minor), 15.2 min (major).

The absolute configuration was attributed on the basis of the obtained enantioselectivity for **2f** and **2h**.

(1*S*,2*S*,3*S*)-2-Cyclohexyl-3-methoxycarbonyl-1-indanol (2c**).** To a solution of active Ru(II) catalyst **B** (2.00 μmol)



prepared from the corresponding (*S,S*)-DPEN-based μ-chlorido Ru(II) dimer (1.40 mg) in HCO₂H/Et₃N 3:2 (1 mL), was added **1c** (272 mg, 1.00 mmol), and stirred at 60 °C for 24 h with continuous mild N₂ sweeping. The reaction mixture was partitioned between EtOAc (10 mL) and H₂O (10 mL), the organic layer was washed with brine (10 mL), filtered through a plug of silica gel/Na₂SO₄, and concentrated. The title compound was obtained

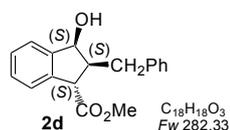
as a white solid (271 mg, 99% yield). Dr = 95:5:0:0 by ¹H NMR (300 MHz, CDCl₃); diagnostic signals (CHOH): δ 5.21 (app t, *J* = 5.5 Hz, *cis,trans*-**2c**), 4.96 (dd, *J* = 12.1, 5.6 Hz, *cis,cis*-**2c**). 99.7% ee (major) by HPLC. The major diastereomer was isolated by recrystallization from toluene/heptane as white needles (220 mg, 81% yield); dr >99; >99.9% ee. ¹H NMR (300 MHz, CDCl₃) δ 7.45–7.37 (m, 1H), 7.33–7.24 (m, 2H), 7.24–7.17 (m, 1H), 5.18 (d, *J* = 5.6 Hz, 1H), 3.97 (d, *J* = 9.1 Hz, 1H), 3.78 (s, 3H), 2.60–2.51 (m, 1H), 2.07 (d, *J* = 12.7 Hz, 1H), 1.88–1.57 (m, 5H), 1.53 (s, 1H), 1.43–0.94 (m, 5H). ¹³C NMR (75 MHz, CDCl₃) δ 174.6, 144.6, 141.9, 129.2, 128.1, 124.9, 123.7, 74.9,

54.4, 52.4, 52.1, 37.0, 32.0, 31.3, 26.4, 26.4, 26.1. Anal. calcd. for C₁₇H₂₂O₃: C, 74.42; H, 8.08. Found: C, 74.12; H, 8.42.

Enantiomeric excess was determined by HPLC analysis on Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, λ = 220 nm, t_R : 12.7 min (minor), 17.2 min (major).

The relative configuration of the major diastereomer was determined by ¹H-¹H NOESY experiment: CHCy has a 10-fold larger NOE with CHOH than with CHCO₂Me. The absolute configuration was assigned according to the generally observed trend of enantioselectivity.

(1S,2S,3S)-2-Benzyl-3-methoxycarbonyl-1-indanol (2d). To a solution of active Ru(II) catalyst **B** (1.00 μ mol)



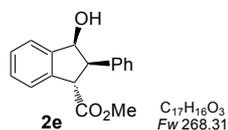
prepared from the corresponding (*S,S*)-DPEN-based μ -chlorido Ru(II) dimer (0.70 mg) in HCO₂H/Et₃N 3:2 (0.50 mL), was added **1d** (139 mg, 0.50 mmol), and stirred at 60 °C for 5 h with continuous mild N₂ sweeping. ¹H NMR analysis of the crude reaction mixture showed full conversion and dr = 65:25:10:0 (*cis,trans/cis,cis/trans,trans,trans,cis*). The stirring was

continued at 60 °C without N₂ sweeping, monitoring the diastereomeric ratio by ¹H NMR: dr = 82:8:10:0 (24 h), dr = 87:3:10:0 (48 h). Thus, after 2 days the reaction mixture was partitioned between EtOAc (5 mL) and H₂O (5 mL), the organic layer was washed with brine (5 mL), filtered through a short plug of silica gel/Na₂SO₄, and concentrated. The title compound was obtained as colorless thick oil (140 mg, quantitative yield). Dr = 87:3:10:0 by ¹H NMR (300 MHz, CDCl₃); diagnostic signals (CHOH): δ 5.09 (d, J = 5.3 Hz, *cis,trans-2d*), 4.88 (d, J = 3.7 Hz, *trans,trans-2d*), 4.85 (d, J = 5.4 Hz, *cis,cis-2d*). 99.8% ee (major), 98.2% ee (minor) by HPLC. HRMS (ESI): calculated for C₁₈H₁₈O₃Na [M+Na]⁺ 305.1154, found 305.1146. Dr was upgraded to 89:0:11:0 by chromatography on silica gel eluting with hexane/EtOAc 7:1 (124 mg, 88%). Major diastereomer: ¹H NMR (300 MHz, CDCl₃) δ 7.41–7.18 (m, 9H), 5.08 (app t, J = 4.9 Hz, 1H), 4.01 (d, J = 8.1 Hz, 1H), 3.66 (s, 3H), 3.18–3.02 (m, 2H), 2.93–2.84 (m, 1H).

Enantiomeric excess was determined by HPLC analysis on Chiralpak IB-3 column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, λ = 220 nm, t_R : 12.0 min (*1S,2S,3R-2d*), 12.7 min (*1S,2R,3R-2d*), 14.1 min (*1S,2S,3S-2d*), 15.8 min (*1R,2R,3R-2d*), 22.9 min (*1R,2S,3S-2d*), 25.7 min (*1R,2R,3S-2d*).

The absolute configuration was attributed on the basis of the obtained enantioselectivity for **2f** and **2h**.

(1S,2R,3S)-2-Phenyl-3-methoxycarbonyl-1-indanol (2e). To a solution of active Ru(II) catalyst **B** (1.88 μ mol)



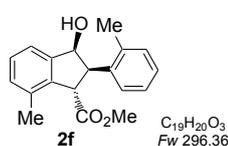
prepared from the corresponding (*S,S*)-DPEN-based μ -chlorido Ru(II) dimer (1.31 mg) in HCO₂H/Et₃N 3:2 (4.0 mL), was added **1e** (1.00 g, 3.76 mmol), and stirred at 60 °C for 24 h with continuous mild N₂ sweeping. HCO₂H/Et₃N 3:2 (1 mL) was added, compensating its evaporation and stirred at 60 °C for 24 h without N₂ sweeping to reach the equilibrium

diastereomeric ratio. The reaction mixture was partitioned between EtOAc (30 mL) and H₂O (30 mL), the organic layer was washed with brine (30 mL), filtered through a short plug of silica gel/Na₂SO₄, and concentrated. The title compound was obtained as a colorless oil (1.00 g, 100% yield); dr = 2:98:0:0 (*cis,cis/cis,trans*) by ¹H NMR (CH-OH)*; >99.9% ee (major) by HPLC. Silica gel chromatography eluting with hexane/EtOAc (7:1 then 1:1) afforded the major diastereomer (0.93 g, 93% yield). D.r >99 by ¹H NMR (300 MHz, CDCl₃); diagnostic signals (CHOH): δ 5.46 (d, J = 5.9 Hz, *cis,cis-2e*), 5.37 (d, J = 6.0 Hz, *cis,trans-2e*). >99.9% ee. ¹H NMR (300 MHz, CDCl₃) δ 7.50–7.24 (m, 9H), 5.36 (d, J = 6.0 Hz, 1H), 4.54 (d, J = 7.5 Hz, 1H), 4.12 (dd, J = 7.4, 6.2 Hz, 1H), 3.73 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 173.1, 143.4, 140.6, 137.3, 129.1, 128.9, 128.8, 128.4, 127.5, 125.5, 124.5, 76.7, 54.5, 53.3, 52.3.

Enantiomeric excess was determined by HPLC analysis on Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, λ = 220 nm, t_R : 18.6 min (minor), 28.6 min (major). HRMS (ESI): calculated for C₁₇H₁₆O₃Na [M+Na]⁺ 291.0997, found 291.0989.

The absolute configuration was attributed on the basis of the obtained enantioselectivity for **2f** and **2h**.

(1S,2R,3S)-2-(*o*-Tolyl)-3-methoxycarbonyl-4-methyl-1-indanol (2f). To a solution of active Ru(II) catalyst



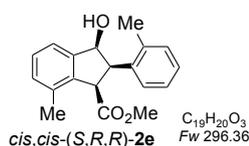
catalyst **A** (2.00 μ mol) prepared from the corresponding (*S,S*)-DPEN-based μ -chlorido Ru(II) dimer (1.37 mg) in HCO₂H/Et₃N 3:2 (1 mL), was added **1f** (294 mg, 1.00 mmol), and stirred at 60 °C for 24 h with continuous mild N₂ sweeping. HCO₂H/Et₃N 3:2 (0.5 mL) was added, compensating its evaporation and stirred at 60 °C for 24 h without N₂ sweeping to reach the equilibrium diastereomeric ratio. The reaction mixture was partitioned between EtOAc

(10 mL) and H₂O (10 mL), the organic layer was washed with brine (10 mL), filtered through a short plug of silica

gel/ Na_2SO_4 , and concentrated. The title compound was obtained as colorless crystals (290 mg, 98% yield). Dr = 92:8:0:0 by ^1H NMR (300 MHz, CDCl_3); diagnostic signals (CHOH): δ 5.57 (app t, $J = 7.2$ Hz, *cis,trans*-**2f**), 5.25 (dd, $J = 11.9, 5.2$ Hz, *cis,cis*-**2f**). 99.6% ee (major) by HPLC. Silica gel chromatography eluting with hexane/EtOAc (9:1 then 1:1) afforded the major diastereomer (252 mg, 85% yield); dr >99. ^1H NMR (300 MHz, CDCl_3) δ 7.34–7.04 (m, 6H), 6.98 (d, $J = 7.5$ Hz, 1H), 5.57 (app t, $J = 7.2$ Hz, 1H), 4.45 (d, $J = 4.7$ Hz, 1H), 4.36 (dd, $J = 6.5, 4.9$ Hz, 1H), 3.69 (s, 3H), 2.44 (s, 3H), 2.34 (s, 3H), 1.36 (d, $J = 8.0$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 174.1, 144.5, 138.6, 137.8, 135.6, 134.6, 130.7, 130.2, 128.7, 127.3, 127.0, 126.3, 122.8, 76.4, 53.6, 52.2, 51.0, 20.3, 18.7.

Enantiomeric excess was determined by HPLC analysis on Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm, t_R : 19.0 min (minor), 25.7 min (major).

The absolute configuration was determined by X-ray analysis (monocrystal grown from toluene/heptane).

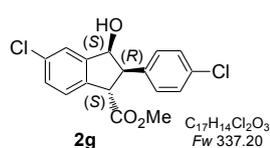


The **minor diastereomer** was isolated by chromatography on silica gel (eluent petroleum ether/EtOAc = 9:1) after quenching the reaction before the equilibrium diastereomeric ratio was reached (96% conversion, dr = 75:25:0:0). ^1H NMR (300 MHz, CDCl_3) δ 7.93–7.84 (m, 1H), 7.45 (d, $J = 7.5$ Hz, 1H), 7.33–7.11 (m, 5H), 5.25 (dd, $J = 11.9, 5.2$ Hz, 1H), 4.39 (d, $J = 7.3$ Hz, 1H), 3.85 (dd, $J = 7.3, 5.2$ Hz, 1H), 3.75 (d, $J = 11.9$ Hz,

1H), 3.54 (s, 3H), 2.42 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 175.4, 146.9, 139.5, 137.0, 135.6, 134.6, 130.5, 129.8, 128.8, 128.6, 127.0, 125.9, 122.8, 77.3, 52.6, 52.4, 48.7, 20.7, 18.7. HRMS (ESI): calculated for $\text{C}_{19}\text{H}_{20}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 319.1310, found 319.1304.

The *cis,cis*-configuration of the minor diastereomer was determined by ^1H - ^1H NOESY experiment: CH -(*o*-tolyl) has a NOE of the same order of magnitude with CH -OH and CH - CO_2Me . The absolute configuration at C1 was assigned according to the generally observed trend of enantioselectivity.

(1*S*,2*R*,3*S*)-2-(*p*-Chlorophenyl)-3-methoxycarbonyl-6-chloro-1-indanol (2g). To a solution of active Ru(II)



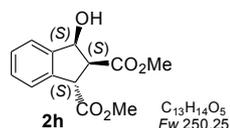
catalyst **B** (2.00 μmol) prepared from the corresponding (*S,S*)-DPEN-based μ -chlorido Ru(II) dimer (1.40 mg) in $\text{HCO}_2\text{H}/\text{Et}_3\text{N}$ 3:2 (1 mL), was added **1g** (335 mg, 1.00 mmol), and stirred at 60 $^\circ\text{C}$ for 24 h with continuous mild N_2 sweeping. $\text{HCO}_2\text{H}/\text{Et}_3\text{N}$ 3:2 (0.5 mL) was added, compensating its evaporation and stirred at 60 $^\circ\text{C}$ for 24 h without N_2 sweeping to reach the equilibrium diastereomeric ratio. The reaction mixture was

partitioned between EtOAc (10 mL) and H_2O (10 mL), the organic layer was washed with brine (10 mL), filtered through a plug of silica gel/ Na_2SO_4 , and concentrated. The title compound was obtained as light brown oil (334 mg, 99% yield). Dr = 97:3:0:0 by ^1H NMR (300 MHz, CDCl_3); diagnostic signals (CO_2Me): δ 3.73 (s, *cis,trans*-**2g**), 3.60 (s, *cis,cis*-**2g**). 99.9% ee (major) by HPLC. ^1H NMR (300 MHz, CDCl_3) δ 7.47–7.43 (m, 1H), 7.39–7.29 (m, 4H), 7.22 (d, $J = 8.4$ Hz, 2H), 5.32 (app t, $J = 5.6$ Hz, 1H), 4.41 (d, $J = 7.4$ Hz, 1H), 4.08 (dd, $J = 7.4, 6.1$ Hz, 1H), 3.73 (s, 3H), 1.49 (d, $J = 5.5$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 172.4, 145.1, 138.6, 135.5, 134.4, 133.5, 130.3, 129.5, 128.9, 125.9, 125.7, 76.2, 54.1, 53.0, 52.5. HRMS (ESI): calculated for $\text{C}_{17}\text{H}_{13}\text{O}_3\text{NaCl}_2$ $[\text{M}+\text{Na}]^+$ 359.0218, found 359.0212.

Enantiomeric excess was determined by HPLC analysis on Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm, t_R : 25.4 min (minor), 30.8 min (major).

The absolute configuration was attributed on the basis of the obtained enantioselectivity for **2f** and **2h**.

(1*S*,2*S*,3*S*)-2,3-Di(methoxycarbonyl)-1-indanol (2h). To a solution of active Ru(II) catalyst catalyst **A** (1.0 μmol)



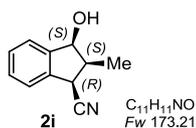
prepared from the corresponding (*S,S*)-DPEN-based μ -chlorido Ru(II) dimer (0.686 mg) in $\text{HCO}_2\text{H}/\text{Et}_3\text{N}$ 3:2 (1.0 mL), was added **1h** (248 mg, 1.0 mmol), and stirred at 60 $^\circ\text{C}$ for 18 h with continuous mild N_2 sweeping. After standard workup, a white solid was obtained (245 mg, 98% yield). Dr = 92:2:2:4 by ^1H NMR (300 MHz, CDCl_3); diagnostic signals (CHOH):

δ 5.47 (d, $J = 6.2$ Hz, *cis,trans*-**2h**), 5.31 (d, $J = 6.1$ Hz), 5.28 (d, $J = 6.1$ Hz), 5.17–5.12 (m). >99.5% ee for all diastereomers (by HPLC). After recrystallization from cyclohexane, the stereopure title compound was obtained as colorless needles (188 mg, 70% yield); dr >99, >99% ee. ^1H NMR (300 MHz, CDCl_3) δ 7.47–7.40 (m, 2H), 7.39–7.29 (m, 2H), 5.46 (app t, $J = 5.9$ Hz, 1H), 4.65 (d, $J = 8.3$ Hz, 1H), 3.89 (dd, $J = 8.3, 6.3$ Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 2.60 (d, $J = 5.7$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 172.3, 171.7, 142.1, 139.3, 129.6, 128.6, 125.4, 124.5, 74.7, 52.9, 52.5, 52.3, 50.0.

Enantiomeric excess was determined by HPLC analysis on Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm, t_R : 20.9 (minor), 21.8 min (major).

The absolute configuration was determined by X-ray analysis (monocrystal grown from cyclohexane).

(1*S*,2*S*,3*R*)-3-Cyano-2-methyl-1-indanol (2i). To a solution of active Ru(II) catalyst **B** (1.0 μmol) prepared from the corresponding (*S,S*)-DPEN-based μ-chlorido Ru(II) dimer (0.700 mg) in HCO₂H/Et₃N 3:2 (1.0 mL), was added **1i** (171 mg, 1.0 mmol), and stirred at 60 °C for 1 h with continuous mild N₂ sweeping. After standard workup, a white solid was obtained (171 mg, 99% yield). Dr = 93:7:0:0 (*cis,cis/cis,trans/trans,trans/trans,cis*) by ¹H NMR (300 MHz, CDCl₃); diagnostic signals (CH₂OH): δ 5.10 (d, *J* = 5.8 Hz, *cis,cis*-**2i**), 5.04 (d, *J* = 5.4 Hz, *cis,trans*-**2i**). >99.5% ee by HPLC. Recrystallization from cyclohexane/CH₂Cl₂ afforded stereomerically pure **2i** (134 mg, 80% yield); dr>99, >99.9% ee. ¹H NMR (300 MHz, CDCl₃) δ 7.51–7.35 (m, 4H), 5.09 (dd, *J* = 7.5 and 6.0 Hz, 1H), 4.08 (d, *J* = 7.3 Hz, 1H), 2.88 (qdd, *J* = 7.2, 7.3, 6.0 Hz, 1H), 1.73 (d, *J* = 7.5 Hz, 1H), 1.30 (d, *J* = 7.2 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 143.6, 136.5, 129.3, 129.2, 125.1, 124.9, 119.0, 76.1, 42.0, 37.9, 10.8. HRMS (ESI): calculated for C₁₁H₁₁NO [M+Na]⁺ 196.0738, found 196.0735.

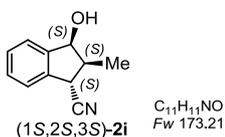


Enantiomeric excess was determined by HPLC analysis on Chiralpak IB-3 column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, λ = 220 nm, *t*_R: 18.9 min (major), 20.4 min (minor).

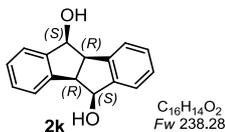
The relative configuration of the major diastereomer was determined by ¹H-¹H NOESY experiment: CH-Me has a NOE of the same order of magnitude with CH-OH and CH-CN, and CH-OH has a NOE with CH-CN.

The absolute configuration was attributed on the basis of the obtained enantioselectivity for **2f** and **2h**.

(1*S*,2*S*,3*R*)- and (1*S*,2*S*,3*S*)-3-Cyano-2-methyl-1-indanol [(1*S*,2*S*,3*R*)-2i**/(1*S*,2*S*,3*S*)-**2i**≅1:1].** The *cis,cis*-(1*S*,2*S*,3*R*)-**2i** stereomer (86 mg, 0.5 mmol) was dissolved in HCO₂H/Et₃N 3:2 (0.5 mL) and stirred at 60 °C for 14 days. After standard workup, a thick oil was obtained; *cis,cis/cis,trans* = 52:48. NMR data for *cis,trans*-(1*S*,2*S*,3*S*)-**2i**: ¹H NMR (300 MHz, CDCl₃) δ 7.52–7.32 (m, 4H), 5.04 (d, *J* = 5.3 Hz, 1H), 3.94 (d, *J* = 9.4 Hz, 1H), 2.80–2.67 (m, 1H), 1.40 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 143.7, 138.1, 129.7, 128.9, 125.3, 124.4, 75.5, 46.3, 39.5, 12.2.



(4*bR*,5*S*,9*b**R*,10*S*)-4*b*,5,9*b*,10-tetrahydroindeno[2,1-*a*]indene-5,10-diol (**2k**).** To a solution of active Ru(II) catalyst **B** (1.0 μmol) prepared from the corresponding (*S,S*)-DPEN-based μ-chlorido Ru(II) dimer (0.700 mg) in HCO₂H/Et₃N 3:2 (1.0 mL), were added indanoindandione **1k** (234 mg, 1.0 mmol) and PhCl (2.0 mL), then stirred at 60 °C for 10 h with continuous mild N₂ sweeping. The reaction mixture was partitioned between EtOAc (10 mL) and H₂O (10 mL), the organic layer was washed with brine (10 mL), filtered through a short plug of silica gel/Na₂SO₄, and concentrated. The title compound was obtained as a white solid (238 mg, 100% yield); dr >99 by ¹H NMR; >99.9% ee by HPLC. ¹H NMR (300 MHz, CDCl₃) δ 7.54–7.28 (m, 8H), 5.24 (m, 2H), 4.16–4.06 (m, 2H), 2.10 (d, *J* = 5 Hz, 2H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 146.4, 139.9, 128.0, 126.7, 126.5, 123.6, 74.8, 50.8.



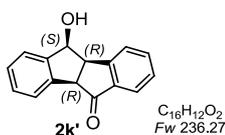
Enantiomeric excess was determined by HPLC analysis on Chiralcel OJ-H column (25 cm). Eluent hexane/2-PrOH 90:10, flow rate 1 mL/min, λ = 220 nm, *t*_R: 26.0 min (*R,S,S,R*), 30.9 min (*S,R,R,S*).

The absolute configuration was determined by X-ray analysis (monocrystal grown from MeOH/CH₂Cl₂).

2-g scale DKR-ATH of **1k** using (*R,R*)-DPEN-based catalyst **A** (*S/C* = 1000):

To a solution of active Ru(II) catalyst **B** (10.0 μmol) prepared from the corresponding (*R,R*)-DPEN-based μ-chlorido Ru(II) dimer (7.0 mg) in HCO₂H/Et₃N 3:2 (10.0 mL), were added indanone **1k** (2.34 g, 10.0 mmol) and PhCl (20.0 mL), then stirred at 60 °C overnight with continuous mild N₂ bubbling through the solution. The reaction mixture was concentrated to 10 mL then poured onto water (150 mL) and sonicated. The white precipitate was collected on glass-frit, washed with water and air-dried overnight, then in high vacuum for 4 h to get pure title compound as a white powder (2.45 g, 97% yield).

(4*bR*,9*b**R*,10*S*)-10-Hydroxy-9*b*,10-dihydroindeno[2,1-*a*]inden-5(4*b**H*)-one (**2k'**).** To a solution of active Ru(II) catalyst **A** (1.0 μmol) prepared from the corresponding (*S,S*)-DPEN-based μ-chlorido Ru(II) dimer (0.686 mg) in HCO₂H/Et₃N 3:2 (0.5 mL), were added **1k** (117 mg, 0.5 mmol) and EtOAc (1.0 mL), then stirred at 50 °C for 10 h with continuous mild N₂ sweeping. The reaction mixture contained (by ¹H NMR) the starting indanoindandione **1k**, mono-reduced 'indanon-indanol' **2k'** and indanoindandiol **2k** in the ratio of 8.5:47:44.5. The mono-reduced compound **2k'** was isolated by silica gel column chromatography eluting with CH₂Cl₂ [*R*_f = 0.1 (**2k**), 0.27 (**2k'**), 0.78 (**1k**)]. White fluffy solid (50 mg, 42% yield); dr >99; >99% ee. ¹H NMR (300 MHz, CDCl₃) δ 7.80–7.58 (m, 4H), 7.46–7.27 (m, 4H), 5.64 (d, *J* = 9.1 Hz, 1H), 4.55–4.30 (m, 1H), 4.19 (d, *J* = 6.6 Hz, 1H), 1.63 (s, 1H). ¹³C



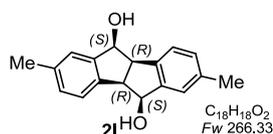
NMR (75 MHz, CDCl₃) δ 204.7, 151.3, 143.7, 137.5, 136.6, 134.6, 129.4, 129.2, 128.7, 128.4, 125.2, 125.1, 124.5, 75.4, 56.8, 46.6. HRMS (ESI): calculated for C₁₆H₁₂O₂ [M+H]⁺ 237.0916, found 237.0913.

Enantiomeric excess was determined by HPLC analysis on Chiralpak IB-3 column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, λ = 220 nm, t_R : 19.1 min (major), 19.9 min (minor).

The relative configuration was determined by ¹H-¹H NOESY experiment: CH-Ar has a NOE of the same order of magnitude with CH-OH and CH-CO. There is a NOE between CH-OH and CH-CO.

The absolute configuration was attributed on the basis of the obtained enantioselectivity for **2k**.

(4bR,5S,9bR,10S)-2,7-Dimethyl-4b,5,9b,10-tetrahydroindeno[2,1-a]indene-5,10-diol (2l). To a solution of

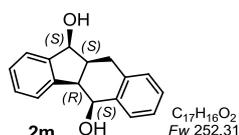


active Ru(II) catalyst **A** (0.5 μ mol) prepared from the corresponding (*S,S*)-DPEN-based μ -chlorido Ru(II) dimer (0.343 mg) in HCO₂H/Et₃N 3:2 (0.5 mL), were added indanoindandione **1l** (131 mg, 0.5 mmol) and PhCl (1.0 mL), then stirred at 60 °C for 10 h with continuous mild N₂ sweeping. The reaction mixture was partitioned between EtOAc (10 mL) and H₂O (10 mL), the organic layer was washed with brine (10 mL), filtered through a short plug of silica gel/Na₂SO₄, and concentrated. The title compound was obtained as a white solid (129 mg, 97% yield); dr >99:1 by ¹H NMR; 99.3% ee by HPLC. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.39 (d, *J* = 7.7 Hz, 2H), 7.00 (s, 2H), 6.93 (d, *J* = 7.7 Hz, 2H), 5.31 (d, *J* = 6.2 Hz, 2H), 5.28–5.16 (m, 2H), 3.95–3.68 (m, 2H), 2.23 (s, 6H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 146.6, 136.9, 135.4, 127.6, 127.4, 124.0, 74.7, 50.6, 20.9. Anal. calcd. for C₁₈H₁₈O₂: C, 81.17; H, 6.81. Found: C, 80.85; H, 6.71.

Enantiomeric excess was determined by HPLC analysis on Chiralcel OJ-H column (25 cm). Eluent hexane/2-PrOH 90:10, flow rate 1 mL/min, λ = 220 nm, t_R : 12.6 min (*R,S,S,R*), 23.9 min (*S,R,R,S*).

The absolute configuration was attributed on the basis of the obtained enantioselectivity for **2k**.

(4bR,5S,10aS,11S)-5,10,10a,4b-tetrahydro-11H-benzo[*b*]fluorene-5,11-diol (2m). To a solution of active Ru(II)



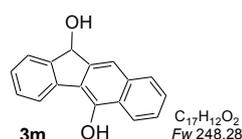
catalyst **B** (5.0 μ mol) prepared from the corresponding (*S,S*)-DPEN-based μ -chlorido Ru(II) dimer (3.50 mg) in HCO₂H/Et₃N 3:2 (0.5 mL), was added indanotetralindione **1m** (124 mg, 0.5 mmol) and stirred at 60 °C for 3.5 h with continuous mild N₂ sweeping. The reaction mixture contained by ¹H NMR the title diol **2m** (55%, dr >20:1) and 11*H*-benzo[*b*]fluorene-5,11-diol (**3m**) (45%). To the reaction mixture was added CH₂Cl₂ (5 mL), the obtained

white precipitate filtered and washed with CH₂Cl₂ to get nearly pure racemic 11*H*-benzo[*b*]fluorene-5,11-diol (**3m**). The filtrate was washed with water (5 mL), 1 M NaOH (3 mL), dried (Na₂SO₄), filtered, and concentrated to get pure diol **2m** (65 mg, 52% yield); dr = 95:5 by ¹H NMR (CH₂OH); >99.9% ee by HPLC. The major diastereomer was isolated by recrystallization from CH₂Cl₂/hexane (57 mg, 45% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.58–7.51 (m, 1H), 7.44–7.15 (m, 7H), 4.97 (t, *J* = 2.5 Hz, 1H), 4.92 (dd, *J* = 11.8, 6.1 Hz, 1H), 3.48 (d, *J* = 11.8 Hz, 1H), 3.49–3.36 (m, 2H), 3.29 (dd, *J* = 8.4, 2.1 Hz, 1H), 3.03–2.87 (m, 2H), 2.15 (dd, *J* = 2.2, 1.0 Hz, 1H). ¹³C NMR (76 MHz, CDCl₃) δ 146.7, 142.1, 138.8, 138.2, 129.3, 128.9, 128.9, 127.9, 127.5, 125.8, 125.8, 124.4, 74.8, 71.8, 49.7, 38.8, 25.7.

Enantiomeric excess was determined by HPLC analysis on Chiralcel OJ-H column (25 cm). Eluent hexane/2-PrOH 90:10, flow rate 1 mL/min, λ = 220 nm, t_R : 14.2 min (minor), 21.1 min (major).

The absolute configuration was determined by X-ray analysis (monocrystal grown from CH₂Cl₂/hexane).

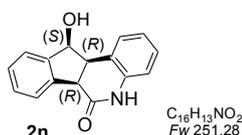
11H-Benzo[*b*]fluorene-5,11-diol (3m). ¹H NMR (300 MHz, acetone-*d*₆) δ 8.80 (s, 1H), 8.41–8.30 (m, 1H), 8.23 (d,



J = 7.6 Hz, 1H), 7.97–7.86 (m, 1H), 7.71 (s, 1H), 7.66–7.60 (m, 1H), 7.54–7.44 (m, 2H), 7.40 (tdd, *J* = 7.5, 1.3, 0.6 Hz, 1H), 7.30 (td, *J* = 7.4, 1.2 Hz, 1H), 5.76 (d, *J* = 7 Hz, 1H), 4.78 (d, *J* = 7 Hz, 1H). ¹³C NMR (75 MHz, acetone-*d*₆) δ 148.2, 147.4, 147.2, 140.2, 135.7, 129.4 (2C), 127.7, 127.0, 126.6, 125.9, 125.7, 124.9, 123.4, 122.0, 117.5, 75.2. HRMS (ESI): calculated for C₁₇H₁₁O₂ [M-H]⁻ 247.0759, found 247.0756.

HPLC analysis on Chiralcel OJ-H column (25 cm). Eluent hexane/2-PrOH 80:20, flow rate 1 mL/min, λ = 220 nm, t_R : 18.6 min (49.7%), 21.6 min (50.3%).

(6aR,11S,11aR)-11-Hydroxy-11,11a-dihydro-5H-indeno[1,2-*c*]quinolin-6(6aH)-one (2n). To a solution of active



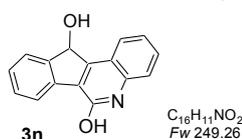
Ru(II) catalyst **B** (5.0 μ mol) prepared from the corresponding (*S,S*)-DPEN-based μ -chlorido Ru(II) dimer (3.50 mg) in HCO₂H/Et₃N 3:2 (0.5 mL), were added indanone **1n** (124 mg, 0.5 mmol) and DMF (1 mL) and stirred at 60 °C for 18 h with continuous mild N₂ sweeping.

The heterogeneous reaction mixture contained the title compound **2n** (37%; dr >99:1) and 11*H*-indeno[1,2-*c*]quinoline-6,11-diol (**3n**) (63%) in a solid form (determined by ¹H NMR). Filtration of the solid **3n** and washing with CH₂Cl₂ (10 mL) afforded it in a pure form (75 mg, 60% yield). The filtrate was washed with H₂O, dried (Na₂SO₄), filtered and concentrated to get the title compound **2n** (44 mg, 35% yield) as colorless crystals; dr >99 (by ¹H NMR); >99.9% ee (by HPLC). ¹H NMR (300 MHz, CDCl₃ + drop of DMSO-*d*₆) δ 8.98 (s, 1H), 7.74 (d, *J* = 7.4 Hz, 1H), 7.47 (d, *J* = 7.4 Hz, 1H), 7.41 (td, *J* = 7.4, 1.3 Hz, 1H), 7.36–7.29 (m, 2H), 7.21 (td, *J* = 7.7, 1.4 Hz, 1H), 7.06 (td, *J* = 7.4, 1.1 Hz, 1H), 6.88 (dd, *J* = 7.9, 0.7 Hz, 1H), 5.18 (dd, *J* = 5.3, 4.2 Hz, 1H), 4.07 (d, *J* = 9.3 Hz, 1H), 3.81 (dd, *J* = 9.3, 5.3 Hz, 1H), 2.77–2.72 (m, 1H). ¹³C NMR (75 MHz, CDCl₃ + drop of DMSO-*d*₆) δ 169.1, 143.1, 141.2, 138.8, 128.8, 128.7, 127.8, 127.7, 124.7, 122.6, 120.6, 115.4, 77.8, 47.9, 46.5.

Enantiomeric excess was determined by HPLC analysis on Chiralcel OJ-H column (25 cm). Eluent hexane/2-PrOH 90:10, flow rate 1 mL/min, λ = 220 nm, *t*_R: 32.9 min (minor), 38.8 min (major).

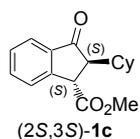
The absolute configuration was determined by X-ray analysis (monocrystal grown from EtOAc/MeOH).

11*H*-Indeno[1,2-*c*]quinoline-6,11-diol (3n**)**. ¹H NMR (300 MHz, DMSO-*d*₆) δ 11.95 (s, 1H), 8.41–7.90 (m, 2H), 7.85–7.07 (m, 6H), 6.14 (s, 1H), 5.82 (s, 1H). ¹³C NMR (75 MHz DMSO-*d*₆) δ 159.3, 153.8, 146.3, 138.9, 137.9, 129.9, 128.3, 128.1, 126.8, 125.2, 124.0, 122.2, 121.9, 117.4, 115.6, 74.2. HRMS (ESI): calculated for C₁₆H₁₂NO₂ [M+H]⁺ 250.0868, found 250.0865.



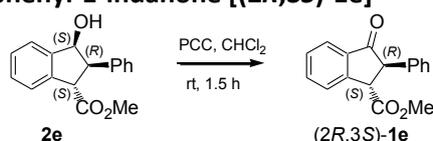
4 Oxidation of **2c**, **2e**, and **2k** to the corresponding stereopure indanones

trans-(1*S*,2*S*)-2-Cyclohexy-3-methoxycarbonyl-1-indanone [(2*S*,3*S*)-1c**]**. Prepared following a similar procedure as for (2*R*,3*S*)-**1e** (see below) starting from **2c** (55 mg, 0.2 mmol). The title compound was isolated as a white powder (52 mg, 95% yield); dr >99; 99.1% ee. ¹H NMR (300 MHz, CDCl₃) δ 7.75 (d, *J* = 7.6 Hz, 1H), 7.65–7.58 (m, 2H), 7.49–7.39 (m, 1H), 4.12 (d, *J* = 3.9 Hz, 1H), 3.79 (s, 1H), 3.12 (app t, *J* = 4.2 Hz, 1H), 2.19–2.06 (m, 1H), 1.84–1.61 (m, 4H), 1.50–0.96 (m, 6H). NMR data is similar to the racemic compound **1c** described above.



Enantiomeric excess was determined by HPLC analysis on Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, λ = 220 nm, *t*_R: 7.5 min (major), 8.3 min (minor).

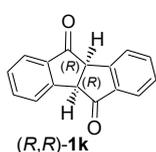
trans-(2*R*,3*S*)-3-Methoxycarbonyl-2-phenyl-1-indanone [(2*R*,3*S*)-1e**]**



To a solution of **2e** (268 mg, 1 mmol) in CH₂Cl₂ (5 mL) was added a mixture of pyridinium chlorochromate (323 mg, 1.5 mmol) and Celite (1.3 g). The resulting slurry was stirred at rt for 1.5 h then filtered through a plug of silica gel eluting with CH₂Cl₂. After concentration, the title compound was obtained as a white solid (242 mg, 91% yield); 99.4% ee. ¹H NMR (300 MHz, CDCl₃) δ 7.85 (d, *J* = 7.7 Hz, 1H), 7.76–7.66 (m, 2H), 7.56–7.48 (m, 1H), 7.38–7.26 (m, 3H), 7.22–7.16 (m, 2H), 4.39 (d, *J* = 4.7 Hz, 1H), 4.37 (d, *J* = 4.7 Hz, 1H), 3.82 (s, 3H). NMR data is similar to the racemic compound **1e** described above.

Enantiomeric excess was determined by HPLC analysis on Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, λ = 220 nm, *t*_R: 13.2 min (major), 16.8 min (minor).

(4*bR*,9*bR*)-Indeno[2,1-*a*]indene-5,10(4*bH*,9*bH*)-dione ((*R,R*)-1k**)**. Prepared following a similar procedure as for (2*R*,3*S*)-**1e** starting from **2k** (80 mg, 0.34 mmol) using 2.5 eq of PCC. The title compound was isolated as a white powder (79 mg, 93% yield); dr >99, 99.2% ee. ¹H NMR (300 MHz, CDCl₃) δ 7.93 (d, *J* = 7.8 Hz, 2H), 7.76–7.63 (m, 4H), 7.44 (app td, *J* = 7.6, 0.9 Hz, 2H), 4.41 (s, 2H). NMR data is the same as for the racemic compound **1k** described above.

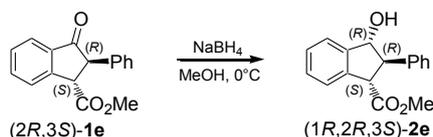


Enantiomeric excess was determined by HPLC analysis on Chiralcel OJ-H column (25 cm). Eluent

hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm, t_R : 26.5 min (major), 30.9 min (minor).

5 Diastereoselective reduction of stereopure (2*R*,3*S*)-**1e** to *trans,trans*-(1*R*,2*R*,3*S*)-**2e** and *cis,cis*-(1*R*,2*S*,3*S*)-**2e**

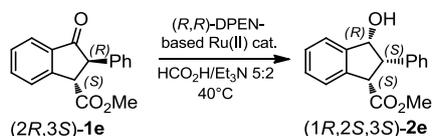
(1*R*,2*R*,3*S*)-3-Methoxycarbonyl-2-phenyl-1-indanone [*trans,trans*-(1*R*,2*R*,3*S*)-**2e**]



To a solution of (2*R*,3*S*)-**1e** (133 mg, 0.5 mmol) in MeOH (5 mL) at 0 °C was added NaBH₄ and stirred for 1 h. The reaction mixture was partitioned between EtOAc (20 mL) and water (20 mL), the organic layer washed with brine, dried (Na₂SO₄), and concentrated affording the title product as colorless oil; dr = 5:12:83:0. The major diastereomer was isolated by chromatography eluting with CH₂Cl₂. Colorless crystals (101 mg, 75% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.52–7.48 (m, 1H), 7.42–7.19 (m, 8H), 5.16 (dd, $J = 9.1, 5.2$ Hz, 1H), 4.15 (d, $J = 6.3$ Hz, 1H), 3.82–3.73 (m, 4H), 2.83 (d, $J = 9.1$ Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 173.7, 143.9, 141.0, 138.9, 128.9, 128.7, 128.6, 127.4, 127.1, 125.0, 124.3, 81.8, 58.3, 55.2, 52.5. HRMS (ESI): calculated for C₁₇H₁₆O₃Na [M+Na]⁺ 291.0997, found 291.1000.

The relative configuration was confirmed by ¹H NOESY: CHOH has NOE with CHCO₂Me confirming their *cis*-disposition, and CH-Ar has NOE with OH confirming the *trans*-disposition at C1/C2.

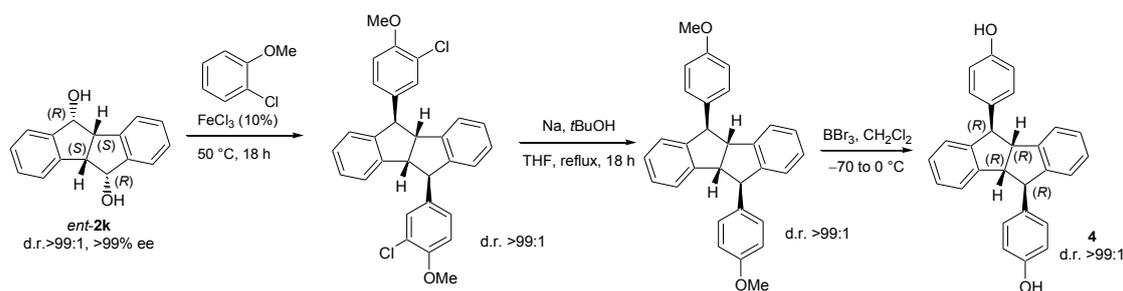
(1*R*,2*S*,3*S*)-3-Methoxycarbonyl-2-phenyl-1-indanol [*cis,cis*-(1*R*,2*S*,3*S*)-**2e**]



To enantiomerically pure (1*S*,2*R*)-**1e** (50 mg, 0.19 mmol) was added a solution of active Ru(II) catalyst **A** (S/C = 100) prepared from the corresponding (*R,R*)-DPEN-based μ -chlorido Ru(II) dimer (1.29 mg) in HCO₂H/Et₃N 5:2 (0.40 mL). After 1 h, 4% conversion to (1*R*,2*S*,3*S*)-**2e** was obtained. After 17 h, 99% conversion was reached with (1*R*,2*S*,3*S*)-**2e**:(1*S*,2*R*,3*S*)-**2e** = 30:70. The minor diastereomer was isolated after chromatography eluting with petroleum ether/EtOAc (7:1) as a thick syrup (contains 3% of the starting ketone). ¹H NMR (300 MHz, CDCl₃) δ 7.65–7.58 (m, 1H), 7.49–7.17 (m, 8H), 5.45 (dd, $J = 11.6, 5.8$ Hz, 1H), 4.54 (d, $J = 7.2$ Hz, 1H), 3.92 (appt, $J = 6.5$ Hz, 1H) 3.62 (d, $J = 11.6$ Hz, 1H), 3.60 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 174.7, 146.0, 140.0, 137.0, 128.8, 128.5, 128.4, 126.8, 125.6, 124.9, 75.4, 53.0, 52.6, 52.2. The signal of one aromatic carbon was not observed due to overlapping. HRMS (ESI): calculated for C₁₇H₁₆O₃Na [M+Na]⁺ 291.0997, found 291.0995.

The relative configuration was assigned on the basis of the one determined by ¹H-¹H NOESY for (1*R*,2*S*,3*S*)-**2e**.

6 Transformation of 1,4-diol *ent*-2k into Pallidol analog (*R,R,R,R*)-4

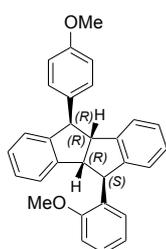


STEP 1: *Friedel-Crafts benzylation*. A mixture of *ent*-2k (1.00 g, 4.2 mmol), anhydrous FeCl₃ (70 mg, 0.43 mmol) and 2-chloroanisole (10 mL) was heated at 50 °C overnight (18 h). The reaction mixture was poured onto water (200 mL) and the product extracted with CH₂Cl₂ (200 mL than 150 mL). The combined organic layers were concentrated, and the yellow residue filtered through silica gel eluting first with hexane to remove the remaining 2-chloroanisole, then with CH₂Cl₂ to elute the product. After concentration, a yellowish stiff syrup (2.20 g, quant.) was obtained tinted with *o*-chloroanisole; dr>99:1, regioselectivity >99:1 (by ¹H NMR). ¹H NMR (300 MHz, CDCl₃) δ 7.38 (d, *J* = 7.4 Hz, 2H), 7.29–7.22 (m, 2H), 7.22–7.15 (m, 4H), 7.04–6.97 (m, 4H), 6.88 (d, *J* = 8.5 Hz, 2H), 4.47 (t, *J* = 2.4 Hz, 2H), 4.13–4.10 (m, 2H), 3.89 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 153.6, 145.6, 145.2, 139.0, 129.5, 127.7, 127.6, 127.0, 125.7, 124.4, 122.6, 112.3, 59.6, 57.4, 56.2.

STEP 2: *Dechlorination*. To a solution of the above prepared compound (2.15 g) in dry THF (100 mL) was added sodium chopped to slices (2.53 g, 110 mmol) then dry *t*BuOH (4.0 mL, 42 mmol). The mixture was vigorously stirred under gentle reflux for 18 h, cooled to rt, and decanted. Partially concentrated residue was partitioned between ice-H₂O (100 mL) and CH₂Cl₂ (100 mL), the organic layer was dried (Na₂SO₄), and concentrated affording dechlorinated product as a white solid (1.73 g). ¹H NMR (300 MHz, CDCl₃) δ 7.38 (d, *J* = 7.3 Hz, 1H), 7.23 (t, *J* = 8.1 Hz, 2H), 7.15 (td, *J* = 7.4, 1.1 Hz, 1H), 7.09 (d, *J* = 8.7 Hz, 2H), 7.00 (d, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.51 (t, *J* = 2.4 Hz, 1H), 4.14–4.12 (m, 1H), 3.79 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 158.2, 145.9, 138.0, 128.7, 127.5, 127.2, 125.7, 124.3, 114.0, 59.8, 57.6, 55.3.

STEP 3: *Demethylation*. To cold (–78 °C) a solution of the above dechlorinated compound (1.72 g, 4.1 mmol) in dry CH₂Cl₂ (80 mL) was added dropwise BBr₃ (1.8 mL, 18.5 mmol). After stirring at this temperature for 30 min, the solution was taken to 0 °C and stirred for 1 h. The solution was poured carefully onto ice-H₂O (150 mL), the phases were separated and the water layer reextracted with CH₂Cl₂ (100 mL). The combined organic layers were dried (Na₂SO₄) and concentrated affording the Pallidol analog (*R,R,R,R*)-4 as a slightly yellowish powder (1.53 g, 96% yield for 3 steps); dr>99 (by ¹H NMR); [α]_D²⁵ = –53.3 (*c* = 1.09 in CHCl₃). ¹H NMR (300 MHz, CDCl₃) δ 7.37 (d, *J* = 7.4 Hz, 2H), 7.23 (ddd, *J* = 7.5, 4.8, 0.6 Hz, 2H), 7.15 (app td, *J* = 7.4, 1.2 Hz, 2H), 7.04 (d, *J* = 8.5 Hz, 4H), 6.99 (d, *J* = 7.5 Hz, 2H), 6.77 (d, *J* = 8.5 Hz, 4H), 4.75 (br s, 2H), 4.56–4.45 (m, 2H), 4.15–4.08 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 154.00, 145.9, 145.8, 138.2, 129.0, 127.5, 127.3, 125.7, 124.3, 115.5, 59.7, 57.6. Anal. Calcd for C₂₈H₂₂O₂ (390.47): C, 86.13; H, 5.68. Found: C, 85.86; H, 5.77.

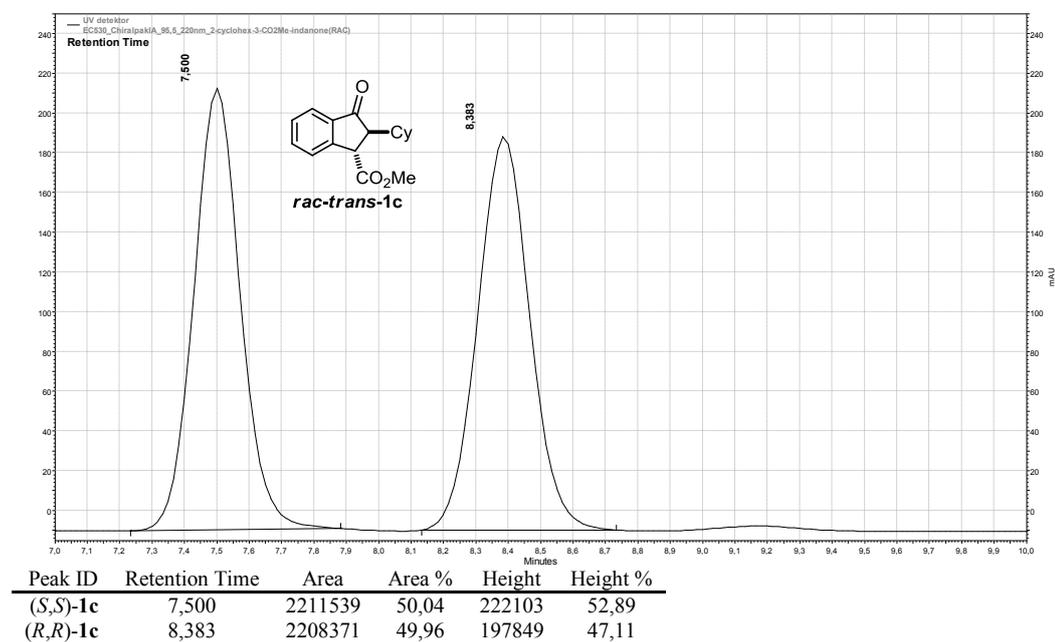
Noteworthy, Friedel-Crafts benzylation of anisole (FeCl₃, 50 °C) was also totally diastereoselective (dr>99), however, the regioselectivity was 75:25 (*p,p/o,p*). The two regioisomers were separated by silica gel chromatography eluting with toluene/hexane 1:1. The minor *o,p*-dianisyl-substituted regioisomer was eluted before the *p,p*-substituted one. *o,p*-dianisyl-substituted product:



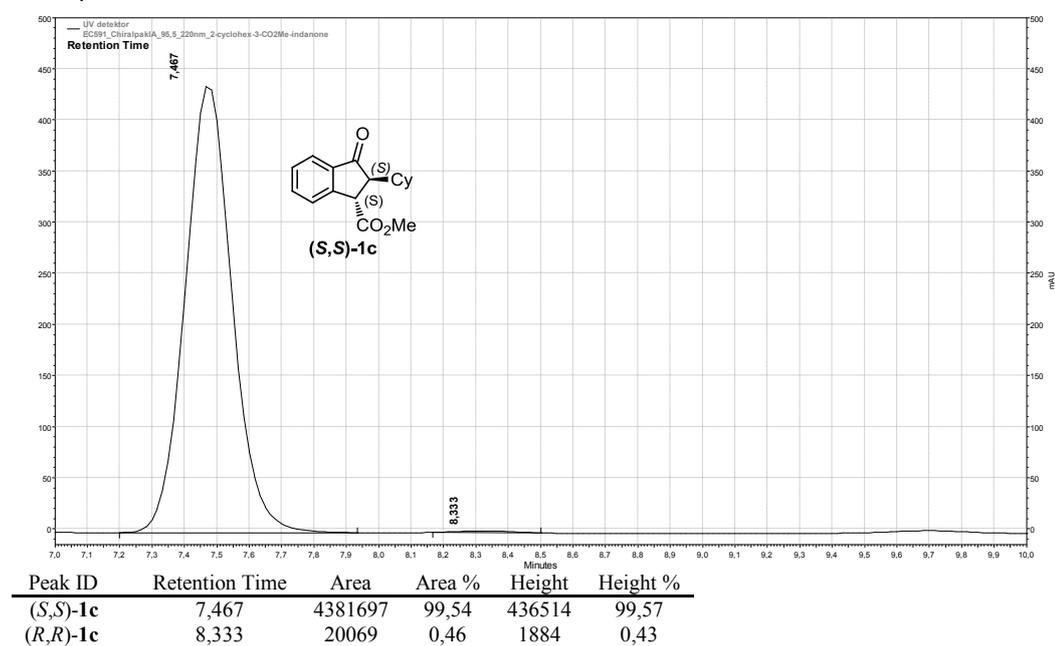
¹H NMR (300 MHz, CDCl₃) δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.31–7.22 (m, 2H), 7.21–7.01 (m, 7H), 6.95 (dd, *J* = 8.1, 0.7 Hz, 1H), 6.83–6.74 (m, 3H), 6.57 (dd, *J* = 7.5, 1.7 Hz, 1H), 5.02 (s, 1H), 4.58 (s, 1H), 4.05 (d, *J* = 7.7 Hz, 1H), 4.02–3.97 (m, 4H), 3.76 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 158.0, 156.8, 147.2, 146.6, 145.4, 144.3, 138.7, 134.5, 128.4, 127.8, 127.4, 127.3, 127.2, 126.1, 125.6, 124.9, 124.3, 120.4, 113.9, 110.2, 58.3, 57.8, 57.5, 55.4, 55.3, 51.6.

7 Chiral HPLC analysis

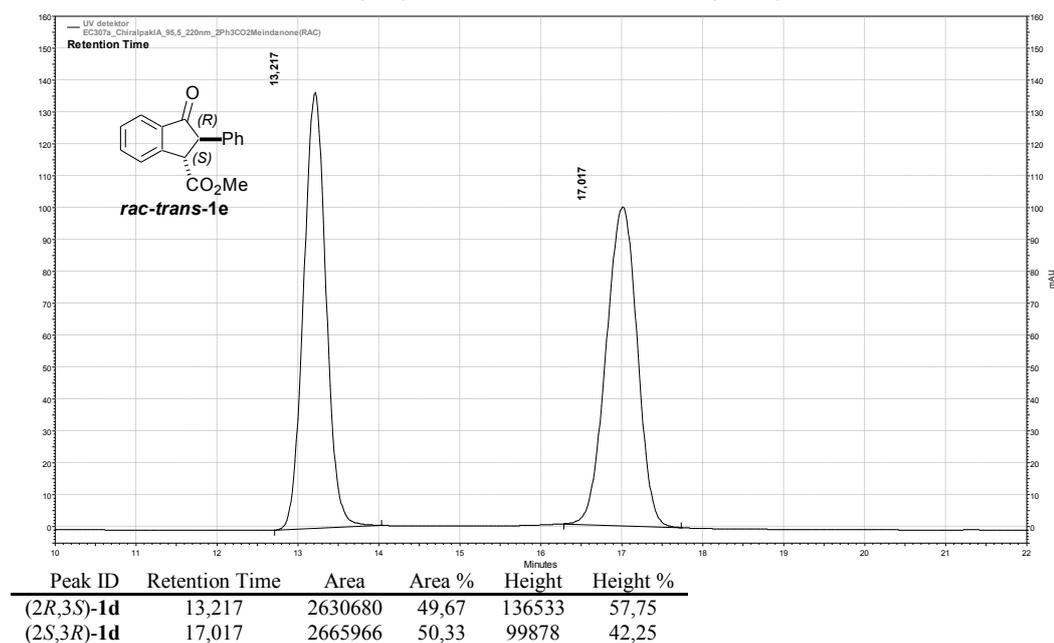
rac-trans-1c. Chiralpak IA column (25 cm), hexane:2-PrOH = 95:5, $\lambda = 220$ nm, flow rate 1 mL/min
The reference racemate was prepared from racemic 2-cyclohexyl-3-phenylsuccinic acid as described above:



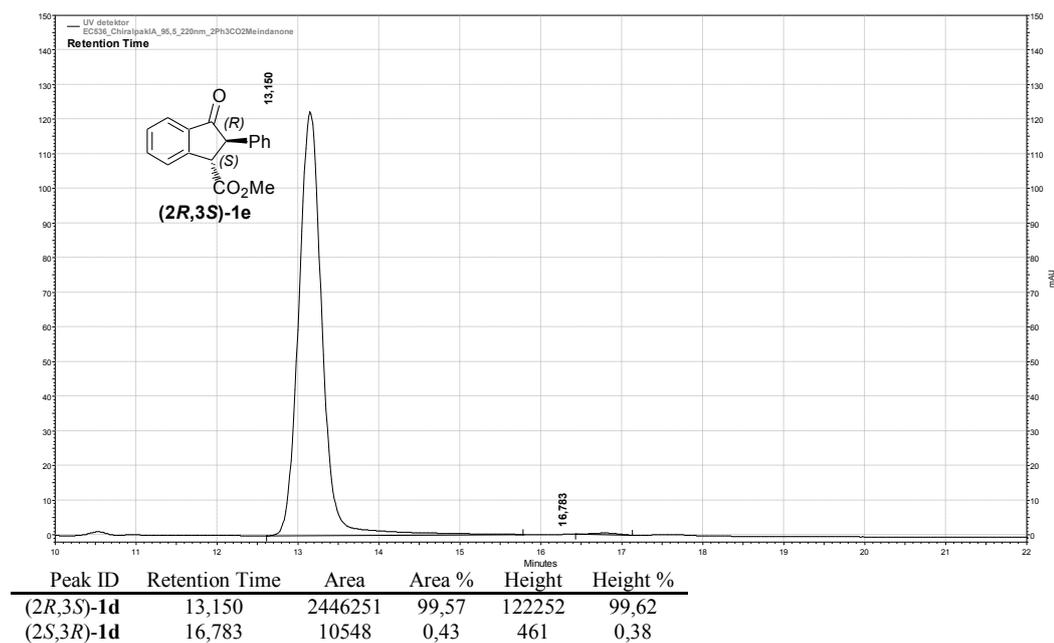
(*2S,3S*)-1c obtained by PCC oxidation of the ATH product 2c (derived from the run with (*S,S*)-DPEN-based Ru(II) cat. **B**):



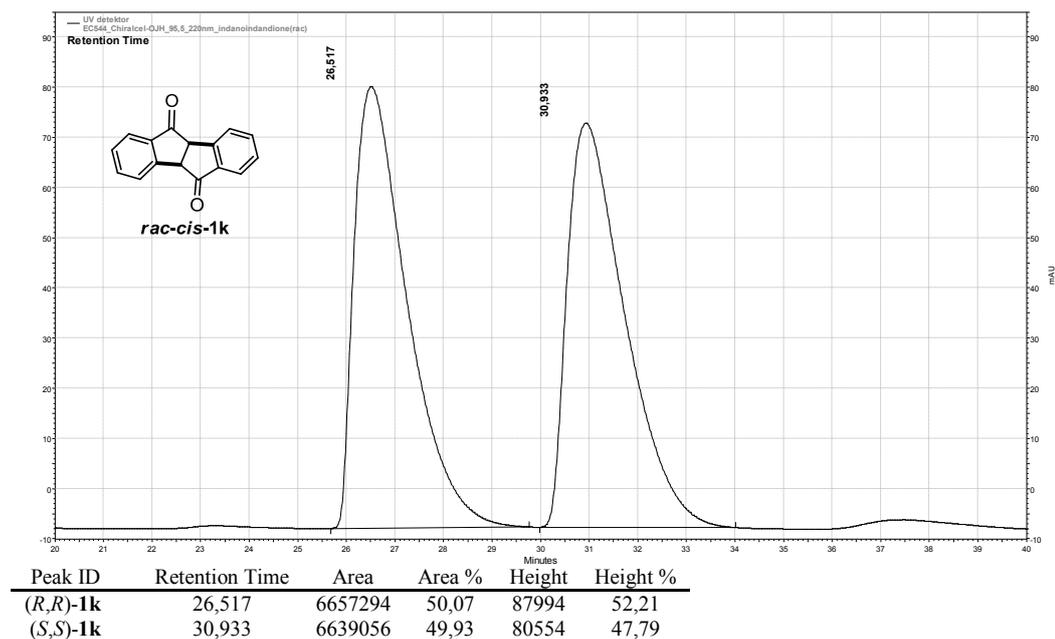
rac-trans-1e. Chiralpak IA column (25 cm), hexane:2-propanol = 95:5, $\lambda = 220$ nm, flow rate 1 mL/min
 The reference racemate was prepared from racemic 2,3-diphenylsuccinic acid as described above:



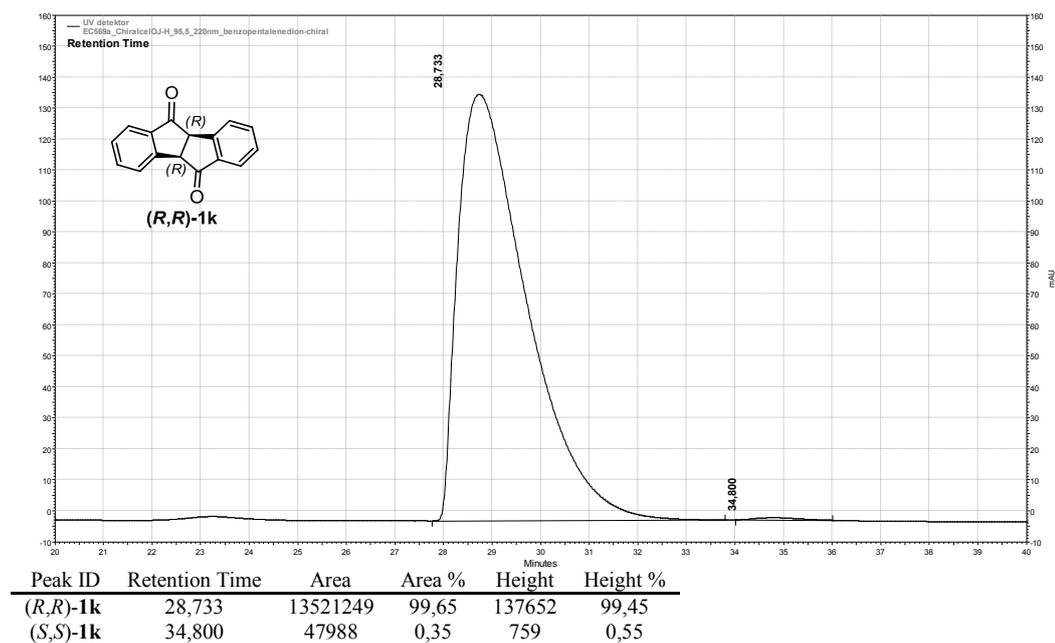
(2*R*,3*S*)-**1e** obtained by PCC oxidation of the ATH product **2e** (derived from the run with (*S,S*)-DPEN-based Ru(II)catalyst **B**):



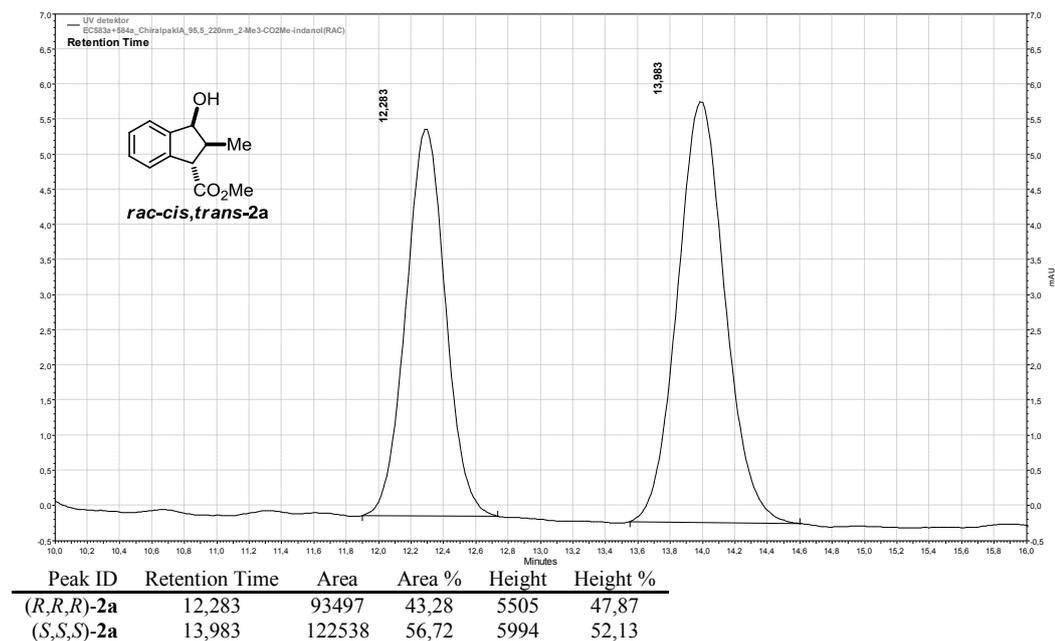
rac-cis-1k. Chiralcel OJ column (25 cm), hexane:2-propanol = 95:5, $\lambda = 220$ nm, flow rate 1 mL/min
 The reference racemate was prepared from racemic 2,3-diphenylsuccinic acid as described above:



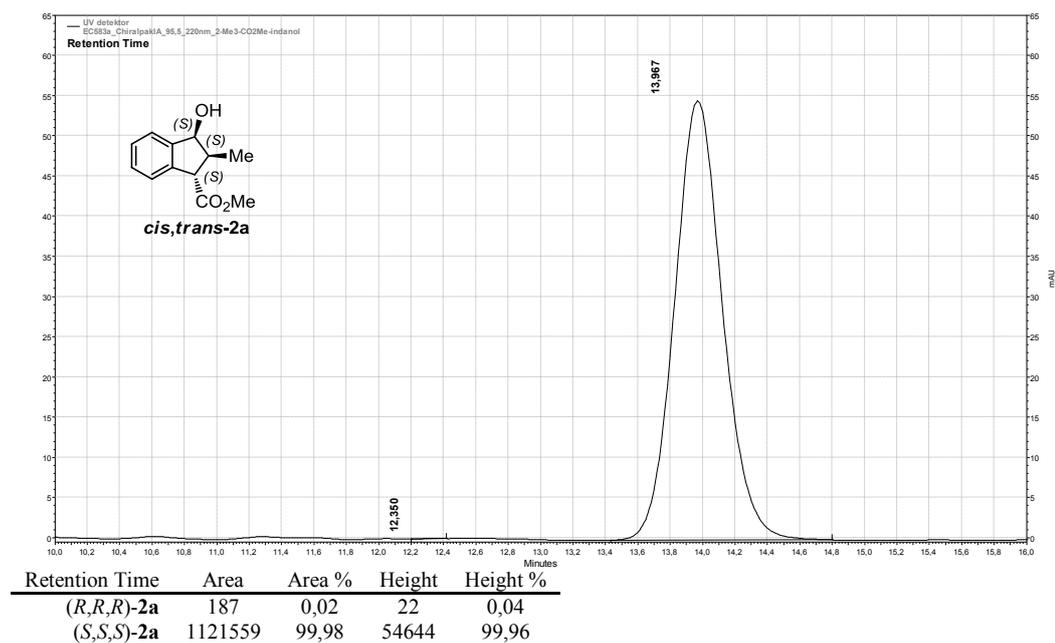
(*R,R*)-**1k** obtained by PCC oxidation of the ATH product **2k** (derived from run with (*S,S*)-DPEN-based Ru(II)catalyst B):



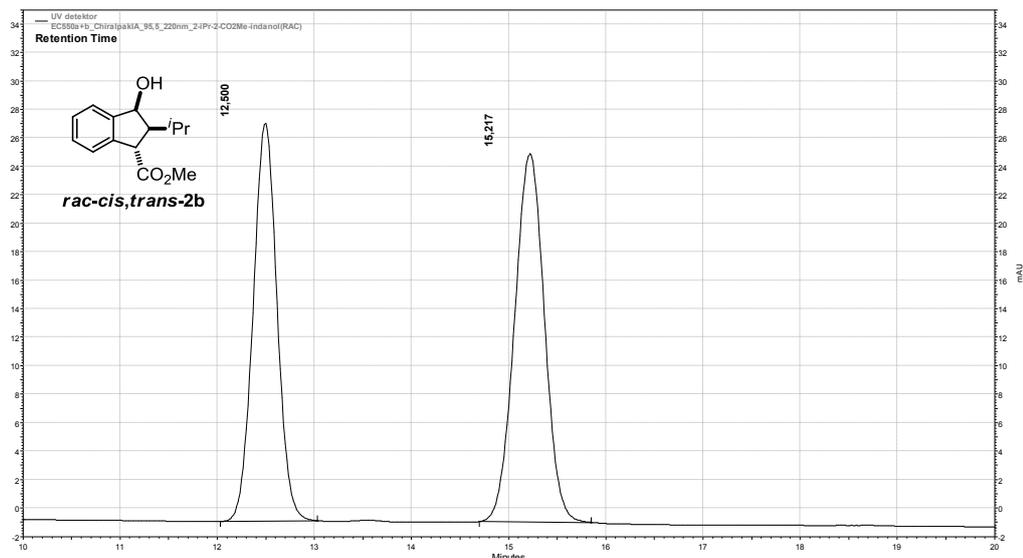
rac-2a. Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)-DPEN-based Ru(II) catalyst **B** and (*R,R*)-DPEN-based Ru(II) catalyst **A**:



Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **B**:

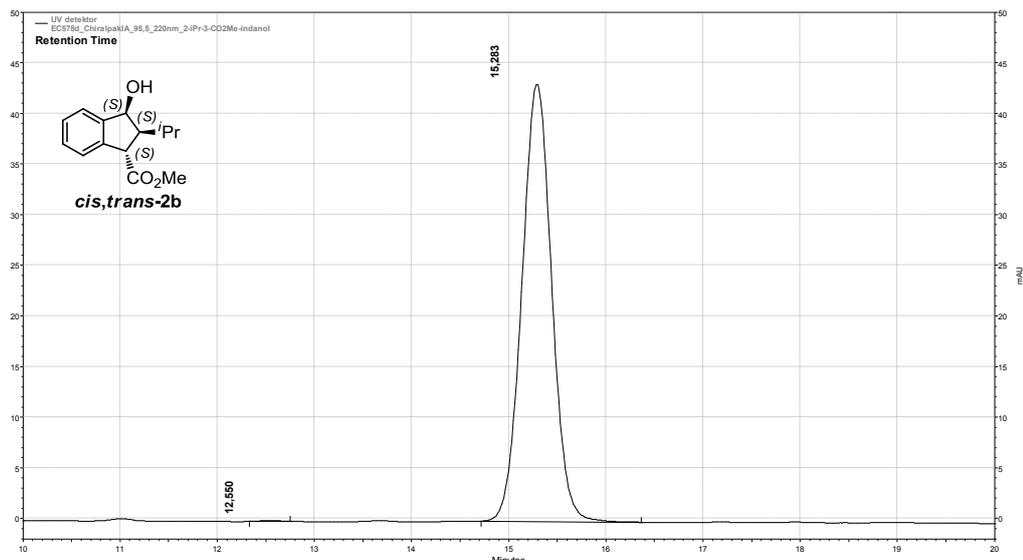


rac-2b. Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)- and (*R,R*)-DPEN-based Ru(II) catalysts **A**:



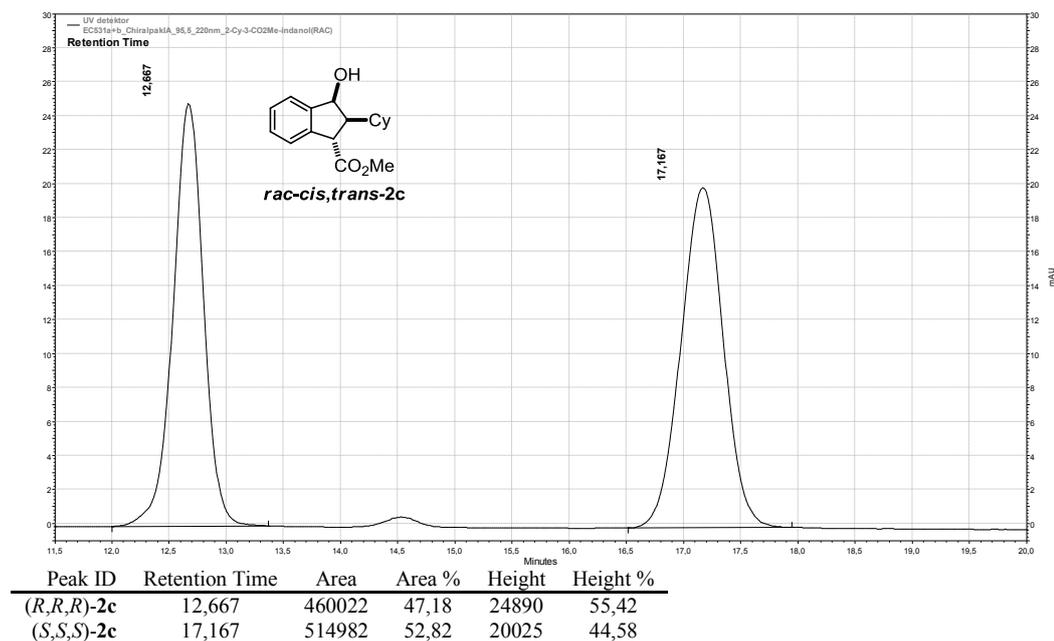
Peak ID	Retention Time	Area	Area %	Height	Height %
(<i>R,R,R</i>)- 2b	12,500	478298	46,39	27956	51,92
(<i>S,S,S</i>)- 2b	15,217	552791	53,61	25887	48,08

Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **B**:

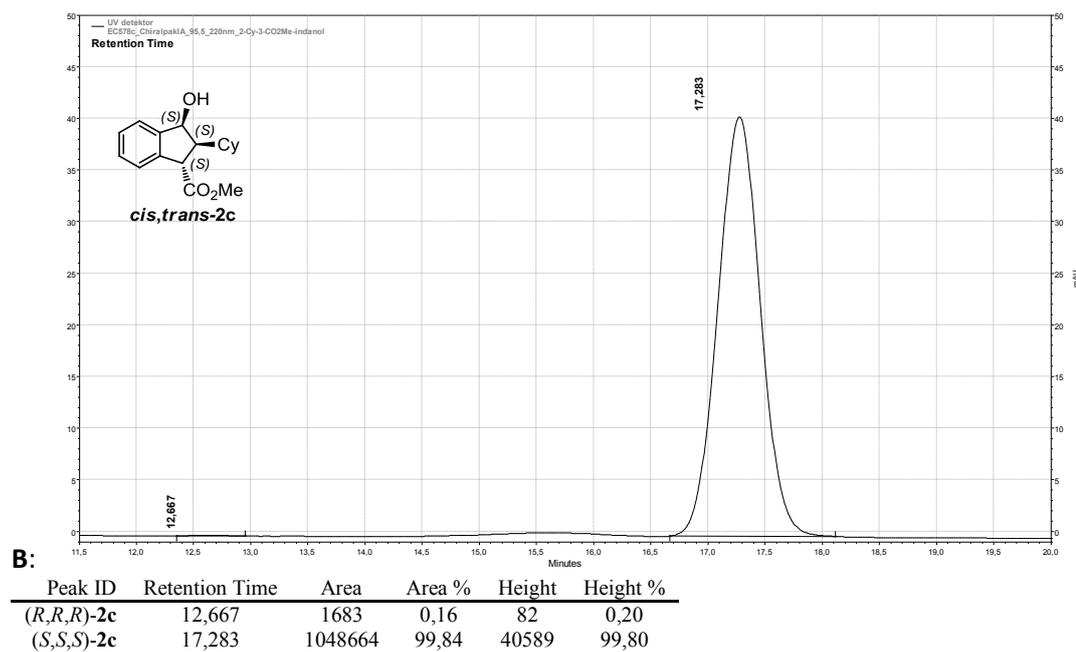


Peak ID	Retention Time	Area	Area %	Height	Height %
(<i>R,R,R</i>)- 2b	12,550	1132	0,12	84	0,19
(<i>S,S,S</i>)- 2b	15,283	917555	99,88	43139	99,81

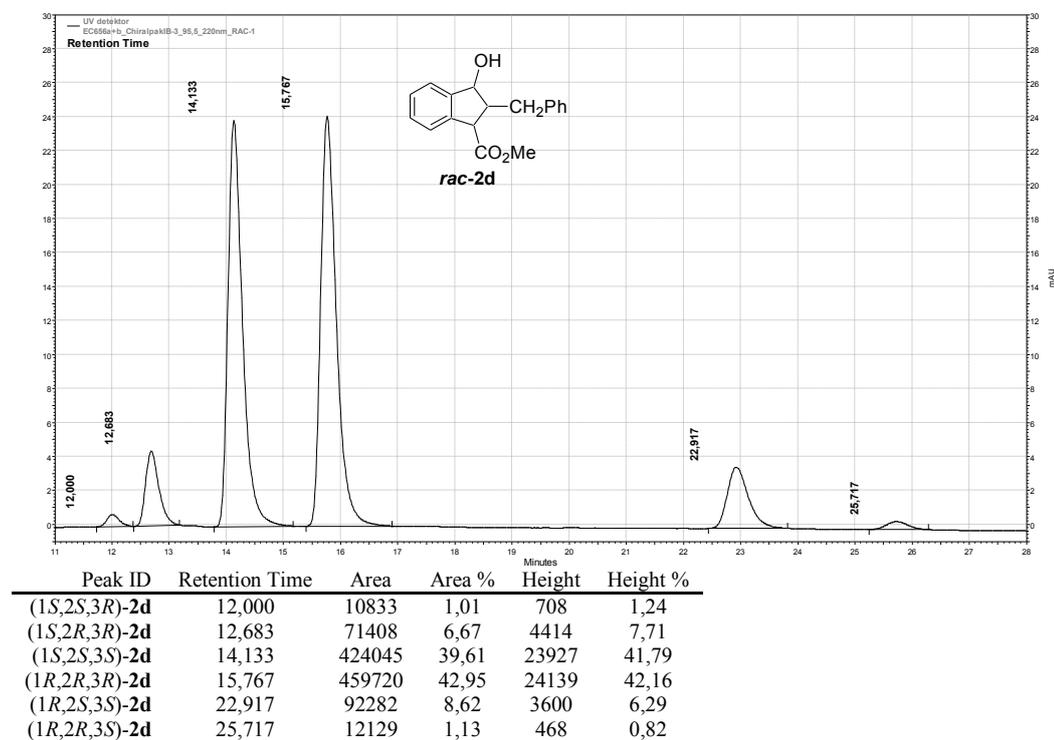
rac-2c. Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)- and (*R,R*)-DPEN-based Ru(II) catalysts **A**:



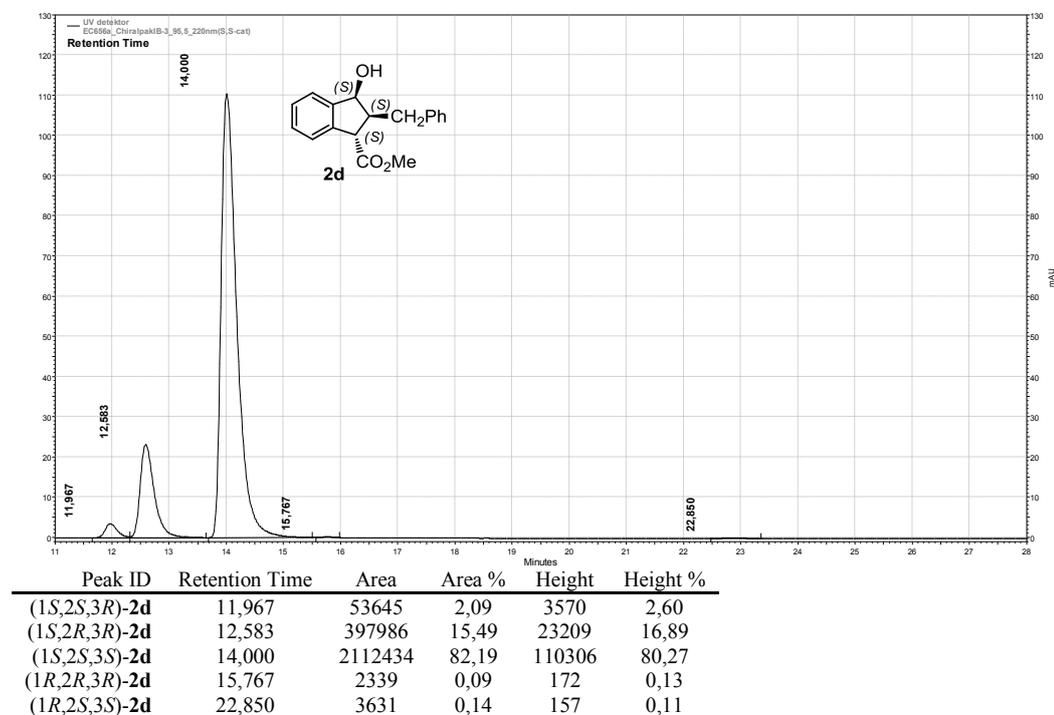
Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst



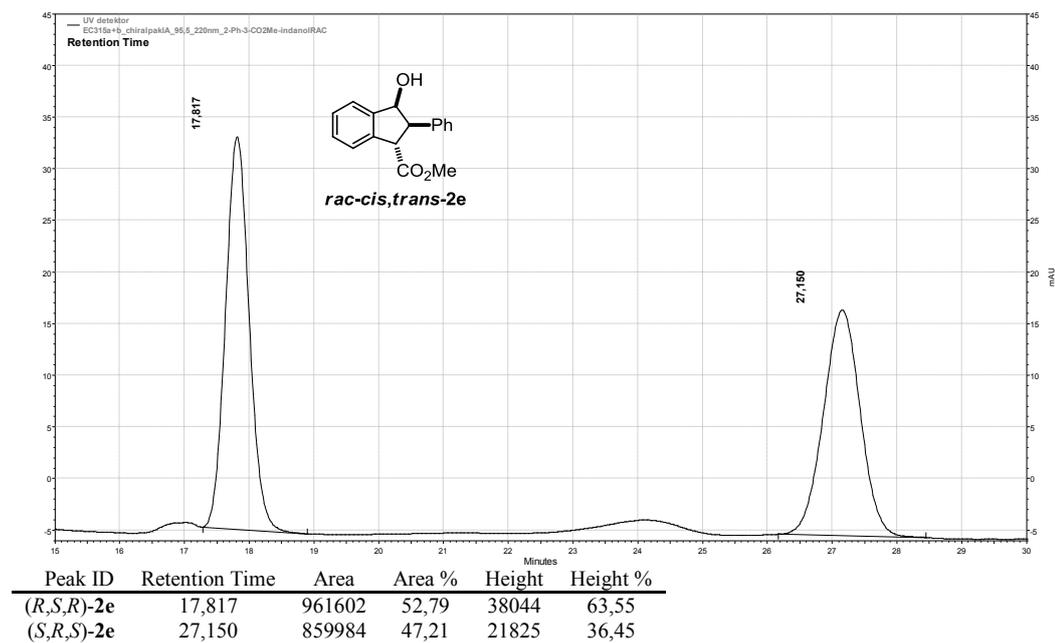
rac-2d. Chiralpak IB-3 column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)-DPEN-based Ru(II) catalyst **B** and (*R,R*)-DPEN-based Ru(II) catalyst **A**:



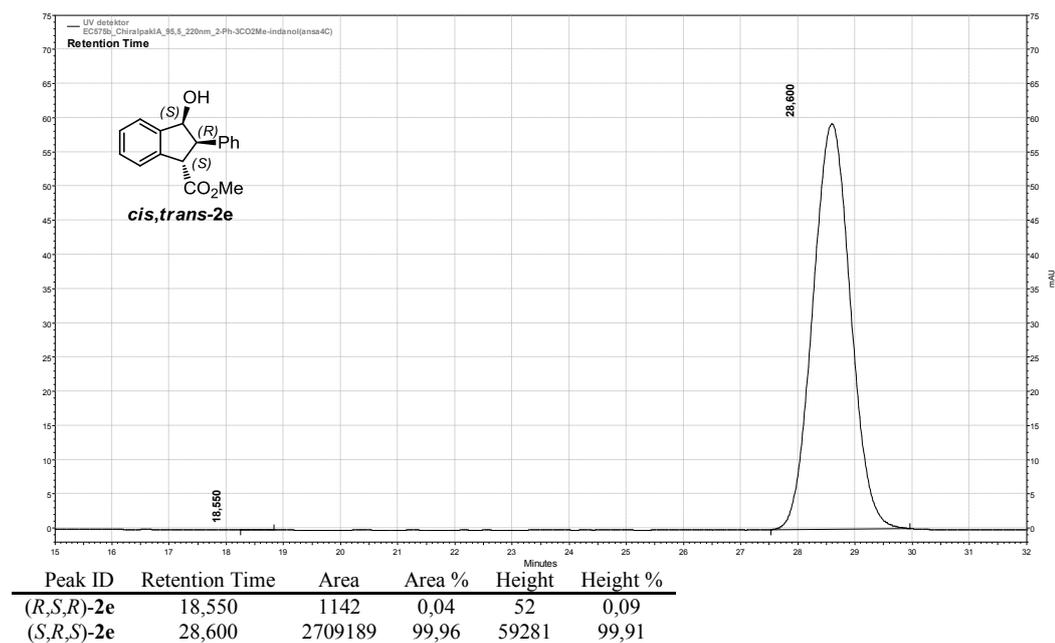
Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **B**:



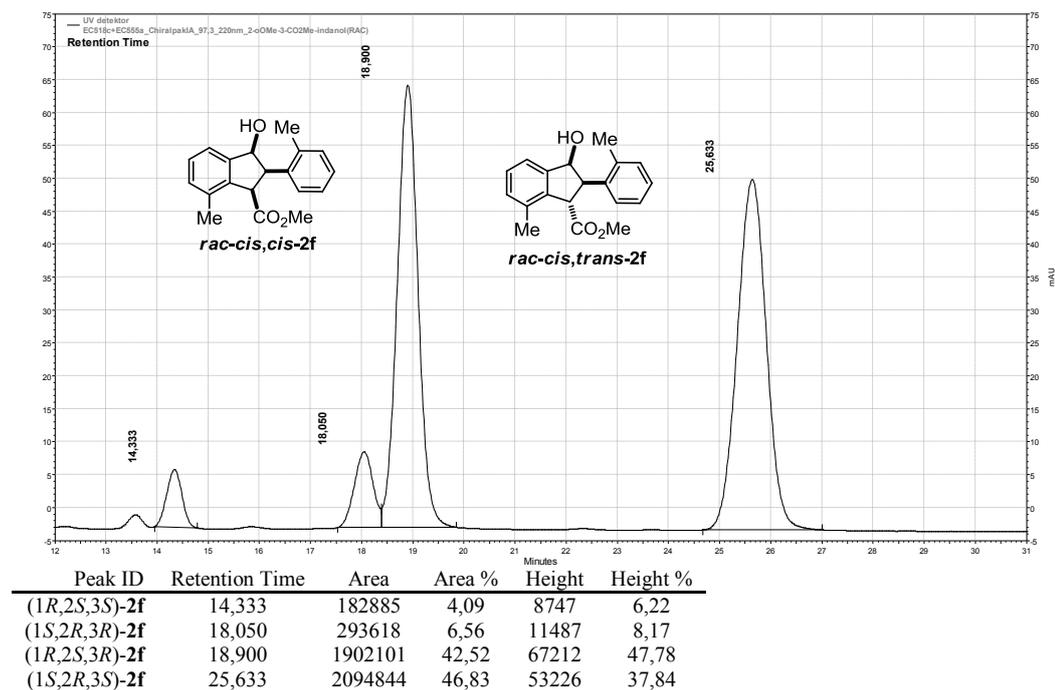
rac-2e. Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)- and (*R,R*)-DPEN-based Ru(II) catalysts **A**:



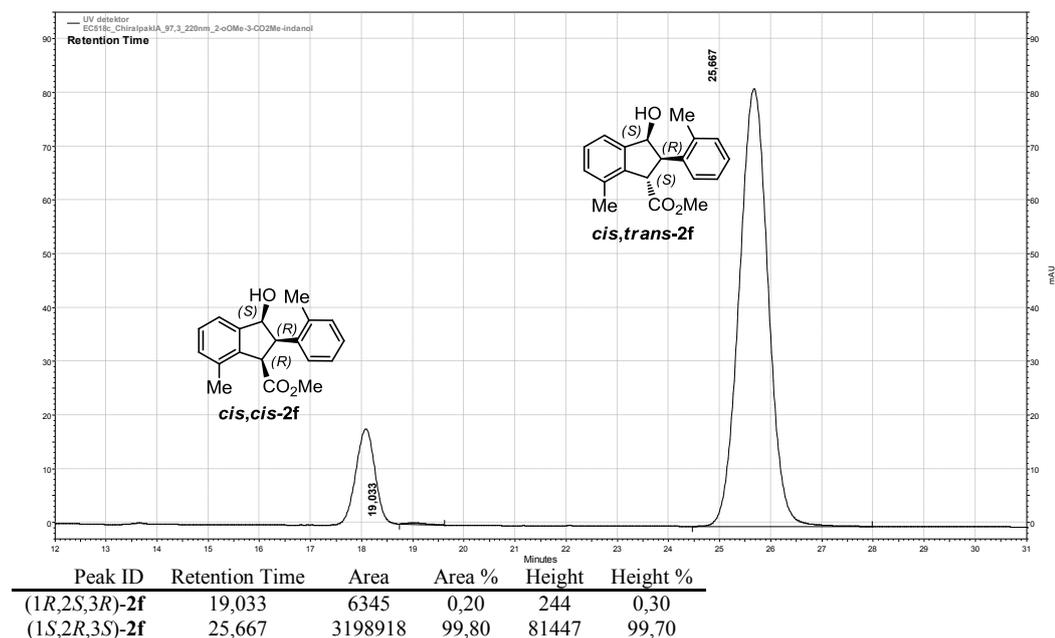
Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **B**:



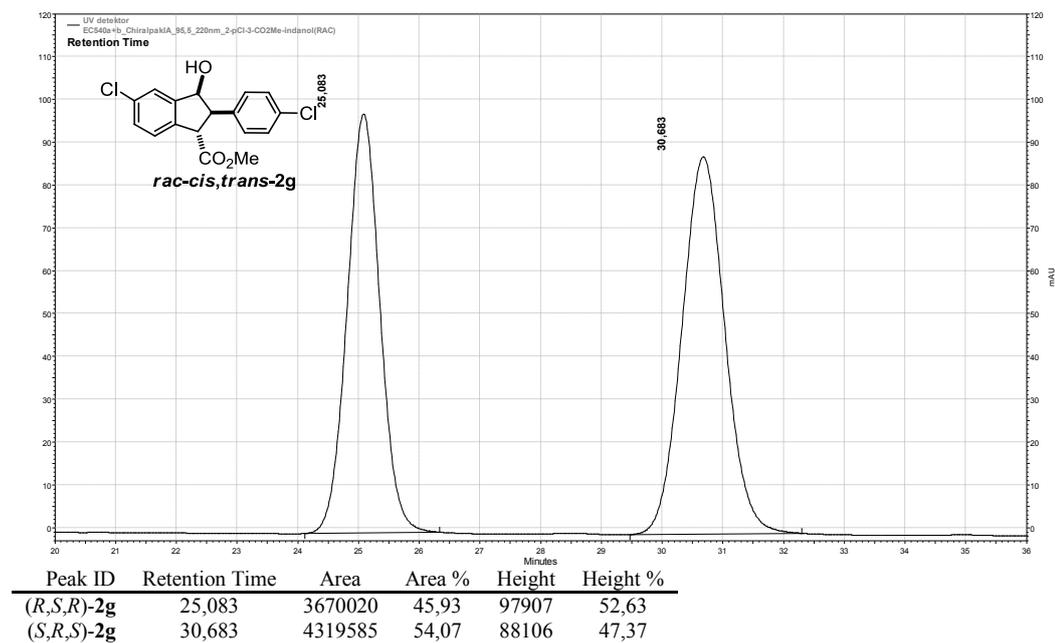
2f. Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 97:3, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)- and (*R,R*)-DPEN-based Ru(II) catalysts **A**:



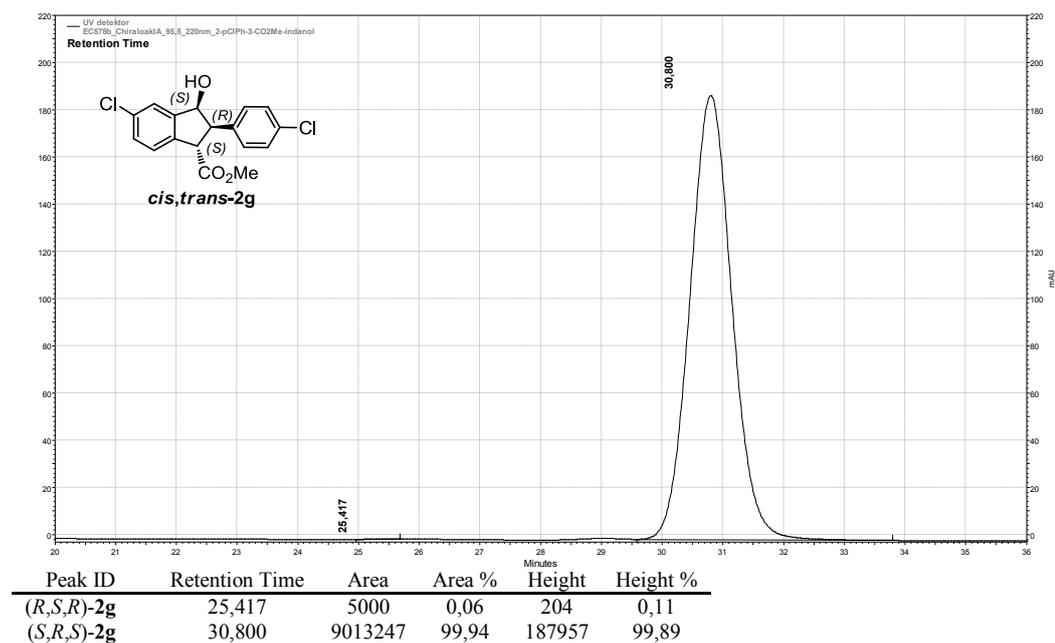
Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **A**:



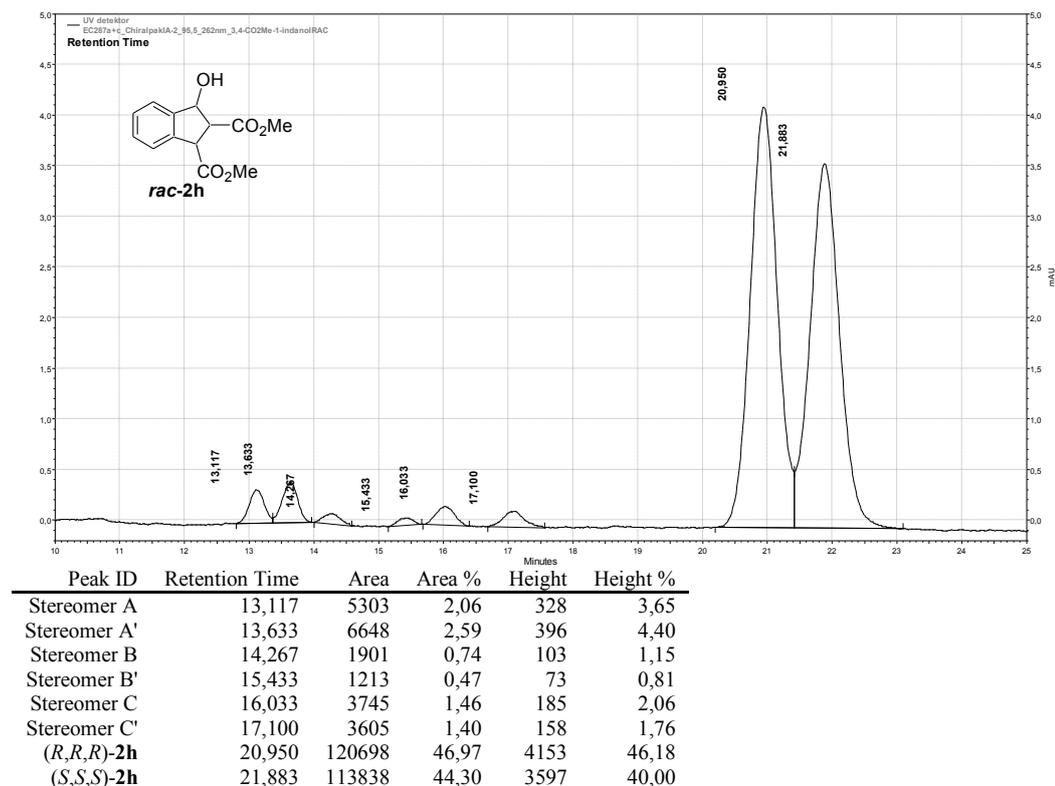
rac-2g. Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)- and (*R,R*)-DPEN-based Ru(II) catalysts **A**:



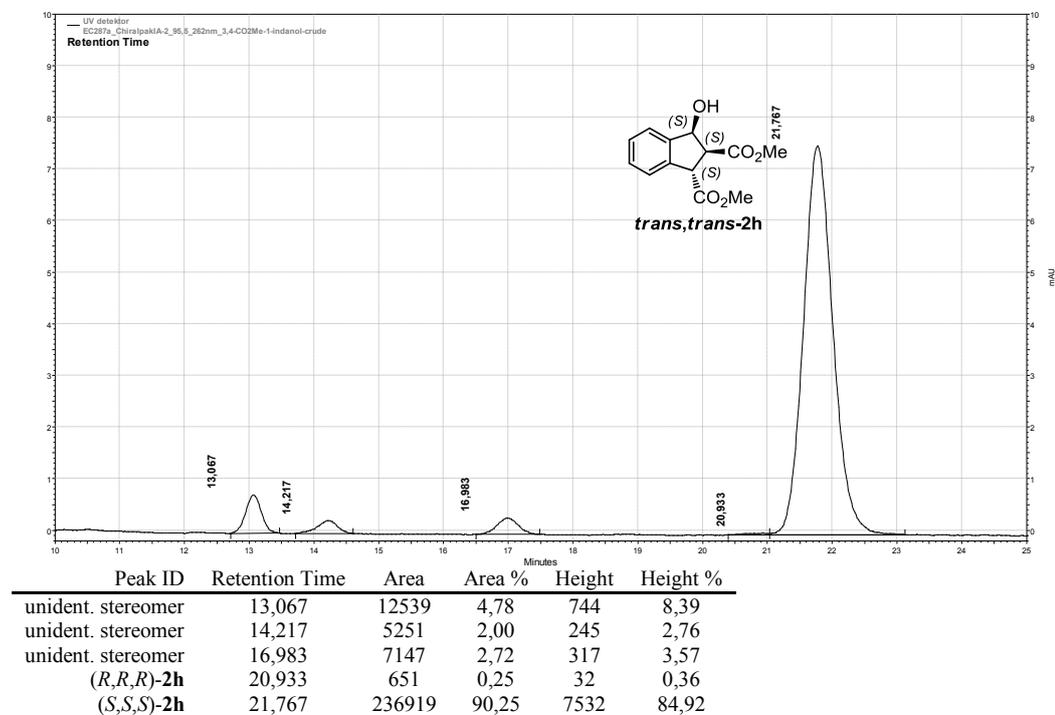
Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **B**:



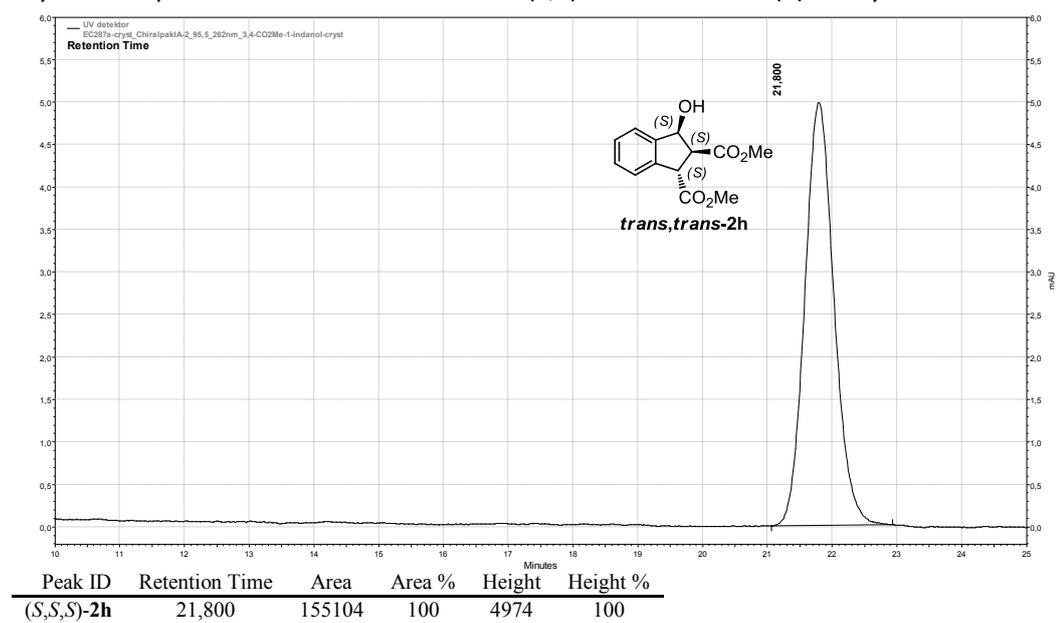
rac-2h. Chiralpak IA column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)- and (*R,R*)-DPEN-based Ru(II) catalysts **A**:



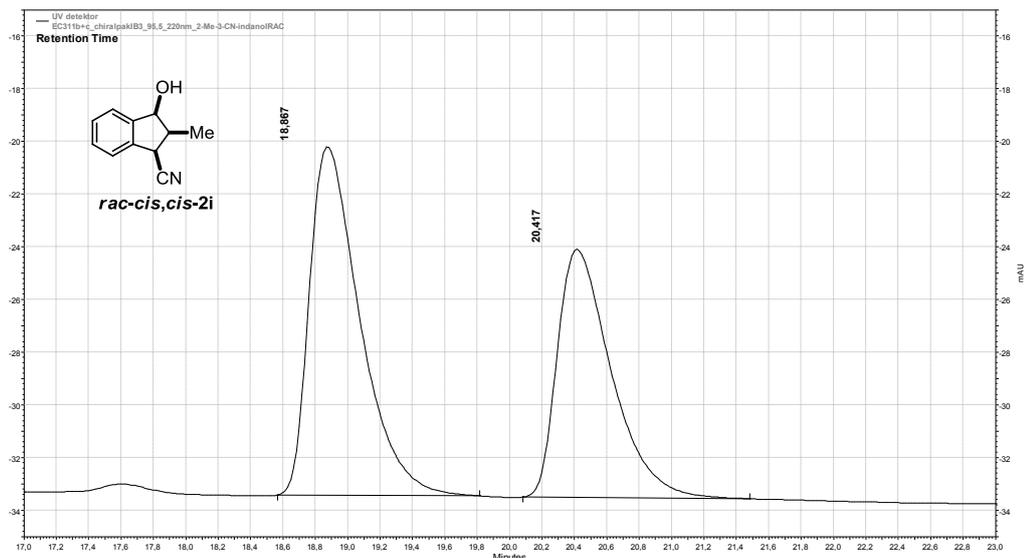
Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **A**:



Crystallized product derived from run with (S,S)-DPEN-based Ru(II) catalyst **A**:

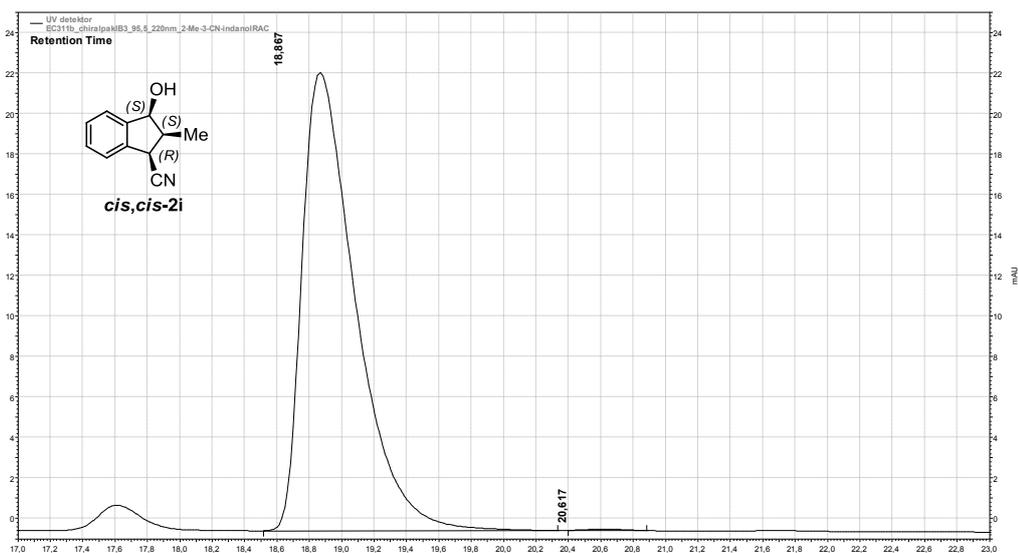


rac-2i. Chiralpak IB-3 column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm. The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)- and (*R,R*)-DPEN-based Ru(II) catalysts **A**:



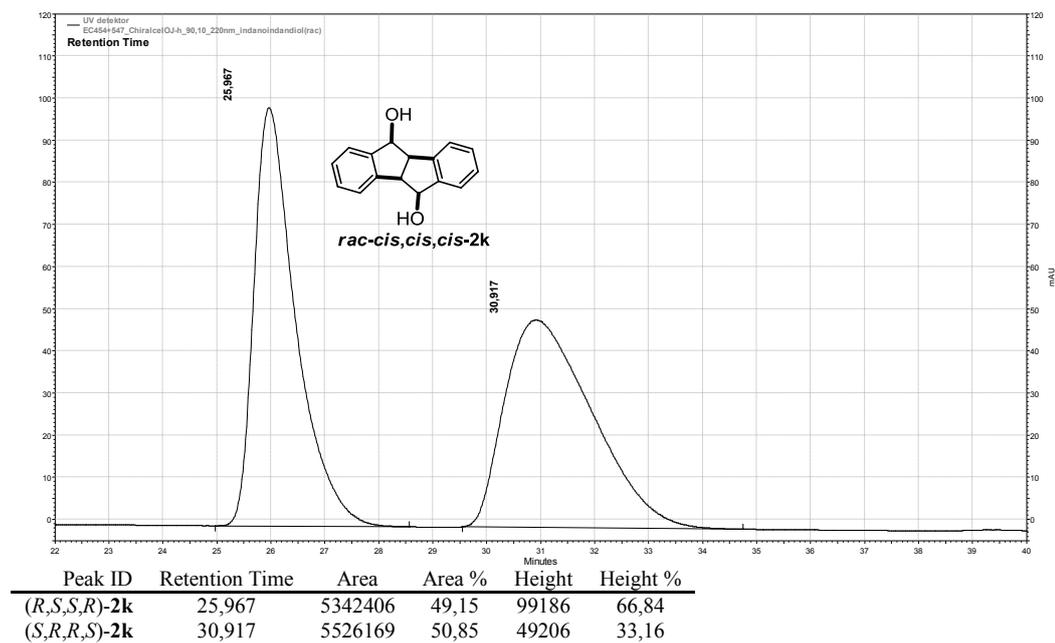
Peak ID	Retention Time	Area	Area %	Height	Height %
(1 <i>S</i> ,2 <i>S</i> ,3 <i>R</i>)- 2i	18,867	286234	56,72	13223	58,39
(1 <i>R</i> ,2 <i>R</i> ,3 <i>S</i>)- 2i	20,417	218412	43,28	9423	41,61

Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **A**:

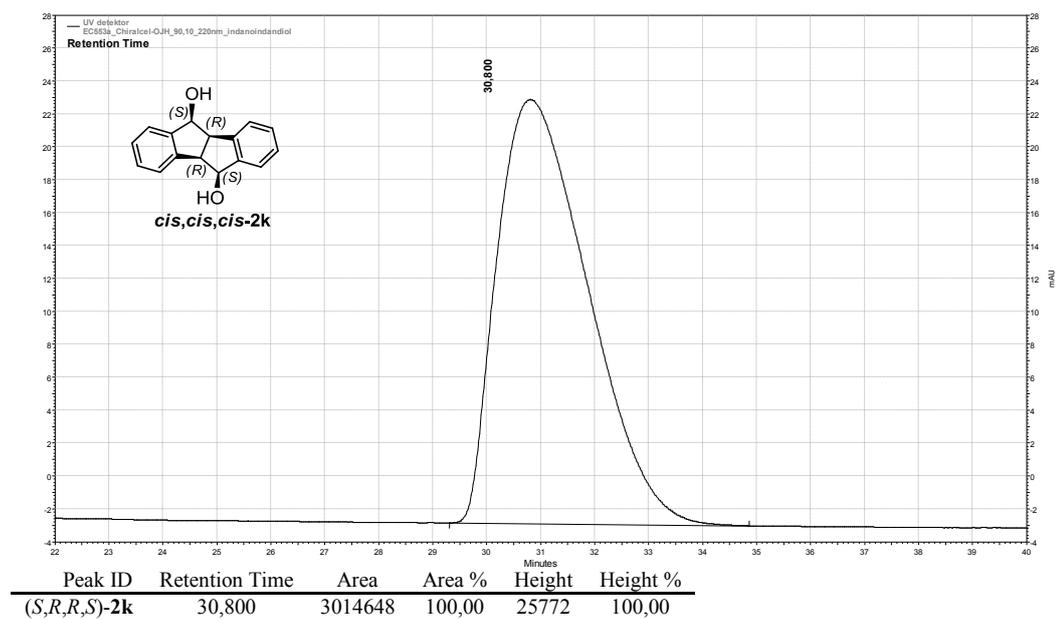


Peak ID	Retention Time	Area	Area %	Height	Height %
(1 <i>S</i> ,2 <i>S</i> ,3 <i>R</i>)- 2i	18,867	517384	99,78	22629	99,68
(1 <i>R</i> ,2 <i>R</i> ,3 <i>S</i>)- 2i	20,617	1144	0,22	72	0,32

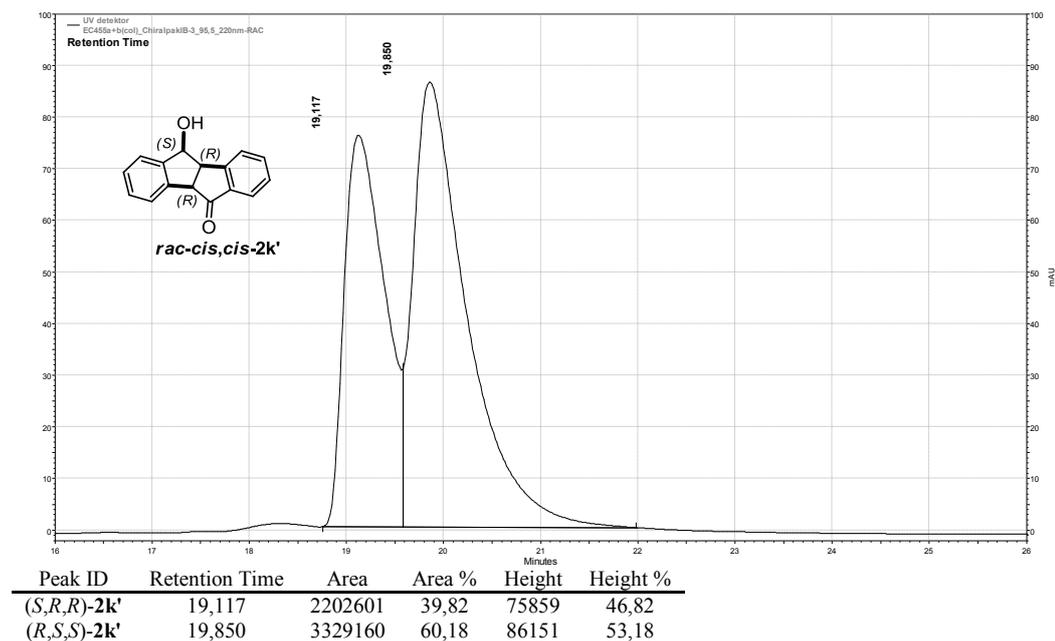
2k. Chiralcel OJ-H column (25 cm). Eluent hexane/2-PrOH 90:10, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)- and (*R,R*)-DPEN-based Ru(II) catalysts **A**:



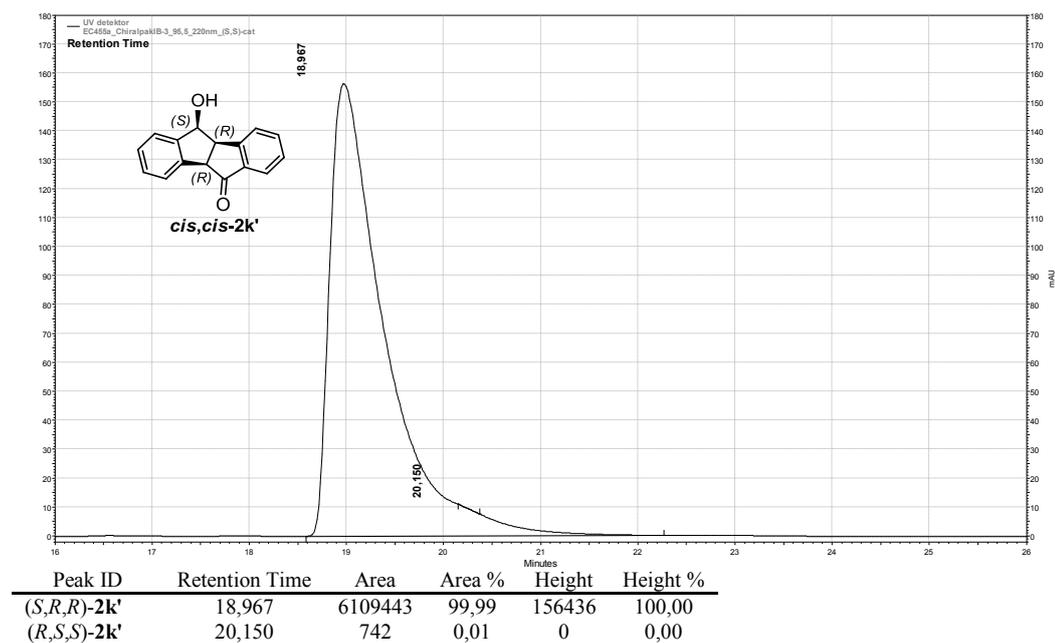
Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **B**:



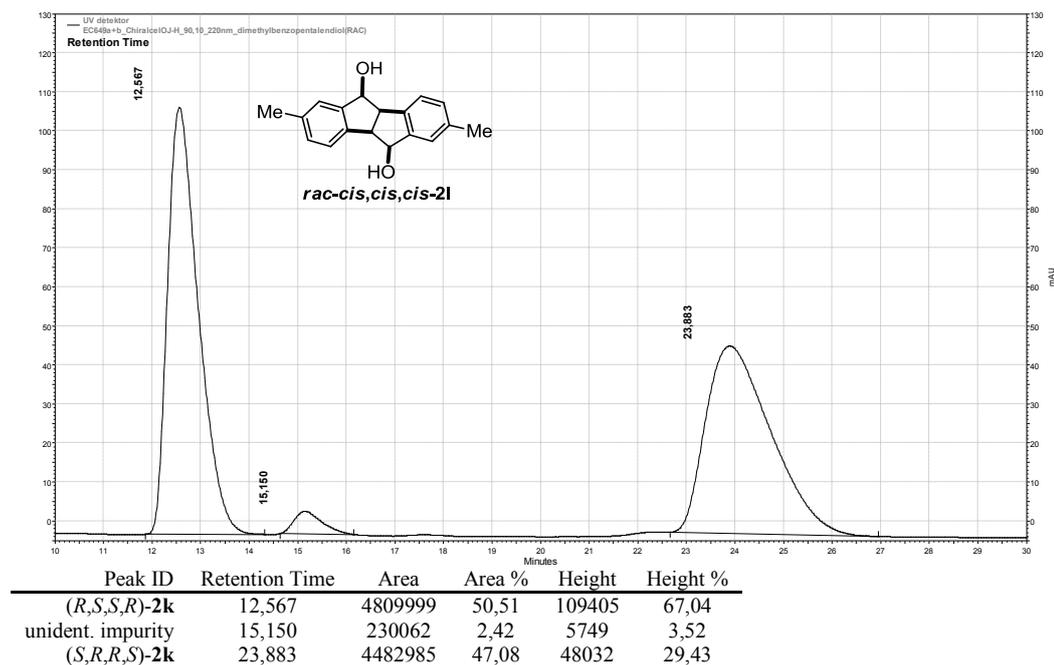
2k'. Chiralpak IB-3 column (25 cm). Eluent hexane/2-PrOH 95:5, flow rate 1 mL/min, $\lambda = 220$ nm.
 The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)-DPEN-based Ru(II) catalyst **A** and (*R,R*)-DPEN-based Ru(II) catalyst **A**:



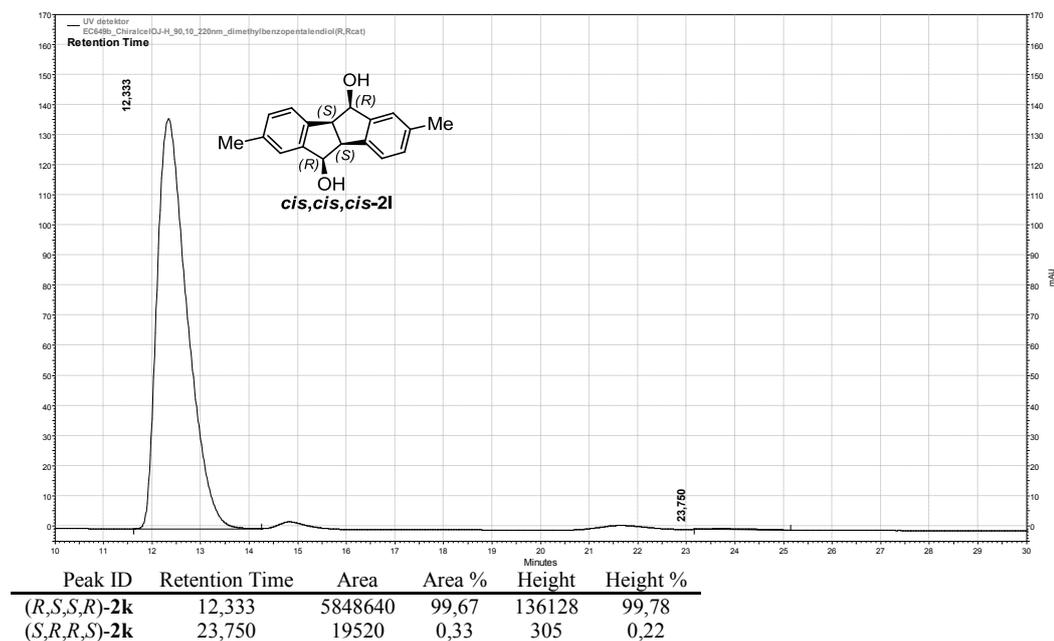
ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **A** after column chromatography:



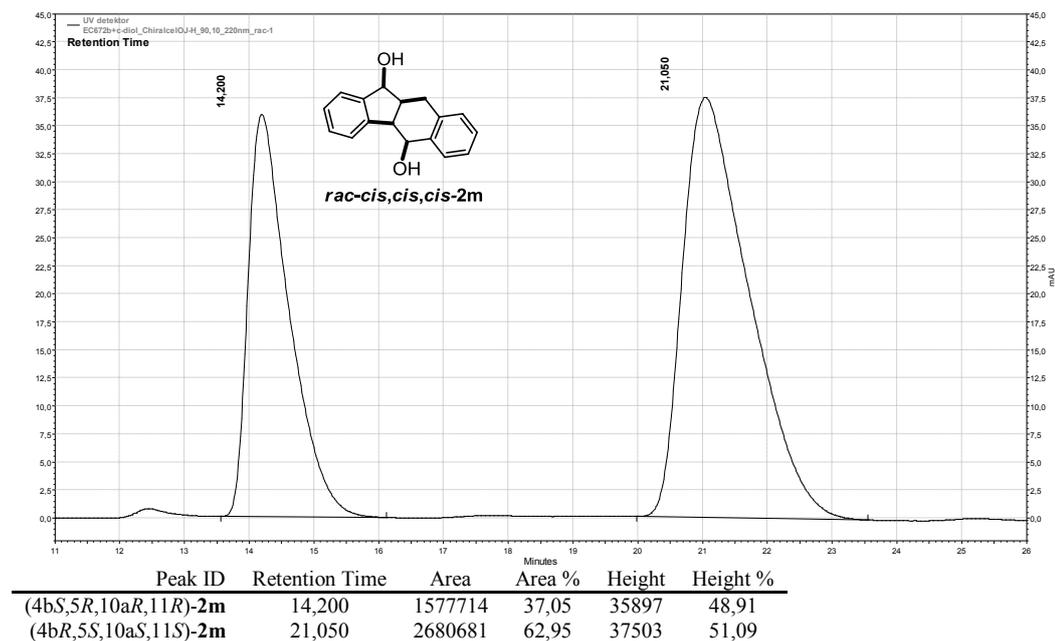
2l. Chiralcel OJ-H column (25 cm). Eluent hexane/2-PrOH 90:10, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)-DPEN-based Ru(II) catalyst **B** and (*R,R*)-DPEN-based Ru(II) catalyst **A**:



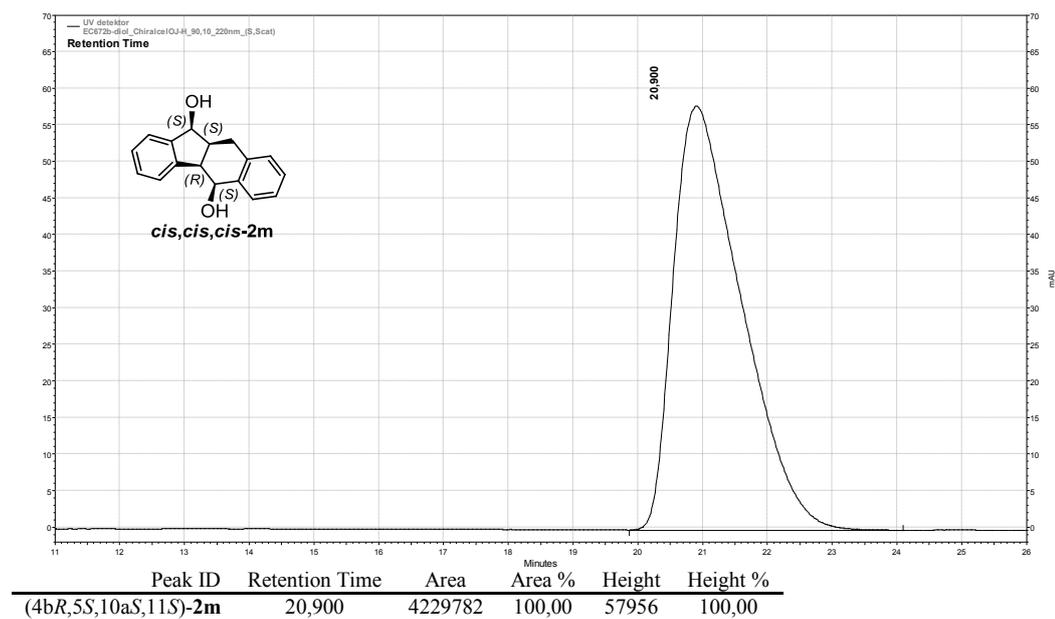
Crude ATH product derived from run with (*R,R*)-DPEN-based Ru(II) catalyst **A**:



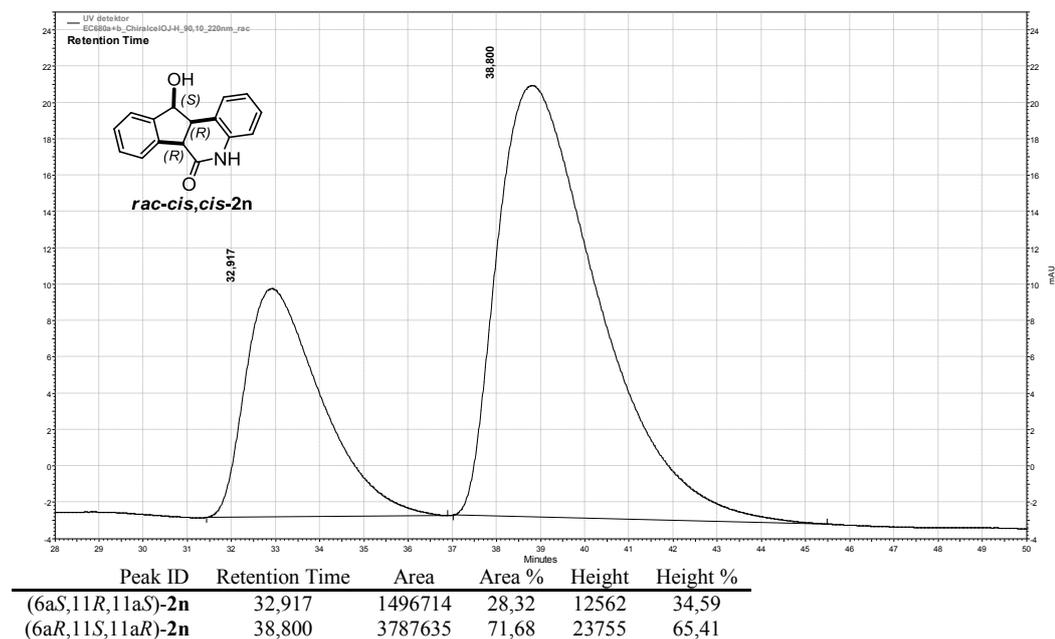
2m. Chiralcel OJ-H column (25 cm). Eluent hexane/2-PrOH 90:10, flow rate 1 mL/min, $\lambda = 220$ nm.
 The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)-DPEN-based Ru(II) catalyst **B** and (*R,R*)-DPEN-based Ru(II) catalyst **A**:



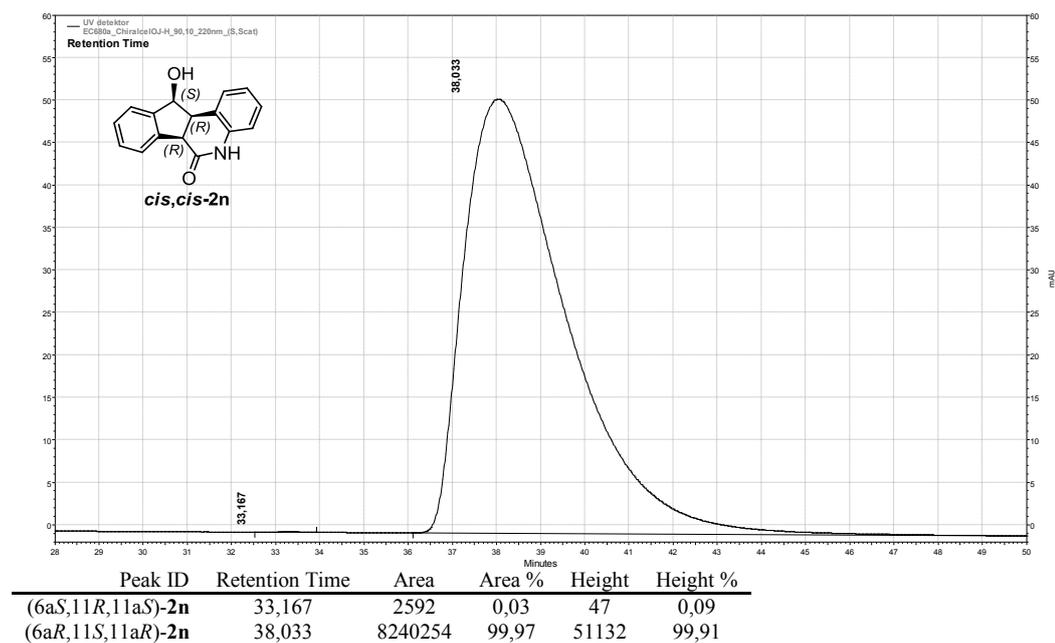
Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **B**:



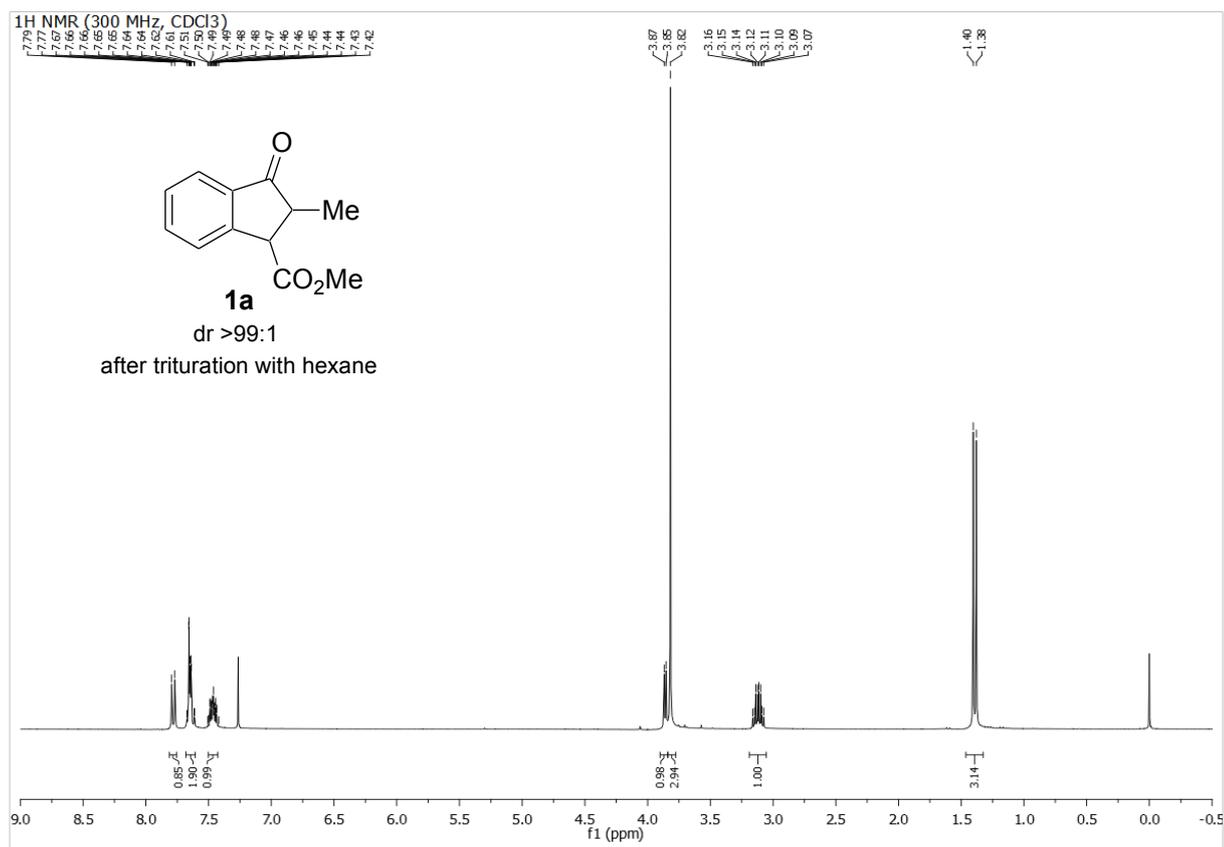
2n. Chiralcel OJ-H column (25 cm). Eluent hexane/2-PrOH 90:10, flow rate 1 mL/min, $\lambda = 220$ nm.
The reference mixture was prepared by mixing the ATH products derived from runs with (*S,S*)-DPEN-based Ru(II) catalyst **B** and (*R,R*)-DPEN-based Ru(II) catalyst **A**:

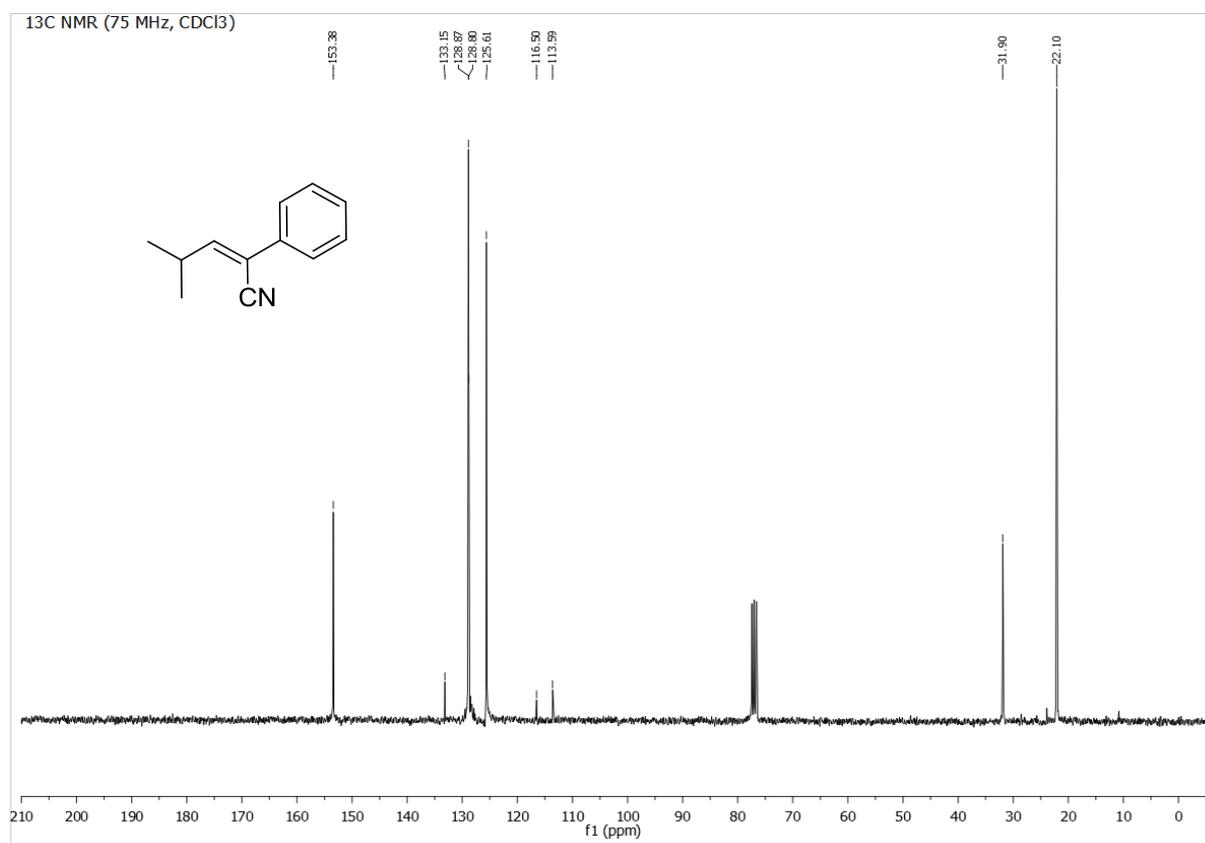
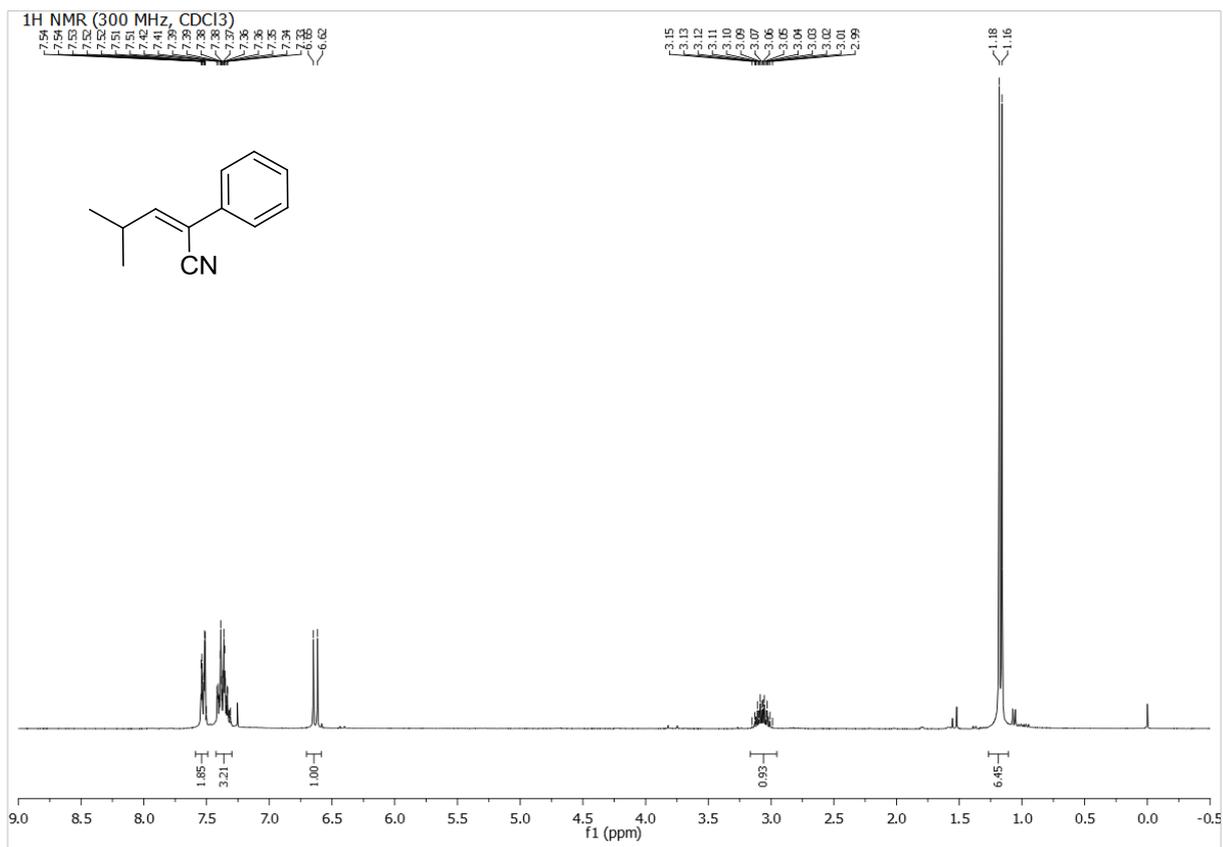


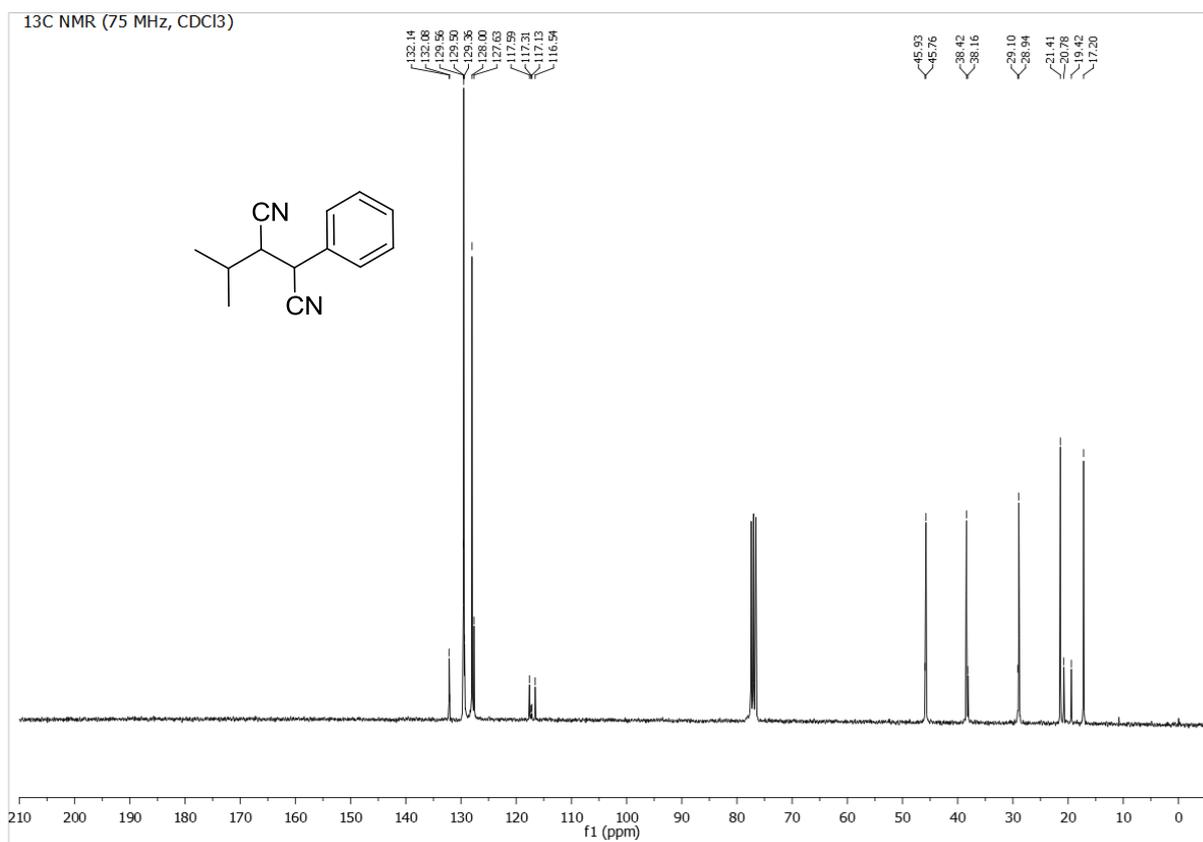
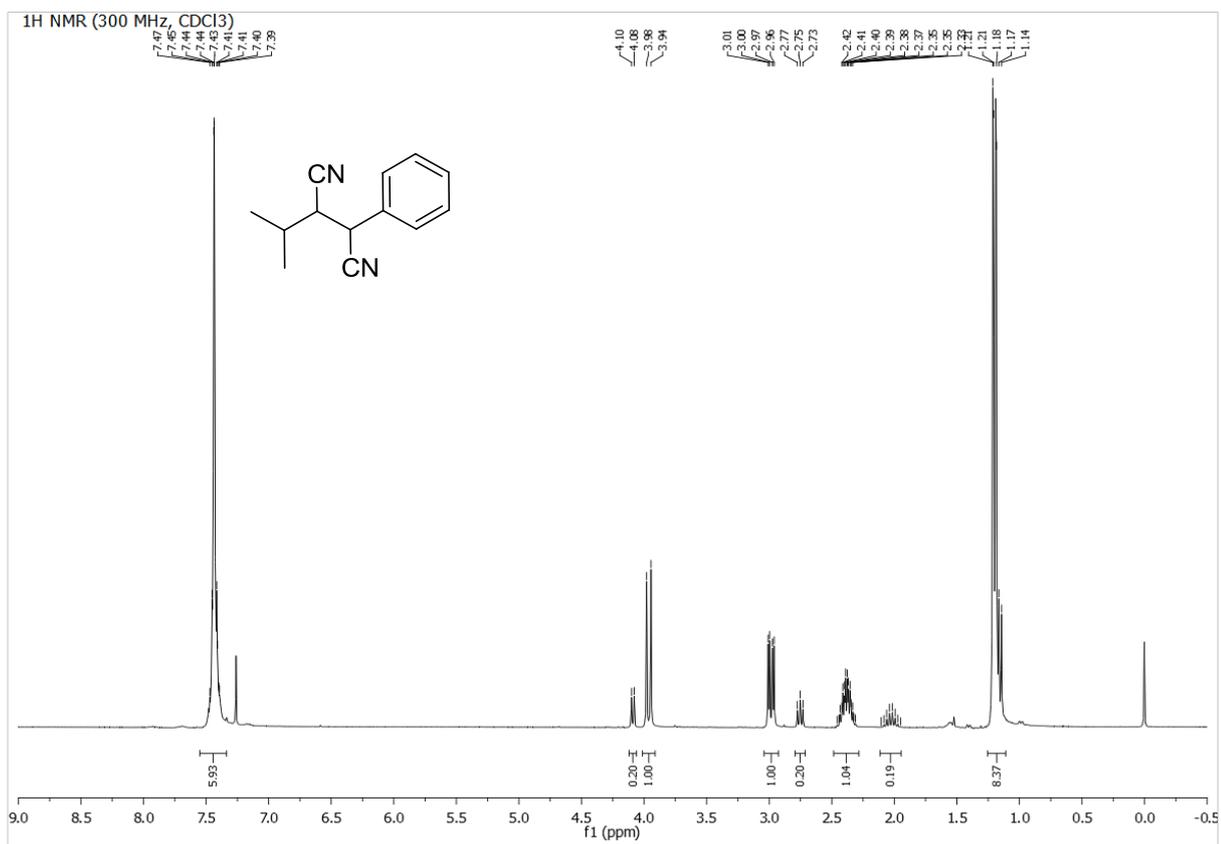
Crude ATH product derived from run with (*S,S*)-DPEN-based Ru(II) catalyst **B**:

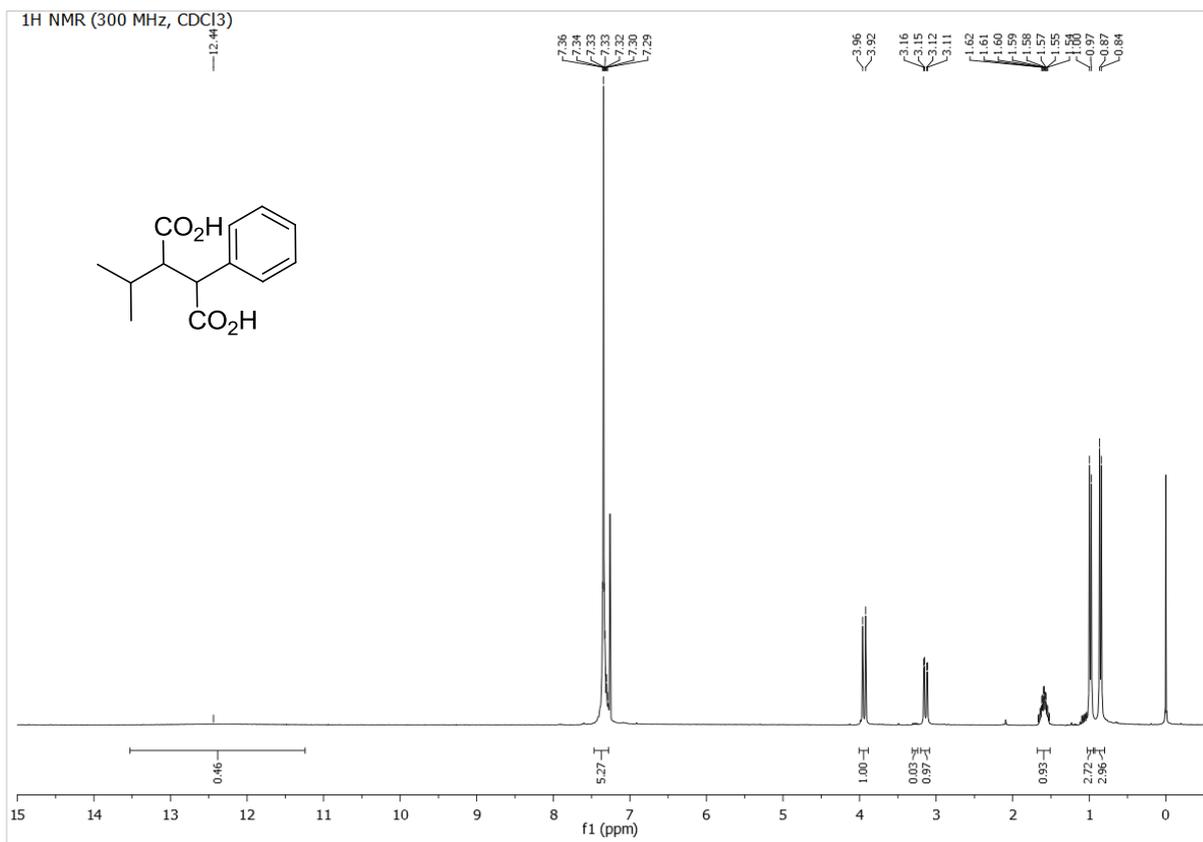


8 ^1H , ^{13}C and NOESY NMR spectra

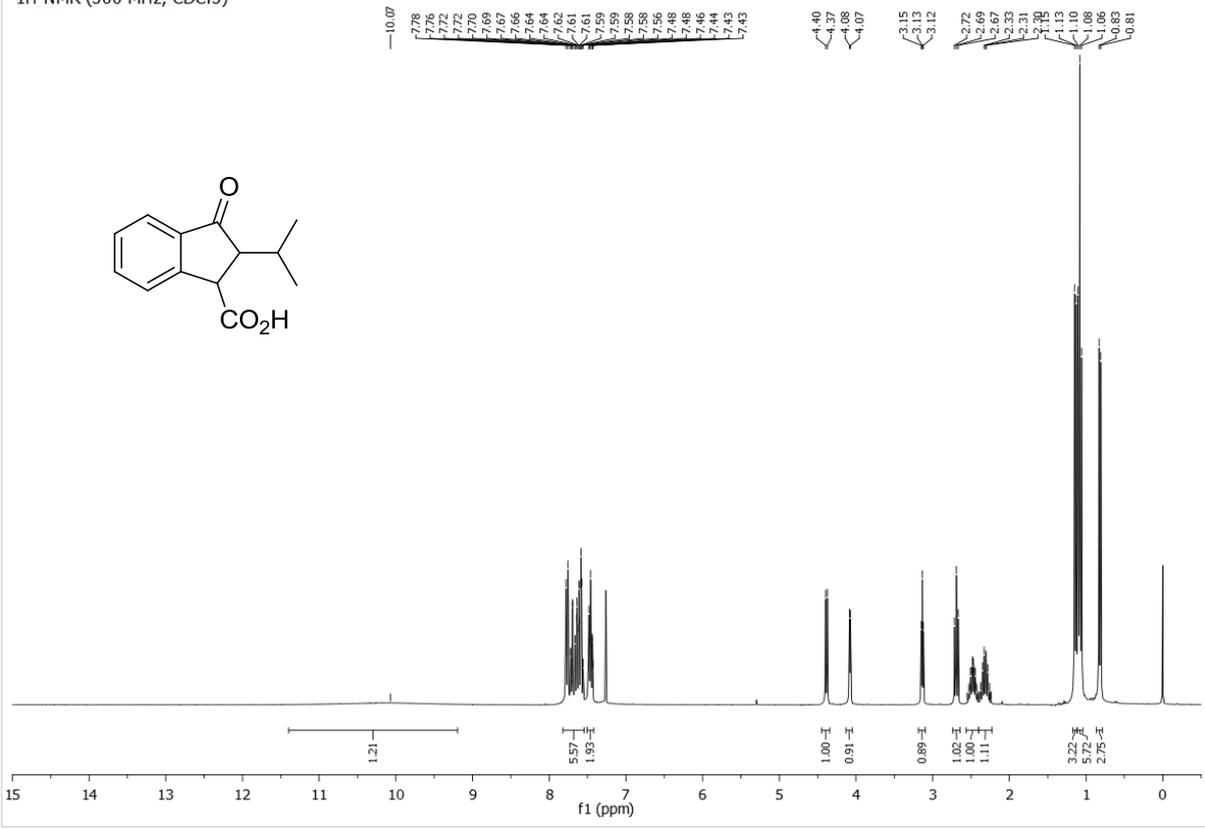
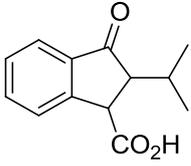




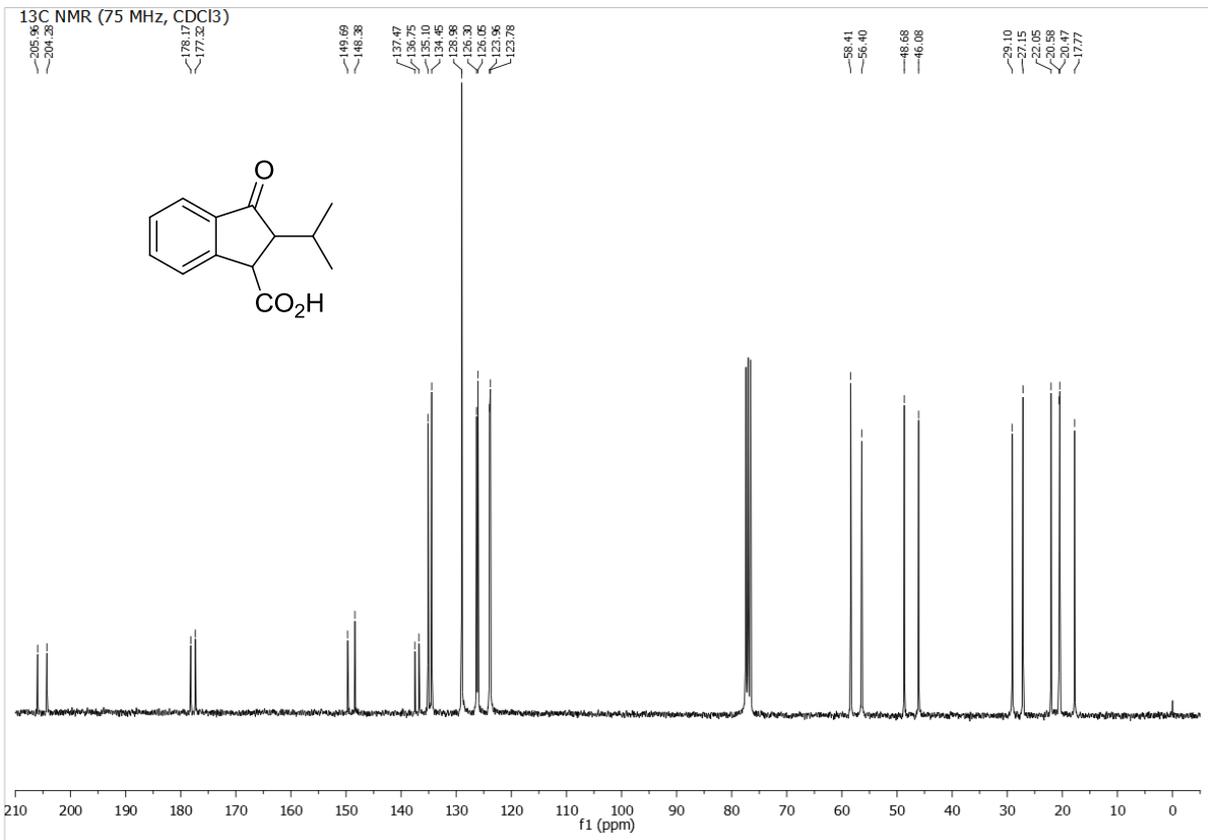
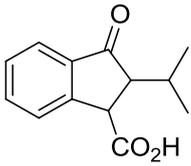


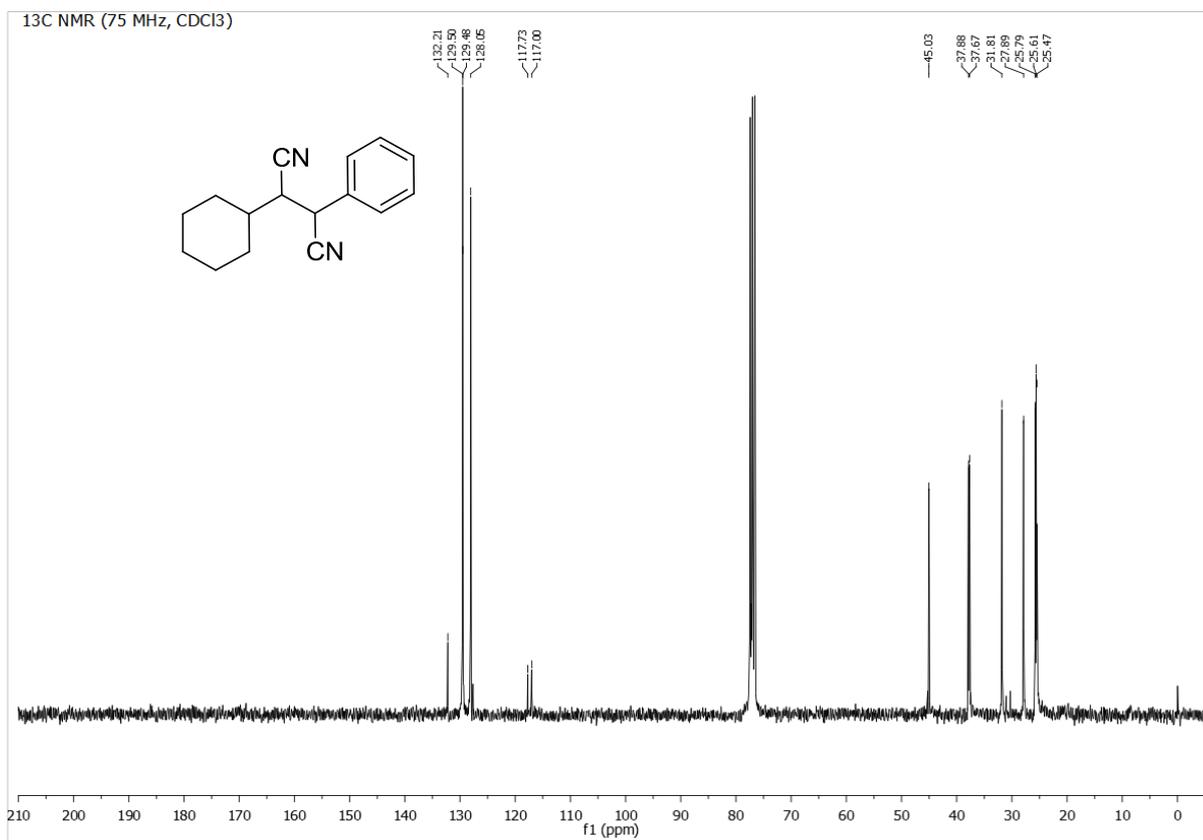
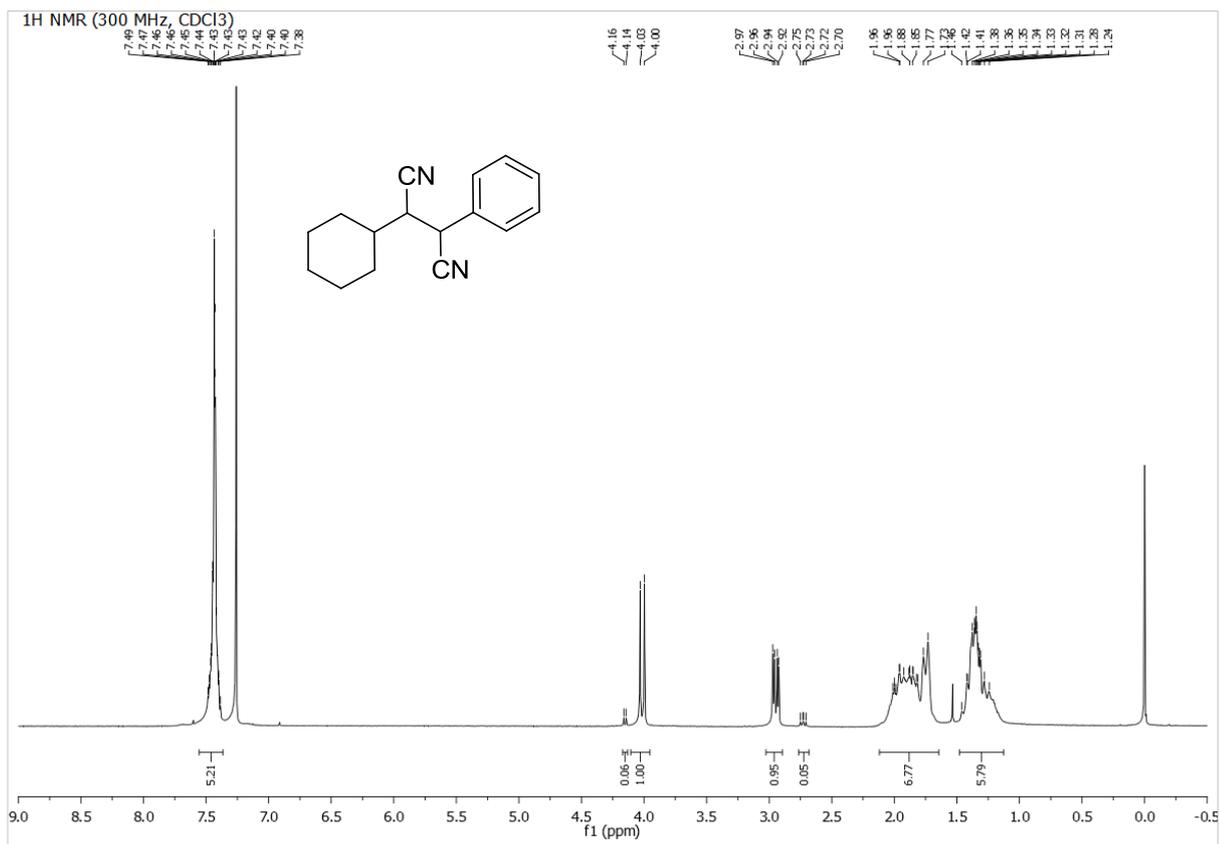


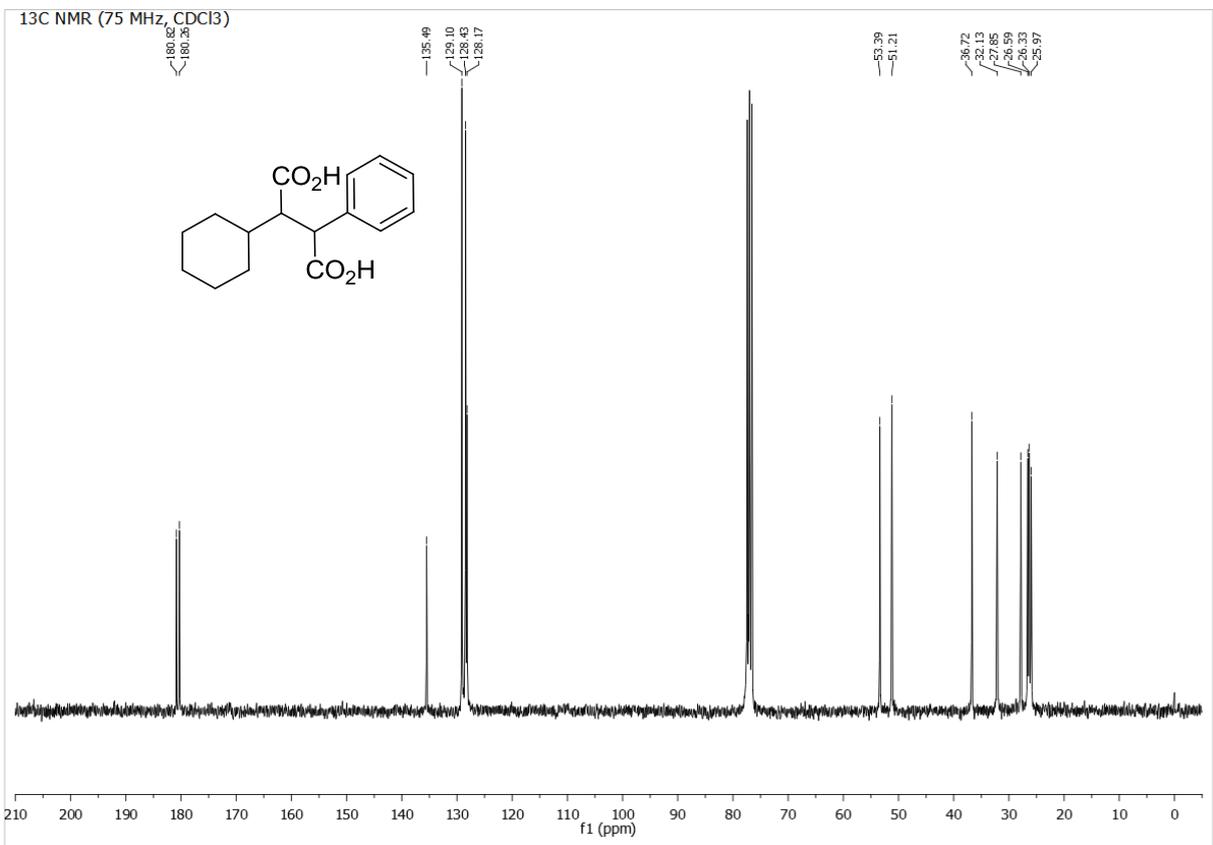
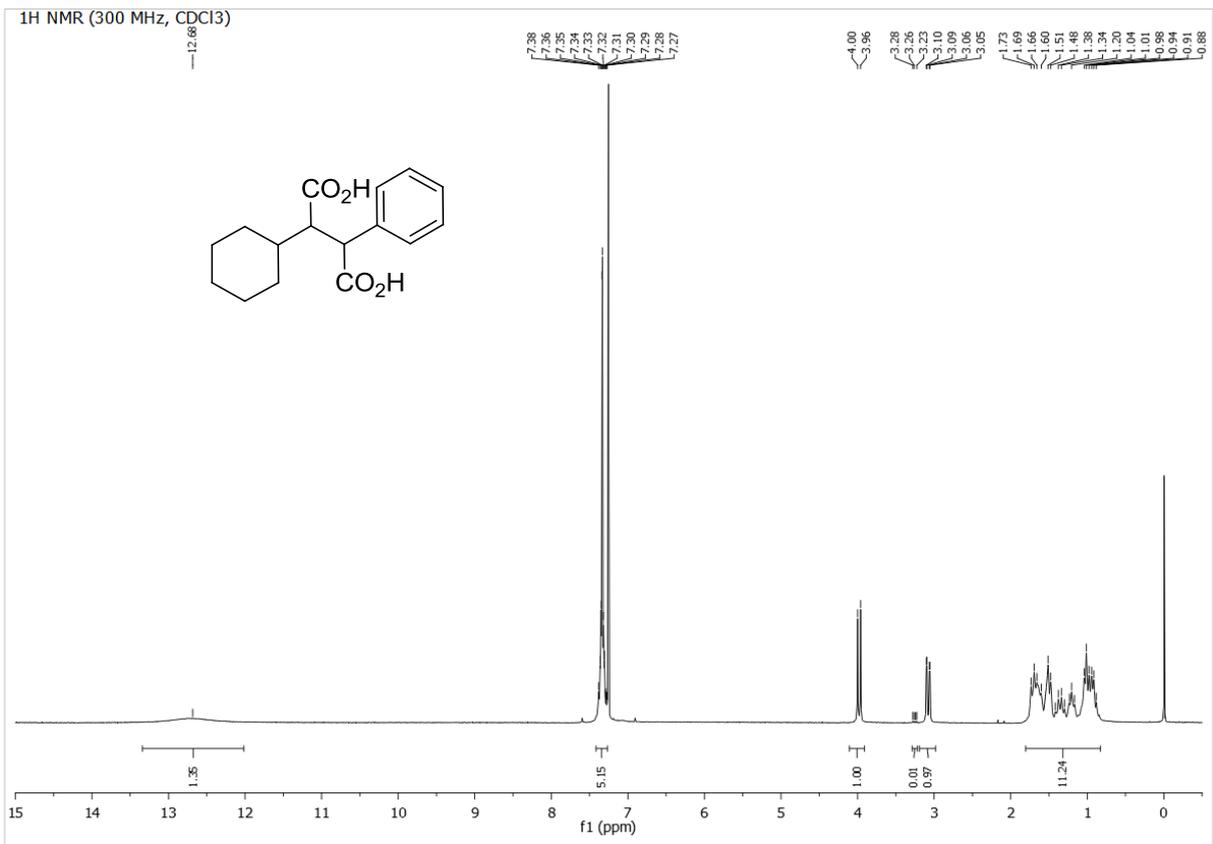
¹H NMR (300 MHz, CDCl₃)

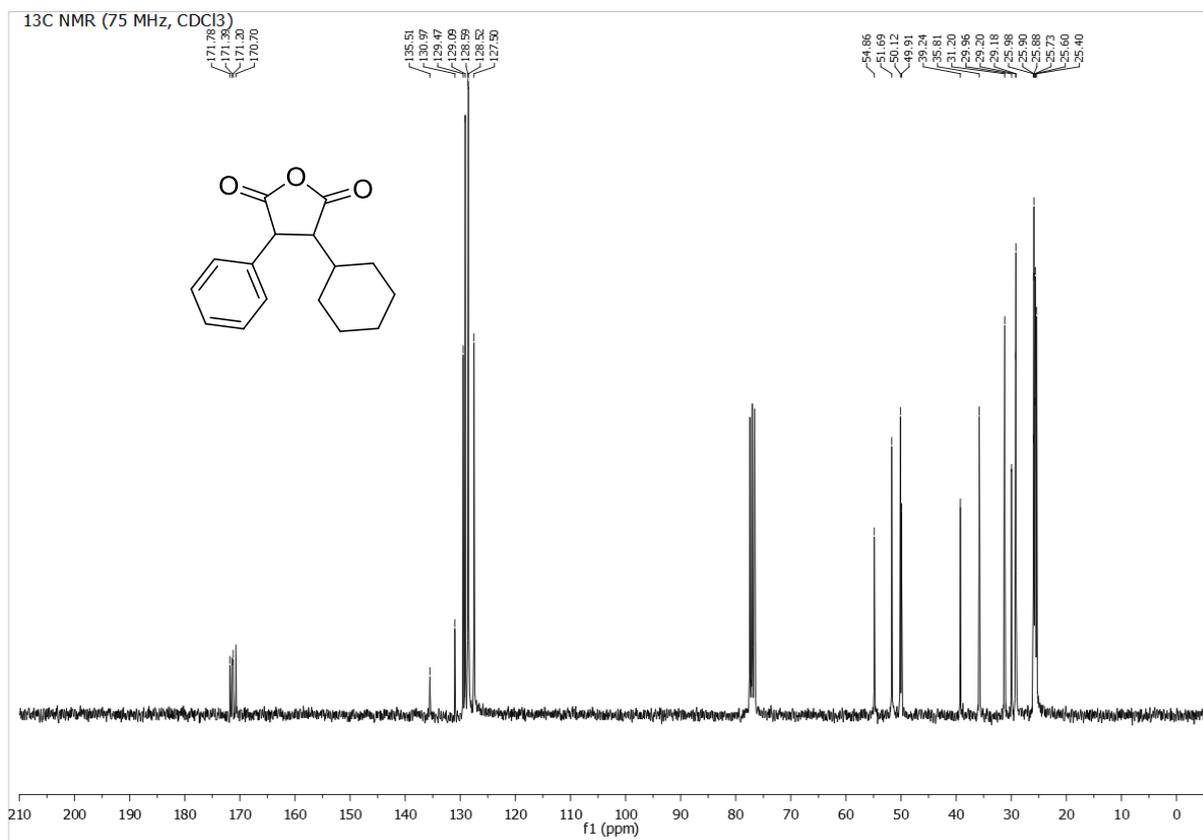
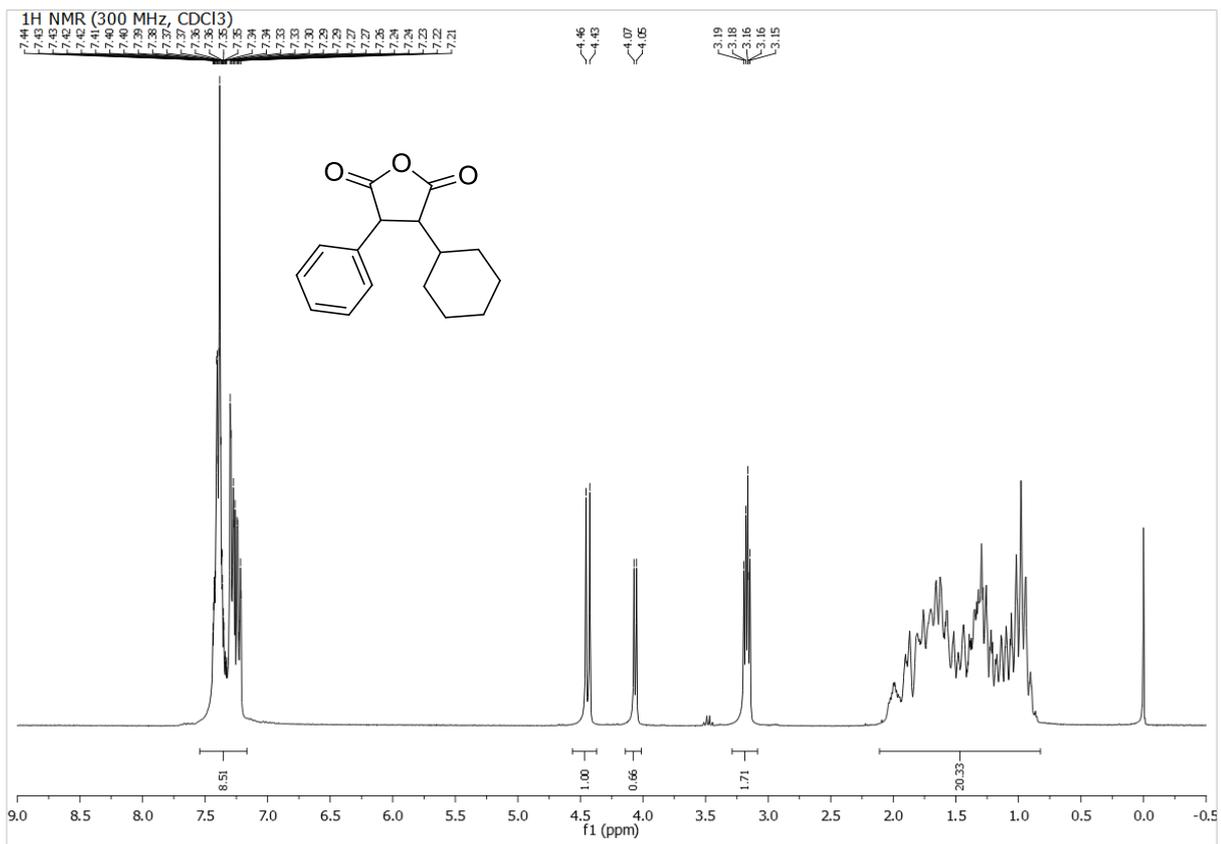


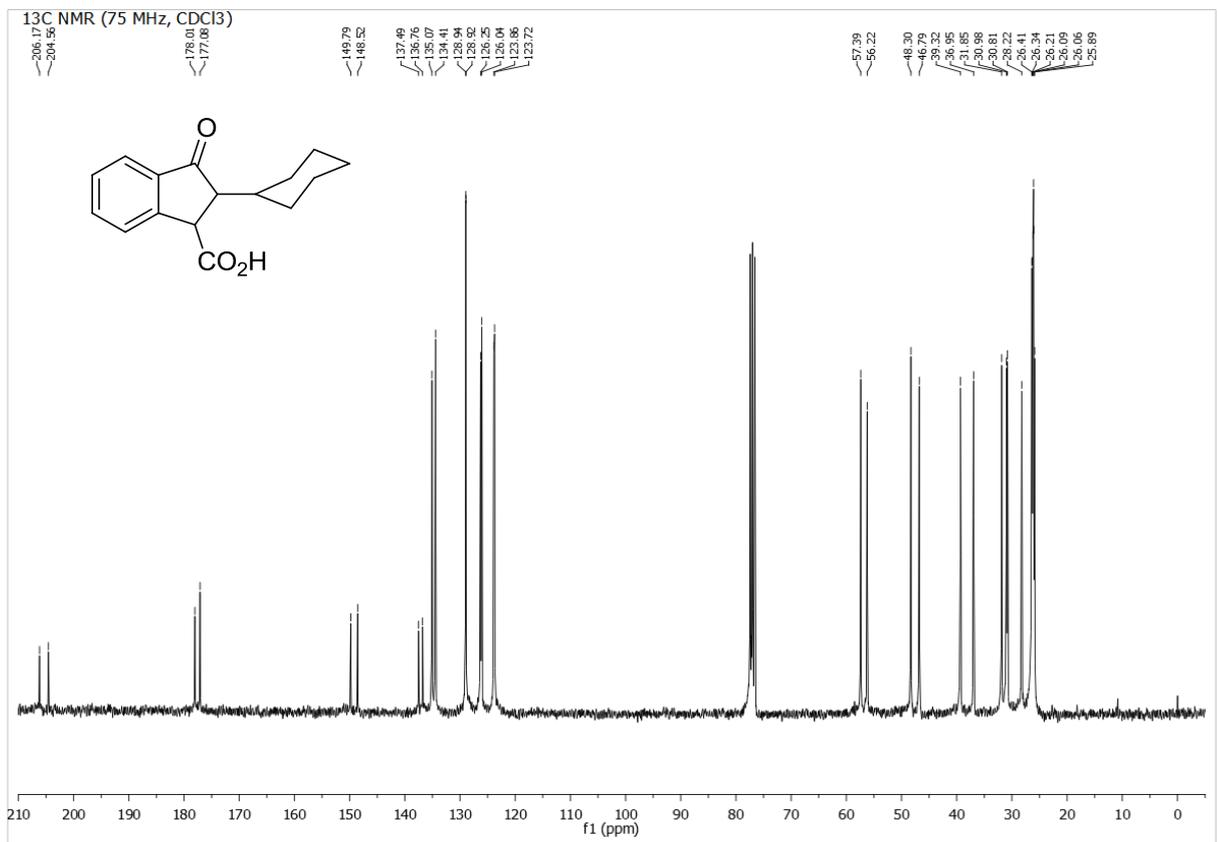
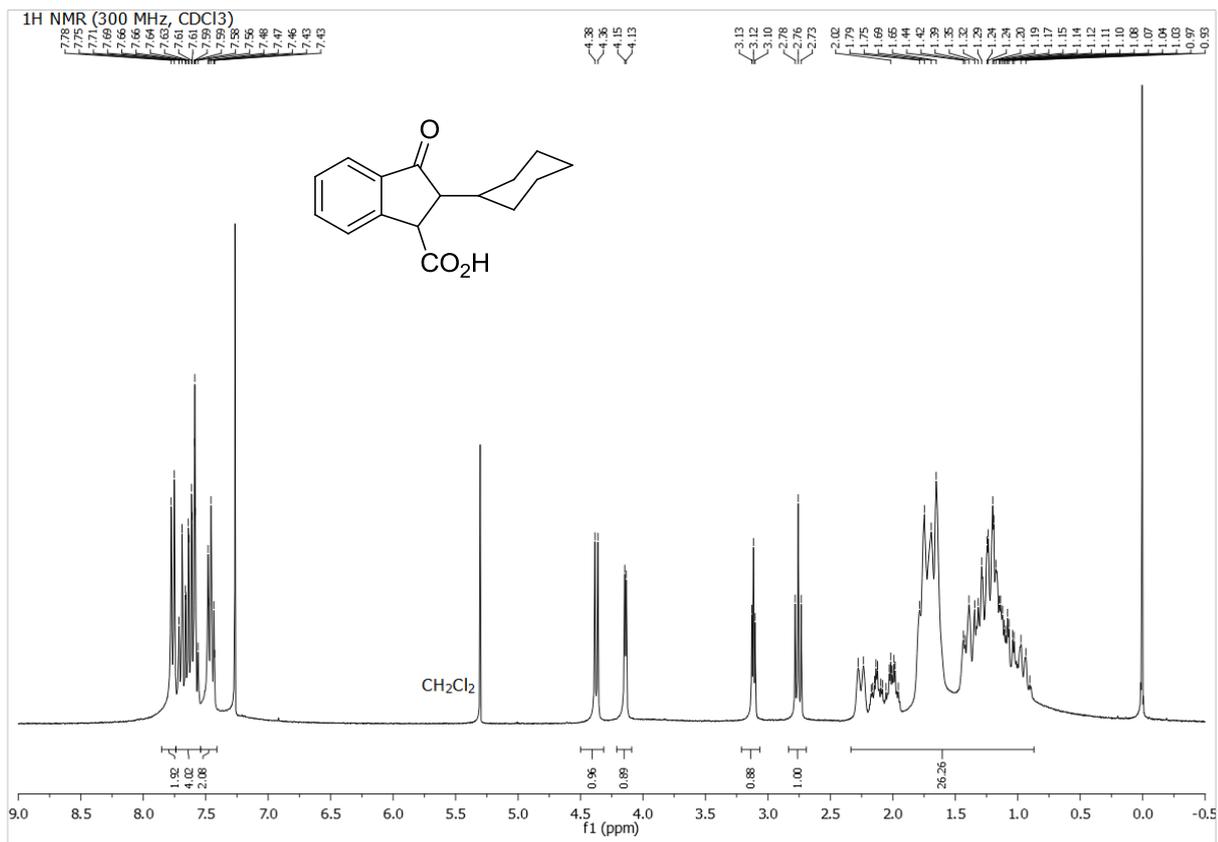
¹³C NMR (75 MHz, CDCl₃)

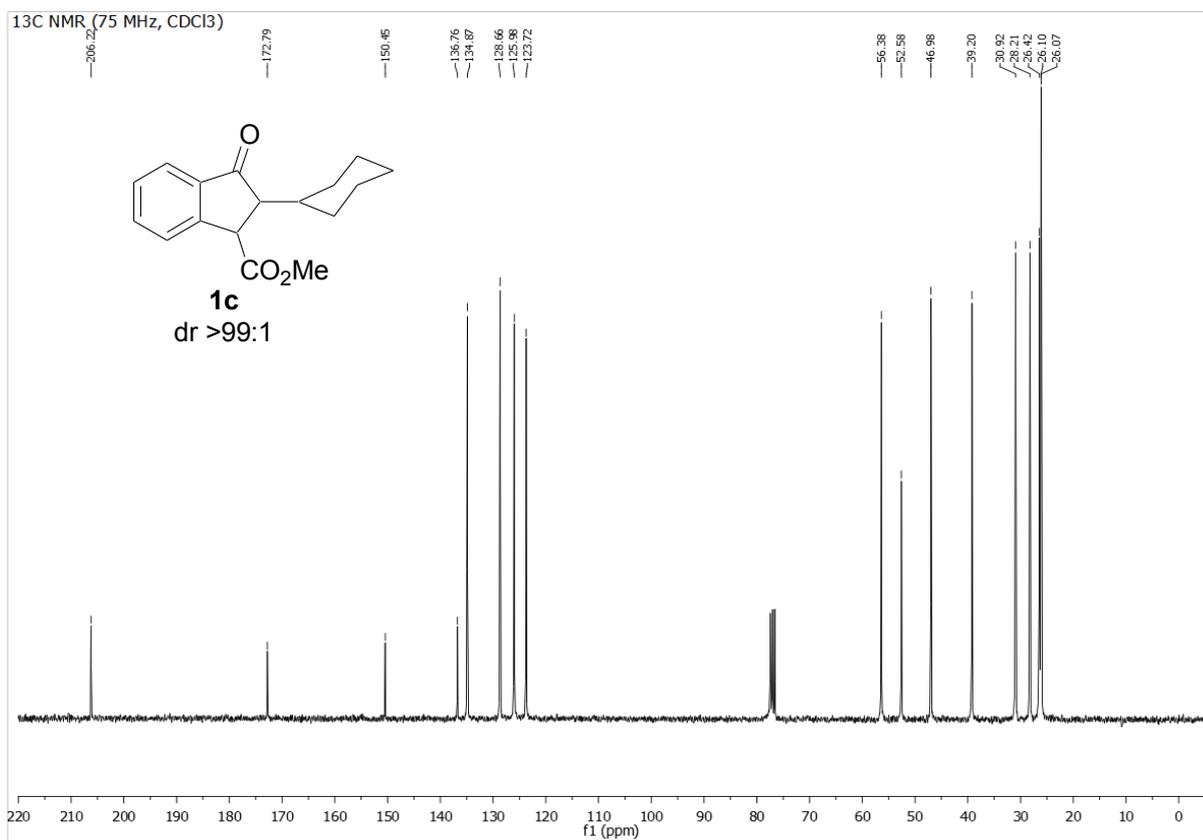
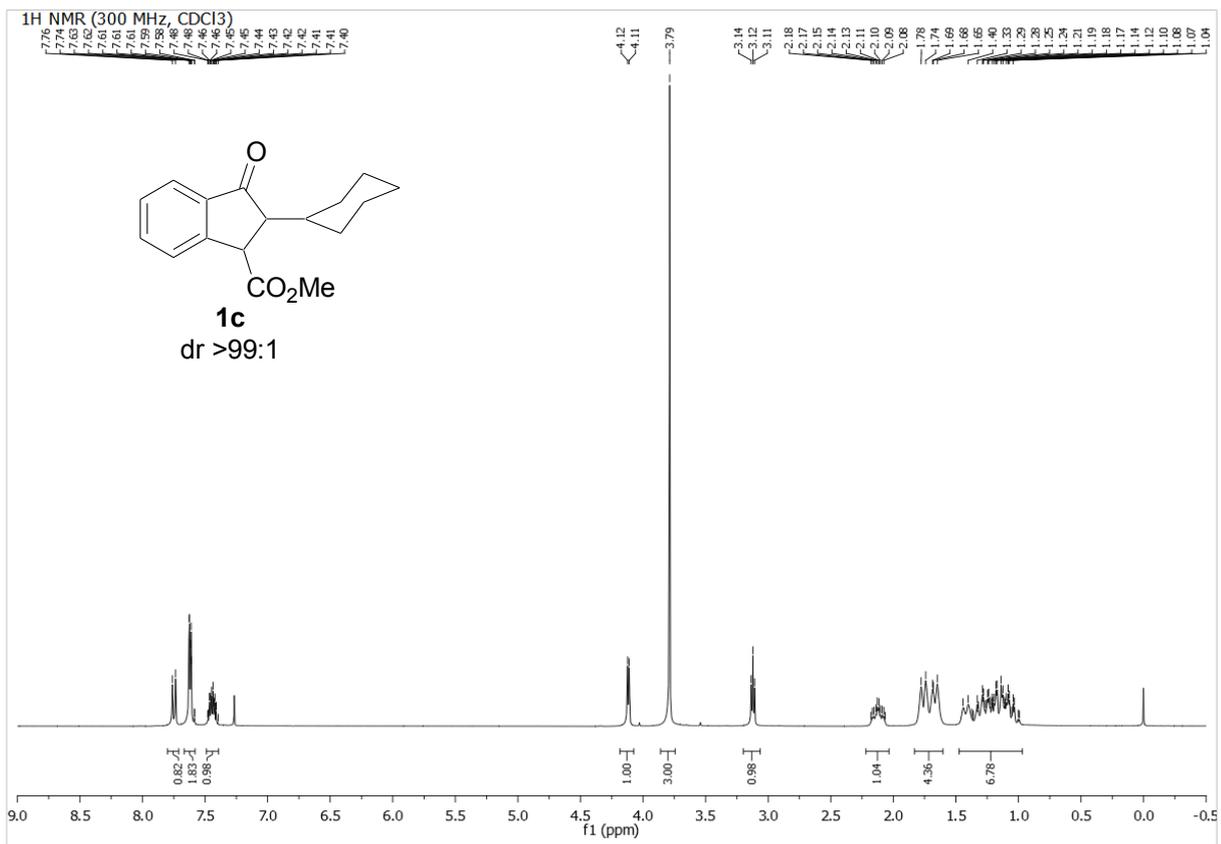


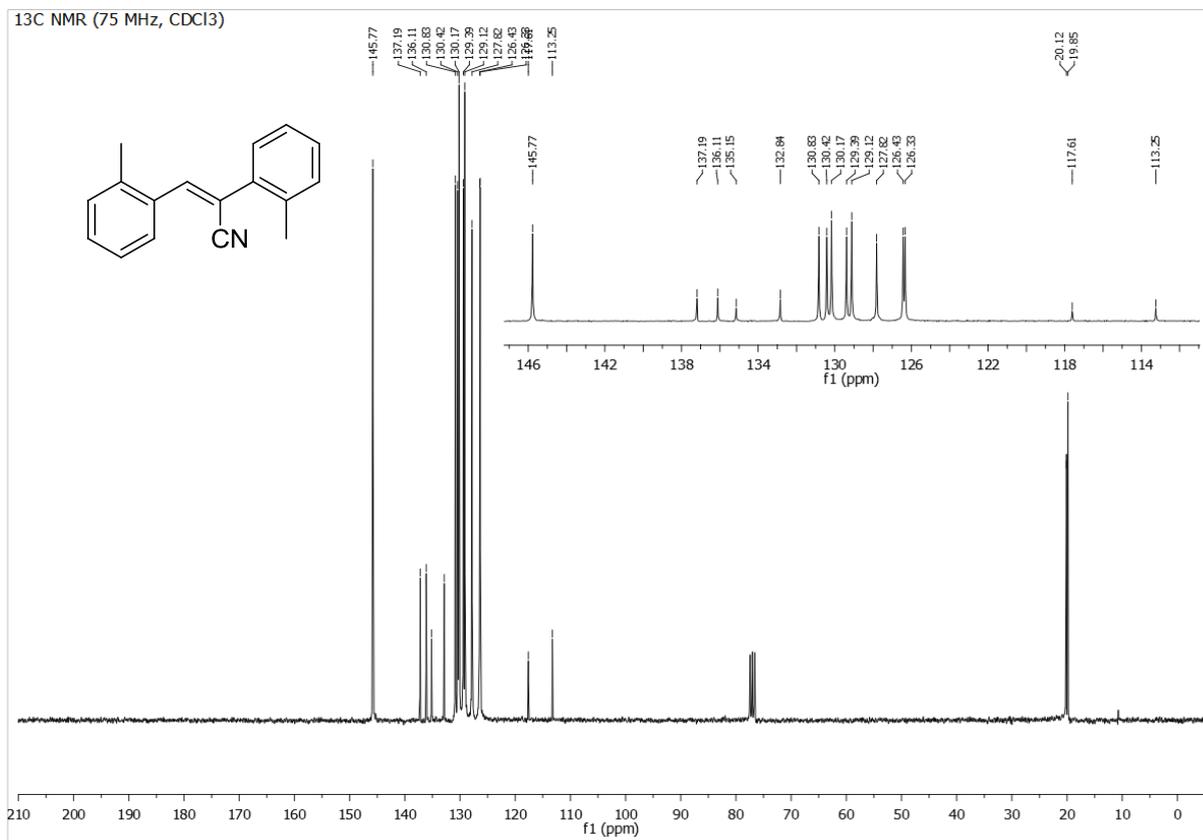
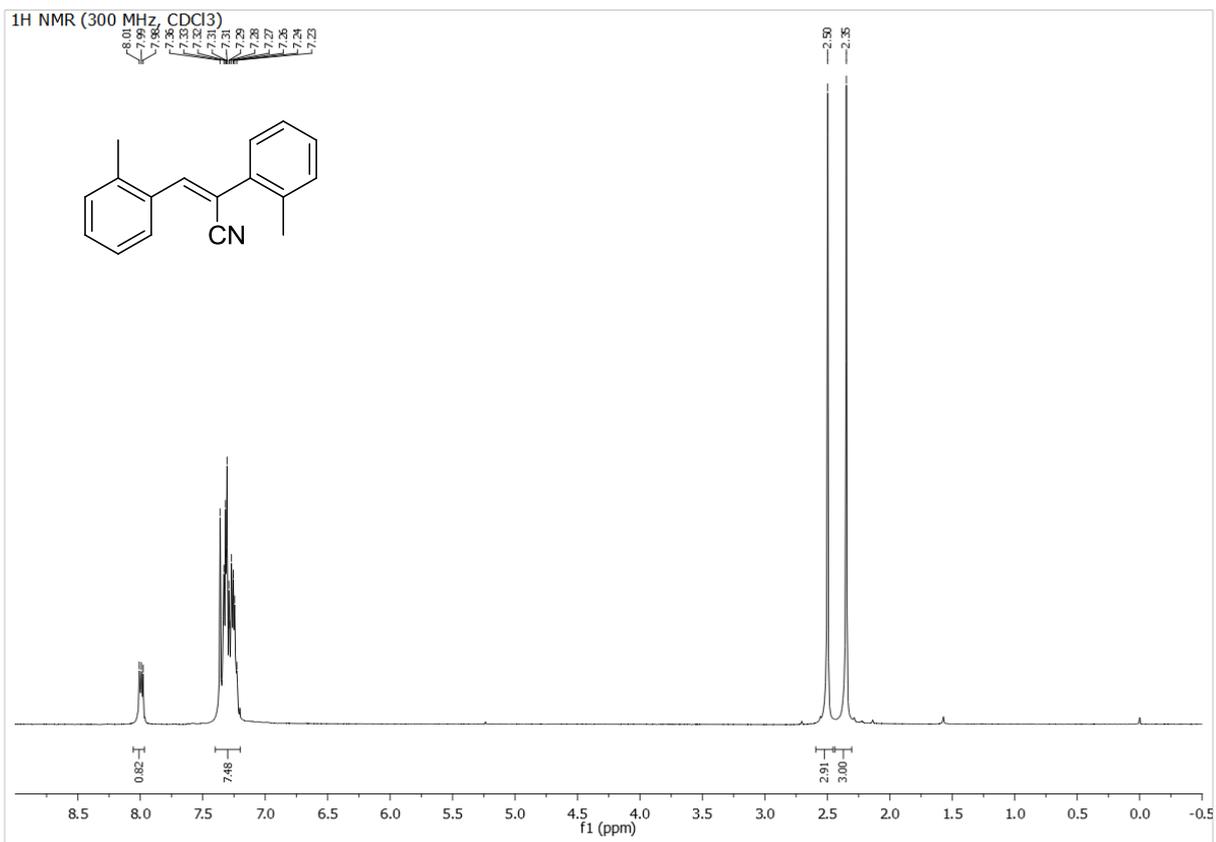


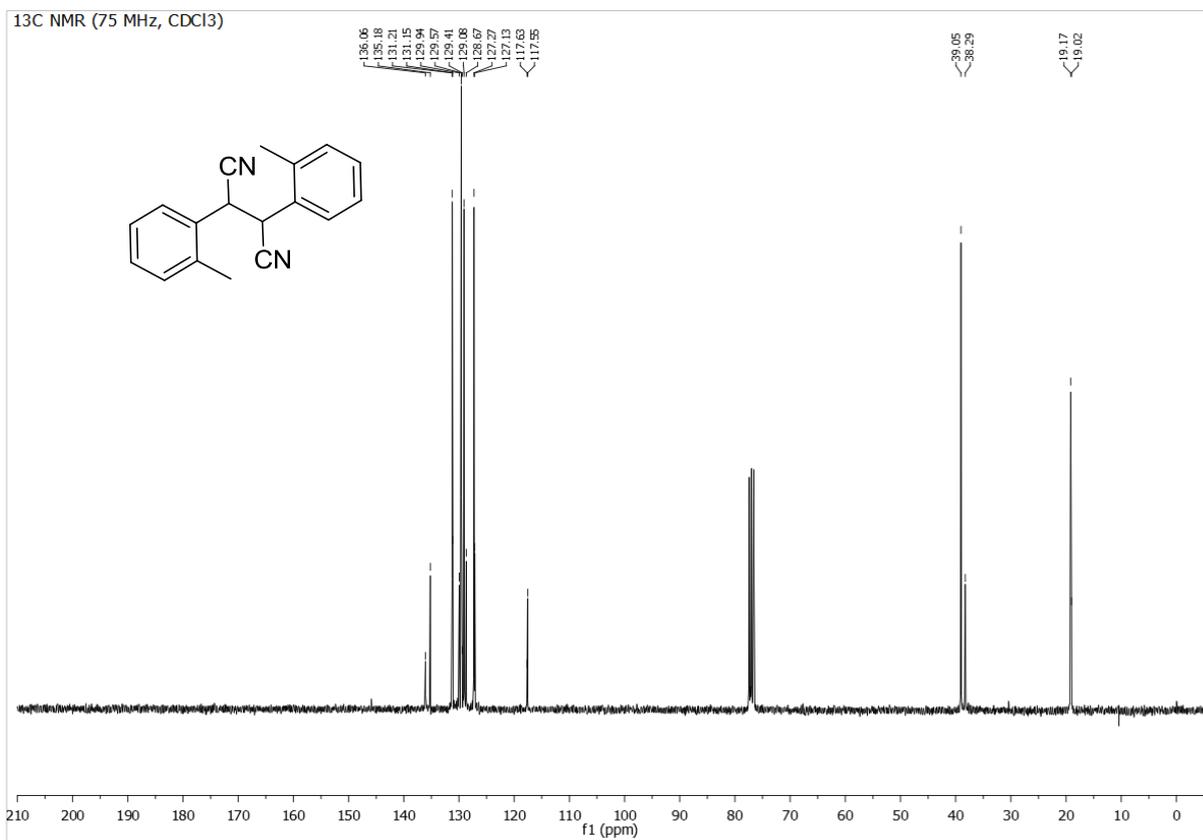
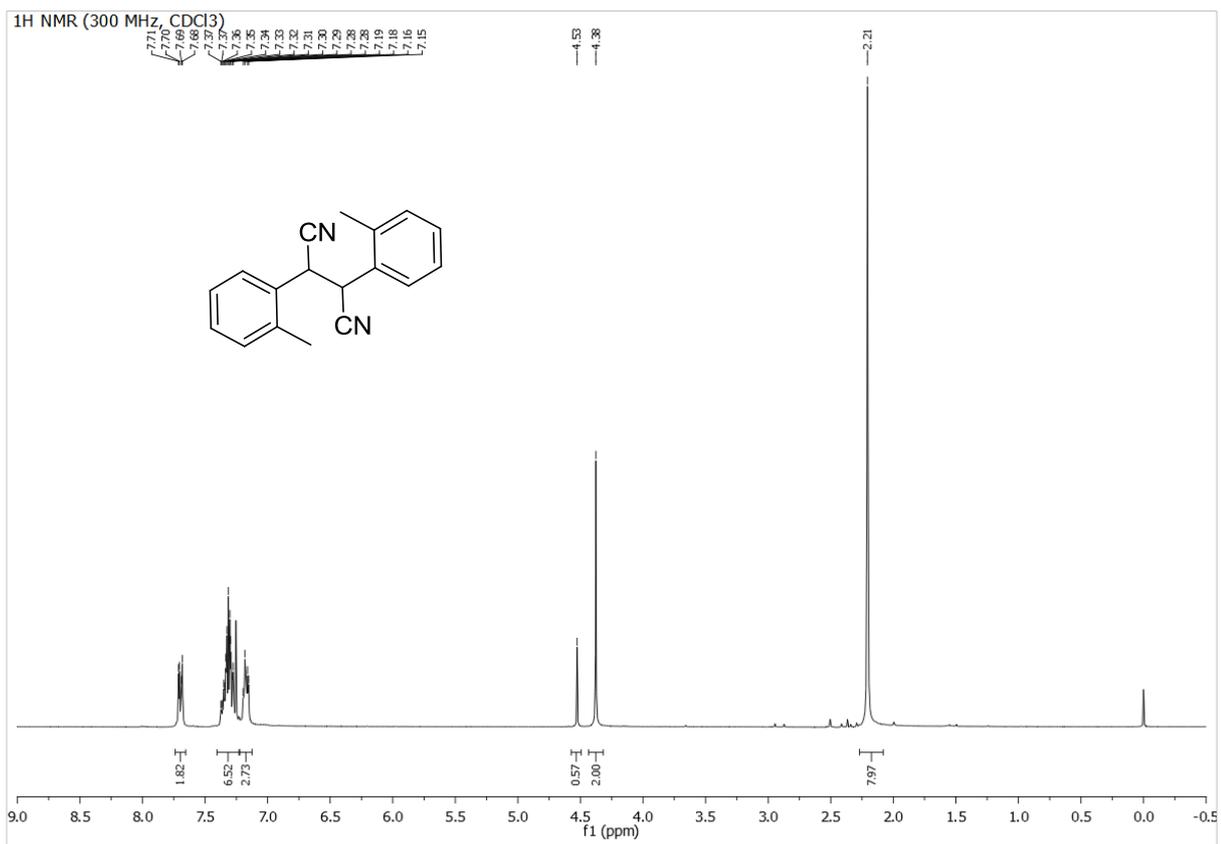


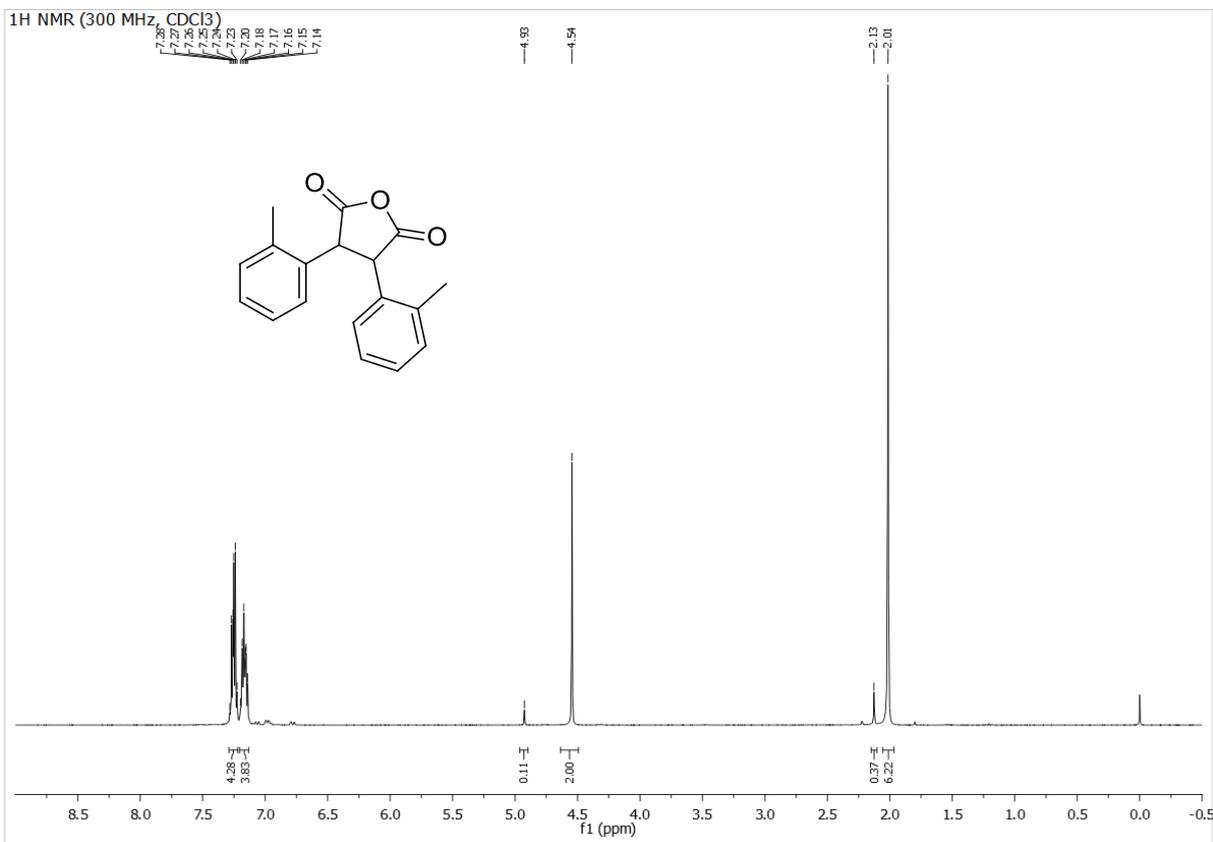
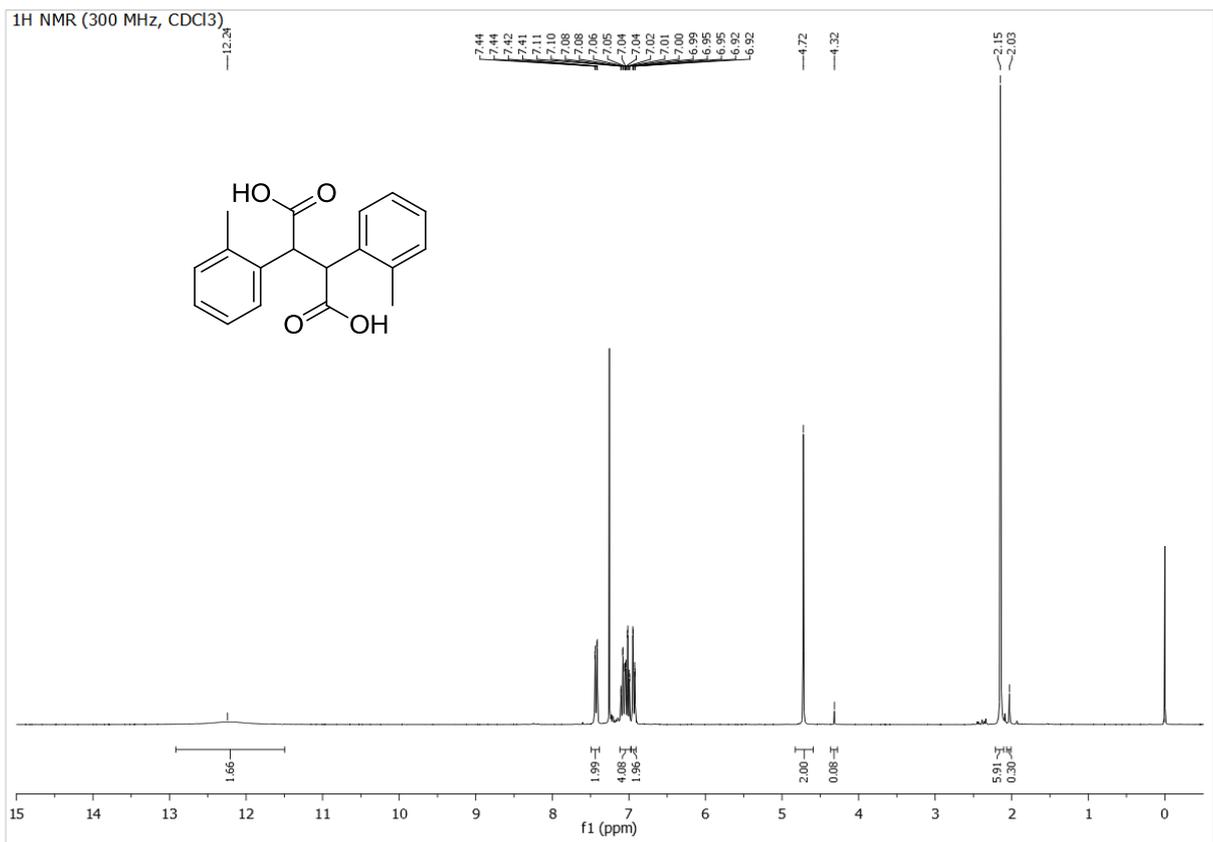


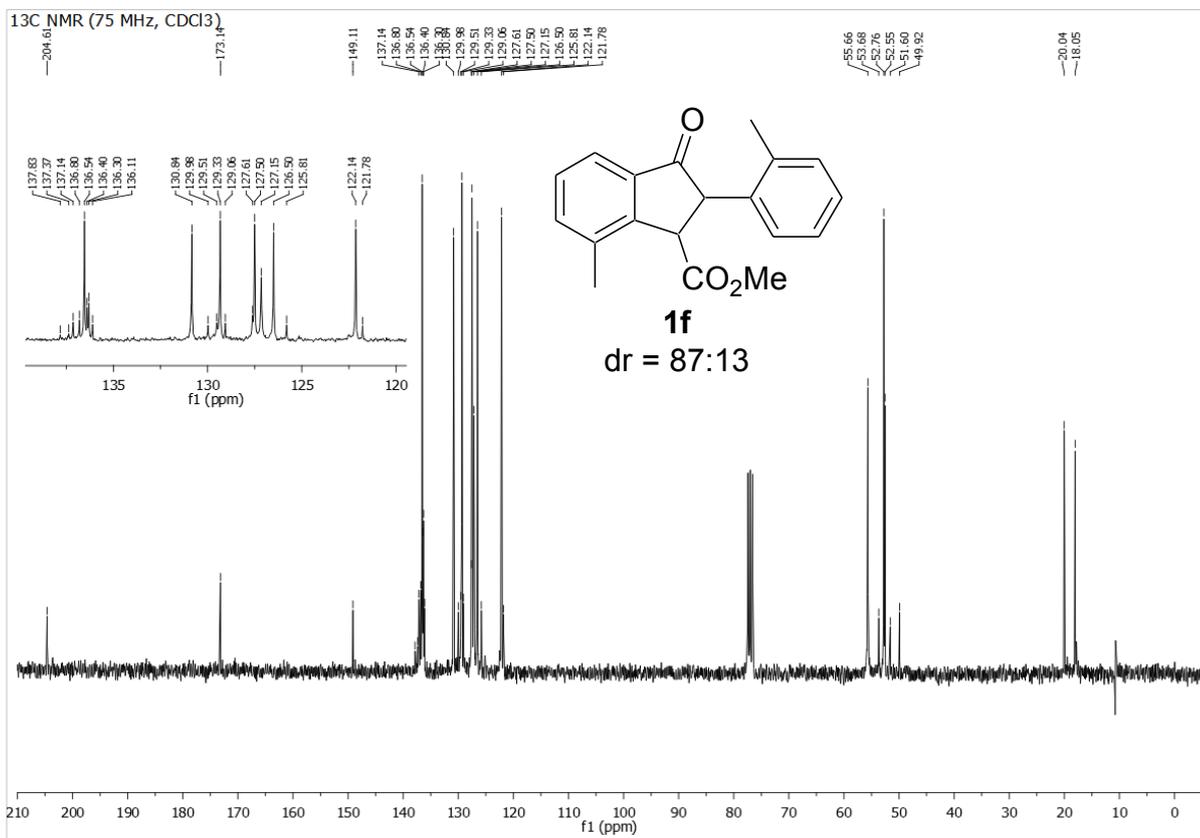
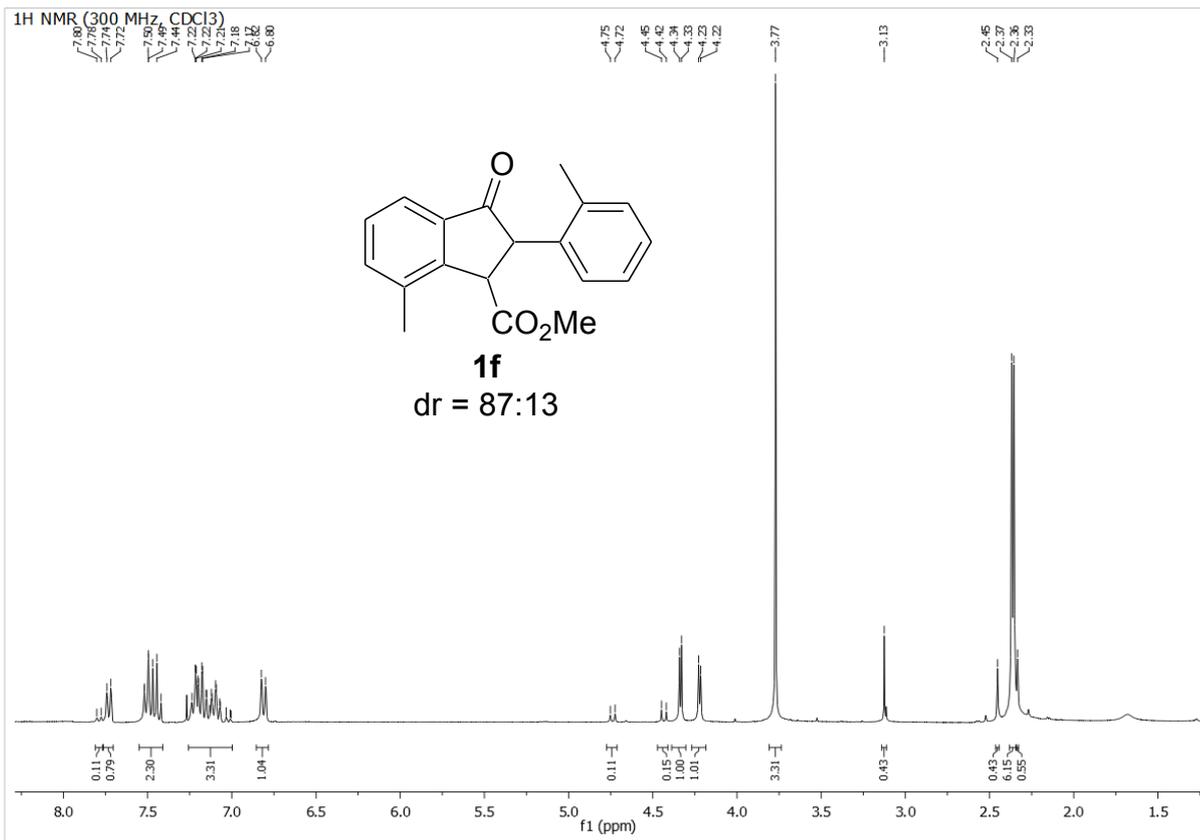


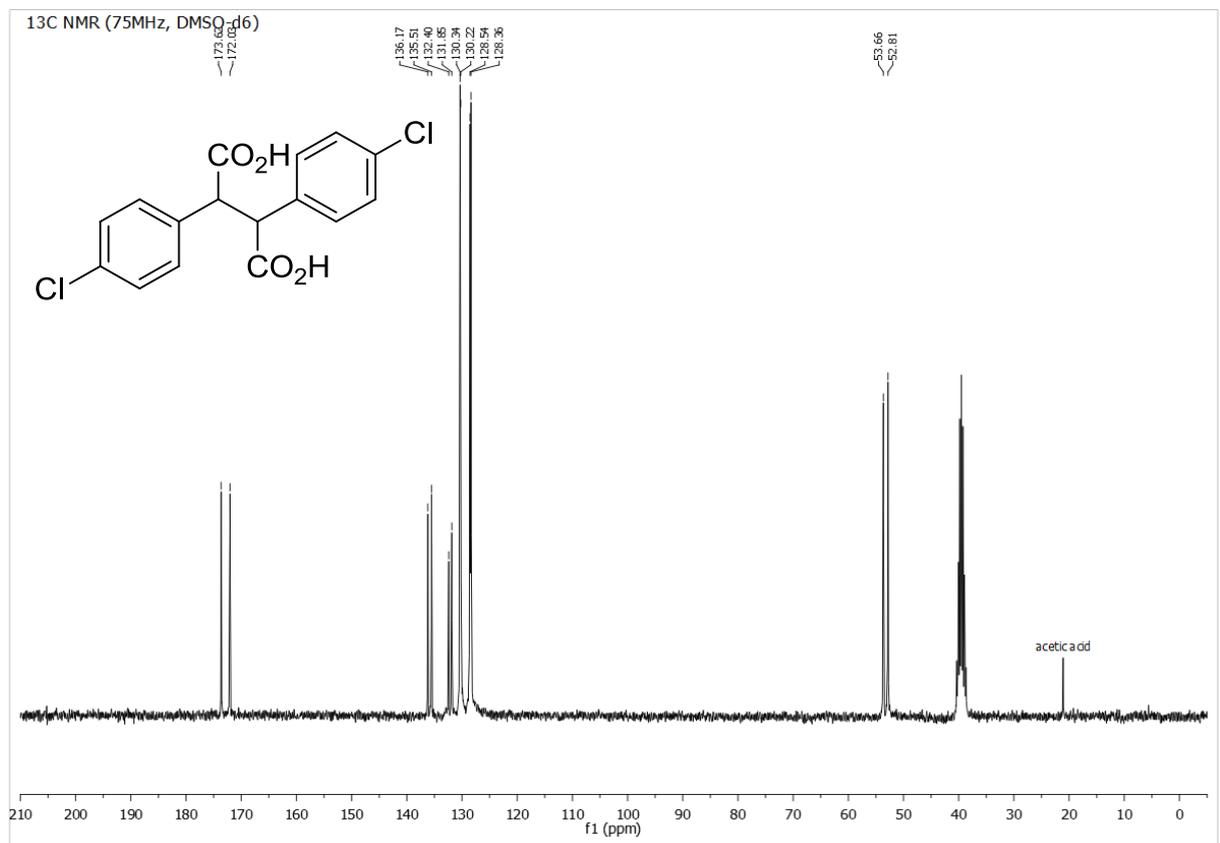
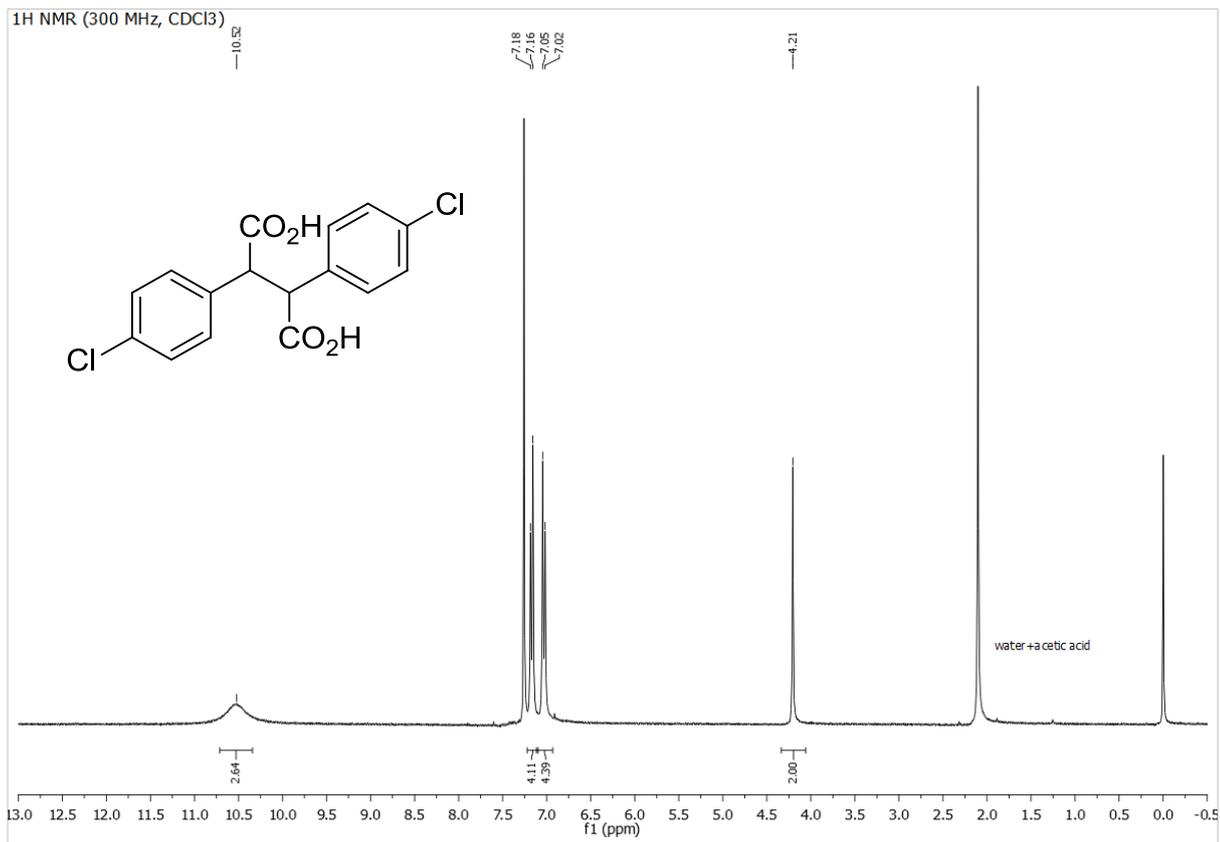


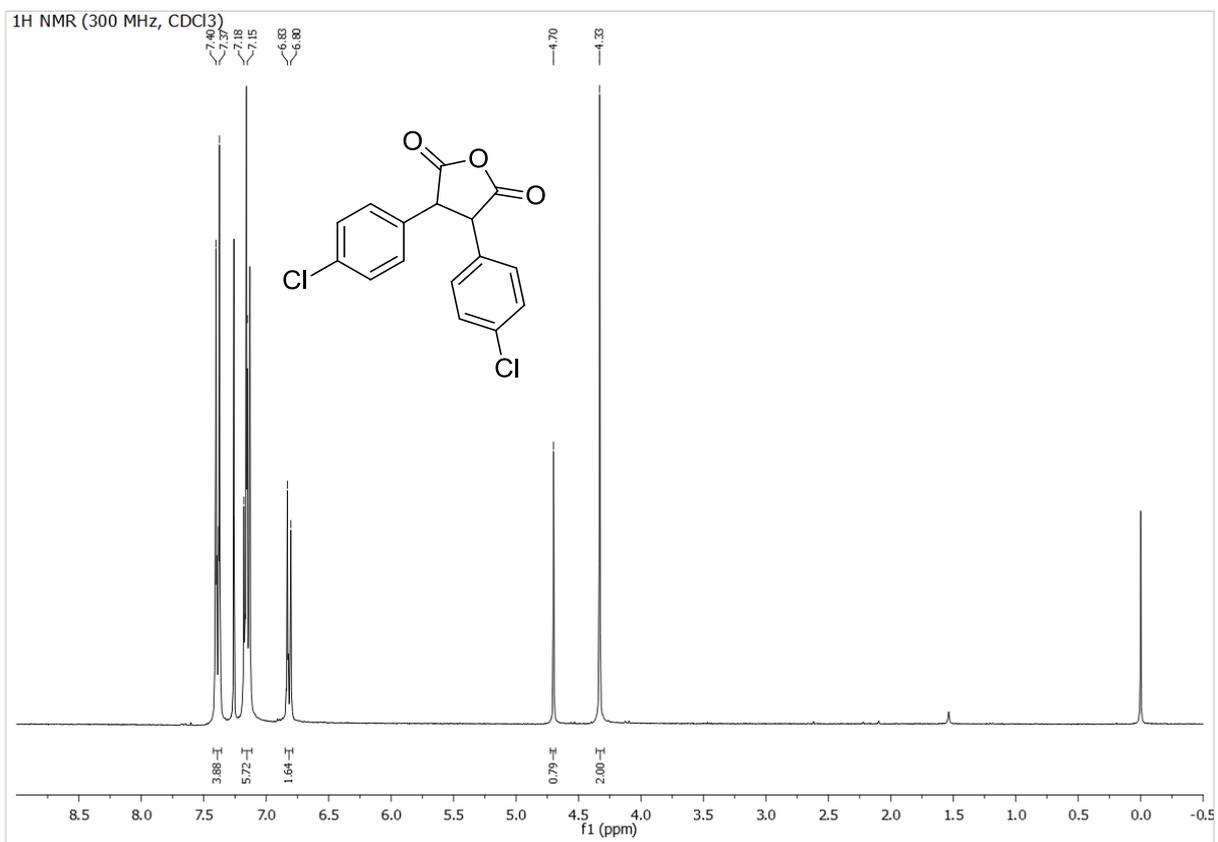


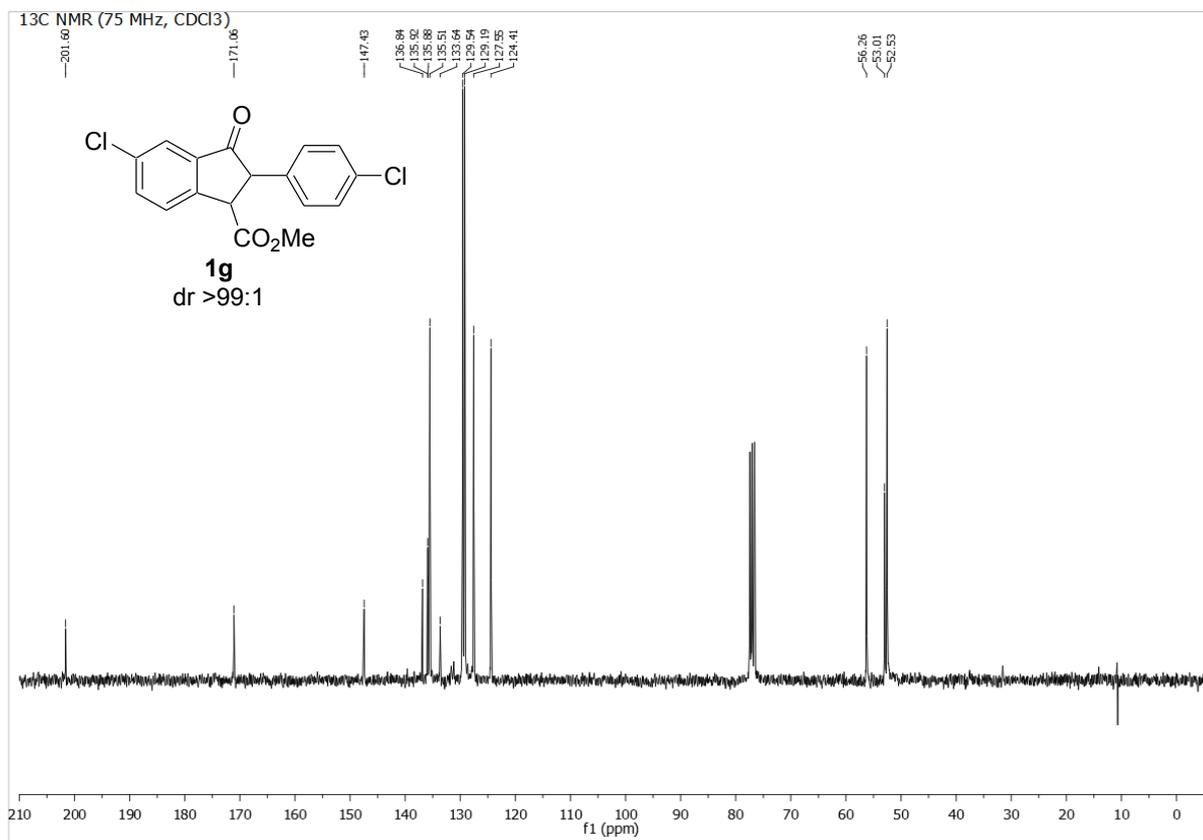
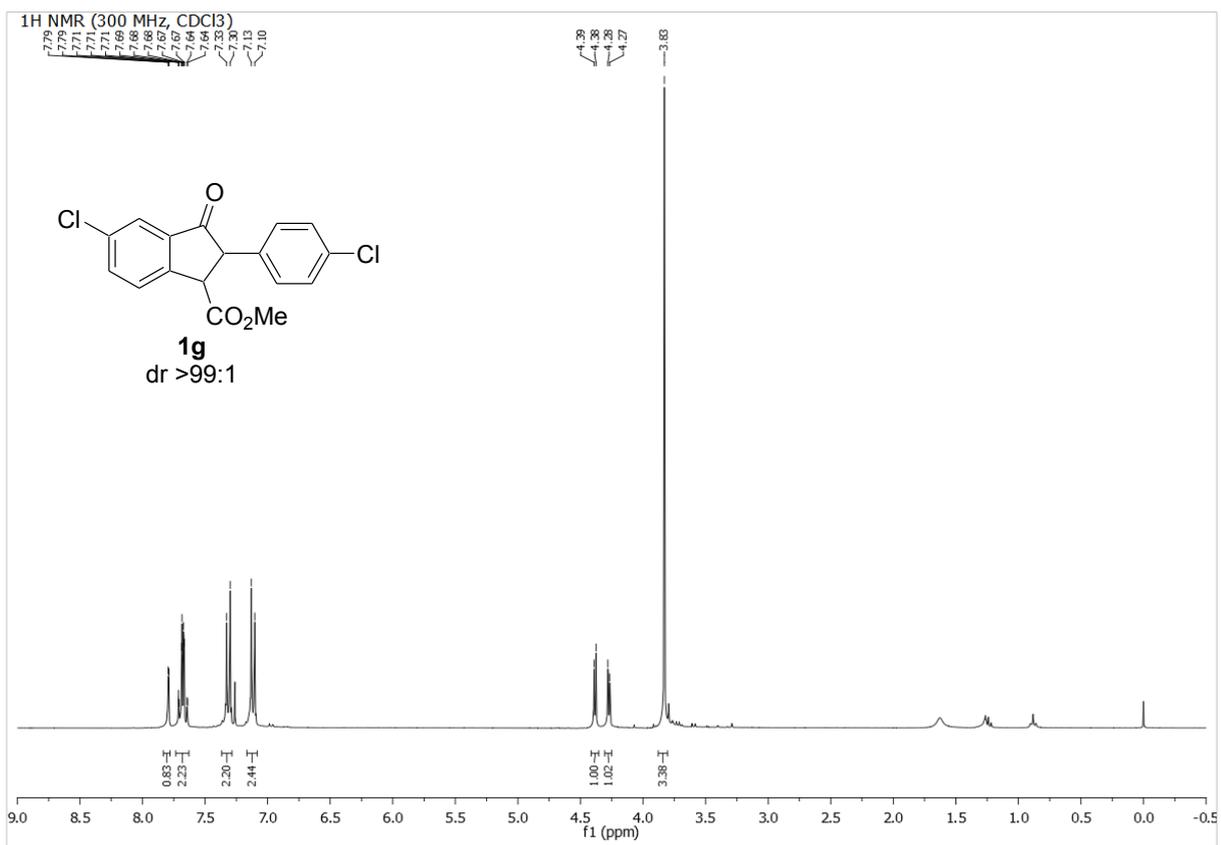


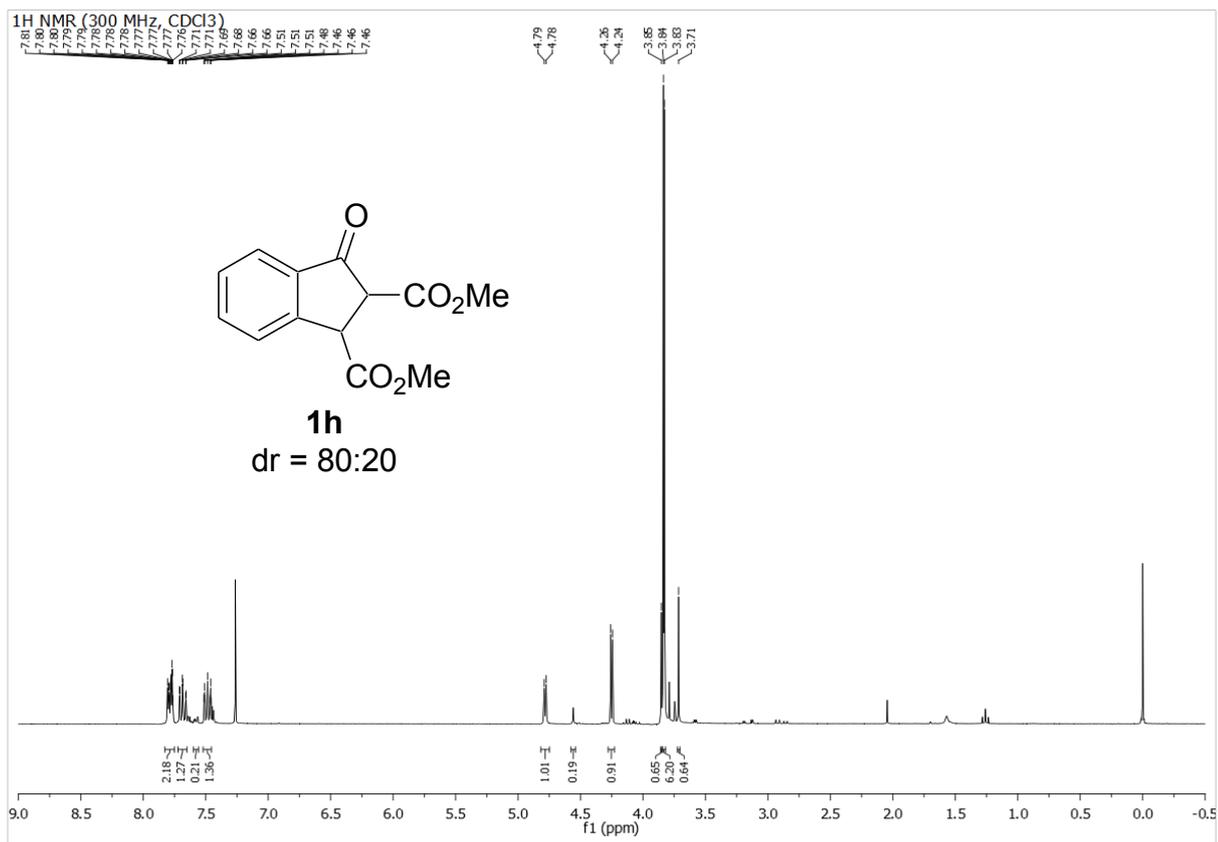


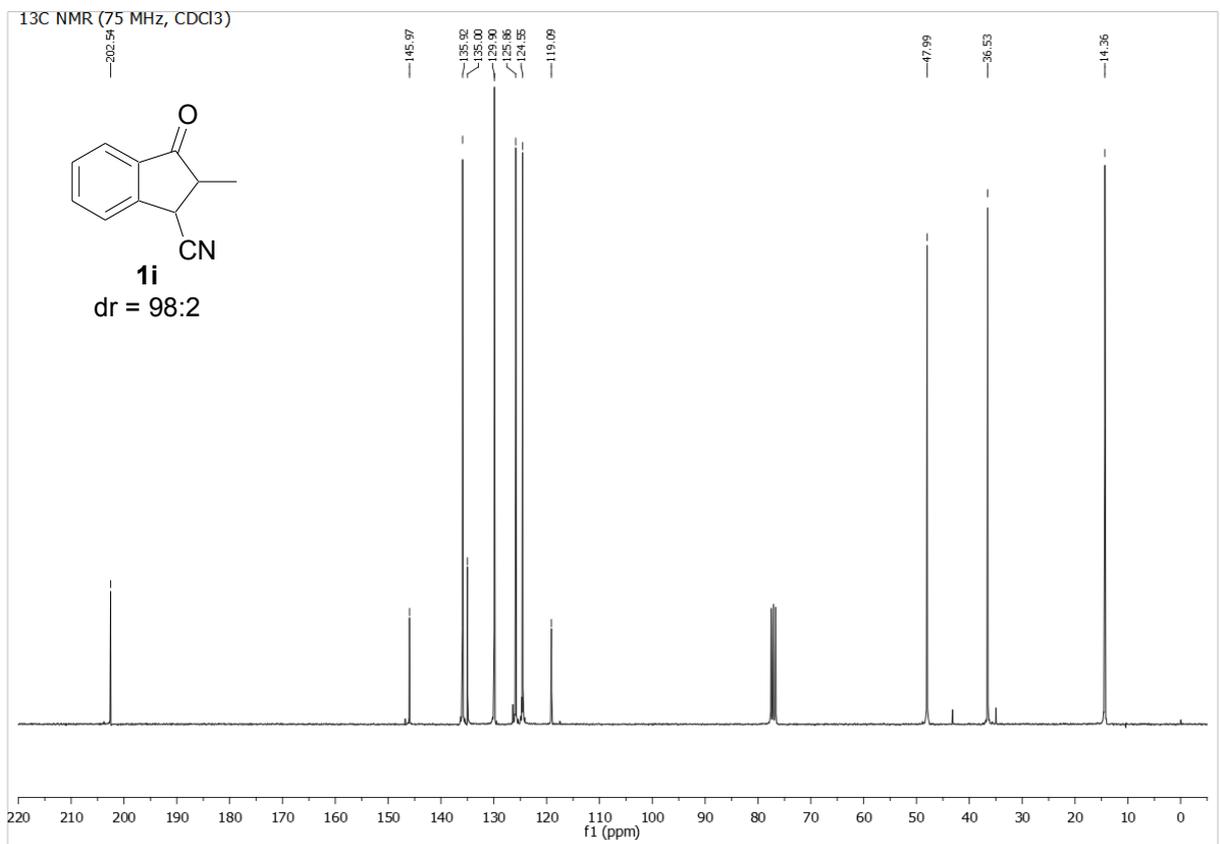
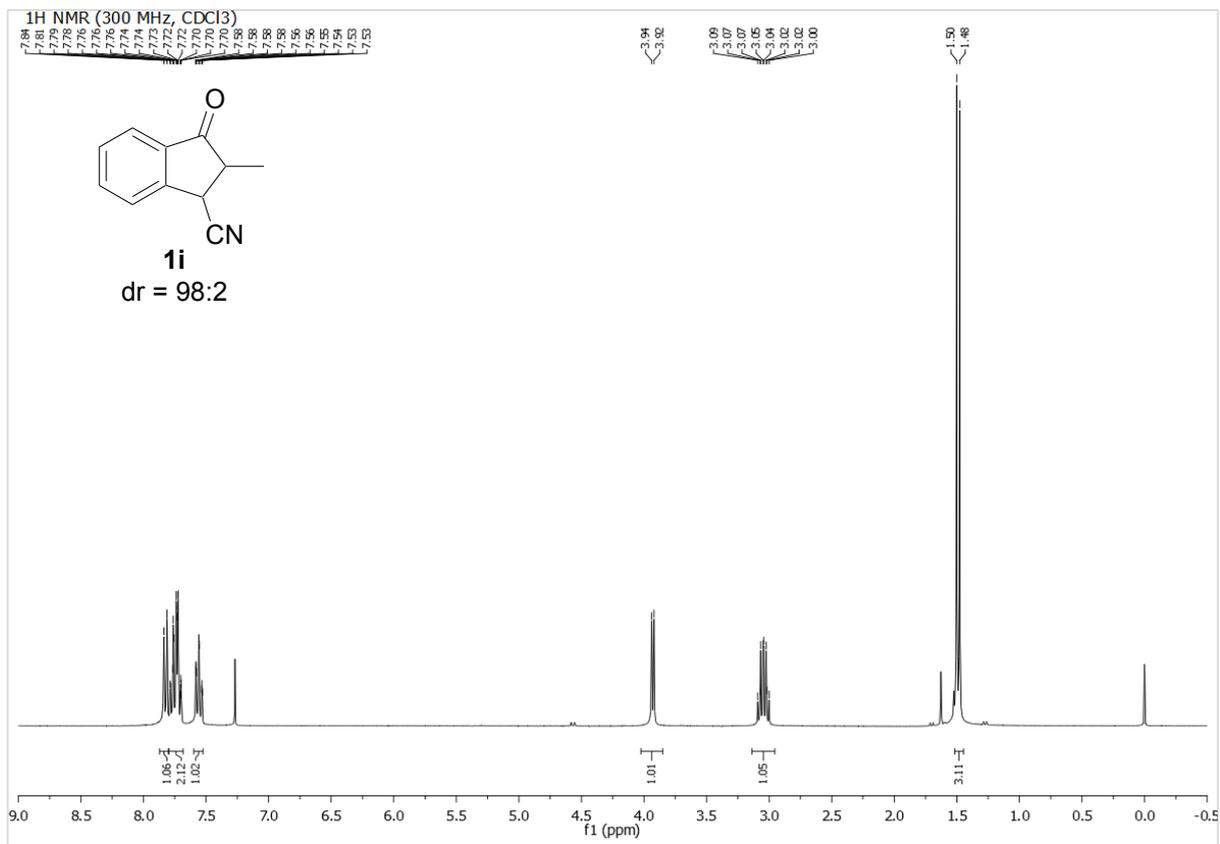


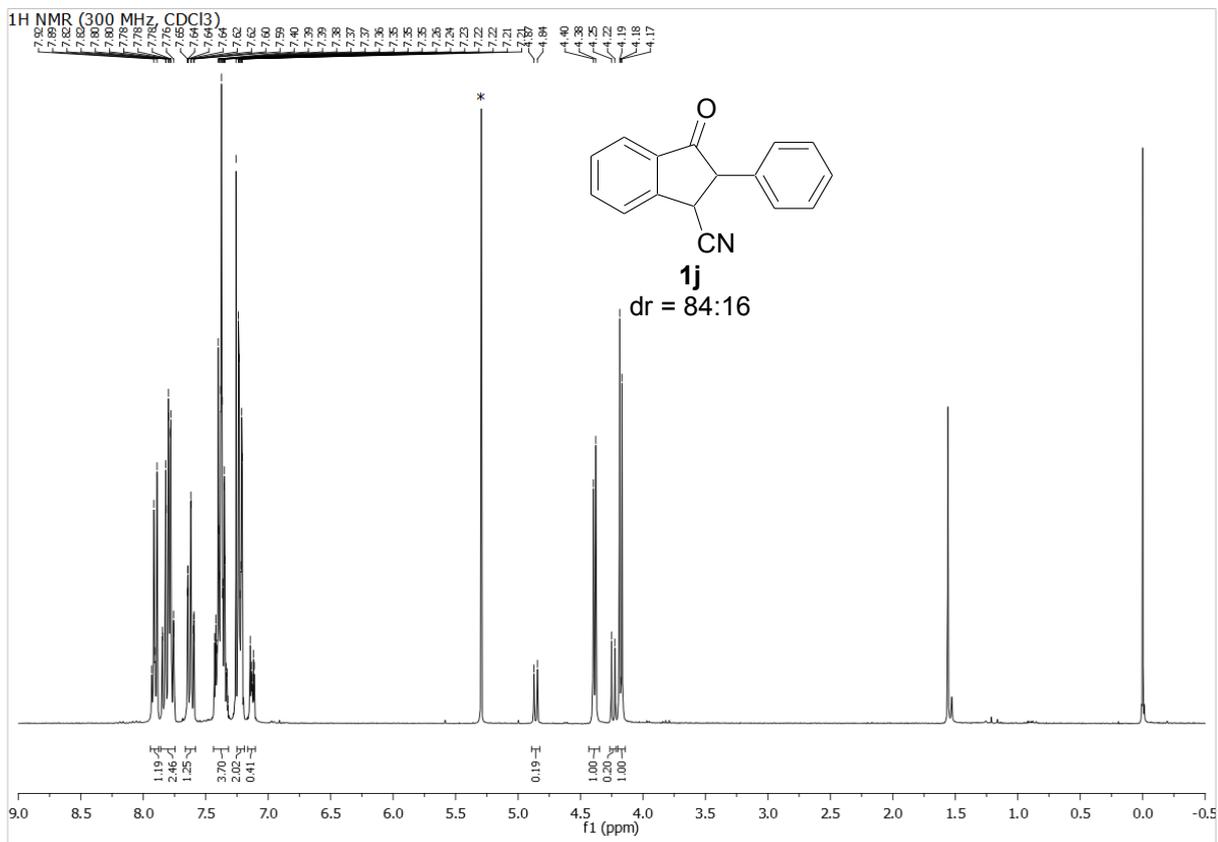
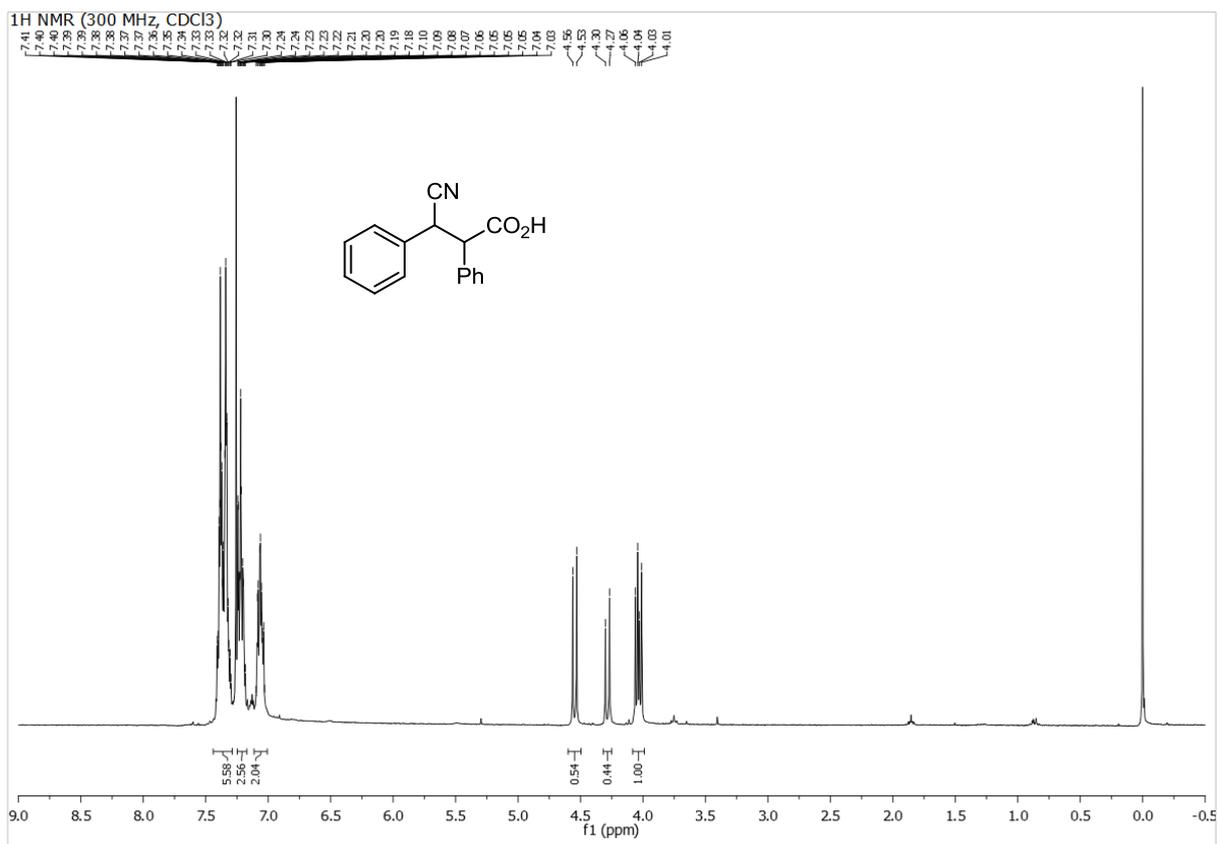




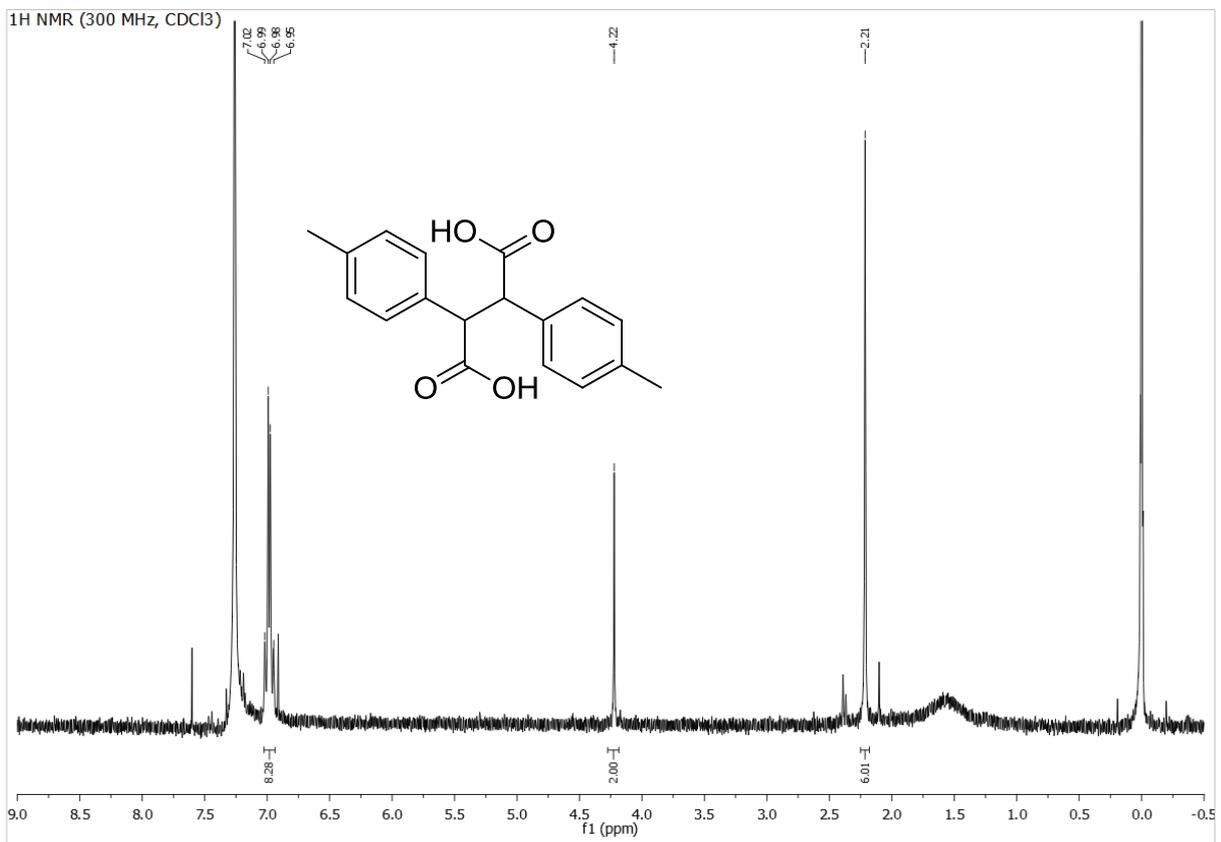
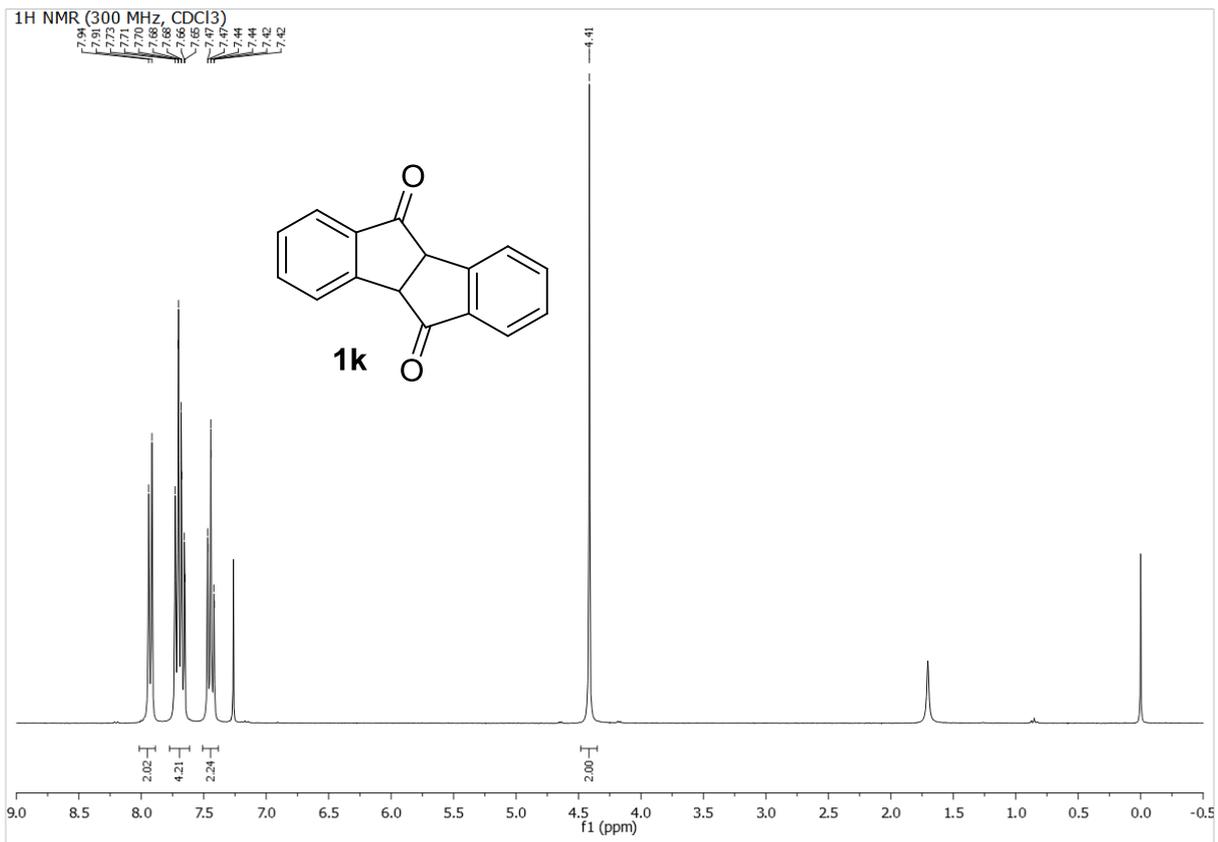








*CH₂Cl₂

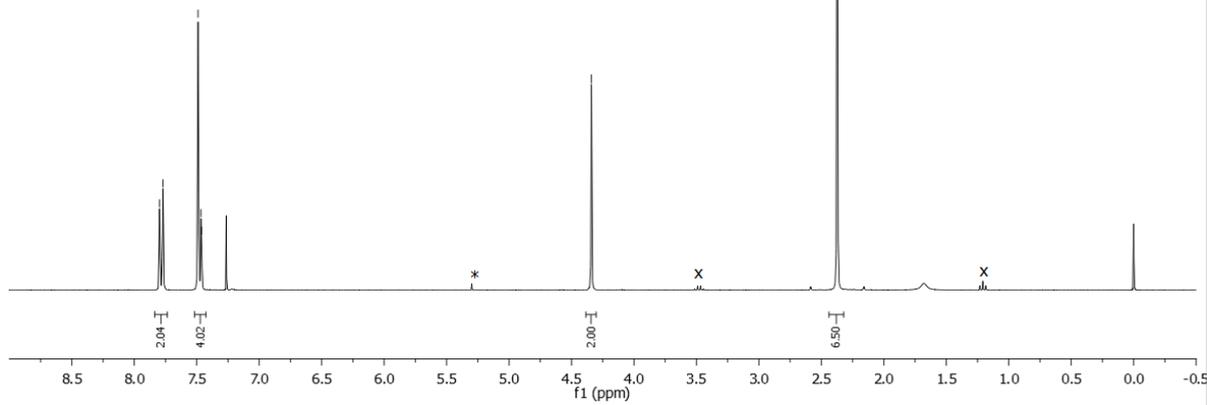
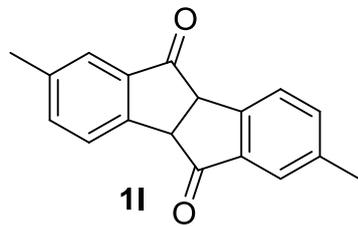


¹H NMR (300 MHz, CDCl₃)

7.80
7.77
7.49
7.47
7.46

4.34

2.37



* CH₂Cl₂, x diethylether

¹³C NMR (75 MHz, CDCl₃)

201.82

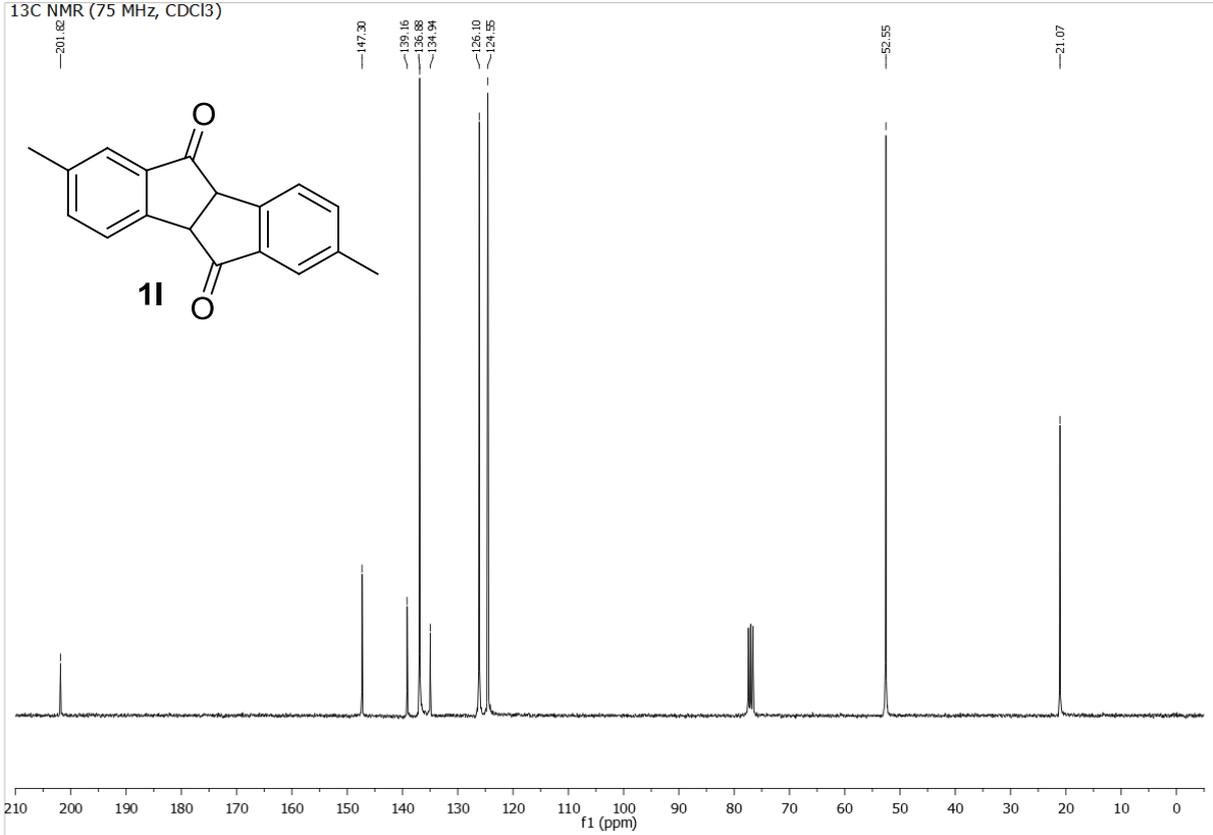
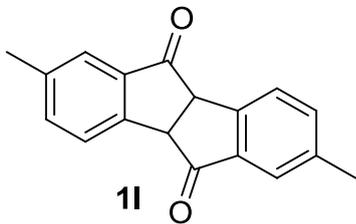
147.30

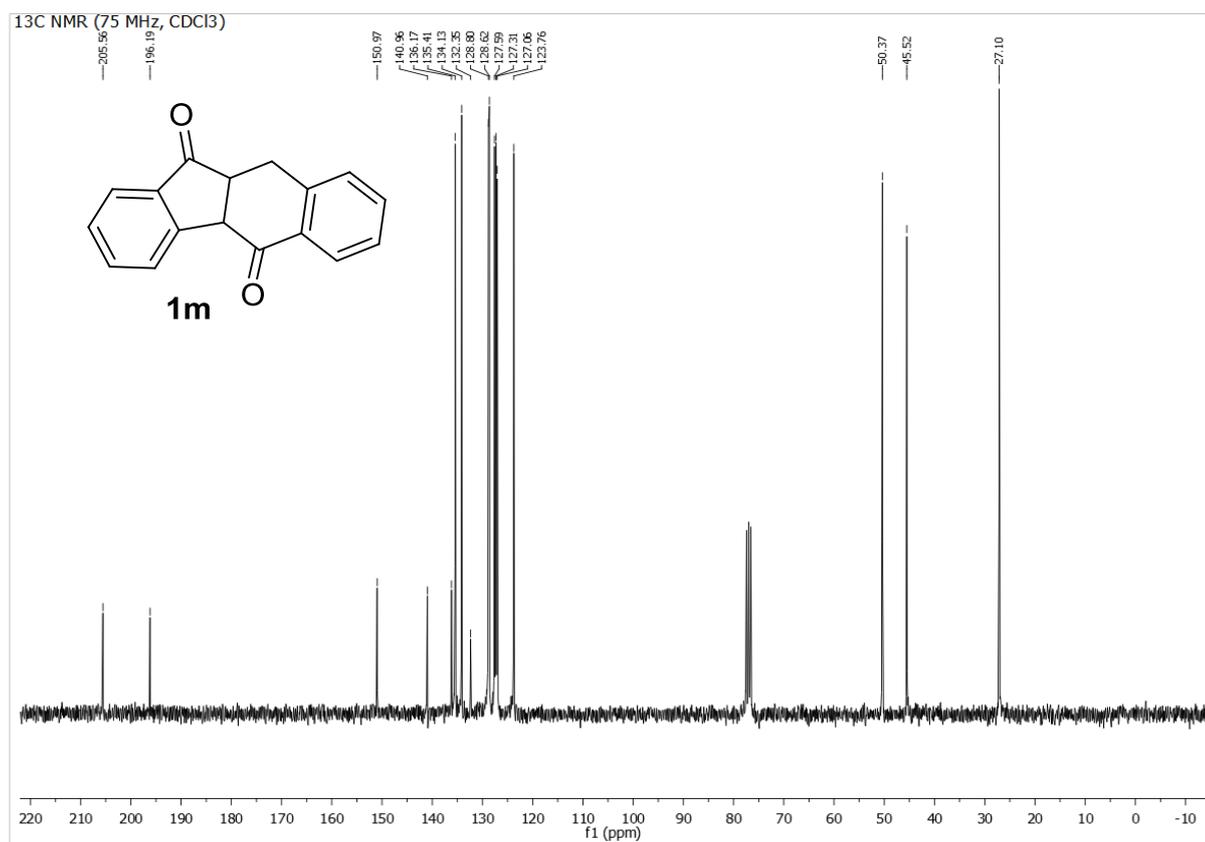
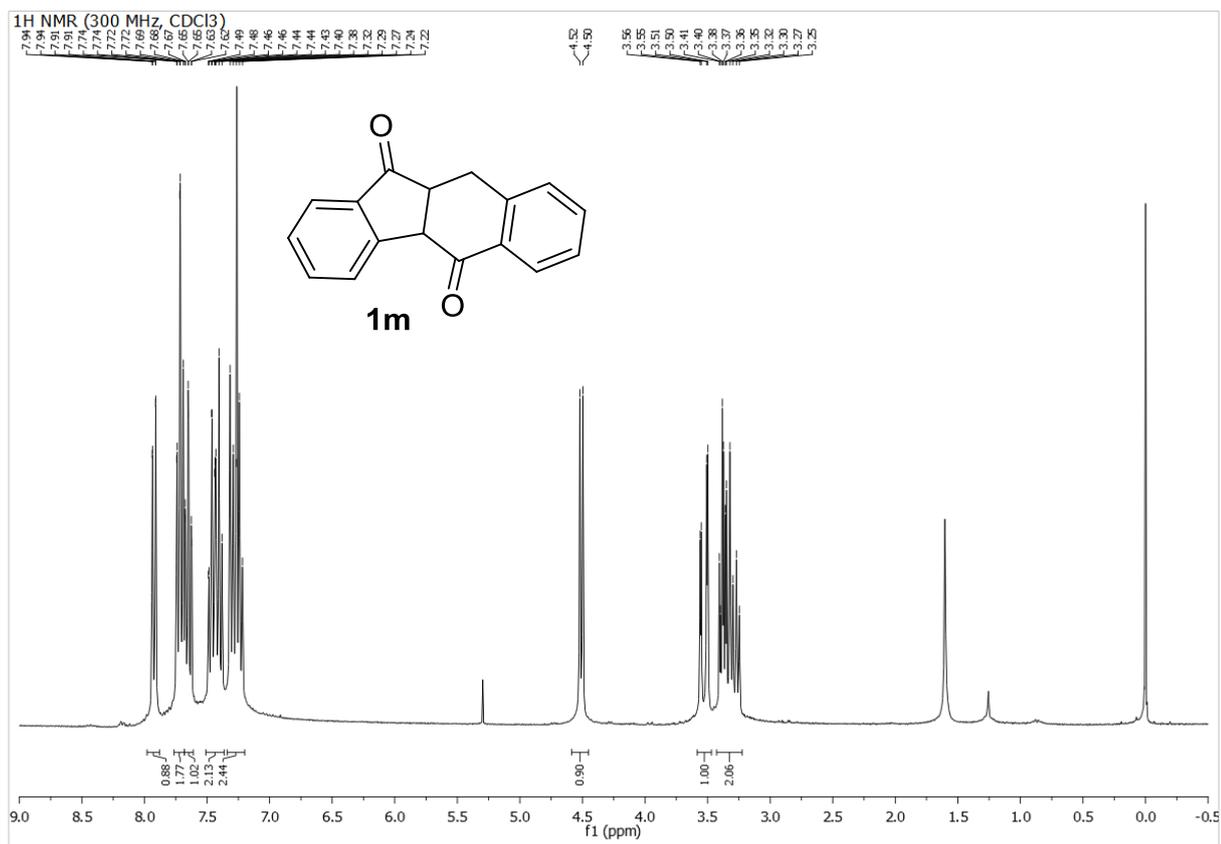
139.16
138.98
138.94

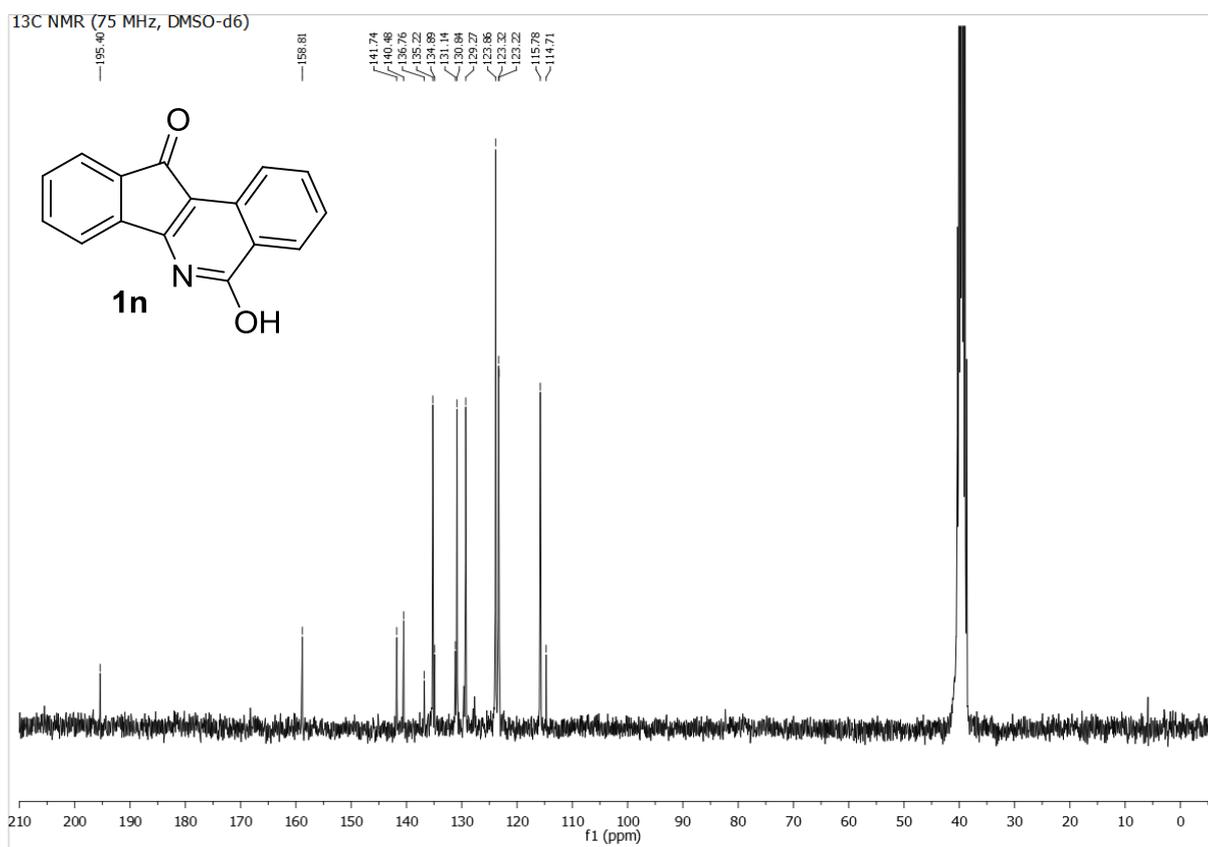
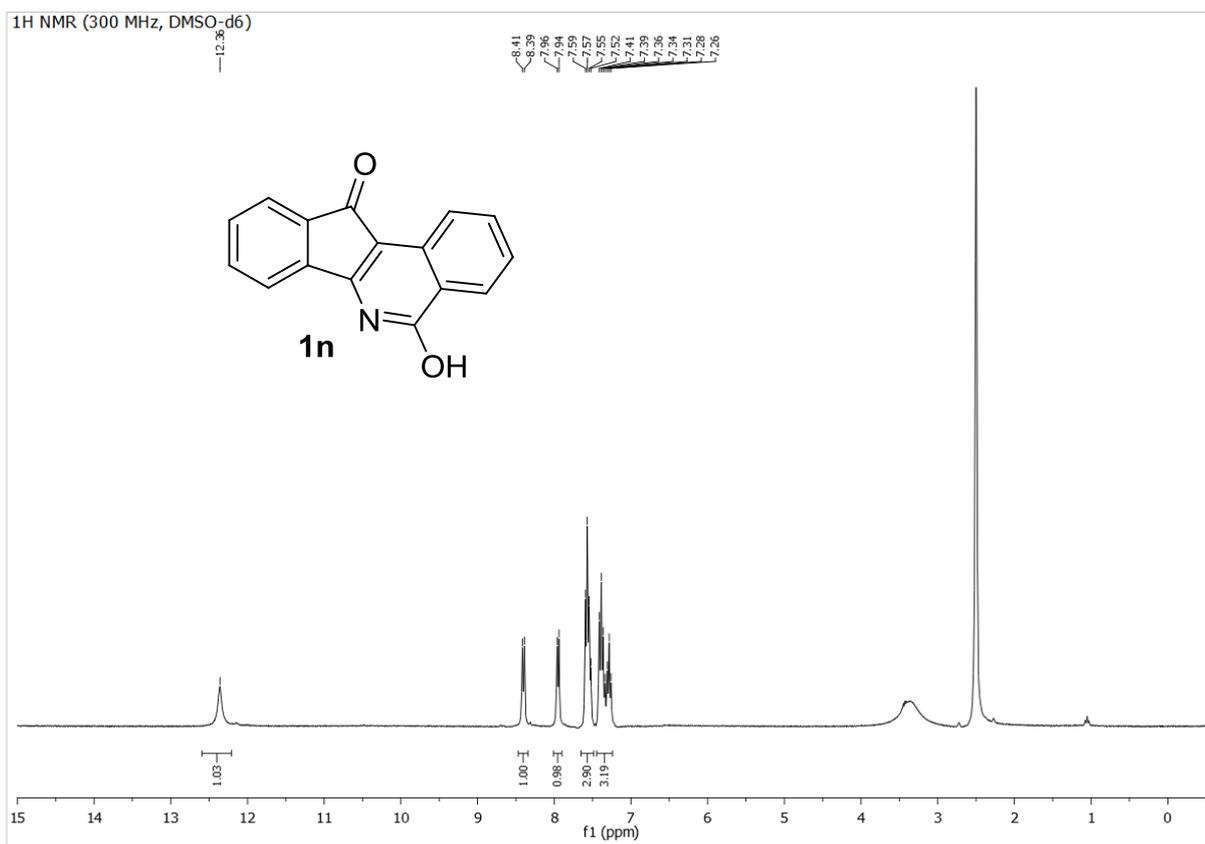
126.10
124.55

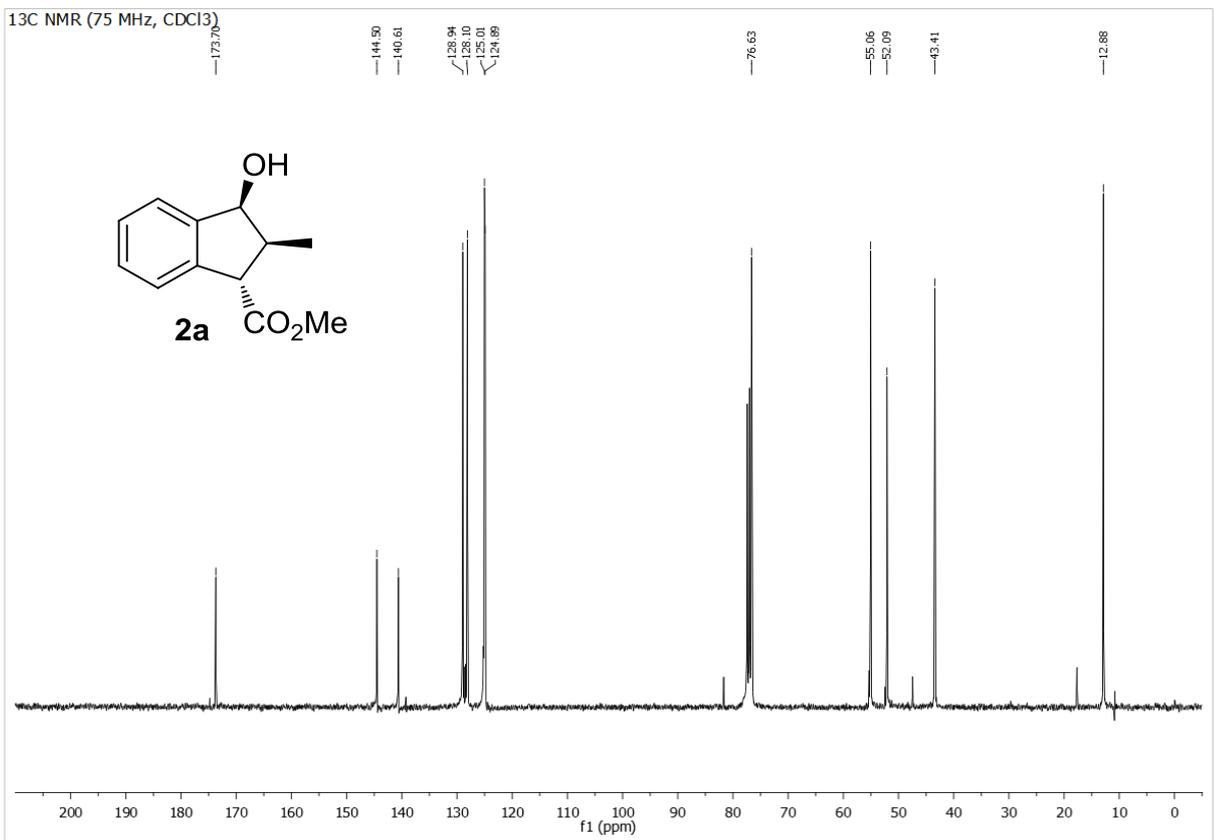
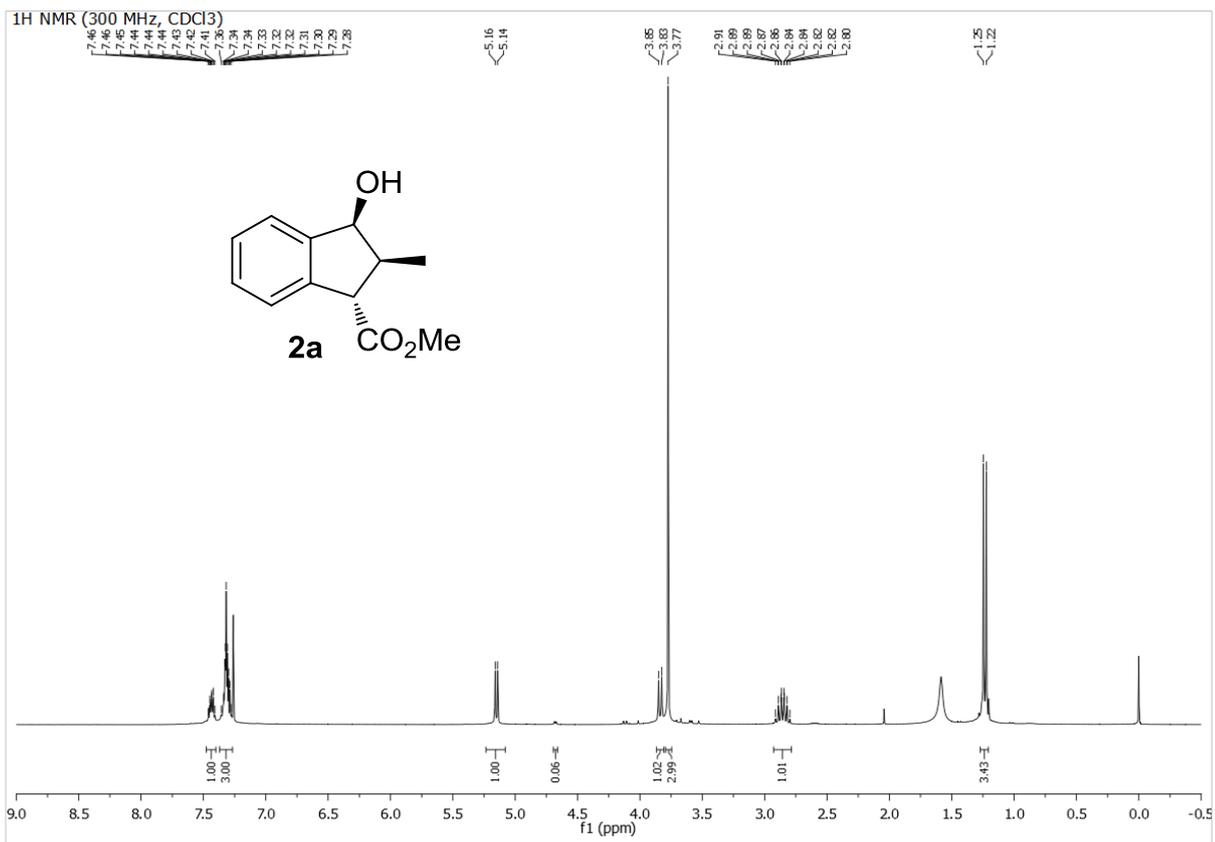
52.95

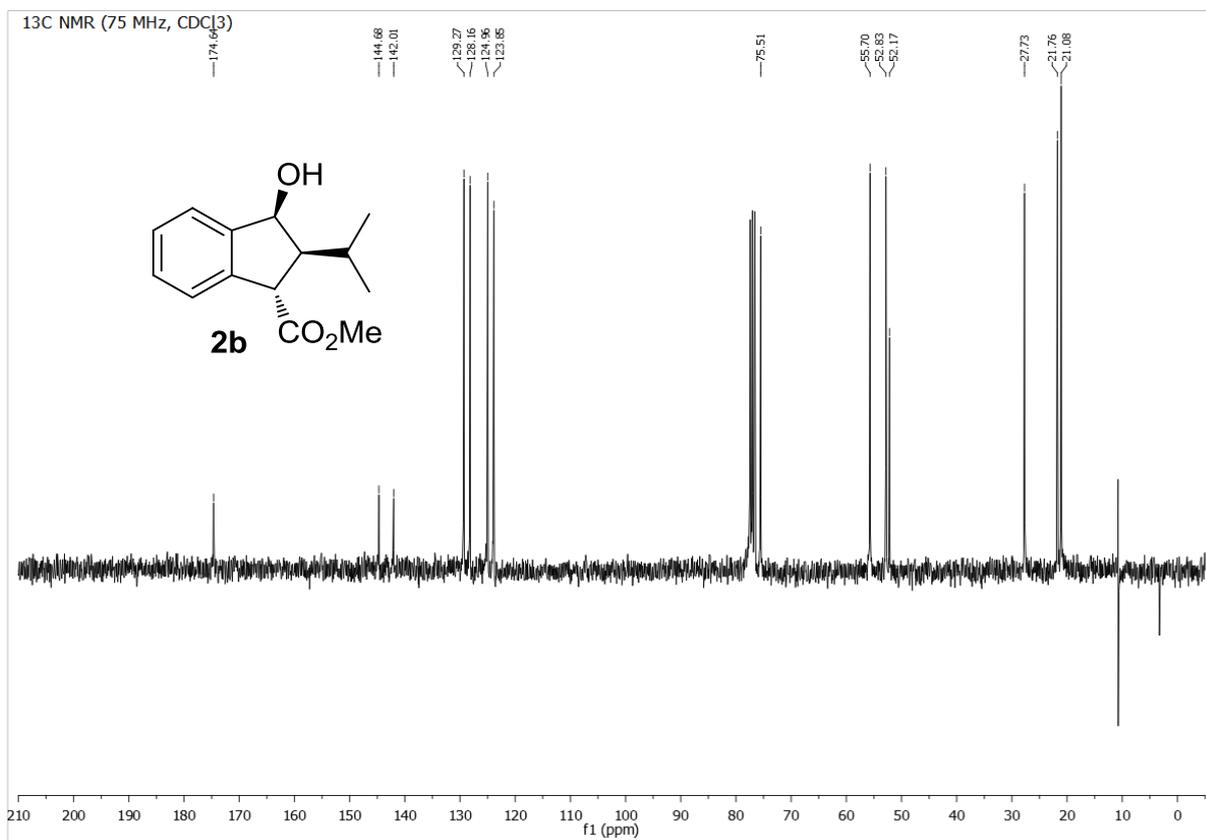
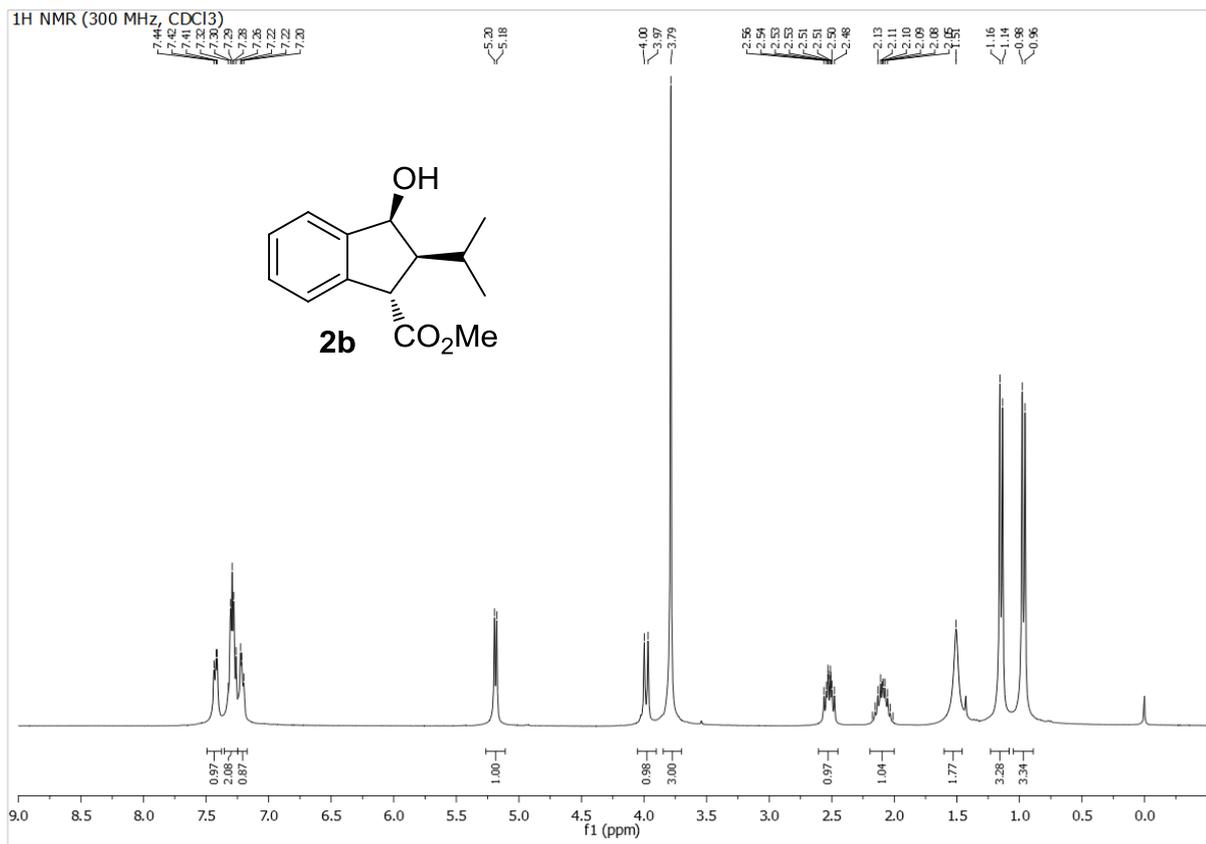
21.07

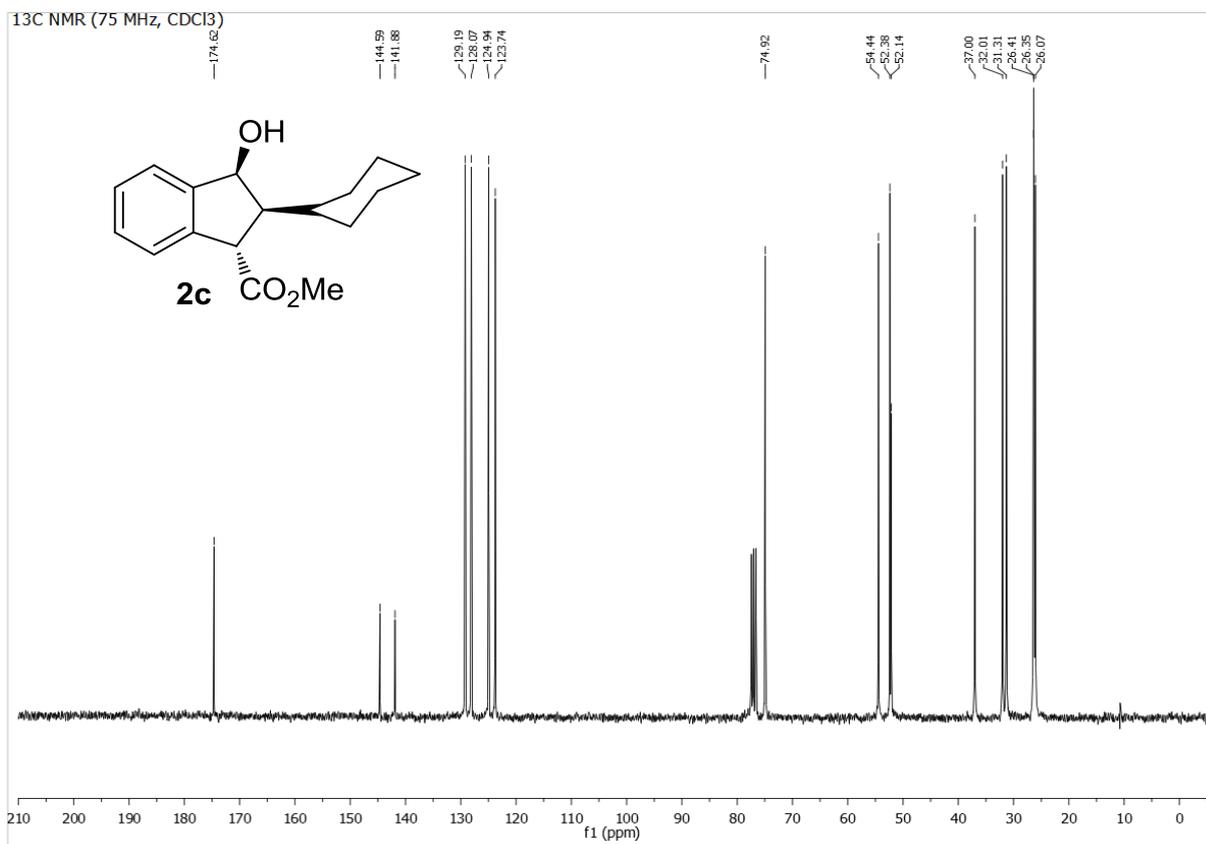
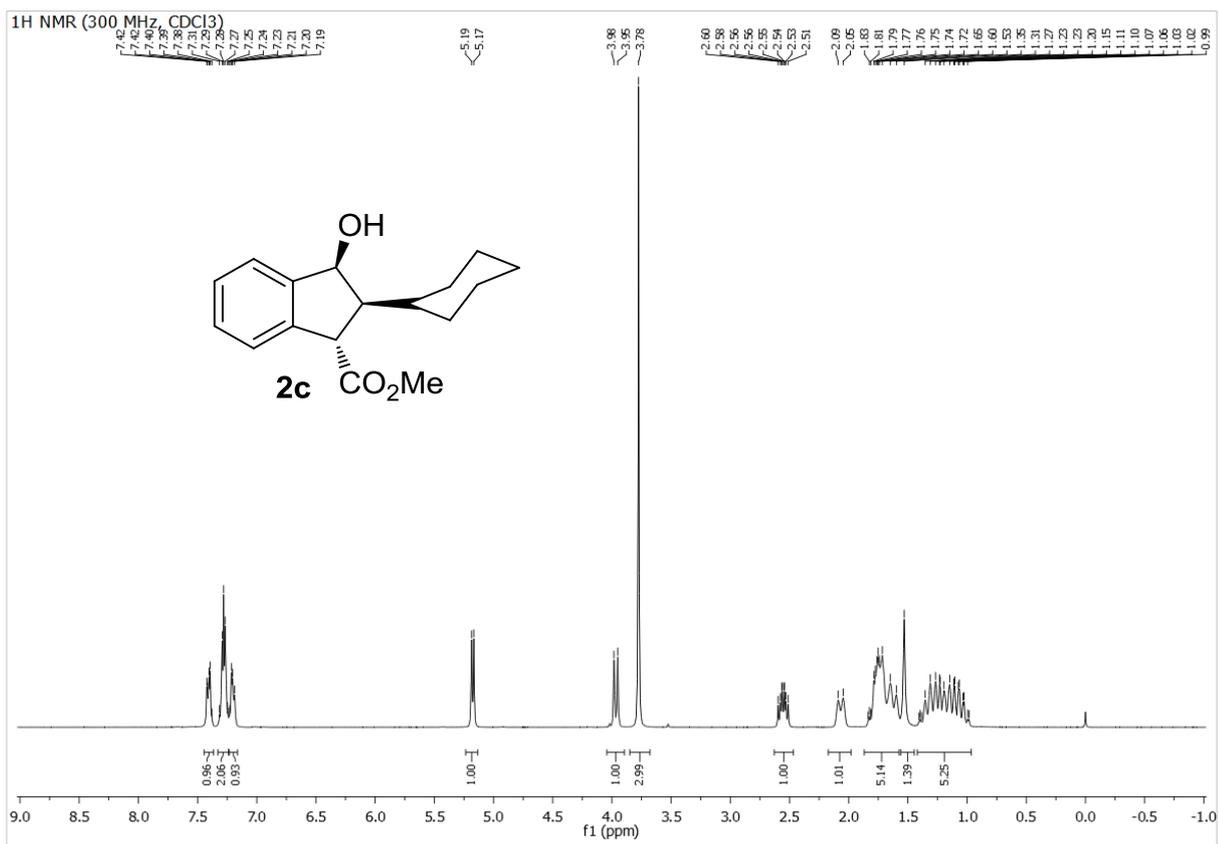






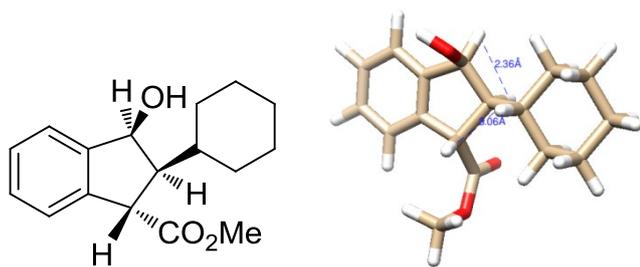




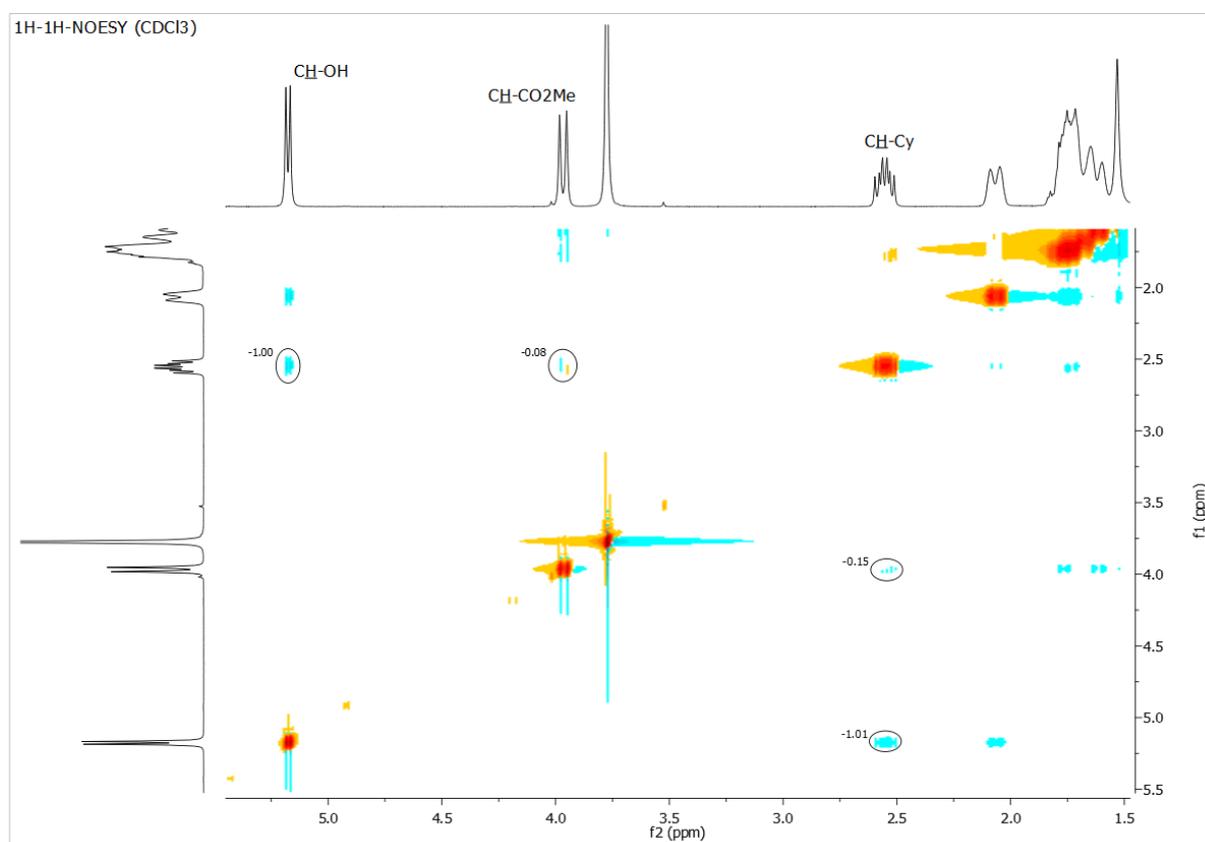


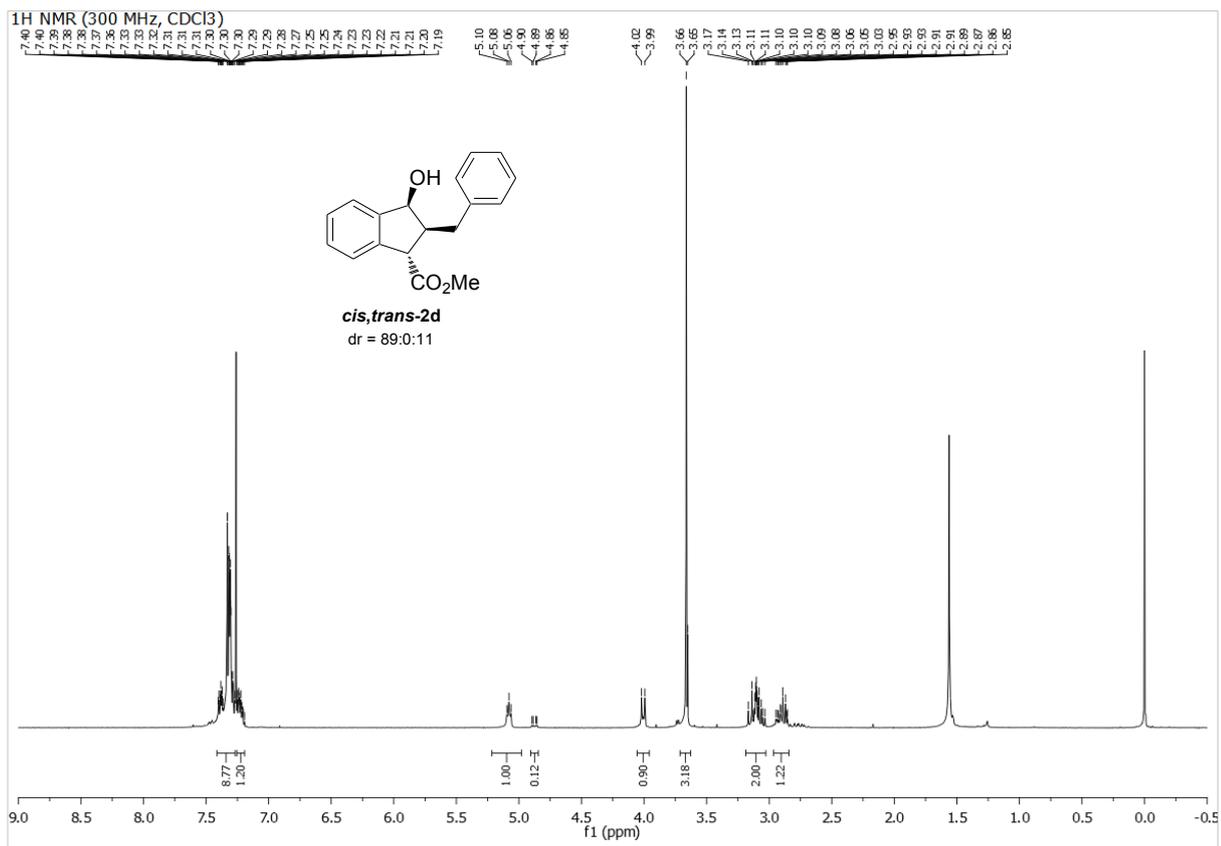
^1H - ^1H NOESY spectrum of 2c

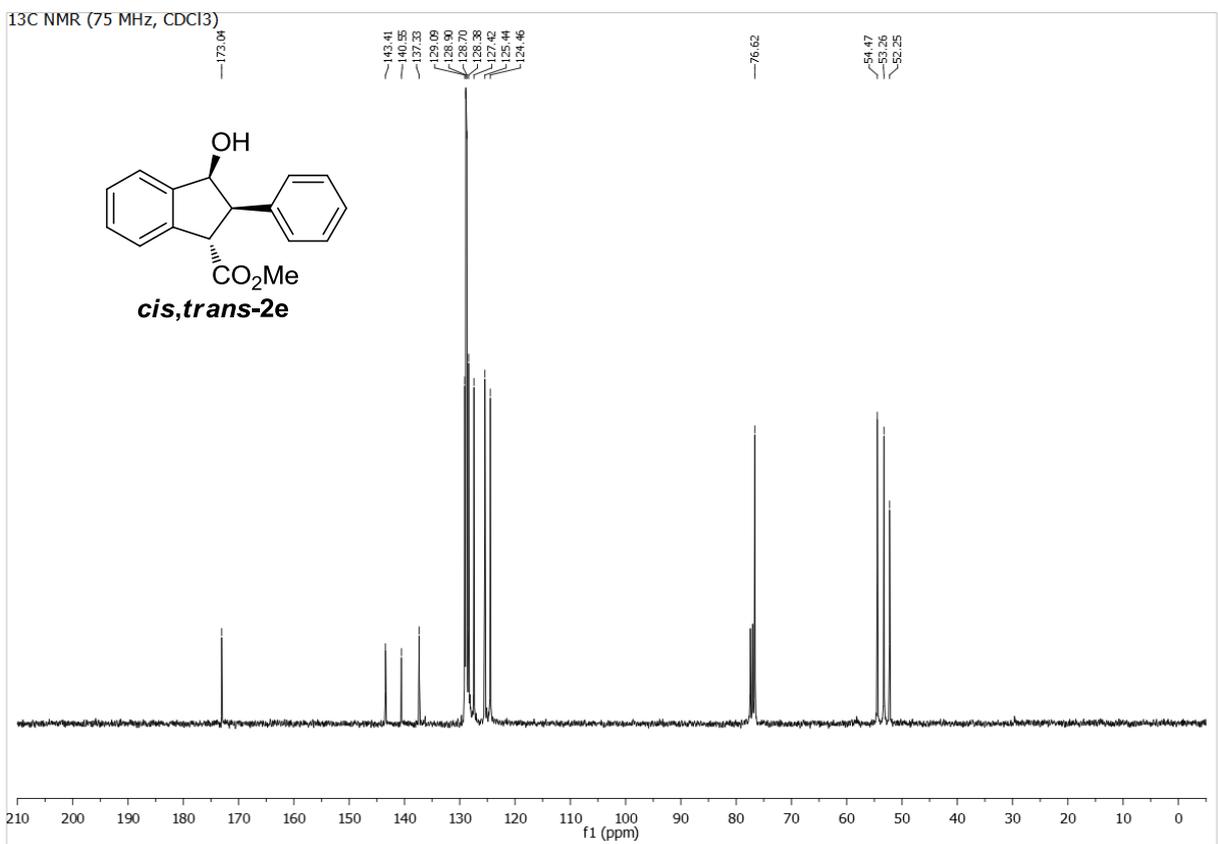
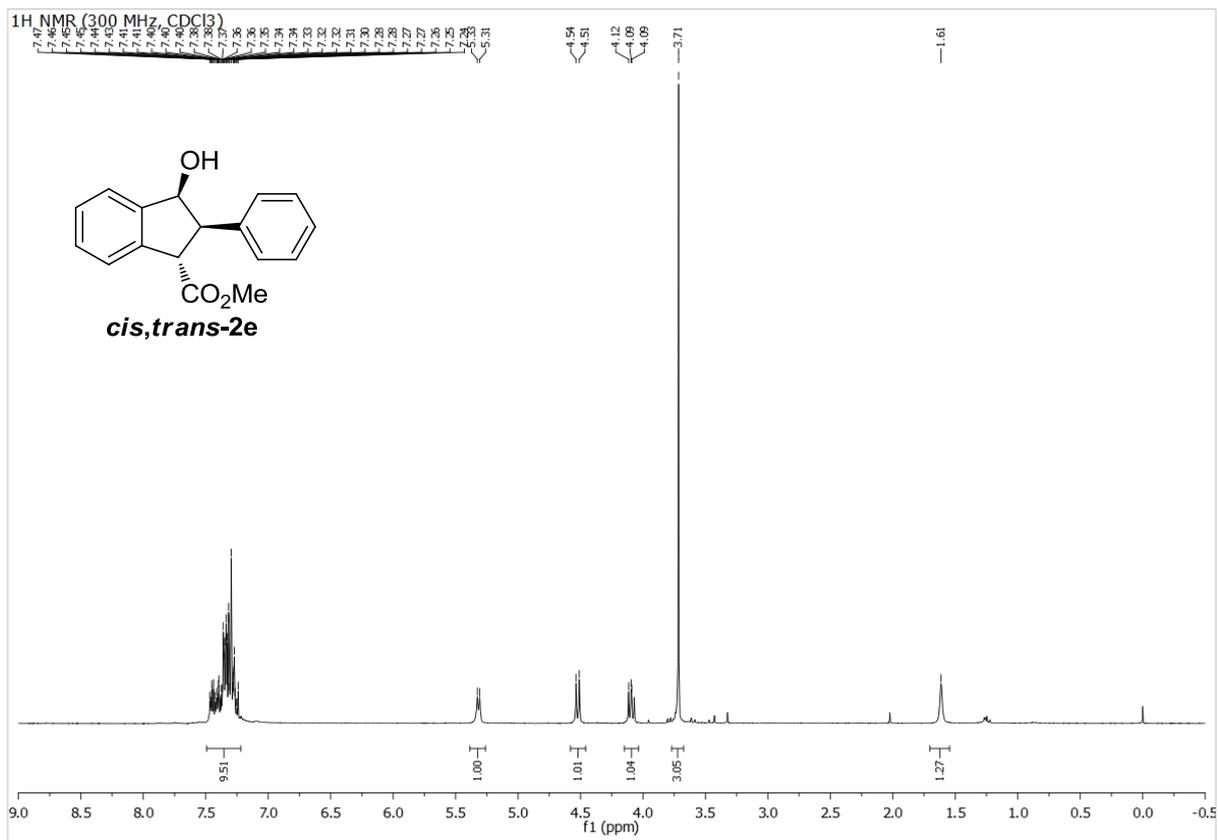
Calculated relevant distances:

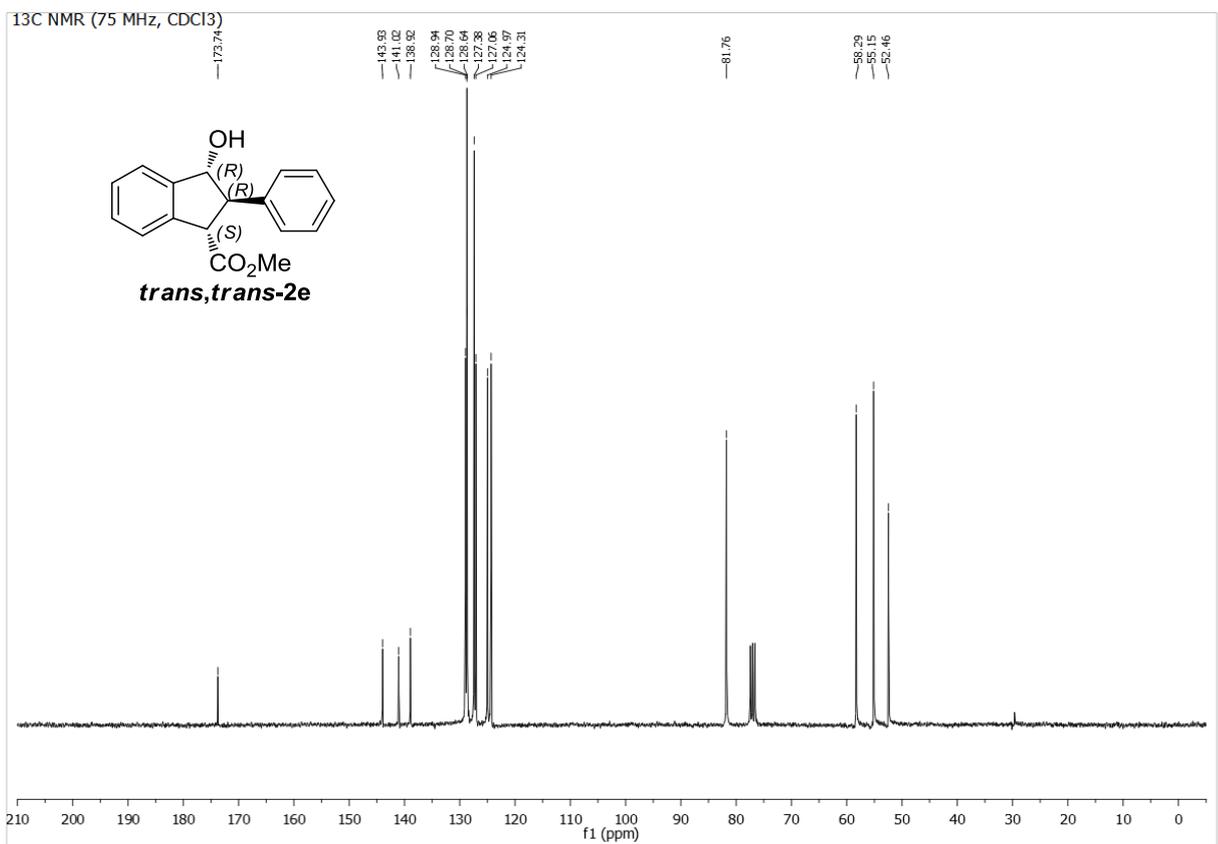
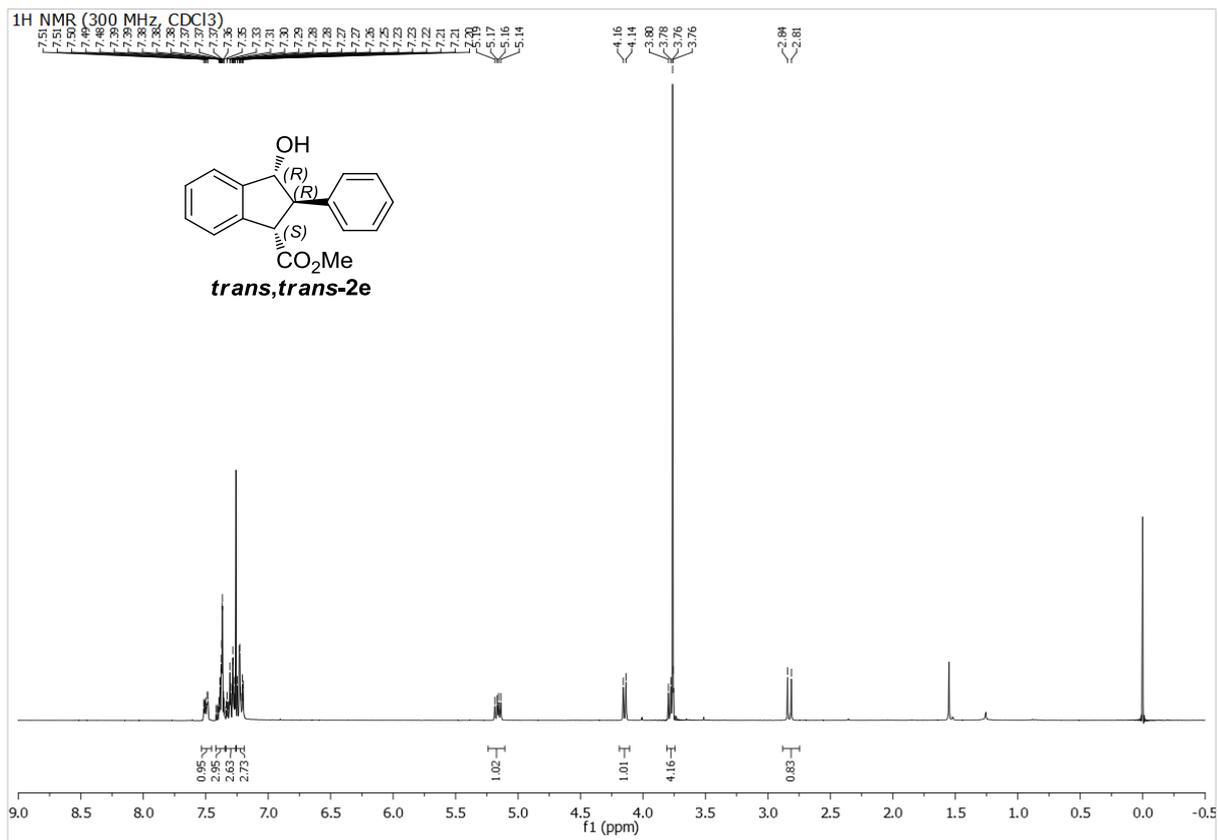


Observation: CH-Cy has a 10 fold larger NOE with CH-OH than with $\text{CH-CO}_2\text{Me}$. The geometries were optimized in ChemBio3D Ultra. Visualization and distance calculation was performed with USCF Chimera.



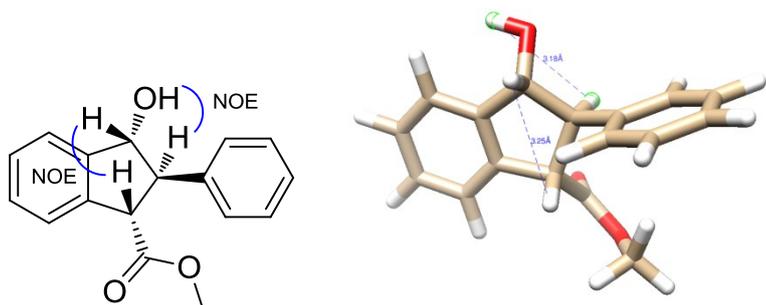




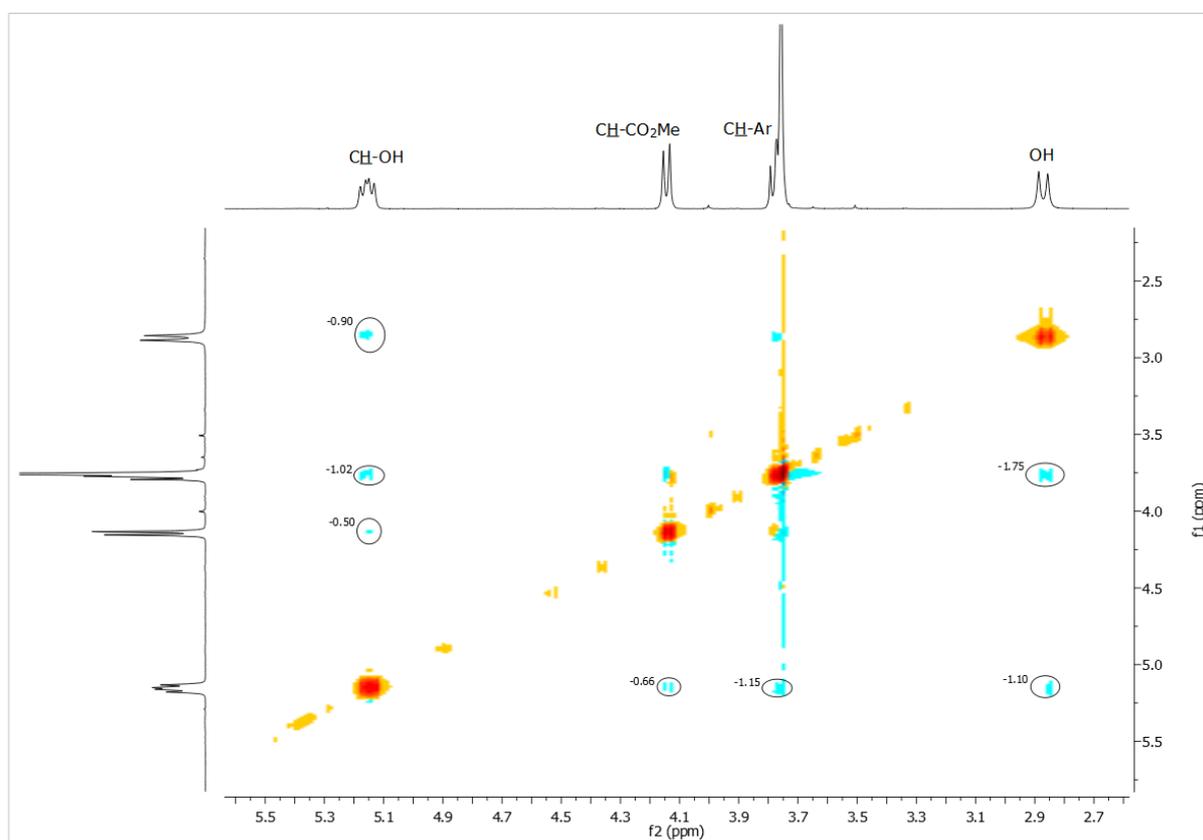


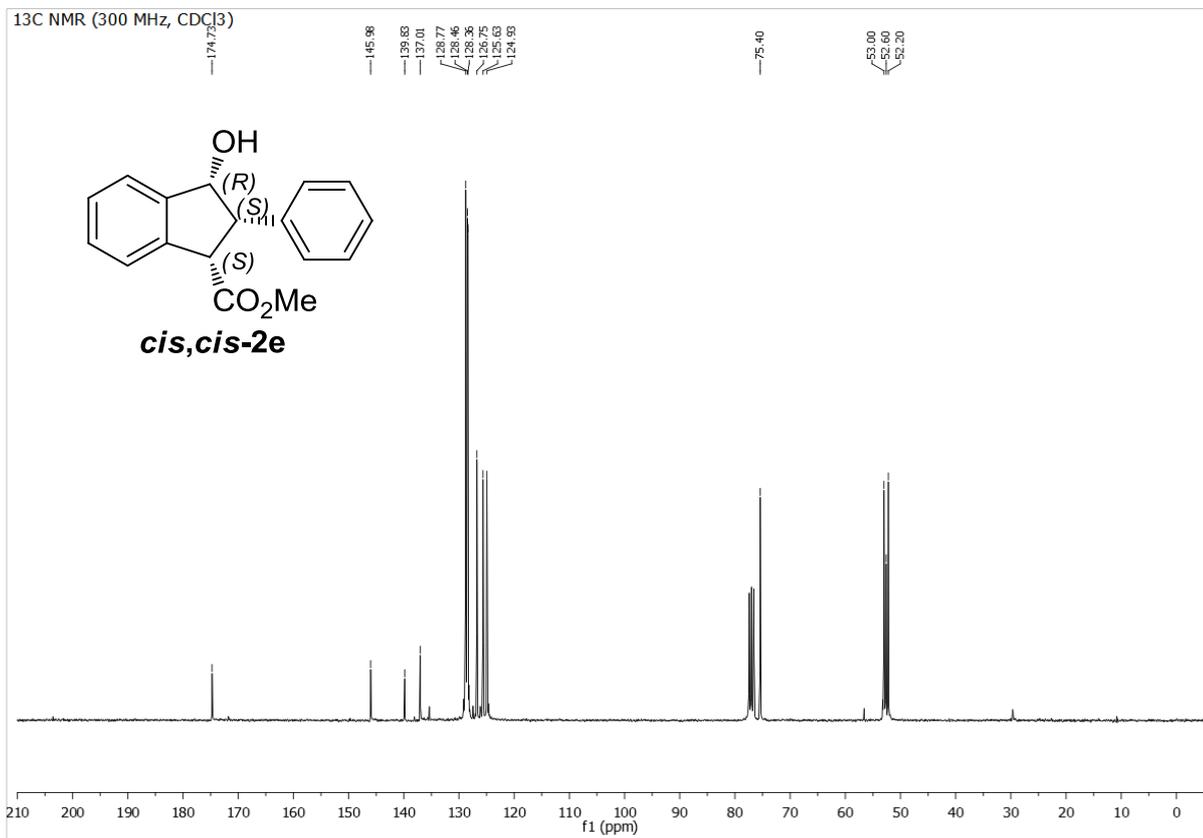
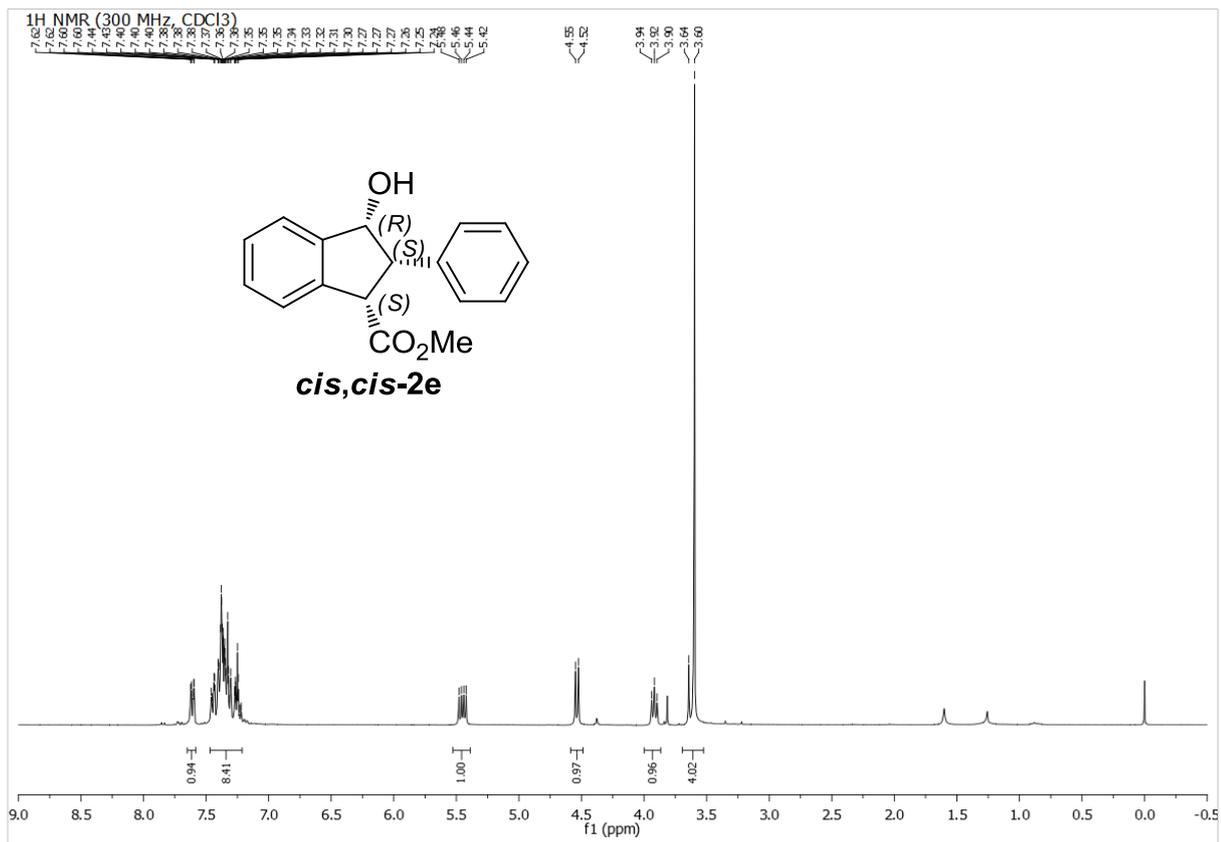
^1H - ^1H NOESY spectrum of *trans,trans*-2e

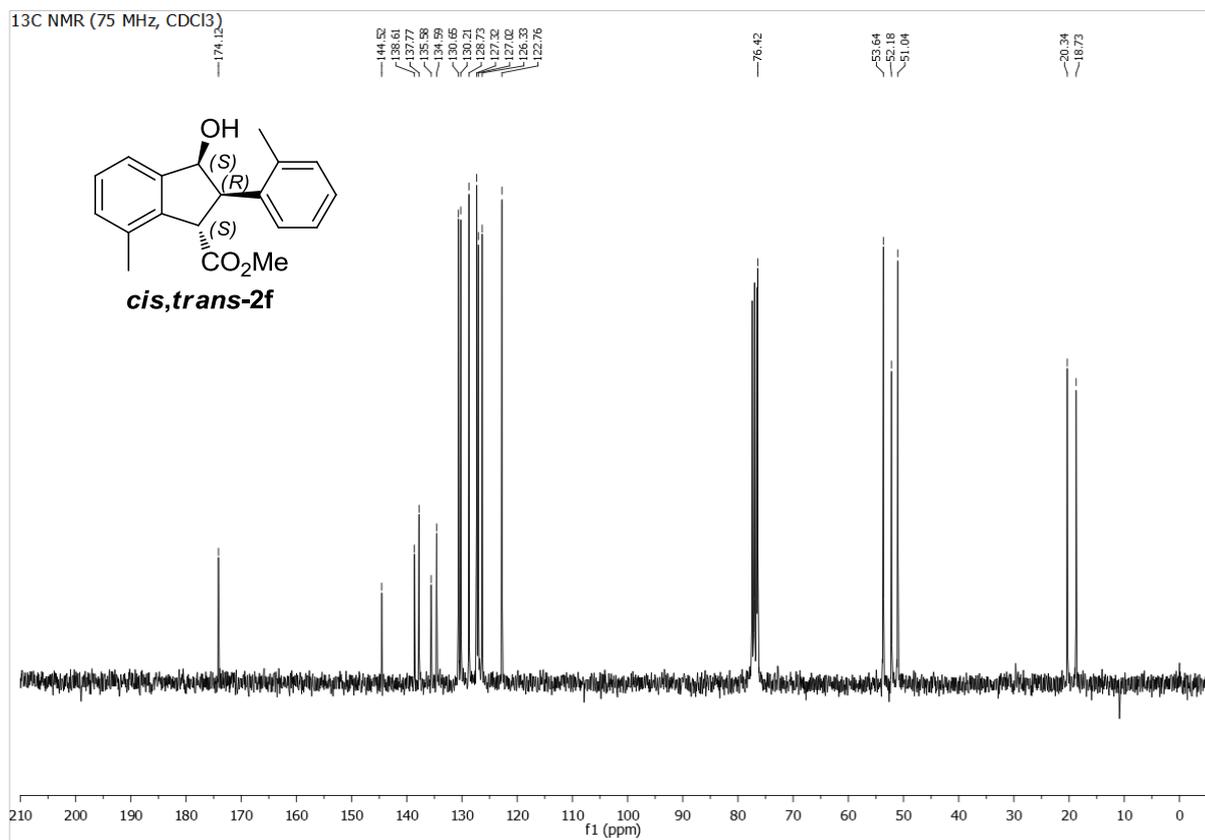
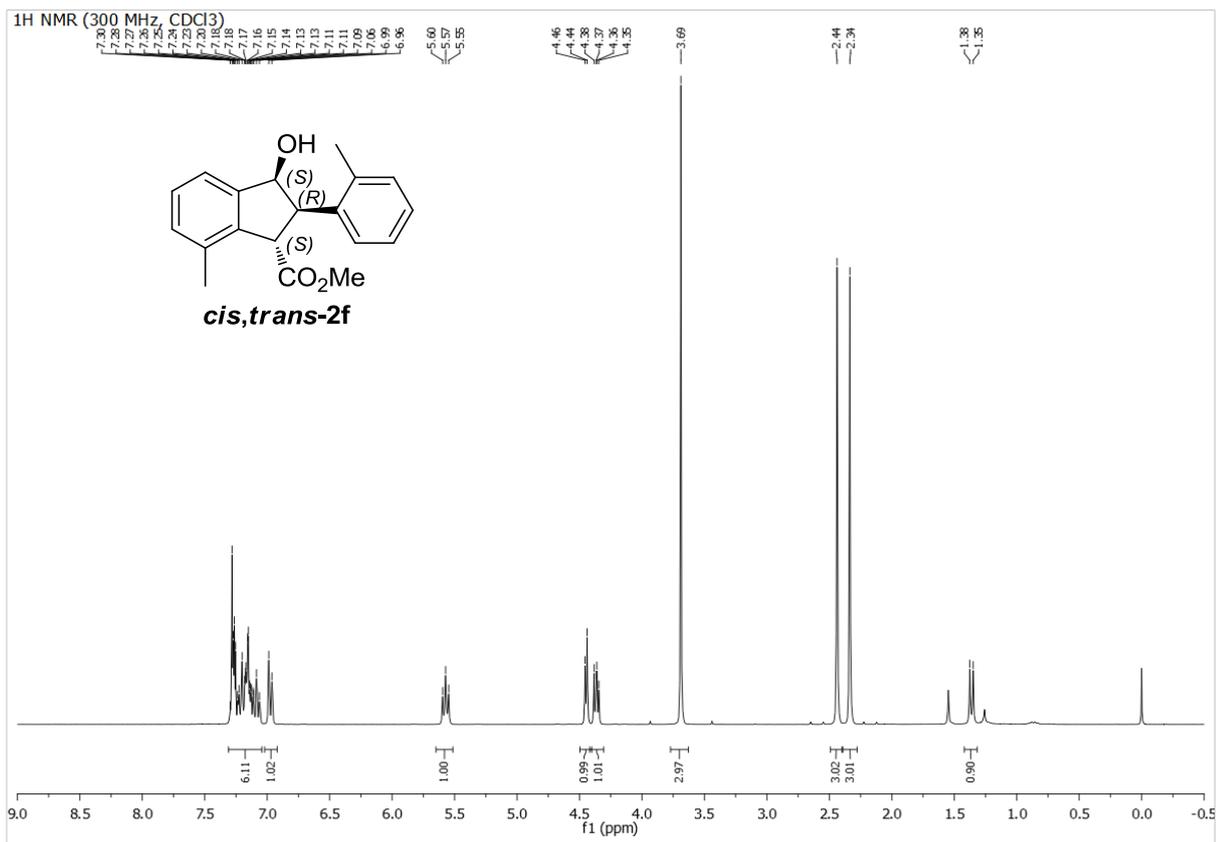
Calculated relevant distances:

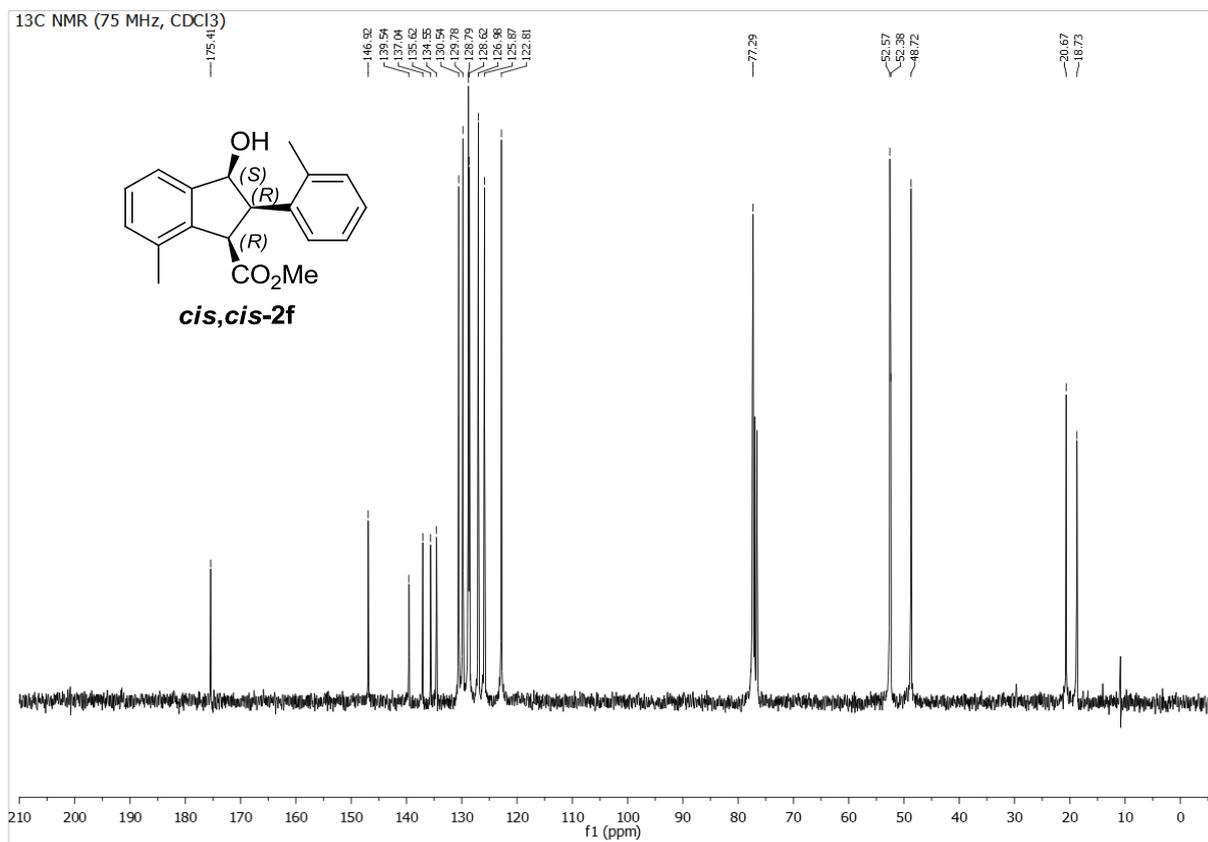
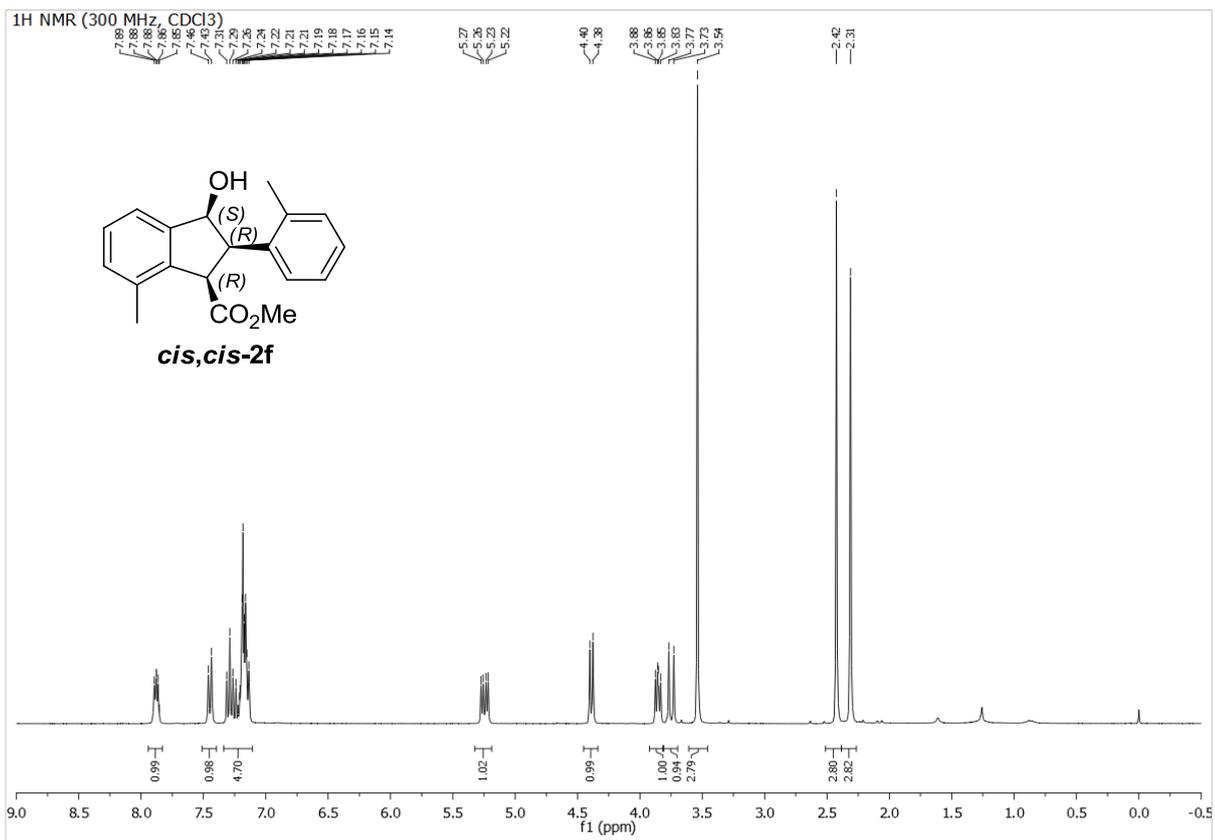


Observation: CH-OH has NOE with CH-CO₂Me, confirming their *cis*-configuration and CH-Ar has NOE with OH confirming the *trans*-configuration of the C1-C2. The geometries were optimized in ChemBio3D Ultra. Visualization and distance calculation was performed with USCF Chimera.



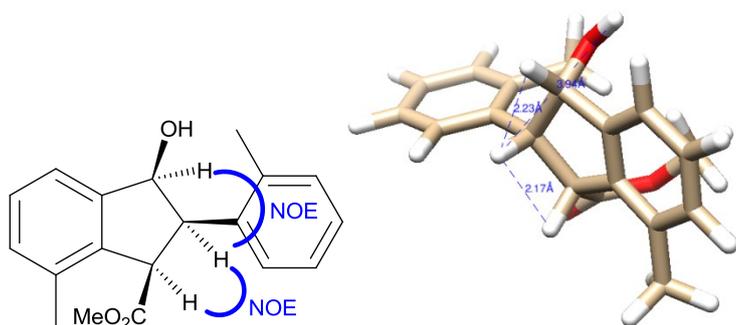




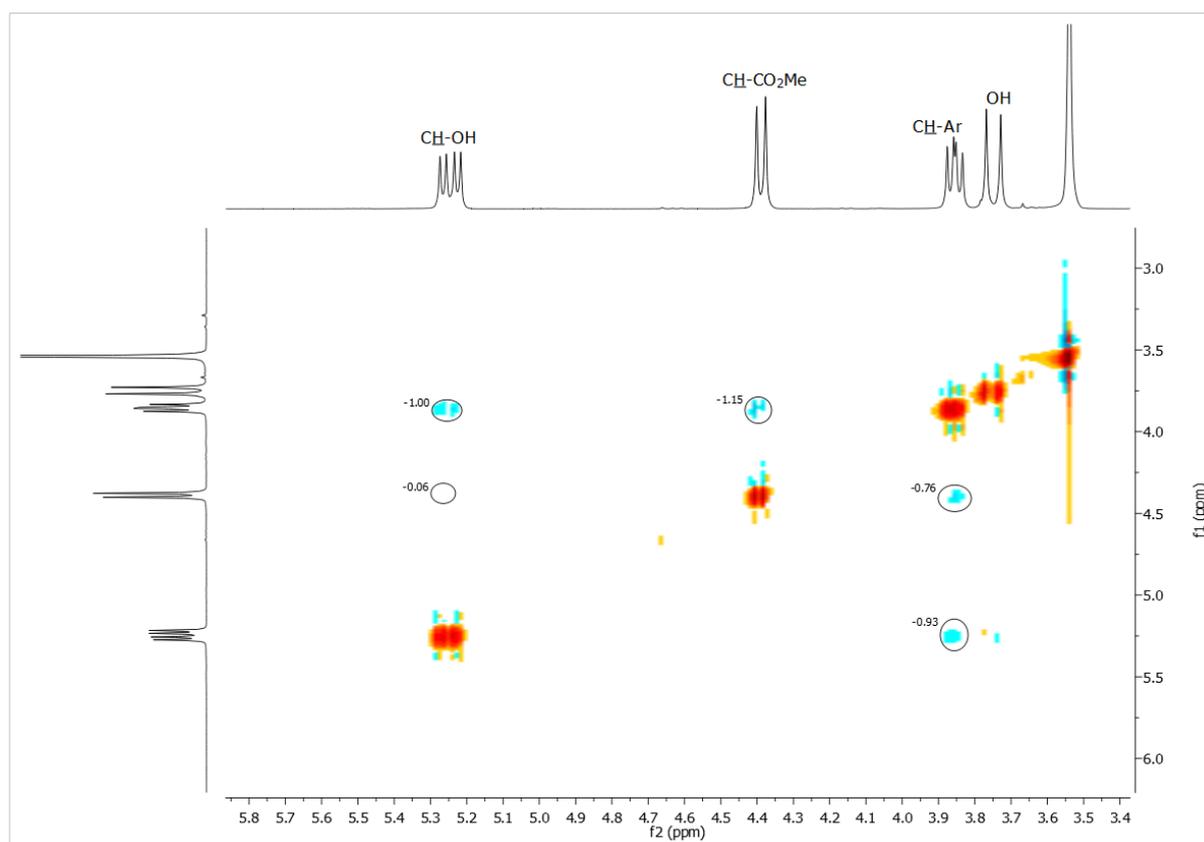


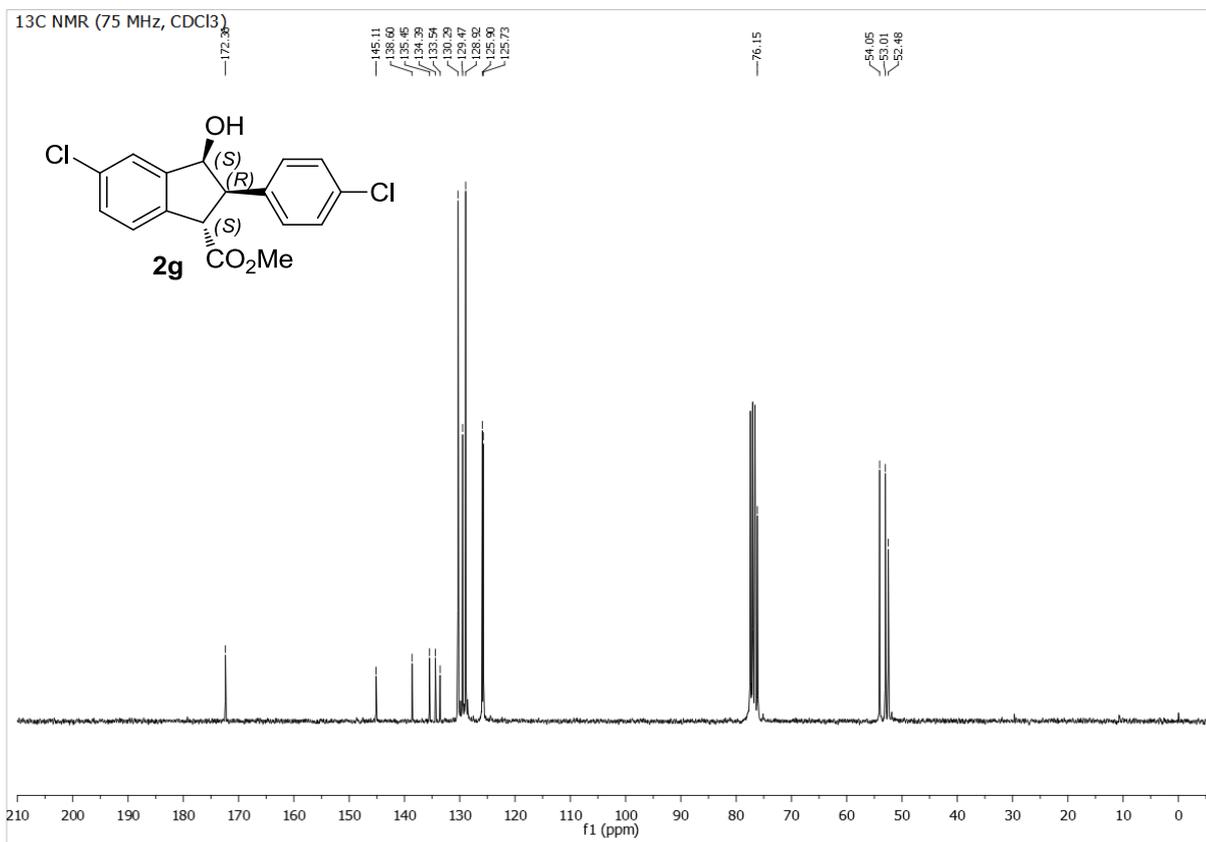
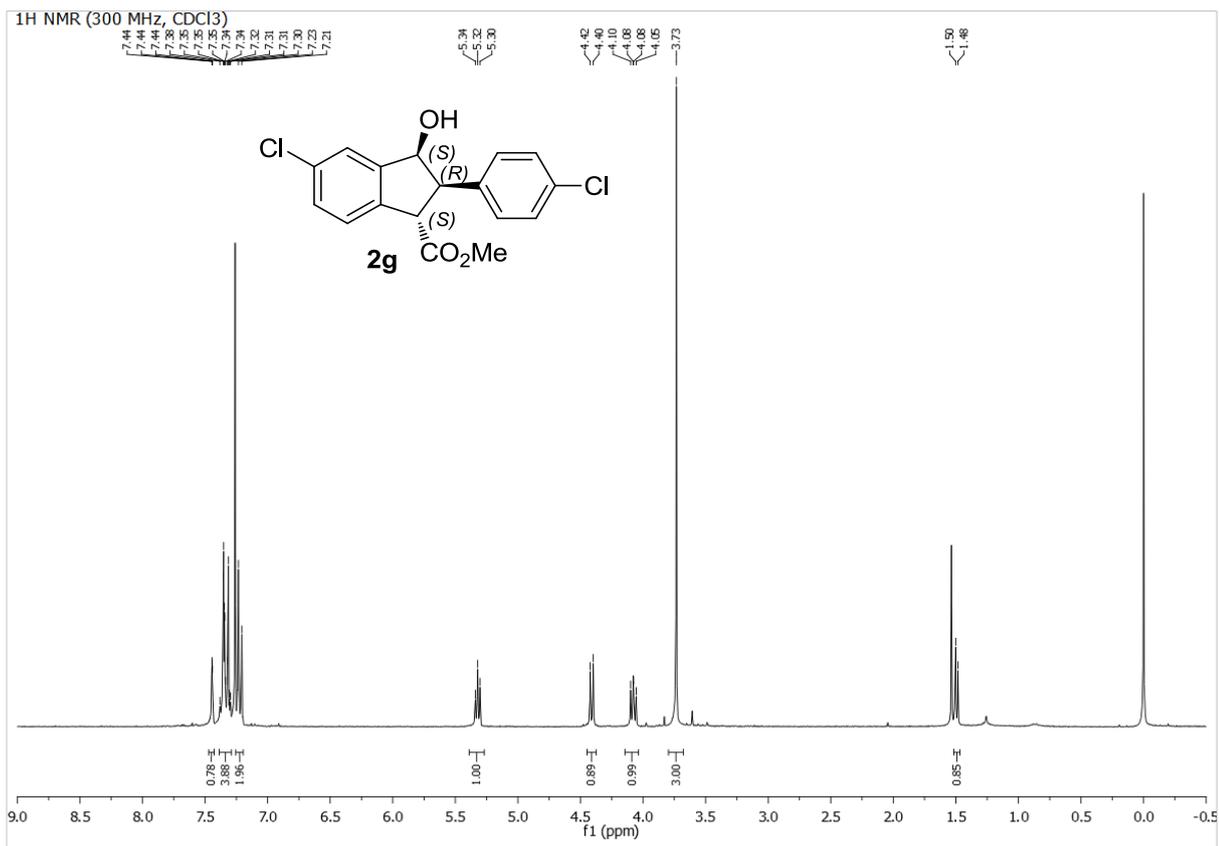
^1H - ^1H NOESY spectrum of *cis,cis*-2f (minor product)

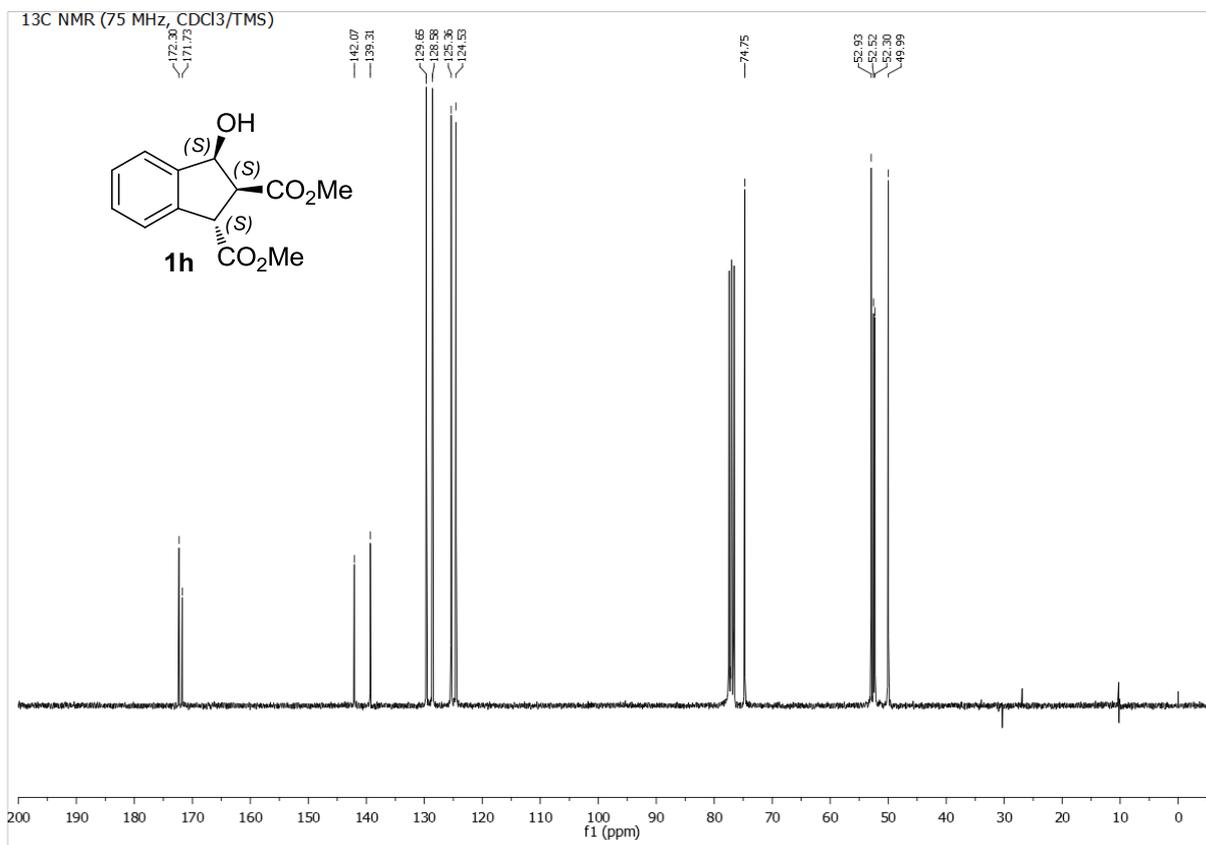
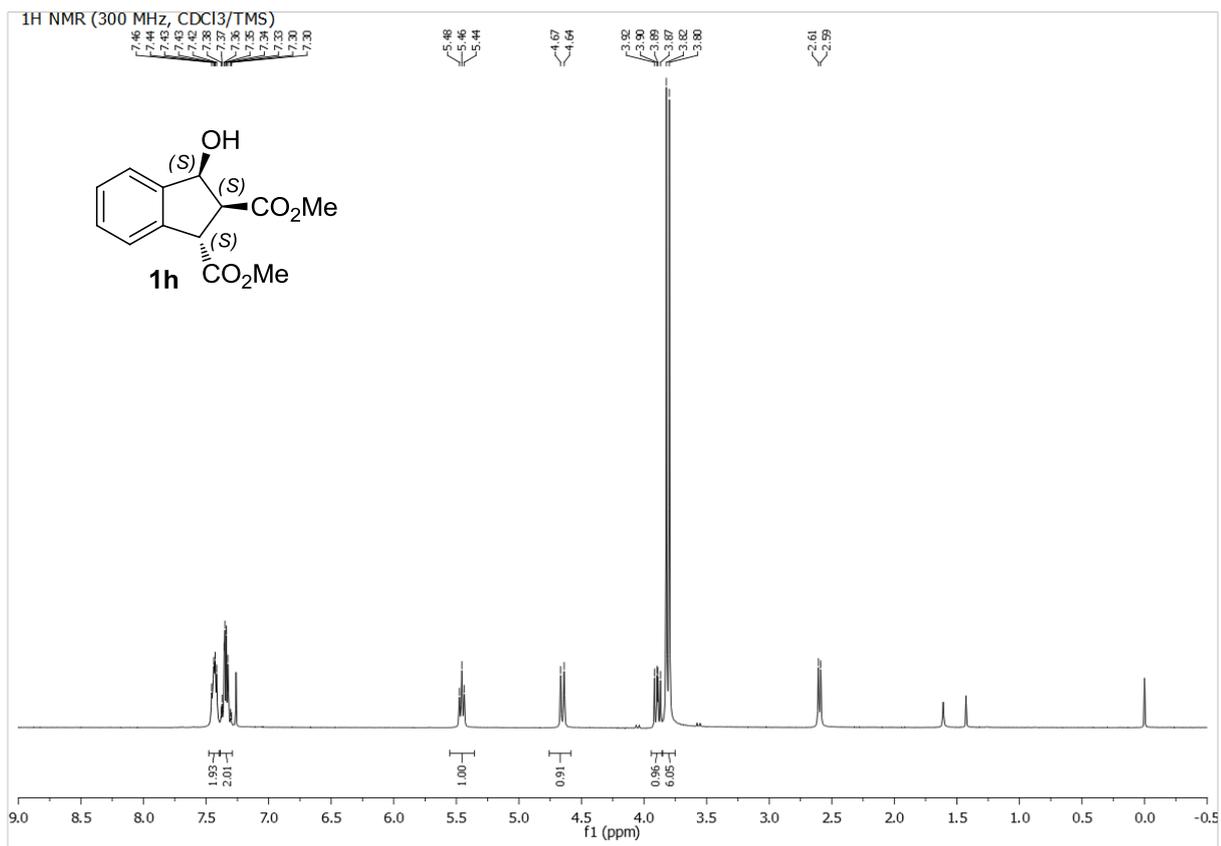
Calculated relevant distances:

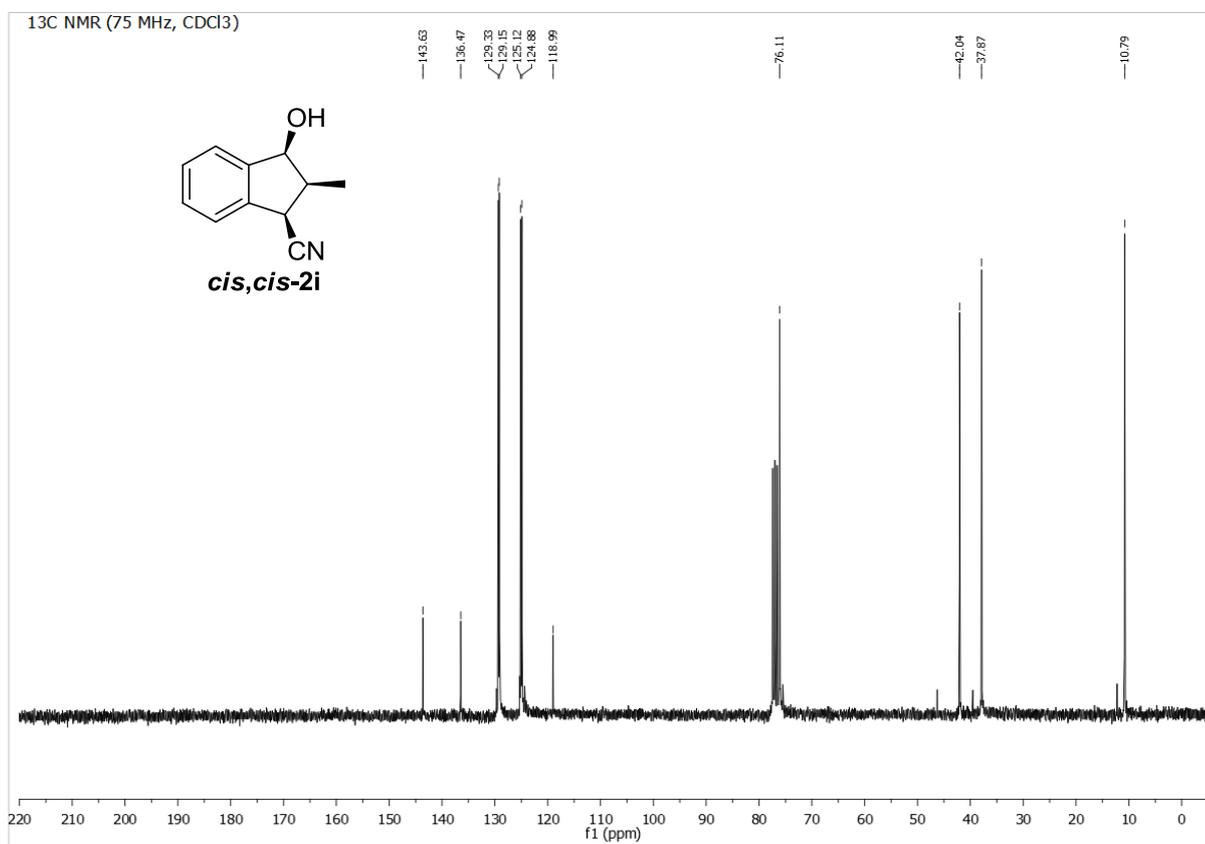
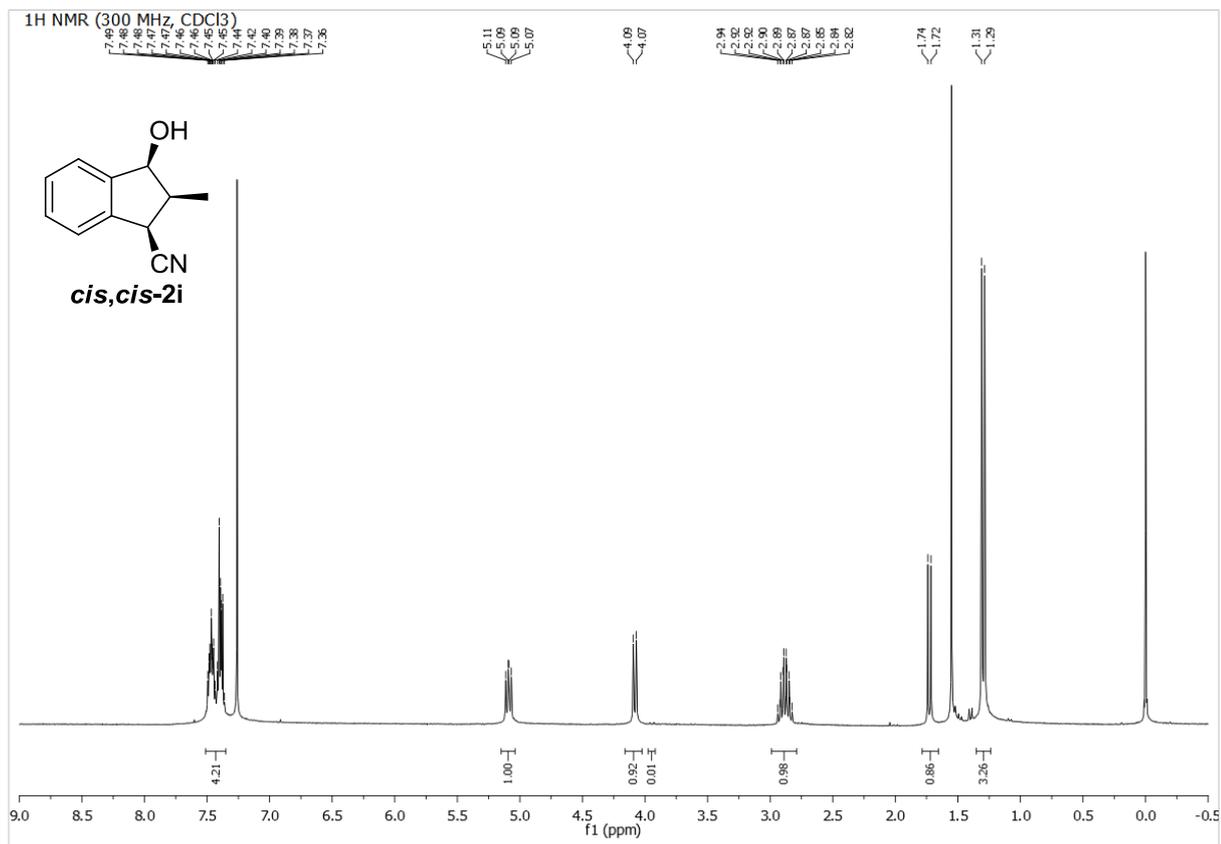


Observation: CH -(*o*-tolyl) has a NOE of the same order of magnitude with CH -OH and CH -CO₂Me. There is no NOE between CH -(*o*-tolyl) and OH. The geometries were optimized in ChemBio3D Ultra. Visualization and distance calculation was performed with USCF Chimera.

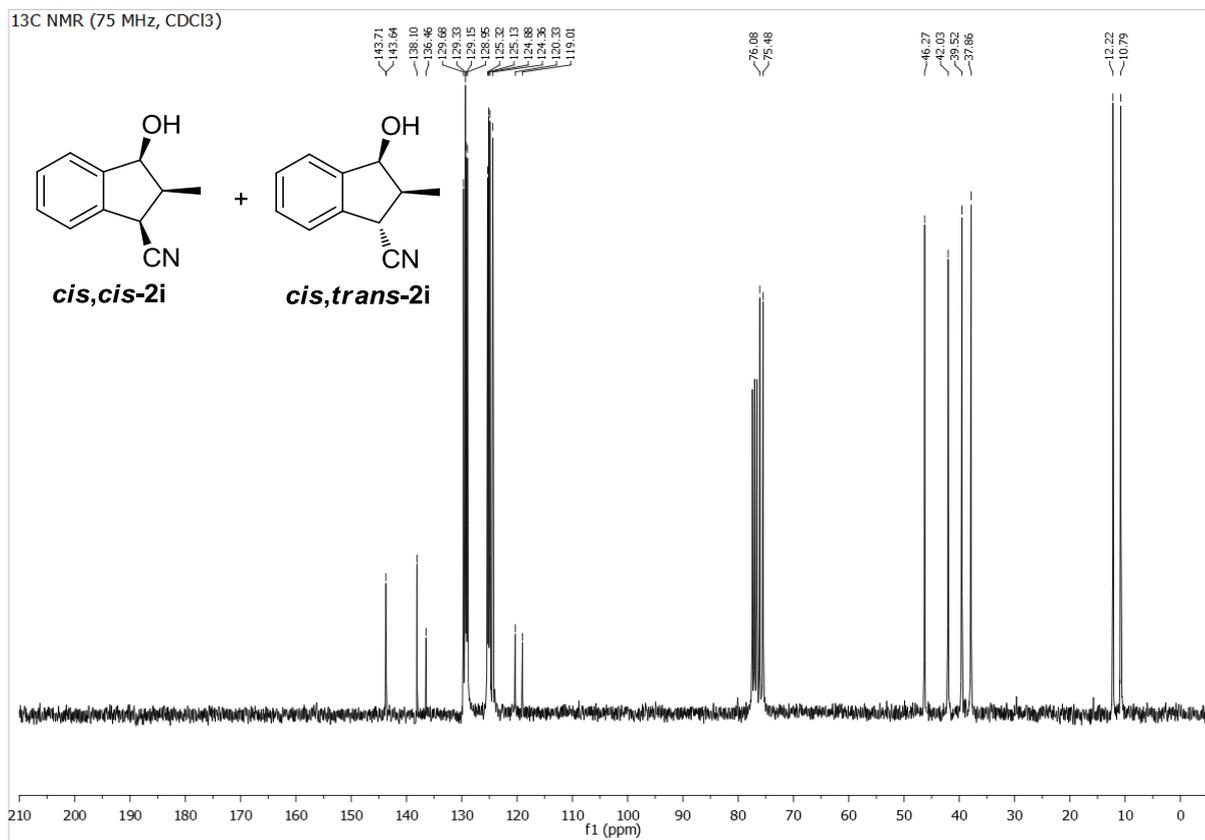
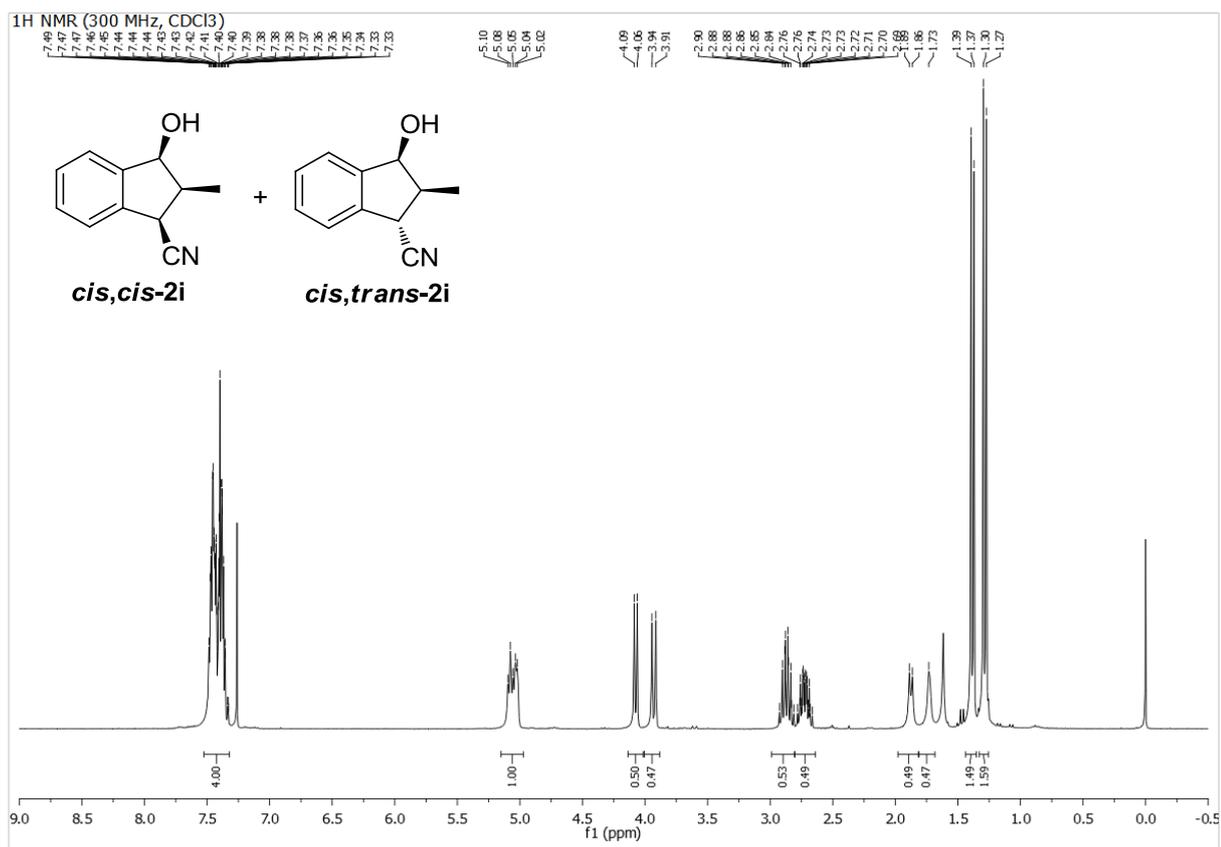






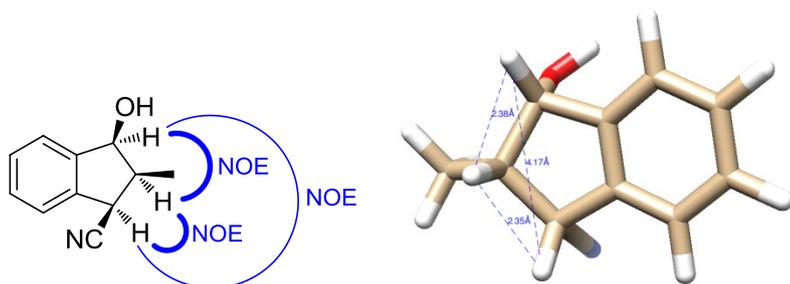


NOTE: ¹³C NMR spectrum of the sample before crystallization. Contains 7% of (1*S*,2*S*,3*S*)-2i

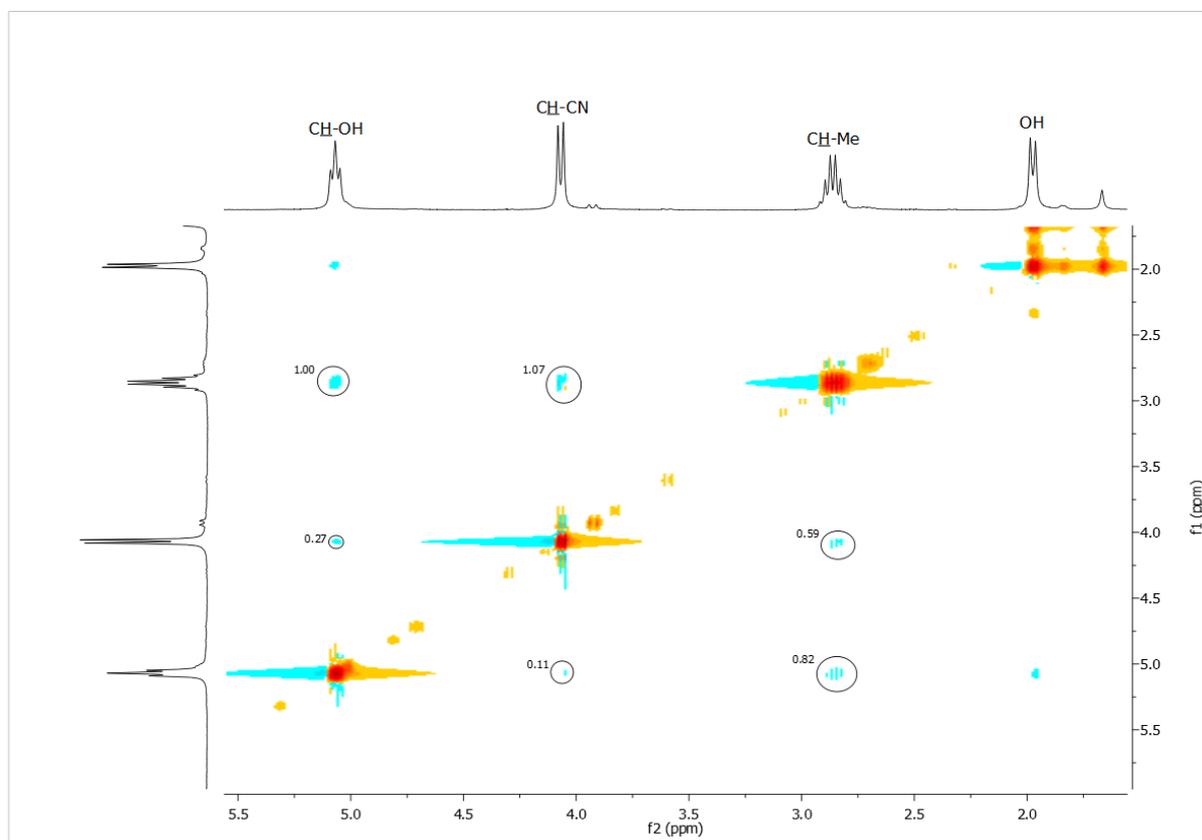


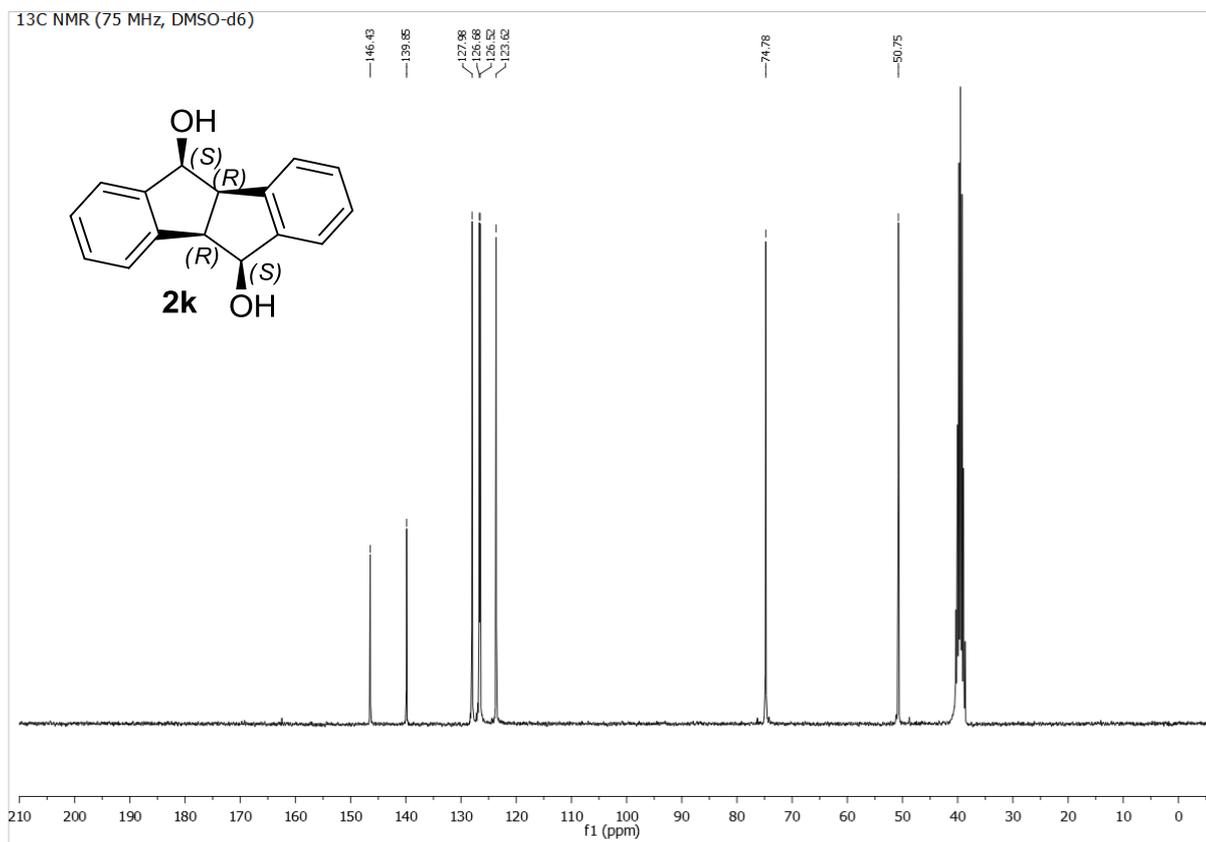
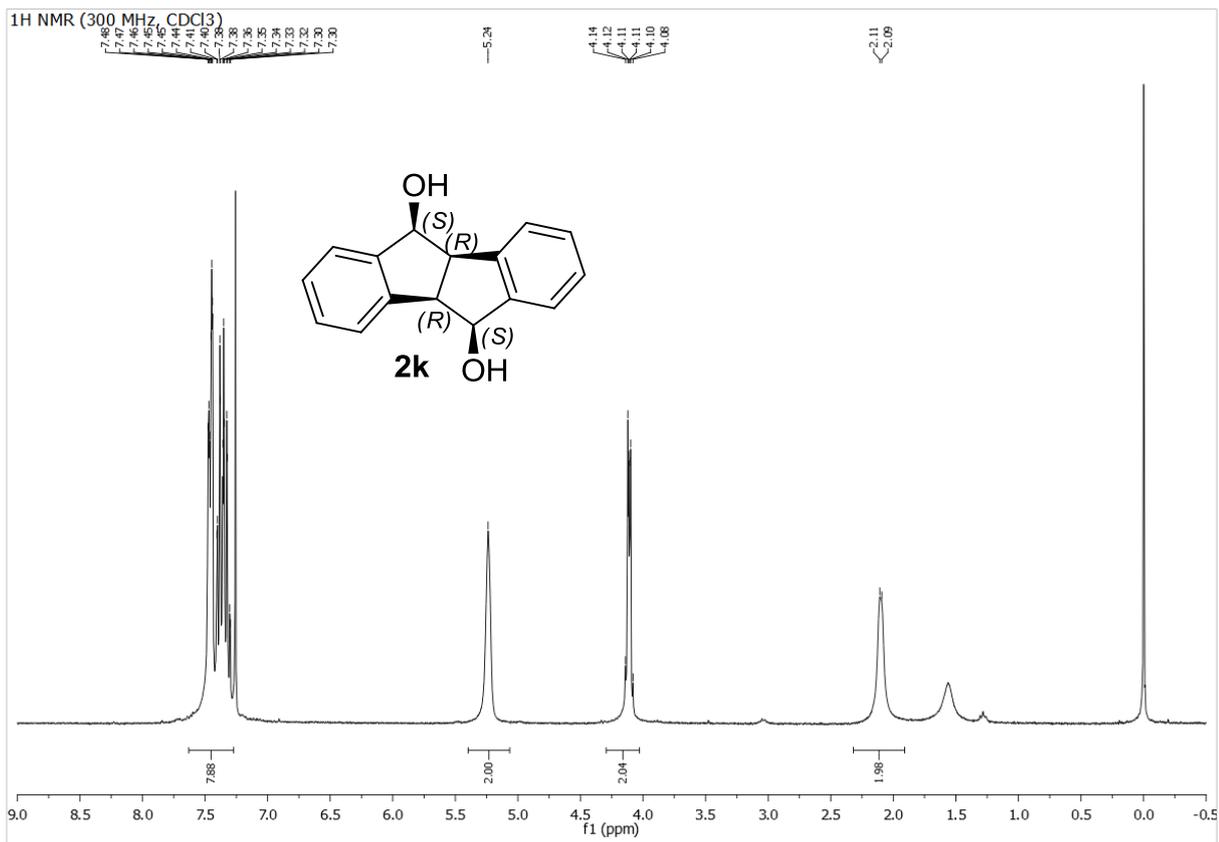
^1H - ^1H NOESY spectrum of *cis,cis*-2i

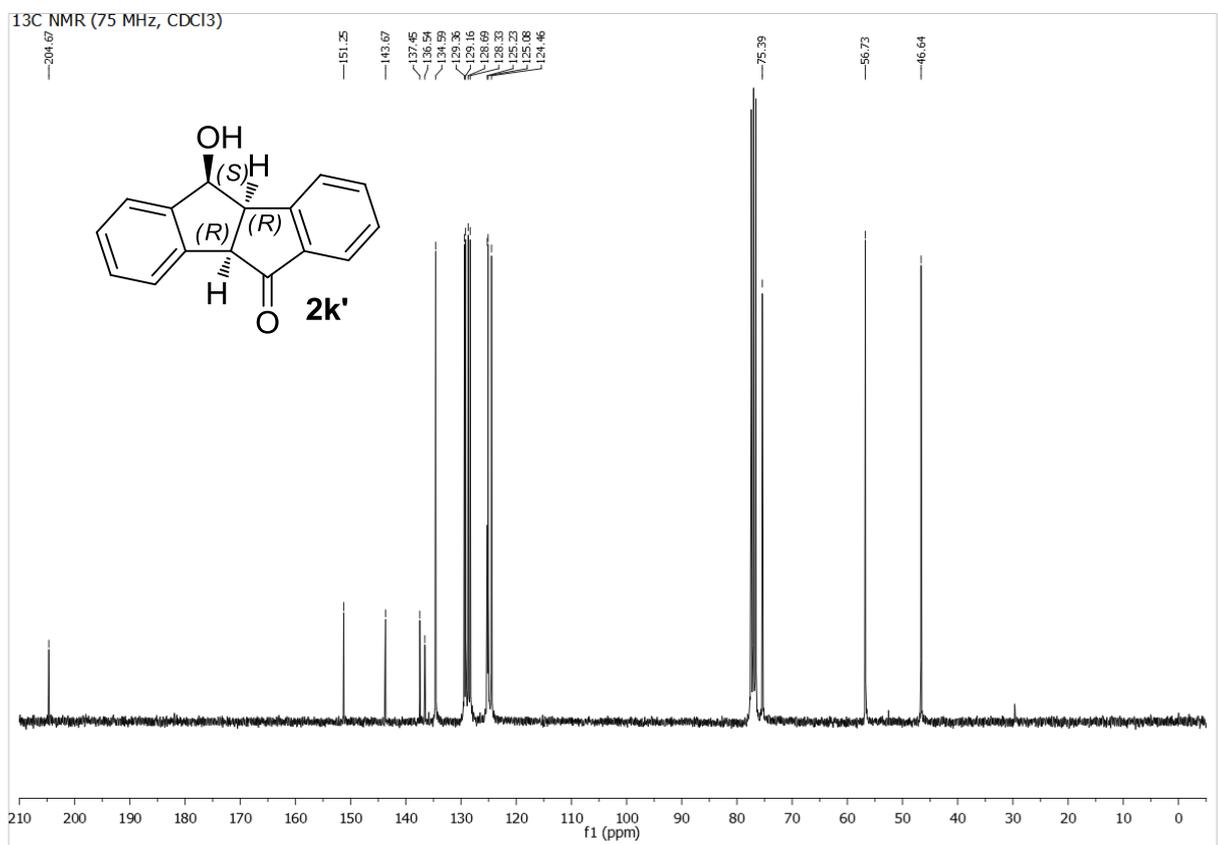
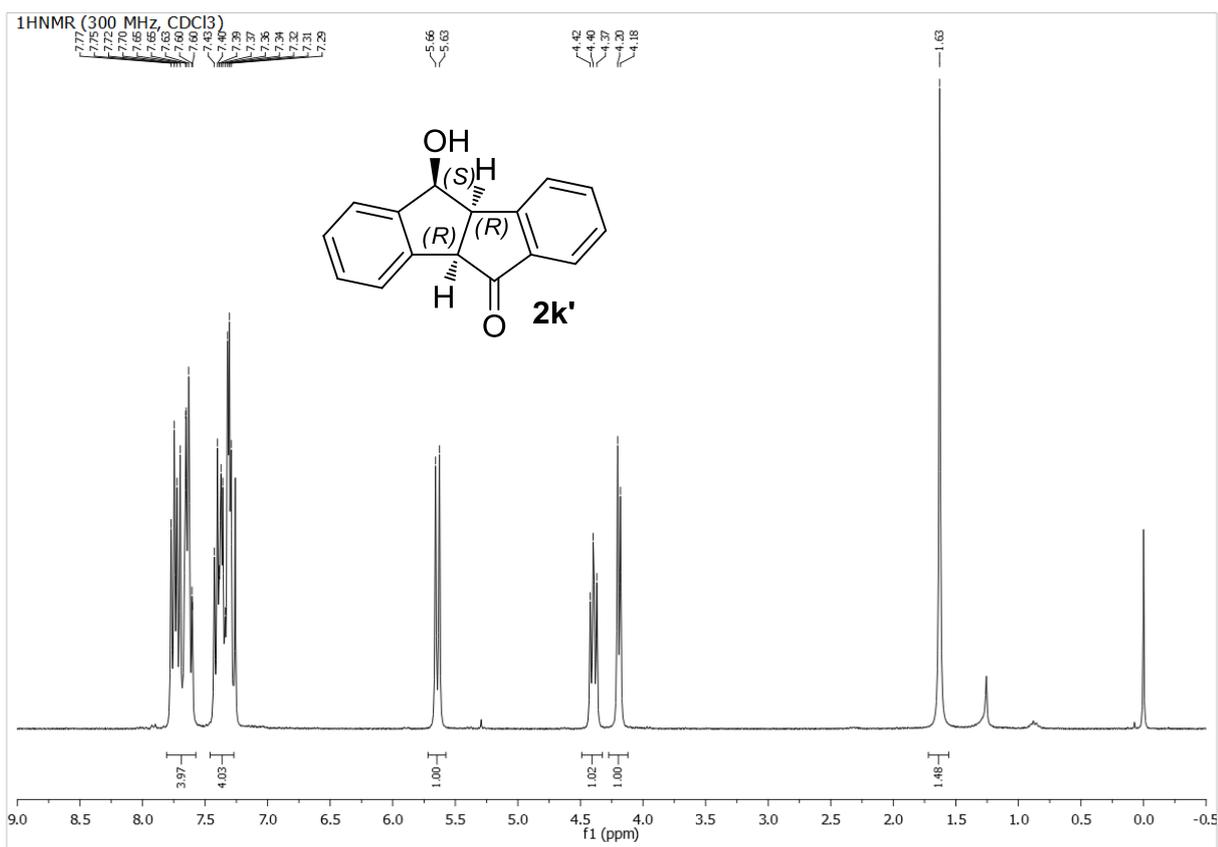
Calculated relevant distances:



Observation: CHMe has a NOE of the same order of magnitude with CHOH and CHCN . There is a NOE between CHOH and CHCN but no NOE between OH and CHMe

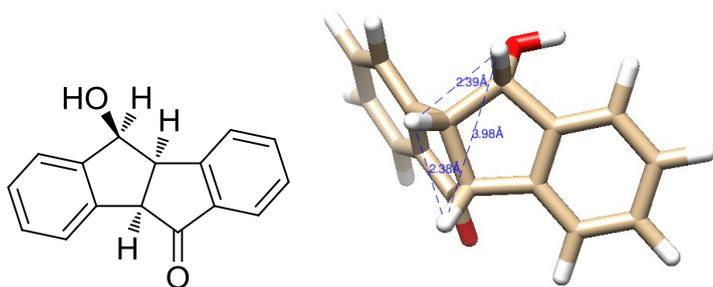






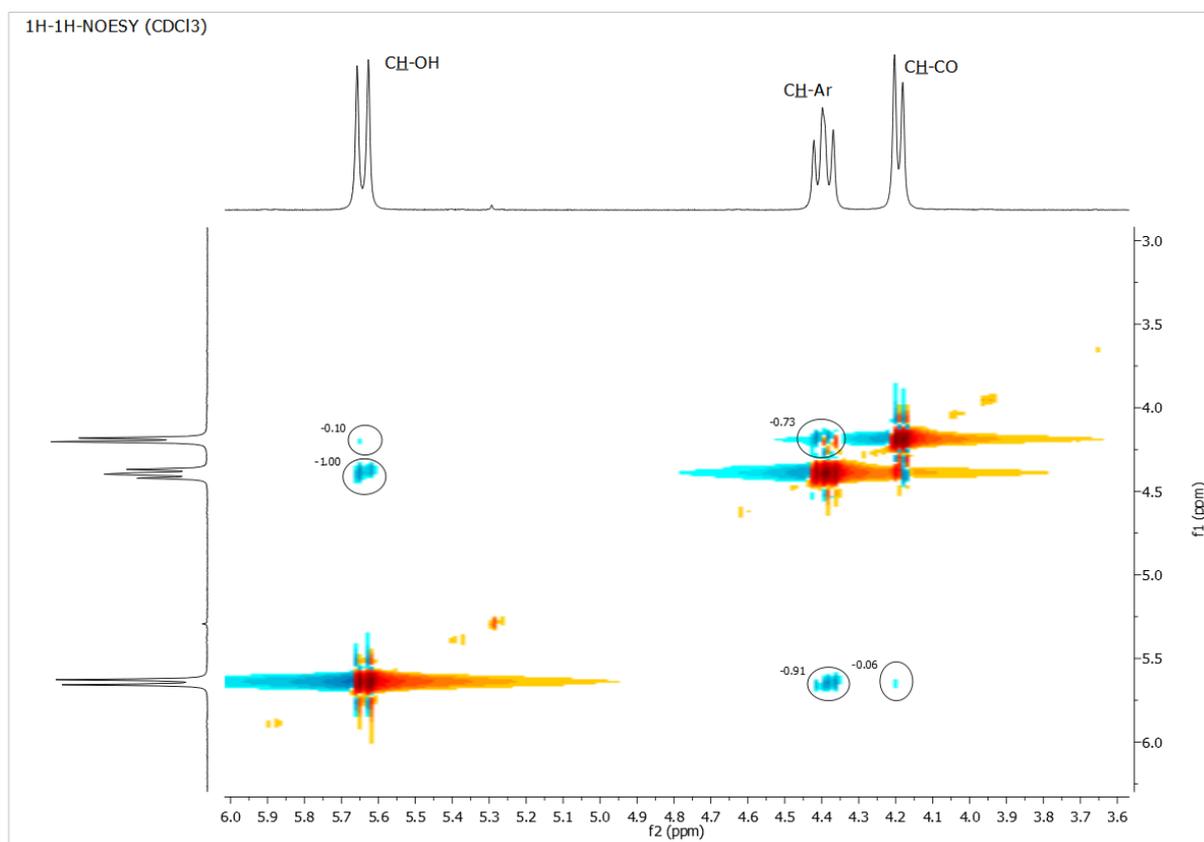
^1H - ^1H NOESY spectrum of *cis,cis*-2k'

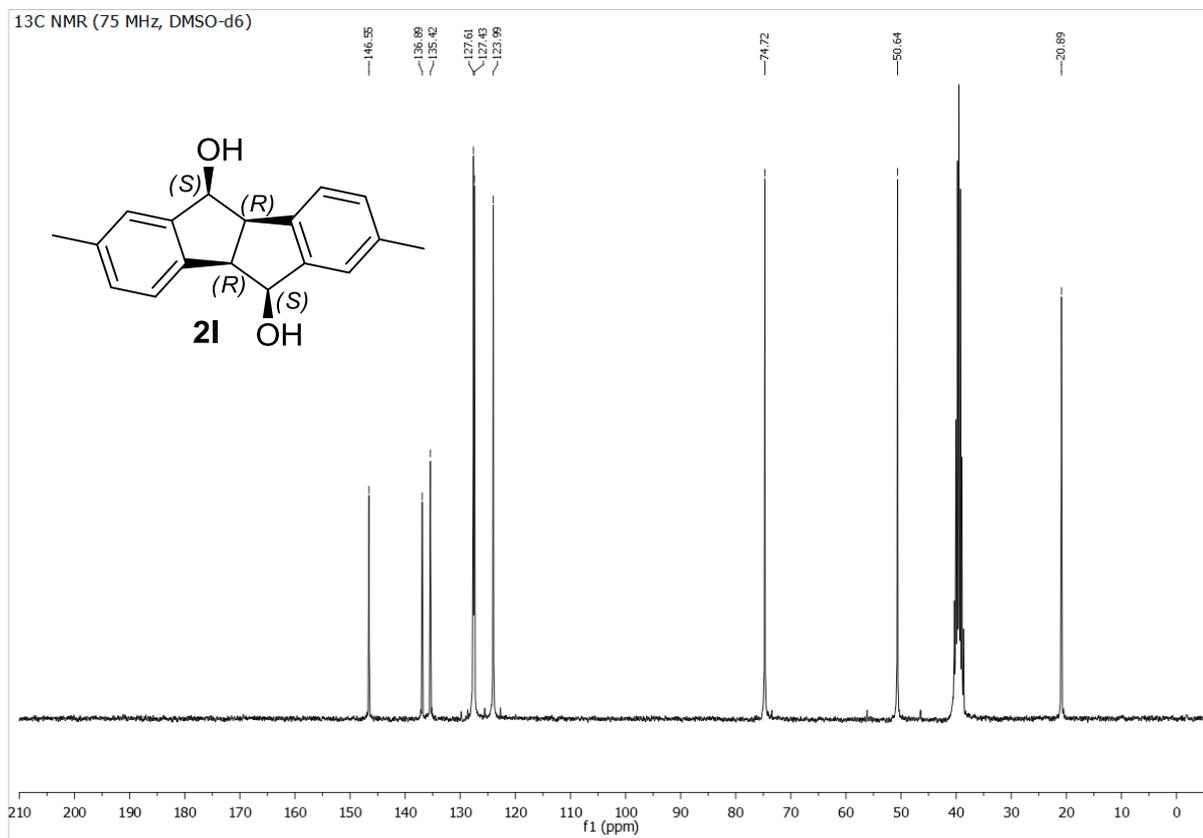
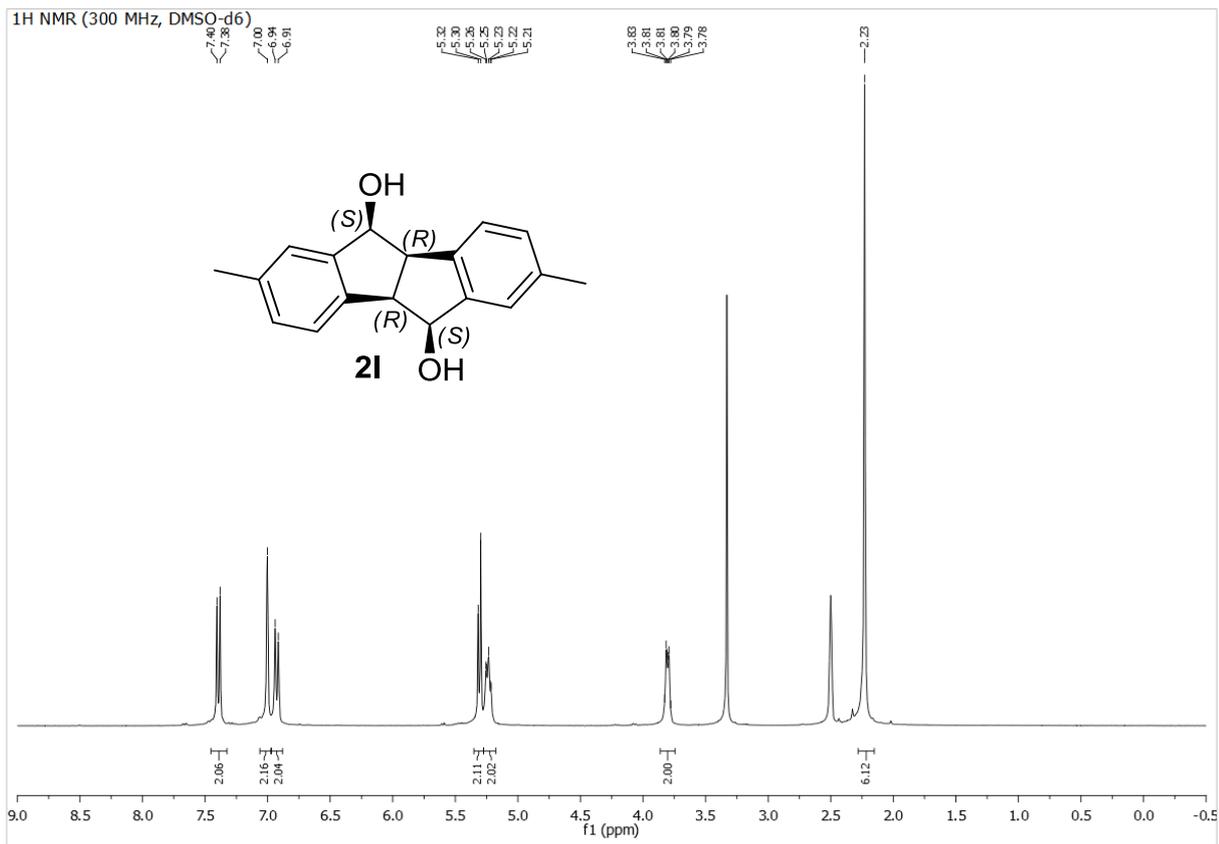
Calculated relevant distances:

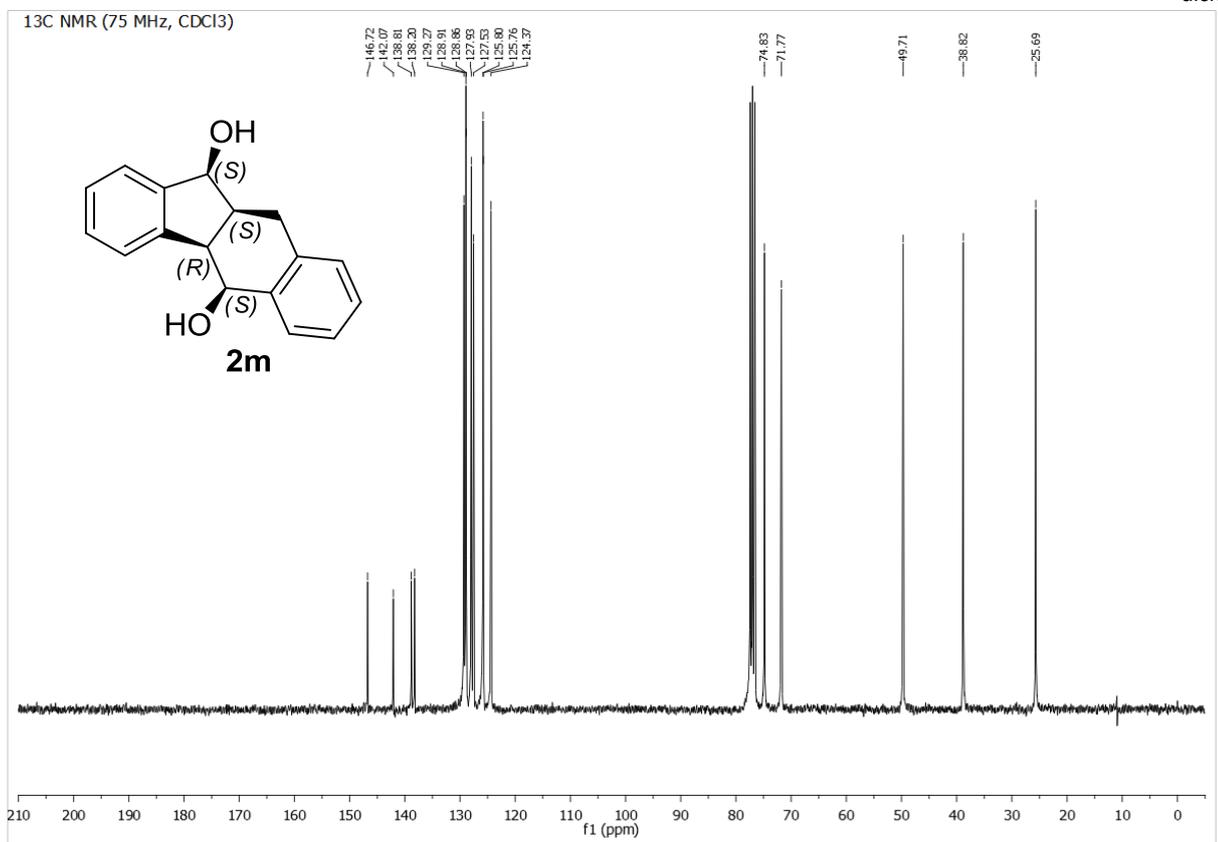
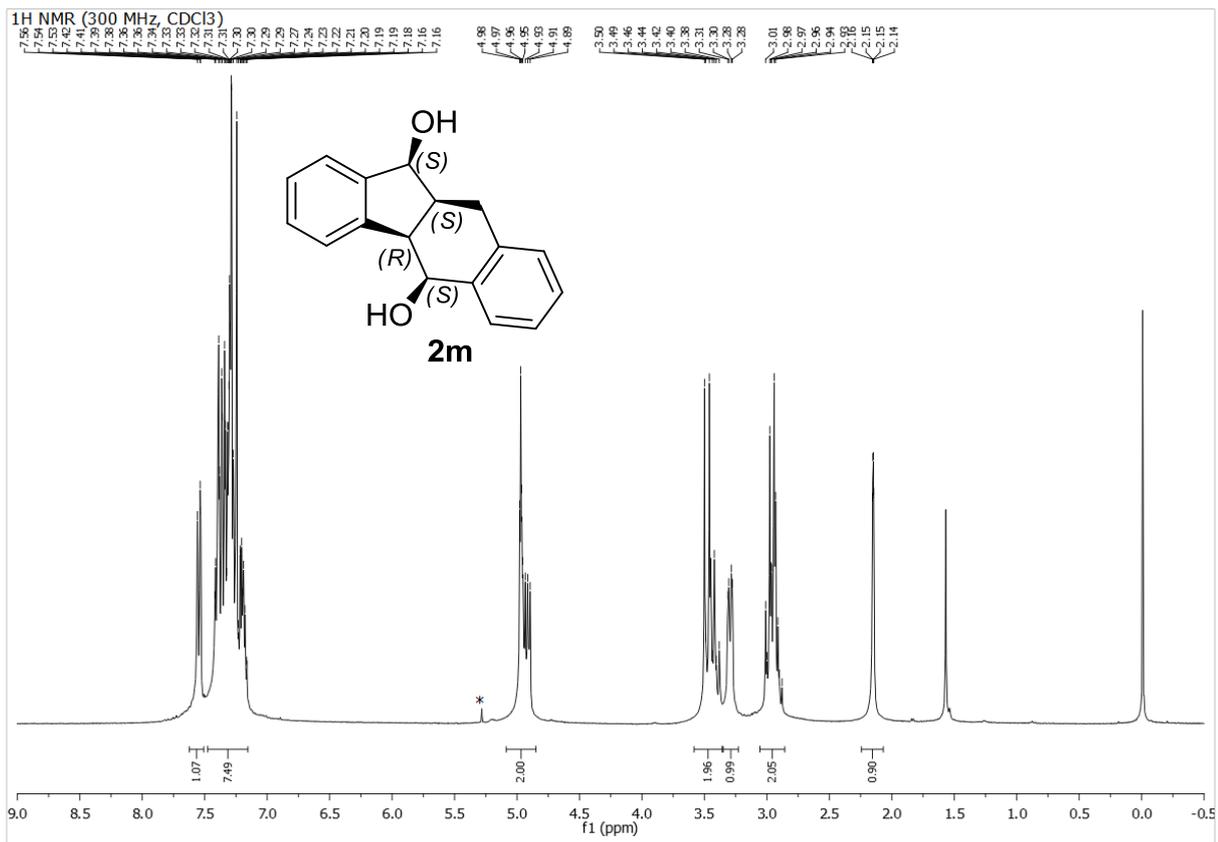


Observation: CH-Ar has a NOE of the same order of magnitude with CH-OH and CH-CO . There is a NOE between CH-OH and CH-CO .

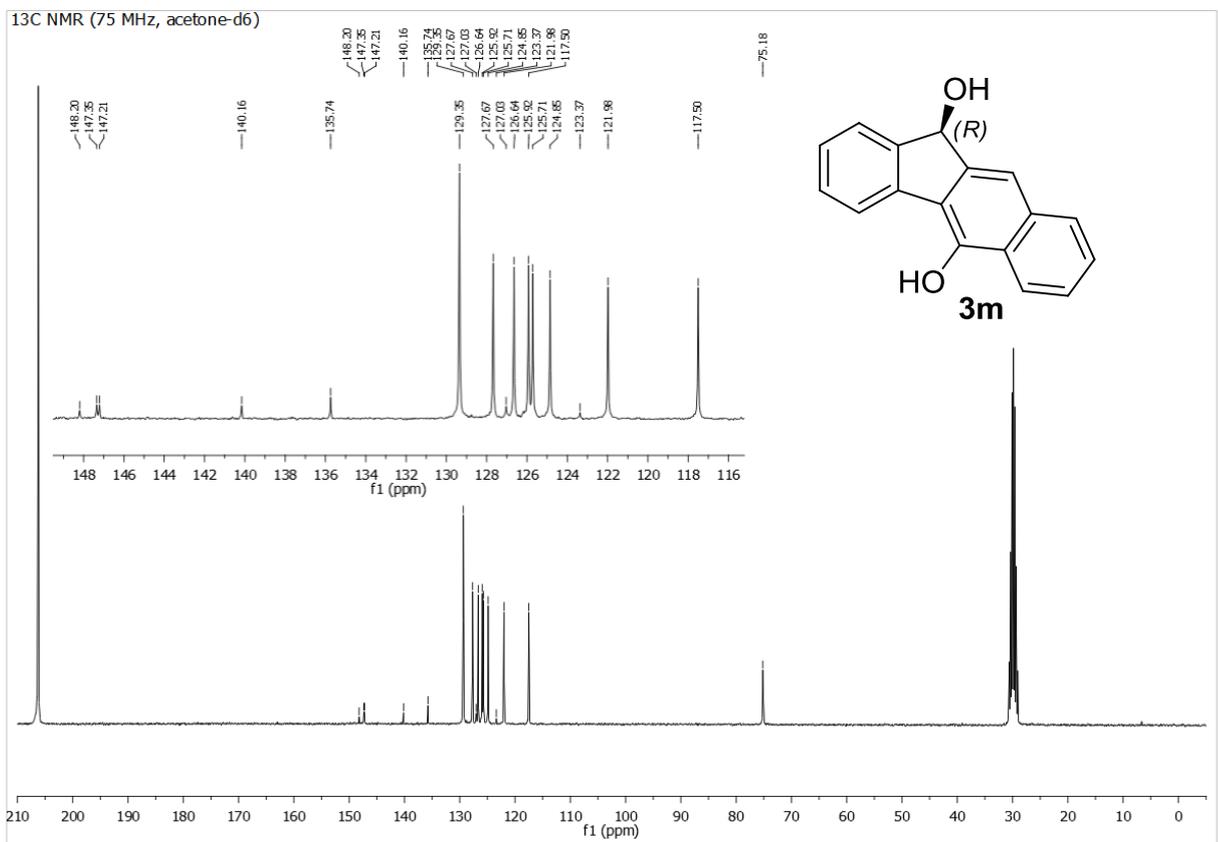
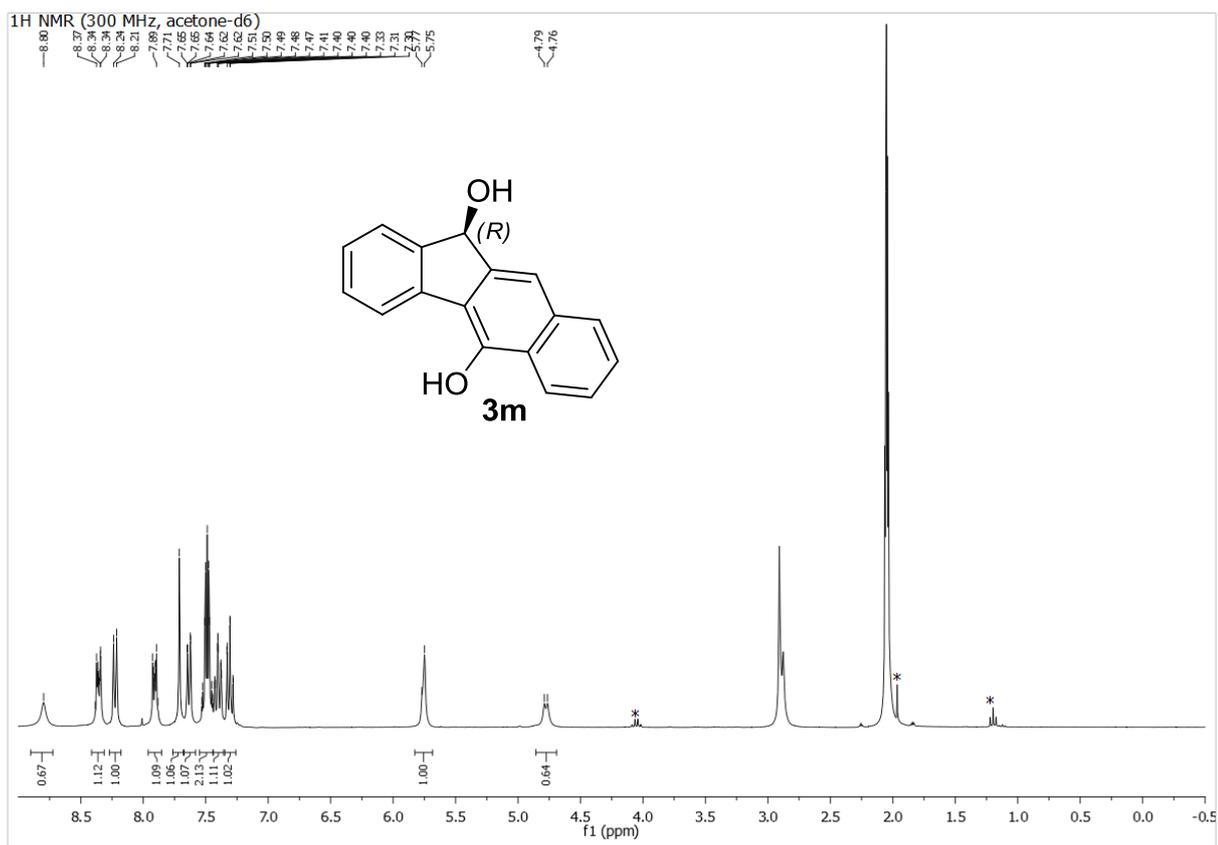
The geometries were optimized in ChemBio3D Ultra. Visualization and distance calculation was performed with UCSF Chimera.

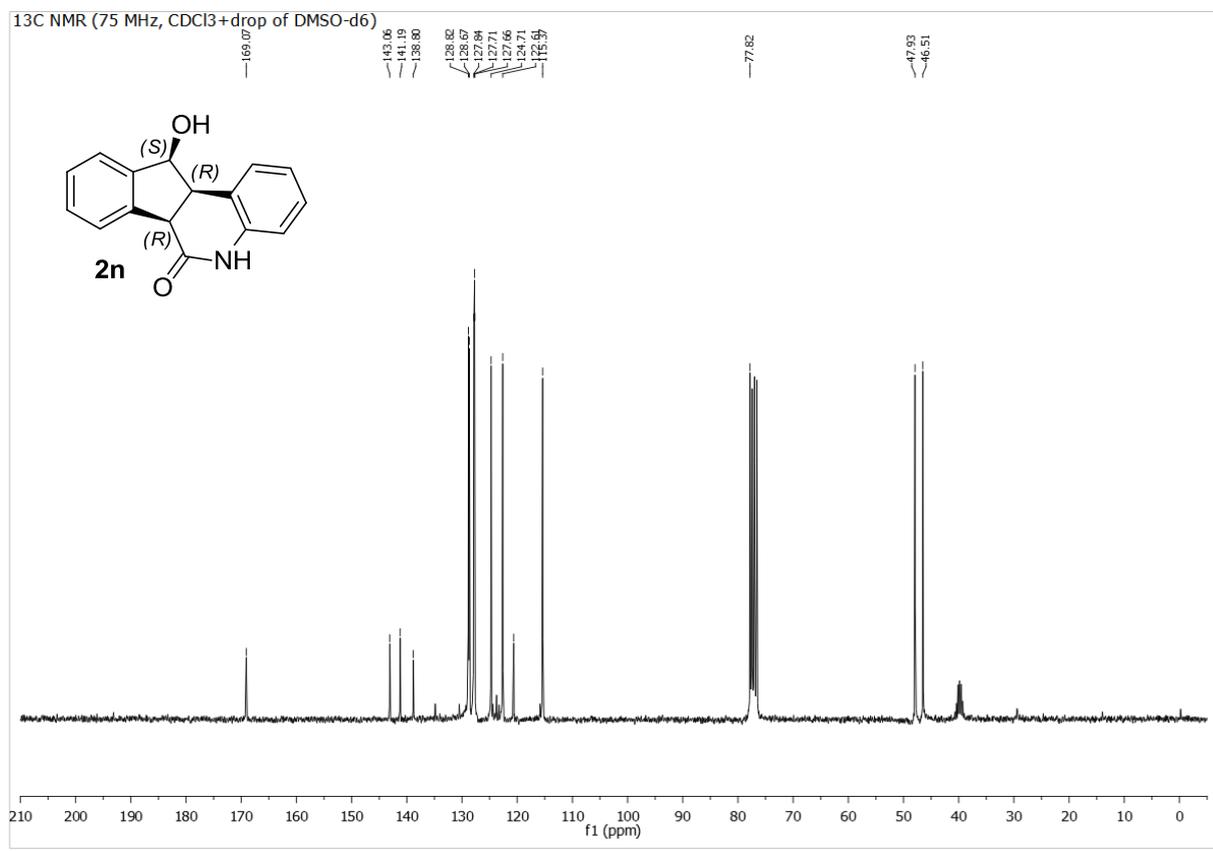
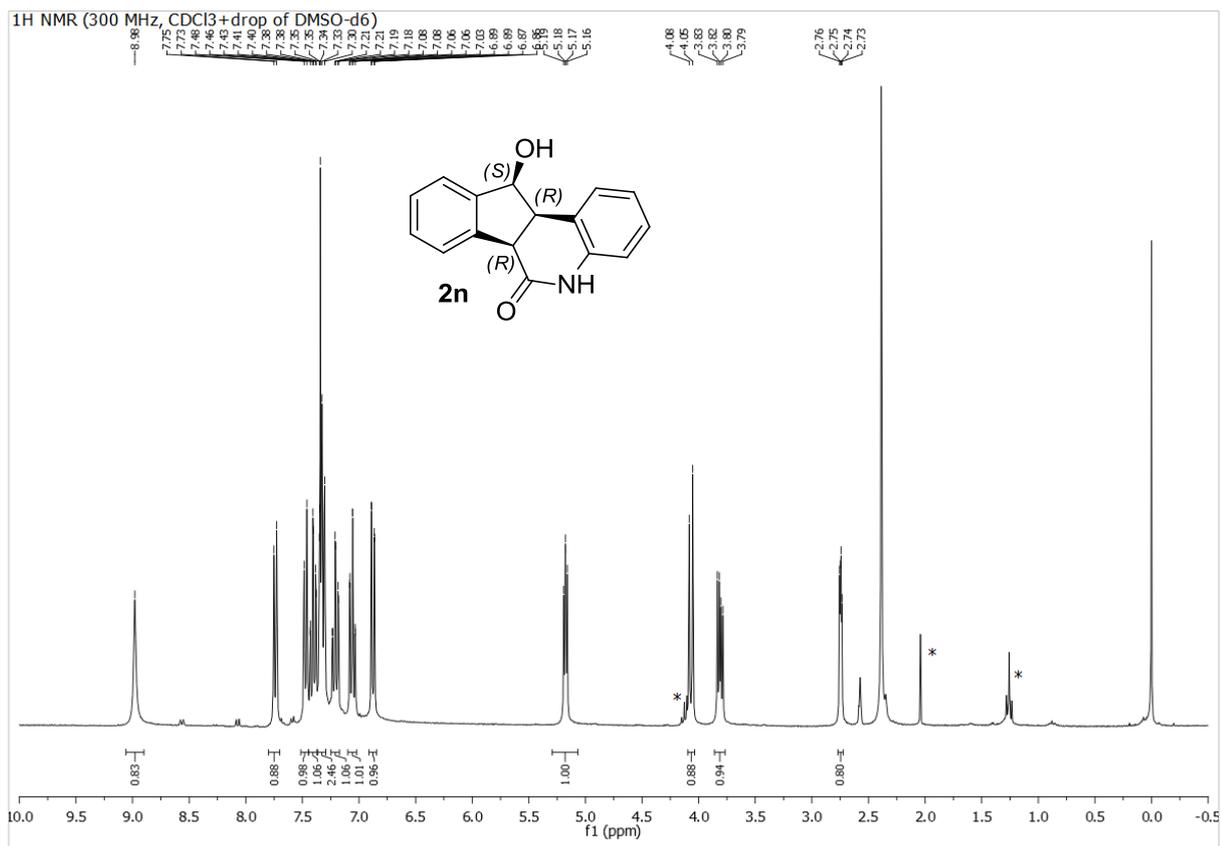






*dichloromethane

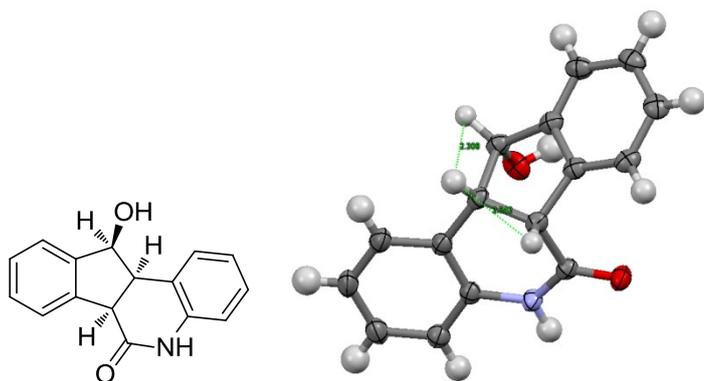




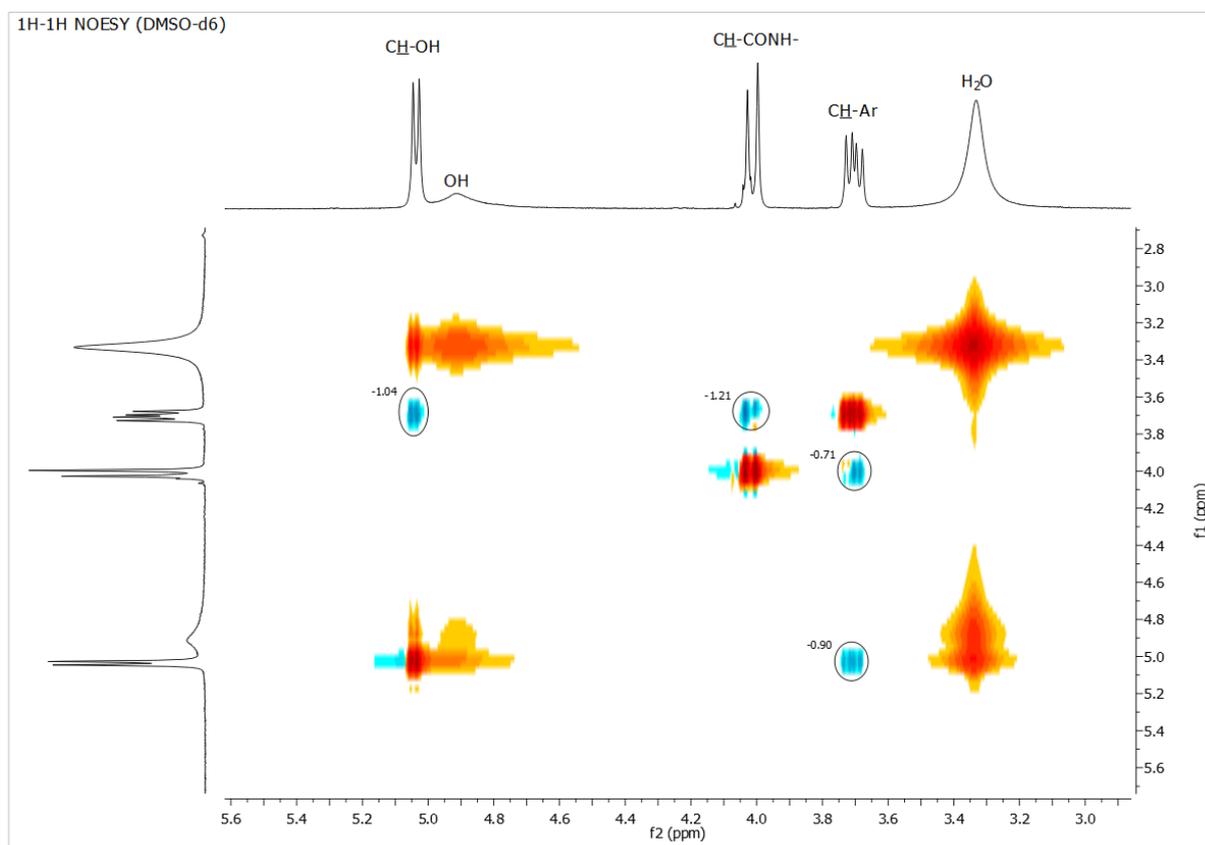
*Ethyl acetate

^1H - ^1H NOESY spectrum of *cis,cis*-2m

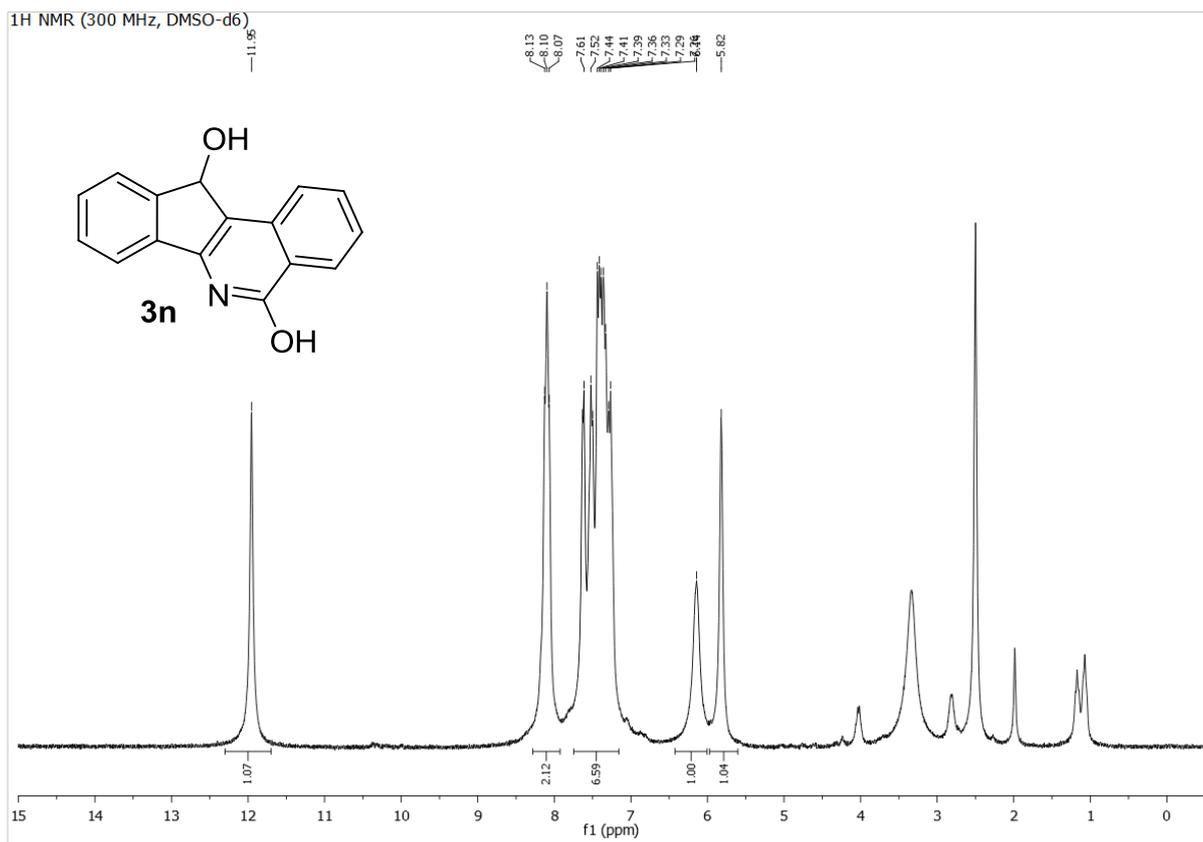
Measured relevant distances:



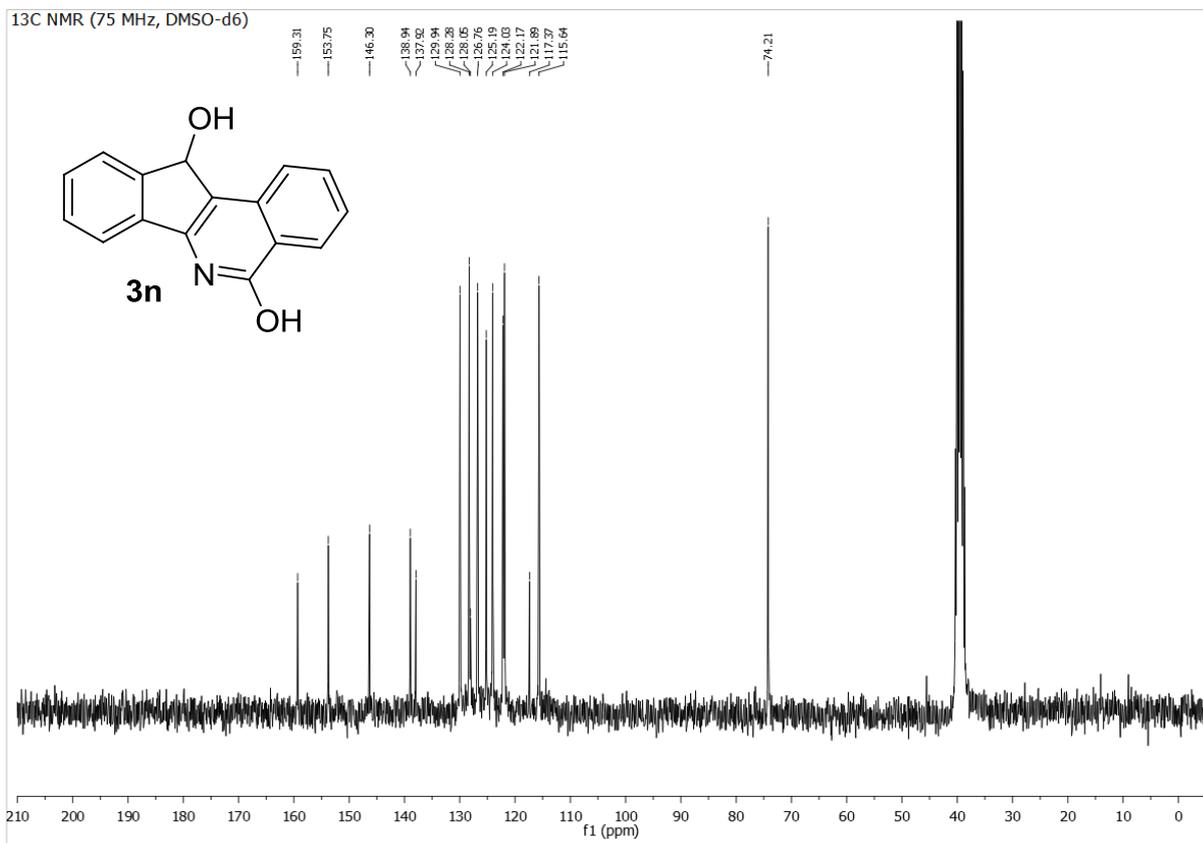
Observation: CH-Ar has a NOE of the same order of magnitude with CH-OH and CH-CONH . The measured distances are based on crystallographic data (see below).

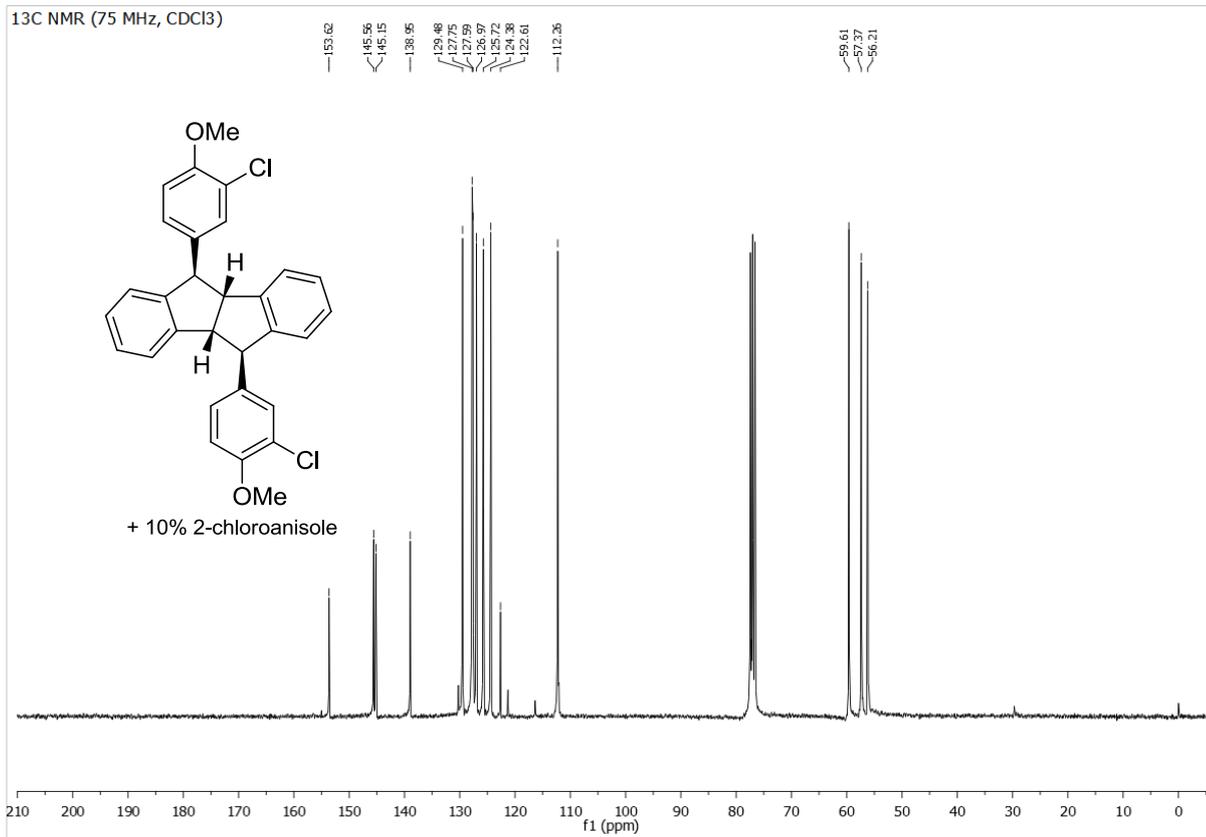
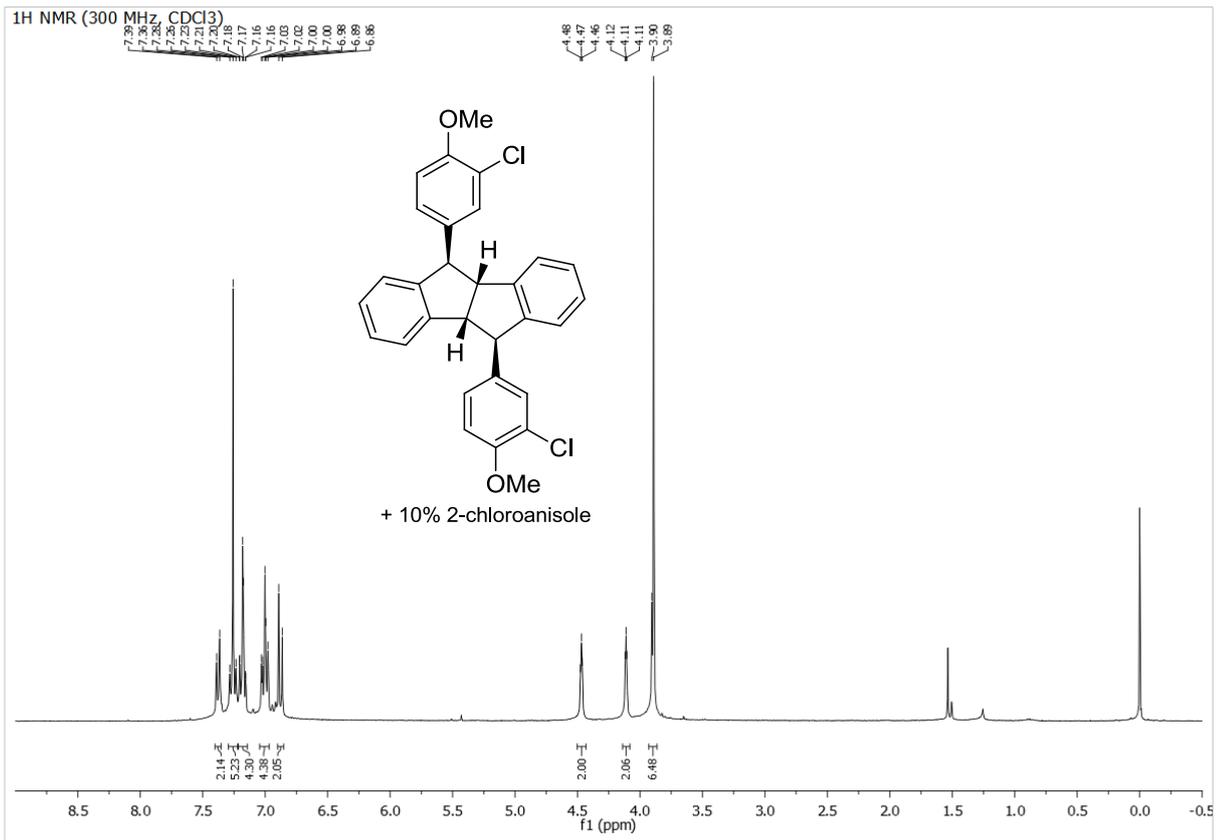


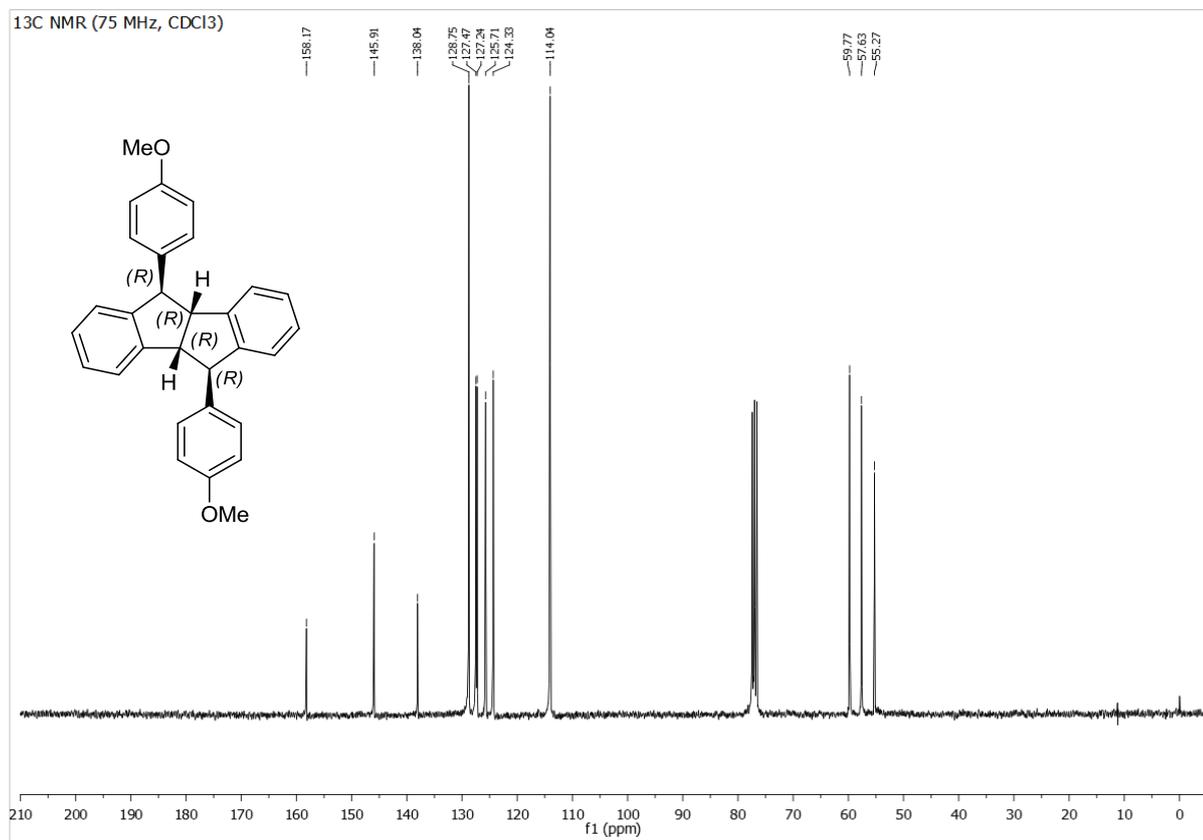
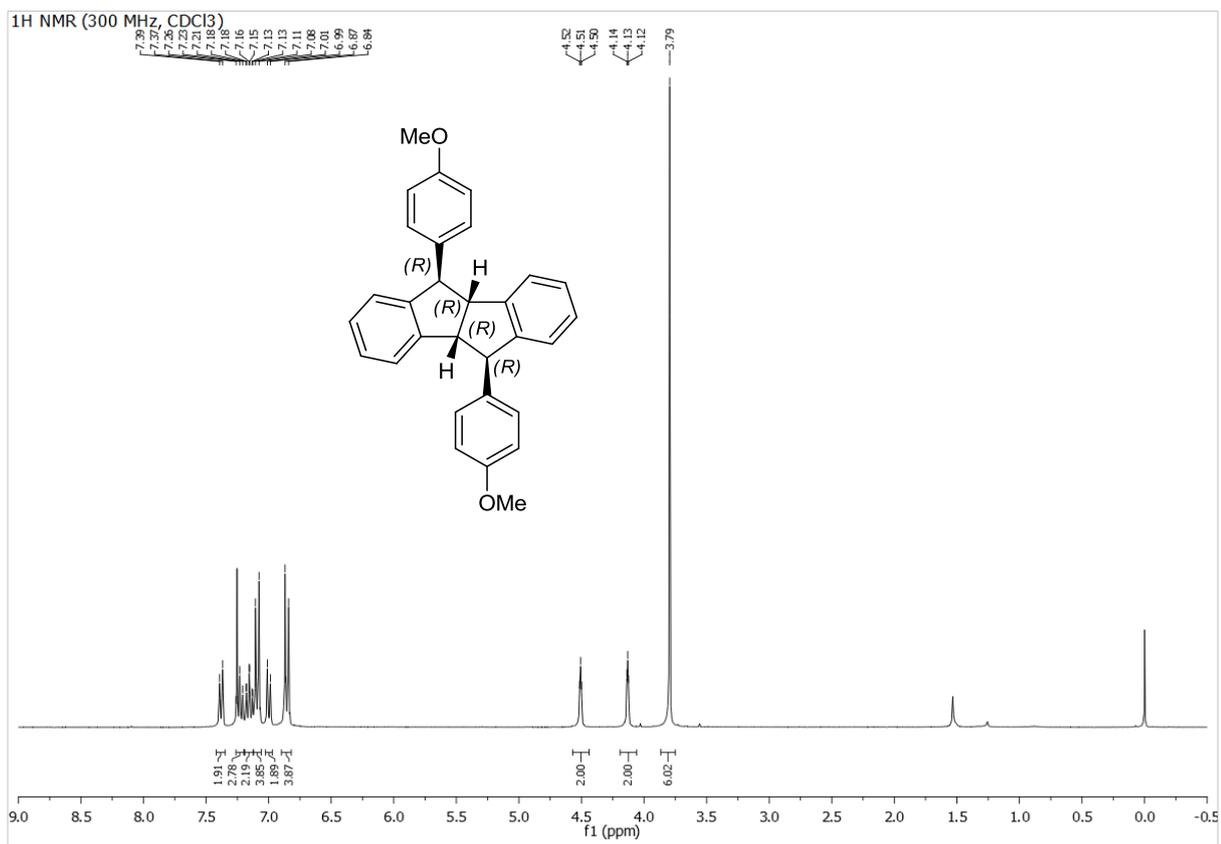
1H NMR (300 MHz, DMSO-d6)



13C NMR (75 MHz, DMSO-d6)

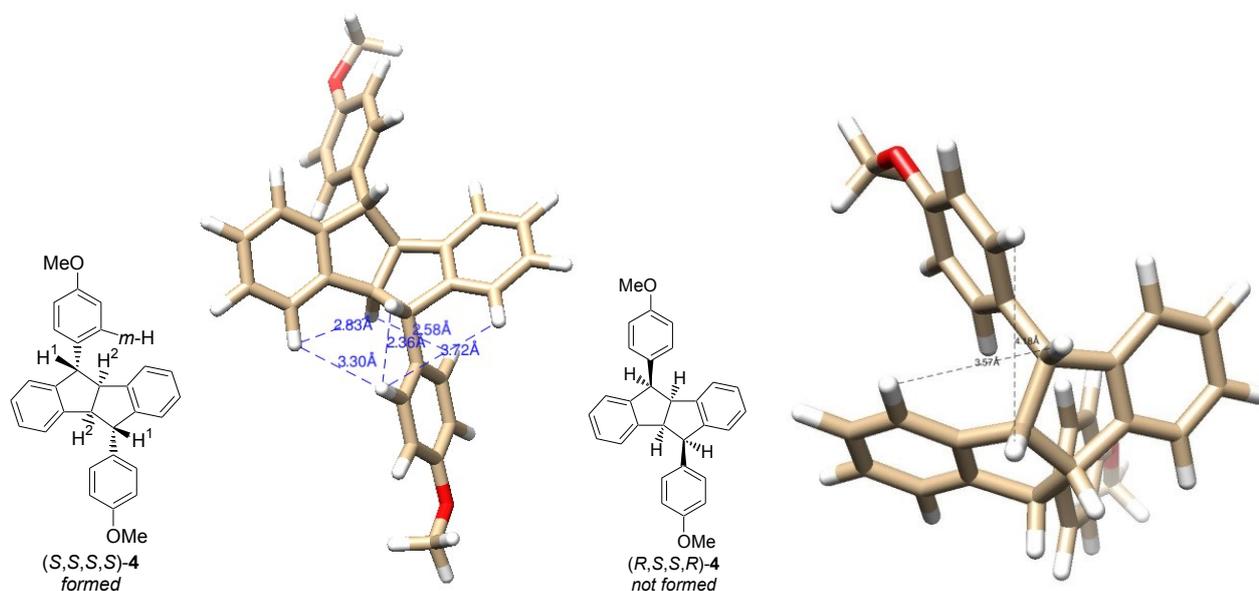






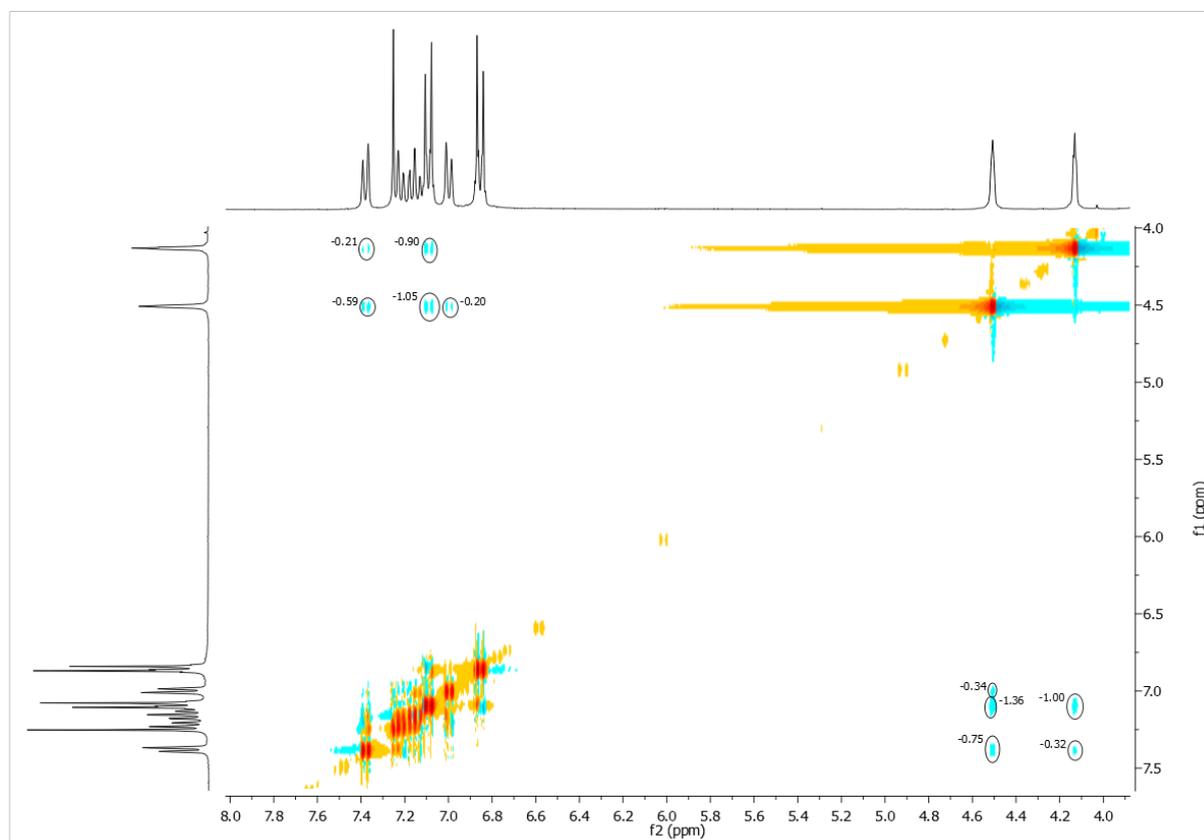
^1H - ^1H NOESY spectrum of the Pallidol analog **4**

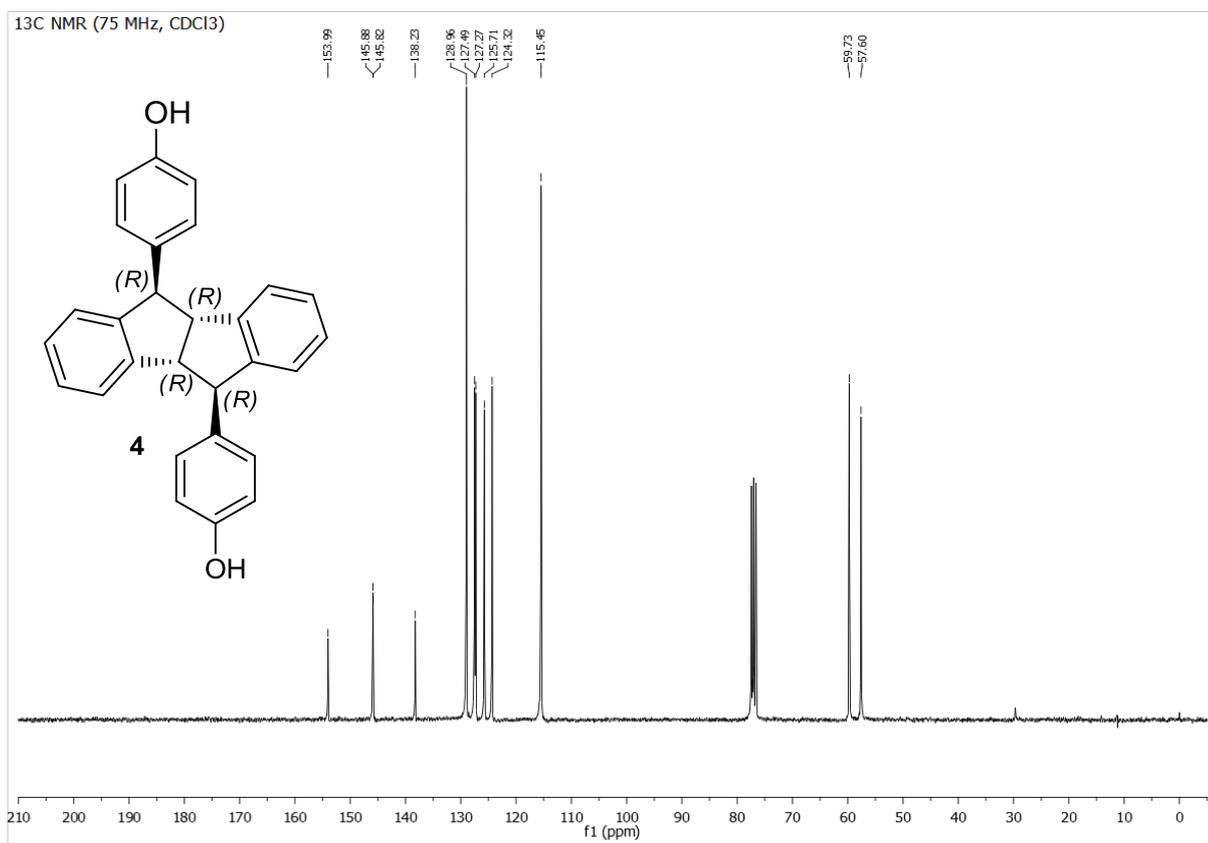
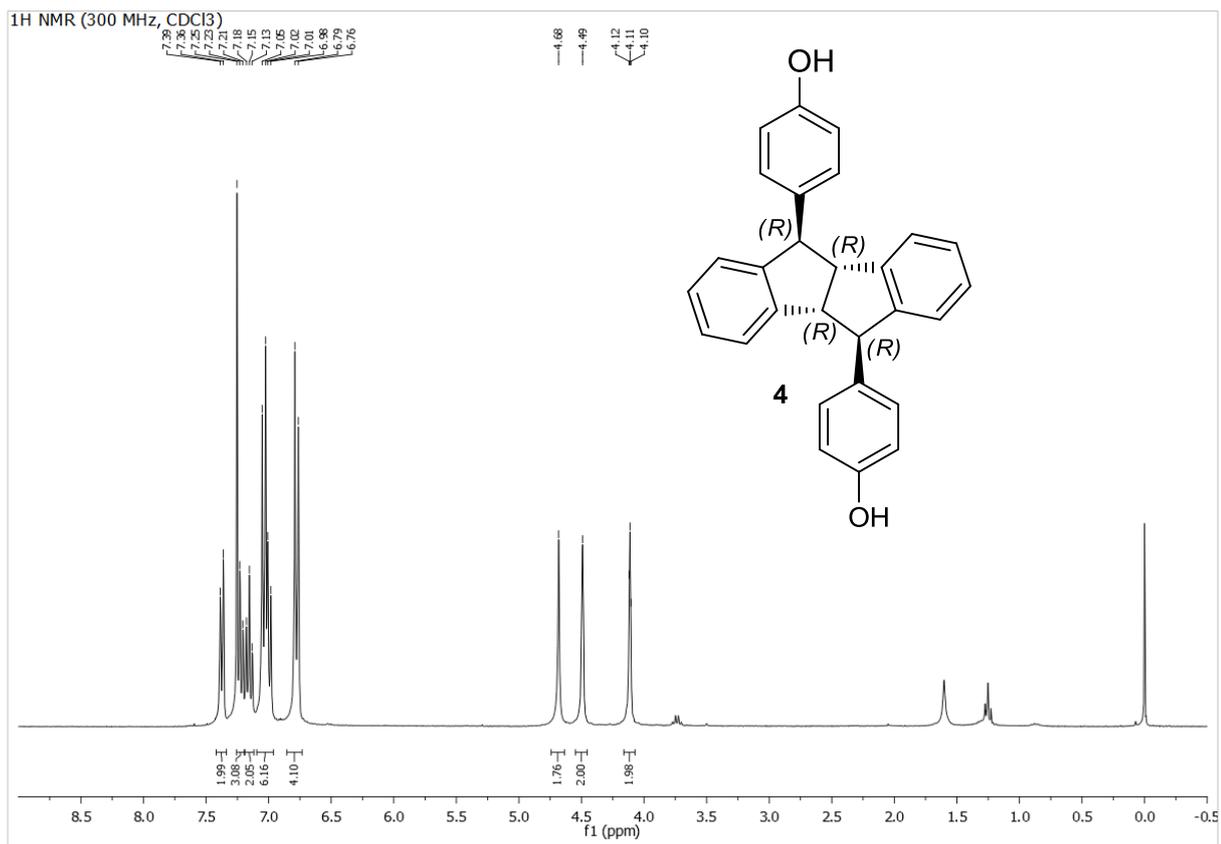
Calculated relevant distances:

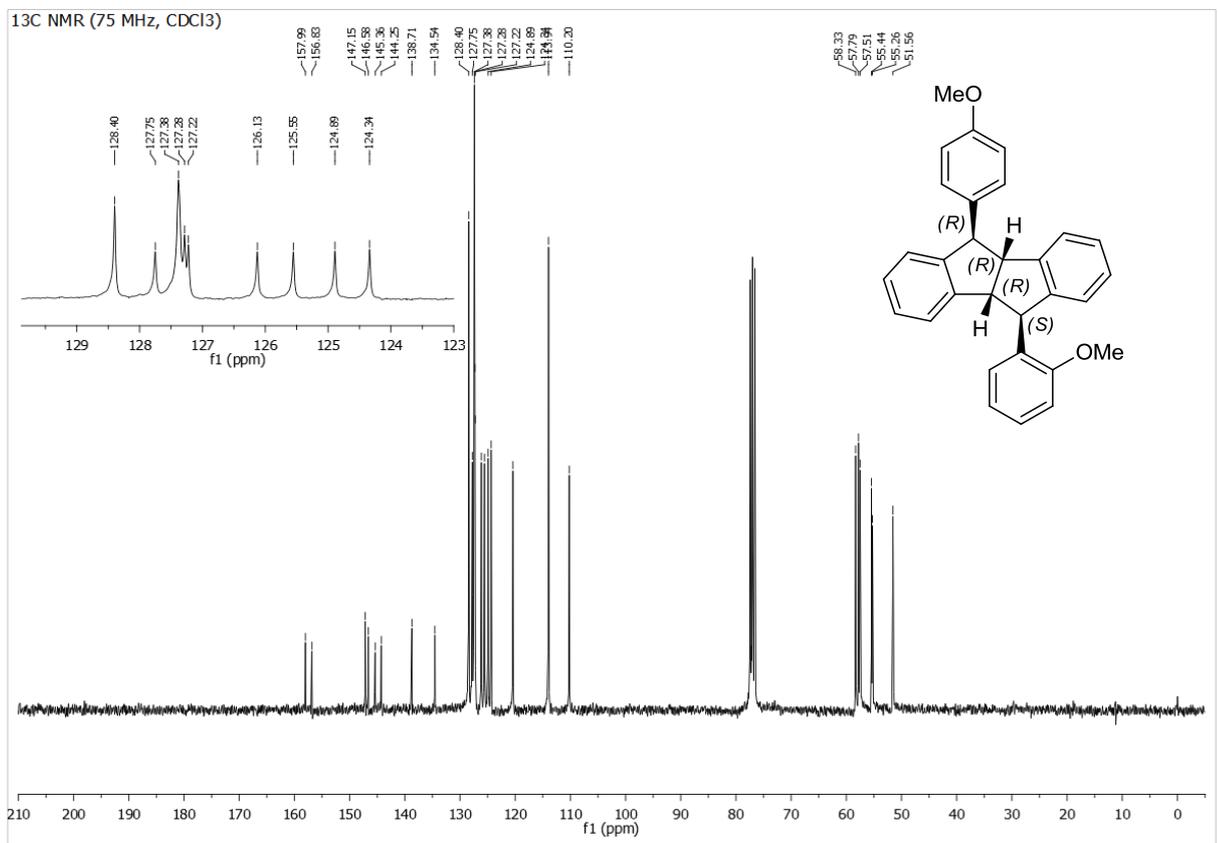
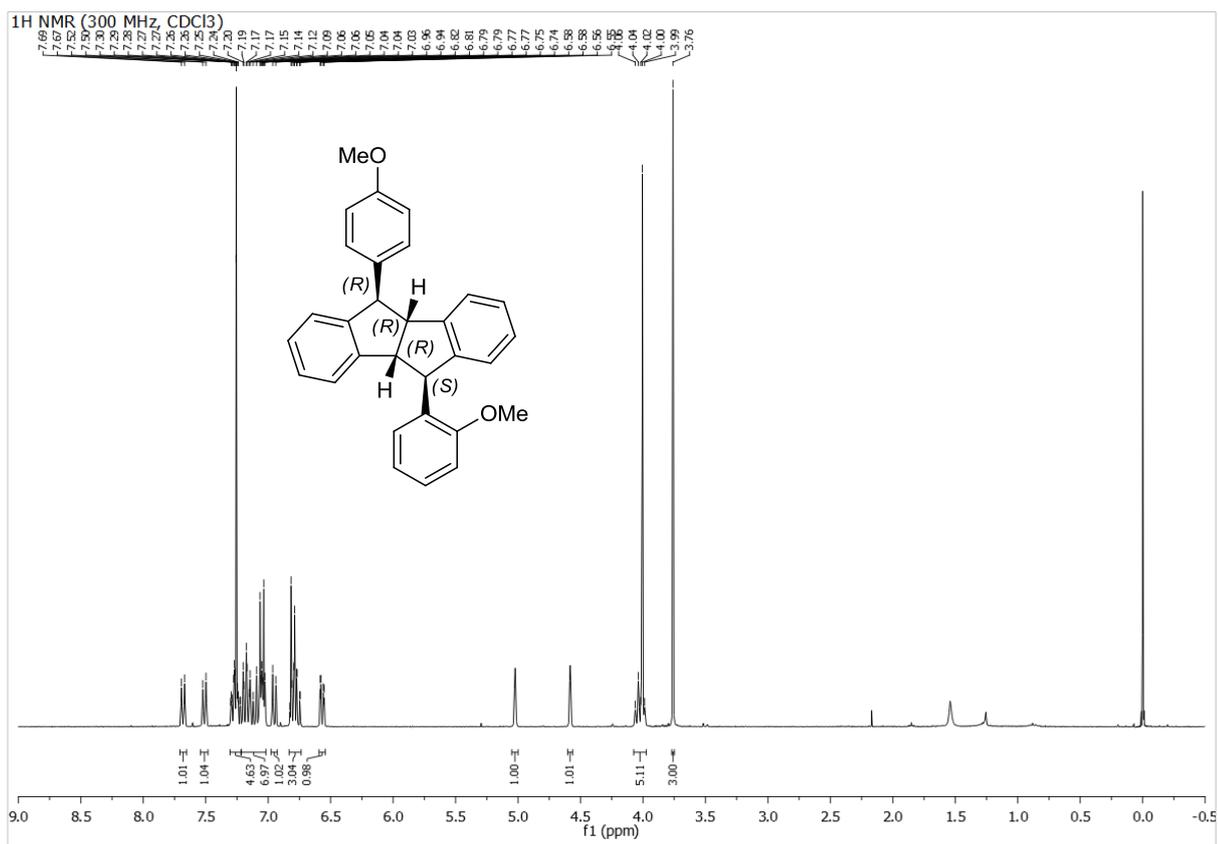


Observation: There is a NOE between H^2 and $m\text{-H}$ of the anisyl moiety in product **4**, which confirms its *trans,cis,trans*-disposition. The calculation revealed that in the *cis,cis,cis*-diastereomer (not formed) the distance between these hydrogens is beyond the 4 Å limit of the NOE range for small molecules. Also, NOEs $\text{H}^2/m\text{-H}$ and $\text{H}^1/m\text{-H}$ are of the same order of magnitude, which is expected for *trans,cis,trans*-disposition.

The geometries were optimized in ChemBio3D Ultra. Visualization and the distance calculation were performed with USCF Chimera.







9 X-ray structures of stereopure **2f**, **2h**, **2k**, **2m**, and **2n**

Determination of X-ray structures

Data for crystals of **2f**, **2h**, **2k**, **2m** and **2n** were collected on Agilent SuperNova diffractometer, using monochromated Cu-K α radiation ($\lambda = 1.54184 \text{ \AA}$) at 150 K. The coordinates of some or all of the non-hydrogen atoms were found *via* direct methods using the structure solution SHELXS-97 program.²⁸ Positions of the remaining non-hydrogen atoms were located by using a combination of least-squares refinement and difference Fourier maps in the SHELXL-97 program.²⁸

The absolute configurations were determined by refinement of the completed models together with the Flack x parameters,²⁹ which refined to values of 0.01(14) (**2f**), 0.3(5) (**2h**), 0.0(2) (**2k**), $-0.04(18)$ (**2m**) and 0.2(2) (**2n**). The values obtained for **2h** and **2n** were inconclusive. Figures depicting the structures were prepared by Ortep³⁰ and Mercury.³¹

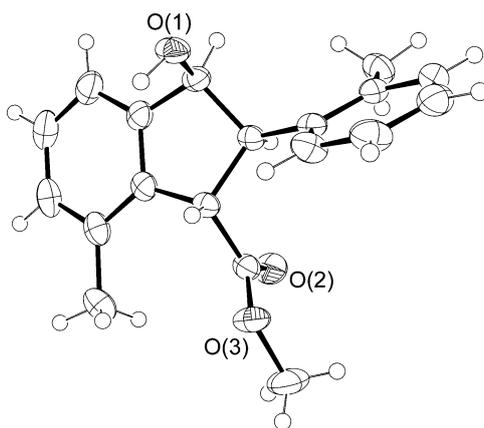


Figure S1. ORTEP drawing of **2f** at the 50% probability level. Selected bond lengths (\AA):

C(8)–O(1) 1.4284(14); C(11)–O(2) 1.2031(15); C(11)–O(3) 1.3327(16).

$\text{C}_{19}\text{H}_{20}\text{O}_3$, $M_r = 296.35$, tetragonal, space group $I4$ (No. 79), $a = 17.2805(2)$, $c = 10.8494(2) \text{ \AA}$,

$V = 3239.80(8) \text{ \AA}^3$, $Z = 8$, $T = 150(2) \text{ K}$, $d_{\text{calcd}} = 1.215 \text{ g cm}^{-3}$, $\mu = 0.650 \text{ mm}^{-1}$, 7231 measured reflections, 3287 unique reflections ($R_{\text{int}} = 0.0154$), 218 refined parameters, $R_1 [I > 2\sigma(I)] = 0.0306$, $wR2 [\text{all data}] = 0.0785$.

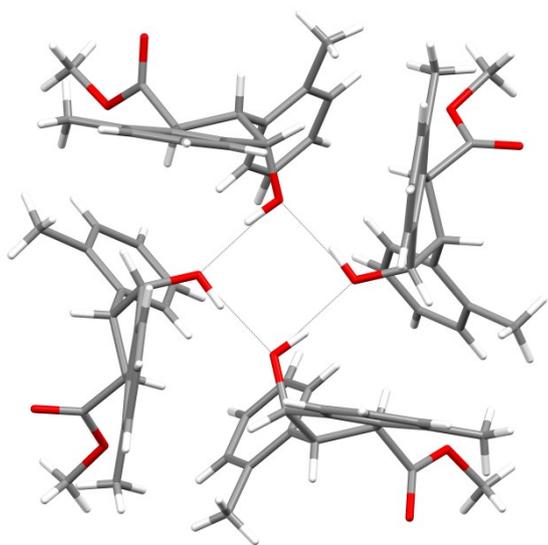


Figure S2. Hydrogen-bonding pattern in **2f**: a linkage of four hydroxyl functional groups into a tetranuclear assembly. The resulting pattern reflects a tetragonal symmetry: molecules are arranged around the central fourfold rotation axis. The distances between the hydroxyl oxygen atom and its two closest symmetry-related counterparts are $2.703(1) \text{ \AA}$ ^[32].

(28) Sheldrick, G. M.; SHELX-97. Programs for Crystal Structure Analysis, University of Göttingen: Göttingen, Germany, **1998**.

(29) Flack, H. D.; *Acta Crystallogr.* **1983**, *A39*, 876–881.

(30) Farrugia, L. J. *Appl. Crystallogr.* **1997**, *30*, 565.

(31) Macrae, C. F.; Bruno, I. J.; Chisholm, J. A.; Edgington, P. R.; McCabe, P.; Pidcock, E.; Rodriguez-Monge, L.; Taylor, R.; van de Streek, J.; Wood, P. A. *J. Appl. Cryst.* **2008**, *41*, 466–470.

(32) The sum of the van der Waals radii for O atoms is 3.04 \AA . Data were taken from Douglas B.; McDaniel, D.; Alexander, J. *Concepts and Models of Inorganic Chemistry*, 3rd Ed., John Wiley and Sons: New York, 1994, p. 102.

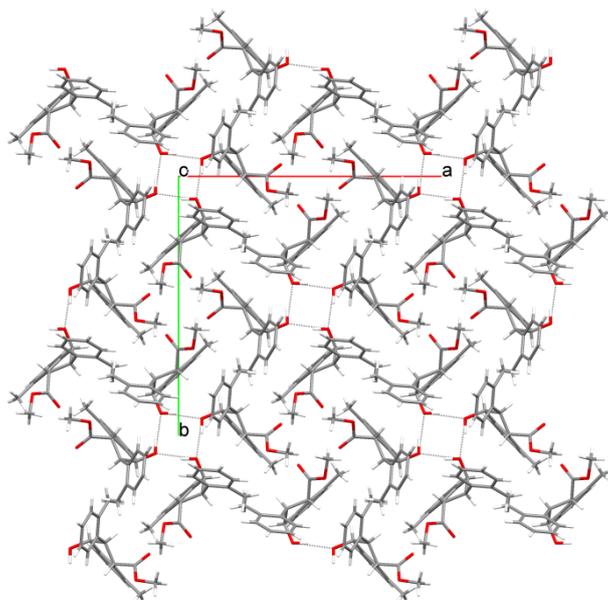


Figure S3. Packing of molecules **2f**; a view along *c* axis.

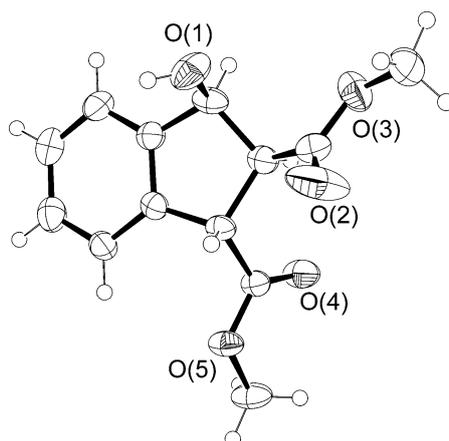


Figure S4. ORTEP drawing of **2h** at the 50% probability level. Selected bond lengths (Å): C(7)–O(1) 1.435(5); C(10)–O(2) 1.200(6); C(10)–O(3) 1.339(5); C(12)–O(4) 1.199(4); C(12)–O(5) 1.328(4). The shortest intermolecular interaction of OH moiety is longer than the sum of the van der Waals radii for oxygen atoms, O(1)⋯O(1) [$x+0.5, -y+0.5, -z$] = 3.060(2) Å. $C_{13}H_{14}O_5$, $M_r = 250.24$, orthorhombic, space group $P 2_1 2_1 2_1$ (No. 19), $a = 5.8404(4)$, $b = 13.9914(12)$, $c = 14.7857(13)$ Å, $V = 1208.22(17)$ Å³, $Z = 4$, $T = 150(2)$ K, $d_{\text{calcd}} = 1.376$ g cm⁻³, $\mu = 0.893$ mm⁻¹, 4697 measured reflections, 2413 unique reflections ($R_{\text{int}} = 0.0521$), 181 refined parameters, $R_1 [I > 2\sigma(I)] = 0.0712$, $wR2$ [all data] = 0.1744.

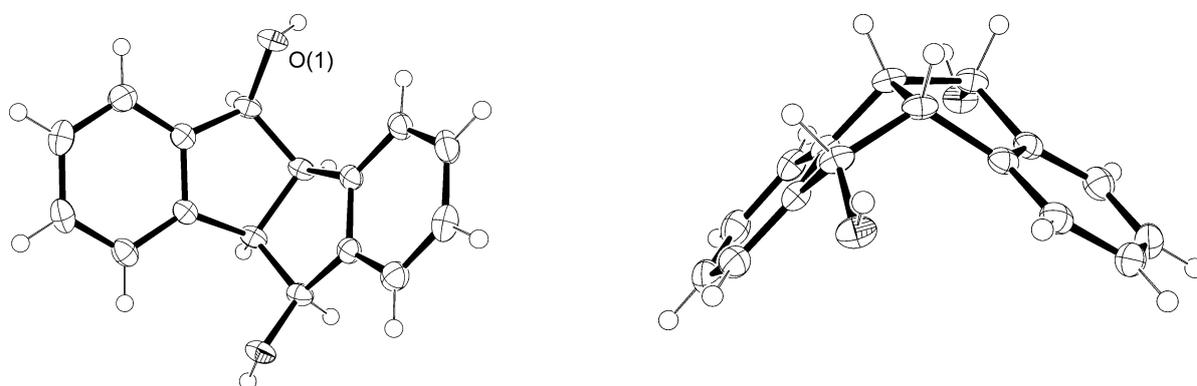


Figure S5. ORTEP drawing of **2k** in two orientations at the 50% probability level. The molecule is disymmetric: a C_2 rotation axis passes through the center of the molecule and relates the two halves. Selected bond length (\AA): C(8)–O(1) 1.4272(13). As shown in the right drawing, the molecule is folded around its center. The value of the dihedral angle between the two aromatic planes is $81.17(3)^\circ$.

$C_{16}H_{14}O_2$, $M_r = 238.27$, monoclinic, space group $I 2$ (No. 5), $a = 13.3374(8)$, $b = 4.7790(3)$, $c = 9.9126(7) \text{\AA}$, $\beta = 110.578(8)^\circ$, $V = 591.51(7) \text{\AA}^3$, $Z = 2$, $T = 150(2) \text{K}$, $d_{\text{calcd}} = 1.338 \text{ g cm}^{-3}$, $\mu = 0.695 \text{ mm}^{-1}$, 2277 measured reflections, 1153 unique reflections ($R_{\text{int}} = 0.0164$), 94 refined parameters, $R_1 [I > 2\sigma(I)] = 0.0270$, $wR2$ [all data] = 0.0685.

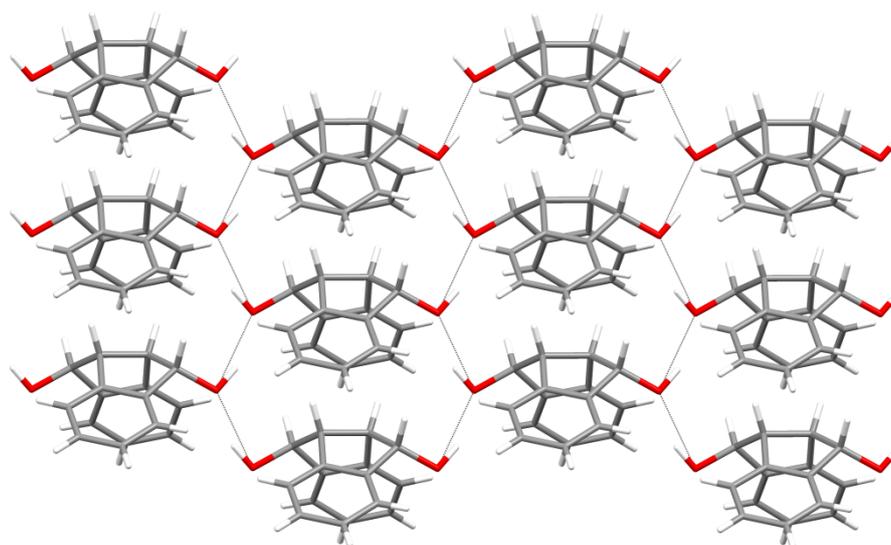


Figure S6. Hydrogen-bonding pattern in **2k**: molecules are linked via OH...OH contacts into layers. The O(1)...O(1) $[-x+0.5, y+0.5, -z+2.5]$ contact is $2.7646(8) \text{\AA}$.

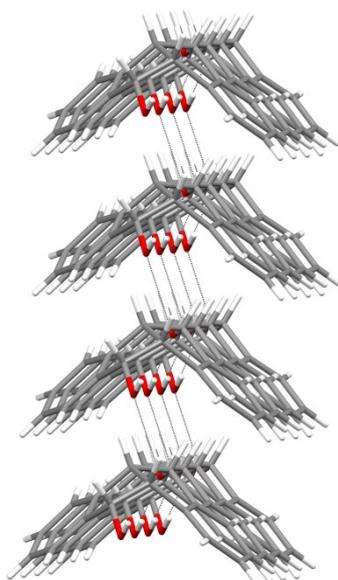


Figure S7. A view along the layer in **2k**: with molecules being folded, a stacking pattern may be observed.

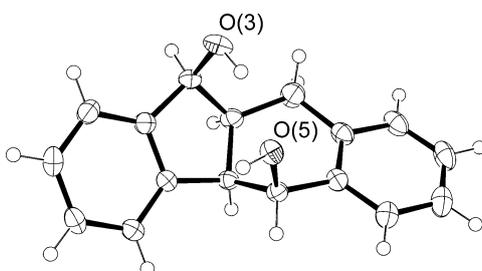


Figure S8. ORTEP drawing of **2m** at the 50% probability level. Selected bond lengths (Å): C(3)–O(3) 1.4361(15); C(5)–O(5) 1.4404(13).

$C_{17}H_{16}O_2$, $M_r = 252.30$, orthorhombic, space group $P 2_1 2_1 2_1$ (No. 19), $a = 8.23270(10)$, $b = 10.4035(2)$, $c = 14.8466(3)$ Å, $V = 1271.59(4)$ Å³, $Z = 4$, $T = 150(2)$ K, $d_{\text{calcd}} = 1.318$ g cm⁻³, $\mu = 0.675$ mm⁻¹, 6788 measured reflections, 2595 unique reflections ($R_{\text{int}} = 0.0202$), 205 refined parameters, $R_1 [I > 2\sigma(I)] = 0.0297$, $wR2$ [all data] = 0.0758.

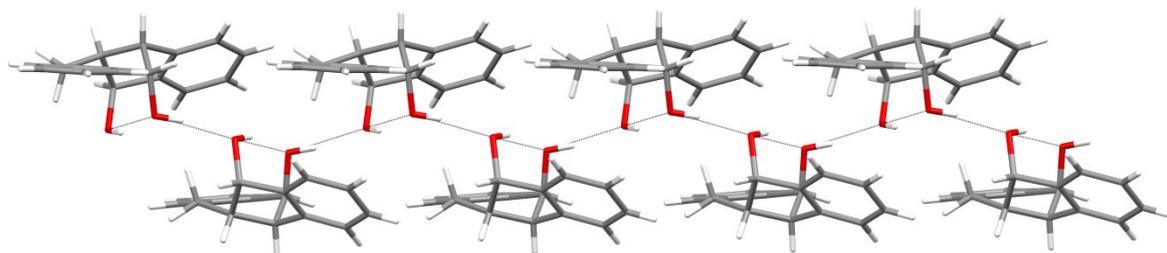


Figure S9. Hydrogen-bonding pattern in **2m**: molecules are linked *via* intra- [O(3)⋯O(5) = 2.732(1) Å] and intermolecular {O(5)⋯O(3) [$x-0.5, -y+0.5, -z+1$] = 2.797(1) Å} hydrogen bonds between adjacent hydroxyl moieties into chains that propagate along a axis.

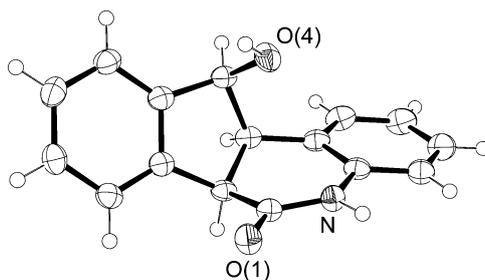


Figure S10. ORTEP drawing of **2n** at the 50% probability level. Selected bond lengths (Å): C(4)–O(4) 1.4275(19); C(1)–O(1) 1.2317(18); C(1)–N 1.346(2); C(15)–N 1.4103(19).

$C_{16}H_{13}NO_2$, $M_r = 251.27$, orthorhombic, space group $P 2_1 2_1 2_1$ (No. 19), $a = 7.8260(2)$, $b = 8.9097(3)$, $c = 17.4520(5)$ Å, $V = 1216.88(6)$ Å³, $Z = 4$, $T = 150(2)$ K, $d_{\text{calcd}} = 1.372$ g cm⁻³, $\mu = 0.732$ mm⁻¹, 5904 measured reflections, 2486 unique reflections ($R_{\text{int}} = 0.0318$), 193 refined parameters, $R_1 [I > 2\sigma(I)] = 0.0340$, $wR2$ [all data] = 0.0881.

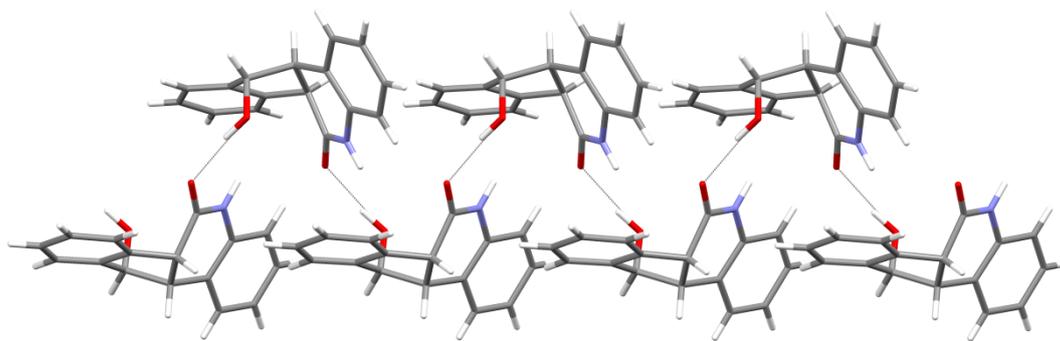


Figure S11. Hydrogen-bonding pattern in **2n**: molecules are linked *via* O–H...O = C interactions into chains that propagate along a axis. The O(4)···O(1) [$x+0.5, -y+0.5, -z+1$] contact is 2.784(2) Å.