Supporting Information

Selective Formation of Functionalized α-Quaternary Malononitriles Towards 5,5-Disubstituted Pyrrolo Pyrimidinones

Alan Whitehead[a,*], Yong Zhang[a,*], Jamie McCabe Dunn[b], Edward Sherer[c], Yu-hong Lam[c], John Stelmach[a], Aaron Sun[a], Melisa Shiroda[a], Robert Orr[b], Sherman T. Waddell[a], and Subharekha Raghavan[a]

[a]*Discovery Chemistry, Merck & Co., Inc., 2000 Galloping Hill Road, Kenilworth, NJ 07033, USA*

[b]*Process Chemistry, Merck & Co., Inc., PO Box 2000, Rahway, NJ 07065, USA*

[c]*Modeling and Informatics, Merck & Co., Inc., PO Box 2000, Rahway, NJ 07065, USA*

* Corresponding author: alan_whitehead@merck.com; yong_zhang@merck.com

Experimental details and characterization data

General Information

All air/moisture sensitive reactions were carried out under an inert atmosphere. The anhydrous solvents were purchased from Aldrich without further treatment. TLC was purchased from Merck KGaA (silica gel 60 with an F254 indicator); visualized under UV light (254 nm) and/or by staining with KMnO4 (10% aq.). Flash column chromatography were performed with Teledyne Isco RediSep Rf Gold® columns (400-632 mesh size, 20-40 um spherical particle size).

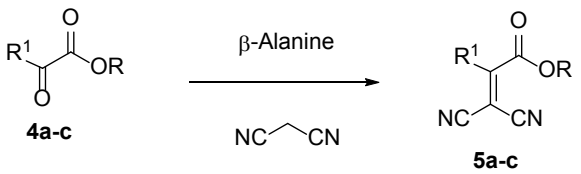
1H NMR (400 or 500 MHz), and 13C NMR (101 MHz) spectra were recorded on Oxford NMR AS400 or 500 in DMSO-d_6 solution. Chemical shifts are reported in δ units using DMSO-d_6 as an internal standard (δ 3.330 ppm 1H, δ 39.520 ppm 13C, respectively). Coupling constants (*J*) are recorded in Hz. The following abbreviations are employed for the multiplicity of the peaks: s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sept (septet), br (broad), and m (multiplet).

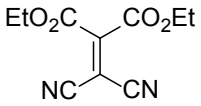
Electrospray mass spectra were obtained using a Micromass platform mass analyser with an electrospray ion source.

Optical rotations were obtained on PerkinElmer Model 341 Polarimeter using Na lamp D line (589nm) at 20 ^{o}C and 1 mL cell with 10 cm length.

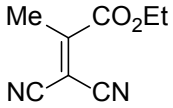
Chiral HPLC analysis and separation were carried out on Diacel Chiralpak® AD-H column or IA column eluting with alcohol/CO_2.

Analytical HPLC were obtained on Hewlett Parkard 1100 Series using Supleco Accentis® Express C18 column (10 cm X 3mm, 2.7 μM).

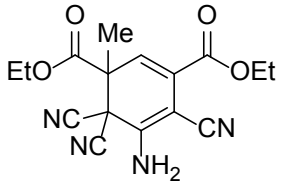




Diethyl 2-(dicyanomethylene)malonate (**5a**). Compound was prepared from commercial available diethyl 2-oxomalonate (**4a**) following reference procedure.[1]
Yield: 74%, pale yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.39 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.28, 149.15, 110.33, 97.68, 63.94, 13.52. LC-MS ($M+H^+$): 222.96.

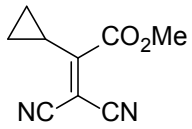


Ethyl 3,3-dicyano-2-methylacrylate (**5b**). Compound was prepared from commercial available ethyl 2-oxopropanoate (**4b**) following reference procedure.[2]
Yield: 89%, colorless oil, stored in benzene (1M or 2M) at –20 ^{o}C.

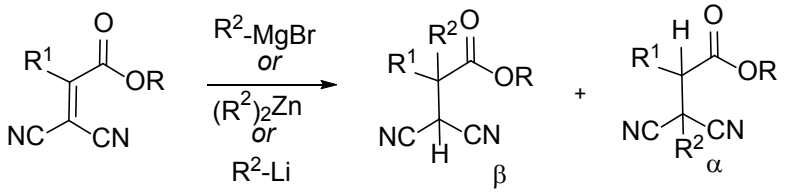


Diethyl 5-amino-4,4,6-tricyano-3-methylcyclohexa-1,5-diene-1,3-dicarboxylate (6).
Product **6** was formed as a byproduct during the reaction to form **5b**. **5b** was purified via distillation according to reference 2 of the SI and attempts to isolate **5b** by silica chromatography significantly promoted formation of **6**. The amount of **6** that was formed during the reaction varied (~5-20% based on 1H NMR yield), and appeared to be influenced by the purity of the ethyl 2-oxopropanoate SM. Drying agent was not used during the workup as this promoted the dimerization event (most noteably $MgSO_4$). A small portion of the reaction was purified by silica gel flash chromatography (0-50% EtOAc in hexanes) to obtain pure **6** for analysis.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.60 (s, 1H), 5.73 (s, 2H), 4.38-4.29 (m, 4H), 1.74 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H), 1.35 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.33, 162.43, 147.19, 127.09, 127.40, 115.15, 110.71, 110.67, 76.38, 63.99, 62.55, 51.52, 44.02, 19.51, 14.11, 13.97. HRMS (ESI) *m/z* calcd for $C_{16}H_{17}N_4O_4$ $[M+H]^+$: 329.1250, found 329.1244.

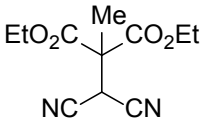


Methyl 3,3-dicyano-2-cyclopropylacrylate (**5c**). Prepared from commercial available methyl 2-cyclopropyl-2-oxoacetate (**4c**) following general procedure for **8**.
Yield: 87%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.87 (s, 3H), 2.26 (tt, J = 8.1, 4.7 Hz, 1H), 1.51 – 1.43 (m, 2H), 1.27 – 1.20 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.14, 162.11, 111.49, 111.36, 85.70, 54.06, 17.12, 13.00. HRMS (ESI) *m/z* calcd for $C_9H_9N_2O_2$ $[M+H]^+$: 177.0664, found 177.0



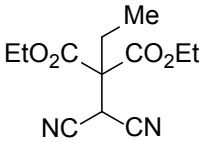
General Procedure:

Dicyano acrylate (1 mmol) was taken up in THF (1 mL) under an atmosphere of N_2, and the solution was cooled (0 °C - 78 °C; see below). Grignard reagent (1.5 mmol) was added and the reaction was monitored by LCMS or TLC. Upon completion, the reaction was quenched with sat'd $NH_4^+Cl^-$ (1 mL) and further diluted with water (1 mL). The layers were separated and the organic layer was extracted with brine. The organic phase was dried (Mg_2SO_4) and concentrated under reduced pressure followed by silica gel flash chromatography.The ratio of regiosiomers was determined by crude product ^{1}H NMR spectra.



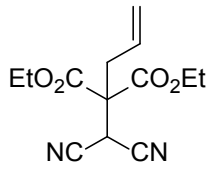
Diethyl 2-(dicyanomethyl)-2-methylmalonate (1a).

The reaction was run at 0 °C for 30 minutes. Front major peak from silica gel column chromatography was isolated (Petroleum ether-EtOAc 1-10%). Yield: 57%, pale yellow oil, β:α (4:1) selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.72 (d, J = 0.7 Hz, 1H), 4.27 (qd, J = 7.1, 3.9 Hz, 4H), 1.62 (s, 3H), 1.22 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.79, 112.08, 63.03, 54.38, 28.54, 18.65, 13.62. HRMS (ESI) *m/z* calcd for $C_{11}H_{13}N_2O_4$ $[M-H]^-$: 237.0876, found 237.0873.

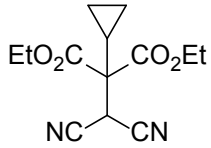


Diethyl 2-(dicyanomethyl)-2-ethylmalonate (1b).

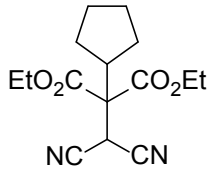
Reaction was run at -78 °C for 20min. Yield: 42%, colorless oil, β:α (2:1) selectivity. Front major peak from silica gel flash column chromatography was isolated (0-30%MTBE/Hexane). ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.76 (s, 1H), 4.29 (qd, J = 7.1, 1.3 Hz, 4H), 2.09 (q, J = 7.5 Hz, 2H), 1.23 (t, J = 7.1 Hz, 6H), 0.95 (t, J = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.43, 112.24, 62.93, 58.56, 26.73, 26.20, 13.67, 8.41. HRMS (ESI) *m/z* calcd for $C_{12}H_{15}N_2O_4$ $[M-H]^-$: 251.1032, found 251.1037.



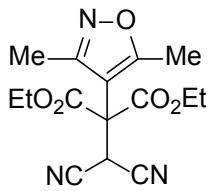
Diethyl 2-allyl-2-(dicyanomethyl)malonate (1c).
Reaction was run at -78 °C for 5min. Yield: 45%, colorless oil, β:α (3:1) selectivity. Front major peak from silica gel flash column chromatography was isolated (0-50%MTBE/Hexane). ^{1}H NMR (500 MHz, DMSO-d6) δ 5.82 - 5.67 (m, 1H), 5.61 (s, 1H), 5.35 - 5.22 (m, 2H), 4.28 (qd, J = 7.1, 1.9 Hz, 4H), 2.81 (d, J = 7.3 Hz, 2H), 1.23 (t, J = 7.1 Hz, 6H). ^{13}C NMR (126 MHz, DMSO-d6) δ 166.01, 129.61, 112.14, 112.10, 63.36, 63.15, 57.80, 36.97, 27.23, 26.77, 13.67. HRMS (ESI) *m/z* calcd for $C_{13}H_{17}N_2O_4$ $[M+H]^+$: 265.1183, found 265.1196.



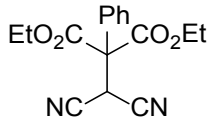
Diethyl 2-cyclopropyl-2-(dicyanomethyl)malonate (1d).
Reaction was run at -20 °C for 1.5 hours. Yield: 61%, colorless oil, β:α >20:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.73 (s, 1H), 4.27 (qd, *J* = 7.1, 1.9 Hz, 4H), 1.41 (tt, *J* = 8.5, 5.4 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 6H), 0.80 – 0.70 (m, 2H), 0.59 – 0.50 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.64, 112.28, 62.94, 59.17, 29.24, 13.97, 13.66, 3.12. HRMS (ESI) *m/z* calcd for $C_{13}H_{15}N_2O_4$ $[M-H]^-$: 263.1032, found 263.1030.



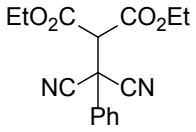
Diethyl 2-cyclopentyl-2-(dicyanomethyl)malonate (1e).
Reaction was run at 0 °C for 1 hour and was purified by silica gel flash column chromatography (0-30% EtOAc/Hexane). Yield: 24% of desired product 1d, pale yellow oil front minor peak. 43% of 1d-α, β:α (1:2) selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.72 (s, 1H), 4.29 (q, *J* = 7.1 Hz, 4H), 2.56 (q, *J* = 8.7 Hz, 1H), 1.87 – 1.72 (m, 2H), 1.68 – 1.43 (m, 6H), 1.24 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.38, 112.50, 62.75, 60.97, 43.13, 28.16, 27.95, 24.95, 13.69. HRMS (ESI) *m/z* calcd for $C_{15}H_{19}N_2O_4$ $[M-H]^-$: cal 291.1345, found 291.1350.



Diethyl 2-(dicyanomethyl)-2-(3,5-dimethylisoxazol-4-yl)malonate (1f).
3,5-dimethyl-4-iodoisoxazole (4 mmol) in THF (2.7 mL) was cooled to -10 °C under N_2, and i-PrMgCl•LiCl (1.3M in THF, 4.4 mmol) was added and was stirred for 2 h, then diethyl-2-(dicyanomethylene)malonate (**5a**, 3 mmol) in THF was added and warmed to room temperature for 2 minutes followed by general workup and separation. Yield: 49%, Off-white solid, β:α >20:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.89 (s, 1H), 4.45 (dq, J = 10.8, 7.1 Hz, 2H), 4.33 (dq, J = 10.8, 7.1 Hz, 2H), 2.30 (s, 3H), 2.12 (s, 3H), 1.25 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.57, 164.42, 157.86, 112.34, 107.11, 64.41, 56.73, 29.76, 13.47, 12.14, 10.54. HRMS (ESI) *m/z* calcd for $C_{15}H_{16}N_3O_5$ [M-H]$^-$: 318.1090, found 318.1086.

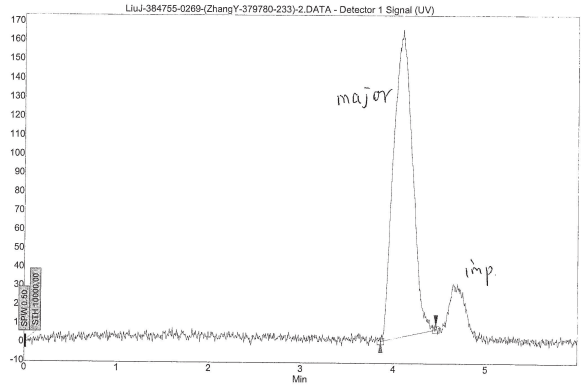


Diethyl 2-(dicyanomethyl)-2-phenylmalonate (1g).
Reaction was run at 0 °C for 30 minutes. Yield: 52%, white solid, β:α >20:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.56 – 7.41 (m, 3H), 7.38 – 7.27 (m, 2H), 6.19 (s, 1H), 4.45 – 4.27 (m, 4H), 1.23 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.94, 132.64, 129.41, 128.93, 127.76, 112.41, 63.78, 63.53, 30.33, 13.58. HRMS (ESI) *m/z* calcd for $C_{16}H_{15}N_2O_4$ [M-H]$^-$: 299.1032, found 299.1035.

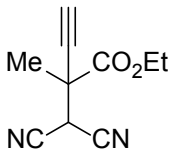


Diethyl 2-(dicyano(phenyl)methyl)malonate (1g-α).
To copper(I) iodide (2.6 mmol), THF (11.3 mL) was added and cooled to 0 °C under N_2. Phenylmagnesium bromide (5 mmol) was added dropwise and the solution was stirred for 30 minutes. Diethyl-2-(dicyanomethylene)malonate (**5a**, 2.3 mmol) in THF was added dropwise and aged for 1 hour before subject to general procedure workup. After silica gel flash column chromatography (0-30%EtOAc-Hexane), the regioisomers were separated by chiral SFC (Diol column, 20% 9:1 Hexane-EtOH/CO_2). β:α (1:5) selectivity. Yield: 47%, white solid, front major peak from chiral separation. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 – 7.67 (m, 2H), 7.63 – 7.50 (m, 3H), 5.44 (s, 1H), 4.21 – 4.07 (m, 4H), 1.07 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.96, 130.56, 129.76, 129.02, 126.62, 113.71, 62.63, 57.38, 40.68, 13.55. HRMS (ESI) *m/z* calcd for $C_{16}H_{15}N_2O_4$ [M-H]$^-$: 299.1032, found 299.1022.

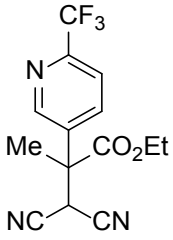
Preparative: Diol (3X25cm), 20% 9:1 Hexane-EtOH/CO_2,70mL/min, 100bar, 210nm, 35 ^oC, 56mg/mL/inj



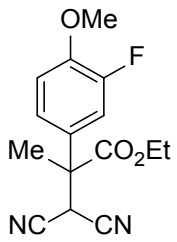
Peak 1 (**1g-α**), rt ~4.1min; peak-2 (**1g-β**), rt ~4.7min



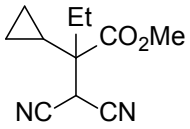
Ethyl 2-(dicyanomethyl)-2-methylbut-3-ynoate (1h).
Reaction was run at -78 ^oC for 1 hour. Yield: 71%, pale yellow oil, β:α >20:1 selectivity. ^1H NMR (400 MHz, DMSO-d_6) δ 5.64 (d, J = 0.7 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3.91 (d, J = 0.7 Hz, 1H), 1.66 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.64, 112.15, 78.75, 78.35, 63.25, 44.20, 31.81, 23.13, 13.67. HRMS (ESI) *m/z* calcd for $C_{10}H_9N_2O_2$ $[M-H]^-$: 189.0664, found 189.0658.



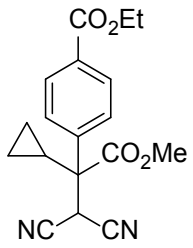
Ethyl 3,3-dicyano-2-methyl-2-(6-(trifluoromethyl)pyridin-3-yl)propanoate (1i).
Magnesium (10 mmol) was placed in a dry 25 mL flask under nitrogen. Lithium chloride (6 mmol) was added, followed by THF (10 mL) and DIBAL-H (0.17 mmol) was added to activate the magnesium. Reaction was stirred at rt for 5 min then cooled to 0 ^oC. 5-bromo-2-(trifluoromethyl)pyridine (5 mmol) was added and the reaction stirred at 0 ^oC for 15 minutes (magnesium is largely consumed). Then methyl 3,3-dicyano-2-methylacrylate (**5b**, 3 mmol) in benzene (2M) was added. The reaction was quenched after 15 minutes and followed general work up and silica gel purification. Yield: 63%, pale yellow solid, β:α >20:1 selectivity. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 2.4 Hz, 1H), 8.21 (dd, J = 8.4, 2.5 Hz, 1H), 8.14 – 8.01 (m, 1H), 5.93 (s, 1H), 4.33 (q, J = 7.1 Hz, 2H), 1.96 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.00, 148.62, 137.32, 120.95, 112.33, 112.26, 63.11, 51.04, 32.20, 20.54, 13.60. HRMS (ESI) *m/z* calcd for $C_{14}H_{11}F_3N_3O_2$ $[M-H]^-$: 310.0804, found 310.0798.



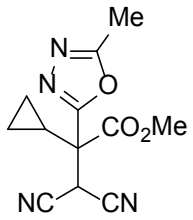
Ethyl 3,3-dicyano-2-(3-fluoro-4-methoxyphenyl)-2-methylpropanoate (1j).
Lithium chloride (4 mmol) was added to a flame dried vial (rubber septa) followed by magnesium (6.4 mmol), and the combined reagents were heated with a heat gun for 10 min under heavy flow of nitrogen until LiCl looked granular). Tetrahydrofuran (5.5 mL), iodine (0.27 mmol) and 1,2-dibromoethane (0.82 mmol) were then added and the solution was heated 35 ^{o}C for 30 minutes until it became near colorless solution. 4-bromo-2-fluoro-1-methoxybenzene (5.5 mmol) was added and the solution was stirred for 60 minutes at room temperature forming a light brown solution. The solution is cooled to -40 ^{o}C and ethyl 3,3-dicyano-2-methylacrylate (**5b**, 2.7 mmol) in benzene (2M) was added dropwise. The reaction was quenched after 30 minutes by saturated ammonium chloride solution and diluted with water and EtOAc. The crude reaction was purified by silica gel flash column chromatography (0-30% EtOAc/Hexane). Yield: 95%, colorless oil, β:α >20:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.31 (dd, J = 12.9, 2.4 Hz, 1H), 7.26 (t, J = 8.8 Hz, 1H), 7.17 (ddd, J = 8.7, 2.5, 1.0 Hz, 1H), 5.75 (s, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.87 (s, 3H), 1.81 (s, 3H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.83, 152.29, 149.86, 147.47, 147.37, 128.98, 128.92, 123.23, 123.20, 114.37, 114.17, 114.02, 114.00, 112.79, 112.65, 62.50, 56.05, 51.64, 32.70, 20.47, 13.65. HRMS (ESI) *m/z* calcd for $C_{15}H_{14}FN_2O_3$ [M-H]$^-$: 289.0989, found 289.0990.



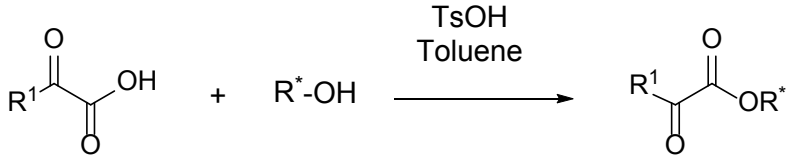
Methyl 2-cyclopropyl-2-(dicyanomethyl)butanoate (1k).
Reaction was run with diethylzinc (1.5 eq) from -78 ^{o}C to room temperature overnight. Yield: 60%, colorless oil, β:α >20:1 selectivity. ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.41 (s, 1H), 3.74 (s, 3H), 1.79 (dq, J = 15.1, 7.6 Hz, 1H), 1.70 (dq, J = 14.7, 7.4 Hz, 1H), 1.16 (tt, J = 8.4, 5.5 Hz, 1H), 0.91 (t, J = 7.5 Hz, 3H), 0.70 – 0.64 (m, 1H), 0.64 – 0.56 (m, 2H), 0.46 – 0.39 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.57, 113.31, 113.16, 52.88, 52.08, 29.68, 26.44, 16.10, 8.32, 2.67, 1.24. HRMS (ESI) *m/z* calcd for $C_{11}H_{13}N_2O_2$ [M-H]$^-$: 205.0977, found 205.0978.



Ethyl 4-(1,1-dicyano-2-cyclopropyl-3-methoxy-3-oxopropan-2-yl)benzoate (1l).
Ethyl 4-iodobenzoate (6.7 mmol) was added THF (15 mL) and cooled to -40 °C under N_2. Turbo Grignard (6.7 mmol) was added and stirred for 2 hours. Methyl 3,3-dicyano-2-cyclopropylacrylate (**5c**, 5.6 mmol) in THF (5 mL) was added. After 20 minutes, reaction was worked up according to general procedure. The reaction crude was purified by silica gel flash column chromatography (0-25% EtOAc/Hexane) to provide the title compound. Yield: 58%, colorless oil, β:α >20:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 – 7.97 (m, 2H), 7.68 – 7.58 (m, 2H), 5.85 (s, 1H), 4.34 (q, J = 7.1 Hz, 2H), 3.74 (s, 3H), 1.70 (tt, J = 8.5, 5.5 Hz, 1H), 0.93 (tt, J = 8.6, 5.5 Hz, 1H), 0.87 – 0.74 (m, 1H), 0.58 (dq, J = 10.6, 5.4 Hz, 1H), 0.35 (dq, J = 9.6, 5.6 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.31, 165.07, 141.63, 130.27, 129.36, 128.11, 112.76, 112.69, 109.52, 60.94, 57.18, 53.40, 33.14, 15.29, 14.12, 4.84, 2.44. HRMS (ESI) *m/z* calcd for $C_{18}H_{17}N_2O_4$ $[M-H]^-$: 325.1189, found 325.1196.



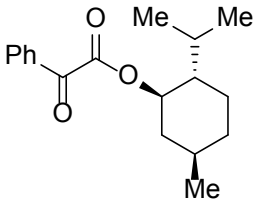
Methyl 3,3-dicyano-2-cyclopropyl-2-(5-methyl-1,3,4-oxadiazol-2-yl)propanoate (1m).
2-methyl-1,3,4-oxadiazole (1.7 mmol) was dissolved in THF (2.3 mL) and cooled to -78 °C under N_2. Butyllithium (1.1 mmol) was added dropwise via syringe. After 1 hour, methyl 3,3-dicyano-2-cyclopropylacrylate (**3c**, 1.1 mmol) in THF (1 mL) was then added drop-wise and the solution was slowly warmed to -50 °C over 1.5 hours. The reaction was then quenched and worked up under general conditions. The reaction crude was purified by silica gel flash column chromatography (0-50% EtOAc/Hexane) to provide the title compound. Yield: 51%, colorless oil, β:α >20:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.09 (s, 1H), 3.81 (s, 3H), 2.57 (s, 3H), 1.63 (tt, J = 8.4, 5.3 Hz, 1H), 0.81 (dd, J = 8.5, 4.4 Hz, 2H), 0.64 – 0.48 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.95, 165.80, 161.25, 111.91, 111.87, 54.36, 53.16, 30.19, 15.27, 10.57, 3.31, 3.13. HRMS (ESI) *m/z* calcd for $C_{12}H_{11}N_4O_3$ $[M-H]^-$: 259.0831, found 259.0822.



7

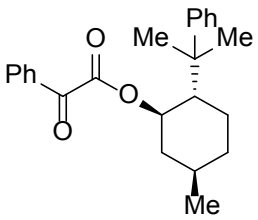
General procedure:

To a flask was added cyclohexanol (1 mmol), followed by α-ketoacid (1 mmol), toluene (10 mL) and lastly *p*-toluenesulfonic acid (0.4 mmol)). The flask was equipped with a Dean-Stark trap and heated at 130 ^{o}C for up to 2 hours. The reaction was cooled to room temperature and concentrated under reduced pressure to remove most of the toluene.[3] The crude mixture was diluted with EtOAc, washed with sat'd $NaHCO_3$ (2x). The organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (0-10% MTBE-hexane or 0-10% EtOAc-hexane) to afford the desired α-ketoesters.



(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl-2-oxo-2-phenylacetate (7a).

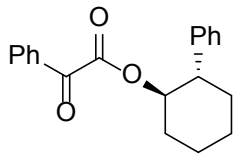
From commercial available L-menthol (*1R, 2S, 5R*) following general procedure. Yield: 41%, pale yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.99 – 7.86 (m, 1H), 7.86 – 7.75 (m, 1H), 7.66 (t, J = 7.8 Hz, 1H), 4.95 (td, J = 11.0, 4.4 Hz, 1H), 2.17 – 2.06 (m, 1H), 1.84 (pd, J = 6.9, 2.6 Hz, 1H), 1.67 (dt, J = 12.1, 2.9 Hz, 1H), 1.57 (tdd, J = 7.9, 5.6, 3.0 Hz, 1H), 1.54 – 1.40 (m, 1H), 1.25 – 1.04 (m, 1H), 0.93 (d, J = 6.6 Hz, 2H), 0.88 (d, J = 7.0 Hz, 2H), 0.81 (d, J = 6.9 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.90, 163.61, 135.60, 131.53, 129.45, 129.41, 76.47, 46.20, 40.03, 33.43, 30.85, 25.93, 22.97, 21.74, 20.31, 16.19. HRMS (ESI) *m/z* calcd for $C_{18}H_{25}O_3$ $[M+H]^+$: 289.1804, found 289.1804; HRMS (ESI) *m/z* calcd for $C_{18}H_{28}NO_3$ $[M+NH_4]^+$: 306.2069, found 306.2071.



(*1R,2S,5R*)-5-methyl-2-(2-phenylpropan-2-yl)cyclohexyl-2-oxo-2-phenylacetate (7b).

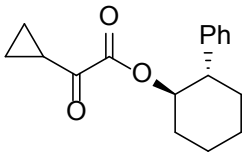
From commercial available (-)-8-phenylmenthol following general procedure. Yield: 25%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 – 7.84 (m, 1H), 7.80 (td, J = 7.3, 1.3 Hz, 1H), 7.70 – 7.60 (m, 1H), 7.28 – 7.21 (m, 1H), 7.09 (dd, J = 8.4, 6.9 Hz, 1H), 4.94 (td, J = 10.7, 4.2 Hz, 1H), 2.12 – 1.97 (m, 1H), 1.68 – 1.42 (m, 2H), 1.26 (d, J = 19.5 Hz, 2H), 1.22 – 1.17 (m, 1H), 1.17 – 1.02 (m, 1H), 0.89 (d, J = 6.3 Hz, 1H). ^{13}C

NMR (101 MHz, DMSO-d_6) δ 186.05, 162.66, 150.04, 135.33, 131.59, 129.57, 129.43, 129.36, 129.24, 127.81, 127.79, 125.28, 125.06, 77.25, 49.66, 40.76, 40.15, 39.94, 39.78, 39.73, 39.59, 39.52, 39.31, 39.10, 38.89, 33.71, 30.83, 27.31, 26.38, 25.79, 21.54. HRMS (ESI) *m/z* calcd for $C_{24}H_{28}NaO_3$ $[M+Na]^+$: 387.1936, found 387.1937.



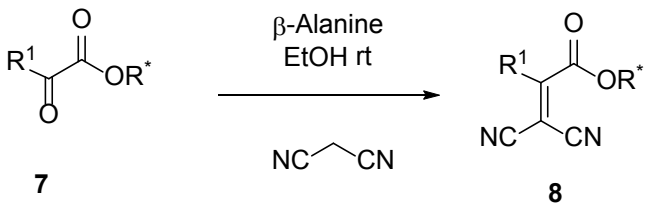
(*1R,2S*)-2-phenylcyclohexyl 2-oxo-2-phenylacetate (7c).

From commercial available (-)-(*1R,2S*)-trans-2-phenylcyclohexanol (Aldrich, 99%ee). Yield: 79%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 16.2 Hz, 6H), 7.16 – 7.03 (m, 2H), 5.41 (dq, *J* = 10.6, 4.6 Hz, 1H), 2.77 (td, *J* = 11.7, 3.7 Hz, 1H), 2.11 (dd, *J* = 8.0, 3.9 Hz, 1H), 1.92 – 1.77 (m, 2H), 1.77 – 1.45 (m, 4H), 1.41 – 1.24 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.51, 163.97, 143.16, 135.81, 131.54, 129.64, 129.54, 129.00, 128.12, 127.18, 78.79, 49.37, 33.96, 32.11, 25.49, 24.52. HRMS (ESI) *m/z* calcd for $C_{20}H_{20}NaO_3$ $[M+Na]^+$: 331.1310, found 331.1310.

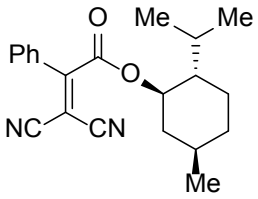


(*1R,2S*)-2-phenylcyclohexyl-2-cyclopropyl-2-oxoacetate (7d).

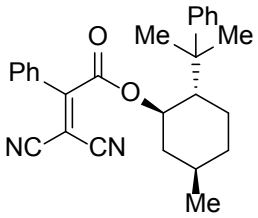
2-cyclopropyl-2-oxoacetic acid (4.3 mmol), (-)-(*1R,2S*)-trans-2-phenylcyclohexanol (Aldrich, 99%ee, 5.2 mmol), DCC (5.2 mmol), DMAP (0.43 mmol) and DCM (22ml) were reacted at room temperature for 2 hours under N_2. Reaction mixture was filterd off solids, concentrated under reduced vacuum. The crude mixture was purified by silica gel flash column chromatography (0-10%MTBE/Hexane) to give title compound as a colorless oil (0.75g, 64%).[4] ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.33 – 7.21 (m, 4H), 7.18 (ddd, *J* = 6.8, 5.7, 2.6 Hz, 1H), 5.08 (td, *J* = 10.6, 4.5 Hz, 1H), 2.78 (ddd, *J* = 12.3, 10.7, 3.6 Hz, 1H), 2.19 (tt, *J* = 7.9, 4.6 Hz, 1H), 2.07 (dp, *J* = 7.3, 2.5 Hz, 1H), 1.90 – 1.77 (m, 2H), 1.78 – 1.60 (m, 1H), 1.60 – 1.43 (m, 2H), 1.36 (tdd, *J* = 12.5, 8.9, 3.4 Hz, 1H), 1.08 – 0.95 (m, 2H), 0.93 – 0.84 (m, 1H), 0.81 – 0.73 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 194.46, 160.19, 142.46, 128.16, 127.45, 126.46, 78.12, 48.75, 32.84, 31.46, 25.07, 24.03, 18.09, 12.72. HRMS (ESI) *m/z* calcd for $C_{17}H_{20}NaO_3$ $[M+Na]^+$: 295.1310, found 295.1311.



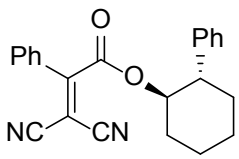
General procedure:
α-Ketoester (1 mmol) and malononitrile (12 mmol) were taken up in EtOH (5 mL), followed by the addition of β-alanine (0.1 mmol). The reaction was stirred at room temperature under N_2 for 16-20 hours. Following completion as determined by LCMS, the reaction was concentration under reduced pressure and a small amount of DCM was added and the excess solid was filtered off. The filtrate was directly loaded onto a silica gel column for purification by flash chromatography (0-10%MTBE-hexane) to provide the desired dicyano acrylate.



(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl-3,3-dicyano-2-phenylacrylate (8a).
Yield: 95%, pale yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.67 (tt, J = 5.3, 1.3 Hz, 3H), 7.64 – 7.58 (m, 2H), 4.90 (td, J = 10.9, 4.3 Hz, 1H), 2.17 – 1.96 (m, 1H), 1.79 (pd, J = 6.8, 2.5 Hz, 1H), 1.65 (dt, J = 12.5, 2.9 Hz, 2H), 1.59 – 1.47 (m, 0H), 1.41 (tt, J = 11.3, 3.1 Hz, 1H), 1.08 (q, J = 11.9 Hz, 2H), 0.90 (d, J = 6.5 Hz, 3H), 0.82 (d, J = 6.9 Hz, 3H), 0.72 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.39, 161.24, 132.90, 130.29, 129.11, 128.86, 112.33, 111.87, 78.07, 46.06, 33.33, 30.76, 25.52, 22.63, 21.72, 20.38, 15.89. HRMS (ESI) *m/z* calcd for $C_{21}H_{25}N_2O_2$ $[M+H]^+$: 337.1916, found: 337.1915.

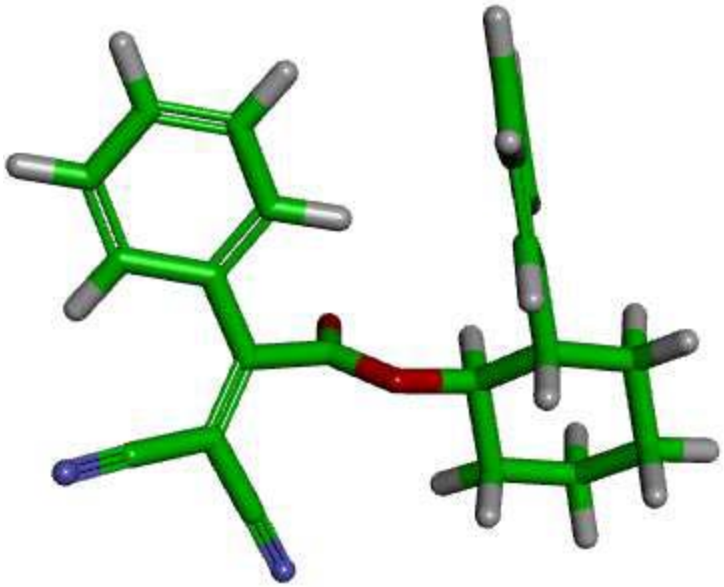


(*1R,2S,5R*)-5-methyl-2-(2-phenylpropan-2-yl)cyclohexyl-3,3-dicyano-2-phenylacrylate (8b).
Yield: 85%, colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65 – 7.59 (m, 2H), 7.59 – 7.52 (m, 2H), 7.42 (dt, J = 7.1, 1.4 Hz, 2H), 7.30 – 7.23 (m, 3H), 7.18 (t, J = 7.6 Hz, 2H), 7.10 (t, J = 7.2 Hz, 1H), 4.90 (td, J = 10.8, 4.2 Hz, 1H), 2.16 (tt, J = 11.2, 5.7 Hz, 1H), 1.92 (d, J = 12.2 Hz, 1H), 1.76 (dd, J = 13.7, 3.3 Hz, 1H), 1.64 (d, J = 13.0 Hz, 1H), 1.49 (s, 1H), 1.20 (s, 4H), 1.11 (d, J = 8.8 Hz, 4H), 1.07 – 0.99 (m, 1H), 0.99 – 0.89 (m, 1H), 0.87 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, dmso) δ 161.22, 160.54, 151.18, 132.54, 130.21, 129.27, 129.06, 128.75, 128.58, 127.84, 125.18, 124.95, 112.34, 111.79, 89.75, 78.22, 49.32, 33.71, 30.69, 28.84, 25.68, 23.29, 21.57. HRMS (ESI) *m/z* calcd for $C_{27}H_{29}N_2O_2$ $[M+H]^+$: 413.2229, found: 413.2231.



(*1R,2S*)-2-phenylcyclohexyl-3,3-dicyano-2-phenylacrylate (8c).
Yield: 94%, White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.57 (ddt, J = 8.7, 7.4, 1.2 Hz, 1H), 7.42 – 7.19 (m, 6H), 6.98 – 6.88 (m, 2H), 5.37 (td, J = 10.6, 4.4 Hz, 1H), 2.77 (td, J = 11.7, 3.6 Hz, 1H), 2.14 (dt, J = 8.0, 4.1 Hz, 1H), 1.92 – 1.77 (m, 2H), 1.77 – 1.60 (m, 2H), 1.55 (dd, J = 10.9, 8.3 Hz, 2H), 1.36 (ddd, J = 12.6, 8.9, 3.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.30, 161.20, 142.40, 133.09, 129.48, 129.05, 128.63, 128.50, 127.53, 126.73, 112.14, 111.68, 87.31, 79.98, 48.74, 33.41, 31.19, 24.96, 23.90. HRMS (ESI) *m/z* calcd for $C_{23}H_{21}N_2O_2$ $[M+H]^+$: 357.1603, found 357.1600.

The absolute configuration of **8c** was further confirmed by VCD study.



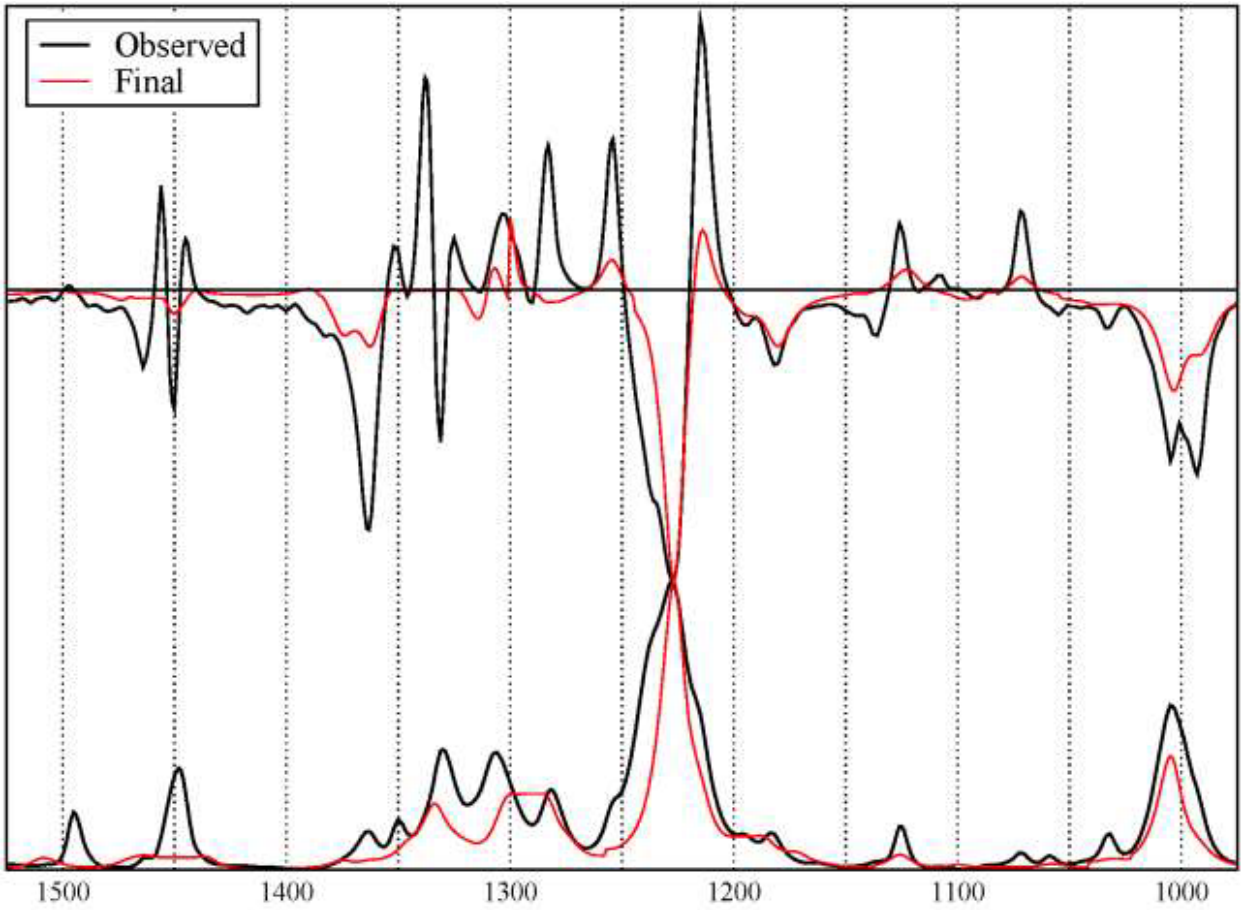
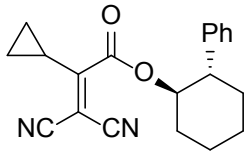
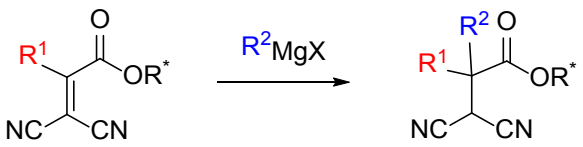


Figure 1. IR (lower frame) and VCD (upper frame) spectra of **8c** in $CDCl_3$. The observed VCD spectrum of **8c** compares better with the Boltzmann population-weighted calculated spectrum (labeled Final) of the (*RS*) configuration for the monomer over the range 1000-1500 cm^{-1}.



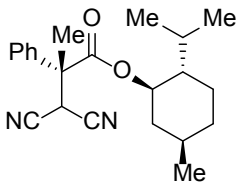
(*1R,2S*)-2-phenylcyclohexyl-3,3-dicyano-2-cyclopropylacrylate (8d).
Yield: 81%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.42 – 7.13 (m, 5H), 5.27 (td, J = 10.6, 4.5 Hz, 1H), 2.78 (td, J = 11.7, 3.7 Hz, 1H), 2.07 (p, J = 4.1 Hz, 1H), 2.04 – 1.94 (m, 1H), 1.89 – 1.75 (m, 2H), 1.70 (d, J = 12.9 Hz, 1H), 1.65 – 1.56 (m, 1H), 1.56 – 1.46 (m, 2H), 1.42 – 1.24 (m, 1H), 1.26 – 1.09 (m, 1H), 1.05 – 0.81 (m, 1H), 0.71 – 0.50 (m, 1H), -0.27 (ddt, J = 9.5, 7.5, 4.6 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.15, 161.06, 142.45, 128.52, 127.38, 126.77, 111.14, 110.93, 84.09, 79.78, 48.59, 33.69, 31.13, 24.95, 23.83, 16.51, 12.87, 12.01. HRMS (ESI) *m/z* calcd for $C_{20}H_{19}N_2O_2$ $[M-H]^+$: 319.1447, found: 319.1447.



8 **9**

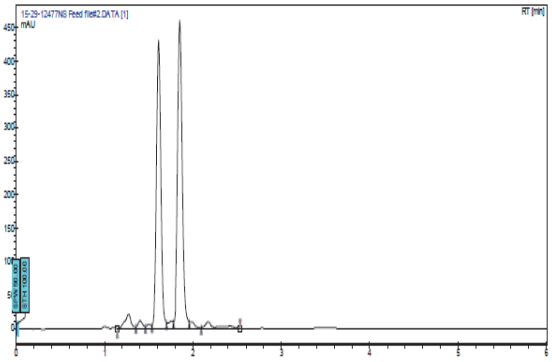
General Procedure:

To chiral malononitrile **8** (1 mmol) was added THF (10 mL) and the solution was cooled to -78 °C under an atmosphere of N_2. Grignard reagent (1.2 mmol) was added drop-wise. After 2 minutes the reaction was quenched with sat'd $NH_4^+Cl^-$ solution and extracted with EtOAc. The organic phase was washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a colorless sticky crude oil. The crude product was analyzed by ^1H NMR. When there was only one major product (selectivity >20:1), the crude was purified by silica gel flash column chromatography (MTBE-Hexane). Otherwise, the crude products were analyzed by SFC analytical for diastereoselectivity, and SFC preparative separation (same condition as analytical) to collect the major peak (**9a-j**) for full characterization. The absolute configuration of the newly formed quaternary carbon was confirmed via coupling of **9e** and **13** to form **14** with known configuration. The absolute configuration assignment of the newly formed quaternary center for compounds (**9a-9j**) is based off of **9e**.

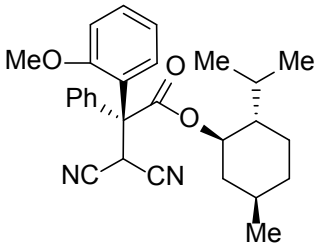


(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (9a).
Yield: 38%, white solid, eluted 2nd, major peak, selectivity 1.2:1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.56 – 7.33 (m, 5H), 5.82 (s, 1H), 4.66 (td, J = 10.9, 4.3 Hz, 1H), 1.97 – 1.88 (m, 1H), 1.84 (s, 3H), 1.68 – 1.52 (m, 2H), 1.52 – 1.39 (m, 0H), 1.27 (ddt, J = 17.3, 11.1, 3.7 Hz, 2H), 1.00 (dddd, J = 21.6, 12.7, 9.1, 2.6 Hz, 2H), 0.88 (d, J = 6.5 Hz, 3H), 0.85 – 0.70 (m, 1H), 0.64 (d, J = 6.9 Hz, 3H), 0.55 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.67, 136.20, 128.94, 128.83, 126.32, 112.97, 112.75, 76.20, 52.10, 46.17, 33.44, 32.61, 30.72, 25.07, 22.46, 21.75, 20.28, 19.96, 15.63. HRMS (ESI) *m/z* calcd for $C_{22}H_{27}N_2O_2$ [M-H]$^-$: 351.2073, found 351.2083.

Analytical: AD-H (25X0.46 cm), 20% isopropanol/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (15X2 cm), 10% isopropanol/CO_2, 100bar, 60mL/min, 220nm, 5mg/0.5mL/inj



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	1.16	1.28	1.36	0.00	2.75	18.9	1.6	2.746
7	UNKNOWN	1.36	1.43	1.60	0.00	2.13	13.0	1.3	2.133
5	UNKNOWN	1.60	1.65	1.73	0.00	41.45	454.5	24.8	41.446
4	UNKNOWN	1.73	1.83	1.85	0.00	1.69	10.3	1.0	1.694
3	UNKNOWN	1.85	1.92	2.02	0.00	48.73	481.6	29.1	48.729
2	UNKNOWN	2.02	2.02	2.33	0.00	2.33	11.8	1.4	2.334
6	UNKNOWN	2.33	2.44	2.71	0.00	0.92	6.8	0.5	0.919
Total						100.00	997.0	59.8	100.000

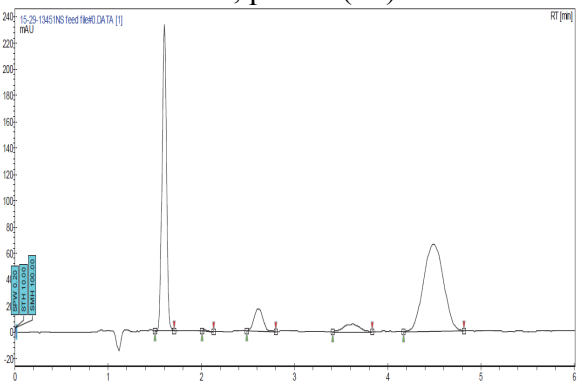


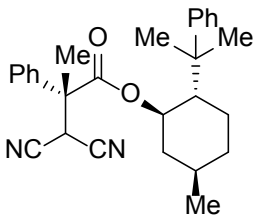
(*1S,2S,5R*)-2-isopropyl-5-methylcyclohexyl-(*R*)-3,3-dicyano-2-(2-methoxyphenyl)-2-phenylpropanoate (9b).

Yield: 25%, white solid, eluted 2nd, major product, selectivity 1.2:1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58 – 7.38 (m, 6H), 7.16 (d, J = 8.3 Hz, 1H), 6.96 (t, J = 7.6 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.40 (s, 1H), 4.65 (td, J = 10.8, 4.3 Hz, 1H), 3.76 (s, 3H), 1.96 (d, J = 12.2 Hz, 1H), 1.65 – 1.50 (m, 2H), 1.44 (s, 1H), 1.24 (s, 1H), 1.18 (t, J = 11.7 Hz, 1H), 0.97 (t, J = 12.1 Hz, 1H), 0.88 (d, J = 6.5 Hz, 3H), 0.86 – 0.71 (m, 2H), 0.66 (d, J = 6.9 Hz, 3H), 0.49 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.35, 156.82, 135.60, 130.78, 130.30, 128.60, 128.17, 125.21, 120.18, 113.51, 111.73, 76.18, 69.97, 59.24, 55.21, 46.20, 33.36, 31.10, 30.68, 24.59, 22.03, 21.85, 20.72, 15.26. HRMS (ESI) *m/z* calcd for $C_{28}H_{31}N_2O_3$ [M-H]$^-$: 443.2335, found 443.2345.

Analytical: AD-H (25X0.46 cm), 30% ethanol/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (25X2 cm), 30% ethanol/CO_2, 100bar, 30mL/min, 220nm, 4mg/1mL/inj

Peak 1: rt 1.67min; peak 2 (**9b**): rt 4.53min.

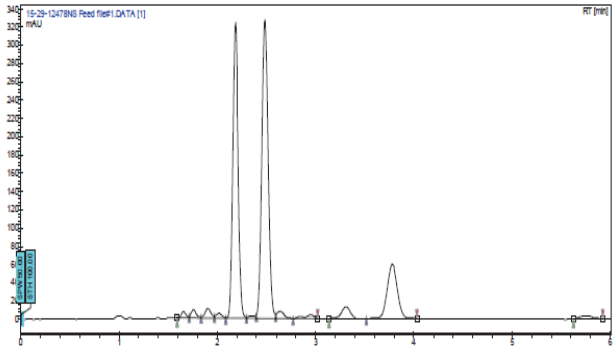




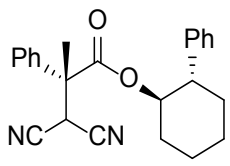
(*1R,2S,5R*)-5-methyl-2-(2-phenylpropan-2-yl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (9c).

Yield: 35%, white solid, second eluting peak characterized; selectivity 1.1:1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45 (ddd, J = 13.1, 7.8, 6.1 Hz, 3H), 7.38 – 7.31 (m, 2H), 7.28 (d, J = 4.3 Hz, 4H), 7.16 (p, J = 4.3 Hz, 1H), 5.65 (s, 1H), 4.86 (td, J = 10.6, 4.2 Hz, 1H), 1.98 (td, J = 11.4, 3.4 Hz, 1H), 1.62 – 1.43 (m, 5H), 1.38 (dd, J = 14.0, 3.9 Hz, 2H), 1.23 (s, 3H), 1.15 (s, 3H), 0.74 (d, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.26, 150.34, 135.81, 128.98, 128.91, 128.10, 126.22, 125.36, 125.31, 112.97, 112.67, 77.17, 52.05, 48.56, 33.50, 32.65, 30.51, 27.50, 26.40, 26.12, 21.50, 18.56. HRMS (ESI) *m/z* calcd for $C_{28}H_{31}N_2O_2$ [M-H]$^-$: 427.2386, found 427.2389.

Analytical: AD-H (25X0.46 cm), 20% isopropanol/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H(15X2cm), 10% isopropanol/CO_2, 100bar, 60mL/min, 220nm, 5mg/0.5mL/inj

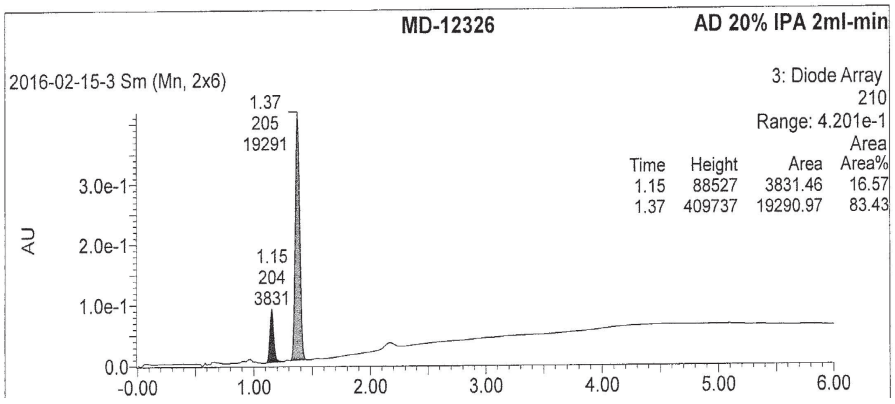


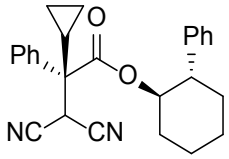
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	1.52	1.91	2.09	0.00	3.18	10.5	1.8	3.182
5	UNKNOWN	2.09	2.19	2.29	0.00	36.90	323.7	21.3	36.899
6	UNKNOWN	2.29	2.40	2.40	0.00	0.43	5.0	0.3	0.433
7	UNKNOWN	2.40	2.49	2.58	0.00	41.42	327.0	23.9	41.419
8	UNKNOWN	2.58	2.65	3.04	0.00	2.12	8.1	1.2	2.121
2	UNKNOWN	3.11	3.31	3.47	0.00	2.46	13.4	1.4	2.461
3	UNKNOWN	3.53	3.78	4.05	0.00	12.70	59.6	7.3	12.696
4	UNKNOWN	5.49	5.75	5.97	0.00	0.79	3.3	0.5	0.789
Total						100.00	750.6	57.8	100.000



(*1R,2S*)-2-phenylcyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (9e).
Yield: 63%, white solid, eluted 2nd, selectivity 6:1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.32 – 7.19 (m, 4H), 7.19 – 7.03 (m, 4H), 6.81 – 6.68 (m, 2H), 5.50 (s, 1H), 5.21 (td, *J* = 10.4, 4.2 Hz, 1H), 2.64 (td, *J* = 11.7, 3.6 Hz, 1H), 2.01 (dt, *J* = 10.7, 3.3 Hz, 1H), 1.86 – 1.72 (m, 2H), 1.65 (s, 4H), 1.62 – 1.50 (m, 1H), 1.46 (t, *J* = 11.3 Hz, 2H), 1.32 (ddd, *J* = 16.0, 8.3, 3.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.57, 142.59, 136.12, 128.53, 128.25, 128.19, 127.28, 126.40, 125.99, 112.71, 112.68, 109.51, 78.02, 52.52, 48.47, 33.81, 32.72, 31.56, 25.06, 23.92, 21.24. HRMS (ESI) *m/z* calcd for $C_{24}H_{23}N_2O_2$ [M-H]$^-$: 371.1760, found 371.1777.

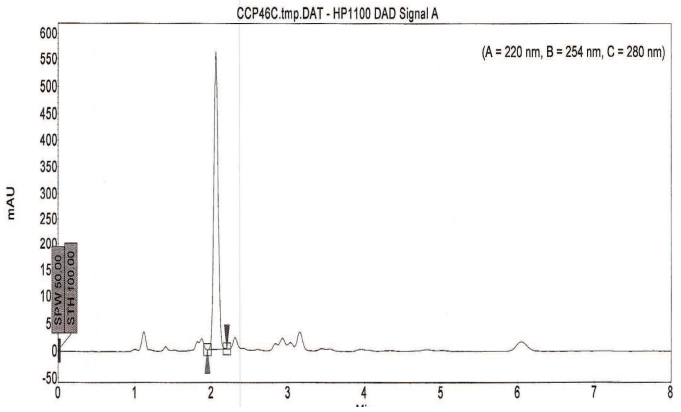
Analytical: AD-H (25X0.46 cm), 20% isopropanol/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H(25X2 cm), 20%isopropanol/CO_2, 100bar, 60mL/min, 220nm, 6mg/0.5mL/inj



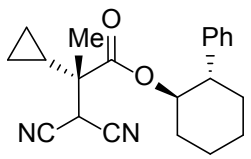


(*1R,2S*)-2-phenylcyclohexyl-(*R*)-3,3-dicyano-2-cyclopropyl-2-Phenylpropanoate (9f).
CyclopropylMgBr was added to (*1R,2S*)-2-phenylcyclohexyl-3,3-dicyano-2-phenylacrylate (**8c**) in THF -78 C for 5 minutes. Purified by chiral SFC method. Yield: 63%, white solid, single major product, selectivity >20:1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.41 – 7.18 (m, 8H), 7.16 – 7.00 (m, 2H), 5.47 (s, 1H), 5.21 (td, *J* = 10.9, 4.3 Hz, 1H), 2.62 (td, *J* = 11.7, 3.7 Hz, 1H), 2.03 (dt, *J* = 11.6, 3.7 Hz, 1H), 1.85 – 1.71 (m, 2H), 1.71 – 1.60 (m, 1H), 1.51 (dtd, *J* = 22.9, 12.9, 6.6 Hz, 2H), 1.39 – 1.16 (m, 3H), 0.51 (tt, *J* = 8.7, 5.5 Hz, 1H), 0.41 – 0.25 (m, 1H), 0.11 (dq, *J* = 10.6, 5.4 Hz, 1H), -0.19 – -0.37 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.17, 142.76, 136.69, 128.51, 128.48, 128.36, 127.49, 127.16, 126.56, 112.95, 112.89, 78.46, 56.44, 48.60, 34.14, 33.43, 31.24, 24.98, 23.85, 14.79, 4.20, 1.86. HRMS (ESI) *m/z* calcd for $C_{26}H_{25}N_2O_2$ $[M-H]^+$: 397.1916, found: 397.1926.

Analytical: AD-H (25X0.46 cm), 20% isopropanol/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H(25X2 cm),20%isopropanol/CO_2, 100bar, 60mL/min,220nm, 10mg/0.5mL/inj

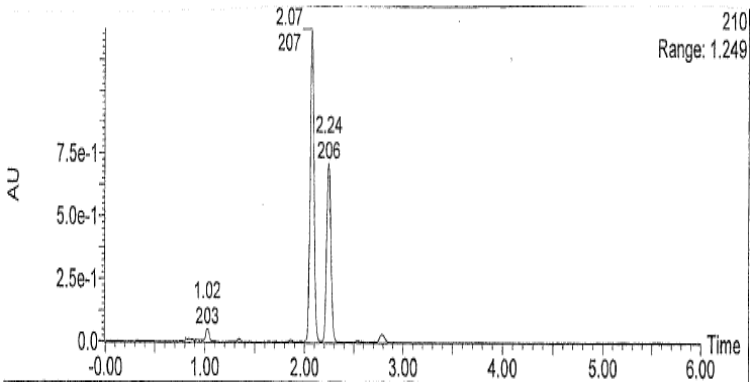


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	1.95	2.06	2.20	0.00	100.00	560.3	36.3	100.000
Total						100.00	560.3	36.3	100.000

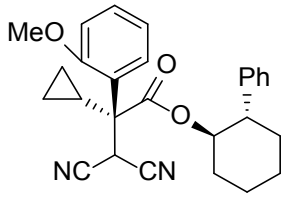


(*1R,2S*)-2-phenylcyclohexyl-(*S*)-3,3-dicyano-2-cyclopropyl-2-methylpropanoate (9g).
Yield: 36%, colorless oil, selectivity ~1.5:1. Front major peak from chiral SFC separation (Chiralcel OJ, 15% 2:1 Hexane-EtOH/CO2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.24 (d, J = 4.3 Hz, 4H), 7.21 – 7.11 (m, 1H), 5.13 (s, 1H), 4.98 (td, J = 10.5, 4.3 Hz, 1H), 2.73 (ddd, J = 12.2, 10.7, 3.6 Hz, 1H), 2.00 (dt, J = 10.8, 3.2 Hz, 1H), 1.87 – 1.75 (m, 2H), 1.75 – 1.66 (m, 1H), 1.60 (td, J = 12.9, 3.4 Hz, 1H), 1.54 – 1.40 (m, 2H), 1.40 – 1.26 (m, 1H), 0.80 (td, J = 8.4, 4.2 Hz, 1H), 0.75 (s, 3H), 0.42 – 0.26 (m, 2H), 0.19 (tt, J = 9.1, 5.5 Hz, 1H), 0.07 – -0.02 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.92, 142.63, 128.13, 127.43, 126.37, 112.81, 112.79, 77.81, 48.93, 47.89, 33.13, 31.57, 31.41, 25.15, 23.93, 16.33, 16.13, 1.65, 0.98. HRMS (ESI) *m/z* calcd for $C_{21}H_{23}N_2O_2$ [M-H]$^-$: 335.1760, found 335.1758.

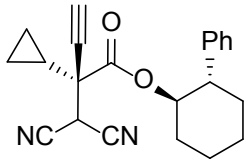
Analytical: Chiralcel OJ (25X0.46cm), 15% 2:1 (Hexane-EtOH)/CO_2, 100bar, 3mL/min, 210nm
Preparative: OJ (25X2.1cm), 15% 2:1(Hexane-EtOH)/CO_2, 100bar, 60mL/min, 210nm, 22mg/mL/inj



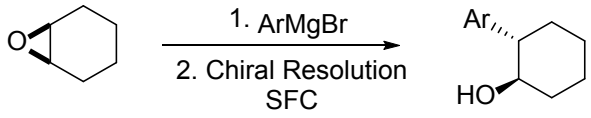
Peak1 (**9g**): rt 2.07min; peak2: rt 2.24min



(*1R,2S*)-2-phenylcyclohexyl-(*S*)-3,3-dicyano-2-cyclopropyl-2-(2-ethoxyphenyl)propanoate (9h).
The product was separated by silica gel flash column chlromatography (0-30% MTBE-Hexane). Yield: 67%, white solid, selectivity >20:1 (by 1H NMR). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.60 (dd, J = 7.8, 1.6 Hz, 1H), 7.31 (td, J = 7.9, 1.6 Hz, 1H), 7.22 – 7.13 (m, 3H), 7.08 (dd, J = 6.6, 3.0 Hz, 2H), 6.97 (t, J = 7.6 Hz, 1H), 6.76 (d, J = 8.2 Hz, 1H), 5.49 (s, 1H), 4.91 (td, J = 10.3, 4.3 Hz, 1H), 3.46 (s, 3H), 2.62 (td, J = 11.5, 3.7 Hz, 1H), 2.12 (dd, J = 7.8, 4.1 Hz, 1H), 1.80 (d, J = 10.4 Hz, 1H), 1.76 – 1.63 (m, 2H), 1.63 – 1.50 (m, 1H), 1.42 (ddd, J = 11.6, 7.0, 2.6 Hz, 3H), 1.36 – 1.15 (m, 1H), 0.69 (tt, J = 9.1, 5.1 Hz, 1H), 0.52 – 0.38 (m, 1H), 0.36 – 0.25 (m, 1H), -0.40 (q, J = 7.8, 7.1 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.53, 155.76, 142.81, 129.95, 128.85, 128.18, 127.49, 126.20, 125.95, 120.25, 113.22, 113.11, 111.14, 78.65, 54.96, 53.34, 48.23, 33.54, 31.41, 31.24, 25.05, 23.85, 14.30, 3.76, 2.37. HRMS (ESI) *m/z* calcd for $C_{27}H_{27}N_2O_3$ [M-H]$^-$: 427.2022, found 427.2033.



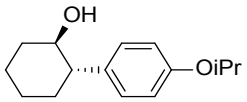
(*1S,2S*)-2-phenylcyclohexyl-(*S*)-2-cyclopropyl-2-(dicyanomethyl)but-3-ynoate (9i).
EthynylMgBr was added to (*1R,2S*)-2-phenylcyclohexyl 3,3-dicyano-2-cyclopropylacrylate (**8d**) in THF from -78 ^{o}C to room temperature overnight. The product was separated by silica gel flash column chlromatography (0-20% MTBE-Hexane). Yield: 67%, white solid, selectivity >20:1(by 1H NMR). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.32 – 7.09 (m, 5H), 5.56 (s, 1H), 5.01 (td, J = 10.4, 4.4 Hz, 1H), 3.63 (s, 1H), 2.75 (td, J = 11.6, 11.2, 3.5 Hz, 1H), 2.03 (d, J = 8.1 Hz, 1H), 1.83 (d, J = 11.6 Hz, 2H), 1.78 – 1.58 (m, 2H), 1.58 – 1.43 (m, 2H), 1.43 – 1.28 (m, 0H), 0.81 (ddd, J = 12.8, 7.2, 3.9 Hz, 1H), 0.61 – 0.47 (m, 2H), 0.25 (ddt, J = 9.5, 6.8, 4.8 Hz, 1H), 0.21 – 0.08 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.00, 142.25, 128.09, 127.51, 126.35, 112.00, 79.04, 73.80, 50.86, 48.69, 32.73, 31.88, 31.42, 25.08, 23.87, 14.90, 2.34, 1.41. HRMS (ESI) *m/z* calcd for $C_{22}H_{21}N_2O_2$ [M-H]$^-$: 345.1603, found 345.1608.



10

General procedure:

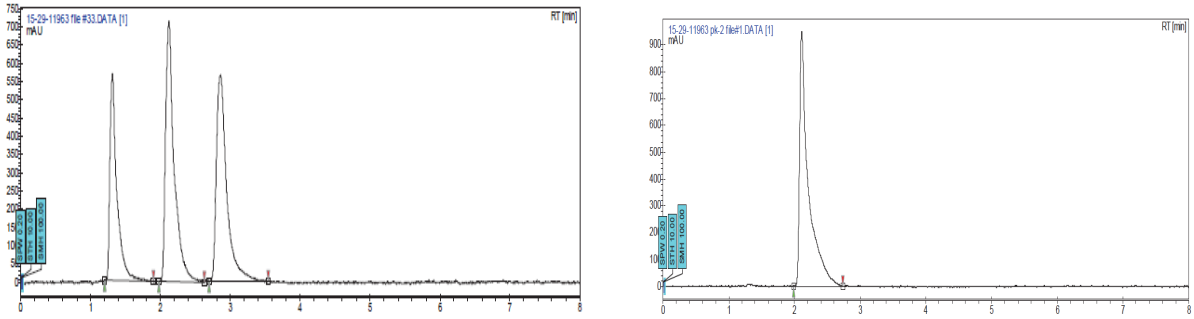
In a three-neck flask, copper(I) bromide-dimethyl sulfide complex (1 mmol) and THF (10 ml) were added under an atmosphere of N_2. Arylmagnesium bromide (15 mmol, 0.5-1 M in THF) was added drop-wise at room temperature via a dropping funnel. The solution was then cooled to <-35 °C and cyclohexene oxide (10 mmol) was added neat via a syringe drop-wise. The reaction was warmed to room temperature over one hour and stirred for another hour. The reaction was cooled to 0 °C and quenched with to sat'd $NH_4^+Cl^-$ (50 mL) and extracted with EtOAc (50 mL). The organic phase was again washed with sat'd $NH_4^+Cl^-$ (50mL) and brine (50mL). The organic phase was dried by $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Silica gel flash chromatography (0-20% MTBE-Hexane), followed by SFC chiral separation afforded the desired alcohols in >99% ee.



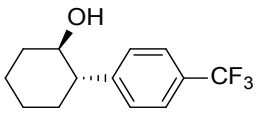
(-)-(*1R,2S*)-2-(4-isopropoxyphenyl)cyclohexan-1-ol (10a).

Yield: 16%, >99% ee, white solid. Separated by AD-H column, front peak. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.13 – 7.04 (m, 1H), 6.84 – 6.74 (m, 1H), 4.52 (hept, J = 6.1 Hz, 1H), 4.19 (d, J = 5.7 Hz, 1H), 3.41 (dq, J = 10.4, 5.2 Hz, 1H), 2.24 (ddd, J = 13.0, 10.0, 3.4 Hz, 1H), 2.01 – 1.86 (m, 1H), 1.79 – 1.56 (m, 2H), 1.46 – 1.30 (m, 1H), 1.24 (d, J = 6.0 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 155.57, 137.16, 128.70, 115.17, 72.63, 69.08, 51.35, 36.29, 34.00, 25.94, 24.90, 22.05. HRMS (ESI) *m/z* calcd for $C_{15}H_{21}O$ $[M\text{-}OH]^+$: 217.1592, found 217.1601. $[\alpha]^{20.0}_D$ = -43.4 (*c* 1.11, CH_3OH), >99% ee.

Analytical: AD-H (25X0.46cm), 40%MeOH(DEA)/CO_2, 100bar, 3mL/min, 220 and 280nm
Preparative: AD-H (25X2cm), 30%MeOH(DEA)/CO_2, 100bar, 60mL/min, 220nm,20mg/mL/inj

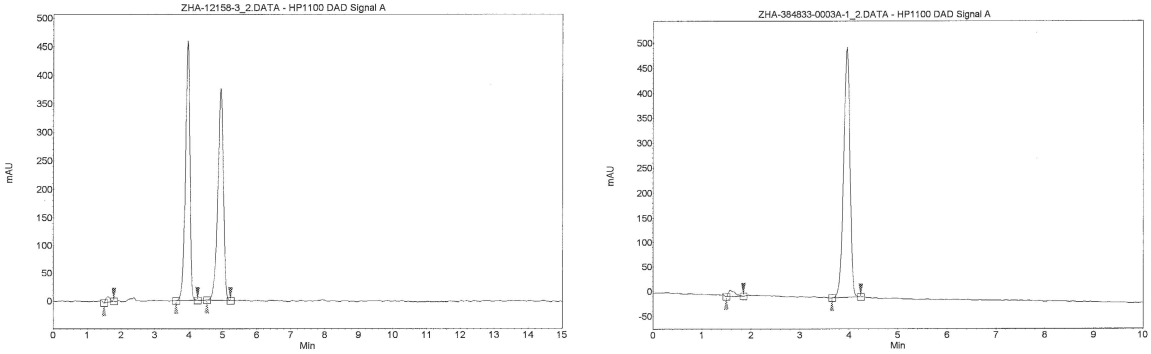


Peak 2 (**10a**) rt 2.11min; Peak 3 (***1S, 2R***) rt 3.23min

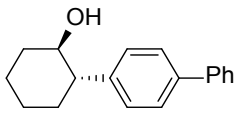


(-)-(*1R,2S*)-2-(4-(trifluoromethyl)phenyl)cyclohexan-1-ol (10b).
Yield: 9%, >99% ee, white solid. Separated by AD-H column, front peak. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H), 4.42 (d, J = 5.8 Hz, 1H), 3.62 – 3.43 (m, 1H), 2.45 (ddd, J = 13.1, 10.0, 3.3 Hz, 1H), 1.95 (dd, J = 12.3, 3.7 Hz, 1H), 1.78 – 1.60 (m, 3H), 1.58 – 1.16 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 150.40, 150.39, 128.71, 126.70, 126.39, 125.99, 124.86, 124.82, 124.78, 124.74, 123.29, 72.31, 52.15, 36.14, 33.41, 25.71, 24.76. HRMS (ESI) *m/z* calcd for $C_{13}H_{14}F_3$ $[M\text{-}OH]^+$: 227.2502, found 227.1041. $[\alpha]^{20.0}_D$ = -42.9 (*c* 1.0, CH_3OH), >99% ee.

Analytical: AD-H (25X0.46cm), 10%MeOH/CO_2, 100bar, 2.1mL/min, 220 and 280nm, 40 ^{o}C
Preparative: AD-H (25X2cm), 18%MeOH/CO_2, 100bar, 60mL/min, 35 ^{o}C, 75mg/mL/inj

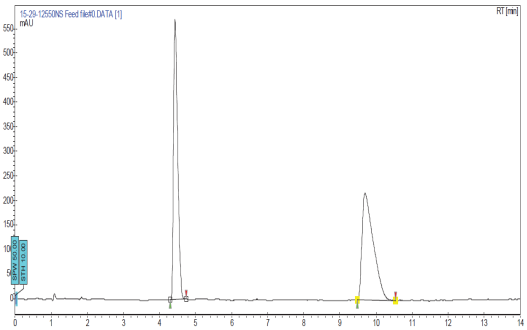


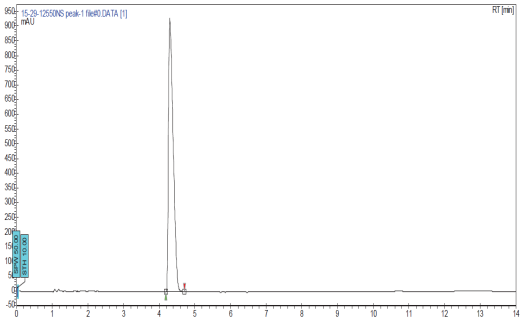
Peak 1 (**10b**) rt 3.96min; Peak 2 (***1S, 2R***) rt 4.93min



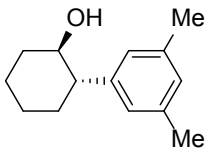
(-)-(*1R,2S*)-2-([1,1'-biphenyl]-4-yl)cyclohexan-1-ol (10c).
Yield: 36%, >99% ee, white solid. Separated by IA column, front peak. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.69 – 7.58 (m, 2H), 7.58 – 7.50 (m, 2H), 7.44 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.37 – 7.32 (m, 1H), 7.32 – 7.26 (m, 2H), 4.33 (d, *J* = 5.8 Hz, 1H), 4.10 (q, *J* = 5.2 Hz, 1H), 3.53 (dtd, *J* = 10.2, 5.9, 3.0 Hz, 1H), 3.16 (d, *J* = 5.2 Hz, 2H), 2.37 (ddd, *J* = 13.0, 9.9, 3.4 Hz, 1H), 1.95 (dt, *J* = 11.1, 3.4 Hz, 1H), 1.69 (ddd, *J* = 25.7, 9.6, 3.5 Hz, 3H), 1.36 (ddtd, *J* = 47.6, 22.9, 12.7, 3.4 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 144.69, 140.35, 137.61, 128.83, 128.34, 126.99, 126.44, 126.22, 72.35, 51.85, 48.57, 36.22, 33.65, 25.79, 24.78. HRMS (ESI) *m/z* calcd for $C_{18}H_{19}$ [M-OH]$^+$: 235.1487, found 235.1490. $[\alpha]^{20.0}_D$ = -30.6 (*c* 3.39, CH_3OH), >99% ee.

Analytical: IA (25X0.46cm), 40%MeOH/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: IA (15X2.1cm), 30%MeOH/CO_2, 100bar, 60mL/min, 254nm, 20mg/0.5mL/inj



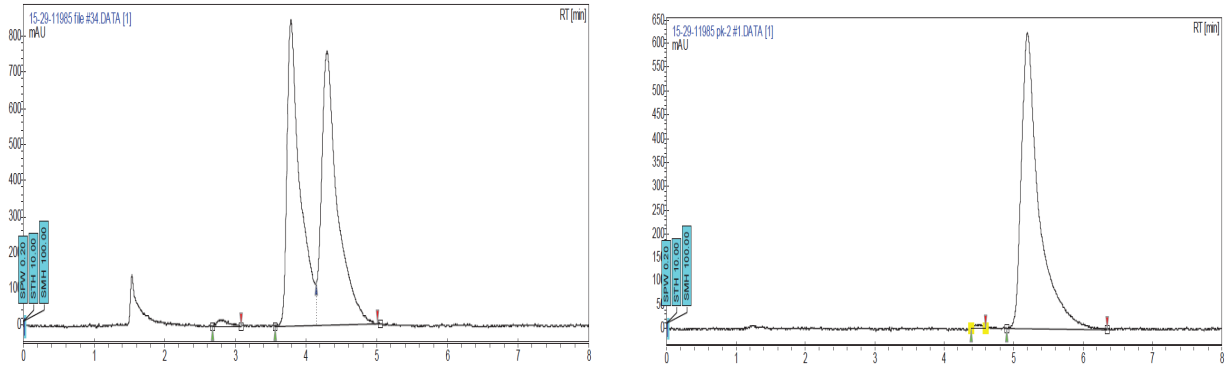


Peak 1 (**10c**) rt 4.30min; Peak 2 (***1S, 2R***) rt 9.26min

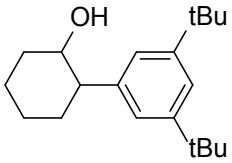


(-)-(*1R,2S*)-2-(3,5-dimethylphenyl)cyclohexan-1-ol (10d).
Yield: 16%, >99% ee, white solid. Separated by AD-H column, later peak. ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.77 (d, J = 9.7 Hz, 3H), 4.18 (d, J = 5.6 Hz, 1H), 3.47 (tt, J = 10.1, 4.9 Hz, 1H), 2.22 (s, 6H), 1.91 (dt, J = 11.2, 3.6 Hz, 1H), 1.80 – 1.56 (m, 3H), 1.45 – 1.06 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.21, 136.50, 127.02, 125.58, 72.27, 52.16, 36.22, 33.91, 25.82, 24.79, 21.00. HRMS (ESI) *m/z* calcd for $C_{14}H_{19}$ [M-OH]$^+$: 187.1487, found 187.1489. $[\alpha]^{20.0}_D$ = -22.2 (*c* 0.073, $CHCl_3$), >99% ee. Ref. $[\alpha]^{20.0}_D$ = -44.8 (*c* 0.070, $CHCl_3$), >99% ee.[6]

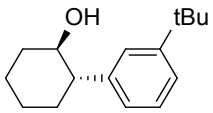
Analytical: AD-H (25X0.46cm), 40%MeOH/CO_2, 100bar, 3mL/min, 220 and 280nm
Preparative: AD-H (25X2cm), 35%MeOH/CO_2, 100bar, 60mL/min, 220nm, 20mg/mL/inj



Peak 1 (***1S, 2R***) rt 4.33min; Peak 2 (**10d**) rt 5.20min

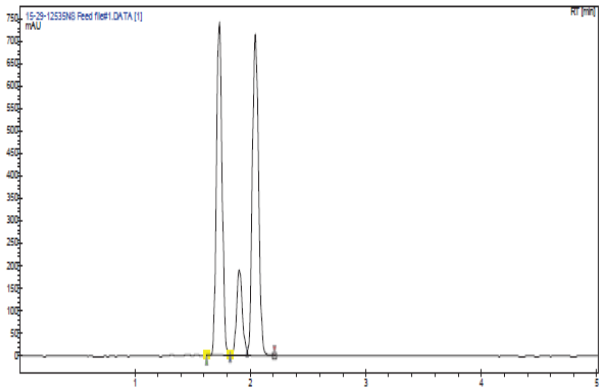


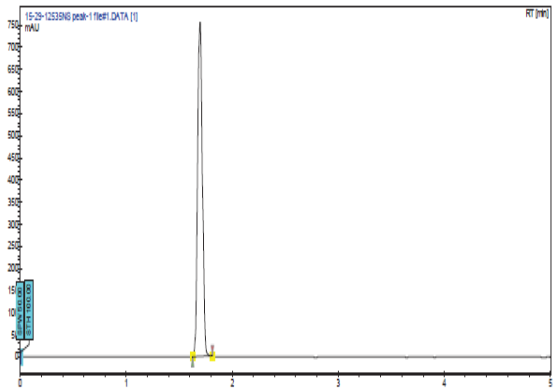
***Trans*-Racemic-2-(3,5-di-tert-butylphenyl)cyclohexan-1-ol (10e).**
No suitable chiral separation condition was found. Yield: 11%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.18 (t, J = 1.8 Hz, 1H), 7.01 (d, J = 1.8 Hz, 2H), 4.20 (d, J = 5.8 Hz, 1H), 3.59 – 3.43 (m, 1H), 2.31 (ddd, J = 13.1, 10.2, 3.3 Hz, 1H), 1.94 (dd, J = 12.5, 3.8 Hz, 1H), 1.68 (q, J = 13.7, 13.2 Hz, 3H), 1.49 – 1.32 (m, 2H), 1.27 (s, 18H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 149.33, 144.30, 121.64, 119.21, 72.23, 52.64, 36.32, 34.38, 34.17, 31.39, 25.85, 24.77. HRMS (ESI) *m/z* calcd for $C_{20}H_{31}$ [M-OH]$^+$: 271.2426, found 271.2431.



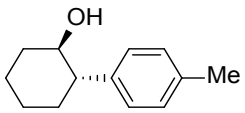
(-)-(*1R,2S*)-2-(3-(tert-butyl)phenyl)cyclohexan-1-ol (10f).
Yield: 26%, >99% ee, pale yellow oil. Separated by AD-H column, front peak. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.25 – 7.12 (m, 3H), 7.02 (dtd, J = 5.4, 3.8, 1.5 Hz, 1H), 4.23 (d, J = 5.8 Hz, 1H), 3.51 (tdd, J = 10.0, 5.7, 4.2 Hz, 1H), 2.50 (p, J = 1.8 Hz, 2H), 2.39 – 2.23 (m, 1H), 2.00 – 1.87 (m, 1H), 1.79 – 1.59 (m, 3H), 1.27 (s, 12H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 149.93, 144.89, 127.49, 124.77, 124.49, 122.40, 72.23, 52.42, 36.27, 34.24, 34.03, 31.26, 25.82, 24.77. HRMS (ESI) *m/z* calcd for $C_{16}H_{23}$ $[M\text{-}OH]^+$: 215.1800, found 215.1801. $[\alpha]^{20.0}_{D}$ = -40.5 (*c* 0.96, CH_3OH), >99% ee.

Analytical: AD-H (25X0.46cm), 15%MeOH/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (25X2cm), 10%MeOH/CO_2, 100bar, 60mL/min, 220nm, 10mg/0.8mL/inj



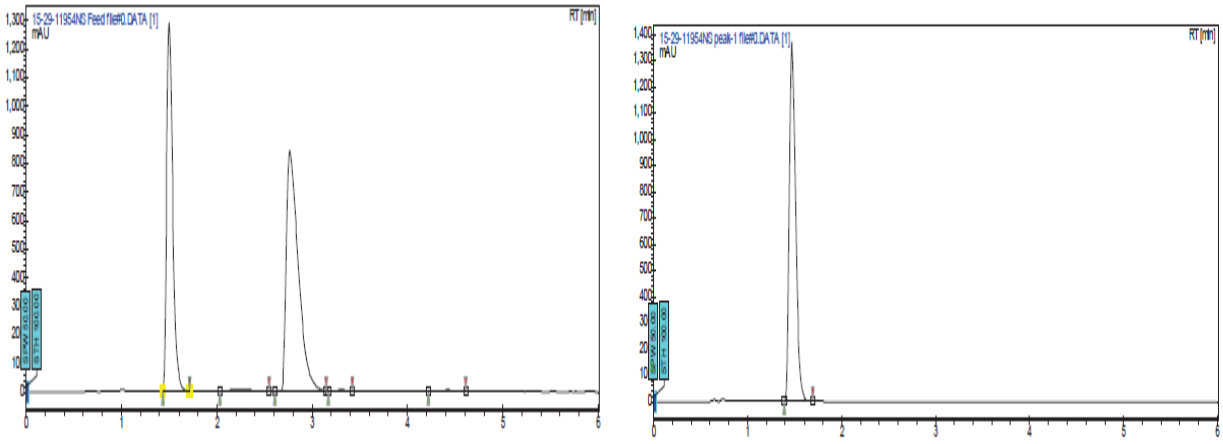


Peak 1 (**10f**) rt 1.69min; Peak 3 (***1S, 2R***) rt 1.99min

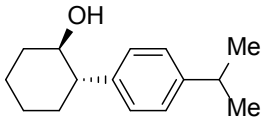


(-)-(*1S,2R*)-2-(p-tolyl)cyclohexan-1-ol (10g).
Yield: 9%, >99% ee, white solid. Separated by IA column, front peak. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.14 – 7.00 (m, 3H), 4.20 (d, J = 5.7 Hz, 1H), 3.45 (tt, J = 9.9, 4.9 Hz, 1H), 2.25 (s, 3H), 1.98 – 1.86 (m, 1H), 1.78 – 1.55 (m, 3H), 1.52 – 1.06 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 142.25, 134.32, 128.42, 127.58, 72.35, 51.76, 36.20, 33.86, 25.81, 24.79, 20.59. HRMS (ESI) *m/z* calcd for $C_{13}H_{17}$ [M-OH]$^{+}$: 173.1330, found 173.1332. $[\alpha]^{20.0}_{D}$ = -55.5 (*c* 1.4, CH_3OH), >99% ee. Ref. $[\alpha]^{20.0}_{D}$ = -59.5 (*c* 1.37, CH_3OH) 99% ee.[7]

Analytical: IA (15X0.46cm), 40%MeOH(DEA)/CO_2, 100bar, 3mL/min, 220 and 280nm
Preparative: IA (150X2cm), 35%MeOH/CO_2, 100bar, 65mL/min, 220nm, 12mg/0.7mL/inj

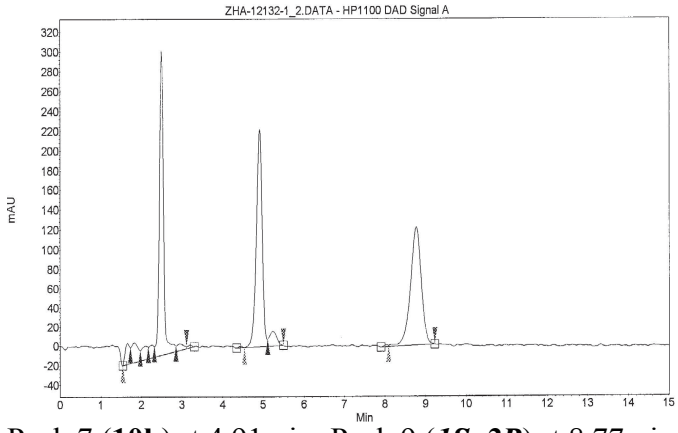


Peak 1 (**10g**) rt 1.47min; Peak 2 (***1S, 2R***) rt 2.71min



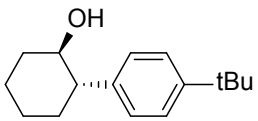
(-)-(*1R,2S*)-2-(4-isopropylphenyl)cyclohexan-1-ol (10h).
Yield: 10%, >99% ee, white solid. Separated by AD-H column, front peak. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.11 (s, 3H), 4.23 (d, J = 5.8 Hz, 1H), 3.55 – 3.41 (m, 1H), 2.83 (p, J = 6.9 Hz, 1H), 2.38 – 2.20 (m, 1H), 2.00 – 1.88 (m, 1H), 1.79 – 1.54 (m, 3H), 1.48 – 1.22 (m, 4H), 1.18 (d, J = 6.9 Hz, 5H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.41, 142.67, 127.61, 125.73, 72.36, 51.77, 36.25, 33.84, 33.03, 25.83, 24.79, 24.00. HRMS (ESI) *m/z* calcd for $C_{15}H_{21}$ $[M\text{-}OH]^+$: 201.1643, found 201.1645. $[\alpha]^{20.0}_D$ = -48.4 (*c* 1.11, CH_3OH), >99% ee.

Analytical: AD-H (25X0.46cm), 20%MeOH/CO_2, 100bar, 2.1mL/min, 40 ^{o}C
Preparative: AD-H (25X3cm), 37%MeOH/CO_2, 100bar, 65mL/min, 220nm, 35 ^{o}C,70mg/mL/inj



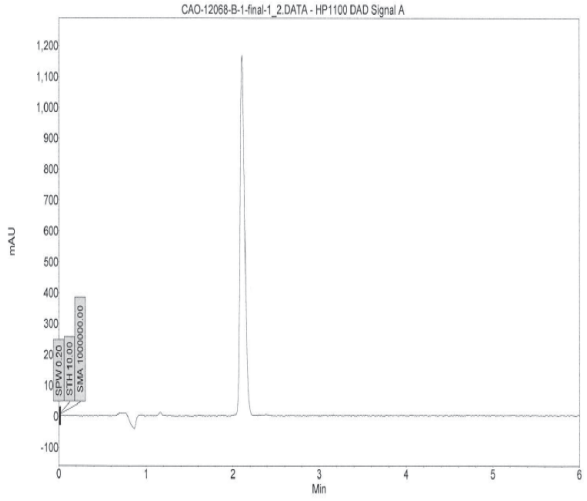
Index	Time [Min]	Area [μV.Min]	Area [%]
1	1.65	2.8	2.218
2	1.83	4.0	3.148
3	2.09	2.6	2.021
4	2.25	1.9	1.447
5	2.49	36.9	28.806
6	2.93	1.3	1.037
7	4.91	37.6	29.336
8	5.24	3.2	2.519
9	8.77	37.7	29.469
Total		128.1	100.000

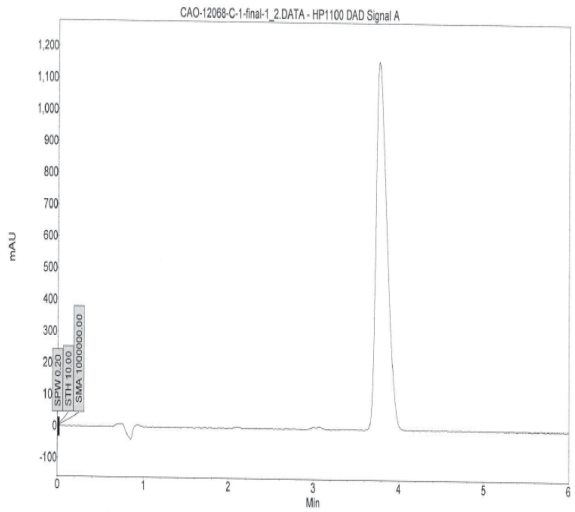
Peak 7 (**10h**) rt 4.91min; Peak 9 (***1S, 2R***) rt 8.77min



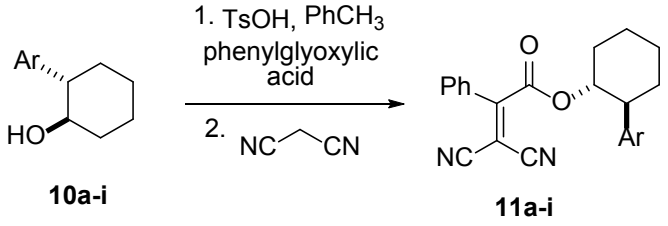
(-)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexan-1-ol (10i).
The crude product was purified by silica gel flash column chromatography (0-20% MTBE/Hexane) to provide *trans* racemic product in near quantitative yield. SFC chiral separation (AD-H column, 20% MeOH/CO_2) afforded title compound. Yield: 39%, >99% ee, white solid, front peak from chiral separation. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.33 – 7.19 (m, 2H), 7.19 – 7.02 (m, 2H), 4.23 (d, J = 5.8 Hz, 1H), 3.46 (tt, J = 10.0, 5.0 Hz, 1H), 2.35 – 2.19 (m, 1H), 1.93 (d, J = 11.4 Hz, 1H), 1.78 – 1.57 (m, 3H), 1.26 (s, 10H), 1.17 – 1.05 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.63, 142.24, 127.35, 124.56, 72.34, 51.64, 36.25, 33.98, 33.79, 31.24, 25.82, 24.79. HRMS (ESI) *m/z* calcd for $C_{15}H_{21}$ $[M\text{-}OH]^+$: 215.1800, found 215.1808. $[\alpha]^{20.0}_D$ = -47.9 (*c* 1.0, CH_3OH), >99% ee.

Analytical: AD-H (25X0.46cm), 20%MeOH(DEA)/CO_2, 100bar, 2.5mL/min, 35 ^oC





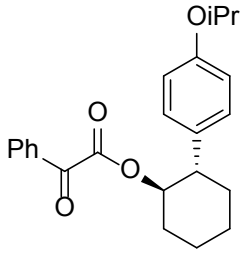
Peak 1 (**1i**) rt ~2.1min; Peak 2 (***1S, 2R***) rt ~3.8min



10a-i **11a-i**

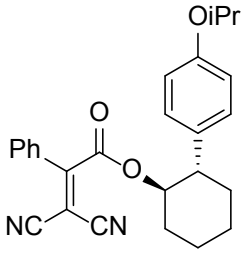
General procedure:

11a-i were prepared from **10a-i** in two steps: 1st step to **11a-i intermediate** chiral α-ketoesters followed the general procedure for **7**; 2nd step to **11a-i** followed the general procedure for **8**.



(*1R,2S*)-2-(4-isopropoxyphenyl)cyclohexyl-2-oxo-2-phenylacetate (11a-intermediate).

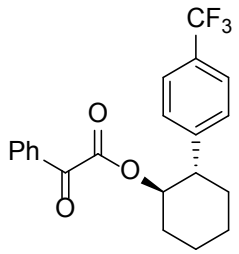
Yield: 60%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 – 7.63 (m, 1H), 7.38 (t, J = 7.8 Hz, 2H), 7.19 (td, J = 8.5, 1.7 Hz, 4H), 6.93 – 6.81 (m, 2H), 5.34 (td, J = 10.6, 4.5 Hz, 1H), 4.59 (p, J = 6.0 Hz, 1H), 2.71 (td, J = 11.6, 3.7 Hz, 1H), 2.12 (dd, J = 8.1, 4.0 Hz, 1H), 1.82 (d, J = 16.1 Hz, 2H), 1.77 – 1.68 (m, 1H), 1.64 (dd, J = 12.9, 3.5 Hz, 1H), 1.56 (dd, J = 11.1, 8.5 Hz, 2H), 1.43 – 1.32 (m, 0H), 1.28 (dd, J = 6.0, 1.5 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.08, 163.52, 156.30, 135.33, 134.30, 131.11, 129.14, 129.03, 128.66, 115.36, 78.52, 69.00, 54.88, 48.07, 33.57, 31.68, 25.08, 24.09, 21.97, 21.90. HRMS (ESI) *m/z* calcd for $C_{23}H_{30}NO_4$ $[M+NH_4]^+$: 384.2175 found: 384.2181.



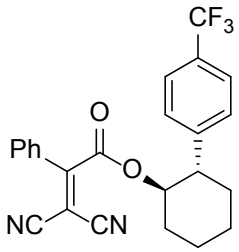
(*1S,2R*)-2-(4-isopropoxyphenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11a).

Yield: 88%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.59 (tt, J = 7.4, 1.2 Hz, 1H), 7.42 – 7.29 (m, 2H), 7.21 – 7.07 (m, 2H), 7.05 – 6.94 (m, 2H), 6.89 – 6.78 (m, 2H), 5.29 (dq, J = 10.5, 4.5 Hz, 1H), 4.58 (hept, J = 6.0 Hz, 1H), 2.69 (td, J = 11.6, 3.7 Hz, 1H), 2.13 (p, J = 4.1 Hz, 1H), 1.92 – 1.75 (m, 2H), 1.70 (d, J = 13.0 Hz, 1H), 1.61 (dd, J = 12.9, 3.4 Hz, 1H), 1.58 – 1.44 (m, 2H), 1.41 – 1.32 (m, 1H), 1.27 (dd, J = 6.0, 2.9 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.29, 161.25, 156.29, 133.99, 133.08, 129.52, 128.90, 128.70, 128.54, 115.35, 112.14, 111.68, 87.26, 80.16, 69.01, 47.91, 33.47, 31.22, 25.02, 23.93, 21.94, 21.90. HRMS (ESI) *m/z*

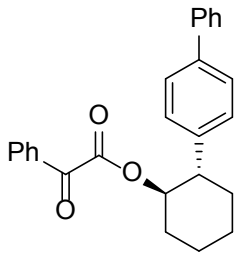
calcd for $C_{26}H_{27}N_2O_3$ $[M+H]^+$: 415.2022, found: 415.2015; HRMS (ESI) *m/z* calcd for $C_{26}H_{26}N_2NaO_3$ $[M+Na]^+$: 437.1841, found: 437.1833.



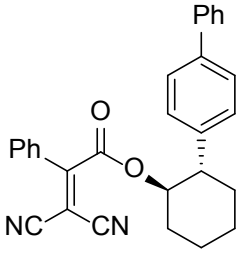
(*1R,2S*)-2-(4-(trifluoromethyl)phenyl)cyclohexyl-2-oxo-2-phenylacetate (11b-intermediate).
Yield: 85%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 – 7.68 (m, 3H), 7.58 (d, J = 8.0 Hz, 2H), 7.36 (t, J = 7.9 Hz, 2H), 7.25 – 7.16 (m, 2H), 5.46 (td, J = 10.6, 4.5 Hz, 1H), 2.95 (td, J = 11.6, 3.7 Hz, 1H), 2.17 (dt, J = 8.3, 4.2 Hz, 1H), 1.93 – 1.80 (m, 2H), 1.80 – 1.66 (m, 2H), 1.65 – 1.50 (m, 2H), 1.37 (tdd, J = 14.1, 9.8, 5.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.74, 163.29, 147.59, 135.48, 131.04, 128.96, 128.94, 128.61, 125.33, 125.29, 125.25, 78.13, 48.62, 32.97, 31.50, 24.85, 23.91. HRMS (ESI) *m/z* calcd for $C_{21}H_{19}F_3NaO_3$ $[M+Na]^+$: 399.1184, found: 399.1185.



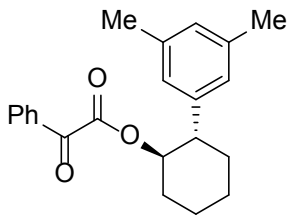
(*1R,2S*)-2-(4-(trifluoromethyl)phenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11b).
Yield: 91%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.64 (d, J = 8.1 Hz, 2H), 7.57 (tt, J = 7.4, 1.2 Hz, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.36 – 7.28 (m, 2H), 7.07 – 7.00 (m, 2H), 5.40 (dq, J = 10.5, 4.5 Hz, 1H), 2.89 (td, J = 11.5, 3.6 Hz, 1H), 2.16 (dd, J = 8.5, 4.1 Hz, 1H), 1.94 – 1.77 (m, 2H), 1.77 – 1.62 (m, 2H), 1.62 – 1.44 (m, 2H), 1.43 – 1.22 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.17, 160.96, 147.20, 133.00, 129.55, 128.81, 128.43, 125.28, 125.24, 125.20, 112.08, 111.58, 87.86, 79.71, 48.45, 32.91, 31.08, 24.80, 23.76. HRMS (ESI) *m/z* calcd for $C_{24}H_{20}F_3N_2O_2$ $[M+H]^+$: 425.14769, found: 425.14783.



(*1R,2S*)-2-([1,1'-biphenyl]-4-yl)cyclohexyl-2-oxo-2-phenylacetate (11c-intermediate).
Yield: 33%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 – 7.68 (m, 2H), 7.66 (d, J = 8.1 Hz, 2H), 7.59 (ddt, J = 8.8, 7.3, 1.9 Hz, 1H), 7.49 (t, J = 7.7 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 7.40 – 7.34 (m, 1H), 7.24 (t, J = 7.8 Hz, 2H), 7.20 – 7.15 (m, 2H), 5.47 (dq, J = 10.5, 4.5 Hz, 1H), 2.85 (td, J = 11.5, 3.6 Hz, 1H), 2.16 (dt, J = 7.9, 4.1 Hz, 1H), 1.87 (q, J = 4.9, 4.4 Hz, 2H), 1.81 – 1.68 (m, 2H), 1.60 (dd, J = 11.0, 8.3 Hz, 2H), 1.47 – 1.30 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.00, 163.48, 142.01, 139.75, 138.54, 135.49, 135.28, 131.09, 129.76, 129.26, 129.07, 128.97, 128.95, 128.28, 127.35, 126.69, 126.46, 78.30, 48.54, 33.41, 31.63, 25.01, 24.04. HRMS (ESI) *m/z* calcd for $C_{26}H_{28}NO_3$ $[M+NH_4]^+$: 402.2069, found: 402.2074.

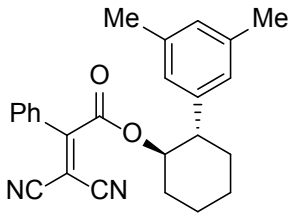


(*1R,2S*)-2-([1,1'-biphenyl]-4-yl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11c).
Yield: 83%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 – 7.65 (m, 2H), 7.65 – 7.56 (m, 2H), 7.48 (q, J = 7.3 Hz, 3H), 7.42 – 7.37 (m, 1H), 7.35 (d, J = 8.1 Hz, 2H), 7.23 (t, J = 7.9 Hz, 2H), 7.04 – 6.97 (m, 2H), 5.41 (dq, J = 10.6, 4.6 Hz, 1H), 2.83 (td, J = 11.5, 3.5 Hz, 1H), 2.17 (p, J = 4.2 Hz, 1H), 1.93 – 1.79 (m, 2H), 1.79 – 1.66 (m, 2H), 1.58 (t, J = 9.5 Hz, 2H), 1.37 (d, J = 12.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.29, 161.15, 141.66, 139.79, 138.56, 132.97, 129.53, 128.96, 128.83, 128.62, 128.13, 127.34, 126.69, 126.48, 112.12, 111.67, 87.48, 79.95, 48.38, 33.26, 31.18, 24.96, 23.90. HRMS (ESI) *m/z* calcd for $C_{29}H_{25}N_2O_2$ $[M+H]^+$: 433.1916, found: 433.1912.

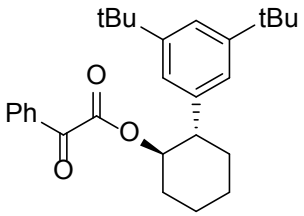


(*1R,2S*)-2-(3,5-dimethylphenyl)cyclohexyl-2-oxo-2-phenylacetate (11d-intermediate).
Yield: 52%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (tt, J = 7.4, 1.3 Hz, 1H), 7.44 – 7.32 (m, 2H), 7.17 – 7.08 (m, 2H), 6.99 – 6.86 (m, 2H), 5.38 (td, J = 10.6, 4.4 Hz, 1H), 2.69 (td, J = 11.6, 3.6 Hz, 1H), 2.21 (s,

5H), 2.16 – 2.06 (m, 1H), 1.92 – 1.78 (m, 2H), 1.78 – 1.60 (m, 2H), 1.56 (dd, *J* = 10.8, 8.2 Hz, 2H), 1.35 (ddt, *J* = 12.5, 7.2, 4.0 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.13, 163.54, 142.52, 137.39, 135.37, 131.12, 129.08, 129.05, 128.09, 125.37, 78.30, 48.79, 33.39, 31.65, 25.04, 24.09, 20.91. HRMS (ESI) *m/z* calcd for $C_{22}H_{28}NO_3$ $[M+NH_4]^+$: 354.2069, found: 354.2064.

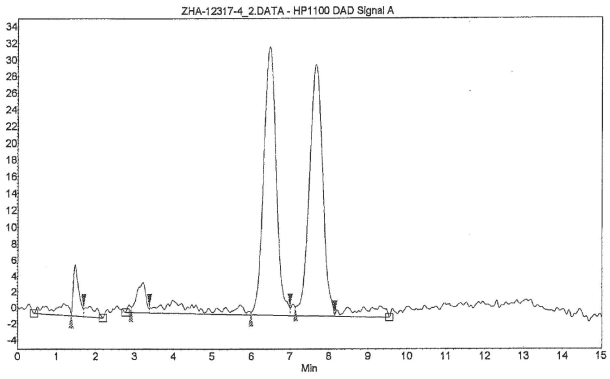


(*1R,2S*)-2-(3,5-dimethylphenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11d).
Yield: 90%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66 – 7.54 (m, 1H), 7.35 (t, *J* = 7.9 Hz, 2H), 7.03 – 6.94 (m, 2H), 6.92 (s, 1H), 6.85 (d, *J* = 1.6 Hz, 2H), 5.34 (dq, *J* = 10.5, 4.4 Hz, 1H), 2.68 (td, *J* = 11.6, 3.6 Hz, 1H), 2.20 (s, 5H), 2.14 (p, *J* = 4.1 Hz, 1H), 1.92 – 1.76 (m, 2H), 1.76 – 1.66 (m, 1H), 1.62 (dd, *J* = 12.8, 3.5 Hz, 1H), 1.59 – 1.43 (m, 2H), 1.41 – 1.22 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.39, 161.31, 142.25, 137.38, 133.22, 129.48, 128.98, 128.60, 128.10, 125.21, 112.13, 111.69, 86.99, 79.97, 48.65, 33.41, 31.18, 25.00, 23.93, 20.93. HRMS (ESI) *m/z* calcd for $C_{25}H_{25}N_2O_2$ $[M+H]^+$: 385.1914, found: 385.1914.



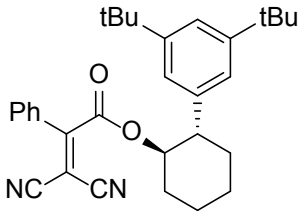
(*1R,2S*)-2-(3,5-di-tert-butylphenyl)cyclohexyl-2-oxo-2-phenylacetate (11e-intermediate).
Yield: 23%, white solid. Started with trans racemic alcohol (**10e**) and the racemic pdt was separated by SFC (IC column, IPA/CO_2), front peak. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66 (tt, *J* = 7.5, 1.4 Hz, 1H), 7.40 – 7.20 (m, 2H), 7.14 (d, *J* = 1.8 Hz, 2H), 7.03 – 6.86 (m, 2H), 5.50 (dq, *J* = 10.4, 4.5 Hz, 1H), 2.77 (td, *J* = 11.6, 3.5 Hz, 1H), 2.10 (q, *J* = 5.7, 4.8 Hz, 1H), 1.84 (d, *J* = 10.8 Hz, 2H), 1.78 – 1.65 (m, 2H), 1.61 (dt, *J* = 16.1, 6.6 Hz, 2H), 1.35 (d, *J* = 11.6 Hz, 2H), 1.21 (s, 12H). ^{13}C NMR (101 MHz, dmso) δ 187.15, 163.50, 150.11, 141.75, 135.16, 131.11, 129.09, 128.95, 121.91, 119.86, 77.97, 49.51, 34.48, 33.64, 31.72, 31.18, 25.09, 24.07. HRMS (ESI) *m/z* calcd for $C_{28}H_{40}NO_3$ $[M+NH_4]^+$: 438.3008, found: 438.3010.

Analytical: IC (25X0.46cm), 5%IPA(0.2%DEA)/CO_2, 100bar, 2.4mL/min, 254nm, 40 ^oC
Preparative: IC (25X2cm), 5%IPA(0.2%DEA)/CO_2, 100bar, 55mL/min, 220nm, 35 ^oC, 10mg/mL/inj

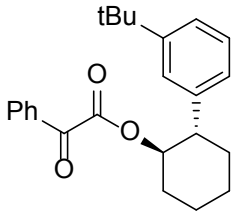


Index	Time [Min]	Area [μV.Min]	Area [%]
1	1.47	1.0	3.936
2	3.21	1.0	3.887
3	6.47	12.2	45.981
4	7.65	12.2	46.196
Total		26.5	100.000

Peak 3 (**11e-intermediate**) rt 6.47min; peak 4 (***1S,2R***) rt 7.65min

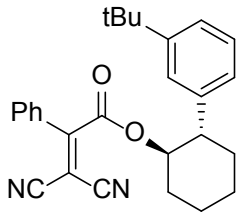


(*1R,2S*)-2-(3,5-di-tert-butylphenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11e).
Yield: 75%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 – 7.49 (m, 1H), 7.33 (t, J = 1.8 Hz, 1H), 7.31 – 7.20 (m, 2H), 7.14 (d, J = 1.8 Hz, 2H), 6.80 – 6.72 (m, 2H), 5.53 (td, J = 10.8, 10.4, 4.3 Hz, 1H), 2.81 (td, J = 11.7, 3.5 Hz, 1H), 2.23 – 2.08 (m, 1H), 1.84 (d, J = 12.9 Hz, 2H), 1.71 (t, J = 10.9 Hz, 1H), 1.67 – 1.50 (m, 2H), 1.45 – 1.30 (m, 1H), 1.22 (s, 18H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.34, 161.36, 150.22, 141.56, 133.27, 129.40, 129.07, 128.57, 121.75, 119.92, 112.09, 111.68, 86.31, 79.65, 49.46, 34.49, 33.78, 31.21, 25.05, 23.89. HRMS (ESI) *m/z* calcd for $C_{31}H_{37}N_2O_2$ $[M+H]^+$: 469.2855, found 469.2848.

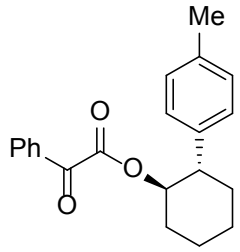


(*1R,2S*)-2-(3-(tert-butyl)phenyl)cyclohexyl-2-oxo-2-phenylacetate (11f-intermediate).
Yield: 45%, colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65 (tt, J = 7.5, 1.3 Hz, 1H), 7.37 – 7.29 (m, 4H), 7.26 (td, J = 7.3, 1.4 Hz, 1H), 7.10 (dt, J = 7.5, 1.5 Hz, 1H), 7.06 – 7.00 (m, 2H), 5.46 (dq, J = 10.6, 4.5 Hz, 1H), 2.77 (td, J = 11.6, 3.5 Hz, 1H), 2.10 (dt, J = 8.3, 4.3 Hz, 1H), 1.94 – 1.77 (m, 2H), 1.77 – 1.64 (m, 2H), 1.64 – 1.48 (m, 2H), 1.35 (dtd, J = 13.7, 9.7, 4.8 Hz, 1H), 1.18 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.07, 163.49, 150.72, 142.21, 135.20, 131.11, 129.12, 128.99, 128.14, 124.78, 124.62, 123.37, 78.11, 49.22,

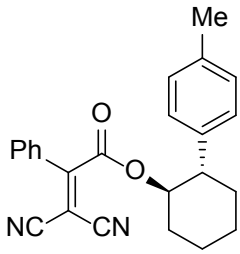
34.31, 33.52, 31.68, 31.01, 25.05, 24.06. HRMS (ESI) *m/z* calcd for $C_{24}H_{32}NO_3$ $[M+NH_4]^+$: 382.2382, found: 382.2382.



(*1R,2S*)-2-(3-(tert-butyl)phenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11f).
Yield: 84%, colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.60 – 7.49 (m, 1H), 7.36 – 7.27 (m, 4H), 7.25 (t, *J* = 7.9 Hz, 1H), 7.08 (dt, *J* = 7.5, 1.5 Hz, 1H), 6.89 – 6.80 (m, 2H), 5.46 (td, *J* = 10.5, 4.6 Hz, 1H), 2.79 (td, *J* = 11.7, 3.6 Hz, 1H), 2.24 – 2.05 (m, 1H), 1.92 – 1.77 (m, 2H), 1.77 – 1.62 (m, 2H), 1.59 (dt, *J* = 10.4, 5.4 Hz, 2H), 1.44 – 1.28 (m, 1H), 1.21 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.33, 161.30, 150.79, 142.00, 133.18, 129.40, 129.07, 128.57, 128.14, 124.69, 124.41, 123.42, 112.10, 111.67, 86.71, 79.79, 49.10, 34.33, 33.62, 31.21, 31.06, 25.01, 23.89. HRMS (ESI) *m/z* calcd for $C_{27}H_{29}N_2O_2$ $[M+H]^+$: 413.2229, found 413.2232.

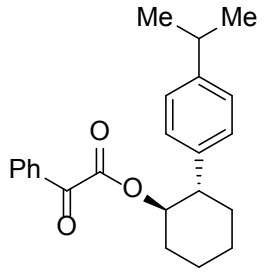


(*1R,2S*)-2-(p-tolyl)cyclohexyl-2-oxo-2-phenylacetate (11g-intermediate).
Yield: 62%, colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.43 – 7.32 (m, 2H), 7.27 – 7.07 (m, 5H), 5.39 (td, *J* = 10.6, 4.5 Hz, 1H), 2.74 (td, *J* = 11.6, 3.7 Hz, 1H), 2.34 (s, 2H), 2.12 (p, *J* = 4.1 Hz, 1H), 1.93 – 1.77 (m, 2H), 1.77 – 1.61 (m, 2H), 1.61 – 1.47 (m, 2H), 1.44 – 1.26 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.07, 163.49, 139.65, 135.68, 135.39, 131.07, 129.13, 129.04, 129.02, 127.53, 109.51, 78.40, 48.52, 33.51, 31.66, 25.03, 24.07, 20.67. HRMS (ESI) *m/z* calcd for $C_{21}H_{22}NaO_3$ $[M+Na]^+$: 345.1467, found: 345.1462; HRMS (ESI) *m/z* calcd for $C_{21}H_{26}NO_3$ $[M+NH_4]^+$: 340.1913, found: 340.1907.

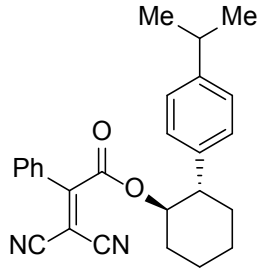


(*1R,2S*)-2-(p-tolyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11g).
Yield: 96%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.59 (tt, *J* = 7.5, 1.2 Hz, 1H), 7.40 – 7.24 (m, 2H), 7.12 (q, *J* = 8.1 Hz, 4H), 7.03 – 6.90 (m, 2H), 5.33 (dq, *J* = 10.6, 4.6 Hz, 1H), 2.72 (td, *J* = 11.6, 3.7 Hz, 1H),

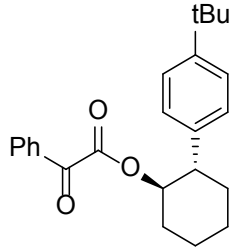
2.32 (s, 3H), 2.13 (p, *J* = 4.8, 4.2 Hz, 1H), 1.91 – 1.75 (m, 2H), 1.75 – 1.66 (m, 1H), 1.63 (dd, *J* = 12.8, 3.4 Hz, 1H), 1.60 – 1.45 (m, 2H), 1.41 – 1.24 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.30, 161.28, 139.32, 135.71, 133.14, 129.45, 129.00, 128.92, 128.66, 127.40, 112.12, 111.67, 87.13, 80.05, 48.36, 33.38, 31.19, 24.98, 23.91, 20.65. HRMS (ESI) *m/z* calcd for $C_{24}H_{23}N_2O_2$ $[M+H]^+$: 371.1754, found: 371.1760.



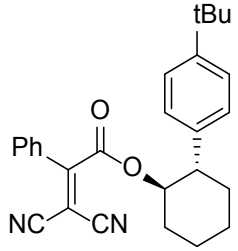
(*1R,2S*)-2-(4-isopropylphenyl)cyclohexyl-2-oxo-2-phenylacetate (11h-intermediate).
Yield: 50%, pale yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.70 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.28 – 7.15 (m, 4H), 5.41 (td, *J* = 10.5, 4.5 Hz, 1H), 2.92 (p, *J* = 6.9 Hz, 1H), 2.76 (td, *J* = 11.6, 3.7 Hz, 1H), 2.12 (p, *J* = 4.3 Hz, 1H), 1.94 – 1.77 (m, 2H), 1.77 – 1.67 (m, 1H), 1.67 – 1.61 (m, 1H), 1.57 (dt, *J* = 12.1, 8.3 Hz, 2H), 1.35 (tdt, *J* = 12.4, 8.7, 3.6 Hz, 1H), 1.22 (dd, *J* = 6.9, 4.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.01, 163.40, 146.58, 140.02, 135.35, 131.13, 129.12, 129.04, 127.45, 126.33, 78.26, 48.43, 33.77, 32.95, 31.66, 25.05, 24.06, 23.91, 23.89. HRMS (ESI) *m/z* calcd for $C_{23}H_{26}NaO_3$ $[M+H]^+$: 373.1780, found: 373.1772; HRMS (ESI) *m/z* calcd for $C_{23}H_{30}NO_3$ $[M+NH_4]^+$: 368.2226, found: 368.2225.



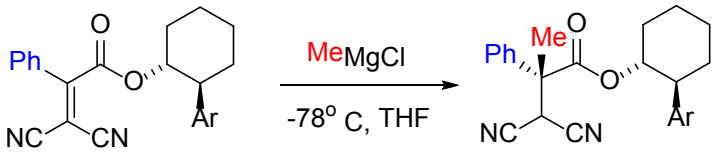
(*1R,2S*)-2-(4-isopropylphenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11h).
Yield: 94%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.41 – 7.30 (m, 2H), 7.22 – 7.13 (m, 3H), 7.07 – 6.97 (m, 2H), 5.35 (dq, *J* = 10.6, 4.6 Hz, 1H), 2.89 (h, *J* = 7.0 Hz, 1H), 2.73 (td, *J* = 11.6, 3.6 Hz, 1H), 2.20 – 2.04 (m, 1H), 1.89 – 1.75 (m, 2H), 1.75 – 1.58 (m, 2H), 1.54 (dd, *J* = 10.8, 8.2 Hz, 2H), 1.43 – 1.28 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 5H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.23, 161.12, 146.60, 139.69, 132.99, 129.58, 128.90, 128.67, 127.34, 126.31, 112.19, 111.68, 87.78, 79.94, 48.29, 33.58, 32.97, 31.23, 25.00, 23.92, 23.88. HRMS (ESI) *m/z* calcd for $C_{26}H_{27}N_2O_2$ $[M+H]^+$: 399.2073, found: 399.2068; HRMS (ESI) *m/z* calcd for $C_{26}H_{26}NaN_2O_2$ $[M+H]^+$: 421.1892, found: 421.1886.



(-)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexyl-2-oxo-2-phenylacetate (11i-intermediate).
Yield: 51%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.68 (tt, J = 7.4, 1.4 Hz, 1H), 7.35 (dt, J = 7.6, 3.5 Hz, 3H), 7.22 (dd, J = 8.4, 1.9 Hz, 3H), 5.40 (dq, J = 10.6, 4.6 Hz, 1H), 2.75 (td, J = 11.6, 3.6 Hz, 1H), 2.11 (p, J = 4.2 Hz, 1H), 1.90 – 1.75 (m, 2H), 1.68 (t, J = 14.6 Hz, 1H), 1.56 (q, J = 11.8, 10.0 Hz, 3H), 1.35 (dt, J = 12.1, 6.5 Hz, 1H), 1.27 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.98, 163.37, 148.87, 139.64, 135.35, 131.16, 129.13, 129.05, 127.16, 125.14, 78.18, 48.28, 34.14, 33.86, 31.65, 31.22, 25.06, 24.06. HRMS (ESI) *m/z* calcd for $C_{24}H_{28}NaO_3$ $[M+Na]^+$: 387.1936, found: 387.1928; HRMS (ESI) *m/z* calcd for $C_{24}H_{28}NaO_3$ $[M+NH_4]^+$: 382.2382, found: 382.2382. $[\alpha]^{20.0}_D$ = -58.7 (*c* 1.12, CH_3OH), >99% ee.

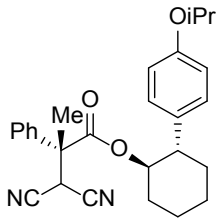


(-)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11i).
Yield: 83%, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.57 (ddt, J = 8.0, 7.2, 1.2 Hz, 1H), 7.41 – 7.26 (m, 3H), 7.22 – 7.09 (m, 2H), 7.09 – 6.96 (m, 1H), 5.34 (td, J = 10.6, 4.3 Hz, 1H), 2.72 (td, J = 11.6, 3.6 Hz, 1H), 2.21 – 2.05 (m, 1H), 1.80 (d, J = 16.0 Hz, 2H), 1.67 (t, J = 14.0 Hz, 1H), 1.56 (ddd, J = 24.4, 12.0, 6.1 Hz, 2H), 1.35 (d, J = 3.1 Hz, 1H), 1.28 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.19, 161.09, 148.87, 139.29, 132.94, 129.63, 128.89, 128.67, 127.05, 125.12, 112.20, 111.67, 88.01, 79.88, 48.15, 34.12, 33.61, 31.20, 25.00, 23.93. HRMS (ESI) *m/z* calcd for $C_{27}H_{29}N_2O_2$ $[M+H]^+$: 413.2229, found: 413.2232. $[\alpha]^{20.0}_D$ = -33.7 (*c* 0.655, CH_3OH), >99% ee.



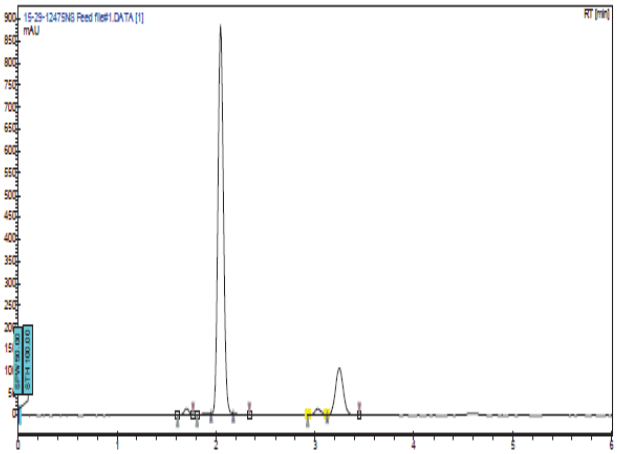
11a-i **12a-i**

General Procedure:
Reactions were performed via same general procedure described for **9**. Selectivity was determined by HPLC of crude reaction mixtures; diastereomers were confirmed by 1H NMR of isolated peaks. The absolute configuration of the newly formed quaternary carbon was confirmed via coupling of **12i** and **13** to form **14** with known configuration.

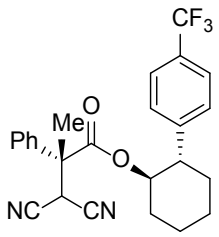


(*1R,2S*)-2-(4-isopropoxyphenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12a).
Yield: 73%, white solid, eluted 1st major peak, 6:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.32 – 7.20 (m, 1H), 7.12 (t, J = 7.8 Hz, 2H), 7.06 – 6.93 (m, 2H), 6.85 – 6.77 (m, 2H), 6.77 – 6.69 (m, 2H), 5.50 (s, 1H), 5.11 (td, J = 10.4, 4.2 Hz, 1H), 4.55 (p, J = 6.0 Hz, 1H), 2.56 (td, J = 11.7, 3.7 Hz, 1H), 1.99 (d, J = 10.1 Hz, 1H), 1.76 (dd, J = 22.0, 12.3 Hz, 1H), 1.65 (s, 4H), 1.60 – 1.35 (m, 3H), 1.27 (t, J = 5.8 Hz, 7H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.56, 156.02, 136.20, 134.28, 128.44, 128.23, 128.17, 126.05, 115.24, 112.74, 112.70, 78.26, 68.95, 52.55, 47.65, 33.90, 32.73, 31.61, 25.12, 23.96, 21.99, 21.89, 21.24. HRMS (ESI) *m/z* calcd for $C_{27}H_{31}N_2O_3$ $[M+H]^+$: 431.2334, found 431.2332.

Analytical: AD-H (25X0.46cm), 20%IPA/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (15X2cm), 15%IPA/CO_2, 100bar, 60mL/min, 220nm, 5mg/0.5mL/inj

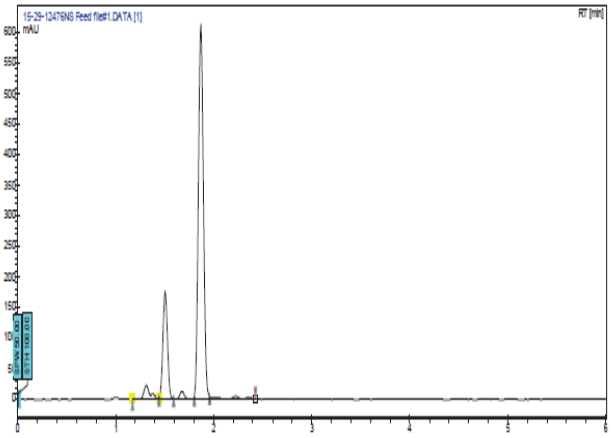


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
3	UNKNOWN	1.61	1.70	1.77	0.00	1.19	14.9	0.8	1.186
4	UNKNOWN	1.81	1.89	1.95	0.00	0.52	4.0	0.4	0.520
5	UNKNOWN	1.95	2.05	2.18	0.00	82.17	884.4	56.2	82.171
6	UNKNOWN	2.18	2.18	2.34	0.00	0.35	3.3	0.2	0.351
1	UNKNOWN	2.93	3.03	3.13	0.00	1.65	13.6	1.1	1.648
2	UNKNOWN	3.13	3.25	3.45	0.00	14.12	107.0	9.7	14.124
Total						100.00	1027.2	68.4	100.000

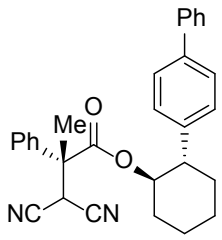


(*1R,2S*)-2-(4-(trifluoromethyl)phenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12b). Yield: 59%, white solid, eluted 2nd major peak, 4:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.50 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.28 – 7.17 (m, 1H), 7.08 (t, J = 7.8 Hz, 2H), 6.91 – 6.76 (m, 2H), 5.55 (s, 1H), 5.18 (td, J = 10.6, 4.2 Hz, 1H), 2.76 (td, J = 11.9, 3.7 Hz, 1H), 2.15 – 2.00 (m, 1H), 1.79 (t, J = 11.7 Hz, 1H), 1.69 (s, 4H), 1.66 – 1.53 (m, 1H), 1.53 – 1.40 (m, 1H), 1.40 – 1.22 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 218.11, 170.47, 135.84, 128.36, 128.31, 128.06, 125.80, 125.04, 125.00, 112.69, 112.62, 77.85, 52.24, 48.25, 33.25, 32.67, 31.40, 24.91, 23.76, 20.57. HRMS (ESI) *m/z* calcd for $C_{25}H_{22}F_3N_2O_2$ [M-H]$^-$: 439.1634, found 439.1638.

Analytical: AD-H (25X0.46cm), 20%IPA/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (15X2cm), 15%IPA/CO_2, 100bar, 60mL/min, 220nm, 5mg/0.5mL/inj

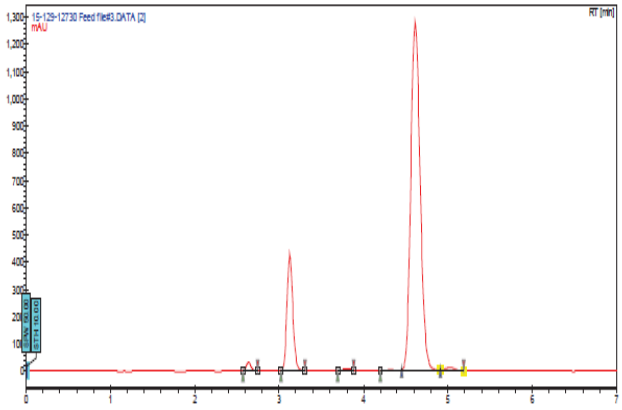


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	1.17	1.31	1.45	0.00	3.26	21.8	1.6	3.258
5	UNKNOWN	1.45	1.51	1.60	0.00	19.22	175.6	9.3	19.223
4	UNKNOWN	1.60	1.67	1.80	0.00	1.43	12.2	0.7	1.434
3	UNKNOWN	1.80	1.87	1.96	0.00	74.55	612.1	36.0	74.546
2	UNKNOWN	1.96	1.96	2.43	0.00	1.54	4.5	0.7	1.538
Total						100.00	826.3	48.3	100.000

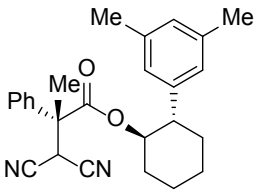


(*1R,2S*)-2-([1,1'-biphenyl]-4-yl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12c).
Yield: 65%, white solid, eluted 2nd major peak, 5:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66 (d, J = 7.6 Hz, 2H), 7.49 (dt, J = 7.5, 3.6 Hz, 4H), 7.37 (t, J = 7.4 Hz, 1H), 7.22 (d, J = 7.8 Hz, 2H), 7.12 (t, J = 7.4 Hz, 1H), 7.01 (t, J = 7.6 Hz, 2H), 6.79 (d, J = 7.7 Hz, 2H), 5.52 (s, 1H), 5.22 (td, J = 10.6, 4.2 Hz, 1H), 2.69 (td, J = 11.5, 3.7 Hz, 1H), 2.05 (d, J = 10.6 Hz, 1H), 1.79 (d, J = 11.8 Hz, 2H), 1.68 (s, 3H), 1.65 – 1.21 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.59, 141.88, 140.06, 138.24, 136.05, 128.92, 128.38, 128.09, 127.83, 127.19, 126.51, 126.45, 125.96, 112.70, 78.03, 52.47, 48.14, 33.67, 32.72, 31.55, 25.06, 23.91, 21.04. HRMS (ESI) *m/z* calcd for $C_{30}H_{27}N_2O_2$ [M-H]$^-$: 447.2073, found 447.2081.

Analytical: AD-H (25X0.46cm), 40%IPA/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (25X2cm), 35%IPA/CO_2, 100bar, 60mL/min, 220nm, 10mg/0.5mL/inj

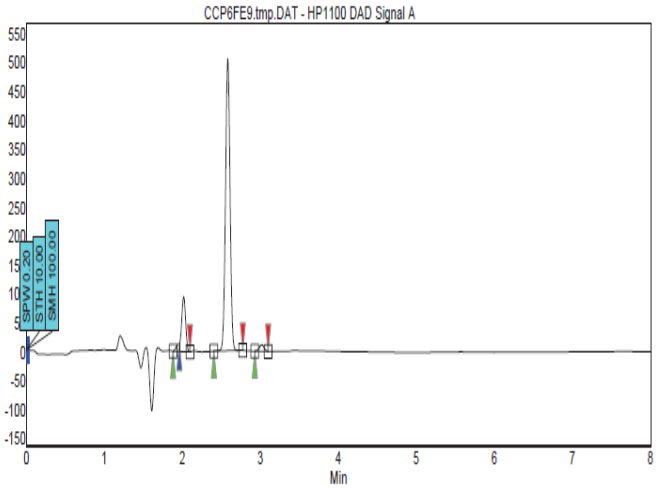


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	2.50	2.63	2.74	0.00	1.01	32.2	2.1	1.013
2	UNKNOWN	2.97	3.13	3.37	0.00	16.82	426.5	34.7	16.818
3	UNKNOWN	3.57	3.80	3.88	0.00	0.24	5.6	0.5	0.243
4	UNKNOWN	4.16	4.33	4.46	0.00	0.29	4.4	0.6	0.290
5	UNKNOWN	4.46	4.61	4.91	0.00	80.74	1281.7	166.3	80.738
6	UNKNOWN	4.91	5.03	5.31	0.00	0.90	13.2	1.8	0.897
Total						100.00	1763.6	206.0	100.000

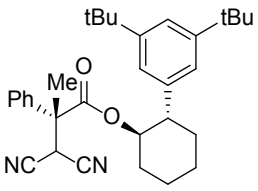


(*1R,2S*)-2-(3,5-dimethylphenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12d).
Yield: 73%, white solid, eluted 2nd major peak, 6:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.25 (t, J = 7.4 Hz, 1H), 7.08 (t, J = 7.9 Hz, 2H), 6.83 (s, 1H), 6.79 – 6.67 (m, 4H), 5.49 (s, 1H), 5.16 (td, J = 10.4, 4.1 Hz, 1H), 2.56 (dd, J = 11.6, 3.5 Hz, 1H), 2.19 (s, 6H), 2.00 (d, J = 10.1 Hz, 1H), 1.76 (dd, J = 23.8, 13.5 Hz, 2H), 1.66 (s, 4H), 1.59 – 1.36 (m, 3H), 1.36 – 1.19 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.63, 142.47, 136.99, 136.08, 128.29, 128.15, 127.88, 125.95, 125.00, 112.71, 77.96, 52.47, 48.45, 33.91, 32.81, 31.54, 25.10, 23.97, 21.15, 20.96. HRMS (ESI) *m/z* calcd for $C_{26}H_{27}N_2O_2$ [M-H]$^-$: 399.2073, found 399.2073.

Analytical: AD-H (25X0.46cm), 20%IPA(DEA)/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (15X2cm), 12%IPA/CO_2, 100bar, 70mL/min, 220nm, 20mg/4mL/inj

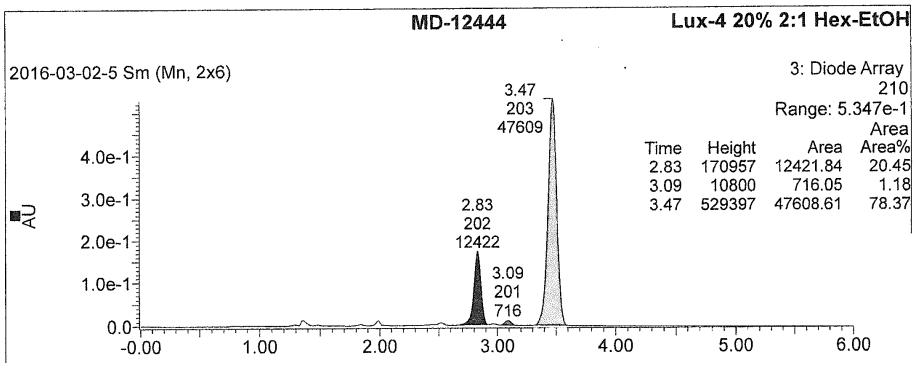


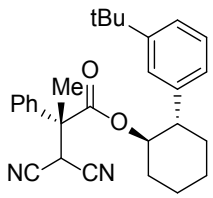
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	1.88	1.96	1.96	0.00	1.43	13.5	0.6	1.427
4	UNKNOWN	1.96	2.01	2.10	0.00	13.69	94.8	5.6	13.694
2	UNKNOWN	2.40	2.58	2.77	0.00	82.89	505.1	33.9	82.889
3	UNKNOWN	2.93	3.02	3.10	0.00	1.99	11.4	0.8	1.990
Total						100.00	624.8	40.9	100.000



(*1R,2S*)-2-(3,5-di-tert-butylphenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12e). Chiral separation by SFC using AD-H column (20% 2:1 Hexane-EtOH/CO_2). Yield: 75%, white solid, eluted 2nd , major peak, 4:1 selectivity). δ ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.28 (t, J = 1.8 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 1.8 Hz, 2H), 6.97 (t, J = 7.7 Hz, 2H), 6.71 – 6.63 (m, 2H), 5.41 (s, 1H), 5.37 (dd, J = 10.5, 4.1 Hz, 1H), 2.73 – 2.62 (m, 1H), 2.06 – 1.97 (m, 1H), 1.79 (t, J = 14.1 Hz, 2H), 1.68 (d, J = 12.9 Hz, 1H), 1.60 (s, 3H), 1.58 – 1.28 (m, 4H), 1.25 (s, 18H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.67, 149.94, 141.88, 136.38, 128.28, 127.99, 126.03, 121.23, 119.92, 112.76, 112.57, 77.31, 52.73, 49.08, 34.86, 34.44, 32.82, 31.71, 31.25, 25.18, 23.97, 21.68. HRMS (ESI) *m/z* calcd for $C_{32}H_{39}N_2O_2$ [M-H]$^-$: 483.3012, found 483.3020.

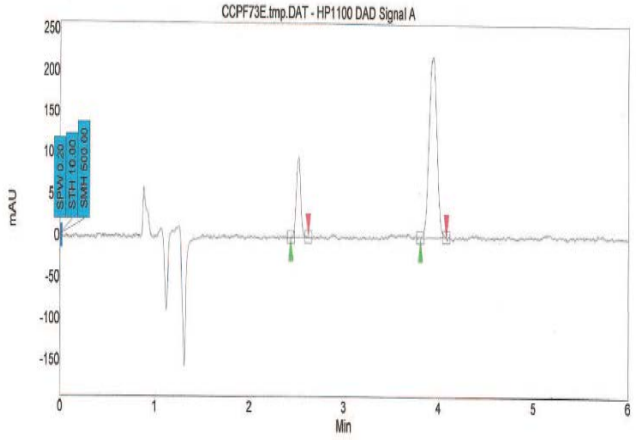
Analytical: Lux Cellulose-4(25X0.46cm), 20% 2:1 Hexane-EtOH/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: Lux Cellulose-4(25X2.1cm), 20% 2:1 Hexane-EtOH/CO_2, 100bar, 50mL/min, 210 nm, 20mg/mL/inj



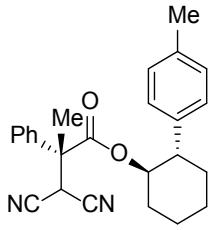


(*1R,2S*)-2-(3-(tert-butyl)phenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12f).
Yield: 69%, white solid, eluted 2nd, major peak, 4:1 selectivity). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.29 – 7.14 (m, 5H), 7.04 (t, J = 7.8 Hz, 2H), 6.94 (dt, J = 7.6, 1.5 Hz, 1H), 6.72 – 6.65 (m, 2H), 5.44 (s, 1H), 5.31 (td, J = 10.6, 4.2 Hz, 1H), 2.66 (td, J = 11.6, 3.6 Hz, 1H), 2.02 (dd, J = 9.2, 4.8 Hz, 1H), 1.87 – 1.72 (m, 2H), 1.68 (d, J = 13.1 Hz, 1H), 1.62 (s, 3H), 1.57 – 1.26 (m, 3H), 1.23 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.59, 150.49, 142.28, 136.29, 128.42, 128.07, 127.96, 125.96, 124.53, 123.88, 123.23, 112.73, 112.60, 77.69, 52.65, 48.84, 34.36, 34.30, 32.76, 31.64, 25.12, 23.94, 21.51. HRMS (ESI) *m/z* calcd for $C_{28}H_{31}N_2O_2$ $[M-H]^-$: 427.2386, found 427.2387.

Analytical: AD-H (25X0.46cm), 10%IPA/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (25X2cm), 10%IPA/CO_2, 100bar, 70mL/min, 220nm, 5mg/mL/inj

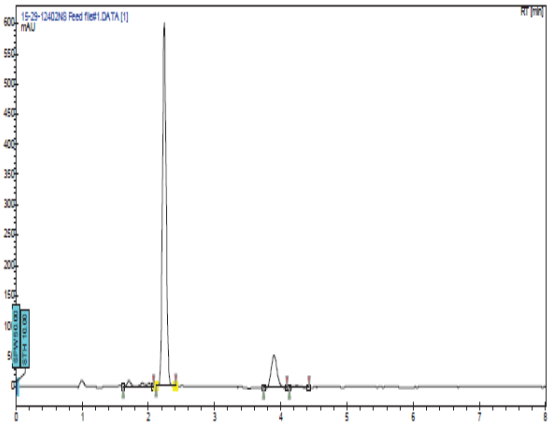


Index	Time	Width	Height	Res. HW	Selectivity	Area	Area
	[Min]	[Min]	[μV]			[μV.Min]	[%]
1	2.52	0.05	94.6	0.00	0.00	5.2	20.061
2	3.94	0.09	220.7	11.88	1.56	20.8	79.939
Total			315.3			26.0	100.000

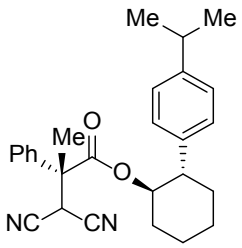


(*1R,2S*)-2-(p-tolyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12g).
Yield: 78%, white solid, eluted 1st major peak, 7:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.33 – 7.21 (m, 1H), 7.08 (t, J = 7.8 Hz, 2H), 6.99 (s, 3H), 6.81 – 6.72 (m, 2H), 5.51 (s, 1H), 5.12 (td, J = 10.4, 4.2 Hz, 1H), 2.58 (td, J = 11.3, 10.8, 3.7 Hz, 1H), 2.29 (s, 3H), 2.01 (dd, J = 8.5, 4.4 Hz, 1H), 1.84 – 1.73 (m, 1H), 1.71 (d, J = 5.0 Hz, 1H), 1.66 (s, 3H), 1.60 – 1.37 (m, 3H), 1.37 – 1.17 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.54, 139.49, 136.09, 135.19, 128.78, 128.43, 128.11, 127.08, 125.94, 112.72, 78.22, 52.51, 48.07, 33.69, 32.73, 31.59, 25.08, 23.93, 21.10, 20.66. HRMS (ESI) *m/z* calcd for $C_{25}H_{25}N_2O_2$ [M-H]$^-$: 385.1916, found 385.1923.

Analytical: AD-H (25X0.46cm), 20%IPA/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (15X2cm), 15%IPA/CO_2, 100bar, 60mL/min, 220nm, 5mg/0.5mL/inj

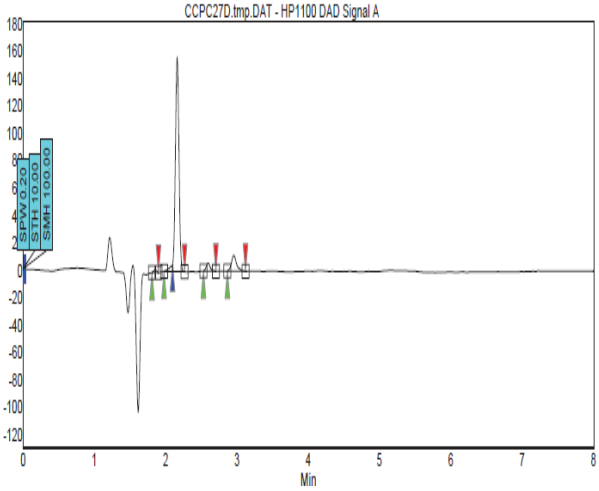


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
3	UNKNOWN	1.62	1.70	2.08	0.00	2.80	9.9	1.3	2.802
1	UNKNOWN	2.11	2.24	2.41	0.00	84.11	598.8	38.2	84.105
2	UNKNOWN	3.74	3.90	4.09	0.00	12.38	53.8	5.6	12.378
4	UNKNOWN	4.13	4.25	4.43	0.00	0.71	3.2	0.3	0.715
Total						100.00	665.7	45.5	100.000

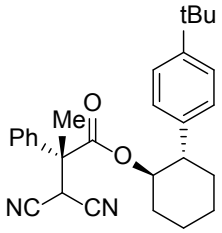


(*1R,2S*)-2-(4-isopropylphenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12h).
Yield: 64%, white solid, eluted 1st major peak, 10:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.25 (t, J = 7.4 Hz, 1H), 7.18 – 6.99 (m, 6H), 6.86 – 6.68 (m, 2H), 5.48 (s, 1H), 5.18 (td, J = 10.5, 4.2 Hz, 1H), 2.87 (p, J = 6.9 Hz, 1H), 2.60 (td, J = 11.6, 3.6 Hz, 1H), 2.01 (dd, J = 8.4, 4.3 Hz, 1H), 1.85 – 1.68 (m, 3H), 1.65 (s, 3H), 1.60 – 1.38 (m, 3H), 1.31 (dd, J = 14.2, 10.7 Hz, 1H), 1.21 (d, J = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.61, 146.17, 139.89, 136.09, 128.41, 128.22, 127.16, 126.17, 126.10, 112.70, 112.67, 77.96, 52.49, 48.07, 33.98, 33.00, 32.76, 31.57, 25.10, 23.94, 23.91, 23.87, 21.19. HRMS (ESI) *m/z* calcd for $C_{27}H_{31}N_2O_2$ $[M+H]^+$: 415.2385, found 415.2389.

Analytical: AD-H (25X0.46cm), 20%IPA(DEA)/CO_2, 100bar, 3mL/min, 220 and 254nm
Preparative: AD-H (15X2cm), 15%IPA/CO_2, 100bar, 60mL/min, 220nm, 7mg/mL/inj

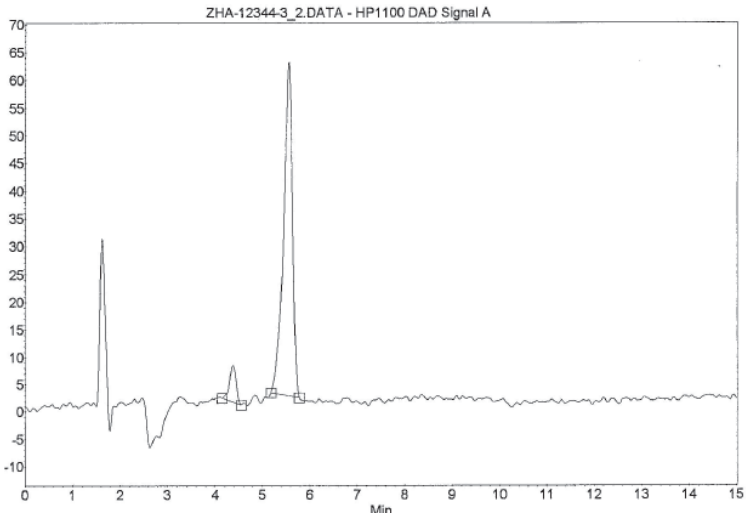


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	1.81	1.85	1.90	0.00	0.84	1.9	0.1	0.836
2	UNKNOWN	1.98	2.10	2.10	0.00	2.21	5.2	0.2	2.206
4	UNKNOWN	2.10	2.16	2.26	0.00	84.70	156.6	9.1	84.702
3	UNKNOWN	2.53	2.59	2.70	0.00	3.31	5.7	0.4	3.313
5	UNKNOWN	2.87	2.95	3.12	0.00	8.94	11.5	1.0	8.943
Total						100.00	180.9	10.7	100.000

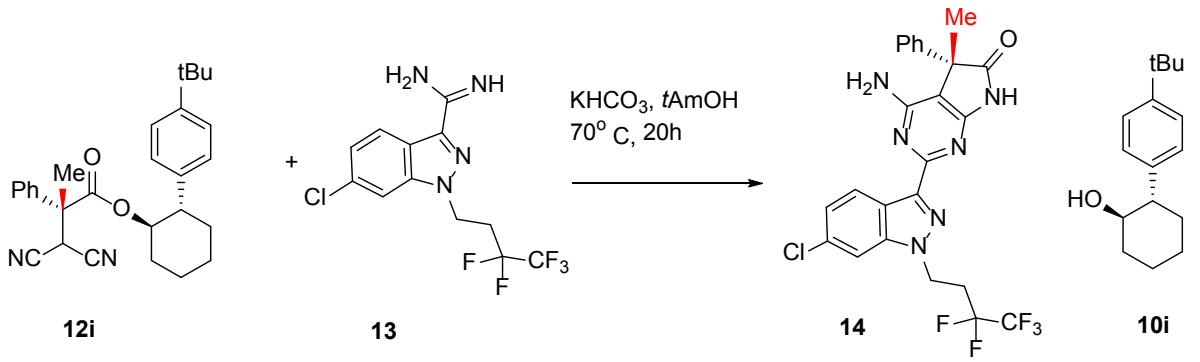


(-)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12i).
Yield: 87%, white solid, eluted 2nd, major peak, 12:1 selectivity. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.30 – 7.19 (m, 3H), 7.11 (t, J = 7.8 Hz, 2H), 7.09 – 7.00 (m, 2H), 6.84 – 6.72 (m, 2H), 5.48 (s, 1H), 5.19 (td, J = 10.5, 4.2 Hz, 1H), 2.60 (td, J = 11.6, 3.6 Hz, 1H), 2.01 (d, J = 10.1 Hz, 1H), 1.77 (t, J = 15.9 Hz, 2H), 1.65 (s, 3H), 1.61 – 1.36 (m, 3H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.62, 148.40, 139.48, 136.07, 128.40, 128.24, 126.91, 126.22, 124.91, 112.69, 112.66, 77.87, 52.47, 47.94, 34.05, 34.00, 32.77, 31.55, 31.18, 25.09, 23.94, 21.19. HRMS (ESI) *m/z* calcd for $C_{28}H_{31}N_2O_2$ [M-H]$^-$: 427.2386, found 427.2386. $[\alpha]^{20.0}_D$ = -48.4 (*c* 0.97, CH_3OH), >99% ee.

Analytical: AD-H (25X0.46cm), 15%IPA(0.1%DEA)/CO_2, 100bar, 2.1mL/min, 40 °C
Preparative: AD-H (25X2cm), 13%IPA/CO_2, 100bar, 60mL/min, 220nm, 10mg/0.6mL/inj



Index	Time [Min]	Area [μV.Min]	Area [%]
1	4.37	1.1	7.582
2	5.56	13.3	92.418
Total		14.4	100.000



(-)-(*S*)-4-amino-2-(6-chloro-1-(3,3,4,4,4-pentafluorobutyl)-1H-indazol-3-yl)-5-methyl-5-phenyl-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one (14).

6-chloro-1-(3,3,4,4,4-pentafluorobutyl)-1H-indazole-3-carboximidamide (**13**, 0.14 mmol),[8] (*R*)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexyl 3,3-dicyano-2-methyl-2-phenylpropanoate (**12i**, 0.12 mmol), potassium bicarbonate (0.35 mmol) and *t*AmOH (2.3 mL) were added into a vial, and heated to 75 °C for 17 hours. The reaction was cooled to room temperature and diluted with EtOAc and aqueous work up, followed by silica gel flash column chromatography ((EtOAc:EtOH 3:1)/Hexane 0-30%) to provide title compound as a white solid in 88% yield. Under these conditions, the alcohol **10i** elutes with early eluting impurities, but can be purified and recovered in high yields as described below. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.13 (s, 1H), 8.71 (d, J = 8.7 Hz, 1H), 8.05 (d, J = 1.7 Hz, 1H), 7.43 – 7.21 (m, 5H), 6.57 (s, 2H), 4.84 (t, J = 6.8 Hz, 2H), 2.92 (tt, J = 19.4, 6.9 Hz, 2H), 1.81 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 180.13, 162.79, 158.92, 156.90, 142.27, 141.09, 138.29, 131.66, 128.46, 127.19, 126.49, 125.35, 122.24, 121.33, 109.88, 101.08, 50.65, 40.91, 29.71, 29.50, 29.30, 19.36. HRMS (ESI) *m/z* calcd for $C_{24}H_{19}ClF_5N_6O$ $[M+H]^+$: 537.1229, found 537.1239. $[\alpha]^{20.0}_D$ = -146.5 (*c* 0.387, CH_3OH), >99% ee.

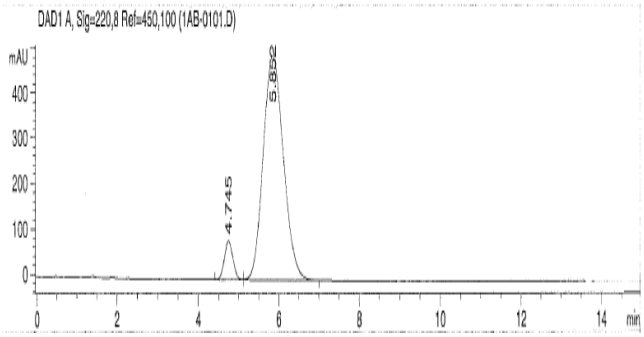
Isolation of 10i:

6-chloro-1-(3,3,4,4,4-pentafluorobutyl)-1H-indazole-3-carboximidamide (**13**, 0.19 mmol), (*R*)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexyl 3,3-dicyano-2-methyl-2-phenylpropanoate (**12i**, 0.16 mmol) and potassium bicarbonate (0.48 mmol) and then *t*AmOH (3.2 mL) was added and heated to 75 °C overnight. The reaction was cooled to room temperature and diluted with EtOAc and aqueous work up, the chiral alcohol could be recovered in high purity using alternative chromatography conditions as described for the isolation of **14** (MTBE)/hexanes 0-20%; UV detection @ 210 nm) affording **10i** in 86%. MTBE was used to enable UV detection @ 210 nm, **14** was not isolated in this experiment.

Confirmation of maintained selectivity from 12i to 14:

12i (10mg, d.e. 92.4:7.58) before separation of diastereomers, was reacted with **13** under the same condition above. The product chiral ratio was analyzed and found to match the diastereoselectivity of 12:1, and matched the retention product of the authentic **14** with previously determined absolute configuration by X-ray structure analysis.

Analytical: ChiralCel OJ (25X0.46cm), 30%MeOH(0.2%DEA)/CO_2, 100bar, 2.1mL/min, 35 ^{o}C, 220 nm



Signal 1: DAD1 A, Sig=220,8 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.745	BV	0.2332	1292.00439	86.03106	6.8645
2	5.852	VB	0.5562	1.75295e4	496.19897	93.1355
Totals :				1.88215e4	582.23003	

Computational Methods

Each transition state was subject to an exhaustive conformational sampling to identify the lowest energy transition state conformation for each configuration. Only the lowest energy conformation for each structure is presented. Transition states were initially optimized using B3LYP/6-31G* with a D3 dispersion correction. Single point energies were calculated using B3LYP-D3/def2tzvpp, M06-2X/def2tzvpp, or B3YLP/6-31G** with implicit SMD tetrahydrofuran (THF).[ref 1-5] Transition states were located using calcall with a reduced stepsize. All stationary points were confirmed with frequency calculations. Transition states were confirmed to have one imaginary vibration corresponding to Grignard addition of methyl. The free energies were corrected using a quasi-harmonic routine.[ref 6] All calculations were run using Gaussian 09.[ref 7] Images were generated using CYLview.[ref 8]

The stereoselectivity was best reproduced when using a dimeric Me-MgCl model (Table S1) and it was determined that the best model chemistry was obtained when pursuing full implicit solvent minimizations using M06-2X/6-31G** incorporating SMD implicit THF (no other energies have been reported). In addition to dimeric Me-MgCl, several conditions have been modeled, including monomeric Me-MgCl or Me-MgBr, monomeric Me-MgCl/Br with explicitly coordinated THF, and monomeric Me-MgCl/Br with an additional LiCl counterion. Structures for the monomeric Grignard in absence of either a coordinating explicit THF solvent molecule or LiCl counterion did not converge and are not reported. The transition-state energy differences for some of these model conditions predicted the opposite sense of stereo-control compared to experiment. For this reason, we consider the models generated from these species to not be relevant to experiment. Only the dimeric species provided energies consistent with experiment. In addition to the structures reported in the main text for the dimeric sysem, we present models below for monomeric Me-MgCl/Br with 1 explicit THF solvent molecule and monomeric Me-MgCl/Br with an additional LiCl counterion. Structures for molecule **9a**:isopropyl are found in Figures S1 and S2; structures for molecule **9e**:phenyl are found in Figure S3.

Table S1: Relative transition state free energies (in kcal/mol) for selected model chemistries of **9a**: isoproyl[1]

System	Grignard	Ion	Explicit Solvent	Energy[2]	Relative $\Delta G^{\ddagger}$
R configuration	Me-MgCl	LiCl	none	-2242.250849	0.00
S	Me-MgCl	LiCl	none	-2242.249256	**0.29**
R	Me-MgCl	none	THF	-2006.807013	0.00
S	Me-MgCl	none	THF	-2006.803865	**0.75**
R	**Me-MgCl dimer**	**none**	**none**	**-2474.647898**	**0.00**
S	**Me-MgCl dimer**	**none**	**none**	**-2474.646764**	**0.02**
R	Me-MgBr	LiCl	none	-4353.876048	0.00
S	Me-MgBr	LiCl	none	-4353.873395	**0.63**
R	Me-MgBr	none	THF	-4118.433611	0.00
S	Me-MgBr	none	THF	-4118.427211	**3.12**

[1] M06-2X/6-31G** (implicit THF) relative free energies are quasi-harmonic corrected

[2] electronic energy

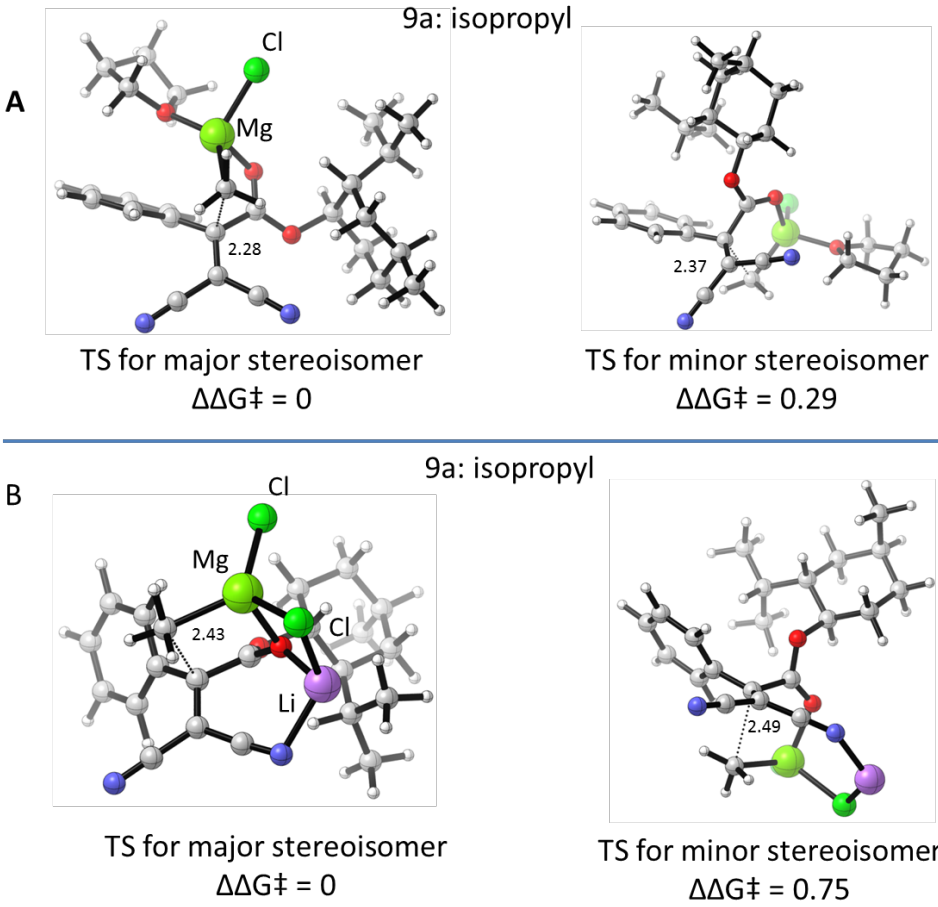


Figure S1. Transition state structures for alternate models of **9a**: isopropyl calculated at the M06-2X/6-31G** level with SMD implicit THF. Bond distances are for forming C-C bond. Panel A corresponds to a model of Me-MgCl with 1 explicit THF while panel B is Me-MgCl + LiCl counterions. Relative energies in kcal/mol.

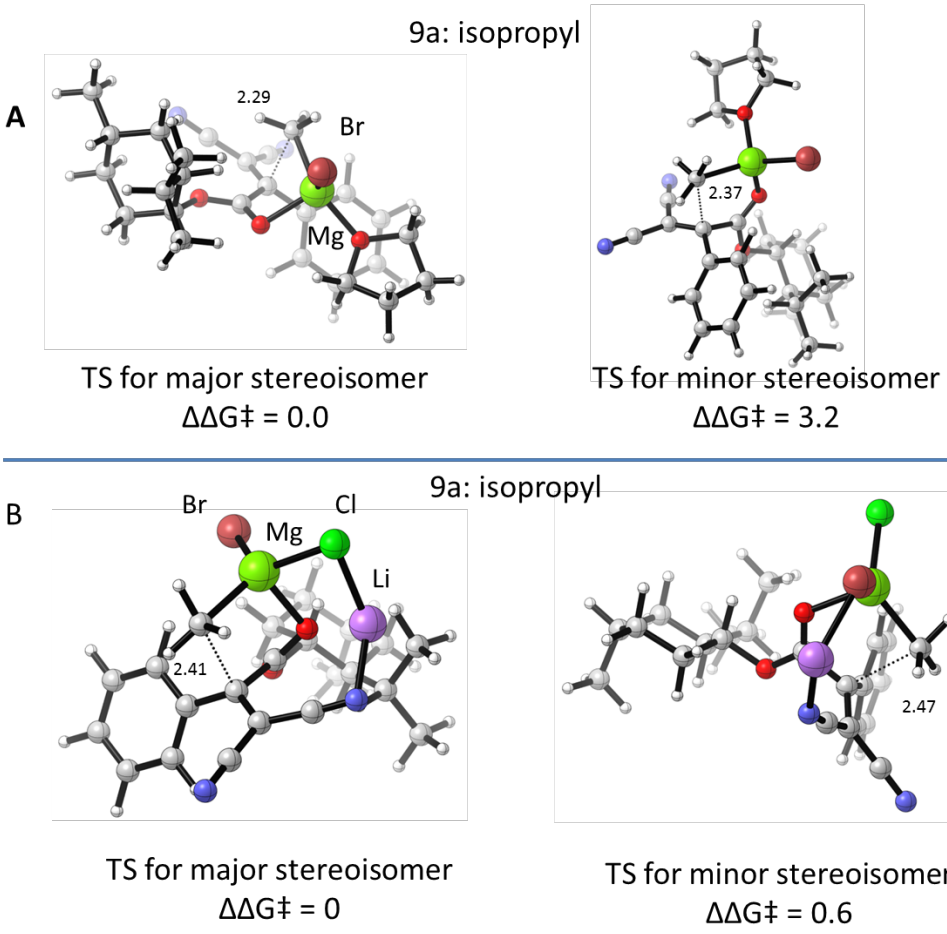


Figure S2. Transition state structures for alternate models of **9a**: isopropyl calculated at the M06-2X/6-31G** level with SMD implicit THF. Bond distances are for forming C-C bond. Panel A corresponds to a model of Me-MgBr with 1 explicit THF while panel B is Me-MgBr + LiCl counterions. Relative energies in kcal/mol.

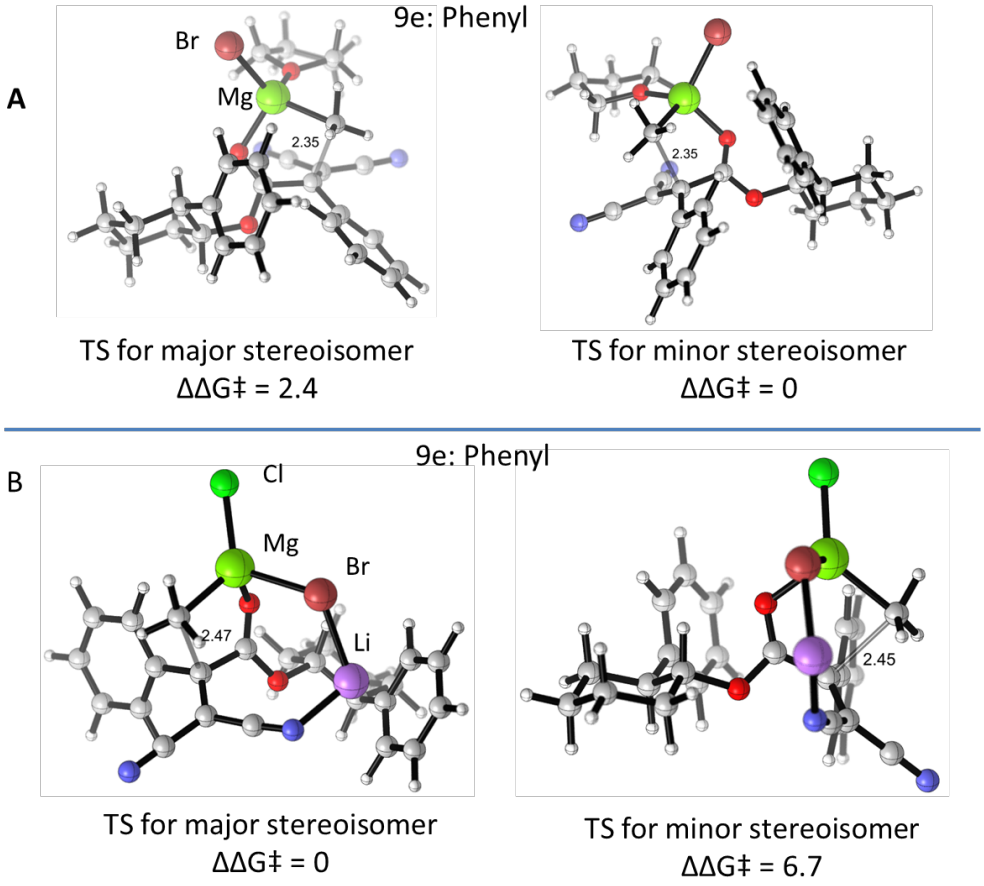


Figure S3. Transition state structures for alternate models of **9e**: phenyl calculated at the M06-2X/6-31G** level with SMD implicit THF. Bond distances are for forming C-C bond. Panel A corresponds to a model of Me-MgBr with 1 explicit THF while panel B is Me-MgBr + LiCl counterions. Relative energies in kcal/mol.

Ref 1
Y. Zhao, D. G. Truhlar, The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: two new functionals and systematic testing of four M06-class functionals and 12 other functionals. Theor. Chem. Acc. 120, 215-241 (2008).

Ref 2
A. V. Marenich, C. J. Cramer, D. G. Truhlar, Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. J. Phys. Chem. B. 113, 6378-6396 (2009).

Ref 3
S. Grimme, J. Antony, S. Ehrlich, H. Krieg, A consistent and accurate ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H-Pu. J. Chem. Phys. 132, 154104-1-19 (2010).

Ref 4
A. D. Becke, Density-functional thermochemistry. III. The Role of Exact Exchange. J. Chem. Phys. 98, 5648-5652 (1993).

Ref 5
C. T. Lee, W. T. Yang, R. G. Parr, Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron-Density. Phys. Rev. B. 37, 785-789 (1988).

Ref 6
R. F. Ribeiro, A. V. Marenich, C. J. Cramer, D. G. Truhlar, Use of solution-phase vibrational frequencies in continuum models for the free energy of solvation. J. Phys. Chem. 115, 14556-14562 (2011).

Ref 7
M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. Montgomery, J.A., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox Gaussian 09, Revision D.01, Gaussian, Inc.: Wallingford, CT, 2009.

Ref 8
C.Y. Legault, CYLview v1.0.561 BETA, 2012.

Coordinates for transition states for 9a, 9e, 12i from Figure 2: M06-2X/6-31G** SCRF=(SMD,solvent=tetrahydrofuran)

Molecule 9a R configuration

Electronic energy: -2474.64789765 hartrees

6 -1.54581 -0.479977 0.851243
6 -1.39634 0.165866 2.07056
6 -2.23245 -0.077276 3.19863
6 -0.604512 1.33666 2.04726
7 -2.90372 -0.277474 4.12142
7 0.028518 2.28735 1.85097
6 -2.25374 -1.77897 0.697811
6 -0.403976 -0.334899 -0.145155
8 0.633383 -0.99647 0.272278
8 -0.45028 0.271807 -1.21065
6 1.817 -1.10573 -0.595846
6 3.04275 -0.94143 0.292698
6 4.28319 -1.12424 -0.59881
6 4.2964 -2.46595 -1.35137
6 3.00419 -2.62571 -2.16524
6 1.75458 -2.45182 -1.29691
6 3.02217 0.38397 1.08675
6 -2.94237 -2.08347 -0.483504
6 -3.52378 -3.33426 -0.643423
6 -3.41606 -4.29168 0.365329
6 -2.72008 -3.99706 1.53379
6 -2.13341 -2.74625 1.70259
1 1.76461 -0.297736 -1.33009
1 3.02378 -1.75664 1.03024
1 5.18651 -1.04411 0.014611
1 4.32114 -0.306772 -1.33083
1 5.13384 -2.4335 -2.0589
1 2.98501 -1.87144 -2.96207
1 1.68663 -3.24232 -0.540942
1 0.848917 -2.50315 -1.91117
1 -3.05746 -1.32552 -1.2537
1 -4.06959 -3.55854 -1.5538
1 -3.8752 -5.26684 0.238101
1 -2.62404 -4.74179 2.31689
1 -1.56354 -2.53381 2.6014
12 -2.04668 1.45413 -1.54795
6 -3.35674 1.07989 0.131215
17 -2.62036 1.23189 -3.74486
1 -3.08334 1.86161 0.851201
1 -3.85712 0.269335 0.656974
1 -4.12703 1.49758 -0.549081
17 -0.929998 3.58141 -1.15357
12 0.559067 3.98035 0.687932
6 4.26821 0.5291 1.96121
1 2.15677 0.328897 1.76047
6 2.84406 1.62604 0.208503
1 2.91825 2.5296 0.826363
1 1.87361 1.64089 -0.307691
1 3.62297 1.70099 -0.557727
1 4.13886 1.34597 2.67761

1 5.15557 0.756044 1.36146
1 4.46695 -0.387351 2.52731
1 2.97899 -3.60613 -2.65228
6 4.53625 -3.65231 -0.415737
1 4.60151 -4.58513 -0.985196
1 5.47479 -3.5292 0.134466
1 3.73632 -3.77389 0.321094
6 2.01477 5.43259 1.00727
1 1.60889 6.45096 1.03581
1 2.77957 5.41969 0.220958
1 2.53704 5.27217 1.95905

Molecule 9a S configuration
Electronic energy: -2474.64676396 hartrees
6 -0.508587 -1.35556 -0.86248
6 -1.27971 -1.23211 -2.00909
6 -1.44667 -2.27579 -2.96505
6 -2.18166 -0.143327 -2.0235
7 -1.57631 -3.11636 -3.75157
7 -2.89498 0.753857 -1.85631
6 0.557237 -2.37329 -0.677696
6 -0.170545 -0.060397 -0.136267
8 0.902038 0.451995 -0.656262
8 -0.791004 0.432158 0.801683
6 1.56166 1.59387 -0.007764
6 3.05453 1.28448 -0.008912
6 3.76913 2.48336 0.636764
6 3.46325 3.81565 -0.070169
6 1.94533 4.04352 -0.137071
6 1.21114 2.85759 -0.771718
6 3.37487 -0.082267 0.639039
6 1.35944 -2.74973 -1.76012
6 2.45379 -3.58474 -1.55094
6 2.7554 -4.03843 -0.269965
6 1.95855 -3.65928 0.81123
6 0.865332 -2.82687 0.611239
1 1.17942 1.65559 1.01567
1 3.37092 1.22001 -1.06008
1 4.85017 2.30974 0.630808
1 3.46251 2.55884 1.68845
6 4.11663 3.90009 -1.45122
1 3.89227 4.61695 0.543819
1 1.55868 4.19026 0.879353
1 1.50174 2.73144 -1.82092
1 0.127683 3.0175 -0.74383
1 1.15529 -2.36636 -2.75464
1 3.07431 -3.87136 -2.39354
1 3.61016 -4.68835 -0.111371
1 2.18615 -4.01481 1.81088
1 0.228433 -2.54309 1.44623
12 -2.19291 -0.725463 1.68083
6 -2.36283 -2.45454 0.401197
17 -1.64482 -0.856166 3.89493
1 -1.78147 -3.26046 -0.041419
1 -3.14894 -2.15579 -0.305126
1 -2.85319 -2.90794 1.28678

17 -4.10917 0.72564 1.34236
12 -4.30205 1.8954 -0.744299
6 4.87782 -0.363032 0.630124
1 2.90109 -0.844987 0.00529
6 2.81147 -0.243222 2.05285
1 1.71646 -0.203632 2.0829
1 3.19209 0.52973 2.72988
1 3.10663 -1.21368 2.46434
1 5.06808 -1.4111 0.882041
1 5.40778 0.253534 1.36373
1 5.31579 -0.169433 -0.355229
1 3.96038 4.88932 -1.8933
1 3.71377 3.16146 -2.15128
1 5.19616 3.73143 -1.38017
1 1.7221 4.95673 -0.698549
6 -5.54589 3.48104 -1.27532
1 -6.53439 3.38403 -0.810356
1 -5.70696 3.53453 -2.35885
1 -5.14315 4.4518 -0.962949

Molecule 9e R configuration
Electronic energy: -2548.43975907 hartrees
6 1.65596 -0.580037 0.822203
6 1.06109 -0.925438 2.02509
6 1.77302 -1.4527 3.14084
6 -0.346932 -1.04855 1.98147
7 2.34891 -1.86984 4.05552
7 -1.47841 -1.13985 1.75139
6 3.10432 -0.27402 0.680375
6 0.812248 0.231381 -0.150431
8 0.583511 1.41264 0.345623
8 0.454089 -0.130972 -1.26531
6 0.000737 2.46505 -0.495706
6 -1.29015 2.92882 0.169517
6 -1.8286 4.15561 -0.597991
6 -0.79023 5.27214 -0.693287
6 0.49453 4.76604 -1.34789
6 1.04899 3.56336 -0.582714
6 3.7787 -0.530184 -0.520677
6 5.10575 -0.148931 -0.665418
6 5.76898 0.494162 0.380047
6 5.09886 0.760071 1.57032
6 3.76785 0.384167 1.72291
1 -0.194249 2.04119 -1.48347
1 -1.03302 3.24922 1.18807
1 -2.73673 4.50612 -0.097478
1 -2.12301 3.83537 -1.60669
1 -1.20281 6.112 -1.26084
1 0.285696 4.47444 -2.38523
1 1.3233 3.86229 0.436441
1 1.94612 3.16289 -1.06573
1 3.27482 -1.06234 -1.32307
1 5.62582 -0.362492 -1.59331
1 6.8076 0.787245 0.264485
1 5.60666 1.26813 2.38334
1 3.23989 0.626593 2.63938

12 0.555462 -2.11046 -1.66451
6 1.636 -2.9426 0.006622
17 1.13269 -2.32234 -3.86444
1 0.859993 -3.24827 0.718961
1 2.58259 -2.82807 0.531492
1 1.79933 -3.78411 -0.698283
1 1.25052 5.55575 -1.38278
1 -0.563066 5.64418 0.314188
6 -2.36412 1.86243 0.259989
6 -3.12702 1.75656 1.43084
6 -2.69721 1.05446 -0.83052
6 -4.21721 0.897951 1.50586
1 -2.86694 2.37229 2.28788
6 -3.79989 0.195306 -0.768992
1 -2.12484 1.10382 -1.7528
6 -4.57343 0.123188 0.395432
1 -4.80351 0.841167 2.41739
1 -4.07547 -0.38829 -1.6436
1 -5.45608 -0.509842 0.42888
17 -1.7765 -2.66909 -1.31925
12 -3.06286 -1.98936 0.627256
6 -4.48431 -3.29604 1.42819
1 -4.95824 -2.88708 2.33104
1 -5.29649 -3.51264 0.721226
1 -4.05639 -4.26597 1.71299

Molecule 9e S configuration
Electronic energy: -2548.43144191 hartrees
6 -0.35734 -1.27456 -1.01606
6 -1.33494 -1.37752 -1.99983
6 -1.43227 -2.46263 -2.91754
6 -2.46115 -0.543701 -1.81926
7 -1.51444 -3.33626 -3.67418
7 -3.32816 0.156488 -1.50091
6 0.933406 -2.00679 -1.04478
6 -0.240425 0.090977 -0.352341
8 0.431621 0.8893 -1.12677
8 -0.7098 0.409154 0.735046
6 0.760192 2.24775 -0.680353
6 0.205061 3.21147 -1.71506
6 0.595134 4.64509 -1.34334
6 2.11141 4.77801 -1.19684
6 2.65765 3.77136 -0.183227
6 2.27863 2.32539 -0.558593
6 1.58328 -2.31141 0.158846
6 2.81758 -2.94522 0.138205
6 3.42394 -3.25798 -1.07869
6 2.79324 -2.93177 -2.27516
6 1.55018 -2.30517 -2.26431
1 0.280529 2.41037 0.28751
1 0.619491 2.95123 -2.69669
1 0.216927 5.33487 -2.10329
1 0.112475 4.91634 -0.395626
1 2.37378 5.79538 -0.890474
1 2.25704 3.99158 0.81567
1 2.69292 2.11307 -1.55366

1 1.10058 -2.08528 1.10716
1 3.30803 -3.1923 1.07384
1 4.38952 -3.75378 -1.0917
1 3.26787 -3.15983 -3.22387
1 1.07944 -2.02764 -3.2016
12 -1.59716 -1.0252 1.83836
6 -1.62114 -2.74479 0.534209
17 -0.7044 -0.932801 3.93728
1 -2.58606 -2.64061 0.020915
1 -0.979892 -3.40284 -0.047564
1 -1.795 -3.28872 1.48521
1 3.74773 3.83968 -0.112035
1 2.58649 4.60359 -2.17112
17 -3.84387 -0.086248 1.86087
12 -4.79331 0.849239 -0.12793
6 -6.5527 1.92292 -0.437536
1 -6.71768 2.14905 -1.49798
1 -6.55479 2.87965 0.09806
1 -7.43207 1.3666 -0.091143
1 -0.882981 3.10007 -1.77054
6 2.85699 1.32199 0.419355
6 4.00748 0.605577 0.076413
6 2.30986 1.13738 1.69462
6 4.60875 -0.259686 0.986548
1 4.4375 0.73413 -0.914099
6 2.90133 0.260742 2.60266
1 1.42087 1.68602 1.99544
6 4.05667 -0.434844 2.25403
1 5.50293 -0.8064 0.701675
1 2.45964 0.129562 3.58566
1 4.51961 -1.11337 2.96412

Molecule 12i R configuration
Electronic energy: -2705.62683128 hartrees
6 -2.45655 -0.708383 -0.648272
6 -2.09016 -1.02699 -1.94551
6 -2.94885 -1.67885 -2.87717
6 -0.704304 -0.952773 -2.21663
7 -3.64496 -2.19822 -3.64395
7 0.450289 -0.866247 -2.25264
6 -3.87088 -0.559765 -0.211582
6 -1.52679 0.221769 0.117919
8 -1.51281 1.39311 -0.447023
8 -0.933582 -0.051276 1.15497
6 -0.936974 2.55126 0.249175
6 0.380493 2.93054 -0.424209
6 0.848341 4.29654 0.129668
6 -0.215715 5.38419 -0.000441
6 -1.50429 4.95791 0.700322
6 -2.0013 3.63282 0.126232
6 -4.25676 -0.849194 1.1039
6 -5.56455 -0.62015 1.50938
6 -6.49646 -0.097144 0.61257
6 -6.11347 0.2045 -0.690741
6 -4.80357 -0.018033 -1.10435
1 -0.780571 2.27368 1.2955

1 0.172163 3.0448 -1.49666
1 1.76749 4.57958 -0.3928
1 1.11046 4.16947 1.18876
1 0.161807 6.31988 0.423576
1 -1.31718 4.84665 1.77617
1 -2.24002 3.75791 -0.937252
1 -2.91 3.29318 0.632829
1 -3.54386 -1.2913 1.79487
1 -5.85849 -0.86103 2.52558
1 -7.5195 0.075036 0.931653
1 -6.83041 0.620757 -1.39056
1 -4.50355 0.25431 -2.1111
12 -0.725818 -2.0197 1.55706
6 -2.03081 -3.03594 0.174478
17 -0.734244 -2.24623 3.83173
1 -1.38368 -3.28688 -0.674675
1 -3.06927 -3.03379 -0.151458
1 -1.95977 -3.86171 0.912355
1 -2.28189 5.71872 0.586719
1 -0.422656 5.57101 -1.06227
6 1.50741 1.92873 -0.253836
6 2.2923 1.56027 -1.34496
6 1.91413 1.48874 1.01459
6 3.48448 0.837204 -1.17279
1 2.00559 1.87515 -2.34548
6 3.08518 0.763285 1.18649
1 1.32008 1.73742 1.89046
6 3.92577 0.451914 0.1041
1 4.09888 0.64149 -2.04724
1 3.3657 0.454393 2.18931
6 5.27944 -0.2223 0.348296
17 1.50355 -2.29722 0.670793
12 2.34213 -1.42041 -1.42725
6 3.54142 -2.5546 -2.71887
1 4.01054 -1.95424 -3.51078
1 4.34907 -3.11139 -2.22672
1 2.92203 -3.30428 -3.23194
6 5.07327 -1.61287 0.967557
6 6.08892 0.650026 1.32331
6 6.08377 -0.375675 -0.945297
1 6.04563 -2.05988 1.20082
1 4.55632 -2.28254 0.271019
1 4.48966 -1.56671 1.89191
1 7.07429 0.201774 1.48792
1 5.59512 0.739532 2.2952
1 6.2347 1.65709 0.919211
1 7.0422 -0.853076 -0.719866
1 6.29418 0.594423 -1.40784
1 5.5638 -1.00498 -1.67526

Molecule 12i S configuration
Electronic energy: -2705.61972935 hartrees
6 1.06266 -0.656255 1.53962
6 2.26226 -0.674369 2.23844
6 2.4346 -1.3106 3.50232
6 3.41172 -0.328936 1.49247

7 2.5816 -1.81473 4.53491
7 4.25453 -0.075412 0.739336
6 -0.25384 -0.90362 2.18168
6 0.991475 0.333642 0.385697
8 0.707546 1.51172 0.852924
8 1.19295 0.084452 -0.798311
6 0.47892 2.63456 -0.062395
6 1.44298 3.74114 0.328733
6 1.18286 4.97842 -0.534926
6 -0.275082 5.42641 -0.42273
6 -1.23154 4.28756 -0.780341
6 -0.982788 3.04273 0.092627
6 -1.29078 -1.52028 1.47091
6 -2.53257 -1.68521 2.07116
6 -2.75855 -1.21536 3.36434
6 -1.73731 -0.575299 4.06022
6 -0.485122 -0.418087 3.47379
1 0.685754 2.28921 -1.07834
1 1.28956 3.98231 1.38774
1 1.85959 5.78302 -0.232985
1 1.41155 4.74272 -1.58218
1 -0.458343 6.2858 -1.07525
1 -1.10464 4.00972 -1.83566
1 -1.12536 3.33056 1.14341
1 -1.11043 -1.89938 0.467654
1 -3.32835 -2.18295 1.52638
1 -3.73226 -1.34625 3.82606
1 -1.90952 -0.195044 5.06172
1 0.300784 0.104085 4.00974
12 1.42819 -1.84191 -1.33598
6 1.50484 -2.90641 0.53568
17 -0.011512 -2.29982 -3.04757
1 2.57814 -2.89732 0.76768
1 0.949403 -3.09233 1.4523
1 1.30109 -3.78836 -0.105686
1 -2.27353 4.59863 -0.655904
1 -0.474762 5.75492 0.605696
17 3.70217 -1.70557 -2.20835
12 5.33119 -0.360308 -1.061
6 7.23408 0.265137 -1.63952
1 7.71583 0.882697 -0.871735
1 7.21254 0.85917 -2.56095
1 7.89972 -0.585594 -1.82858
1 2.47237 3.38642 0.21161
6 -1.95388 1.92428 -0.225644
6 -3.03588 1.67592 0.6174
6 -1.84515 1.15528 -1.39113
6 -3.99153 0.709882 0.303735
1 -3.13994 2.2503 1.53528
6 -2.79243 0.18416 -1.69536
1 -1.02269 1.31831 -2.08351
6 -3.8919 -0.057548 -0.859382
1 -4.81481 0.555213 0.993129
1 -2.67063 -0.389539 -2.61016
6 -4.9285 -1.11228 -1.25634
6 -5.63106 -0.655994 -2.54585

6 -5.98916 -1.31461 -0.170455
6 -4.23297 -2.45826 -1.51629
1 -6.37762 -1.39658 -2.85367
1 -4.91751 -0.534833 -3.36679
1 -6.14018 0.301676 -2.39541
1 -6.69181 -2.09184 -0.487223
1 -6.56429 -0.400859 0.011182
1 -5.54244 -1.63304 0.778121
1 -4.97523 -3.21563 -1.79117
1 -3.70379 -2.8101 -0.62392
1 -3.507 -2.39142 -2.3315

Alternate model chemistries

R 9a:isopropyl Me-MgCl with LiCl
M06-2X/6-31G (implicit THF)**
6 1.6973 0.482696 0.470556
6 2.24884 -0.005384 1.65553
6 3.4098 0.567673 2.25199
6 1.79284 -1.23603 2.19915
7 4.35274 1.01933 2.75255
7 1.35622 -2.24567 2.57482
6 1.90692 1.88602 0.019912
6 0.382441 -0.136893 0.071575
8 -0.5759 0.710853 -0.062966
8 0.238937 -1.36502 -0.080877
6 -1.93146 0.232939 -0.397136
6 -2.75642 0.182837 0.890356
6 -4.19572 -0.196719 0.499006
6 -4.8197 0.763064 -0.52656
6 -3.92017 0.840846 -1.76855
6 -2.47975 1.22027 -1.41239
6 -2.15847 -0.732983 1.98145
6 1.86489 2.20335 -1.34405
6 1.98023 3.523 -1.75618
6 2.13555 4.54086 -0.813555
6 2.16222 4.23264 0.54221
6 2.04151 2.91024 0.961987
1 -1.82565 -0.759324 -0.84496
1 -2.75715 1.20376 1.29785
1 -4.81891 -0.236881 1.39908
1 -4.18856 -1.20756 0.070246
1 -5.77907 0.330493 -0.836375
1 -3.91279 -0.135404 -2.26981
1 -2.43512 2.22866 -0.986125
1 -1.84678 1.21031 -2.30475
1 1.76134 1.40566 -2.07528
1 1.9556 3.75837 -2.81512
1 2.23096 5.57185 -1.13928
1 2.26869 5.01956 1.28156
1 2.02485 2.68537 2.02321
12 1.57094 -1.89665 -1.61906
6 3.24383 -0.660363 -1.01733
17 0.264588 -1.40458 -3.4304
1 3.64353 -1.37811 -0.285175

1 3.70391 0.306109 -0.831251
1 3.59766 -0.943211 -2.03061
17 1.57716 -4.08891 -0.734269
3 0.358818 -3.06755 0.951799
6 -2.79023 -0.448205 3.34562
1 -1.09356 -0.475655 2.08064
6 -2.26379 -2.22794 1.66109
1 -1.65037 -2.80828 2.3634
1 -1.9737 -2.46445 0.629884
1 -3.29059 -2.58671 1.78482
1 -2.29407 -1.03356 4.12608
1 -3.8518 -0.715353 3.35745
1 -2.70239 0.610166 3.60971
1 -4.3202 1.56463 -2.48596
6 -5.11182 2.14363 0.06356
1 -5.62004 2.77604 -0.671368
1 -5.76063 2.06187 0.941576
1 -4.20267 2.66791 0.373118

S 9a:isopropyl Me-MgCl with LiCl
M06-2X/6-31G (implicit THF)**
6 1.26696 0.870576 -0.804399
6 1.86577 0.774745 -2.05052
6 2.45659 1.88832 -2.7163
6 2.18219 -0.527744 -2.51081
7 2.92877 2.79027 -3.26986
7 2.43206 -1.63357 -2.75599
6 0.758861 2.14547 -0.230094
6 0.422966 -0.31667 -0.36466
8 -0.795998 -0.163702 -0.789236
8 0.806639 -1.27328 0.300922
6 -1.85391 -1.05539 -0.299025
6 -3.05661 -0.169634 0.009009
6 -4.17893 -1.08889 0.517738
6 -4.53608 -2.20995 -0.475197
6 -3.27819 -3.01166 -0.844544
6 -2.14452 -2.11246 -1.34926
6 -2.70259 0.997467 0.958852
6 0.153985 3.08827 -1.06845
6 -0.461519 4.20995 -0.519505
6 -0.48384 4.39207 0.860546
6 0.115822 3.45098 1.69784
6 0.732264 2.3292 1.15767
1 -1.48324 -1.53159 0.613907
1 -3.38123 0.279907 -0.940781
1 -5.07327 -0.493496 0.728411
1 -3.86537 -1.54176 1.46767
6 -5.25835 -1.67746 -1.71486
1 -5.22562 -2.89272 0.036483
1 -2.9248 -3.55355 0.04189
1 -2.42091 -1.61801 -2.28752
1 -1.24124 -2.70289 -1.53849
1 0.133432 2.93197 -2.14234
1 -0.930133 4.93622 -1.17547
1 -0.965326 5.26702 1.28573
1 0.106661 3.59132 2.77384

1 1.21418 1.60147 1.80657
12 2.59102 -1.08376 1.24869
6 3.43961 0.703977 0.39165
17 2.11616 -1.2732 3.48388
1 3.27028 1.76751 0.236993
1 3.98675 0.303742 -0.472523
1 4.1064 0.647756 1.27631
17 3.72328 -2.99082 0.363153
3 3.3251 -3.17291 -1.8616
6 -3.92647 1.86236 1.26325
1 -1.98626 1.63115 0.418041
6 -2.03281 0.551424 2.26019
1 -1.07006 0.05404 2.09569
1 -2.67135 -0.134287 2.82802
1 -1.83419 1.42002 2.89614
1 -3.61762 2.79526 1.74575
1 -4.62061 1.35555 1.94214
1 -4.47323 2.12154 0.349969
1 -5.56161 -2.50244 -2.36775
1 -4.63122 -1.00462 -2.30791
1 -6.15991 -1.12399 -1.43303
1 -3.51681 -3.7638 -1.60394

R 9a:isopropyl Me-MgCl with explicit THF
M06-2X/6-31G (implicit THF)**
6 -0.396622 1.64525 -0.034916
6 0.220537 2.86735 -0.311548
6 -0.560749 4.03563 -0.551952
6 1.61051 3.02856 -0.579376
7 -1.17626 5.00119 -0.741885
7 2.72643 3.22167 -0.835489
6 -1.8604 1.65878 0.30038
6 0.369703 0.504766 0.580919
8 1.59842 0.754861 0.909835
8 -0.169875 -0.598902 0.765491
6 2.43183 -0.388723 1.34024
6 2.84385 -1.16828 0.084034
6 3.73161 -0.268663 -0.79045
6 4.97284 0.249646 -0.054628
6 4.54046 1.01814 1.19989
6 3.61072 0.198676 2.09683
6 3.48473 -2.5277 0.450188
6 -2.82142 2.00977 -0.65274
6 -4.16706 2.06453 -0.30312
6 -4.56535 1.76833 0.999111
6 -3.61037 1.43307 1.9559
6 -2.26378 1.37776 1.61045
1 1.8019 -0.986798 1.99799
1 1.92731 -1.41049 -0.476257
1 4.01916 -0.798685 -1.70369
1 3.14515 0.602812 -1.11173
1 5.58314 -0.610928 0.256941
1 5.42008 1.32943 1.77435
1 3.23965 0.800783 2.9323
1 4.15345 -0.648837 2.53361
1 -2.51579 2.24234 -1.66815

1 -4.904 2.33909 -1.05146
1 -5.61585 1.8108 1.26996
1 -3.91016 1.21521 2.97624
1 -1.5269 1.12014 2.3662
12 -1.29346 -0.95957 -0.874087
6 -0.215995 0.625275 -2.06798
17 -0.807841 -3.07352 -1.61249
1 0.876559 0.675483 -2.03301
1 -0.613706 1.53434 -2.51507
1 -0.454292 -0.20654 -2.76493
8 -3.14849 -1.18341 -0.167523
6 -3.29082 -2.00977 1.02495
6 -4.5944 -2.77359 0.823628
6 -5.38601 -1.84734 -0.103565
6 -4.2978 -1.35189 -1.03629
1 -2.41614 -2.6621 1.1012
1 -3.32374 -1.33133 1.88111
1 -4.40022 -3.72792 0.325595
1 -5.09668 -2.96816 1.77245
1 -6.18644 -2.35791 -0.641075
1 -5.8089 -1.00721 0.456368
1 -4.49622 -0.383843 -1.49986
1 -4.05404 -2.0957 -1.80385
6 2.5475 -3.37806 1.31315
1 4.40505 -2.34742 1.02106
6 3.85923 -3.30213 -0.815918
1 4.21257 -4.30485 -0.557241
1 4.65308 -2.81144 -1.38486
1 2.98634 -3.41248 -1.47102
1 2.3957 -2.95828 2.3116
1 2.96093 -4.38245 1.4459
1 1.56681 -3.47997 0.832423
1 4.02352 1.93298 0.883241
6 5.81381 1.1342 -0.97041
1 6.7093 1.49997 -0.45719
1 6.13524 0.588288 -1.86357
1 5.23205 2.0042 -1.29559

S 9a:isopropyl Me-MgCl with explicit THF
M06-2X/6-31G (implicit THF)**
6 -0.397019 1.43716 0.887197
6 -0.769972 1.53251 2.22136
6 -0.85222 2.78576 2.89192
6 -1.28481 0.380269 2.88044
7 -0.918239 3.80644 3.43951
7 -1.68982 -0.596414 3.36038
6 0.505064 2.4362 0.229482
6 -0.0713 0.031765 0.406547
8 1.1104 -0.318349 0.813662
8 -0.790937 -0.673537 -0.300989
6 1.74392 -1.53009 0.281628
6 3.14348 -1.12938 -0.172901
6 3.82888 -2.39866 -0.707534
6 3.86721 -3.54242 0.321951
6 2.4511 -3.84358 0.835856

6 1.74907 -2.58985 1.36791
6 3.12687 0.056648 -1.16526
6 1.54271 2.99944 0.98165
6 2.50089 3.79802 0.363607
6 2.4437 4.02649 -1.0085
6 1.41606 3.46194 -1.76263
6 0.450726 2.67164 -1.14848
1 1.14899 -1.86779 -0.571488
1 3.69012 -0.789783 0.718762
1 4.85098 -2.15858 -1.01869
1 3.29438 -2.74212 -1.60329
6 4.84319 -3.2579 1.46531
1 4.22803 -4.43805 -0.198694
1 1.85161 -4.25828 0.015321
1 2.26604 -2.19418 2.24966
1 0.719709 -2.81906 1.66379
1 1.62022 2.78863 2.04334
1 3.29934 4.23105 0.957449
1 3.1962 4.64332 -1.48974
1 1.36099 3.63898 -2.83197
1 -0.357091 2.25103 -1.74101
12 -2.35179 0.24518 -1.15979
6 -2.48432 2.07831 -0.024157
17 -2.28705 0.023315 -3.42628
1 -2.01883 3.03753 0.192667
1 -3.09014 1.77895 0.840401
1 -3.17261 2.30122 -0.870404
8 -3.82482 -0.919982 -0.490243
6 -3.9796 -1.27009 0.912462
6 -5.35995 -1.89959 0.992066
6 -5.46362 -2.6067 -0.361099
6 -4.82187 -1.60004 -1.30452
1 -3.86878 -0.357813 1.50202
1 -3.18789 -1.97755 1.17866
1 -6.12534 -1.1226 1.07917
1 -5.44625 -2.57728 1.84272
1 -6.49034 -2.83479 -0.65155
1 -4.88645 -3.53602 -0.349627
1 -5.5345 -0.84873 -1.65701
1 -4.31174 -2.04896 -2.15814
6 4.53772 0.413673 -1.6333
1 2.74529 0.922616 -0.607357
6 2.20557 -0.156025 -2.3688
1 1.15154 -0.257129 -2.08565
1 2.48404 -1.04912 -2.93979
1 2.27076 0.700588 -3.04753
1 4.53164 1.38057 -2.14636
1 4.92951 -0.329169 -2.3361
1 5.23427 0.483315 -0.790496
1 4.89702 -4.11304 2.14679
1 4.55288 -2.3848 2.05785
1 5.85037 -3.07303 1.07773
1 2.48764 -4.60659 1.62081

R 9a:isopropyl Me-MgCl dimer
M06-2X/6-31G (implicit THF)**

6 1.3963 -0.767395 -0.852891
6 1.29185 -0.151516 -2.10893
6 1.96352 -0.618238 -3.2716
6 0.787241 1.16161 -2.07683
7 2.50314 -1.00409 -4.22264
7 0.382458 2.2271 -1.85544
6 1.76327 -2.20523 -0.688953
6 0.334613 -0.360423 0.162875
8 -0.826719 -0.806854 -0.217457
8 0.527411 0.254866 1.20637
6 -1.98828 -0.670411 0.671452
6 -3.18034 -0.3049 -0.204128
6 -4.41926 -0.233809 0.704704
6 -4.66938 -1.53783 1.48166
6 -3.417 -1.91848 2.28523
6 -2.16659 -1.99038 1.40363
6 -2.92983 0.968502 -1.04224
6 2.44322 -2.64386 0.453857
6 2.68617 -3.99865 0.639832
6 2.25027 -4.92568 -0.306637
6 1.56373 -4.49378 -1.43734
6 1.31258 -3.13787 -1.62936
1 -1.77371 0.131661 1.38323
1 -3.32148 -1.12824 -0.919101
1 -5.30101 0.003062 0.100405
1 -4.29241 0.587744 1.42242
1 -5.47804 -1.34467 2.19705
1 -3.25187 -1.16901 3.06964
1 -2.25463 -2.79426 0.663827
1 -1.27854 -2.19745 2.01081
1 2.80977 -1.91974 1.17718
1 3.22509 -4.32902 1.52174
1 2.44633 -5.9831 -0.160325
1 1.21271 -5.21056 -2.17239
1 0.746879 -2.81094 -2.49604
12 2.44858 1.06797 1.41509
6 3.50122 0.263541 -0.303044
17 3.10779 0.739996 3.56453
1 3.4348 1.14748 -0.950075
1 3.79368 -0.594647 -0.902206
1 4.32839 0.395013 0.424107
17 1.88929 3.37822 0.991838
12 0.277651 3.98146 -0.692954
6 -4.1398 1.30997 -1.91327
1 -2.09653 0.732616 -1.71712
6 -2.51899 2.18758 -0.21153
1 -2.41336 3.06129 -0.865489
1 -1.56553 2.03489 0.313525
1 -3.27218 2.43817 0.543445
1 -3.87261 2.06951 -2.6542
1 -4.96367 1.71106 -1.3141
1 -4.50782 0.428919 -2.45001
1 -3.56597 -2.8795 2.78861
6 -5.13235 -2.67297 0.566077
1 -5.37311 -3.56695 1.15012
1 -6.0308 -2.38219 0.01198

1 -4.37018 -2.95393 -0.167077
6 -0.906343 5.69057 -0.81826
1 -0.328076 6.61862 -0.734387
1 -1.65951 5.71474 -0.020873
1 -1.4516 5.73928 -1.76916

S 9a:isopropyl Me-MgCl dimer
M06-2X/6-31G (implicit THF)**
6 -0.508587 -1.35556 -0.86248
6 -1.27971 -1.23211 -2.00909
6 -1.44667 -2.27579 -2.96505
6 -2.18166 -0.143327 -2.0235
7 -1.57631 -3.11636 -3.75157
7 -2.89498 0.753857 -1.85631
6 0.557237 -2.37329 -0.677696
6 -0.170545 -0.060397 -0.136267
8 0.902038 0.451995 -0.656262
8 -0.791004 0.432158 0.801683
6 1.56166 1.59387 -0.007764
6 3.05453 1.28448 -0.008912
6 3.76913 2.48336 0.636764
6 3.46325 3.81565 -0.070169
6 1.94533 4.04352 -0.137071
6 1.21114 2.85759 -0.771718
6 3.37487 -0.082267 0.639039
6 1.35944 -2.74973 -1.76012
6 2.45379 -3.58474 -1.55094
6 2.7554 -4.03843 -0.269965
6 1.95855 -3.65928 0.81123
6 0.865332 -2.82687 0.611239
1 1.17942 1.65559 1.01567
1 3.37092 1.22001 -1.06008
1 4.85017 2.30974 0.630808
1 3.46251 2.55884 1.68845
6 4.11663 3.90009 -1.45122
1 3.89227 4.61695 0.543819
1 1.55868 4.19026 0.879353
1 1.50174 2.73144 -1.82092
1 0.127683 3.0175 -0.74383
1 1.15529 -2.36636 -2.75464
1 3.07431 -3.87136 -2.39354
1 3.61016 -4.68835 -0.111371
1 2.18615 -4.01481 1.81088
1 0.228433 -2.54309 1.44623
12 -2.19291 -0.725463 1.68083
6 -2.36283 -2.45454 0.401197
17 -1.64482 -0.856166 3.89493
1 -1.78147 -3.26046 -0.041419
1 -3.14894 -2.15579 -0.305126
1 -2.85319 -2.90794 1.28678
17 -4.10917 0.72564 1.34236
12 -4.30205 1.8954 -0.744299
6 4.87782 -0.363032 0.630124
1 2.90109 -0.844987 0.00529
6 2.81147 -0.243222 2.05285

1 1.71646 -0.203632 2.0829
1 3.19209 0.52973 2.72988
1 3.10663 -1.21368 2.46434
1 5.06808 -1.4111 0.882041
1 5.40778 0.253534 1.36373
1 5.31579 -0.169433 -0.355229
1 3.96038 4.88932 -1.8933
1 3.71377 3.16146 -2.15128
1 5.19616 3.73143 -1.38017
1 1.7221 4.95673 -0.698549
6 -5.54589 3.48104 -1.27532
1 -6.53439 3.38403 -0.810356
1 -5.70696 3.53453 -2.35885
1 -5.14315 4.4518 -0.962949

R 9a:isopropyl Me-MgBr with LiCl
M06-2X/6-31G (implicit THF)**
6 1.79603 0.419534 0.670306
6 2.35615 -0.059981 1.85974
6 3.60232 0.409353 2.36627
6 1.82069 -1.22218 2.47428
7 4.61513 0.778728 2.79316
7 1.31746 -2.1789 2.903
6 2.11335 1.76399 0.113611
6 0.407801 -0.090754 0.377981
8 -0.477216 0.826881 0.216845
8 0.147644 -1.30743 0.321431
6 -1.86688 0.44244 -0.106336
6 -2.70237 0.467388 1.17375
6 -4.1617 0.188016 0.770345
6 -4.70527 1.17402 -0.275619
6 -3.79107 1.16887 -1.50925
6 -2.33077 1.44823 -1.14442
6 -2.18902 -0.481223 2.2805
6 1.92554 2.00312 -1.25556
6 2.16795 3.26172 -1.78404
6 2.59703 4.29942 -0.954252
6 2.76409 4.07353 0.407187
6 2.51766 2.81175 0.945191
1 -1.82826 -0.559935 -0.54225
1 -2.63451 1.48906 1.57337
1 -4.79495 0.205295 1.66403
1 -4.22244 -0.826912 0.355813
1 -5.6906 0.807188 -0.588374
1 -3.84826 0.186977 -1.99686
1 -2.21375 2.45984 -0.739494
1 -1.68909 1.35791 -2.02595
1 1.58987 1.19446 -1.90145
1 2.02547 3.43376 -2.84591
1 2.79131 5.28255 -1.37138
1 3.07976 4.87974 1.06111
1 2.61969 2.66087 2.01425
12 1.30353 -1.99242 -1.28814
6 3.13317 -0.928617 -0.809459
35 -0.089398 -1.00901 -3.0033
1 3.50022 -1.67698 -0.090364

1 3.7118 -0.018955 -0.676548
1 3.3801 -1.25881 -1.84143
17 0.988336 -4.16788 -0.464016
3 0.153086 -2.96743 1.36624
6 -2.80982 -0.132564 3.63473
1 -1.10826 -0.308895 2.38914
6 -2.40934 -1.96631 1.97118
1 -1.84552 -2.58787 2.68131
1 -2.13396 -2.23196 0.943096
1 -3.46093 -2.24464 2.09587
1 -2.37567 -0.75321 4.42493
1 -3.89078 -0.305998 3.63638
1 -2.63181 0.915949 3.89258
1 -4.13289 1.9078 -2.24144
6 -4.90045 2.58044 0.293156
1 -5.34415 3.24211 -0.457628
1 -5.56984 2.56018 1.15927
1 -3.95899 3.03573 0.615671

S 9a:isopropyl Me-MgBr with LiCl
M06-2X/6-31G (implicit THF)**
6 0.693497 1.2421 -0.897387
6 1.16944 1.2028 -2.20009
6 1.46353 2.3688 -2.96456
6 1.68777 -0.040301 -2.63864
7 1.69577 3.31031 -3.59918
7 2.11969 -1.09615 -2.85168
6 -0.016301 2.40695 -0.304261
6 0.146669 -0.065824 -0.343704
8 -1.07433 -0.230942 -0.754403
8 0.734014 -0.842534 0.402892
6 -1.88914 -1.31702 -0.196636
6 -3.25962 -0.719055 0.097897
6 -4.14938 -1.85086 0.638955
6 -4.23999 -3.05276 -0.318095
6 -2.83369 -3.56676 -0.661729
6 -1.92839 -2.45476 -1.20039
6 -3.17254 0.526572 1.01075
6 -0.843059 3.20229 -1.10579
6 -1.62255 4.19836 -0.523607
6 -1.59291 4.3972 0.853827
6 -0.776628 3.5987 1.65591
6 0.00675 2.60597 1.08206
1 -1.40881 -1.64843 0.728576
1 -3.67725 -0.379406 -0.86116
1 -5.15581 -1.46334 0.828829
1 -3.75145 -2.19202 1.60396
6 -5.05688 -2.73102 -1.57145
1 -4.76502 -3.85562 0.213744
1 -2.37431 -3.98597 0.24254
1 -2.30241 -2.07315 -2.15725
1 -0.912809 -2.83132 -1.36741
1 -0.906292 3.02547 -2.17455
1 -2.26095 4.8115 -1.15109
1 -2.20377 5.1731 1.30435
1 -0.745934 3.75135 2.72978

1 0.656089 1.99737 1.70719
12 2.49927 -0.224482 1.16547
6 2.95124 1.57287 0.048079
17 2.21916 -0.215858 3.43673
1 3.73361 1.66632 0.831066
1 2.58084 2.58605 -0.099451
1 3.44398 1.22882 -0.869061
35 4.06131 -2.00456 0.286743
3 3.40491 -2.34962 -2.00031
6 -4.55972 1.09435 1.31264
1 -2.62839 1.29179 0.439612
6 -2.39877 0.28855 2.31038
1 -1.34462 0.04057 2.13877
1 -2.84152 -0.521324 2.9009
1 -2.41532 1.19266 2.92731
1 -4.47066 2.08764 1.76364
1 -5.111 0.460585 2.01537
1 -5.16015 1.19161 0.401279
1 -5.15584 -3.61859 -2.20471
1 -4.60114 -1.94281 -2.17833
1 -6.06403 -2.39719 -1.30148
1 -2.8961 -4.37823 -1.39441

R 9a:isopropyl Me-MgBr with THF
M06-2X/6-31G (implicit THF)**
6 -0.282578 1.94127 -0.102774
6 0.391883 3.10637 -0.466451
6 -0.342234 4.27648 -0.820052
6 1.79033 3.171 -0.735146
7 -0.926976 5.23715 -1.1062
7 2.9181 3.2671 -0.993474
6 -1.74544 2.03251 0.229098
6 0.428295 0.816154 0.600307
8 1.66855 1.02236 0.917386
8 -0.168753 -0.239301 0.866544
6 2.41314 -0.138943 1.45165
6 2.75267 -1.0573 0.27095
6 3.73911 -0.334268 -0.661423
6 5.00476 0.161517 0.048506
6 4.61843 1.08344 1.20935
6 3.63077 0.416758 2.16631
6 3.22911 -2.45331 0.738585
6 -2.71224 2.26838 -0.753243
6 -4.05578 2.36474 -0.401776
6 -4.44491 2.2236 0.928388
6 -3.48298 2.00376 1.91189
6 -2.13909 1.90877 1.56565
1 1.73641 -0.623203 2.15451
1 1.81878 -1.23858 -0.282438
1 4.00561 -0.981491 -1.50325
1 3.23683 0.543042 -1.0938
1 5.54344 -0.704582 0.46016
1 5.51348 1.39102 1.76153
1 3.3063 1.10943 2.94941
1 4.10917 -0.433438 2.66975
1 -2.4155 2.36935 -1.79234

1 -4.79863 2.54517 -1.17239
1 -5.49407 2.29288 1.19891
1 -3.77672 1.90615 2.95239
1 -1.39483 1.73785 2.33909
12 -1.27502 -0.67666 -0.76774
6 -0.170224 0.783075 -2.07875
35 -0.785501 -2.92348 -1.49526
1 0.923284 0.730572 -2.05319
1 -0.485664 1.71144 -2.55073
1 -0.499218 -0.040474 -2.74642
8 -3.04502 -0.865214 0.143591
6 -3.01608 -1.56377 1.42199
6 -4.18177 -2.53719 1.35479
6 -5.1793 -1.78256 0.473512
6 -4.26534 -1.17972 -0.579137
1 -2.04173 -2.04864 1.53298
1 -3.14025 -0.811368 2.20599
1 -3.87001 -3.46542 0.865933
1 -4.57055 -2.77301 2.34672
1 -5.94108 -2.42655 0.031477
1 -5.67074 -0.987471 1.04353
1 -4.63165 -0.250562 -1.0193
1 -4.02594 -1.90075 -1.36973
6 2.33293 -3.02792 1.8415
1 4.2498 -2.36924 1.13491
6 3.2429 -3.42155 -0.447505
1 3.58737 -4.41084 -0.130712
1 3.90002 -3.08727 -1.25464
1 2.22877 -3.52694 -0.852084
1 2.46149 -2.51583 2.79986
1 2.56516 -4.08448 2.00642
1 1.27503 -2.95906 1.55631
1 4.16659 1.99427 0.795499
6 5.92348 0.882344 -0.933243
1 6.83827 1.2281 -0.440586
1 6.21235 0.228856 -1.76295
1 5.41607 1.75835 -1.354

S 9a:isopropyl Me-MgBr with THF
M06-2X/6-31G (implicit THF)**
6 -0.156108 1.20629 1.33847
6 -0.341606 1.08771 2.70924
6 -0.36752 2.22288 3.56811
6 -0.734456 -0.172588 3.24312
7 -0.385543 3.14913 4.26643
7 -1.05107 -1.22799 3.60913
6 0.603162 2.33463 0.711475
6 0.148435 -0.095265 0.613514
8 1.37735 -0.449793 0.829031
8 -0.62643 -0.714682 -0.116398
6 1.97658 -1.53976 0.051315
6 3.33042 -1.02913 -0.430567
6 4.00728 -2.17493 -1.20043
6 4.14277 -3.46031 -0.365024
6 2.76824 -3.89202 0.169591
6 2.07177 -2.76612 0.940628

6 3.2122 0.296464 -1.21904
6 1.70163 2.87439 1.39
6 2.52079 3.80878 0.761702
6 2.26529 4.19619 -0.550761
6 1.17762 3.65328 -1.23367
6 0.349235 2.73017 -0.606627
1 1.31988 -1.7425 -0.799542
1 3.93037 -0.811118 0.464789
1 4.99917 -1.85367 -1.53487
1 3.42171 -2.39633 -2.10289
6 5.16996 -3.31 0.759304
1 4.50401 -4.25049 -1.03492
1 2.1311 -4.18758 -0.673758
1 2.6316 -2.50657 1.84617
1 1.06684 -3.07173 1.25169
1 1.93482 2.54436 2.39721
1 3.36734 4.22386 1.2991
1 2.90977 4.91959 -1.04019
1 0.96637 3.95026 -2.25594
1 -0.507269 2.33093 -1.14445
12 -2.30021 0.263807 -0.60655
6 -2.36835 1.87496 0.828885
35 -2.51279 0.66367 -2.95529
1 -1.90506 2.80539 1.15029
1 -2.85246 1.40476 1.69466
1 -3.16225 2.20218 0.121193
8 -3.63909 -1.0761 -0.00982
6 -3.60114 -1.67505 1.31385
6 -4.95216 -2.35518 1.45356
6 -5.22498 -2.81703 0.020301
6 -4.71643 -1.64458 -0.806291
1 -3.42464 -0.87731 2.0382
1 -2.77027 -2.38754 1.34423
1 -5.70651 -1.6302 1.77369
1 -4.921 -3.17405 2.17387
1 -6.27909 -3.01993 -0.174712
1 -4.64654 -3.71763 -0.205578
1 -5.47407 -0.867754 -0.942142
1 -4.30663 -1.92815 -1.77721
6 4.58011 0.782256 -1.69917
1 2.83348 1.04636 -0.511105
6 2.22856 0.236656 -2.39072
1 1.19829 0.040413 -2.07145
1 2.50926 -0.537795 -3.11346
1 2.21911 1.19483 -2.92017
1 4.51095 1.81558 -2.05365
1 4.95543 0.173804 -2.52892
1 5.32214 0.751624 -0.893629
1 5.3101 -4.26076 1.28348
1 4.86606 -2.56674 1.5026
1 6.14081 -2.99902 0.359792
1 2.87111 -4.77072 0.

Compound 14: X-ray structure analysis.

Crystal Data and Structure Refinement for Compound 14 (CCDC 1540792)

A single crystal grown from ethanol by slow evaporation was selected for single crystal X-ray analysis. The crystal was a small colourless block with dimensions of 0.09 mm x 0.09 mm x 0.06mm. Data collection was performed on an Oxford Gemini system at 273K. The unit cell was determined to be hexagonal in the chiral space group $P6_5$. The structure contained one molecule of Compound 14 in the asymmetric unit. Crystallographic data is summarized in Table 1. Absolute configuration was determined by resonant-scattering effect in the diffraction measurements on the crystal and confirmed that the stereochemistry at the stereogenic centre was *S*. Figure 1 shows a thermal ellipsoid representation of Compound 14 with thermal ellipsoids set at the 50% probability level. Coordinates, refinement details and structure factors have been deposited with the Cambridge Crystallographic Data Centre (CCDC 1540792).

Figure 1: Thermal ellipsoid representation of Compound 14 with thermal ellipsoids set at the 50% probability level.

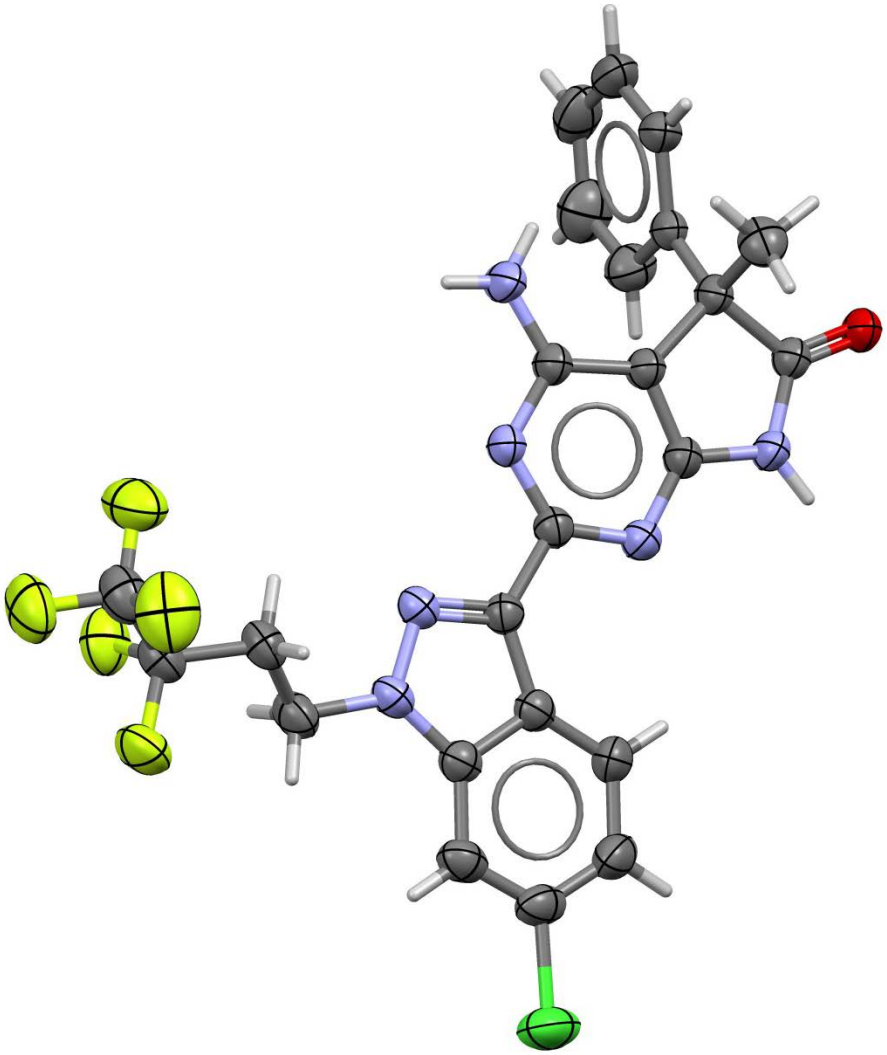


Table 1. Crystal data and structure refinement Compound 14 (CCDC 1540792)

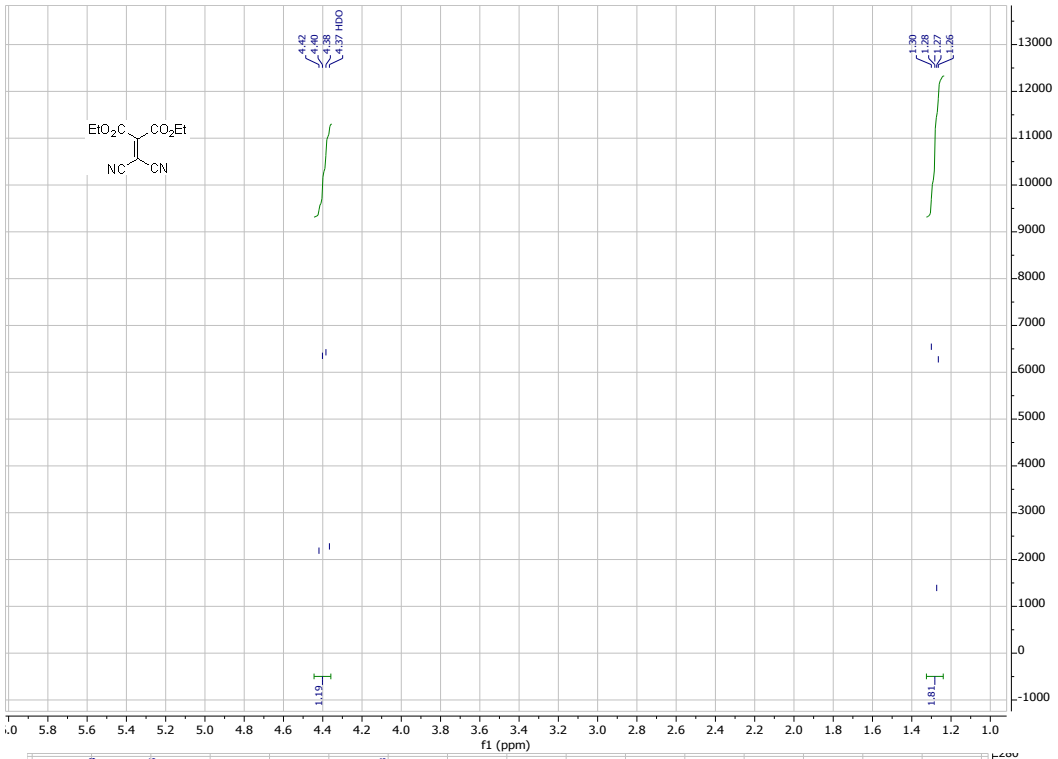
Identification code	mde120	
Empirical formula	C24 H18 Cl F5 N6 O	
Formula weight	536.89	
Temperature	273(2) K	
Wavelength	1.54178 Å	
Crystal system	Hexagonal	
Space group	$P6_5$	
Unit cell dimensions	a = 17.3410(12) Å	α= 90°
	b = 17.34103(12) Å	β= 90°
	c = 15.00551(10) Å	γ = 120°.
Volume	3907.79(5) $Å^3$	
Z	6	
Density (calculated)	1.369 g/cm^3	
Absorption coefficient	1.879mm^{-1}	
F(000)	1644	
Crystal size	0.06 x 0.09 x 0.09 mm^3	
Theta range for data collection	2.939 to 66.27°.	
Index ranges	-20<=h<=20, -20<=k<=20, -17<=l<=17	
Reflections collected	46742	
Independent reflections	4584 [R(int) = 0.0402]	
Completeness	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.897 and 0.800	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4584 / 1 / 335	
Goodness-of-fit on F^2	1.03	
Final R indices [I>2sigma(I)]	R1 = 0.0288, wR2 = 0.0757	
R indices (all data)	R1 = 0.0313, wR2 = 0.0769	
Absolute structure parameter	-0.004(12)	
Largest diff. peak and hole	0.201 and -0.167 e.$Å^{-3}$	

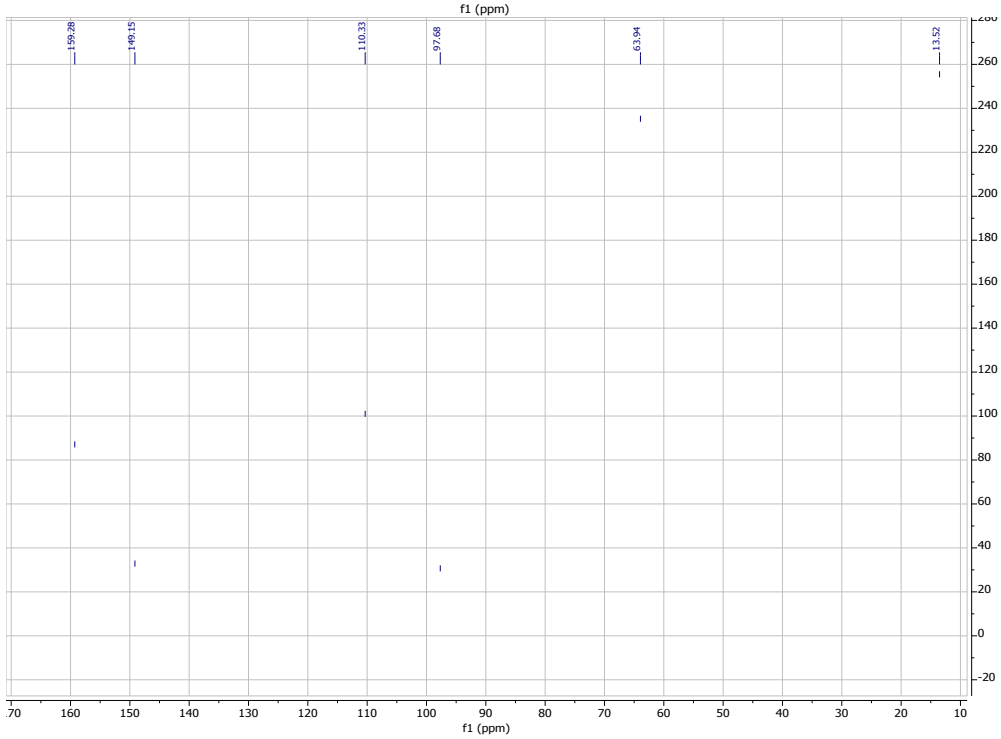
References

(1) Donckele, E.J.; Reekie, T.A.; Trapp, N. and Diederich, F. *Eur. JOC.* **2016**, *4*, 716-724.
(2) Yamada, Y.; Iguchi, K.; Hosaka, K.; Hagiwara, K.. *Synthesis*, **1974**, *9*, 669-70.
(3) Song, J.J.; Tan, Z.; Xu, J.; Reeves, J.T.; Yee, N.K.; Ramdas, R.; Gallou, F.; Kuzmich, K.; DeLattre, L.; Lee, H.; Feng, X. and Senanayake, C.H. *J. Org. Chem.* **2007**, *72*, 292-294.
(4) Feng Cai, Xiaotao Pu, Xiangbing Qi, Vincent Lynch, Akella Radha and Joseph M. Ready. *JACS.* **2011**, *45*, 18966-18069.
(5) Ali, M.; Hazmi, A.; Sheikh, N.S.; Bataille, C.J.R.; Al-Hadedi, A.A.M.; Watkin, S.V.; Luker, T.J.; Camp, N.P. and Brown, R.C.D. *Org. Lett.* **2014**, *16*, 5104−5107.
(6) Kumazawa, K.; Ishihara, K. and Yamamoto, H.. *Org. Lett*. **2004**, *6*, 2551-2554.
(7) Vrancken, E.E.; Alexakis, A; and Mangeney, P. *Eur. JOC.* **2005**, *7*, 1354-1366.
(8) Raghavan S.; Stelmach J.E.; Smith, C.J.; Li, H.; Whitehead, A.; Waddell, S.T.; Chen, Y-H.; Miao, S.; Ornoski, O.A.; Garfunkle, J.; Liao, X.; Chang, J.; Han, X.; ,Guo, J.; Groeper, J.A.; Brockunier, L.L.; Rosauer, K.; Parmee E. R. *PCT. Int. Appl.,* **2011** WO 2011149921.

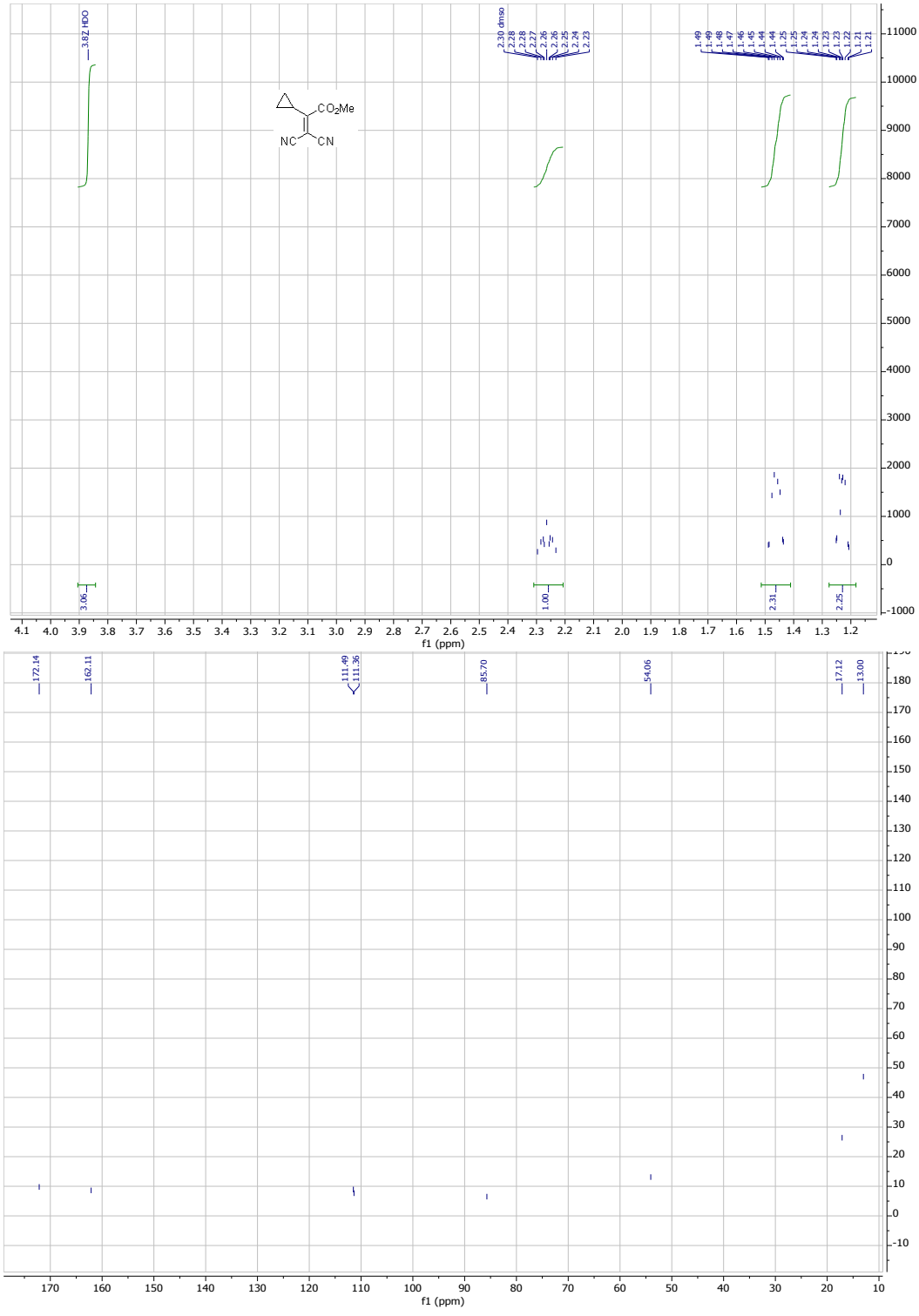
NMR Spectra

Diethyl 2-(dicyanomethylene)malonate (5a)

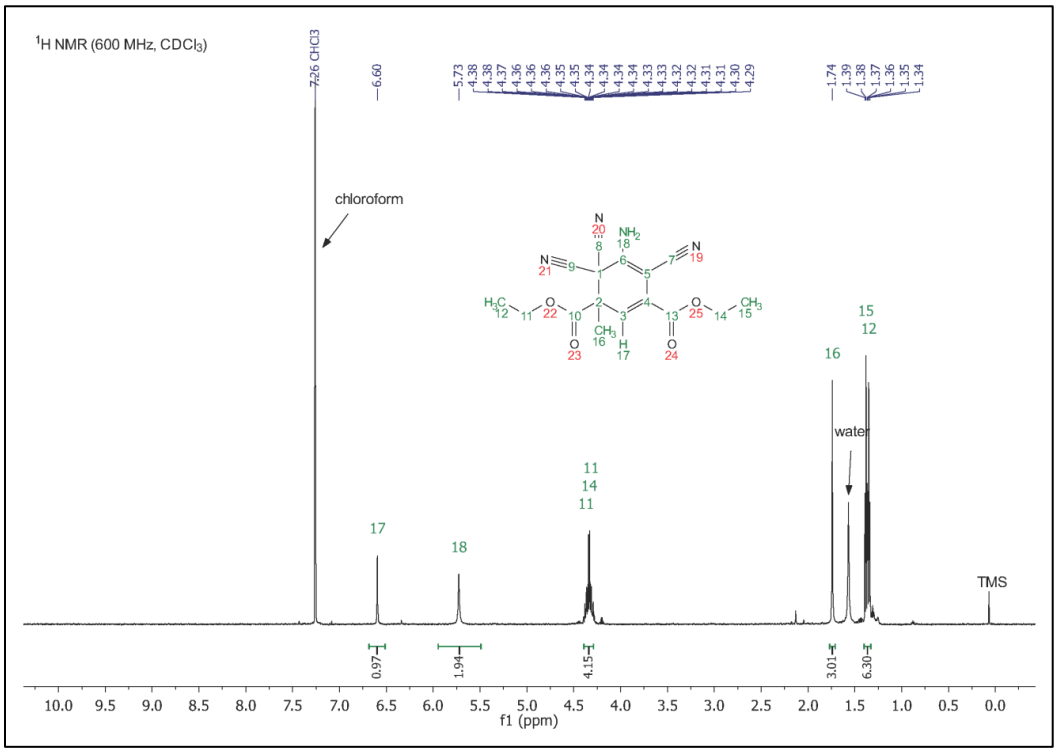


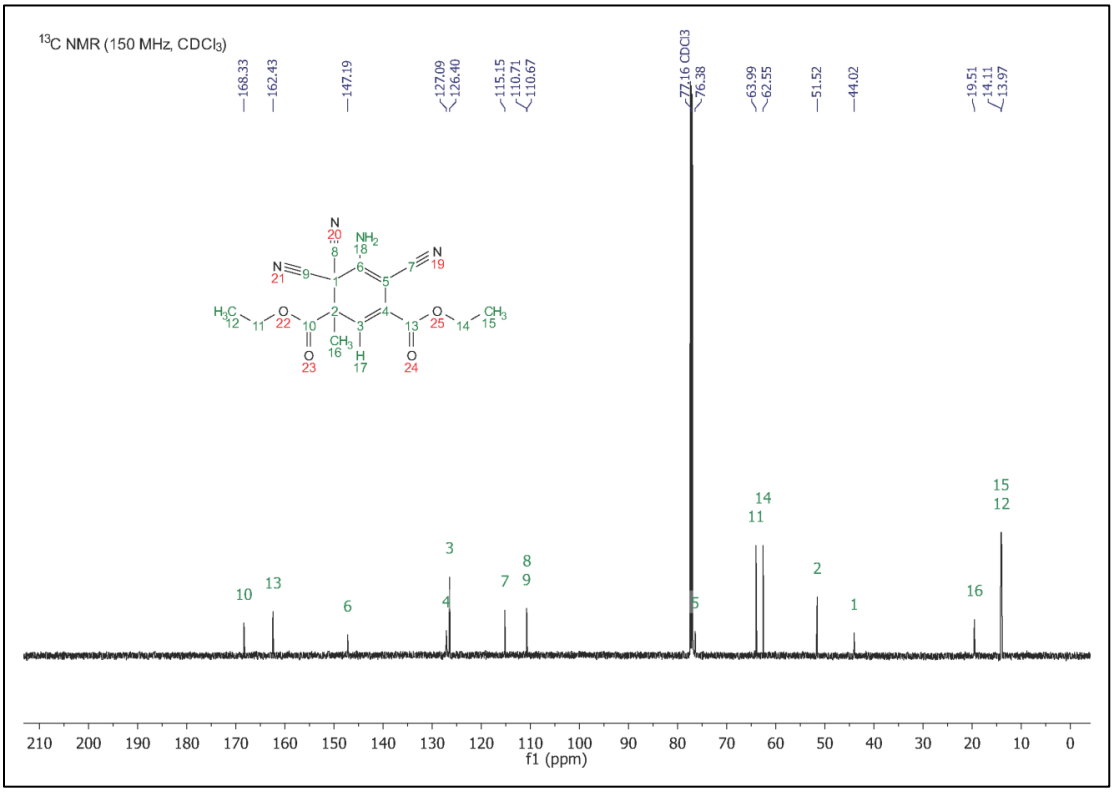


Methyl 3,3-dicyano-2-cyclopropylacrylate (5c).

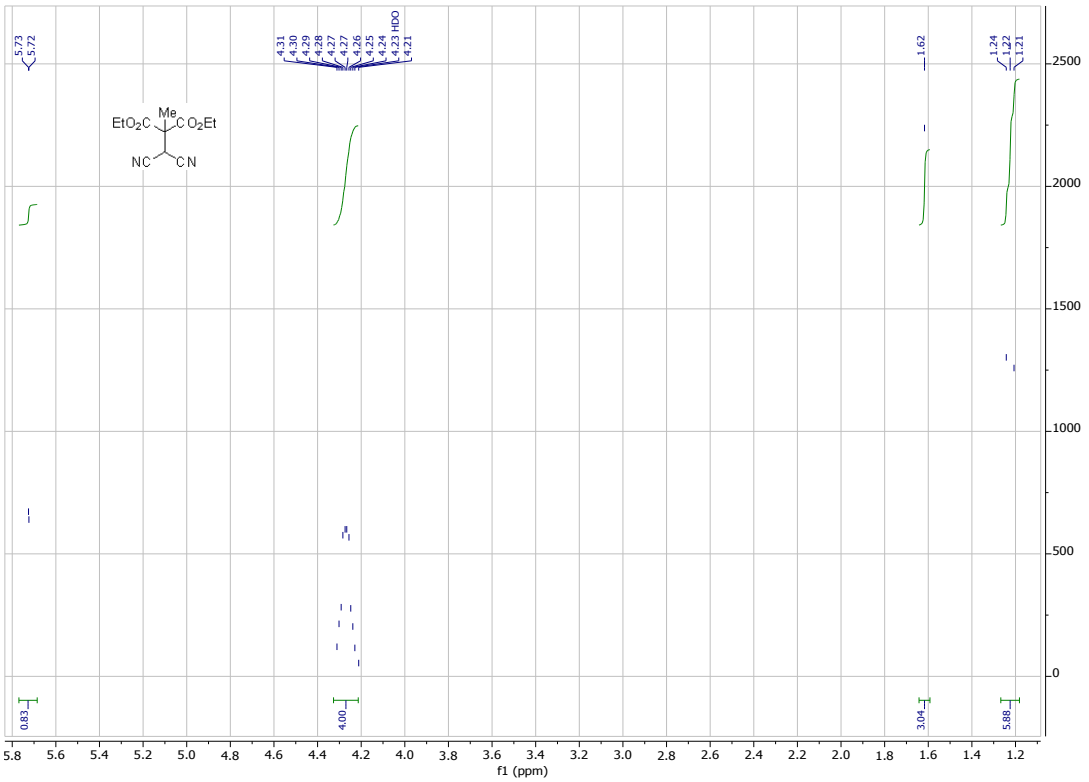


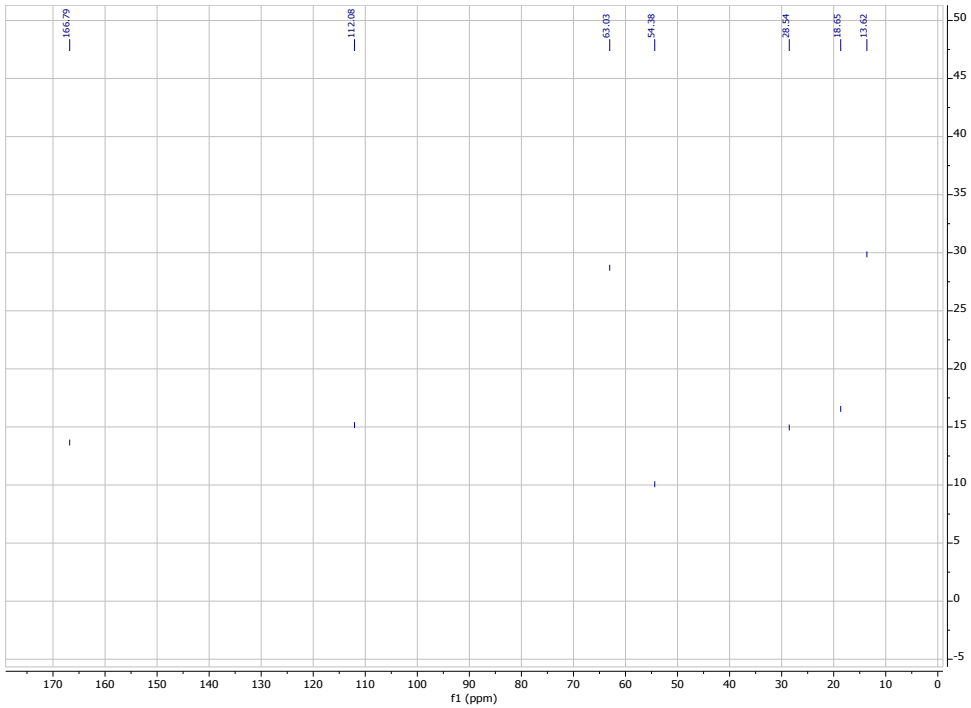
Diethyl 5-amino-4,4,6-tricyano-3-methylcyclohexa-1,5-diene-1,3-dicarboxylate (6).



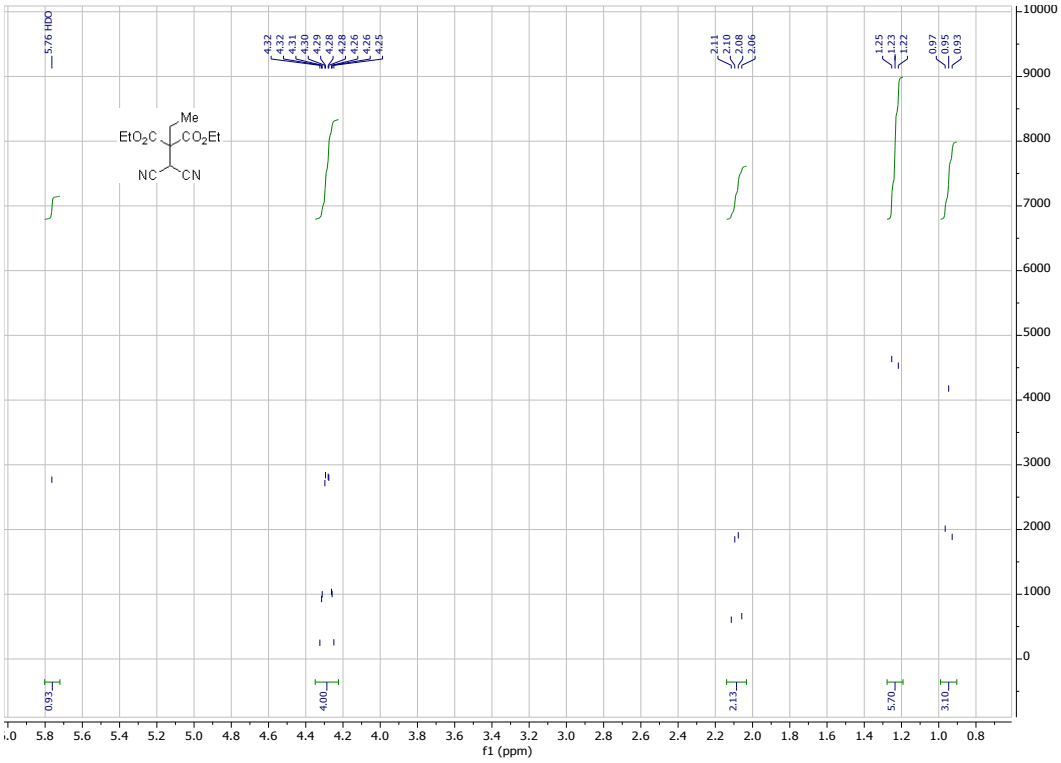


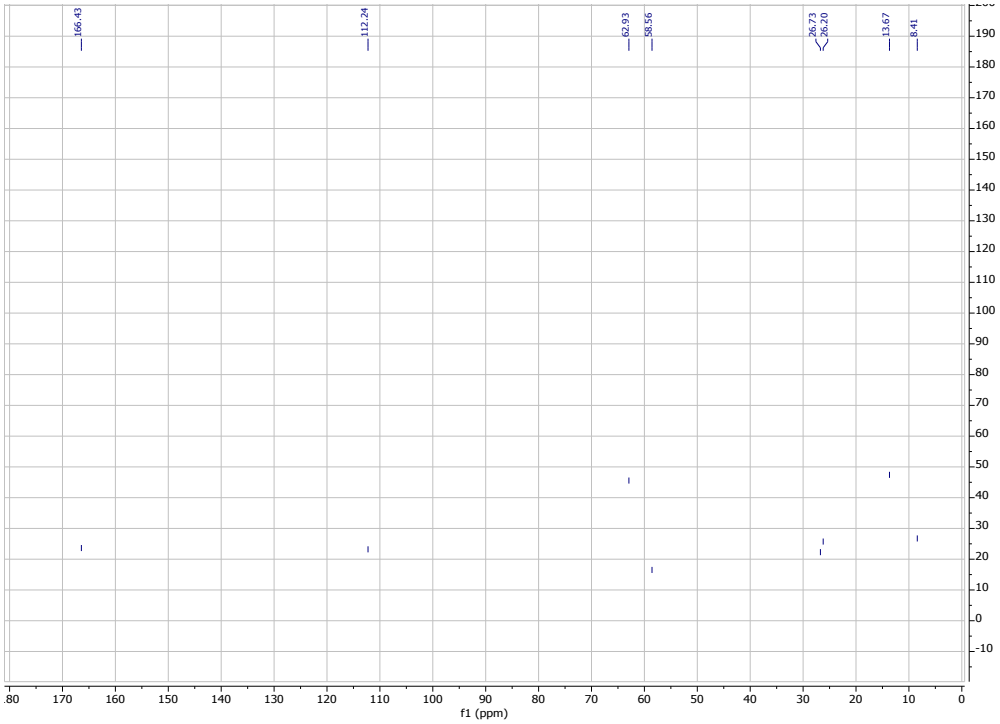
Diethyl 2-(dicyanomethyl)-2-methylmalonate (1a)



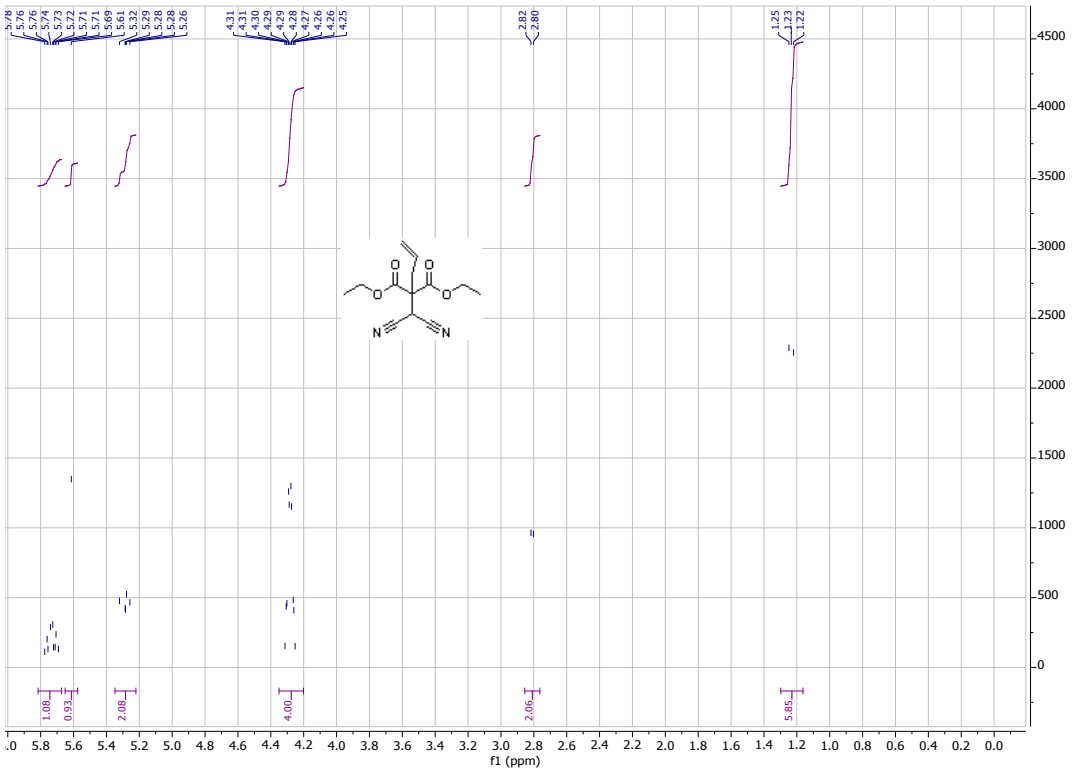


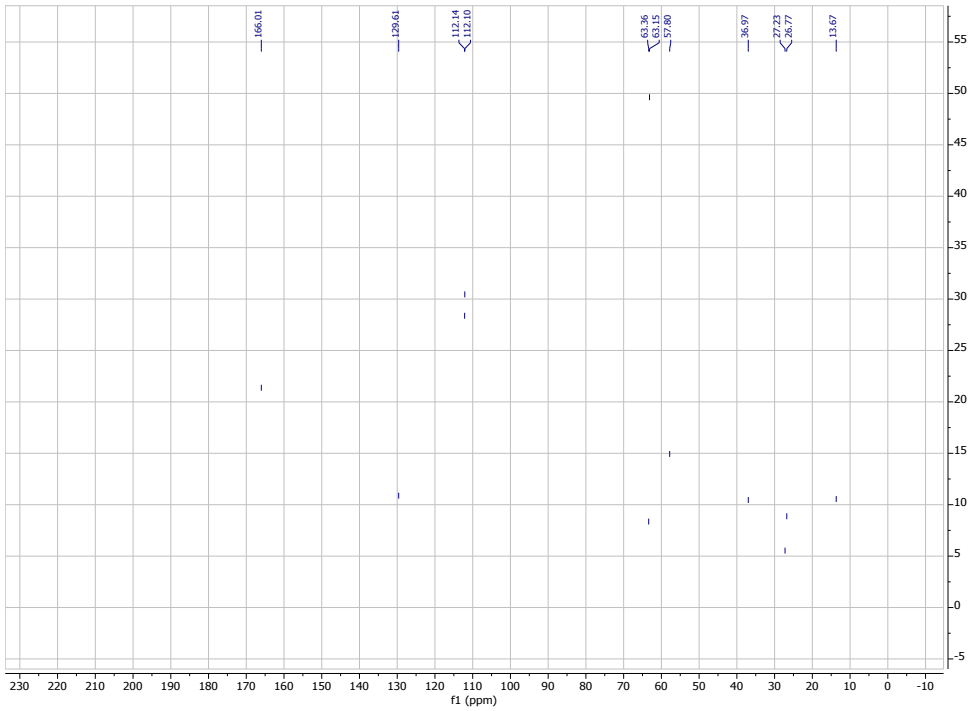
Diethyl 2-(dicyanomethyl)-2-ethylmalonate (1b)



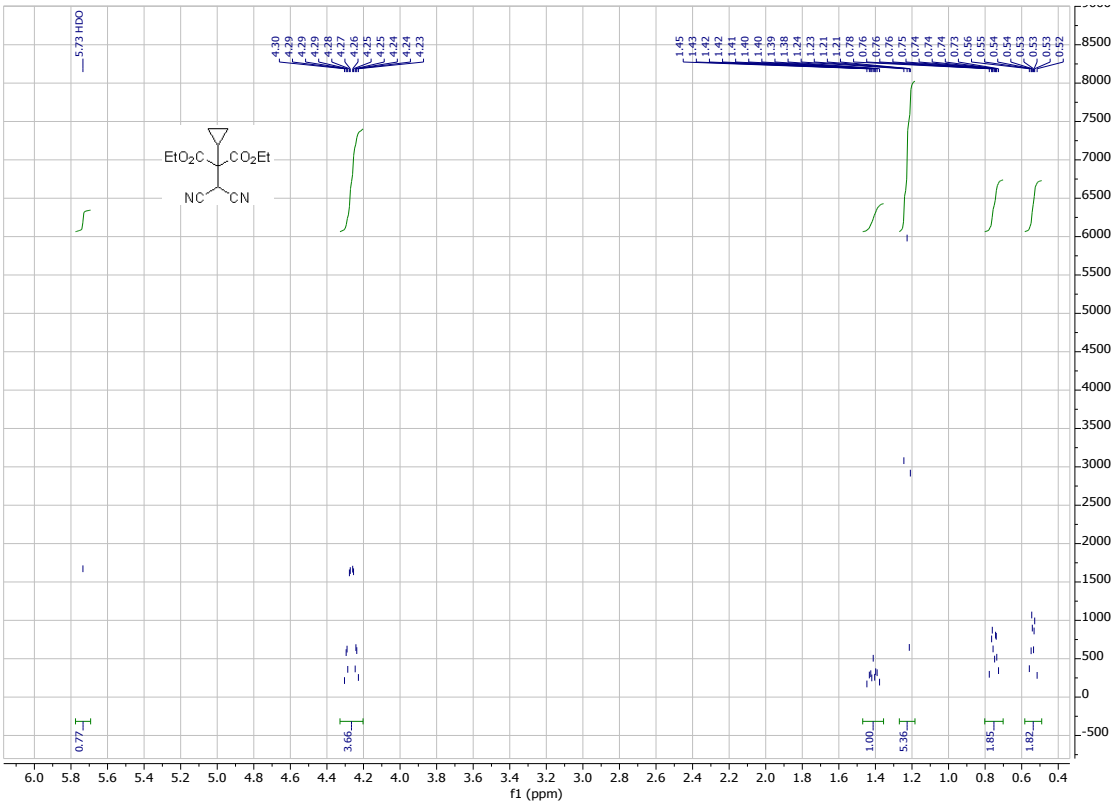


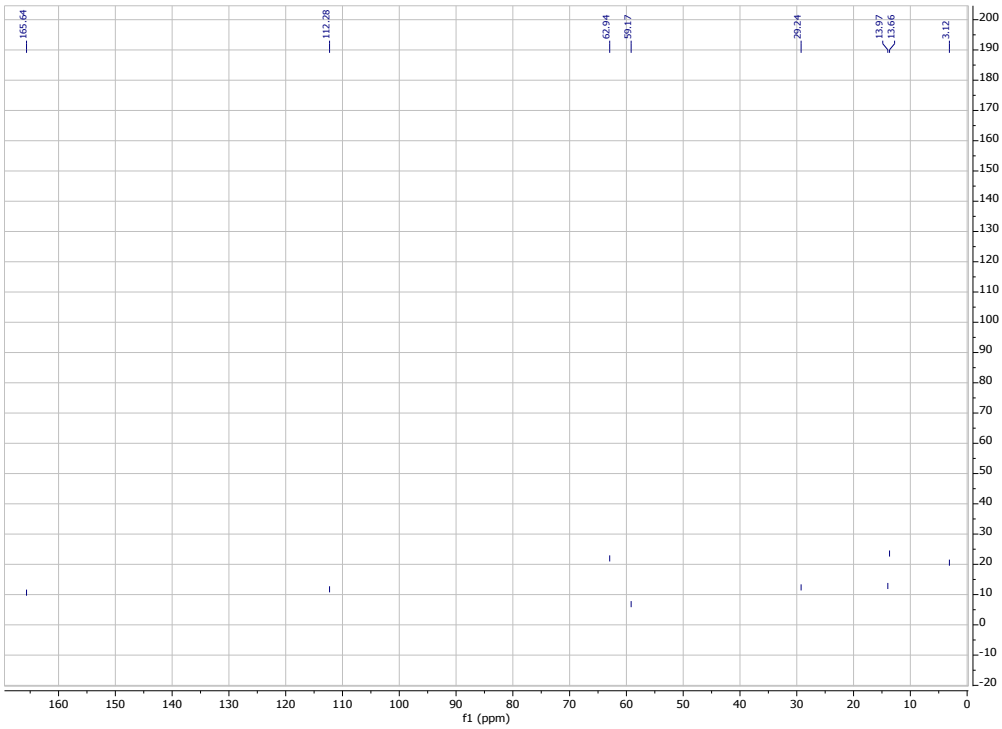
Diethyl 2-allyl-2-(dicyanomethyl)malonate (1c)



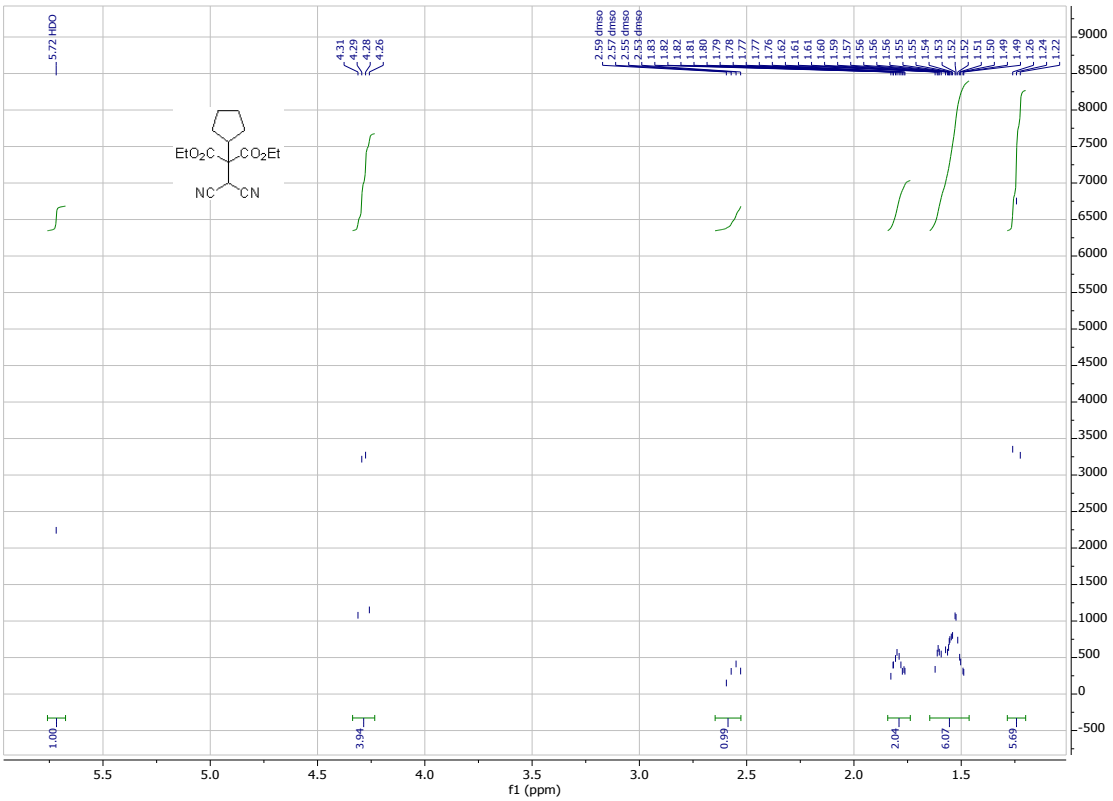


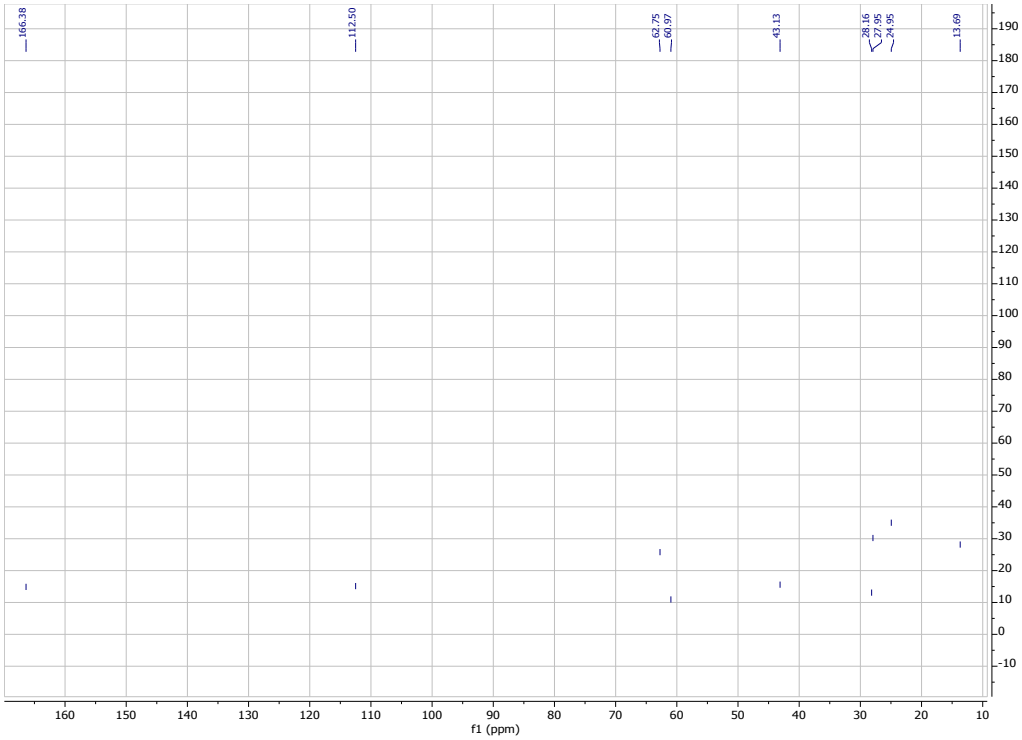
Diethyl 2-cyclopropyl-2-(dicyanomethyl)malonate (1d)



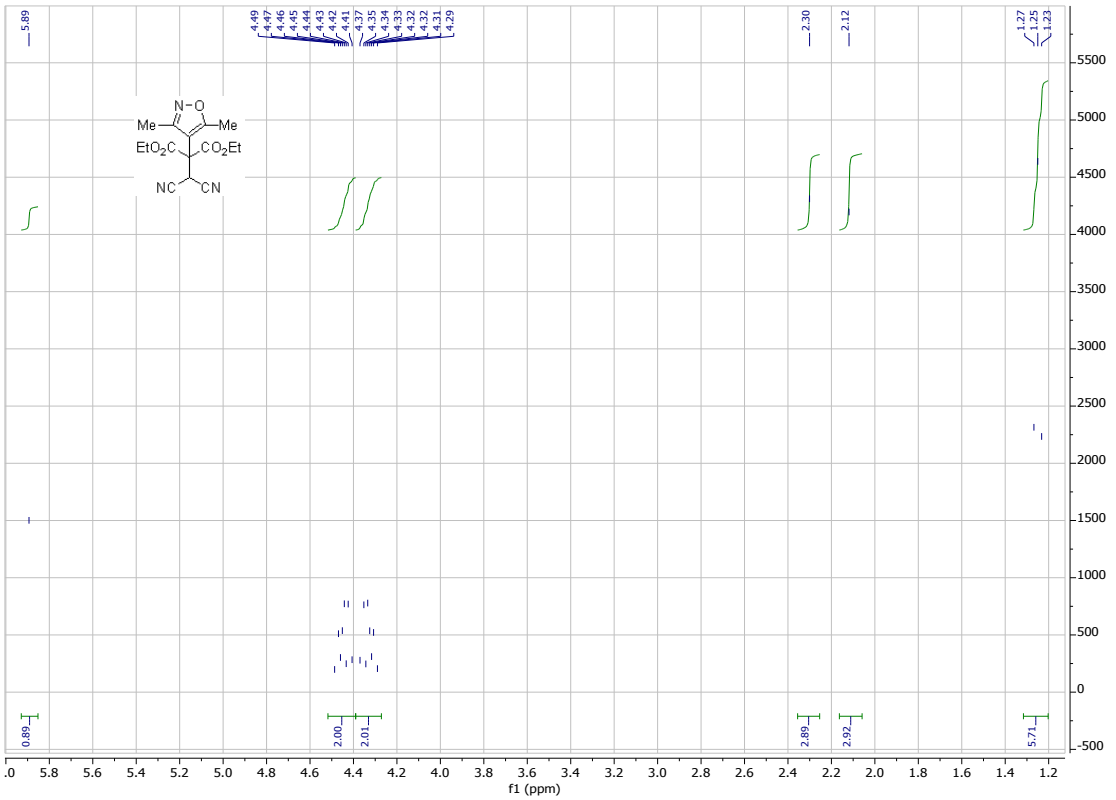


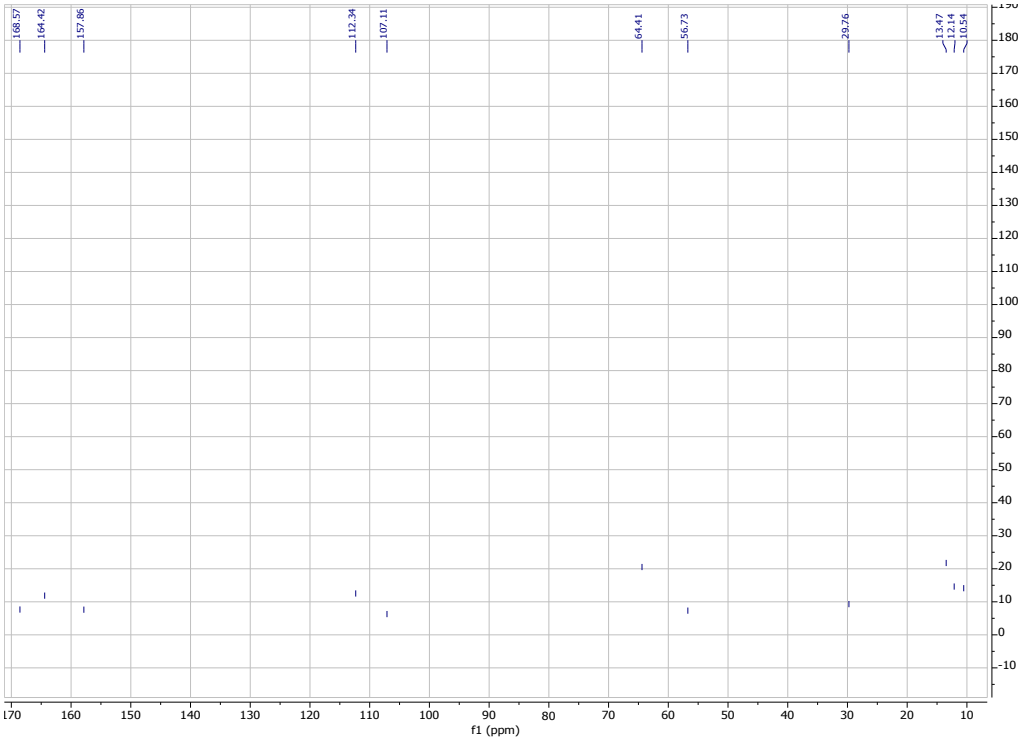
Diethyl 2-cyclopentyl-2-(dicyanomethyl)malonate (1e)



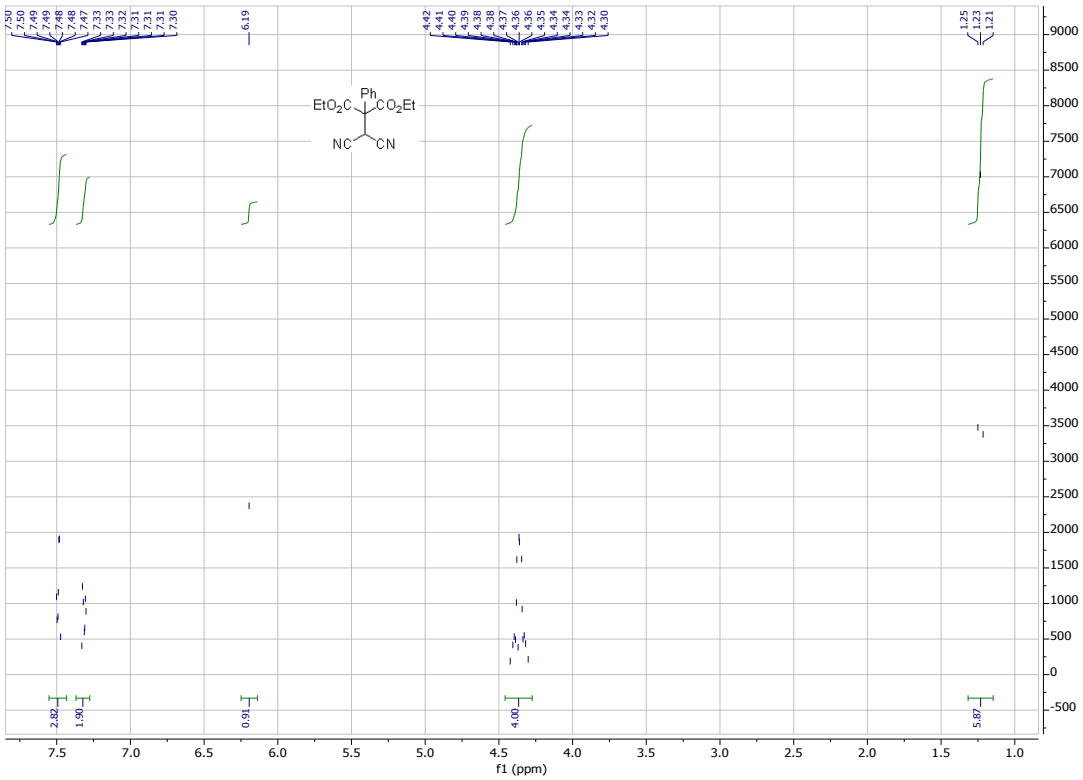


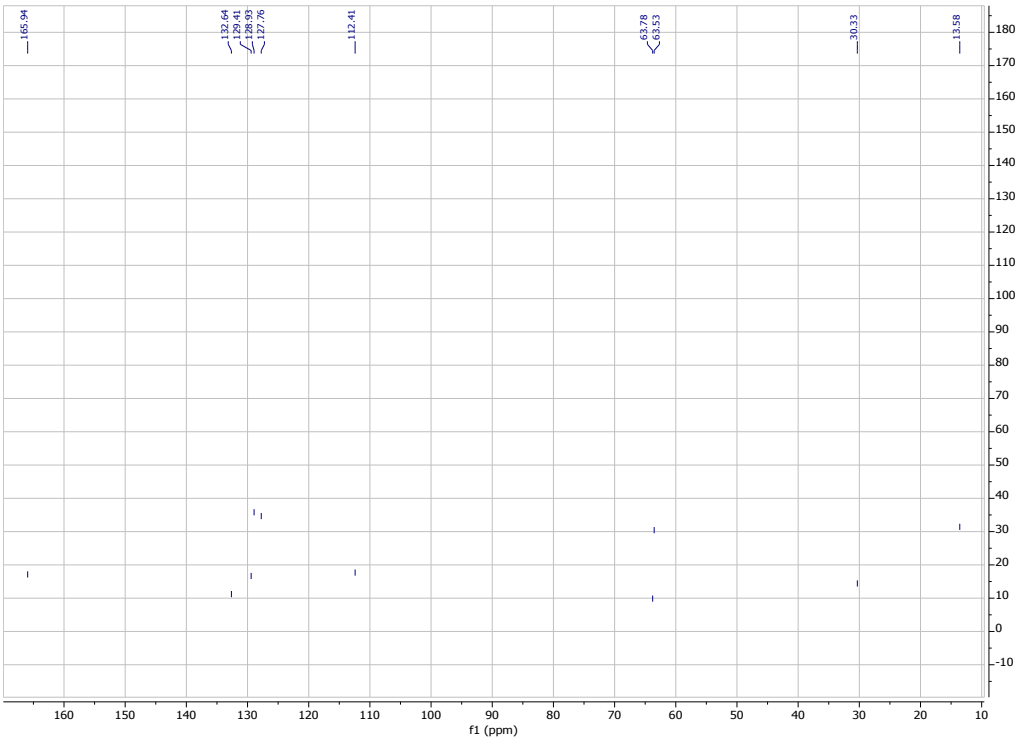
Diethyl 2-(dicyanomethyl)-2-(3,5-dimethylisoxazol-4-yl)malonate (1f)



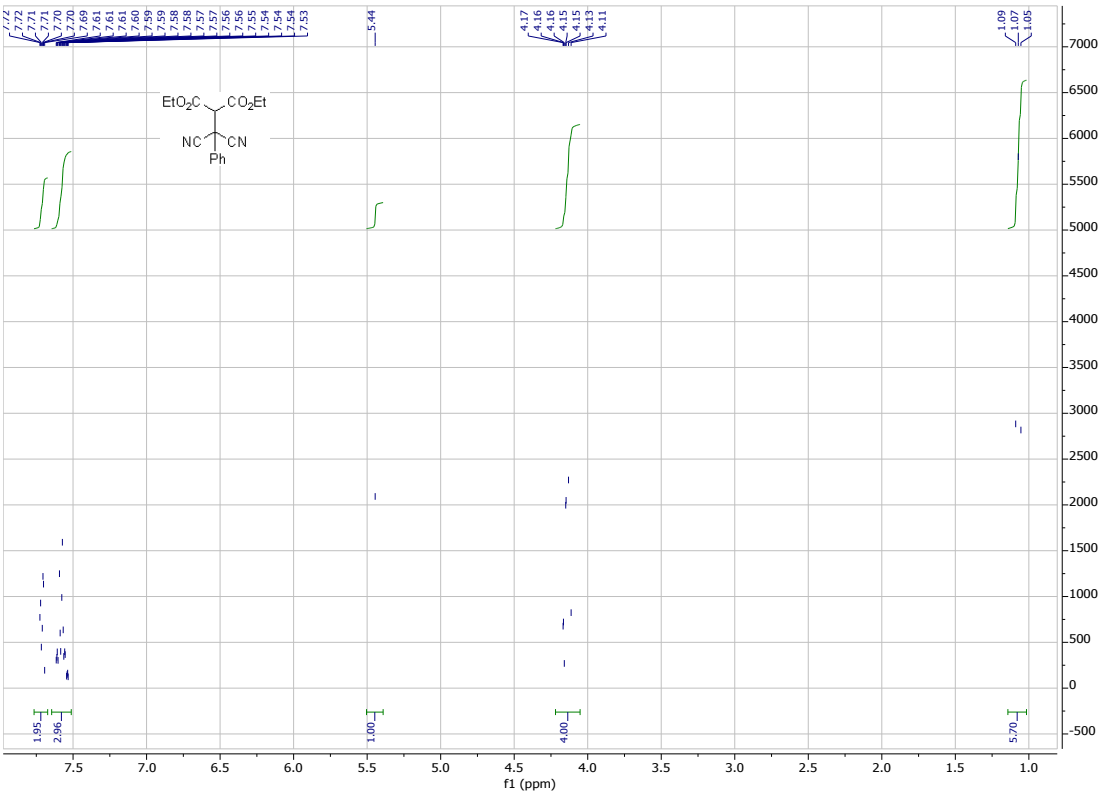


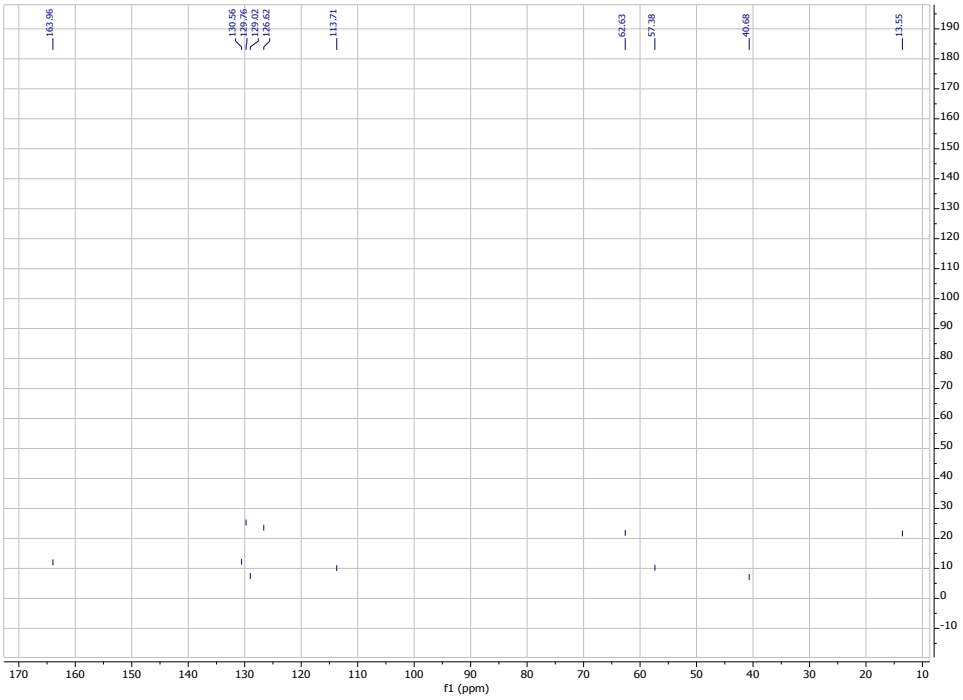
Diethyl 2-(dicyanomethyl)-2-phenylmalonate (1g)



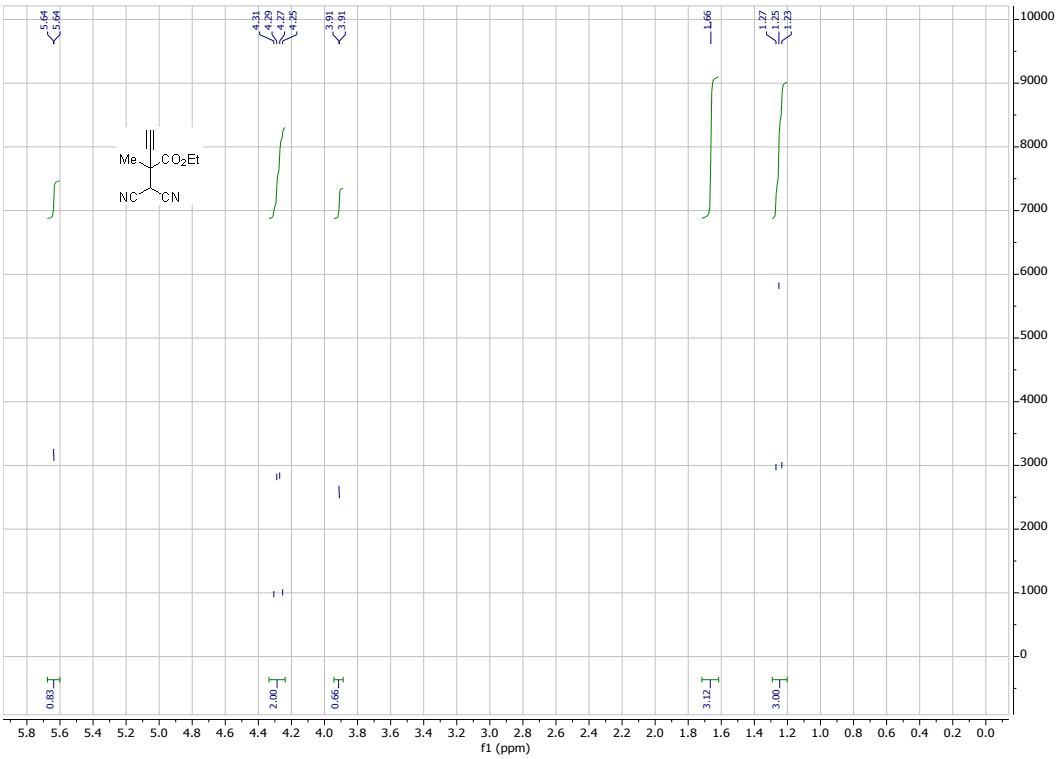


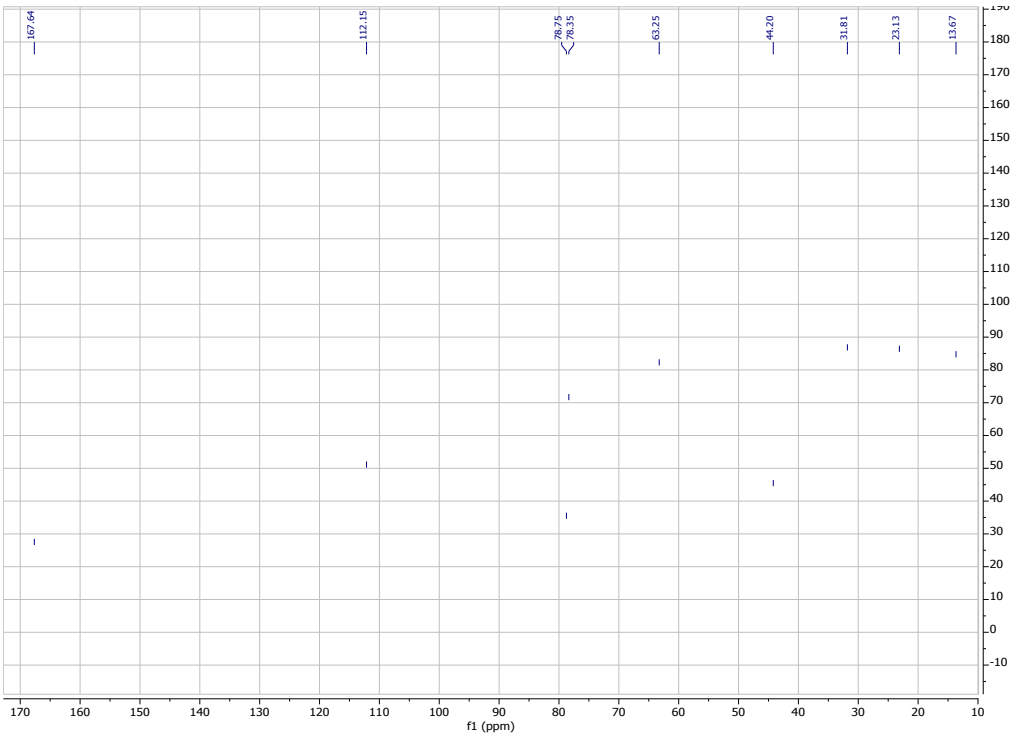
Diethyl 2-(dicyano(phenyl)methyl)malonate (1g-α)



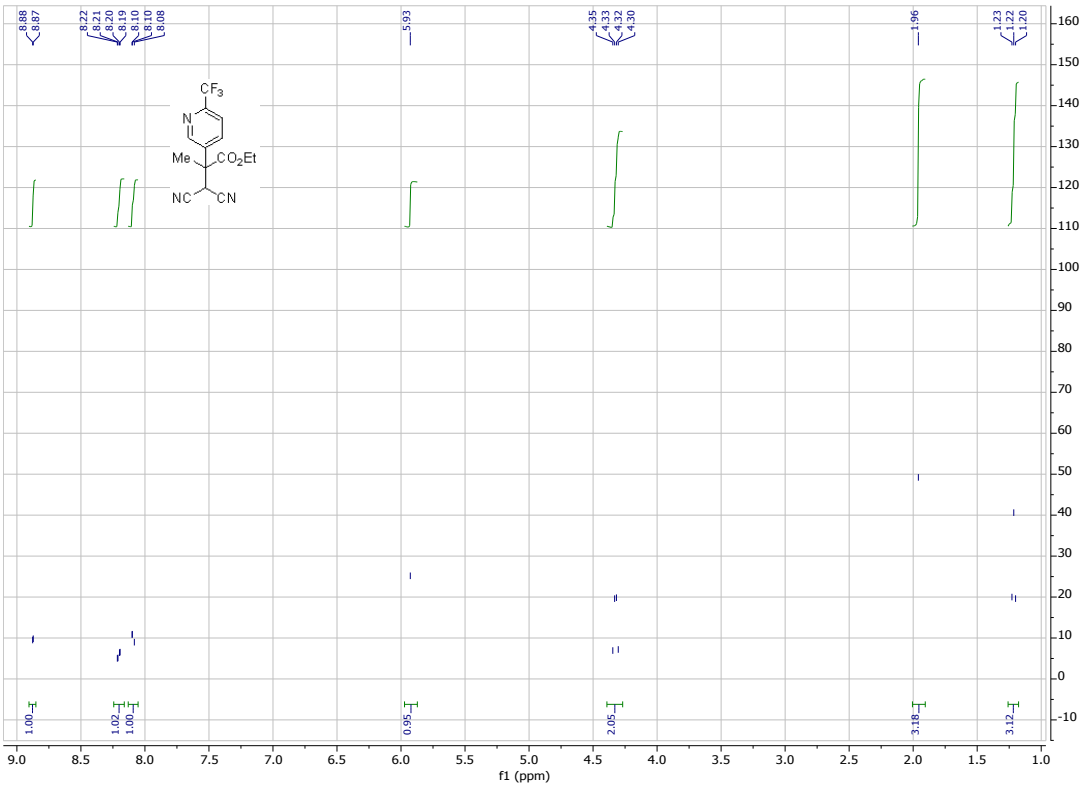


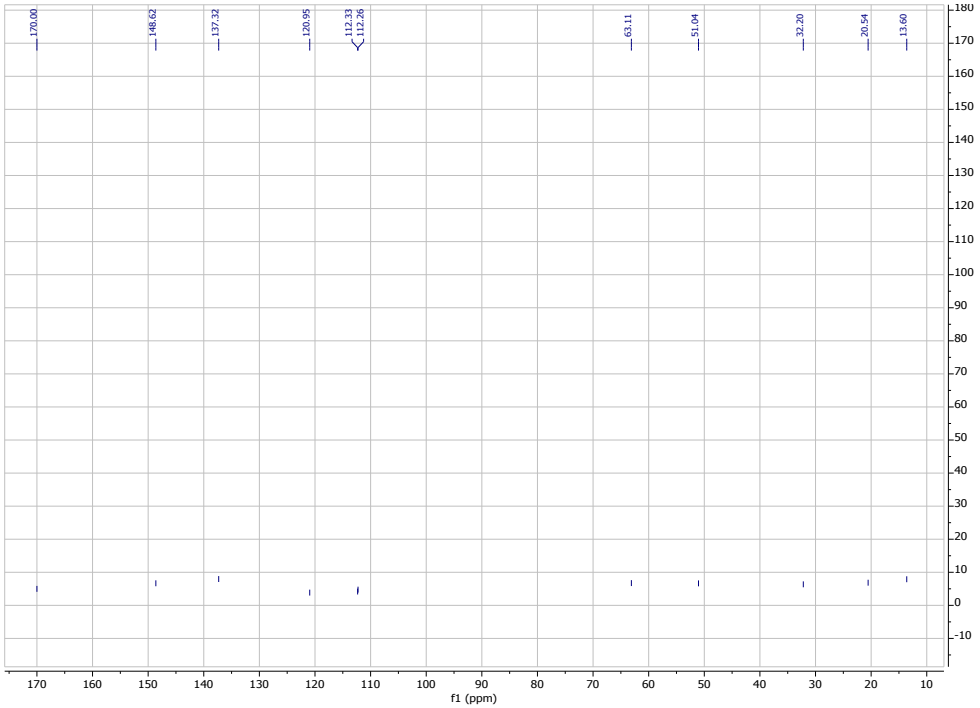
Ethyl 2-(dicyanomethyl)-2-methylbut-3-ynoate (1h)



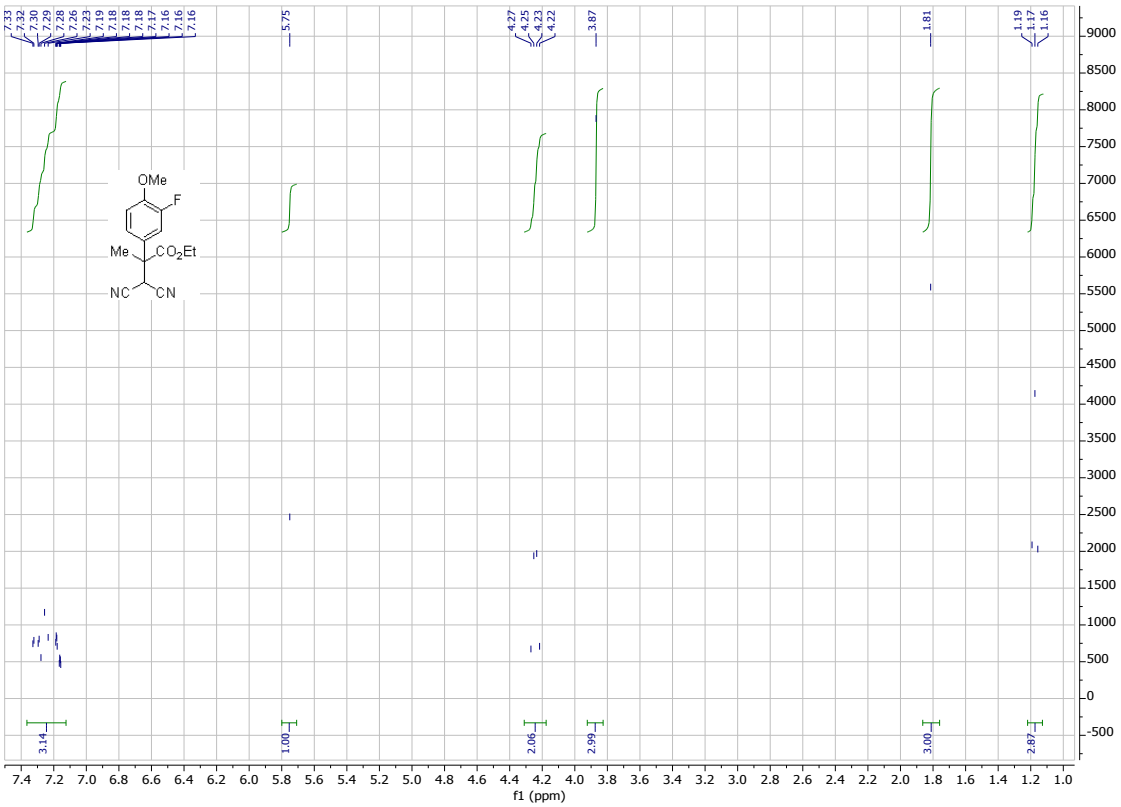


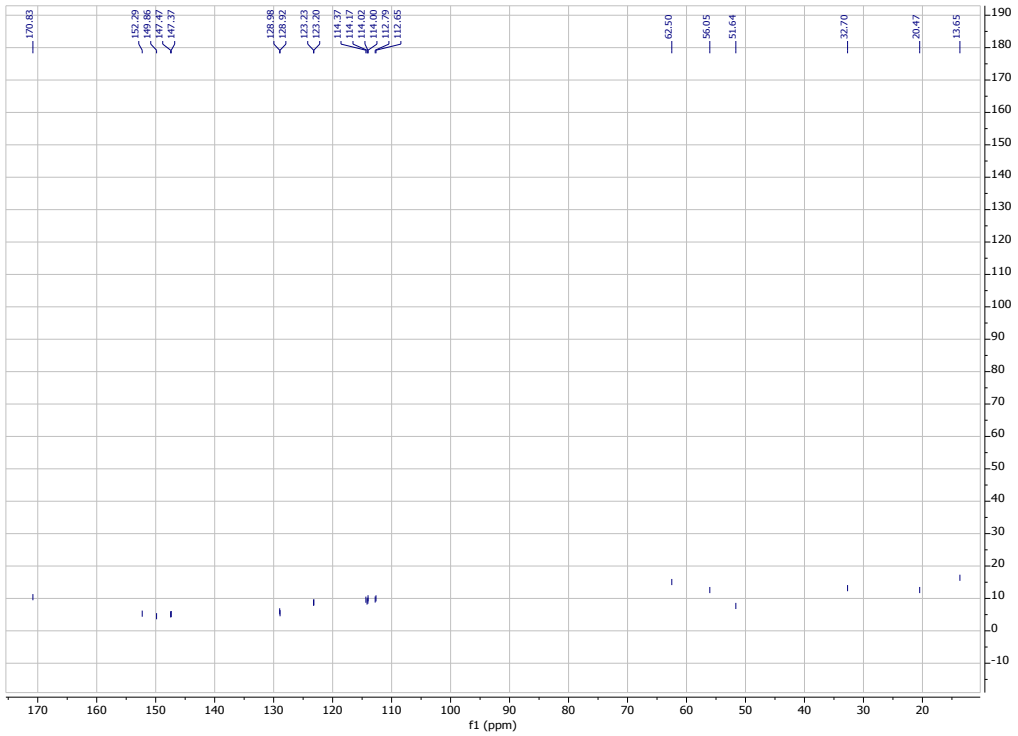
Ethyl 3,3-dicyano-2-methyl-2-(6-(trifluoromethyl)pyridin-3-yl)propanoate (1i)



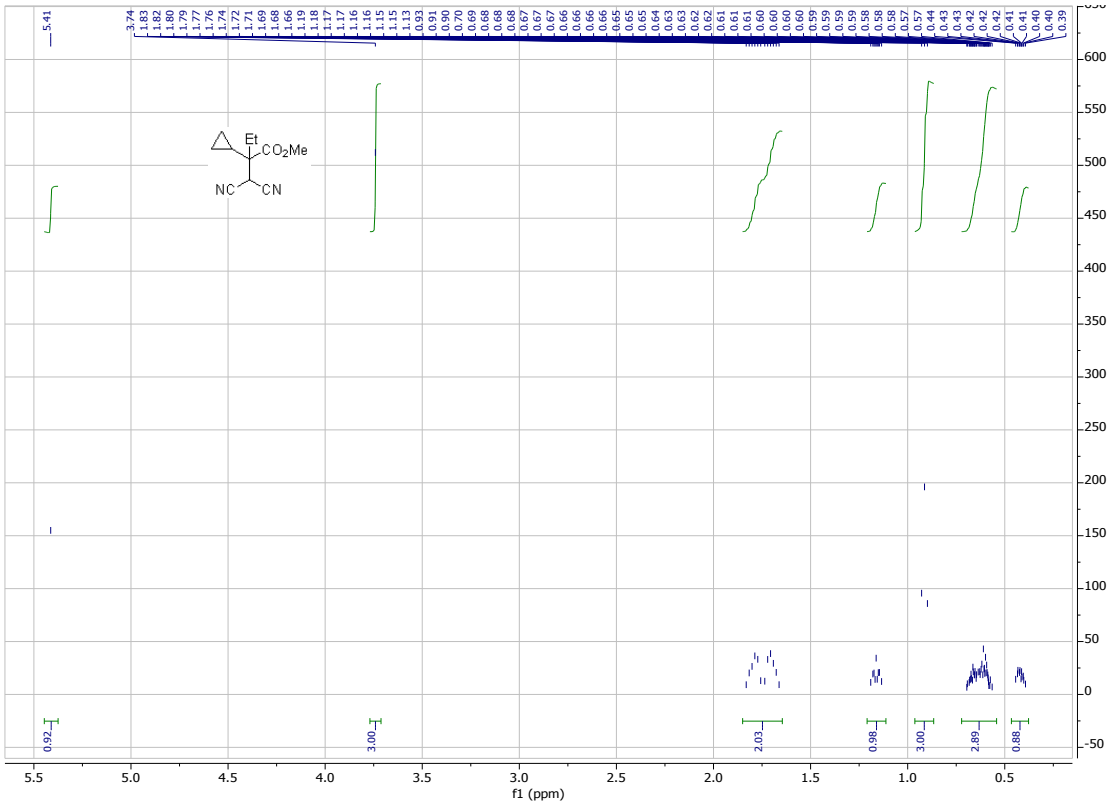


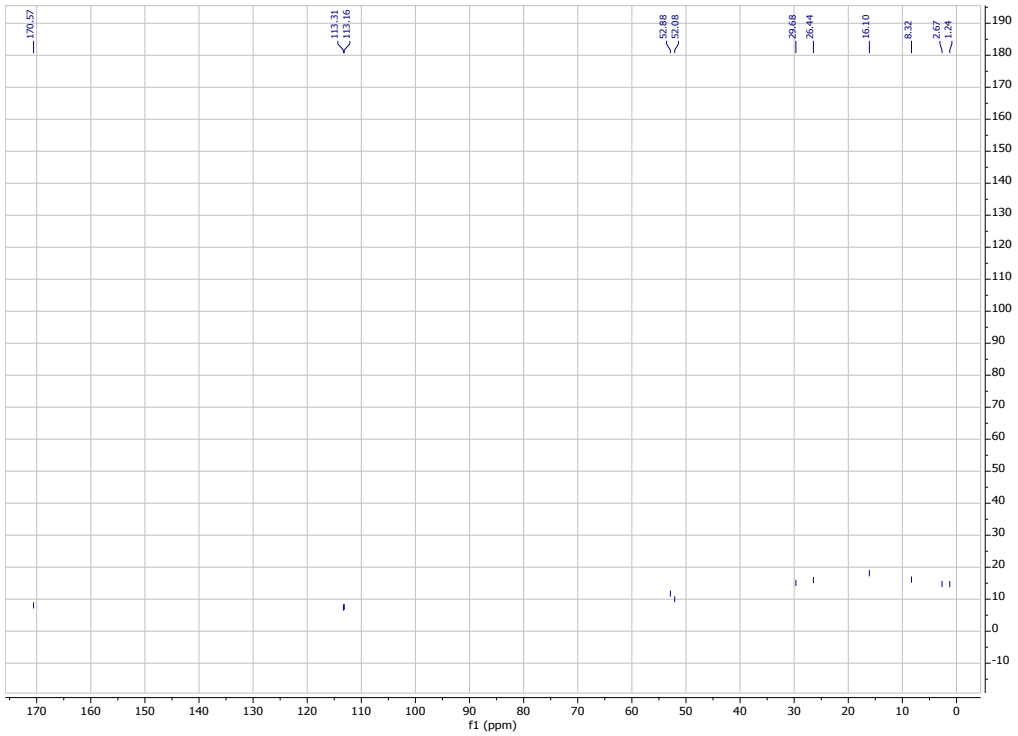
Ethyl 3,3-dicyano-2-(3-fluoro-4-methoxyphenyl)-2-methylpropanoate (1j)



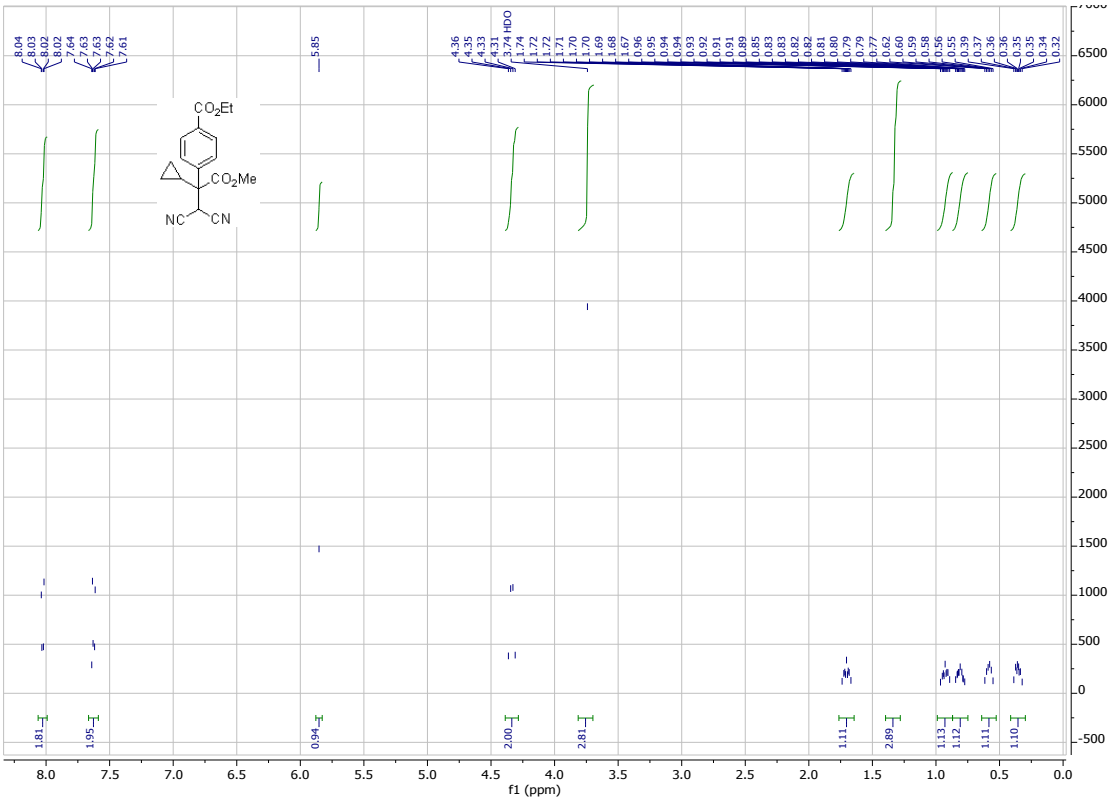


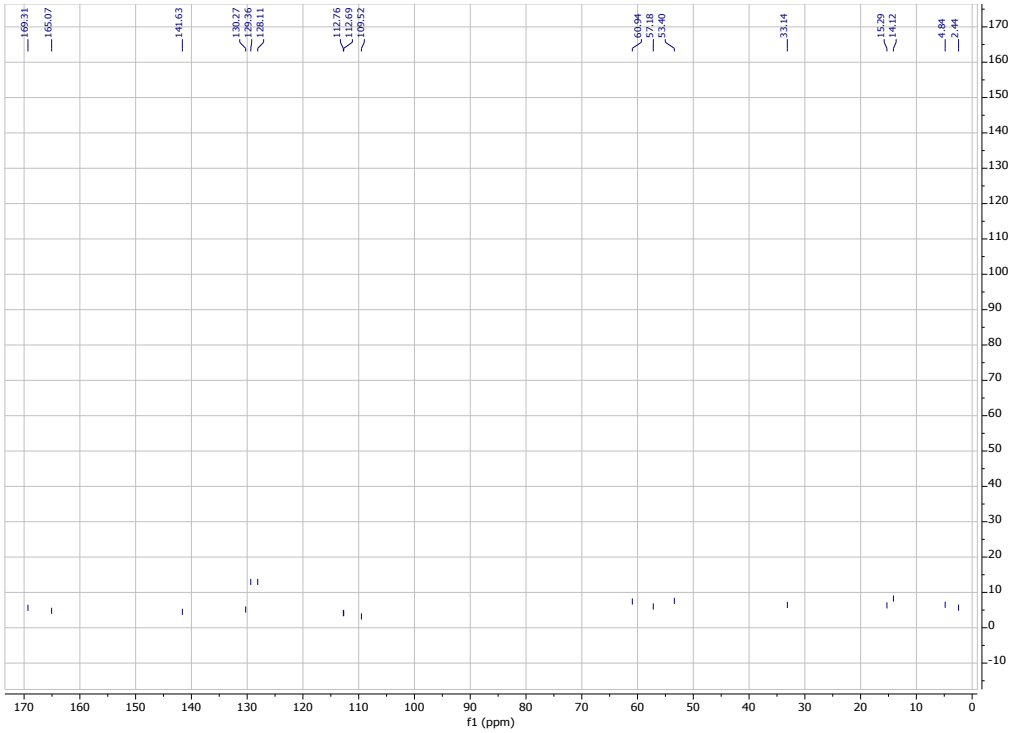
Methyl 2-cyclopropyl-2-(dicyanomethyl)butanoate (1k)



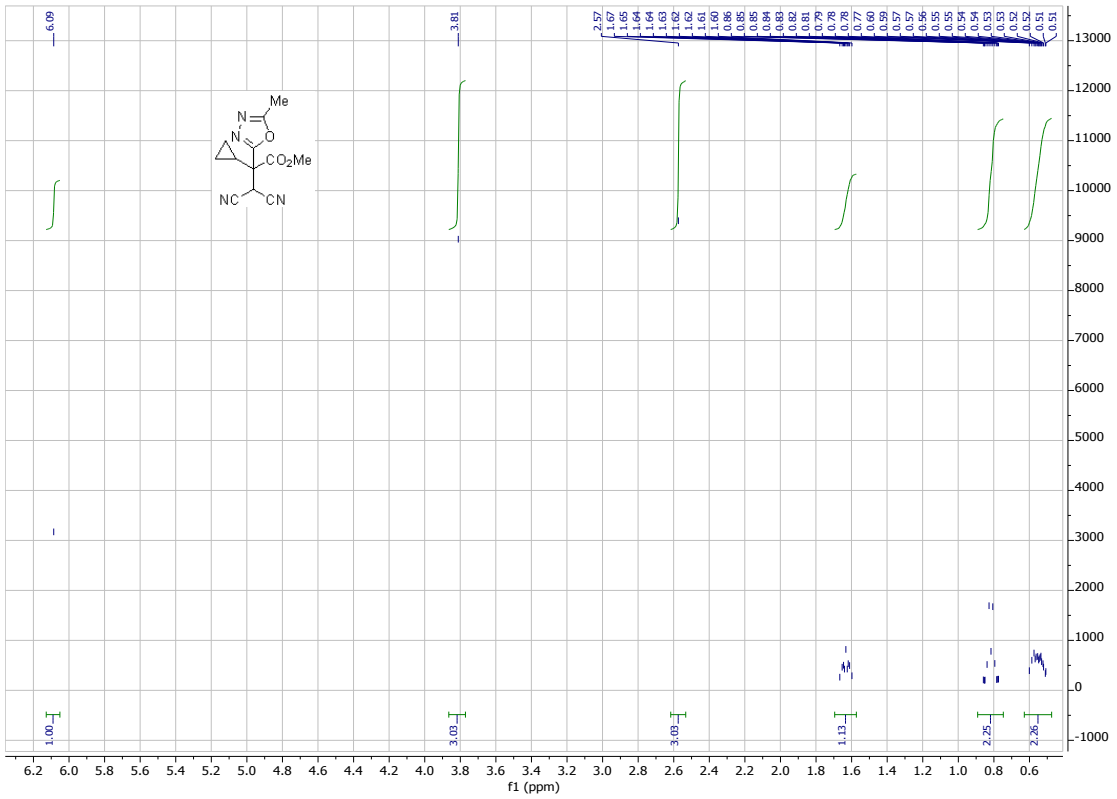


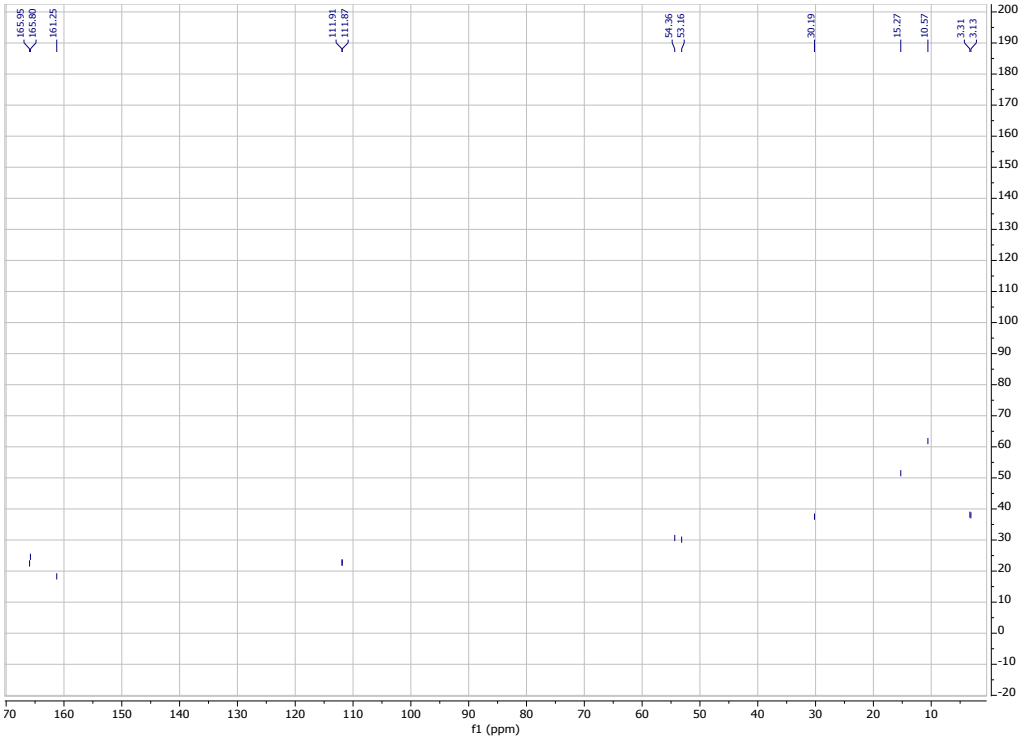
Ethyl 4-(1,1-dicyano-2-cyclopropyl-3-methoxy-3-oxopropan-2-yl)benzoate (1l)



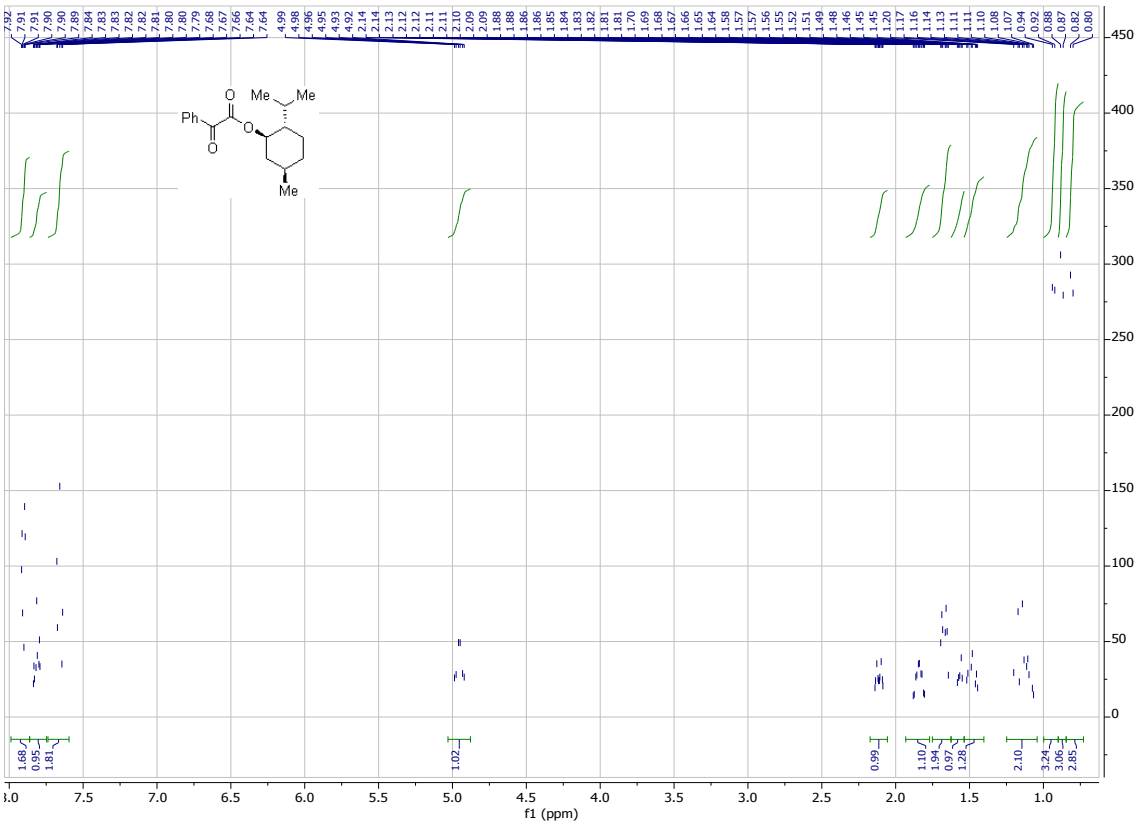


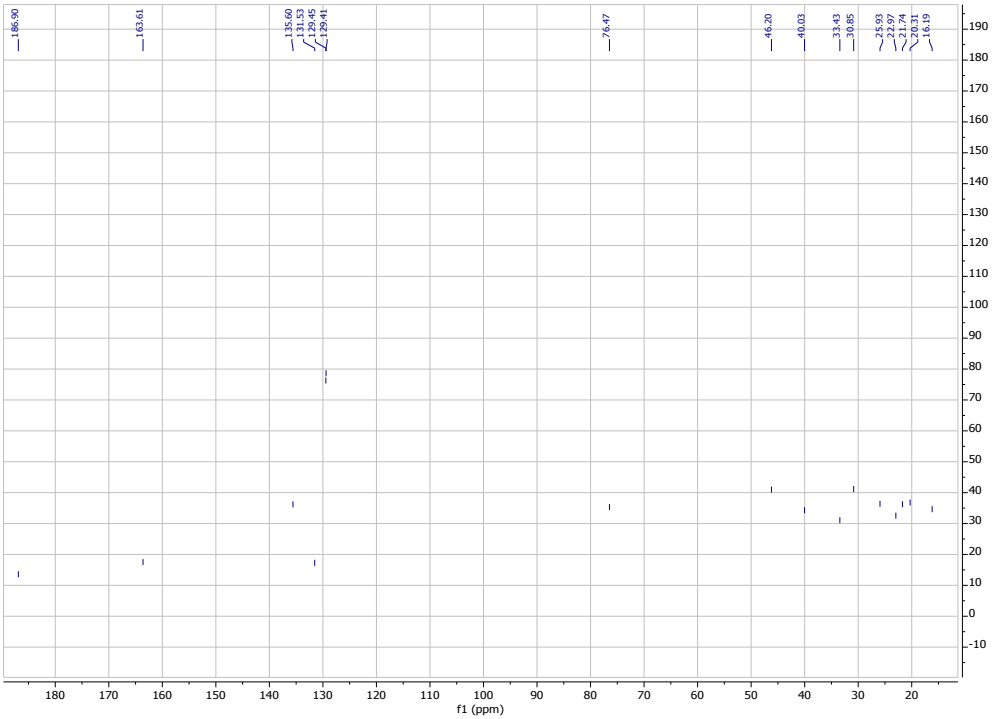
Methyl 3,3-dicyano-2-cyclopropyl-2-(5-methyl-1,3,4-oxadiazol-2-yl)propanoate (1m)



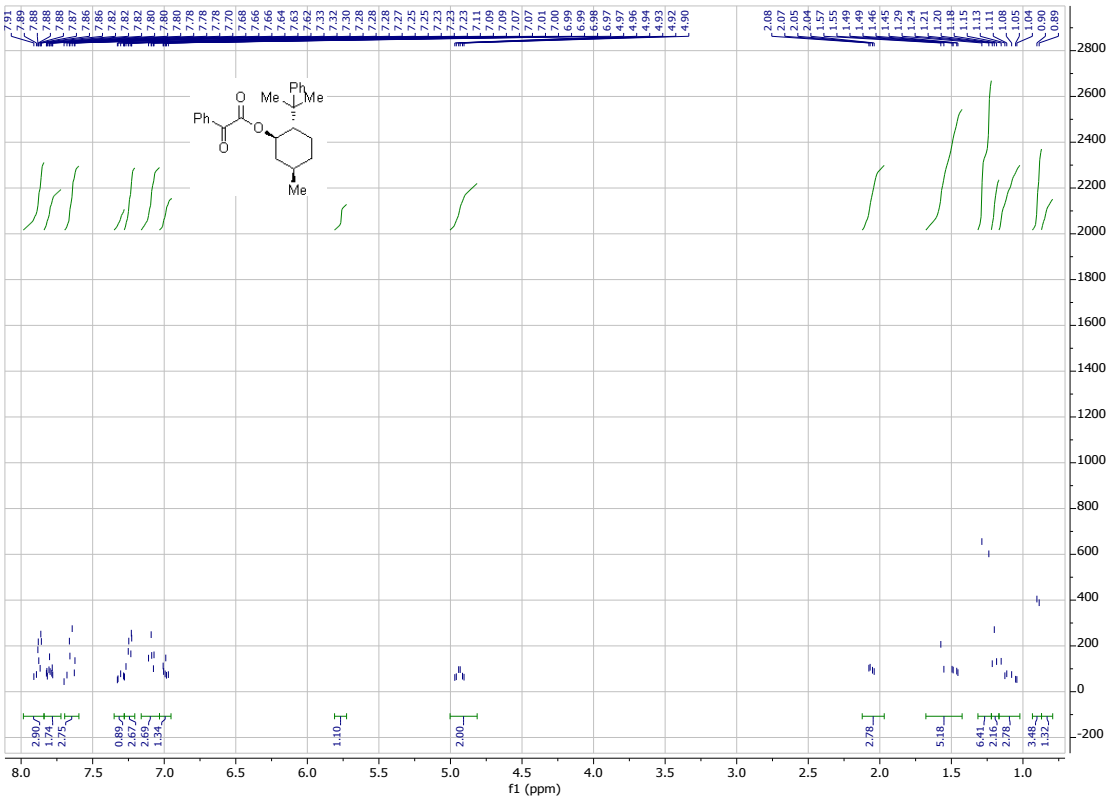


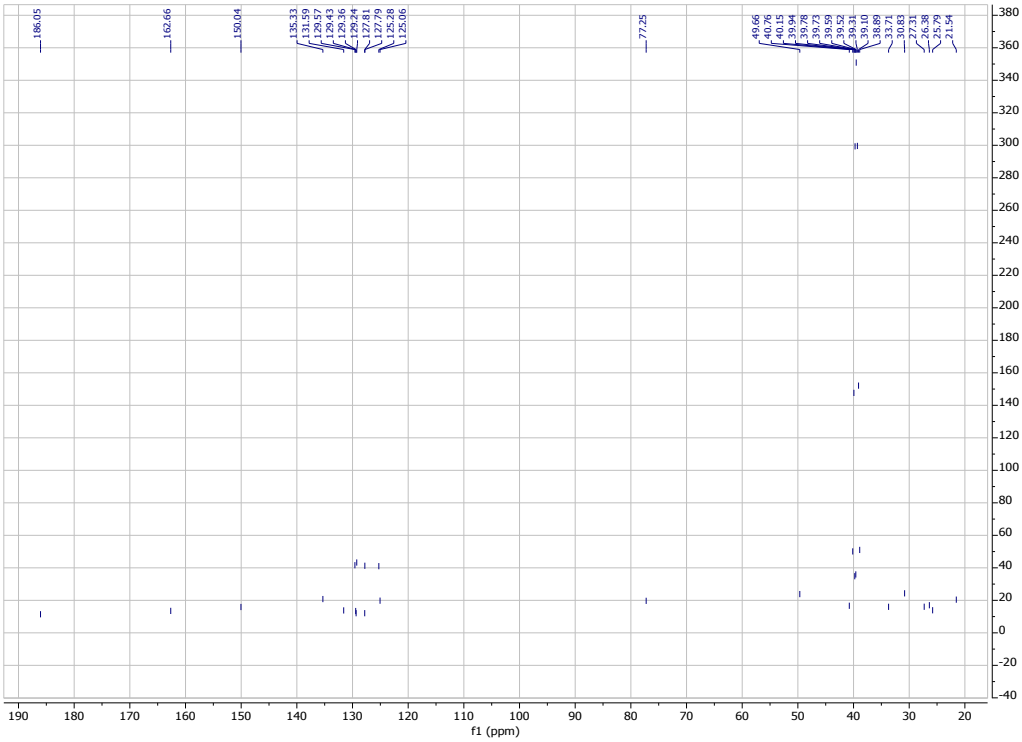
(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl-2-oxo-2-phenylacetate (7a)



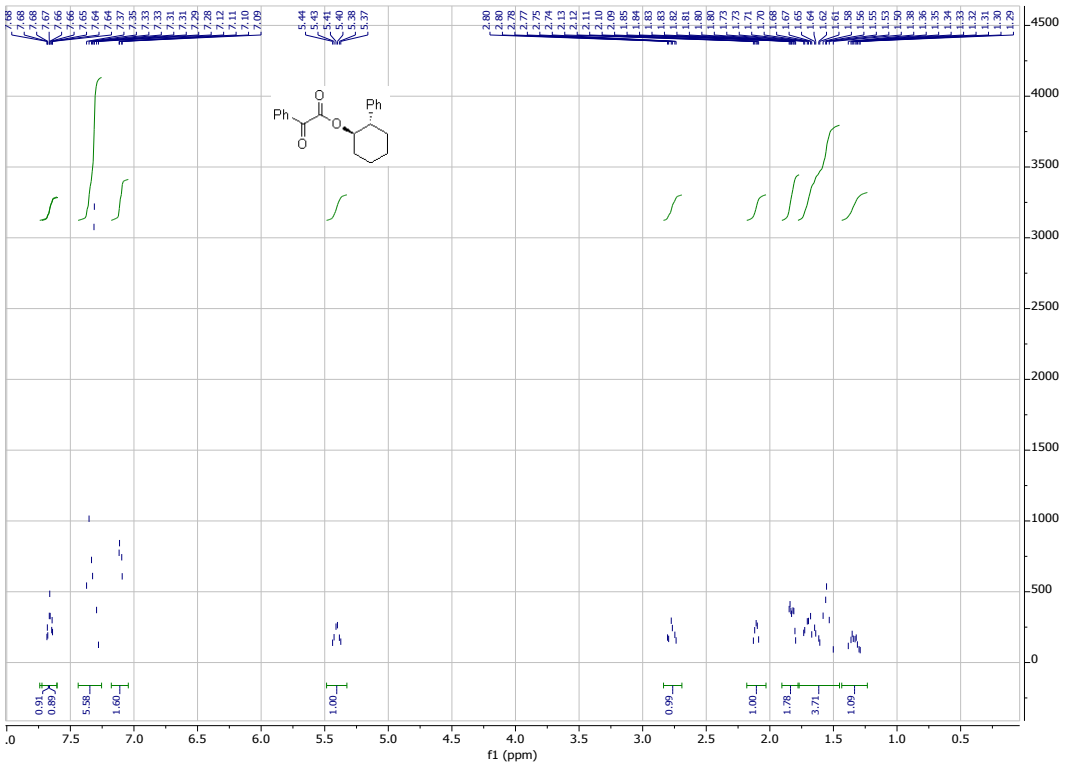


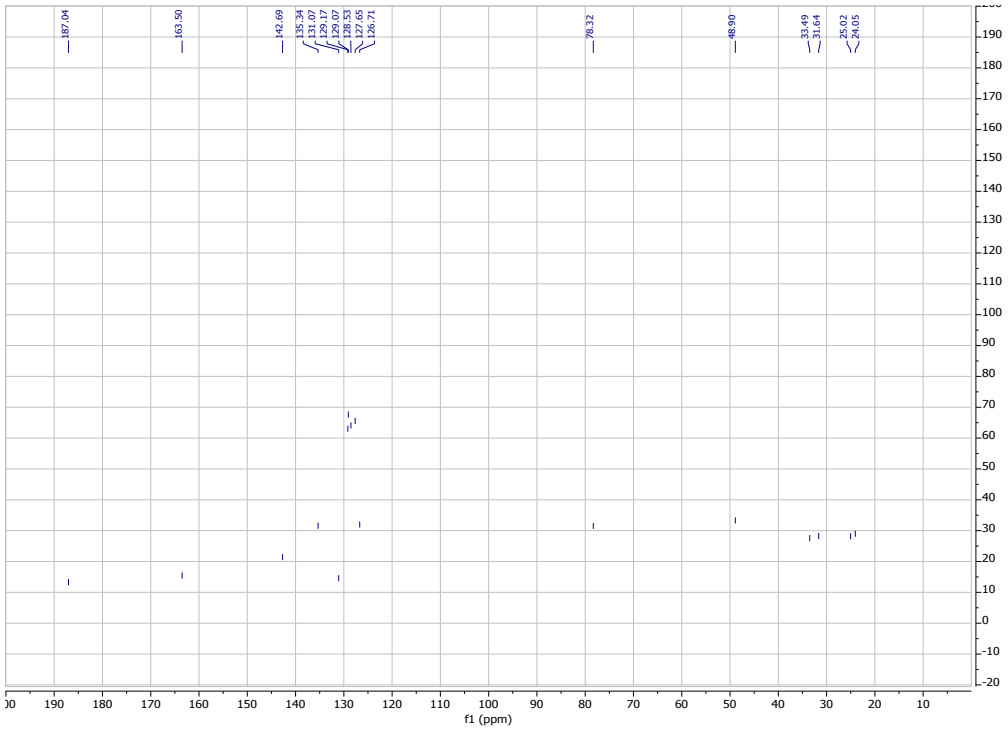
(*1R,2S,5R*)-5-methyl-2-(2-phenylpropan-2-yl)cyclohexyl-2-oxo-2-phenylacetate (7b)



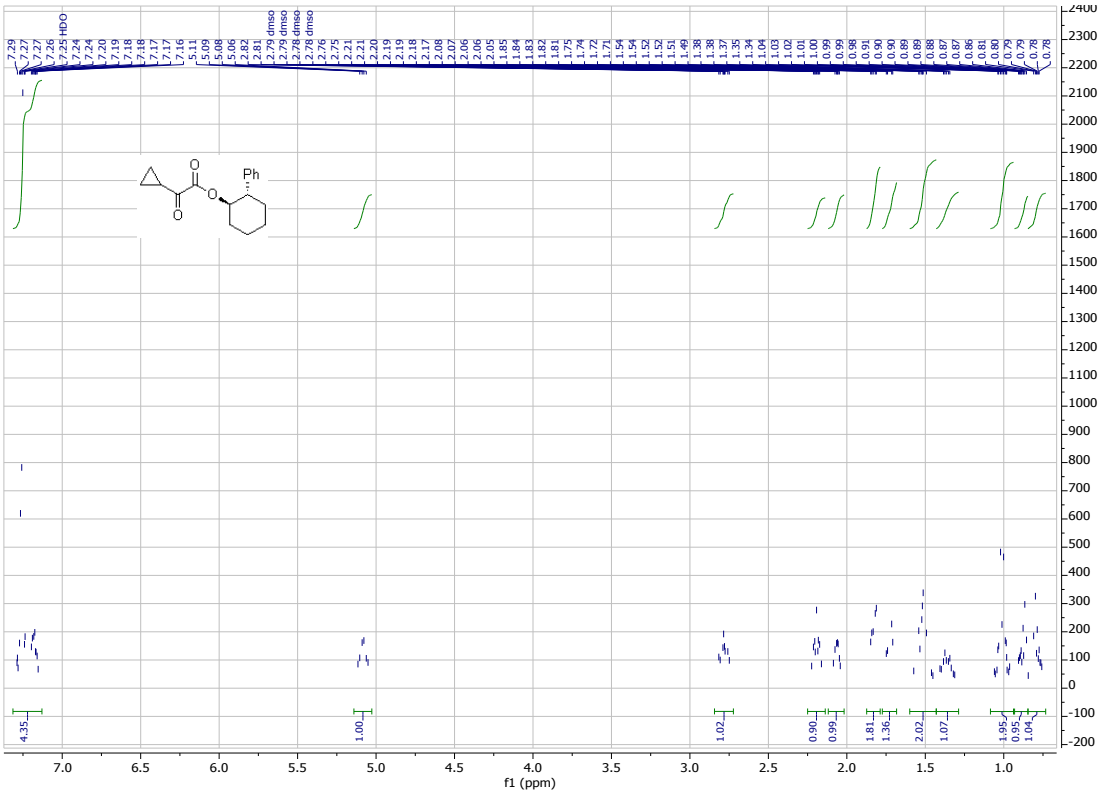


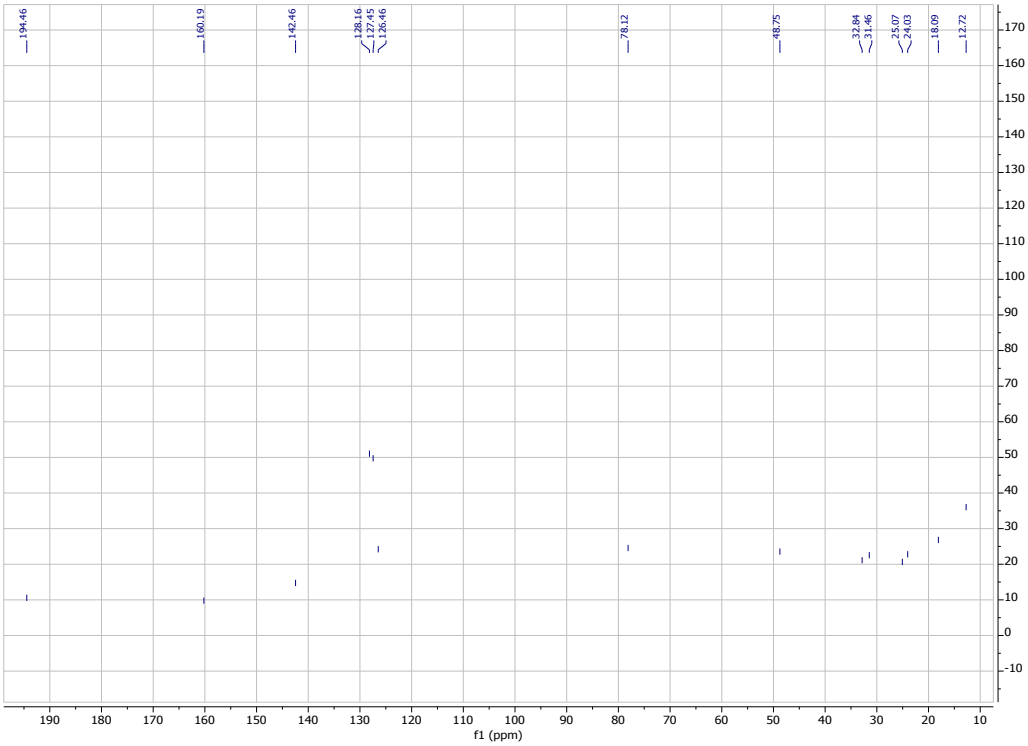
(*1R,2S*)-2-phenylcyclohexyl 2-oxo-2-phenylacetate (7c)



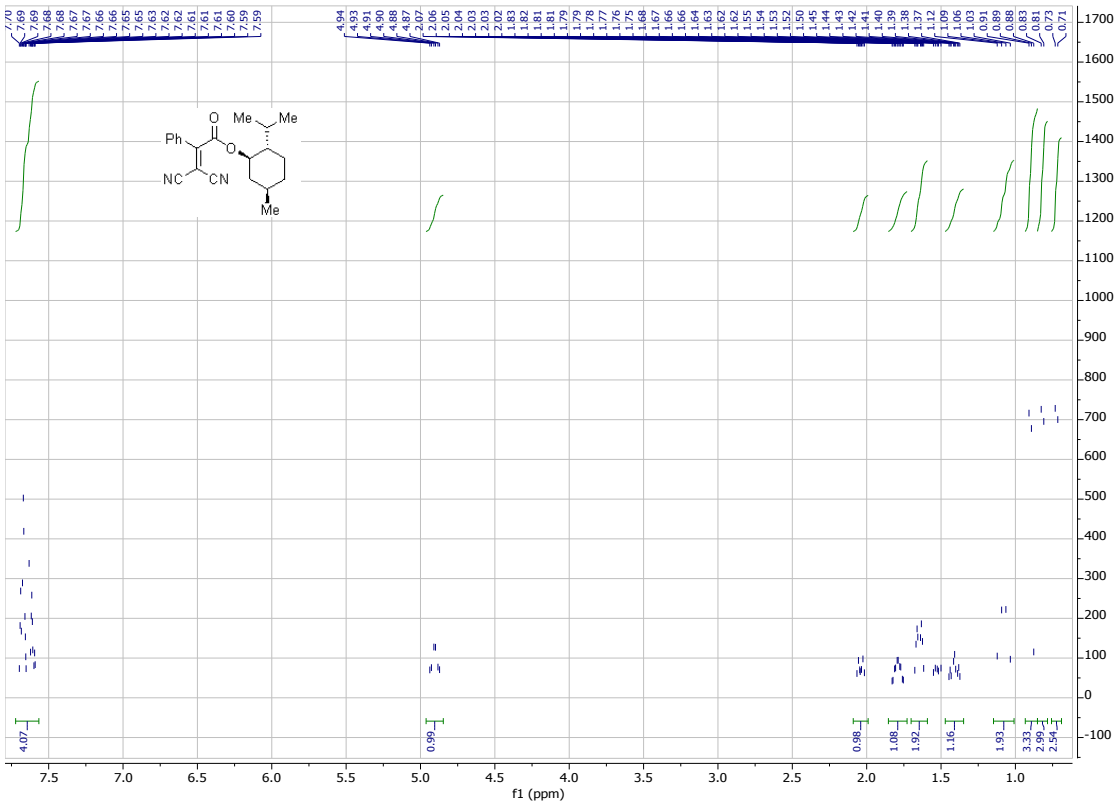


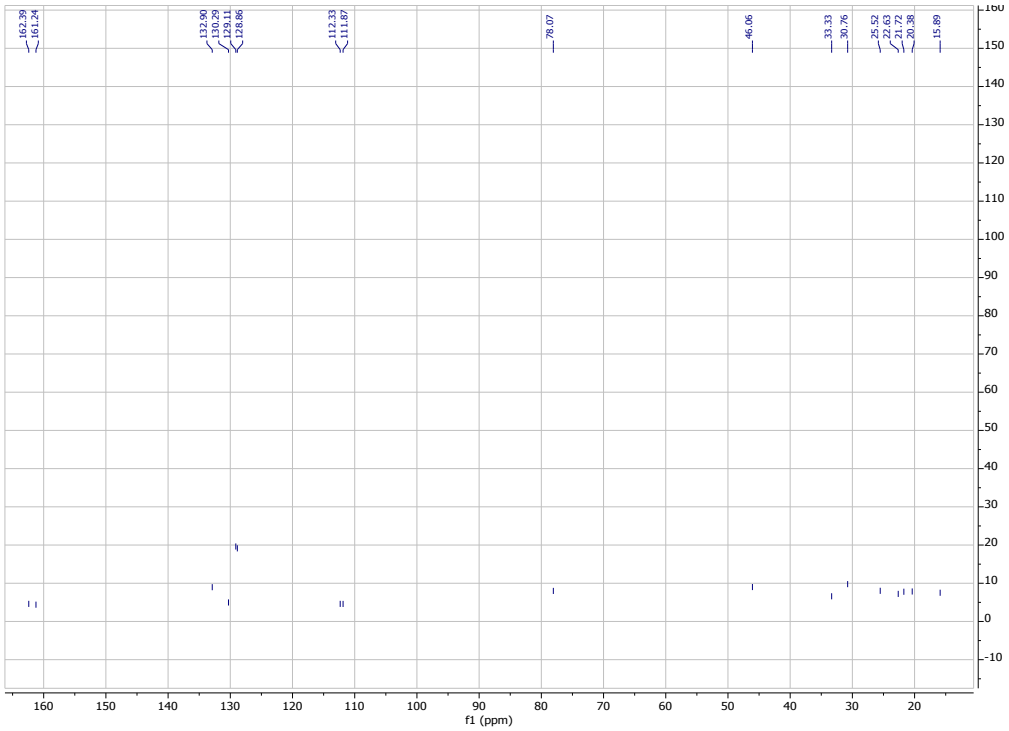
(*1R,2S*)-2-phenylcyclohexyl-2-cyclopropyl-2-oxoacetate (7d)



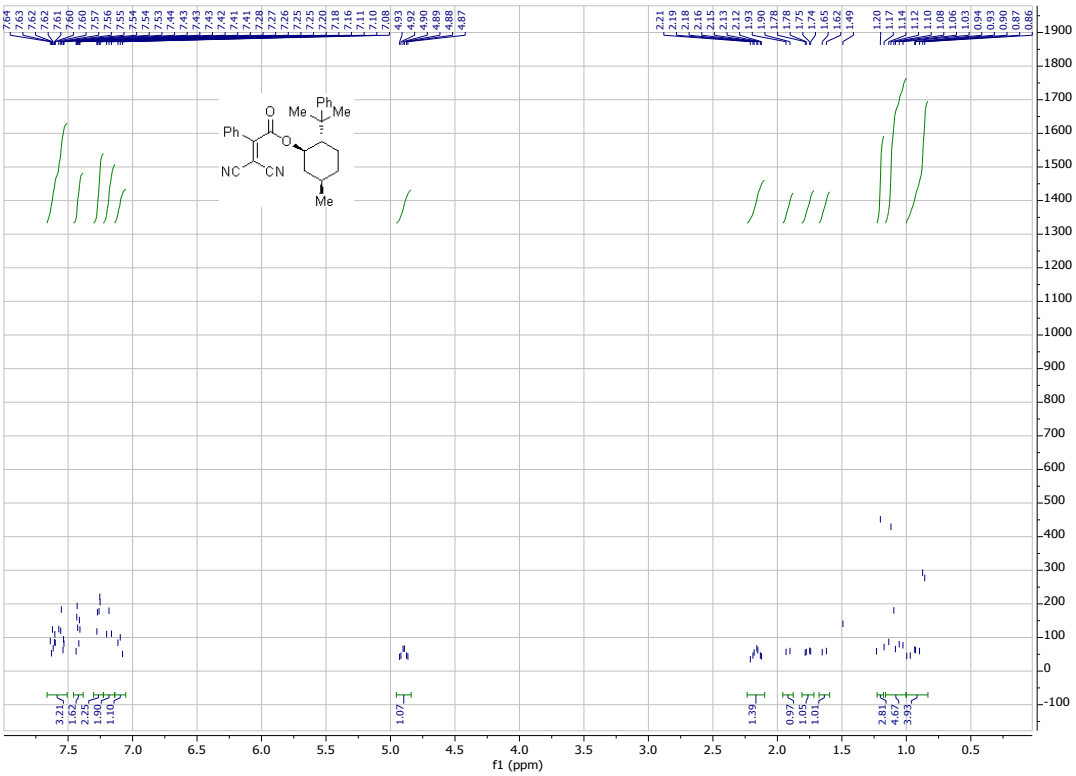


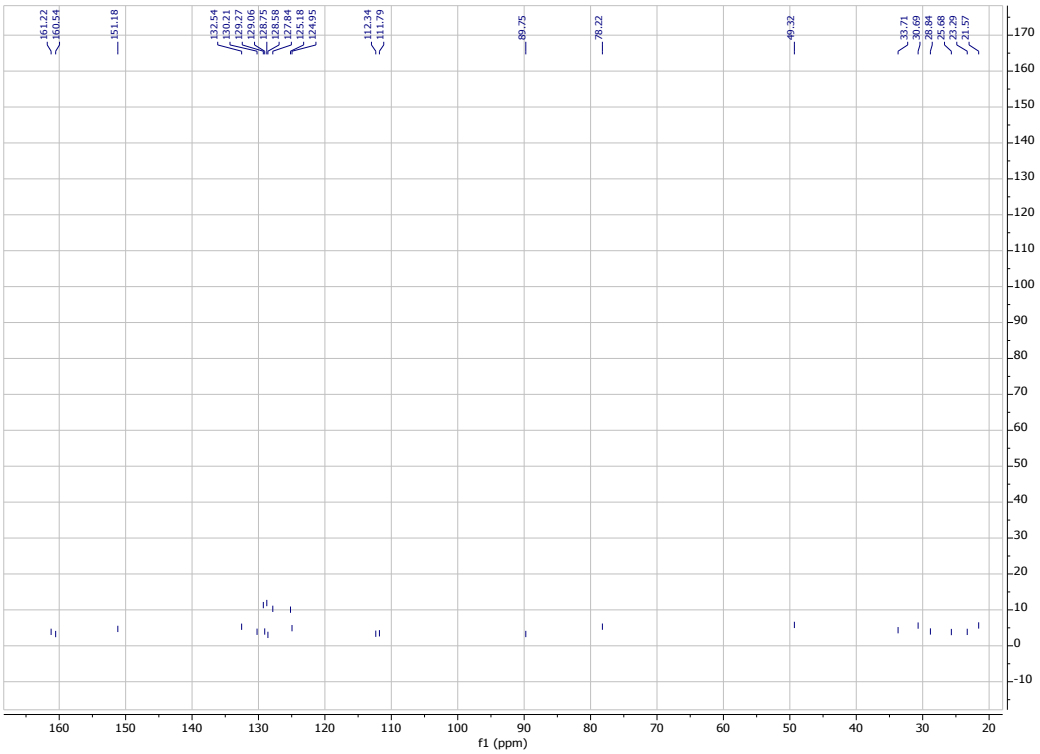
(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl-3,3-dicyano-2-phenylacrylate (8a)



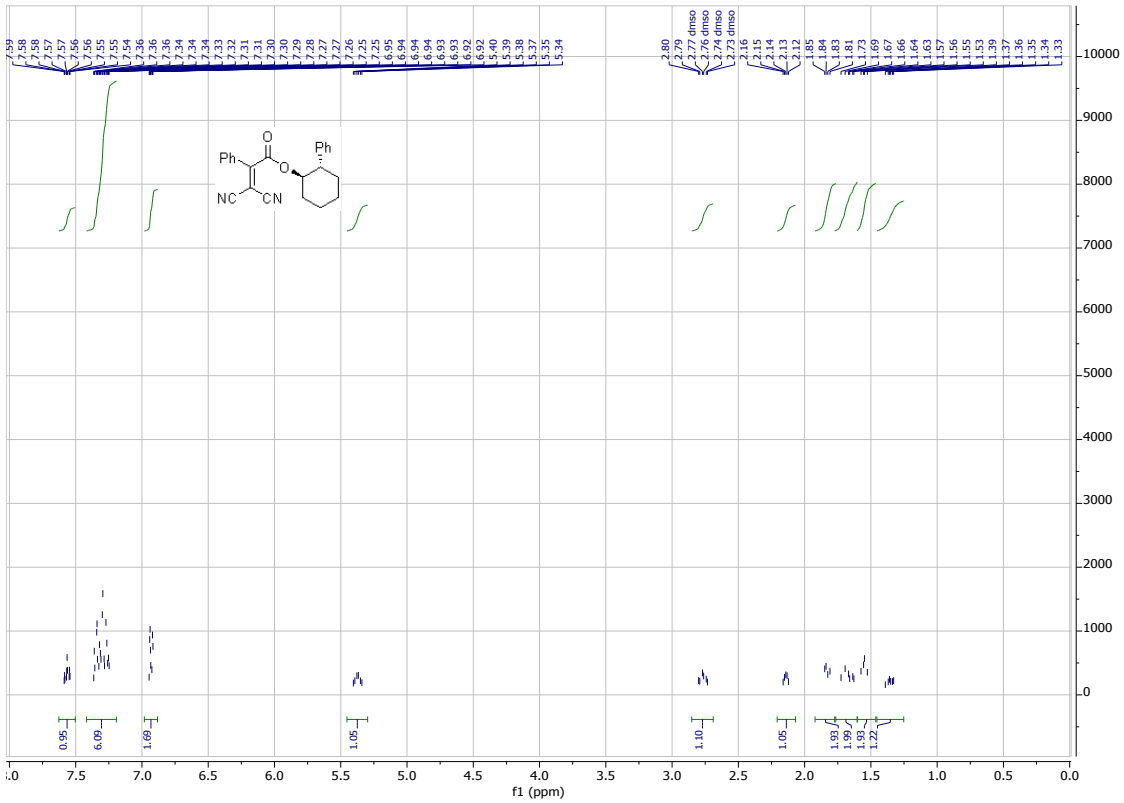


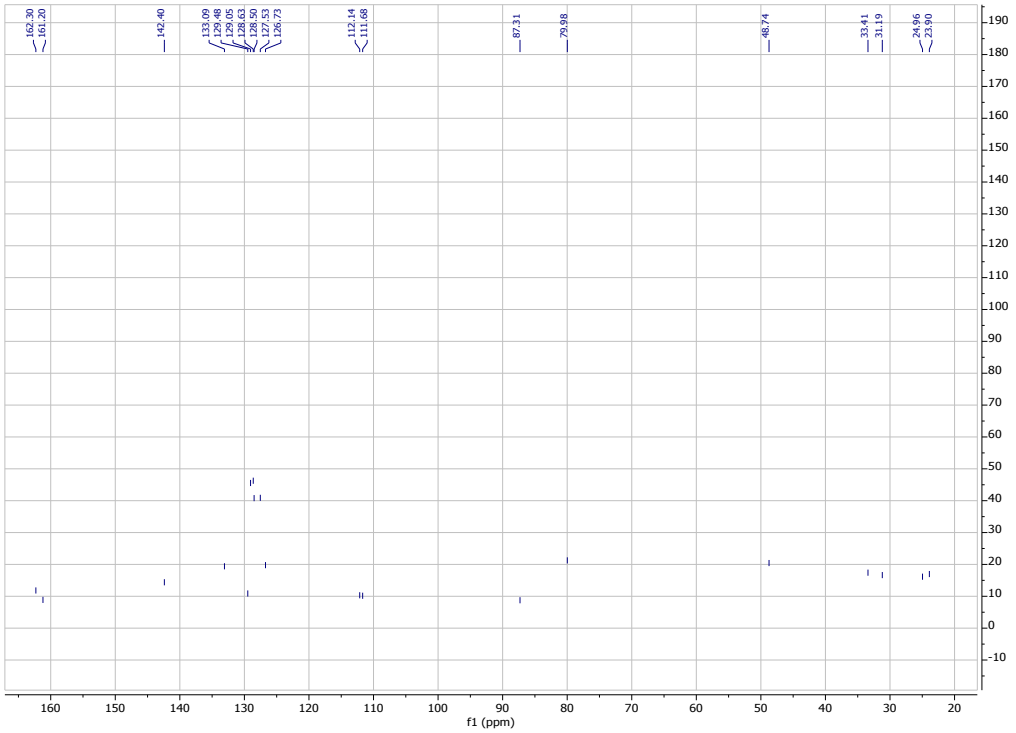
(*1R,2S,5R*)-5-methyl-2-(2-phenylpropan-2-yl)cyclohexyl-3,3-dicyano-2-phenylacrylate (8b)



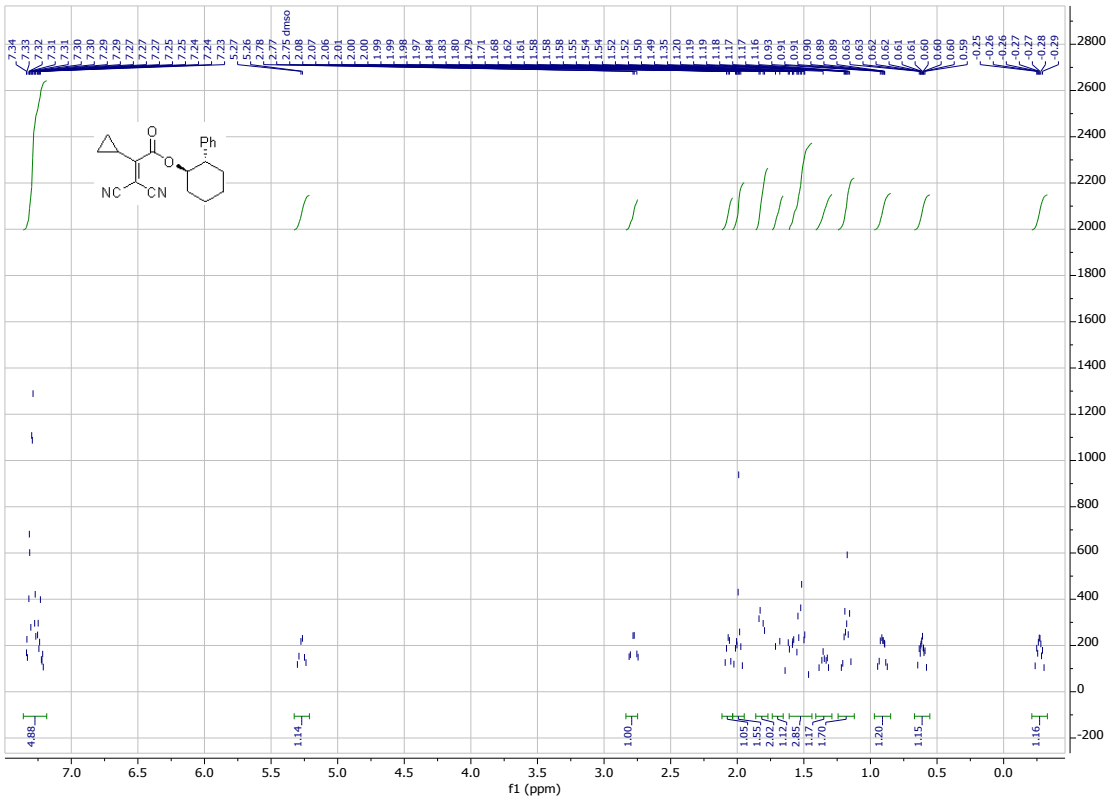


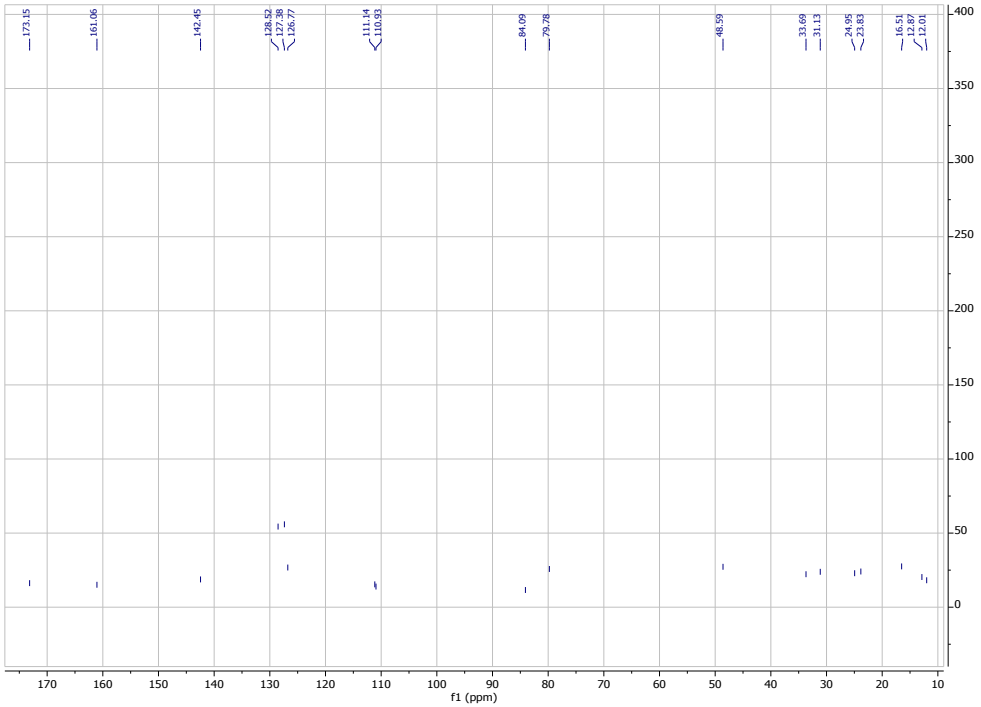
(*1R,2S*)-2-phenylcyclohexyl-3,3-dicyano-2-phenylacrylate (8c)



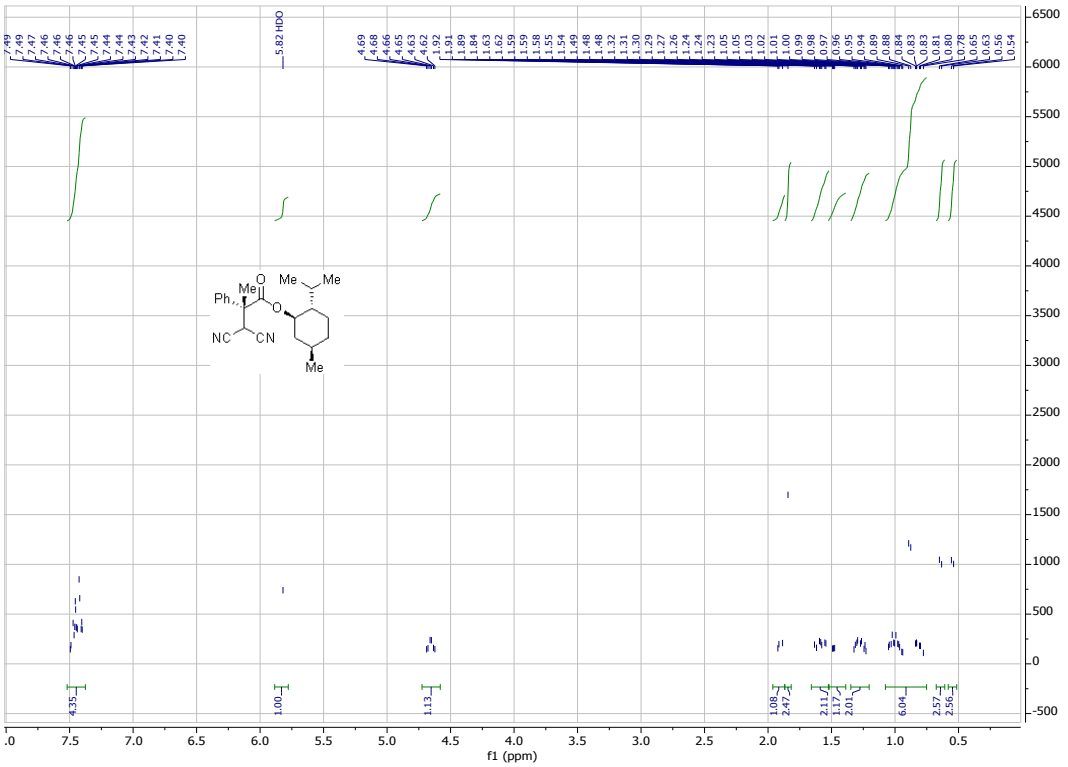


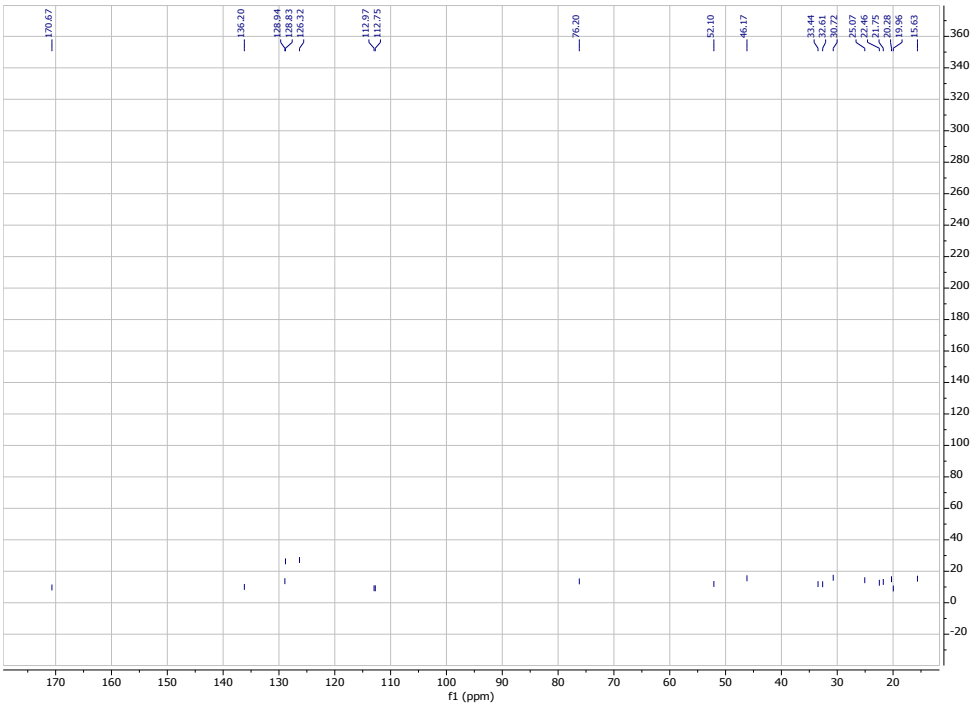
(*1R,2S*)-2-phenylcyclohexyl-3,3-dicyano-2-cyclopropylacrylate (8d)



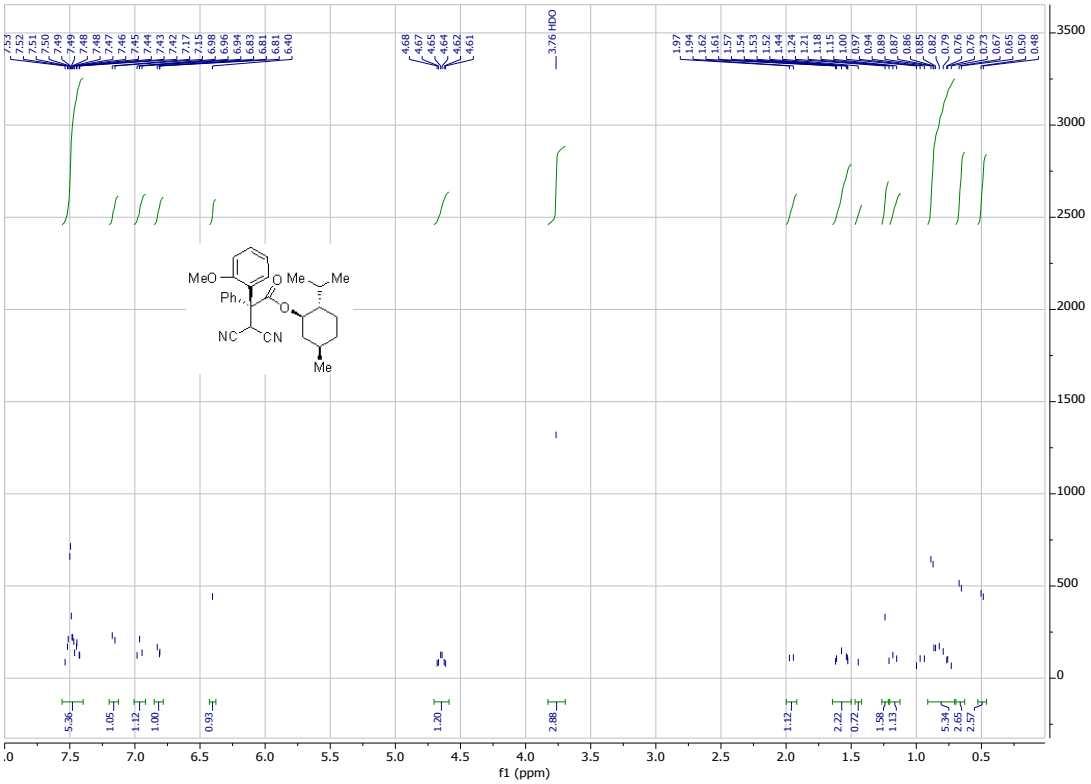


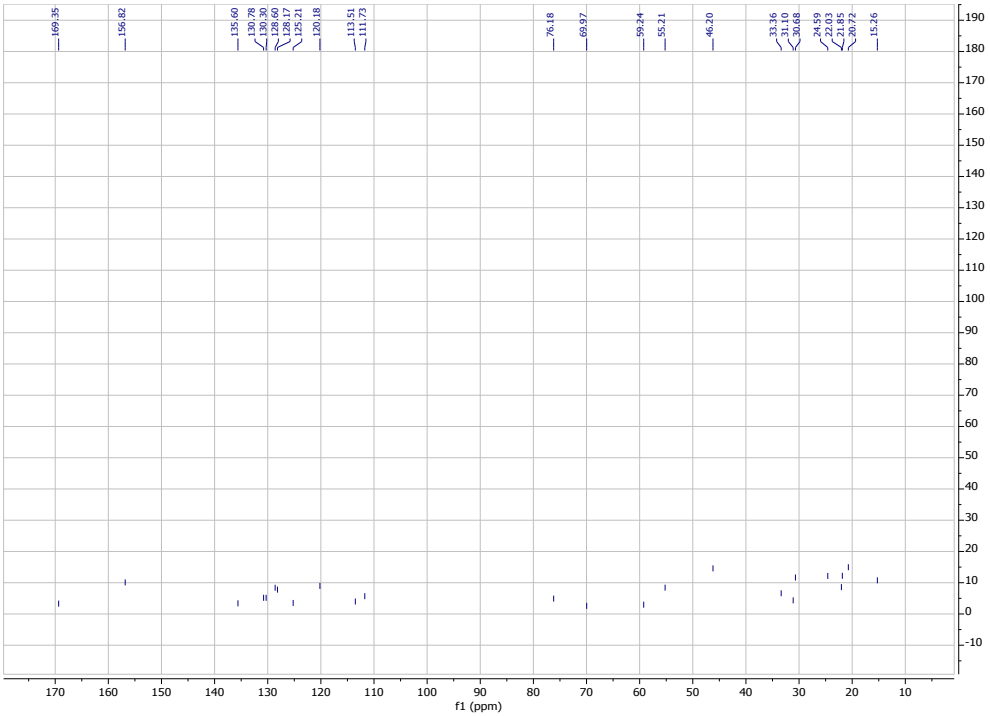
(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (9a)



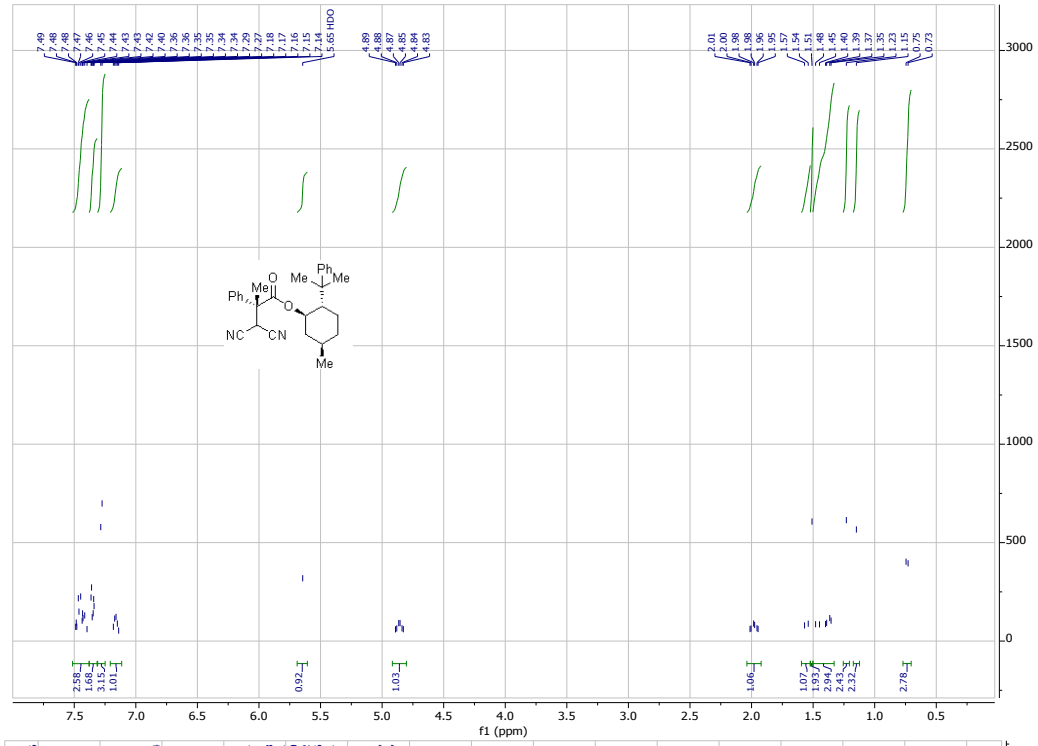


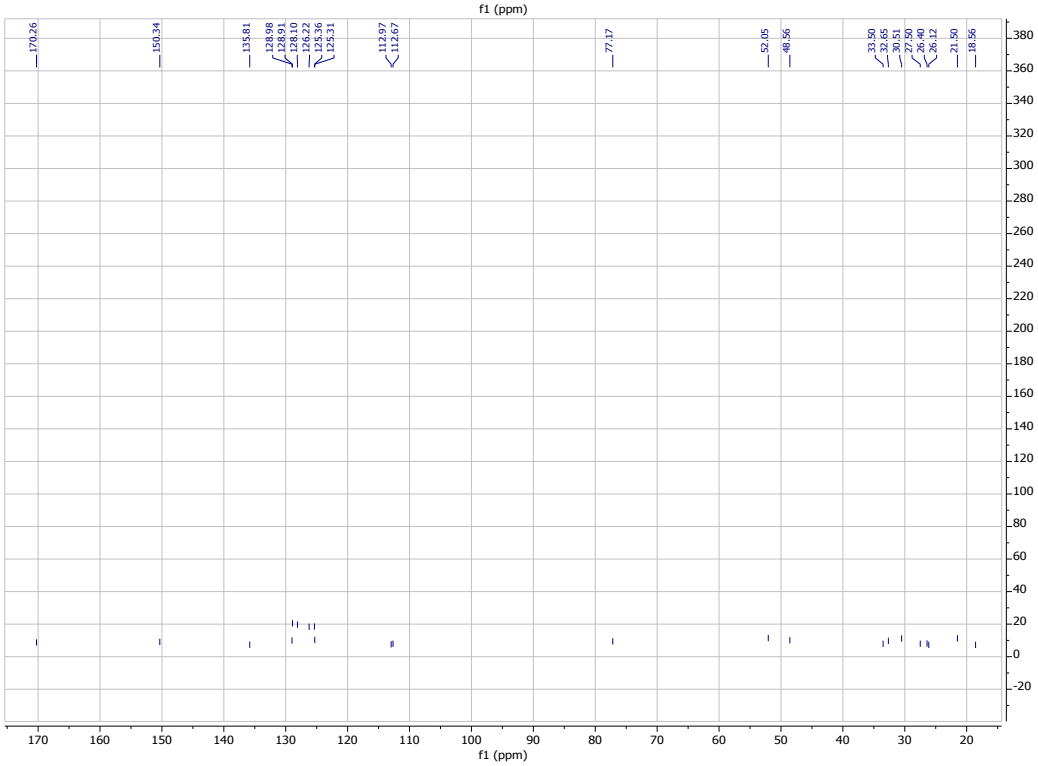
(*1S,2S,5R*)-2-isopropyl-5-methylcyclohexyl-(*R*)-3,3-dicyano-2-(2-methoxyphenyl)-2-phenylpropanoate (9b).



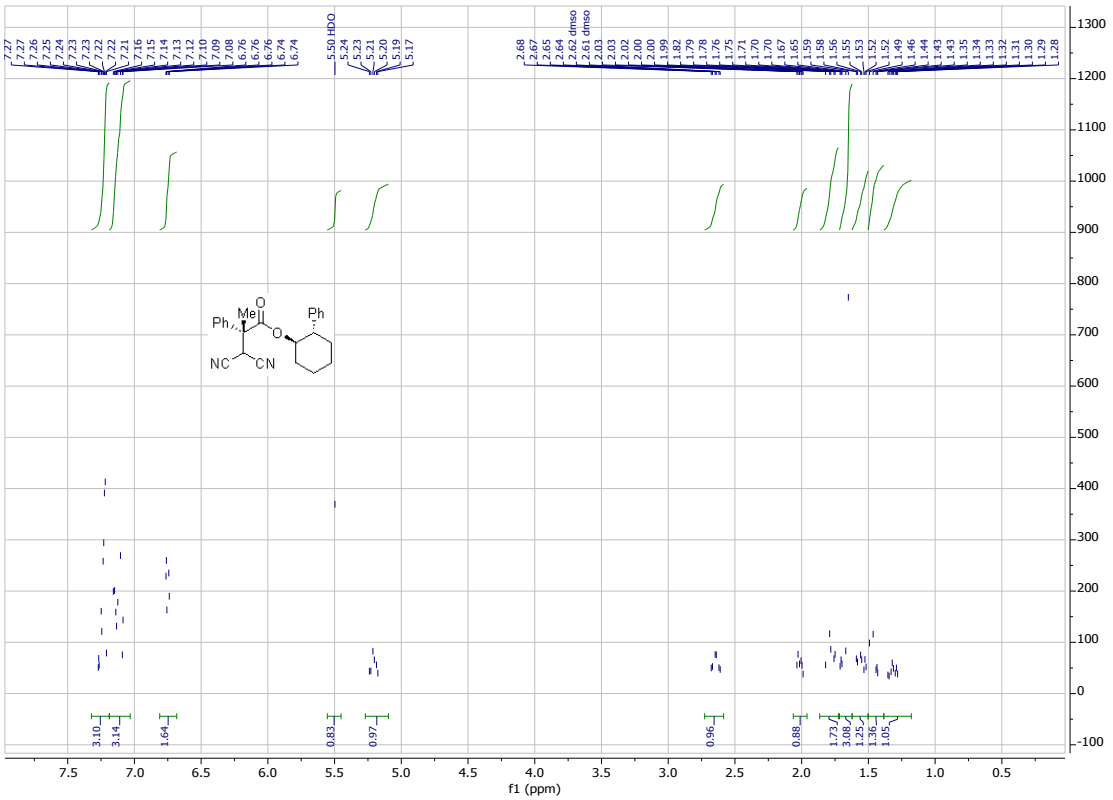


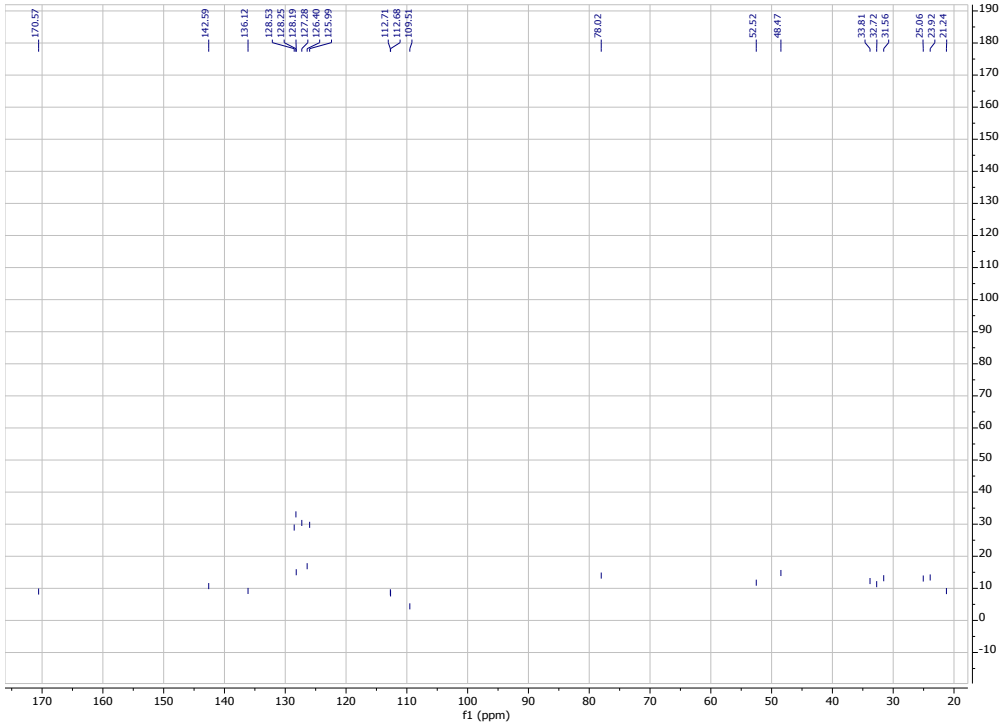
(*1R,2S,5R*)-5-methyl-2-(2-phenylpropan-2-yl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (9c)



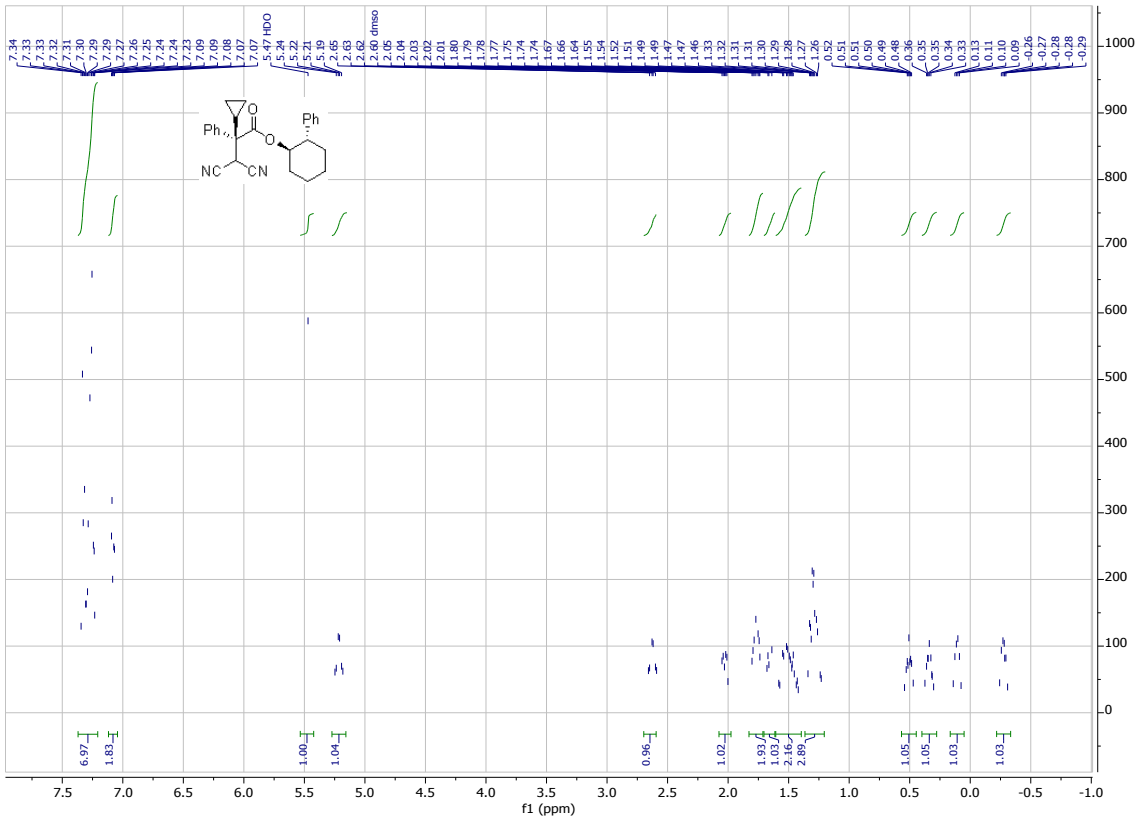


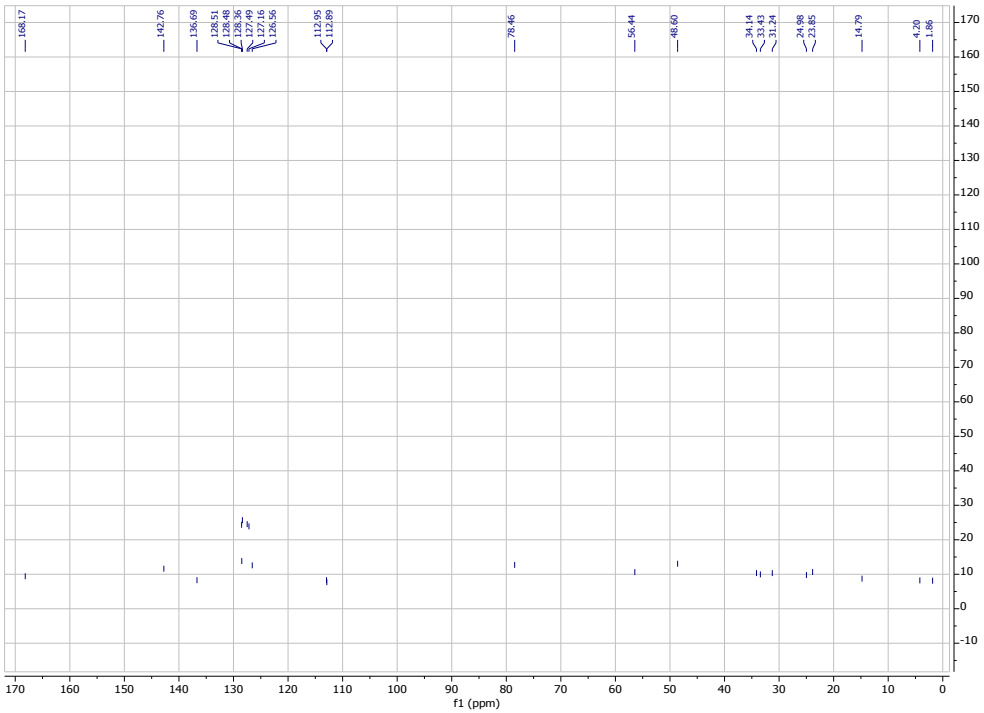
(*1R,2S*)-2-phenylcyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (9e)



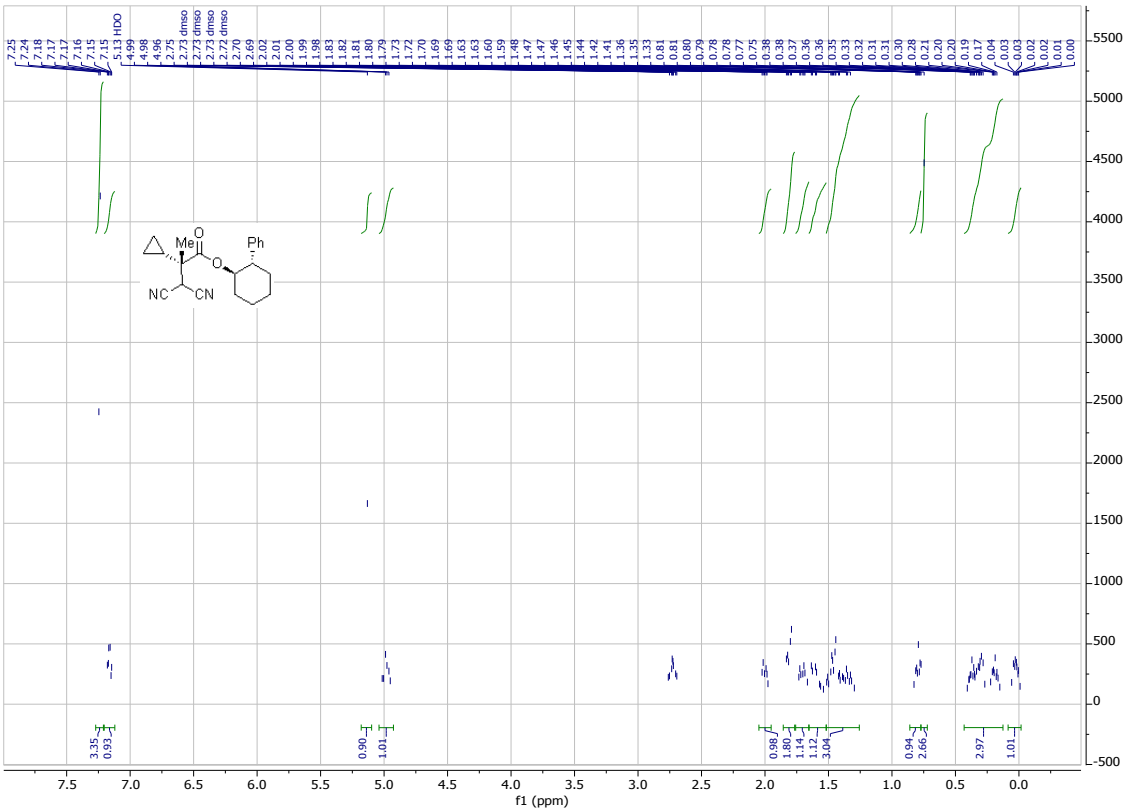


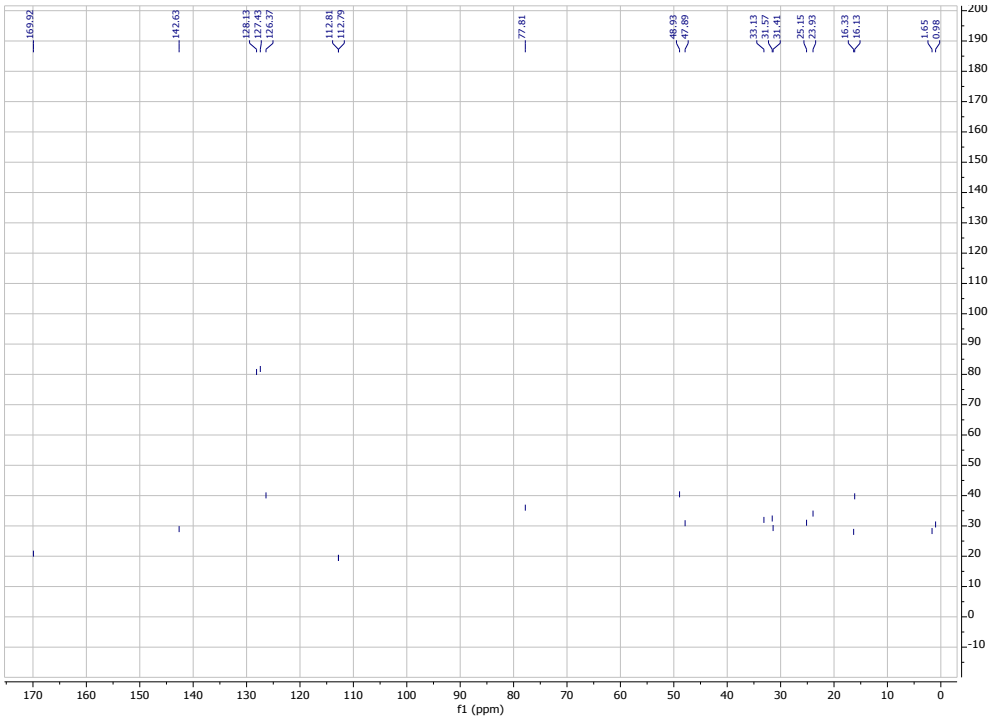
(*1R,2S*)-2-phenylcyclohexyl-(*R*)-3,3-dicyano-2-cyclopropyl-2-Phenylpropanoate (9f)



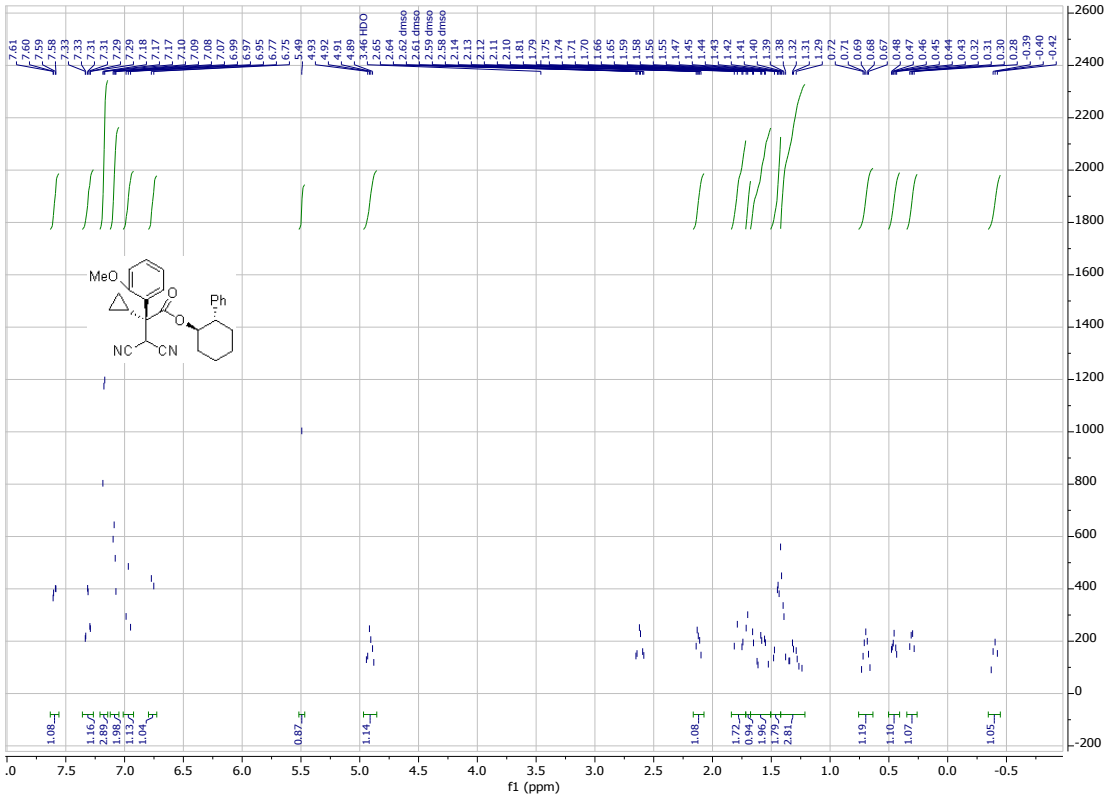


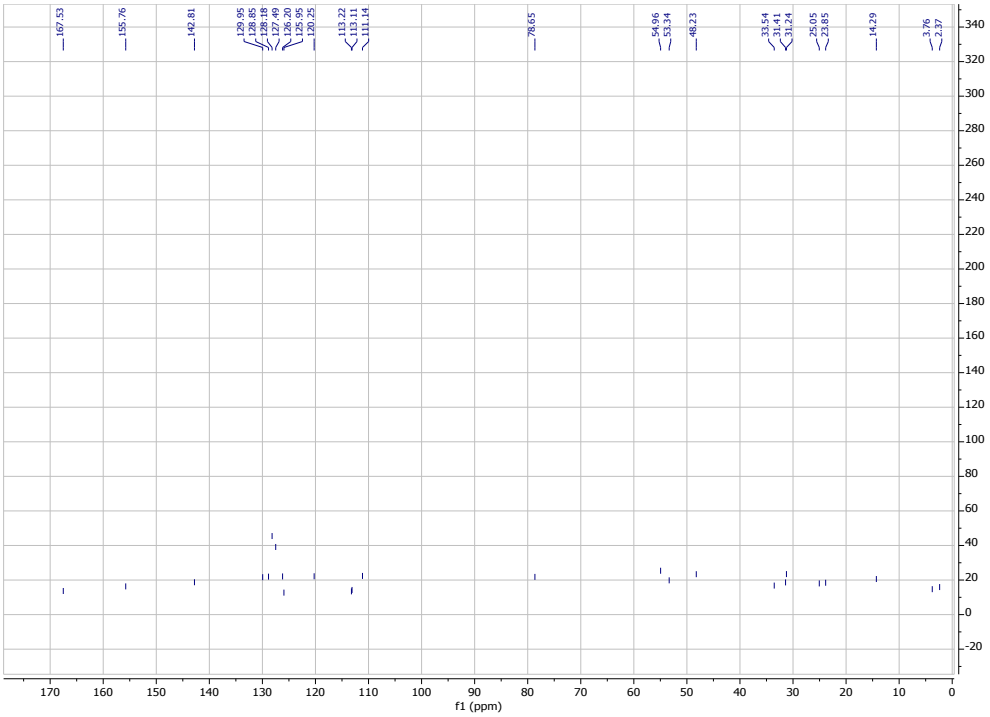
(*1R,2S*)-2-phenylcyclohexyl-(*S*)-3,3-dicyano-2-cyclopropyl-2-methylpropanoate (9g)



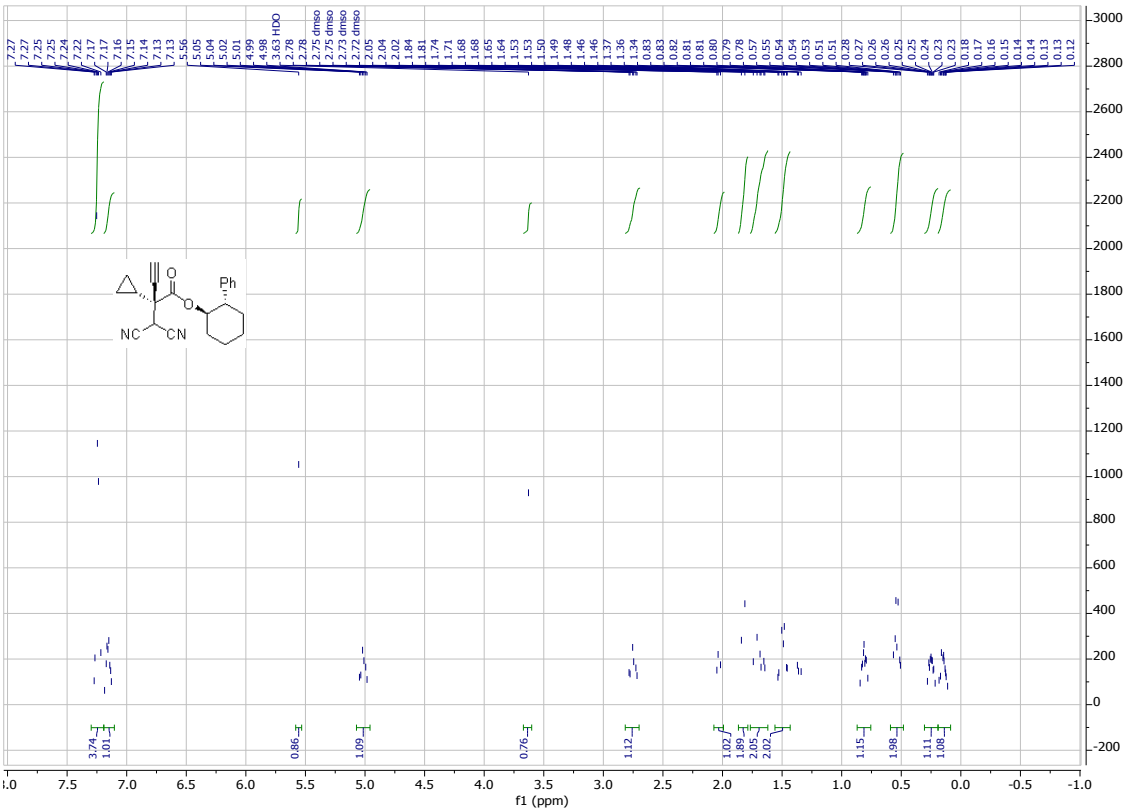


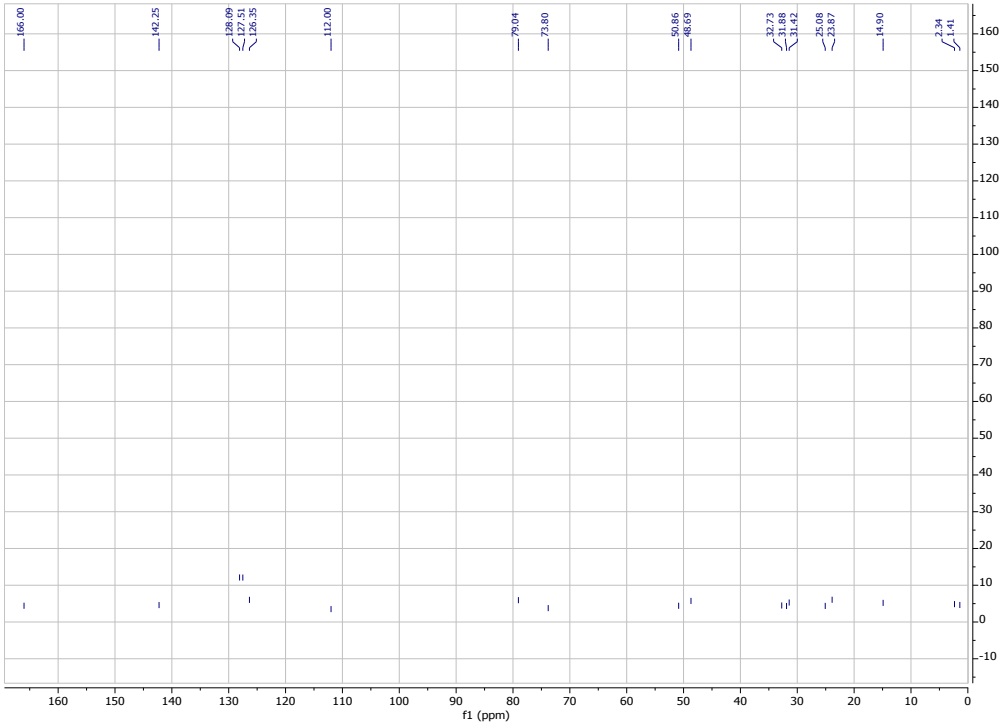
(*1R,2S*)-2-phenylcyclohexyl-(*S*)-3,3-dicyano-2-cyclopropyl-2-(2-ethoxyphenyl)propanoate (9h)



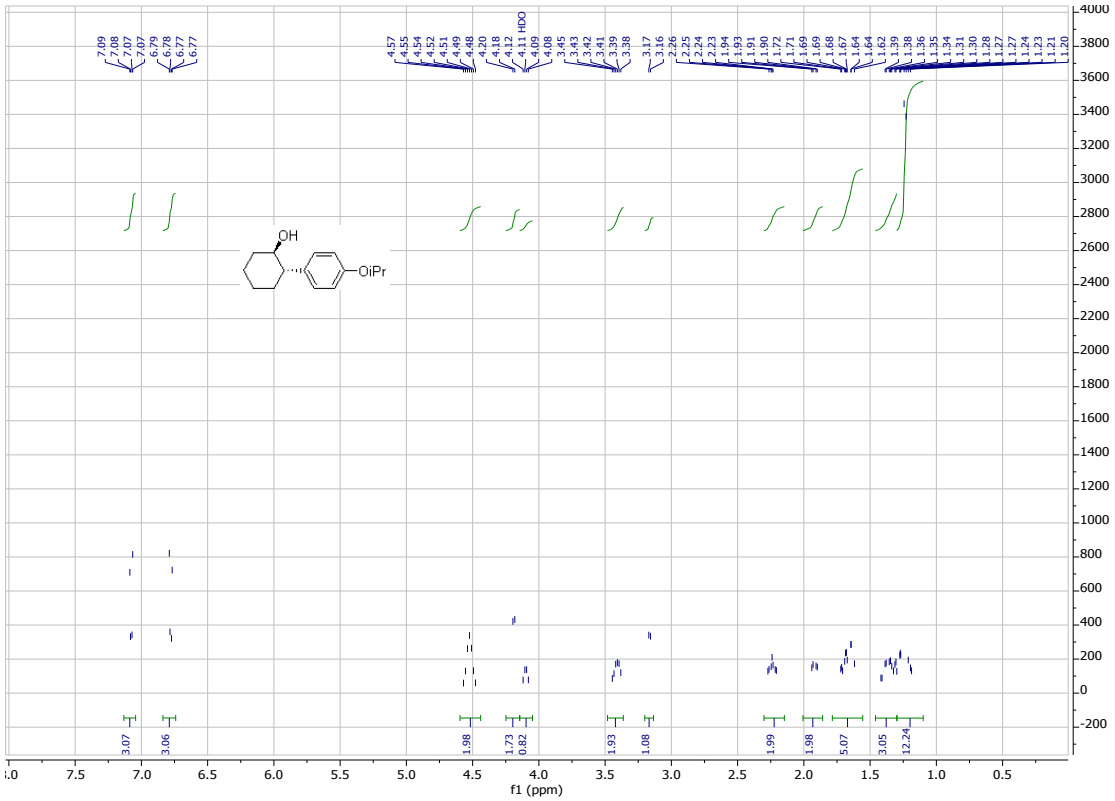


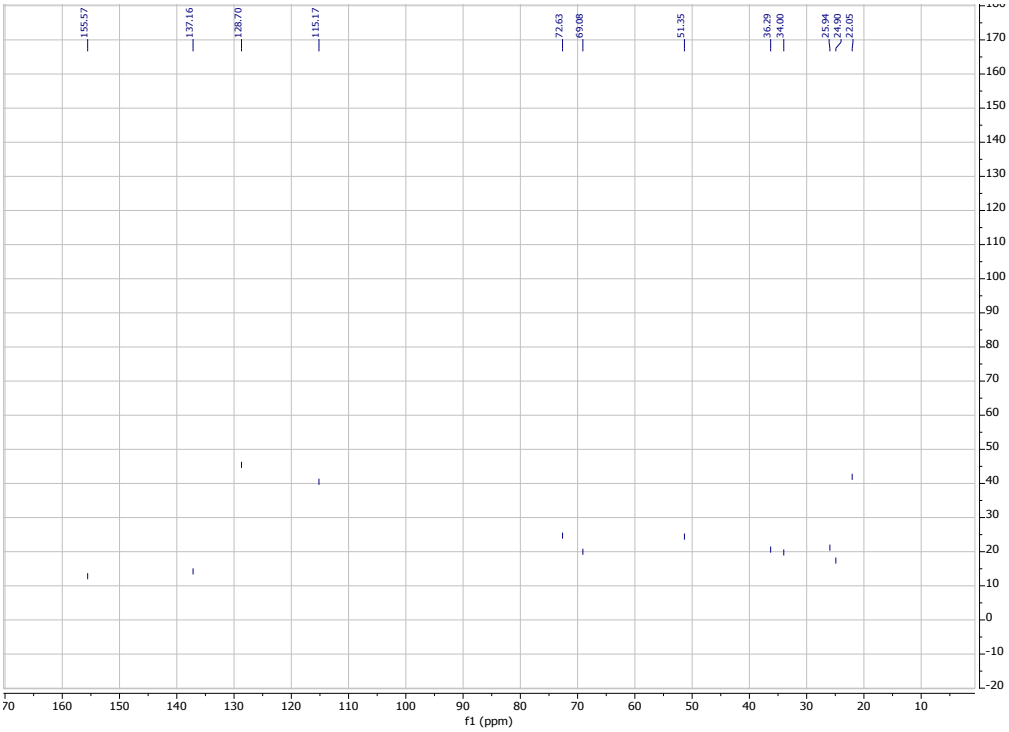
(*1S,2S*)-2-phenylcyclohexyl-(*S*)-2-cyclopropyl-2-(dicyanomethyl)but-3-ynoate (9i)



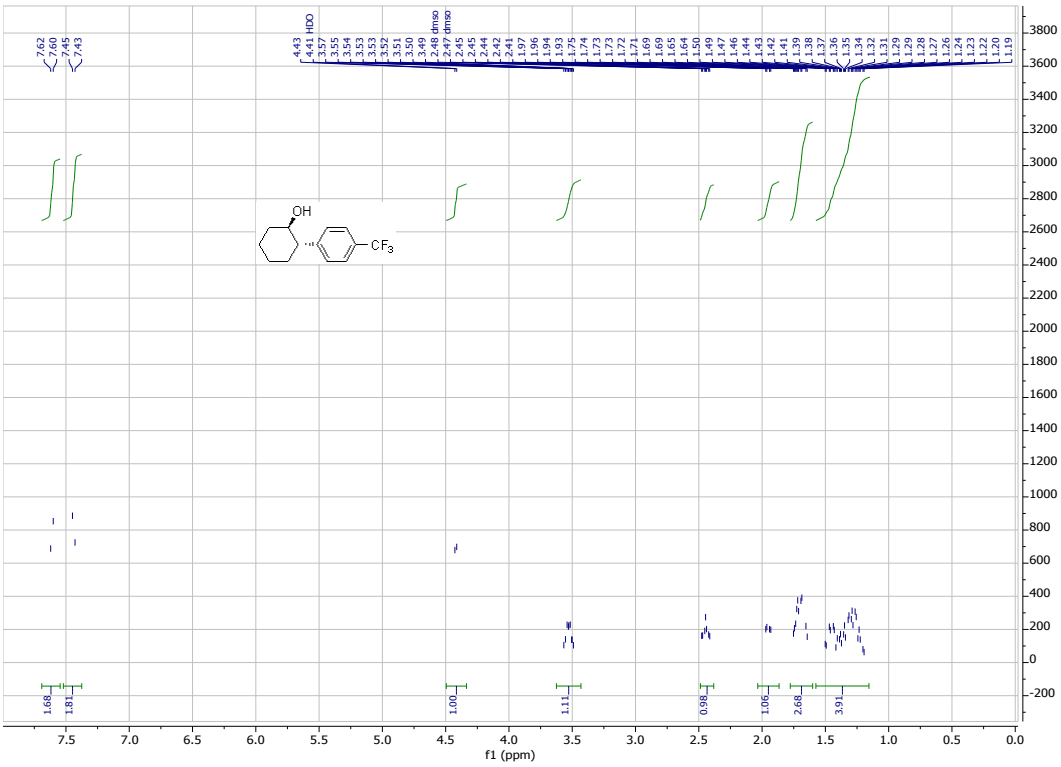


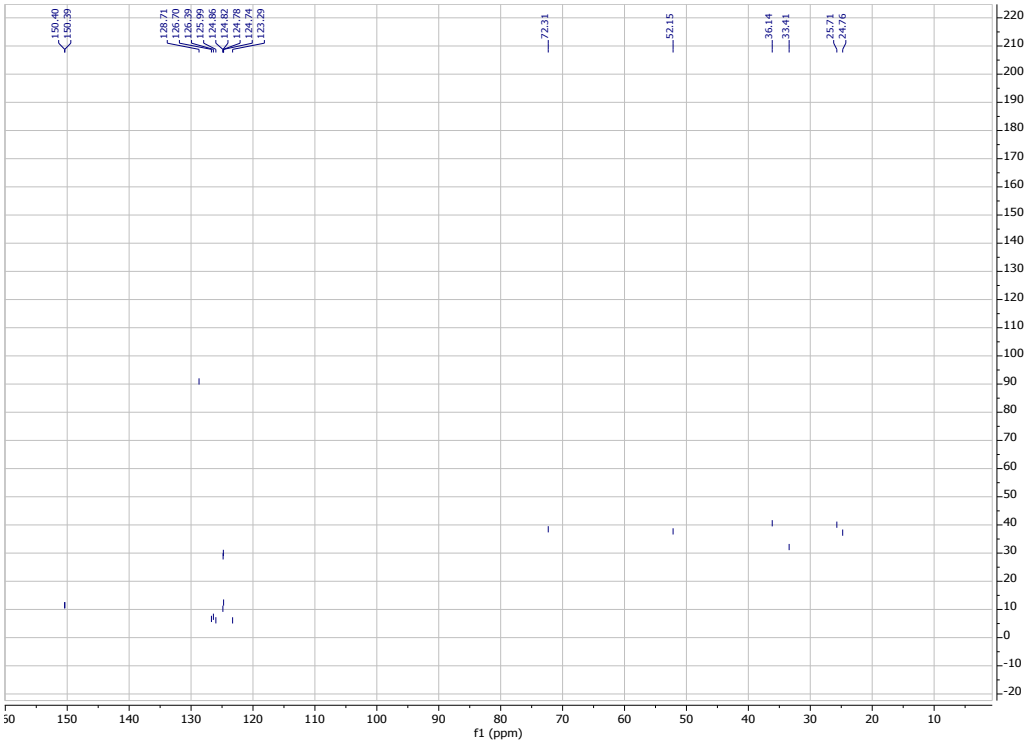
(-)-(*1R,2S*)-2-(4-isopropoxyphenyl)cyclohexan-1-ol (10a)



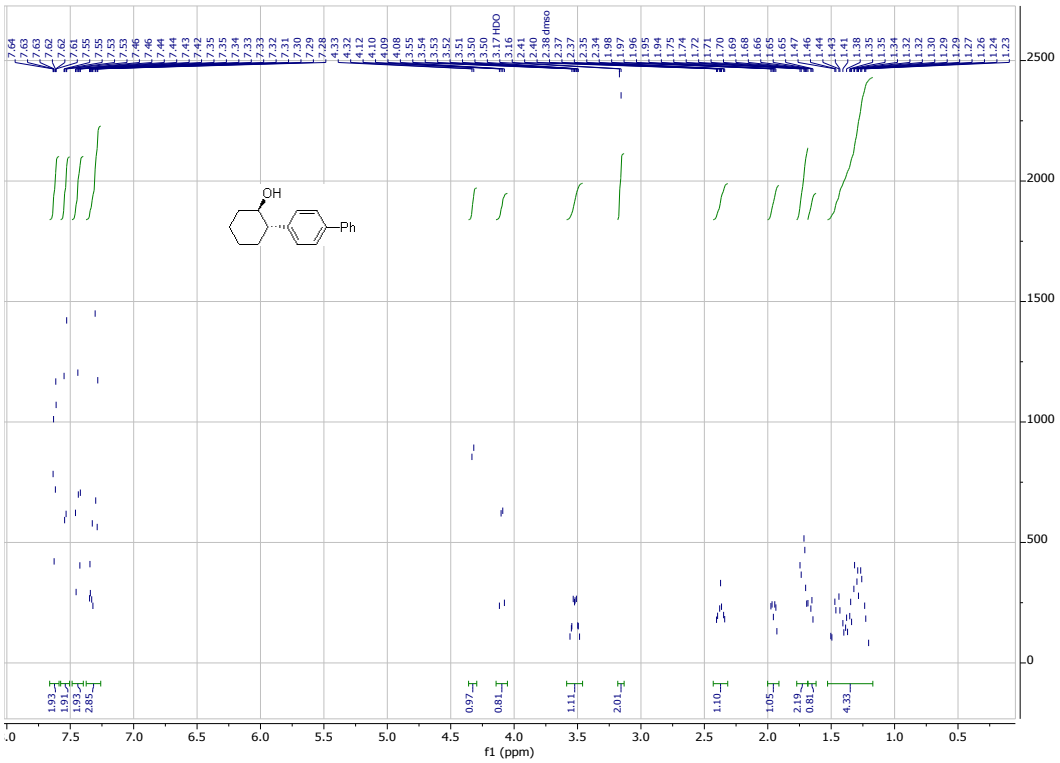


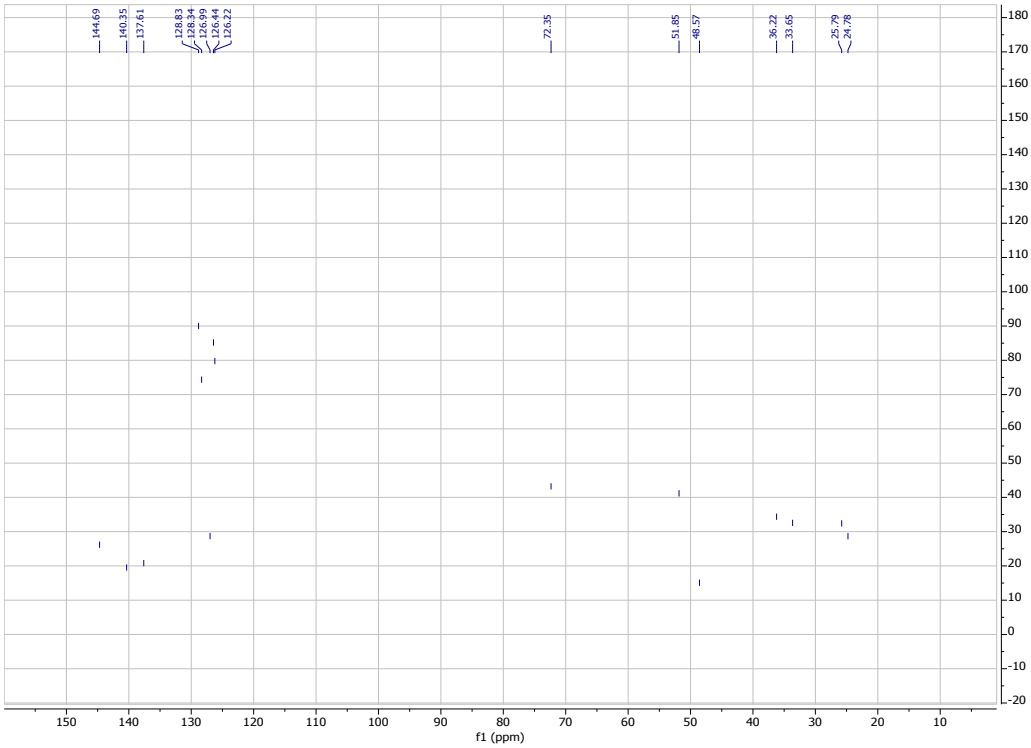
(-)-(*1R,2S*)-2-(4-(trifluoromethyl)phenyl)cyclohexan-1-ol (10b)



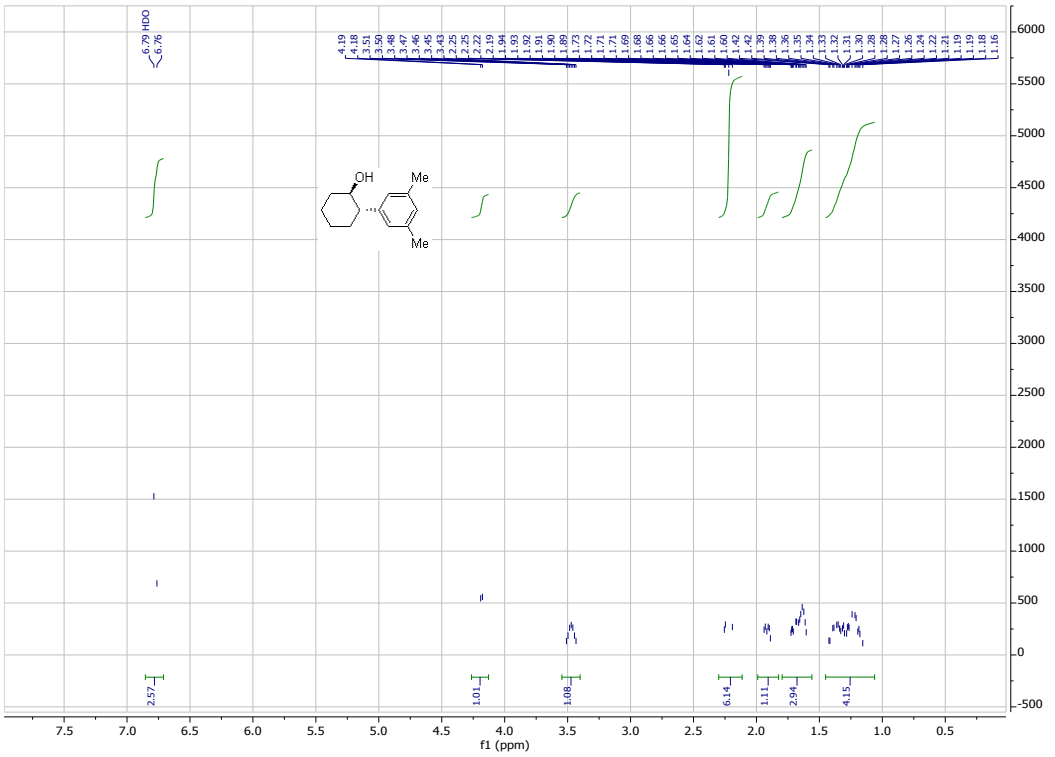


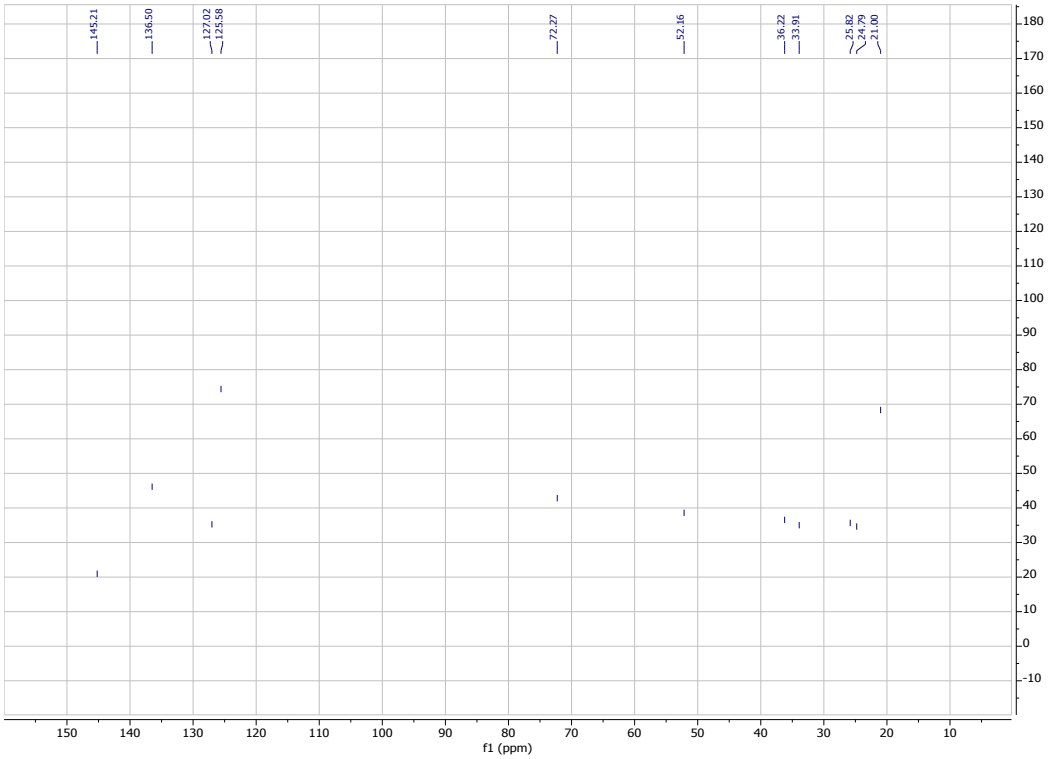
(-)-(*1R,2S*)-2-([1,1'-biphenyl]-4-yl)cyclohexan-1-ol (10c)



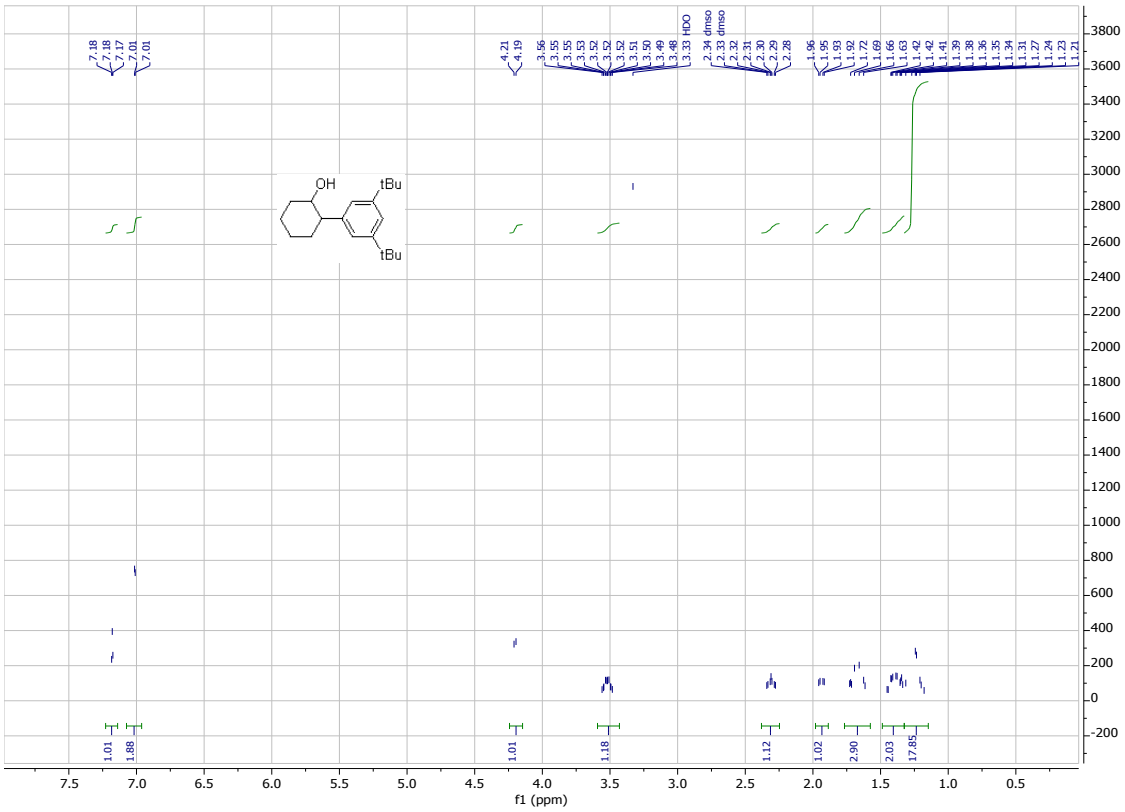


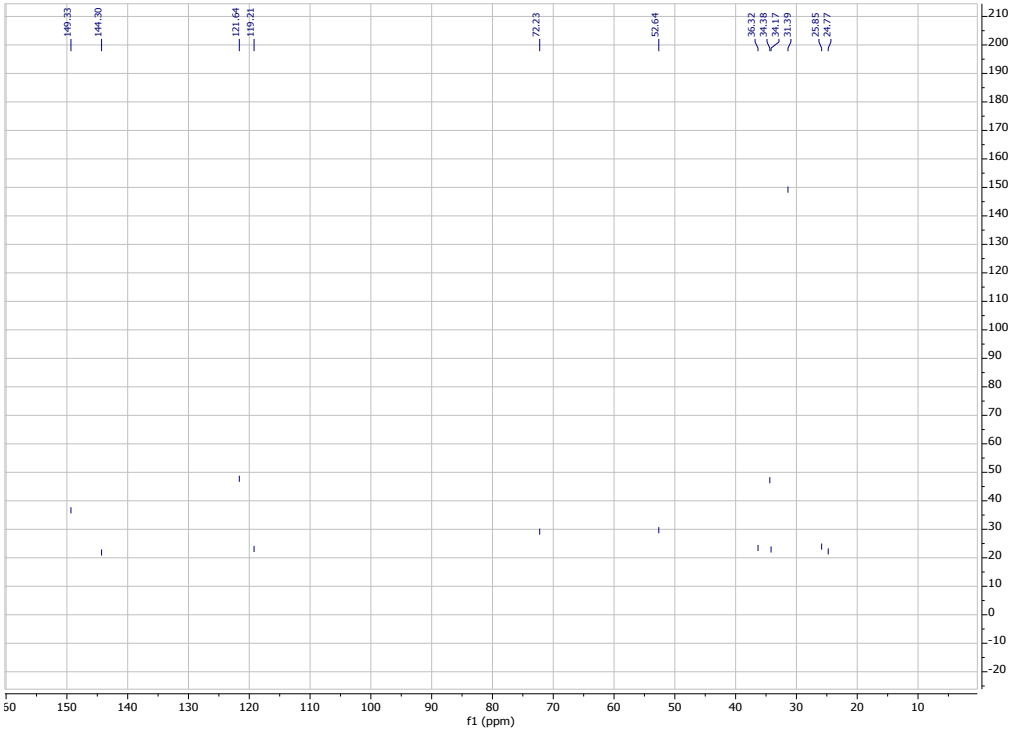
(-)-(*1R,2S*)-2-(3,5-dimethylphenyl)cyclohexan-1-ol (10d)



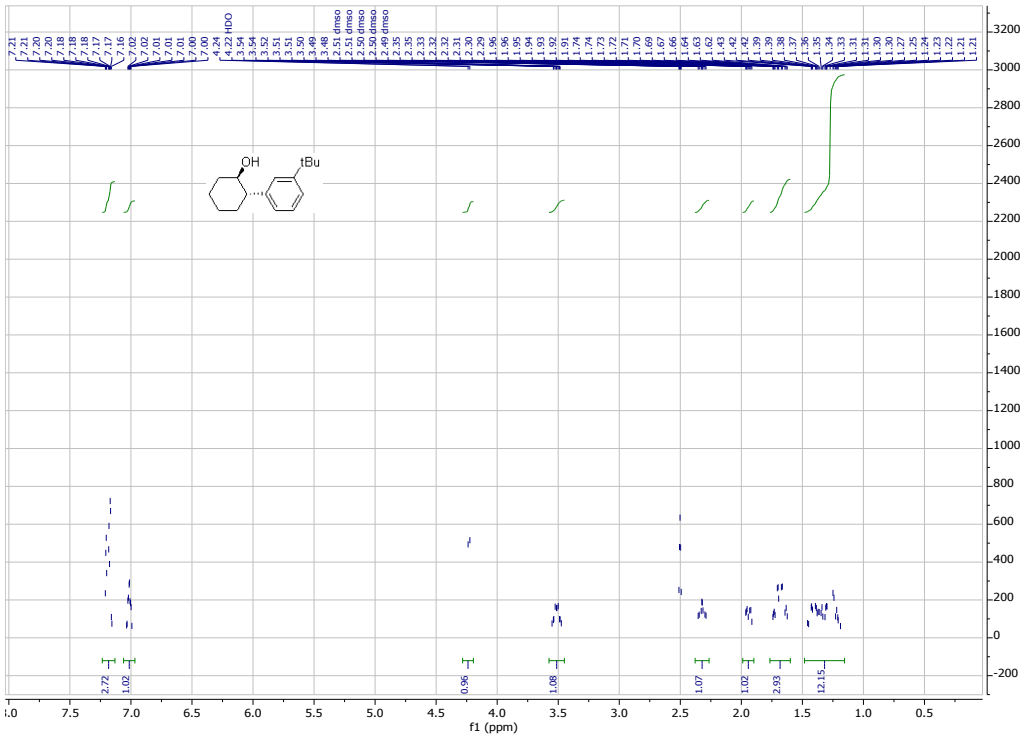


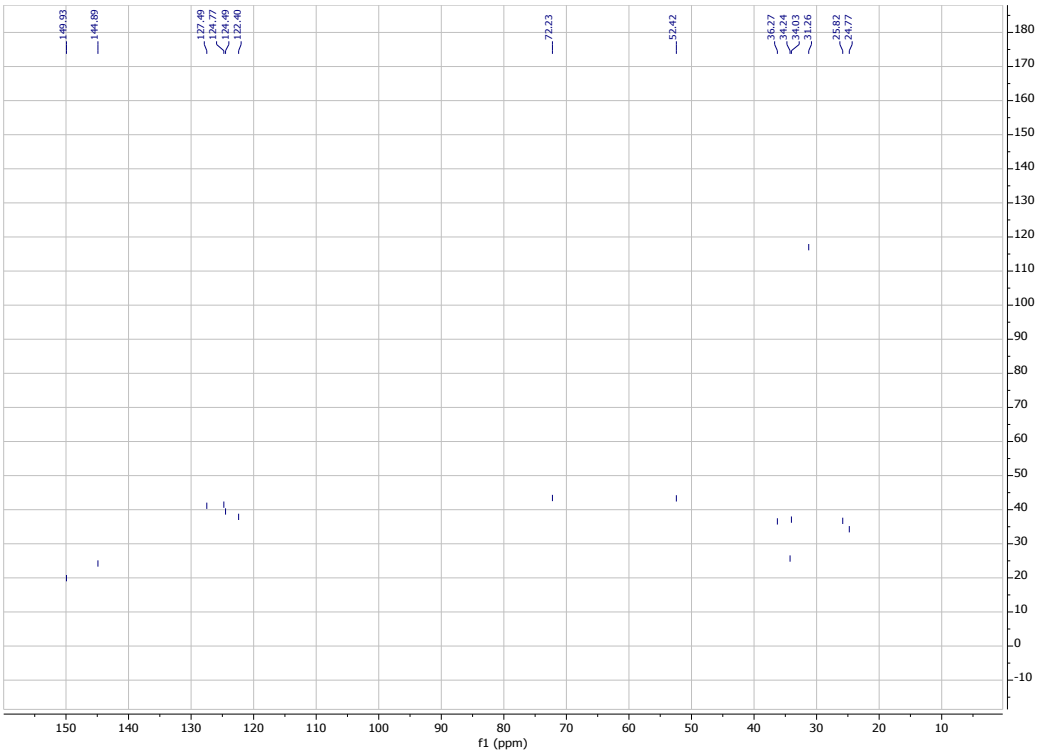
Trans-Racemic-2-(3,5-di-tert-butylphenyl)cyclohexan-1-ol (10e)



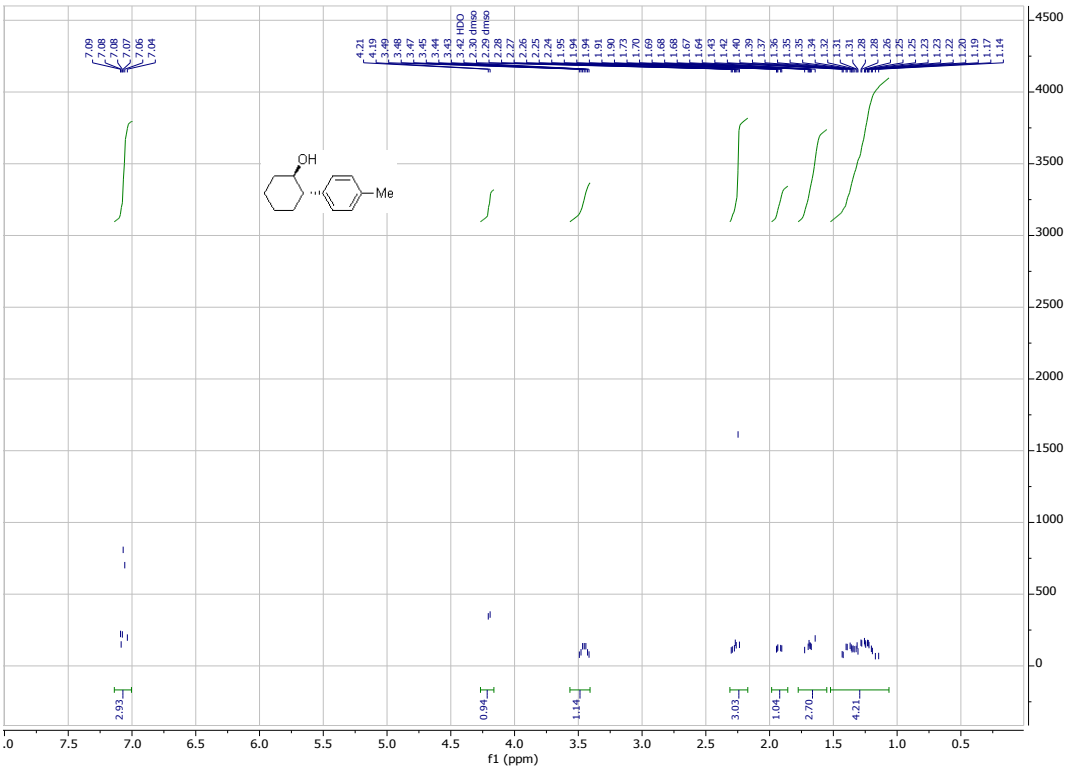


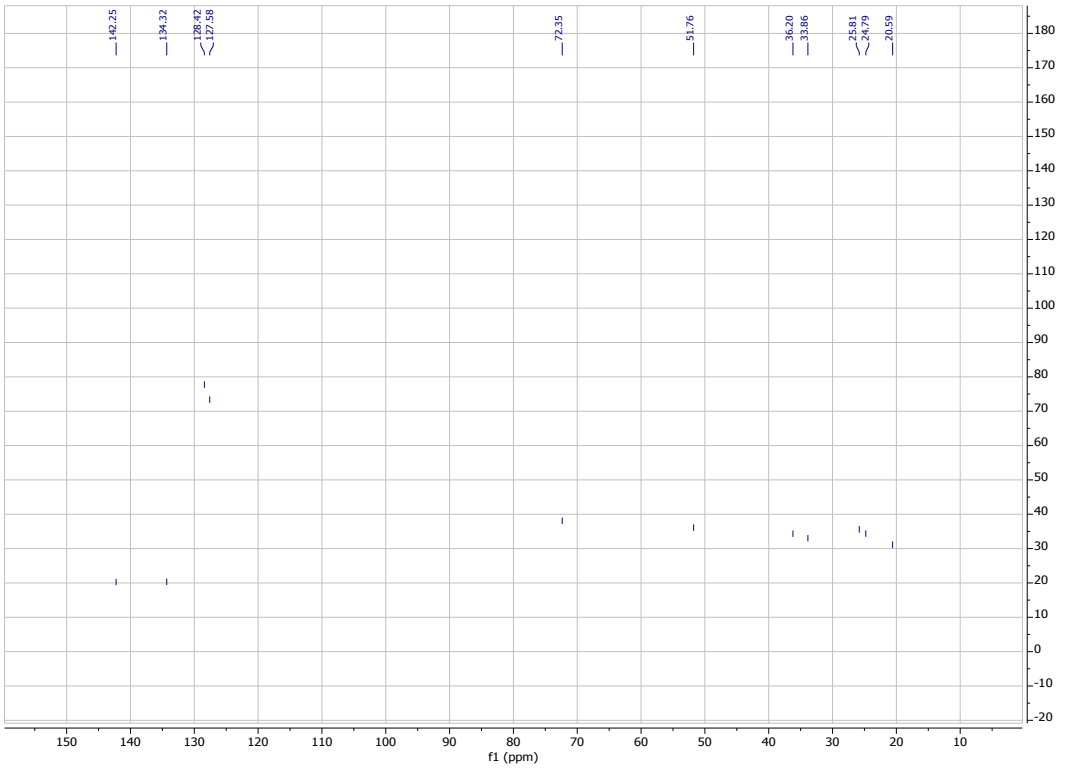
(-)-(*1R,2S*)-2-(3-(tert-butyl)phenyl)cyclohexan-1-ol (10f)



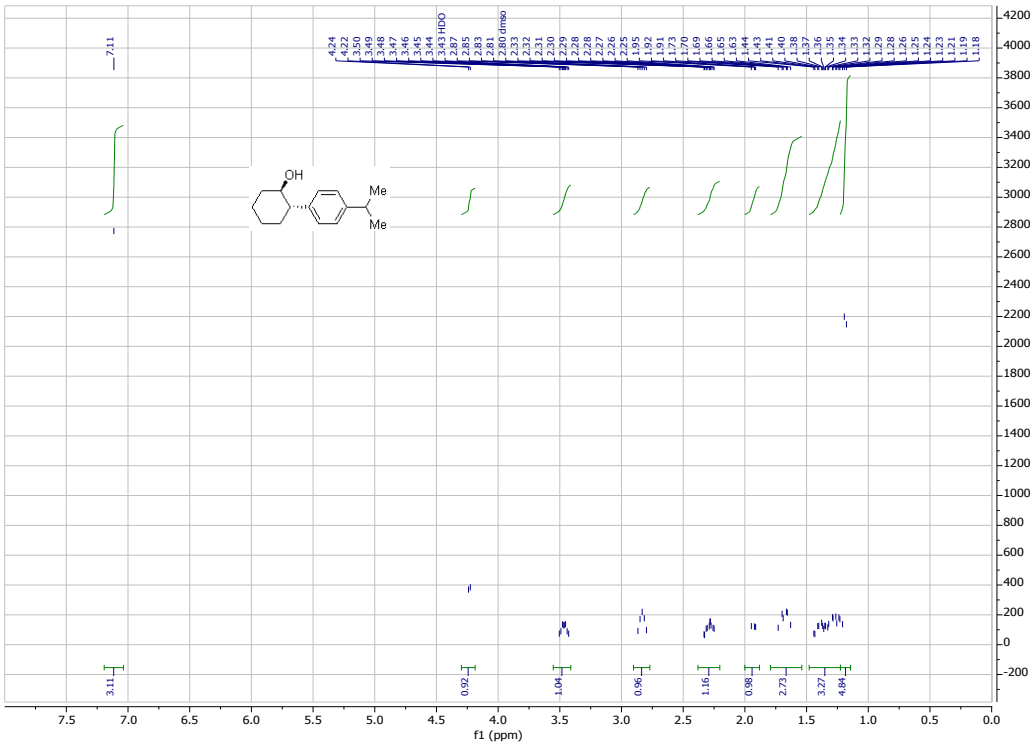


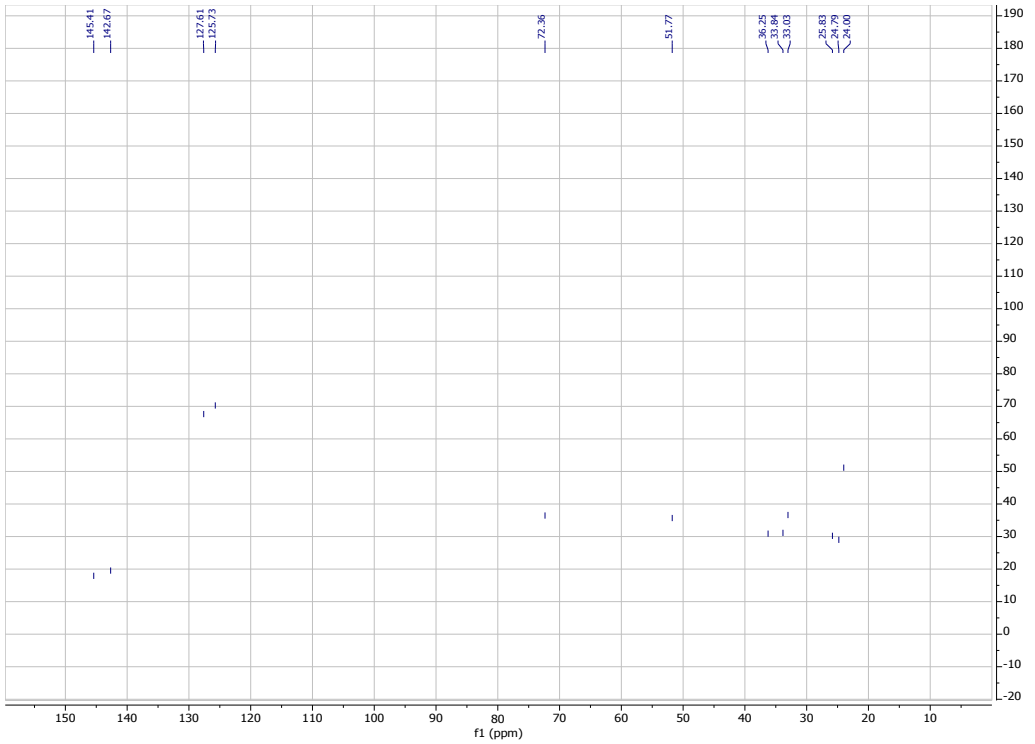
(-)-(*1S,2R*)-2-(p-tolyl)cyclohexan-1-ol (10g)



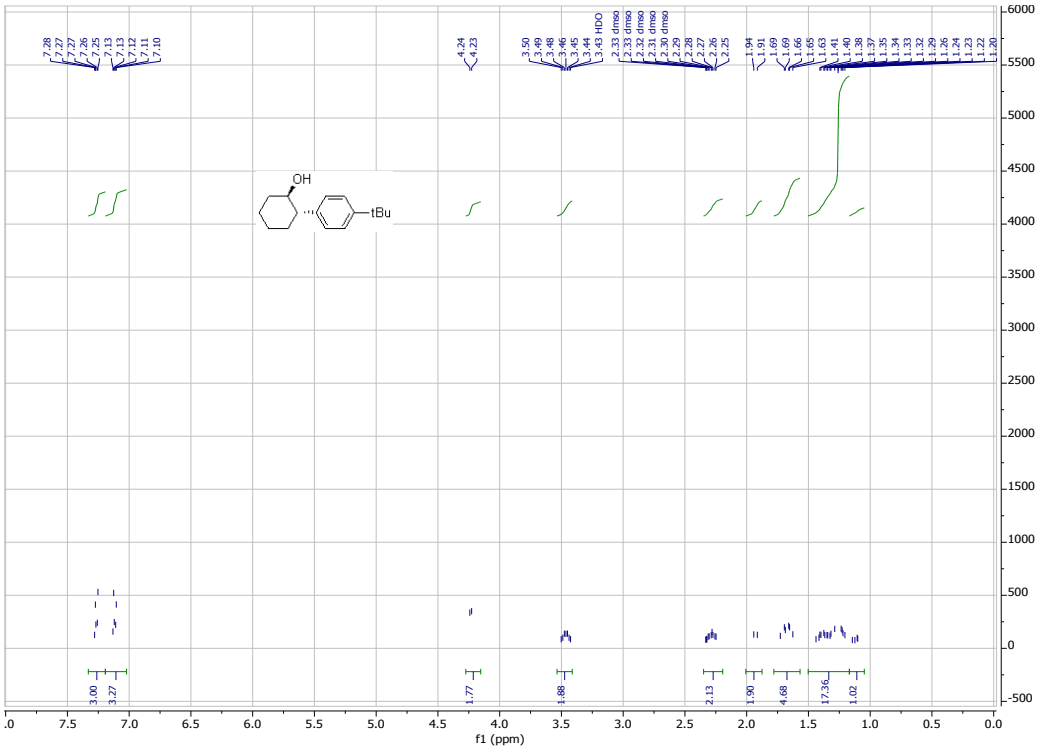


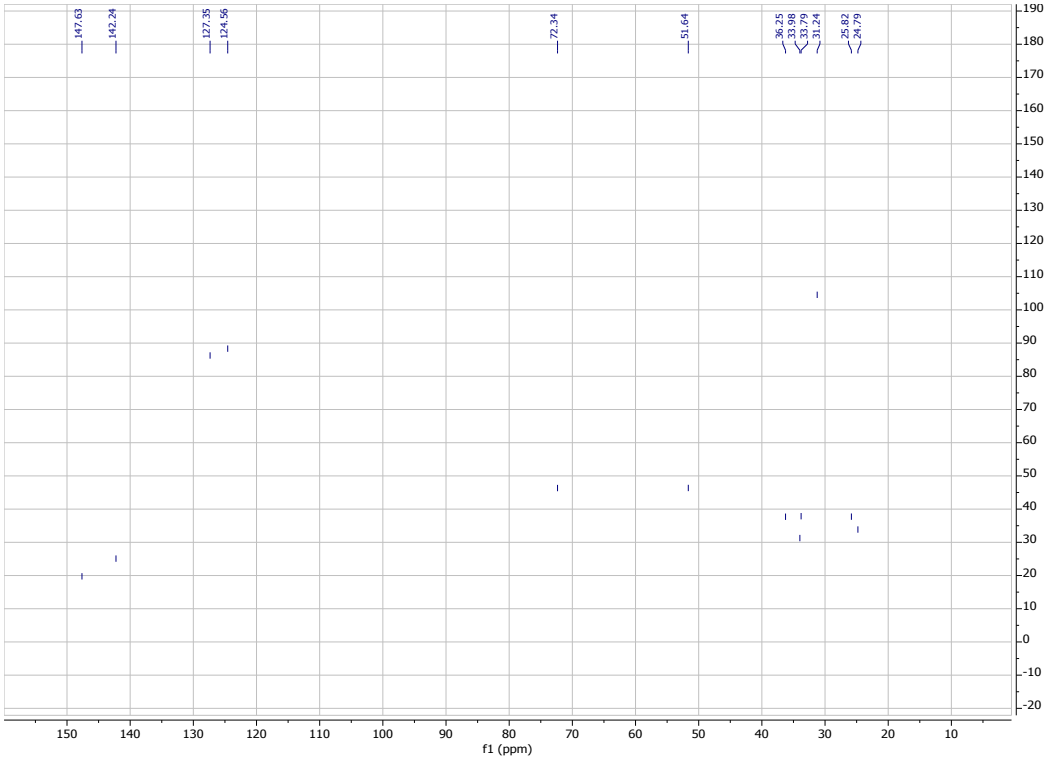
(-)-(*1R,2S*)-2-(4-isopropylphenyl)cyclohexan-1-ol (10h)



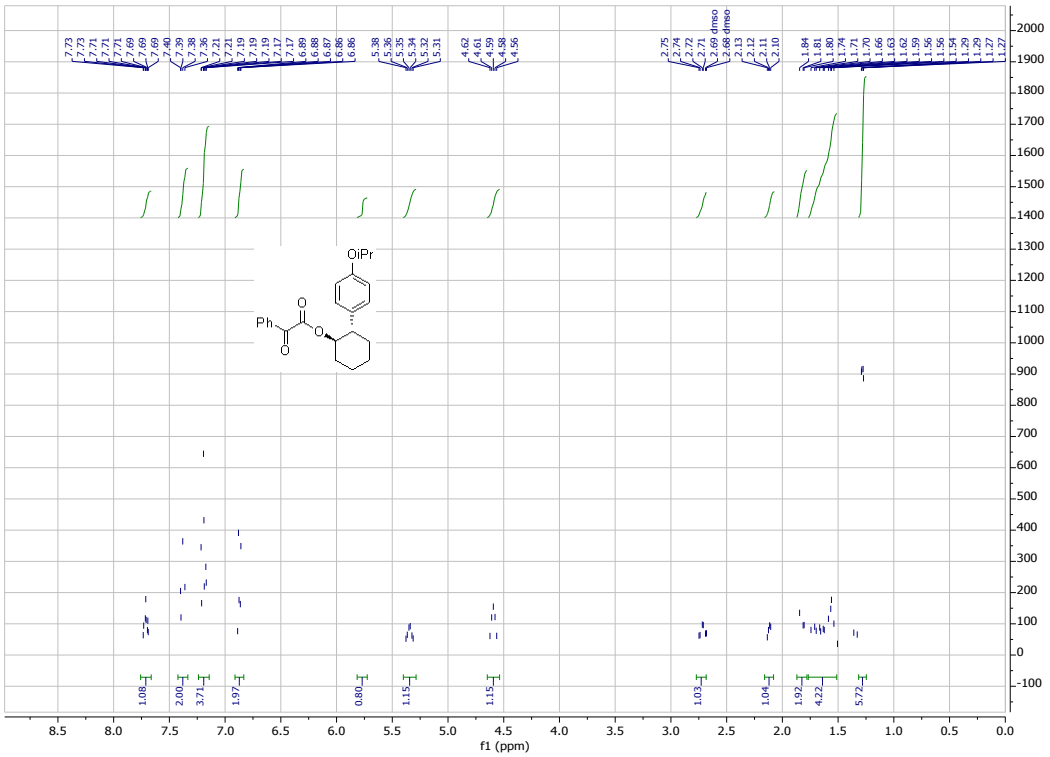


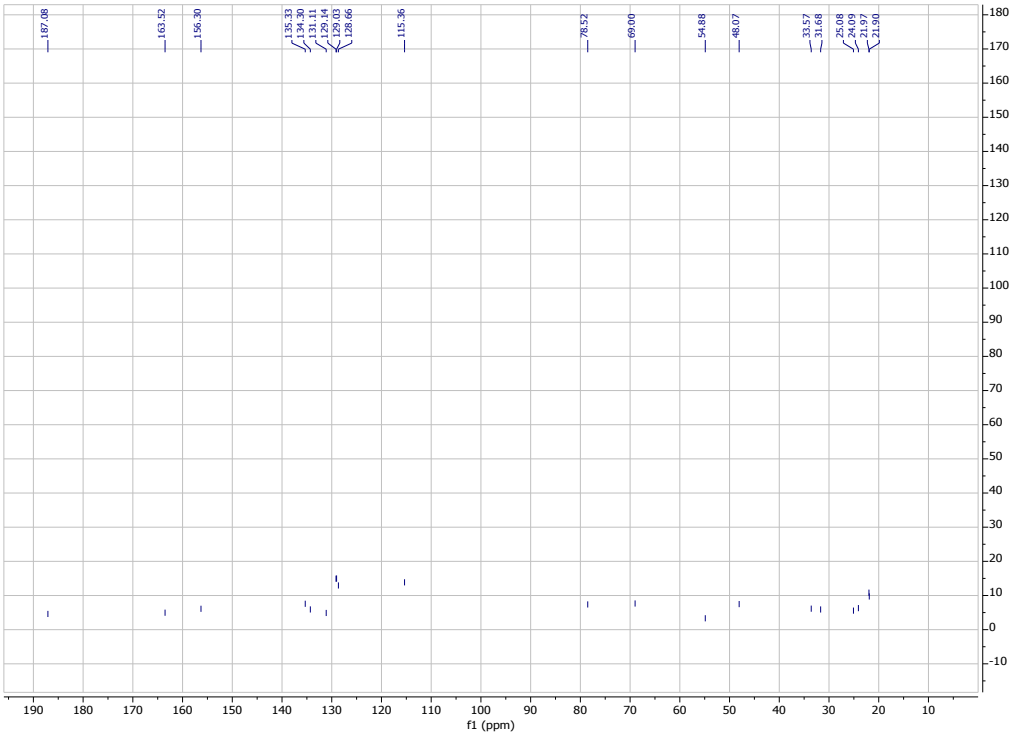
(-)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexan-1-ol (10i)



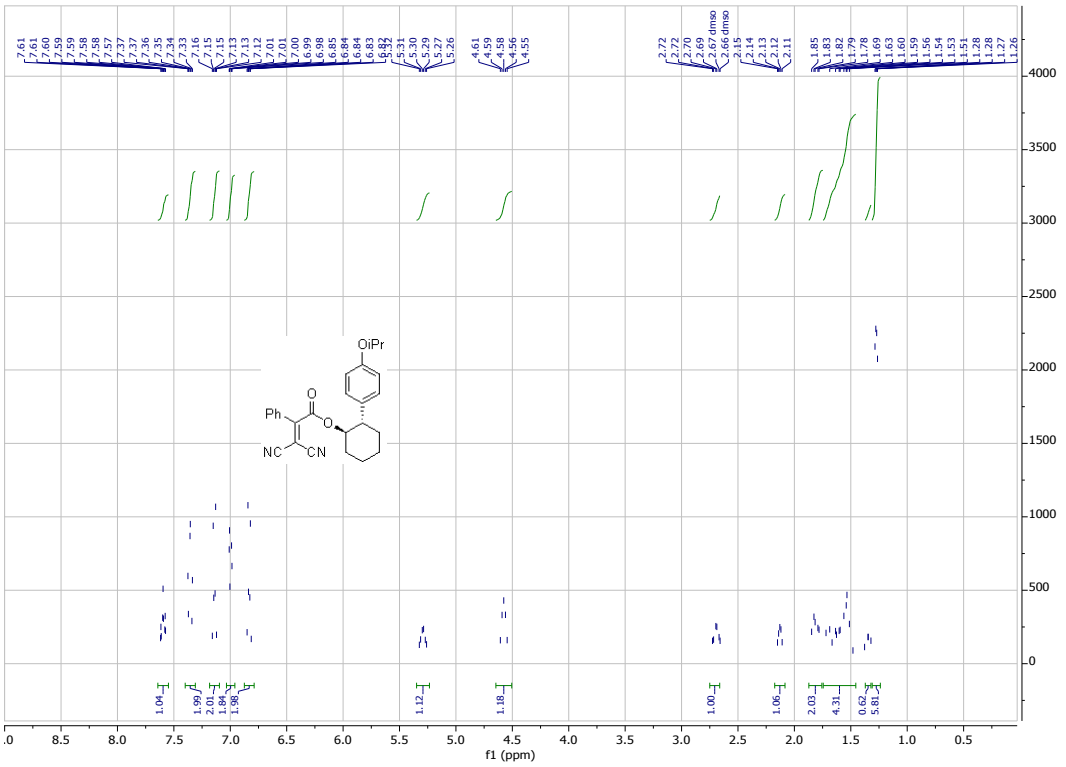


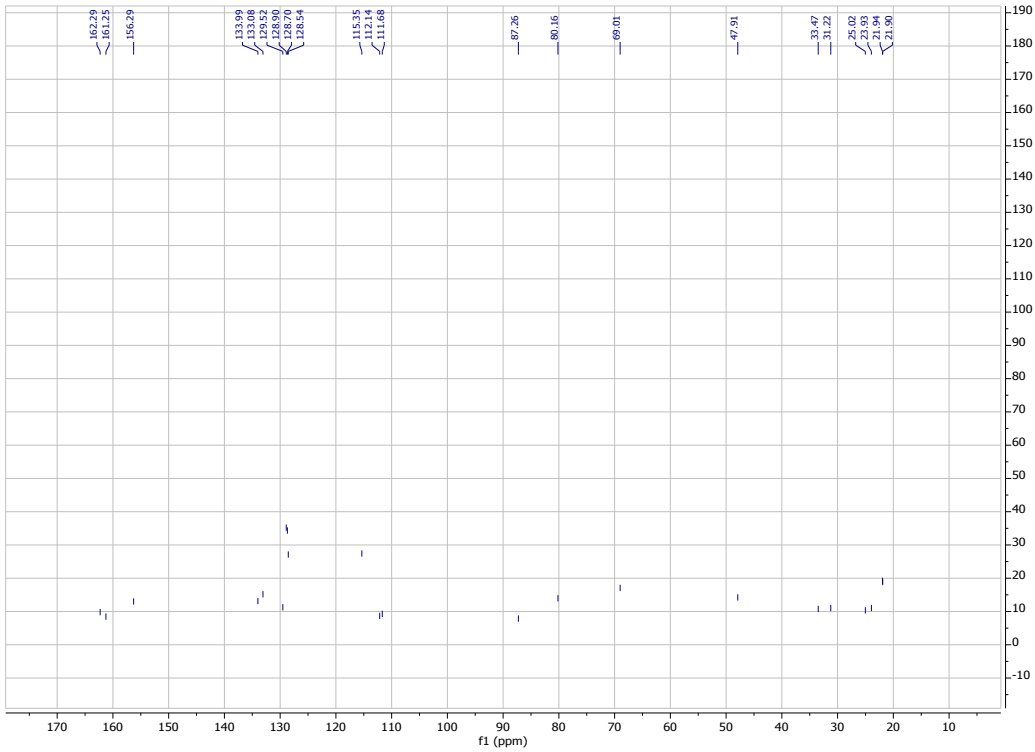
(*1R,2S*)-2-(4-isopropoxyphenyl)cyclohexyl-2-oxo-2-phenylacetate (11a-intermediate)



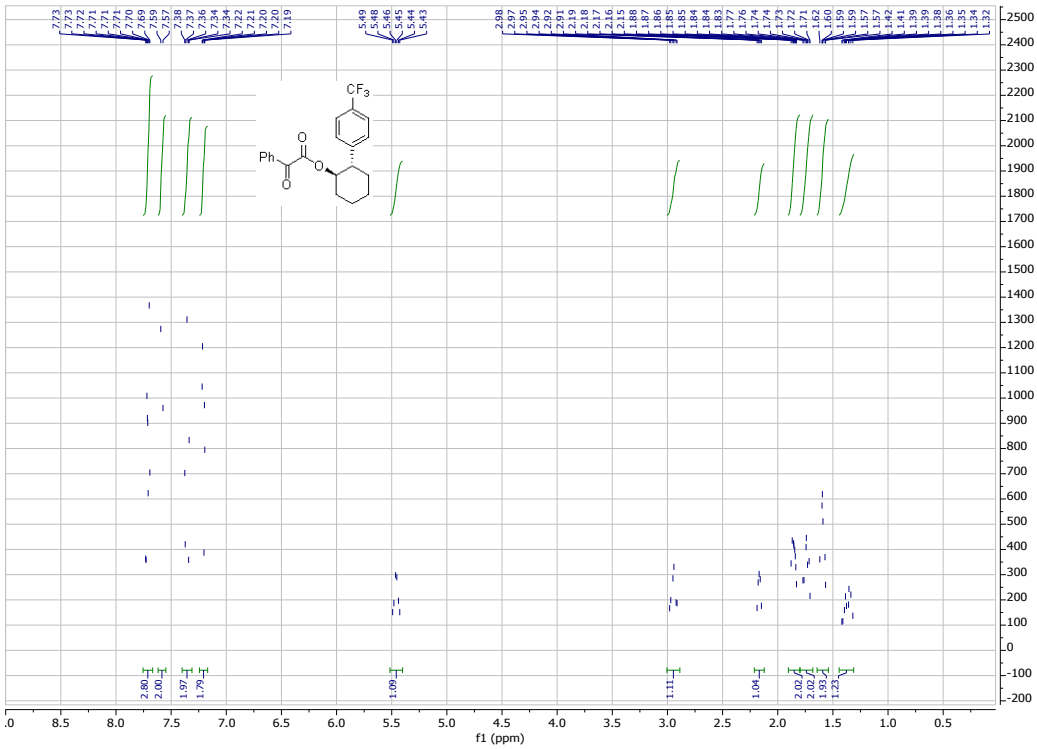


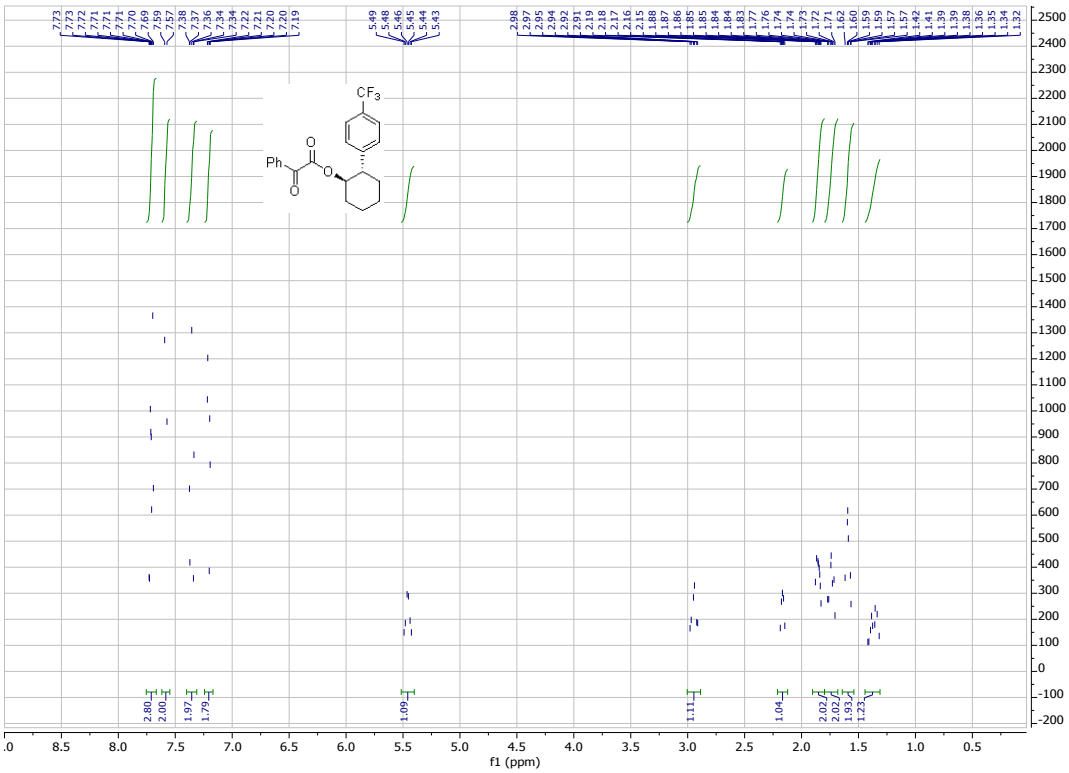
(*1S,2R*)-2-(4-isopropoxyphenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11a)



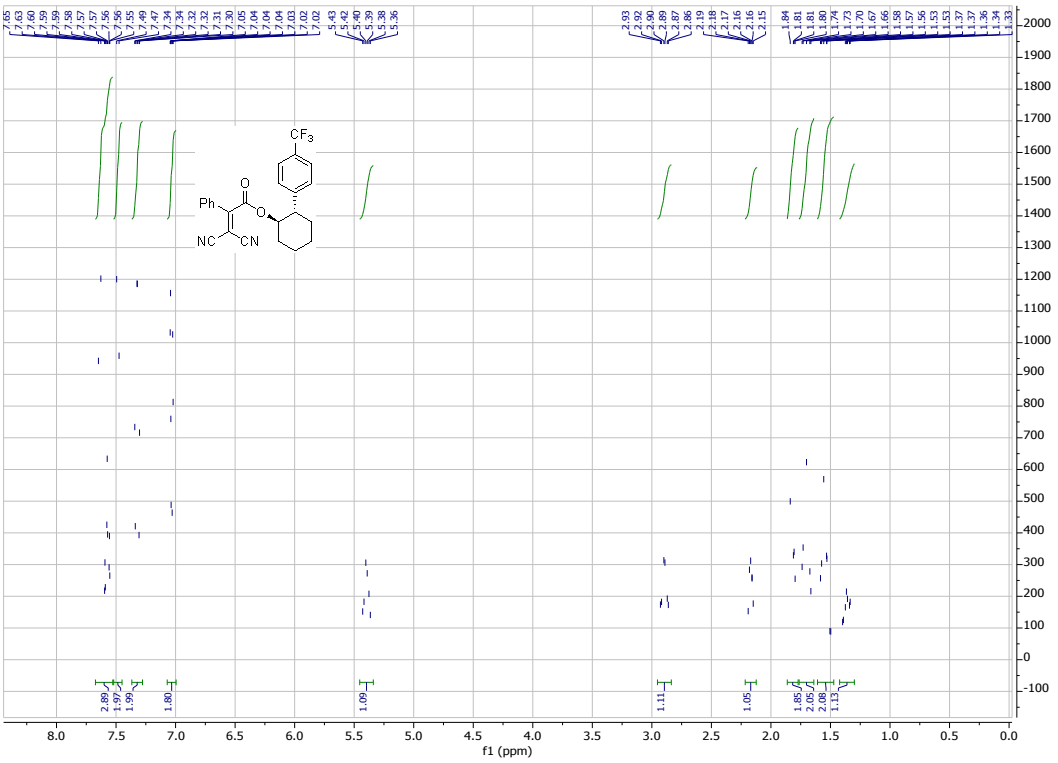


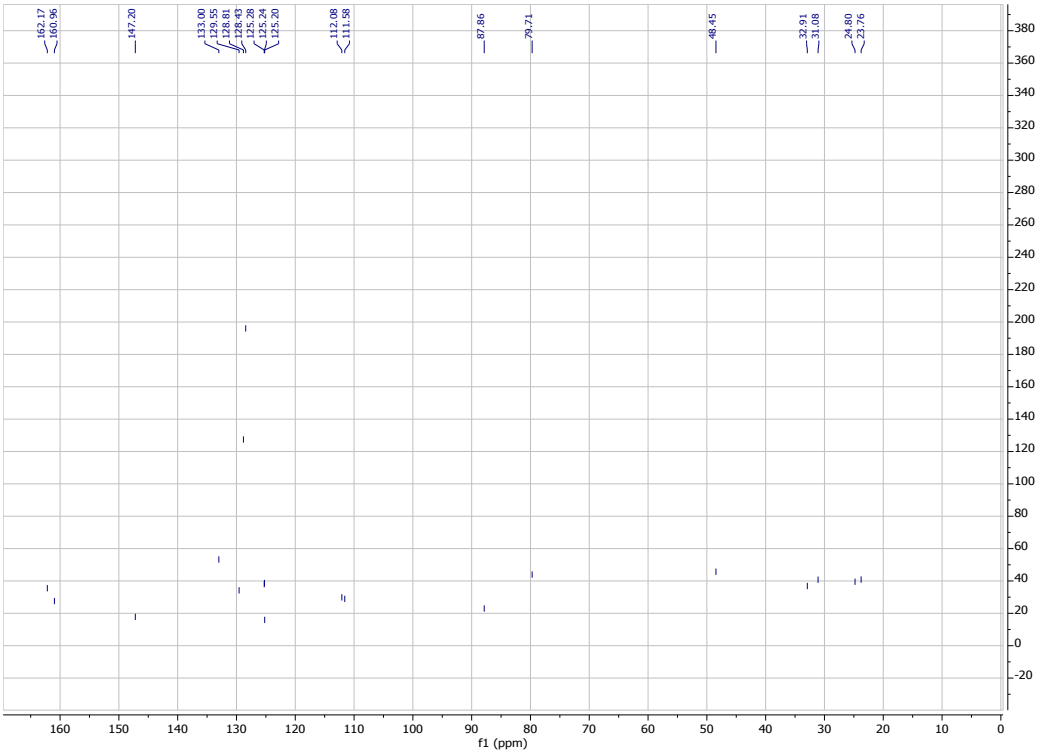
(*1R,2S*)-2-(4-(trifluoromethyl)phenyl)cyclohexyl-2-oxo-2-phenylacetate (11b-intermediate)



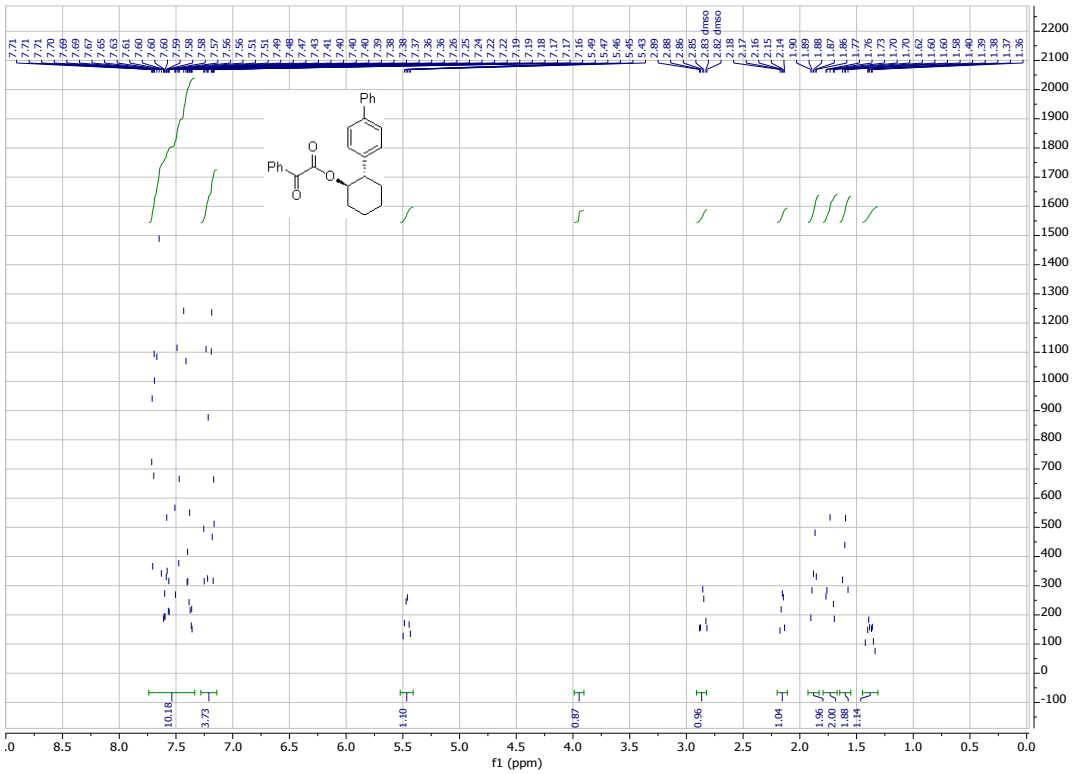


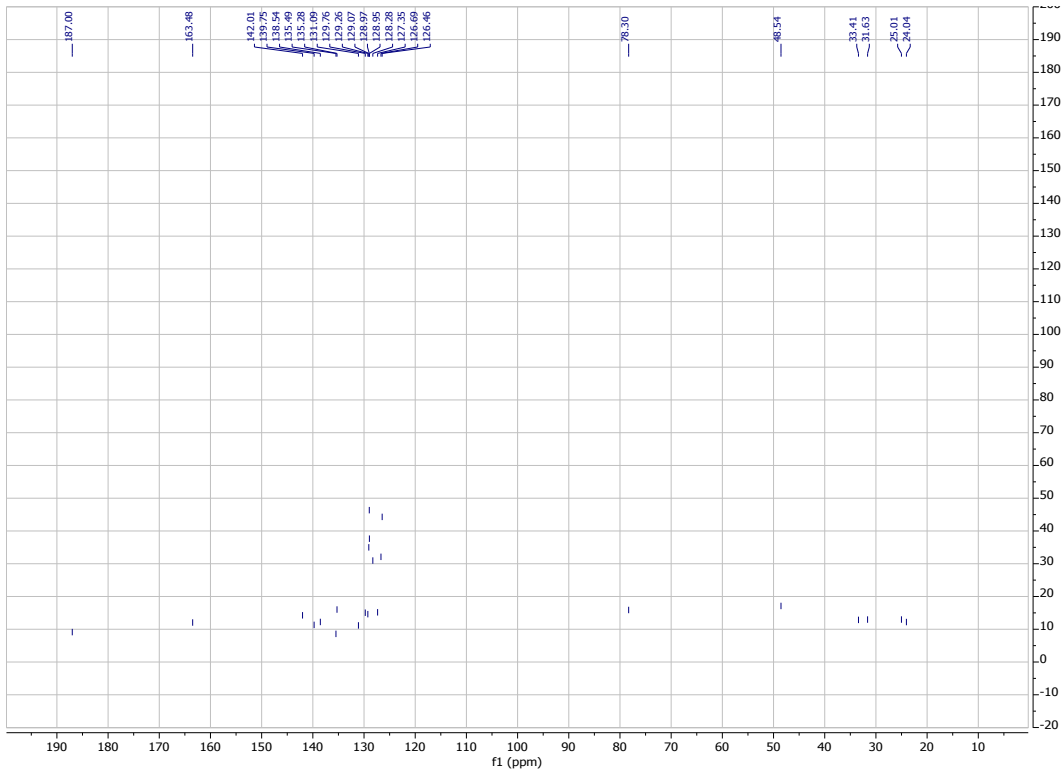
(*1R,2S*)-2-(4-(trifluoromethyl)phenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11b)



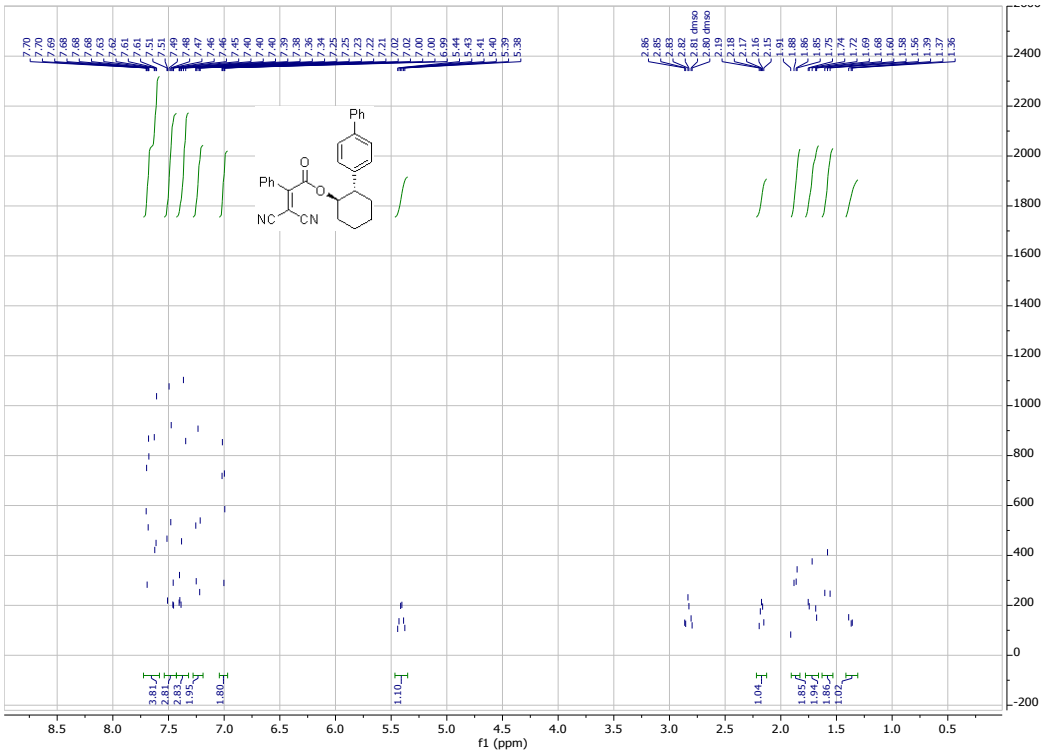


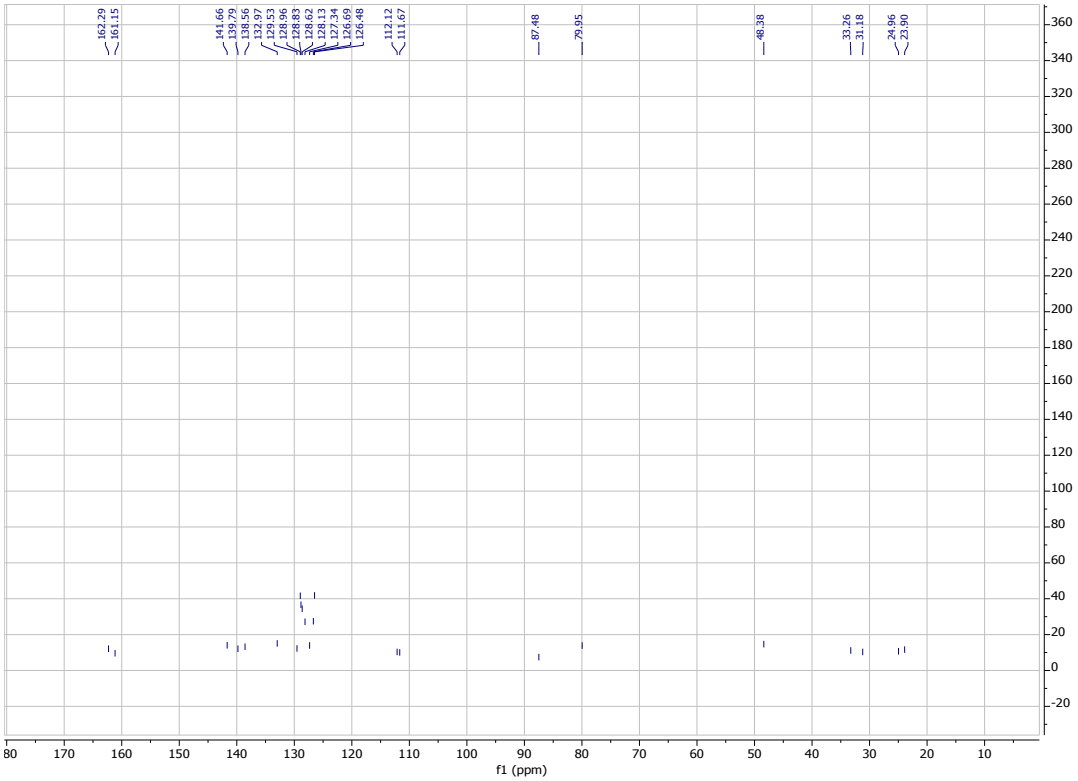
(*1R,2S*)-2-([1,1'-biphenyl]-4-yl)cyclohexyl-2-oxo-2-phenylacetate (11c-intermediate)



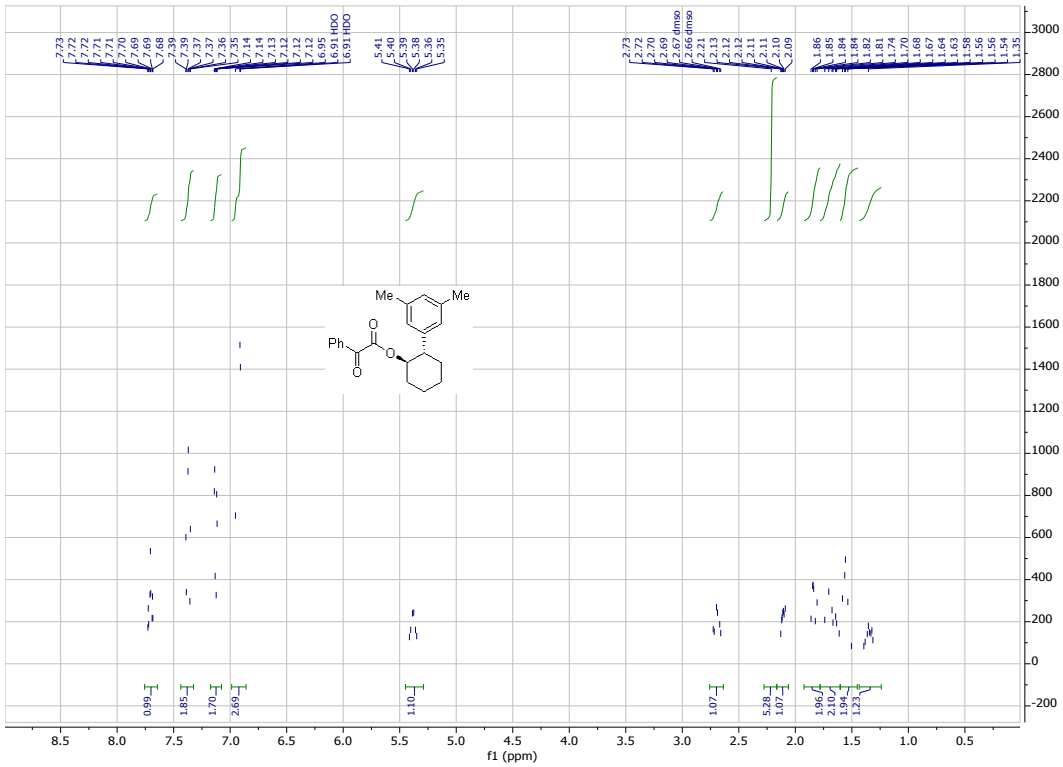


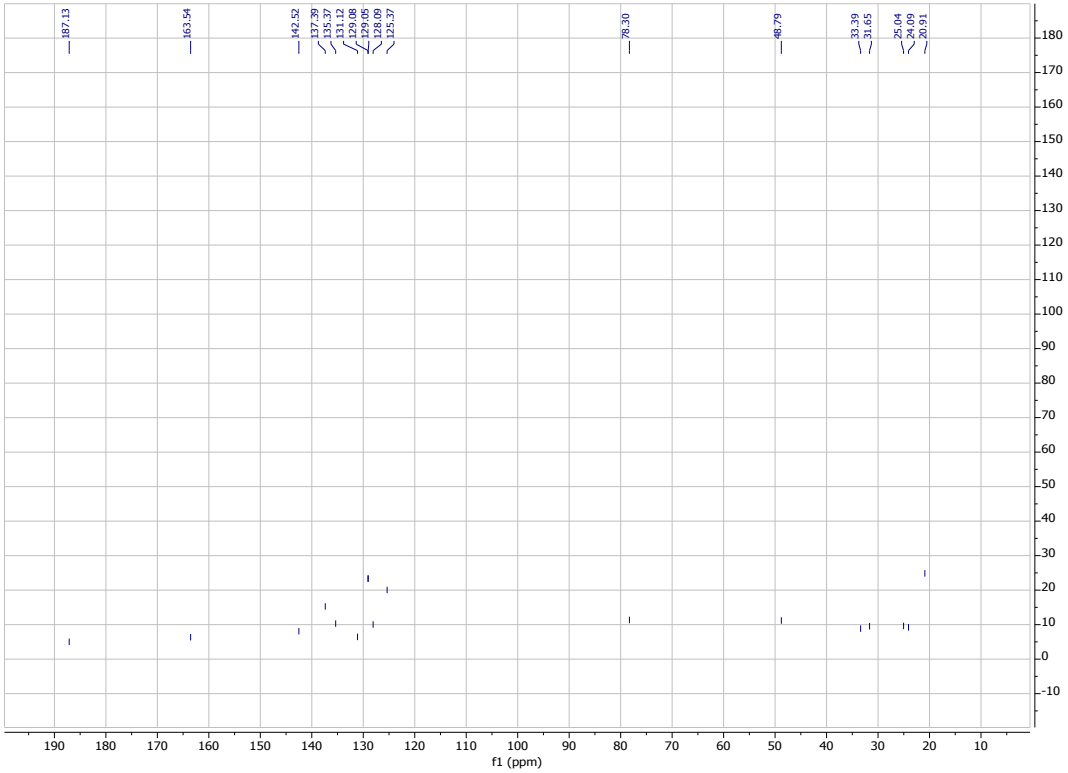
(*1R,2S*)-2-([1,1'-biphenyl]-4-yl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11c)



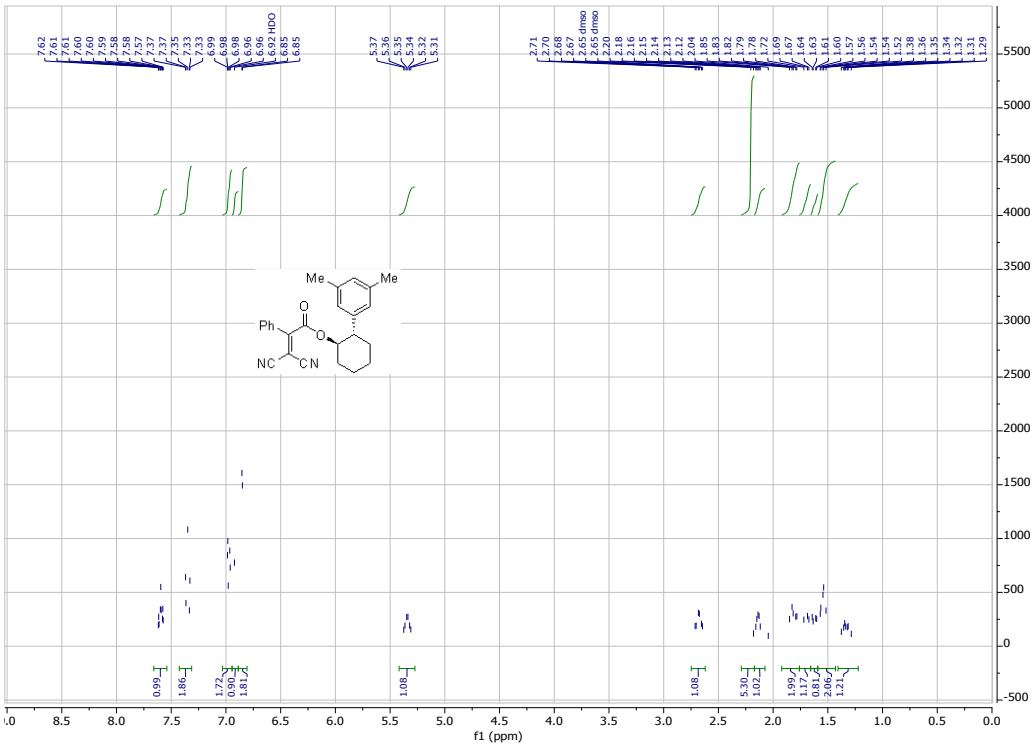


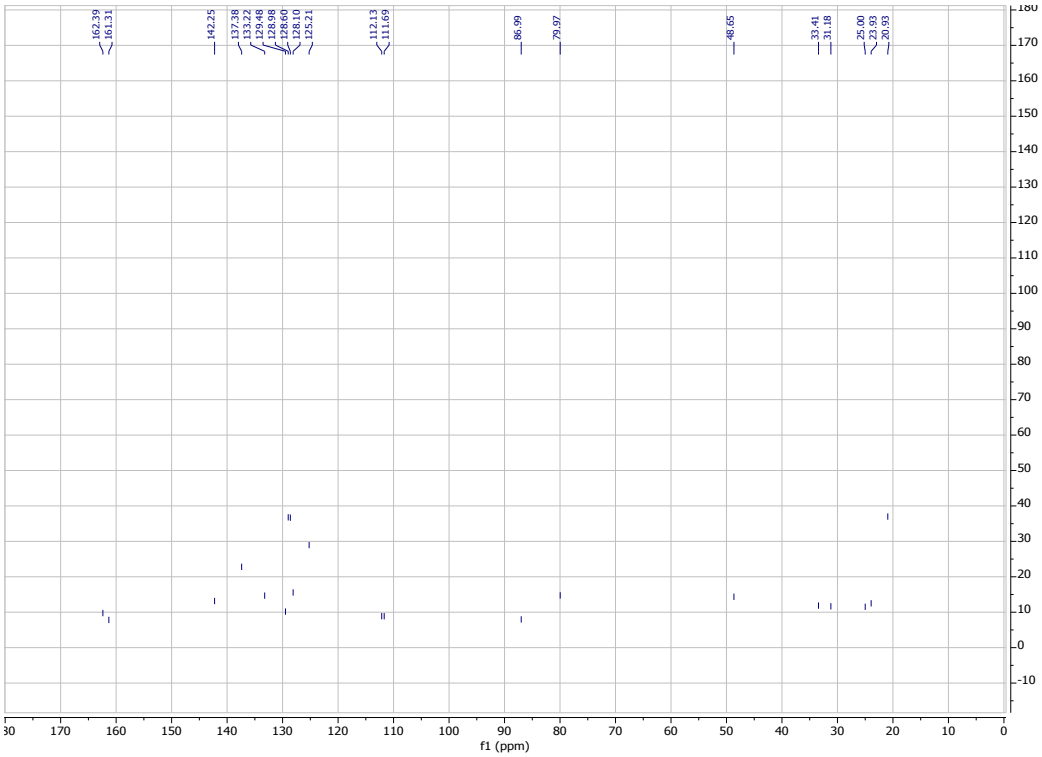
(*1R,2S*)-2-(3,5-dimethylphenyl)cyclohexyl-2-oxo-2-phenylacetate (11d-intermediate)



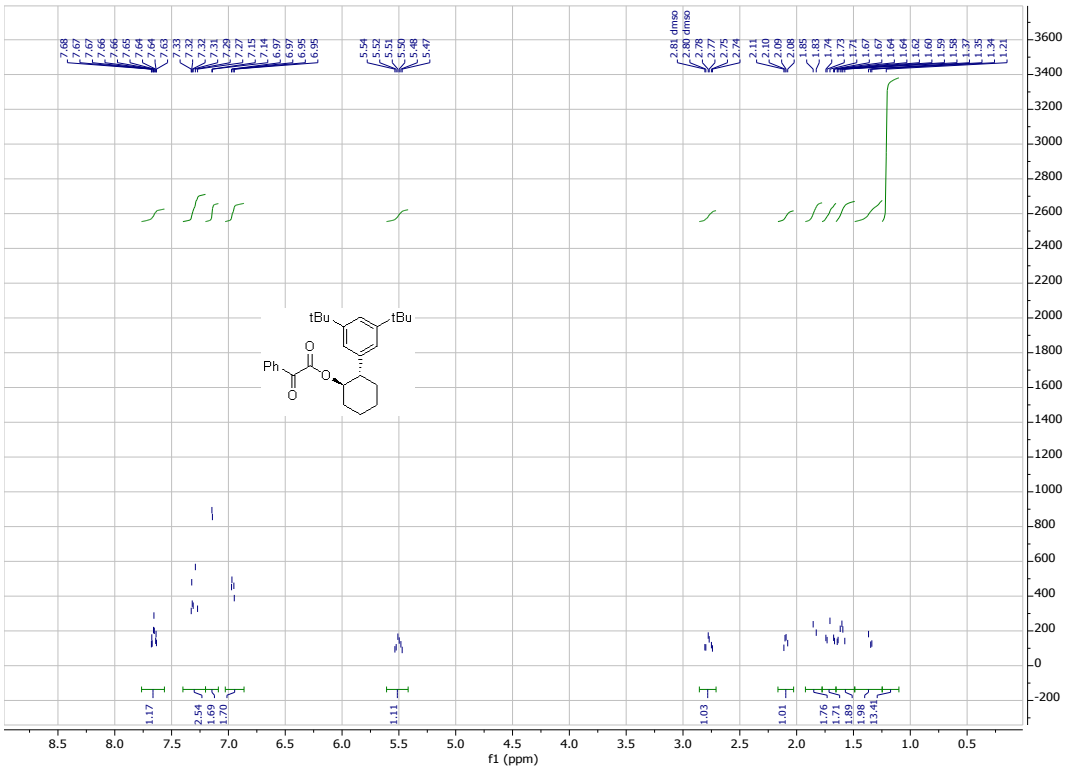


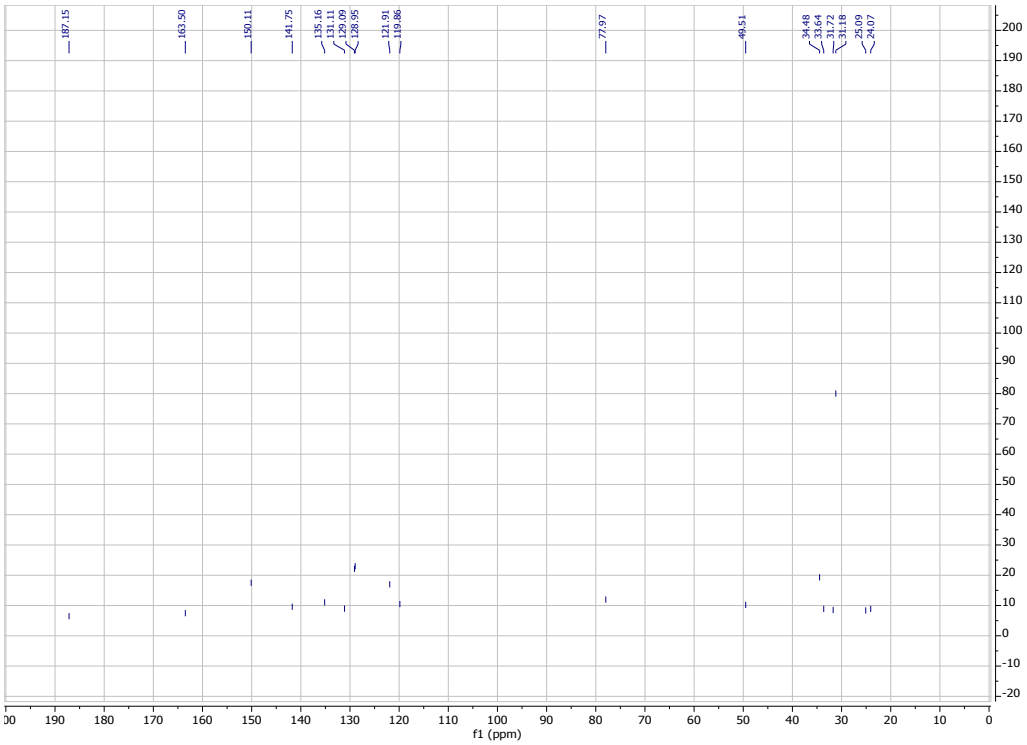
(*1R,2S*)-2-(3,5-dimethylphenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11d)



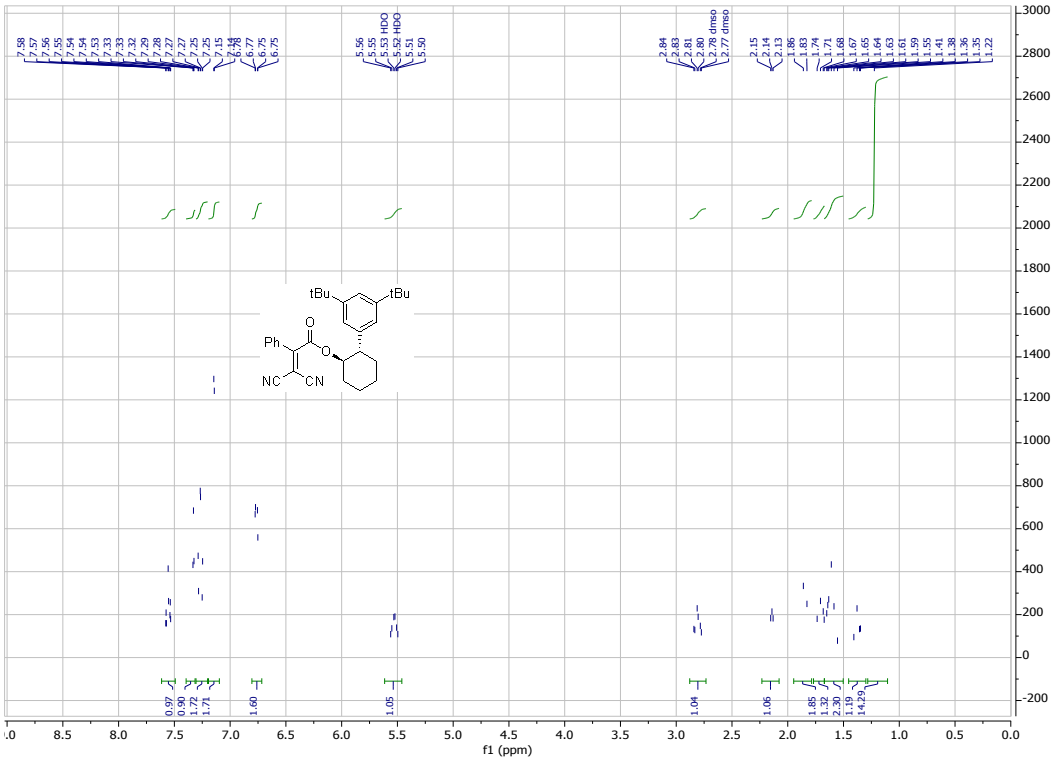


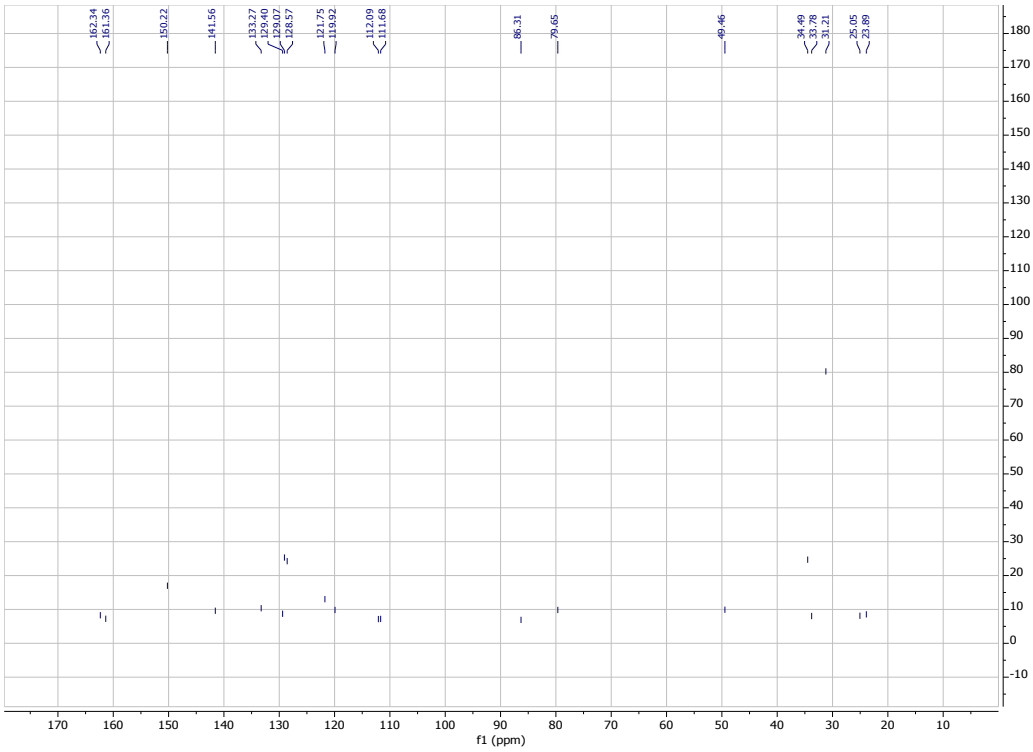
(*1R,2S*)-2-(3,5-di-tert-butylphenyl)cyclohexyl-2-oxo-2-phenylacetate (11e-intermediate)



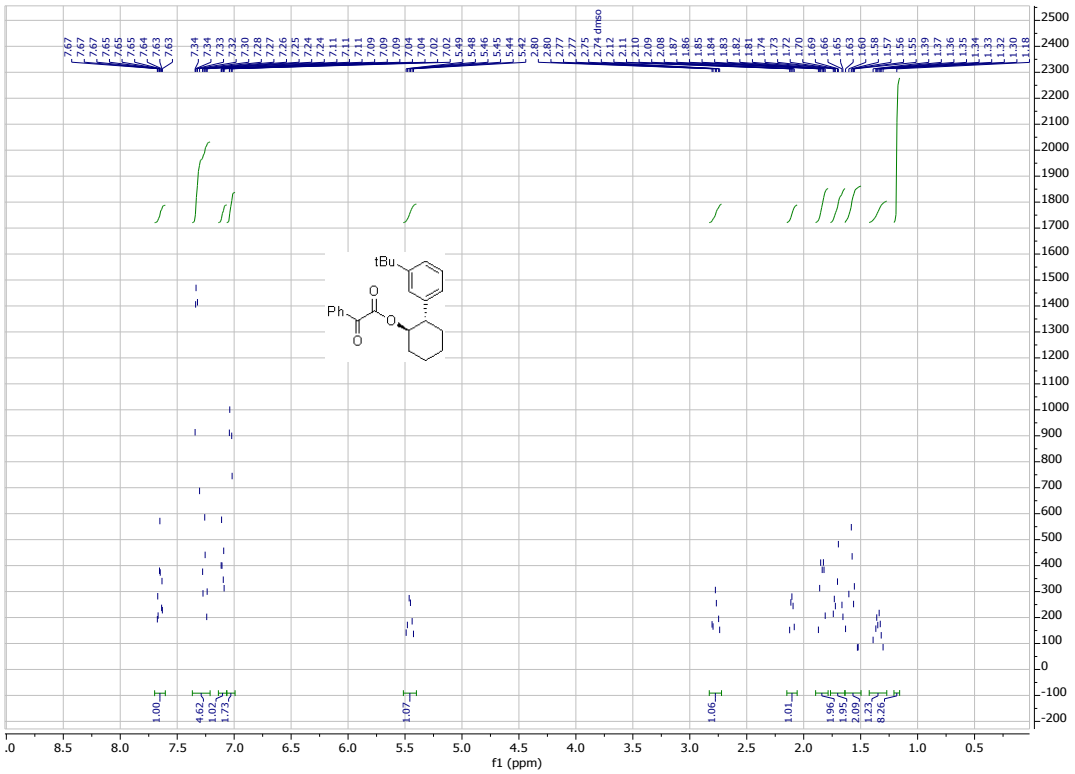


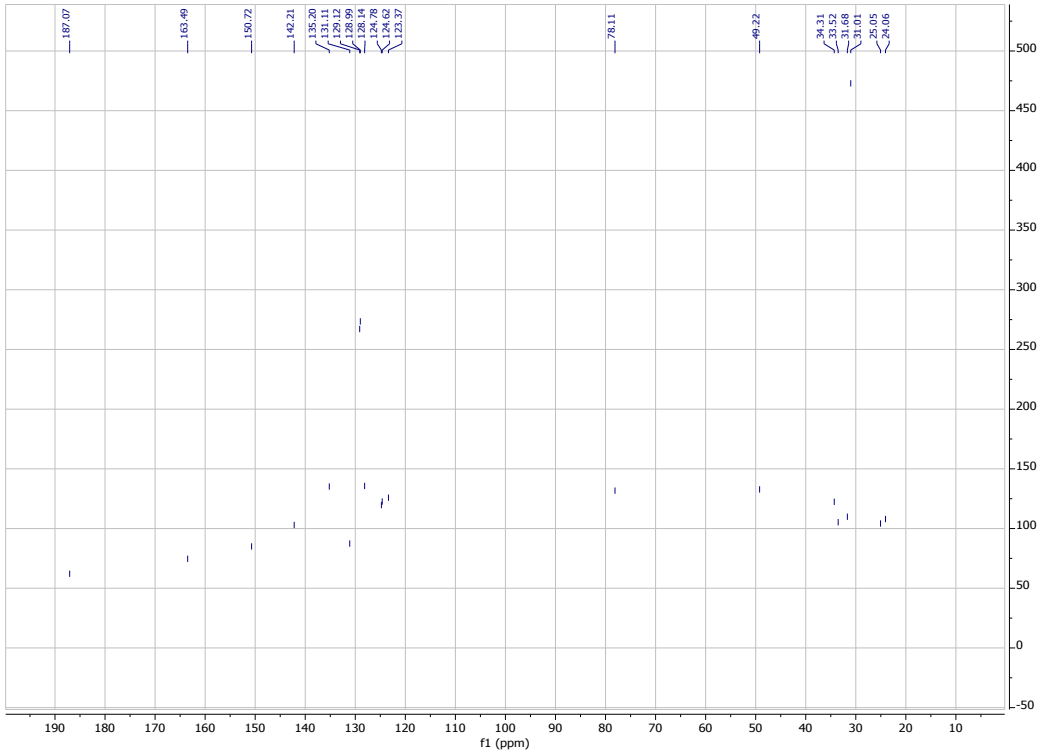
(*1R,2S*)-2-(3,5-di-tert-butylphenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11e)



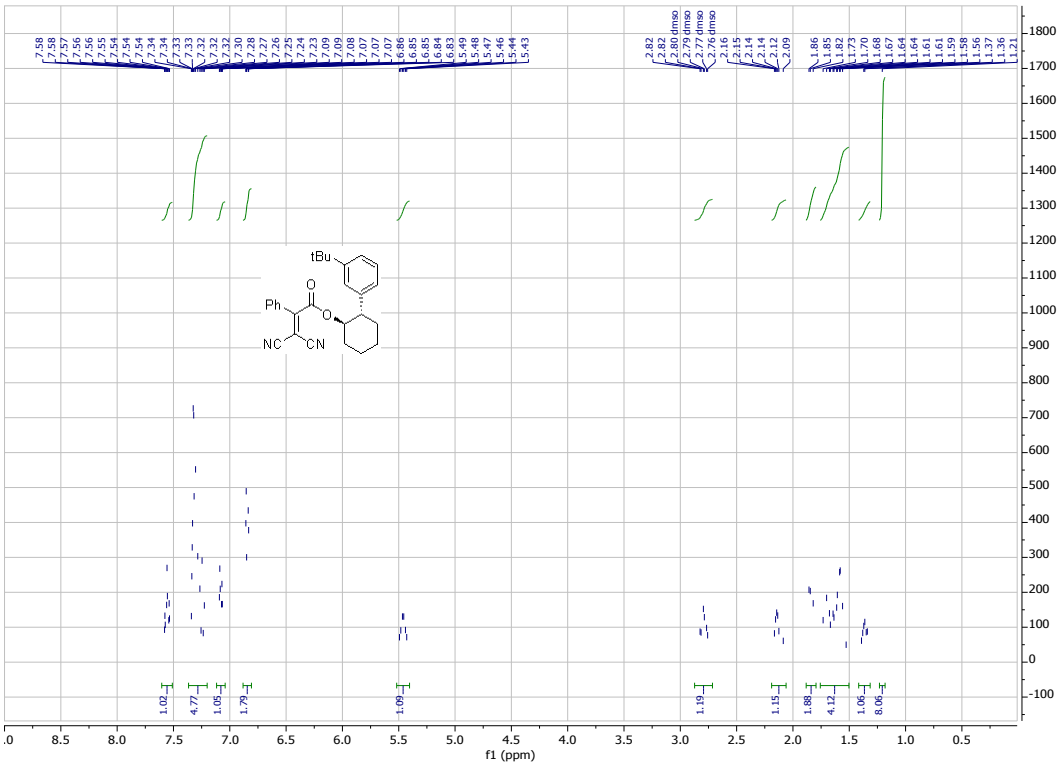


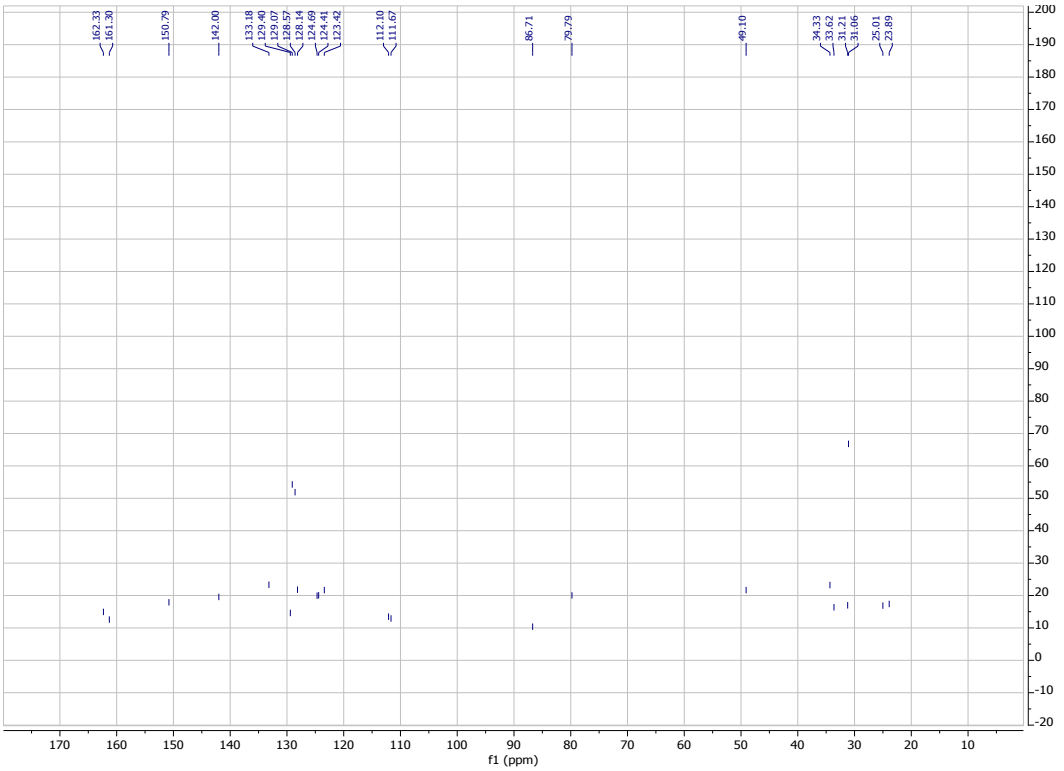
(*1R,2S*)-2-(3-(tert-butyl)phenyl)cyclohexyl-2-oxo-2-phenylacetate (11f-intermediate)



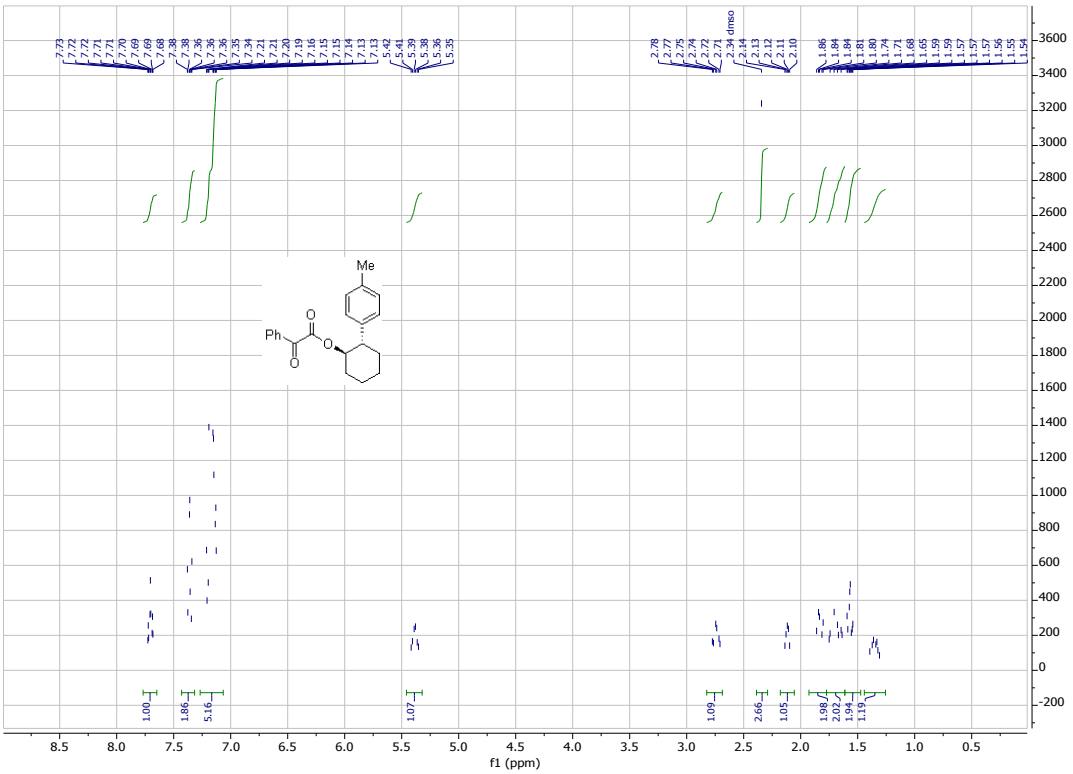


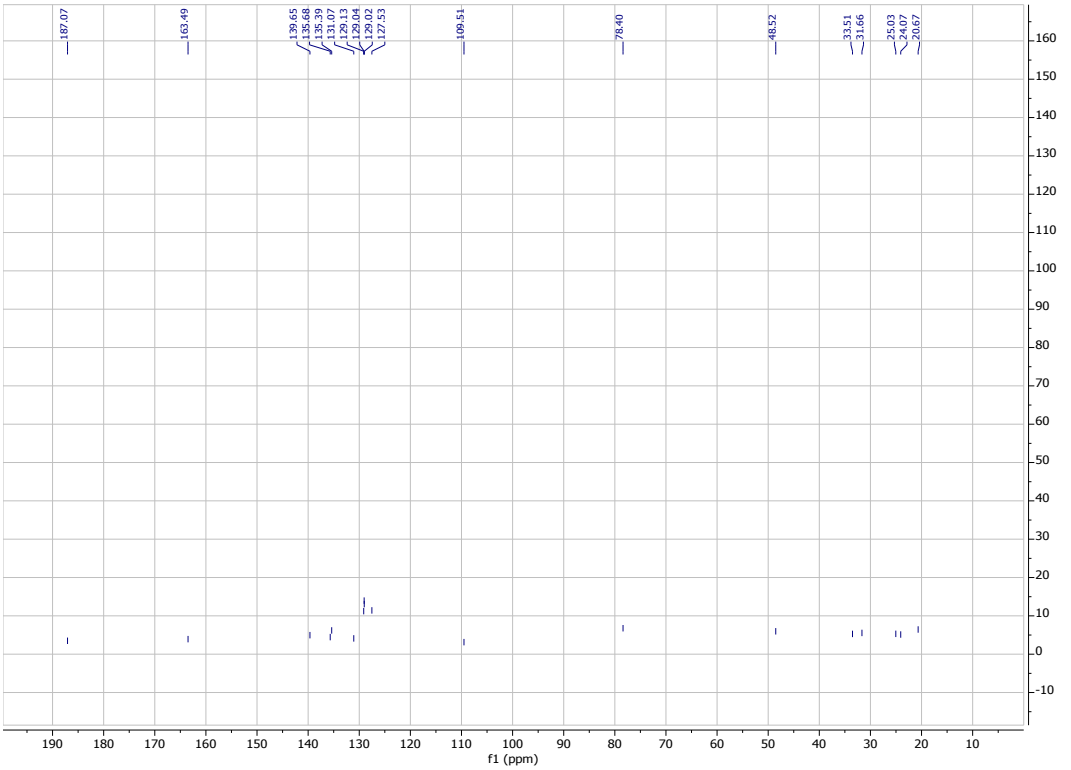
(*1R,2S*)-2-(3-(tert-butyl)phenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11f)



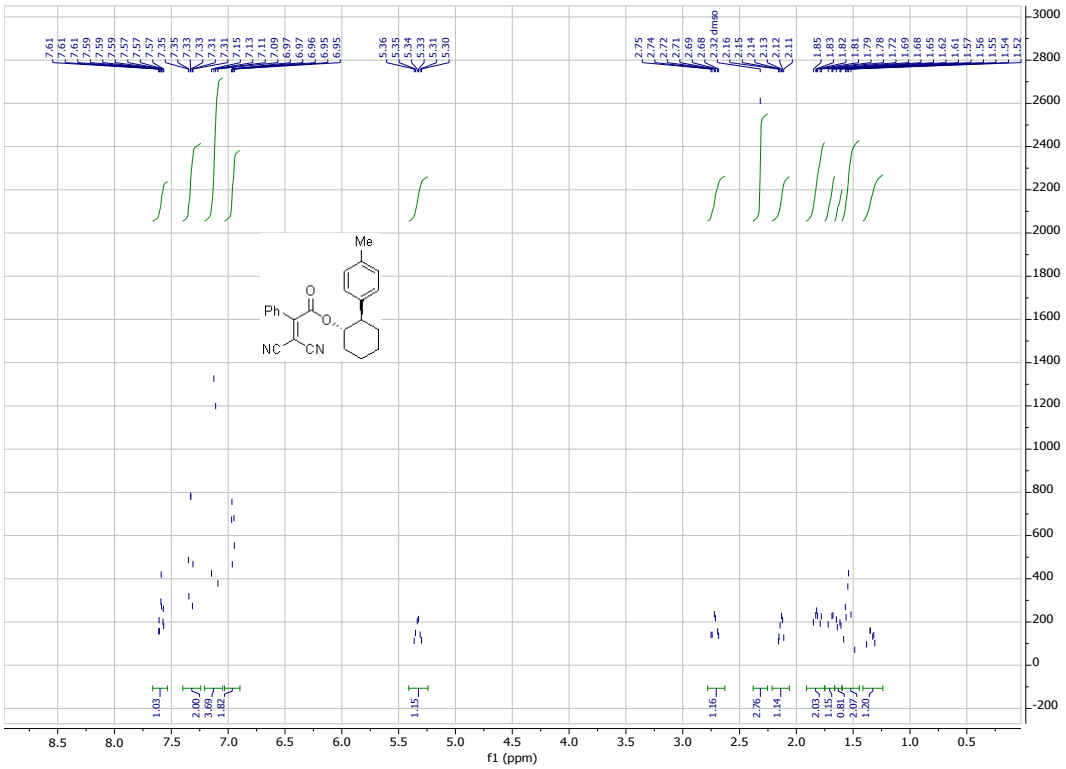


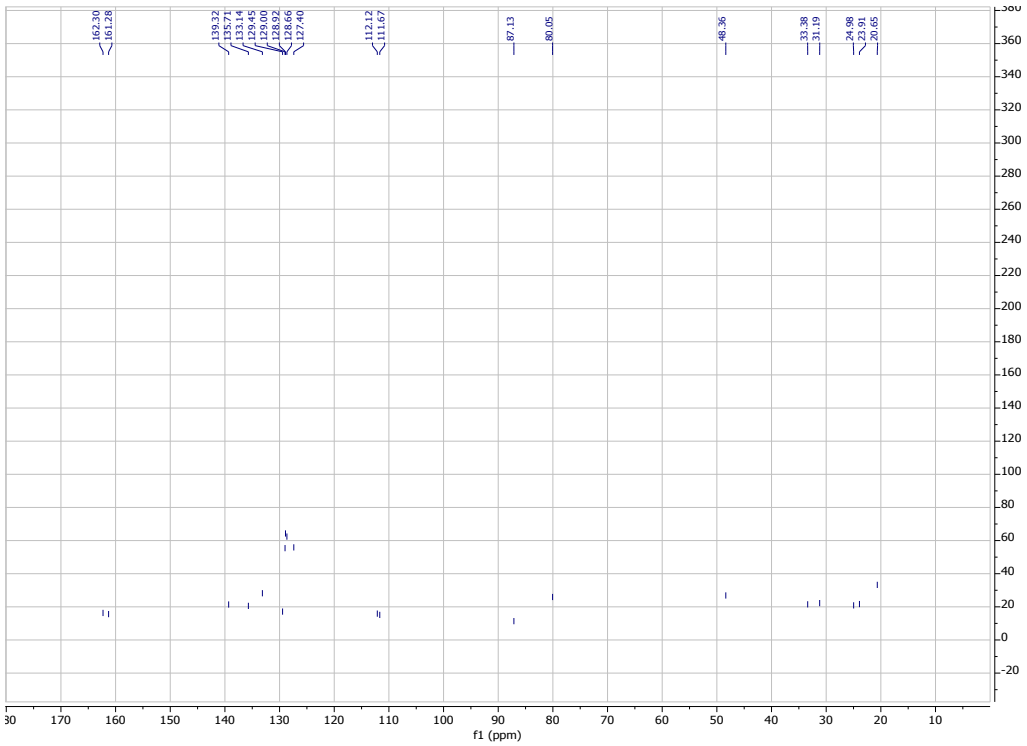
(*1R,2S*)-2-(p-tolyl)cyclohexyl-2-oxo-2-phenylacetate (11g-intermediate)



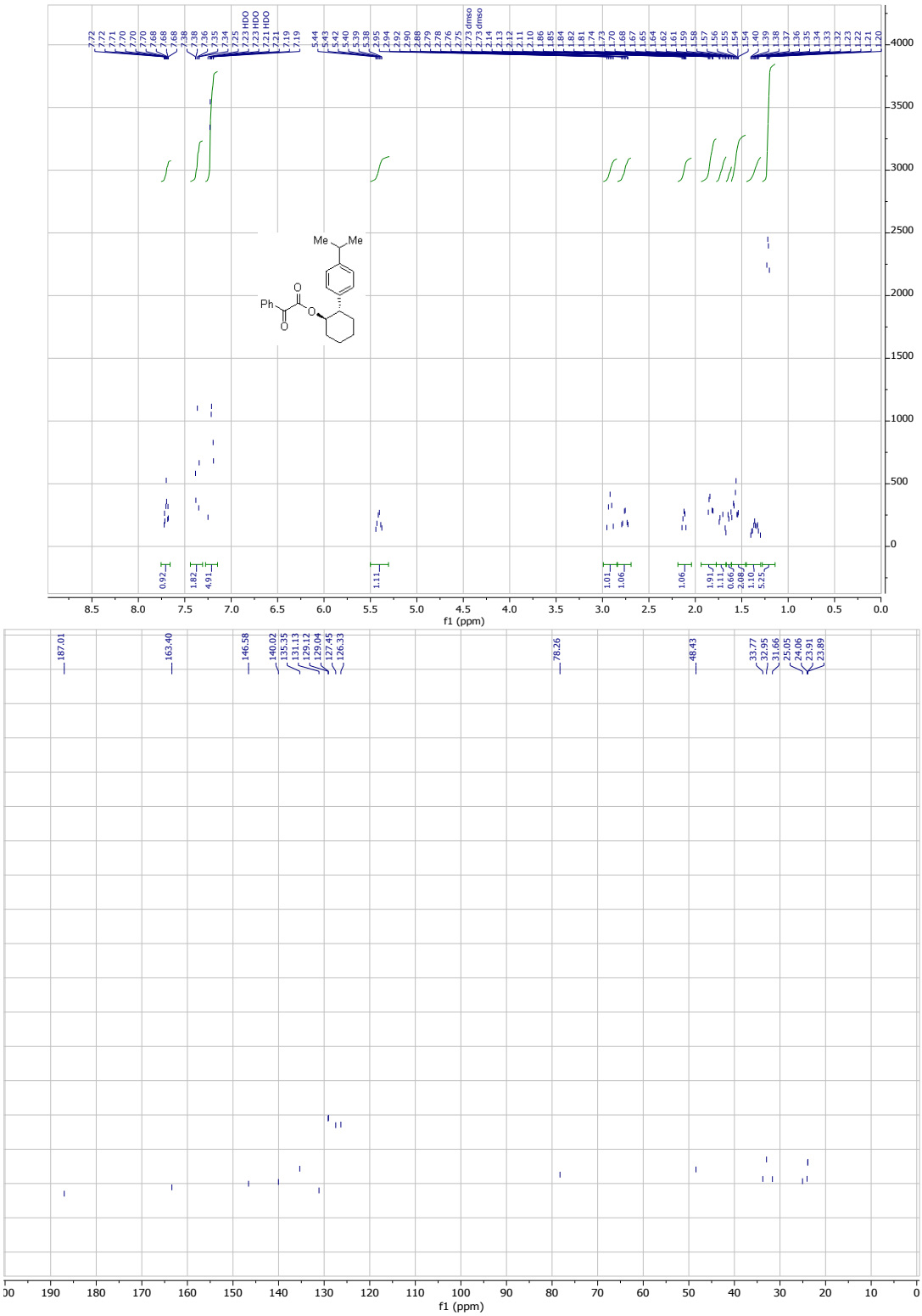


(*1S,2R*)-2-(p-tolyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11g)

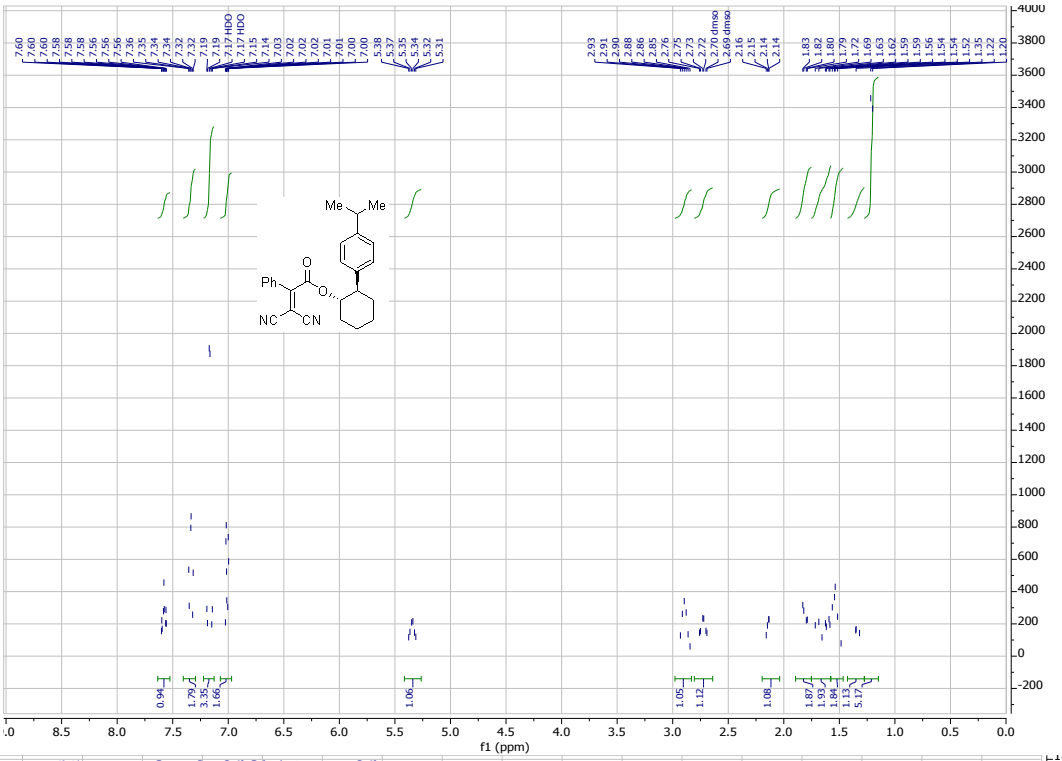


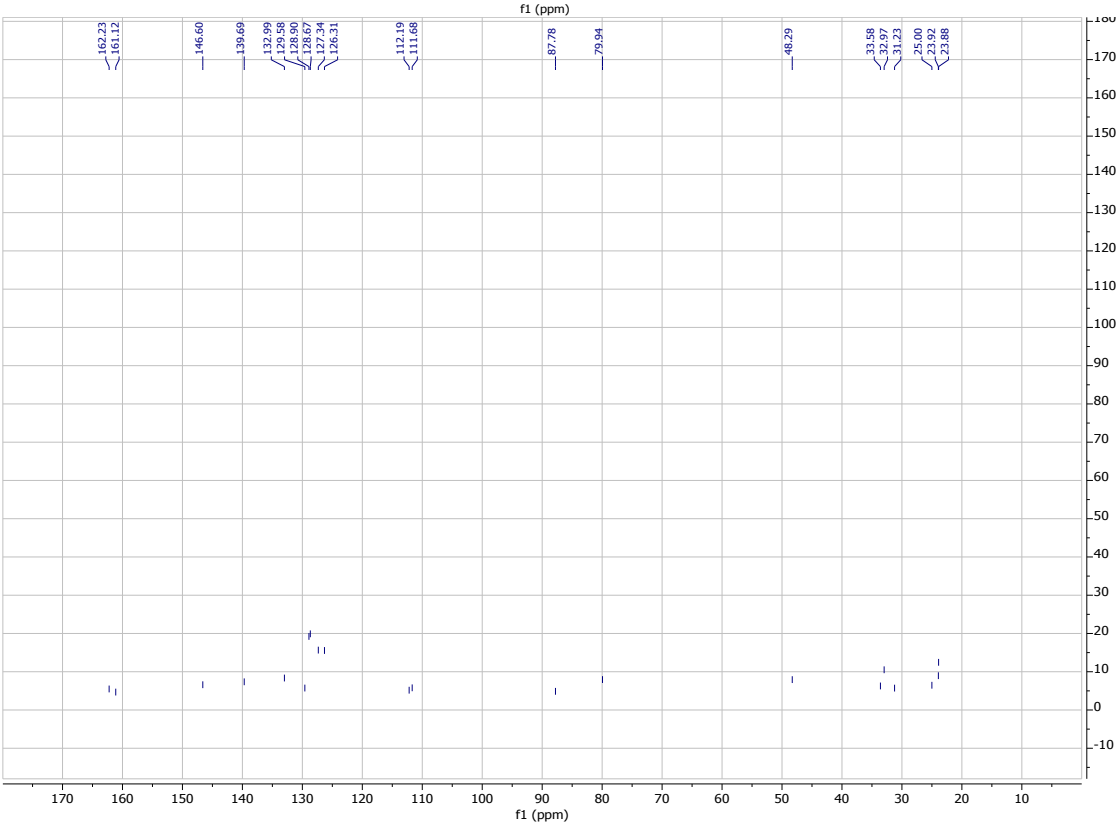


(*1R,2S*)-2-(4-isopropylphenyl)cyclohexyl-2-oxo-2-phenylacetate (11h-intermediate)

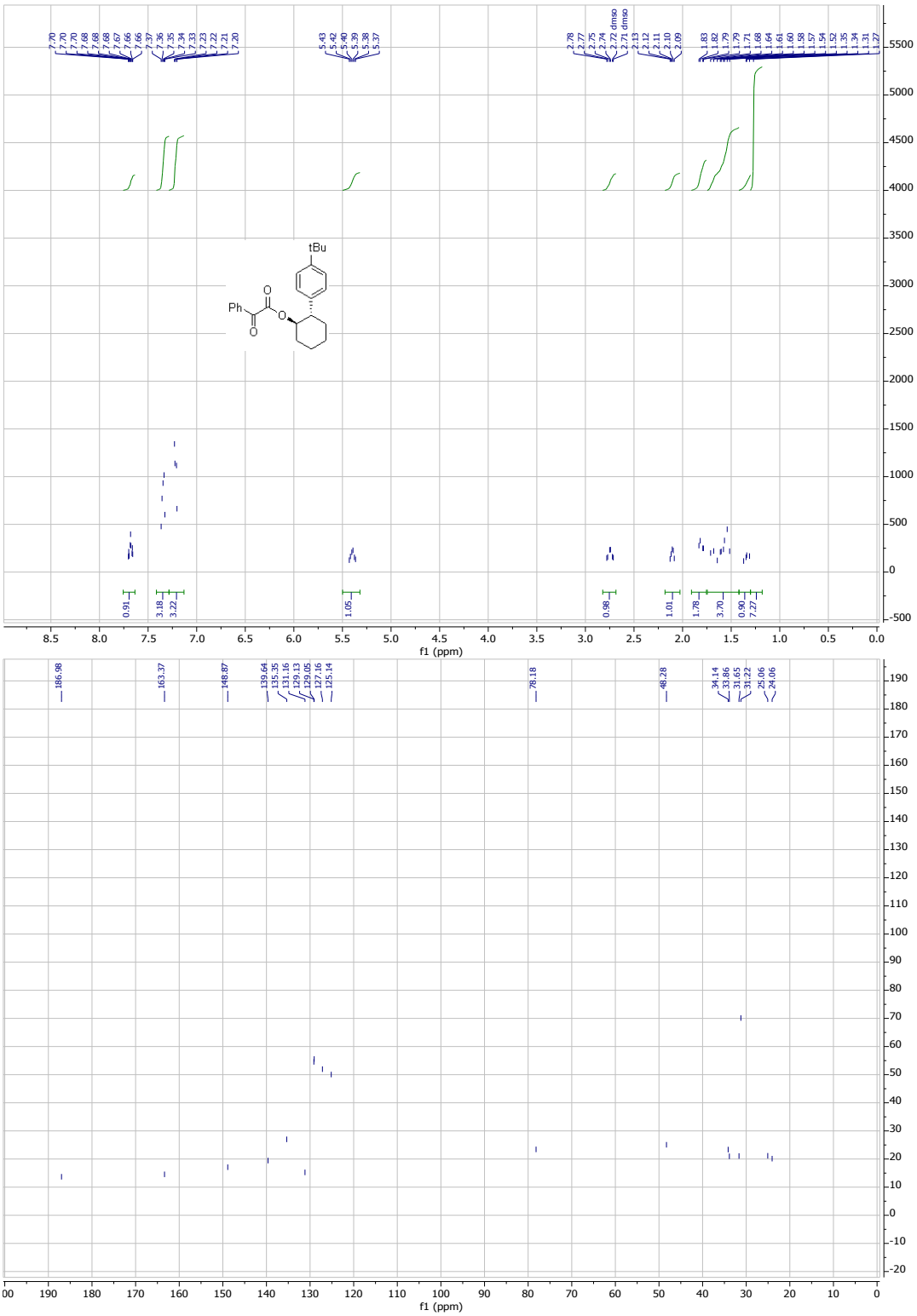


(*1S,2R*)-2-(4-isopropylphenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11h)

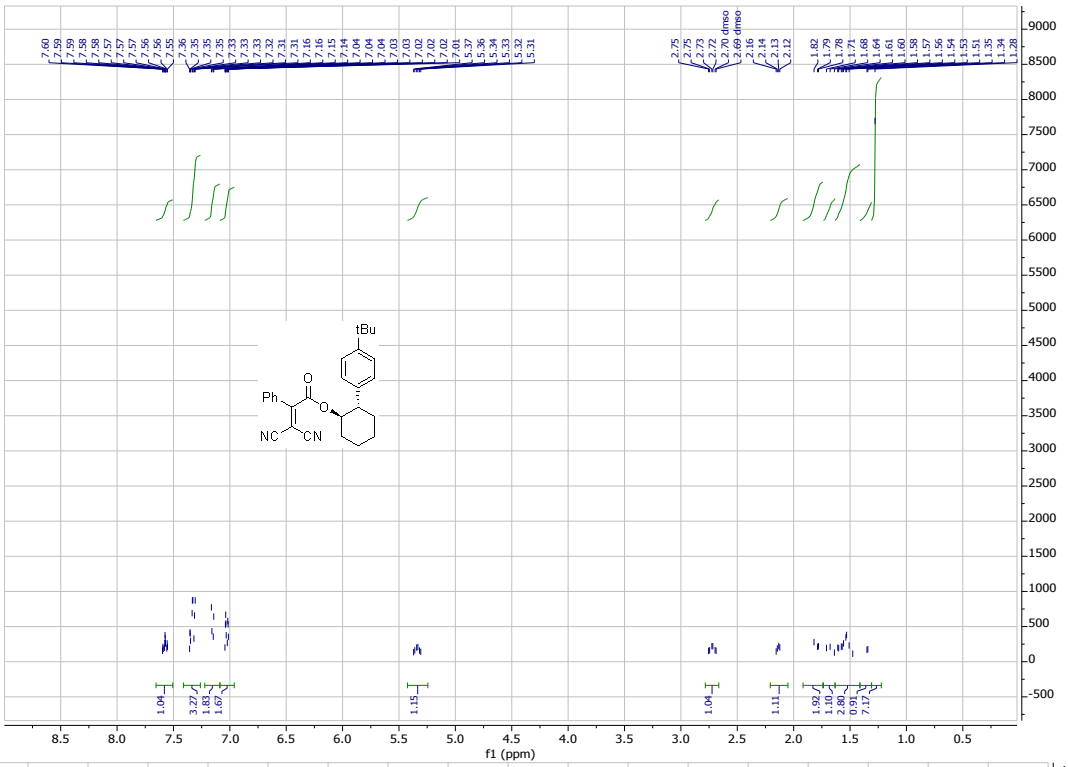


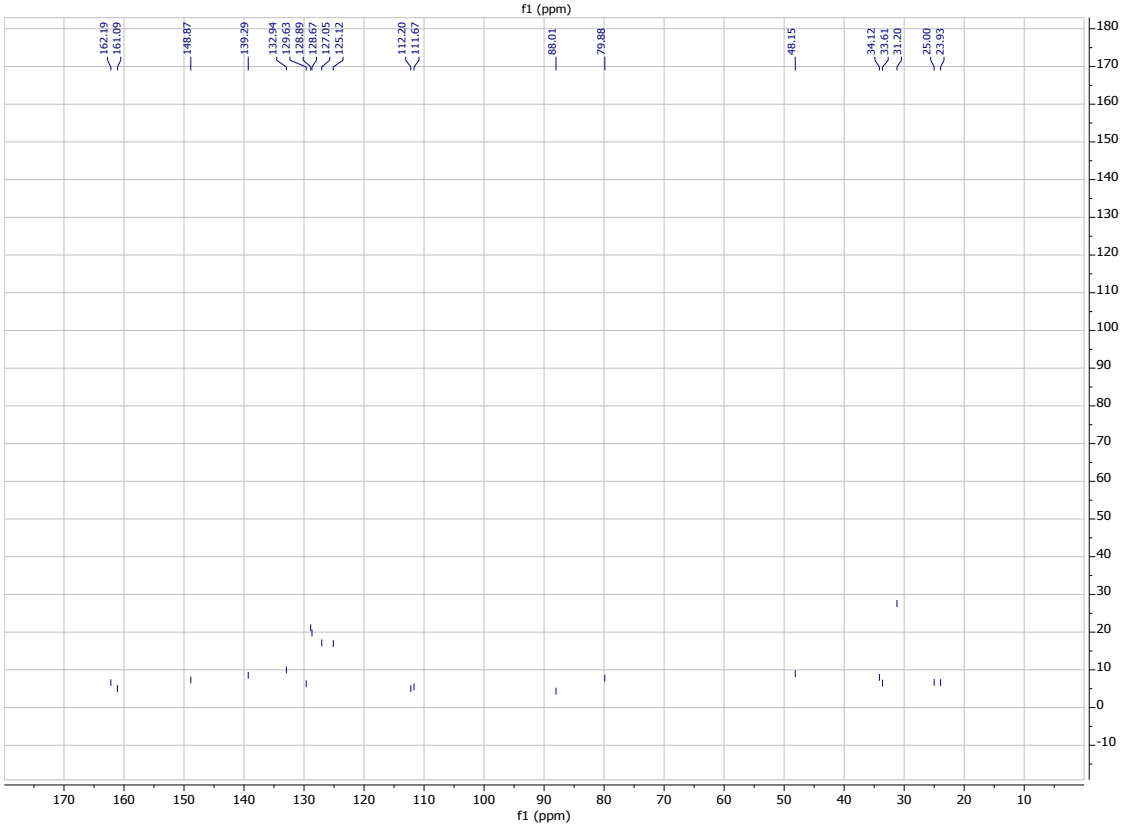


(-)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexyl-2-oxo-2-phenylacetate (11i-intermediate)

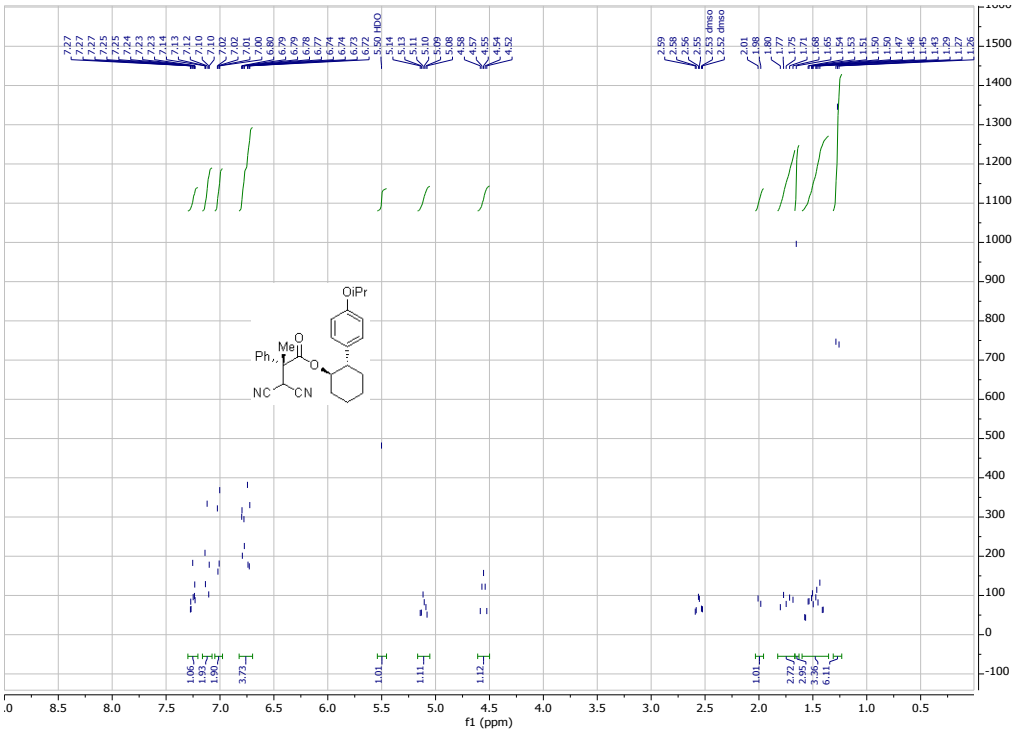


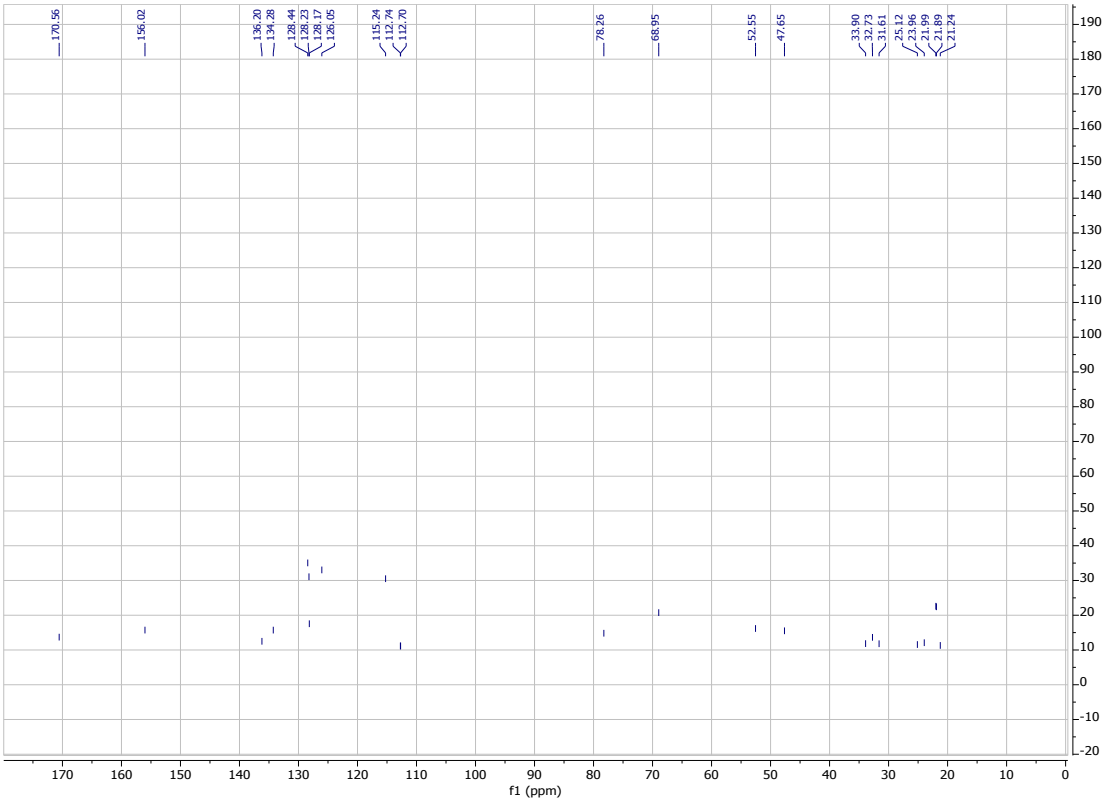
(-)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexyl-3,3-dicyano-2-phenylacrylate (11i)



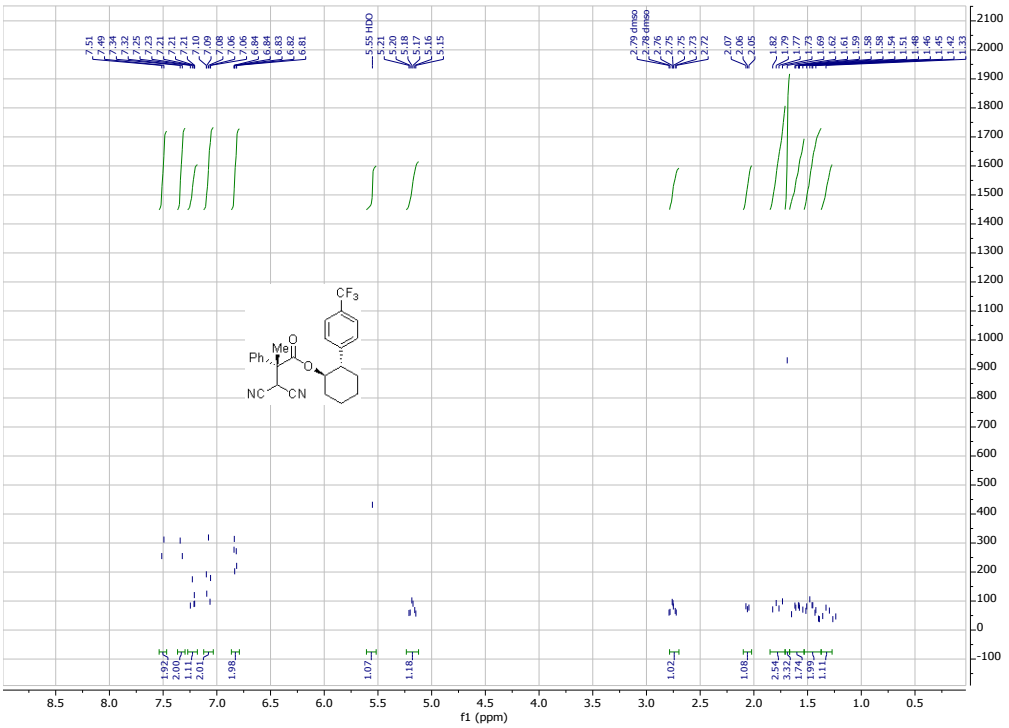


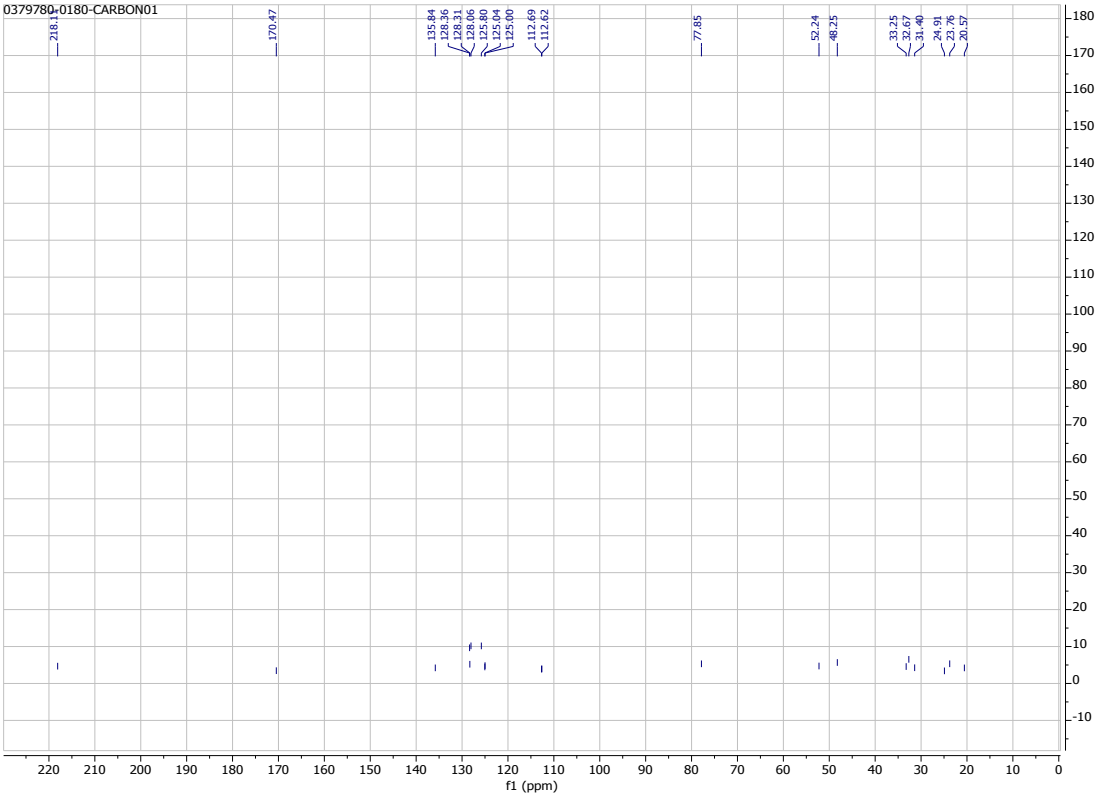
(*1R,2S*)-2-(4-isopropoxyphenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12a)



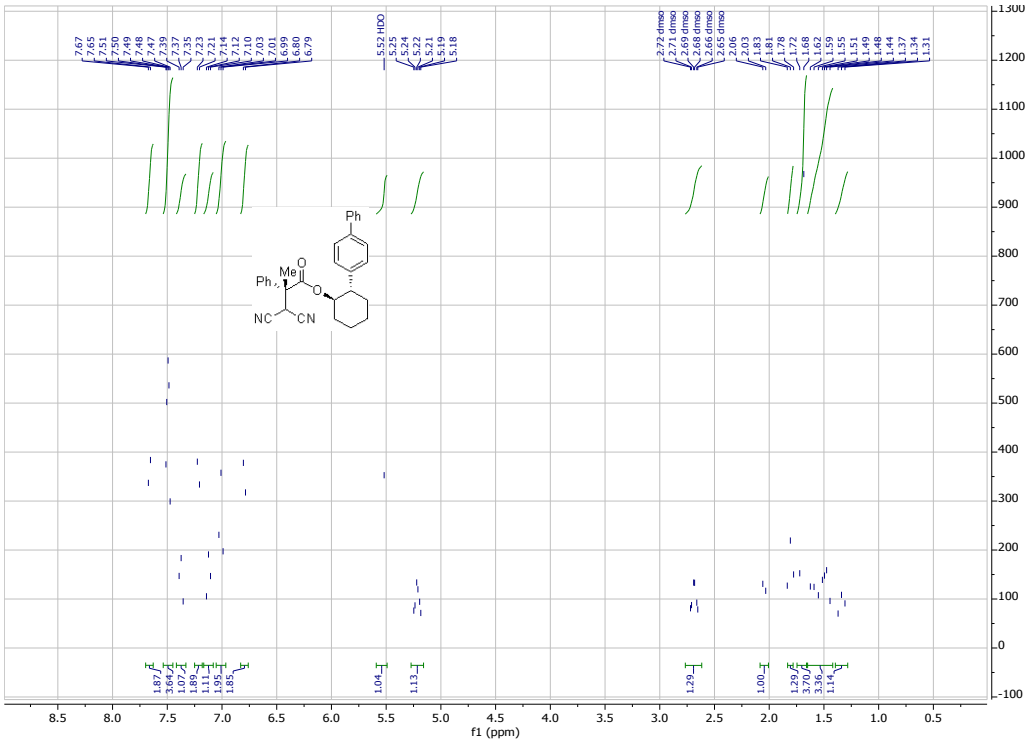


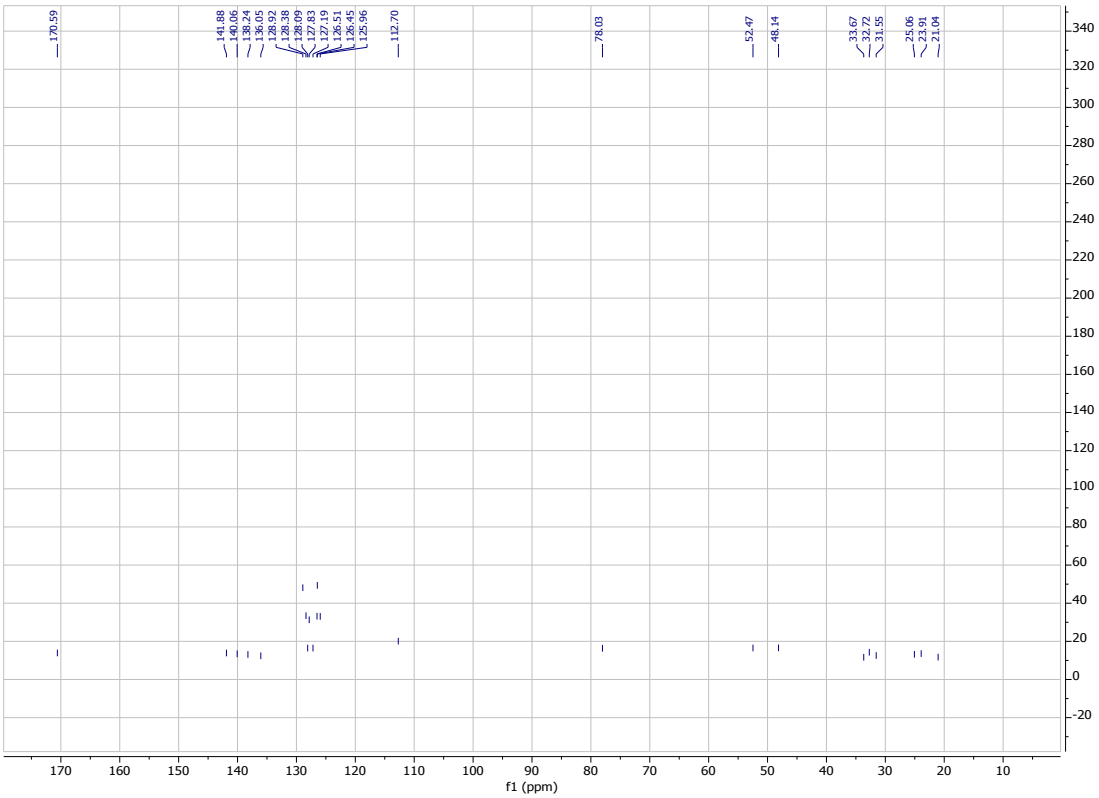
(*1R,2S*)-2-(4-(trifluoromethyl)phenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12b)



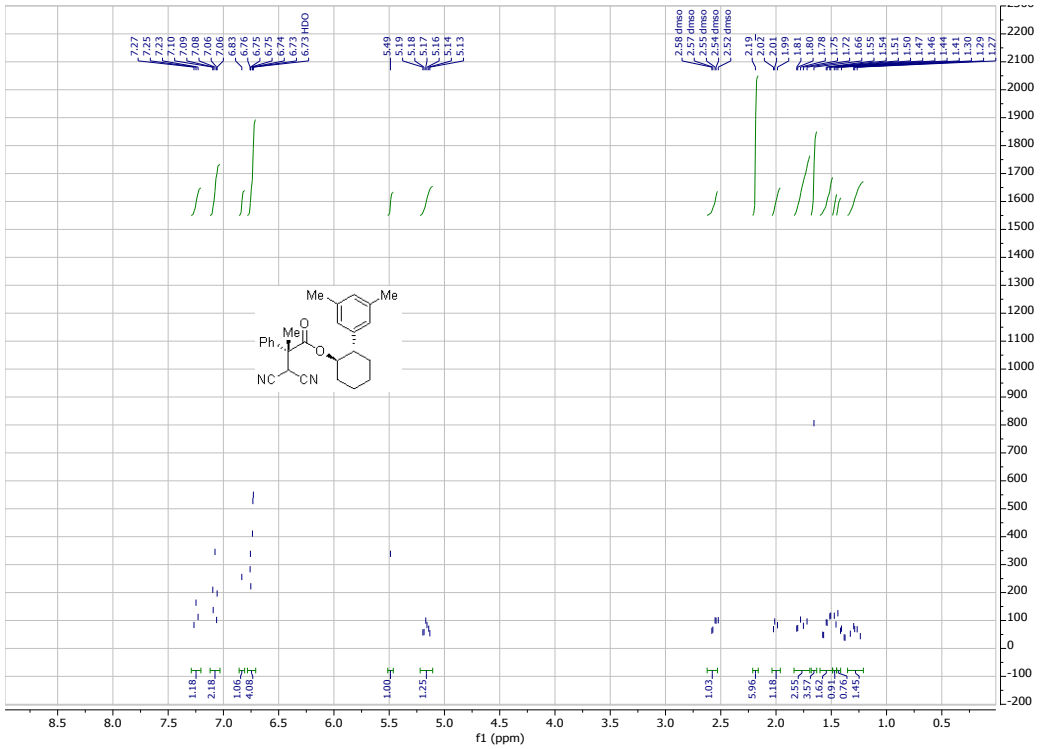


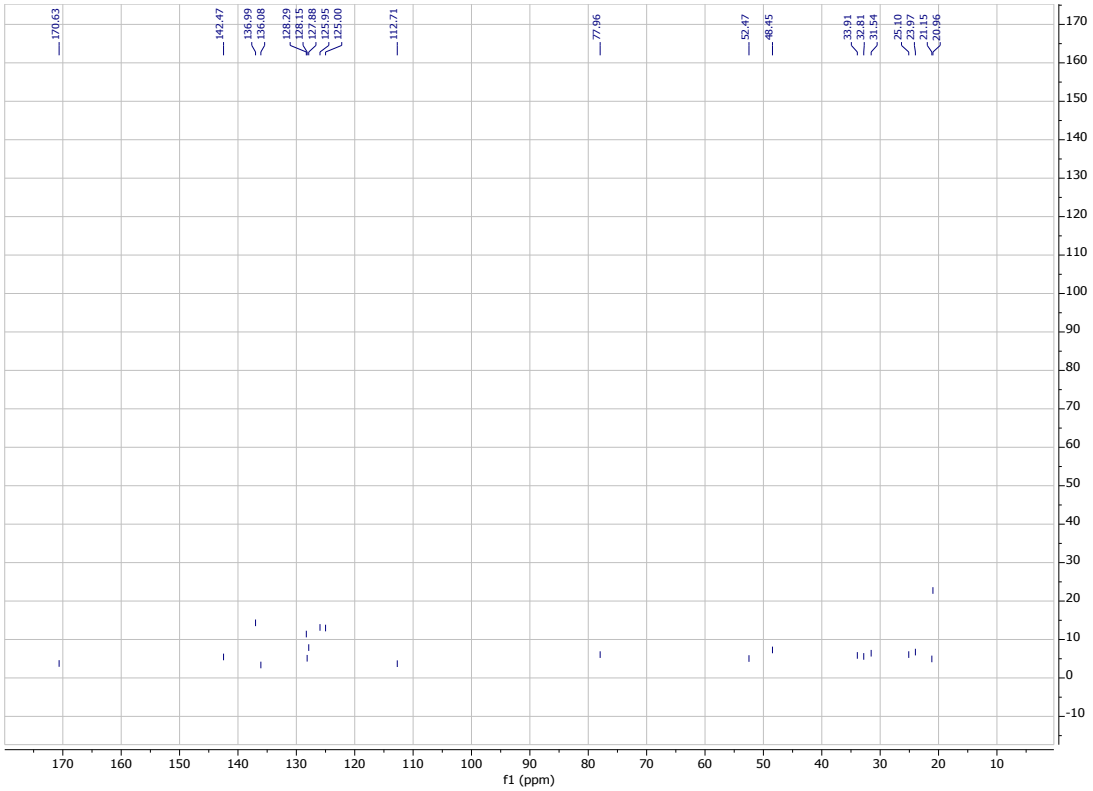
(*1R,2S*)-2-([1,1'-biphenyl]-4-yl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12c)



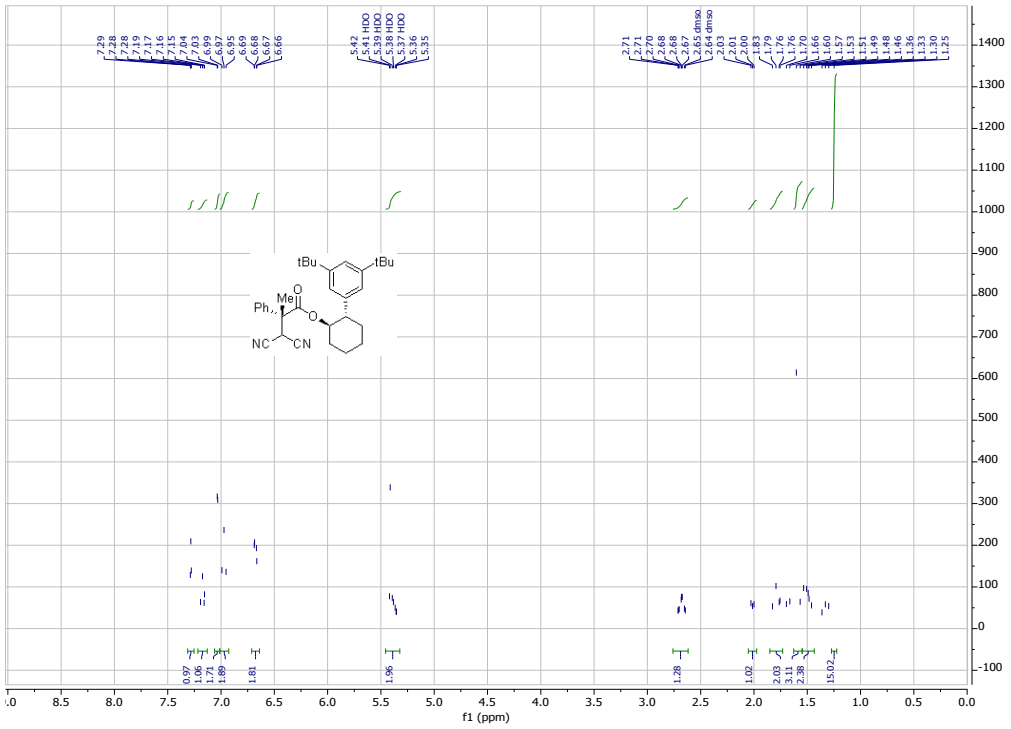


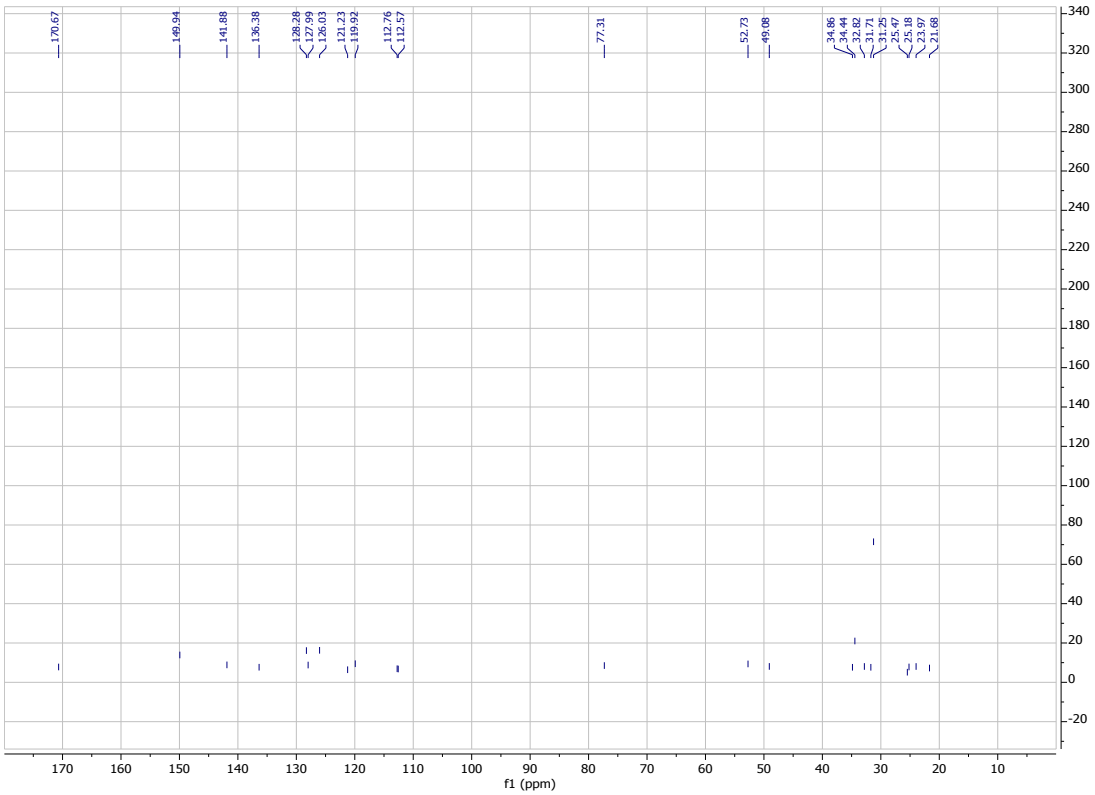
(*1R,2S*)-2-(3,5-dimethylphenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12d)



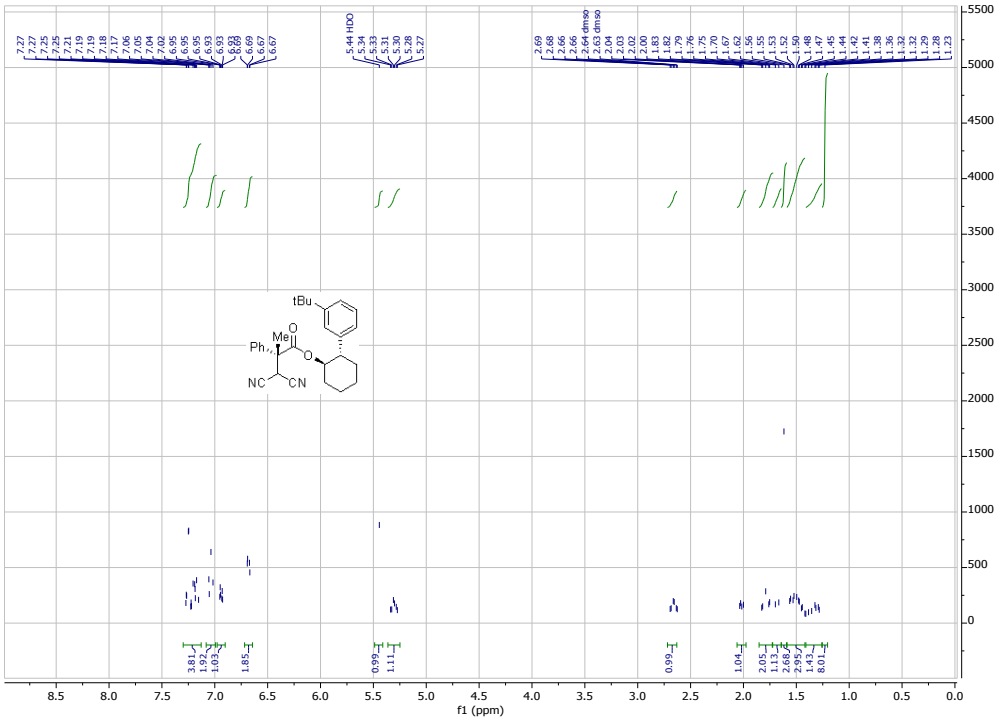


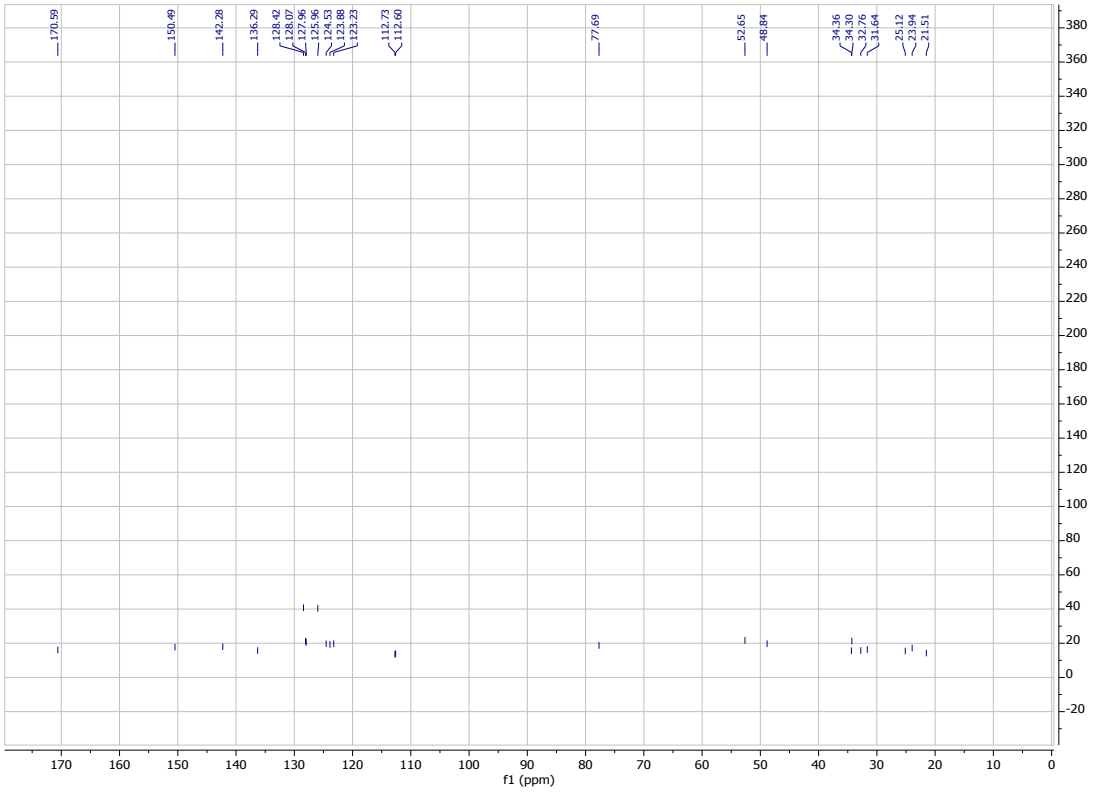
(*1R,2S*)-2-(3,5-di-tert-butylphenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12e)



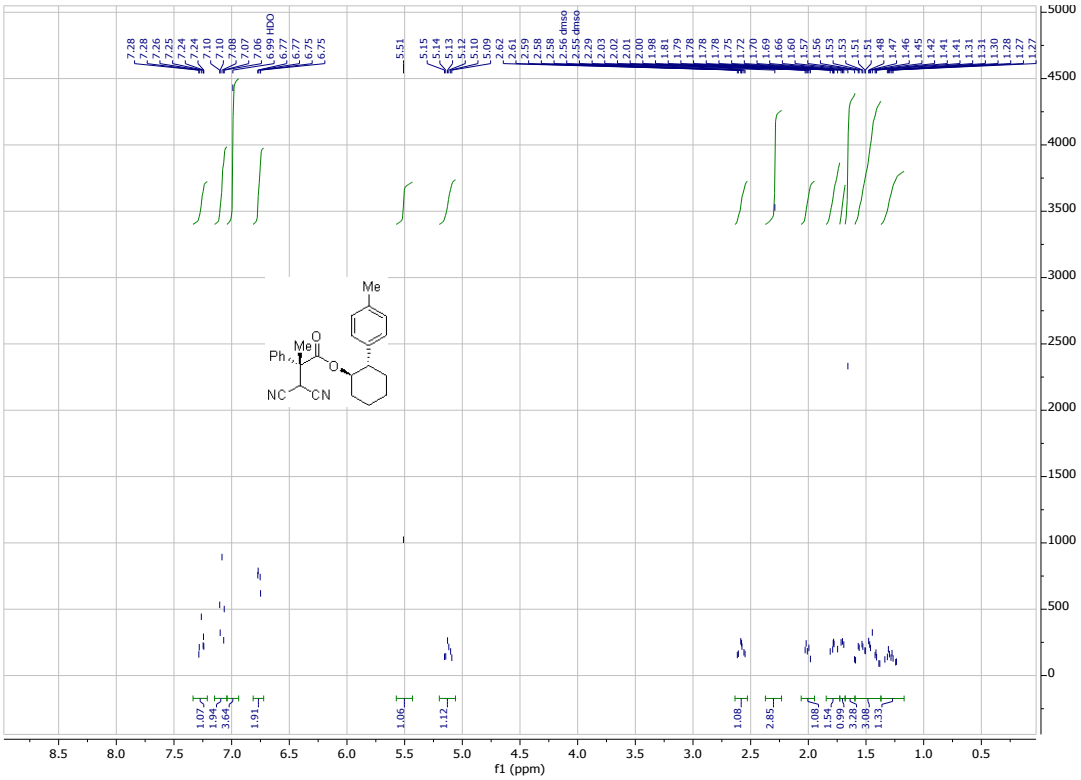


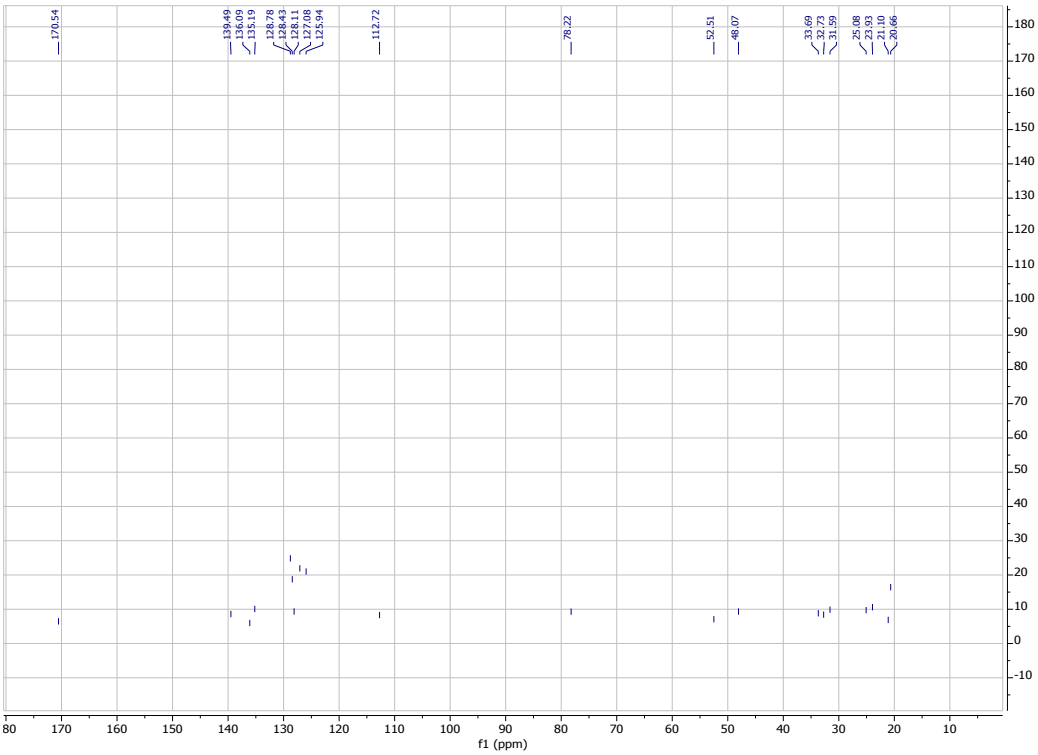
(*1R,2S*)-2-(3-(tert-butyl)phenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12f).



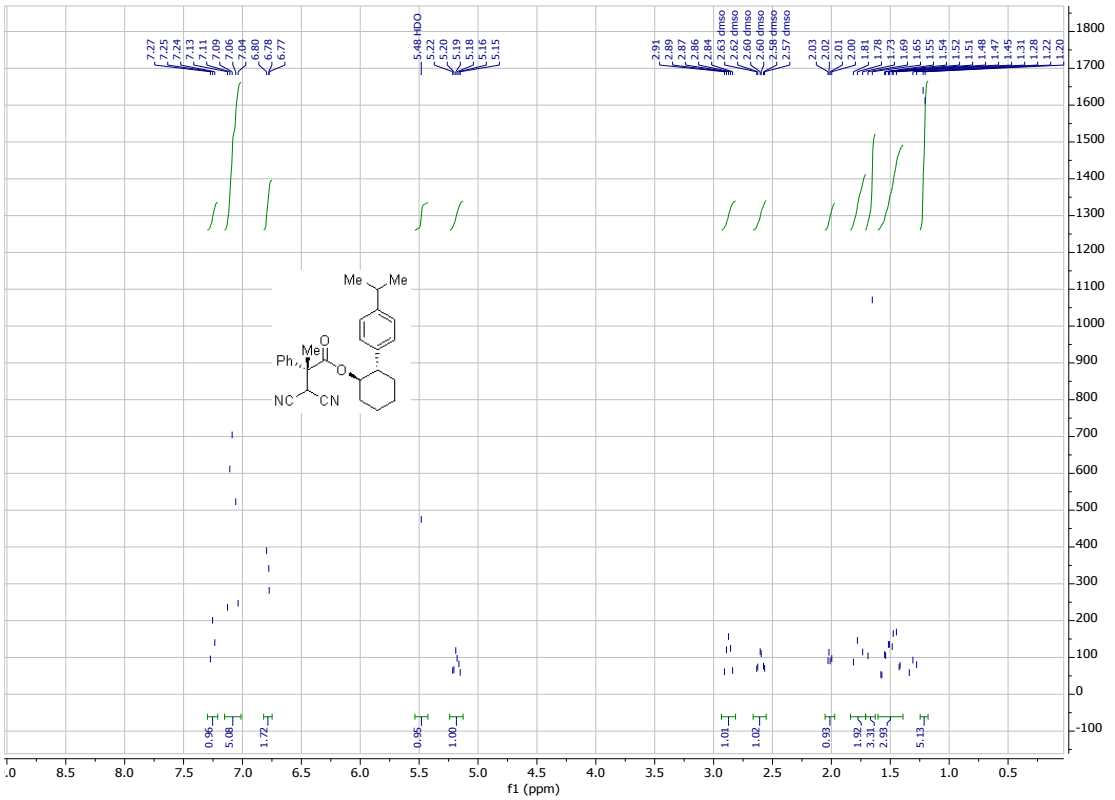


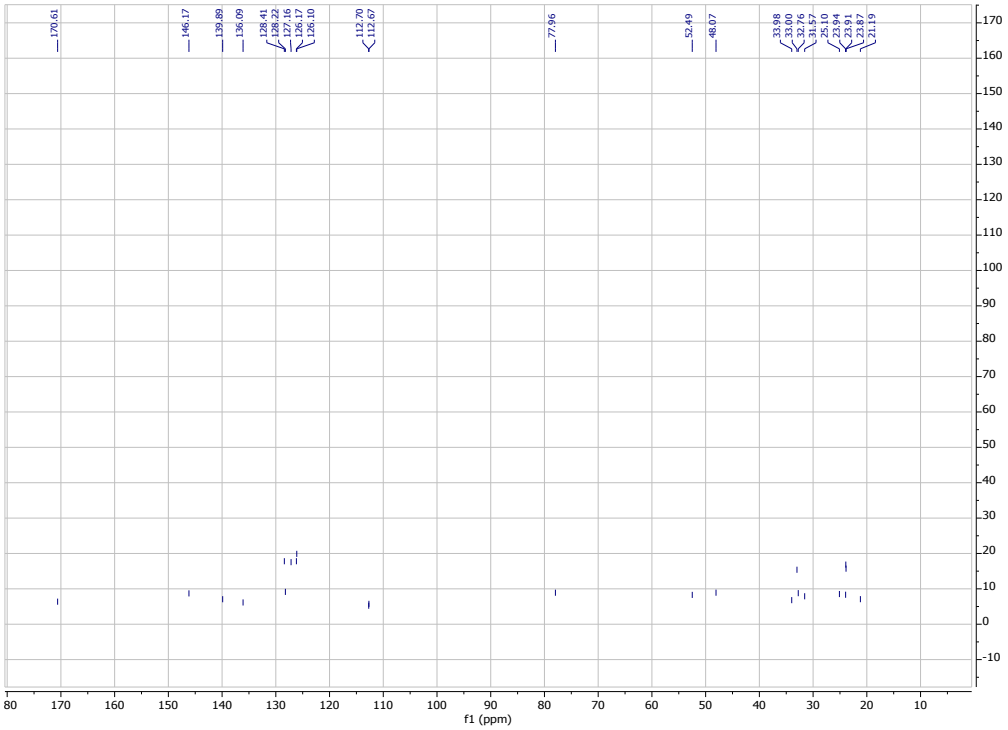
(*1R,2S*)-2-(p-tolyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12g)



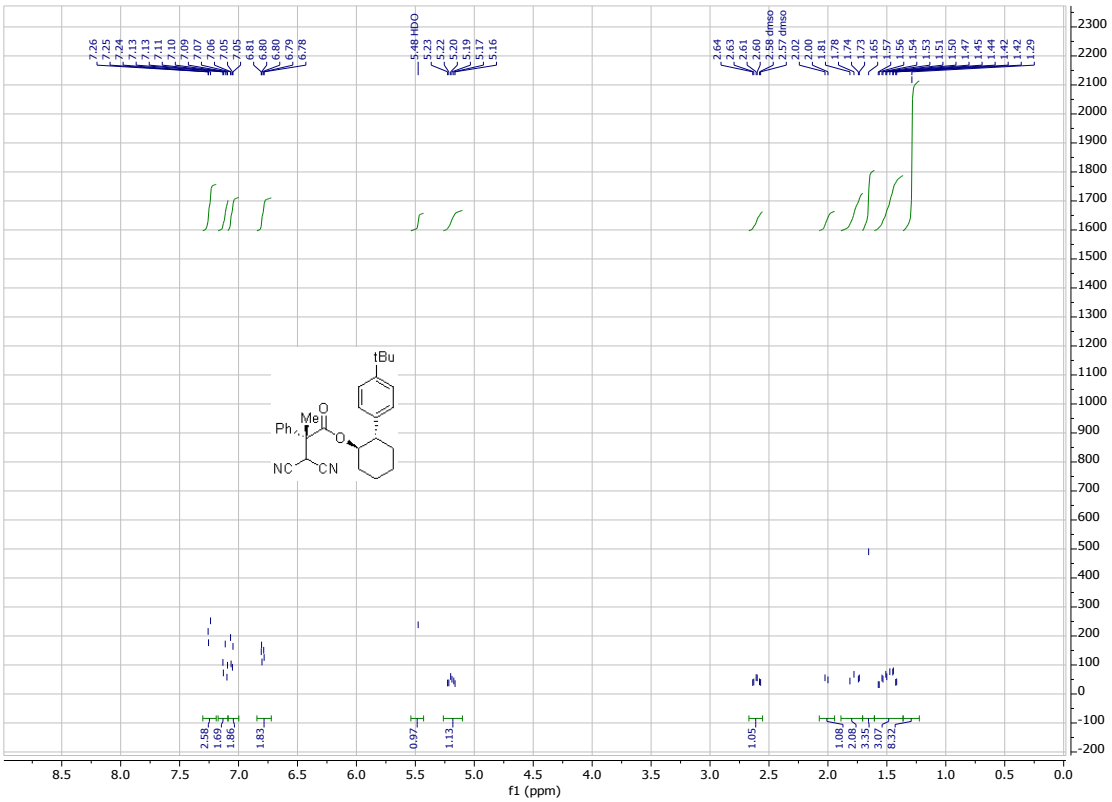


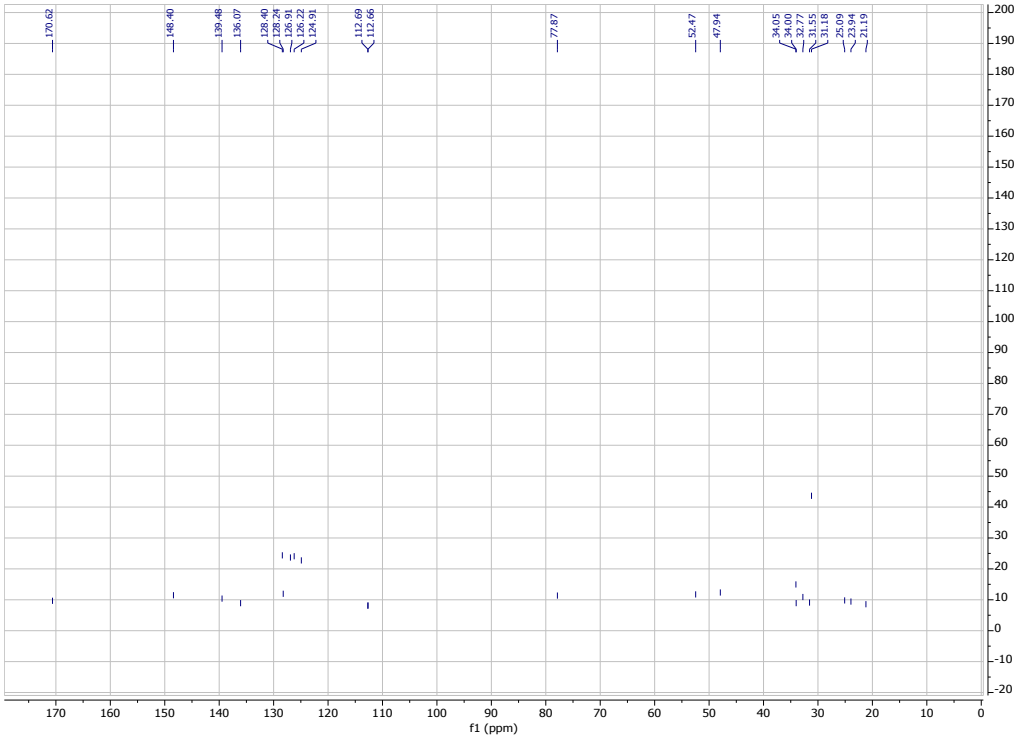
(*1R,2S*)-2-(4-isopropylphenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12h)





(-)-(*1R,2S*)-2-(4-(tert-butyl)phenyl)cyclohexyl-(*R*)-3,3-dicyano-2-methyl-2-phenylpropanoate (12i)





(-)-(*S*)-4-amino-2-(6-chloro-1-(3,3,4,4,4-pentafluorobutyl)-1H-indazol-3-yl)-5-methyl-5-phenyl-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one (14)