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SUPPORTING INFORMATION

Scalable organocatalytic one-pot asymmetric Strecker reaction *via* camphor sulfonyl functionalized crown-ether-tethered calix[4]arene

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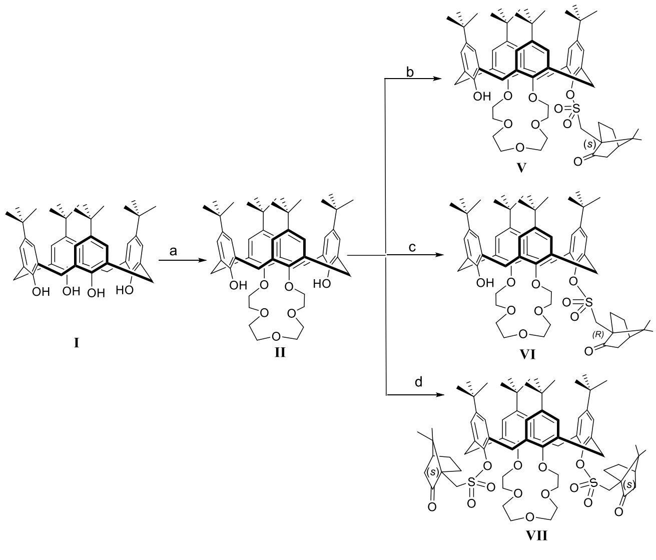
1. General Information

Starting materials and reagents were used without purification unless otherwise mentioned and were purchased from commercial suppliers. Reaction temperatures were measured externally; reactions were monitored by analytical thin layer chromatography (TLC), Merk 60 F_{254} Aluminium coated plates and visualized by UV light. Column chromatography was performed on silica gel (60-120 mesh) and the solvents employed were of analytical grade purified before Use. The enantiomeric excess(ee) of the cyanated products was determined by HPLC measurements carried out using a thermos scientific Vanquish detector Model: VC-D11-A equipped with chiral columns DAICEL 4.6 mm × 250 mm Chiralpak- AD-H using condition n-Hexane/isopropanol solvent system. Optical rotation values were measured on a JASCO P-1010 polarimeter at λ = 589 nm, corresponding to the sodium D line, at the temperatures indicated. NMR spectra were recorded on a Bruker 500 spectrophotometer ^{1}H NMR, ^{13}C and ^{29}Si spectra were recorded on 500, 126 and,500 MHz respectively. Chemical shifts (δ) are reported in ppm relative to the residual solvent peak (^{1}H $CDCl_3$, δ = 7.26; ^{13}C $CDCl_3$, δ = 77.0) and the following abbreviations designate the multiplicity of each signal: s, singlet; d, doublet; t, triplet; m, multiplet; bs, broad singlet; bd, broad doublet. Coupling constants (J) are quoted in Hertz. High-resolution mass spectra (HRMS) were acquired using an Agilent technologies model G6564 QTOF. The samples were ionized in positive ion mode using a MALDI or ESI ionization source. Calix[4] arene was synthesised via reported procedure [1]

2. Synthesis of catalyst



Reaction conditions: (a) dry toluene, p-tert-butylcalix[4]arene (1.46 g, 2.25 mmol), ^{t}BuOK (0.46 g, 4 mmol), reflux, tetraethylene glycol ditosylate (1.06g, 2 mmol); (b) **II**, Dry THF/DMF (16:1), NaH (0.06g, 1.62 mmol), (+)-10-Camphorsulfonyl chloride (0.4g,1.65 mmol).(c) **II**,Dry THF/DMF (16:1), NaH (0.06g, 1.62 mmol), (-)-10-Camphorsulfonyl chloride (0.4g,1.65 mmol) (d) **II**, Dry THF/DMF (16:1), NaH (0.14g, 3.24 mmol), (+)-10-Camphorsulfonyl chloride (0.8g, 3.3 mmol)

Step a: Synthesis of p-tert-butylcalix[4]arene-crown-5 (II) :

A mixture of p-tert-butylcalix[4]arene (**I**, 1.46 g, 2.25 mmol) and ^{t}BuOK (0.23 g, 2 mmol) in 50 mL of dry toluene was refluxed (using heating blocks) under nitrogen gas with stirring for 1.5 h, then tetraethylene glycol ditosylate (1.06 g, 2 mmol) was added. After refluxing for 24 h, a second portion of $^{t}BuOK$ (0.23 g, 2 mmol) was added, and the reaction mixture was refluxed for an additional 24 h. It was then cooled to room temperature, treated with 1 N HCl (125 mL), and extracted five or six times with 30 mL of diethyl ether each time. The combined organic layers were finally washed three times with water (100 mL each time), and the solvent was removed by rotary evaporation. The crude product was purified by column chromatography using silica as packing material and dichloromethane/ethyl acetate (4:1) as eluent gives white solid, 1.17 g, 65% yield of I, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (s, 4H), 6.75 (s, 4H), 4.38 (d, *J* = 13.0 Hz, 4H), 4.08 (s, 8H), 3.97 (t, *J* = 5.5 Hz, 4H), 3.85 (t, *J* = 5.5 Hz, 4H), 3.30 (d, *J* = 13.0 Hz, 4H), 1.31 (s, 20H), 0.91 (s, 16H);^{13}C NMR (126 MHz, Chloroform-d): 150.8, 149.8, 146.8, 141.2, 132.5, 129.8, 127.8, 125.4, 124.9, 71.0, 70.8, 70.3, 33.8, 31.7, 31.0

Step b: Synthesis of calix[4]arene-crown-5 tethered with (+)-10-camphorsulfonyl catalyst (V):

To a solution of calix[4]crown-5 **II** (1.2g, 1.5 mmol) in DryTHF/DMF mixture (16/1), a 60% suspension of sodium hydride in mineral oil was added (0.06g, 1.62 mmol). After stirring the reaction mixture at room temperature for 2 hours, (+)-10-camphor sulfonyl chloride (0.40g, 1.65 mmol; mp 69°C ($[\alpha]^{28}_{D}$ = +36° C2, $CHCl_3$)) in THF (2.5 mL) was added. The reaction mixture was stirred at ambient temperature for 18h. The solvent was removed under vacuum and the oily residue was dissolved into chloroform and washed with saturated NH_4Cl solution. Then the organic layer was dried over Na_2SO_4. The residue was further purified through column chromatography CH_2Cl_2/MeOH = 95/5 to 60/40 as eluent to afford **V** as a white crystalline solid (1.14 g, 76%); $[\alpha]^{28}_{D}$ = +52° (c 1, $CHCl_3$); ^{1}H NMR (500 MHz, Chloroform-*d*) δ7.19 (s,1H), 7.07 (s, 4H), 6.75 (s, 4H), 4.60 (m,1H), 4.37 (d, *J* = 13.0 Hz, 4H), 4.08 (s, 8H), 3.97 (t, *J* = 5.3 Hz, 4H), 3.84 (t, *J* = 5.5 Hz, 4H), 3.29 (d, *J* = 13.0 Hz, 4H),3.18(s,1H) 2.06 – 1.94 (m, 3H), 1.31 (s, 18H), 1.19 (s, 3H), 1.11 (s, 3H), 1.04 (d, *J* = 7.4 Hz, 6H), 0.91 (s, 18H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 214.73,214.17, 150.82, 149.82, 146.85, 141.23, 135.12, 134.93, 134.83, 134.30, 134.24, 132.51, 127.85, 125.56, 125.35, 125.01, 124.96, 71.26, 71.07, 70.90, 70.69, 70.37, 70.06, 58.66, 58.39, 47.81, 47.70, 43.37, 43.11, 42.49, 33.89, 33.85, 31.68, 31.34, 31.04, 30.97, 20.35, 20.17, 20.07, 19.96, 19.78. HRMS (ESI+) m/z $[M + H]^{+}$ calcd for $C_{62}H_{84}O_{10}S$, 1020.5800; found 1020.5805

Step c: Synthesis of calix[4]arene-crown-5 tethered with (-)-10-camphor sulfonyl catalyst(VI):

The synthetic procedure is the same as catalyst **V** using (-)-10-camphor sulfonyl chloride; mp 67°C ($[\alpha]^{28}_{D}$=-34° C2, $CHCl_3$). The residue was purified through column chromatography CH_2Cl_2/MeOH = 95/5 to 60/40 as eluent to afford VI as a white crystalline solid (1.11 g, 74%); $[\alpha]^{28}_{D}$ = - 50° (c 1, $CHCl_3$); ^{1}H NMR (500 MHz, Chloroform-*d*) δ7.29(s,1H), 7.07 (s, 4H), 6.75 (s, 4H),4.60(m, 1H) ,4.37 (d, J = 13.0 Hz, 4H), 4.07 (s, 8H), 3.96 (t, J = 5.4 Hz, 4H), 3.84 (d, J = 5.4 Hz, 4H), 3.29 (d, J = 13.1 Hz, 4H),3.18 (m,1H), 2.00 (m,1H),1.31 (s, 20H), 1.11 (s, 4H), 1.04 (s, 4H), 1.03 (s, 4H), 0.91 (s, 16H).^{13}C NMR (126 MHz, Chloroform-*d*) δ 213.73, 213.17, 149.82,148.82, 145.85, 140.23,131.511, 126.85, 124.56, 124.35, 124.01, 123.96, 57.66, 57.39, 46.81, 46.70, 46.26,42.37, 41.49,32.89,32.86, 30.88, 30.68, 30.35, 29.97, 18.96, 18.87 HRMS (ESI+) m/z [M + H] $^+$ calcd for $C_{62}H_{84}O_{10}S$, 1020.5800; found 1020.5803

Step d: Synthesis of calix[4]arene-crown-5 tethered with (+)-10-camphorsulfonyl catalyst (VII):

To a solution of calix[4]crown-5 **II** (1.2g, 1.5 mmol) in DryTHF/DMF mixture (16/1), a 60% suspension of sodium hydride in mineral oil was added (0.14g, 6.0 mmol). After stirring the reaction mixture at room temperature for 2 hours, D-(+)-10-camphor sulfonyl chloride (1.50g, 8.0 mmol mp 69^{o}C ($[\alpha]^{28}_D$ = +36^o C2, $CHCl_3$)) in THF (2.5 mL) was added. The reaction mixture was stirred at ambient temperature for 5h followed by heating at 70 ^{o}C for 12h. Recation was monitoried via TLC. After completion of reaction, reaction mixture was cooled to room temparture and solvent was removed under vacuum and the oily residue was dissolved into chloroform and washed with saturated NH_4Cl solution. Then the organic layer was dried over Na_2SO_4. The residue was further purified through column chromatography CH_2Cl_2/MeOH = 95/5 to 60/40 as eluent to afford **VII** as a white crystalline solid (1.47 g, 80%); $[\alpha]^{28}_D$ = +78^o (c 1, $CHCl_3$); ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.07 (s, 4H), 6.75 (s, 4H), 4.38 (d, *J* = 13.0 Hz, 4H), 4.37-4.25 (m,2H), 4.10 – 4.06 (m, 4H), 3.96 (d, *J* = 5.4 Hz, 4H), 3.85 (d, *J* = 5.4 Hz, 4H), 3.30 (d, *J* = 13.1 Hz, 4H), 2.83 (s, 2H), 2.17 – 1.90 (m, 2H), 1.78 (s, 4H), 1.34 (s, 2H), 1.31 (s, 20H), 1.21 (s, 4H), 0.94 (s, 4H), 0.91 (s, 16H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 214.41, 214.15, 150.82, 149.81, 146.85, 141.22, 132.51, 127.84, 125.44, 124.97, 71.07, 70.90, 70.37, 43.26, 42.82, 42.52,42.4, 37.12, 34.15, 33.92, 33.89, 33.85, 33.82, 33.06, 31.76, 31.50, 31.35, 31.27, 31.04, 30.99, 29.72, 26.90, 24.93,22.72, 20.25, 20.25, 19.86,19.71, 14.14. HRMS (ESI+) m/z [M + H] $^+$ calcd for $C_{72}H_{98}O_{13}S_2$ 1234.6400; found 1234.6406

3. General procedure for one-pot three-component Strecker reaction.

In an inert environment, benzaldehyde (84 mg, 0.8 mmol), aniline (74 mg, 0.8 mmol), trimethylsilyl cyanide (79 mg, 0.8 mmol), and catalyst (2 mol%) were introduced in a dry glass tube with dichloromethane (0.4ml) as a solvent. The reaction mixture was stirred continuously for 15 minutes and monitored through TLC. The reaction mixture was treated with chloroform and washed with a saturated solution of sodium bisulphite. The organic phase was dried over anhydrous sodium sulphate. The solvent was then evaporated under reduced pressure and the crude was purified through column chromatography (hexane/Ethyl acetate 80/20) .The enantiomeric excess was determined by chiral stationary-phase HPLC analysis.

Table S1-Effects of the ratio of aldehyde/amine to TMSCN on enantioselective Strecker reaction*

Entry[a]	Ratio of benzaldehyde/aniline /TMSCN	Time[min]	Yield[b]	ee[c]
1	1/1/1	15	99.9	99.2
2	1/0.9/1.2	15	99.9	99.1
3	1/0.9/1.5	30	99.9	98.9

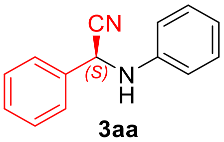
*Reaction Conditions: 1 equiv of catalyst **V**. benzaldehyde, aniline and TMSCN in DCM at 25°C [b] Isolated yield.[c]Determined by HPLC analysis on Diacel chiralpak AD-H

Table S2- Limitation Table for Substrate scope using catalyst V*

Entry[a]	aldehyde	Time[min]	Yield[b]	$[\alpha]^{28}_{D}$[c]
1	Propionaldehyde	15	90	+51 (C 0.5, MeOH)
2	butyraldehyde	15	94	+23 (C 0.5, $CHCl_3$)
3	Hexanal	15	97	+46 (C 0.5, $CHCl_3$)

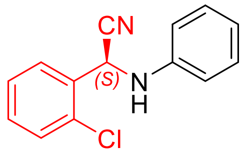
*Reaction Conditions: 1 equiv of catalyst **V**. aldehyde, aniline and TMSCN in DCM at 25°C [b] Isolated yield. [c] Optical rotation values were measured on a JASCO P-1010 polarimeter at λ = 589 nm.

4. Characterisation of Strecker products



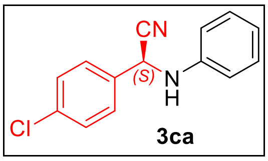
3aa

(S)-2-phenyl-2-(phenylamino)acetonitrile(3aa). Colourless solid; 164.3 mg, 99.9% yield; 99.2% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) =12.5min, tR (minor) = 18.9 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 (dd, *J* = 7.5, 1.9 Hz, 2H), 7.47 (d, *J* = 7.4 Hz, 3H), 7.31 – 7.27 (m, 2H), 7.17 (dd, *J* = 8.5, 7.4 Hz, 1H), 6.96 – 6.88 (m, 1H), 6.82 – 6.77 (m, 2H), 6.73 – 6.69 (m, 1H), 5.44 (s, 1H), 4.00 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 143.62, 132.87, 128.54, 128.51, 128.31, 126.23, 119.24, 113.09, 49.16. HRMS (ESI+) m/z $[M + H]^+$ calcd for $C_{14}H_{12}N_2$, 208.1000 ; found 208.1009.

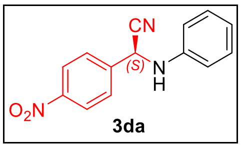


3ba

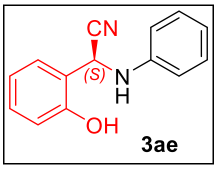
(S)-2-(2-chlorophenyl)-2-(phenylamino)acetonitrile (3ba). Colourless solid; 171.8 mg, 99.9% yield; 89.6% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 4.1 min, tR (minor) = 7.1 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.35 (m, 5H), 7.31 – 7.28 (m, 4H), 5.75 (s, 1H), 4.07 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 144.39, 135.64, 132.43, 129.65, 128.63, 126.25, 120.60, 117.86, 114.33, 49.69. HRMS (ESI+) m/z $[M + H]^+$ calcd for $C_{14}H_{11}ClN_2$, 242.0600; found 242.0602.



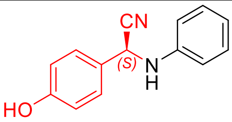
(S)-2-(4-chlorophenyl)-2-(phenylamino)acetonitrile (3ca). Colourless solid; 151.4 mg, 92% yield; 88.4% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 4.2 min, tR (minor) = 4.4 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.48 – 7.39 (m, 5H), 7.29 (d, *J* = 7.9 Hz, 1H), 7.24 – 7.20 (m, 2H), 6.93 (t, *J* = 7.4 Hz, 1H), 5.42 (s, 1H), 4.10 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 157.92, 150.67, 143.37, 136.41, 133.69, 131.42, 128.98, 128.65, 128.57, 128.23, 128.11, 127.62, 125.24, 119.87, 119.62, 116.82, 113.32, 48.68, 28.73 HRMS (ESI+) m/z [M + H]$^{+}$ calcd for $C_{14}H_{11}ClN_2$, 242.0600; found 242.0603



(S)-2-(4-nitrophenyl)-2-(phenylamino)acetonitrile(3da). Yellow solid; 207.3 mg, 99.9% yield; 47.0% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 26.3 min, tR (minor) = 39.3 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 8.7 Hz, 2H), 8.09 – 8.06 (m, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.27 (dd, *J* = 13.4, 6.9 Hz, 3H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.76 (d, *J* = 7.9 Hz, 2H), 5.64 – 5.48 (m, 1H), 4.22 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 141.59, 138.75, 129.73, 129.51, 129.43, 129.36, 129.15, 128.68, 128.24, 127.11, 124.49, 124.21, 124.04, 120.98, 120.79, 114.62, 49.76. HRMS (ESI+) m/z [M + H]$^{+}$ calcd for $C_{14}H_{11}N_3O_2$, 253.0900; found 253.0907.

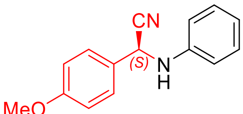


(S)-2-(2-hydroxyphenyl)-2-(phenylamino)acetonitrile (3ea). Colourless solid; 157.9 mg, 92% yield; 89.1% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 8.9 min, tR (minor) =18.8 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.63 (s, 1H), 7.56 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.31 – 7.27 (m, 3H), 7.03 (dd, *J* = 7.7, 3.6 Hz, 3H), 6.92 (d, *J* = 8.0 Hz, 2H), 5.63 (d, *J* = 9.1 Hz, 1H), 4.23 (d, *J* = 9.6 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.66, 153.76, 132.15, 131.26, 128.71, 128.40, 127.13, 125.89, 121.23, 120.15, 118.07, 116.30, 115.41, 47.61. HRMS (ESI+) m/z [M + H] + calcd for $C_{14}H_{12}N_2O$, 224.0900; found 224.0903



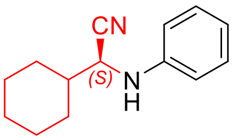
3fa

(S)-2-(4-hydroxyphenyl)-2-(phenylamino)acetonitrile (3fa). Colourless solid; 171.3 mg, 95% yield; 95.5% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 26.9 min, tR (minor) =33.3 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.46 (d, *J* = 8.5 Hz, 2H), 7.31 – 7.27 (m, 2H), 6.91 (t, *J* = 8.1 Hz, 3H), 6.78 (dt, *J* = 7.7, 3.4 Hz, 2H), 5.36 (d, *J* = 7.5 Hz, 1H), 4.01 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.65, 143.66, 128.56, 127.85, 124.99, 119.22, 117.38, 115.13, 113.08, 48.66. HRMS (ESI+) m/z [M + H] + calcd for $C_{14}H_{12}N_2O$, 224.0900; found 224.0905



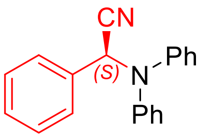
3ga

(S)-2-(4-methoxyphenyl)-2-(phenylamino)acetonitrile (3ga). Colourless solid; 151.5 mg, 97% yield; 97.9% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 11.8 min, tR (minor) =12.5min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.51 (d, *J* = 8.7 Hz, 2H), 7.28 (dd, *J* = 8.5, 7.3 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.90 (t, *J* = 7.4 Hz, 1H), 6.80 – 6.75 (m, 2H), 5.37 (s, 1H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.38, 143.69, 128.52, 127.60, 124.88, 119.13, 117.39, 113.59, 113.04, 54.39, 48.60. HRMS (ESI+) m/z [M + H] + calcd for $C_{15}H_{14}N_2O$, 238.1100; found 238.1107.



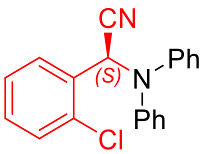
3ha

(S)-2-cyclohexyl-2-(phenylamino)acetonitrile (3ha). Colourless solid; 141.1 mg, 99.9% yield; 98.5% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 22.9 min, tR (minor) =25.6 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.29 – 7.27 (m, 2H), 7.20 – 7.17 (m, 1H), 6.90 – 6.87 (m, 1H), 6.73 (ddt, *J* = 11.0, 8.5, 1.1 Hz, 3H), 3.88 – 3.79 (m, 1H), 1.36 – 1.21 (m, 12H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 145.19, 129.55, 119.89, 118.86, 114.06, 51.75, 40.80, 29.69, 28.94, 25.94, 25.66, 25.59. HRMS (ESI+) m/z [M + H] + calcd for $C_{14}H_{18}N_2$, 214.1500; found 214.1504



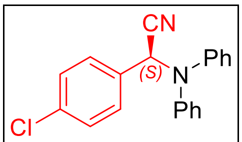
3ab

(S)-2-(diphenylamino)-2-phenylacetonitrile (3ab). Colourless solid; 217.1 mg, 98% yield; 93.1% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) =18.8 min, tR (minor) = 34.2 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 – 7.50 (m, 2H), 7.43 (s, 3H), 7.07 (d, *J* = 7.9 Hz, 9H), 6.93 (d, *J* = 7.4 Hz, 5H), 5.50 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.19, 135.38, 129.41, 126.81, 126.63, 121.12, 121.11, 121.01, 118.89, 117.88, 63.76. HRMS (ESI+) m/z [M + H]$^+$ calcd for $C_{20}H_{16}N_2$, 284.1300; found 284.1308.



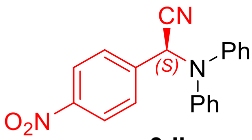
3bb

(S)-2-(2-chlorophenyl)-2-(diphenylamino)acetonitrile (3bb). Colourless solid; 225.8 mg, 99.9% yield; 95.5% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 9.1 min, tR (minor) =19.1 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.30 (t, *J* = 7.8 Hz, 6H), 7.10 (d, *J* = 8.0 Hz, 6H), 6.96 (t, *J* = 7.4 Hz, 3H), 5.85 (d, *J* = 4.6 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 144.17, 142.09, 130.13, 130.03, 129.59, 129.10, 128.85, 128.31, 127.41, 126.69, 125.78, 122.95, 121.98, 119.97, 116.78, 59.99. HRMS (ESI+) m/z [M + H]$^+$ calcd for $C_{20}H_{15}ClN_2$, 318.0900; found 318.0902.



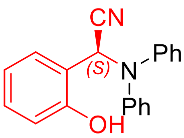
3cb

(S)-2-(4-chlorophenyl)-2-(diphenylamino)acetonitrile (3cb). Colourless solid; 209.8 mg, 97% yield; 98.4% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) =17.2 min, tR (minor) = 22.4 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (d, *J* = 7.9 Hz, 9H), 6.92 (t, *J* = 7.4 Hz, 5H), 5.51 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 143.12, 133.73,131.09, 129.38, 127.98, 121.09, 120.97, 118.38, 117.81, 63.08. HRMS (ESI+) m/z [M + H]$^+$ calcd for $C_{20}H_{15}ClN_2$, 318.0900; found 318.0909.



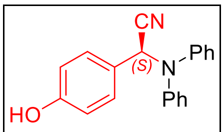
3db

(S)-2-(diphenylamino)-2-(4-nitrophenyl)acetonitrile (3db). ellow solid; 248.1 mg, 92% yield; 66.4 % ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) =17.0 min, tR (minor) = 18.6 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.33 (d, *J* = 8.8 Hz, 1H), 7.80 – 7.73 (m, 2H), 7.29 (s, 1H), 7.28 (d, *J* = 1.2 Hz, 2H), 7.27 (s, 3H), 7.11 – 7.06 (m, 4H), 6.94 (s, 2H), 5.71 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 143.13, 141.44, 129.36, 127.51, 124.37, 121.03, 117.83, 62.54. HRMS (ESI+) m/z [M + H]$^{+}$ calcd for $C_{20}H_{15}N_{3}O$, 329.1200; found 329.1204.



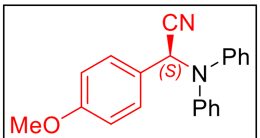
3eb

(S)-2-(diphenylamino)-2-(2-hydroxyphenyl)acetonitrile (3eb). Colourless solid; 218.4 mg, 95% yield; 98% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) =18.1 min, tR (minor) = 20.8 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.52 – 7.48 (m, 1H), 7.27 (d, *J* = 7.8 Hz, 4H), 7.08 (d, *J* = 7.9 Hz, 7H), 6.94 (t, *J* = 7.4 Hz, 3H), 5.70 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.07, 141.56, 130.46, 128.39, 127.77, 126.75, 119.42, 116.24, 112.97, 112.76, 61.82, 54.03. HRMS (ESI+) m/z [M + H]$^{+}$ calcd for $C_{20}H_{16}N_{2}O$, 300.1300; found 300.1304.



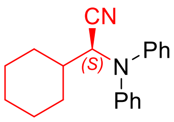
3fb

(S)-2-(diphenylamino)-2-(4-hydroxyphenyl)acetonitrile (3fb) Colourless solid; 241.3 mg, 99.9% yield; 94.6% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 18.8 min, tR (minor) =28.3 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 8.2 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 5H), 7.08 (d, *J* = 8.0 Hz, 5H), 6.95 (q, *J* = 8.0 Hz, 3H), 5.73 (s, 1H); ^{13}C NMR (126 MHz, Chloroform-*d*) 163.59, 142.07, 131.00, 128.91, 128.31, 127.29, 119.95, 116.75, 113.50, 113.29, 62.36 HRMS (ESI+) m/z [M + H]$^{+}$ calcd for $C_{20}H_{16}N_{2}O$, 300.1300; found 300.1305.



3gb

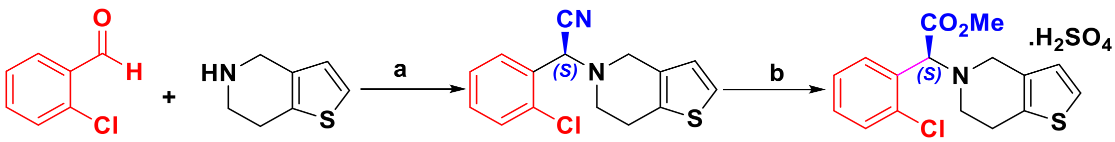
(S)-2-(diphenylamino)-2-(4-methoxyphenyl)acetonitrile (3gb). Colourless solid; 189.5 mg, 92% yield; 96.2% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) =5.0 min, tR (minor) = 5.6 min; ^{1}H NMR (500 MHz, Chloroform-d) δ 7.30 – 7.26 (m, 4H), 7.11 – 7.07 (m, 6H), 7.02 (d, J = 8.8 Hz, 2H), 6.96 – 6.90 (m, 3H), 5.76 (s, 1H), 3.90 (s, 3H).^{13}C NMR (126 MHz, Chloroform-d) δ 163.59, 142.07, 131.00, 128.31,127.29, 119.95, 116.75, 113.50, 113.29,62.36, 54.56. HRMS (ESI+) m/z [M + H]$^{+}$ calcd for $C_{21}H_{18}N_2O$, 314.1400; found 314.1402.



3hb

(S)-2-cyclohexyl-2-(diphenylamino)acetonitrile (3hb). Colourless solid; 176.1 mg, 92% yield; 96.1% ee; determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 90/10, flow rate: 1 mL/min, wavelength=210 nm: tR (major) = 9.5 min, tR (minor) = 13.0 min; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 7.8 Hz, 3H), 7.08 (d, *J* = 7.9 Hz, 5H), 6.93 (t, *J* = 7.4 Hz, 2H), 4.27 (d, *J* = 6.2 Hz, 1H), 1.89 (s, 1H), 1.85 – 1.80 (m, 2H), 1.75 – 1.70 (m, 3H), 1.27 (q, *J* = 5.0 Hz, 5H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 141.55, 127.77, 119.43, 116.24, 64.84, 40.72, 26.52, 26.20, 24.35, 23.87, 23.84 HRMS (ESI+) m/z [M + H]$^{+}$ calcd for $C_{20}H_{22}N_2$, 290.1800; found 290.1800.

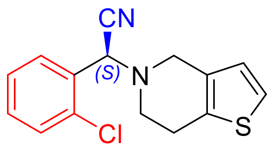
5. Procedure for the Synthesis of *S*-Clopidogrel*



4 **5** **6** **7**

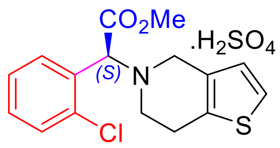
*Reaction Conditions (a) **4**(3 g, 21mmol), **5**(2.9 g, 21 mmol), TMSCN (2.0 g,21 mmol) DCM (20 ml) to give **6** (98% yield, 99.3% ee) ;(b) MeOH, H_2SO_4 to give **7** (73.2% yield,98.5% ee) ;(c) % ee determined by HPLC equipped with AD-H chiral columns and configuration was determined by relative retention time and specific rotation with literature data

In an inert environment 2-Chlorobenzaldehyde (3 g, 21mmol),4,5,6,7-tetrahydrothieno[3,2-c]pyridine (2.9 g, 21 mmol) TMSCN (2.0 g, 21 mmol), were introduced in a round bottom flask with dichloromethane (20 ml) as a solvent and catalyst V (0.2 mol%)The reaction mixture was stirred continuously for 15 minutes and monitored through TLC. The reaction mixture was treated with chloroform and washed with a saturated solution of sodium bisulphite. The organic phase was dried over anhydrous sodium sulphate. The solvent was then evaporated under reduced pressure and the crude was purified through column chromatography (n-hexane/ethyl acetate 80:20) to give (S)-2-(2-chlorophenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetonitrile (5.9 g , 98% yield).To this compound 6 esterification was done with MeOH(40 ml), and H_2SO_4(1 ml) and the reaction was continued for 4 days and monitored through TLC. The reaction mixture was treated with water followed by the addition of sodium carbonate and dichloromethane. After drying over Na_2SO_4 solvent was evaporated to obtain S-Clopidogrel (4.8 g,73.2% yield). The enantiomeric excess was determined by chiral stationary-phase HPLC analysis using AD-H chiral column.



6

(S)-2-(2-chlorophenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetonitrile(6): colourless solid 5.9 g,98% yield; 99.3%ee determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 60/40, flow rate: 1 mL/min, wavelength=210 nm : tR (major) =10.6min, tR (minor) = 12.2 min;^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.71 (s, 1H), 7.48 – 7.33 (m, 3H), 7.09 (d, *J* = 5.2 Hz, 1H), 6.71 (d, *J* = 5.2 Hz, 1H), 5.33 (s, 1H), 3.81 (d, *J* = 13.7 Hz, 1H), 3.67 (d, *J* = 13.7 Hz, 1H), 3.03 – 2.90 (m, 3H), 2.86 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 133.06, 131.36, 130.95, 129.02, 128.96, 128.47, 125.29, 123.51, 121.57, 113.65, 57.69, 47.88, 46.24, 24.04. HRMS (ESI+) m/z [M + H] $^+$ calcd for $C_{15}H_{13}ClN_2S$, 288.0500; found. 288.0502



7

methyl(S)-2-(2-chlorophenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetate(7): colourless solid 4.8 g,73.2% yield;98.5%ee determined by HPLC analysis (Daicel Chiralpak AD-H column, hexane/2-propanol = 60/40, flow rate: 1 mL/min, wavelength=210 nm: tR (major) =12.3 min, tR (minor) = 13.7 min;^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (dd, J = 7.3, 2.2 Hz, 1H), 7.41 (dd, J = 7.4, 1.9 Hz, 1H), 7.30 (d, J = 1.8 Hz, 1H), 7.28 (d, J = 2.3 Hz, 1H), 7.06 (d, J = 5.2 Hz, 1H), 6.67 (d, J = 5.2 Hz, 1H), 4.92 (s, 1H), 3.76 (d, J = 14.0 Hz, 1H), 3.73 (s, 3H), 3.63 (d, J = 14.1 Hz, 1H), 2.88 (s, 4H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 129.98, 129.82, 129.46, 127.21, 125.27, 122.78, 67.90, 52.24, 50.74, 48.34, 29.73, 25.53. HRMS (ESI+) m/z [M + H] $^+$ calcd for $C_{16}H_{16}ClN_2S$, 321.0600; found 321.0608

6. Recyclability Test (under scale-up condition)

The reaction was performed in a 250 mL round bottom flask at 25 ^{o}C in an inert environment, benzaldehyde **1a** (8.4 g, 80 mmol), aniline **2a** (7.4 g, 80 mmol), trimethylsilyl cyanide (7.9 g, 80 mmol), and catalyst **V** (0.2 mol%) were introduced in a dry glass tube with dichloromethane (120 ml) as a solvent. The reaction mixture was stirred continuously for 15 minutes and monitored through TLC. After completion of reaction, solvent was removed *in-vacuo*. The reaction mixture was dissolved in cold diethyl ether (100x3 times) and organic layer was washed with saturated solution of sodium bisulphite. The organic phase was dried over anhydrous sodium sulphate. The solvent was then evaporated under reduced pressure to afford 3aa (16.4g; 99.2% yield). For the next cycle, in the same flask (containing catalyst), 120 mL dichloromethane was charged and stirred for 15 min, followed by subsequent catalytic cycles under similar conditions as described above.

7. Time-dependent NMR:

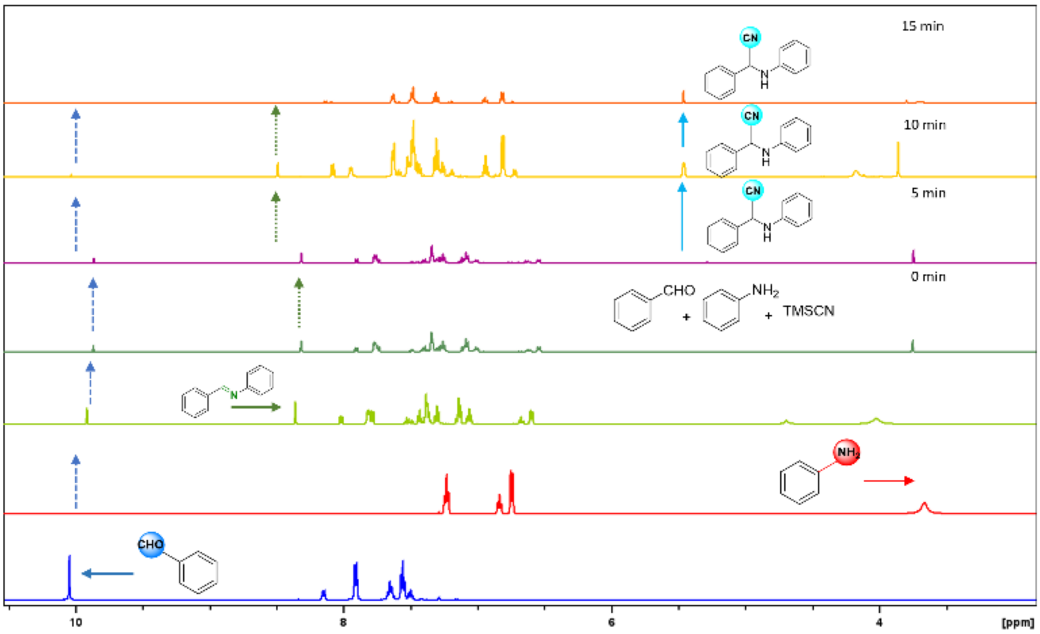
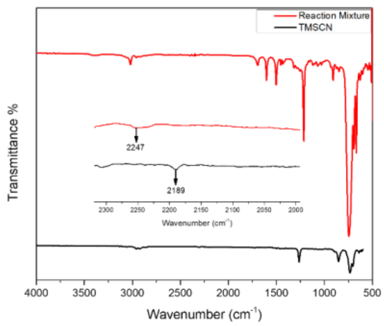


Figure 1

In Figure S1 The time dependent NMR showed the formation of imine intermediate and it was ascertained by the downfield value of chemical shift i.e. 8.91 ppm. As the reaction progresses the α-aminonitrile moiety starts forming as the upfield value of 5.02 ppm of Hydrogen attached to quaternary carbon of α-aminonitrile starts appearing. Within the due course of time eventually, the chemical shift value of the imine intermediate and aldehyde would disappear completely within 15 minutes of time

8. IR and UV-visible spectroscopic study-



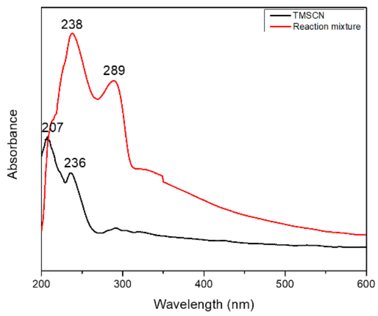


Figure 2 **Figure 3**

In figure S2: IR spectrum, the peak intensities at 1697cm^{-1}(CO), 2189cm^{-1} (CN) for aldehyde and TMSCN respectively were diminished in the cyanated product. The characteristic peaks at 3021cm^{-1} (N-H) and 2247cm^{-1} (CN) indicate the formation of the α-aminonitrile moiety.

In Figure S3: of the UV absorbance spectrum, TMSCN shows a low-intensity band at 207 nm and a high-intensity band at 236 nm due to n-π* and π- π* transition respectively. In a similar way, the formation of α-aminonitrile moiety was confirmed by the shift in n-π*(238 nm) and π- π* transition (289 nm). The shift in absorbance maxima is due to the presence of a benzene chromophore.

9. ^{29}Si-NMR

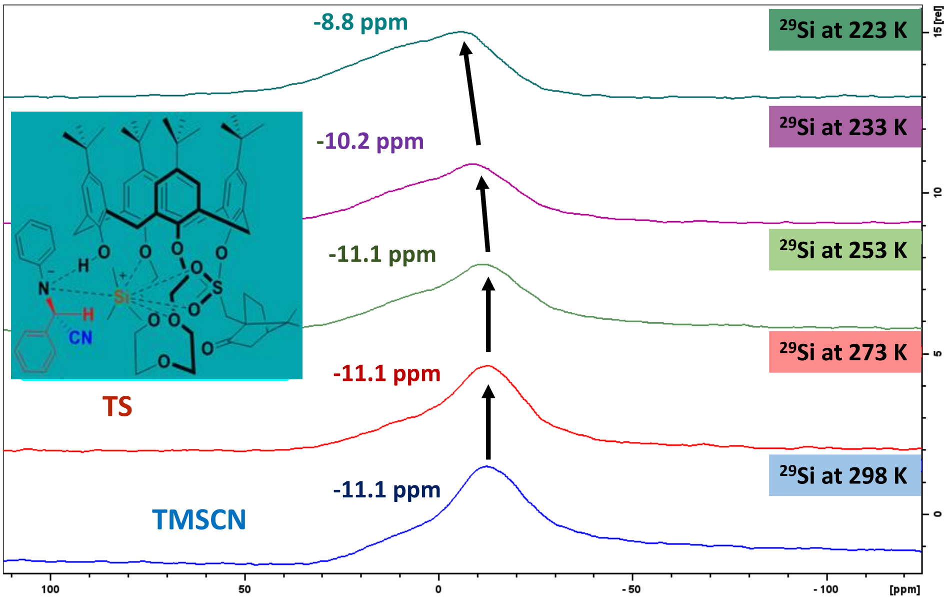


Figure S4: ^{29}Si(500MHz) analysis was carried out at a temperature range of rt to -50 °C. All experiments were performed in $CDCl_3$.^{29}Si-NMR Spectra were recorded and scaled from TMS[2]

10. HRMS

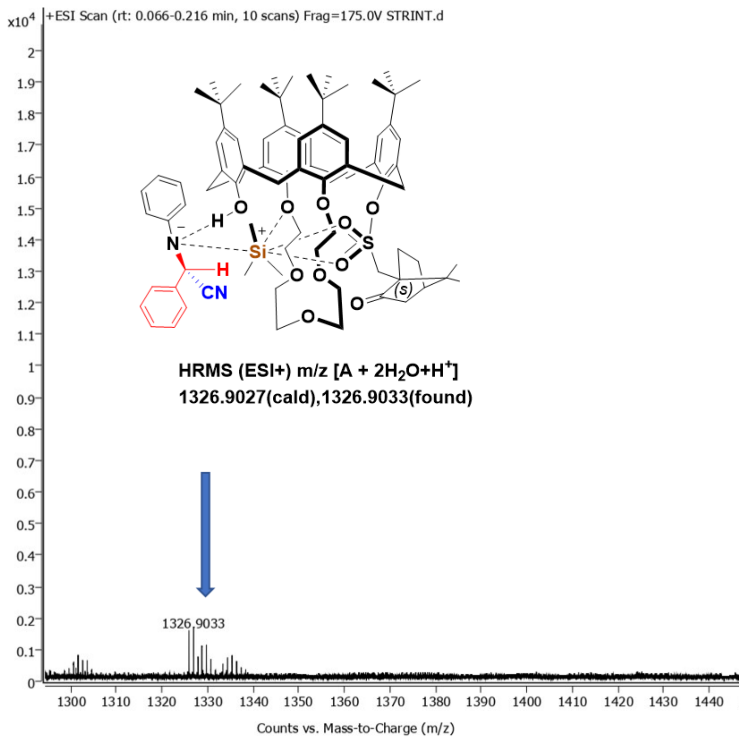
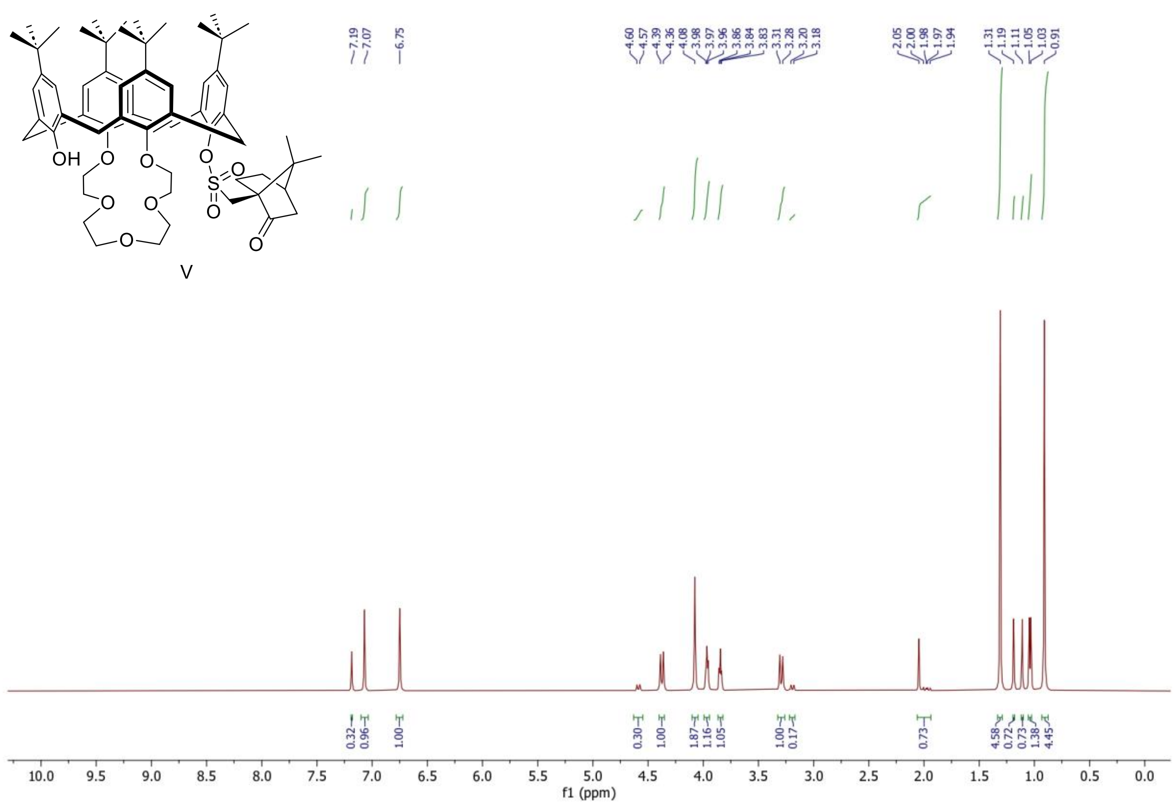
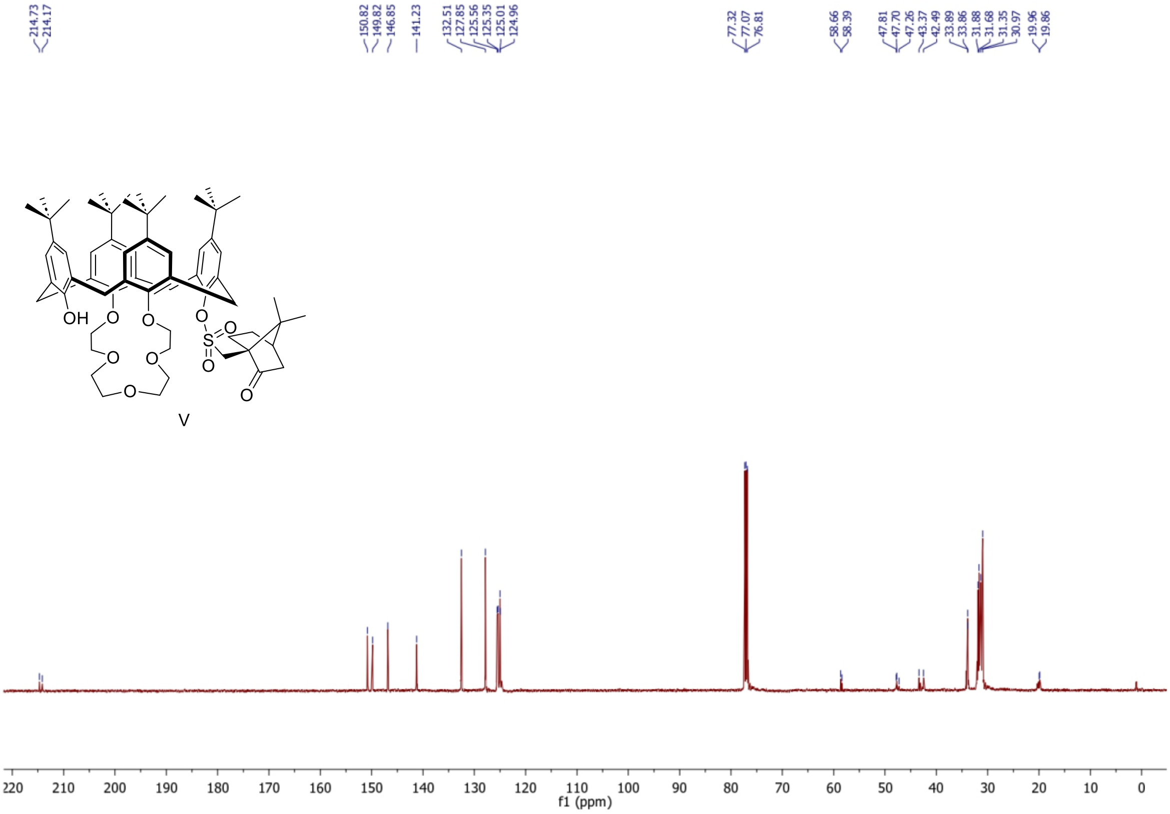


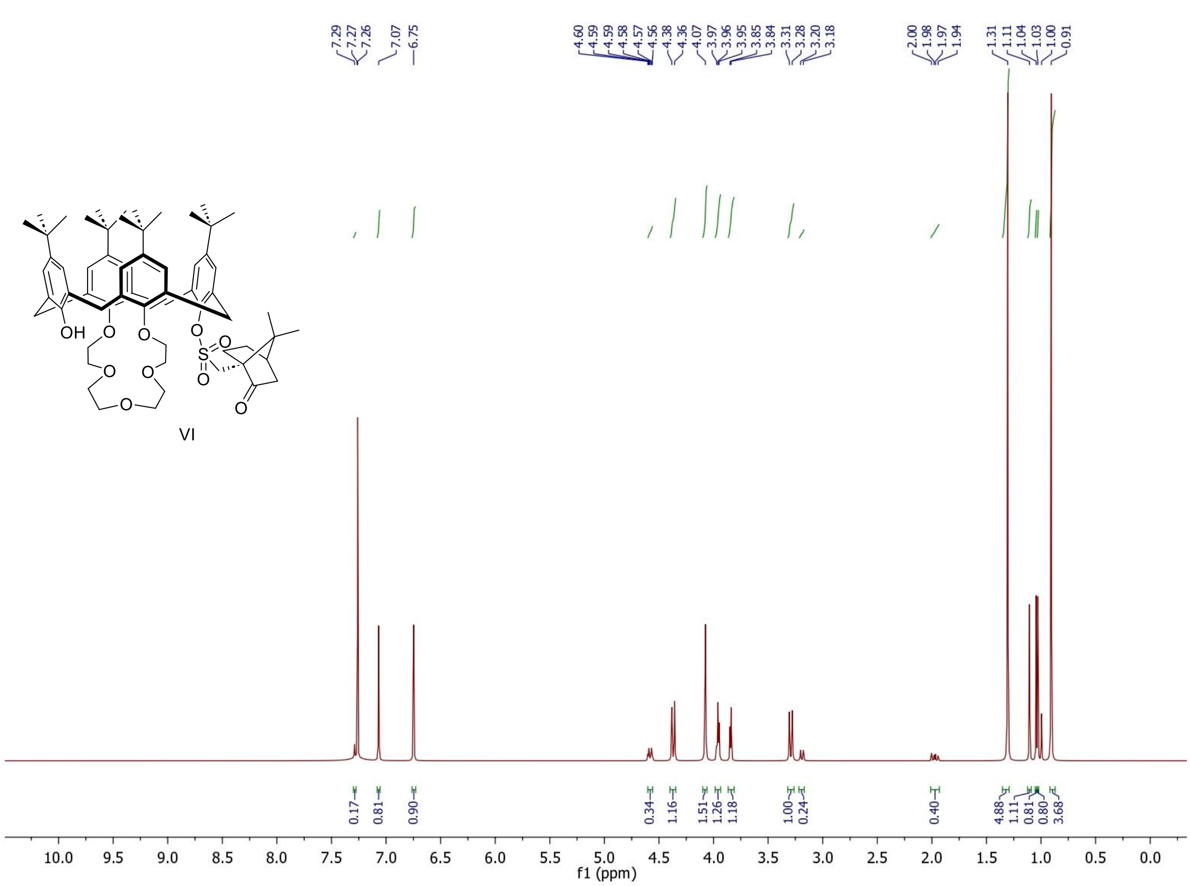
Figure S5: ESI-MS analysis of Transition state

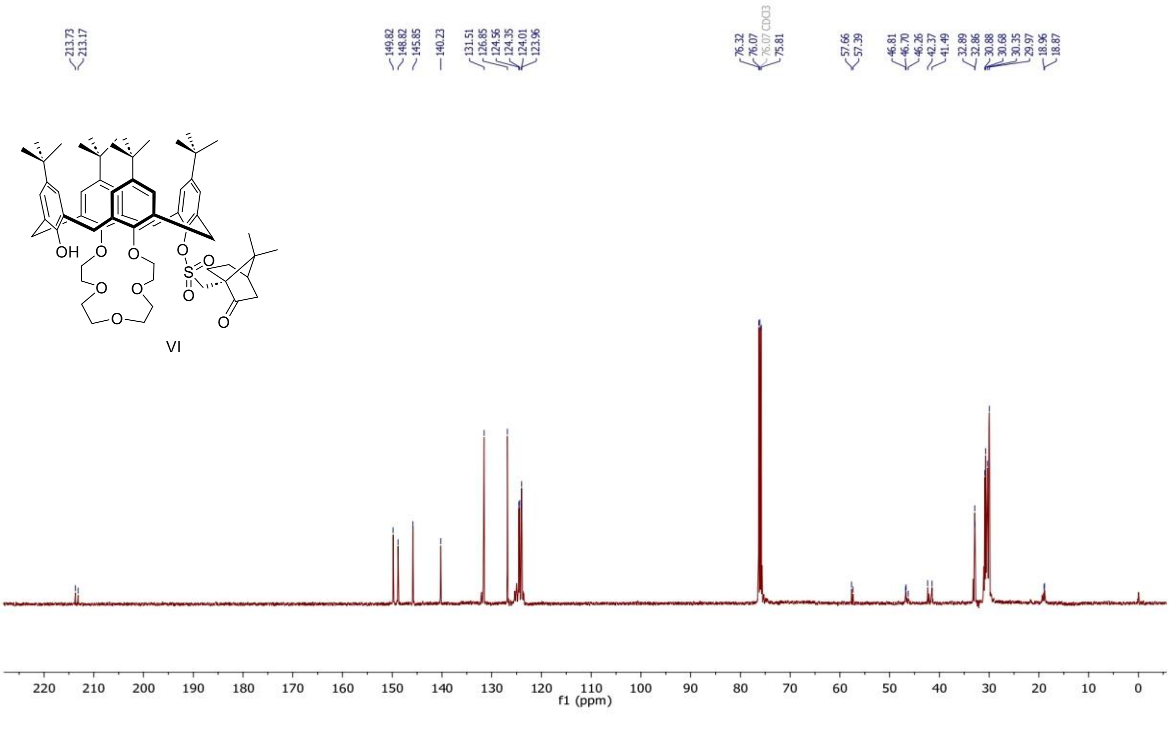
11. NMR (Catalyst-V)



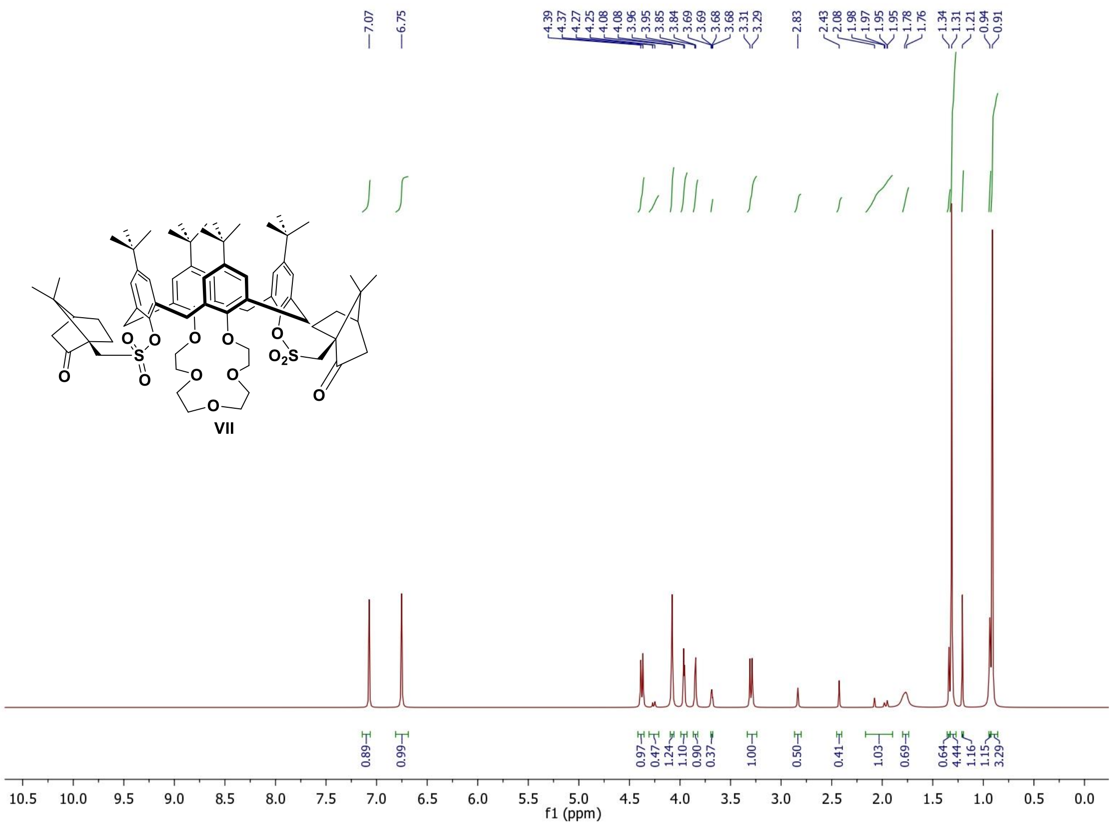


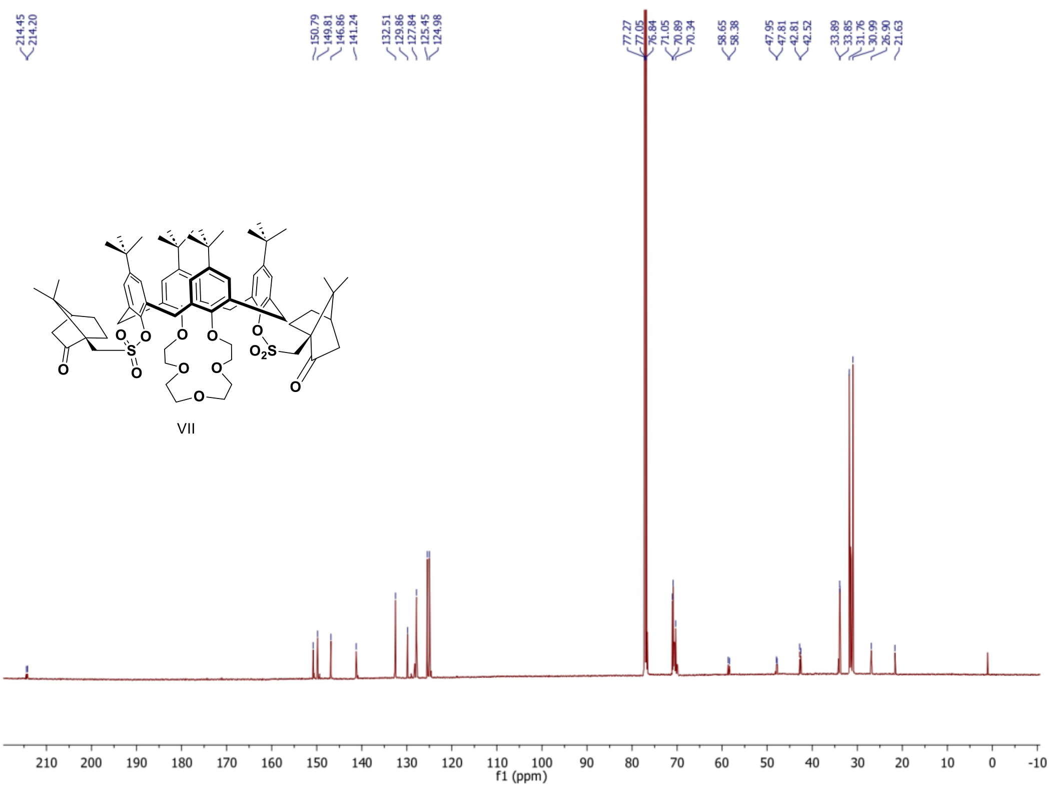
Catalyst-VI



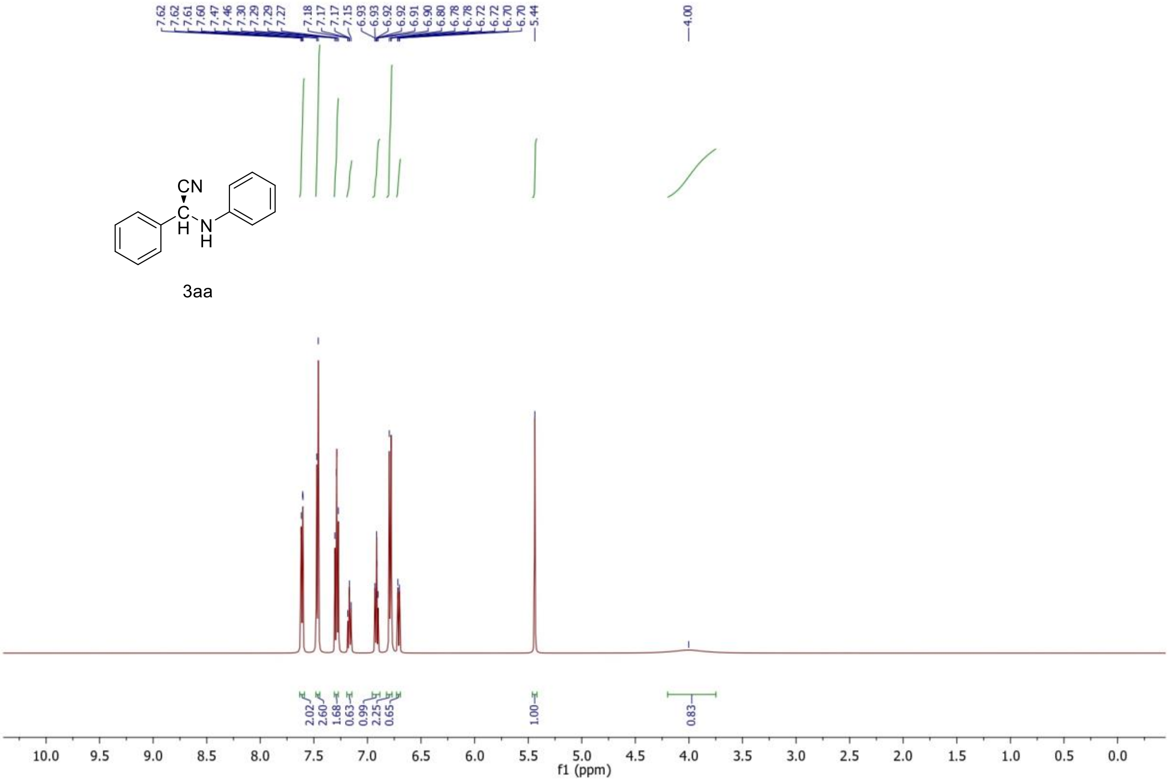


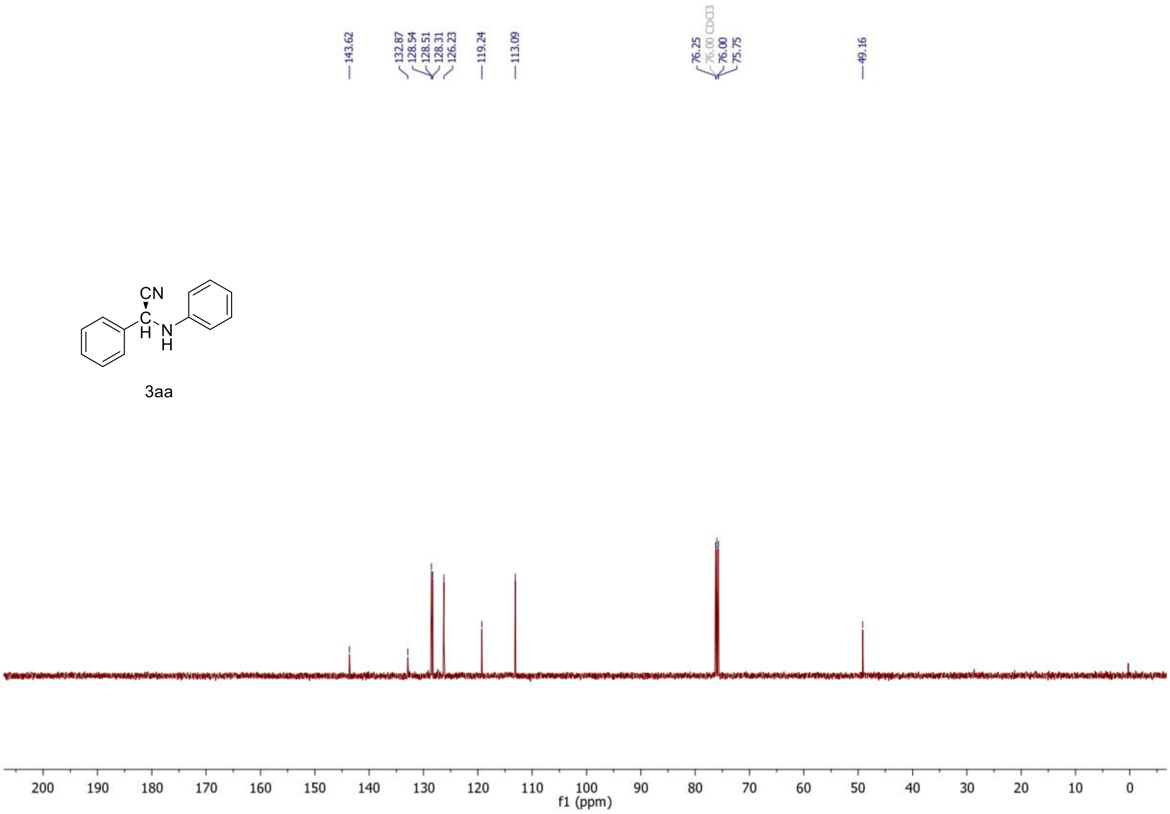
Catalyst VII



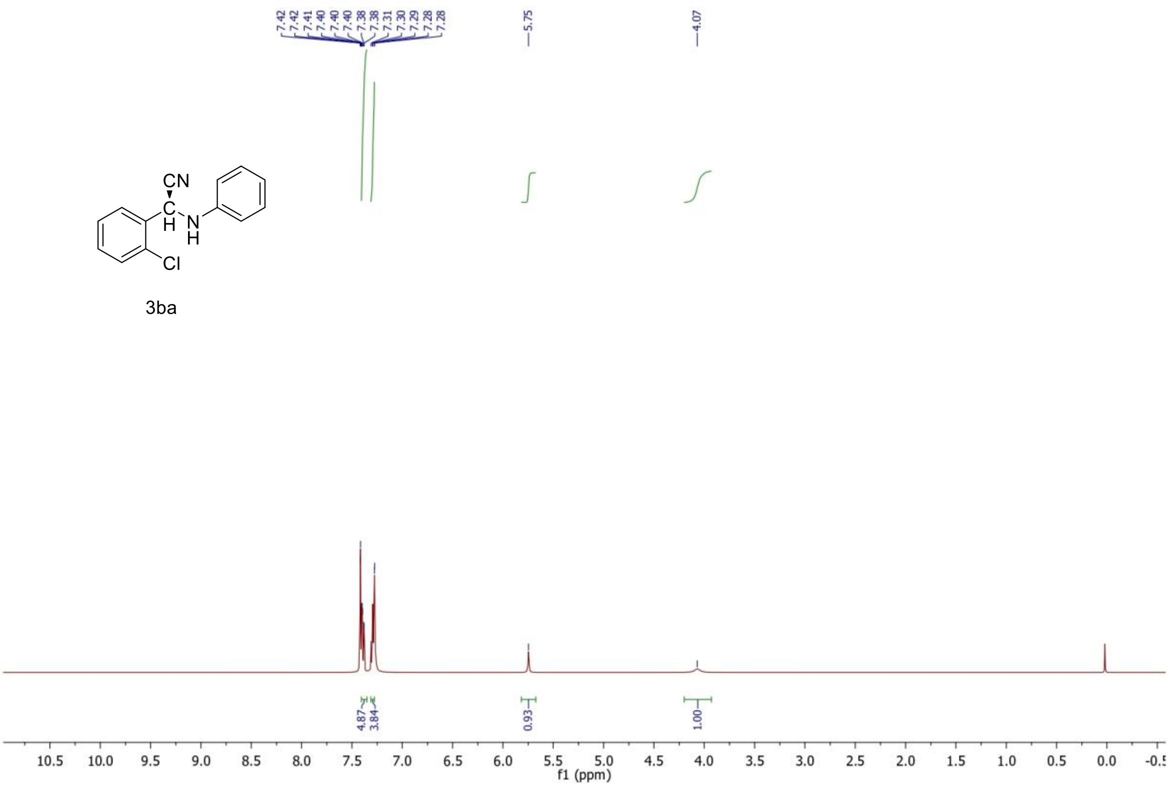


3aa





3ba



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7.38
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7.29
7.28
7.28
5.75
4.07
CN
C
H
N
H
Cl
3ba
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3.84
0.93
1.00
10.5
10.0
9.5
9.0
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6.5
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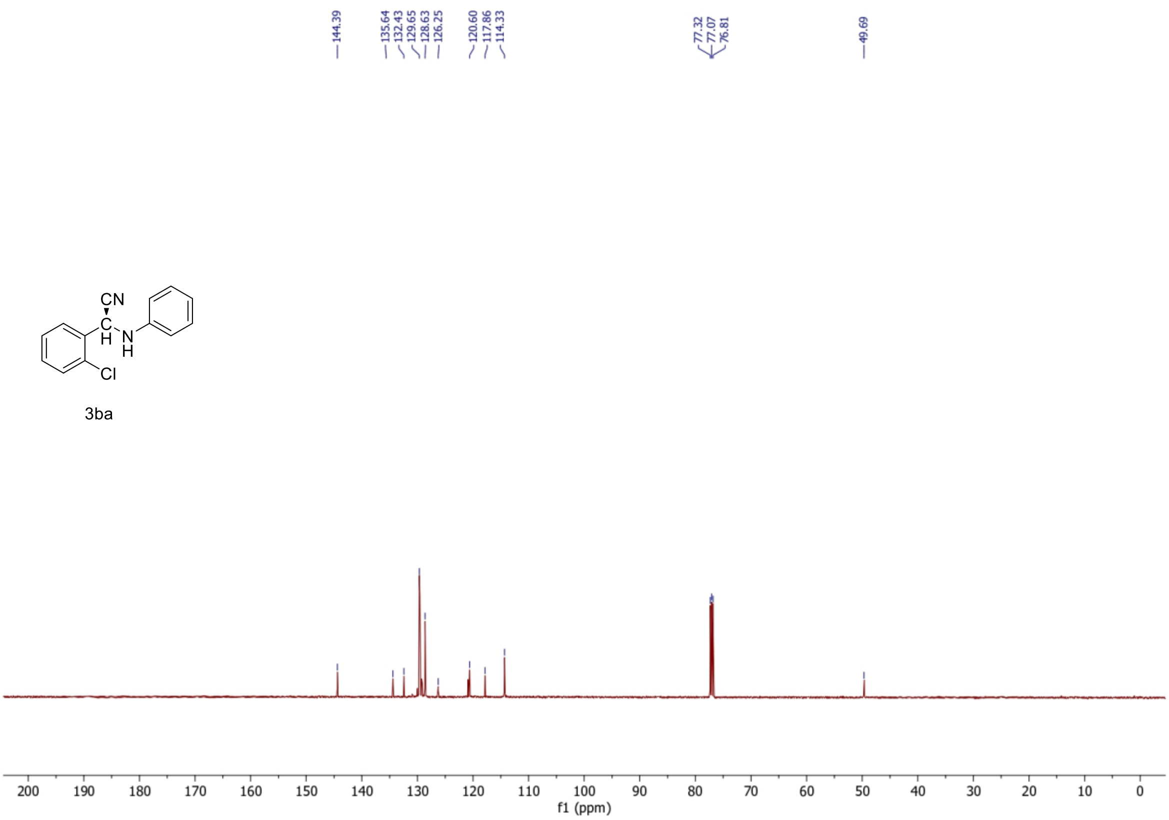
f1 (ppm)



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N
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Cl
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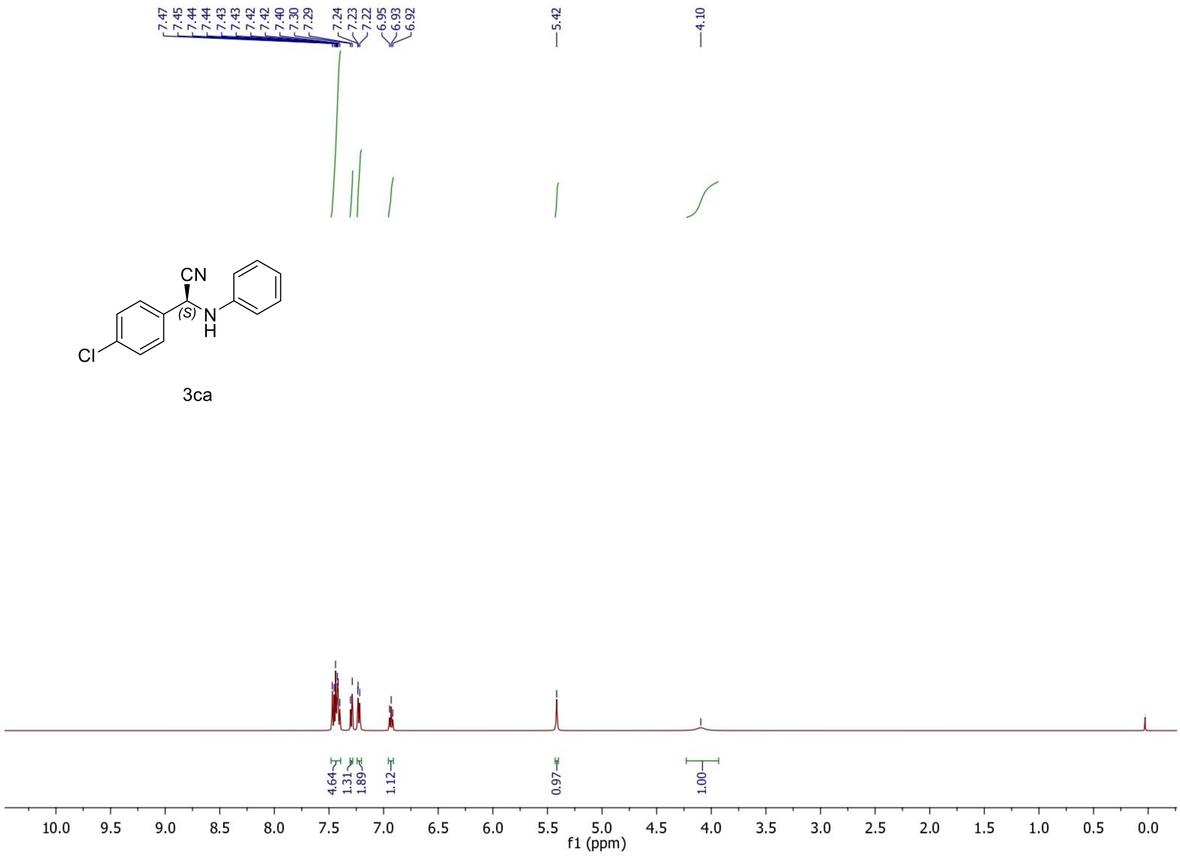
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3ca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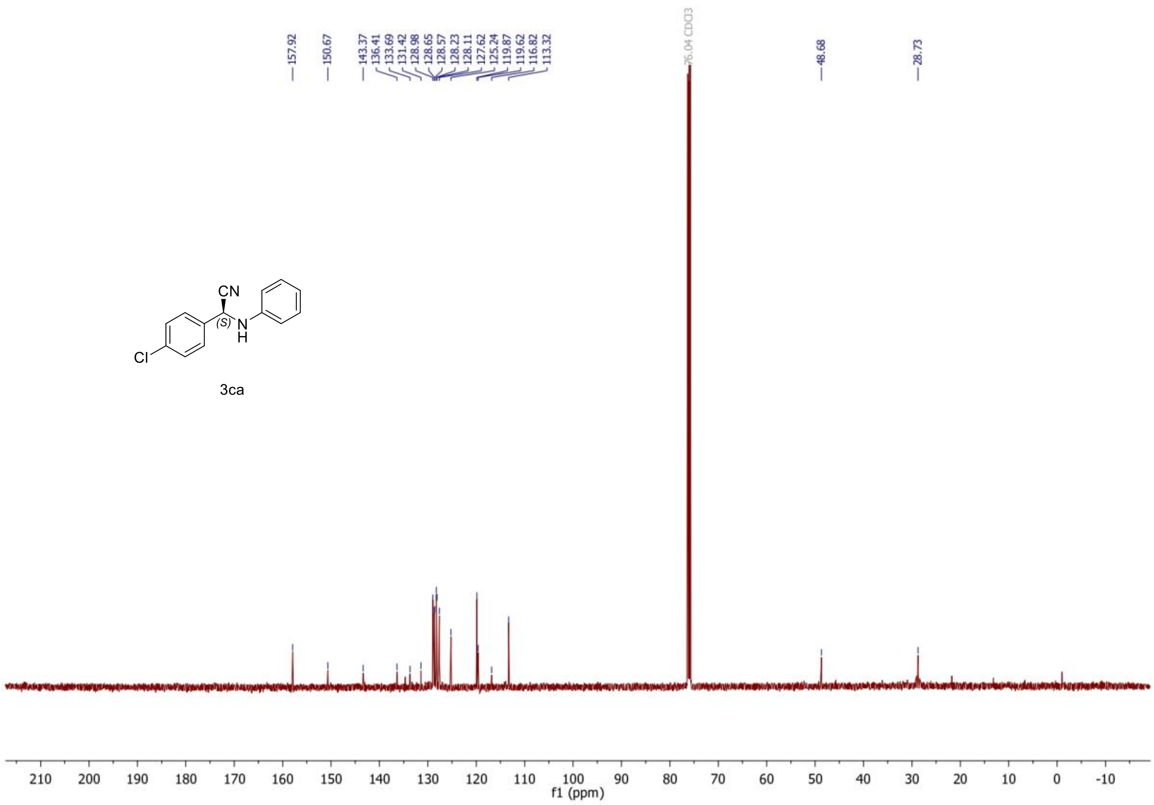
5.42
4.10
CN
(S)
N
H
Cl
3ca
4.64 1.31 1.89 1.12 0.97 1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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48.68
28.73
CN
(S)
N
H
Cl
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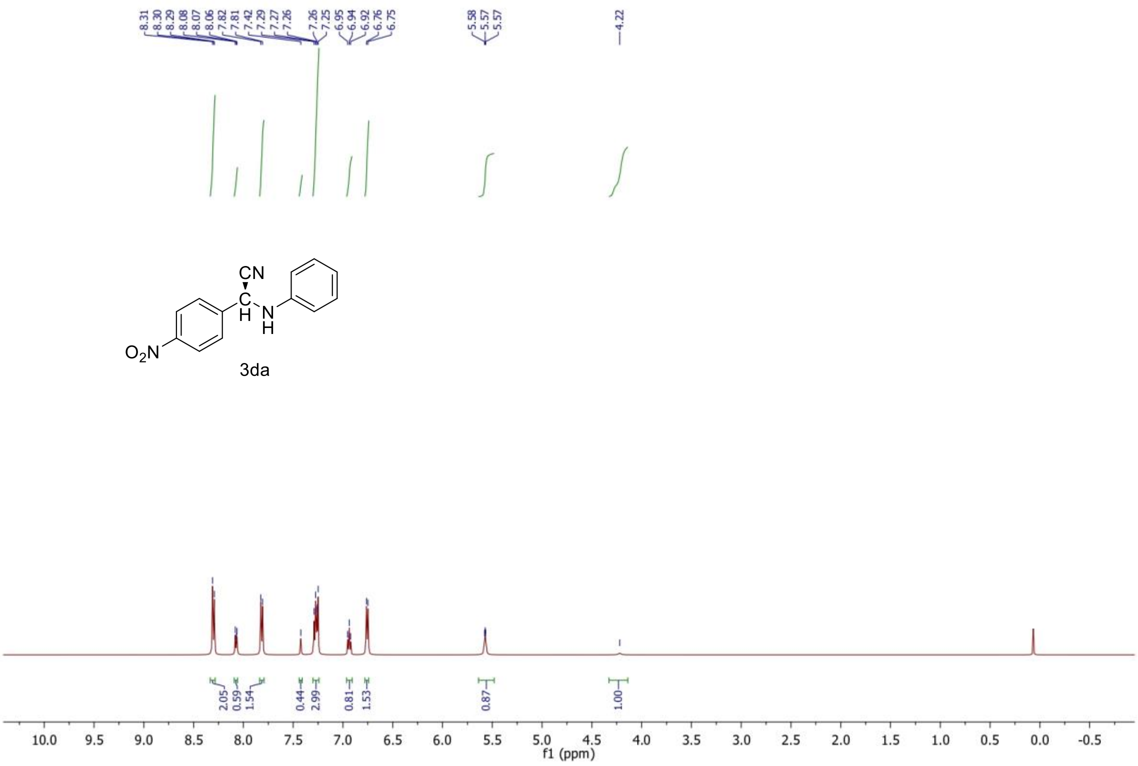
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

3da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5.57
5.57
4.22
CN
H
N
H
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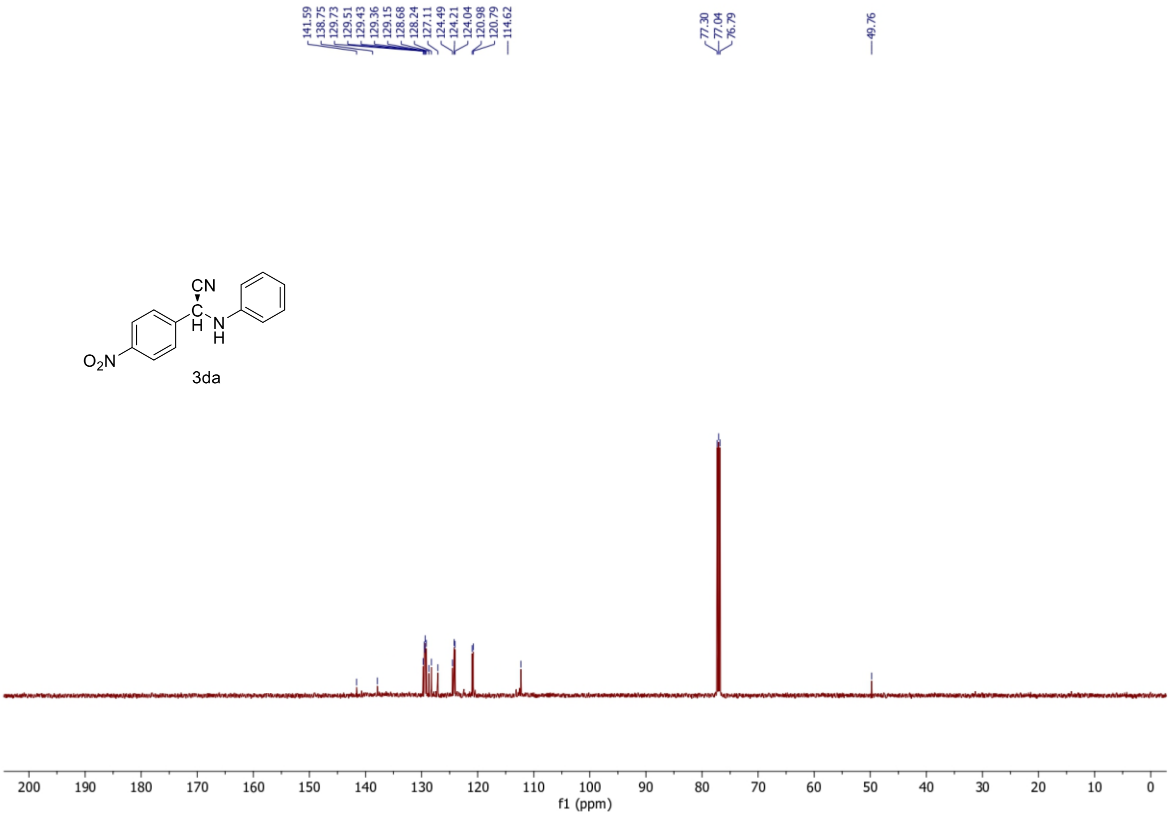
f1 (ppm)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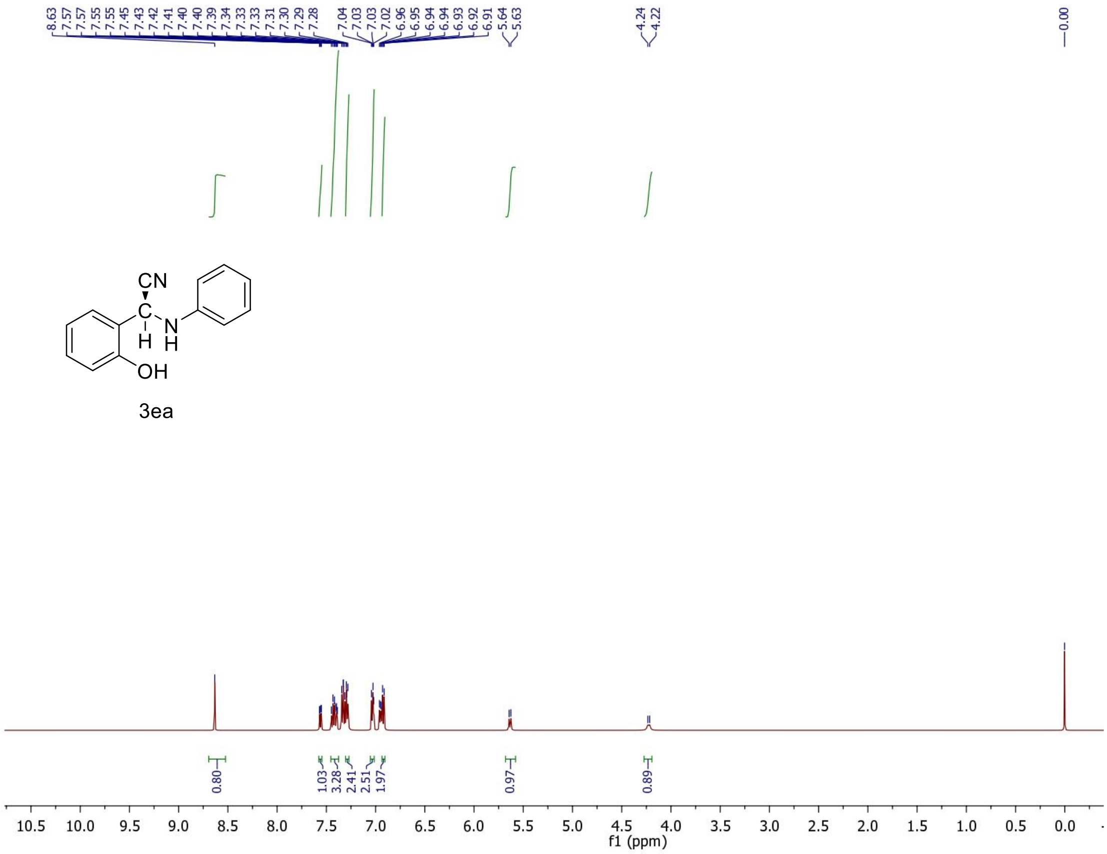
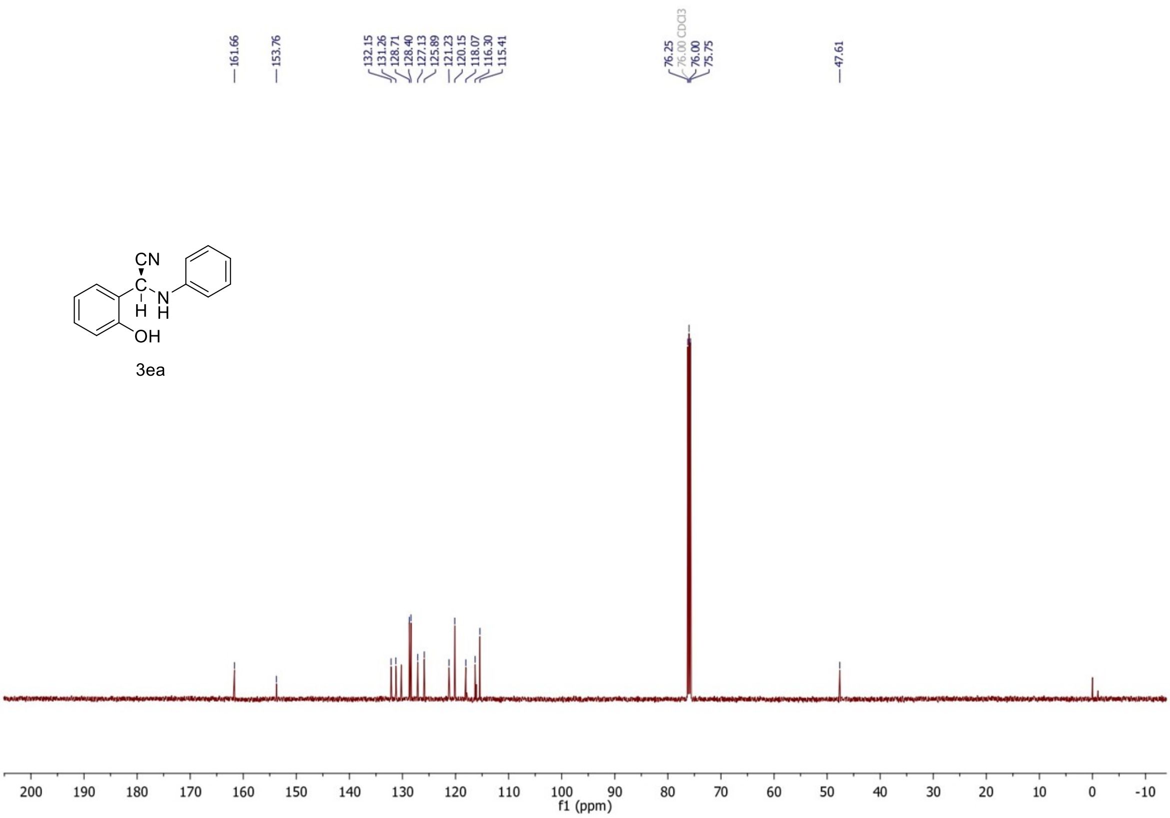
77.30
77.04
76.79
49.76
CN
H
N
H
O_2N
3da
f1 (ppm)

3ea

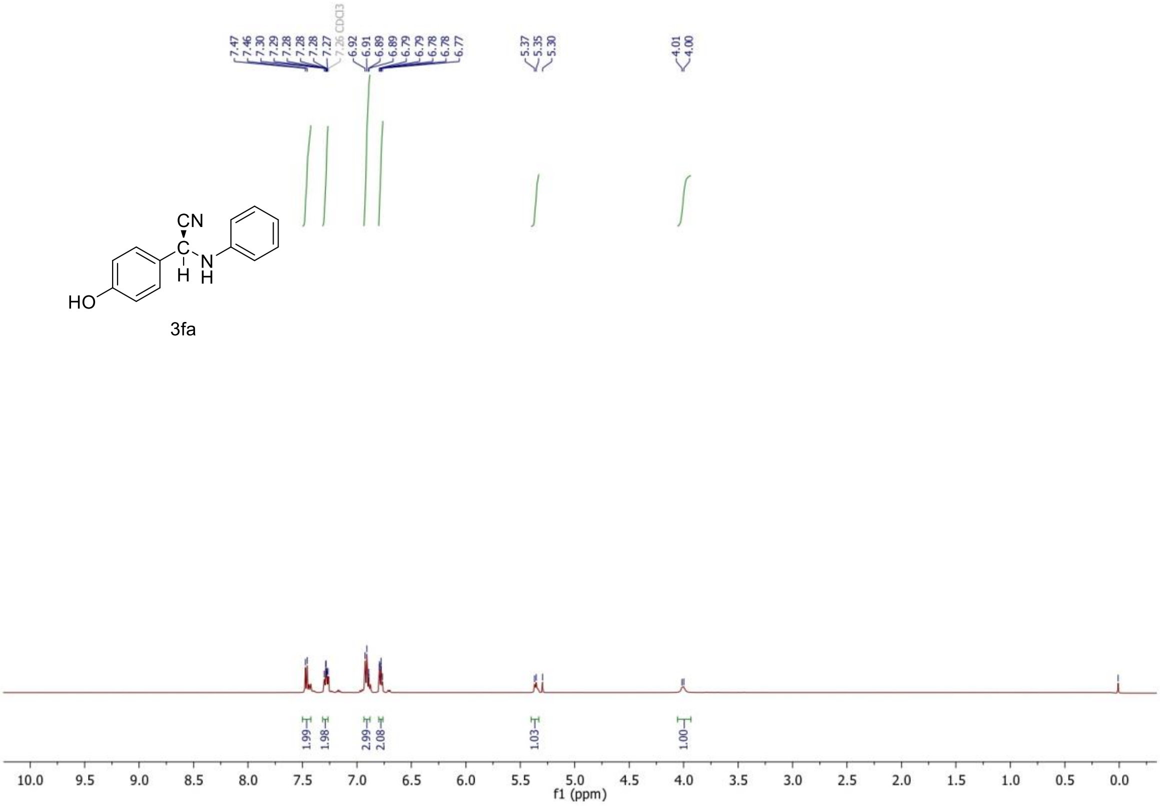


8.63 7.57 7.57 7.55 7.55 7.45 7.43 7.42 7.41 7.40 7.40 7.39 7.34 7.33 7.33 7.31 7.30 7.29 7.28 7.04 7.03 7.03 7.02 6.96 6.95 6.94 6.94 6.93 6.92 6.91 5.64 5.63
4.24 4.22
0.00
CN
C
H
N
H
OH
3ea
0.80
1.03 3.28 2.41 2.51 1.97
0.97
0.89
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

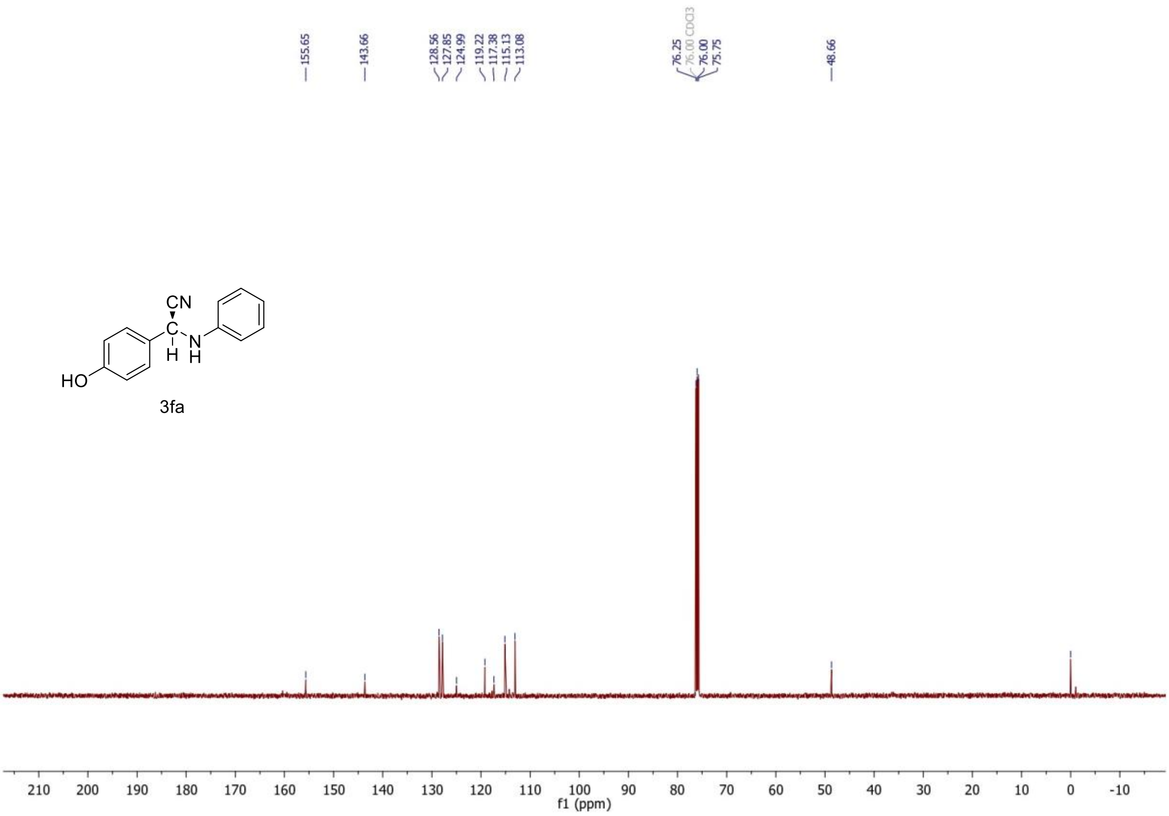


161.66
153.76
132.15 131.26 128.71 128.40 127.13 125.89 121.23 120.15 118.07 116.30 115.41
76.25 76.00 CDCl3 76.00 75.75
47.61
CN
C
H
N
H
OH
3ea
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

3fa

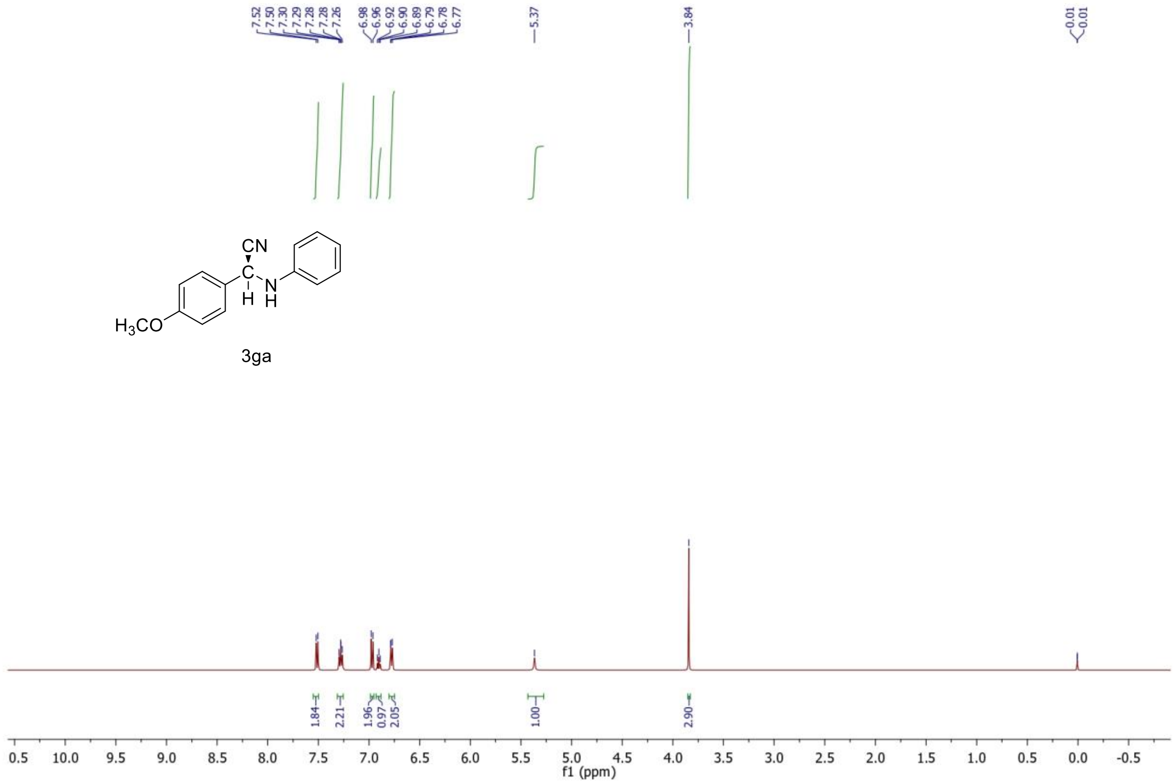


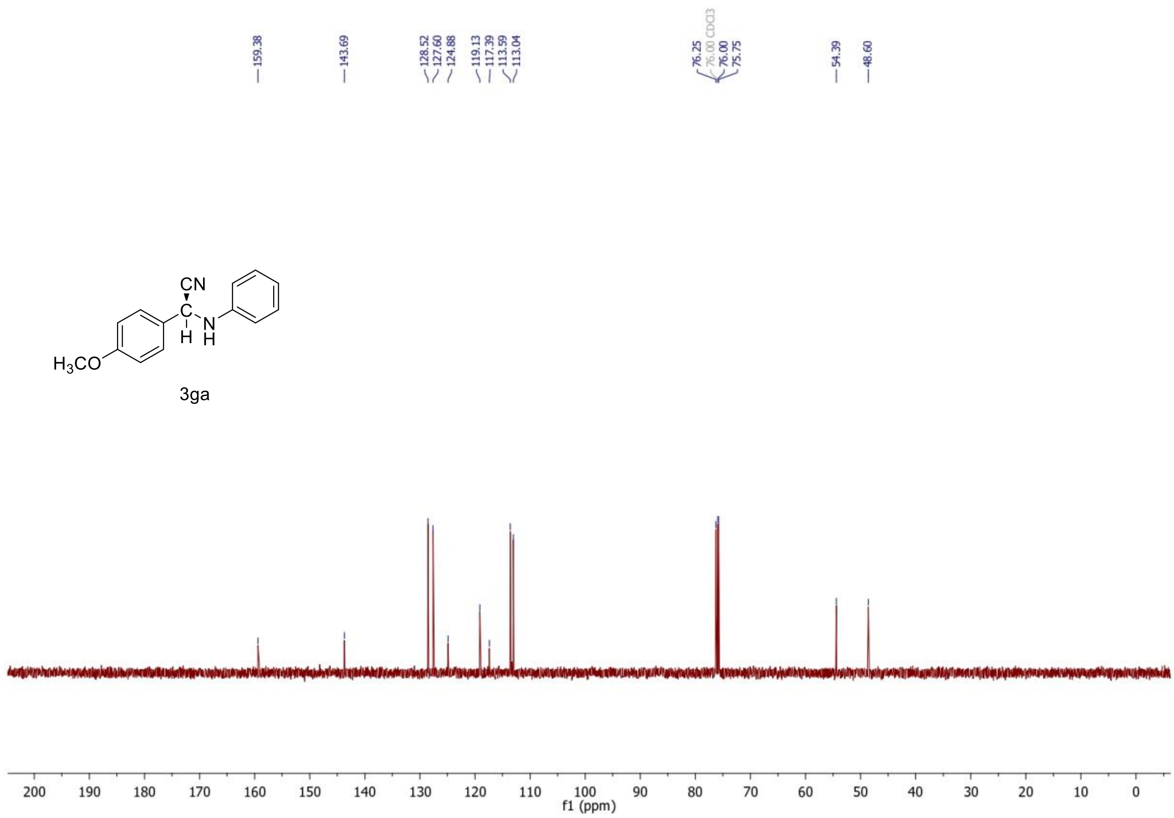
7.47
7.46
7.30
7.29
7.28
7.28
7.28
7.27
7.26 CDCl3
6.92
6.91
6.89
6.89
6.79
6.79
6.78
6.78
6.77
5.37
5.35
5.30
4.01
4.00
CN
C
H
N
H
HO
3fa
1.99
1.98
2.99
2.08
1.03
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



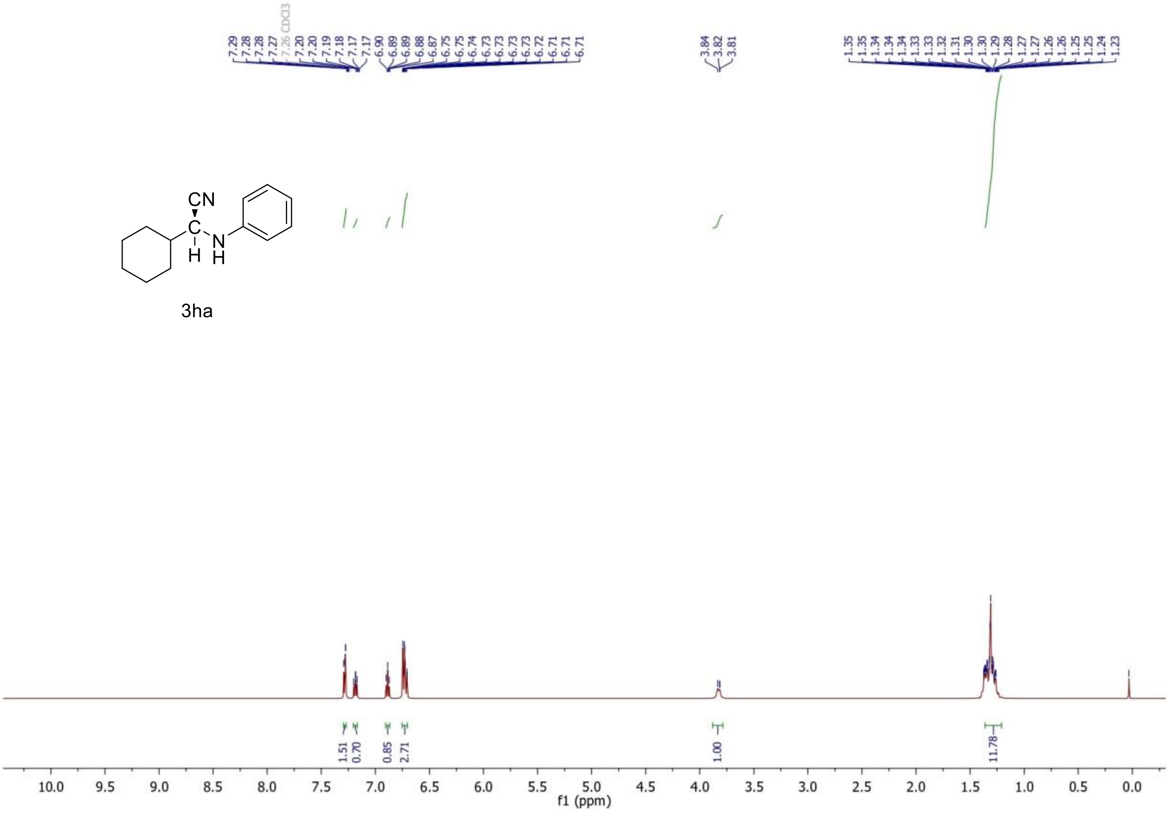
155.65
143.66
128.56
127.85
124.99
119.22
117.38
115.13
113.08
76.25
76.00 CDCl3
76.00
75.75
48.66
CN
C
H
N
H
HO
3fa
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

3ga

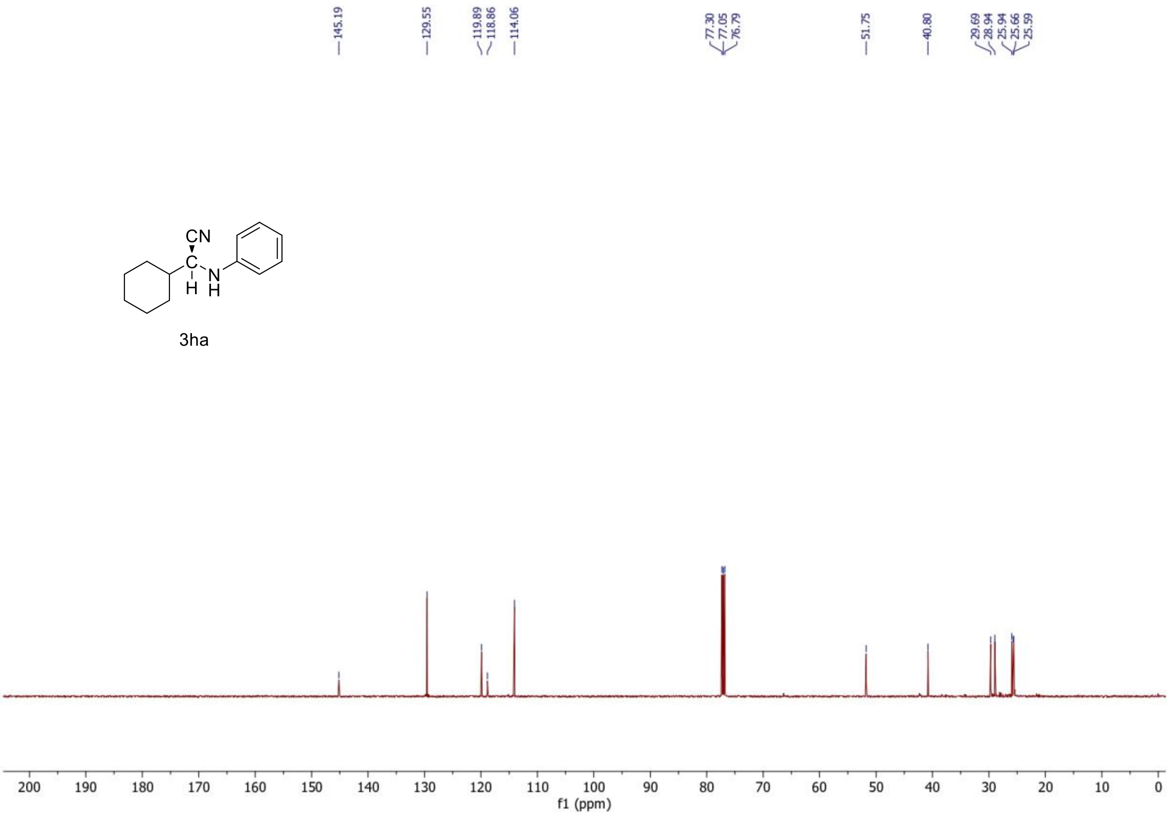

7.52 7.50 7.30 7.29 7.28 7.28 7.26 6.98 6.96 6.92 6.90 6.89 6.79 6.78 6.77
5.37
3.84
0.01 0.01
H_3CO
CN
C
H
N
H
3ga
1.84 2.21 1.96 0.97 2.05
1.00
2.90
f1 (ppm)


159.38
143.69
128.52 127.60 124.88
119.13 117.39 113.59 113.04
76.25 76.00 CDCl3 76.00 75.75
54.39
48.60
H_3CO
CN
C
H
N
H
3ga
f1 (ppm)

3ha

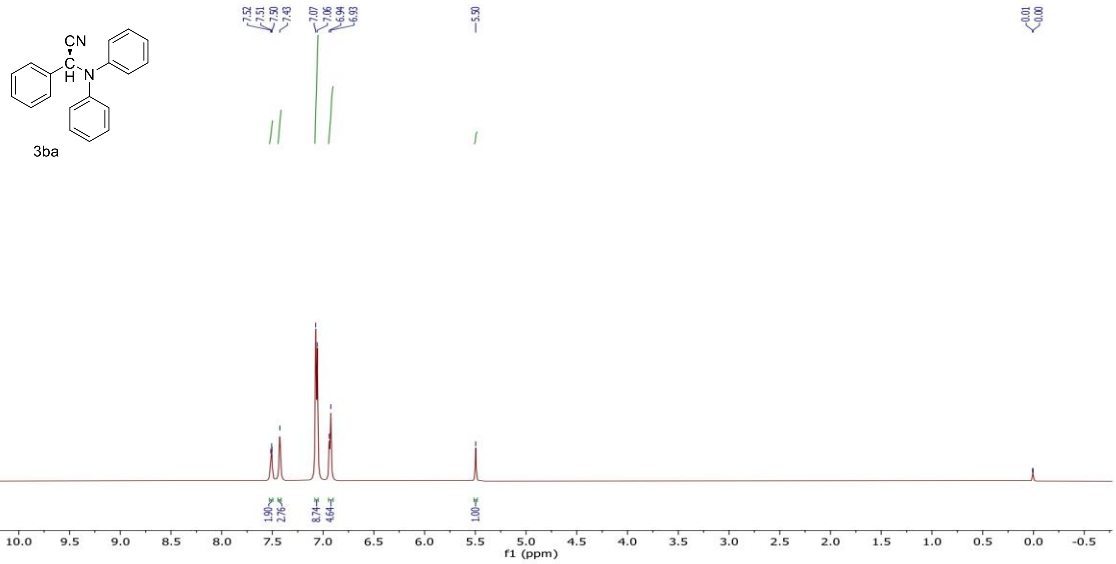


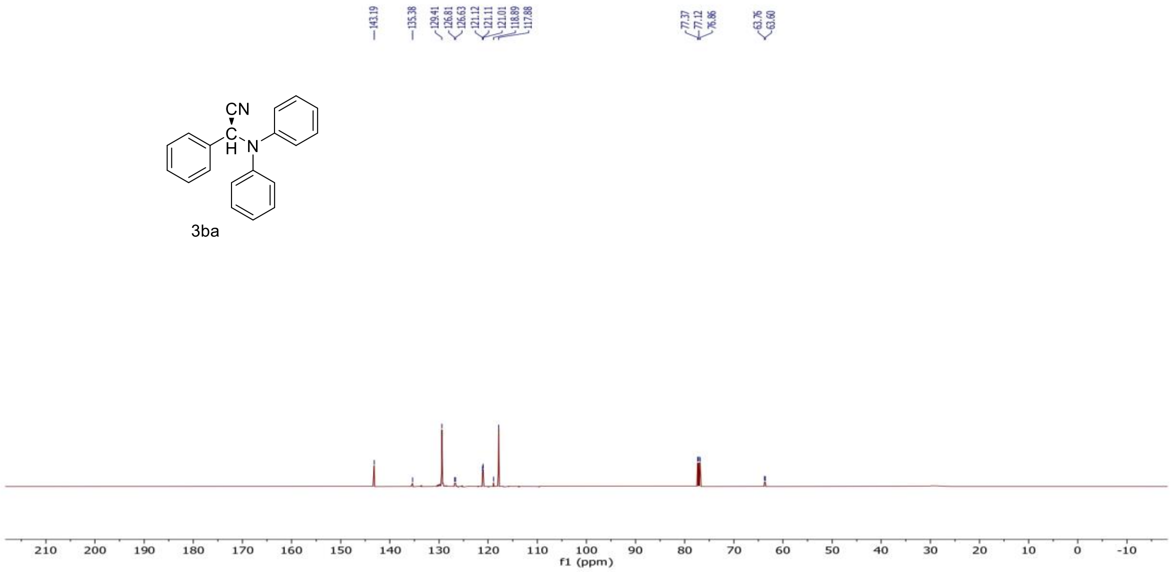
CN
C
H
N
H
3ha
7.29 7.28 7.28 7.27 7.26 CDCl3 7.20 7.20 7.19 7.18 7.17 7.17 6.90 6.89 6.89 6.88 6.87 6.75 6.75 6.74 6.73 6.73 6.73 6.72 6.71 6.71 6.71
3.84 3.82 3.81
1.35 1.35 1.34 1.34 1.33 1.33 1.32 1.31 1.30 1.30 1.29 1.28 1.27 1.27 1.26 1.26 1.25 1.25 1.24 1.23
1.51 0.70 0.85 2.71 1.00 11.78
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



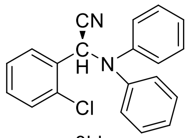
CN
C
H
N
H
3ha
145.19
129.55
119.89 118.86
114.06
77.30 77.05 76.79
51.75
40.80
29.69 28.94 25.94 25.66 25.59
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3ba

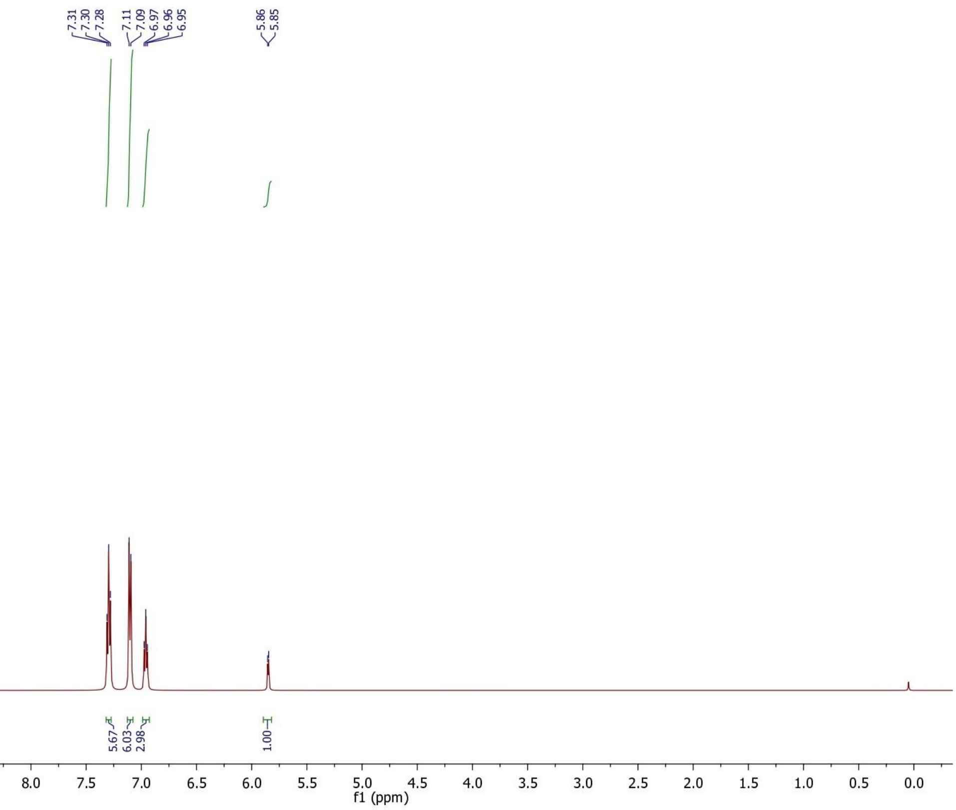


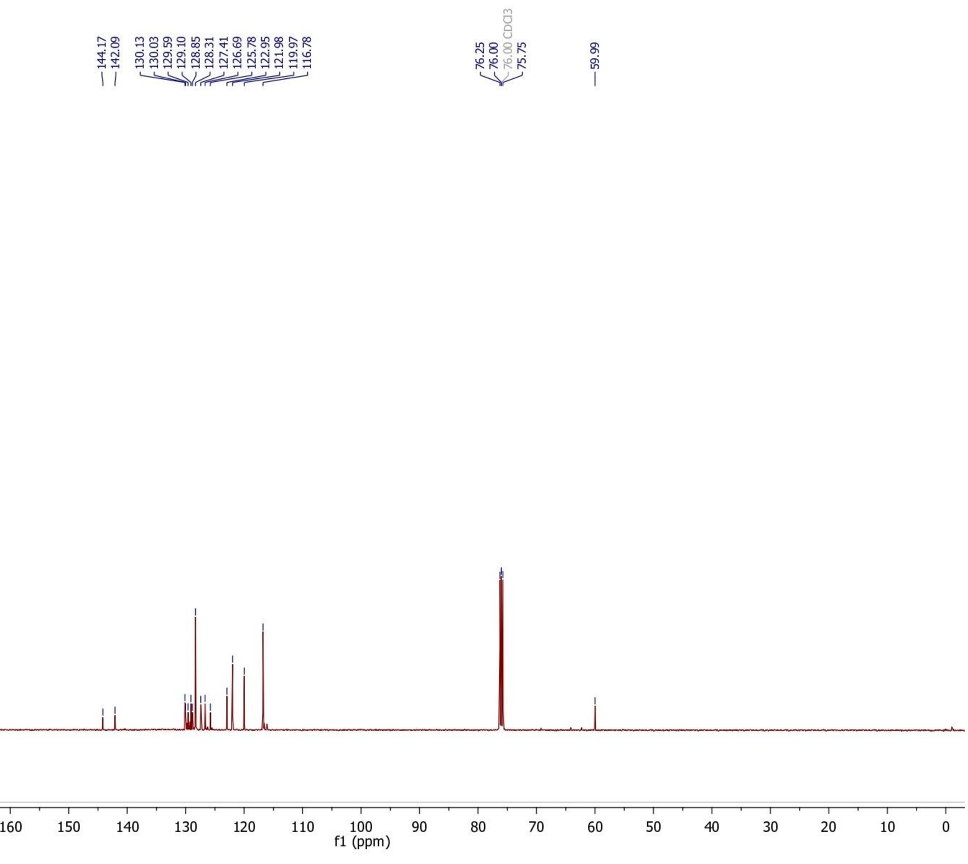


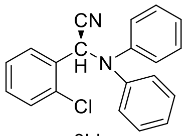
3bb


CN
C
H
N
Cl

3bb

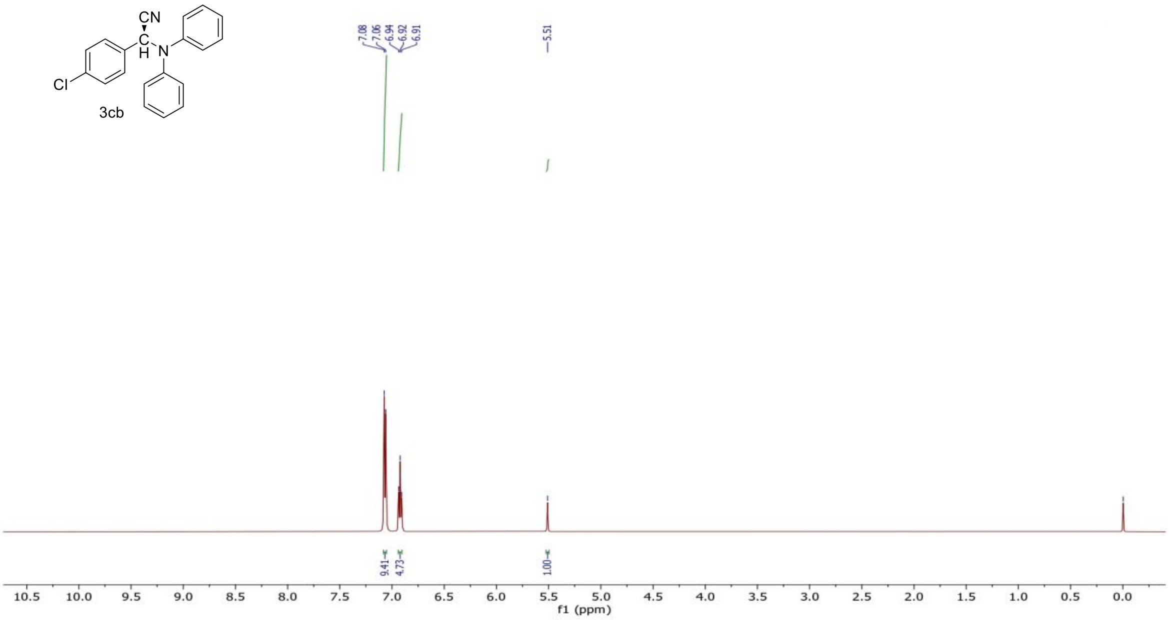

7.31
7.30
7.28
7.11
7.09
6.97
6.96
6.95
5.86
5.85
5.67
6.03
2.98
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

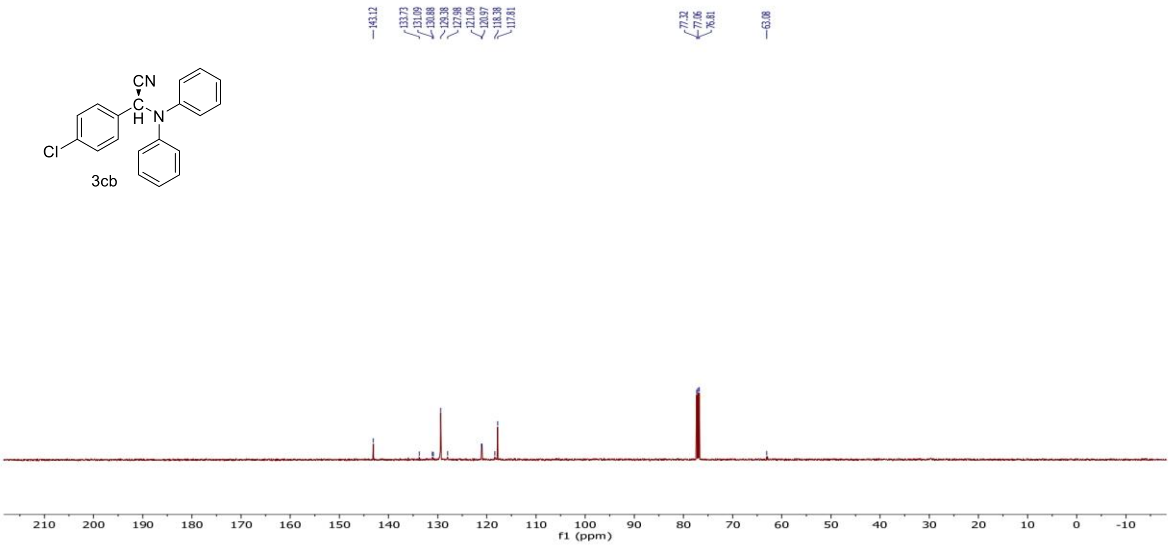

144.17
142.09
130.13
130.03
129.59
129.10
128.85
128.31
127.41
126.69
125.78
122.95
121.98
119.97
116.78
76.25
76.00
76.00 CDCl3
75.75
59.99
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CN
C
H
N
Cl

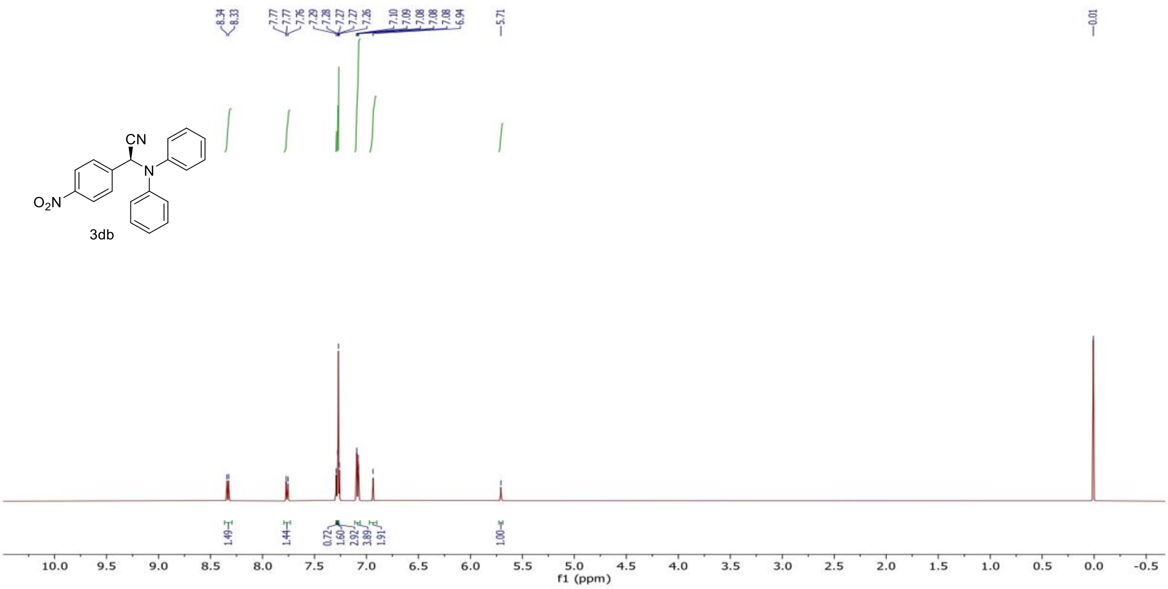
3bb

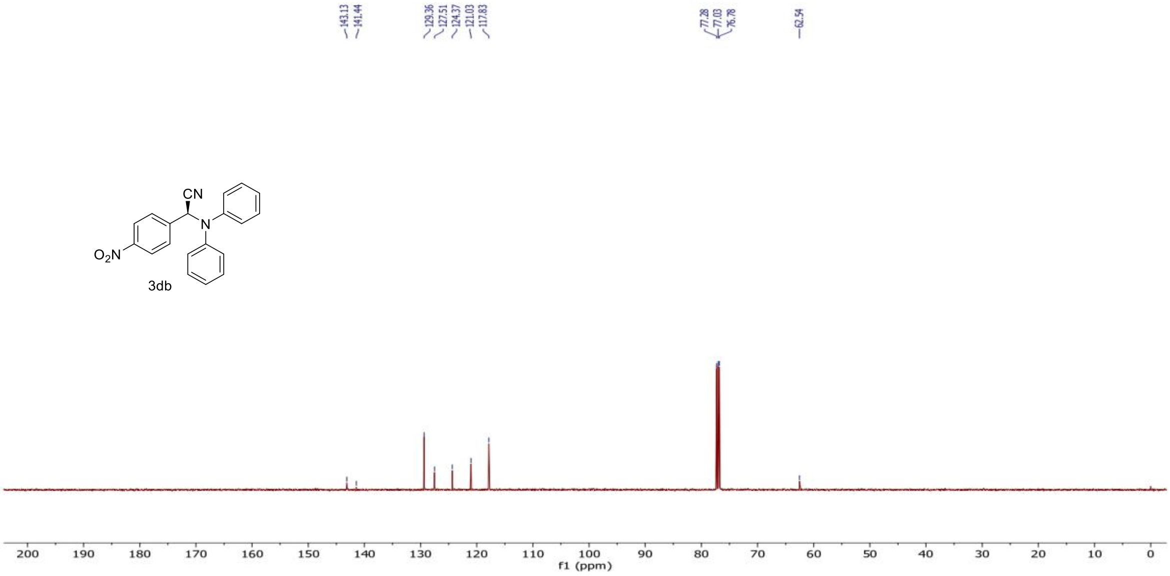
3cb



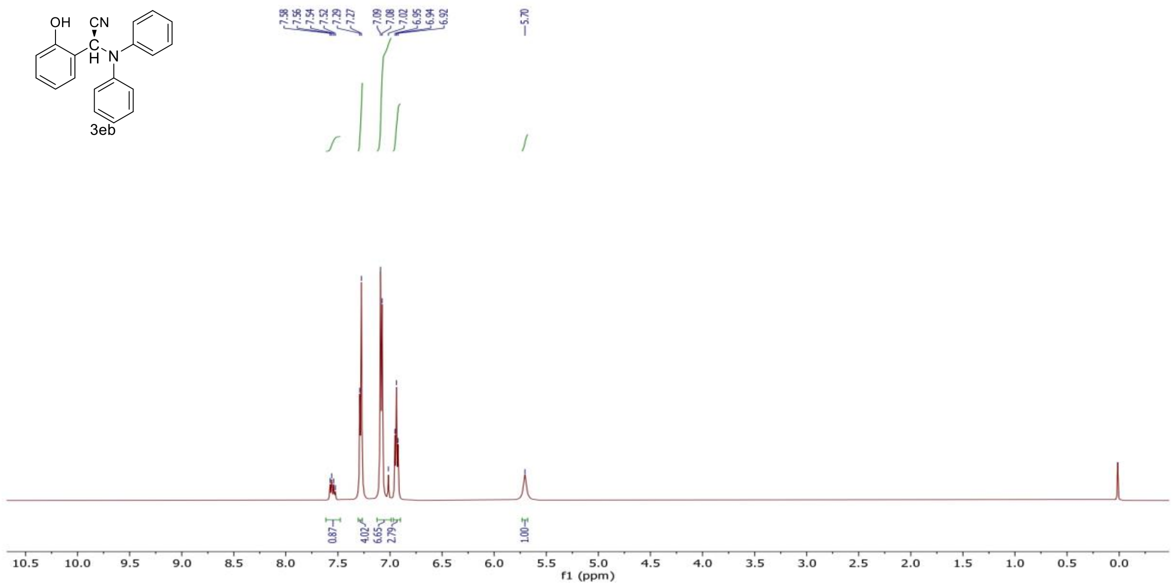


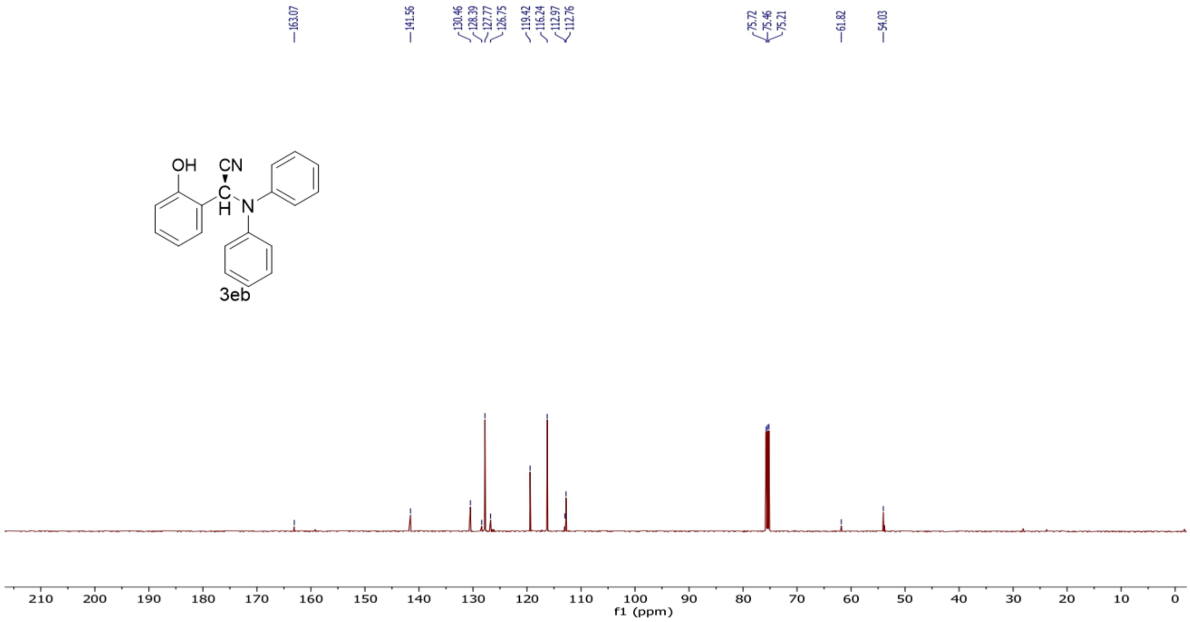
3db


8.34
8.33
7.77
7.77
7.76
7.29
7.28
7.27
7.27
7.26
7.10
7.09
7.08
7.08
7.08
6.94
5.71
0.01
CN
N
O_2N
3db
1.49
1.44
0.72
1.60
2.92
3.89
1.91
1.00
f1 (ppm)

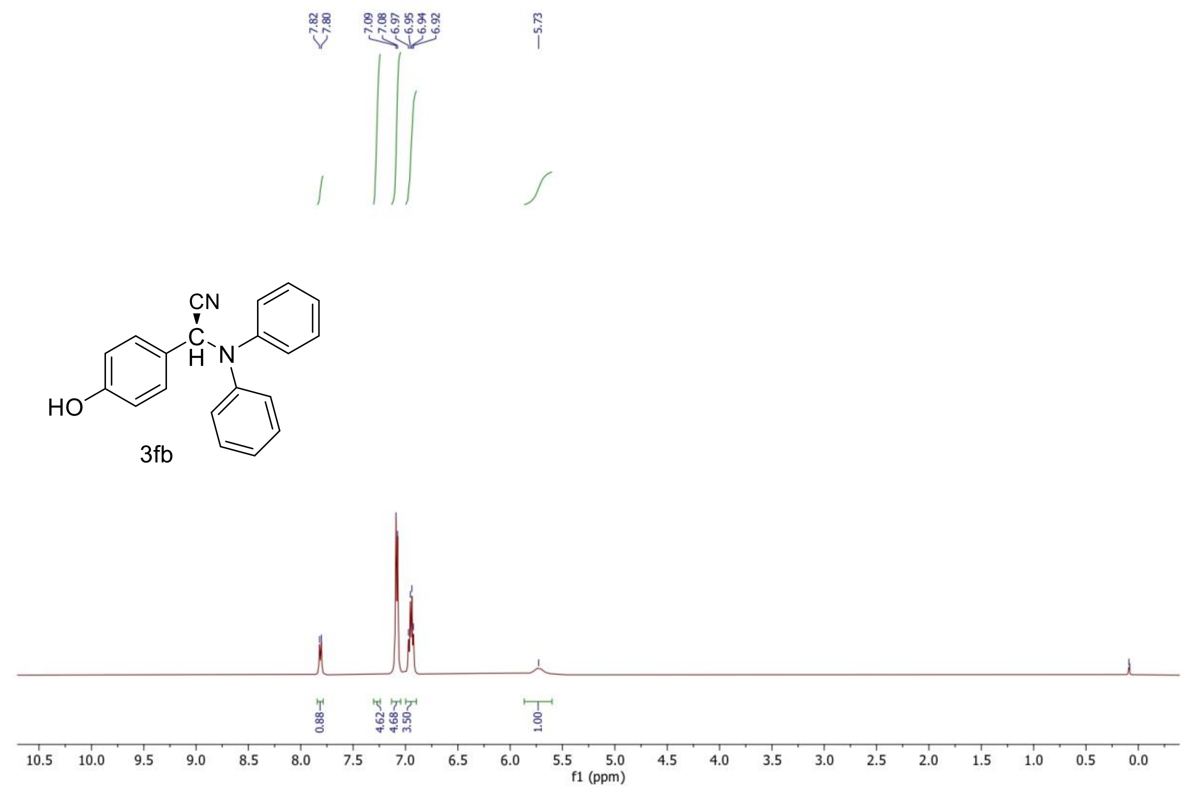

143.13
141.44
129.36
127.51
124.37
121.03
117.83
77.28
77.03
76.78
62.54
CN
N
O_2N
3db
f1 (ppm)

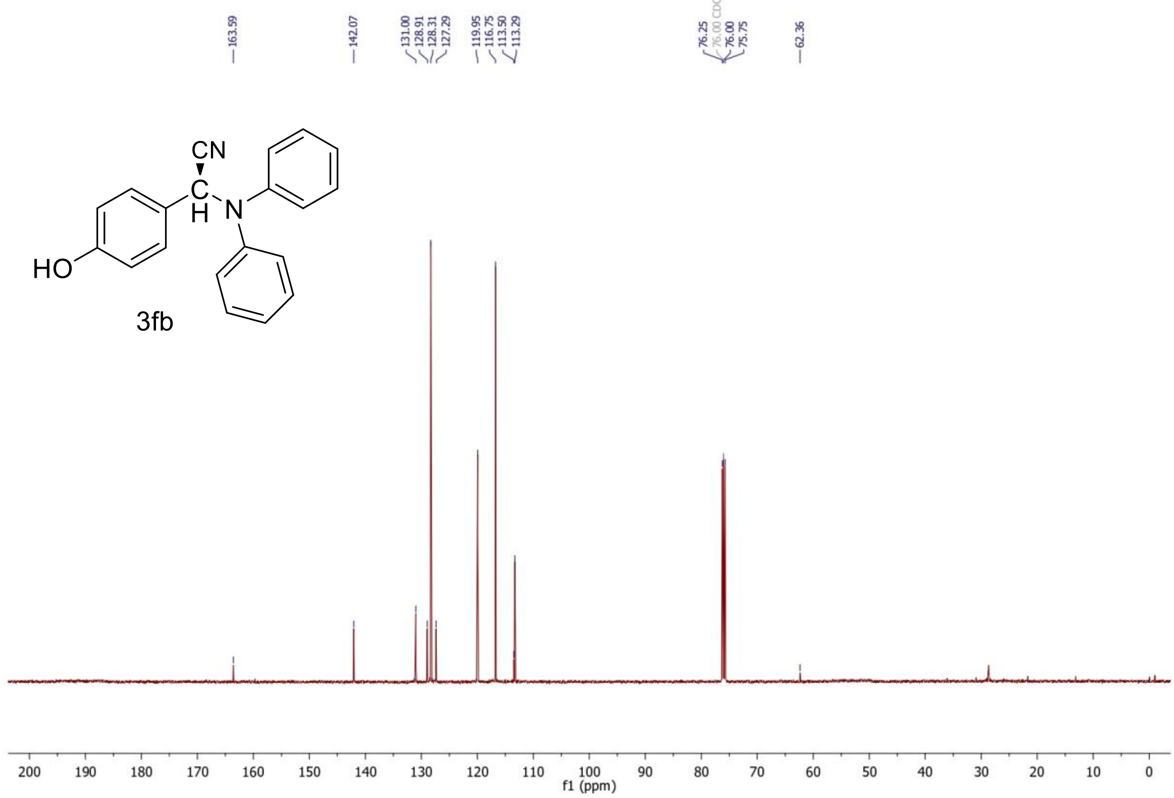
3eb



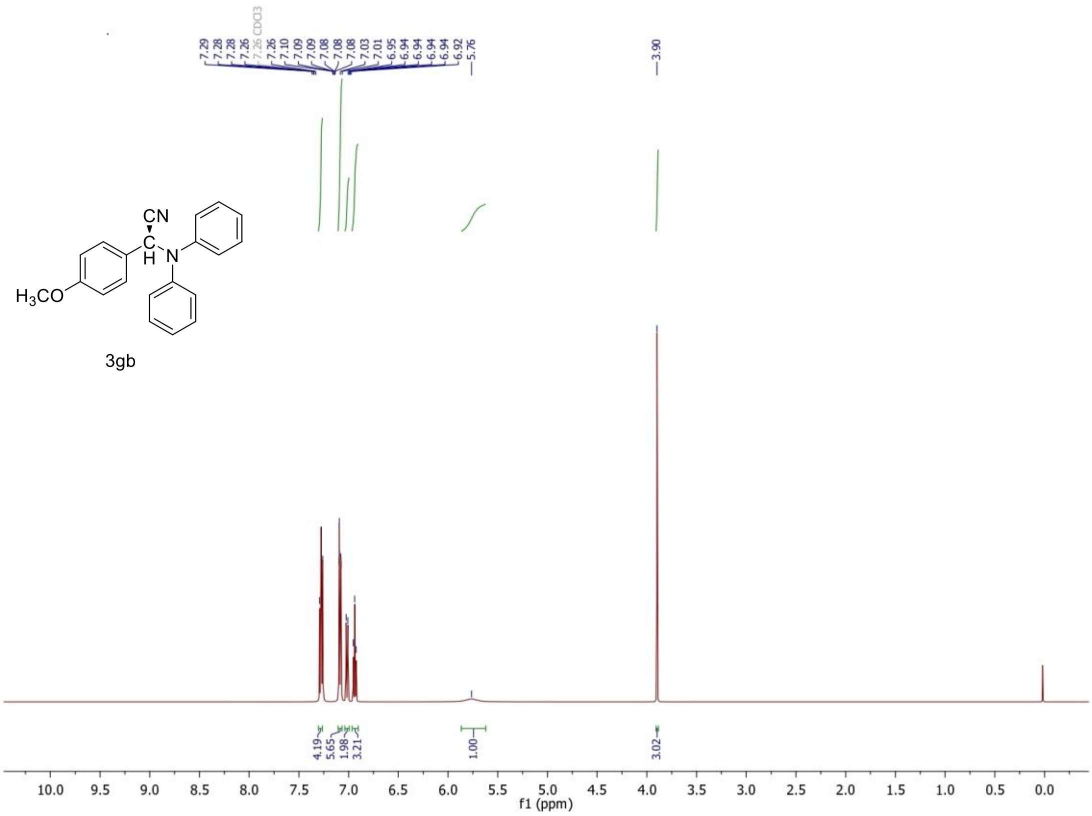


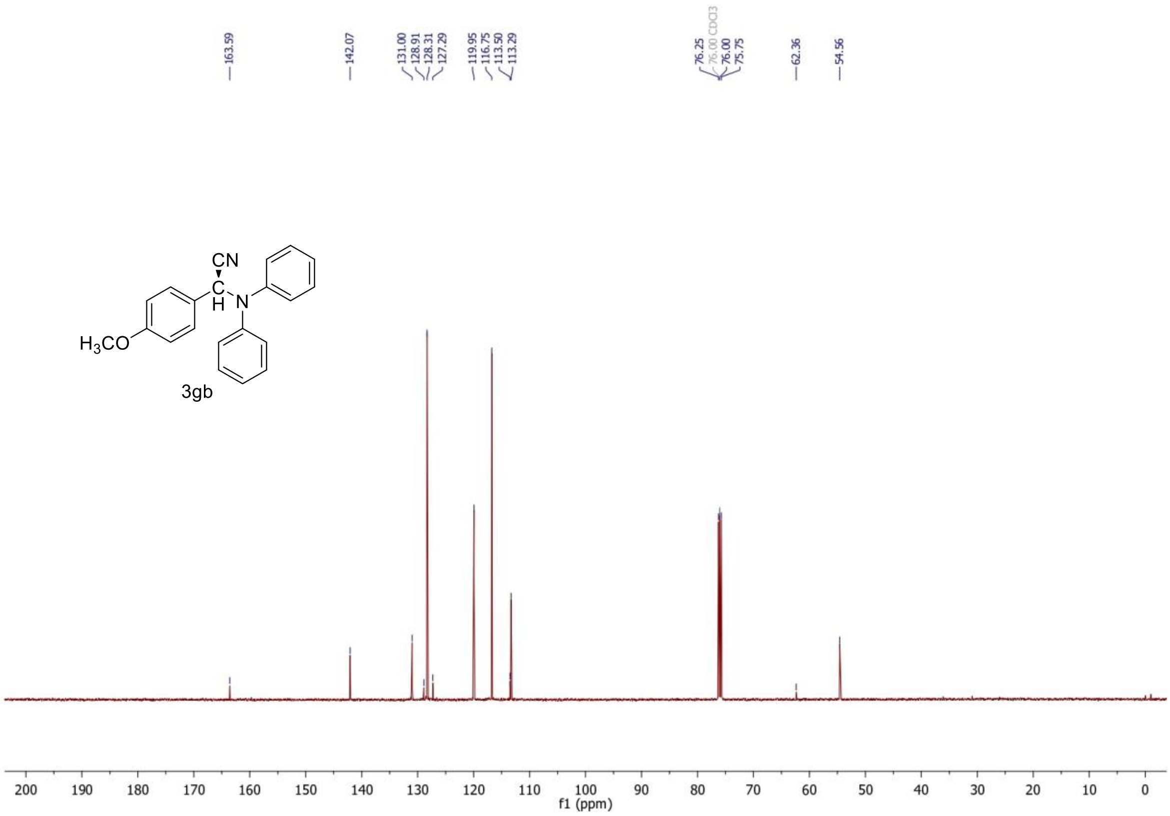
3fb


7.82
7.80
7.09
7.08
6.97
6.95
6.94
6.92
5.73
CN
C
H
N
HO
3fb
0.88
4.62
4.68
3.50
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

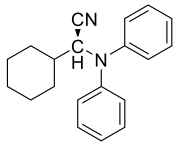

163.59
142.07
131.00
128.91
128.31
127.29
119.95
116.75
113.50
113.29
76.25
76.00 CDCl3
76.00
75.75
62.36
CN
C
H
N
HO
3fb
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3bg

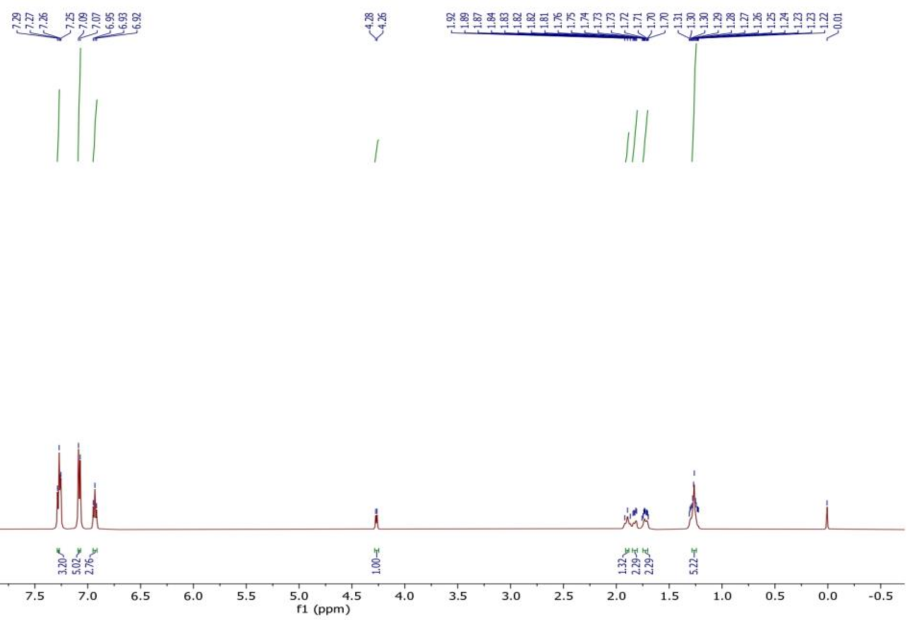

7.29
7.28
7.28
7.26
7.26 CDCl3
7.26
7.10
7.09
7.09
7.08
7.08
7.08
7.03
7.01
6.95
6.94
6.94
6.94
6.94
6.92
5.76
3.90
CN
C
H
N
H_3CO
3gb
4.19
5.65
1.98
3.21
1.00
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

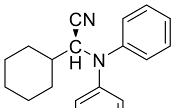

163.59
142.07
131.00
128.91
128.31
127.29
119.95
116.75
113.50
113.29
76.25
76.00 CDCl3
76.00
75.75
62.36
54.56
CN
C
H
N
H_3CO
3gb
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

3hb

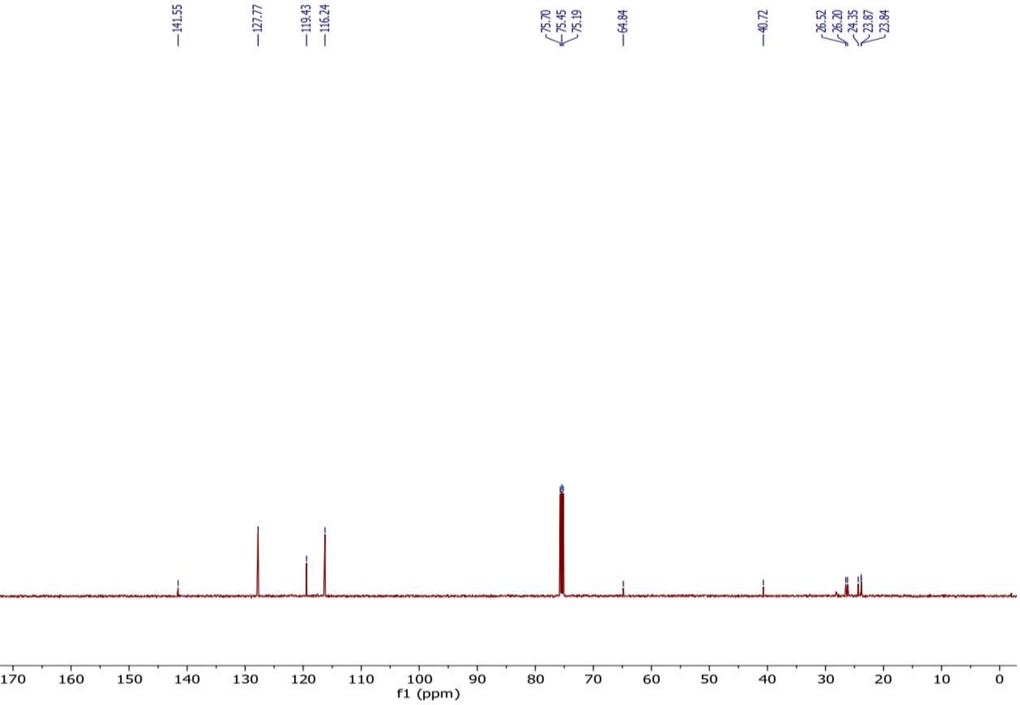

CN
C
H
N

3hb

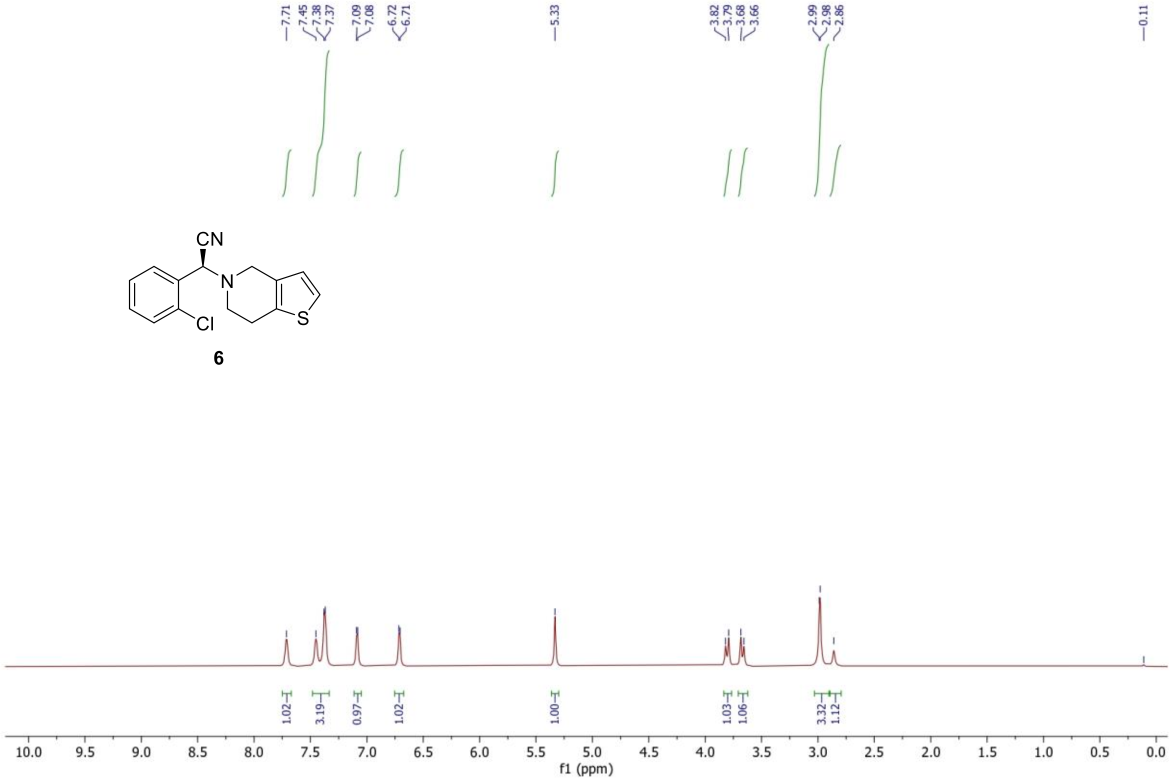

7.29
7.27
7.26
7.25
7.09
7.07
6.95
6.93
6.92
4.28
4.26
1.92
1.89
1.87
1.84
1.83
1.82
1.82
1.81
1.76
1.75
1.74
1.73
1.73
1.72
1.71
1.70
1.70
1.31
1.30
1.30
1.29
1.28
1.27
1.26
1.25
1.24
1.23
1.23
1.22
0.01
3.20
5.02
2.76
1.00
1.32
2.29
2.29
5.22
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


CN
C
H
N

3hb

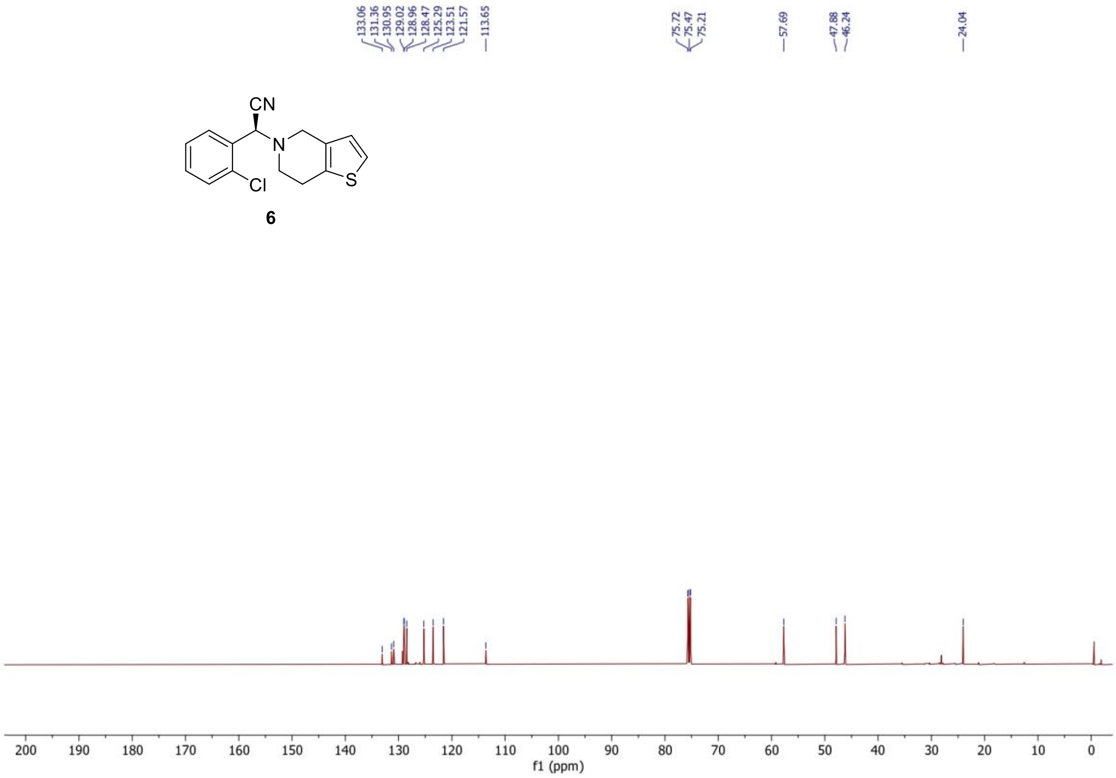

141.55
127.77
119.43
116.24
75.70
75.45
75.19
64.84
40.72
26.52
26.20
24.35
23.87
23.84
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

NMR of 6



7.71
7.45
7.38
7.37
7.09
7.08
6.72
6.71
5.33
3.82
3.79
3.68
3.66
2.99
2.98
2.86
0.11
1.02
3.19
0.97
1.02
1.00
1.03
1.06
3.32
1.12
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
CN
N
Cl
S

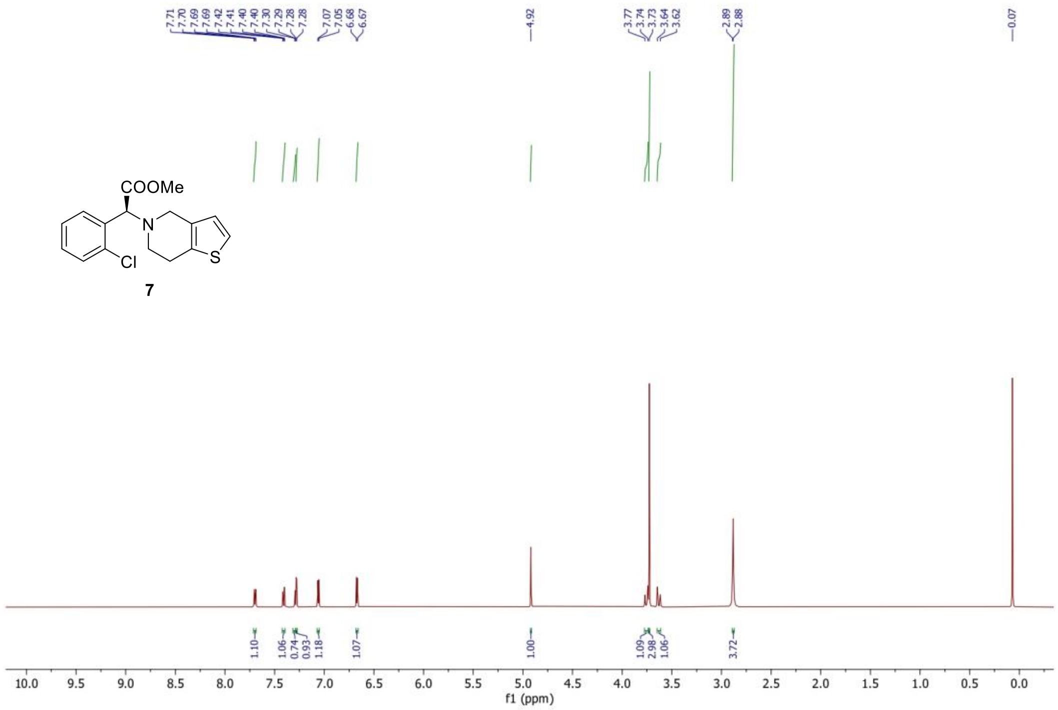
6

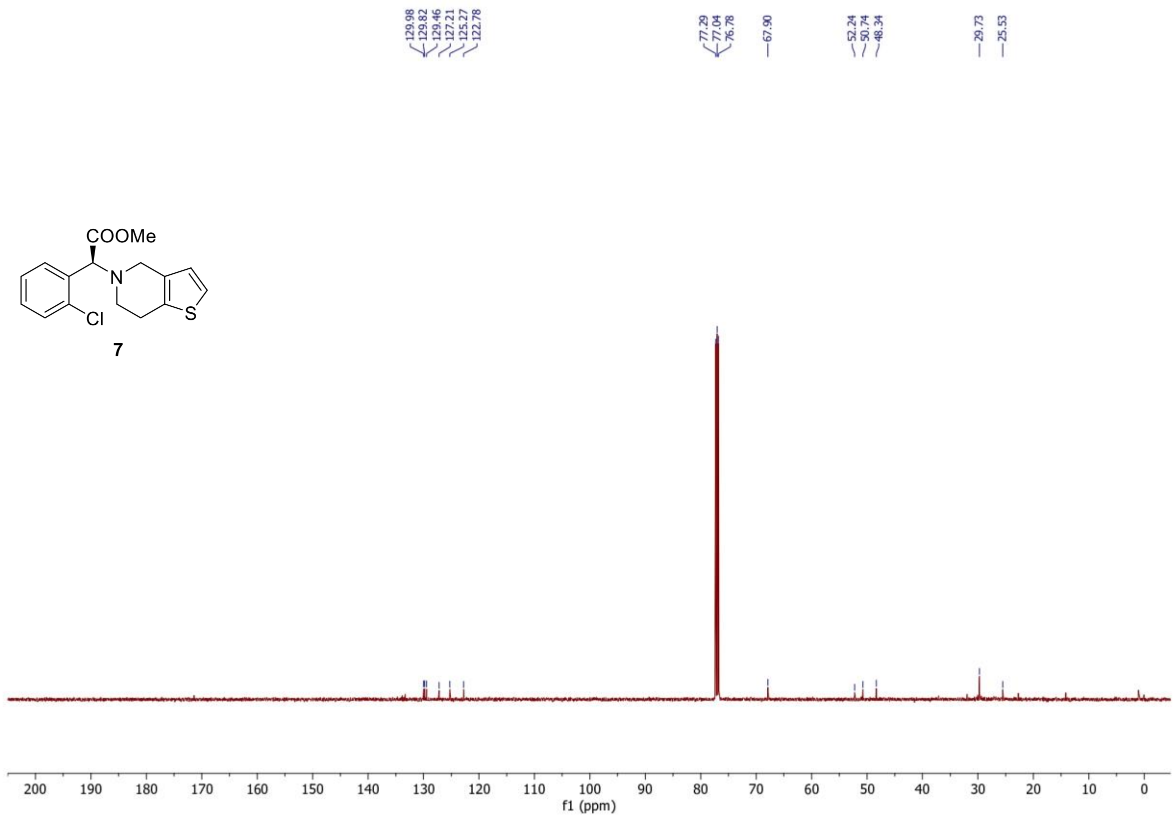


133.06
131.36
130.95
129.02
128.96
128.47
125.29
123.51
121.57
113.65
75.72
75.47
75.21
57.69
47.88
46.24
24.04
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CN
N
Cl
S

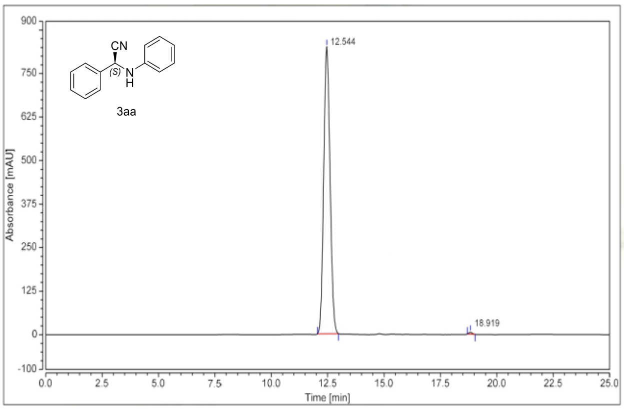
6

NMR 7


7.71
7.70
7.69
7.69
7.42
7.41
7.40
7.40
7.30
7.29
7.28
7.28
7.07
7.05
6.68
6.67
4.92
3.77
3.74
3.73
3.64
3.62
2.89
2.88
0.07
COOMe
N
Cl
S
7
1.10
1.06
0.74
0.93
1.18
1.07
1.00
1.09
2.98
1.06
3.72
f1 (ppm)

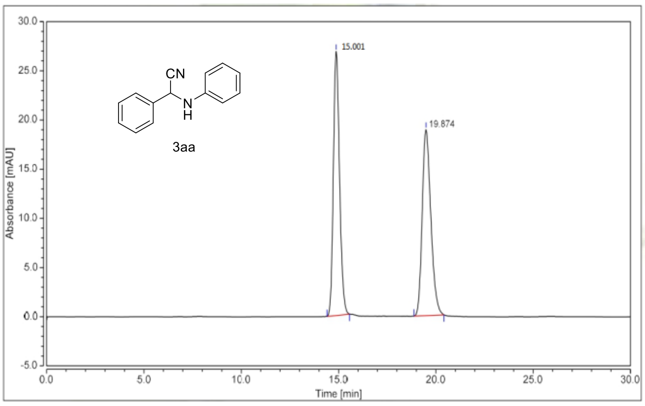

129.98
129.82
129.46
127.21
125.27
122.78
77.29
77.04
76.78
67.90
52.24
50.74
48.34
29.73
25.53
COOMe
N
Cl
S
7
f1 (ppm)

12. HPLC



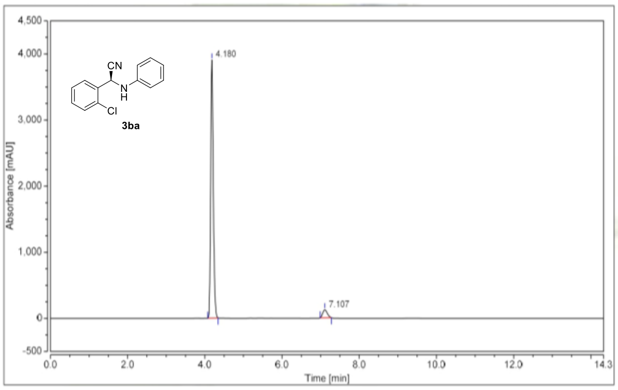
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	12.544	268.550	824.576	99.63	99.32	n.a.
2	18.919	0.996	5.681	0.37	0.68	n.a.
		269.546	**830.257**	**100.00**	**100.00**	



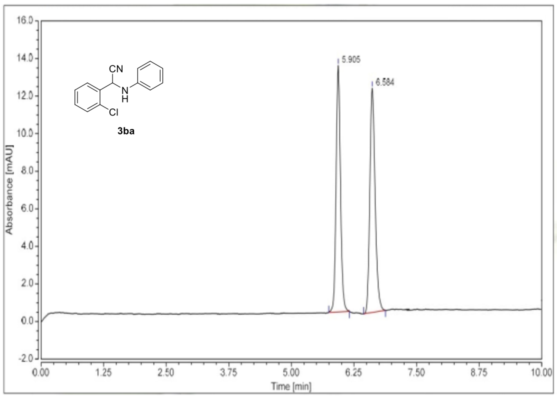
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	15.001	9.830	26.865	50.30	58.65	n.a.
2	19.874	9.714	18.939	49.70	41.35	n.a.
		19.544	**45.804**	**100.00**	**100.00**	



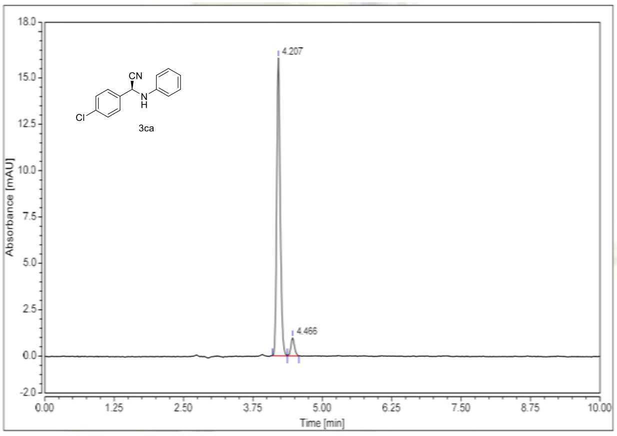
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	4.180	300.203	3903.642	94.80	97.02	n.a.
2	7.107	16.471	119.940	5.20	2.98	n.a.
		316.674	**4023.581**	**100.00**	**100.00**	

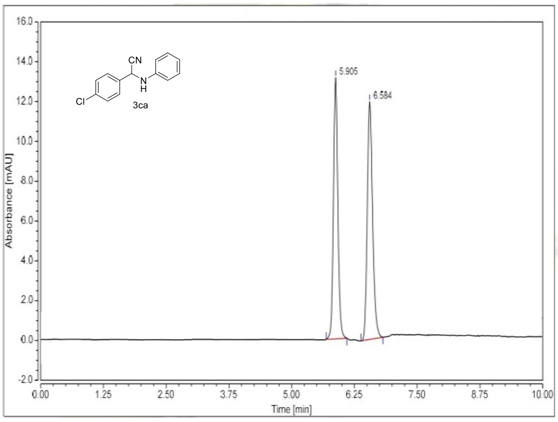


Integration Results

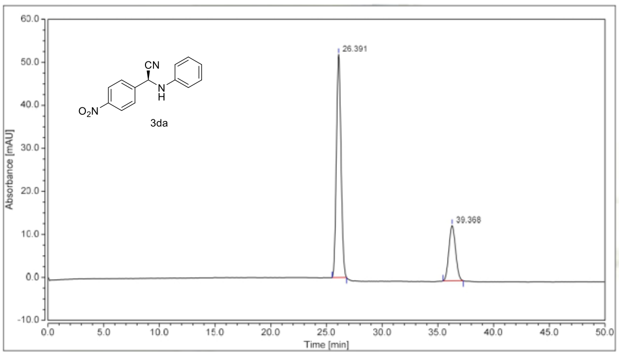
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	6.584	1.470	11.934	52.47	47.63	n.a.
2	5.905	1.332	13.121	47.53	52.37	n.a.
		2.802	**25.055**	**100.00**	**100.00**	



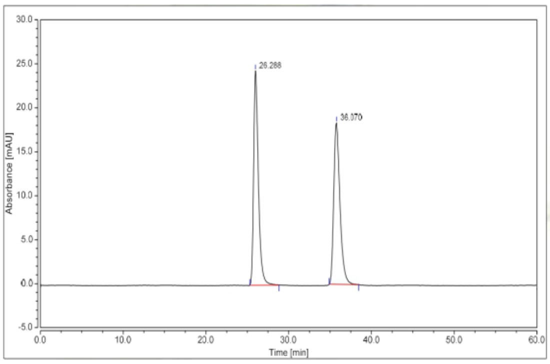
Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	4.207	1.184	16.065	94.22	94.28	n.a.
2	4.466	0.073	0.975	5.78	5.72	n.a.
		1.257	**17.040**	**100.00**	**100.00**	



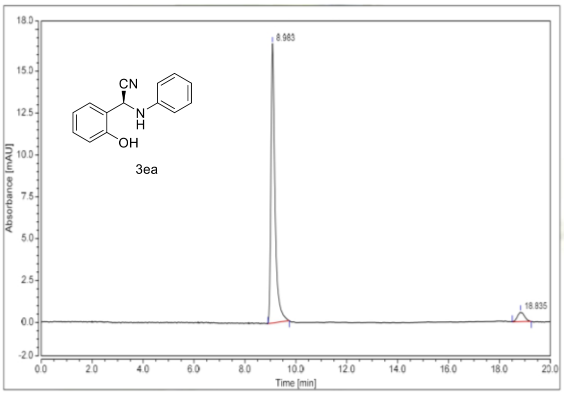
Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	5.905	1.470	11.934	52.47	47.63	n.a.
2	6.584	1.332	13.121	47.53	52.37	n.a.
		2.802	**25.055**	**100.00**	**100.00**	



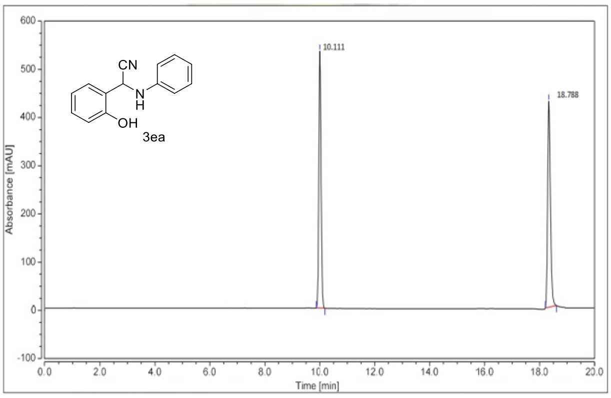
Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	26.391	24.970	51.876	73.53	80.08	n.a.
2	39.368	8.990	12.903	26.47	19.92	n.a.
		33.960	**64.778**	**100.00**	**100.00**	



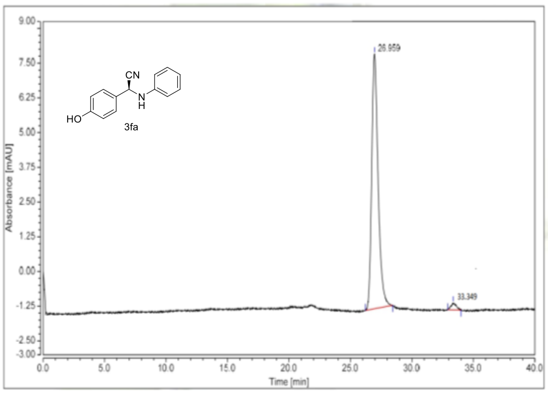
Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	26.288	16.192	24.380	50.47	57.02	n.a.
2	36.070	15.892	18.377	49.53	42.98	n.a.
		32.084	**42.757**	**100.00**	**100.00**	



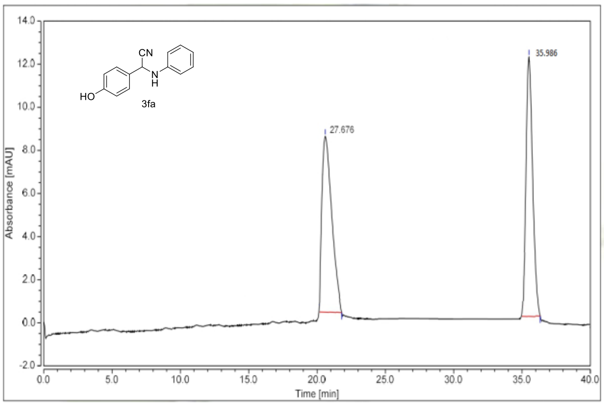
Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	8.983	3.084	16.684	94.58	96.64	n.a.
2	18.835	0.177	0.580	5.42	3.36	n.a.
		3.261	**17.264**	**100.00**	**100.00**	



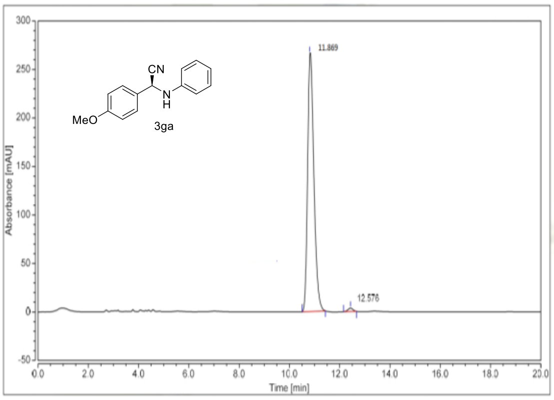
Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	10.111	42.543	427.287	50.28	44.50	n.a.
2	18.788	42.074	532.961	49.72	55.50	n.a.
		84.617	**960.248**	**100.00**	**100.00**	



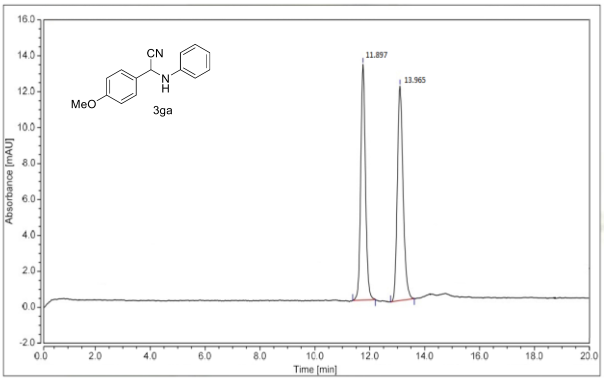
Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	26.959	5.522	9.173	97.78	97.38	n.a.
2	33.349	0.125	0.247	2.22	2.62	n.a.
		5.648	**9.420**	**100.00**	**100.00**	



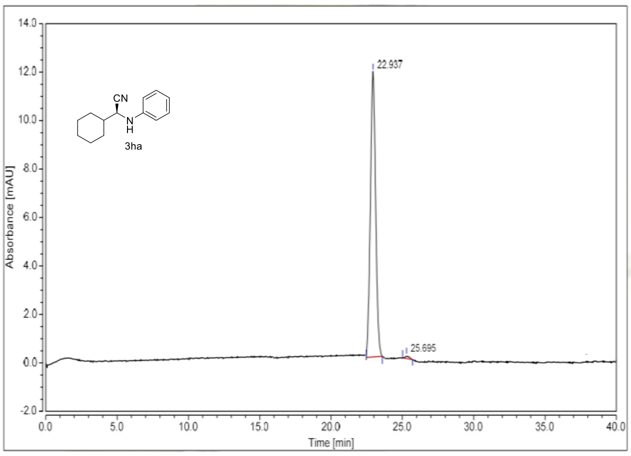
Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	27.676	7.083	8.244	51.28	40.70	n.a.
2	35.986	6.730	12.010	48.72	59.30	n.a.
		13.813	**20.254**	**100.00**	**100.00**	



Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	11.869	77.155	268.950	98.96	98.72	n.a.
2	12.576	0.808	3.500	1.04	1.28	n.a.
		77.963	**272.449**	**100.00**	**100.00**	

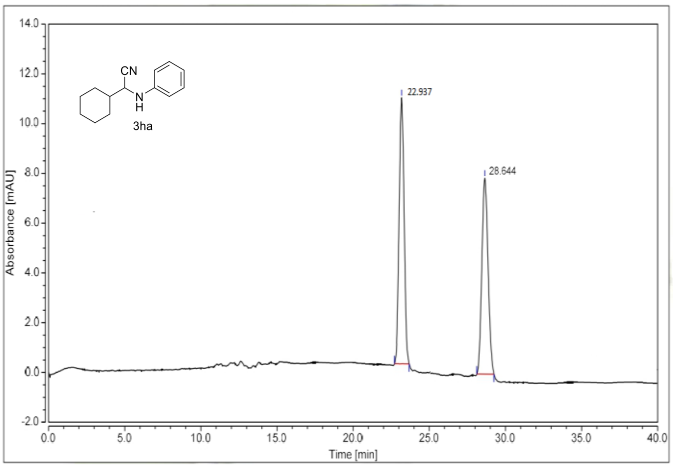


Integration Results						
Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	11.897	1.470	11.934	52.47	47.63	n.a.
2	13.965	1.332	13.121	47.53	52.37	n.a.
		2.802	**25.055**	**100.00**	**100.00**	



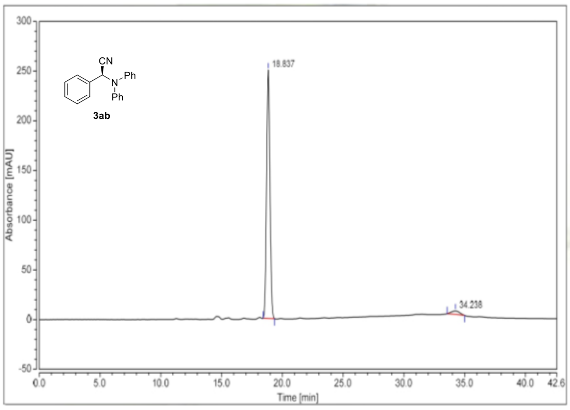
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	22.937	4.974	11.780	99.28	98.92	n.a.
2	25.695	0.036	0.128	0.72	1.08	n.a.
		5.010	**11.908**	**100.00**	**100.00**	



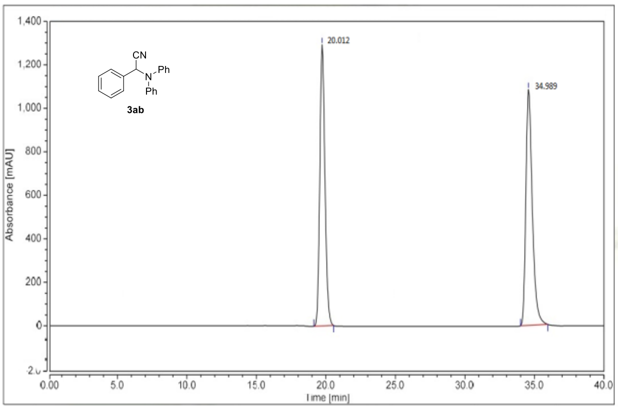
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	22.937	4.007	10.692	51.89	57.57	n.a.
2	28.644	3.715	7.880	48.11	42.43	n.a.
		7.722	**18.572**	**100.00**	**100.00**	



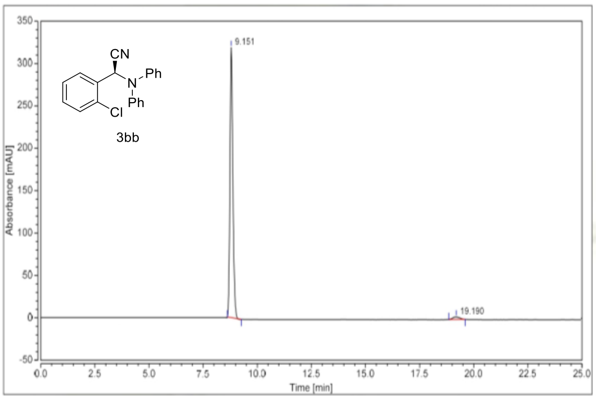
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	18.837	79.379	249.831	96.58	98.58	n.a.
2	34.238	2.812	3.597	3.42	1.42	n.a.
		82.191	**253.427**	**100.00**	**100.00**	



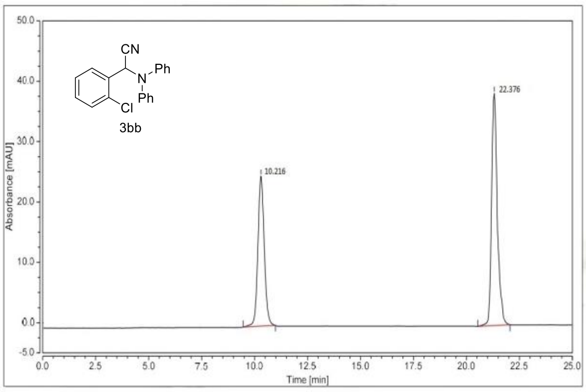
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	20.012	116.913	1084.075	51.17	45.60	n.a.
2	34.989	111.546	1293.323	48.83	54.40	n.a.
		228.459	**2377.398**	**100.00**	**100.00**	



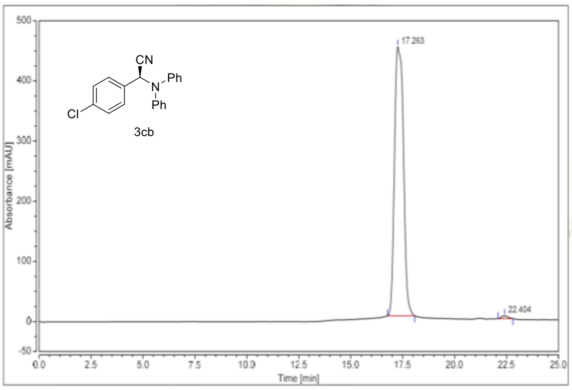
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	9.151	49.735	318.597	97.77	99.07	n.a.
2	19.190	1.135	2.993	2.23	0.93	n.a.
		50.870	**321.590**	**100.00**	**100.00**	



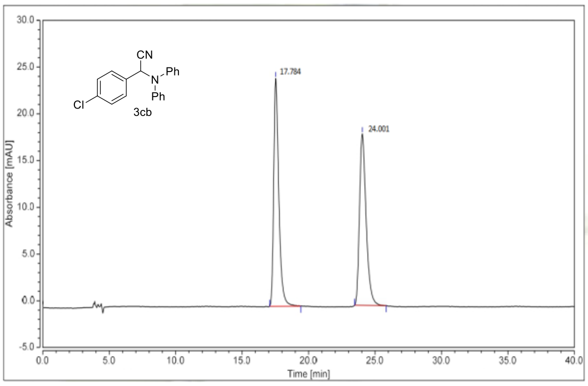
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	10.216	8.639	24.835	50.10	42.03	n.a.
2	22.376	8.605	34.258	49.90	57.97	n.a.
		17.244	**59.093**	**100.00**	**100.00**	



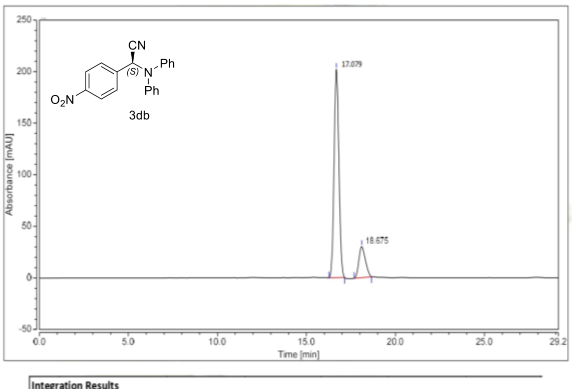
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	17.263	223.887	447.837	99.24	98.92	n.a.
2	22.404	1.703	4.899	0.76	1.08	n.a.
		225.590	**452.736**	**100.00**	**100.00**	



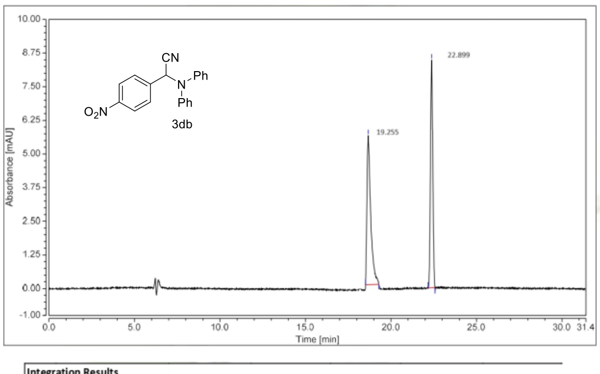
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	17.784	16.192	24.380	50.47	57.02	n.a.
2	24.001	15.892	18.377	49.53	42.98	n.a.
		32.084	**42.757**	**100.00**	**100.00**	



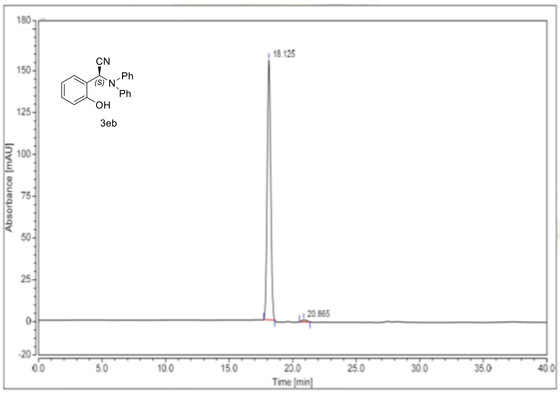
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	17.079	12.811	30.280	83.23	13.04	n.a.
2	18.675	63.581	202.021	16.77	86.96	n.a.
		76.393	**232.301**	**100.00**	**100.00**	



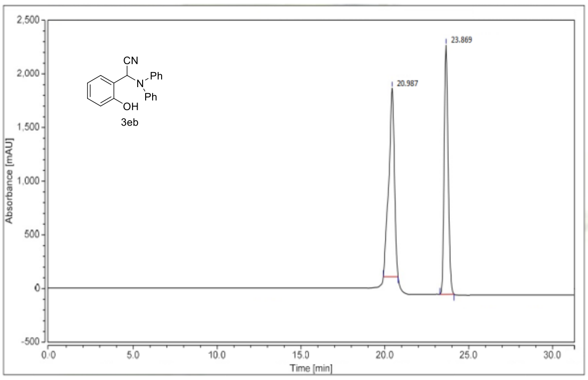
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	19.255	1.422	5.548	51.44	38.45	n.a.
2	22.899	1.342	8.880	48.56	61.55	n.a.
		2.764	**14.428**	**100.00**	**100.00**	



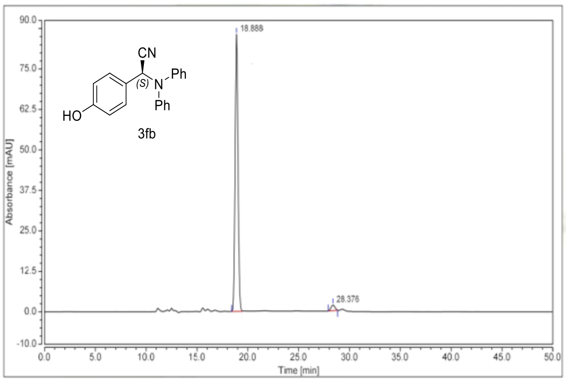
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	18.125	49.142	155.402	99.00	99.28	n.a.
2	20.865	0.498	1.127	1.00	0.72	n.a.
		49.639	**156.529**	**100.00**	**100.00**	



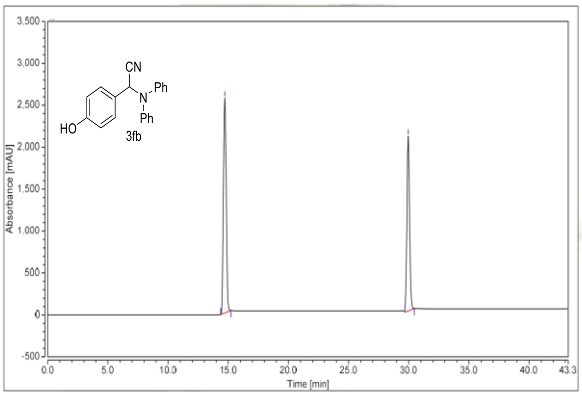
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	20.987	393.531	1757.120	52.01	43.10	n.a.
2	23.869	363.068	2319.919	47.99	56.90	n.a.
		756.599	**4077.039**	**100.00**	**100.00**	



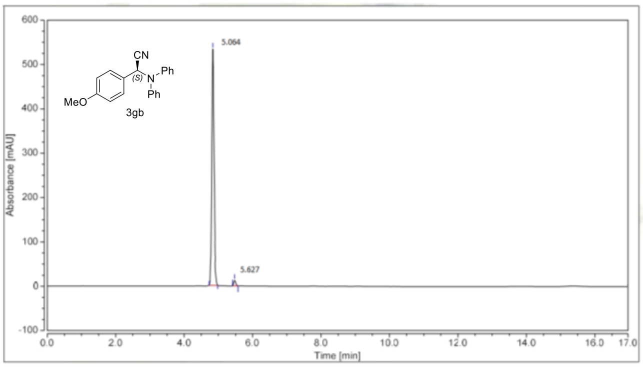
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	18.888	28.123	85.540	97.33	98.01	n.a.
2	28.376	0.771	1.737	2.67	1.99	n.a.
		28.894	**87.277**	**100.00**	**100.00**	



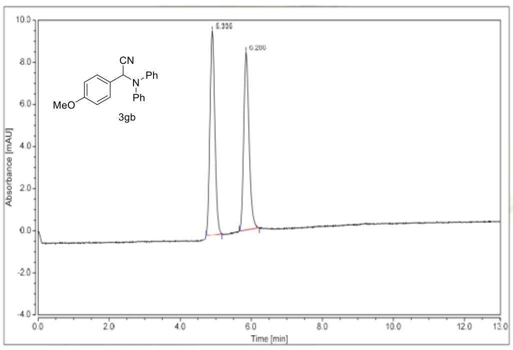
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	19.234	536.389	2084.317	51.29	50.97	n.a.
2	30.115	509.368	2005.074	48.71	49.03	n.a.
		1045.757	**4089.391**	**100.00**	**100.00**	



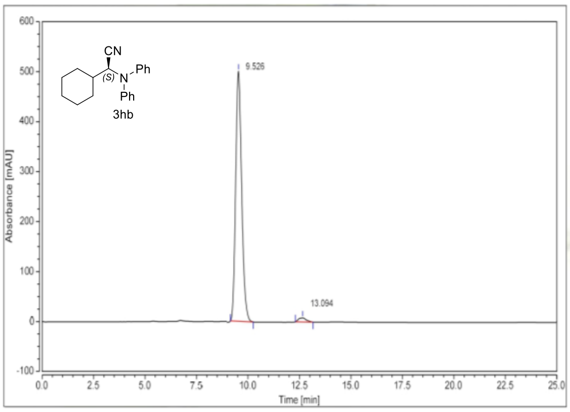
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	5.064	42.011	532.753	98.07	97.76	n.a.
2	5.627	0.828	12.216	1.93	2.24	n.a.
		42.839	**544.969**	**100.00**	**100.00**	



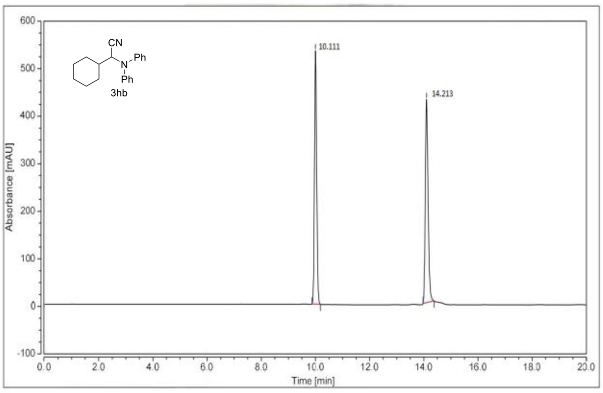
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	5.335	1.765	11.009	51.53	53.50	n.a.
2	6.286	1.661	9.569	48.47	46.50	n.a.
		3.426	**20.578**	**100.00**	**100.00**	



Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	9.526	3.367	7.785	98.05	1.53	n.a.
2	13.094	169.371	500.505	1.95	98.47	n.a.
		172.738	508.290	100.00	100.00	



Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	10.111	42.543	427.287	50.28	44.50	n.a.
2	14.213	42.074	532.961	49.72	55.50	n.a.
		84.617	960.248	100.00	100.00	

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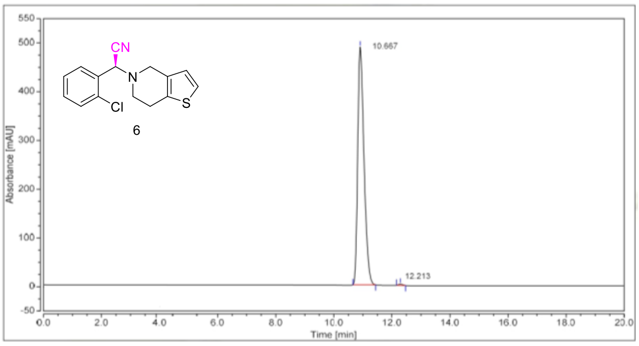
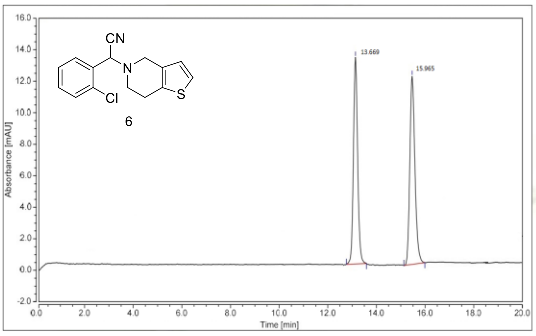


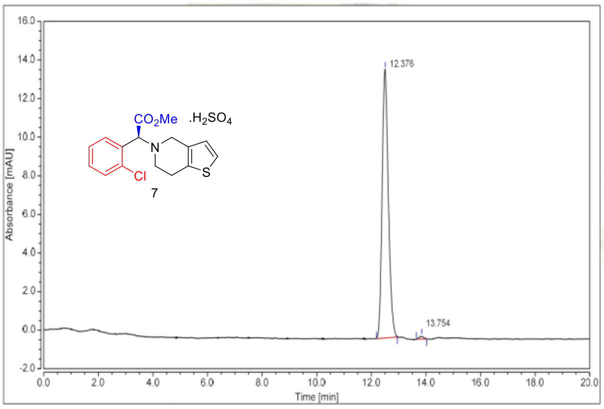
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	10.667	122.419	487.866	99.67	99.52	n.a.
2	12.213	0.400	2.356	0.33	0.48	n.a.
		122.819	490.222	100.00	100.00	



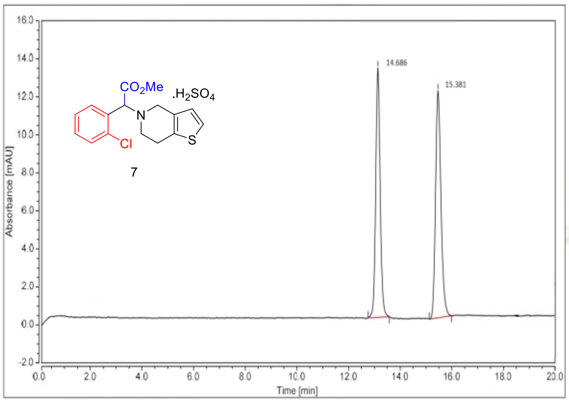
Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	13.669	1.470	11.934	52.47	47.63	n.a.
2	15.965	1.332	13.121	47.53	52.37	n.a.
		2.802	25.055	100.00	100.00	



Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	12.376	3.673	13.941	99.25	98.84	n.a.
2	13.754	0.028	0.163	0.75	1.16	n.a.
		3.701	14.104	100.00	100.00	



Integration Results

Peak	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	14.686	1.470	11.934	52.47	47.63	n.a.
2	15.381	1.332	13.121	47.53	52.37	n.a.
		2.802	25.055	100.00	100.00	

13. References:

1. C. D. Gutsche, M. I., P-Tert-BUTYLCALIX[4]ARENE. *Organic Synthesis* **1990,** *68*, 234.
2. Jiao, Z.; Feng, X.; Liu, B.; Chen, F.; Zhang, G.; Jiang, Y., Enantioselective Strecker Reactions between Aldimines and Trimethylsilyl Cyanide Promoted by Chiral N,N'-Dioxides. *Eur. J. Org. Chem.* **2003,** *2003*, 3818-3826