First application of chiral phosphotriesters in asymmetric metal catalysis: enantioselective Zn-catalyzed hydrosilylation of ketones in the presence of BINOL-derived phosphates

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SUPPORTING INFORMATION

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I - General information

All the reactions were performed in dried glassware, under argon atmosphere, and sealed with a rubber septum. Reagents were obtained from commercial suppliers and used without further purification unless otherwise noted. TLC analyses were performed using precoated Merck TLC Silica Gel 60 F254 plates. Purifications by column chromatography on silica gel were performed using Merck Silica Gel 60 (0,040-0,063 nm). Petroleum ether (PE) used for purifications was the low boiling point fraction (40-60 °C). ^{1}H and ^{13}C spectra were recorded on a Bruker Avance 300 instruments using TMS and $CDCl_3$ respectively as internal standard. ^{31}P NMR spectra were recorded on a Bruker DMX 500. Chemical shifts (δ) are reported in parts per million (ppm) relatively to TMS and residual solvent as internal standards. The following abbreviations are used for multiplicities: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; td, triplet of doublets; m, multiplet. Coupling constants (*J*) are reported in Hertz (Hz). HRMS analyses were obtained using a Waters Q-TOF 2 or a Micromass ZABSpec TOF or a Bruker Micro-TOF Q II or a LTQ Orbitrap XL instrument for ESI. X-ray crystallographic data were collected on a D8 Venture Bruker AXS diffractometers at 150 K. Optical rotations were recorded on a Perkin Elmer Model 341 polarimeter. Melting points were obtained on a hot bench. IR spectra were recorded on a Perkin Elmer FT-IR Spectrometer UATR Spectrum Two.

II - Synthesis of monophosphates G and H

Under an atmosphere of argon, to a solution of 3-I-(*R*)-BINOL (1) (190 mg, 0.46 mmol) and Et_3N (0.13 mL, 0.92 mmol, 2 equiv.) in dry CH_2Cl_2 (5 mL) was added at 0 °C phenyl phosphorodichloridate (2) (83 □L, 0.55 mmol, 1.2 equiv.). The mixture was stirred at room temperature overnight, then hydrolyzed with an aqueous 2 N HCl solution (5 mL), and extracted with CH_2Cl_2 (2 x 10 mL). The organic phases were washed with H_2O (1 x 10 mL), then dried over anhydrous $MgSO_4$. After filtration, the solvent was removed under vacuum and the residue was purified by column chromatography on silica gel using a mixture of petroleum ether/diethylether 1/1 as eluent, to give two white solids. Yield: 228 mg, 90%.

Diastereomer **G**: M.p. 240 °C; $[\alpha]^{20}_D$ - 264 (c = 1.0, $CHCl_3$); IR (neat, cm^{-1}) 3064, 1592, 1489, 1311, 1299, 1198, 968, 949, 895, 750; ESI-HRMS calculated for $C_{26}H_{16}O_4INaP$ $[M+Na]^+$ 572.9723, found 572.9718; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.57 (s, 1H), 8.02 (d, *J* = 9.0 Hz, 1H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 6.0 Hz, 1H), 7.50-7.45 (m, 3H), 7.37-7.20 (m, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.4 (d, J_{CP} = 6.7 Hz), 147.5 (d, J_{CP} = 11.2 Hz), 145.2 (d, J_{CP} = 8.2 Hz), 140.9, 133.2 (d, J_{CP} = 1.5 Hz), 132.3 (d, J_{CP} = 0.8 Hz), 132.2 (d, J_{CP} = 1.5 Hz), 131.7, 130.0, 128.6, 127.5, 127.4, 127.2, 127.1, 127.0, 126.8, 126.1, 125.8, 122.2 (d, J_{CP} = 2.2 Hz), 121.1 (d, J_{CP} = 2.2 Hz), 120.1 (d, J_{CP} = 3.8 Hz), 119.9 (d, J_{CP} = 5.2 Hz), 87.9 (d, J_{CP} = 3.8 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ = - 4.21 ppm. Crystals suitable for X-ray diffraction study were grown by slow diffusion of a CH_2Cl_2 solution layered with pentane.

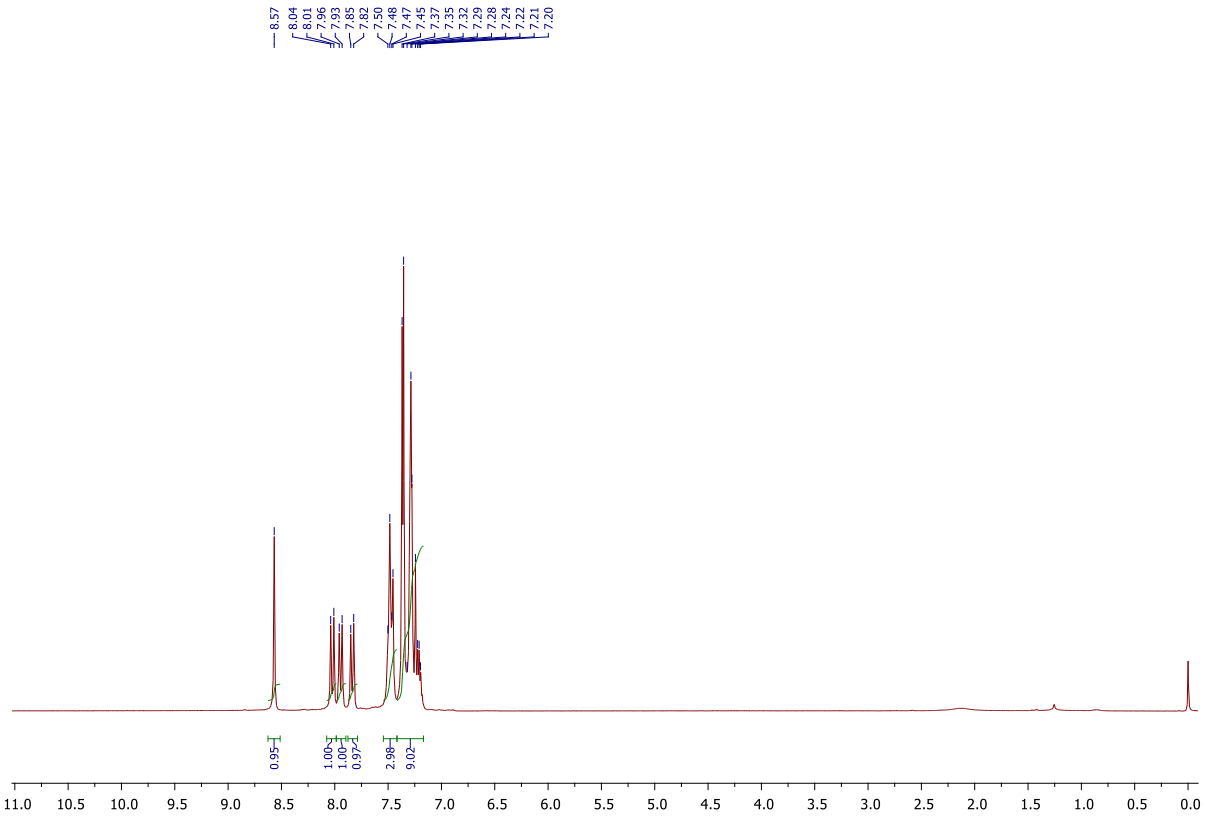
Diastereomer **H**: M.p. 236 °C; $[\alpha]^{20}_D$ - 255 (c = 1.0, $CHCl_3$); IR (neat, cm^{-1}) 3067, 1586, 1486, 1304, 1183, 960, 897; ESI-HRMS calculated for $C_{26}H_{16}O_4INaP$ $[M+Na]^+$ 572.9723, found 572.9725; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.57 (s, 1H), 8.06 (d, *J* = 9.0 Hz, 1H), 7.96 (d, *J* = 9.0 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.63 (dd, *J* = 9.0 and 3.0 Hz, 1H), 7.51-7.47 (m, 2H), 7.37-7.28 (m, 8H), 7.22-7.17 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.7 (d, J_{CP} = 6.7 Hz), 146.3 (d, J_{CP} = 8.2 Hz), 146.1, 140.9, 132.9 (d, J_{CP} = 0.8 Hz), 132.3 (d, J_{CP} = 1.5 Hz), 132.2 (d, J_{CP} = 1.5 Hz), 132.1, 132.0 (d, J_{CP} = 0.8 Hz), 129.9, 128.7, 127.5, 127.5, 127.4, 127.0, 126.9, 126.8, 126.2, 125.7, 122.0 (d, J_{CP} = 2.2 Hz), 121.5 (d, J_{CP} = 2.2 Hz), 120.6 (d, J_{CP} = 3.0 Hz), 120.2 (d, J_{CP} = 4.5 Hz), 87.6 (d, J_{CP} = 4.5 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ = - 3.53 ppm. Crystals suitable for X-ray diffraction study were grown by slow diffusion of a CH_2Cl_2 solution layered with pentane.

III - Synthesis of bisphosphate I

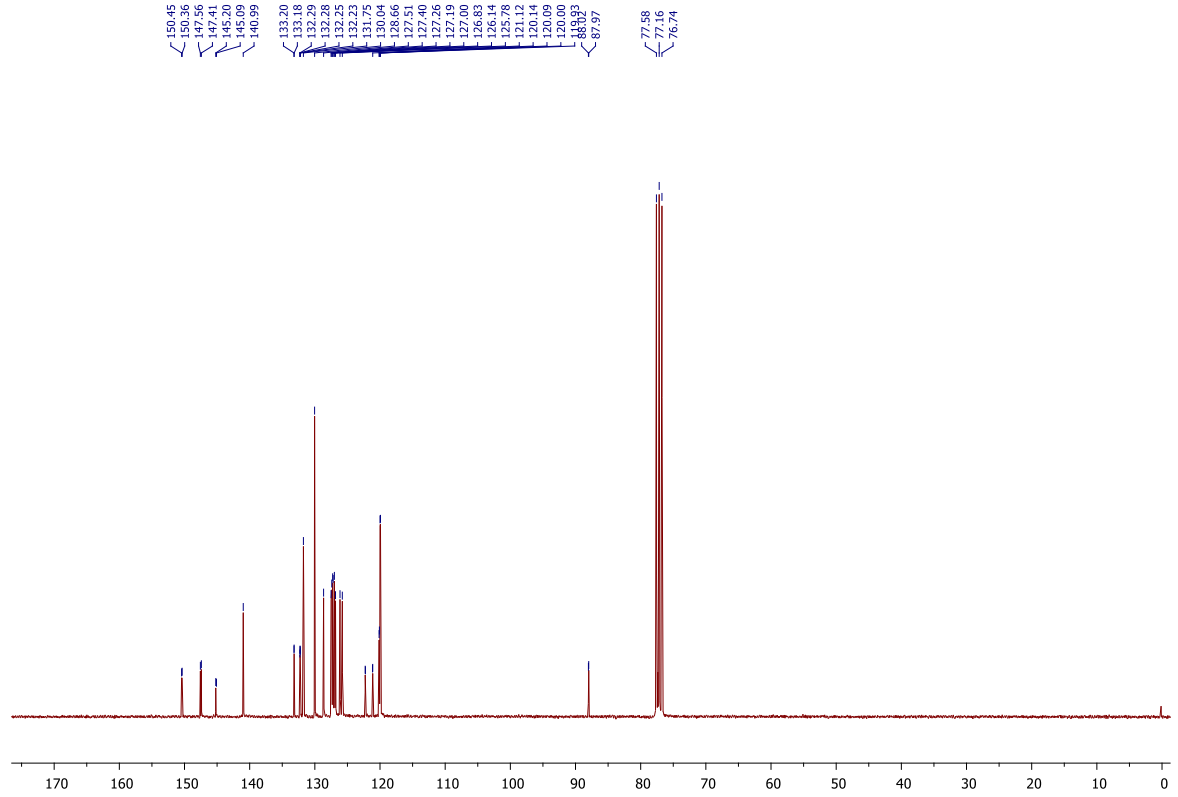
Under an atmosphere of argon, to a solution of PCl_3 (0.5 mL, 5.7 mmol, 1 equiv.) and **3** (1.64 g, 5.7 mmol, 1 equiv.) in toluene (100 mL) was added dropwise Et_3N (4.5 mL, excess) at 0 °C. The mixture was stirred at 0 °C for 30 min before addition of ethylene glycol (0.16 mL, 2.85 mmol, 0.5 equiv.). The reaction was stirred at room temperature for 1 h, then the mixture was filtered over a short pad of celite, rinced with toluene (20 mL), and the solvent was removed under vacuum. The crude product was taken up in EtOAc (40 mL), washed with H_2O (2 x 20 mL), aqueous 5% NaOCl solution (2 x 30 mL), brine (2 x 20 mL), and then dried over anhydrous $MgSO_4$. After filtration, the solvent was removed under vacuum and the residue was purified by column chromatography on silica gel using a mixture of petroleum ether/ethyl acetate 1/2 as eluent to give a white solid. Yield: 1.2 g, 58%. M.p. 180-182 °C; $[\alpha]^{20}_D$ +468 (c = 1.0, $CHCl_3$); IR (neat, cm^{-1}) 3056, 2956, 2925, 1590, 1506, 1463, 1297, 1226, 1201, 1067, 1038, 961, 948, 891, 813, 746; ESI-HRMS calculated for $C_{42}H_{29}O_8P_2$ $[M+H]^+$ 723.1332, found 723.1339; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 9.0 Hz, 2H), 7.92 (d, *J* = 8.1 Hz, 2H), 7.83 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 9.0 Hz, 2H), 7.53 (dd, *J* = 8.7 and 0.6 Hz, 2H), 7.50-7.43 (m, 6H), 7.37-7.26 (m, 8H), 4.65-4.59 (m, 2H), 4.52-4.46 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.5 (d, J_{CP} = 11.3 Hz), 146.3 (d, J_{CP} = 8.3 Hz), 132.3 (d, J_{CP} = 0.9 Hz), 132.2 (d, J_{CP} = 0.9 Hz), 132.0 (d, J_{CP} = 1.0 Hz), 131.8 (d, J_{CP} = 1.0 Hz), 131.6, 131.4, 128.6, 127.3, 127.2, 126.9, 126.0, 125.9, 121.6 (d, J_{CP} = 2.2 Hz), 121.1 (d, J_{CP} = 2.2 Hz), 120.6 (d, J_{CP} = 2.9 Hz), 120.4 (d, J_{CP} = 3.2 Hz), 67.9 (t, J_{CP} = 5.8 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ = 2.70 ppm.

IV - ^{1}H, ^{13}C and ^{31}P NMR data of compounds G, H and I

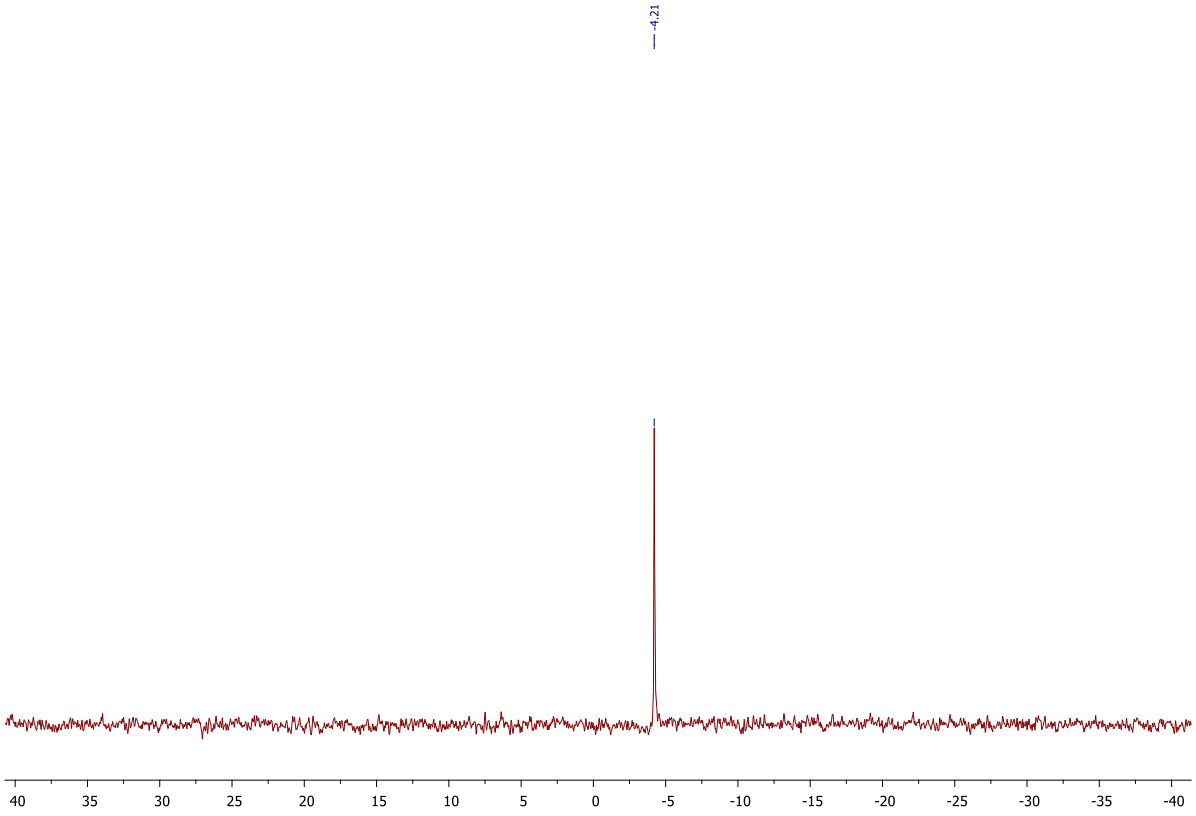
^{1}H NMR (300 MHz, $CDCl_3$) of compound G



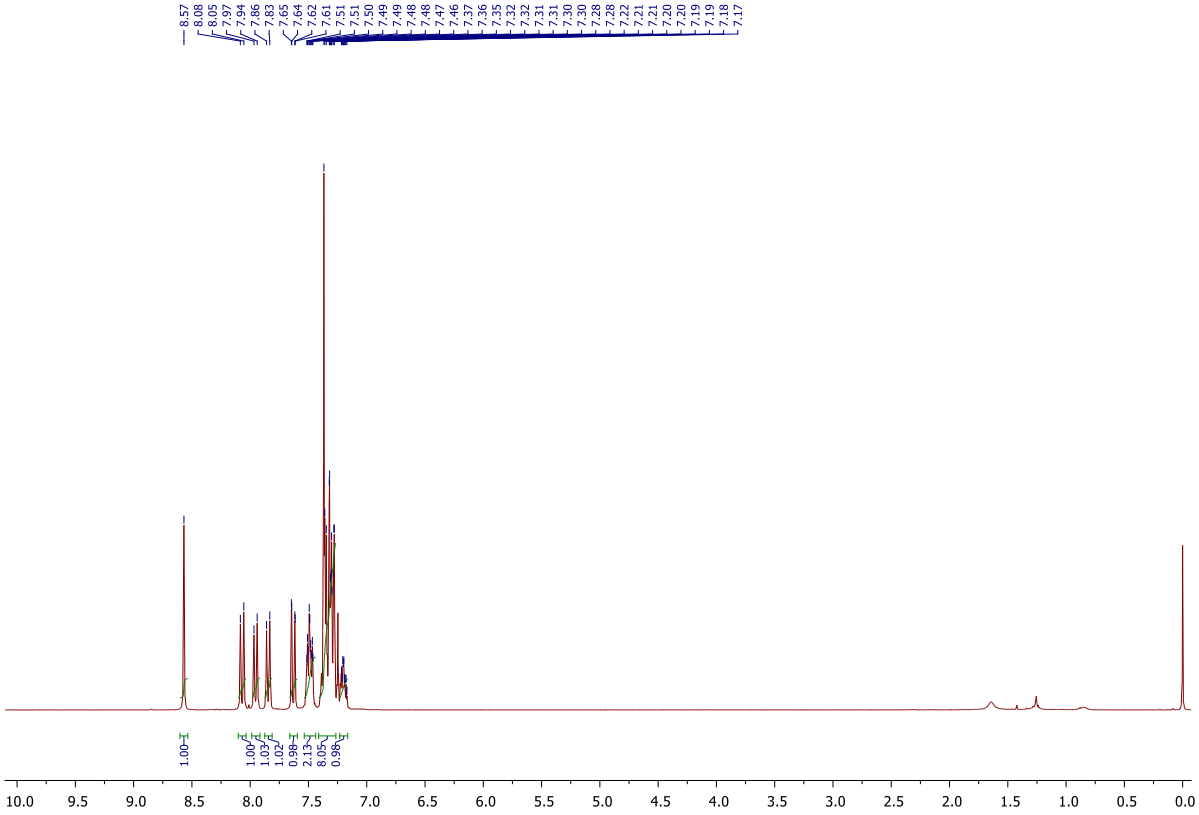
^{13}C NMR (75 MHz, $CDCl_3$) of compound G



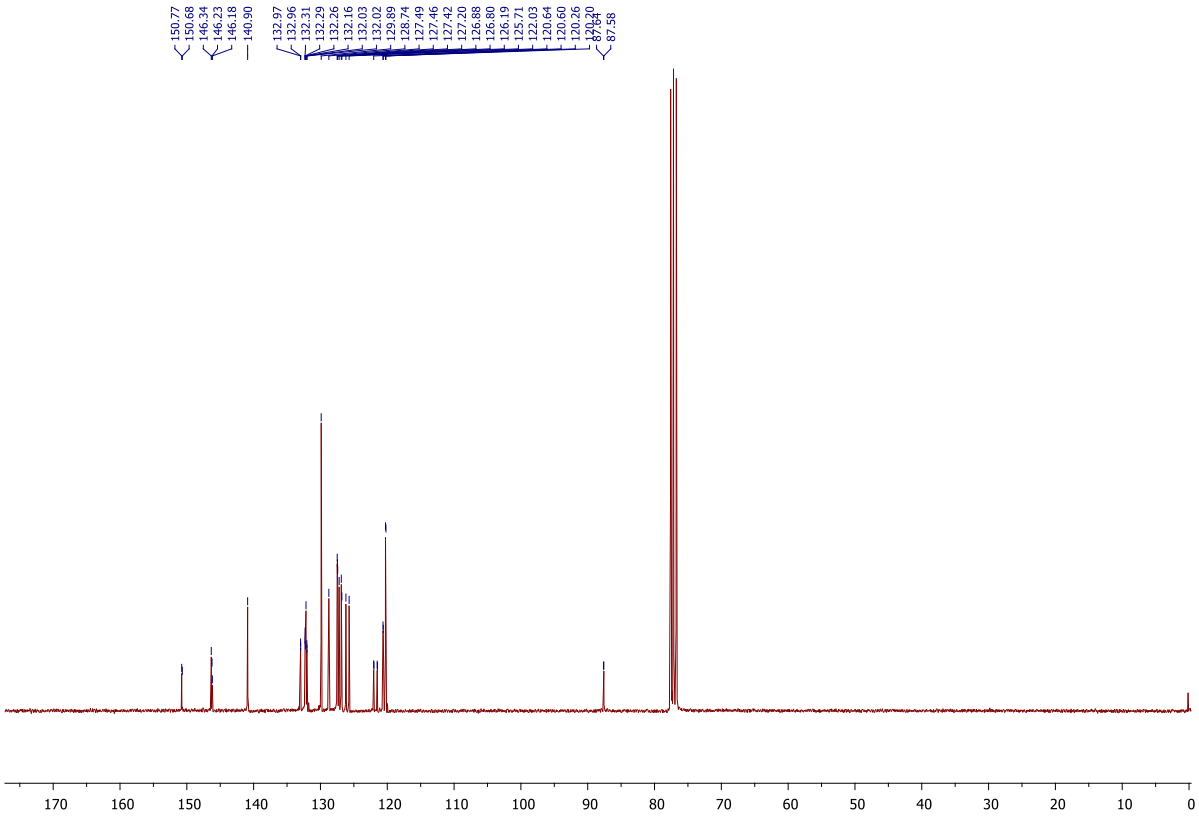
^{31}P NMR (202 MHz, $CDCl_3$) of compound G



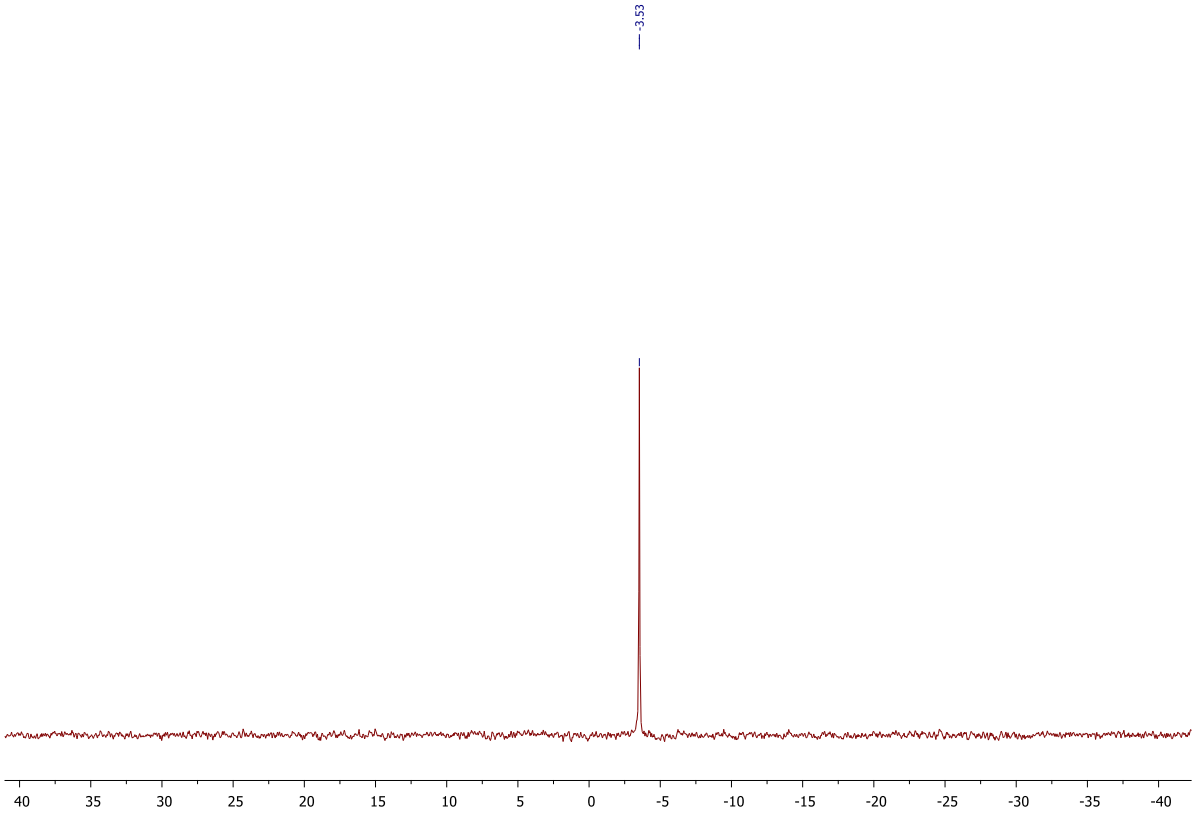
^{1}H NMR (300 MHz, $CDCl_3$) of compound H



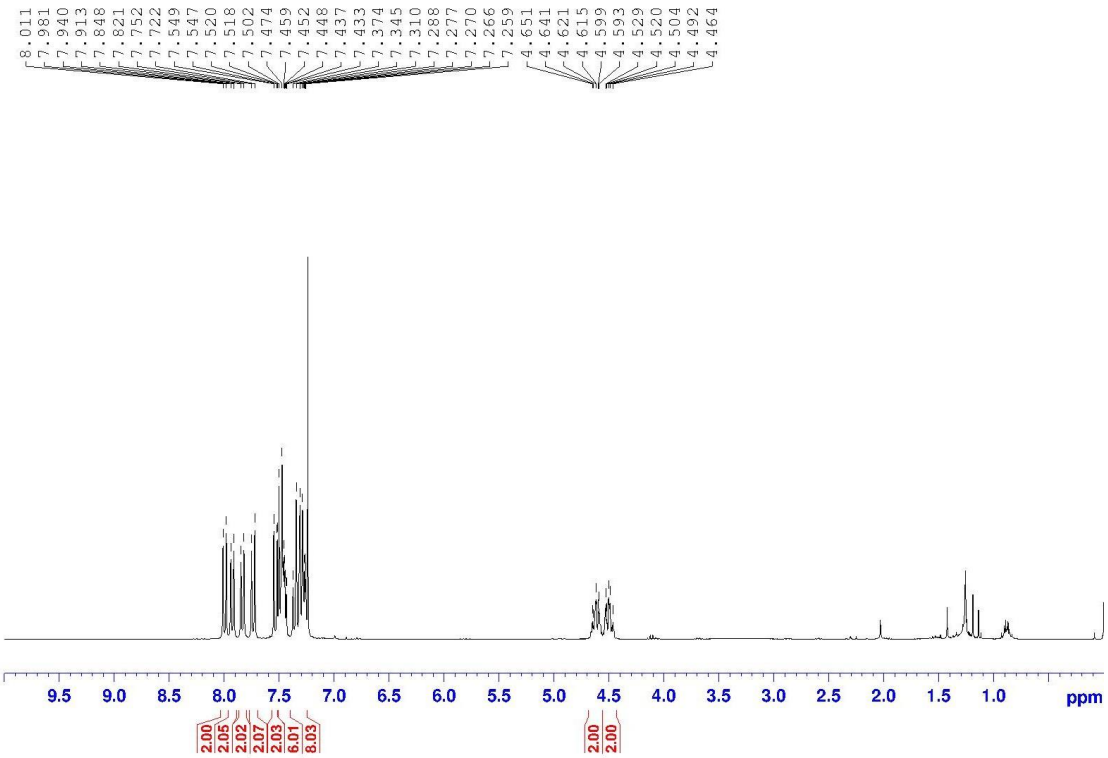
^{13}C NMR (75 MHz, $CDCl_3$) of compound H



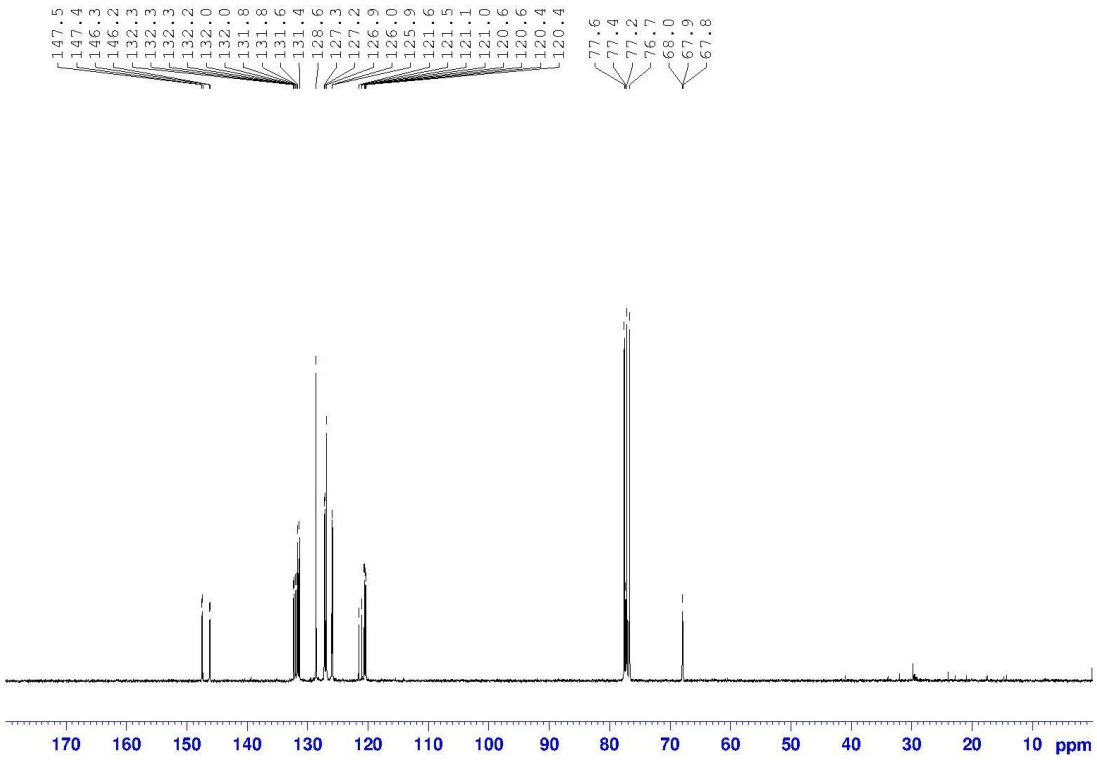
^{31}P NMR (202 MHz, $CDCl_3$) of compound H



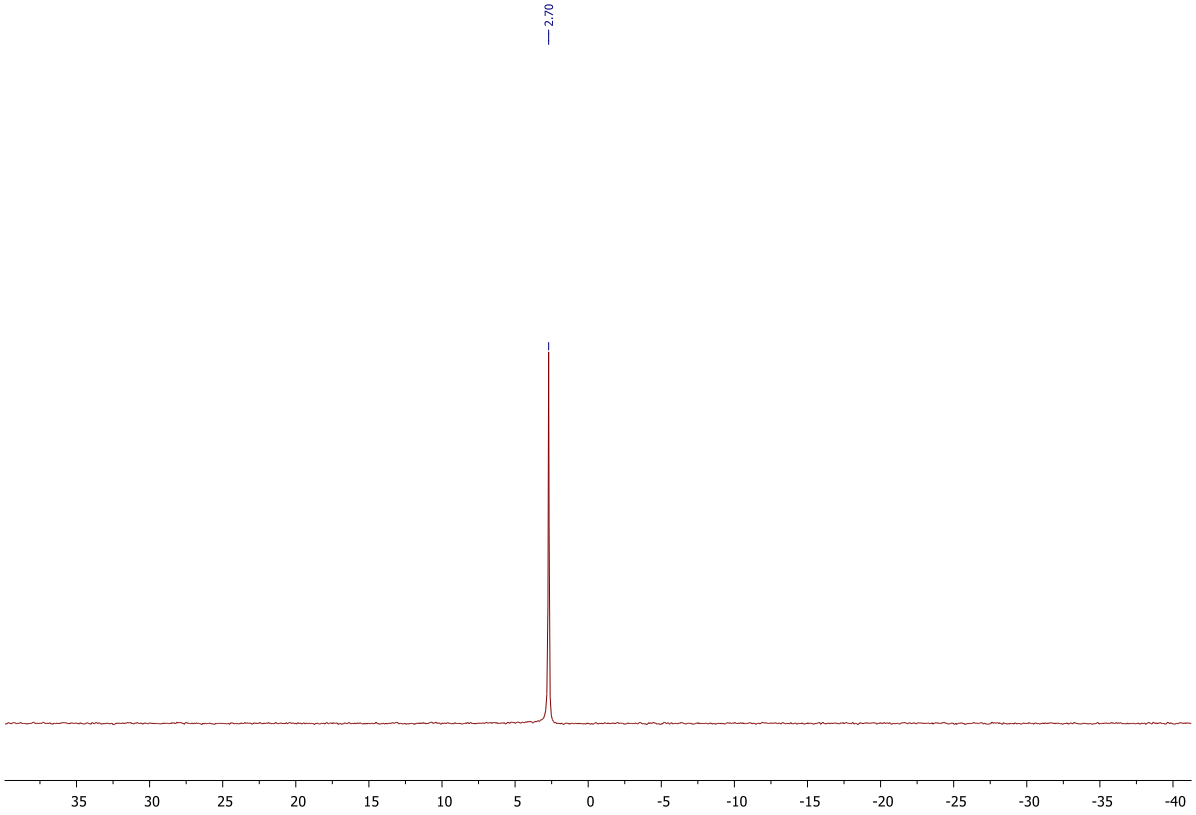
^{1}H NMR (300 MHz, $CDCl_3$) of compound I



^{13}C NMR (75 MHz, $CDCl_3$) of compound I



^{31}P NMR (202 MHz, $CDCl_3$) of compound I

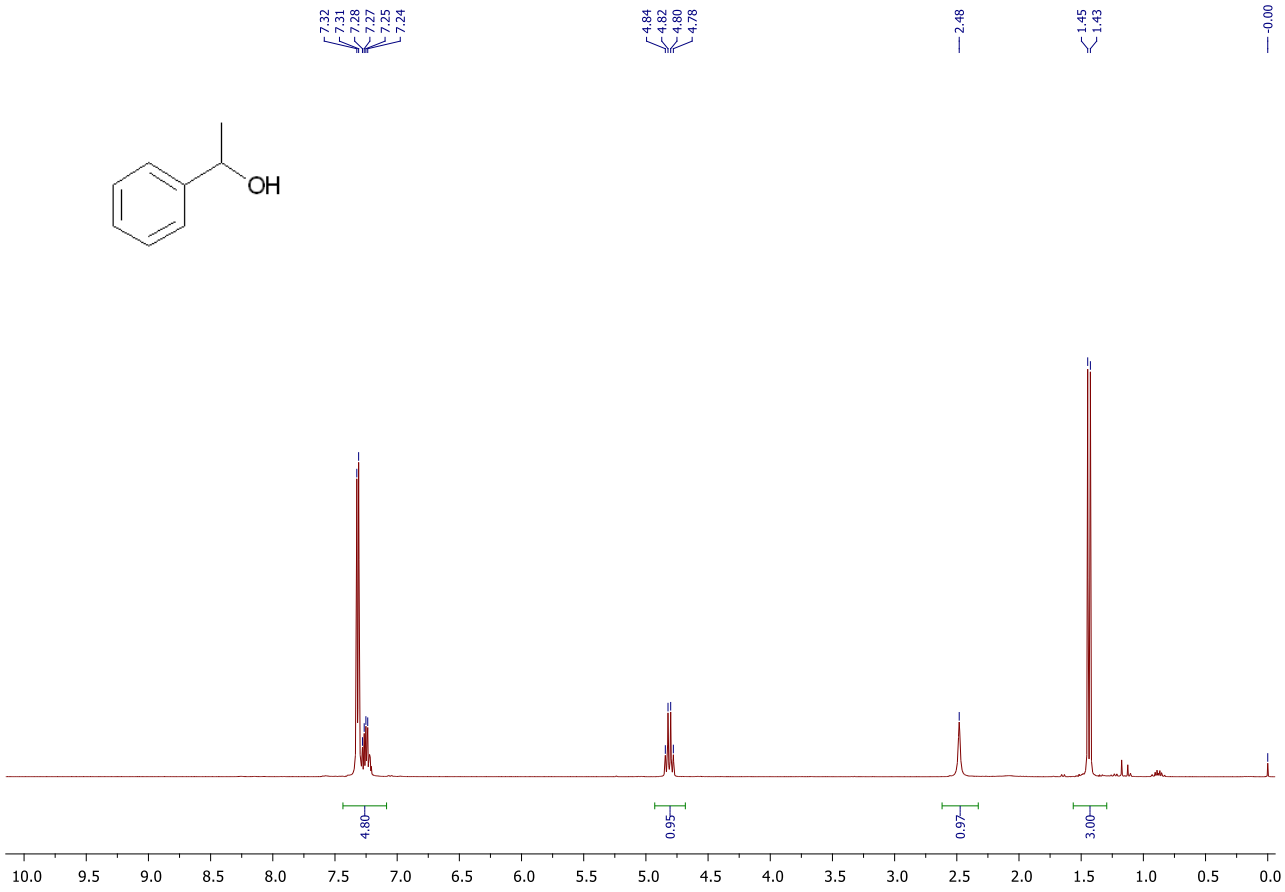


V – General procedure for the hydrosilylation of ketones

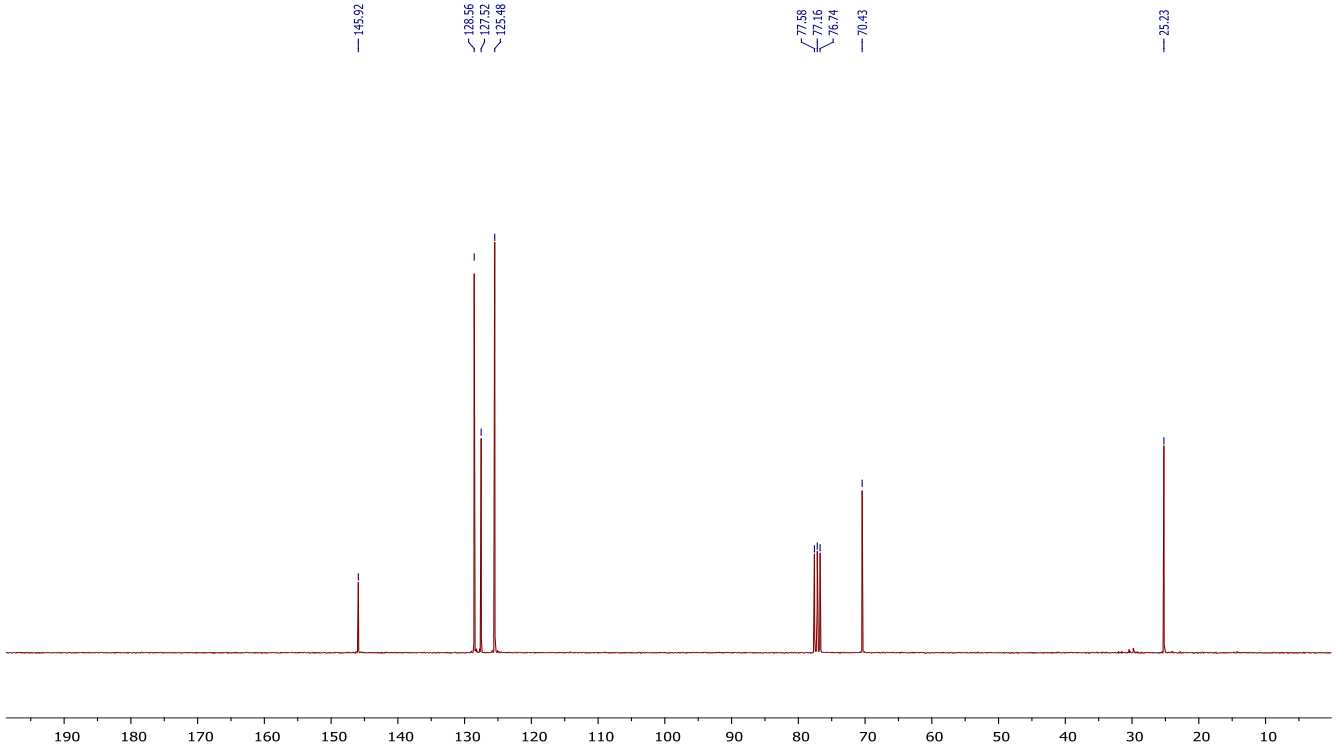
In a flame-dried round-bottom flask, to a solution of the ligand (0.05 mmol) in dry THF (5 mL) under an atmosphere of argon was added $ZnEt_2$ (50 µL, 1 M solution in *n*-hexane, 0.05 mmol). After 10 min, the ketone (1 mmol) and $(EtO)_2MeSiH$ (0.24 mL, 1.5 mmol) were injected and the reaction mixture was stirred overnight at room temperature. After removal of the solvent under reduced pressure, MeOH (4 mL) and an aqueous 1 N NaOH solution (4 mL) were added and the resulting solution was stirred for 12 h. The reaction medium was quenched with brine (10 mL) and an aqueous 1 N HCl solution (10 mL), and extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with an aqueous 1 N NaOH solution (10 mL) and brine (10 mL). After drying over anhydrous $MgSO_4$, filtration and evaporation to dryness, the residue was subjected to ^1H NMR analysis to determine the conversion. The crude product was then purified by silica gel column chromatography using petroleum ether/ Et_2O mixtures. ^1H and ^{13}C NMR data for purified products are in agreement with reported values.

VI - ^{1}H, ^{13}C NMR and HPLC data of compounds 5a-f

^{1}H NMR (300 MHz, $CDCl_3$) of compound 5a



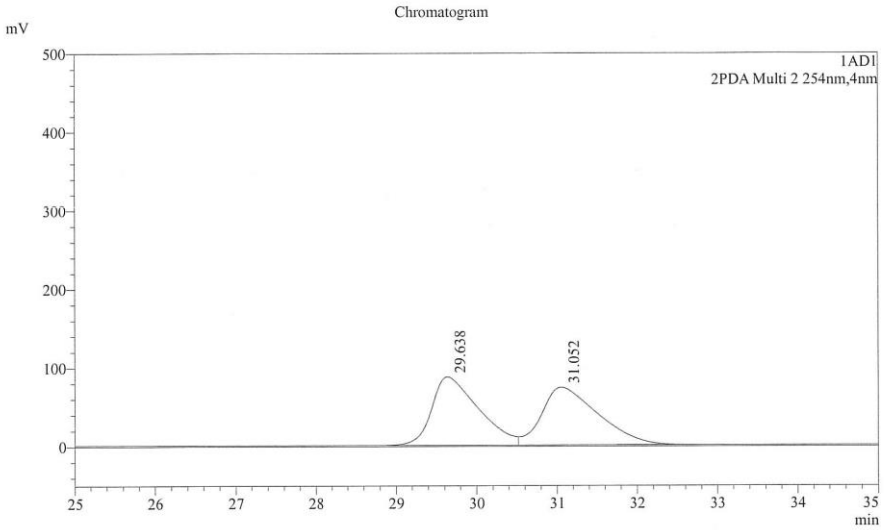
^{13}C NMR (75 MHz, $CDCl_3$) of compound 5a



Chiralpak IA, Heptane/Isopropanol = 99/1, 0.8mL/min, 254nm $[\alpha]^{20}_{D}$ -17.3 (c = 1.0, $CHCl_3$)

Sample Information

Sample Name	: phenylethanol IA 99-1 0.8mlmin
Date Acquired	: 29/02/2016 15:06:37
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm



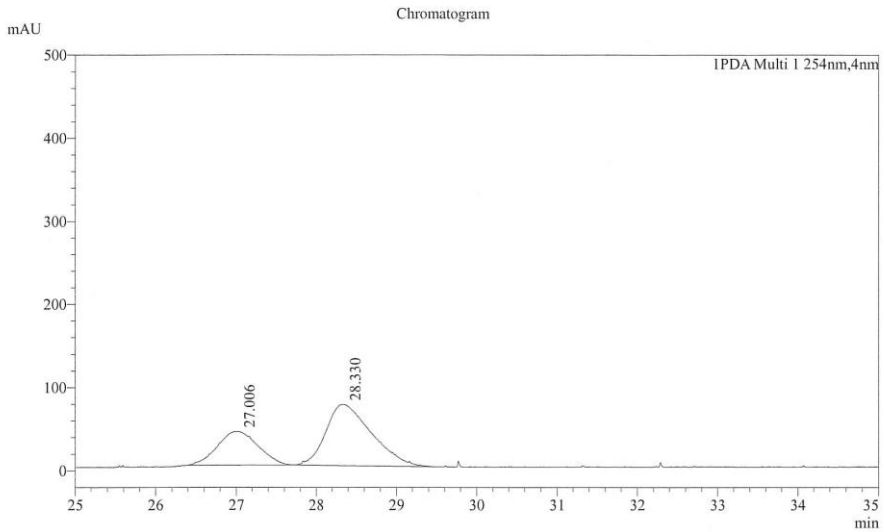
Peak Table

PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	29.638	86907	3498117	49.463
2	31.052	73281	3574129	50.537
Total		160188	7072246	100.000

Sample Information

Sample Name	: ANN 49
Date Acquired	: 21/03/2016 12:37:20
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm

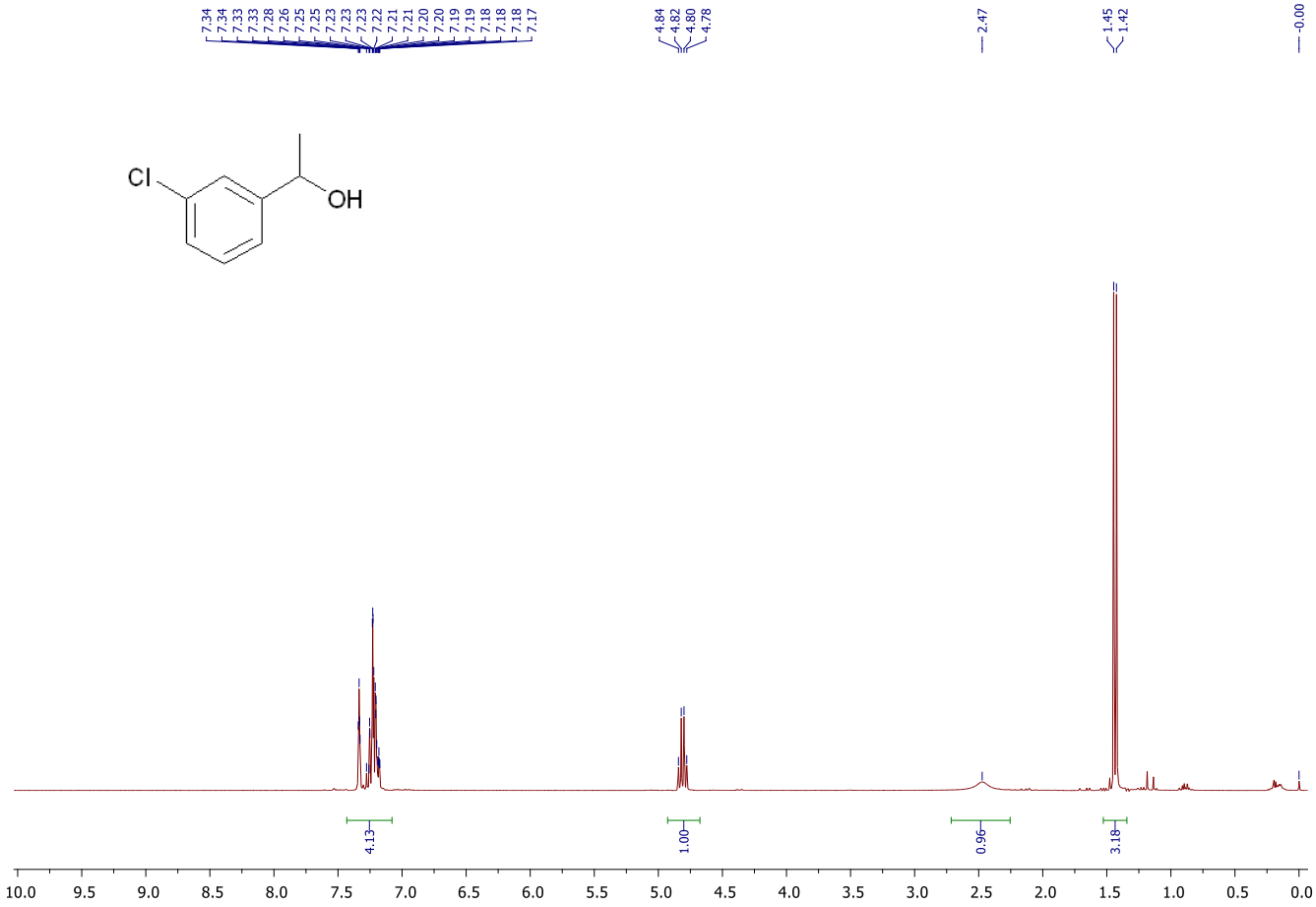


Peak Table

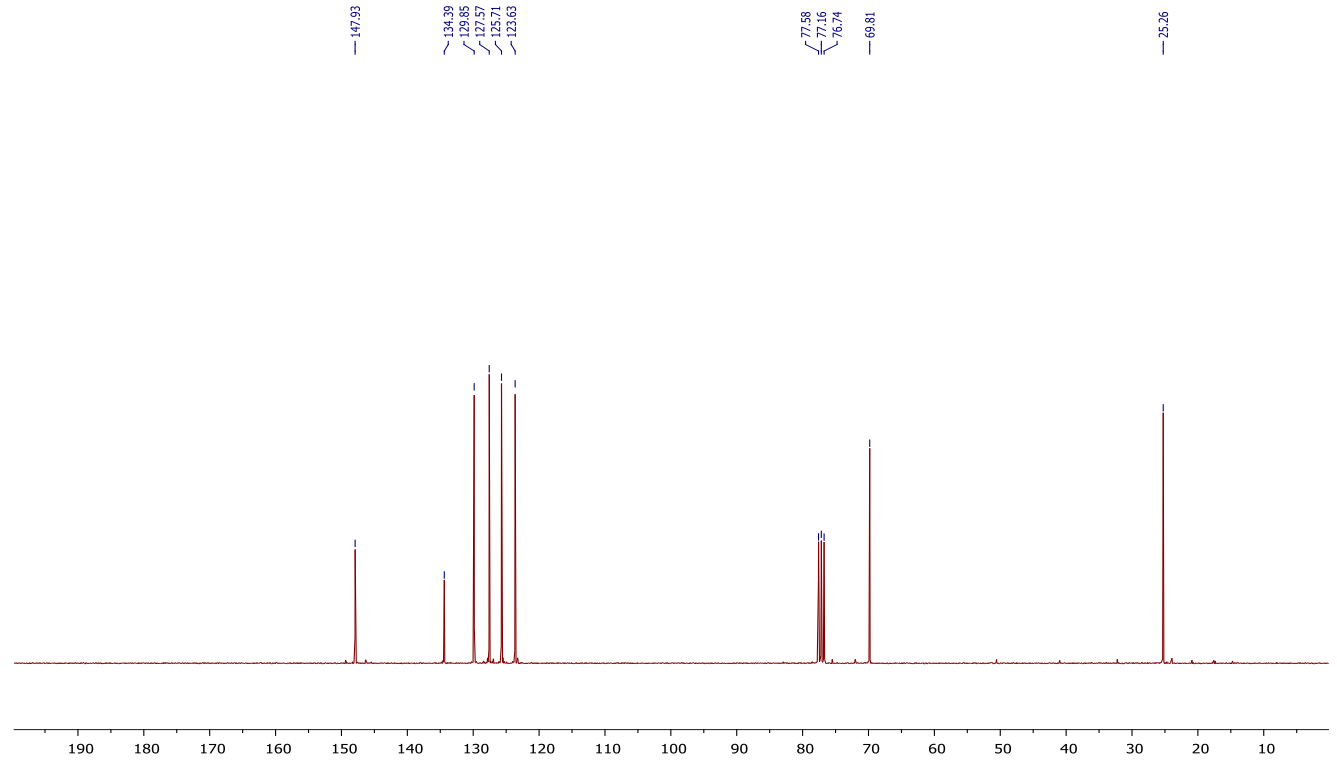
PDA Ch1 254nm

Peak#	Ret. Time	Height	Area	Area%
1	27.006	40414	1417085	32.798
2	28.330	73427	2903620	67.202
Total		113841	4320704	100.000

^{1}H NMR (300 MHz, $CDCl_3$) of compound 5b



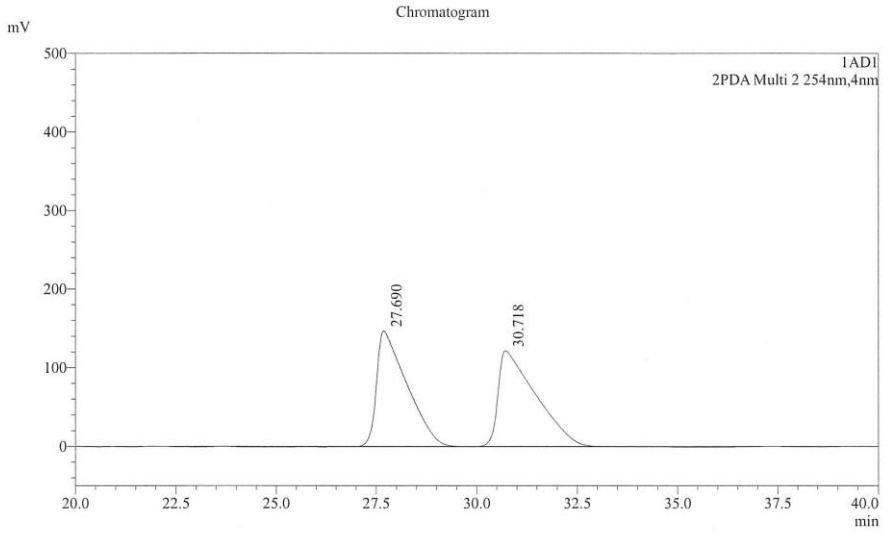
^{13}C NMR (75 MHz, $CDCl_3$) of compound 5b



Chiralpak IA, Heptane/Isopropanol = 99/1, 0.8mL/min, 254nm $[\alpha]^{20}_{D}$ -6.8 (c = 1.0, $CHCl_3$)

Sample Information

Sample Name	: GA 232
Date Acquired	: 12/04/2016 12:16:03
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm



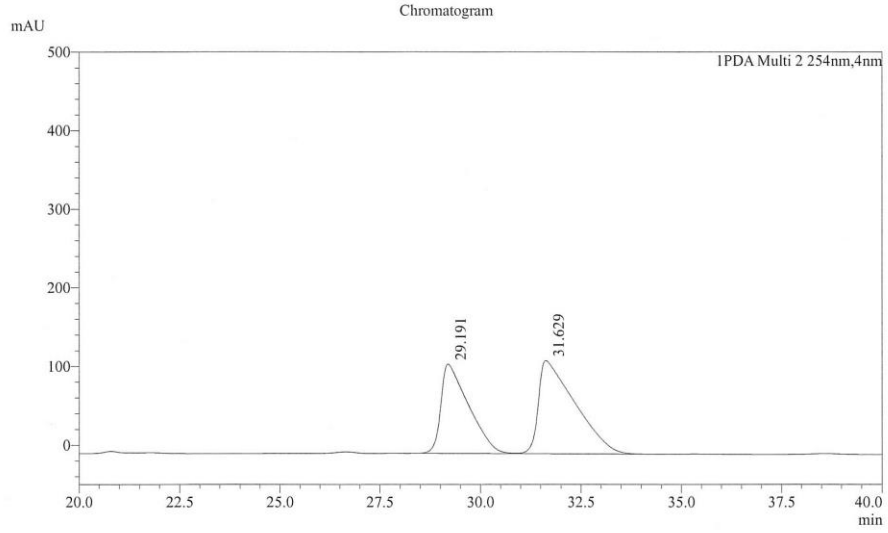
Peak Table

PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	27.690	147191	7731962	49.186
2	30.718	122091	7987768	50.814
Total		269282	15719731	100.000

Sample Information

Sample Name	: ANN 97
Date Acquired	: 26/05/2016 15:13:53
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm

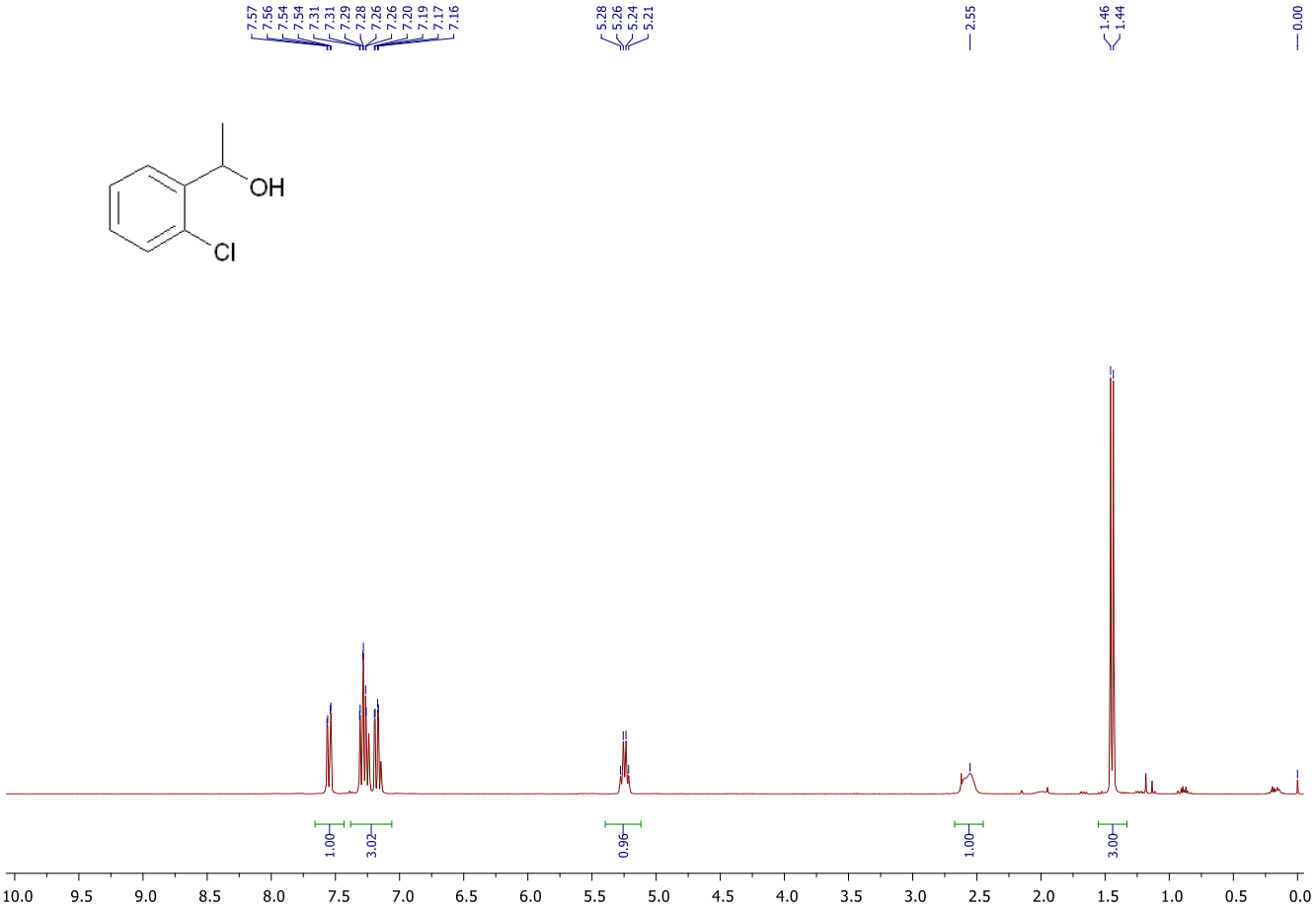


Peak Table

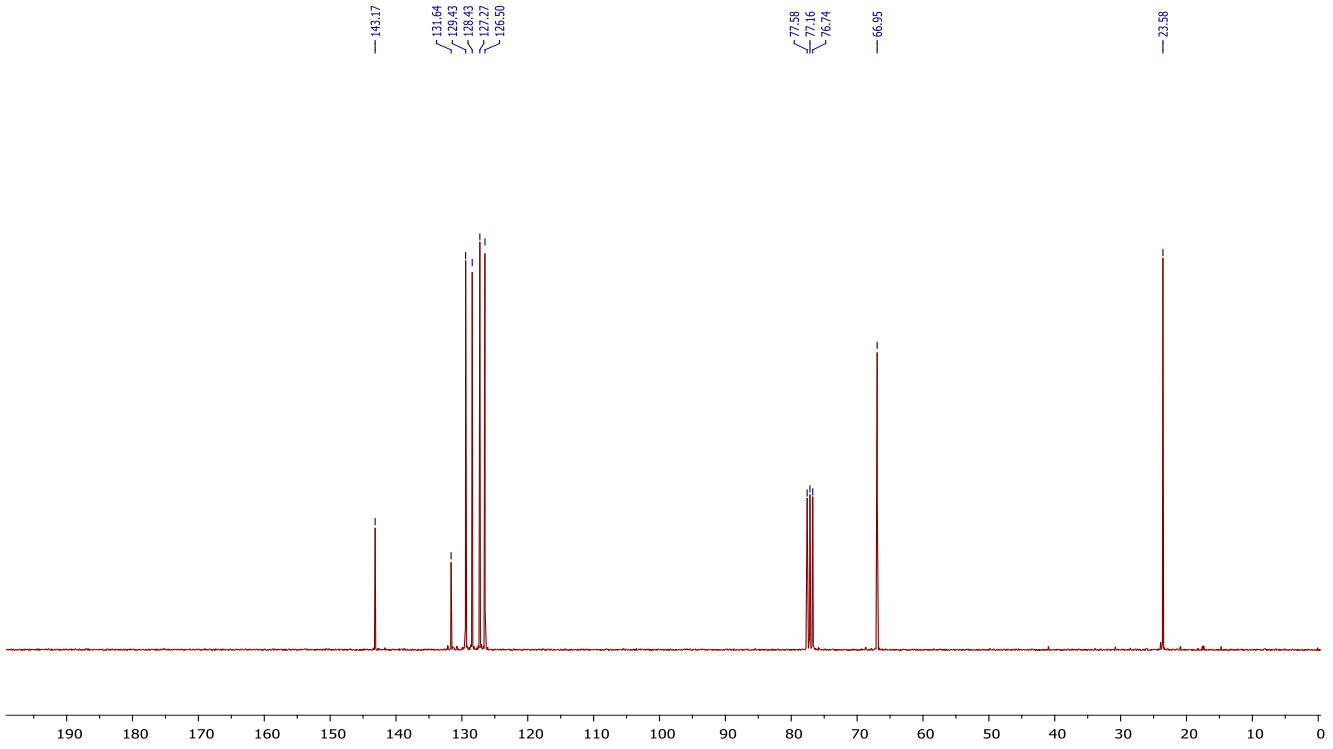
PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	29.191	113476	5450843	42.167
2	31.629	118315	7475900	57.833
Total		231791	12926743	100.000

^{1}H NMR (300 MHz, $CDCl_3$) of compound 5c



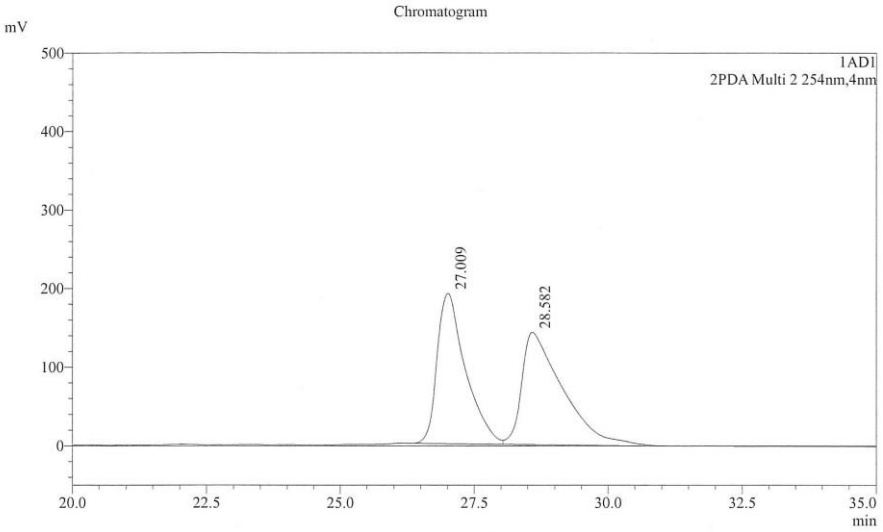
^{13}C NMR (75 MHz, $CDCl_3$) of compound 5c



Chiralpak IA, Heptane/Isopropanol = 99/1, 0.8mL/min, 254nm $[\alpha]^{20}_{D}$ -5.8 (c = 1.0, $CHCl_3$)

Sample Information

Sample Name	: TJ 27
Date Acquired	: 12/04/2016 10:14:47
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm



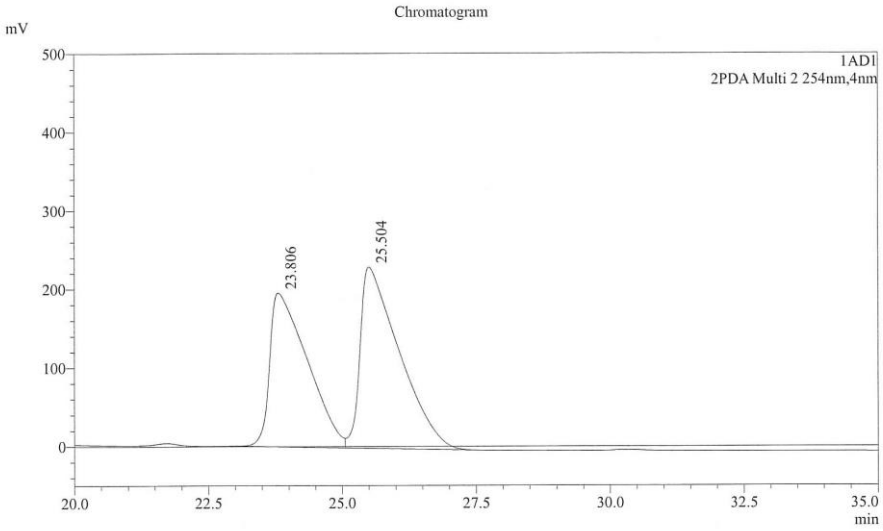
Peak Table

PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	27.009	191312	7034217	48.159
2	28.582	142901	7571922	51.841
Total		334213	14606138	100.000

Sample Information

Sample Name	: ANN 96
Date Acquired	: 26/05/2016 14:33:28
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm

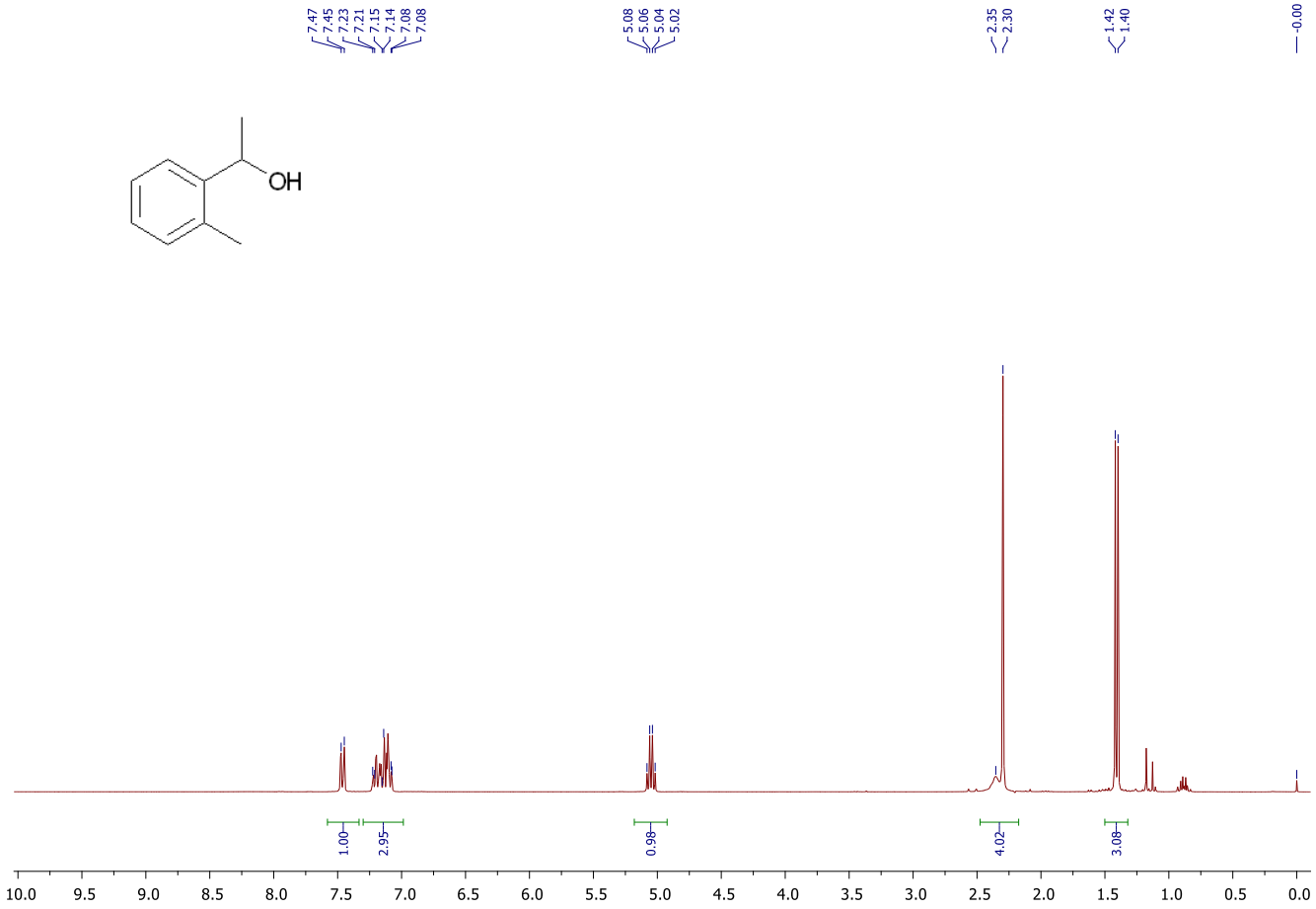


Peak Table

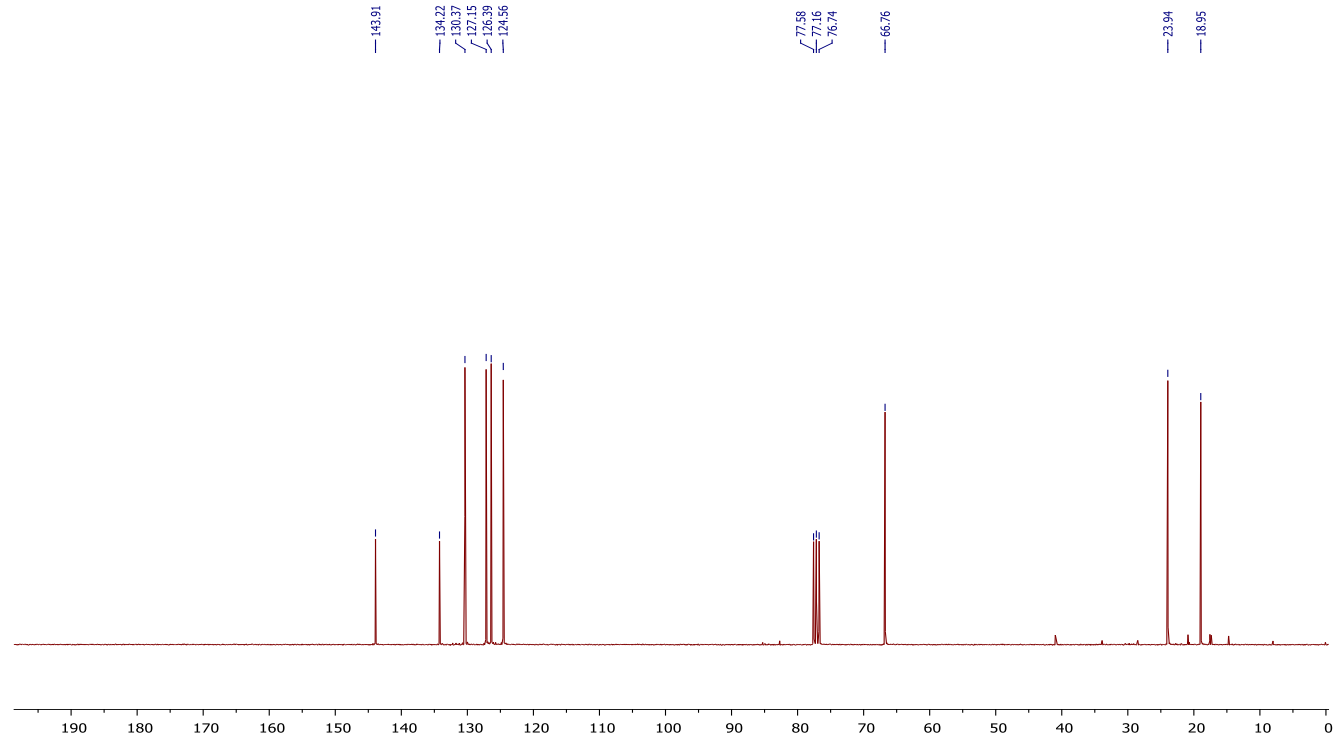
PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	23.806	195557	9576513	44.851
2	25.504	230734	11775523	55.149
Total		426291	21352036	100.000

^{1}H NMR (300 MHz, $CDCl_3$) of compound 5d



^{13}C NMR (75 MHz, $CDCl_3$) of compound 5d



Chiralpak IA, Heptane/Isopropanol = 99/1, 0.8mL/min, 254nm $[\alpha]^{20}_{D}$ +11.2 (c = 1.0, $CHCl_3$)

Sample Information

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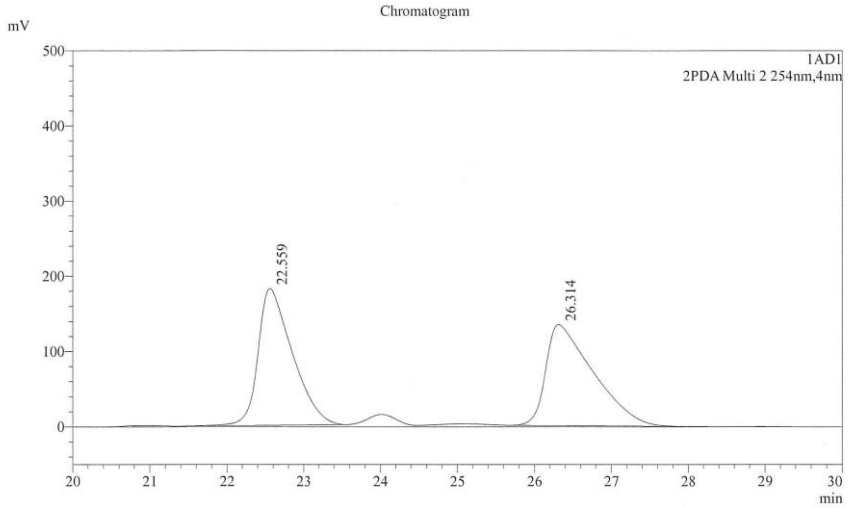
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm



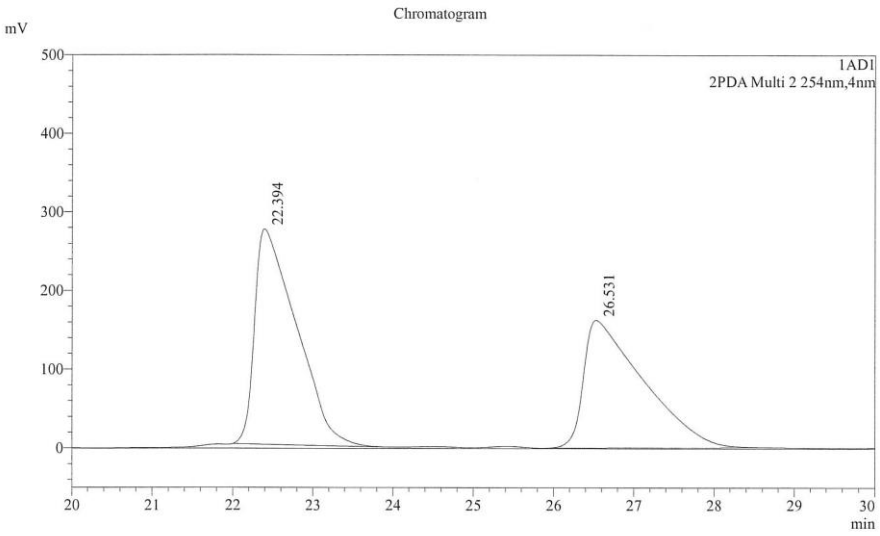
Peak Table

PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	22.559	181593	5630475	49.534
2	26.314	134053	5736385	50.466
Total		315647	11366860	100.000

Sample Information

Sample Name	: ANN 99
Date Acquired	: 26/05/2016 15:54:19
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm

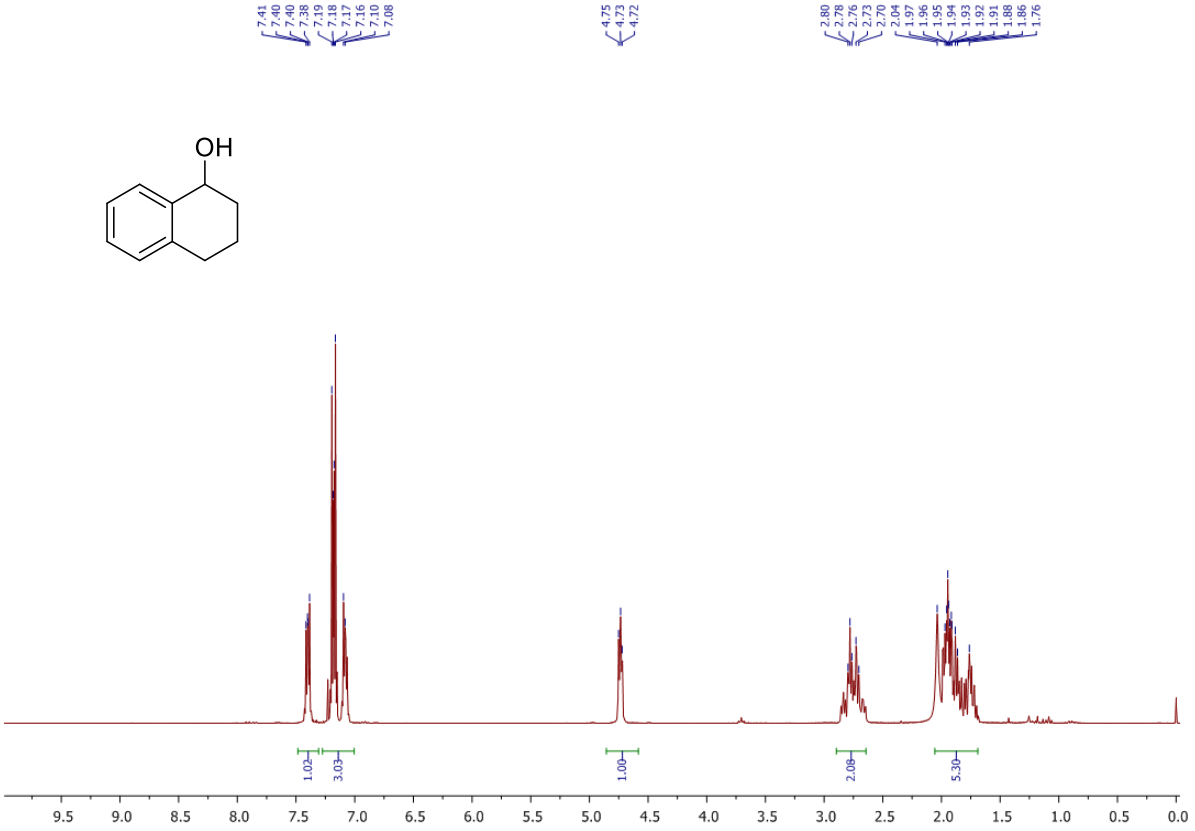


Peak Table

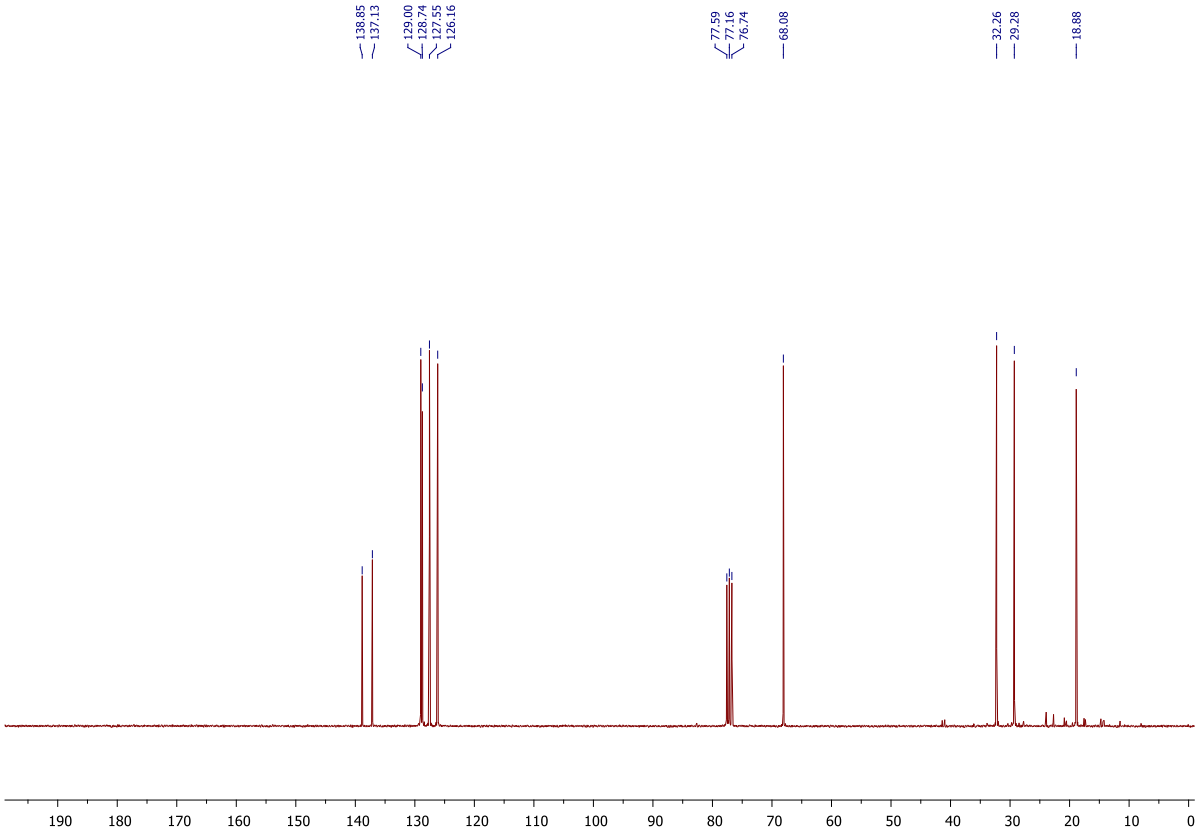
PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	22.394	273492	9893972	54.183
2	26.531	161969	8366203	45.817
Total		435460	18260175	100.000

^{1}H NMR (300 MHz, $CDCl_3$) of compound 5e



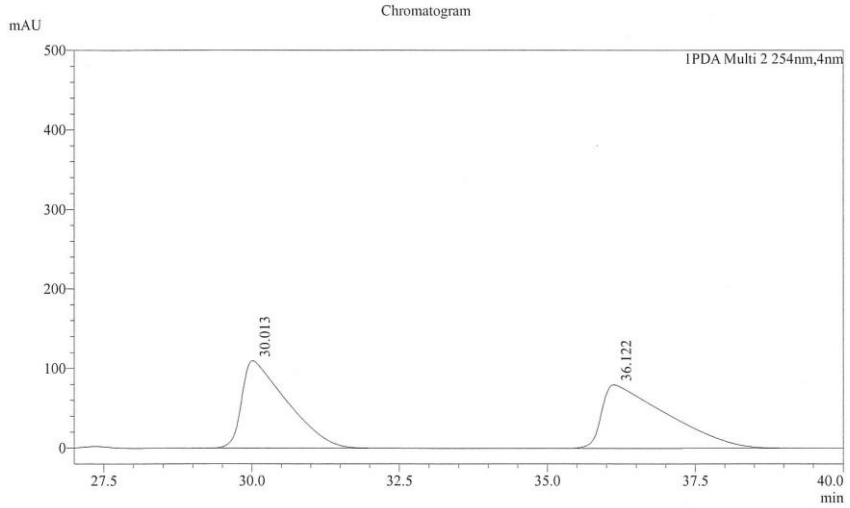
^{13}C NMR (75 MHz, $CDCl_3$) of compound 5e



Chiralpak IA, Heptane/Isopropanol = 99/1, 0.8mL/min, 254nm $[\alpha]^{20}_{D}$ +8.3 (c = 1.0, $CHCl_3$)

Sample Information

Sample Name	: GA 281
Date Acquired	: 12/04/2016 14:17:19
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm



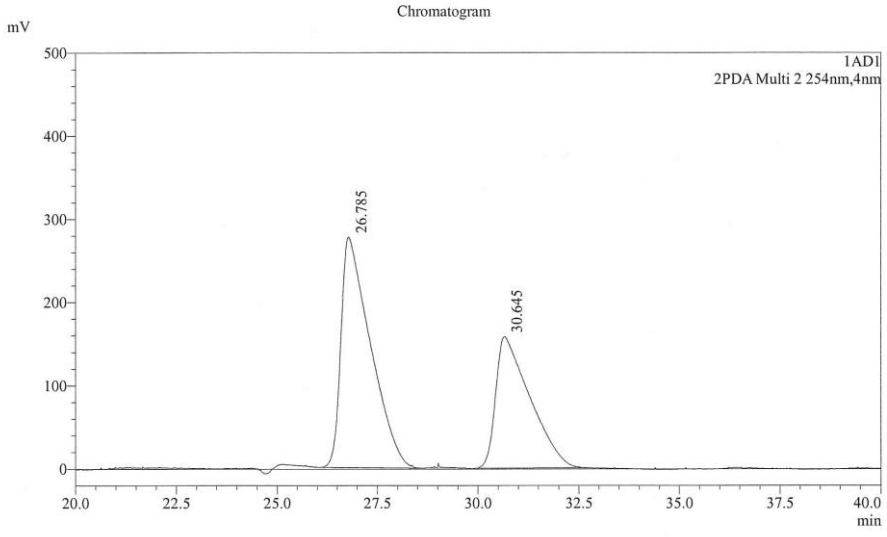
Peak Table

PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	30.013	109745	5847179	48.990
2	36.122	79782	6088260	51.010
Total		189527	11935439	100.000

Sample Information

Sample Name	: ANN101
Date Acquired	: 02/06/2016 11:40:49
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm

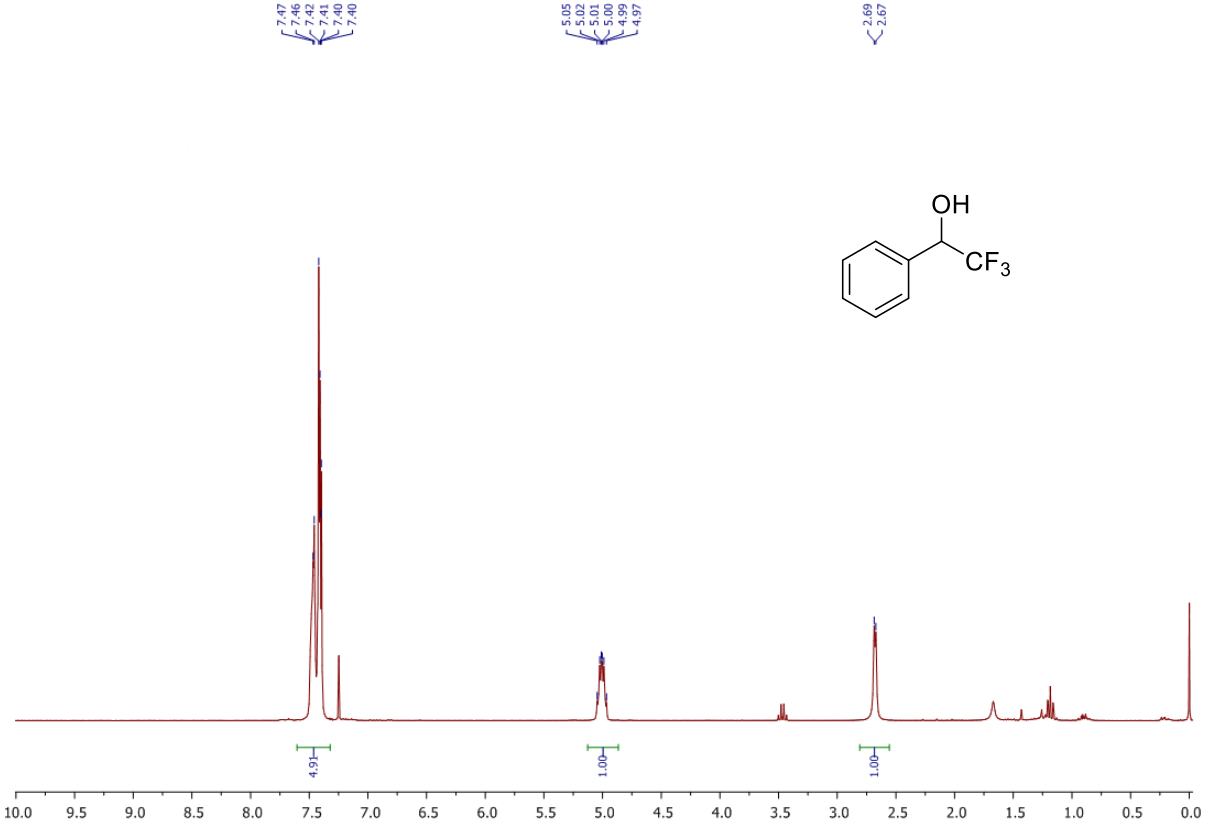


Peak Table

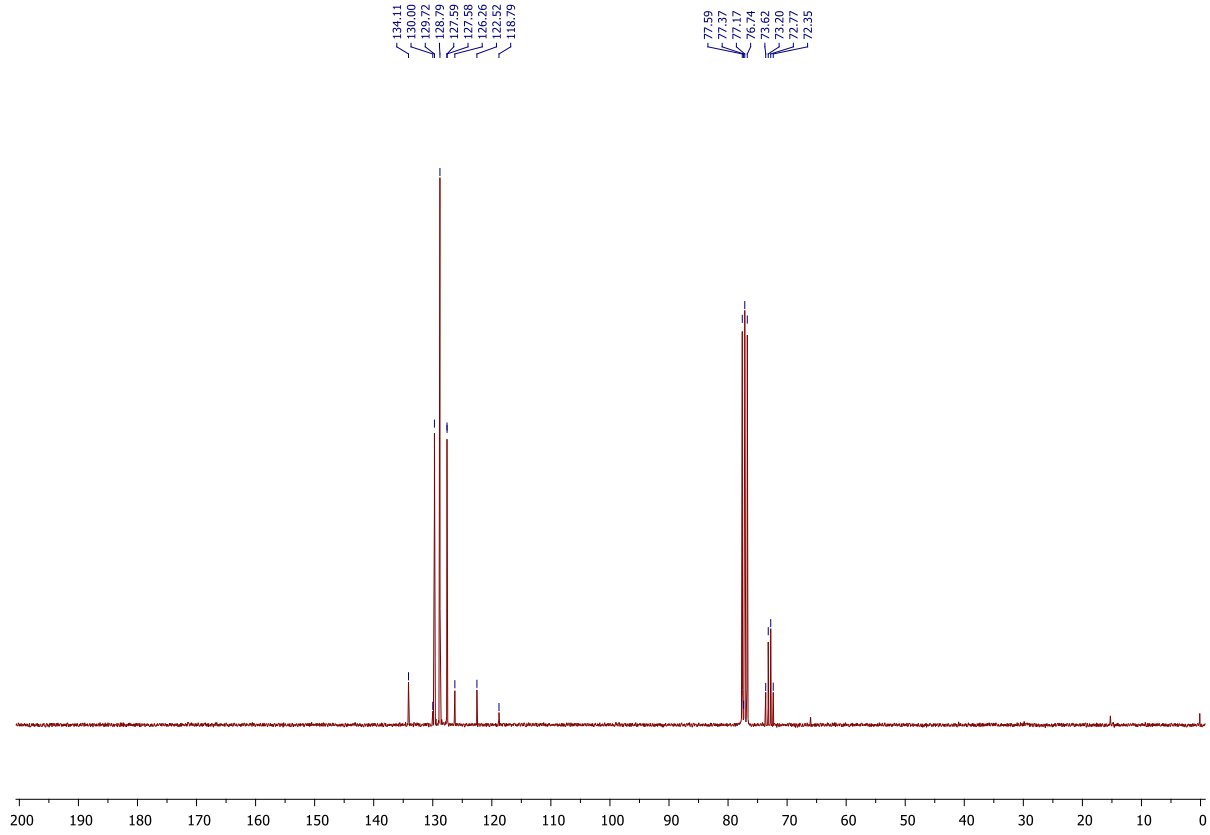
PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	26.785	276822	14099301	60.249
2	30.645	157372	9302456	39.751
Total		434194	23401757	100.000

^{1}H NMR (300 MHz, $CDCl_3$) of compound 5f



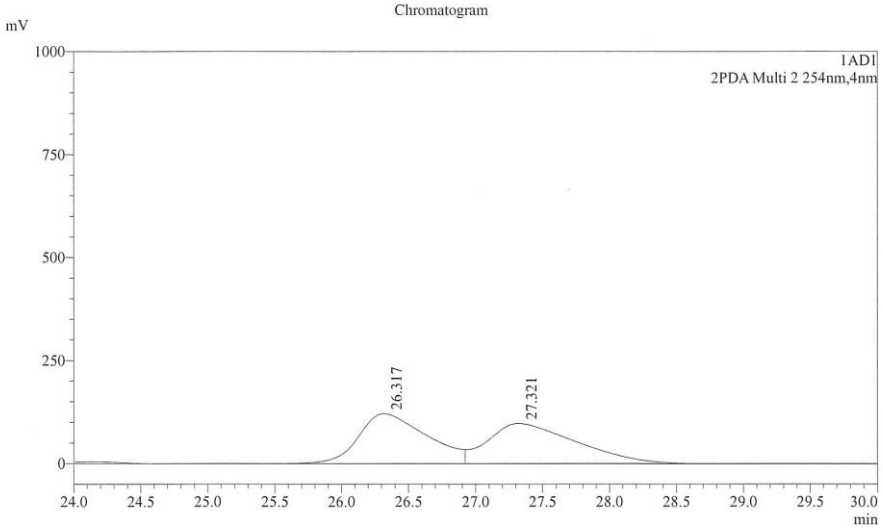
^{13}C NMR (75 MHz, $CDCl_3$) of compound 5f



Chiralpak IA, Heptane/Isopropanol = 99/1, 0.8mL/min, 254nm $[\alpha]^{20}_{D}$ +0.9 (c = 1.0, $CHCl_3$)

Sample Information

Sample Name	: VS 49
Date Acquired	: 12/04/2016 12:56:28
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm



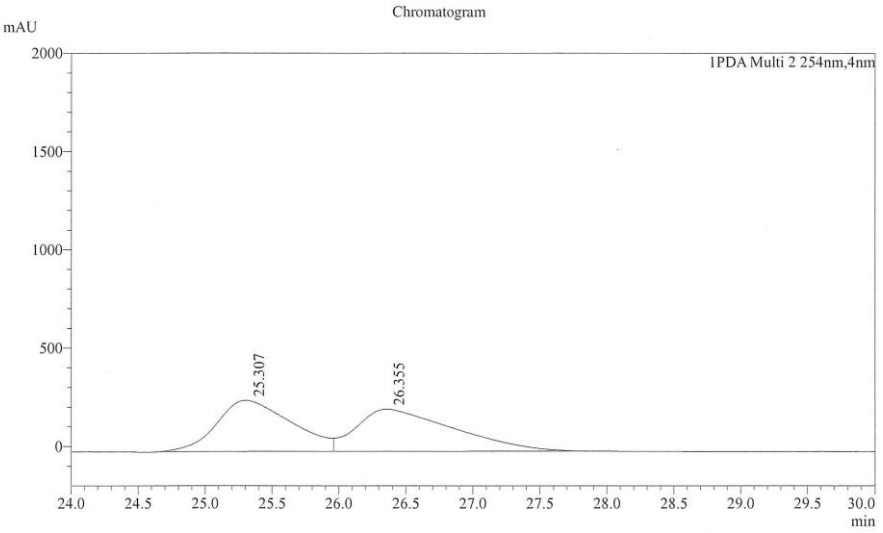
Peak Table

PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	26.317	121266	4343567	49.111
2	27.321	97599	4500845	50.889
Total		218865	8844412	100.000

Sample Information

Sample Name	: ANN100
Date Acquired	: 02/06/2016 11:00:22
Method File	: IA hept-IPA 99-1 flow0.8mlmin.lcm



Peak Table

PDA Ch2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	25.307	259030	10091657	48.441
2	26.355	213996	10741274	51.559
Total		473026	20832931	100.000

VII - X-ray diffraction study for compounds G and H

Data collections for compounds **G** and **H** were carried out on a D8 Venture Bruker AXS diffractometer at 150 K. The structures were solved by direct methods using the *SHELXT* program[1] and then refined with full-matrix least-square methods based on F^2 (*SHELXL-2014*).[2] All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions. Details of the data collection, cell dimensions, and structure refinements are given in Table 1.

[1] Sheldrick, G. M. *Acta Cryst.* **2015**, *A71*, 3–8.

[2] Sheldrick, G. M. *Acta Cryst.* **2015**, *C71*, 3–8.

Compound	**G**	**H**
Formula	C_{26} H_{16} I O_4 P	C_{26} H_{16} I O_4 P
Fw, g/mol	550.26	550.26
Crystal size, mm	0.58 x 0.53 x 0.40	0.58 x 0.51 x 0.22
Color	colourless	colourless
space group	*P* 2_1	*P* 2_1 2_1 2_1
a, Å	6.9836(9)	7.2039(8)
b, Å	18.211(3)	9.9713(11)
c, Å	8.7011(14)	30.095(4)
α, deg	90	90
β, deg	103.450(5)	90
γ, deg	90	90
V, $Å^3$	1076.2(3)	2161.8(4)
Z	2	4
d_{calcd}, g/cm^3	1.698	1.691
θ range, deg	2.237 to 27.547	2.152 to 27.518
μ, mm^{-1}	1.594	1.587
no. of obsd data, I > 2σ (I)	4429	4781
data / restraints / parameters	4548 / 1 / 289	4939 / 0 / 289
R1 (all data)[a]	0.0325	0.0251
wR2 (all data)[b]	0.0764	0.0543
$(\Delta\rho)_{min}$, $e.Å^{-3}$	-1.324	-0.603
$(\Delta\rho)_{max}$, $e.Å^{-3}$	0.850	0.286

Table 1. Selected crystallographic data and collection parameters for **G** and **H**.

[a] $R1 = \sum | |F_o| - |F_c| | / \sum |F_o|$. [b] $wR2 = \{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}^{1/2}$.