A versatile indium trichloride mediated Prins-type reaction to unsaturated heterocycles

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Supporting Information

Representative experimental proceedures and spectral data for compounds 2-4 & 6 and those in Tables 1 and 2 are provided and crystallographic CIF files for compounds 3 & 6.

A. General

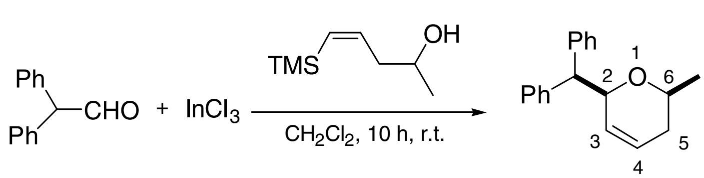
Dichloromethane was distilled over calcium hydride; diethyl ether, THF and toluene were distilled over sodium and benzophenone, which was used as an indicator. All other solvents were obtained anhydrous from Aldrich and used directly into the reaction vessel. All reactions were carried out under an atmosphere of nitrogen unless otherwise stated, using a vacuum/nitrogen manifold. All glassware, syringes and needles were predried in an oven (120-140 °C) and cooled in a nitrogen atmosphere prior to use. Stirring was by internal magnetic follower. All chemicals were purified by distillation or recrystallisation where appropriate. Commercially available compounds were generally used without further purification.

All reactions were followed by TLC. Analytical thin layer chromatography was carried out using aluminium backed plates coated with Merck Kieselgel 60 GF_{254}. Plates were visualised under UV light (at 254 nm) or by staining with acidic ceric ammonium molybdate or acidic potassium permanganate followed by heating. Flash chromatography was carried out using Matrex silica 60, 230-400 mesh; samples were applied as a saturated solution in an appropriate solvent.

Proton (^1H) NMR spectra were recorded at either 300 MHz or 400 MHz and carbon (^{13}C) NMR spectra at 75 MHz or 100 MHz in deuterated. NMR chemical shifts (δ) are quoted in ppm (parts per million) relative to an internal standard ($CDCl_3$). Spectroscopic data is annotated with the following abbreviations: br - broad, s – singlet, d – doublet, t – triplet, and m - multiplet. Coupling constants are expressed in Hz. ^1H and ^{13}C NMR assignments were made using COSY (^1H-^1H correlation) and HMQC (^1H-^{13}C correlation) NMR techniques.

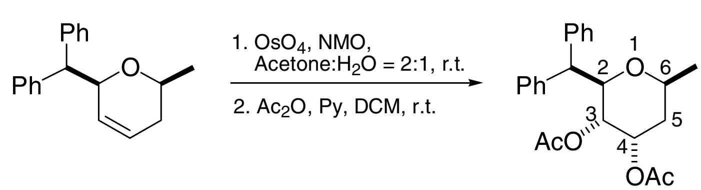
Compounds characterised by high-resolution mass spectrometry were chromatographically homogeneous. Infrared (IR) spectra were recorded in the range 4000-600 cm^{-1} with internal calibration. Spectra were recorded as KBr discs or as thin films between NaCl plates.

(±)-Cis-2-Benzhydryl-6-methyl-5,6-dihydro-2H-pyran (2)



Indium (III) chloride (0.44 g, 2 mmol) was added to a 50 ml round bottom flask containing diphenylacetaldehyde (1 eq., 0.39 g, 2 mmol) dissolved in dry DCM (20 ml) under an atmosphere of nitrogen and the resulting solution was stirred for 1 hour. After this time *Z*-5-trimethylsilylpent-4-en-2-ol (1 eq., 0.32g, 2 mmol) was added and the reaction mixture was stirred at room temperature for a further 16 hours. The reaction mixture was then quenched with distilled water (10 ml) and the water layer was extracted with dichloromethane (40 ml). The combined organic extracts were dried with magnesium sulfate. The solvent was removed *in vacuo* and the reaction mixture purified by flash column chromatography (hexane:diethyl ether 10:1) to give the *title compound* isolated as a colourless solid (0.41 g, 78%); R_f 0.43 (petrol:diethyl ether 10:1); Mp 75-77 °C (from petrol); Found $[M+H]^+$ 265.1590: $C_{19}H_{20}O+H$ requires 265.1592; Found: C, 86.3; H, 7.7. Calc. for $C_{19}H_{20}O$: C, 86.3; H, 7.6%; ν_{max}/cm^{-1} (KBr) 3027 [Ar(C-H)], 2970 (OCH), 1654 (C=C), 1598, 1495, 1449, 1388, 1183 (C-O), 1086; δ_H (400 MHz; $CDCl_3$) 7.19-7.39 (10H, m, Ar-H), 5.77 (1H, m, C(4)H), 5.58 (1H, dt, *J* 10.3, 1.9, C(3)H), 4.87 (1H, m, C(2)H), 4.02 (1H, d, *J* 8.1, $Ph_2C\underline{H}$), 3.75 (1H, m, C(6)H), 1.95 (2H, m, $C(5)H_2$), 1.23 (3H, d, *J* 6.4, $C(6)C\underline{H}_3$); δ_C (100 MHz; $CDCl_3$) 142.5 (C_{ipso}), 142.0 (C_{ipso}), 127.9-128.9 [overlapping 8×(C-Ar), C(3)H], 126.3 (C(4)H), 126.1 (C-Ar), 125.9 (C-Ar), 77.3 (C(2)H), 70.3 (C(6)H), 56.3 ($Ar_2\underline{C}H$), 32.8 ($C(5)H_2$), 21.7 ($C(6)\underline{C}H_3$); *m/z* (CI) 265 [$(MH)^+$, 90%], 247 [$(MH)^+$-H_2O, 100].

(±)-2β-Benzhydryl-3α,4α-diacetoxy-6β-methyltetrahydropyran (3)

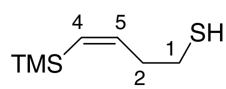


(±)-*Cis*-2-Benzhydryl-6-methyloxacyclohex-3-ene (0.09 g, 0.3 mmol) was placed into a round bottom flask (25 ml) and dissolved in acetone:water 2:1 (9 ml). 4-Methylmorpholine *N*-oxide was added (0.09 g, 0.7 mmol, 2eq.), followed by two crystals of osmium tetroxide. The flask was sealed with a stopper and the reaction mixture stirred for 48 hours at room temperature. After this time the reaction mixture was cooled to 0 °C, saturated aqueous sodium bisulfite (6 ml) was added and the reaction mixture allowed to warm to room temperature. The aqueous layer was extracted with ethyl acetate (3×20 ml). The combined organic layers were washed with brine (2×10 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* to give (±)-2β-benzhydryl-3α,4α-dihydroxy-6β-methyloxacyclohexane (0.06 g, 61%) which was used without further purification. (±)-2β-benzhydryl-3α,4α-dihydroxy-6β-methyloxacyclohexane (0.06 g) was dissolved in pyridine:DCM 1:1 (10 ml), acetic anhydride was added (0.61 ml, 6.4 mmol, 16 eq.) and the reaction mixture was stirred overnight (19 hours). After this time the reaction mixture was quenched with saturated aqueous sodium hydrogencarbonate solution (5 ml), the layers were separated and the aqueous layer was extracted with DCM (3×10 ml). The organic layer was washed with 2M hydrochloric acid (2×10 ml), saturated brine solution (10 ml) and dried over $MgSO_4$. The solvent was removed *in vacuo* to give *(±)-2β-benzhydryl-3α,4α-diacetoxy-6β-methyltetrahydropyran* as colourless crystals (0.04 g, 57%; overall yield 35%); Mp 144-146 °C (from hexane/diethyl ether); Found $[M+H]^+$ 383.1851; $C_{23}H_{26}O_5$+H requires 383.1858; Found: C, 72.3; H, 6.8. Calc. for $C_{23}H_{26}O_5$: C, 72.2; H, 6.8%; ν_{max}/cm^{-1} (KBr) 3088, 3052, 3027 [Ar(C-H)], 2883 (OCH), 1736, (C=O), 1598, 1495, 1449, 1367, 1137 (C-O), 1055; δ_H (400 MHz; $CDCl_3$) 7.19-7.44 (10H, m, Ar-H), 5.40 (1H, m, $Ph_2C\underline{H}$), 4.48 (2H, m, C(2)H, C(3)H), 4.09 (1H, m, C(4)H), 3.96 (1H, m, C(6)H), 2.11 (3H, s, $OCOC\underline{H}_3$), 1.96 (3H, s, $OCOC\underline{H}_3$), 1.79 (1H, m, C(5)$\underline{H}$H), 1.58 (1H, m, C(5)H$\underline{H}$), 1.20 (3H, d, *J* 6.2, C(6)$C\underline{H}_3$); δ_C (100 MHz; $CDCl_3$) 170.3 [$C_{quat}(O\underline{C}OCH_3)$], 169.6 [$C_{quat}(O\underline{C}OCH_3)$], 143.1 ($C_{ipso}$), 139.7 ($C_{ipso}$), 130.2 [overlapping 2×C(Ar)], 128.7 [overlapping 2×C(Ar)], 128.2 [overlapping 2×C(Ar)], 128.0 [overlapping 2×C(Ar)], 126.6 C(Ar), 126.2 C(Ar), 74.9 and 69.8 [C(3 and 2)H], 68.4 (C(6)H), 67.7 ($Ph_2\underline{C}H$), 51.1 (C(4)H), 37.4 ($C(5)H_2$), 21.1 [overlapping C(3 and 4)$CHOCO\underline{C}H_3$], 20.8 [C(6)$\underline{C}H_3$]; *m/z* (CI) 383 [$(MH)^+$, 5%], 323 [$(MH)^+-C_2H_4O_2$, 10], 263 [$(MH)^+-2\times(C_2H_4O_2)$, 35], 245 [$(MH)^+-C_4H_{10}O_5$, 25], 215 [$(MH)^+-C_6H_{16}O_5$, 25], 143 [$(MH)^+-C_{12}H_{16}O_5$, 100].

General method for the preparation of thiols (4) from alcohols

Diethyl azodicarboxylate (2 eq., 1.9 ml, 12 mmol) was added to a vigorously stirred solution of triphenylphosphine (2 eq., 3.32 g, 12 mmol) in THF (100 ml) at 0 °C. The mixture was stirred at 0 °C for 30 minutes. A solution of 4- trimethylsilylbut-3-en-1-ol (1 eq., 6 mmol) *or* (±)-*Z*-5-trimethylsilylpent-4-en-2-ol (1 eq., 6 mmol) and thioacetic acid (2 eq., 0.9 ml, 12 mmol) in THF (50 ml) was added dropwise over 10 minutes and the resulting mixture stirred for 1 hour at 0 °C and 1 hour at ambient temperature. A clear yellow solution was formed. The solution was concentrated *in vacuo* and the residue was purified by flash chromatography over silica gel, eluting with petrol:diethyl ether 7:1 to give the thioacetate (0.83 g, 61%). The thioacetate (1 eq., 2 mmol) was then dissolved in anhydrous THF (25 ml) and added dropwise to a suspension of lithium aluminium hydride (4 eq., 0.25 g, 8 mmol) in anhydrous ether (15 ml) under a nitrogen atmosphere. The reaction mixture was stirred at ambient temperature for 30 minutes, and the excess lithium aluminium hydride was destroyed by careful addition of 1 M solution of hydrochloric acid (10 ml). The ether layer was separated and dried ($MgSO_4$). After evaporation of the solvent, the crude reaction mixture was purified by flash chromatography (petrol:diethyl ether 7:1) to afford the product.

Z-4-Trimethylsilylbut-3-en-1-thiol



Clear oil

Overall yield for two steps 61%

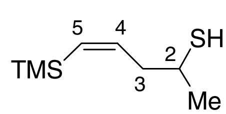
R_f 0.51 (petrol:ether 7:1)

Found $[M+H]^+$ 161.0817; $C_7H_{16}SSi$+H requires 161.0821.

ν_{max}/cm^{-1} (neat) 2969, 1601 (C=C), 843 (S-H), 687 (C-S)

δ_H (300 MHz; $CDCl_3$) 6.11 (1H, dt, *J* 14.0, 7.2, C(3)H), 5.52 (1H, d, *J* 14.0, C(4)H), 2.44 (2H, m, C(1)H_2), 2.31 (2H, m, C(2)H_2), 1.27 (1H, t, *J* 7.6, SH), 0.06 (9H, s, 3×CH_3); δ_C (100 MHz; $CDCl_3$) 145.3 (C(3)H), 131.7 (C(4)H), 37.1 (C(1)H_2), 24.2 (C(2)H_2), 0.00 (TMS).

(±)-Z-5-trimethylsilylpent-4-en-2-thiol



Clear oil

Overall yield for two steps 56%

R_f 0.58 (petrol:ether 7:1)

Found $[M+H]^+$ 175.0961; $C_8H_{18}SSi+H$ requires 175.0977

ν_{max}/cm^{-1} (neat) 2960, 1608 (C=C), 840 (S-H), 686 (C-S)

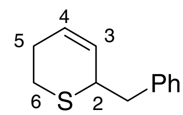
δ_H (300 MHz; $CDCl_3$) 6.18 (1H, ddd, *J* 14.1, 7.2, 6.9, C(4)H), 5.51 (1H, d, *J* 14.1, C(5)H), 2.91 (1H, m, C(2)H), 2.26 (2H, m, $C(3)H_2$), 1.47 (1H, d, *J* 5.6, SH), 1.20 (3H, d, *J* 6.7, $C(1)H_3$), 0.02 (9H, s, $3\times CH_3$); δ_C (100 MHz; $CDCl_3$) 144.9 (C(4)H), 131.7 (C(5)TMS), 43.9 ($C(3)H_2$), 35.1 (C(2)H), 24.6 ($C(1)H_3$), -0.21 ($3\times CH_3$).

m/z (CI) 175 [$(MH)^+$, 70%], 174 [$(M-H)^+$, 100], 159 [$(MH)^+-CH_3$, 55], 133 [$(MH)^+-C_3H_6$, 75].

General method for cyclisation reactions of aldehydes with *Z*-vinylsilyl thiols

Indium chloride (1 mmol) was added to a solution of aldehyde (1 mmol) in dry dichloromethane (20 ml), under an atmosphere of nitrogen and the reaction mixture was stirred for 1 hour. After this time, the homoallylic thiol (1 mmol) was added and the reaction mixture stirred at room temperature for a further 5-16 hours. The reaction was monitored by TLC. Upon completion, the reaction mixture was quenched with distilled water (10 ml). The water layer was extracted with dichloromethane (2x40 ml) and the combined organic layer dried with magnesium sulfate. The solvent was removed *in vacuo* and the reaction mixture purified by flash column chromatography (hexane:diethyl ether 10:1) affording the cyclisation product as an oil.

(±)-2-Benzyl-5,6-dihydro-2H-thiopyran (Table 1 entry 1)



Pale yellow oil.

51%

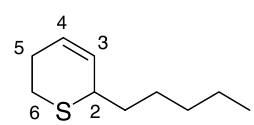
R_f (hexane:diethyl ether 10:1).

Found $[M+H]^+$ 191.0888; $C_{14}H_{18}S$+H requires 191.0895.

ν_{max}/cm^{-1} (neat) 3015 [Ar(C-H)], 2834 (S-CH), 1651 (C=C), 1460, 741 (C-S), 696 (C-S)

δ_H (400 MHz; $CDCl_3$) 7.36-7.17 (5H, m, Ar-H), 5.75-5.71 (2H, m, C(3)H & C(4)H), 3.42 (1H, m, C(2)H), 2.88 (2H, m, $PhCH_2$), 2.61 (2H, m, C(6)H_2), 2.23 (2H, m, C(5)H_2).

(±)-2-Pentyl-5,6-dihydro-2H-thiopyran (Table 1 entry 2)



Pale yellow oil

53%

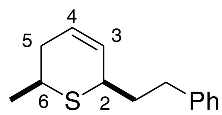
R_f 0.85 (petrol:diethyl ether 10:1).

Found $[M+H]^+$ 171.1199; $C_{10}H_{18}S$+H requires 171.1208.

ν_{max}/cm^{-1} (neat) 2955, 2858 (S-CH), 1649 (C=C), 700 (C-S).

δ_H (400 MHz; $CDCl_3$) 5.71 (2H, m, C(3)H and C(4)H), 3.23 (1H, m, C(2)H), 2.67 (2H, m, C(6)H_2), 2.22 (2H, m, C(5)H_2), 1.51-1.21 (8H, m, overlapping 4xCH_2), 0.83 (3H, t, *J* 6.8, CH_3).

(±)-6-Methyl-2-(2-phenylethyl)-5,6-dihydro-2H-thiopyran (Table 1 entry 3)



Pale yellow oil.

68%

R_f 0.81 (hexane:diethyl ether 10:1).

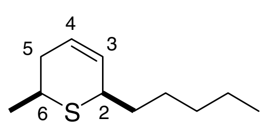
Found $[M+H]^+$ 219.1212. $C_{14}H_{18}S$+H requires 219.1207.

ν_{max}/cm^{-1} (neat) 3021 [Ar(C-H)], 2824 (S-CH), 1644 (C=C), 1460, 1255, 737 (C-S), 697 (C-S).

δ_H (400 MHz; $CDCl_3$) 7.19-7.32 (5H, m, Ar-H), 5.82 (1H, m, C(3)H), 5.72 (1H, dt, 12.7, 1.9, C(4)H), 3.66 (1H, m, C(2)H), 3.03 (1H, m, C(6)H), 2.78 (2H, m, ArC$\underline{H}_2$CH$_2$), 2.47 (1H, m, C(5)$\underline{H}$H), 1.86-2.28 (3H, m, ArCH$_2$C$\underline{H}_2$, C(5)H$\underline{H}$), 1.30 (3H, d, *J* 6.8, C(6)CH$_3$); δ_C (100 MHz; $CDCl_3$) 141.7 (C_{ipso}), 129.5 (C(4)H), 128.6 [overlapping 2×C(Ar)], 127.8 (C(3)H), 127.3 (C(Ar)), 125.9 [overlapping 2×C(Ar)], 40.1 (C(2)H), 38.6 (C(5)H$_2$), 34.9 (Ar$\underline{C}$H$_2$CH$_2$), 34.5 (C(6)H), 32.8 (ArCH$_2\underline{C}$H$_2$), 21.3 (C(6)$\underline{C}$H$_3$).

m/z (CI) 219 [$(MH)^+$, 100%], 127 [$(MH)^+$-C_7H_8, 10].

(±)-6-Methyl-2-pentyl-5,6-dihydro-2H-thiopyran (Table 1 entry 4)



Pale yellow oil

54%

R_f 0.85 (petrol:diethyl ether 10:1).

Found $[M+H]^+$ 185.1365. $C_{11}H_{20}S$+H requires 185.1364.

ν_{max}/cm^{-1} (neat) 2960, 2852 (S-CH), 1654 (C=C), 702 (C-S).

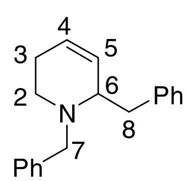
δ_H (400 MHz; $CDCl_3$) 5.75 (1H, m, C(3)H), 5.67 (1H, dt, *J* 12.6, 6.6, C(4)H), 3.61 (1H, m, C(2)H), 3.01 (1H, m, C(6)H), 2.25 (1H, m, C(5)H), 1.99 (1H, m, C(5)H), 1.25-1.62

(overlapping 11H, m, C(6)CH_3, C(2)C$\underline{H}_2$C$\underline{H}_2$C$\underline{H}_2$C$\underline{H}_2$$CH_3$), 0.88 (3H, t, *J* 7.0, C(2)$CH_2CH_2CH_2CH_2C\underline{H}_3$); δ_C (100 MHz; $CDCl_3$) 129.9 C(4)H, 127.3 C(3)H, 40.9 C(2)H, 35.7 [1×CH_2, C(2)$CH_2CH_2CH_2CH_2CH_3$], 35.0 C(5)H_2, 34.5 C(6)H, 31.7, 26.5 and 22.6 [3×CH_2, C(2) $CH_2CH_2CH_2CH_2CH_3$], 21.2 C(6)$\underline{C}H_3$, 14.1 C(2)$CH_2CH_2CH_2CH_2\underline{C}H_3$.
m/z (CI) 185 [$(MH)^+$, 100%], 128 [$(MH)^+$-C_4H_9, 6].

General procedure for the cyclisation of homoallyl amines with aldehydes

To a solution of indium trichloride (221 mg, 1.0 mmol) and aldehyde (1.0 mmol) in anhydrous acetonitrile (20 mL) at reflux was added dropwise the secondary amine (1.0 mmol). Once the reaction was completed (TLC check) the solution was concentrated and the residue obtained partioned between dichloromethane (20 mL) and 1 M NaOH (20 mL). The aqueous layer was extracted with dichloromethane. The combined organic layers were washed with 1 M NaOH, dried (magnesium sulfate) and concentrated under reduced pressure. The residue was then purified by flash chromatography to give the corresponding tetrahydropyridine.

(±)-1,6-Dibenzyl-1,2,3,6-tetrahydropyridine (Table 2 entry 1)

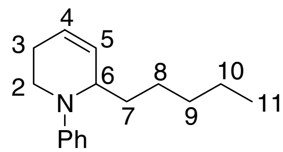


Yellow oil
95% yield
R_f 0.35 (hexane:ethyl acetate:triethylamine 94:5:1)
Found: $[MH]^+$ 264.1752; $C_{19}H_{21}N$+H requires 264.1764.
ν_{max}/cm^{-1} (neat) 3084, 3060, 3025, 2921, 2800, 1635, 1602, 1494, 1452, 1363, 728, 698.
δ_H (400 MHz; $CDCl_3$) 7.35-7.16 (m, 10H, H_{Ph}), 5.76-5.73 (m, 1H, H_4), 5.53-5.49 (m, 1H, H_5), 4.00 (d, *J* 13.2, 1H, H_7), 3.56 (d, *J* 13.2, 1H, H_7), 3.22-3.18 (m, 1H, H_6), 3.11 (dd, *J* 5.4 and 13.1, 1H, H_8), 2.99-2.93 (m, 1H, H_2), 2.65 (dd, *J* 8.8 and 13.1, 1H, H_8), 2.52-2.46 (m, 1H, H_2), 2.12-1.96 (m, 2H, H_3); δ_C (100.6 MHz; $CDCl_3$) 139.7 (C_{Ph}), 139.5 (C_{Ph}),

129.6 (C_{Ph}), 129.1 (C_5), 128.9 (C_{Ph}), 128.3 (C_{Ph}), 128.2 (C_{Ph}), 126.9 (C_{Ph}), 126.0 (C_{Ph}), 125.3 (C_4), 60.5 (C_6), 58.5 (C_7), 45.7 (C_2), 39.7 (C_8), 23.8 (C_3).

m/z 264 (MH^+, 80), 172 (100), 120 (20).

(±)-6-Pentyl-1-phenyl-1,2,3,6-tetrahydropyridine (Table 2 entry 3)



Yellow oil

95% yield

R_f 0.5 (hexane)

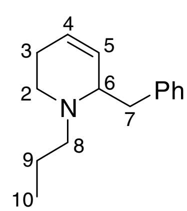
Found: $[M+H]^+$, 230.1908. $C_{16}H_{23}N$+H requires 230.1908.

ν_{max}/cm^{-1} (neat) 3027, 2954, 2927, 1596, 1502, 1457, 1388, 1319, 1247, 746, 692.

δ_H (400 MHz; $CDCl_3$) 7.29-7.34 (m, 2H, H_{Ph}), 6.89 (d, *J* 7.8, 2H, H_{Ph}), 6.78-6.74 (m, 1H, H_{Ph}), 5.91-5.84 (m, 2H, H_4 and H_5), 4.07 (br s, 1H, H_6), 3.68-3.63 (m, 1H, H_2), 3.28-3.21 (m, 1H, H_2), 2.41-2.30 (m, 1H, H_3), 2.06-1.98 (m, 1H, H_3), 1.68-1.57 (m, 2H, H_7), 1.45-1.41 (m, 2H, H_8), 1.36-1.29 (m, 4H, H_9 and H_{10}), 0.91 (t, *J* 6.9, 3H, H_{11}); δ_C (100.6 MHz; $CDCl_3$) 150.3 (C_{Ph}), 130.0 (C_5), 129.3 (C_{Ph}), 125.5 (C_4), 117.6 (C_{Ph}), 115.2 (C_{Ph}), 56.3 (C_6), 40.5 (C_2), 32.9 (C_7), 32.2 (C_8), 26.2 (C_9), 24.3 (C_3), 22.8 (C_{10}), 14.2 (C_{11})

m/z 230 (MH^+, 100), 158 (31)

(±)-6-Benzyl-1-propyl-1,2,3,6-tetrahydropyridine (Table 2 entry 4)



Yellow oil

55% yield

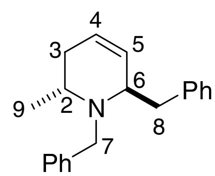
R_f 0.3 (hexane:ethyl acetate:triethylamine 94:5:1)

Found: $[M+H]^+$ 216.1752; $C_{15}H_{21}N$+H requires 216.1770.

ν_{max}/cm^{-1} (neat) 3060, 3027, 2958, 2931, 2802, 1604, 1494, 1454, 742, 698.

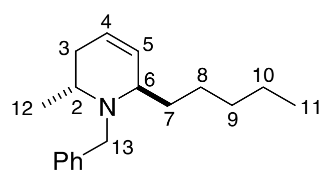
δ_H (400 MHz; $CDCl_3$) 7.25-7.13 (m, 5H, H_{Ph}), 5.70-5.66 (m, 1H, H_4), 5.43-5.40 (m, 1H, H_5), 3.12-3.09 (m, 1H, H_6), 3.02 (dd, *J* 4.6 and 13.0, 1H, H_7), 2.93 (dt, *J* 5.8 and 12.0, 1H, H_2), 2.69-2.62 (m, 1H, H_8), 2.51-2.38 (m, 3H, H_2 H_7 and H_8), 2.10-1.98 (m, 2H, H_3), 1.55-1.44 (m, 2H, H_9), 0.86 (t, *J* 7.3, 3H, H_{10}); δ_C (100.6 MHz; $CDCl_3$) 139.8 (C_{Ph}), 129.6 (C_5), 129.1 (C_{Ph}), 128.3 (C_{Ph}), 126.0 (C_4), 125.1 (C_{Ph}), 60.7 (C_6), 56.5 (C_8), 46.4 (C_2), 39.4 (C_7), 24.5 (C_3), 20.7 (C_9), 12.1 (C_{10}).
m/z 216 (MH^+, 55), 124 (100).

(±)-1,6-Dibenzyl-2-methyl-1,2,3,6-tetrahydropyridine (Table 2 entry 5); compound 6



White solid
68% yield
R_f 0.4 (hexane:ethyl acetate:triethylamine 94:5:1)
Mp 66-67°C
Found: [M+H[$^+$ 278.1908; $C_{19}H_{21}N$+H requires 278.1917.
ν_{max}/cm^{-1} (ethyl acetate) 3025, 2962, 2912, 2829, 1739, 1602, 1494, 1452, 1360, 740, 727, 696.
δ_H (400 MHz; $CDCl_3$) 7.26-7.17 (m, 8H, H_{Ph}), 7.08-7.06 (m, 2H, H_{Ph}), 5.84-5.81 (m, 1H, H_4), 5.57-5.53 (m, 1H, H_5), 3.78 (d, *J* 14.1, 1H, H_7), 3.55 (d, *J* 14.1, 1H, H_7), 3.36-3.28 (m, 1H, H_2), 3.18 (br s, 1H, H_6), 2.94 (dd, *J* 6.9 and 13.2, 1H, H_8), 2.66 (dd, *J* 7.7 and 13.2, 1H, H_8), 2.06-1.91 (m, 2H, H_3), 1.18 (d, *J* 6.7, 3H, H_9); δ_C (100.6 MHz; $CDCl_3$) 140.8 (C_{Ph}), 140.1 (C_{Ph}), 129.7 (C_5), 128.7 (C_{Ph}), 128.4 (C_{Ph}), 128.1 (C_{Ph}), 126.4 (C_{Ph}), 125.8 (C_{Ph}), 125.4 (C_4), 59.3 (C_6), 50.7 (C_7), 47.0 (C_2), 40.7 (C_8), 29.3 (C_3), 17.5 (C_9).
m/z 278 (MH^+, 78), 186 (100).

(±)-1-Benzyl-2-methyl-6-pentyl-1,2,3,6-tetrahydropyridine (Table 2 entry 6)



Yellow oil

70% yield

R_f 0.3 (hexane:ethyl acetate:triethylamine 94:5:1)

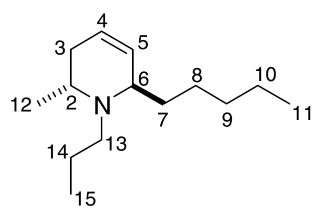
Found: $[M+H]^+$ 258.2222; $C_{17}H_{25}N$+H requires 258.2229.

ν_{max}/cm^{-1} (neat) 3023, 2958, 2927, 2856, 1646, 1456, 1361, 696.

δ_H (400 MHz; $CDCl_3$) 7.40-7.38 (m, 2H, H_{Ph}), 7.32-7.28 (m, 2H, H_{Ph}), 7.26-7.21 (m, 1H, H_{Ph}), 5.80-5.77 (m, 1H, H_4), 5.63-5.59 (m, 1H, H_5), 3.71 (d, *J* 13.8, 1H, H_{13}), 3.50 (d, *J* 13.8, 1H, H_{13}), 3.18-3.13 (m, 1H, H_2), 2.93 (br s, 1H, H_6), 2.06-1.97 (m, 1H, H_3), 1.92-1.84 (m, 1H, H_3), 1.54-1.37 (m, 2H, H_7), 1.36-1.17 (m, 6H, H_8 H_9 and H_{10}), 1.13 (d, *J* 6.7, 3H, H_{12}), 0.84 (t, *J* 7.1, 3H, H_{11}); δ_C (100.6 MHz; $CDCl_3$) 141.3 (C_{Ph}), 129.8 (C_5), 128.9 (C_{Ph}), 128.1 (C_{Ph}), 126.5 (C_{Ph}), 124.8 (C_4), 56.8 (C_6), 50.8 (C_{13}), 46.7 (C_2), 33.9 (C_7), 32.0 (C_3), 29.5 (C_8), 25.7 (C_9), 22.8 (C_{10}), 16.8 (C_{12}), 14.3 (C_{11}).

m/z 258 (MH^+, 98), 186 (100).

(±)-6-Pentyl-2-methyl-1-propyl-1,2,3,6-tetrahydropyridine (Table 2 entry 7)



Yellow oil

73% yield

R_f 0.35 (hexane:ethyl acetate:triethylamine 94:5:1)

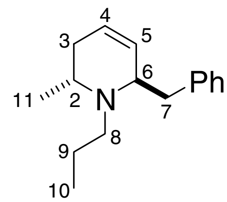
Found: $[M+H]^+$ 210.2222; $C_{14}H_{19}N$+H requires 210.2195.

ν_{max}/cm^{-1} (neat) 3020, 2958, 2929, 2871, 1733, 1465, 1375, 1149, 703.

δ_H (400 MHz; $CDCl_3$) 5.72-5.69 (m, 1H, H_4), 5.62-5.58 (m, 1H, H_5), 3.11-3.05 (m, 1H, H_2), 2.93-2.92 (m, 1H, H_6), 2.41-2.26 (m, 2H, H_{13}), 1.98-1.89 (m, 1H, H_3), 1.85-1.75 (m, 1H, H_3), 1.44-1.25 (m, 10H, H_7 H_8 H_9 H_{10} and H_{14}), 1.02 (d, *J* 6.7, 3H, H_{12}), 0.90-0.86 (m, 6H, H_{11} and H_{15}); δ_C (100.6 MHz; $CDCl_3$) 129.9 (C_5), 124.7 (C_4), 57.7 (C_6), 48.9 (C_{13}), 47.0 (C_2), 33.8 (C_7), 32.3 (C_8), 29.7 (C_3), 26.2 (C_9), 22.8 (C_{10}), 22.2 (C_{14}), 16.9 (C_{12}), 14.2 (C_{11}), 12.2 (C_{15}).

m/z 210 (MH^+, 89), 138 (76).

(±)-6-Benzyl-2-methyl-1-propyl-1,2,3,6-tetrahydropyridine (Table 2 entry 8)



Yellow oil

85% yield

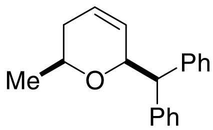
R_f 0.3 (hexane:ethyl acetate:triethylamine 94:5:1)

Found: $[M+H]^+$ 230.1908; $C_{15}H_{21}N$+H requires 230.1903.

ν_{max}/cm^{-1} (neat) 3028, 2957, 1660, 1604, 1490, 1452, 1371, 1080, 696.

δ_H (400 MHz; $CDCl_3$) 7.33-7.18 (m, 5H, H_{Ph}), 5.77-5.74 (m, 1H, H_4), 5.52-5.49 (m, 1H, H_5), 3.25-3.21 (m, 2H, H_2 and H_6), 2.99 (dd, *J* 6.1 and 12.9, 1H, H_7), 2.62 (dd, *J* 8.5 and 12.9, 1H, H_7), 2.47-2.40 (m, 2H, H_8), 2.04-1.99 (m, 1H, H_3) 1.91-1.88 (m, 1H, H_3), 1.41-1.35 (m, 2H, H_9), 1.09 (d, *J* 6.6, 3H, H_{11}), 0.81 (t, *J* 7.3, 3H, H_{10}); δ_C (100.6 MHz; $CDCl_3$) 140.3 (C_{Ph}), 129.6 (C_5), 128.6 (C_{Ph}), 128.1 (C_{Ph}), 125.9 (C_{Ph}), 125.2 (C_4), 59.8 (C_6), 49.0 (C_8), 47.3 (C_2), 40.4 (C_7), 29.8 (C_3), 22.0 (C_9), 17.1 (C_{11}) 12.0 (C_{10}).

m/z 230 (MH^+, 81), 138 (100).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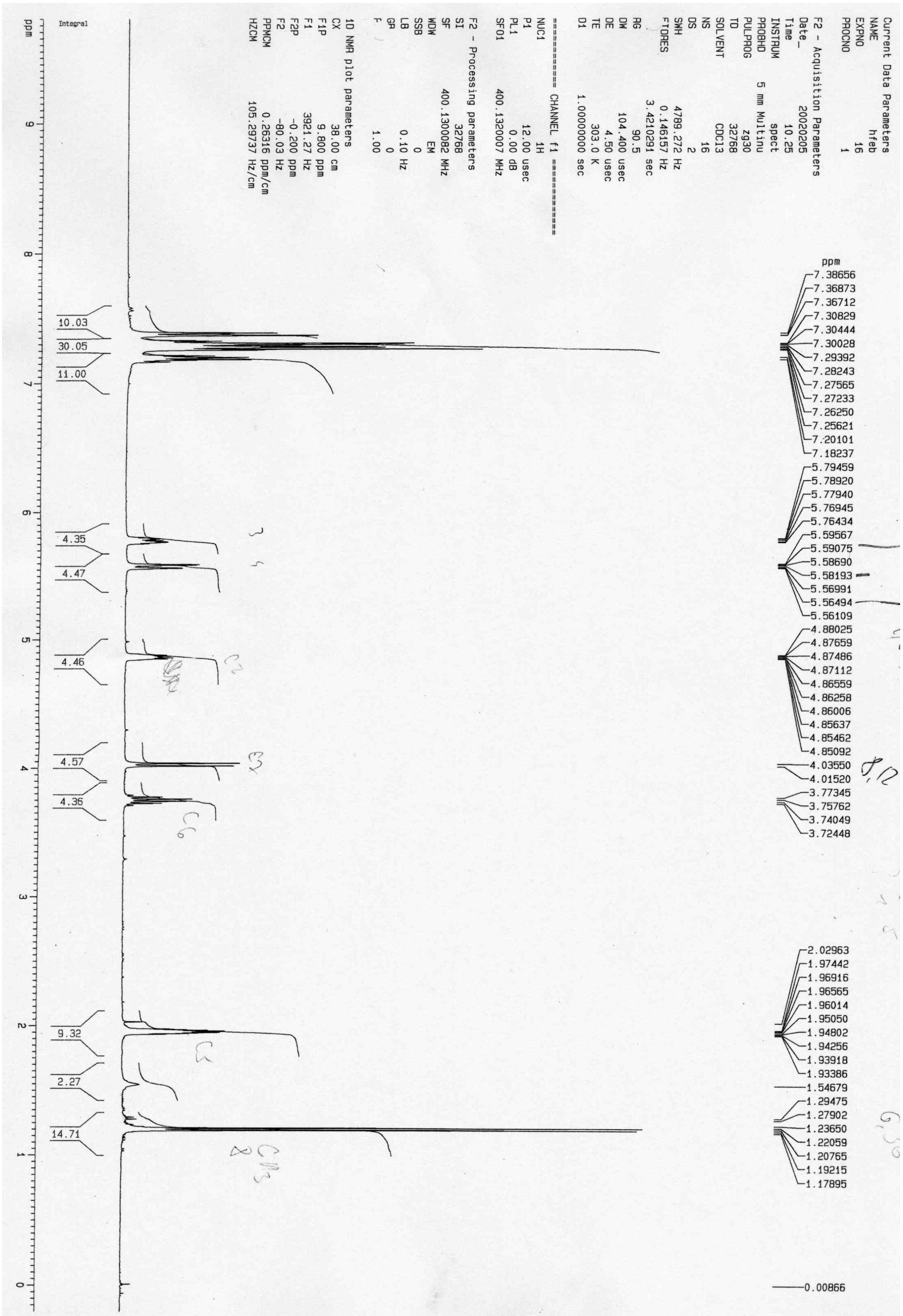
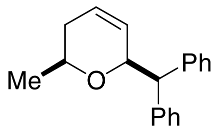
Ph

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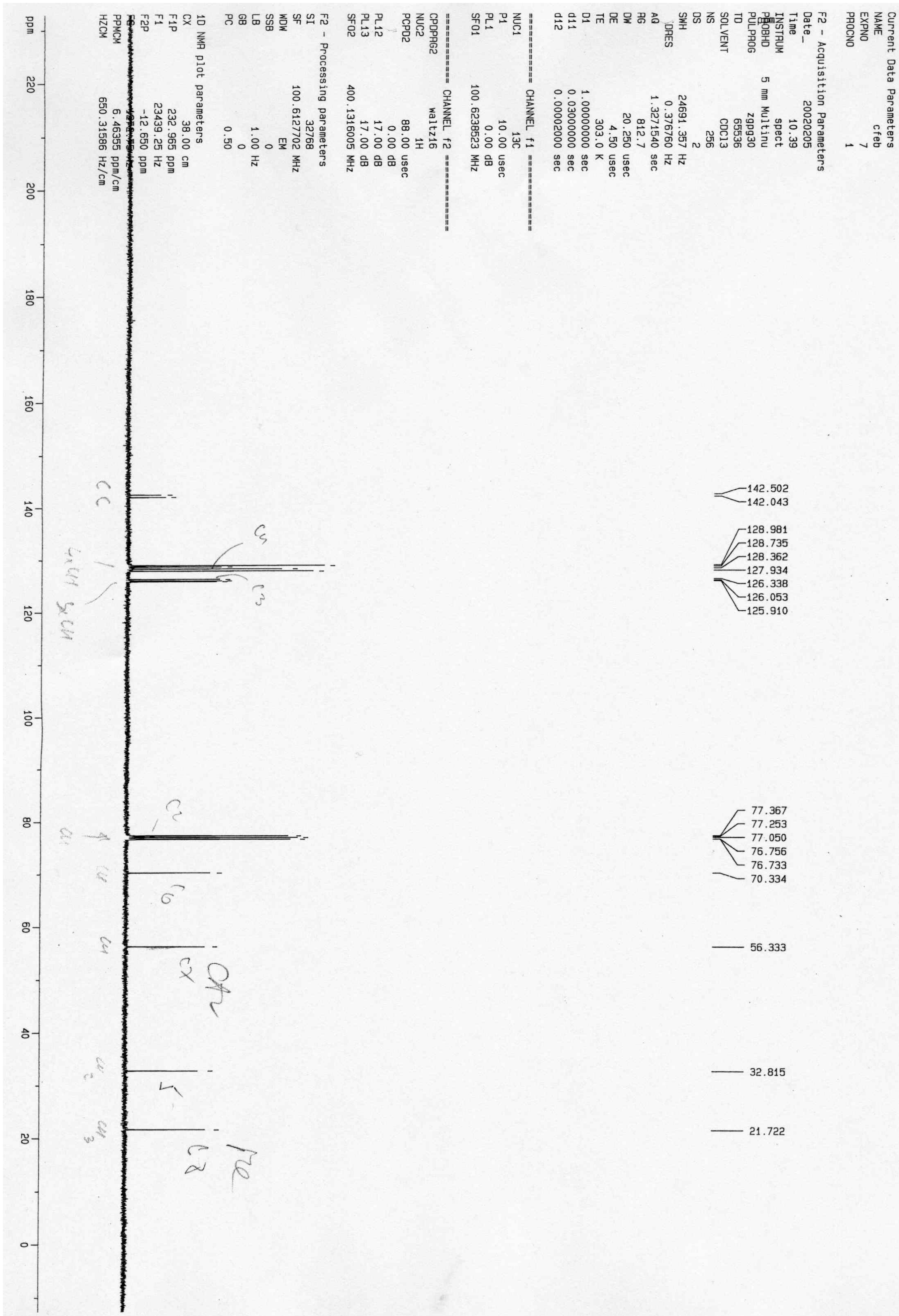
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DE 4.50 usec
TE 303.0 K
D1 1.0000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
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PL1 0.00 dB
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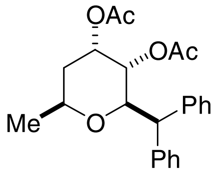
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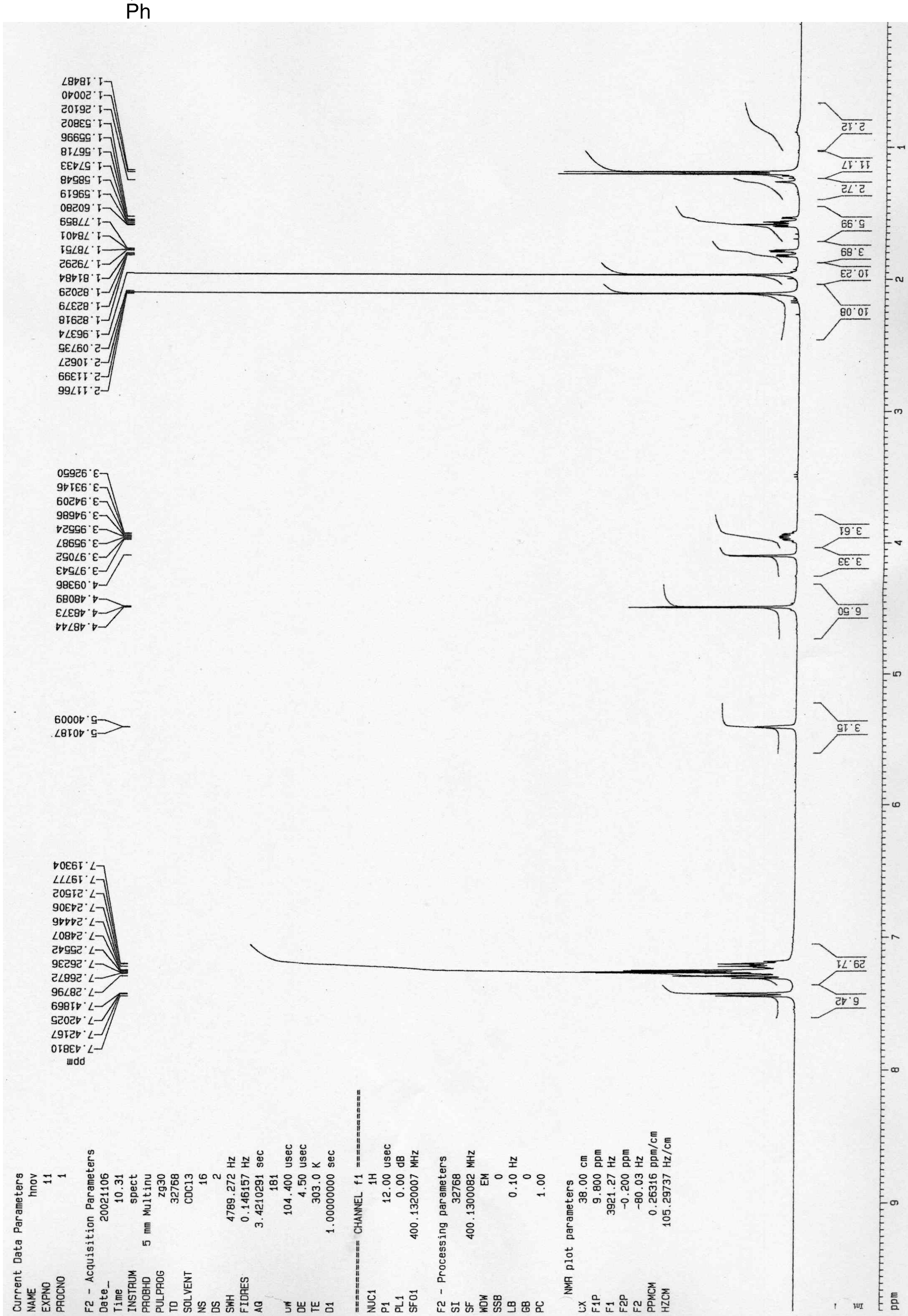

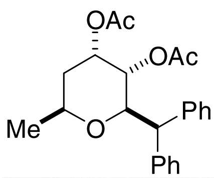
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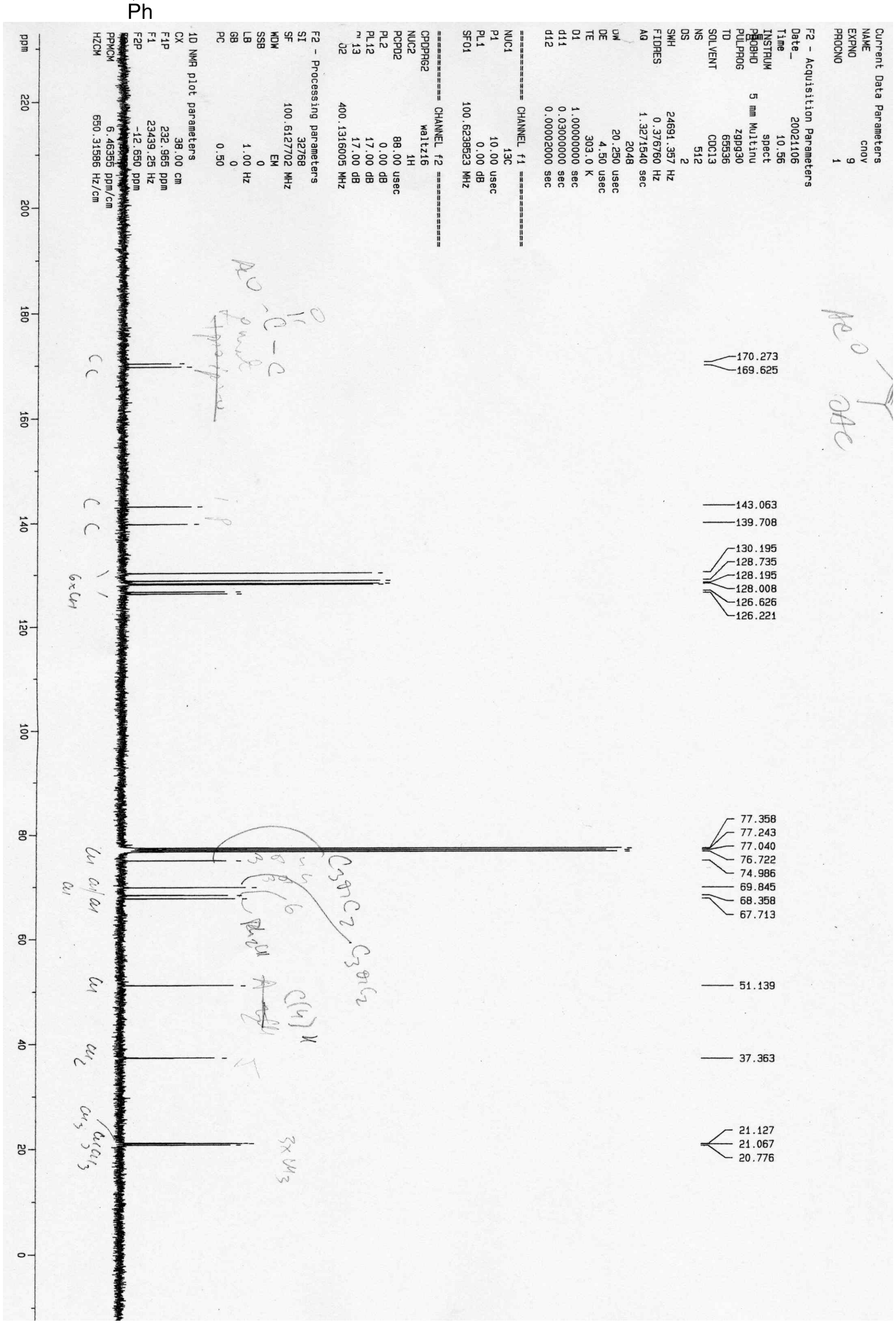
O
Ph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DE 4.50 usec
TE 303.0 K
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d11 0.03000000 sec
d12 0.00002000 sec
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P1 10.00 usec
PL1 0.00 dB
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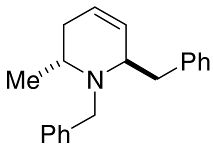
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