Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Synthesis of (*S*)-(+)-cericlamine through lipase-catalyzed aminolysis of azo acetates

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Contents

1. General remarks

Solvents and reagents were used as received. 2-Methallyl acetate was obtained through acetylation of 2-methallyl alcohol. Diazonium tetrafluoroborates were prepared by previously reported procedures.[1] ^{1}H NMR were recorded on 360 and 600 MHz spectrometers using $CDCl_3$ and C_6D_6 as solvents referenced to TMS (0 ppm), $CHCl_3$ (7.26 ppm) or C_6HD_5 (7.15 ppm). Chemical shifts are reported in parts per million (ppm). Coupling constants are in Hertz (*J* Hz). The following abbreviations are used for the description of signals: s (singlet), d (doublet), dd (double doublet), t (triplet), m (multiplet), br (broad). ^{13}C NMR were recorded at 90.6 and 151 MHz in $CDCl_3$ and C_6D_6 using $CDCl_3$ (77.0 ppm) and C_6D_6 (128.0 ppm) as standard. Chemical shifts are given in parts per million (ppm). Mass spectra were recorded using electron impact (EI). Analytical TLC was carried out on Merck silica gel plates using short wave (254 nm) UV light to visualise components. Silica gel (Kieselgel 60, 40-63 μm, Merck) was used for flash column chromatography. Analytical HPLC was carried out using a Daicel Chiralpak® column IC or a Daicel Chiralpak® column IA.

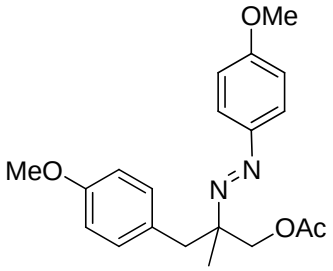
2. Syntheses

2.1 General procedure for the preparation of racemic azo acetates 7 and alcohols 8[2]

To a mixture of DMSO/H_2O (3 mL, 5:2, v/v, previously degassed with argon) were added $FeSO_4 \cdot 7H_2O$ (3 mmol, 834 mg) and 2-methallyl acetate or 2-methallyl alcohol (6 mmol) under an argon atmosphere. A solution of diazonium tetrafluoroborate (1 mmol) in a mixture of DMSO/H_2O (1.5 mL, 5:2, v/v, previously degassed with argon) was added dropwise. The reaction mixture was stirred for 15 minutes, then diluted with water (25 mL) and extracted with diethyl ether (3 × 25 mL). The combined organic phases were washed with brine (1 × 50 mL) and dried over sodium sulfate. The solvent was evaporated and the products were purified by column chromatography.

2.2 Compounds

2.2.1 Acetic acid 3-(4-methoxyphenyl)-2-(4-methoxyphenylazo)-2-methylpropyl ester (7a)[3]



$C_{20}H_{24}N_2O_4$
M = 356.42 g/mol

Prepared from 4-methoxybenzenediazonium tetrafluoroborate (10.0 mmol, 2.22 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 4:1) gave **7a** (3.17 mmol, 1.13 g, 63%) as a yellow oil.

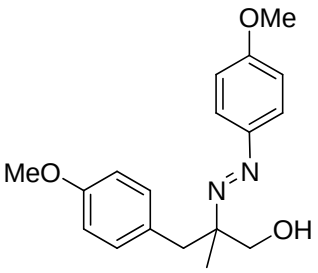
***R*f** 0.40 (hexane/ethyl acetate = 4:1)

^{1}H-NMR (600 MHz, C_6D_6): δ = 1.33 (s, 3 H), 1.65 (s, 3 H), 3.09 (d, J = 13.6 Hz, 1 H), 3.16 (d, J = 13.6 Hz, 1 H), 3.19 (s, 3 H), 3.27 (s, 3 H), 4.57 (d, J = 11.2 Hz, 1 H), 4.62 (d, J = 11.2 Hz, 1 H), 6.70 (d, J = 8.7 Hz, 2 H), 6.72 (d, J = 9.0 Hz, 2 H), 7.00 (d, J = 8.7 Hz, 2 H), 7.85 (d, J = 9.0 Hz, 2 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 90:10; 0.8 mL/min, 280 nm): t_R = 9.4 min.

The analytical data is in agreement with literature.[3]

2.2.2 3-(4-Methoxyphenyl)-2-(4-methoxyphenylazo)-2-methylpropan-1-ol (8a)[3]



$C_{18}H_{22}N_2O_3$
M = 314.38 g/mol

Prepared from 4-methoxybenzenediazonium tetrafluoroborate (2.00 mmol, 444 mg) and 2-methallyl alcohol (12.0 mmol, 865 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 3:1) gave **8a** (0.44 mmol, 137 mg, 44%) as a yellow oil.

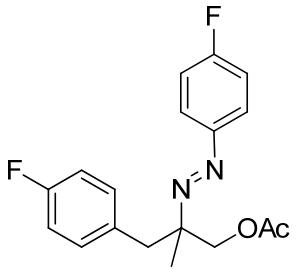
***R*f** 0.25 (hexane/ethyl acetate = 4:1)

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.22 (s, 3 H), 2.94 (d, J = 13.5 Hz, 1 H), 3.09 (d, J = 13.5 Hz, 1 H), 3.70-3.78 (m, 2 H), 3.78 (s, 3 H), 3.87 (s, 3 H), 6.81 (d, J = 8.7 Hz, 2 H), 6.97 (d, J = 9.0 Hz, 2 H), 7.15 (d, J = 8.7 Hz, 2 H), 7.70 (d, J = 9.0 Hz, 2 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 90:10; 0.8 mL/min, 280 nm): t_R = 11.5 min, 19.2 min.

The analytical data is in agreement with literature.[3]

2.2.3 Acetic acid 3-(4-fluorophenyl)-2-(4-fluorophenylazo)-2-methylpropyl ester (7b)[2]



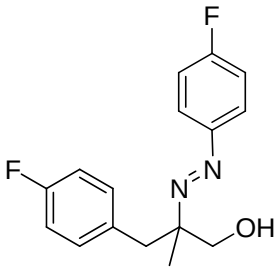
$C_{18}H_{18}F_2N_2O_2$
M = 332.34 g/mol

Prepared from 4-fluorobenzenediazonium tetrafluoroborate (10.0 mmol, 2.10 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 5:1) gave **7b** (3.08 mmol, 1.02 g, 62%) as a yellow oil.

R_f	0.60 (hexane/ethyl acetate = 5:1)
^{1}H-NMR	(600 MHz, $CDCl_3$): δ = 1.24 (s, 3 H), 2.06 (s, 3 H), 3.11 (d, J = 13.7 Hz, 1 H), 3.15 (d, J = 13.7 Hz, 1 H), 4.32 (d, J = 11.2 Hz, 1 H), 4.36 (d, J = 11.2 Hz, 1 H), 6.92 (dd, $J_{H,F}$ = 8.7 Hz, J = 8.7 Hz, 2 H), 7.04 (dd, $J_{H,F}$ = 5.4 Hz, J = 8.7 Hz, 2 H), 7.14 (dd, $J_{H,F}$ = 8.4 Hz, J = 8.8 Hz, 2 H),7.68 (dd, $J_{H,F}$ = 5.2 Hz, J = 9.0 Hz, 2 H).
HPLC	(Chiralpak® IC column; hexane/2-propanol = 99:1; 0.8 mL/min, 280 nm): t_R = 8.6 min.

The analytical data is in agreement with literature.[2]

2.2.4 3-(4-Fluorophenyl)-2-(4-fluorophenylazo)-2-methylpropan-1-ol (8b)[2]



$C_{16}H_{16}F_2N_2O$
M = 290.31 g/mol

Prepared from 4-fluorobenzenediazonium tetrafluoroborate (2.00 mmol, 420 mg) and 2-methallyl alcohol (12.0 mmol, 865 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 3:1) gave **8b** (0.66 mmol, 191 mg, 66%) as a yellow oil.

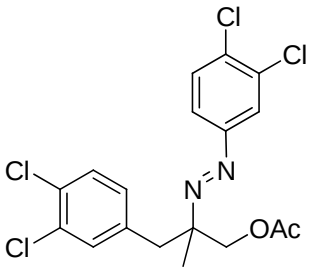
***R*f** 0.60 (hexane/ethyl acetate = 2:1)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.22 (s, 3 H), 3.00 (d, J = 13.5 Hz, 1 H), 3.13 (d, J = 13.5 Hz, 1 H), 3.72 (d, J = 11.9 Hz, 1 H), 3.79 (d, J = 11.9 Hz, 1 H), 6.95 (dd, $J_{H,F}$ = 8.7 Hz, J = 8.7 Hz, 2 H), 7.13-7.20 (m, 4 H), 7.71 (dd, $J_{H,F}$ = 5.2 Hz, J = 9.0 Hz, 2 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.8 mL/min, 280 nm): t_R = 11.1 min, 12.6 min.

The analytical data is in agreement with literature.[2]

2.2.5 Acetic acid 3-(3,4-dichlorophenyl)-2-(3,4-dichlorophenylazo)-2-methylpropyl ester (7c)



$C_{18}H_{16}Cl_4N_2O_2$
M = 434.14 g/mol

Prepared from 3,4-dichlorobenzenediazonium tetrafluoroborate (10.0 mmol, 2.61 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 5:1) gave **7c** (3.79 mmol, 1.65 g, 76%) as a yellow oil.

***R*$_f$** 0.50 (hexane/ethyl acetate = 5:1)

^{1}H-NMR (360 MHz, C_6D_6): δ = 1.00 (s, 3 H), 1.61 (s, 3 H), 2.65 (d, J = 13.6 Hz, 1 H), 2.80 (d, J = 13.6 Hz, 1 H), 4.25 (d, J = 11.3 Hz, 1 H), 4.30 (d, J = 11.3 Hz, 1 H), 6.45 (dd, J = 2.0 Hz, J = 8.2 Hz, 1 H), 6.91 (d, J = 8.2 Hz, 1 H), 6.96-7.00 (m, 2 H), 7.20 (dd, J = 2.3 Hz, J = 8.5 Hz, 1 H), 7.70 (d, J = 2.3 Hz, 1 H).

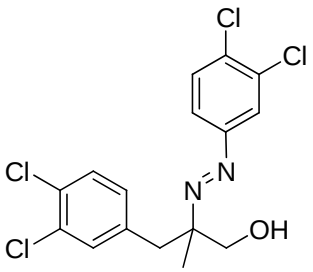
^{13}C-NMR (151 MHz, C_6D_6): δ = 19.4 (CH_3), 20.2 (CH_3), 41.1 (CH_2), 67.7 (CH_2), 72.9 (C_q), 122.4 (CH), 123.8 (CH), 130.1 (CH), 130.2 (CH), 131.1 (CH), 131.2 (C_q), 132.4 (C_q), 132.9 (CH), 133.9 (C_q), 135.3 (C_q), 136.9 (C_q), 150.7 (C_q), 169.6 (C_q).

MS (EI) *m/z* (%): 434 (<1) [M^+], 261 (35), 259 (55), 201 (51), 199 (80), 175 (51), 173 (83), 165 (11), 164 (26), 163 (14), 161 (22), 159 (30), 149 (10), 47 (52), 145 (82), 129 (24), 128 (10), 124 (11), 109 (15), 83 (16), 45 (11), 44 (100).

HRMS (EI) calcd. for $C_{18}H_{16}Cl_4N_2O_2$ [M^+]: 431.9966, found: 431.9967.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 12.0 min.

2.2.6 3-(3,4-Dichlorophenyl)-2-(3,4-dichlorophenylazo)-2-methylpropan-1-ol (8c)



$C_{16}H_{14}Cl_4N_2O$
M = 392.11 g/mol

Prepared from 3,4-dichlorobenzenediazonium tetrafluoroborate (2.00 mmol, 522 mg) and 2-methallyl alcohol (12.0 mmol, 865 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 2.5:1) gave **8c** (0.80 mmol, 312 mg, 80%) as a yellow oil.

***R*$_f$** 0.55 (hexane/ethyl acetate = 2:1)

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.22 (s, 3 H), 3.01 (d, J = 13.4 Hz, 1 H), 3.12 (d, J = 13.4 Hz, 1 H), 3.71 (d, J = 11.8 Hz, 1 H), 3.83 (d, J = 11.8 Hz, 1 H), 7.04 (dd, J = 2.1 Hz, J = 8.2 Hz, 1 H), 7.28-7.37 (m, 2 H), 7.54-7.62 (m, 2 H), 7.76-7.80 (m, 1 H).

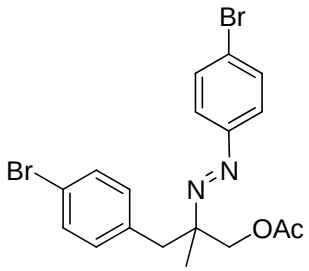
^{13}C-NMR (90.6 MHz, $CDCl_3$): δ = 19.5 (CH_3), 40.4 (CH_2), 66.6 (CH_2), 74.4 (C_q), 122.1 (CH), 123.4 (CH), 130.0 (CH), 130.1 (CH), 130.7 (C_q), 130.9 (CH), 132.0 (C_q), 132.6 (CH), 133.6 (C_q), 135.1 (C_q), 137.0 (C_q), 150.3 (C_q).

MS (EI) *m/z* (%): 392 (<1) [M^+], 362 (20), 360 (16), 173 (15), 163 (39), 162 (24), 161 (100), 160 (35), 159 (92), 147 (15), 145 (23), 133 (12), 125 (16), 124 (15), 123 (16), 89 (15), 85 (15), 83 (22).

HRMS (EI) calcd. for $C_{16}H_{14}Cl_4N_2O$ [M^+]: 389.9860, found: 389.9861.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 21.6 min, 23.6 min.

2.2.7 Acetic acid 3-(4-bromophenyl)-2-(4-bromophenylazo)-2-methylpropyl ester (7d)

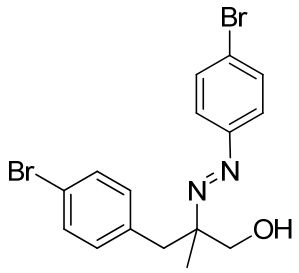


$C_{18}H_{18}Br_2N_2O_2$
M = 454.16 g/mol

Prepared from 4-bromobenzenediazonium tetrafluoroborate (10.0 mmol, 2.71 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 5:1) gave **7d** (2.99 mmol, 1.36 g, 60%) as a yellow oil.

R_f	0.65 (hexane/ethyl acetate = 4:1)
^{1}H-NMR	(600 MHz, C_6D_6): δ = 1.10 (s, 3 H), 1.61 (s, 3 H), 2.78 (d, J = 13.5 Hz, 1 H), 2.90 (d, J = 13.5 Hz, 1 H), 4.35-4.40 (m, 2 H), 6.61 (d, J = 8.5 Hz, 2 H), 7.14-7.17 (m, 2 H), 7.22 (d, J = 8.8 Hz, 2 H), 7.36 (d, J = 8.8 Hz, 2 H).
^{13}C-NMR	(151 MHz, C_6D_6): δ = 19.5 (CH_3), 20.3 (CH_3), 41.6 (CH_2), 67.9 (CH_2), 72.7 (C_q), 121.0 (C_q), 124.1 (2×CH), 125.5 (C_q), 131.4 (2×CH), 132.5 (2×CH), 132.6 (2×CH), 135.7 (C_q), 150.6 (C_q), 169.7 (C_q).
MS (EI)	*m/z* (%): 454 (<1) [M^+], 271 (35), 269 (35), 211 (30), 209 (30), 185 (77), 183 (78), 171 (26), 169 (23), 157 (58), 155 (60), 131 (23), 130 (100), 129 (25), 116 (13), 115 (20), 91 (16), 90 (29), 89 (13), 83 (16), 76 (21), 75 (18), 44 (100).
HRMS (EI)	calcd. for $C_{18}H_{18}Br_2N_2O_2$ [M^+]: 451.9735, found: 451.9735.
HPLC	(Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 12.2 min.

2.2.8 3-(4-Bromophenyl)-2-(4-bromophenylazo)-2-methylpropan-1-ol (8d)



$C_{16}H_{16}Br_2N_2O$
M = 412.12 g/mol

Prepared from 4-bromobenzenediazonium tetrafluoroborate (2.00 mmol, 542 mg) and 2-methallyl alcohol (12.0 mmol, 865 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 2:1) gave **8d** (0.71 mmol, 292 mg, 71%) as a dark yellow oil.

***R*f** 0.55 (hexane/ethyl acetate = 2:1)

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.21 (s, 3 H), 2.99 (d, J = 13.4 Hz, 1 H), 3.11 (d, J = 13.4 Hz, 1 H), 3.71 (d, J = 11.8 Hz, 1 H), 3.79 (d, J = 11.8 Hz, 1 H), 7.08 (d, J = 8.5 Hz, 2 H), 7.39 (d, J = 8.5 Hz, 2 H), 7.56 (d, J = 8.9 Hz, 2 H), 7.61 (d, J = 8.9 Hz, 2 H).

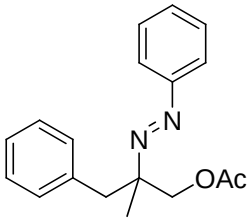
^{13}C-NMR (90.6 MHz, $CDCl_3$): δ = 19.6 (CH_3), 40.8 (CH_2), 66.8 (CH_2), 74.0 (C_q), 120.5 (C_q), 123.7 (2×CH), 125.3 (C_q), 131.1 (2×CH), 132.3 (2×CH), 132.5 (2×CH), 135.8 (C_q), 150.2 (C_q).

MS (EI) *m/z* (%): 412 (<1) [M^+], 384 (25), 382 (59), 380 (27), 185 (24), 183 (22), 173 (73), 172 (47), 171 (100), 170 (48), 169 (89), 157 (25), 155 (25), 131 (12), 130 (29), 116 (11), 115 (14), 91 (49), 90 (60), 89 (43), 85 (22), 83 (34).

HRMS (EI) calcd. for $C_{16}H_{16}Br_2N_2O$ [M^+]: 409.9630, found: 409.9626.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 20.6 min, 23.8 min.

2.2.9 Acetic acid 2-methyl-3-phenyl-2-phenylazopropyl ester (7e)[4]



$C_{18}H_{20}N_2O_2$
M = 296.36 g/mol

Prepared from benzenediazonium tetrafluoroborate (10.0 mmol, 1.92 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 5:1) gave **7e** (2.05 mmol, 608 mg, 41%) as a yellow oil.

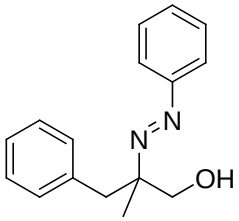
***R*f** 0.50 (hexane/diethyl ether = 5:1)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.27 (s, 3 H), 2.05 (s, 3 H), 3.13-3.19 (m, 2 H), 4.36 (d, J = 11.2 Hz, 1 H), 4.39 (d, J = 11.2 Hz, 1 H), 7.10-7.13 (m, 2 H), 7.17-7.26 (m, 3 H), 7.41-7.48 (m, 3 H), 7.64-7.68 (m, 2 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.8 mL/min, 280 nm): t_R = 7.5 min.

The analytical data is in agreement with literature.[4]

2.2.10 2-Methyl-3-phenyl-2-phenylazopropan-1-ol (8e)[4]



$C_{16}H_{18}N_2O$
M = 254.33 g/mol

Prepared from benzenediazonium tetrafluoroborate (2.00 mmol, 384 mg) and 2-methallyl alcohol (12.0 mmol, 865 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 3:1) gave **8e** (0.54 mmol, 137 mg, 54%) as a yellow oil.

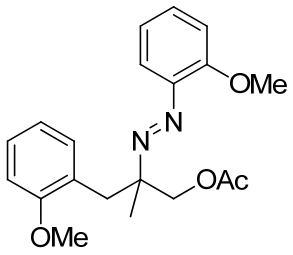
***R*f** 0.20 (hexane/diethyl ether = 5:1)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.25 (s, 3 H), 2.61 (br, 1 H), 3.03 (d, J = 13.4 Hz, 1 H), 3.17 (d, J = 13.4 Hz, 1 H), 3.76 (d, J = 11.9 Hz, 1 H), 3.79 (d, J = 11.9 Hz, 1 H), 7.19-7.30 (m, 5 H), 7.43-7.50 (m, 3 H), 7.67-7.71 (m, 2 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.8 mL/min, 280 nm): t_R = 15.1 min, 18.3 min.

The analytical data is in agreement with literature.[4]

2.2.11 Acetic acid 3-(2-methoxyphenyl)-2-(2-methoxyphenylazo)-2-methylpropyl ester (7f)[4]



$C_{20}H_{24}N_2O_4$
M = 356.42 g/mol

Prepared from 2-methoxybenzenediazonium tetrafluoroborate (10.0 mmol, 2.22 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 3:1) gave **7f** (3.34 mmol, 1.19 g, 67%) as a yellow oil.

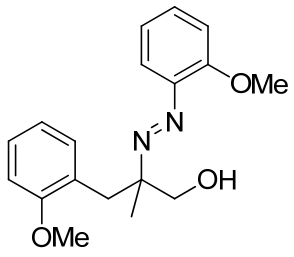
R_f 0.50 (hexane/ethyl acetate = 3:1)

^{1}H-NMR (360 MHz, C_6D_6): δ = 1.45 (s, 3 H), 1.61 (s, 3 H), 3.27 (s, 3 H), 3.30 (d, J = 13.3 Hz, 1 H), 3.38 (s, 3 H), 3.41 (d, J = 13.3 Hz, 1 H), 4.61 (d, J = 11.2 Hz, 1 H), 4.81 (d, J = 11.2 Hz, 1 H), 6.50 (dd, J = 0.9 Hz, J = 8.2 Hz, 1 H), 6.62 (dd, J = 1.2 Hz, J = 8.3 Hz, 1 H), 6.73-6.81 (m, 2 H), 6.99-7.13 (m, 3 H), 7.60 (dd, J = 1.8 Hz, J = 7.9 Hz, 1 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 90:10; 0.6 mL/min, 280 nm): t_R = 11.6 min.

The analytical data is in agreement with literature.[4]

2.2.12 3-(2-Methoxyphenyl)-2-(2-methoxyphenylazo)-2-methylpropan-1-ol (8f)[4]



$C_{18}H_{22}N_2O_3$
M = 314.38 g/mol

Prepared from 2-methoxybenzenediazonium tetrafluoroborate (2.00 mmol, 444 mg) and 2-methallyl alcohol (12.0 mmol, 865 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 2:1) gave **8f** (0.50 mmol, 156 mg, 50%) as a yellow oil.

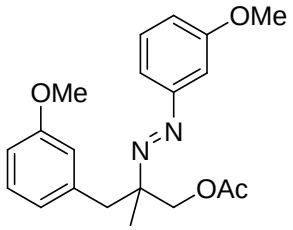
***R*f** 0.55 (hexane/ethyl acetate = 2:1)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.32 (s, 3 H), 3.17 (d, J = 13.4 Hz, 1 H), 3.21 (d, J = 13.4 Hz, 1 H), 3.30-3.38 (m, 1 H), 3.72-3.76 (m, 2 H), 3.82 (s, 3 H), 3.94 (s, 3 H), 6.85-6.89 (m, 2 H), 6.96 (ddd, J = 1.1 Hz, J = 7.4 Hz, J = 7.7 Hz, 1 H), 7.03 (dd, J = 1.1 Hz, J = 8.3 Hz, 1 H), 7.18-7.23 (m, 2 H), 7.31 (dd, J = 1.7 Hz, J = 7.8 Hz, 1 H), 7.39 (ddd, J = 1.7 Hz, J = 7.4 Hz, J = 8.3 Hz, 1 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 90:10; 0.6 mL/min, 280 nm): t_R = 15.8 min, 17.0 min.

The analytical data is in agreement with literature.[4]

2.2.13 Acetic acid 3-(3-methoxyphenyl)-2-(3-methoxyphenylazo)-2-methylpropyl ester (7g)[4]



$C_{20}H_{24}N_2O_4$
M = 356.42 g/mol

Prepared from 3-methoxybenzenediazonium tetrafluoroborate (10.0 mmol, 2.22 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 3:1) gave **7g** (1.62 mmol, 576 mg, 32%) as a yellow oil.

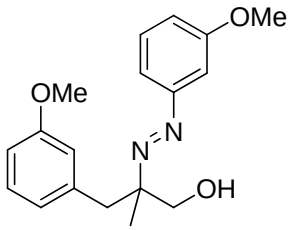
***R*f** 0.60 (hexane/ethyl acetate = 3:1)

^{1}H-NMR (360 MHz, C_6D_6): δ = 1.28 (s, 3 H), 1.62 (s, 3 H), 3.08 (d, J = 13.4 Hz, 1 H), 3.17 (d, J = 13.4 Hz, 1 H), 3.28-3.30 (m, 6 H), 4.53 (d, J = 11.2 Hz, 1 H), 4.57 (d, J = 11.2 Hz, 1 H), 6.67 (ddd, J = 0.9 Hz, J = 2.6 Hz, J = 8.2 Hz, 1 H), 6.70-6.74 (m, 1 H), 6.74-6.77 (m, 1 H), 6.83 (ddd, J = 1.0 Hz, J = 2.6 Hz, J = 8.2 Hz, 1 H), 6.98-7.05 (m, 1 H), 7.05-7.11 (m, 1 H), 7.44-7.47 (m, 1 H), 7.50 (ddd, J = 1.0 Hz, J = 1.7 Hz, J = 7.8 Hz, 1 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 90:10; 0.6 mL/min, 280 nm): t_R = 11.0 min.

The analytical data is in agreement with literature.[4]

2.2.14 3-(3-Methoxyphenyl)-2-(3-methoxyphenylazo)-2-methylpropan-1-ol (8g)[4]



$C_{18}H_{22}N_2O_3$
M = 314.38 g/mol

Prepared from 3-methoxybenzenediazonium tetrafluoroborate (2.00 mmol, 444 mg) and 2-methallyl alcohol (12.0 mmol, 865 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 2:1) gave **8g** (0.38 mmol, 121 mg, 38%) as a red oil.

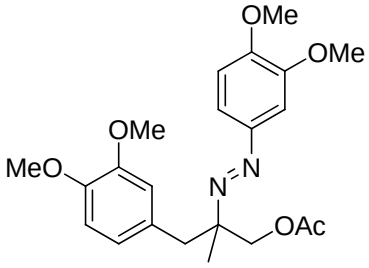
***R*f** 0.40 (hexane/ethyl acetate = 3:1)

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.26 (s, 3 H), 3.02 (d, *J* = 13.3 Hz, 1 H), 3.15 (d, *J* = 13.3 Hz, 1 H), 3.74 (s, 3 H), 3.78-3.80 (m, 2 H), 3.86 (s, 3 H), 6.74-6.80 (m, 2 H), 6.81-6.85 (m, 1 H), 7.01(ddd, *J* = 1.3 Hz, *J* = 2.6 Hz, *J* = 8.0 Hz, 1 H), 7.15-7.22 (m, 2 H), 7.33 (td, *J* = 1.4 Hz, *J* = 7.8 Hz, 1 H), 7.38 (t, *J* = 7.9 Hz, 1 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 90:10; 0.6 mL/min, 280 nm): t_R = 15.8 min, 16.3 min.

The analytical data is in agreement with literature.[4]

2.2.15 Acetic acid 3-(3,4-dimethoxyphenyl)-2-(3,4-dimethoxyphenylazo)-2-methylpropyl ester (7h)[4]



$C_{22}H_{28}N_2O_6$
M = 416.47 g/mol

Prepared from 3,4-dimethoxybenzenediazonium tetrafluoroborate (10.0 mmol, 2.52 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 1:1) gave **7h** (3.22 mmol, 1.34 g, 64%) as a yellow oil.

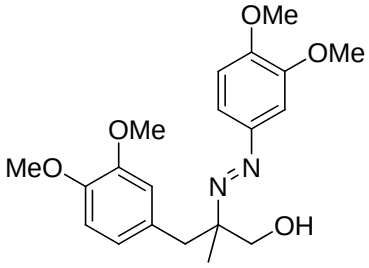
***R*$_f$** 0.60 (hexane/ethyl acetate = 1:1)

^{1}H-NMR (600 MHz, C_6D_6): δ = 1.42 (s, 3 H), 1.67 (s, 3 H), 3.14 (d, J = 13.6 Hz, 1 H), 3.24 (d, J = 13.6 Hz, 1 H), 3.30 (s, 3 H), 3.37 (s, 3 H), 3.38 (s, 3 H), 3.39 (s, 3 H), 4.63 (d, J = 11.2 Hz, 1 H), 4.71 (d, J = 11.2 Hz, 1 H), 6.52 (d, J = 8.4 Hz, 1 H), 6.54 (d, J = 8.1 Hz, 1 H), 6.62 (d, J = 2.0 Hz, 1 H), 6.70 (dd, J = 2.0 Hz, J = 8.1 Hz, 1 H), 7.51 (d, J = 2.2 Hz, 1 H), 7.61 (dd, J = 2.2 Hz, J = 8.4 Hz, 1 H).

HPLC (Chiralpak® IA column; hexane/2-propanol = 90:10; 0.8 mL/min, 280 nm): t_R = 16.7 min, 19.0 min.

The analytical data is in agreement with literature.[4]

2.2.16 3-(3,4-Dimethoxyphenyl)-2-(3,4-dimethoxyphenylazo)-2-methylpropan-1-ol (8h)[4]



$C_{20}H_{26}N_2O_5$
M = 374.43 g/mol

Prepared from 3,4-dimethoxybenzenediazonium tetrafluoroborate (2.00 mmol, 504 mg) and 2-methallyl alcohol (12.0 mmol, 865 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 1:2) gave **8h** (0.56 mmol, 211 mg, 56%) as a dark red solid.

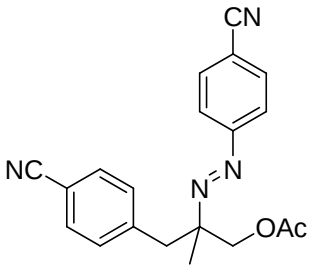
***R*f** 0.25 (hexane/ethyl acetate = 1:1)

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.26 (s, 3 H), 2.96 (d, J = 13.5 Hz, 1 H), 3.11 (d, J = 13.5 Hz, 1 H), 3.76 (s, 3 H), 3.76-3.78 (m, 2 H), 3.85 (s, 3 H), 3.94 (s, 3 H), 3.96 (s, 3 H), 6.72-6.74 (m, 1 H), 6.77-6.79 (m, 2 H), 6.95 (d, J = 8.5 Hz, 1 H), 7.23 (d, J = 2.2 Hz, 1 H), 7.42 (dd, J = 2.2 Hz, J = 8.5 Hz, 1 H).

HPLC **(**Chiralpak® IA column; hexane/2-propanol = 90:10; 0.8 mL/min, 280 nm): t_R = 34.6 min, 40.2 min.

The analytical data is in agreement with literature.[4]

2.2.17 Acetic acid 3-(4-cyanophenyl)-2-(4-cyanophenylazo)-2-methylpropyl ester (7i)[4]



$C_{20}H_{18}N_4O_2$
M = 346.38 g/mol

Prepared from 4-cyanobenzenediazonium tetrafluoroborate (10.0 mmol, 2.17 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 2:1) gave **7i** (3.78 mmol, 1.31 g, 76%) as a yellow oil.

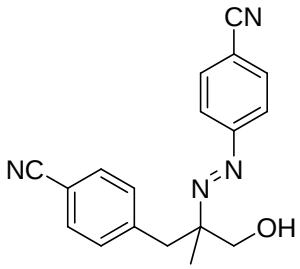
***R*$_f$** 0.50 (hexane/ethyl acetate = 2:1)

^{1}H-NMR (600 MHz, C_6D_6): δ = 0.99 (s, 3 H), 1.61 (s, 3 H), 2.71 (d, J = 13.4 Hz, 1 H), 2.84 (d, J = 13.4 Hz, 1 H), 4.25 (d, J = 11.4 Hz, 1 H), 4.29 (d, J = 11.4 Hz, 1 H), 6.57 (d, J = 8.4 Hz, 2 H), 6.93 (d, J = 8.4 Hz, 2 H), 6.99 (d, J = 8.7 Hz, 2 H), 7.25 (d, J = 8.7 Hz, 2 H).

HPLC (Chiralpak® IA column; hexane/2-propanol = 90:10; 0.8 mL/min, 280 nm): t_R = 20.7 min.

The analytical data is in agreement with literature.[4]

2.2.18 4-((1-(4-Cyanophenyl)-3-hydroxy-2-methylpropan-2-yl)diazenyl)-benzonitrile (8i)[4]



$C_{18}H_{16}N_4O$
M = 304.35 g/mol

Prepared from 4-cyanobenzenediazonium tetrafluoroborate (2.00 mmol, 434 mg) and 2-methallyl alcohol (12.0 mmol, 865 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 1:1) gave **8i** (0.77 mmol, 233 mg, 77%) as a yellow solid.

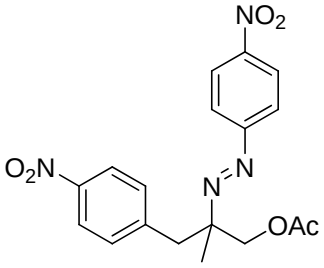
***R*f** 0.35 (hexane/ethyl acetate = 1:1)

^{1}H-NMR (600 MHz, C_6D_6): δ = 0.94 (s, 3 H), 1.62 (br, 1 H), 2.77 (d, J = 13.1 Hz, 1 H), 2.89 (d, J = 13.1 Hz, 1 H), 3.40 (d, J = 11.6 Hz, 1 H), 3.54 (d, J = 11.6 Hz, 1 H), 6.76 (d, J = 8.4 Hz, 2 H), 6.99 (d, J = 8.4 Hz, 2 H), 7.00 (d, J = 8.7 Hz, 2 H), 7.19 (d, J = 8.7 Hz, 2 H).

HPLC (Chiralpak® IA column; hexane/2-propanol = 90:10; 0.8 mL/min, 240 nm): t_R = 29.0 min, 32.0 min.

The analytical data is in agreement with literature.[4]

2.2.19 Acetic acid 2-methyl-3-(4-nitrophenyl)-2-(4-nitrophenylazo)propyl ester (7j)

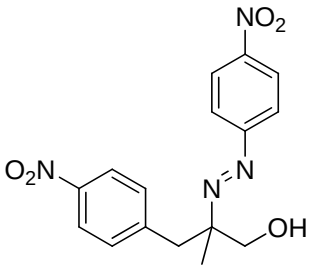


$C_{18}H_{18}N_4O_6$
M = 386.36 g/mol

Prepared from 4-nitrobenzenediazonium tetrafluoroborate (1.00 mmol, 237 mg) and 2-methallyl acetate (6.00 mmol, 685 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 2:1) gave **7j** (0.18 mmol, 68.5 mg, 36%) as a yellow oil.

R_f	0.55 (hexane/ethyl acetate = 2:1)
^{1}H-NMR	(600 MHz, $CDCl_3$): δ = 1.31 (s, 3 H), 2.08 (s, 3 H), 3.30 (d, J = 13.5 Hz, 1 H), 3.39 (d, J = 13.5 Hz, 1 H), 4.35 (d, J = 11.4 Hz, 1 H), 4.44 (d, J = 11.4 Hz, 1 H), 7.27 (d, J = 8.8 Hz, 2 H), 7.77 (d, J = 9.1 Hz, 2 H), 8.12 (d, J = 8.8 Hz, 2 H), 8.36 (d, J = 9.1 Hz, 2 H).
^{13}C-NMR	(151 MHz, $CDCl_3$): δ = 19.9 (CH_3), 20.8 (CH_3), 41.7 (CH_2), 67.4 (CH_2), 73.6 (C_q), 122.9 (2×CH), 123.3 (2×CH), 124.8 (2×CH), 131.4 (2×CH), 144.0 (C_q), 147.0 (C_q), 148.9 (C_q), 154.5 (C_q), 170.4 (C_q).
MS (EI)	*m/z* (%): 386 (1) [M^+], 237 (19), 236 (100), 194 (39), 176 (14), 164 (10), 151 (12), 150 (72), 131 (11), 130 (93), 129 (18), 122 (57), 115 (14), 83 (11), 76 (13), 75 (11).
HRMS (EI)	calcd. for $C_{18}H_{18}N_4O_6$ [M^+]: 386.1226, found: 386.1226.
HPLC	(Chiralpak® IC column; hexane/2-propanol = 70:30; 0.8 mL/min, 280 nm): t_R = 50.9 min, 54.2 min.

2.2.20 2-Methyl-3-(4-nitrophenyl)-2-(4-nitrophenylazo)propan-1-ol (8j)

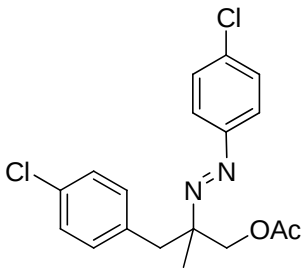


$C_{16}H_{16}N_4O_5$
M = 344.32 g/mol

Prepared from 4-nitrobenzenediazonium tetrafluoroborate (1.00 mmol, 237 mg) and 2-methallyl alcohol (6.00 mmol, 433 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 1:1) gave **8j** (0.13 mmol, 43.5 mg, 26%) as a dark yellow solid.

***R*f**	0.50 (hexane/ethyl acetate = 1:1)
^{1}H-NMR	(600 MHz, $CDCl_3$): δ = 1.27 (s, 3 H), 3.24 (d, J = 13.2 Hz, 1 H), 3.33 (d, J = 13.2 Hz, 1 H), 3.75 (d, J = 11.9 Hz, 1 H), 3.92 (d, J = 11.9 Hz, 1 H), 7.40 (d, J = 8.8 Hz, 2 H), 7.81 (d, J = 9.1 Hz, 2 H), 8.14 (d, J = 8.8 Hz, 2 H), 8.37 (d, J = 9.1 Hz, 2 H).
^{13}C-NMR	(151 MHz, $CDCl_3$): δ = 19.6 (CH_3), 40.9 (CH_2), 66.5 (CH_2), 75.4 (C_q), 122.9 (2×CH), 123.3 (2×CH), 124.8 (2×CH), 131.6 (2×CH), 144.6 (C_q), 146.9 (C_q), 149.0 (C_q), 154.4 (C_q).
MS (EI)	*m/z* (%): 344 (2) [M^+], 315 (38), 314 (100), 195 (11), 194 (98), 176 (12), 164 (16), 151 (21), 150 (41), 138 (42), 137 (24), 136 (48), 132 (10), 130 (23), 123 (12), 122 (41), 115 (14), 106 (20), 92 (10), 91 (14), 90 (26), 89 (25), 78 (23).
HRMS (EI)	calcd. for $C_{16}H_{16}N_4O_5$ [M^+]: 344.1121, found: 344.1122.
HPLC	(Chiralpak® IC column; hexane/2-propanol = 80:20; 0.8 mL/min, 280 nm): t_R = 21.8 min, 22.8 min.

2.2.21 Acetic acid 3-(4-chlorophenyl)-2-(4-chlorophenylazo)-2- methylpropyl ester (7k)



$C_{18}H_{18}Cl_2N_2O_2$
M = 365.25 g/mol

Prepared from 4-chlorobenzenediazonium tetrafluoroborate (5.00 mmol, 1.13 g) and 2-methallyl acetate (30.0 mmol, 3.42 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 8:1) gave **7f** (1.78 mmol, 649 mg, 71%) as a yellow oil.

R_f 0.45 (hexane/ethyl acetate = 8:1)

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.24 (s, 3 H), 2.05 (s, 3 H), 3.10 (d, J = 13.6 Hz, 1 H), 3.16 (d, J = 13.6 Hz, 1 H), 4.32 (d, J = 11.2 Hz, 1 H), 4.36 (d, J = 11.2 Hz, 1 H), 7.01 (d, J = 8.5 Hz, 2 H), 7.12 (d, J = 8.5 Hz, 2 H), 7.44 (d, J = 8.8 Hz, 2 H), 7.61 (d, J = 8.8 Hz, 2 H).

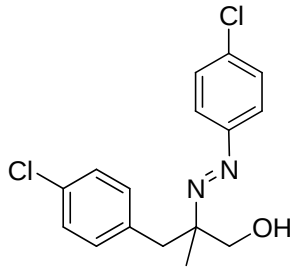
^{13}C-NMR (151 MHz, $CDCl_3$): δ = 19.8 (CH_3), 20.9 (CH_3), 41.4 (CH_2), 67.8 (CH_2), 72.4 (C_q), 123.5 (2×CH), 128.2 (2×CH), 129.2 (2×CH), 131.9 (2×CH), 132.5 (C_q), 134.9 (C_q), 136.7 (C_q), 150.0 (C_q), 170.7 (C_q).

MS (EI) *m/z* (%): 365 (<1) [M^+], 227 (15), 225 (51), 167 (29), 166 (12), 165 (83), 141 (27), 139 (83), 130 (18), 129 (16), 127 (18), 125 (39), 113 (24), 111 (82), 89 (10), 75 (15), 43 (100).

HRMS (EI) calcd. for $C_{18}H_{18}Cl_2N_2O_2$ [M^+]: 364.0745, found: 364.0747.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 11.4 min.

2.2.22 3-(4-Chlorophenyl)-2-(4-chlorophenylazo)-2-methylpropan-1-ol (8k)



$C_{16}H_{16}Cl_2N_2O$
M = 323.22 g/mol

Prepared from 4-chlorobenzenediazonium tetrafluoroborate (1.00 mmol, 226 mg) and 2-methallyl alcohol (6.0 mmol, 433 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 4:1) gave **8f** (0.32 mmol, 104 mg, 64%) as a yellow oil.

***R*f** 0.35 (hexane/ethyl acetate = 4:1)

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.22 (s, 3 H), 3.00 (d, J = 13.4 Hz, 1 H), 3.13 (d, J = 13.4 Hz, 1 H), 3.71 (d, J = 11.9 Hz, 1 H), 3.80 (d, J = 11.9 Hz, 1 H), 7.15 (d, J = 8.5 Hz, 2 H), 7.24 (d, J = 8.5 Hz, 2 H), 7.45 (d, J = 8.8 Hz, 2 H), 7.64 (d, J = 8.8 Hz, 2 H).

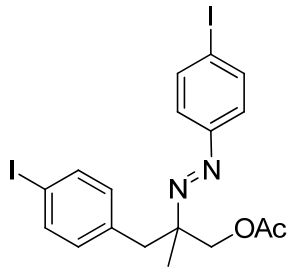
^{13}C-NMR (90.6 MHz, $CDCl_3$): δ = 19.6 (CH_3), 40.7 (CH_2), 66.8 (CH_2), 74.0 (C_q), 123.5 (2×CH), 128.2 (2×CH), 129.3 (2×CH), 132.1 (2×CH), 132.4 (C_q), 135.3 (C_q), 136.9 (C_q), 149.8 (C_q).

MS (EI) *m/z* (%): 323 (<1) [M^+], 294 (32), 292 (49), 139 (12), 129 (21), 128 (22), 127 (100), 126 (54), 125 (93), 111 (20), 99 (21), 90 (11), 89 (22).

HRMS (EI) calcd. for $C_{16}H_{16}Cl_2N_2O$ [M^+]: 322.0640, found: 322.0640.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 17.2 min, 18.9 min.

2.2.23 Acetic acid 3-(4-iodophenyl)-2-(4-iodophenylazo)-2-methylpropyl ester (7l)



$C_{18}H_{18}I_2N_2O_2$
M = 548.16 g/mol

Prepared from 4-iodobenzenediazonium tetrafluoroborate (10.0 mmol, 3.18 g) and 2-methallyl acetate (60.0 mmol, 6.85 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 8:1) gave **7k** (3.48 mmol, 1.91 g, 70%) as a yellow oil.

***R*f** 0.50 (hexane/ethyl acetate = 8:1)

^{1}H-NMR (360 MHz, C_6D_6): δ = 1.08 (s, 3 H), 1.59 (s, 3 H), 2.75 (d, J = 13.5 Hz, 1 H), 2.88 (d, J = 13.5 Hz, 1 H), 4.31-4-40 (m, 2 H), 6.49 (d, J = 8.4 Hz, 2 H), 7.21 (d, J = 8.7 Hz, 2 H), 7.34 (d, J = 8.4 Hz, 2 H), 7.43 (d, J = 8.7 Hz, 2 H).

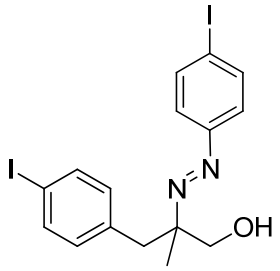
^{13}C-NMR (90.6 MHz, C_6D_6): δ = 19.5 (CH_3), 20.3 (CH_3), 41.8 (CH_2), 67.9 (CH_2), 72.7 (C_q), 92.4 (C_q), 97.6 (C_q), 124.2 (2×CH), 132.9 (2×CH), 136.3 (C_q), 137.4 (2×CH), 138.6 (2×CH), 151.3 (C_q), 169.7 (C_q).

MS (EI) *m/z* (%): 548 (<1) [M^+], 317 (67), 257 (12), 231 (100), 217 (19), 203 (62), 131 (12), 130 (89), 129 (11), 115 (11), 90 (13), 76 (23).

HRMS (EI) calcd. for $C_{18}H_{18}I_2N_2O_2$ [M^+]: 547.9458, found: 547.9457.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 14.1 min.

2.2.24 3-(4-Iodophenyl)-2-(4-iodophenylazo)-2-methylpropan-1-ol (8l)

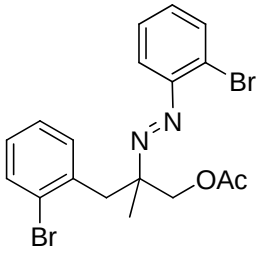


$C_{16}H_{16}I_2N_2O$
M = 506.12 g/mol

Prepared from 4-iodobenzenediazonium tetrafluoroborate (1.00 mmol, 318 mg) and 2-methallyl alcohol (6.00 mmol, 433 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 4:1) gave **8k** (0.33 mmol, 169 mg, 66%) as a yellow oil.

***R*f**	0.30 (hexane/ethyl acetate = 4:1)
^{1}H-NMR	(360 MHz, $CDCl_3$): δ = 1.21 (s, 3 H), 2.97 (d, J = 13.3 Hz, 1 H), 3.09 (d, J = 13.3 Hz, 1 H), 3.70 (d, J = 11.9 Hz, 1 H), 3.79 (d, J = 11.9 Hz, 1 H), 6.96 (d, J = 8.3 Hz, 2 H), 7.41 (d, J = 8.7 Hz, 2 H), 7.58 (d, J = 8.3 Hz, 2 H), 7.83 (d, J = 8.7 Hz, 2 H).
^{13}C-NMR	(151 MHz, $CDCl_3$): δ = 19.6 (CH_3), 40.9 (CH_2), 66.7 (CH_2), 74.0 (C_q), 91.9 (C_q), 97.5 (C_q), 123.8 (2×CH), 132.8 (2×CH), 136.5 (C_q), 137.1 (2×CH), 138.3 (2×CH), 150.8 (C_q).
MS (EI)	*m/z* (%): 506 (<1) [M^+], 476 (18), 475 (100), 347 (12), 275 (12), 231 (22), 219 (70), 218 (44), 217 (69), 203 (28), 130 (13), 115 (14), 91 (27), 90 (35), 89 (19), 76 (16).
HRMS (EI)	calcd. for $C_{16}H_{16}I_2N_2O$ [M^+]: 505.9353, found: 505.9353.
HPLC	(Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 24.7 min, 30.9 min.

2.2.25 Acetic acid 3-(2-bromophenyl)-2-(2-bromophenylazo)-2-methylpropyl ester (7m)



$C_{18}H_{18}Br_2N_2O_2$
M = 454.16 g/mol

Prepared from 2-bromobenzenediazonium tetrafluoroborate (3.18 mmol, 860 mg) and 2-methallyl acetate (19.1 mmol, 2.18 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 8:1) gave **7i** (1.14 mmol, 518 mg, 72%) as a yellow oil.

R_f 0.35 (hexane/ethyl acetate = 8:1)

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.35 (s, 3 H), 2.04 (s, 3 H), 3.42 (d, J = 13.9 Hz, 1 H), 3.51 (d, J = 13.9 Hz, 1 H), 4.44-4.52 (m, 2 H), 7.03-7.09 (m, 1 H), 7.13-7.21 (m, 2 H), 7.25-7.38 (m, 3 H), 7.52-7.57 (m, 1 H), 7.69 (dd, J = 1.0 Hz, J = 7.8 Hz, 1 H).

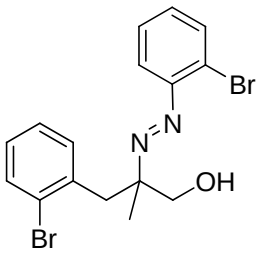
^{13}C-NMR (151 MHz, $CDCl_3$): δ = 19.6 (CH_3), 20.9 (CH_3), 40.8 (CH_2), 68.0 (CH_2), 74.3 (C_q), 117.9 (CH), 124.1 (C_q), 126.1 (C_q), 127.0 (CH), 128.0 (CH), 128.3 (CH), 131.4 (CH), 132.5 (CH), 133.1 (CH), 133.5 (CH), 136.4 (C_q), 149.1 (C_q), 170.8 (C_q).

MS (EI) *m/z* (%): 454 (1) [M^+], 272 (13), 271 (86), 270 (12), 269 (88), 211 (63), 209 (66), 185 (56), 183 (58), 171 (36), 169 (35), 157 (49), 155 (51), 131 (23), 130 (100), 129 (25), 116 (11), 115 (22), 91 (21), 90 (23), 76 (15), 75 (12).

HRMS (EI) calcd. for $C_{18}H_{18}Br_2N_2O_2$ [M^+]: 451.9735, found: 451.9734.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 13.7 min.

2.2.26 3-(2-Bromophenyl)-2-(2-bromophenylazo)-2-methylpropan-1-ol (8m)



$C_{16}H_{16}Br_2N_2O$
M = 412.12 g/mol

Prepared from 2-bromobenzenediazonium tetrafluoroborate (1.00 mmol, 271 mg) and 2-methallyl alcohol (6.00 mmol, 433 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 4:1) gave **8i** (0.37 mmol, 152 mg, 74%) as a yellow oil.

***R*$_f$** 0.35 (hexane/ethyl acetate = 4:1)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.39 (s, 3 H), 2.92 (br, 1 H), 3.32 (d, J = 13.8 Hz, 1 H), 3.47 (d, J = 13.8 Hz, 1 H), 3.81-3.87 (m, 2 H), 7.08 (ddd, J = 1.7 Hz, J = 7.5 Hz, J = 7.9 Hz, 1 H), 7.23 (ddd, J = 1.3 Hz, J = 7.5 Hz, J = 7.6 Hz, 1 H), 7.29-7.41 (m, 4 H), 7.57 (dd, J = 1.3 Hz, J = 8.0 Hz, 1 H), 7.71 (dd, J = 1.2 Hz, J = 7.9 Hz, 1 H).

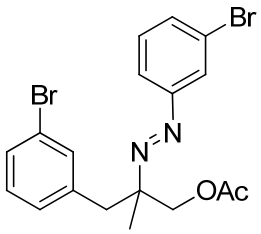
^{13}C-NMR (151 MHz, $CDCl_3$): δ = 19.8 (CH_3), 40.4 (CH_2), 66.9 (CH_2), 75.8 (C_q), 117.8 (CH), 124.5 (C_q), 126.1 (C_q), 127.1 (CH), 128.1 (CH), 128.2 (CH), 131.9 (CH), 132.8 (CH), 133.0 (CH), 133.4 (CH), 136.7 (C_q), 148.4 (C_q).

MS (EI) *m/z* (%): 412 (<1) [M^+], 384 (16), 382 (22), 380 (12), 222 (11), 181 (22), 173 (17), 172 (47), 171 (100), 170 (42), 169 (35), 157 (14), 155 (13), 147 (29), 131 (12), 130 (14), 115 (12), 91 (35), 90 (46), 89 (22).

HRMS (EI) calcd. for $C_{16}H_{16}Br_2N_2O$ [M^+]: 409.9630, found: 409.9628.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 19.3 min, 20.2 min.

2.2.27 Acetic acid 3-(3-bromophenyl)-2-(3-bromophenylazo)-2-methylpropyl ester (7n)



$C_{18}H_{18}Br_2N_2O_2$
M = 454.16 g/mol

Prepared from 3-bromobenzenediazonium tetrafluoroborate (5.00 mmol, 1.35 g) and 2-methallyl acetate (30.0 mmol, 3.42 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 8:1) gave **7j** (1.90 mmol, 861 mg, 76%) as a yellow oil.

***R*f** 0.45 (hexane/ethyl acetate = 8:1)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.26 (s, 3 H), 2.07 (s, 3 H), 3.11 (d, J = 13.6 Hz, 1 H), 3.16 (d, J = 13.6 Hz, 1 H), 4.32 (d, J = 11.3 Hz, 1 H), 4.38 (d, J = 11.3 Hz, 1 H), 7.00-7.03 (m, 1 H), 7.11 (t, J = 7.8 Hz, 1 H), 7.27 (t, J = 1.8 Hz, 1 H), 7.33-7.38 (m, 2 H), 7.58 (ddd, J = 1.0 Hz, J = 1.9 Hz, J = 7.9 Hz, 1 H), 7.62 (ddd, J = 1.0 Hz, J = 1.8 Hz, J = 7.8 Hz, 1 H), 7.78 (t, J = 1.9 Hz, 1 H).

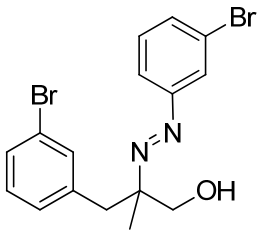
^{13}C-NMR (151 MHz, $CDCl_3$): δ = 19.9 (CH_3), 20.9 (CH_3), 41.7 (CH_2), 67.7 (CH_2), 72.6 (C_q), 122.0 (CH), 122.1 (C_q), 123.0 (C_q), 124.4 (CH), 129.2 (CH), 129.6 (CH), 129.7 (CH), 130.4 (CH), 133.4 (CH), 133.7 (CH), 138.7 (C_q), 152.6 (C_q), 170.7 (C_q).

MS (EI) *m/z* (%): 454 (<1) [M^+], 271 (61), 269 (61), 211 (37), 209 (36), 185 (46), 183 (47), 171 (15), 169 (12), 157 (45), 155 (46), 131 (18), 130 (100), 129 (16), 115 (14), 91 (12), 90 (15), 76 (13).

HRMS (EI) calcd. for $C_{18}H_{18}Br_2N_2O_2$ [M^+]: 451.9735, found: 451.9735.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 11.7 min.

2.2.28 3-(3-Bromophenyl)-2-(3-bromophenylazo)-2-methylpropan-1-ol (8n)



$C_{16}H_{16}Br_2N_2O$
M = 412.12 g/mol

Prepared from 3-bromobenzenediazonium tetrafluoroborate (1.00 mmol, 271 mg) and 2-methallyl alcohol (6.00 mmol, 433 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 4:1) gave **8j** (0.37 mmol, 153 mg, 74%) as a yellow oil.

R_f 0.35 (hexane/ethyl acetate = 4:1)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.23 (s, 3 H), 2.33 (br, 1 H), 3.01 (d, J = 13.4 Hz, 1 H), 3.13 (d, J = 13.4 Hz, 1 H), 3.74 (d, J = 11.9 Hz, 1 H), 3.81 (d, J = 11.9 Hz, 1 H), 7.12-7.17 (m, 2 H), 7.34-7.40 (m, 3 H), 7.59 (ddd, J = 1.0 Hz, J = 2.0 Hz, J = 7.9 Hz, 1 H), 7.65 (ddd, J = 1.0 Hz, J = 1.9 Hz, J = 7.9 Hz, 1 H) 7.79-7.82 (m, 1 H).

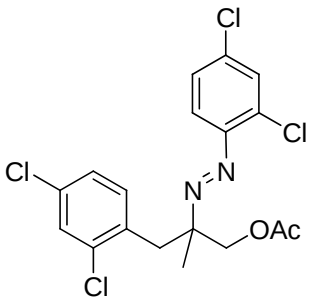
^{13}C-NMR (151 MHz, $CDCl_3$): δ = 19.6 (CH_3), 40.9 (CH_2), 66.7 (CH_2), 74.3 (C_q), 122.1 (C_q), 122.2 (CH), 123.1 (C_q), 124.2 (CH), 129.4 (CH), 129.5 (CH), 129.6 (CH), 130.5 (CH), 133.6 (CH), 133.7 (CH), 139.2 (C_q), 152.4 (C_q).

MS (EI) *m/z* (%): 412 (<1) [M^+], 384 (40), 383 (14), 382 (82), 380 (43), 229 (14), 227 (13), 211 (13), 210 (11), 185 (15), 183 (15), 173 (72), 172 (52), 171 (100), 170 (48), 169 (80), 157 (21), 155 (21), 132 (12), 131 (17), 130 (32), 116 (11), 115 (13), 91 (52), 90 (58), 89 (33).

HRMS (EI) calcd. for $C_{16}H_{16}Br_2N_2O$ [M^+]: 409.9630, found: 409.9629.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.6 mL/min, 280 nm): t_R = 20.4 min, 22.1 min.

2.2.29 Acetic acid 3-(2,4-dichlorophenyl)-2-(2,4-dichlorophenylazo)-2-methyl-propyl ester (7o)



$C_{18}H_{16}Cl_4N_2O_2$
M = 434.14 g/mol

Prepared from 2,4-dichlorobenzenediazonium tetrafluoroborate (5.00 mmol, 1.30 g) and 2-methallyl acetate (30.0 mmol, 3.42 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 8:1) gave **7g** (2.03 mmol, 881 mg, 81%) as a yellow oil.

***R*f** 0.40 (hexane/ethyl acetate = 8:1)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.31 (s, 3 H), 2.04 (s, 3 H), 3.31 (d, J = 14.0 Hz, 1 H), 3.41 (d, J = 14.0 Hz, 1 H), 4.42 (d, J = 11.3 Hz, 1 H), 4.45 (d, J = 11.3 Hz, 1 H), 7.07 (d, J = 8.3 Hz, 1 H), 7.12 (dd, J = 2.2 Hz, J = 8.3 Hz, 1 H), 7.28 (dd, J = 2.1 Hz, J = 8.6 Hz, 1 H), 7.31 (d, J = 8.6 Hz, 1 H), 7.37 (d, J = 2.2 Hz, 1 H), 7.52 (d, J = 2.1 Hz, 1 H).

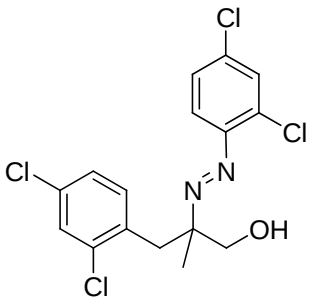
^{13}C-NMR (151 MHz, $CDCl_3$): δ = 19.6 (CH_3), 20.8 (CH_3), 37.8 (CH_2), 67.8 (CH_2), 74.3 (C_q), 118.5 (CH), 126.7 (CH), 127.7 (CH), 129.5 (CH), 130.3 (CH), 133.1 (C_q), 133.2 (C_q), 133.3 (CH), 135.1 (C_q), 135.8 (C_q), 137.0 (C_q), 146.4 (C_q), 170.6 (C_q).

MS (EI) *m/z* (%): 434 (<1) [M^+], 261 (53), 260 (11), 259 (80), 201 (47), 200 (10), 199 (67), 175 (64), 173 (100), 164 (21), 163 (15), 161 (31), 159 (45), 147 (35), 145 (46), 129 (18), 124 (10), 109 (11).

HRMS (EI) calcd. for $C_{18}H_{16}Cl_4N_2O_2$ [M^+]: 431.9966, found: 431.9966.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.8 mL/min, 280 nm): t_R = 8.2 min.

2.2.30 3-(2,4-Dichlorophenyl)-2-(2,4-dichlorophenylazo)-2-methylpropan-1-ol (8o)

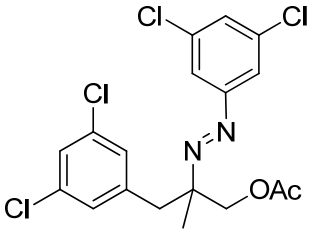


$C_{16}H_{14}Cl_4N_2O$
M = 392.11 g/mol

Prepared from 2,4-dichlorobenzenediazonium tetrafluoroborate (1.00 mmol, 261 mg) and 2-methallyl alcohol (6.00 mmol, 433 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 4:1) gave **8g** (0.35 mmol, 137 mg, 70%) as a yellow oil.

***R*$_f$**	0.35 (hexane/ethyl acetate = 4:1)
^{1}H-NMR	(600 MHz, $CDCl_3$): δ = 1.33 (s, 3 H), 3.20 (d, J = 13.7 Hz, 1 H), 3.39 (d, J = 13.7 Hz, 1 H), 3.77 (d, J = 12.3 Hz, 1 H), 3.84 (d, J = 12.3 Hz, 1 H), 7.17 (dd, J = 2.2 Hz, J = 8.3 Hz, 1 H), 7.27 (d, J = 8.3 Hz, 1 H), 7.30 (dd, J = 2.1 Hz, J = 8.6 Hz, 1 H), 7.36 (d, J = 8.6 Hz, 1 H), 7.39 (d, J = 2.2 Hz, 1 H), 7.55 (d, J = 2.1 Hz, 1 H).
^{13}C-NMR	(151 MHz, $CDCl_3$): δ = 19.7 (CH_3), 37.3 (CH_2), 66.8 (CH_2), 75.9 (C_q), 118.2 (CH), 126.8 (CH), 127.9 (CH), 129.4 (CH), 130.2 (CH), 133.1 (C_q), 133.4 (C_q), 133.6 (CH), 135.2 (C_q), 135.8 (C_q), 137.4 (C_q), 145.8 (C_q).
MS (EI)	*m/z* (%): 392 (<1) [M^+], 363 (20), 361 (44), 359 (33), 164 (12), 163 (39), 162 (45), 161 (100), 160 (64), 159 (80), 135 (12), 124 (12), 123 (11).
HRMS (EI)	calcd. for $C_{16}H_{14}Cl_4N_2O$ [M^+]: 389.9860, found: 389.9860.
HPLC	(Chiralpak® IC column; hexane/2-propanol = 99:1; 0.8 mL/min, 280 nm): t_R = 10.6 min.

2.2.31 Acetic acid 3-(3,5-dichlorophenyl)-2-(3,5-dichlorophenylazo)-2-methyl-propyl ester (7p)



$C_{18}H_{16}Cl_4N_2O_2$
M = 434.14 g/mol

Prepared from 3,5-dichlorobenzenediazonium tetrafluoroborate (5.00 mmol, 1.30 g) and 2-methallyl acetate (30.0 mmol, 3.42 g) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 8:1) gave **7h** (2.08 mmol, 904 mg, 83%) as a yellow oil.

R_f 0.45 (hexane/ethyl acetate = 8:1)

^{1}H-NMR (360 MHz, C_6D_6): δ = 0.93 (s, 3 H), 1.59 (s, 3 H), 2.58 (d, J = 13.5 Hz, 1 H), 2.75 (d, J = 13.5 Hz, 1 H), 4.17 (d, J = 11.4 Hz, 1 H), 4.26 (d, J = 11.4 Hz, 1 H), 6.76 (d, J = 1.9 Hz, 2 H), 6.99 (t, J = 1.9 Hz, 1 H), 7.02 (t, J = 1.9 Hz, 1 H), 7.46 (d, J = 1.9 Hz, 2 H).

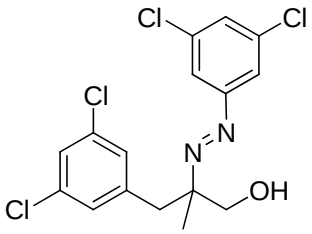
^{13}C-NMR (151 MHz, C_6D_6): δ = 19.4 (CH_3), 20.1 (CH_3), 41.3 (CH_2), 67.5 (CH_2), 73.0 (C_q), 121.3 (2×CH), 127.2 (CH), 129.4 (2×CH), 130.6 (CH), 134.8 (2×C_q), 136.0 (2×C_q), 140.0 (C_q), 152.8 (C_q), 169.6 (C_q).

MS (EI) *m/z* (%): 434 (<1) [M^+], 263 (10), 261 (64), 260 (14), 259 (99), 203 (11), 201 (65), 200 (12), 199 (100), 175 (38), 173 (58), 165 (13), 164 (24), 163 (12), 161 (17), 159 (24), 147 (44), 145 (77), 129 (22), 128 (11), 109 (14).

HRMS (EI) calcd. for $C_{18}H_{16}Cl_4N_2O_2$ [M^+]: 431.9966, found: 431.9966.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.8 mL/min, 280 nm): t_R = 7.3 min.

2.2.32 3-(3,5-Dichlorophenyl)-2-(3,5-dichlorophenylazo)-2-methylpropan-1-ol (8p)



$C_{16}H_{14}Cl_4N_2O$
M = 392.11 g/mol

Prepared from 3,5-dichlorobenzenediazonium tetrafluoroborate (1.00 mmol, 261 mg) and 2-methallyl alcohol (6.00 mmol, 433 mg) according to the general procedure. Purification by column chromatography (hexane/ethyl acetate = 4:1) gave **8h** (0.39 mmol, 152 mg, 78%) as a yellow oil.

***R*f** 0.40 (hexane/ethyl acetate = 4:1)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.22 (s, 3 H), 3.01 (d, J = 13.4 Hz, 1 H), 3.11 (d, J = 13.4 Hz, 1 H), 3.72 (d, J = 11.9 Hz, 1 H), 3.85 (d, J = 11.9 Hz, 1 H), 7.11 (d, J = 1.9 Hz, 2 H), 7.24 (t, J = 1.9 Hz, 1 H), 7.46 (t, J = 1.9 Hz, 1 H), 7.58 (d, J = 1.9 Hz, 2 H).

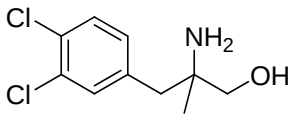
^{13}C-NMR (151 MHz, $CDCl_3$): δ = 19.5 (CH_3), 40.6 (CH_2), 66.5 (CH_2), 74.7 (C_q), 121.0 (2×CH), 126.9 (CH), 129.2 (2×CH), 130.5 (CH), 134.5 (2×C_q), 135.7 (2×C_q), 140.1 (C_q), 152.5 (C_q).

MS (EI) *m/z* (%): 392 (1) [M^+], 364 (28), 362 (59), 360 (50), 219 (31), 218 (16), 217 (44), 216 (16), 203 (15), 201 (47), 200 (20), 199 (53), 198 (20), 189 (16), 187 (24), 175 (28), 173 (41), 165 (17), 164 (23), 163 (65), 162 (51), 161 (100), 160 (80), 159 (100), 147 (36), 145 (55), 135 (16), 133 (26), 125 (28), 124 (30), 123 (26), 115 (16), 89 (23).

HRMS (EI) calcd. for $C_{16}H_{14}Cl_4N_2O$ [M^+]: 389.9860, found: 389.9860.

HPLC (Chiralpak® IC column; hexane/2-propanol = 99:1; 0.8 mL/min, 280 nm): t_R = 10.4 min.

2.2.33 2-Amino-3-(3,4-dichlorophenyl)-2-methylpropan-1-ol (9)[5]



$C_{10}H_{13}Cl_2NO$
M = 234.12 g/mol

Racemic synthesis of amino alcohol *rac*-9 from acetate *rac*-7c

Acetate *rac*-**7c** (0.50 mmol, 217 mg) was dissolved in methanol (5 mL) and zinc dust (15.0 mmol, 981 mg) and hydrochloric acid (6 M, 5 mL) were added. The resulting mixture was heated to reflux for 4 hours, after which additional hydrochloric acid (6 M, 5 mL) was added. The mixture was refluxed for another 15 hours, then allowed to cool to room temperature and diluted with water (20 mL). The pH was adjusted with aqueous sodium hydroxide (20%) to a value >12 and the reaction mixture was extracted with dichloromethane (3 × 30 mL). The combined organic phases were dried over sodium sulfate and the solvent was evaporated under reduced pressure. The pure product was obtained after column chromatography (chloroform/methanol = 10:1, 1% diethyl amine) as a white solid (0.39 mmol, 91.0 mg, 78%).

Synthesis of the enantiomerically enriched amino alcohol (*S*)-9 from acetate 7c

Acetate **7c** (0.12 mmol, 51.1 mg, >99% ee) was dissolved in methanol (2 mL) and zinc dust (3.5 mmol, 229 mg) and hydrochloric acid (6 M, 2 mL) were added. The resulting mixture was heated to reflux for 20 hours, then allowed to cool to room temperature and diluted with water (20 mL) The pH was adjusted with aqueous sodium hydroxide (20%) to a value >12 and the reaction mixture was extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried over sodium sulfate and the solvent was evaporated under reduced pressure. The pure product was obtained after column chromatography (chloroform/methanol = 10:1, 1% diethyl amine) as a white solid (61.5 µmol, 14.4 mg, 51%, >99% ee).

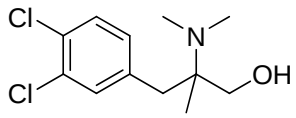
R_f 0.35 (chloroform/methanol = 10:1, 1% diethyl amine)

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.03 (s, 3 H), 1.88 (br, 3 H), 2.64 (d, J = 13.2 Hz, 1 H), 2.69 (d, J = 13.2 Hz, 1 H), 3.26-3.36 (m, 2 H), 7.06 (dd, J = 2.0 Hz, J = 8.2 Hz, 1 H), 7.31 (d, J = 2.0 Hz, 1 H), 7.37 (d, J = 8.2 Hz, 1 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 95:5, 0.1% diethyl amine; 0.8 mL/min, 230 nm): t_R = 15.5 min, 17.6 min.

The analytical data is in agreement with literature.[5]

2.2.34 3-(3,4-Dichlorophenyl)-2-dimethylamino-2-methylpropan-1-ol (Cericlamine) (10)[5]



$C_{12}H_{17}Cl_2NO$
M= 262.18 g/mol

Racemic synthesis of compound *rac*-10 from amino alcohol *rac*-9

To amino alcohol *rac*-**9** (0.38 mmol, 89.6 mg) were added aqueous formaldehyde (37% solution, 3.70 mmol, 300 mg) and formic acid (13.0 mmol, 600 mg). The mixture was refluxed for 4 hours. After cooling to room temperature, the reaction mixture was diluted with water (15 mL), the pH was adjusted with aqueous sodium hydroxide (20%) to a value >12 and the reaction mixture was extracted with chloroform (3 × 15 mL). The combined organic phases were dried over sodium sulfate and the solvent was evaporated under reduced pressure. The pure product was obtained after column chromatography (chloroform/methanol = 10:1, 1% diethyl amine) as a yellowish solid (0.27 mmol, 70.4 mg, 71%).

Synthesis of the enantiomerically enriched compound (*S*)-10 from amino alcohol (*S*)-9

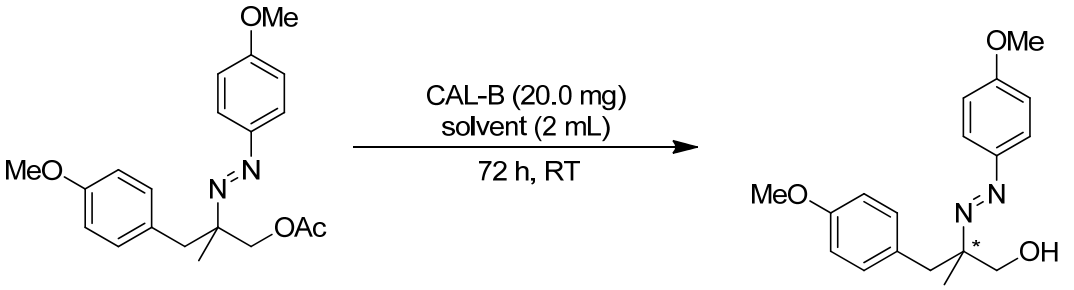
To amino alcohol (*S*)-**9** (61.5 µmol, 14.4 mg, >99% ee) were added aqueous formaldehyde (37% solution, 0.62 mmol, 50 mg) and formic acid (2.17 mmol, 100 mg). The mixture was refluxed for 4.5 hours. After cooling to room temperature, the reaction mixture was diluted with water (15 mL), the pH was adjusted with aqueous sodium hydroxide (20%) to a value >12 and reaction mixture was extracted with chloroform (4 × 15 mL). The combined organic phases were dried over sodium sulfate and the solvent was evaporated under reduced pressure. The pure product was obtained after column chromatography (chloroform/methanol = 10:1, 1% diethyl amine) as a colourless, slowly crystallizing oil (46.2 µmol, 12.1 mg, 75%, >99% ee).

R_f	0.30 (chloroform/methanol = 10:1, 1% diethyl amine)
^{1}H-NMR	(360 MHz, $CDCl_3$): δ = 0.90 (s, 3 H), 2.35 (s, 6 H), 2.64 (d, J = 12.9 Hz, 1 H), 2.77 (d, J = 12.9 Hz, 1 H), 3.23 (d, J = 11.0 Hz, 1 H), 3.29 (d, J = 11.0 Hz, 1 H), 7.06 (dd, J = 2.1 Hz, J = 8.2 Hz, 1 H), 7.30 (d, J = 2.1 Hz, 1 H), 7.34 (d, J = 8.2 Hz, 1 H).
HPLC	(Chiralpak® IC column; hexane/2-propanol = 99.5:0.5; 0.4 mL/min, 250 nm): t_R = 30.6 min, 31.7 min.
$[\alpha]^{20}_D$	+6.8 (c 0.8, EtOH) [Lit: $[\alpha]^{20}_D$ +6.3 (c 1, EtOH)][5]

The analytical data is in agreement with literature.[5]

3. Optimization and screening experiments for the enzymatic kinetic resolution

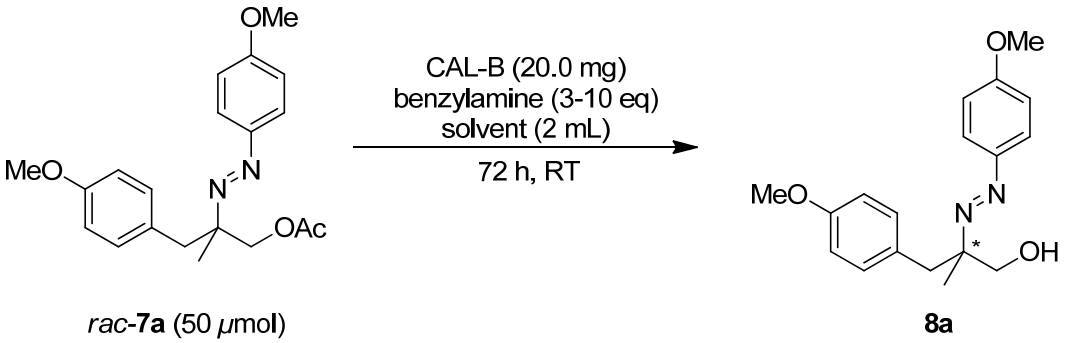
3.1 Solvent screening (Table 1)



rac-**7a** (50.0 μmol) **8a**

Rac-**7a** (0.05 mmol, 17.8 mg) was dissolved in 2 mL of the solvent given in Table 1 (see article). Lipase *Candida antarctica* B (CAL-B, formulation Novozym 435, 20.0 mg) was added, the reaction vessel was stoppered and the mixture stirred at room temperature for 3 days. The reaction mixture was filtered and the solvent evaporated under reduced pressure. The conversion and enantiomeric excess of the product **8a** were determined by chiral HPLC-chromatography.

3.2 Solvent screening with addition of benzylamine (Table 1)



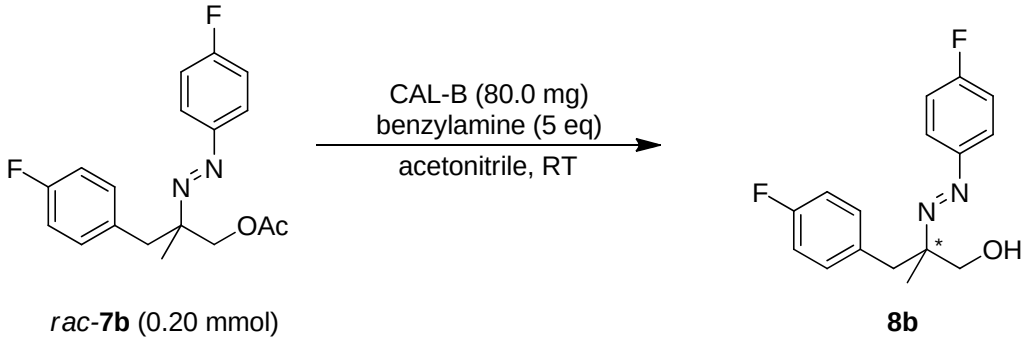
rac-**7a** (50 μmol) **8a**

Rac-**7a** (0.05 mmol, 17.8 mg) was dissolved in 2 mL of the solvent given in Table 1 (see article). Benzylamine (3-10 eq) and lipase *Candida antarctica* B (CAL-B, formulation Novozym 435, 20.0 mg) were added, the reaction vessel was stoppered and the mixture stirred at room temperature for 3 days. The reaction mixture was filtered and the solvent evaporated under reduced pressure. The conversion and enantiomeric excess of the product **8a** were determined by chiral HPLC-chromatography.

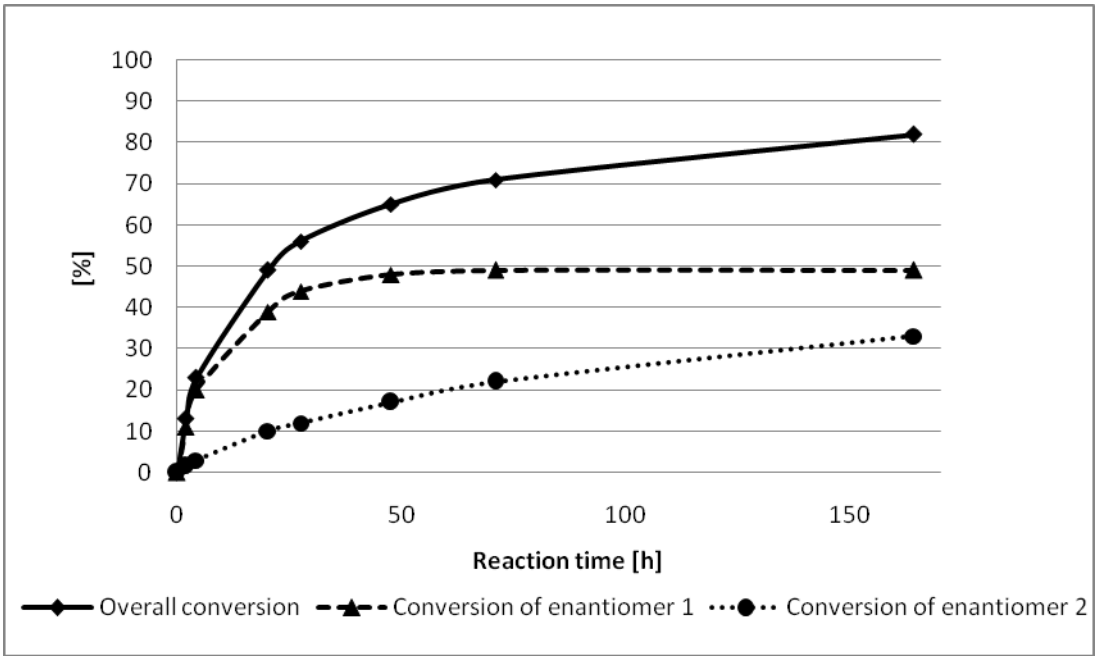
3.3 Reaction monitoring by HPLC for azo acetate 7b

Rac-**7b** (0.20 mmol, 66.5 mg) was dissolved in acetonitrile (8 mL). Benzylamine (1.00 mmol, 5 eq, 107 mg) and lipase *Candida antarctica* B (CAL-B, formulation Novozym 435, 80.0 mg) were added, the reaction vessel was stoppered and the mixture stirred at room temperature for 7 days. Aliquots of the reaction mixture were drawn at intervals, filtered and the solvent evaporated under reduced pressure. Conversion and enantiomeric excess of the product **8b** were determined by chiral HPLC.

Figure 1. Reaction monitoring by HPLC for **7b**.



rac-**7b** (0.20 mmol) **8b**



3.4 Substrate screening I (Table 2)

General procedure for compounds 7b-i: To a solution of azo acetate *rac*-**7** (0.30 mmol) in acetonitrile (12 mL) was added benzylamine (1.50 mmol, 5 eq, 161 mg) and lipase *Candida antarctica* B (CAL-B, formulation Novozym 435, 120 mg). The reaction vessel was sealed, and stirring was continued for 3 days. The reaction mixture was filtered and the solvent evaporated under reduced pressure. The crude product was analyzed by HPLC to determine conversion and enantiomeric excess of the product **8**. For determination of the enantiomeric excess of remaining azo acetate **7**, the acetate was first separated by column chromatography on silica gel (hexane/ethyl acetate = 4:1) and then converted to its corresponding alcohol **8** (see below).

Procedure for compound 7j: To a solution of azo acetate *rac*-**7j** (0.06 mmol, 23.2 mg) in acetonitrile (2.4 mL) was added benzylamine (0.30 mmol, 5 eq, 32.2 mg) and lipase *Candida antarctica* B (CAL-B, formulation Novozym 435, 24 mg). The reaction vessel was sealed, and stirring was continued for 3 days. The reaction mixture was filtered and the solvent evaporated under reduced pressure. The crude product was analyzed by HPLC to determine conversion and the enantiomeric excess of the remaining substrate **7j** and the product **8j**.

Conversion of azo acetate 7b to azo alcohol 8b: To azo acetate **7b** (0.07 mmol, 23.8 mg) were added methanol (2 mL), water (2 mL) and methanolic potassium hydroxide (3 M, 2 mL). The resulting mixture was stirred at room temperature for 2 hours, then diluted with water (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic phases were washed with brine (1 × 15 mL) and dried over sodium sulfate. The solvent was evaporated yielding a crude yellow oil containing the alcohol **8b**, which was then analyzed by chiral HPLC.

Conversion of azo acetates 7c-i to azo alcohols 8c-i: To the acetates **7c-i** (0.03-0.07 mmol) were added methanol (1 mL), water (0.5 mL) and potassium carbonate (0.14 mmol, 20.0 mg). The resulting mixture was stirred at room temperature for 1 hour, then diluted with water (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic phases were washed with brine (1 × 15 mL) and dried over sodium sulfate. The solvent was evaporated yielding a crude yellow oil containing the alcohol **8c-i**, which was then analyzed by chiral HPLC.

3.5 Substrate screening II (Table 3)

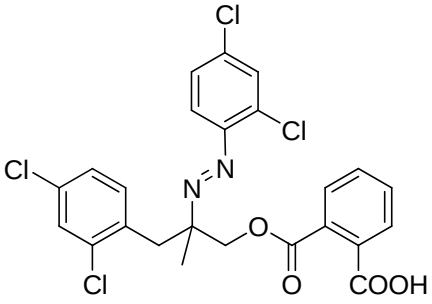
General procedure for compounds 7c-d, k-p: To a solution of acetate *rac*-**7** (0.20 mmol) in acetonitrile (8 mL) was added benzylamine (1.00 mmol, 5 eq, 107 mg) and lipase *Candida antarctica* B (CAL-B, formulation Novozym 435, 80.0 mg). The reaction vessel was sealed and the mixture stirred for several hours. Aliquots of the reaction mixture were drawn at various intervals, filtered and the solvent evaporated under reduced pressure. Conversion of the product **8** was determined by HPLC.

Determination of the enantiomeric excess of compounds 7c-d, k-n, and 8c-d, k-n: Enantiomeric excess of **8c-d**, **k-n** was determined by chiral HPLC. For determination of the enantiomeric excess of remaining azo acetates **7c-d, k-n**, the aliquots drawn from the reaction mixture were subjected to small scale column chromatography on silica gel (hexane/ethyl

acetate = 8:1) and the isolated acetate **7** saponified by addition of 0.3 mL of a mixture of MeOH (9 mL), water (1 mL) and sodium carbonate (1.89 mmol, 200 mg). After standing for 2 hours, the reaction mixture was diluted with water (2 mL) and extracted with diethyl ether (2 × 2 mL). The solvent was evaporated and the obtained alcohol **8** was analyzed by chiral HPLC.

Determination of the enantiomeric excess of compound 7o: For determination of the enantiomeric excess of azo acetate **7o**, the aliquots drawn from the reaction mixture were separated by small scale column chromatography on silica gel (hexane/ethyl acetate = 8:1). Acetate **7o** was saponified by addition of 0.3 mL of a mixture of MeOH (9 mL), water (1 mL) and sodium carbonate (1.89 mmol, 200 mg). After standing for 2 hours, the reaction mixture was diluted with water (2 mL), extracted with diethyl ether (2 × 2 mL) and the solvent evaporated. The obtained crude alcohol **8o** was then dissolved in dichloromethane (1 mL) and converted to its phthalic acid monoester by addition of triethylamine (0.20 mmol, 20.0 mg) and phthalic anhydride (0.14 mmol, 20.0 mg). The reaction mixture was stirred for 2 hours at room temperature, then diluted with water (1 ml) and extracted with diethyl ether (2 × 1 mL). The solvent was evaporated and the crude reaction mixture containing the phthalic acid monoester was analyzed by chiral HPLC.

Phthalic acid mono-[3-(2,4-dichlorophenyl)-2-(2,4-dichlorophenylazo)-2-methylpropyl]ester



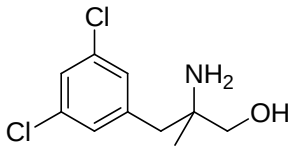
$C_{24}H_{18}Cl_4N_2O_4$
M = 540.22 g/mol

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.38 (s, 3 H), 3.36 (d, J = 13.9 Hz, 1 H), 3.45 (d, J = 13.9 Hz, 1 H), 4.67 (d, J = 11.3 Hz, 1 H), 4.71 (d, J = 11.3 Hz, 1 H), 7.08-7.12 (m, 2 H), 7.25 (dd, J = 2.2 Hz, J = 8.6 Hz, 1 H), 7.30-7.34 (m, 2 H), 7.48 (d, J = 2.1 Hz, 1 H), 7.55-7.60 (m, 2 H), 7.61-7.65 (m, 1 H), 7.83-7.86 (m, 1 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 95:5, 0.1% trifluoroacetic acid; 0.6 mL/min, 280 nm): t_R = 20.2 min, 21.0 min.

Determination of the enantiomeric excess of 7p and 8p: For determination of the enantiomeric excess of azo acetate **7p** and azo alcohol **8p**, the reaction mixture was filtered after 12.5 hours, the solvent was evaporated, and the conversion was determined by HPLC. Azo acetate **7p** and azo alcohol **8p** were separated by column chromatography on silica gel (hexane/ethyl acetate = 4:1). **7p** (0.06 mmol, 26.5 mg) and **8p** (0.11 mmol, 43.3 mg) were each dissolved in methanol (2 ml) and zinc dust (1.74/3.50 mmol, 114/229 mg) and hydrochloric acid (6 M, 1/2 mL) were added. The two resulting mixtures were heated to reflux for 17 hours, then allowed to cool to room temperature and diluted with water (10 mL). The pH was adjusted with aqueous sodium hydroxide (20%) to a value >12 and the reaction mixtures were extracted with dichloromethane (3 × 10 mL). The combined organic phases were dried over sodium sulfate and the solvent was evaporated under reduced pressure. The amino alcohols resulting from the reduction were purified by column chromatography (chloroform/methanol = 10:1, 1% diethyl amine) to give colorless, slowly crystallizing oils (0.04/0.05 mmol, 9.4/12.5 mg, 67/45%). The enantiomeric excess was determined by chiral HPLC.

2-Amino-3-(3,5-dichlorophenyl)-2-methylpropan-1-ol



$C_{10}H_{13}Cl_2NO$
M = 234.12 g/mol

^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.05 (s, 3 H), 2.11 (br, 3 H), 2.60-2.76 (m, 2 H), 3.21–3.49 (m, 2 H), 7.11 (d, J = 1.9 Hz, 2 H), 7.25-7.27 (m, 1 H).

HPLC (Chiralpak® IC column; hexane/2-propanol = 95:5, 0.1% diethyl amine; 0.8 mL/min, 230 nm): t_R = 13.7 min, 15.4 min.

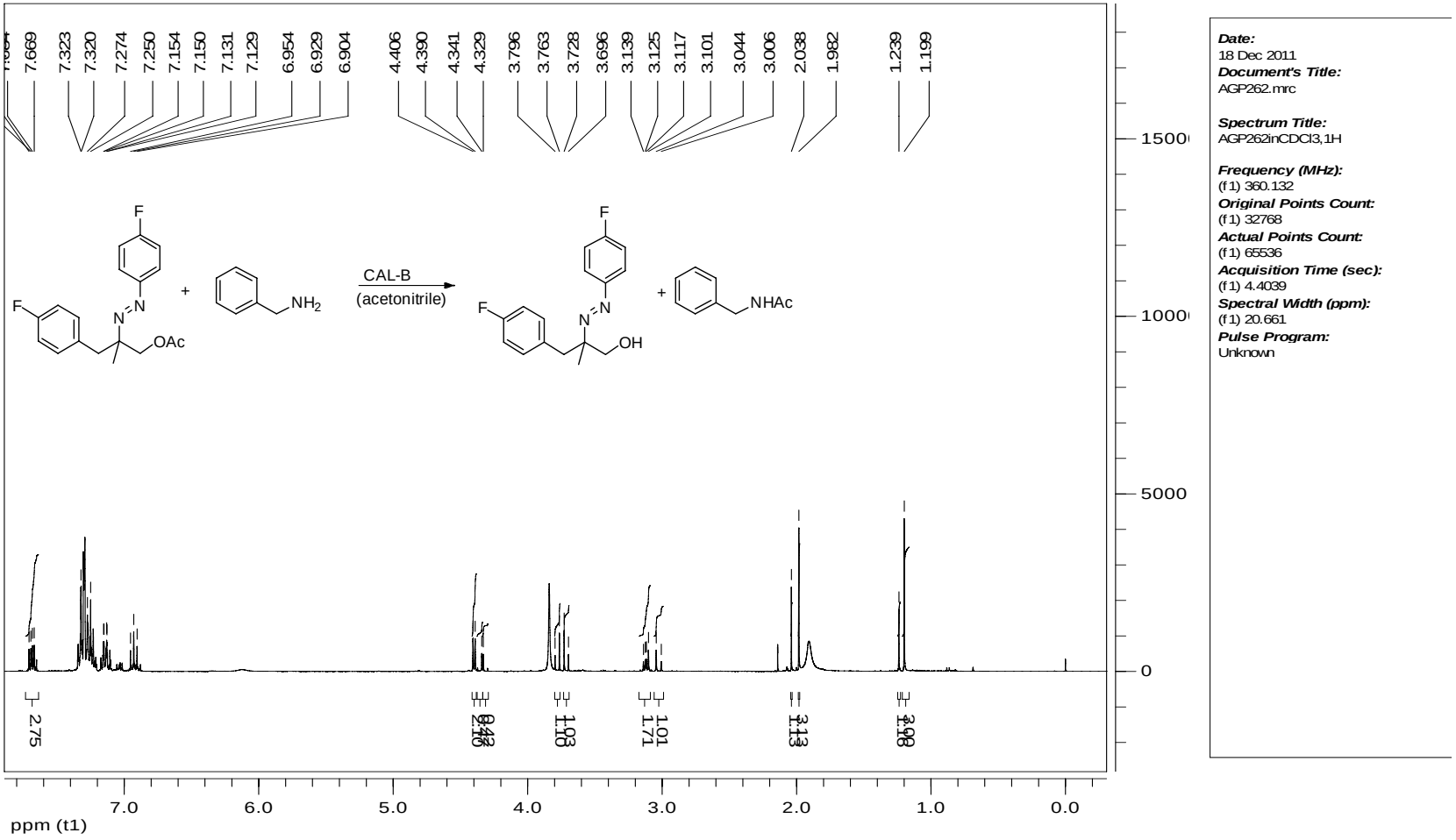
3.6 Large-Scale enzymatic kinetic resolution of azo acetate 7c

Azo acetate *rac*-**7c** (5.00 mmol, 2.17 g) and benzylamine (25.0 mmol, 5 eq, 2.68 g) were dissolved in acetonitrile (200 mL), and lipase *Candida antarctica* B (CAL-B, formulation Novozym 435, 2.0 g) was added. The reaction course was followed by HPLC until a probe taken from the reaction mixture (19.5 h) showed a conversion of 60%. The reaction mixture was filtered and the solvent evaporated under reduced pressure. Column chromatography (hexane/ethyl acetate = 8:1→ hexane/ethyl acetate = 2:1) gave the acetate (*S*)-**7c** (1.92 mmol, 835 mg, 38%, 97% ee) and the alcohol (*R*)-**8c** (2.86 mmol, 1.12 g, 57%, 59% ee) as yellow oils. The enantiomeric excess of the alcohol **8c** was determined by chiral HPLC. For determination of the enantiomeric excess of azo acetate **7c**, 5 mg (0.01 mmol) of the compound were treated according to the procedure described in section 3.5 (page 42).

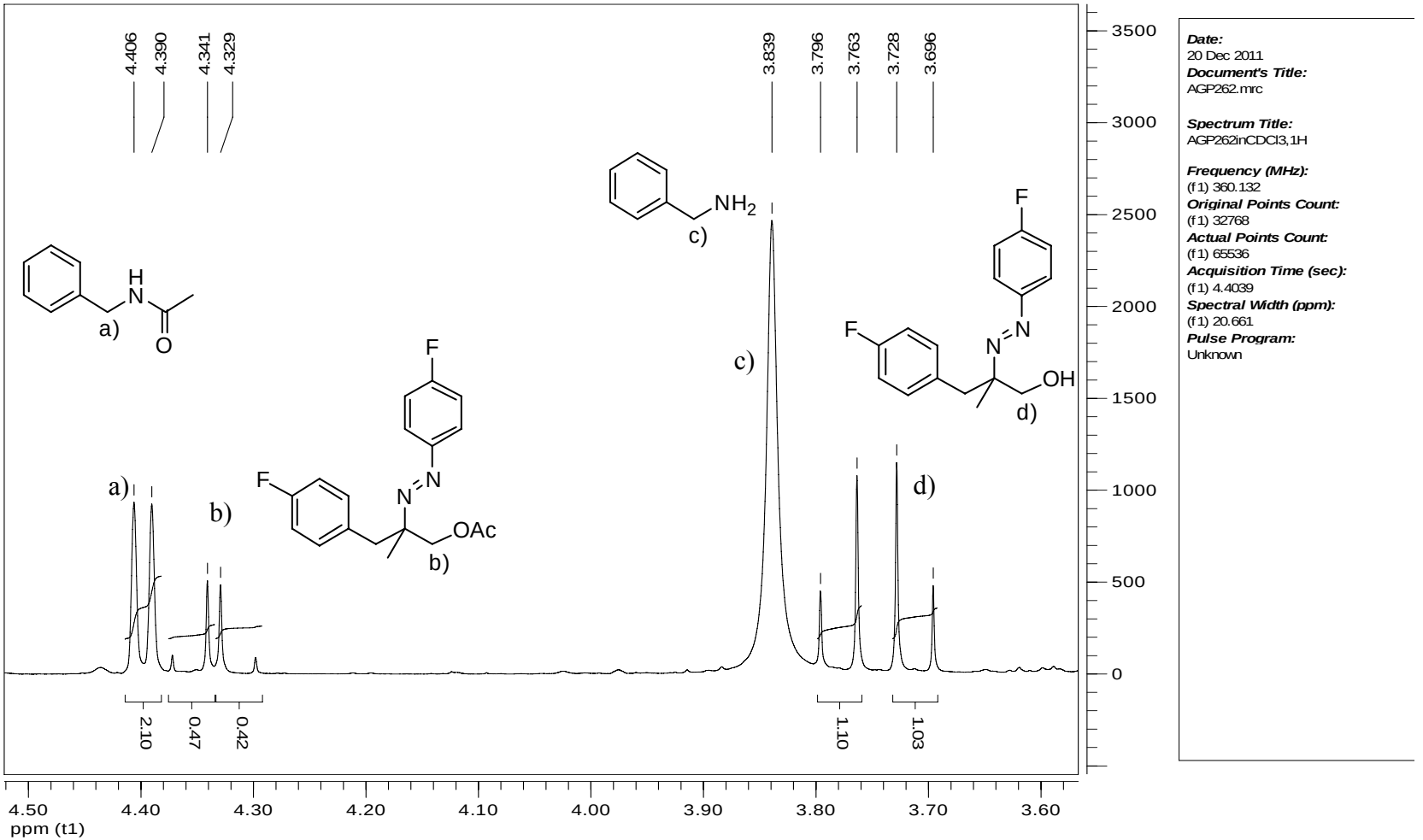
4. NMR-Spectra

4.1 Formation of N-benzylacetamide during enzymatic aminolysis

^{1}H-NMR spectrum of enzymatic kinetic resolution of **7b** as described in 3.4 (page 30) after 3 days



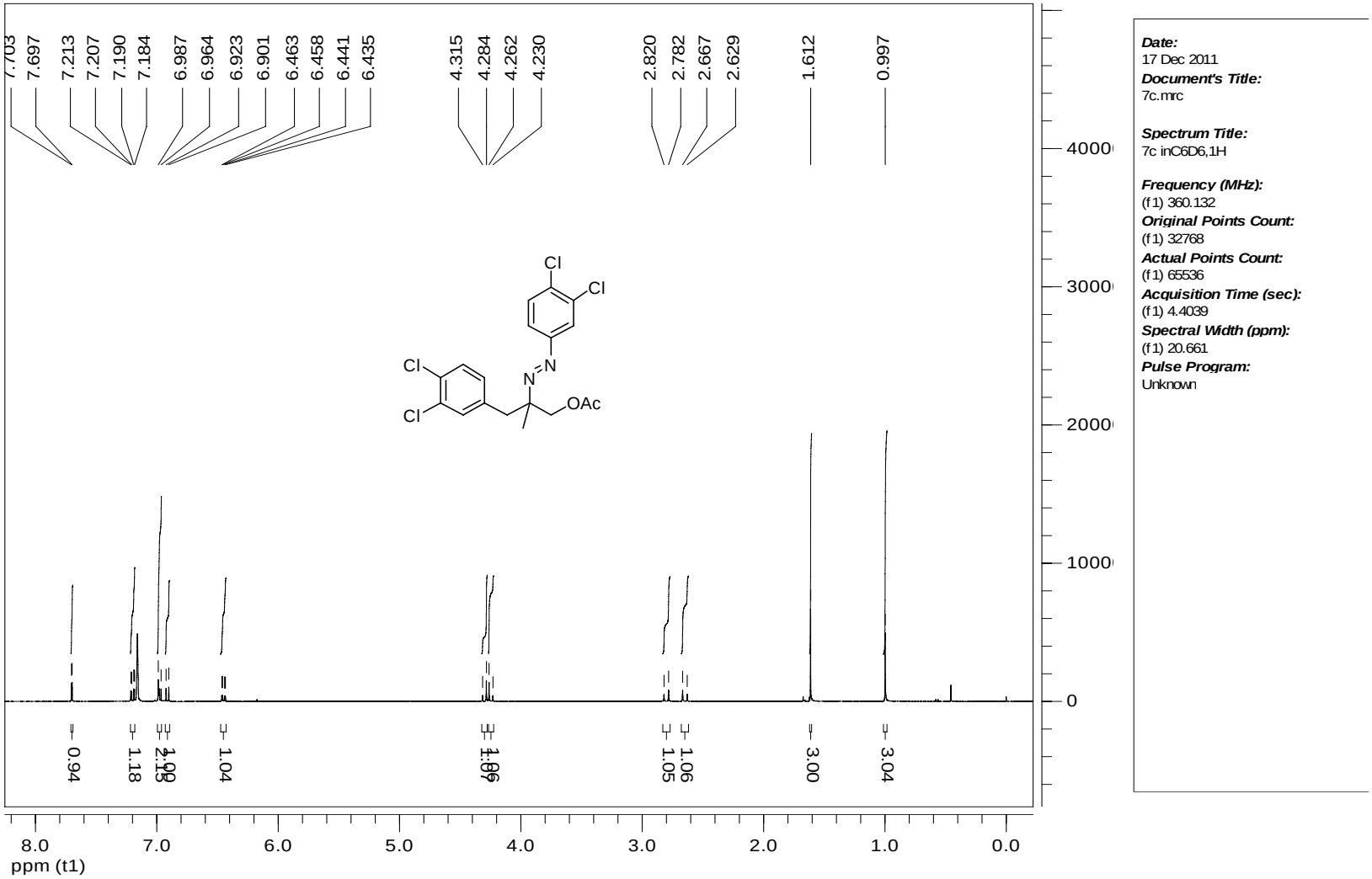
^{1}H-NMR spectrum of enzymatic kinetic resolution of **7b** as described in 3.4 (page 30) after 3 days (magnification of 3.60-4.50 ppm)



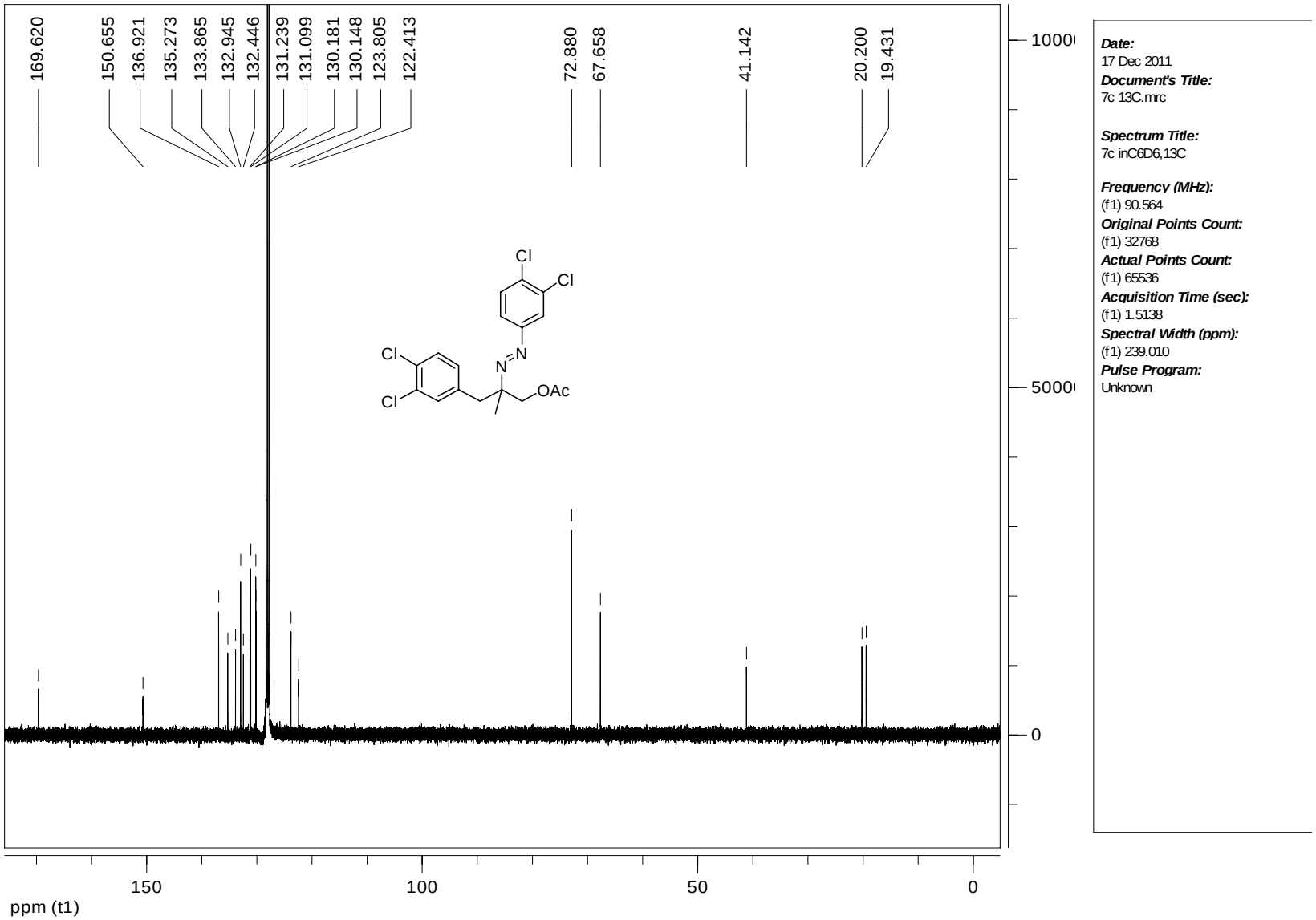
Signals at 3.71 (d, J = 11.7 Hz, 1 H) and 3.78 (d, J = 11.7 Hz, 1 H) are related to alcohol **8b**, signal at 4.40 (d, J = 5.7 Hz, 2 H) to *N*-benzylacetamide, signals at 4.31 (d, J = 11.2 Hz, 1 H) and 4.36 (d, J = 11.2 Hz, 1 H) are related to remaining acetate **7b**. Signal at 3.84 (s, 2 H) caused by excess benzylamine.

4.2 Compounds

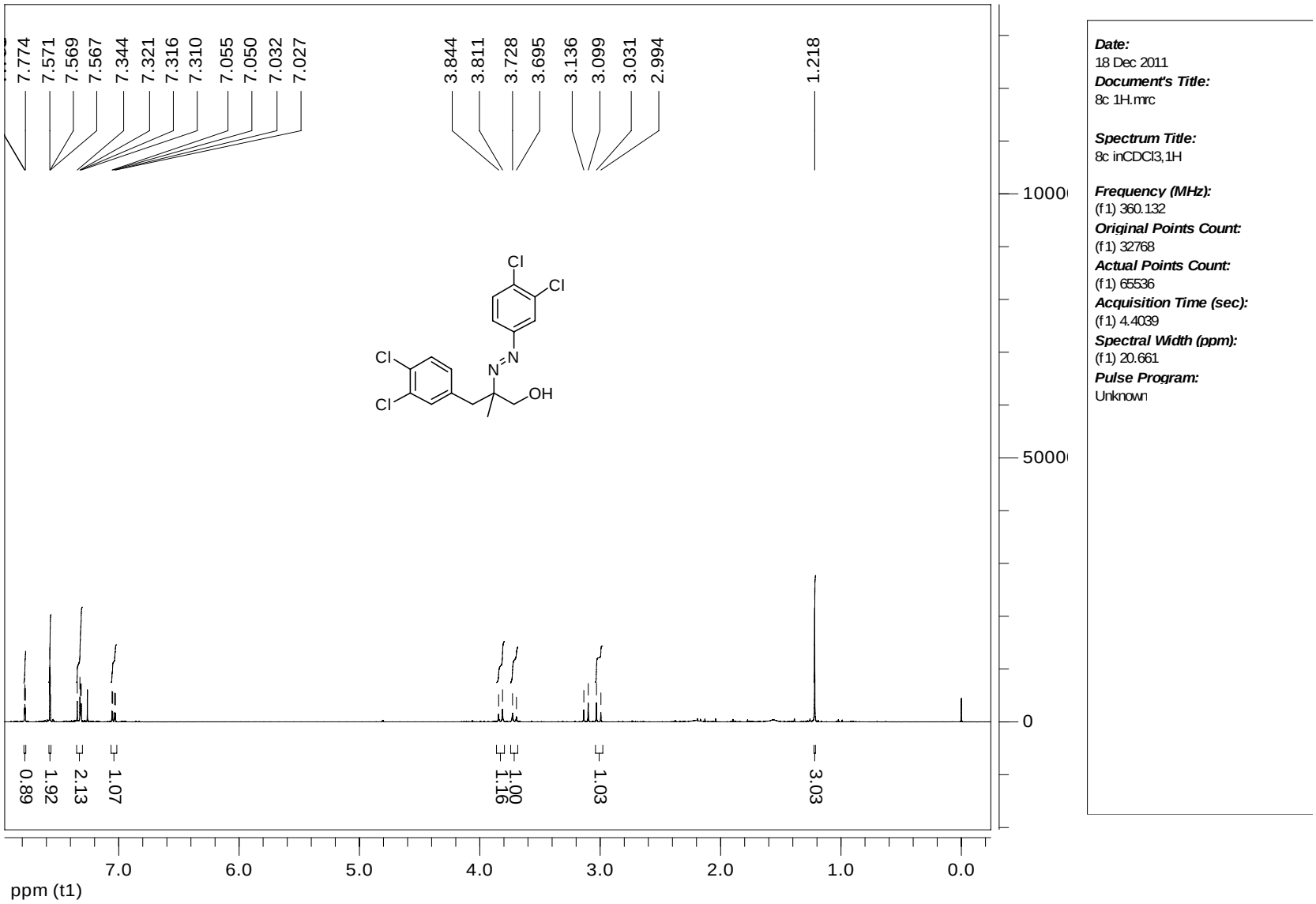
^{1}H-Spectrum of **7c**



^{13}C-Spectrum of **7c**



^{1}H-Spectrum of **8c**



Date:
18 Dec 2011
Document's Title:
8c 1H.mrc

Spectrum Title:
8c inCDCl3,1H

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Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
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Spectral Width (ppm):
(f1) 20.661
Pulse Program:
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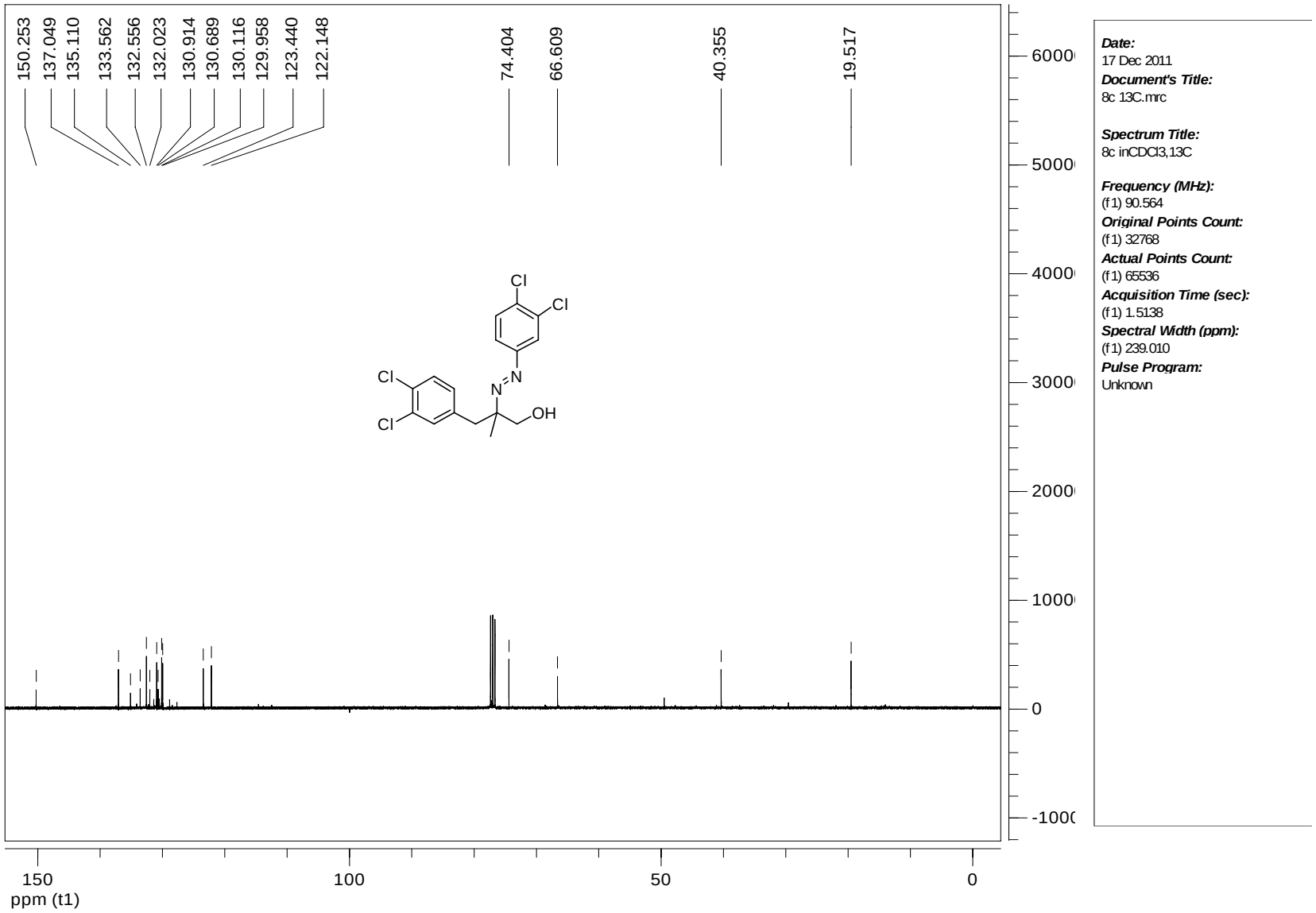
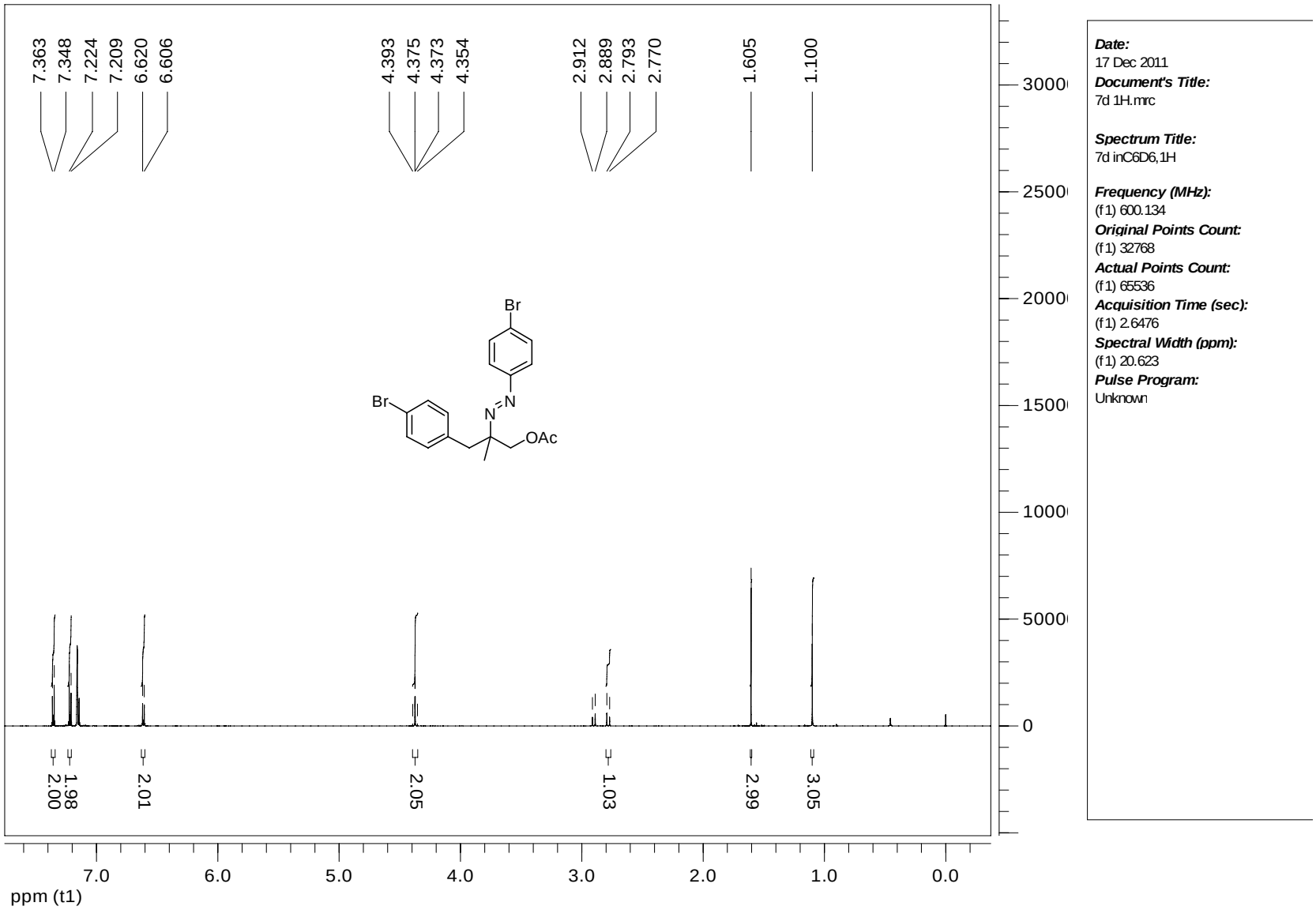


^{1}H-Spectrum of **7d**



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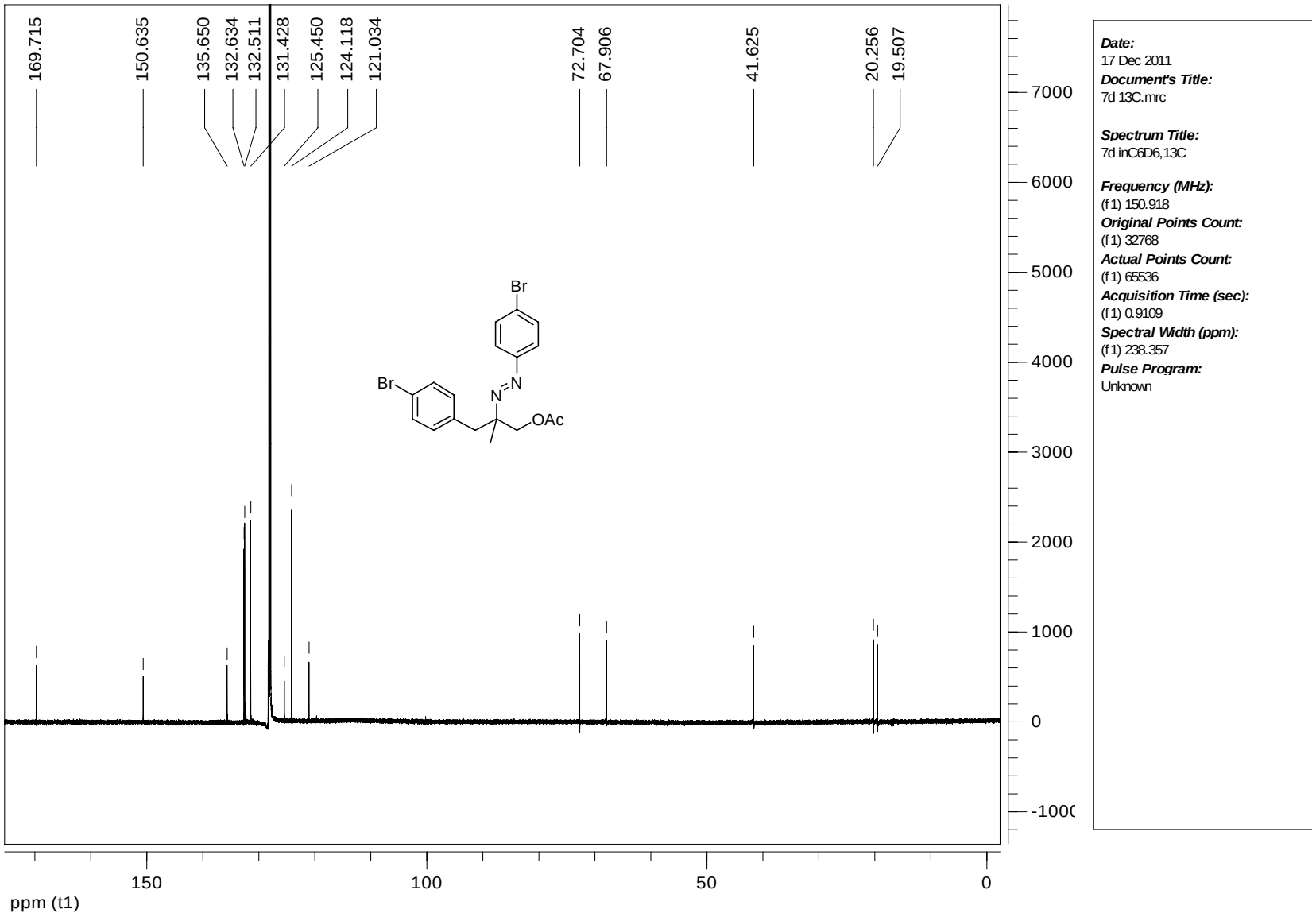

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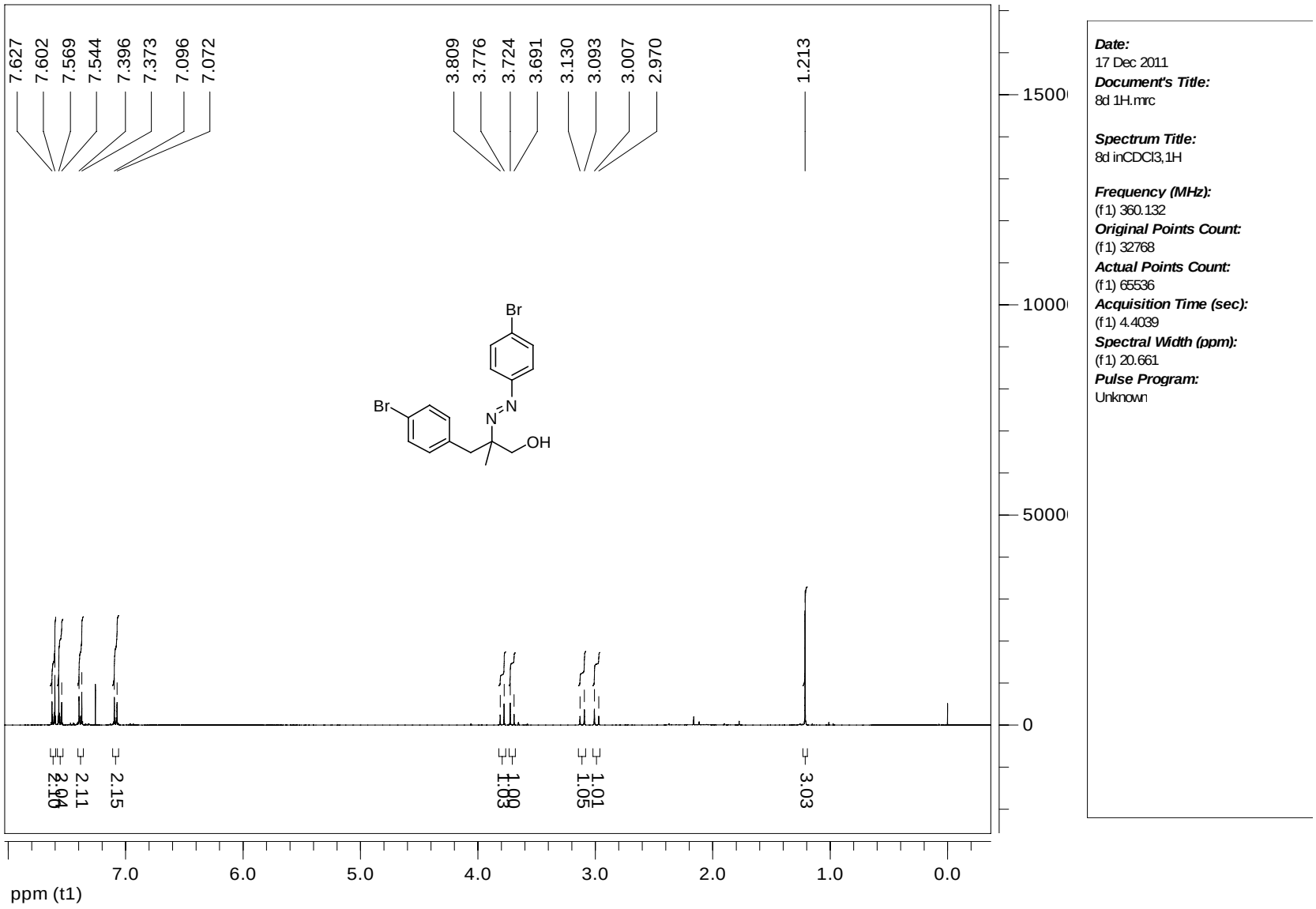

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17 Dec 2011
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Spectrum Title:
8d inCDCl3,1H

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Spectral Width (ppm):
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Pulse Program:
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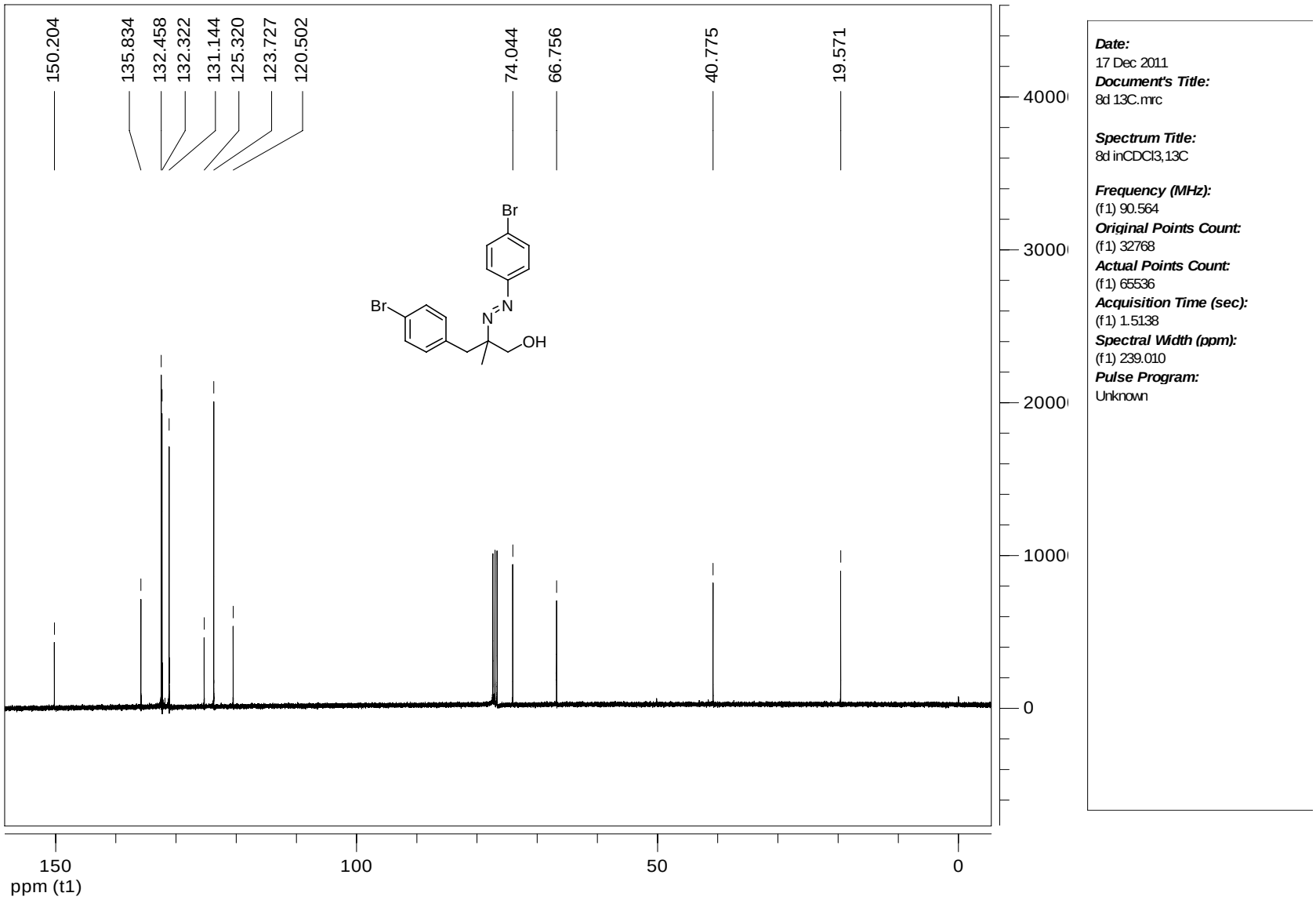
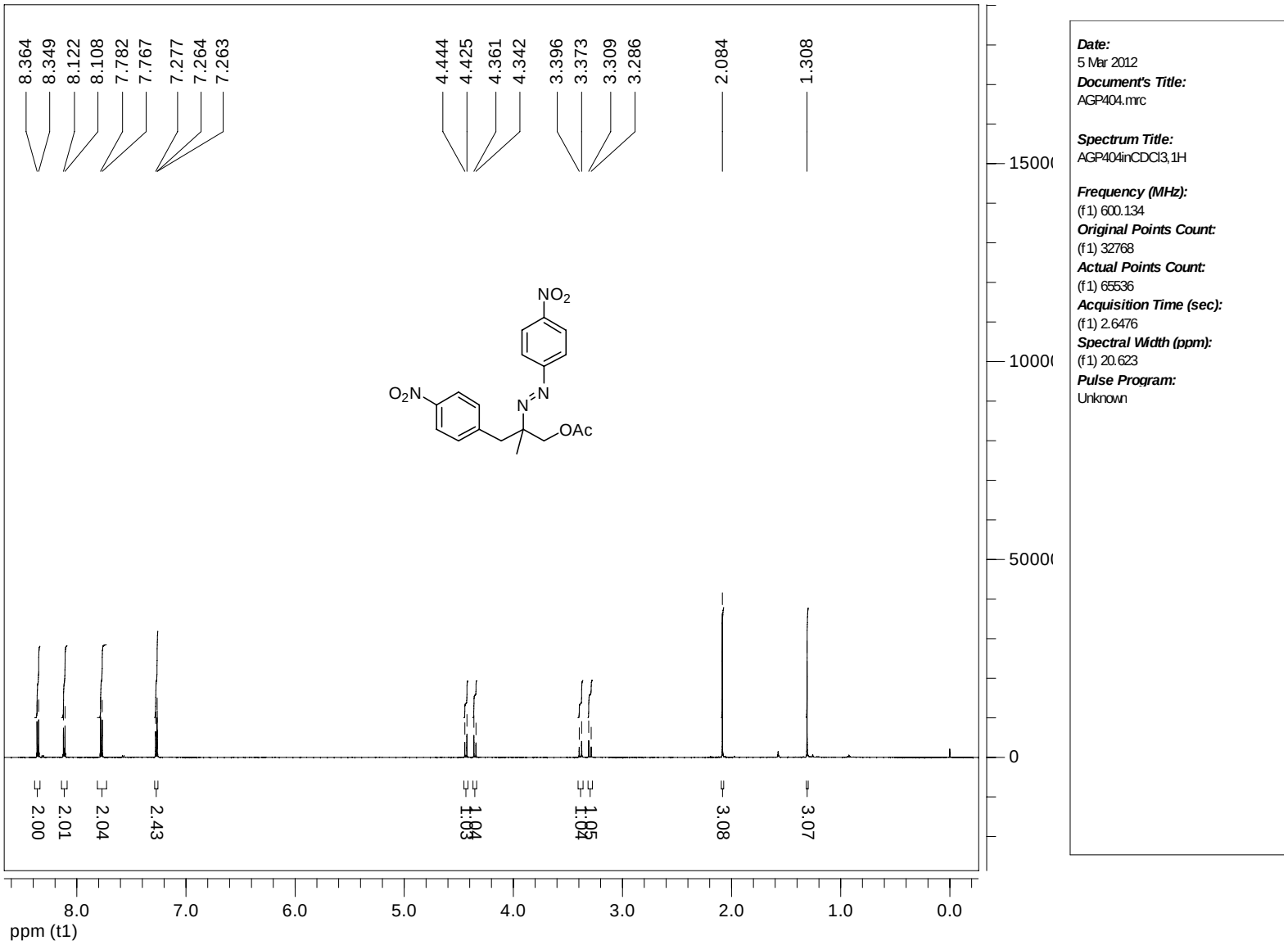


^{1}H-Spectrum of **7j**



Date:
5 Mar 2012
Document's Title:
AGP404.mrc

Spectrum Title:
AGP404inCDCl3,1H

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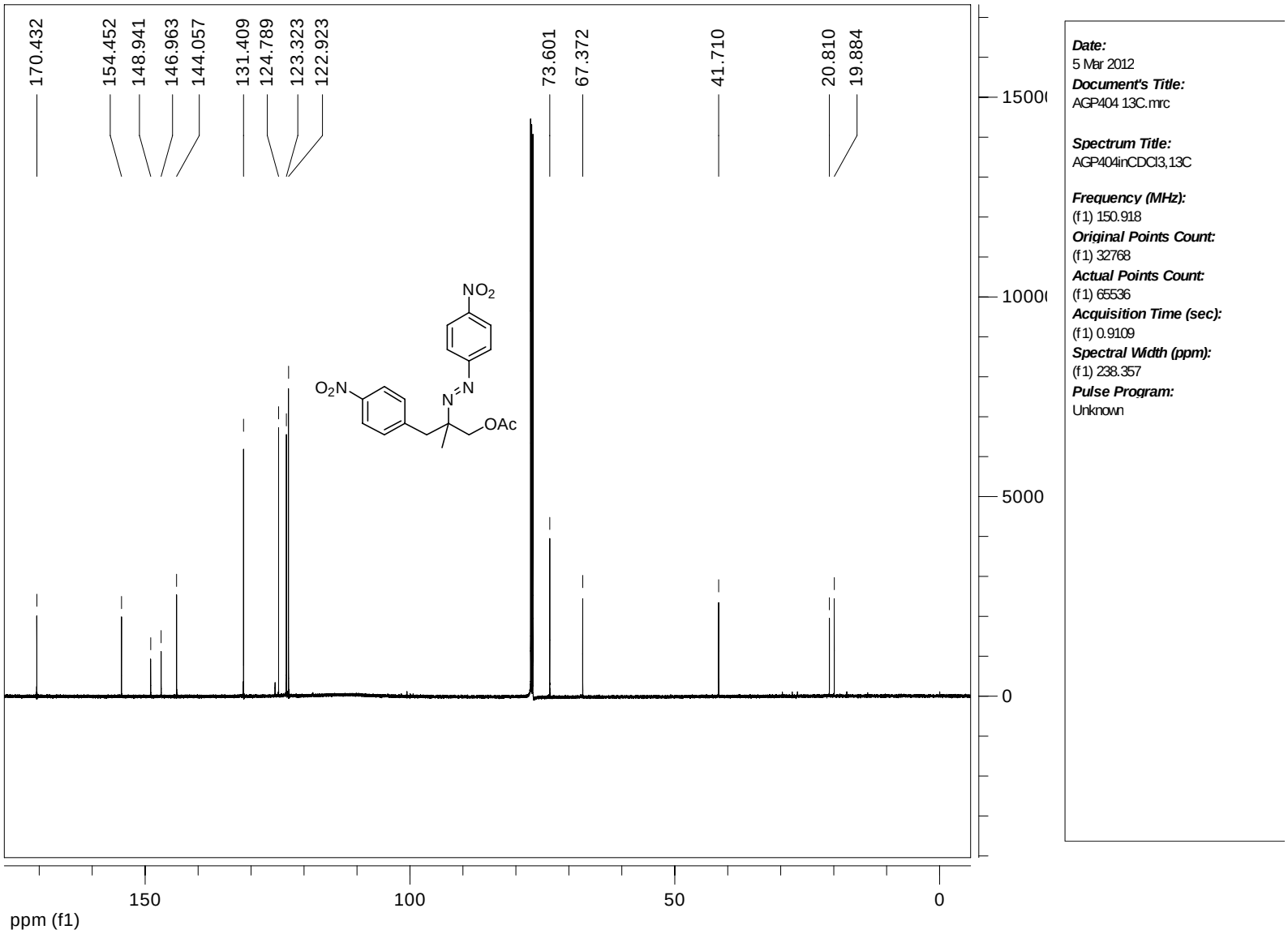

Date:
5 Mar 2012
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AGP404 13C.mrc

Spectrum Title:
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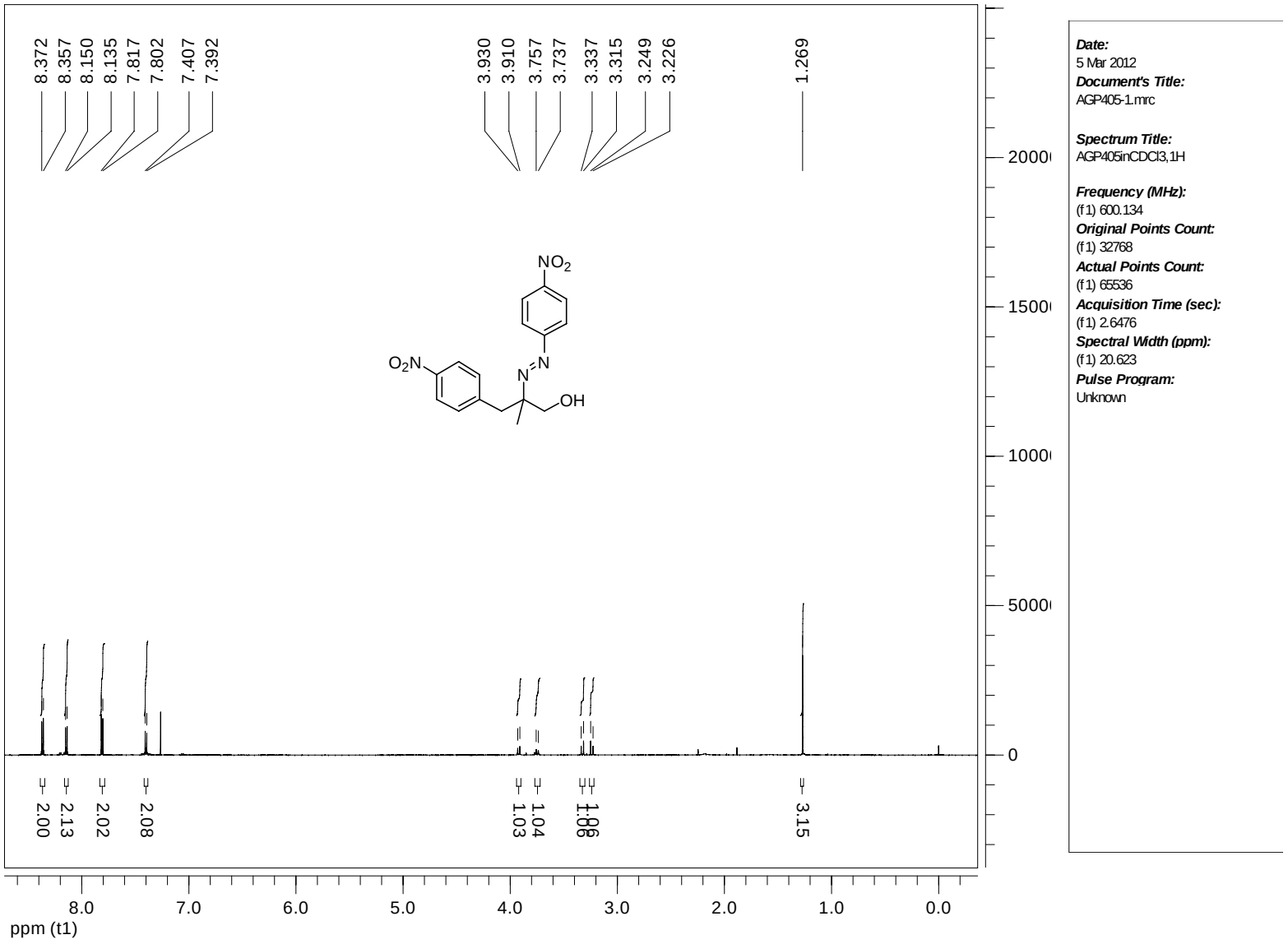
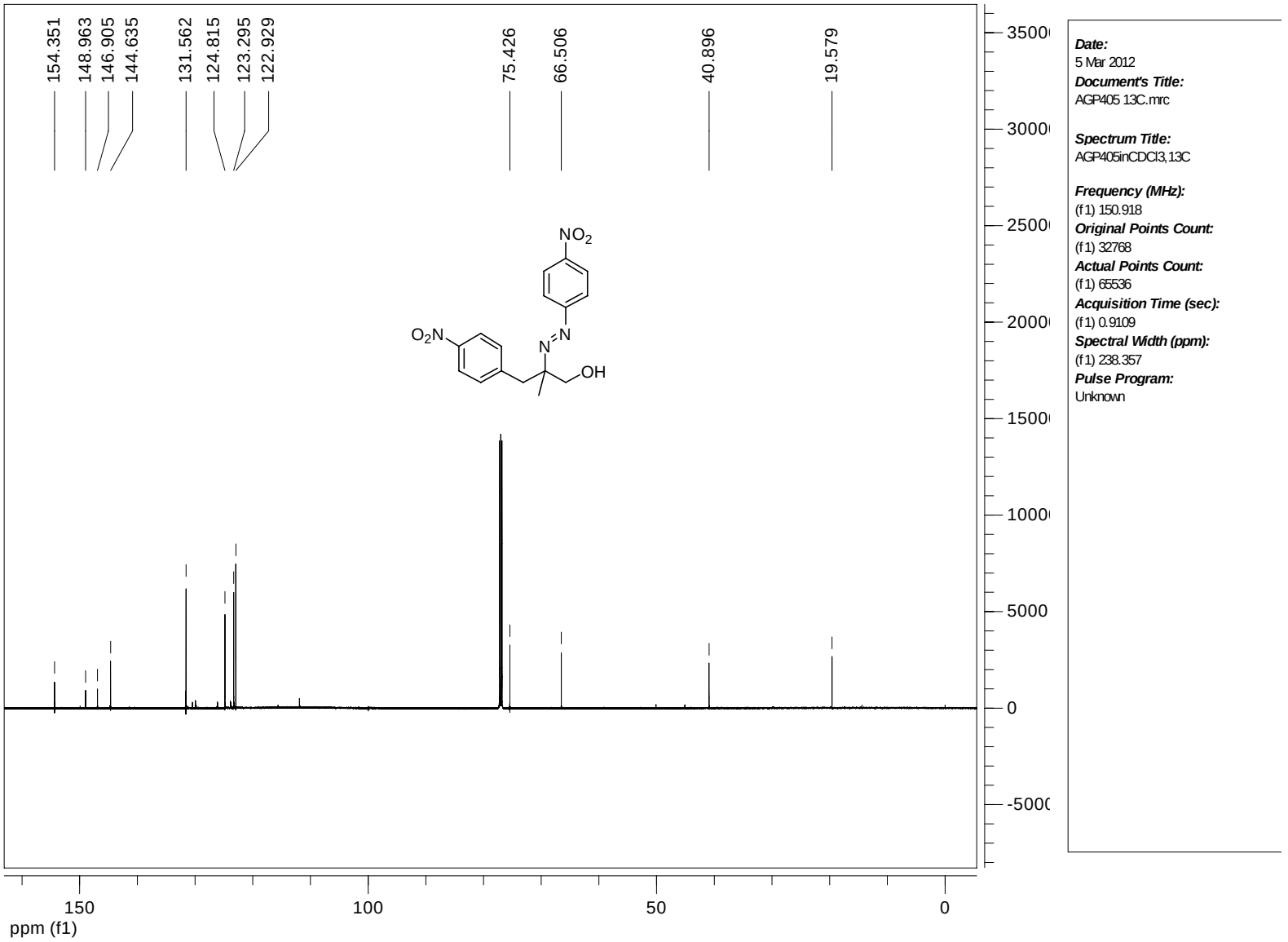
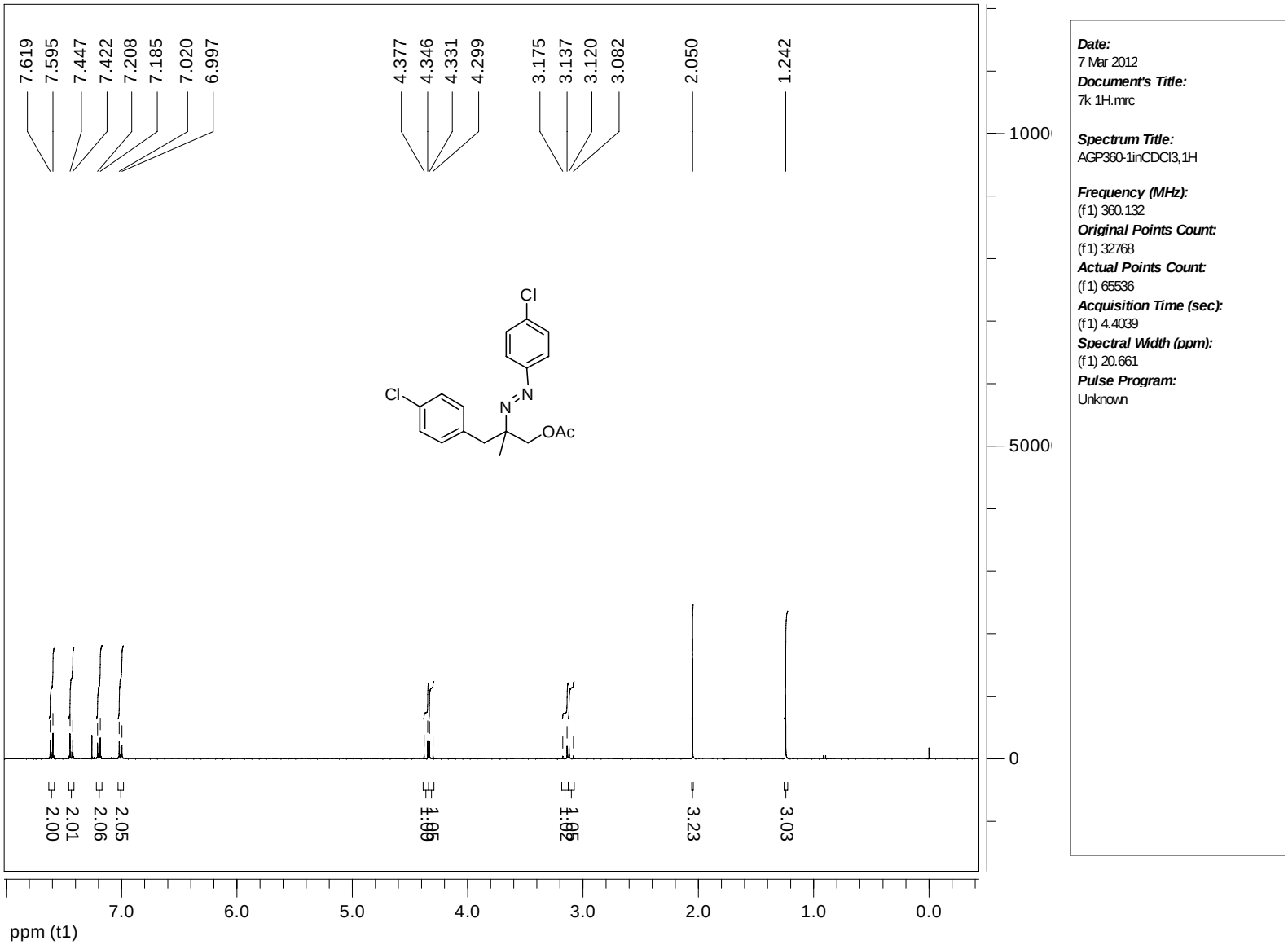


^{13}C-Spectrum of **8j**



^{1}H-Spectrum of **7k**



Date:
7 Mar 2012
Document's Title:
7k 1H.mrc

Spectrum Title:
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Spectral Width (ppm):
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Pulse Program:
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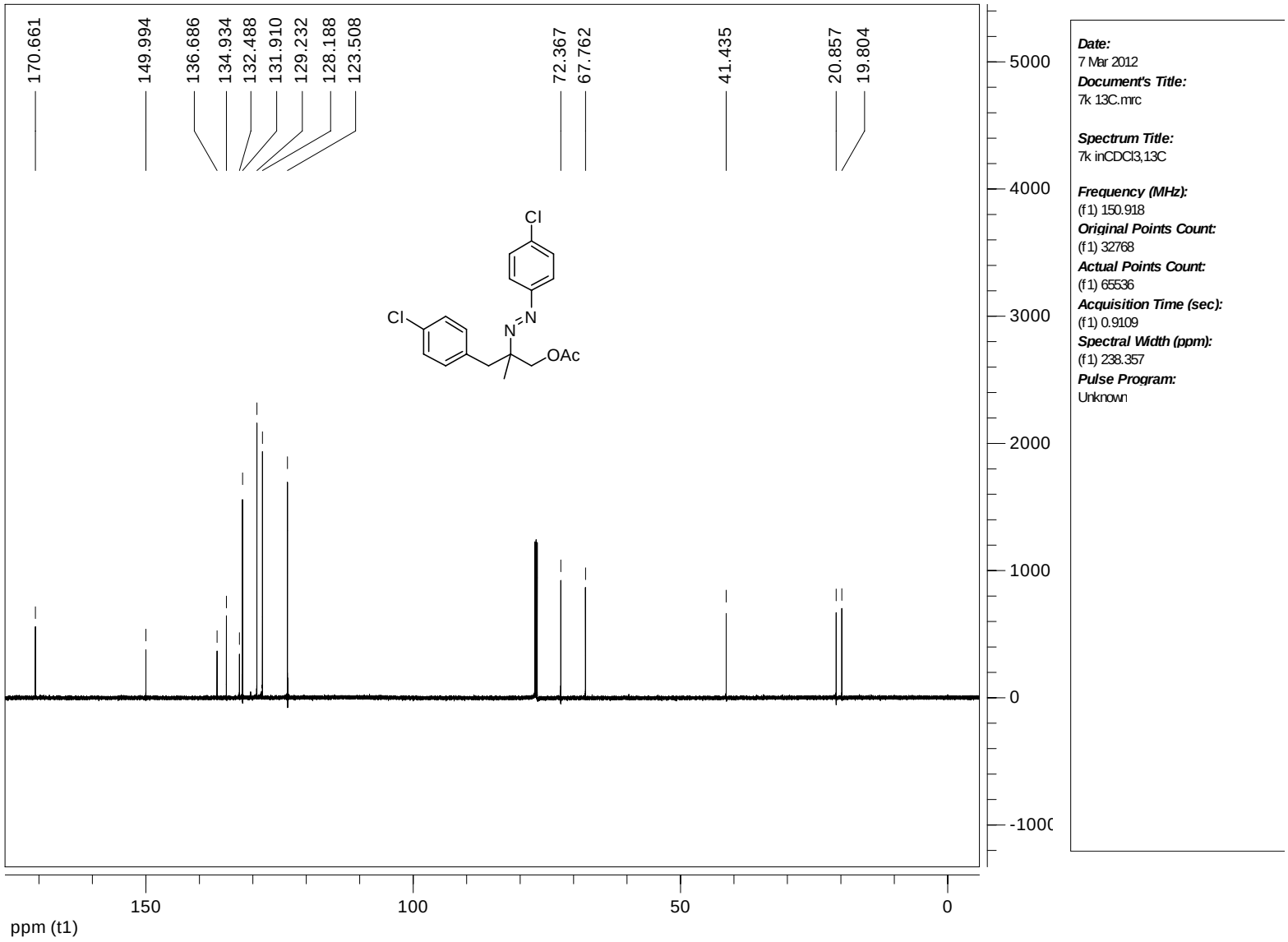
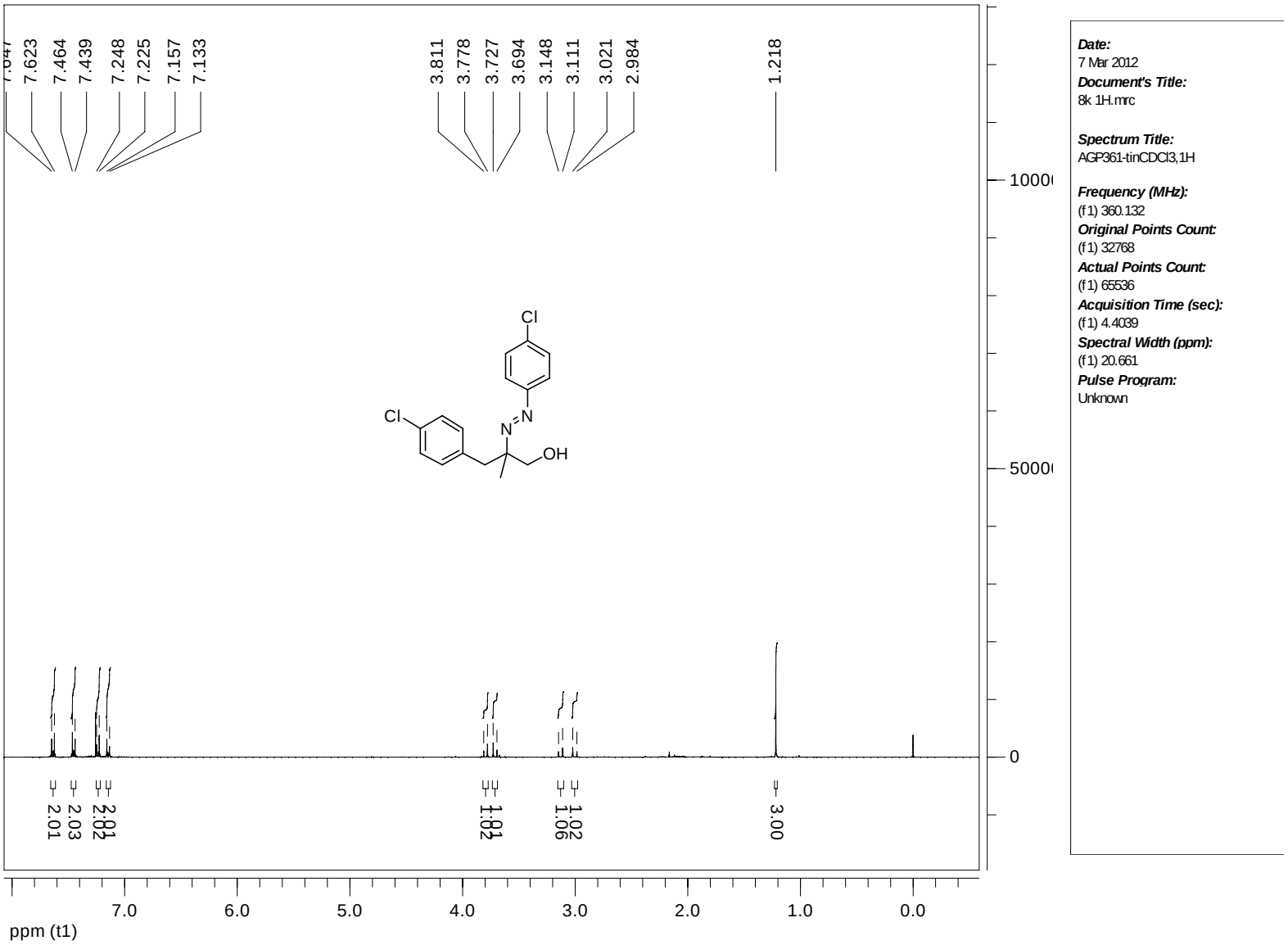


^{1}H-Spectrum of **8k**



Date:
7 Mar 2012
Document's Title:
8k 1H.mrc

Spectrum Title:
AGP361-tinCDCl3,1H

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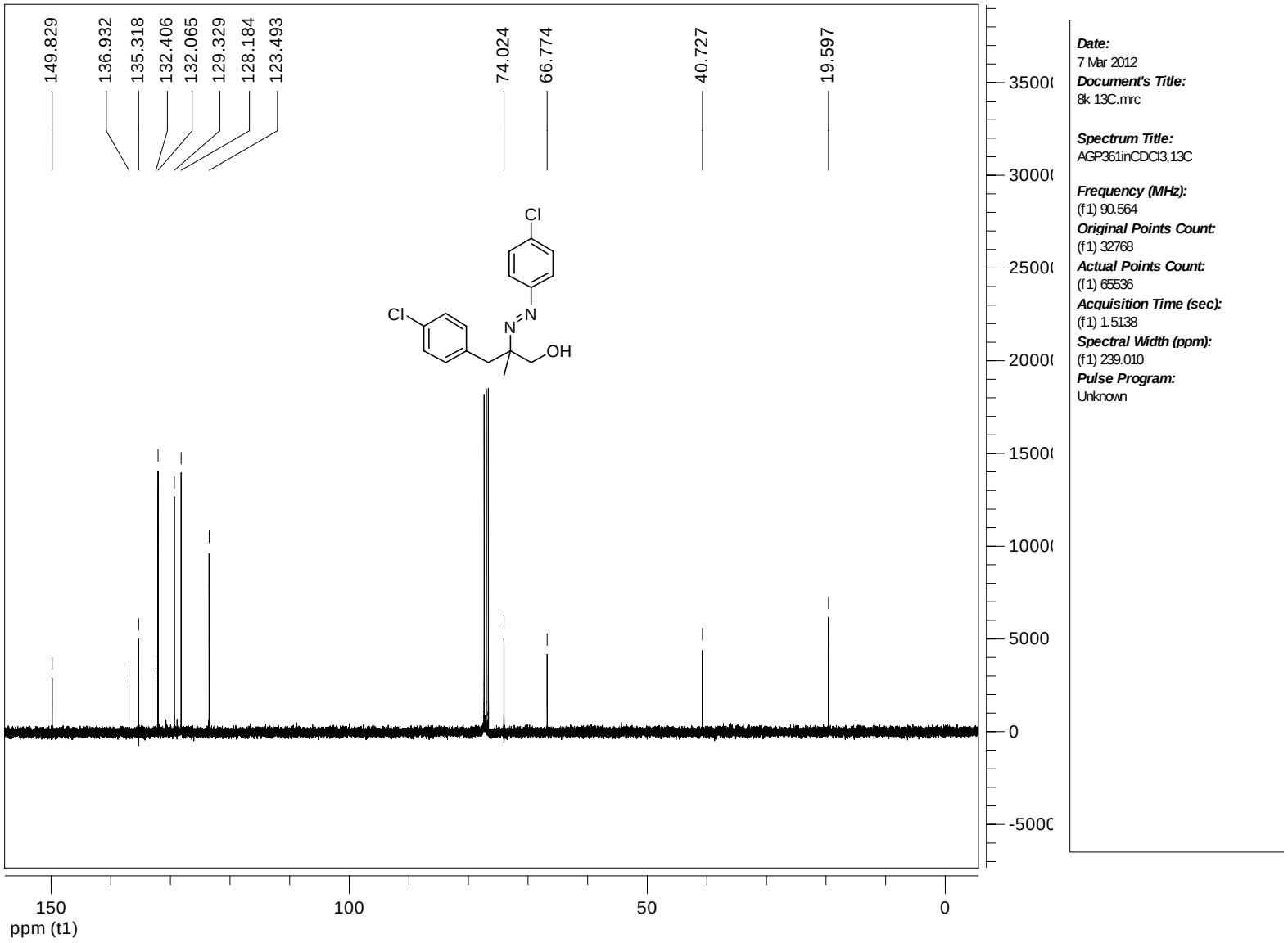
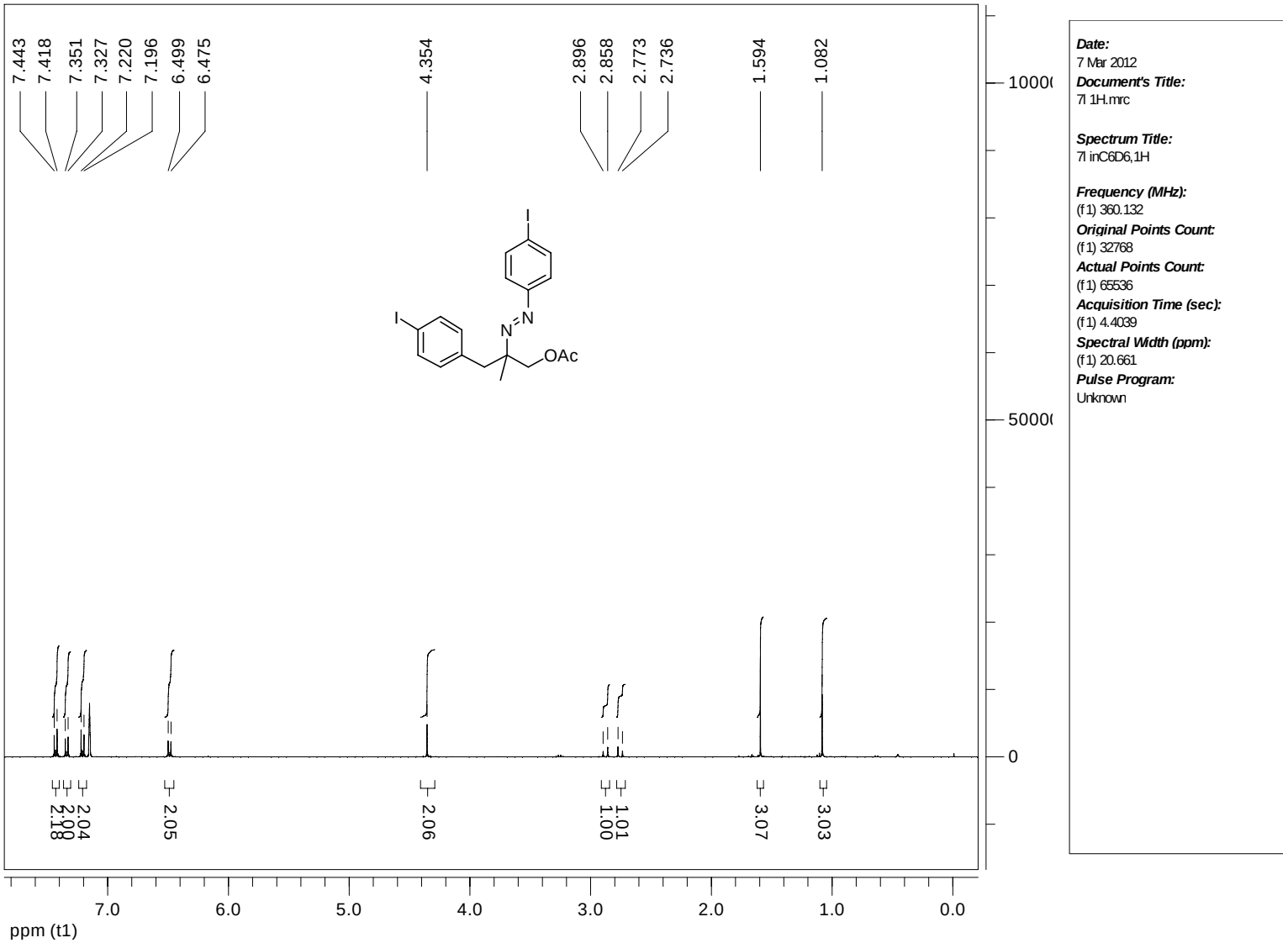
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 4.4039
Spectral Width (ppm):
(f1) 20.661
Pulse Program:
Unknown

^{13}C-Spectrum of **8k**



^{1}H-Spectrum of **7l**

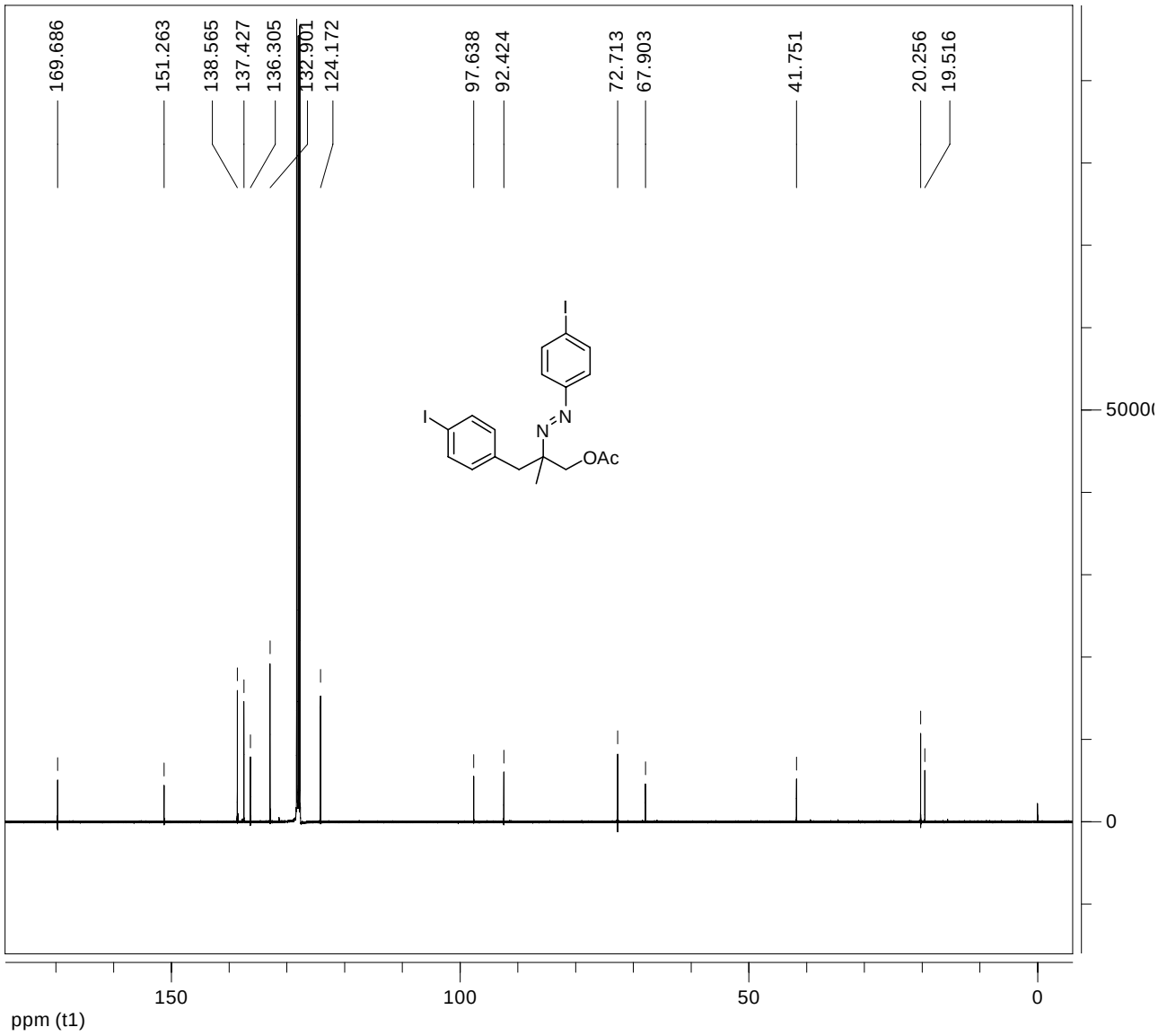


Date:
7 Mar 2012
Document's Title:
7l 1H.mrc

Spectrum Title:
7l inC6D6,1H

Frequency (MHz):
(f1) 360.132
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 4.4039
Spectral Width (ppm):
(f1) 20.661
Pulse Program:
Unknown

^{13}C-Spectrum of **7l**

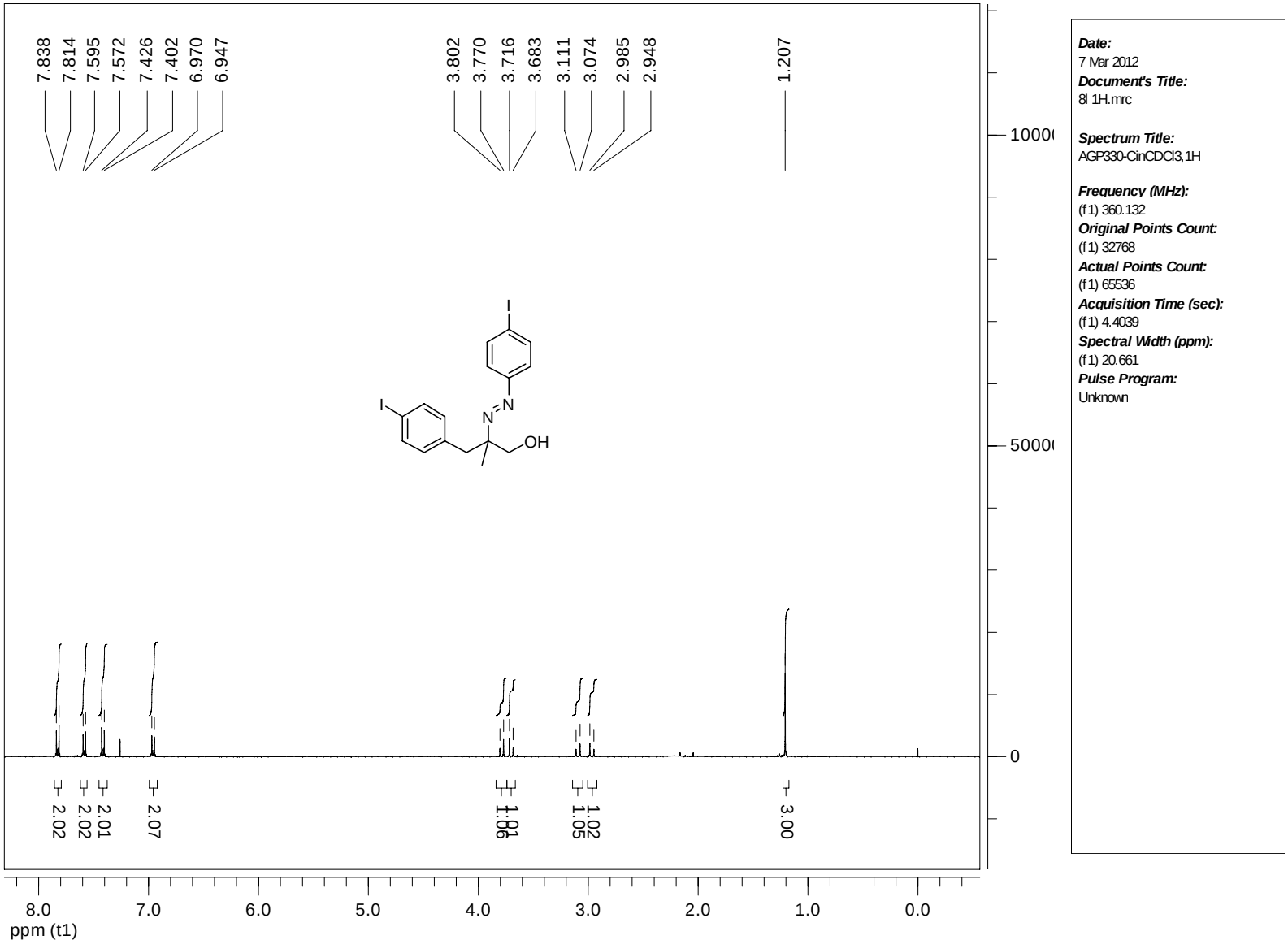


Date:
7 Mar 2012
Document's Title:
7l 13C.mrc

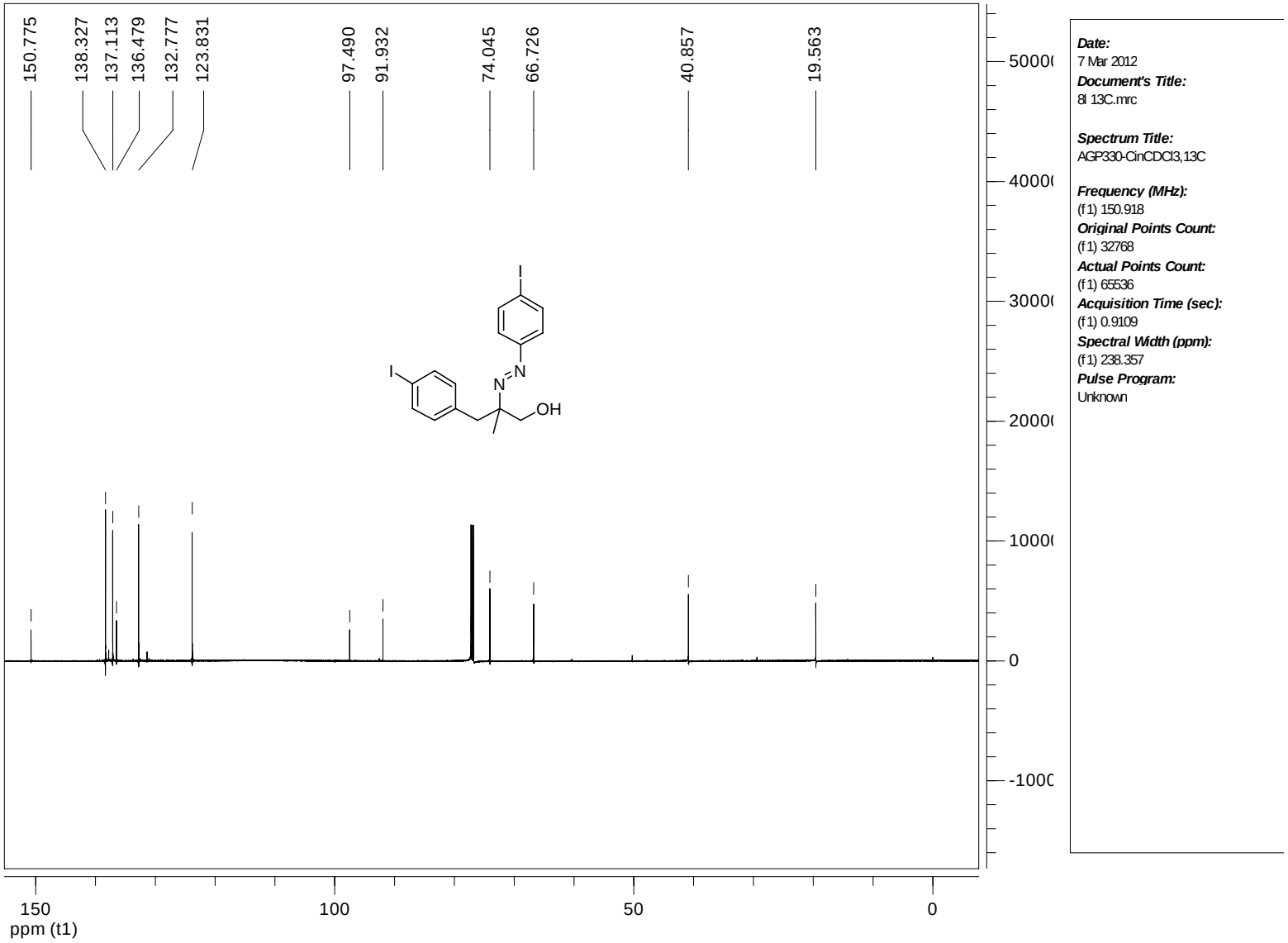
Spectrum Title:
7l inC6D6,13C

Frequency (MHz):
(f1) 90.564
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.5138
Spectral Width (ppm):
(f1) 239.010
Pulse Program:
Unknown

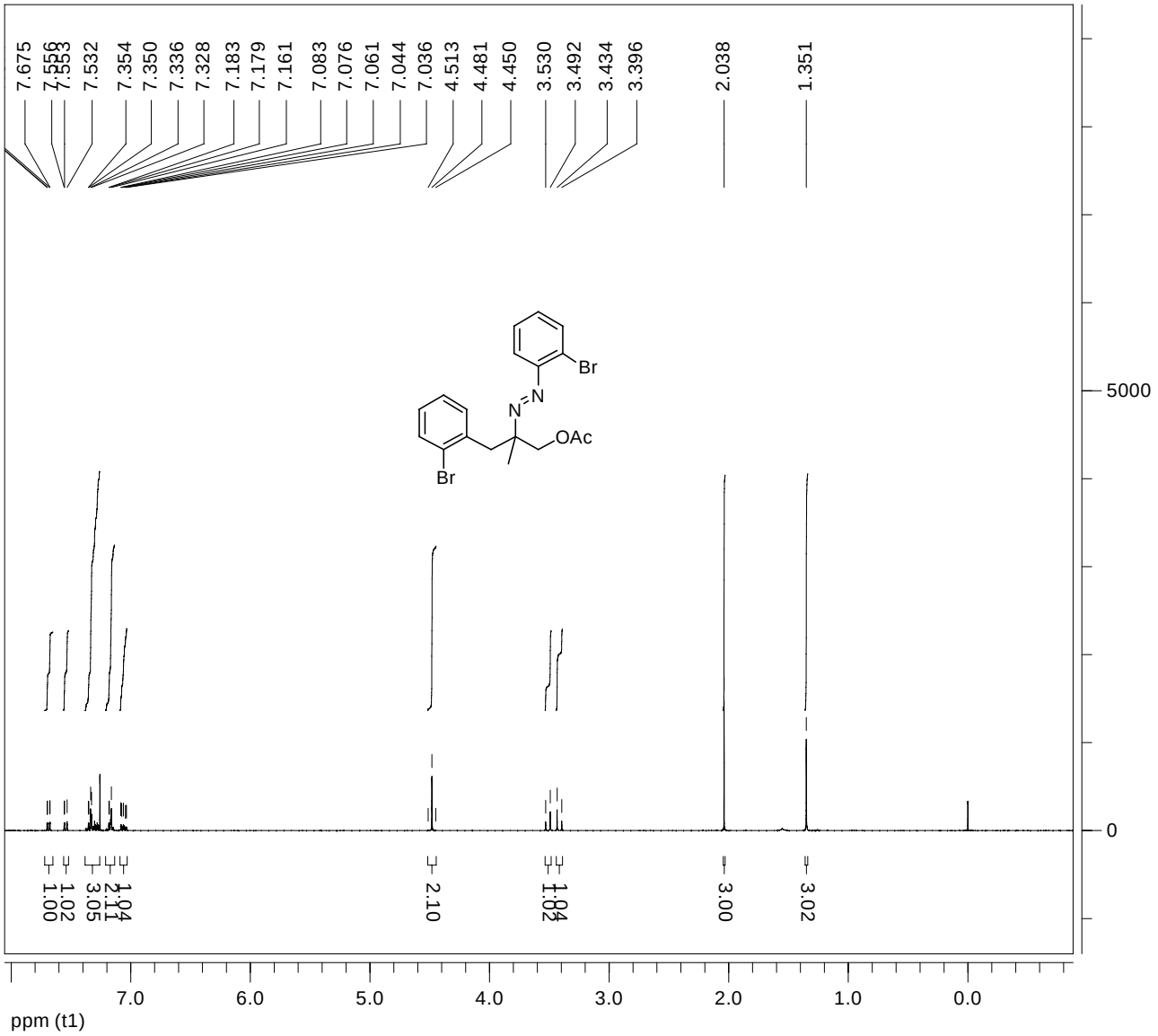
^{1}H-Spectrum of **8l**



^{13}C-Spectrum of **8l**



^{1}H-Spectrum of **7m**

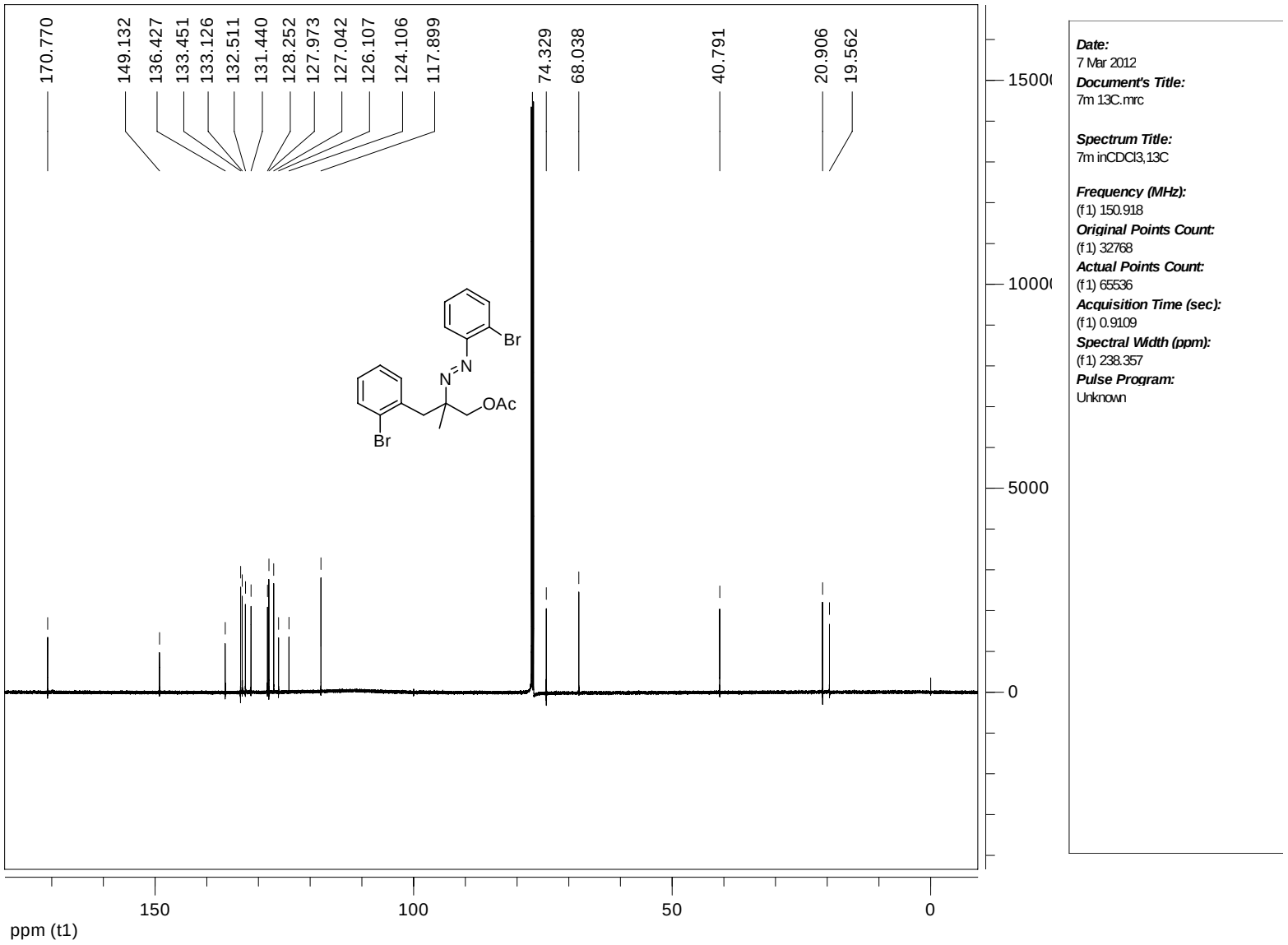


Date:
7 Mar 2012
Document's Title:
7m 1H.mrc

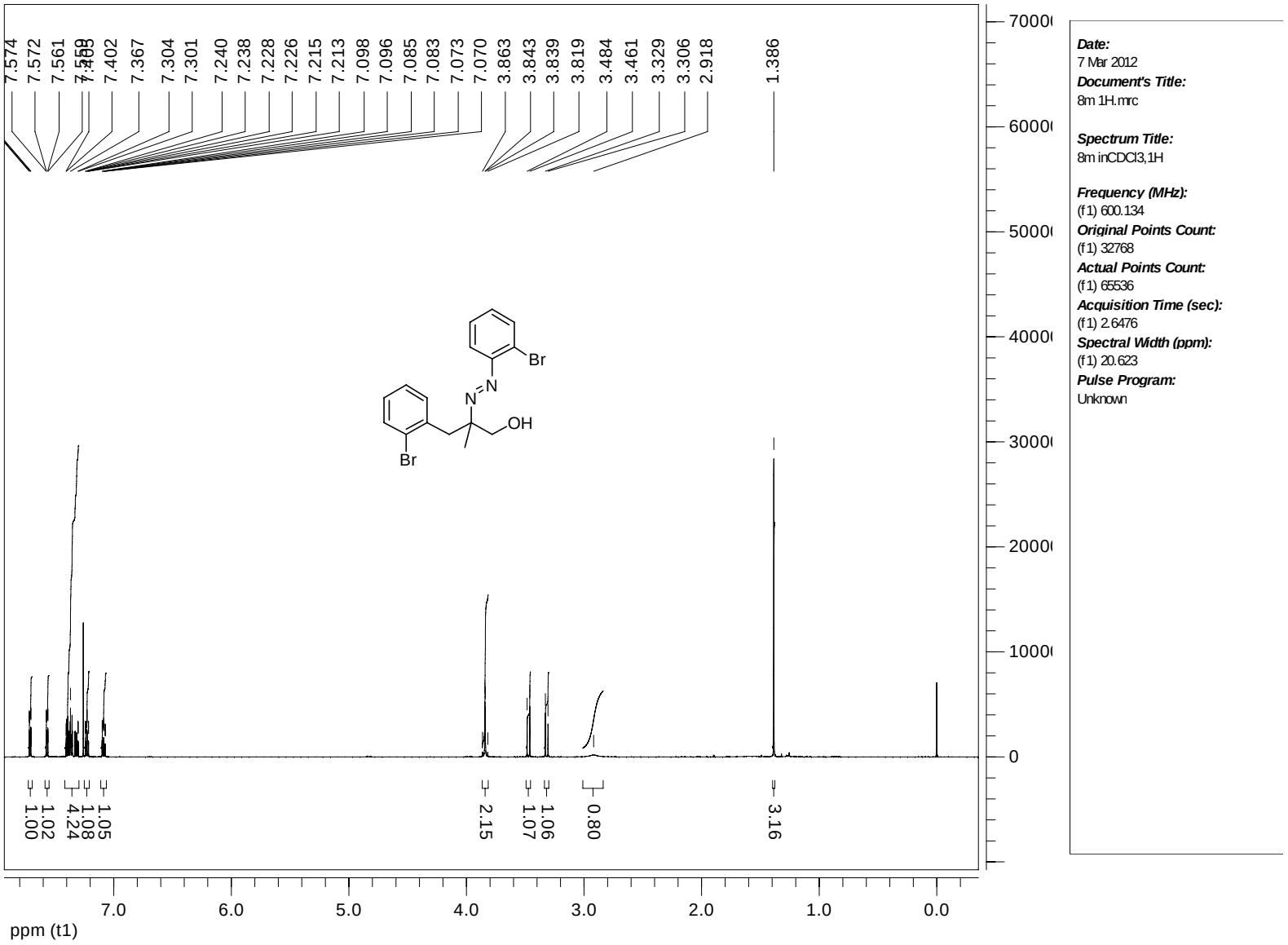
Spectrum Title:
7m inCDCl3,1H

Frequency (MHz):
(f1) 360.132
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 4.4039
Spectral Width (ppm):
(f1) 20.661
Pulse Program:
Unknown

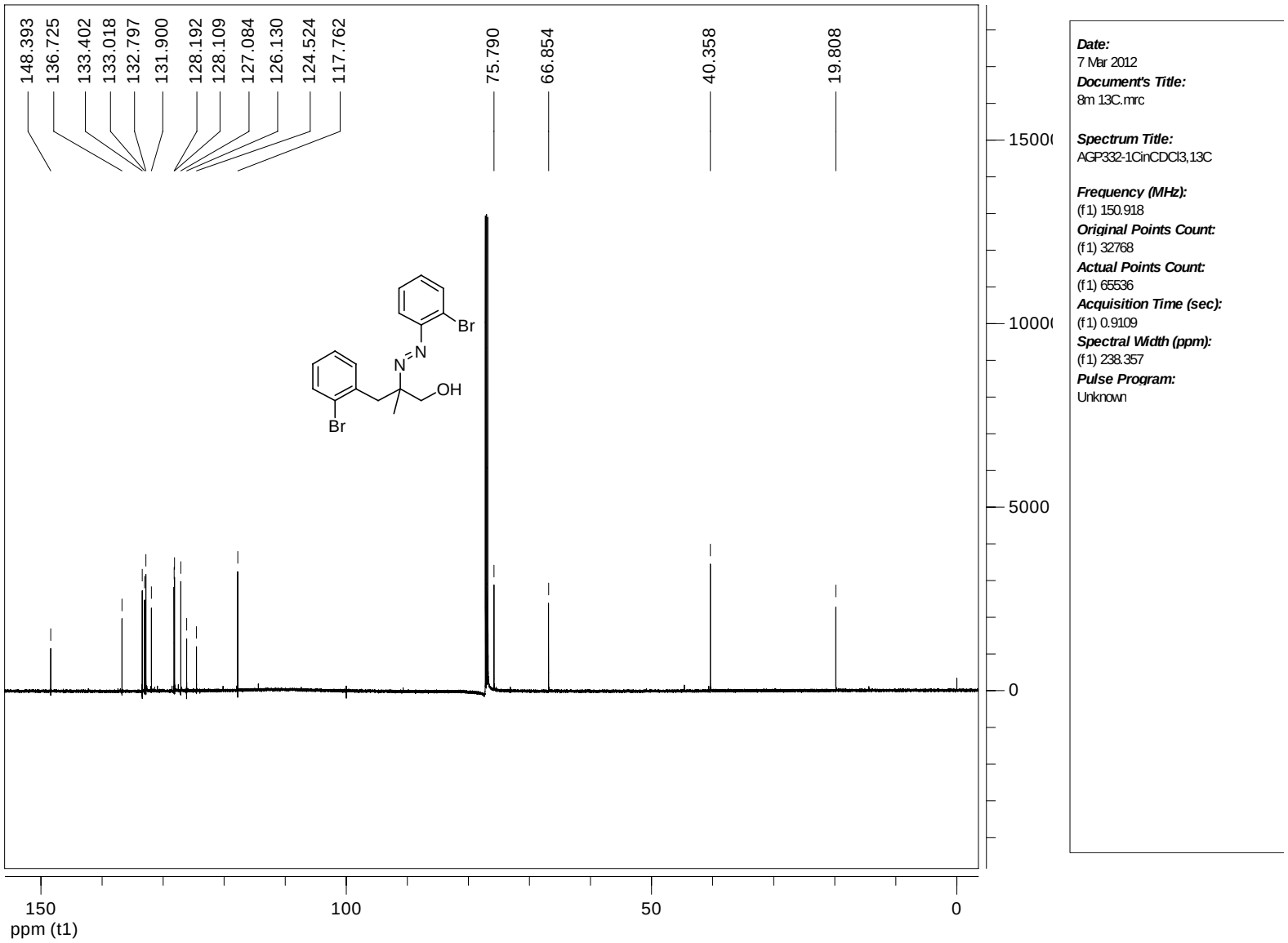
^{13}C-Spectrum of **7m**



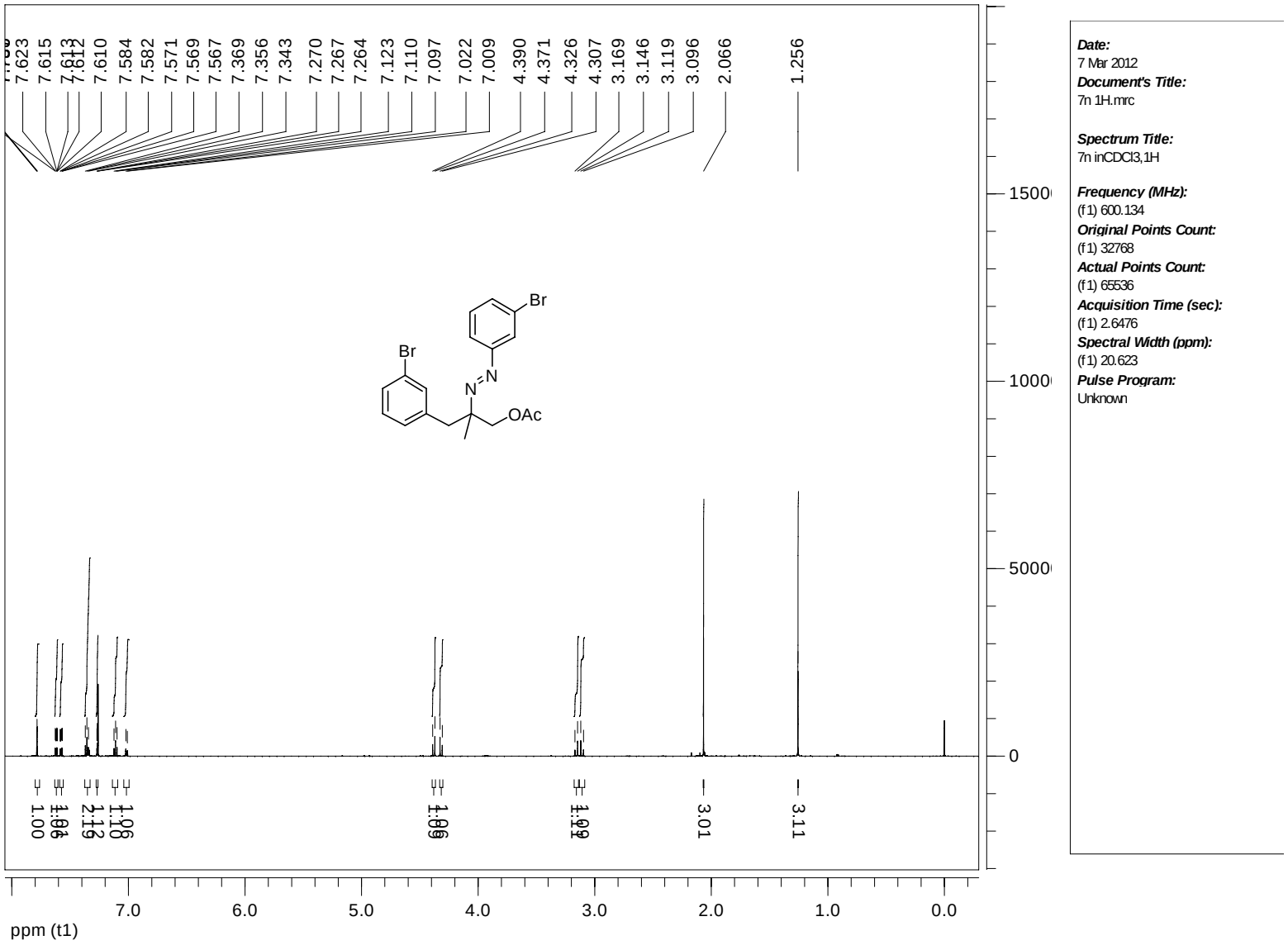
^{1}H-Spectrum of **8m**



^{13}C-Spectrum of **8m**



^{1}H-Spectrum of **7n**

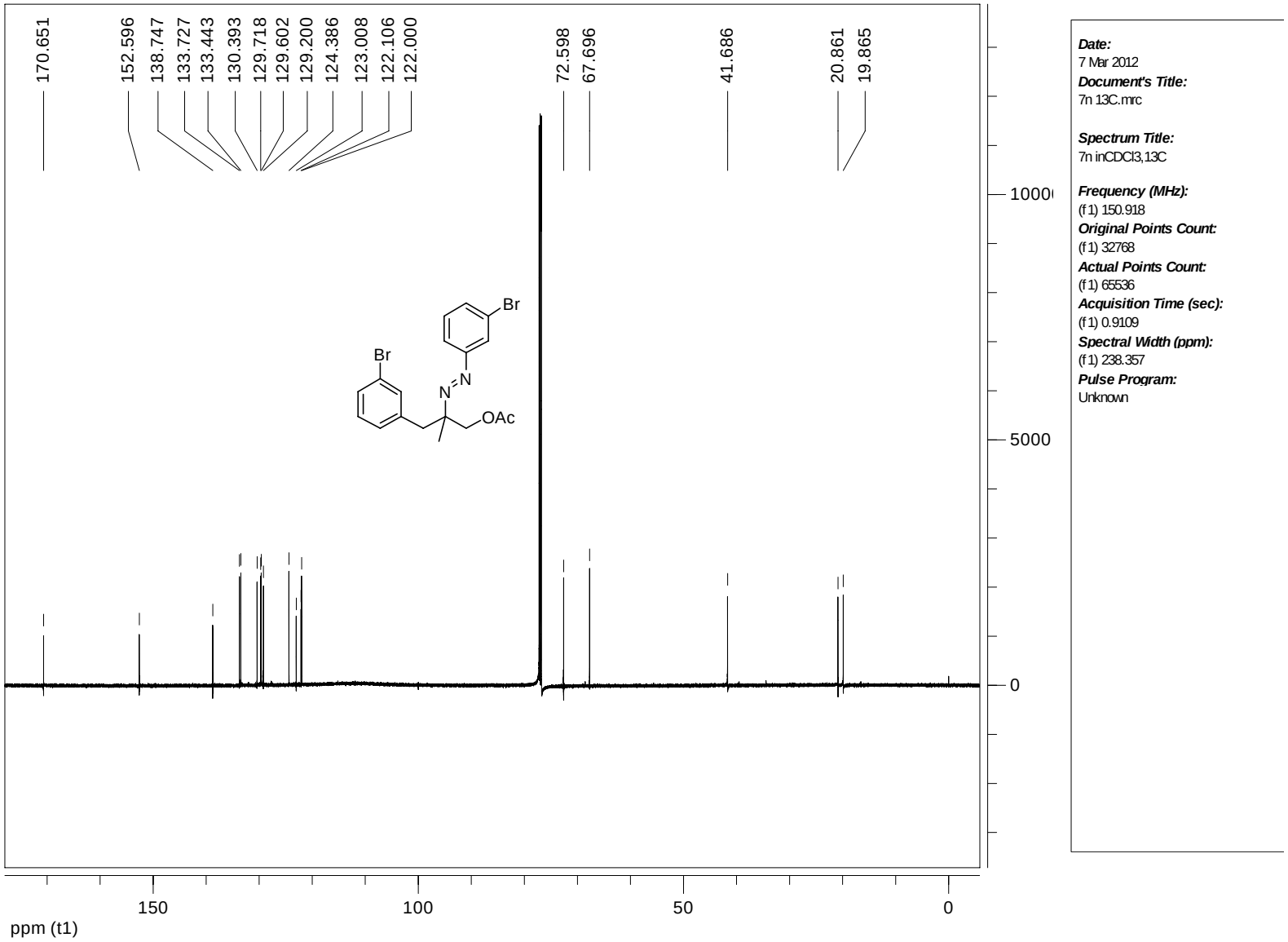


Date:
7 Mar 2012
Document's Title:
7n 1H.mrc

Spectrum Title:
7n inCDCl3,1H

Frequency (MHz):
(f1) 600.134
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 2.6476
Spectral Width (ppm):
(f1) 20.623
Pulse Program:
Unknown

^{13}C-Spectrum of **7n**

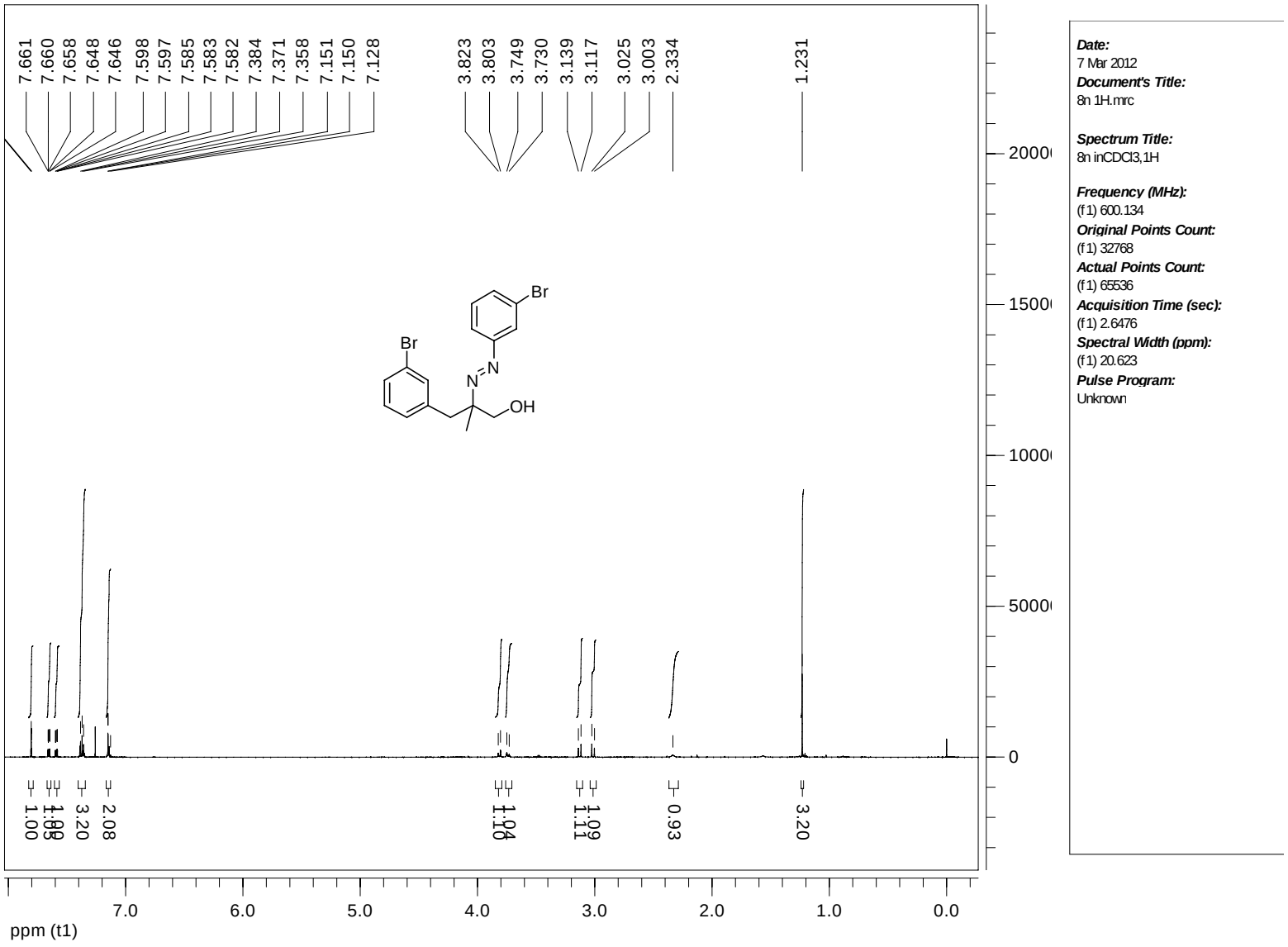


Date:
7 Mar 2012
Document's Title:
7n 13C.mrc

Spectrum Title:
7n inCDCl3,13C

Frequency (MHz):
(f1) 150.918
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.9109
Spectral Width (ppm):
(f1) 238.357
Pulse Program:
Unknown

^{1}H-Spectrum of **8n**

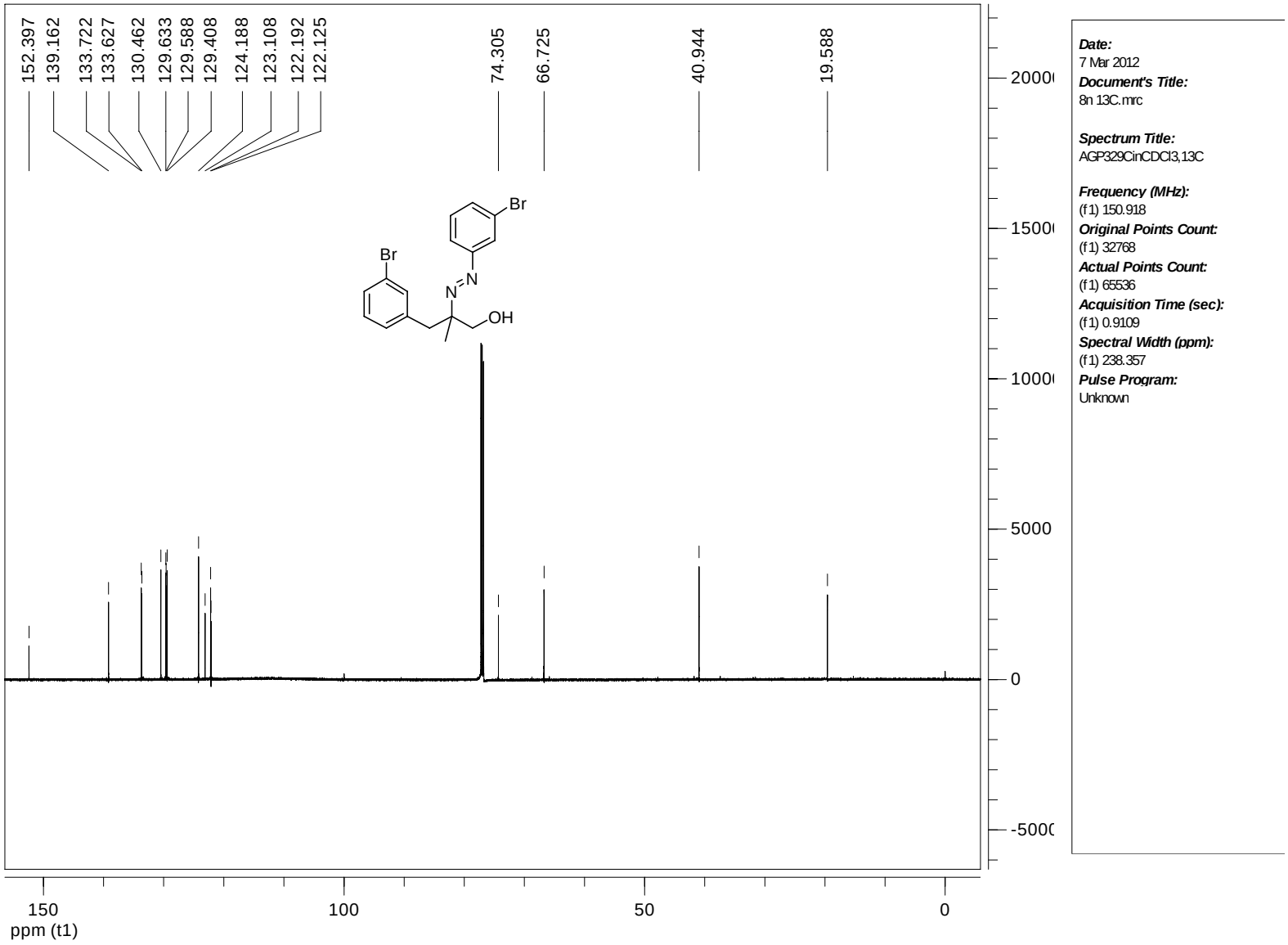


Date:
7 Mar 2012
Document's Title:
8n 1H.mrc

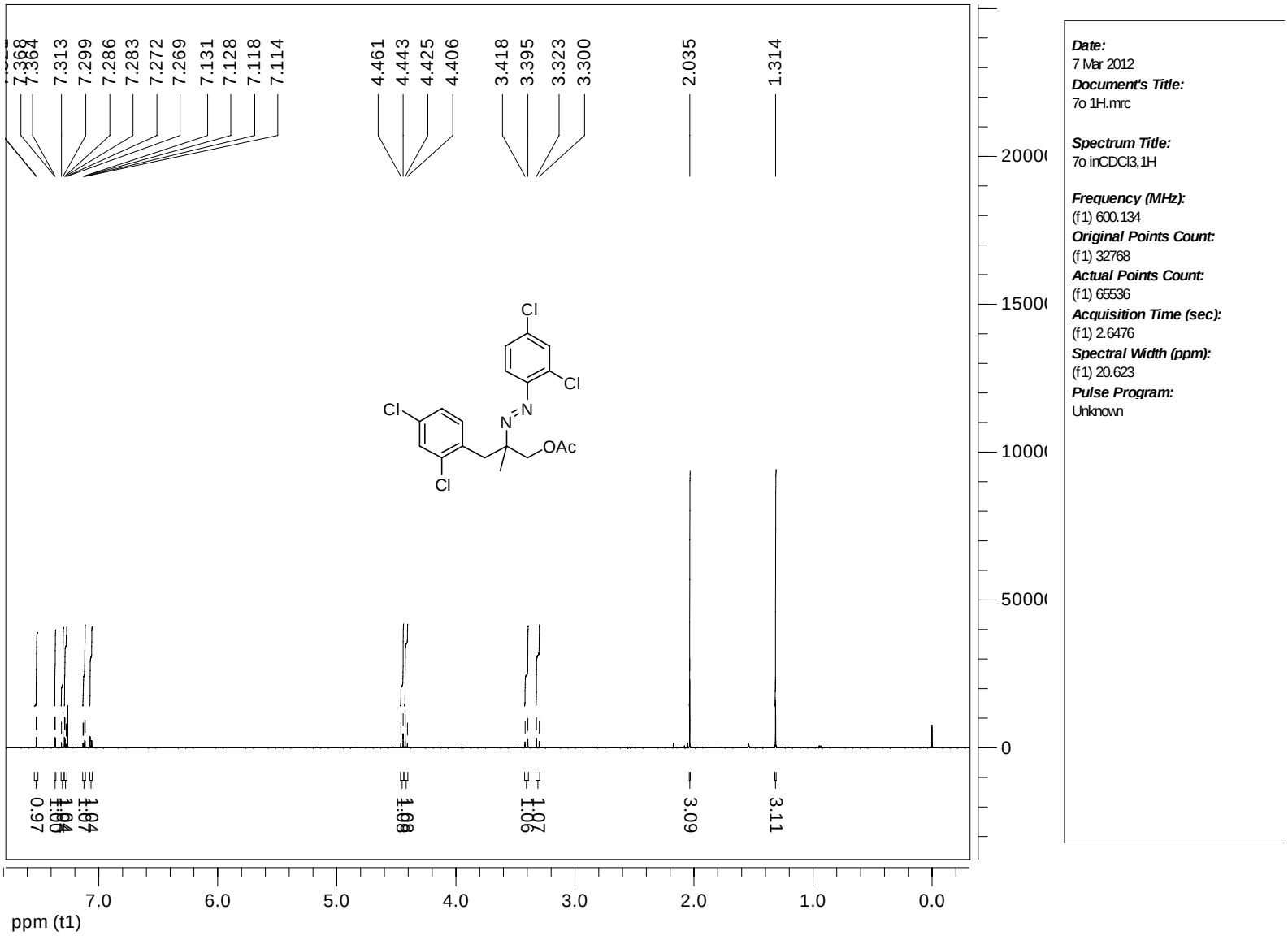
Spectrum Title:
8n inCDCl3,1H

Frequency (MHz):
(f1) 600.134
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 2.6476
Spectral Width (ppm):
(f1) 20.623
Pulse Program:
Unknown

^{13}C-Spectrum of **8n**



^{1}H-Spectrum of **7o**

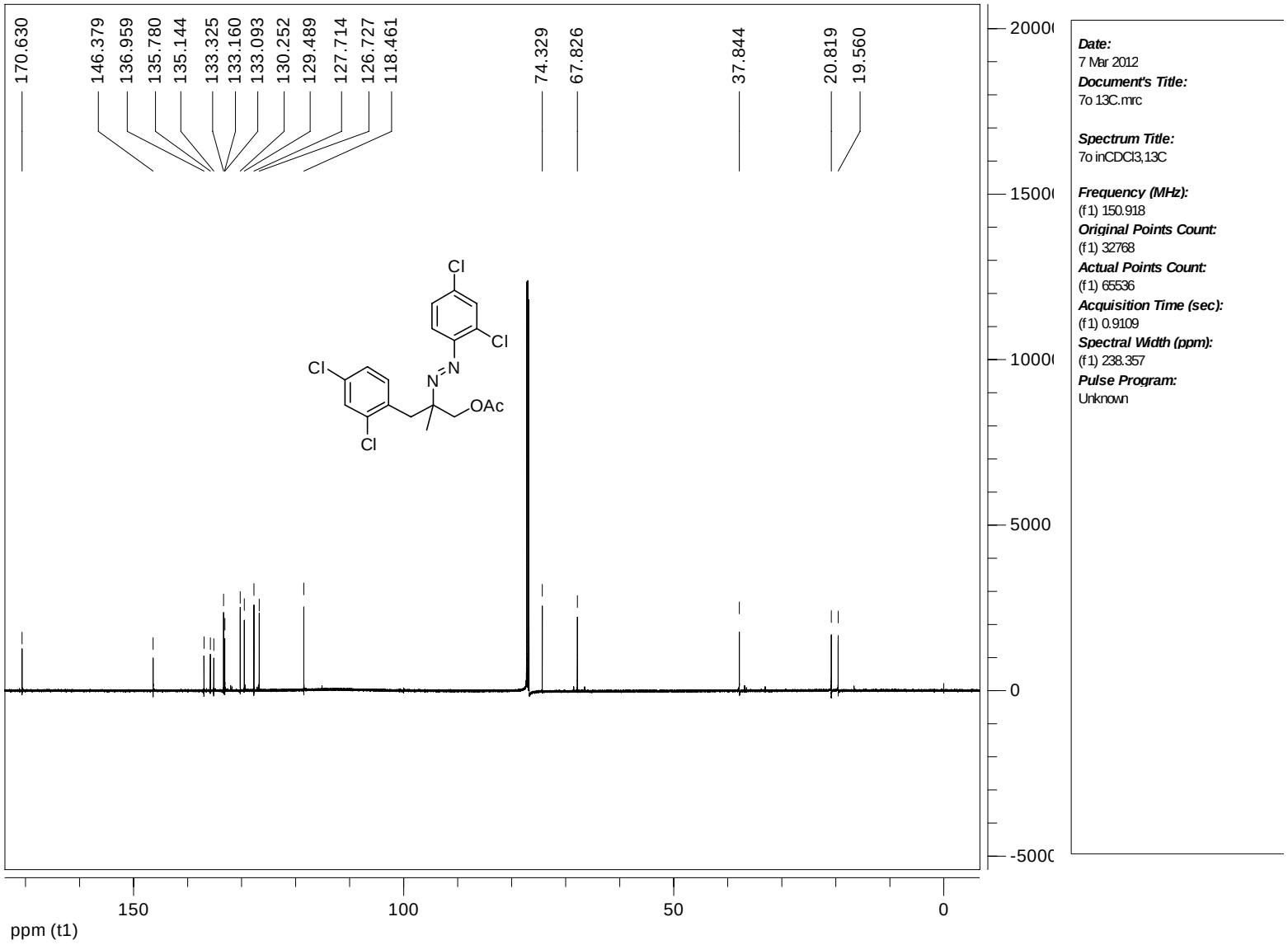


Date:
7 Mar 2012
Document's Title:
7o 1H.mrc

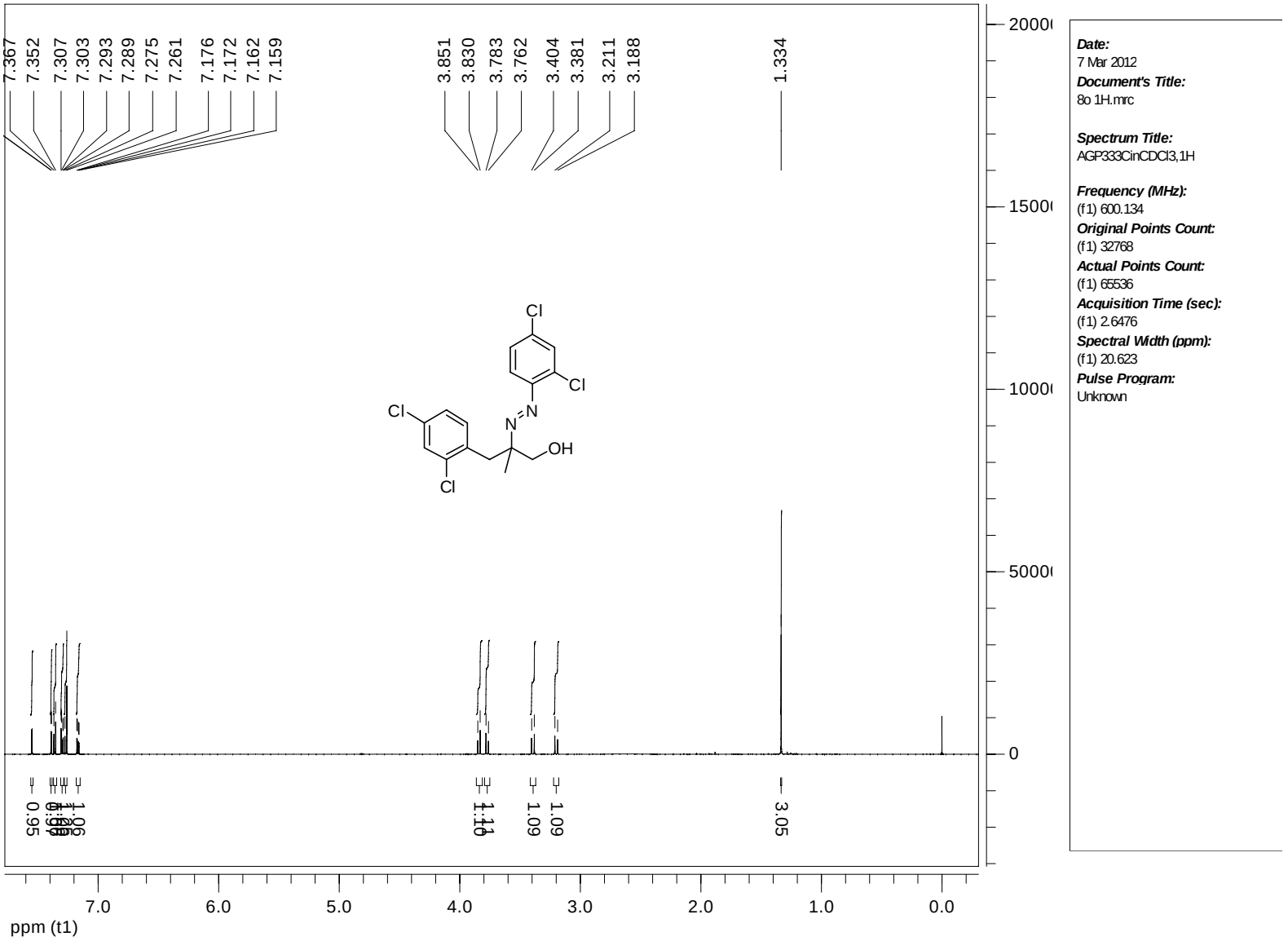
Spectrum Title:
7o inCDCl3,1H

Frequency (MHz):
(f1) 600.134
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 2.6476
Spectral Width (ppm):
(f1) 20.623
Pulse Program:
Unknown

^{13}C-Spectrum of **7o**



^{1}H-Spectrum of **8o**

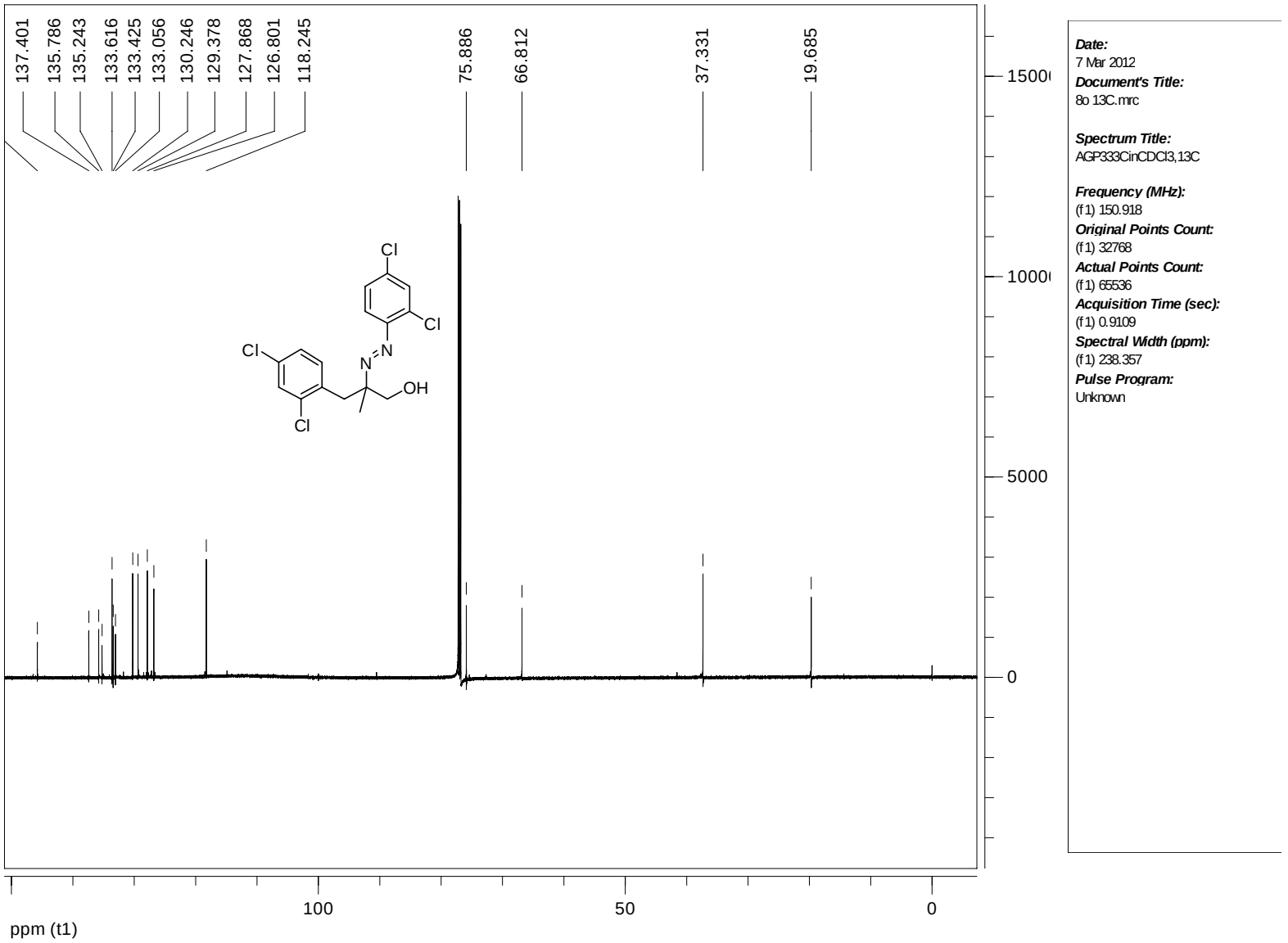


Date:
7 Mar 2012
Document's Title:
8o 1H.mrc

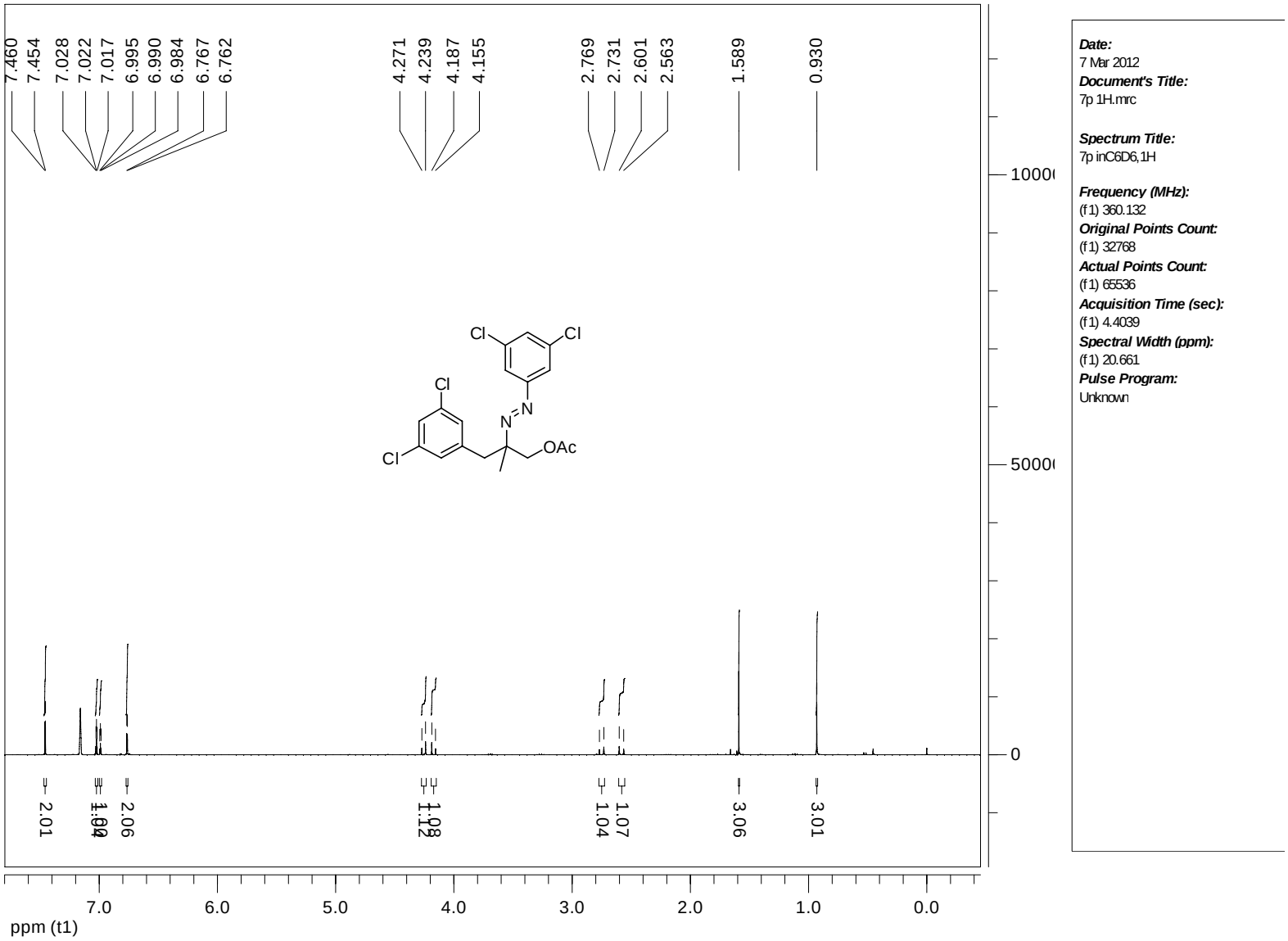
Spectrum Title:
AGP333CinCDCl3,1H

Frequency (MHz):
(f1) 600.134
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 2.6476
Spectral Width (ppm):
(f1) 20.623
Pulse Program:
Unknown

^{13}C-Spectrum of **8o**



^{1}H-Spectrum of **7p**

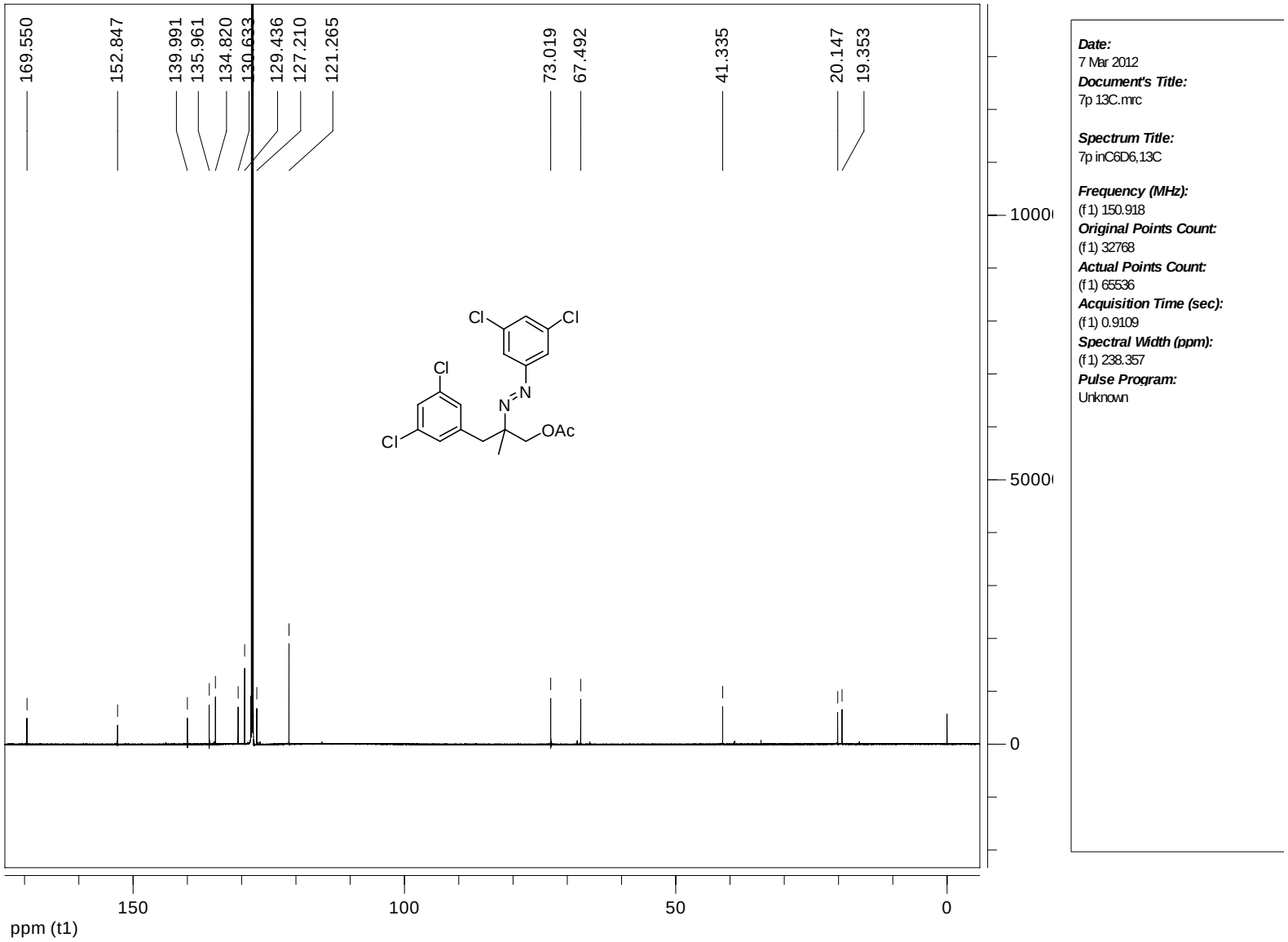


Date:
7 Mar 2012
Document's Title:
7p 1H.mrc

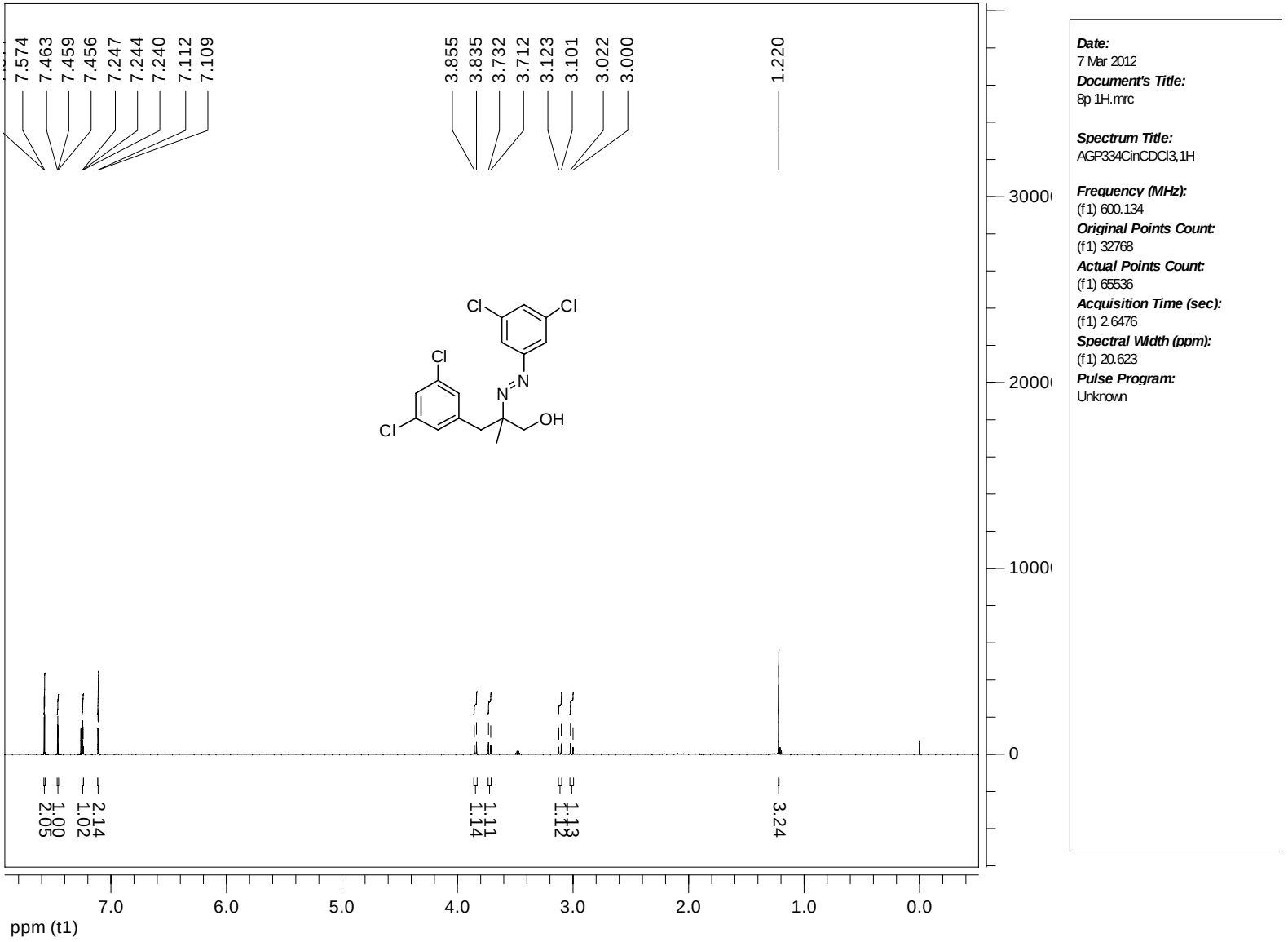
Spectrum Title:
7p inC6D6,1H

Frequency (MHz):
(f1) 360.132
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 4.4039
Spectral Width (ppm):
(f1) 20.661
Pulse Program:
Unknown

^{13}C-Spectrum of **7p**



^{1}H-Spectrum of **8p**

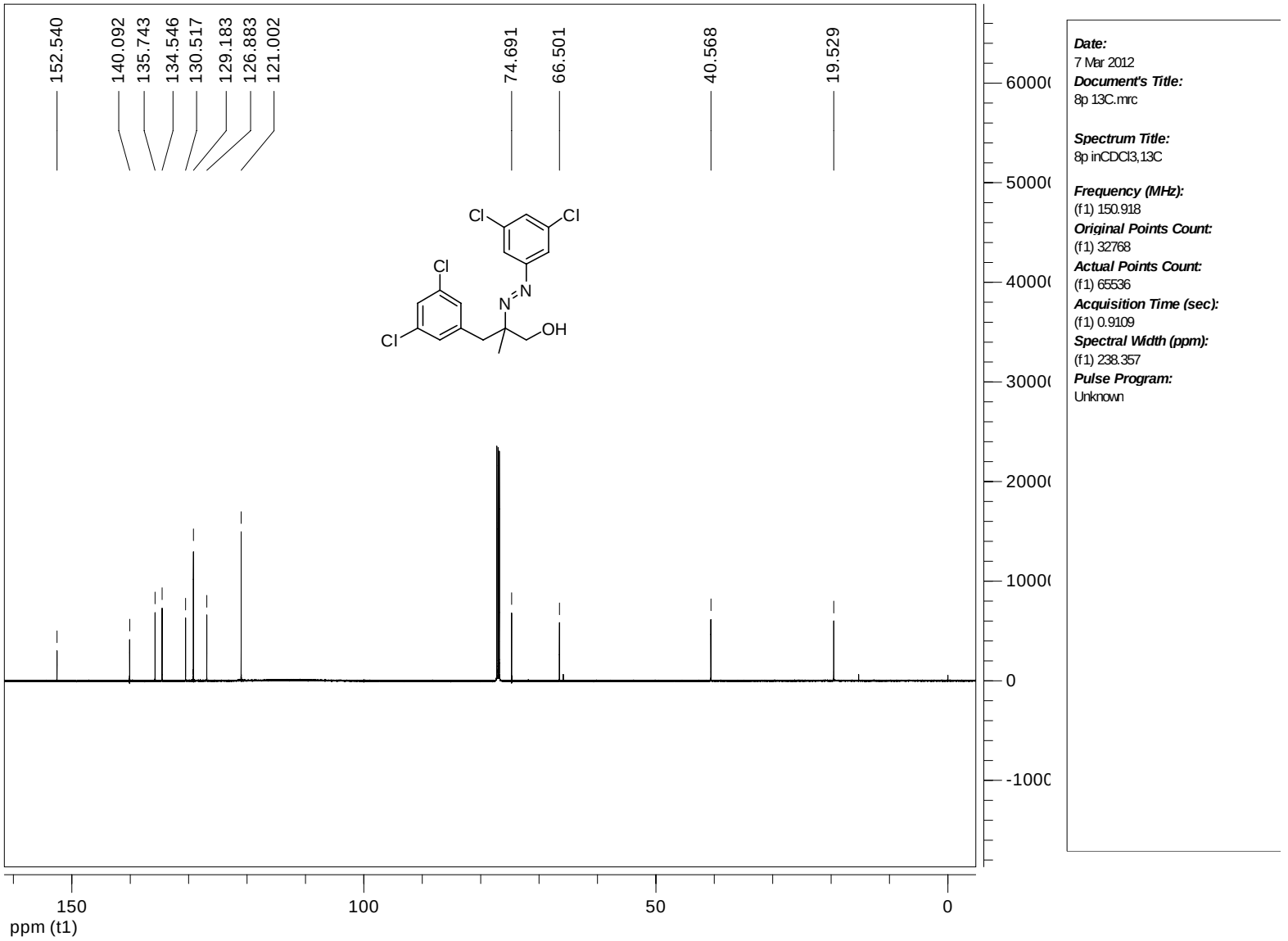


Date:
7 Mar 2012
Document's Title:
8p 1H.mrc

Spectrum Title:
AGP334CinCDCl3,1H

Frequency (MHz):
(f1) 600.134
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 2.6476
Spectral Width (ppm):
(f1) 20.623
Pulse Program:
Unknown

^{13}C-Spectrum of **8p**



5. References

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[2] O. Blank, A. Wetzel, D. Ullrich, M. R. Heinrich, *Eur. J. Org. Chem.* **2008**, 3179–3189.

[3] M. R. Heinrich, O. Blank, A. Wetzel, *J. Org. Chem.* **2007**, *72*, 476–484.

[4] Dietz, F. R.; Prechter, A.; Gröger, H.; Heinrich, M. R. *Tetrahedron Lett.* **2011**, *52*, 655–657.

[5] B. Kaptein, H. M. Moody, Q. B. Broxterman, J. Kamphuis, *J. Chem. Soc. Perkin Trans. I* **1994**, 1495–1498.