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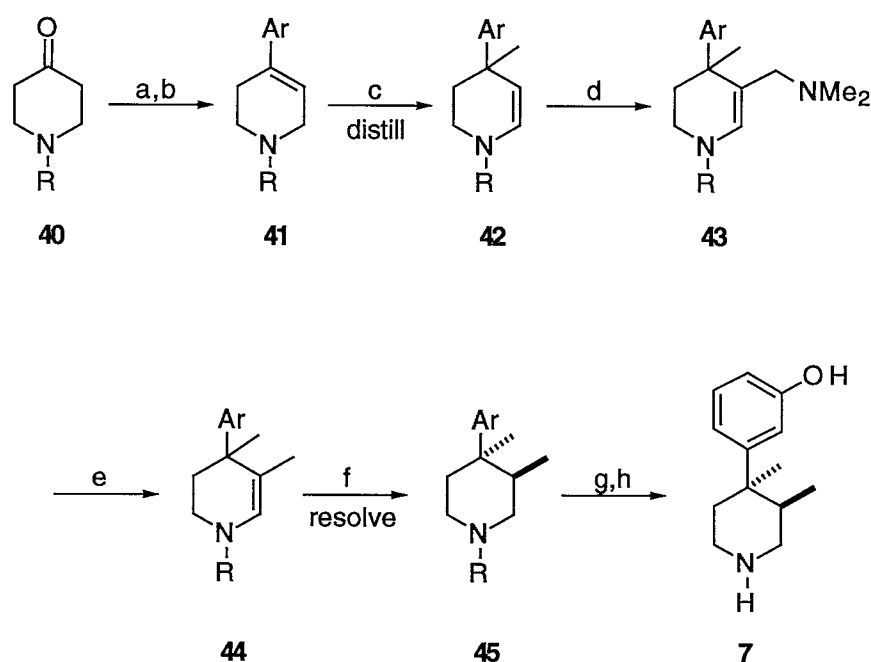
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Supporting Information

Synthesis of the *trans*-3,4-Dimethyl-4-aryl Piperidine Nucleus Using a Modification of the Literature Procedure. Two synthetic approaches to (3*R*,4*R*)-3,4-dimethyl-4-(3-hydroxyphenyl)piperidine (**7**) were successfully implemented on a pilot plant scale. The process described below is a modification of the approach used by Mitch in his lab-scale synthesis of **1** (Scheme 5).¹ The second is a stereospecific synthesis, beginning with 1,3-dimethyl-4-piperidinone (**8**), as described in the body of this paper.

Scheme 5.^a Synthesis of **1 from *N*-Ethyl-4-piperidinone.**



8.3% from **40a**

5.5% from **40b**

40a - 45a: R = Me; Ar = 3-methoxyphenyl

40b - 45b: R = Et; Ar = 3-isopropoxyphenyl

^a Conditions and yields for **40b-7**: (a) ArLi, THF, -70 °C, 66%; (b) MsOH, PhMe, reflux, 85%; (c) *n*-BuLi, THF, -10 °C; MeBr; distill, 64%; (d) Me₂NH, CH₂O, H⁺, 86%; (e) H₂, 1.4% loading of 5% Pd/C, EtOH, 2 h, 94%; (f) NaBH₄, MeOH, rt, (80:15:5 β/α/exo), 98%; (-)-dibenzoyl-L-tartaric acid, EtOH; recryst. 3 times in hot EtOH (4 mL/g, heterogeneous throughout), 26.5%; (g) PhO₂CCl, PhMe, 2 h, 90 °C, 100%; (h) HBr (4 equiv), HOAc, reflux, 15 h, 73%.

Establishing the *trans*-diaxial relationship between the two methyl groups has been a major challenge in the synthesis of **7**. Mitch used a two-step reduction strategy to prepare piperidine **45a** from the dimethylaminomethyl enamine **43a**, which was prepared in four steps using methodology adapted from Barnett's synthesis of Picenadol,² a *cis*-3,4-dialkyl-4-arylpiperidine. Hydrogenolysis of the dimethylamino group in **43a** followed by reduction of enamine **44a** with NaBH₃CN in MeOH afforded **45a** in 94% yield as a 13:1 mixture of diastereomers. The one-step hydrogenation of **43a** to **45a** afforded 1:1 mixture of diastereomers on a multi-gram scale (5% Pt/C, EtOH, 50 psi H₂, 18 h, rt). After separation of the diastereomers by recrystallization of the HBr salt, **45a** was resolved and carried on to **7** (8.3% overall yield from **40a** on a lab scale).

Safe implementation of this strategy on a large scale requires changing the nitrogen and oxygen protecting groups to ethyl and isopropyl, respectively, as **41a** is known to possess neurotoxicity similar to MPTP³ (which leads to Parkinson's-like symptoms) while **41b** does not. Substituents larger than methyl on either the piperidine nitrogen⁴ or the aryl oxygen⁵ are known to prevent MPTP-like neurotoxicity in animals. C-Methyl substitution on the piperidine ring also eliminates all neurotoxicity.⁶

This strategy was successfully implemented on a pilot plant scale and afforded the piperidine nucleus **7** in 5.5% yield from **40b**. Some of the process improvements in this synthesis included a modification of the procedures used for the preparation and purification of **45b** and for the deprotection of the *N*-methyl piperidine **45b**. The hydrogenolysis of **43b** was achieved with only a 1.4% catalyst loading by weight of 5% Pd/C in 94% yield (cf. 10% loading by weight of 5% Pd/BaSO₄ used by Mitch). Use of NaBH₄ instead of NaBH₃CN in the reduction of **44b** gave an 80:15 mixture of the C3-β-methyl/C3-α-methyl diastereomer, respectively, and 5% of the C3-*exo*-olefin. The cyanide waste problem was also eliminated by this change. Purification of this crude mixture by recrystallization of the (-)-dibenzoyl-L-tartaric acid (DBTA) salt from 3A ethanol provided *both* resolution and

purification, and gave the desired β -isomer **45b** in 27% yield. In the *N*-dealkylation step, replacement of vinyl chloroformate with phenyl chloroformate⁷ to demethylate **45b** not only provided a more cost effective procedure but gave the phenyl carbamate in quantitative yield as a crystalline solid.

Experimental Procedures for Compounds in Eq. 2 and Table 1.

Carbonic Acid, Phenyl *cis*-($\pm$)-1-Ethyl-3-methyl-4-[3-(1-methylethoxy)phenyl]-4-piperidinyl Ester (13). Phenyl chloroformate (87 mL, 0.70 mol) in toluene (100 mL) was added over 25 min at 15 °C to a solution of the *N*-ethyl-3-methylpiperidinol (175 g, 0.632 mol of a 88:12 mixture of diastereomers), which was prepared from *N*-ethyl-3-methyl-4-piperidinone using the procedure described for **22**. The mixture was stirred overnight at room temperature and then poured into hexane (1.5 L) to precipitate the hydrochloride salt. Recrystallization from EtOAc (13.5 mL/g) afforded 160.8 g (59%) of the pure hydrochloride **16**. The salt (156 g, 0.359 mol) was neutralized with 1 N NaOH and the free base partitioned into hexane/ether. The solvent volume was reduced to 600 mL, the mixture heated to reflux to redissolve the precipitate, and the product allowed to crystallize. Filtration afforded 121.7 g of **13** (85% yield) as a single, crystalline diastereomer, mp 86.0-88.4 °C. Spectral data: ¹H NMR (CDCl₃) δ 0.74 (d, *J* = 6.9 Hz, 3H), 1.14 (t, *J* = 7.2 Hz, 3H), 1.32 (d, *J* = 6.0 Hz, 3H), 1.33 (d, *J* = 6.0 Hz, 3H), 1.93-2.00 (m, 1H), 2.18 (t, *J* = 11.4 Hz, 1H), 2.23 (td, *J* = 12.0, 1.8 Hz, 1H), 2.40 (td, *J* = 13.5, 3.9 Hz, 1H), 2.49 (q, *J* = 7.2 Hz, 2H), 2.75 (dd, *J* = 11.5, 3.4 Hz, 1H), 2.94 (br d, *J* = 11.6 Hz, 1H), 3.02 (dt, *J* = 14.5, 2.3 Hz, 1H), 4.51 (septet, *J* = 6.1 Hz, 1H), 6.79 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.83 (t, *J* = 1.9 Hz, 1H), 6.86 (br d, *J* = 7.8 Hz, 1H), 7.17-7.26 (m, 4H), 7.36 (t, *J* = 7.8 Hz, 2H); ¹³C NMR (CDCl₃) δ 12.2, 12.7, 22.09, 22.13, 32.8, 42.6, 48.6, 52.3, 56.6, 70.0, 86.7, 113.3, 114.5, 117.3, 121.2 (2C), 125.9, 129.2, 129.4 (2C), 143.0, 151.25, 151.27, 157.9; IR (KBr) 2974, 1761,

1581, 1192, 925, 784 cm^{-1} . Anal. Calcd for $\text{C}_{24}\text{H}_{31}\text{NO}_4$: C, 72.52; H, 7.86; N, 3.52.

Found: C, 72.79; H, 8.13; N, 3.48.

Carbonic Acid, Phenyl *cis*-($\pm$)-1-(Phenylcarboxylate)-3-methyl-4-[3-(1-methylethoxy)phenyl]-4-piperidinyl Ester (19). Phenyl chloroformate (0.95 mL, 7.6 mmol) was added over 2 min via syringe to a solution of **13** (2.50 g, 6.29 mmol) in toluene (30 mL) at 90 °C. The reaction mixture was heated under reflux for 1 h.

Analysis by TLC (1:10 MeOH/EtOAc) showed some residual starting material so an additional 0.25 equiv of phenyl chloroformate (0.2 mL, 1.6 mmol) was added and the solution heated for an additional 2 h. The reaction mixture was cooled to room temperature, diluted with ether (60 mL) and extracted with 1 N NaOH (20 mL), 5% HCl (20 mL), saturated NaHCO_3 (2 x 20 mL) and saturated NaCl (2 x 20 mL). The organic layer was dried over MgSO_4 . Filtration, followed by rotary evaporation afforded ca. 4 g of crude product. Purification by flash chromatography (1:5 EtOAc/hexane) afforded 2.70 g of **19** (87% yield) as a foam. Spectral data: ^1H NMR (CDCl_3 , mixture of rotamers) δ 0.83 (br s, 3H), 1.34-1.36 (br s, 6H), 1.97 (br s, 1H), 2.37 (td, $J = 14.0, 4.1$ Hz, 1H), 3.09-3.36 (m, 3H), 4.12 (br s, 1H), 4.32 (m, 1H), 4.56 (septet, $J = 6.0$ Hz, 1H), 6.82-6.84 (m, 2H), 6.87 (d, $J = 7.9$ Hz, 1H), 7.10-7.25 (m, 6H), 7.29 (t, $J = 8.2$ Hz, 1H), 7.37-7.40 (m, 4H); ^{13}C NMR (CDCl_3 , mixture of rotamers) δ 12.2, 22.0, 22.1, 32.2, 32.7, 39.9, 40.2, 42.3, 42.4, 46.5, 46.9, 70.0, 86.0, 113.6, 114.3, 117.2, 121.1, 121.7, 125.4, 126.1, 129.3, 129.4, 129.5, 142.1, 151.0, 151.3, 151.4, 153.7, 158.0; IR (CHCl_3) 3020, 1761, 1711, 1364, 1199, 925 cm^{-1} . Anal. Calcd for $\text{C}_{29}\text{H}_{31}\text{NO}_6$: C, 71.15; H, 6.38; N, 2.86. Found: C, 71.41; H, 6.34; N, 2.69.

General Procedure for Preparation of Carbonates. The chloroformate (1.2 equiv) was added slowly at 0 °C to a solution of alcohol **23** (1.0 equiv) in EtOAc (5 mL/g of alcohol). The mixture was warmed to room temperature and stirred until the reaction stops. If the hydrochloride precipitated, it was isolated by filtration. If the hydrochloride could

not be filtered, the solvent was removed and the crude product carried on. The hydrochloride was neutralized by adding to a mixture of 1 N NaOH (1.3 equiv) and hexane (5 mL/g HCl salt) at 0 °C. The layers were separated, the organic layer washed with brine, and dried over MgSO₄. If the crude free base contained unreacted alcohol it was purified by flash chromatography (silica gel, 1:10 MeOH/EtOAc).

Carbonic Acid, Methyl *cis*-(±)-1,3-Dimethyl-4-[3-(1-methylethoxy)-phenyl]-4-piperidinyl Ester (22a). Yield: 81% (88% conversion, purified by silica gel flash chromatography, 1:10 MeOH/EtOAc) as a viscous oil. Spectral data: ¹H NMR (CDCl₃) δ 0.73 (d, *J* = 6.7 Hz, 3H), 1.31 (d, *J* = 6.3 Hz, 3H), 1.32 (d, *J* = 6.3 Hz, 3H), 1.91-1.96 (m, 1H), 2.19 (br t, *J* = 11.2 Hz, 1H), 2.23 (t, *J* = 11.4 Hz, 1H), 2.33 (s, 3H), 2.34-2.40 (m, 1H), 2.66 (dd, *J* = 11.4, 3.95 Hz, 1H), 2.79 (br d, *J* = 11.5 Hz, 1H), 2.97 (dt, *J* = 14.3, 2.3 Hz, 1H), 3.76 (s, 3H), 4.51 (septet, *J* = 6.0 Hz, 1H), 6.74-6.80 (m, 3H), 7.22 (t, *J* = 8.0 Hz, 1H); ¹³C NMR (CDCl₃) δ 12.6, 22.0, 22.1, 32.8, 42.6, 45.9, 51.0, 54.4, 58.9, 69.9, 84.6, 113.2, 114.3, 117.3, 129.1, 143.3, 153.8, 157.7; IR (CHCl₃) 2979, 2943, 2807, 1749, 1282, 1262, 940, 921 cm⁻¹. Anal. Calcd for C₁₈H₂₇NO₄: C, 67.26; H, 8.47; N, 4.36. Found: C, 67.15; H, 8.46; N, 4.38.

Carbonic Acid, 2-Methylpropyl *cis*-(±)-1,3-Dimethyl-4-[3-(1-methylethoxy)phenyl]-4-piperidinyl Ester (22c). The HCl salt was isolated in quantitative yield (95% purity) by filtration prior to generation of the free base. The free base solidified upon standing, mp 41.5-44.5 °C. Spectral data: ¹H NMR (CDCl₃) δ 0.74 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 7.3 Hz, 6H), 1.30 (d, *J* = 6.1 Hz, 3H), 1.31 (d, *J* = 6.1 Hz, 3H), 1.89-1.99 (m, 1H), 1.99 (septet, *J* = 6.7 Hz, 1H), 2.19 (td, *J* = 11.2, 1.8 Hz, 1H), 2.25 (t, *J* = 11.4 Hz, 1H), 2.33 (s, 3H), 2.37 (td, *J* = 12.7, 4.1 Hz, 1H), 2.65 (dd, *J* = 11.5, 3.6 Hz, 1H), 2.79 (br d, *J* = 11.5 Hz, 1H), 2.97 (dt, *J* = 14.3, 2.3 Hz, 1H), 3.88 (dd, *J* = 10.5, 6.8 Hz, 1H), 3.91 (dd, *J* = 10.6, 6.9 Hz, 1H), 4.49 (septet, *J* = 6.1 Hz, 1H), 6.76-6.79 (m, 3H), 7.21 (t, *J* = 8.3 Hz, 1H); ¹³C NMR (CDCl₃) δ 12.6, 18.9 (2C), 22.0, 22.1, 27.9, 32.9, 42.7, 46.0, 51.1, 58.9, 69.9, 73.6, 84.2, 113.2, 114.3, 117.3,

129.0, 143.5, 153.4, 157.7; IR (CHCl₃) 3010, 2974, 2808, 1741, 1604, 1583, 1219 cm⁻¹. Anal. Calcd for C₂₁H₃₃NO₄: C, 69.39; H, 9.15; N, 3.85. Found: C, 69.59; H, 9.21; N, 3.90.

Carbonic Acid, Phenylmethyl *cis*-(±)-1,3-Dimethyl-4-[3-(1-methoxyethoxy)phenyl]-4-piperidinyl Ester (22d). The crude HCl salt was isolated in 54% yield (88% purity) by removing the solvent. The material was dissolved in EtOAc/hexane and stirred over the weekend. The precipitated HCl salt was isolated by filtration (23% yield, 96% purity), neutralized with NaOH, and the crude free base purified by chromatography. Viscous oil. Spectral data: ¹H NMR (CDCl₃) δ 0.71 (d, *J* = 6.9 Hz, 3H), 1.28 (d, *J* = 6.0 Hz, 3H), 1.29 (d, *J* = 6.0 Hz, 3H), 1.86-1.96 (m, 1H), 2.16 (td, *J* = 12.1, 2.0 Hz, 1H), 2.22 (t, *J* = 7.8 Hz, 1H), 2.31 (s, 3H), 2.36 (td, *J* = 13.6, 4.1 Hz, 1H), 2.64 (dd, *J* = 11.5, 3.0 Hz, 1H), 2.77 (br d, *J* = 11.6 Hz, 1H), 2.97 (dt, *J* = 14.3, 2.5 Hz, 1H), 4.43 (septet, *J* = 6.0 Hz, 1H), 5.10 (d, *J* = 12.4 Hz, 1H), 5.18 (d, *J* = 12.2 Hz, 1H), 6.72 (t, *J* = 2.0 Hz, 1H), 6.74-6.77 (m, 2H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.32-7.39 (m, 5H); ¹³C NMR (CDCl₃) δ 12.6, 22.03, 22.06, 32.8, 42.7, 45.9, 51.0, 58.8, 69.1, 69.8, 84.9, 113.1, 114.4, 117.3, 128.3 (2C), 128.4, 128.6 (2C), 129.1, 135.7, 143.3, 153.2, 157.7; IR (CHCl₃) 3010, 2979, 2807, 1744, 1604, 1583, 1277, 1260, 1233 cm⁻¹. Anal. Calcd for C₂₄H₃₁NO₄: C, 72.52; H, 7.86; N, 3.52. Found: C, 72.24; H, 7.84; N, 3.71.

Carbonic Acid, 2-Propyl *cis*-(±)-1,3-Dimethyl-4-[3-(1-methoxyethoxy)phenyl]-4-piperidinyl Ester (22e). 2-Propanol (200 mL) was added to NaH (6.43 g, 161 mmol, 60% dispersion in mineral oil), which had been washed with 3 x 30 mL portions of hexane, and the mixture was stirred at 25 °C. When the hydrogen gas evolution ceased (ca. 15 min) the phenyl carbonate hydrochloride **22g**•HCl (30.0 g, 71.4 mmol) was added in one portion and the solution heated to 60 °C overnight. After 16 h about 150 mL of the 2-propanol was removed by rotary evaporation and the product partitioned between hexane (200 mL) and water (200 mL). The organic fraction was

washed with 1 N NaOH (1 x 30 mL) and a saturated solution of NaCl (3 x 30 mL) and was dried over MgSO₄. Removal of the solvent by rotary evaporation followed by purification of the crude product by flash chromatography (1:10 MeOH/EtOAc) afforded 13.5 g of **22e** (54% yield) as a white solid, mp 108.5-110.4 °C. Spectral data: ¹H NMR (CDCl₃) δ 0.73 (d, *J* = 6.9 Hz, 3H), 1.28-1.32 (m, 12 H), 1.90-1.94 (m, 1H), 2.19 (td, *J* = 12.0, 1.9 Hz, 1H), 2.26 (t, *J* = 11.4 Hz, 1H), 2.33 (s, 3H), 2.37 (dd, *J* = 12.6, 4.0 Hz, 1H), 2.64 (dd, *J* = 11.5, 3.4 Hz, 1H), 2.79 (br d, *J* = 11.5 Hz, 1H), 2.98 (dt, *J* = 14.3, 4.8 Hz, 1H), 4.49 (septet, *J* = 6.1 Hz, 1H), 4.83 (septet, *J* = 6.3 Hz, 1H), 6.76-6.79 (m, 3H), 7.21 (t, *J* = 8.2 Hz, 1H); ¹³C NMR (DMSO-*d*₆) δ 12.2, 21.4 (2C), 21.7, 21.8, 32.1, 41.6, 45.5, 50.4, 58.3, 69.2, 70.8, 83.8, 112.7, 113.9, 117.0, 129.0, 143.6, 152.0, 157.1; IR (CHCl₃) 3010, 2982, 2808, 1739, 1604, 1583, 1279, 1265, 1112, 1097, 912 cm⁻¹. Anal. Calcd for C₂₀H₃₁NO₄: C, 68.74; H, 8.94; N, 4.01. Found: C, 68.74; H, 9.02; N, 3.98.

Carbonic Acid, 1,1-Dimethylethyl *cis*-(±)-1,3-Dimethyl-4-[3-(1-methylethoxy)phenyl]-4-piperidiny Ester (22f). Di-*t*-butyl dicarbonate (9.6 mL, 42 mmol) was added via syringe to a solution of alcohol **23** (10.0 g, 38.0 mmol) in THF (50 mL) at 25 °C and the solution stirred for 20 h (slow gas evolution). The solvent was removed by rotary evaporation and the crude product partitioned between ether (100 mL) and 1 N NaOH (50 mL). The layers were separated and the aqueous phase extracted with 25 mL of ether. The combined organic fractions were washed with a saturated solution of NaCl (3 x 25 mL) and dried over MgSO₄. Removal of the solvent by rotary evaporation afforded an tan solid which was dried overnight (40 °C/5 Torr). Yield: 13.26 g (96%). mp 108.5-110.4 °C. Spectral data: ¹H NMR (CDCl₃) δ 0.71 (d, *J* = 6.9 Hz, 3H), 1.31 (d, *J* = 6.0 Hz, 6H), 1.45 (s, 9H), 1.88-1.92 (m, 1H), 2.21 (td, *J* = 12.0, 1.6 Hz, 1H), 2.27 (t, *J* = 11.3 Hz, 1H), 2.34 (s, 3H), 2.34 (td, *J* = 13.4, 4.0 Hz, 1H), 2.63 (dd, *J* = 11.4, 3.5 Hz, 1H), 2.79 (br d, *J* = 11.3 Hz, 1H), 2.95 (dt, *J* = 14.2, 4.7 Hz, 1H), 4.49 (septet, *J* = 6.1 Hz, 1H), 6.75-6.77 (m, 2H), 6.79 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 8.1 Hz, 1H);

^{13}C NMR (DMSO- d_6) δ 12.3, 21.75, 21.80, 27.4 (3C), 32.1, 41.7, 45.5, 50.4, 58.3, 69.2, 80.9, 83.2, 112.8, 113.9, 117.1, 128.9, 143.8, 151.1, 157.1; IR (CHCl₃) 3010, 2981, 2808, 1738, 1603, 1583, 1288, 1138 cm⁻¹. Anal. Calcd for C₂₁H₃₃NO₄: C, 69.39; H, 9.15; N, 3.85. Found: C, 69.10; H, 9.29; N, 3.55.

Carbonic Acid, Phenyl *cis*-($\pm$)-1,3-Dimethyl-4-[3-(1-methylethoxy)-phenyl]-4-piperidinyl Ester (22g). The HCl salt was isolated in 92% yield (95% purity) by filtration prior to generation of the free base. Chromatography of the free base afforded **22g** as a white solid (75% yield); mp 95.3-98.0 °C. Spectral data: ^1H NMR (CDCl₃) δ 0.74 (d, J = 6.8 Hz, 3H), 1.32 (d, J = 5.7 Hz, 3H), 1.33 (d, J = 5.7 Hz, 3H), 1.92-2.02 (m, 1H), 2.22 (t, J = 11.4 Hz, 1H), 2.28 (t, J = 11.5 Hz, 1H), 2.36 (s, 3H), 2.41 (td, J = 13.4, 3.7 Hz, 1H), 2.67 (dd, J = 11.5, 3.8 Hz, 1H), 2.85 (br d, J = 11.4 Hz, 1H), 3.01 (br d, J = 14.4 Hz, 1H), 4.52 (septet, J = 6.0 Hz, 1H), 6.79 (dd, J = 8.2, 2.2 Hz, 1H), 6.82 (br s, 1H), 6.85 (d, J = 8.0 Hz, 1H), 7.14-7.21 (m, 2H), 7.22 (d, J = 6.7 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.37 (t, J = 7.8 Hz, 2H); ^{13}C NMR (DMSO- d_6) δ 12.1, 21.7, 21.8, 31.9, 41.6, 45.5, 50.3, 58.1, 69.2, 85.9, 112.6, 114.1, 117.1, 121.3 (2C), 126.1, 129.2, 129.6 (2C), 142.7, 150.4, 150.7, 157.3; IR (CHCl₃) 3010, 2927, 2808, 1760, 1602, 1584, 1494, 928 cm⁻¹. Anal. Calcd for C₂₃H₂₉NO₄: C, 72.04; H, 7.65; N, 3.65. Found: C, 71.75; H, 7.65; N, 3.57.

***cis*-($\pm$)-1,3-Dimethyl-4-[3-(1-methylethoxy)-phenyl]-4-piperidinyl Propanoate.** Propionyl chloride (19.8 mL, 228 mmol) was added slowly to a solution of alcohol **23** (50.0 g, 190 mmol) in EtOAc (250 mL) at 0 °C. The slurry was stirred for 30 min, warmed to room temperature, and stirred for an additional 3 h. The precipitate was isolated by filtration (57.6 g, 85% yield). The free base was generated by adding the hydrochloride salt to a mixture of 1 N NaOH and hexane, separating the phases, and concentrating the organic phase by rotary evaporation. A colorless oil was obtained in 98% yield. Spectral data: ^1H NMR (CDCl₃) δ 0.70 (d, J = 6.9 Hz, 3H), 1.23 (t, J = 7.6 Hz, 3H), 1.31 (d, J = 5.8 Hz, 3H), 1.32 (d, J = 5.8 Hz, 3H), 1.87-1.93 (m, 1H), 2.08 (td, J

= 12.1, 2.0 Hz, 1H), 2.18 (t, J = 11.3 Hz, 1H), 2.32 (s, 3H), 2.35 (dd, J = 12.6, 4.0 Hz, 1H), 2.48 (q, J = 7.6 Hz, 2H), 2.67 (dd, J = 11.4, 3.9 Hz, 1H), 2.79 (br d, J = 11.6 Hz, 1H), 3.01 (dt, J = 14.3, 2.5 Hz, 1H), 4.48 (septet, J = 6.1 Hz, 1H), 6.68 (m, 1H), 6.72 (d, J = 7.8 Hz, 1H), 6.75 (dd, J = 8.2, 2.3 Hz, 1H), 7.19 (t, J = 8.0 Hz, 1H); ^{13}C NMR (CDCl_3) δ 9.5, 12.7, 22.0, 22.1, 28.8, 32.7, 42.8, 46.1, 51.3, 59.2, 69.9, 83.2, 113.4, 114.0, 117.4, 128.9, 143.5, 157.6, 172.7; IR (CHCl_3) 3010, 2980, 2805, 1731, 1608, 1583, 1190, 964 cm^{-1} . Anal. Calcd for $\text{C}_{19}\text{H}_{29}\text{NO}_3$: C, 71.44; H, 9.16; N, 4.38. Found: C, 71.31; H, 9.27; N, 4.43.

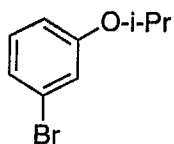
Footnotes for Supplementary Material

1. For the synthesis of **1** see: Mitch, C. H.; Zimmerman, D. M.; Snoddy, J. D.; Reel, J. K.; Cantrell, B. E. *J. Org. Chem.* **1991**, *56*, 1660.
2. Barnett, C. J.; Copley-Merriman, C. R.; Maki, J. *J. Org. Chem.* **1989**, *54*, 4795.
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4. Zimmerman, D. M.; Cantrell, B. E.; Reel, J. K.; Hemrick-Luecke, S. K.; Fuller, R. W. *J. Med. Chem.* **1986**, *29*, 1517, and references cited therein.
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6. Fries, D. S.; de Vries, J.; Hazelhoff, B.; Horn, A. S. *J. Med. Chem.* **1986**, *29*, 424.
7. (a) For a review of amine dealkylations see: Cooley, J. H.; Evain, E. *J. Synthesis* **1989**, 1. (b) Hobson, J. D.; McCluskey, J. G. *J. Chem. Soc. (C)* **1967**, 2015.

Lot# V44-CCW-284-1, CDC13

7.2514
7.1264
7.1099
7.0934
7.0471
7.0450
7.0429
7.0387
7.0345
6.8144
6.8127
6.8097
6.8080
6.7980
6.7961
6.7933
6.7914

4.5328
4.5205
4.5086
4.4963
4.4844



1.5177
1.3297
1.3177

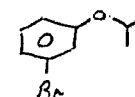
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Current Data Parameters
NAME CCW2841
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date 940624
Time 9.11
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DW 48.0 usec
RG 360
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters
SI 16384
SF 500.1300173 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



4-597-16

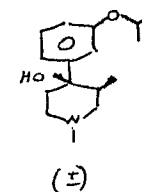
Compound Lot# V44-CCW-279-1, CDC13

Current Data Parameters
 NAME Werner
 EXPNO 10
 PROCNO 1

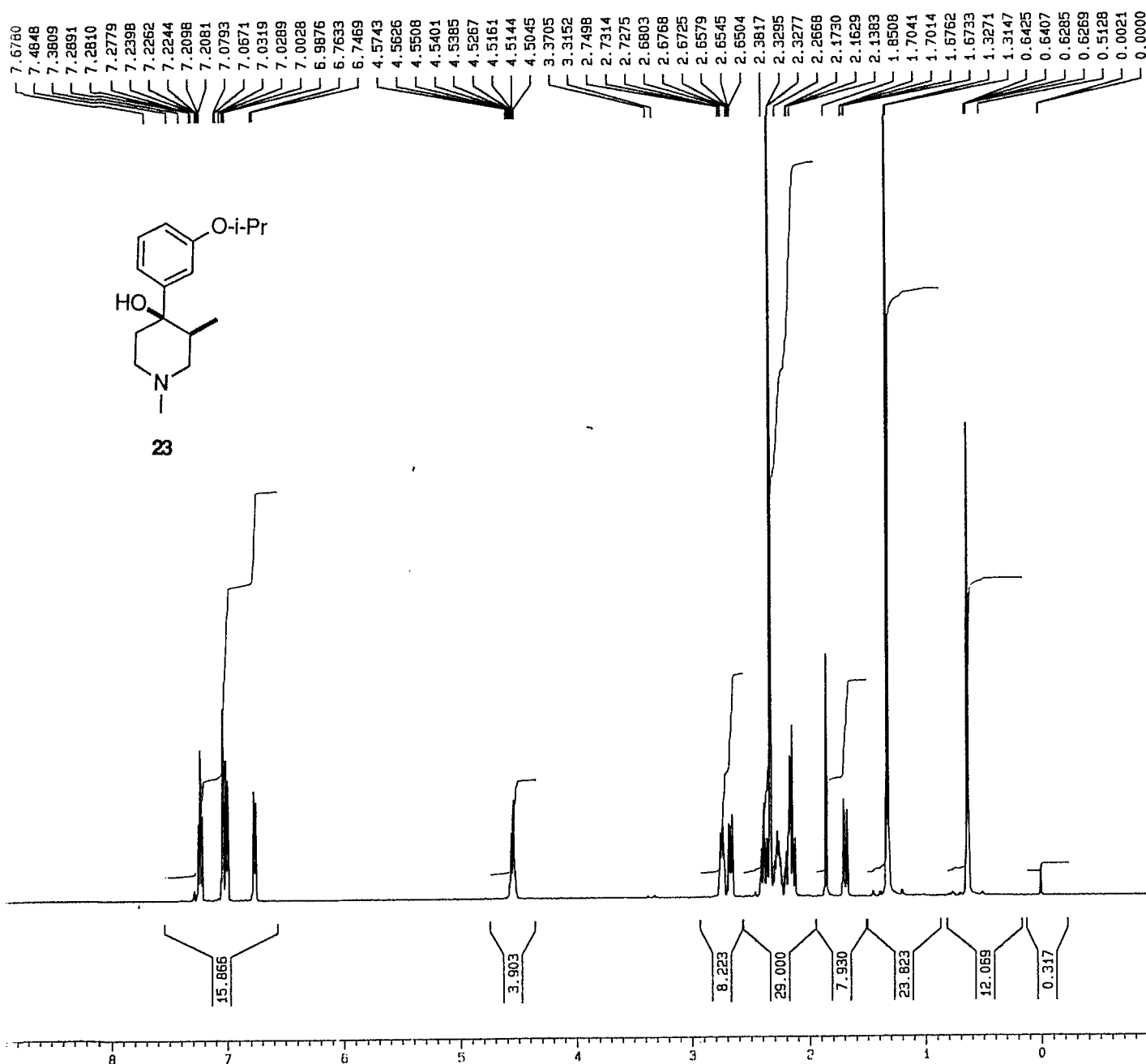
F2 - Acquisition Parameters
 Date 940624
 Time 12.54
 PULPROG zg30
 SOLVENT CDC13
 AQ 1.5728840 sec
 FIDRES 0.317891 Hz
 DM 48.0 usec
 RG 64
 NUCLEUS 1H
 D1 1.0000000 sec
 P1 11.0 usec
 DE 68.6 usec
 SF01 500.1330634 MHz
 SWH 10416.67 Hz
 TD 32768
 NS 16
 DS 2

F2 - Processing parameters
 SI 16384
 SF 500.1300034 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

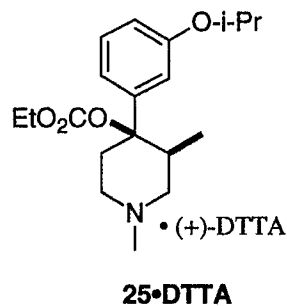
1D NMR plot parameters
 CX 30.00 cm
 F1P 11.000 ppm
 F1 5501.43 Hz
 F2P -1.000 ppm
 F2 -500.13 Hz



6-597-11



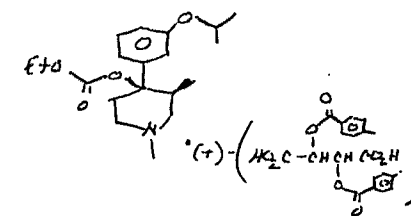
Compound . , Lot# V44-CCW-280-1



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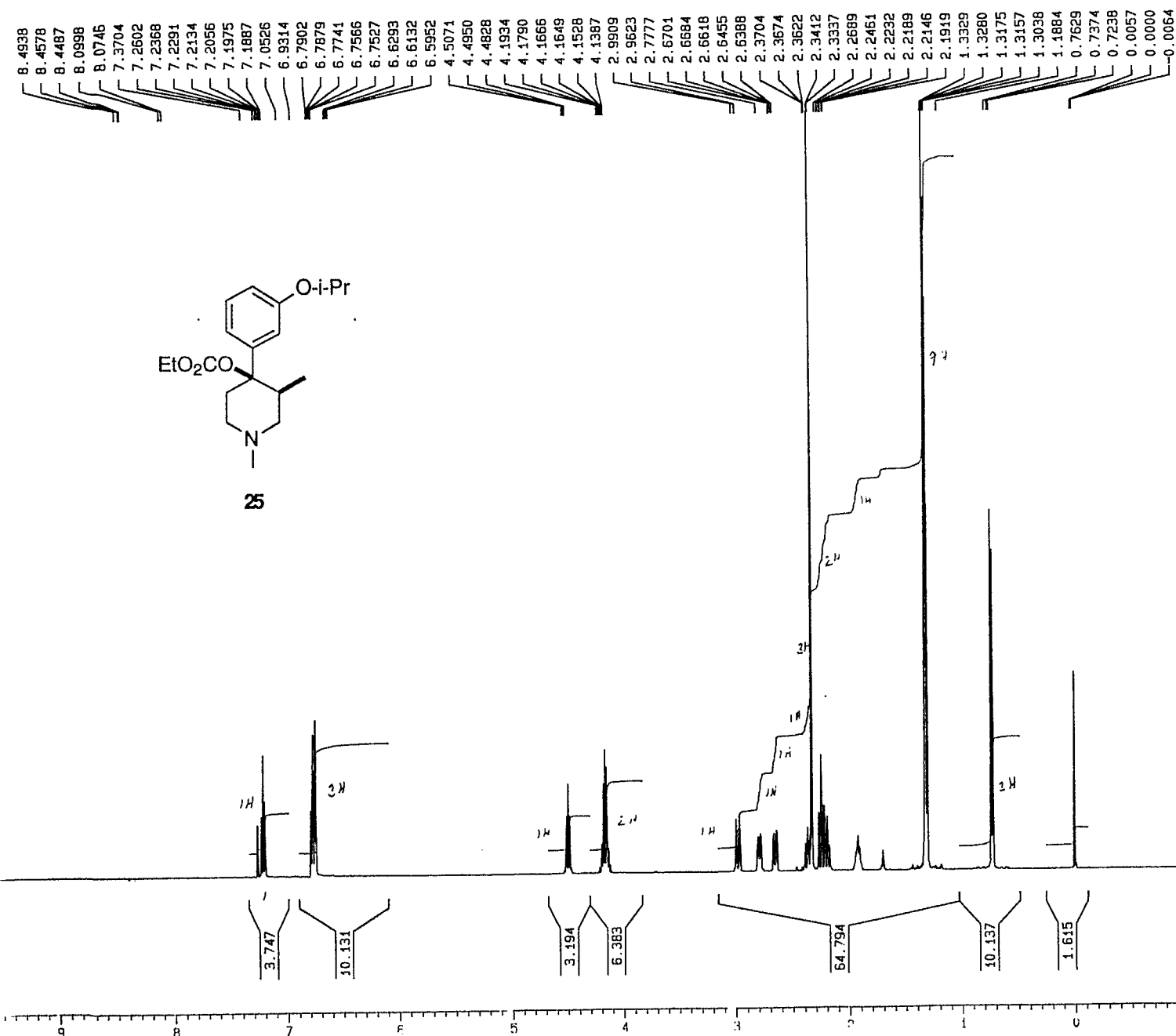
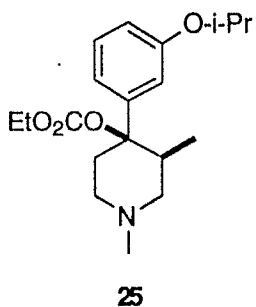
1D NMR plot parameters
CX              30.00 cm
F1P             11.000 ppm
F1              5501.43 Hz
F2P             -1.000 ppm
F2             -500.13 Hz

```



Compound

Lot# V44-8EZ-231-1



Current Data Parameters

NAME	Werner
EXPNO	120
PROCNO	1

F2 - Acquisition Parameters

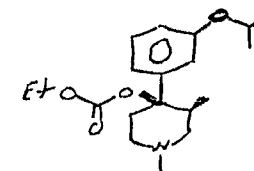
Date	940627
Time	12.31
PULPROG	zg30
SOLVENT	CDCl3
AQ	1.5728840 sec
FIDRES	0.317891 Hz
DW	48.0 usec
RG	360
NUCLEUS	1H
D1	1.0000000 sec
P1	11.0 usec
DE	68.6 usec
SF01	500.1330634 MHz
SWH	10416.67 Hz
TD	32768
NS	16
DS	2

F2 - Processing parameters

SI	16384	
SF	500.1300129	MHz
WDW	EM	
SSB	0	
LB	0.30	Hz
GB	0	
PC	1.00	

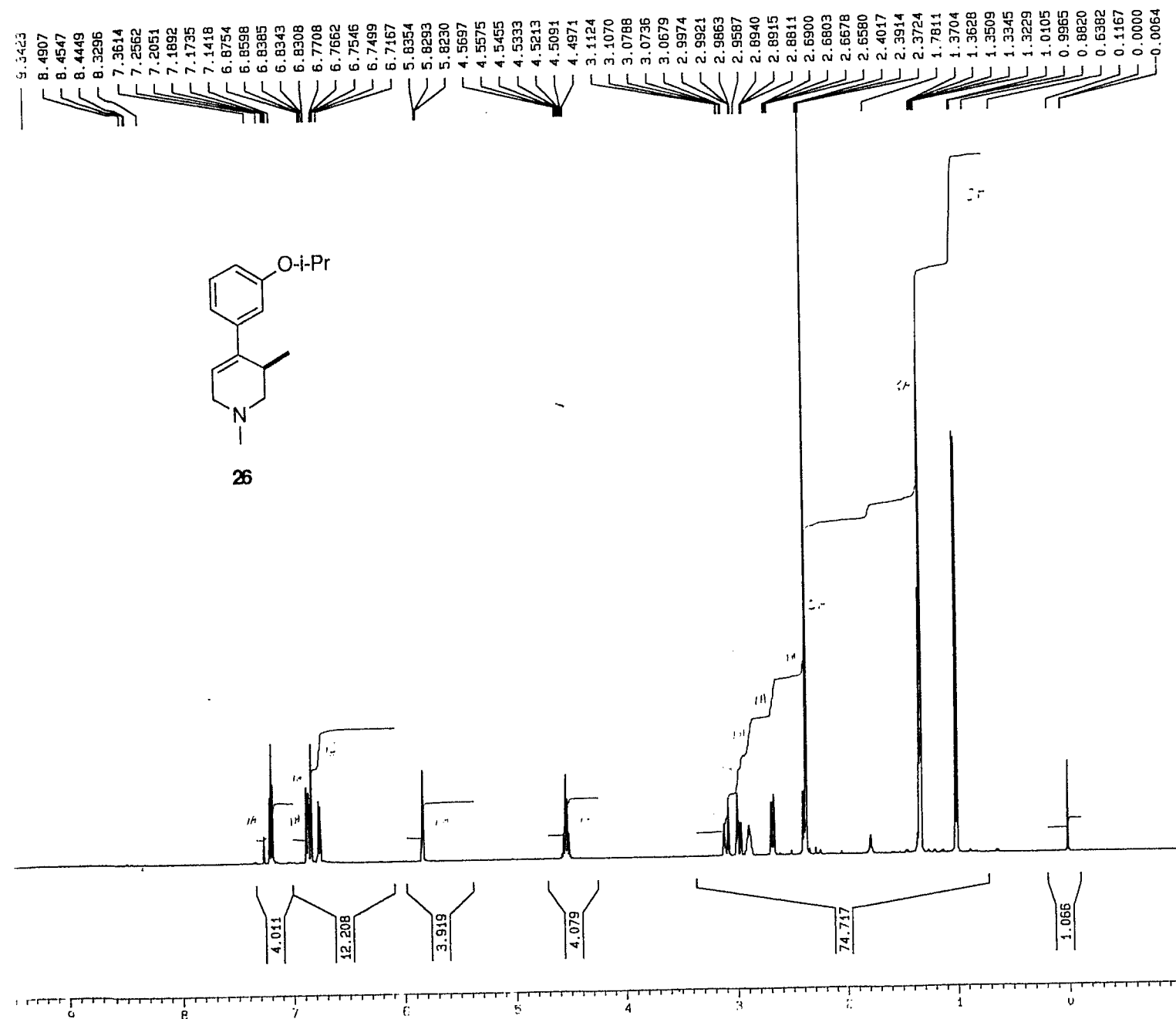
1D NMR plot parameters

CX	30.00 cm
F1P	11.000 ppm
F1	5501.43 Hz
F2P	-1.000 ppm
F2	-500.13 Hz



Compound

Lot# V44-CCW-278-1, CDC1



NAME Werner

EXP NO	1
PROCNO	1

F2 - Acquisition Parame

Date 2-10-22
Time 13.02

SOLVENT CDC13

AG	1.372275 Hz
FIDRES	0.317891 Hz

BW	1270
BG	360

NUCLEUS	IN
D1	1.0000000 sec

F1	21.6 use
DE	68.6 use

SWH 10416.67 Hz

TD	SE788
NS	64

05 2

F2 - Processing parameters
ST 16384

SF 300.150014B AM
HDE FM

SSB 0
1.8 0.30 Hz

GB	0
DC	1.00

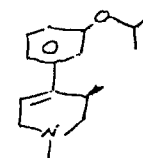
4D NMR plot parameters

CX	30.00 CM
E1P	11.000 PD

F1	3301.45 Hz
F2B	-1.000 pp

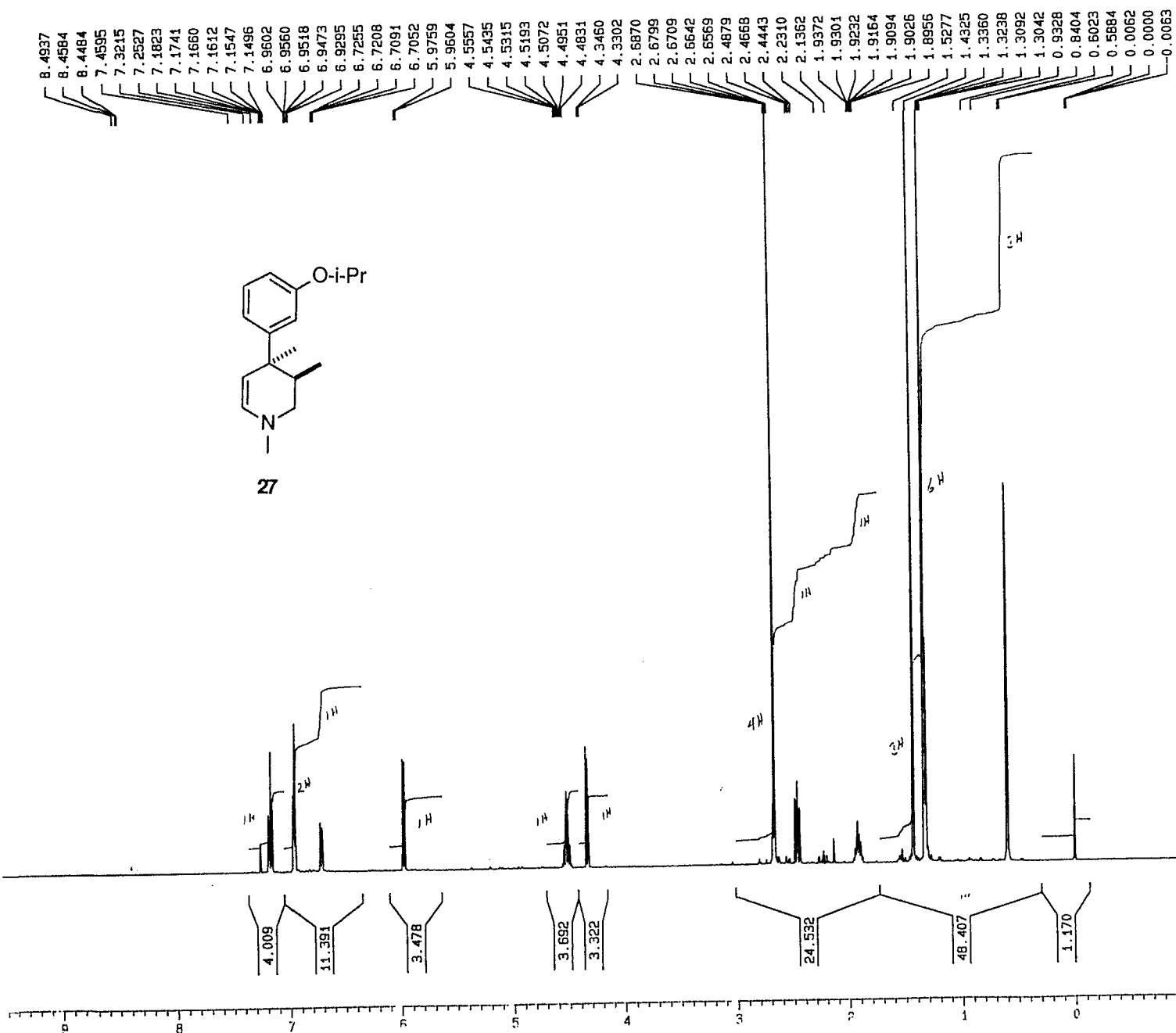
FE 300.15 112

10/10/10



4-547-15

Compound , Lot# V44-CCW-283-1

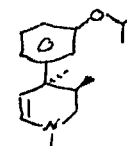


Current Data Parameters
 NAME Werner
 EXPNO 30
 PROCNO 1

F2 - Acquisition Parameters
 Date 940624
 Time 13.14
 PULPROG zg30
 SOLVENT CDC13
 AQ 1.5728840 sec
 FIDRES 0.317891 Hz
 DW 48.0 usec
 RG 256
 NUCLEUS 1H
 D1 1.0000000 sec
 P1 11.0 usec
 DE 68.6 usec
 SF01 500.1330634 MHz
 SMH 10416.67 Hz
 TD 32768
 NS 16
 DS 2

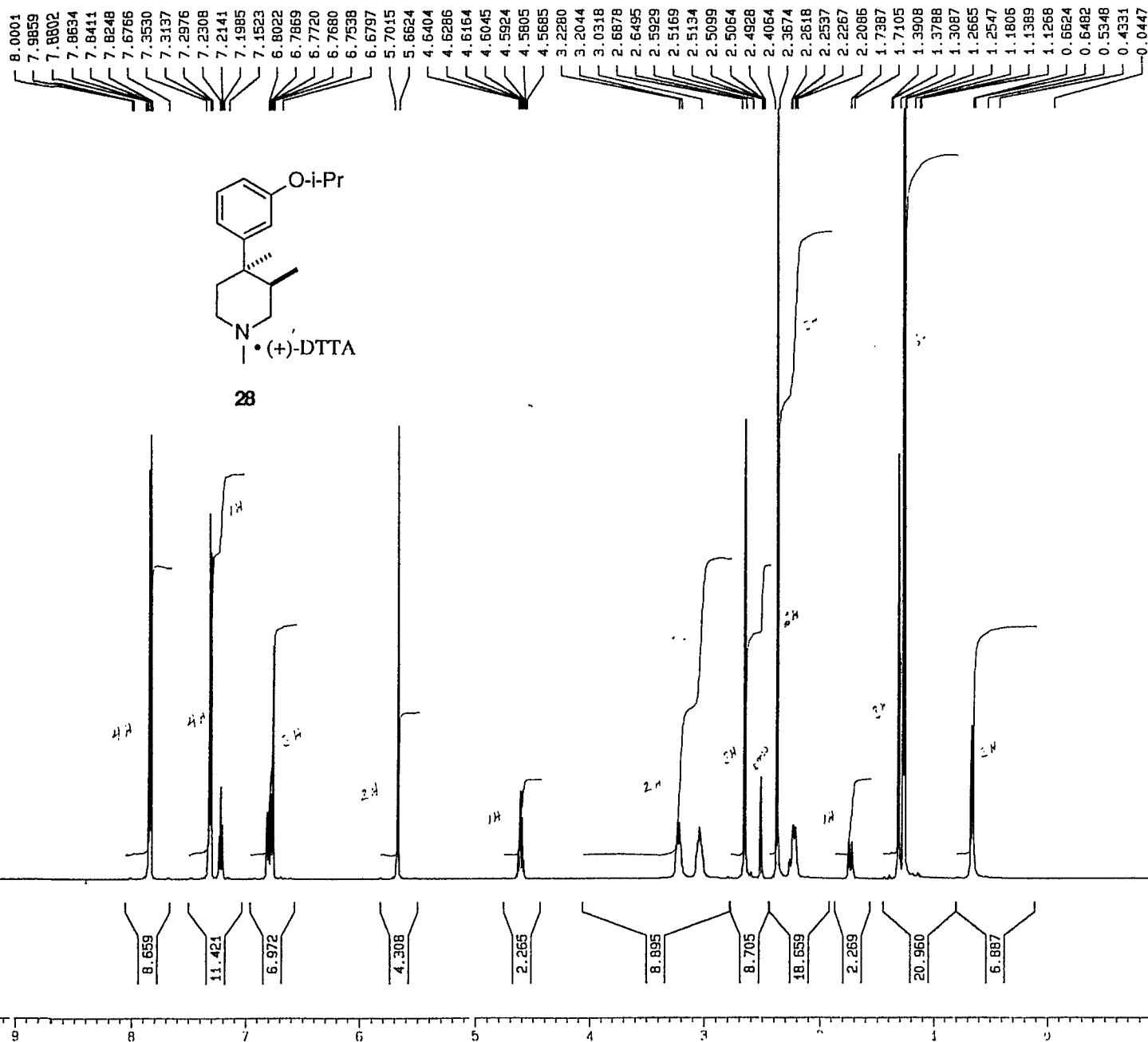
F2 - Processing parameters
 SI 16384
 SF 500.1300167 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 30.00 cm
 F1P 11.000 ppm
 F1 5501.43 Hz
 F2P -1.000 ppm
 F2 -500.13 Hz



Compound

Lot# V44-CCW-282-1, DMSO



Current Data Parameters

NAME Werner
EXPNO 210
PROCNO 1

F2 - Acquisition Parameters

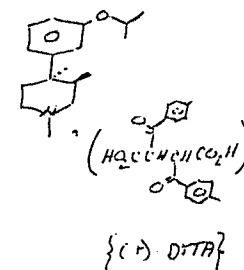
Date 940629
Time 13.29
PULPROG zg30
SOLVENT DMSO
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DQ 48.0 usec
RG 715
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SMH 10416.67 Hz
TD 32768
NS 64
DS 2

F2 - Processing parameters

SI 16384
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

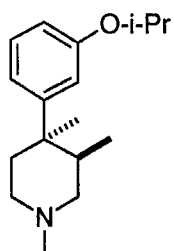
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



45-111
16
4-577-16

Compound Lot# V44-CCW-287-1, CDC13

7.4633
7.2565
7.2119
7.1961
7.1800
6.8635
6.8480
6.8281
6.8240
6.8203
6.7566
6.7411
6.7208
6.7082
6.7036
6.6921
6.6875
6.6747
6.6679
6.5314
4.5665
4.5546
4.5423
4.5304
4.5181
4.5061
4.4939
4.3854
2.7956
2.7901
2.7839
2.5205
2.5142
2.5090
2.3294
2.3230
2.3129
2.3076
2.2957
2.2936
2.2721
1.9909
1.9794
1.9769
1.6060
1.5824
1.3403
1.3360
1.3283
1.3237
1.3043
0.8276
0.8059
0.7919
0.6647
0.0061
0.0000
-0.0062



28 free base

Current Data Parameters

NAME Werner
EXPNO 40
PROCNO 1

F2 - Acquisition Parameters

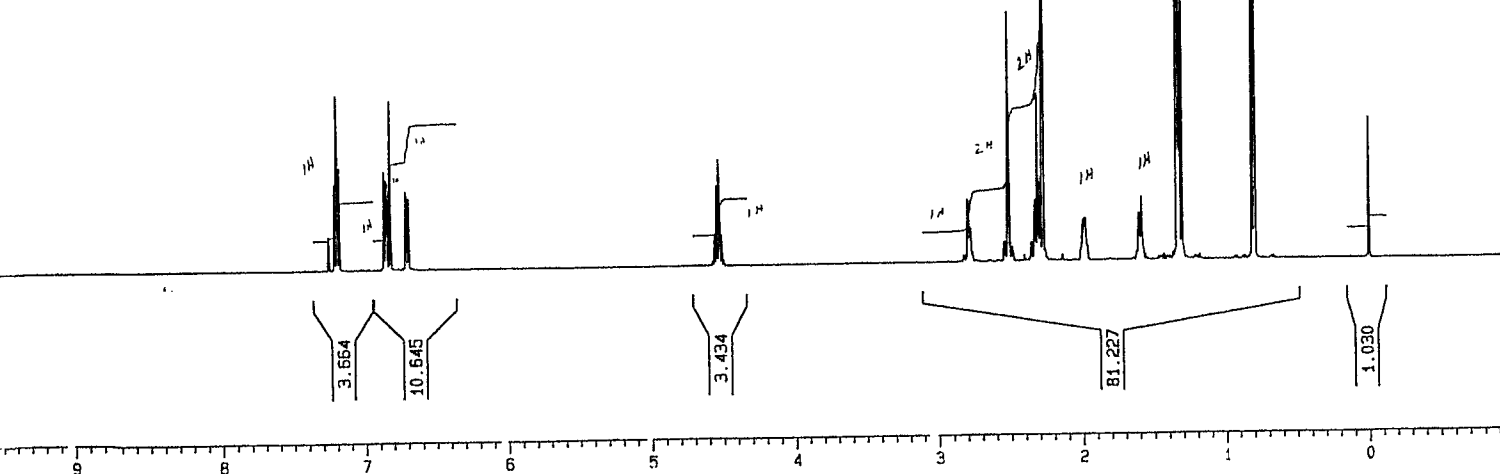
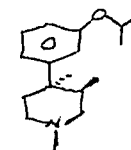
Date 940624
Time 13.24
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DQ 48.0 usec
RG 256
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters

SI 16384
SF 500.1300148 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

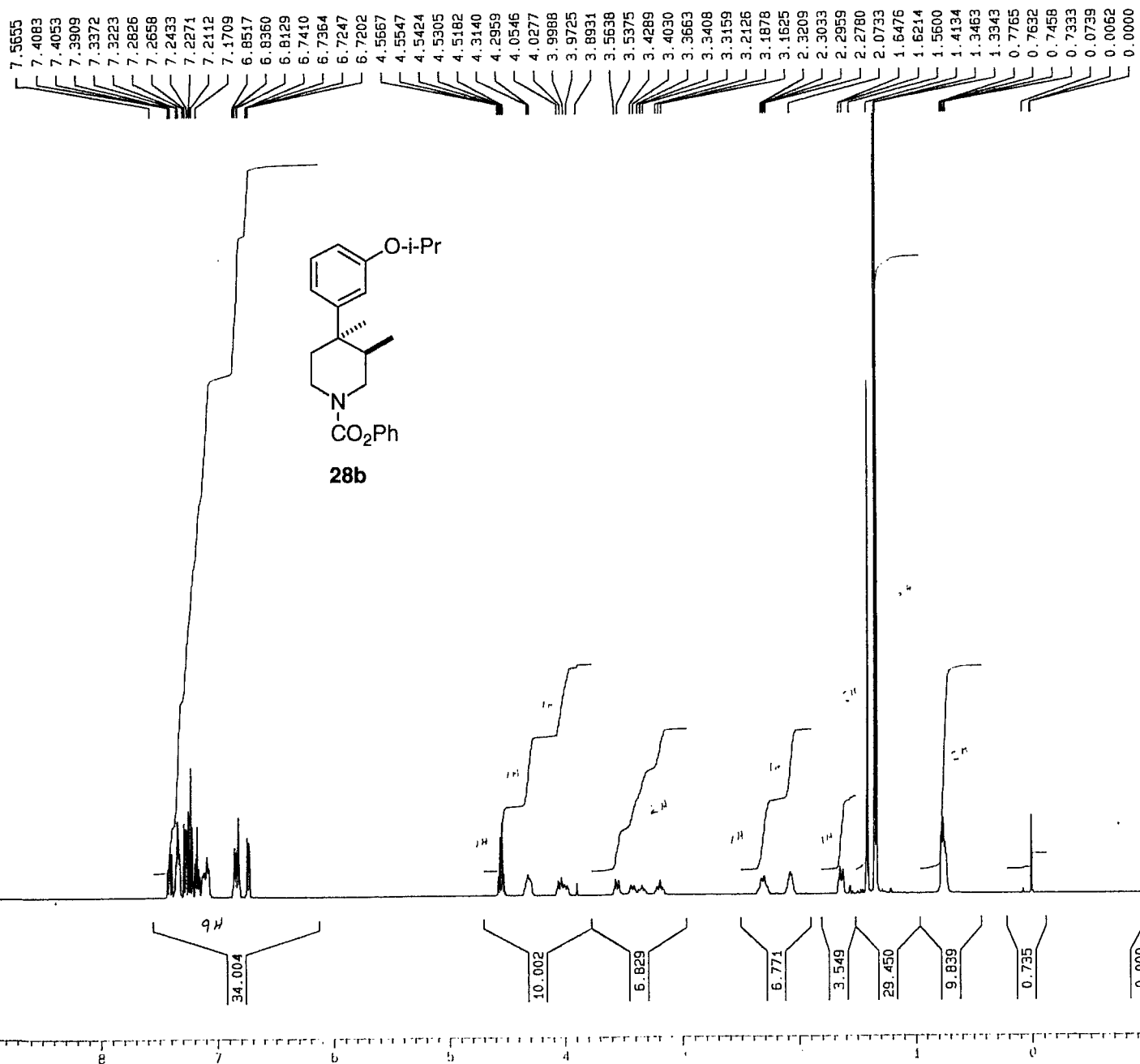
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



S-577-18

Compound

Lot# V44-CCW-286-1, CDC13



Current Data Parameters

NAME Werner
EXPNO 70
PROCNO 1

F2 - Acquisition Parameters

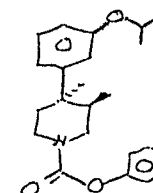
Date 940627
Time 7.59
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DM 48.0 usec
RG 180
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters

SI 16384
SF 500.1300212 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



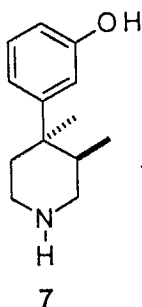
4-577-19

Compound

Lot# 216MH0, DMSO

444-CW-287-1

7.12057
7.10488
7.08919
6.72792
6.71212
6.69047
6.58246
6.57872
6.56672
6.56304



3.10669
3.10059
3.08126
3.07543
2.90407
2.88108
2.85066
2.84544
2.82618
2.82109
2.80138
2.57837
2.55457
2.02875
2.01891
2.00385
1.99405
1.97910
1.96921
1.83363
1.82648
1.82000
1.41049
1.38471
1.29683
1.13693
0.67626
0.66227

Current Data Parameters

NAME Werner
EXPNO 50
PROCNO 1

F2 - Acquisition Parameters

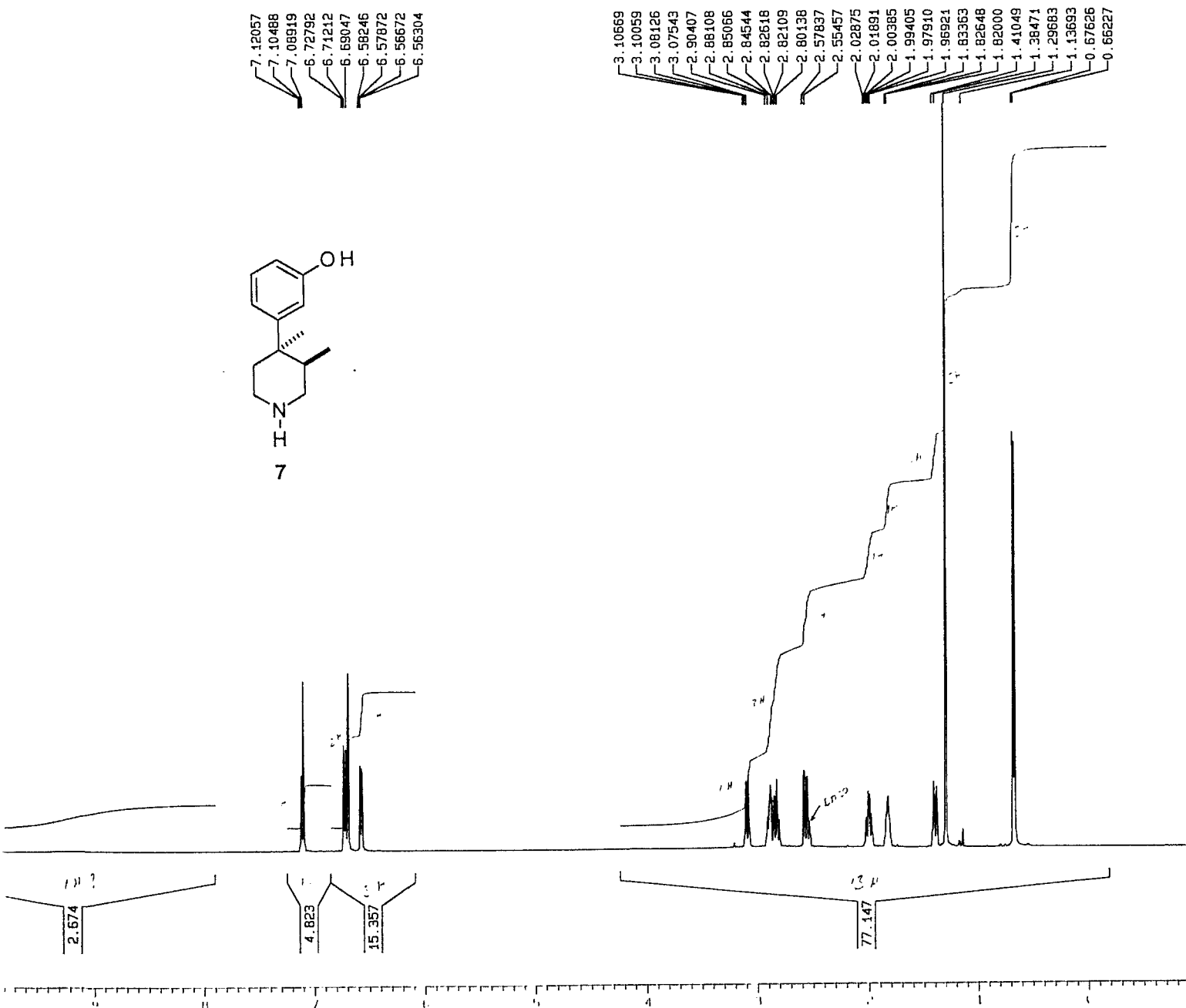
Date 940627
Time 7.37
PULPROG zg30
SOLVENT DMSO
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DM 48.0 usec
RG 256
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters

SI 16384
SF 500.1299894 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



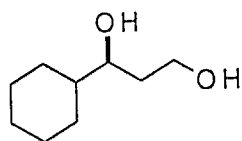
Compound

Lot #

CDC13

8.7953

7.4793
7.2723
7.2492
7.2341
7.1775
7.1636
7.1522
7.0605



31

3.8812
3.8711
3.8618
3.8147
3.8077
3.6022
3.5972
3.5913
3.5858
2.8860
2.6609
2.6556
1.9603
1.7687
1.7614
1.7535
1.7019
1.6927
1.6856
1.6773
1.6754
1.6678
1.6631
1.6593
1.2556
1.2477
1.2301
1.2223
1.1533
1.0391
1.0147
0.9908
0.1167
0.0696
0.0057
0.0000
-0.0066

Current Data Parameters

NAME Werner
EXPNO 80
PROCNO 1

F2 - Acquisition Parameters

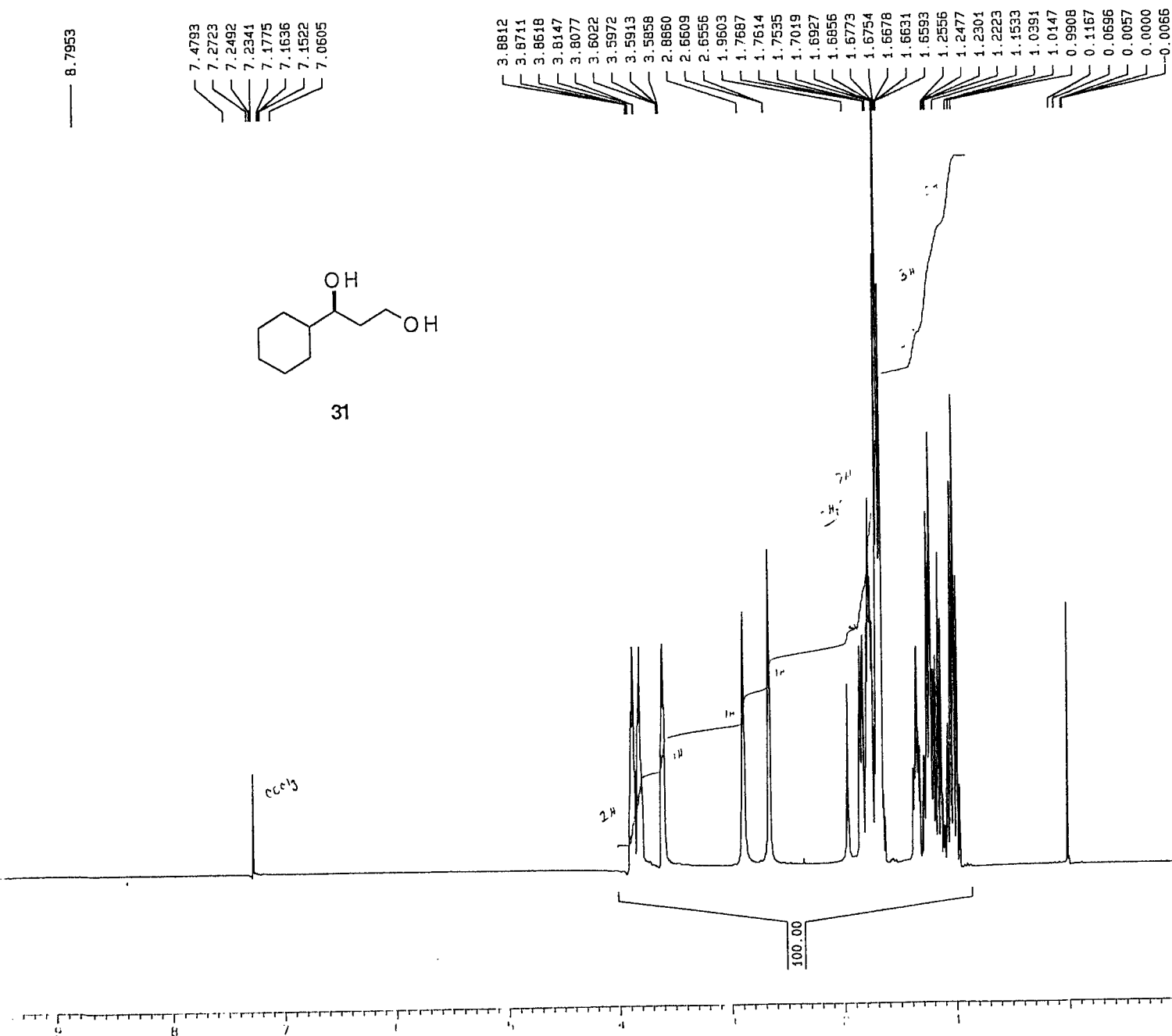
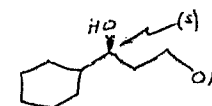
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Time 8.07
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SOLVENT CDC13
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FIDRES 0.317891 Hz
DQ 48.0 usec
RG 128
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters

SI 16384
SF 500.1300067 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

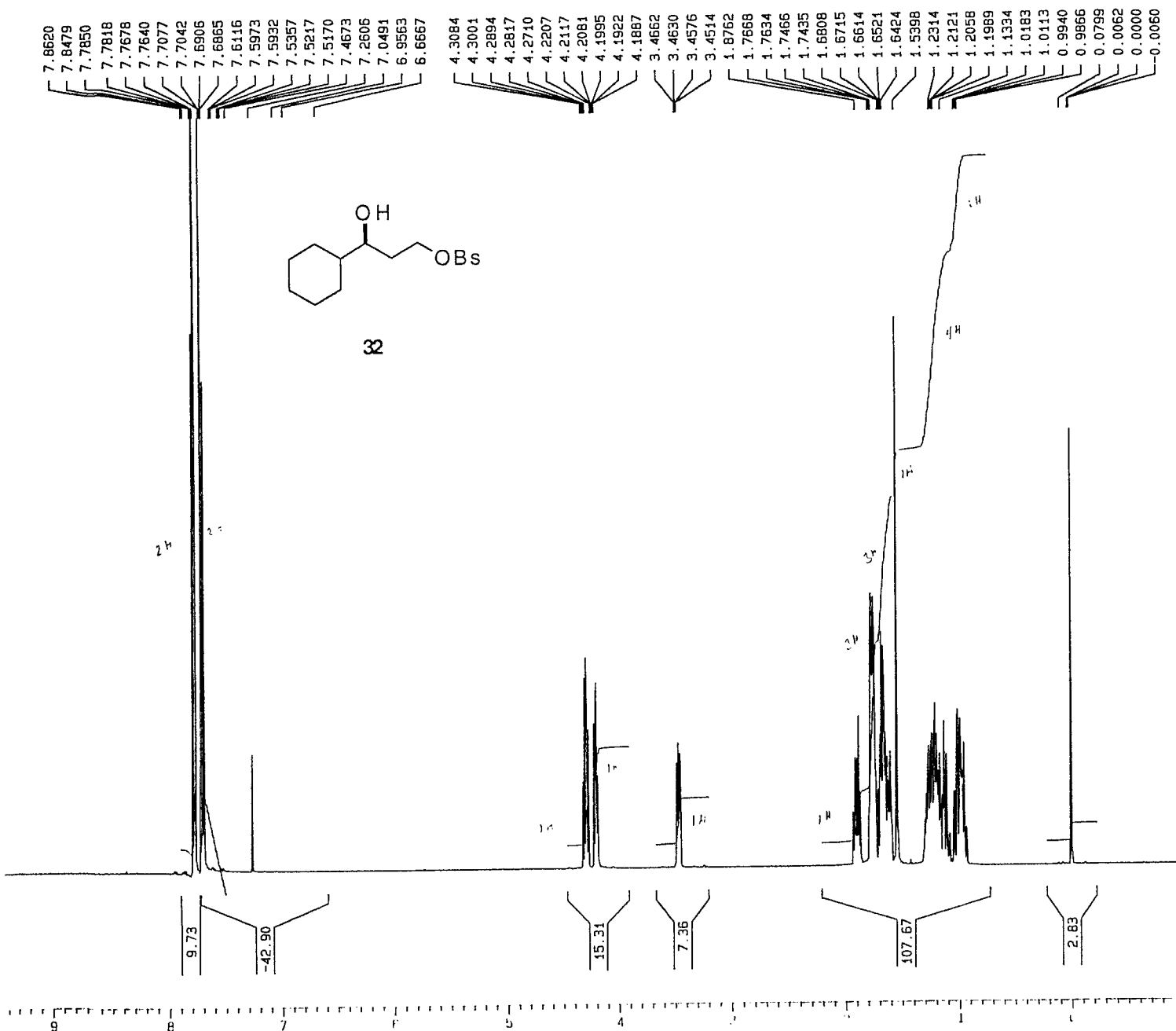
1D NMR plot parameters

CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



5-5977-21

Compound , Lot# V44-1FT-100, CDC13



Current Data Parameters

NAME Werner
EXPNO 90
PROCNO 1

F2 - Acquisition Parameters

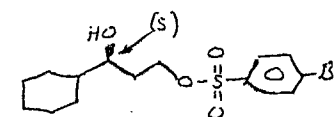
Date 940627
Time 8.16
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DW 48.0 usec
RG 360
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1300128 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters

SI 16384
SF 500.1300128 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

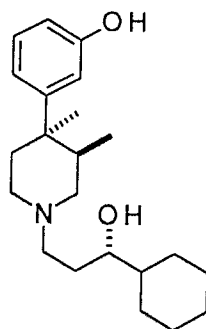
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



Compound

Lot# V44-1FT-93-1, CDC13

7.4114
7.2550
7.2343
7.0945
7.0787
7.0629
7.0230
6.7073
6.6913
6.6727
6.6201
6.6067
6.6025
6.5908
6.5866
6.5503
6.5346
6.5174
6.4462
6.4304
6.1962
6.1301
4.1159
4.1159
3.9963
3.9817
3.9776
3.9668
3.9636
2.8150
2.6756
2.6709
2.5986
2.4586
2.4549
2.3848
2.3790
2.3619
2.3560
1.9281
1.9250
1.7291
1.7044
1.6900
1.6567
1.6507
1.6367
1.6314
1.5590
1.5576
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1.2773
1.2010
1.0094
0.5447
0.5305
0.5089
0.0060
0.0000



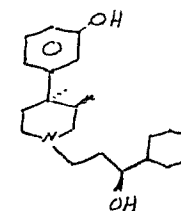
LY255582 (1)

Current Data Parameters
NAME Werner
EXPNO 60
PROCNO 1

F2 - Acquisition Parameters
Date 940627
Time 7.50
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DQ 48.0 usec
RG 128
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

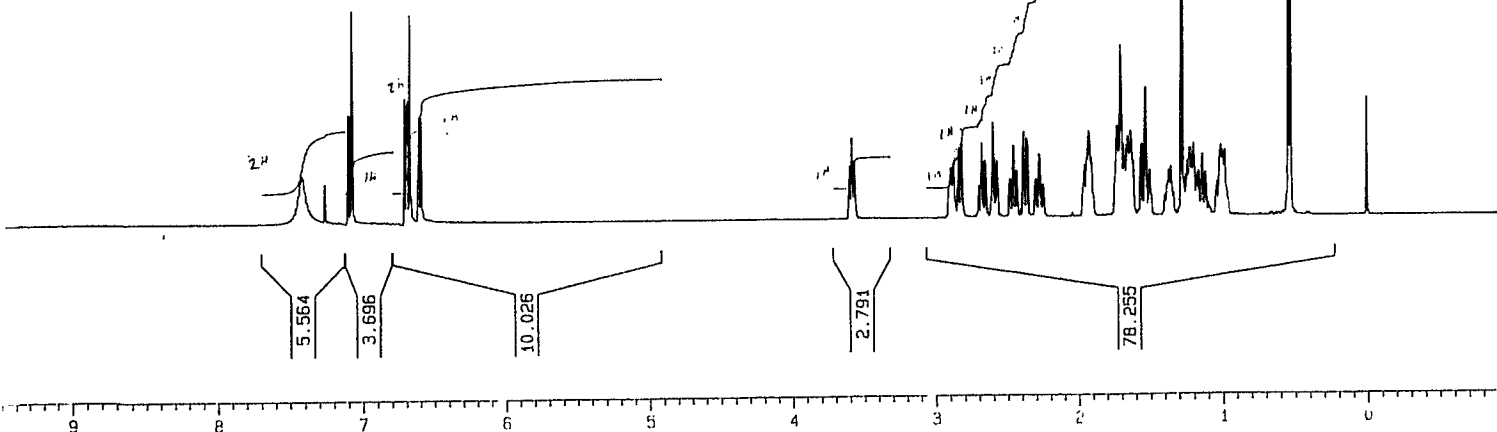
F2 - Processing parameters
SI 16384
SF 500.1300155 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



35-150407

9-547-22



Compound

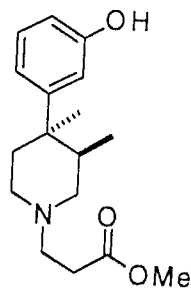
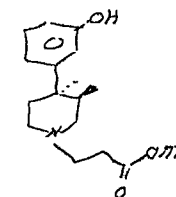
Lot# AV3-CIW-191A, CDC13

Current Data Parameters
 NAME Werner
 EXPNO 260
 PROCNO 1

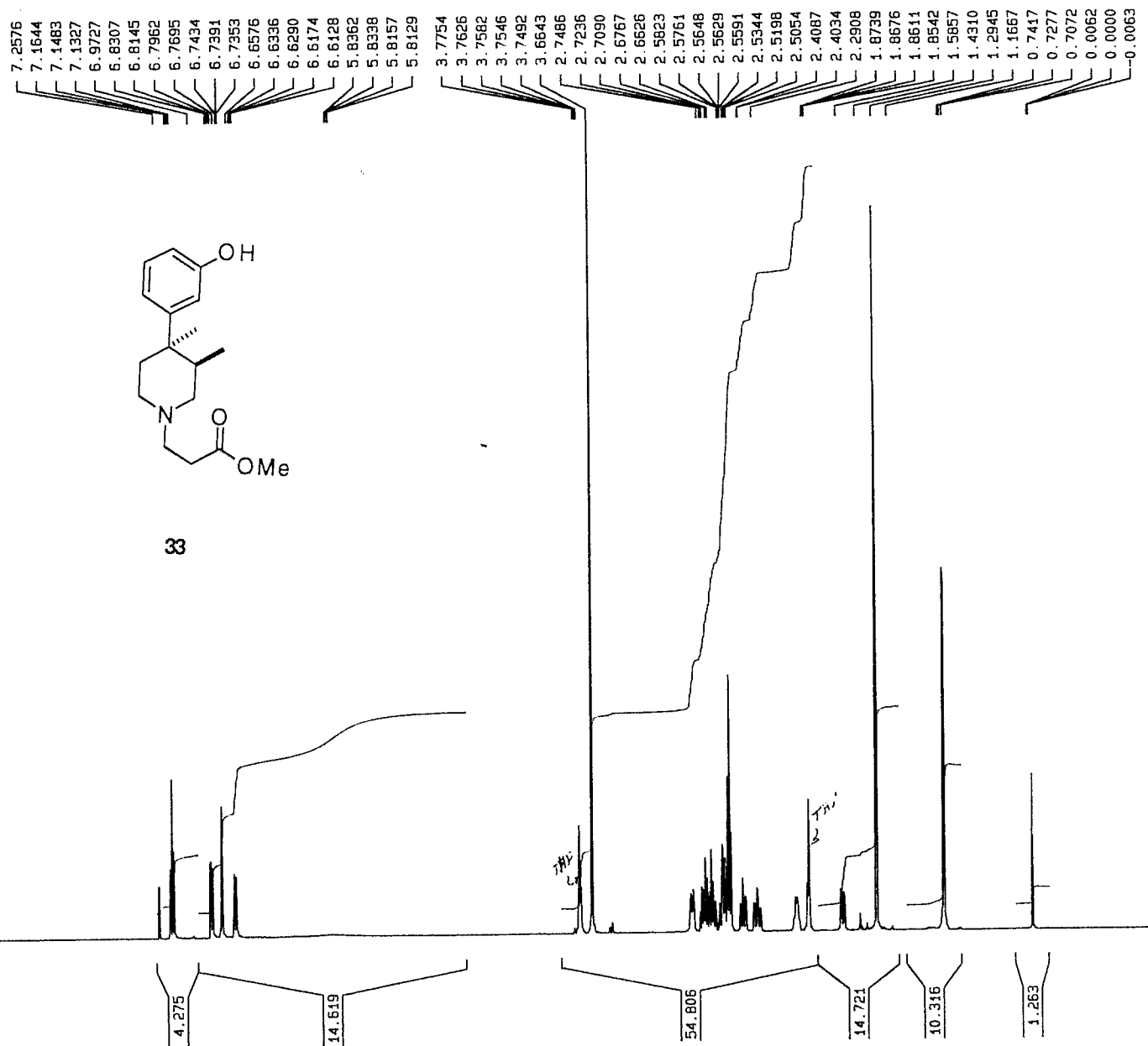
F2 - Acquisition Parameters
 Date 940706
 Time 13.41
 PULPROG zg30
 SOLVENT CDC13
 AQ 1.5728840 sec
 FIDRES 0.317891 Hz
 DW 48.0 usec
 RG 360
 NUCLEUS 1H
 D1 1.0000000 sec
 P1 11.0 usec
 DE 68.6 usec
 SFO1 500.1330634 MHz
 SWH 10416.67 Hz
 TD 32768
 NS 64
 DS 2

F2 - Processing parameters
 SI 16384
 SF 500.1300141 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 30.00 cm
 F1P 11.000 ppm
 F1 5501.43 Hz
 F2P -1.000 ppm
 F2 -500.13 Hz

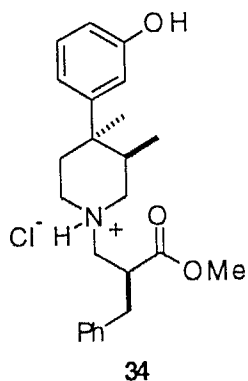


33



4-597-24

Compound , Lot# V44-1FT-271-1, DMSO

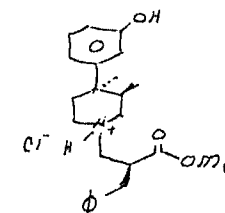


Current Data Parameters
NAME Werner
EXPNO 310
PROCNO 1

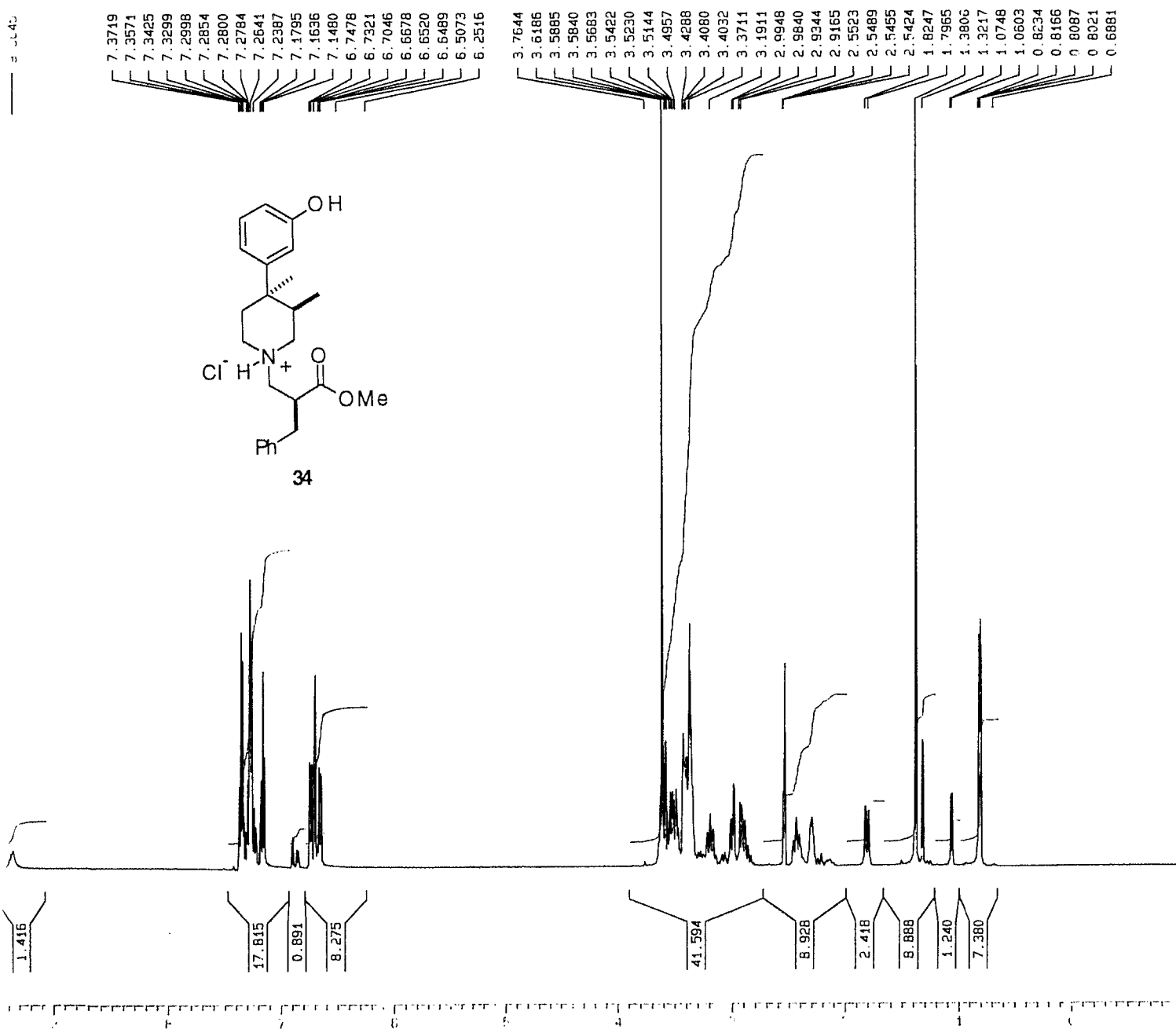
F2 - Acquisition Parameters
Date 940707
Time 8.20
PULPROG zg30
SOLVENT DMSO
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DW 48.0 usec
RG 715
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters
SI 16384
SF 500.1299823 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz

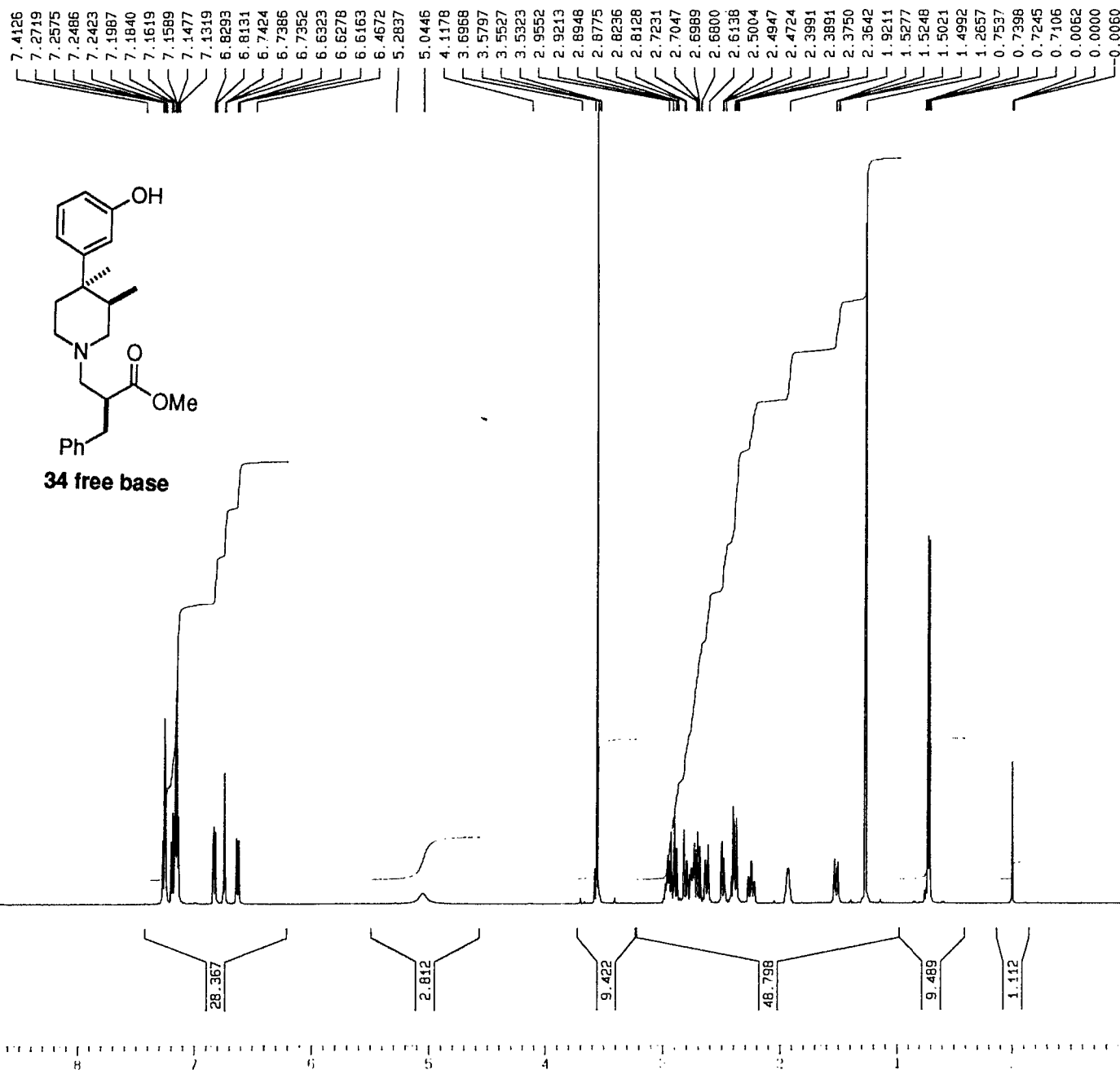


3R,4R,αS



6-597-25
25

Compound # . Lot# V44-CCw-4-1, CDC13

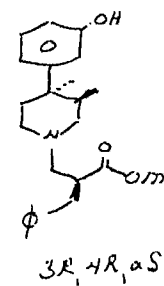


Current Data Parameters
NAME Werner
EXPNO 240
PROCNO 1

F2 - Acquisition Parameters
Date 940706
Time 13.19
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DW 48.0 usec
RG 360
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 64
DS 2

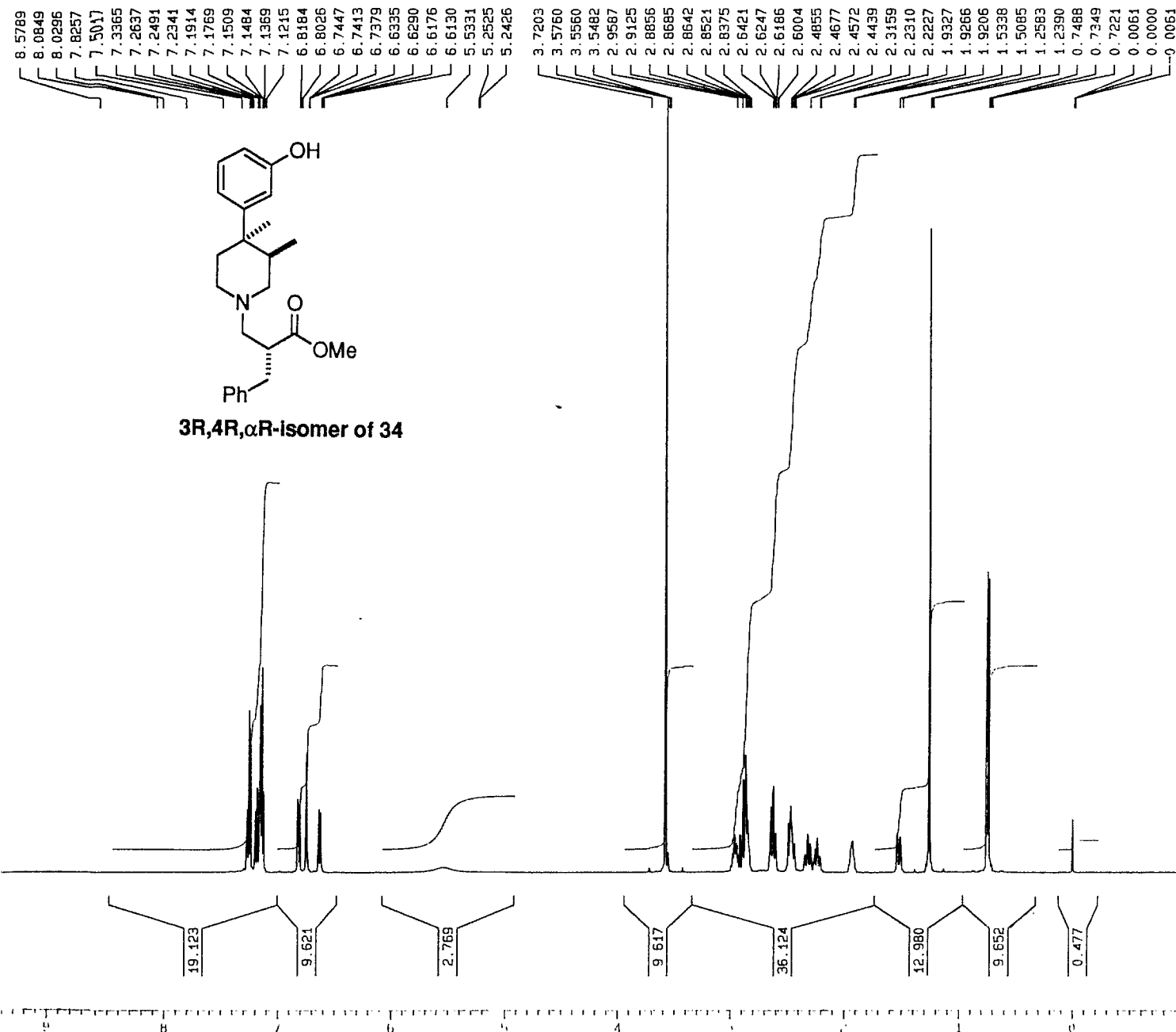
F2 - Processing parameters
SI 16384
SF 500.1300186 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



4-597-26
26

Compound # , Lot# V44-CCW-2-1, CDC13

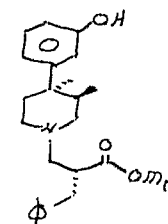


Current Data Parameters
NAME Werner
EXPNO 250
PROCNO 1

F2 - Acquisition Parameters
Date 940706
Time 13.30
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DN 48.0 usec
RG 180
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SFO1 500.1330634 MHz
SMH 10416.67 Hz
TD 32768
NS 64
DS 2

F2 - Processing parameters
SI 16384
SF 500.1300231 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



3R,4R,αR

Compound , Lot# AV3-4YL-97B, DMSO

Current Data Parameters

NAME Werner
EXPNO 320
PROCNO 1

F2 - Acquisition Parameters

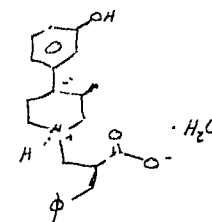
Date 940707
Time 8.30
PULPROG zg30
SOLVENT DMSO
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DQ 48.0 usec
RG 360
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters

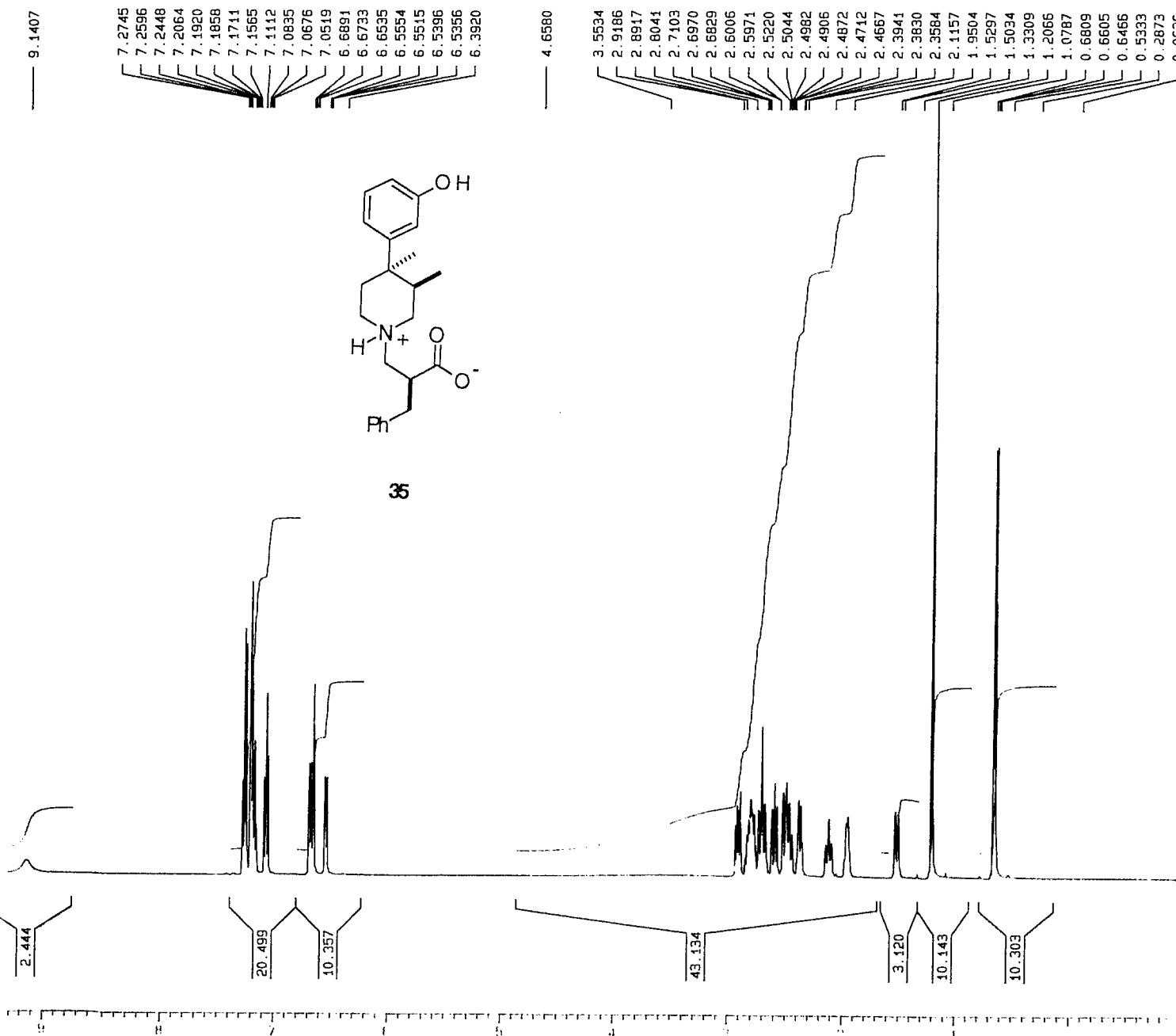
SI 16384
SF 500.1300115 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz

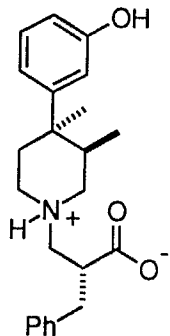


32, 42, xS

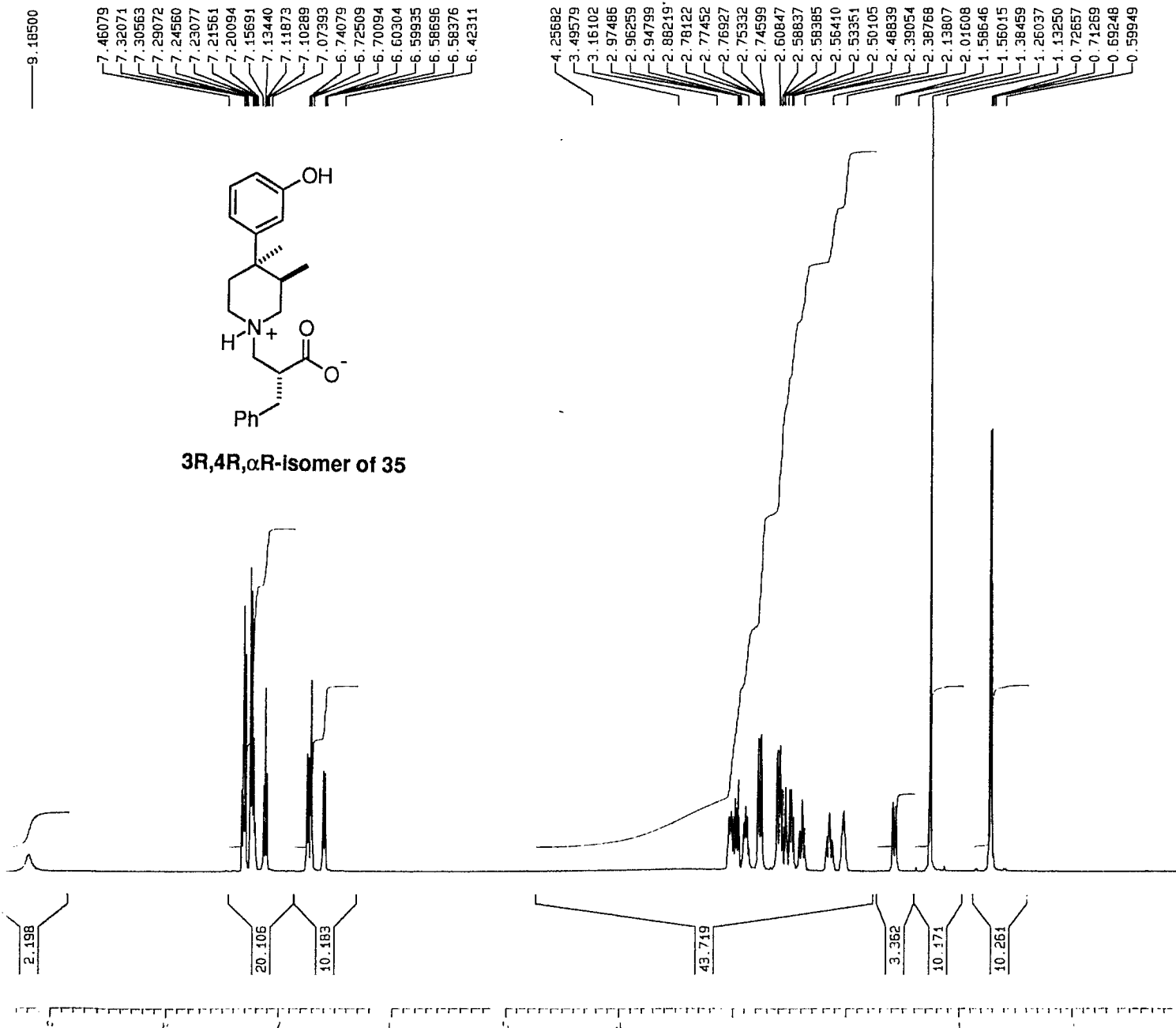


4-577-28

Compound Lot # AV3-6YN-28A, DMSO



3R,4R,αR-isomer of 35

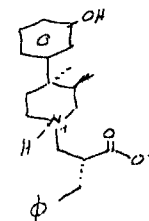


Current Data Parameters
NAME Werner
EXPNO 340
PROCNO 1

F2 - Acquisition Parameters
Date 940707
Time 8.49
PULPROG zg30
SOLVENT DMSO
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DW 48.0 usec
RG 512
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SNH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters
SI 16384
SF 500.1299881 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



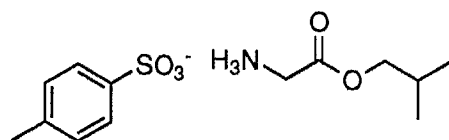
3R,4R,αR

Compound

V44-1FT-173-1, CDC13

8.0358
7.9466
7.8935
7.8756
7.7698
7.7529
7.7295
7.7133
7.5639
7.5506
7.4636
7.2972
7.2572
7.1523
7.1132
7.0972
7.0454
6.9525
6.9385

4.0097
3.9478
3.9344
3.8431
3.8295
3.8029
3.7897
3.6701
3.5213
3.4060
2.4552
2.3706
2.3304
2.2894
2.2020
2.0275
1.8529
1.8395
1.8259
1.8126
1.7991
1.7857
1.7722
1.7588
1.7454
1.4558
0.9590
0.9458
0.9064
0.8755
0.8620
0.8353
0.8217
0.7079
0.6943
0.0001
0.0000
-0.0000



36

Current Data Parameters

NAME Werner
EXPNO 440
PROCNO 1

F2 - Acquisition Parameters

Date 941223
Time 10.33
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DQ 48.0 usec
RG 715
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters

SI 16384
SF 500.1300153 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz
PPMCM 0.40000 ppm/cm
HZCM 200.05200 Hz/cm

23.059

9.643

18.482

13.546

4.127

1.754

26.769

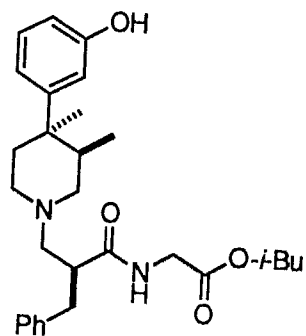
2.420

4-597-29

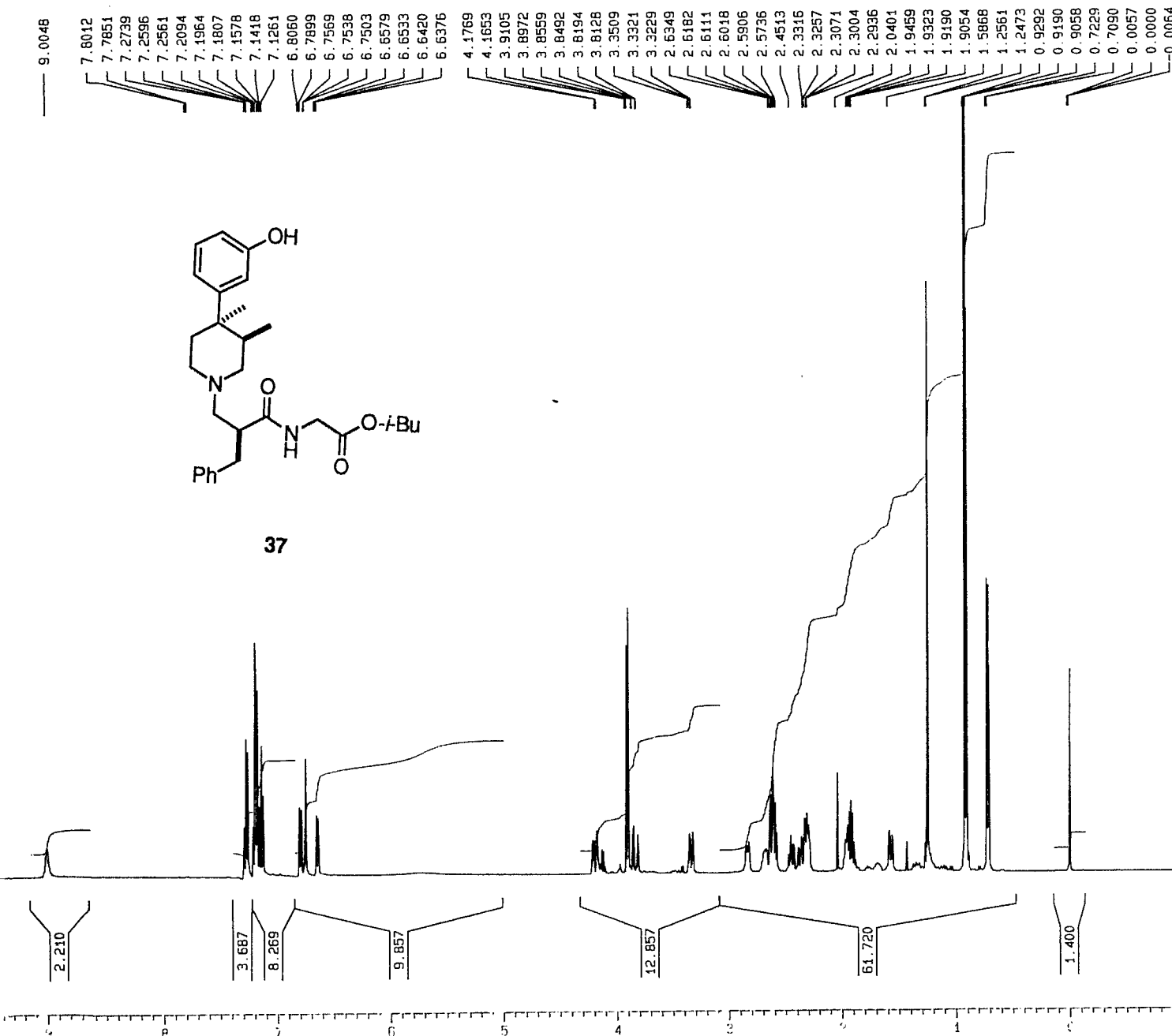
9-571-30
30

Compound

Lot# E29-144NK2, CDC13



37

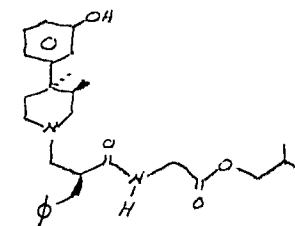


Current Data Parameters
NAME Werner
EXPNO 270
PROCNO 1

F2 - Acquisition Parameters
Date 940705
Time 13.52
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DW 48.0 usec
RG 512
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SMH 10416.67 Hz
TD 32768
NS 64
DS 2

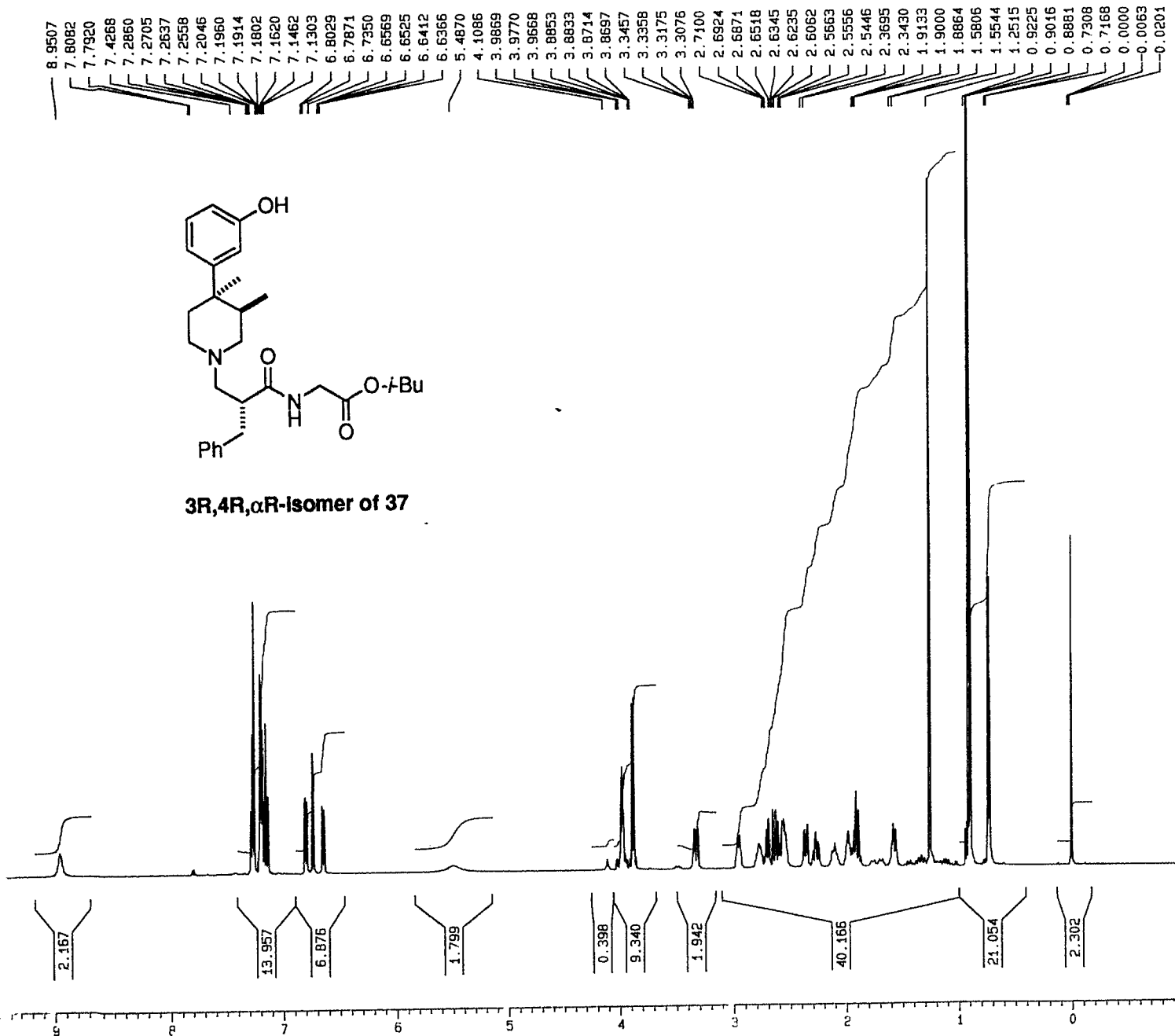
F2 - Processing parameters
SI 16384
SF 500.1300150 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



3R, 4R, & S

Compound Lot# V44-CCW-14-1, CDC13

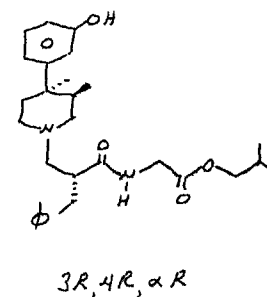


Current Data Parameters
NAME Werner
EXPNO 280
PROCNO 1

F2 - Acquisition Parameters
Date 940706
Time 14.05
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DM 48.0 usec
RG 715
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

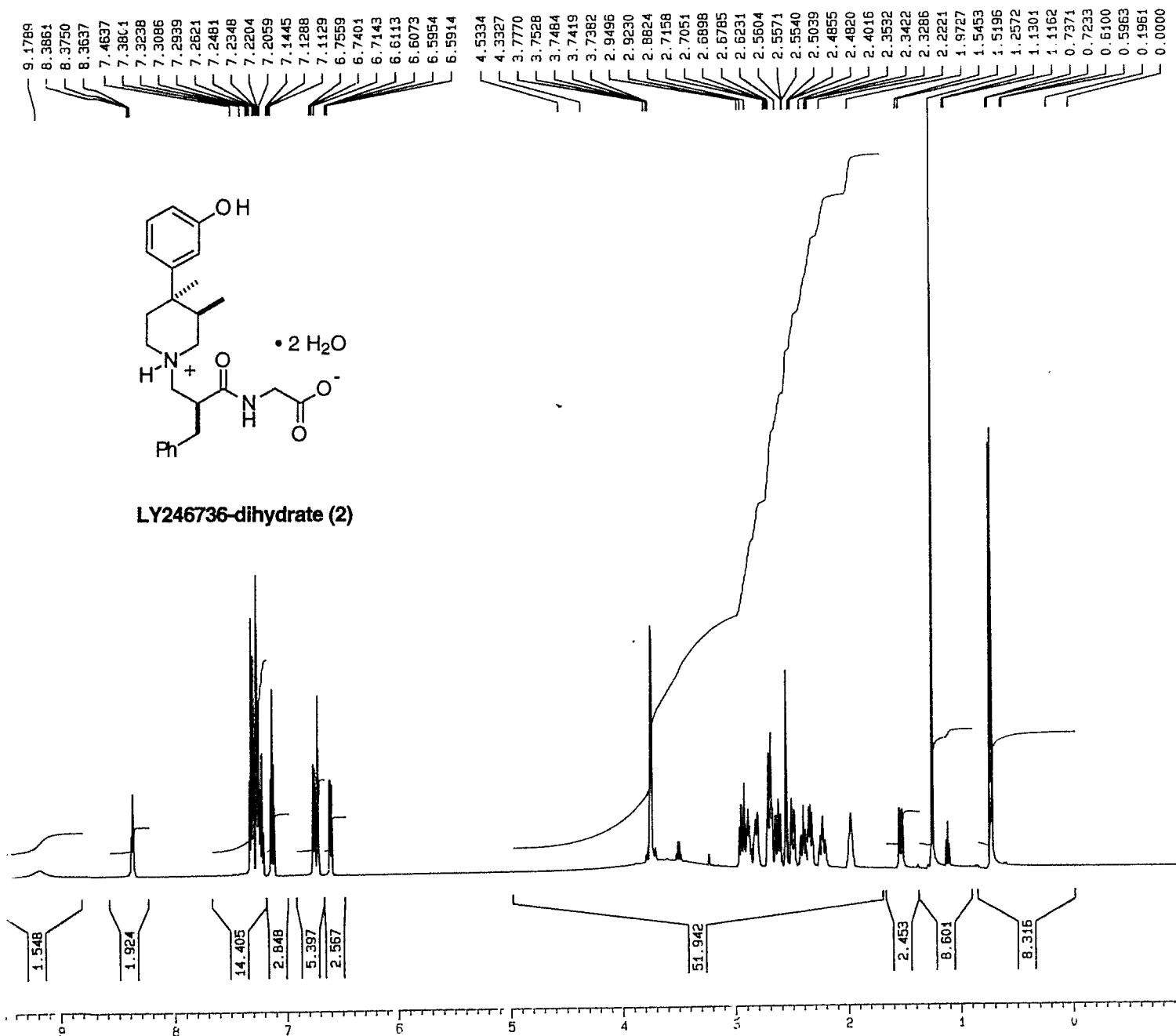
F2 - Processing parameters
SI 16384
SF 500.1300150 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



Compound

Lot# 284MH2, DMSO



Current Data Parameters

NAME Werner
EXPNO 290
PROCNO 1

F2 - Acquisition Parameters

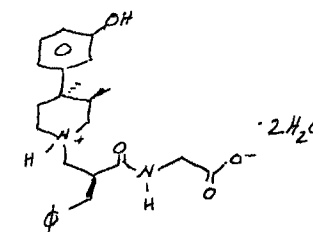
Date 940707
Time 7.57
PULPROG zg30
SOLVENT DMSO
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DW 48.0 usec
RG 715
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SMH 10416.67 Hz
TD 32768
NS 64
DS 2

F2 - Processing parameters

SI 16384
SF 500.1299765 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

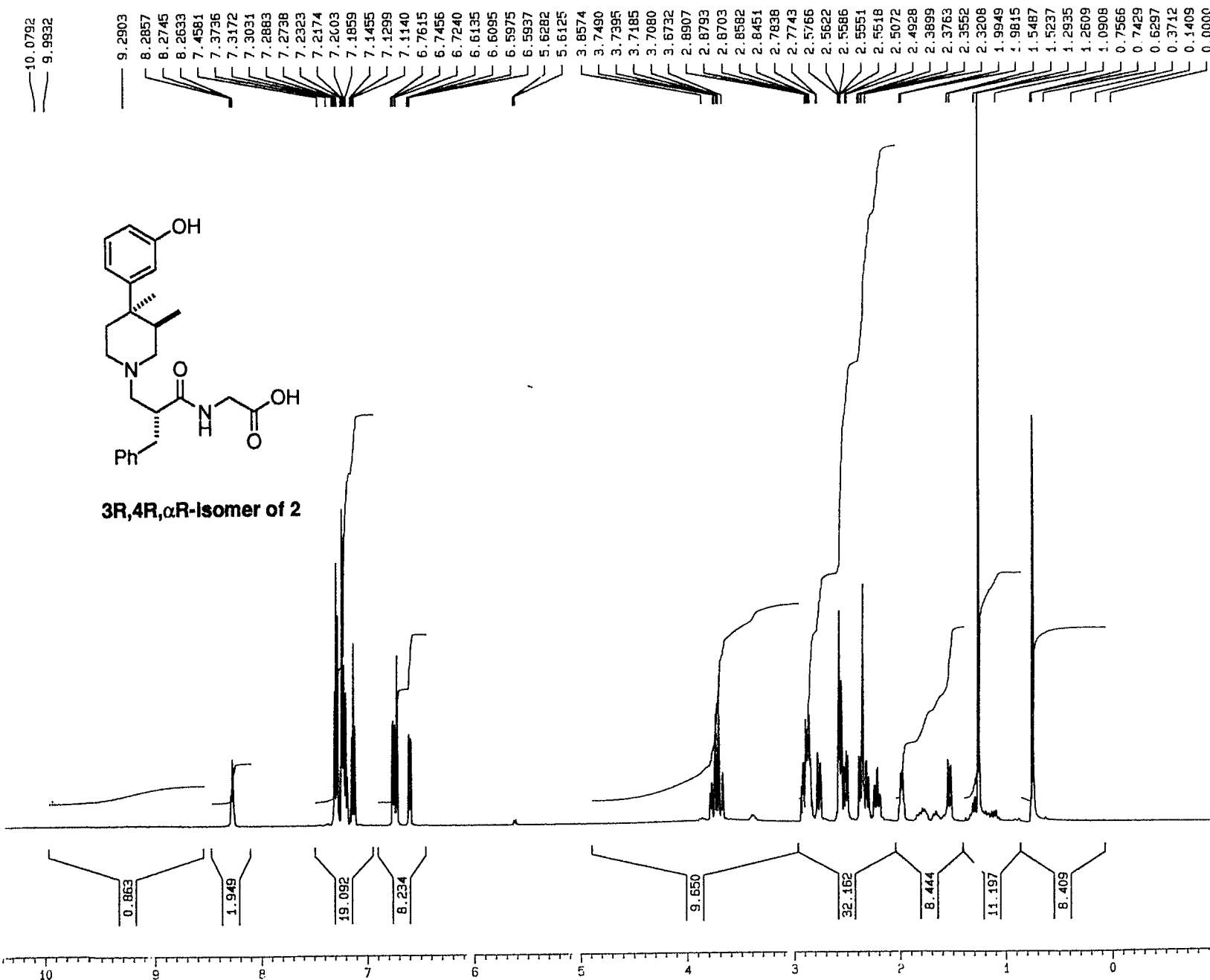
CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



4-5977-32

Compound

Lot# V44-CCW-17-1, DMSO

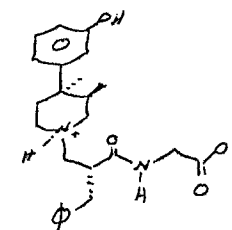


Current Data Parameters
 NAME Werner
 EXPNO 300
 PROCNO 1

F2 - Acquisition Parameters
 Date 940707
 Time 8.09
 PULPROG zg30
 SOLVENT DMSO
 AQ 1.5728840 sec
 FIDRES 0.317891 Hz
 DW 48.0 usec
 RG 512
 NUCLEUS 1H
 D1 1.0000000 sec
 P1 11.0 usec
 DE 68.6 usec
 SF01 500.1330634 MHz
 SWH 10416.67 Hz
 TD 32768
 NS 64
 DS 2

F2 - Processing parameters
 SI 16384
 SF 500.1299774 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 30.00 cm
 F1P 11.000 ppm
 F1 5501.43 Hz
 F2P -1.000 ppm
 F2 -500.13 Hz



3R,4R,αR

Compound , Lot# V44-US1-138-1, CDC13

Current Data Parameters

NAME Werner
EXPNO 140
PROCNO 1

F2 - Acquisition Parameters

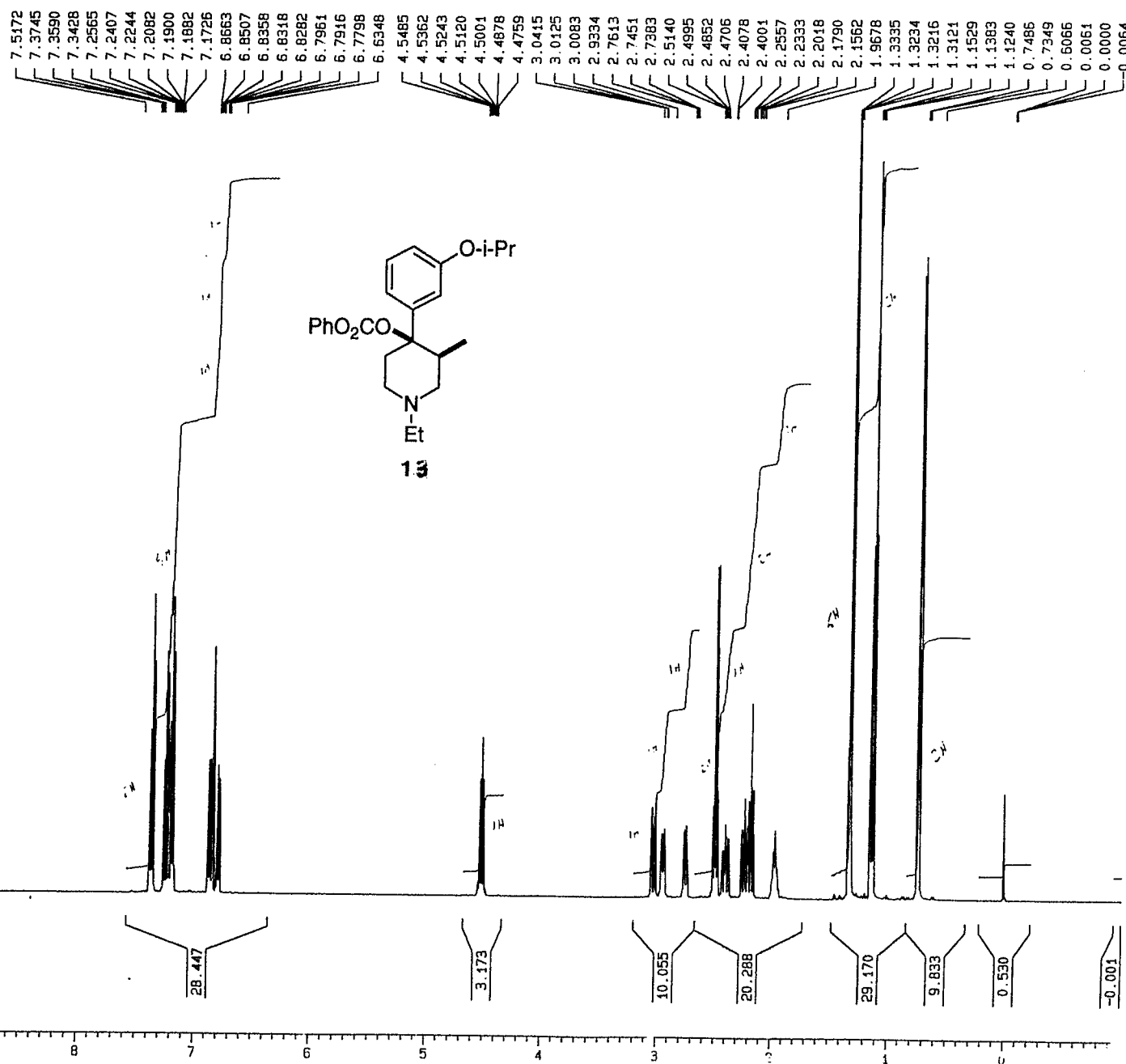
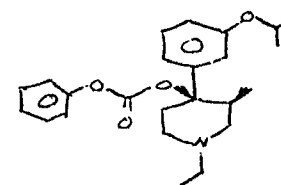
Date 940627
Time 12.47
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DQ 48.0 usec
RG 128
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SMH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters

SI 16384
SF 500.1300166 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz



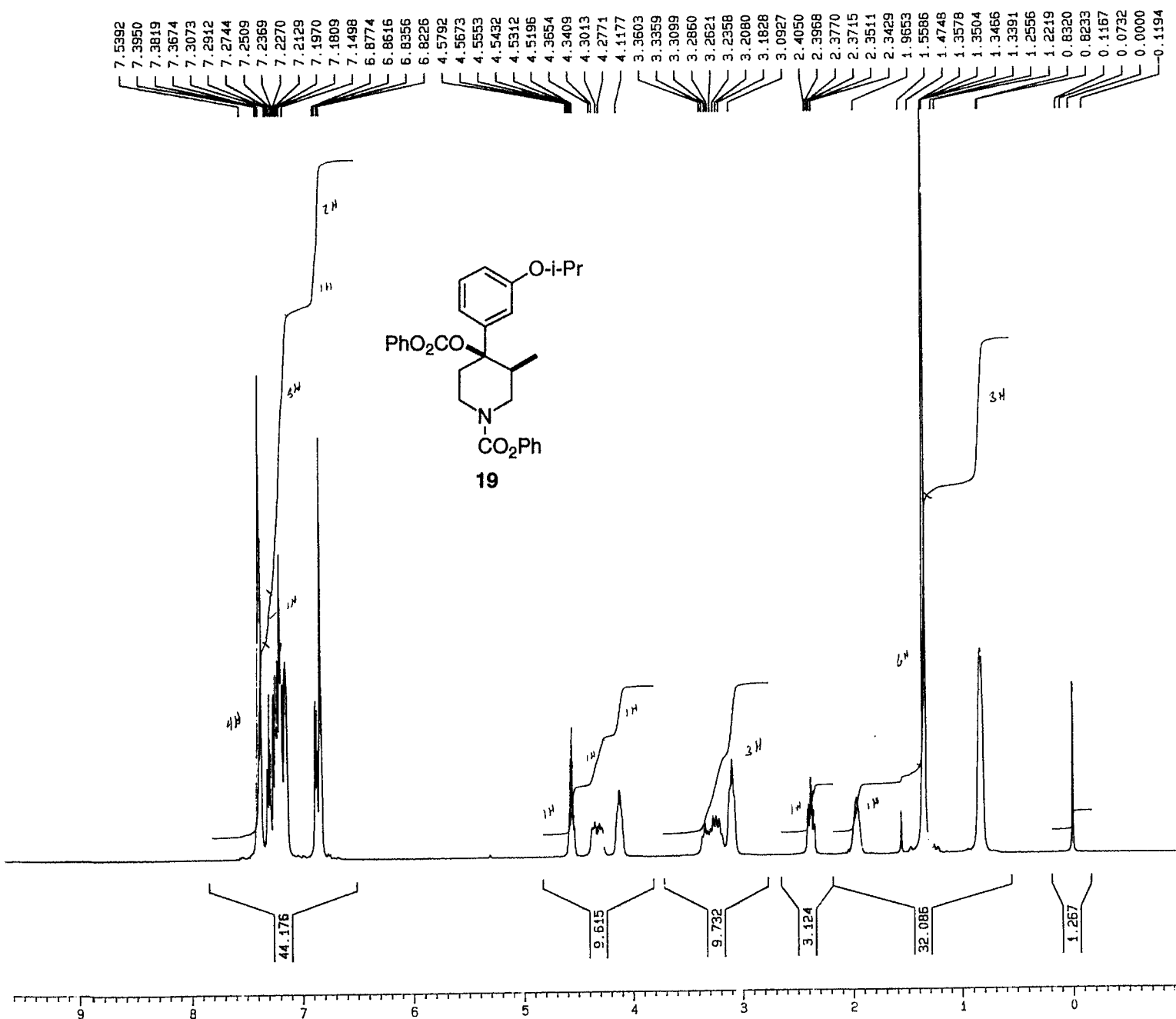
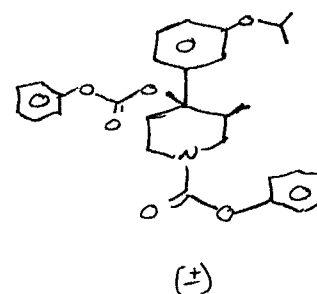
V44-US1-76-4, CDC13

Current Data Parameters
 NAME Werner
 EXPNO 360
 PROCNO 1

F2 - Acquisition Parameters
 Date 940922
 Time 10.18
 PULPROG zg30
 SOLVENT CDC13
 AQ 1.5728840 sec
 FIDRES 0.317891 Hz
 DM 48.0 usec
 RG 360
 NUCLEUS 1H
 D1 1.0000000 sec
 P1 11.0 usec
 DE 68.6 usec
 SF01 500.1330634 MHz
 SWH 10416.67 Hz
 TD 32768
 NS 16
 DS 2

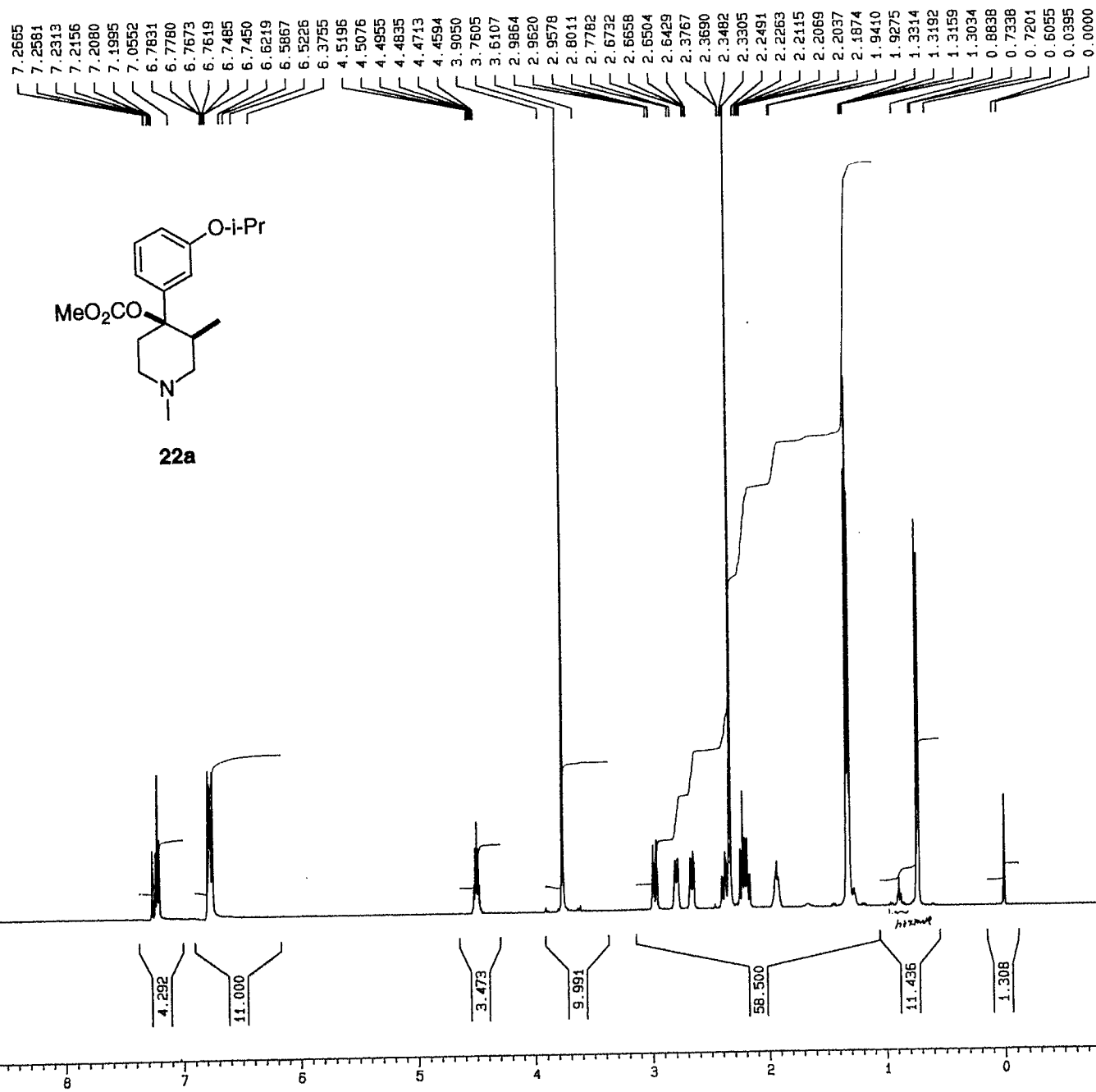
F2 - Processing parameters
 SI 16384
 SF 500.1300183 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 30.00 cm
 F1P 11.000 ppm
 F1 5501.43 Hz
 F2P -1.000 ppm
 F2 -500.13 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 200.05200 Hz/cm



Compound

Lot # V44-CCW-288-1

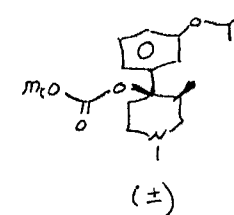


Current Data Parameters
 NAME Werner
 EXPNO 350
 PROCNO 1

F2 - Acquisition Parameters
 Date 940801
 Time 13.18
 PULPROG zg30
 SOLVENT CDC13
 AQ 1.5728840 sec
 FIDRES 0.317891 Hz
 DM 48.0 usec
 RG 715
 NUCLEUS 1H
 D1 1.0000000 sec
 P1 11.0 usec
 DE 68.6 usec
 SF01 500.1330634 MHz
 SWH 10416.67 Hz
 TD 32768
 NS 16
 DS 2

F2 - Processing parameters
 SI 16384
 SF 500.1300134 MHz
 WDM EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

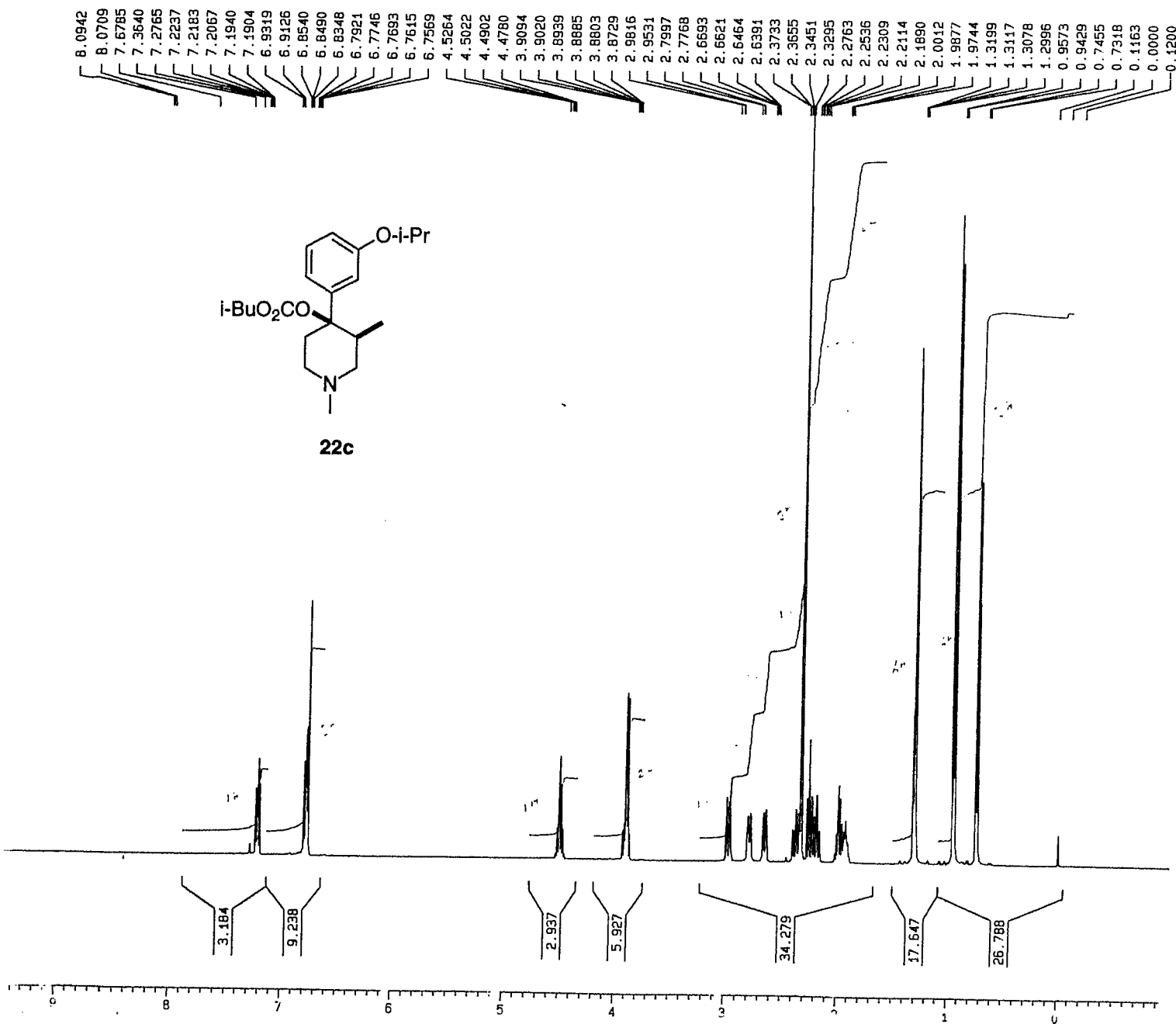
1D NMR plot parameters
 CX 30.00 cm
 F1P 11.000 ppm
 F1 5501.43 Hz
 F2P -1.000 ppm
 F2 -500.13 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 200.05200 Hz/cm



57-36
36

Compound

Lot# V44-219-1, CDC13

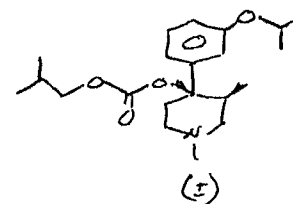


Current Data Parameters
 NAME Werner
 EXPNO 110
 PROCNO 1

F2 - Acquisition Parameters
 Date 940627
 Time 8.31
 PULPROG zg30
 SOLVENT CDC13
 AQ 1.5728840 sec
 FIDRES 0.317891 Hz
 DW 48.0 usec
 RG 45
 NUCLEUS 1H
 D1 1.0000000 sec
 P1 11.0 usec
 DE 68.6 usec
 SFO1 500.1330634 MHz
 SWH 10416.67 Hz
 TD 32768
 NS 16
 DS 2

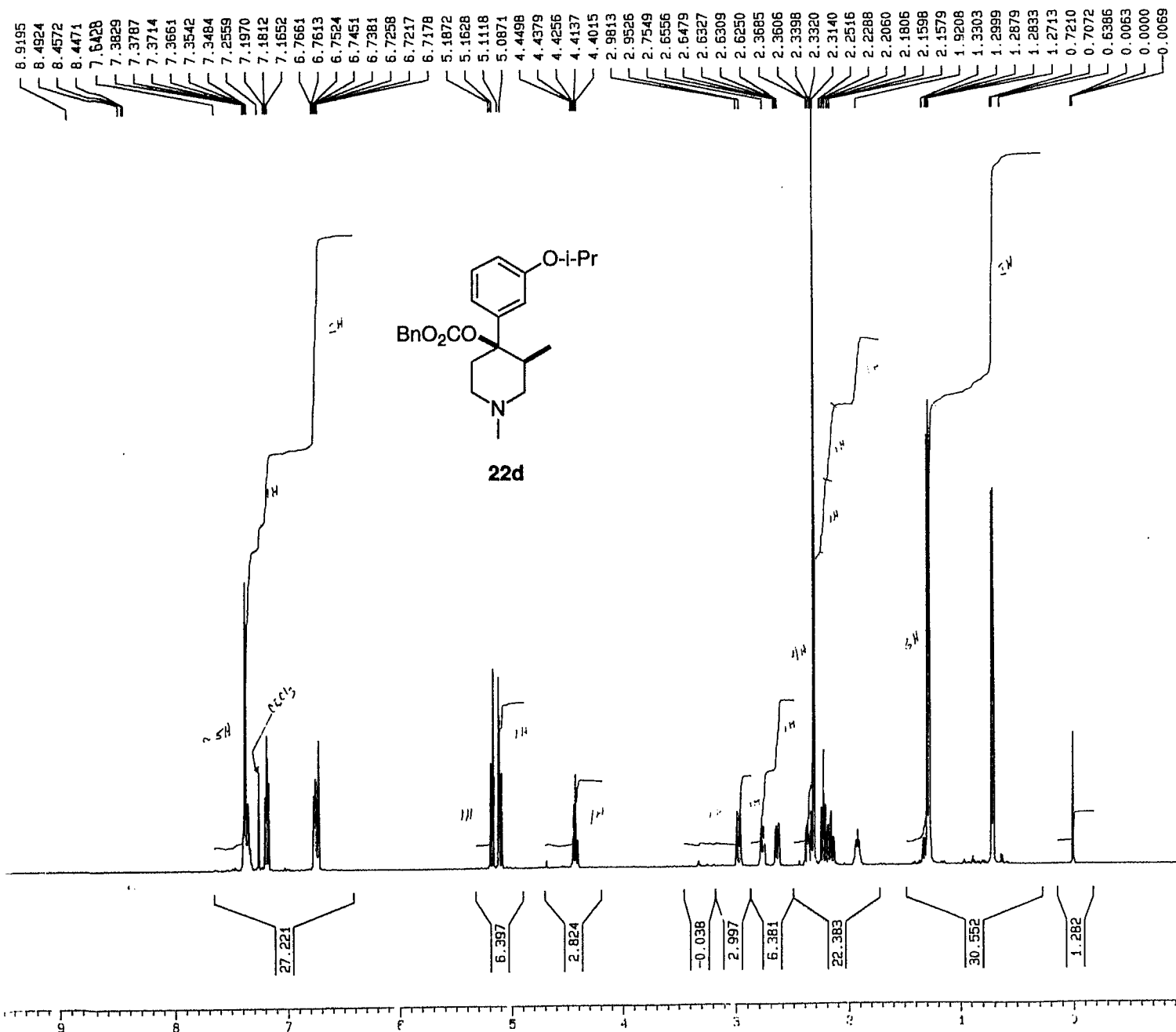
F2 - Processing parameters
 SI 16384
 SF 500.1300051 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 30.00 cm
 F1P 11.000 ppm
 F1 5501.43 Hz
 F2P -1.000 ppm
 F2 -500.13 Hz



4-577-38
38

Compound , Lot#V44-8EZ-223-3, CDC13

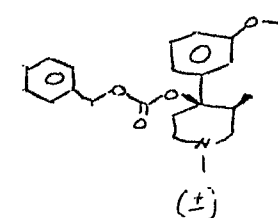


Current Data Parameters
 NAME Werner
 EXPNO 180
 PROCNO 1

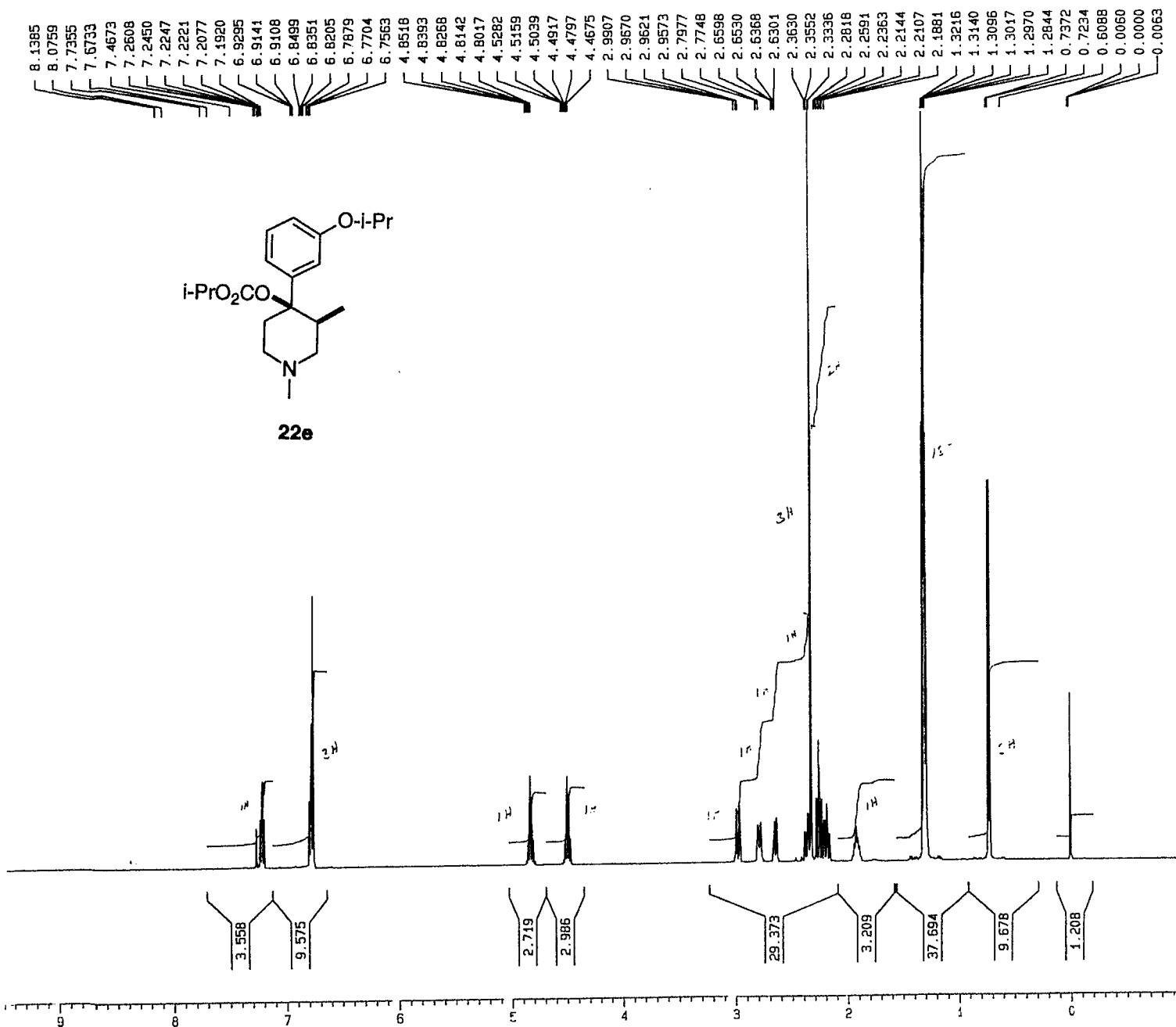
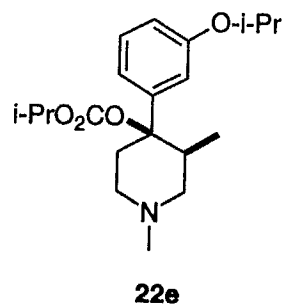
F2 - Acquisition Parameters
 Date 940627
 Time 13.40
 PULPROG zg30
 SOLVENT CDC13
 AQ 1.5728840 sec
 FIDRES 0.317891 Hz
 DW 48.0 usec
 RG 256
 NUCLEUS 1H
 D1 1.0000000 sec
 P1 11.0 usec
 DE 68.6 usec
 SF01 500.1330634 MHz
 SWH 10416.67 Hz
 TD 32768
 NS 16
 DS 2

F2 - Processing parameters
 SI 16384
 SF 500.1300152 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 30.00 cm
 F1P 11.000 ppm
 F1 5501.43 Hz
 F2P -1.000 ppm
 F2 -500.13 Hz



31 peaks

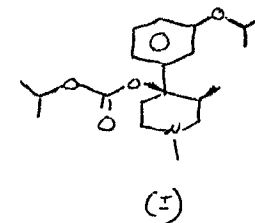
4-547-39
39Compound , Lot# V44-8EZ-²³⁰⁻¹~~229-2~~, CDCL₃

Current Data Parameters
 NAME Werner
 EXPNO 160
 PROCNO 1

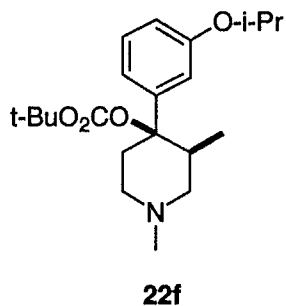
F2 - Acquisition Parameters
 Date 940627
 Time 13.12
 PULPROG zg30
 SOLVENT CDCL₃
 AQ 1.5728840 sec
 FIDRES 0.317891 Hz
 DW 48.0 usec
 RG 256
 NUCLEUS ¹H
 D1 1.0000000 sec
 P1 11.0 usec
 DE 68.6 usec
 SF01 500.1330634 MHz
 SNH 10416.67 Hz
 TD 32768
 NS 64
 DS 2

F2 - Processing parameters
 SI 16384
 SF 500.1300128 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 30.00 cm
 F1P 11.000 ppm
 F1 5501.43 Hz
 F2P -1.000 ppm
 F2 -500.13 Hz



Compound , Lot# V44-8EZ-224-1, CDC13



Current Data Parameters

NAME Werner
EXPNO 100
PROCNO 1

F2 - Acquisition Parameters

Date 940627
Time 8.23
PULPROG zg30
SOLVENT CDC13
AQ 1.5728840 sec
FIDRES 0.317891 Hz
DW 48.0 usec
RG 180
NUCLEUS 1H
D1 1.0000000 sec
P1 11.0 usec
DE 68.6 usec
SF01 500.1330634 MHz
SWH 10416.67 Hz
TD 32768
NS 16
DS 2

F2 - Processing parameters

SI 16384
SF 500.1300112 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 30.00 cm
F1P 11.000 ppm
F1 5501.43 Hz
F2P -1.000 ppm
F2 -500.13 Hz

