Synthesis of Tetrahydroisoquinoline Alkaloids via Anodic Cyanation as Key Step

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Supporting Information

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Experimental Section

General Techniques: Purification by column chromatography was performed with 70–230 mesh silica gel. TLC analyses were carried out on alumina sheets precoated with silica gel 60 F254 and visualized with UV light; R_f values are given for guidance. The ^{1}H NMR spectra were recorded with a 500 MHz or a 300 MHz spectrometer and the ^{13}C NMR spectra were recorded with a 100 MHz or a 75 MHz spectrometer. Chemical shifts are expressed in ppm downfield from TMS. Data are reported as follows: Chemical shift [multiplicity (s: singlet, d: doublet, dd: double doublet, ddd: double double doublet, dm: double multiplet, dt: double triplet, t: triplet, td triple doublet, tm, triple multiplet, tt: triple triplet, q: quartet, quint: quintuplet, m: multiplet, br: broad), coupling constants (*J*) in Hertz, integration]. Number of attached proton(s) in the ^{13}C NMR spectra was elucidated using DEPT and are described as: (p) primary, RCH_3; (s) secondary, R_2CH_2; (t) tertiary, R_3CH; (q) quaternary, R_4C. High resolution mass spectra were obtained with double focussing instrument with a source temperature of 170 °C. An ion accelerating potential of 3 kV and ionizing electrons of 70 eV were used. Elemental analyses are expressed as percentage values with the abbreviations calc.: calculated. Melting points were measured on a Kofler apparatus, the values reported in °C, and were uncorrected. For air sensitive reactions, all glassware was oven dried (120 °C) over a 24 h period and cooled under a stream of argon. All commercially available reagents were used as supplied. THF was distilled over sodium benzophenone ketyl and stored under an atmosphere of argon. Diisopropylamine was distilled from potassium hydroxide. Air-sensitive reagents were transferred by syringe or with a double-ended needle. Yields refer to chromatographically and spectroscopically (^{1}H, ^{13}C) homogeneous material. Electrolyses were carried out using a homemade undivided electrolysis cell (see the schematic diagram below).

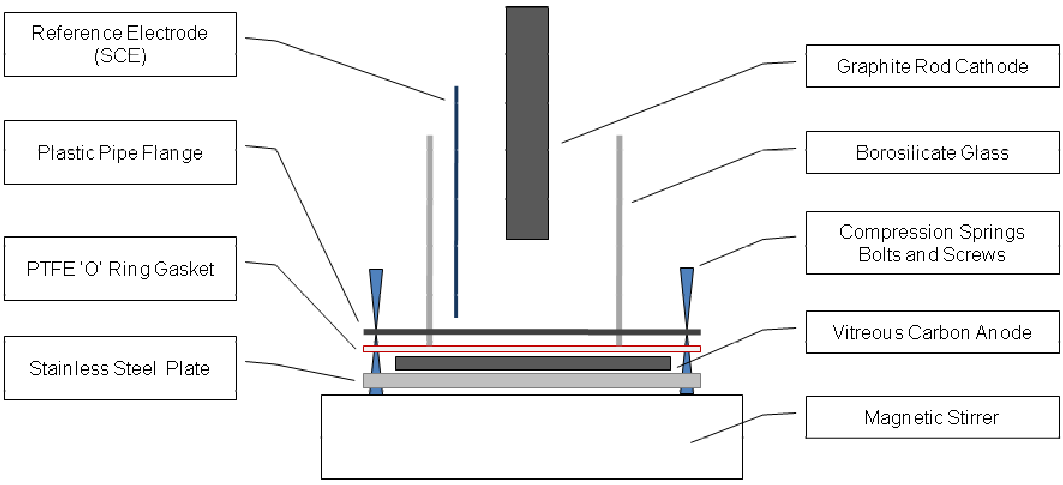

Figure 1 : Macroscale Undivided Electrolysis Cell

6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline : 3,4-Dimethoxyphenylethylamine (10.0 g, 55.17 mmol) was slowly added at 0 °C to 30 mL of formic acid. The orange solution was stirred for 10 min at that temperature until complete dissolution of the amine. Paraformaldehyde (1.65 g, 54.94 mmol) was added to that solution which was heated at 50 °C for 12 h. The resulting viscous mixture was poured into 50 mL of water and the solution was made basic by the addition of NaOH pellets to yield an oily residue which was extracted with dichloromethane (50 mL × 3). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by column chromatography (dichloromethane/methanol, 70:30) to afford 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (10.13 g, 95%) as a highly viscous oil. R_f (dichloromethane/methanol, 70:30) = 0.1. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 2.71 (t, J = 5.8 Hz, 3 H), 3.12 (t, J = 5.8 Hz, 3 H), 3.84 (s, 3 H), 3.85 (s, 3 H), 3.94 (s, 2 H), 6.51 (s, 1 H), 6.58 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 28.5 (s), 43.7 (s), 47.7 (s), 55.9 (p, 2 C), 109.1 (t), 111.1 (t), 126.4 (q), 127.4 (q), 147.3 (q), 147.4 (q) ppm.

6,7-dimethoxy-2-(1-phenyl-ethyl)-1,2,3,4-tetrahydroisoquinoline (1) : 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (5.0 g, 25.87 mmol) was dissolved in 30 mL of acetonitrile containing 7.60 mL (5.93 g, 45.86 mmol) of diisopropylethylamine (Hünig's base). Then, 4.11 mL (5.55 g, 28.44 mmol, 1.1 equiv.) of α-methylbenzylbromide were added and the resulting solution was stirred at 20 °C until TLC indicated the absence of starting material (12 h). The solvent was evaporated under reduced pressure and the crude material was purified by column chromatography (diethyl ether/petroleum ether, 60:40) to yield tetrahydroisoquinoline **1** (6.45 g, 84%) as a solid. White powder, m. p. 94–96 °C (petroleum ether); R_f (diethyl ether/petroleum ether, 70:30) = 0.7. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 1.46 (d, J = 6.7 Hz, 3 H), 2.55–2.82 (m, 4 H), 3.48 (d, J_{AB} = 14.5 Hz, 1 H), 3.53 (q, J = 6.7 Hz, 1 H), 3.72 (d, J_{AB} = 14.5 Hz, 1 H), 3.80 (s, 3 H), 3.82 (s, 3 H), 6.48 (s, 1 H), 6.57 (s, 1 H), 7.21–7.39 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 20.3 (p), 28.9 (s), 48.1 (s), 53.3 (s), 55.9 (p, 2 C), 64.5 (s), 109.6 (t), 111.3 (t), 126.4 (q), 126.9 (t), 127.0 (q), 127.5 (t), 128.3 (t), 144.4 (q), 147.1 (q), 147.4 (q) ppm. HRMS ($C_{19}H_{23}NO_2$ [M^+]): calc. for 297.1729; found: 297.1721. $C_{19}H_{23}NO_2$: calc. C 76.73, H 7.80, N 4.71; found C 76.61, H 7.81, N 4.70.

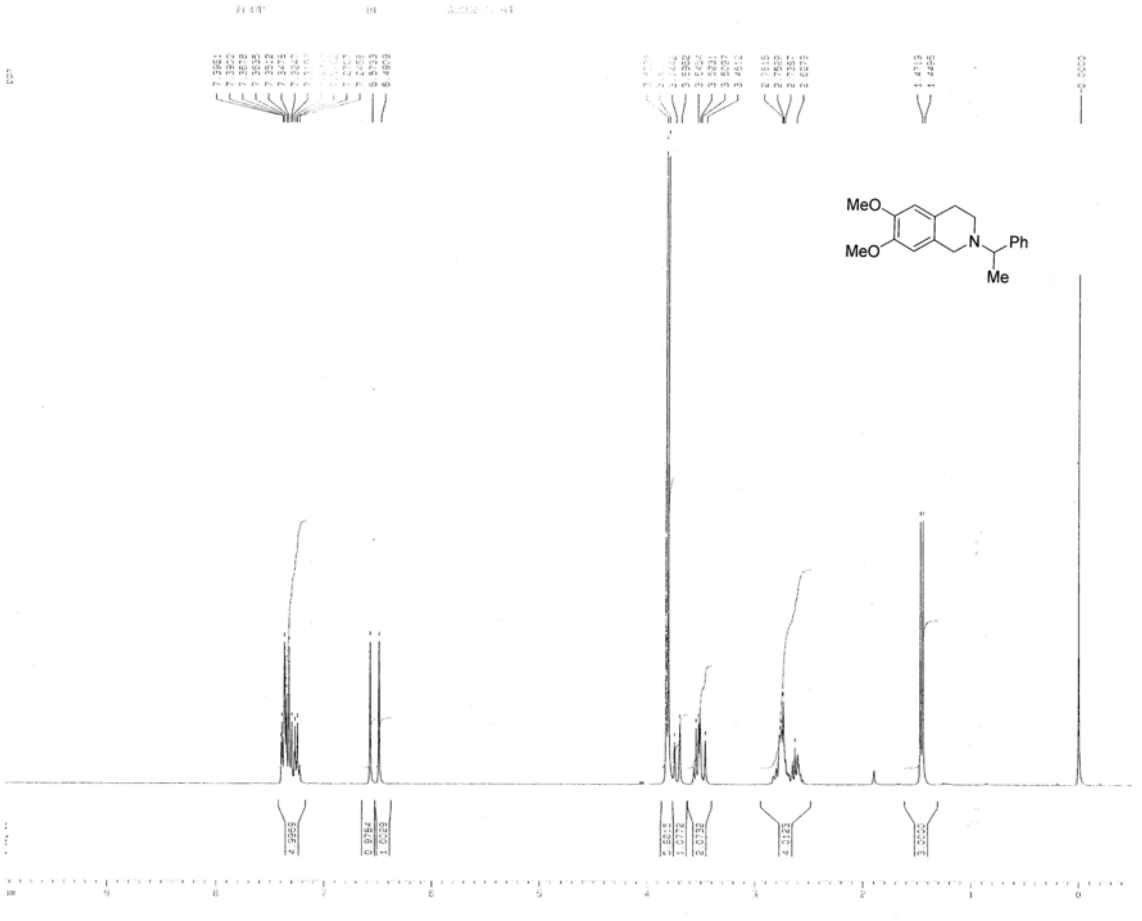

Figure 2 : ^{1}H NMR spectrum of derivative **1**

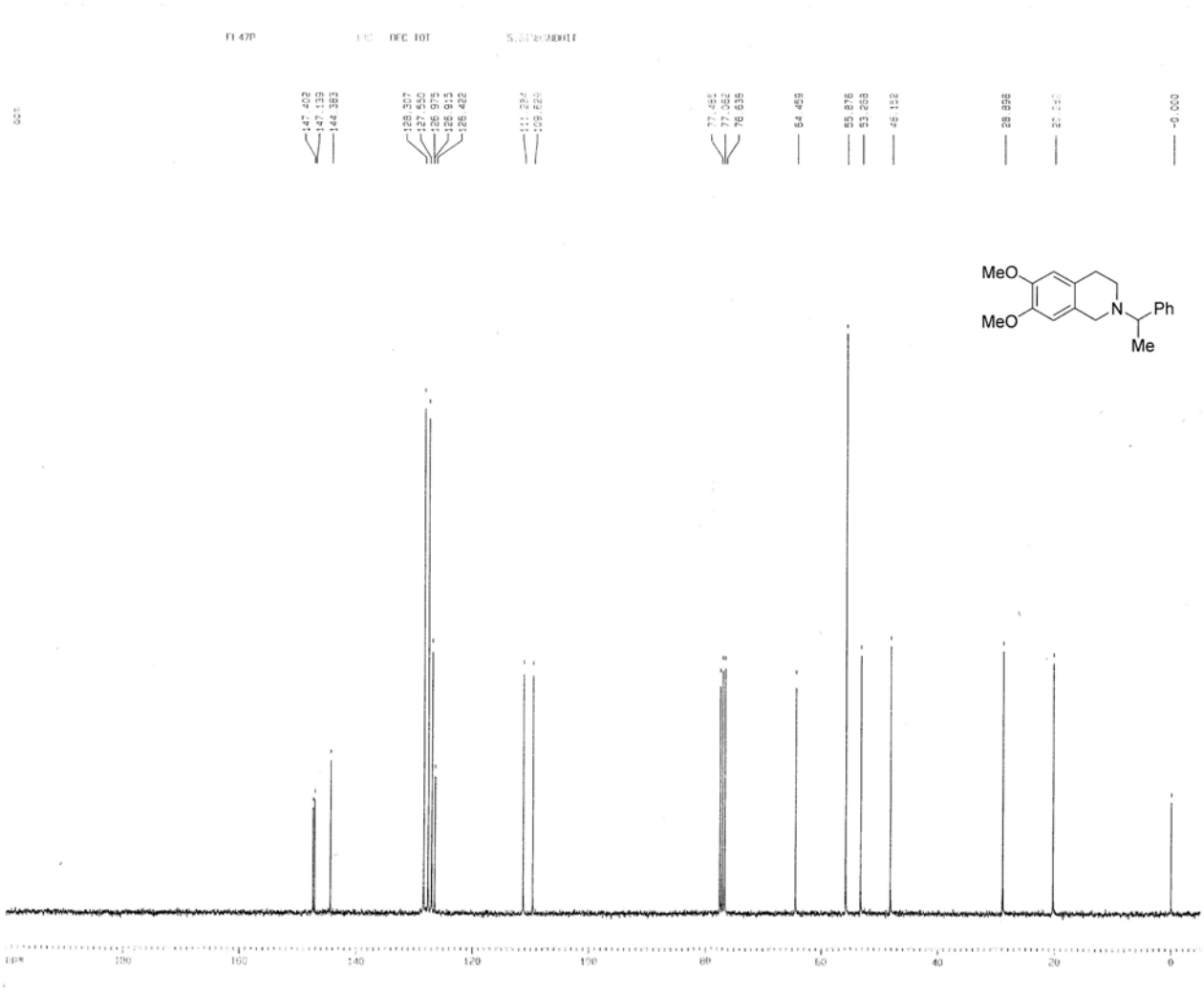

Figure 3 : ^{13}C NMR spectrum of derivative **1**

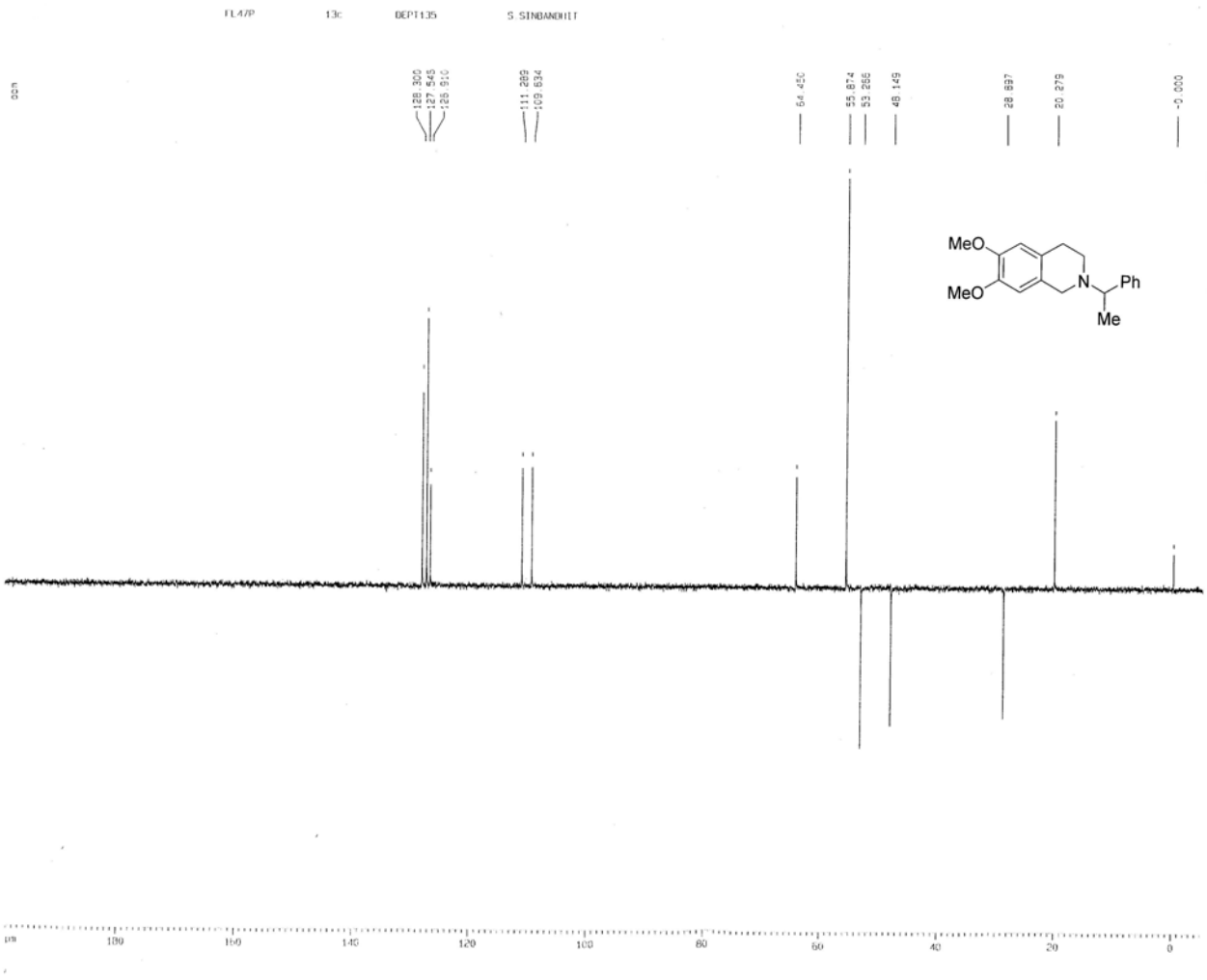

Figure 4 : DEPT spectrum of derivative **1**

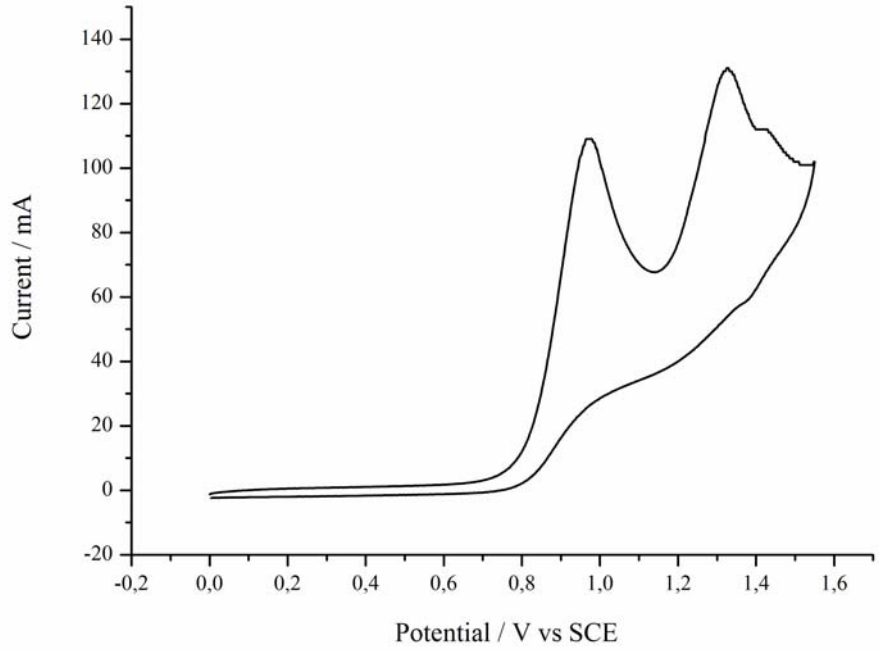

Figure 5 : Cyclic voltammogram of THIQ **5**. Glassy carbon electrode (diameter 3.0 mm); solvent: MeOH; supporting electrolyte: $LiClO_4$ (0.1 M); product concentration: 20 $mmolL^{-1}$; NaCN: 4 equiv. per mol of substrate; scan rate: 50 mVs^{-1}.

(*R,*R**)-6,7-dimethoxy-2-(1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2) :**
Tetrahydroisoquinoline **1** (2.0 g, 6.72 mmol) was dissolved in a 0.1 M $LiClO_4$ in MeOH electrolyte solution (0.3 L), 0.82 g (16.73 mmol) of NaCN and 0.19 mL (0.19 g, 3.32 mmol) of glacial acetic acid. The solution was placed in an undivided cell equipped with a planar vitreous carbon electrode (diameter = 100 mm, Carbone Lorraine®) as anode and a carbon rod as cathode. The working potential was adjusted to +1.0 V/SCE and after the consumption of 1360 C (2.1 F/mol), the electrolysis was stopped. Then, water (150 mL) was added to the filtrate (**Caution**: *$LiClO_4$ may lead to severe explosions when the material is evaporated to dryness. NaCN was destroyed by adding an excess of $KMnO_4$ onto the aqueous phase. Due to the possible release of HCN, the electrolyses should be carried out under a well ventilated hood*) and methanol was evaporated under reduced pressure at +50 °C. The resulting aqueous phase was extracted with dichloromethane (50 mL × 3) and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The resulting white solid was triturated with diethyl ether and was recrystallized from 50 mL of hot ethanol to give 1.87 g (86%) of a crystalline white powder. A further slow crystallization (24 h) of this powder from ethanol afforded single colourless plates which were analyzed by X-ray diffraction. Colourless plates, m.p. 172–174 °C (ethanol); R_f (diethyl ether/petroleum ether, 70:30) = 0.3, α-aminonitrile **2** decomposed readily on silica plates, R_f value is given for guidance. ^{1}H NMR (C_6D_6, 500 MHz) δ = 1.37 (d, J = 6.5 Hz, 3 H), 2.46 (dd, J = 16.5, 3.5 Hz, 1 H), 2.79 (td, J = 11.8, 3.8 Hz, 1 H), 2.96 (ddd, J = 16.5, 11.8, 6.3 Hz, 1 H), 3.15 (s, 3 H), 3.21 (ddm, J = 11.8, 6.3 Hz, 1 H), 3.46 (s, 3 H), 3.97 (q, J = 6.5 Hz, 1 H), 4.73 (s, 1 H), 6.12 (s, 1 H), 6.42 (s, 3 H), 7.20 (tt, J = 6.8, 1.5 Hz, 1 H), 7.29, (tm, J = 6.8 Hz, 2 H), 7.55 (dm, J = 6.8 Hz, 2 H) ppm. ^{13}C NMR (isomeric mixture, 85:15, major diastereoisomer, C_6D_6, 125 MHz) δ = 21.7 (p), 28.6 (s), 42.8 (s), 54.1 (t), 55.2 (p), 55.3 (p), 62.1 (t), 110.1 (t), 112.0 (t), 117.1 (q), 122.1 (q), 126.3 (q), 129.1 (t), 143.9 (q), 148.7 (q), 149.9 (q) ppm. ^{1}H NMR (isomeric mixture, 60:40, $CDCl_3$, 500 MHz) δ = 1.50 (J = 6.6 Hz, 1.8 H), 1.53 (J = 6.6 Hz, 1.2 H), 2.62–2.52 (m, 1.0 H), 2.75–2.87 (m, 1.5 H), 2.90–2.93 (m, 0.6 H), 3.02–3.10 (m, 0.4 H), 3.48–

3.52 (m, 1.8 H), 3.75 (q, J = 6.6 Hz, 0.6 H), 3.79 (s, 1.2 H), 3.82 (q, J = 6.6 Hz, 0.4 H), 3.87 (s, 1.2 H), 3.88 (s, 1.8 H), 3.92 (s, 1.8 H), 4.43 (s, 0.4 H), 5.12 (s, 0.6 H), 6.46 (s, 0.4 H), 6.62 (0.6 H), 6.64 (s, 0.4 H), 6.75 (s, 0.6 H), 7.31–7.46 (m, 5 H) ppm. ^{13}C NMR (isomeric mixture, 60:40, $CDCl_3$, 125 MHz) δ = 21.8 (p), 21.8 (p), 28.1 (s), 28.6 (s), 42.8 (s), 45.1 (s), 52.4 (s), 53.9 (t), 55.9 (p, 3 C), 56.1 (p), 62.0 (t), 62.4 (t), 109.5 (t), 109.7 (t), 117.0 (q), 121.4 (q), 121.7 (q), 127.1 (s, 2 C), 127.4 (t), 127.5 (t), 128.7 (t), 128.9 (t), 143.2 (q), 144.5 (q), 147.7 (q), 147.8 (q), 149.1 (q), 149.2 (q) ppm. HRMS ($C_{20}H_{22}N_2O_2$ [M^+]): calc. for 322.1681; found: 322.1679. $C_{20}H_{22}N_2O_2$: calc. C 74.51, H 6.88, N 8.69; found C 74.29, H 6.82, N 8.74.

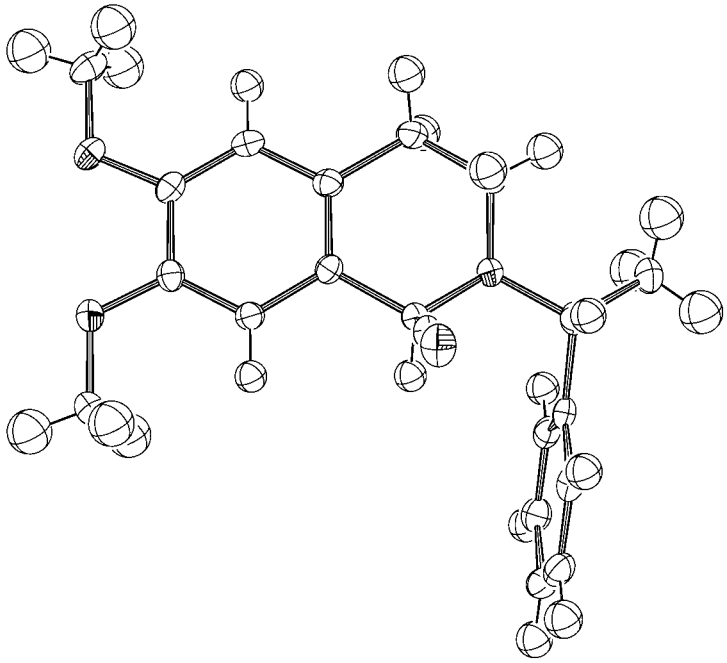

Figure 6 : ORTEP drawing of derivative **2** (Ellipsoid plots are drawn with 40% of probability)

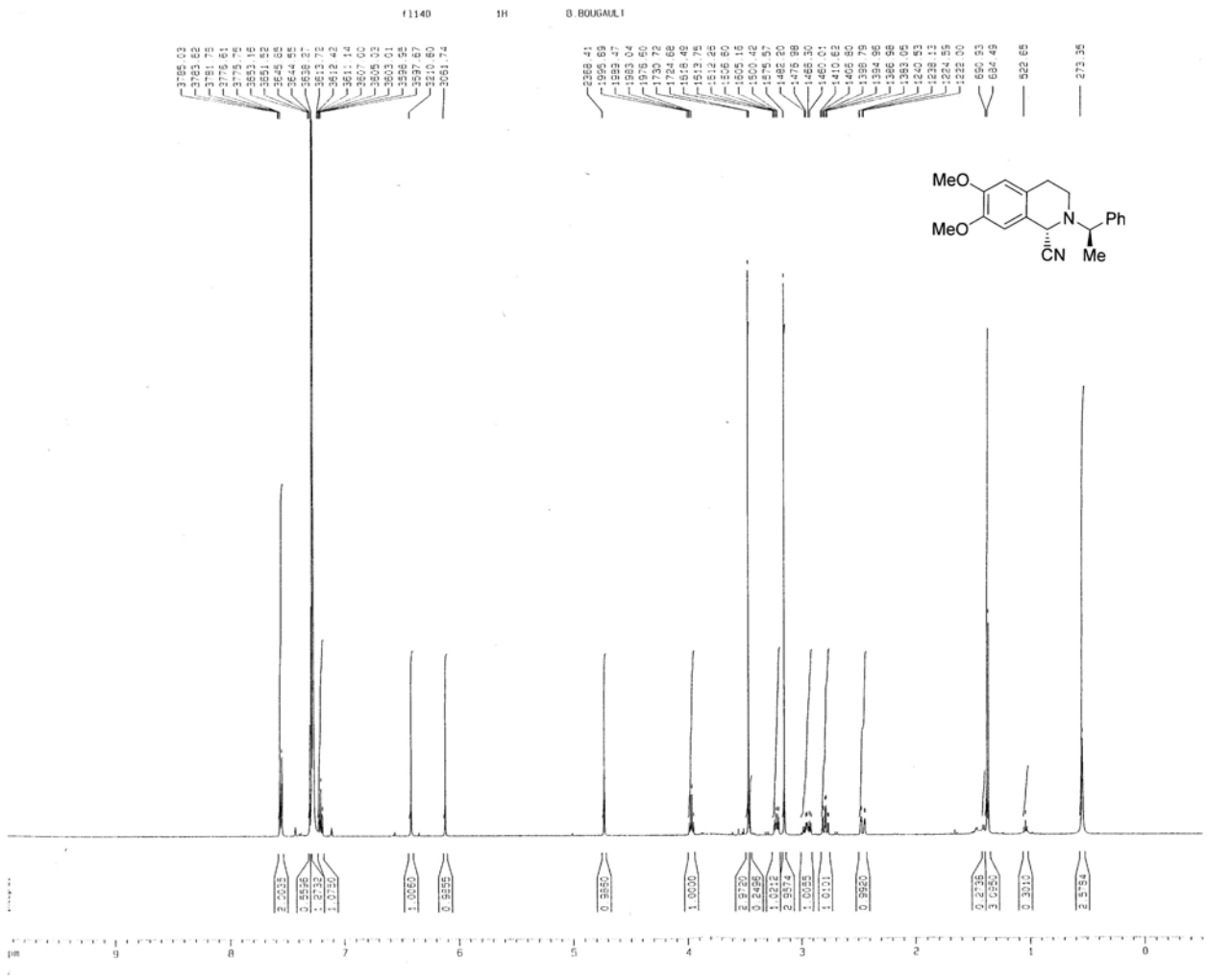

Figure 7 ^{1}H NMR spectrum of derivative **2** after a 5 min standing in C_6D_6

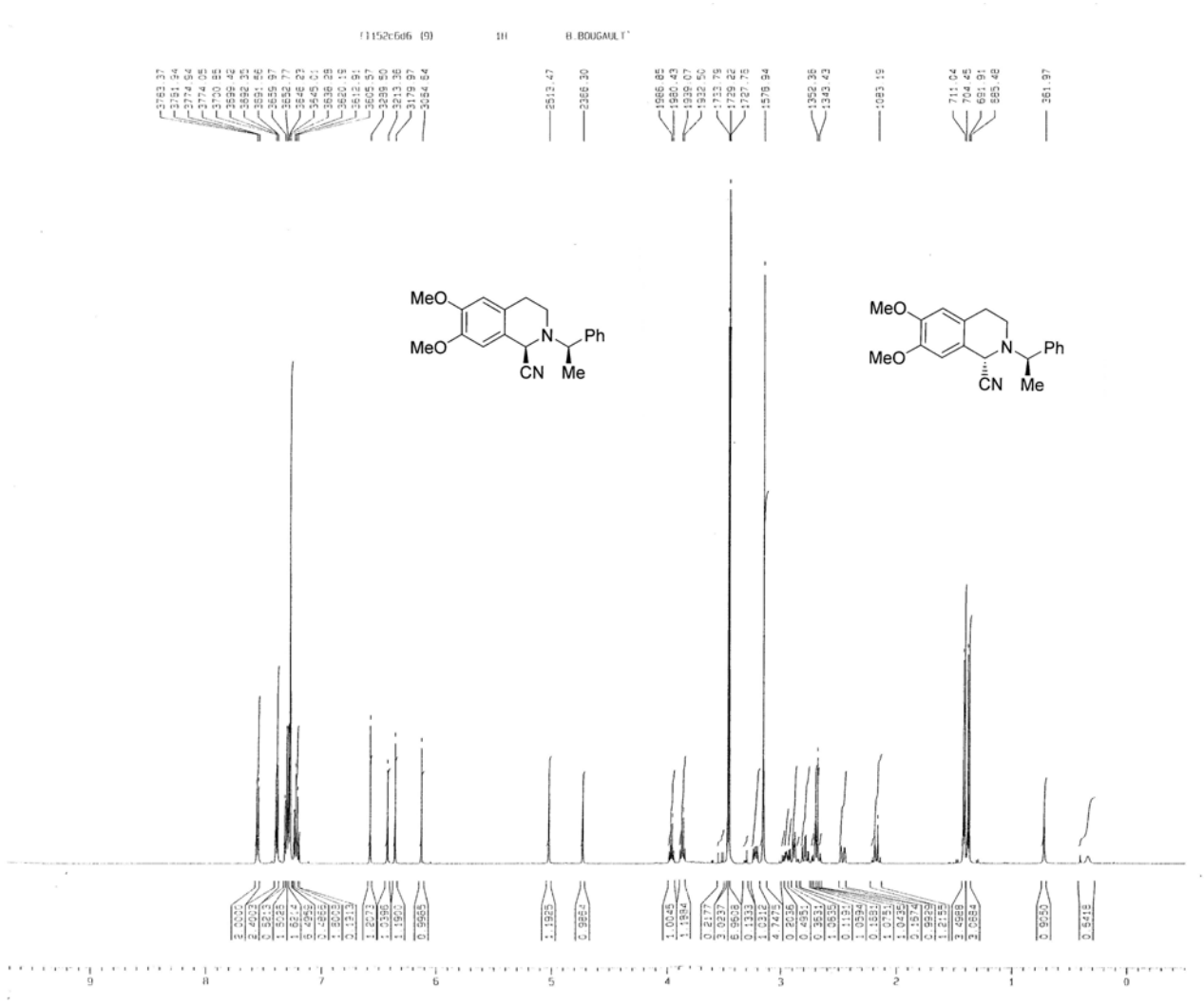

Figure 8 : ^{1}H NMR spectrum of derivatives (*R**,*R**)-**2** and (*R**,*S**)-**2** after a 48 h standing in C_6D_6

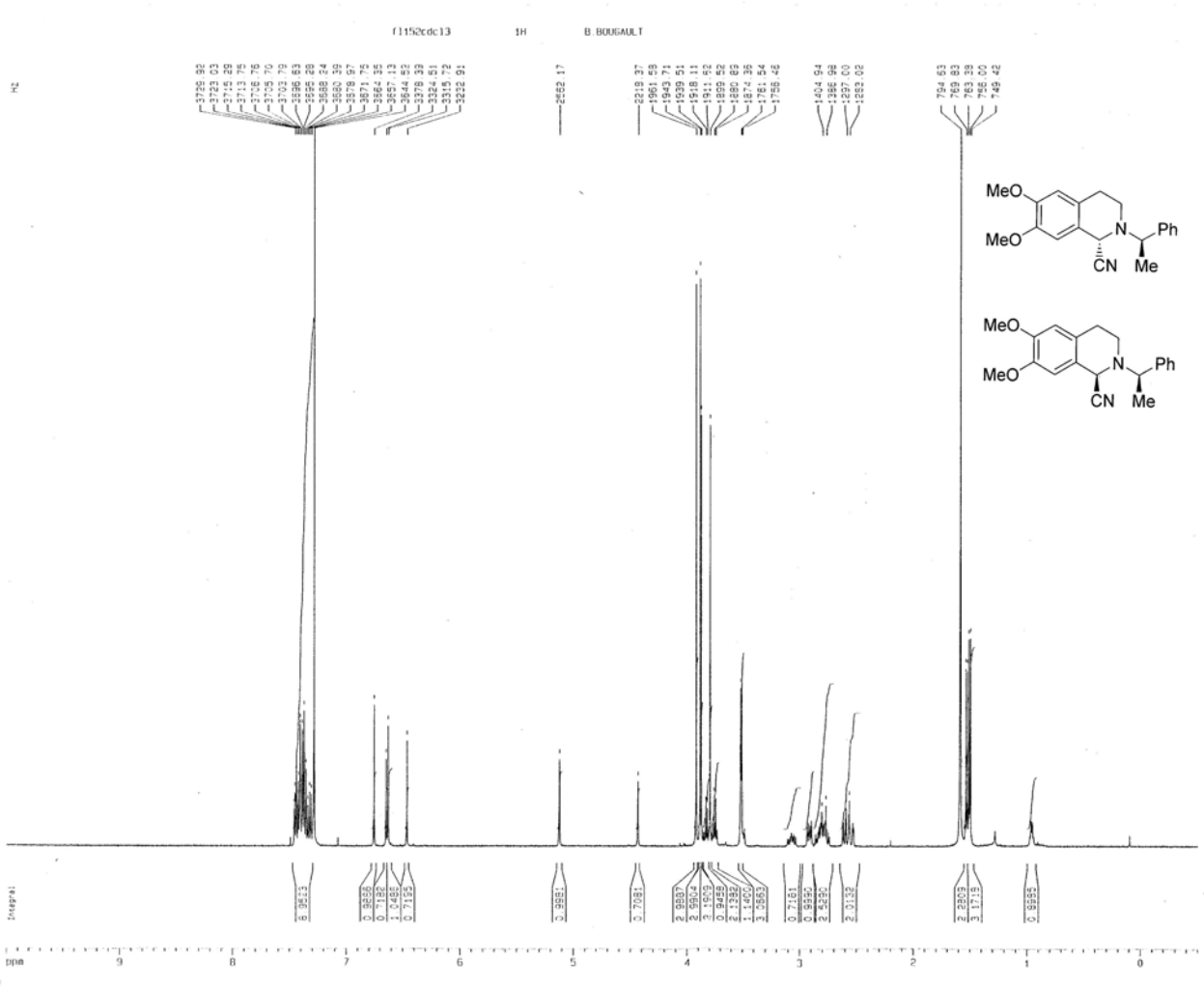

Figure 9 : ^{1}H NMR spectrum of derivatives (*R**,*R**)-**2** and (*R**,*S**)-**2** after a 5 min standing in $CDCl_3$

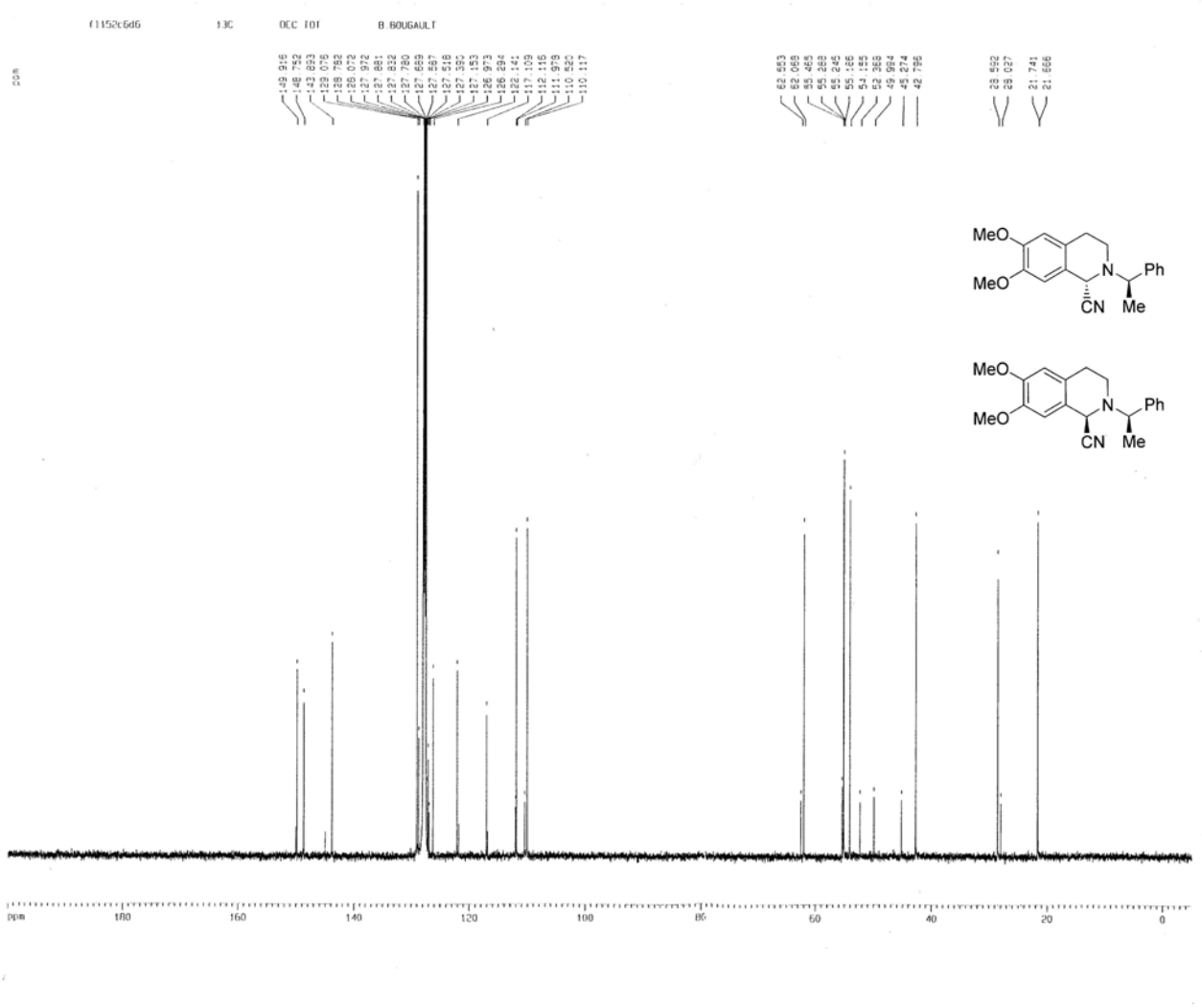

Figure 10 : ^{13}C NMR spectrum of derivatives (*R**,*R**)-**2** and (*R**,*S**)-**2** after a 30 min standing in C_6D_6

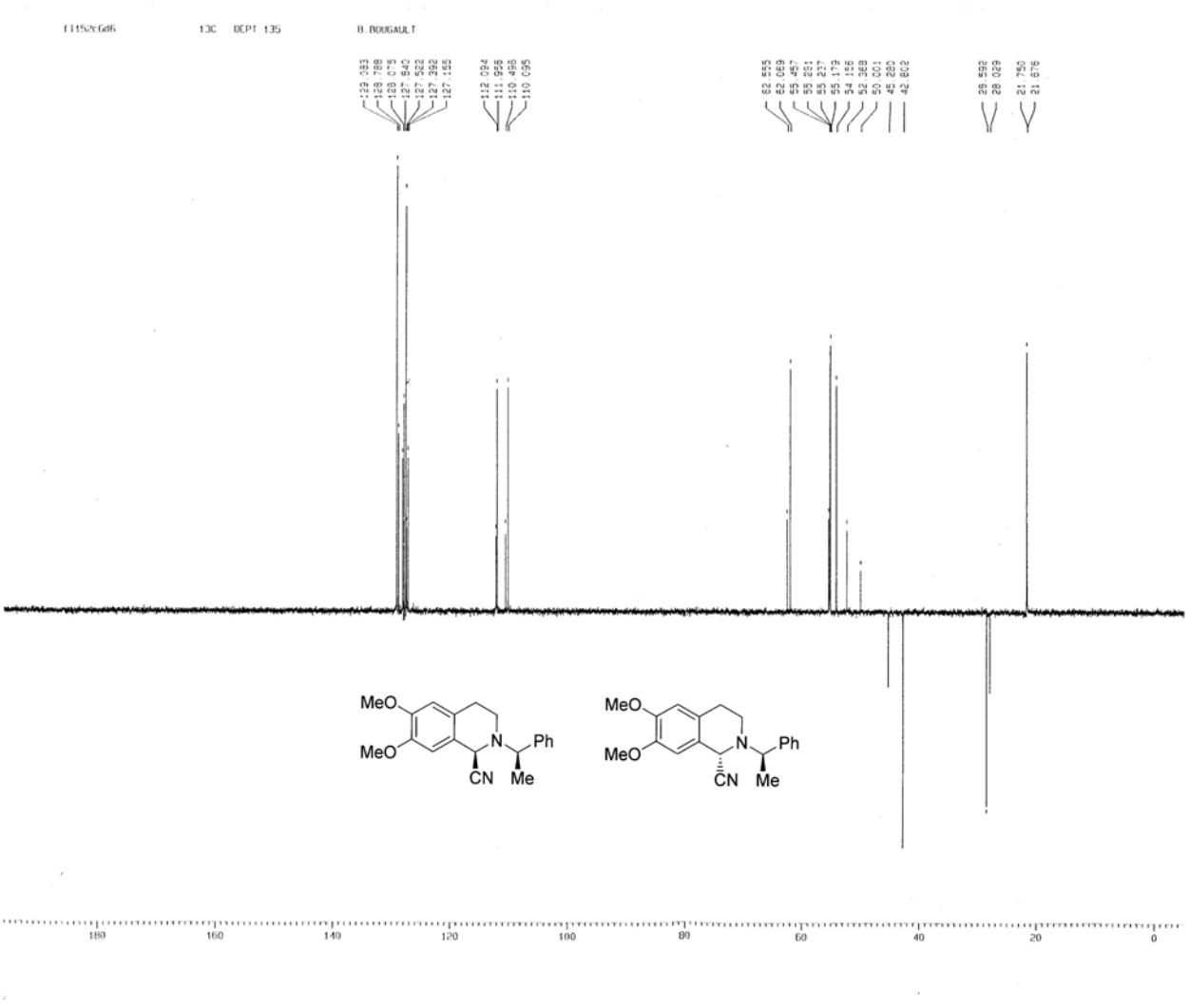

Figure 11 : DEPT spectrum of derivatives (*R**,*R**)-**2** and (*R**,*S**)-**2** after a 15 min standing in C_6D_6

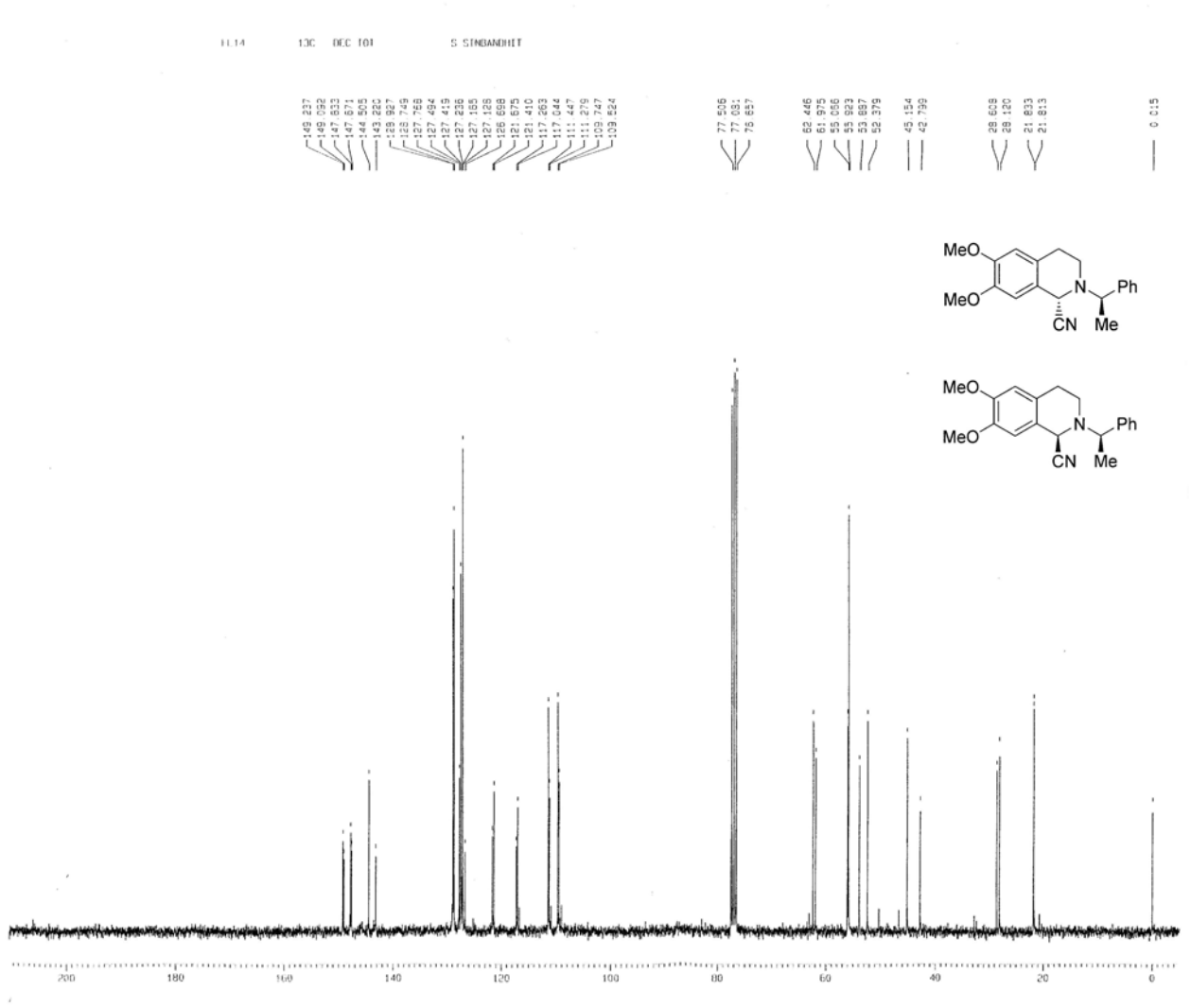

Figure 12 : ^{13}C NMR spectrum of derivatives (*R**,*R**)-**2** and (*R**,*S**)-**2** after a 20 min standing in $CDCl_3$

(*R*,R)-6,7-dimethoxy-2-(1-phenyl-ethyl)-1,2,3,4-tetrahydroisoquinoline-3-carbonitrile (5).**

Tetrahydroisoquinoline **1** (1.0 g, 3.36 mmol) was dissolved in a 0.1 M $LiClO_4$ in MeOH electrolyte solution (0.2 L), and 2.97 g (60.60 mmol) of NaCN. The solution was placed in an undivided cell equipped with a planar vitreous carbon electrode (diameter = 100 mm, Carbone Lorraine®) as anode and a carbon rod as cathode. The working potential was adjusted to +1.0 V/SCE and after the consumption of 680 C (2.1 F/mol), the electrolysis was stopped. Then, water (150 mL) was added to the solution (**Caution**: *$LiClO_4$ may lead to severe explosions when the material is evaporated to dryness. NaCN was destroyed by adding an excess of $KMnO_4$*) and methanol was evaporated under reduced pressure at +50 °C. The resulting aqueous phase was extracted with dichloromethane (50 mL × 3) and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The resulting white solid was triturated with methanol (30 mL) for 12 h to yield α-aminonitriles **2** and **5** (0.95 g, 87%) as a (65:35) mixture. This powder was dissolved in 30 mL of ethanol and the solution was cooled to 0 °C. Then, $NaBH_4$ (0.43 g, 11.37 mmol) was added in portions and the resulting suspension was stirred at that temperature for 12 h. The solvents were evaporated under reduced pressure and the resulting paste was taken-up with a 15% ammonia solution. The solution was extracted with dichloromethane (50 mL × 3) and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The resulting paste was triturated with diethyl ether (50 mL) to yield 0.22 g of α-aminonitrile **5** as a mixture (50:50) of diastereoisomers. This mixture was refluxed for 5 h in 50 mL of diethyl ether in the presence of 0.5 g of NaCN. Water was added to the

solution and the organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to yield α-aminonitrile **9** (0.2 g, 18%) as a mixture (90/10) of diastereoisomers. A further slow crystallization (24 h) of this powder from diethyl ether afforded single colourless plates which were analyzed by X-ray diffraction. Colourless plates; m.p. 158–160 °C (diethyl ether); R_f (diethyl ether/petroleum ether, 70:30) = 0.3. ^{1}H NMR (isomeric mixture, 90:10, major diastereoisomer, $CDCl_3$, 300 MHz) δ = 1.49 (d, J = 6.5 Hz, 3 H), 2.75 (d, J = 16.2 Hz, 1 H), 3.09 (dd, J = 16.2, 5.6 Hz, 1 H), 3.64 (q, J = 6.5 Hz, 1 H), 3.73 (d, J_{AB} = 14.2 Hz, 1 H), 3.83 (s, 3 H), 3.86 (s, 3 H), 3.88 (d, J = 5.6 Hz, 1 H), 4.25 (d, J_{AB} = 14.2 Hz, 1 H), 6.55 (s, 1 H), 6.62 (s, 1 H), 7.25–7.40 (m, 5 H) ppm. ^{13}C NMR (isomeric mixture, 90:10, major diastereoisomer, $CDCl_3$, 75 MHz) δ = 21.6 (p), 32.4 (s), 48.6 (s), 48.7 (t), 55.9 (p, 2 C), 63.5 (t), 109.4 (t), 111.1 (t), 116.7 (q), 121.9 (q), 124.9 (q), 127.1 (t), 127.9 (t), 129.0 (t), 143.6 (q), 148.0 (q), 148.1 (q) ppm. $C_{20}H_{22}N_2O_2$: calc. C 74.51, H 6.88, N 8.69; found C 74.49, H 6.92, N 8.66.

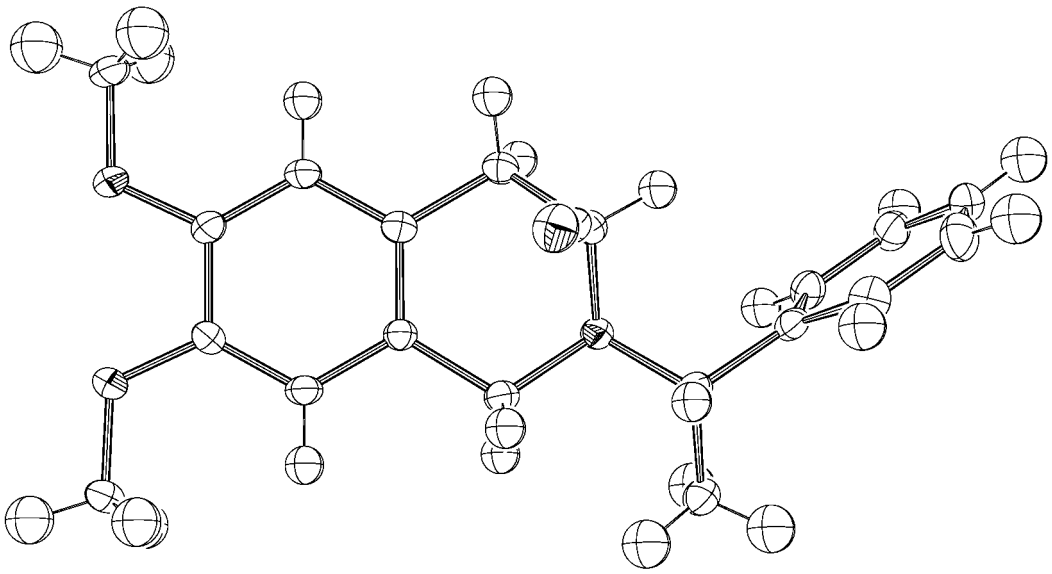

Figure 13 : ORTEP drawing of derivative **5** (Ellipsoid plots are drawn with 40% of probability)

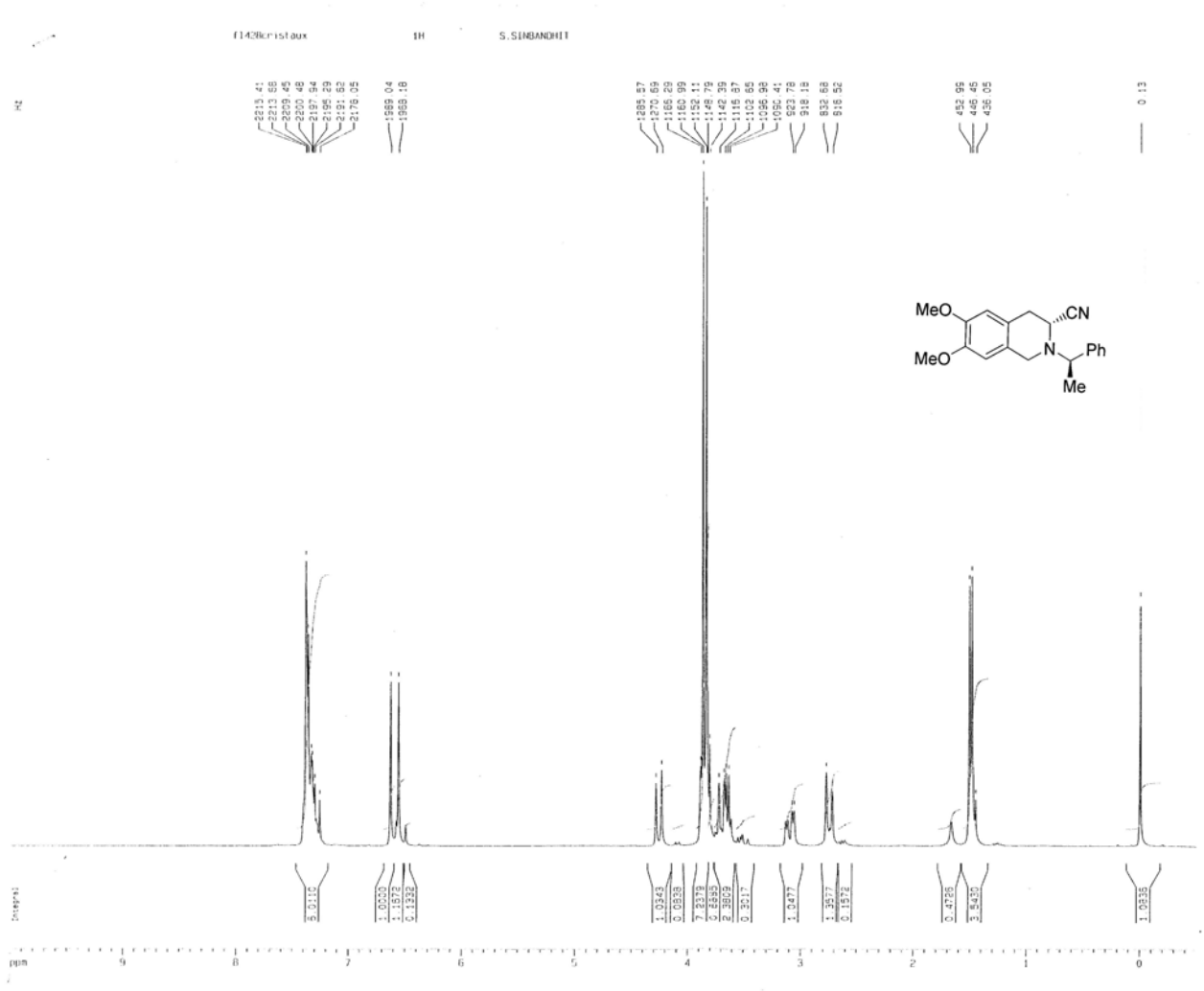

Figure 14 : ^{1}H NMR spectrum of derivative **5**

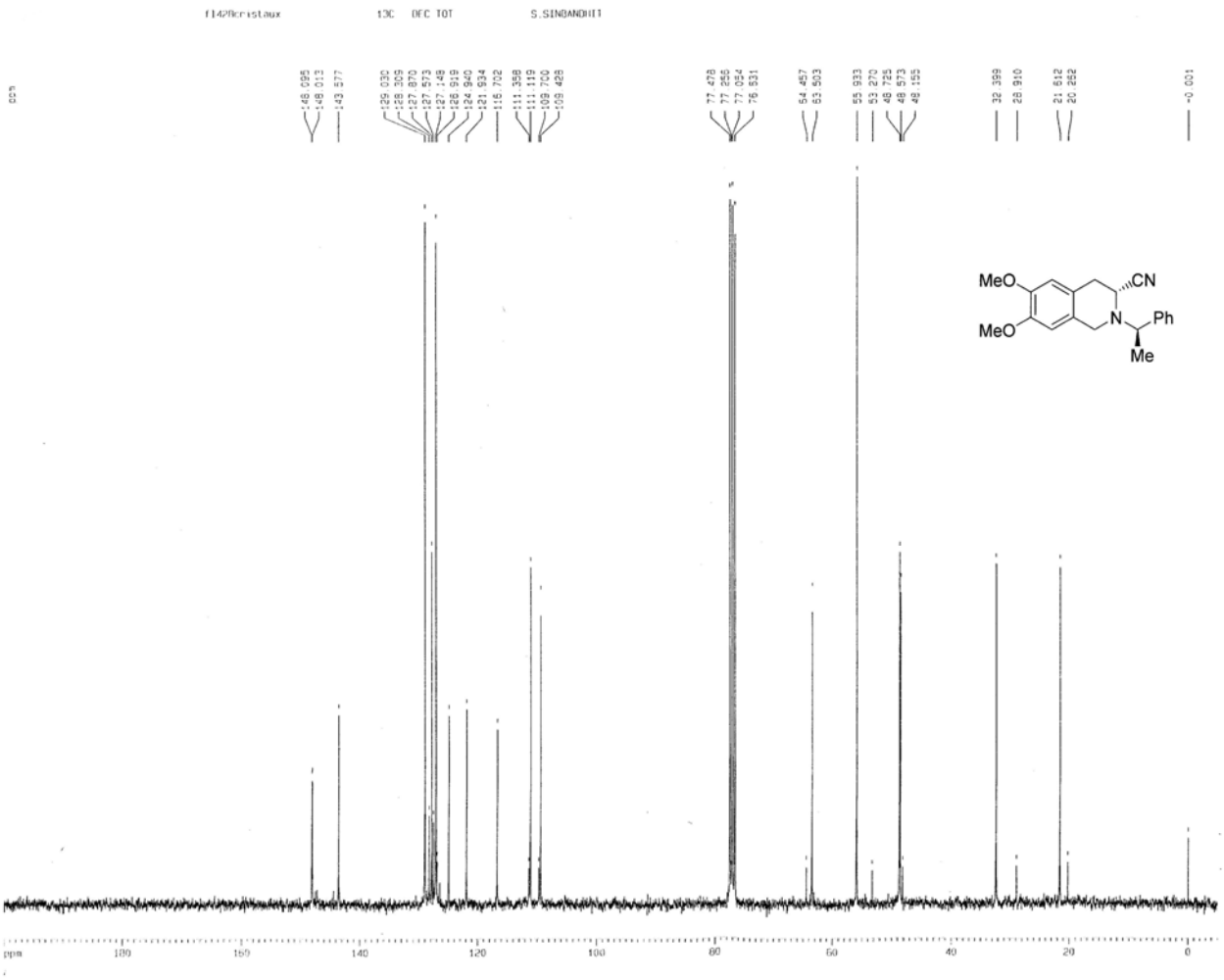

Figure 15 : ^{13}C NMR spectrum of derivative **5**

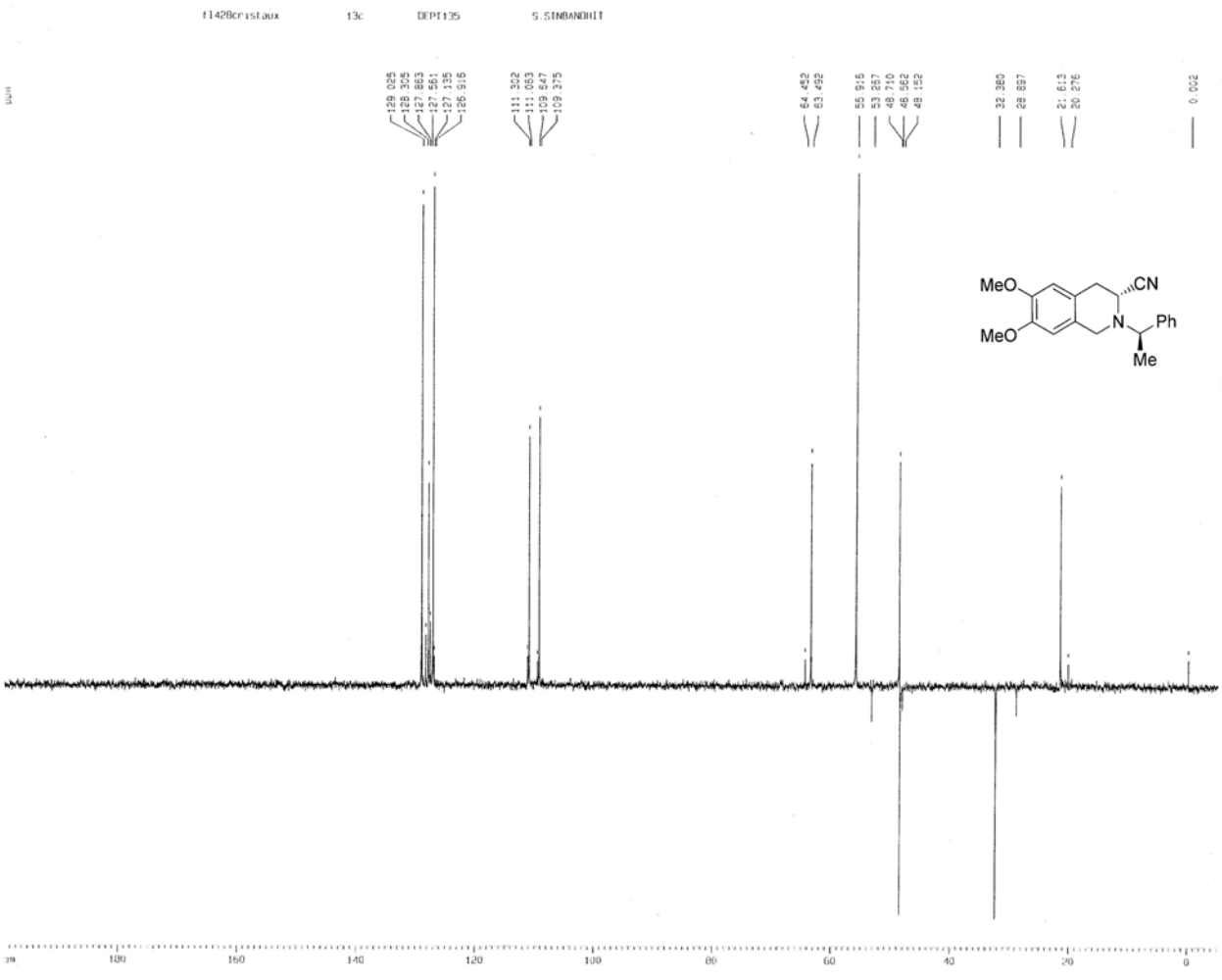

Figure 16 : DEPT spectrum of derivative **5**

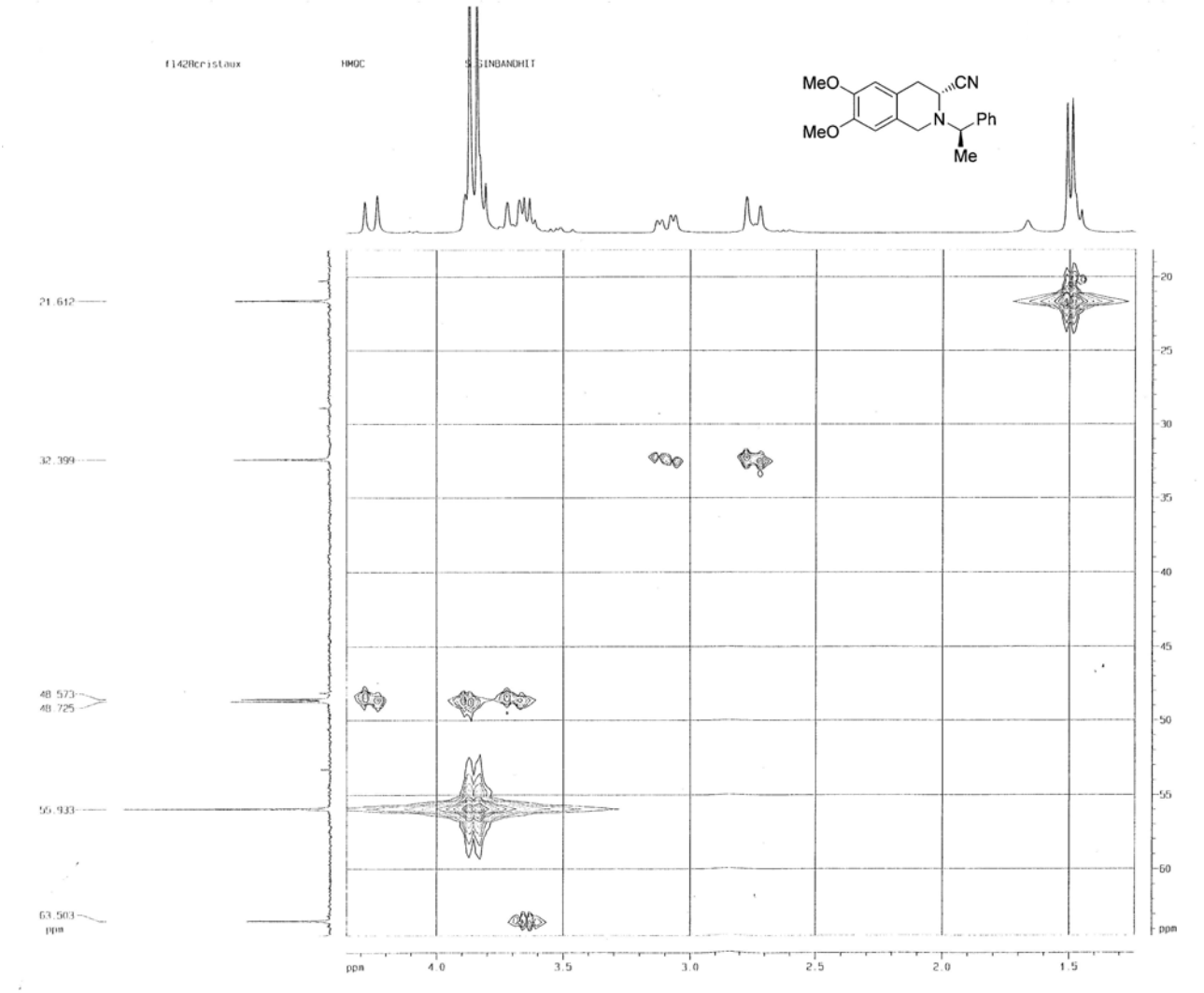

Figure 17 : HMQC spectrum of derivative **5**

(*R,*R**)-6,7-dimethoxy-1-methyl-2-(1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (6a) (Procedure A):** In a Schlenk tube**,** α-aminonitrile **2** (1.10 g, 3.41 mmol) was added to 10 mL of dry THF. The suspension was cooled to –80 °C and a THF solution (5 mL) of LDA [prepared from 2.5 M *n*BuLi in hexane (1.77 mL, 4.42 mmol, 1.30 equiv.) and 0.66 g of diisopropylamine (0.84 ml, 5.11 mmol] was added with a syringe at that temperature over a 10 min period. The suspension was warmed up to –10 °C over a 2 h period upon which we noticed the progressive formation of a clear deep-red anion solution. Then, the temperature was brought once again at –80 °C and iodomethane (1.27 mL, 2.89 g, 20.40 mmol) was added at that temperature. The solution turned rapidly yellow and was allowed to warm-up to 20 °C over a 2 h period. The solution was poured onto 10 mL of water containing 0.25 g of NaCN. The THF was evaporated at 20 °C under reduced pressure to yield an oily residue which was extracted with diethyl ether. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was taken-up in 20 mL of ethanol at 5 °C to yield α-aminonitrile **6a** (0.77 g, 67%) as a white powder. A further slow crystallization (24 h) of this powder from ethanol afforded single yellow plates which were analyzed by X-ray diffraction. Yellow plates; m.p. 120–122 °C (dec.). ^{1}H NMR (isomeric mixture, 90:10, major diastereoisomer, $CDCl_3$, 500 MHz) δ = 1.67 (d, J = 6.8 Hz, 3 H), 1.89 (s, 3 H), 2.53 (d, J = 13.6 Hz, br. 1 H), 2.80–2.90 (m, 3 H), 3.86 (s, 3 H), 3.90 (s, 3 H), 4.60 (q, J = 6.8 Hz, 1 H), 6.56 (s, 1 H), 6.88 (s, 1 H), 7.24 (t, J = 7.2 H, 1 H), 7.33 (t, J = 7.2 Hz, 2 H), 7.46 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (isomeric

mixture, 90:10, major diastereoisomer, $CDCl_3$, 125 MHz) δ = 13.7 (p), 29.2 (p), 29.3 (s), 40.4 (s), 55.4 (t), 55.9 (p), 56.2 (p), 57.6 (q), 109.6 (t), 111.2 (t), 123.0 (q), 126.7 (t), 126.7 (t), 128.2 (t), 144.8 (q), 147.8 (q), 148.7 (q) ppm. HRMS ($C_{20}H_{23}NO_2$ $[M–HCN]^+$): calc. for 309.17288; found: 309.1753. $C_{21}H_{24}N_2O_2$: calc. C 74.97, H 7.19, N 8.33; found C 74.89, H 7.12, N 8.18.

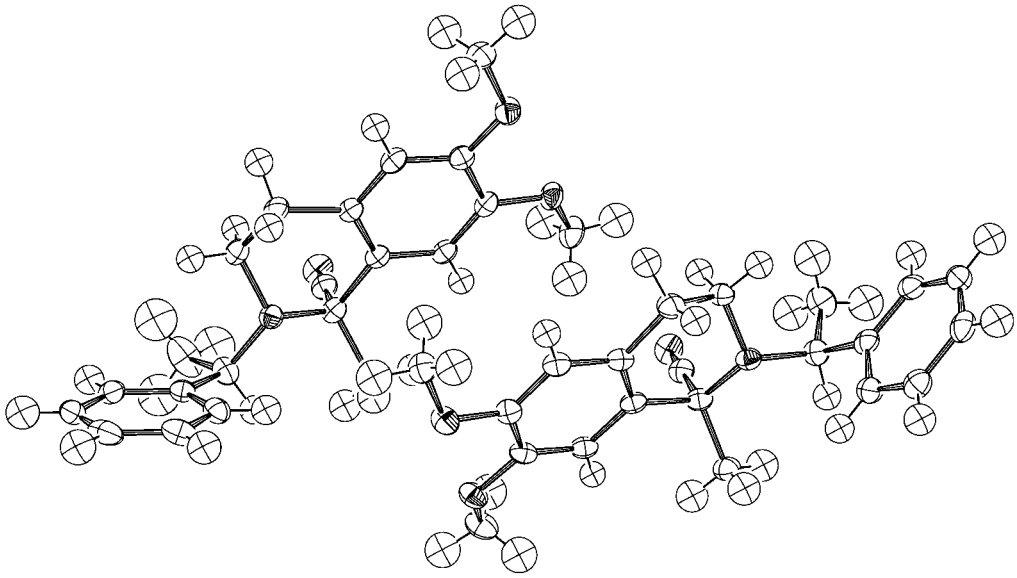

Figure 18 : ORTEP drawing of derivative **6a** (Ellipsoid plots are drawn with 40% of probability)

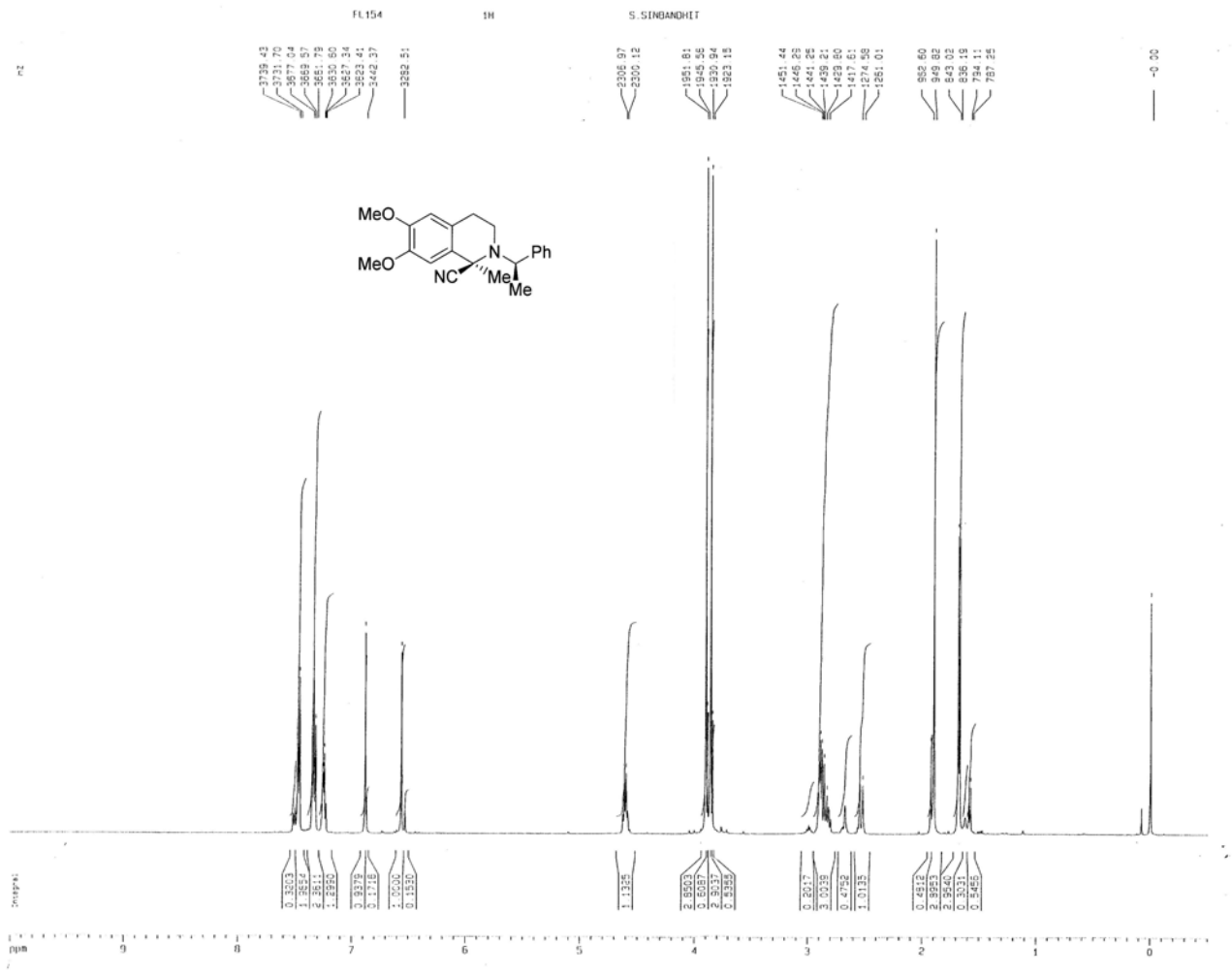

Figure 19 : ^{1}H NMR spectrum of derivative **6a**

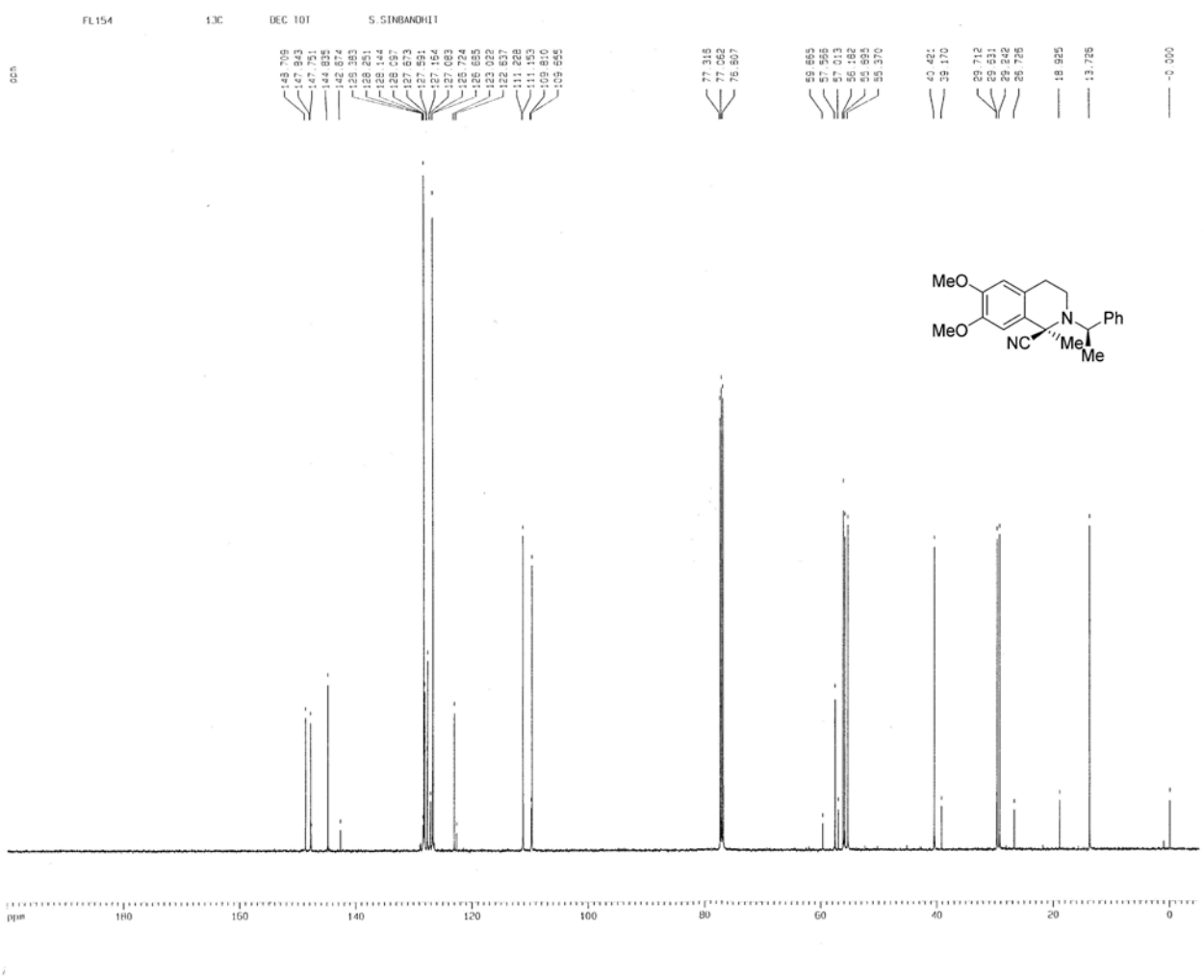

Figure 20 : ^{13}C NMR spectrum of derivative **6a**

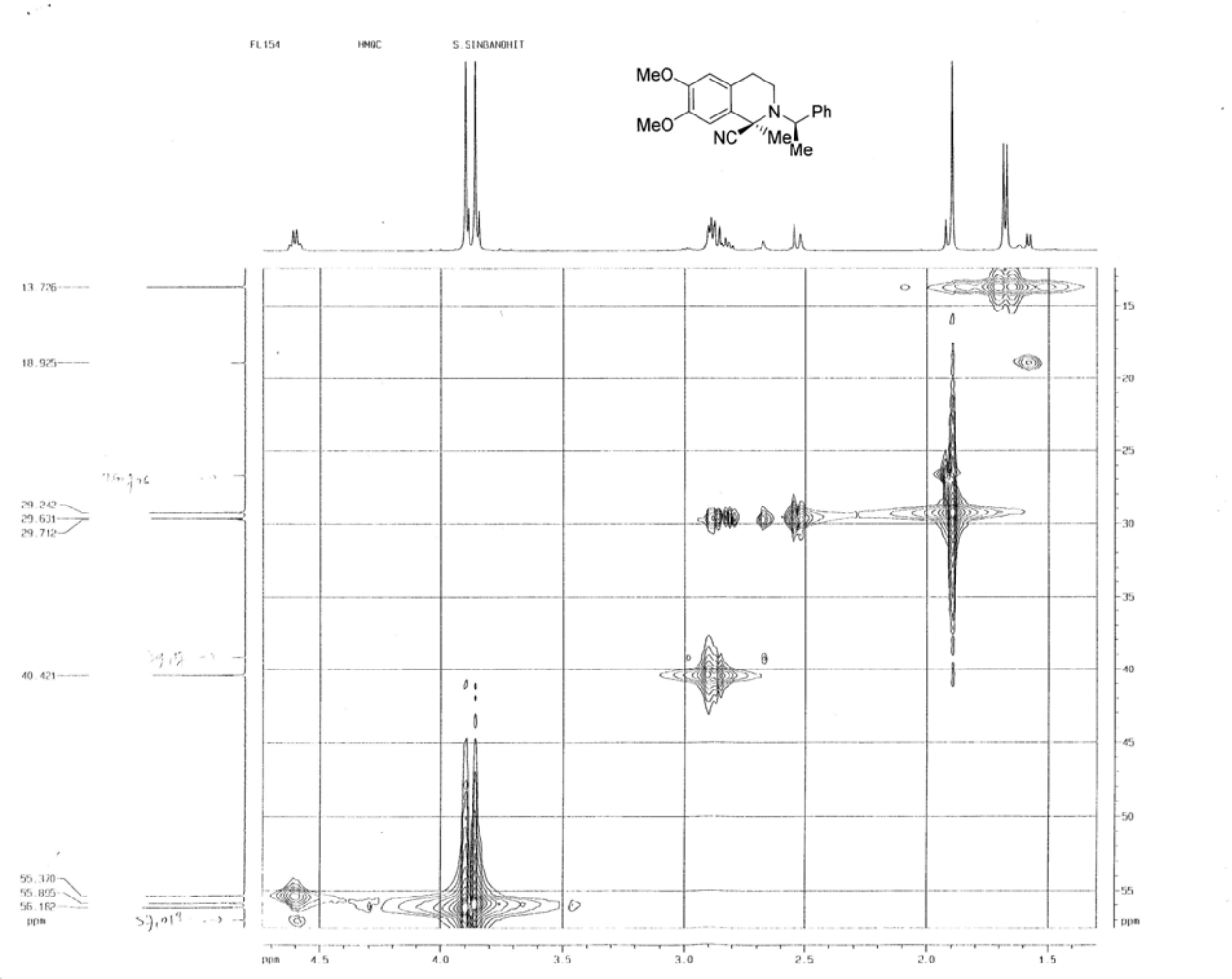

Figure 21 : HMQC spectrum of derivative **6a**

1-(bromomethyl)-4-methoxybenzene (7). In a Schlenk tube under argon, 4-methoxybenzylalcohol (2.0 g, 14.47 mmol) was dissolved in 20 mL of dichloromethane and the solution was cooled to 0 °C. Then, 20.26 mL (20.26 mmol, 1.4 equiv.) of a solution (1.0 M) of PBr_3 in dichloromethane were added by syringe over a 5 min period, and the resulting solution was stirred at 20 °C for 4 h. The reaction was quenched by the addition of 10 mL of absolute ethanol and the solution was stirred for 30 min. Then, 1.0 g of powdered Na_2CO_3 was added to the solution which was stirred for an additional 30 min period. The solution was filtered rapidly over a sintered glass funnel and the filtrate was evaporated under argon at a temperature lower than 10 °C (bromide **7** decomposed readily upon heating at 50 °C). The viscous paste was purified by a rapid filtration over a column chromatography [SiO_2 (30 g); (diethyl ether/petroleum ether, 50:50)]. The fractions were concentrated at 10 °C under argon to yield bromide **7** (2.36 g, 81%) as a colourless oil which can be stored for one week under argon at 5 °C without loss of quality. Bromide **7** readily decomposed on silica sheets, R_f value [0.8, (diethyl ether/petroleum ether, 50:50)] is given for guidance. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H), 4.53 (s, 2 H), 6.90 (d, J = 6.6 Hz, 2 H), 7.36 (d, J = 6.6 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 34.1 (s), 55.3 (p), 114.2 (t), 120.0 (q), 130.5 (t), 159.7 (q) ppm.

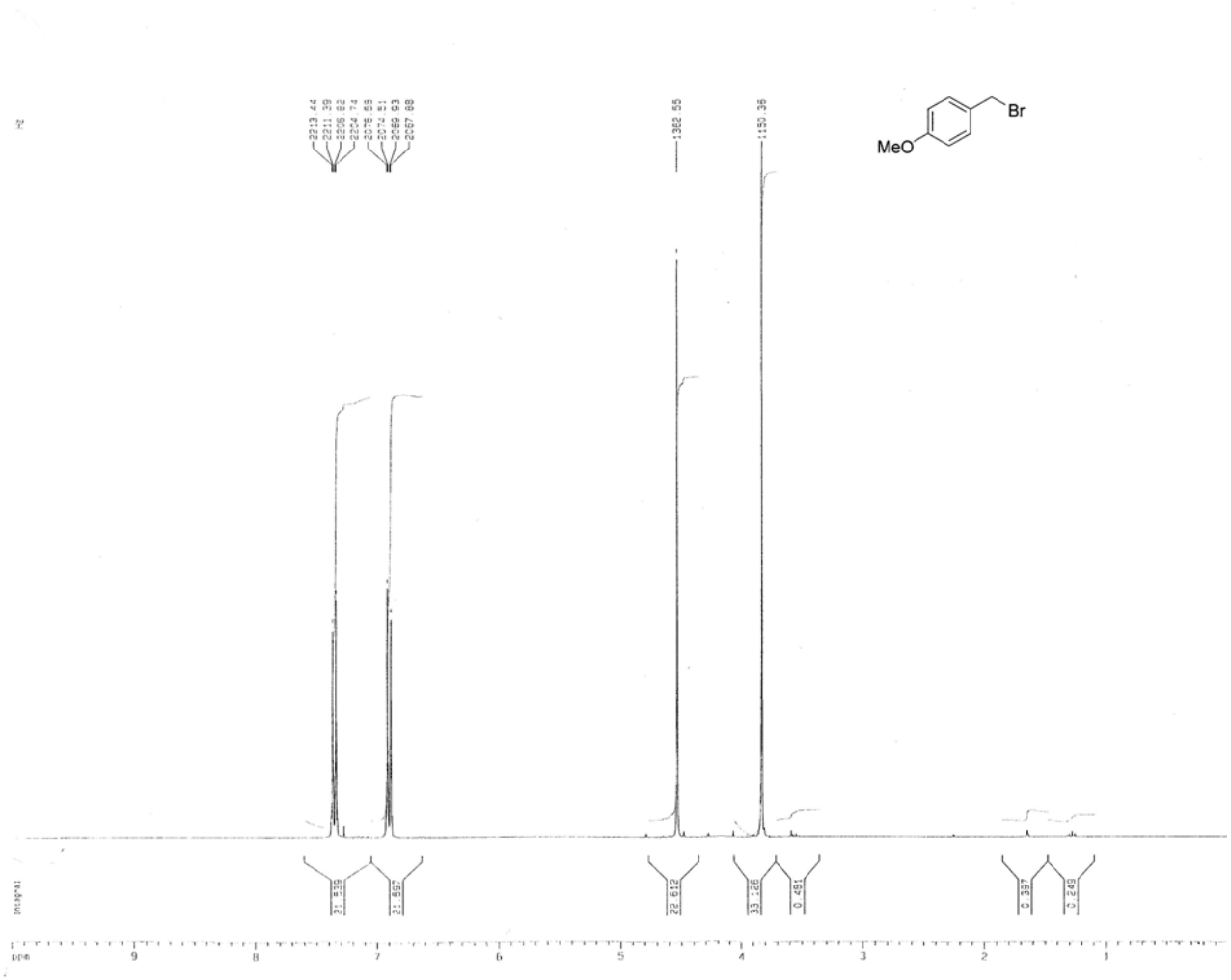

Figure 22 : ^{1}H NMR spectrum of derivative **7**

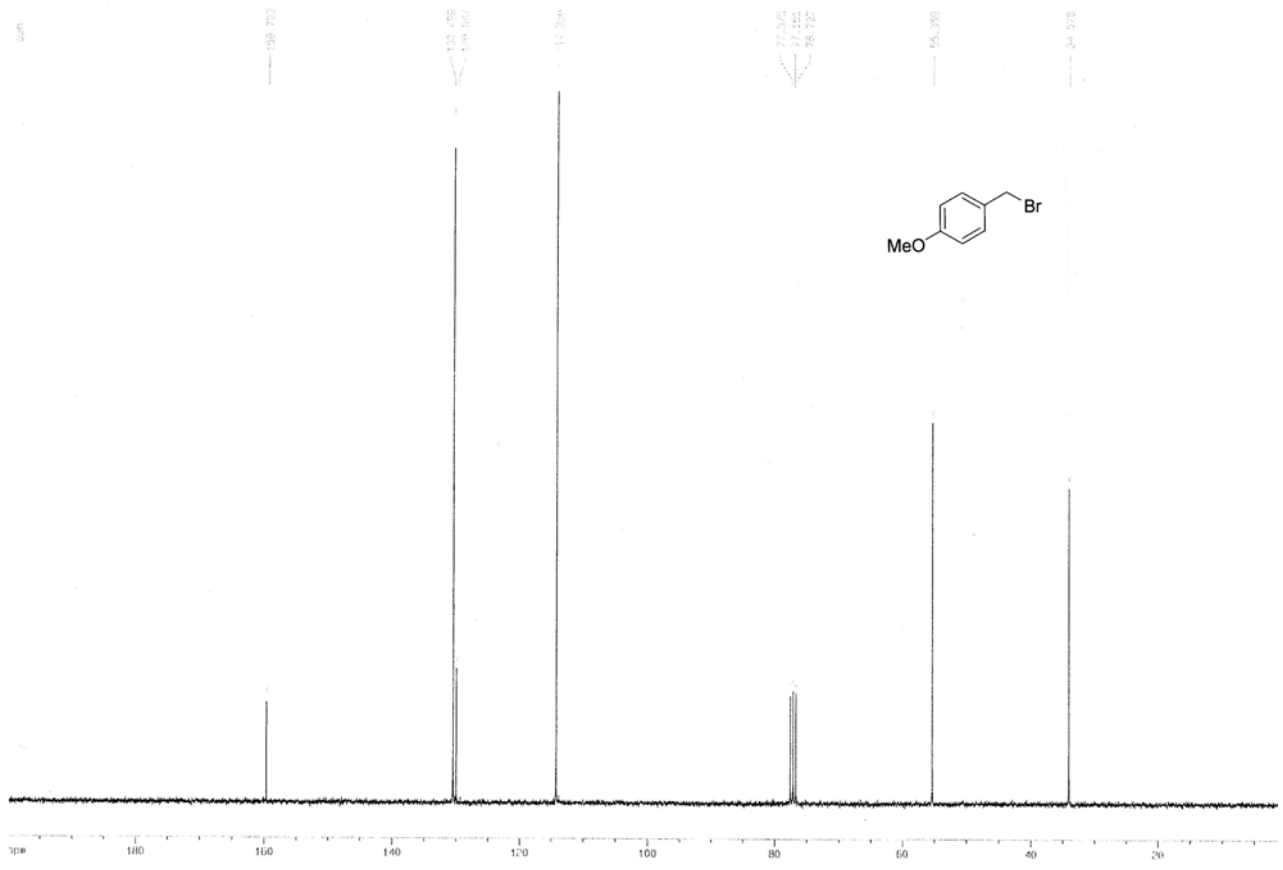

Figure 23 : ^{13}C NMR spectrum of derivative **7**

4-(Bromomethyl)-1,2-dimethoxybenzene (8). This was prepared according the previous protocol using 2.0 g (11.89 mmol) of 3,4-dimethoxybenzylalcohol and 20.26 mL (20.26 mmol, 1.4 equiv.) of a solution (1.0 M) of PBr_3 in dichloromethane. White powder (2.20 g, 80%); m.p. 57–58 °C (dec.). Bromide **8** readily decomposed on silica sheets, R_f value [0.7, (diethyl ether/petroleum ether, 50:50)] is given for guidance. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.89 (s, 3 H), 3.91 (s, 3 H), 4.52 (s, 2 H), 6.82 (d, J = 8.1 Hz, 1 H), 6.93 (d, J = 2.0 Hz, 1 H), 6.97 (dd, J = 8.1, 2.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 34.4 (s), 55.9 (p, 2 C), 111.0 (t), 112.1 (t), 121.6 (t), 130.2 (q), 149.1 (q), 149.2 (q) ppm.

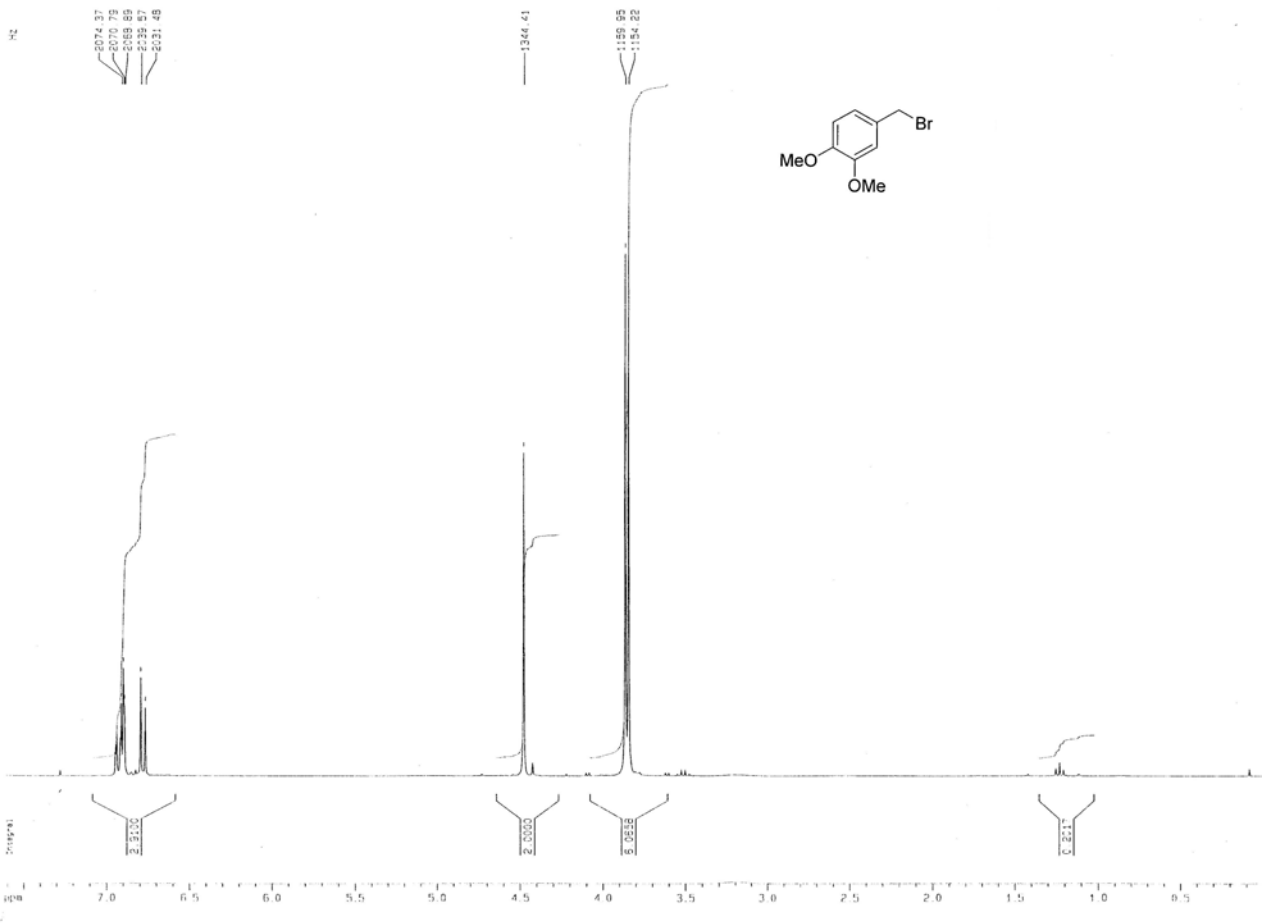

Figure 24 : ^{1}H NMR spectrum of derivative **8**

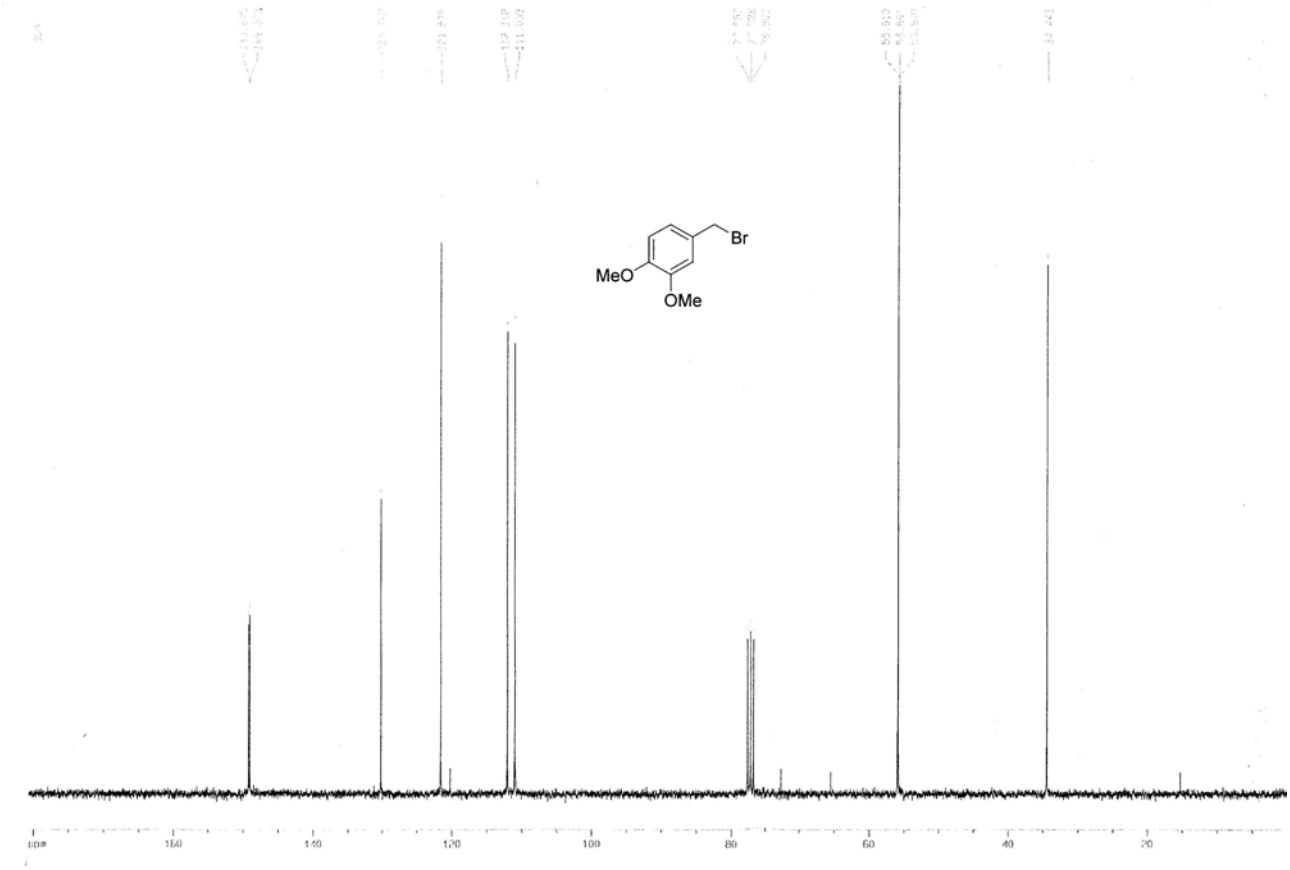

Figure 25 : ^{13}C NMR spectrum of derivative **8**

(*R,*R**)-6,7-dimethoxy-1-(4-methoxy-benzyl)-2-(1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (6b).** This has been prepared according to the procedure A using 1.5 g (4.65 mmol) of α-aminonitrile **2** and 1.38 g (6.86 mmol) of bromide **7** which was added directly (by syringe) onto the anion solution. Work-up afforded a yellow paste which was taken-up in 15 mL of ethanol to afford α-aminonitrile **6b** (1.6 g, 77%) as a crystalline yellow powder. A further slow crystallization (24 h) of this powder from ethanol afforded single yellow plates which were analyzed by X-ray diffraction. Yellow plates; m.p. 121–122 °C. ^{1}H NMR (isomeric mixture, 90:10, major diastereoisomer, $CDCl_3$, 500 MHz) δ = 1.72 (d, J = 6.8 Hz, 3 H), 2.46 (dt, J = 15.2, 2.5 Hz, 1 H), 2.62 (ddd, J = 15.2, 10.7, 6.5 Hz, 1 H), 2.85 (td, J = 10.7, 2.5 Hz, 1 H), 2.89 (ddd, J = 11.7, 7.7, 2.5 Hz, 1 H), 3.25 (d, J = 14.0 Hz, 1 H), 3.49 (d, J = 14.0 Hz, 1 H), 3.71 (s, 3 H), 3.73 (s, 3 H), 3.87 (s, 3 H), 4.74 (q, J = 6.8 Hz, 1 H), 6.53 (s, 1 H), 6.56 (dm, $J_{AA'BB'}$ = 9.0 Hz, 2 H), 6.61 (dm, $J_{AA'BB'}$ = 9.0 Hz, 2 H), 6.64 (s, 1 H), 7.21–7.35 (m, 5 H) ppm. ^{13}C NMR (isomeric mixture, 90:10, major diastereoisomer, $CDCl_3$, 125 MHz): δ = 15.3 (p), 29.6 (s), 40.6 (s), 46.7 (s), 55.2 (p), 55.8 (p), 56.5 (p), 56.5 (t), 62.9 (q), 110.9 (t), 111.0 (t), 113.1 (t), 122.6 (q), 125.4 (q), 126.3 (q), 126.6 (t), 126.8 (t), 128.1 (t), 129.1 (q), 132.0 (t), 144.2 (q), 147.1 (q), 148.4 (q), 158.6 (q) ppm. HRMS: $C_{27}H_{29}NO_3$ $[M–HCN]^+$: calc. for 415.2147; found: 415.2138; $C_{28}H_{30}N_2O_3$: calc. C 75.99, H 6.83, N 6.33; found C 75.76, H 6.73, N 6.32.

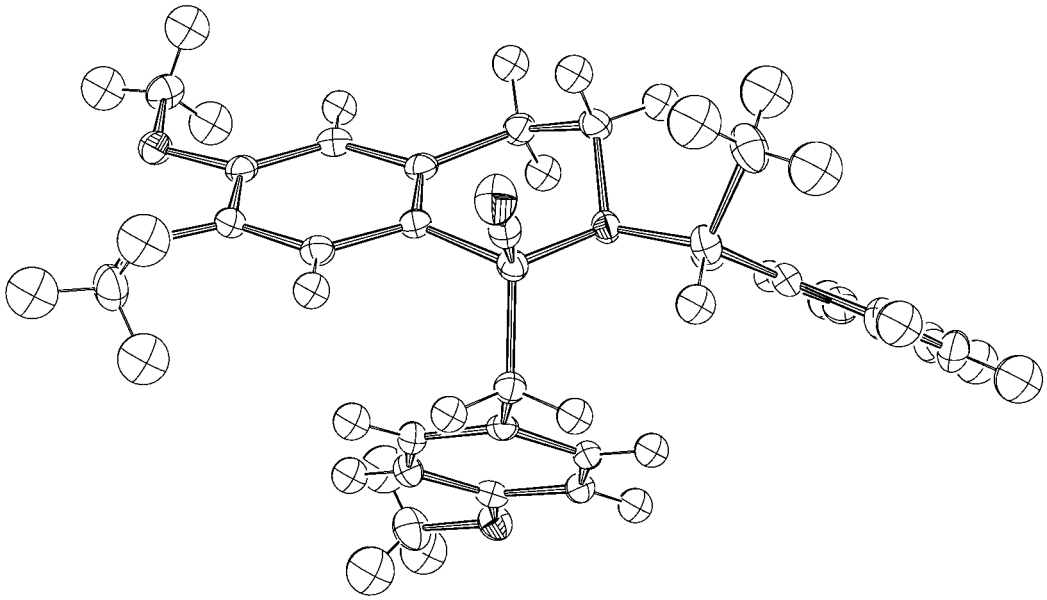

Figure 26 : ORTEP drawing of derivative **6b** (Ellipsoid plots are drawn with 40% of probability)

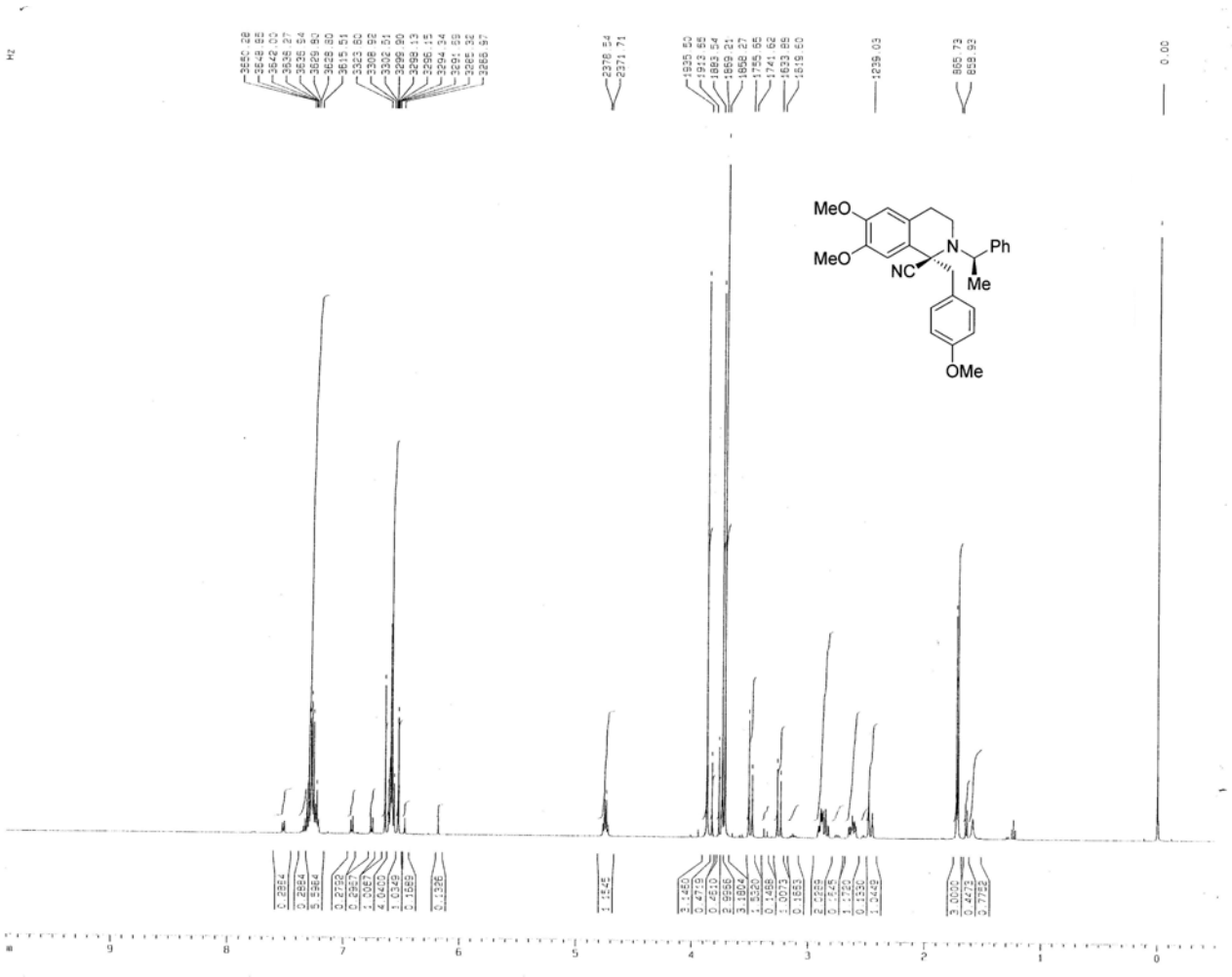

Figure 27 : ^{1}H NMR spectrum of derivative **6b**

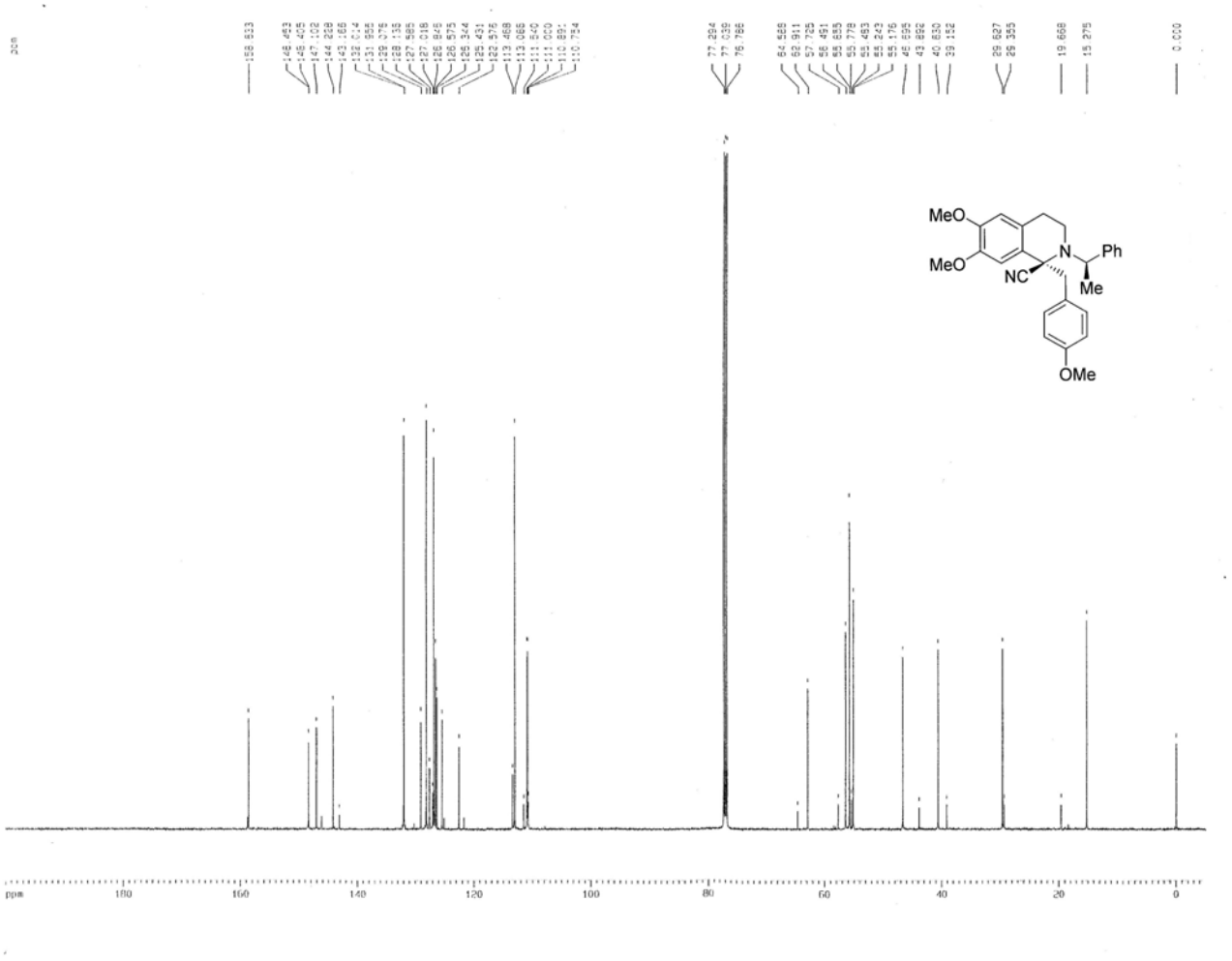

Figure 28 : ^{13}C NMR spectrum of derivative **6b**

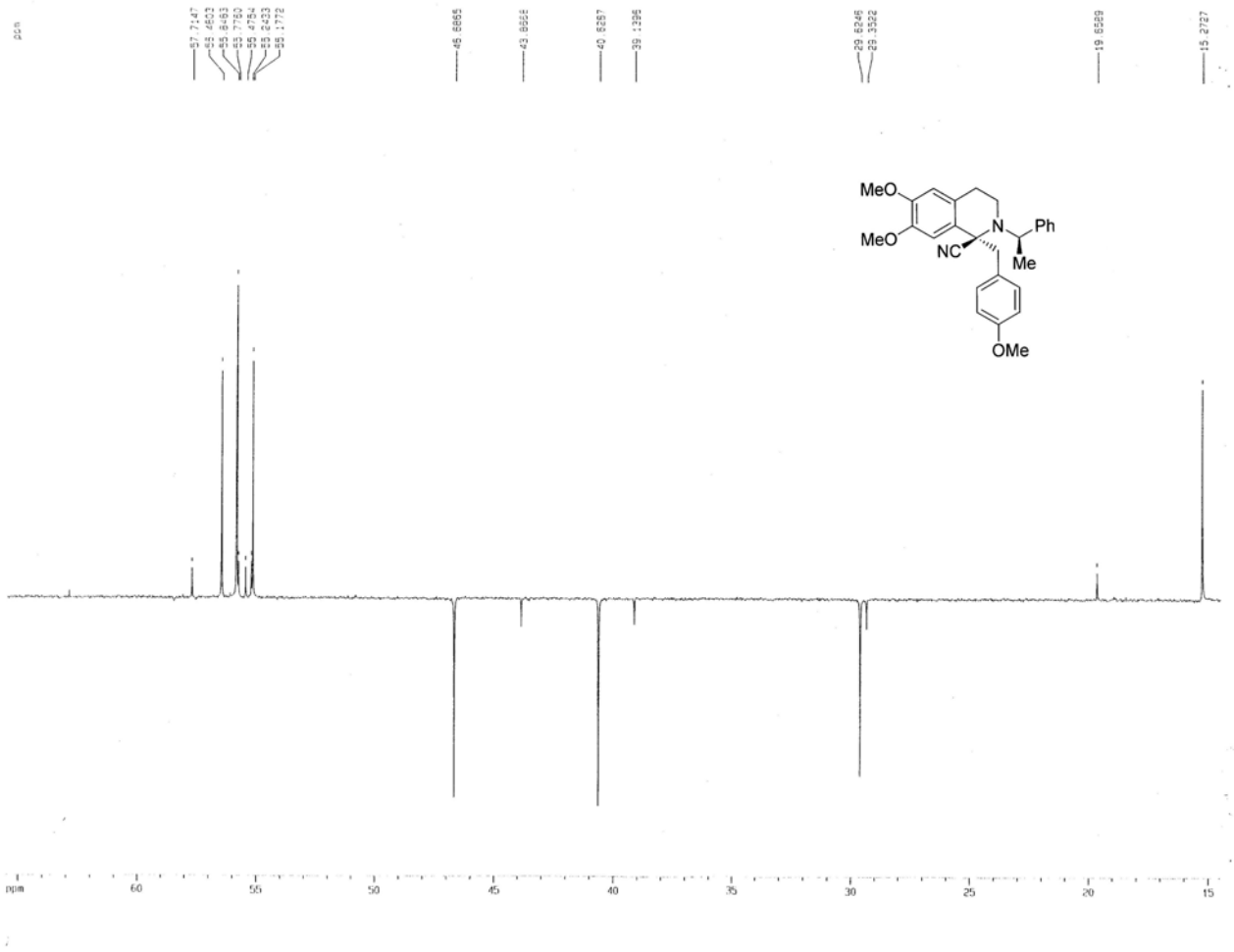

Figure 29 : DEPT spectrum of derivative **6b**

(*R,*R**)-1-(3,4-dimethoxy-benzyl)-6,7-dimethoxy-2-(1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (6c).** This has been prepared according to the procedure A using 1.30 g (4.03 mmol) of α-aminonitrile **2** and a THF solution (3 mL) of bromide **8** (1.30 g, 5.62 mmol) which was added dropwise (by syringe) onto the anion solution. Work-up afforded a yellow paste which was recrystallized in 15 mL of hot ethanol to afford α-aminonitrile **6c** (1.36 g, 71%) as a crystalline yellow powder. A further slow crystallization (24 h) of this powder from ethanol afforded single yellow plates which were analyzed by X-ray diffraction. Yellow plates; m.p. 130–132 °C. ^{1}H NMR (isomeric mixture, 90:10, major diastereoisomer, $CDCl_3$, 300 MHz) δ = 1.72 (d, J = 6.8 Hz, 3 H), 2.45 (dt, J = 15.2, 2.5 Hz, 1 H), 2.59 (ddd, J = 15.2, 10.9, 6.5 Hz, 1 H), 2.85 (td, J = 10.7, 2.5 Hz, 1 H), 2.89 (ddd, J = 10.7, 7.7, 2.5 Hz, 1 H), 3.36 (d, J = 14.2 Hz, 1 H), 3.41 (s, 3 H), 3.47 (d, J = 14.2 Hz, 1 H), 3.77 (s, 3 H), 3.80 (s, 3 H), 3.85 (s, 3 H), 4.75 (q, J = 6.8 Hz, 1 H), 6.17–6.19 (m, 2 H), 6.47–6.51 (m, 2 H), 6.76 (s, 1 H), 7.14–7.28 (m, 5 H) ppm. ^{13}C NMR (isomeric mixture, 90:10, major diastereoisomer, $CDCl_3$, 75 MHz): δ = 15.2 (p), 29.5 (s), 40.7 (s), 46.8 (s), 55.3 (p), 55.7 (p), 55.9 (p), 56.0 (p), 56.5 (t), 62.8 (q), 110.2 (t), 110.8 (t), 111.0 (t), 113.5 (t), 122.6 (q), 123.4 (t), 125.5 (q), 126.6 (t), 126.7 (q), 126.8 (t), 128.2 (t), 129.3 (q), 144.2 (q), 147.3 (q), 147.9 (q), 148.5 (q) ppm. HRMS: $C_{28}H_{31}NO_4$ $[M–HCN]^+$: calc. for 445.2253; found: 445.2231; $C_{29}H_{32}N_2O_4$: calc. C 73.70, H 6.83, N 5.93; found C 73.60, H 6.73, N 5.80.

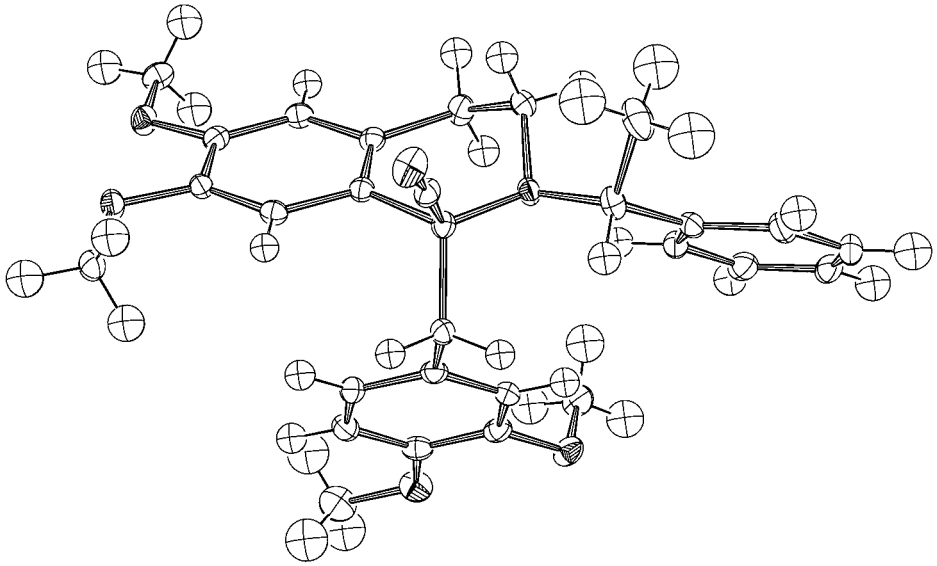

Figure 30 : ORTEP drawing of derivative **6c** (Ellipsoid plots are drawn with 40% of probability)

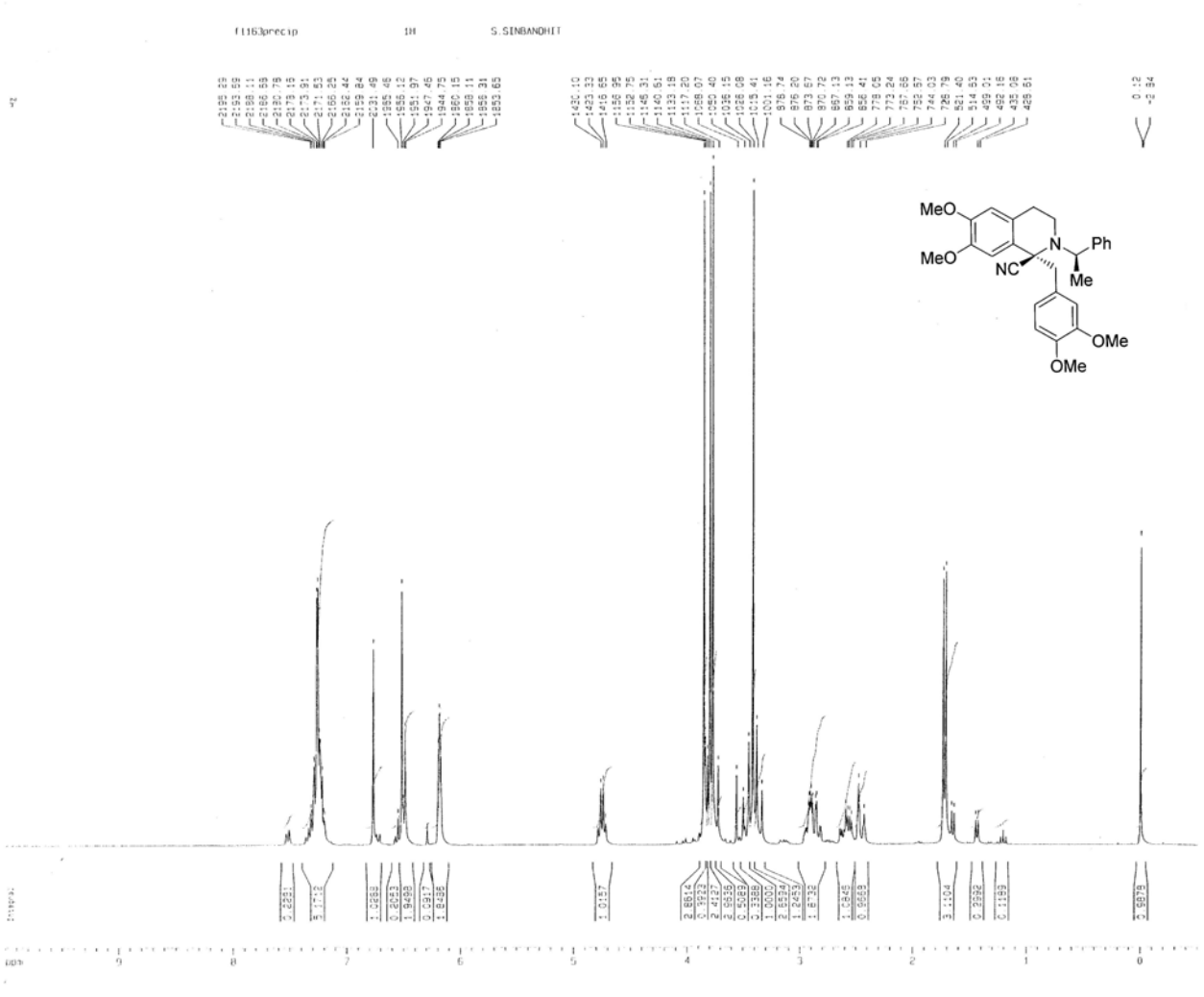

Figure 31 : ^{1}H NMR spectrum of derivative **6c**

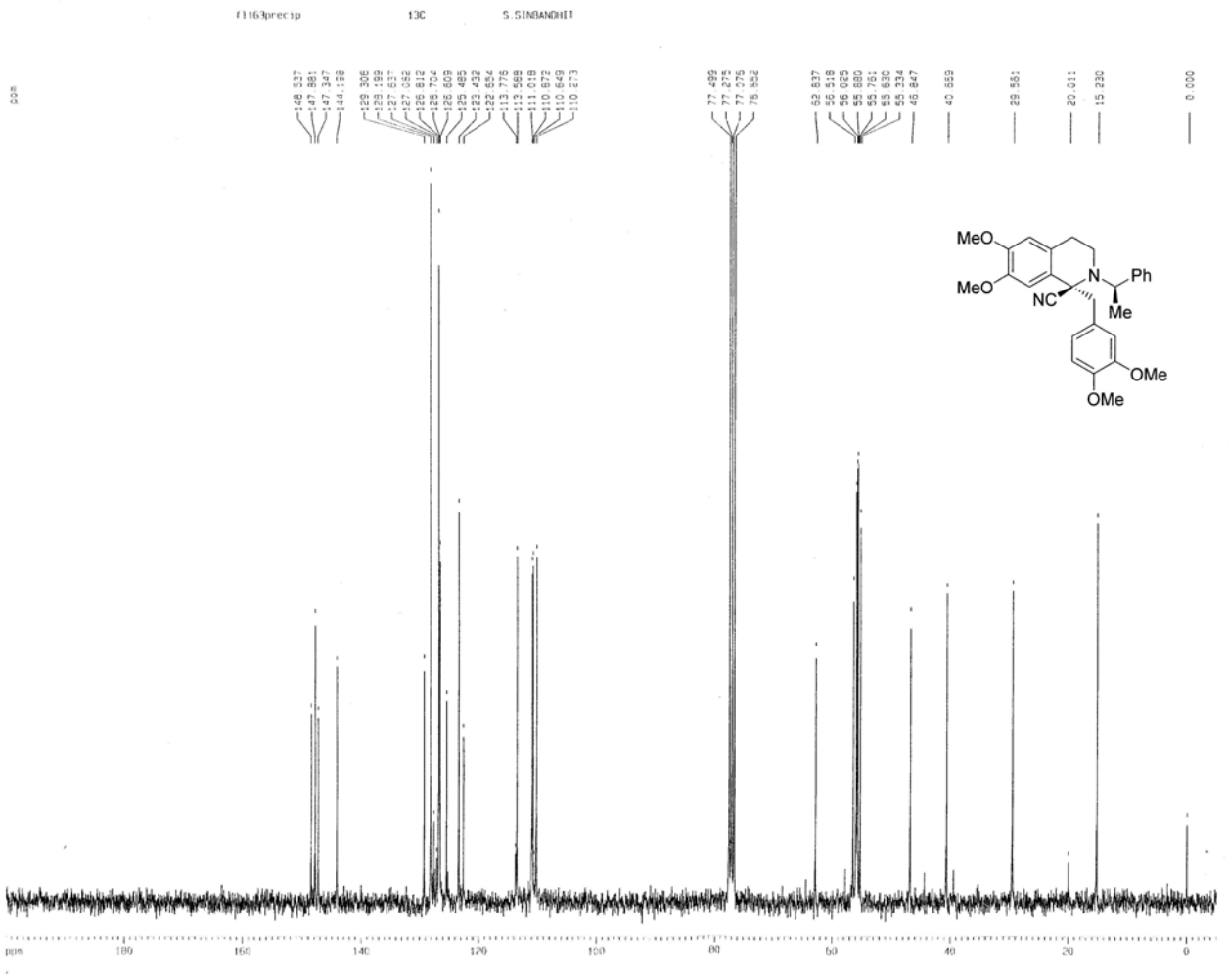

Figure 32 : ^{13}C NMR spectrum of derivative **6c**

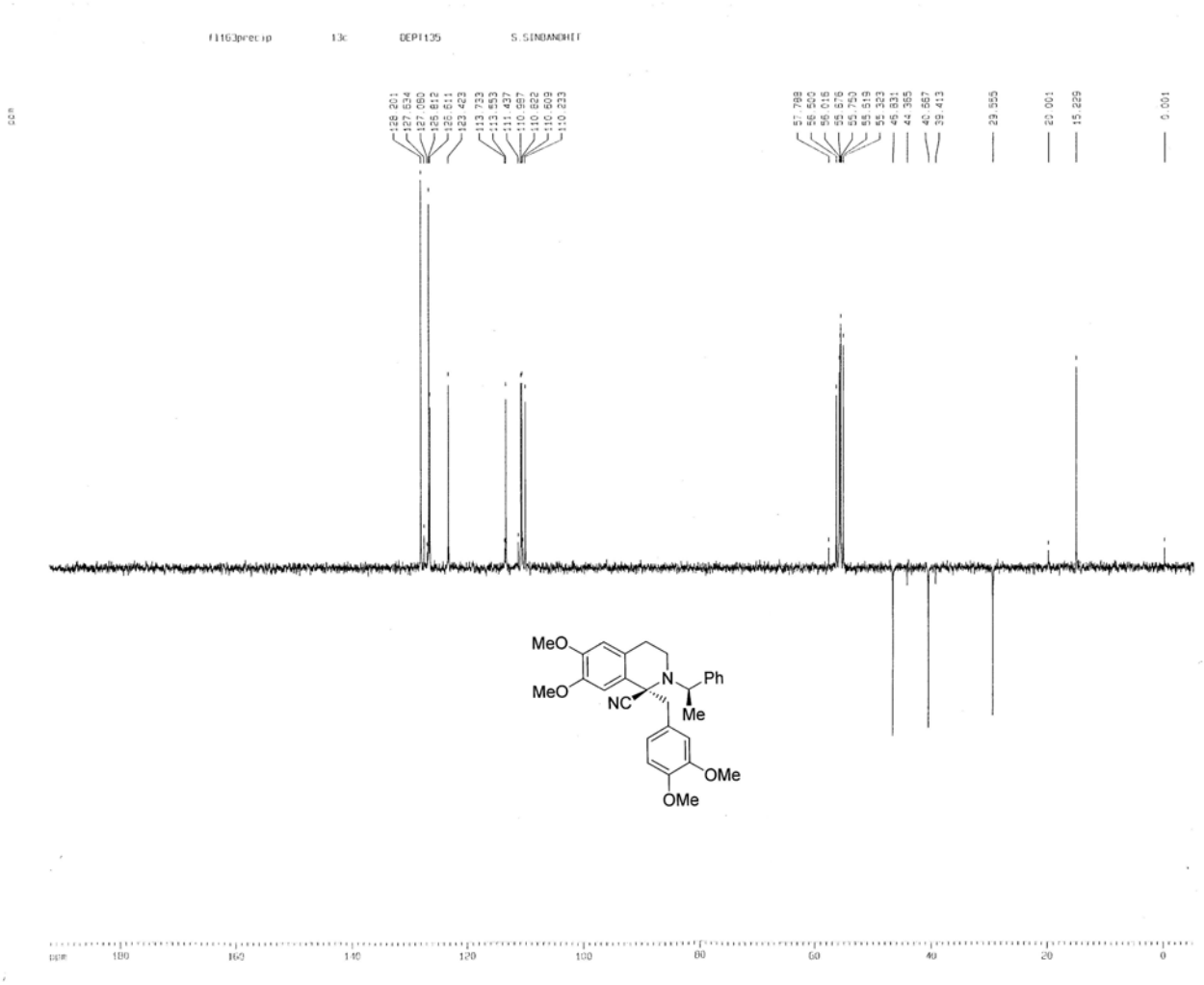

Figure 33 : DEPT spectrum of derivative **6c**

General procedure for the reductive decyanation of α-aminonitriles 6a-c (Procedure B). $NaBH_4$ (4 equiv.) was added in portions at –20 °C to a suspension of α-aminonitriles **6a-c** (4.0 mmol) in 20 mL of ethanol. The reaction mixture was warmed up to 0 °C and was stirred at that temperature over a 12 h period. The solvent was removed under reduced pressure, and the crude material was taken-up with a 15% ammonia solution (20 mL) and was extracted with dichloromethane (50 mL × 3). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture of tetrahydroisoquinolines **9a-c** was purified by column chromatography over a silica column.

(*R,*R**)-6,7-dimethoxy-1-methyl-2-(1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline (9a).** White powder (1.02 g, 76%); m.p. 70–72 °C (petroleum ether). R_f = 0.4 (diethyl ether/petroleum ether, 50:50)]. ^{1}H NMR (isomeric mixture, 98:2, major diastereoisomer, $CDCl_3$, 300 MHz): δ = 1.31 (d, J = 6.7 Hz, 3 H), 1.38 (d, J = 6.5 Hz, 3 H), 2.42 (dt, J = 16.0, 2.6 Hz, 1 H), 2.82 (ddd, J = 16.0, 10.3, 6.4 Hz, 1 H), 2.95–3.00 (m, 2 H), 3.74 (q, J = 6.5 Hz, 1 H), 3.81 (s, 3 H), 3.84 (s, 3 H), 3.95 (q, J = 6.7 Hz, 1 H), 6.47 (s, 1 H), 6.57 (s, 1 H), 7.20–7.38 (m, 5 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.5 (p), 21.6 (p), 25.8 (s), 39.8 (s), 53.3 (t), 55.8 (p), 55.9 (p), 59.4 (t), 110.6 (t), 111.3 (t), 126.4 (q), 126.7 (t), 127.2 (t), 128.3 (t), 132.2 (q), 146.7 (q), 147.1 (q), 147.2 (q) ppm. HRMS: $C_{20}H_{25}NO_2$ $[M]^+$: calc. for 311.1885; found: 311.1877; $C_{20}H_{25}NO_2$: calc. C 77.14, H 8.09, N 4.50; found C 76.80, H 8.07, N 4.48.

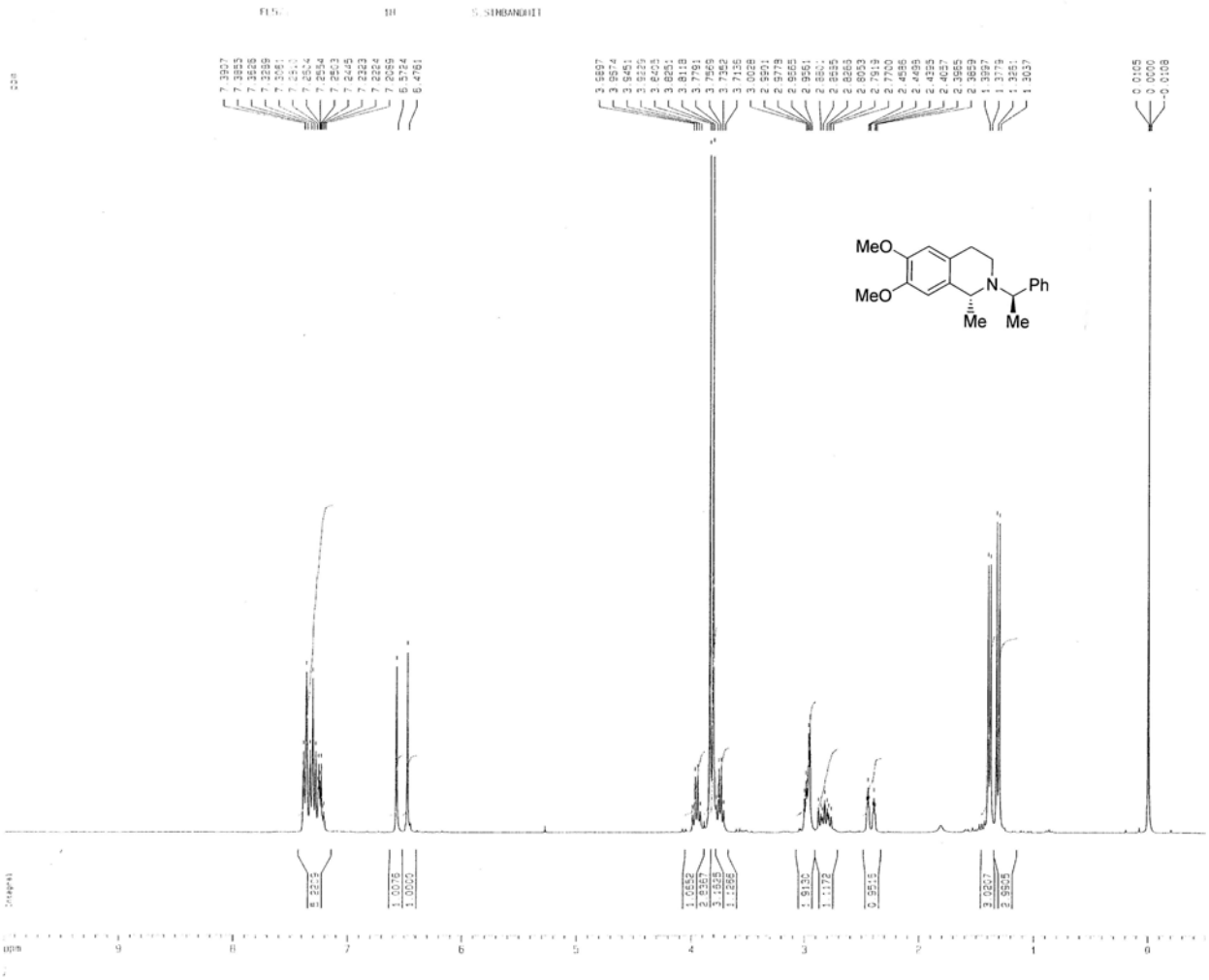

Figure 34 : ^{1}H NMR spectrum of derivative **9a**

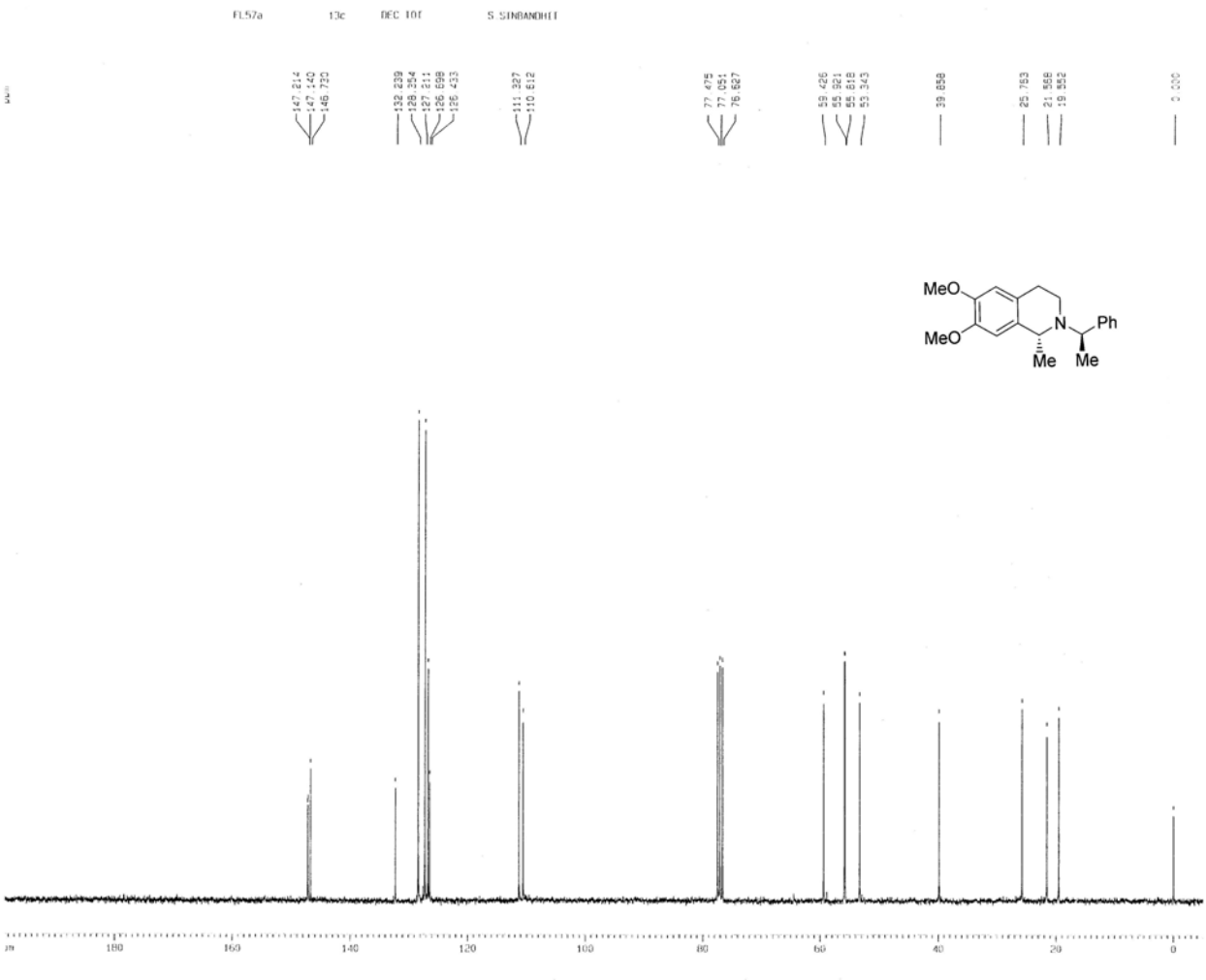

Figure 35 : ^{13}C NMR spectrum of derivative **9a**

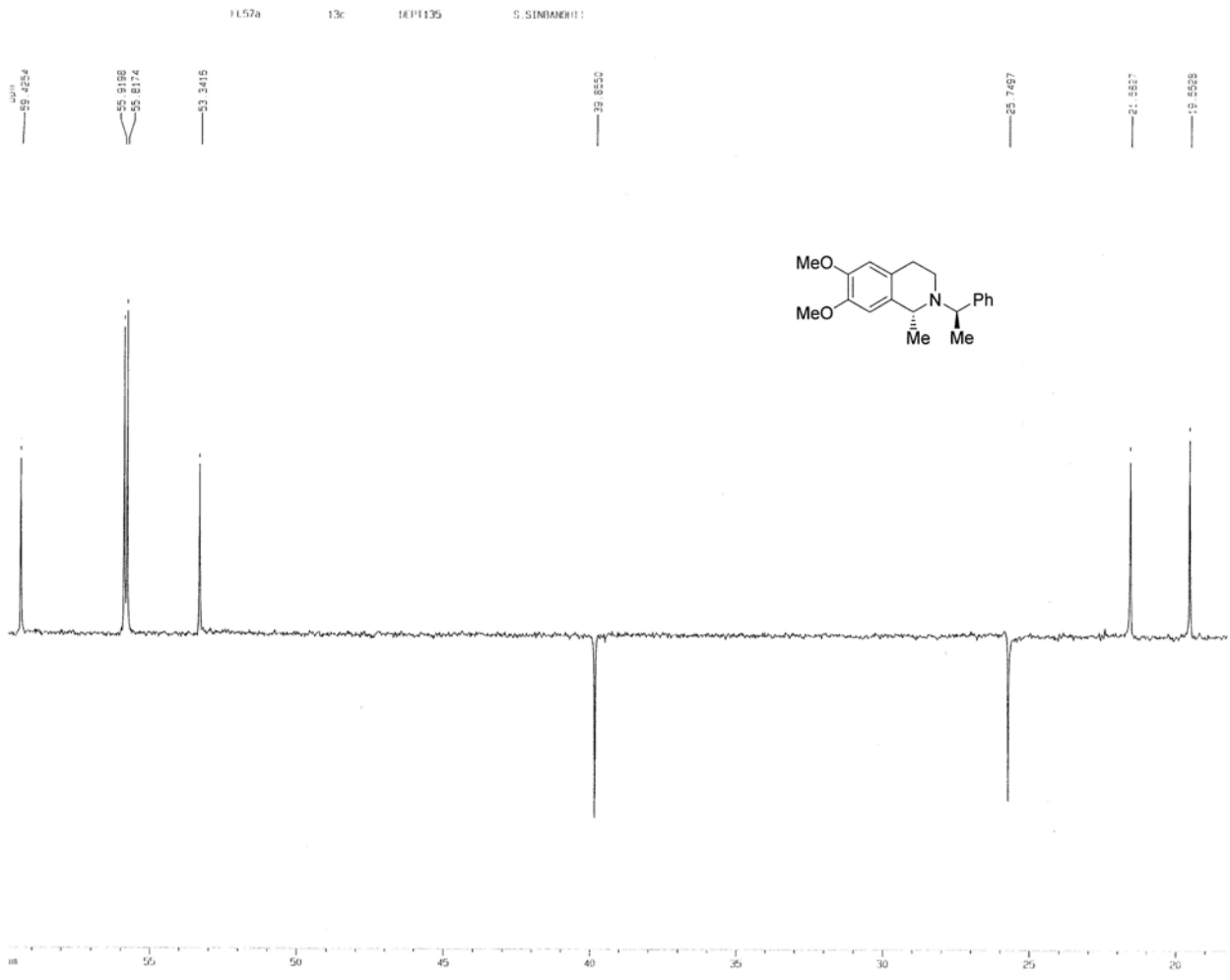

Figure 36 : DEPT spectrum of derivative **9a**

(*R,*R**)-6,7-dimethoxy-1-(4-methoxy-benzyl)-2-(1-phenyl-ethyl)- 1,2,3,4-tetrahydroisoquinoline (9b).** This was prepared according to procedure B to afford tetrahydroisoquinoline **9b** as a white powder (1.41 g, 84%, isomeric mixture 90:10). A further crystallization in hot ethanol afforded single crystals which analyzed by X-ray diffraction. Colourless plates; m.p. 137–138 °C (ethanol). R_f = 0.2 (diethyl ether/petroleum ether, 50:50). ^{1}H NMR (isomeric mixture, 95:5, major diastereoisomer, $CDCl_3$, 300 MHz): δ = 1.37 (d, J = 6.5 Hz, 3 H), 2.49 (dd, J = 16.5, 2.8 Hz, 1 H), 2.70 (dd, J = 13.3, 7.7 Hz, 1 H), 2.88 (ddd, J = 16.5, 11.7, 6.1 Hz, 1 H), 3.05 (dd, J = 13.3, 6.5 Hz, 1 H), 3.15–3.33 (m, 2 H), 3.51 (s, 3 H), 3.67–3.79 (m, 2 H), 3.77 (s, 3 H), 3.83 (s, 3 H), 5.85 (s, 1 H), 6.58 (s, 1 H), 6.78 (d, J_{AB} = 8.6 Hz, 1 H), 6.81 (d, J_{AB} = 8.6 Hz, 1 H), 7.09–7.20 (m, 2 H), 7.17–7.20 (m, 3 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.1 (p), 24.1 (s), 39.8 (s), 41.1 (s), 55.3 (p), 55.5 (p), 55.7 (p), 59.2 (t), 60.7 (t), 111.2 (t), 111.5 (t), 113.4 (t), 126.5 (q), 126.5 (t), 127.3 (t), 128.2 (t), 129.7 (q), 130.8 (t), 132.2 (q), 146.1 (q), 146.4 (q), 147.2 (q), 157.90 (q) ppm. HRMS: $C_{19}H_{22}NO_2$ $[M–C_8H_9O]^+$: calc. for 296.1650; found: 296.1642; $C_{27}H_{31}NO_3$: calc. C 77.67, H 7.48, N 3.35; found C 77.42, H 7.48, N 3.35.

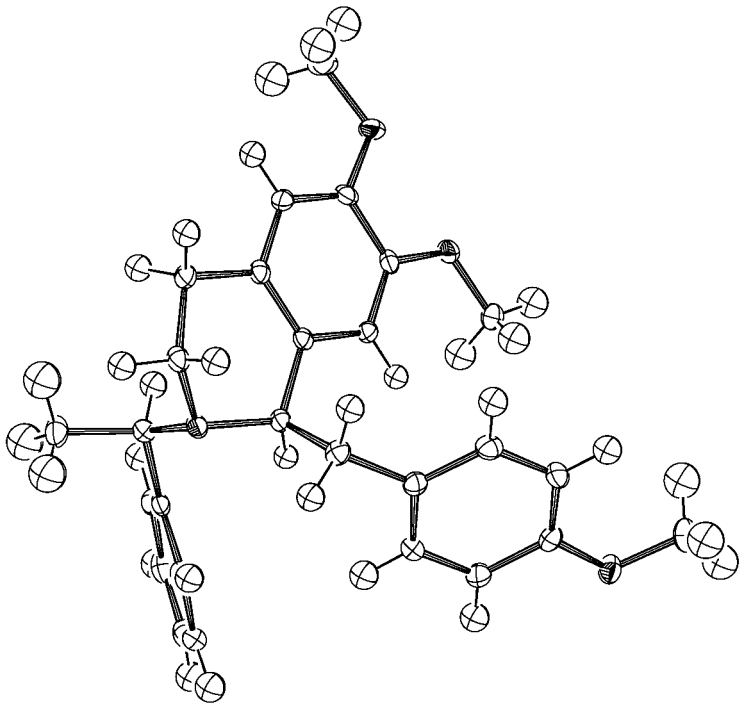

Figure 37 : ORTEP drawing of derivative **9b** (Ellipsoid plots are drawn with 40% of probability)

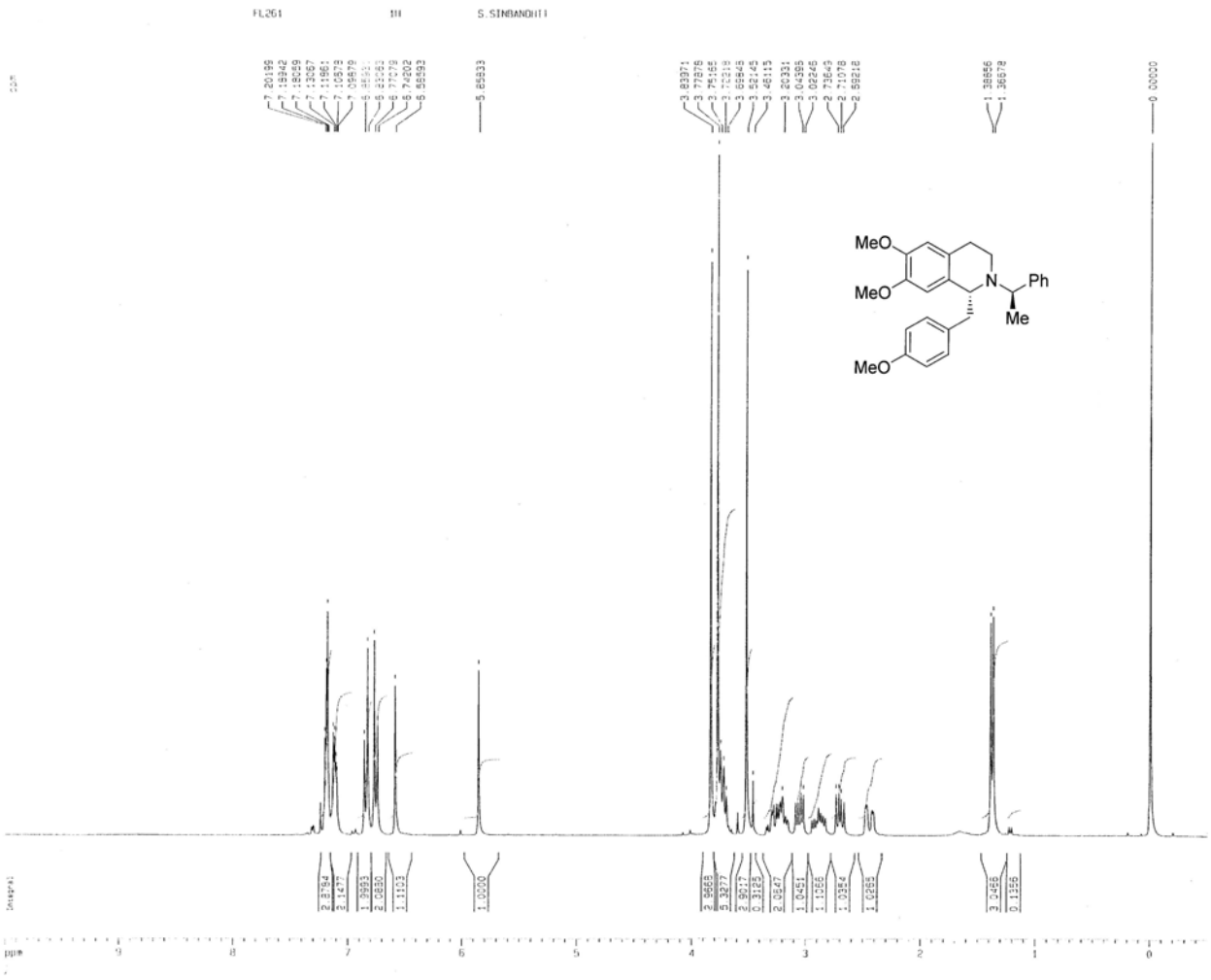

Figure 38 : ^{1}H NMR spectrum of derivative **9b**

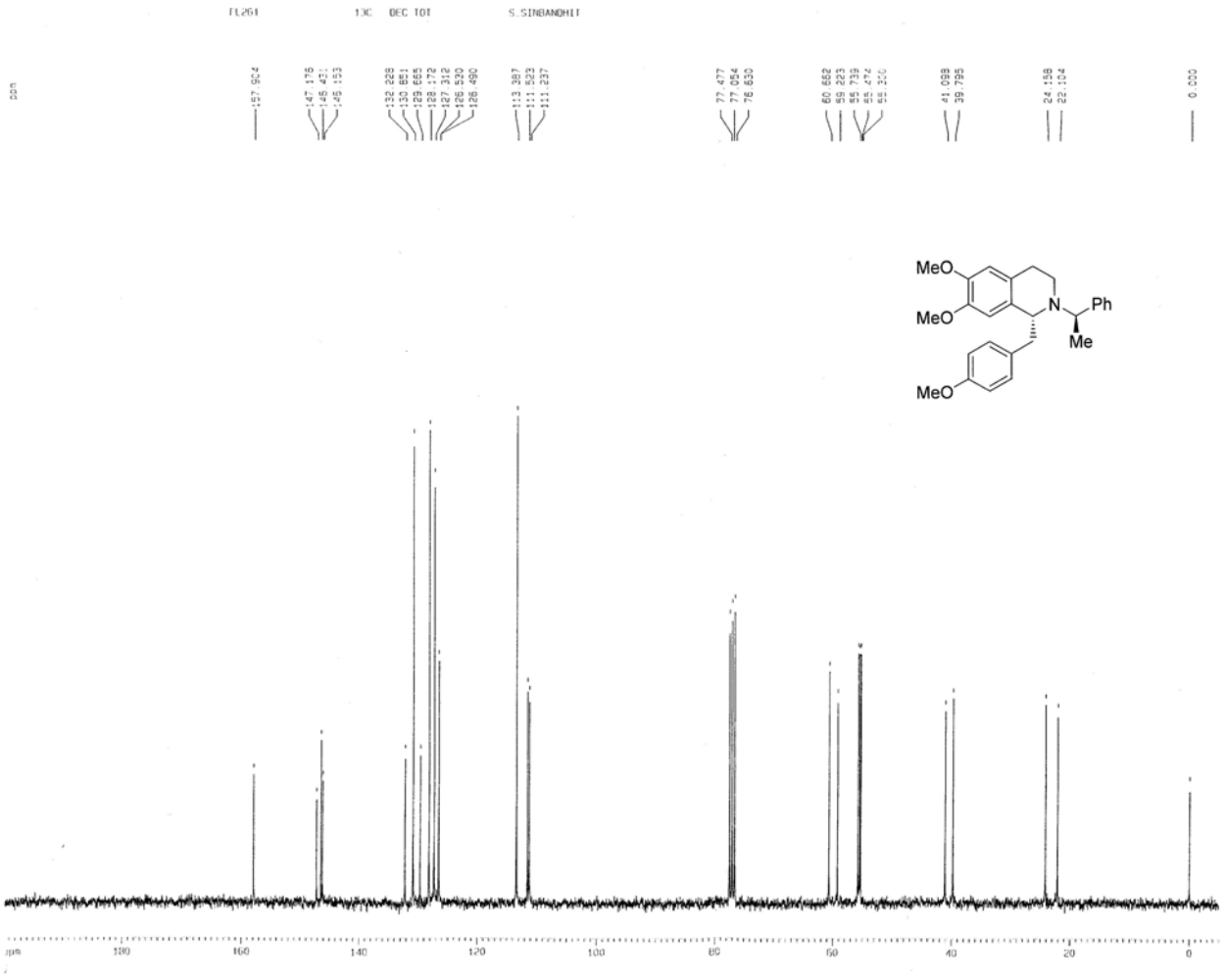

Figure 39 : ^{13}C NMR spectrum of derivative **9b**

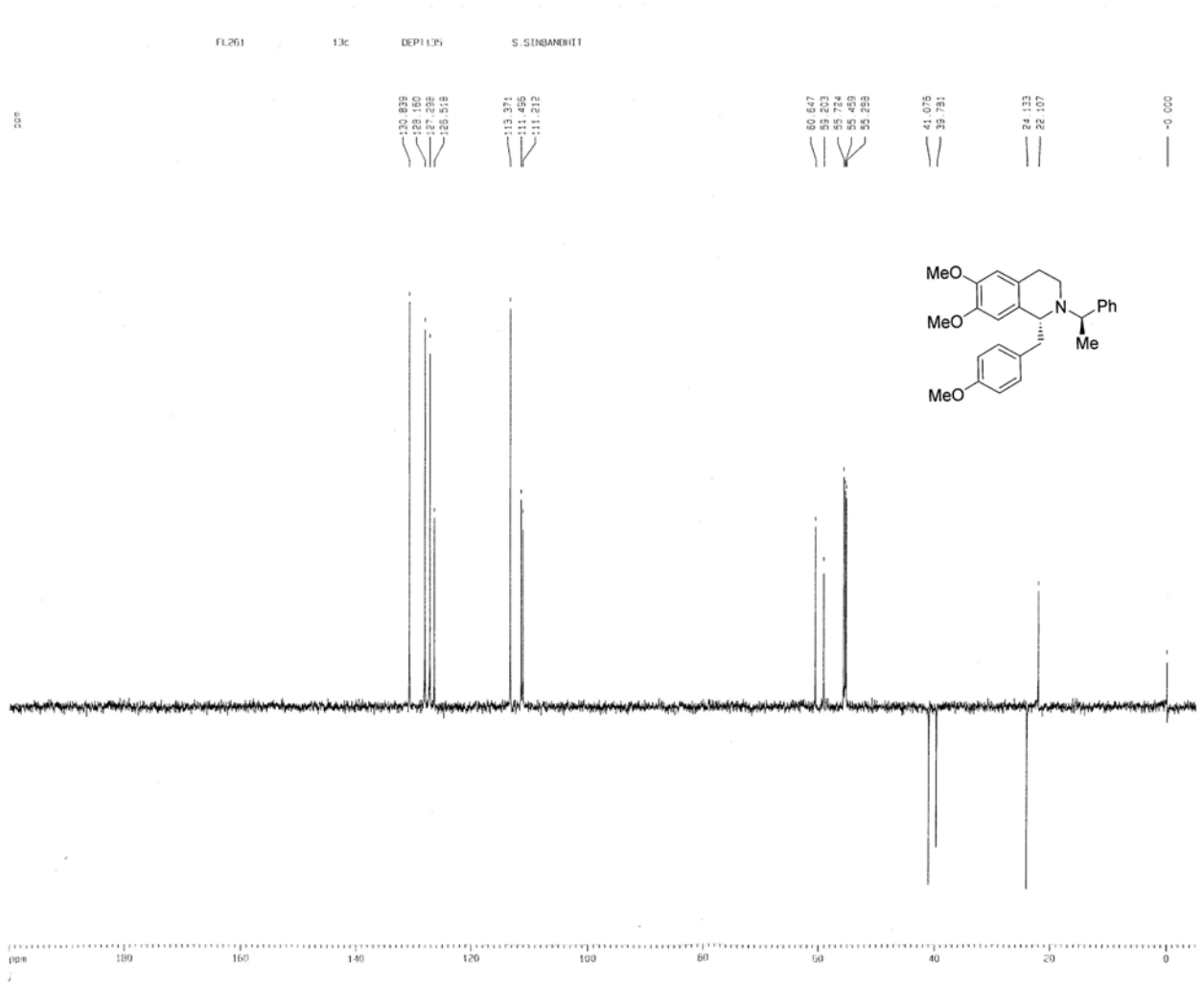

Figure 40 : DEPT spectrum of derivative **9b**

(*R,*R**)-1-(3,4-dimethoxy-benzyl)-6,7-dimethoxy-2-(1-phenyl-ethyl)-1,2,3,4-tetrahydroisoquinoline (9c).** This was prepared according to procedure B to afford tetrahydroisoquinoline **9c** as a white powder (1.57 g, 88%, isomeric mixture 85:15) which was recrystallized in ethanol. White powder; m.p. 102–104 °C (ethanol). R_f = 0.2 (diethyl ether/petroleum ether, 50:50)]. ^{1}H NMR (isomeric mixture, 95:5, major diastereoisomer, $CDCl_3$, 300 MHz): δ = 1.37 (d, J = 6.5 Hz, 3 H), 2.44 (dm, J = 16.5, Hz, 1 H), 2.70 (dd, J = 13.3, 7.7 Hz, 1 H), 2.88 (ddd, J = 16.5, 11.7, 6.1 Hz, 1 H), 3.05 (dd, J = 13.3, 6.1 Hz, 1 H), 3.15–3.33 (m, 2 H), 3.54 (s, 3 H), 3.67–3.79 (m, 2 H), 3.69 (s, 3 H), 3.84 (s, 3 H), 3.85 (s, 3 H), 5.90 (s, 1 H), 6.37 (d, J = 1.8 Hz, 1 H), 6.49 (dd, J = 8.1, 1.8 Hz, 1 H), 6.59 (s, 1 H), 6.72 (d, J = 8.1 Hz, 1 H), 7.11–7.20 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.9 (p), 23.9 (s), 39.8 (s), 42.2 (s), 55.6 (p), 55.7 (p), 55.8 (p), 56.0 (p), 59.1 (t), 60.8 (t), 110.8 (t), 111.3 (t), 111.5 (t), 112.9 (t), 121.9 (t), 126.5 (t), 127.4 (t), 128.1 (t), 129.6 (q), 132.8 (q), 146.3 (q), 146.5 (q), 147.2 (q), 148.4 (q) ppm. HRMS: $C_{19}H_{22}NO_2$ $[M–C_9H_{11}O_2]^+$: calc. for 296.1650; found: 296.1639; $C_{28}H_{33}NO_4$: calc. C 75.14, H 7.43, N 3.13; found C 74.65, H 7.48, N 3.13.

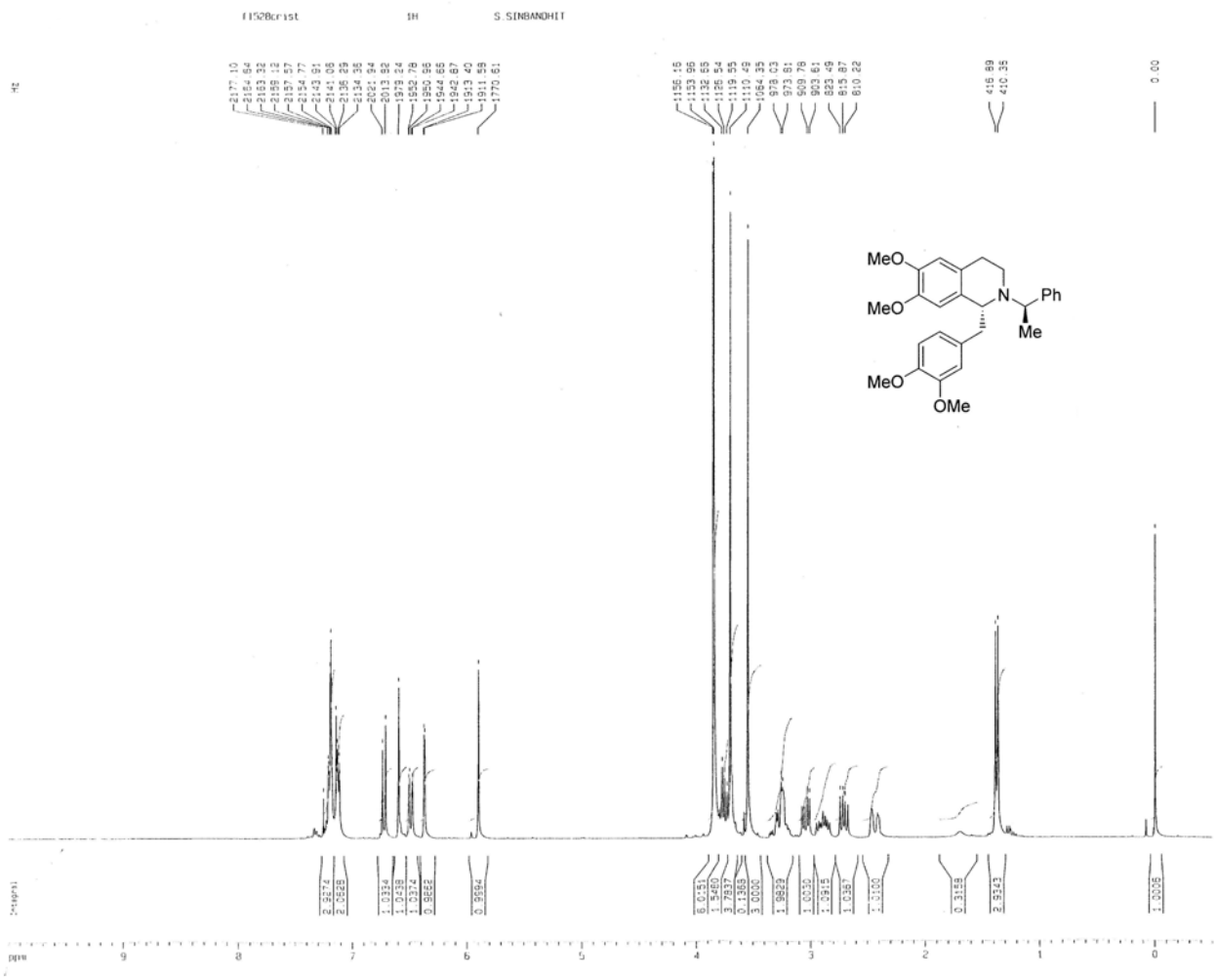

Figure 41 : ^{1}H NMR spectrum of derivative **9c**

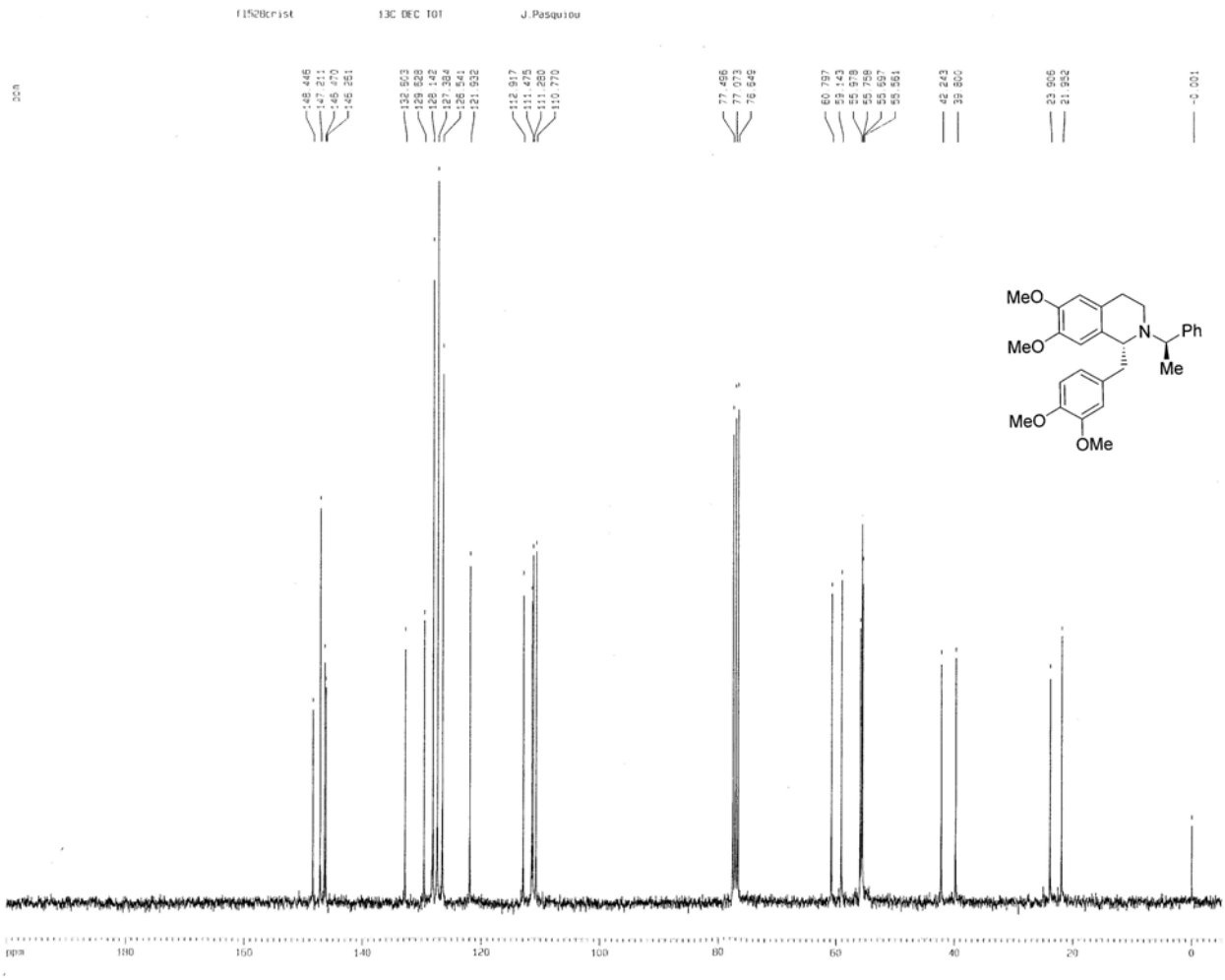

Figure 42 : ^{13}C NMR spectrum of derivative **9c**

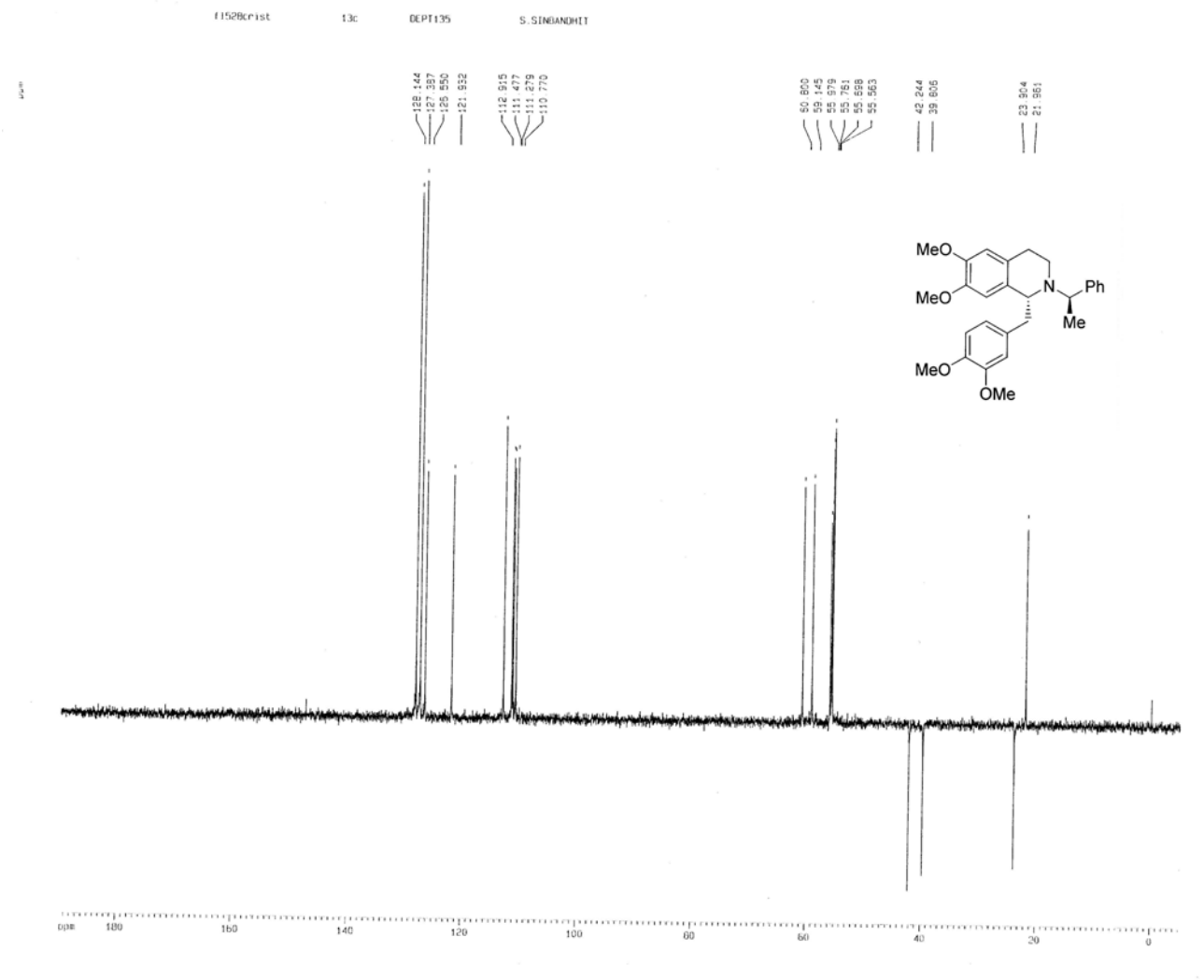

Figure 43 : DEPT spectrum of derivative **9c**

General hydrogenolysis procedure (Procedure C). Tetrahydroisoquinolines **9a-c** (4.0 mmol) were dissolved in 8 mL of ethanol containing 2 mL of 10% HCl. The resulting solution was placed in a low-pressure hydrogenator in the presence of 10% Pd/C (20% in weight) and a stir bar. Air was removed from the reactor by alternately filling it with hydrogen and venting it three times. The desired hydrogen pressure (2.25×10^3 Torr, 3 bars) was applied, and the suspension was stirred for 48 h at room temperature. The suspension was filtered over a small pad of Celite, and the vessel was washed thoroughly with ethanol. The filtrate was concentrated *in vacuo* and the resulting paste was dissolved in 10 mL of water. The solution was cooled in an ice bath and basified with solid KOH. The white oily residue was extracted with dichloromethane (50 mL × 3) and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixtures of tetrahydroisoquinolines **10a-c** were purified by column chromatography (dichloromethane/methanol, 8:2). Analyses should be carried out immediately after chromatographic purifications. Tetrahydroisoquinolines **10a-c** are sensitive to aerial oxidation and should kept at –20 °C for storage.

6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline (10a). This was prepared according to procedure C to afford *rac*-salsolidine (**10a**) as clear oil (0.78 g, 94%). R_f = 0.4 (dichloromethane/methanol, 80:20). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.43 (d, J = 6.7 Hz, 3 H), 2.64 (td, J = 16.0, 4.7 Hz, 1 H), 2.78 (ddd, J = 16.0, 8.7, 4.7 Hz, 1 H), 2.98 (ddd, J = 12.8, 8.70, 4.7 Hz, 1 H), 3.24 (td, J = 12.8, 4.7 Hz, 1 H), 3.84 (s, 3 H), 3.95 (s, 3 H), 4.03 (q, J = 6.7 Hz, 1 H), 6.56 (s,

1 H), 6.62 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 22.8 (p), 29.5 (s), 41.8 (s), 51.2 (t), 55.9 (p), 56.0 (p), 109.1 (t), 111.8 (t), 126.8 (q), 132.5 (q), 147.3 (q), 147.3 (q) ppm. HRMS: $C_{12}H_{17}NO_2$ $[M]^+$: calc. for 207.1259; found: 207.1276; $C_{12}H_{17}NO_2$: calc. C 69.54, H 8.27, N 6.76; found C 68.61, H 8.12, N 6.34.

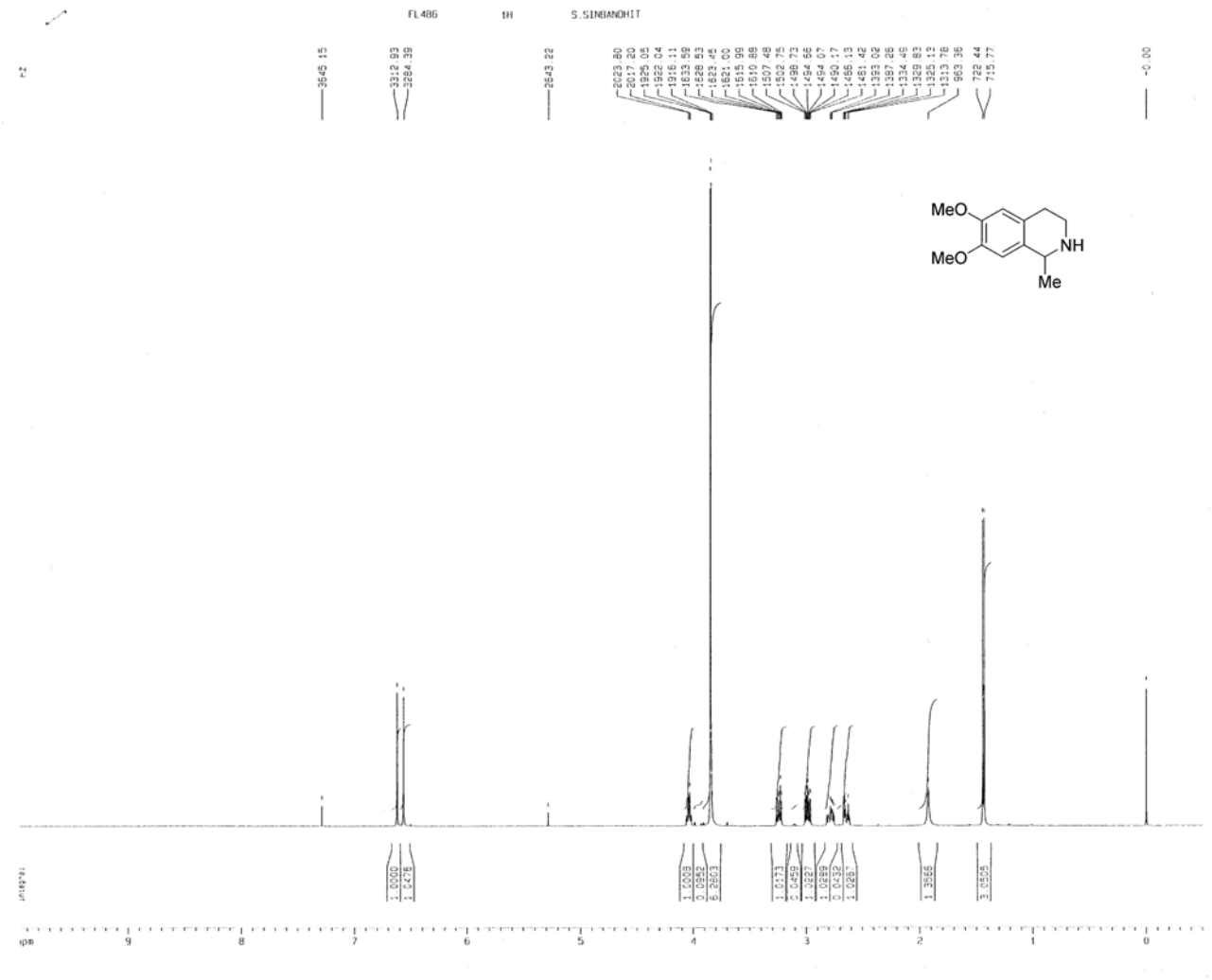

Figure 44 : ^{1}H NMR spectrum of *rac*-salsolidine (**10a**)

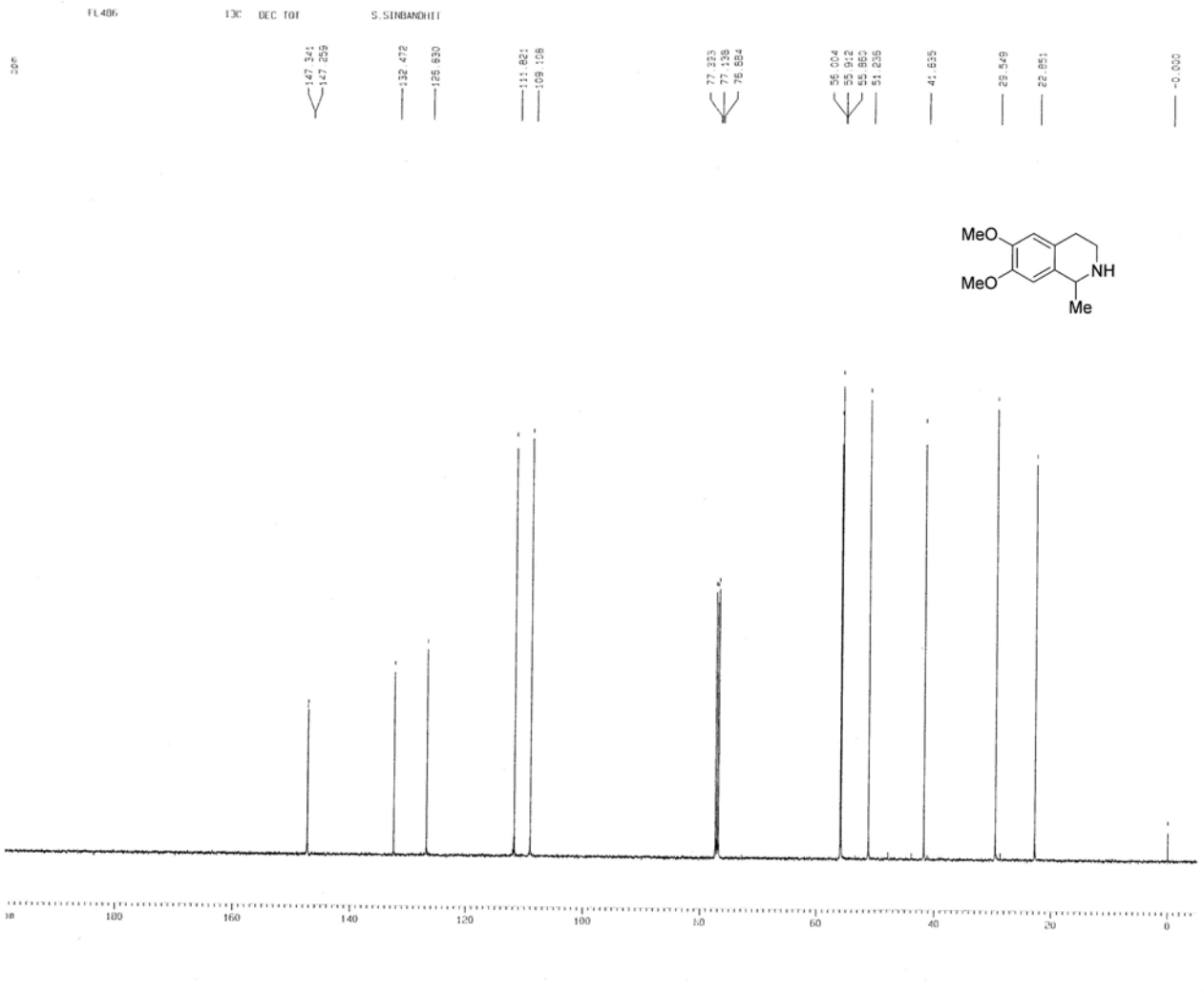

Figure 45 : ^{13}C NMR spectrum of *rac*-salsolidine (**10a**)

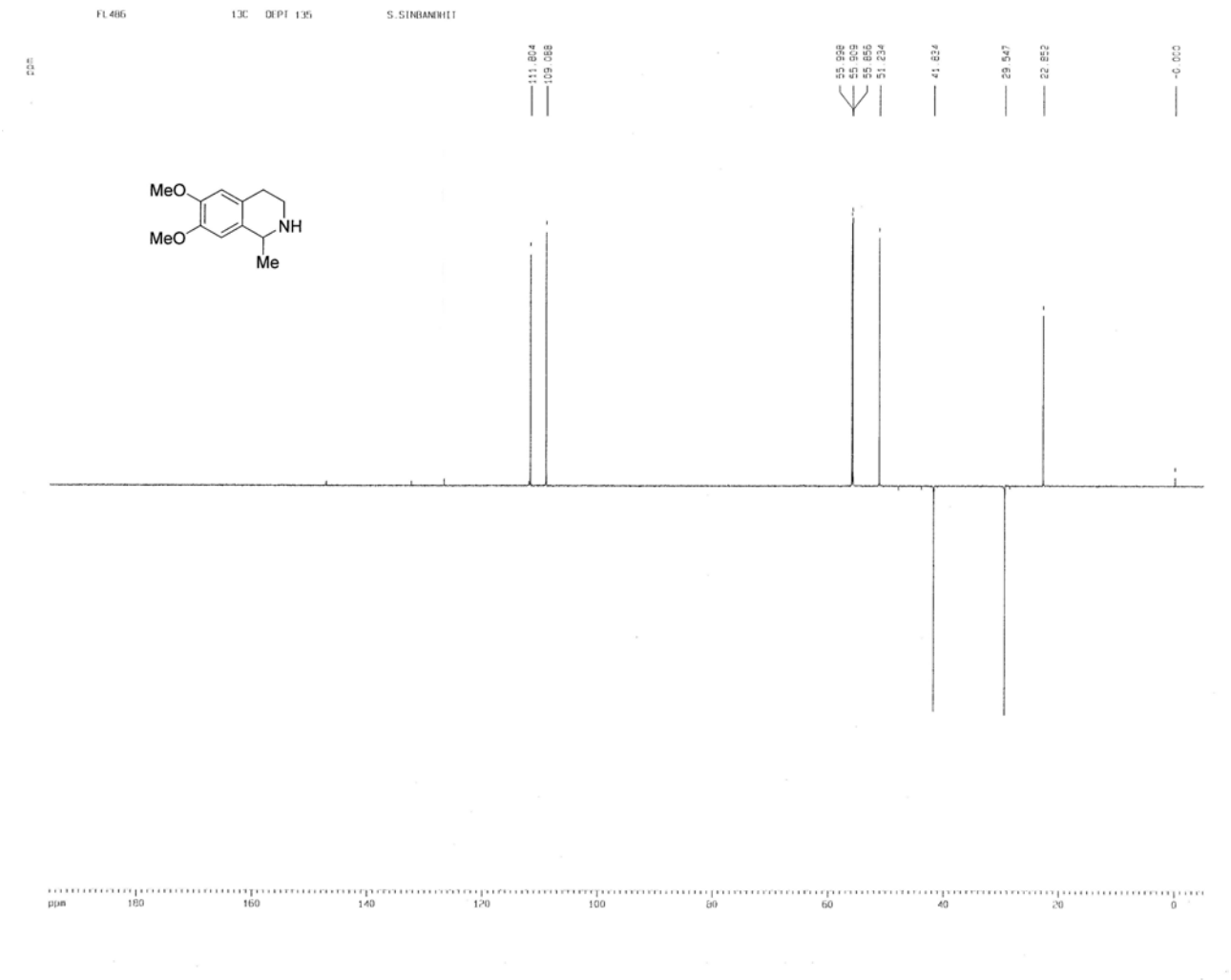

Figure 46 : DEPT spectrum of *rac*-salsolidine (**10a**)

6,7-dimethoxy-1-(4-methoxy-benzyl)-1,2,3,4-tetrahydroisoquinoline (10b). This was prepared according to procedure C to afford *rac-O,O*-dimethylcoclaurine (**10b**) as a viscous clear oil (1.0 g, 80%). R_f = 0.3 (dichloromethane/methanol, 90:10). ^{1}H NMR ($CDCl_3$, 300 MHz): 2.61–2.75 (m, 2 H), 2.79–2.94 (m, 2 H), 3.11–3.23 (m, 2 H), 3.79 (s, 3 H), 3.81 (s, 3 H), 3.87 (s, 3 H), 4.10 (dd, J = 9.4, 4.3 Hz, 1 H), 6.58 (s, 1 H), 6.62 (s, 1 H), 6.86 (d, J = 8.6 Hz, 2 H), 7.16 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 29.4 (s), 40.7 (s), 41.8 (s), 55.3 (p), 55.8 (p), 56.0 (p), 56.9 (t), 109.5 (t), 111.8 (t), 114.0 (t), 127.3 (q), 130.3 (t), 130.5 (q), 131.0 (q), 147.0 (q), 147.4 (q), 158.3 (q) ppm. HRMS: $C_{11}H_{14}NO_2$ $[M–C_8H_9O]^+$: calc. for 192.1024; found: 192.1014; $C_{19}H_{23}NO_3$: calc. C 72.82, H 7.40, N 4.47; found C 72.76, H 7.24, N 4.38.

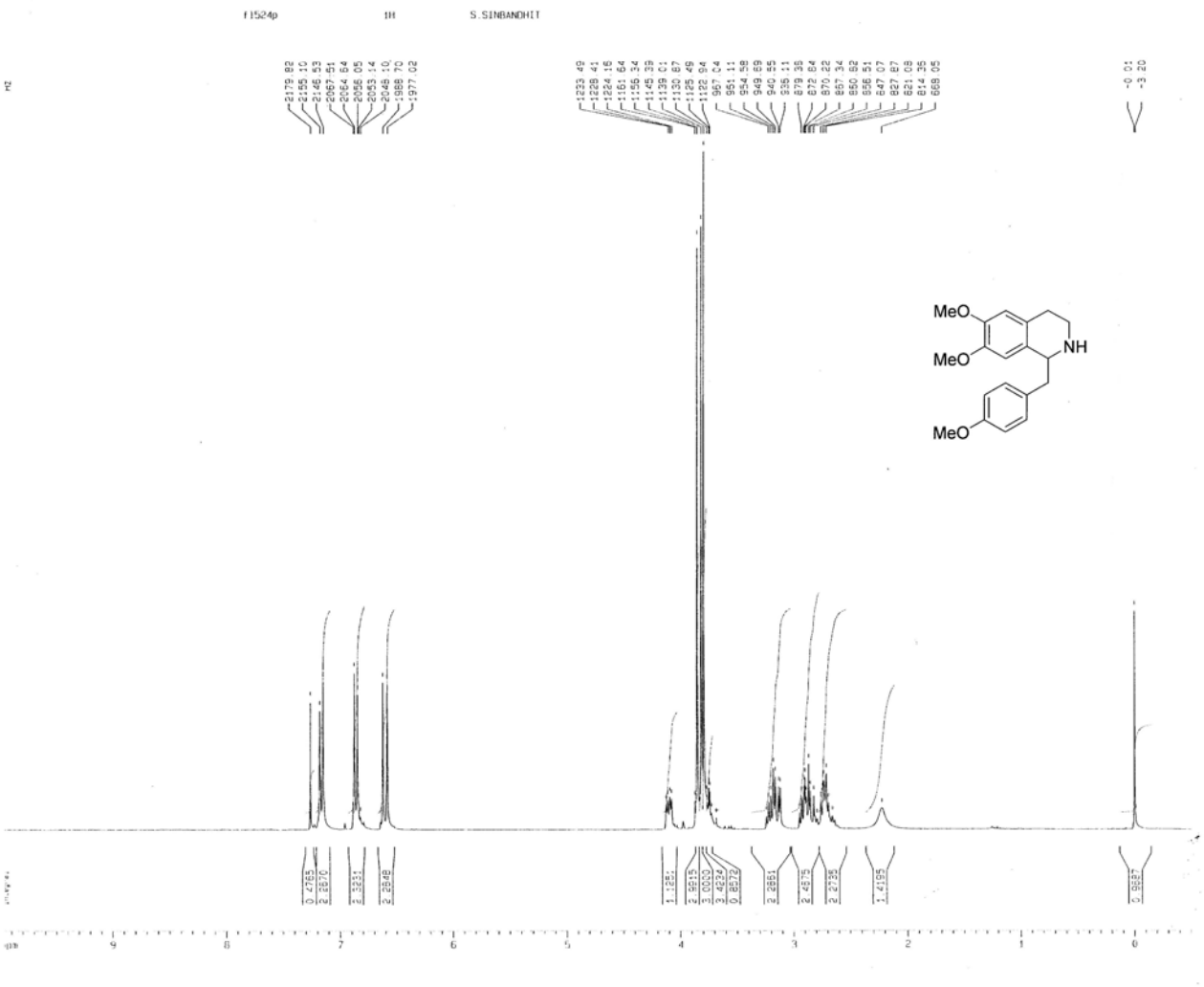

Figure 47 : ^{1}H NMR spectrum of *rac*-*O*,*O*-dimethylcoclaurine (**10b**)

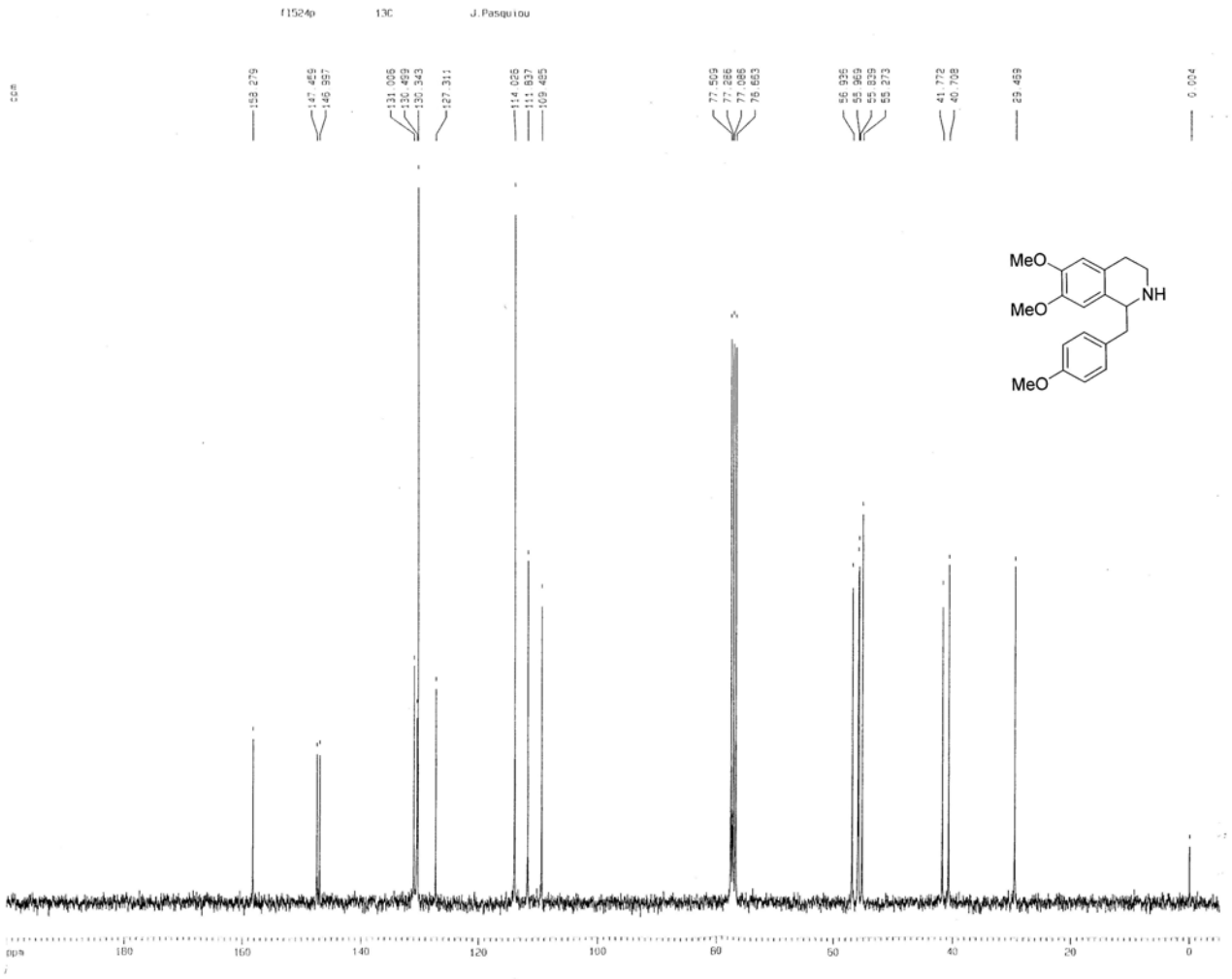

Figure 48 : ^{13}C NMR spectrum of *rac*-*O*,*O*-dimethylcoclaurine (**10b**)

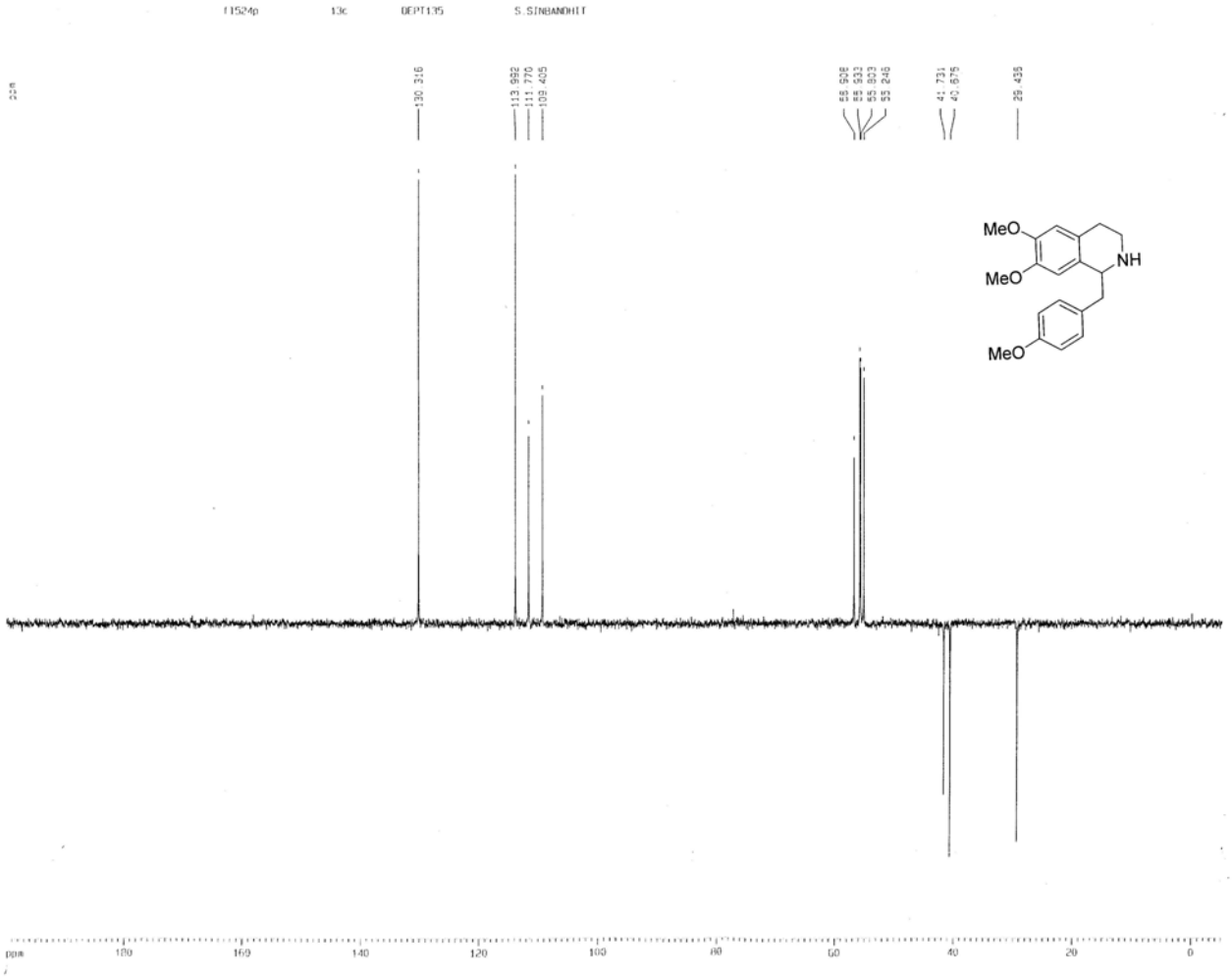

Figure 49 : DEPT spectrum of *rac*-*O*,*O*-dimethylcoclaurine (**10b**)

1-(3,4-dimethoxy-benzyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (10c). This was prepared according to procedure C to afford *rac*-norlaudanosine (**10c**) as viscous clear oil (1.23 g, 90%). R_f = 0.25 (dichloromethane/methanol, 95:5). ^{1}H NMR ($CDCl_3$, 300 MHz): 2.61–2.75 (m, 2 H), 2.79–2.94 (m, 2 H), 3.11–3.25 (m, 2 H), 3.82 (s, 3 H), 3.84 (s, 6 H), 3.86 (s, 3 H), 4.13 (dd, J = 8.9, 4.3 Hz, 1 H), 6.59 (s, 1 H), 6.65 (s, 1 H), 6.79 (s, br., 1 H), 6.78 (d, J_{AB} = 8.0 Hz, 1 H), 6.82 (d, J_{AB} = 8.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 29.4 (s), 40.9 (s), 42.2 (s), 55.8 (p), 55.8 (p), 55.9 (p), 56.0 (p), 56.8 (t), 109.4 (t), 111.3 (t), 111.8 (t), 112.5 (t), 121.4 (t), 127.4 (q), 130.3 (q), 131.4 (q), 147.0 (q), 147.5 (q), 147.7 (q), 149.0 (q) ppm. $C_{11}H_{14}NO_2$ $[M–C_9H_{11}O_2]^+$: calc. for 192.1025; found: 192.1014; $C_{20}H_{25}NO_4$: calc. C 69.95, H 7.34, N 4.08; found C 68.15, H 7.28, N 4.02.

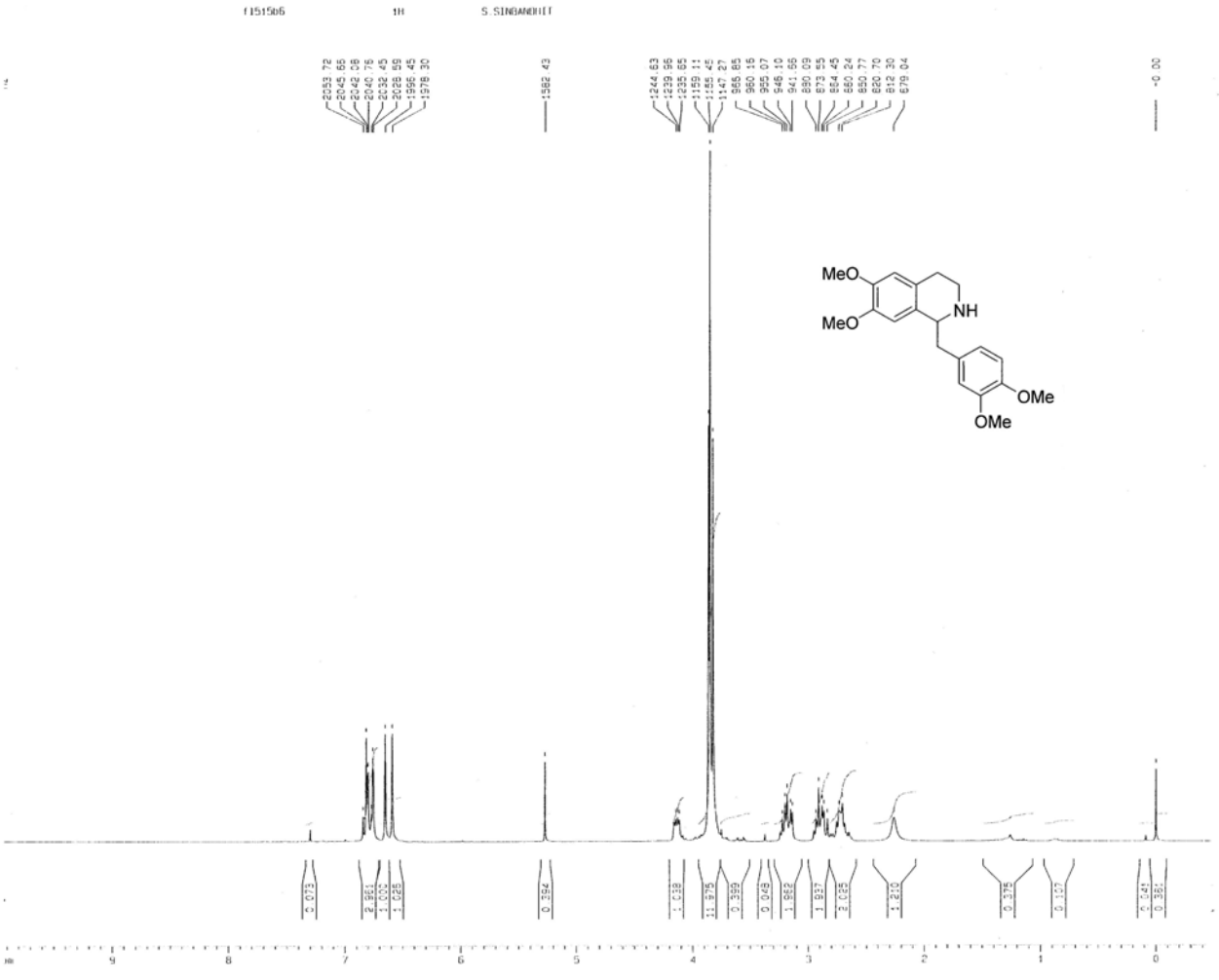

Figure 50 : ^{1}H NMR spectrum of *rac*-norlaudanosine (**10c**)

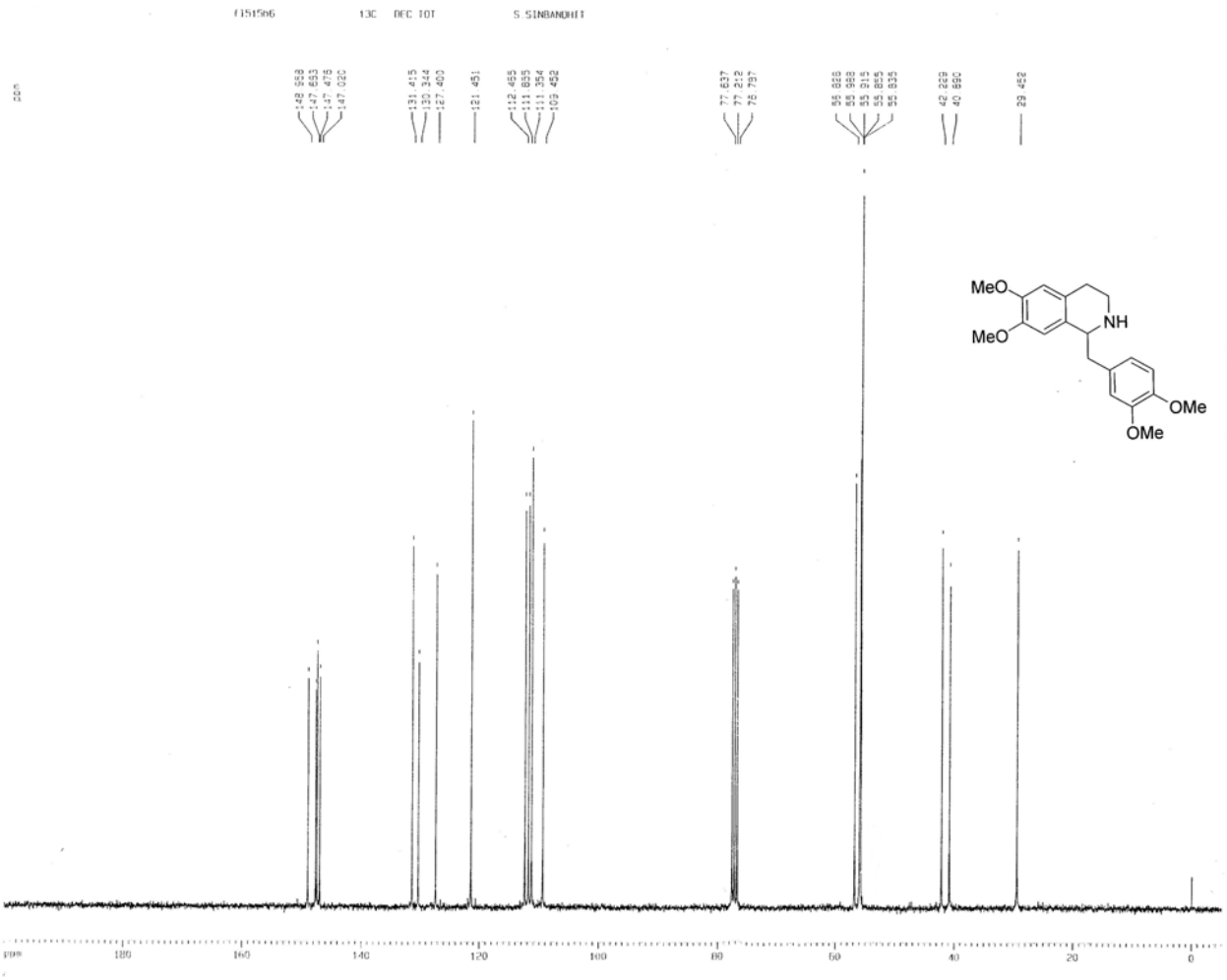

Figure 51 : ^{13}C NMR spectrum of *rac*-norlaudanosine (**10c**)

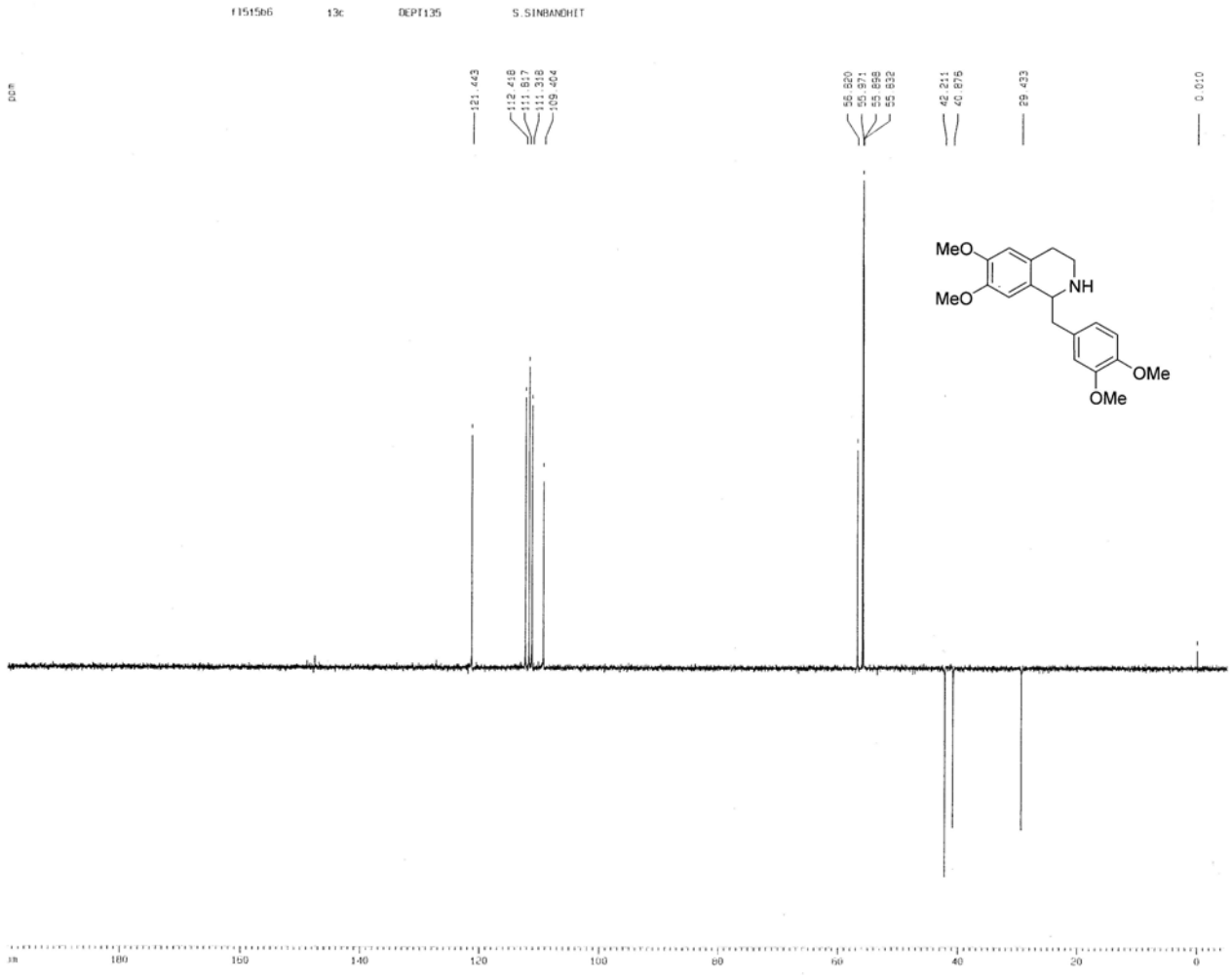

Figure 52 : DEPT spectrum of *rac*-norlaudanosine (**10c**)

X-ray Crystallographic Study: Crystallographic data were collected on a diffractometer with graphite monochromated Mo–K_α radiation. Details are given in table 1. The structures were solved by direct methods with SIR-97,[1] which revealed the non-hydrogen atoms of the molecules. Refinement was performed by full-matrix least-square techniques based on F^2 with SHELXL-97[2] with the aid of the WINGX[3] program. All non-hydrogen atoms were refined with anisotropic thermal parameters. H atoms were finally included in their calculated positions. Figures were drawn with ORTEP-3 for Windows.[4] CCDC-749116 [(*R**,*R**)-**2**] ; CCDC-749119 [(*R**,*R**)-**5**]) ; CCDC-749115 [(*R**,*R**)-**6a**] ; CCDC-749117 [(*R**,*R**)-**6b**]) ; CCDC-749118 [(*R**,*R**)-**6c**]) ; CCDC-749114 [(*R**,*R**)-**9b**]) contain the supplementary crystallographic data for this paper. These data can be obtained from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[1] A. Altomare, M.C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guargliardi, A. G. G. Moliterni, G. Polidori, R. Spagna, *J. Appl. Cryst.* **1999**, *32*, 115–119.

[2] G. M. Sheldrick, *SHELX97*, Programs for Crystal Structure Analysis (Release 97-2), University of Göttingen, Germany, **1998**.

[3] L. J. Farrugia, *J. Appl. Crystallogr*. **1999**, *32*, 837–838.

[4] L. J. Farrugia, *J. Appl. Crystallogr*. **1998**, *30*, 565–567.

	(*R**,*R**)-**2**	(*R**,*R**)-**5**	(*R**,*R**)-**6a**	(*R**,*R**)-**6b**	(*R**,*R**)-**6c**	(*R**,*R**)-**9b**
Formula	$C_{20}H_{22}N_2O_2$	$C_{20}H_{22}N_2O_2$	$C_{22}H_{48}N_4O_4$	$C_{28}H_{30}N_2O_3$	$C_{29}H_{32}N_2O_4$	$C_{27}H_{31}N_1O_3$
Mol. mass	322.4	322.4	672.84	444.54	472.57	417.53
Cryst. Syst.	Orthorhombic	Monoclinic	Triclinic	Monoclinic	Monoclinic	Monoclinic
Space group	*P* c a b	*P* 21/c	P-1	*P* 21/c	*P* 21/c	*P* 21/n
D_X [Mg m^{-3}]	1.289	1.266	1.237	1.248	1.294	1.23
a [Å]	8.4509(2)	10.3512(4)	9.6959(5)	15.5110(8)	12.8819(6)	9.6750(4)
b [Å]	15.2906(3)	10.7981(4)	13.0494	10.4033(6)	13.6556(7)	20.4801(10)
c [Å]	25.7074(4)	15.9585(5)	15.4053	16.1882(7)	14.1026(6)	11.5788(5)
α [°]	90	90	104.685(3)	90	90	90
β [°]	90	108.519(2)	105.272(3)	115.612(2)	102.184(2)	100.550(2)
γ [°]	90	90	92.556(3)	90	90	90
V [Å^{-3}]	3321.89(11)	1691.37(10)	1805.91(17)	2355.5(2)	2424.9(2)	2255.50(17)
Z	8	4	2	4	4	4
F(000)	1376	688	720	944	1008	896
μ [cm^{-1}]	0.84	0.82	0.80	0.81	0.86	0.79
λ (Mo–*K*α) [Å]	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
T [K]	120(2)	100(2)	100(2)	100(2)	100(2)	100(2)
Crystal size (mm)	0.55×0.32×0.25	0.53×0.35×0.25	0.43×0.29×0.23	0.56×0.42×0.31	0.55×0.51×0.11	0.6×0.45×0.24
Radiation	Mo–K_α	Mo–K_α	Mo–K_α	Mo–K_α	Mo–K_α	Mo–K_α
Max. θ [°]	27.47	27.47	27.45	27.42	27.48	27.48
Range of *hkl*	–10→10, –19→19, –33→33	–10→13, –14→13, –20→20	–12→12, –16→16, –19→19	–20→20, –13→13, –20→20	–16→16, –17→17, –18→11	–12→12, –21→26, –15→15
Reflection measured	3778	3863	8222	5344	5520	5161

Reflections independent observed [I>2.0σ(I)]	2792	3190	5549	4879	4537	4700
Final R_1	0.0588	0.0413	0.0512	0.0472	0.0472	0.054
wR_2	0.1553	0.1049	0.1386	0.0973	0.0973	0.1121

Table 1 : X-ray crystallographic data for compounds **2**, **5**, **6a-c**, **9b**