Electronic Supplementary Information (ESI) for

Hypervalent Iodine(III)-Induced Oxidative [4+2] Annulation of *o*-Phenylenediamines and Electron-Deficient Alkynes: Direct Synthesis of Quinoxalines from Alkyne Substrates under Metal-Free Conditions

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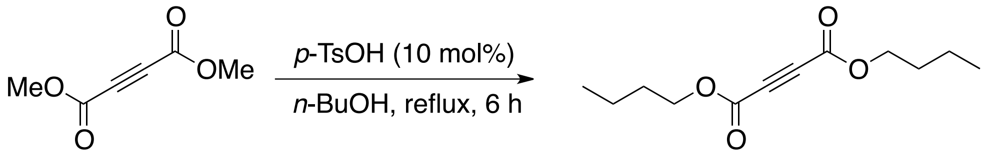
Table of Contents

General remarks S2
Procedures for the preparation of alkyne substrates S2–S3
A typical procedure for the oxidative [4+2] annulation S3
Procedure for the derivatization of **3a** into **6–8** S4
Procedure for the preparation of **9** S4–S5
Procedure for the reaction of **9** with PIDA S5
Optimization study of reaction conditions (Table S1) S6
The reaction of **9** with trifluoroacetic acid at –20 °C S6
Explanation of Solvent Effect (Scheme S1) S7
Spectra data of products S8–S15
^{1}H and ^{13}C NMR charts of products S16–S67
References S68

General remarks

Melting points were determined on a Stanford Research Systems MPA100 OptiMelt Automated Melting Point System and are uncorrected. Infrared spectra were recorded on a SHIMADZU IRAffinity-1 FT-IR Spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JMTC-400/54/SS spectrometer (^{1}H NMR, 400 MHz; ^{13}C NMR, 100 MHz) using tetramethylsilane as an internal standard. Mass spectra were obtained on a JEOL JMS-DX303HF mass spectrometer. High-resolution mass spectra were obtained on a JEOL JMS-DX303HF mass spectrometer. Products were purified by chromatography on silica gel BW-300 (Fuji Silysia Chemical Ltd.). Analytical thin-layer chromatography (TLC) was performed on pre-coated silica gel glass plates (Merck silica gel 60 F_{254}, 0.25 mm thickness). Compounds were visualized with UV lamp or treatment with an ethanolic solution of phosphomolybdic acid followed by heating. Dimethyl acetylenedicarboxylate (DMAD) was purchased and distilled before using. *o*-Phenylenediamines and $PhI(OAc)_2$ were purchased and used as received.

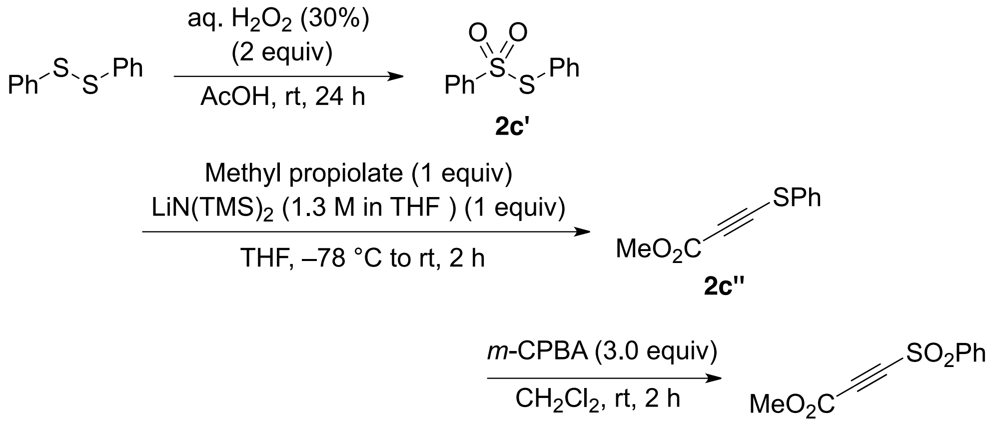
Procedure for the preparation of alkyne 2b[S1]



2a **2b**

To a *n*-butyl alcohol solution (40 mL) of *p*-toluenesulfonic acid (2.5 mmol), was added dimethyl acetylenedicarboxylate (25 mmol) at room temperature. The mixture was stirred under reflux for 6 hour. *n*-Butyl alcohol was removed under vacuum to give the crude product. Purification by flash column chromatography on silica gel (eluent: ethyl acetate in hexane) gave alkyne **2b** (4.38 g, 77%).

Procedure for the preparation of alkyne 2c[S3,S4]



2c

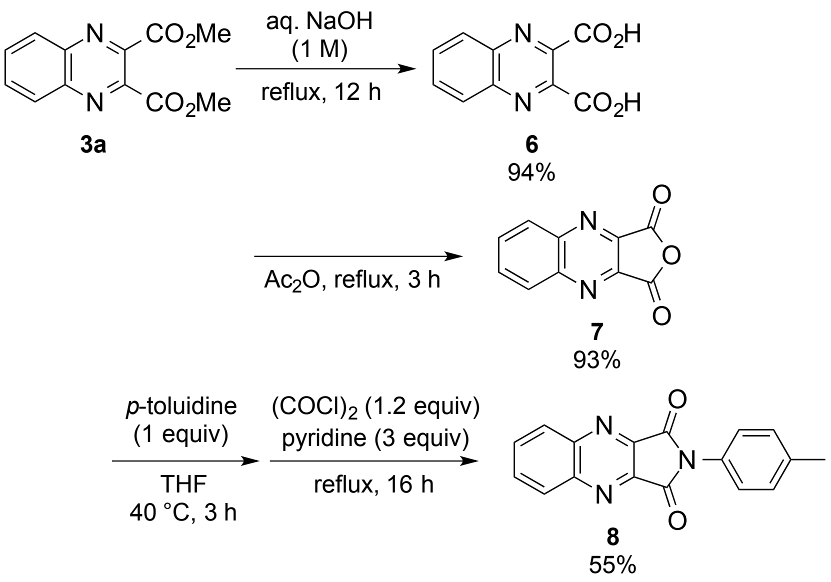
To a suspension of diphenyl disulfide (100 mmol) in acetic acid (80 mL), was dropwise added 30% aqueous hydrogen peroxide (200 mmol) over 30 min. After stirring at room temperature for 24 hour, the reaction mixture was cooled and filtered. Dilution of the filtrate with water (100 mL) caused phase-separation. The precipitates and oil layer were combined and dissolved in chloroform (100 mL). The solution was washed with aqueous sat. $NaHCO_3$ (100mL), dried over Na_2SO_4, and concentrated under vacuum to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc 99:1 to 7:3) gave **2c'** (21.4 g, 86%). The spectroscopic data for **2c'** was in agreement with the reported data.[S2]

To a THF solution (32 mL) of methyl propiolate (16 mmol), was slowly added a solution of lithium bis(trimethylsilyl)amide (1.3 M in THF, 16 mmol) at –78 °C. After 30 min of stirring at –78 ˚C, a THF solution (24 mL) of **2c'** (16 mmol) was added dropwise at the same temperature, and the resulting mixture was left to react at room temperature for 2 hour. After the completion of the reaction, the reaction mixture was quenched with aqueous sat. NH_4Cl (30 mL) and extracted with Et_2O (50 mL × 3). The combined organic extracts was dried over Na_2SO_4 and concentrated under vacuum to give the crude product **2c''**, which was used in the following step without further purification. To a CH_2Cl_2 solution (45 mL) of 2**c''**, was added a CH_2Cl_2 solution (45 mL) of *m*-CPBA (70%, 48 mmol). The reaction mixture was stirred at room temperature for 2 hour and quenched with aqueous $Na_2S_2O_3$ (1.0 M, 50 mL), and the resulting solution was extracted with CH_2Cl_2 (50 mL × 3). The combined organic extracts was dried over Na_2SO_4 and concentrated under vacuum to give the crude product. Purification by flash column chromatography on silica gel (eluent: ethyl acetate in hexane) gave alkyne **2c** (1.82 g, 50%).

A typical procedure for the oxidative [4+2] annulation

To a mixture of *o*-phenylenediamine (0.25 mmol) and alkyne (0.25 mmol) in DMF (3 mL), was added $PhI(OAc)_2$ (0.5 mmol, 161.0 mg) under N_2 atmosphere at –20 °C. The mixture was stirred in the dark for 24 hour and quenched with aqueous $Na_2S_2O_3$ (1.0 M, 5 mL), and the resulting solution was extracted with CH_2Cl_2 (20 mL × 3). The combined organic extracts was washed with aqueous sat. $NaHCO_3$ (10 mL), dried over Na_2SO_4, and concentrated under vacuum to give the crude product. Purification by flash column chromatography on silica gel (eluent: ethyl acetate in hexane) gave quinoxaline product (for example, compound **3a**: 56.6 mg, 92%).

Procedure for the derivatization of 3a into 6–8

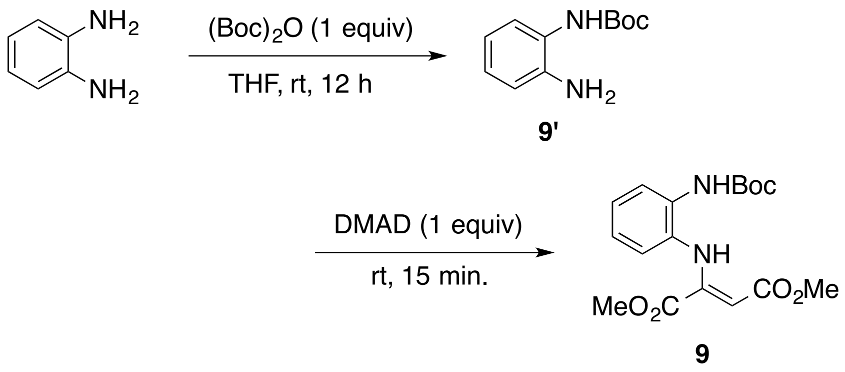


The mixture of quinoxaline **3a** (3 mmol) and aqueous NaOH (1 M, 45 mL) was stirred under reflux for 12 hour before quenched with aqueous HCl (2 M, 30 mL). The mixture was extracted with EtOAc/MeOH = 9/1 (v/v), dried over Na_2SO_4, and concentrated under vacuum to give the crude product, which was washed with Et_2O and $CHCl_3$ to give **6** (614 mg, 94%).

Quinoxaline-2,3-dicarcoxylic acid (**6**) (1 mmol) was dissolved in acetic anhydride (1 mL) and the solution was heated at reflux for 3 hour. The excess of acetic anhydride was distilled off. The crude was washed with water, Et_2O and $CHCl_3$ to give **7** (186 mg, 93%).

A solution of **7** (0.25 mmol) and *p*-toluidine (0.25 mmol) in THF (3 mL) was heated to 40 °C for 3 hour. After cooling to room temperature, oxalyl chloride (0.3 mmol) and pyridine (0.75 mmol) were added, and the reaction mixture was stirred for 16 h under reflux. The solvent was evaporated to give the crude product. Purification by flash column chromatography on silica gel (eluent: CH_2Cl_2) gave imide **8** (39.8 mg, 55%).

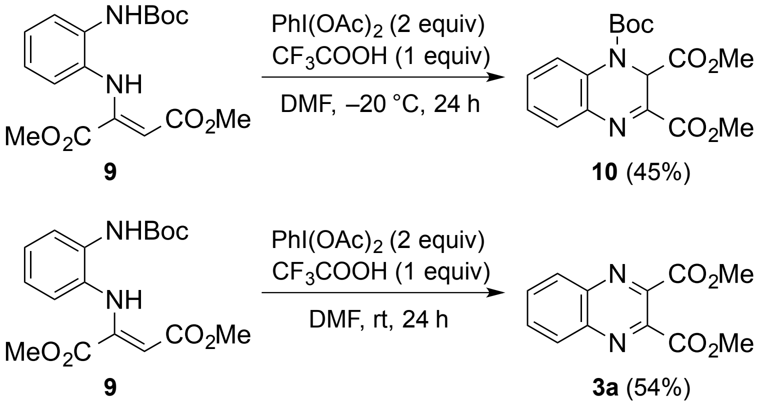
Procedure for the preparation of 9[S5, S6]



To a THF solution (15 mL) of *o*-phenylenediamine (100 mmol), was dropwise added di-*tert*-butyl dicarbonate (2 M in THF, 50 mL). The mixture was stirred at room temperature for 12 hour. After the mixture was concentrated under vacuum, the resulting residue was diluted with hexane/EtOAc = 4/1 (v/v), and the precipitate was removed thorough filtration. The resulting solution was concentrated to give the crude product. Purification by flash column chromatography on silica gel (eluent: ethyl acetate in hexane) gave *N*-Boc protected phenylenediamine product **9’** (10.8 g, 52%).

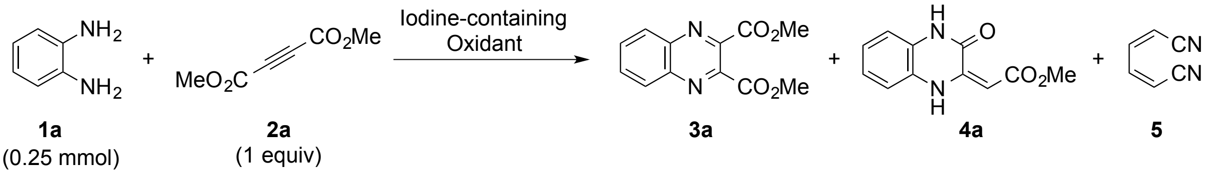
The mixture of **9’** (10 mmol) and dimethyl acetylenedicarboxylate (10 mmol) was stirred at room temperature for 15 min. Purification by flash column chromatography on silica gel (eluent: ethyl acetate in hexane) gave product **9** (2.2 g, 62%).

Procedure for the reaction of 9 with PIDA



To a mixture of **9** (0.25 mmol) and trifluoroacetic acid (0.25 mmol) in DMF (3 mL), was added PhI(OAc)$_2$ (0.5 mmol, 161.0 mg) under N_2 atmosphere at the temperature indicated. The mixture was stirred in the dark for 24 hour and quenched with aqueous $Na_2S_2O_3$ (1.0 M, 5 mL), and the solution was extracted with CH_2Cl_2 (20 mL × 3). The combined organic extracts was washed with aqueous sat. $NaHCO_3$ (10 mL), dried over Na_2SO_4, and concentrated under vacuum to give the crude product. Purification by flash column chromatography on silica gel (eluent: ethyl acetate in hexane) gave **10** or **3a**.

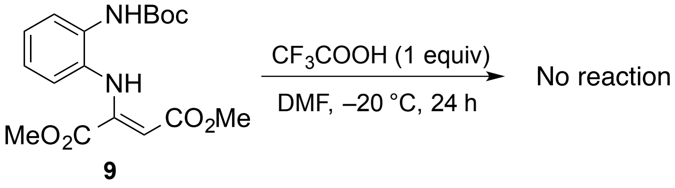
Table S1. Optimization study of reaction parameters



entry	oxidant (equiv)	solvent	temp. (°C)	time (h)	yield (%)[a]		
					3a	4a	5
1	*t*-BuOI (4)	THF	–20	24	12	0	64
2	*t*-BuOI (4)	DME	–20	24	2	0	33
3	$PhI(OAc)_2$ (2)	DME	–20	24	60[b]	4[b]	0
4	$PhI(OAc)_2$ (2)	MeCN	–20	24	trace	38	0
5	$PhI(OAc)_2$ (2)	THF	–20	24	63	18	0
6	$PhI(OAc)_2$ (2)	DMF	–20	24	**92**[b]	4[b]	0
7	$PhI(OAc)_2$ (2)	CH_2Cl_2	–20	24	trace	40	0
8	$PhI(OAc)_2$ (2)	toluene	–20	24	5	36	0
9	$PhI(OAc)_2$ (2)	Et_2O	–20	24	17	24	0
10	$PhI(OAc)_2$ (2)	DMF	0	24	72	10	0
11	$PhI(OAc)_2$ (2)	DMF	25	24	45	28	trace
12	$PhI(OAc)_2$ (2)	DMF	–40	24	82	3	0
13	$PhI(OAc)_2$ (2)	DMF	–20	1	46	trace	0
14	$PhI(OAc)_2$ (2)	DMF	–20	3	65	trace	0
15	$PhI(OAc)_2$ (2)	DMF	–20	6	71	trace	0
16	$PhI(OAc)_2$ (2)	DMF	–20	12	84	trace	0

[a] ^1H NMR yields. [b] Isolated yield.

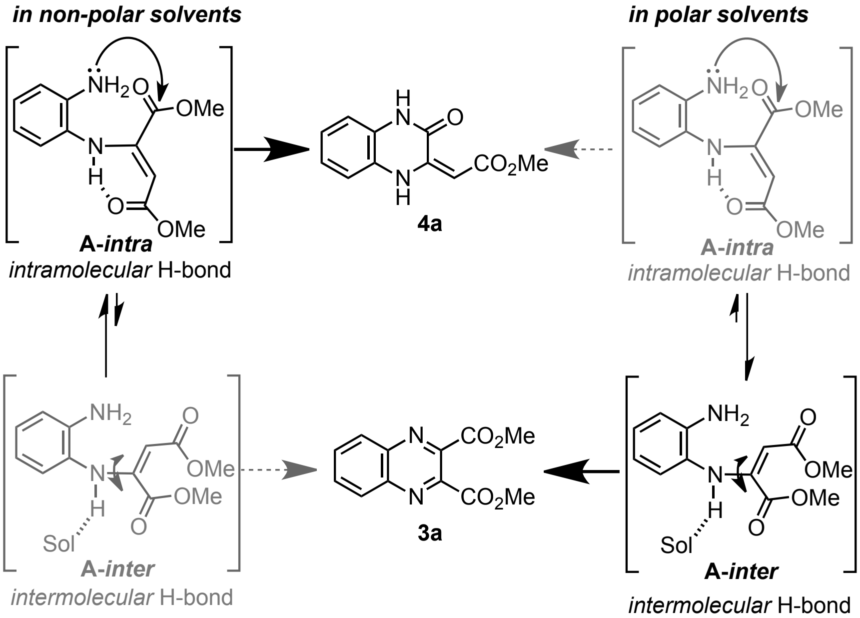
The reaction of 9 with trifluoroacetic acid at –20 °C



At –20 ˚C, **9** was not deprotected and starting material was recovered quantitatively (97%) in the presence of trifluoroacetic acid alone.

Explanation of Solvent Effect

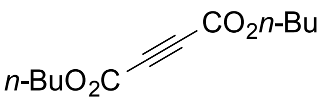
Intramolecular hydrogen-bond (H-bond) between enaminone N–H and conjugated carbonyl oxygen[S8] would be preferentially operative (**A-*intra***) in non-polar solvents. However, in polar solvents such as DME and DMF, solvent molecules are capable of serving as a Lewis base to form *intermolecular* H-bond with enaminone N–H (**A-*inter***). Such *intermolecular* H-bond would not only allow for free-rotation around the N–C single bond, but also enhance the anionic (nucleophilic) character of the β-carbon.[S9] Therefore, the solvent effect can be summarized as follows: non-polar solvents would favor the *intramolecular* H-bond that locks the enamine moiety into the 6-membered plane (**A-*intra***), and thereby nucleophilic cyclization exclusively takes place at the carbonyl carbon to give **4a** as a major product. As the polarity of solvent increases, *intermolecular* H-bond would compete with *intramolecular* H-bond (**A-*inter***), suppressing the production of **4a** and promoting electrophilic attack by PIDA on the nucleophilicity-enhanced β-carbon.



Scheme S1 Illustrative Explanation of Solvent Effect in the Oxidative Annulation

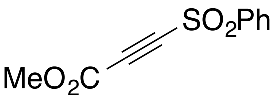
Spectra Data of Products

Dibutyl acetylenedicarboxylate (2b)[S1]



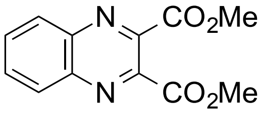
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 9:1); Colorless oil; R_f 0.45 (hexane/EtOAc 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, J = 7.2 Hz, 6H), 1.41 (tq, J = 7.2, 7.6 Hz, 4H), 1.68 (tt, J = 6.8, 7.6 Hz, 4H), 4.25 (t, J = 6.8 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.2, 18.6, 29.9, 66.4, 74.3, 151.5; IR (ATR) ν 2963, 1721, 1244, 1059, 1036, 746 cm^{-1}; MS (CI): m/z (relative intensity, %) 227 ($[M]^+ + H^+$, 100), 171 (25); HRMS (CI): m/z calcd for $C_{12}H_{10}O_4$ (M) 227.1283, found 227.1285.

Methyl 2-(phenylsulfonyl)propiolate (2c)



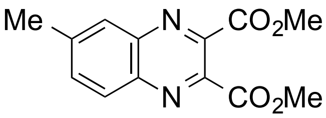
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow oil; R_f 0.08 (hexane/EtOAc 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 3H), 7.64 (m, 2H), 7.77 (m, 1H), 8.03 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.8, 79.35, 79.42, 128.0, 129.7, 135.3, 139.6, 151.3; IR (ATR) ν 3066, 1724, 1448, 1435, 1348, 1242, 1165, 1086, 883, 742 cm^{-1}; MS (EI): m/z (relative intensity, %) 224 ($[M]^+$, 48), 193 (14), 125 (100), 77 (99); HRMS (EI): m/z calcd for $C_{10}H_8O_4S$ (M) 224.0143, found 224.0141.

Dimethyl quinoxaline-2,3-dicarboxylate (3a)[S7]



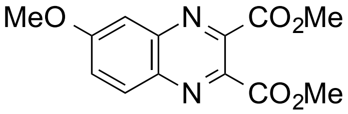
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow solid (56.6 mg, 92%); mp 132.6–133.0 °C; R_f 0.20 (hexane/EtOAc 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (s, 6H), 7.96 (dd, J = 3.6, 6.8 Hz, 2H), 8.27 (dd, J = 3.6, 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.6, 129.8, 132.7, 141.3, 143.7, 165.1; IR (ATR) ν 2954, 1718, 1442, 1325, 1290, 1228, 1193, 1166, 1114, 954, 852, 781, 767 cm^{-1}; MS (EI): m/z (relative intensity, %) 246 ($[M]^+$, 32), 215 ($[M]^+ -$ OMe, 26), 188 ($[M]^+ - CO_2Me + H^+$, 31), 130 ($[M]^+ - 2CO_2Me + 2H^+$, 100); HRMS (EI): m/z calcd for $C_{12}H_{10}N_2O_4$ (M) 246.0641, found 246.0639.

Dimethyl 6-methylquinoxaline-2,3-dicarboxylate (3b)



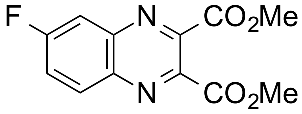
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow solid (55.4 mg, 85%); mp 84.4–85.4 °C; R_f 0.18 (hexane/EtOAc 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.65 (s, 3H), 4.09 (s, 6H), 7.77 (dd, J = 2.0, 8.8 Hz, 1H), 8.02 (s, 1H), 8.15 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 53.47, 53.53, 128.4, 129.3, 135.0, 135.1, 139.8, 141.5, 142.5, 144.0, 165.1, 165.3; IR (ATR) ν 2954, 1738, 1720, 1446, 1342, 1311, 1288, 1224, 1192, 1170, 1148, 1121, 1068, 858, 831, 810 cm^{-1}; MS (EI): m/z (relative intensity, %) 260 ($[M]^+$, 43), 229 ([M]$^+$ – OMe, 19), 202 ([M]$^+$ – CO_2Me + H$^+$, 23), 144 ([M]$^+$ – $2CO_2Me$ + 2H$^+$, 100); HRMS (EI): *m/z* calcd for $C_{13}H_{12}N_2O_4$ (M) 260.0797, found 260.0800.

Dimethyl 6-methoxylquinoxaline-2,3-dicarboxylate (3c)



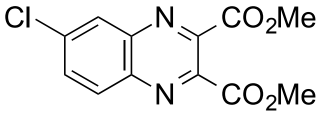
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow solid (66.8 mg, 97%); mp 113.3–113.7 °C; R_f 0.18 (hexane/EtOAc 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (s, 3H), 4.084 (s, 3H), 4.089 (s, 3H), 7.49 (s, 1H), 7.57 (d, *J* = 9.6 Hz, 1H), 8.13 (d, *J* = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.49, 53.52, 56.1, 106.5, 126.6, 130.8, 137.7, 140.3, 143.5, 144.6, 163.1, 165.1, 165.6; IR (ATR) ν 296.1, 1739, 1726, 1616, 1491, 1450, 1440, 1413, 1287, 1222, 1198, 1182, 1121, 1067, 1018, 862, 837, 810 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 276 ([M]$^+$, 41), 245 ([M]$^+$ – OMe, 12), 218 ([M]$^+$ – CO_2Me + H$^+$, 7), 160 ([M]$^+$ – $2CO_2Me$ + 2H$^+$, 100); HRMS (EI): *m/z* calcd for $C_{13}H_{12}N_2O_5$ (M) 276.0746, found 276.0744.

Dimethyl 6-fluoroquinoxaline-2,3-dicarboxylate (3d)



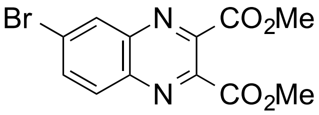
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 8:2); Yellow solid (62.3 mg, 94%); mp 88.3–89.0 °C; R_f 0.15 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.101 (s, 3H), 4.105 (s, 3H), 7.74 (m, 1H), 7.88 (dd, *J* = 2.4, 9.2 Hz, 1H), 8.29 (dd, *J* = 5.6, 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.6 (s), 53.8 (s), 113.3 (d, *J* = 22.2 Hz), 123.4 (d, *J* = 26.3 Hz), 132.3 (d, *J* = 10.7 Hz), 138.6 (s) 142.5 (d, *J* = 14.0 Hz), 142.7 (d, *J* = 2.3 Hz), 145.0 (s), 164.3 (d, *J* = 257.7 Hz), 164.8 (s), 165.0 (s); IR (ATR) ν 2953, 1715, 1721, 1449, 1298, 1200, 1179, 1115, 1064, 885, 856, 839, 826, 787 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 264 ([M]$^+$, 37), 233 ([M]$^+$ – OMe, 35), 206 ([M]$^+$ – CO_2Me + H$^+$, 32), 148 ([M]$^+$ – $2CO_2Me$ + 2H$^+$, 100); HRMS (EI): *m/z* calcd for $C_{12}H_9FN_2O_4$ (M) 264.0546, found 264.0545.

Dimethyl 6-chloroquinoxaline-2,3-dicarboxylate (3e)



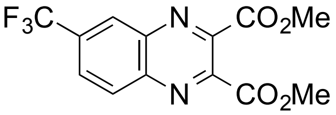
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow solid (60.8 mg, 87%); mp 93.5–94.4 °C; R_f 0.28 (hexane/EtOAc 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (s, 6H), 7.88 (dd, *J* = 2.0, 8.8 Hz, 1H), 8.20 (d, *J* = 8.8 Hz, 1H), 8.25 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.70, 53.77, 128.6, 131.0, 133.8, 139.0, 139.8, 141.6, 143.5, 144.9, 164.7, 164.9; IR (ATR) ν 2956, 1736, 1721, 1443, 1289, 1279, 1234, 1220, 1153, 1124, 876, 856, 835, 816, 804 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 280 ([M]$^+$, 40), 249 ([M]$^+$ – OMe, 31), 222 ([M]$^+$ – CO_2Me + H$^+$, 29), 164 ([M]$^+$ – $2CO_2Me$ + 2H$^+$, 100); HRMS (EI): *m/z* calcd for $C_{12}H_9ClN_2O_4$ (M) 280.0250, found 280.0251.

Dimethyl 6-bromoquinoxaline-2,3-dicarboxylate (3f)



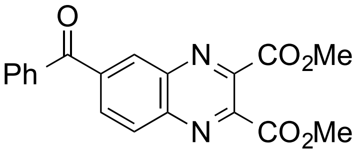
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow solid (69.0 mg, 85%); mp 99.6–100.3 °C; R$_f$ 0.20 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.10 (s, 6H), 8.02 (d, *J* = 8.8 Hz, 1H), 8.12 (d, *J* = 8.8 Hz, 1H), 8.44 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 53.7, 127.4, 131.0, 132.0, 136.3, 140.1, 141.8, 143.6, 144.8, 164.7, 164.8; IR (ATR) *ν* 2957, 1738, 1722, 1440, 1298, 1219, 1153, 1124, 1065, 813 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 324 ([M]$^+$, 66), 293 ([M]$^+$ – OMe, 31), 266 ([M]$^+$ – CO$_2$Me + H$^+$, 52), 208 ([M]$^+$ – 2CO$_2$Me + 2H$^+$, 100); HRMS (EI): *m/z* calcd for $C_{12}H_9BrN_2O_4$ (M) 323.9746, found 323.9749.

Dimethyl 6-(trifluoromethyl)quinoxaline-2,3-dicarboxylate (3g)



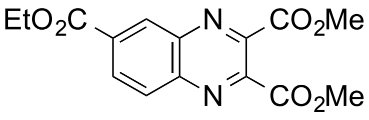
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Orange solid (71.2 mg, 91%); mp 82.6–83.8 °C; R$_f$ 0.21 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.12 (s, 6H), 8.12 (d, *J* = 8.8 Hz, 1H), 8.40 (d, *J* = 8.8 Hz, 1H), 8.60 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 53.7 (s), 123.0 (q, *J* = 271.7 Hz), 127.7 (q, *J* = 4.9 Hz), 128.2 (q, *J* = 2.5 Hz), 131.1 (s), 134.0 (q, *J* = 32.9 Hz), 140.3 (s), 142.2 (s), 144.8 (s), 145.7 (s), 164.4 (s), 164.5 (s); IR (ATR) *ν* 2922, 1751, 1732, 1443, 1350, 1175, 1138, 1118, 1070, 1055, 902, 847 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 314 ([M]$^+$, 34), 283 ([M]$^+$ – OMe, 32), 256 ([M]$^+$ – CO$_2$Me + H$^+$, 16), 198 ([M]$^+$ – 2CO$_2$Me + 2H$^+$, 100); HRMS (EI): *m/z* calcd for $C_{13}H_9F_3N_2O_4$ (M) 314.0514, found 314.0512.

Dimethyl 6-benzoylquinoxaline-2,3-dicarboxylate (3h)



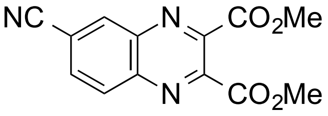
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 6:4); Yellow solid (69.6 mg, 80%); mp 119.2–120.0 °C; R$_f$ 0.10 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.10 (s, 3H), 4.12 (s, 3H), 7.54 (t, *J* = 8.0 Hz, 2H), 7.67 (m, 1H), 7.88 (dd, *J* = 1.2, 6.8 Hz, 2H), 8.38 (d, *J* = 8.8 Hz, 1H), 8.42 (d, *J* = 8.8 Hz, 1H), 8.59 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 53.8, 128.7, 130.1, 130.4, 132.4, 132.6, 133.3, 136.3, 140.5, 140.7, 142.9, 144.5, 145.5, 164.7, 164.9, 194.9; IR (ATR) *ν* 2976, 1740, 1726, 1659, 1445, 1296, 1229, 1150, 1117, 1065, 895, 849 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 350 ([M]$^+$, 29), 319 ([M]$^+$ – OMe, 18), 292 ([M]$^+$ – CO$_2$Me + H$^+$, 8), 234 ([M]$^+$ – 2CO$_2$Me + 2H$^+$, 78), 105 (PhCO, 100); HRMS (EI): *m/z* calcd for $C_{19}H_{14}N_2O_5$ (M) 350.0903, found 350.0905.

6-Ethyl 2,3-dimethyl quinoxaline-2,3,6-tricarboxylate (3i)



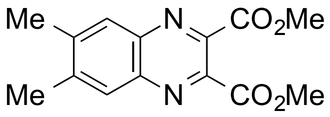
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 6:4); Yellow solid (75.6 mg, 95%); mp 112.8–113.4 °C; R_f 0.10 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (t, *J* = 7.2 Hz, 3H), 4.11 (s, 6H), 4.49 (q, *J* = 7.2 Hz, 2H), 8.31 (d, *J* = 8.8 Hz, 1H), 8.54 (d, *J* = 8.8 Hz, 1H), 8.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 53.7, 61.9, 129.9, 132.08, 132.10, 134.0, 140.6, 143.0, 144.2, 145.4, 164.56, 164.77, 164.80; IR (ATR) *v* 3001, 1751, 1719, 1443, 1342, 1294, 1231, 1146, 1120, 1169 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 318 ($[M]^+$, 26), 287 ($[M]^+$ – OMe, 19), 273 ($[M]^+$ – OEt, 28), 260 ($[M]^+$ – CO_2Me + H^+, 16), 245 ($[M]^+$ – CO_2Et, 2), 202 ($[M]^+$ – $2CO_2Me$ + $2H^+$, 100); HRMS (EI): *m/z* calcd for $C_{15}H_{14}N_2O_6$ (M) 318.0852, found 318.0851.

Dimethyl 6-cyanoquinoxaline-2,3-dicarboxylate (3j)



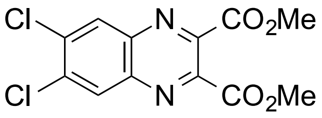
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 5:5); Yellow solid (60.2 mg, 89%); mp 128.5–129.1 °C; R_f 0.20 (hexane/EtOAc 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (s, 6H), 8.10 (dd, *J* = 2.0, 8.8 Hz, 1H), 8.37 (d, *J* = 8.8 Hz, 1H), 8.63 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.8, 116.1, 117.0, 131.4, 133.0, 135.4, 140.3, 142.4, 145.3, 145.9, 164.2, 164.2; IR (ATR) *v* 2955, 2230, 1732, 1443, 1307, 1227, 1167, 1125, 1067, 849, 814 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 271 ($[M]^+$, 47), 240 ($[M]^+$ – OMe, 54), 213 ($[M]^+$ – CO_2Me + H^+, 24), 155 ($[M]^+$ – $2CO_2Me$ + $2H^+$, 100); HRMS (EI): *m/z* calcd for $C_{13}H_9N_3O_4$ (M) 271.0593, found 271.0594.

Dimethyl 6,7-dimethylquinoxaline-2,3-dicarboxylate (3k)



Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow solid (56.9 mg, 83%); mp 118.0–119.1 °C; R_f 0.13 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.55 (s, 6H), 4.08 (s, 6H), 7.99 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 53.5, 128.7, 140.4, 142.9, 144.1, 165.5; IR (ATR) *v* 2957, 1732, 1717, 1445, 1348, 1296, 1225, 1203, 1136, 1076, 871 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 274 ($[M]^+$, 35), 243 ($[M]^+$ – OMe, 14), 216 ($[M]^+$ – CO_2Me + H^+, 16), 158 ($[M]^+$ – $2CO_2Me$ + $2H^+$, 100); HRMS (EI): *m/z* calcd for $C_{14}H_{14}N_2O_4$ (M) 274.0954, found 274.0952.

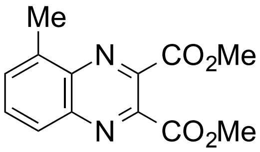
Dimethyl 6,7-dichloroquinoxaline-2,3-dicarboxylate (3l)



Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow solid (59.7 mg, 76%); mp 152.9–153.9 °C; R_f 0.35 (hexane/EtOAc 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (s, 6H), 8.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.7, 130.1, 137.8, 139.9, 144.5, 164.5; IR

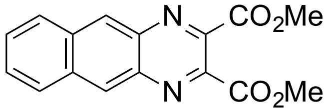
(ATR) *ν* 1740, 1437, 1221, 1069, 976, 881, 851, 810 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 314 ([M]$^+$, 58), 283 ([M]$^+$ – OMe, 44), 256 ([M]$^+$ – CO$_2$Me + H$^+$, 32), 198 ([M]$^+$ – 2CO$_2$Me + 2H$^+$, 100); HRMS (EI): *m/z* calcd for $C_{12}H_8Cl_2N_2O_4$ (M) 313.9861, found 313.9858.

Dimethyl 5-methylquinoxaline-2,3-dicarboxylate (3m)



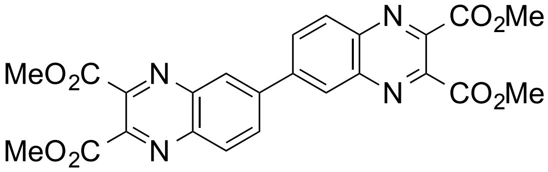
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow solid (63.6 mg, 98%); mp 111.9–112.8 °C; R$_f$ 0.20 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.85 (s, 3H), 4.087 (s, 3H), 4.095 (s, 3H), 7.76–7.84 (m, 2H), 8.10 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 17.1, 53.4, 53.6, 127.7, 132.3, 132.6, 138.7, 140.8, 141.5, 142.3, 143.5, 165.1, 165.8; IR (ATR) *ν* 2959, 1744, 1719, 1225, 1167, 1134, 1092, 1032, 831, 797, 779 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 260 ([M]$^+$, 100), 229 ([M]$^+$ – OMe, 43), 202 ([M]$^+$ – CO$_2$Me + H$^+$, 29), 144 ([M]$^+$ – 2CO$_2$Me + 2H$^+$, 87); HRMS (EI): *m/z* calcd for $C_{13}H_{12}N_2O_4$ (M) 260.0797, found 260.0796.

Dimethyl benzo[*g*]quinoxaline-2,3-dicarboxylate (3n)



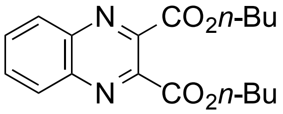
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Orange solid (41.3 mg, 56%); mp 169.8–170.9 °C; R$_f$ 0.23 (hexane/EtOAc 7:3); ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.13 (s, 3H), 7.67 (dd, *J* = 3.2, 6.4 Hz, 2H), 8.15 (dd, *J* = 3.2, 6.4 Hz, 2H), 8.31 (s, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 53.6, 128.3, 128.8, 129.0, 135.2, 136.8, 143.8, 165.2; IR (ATR) *ν* 3030, 1736, 1719, 1439, 1202, 1142, 1072, 883, 872, 752 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 296 ([M]$^+$, 100), 265 ([M]$^+$ – OMe, 9), 238 ([M]$^+$ – CO$_2$Me + H$^+$, 5), 180 ([M]$^+$ – 2CO$_2$Me + 2H$^+$, 83); HRMS (EI): *m/z* calcd for $C_{16}H_{12}N_2O_4$ (M) 296.0797, found 296.0793.

Tetramethyl [6,6'-biquinoxaline]-2,2',3,3'-tetracarboxylate (3o)



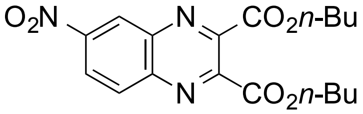
Purified by silica gel column chromatography (CHCl$_3$/MeOH 99:1 to 95:5); Brown solid (86.7 mg, 71%); mp 225.0–225.5 °C (dec.); R$_f$ 0.50 (CHCl$_3$/MeOH 95:5); ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.13 (s, 12H), 8.35 (dd, *J* = 2.0, 8.8 Hz, 2H), 8.44 (d, *J* = 8.8 Hz, 2H), 8.64 (d *J* = 2.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 53.8, 128.3, 131.0, 132.0, 141.2, 141.6, 142.9, 144.1, 144.8, 165.0; IR (ATR) *ν* 1726, 1437, 1221, 1132, 1068, 812 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 490 ([M]$^+$, 71), 459 ([M]$^+$ – OMe, 13), 432 ([M]$^+$ – CO$_2$Me + H$^+$, 3), 374 ([M]$^+$ – 2CO$_2$Me + 2H$^+$, 100); HRMS (EI): *m/z* calcd for $C_{24}H_{18}N_4O_8$ (M) 490.1125, found 490.1123.

Dibutyl quinoxaline-2,3-dicarboxylate (3p)



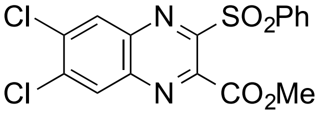
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow oil (63.8 mg, 77%); R$_f$ 0.30 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.99 (t, *J* = 7.2 Hz, 6H), 1.49 (tq, *J* = 7.2, 7.6 Hz, 4H), 1.83 (tt, *J* = 7.2, 7.6 Hz, 4H), 4.50 (t, *J* = 7.2 Hz, 4H), 7.93 (dd, *J* = 3.6, 6.4 Hz, 2H), 8.26 (dd, *J* = 3.6, 6.4 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 13.6, 18.9, 30.3, 66.6, 129.7, 132.3, 141.2, 144.1, 164.8; IR (ATR) *ν* 2961, 2934, 1749, 1722, 1466, 1331, 1234, 1174, 1132, 1062, 764 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 330 ([M]$^+$, 24), 202 (100), 130 ([M]$^+$ – 2CO$_2$Bu + 2H$^+$, 77); HRMS (EI): *m/z* calcd for $C_{18}H_{22}N_2O_4$ (M) 330.1580, found 330.1577.

Dibutyl 6-nitroquinoxaline-2,3-dicarboxylate (3q)



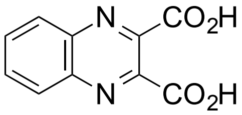
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Red oil (41.2 mg, 44%); R$_f$ 0.35 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.00 (m, 6H), 1.50 (m, 4H), 1.84 (m, 4H), 4.52 (t, *J* = 6.8 Hz, 4H), 8.43 (d, *J* = 9.2 Hz, 1H), 8.69 (dd, *J* = 2.4, 9.2 Hz, 1H), 9.16 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 13.6, 19.0, 30.3, 30.4, 67.08, 67.09, 125.6, 125.9, 131.6, 140.3, 143.4, 145.9, 146.9, 149.2, 163.9, 164.0; IR (ATR) *ν* 2960, 2935, 1742, 1728, 1533, 1348, 1219, 1159, 1116, 1064 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 375 ([M]$^+$, 33), 247 (100), 175 ([M]$^+$ – 2CO$_2$Bu + 2H$^+$, 56); HRMS (EI): *m/z* calcd for $C_{18}H_{21}N_3O_6$ (M) 375.1430, found 375.1432.

Butyl 6,7-dichloro-3-(phenylsulfonyl)quinoxaline-2-carboxylate (3r)



Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Red solid (64.8 mg, 65%); mp 133.0–134.8 °C (dec.); R$_f$ 0.43 (hexane/EtOAc 7:3); ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.18 (s, 3H), 7.58–7.71 (m, 3H), 8.15 (d, *J* = 8.0 Hz, 2H), 8.26 (s, 1H), 8.30, (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 54.0, 129.2, 129.6, 129.8, 130.2, 143.6, 137.5, 138.1, 139.1, 139.4, 139.9, 144.7, 151.8, 164.4; IR (ATR) *ν* 1754, 1441, 1325, 1159, 1138, 1085, 1043, 882, 849, 733 cm^{-1}; MS (FAB): *m/z* (relative intensity, %) 397 ([M]$^+$ + H$^+$, 10), 307 (24), 154 (100), 136 (87); HRMS (FAB): *m/z* calcd for $C_{16}H_{12}Cl_2N_2O_4S$ (M) 396.9817, found 396.9818.

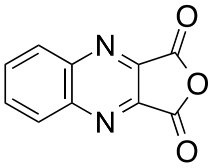
Quinoxaline-2,3-dicarcoxylic acid (6)



Purple solid; mp 188.6–188.8 °C (dec.); ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.04 (dd, *J* = 3.2, 6.4 Hz, 2H), 8.22 (dd, *J* = 3.2, 6.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 129.3, 132.7, 140.5, 145.1, 166.1; IR (ATR) *ν* 3028, 2554, 1682, 1474, 1275, 1240, 1169, 1063, 906, 781, 770, 742 cm^{-1}; MS (FAB): *m/z* (relative intensity, %) 219 ([M]$^+$ + H$^+$, 33), 154 (100), 136 (77); HRMS (FAB): *m/z* calcd for

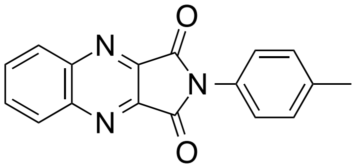
$C_{10}H_7N_2O_4$ (M) 219.0406, found 219.0410.

Quinoxaline-2,3-dicarcoxylic acid anhydride (7)



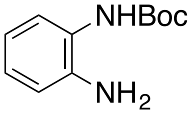
Brown solid; mp 250.5–251.5 °C (dec.); ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.22 (dd, *J* = 3.6, 6.8 Hz, 2H), 8.47 (dd, *J* = 3.6, 6.8 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 130.8, 134.5, 143.3, 144.9, 159.9; IR (ATR) *ν* 1876, 1788, 1647, 1585, 1368, 1177, 1103, 927, 887, 775 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 200 ([M]$^+$, 40), 156 (58), 128 (100); HRMS (EI): *m/z* calcd for $C_{10}H_4N_2O_3$ (M) 200.0222, found 200.0220.

2-(*p*-Tolyl)-1*H*-pyrrolo[3,4-*b*]quinoxaline-1,3(2*H*)-dione (8)



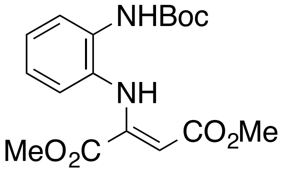
Purified by silica gel column chromatography (CH_2Cl_2); Yellow solid; 374.4–375.5 °C (dec.); R$_f$ 0.55 (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 8.06 (dd, *J* = 3.6, 5.4 Hz, 2H), 8.48 (dd, *J* = 3.6, 5.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 20.8, 127.0, 128.8, 129.5, 130.6, 133.1, 138.3, 143.0, 146.3, 163.6; IR (ATR) *ν* 3069, 2918, 1788, 1720, 1510, 1379, 1143, 1117, 1089, 885, 795, 779 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 289 ([M]$^+$, 100), 245 (13), 128 (24); HRMS (EI): *m/z* calcd for $C_{17}H_{11}N_3O_2$ (M) 289.0851, found 289.0850.

tert-Butyl (2-aminophenyl)carbamate (9')[S5]



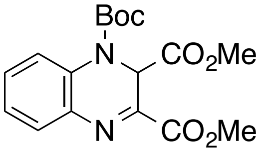
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 5:5); Colorless solid; mp 112.3–113.8 °C; R$_f$ 0.13 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (s, 9H), 3.73 (br, s, 2H), 6.37 (br, s, 1H), 6.72–6.78 (m, 2H), 6.97 (t, *J* = 7.2 Hz, 1H), 7.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 80.4, 117.5, 119.4, 124.7, 126.0 (2C), 139.9, 153.8; IR (ATR) *ν* 3354, 1678, 1516, 1491, 1456, 1288, 1254, 1153, 1055, 748 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 208 ([M]$^+$, 16), 152 ([M]$^+$ – C_4H_9 + H$^+$, 57), 108 ([M]$^+$ – Boc + H$^+$, 100); HRMS (EI): *m/z* calcd for $C_{11}H_{16}N_2O_2$ (M) 208.1212, found 208.1211.

Dimethyl 2-((2-((*tert*-butoxycarbonyl)amino)phenyl)amino)fumarate (9)

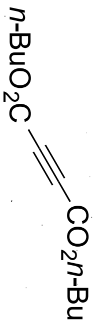


Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Yellow solid; mp 80.2–81.0 °C; R$_f$ 0.40 (hexane/EtOAc 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.53 (s, 9H), 3.59 (s, 3H), 3.76 (s, 3H), 5.59 (s, 1H), 6.83–6.96 (m, 3H), 7.17 (m, 1H), 7.95 (d, *J* = 7.6 Hz, 1H), 9.05 (br, s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0, 51.0, 52.4, 80.4, 95.2, 120.4, 123.0, 124.2, 126.5, 130.5, 133.2, 149.5, 152.6, 163.9, 169.4; IR (ATR) *ν* 3377, 2970, 1740, 1721, 1670, 1612, 1595, 1516, 1437, 1363, 1271, 1217, 1143, 1022, 777, 764 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 350 ([M]$^+$, 11), 294 ([M]$^+$ – C_4H_9 + H$^+$, 12), 250 ([M]$^+$ – Boc + H$^+$, 24), 191 ([M]$^+$ – Boc – CO_2Me + H$^+$, 98), 159 (92), 57 (100); HRMS (EI): *m/z* calcd for $C_{17}H_{22}N_2O_6$ (M) 350.1478, found 350.1474.

1-(*tert*-Butyl) 2,3-dimethyl quinoxaline-1,2,3(2*H*)-tricarboxylate (10)

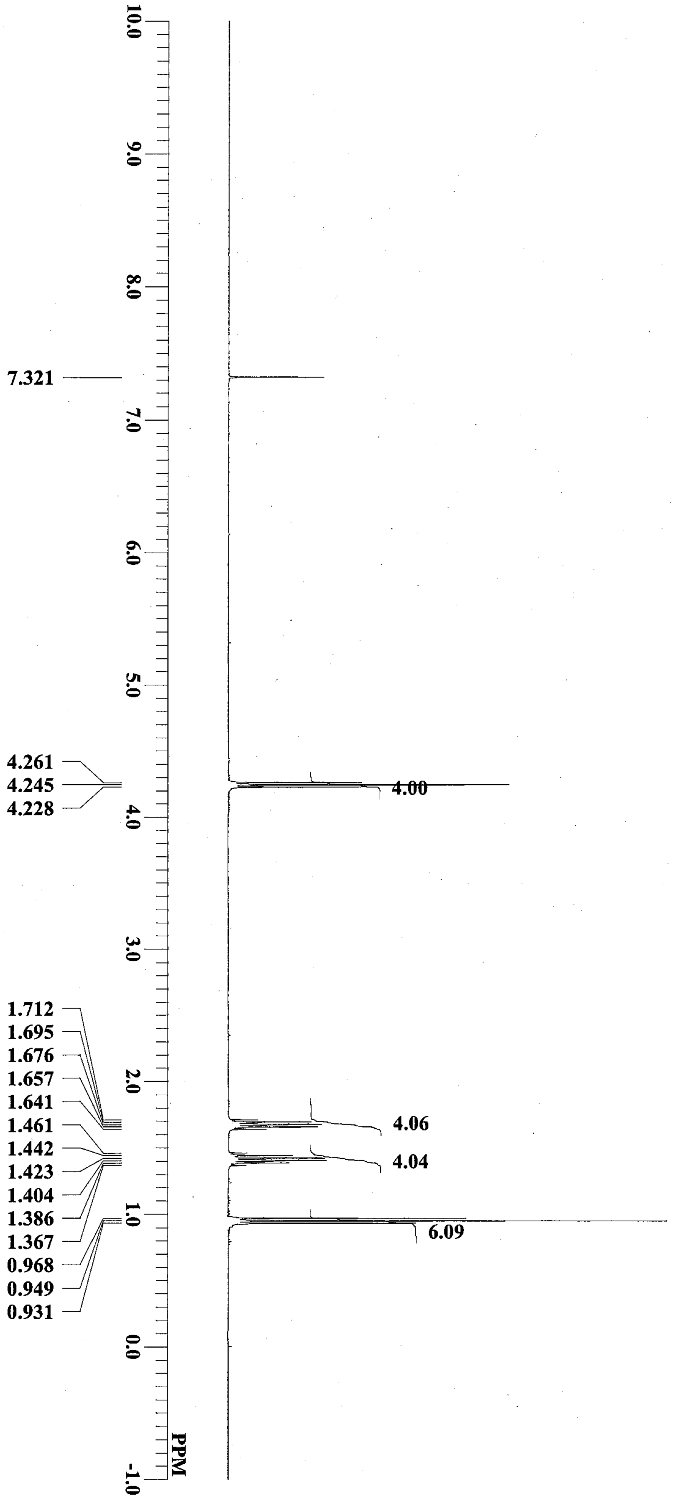


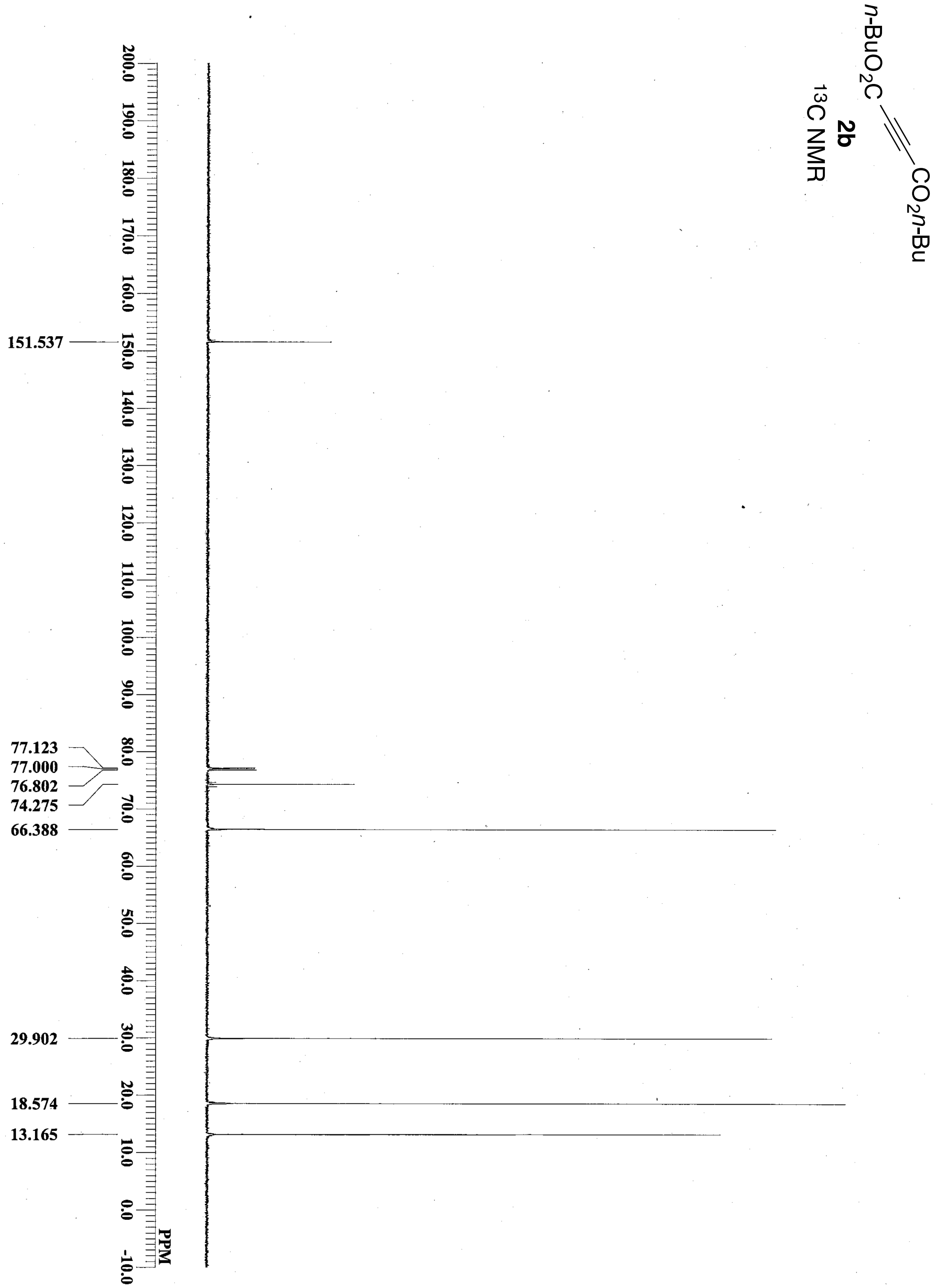
Purified by silica gel column chromatography (hexane/EtOAc 99:1 to 7:3); Colorless solid; mp 110.6–111.3 °C; R_f 0.19 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57 (s, 9H), 3.64 (s, 3H), 4.03 (s, 3H), 6.47 (br, s, 1H), 7.18 (m, 1H), 7.37 (m, 1H), 7.61 (m, 1H), 7.88 (br, s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.1, 51.3, 53.0, 53.5, 83.5, 122.7, 124.6, 129.0, 129.2, 130.4, 135.4, 150.1, 151.6, 163.3, 167.2; IR (ATR) *ν* 2959, 1726, 1712, 1476, 1440, 1367, 1338, 1269, 1226, 1157, 1123, 1010, 870, 799, 770, 754 cm^{-1}; MS (EI): *m/z* (relative intensity, %) 348 ([M]$^+$, 3), 289 ([M]$^+$ – CO_2Me, 2), 247 ([M]$^+$ – Boc, 2), 189 ([M]$^+$ – Boc – CO_2Me + H$^+$, 100), 57 (54); HRMS (EI): *m/z* calcd for $C_{17}H_{20}N_2O_6$ (M) 348.1321, found 348.1325.

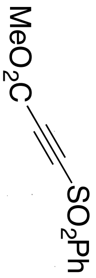

n-BuO$_2$C
CO$_2$$n$-Bu

2b

^{1}H NMR

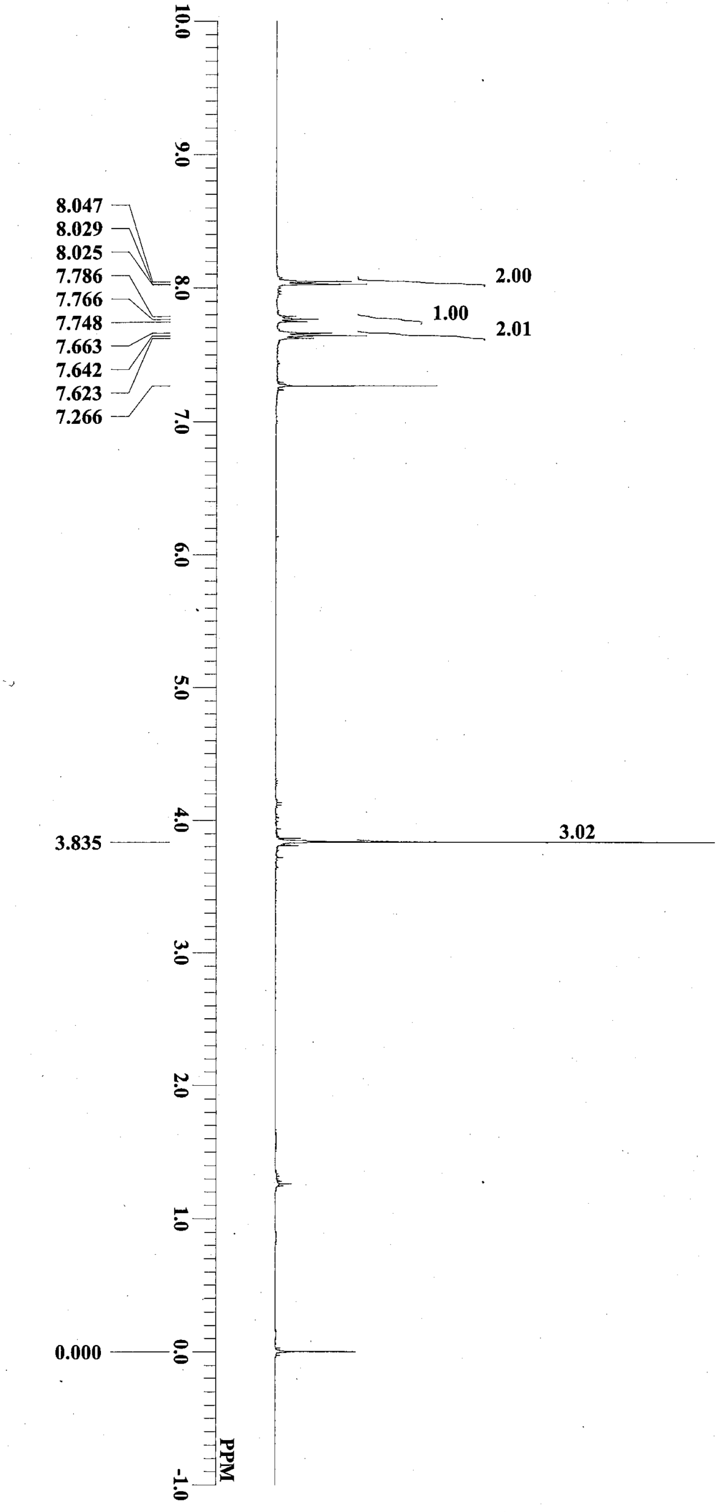

10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
7.321
4.261
4.245
4.228
1.712
1.695
1.676
1.657
1.641
1.461
1.442
1.423
1.404
1.386
1.367
0.968
0.949
0.931
4.00
4.06
4.04
6.09

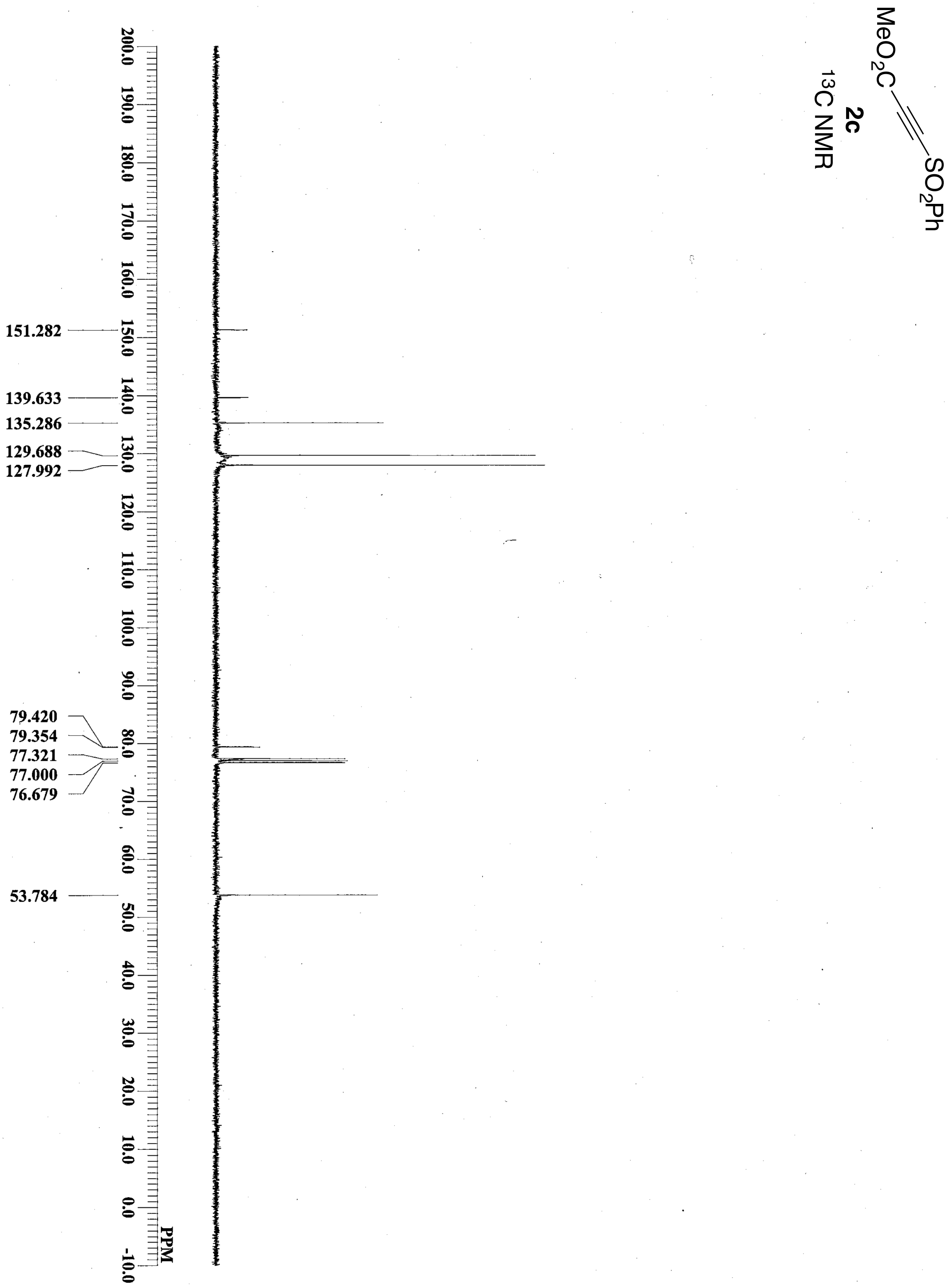

n-BuO2C
CO2n-Bu
2b
13C NMR
151.537
77.123
77.000
76.802
74.275
66.388
29.902
18.574
13.165
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM



2c

^{1}H NMR

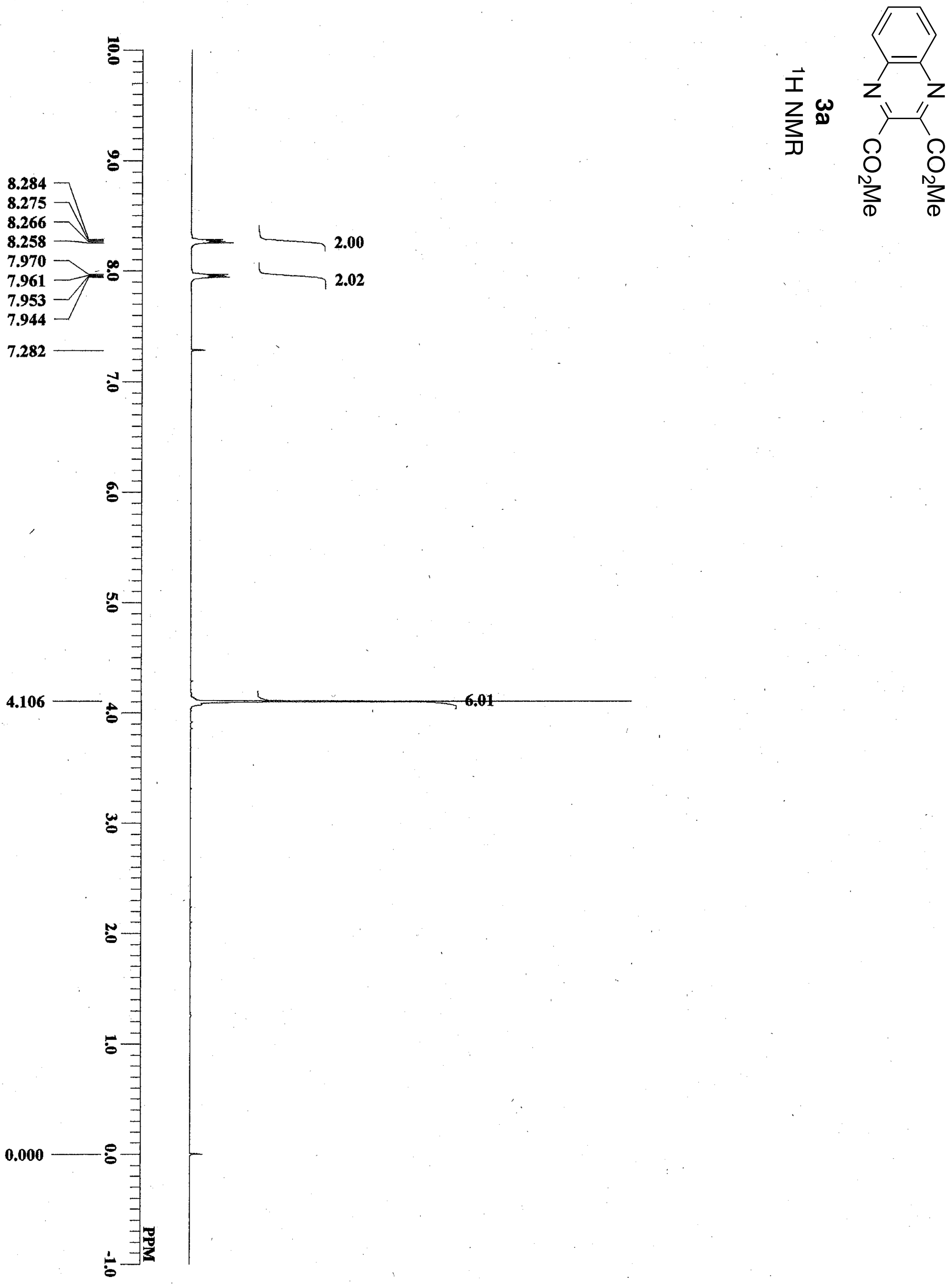

8.047
8.029
8.025
7.786
7.766
7.748
7.663
7.642
7.623
7.266
3.835
0.000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
2.00
1.00
2.01
3.02



2c

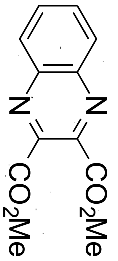
^{13}C NMR

MeO$_2$C
SO$_2$Ph
151.282
139.633
135.286
129.688
127.992
79.420
79.354
77.321
77.000
76.679
53.784
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


CO2Me
CO2Me
N
N
8.284
8.275
8.266
8.258
7.970
7.961
7.953
7.944
7.282
4.106
0.000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
2.00
2.02
6.01

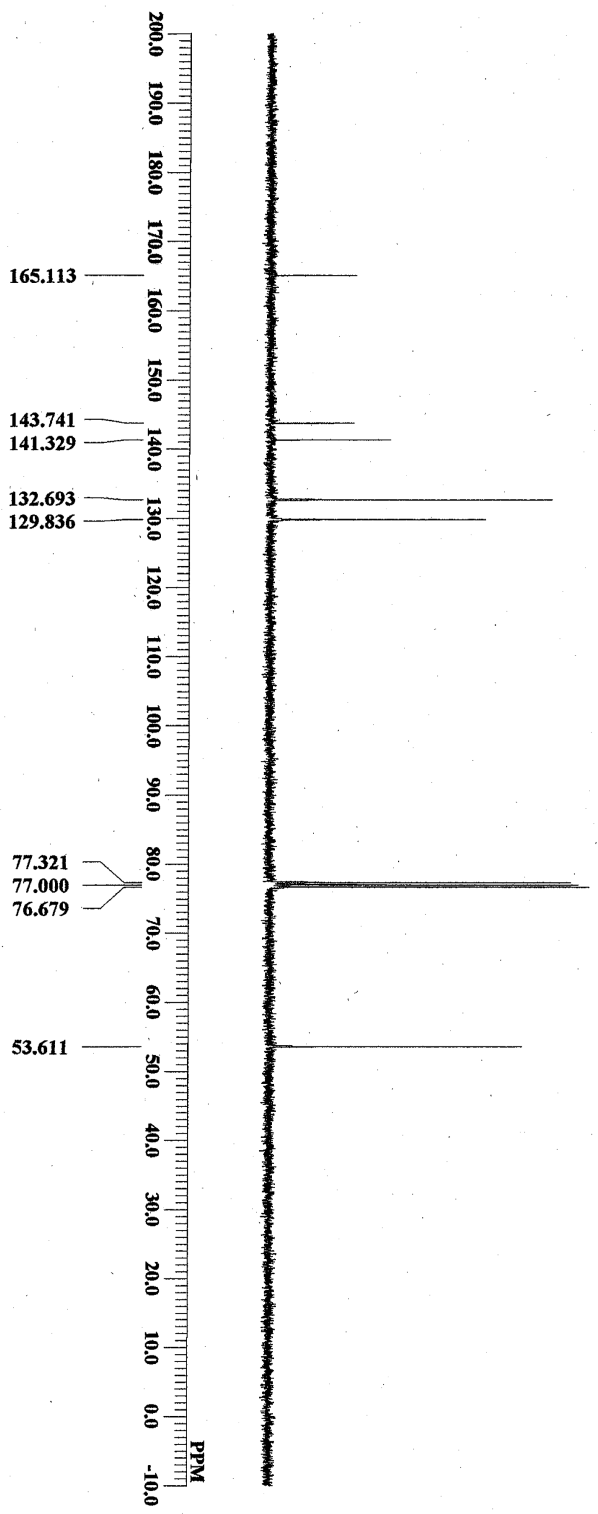
3a

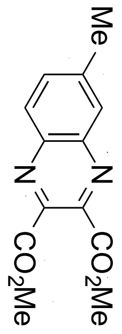
^{1}H NMR


N
N
CO2Me
CO2Me

3a

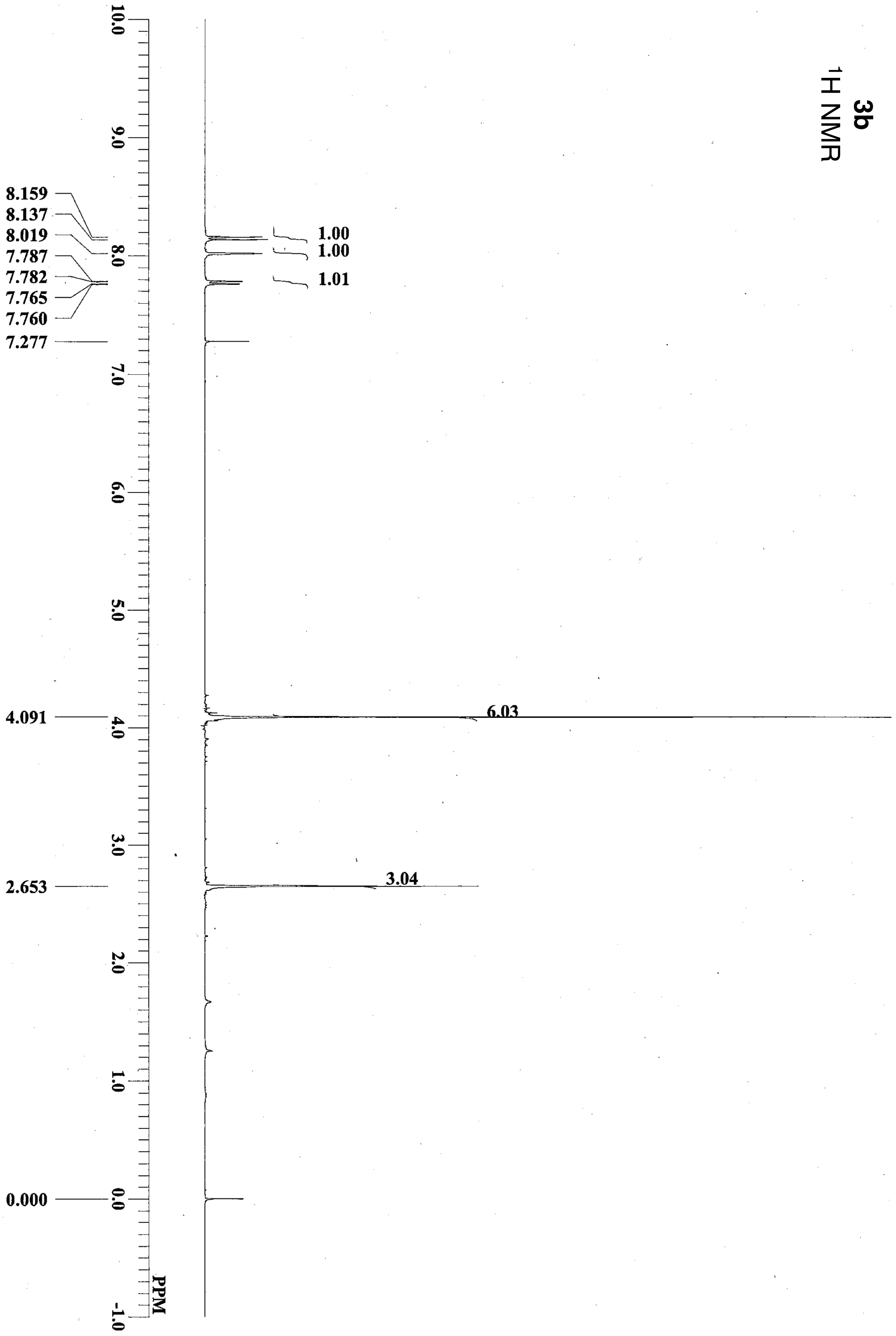
^{13}C NMR

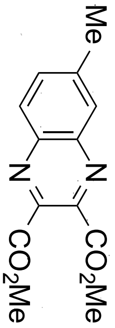

165.113
143.741
141.329
132.693
129.836
77.321
77.000
76.679
53.611
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


Me
N
N
CO2Me
CO2Me

3b

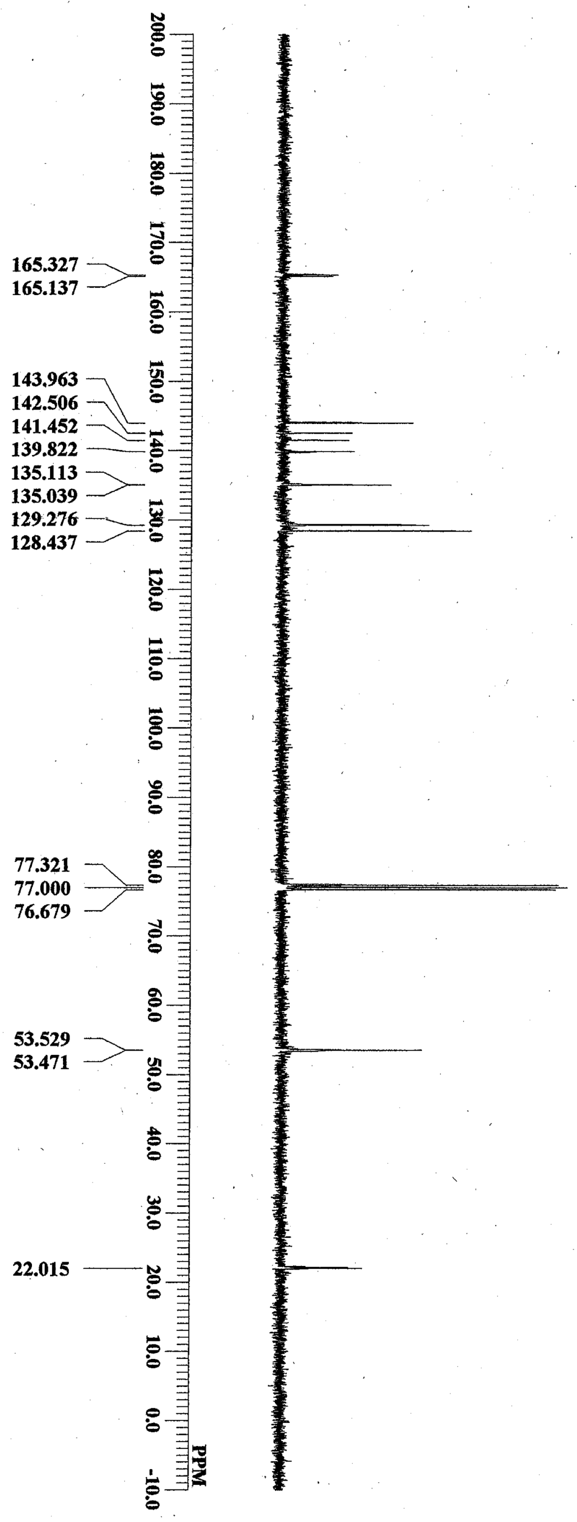
^{1}H NMR

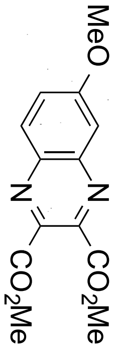

8.159
8.137
8.019
7.787
7.782
7.765
7.760
7.277
4.091
2.653
0.000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
1.00
1.00
1.01
6.03
3.04


Me
N
N
CO2Me
CO2Me

3b

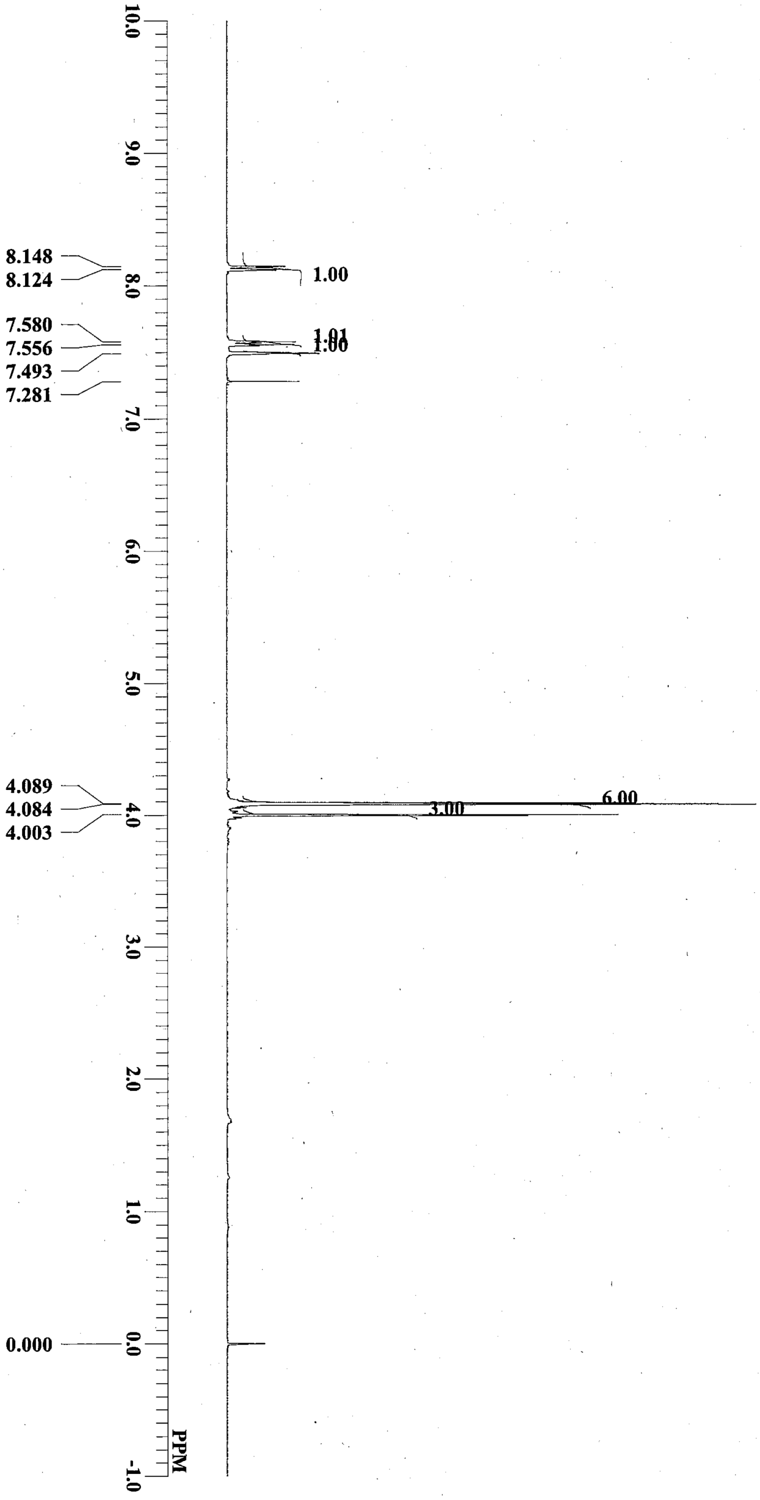
^{13}C NMR

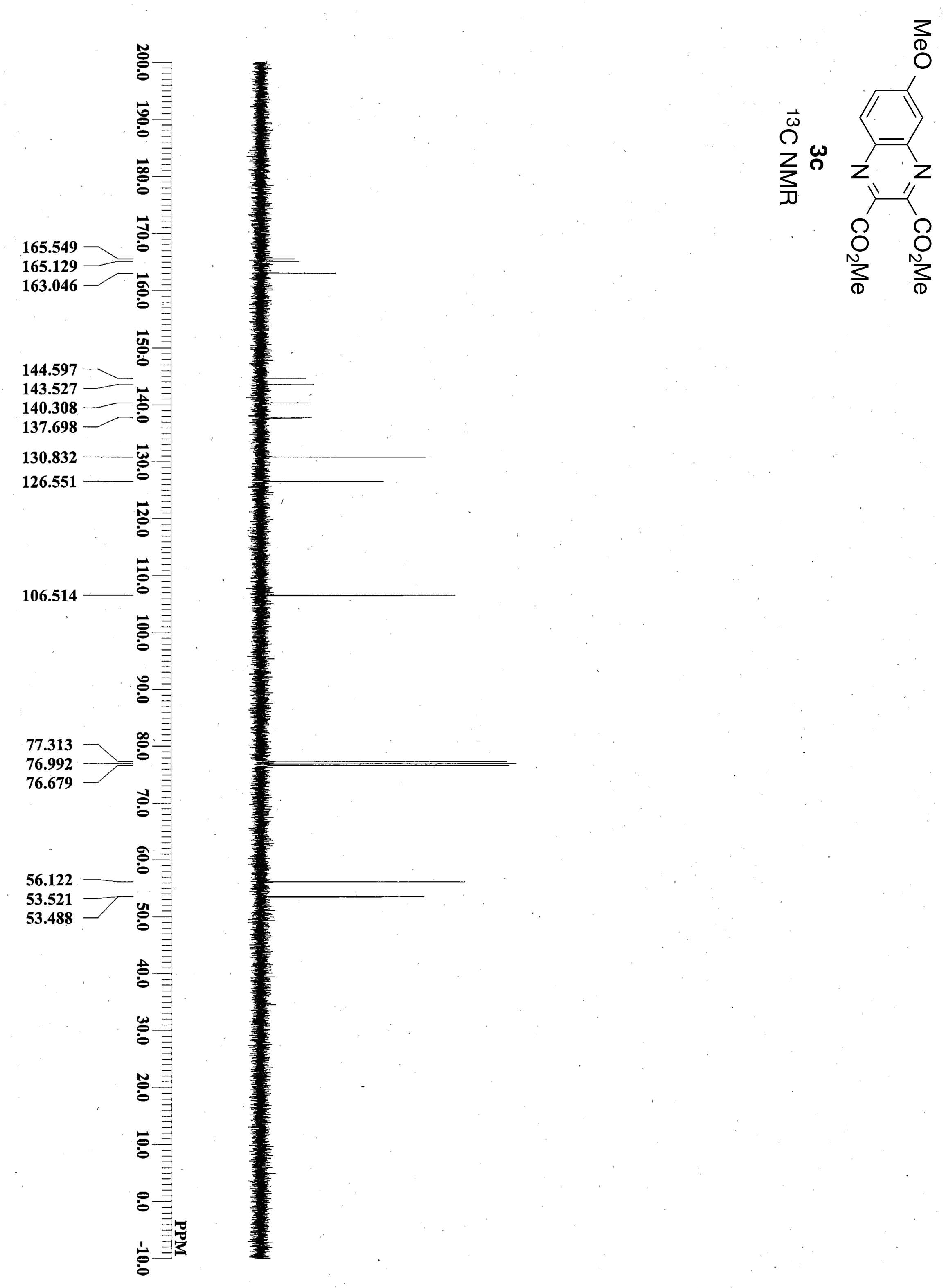

165.327
165.137
143.963
142.506
141.452
139.822
135.113
135.039
129.276
128.437
77.321
77.000
76.679
53.529
53.471
22.015
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM



3c

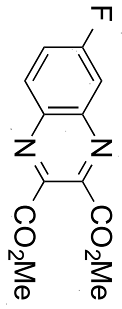
^{1}H NMR


8.148
8.124
7.580
7.556
7.493
7.281
4.089
4.084
4.003
0.000
1.00
1.01
1.00
3.00
6.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


MeO
N
N
CO2Me
CO2Me
165.549
165.129
163.046
144.597
143.527
140.308
137.698
130.832
126.551
106.514
77.313
76.992
76.679
56.122
53.521
53.488
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM

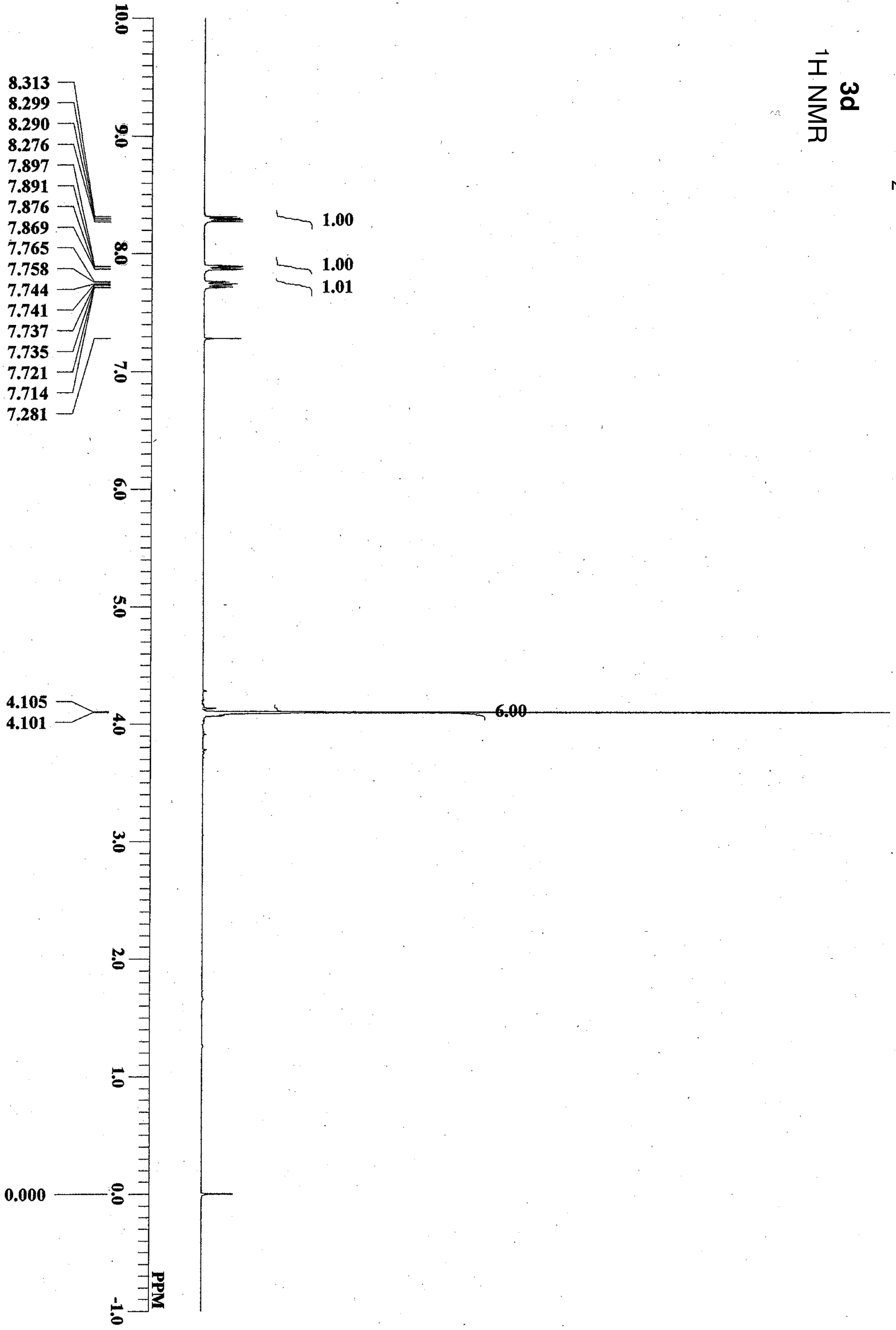
3c

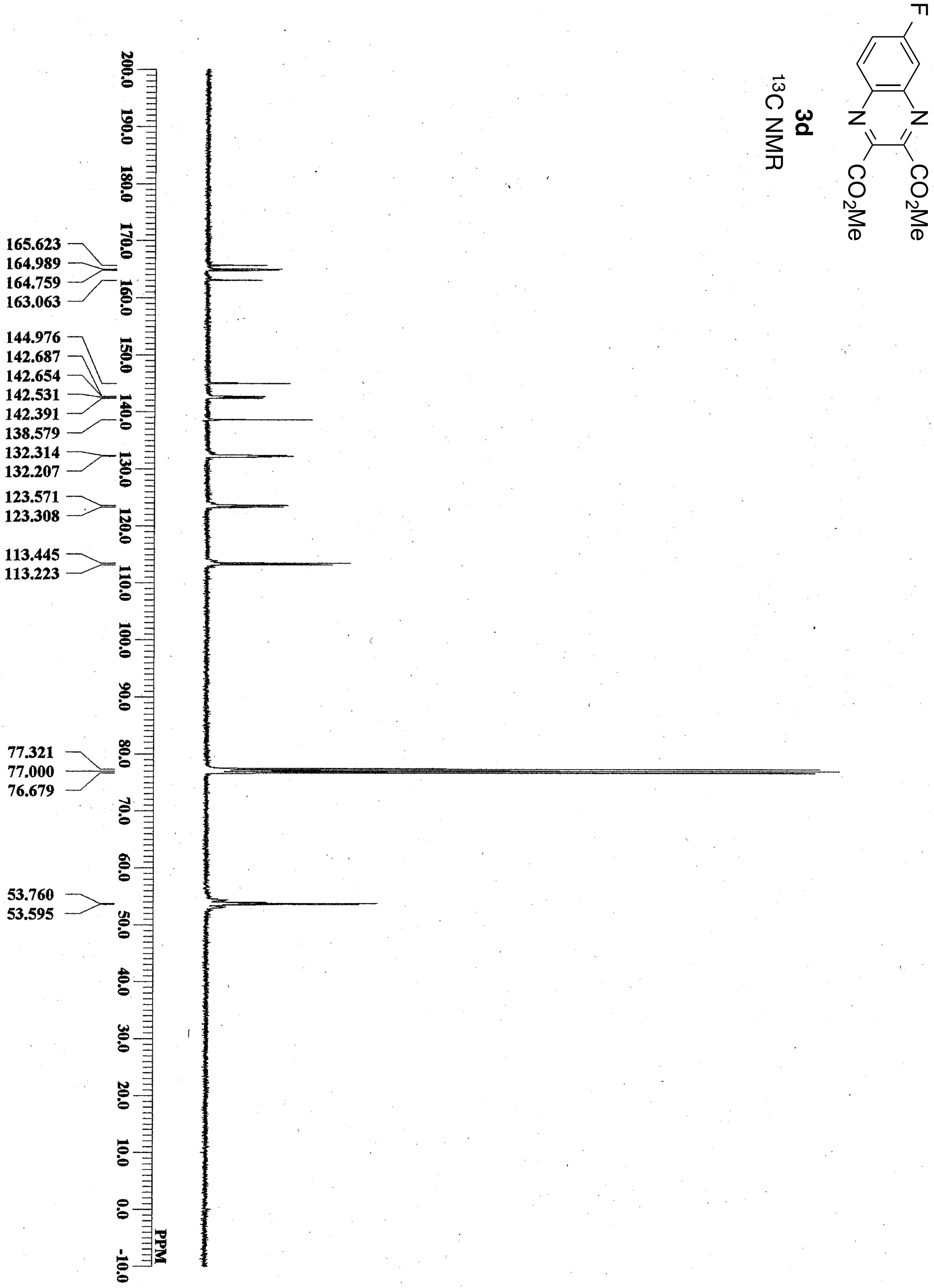
^{13}C NMR


F
N
N
CO2Me
CO2Me

3d

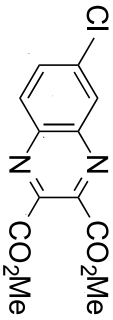
^{1}H NMR


8.313
8.299
8.290
8.276
7.897
7.891
7.876
7.869
7.765
7.758
7.744
7.741
7.737
7.735
7.721
7.714
7.281
4.105
4.101
0.000
1.00
1.00
1.01
6.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


F
N
N
CO2Me
CO2Me
165.623
164.989
164.759
163.063
144.976
142.687
142.654
142.531
142.391
138.579
132.314
132.207
123.571
123.308
113.445
113.223
77.321
77.000
76.679
53.760
53.595
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM

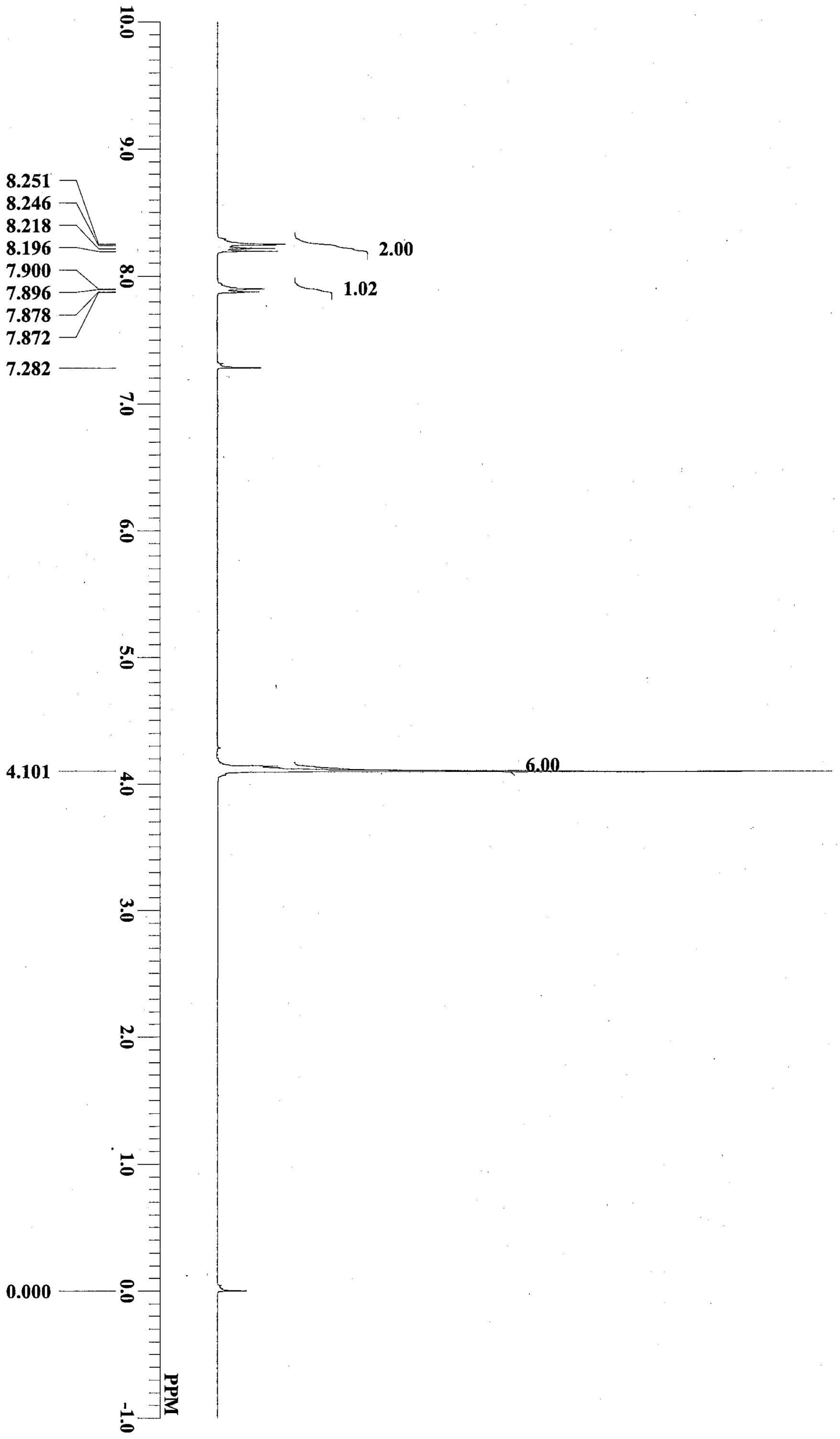
3d

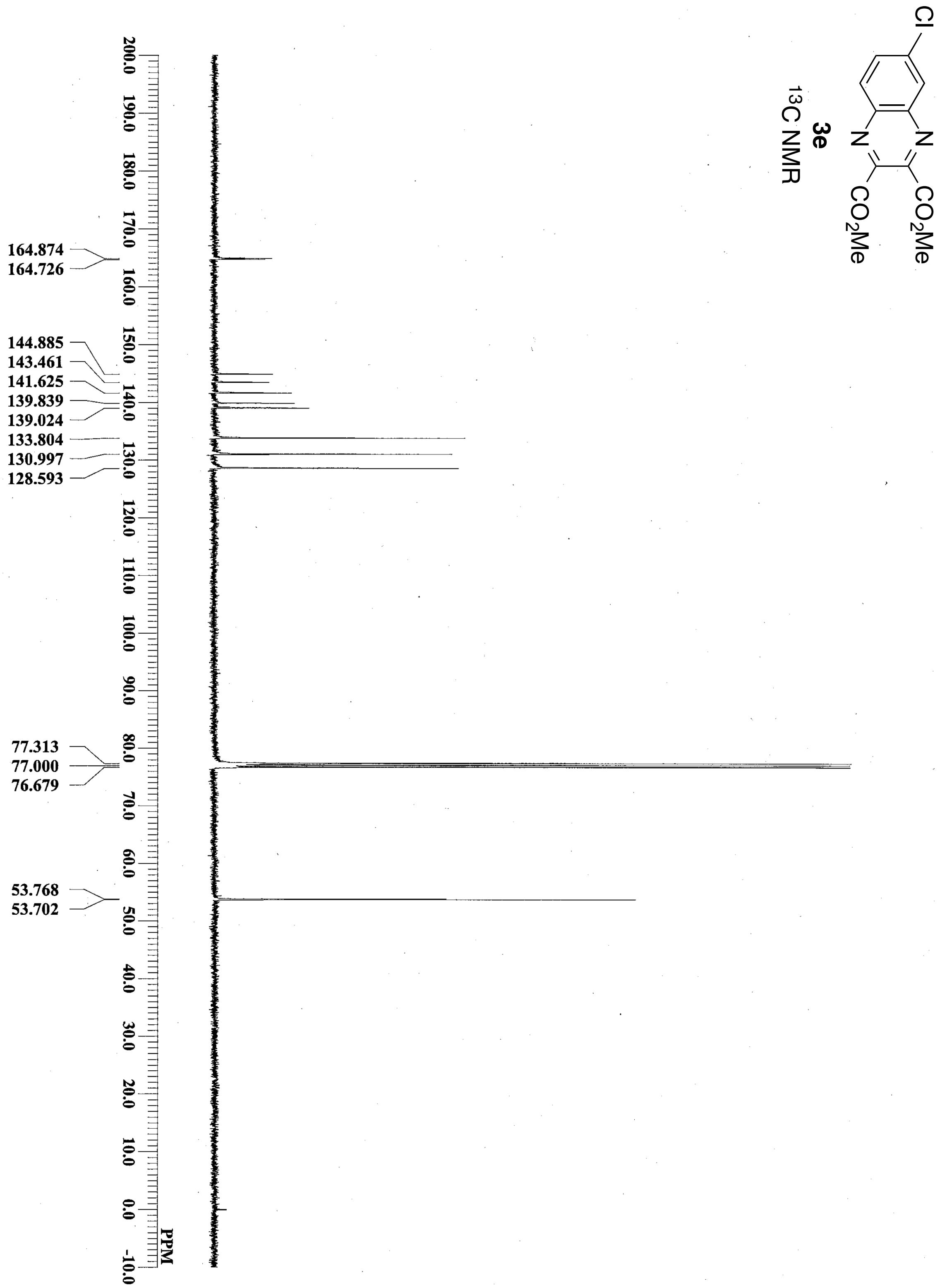
^{13}C NMR


Cl
N
N
CO2Me
CO2Me

3e

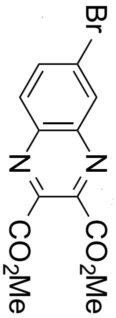
^{1}H NMR


8.251
8.246
8.218
8.196
7.900
7.896
7.878
7.872
7.282
4.101
0.000
2.00
1.02
6.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


Cl
N
N
CO2Me
CO2Me
164.874
164.726
144.885
143.461
141.625
139.839
139.024
133.804
130.997
128.593
77.313
77.000
76.679
53.768
53.702
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM

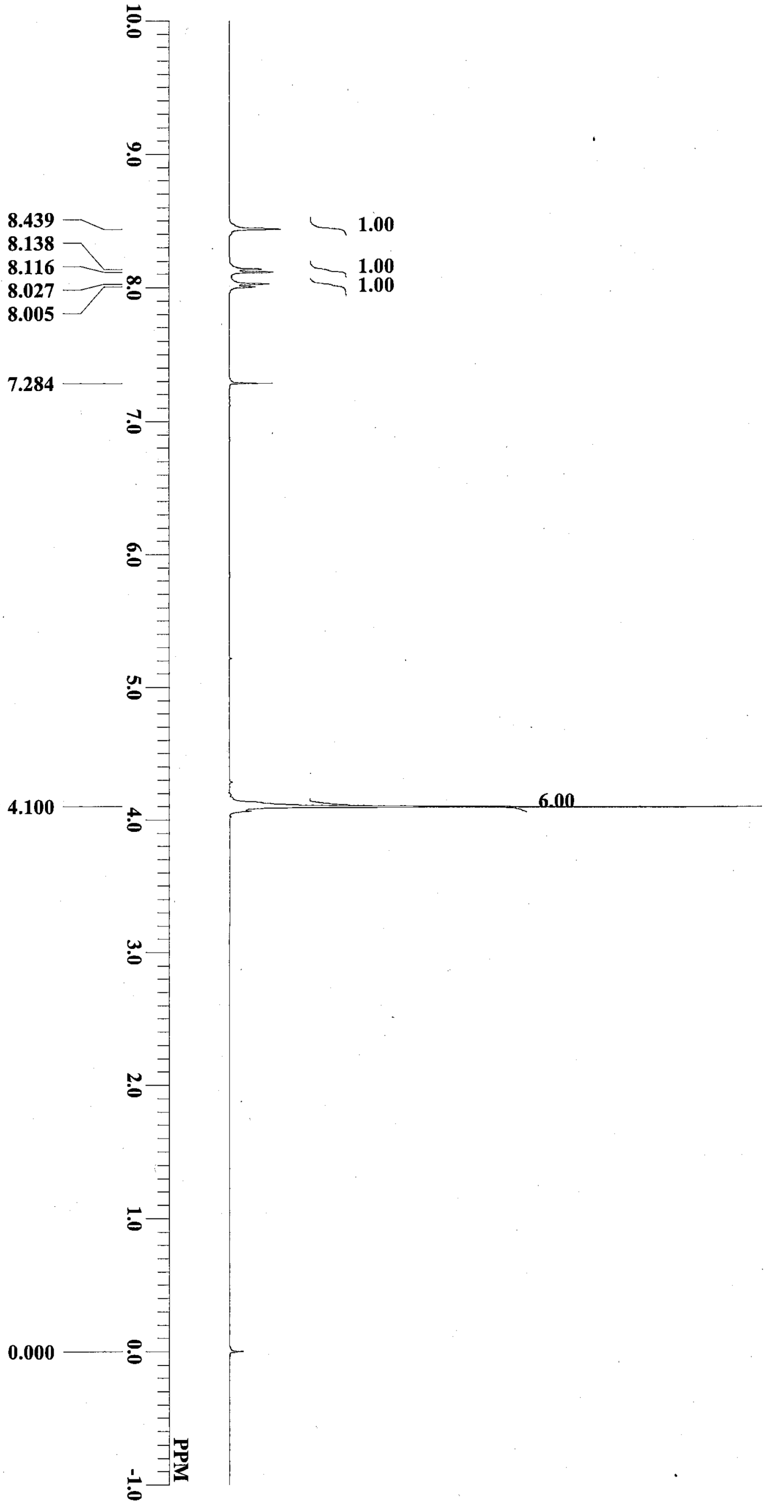
3e

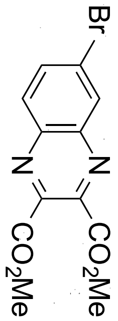
^{13}C NMR


Br
N
N
CO2Me
CO2Me

3f

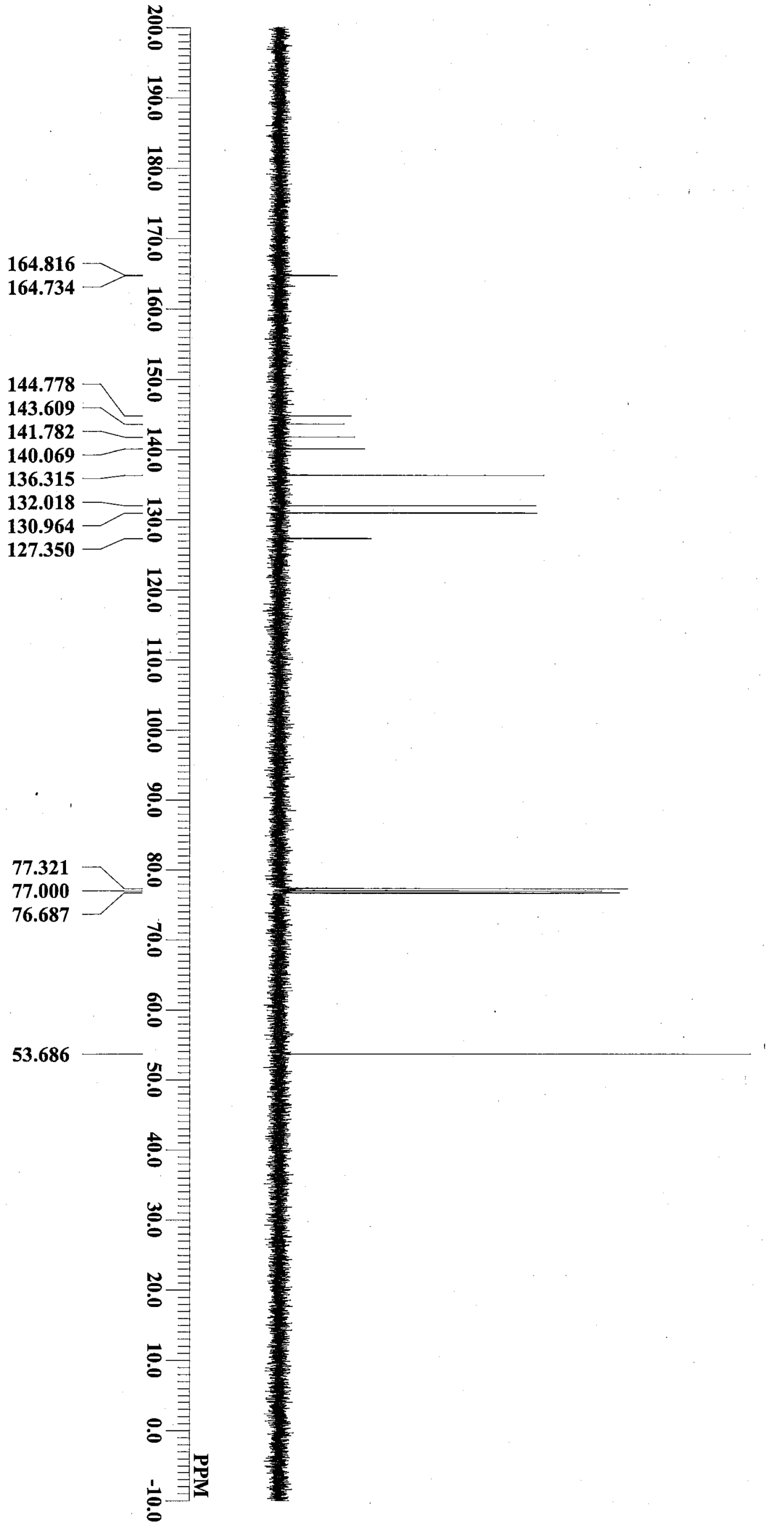
^{1}H NMR

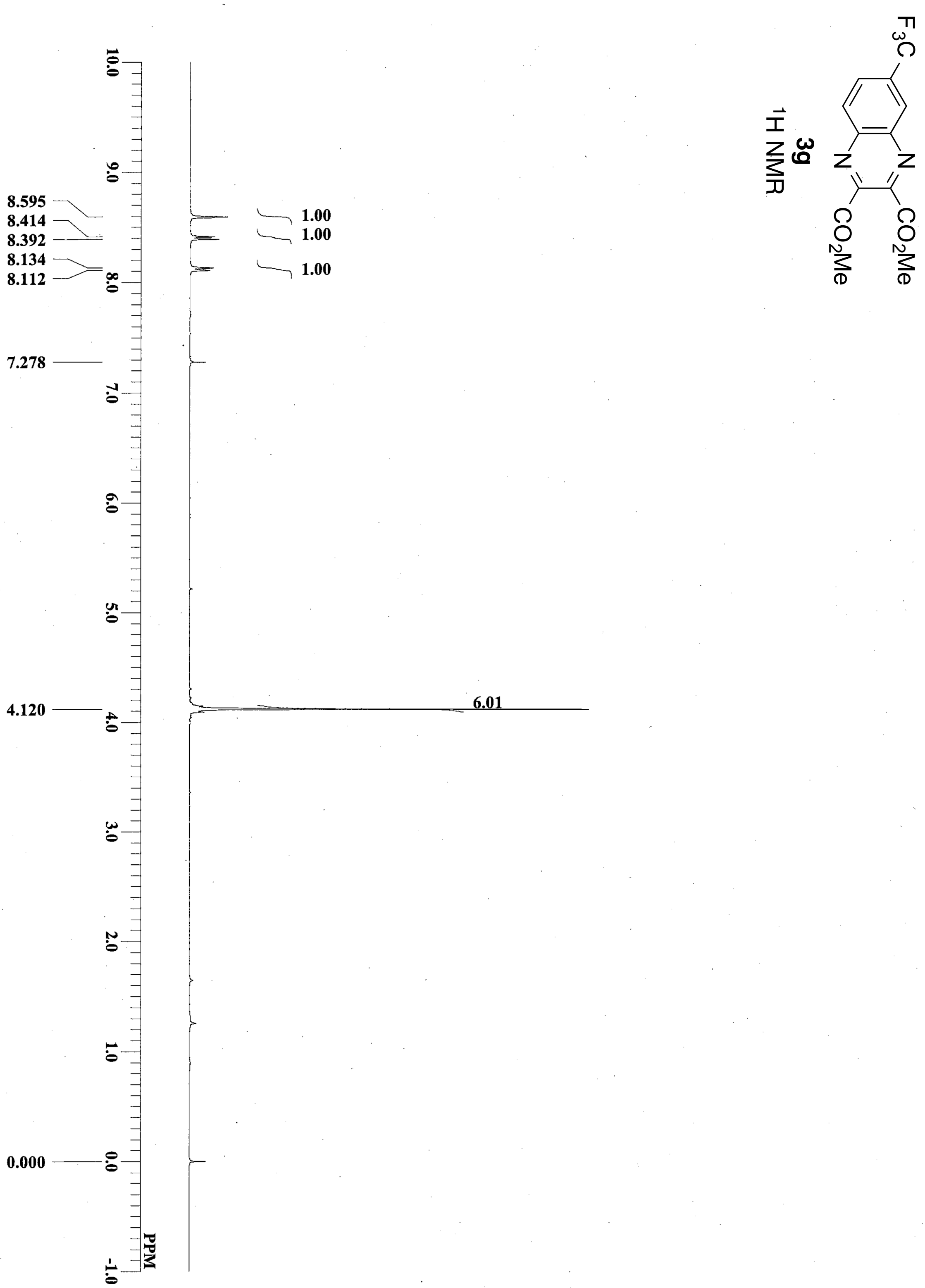

8.439
8.138
8.116
8.027
8.005
7.284
4.100
0.000
1.00
1.00
1.00
6.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


Br
N
N
CO2Me
CO2Me

3f

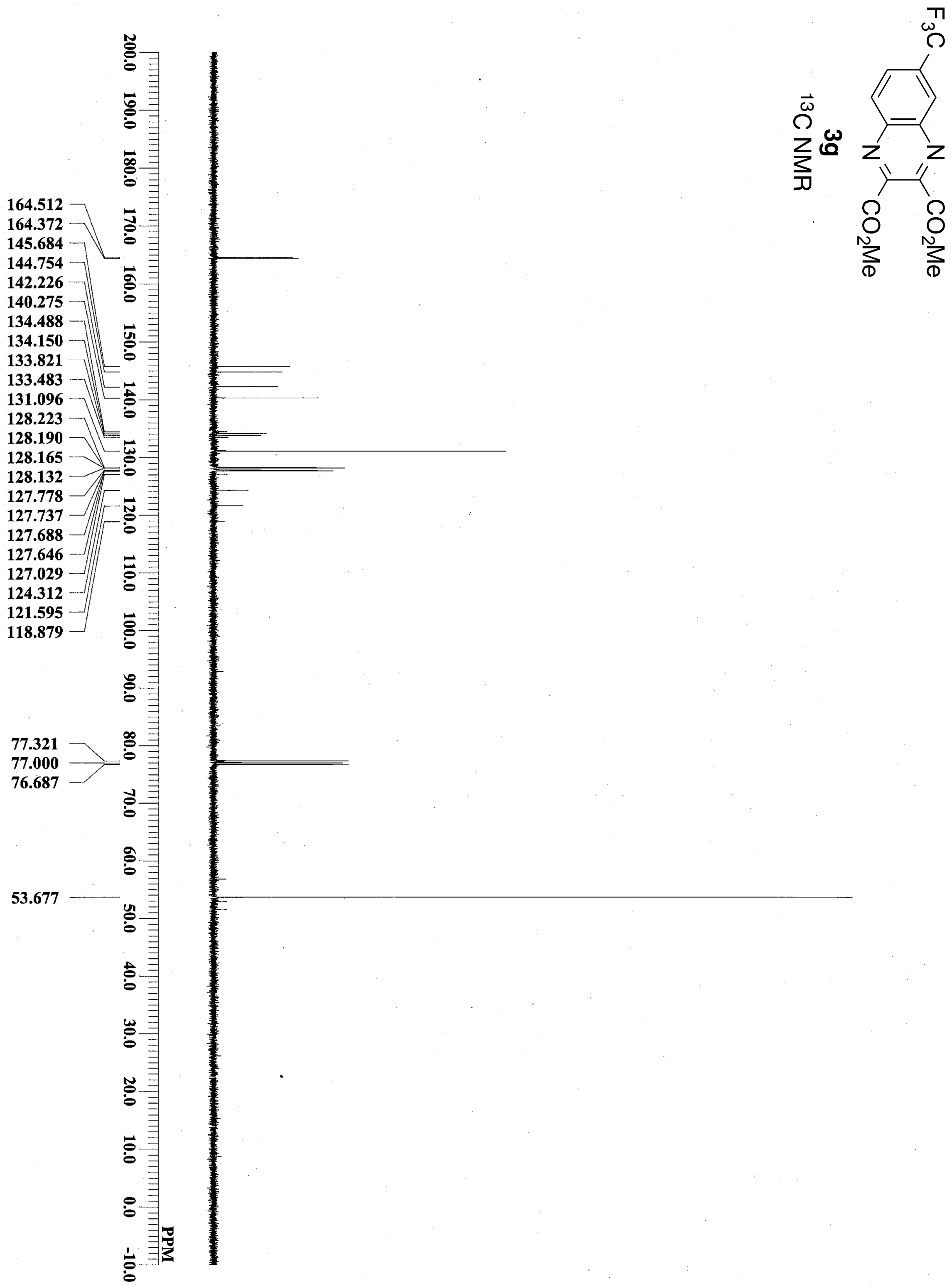
^{13}C NMR


164.816
164.734
144.778
143.609
141.782
140.069
136.315
132.018
130.964
127.350
77.321
77.000
76.687
53.686
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


F$_3$C
N
N
CO$_2$Me
CO$_2$Me
8.595
8.414
8.392
8.134
8.112
7.278
4.120
0.000
1.00
1.00
1.00
6.01
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM

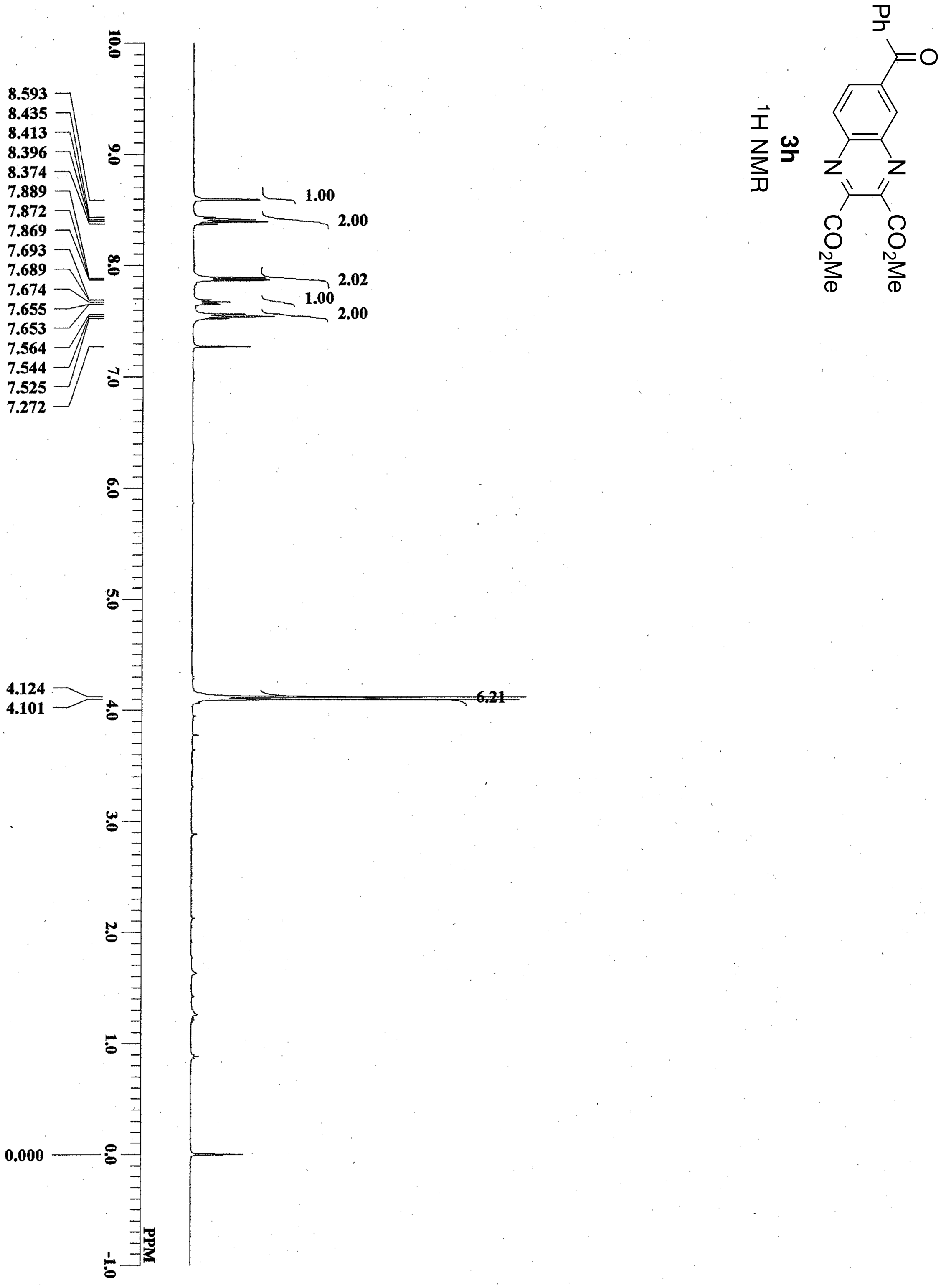
3g

^{1}H NMR


F3C
N
N
CO2Me
CO2Me
164.512
164.372
145.684
144.754
142.226
140.275
134.488
134.150
133.821
133.483
131.096
128.223
128.190
128.165
128.132
127.778
127.737
127.688
127.646
127.029
124.312
121.595
118.879
77.321
77.000
76.687
53.677
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM

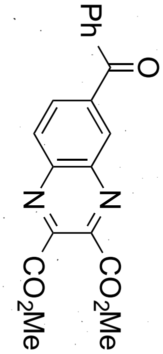
3g

^{13}C NMR


Ph
O
N
N
CO2Me
CO2Me
8.593
8.435
8.413
8.396
8.374
7.889
7.872
7.869
7.693
7.689
7.674
7.655
7.653
7.564
7.544
7.525
7.272
4.124
4.101
0.000
1.00
2.00
2.02
1.00
2.00
6.21
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM

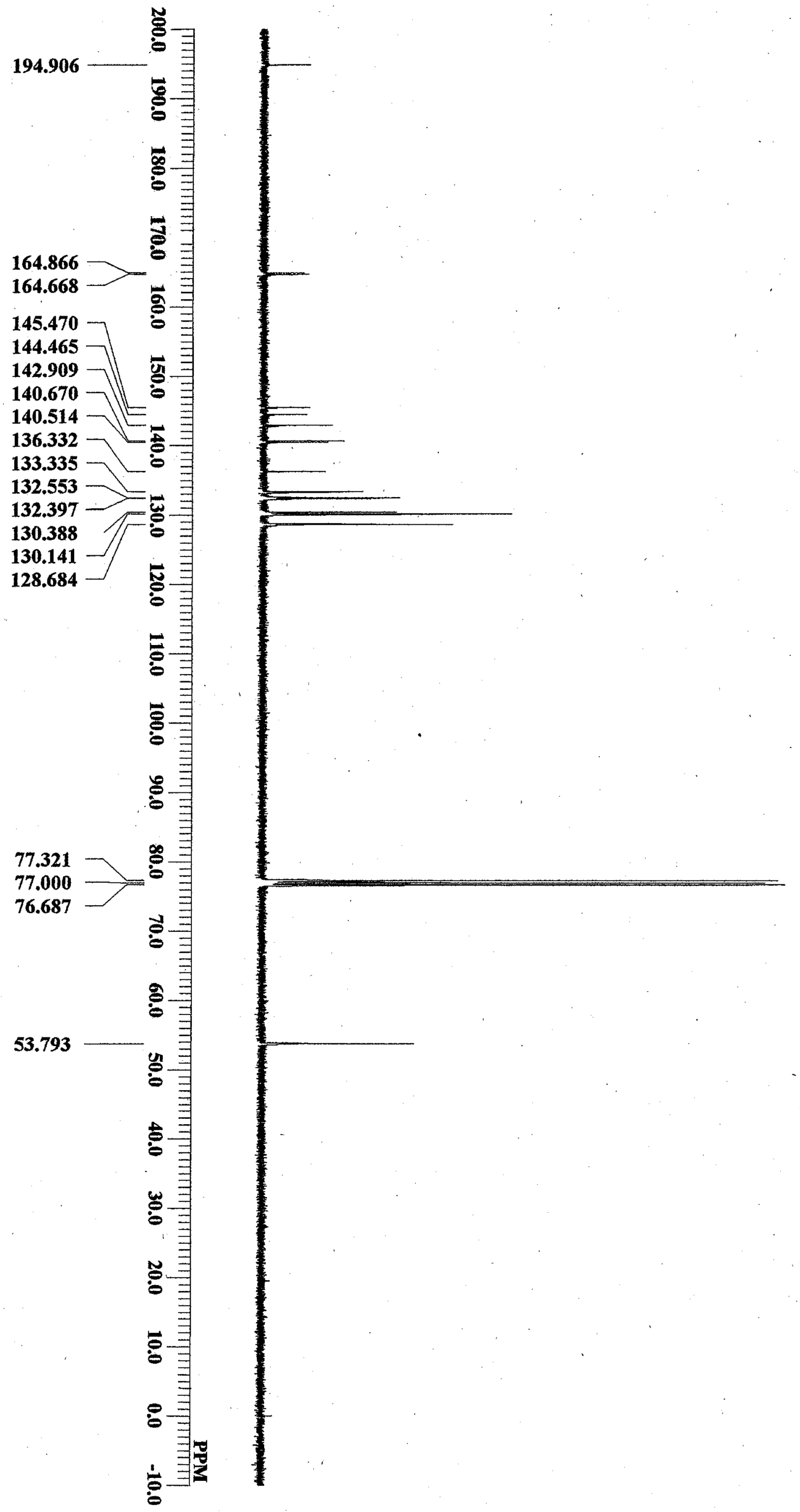
3h

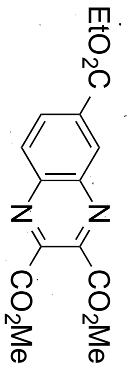
^{1}H NMR


Ph
O
N
N
CO2Me
CO2Me

3h

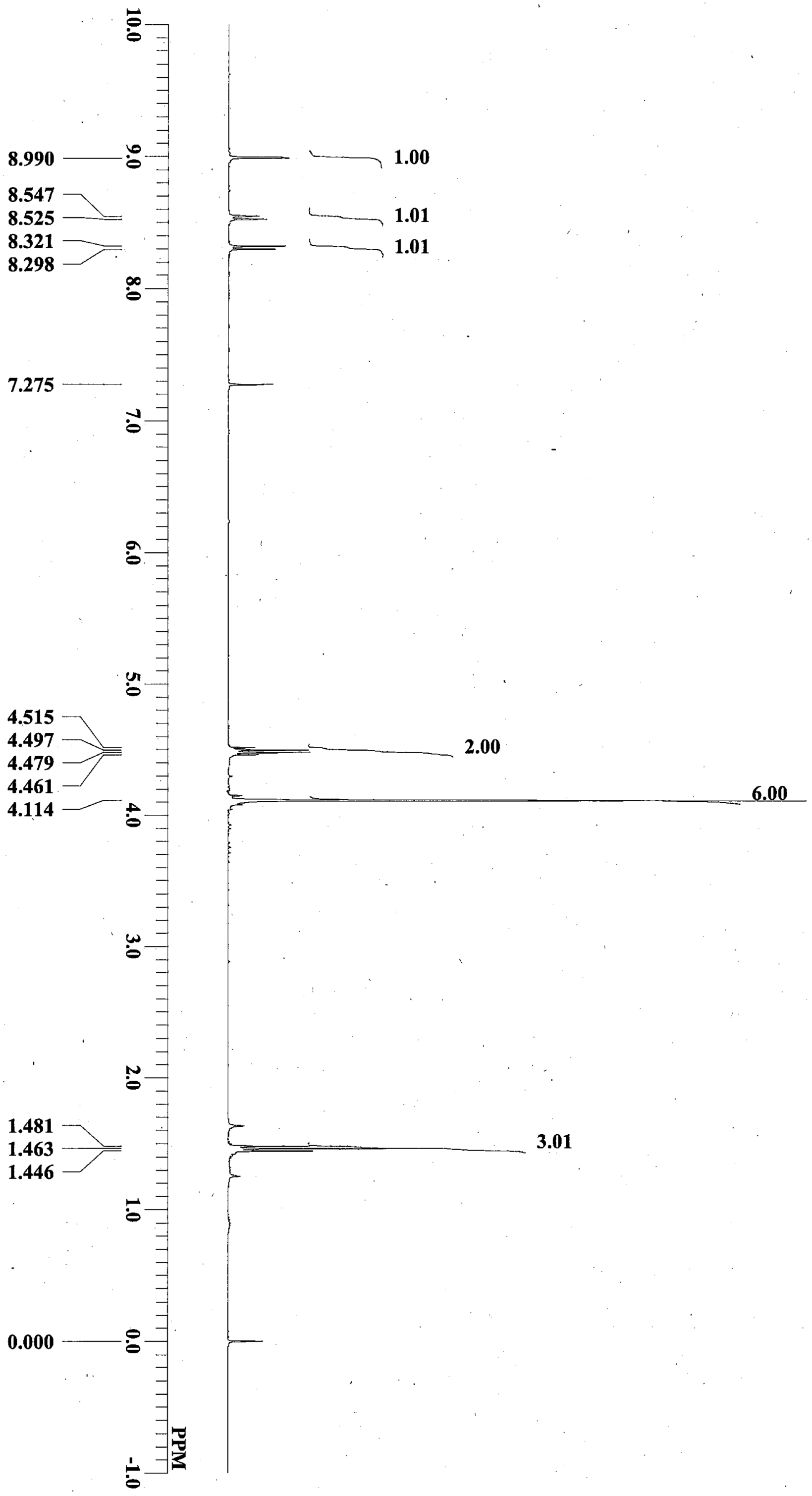
^{13}C NMR

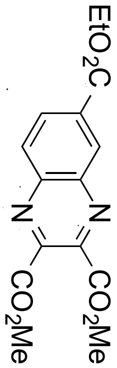

194.906
164.866
164.668
145.470
144.465
142.909
140.670
140.514
136.332
133.335
132.553
132.397
130.388
130.141
128.684
77.321
77.000
76.687
53.793
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


EtO2C
N
N
CO2Me
CO2Me

3i

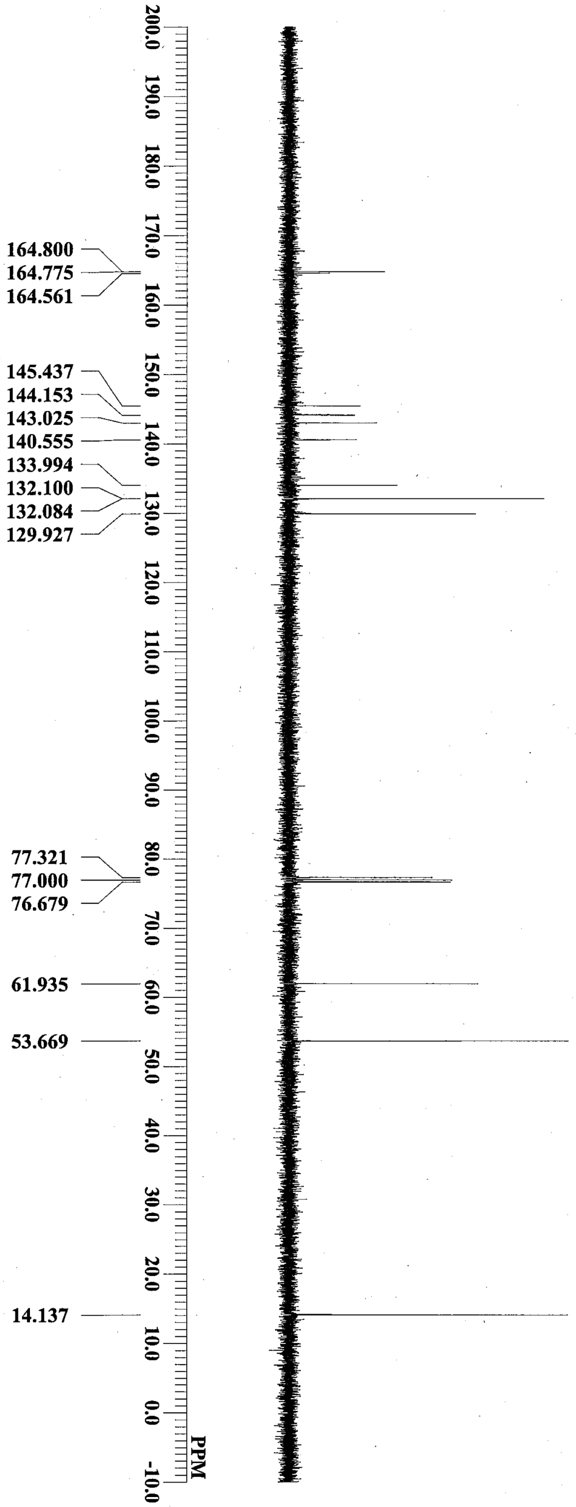
^{1}H NMR

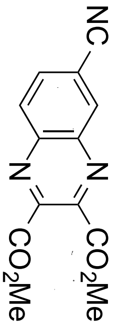

8.990
8.547
8.525
8.321
8.298
7.275
4.515
4.497
4.479
4.461
4.114
1.481
1.463
1.446
0.000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
1.00
1.01
1.01
2.00
6.00
3.01


EtO2C
N
N
CO2Me
CO2Me

3i

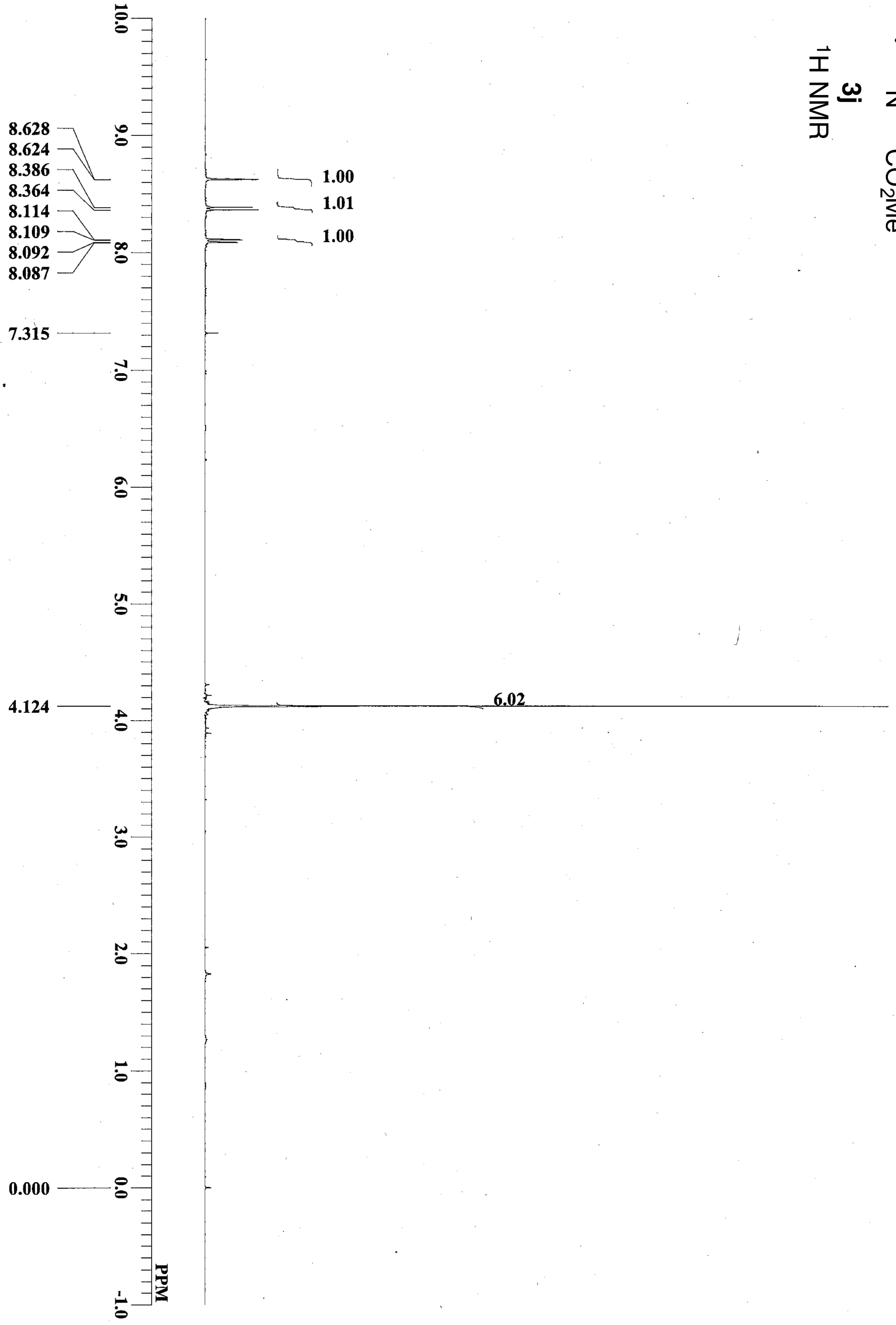
^{13}C NMR

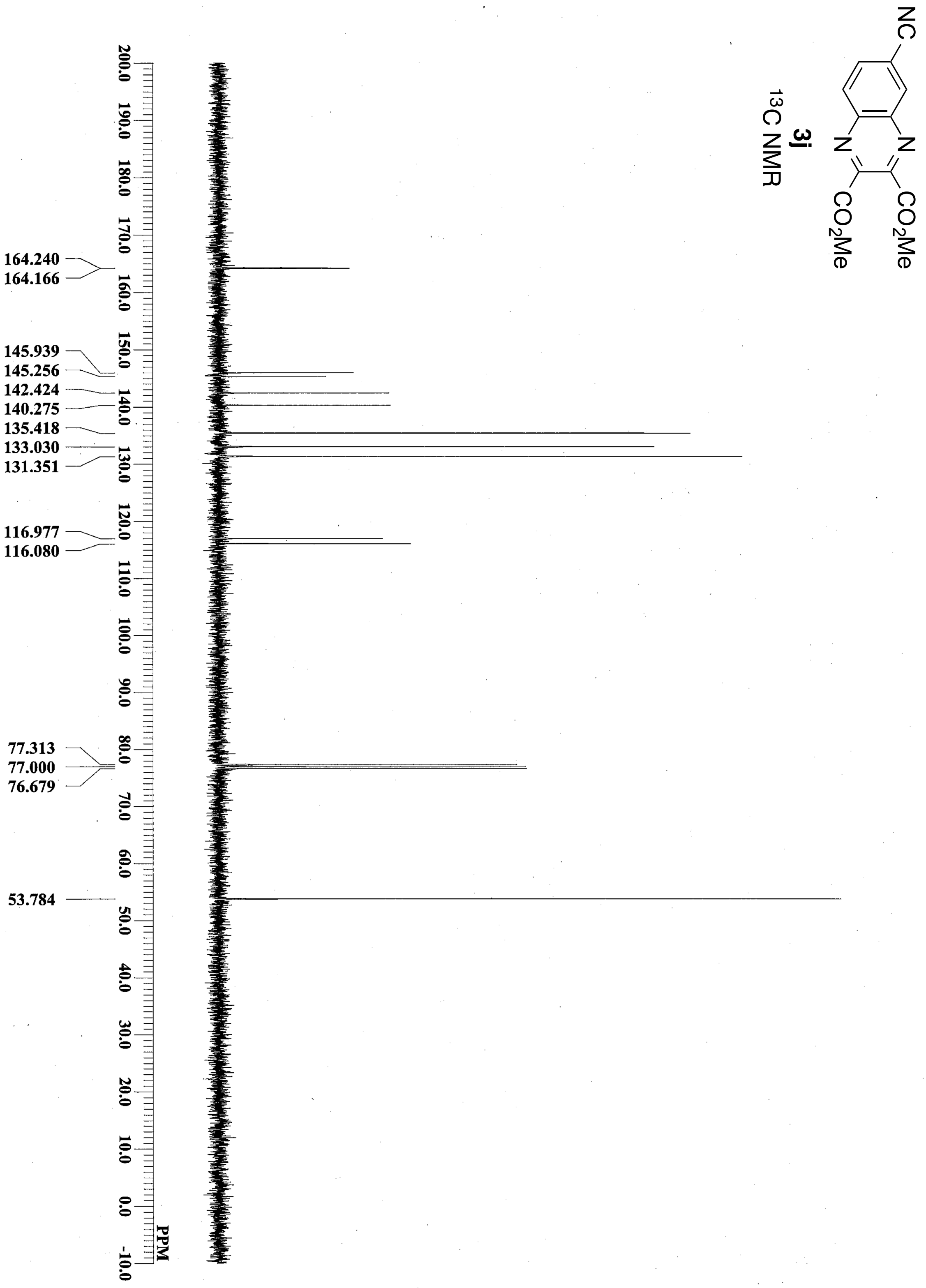

164.800
164.775
164.561
145.437
144.153
143.025
140.555
133.994
132.100
132.084
129.927
77.321
77.000
76.679
61.935
53.669
14.137
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


NC
N
N
CO2Me
CO2Me

3j

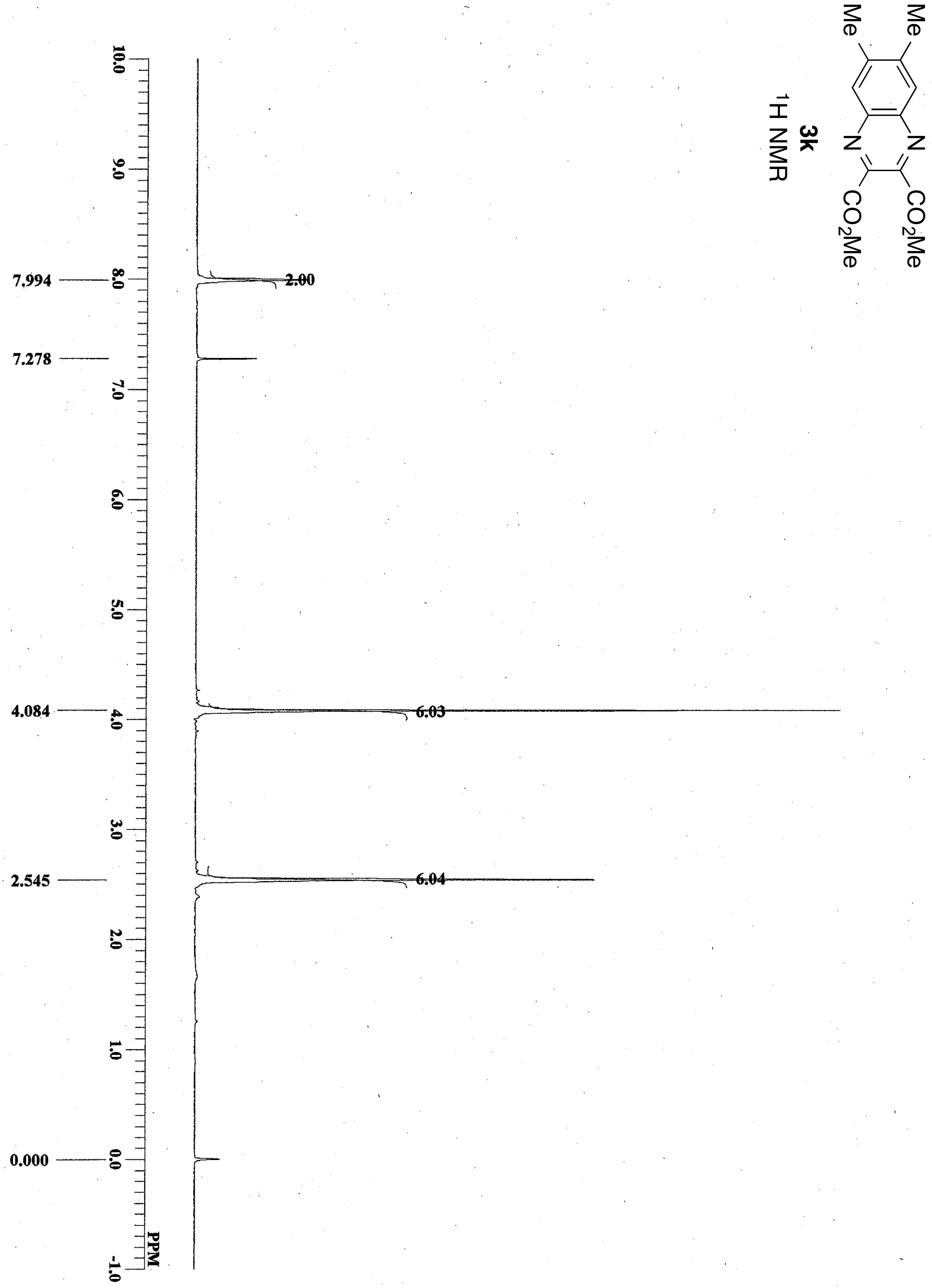
^{1}H NMR


8.628
8.624
8.386
8.364
8.114
8.109
8.092
8.087
7.315
4.124
0.000
1.00
1.01
1.00
6.02
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


NC
N
N
CO_2Me
CO_2Me
164.240
164.166
145.939
145.256
142.424
140.275
135.418
133.030
131.351
116.977
116.080
77.313
77.000
76.679
53.784
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM

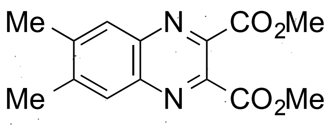
3j

^{13}C NMR


Me
Me
N
N
CO2Me
CO2Me
7.994
7.278
4.084
2.545
0.000
2.00
6.03
6.04
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM

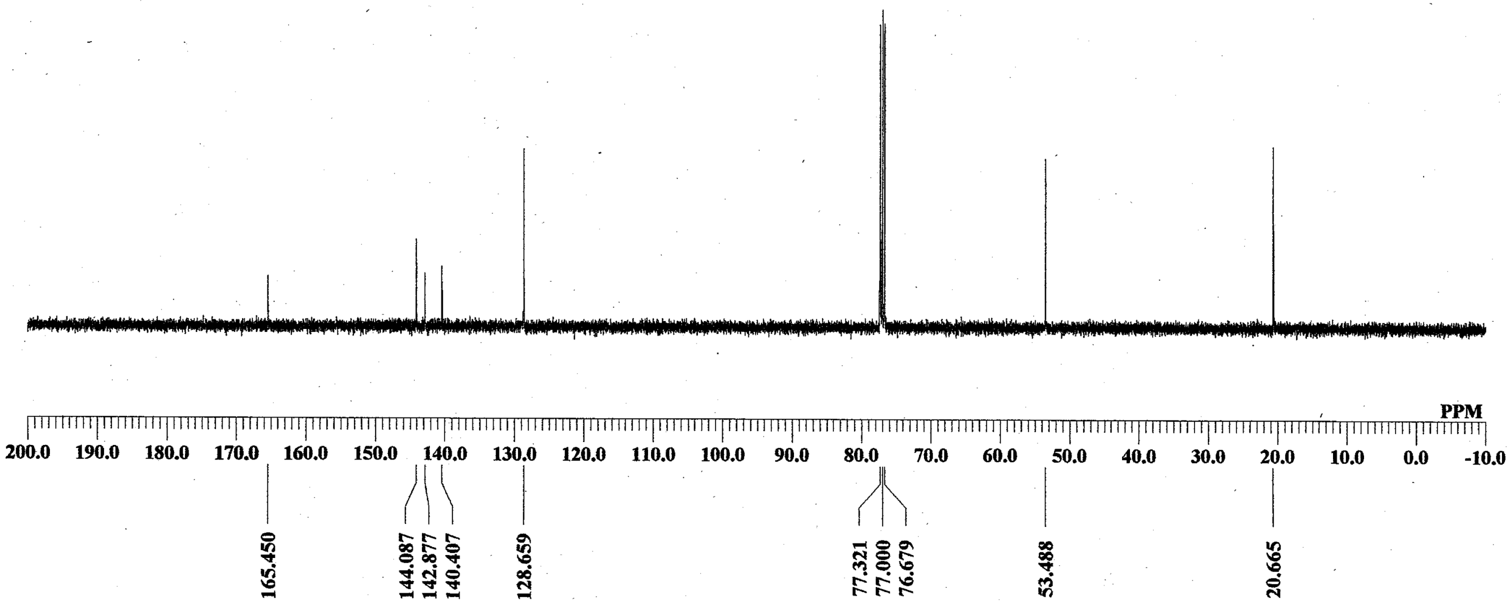
3k

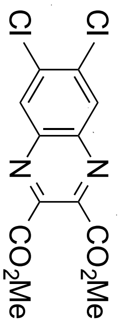
^{1}H NMR


Me
Me
N
N
CO2Me
CO2Me

3k

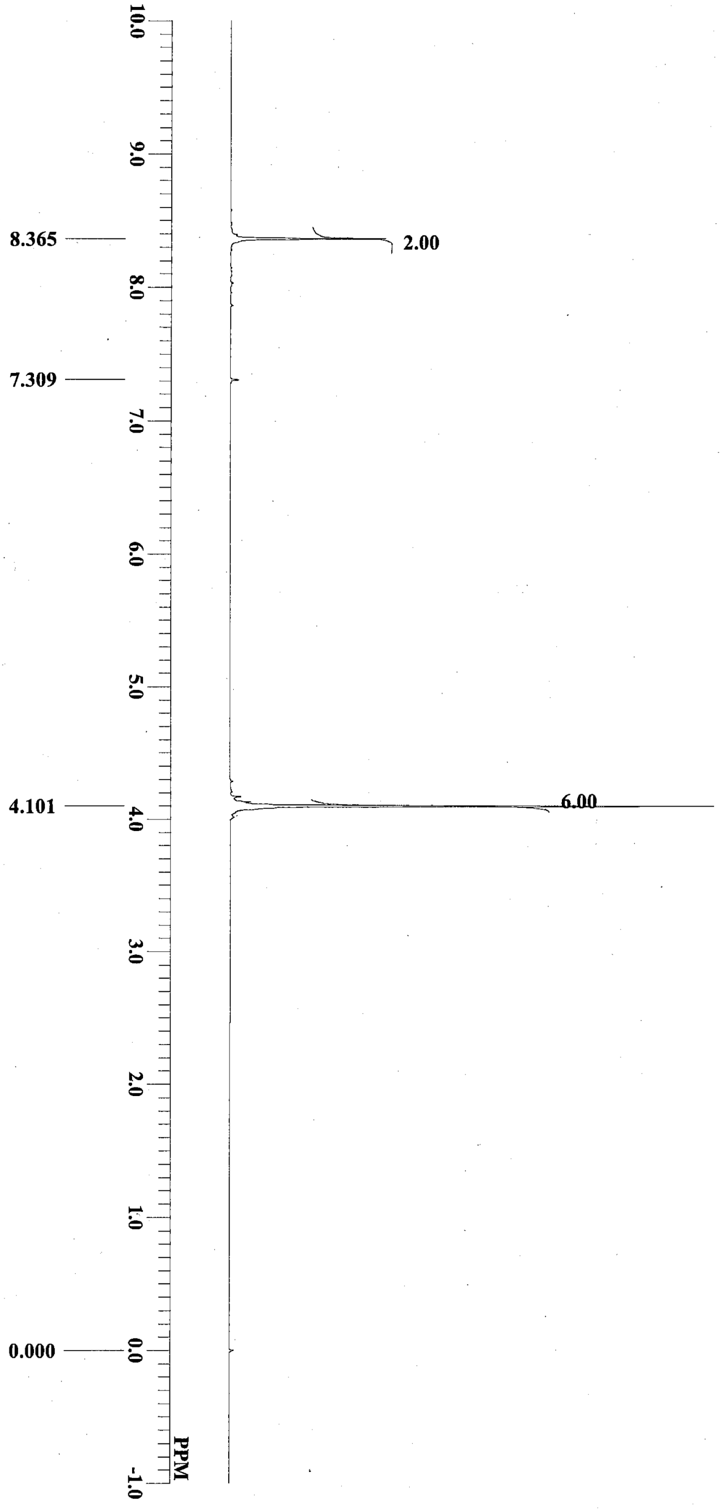
^{13}C NMR

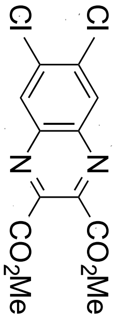

165.450
144.087
142.877
140.407
128.659
77.321
77.000
76.679
53.488
20.665
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


Cl
Cl
N
N
CO2Me
CO2Me

3l

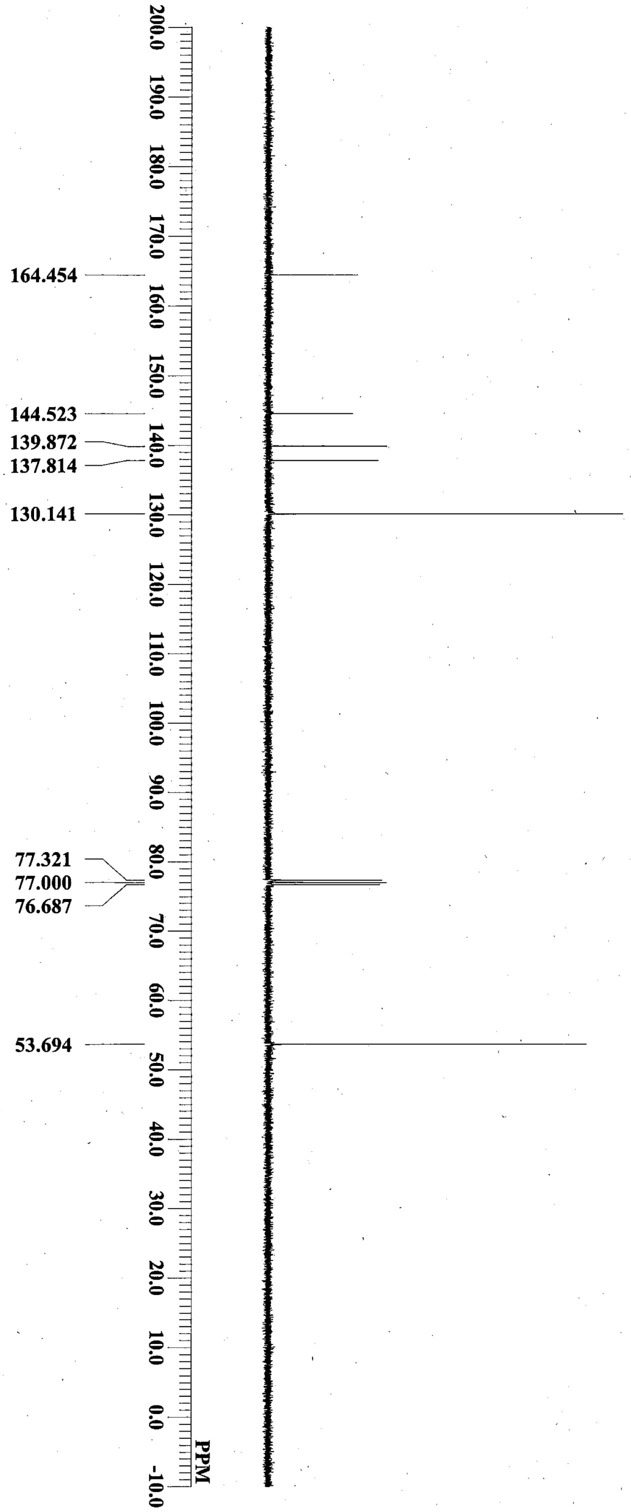
^{1}H NMR

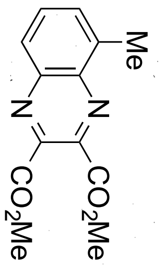

8.365
7.309
4.101
0.000
2.00
6.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


Cl
Cl
N
N
CO$_2$Me
CO$_2$Me

3l

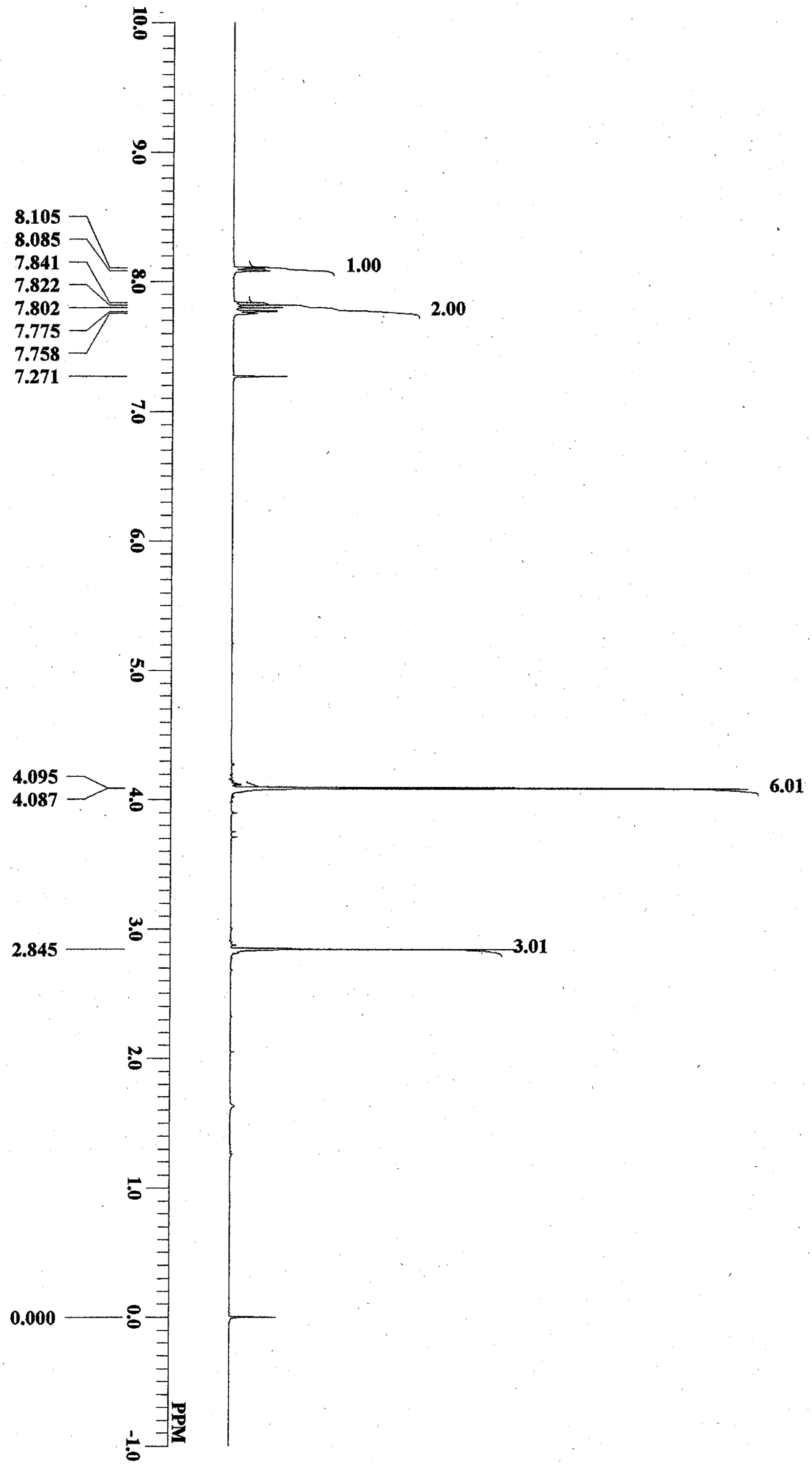
^{13}C NMR

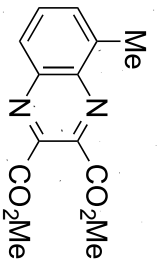

164.454
144.523
139.872
137.814
130.141
77.321
77.000
76.687
53.694
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


Me
N
N
CO2Me
CO2Me

3m

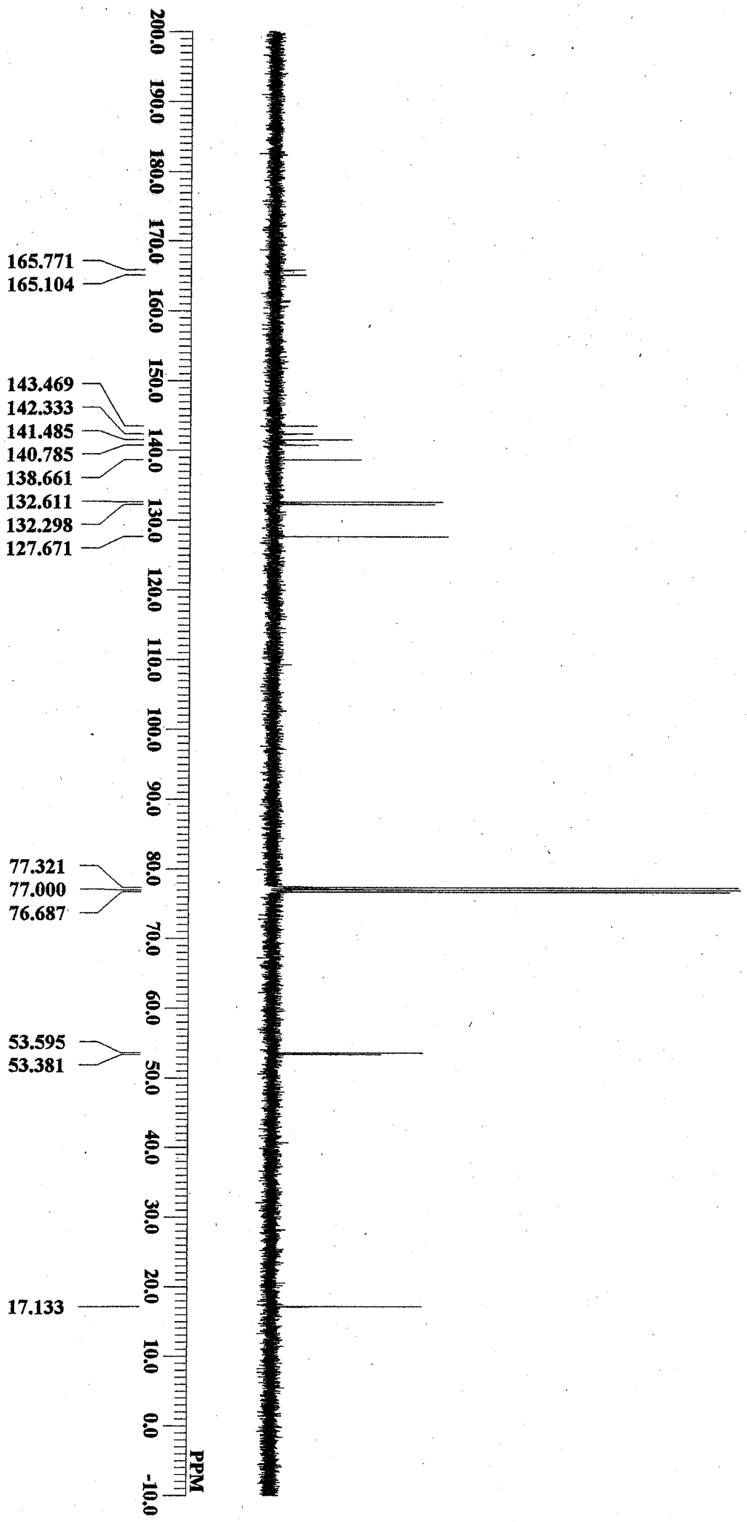
^{1}H NMR

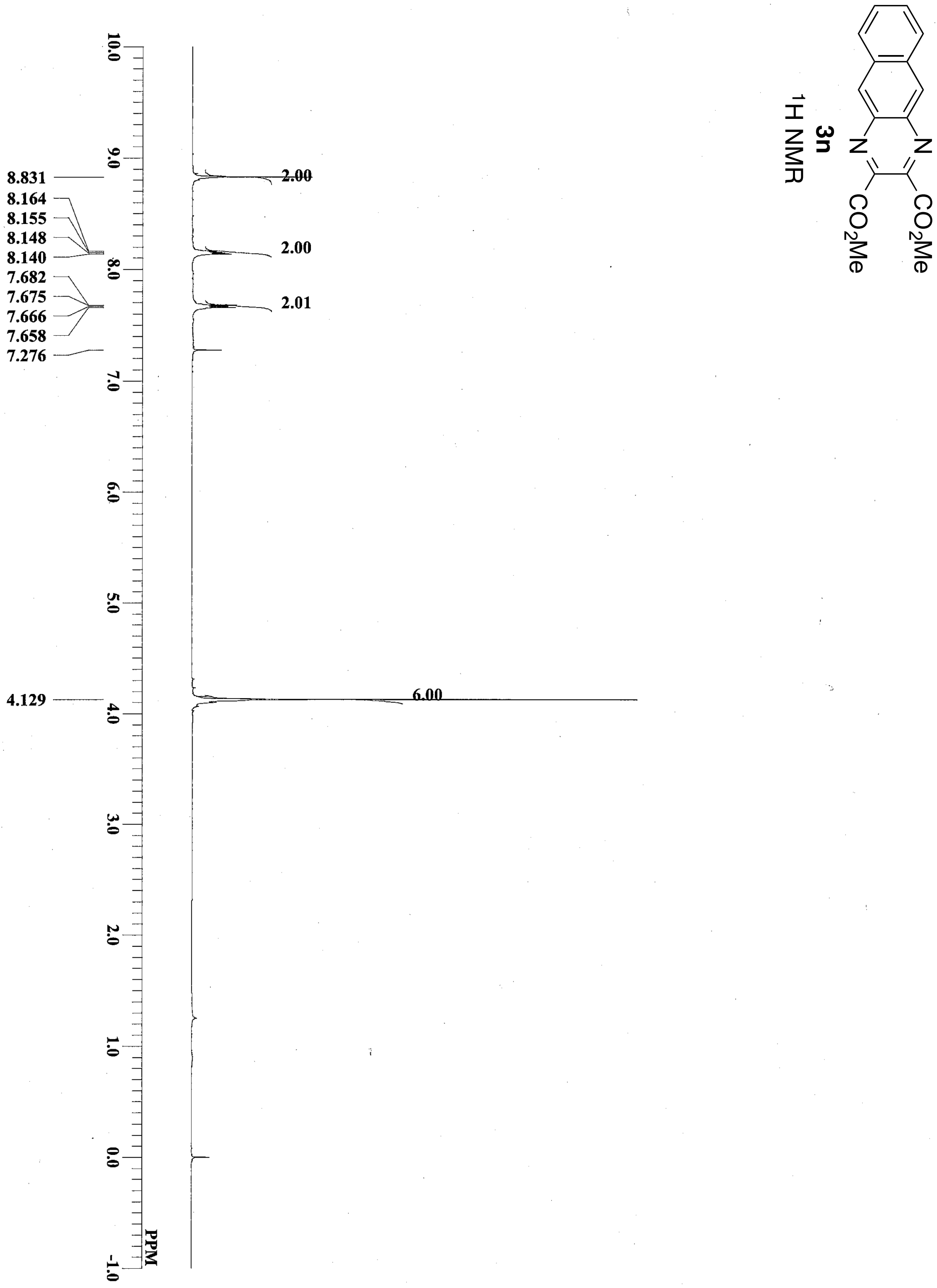

8.105
8.085
7.841
7.822
7.802
7.775
7.758
7.271
4.095
4.087
2.845
0.000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
1.00
2.00
6.01
3.01


Me
N
N
CO$_2$Me
CO$_2$Me

3m

^{13}C NMR

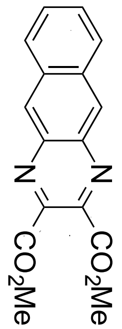

165.771
165.104
143.469
142.333
141.485
140.785
138.661
132.611
132.298
127.671
77.321
77.000
76.687
53.595
53.381
17.133
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM



3n

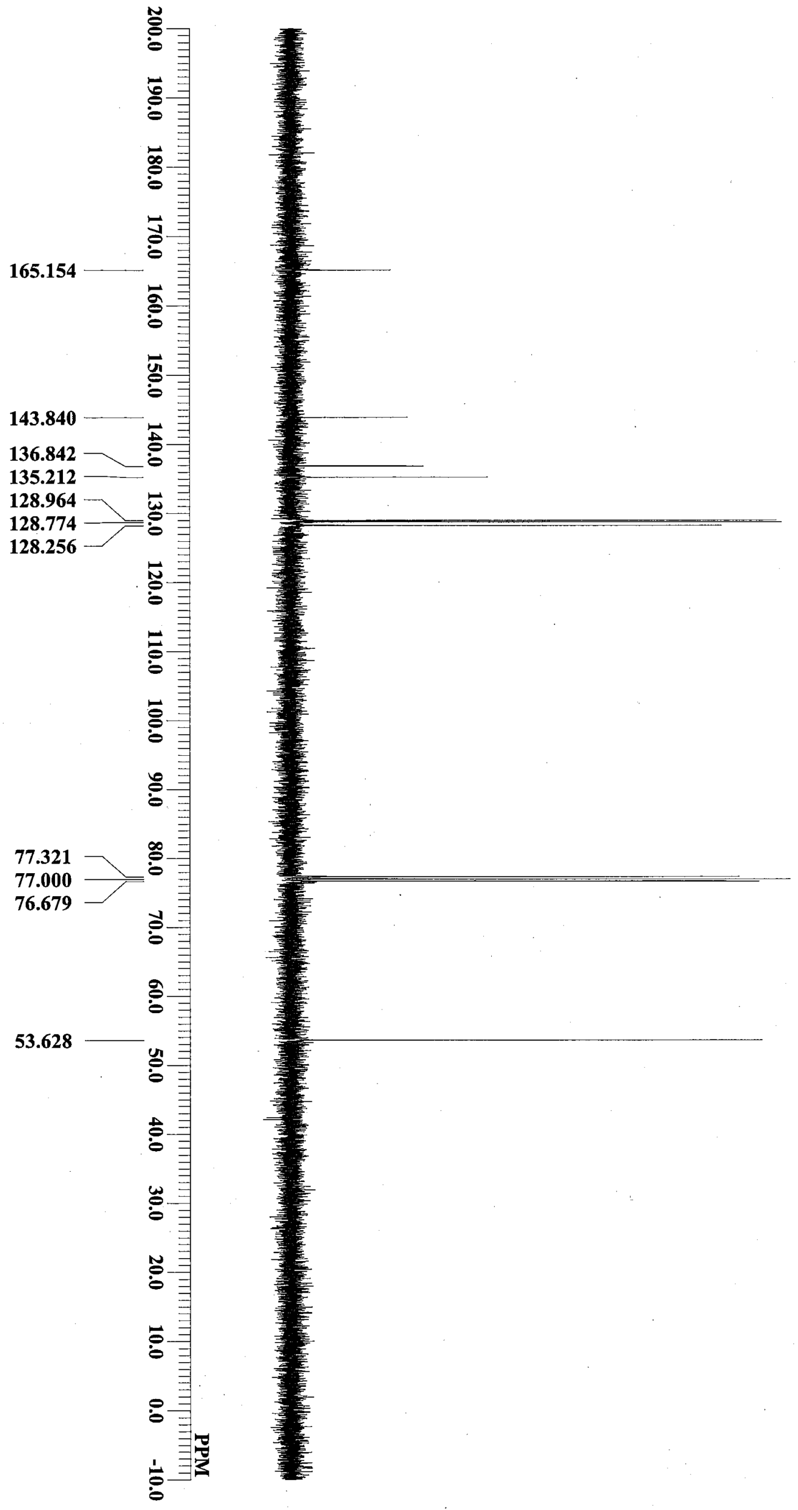
^{1}H NMR

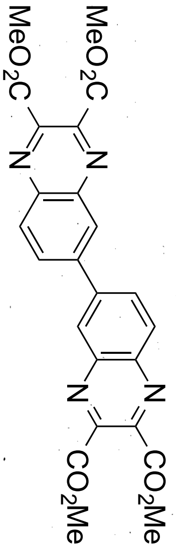
CO$_2$Me
CO$_2$Me
N
N
8.831
8.164
8.155
8.148
8.140
7.682
7.675
7.666
7.658
7.276
4.129
2.00
2.00
2.01
6.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


N
N
CO2Me
CO2Me

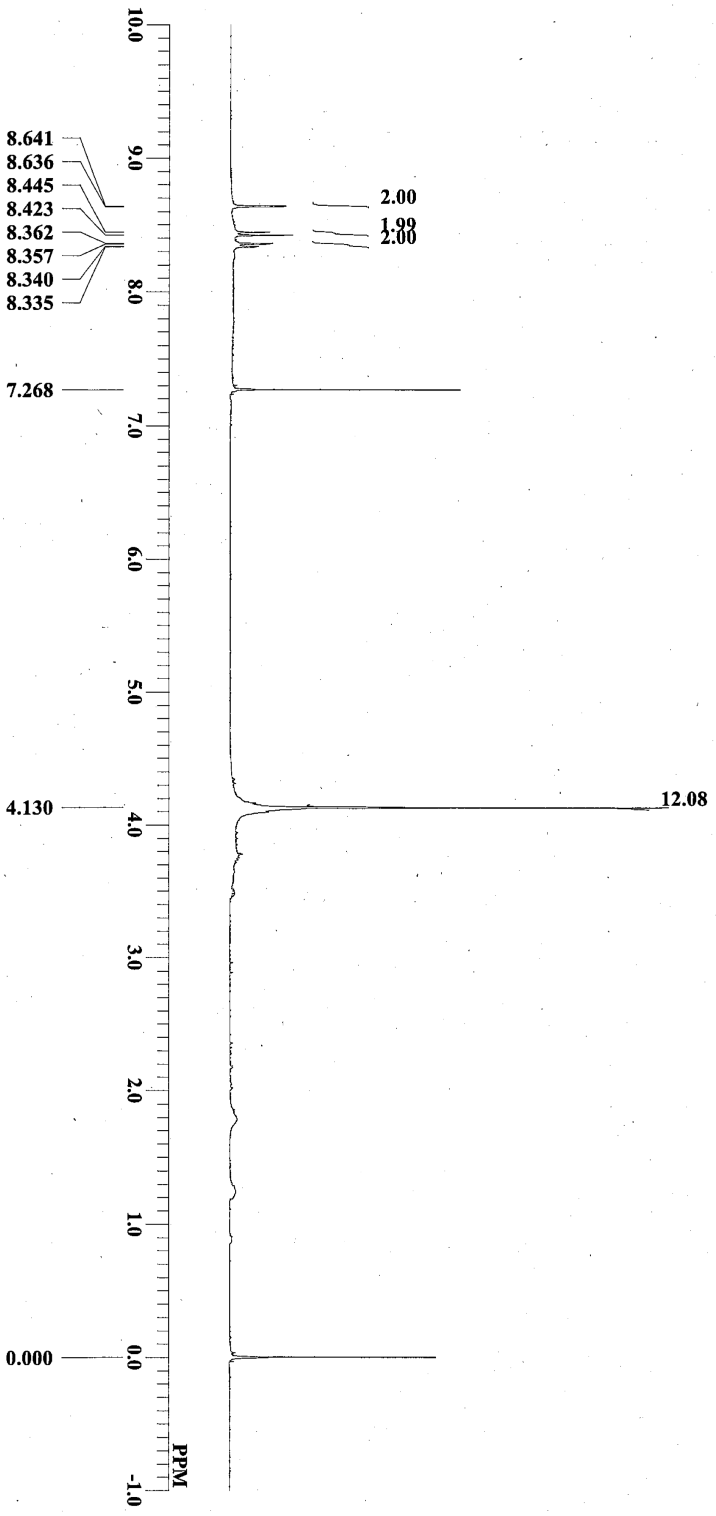
3n

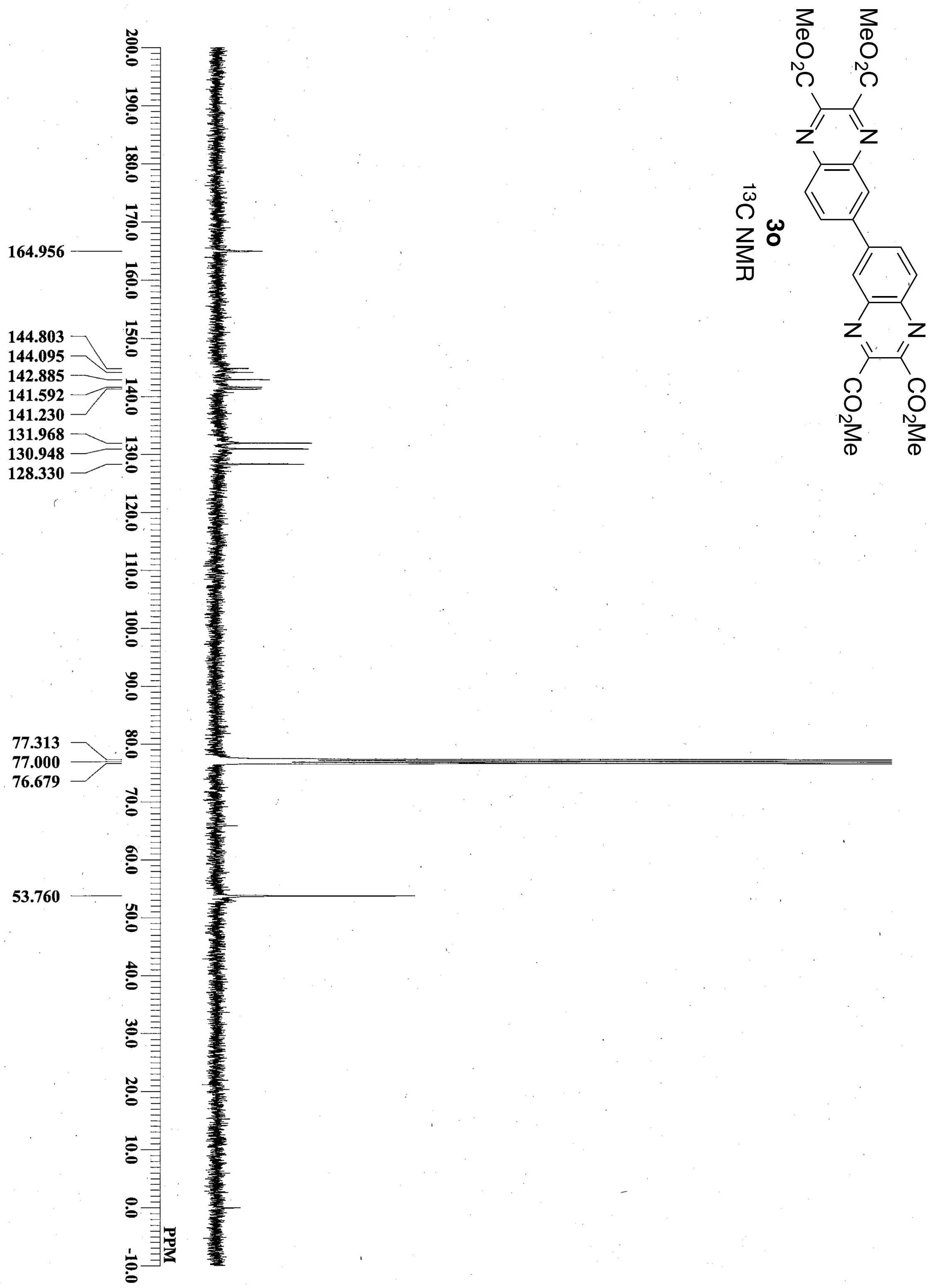
^{13}C NMR


165.154
143.840
136.842
135.212
128.964
128.774
128.256
77.321
77.000
76.679
53.628
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


MeO$_2$C
MeO$_2$C
N
N
N
N
CO$_2$Me
CO$_2$Me

3o
^{1}H NMR

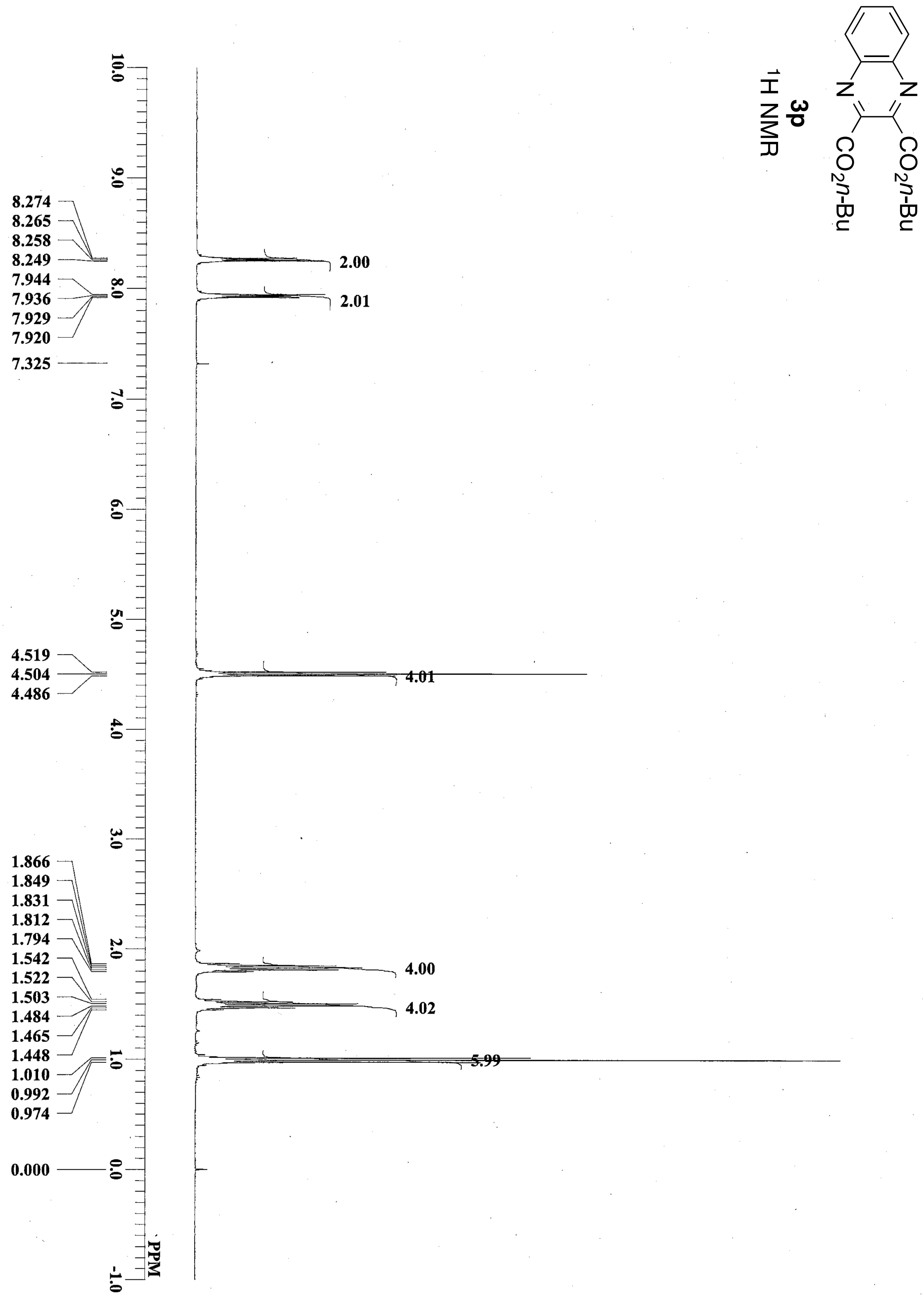

8.641
8.636
8.445
8.423
8.362
8.357
8.340
8.335
7.268
4.130
0.000
2.00
1.99
2.00
12.08
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM



3o

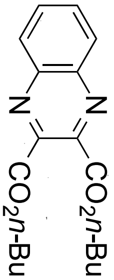
^{13}C NMR

164.956
144.803
144.095
142.885
141.592
141.230
131.968
130.948
128.330
77.313
77.000
76.679
53.760
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM
MeO2C
MeO2C
N
N
N
N
CO2Me
CO2Me



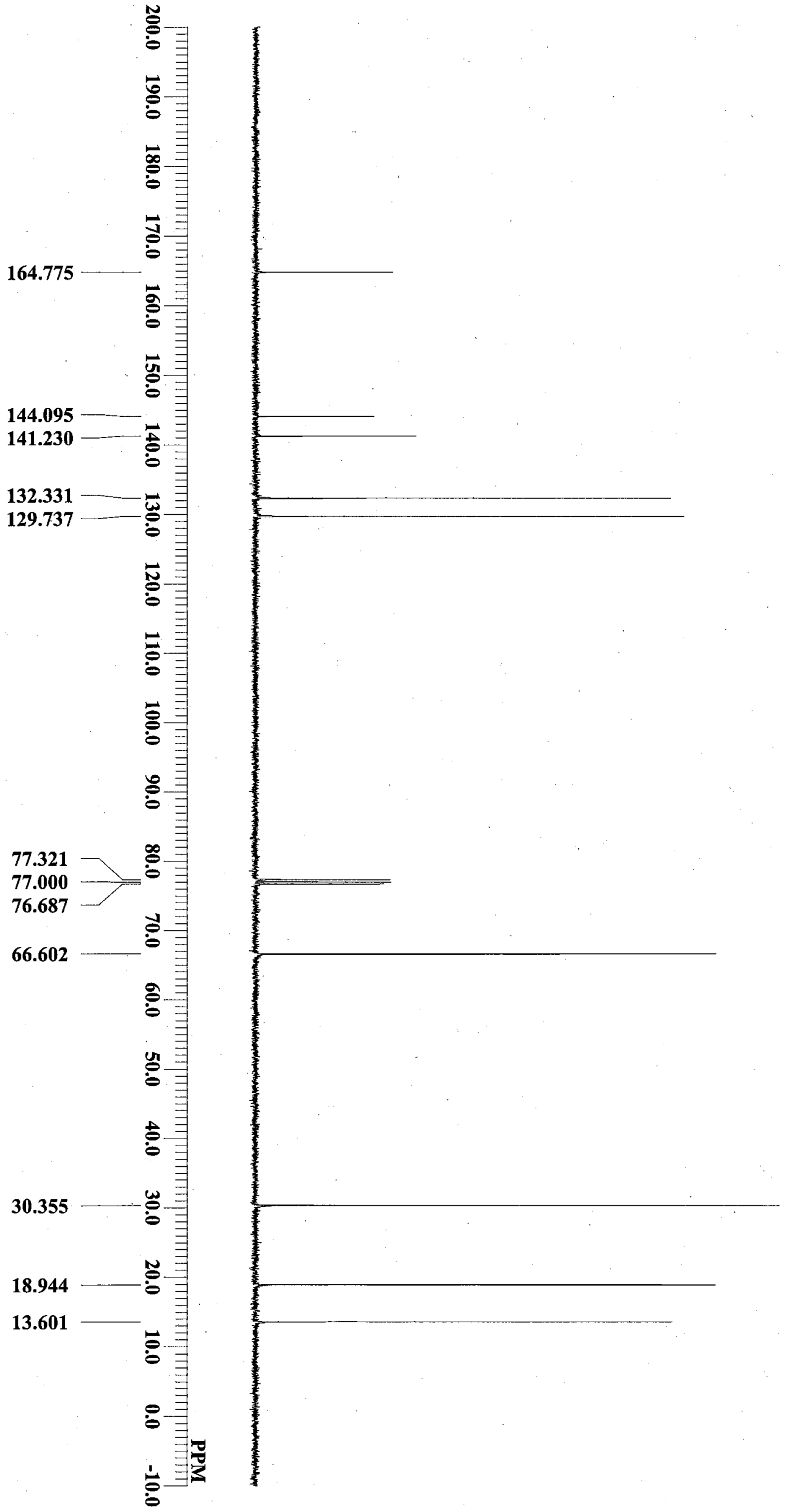
3p
^1H NMR

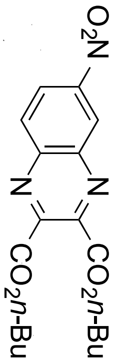
CO2n-Bu
CO2n-Bu
N
N
8.274
8.265
8.258
8.249
7.944
7.936
7.929
7.920
7.325
4.519
4.504
4.486
1.866
1.849
1.831
1.812
1.794
1.542
1.522
1.503
1.484
1.465
1.448
1.010
0.992
0.974
0.000
2.00
2.01
4.01
4.00
4.02
5.99
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


N
N
CO2n-Bu
CO2n-Bu

3p

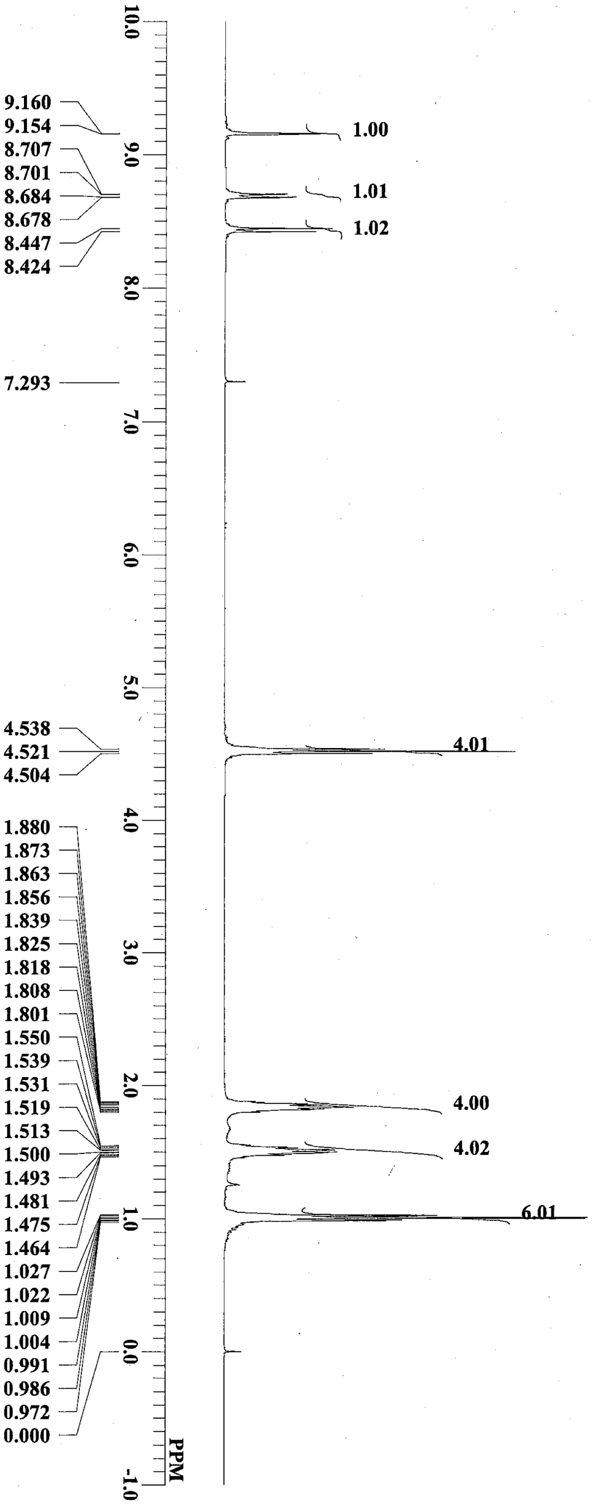
^{13}C NMR

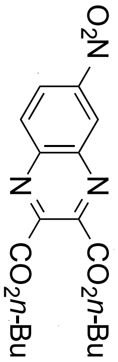

164.775
144.095
141.230
132.331
129.737
77.321
77.000
76.687
66.602
30.355
18.944
13.601
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


O2N
N
N
CO2n-Bu
CO2n-Bu

3q

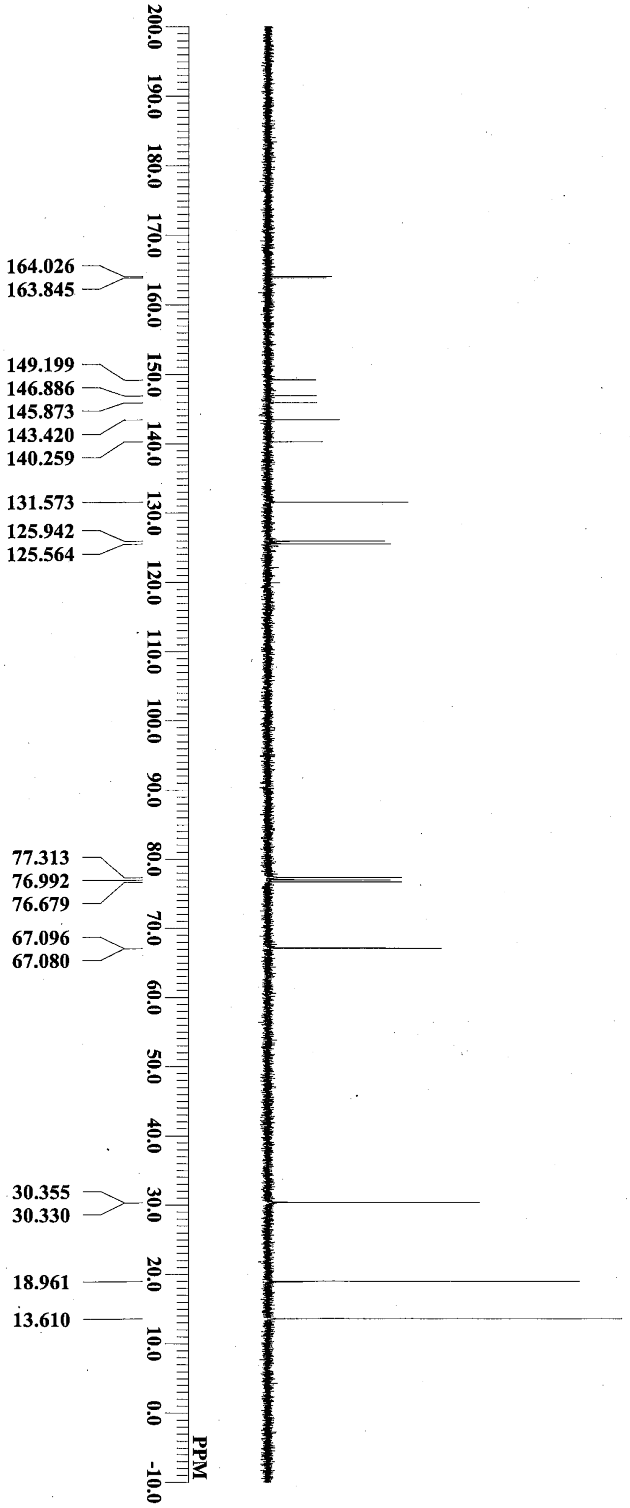
^{1}H NMR

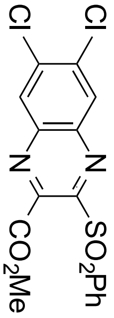

9.160
9.154
8.707
8.701
8.684
8.678
8.447
8.424
7.293
4.538
4.521
4.504
1.880
1.873
1.863
1.856
1.839
1.825
1.818
1.808
1.801
1.550
1.539
1.531
1.519
1.513
1.500
1.493
1.481
1.475
1.464
1.027
1.022
1.009
1.004
0.991
0.986
0.972
0.000
1.00
1.01
1.02
4.01
4.00
4.02
6.01
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


O$_2$N
N
N
CO$_2$n-Bu
CO$_2$n-Bu

3q

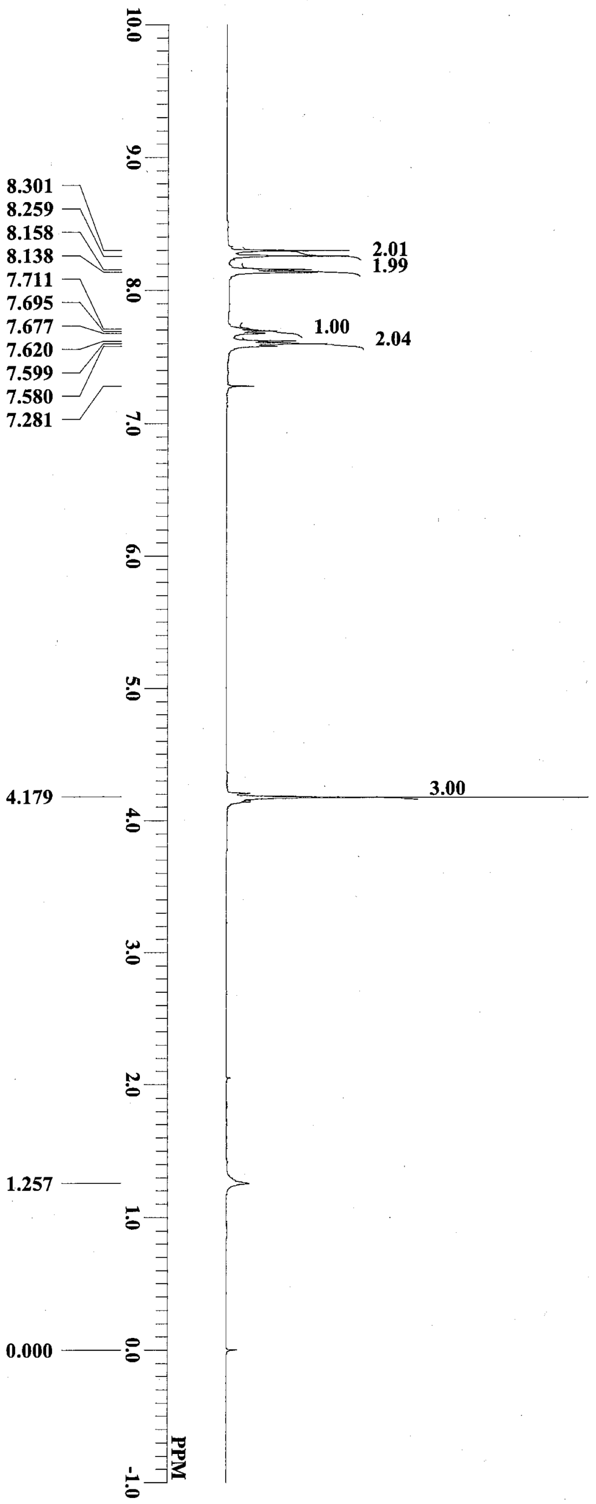
^{13}C NMR

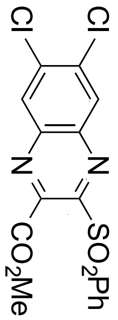

164.026
163.845
149.199
146.886
145.873
143.420
140.259
131.573
125.942
125.564
77.313
76.992
76.679
67.096
67.080
30.355
30.330
18.961
13.610
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


Cl
Cl
N
N
SO2Ph
CO2Me

3r

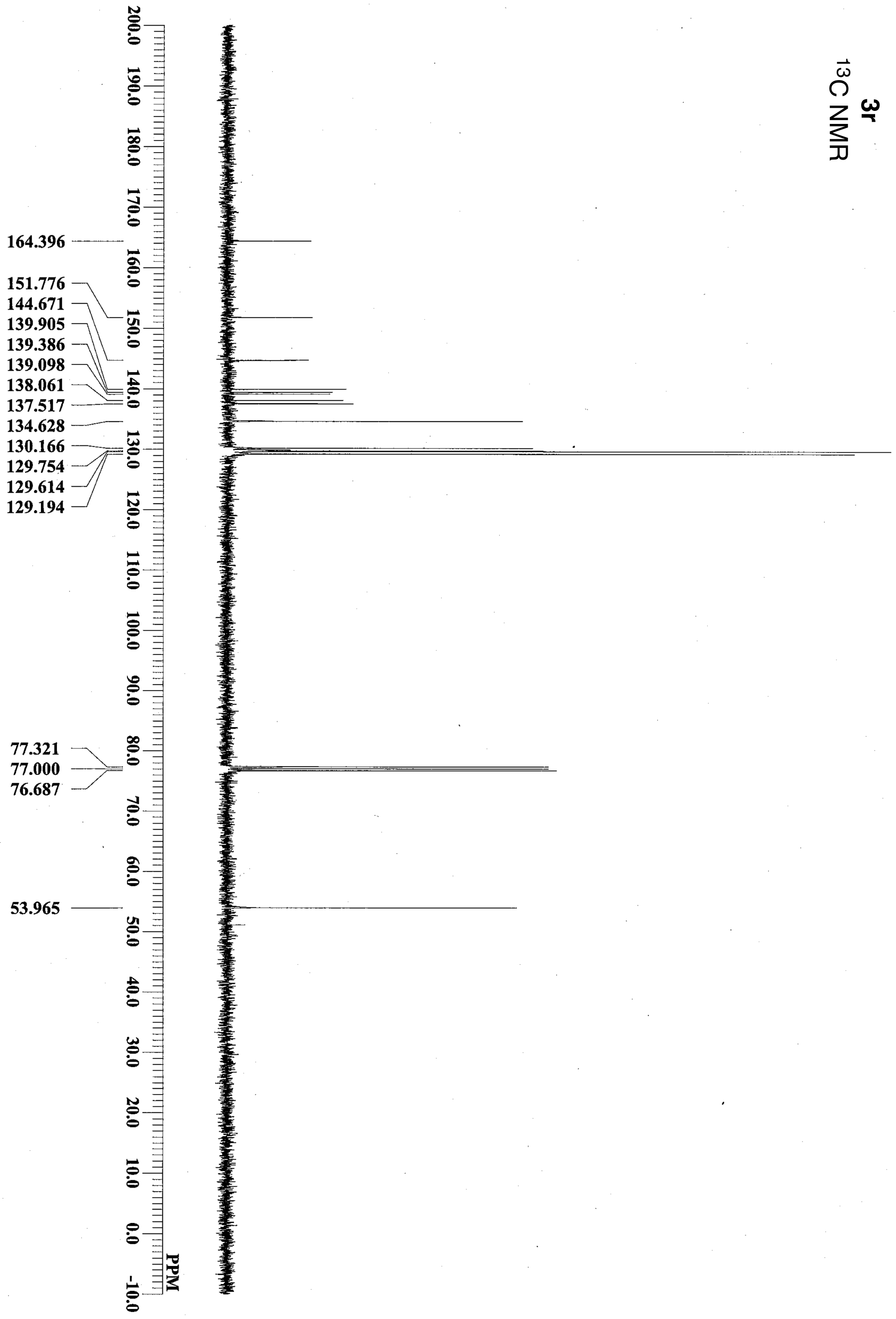
^{1}H NMR

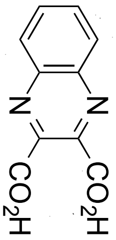

8.301
8.259
8.158
8.138
7.711
7.695
7.677
7.620
7.599
7.580
7.281
4.179
1.257
0.000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
2.01
1.99
1.00
2.04
3.00


Cl
Cl
N
N
SO2Ph
CO2Me

3r

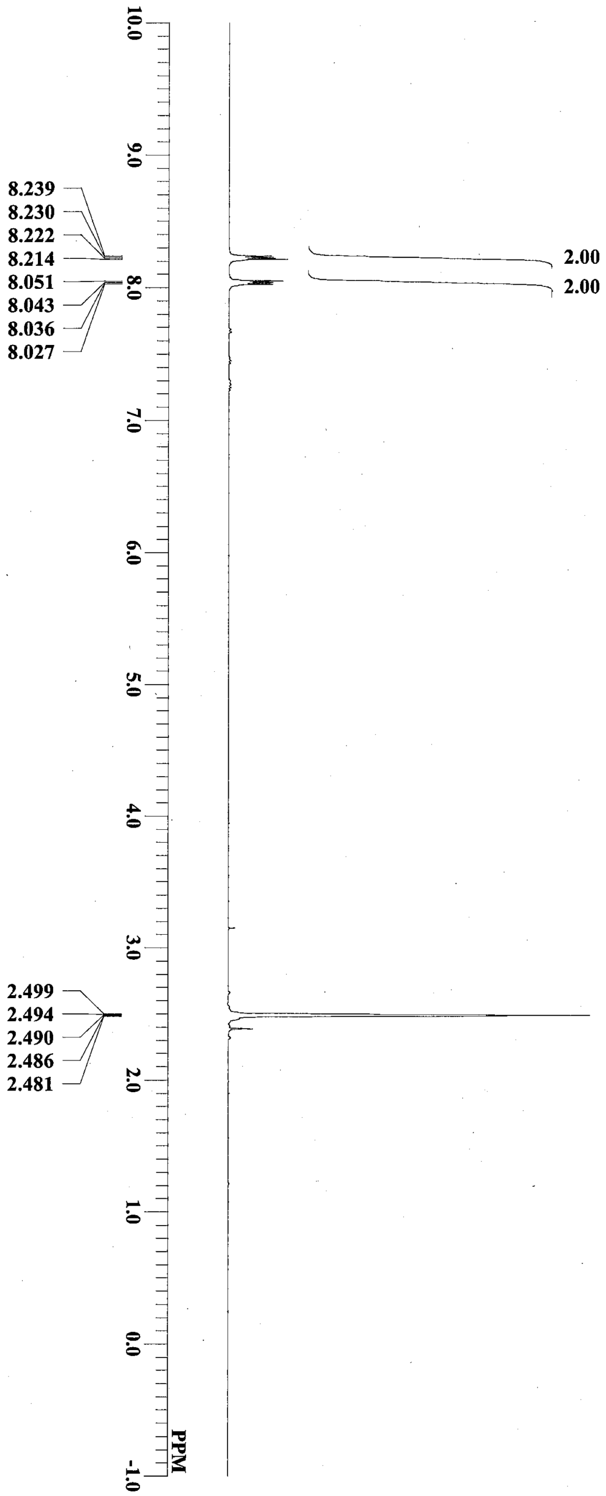
^{13}C NMR

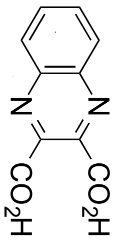

164.396
151.776
144.671
139.905
139.386
139.098
138.061
137.517
134.628
130.166
129.754
129.614
129.194
77.321
77.000
76.687
53.965
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM



6

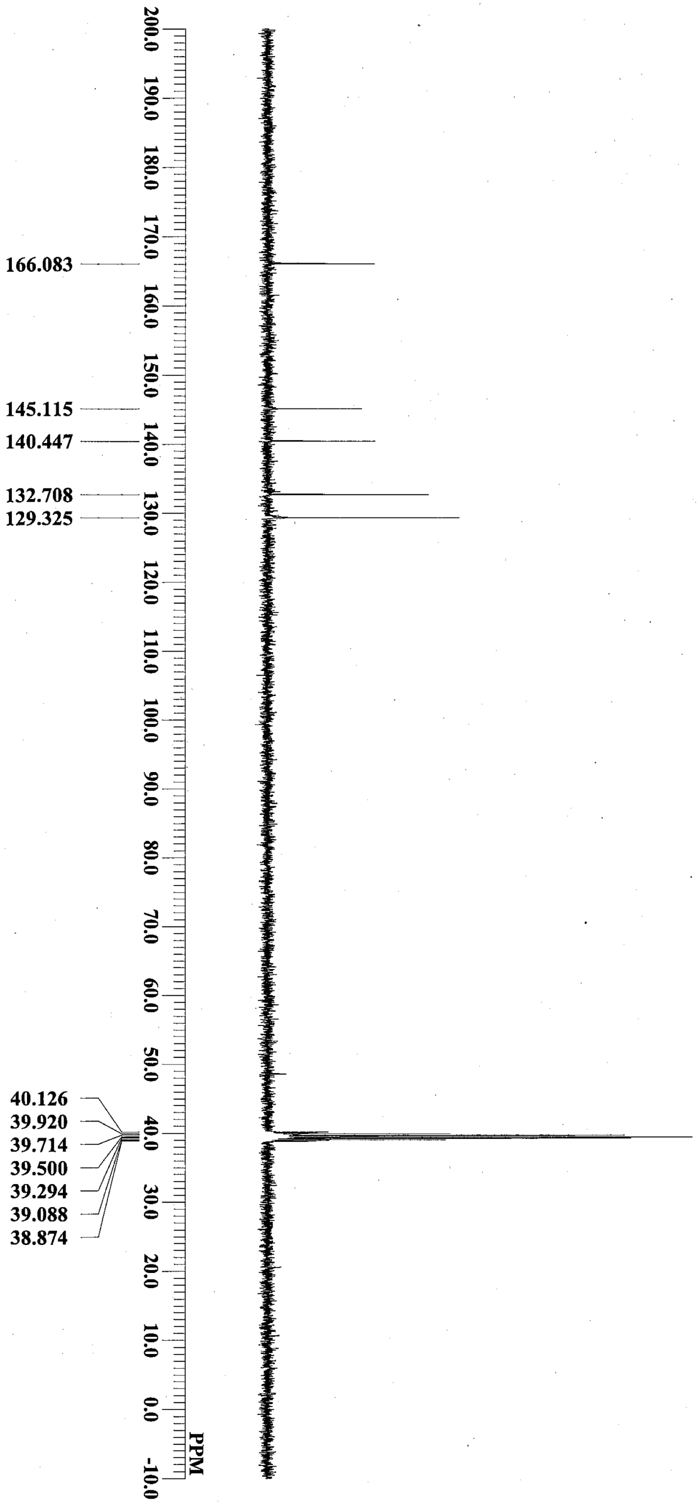
^1H NMR

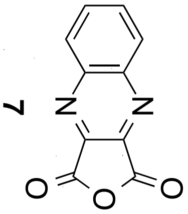

8.239
8.230
8.222
8.214
8.051
8.043
8.036
8.027
2.499
2.494
2.490
2.486
2.481
2.00
2.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


N
N
CO2H
CO2H

6

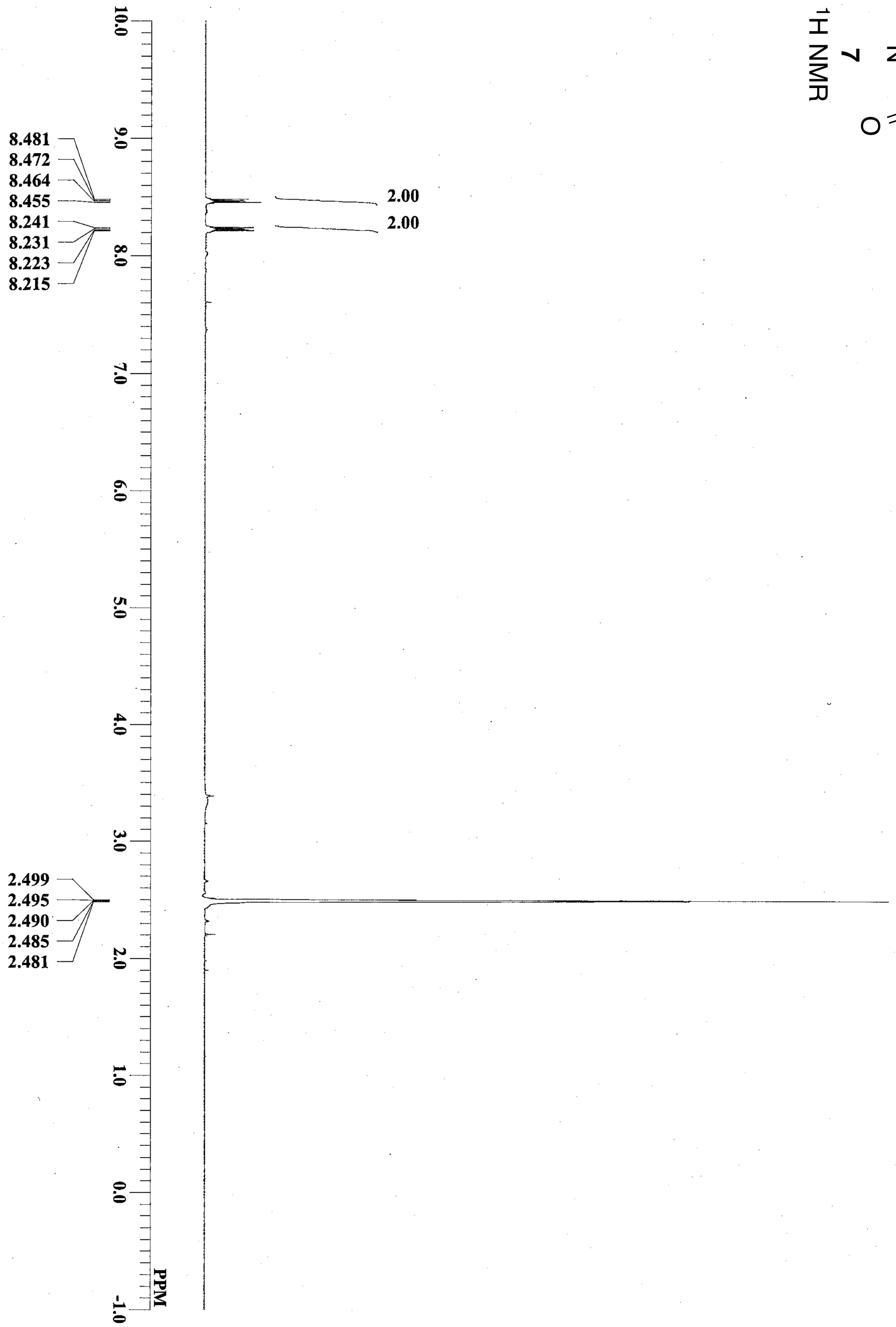
^{13}C NMR

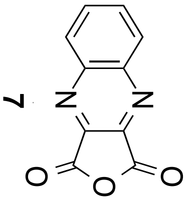

166.083
145.115
140.447
132.708
129.325
40.126
39.920
39.714
39.500
39.294
39.088
38.874
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM



7

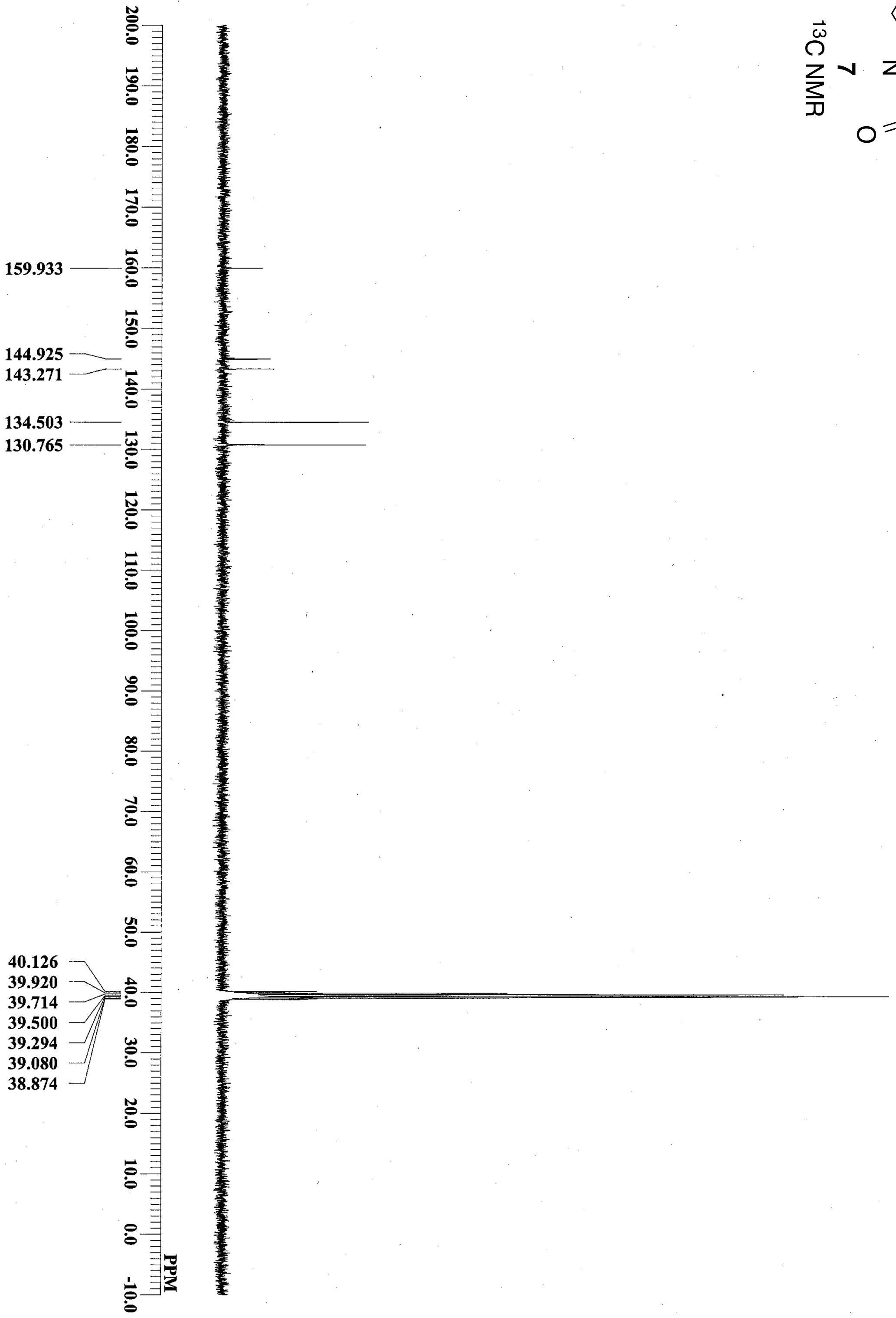
^{1}H NMR

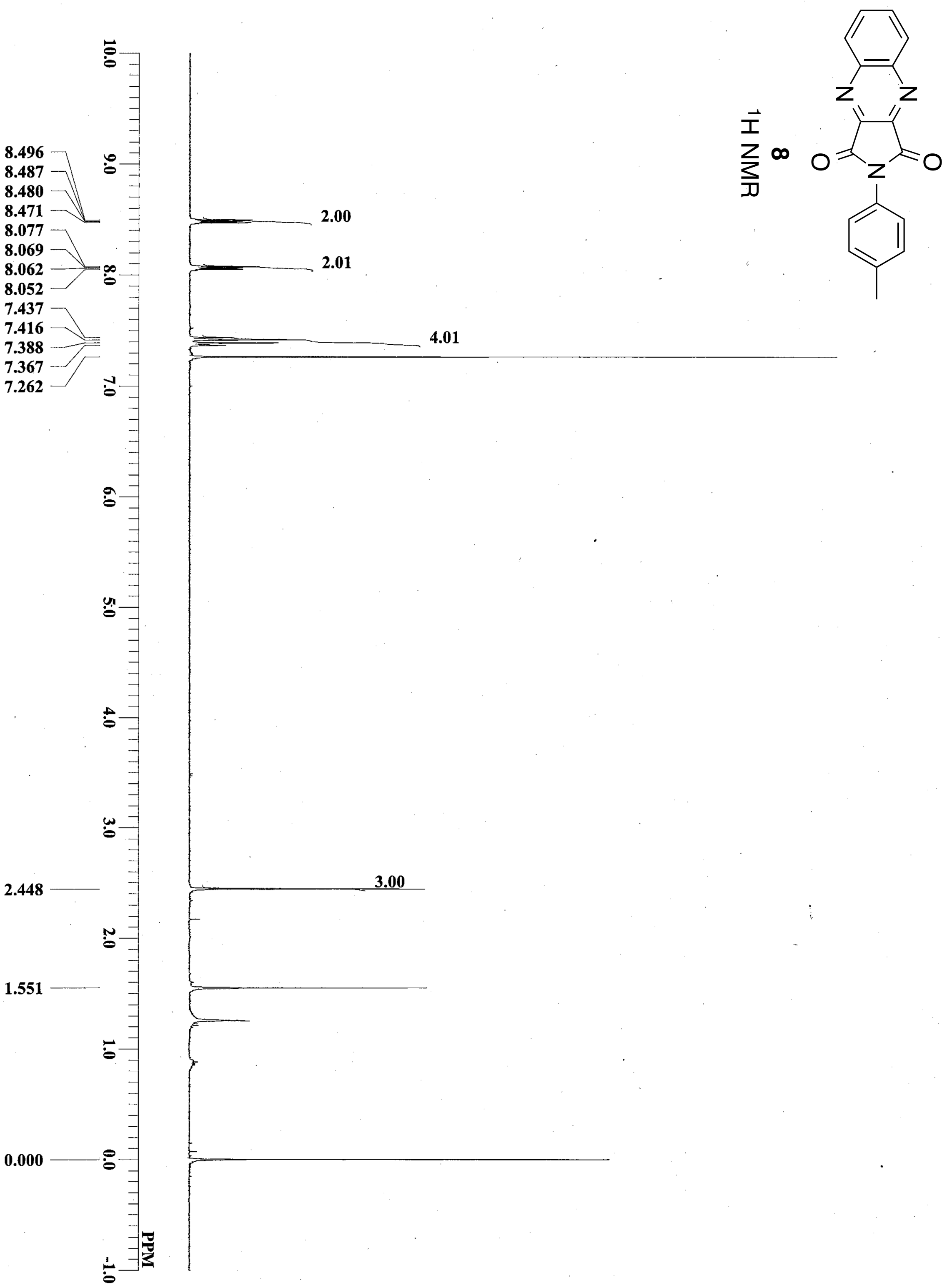

8.481
8.472
8.464
8.455
8.241
8.231
8.223
8.215
2.499
2.495
2.490
2.485
2.481
2.00
2.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM


N
N
O
O
O

7

^{13}C NMR

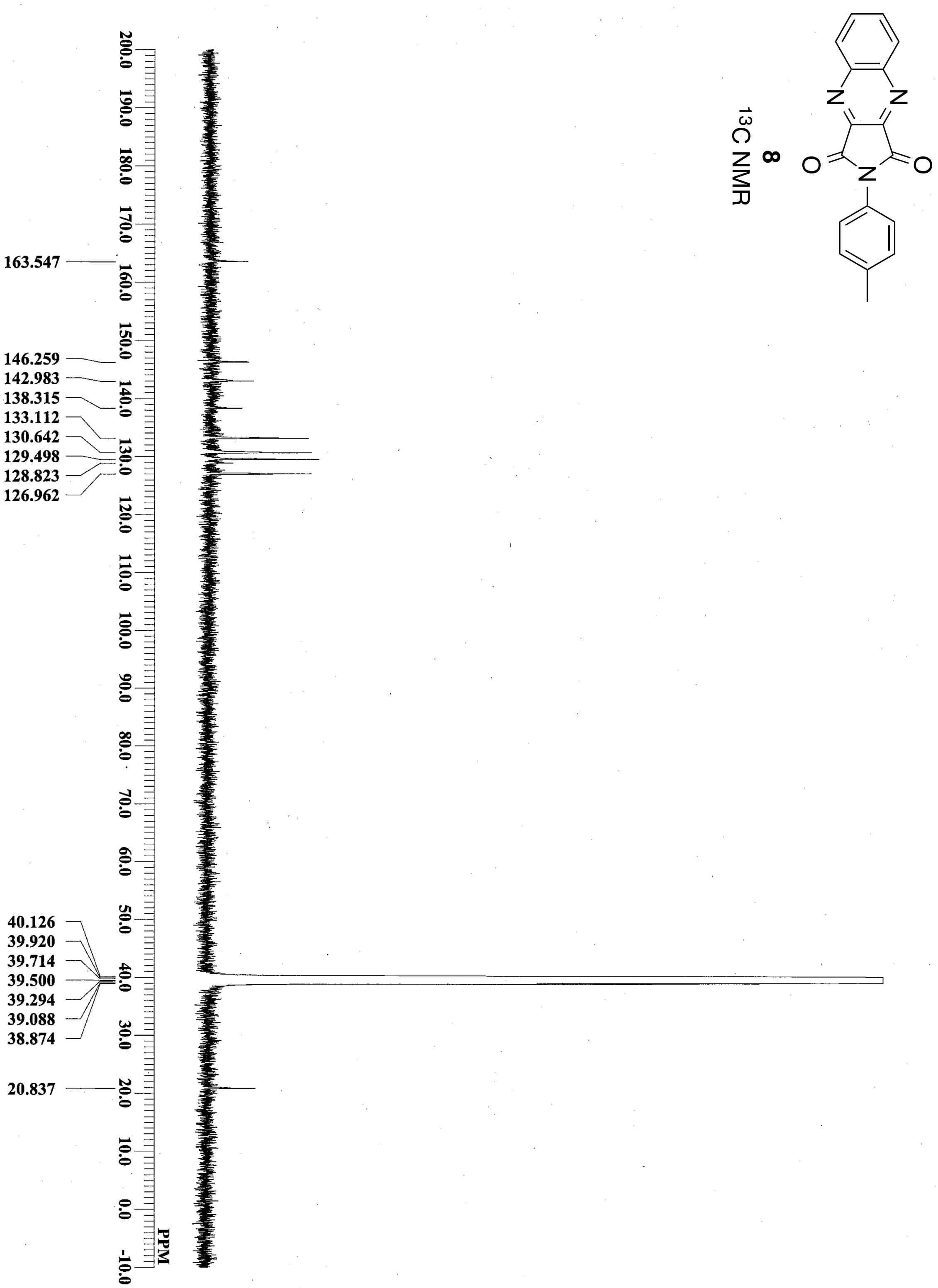

159.933
144.925
143.271
134.503
130.765
40.126
39.920
39.714
39.500
39.294
39.080
38.874
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM



8

^{1}H NMR

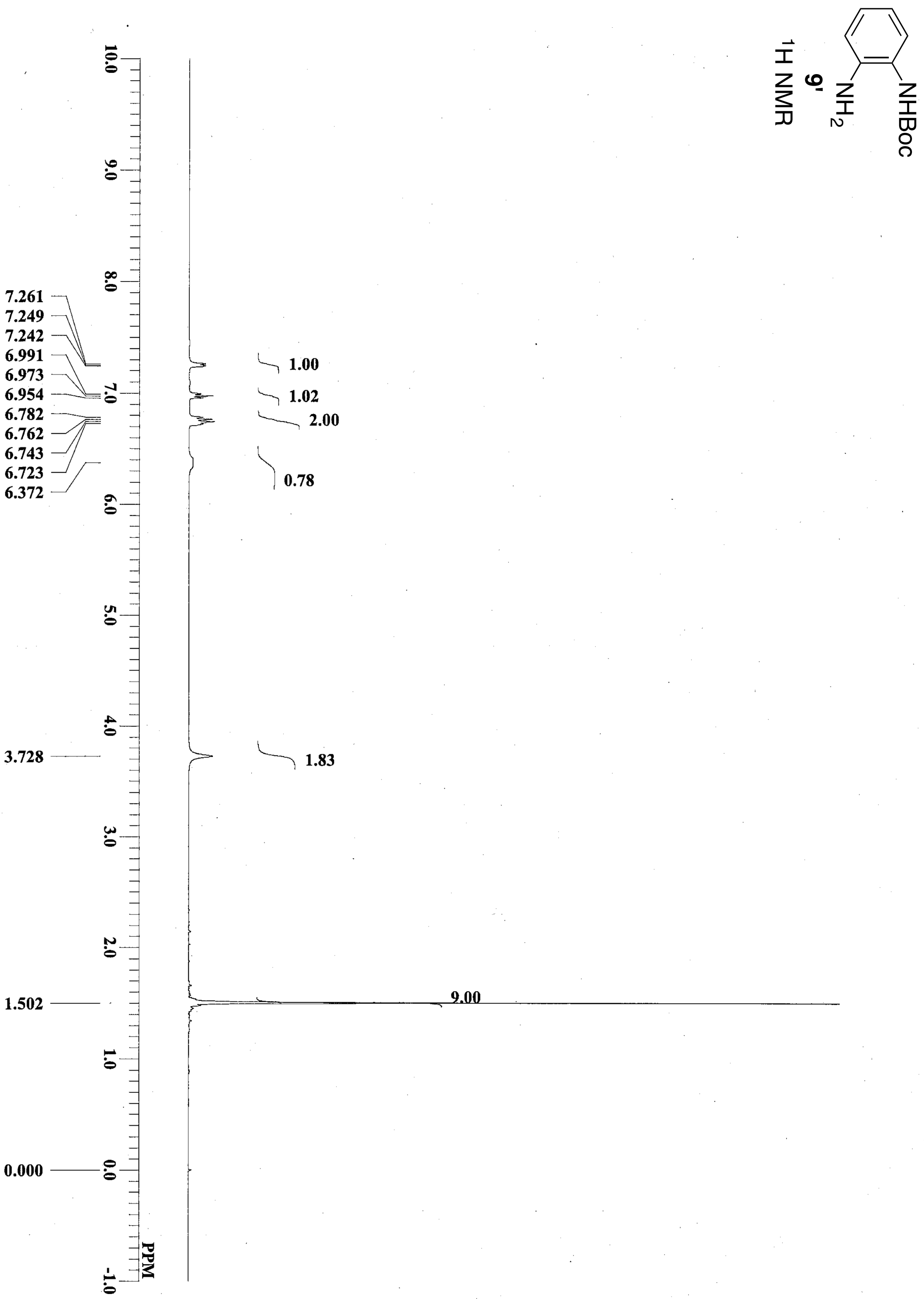
8.496
8.487
8.480
8.471
8.077
8.069
8.062
8.052
7.437
7.416
7.388
7.367
7.262
2.448
1.551
0.000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
2.00
2.01
4.01
3.00
N
N
O
O
N

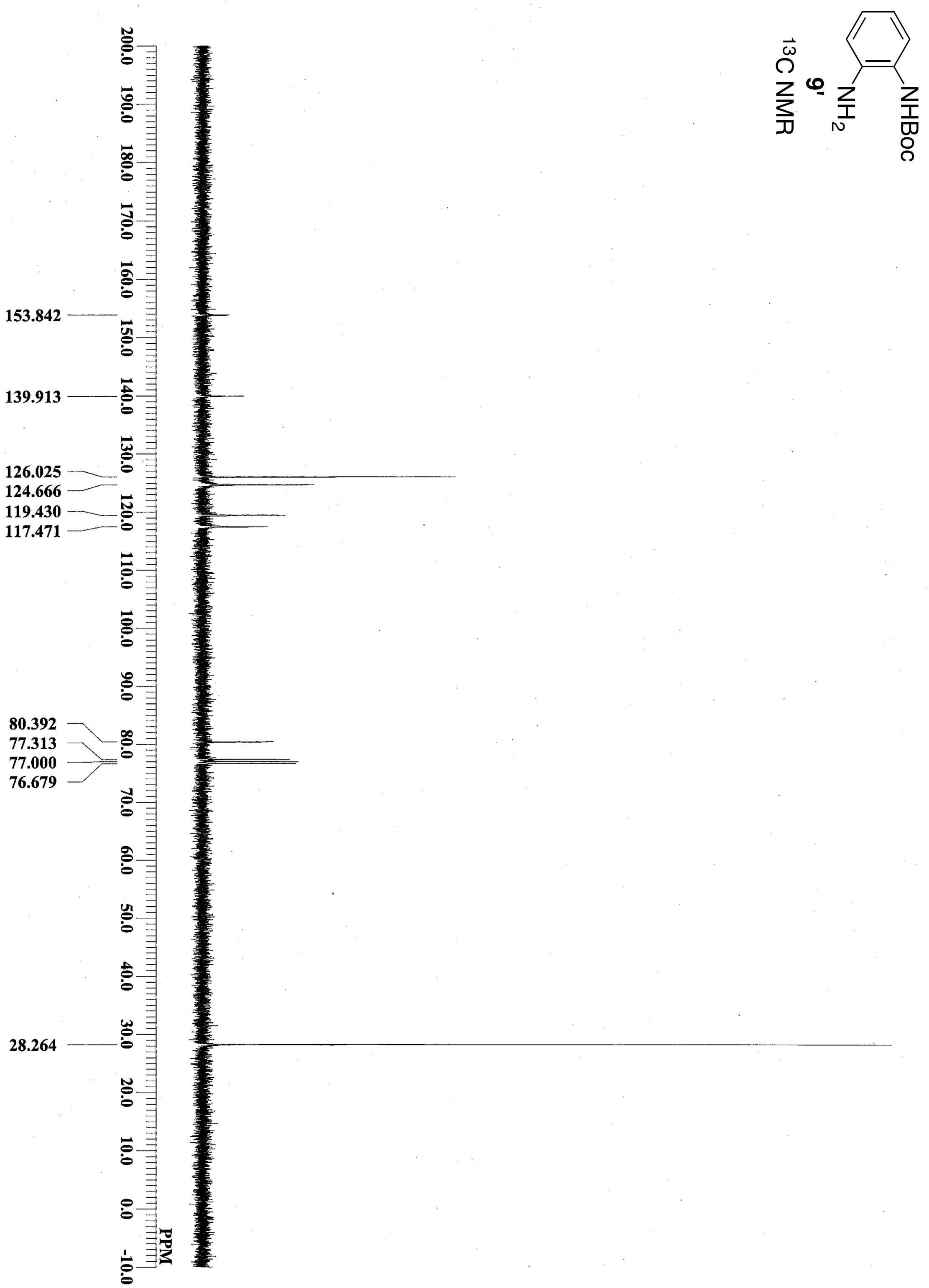

N
N
O
N
O

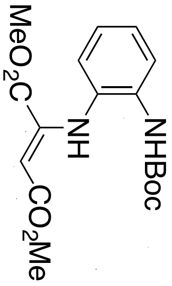
8

^{13}C NMR

163.547
146.259
142.983
138.315
133.112
130.642
129.498
128.823
126.962
40.126
39.920
39.714
39.500
39.294
39.088
38.874
20.837
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM

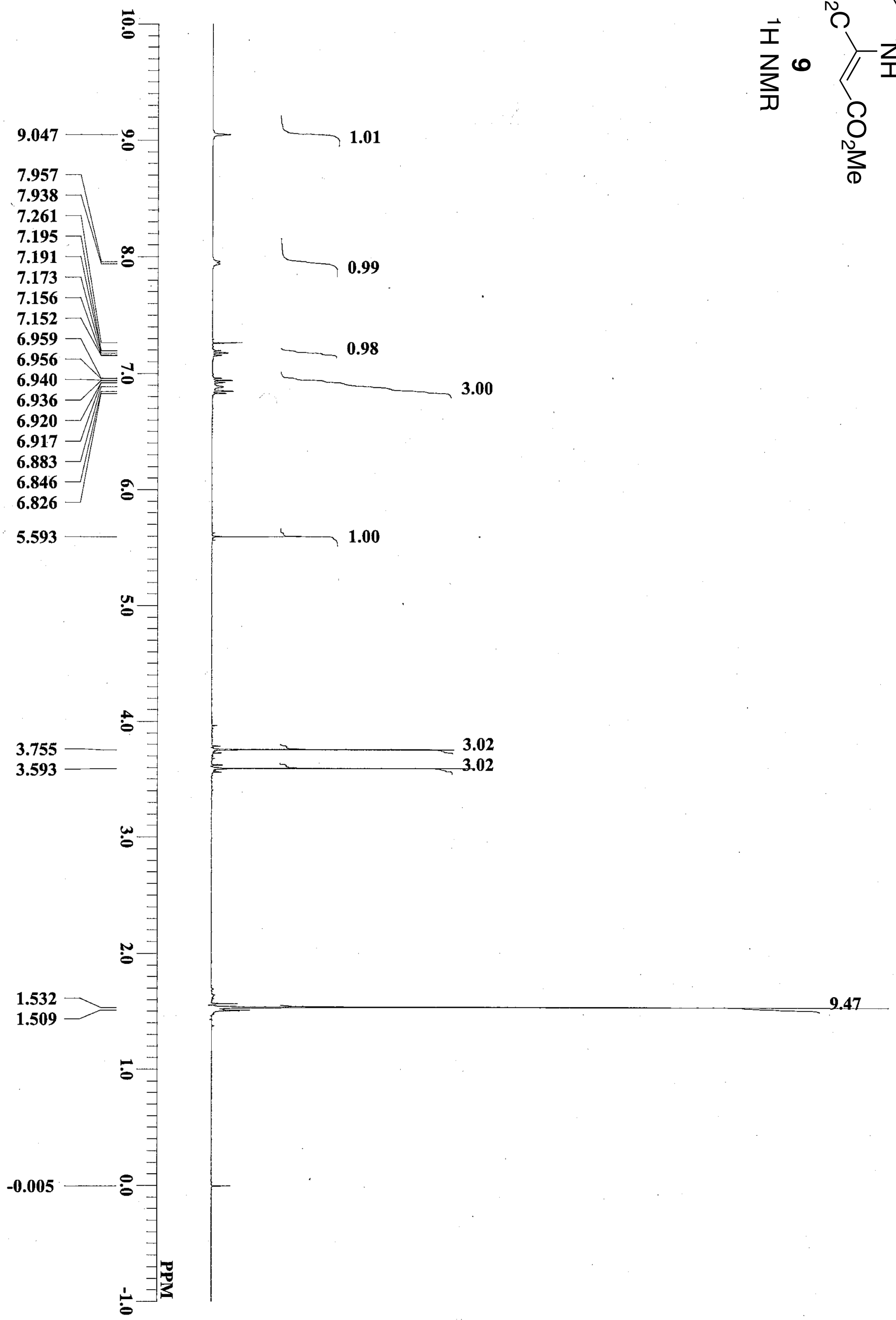

NHBoc
NH_2
9'
^1H NMR
7.261
7.249
7.242
6.991
6.973
6.954
6.782
6.762
6.743
6.723
6.372
3.728
1.502
0.000
1.00
1.02
2.00
0.78
1.83
9.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM

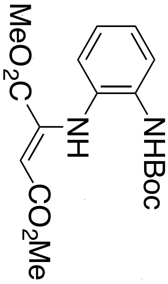

NHBoc
NH_2
9'
^{13}C NMR
153.842
139.913
126.025
124.666
119.430
117.471
80.392
77.313
77.000
76.679
28.264
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM


NHBoc
NH
MeO2C
CO2Me

9

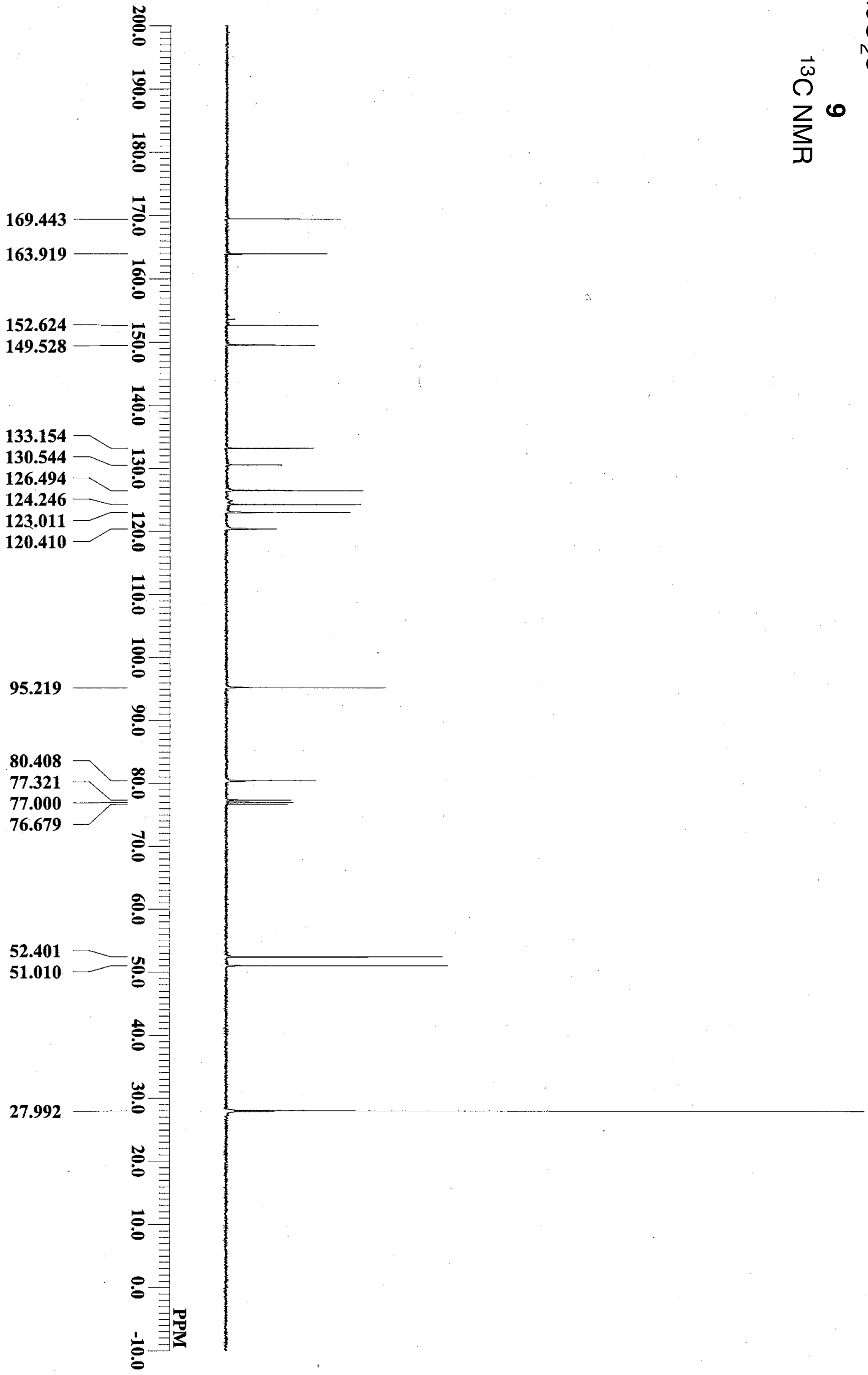
^{1}H NMR

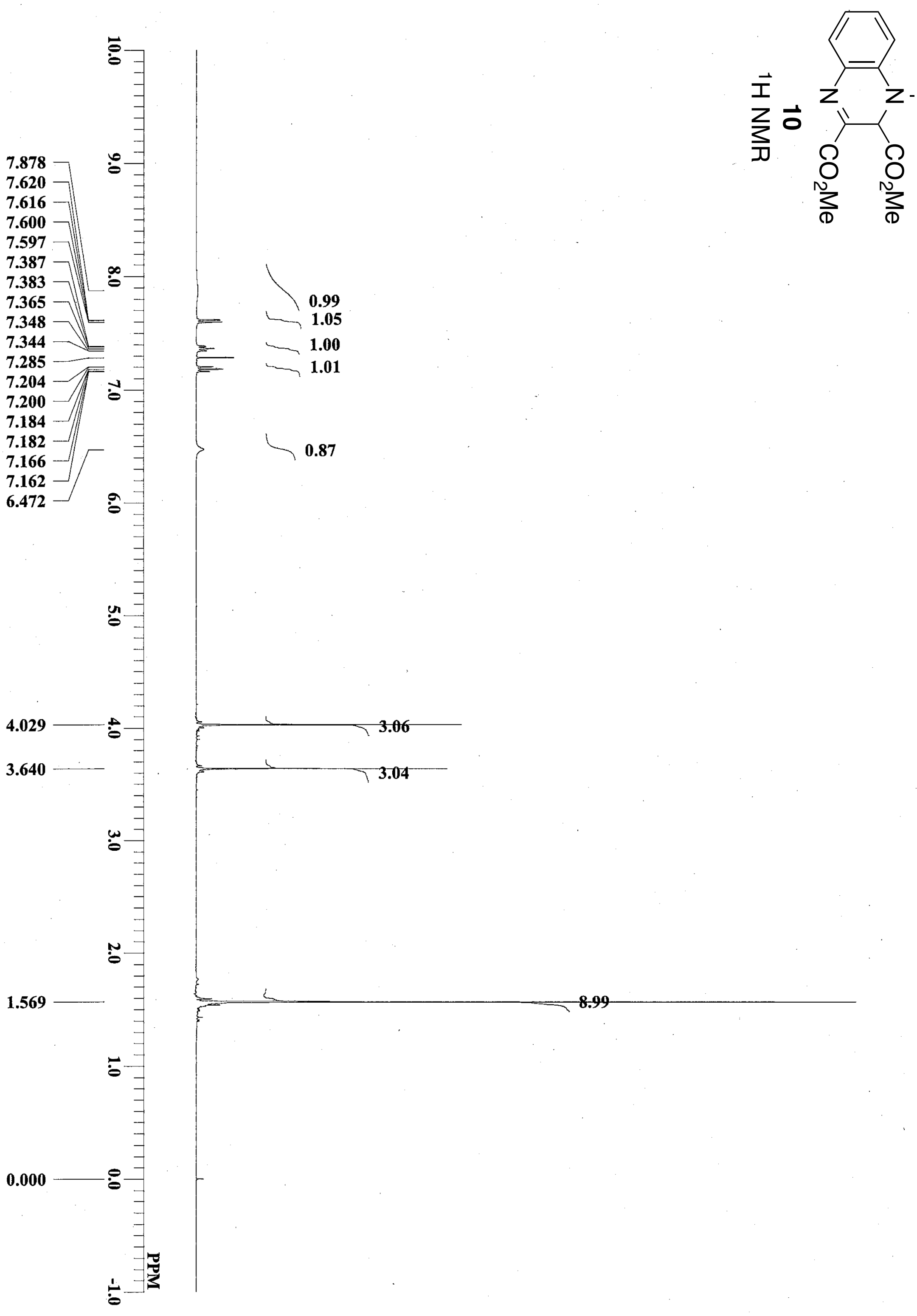

9.047
7.957
7.938
7.261
7.195
7.191
7.173
7.156
7.152
6.959
6.956
6.940
6.936
6.920
6.917
6.883
6.846
6.826
5.593
3.755
3.593
1.532
1.509
-0.005
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
1.01
0.99
0.98
3.00
1.00
3.02
3.02
9.47


NHBoc
NH
MeO$_2$C
CO$_2$Me

9

^{13}C NMR

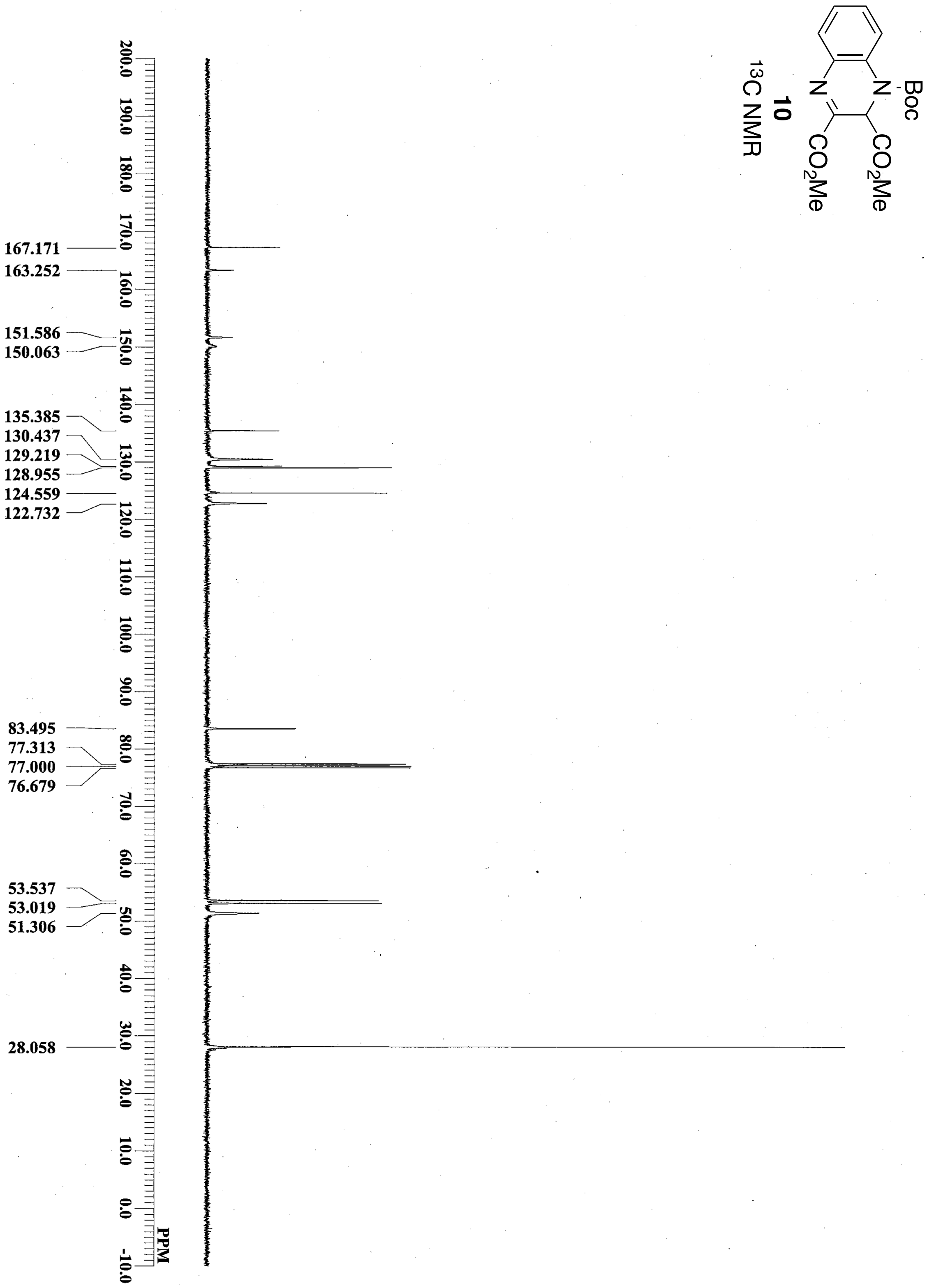

169.443
163.919
152.624
149.528
133.154
130.544
126.494
124.246
123.011
120.410
95.219
80.408
77.321
77.000
76.679
52.401
51.010
27.992
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM



10

^{1}H NMR

Boc
N
N
CO$_2$Me
CO$_2$Me
7.878
7.620
7.616
7.600
7.597
7.387
7.383
7.365
7.348
7.344
7.285
7.204
7.200
7.184
7.182
7.166
7.162
6.472
4.029
3.640
1.569
0.000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
PPM
0.99
1.05
1.00
1.01
0.87
3.06
3.04
8.99


Boc
N
N
CO2Me
CO2Me
10
13C NMR
167.171
163.252
151.586
150.063
135.385
130.437
129.219
128.955
124.559
122.732
83.495
77.313
77.000
76.679
53.537
53.019
51.306
28.058
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
PPM

References

S1 Sultan, N.; Thomas, C.; Blanco, L.; Deloisy, S.; *Tetrahedron Lett*. **2011**, *52*, 3443.

S2 Sobhani, S.; Aryanejad, S.; Maleki, M. F. *Synlett* **2011**, 319.

S3 Trost, B. M.; Massiot, G. S. *J. Am*. *Chem*. *Soc*. **1977**, *99*, 4405.

S4 Chandanshive, J. Z.; Bonini, B. F.; Gentili, D.; Fochi, M.; Bernardi, L.; Franchini, M. C. *Eur*. *J*. *Org*. *Chem*. **2010**, 6440.

S5 Wong, J. C.; Tang, G.; Wu, X.; Liang, C.; Zhang, Z.; Guo, L.; Peng, Z.; Zhang, W.; Lin, X.; Wang, Z.; Mei, J.; Chen, J.; Pan, S.; Zhang, N.; Liu, Y.; Zhou, M.; Feng, L.; Zhao, W.; Li, S.; Zhang, C.; Zhang, M.; Rong, Y.; Jin, T.-G.; Zhang, X.; Ren, S.; Ji, Y.; Zhao, R.; She, J.; Ren, Y.; Xu, C.; Chen, D.; Cai, J.; Shan, S.; Pan, D.; Ning, Z.; Lu, X.; Chen, T.; He, Y.; Chen, L. *J. Med*. *Chem*. **2012**, *55*, 8903.

S6 Choudhary, G.; Peddinti, R. K. *Green Chem*. **2011**, *13*, 3290.

S7 Pinho e Melo, T. M. V. D.; Lopes, C. S. J.; Rocha Gonsalves, A. M. d'A.; Beja, A. M.; Paixão, J. A.; Silva, M. R.; Alte da Veiga, L. *J. Org*. *Chem*. **2002**, *67*, 66.

S8 Gilli, P.; Bertolasi, V.; Ferretti, V.; Gilli, G. *J. Am. Chem. Soc.* **2000**, *122,* 10405.

S9 Gamble, A. B.; Keller, P. A. *Chem*. *Commun*. **2010**, *46*, 4076.