Lewis Acid Promoted Carbon-Carbon bond Cleavage of Aziridines: Divergent Cycloaddition Pathways of the Derived Ylides

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Supporting Information

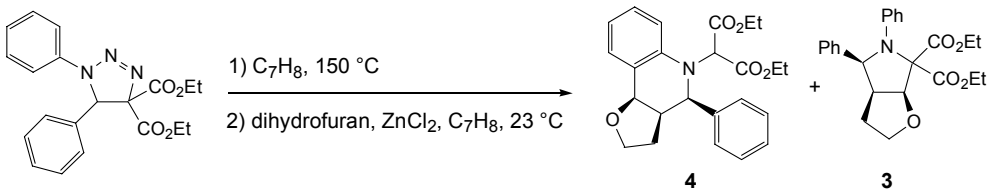
Experimental Section

Materials and Methods: General. Infrared (IR) spectra were obtained using a Nicolet 560-E.S.P. infrared spectrometer. Proton and carbon nuclear magnetic resonance spectra (^{1}H and ^{13}C NMR) were recorded on the following instruments: Bruker model Avance 400 (^{1}H NMR at 400 MHz and ^{13}C NMR at 100 MHz) and Varian Gemini 300 (^{1}H NMR at 300 MHz and ^{13}C at 75 MHz) spectrometers with tetramethylsilane (TMS) as the internal standard for ^{1}H NMR at 0.00 ppm and $CDCl_3$ solvent resonance as the internal standard for ^{13}C NMR at 77.16 ppm. ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, m = multiplet), coupling constants (Hz), and integration. Structural assignments were made using a combination of COSY, NOESY, HMQC, and HMBC experiments (see Appendix for spectra). Combustion analyses were performed by Atlantic Microlab Inc., Norcross, GA. Analytical thin layer chromatography (TLC) was performed on Whatman 0.25 mm silica gel 60 plates. Visualization was accomplished with UV light and aqueous ceric ammonium molybdate solution followed by heating. Purification of the reaction products was carried out by flash chromatography using Sorbent Technologies silica gel 60 (32-63 μm). All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring. Yield refers to isolated yield of analytically pure material. Yields are reported for a specific experiment and as a result may differ slightly from those found in the tables and equations, which are averages of at least two experiments. Toluene, tetrahydrofuran, and methylene chloride were dried by passage through a column of neutral alumina under nitrogen prior to use. Triazolines were prepared using Carrie's procedure from the corresponding aryl azide and benzylidene malonate.[1] Aryl azides were prepared from a known procedure.[2] Benzylidene malonates were prepared via Knoevenagel condensations.[3] Unless otherwise noted, reagents were obtained from commercial sources and used without further purification. Zinc (II) chloride was dried at 150 °C under vacuum overnight.

General procedure (A) for aziridine synthesis and Lewis acid-promoted cycloaddition. In an inert atmosphere glove box, a flame-dried Schlenk tube with a magnetic stir bar was charged with 0.22 mmol of triazoline and 3 mL of toluene. Outside of the glove box, this solution was heated to 150 °C for 14 h. After cooling, the tube was transferred into the glove box where it was concentrated in vacuo. To the remaining residue was added $ZnCl_2$ (1.2 equiv), 1.6 mL of solvent, and the dipolarophile (3-22 equiv). The tube was sealed and the reaction was stirred for 76 h at 23 °C outside of the glove box. The reaction was diluted with 20 mL of CH_2Cl_2 and washed with 10 ml of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with 10 mL of CH_2Cl_2. The organic extracts were combined, washed with 20 mL of saturated aqueous NaCl,

dried over Na_2SO_4, and the solvent was removed with a rotary evaporator. The product was purified by flash chromatography, eluting with the indicated solvent system to afford the pure pyrrolidine or tetrahydroquinoline product.

General procedure (B) for aziridine synthesis and Lewis acid–catalyzed cycloaddition. In an inert atmosphere glove box, a flame-dried Schlenk tube with a magnetic stir bar was charged with 0.22 mmol of triazoline and 3 mL of toluene. Outside of the glove box, this solution was heated to 150 °C for 14 h. After cooling the tube was transferred into the glove box where it was concentrated in vacuo. The catalyst was prepared in the glovebox by stirring 0.04 mmol of $ZnCl_2$ and 0.04 mmol of *N,N*-dibenzylidene-cyclohexane-1,2-diamine in 2 mL of THF for one hour. To the aziridine generated from the triazoline thermolysis was added (*N,N*-dibenzylidene-cyclohexane-1,2-diamine)$ZnCl_2$ (0.2 equiv) as a heterogeneous mixture in THF and concentrated in vacuo. The residue was treated with 1.6 mL of solvent and the dipolarophile (3-22 equiv). The tube was sealed and the reaction was stirred for 76 h at 45 °C outside of the glove box. The reaction was diluted with 20 mL of CH_2Cl_2 and washed with 10 ml of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with 10 mL of CH_2Cl_2. The organic extracts were combined, washed with 20 mL of saturated aqueous NaCl, dried over Na_2SO_4, and the solvent was removed with a rotary evaporator. The product was purified by flash chromatography, eluting with the indicated solvent system to afford the pure pyrrolidine or tetrahydroquinoline product.

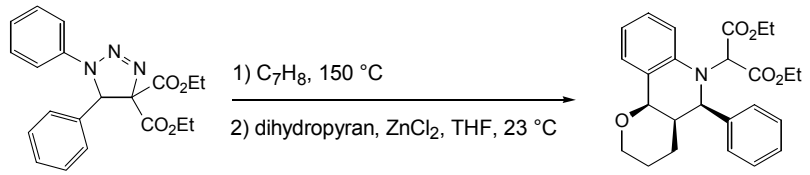


2-(4-Phenyl-2,3,3a,9b-tetrahydro-4H-furo[3,2-c]quinolin-5-yl)-malonic acid diethyl ester (4). The title compound was prepared according to General Procedure **A** using 80.0 mg (0.218 mmol) of triazoline, 3 mL of C_7H_8, then 35.3 mg (0.259 mmol) of $ZnCl_2$, 360 μL (4.73 mmol) of dihydrofuran, and 1.6 mL of C_7H_8. After 76 h at 23 °C and extractive workup, ^{1}H NMR of the unpurified product (δ 4.66 vs. δ 5.14) gave the isomeric composition of the product: **4/3** = 3.2:1. ^{1}H NMR (δ 4.66 vs. δ 5.04) gave the diastereomer ratio of **4** with respect to another isomer of unknown relative stereochemistry: 10:1. The isomers were separated and purified by flash chromatography with a 5-20% EtOAc/hexanes linear gradient to afford 49.5 mg (55%) of the product (**4+3),** as a clear oil which contained 3% of a [4+2] adduct of unknown relative stereochemistry.

Analytical data for **4**: **IR** (thin film, cm^{-1}) 3057, 2983, 2937, 2872, 1755, 1738, 1605, 1581, 1497, 1456, 1369, 1265, 1178, 1161, 1103, 1032, 737, 704; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.35-7.24 (m, 5H), 7.15 (ddd, *J* = 8.3, 7.5, 1.8 Hz, 1H), 6.83 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.77 (d, *J* = 8.5 Hz, 1H), 4.83 (s, 1H), 4.66 (d, *J* = 5.7 Hz, 1H), 4.41 (d, *J* = 7.8 Hz, 1H), 4.23-4.12 (m, 2H), 3.98-3.76 (m, 4H), 2.66 (dddd, *J* = 7.7, 7.7. 5.7, 5.7 Hz, 1H), 2.16-2.04 (m, 1H), 2.00-1.89 (m, 1H), 1.19 (t, *J*

= 7.0 Hz, 3H), 0.98 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.72, 167.69, 143.68, 141.71, 130.90, 128.90, 128.78, 128.11, 128.01, 122.30, 118.80, 113.18, 74.39, 65.71, 65.00, 63.18, 61.76, 44.14, 29.82, 29.77, 14.15, 13.87; TLC (20% EtOAc/pet. ether) R_f 0.31; **Anal.** Calcd. for $C_{24}H_{27}NO_5$: C, 70.40; H, 6.65; N, 3.42. Found: C, 70.07; H, 6.65; N, 3.34.

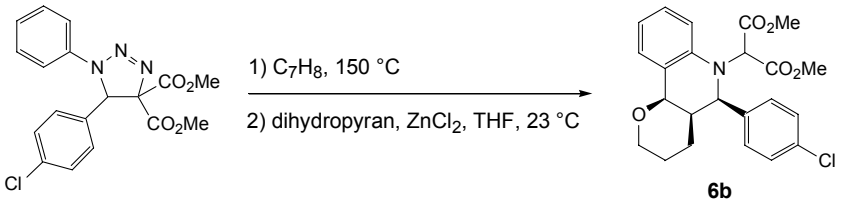
Analytical data for **4,5-Diphenyl-hexahydro-furo[2,3-c]pyrrole-6,6-dicarboxylic acid diethyl ester (3)**: **IR** (thin film, cm^{-1}) 3061, 3028, 2980, 2937, 2895, 1755, 1720, 1601, 1581, 1504, 1454, 1389, 1367, 1292, 1267, 1225, 1176, 1138, 1117, 1059, 1034, 928, 862, 750, 704; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42-7.40 (m, 2H), 7.28-7.24 (m, 2H), 7.20-7.16 (m, 1H), 7.07-7.02 (m, 2H), 6.85-6.82 (m, 2H), 6.78 (tt, *J* = 7.3, 1.1 Hz, 1H), 5.14 (d, *J* = 9.0 Hz, 1H), 4.97 (d, *J* = 6.4 Hz, 1H), 4.51-4.43 (m, 1H), 4.37-4.29 (m, 1H), 4.06-3.98 (m, 1H), 3.92-3.84 (m, 1H); 3.64 (ddd, *J* = 8.1, 8.1, 4.4 Hz, 1H), 3.54-3.45 (m, 2H), 1.73-1.57 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.42, 167.62, 145.18, 140.02, 128.52, 128.30, 127.74, 127.18, 121.00, 119.76, 87.97, 81.47, 69.35, 67.76, 61.63, 61.42, 47.06, 28.81, 14.36, 13.84; TLC (20% EtOAc/pet. ether) R_f 0.36; **Anal.** Calcd. for $C_{24}H_{27}NO_5$: C, 70.40; H, 6.65; N, 3.42. Found: C, 70.25; H, 6.73; N, 3.35.



6a

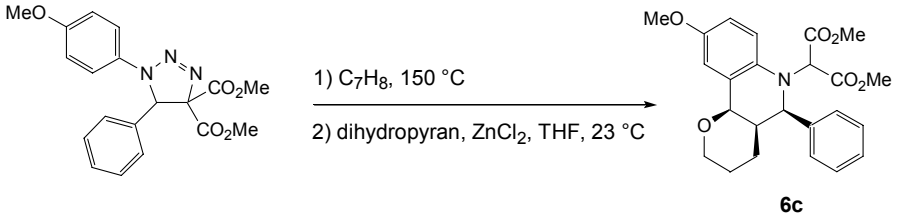
2-(5-Phenyl-3,4,4a,10b-tetrahydro-2H,5H-pyrano[3,2-c]quinolin-6-yl)-malonic acid diethyl ester (6a). The title compound was prepared according to General Procedure A using 80.0 mg (0.218 mmol) of triazoline, 3 mL of C_7H_8, then 35.6 mg (0.261 mmol) of $ZnCl_2$, 300 μL (3.29 mmol) of dihydropyran, and 1.6 mL of THF. After 76 h at 23 °C and extractive workup, ^{1}H NMR of the unpurified product (δ 4.50 vs. δ 4.94) gave the ratio of **6a** with respect to a [3+2] isomer of unknown relative stereochemistry: 12:1. The crude product was purified by flash chromatography with a 7.5-17.5% EtOAc/hexanes linear gradient to afford 77.0 mg (83%) of the product as a clear oil.

Analytical data for **6a**: **IR** (thin film, cm^{-1}) 3062, 3030, 2980, 2939, 2862, 1759, 1736, 1603, 1579, 1495, 1464, 1454, 1390, 1367, 1304, 1271, 1217, 1176, 1159, 1090, 1072, 1041, 1030, 943, 916, 893, 866, 779, 739, 704; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.4 Hz, 1H), 7.30-7.21 (m, 5H), 7.15 (ddd, *J* = 8.6, 7.4, 1.8 Hz, 1H), 6.80 (ddd, *J* = 7.4, 7.4, 0.6 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 4.81 (s, 1H), 4.72 (d, *J* = 6.9 Hz, 1H), 4.50 (d, *J* = 3.7 Hz, 1H), 4.21-4.09 (m, 2H), 3.92-3.71 (m, 3H), 3.67-3.61 (m, 1H), 2.19 (dddd, *J* = 6.3, 6.3, 4.1, 4.1 Hz, 1H), 1.78-1.68 (m, 2H), 1.57-1.47 (m, 2H), 1.17 (t, *J* = 7.0 Hz, 3H), 0.95 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$); 167.92, 167.51, 143.87, 142.18, 129.42, 128.78, 128.60, 127.70, 127.58, 121.87, 118.18, 112.57, 71.33, 66.22, 64.76, 64.57, 61.83, 61.65, 39.33, 25.37, 23.99, 14.13, 13.77; TLC (20% EtOAc/pet. ether) R_f 0.40; **Anal.** Calcd. for $C_{25}H_{29}NO_5$: C, 70.90; H, 6.90; N, 3.31. Found: C, 70.69; H, 6.95; N, 3.24.



2-[5-(4-Chloro-phenyl)-3,4,4a,10b-tetrahydro-2H,5H-pyrano[3,2-c]quinolin-6-yl]-malonic acid dimethyl ester (6b). The title compound was prepared according to General Procedure A using 81.5 mg (0.218 mmol) of triazoline, 3 mL of C_7H_8, then 35.6 mg (0.261 mmol) of $ZnCl_2$, 300 μL (3.29 mmol) of dihydropyran, and 1.6 mL of THF. After 76 h at 23 °C and extractive workup, ^{1}H NMR of the unpurified product (δ 4.51 vs. δ 4.93) gave the ratio of **6b** with respect to a [3+2] isomer of unknown relative stereochemistry: 7.6:1. The crude product was purified by flash chromatography with a 10-20% EtOAc/hexanes gradient to afford 68.3 mg (73%) of the product as a white foam.

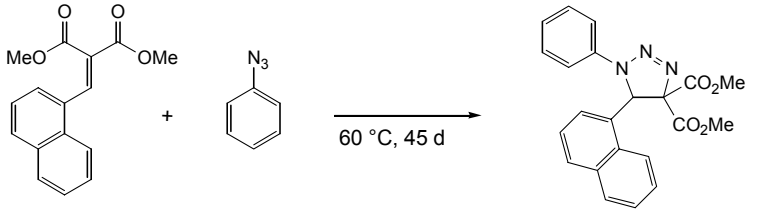
Analytical data for **6b**: **IR** (thin film, cm^{-1}) 3654, 3488, 3044, 2951, 2861, 2724, 1907, 1743, 1603, 1578, 1492, 1496, 1435, 1397, 1368, 1305, 1162, 1090, 1041, 1014, 921, 896, 839, 826, 750, 705, 660, 645, 608; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.5 Hz, 1H), 7.29-7.24 (m, 2H), 7.20-7.14 (m, 3H), 6.83 (ddd, *J* = 7.5, 7.5, 0.8 Hz, 1H), 6.69 (d, *J* = 8.3 Hz, 1H), 4.88 (s, 1H), 4.69 (d, *J* = 6.2 Hz, 1H), 4.51 (d, *J* = 4.1 Hz, 1H), 3.80-3.71 (m, 1H), 3.71 (s, 3H), 3.66-3.59 (m, 1H), 3.37 (s, 3H), 2.19-2.11 (m, 1H), 1.80-1.49 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$); 168.14, 167.66, 143.36, 140.71, 133.45, 129.35, 128.91, 128.73(two overlapping resonances), 121.52, 118.53, 112.01, 70.56, 65.30, 64.15, 63.91, 52.68, 52.60, 39.33, 25.23, 24.25; TLC (20% EtOAc/pet. ether) R_f 0.26; **Anal.** Calcd. for $C_{25}H_{28}ClNO_5$: C, 64.26; H, 5.63; N, 3.26. Found: C, 64.03; H, 5.73; N, 3.15.



2-(9-Methoxy-5-phenyl-3,4,4a,10b-tetrahydro-2H,5H-pyrano[3,2-c]quinolin-6-yl)-malonic acid dimethyl ester (6c). The title compound was prepared according to General Procedure A using 80.5 mg (0.218 mmol) of triazoline, 3 mL of C_7H_8, then 35.6 mg (0.261 mmol) of $ZnCl_2$, 300 μL (3.29 mmol) of dihydropyran, and 1.6 mL of THF. After 76 h at 23 °C and extractive workup, ^{1}H NMR of the unpurified product (δ 4.49 vs. δ 4.89) gave the ratio of **6c** with respect to a [3+2] isomer of unknown relative stereochemistry: 26:1. The crude product was purified by flash chromatography with a 15-25% EtOAc/hexanes linear gradient to afford 60.8 mg (66%) of the product as a white foam.

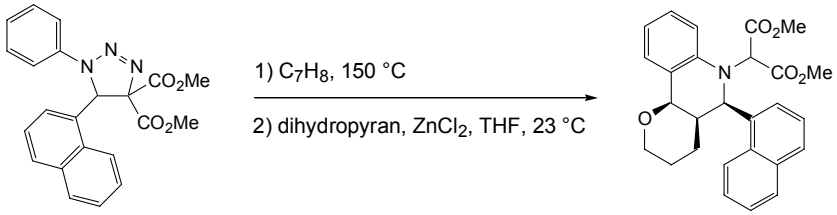
Analytical data for title **6c**: **IR** (thin film, cm^{-1}) 2999, 2950, 2859, 1742, 1505, 1453, 1434, 1357, 1229, 1160, 1087, 1066, 1043, 923, 905, 870, 805, 760, 737, 704; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H), 7.25-7.21 (m, 3H), 6.95 (d, *J* = 2.9 Hz, 1H), 6.77 (dd, *J* = 9.0, 2.9 Hz, 1H), 6.66 (d, *J* = 9.0 Hz, 1H), 4.84 (s, 1H), 4.68 (d, *J* = 6.6

Hz, 1H), 4.49 (d, *J* = 4.0 Hz, 1H), 3.84-3.77 (m, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 3.68-3.62 (m, 1H), 3.37 (s, 3H), 2.19 (dddd, *J* = 7.1, 7.1, 4.1, 4.1 Hz, 1H), 1.77-1.69 (m, 2H), 1.59-1.48 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$); 168.53, 168.08, 152.36, 142.16, 137.71, 128.58, 127.67, 127.42, 122.67, 115.09, 114.35, 113.19, 71.30, 65.74, 64.70, 64.38, 55.81, 52.52, 52.50, 39.47, 25.35, 24.04; TLC (20% EtOAc/pet. ether) R_f 0.16; **Anal.** Calcd. for $C_{24}H_{27}NO_6$: C, 67.75; H, 6.40; N, 3.29. Found: C, 67.83; H, 6.48; N, 3.28.



5-Naphthalen-1-yl-1-phenyl-1,5-dihydro-[1,2,3]triazole-4,4-dicarboxylic acid dimethyl ester. The title compound was prepared by combining 2.9 g of 2-Naphthalen-1-ylmethylene-malonic acid dimethyl ester (10.9 mmol) and 2.6 g of phenyl azide (21.8 mmol) in a small vial. After 42 d at 60 °C, the crude product was purified by flash chromatography with a 15-20% EtOAc/hexanes gradient to afford 667 mg (16%) of the product as a yellow solid.

Analytical data for title compound: **IR** (Nujol mull, cm^{-1}) 1742, 1598, 1461, 1377, 1282, 1228, 1130, 750; **^{1}H NMR** (400 MHz, $CDCl_3$); δ 8.39 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.67 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.57 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.30 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.20-7.14 (m, 4H), 7.09 (dd, *J* = 7.2, 0.98 Hz, 1H), 6.98 (tt, *J* = 6.7, 1.8 Hz, 1H), 6.79 (s, 1H), 3.96 (s, 3H), 2.84 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$); δ 166.10, 164.75, 138.63, 133.84, 131.44, 129.60, 129.44, 128.98, 128.76, 127.27, 126.29, 125.81, 125.34, 123.72, 123.25, 115.80, 95.97, 59.22, 54.45, 52.37; TLC (20% EtOAc/pet. ether) R_f 0.22; **Anal.** Calcd. for $C_{22}H_{19}N_3O_4$: C, 67.86; H, 4.92; N, 10.79. Found: C, 67.93; H, 5.05; N, 10.55.

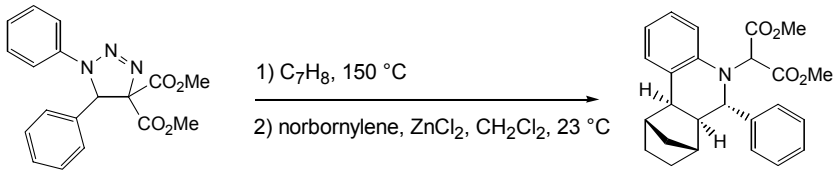


6d

2-(5-Naphthalen-1-yl-3,4,4a,10b-tetrahydro-2H,5H-pyrano[3,2-c]quinolin-6-yl)-malonic acid dimethyl ester (6d). The title compound was prepared according to General Procedure A using 84.9 mg (0.218 mmol) of triazoline, 3 mL of C_7H_8, then 33.0 mg (0.242 mmol) of $ZnCl_2$, 300 μL (3.29 mmol) of dihydropyran, and 1.6 mL of THF. After 76 h at 23 °C and extractive workup, ^{1}H NMR of the unpurified product (δ 4.64 vs. δ 4.90) gave the diastereomer ratio of **6d** with respect to another isomer of unknown relative stereochemistry: 4.2:1. The material was purified by flash chromatography with

a 5-20% EtOAc/hexanes linear gradient to afford 49.0 mg (51%) of the product as clear crystals that contained 13% of a diastereomer.

Analytical data for **6d**: **IR** (Nujol mull, cm^{-1}) 2357, 1753, 1742, 1604, 1501, 1460, 1377, 1335, 1242, 1202, 1170, 1126, 1081, 1067, 783, 748; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.3 Hz, 1H), 7.87 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.72 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.61-7.55 (m, 1H), 7.53-7.50 (m, 1H), 7.45 (ddd, *J* = 7.5, 1.3, 1.3 Hz, 1H), 7.37-7.29 (m, 2H), 7.26-7.19 (m, 1H), 6.87 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.69 (d, *J* = 8.3 Hz, 1H), 5.49 (d, *J* = 3.1 Hz, 1H), 5.07 (s, 1H), 4.64 (d, *J* = 4.9 Hz, 1H), 3.73 (s, 3H), 3.59-3.56 (m, 2H), 3.05 (s, 3H), 2.47-2.39 (m, 1H), 1.98-1.93(m, 1H), 1.82-1.58 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$); 168.23, 167.42, 143.67, 137.25, 134.08, 130.60, 129.31, 128.57, 128.07, 126.66, 125.70, 125.22(two overlapping resonances), 124.55, 122.44, 120.32, 118.13, 110.70, 69.37, 64.52, 61.91, 60.76, 52.69, 52.47, 37.84, 25.81, 25.24; TLC (20% EtOAc/Pet. Ether) R_f 0.31; **Anal.** Calcd. for $C_{27}H_{27}NO_5$: C,72.79; H, 6.11; N, 3.14. Found: C, 72.55; H, 6.15; N, 3.09.



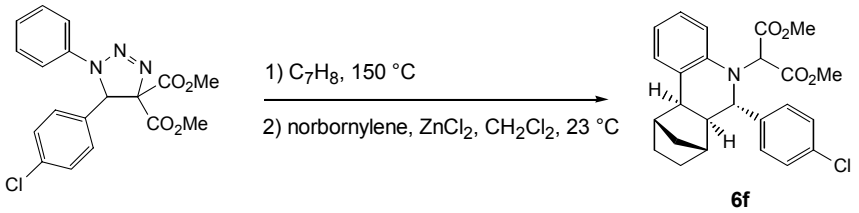
6e

2-((6α,6aβ,7α,10α,10aβ)-5,6,6a,7,8,9,10,10a-octahydro-7,10-methano-6-phenyl-phenanthridin-5-yl)malonic acid dimethyl ester (6e). The title compound was prepared according to General Procedure A using 80 mg (0.236 mmol) of triazoline, 3 mL of C_7H_8, then 35 mg (0.26 mmol) of $ZnCl_2$, 67.0 mg (0.708 mmol) of norbornylene, and 1.6 mL of CH_2Cl_2. After 76 h at 23 °C and extractive workup, ^{1}H NMR of the unpurified product (δ 2.80 vs. δ 2.72) gave the diastereomer ratio of **6e** with respect to another isomer of unknown relative stereochemistry: 9:1. The isomers were purified by flash chromatography with a 15-22.5% EtOAc/hexanes linear gradient to afford 80.9 mg (85%) of the product as a white foam which contained 10% of a diastereomer.

Alternatively, the title compound was prepared according to General Procedure B using 80 mg (0.236 mmol) of triazoline, 3 mL of C_7H_8, 20 mg (0.047 mmol) of (*N,N*-dibenzylidene-cyclohexane-1,2-diamine)$ZnCl_2$, 67.0 mg (0.708 mmol) of norbornylene, and 1.6 mL of CH_2Cl_2. After 76 h at 45 °C and extractive workup, the crude product was purified by flash chromatography with a 15-22.5% EtOAc/hexanes linear gradient to afford 83.0 mg (86%) of the product as a white foam which contained 15% of a diastereomer.

Analytical data for **6e**: **IR** (thin film, cm^{-1}), 3060, 3027, 2952, 2869, 1762, 1741, 1598, 1496, 1452, 1434, 1371, 1340, 1282, 1247, 1230, 1193, 1120, 1072, 1029, 938, 929, 890, 827, 806, 750, 736, 700; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19-7.03 (m, 7H), 6.83-6.80 (m, 2H), 5.07 (s, 1H), 4.49 (d, *J* = 3.5 Hz, 1H), 3.69 (s, 3H), 3.24 (s, 3H), 2.80 (d, *J* = 12.0 Hz, 1H), 2.41-2.38 (m, 2H), 2.24 (dd, *J* = 9.1, 3.6 Hz, 1H), 1.79 (d, *J* = 9.7 Hz, 1H), 1.67-1.60 (m, 1H), 1.56-1.48 (m, 1H), 1.39-1.26 (m, 2H), 1.04 (d, *J* = 9.9 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$); 168.17, 167.95, 144.75, 144.05, 130.48,

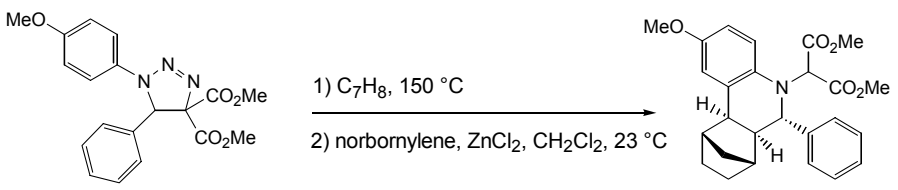
129.72, 128.41, 127.63, 126.87, 126.61, 119.27, 113.63, 63.90(two overlapping resonances), 52.90, 52.57, 52.10, 47.32, 44.02, 43.76, 34.29, 30.80, 28.93; TLC (20% EtOAc/pet. ether) R_f 0.42; **Anal.** Calcd. for $C_{25}H_{27}NO_4$: C, 74.05; H, 6.71; N, 3.45. Found: C, 74.20; H, 6.77; N, 3.49



6f

2-((6α,6aβ,7α,10α,10aβ)-5,6,6a,7,8,9,10,10a-octahydro-7,10-methano-6-(4-chlorophenyl)-phenanthridin-5-yl)malonic acid dimethyl ester (6f). The title compound was prepared according to General Procedure A using 88 mg (0.236 mmol) of triazoline, 3 mL of C_7H_8, then 35 mg (0.26 mmol) of $ZnCl_2$, 67.0 mg (0.708 mmol) of norbornylene, and 1.6 mL of CH_2Cl_2. After 76 h at 23 °C and extractive workup, ^{1}H NMR of the unpurified product (δ 2.78 vs. δ 2.70) gave the diastereomer ratio of **6f** with respect to another isomer of unknown relative stereochemistry: 2.8:1. The isomers were purified by flash chromatography with a 10-25% EtOAc/hexanes linear gradient to afford 78 mg (75%) of the product as a white foam which contained 23% of a diastereomer.

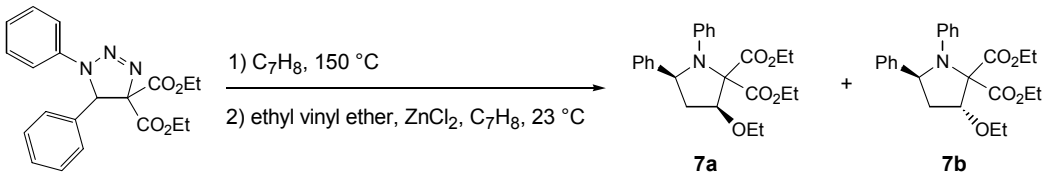
Analytical data for title **6f**: **IR** (thin film, cm^{-1}), 3062, 2952, 2869, 1764, 1739, 1598, 1579, 1490, 1454, 1434, 1396, 1371, 1340, 1295, 1282, 1232, 1170, 1091, 1031, 1014, 910, 823, 750, 730; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.15-7.06 (m, 4H), 6.95 (d, J = 8.1 Hz, 2H), 6.84-6.80 (m, 2H), 5.10 (s, 1H), 4.55 (d, J = 2.5 Hz, 1H), 3.71 (s, 3H), 3.28 (s, 3H), 2.78 (d, J = 9.0 Hz, 1H), 2.44 (s, 1H), 2.34 (d, J = 3.5 Hz, 1H), 2.19-2.11 (m, 1H), 1.77 (d, J = 9.9 Hz, 1H), 1.68-1.60 (m, 1H), 1.57-1.49 (m, 1H), 1.39-1.26 (m, 2H), 1.04 (d, J = 9.9 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$); 167.98, 167.76, 144.33, 142.85, 132.41, 130.44, 129.87, 128.86, 128.41, 126.82, 119.49, 113.54, 63.81, 62.76, 52.90, 52.62, 52.18, 47.68, 43.91(two overlapping resonances), 34.28, 30.93, 28.78; TLC (20% EtOAc/Pet. Ether) R_f 0.41; **Anal.** Calcd. for $C_{25}H_{26}NO_4Cl$: C, 68.25; H, 5.96; N, 3.18. Found: C, 67.99; H, 5.99; N, 3.20. The relative stereochemistry of the major isomer was further confirmed by X-ray crystallography: see Appendix.



6g

2-((6α,6aβ,7α,10α,10aβ)-5,6,6a,7,8,9,10,10a-octahydro-7,10-methano-2-methoxy-6-phenyl-phenanthridin-5-yl)malonic acid dimethyl ester (6g). The title compound was prepared according to General Procedure A using 87 mg (0.236 mmol) of triazoline, 3 mL of C_7H_8, then 35 mg (0.26 mmol) of $ZnCl_2$, 67.0 mg (0.708 mmol) of norbornylene, and 1.6 mL of CH_2Cl_2. After 76 h at 23 °C and extractive workup, the crude product was purified by flash chromatography with a 10-25% EtOAc/hexanes linear gradient to afford 85 mg (82%) of the product as a white foam.

Analytical data for **6g**: **IR** (thin film, cm^{-1}), 2950, 2869, 2834, 1762, 1739, 1506, 1452, 1432, 1303, 1295, 1226, 1195, 1162, 1043, 1031, 910, 802, 734, 700; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23-7.14 (m, 3H), 7.07 (d, *J* = 6.6 Hz, 2H), 6.79-6.76 (m, 2H), 6.64 (dd, *J* = 9.0, 2.9 Hz, 1H), 4.94 (s, 1H), 4.38 (d, *J* = 4.2 Hz, 1H), 3.77 (s, 3H), 3.66 (s, 3H), 3.29 (s, 3H), 2.78 (d, *J* = 9.3 Hz, 1H), 2.43 (d, *J* = 3.8Hz, 1H), 2.33 (d, *J* = 2.2 Hz, 1H), 2.26 (dd, *J* = 9.1, 4.67 Hz, 1H), 1.79 (d, *J* = 10.3 Hz, 1H), 1.69-1.61 (m, 1H), 1.57-1.49 (m, 1H), 1.41-1.27 (m, 2H), 1.05 (d, *J* = 9.7 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$); 168.3, 168.21, 152.98, 143.60, 138.82, 131.90, 128.4, 127.88, 126.97, 115.18, 115.02, 111.67, 64.29, 64.21, 55.60, 52.63, 52.49, 52.05, 46.67, 44.51, 43.36, 34.29, 30.58, 29.04; TLC (20% EtOAc/pet. ether) R_f 0.32; **Anal.** Calcd. for $C_{26}H_{29}NO_5$: C, 71.70; H, 6.71; N, 3.22. Found: C, 71.51; H, 6.72; N, 3.14

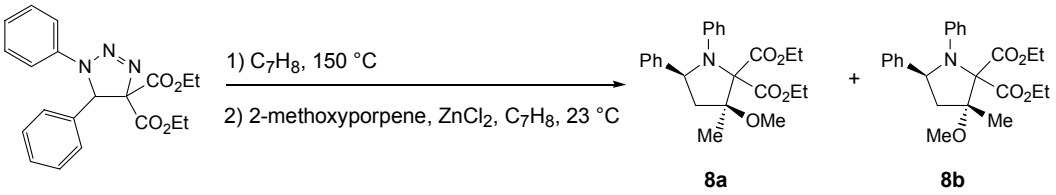


(±)-(3*S*,5*S*)-3-Ethoxy-1,5-diphenyl-pyrrolidine-2,2-dicarboxylic acid diethyl ester (7a). The title compound was prepared according to General Procedure A using 80.0 mg (0.218 mmol) of triazoline, 3 mL of C_7H_8, then 35.6 mg (0.261 mmol) of $ZnCl_2$, 340 μL (3.55 mmol) of ethyl vinyl ether, and 1.6 mL of C_7H_8. After 76 h at 23 °C, and extractive workup, ^{1}H NMR of the unpurified product (δ 4.97 vs. δ 5.05) gave the diastereomer ratio of the product: **7a**/**7b** = 1.6:1. The isomers were purified by adsorption onto SiO_2 followed by flash chromatography with a 5-20% EtOAc/hexanes linear gradient to afford 54.5 mg (61%) of the product (**7a**+**7b**) as a clear oil.

Analytical data for **7a**: **IR** (thin film, cm^{-1}) 3062, 3026, 2980, 2929, 2902, 2873, 1741, 1732, 1601, 1504, 1454, 1367, 1350, 1327, 1302, 1242, 1178, 1128, 1080, 1061, 1028, 926, 868, 816, 750, 700; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53-7.50 (m, 2H), 7.28-7.23 (m, 2H), 7.18-7.14 (m, 1H), 7.05-7.00 (m, 2H), 6.68 (tt, *J* = 7.2, 1.0 Hz, 1H), 6.55-6.51 (m, 2H), 4.97 (dd, *J* = 7.6, 6.3 Hz, 1H), 4.51 (dd, *J* = 5.9, 5.9 Hz, 1H), 4.47-4.41 (m, 1H), 4.37-4.29 (m, 1H), 4.12-3.99 (m, 2H), 3.55-3.48 (m, 1H), 3.39-3.32 (m, 1H), 2.79 (ddd, *J* = 12.7, 7.6, 5.5 Hz, 1H), 2.18 (ddd, *J* = 12.7, 6.1, 6.1 Hz, 1H), 1.37 (t, *J* = 7.0 Hz, 3H), 1.02 (t, *J* = 7.0 Hz, 3H), 1.00 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$); 169.59, 167.82, 144.93, 143.52, 128.41, 128.30, 126.85, 126.81, 118.76, 116.61, 85.11, 79.55, 65.88, 64.02, 61.80, 61.64, 40.32, 15.06, 14.40, 13.93; TLC (10% EtOAc/pet.

ether) R_f 0.18; **Anal.** Calcd. for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: Combustion analysis failed.

Analytical data for **(±)-(3*R*,5*S*)-3-Ethoxy-1,5-diphenyl-pyrrolidine-2,2-dicarboxylic acid diethyl ester (7b)**: **IR** (thin film, cm^{-1}) 2981, 2924, 1741, 1601, 1504, 1450, 1350, 1329, 1242, 1211, 1178, 1161, 1122, 1095, 1063, 748, 692; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41-7.38 (m, 2H), 7.33-7.30 (m, 2H), 7.25-7.21 (m, 1H) 7.08-7.03 (m, 2H), 6.68 (tt, *J* = 7.4, 1.0 Hz, 1H), 6.54-6.50 (m, 2H), 5.05 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.62 (dd, *J* = 9.6, 6.5 Hz, 1H), 4.42-4.30 (m, 2H), 4.30-4.15 (m, 2H), 3.77-3.69 (m, 1H), 3.55-3.48 (m 1H), 2.74 (ddd, *J* = 12.1, 9.4, 9.4 Hz, 1H), 2.24 (ddd, *J* = 12.1, 6.3, 2.7 Hz, 1H), 1.34 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$); δ 170.19, 167.72, 145.43, 144.08, 128.84, 128.44, 127.05, 126.08, 118.03, 114.74, 84.13, 66.87, 63.87, 62.10, 61.75, 39.94, 29.86, 15.44, 14.24, 14.22; TLC (10% EtOAc/Pet. Ether) R_f 0.20; **Anal.** Calcd. for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: Combustion analysis failed.



(±)-(3*S*,5*S*)-3-Methoxy-3-methyl-1,5-diphenyl-pyrrolidine-2,2-dicarboxylic acid diethyl ester (8a). The title compound was prepared according to General Procedure A using 80.0 mg (0.218 mmol) of triazoline, 3 mL of C_7H_8, then 33.0 mg (0.242 mmol) of $ZnCl_2$, 313 μL (3.27 mmol) of 2-methoxypropene, and 1.6 mL of C_7H_8. After 76 h at 23 °C, and extractive workup, ^{1}H NMR of the unpurified product (δ 4.99 vs. δ 5.12) gave the diastereomer ratio of the product: **8a**/**8b** = 1.4:1. The isomers were purified by adsorption onto SiO_2 followed by flash chromatography with a 5-20% EtOAc/hexanes linear gradient to afford 67.0 mg (75%) of the product (**8a**+**8b**) as a clear oil.

Alternatively, the title compound was prepared according to General Procedure B using 80.0 mg (0.218 mmol) of triazoline, 3 mL of C_7H_8, then 18.6 mg (0.044 mmol) of (*N,N*-dibenzylidene-cyclohexane-1,2-diamine)$ZnCl_2$, 313 μL (3.27 mmol) of 2-methoxypropene, and 1.6 mL of C_7H_8. After 76 h at 23 °C, and extractive workup, ^{1}H NMR of the unpurified product gave the diastereomer ratio of the product: **8a**/**8b** = 1.2:1. The isomers were purified by adsorption onto SiO_2 followed by flash chromatography with a 5-20% EtOAc/hexanes linear gradient to afford 68.0 mg (76%) of the product (**8a**+**8b**) as a clear oil.

Analytical data for **8a**: **IR** (thin film, cm^{-1}) 3061, 3026, 2980, 2937, 2902, 2829, 1751, 1601, 1578, 1506, 1464, 1452, 1379, 1350, 1329, 1261, 1232, 1205, 1192, 1167, 1136, 1109, 1078, 1039, 993, 891, 866, 764, 748, 702, 646; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.54-7.50 (m, 2H), 7.31-7.25 (m, 2H), 7.20-7.15 (m, 1H), 7.09-7.02 (m, 2H), 6.66 (tt, *J* = 7.5, 1.0 Hz, 1H), 6.40-6.36 (m, 2H), 4.99 (d, *J* = 9.6 Hz, 1H), 4.47-4.23 (m, 2H), 4.22-4.11 (m, 2H), 2.73 (dd, *J* = 13.5, 9.8 Hz, 1H), 2.62 (s, 3H), 2.38 (dd, *J* = 13.2, 1.0 Hz, 1H), 1.42 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$); δ 169.56, 166.59, 146.07, 144.14, 128.44, 128.22, 126.69, 126.38, 117.46, 114.19, 88.80, 83.54, 65.16, 61.94, 61.24, 49.28, 39.99, 17.94, 14.33, 14.12; TLC (20%

EtOAc/Pet. Ether) R_f 0.41; **Anal.** Calcd. for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: Analysis Failed

Analytical data for **(±)-(3*R*,5*S*)-3-Methoxy-3-methyl-1,5-diphenyl-pyrrolidine-2,2-dicarboxylic acid diethyl ester (8b)**: **IR** (thin film, cm^{-1}) 3061, 3026, 2981, 2956, 2931, 2850, 1763, 1743, 1601, 1504, 1450, 1377, 1365, 1323, 1265, 1219, 1186, 1155, 1126, 1076, 1038, 908, 864, 750, 704, 692; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47-7.44 (m, 2H), 7.32-7.28 (m, 2H), 7.23-7.19 (m, 1H), 7.06-7.01 (m, 2H), 6.67 (tt, J = 7.3, 0.9 Hz, 1H), 6.36-6.33 (m, 2H), 5.12 (dd, J = 9.3, 3.3 Hz, 1H), 4.47-4.29 (m, 2H), 4.23-4.10 (m, 2H), 3.32 (s, 3H), 3.13 (dd, J = 11.9, 9.5 Hz, 1H), 2.17 (dd, J = 12.3, 3.5 Hz, 1H), 1.35 (t, J = 7.1 Hz, 3H), 1.29 (s, 3H), 1.11 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.95, 167.97, 145.88, 143.76, 128.58, 128.36, 126.84, 126.62, 117.87, 114.90, 86.42, 82.23, 63.64, 61.85, 61.47, 51.23, 45.41, 20.48, 14.30, 14.10; TLC (20% EtOAc/Pet. Ether) R_f 0.34; **Anal**. Calcd. for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: C, 70.10; H, 7.03; N, 3.40.

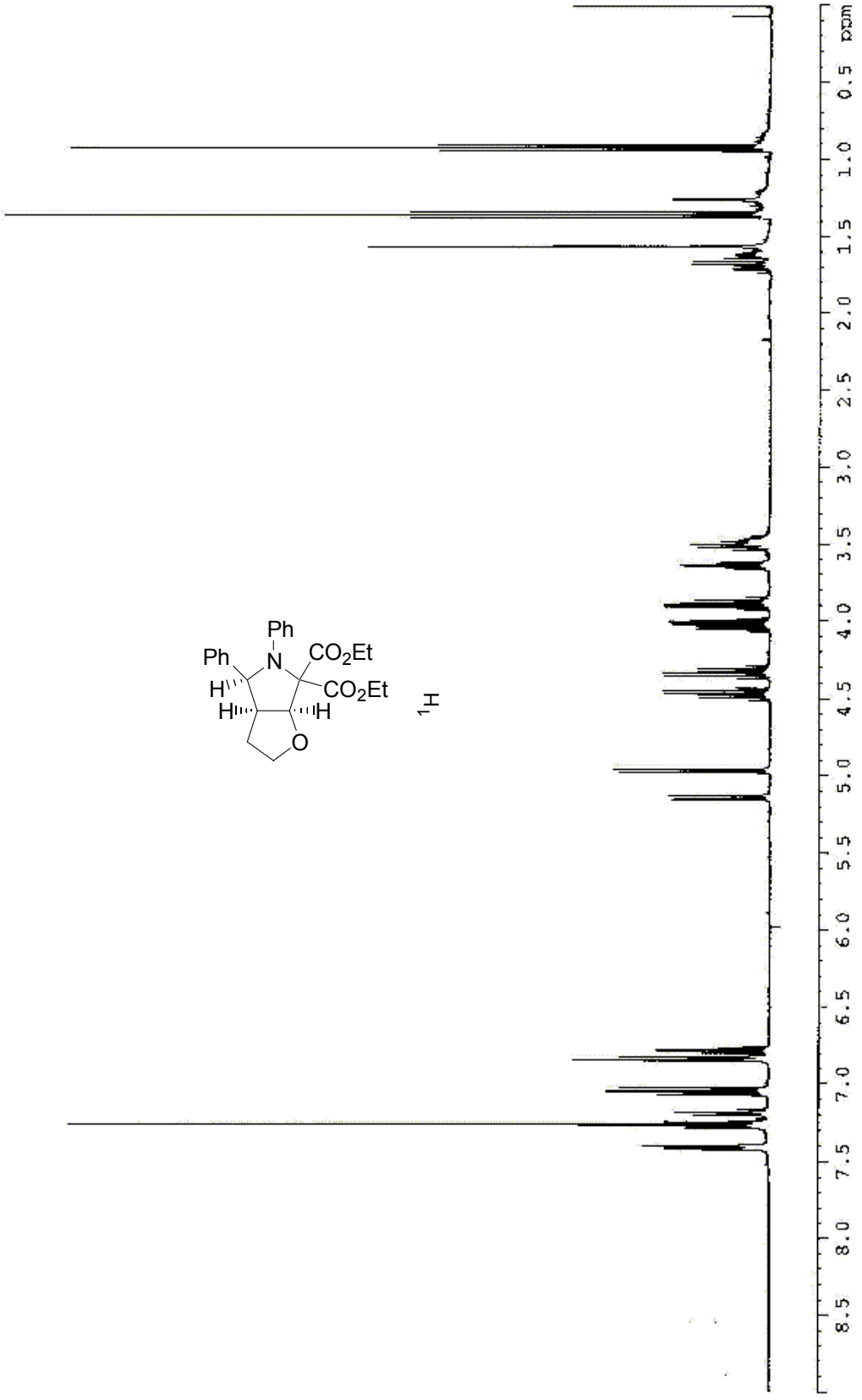
Literature Cited

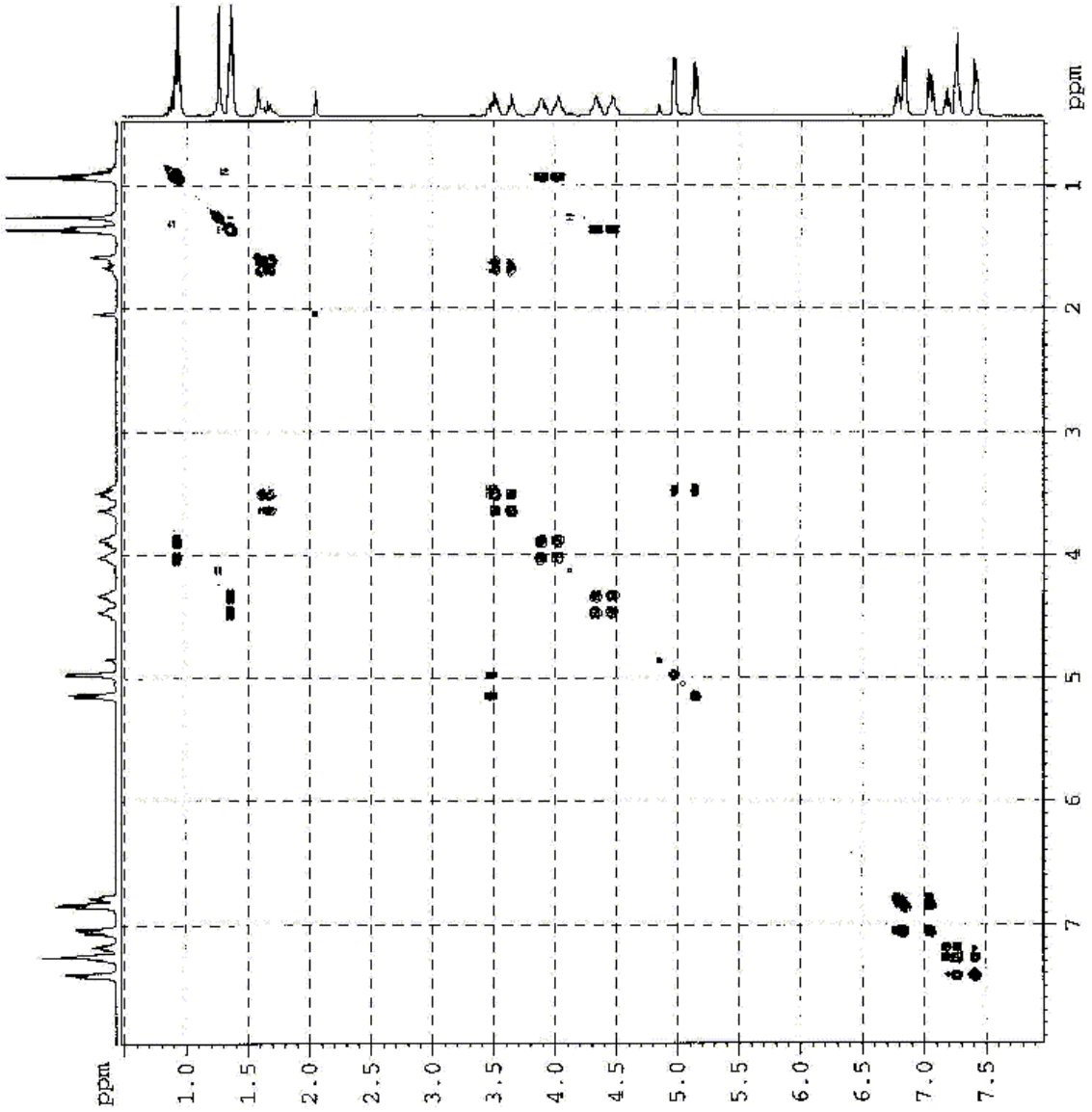
(1) Texier, F.; Carrie, R. *Bull. Soc. Chim. Fr.* **1971**, 4119-4128.

(2) Tanno, M.; Sueyoshi, S.; Kamiya, S. *Chem. Pharm. Bull.* **1982**, *30,* 3125-3132.

(3) Fraser, W.; Suckling, C. J.; Wood, H. C. S. *J. Chem. Soc. Perkin Trans. 1*. **1990**, 3137-3144.

Appendix. NMR spectra

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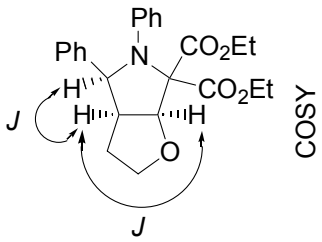
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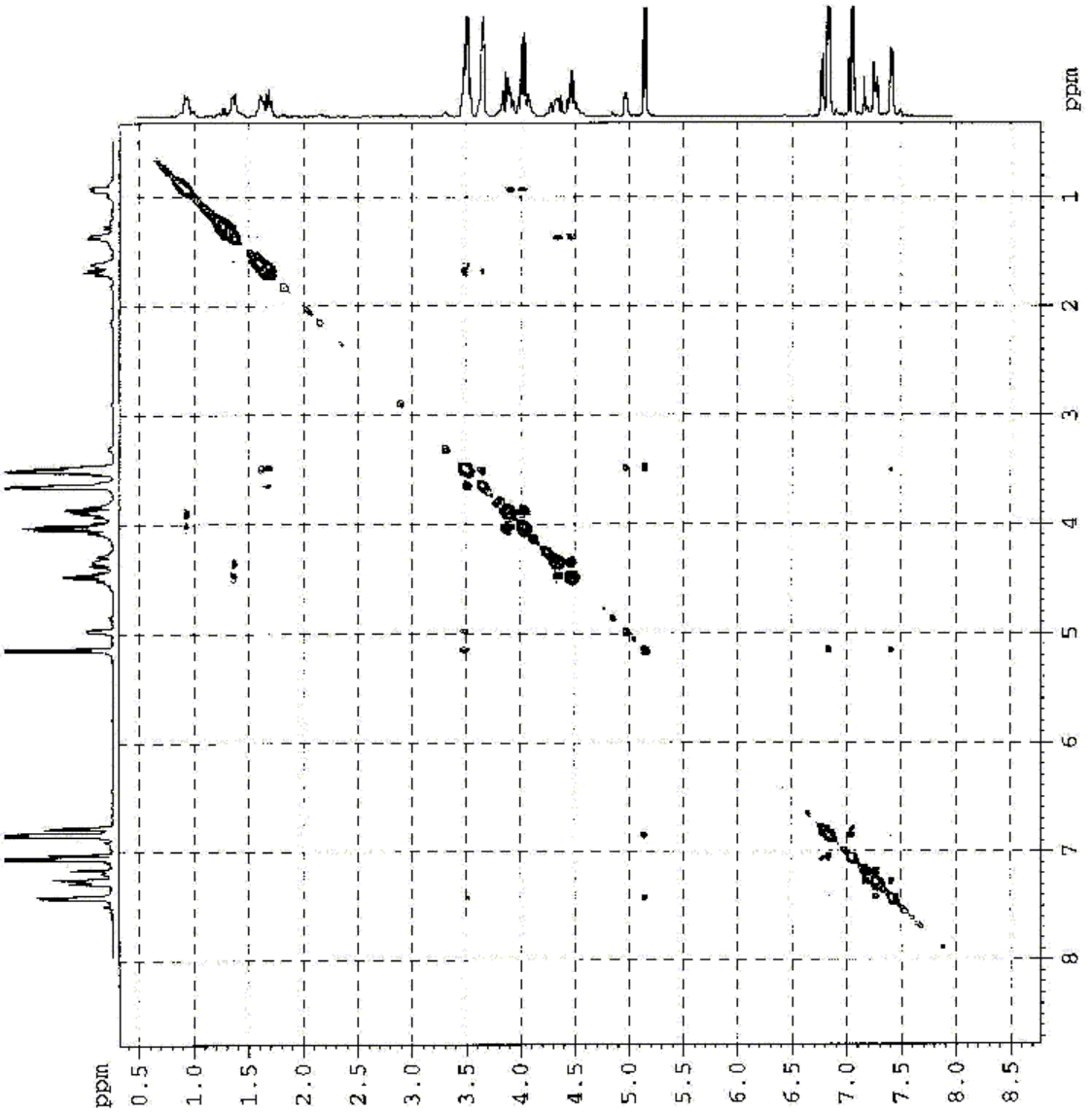
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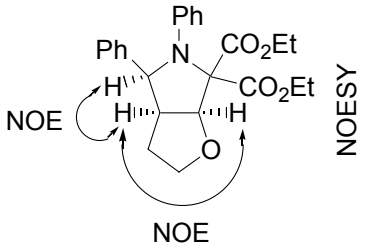
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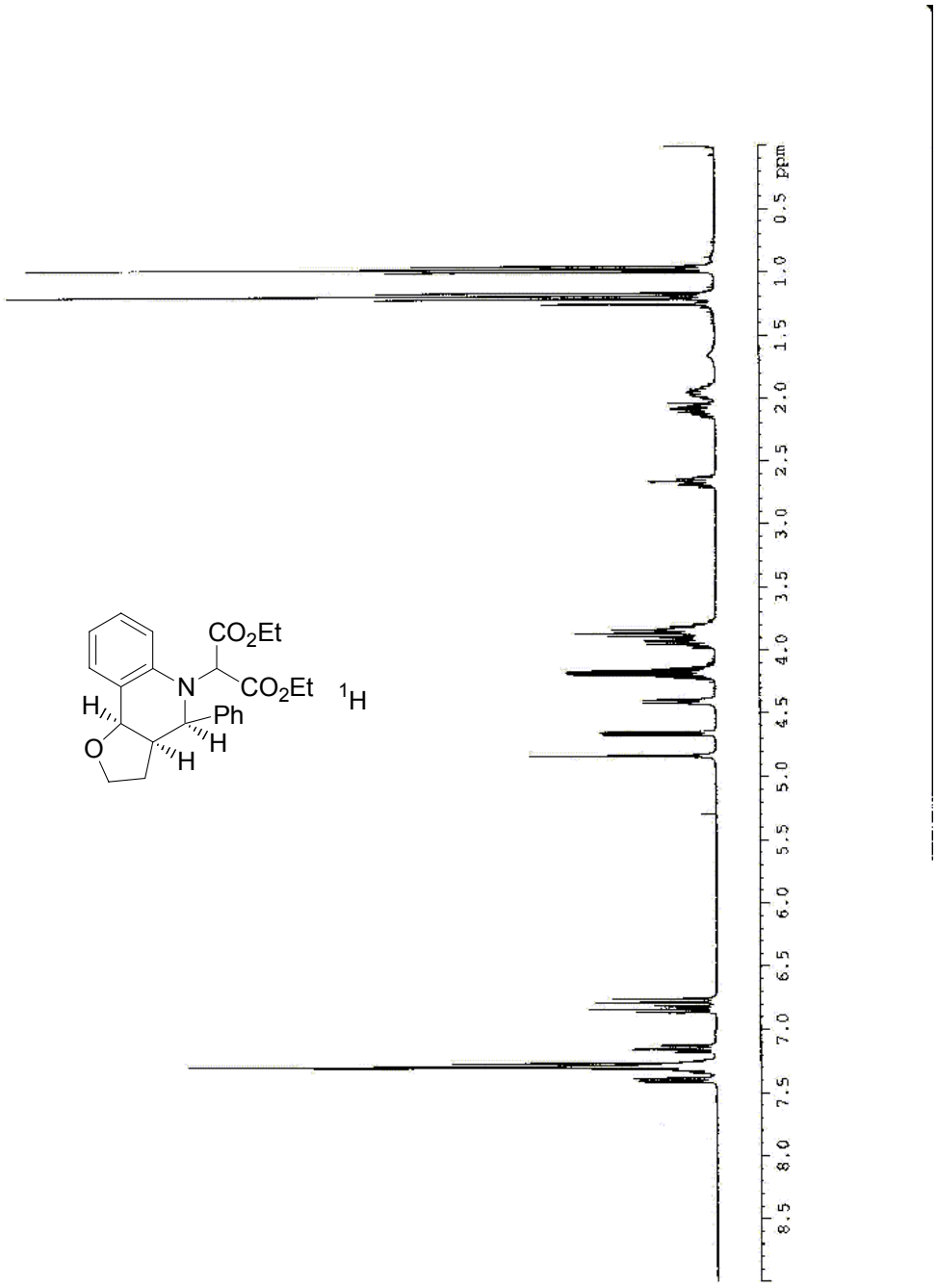
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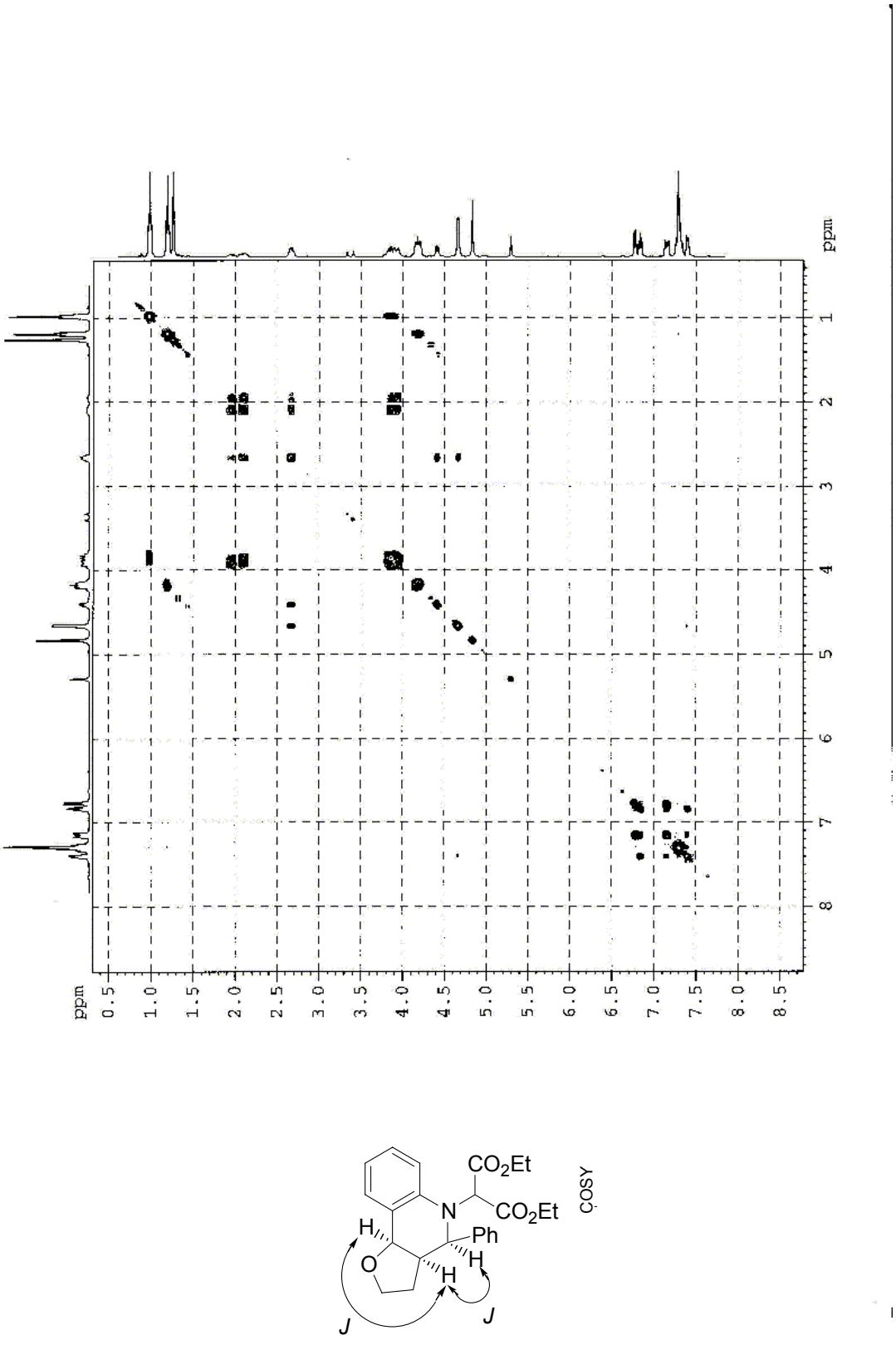
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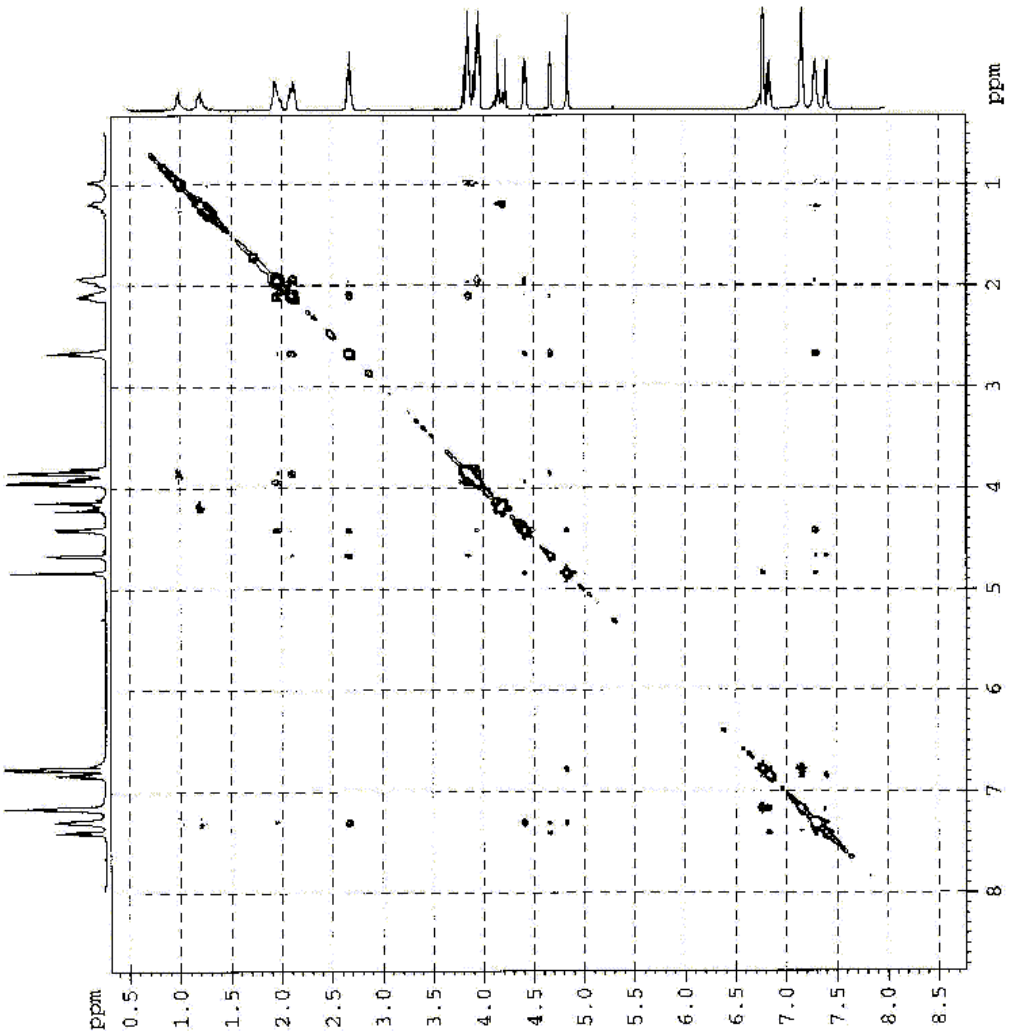
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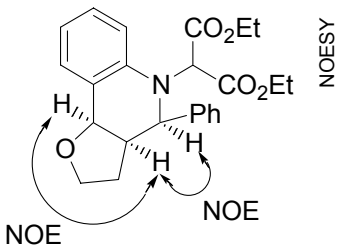
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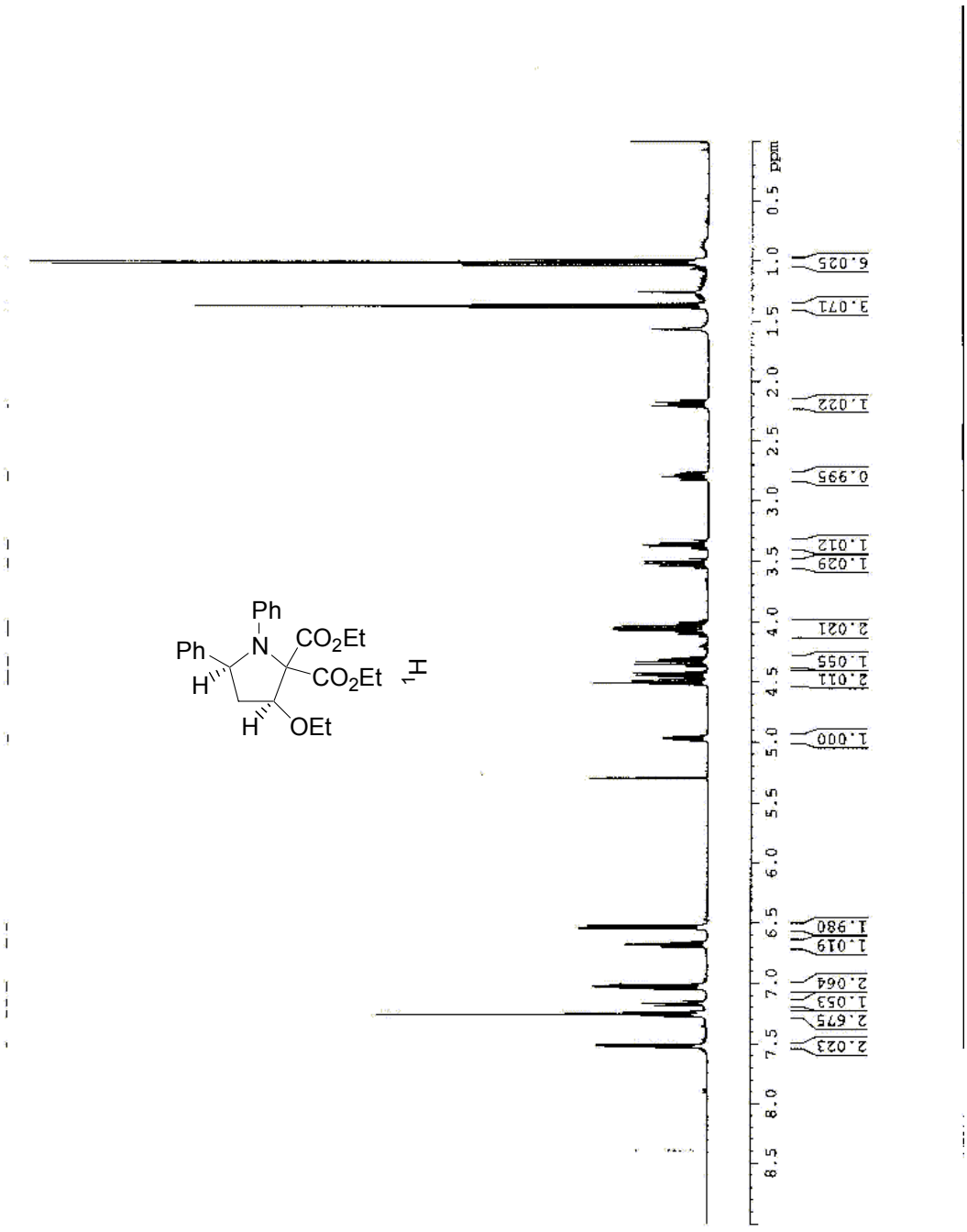
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1.5
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2.5
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1.022
0.995
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1.000
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1.019
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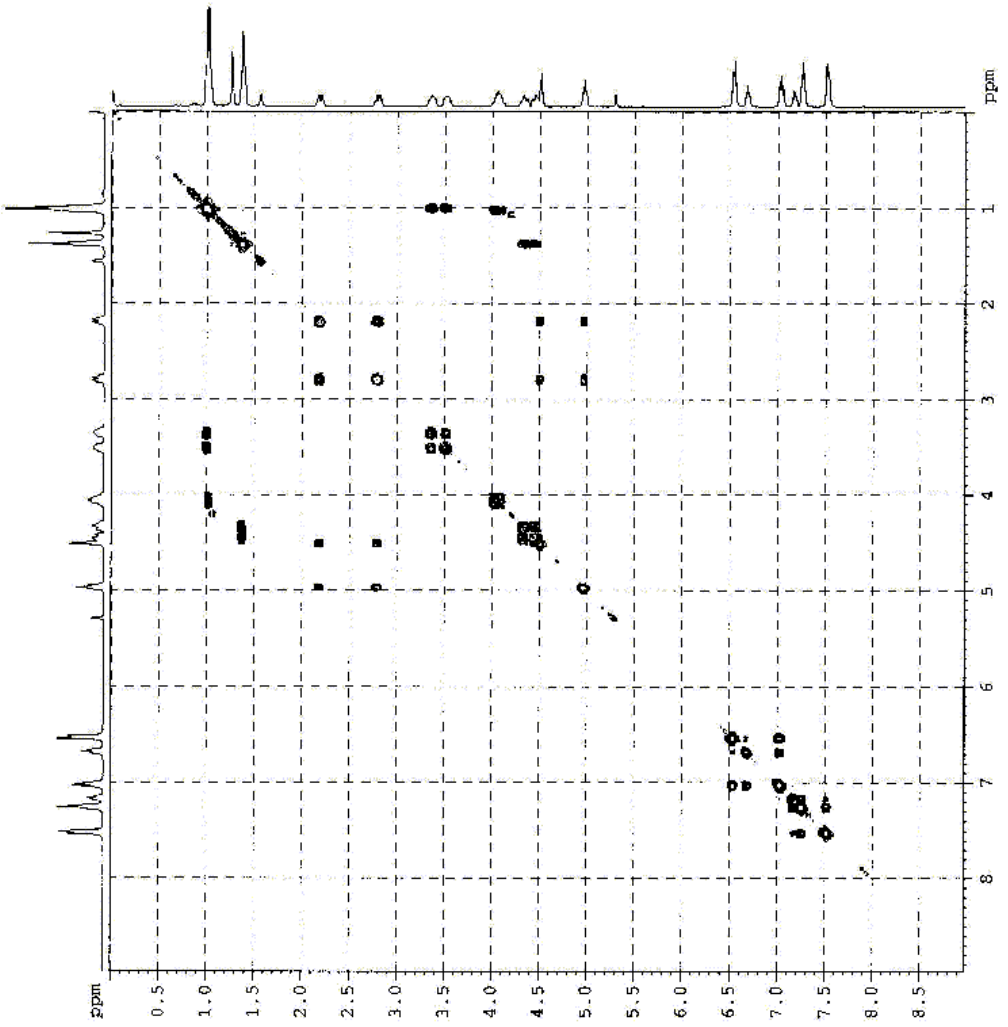
2.023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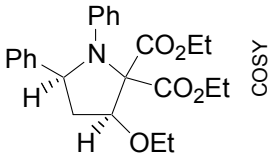
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Ph
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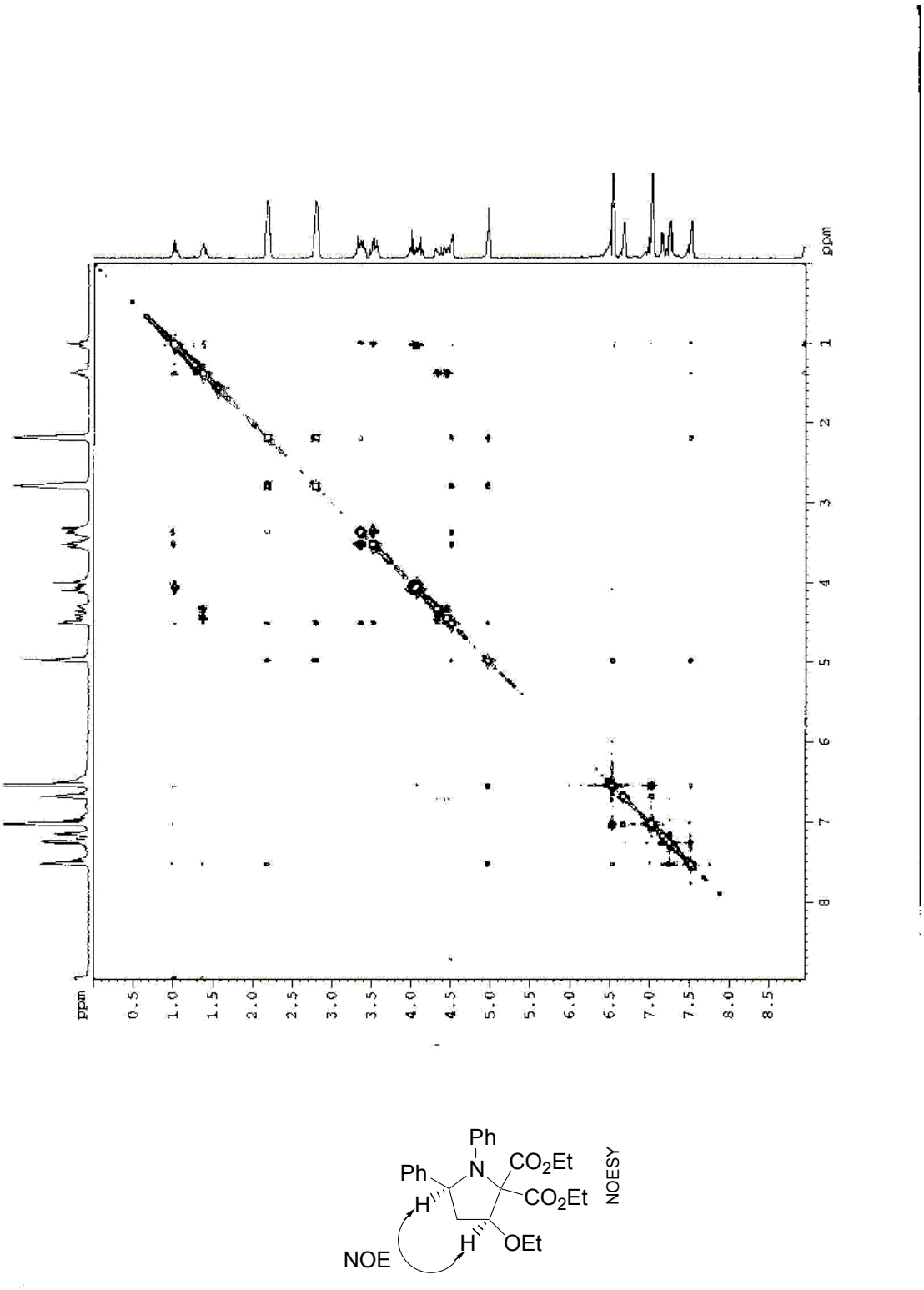
CO2Et
CO2Et
H
OEt

COSY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6.5
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7.5
8.0
8.5
ppm
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7
8
Ph
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CO2Et
CO2Et
Ph
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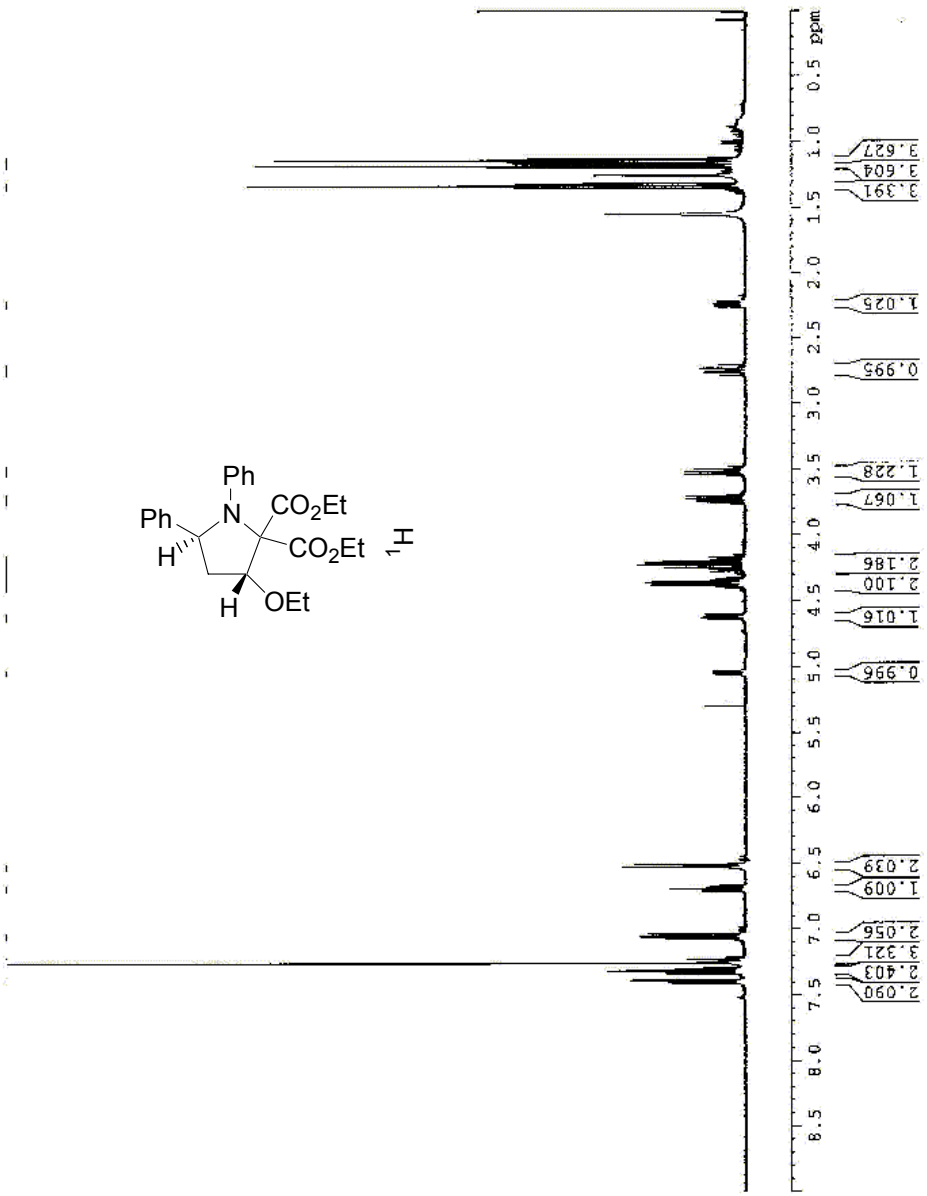
H
OEt
NOE
NOESY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CO2Et
CO2Et
Ph
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H
OEt
1H
ppm
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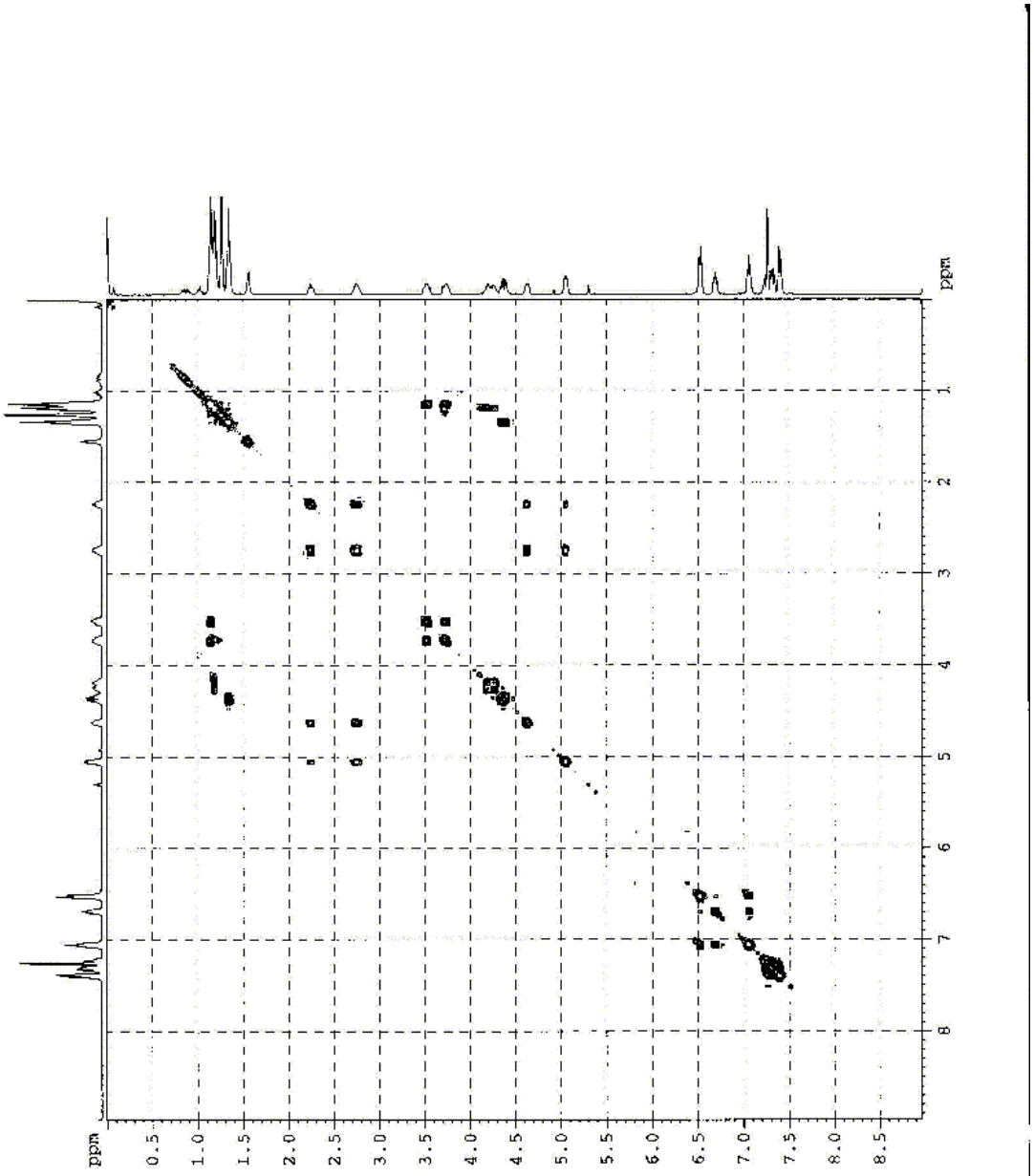
2.090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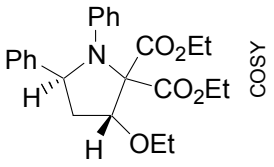
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Ph
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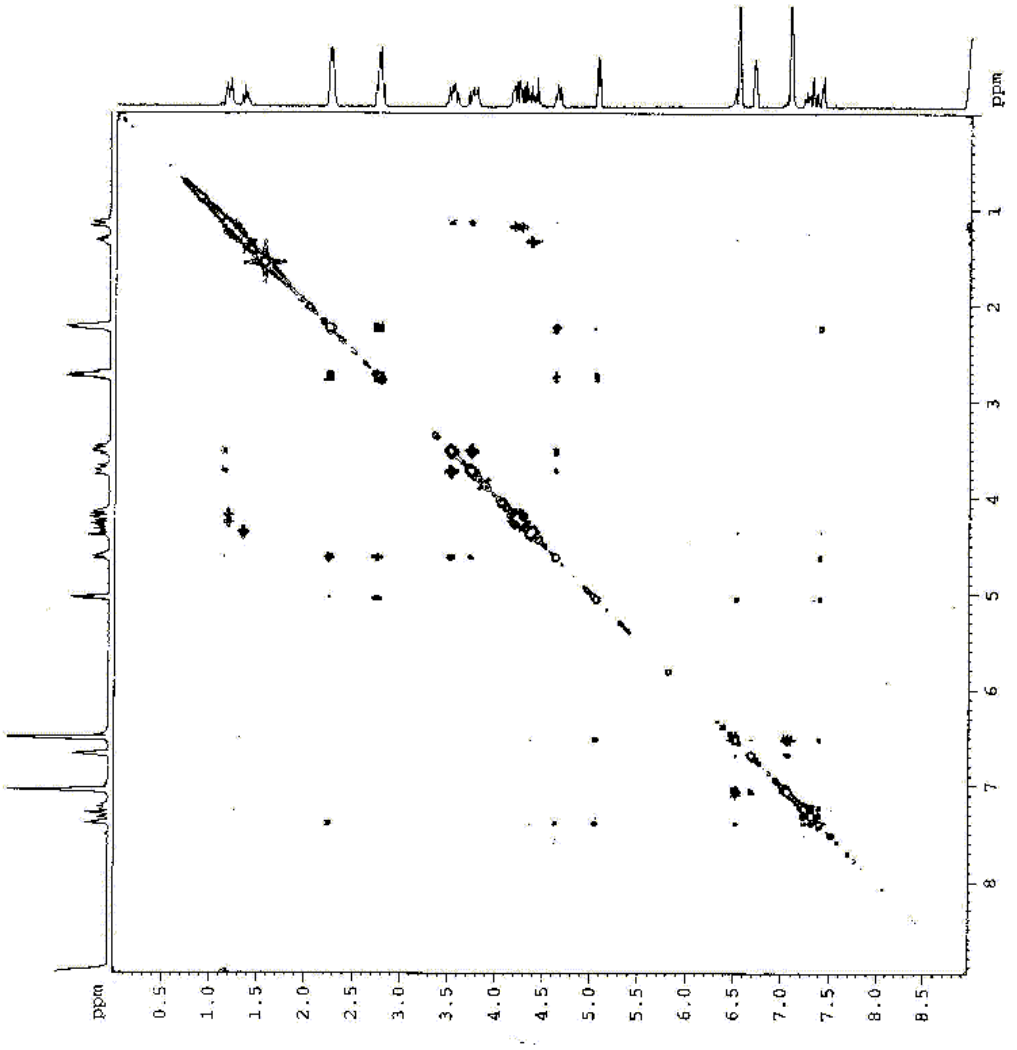
CO2Et
CO2Et
H
OEt

COSY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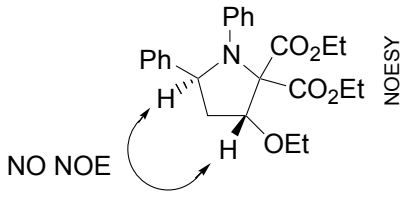
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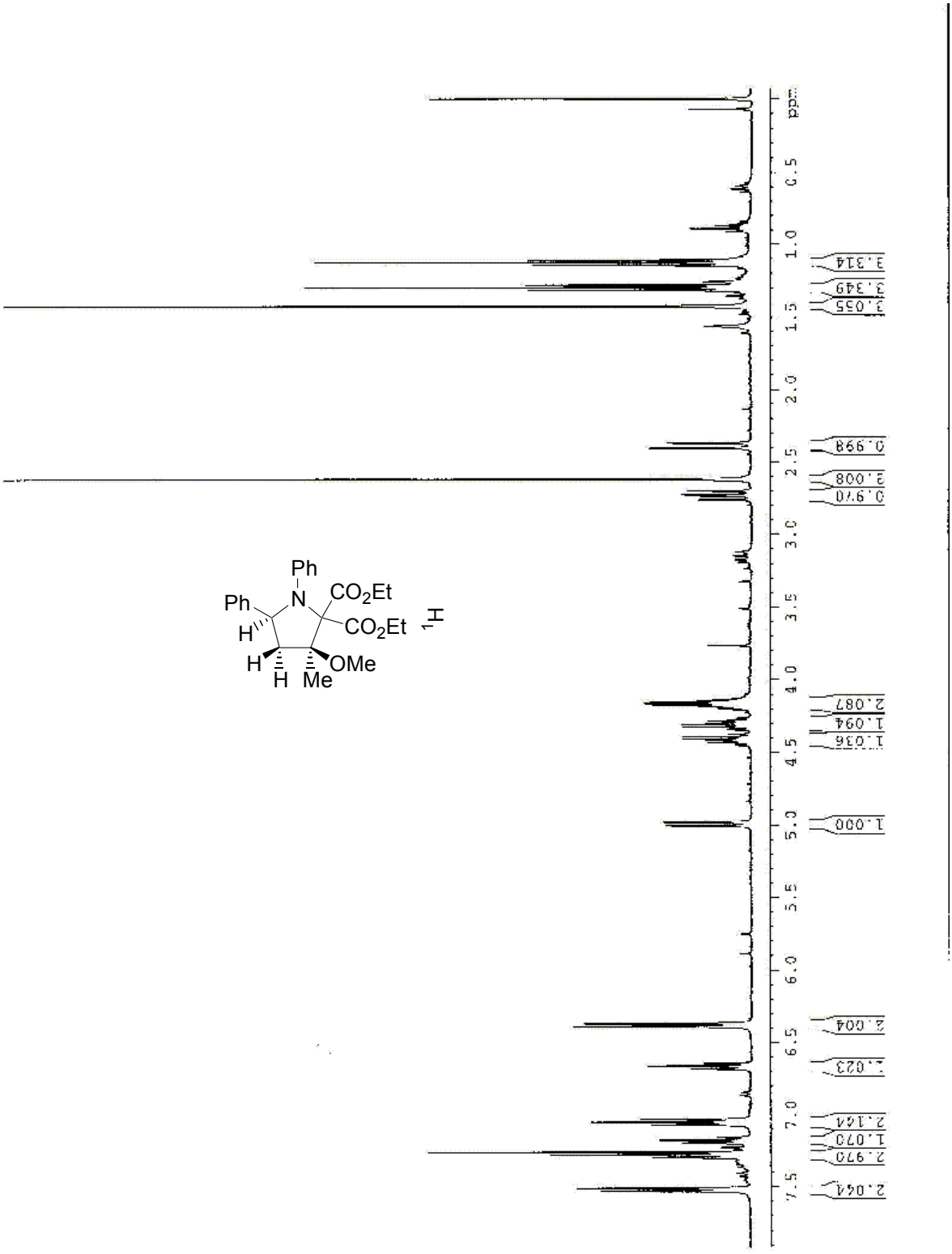
CO2Et
CO2Et
Ph
H
H
OEt
NO NOE
NOESY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CO2Et
CO2Et
Ph
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H
H
Me
OMe
1H
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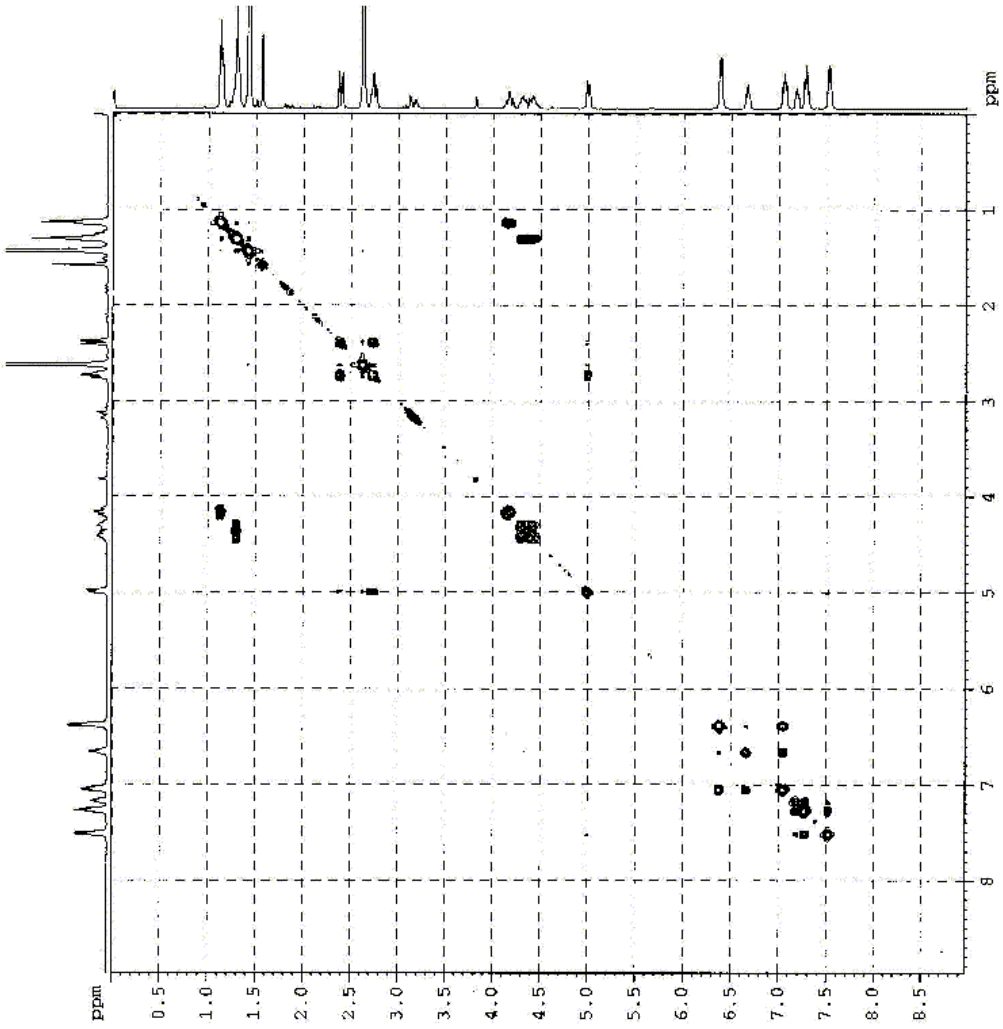
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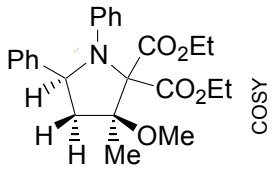
7
8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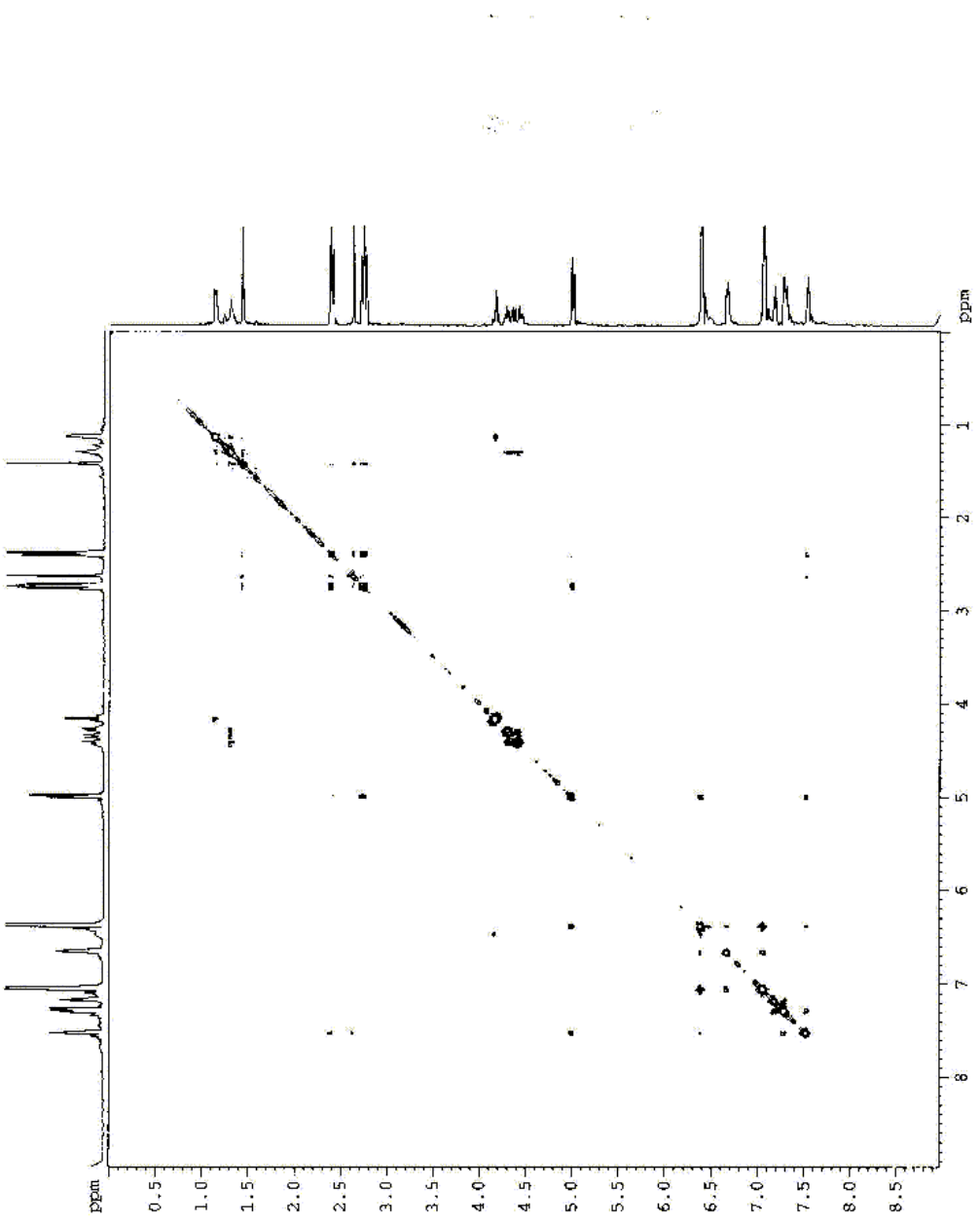
CO2Et
CO2Et
Ph
H
H
H
OMe
Me
COSY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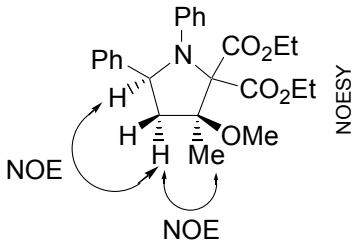
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CO2Et
CO2Et
Ph
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H
OMe
H
Me
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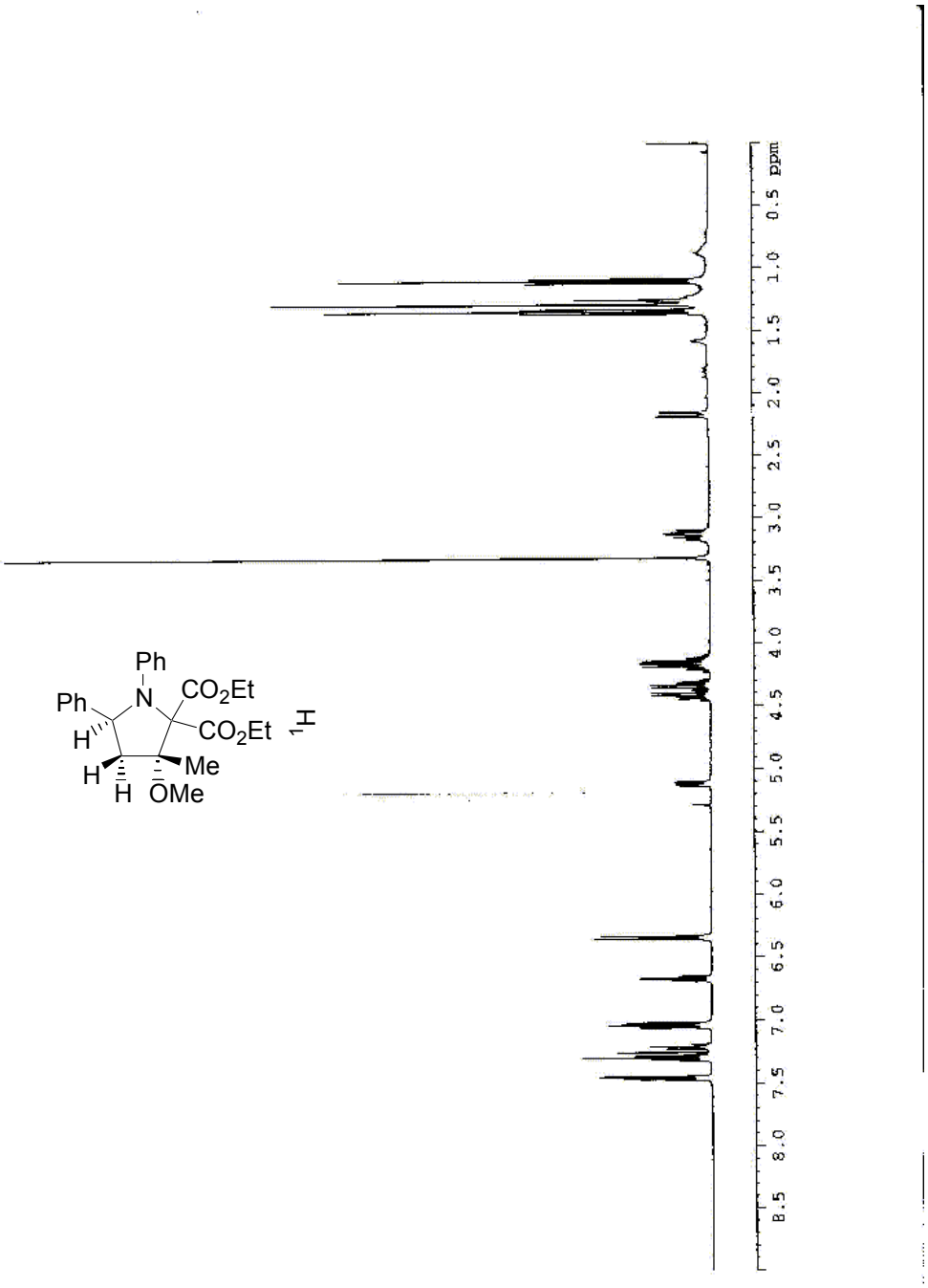
NOE
NOESY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CO2Et
CO2Et
Ph
H
H
H
Me
OMe
1H
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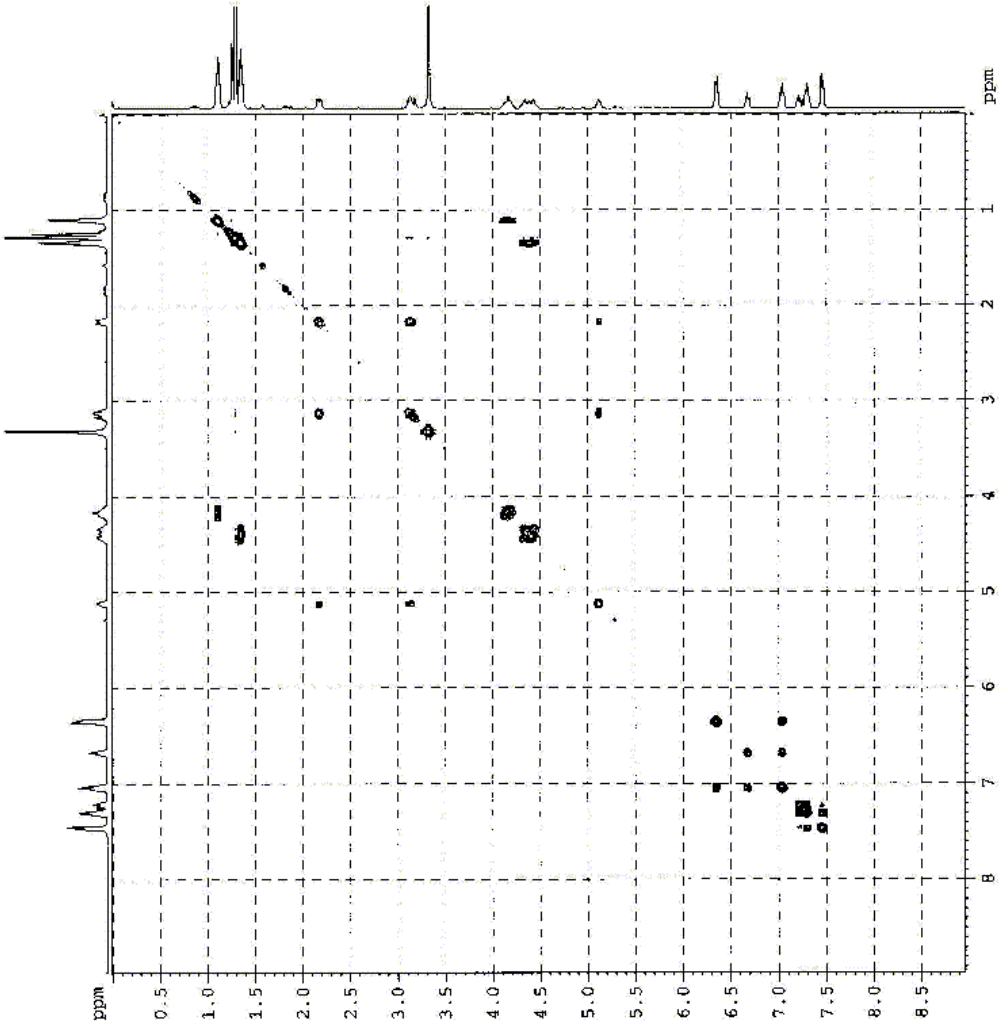
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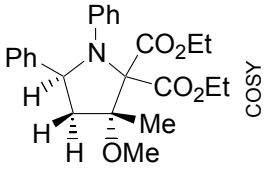
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CO2Et
CO2Et
Ph
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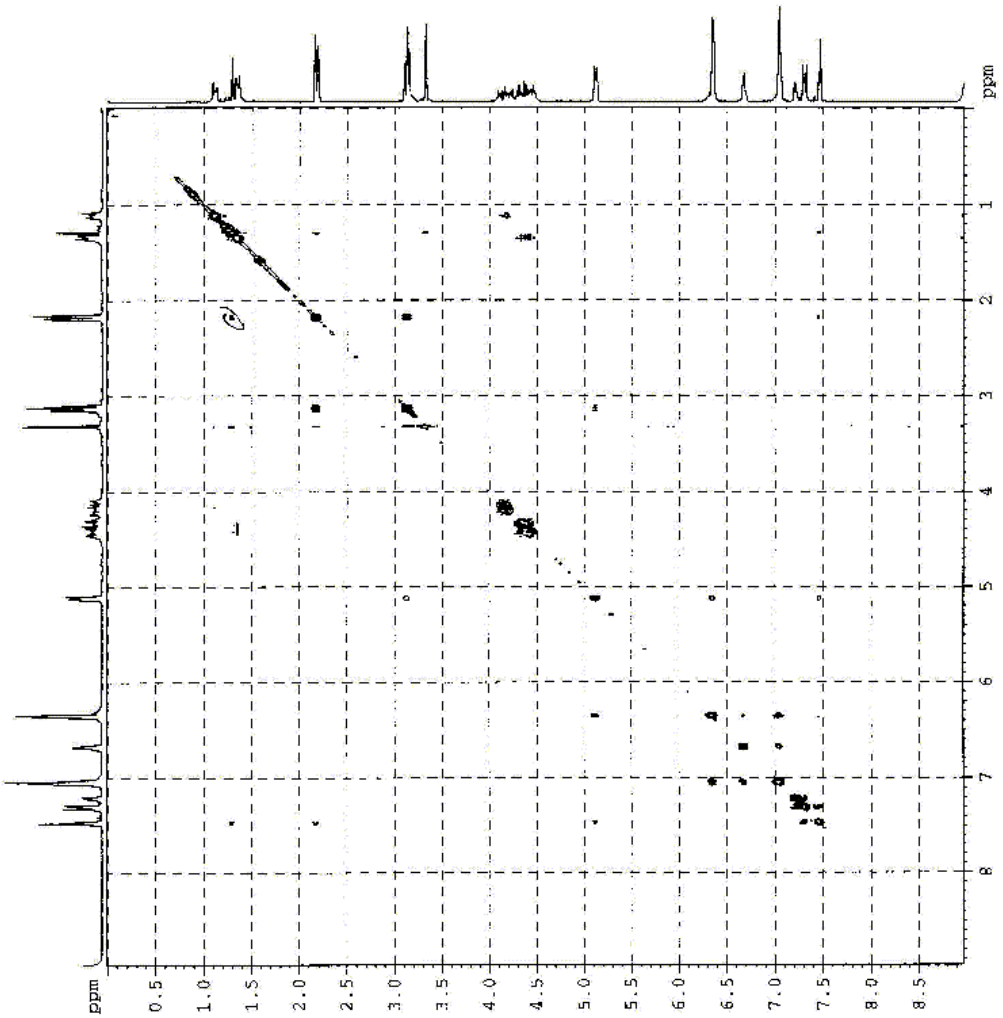
H
Me
H
OMe

COSY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ppm
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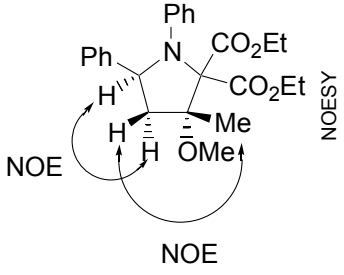
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CO2Et
CO2Et
Ph
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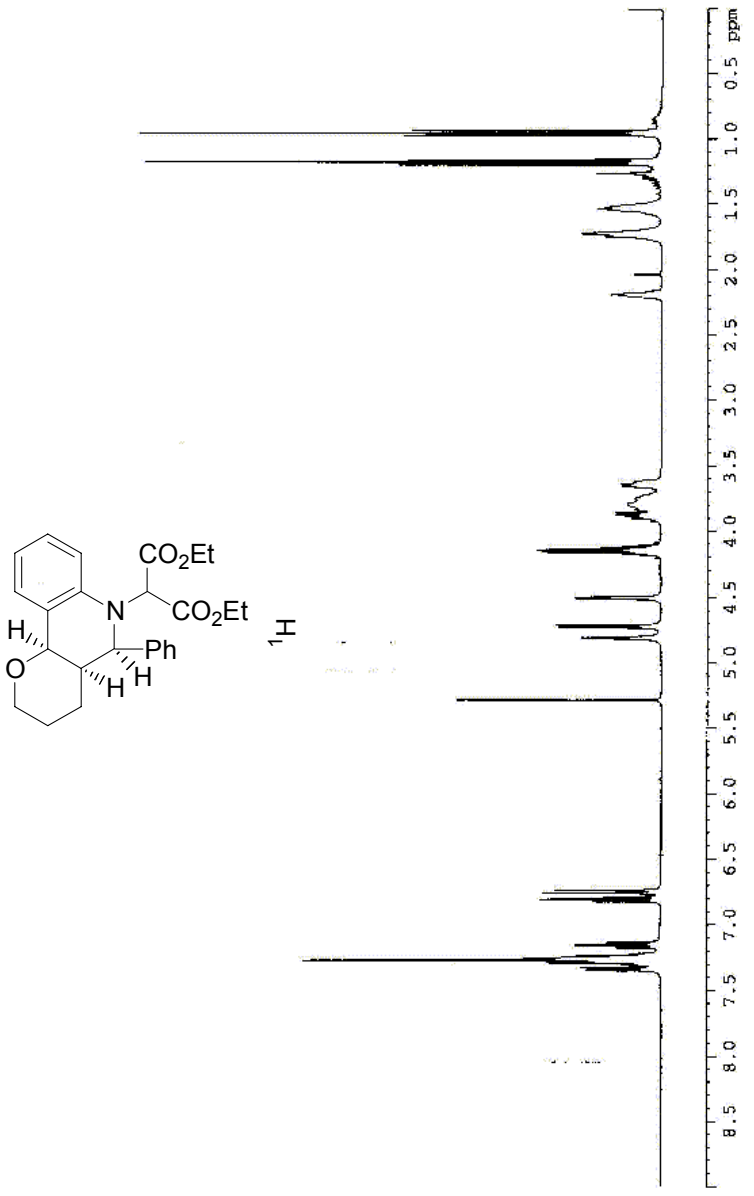
Me
H
OMe
NOE
NOE
NOESY


CO2Et
CO2Et
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H
O
Ph
H
H
1H
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7.0
6.5
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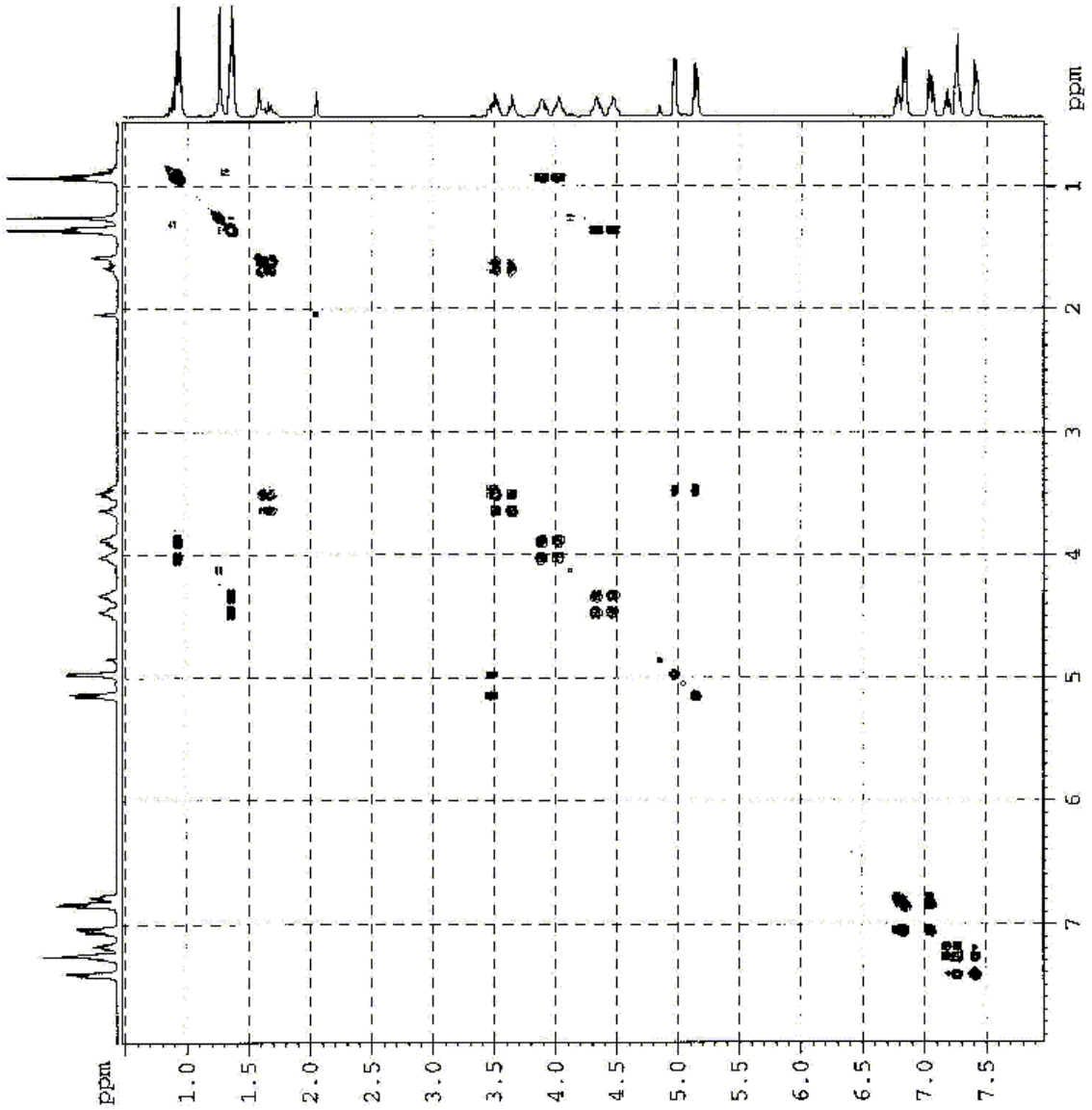
1.0
0.5
ppm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ppm
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6
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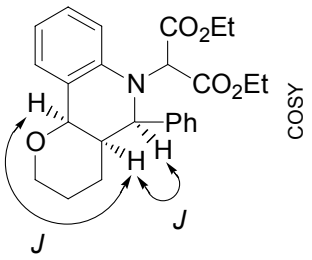
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CO2Et
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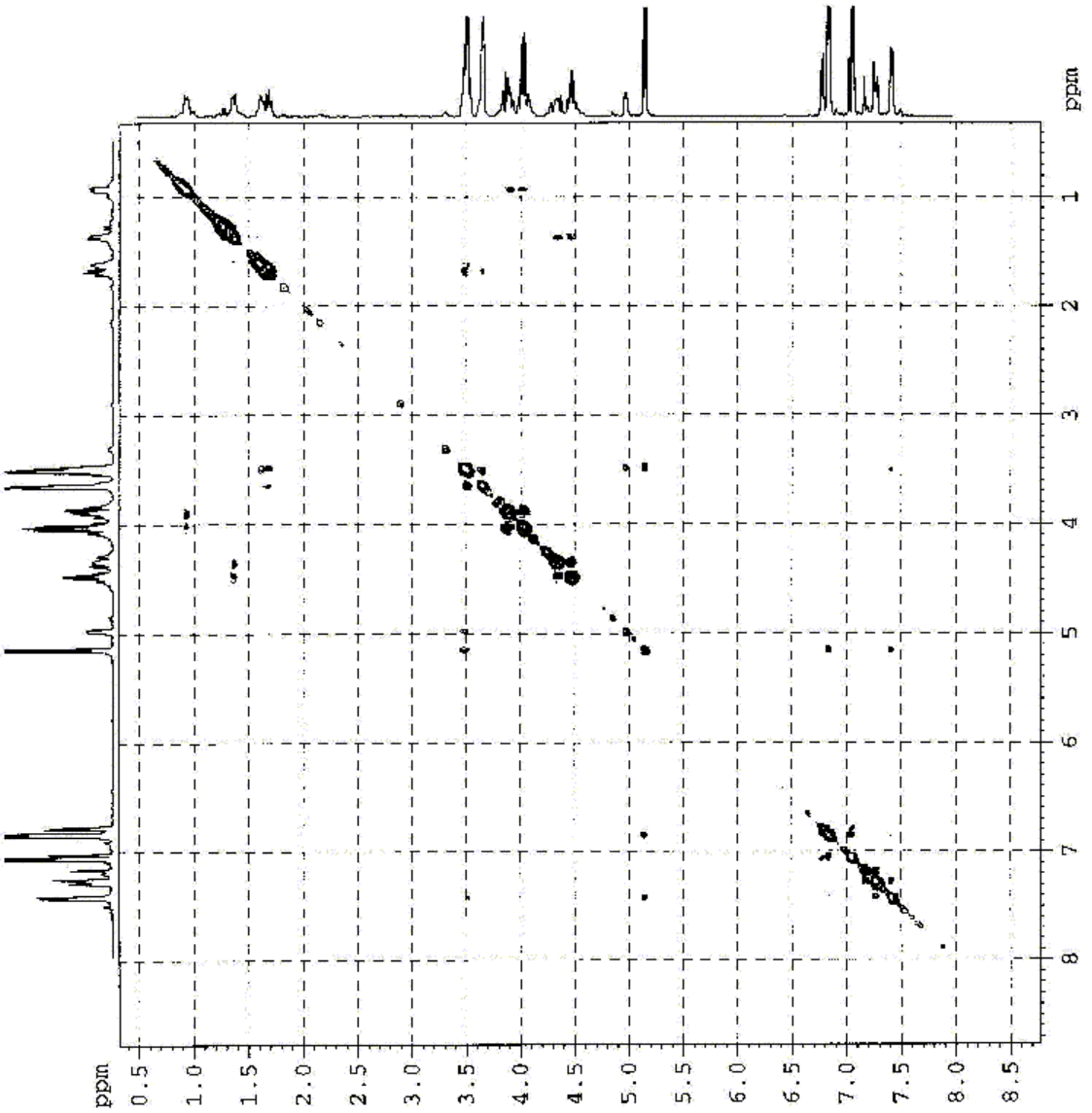
H
O
Ph
H
H
J
J

COSY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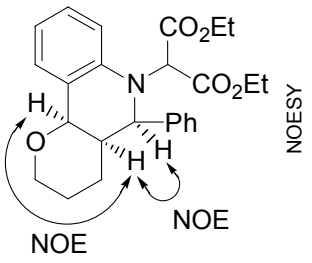
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CO2Et
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Ph
O
H
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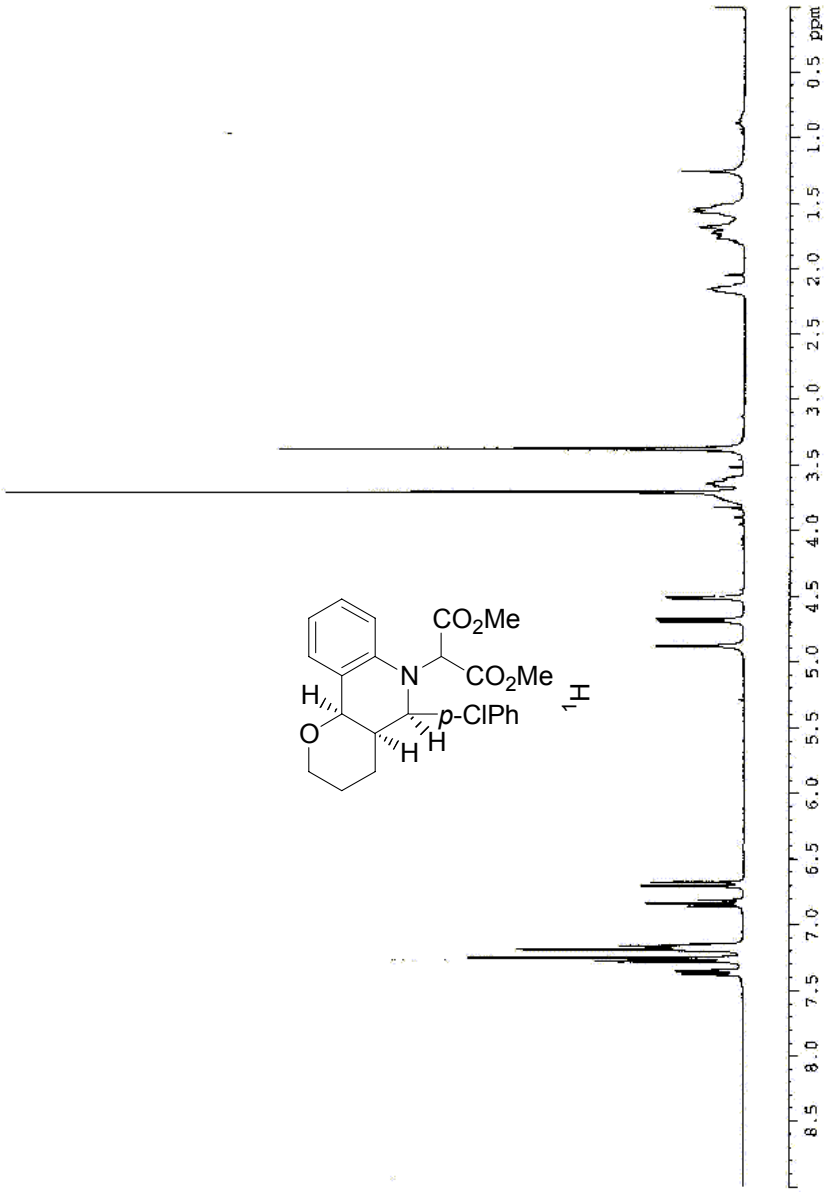
NOE
NOESY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CO2Me
H
O
p-ClPh
H
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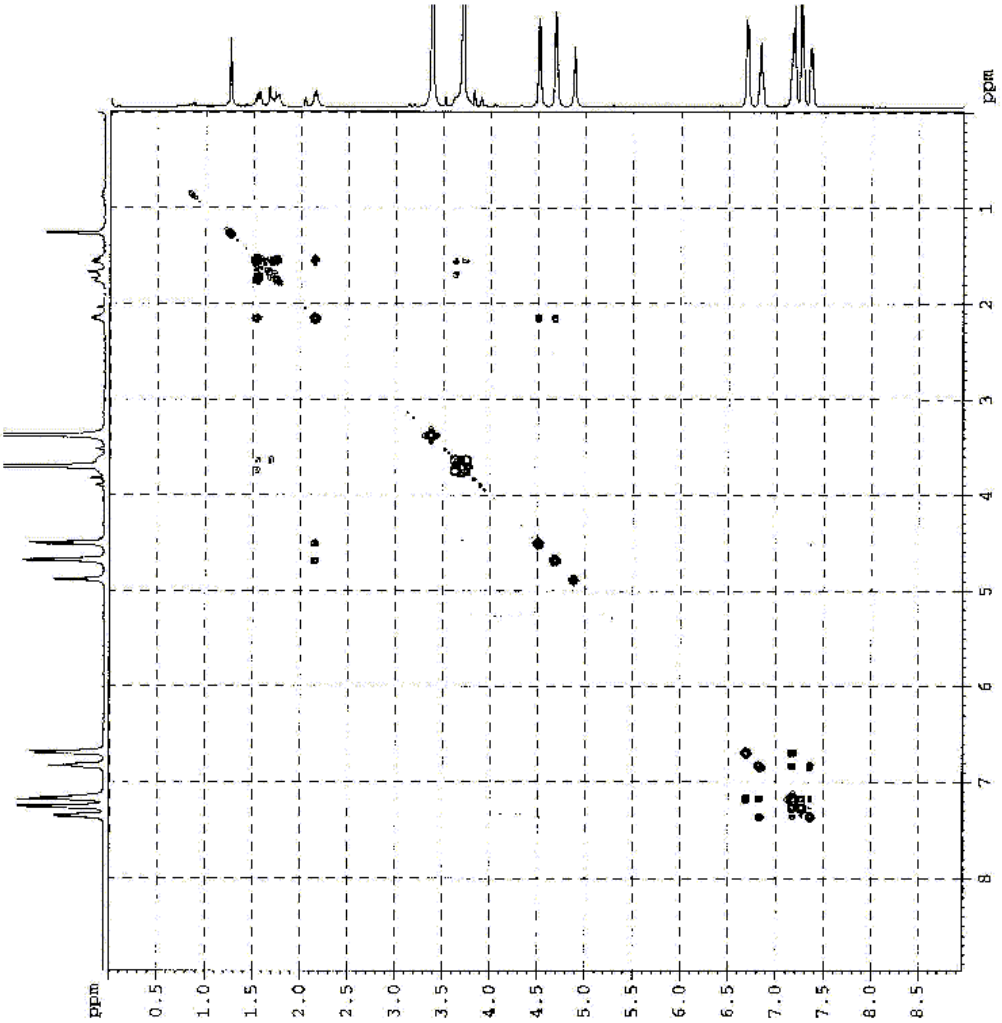
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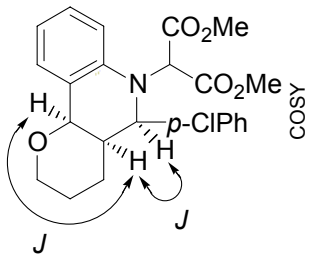
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CO2Me
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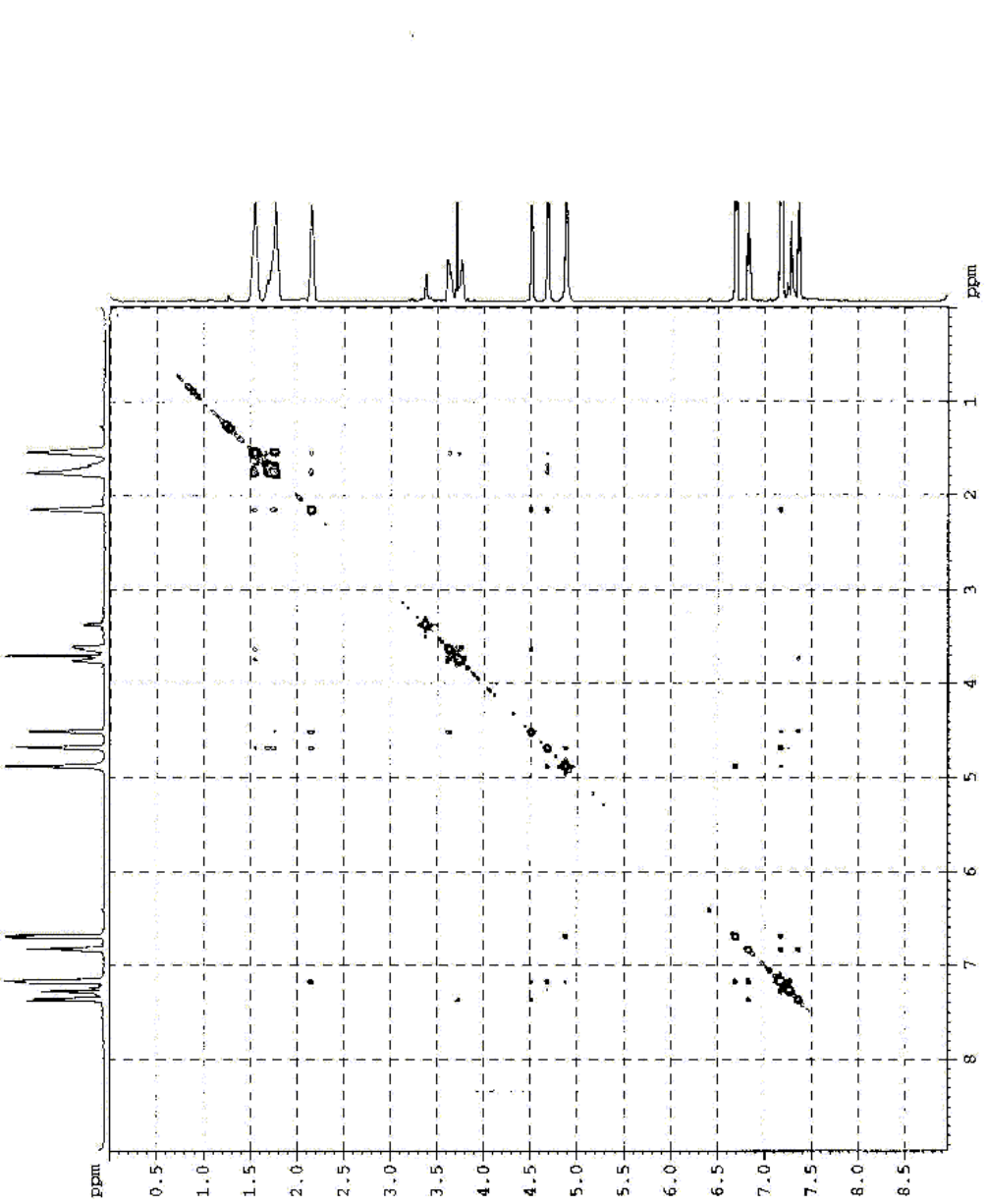
J
COSY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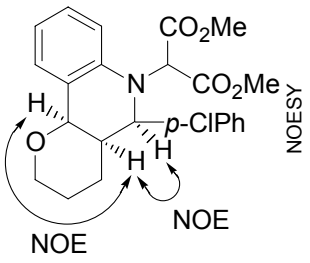
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CO2Me
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O
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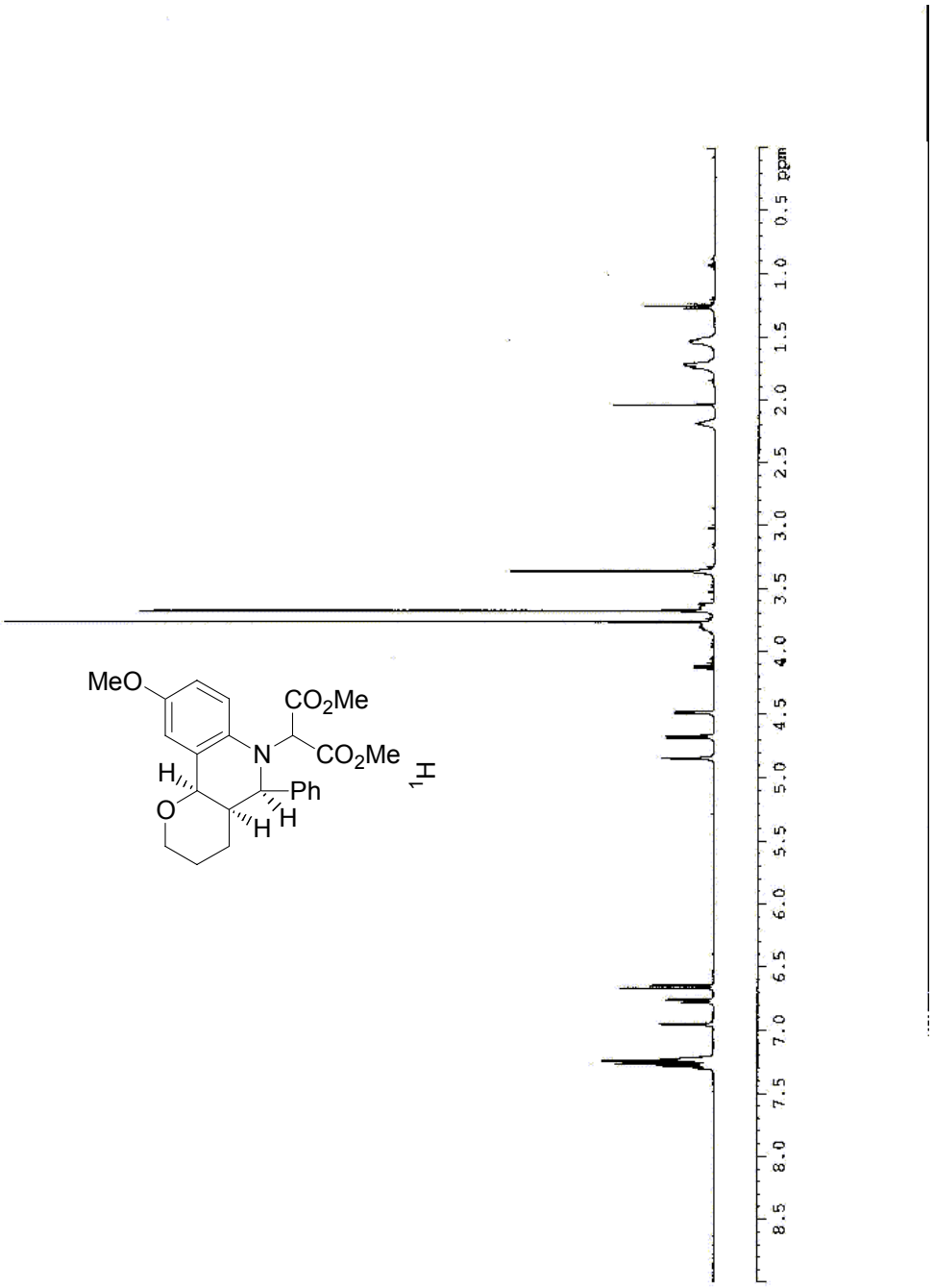
NOE
NOESY


MeO
CO2Me
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CO2Me
H
Ph
O
H
H
1H
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7.5
7.0
6.5
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1.0
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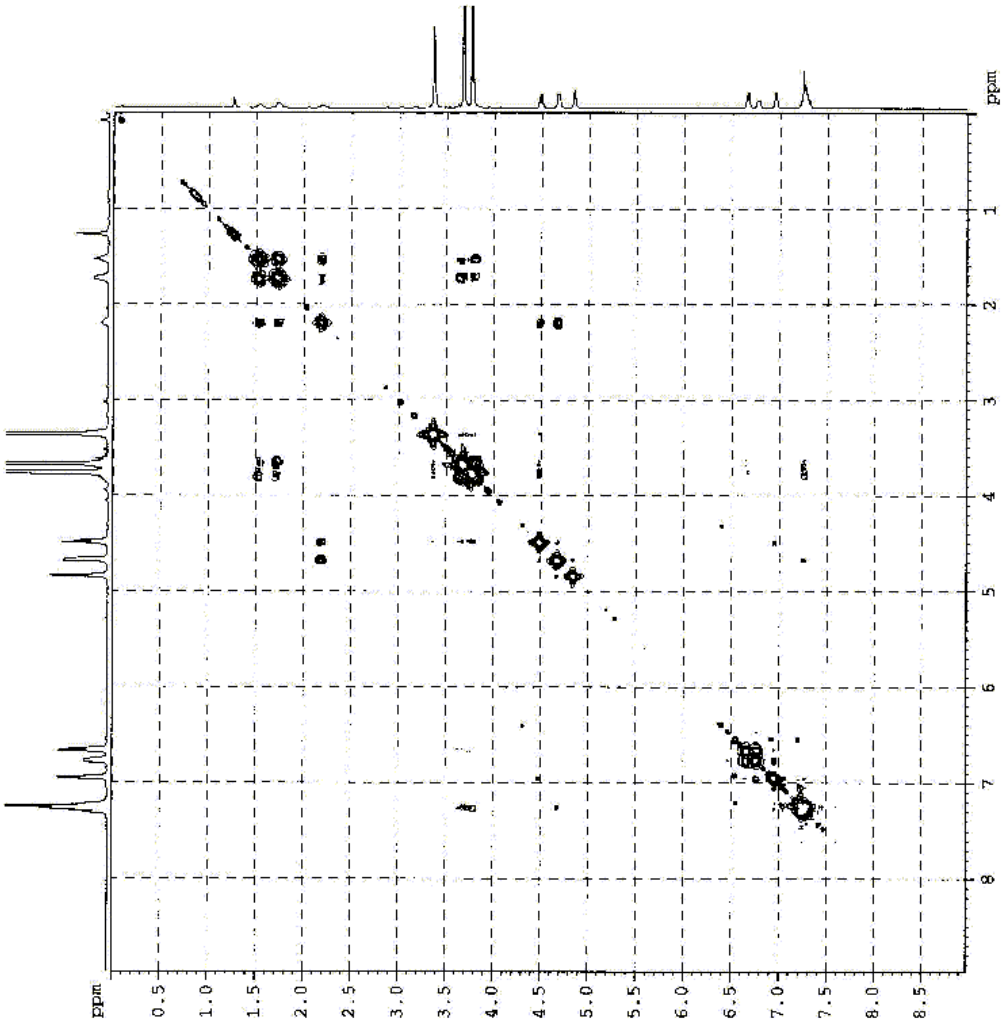
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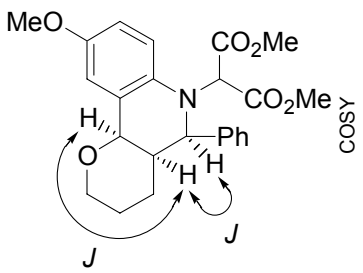
MeO
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CO2Me
H
Ph
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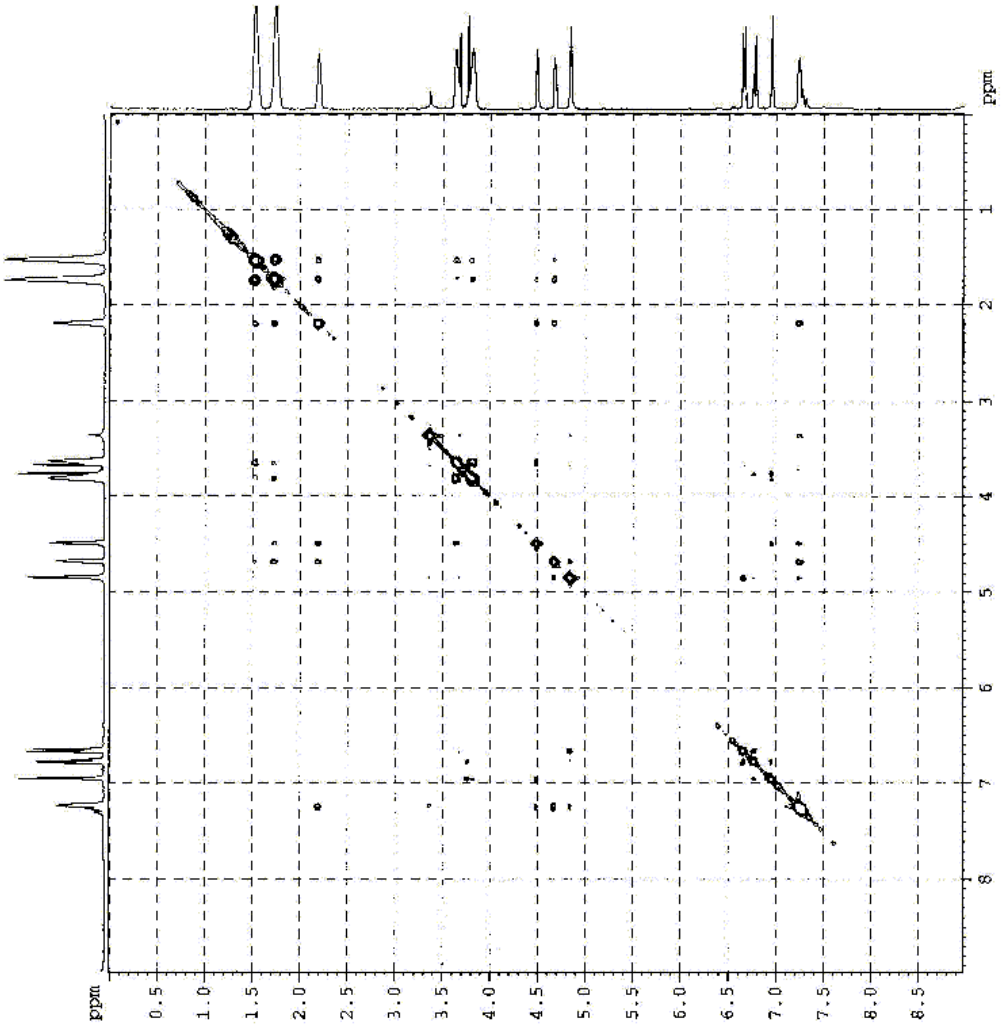
H
H
J
J
COSY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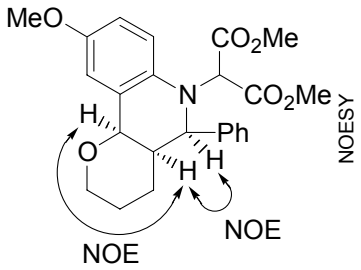
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CO2Me
N
CO2Me
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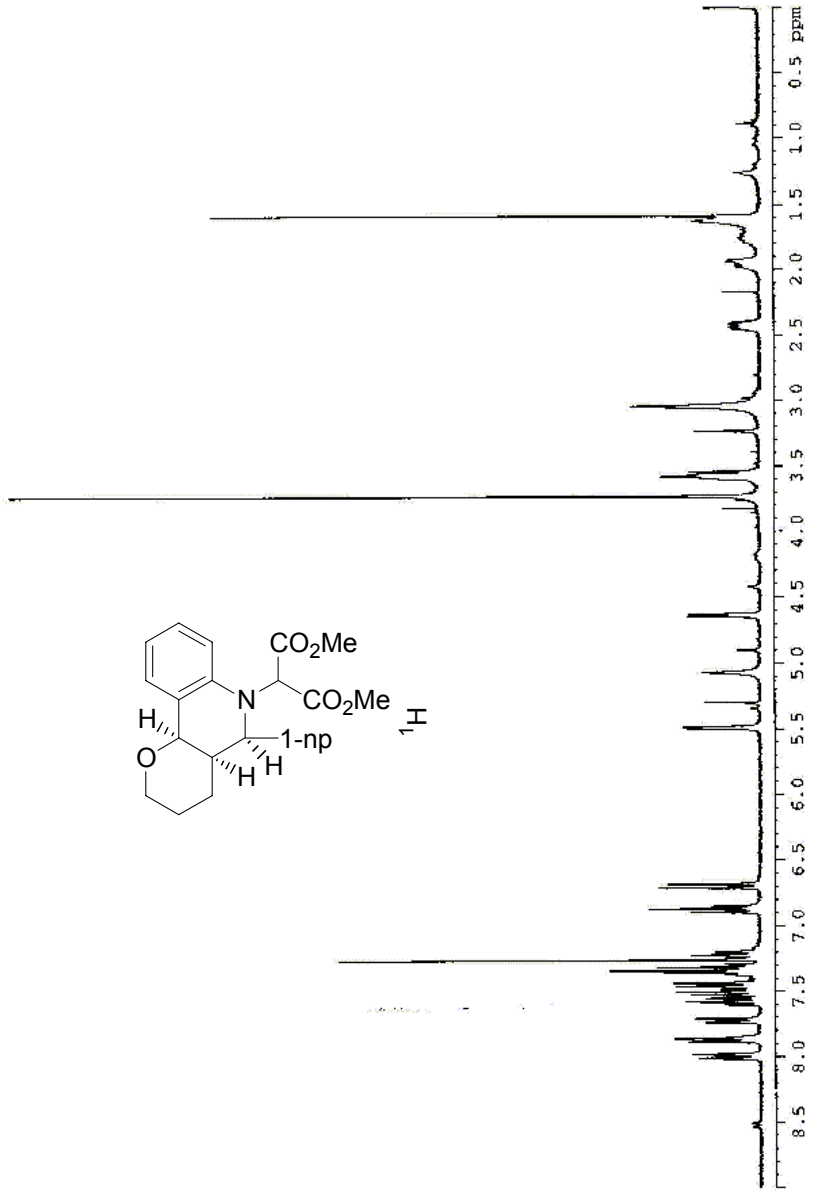
NOE
NOESY


CO2Me
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CO2Me
H
1-np
O
H
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1H
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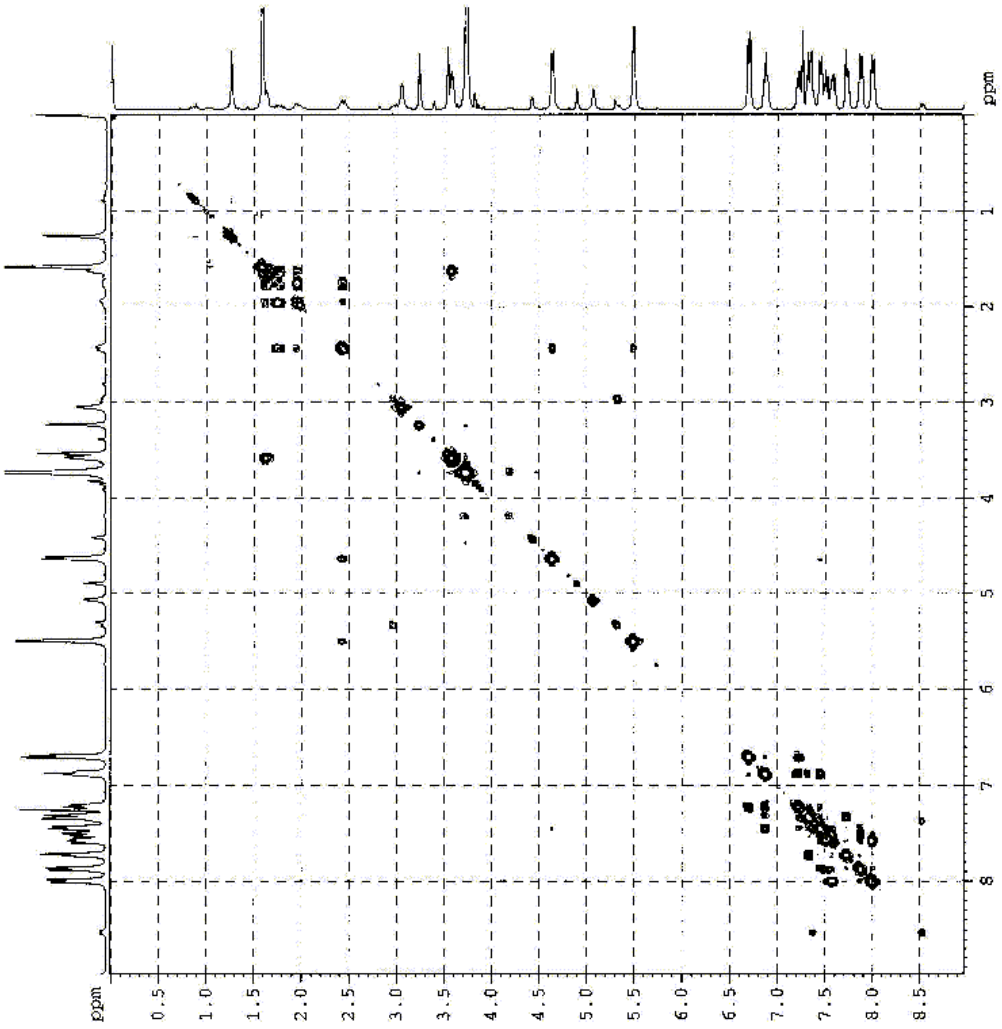
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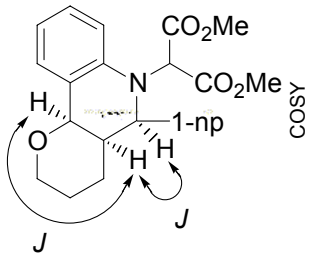
CO2Me
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CO2Me
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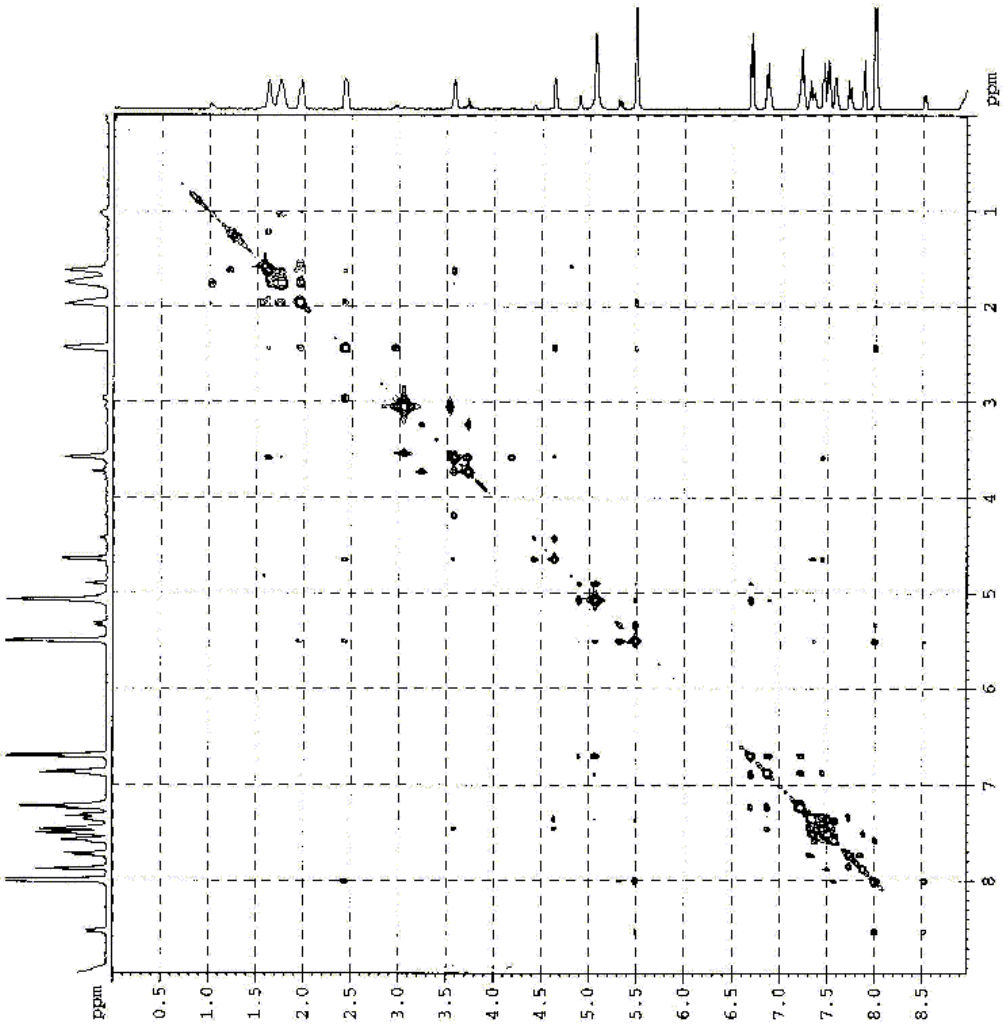
1-np
O
H
H
J
J
COSY


ppm
ppm
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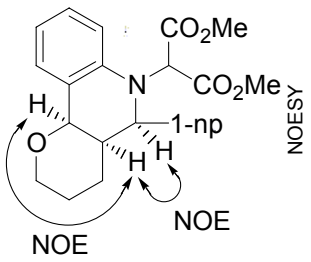
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CO2Me
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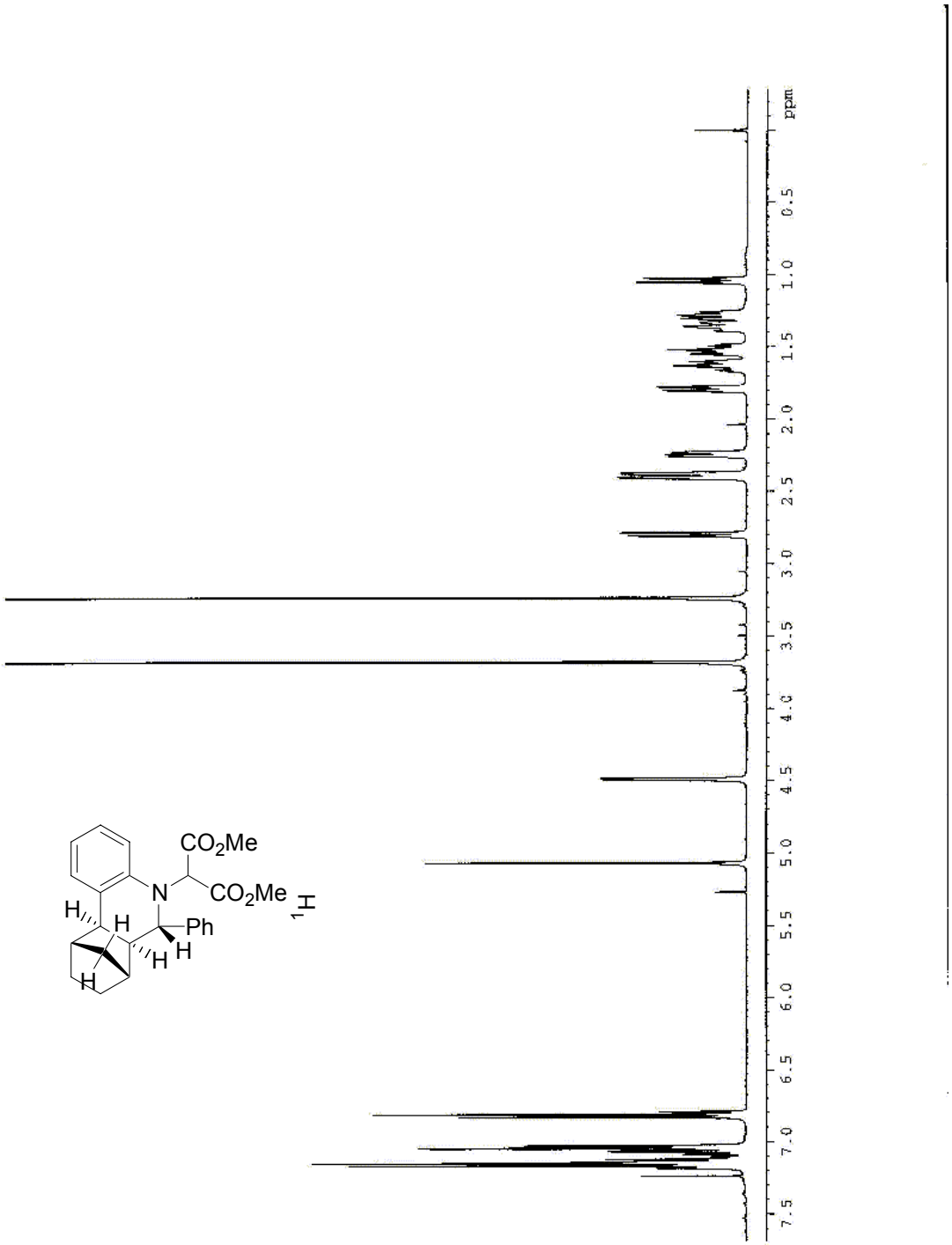
O
H
H
NOE
NOE
NOESY


CO2Me
CO2Me
N
H
H
Ph
H
H
H
1H
ppm
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1.5
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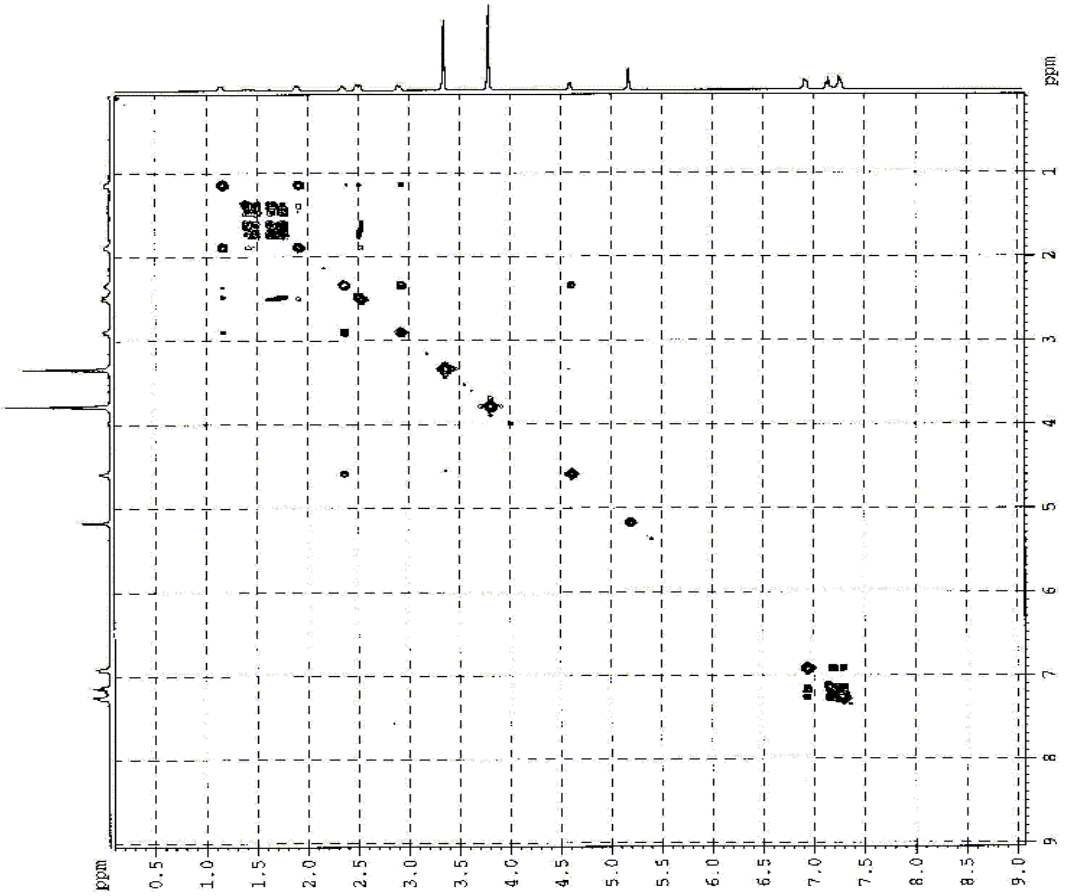
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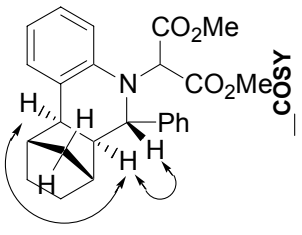
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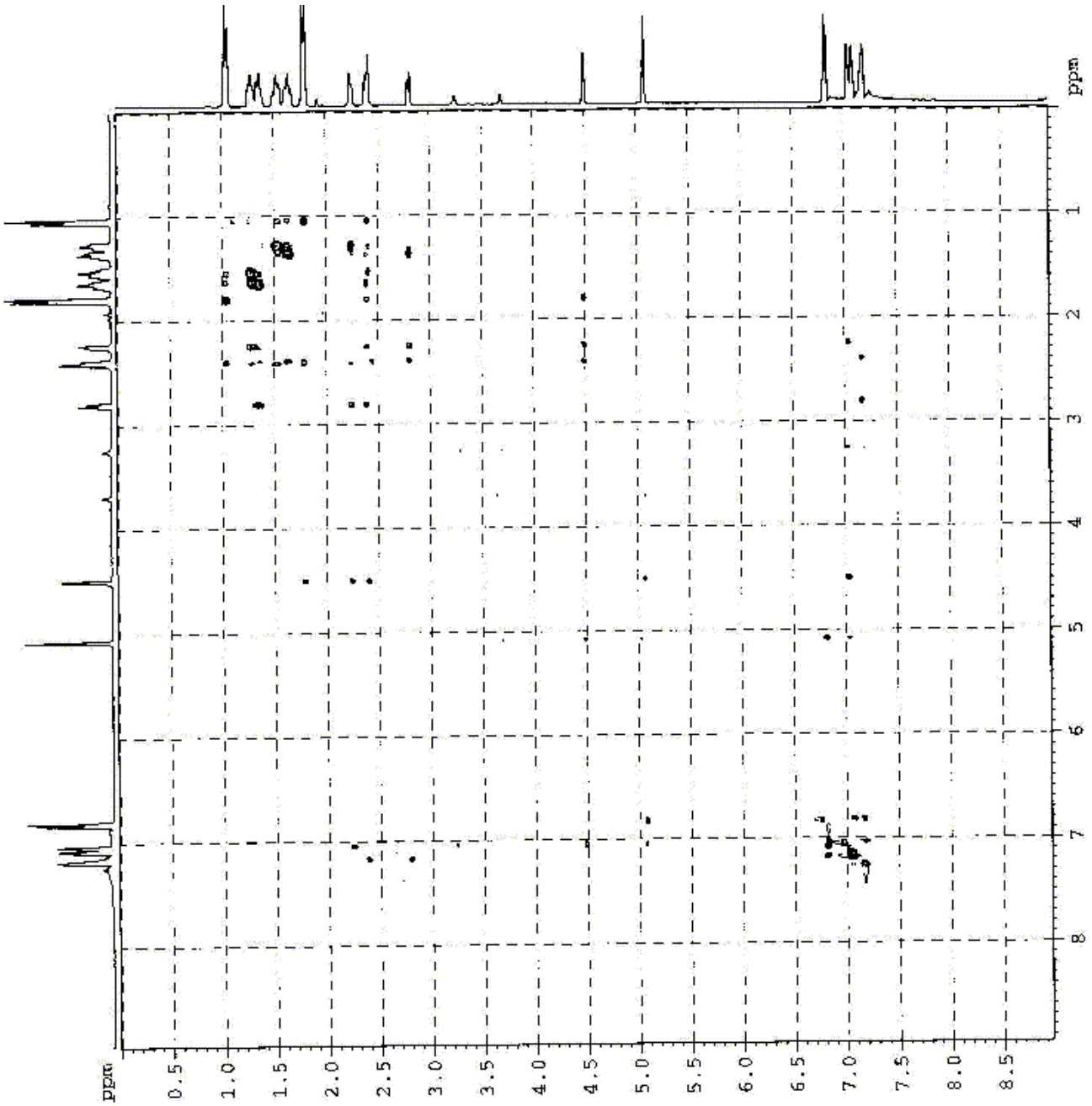
N
CO2Me
H
H
Ph
H
H
H
COSY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7
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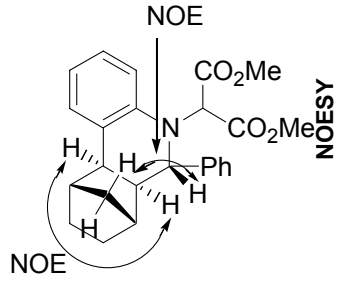
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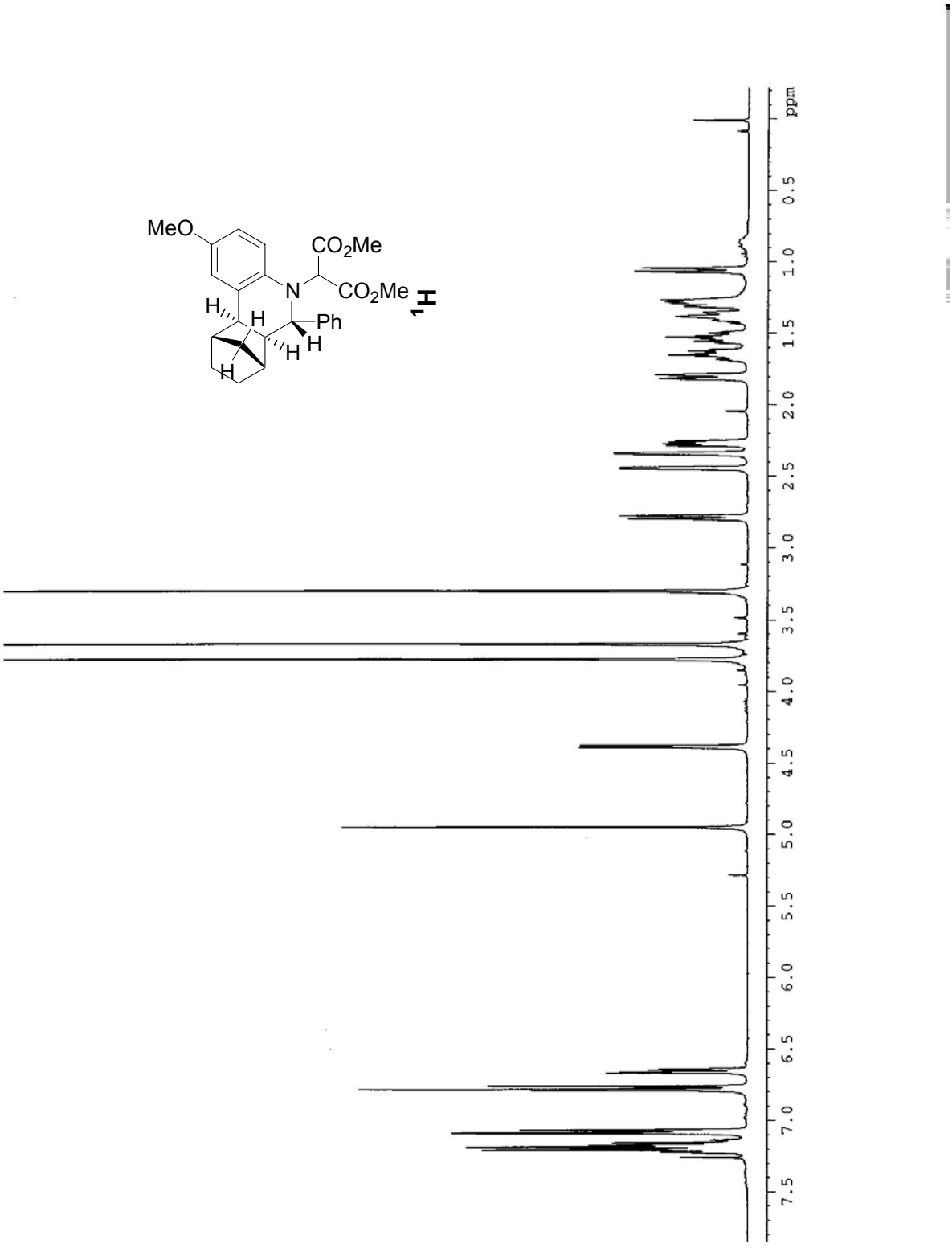
N
CO2Me
H
H
Ph
H
H
H
NOE
NOESY


MeO
CO2Me
N
CO2Me
H
H
Ph
H
H
H
1H
ppm
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1.5
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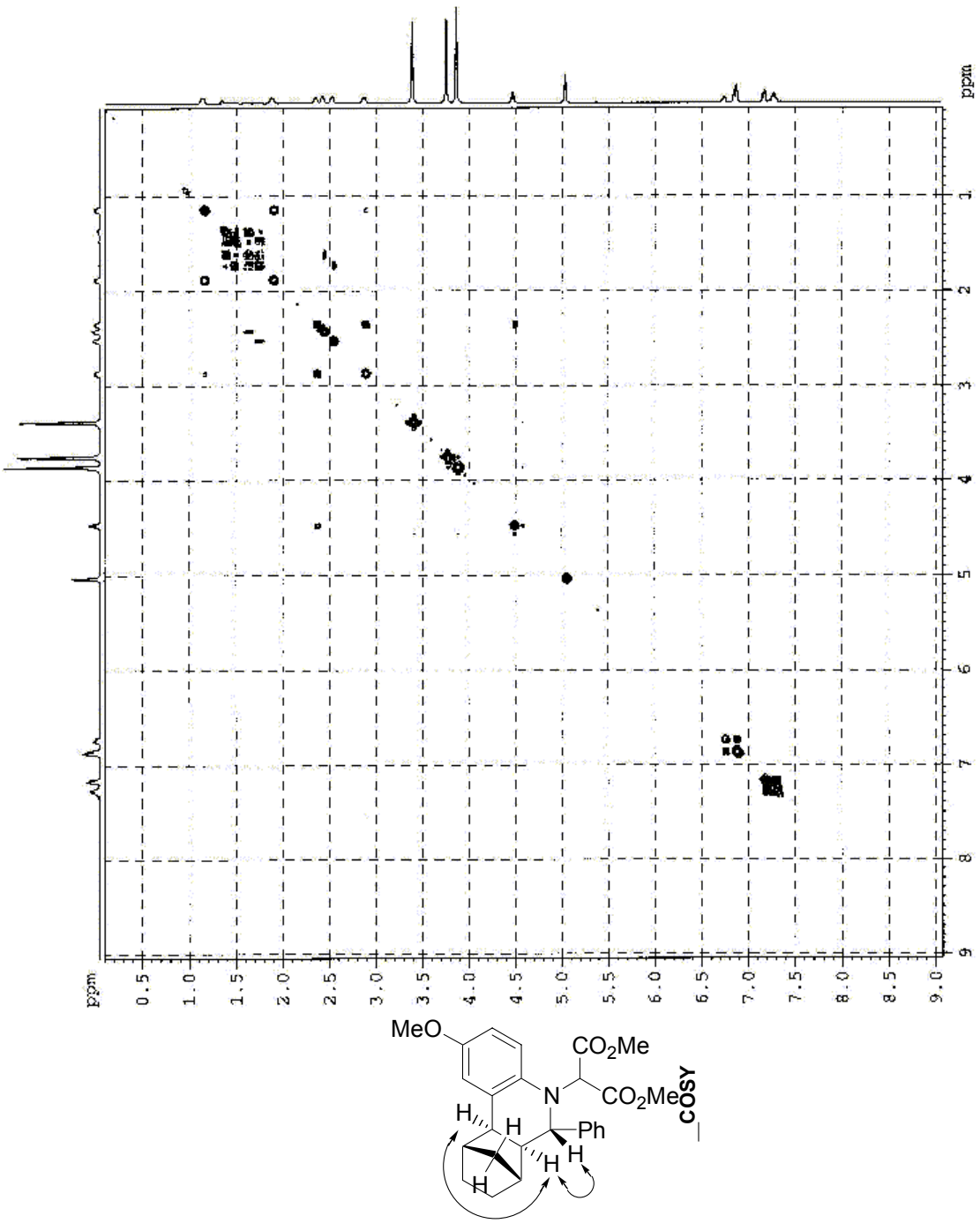
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6.5
7.0
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8.5
9.0
ppm
1
2
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8
9
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H
H
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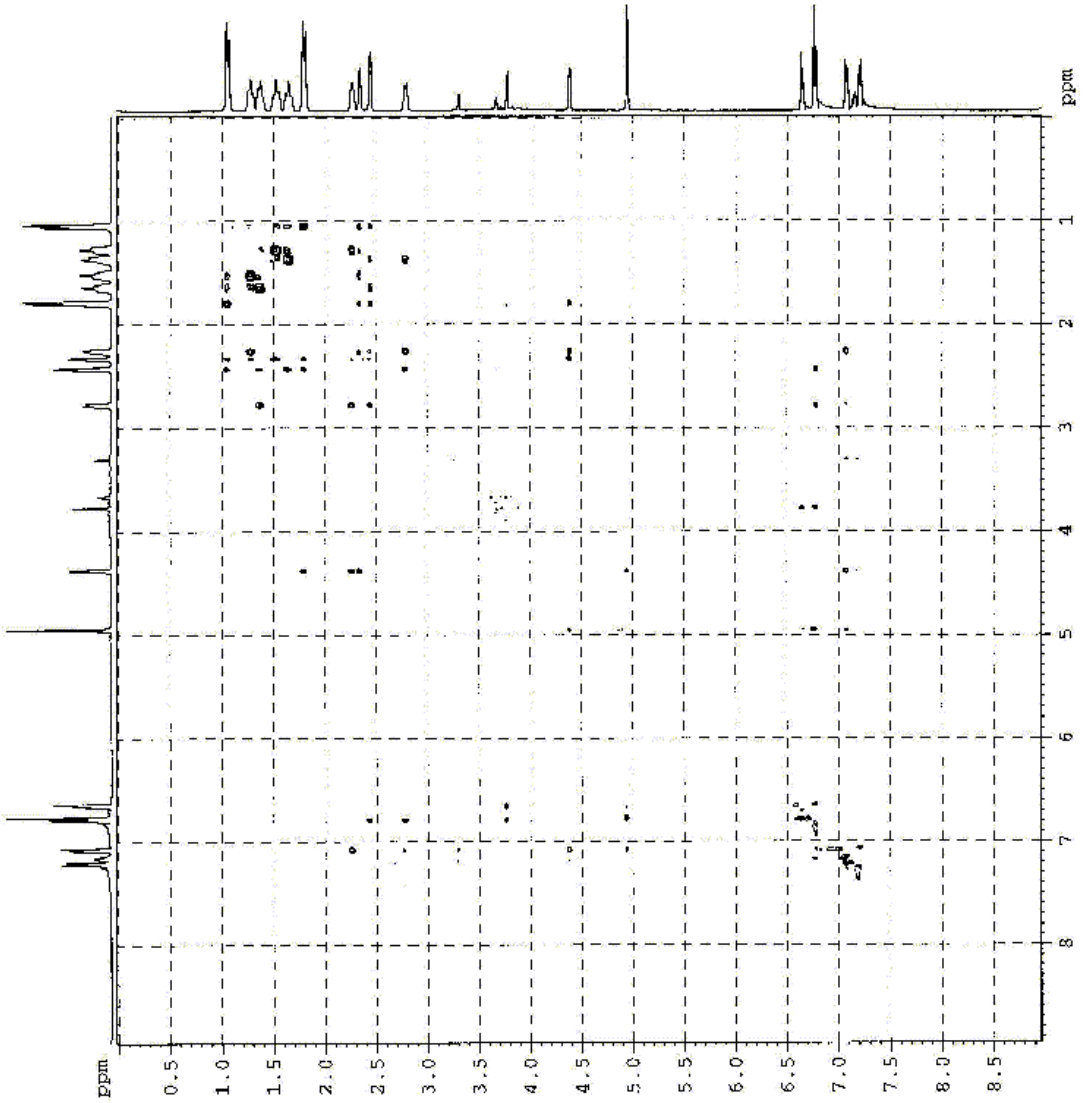
H
H
H
COSY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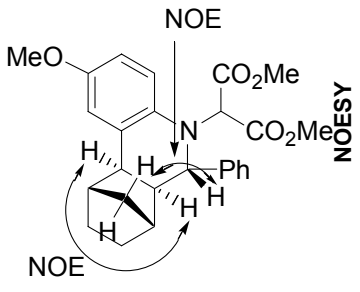
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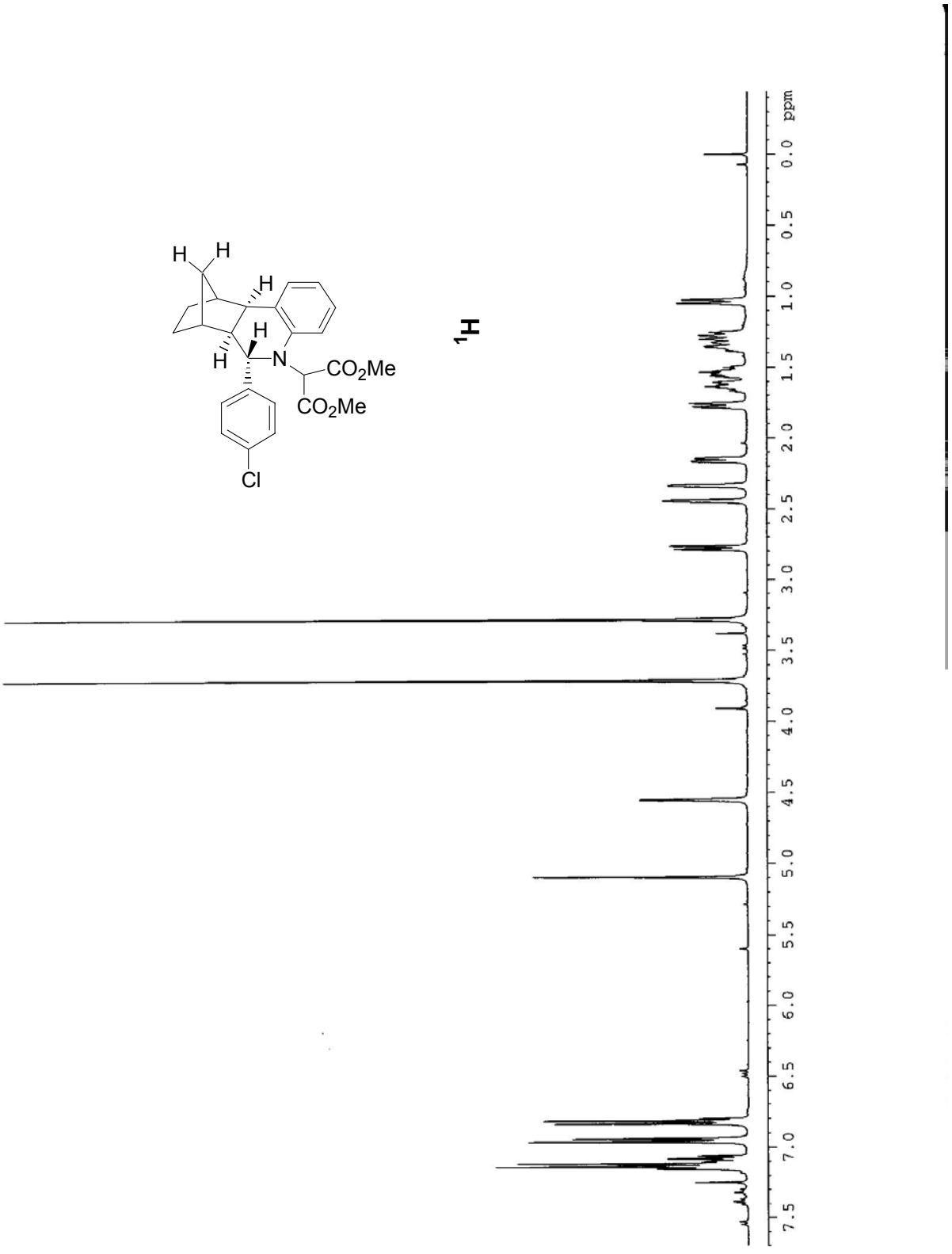
CO2Me
N
CO2Me
H
H
Ph
H
H
H
NOE
NOESY


H
H
H
H
H
N
CO2Me
CO2Me
Cl
1H
ppm
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0.5
1.0
1.5
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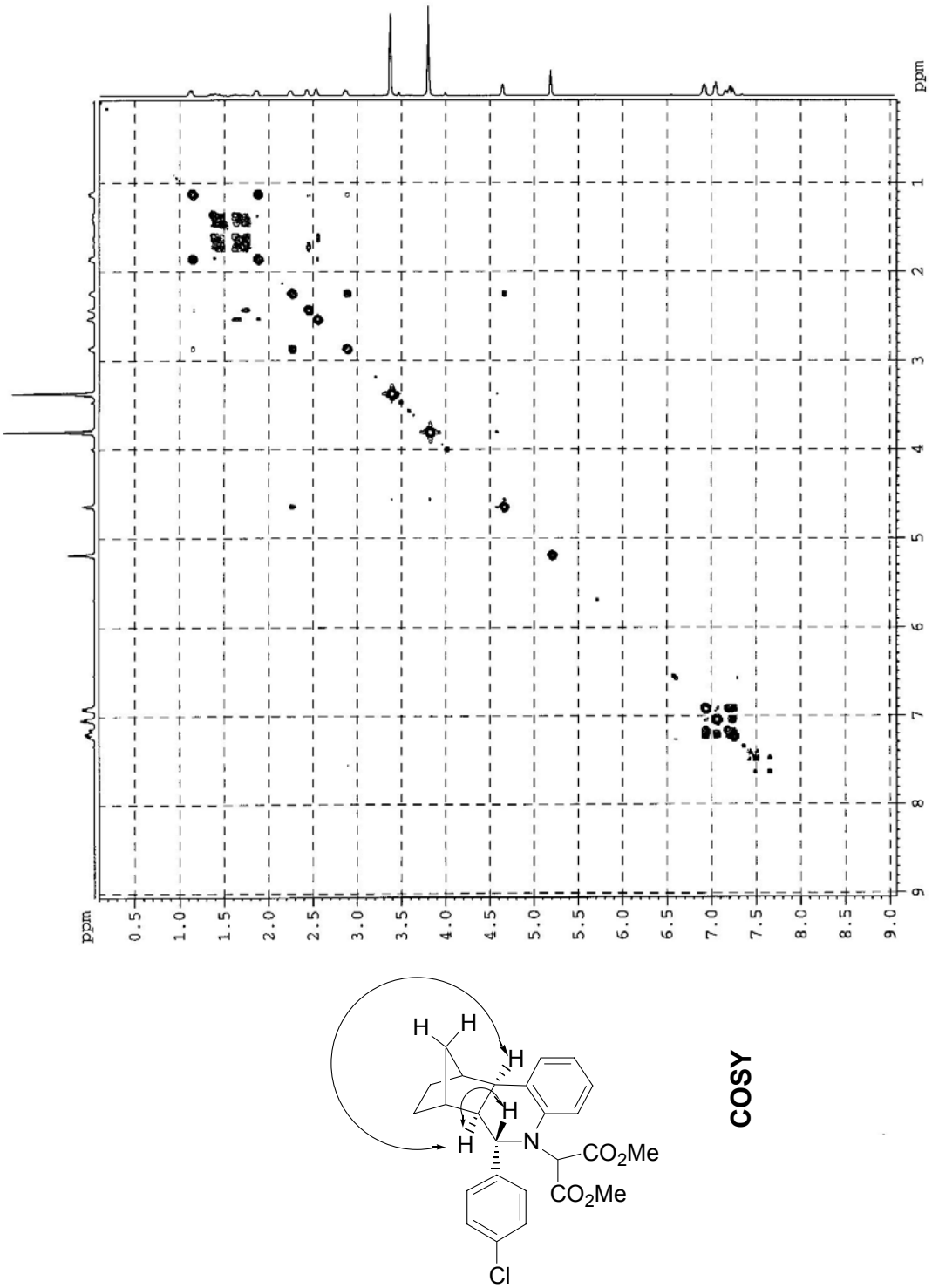
7.5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4.5
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6.0
6.5
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7.5
8.0
8.5
9.0
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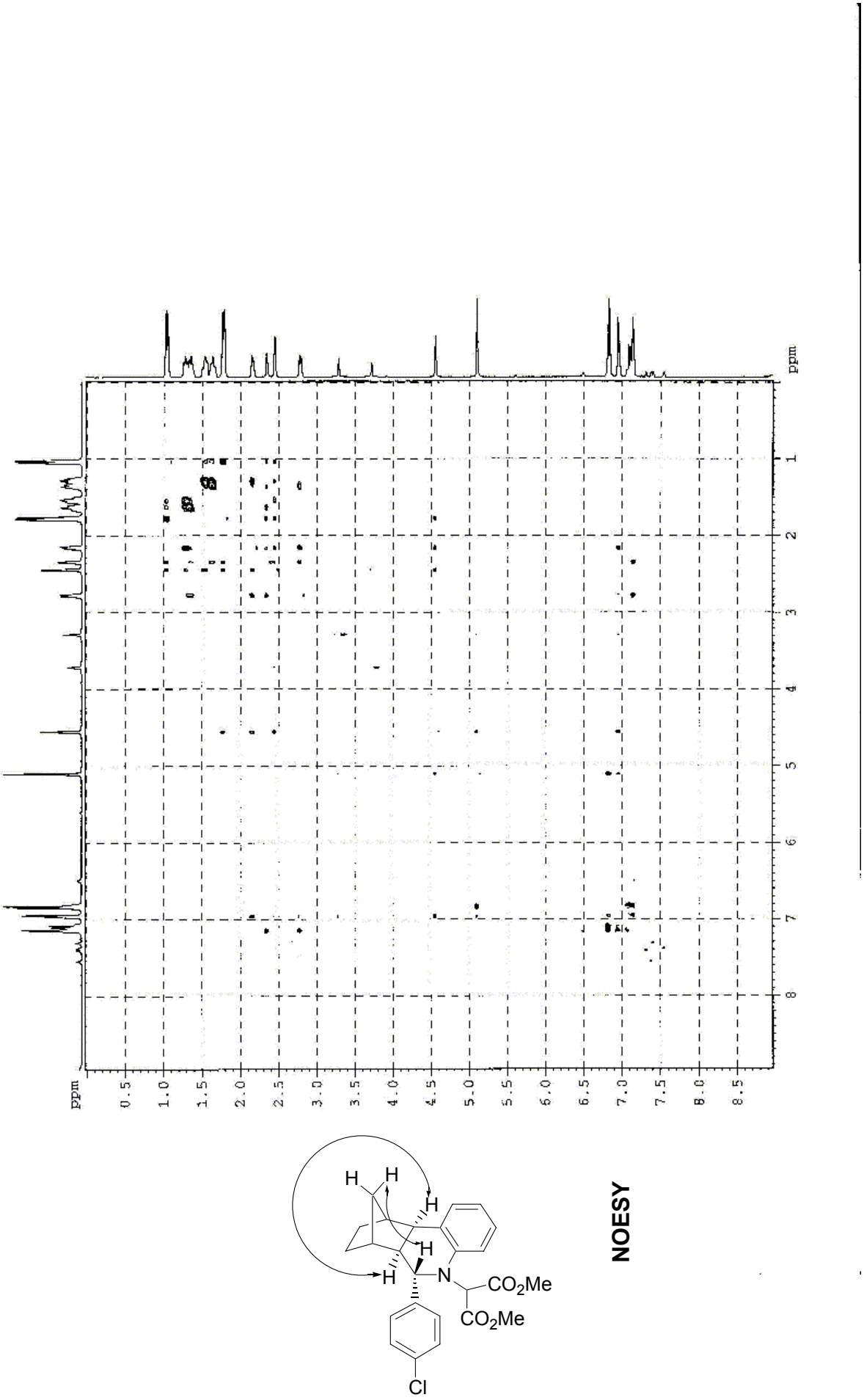
6
7
8
9
H
H
H
H
H
N
CO2Me
CO2Me
Cl
COSY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6.5
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7.5
8.0
8.5
ppm
1
2
3
4
5
6
7
8
H
H
H
H
H
N
CO2Me
CO2Me
Cl
NOESY

Ortep diagram for **6f**