Rhodium-Catalyzed [2+2+2] Cycloaddition of 1,6-Diynes with Isothiocyanates and Carbon Disulfide

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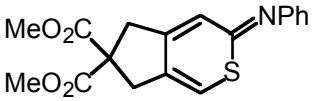
I. General

Anhydrous CH_2Cl_2 (No. 27,099-7) and $(CH_2Cl)_2$ (No. 28,450-5) were obtained from Aldrich and used as received. All reagents were obtained from commercial sources and used as received. All reactions were carried out under an atmosphere of argon or nitrogen in oven-dried glassware with magnetic stirring. Diynes **1a**,[1] **1b**,[2] **1c**,[3] and **1d**[4] were prepared according to the literatures.

II. Rhodium-Catalyzed [2+2+2] Cycloaddition of 1,6-Diynes with Isothiocyanates and Carbon Disulfide (Table 2)

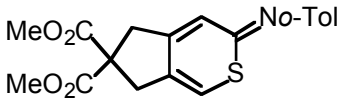
General Procedure (Table 2, entry 1). Under an Ar atmosphere, BINAP (9.3 mg, 0.015 mmol) and $[Rh(cod)Cl]_2$ (3.7 mg, 0.0075 mmol) were dissolved in CH_2Cl_2 (1.0 mL) and the mixture was stirred for 5 min. H_2 was introduced to the resulting solution in a Schlenk tube. After stirring for 0.5 h at room temperature, the resulting solution was concentrated to dryness and dissolved in $(CH_2Cl)_2$ (0.5 mL). To this solution was added dropwise over 1 min a solution of 2,2-dibut-2-ynylmalonic acid dimethyl ester (**1a**, 62.5 mg, 0.30 mmol) and phenyl isothiocyanate (**2a**, 44.6 mg, 0.33 mmol) in $(CH_2Cl)_2$ (0.5 mL) and washed remaining substrates away by using CH_2Cl_2 (0.5 mL). The mixture was stirred at 80 °C for 15 h. The resulting solution was concentrated and purified by silica gel column chromatography (hexane:EtOAc = 5:1), which furnished 3-phenylimino-3,5-dihydro-7H-cyclopentan[c]thiopyran-6,6-dicarboxylic acid dimethyl ester (**3aa**, 91.0 mg, 0.265 mmol, 88% yield) as a yellow solid.

3-Phenylimino-3,5-dihydro-7H-cyclopentan[*c*]thiopyran-6,6-dicarboxylic acid dimethyl ester (3aa, entry 1, reaction time: 12 h).[1]



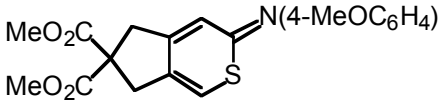
Mp 95.0–95.5 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30–7.42 (m, 2H), 7.05–7.13 (m, 1H), 6.85–6.90 (m, 2H), 6.61 (s, 1H), 6.56 (s, 1H), 3.78 (s, 6H), 3.35 (d, J = 1.8 Hz, 2H), 3.24 (d, J = 1.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.1, 157.9, 151.2, 149.5, 130.8, 130.0, 124.3, 121.5, 121.1, 119.8, 58.8, 55.7, 40.9, 39.8.

3-*o*-Tolylimino-3,5-dihydro-7H-cyclopenta[c]thiopyran-6,6-dicarboxylic acid dimethyl ester (3ab, entry 2, reaction time: 13 h).



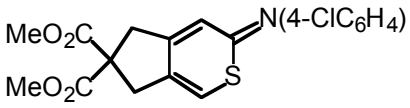
Yellow oil; IR (neat) 3300, 2900, 1710, 1530, 1420, 1235, 1200, 890, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.15–7.24 (m, 2H), 7.02 (dt, J = 7.5, 1.5 Hz, 1H), 6.73 (dd, J = 7.5, 1.5 Hz, 1H), 6.55–6.65 (m, 2H), 3.76 (s, 6H), 3.36 (d, J = 1.5 Hz, 2H), 3.23 (d, J = 1.5 Hz, 2H), 2.08 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 157.3, 149.7, 149.0, 131.1, 130.5, 128.0, 127.2, 124.0, 121.3, 120.8, 118.7, 58.7, 53.1, 40.8, 39.7, 17.2; HRMS (EI) calcd for $C_{23}H_{21}NO_4S$ $[M]^+$ 357.1035, found 357.1025.

3-(4-Methoxyphenylimino)-3,5-dihydro-7H-cyclopenta[c]thiopyran-6,6-dicarboxylic acid dimethyl ester (3ac, entry 3, reaction time: 13 h).



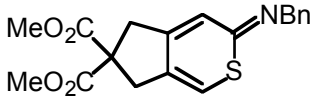
Yellow solid; Mp 153.5–154.0 °C; IR (neat) 3000, 2850, 1710, 1530, 1480, 1200, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.88–6.97 (m, 2H), 6.82–6.88 (m, 2H), 6.62 (s, 1H), 6.54 (s, 1H), 3.79 (s, 3H), 3.77 (s, 6H), 3.34 (d, J = 1.8 Hz, 2H), 3.23 (d, J = 1.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 157.6, 156.3, 148.9, 144.0, 130.6, 121.4, 120.8, 120.7, 114.9, 58.7, 55.3, 53.1, 40.8, 39.7; HRMS (EI) calcd for $C_{19}H_{19}NO_5S$ $[M]^+$ 373.0984, found 373.1013.

3-(4-Methoxyphenylimino)-3,5-dihydro-7H-cyclopenta[c]thiopyran-6,6-dicarboxylic acid dimethyl ester (3ad, entry 4, reaction time: 12 h).



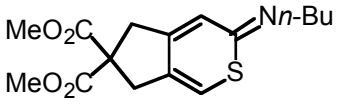
Yellow solid; Mp 153.5–154.0 °C; IR (neat) 3000, 2850, 1710, 1530, 1470, 1240, 1050, 820 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.32 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 6.65 (s, 1H), 6.55 (s, 1H), 3.77 (s, 6H), 3.35 (d, J = 1.5 Hz, 2H), 3.25 (d, J = 1.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.7, 158.3, 149.7, 149.3, 130.8, 129.9, 129.1, 121.3, 121.2, 120.8, 58.7, 53.2, 40.9, 39.7; HRMS (EI) calcd for $C_{18}H_{16}ClNO_4S$ $[M]^+$ 377.0489, found 377.0565.

3-Benzylimino-3,5-dihydro-7H-cyclopentan[c]thiopyran-6,6-dicarboxylic acid dimethyl ester (3ae, entry 5, reaction time: 12 h).



Yellow solid; Mp 68.5–69.3 °C; IR (neat) 3300, 2900, 1720, 1540, 1420, 1240, 1180, 1160, 720 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.30–7.43 (m, 4H), 7.20–7.28 (m, 1H), 6.78 (s, 1H), 6.55 (s, 1H), 4.25 (s, 2H), 3.76 (s, 6H), 3.32 (d, J = 1.8 Hz, 2H), 3.23 (d, J = 1.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.7, 155.4, 146.2, 139.7, 131.3, 128.3, 127.9, 126.7, 121.3, 120.2, 58.8, 57.1, 53.2, 40.8, 40.0; HRMS (EI) calcd for $C_{19}H_{19}NO_4S$ $[M]^+$ 357.1035, found 357.1055.

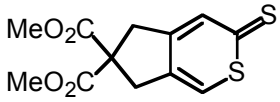
3-Butylimino-3,5-dihydro-7H-cyclopenta[c]thiopyran-6,6-dicarboxylic acid dimethyl ester (3af, entry 5, reaction time: 20 h).



Yellow solid; Mp 76.5–77.0 °C; IR (neat) 3200, 2900, 1720, 1540, 1420, 1240, 1180, 1150, 720 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.74 (s, 1H), 6.42 (s, 1H), 3.75 (s, 6H), 3.28 (d, J = 1.2 Hz, 2H), 3.24 (d, J = 1.2 Hz, 2H), 3.00 (t, J = 5.1 Hz, 2H), 1.74 (quintet, J = 5.1 Hz, 2H), 1.48–1.65 (sextet, J = 5.1 Hz, 2H), 0.95 (t, J = 5.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 154.5, 145.7, 131.9, 121.0, 120.4, 58.7, 53.2, 53.1, 40.7, 40.0, 32.7, 20.9, 14.0; HRMS (EI) calcd for $C_{16}H_{21}NO_4S$ $[M]^+$ 323.1191, found 323.1167.

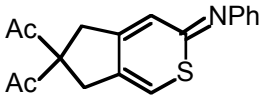
3-Thioxo-3,5-dihydro-7H-cyclopenta[c]thiopyran-6,6-dicarboxylic acid dimethyl

ester (3ag, entry 7, reaction time: 12 h).[1]



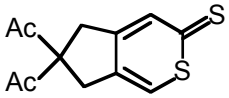
Red solid; Mp 127.2–127.8 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.44 (d, J = 1.2 Hz, 1H), 7.40 (d, J = 1.2 Hz, 1H), 3.78 (s, 6H), 3.45 (d, J = 1.5 Hz, 2H), 3.40 (d, J = 1.5 Hz, 2H);^{13}C NMR ($CDCl_3$, 75 MHz) δ 204.4, 170.3, 150.8, 136.2, 135.1, 134.6, 58.7, 53.4, 41.0, 40.0.

1-(6-Acetyl-3-phenylimino-3,5,6,7-tetrahydrocyclopenta[c]thiopyran-6-yl)ethanone (3ba, entry 8, reaction time: 12 h).[1]



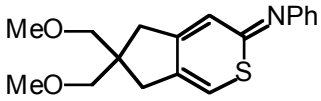
Red solid; Mp 121.5–122.0 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30–7.40 (m, 2H), 7.05–7.15 (m, 1H), 6.83–6.88 (m, 2H), 6.63 (s, 1H), 6.57 (s, 1H), 3.27 (d, J = 1.5 Hz, 2H), 3.16 (d, J = 1.5 Hz, 2H), 2.17 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 203.5, 157.5, 150.8, 149.1, 130.4, 129.8, 124.1, 121.5, 121.2, 119.6, 73.2, 38.1, 37.0, 26.5

1-(6-Acetyl-3-thioxo-3,5,6,7-tetrahydrocyclopenta[c]thiopyran-6-yl)ethanone (3bg, entry 9, reaction time: 12 h).



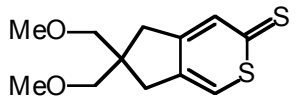
Red solid; Mp 111.4-112.0 °C; IR (neat) 3200, 2950, 1500, 1400, 1350, 1170, 950 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43 (s, 1H), 7.41 (s, 1H), 3.38 (d, J = 1.2 Hz, 2H), 3.34 (d, J = 1.2 Hz, 2H), 2.19 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 204.2, 202.6, 150.6, 136.0, 135.3, 134.9, 73.3, 38.1, 37.1, 26.4; HRMS (EI) calcd for $C_{12}H_{12}O_2S_2$ $[M\text{-}Ac]^+$ 209.0095, found 209.0175.

(6,6-Dimethoxymethyl-6,7-dihydro-5H-cyclopenta[c]thiopyran-3-ylidene)phenyl-amine (3ca, entry 10, reaction time: 12 h).



Yellow solid; Mp 94.5–95.5 °C; IR (neat) 3300, 2800, 1520, 1090, 940, 860 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.30–7.40 (m, 2H), 7.05–7.12 (m, 1H), 6.85–6.93 (m, 2H), 6.52–6.56 (m, 2H), 3.35 (s, 6H), 3.29 (s, 4H), 2.67 (d, J = 1.5 Hz, 2H), 2.55 (d, J = 1.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.5, 151.1, 133.3, 129.8, 123.9, 121.5, 120.0, 119.9, 74.9, 59.3, 47.1, 39.3, 37.8; HRMS (EI) calcd for $C_{18}H_{21}NO_2S$ $[M]^+$ 315.1293, found 315.1333.

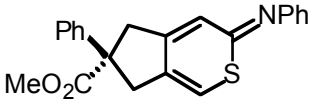
6,6-Dimethoxymethyl-6,7-dihydro-5H-cyclopenta[c]thiopyran-3-thione (3cg, entry 11, reaction time: 12 h).



Yellow solid; Mp 80.4–80.9 °C; IR (neat) 3300, 2800, 1580, 1400, 1150, 940 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.42–7.48 (m, 1H), 7.32–7.38 (m, 1H), 3.34 (s, 6H), 3.30 (s, 4H), 2.77 (d, J = 1.2 Hz, 2H), 2.74 (d, J = 1.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 204.0, 154.8, 139.2, 135.8, 134.4, 74.9, 59.2, 47.3, 39.5, 38.1; HRMS (EI) calcd for $C_{12}H_{16}O_2S_2$ $[M]^+$ 256.0592, found 256.0522.

III. Rhodium-Catalyzed Enantioselective [2+2+2] Cycloaddition of 1,6-Diyne 1d with Isothiocyanate 2a (eq 3)

(*R*)-(–)-6-Phenyl-3-phenylimino-3,5,6,7-tetrahydro-cyclopenta[c]thiopyran-6-carboxylic acid methyl ester [(*R*)-(–)-3da].



Under an Ar atmosphere, (*R*)-BINAP (18.7 mg, 0.030 mmol) and $[Rh(cod)Cl]_2$ (7.4 mg, 0.0150 mmol) were dissolved in CH_2Cl_2 (2.0 mL) and the mixture was stirred at rt for 5 min. H_2 was introduced to the resulting solution in a Schlenk tube. After stirring at rt for 0.5 h, the resulting mixture was concentrated to dryness. To the $(CH_2Cl)_2$ (4.0 mL) solution of the residue was added a $(CH_2Cl)_2$ (1.0 mL) solution of 2-phenyl-2-prop-2-ynylpent-4-ynoic acid methyl ester (**1d**, 67.9 mg, 0.30 mmol) and phenyl isothiocyanate (**2a**, 44.6 mg, 0.33 mmol) at rt, and washed remaining substrates away by using $(CH_2Cl)_2$ (1.0 mL). The mixture was stirred at 60 °C for 12 h. The resulting mixture was concentrated and purified by silica gel

column chromatography (CH_2Cl_2), which furnished (*R*)-(–)-6-phenyl-3-phenylimino-3,5,6,7-tetrahydrocyclopenta[*c*]thiopyran-6-carboxylic acid methyl ester [**(*R*)-(–)-3da**, 106.8 mg, 0.295 mmol, 98% yield, 61% ee] as a yellow solid.

Mp 141.2–141.5 °C; $[\alpha]^{25}_{D}$ –6.40° ($CHCl_3$, *c* 2.405, 61% ee); IR (neat) 3200, 2900, 1700, 1450, 1100, 680 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.26–7.42 (m, 7H), 7.10 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 7.2 Hz, 2H), 6.66 (s, 1H), 6.63 (s, 1H), 3.74 (d, *J* = 16.5 Hz, 1H), 3.66 (d, *J* = 16.5 Hz, 1H), 3.65 (s, 3H), 3.14 (dd, *J* = 16.5, 1.2 Hz, 1H), 3.00 (dd, *J* = 16.5, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.5, 158.1, 151.0, 150.4, 140.8, 131.6, 129.8, 128.7, 127.6, 126.5, 124.0, 121.2, 120.6, 119.7, 57.1, 52.9, 43.0, 42.1; HRMS (EI) calcd for $C_{22}H_{19}NO_2S$ $[M]^+$ 361.1136, found 361.1094. CHIRALPAK AD, hexane:2-PrOH = 85:15, 1.0 mL/min, retention times: 12.1 min (major isomer) and 15.1 min (mimor isomer).

IV. References

(1) Yamamoto, Y.; Kinpara, K.; Saigoku, T.; Takagishi, H.; Okuda, S.; Nishiyama, H.; Itoh, K. *J. Am. Chem. Soc*. **2005**, *127*, 605–613.

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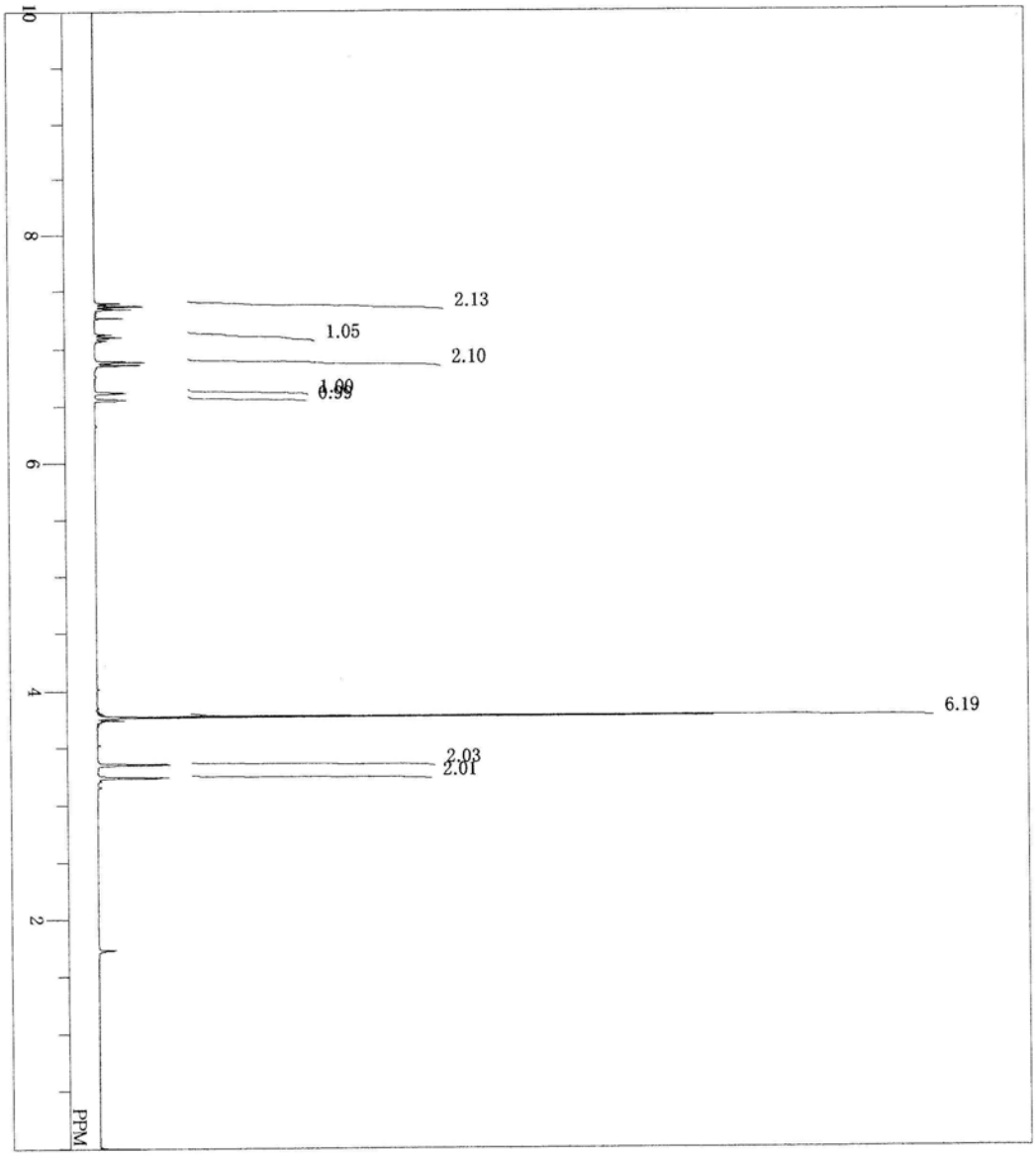
(3) Cadran, N.; Cariou, K.; Herve, G.; Aubert, C.; Fensterbank, L.; Malacria, M.; Marco-Contelles, J. *J. Am. Chem. Soc*. **2004**, *126*, 3408–3409.

(4) Madine, J. W.; Wang, X.; Widenhoefer, R. A. *Org. Lett*. **2001**, *3*, 385–388.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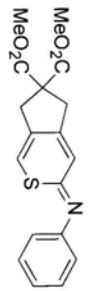
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MeO2C
S
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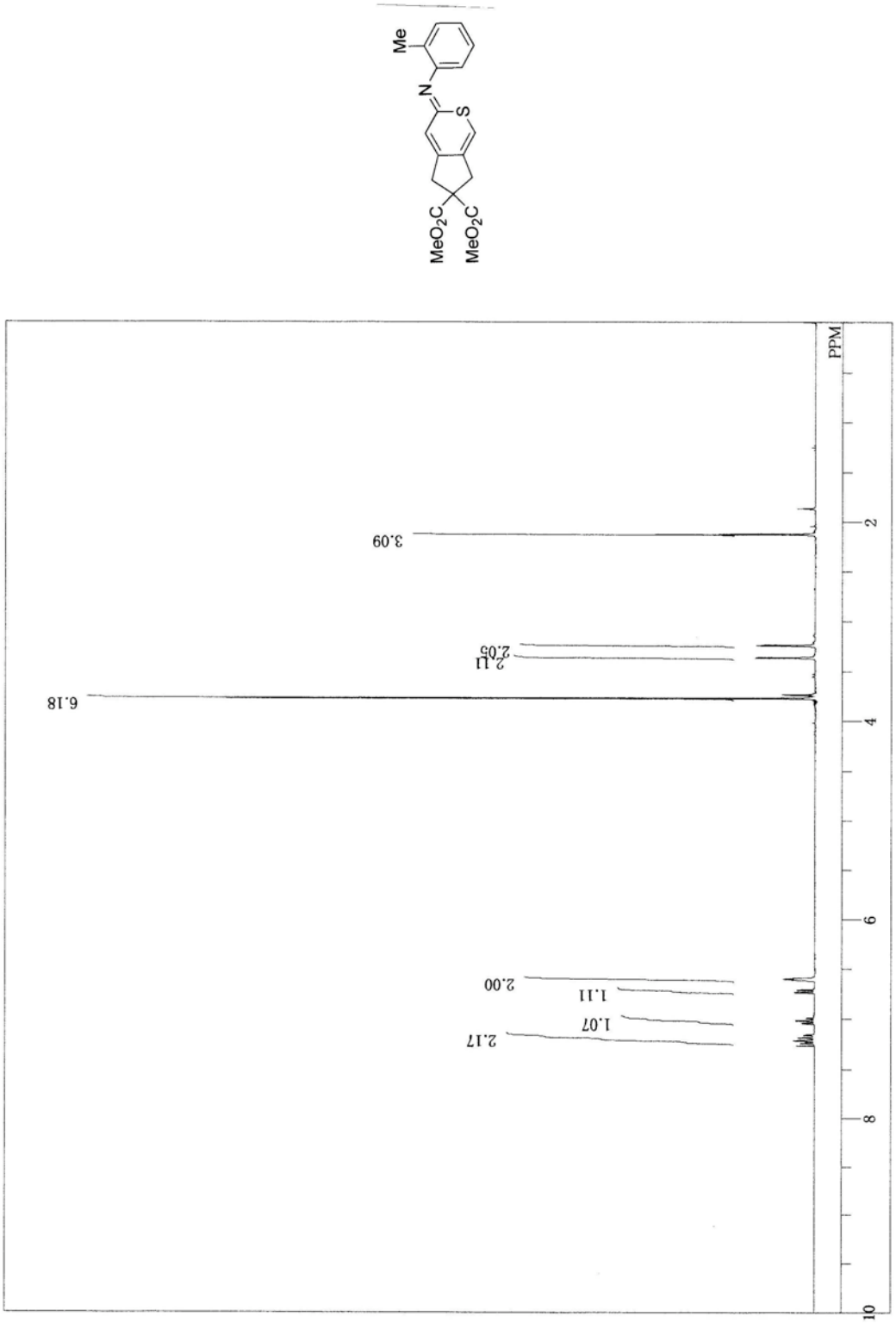
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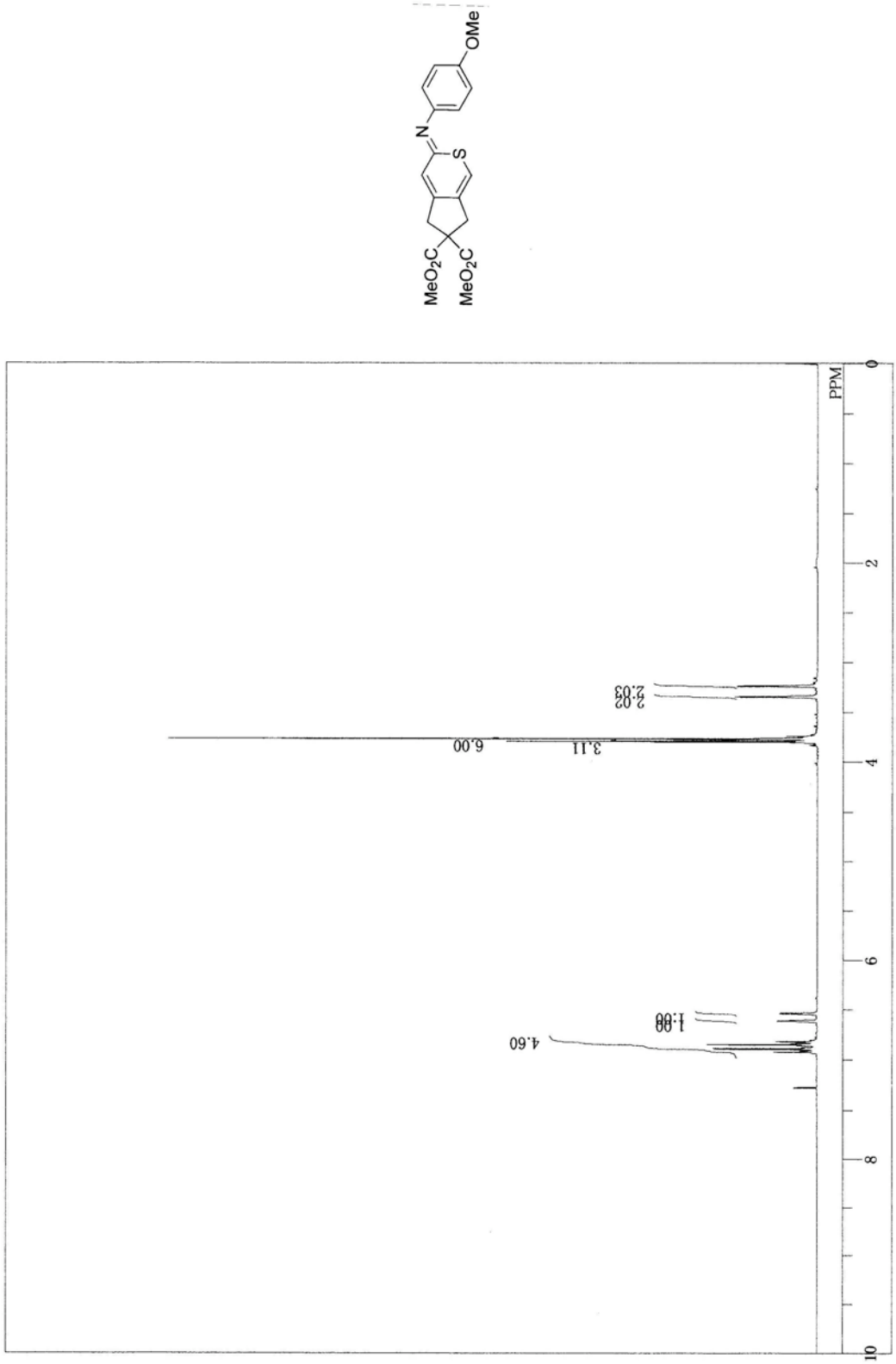
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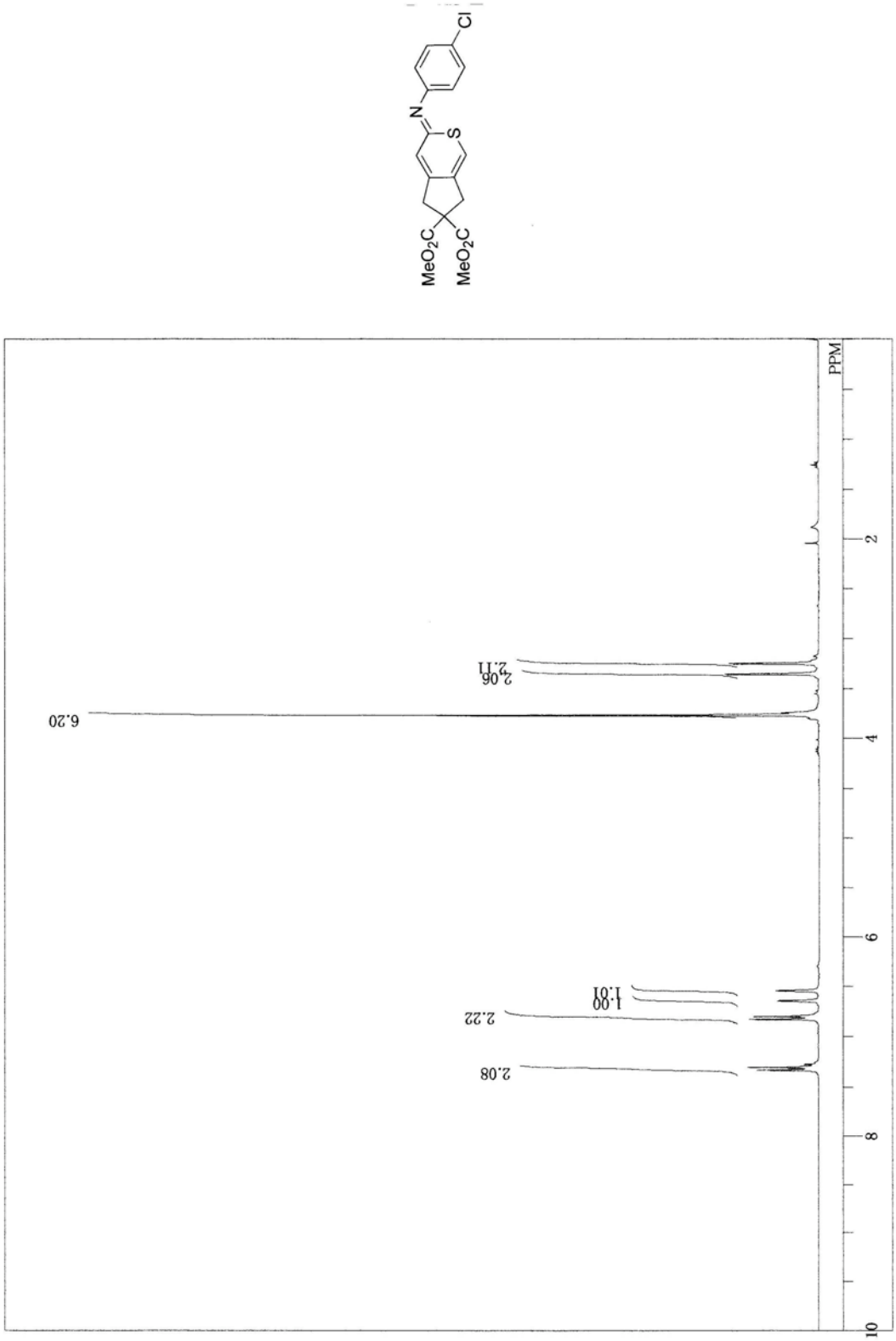
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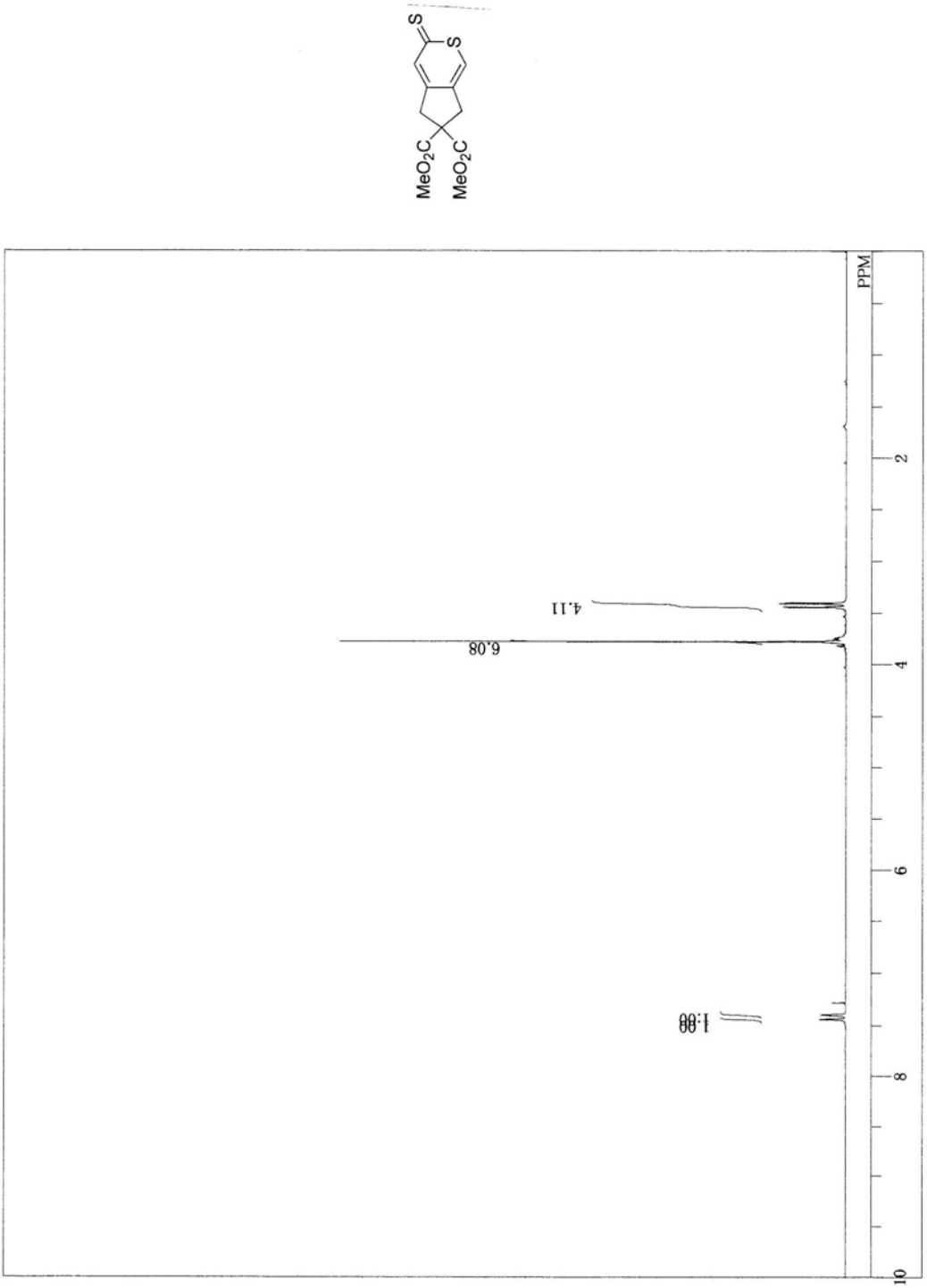
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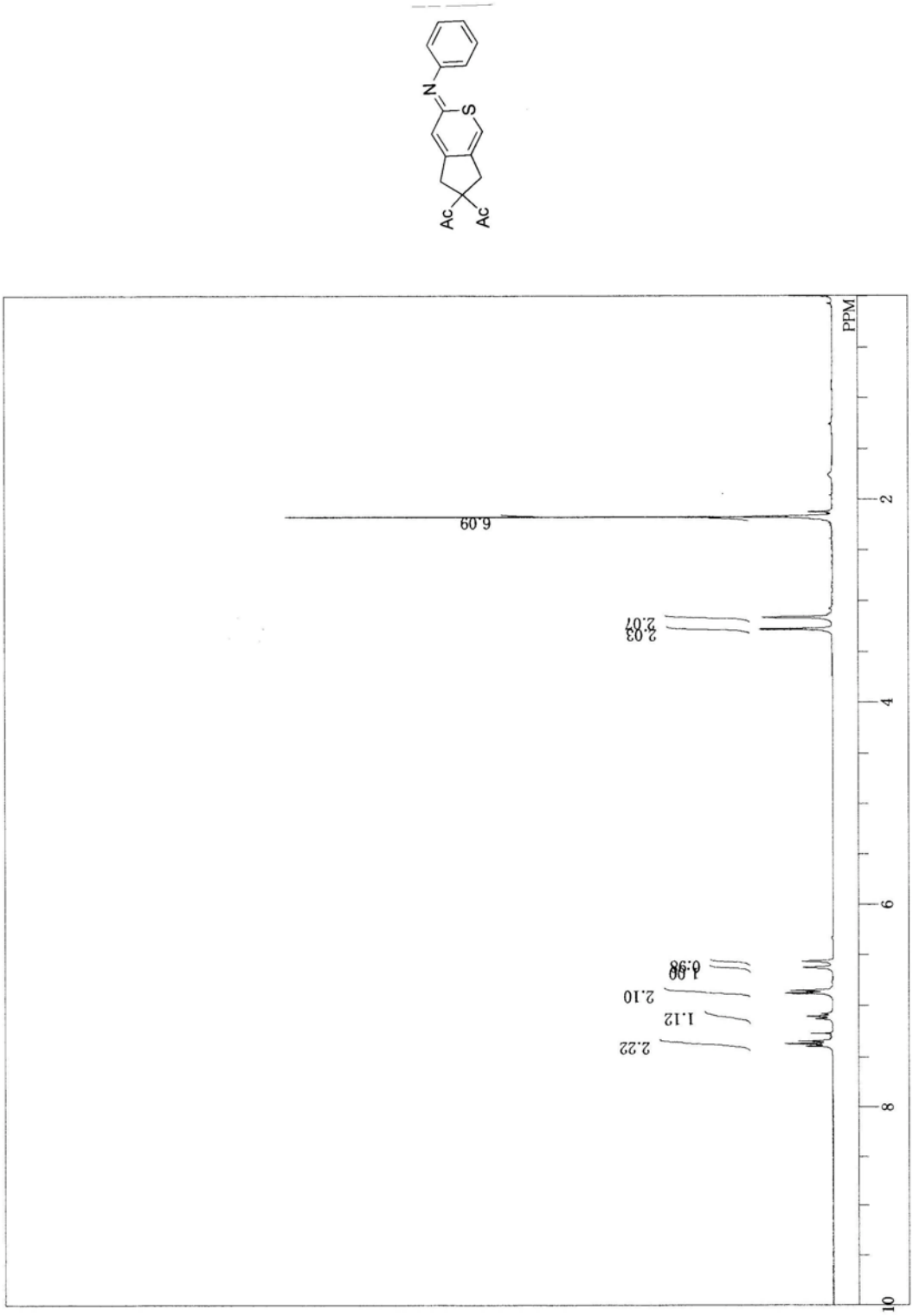
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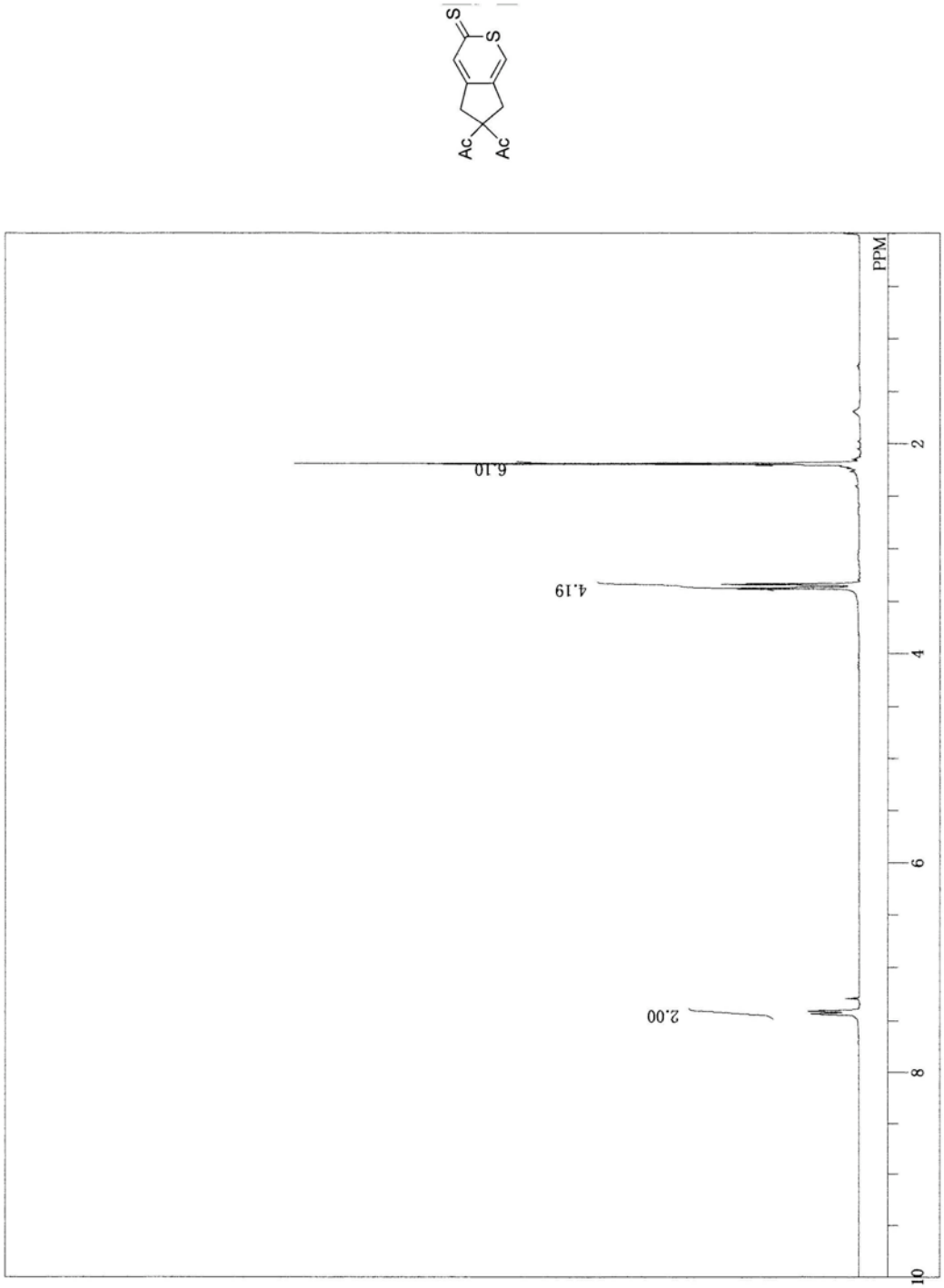
2.22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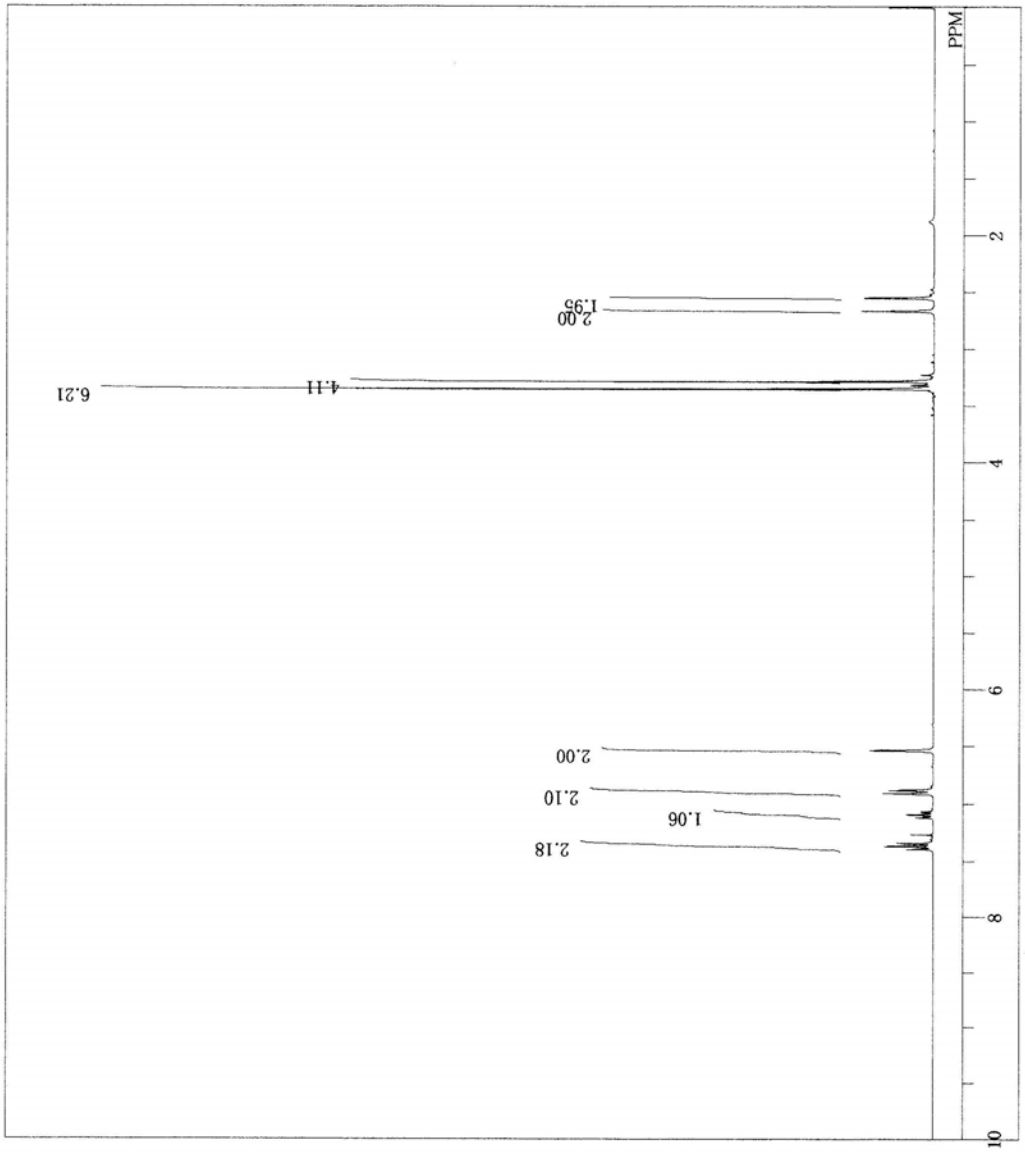
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MeO
MeO
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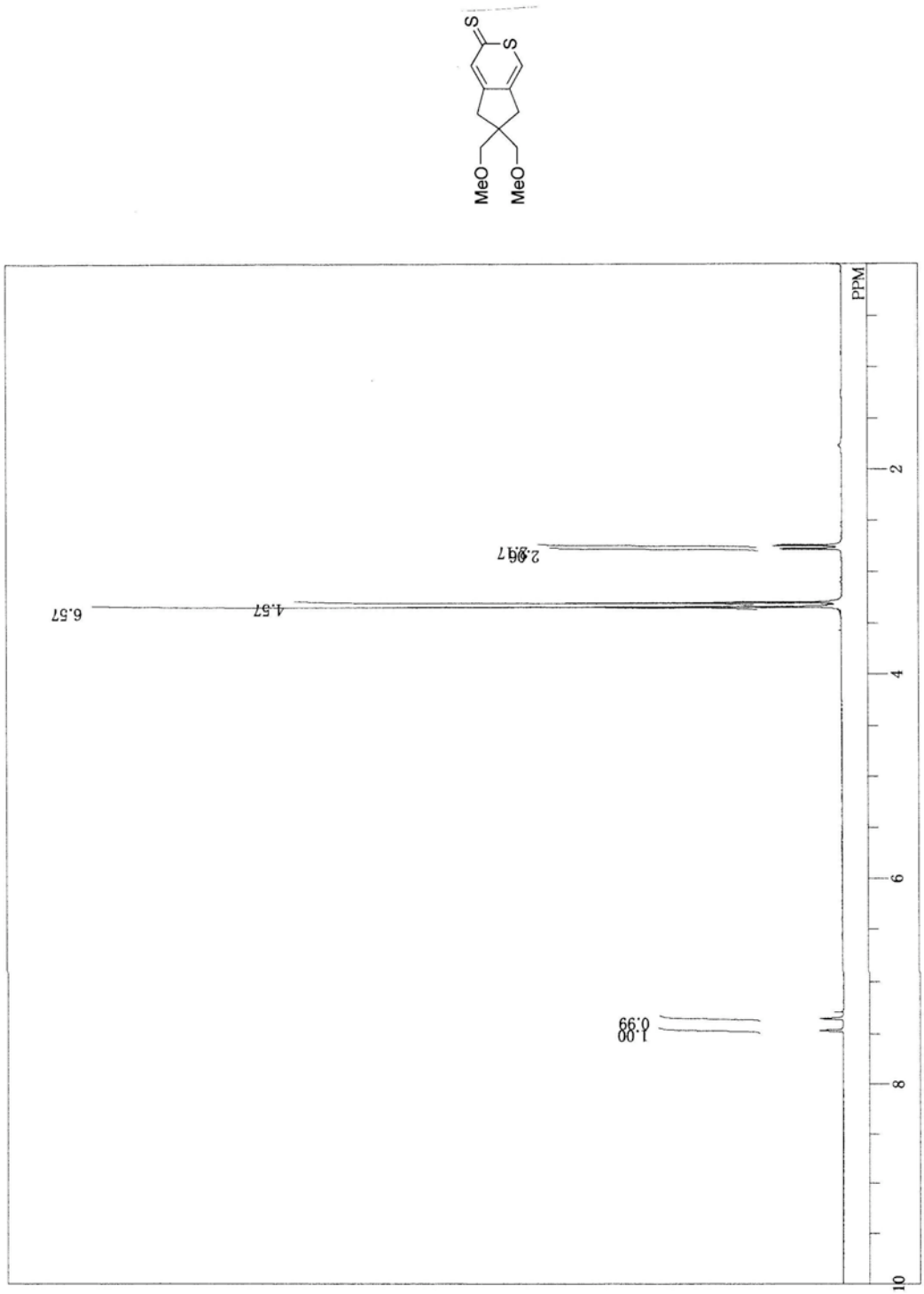
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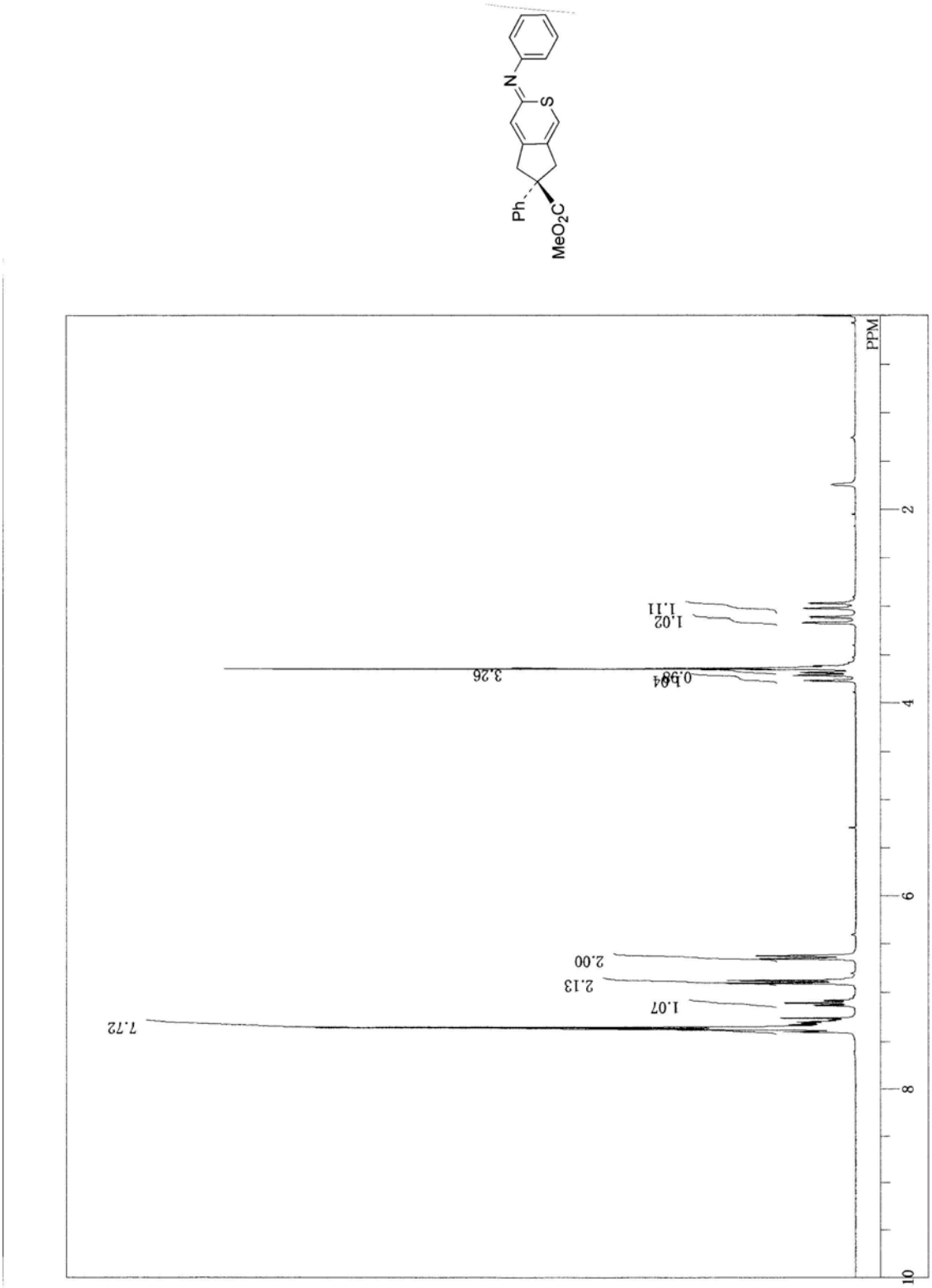
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8
6
4
2