

Supporting Information

An efficient synthetic route to 1,3-bis(arylethynyl)isobenzofuran by using alkoxybenzocyclobuteneone as a reactive platform

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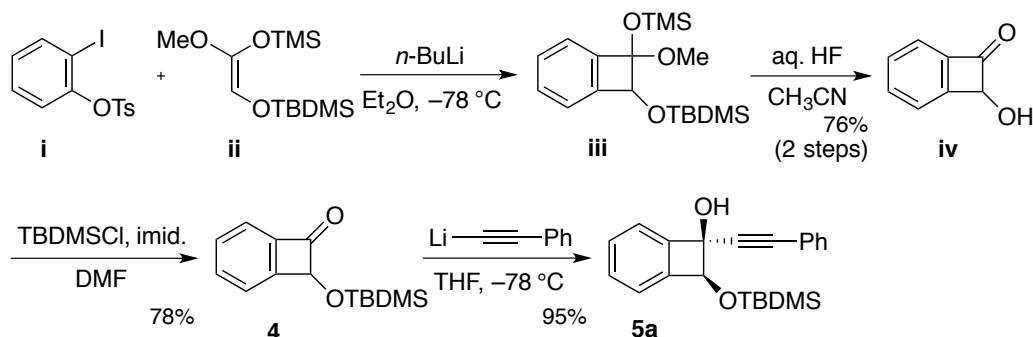
General Experimental Procedures

All experiments dealing with air- and moisture-sensitive compounds were conducted under an atmosphere of dry argon. THF (anhydrous; Wako Pure Chemical Industries, Ltd.) was used as received.

For thin-layer chromatography (TLC) analysis, Merck pre-coated plates (silica gel 60 F₂₅₄, Art 5715, 0.25 mm) were used. For flash column chromatography, silica gel 60 N (spherical, neutral, 63–210 µm) from Kanto Chemical was used. Silica gel preparative TLC (PTLC) was performed on Merck silica gel 60 PF₂₅₄ (Art 7749).

¹H NMR and ¹³C NMR were measured on a JEOL JNM ECA-300 and a JEOL JNM ECA-400 spectrometer. Attenuated Total Reflectance Fourier Transformation Infrared (ATR-FTIR) spectra were recorded on a Perkin Elmer 1600 FTIR. High resolution mass spectra were obtained with a JEOL The AccuTOF LC-plus JMS-T100LP, Bruker solariX, and Bruker micrOTOF-Q. Melting point (mp) determinations were performed by using a Yanako MP-S3 instrument and are uncorrected.

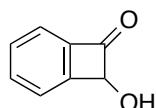
General Procedure for Preparation of Alkynylbenzocyclobutanol



Scheme 1.

Synthesis of hydroxybenzocyclobutenone **iv**:

To a mixture of tosylate **i** (39.7 g, 0.106 mol) and ketene silyl acetal **ii** (35.1 g, 0.127 mmol) in Et₂O (366 mL) was added *n*-BuLi (1.55 M in hexane, 94.1 mL, 0.146 mol) at -78 °C. After gradually warmed up to room temperature for 72 h, the reaction was stopped by adding water. Extractive workup (EtOAc) followed by evaporation gave crude cycloadduct **iii**. To a solution of cycloadduct **iii** (46.9 g) in MeCN (300 mL) was added 46% aq. HF (20.2 mL, 0.532 mol) at 0 °C. After warmed up to room temperature, the reaction was further stirred for 6.5 h. The reaction was stopped by adding sat. aq. NaHCO₃ at 0 °C. The products were extracted with EtOAc (X3) and the combined organic extracts were washed brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 7/3) to give **iv** (10.8 g, 75.9%) as white solids.



hydroxybenzocyclobutenone **iv**

¹H NMR (CDCl₃, δ)

3.97 (d, 1H, J = 5.9 Hz), 5.81 (d, 1H, J = 5.9 Hz), 7.49 (d, 1H, J = 7.2 Hz), 7.51–7.67 (m, 2H), 7.77 (d, 1H, J = 7.2 Hz);

¹³C NMR (CDCl₃, δ)

86.0, 121.7, 123.9, 131.4, 135.9, 146.8, 157.3, 191.6;

IR (ATR)

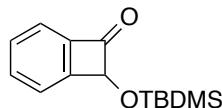
3415, 2952, 1755, 1584, 1465, 1440, 1338, 1280, 1259, 1181, 1144, 1111, 1050, 942, 851, 795, 752 cm⁻¹;

HRMS (ESI) *m/z* 157.0260 (157.0265 calcd for C₈H₆O₂Na [M+Na]⁺).

Synthesis of siloxybenzocyclobutenone **4**:

To a solution of hydroxyketone **iv** (412 mg, 3.07 mmol) in DMF (3.0 mL) was added TBDMSCl (689 mg, 4.65 mmol) and imidazole (417 mg, 6.13 mmol) at 0 °C. After warmed up to room temperature, the reaction was further stirred for 3 h. The reaction was stopped by adding sat. aq. NaHCO₃ at 0 °C. The products were extracted with Et₂O (X3) and the combined organic extracts were washed with brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 19/1) to

give siloxyketone **4** (592 mg, 77.5%) as a colorless oil.



siloxycyclobuteneone **4**

¹H NMR (CDCl₃, δ)

0.19 (s, 3H), 0.22 (s, 3H), 0.96 (s, 9H), 5.78 (s, 1H), 7.47 (dt, 1H, J₁ = 1.4 Hz, J₂ = 7.6 Hz), 7.53 (t, 1H, J = 7.6 Hz), 7.59 (td, 1H, J₁ = 1.4 Hz, J₂ = 6.9 Hz), 7.67 (d, 1H, J = 6.9 Hz);

¹³C NMR (CDCl₃, δ)

-4.8, -4.6, 18.3, 25.7, 86.2, 121.6, 123.6, 131.0, 135.4, 146.8, 158.0, 190.6;

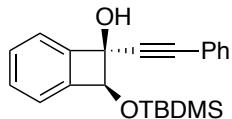
IR (ATR)

2955, 2929, 2886, 2857, 1767, 1586, 1464, 1345, 1254, 1189, 1144, 1122, 1068, 949, 894, 837, 779, 750, 709 cm⁻¹;

HRMS (ESI) *m/z* 271.1125 (271.1130 calcd for C₁₄H₂₀O₂SiNa [M+Na]⁺).

*Synthesis of benzocyclobutenol **5a**:*

To a solution of phenylacetylene (574 mg, 5.64 mmol) in THF (13.5 mL) was added *n*-BuLi (1.6 M in hexane, 2.8 ml, 4.6 mmol) at 0 °C. After 30 min, the reaction was cooled to -78 °C, to which was added benzocyclobuteneone **4** (1.00 g, 4.03 mmol) in THF (10 mL). After warmed up to -30 °C, the reaction was stopped by adding water. The products were extracted with EtOAc (X3) and the combined organic extracts were washed with brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 19/1) to give the benzocyclobutenol **5a** (1.34 g, 95.0%) as a colorless oil.



benzocyclobutenol **5a**

¹H NMR (CDCl₃, δ)

0.27 (s, 3H), 0.29 (s, 3H), 1.00 (s, 9H), 3.70 (s, 1H), 5.49 (s, 1H), 7.27–7.30 (m, 4H), 7.33–7.40 (m, 2H), 7.42–7.46 (m, 3H);

¹³C NMR (CDCl₃, δ)

-4.6, -4.5, 18.3, 25.8, 73.5, 79.9, 86.0, 88.2, 122.2, 122.6, 123.7, 128.1, 128.3, 130.0, 130.3, 131.7, 145.8, 148.6;

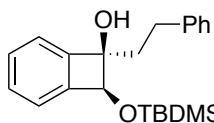
IR (ATR)

3479, 2954, 2930, 2857, 2226, 2198, 1490, 1461, 1362, 1255, 1219, 1078, 837, 771 cm⁻¹;

HRMS (ESI) *m/z* 373.1602 (373.1600 calcd for C₂₂H₂₆O₂SiNa [M+Na]⁺).

*Synthesis of benzocyclobutenol **6a**:*

To a solution of alkynylbenzocyclobutenol **5a** (38.1 mg, 0.109 mmol) in EtOH (2 mL) was added 10% Pd/C (11.4 mg), and the reaction mixture was stirred at room temperature under ambient pressure of hydrogen for 2 h. After removing Pd/C by filtration, the filtrate was concentrated in vacuo. The residue was purified by PTLC (hexane / EtOAc = 7 / 3) to give the benzocyclobutenol **6a** (29.0 mg, 75.2%) as a colorless oil.



benzocyclobutanol **6a**

¹H NMR (CDCl₃, δ)

0.20 (s, 3H), 0.22 (s, 3H), 0.97 (s, 9H), 2.05–2.23 (m, 2H), 2.81–2.97 (m, 2H), 3.54 (s, 1H), 5.10 (s, 1H), 7.14–7.39 (m, 9H);

¹³C NMR (CDCl₃, δ)

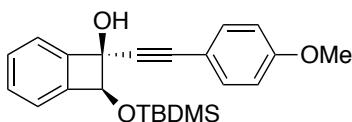
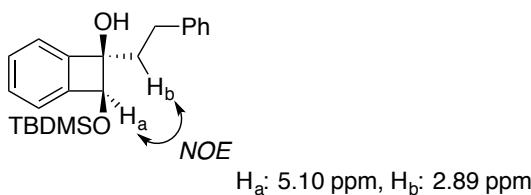
–4.6, –4.4, 18.3, 25.9, 31.1, 39.7, 77.5, 81.9, 122.3, 123.5, 125.8, 128.4, 129.3, 129.7, 142.3, 144.9, 150.9;

IR (ATR)

3509, 2929, 2857, 1602, 1456, 1345, 1254, 1113, 1089, 837, 752 cm^{–1};

HRMS (ESI) *m/z* 377.1921 (377.1913 calcd for C₂₂H₃₀O₂SiNa [M+Na]⁺).

*The stereochemistry of **5a** was determined by NOE after conversion to **6a** as shown below.*



benzocyclobutanol **5b**

¹H NMR (CDCl₃, δ)

0.27 (s, 3H), 0.28 (s, 3H), 1.00 (s, 9H), 3.70 (s, 1H), 3.79 (s, 3H), 5.48 (s, 1H), 6.80 (d, 2H, J = 9.0 Hz), 7.25–7.43 (m, 6H);

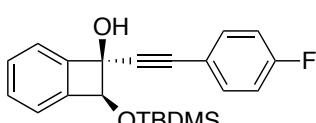
¹³C NMR (CDCl₃, δ)

–4.6, –4.5, 18.3, 25.8, 55.2, 73.6, 80.0, 86.0, 86.8, 113.8, 114.7, 122.2, 123.7, 129.9, 130.3, 133.2, 145.8, 148.7, 159.6;

IR (ATR)

3494, 2954, 2929, 2224, 2191, 1606, 1509, 1463, 1362, 1248, 1207, 1172, 1151, 1079, 1033, 831, 781, 754 cm^{–1};

HRMS (ESI) *m/z* 403.1694 (403.1705 calcd for C₂₃H₂₈O₃SiNa [M+Na]⁺).



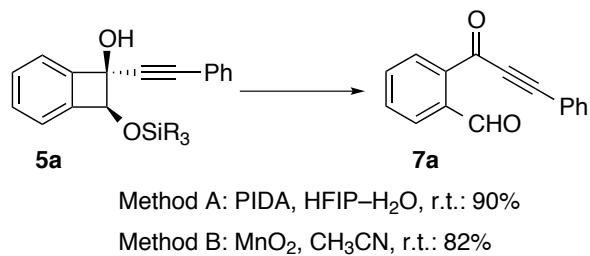
benzocyclobutanol **5c**

¹H NMR (CDCl₃, δ)

0.27 (s, 3H), 0.28 (s, 3H), 1.00 (s, 9H), 3.71 (s, 1H), 5.48 (s, 1H), 6.97 (t, 2H, J = 8.6 Hz), 7.26–7.29 (m, 1H), 7.30–7.46 (m, 5H);

¹³C NMR (CDCl₃, δ) –4.59, –4.56, 18.3, 25.8, 73.5, 79.8, 85.0, 87.9, 115.6 (d, J_{C–F} = 22.4 Hz), 118.9 (d, J_{C–F} = 3.6 Hz), 122.3, 123.9, 130.1, 130.5, 133.8 (d, J_{C–F} = 8.7 Hz), 145.9, 148.6, 161.2 (d, J_{C–F} = 249.3 Hz);
 IR (ATR) 3487, 2953, 2929, 2228, 2201, 1600, 1507, 1463, 1362, 1230, 1154, 1081, 834, 781, 757 cm⁻¹;
 HRMS (ESI) *m/z* 391.1523 (391.1506 calcd for C₂₂H₂₅FO₂SiNa [M+Na]⁺).

General Procedure for Oxidative Ring Cleavage of Alkynylbenzocyclobutenol into keto-aldehyde



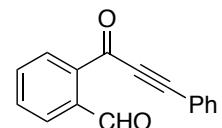
Scheme 2.

Synthesis of keto-aldehyde 7a (Method A):

To a solution of alkynylbenzocyclobutenol **5a** (75.4 mg, 0.215 mmol) in HFIP–H₂O (1.8–0.2 mL) was added PIDA (72.9 mg, 0.226 mmol) at room temperature, and the reaction mixture was stirred for further 10 min. The reaction was stopped by adding sat. aq. NaHCO₃. The products were extracted with EtOAc (X3), washed with sat. aq. NaHCO₃, brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by PTLC (hexane/EtOAc = 8/2) to give keto-aldehyde **7a** (45.5 mg, 90.2%) as yellow solids.

Synthesis of keto-aldehyde 7a (Method B):

To a solution of alkynylbenzocyclobutenol **5a** (195 mg, 0.558 mmol) in CH₃CN (10.5 mL) was added MnO₂ (970 mg, 11.2 mmol) at room temperature, and the reaction mixture was stirred for further 2 h. After removing MnO₂ by filtration, the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 9/1) to give keto-aldehyde **7a** (107 mg, 81.5%) as yellow solids.



keto-aldehyde **7a**

Mp 71.5–73.2 °C;

¹H NMR (CDCl₃, δ)

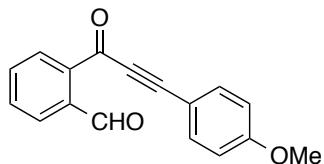
7.44–7.55 (m, 3H), 7.67–7.79 (m, 4H) 7.93–7.96 (m, 1H), 8.31–8.34 (m, 1H), 10.56 (s, 1H);

¹³C NMR (CDCl₃, δ)

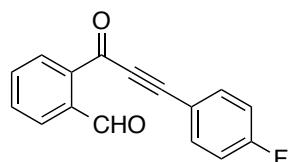
87.5, 94.4, 128.4, 128.8, 131.2, 131.9, 132.8, 133.2, 133.4, 137.4, 138.4, 178.3, 192.0;

IR (ATR)

3062, 2905, 2195, 1691, 1592, 1573, 1489, 1444, 1303, 1286, 1205, 1114, 1028, 1012, 995, 758, 743, 705 cm^{-1} ;
 HRMS (ESI) m/z 257.0567 (257.0578 calcd for $\text{C}_{16}\text{H}_{10}\text{O}_2\text{Na} [\text{M}+\text{Na}]^+$).

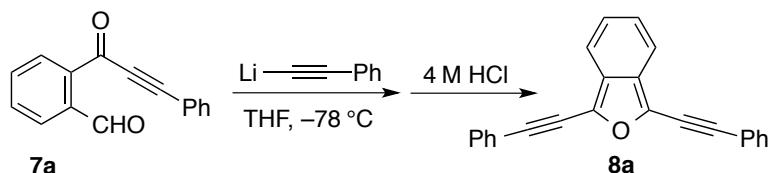


keto-aldehyde 7b
 Mp 112.5–114.0 °C;
 ^1H NMR (CDCl_3 , δ)
 3.87 (s, 3H), 6.95 (d, 2H, $J = 9.0$ Hz), 7.64 (d, 2H, $J = 9.0$ Hz), 7.67–7.78 (m, 2H), 7.93 (dd, 1H, $J_1 = 2.4$ Hz, $J_2 = 6.6$ Hz), 8.30 (dd, 1H, $J_1 = 1.7$ Hz, $J_2 = 7.3$ Hz), 10.57 (s, 1H);
 ^{13}C NMR (CDCl_3 , δ)
 55.5, 87.9, 95.9, 111.2, 114.5, 128.3, 131.7, 132.7, 133.1, 135.4, 137.4, 138.7, 162.1, 178.3, 192.1;
 IR (ATR)
 3015, 2935, 2190, 1697, 1622, 1600, 1571, 1509, 1293, 1254, 1214, 1190, 1173, 1112, 1025, 833, 753 cm^{-1} ;
 HRMS (ESI) m/z 287.0672 (287.0684 calcd for $\text{C}_{17}\text{H}_{12}\text{O}_3\text{Na} [\text{M}+\text{Na}]^+$).



keto-aldehyde 7c
 Mp 116.6–118.3 °C;
 ^1H NMR (CDCl_3 , δ)
 7.14 (t, 2H, $J = 8.6$ Hz), 7.60–7.79 (m, 4H), 7.94 (m, 1H), 8.30 (m, 1H), 10.56 (s, 1H);
 ^{13}C NMR (CDCl_3 , δ)
 87.5, 93.3, 115.7, 116.4 (d, $J_{\text{C}-\text{F}} = 22.4$ Hz), 128.5, 131.8, 132.8, 133.4, 135.5 (d, $J_{\text{C}-\text{F}} = 9.4$ Hz), 137.4, 138.4, 164.3 (d, $J_{\text{C}-\text{F}} = 255.0$ Hz), 178.2, 192.0;
 IR (ATR)
 3102, 2857, 2203, 1698, 1625, 1595, 1573, 1507, 1304, 1227, 1212, 1193, 1159, 1112, 1096, 1013, 837, 781, 735 cm^{-1} ;
 HRMS (ESI) m/z 275.0469 (275.0484 calcd for $\text{C}_{16}\text{H}_9\text{FO}_2\text{Na} [\text{M}+\text{Na}]^+$).

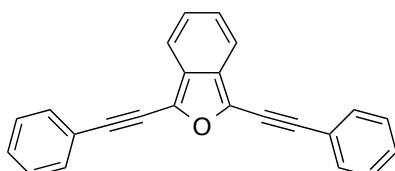
General Procedure for Preparation of Dialkynylisobenzofuran



Scheme 3.

Synthesis of dialkynylisobenzofuran 8a:

To a solution of keto-aldehyde **7a** (34.7 mg, 0.148 mmol) in THF (2.0 mL) was added (phenylethynyl)lithium (0.54 M in THF, 0.41 mL, 0.22 mmol), prepared by treatment of phenylacetylene (127 mg, 1.25 mmol) with *n*-BuLi (1.63 M in hexane, 0.66 mL, 1.1 mmol) in THF (1.3 mL) at -78 °C. After stirring for 1 h, 4 M HCl (0.5 mL) was added to the reaction mixture at 0 °C, and the reaction was warmed to room temperature. After 2 h, the reaction was stopped by adding sat. aq. NaHCO₃. The products were extracted with EtOAc (X3), washed with brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/CH₂Cl₂ = 9/1) to give dialkynylisobenzofuran **8a** (32.0 mg, 67.8%) as yellow solids.



dialkynylisobenzofuran **8a**

Mp 82.0–83.5 °C;

¹H NMR (CDCl₃, δ)

7.10 (dd, 2H, J₁ = 3.1 Hz, J₂ = 6.7 Hz), 7.37–7.39 (m, 6H), 7.59–7.63 (m, 6H);

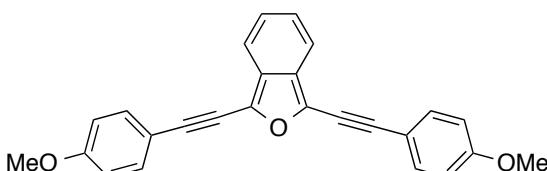
¹³C NMR (acetone-*d*₆, δ)

79.9, 100.7, 120.2, 123.0, 127.9, 128.9, 129.8, 130.2, 131.1, 132.2;

IR (ATR)

3053, 3032, 2195, 1634, 1595, 1485, 1441, 1288, 1155, 1073, 1027, 1010, 755, 743 cm⁻¹;

HRMS (DART) *m/z* 319.1122 (319.1123 calcd for C₂₄H₁₅O [M+H]⁺).



dialkynylisobenzofuran **8b**

Mp 111.4–113.0 °C;

¹H NMR (CDCl₃, δ)

3.84 (s, 6H), 6.90 (d, 4H, J = 8.6 Hz), 7.05 (dd, 2H, J₁ = 2.8 Hz, J₂ = 6.5 Hz), 7.52 (d, 4H, J = 8.6 Hz), 7.56 (dd, 2H, J₁ = 2.8 Hz, J₂ = 6.5 Hz);

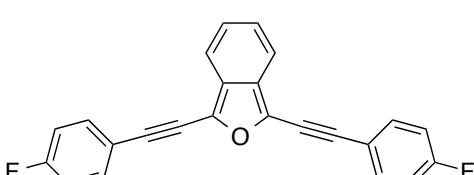
¹³C NMR (CDCl₃, δ)

55.4, 78.3, 99.3, 114.2, 114.5, 119.5, 125.9, 127.4, 130.2, 132.9, 160.1;

IR (ATR)

3011, 2934, 2838, 2190, 1604, 1508, 1291, 1251, 1173, 1032, 831, 752 cm⁻¹;

HRMS (ESI) *m/z* 379.1326 (379.1334 calcd for C₂₆H₁₉O₃ [M+H]⁺).



dialkynylisobenzofuran **8c**

Mp decomposed at 151 °C;

¹H NMR (acetone-*d*₆, δ)

7.20–7.30 (m, 6H), 7.66–7.76 (m, 6H);

¹³C NMR (acetone-*d*₆, δ)

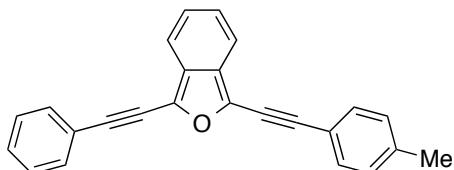
79.5, 99.4, 117.0 (d, J_{C-F} = 21.7 Hz), 119.3 (d, J_{C-F} = 2.9 Hz), 120.1, 127.9, 128.8, 130.9,

134.5 (d, J_{C-F} = 8.7 Hz), 163.9 (d, J_{C-F} = 249.3 Hz);

IR (ATR)

2925, 2853, 2200, 1600, 1542, 1261, 1256, 1154, 1092, 1074, 1013, 908, 836, 752, 734 cm⁻¹;

HRMS (ESI) *m/z* 354.0868 (354.0856 calcd for C₂₄H₁₂F₂O [M⁺]).



dialkynylisobenzofuran **9a**

Mp 100.5–102.0 °C;

¹H NMR (CDCl₃, δ)

2.39 (s, 3H), 7.09 (dd, 2H, J_1 = 2.8 Hz, J_2 = 6.7 Hz), 7.19 (d, 2H, J = 7.9 Hz), 7.36–7.39 (m, 3H), 7.48 (d, 2H, J = 7.9 Hz), 7.55–7.63 (m, 4H);

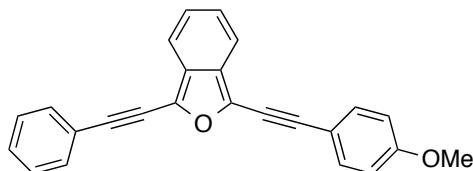
¹³C NMR (acetone-*d*₆, δ)

21.7, 79.2, 79.9, 100.5, 100.8, 119.9, 120.1, 120.2, 123.0, 127.7, 127.8, 128.6, 128.8, 129.8, 130.1, 130.5, 130.8, 132.1, 140.6;

IR (ATR)

3057, 2923, 2195, 1631, 1596, 1543, 1510, 1493, 1442, 1152, 1076, 815, 751 cm⁻¹;

HRMS (ESI) *m/z* 355.1108 (355.1099 calcd for C₂₅H₁₆ONa [M+Na]⁺).



dialkynylisobenzofuran **9b**

Mp 102.4–103.6 °C;

¹H NMR (CDCl₃, δ)

3.86 (s, 3H), 6.93 (d, 2H, J = 9.0 Hz), 7.05–7.12 (m, 2H), 7.38–7.41 (m, 4H), 7.54 (d, 2H, J = 8.6 Hz) 7.55–7.61 (m, 3H);

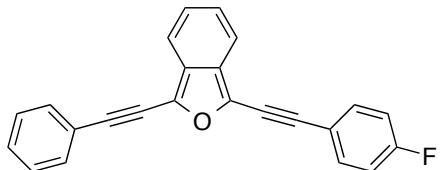
¹³C NMR (CDCl₃, δ)

55.3, 78.2, 79.6, 99.4, 99.5, 114.2, 114.3, 119.3, 119.5, 122.4, 125.9, 126.1, 127.3, 127.8, 128.5, 128.6, 129.8, 130.6, 131.2, 132.9, 160.1;

IR (ATR)

3058, 2929, 2191, 1636, 1603, 1511, 1493, 1293, 1251, 1173, 1173, 1075, 1031, 831, 754 cm⁻¹;

HRMS (ESI) *m/z* 387.0808 (387.0787 calcd for C₂₅H₁₆O₂K [M+K]⁺).



dialkynylisobenzofuran **9c**

Mp 72.2–74.5 °C;

¹H NMR (CDCl₃, δ)

7.05–7.14 (m, 4H), 7.39 (d, 2H, J = 2.1 Hz) 7.41 (d, 1H, J = 1.7 Hz), 7.54–7.63 (m, 6H);

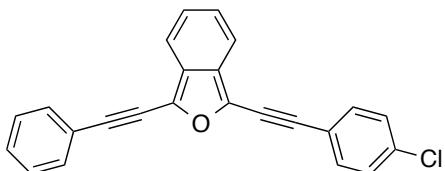
¹³C NMR (CDCl₃, δ)

79.2, 79.4, 98.3, 99.5, 115.9 (d, J_{C-F} = 22.4 Hz), 118.4, 119.3, 119.5, 122.3, 126.2 (d, J_{C-F} = 4.3 Hz), 127.8, 128.5, 128.8, 130.0, 130.3, 131.3, 133.2 (d, J_{C-F} = 8.7 Hz), 162.8 (d, J_{C-F} = 250.7 Hz);

IR (ATR)

3033, 2926, 2199, 1635, 1600, 1542, 1509, 1493, 1261, 1215, 1155, 1077, 1013, 908, 836, 752 cm⁻¹;

HRMS (ESI) *m/z* 375.0600 (375.0587 calcd for C₂₄H₁₃FOK [M+K]⁺).



dialkynylisobenzofuran **9d**

Mp 121.6–122.5 °C;

¹H NMR (CDCl₃, δ)

7.09 (dd, 2H, J₁ = 2.4 Hz, J₂ = 6.2 Hz), 7.33–7.42 (m, 5H), 7.49 (d, 2H, J = 8.6 Hz), 7.53–7.60 (m, 4H);

¹³C NMR (CDCl₃, δ)

79.4, 80.5, 98.4, 99.6, 119.3, 119.5, 120.8, 122.2, 126.2, 126.4, 127.8, 128.0, 128.5, 128.8, 128.9, 129.9, 130.5, 131.3, 132.3, 134.8;

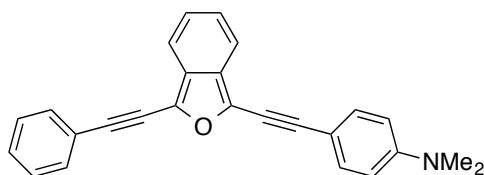
IR (ATR)

3059, 2197, 1641, 1488, 1290, 1213, 1092, 1013, 827, 754 cm⁻¹;

HRMS (ESI) *m/z* 353.0751 (353.0733 calcd for C₂₄H₁₄ClO [M+H]⁺).

Synthesis of dialkynylisobenzofuran 9e:

To a solution of keto-aldehyde **7a** (21.0 mg, 0.090 mmol) in THF (1.5 mL) was added [4-(dimethylamino)phenylethynyl]lithium (0.56 M in THF, 0.32 mL, 0.179 mmol), prepared by treatment of 4-ethynyl-*N,N*-dimethylaniline (88.1 mg, 0.60 mmol) with *n*-BuLi (1.55 M in hexane, 0.39 mL, 0.605 mmol) in THF (0.7 mL) at –78 °C. After gradually warmed up to –40 °C for 3 h, acetic anhydride (1.0 mL) was added to the reaction mixture at 0 °C, and the reaction was stirred at room temperature. After 3 h, the reaction was stopped by adding sat. aq. NaHCO₃. The products were extracted with EtOAc (X3), washed with brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/CH₂Cl₂ = 95/5) to give dialkynylisobenzofuran **9e** (13.9 mg, 42.9%) as a red oil.



dialkynylisobenzofuran **9e**

¹H NMR (acetone-*d*₆, δ)

3.03 (s, 6H), 6.78 (d, 2H, J = 8.9 Hz), 7.12–7.21 (m, 2H), 7.45–7.49 (m, 5H), 7.61–7.67 (m, 4H);

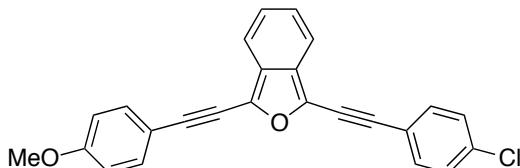
¹³C NMR (acetone-*d*₆, δ)

40.1, 77.9, 80.0, 100.3, 102.3, 108.7, 112.8, 119.8, 120.3, 123.1, 127.0, 127.57, 127.64, 128.9, 129.6, 129.8, 131.9, 132.1, 133.4, 151.8;

IR (ATR)

2925, 2177, 1605, 1545, 1522, 1364, 1197, 1159, 1070, 946, 817, 753 cm⁻¹;

HRMS (ESI) *m/z* 400.1090 (400.1104 calcd for C₂₆H₁₉NOK [M+K]⁺).



dialkynylisobenzofuran **9f**

Mp 110.7–112.2 °C;

¹H NMR (CDCl₃, δ)

3.85 (s, 3H), 6.92 (d, 2H, J = 8.6 Hz), 7.05–7.12 (m, 2H), 7.36 (d, 2H, J = 8.6 Hz), 7.48–7.60 (m, 6H);

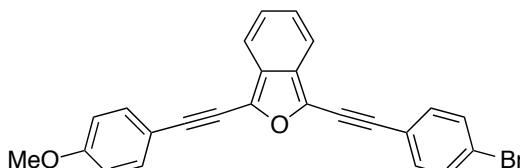
¹³C NMR (CDCl₃, δ)

55.3, 78.2, 80.6, 98.3, 99.6, 114.2, 119.2, 119.6, 120.9, 126.0, 126.4, 127.3, 128.1, 128.9, 129.4, 130.9, 132.3, 133.0, 134.7, 160.2;

IR (ATR)

2928, 2192, 1604, 1511, 1493, 1295, 1251, 1173, 1091, 1031, 909, 820, 739 cm⁻¹;

HRMS (ESI) *m/z* 421.0395 (421.0398 calcd for C₂₅H₁₅ClO₂K [M+K]⁺).



dialkynylisobenzofuran **9g**

Mp 106.4–109.1 °C;

¹H NMR (CDCl₃, δ)

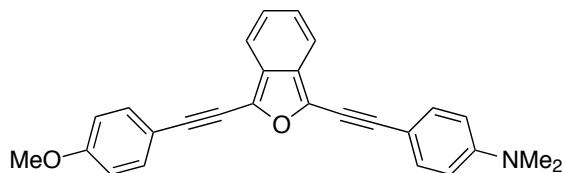
3.85 (s, 3H), 6.92 (d, 2H, J = 8.9 Hz), 7.05–7.12 (m, 2H), 7.43 (d, 2H, J = 8.9 Hz), 7.49–7.60 (m, 6H);

¹³C NMR (CDCl₃, δ)

55.4, 78.2, 80.8, 98.4, 99.7, 114.2, 114.4, 119.2, 119.6, 121.4, 122.9, 126.0, 126.4, 127.3, 128.1, 129.4, 131.0, 131.8, 132.5, 133.0, 160.2;

IR (ATR)

2956, 2929, 2192, 1603, 1509, 1292, 1252, 1173, 1010, 827, 759 cm^{-1} ;
 HRMS (ESI) m/z 464.9902 (464.9892 calcd for $\text{C}_{25}\text{H}_{15}\text{BrO}_2\text{K} [\text{M}+\text{K}]^+$).



dialkynylisobenzofuran **9h**

Mp 118.8–121.1 °C;

^1H NMR (CDCl_3 , δ)

3.01 (s, 6H), 3.84 (s, 3H), 6.67 (d, 2H, $J = 8.9$ Hz), 6.90 (d, 2H, $J = 8.9$ Hz), 7.00–7.07 (m, 2H), 7.44–7.58 (m, 6H);

^{13}C NMR (CDCl_3 , δ)

40.1, 55.3, 77.7, 78.5, 99.2, 100.7, 108.8, 111.8, 114.2, 114.6, 119.3, 119.7, 125.5, 125.8, 126.8, 127.5, 129.6, 130.8, 132.6, 132.8, 150.4, 159.9;

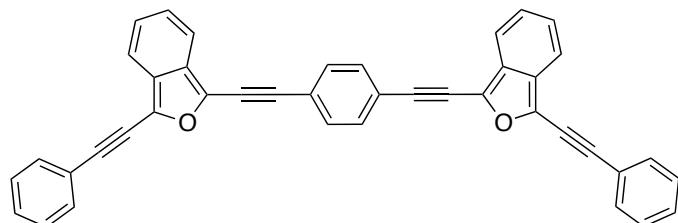
IR (ATR)

2928, 2177, 1604, 1543, 1508, 1364, 1250, 1173, 1074, 1031, 946, 831, 816, 745 cm^{-1} ;

HRMS (ESI) m/z 391.1585 (391.1572 calcd for $\text{C}_{27}\text{H}_{21}\text{NO}_2 [\text{M}]^+$).

Synthesis of dialkynylisobenzofuran **11**:

To a solution of 1,4-diethynylbenzene (22.3 mg, 0.177 mmol) in THF (2.0 mL) was added *n*-BuLi (1.63 M in hexane, 0.220 mL, 0.352 mmol) at 0 °C. After 10 min, the reaction was cooled to –78 °C, to which was added keto-aldehyde **7a** (99.4 mg, 0.424 mmol) in THF (2.0 mL). After gradually warmed up to room temperature for 6 h, the reaction was stopped by adding water. The products were extracted with EtOAc (X3) and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 7/3 → 6/4) to give the bis-adduct (53.8 mg, 50.8%) as a yellow oil. To a solution of bis-adduct (53.8 mg) in THF (2.0 mL) was added 4 M HCl (0.5 mL) at 0 °C. After warmed up to room temperature, the reaction was further stirred for 3 h. The reaction was stopped by adding sat. aq. NaHCO_3 at 0 °C. The products were extracted with CHCl_3 (X3) and the combined organic extracts were washed brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was triturated in hexane and filtrated to give the essentially pure product **11** (49.6 mg, 98.8%) as orange solids.



bis-isobenzofuran **11**

Mp decomposed at 370 °C;

^1H NMR (CDCl_3 , δ)

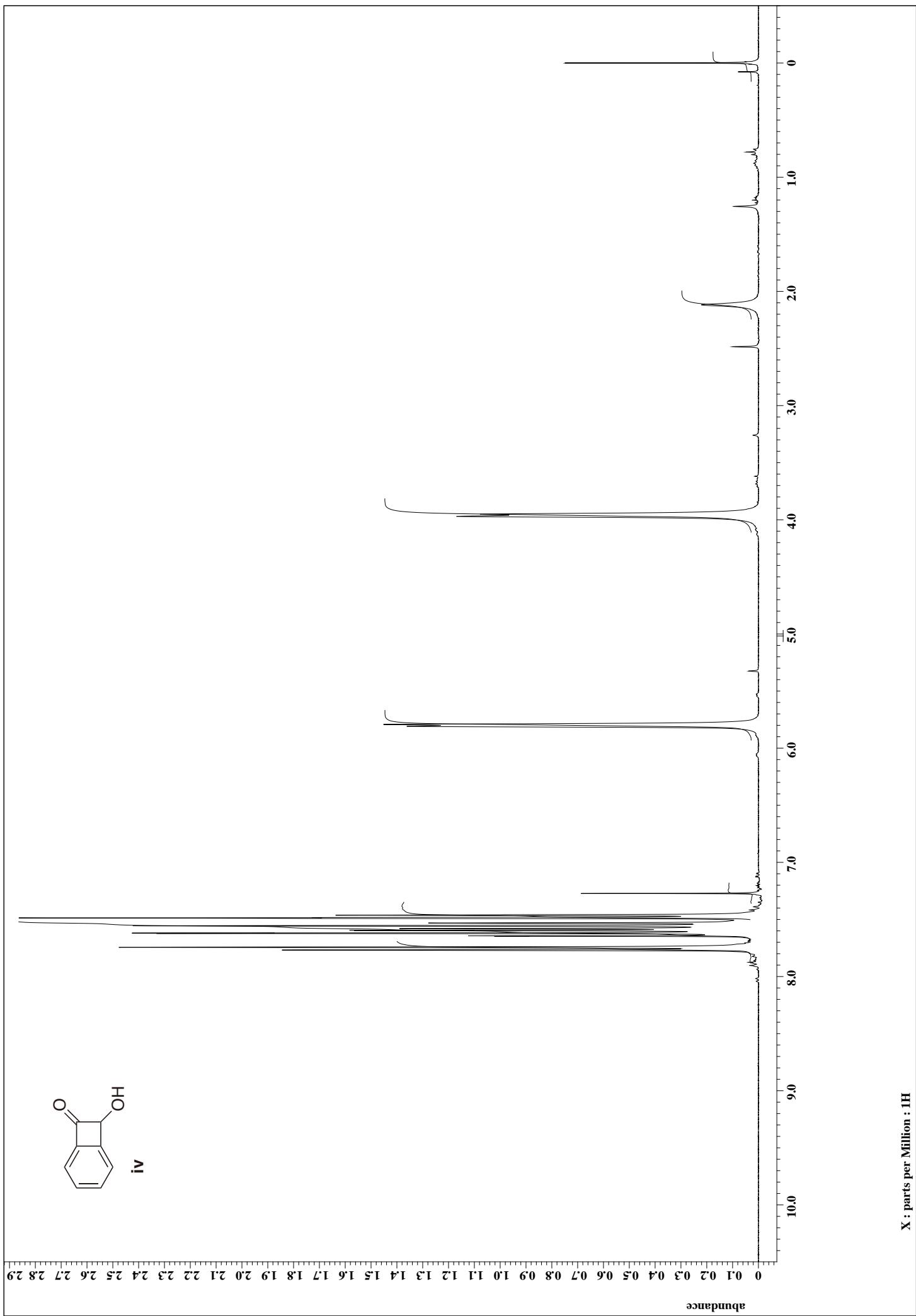
7.09–7.12 (m, 4H), 7.36–7.39 (m, 6H), 7.57–7.62 (m, 12H);

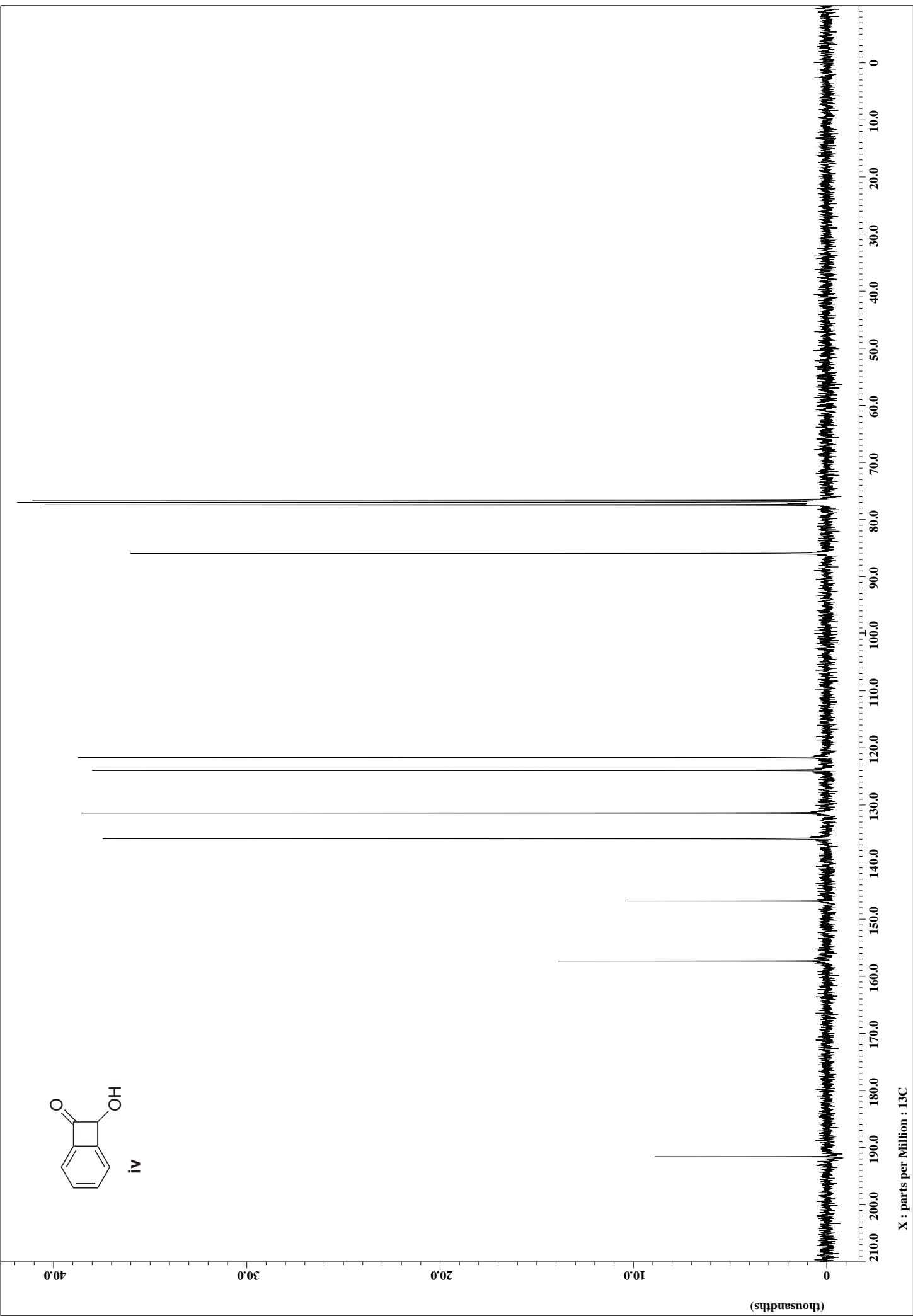
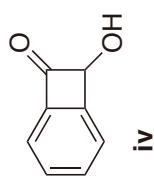
^{13}C NMR (CDCl_3 , δ)

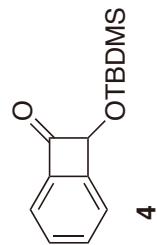
79.5, 82.0, 99.6, 99.8, 119.4, 119.6, 122.4, 122.6, 126.3, 126.5, 128.0, 128.3, 128.5, 128.8,

130.1, 130.8, 131.2, 131.4;
IR (ATR)
2925, 2854, 2194, 1595, 1489, 1262, 1075, 1011, 835, 802, 755, 744 cm⁻¹;
HRMS (MALDI) *m/z* 558.1612 (558.1614 calcd for C₄₂H₂₂O₂ [M⁺]).

X : parts per Million : 1H

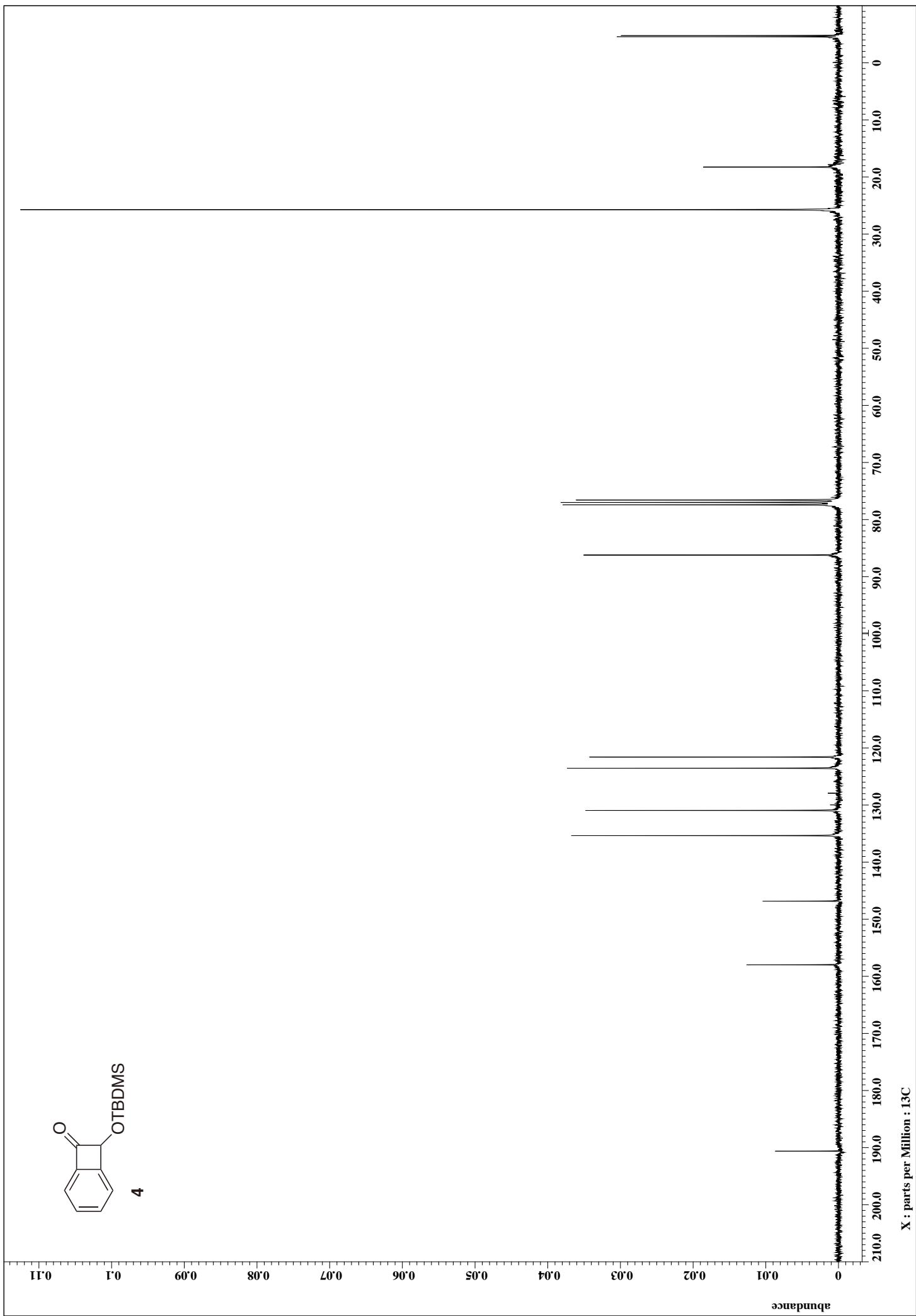
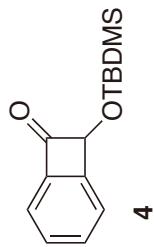


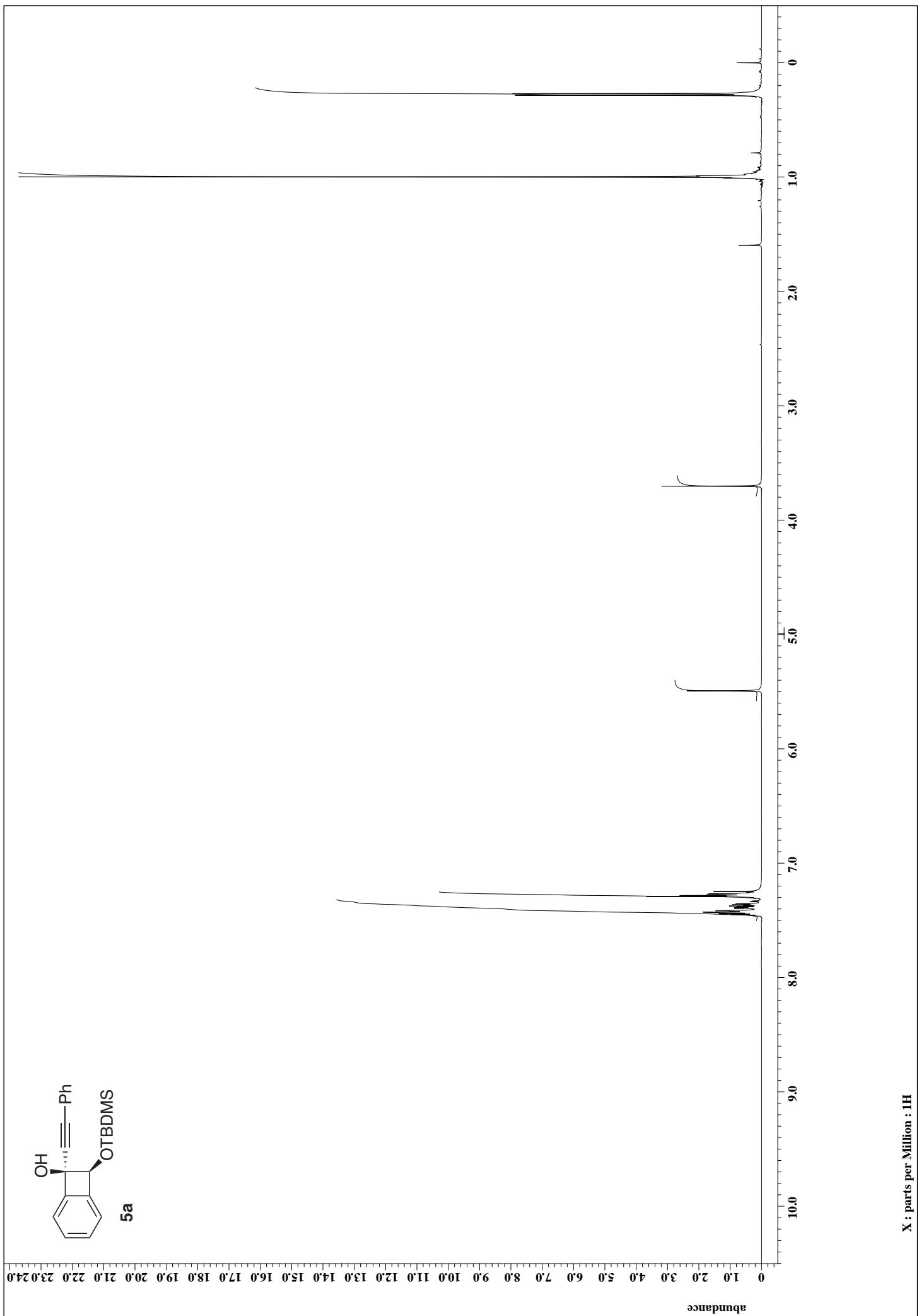


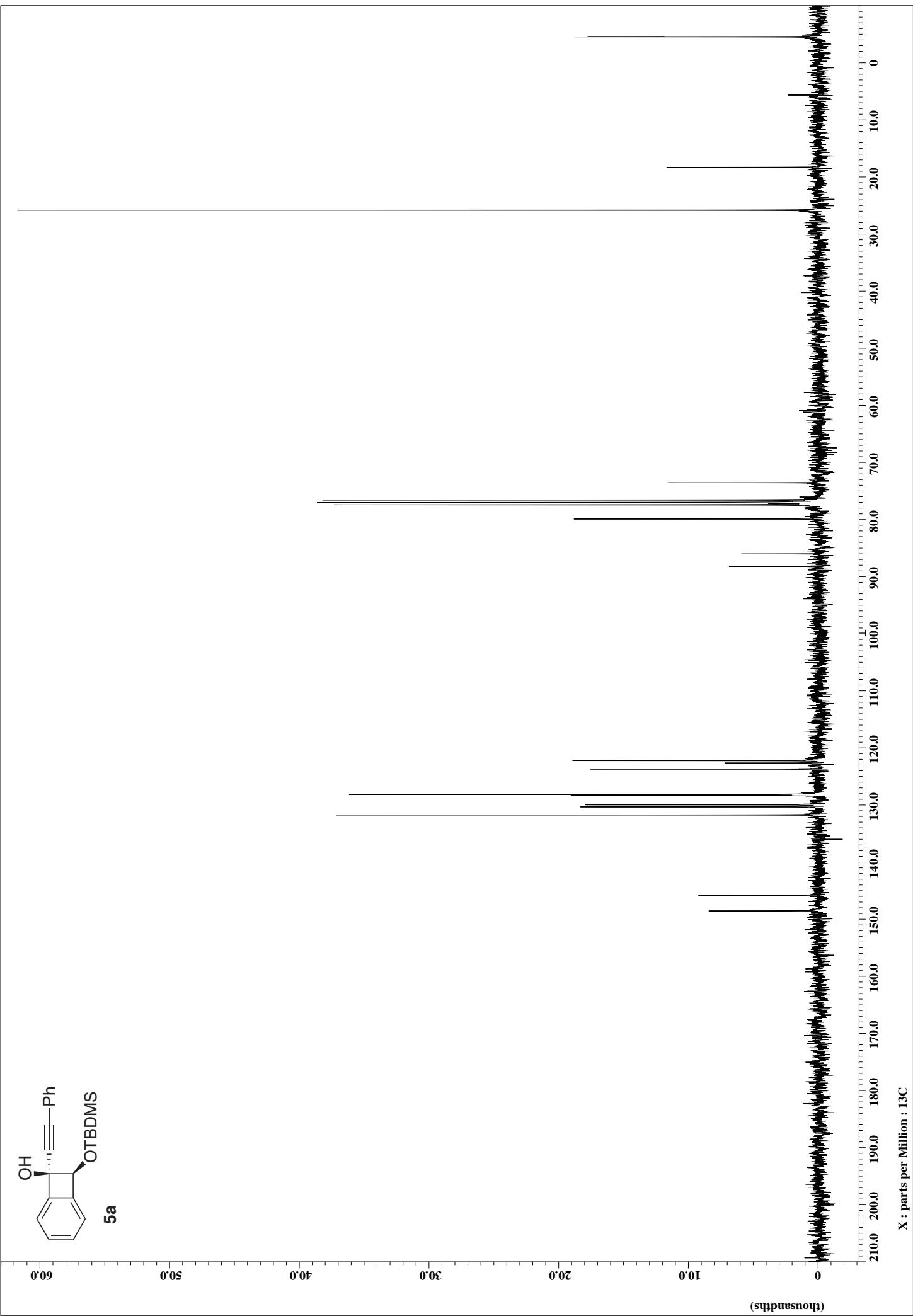
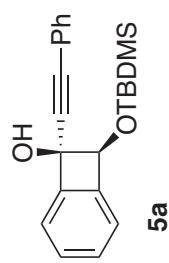


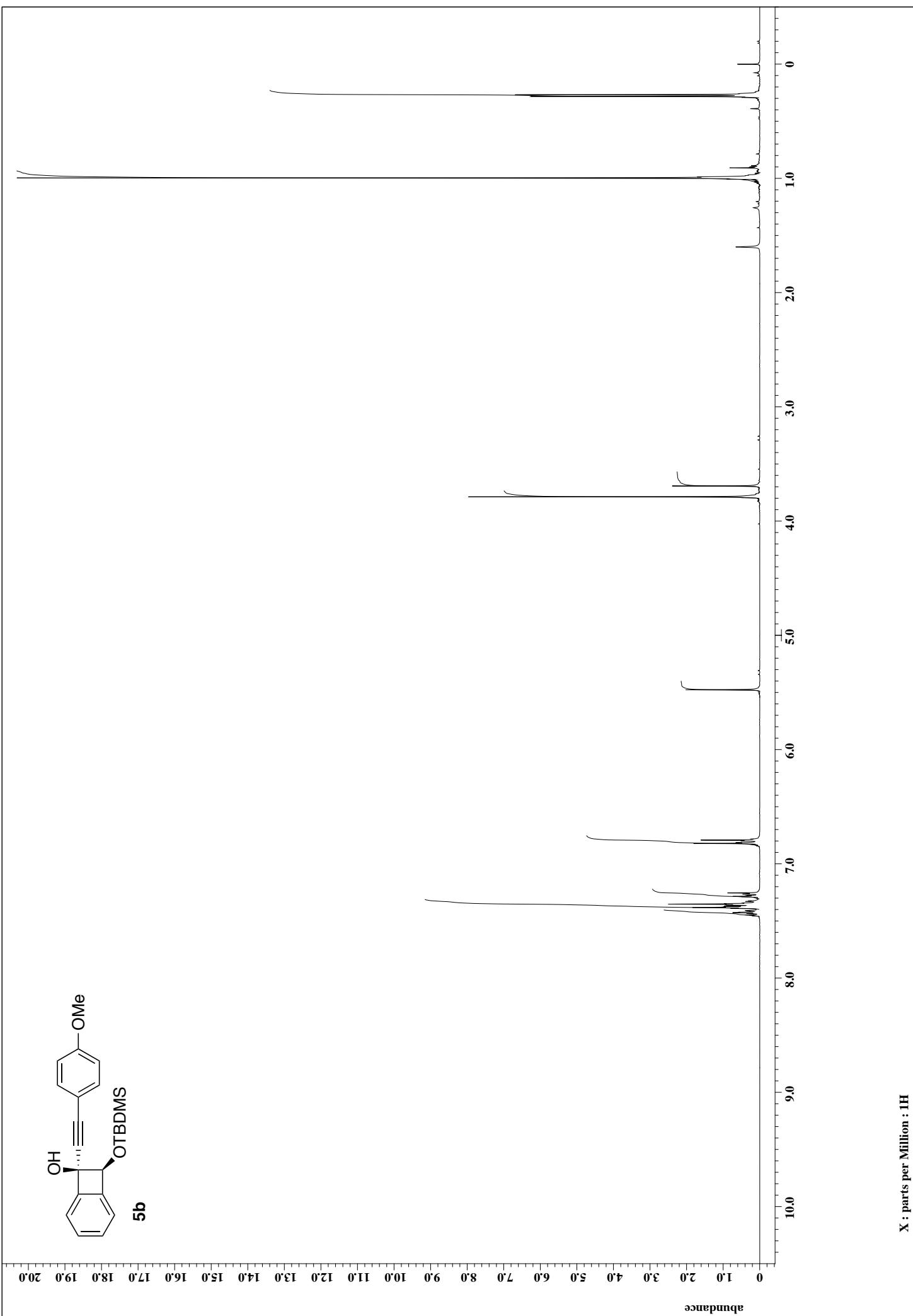
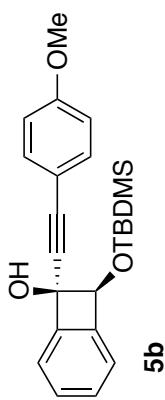
abundance

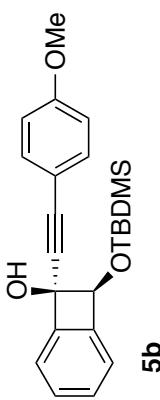
X : parts per Million : 1H











40.0

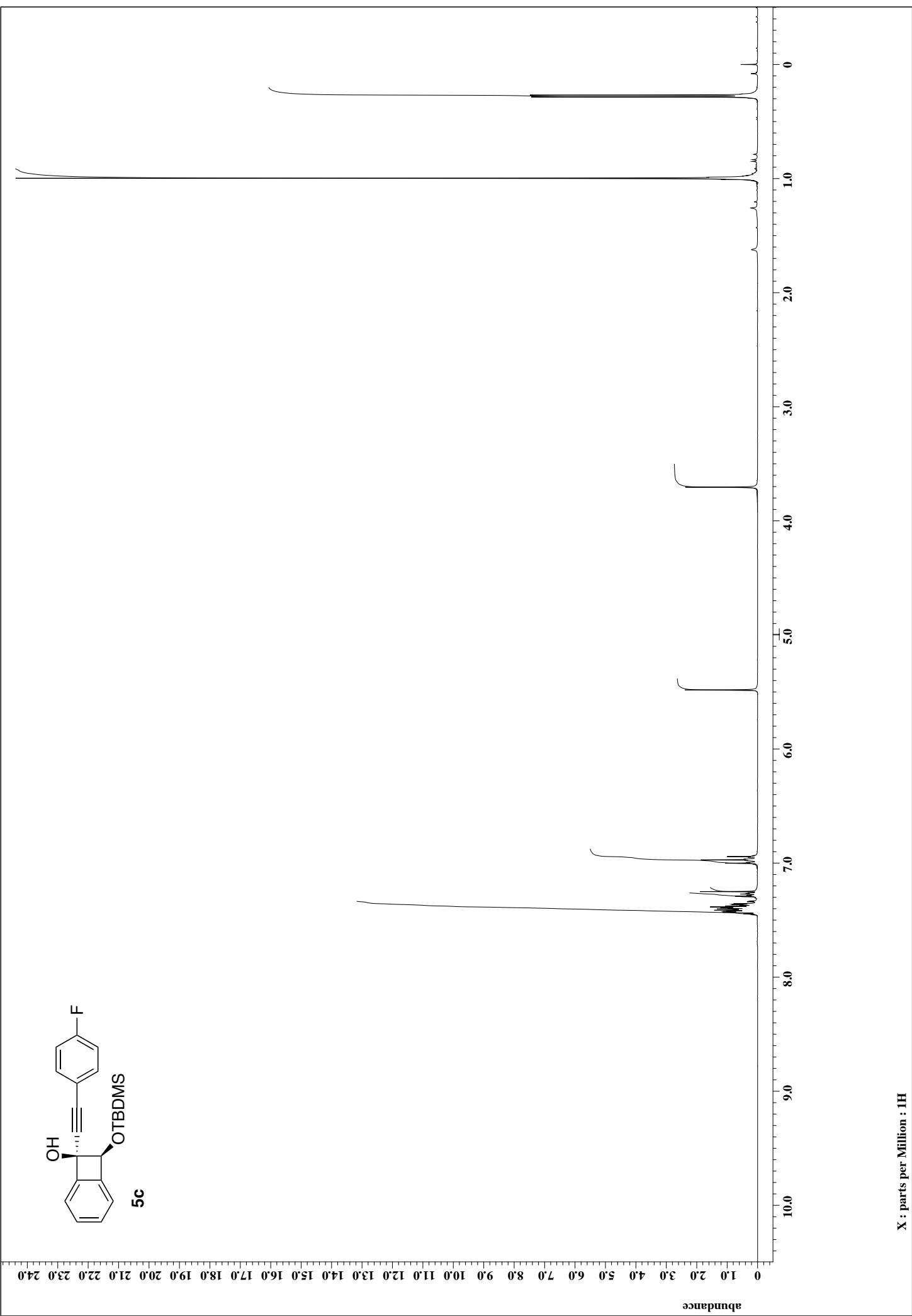
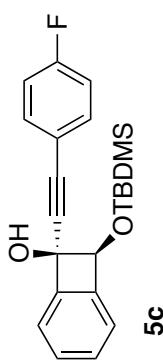
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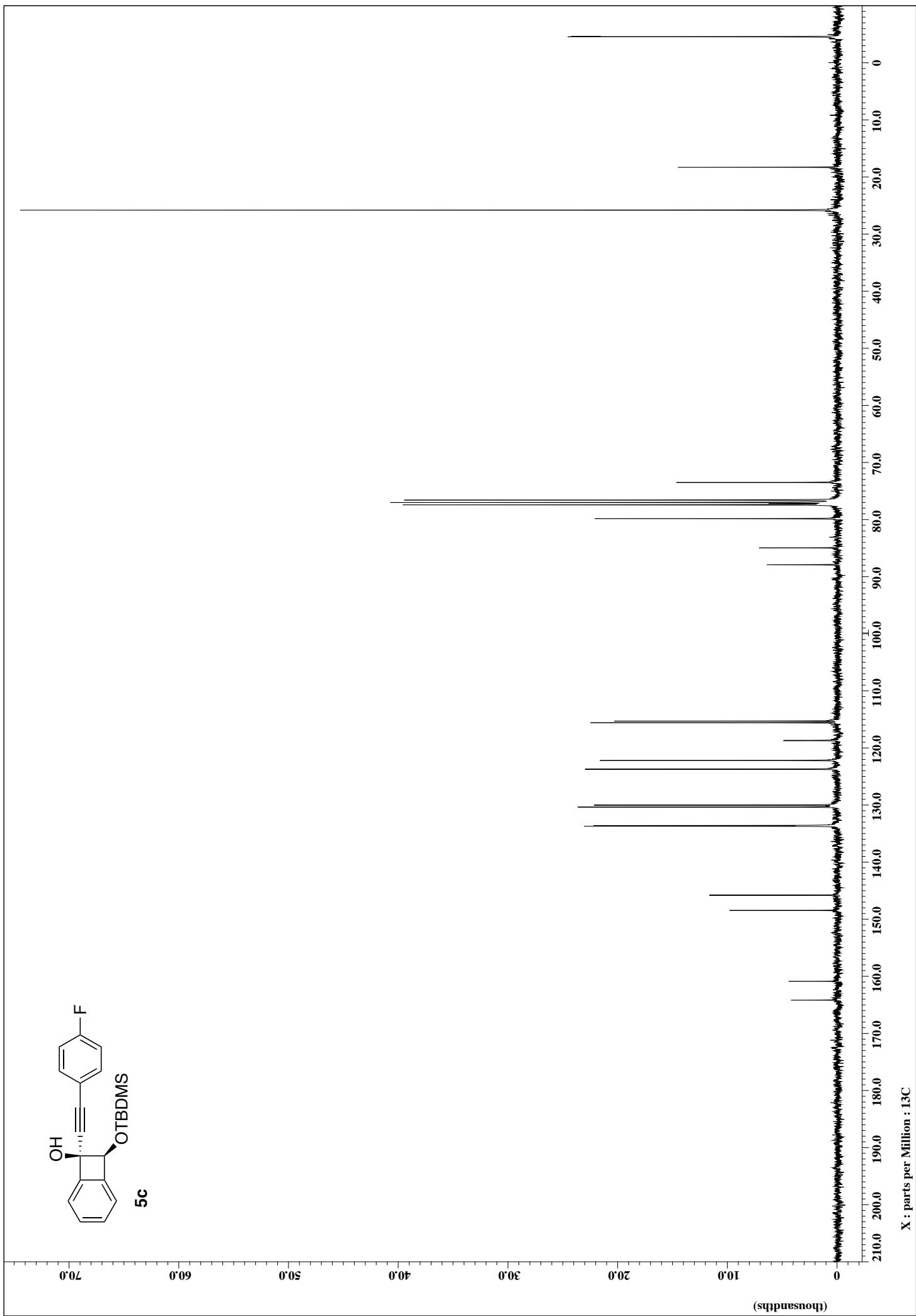
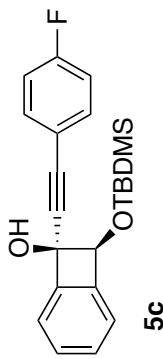
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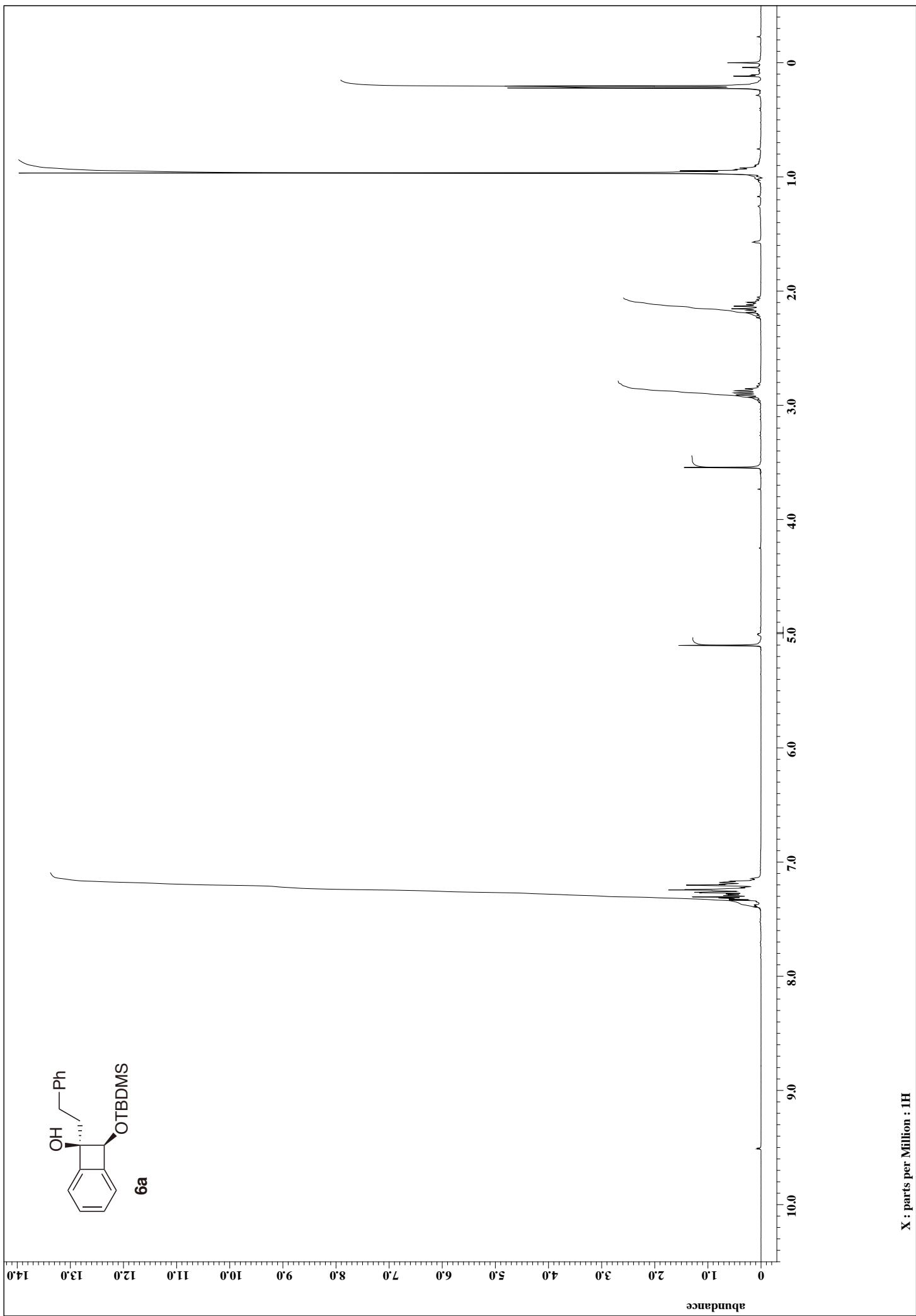
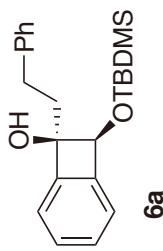
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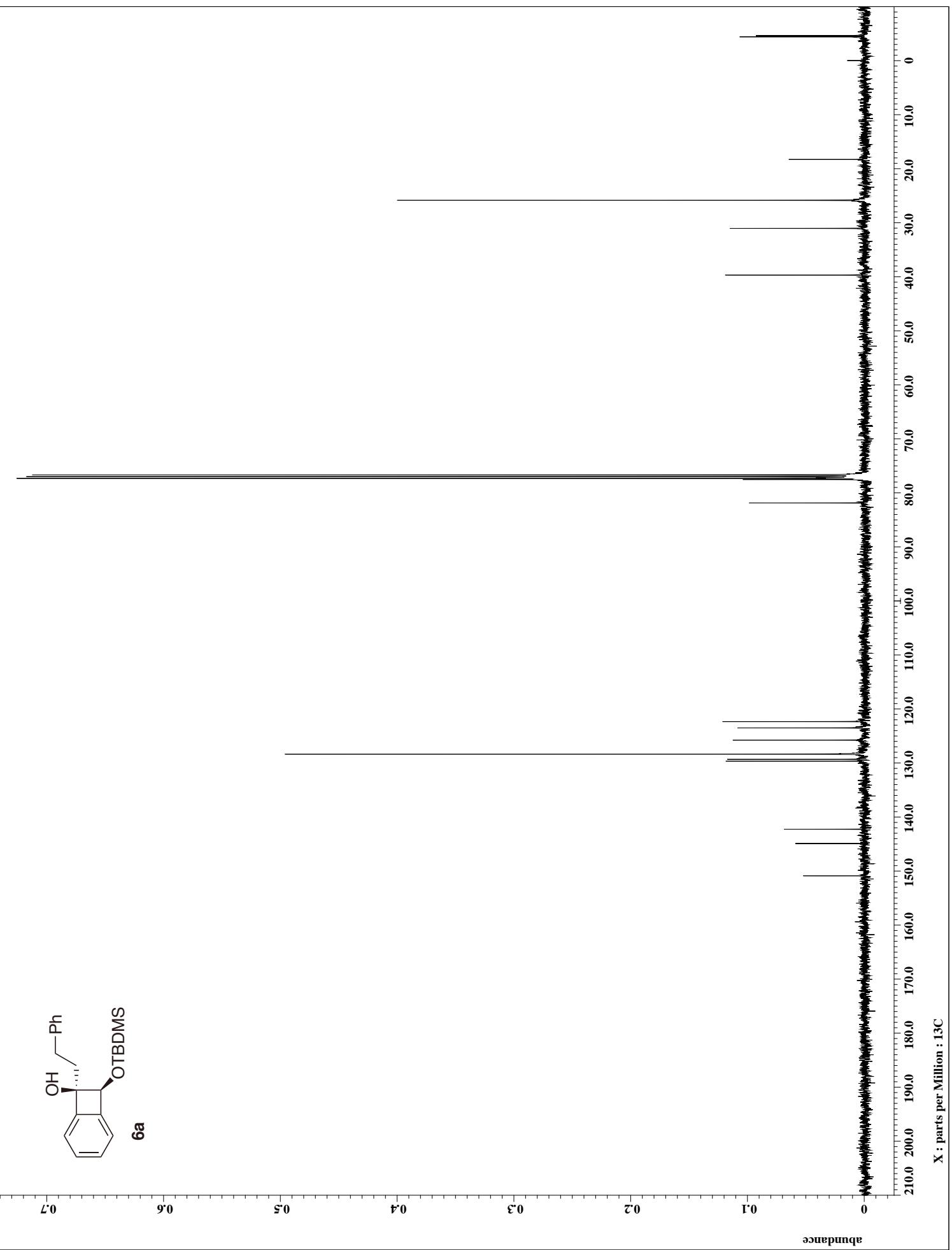
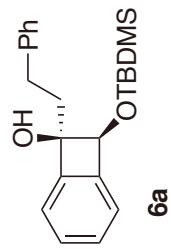
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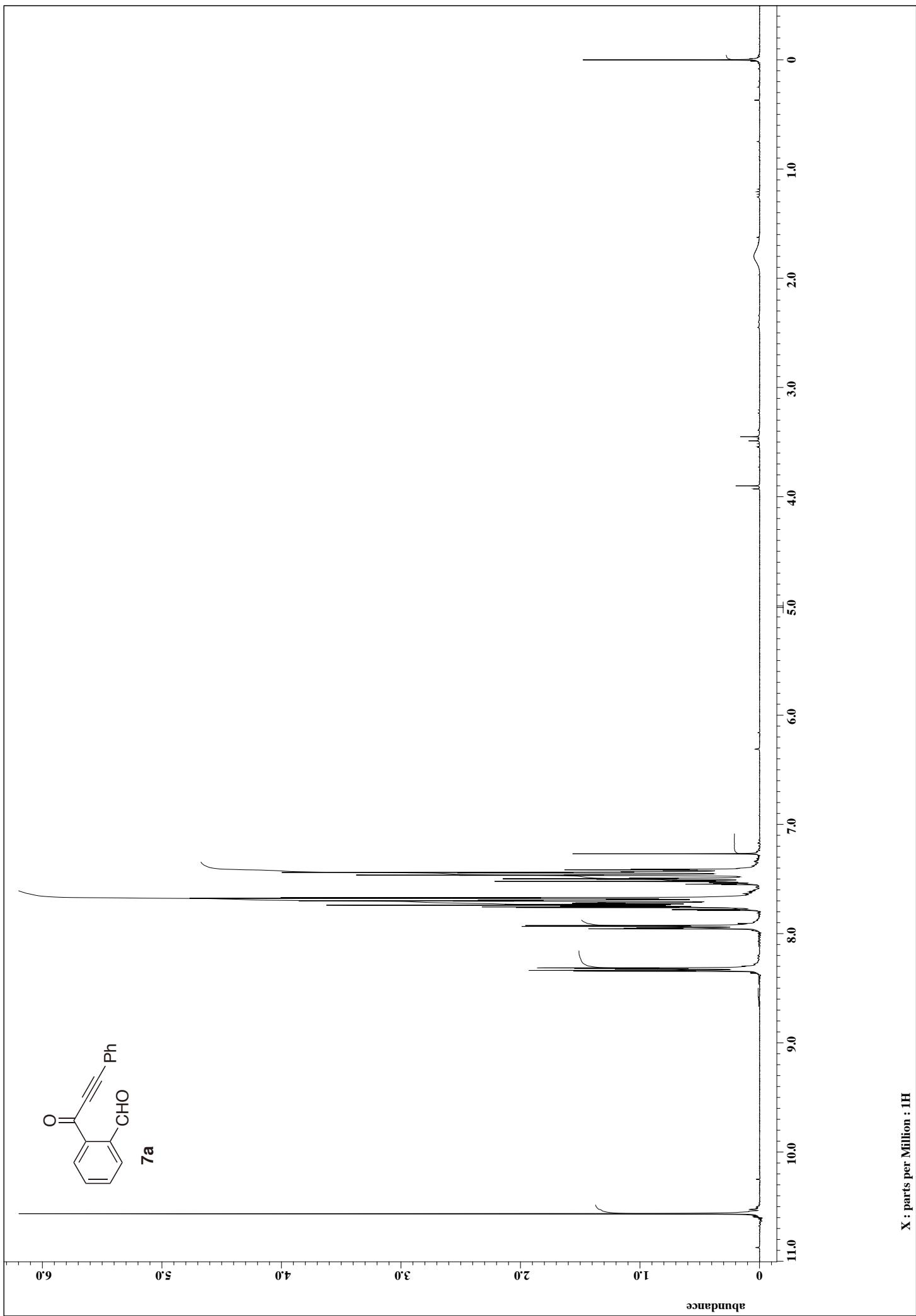
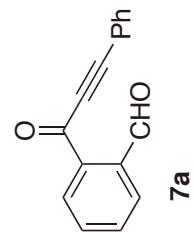
(thousandths)

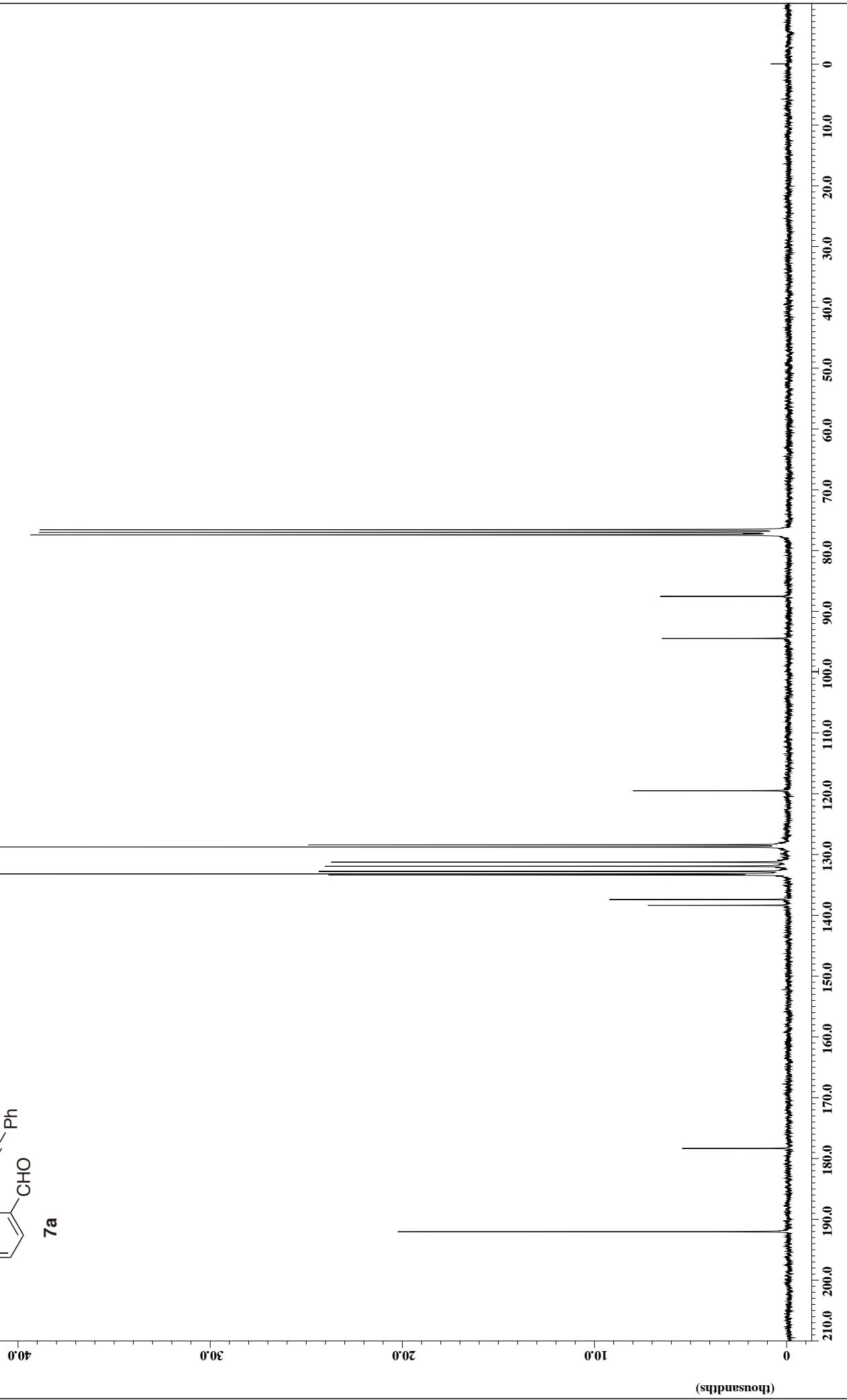
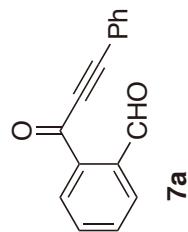


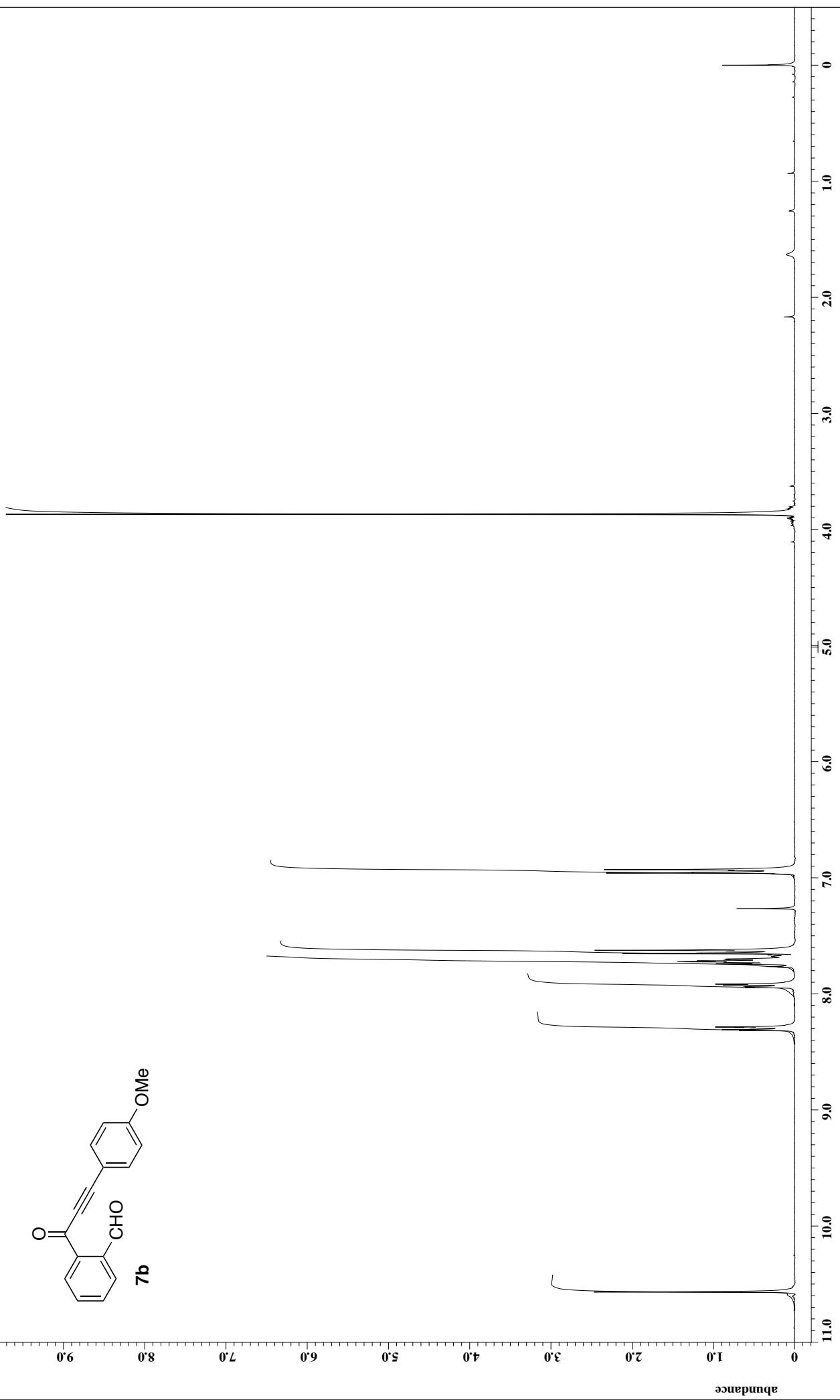
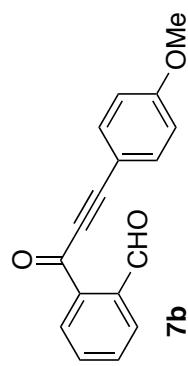




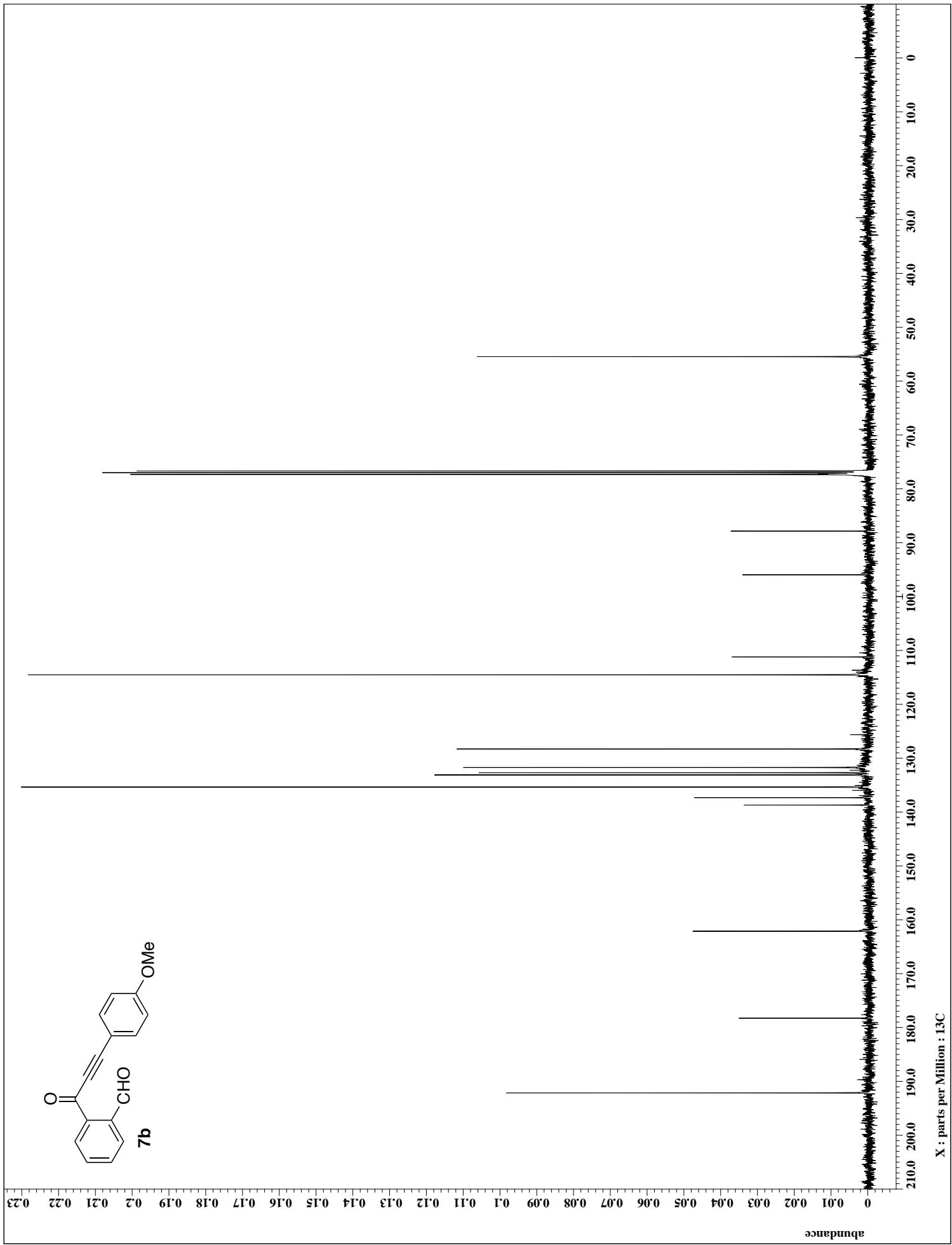
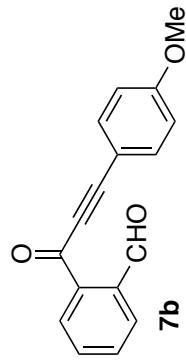


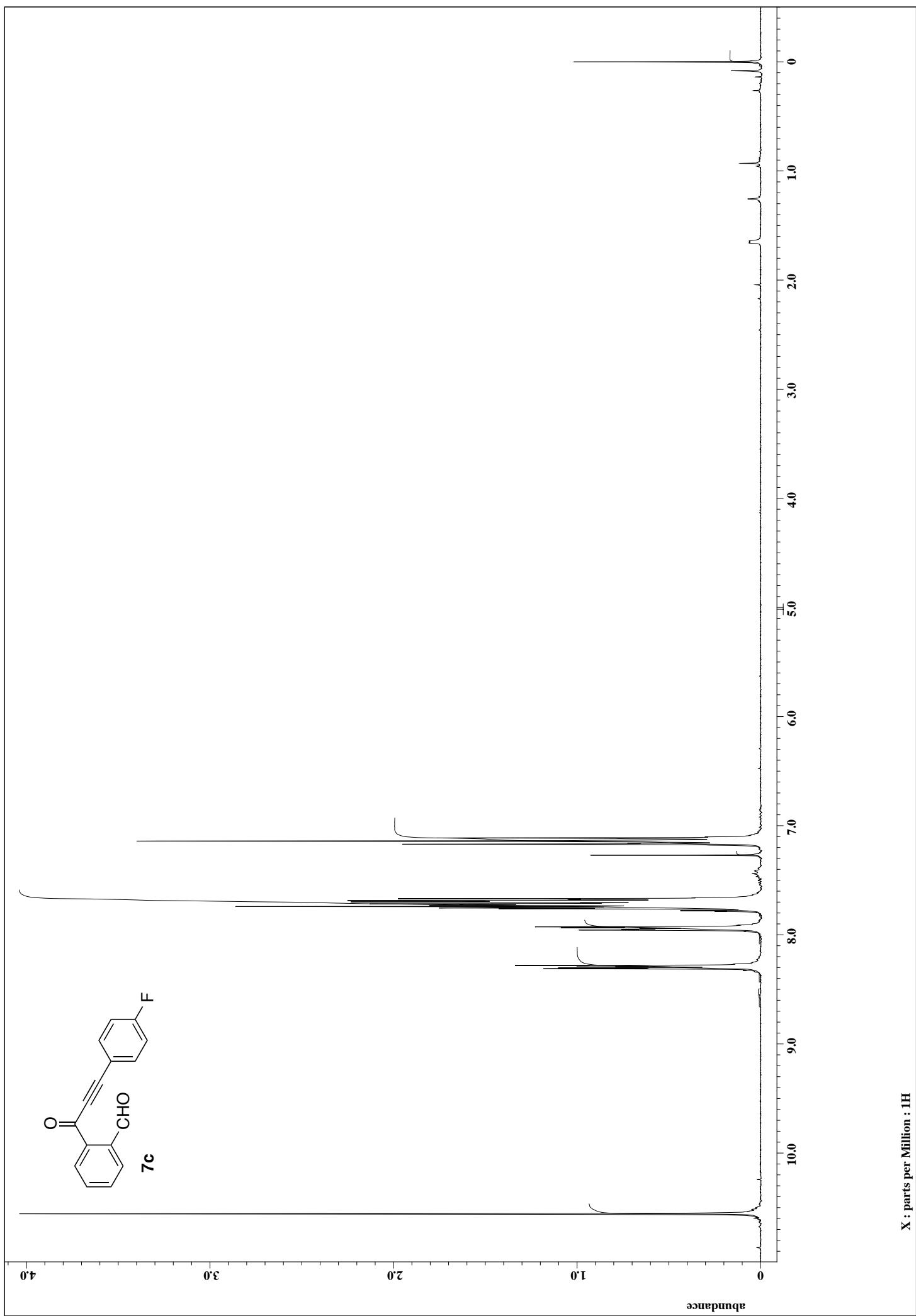
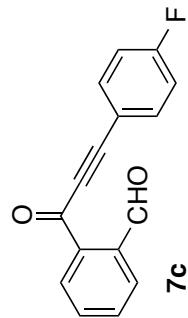


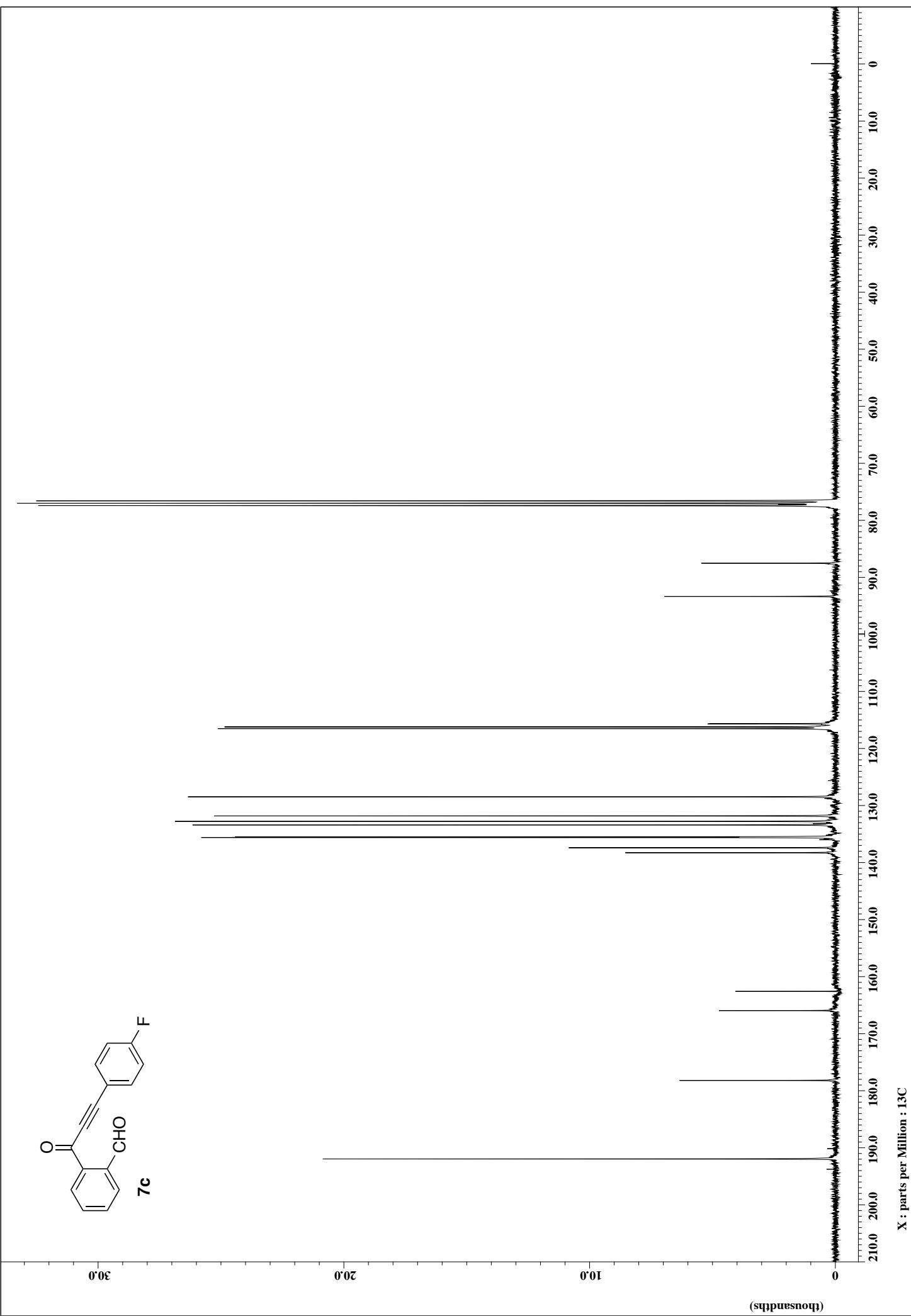
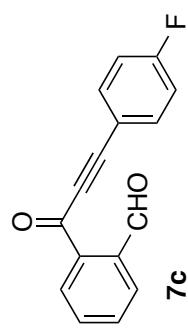


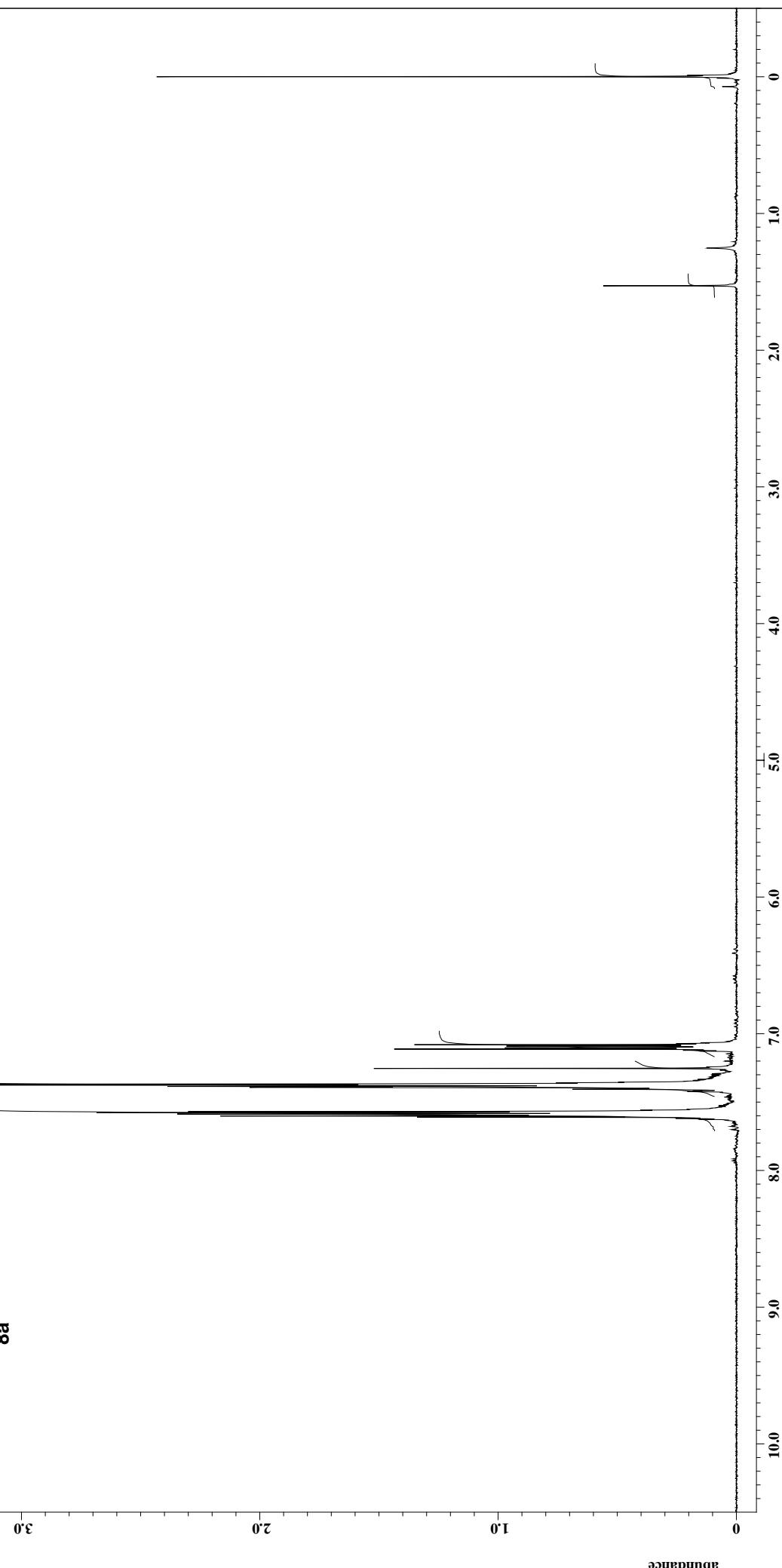
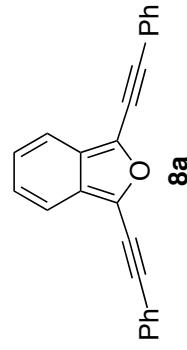


X : parts per Million : 1H

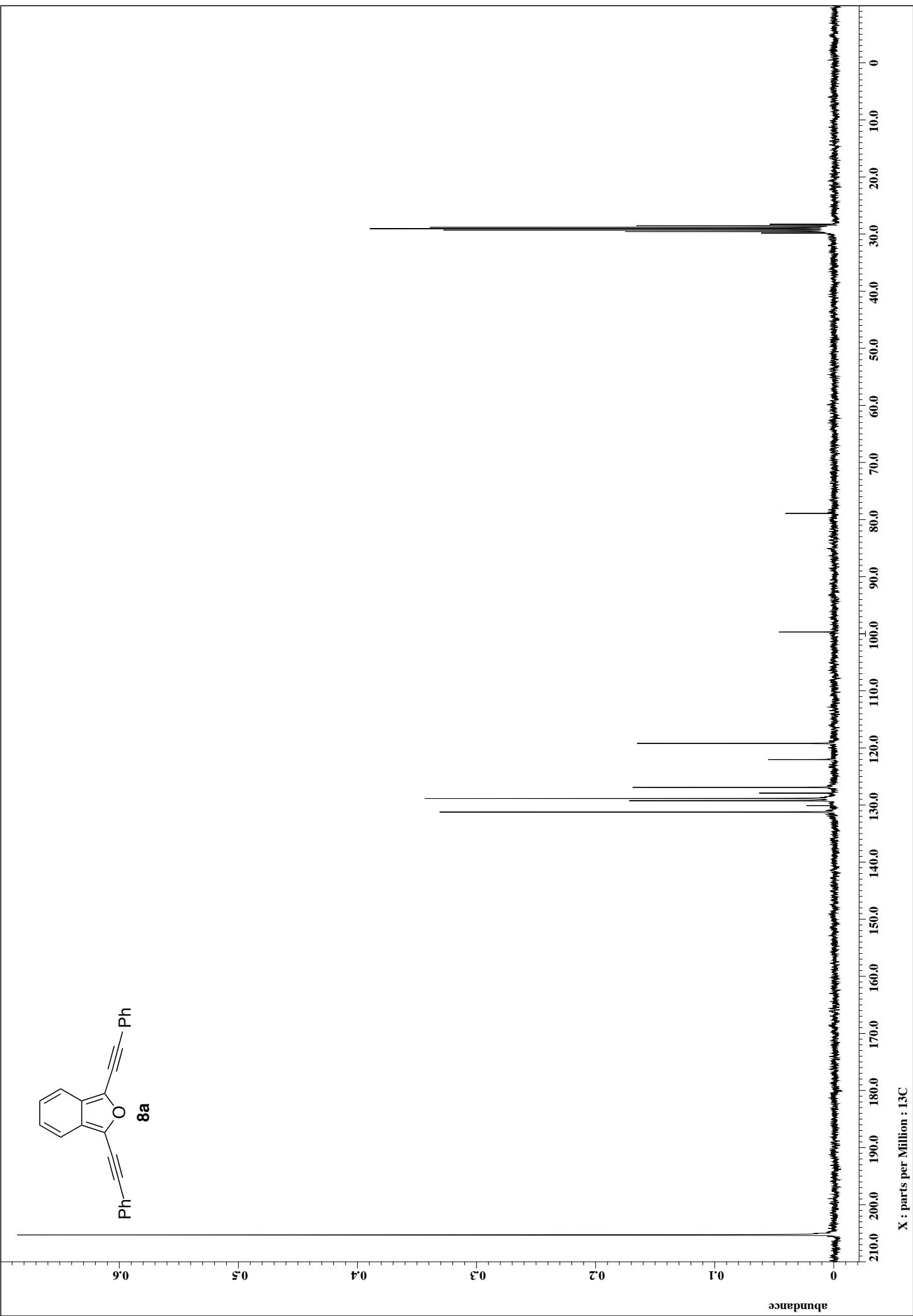
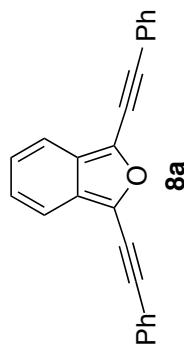


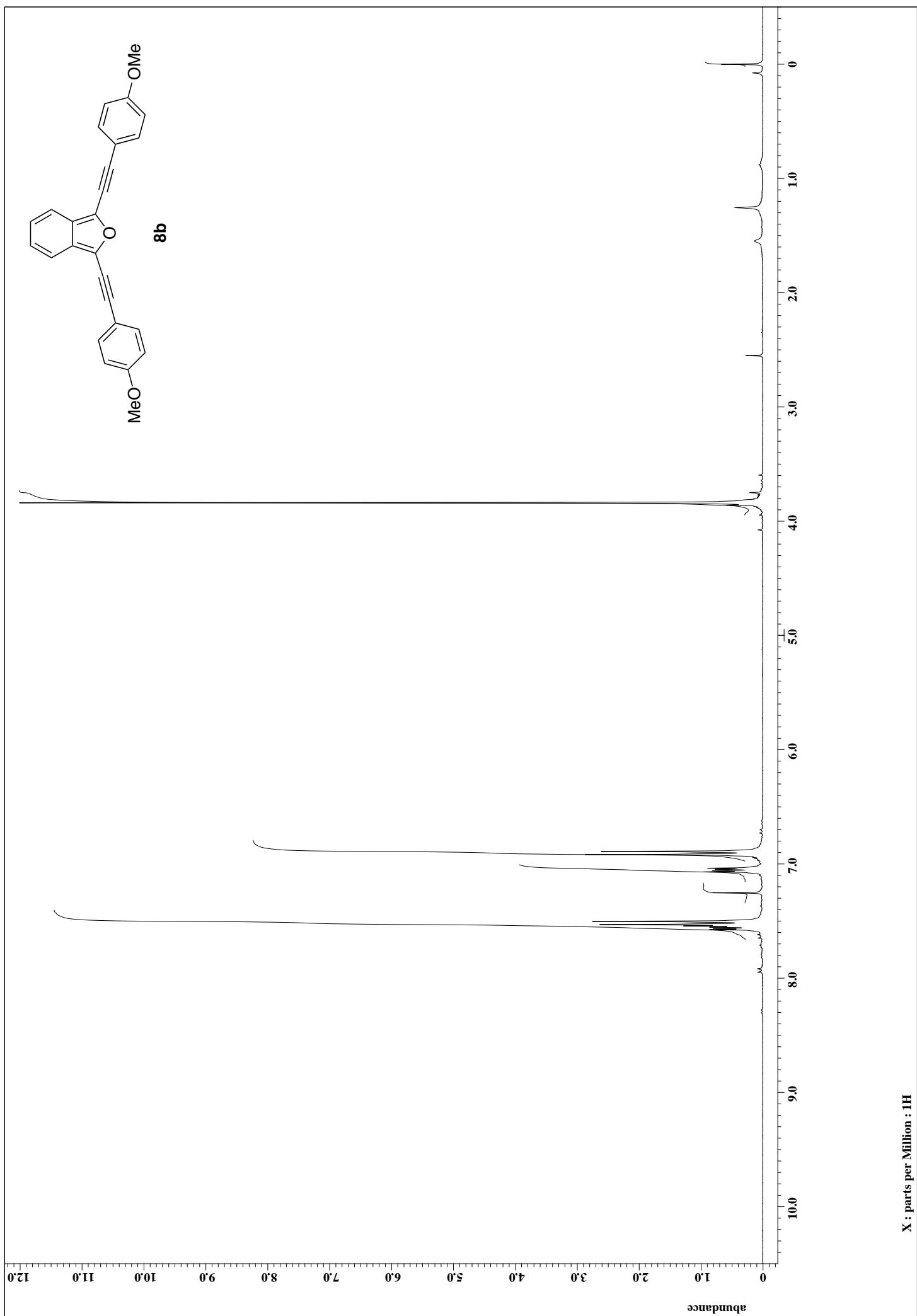
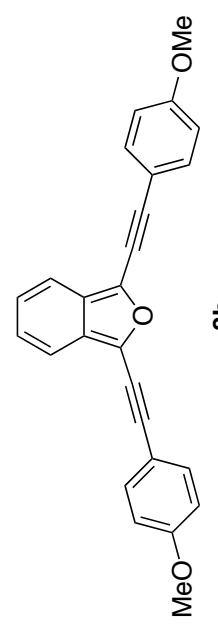


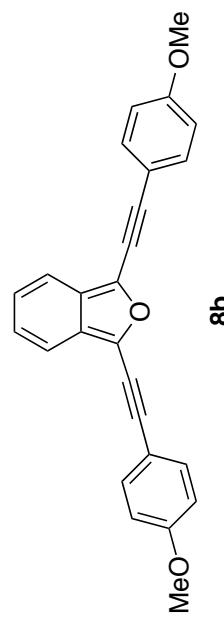




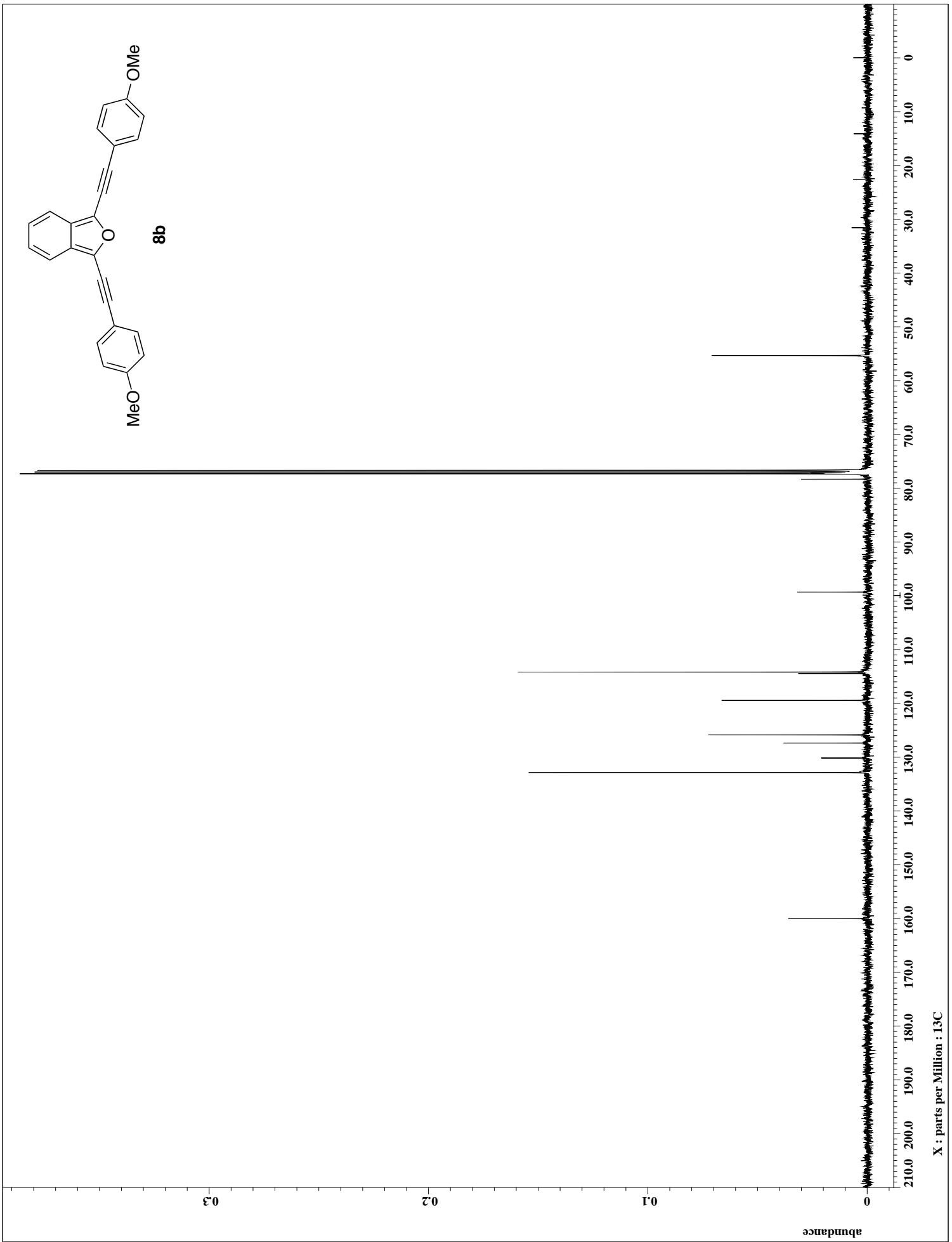
X : parts per Million : 1H

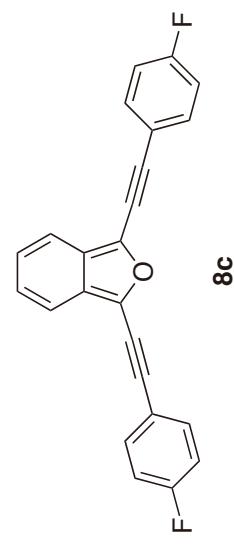




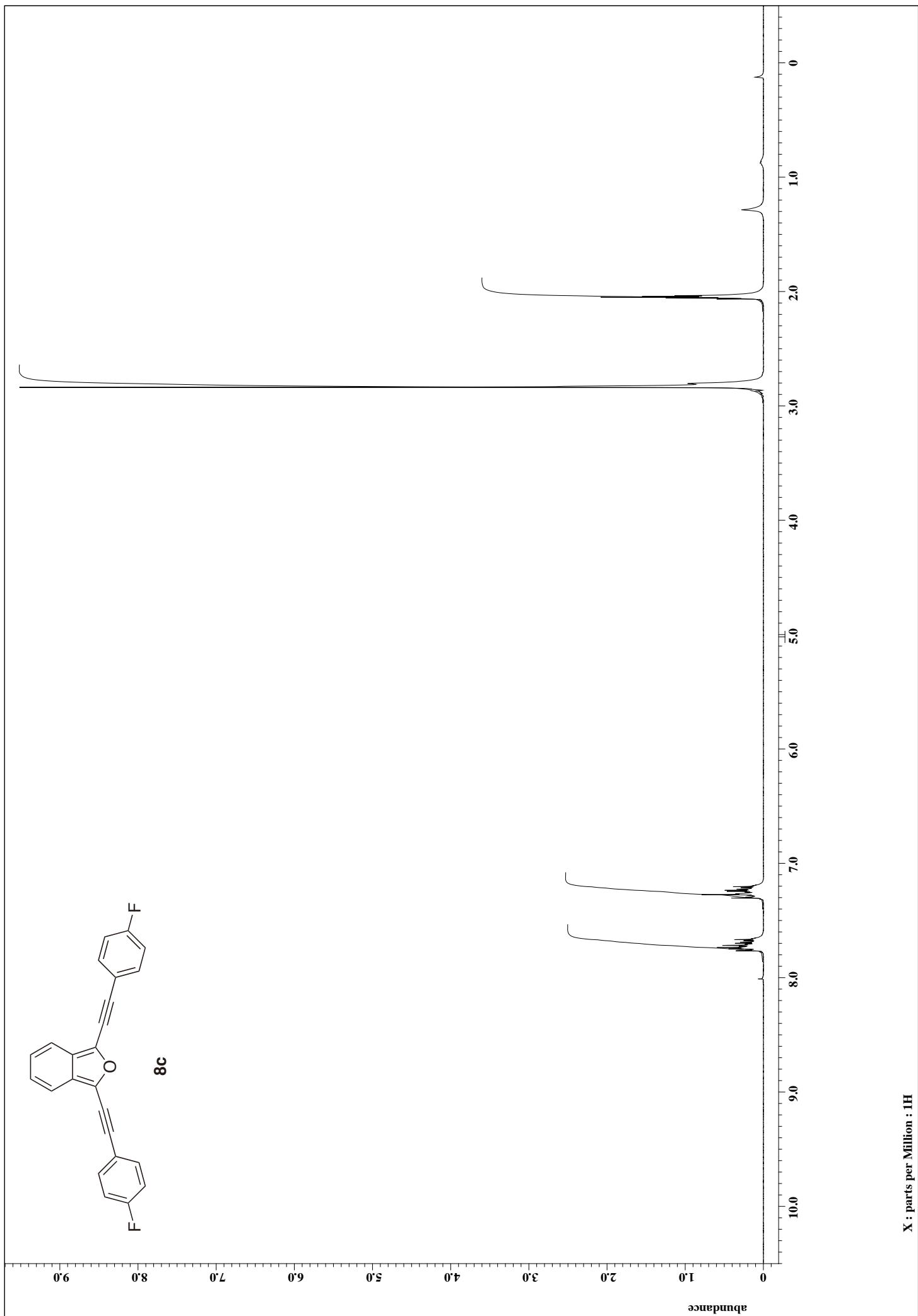


8b

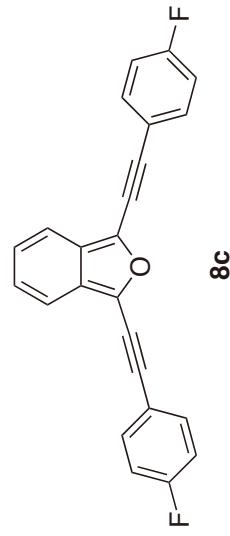




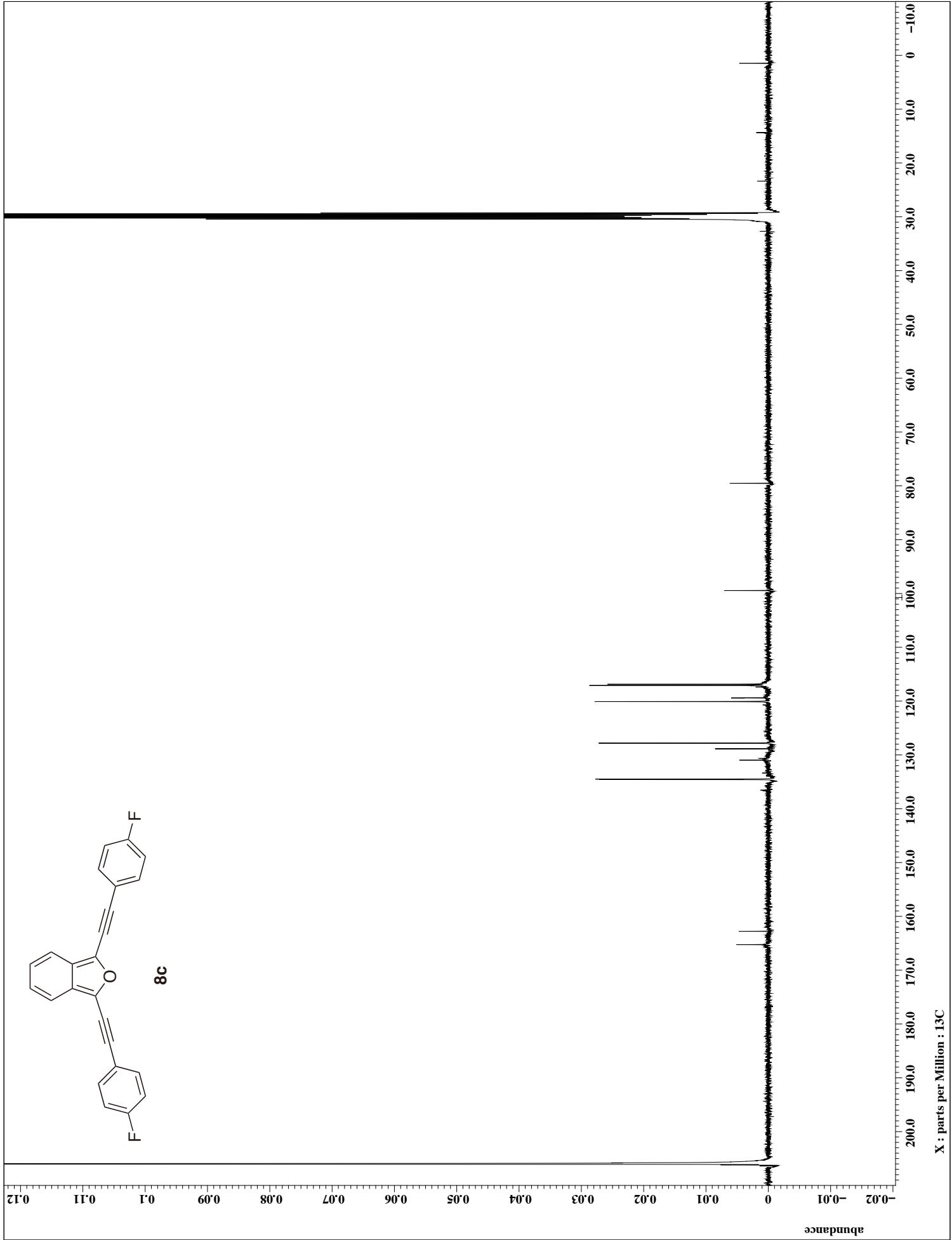
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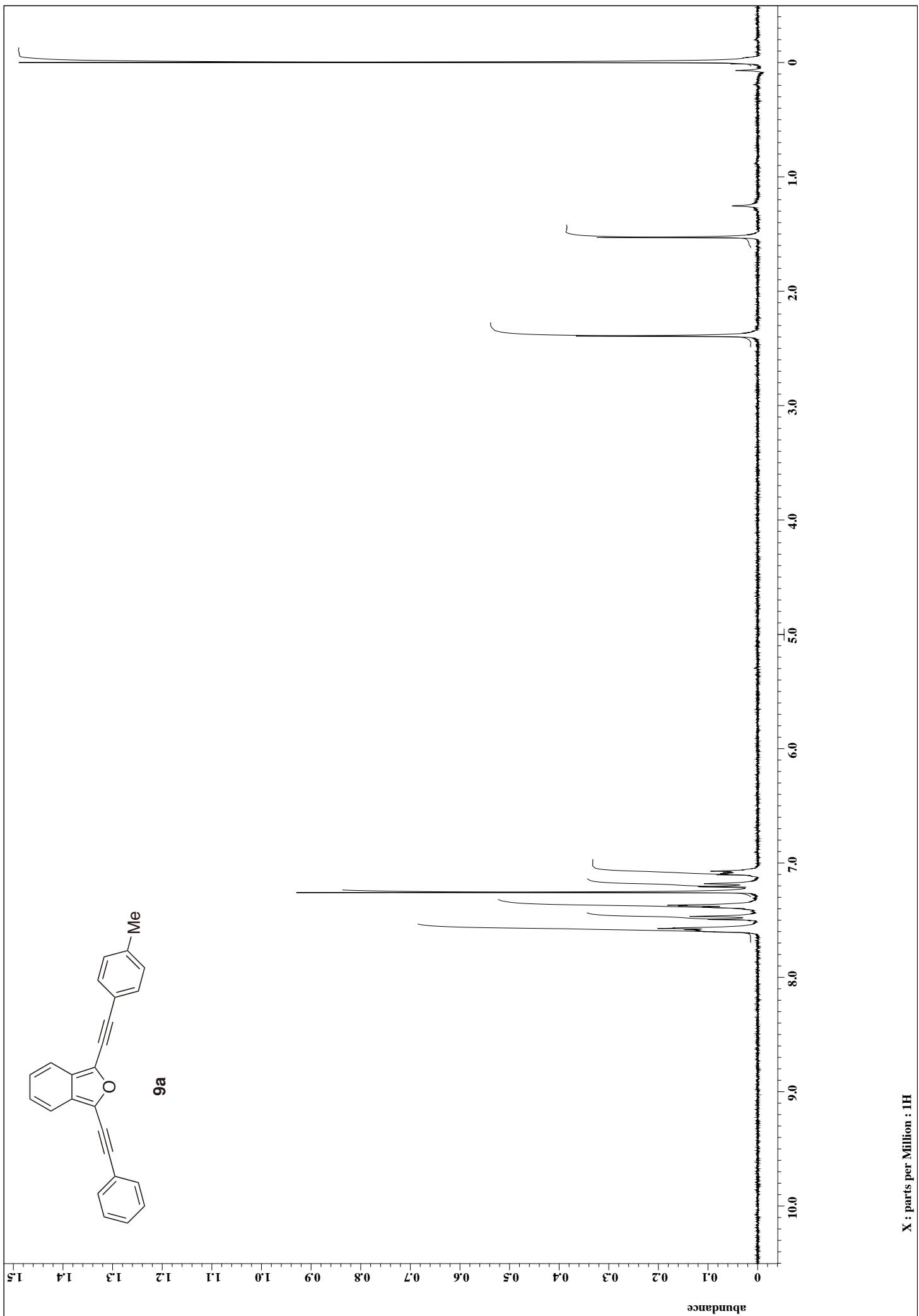


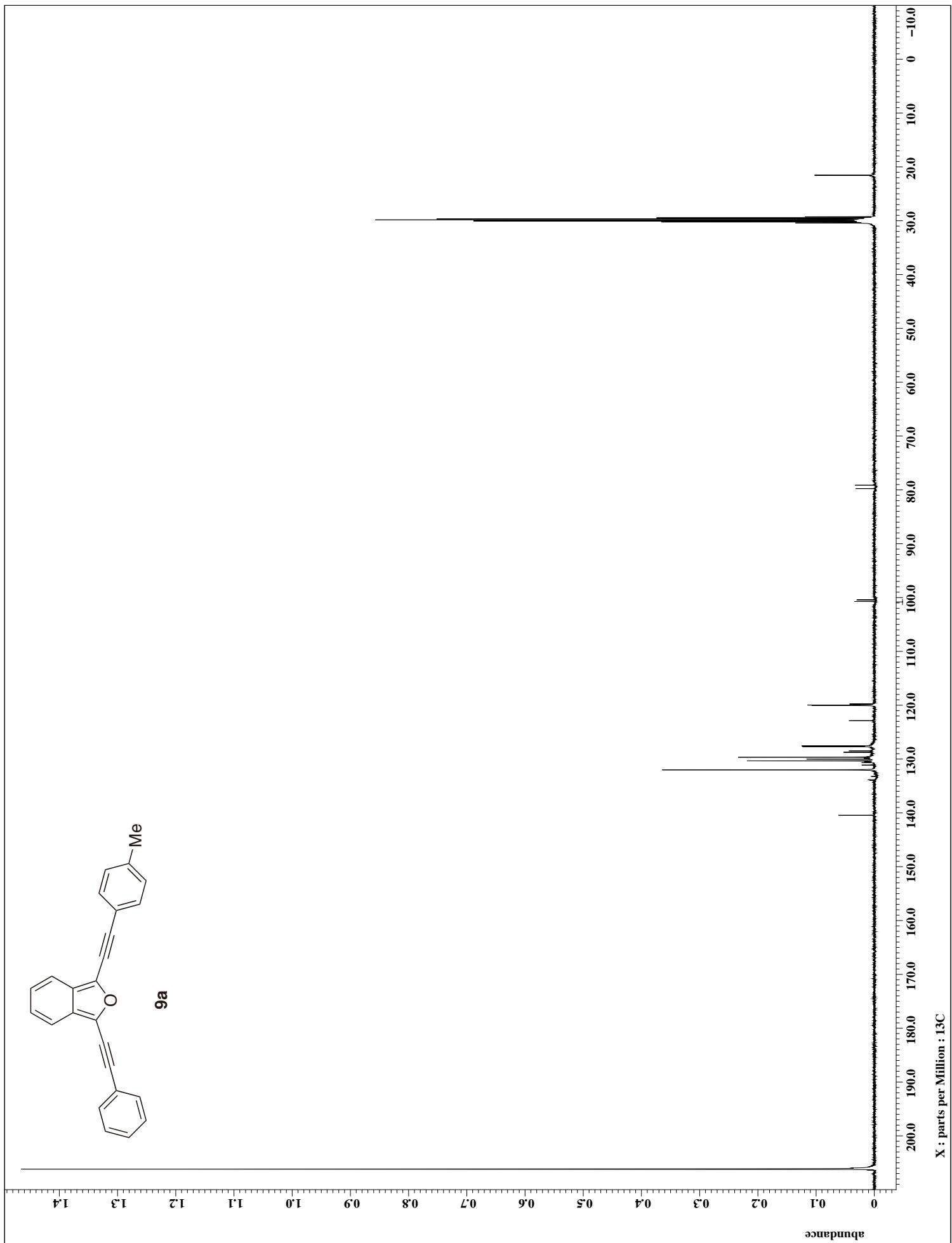
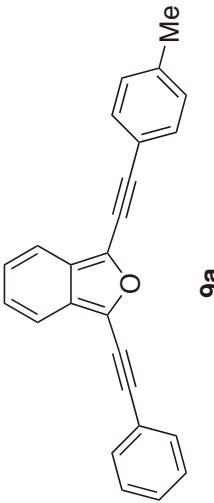
X : parts per Million : ^1H

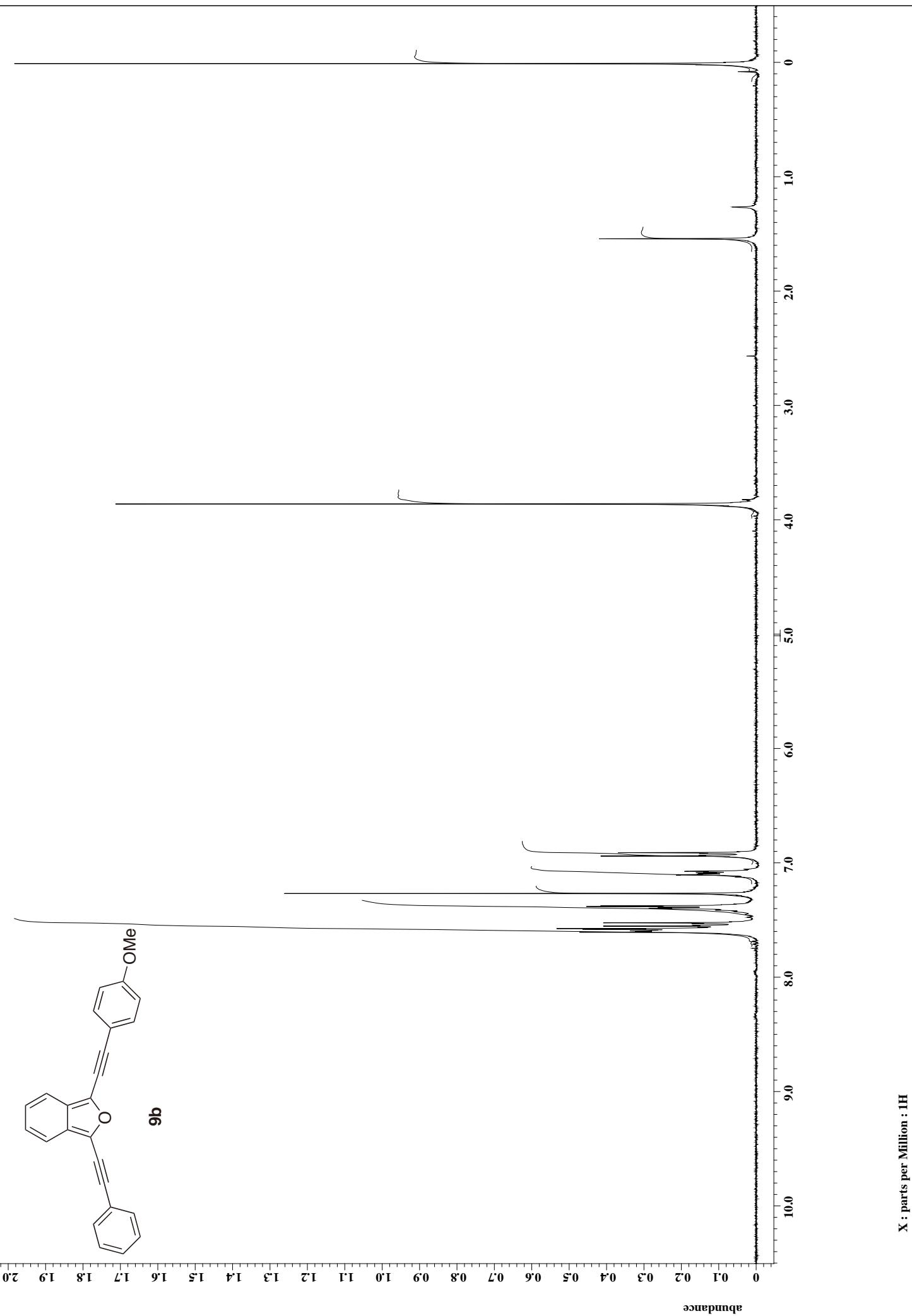


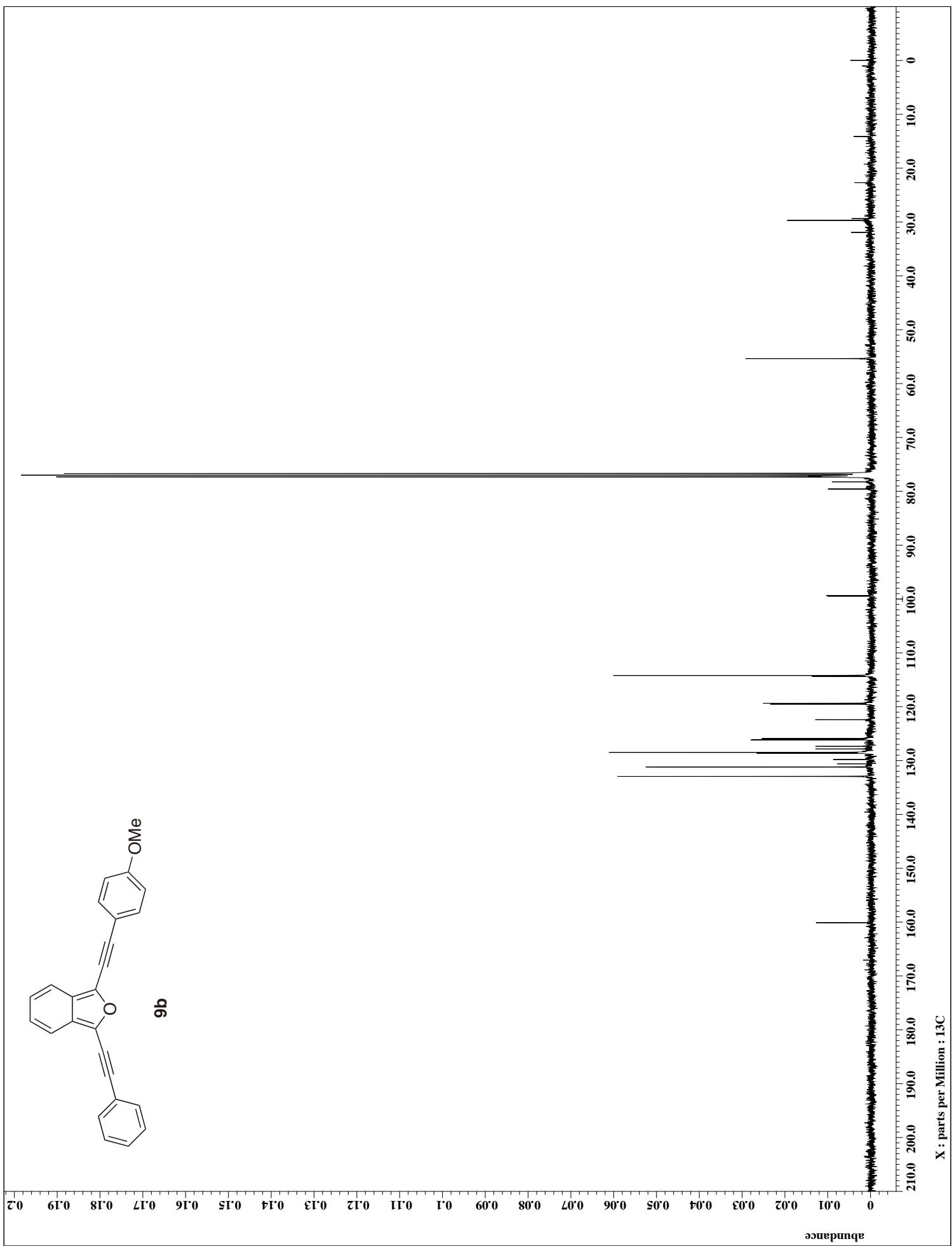
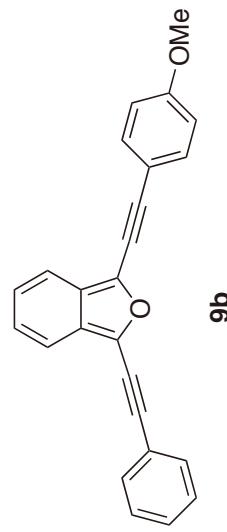
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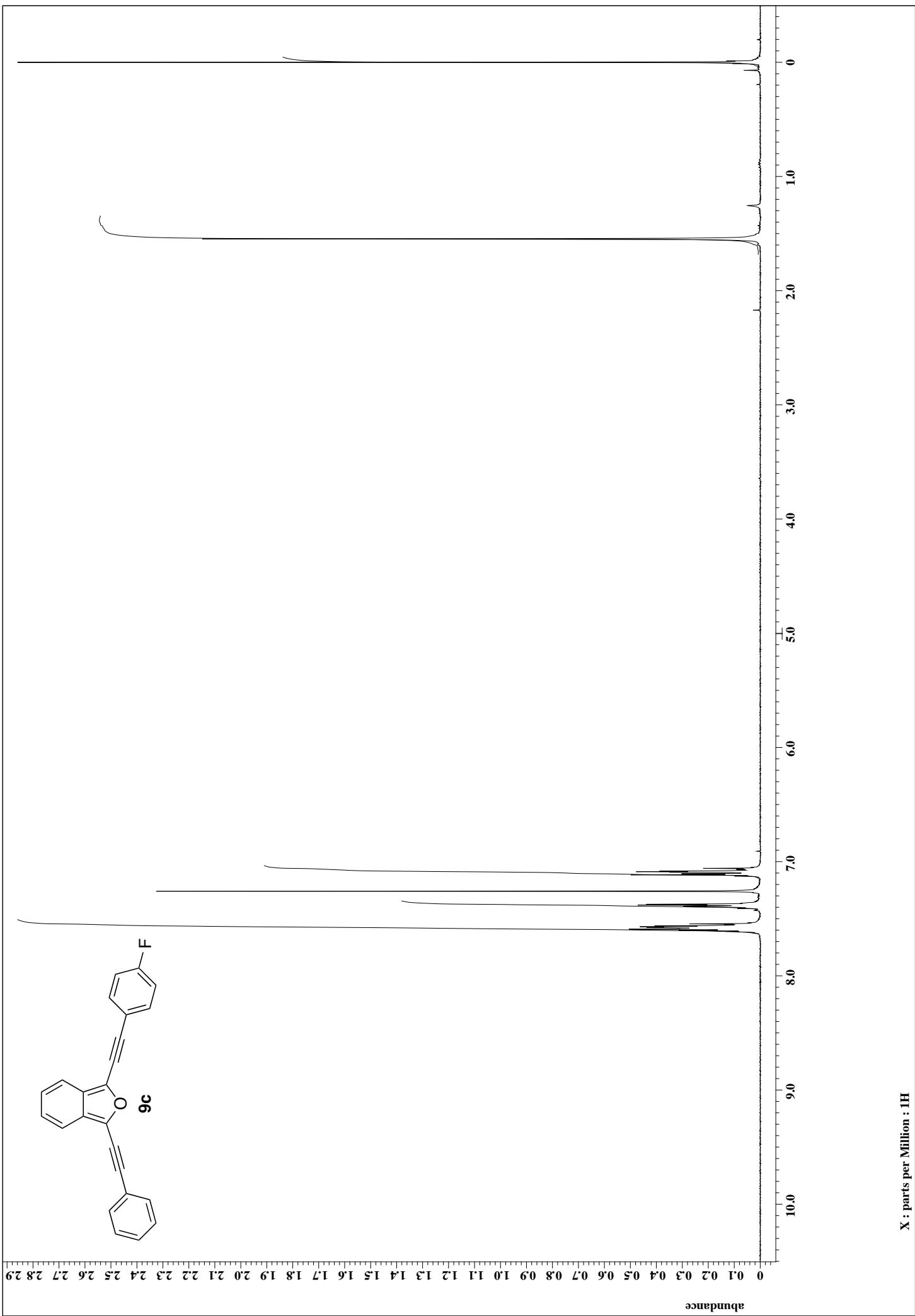
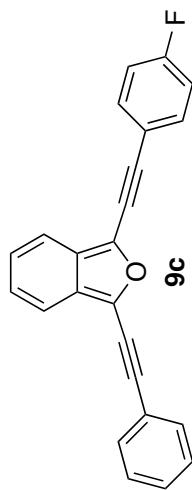




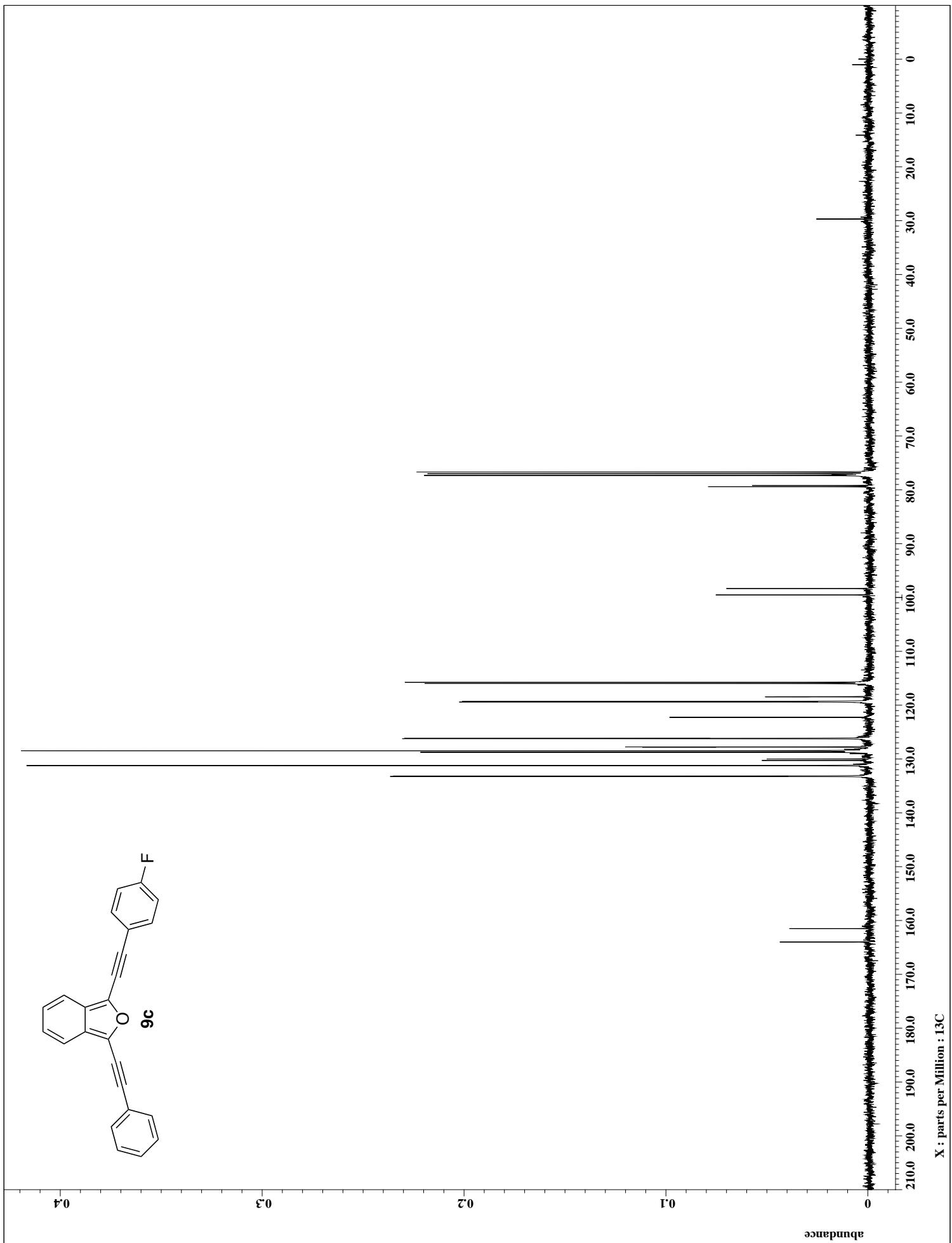
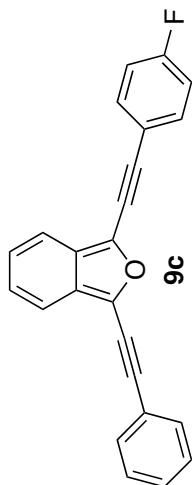


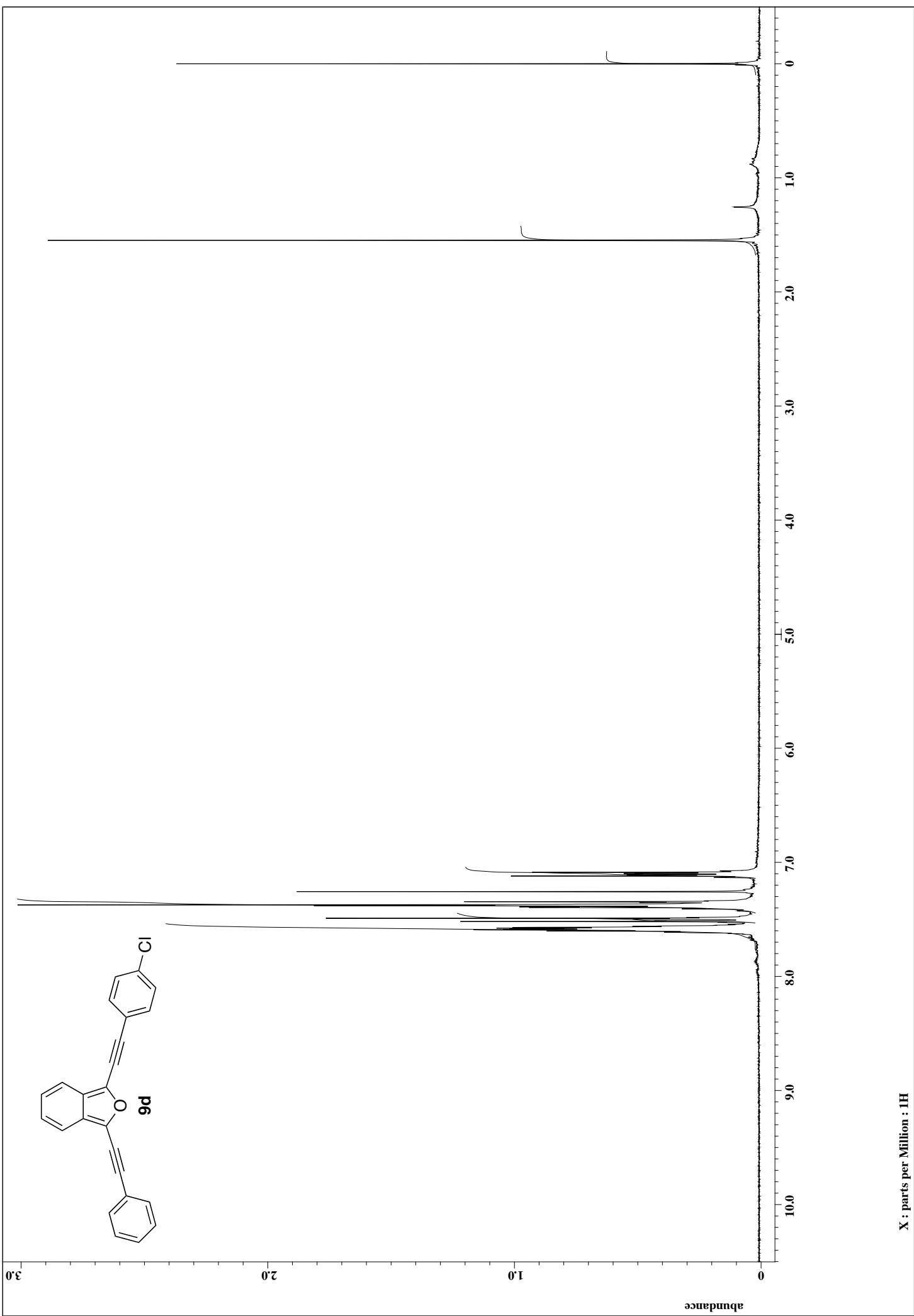
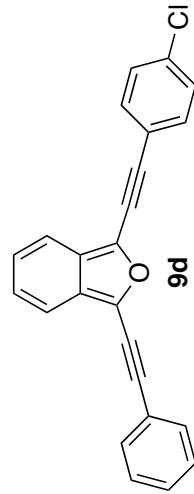




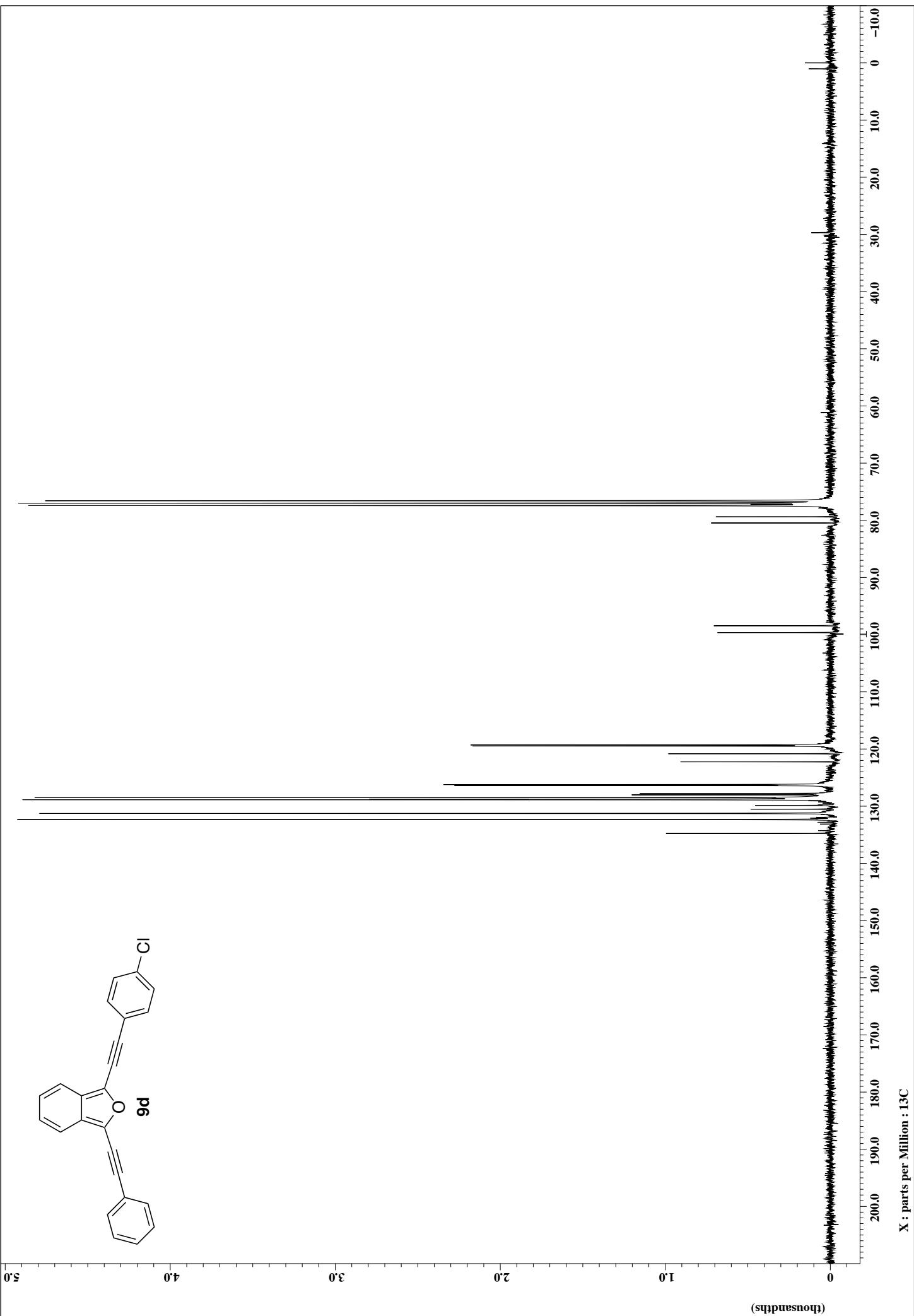
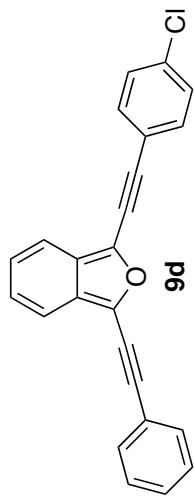


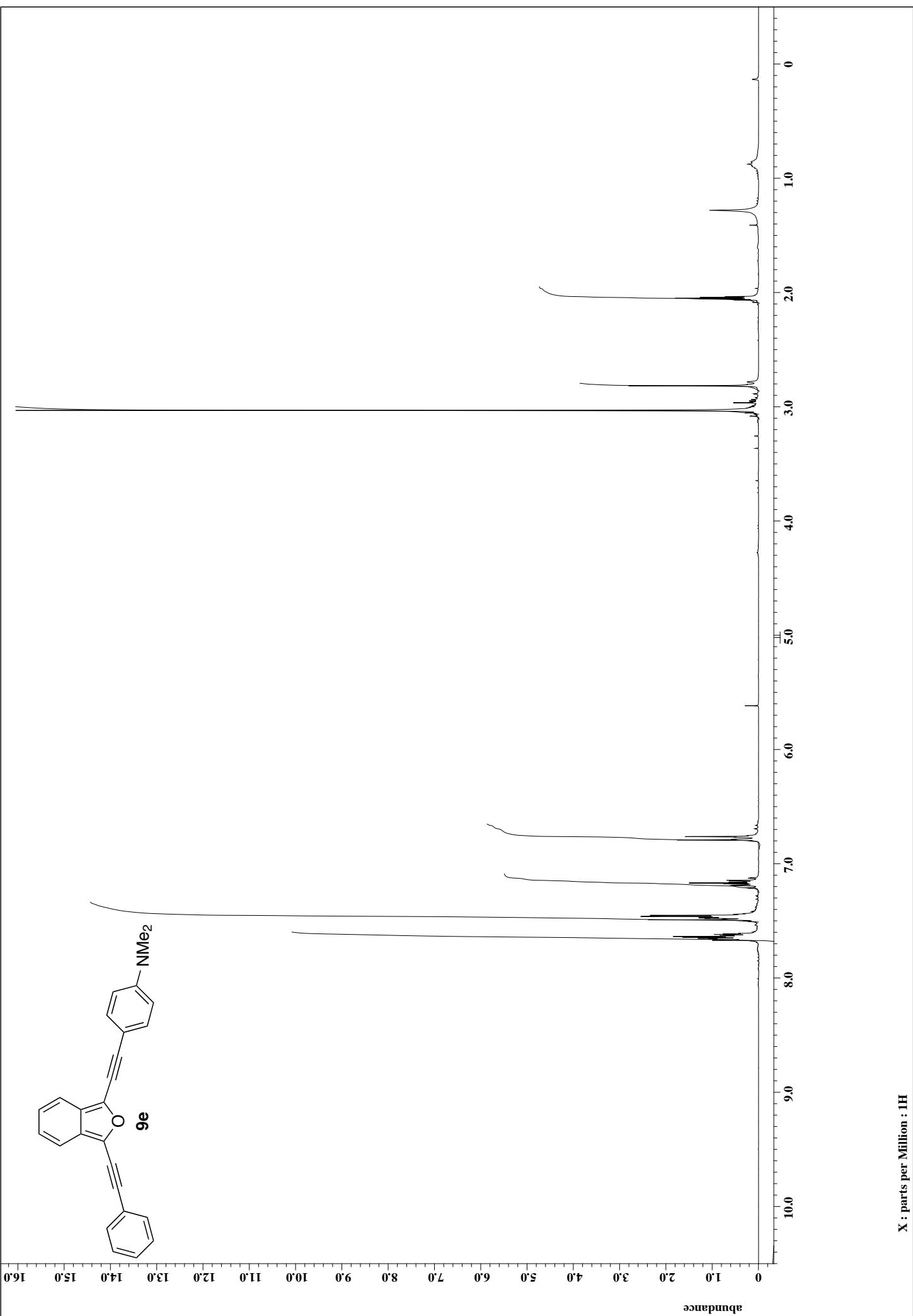
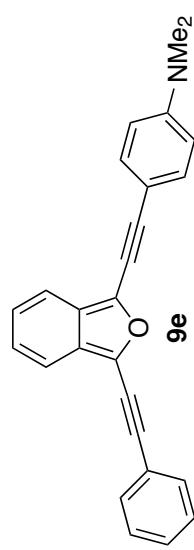
X : parts per Million : 1H

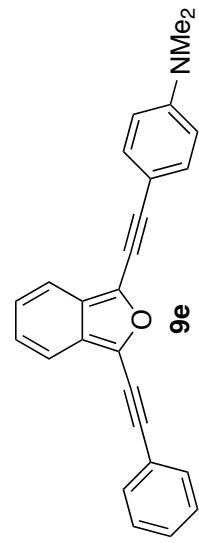




X : parts per Million : 1H







30.0

20.0

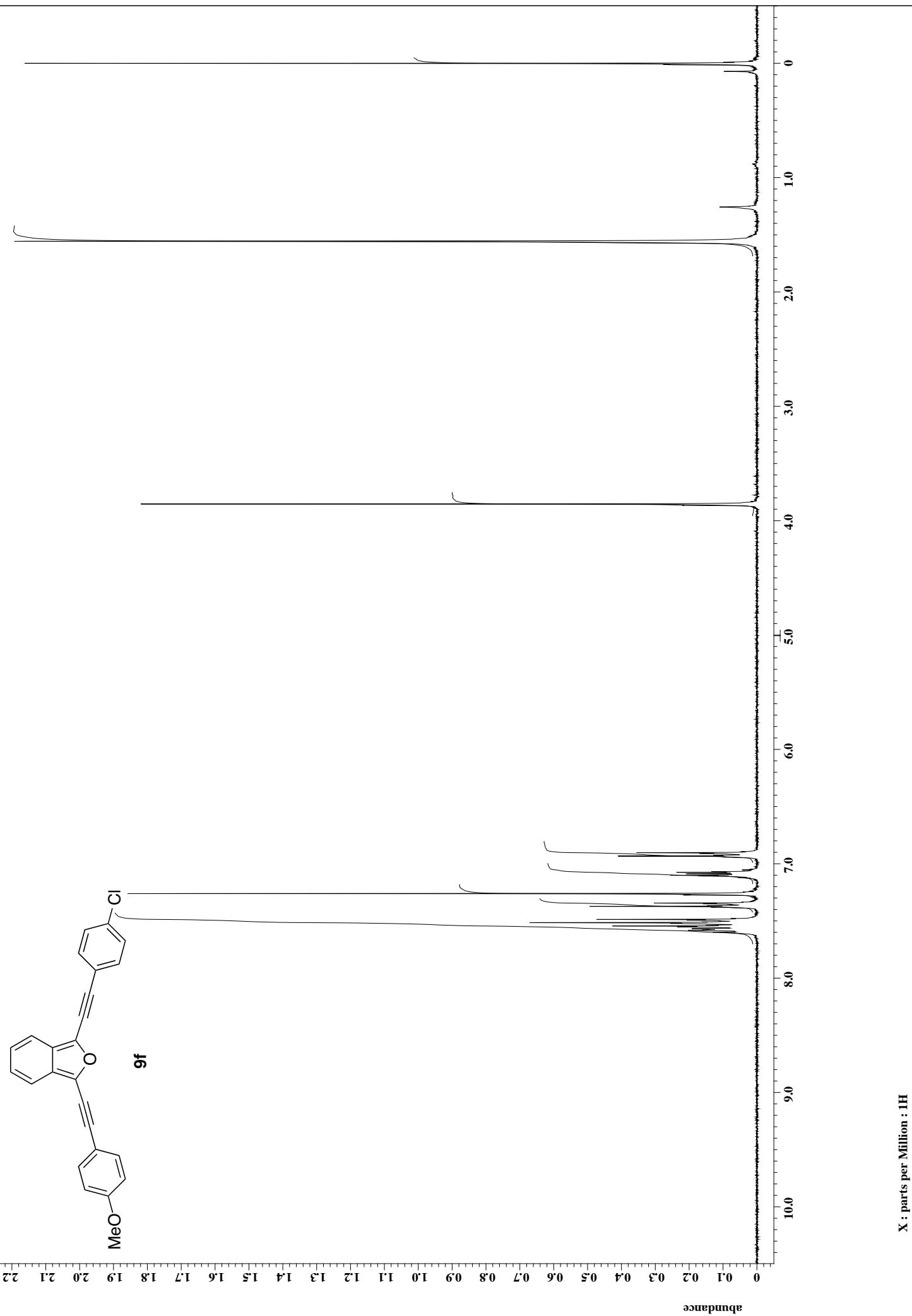
10.0

0

X : parts per Million : ^{13}C

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 -10.0

(thousandths)



X : parts per Million : 1H

abundance

