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Cyanoacetylene-driven base catalyzed synthesis of dihydropyrimidophenanthridinones from phenanthridine and water

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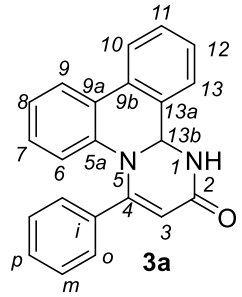
Contents

General Experimental

^{1}H and ^{13}C NMR spectra were recorded with an AV-400 Bruker BioSpin spectrometer with HMDS as an internal standard. IR spectra were recorded on a Bruker Vertex-70 instrument. Phenanthridine (**1**) is a commercial reagent. 3-Arylprop-2-ynenitriles **2a-d** were prepared by literature method [S1]. Column and thin-layer chromatography were carried out on silica gel 60 (0.060-0.200 mm) with chloroform/toluene/ethanol (20:4:1) mixture as eluent.

Experimental Procedures, Spectral and Analytical data

*4-Phenyl-1,13b-dihydro-2H-pyrimido[1,2-f]phenanthridin-2-one (**3a**).* A mixture of phenanthridine (**1**) (90 mg, 0.5 mmol), acetylene **2a** (64 mg, 0.5 mmol), H_2O (45 mg, 2.5 mmol), KOH (6 mg, 20 mol%) in MeCN (0.1 ml) was stirred at 20-25 °C for 120 h. The solvents were removed under reduced pressure, column chromatography afforded pyrimidophenanthridin-2-one **3a** (53 mg, 33%) as a light-beige powder, mp 251-253 °C (EtOH). Starting phenanthridine (**1**) (47 mg, conversion was 48%) was recovered.



IR (microlayer): 1602 (C=C), 1660 (C=O) cm^{-1}.

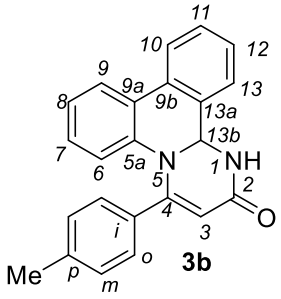
^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.93 (d, $^{3}J_{H10,H11}$ = 7.8 Hz, 1H, H-10), 7.78 (m, 1H, H-9), 7.69 (m, 2H, H_o from Ph), 7.52 (m, 1H, H-11), 7.45-7.35 (m, 5H, H-12, H-13, $H_{m,p}$ from Ph), 6.94 (m, 2H, H-7, H-8), 6.40 (d, $^{3}J_{H6,H7}$ = 8.2 Hz, 1H, H-6), 6.39 (s, 1H, H-3), 6.08 (s, 1H, H-13b), 5.96 (br s, 1H, NH) ppm.

^{13}C NMR (100.62 MHz, $CDCl_3$): δ 165.4 (C-2), 154.8 (C-4), 138.1 (C-5a), 134.5 (C_i from Ph), 131.0 (C-9b, C_p from Ph), 130.2 (C-7), 129.4 (C_m from Ph), 129.0 (C-11), 128.3 (C-13),

128.1 (C-13a), 127.7 (C-9), 127.2 (C_o from Ph), 123.8 (C-12), 122.8 (C-10), 122.5 (C-9a), 121.9 (C-8), 119.5 (C-6), 112.6 (C-3), 67.9 (C-13b) ppm.

$C_{22}H_{16}N_2O$ (324.38): calcd C 81.46, H 4.97, N 8.64; found C 81.59, H 4.75, N 8.48.

*4-(4-Methylphenyl)-1,13b-dihydro-2H-pyrimido[1,2-f]phenanthridin-2-one (**3b**)*: Analogously from phenanthridine (**1**) (179 mg, 1.0 mmol), acetylene **2b** (141 mg, 1.0 mmol), H_2O (90 mg, 5.0 mmol), KOH (12 mg, 20 mol%) in MeCN (0.2 ml) (20-25 °C, 144 h) pyrimidophenanthridin-2-one **3b** was obtained (111 mg, 33%) as a light-yellow powder, mp 238-240 °C (MeCN). Starting phenanthridine (**1**) (84 mg, conversion was 53%) and acetylene **2b** (19 mg, conversion was 87%) were recovered.



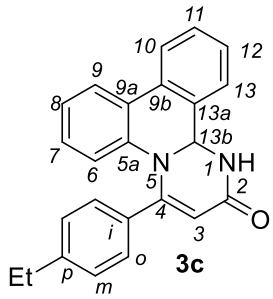
IR (microlayer): 1605 (C=C), 1659 (C=O) cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.89 (d, $^3J_{H10,H11}$ = 7.9 Hz, 1H, H-10), 7.74 (m, 1H, H-9), 7.55 (m, 2H, H_o from Ph), 7.47 (m, 1H, H-11), 7.36 (m, 1H, H-12), 7.33 (m, 1H, H-13), 7.16 (m, 2H, H_m from Ph), 6.91 (m, 2H, H-7, H-8), 6.39 (m, 1H, H-6), 6.30 (s, 1H, H-3), 6.27 (br s, 1H, NH), 6.02 (s, 1H, H-13b), 2.34 (s, 3H, Me) ppm.

^{13}C NMR (100.62 MHz, $CDCl_3$): δ 165.7 (C-2), 154.9 (C-4), 141.4 (C_p from Ph), 138.3 (C-5a), 131.6 (C_i from Ph), 131.0 (C-9b), 130.1 (C-7, C_m from Ph), 128.9 (C-11), 128.3 (C-13), 128.2 (C-13a), 127.7 (C-9), 127.1 (C_o from Ph), 123.8 (C-12), 122.7 (C-10), 122.4 (C-9a), 121.8 (C-8), 119.5 (C-6), 111.8 (C-3), 67.8 (C-13b), 21.5 (Me) ppm.

$C_{23}H_{18}N_2O$ (338.41): calcd C 81.63, H 5.36, N 8.28; found C 81.37, H 5.52, N 8.33.

*4-(4-Ethylphenyl)-1,13b-dihydro-2H-pyrimido[1,2-f]phenanthridin-2-one (**3c**):* Analogously from phenanthridine (**1**) (179 mg, 1.0 mmol), acetylene **2c** (155 mg, 1.0 mmol), H_2O (90 mg, 5.0 mmol), KOH (12 mg, 20 mol%) in MeCN (0.2ml) (20-25 °C, 144 h) pyrimidophenanthridin-2-one **3c** was obtained (42 mg, 12%) as a white powder, mp 238-240 °C (MeCN). Starting phenanthridine (**1**) (136 mg, conversion was 24%) and acetylene **2c** (66 mg, conversion was 57%) were recovered.



IR (microlayer): 1601 (C=C), 1659 (C=O) cm^{-1}.

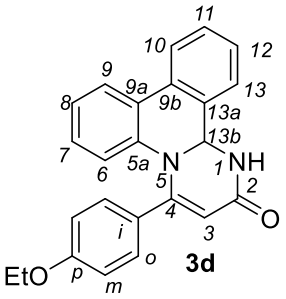
^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.92 (d, $^3J_{H10,H11}$ = 7.9 Hz, 1H, H-10), 7.76 (m, 1H, H-9), 7.59 (m, 2H, H_o from Ph), 7.50 (m, 1H, H-11), 7.38 (m, 1H, H-12), 7.35 (m, 1H, H-13), 7.20 (m, 2H, H_m from Ph), 6.93 (m, 2H, H-7, H-8), 6.42 (m, 1H, H-6), 6.33 (s, 1H, H-3), 6.05 (s, 2H, NH, H-13b), 2.65 (q, $^3J_{H,H}$ = 7.2 Hz, 2H, CH_2 from Et), 1.22 (t, 3H, Me from Et) ppm.

^{13}C NMR (100.62 MHz, $CDCl_3$): δ 165.7 (C-2), 155.0 (C-4), 147.7 (C_p from Ph), 138.3 (C-5a), 131.9 (C_i from Ph), 131.1 (C-9b), 130.2 (C-7), 129.0 (C-11), 128.9 (C_m from Ph), 128.3

(C-13), 128.2 (C-13a), 127.7 (C-9), 127.3 (C_o from Ph), 123.8 (C-12), 122.8 (C-10), 122.4 (C-9a), 121.8 (C-8), 119.6 (C-6), 111.9 (C-3), 67.9 (C-13b), 28.8 (CH_2 from Et), 15.3 (Me from Et) ppm.

$C_{24}H_{20}N_2O$ (352.44): C 81.79, H 5.72, N 7.95; found 81.54, H 5.80, N 7.90.

*4-(4-Ethoxyphenyl)-1,13b-dihydro-2H-pyrimido[1,2-f]phenanthridin-2-one (**3d**):* Analogously from phenanthridine (**1**) (90 mg, 0.5 mmol), acetylene **2d** (86 mg, 0.5 mmol), H_2O (45 mg, 2.5 mmol), KOH (6 mg, 20 mol%) in MeCN (0.1 ml) (20-25 °C, 144 h) pyrimidophenanthridin-2-one **3d** was obtained (47 mg, 26%) as a white powder, mp 288-290 °C (MeCN). Starting phenanthridine (**1**) (58 mg, conversion was 36%) was recovered.



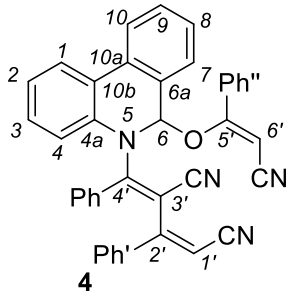
IR (microlayer): 1601 (C=C), 1659 (C=O) cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.94 (d, $^3J_{H10,H11}$ = 7.9 Hz, 1H, H-10), 7.78 (m, 1H, H-9), 7.61 (m, 2H, H_o from Ph), 7.52 (m, 1H, H-11), 7.40 (m, 1H, H-12), 7.37 (m, 1H, H-13), 6.95 (m, 2H, H-7, H-8), 6.88 (m, 2H, H_m from Ph), 6.44 (m, 1H, H-6), 6.29 (s, 1H, H-3), 6.06 (s, 1H, H-13b), 5.72 (br s, 1H, NH), 4.04 (m, 2H, CH_2 from OEt), 1.41 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, Me from OEt) ppm.

^{13}C NMR (100.62 MHz, $CDCl_3$): δ 165.8 (C-2), 161.5 (C_p from Ph), 154.9 (C-4), 138.4 (C-5a), 131.2 (C-9b), 130.3 (C-7), 129.1 (C-11), 128.9 (C_o from Ph), 128.3 (C-13, C-13a), 127.7 (C-9), 126.9 (C_i from Ph), 123.9 (C-12), 122.9 (C-10), 122.5 (C-9a), 121.9 (C-8), 119.7 (C-6), 115.3 (C_m from Ph), 110.7 (C-3), 67.9 (C-13b), 63.8 (CH_2 from OEt), 14.9 (Me from OEt) ppm.

$C_{24}H_{20}N_2O_2$ (368.44): calcd C 78.24, H 5.47, N 7.60; found 78.45, H 5.38, N 7.57.

*(2Z,4Z)-4-(1-{6-[(Z)-2-cyano-1-phenylvinyloxy]phenanthridin-5(6H)-yl}-1-phenylmethylidene)-3-phenylpent-2-enedinitrile (**4**).* A mixture of phenanthridine (**1**) (90 mg, 0.5 mmol), acetylene **2a** (64 mg, 0.5 mmol), H_2O (45 mg, 2.5 mmol), KOH (6 mg, 20 mol%) in MeCN (0.5 ml) was processed at 20-25 °C for 120 h. Along with pyrimidophenanthridin-2-one **3a** (23 mg, 14%), product **4** (12 mg, 12%) was isolated as a light-beige powder, mp 148-149 °C (EtOH). Starting phenanthridine (**1**) (61 mg, conversion was 31%) was recovered.



IR (microlayer): 1618 (C=C), 2210 (C≡N) cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.90 (m, 2H, H_o from Ph), 7.45-6.90 (m, 21H, H-1-4, H-7-9, $H_{m,p,o',m',p',o'',m'',p''}$ from Ph), 6.20 (s, 1H, H-6), 5.03 (s, 1H, H-6'), 4.86 (s, 1H, H-1') ppm.

^{13}C NMR (100.62 MHz, $CDCl_3$): δ 166.4 (C-5'), 163.7 (C-2'), 162.3 (C-4'), 138.8 (C-4a), 136.6 (C_i from Ph''), 132.2 (C_i from Ph), 132.1 (C_i from Ph'), 131.7 (C_p from Ph'), 131.0 (C-10a), 130.9 (C-6a, C_p from Ph), 130.8 (C-3), 129.4 (C-9), 128.9-128.8 ($C_{o',m',o'',m'',p''}$ from Ph), 128.3 (C_m from Ph), 128.1 (C-7), 127.7 (C-10b), 127.5 (C-1), 126.3 (C_o from Ph), 126.2 (C-8), 125.1 (C-10), 124.2 (C-2), 123.9 (C-4), 117.2 (CN-1'), 116.9 (CN-3'), 114.5 (CN-6'), 102.2 (C-3'), 82.6 (C-6), 80.8 (C-6'), 60.7 (C-1') ppm.

$C_{40}H_{26}N_4O$ (578.68): calcd C 83.02, H 4.53, N 9.68; found C 82.82, H 4.35, N 9.79.

The spectral and configurational assignments in compound **4** based on the 2D NMR spectroscopy are extremely difficult due to the overlapping of numerous proton signals in the region of 6.9–7.4 ppm of the ^{1}H NMR spectrum. For this reason, the ^{13}C NMR signals and configuration of compound **4** were assigned using the reference data [S2–S7].

References

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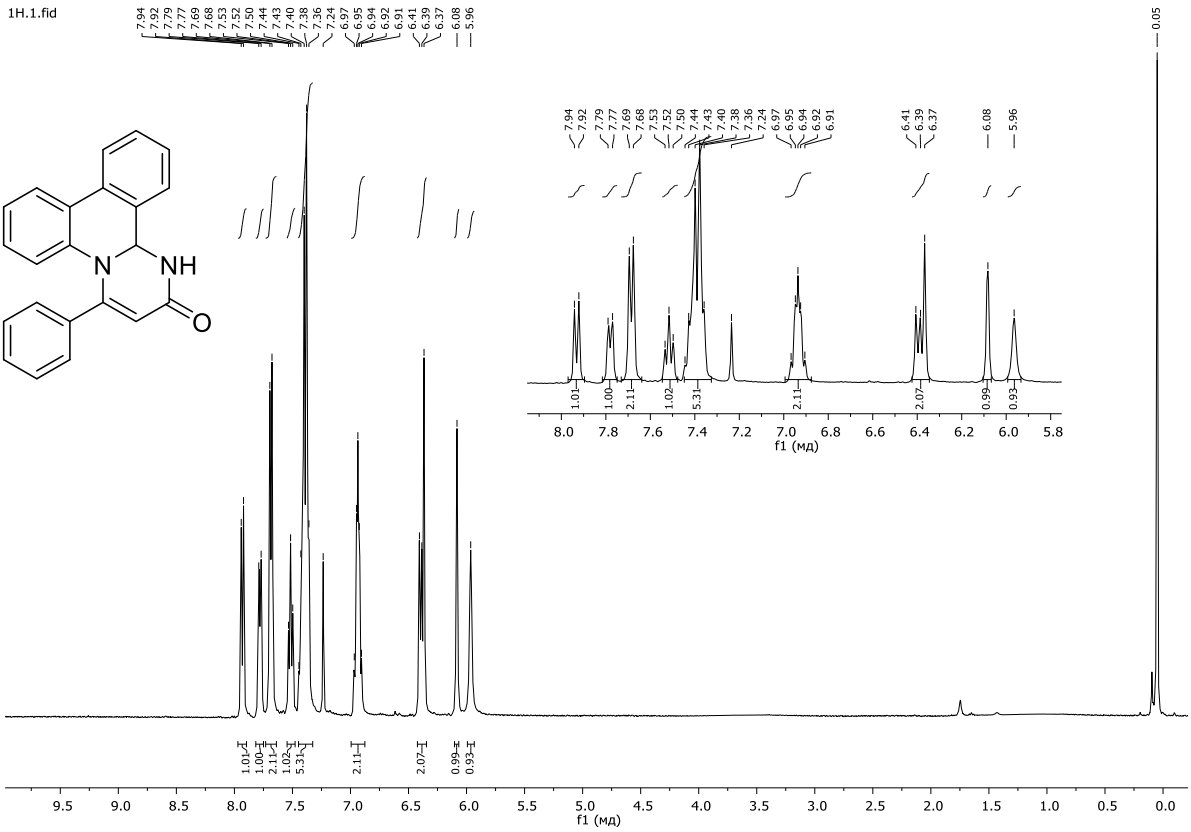
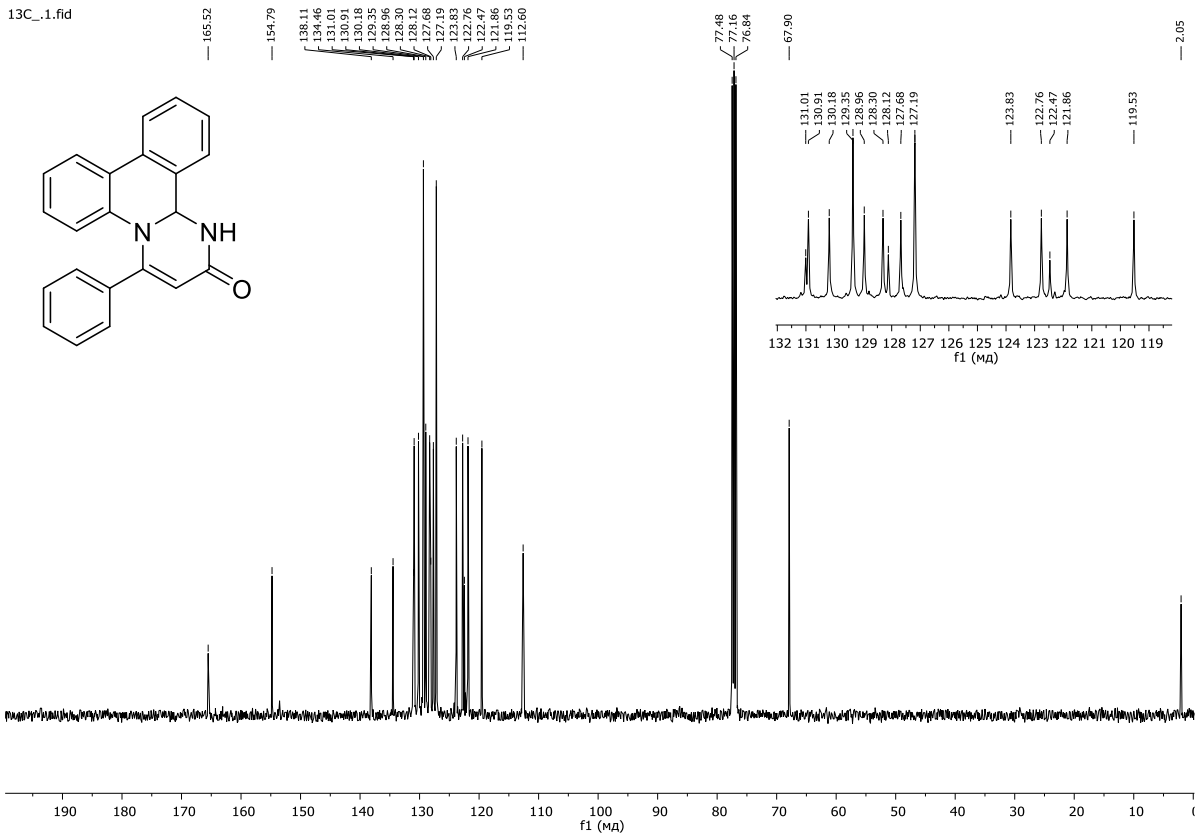
[S6] B. A. Trofimov, L. V. Andriyankova, K. V. Belyaeva, A. G. Mal'kina, L. P. Nikitina, A. V. Afonin, I. A. Usakov, *Eur. J. Org. Chem*., 2010, 1772.

[S7] L. V. Andriyankova, A. G. Mal'kina, A. V. Afonin and B. A. Trofimov, *Mendeleev Commun*., 2003, **13**, 186.

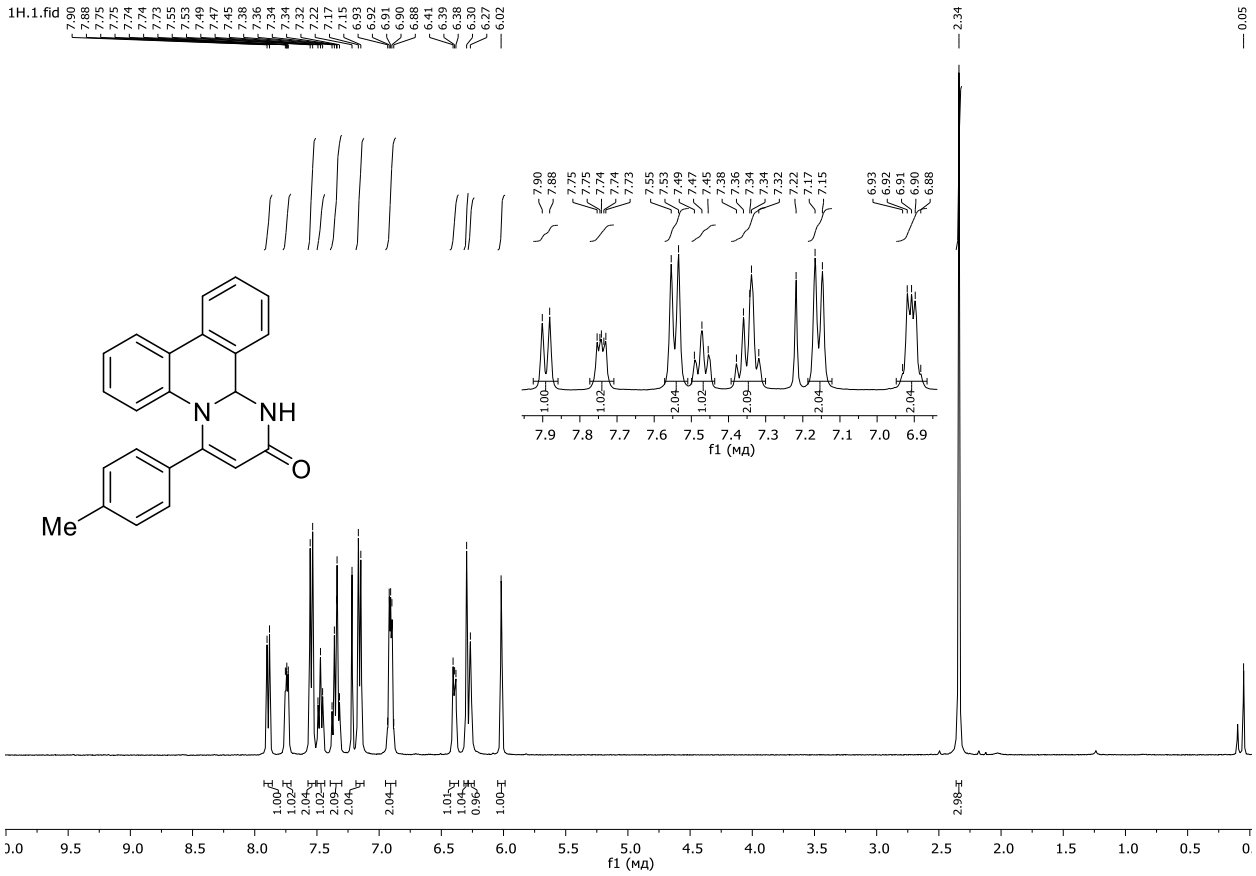
Copies of NMR Spectra



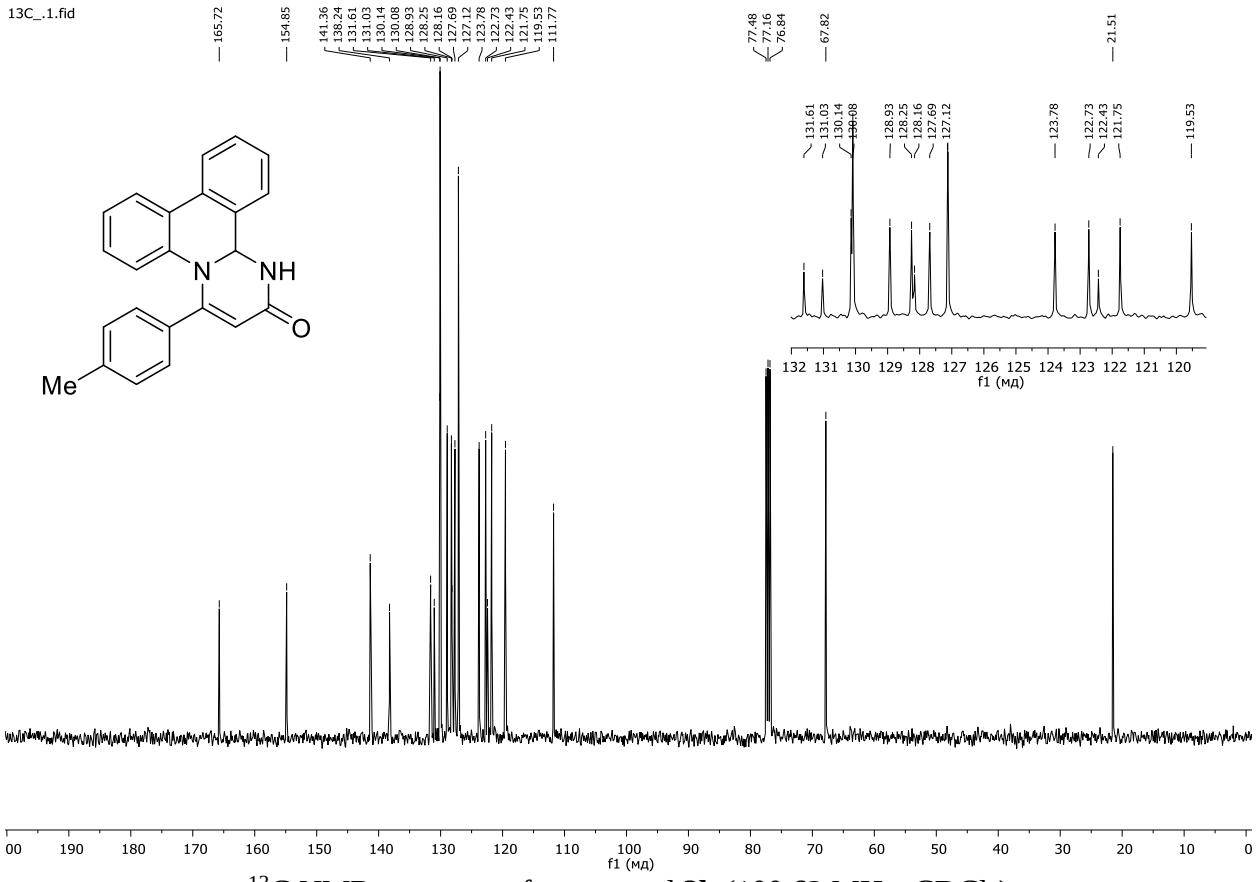
^{1}H NMR spectrum of compound **3a** (400.13 MHz, $CDCl_3$)



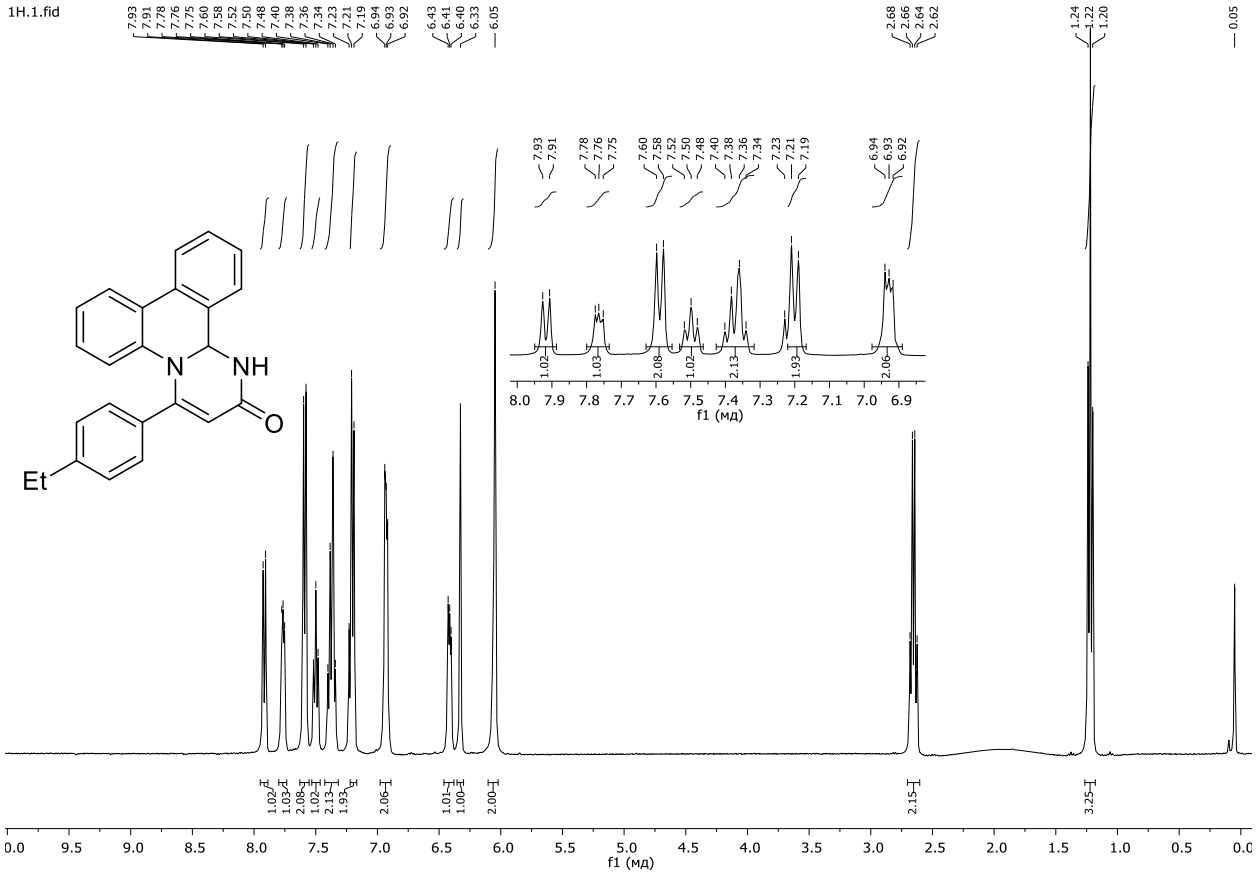
^{13}C NMR spectrum of compound **3a** (100.62 MHz, $CDCl_3$)



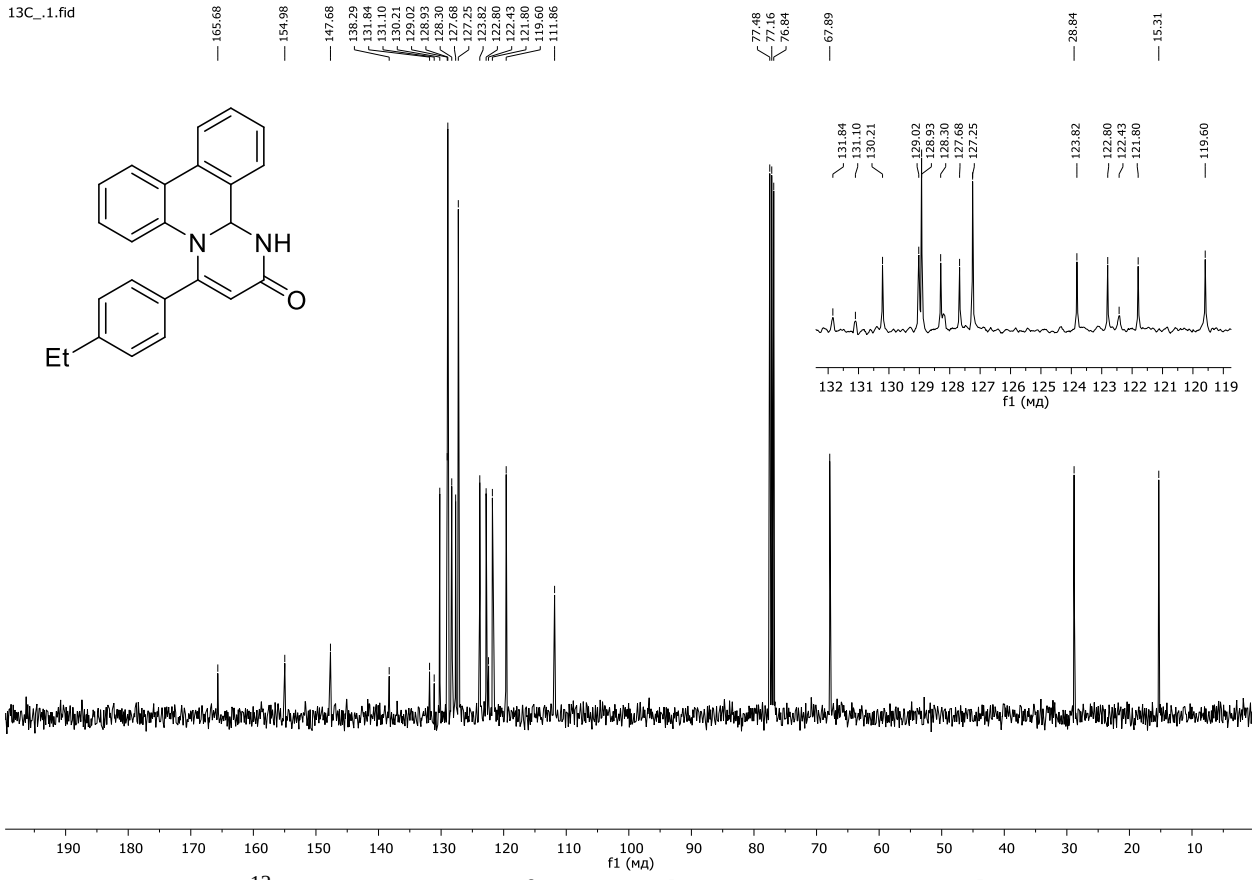
^{1}H NMR spectrum of compound **3b** (400.13 MHz, $CDCl_3$)



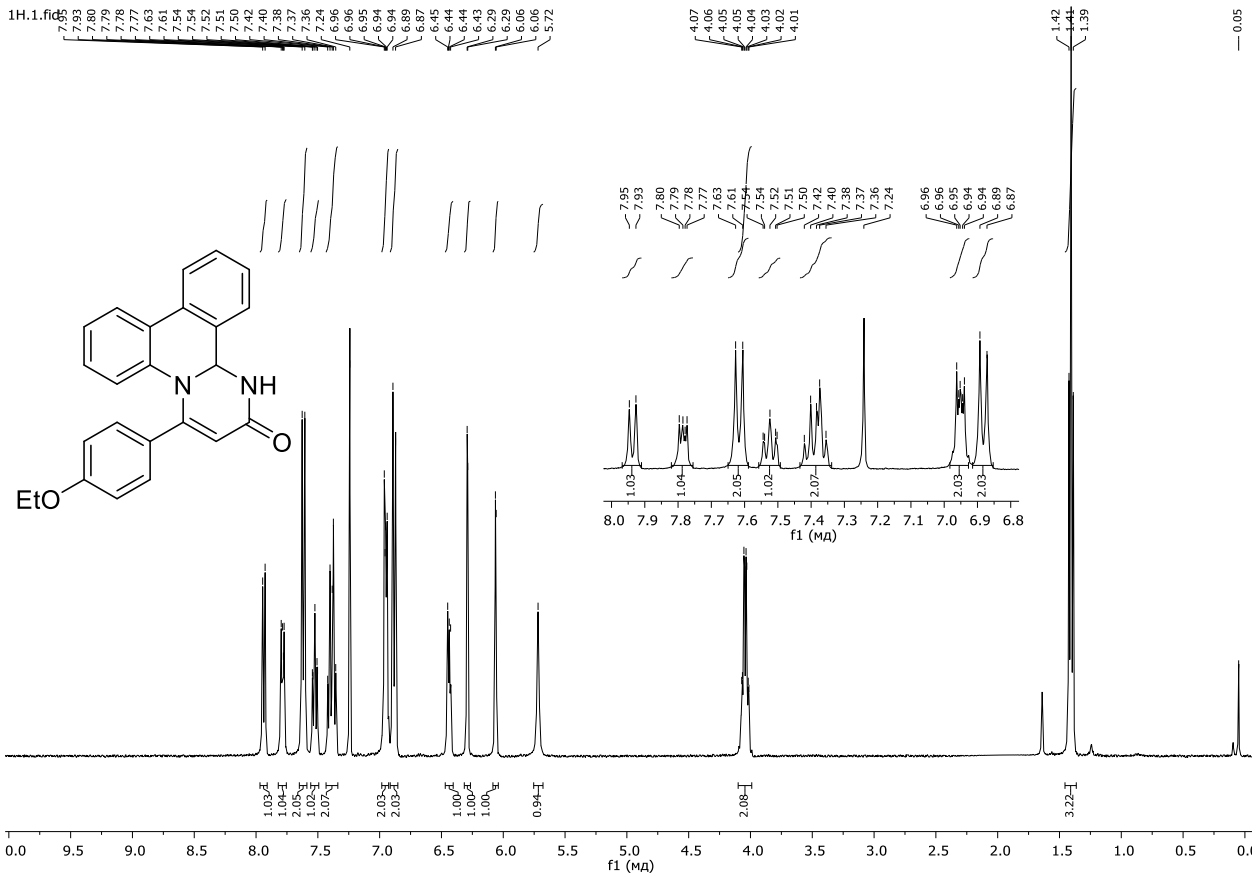
^{13}C NMR spectrum of compound **3b** (100.62 MHz, $CDCl_3$)



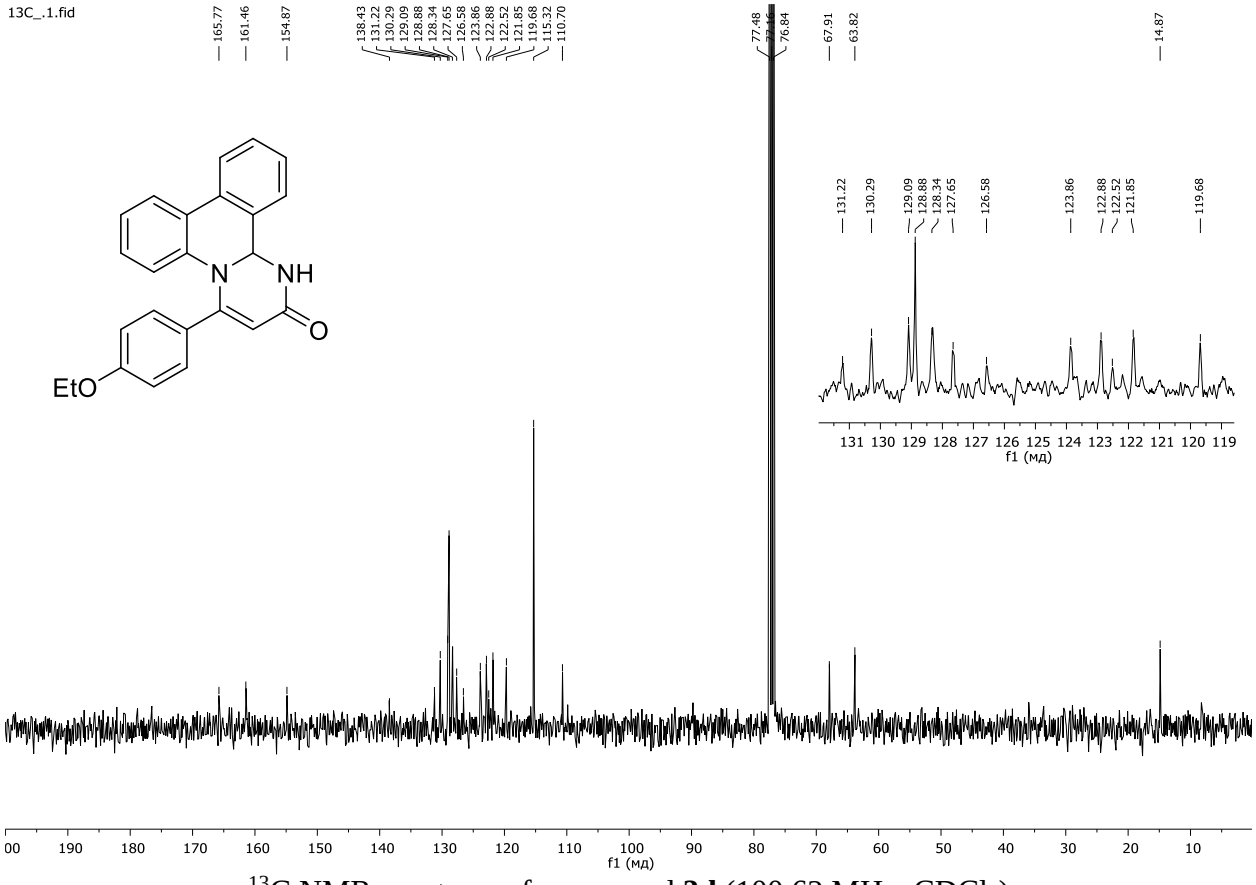
^{1}H NMR spectrum of compound **3c** (400.13 MHz, $CDCl_3$)



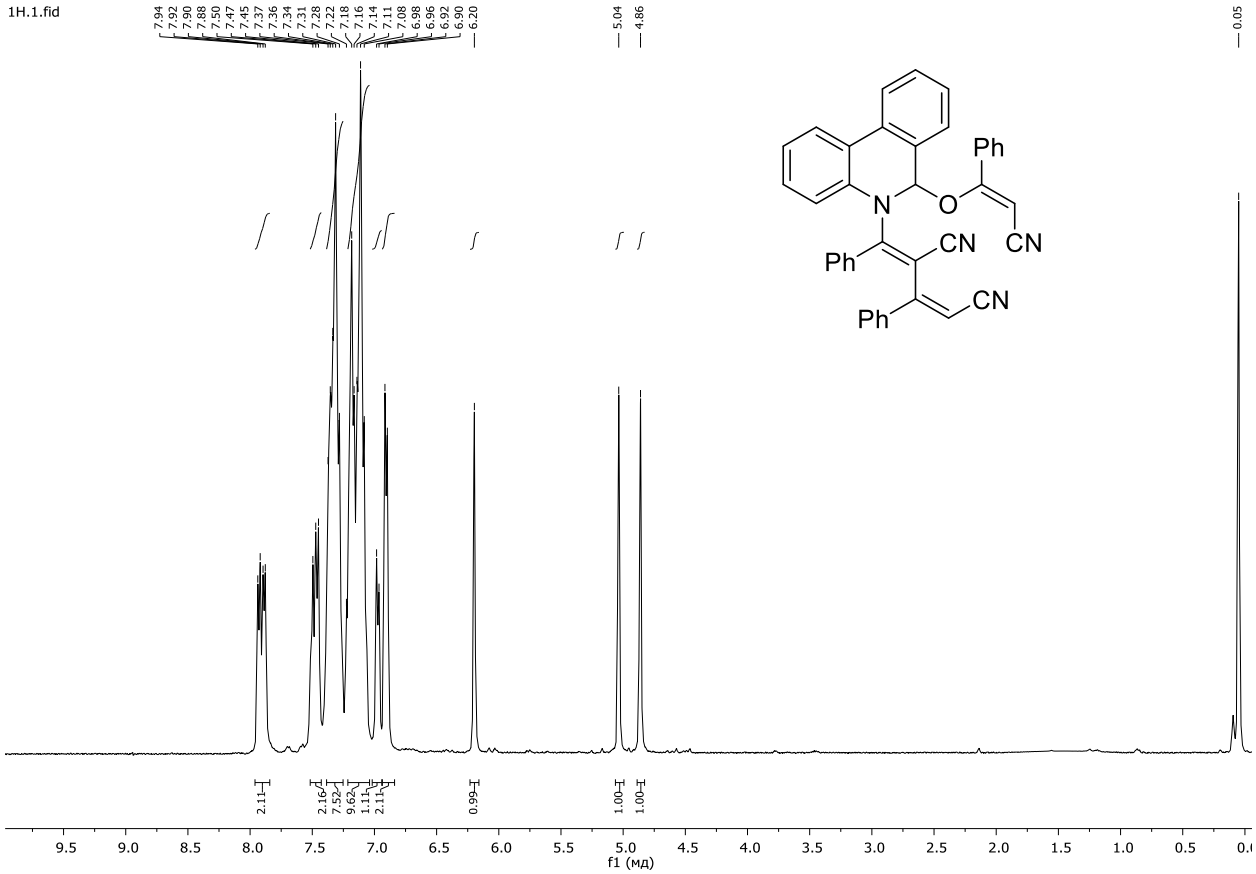
^{13}C NMR spectrum of compound **3c** (100.62 MHz, $CDCl_3$)



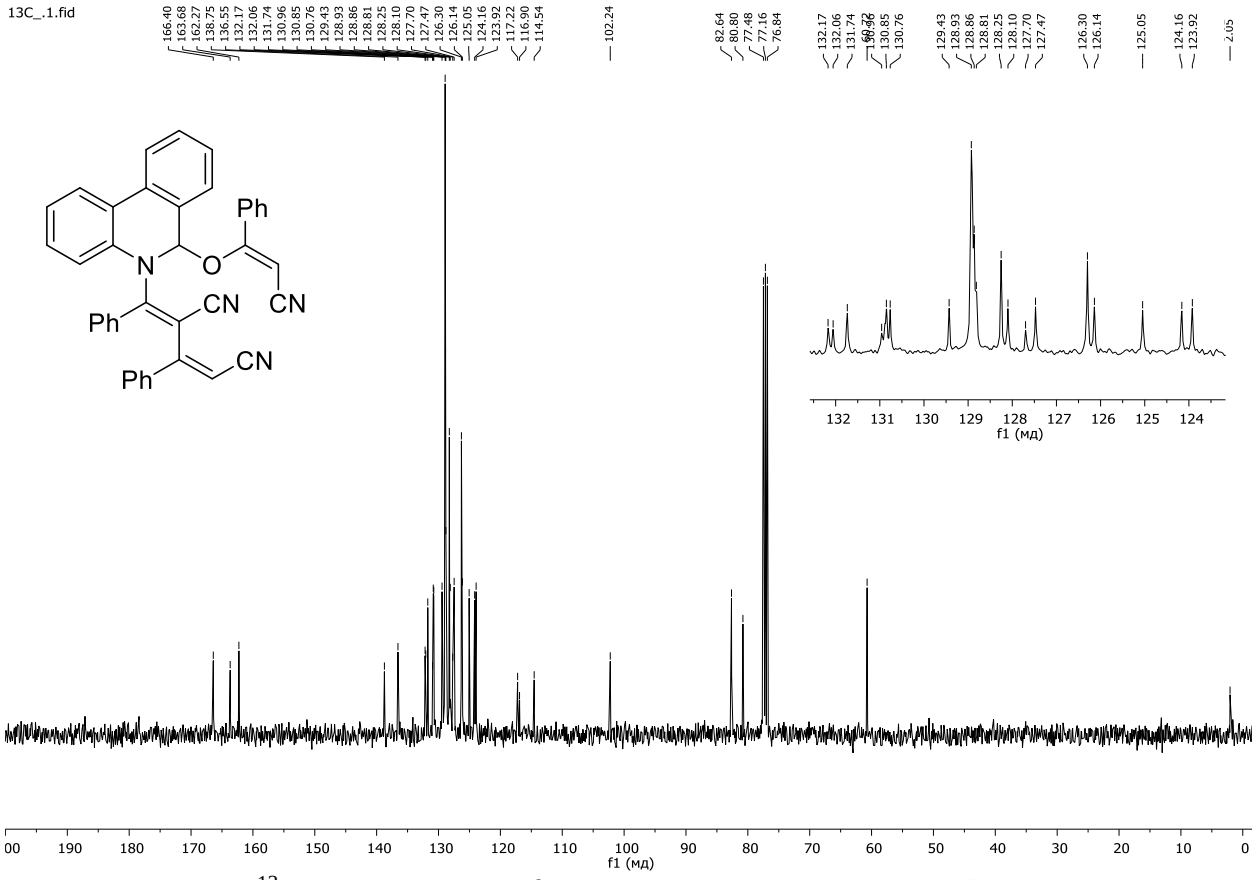
^{1}H NMR spectrum of compound **3d** (400.13 MHz, $CDCl_3$)



^{13}C NMR spectrum of compound **3d** (100.62 MHz, $CDCl_3$)



^{1}H NMR spectrum of compound **4** (400.13 MHz, $CDCl_3$)



^{13}C NMR spectrum of compound **4** (100.62 MHz, $CDCl_3$)