Ru-catalyzed synthesis of fused heterocycle-pyridinones and -pyrones by C-H/X-H (X = N, O) oxidative coupling between internal alkynes and amides or acids

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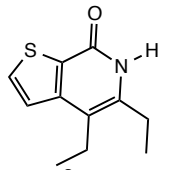
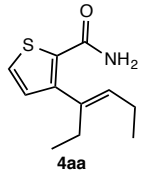
Electronic Supplementary Information

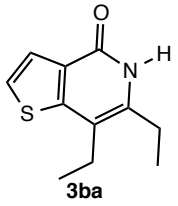
1.- Characterization of all prepared compounds

 **3aa**	4,5-diethylthieno[2,3-*c*]pyridin-7(6*H*)-one **3aa**

White solid (179 mg, 87%). Column chromatography: elution with hexane/ethyl acetate (90/10) allows to obtain compound **4aa**. After exhaustive washing with this mixture compound **3aa** remains in the column. Therefore, elution is carried out with a mixture hexane/ethylacetate (50/50), which allows to obtain compound **3aa**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.16 (s, 1H, NH), 7.65 (d, 1H, H_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 7.22 (d, 1H, H_{thio} $^{3}J_{HH}$ = 5.2 Hz), 2.65 (m, 4H, CH_2CH_3), 1.25 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz,), 1.14 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$): δ 148.1 (C), 140.7 (C), 133.3 (CH), 127.2 (C), 122.9 (CH), 114.6 (C), 23.6 (CH_2), 21.4 (CH_2), 15.3 (CH_3), 14.4 (CH_3). The carbonyl C was not observed in spite of long accumulation trials, changes in the relaxation delay, or attempts to inverse detection through ^{1}H-^{13}C HMBC. IR (ν, cm^{-1}): 1632 (vs, CO). HRMS (ESI-TOF) m/z: $[M+H]^+$ calc. $C_{11}H_{14}NOS$ 208.0791, found 208.0786.

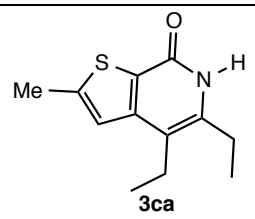
 **4aa**	(*E*)-3-(hex-3-en-3-yl)thiophene-2-carboxamide **4aa**

White solid (11 mg, 6%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34 (d, 1H, H_{thio}, $^{3}J_{HH}$ = 5.1 Hz), 6.78 (d, 1H, H_{thio}, $^{3}J_{HH}$ = 5.1 Hz), 5.52 (t, 1H, *H*C=C, $^{3}J_{HH}$ = 7.3 Hz), 2.35 (q, 2H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 2.15 (m, 2H, C=CH-CH_2), 0.99 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 0.89 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.0 (CH), 130.3 (CH), 129.2 (CH), 25.1 (CH_2), 21.3 (CH_2), 14.0 (CH_3), 13.1 (CH_3). Only CH nuclei were observed due to low amount of sample. IR (ν, cm^{-1}): 1650 (vs, CO). HRMS (ESI-TOF) m/z: $[M-H]^+$ calc. $C_{11}H_{14}NOS$ 208.0791, found 208.0793.

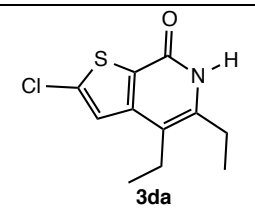
 **3ba**	6,7-diethylthieno[3,2-*c*]pyridin-4(5*H*)-one **3ba**

Orange solid (191 mg, 92%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.87 (s, 1H, NH), 7.56 (d, 1H, H_{thio}, $^{3}J_{HH}$ = 5.4 Hz), 7.14 (d, 1H, H_{thio}, $^{3}J_{HH}$ = 5.4 Hz), 2.61 (m, 4H, CH_2CH_3), 1.23 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz), 1.15 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.9 (CO), 152.3 (C), 140.4 (C), 128.7 (C),

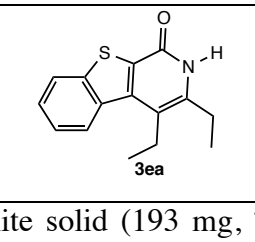
124.9 (CH), 123.1 (CH), 113.8 (C), 23.5(CH_2), 23.0 (CH_2), 14.3 (CH_3), 14.2 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{11}H_{13}NNaOS$ 230.0610, found 230.0609.

 **3ca**	4,5-diethyl-2-methylthieno[2,3-*c*]pyridin-7(6*H*)-one **3ca**

Yellow solid (197 mg, 89%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.86 (s, 1H, NH), 6.84 (d, 1H, H_{thio}, $^4J_{HH}$ = 1.2 Hz), 2.60 (m, 4H, CH_2CH_3), 2.52 (d, 3H, $^4J_{HH}$ = 1.2 Hz), 1.20 (t, 3H, CH_2CH_3, $^3J_{HH}$ = 7.6 Hz), 1.09 (t, 3H, CH_2CH_3, $^3J_{HH}$ = 7.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.9 (CO), 148.8 (C), 148.4 (C), 141.4 (C), 125.7 (C), 121.1 (CH), 114.2 (C), 23.6 (CH_2), 21.3 (CH_2), 16.5 (CH_3), 15.3 (CH_3), 14.6 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{12}H_{15}NNaOS$ 244.0767, found 244.0763.

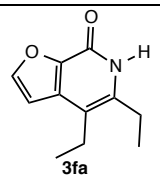
 **3da**	2-chloro-4,5-diethylthieno[2,3-*c*]pyridin-7(6*H*)-one **3da**

White solid (123 mg, 51%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.25 (s, 1H, N*H*), 7.05 (s, 1H, H_{thio}), 2.59 (m, 4H, CH_2CH_3), 1.23 (t, 3H, CH_2CH_3, $^3J_{HH}$ = 7.6 Hz), 1.11 (t, 3H, CH_2CH_3, $^3J_{HH}$ = 7.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.8 (CO), 147.5 (C), 141.8 (C), 139.2 (C), 125.7 (C), 122.2 (CH), 114.0 (C), 23.7 (CH_2), 21.3 (CH_2), 15.2 (CH_3), 14.3 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{11}H_{12}NNaOS$ 264.0220, found 264.0213.

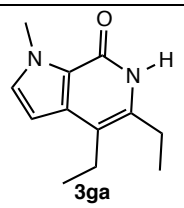
 **3ea**	3,4-diethylbenzo[4,5]thieno[2,3-*c*]pyridin-1(2*H*)-one **3ea**

White solid (193 mg, 75%). This compound was purified by precipitation from an ethyl acetate solution. No column chromatography was needed. ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.79 (s, 1H, NH), 8.34 (m, 1H, CH_{Ph}), 8.13 (m, 1H, CH_{Ph}), 7.58 (m, 2H, CH_{Ph}), 3.00 (q, 2 H, CH_2CH_3, $^3J_{HH}$ = 7.3 Hz), 2.67 (q, 2 H, CH_2CH_3, $^3J_{HH}$ = 7.5 Hz), 1.23 (m, 6H, CH_2CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ 158.8 (CO), 143.2 (C), 141.9 (C), 141.5 (C), 135.6 (C), 127.8 (CH), 126.2 (CH), 125.7 (CH),

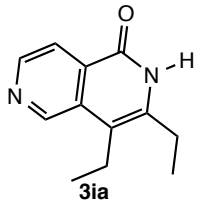
124.4 (CH), 114.5 (C), 110.0 (C), 23.3 (CH_2), 20.4 (CH_2), 15.5 (CH_3), 15.2 (CH_3). HRMS (ESI-TOF) m/z: $[M + Na]^+$ calc. $C_{15}H_{15}NNaOS$ 280.0767, found 280.0765.

	4,5-diethylfuro[2,3-*c*]pyridin-7(6*H*)-one **3fa**

White solid (71 mg, 37%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^1H NMR (300 MHz, $CDCl_3$): δ 11.69 (s, 1H, NH), 7.66 (d, 1H, H_{fur}, $^3J_{HH}$ = 1.1 Hz), 6.62 (d, 1H, H_{fur}, $^3J_{HH}$ = 1.1 Hz), 2.65 (q, 2H, C*H*$_2$CH$_3$, $^3J_{HH}$ = 7.5 Hz), 2.55 (q, 2H, C*H*$_2$CH$_3$, $^3J_{HH}$ = 7.5 Hz), 1.23 (t, 3H, CH$_2$C*H*$_3$, $^3J_{HH}$ = 7.5 Hz), 1.11 (t, 3H, CH$_2$C*H*$_3$, $^3J_{HH}$ = 7.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.2 (CO), 148.4 (CH), 141.6 (C), 140.2 (C), 136.4 (C), 112.6 (C), 106.1 (CH), 23.4 (CH_2), 21.1 (CH_2), 15.1 (CH_3), 14.6 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{11}H_{13}NNaO_2$ 214.0838, found 214.0835.

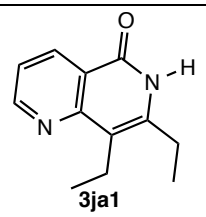
	4,5-diethyl-1-methyl-1,6-dihydro-7*H*-pyrrolo[2,3-*c*]pyridin-7-one **3ga**

White solid (157 mg, 77%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^1H NMR (300 MHz, $CDCl_3$): δ 10.60 (s, 1H, N*H*), 6.91 (d, 1H, H_{pyrr}, $^3J_{HH}$ = 2.8 Hz), 6.18 (d, 1H, H_{pyrr}, $^3J_{HH}$ = 2.8 Hz), 4.09 (s, 3H, N-C*H*$_3$), 2.54 (m, 4H, C*H*$_2$CH$_3$), 1.18 (t, 3H, CH$_2$C*H*$_3$, $^3J_{HH}$ = 7.6 Hz), 1.10 (t, 3H, CH$_2$C*H*$_3$, $^3J_{HH}$ = 7.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.8 (CO), 134.9 (C), 134.2 (C), 131.2 (CH), 121.6 (C), 112.6 (C), 100.4 (CH), 35.6 (CH_3), 23.2 (CH_2), 20.9 (CH_2), 15.1 (CH_3), 14.5 (CH_3). HRMS (ESI-TOF) m/z: $[M + Na]^+$ calc. $C_{12}H_{16}N_2NaO$ 227.1155, found 227.1149.

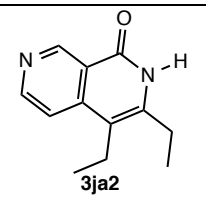
	3,4-diethyl-2,6-naphthyridin-1(2*H*)-one **3ia**

Orange solid (40 mg, 20%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^1H NMR (300 MHz, $CDCl_3$): δ 10.80 (s, 1H, NH), 9.10 (s, 1H, H_{py}), 8.58 (d, 1H, H_{py}, $^3J_{HH}$ = 5.3 Hz), 8.11 (dd, 1H, H_{py}, $^3J_{HH}$ = 5.3, $^5J_{HH}$ = 0.9 Hz), 2.77 (q, 2H, C*H*$_2$CH$_3$, $^3J_{HH}$ = 7.6 Hz), 2.67 (q, 2H, C*H*$_2$CH$_3$, $^3J_{HH}$ = 7.6 Hz), 1.28 (t, 3H, CH$_2$C*H*$_3$, $^3J_{HH}$ = 7.6 Hz), 1.20 (t, 3H, CH$_2$C*H*$_3$, $^3J_{HH}$ = 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.6 (CO), 147.1 (CH), 145.1 (CH), 140.7 (C), 132.2 (C), 129.9

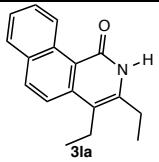
(C), 119.7 (CH), 112.8 (C), 24.1 (CH_2), 18.9 (CH_2), 15.1 (CH_3), 13.8 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{12}H_{14}N_2NaO$ 225.0998, found 225.0995.

 **3ja1**	7,8-diethyl-1,6-naphthyridin-5(6*H*)-one **3ja1**

Yellow solid (51 mg, 25%). Column chromatography: elution with hexane/ethyl acetate (50/50) allows to obtain compound **3ja1**. After exhaustive washing with this mixture compound **3ja2** remains in the column. Therefore elution is carried out with pure ethylacetate, which allows to obtain compound **3ja2**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.16 (s, 1H, NH), 8.89 (dd, 1H, H_{py}, $^3J_{HH}$= 4.5, $^4J_{HH}$=1.9 Hz), 8.59 (dd, 1H, H_{py}, $^3J_{HH}$= 8.0, $^4J_{HH}$=1.9 Hz), 7.28 (dd, 1H, H_{py}, $^3J_{HH}$= 8.0, $^3J_{HH}$= 4.5 Hz), 2.88 (q, 2H, C*H*$_2$CH$_3$, $^3J_{HH}$ = 7.4 Hz), 2.68 (q, 2H, C*H*$_2$CH$_3$, $^3J_{HH}$ = 7.6 Hz), 1.29 (t, 3H, CH$_2$C*H*$_3$, $^3J_{HH}$ = 7.6 Hz), 1.15 (t, 3H, CH$_2$C*H*$_3$, $^3J_{HH}$ = 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.8 (CO), 163.5 (C), 154.2 (C), 154.0 (CH), 142.4 (C), 135.7 (CH), 120.5 (CH), 117.2 (C), 24.4 (CH_2), 18.7 (CH_2), 15.1 (CH_3), 13.7 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{12}H_{14}N_2NaO$ 225.0998, found 225.1004.

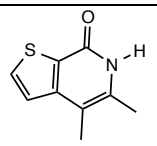
 **3ja2**	3,4-diethyl-2,7-naphthyridin-1(2*H*)-one **3ja2**

White solid (16 mg, 8%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.45 (s, broad, 1H, NH), 9.61 (s, 1H, H_{py}), 8.76 (d, 1H, H_{py}, $^3J_{HH}$ = 5.8 Hz), 7.50 (dd, 1H, H_{py}, $^3J_{HH}$ = 5.8, $^5J_{HH}$ = 0.9 Hz), 2.75 (m, 4H, C*H*$_2$CH$_3$), 1.38 (t, 3H, $^3J_{HH}$ = 7.6 Hz, CH$_2$C*H*$_3$), 1.23 (t, 3H, $^3J_{HH}$ = 7.5 Hz, CH$_2$C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.0 (CO), 151.4 (CH), 151.1 (CH), 144.2 (C), 143.6 (C), 120.1 (C), 116.2 (CH), 112.8 (C), 24.6 (CH_2), 19.1 (CH_2), 14.7 (CH_3), 13.6 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ calc. $C_{12}H_{15}N_2O$ 203.1179, found 203.1179.

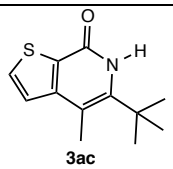
 **3la**	3,4-diethylbenzo[*h*]isoquinolin-1(2*H*)-one **3la**

Light yellow solid (201 mg, 80%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.11 (s, 1H, N*H*), 10.38 (d, 1H, C_6H_4, $^3J_{HH}$= 8.7 Hz), 8.08

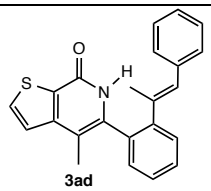
(d, 1H, C_6H_2, $^3J_{HH}$= 9.0 Hz), 7.93 (d, 1H, C_6H_4, $^3J_{HH}$= 7.9 Hz), 7.83 (d, 1H, C_6H_2, $^3J_{HH}$= 9.0 Hz), 7.76 (m, 1H, C_6H_4), 7.62 (m, 1H, C_6H_4), 2.93 (m, 4H, CH_2CH$_3$), 1.49 (t, 3H, CH$_2$CH_3, $^3J_{HH}$ = 7.5 Hz), 1.30 (t, 3H, CH$_2$CH_3, $^3J_{HH}$ = 6.7 Hz). ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.5 (CO), 141.6 (C), 140.1 (C), 133.7 (CH), 132.5 (C), 131.4 (C), 128.0 (CH), 127.9 (CH), 127.4 (CH), 125.9 (CH), 121.3 (CH), 118.3 (C), 114.7 (C), 24.3 (CH_2), 20.1 (CH_2), 15.3 (CH_3), 14.2 (CH_3). HRMS (ESI-TOF) m/z: $[M + Na]^+$ calc. $C_{17}H_{17}NNaO$ 274.1202, found 274.1203.

 3ab	4,5-dimethylthieno[2,3-*c*]pyridin-7(6*H*)-one **3ab**

White solid (45 mg, 25%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.09 (s, 1H, NH), 7.63 (d, 1H, H_{thio}, $^3J_{HH}$ = 5.1 Hz), 7.18 (d, 1H, H_{thio}, $^3J_{HH}$ = 5.1 Hz), 2.35 (s, 3H, CH_3), 2.19 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.2 (CO), 148.7 (C), 135.7 (C), 133.1 (CH), 126.6 (C), 122.9 (CH), 108.8 (C), 16.7 (CH_3), 13.6 (CH_3). HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. $C_9H_{10}NOS$ 180.0483, found 180.0483.

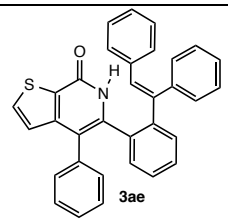
 3ac	5-(*tert*-butyl)-4-methylthieno[2,3-*c*]pyridin-7(6*H*)-one **3ac**.

White solid (202 mg, 92%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.85 (s, broad, 1H, NH), 7.57 (s, broad, 1H, H_{thio}), 7.18 (s, broad, 1H, H_{thio}), 2.36 (s, 3H, CH_3), 1.37 (s, 9H, C(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.2 (C), 150.1 (C), 144.5 (2C, overlapped), 133.1 (CH_{tio}), 127.0 (C), 123.4 (CH_{tio}), 108.5 (C), 35.7 (*C*(CH_3)$_3$), 29.6 (C(*C*H$_3$)$_3$), 16.0 (CH_3). HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. $C_{12}H_{16}NOS$ 222.0953, found 222.0957.

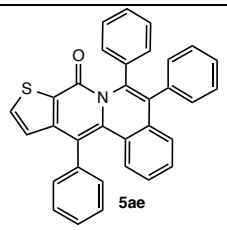
 3ad	(*E*)-4-methyl-5-(2-(1-phenylprop-1-en-2-yl)phenyl)thieno[2,3-*c*]pyridin-7(6*H*)-one **3ad**

Yellow solid (98 mg, 28%). Column chromatography: elution with hexane/ethyl acetate (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.98 (s, 1H, NH), 7.62 (d, 1H, H_{thio}, $^3J_{HH}$ = 5.2 Hz), 7.40-7.35 (m, 2H, H-Ar), 7.33-7.21 (m, 2H, H-Ar), 7.19-7.12 (m, 3H, H-Ar), 7.08-6.98 (m, 3H, H-Ar), 6.40 (s, broad, 1H, HC=C), 2.03 (s, 3H, CH_3), 1.81 (d, 3H, CH_3, $^4J_{HH}$ = 1.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ =

158.7 (C), 148.1 (C), 145.9 (C), 138.2 (C), 137.6 (2C, overlapped), 133.5 (CH_{thio}), 132.0 (2C, overlapped), 131.0 (CH), 130.6 (CH), 129.6 (CH), 129.1 (CH), 128.8 (CH), 128.1 (CH), 127.2 (CH), 126.6 (CH), 123.4 (CH_{tio}), 110.0 (C), 18.9 (CH_3), 14.8 (CH_3). HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. $C_{23}H_{20}NOS$ 358.1260, found 358.1265.

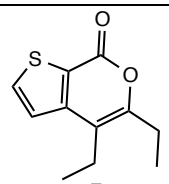
 3ae	(*E*)-5-(2-(1,2-diphenylvinyl)phenyl)-4-phenylthieno[2,3-*c*]pyridin-7(6*H*)-one **3ae**

Dark yellow oil (91 mg, 19%). Column chromatography over neutral alumina, eluting with dichloromethane/methanol 95:5. Further purification by silica gel chromatography, eluting with hexane/ethyl acetate (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39 (s, 1H, NH), 7.54 (d, 1H, CH_{thio}, $^3J_{HH}$ = 5.3 Hz), 7.37 – 7.20 (m, 8H, C_{arom}), 7.06 – 7.00 (m, 4H, C_{arom}), 6.97 (d, 1H, CH_{thio}, $^3J_{HH}$ = 5.3) 6.93 – 6.83 (m, 5H, C_{arom}), 6.64 (s,1H, C_{arom}), 6.62 (s, 1H, C_{arom}), 5.85 (s, 1H, HC=C). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.4 (C), 141.3 (C), 139.6 (C), 138.1 (C), 136.7 (C), 135.7 (C), 133.3 (CH), 133.1 (C), 131.1 (CH), 130.8 (CH), 130.5 (CH) , 130.3 (CH), 129.6 (CH), 129.4 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 127.6 (CH), 127.4 (CH), 127.0 (CH), 127.0 (CH), 124.8 (CH). Signals due to 4 quaternary C atoms were not observed in spite of long accumulation trials, changes in the relaxation delay, or attempts to inverse detection through ^{1}H-^{13}C HMBC. HRMS (ESI-TOF) m/z: $[M+H]^+$ calc. $C_{33}H_{24}NOS$ 482.1573, found 482.1577.

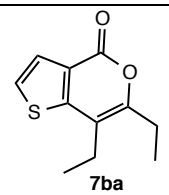
 5ae	5,6,12-triphenyl-8*H*-thieno[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8-one **5ae**

Yellow solid (104 mg, 22%). Column chromatography over neutral alumina, eluting with dichloromethane/methanol 90/10. Further purification by silica gel chromatography, eluting with hexane/diethyl ether (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, 1H, C_{thio}, $^3J_{HH}$ = 5.3 Hz), 7.50 – 7.37 (m, 5H, C_{arom}), 7.23 – 7.12 (m, 5H, C_{arom}), 7.11 – 7.04 (m, 4H, C_{arom}), 7.00 (m, 4H, C_{arom}), 6.97 (d, 1H, C_{thio}, $^3J_{HH}$ = 5.3 Hz), 6.84 (ddd, 1H, C_{arom}, J = 8.5, 6.2, 2.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.7 (C), 145.7 (C), 139.2 (C), 137.3 (C), 136.2 (C), 135.6 (C), 133.2 (CH_{thio}), 132.6 (C), 131.4 (CH), 131.1 (CH), 129.7 (CH), 128.9 (CH), 128.8 (CH), 128.5 (CH), 128.1 (CH), 127.9 (CH), 127.5 (C), 127.1 (CH), 127.0 (CH), 126.8 (CH), 126.3 (CH), 125.8 (CH), 125.2 (CH_{thio}), 115.5 (C). Signals due to 3 quaternary C atoms were not observed in spite of long accumulation

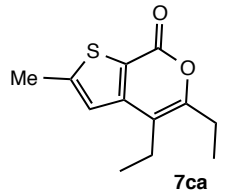
trials, changes in the relaxation delay, or attempts to inverse detection through ^{1}H-^{13}C HMBC. HRMS (ESI-TOF) m/z: $[M+H]^+$ calc. $C_{33}H_{22}NOS$ 480.1417, found 480.1412.

 **7aa**	4,5-diethyl-7*H*-thieno[2,3-*c*]pyran-7-one **7aa**

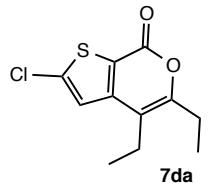
White solid (123 mg, 59 %). Column chromatography: elution with hexane/diethylether (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (d, 1H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 7.13 (d, 1H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 2.54 (m, 4H, CH_2CH_3), 1.21 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.13 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.1 (C), 157.3 (C), 149.0 (C), 136.3 (CH), 122.9 (CH), 122.6 (C), 113.4 (C), 23.5 (CH_2), 21.1 (CH_2), 14.7 (CH_3), 12.8 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{11}H_{12}NaO_2S$ 231.0450, found 231.0451.

 **7ba**	6,7-diethyl-4*H*-thieno[3,2-*c*]pyran-4-one **7ba**

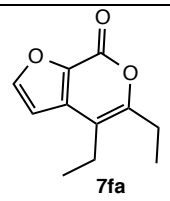
Orange solid (156 mg, 75%). Column chromatography: elution with hexane/diethylether (50/50). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, 1H, CH_{thio}, $^{3}J_{HH}$ = 5.3 Hz), 7.28 (d, 1H, CH_{thio}, $^{3}J_{HH}$ = 5.3 Hz), 2.60 (m, 4H, CH_2CH_3), 1.28 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.24 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.2 (C), 156.4 (C), 153.4 (C), 126.1 (CH), 124.5 (CH), 123.4 (C), 112.9 (C), 23.6 (CH_2), 22.4 (CH_2), 13.9 (CH_3), 12.6 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{11}H_{12}NaO_2S$ 231.0450, found 231.0451.

 **7ca**	4,5-diethyl-2-methyl-7*H*-thieno[2,3-*c*]pyran-7-one **7ca**

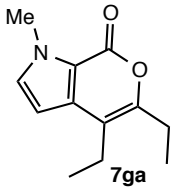
Dark yellow solid (198 mg, 89%). Column chromatography: elution with hexane/diethylether (50/50). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.80 (q, 1H, CH_{thio}, $^{4}J_{HH}$ = 1.1 Hz), 2.55 (d, 3H, C-CH_3, $^{4}J_{HH}$ = 1.1 Hz), 2.51 (m, 4H, CH_2CH_3), 1.20 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.11 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz). ^{13}C NMR (126 MHz, $CDCl_3$): δ 158.9 (C), 157.4 (C), 152.4 (C), 149.8 (C), 121.3 (CH), 120.8 (C), 113.2 (C), 23.6 (CH_2), 21.1 (CH_2), 16.5 (CH_3), 14.7 (CH_3), 12.8 (CH_3). HRMS (ESI-TOF) m/z: $[M + Na]^+$ calc. $C_{12}H_{14}NaO_2S$ 245.0607, found 245.0608.

 **7da**	2-chloro-4,5-diethyl-7*H*-thieno[2,3-*c*]pyran-7-one **7da**

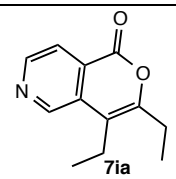
White solid (90 mg, 37%). Column chromatography: elution with hexane/diethylether (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.97 (s, 1H, CH_{thio}), 2.50 (m, 4H, CH_2CH_3), 1.20 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.11 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.4 (C), 157.6 (C), 148.7 (C), 142.4 (C), 122.3 (CH), 121.0 (C), 112.8 (C), 23.7 (CH_2), 21.0 (CH_2), 14.6 (CH_3), 12.6 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{11}H_{11}ClNaO_2S$ 265.0060, found 265.0050.

 **7fa**	4,5-diethyl-7*H*-furo[2,3-*c*]pyran-7-one **7fa**

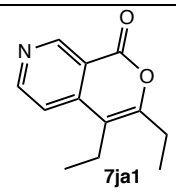
Yellow oil (81 mg, 42%). Column chromatography: elution with hexane/diethylether (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, 1 H, CH_{fur}, $^{3}J_{HH}$ = 1.9 Hz), 6.57 (d, 1 H, CH_{fur}, $^{3}J_{HH}$ = 1.9 Hz), 2.50 (m, 4H, CH_2CH_3), 1.19 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.12 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.5 (C), 157.3 (C), 150.1 (CH), 137.3 (C), 136.53 (C), 111.7 (C), 106.5 (CH), 23.6 (CH_2), 20.8, (CH_2) 14.5 (CH_3), 12.8 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{11}H_{13}O_3$ 193.0859, found 193.0863.

 **7ga**	4,5-diethyl-1-methylpyrano[3,4-*b*]pyrrol-7(1*H*)-one **7ga**

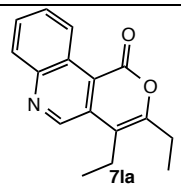
Yellow solid (195 mg, 95%). This compound was obtained pure after filtration over alumina. No column chromatography was needed. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.94 (d, 1H, CH_{pyrr}, $^{3}J_{HH}$ = 2.7 Hz), 6.09 (d, 1H, CH_{pyrr}, $^{3}J_{HH}$ = 2.7 Hz), 3.95 (s, 3H, NMe), 2.44 (m, 4H, CH_2CH_3), 1.13 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.08 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$): δ 156.9 (C), 152.9 (C), 134.2 (C), 132.7 (CH), 116.8 (C), 112.4 (C), 101.2 (CH), 35.7 (CH_3), 23.2 (CH_2), 20.5 (CH_2), 14.5 (CH_3), 13.0 (CH_3). HRMS (ESI-TOF) m/z: $[M + Na]^+$ calc. $C_{12}H_{15}NNaO_2$ 228.0995, found 228.1000.

 **7ia**	3,4-diethyl-1*H*-pyrano[4,3-*c*]pyridin-1-one **7ia**

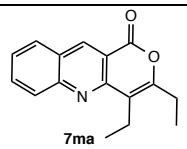
White solid (55 mg, 27 %). Column chromatography: elution with hexane/diethylether (50/50). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.94 (s, broad, 1H, CH_{pyr}), 8.67 (d, 1H, CH_{pyr}, $^{3}J_{HH}$ = 5.1 Hz), 8.00 (dd, 1H, CH_{pyr}, $^{3}J_{HH}$ = 5.1, $^{5}J_{HH}$= 0.9 Hz), 2.67 (q, 2H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz), 2.58 (q, 2H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.23 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.19 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.3 (C), 157.0 (C), 147.3 (CH), 145.9 (CH), 131.6 (C), 126.5 (C), 121.6 (CH), 111.4 (C), 24.0 (CH_2), 18.8 (CH_2), 14.4 (CH_3), 12.4 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ calc. $C_{12}H_{14}NO_2$ 204.1019, found 204.1013.

 **7ja1**	3,4-diethyl-1*H*-pyrano[3,4-*c*]pyridin-1-one **7ja1**

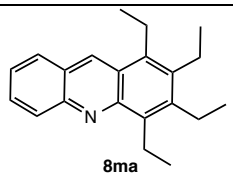
White solid, (63 mg, 31%). Column chromatography: elution with hexane/ diethylether (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.39 (d, 1H, CH_{pyr}, $^{5}J_{HH}$ = 0.8 Hz), 8.76 (d, 1H, CH_{pyr}, $^{3}J_{HH}$ = 5.6 Hz), 7.29 (dd, 1H, $^{3}J_{HH}$ = 5.6, $^{5}J_{HH}$= 0.9 Hz), 2.57 (m, 4H, CH_2CH_3), 1.23 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.13 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.4 (C), 160.0 (C), 153.8 (CH), 152.6 (CH), 144.1 (C), 116.1 (C), 115.8 (CH), 112.1 (C), 24.5 (CH_2), 18.9 (CH_2), 14.1 (CH_3), 12.2 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{12}H_{13}NNaO_2$ 226.0838, found 226.0831.

 **7la**	3,4-diethyl-1*H*-pyrano[4,3-*c*]quinolin-1-one **7la**

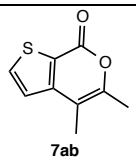
Yellow solid, (116.4 mg, 46%). Column chromatography: elution with hexane/diethylether (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.52 (m, 1H, C_6H_4), 9.20 (s, 1H, CH_{pyr}), 8.12 (m, 1H, C_6H_4), 7.72 (m, 2H, C_6H_4), 2.79 (q, 2H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 2.66 (q, 2H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz), 1.28 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.6 Hz), 1.24 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.1 (C), 158.9 (C), 146.6 (C), 146.6 (CH), 131.9 (C), 129.9 (CH) 129.7 (CH), 129.4 (CH), 126.3 (CH), 124.3 (C), 119.2 (C), 112.3 (C), 24.1 (CH_2), 19.1 (CH_2), 14.8 (CH_3), 12.5 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{16}H_{15}NNaO_2$ 276.0995, found 276.0995.

 7ma	3,4-diethyl-1*H*-pyrano[4,3-*b*]quinolin-1-one **7ma**

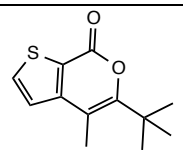
Yellow solid (73 mg, 29%). Column chromatography: elution with hexane/diethyl ether (80/20) allows to obtain compound **8ma**. After washing with this mixture compound **7ma** remains in the column. Therefore, elution is carried out with a mixture hexane/diethyl ether (50/50), which allows to obtain compound **7ma**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.05 (s, 1H, CH_{pyr}), 8.08 (dd, 1H, C_6H_4, $^{3}J_{HH}$ = 8.6, $^{4}J_{HH}$ = 1.0 Hz), 7.90 (dd, 1H, C_6H_4, $^{3}J_{HH}$ = 8.2, $^{4}J_{HH}$ = 1.5 Hz), 7.78 (ddd, 1H, C_6H_4, $^{3}J_{HH}$ = 8.2, $^{3}J_{HH}$ = 6.8, $^{4}J_{HH}$ =1.0 Hz), 7.50 (ddd, 1H, C_6H_4, $^{3}J_{HH}$ = 8.6, $^{3}J_{HH}$ = 6.8, $^{4}J_{HH}$ =1.5 Hz), 2.88 (q, 2H, CH_2CH_3, $^{3}J_{HH}$ = 7.4 Hz), 2.64 (q, 2H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.27 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.5 Hz), 1.19 (t, 3H, CH_2CH_3, $^{3}J_{HH}$ = 7.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.0 (C), 158.5 (C), 152.2 (C), 151.4 (C), 140.1 (CH), 132.8 (CH), 129.6 (CH), 129.2 (CH), 126.6 (CH), 126.4 (C), 116.6 (C), 115.6 (C), 24.4 (CH_2), 18.5 (CH_2), 14.5 (CH_3), 12.3 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{16}H_{15}NNaO_2$ 276.0995, found 276.0989.

 8ma	1,2,3,4-tetraethylacridine **8ma**

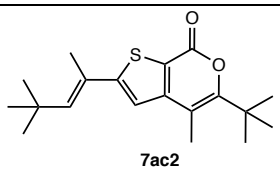
Yellow solid (119 mg, 41%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.75 (s, 1H, CH_{pyr}), 8.13 (d, 1H, C_6H_4, $^{3}J_{HH}$ = 8.7 Hz), 7.90 (d, 1H, C_6H_4, $^{3}J_{HH}$ = 8.3 Hz), 7.62 (m, 1H, C_6H_4), 7.39 (m, 1H, C_6H_4), 3.43 (q, 2H, $^{3}J_{HH}$ = 7.2 Hz), 3.15 (q, 2H, $^{3}J_{HH}$ = 7.4 Hz), 2.86 (m, 4H), 1.25 (m, 12H). The product is unstable towards protonation in solution, affording very broad peaks, and no reliable ^{13}C measurements could be performed. HRMS (ESI-TOF) m/z: $[M+H]^+$ calc. $C_{21}H_{26}N$ 292.2065, found 292.2061.

 7ab	4,5-dimethyl-7*H*-thieno[2,3-*c*]pyran-7-one **7ab**

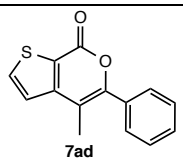
Yellow solid (41 mg, 23%). Column chromatography: elution with hexane/diethylether (50/50). Two consecutive purifications were needed in order to obtain a pure product. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (d, 1 H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 7.10 (d, 1 H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 2.23 (s, 3H, CH_3), 2.13 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.0 (C). 152.5 (C), 149.7 (C), 136.4 (CH), 123.0 (CH), 122.0 (C), 107.8 (C), 16.7 (CH_3), 13.2 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_9H_8NaO_2S$ 203.0137, found 203.0131.

 7ac	5-(*tert*-butyl)-4-methyl-7*H*-thieno[2,3-*c*]pyran-7-one **7ac**

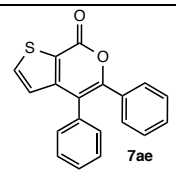
Yellow solid (151 mg, 68% the reaction is performed with only 1 equivalent of alkyne). Column chromatography: elution with hexane/diethyl ether (50/50) develops a first fraction containing compound **7ac2**. Further elution carried out with the same mixture hexane/diethyl ether (50/50), allowed to obtain compound **7ac**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, 1 H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 7.14 (d, 1 H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 2.30 (s, 3H, CH_3), 1.36 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.8 (C) 158.6 (C), 151.3 (C), 135.9 (CH), 123.4 (CH), 121.9 (C), 107.5 (C), 37.3 (C), 29.6 (CH_3, *t*Bu), 14.40 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{12}H_{14}NaO_2S$ 245.0607, found 245.0609.

 7ac2	(*E*)-5-(tert-butyl)-2-(4,4-dimethylpent-2-en-2-yl)-4-methyl-7*H*-thieno[2,3-*c*]pyran-7-one **7ac2**

Yellow oil (64 mg, 20%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.92 (s, 1H, CH_{thio}), 6.13 (q, 1H, CH_{alkene}, $^{3}J_{HH}$ = 1.3 Hz), 2.26 (s, 3H, C-CH_3), 2.12 (d, 3H, CH-CH_3, $^{3}J_{HH}$ = 1.3 Hz), 1.35 (s, 9H, C-C(CH_3)$_3$), 1.16 (s, 9H, CH-C(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.9 (C), 160.0 (C), 158.4 (C), 151.7 (C), 142.9 (CH), 128.1 (C), 119.2 (C), 117.5 (CH), 107.2 (C), 37.3 (C), 33.1 (C), 30.7 (CH_3), 29.6 (CH_3), 16.8 (CH_3), 14.3 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{19}H_{26}NaO_2S$ 341.1546, found 341.1544.

 7ad	4-methyl-5-phenyl-7*H*-thieno[2,3-*c*]pyran-7-one **7ad**

Yellow solid (36 mg, 15%). Column chromatography: elution with hexane/diethylether (50/50).
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, 1 H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 7.53 (m, 2H, Ph), 7.40 (m, 3H, Ph), 7.23 (d, 1 H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 2.29 (s, 3H, Me). ^{13}C NMR (75 MHz, $CDCl_3$): 158.5 (C), 153.9 (C), 149.8 (C), 136.5 (CH), 132.6 (C) 129.4 (CH), 129.3 (CH), 128.3 (CH), 123.7 (CH), 121.9 (C), 108.8 (C), 14.5 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calc. $C_{14}H_{10}NaO_2S$ 265.0294, found 265.0286.

 7ae	4,5-diphenyl-7*H*-thieno[2,3-*c*]pyran-7-one **7ae**

Yellow solid (30 mg, 10%). Column chromatography: elution with hexane/diethylether (50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, 1 H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz), 7.30 (m, 6H, Ph), 7.21 (m, 2H, Ph), 7.15 (m, 2H, Ph), 6.89 (d, 1 H, CH_{thio}, $^{3}J_{HH}$ = 5.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.4 (C), 153.4 (C), 149.5 (C), 136.2 (CH), 134.9 (C), 130.3 (CH), 129.3 (CH), 129.2 (CH), 129.1 (CH), 128.2 (CH), 128.0 (CH), 125.2 (CH), 123.8 (C), 122.5 (C), 115.8 (C). HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. $C_{19}H_{13}O_2S$ 305.0631, found 305.0641.

2. X-ray crystallography.

The relative lack of attention undergone by this type of fused heterocycles, noted in the introductory paragraphs, is also reflected here, because only five molecular structures (among more than 1.500.000 in the CCDC database) having the same molecular core have been reported to date.[1] Single-crystals of each compound adequate for structure determination were grown by slow evaporation of their respective solutions in ethyl acetate. In all cases the structural determination confirms the expected structures for the fused thienopyridinones. Thermal ellipsoid drawings of **3aa**, **3ab**, **3ac** and **5ae** are shown in Figures S1, S2, S3, and S4, respectively, as well as selected bond distances and angles of each one.

Compounds **3aa**, **3ab** and **3ac** can be considered as planar, as deduced from the values of the respective dihedral angles between the best least-square planes calculated with the atoms of the thiophene ring and those of the pyridinone ring (excluding substituents in 4 and 5 positions). For instance, the values of the mentioned dihedral angle in **3aa**, **3ab**, and **3ac** are 1.29(8)°, 0.5(1)°, and 5.6(1)°, respectively. The higher value in the case of **3ac** is probably related with the higher steric requirements of the ^{t}Bu group, which is located adjacent to the N atom, in agreement with the 1D-NOESY spectra of this compound. In the crystal network, pairs of molecules of **3aa** interact through hydrogen bonds. These hydrogen bonds are established between the N-H bond of one molecule and the carbonyl oxygen of the other molecule. The bond distances involved in this hydrogen bond are characterized as d(O···H) = 1.91(2) Å, d(O···N) = 2.806(2) Å, and the bond angle is defined as N-H···O = 174(2)°. According with the Jeffrey criteria, this hydrogen bond shows a moderate strength, having an energy in the range 4-15 kcal/mol.[2] This structural arrangement has also been observed in **3ab** and **3ac**. In these cases the parameters defining the respective hydrogen bonds are d(O···H) = 1.951(8) Å and 2.006(8) Å, d(O···N) = 2.86(1) Å and 2.81(1) Å, and N-H···O = 174.2(7)° and 173.1(7)° for **3ab** (two molecules in the asymmetric unit), while d(O···H) = 2.15(2) Å, d(O···N) = 2.929(2) Å, N-H···O = 160(2)° were found for **3ac**.

The analysis of the bond distances in the thiophene ring of **3aa** shows that C1-C2 bond distance (1.353(3) Å) is shorter than C3-C4 bond distance (1.386(2) Å), reflecting the delocalization of the C3-C4 bond through the pyridinone ring. The same analysis in the pyridinone ring confirms this delocalization, since the values of the bond distances C5-C4 = 1.424(2) Å, C4-C3 = 1.386(2) Å, C3-C7 = 1.439(2) Å, and C7-C6 = 1.363(2) Å, show a long-short-long-short distribution of bond distances, typical for a conjugated but non-aromatic system where the bond order is intermediate between 1 and 2.[3] The bond distance of the carbonyl group (C5-O1 = 1.249(2) Å) is identical, within experimental error, to that found in related δ-lactams (averaged 1.240(3) Å).[3] Other bonding parameters of the thienopyridinone moiety do not show remarkable deviations from values found in the literature and are not worthy of further discussion.[1,4] The analysis of bond distances and angles

in compounds **3ab** and **3ac** is strictly identical to that described for **3aa**, and suggests similar delocalizations.

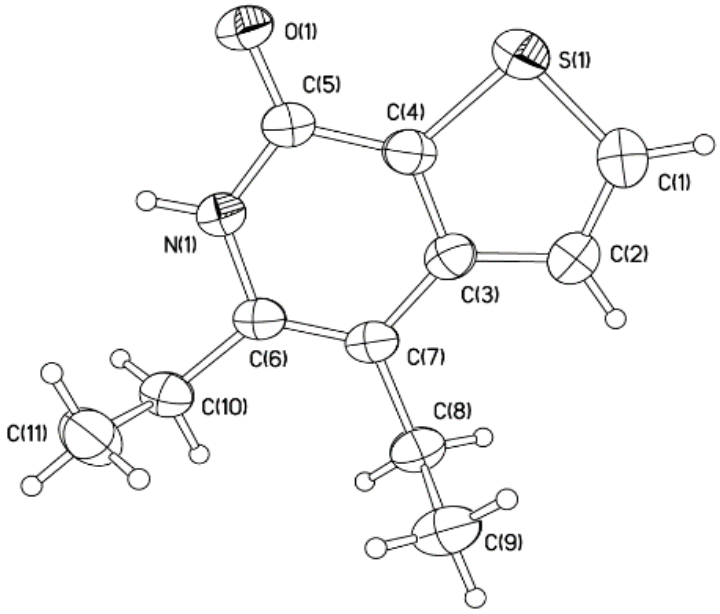


Figure S1. Molecular structure of **3aa** with thermal ellipsoids at 50% probability level. Selected bond distances [Å] and angles [°]: C1-C2 1.353(3) Å, C1-S1 1.712(2) Å, C2-C3 1.432(2) Å, C3-C4 1.386(2) Å, C3-C7 1.439(2) Å, C4-C5 1.424(2) Å, C4-S1 1.7209(17) Å, C5-O1 1.2491(19) Å, C5-N1 1.369(2) Å, C6-C7 1.363(2) Å, C6-N1 1.390(2) Å, C1-S1-C4 90.23(9)°, C2-C1-S1 113.91(15)°, C1-C2-C3 112.17(17)°, C4-C3-C2 110.64(15)°, C4-C3-C7 120.00(15)°, C2-C3-C7 129.36(15)°, C3-C4-C5 123.22(15)°, C3-C4-S1 113.04(13)°, C5-C4-S1 123.73(13)°, O1-C5-N1 121.59(15)°, O1-C5-C4 125.39(15)°, N1-C5-C4 113.01(14)°, C7-C6-N1 120.07(15)°, C6-C7-C3 117.31(14)°, C6-C7-C8 123.63(15)°, C5-N1-C6 126.35(15)°.

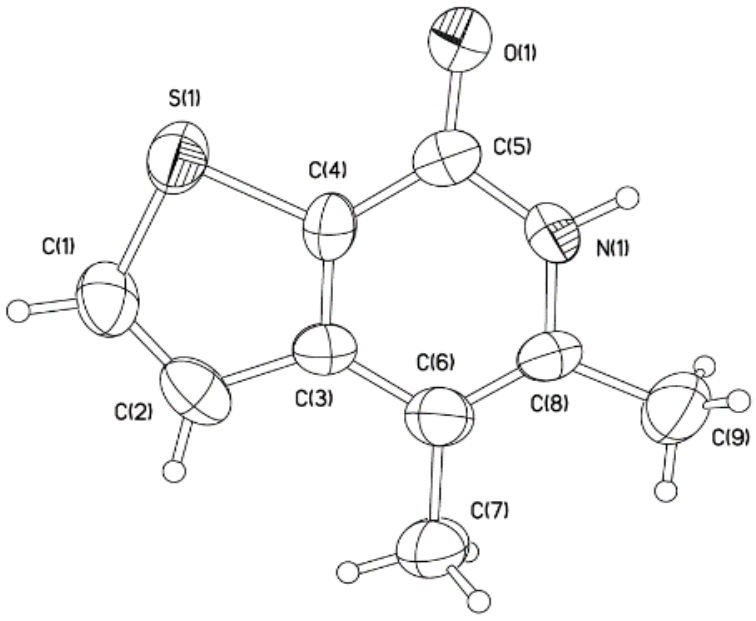


Figure S2. Molecular structure of **3ab** with thermal ellipsoids at 50% probability level. Selected bond distances [Å] and angles [°]: S1-C1 1.699(12) Å, S1-C4 1.727(11) Å, C1-C2 1.359(16) Å, C2-C3 1.430(15) Å, C3-C4 1.348(14) Å, C3-C6 1.443(15) Å, C4-C5 1.418(16) Å, C5-O1 1.259(13) Å, C5-N1 1.372(14) Å, N1-C8 1.374(15) Å, C6-C8 1.347(16) Å, C1-S1-C4 90.8(6)°, C2-C1-S1 112.3(9)°, C1-C2-C3 113.0(11)°, C4-C3-C2 110.8(10)°, C4-C3-C6 120.1(10)°, C2-C3-C6 129.1(11)°, C3-C4-C5 123.7(11)°, C3-C4-S1 113.1(9)°, C5-C4-S1 123.2(9)°, O1-C5-N1 120.6(11)°, O1-C5-C4 127.0(11)°, N1-C5-C4 112.4(10)°, C5-N1-C8 126.5(10)°, C8-C6-C3 117.5(11)°, C6-C8-N1 119.6(11)°.

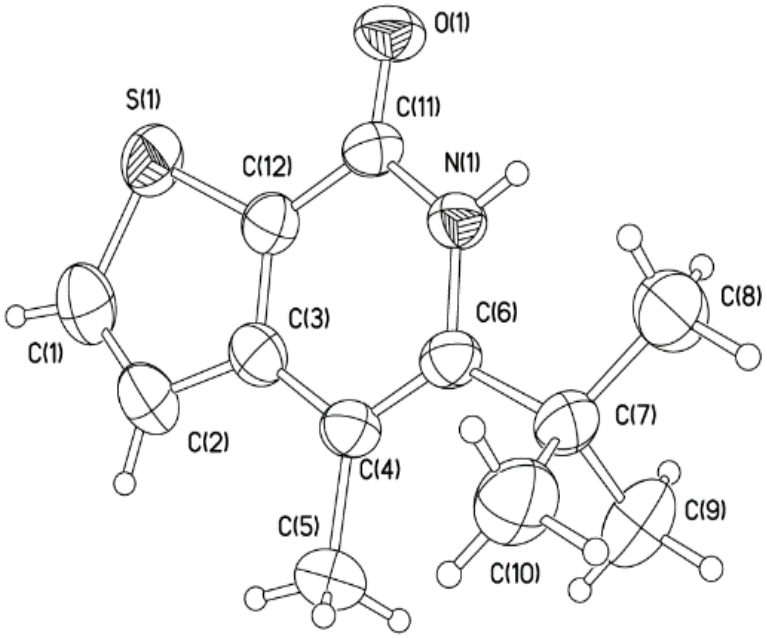


Figure S3. Molecular structure of **3ac** with thermal ellipsoids at 50% probability level. Selected bond distances [Å] and angles [°]: O1-C11 1.237(2) Å, N1-C11 1.372(2) Å, N1-C6 1.390(2) Å, C12-C3 1.375(3) Å, C12-C11 1.419(3) Å, C12-S1 1.719(2) Å, C3-C2 1.428(3) Å, C3-C4 1.431(3) Å, C6-C4 1.367(3) Å, C1-C2 1.345(3) Å, C1-S1 1.709(3) Å, C11-N1-C6 127.07(18)°, C3-C12-C11 122.96(18)°, C3-C12-S1 113.06(16)°, C11-C12-S1 123.94(16)°, C12-C3-C2 110.72(19)°, C12-C3-C4 120.54(18)°, C2-C3-C4 128.7(2)°, O1-C11-N1 122.14(19)°, O1-C11-C12 125.12(18)°, N1-C11-C12 112.73(17)°, C4-C6-N1 118.65(18)°, C4-C6-C7 125.65(18)°, N1-C6-C7 115.70(18)°, C2-C1-S1 113.74(19)°, C6-C4-C3 117.73(18)°, C1-C2-C3 112.3(2)°, C1-S1-C12 90.12(11)°.

The molecular structure of **5ae**, shown in Figure S4, confirms the double oxidative coupling of **1a** with two equivalents of diphenylacetylene **2e**, forming a thienopyridoisoquinoline tetracyclic unit. Two crystallographically independent molecules appear in the asymmetric unit, but both are identical within experimental error. In the two molecules the fused thiophene and pyridinone rings are coplanar, as it is deduced from the values of the dihedral angles between the respective best

least-square planes (1.7(2)° and 2.1(1)°). Beyond the bicyclic thienopyridinone system, the molecule loses planarity. The angle between the best least-square planes defined with the thienopyridinone and the isoquinoline moieties is 29.0(2)°, showing a notable distortion.

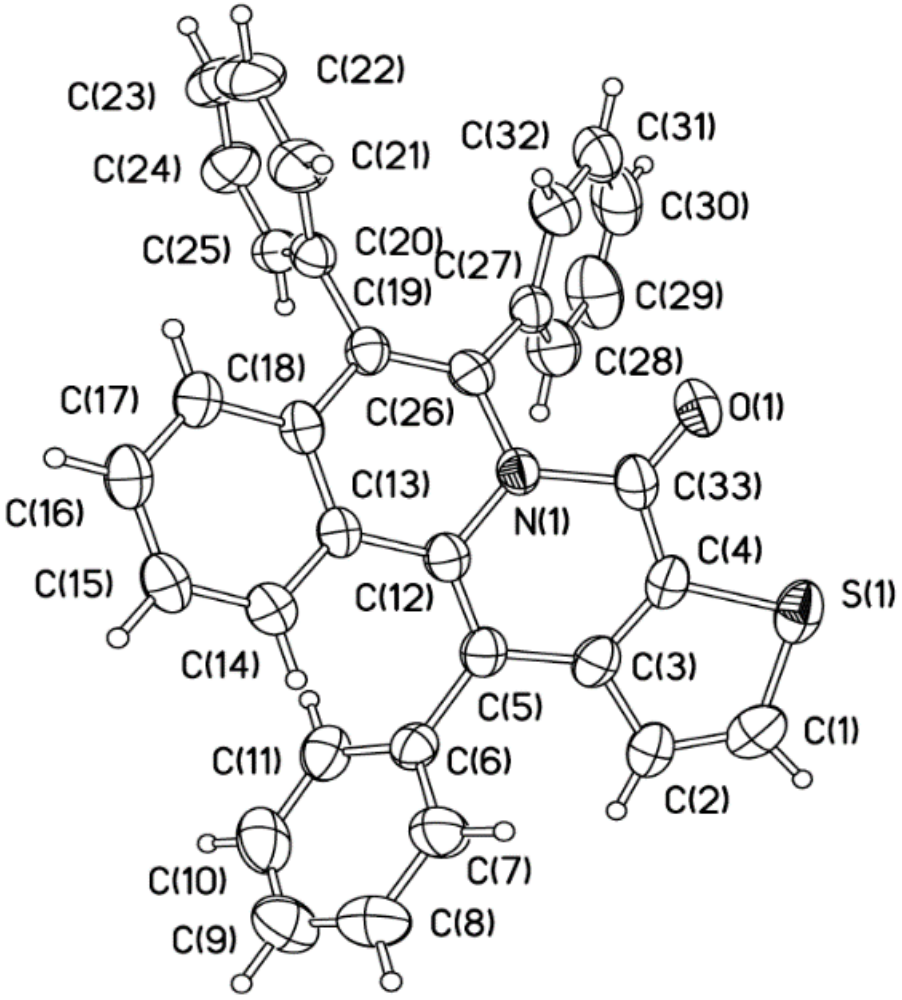


Figure 7. Molecular structure of **5ae** with thermal ellipsoids at 50% probability level. Selected bond distances [Å] and angles [°]: S1-C1 1.718(4) Å, S1-C4 1.714(3) Å, C1-C2 1.346(4) Å, C2-C3 1.443(4) Å, C3-C4 1.363(4) Å, C4-C33 1.424(4) Å, O1-C33 1.223(4) Å, N1-C33 1.430(4) Å, N1-C12 1.421(4) Å, N1-C26 1.425(4) Å, C3-C5 1.435(4) Å, C5-C12 1.367(4) Å, C12-C13 1.471(4) Å, C13-C18 1.405(4) Å, C18-C19 1.453(4) Å, C19-C26 1.333(4) Å, C4-S1-C1 89.5(2)°, C2-C1-S1 114.6(3)°, C1-C2-C3 111.0(4)°, C4-C3-C5 120.4(3)°, C4-C3-C2 111.1(3)°, C5-C3-C2 128.2(4)°, C3-C4-C33 123.6(3)°, C3-C4-S1 113.9(3)°, C33-C4-S1 122.6(3)°, C12-N1-C33 122.1(3)°, C26-N1-C33 118.0(3)°, C12-N1-C26 119.7(3)°, C12-C5-C3 118.3(3)°, C5-C12-N1 118.7(3)°, C5-C12-C13 127.0(3)°, N1-C12-C13 114.1(3)°, C14-C13-C18 117.6(3)°, C14-C13-C12 122.8(3)°, C18-C13-C12 119.5(3)°, C13-C18-C19 119.0(3)°, C26-C19-C18 120.0(3)°, C19-C26-N1 120.0(3)°, O1-C33-C4 127.1(3)°, O1-C33-N1 120.5(4)°, C4-C33-N1 112.4(3)°.

References corresponding to the crystallographic work

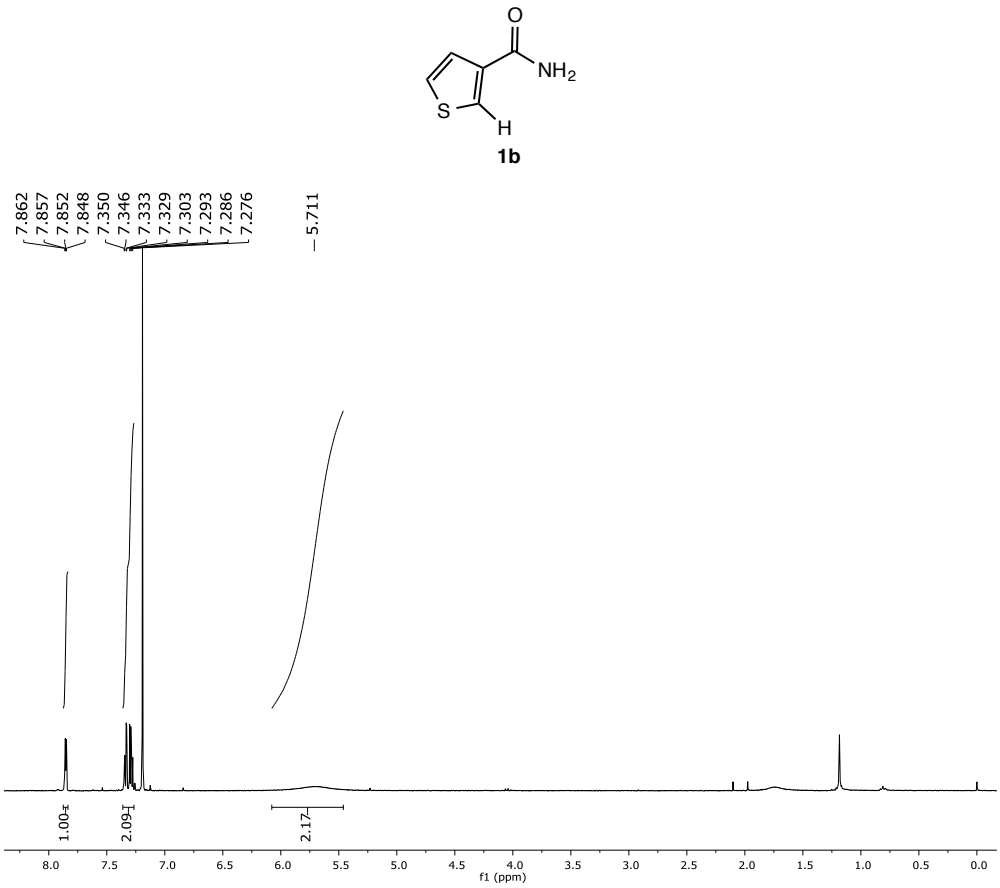
1.- (a) C. R. Groom, I. J. Bruno, M. P. Lightfoot and S. C. Ward, *Acta Crystallogr*. 2016, **B72**, 171; (b) A. M. Martínez, J. Echavarren, I. Alonso, N. Rodríguez, R. Gómez Arrayás and J. C. Carretero, *Chem. Sci*. 2015, **6**, 5802; (c) R. S. Phatake, P. Patel and C. V. Ramana, *Org. Lett*. 2016, **18**, 2828; (d) V. O. Iaroshenko, S. Ali, T. M. Babar, M. S. A. Abbasi, V. Y. Sosnovskikh, A. Villinger, A. Tolmachev and P. Langer, *Tetrahedron* 2013, **69**, 3167; (e) I. Jarak, M. Kralj, L. Suman, G. Pavlovic, J. Dogan, I. Piantanida, M. Zinic, K. Pavelic and G. Karminski-Zamola, *J. Med. Chem*. 2005, **48**, 2346; (f) M. I. Sarker, T. Shahrin, M. G. Steinmetz and Q. K. Timerghazin, *Photochem. Photobiol. Sci*. 2013, **12**, 309.

2.- T. Steiner, *Angew. Chem. Int. Ed*. 2002, **41**, 48.

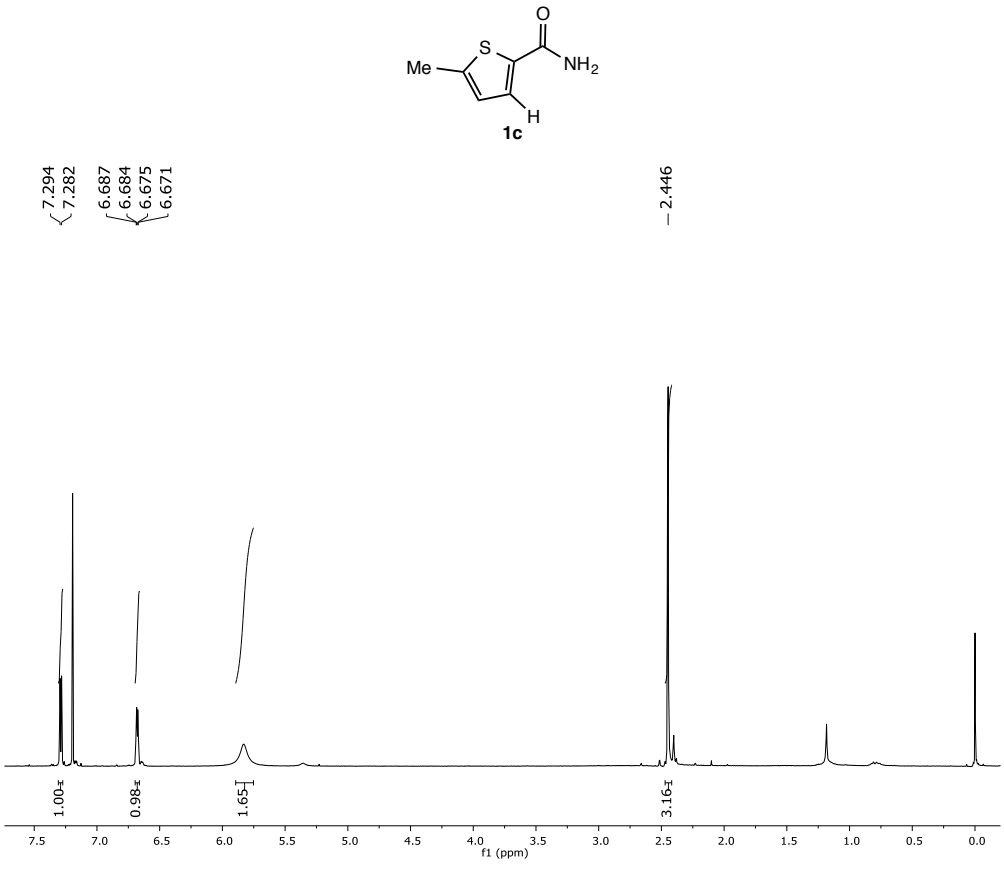
3.- F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen and R. Taylor, *J. Chem. Soc., Perkin Trans. 2* 1987, S1.

4.- R. S. Phatake, P. Patel and C. V. Ramana, *Org. Lett*. 2016, **18**, 2828.

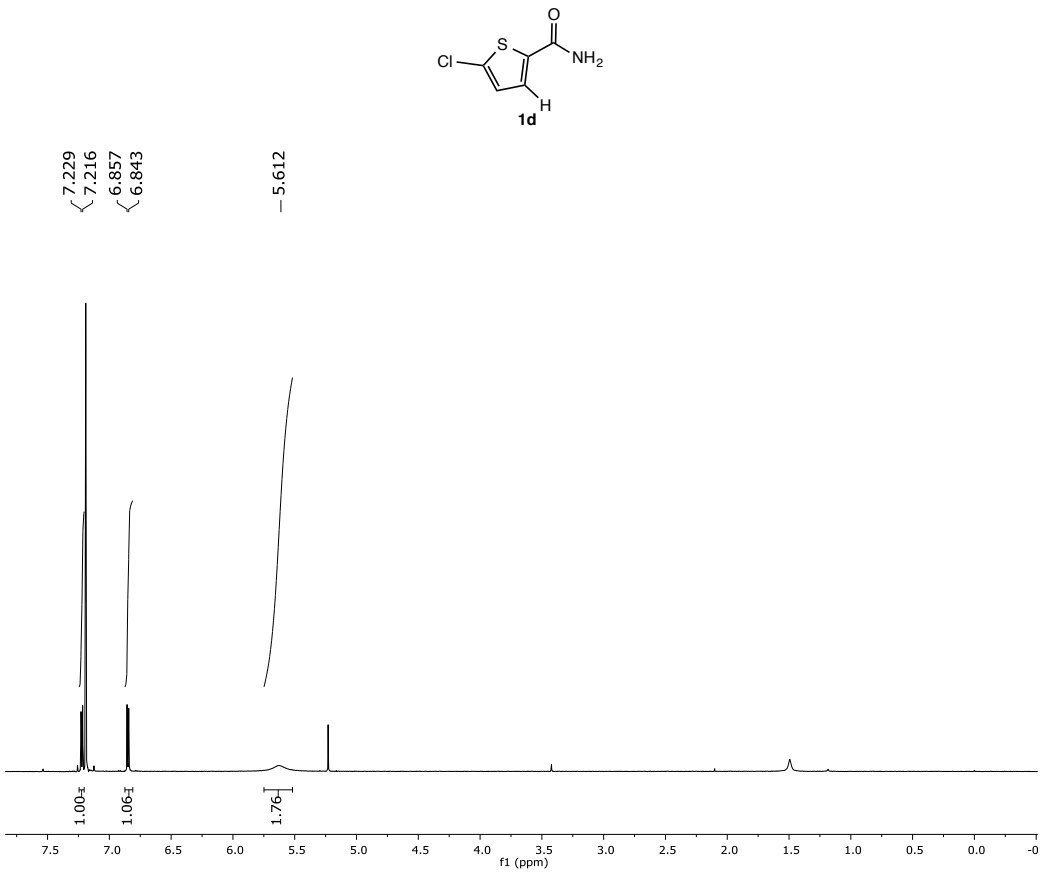
3.- NMR of starting amides **1b**, **1c**, **1d** and **1g**



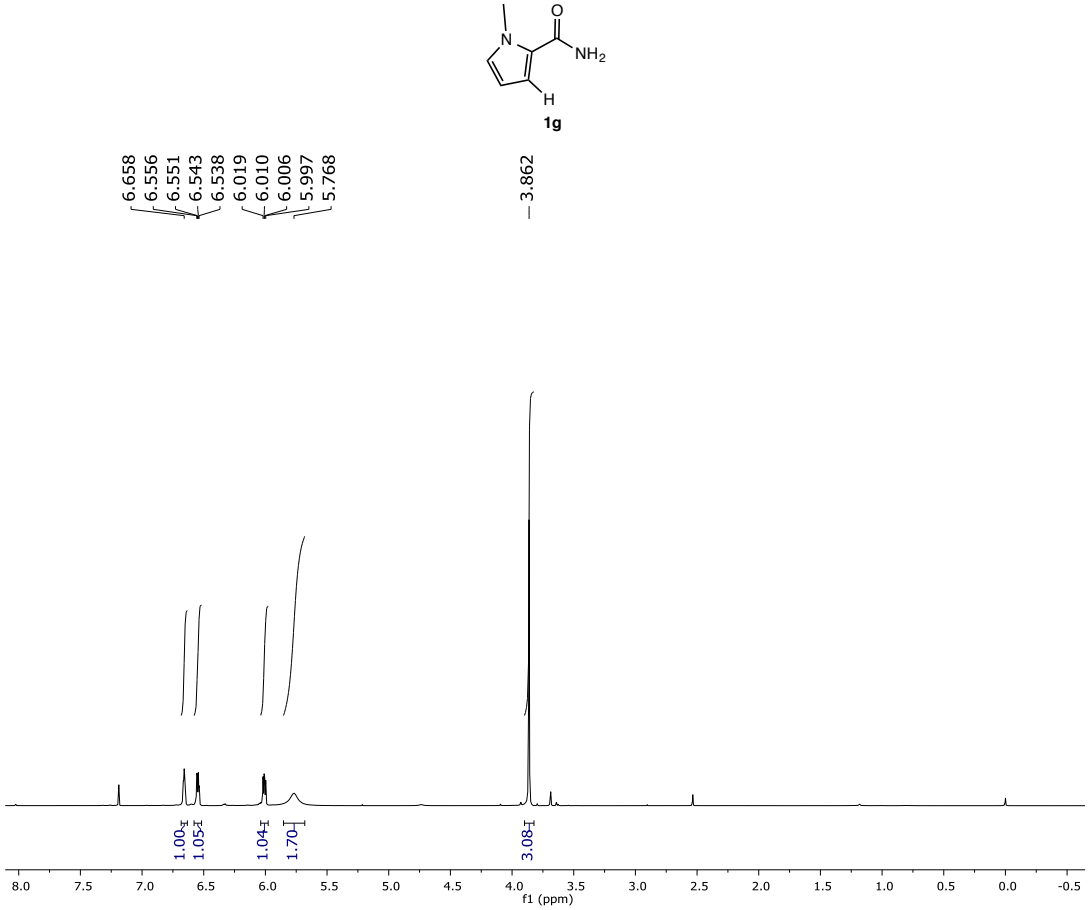
^{1}H NMR spectrum of amide **1b**



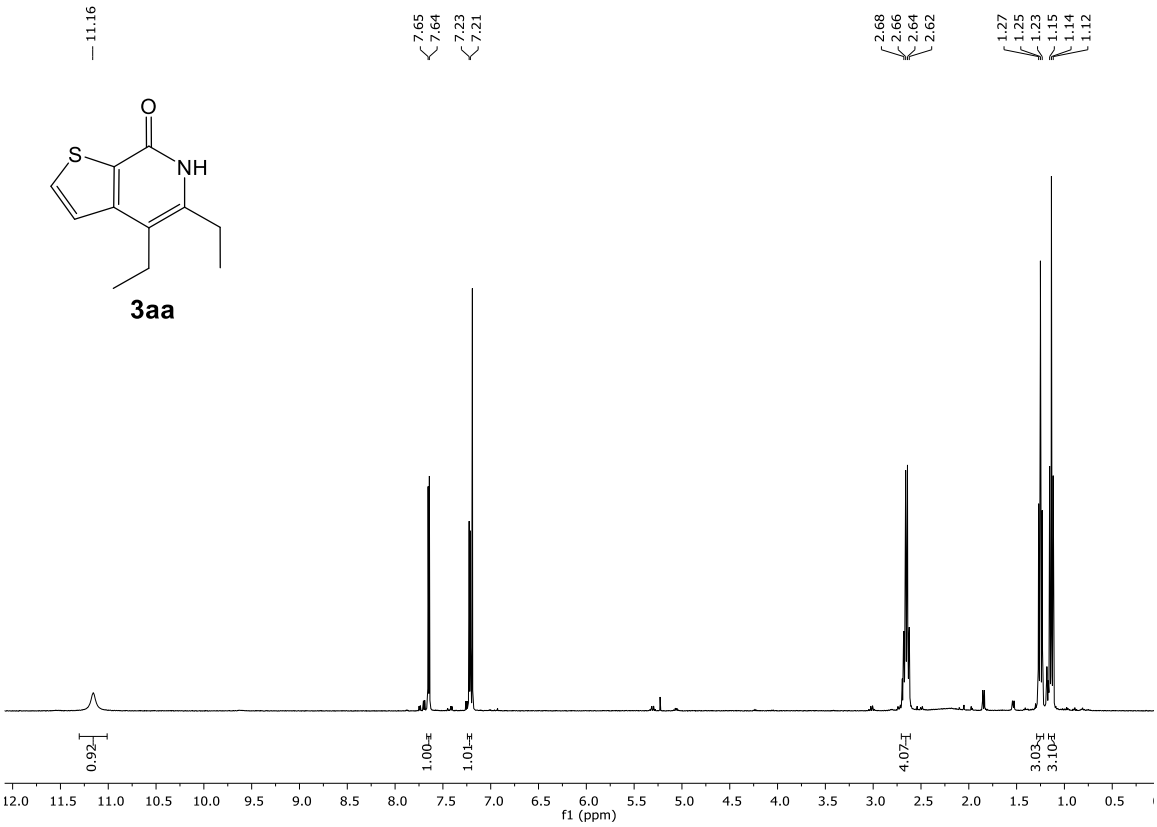
^{1}H NMR spectrum of amide **1c**



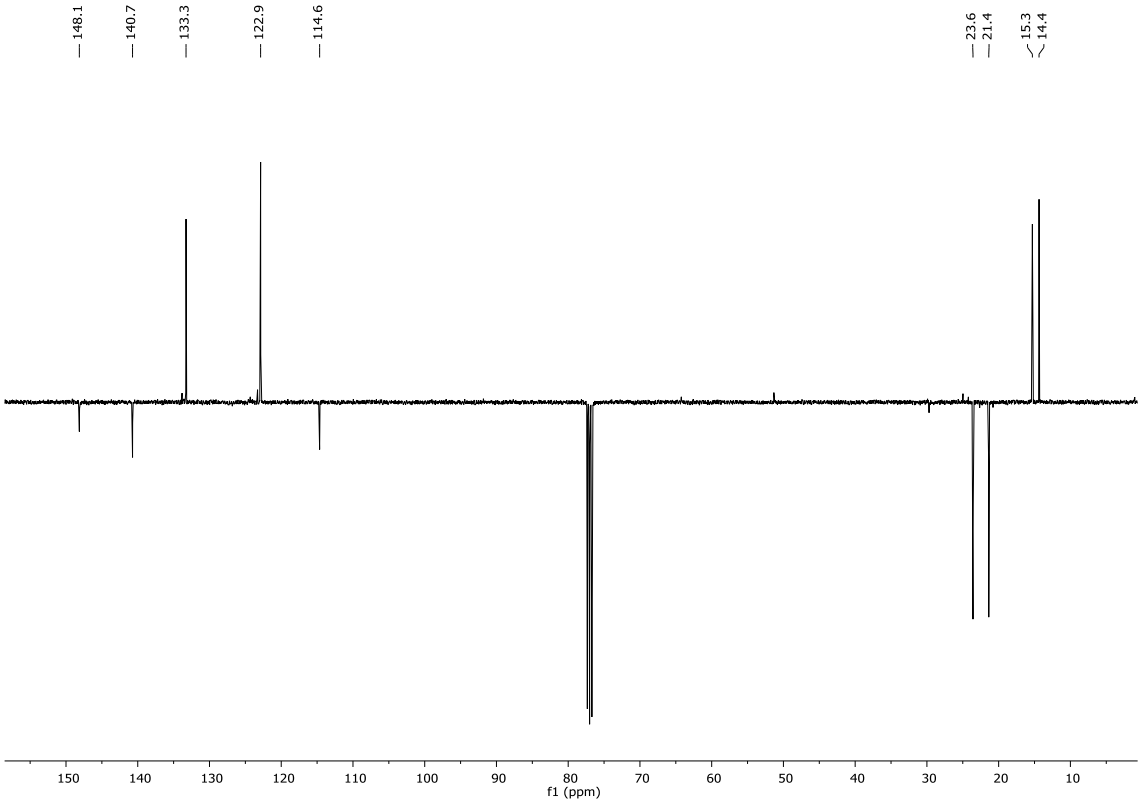
^{1}H NMR spectrum of amide **1d**



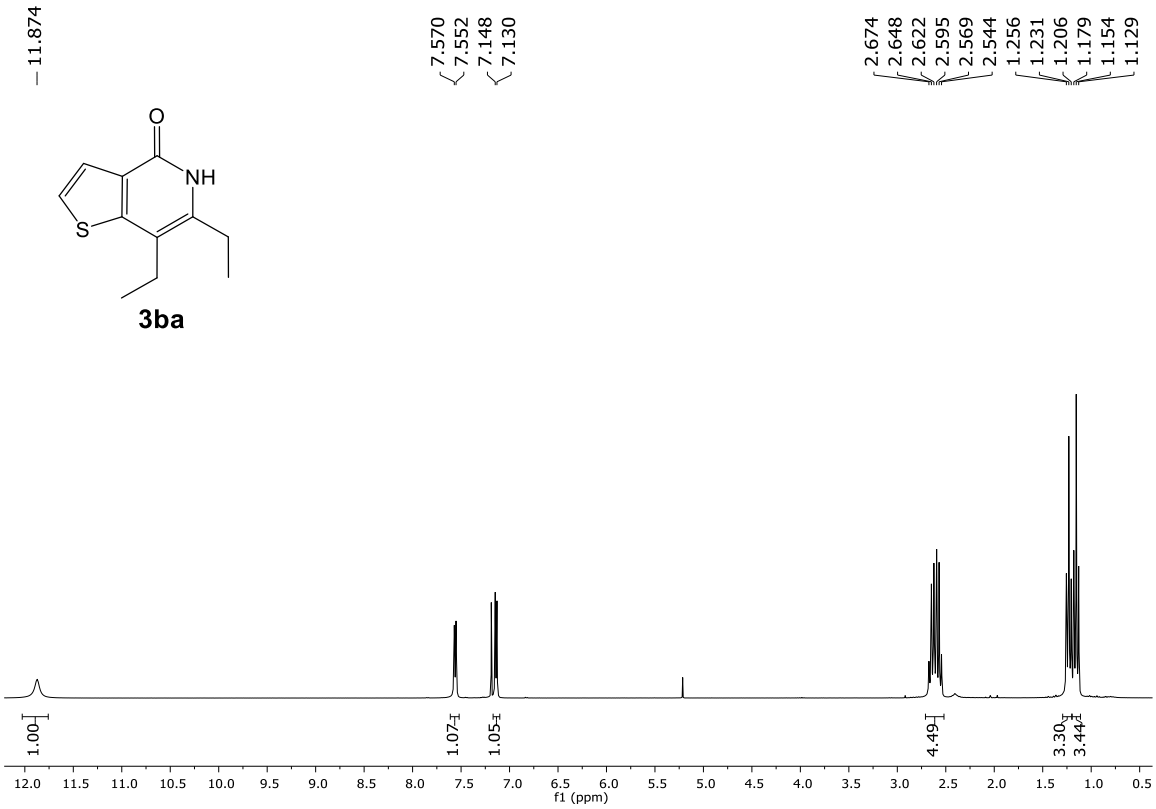
^{1}H NMR spectrum of amide **1g**



^{1}H-NMR spectrum of 3aa

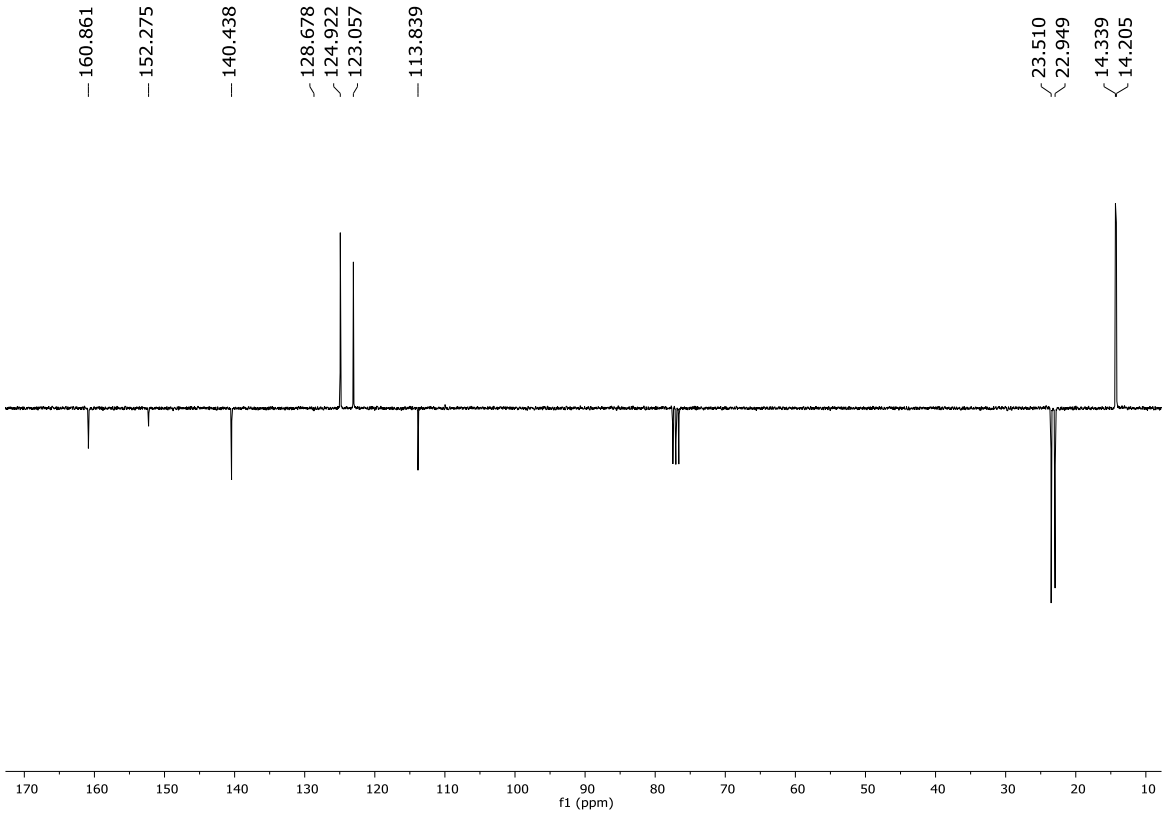


^{13}C(APT)-NMR spectrum of 3aa

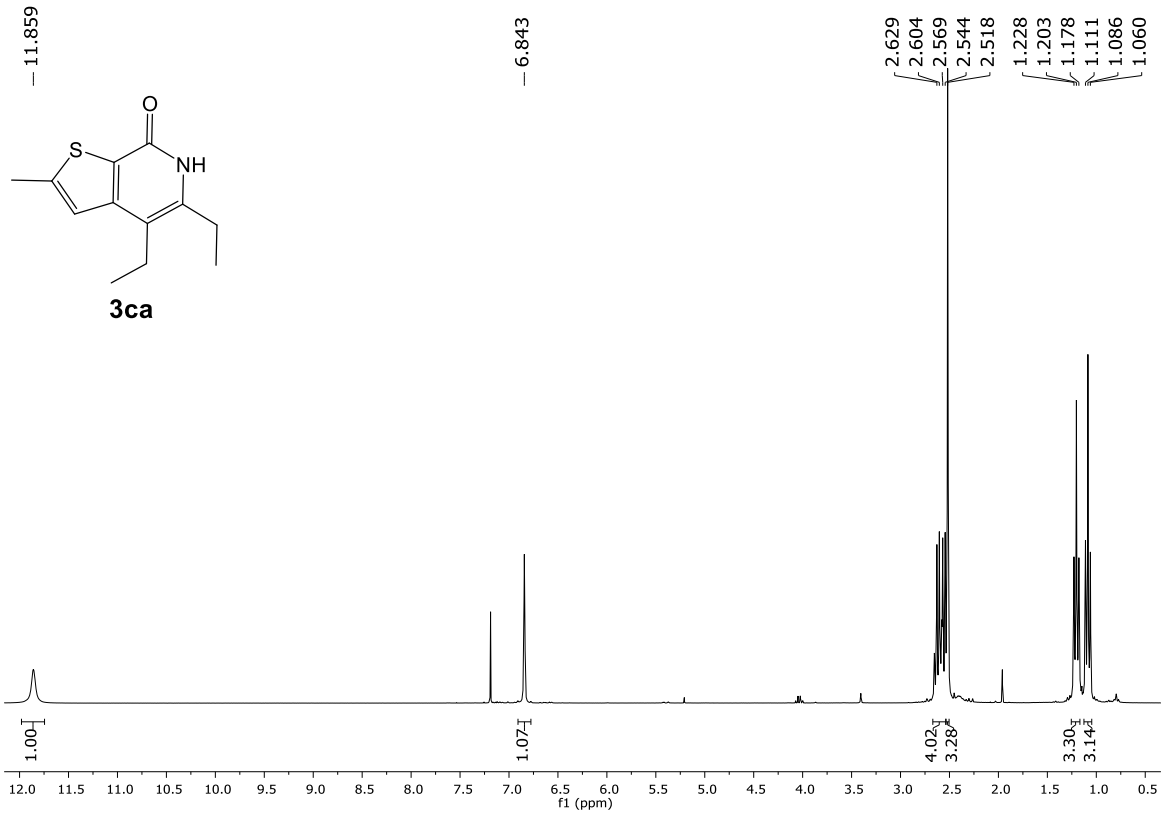


3ba

^{1}H-NMR spectrum of 3ba

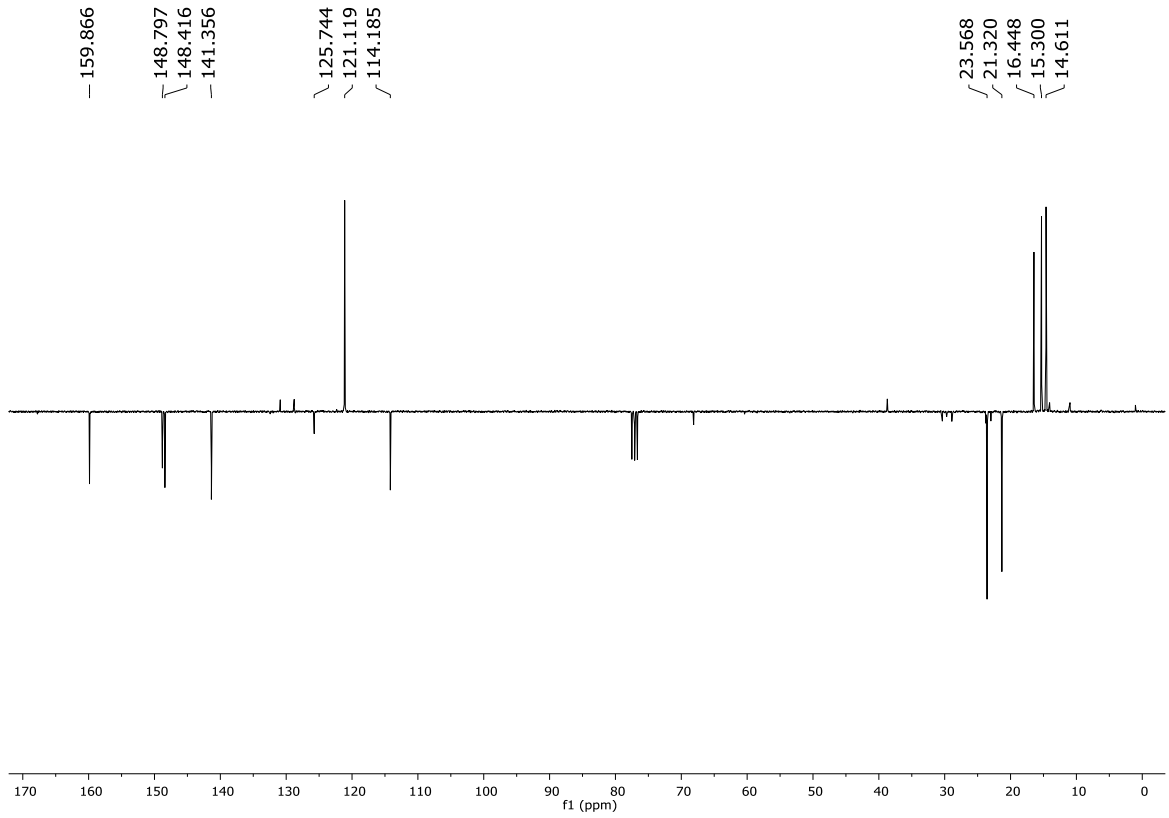


^{13}C(APT)-NMR spectrum of 3ba



3ca

^{1}H-NMR spectrum of 3ca



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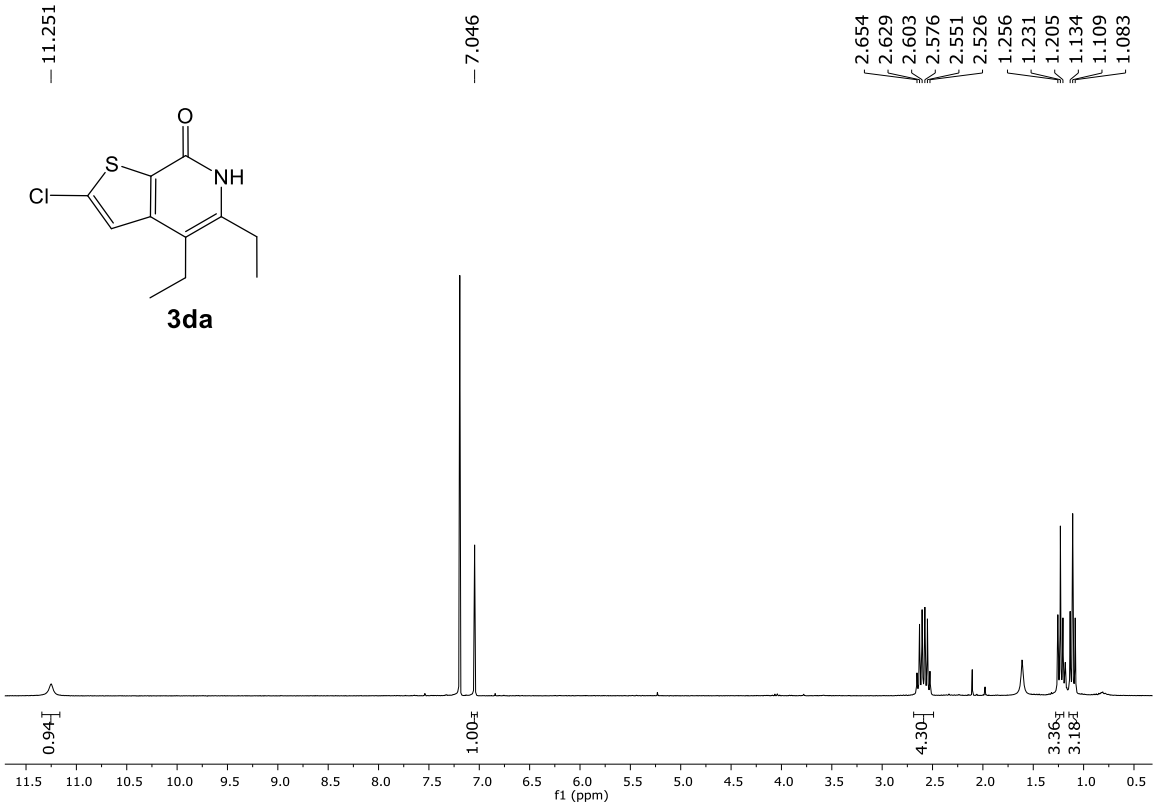

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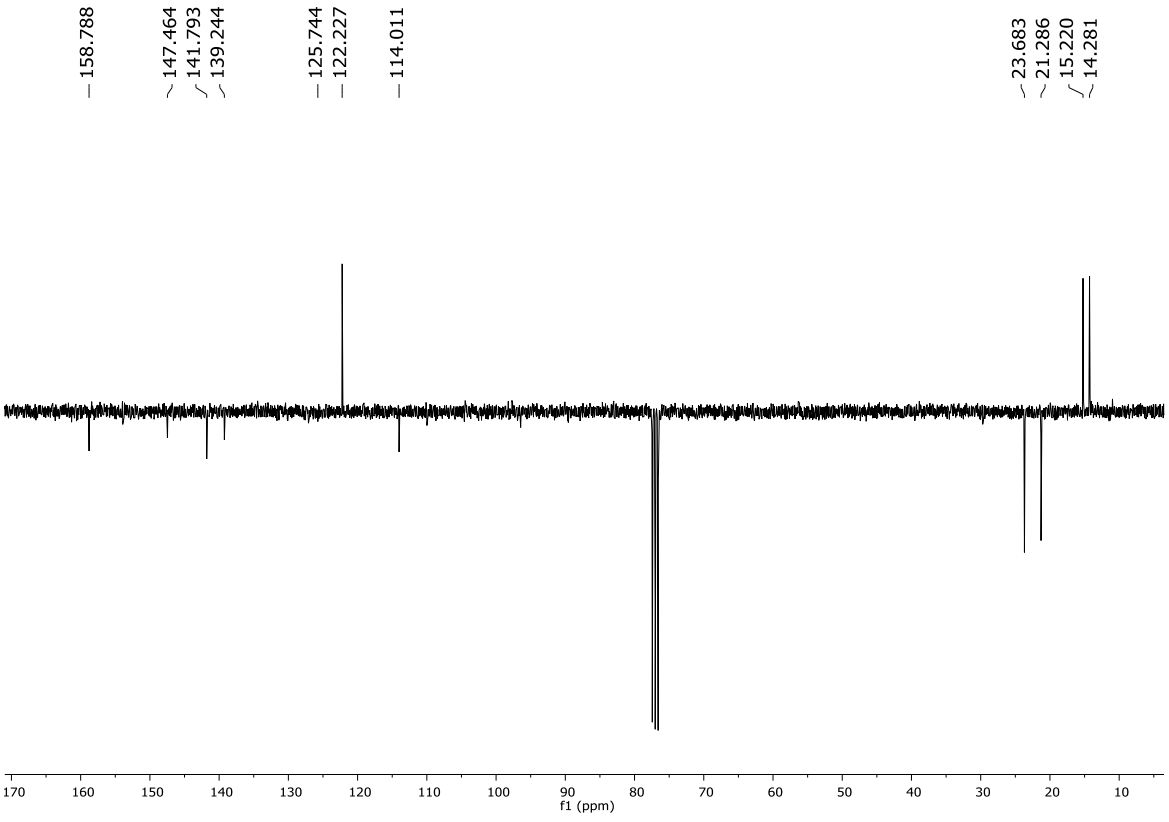

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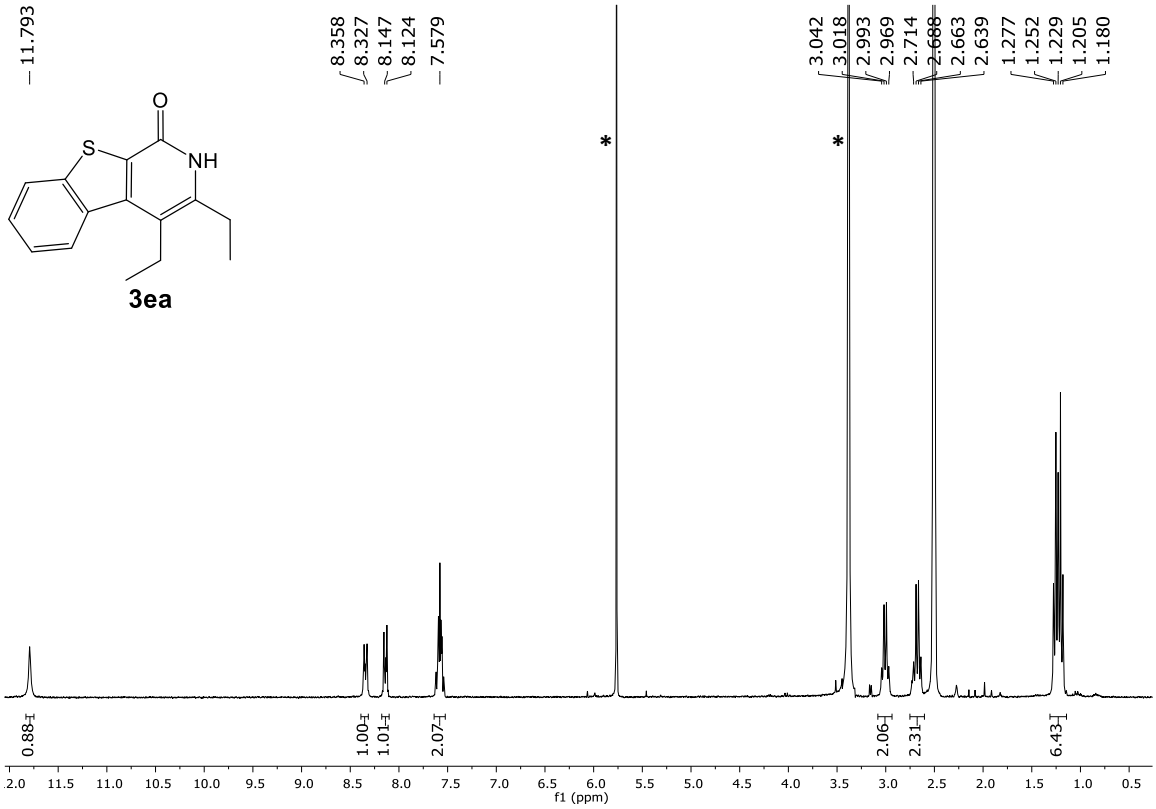
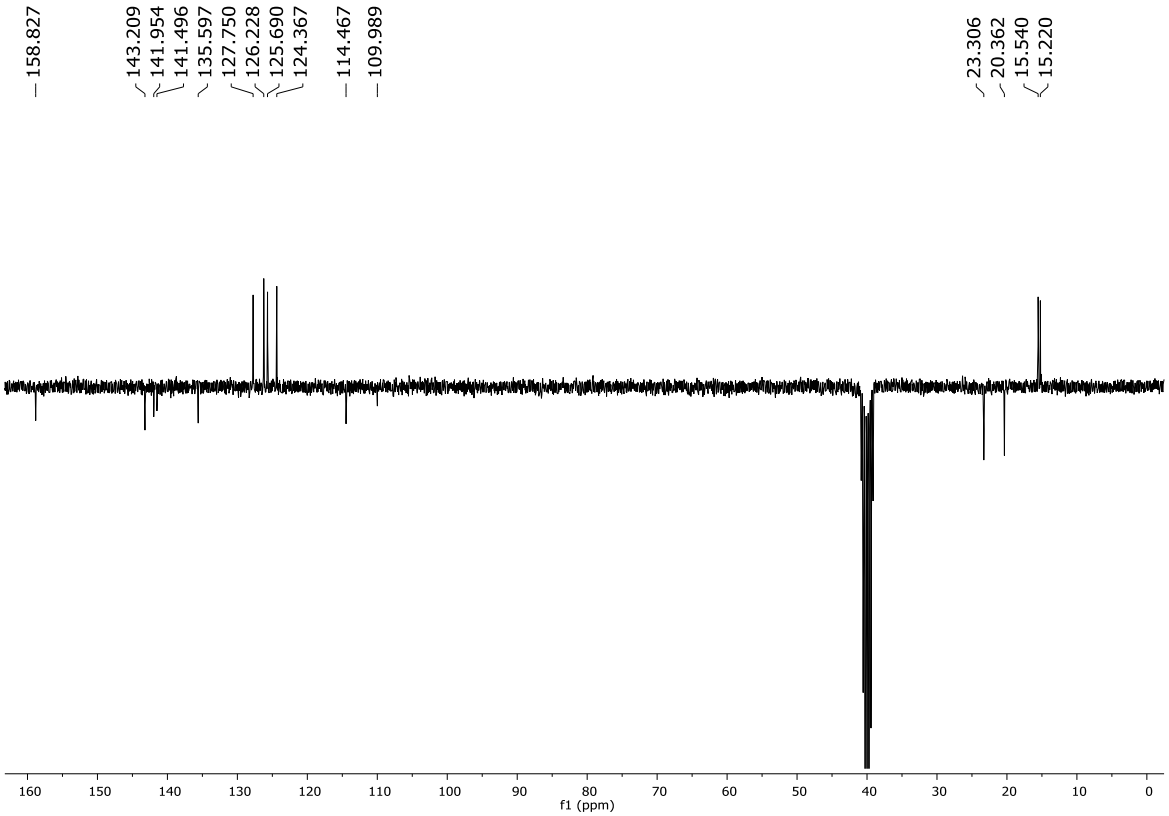
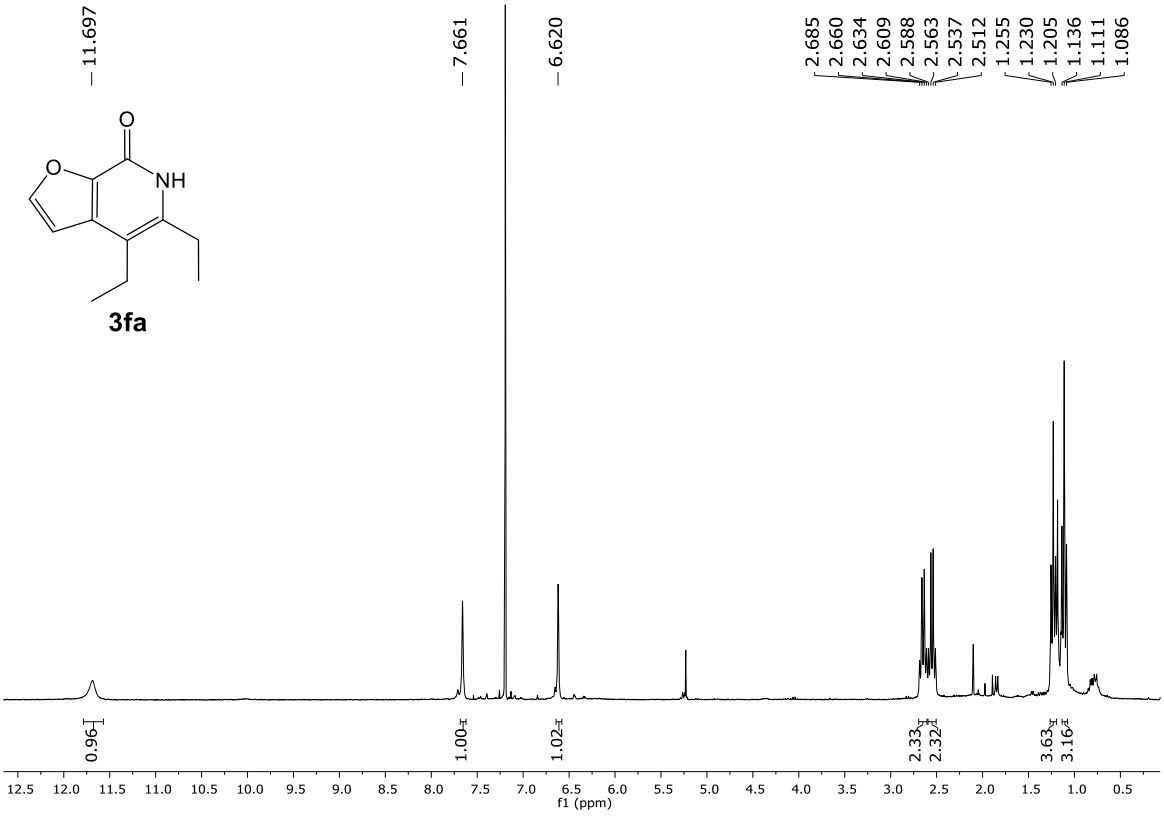


^{1}H-NMR spectrum of 3ea (* Solvent impurities)

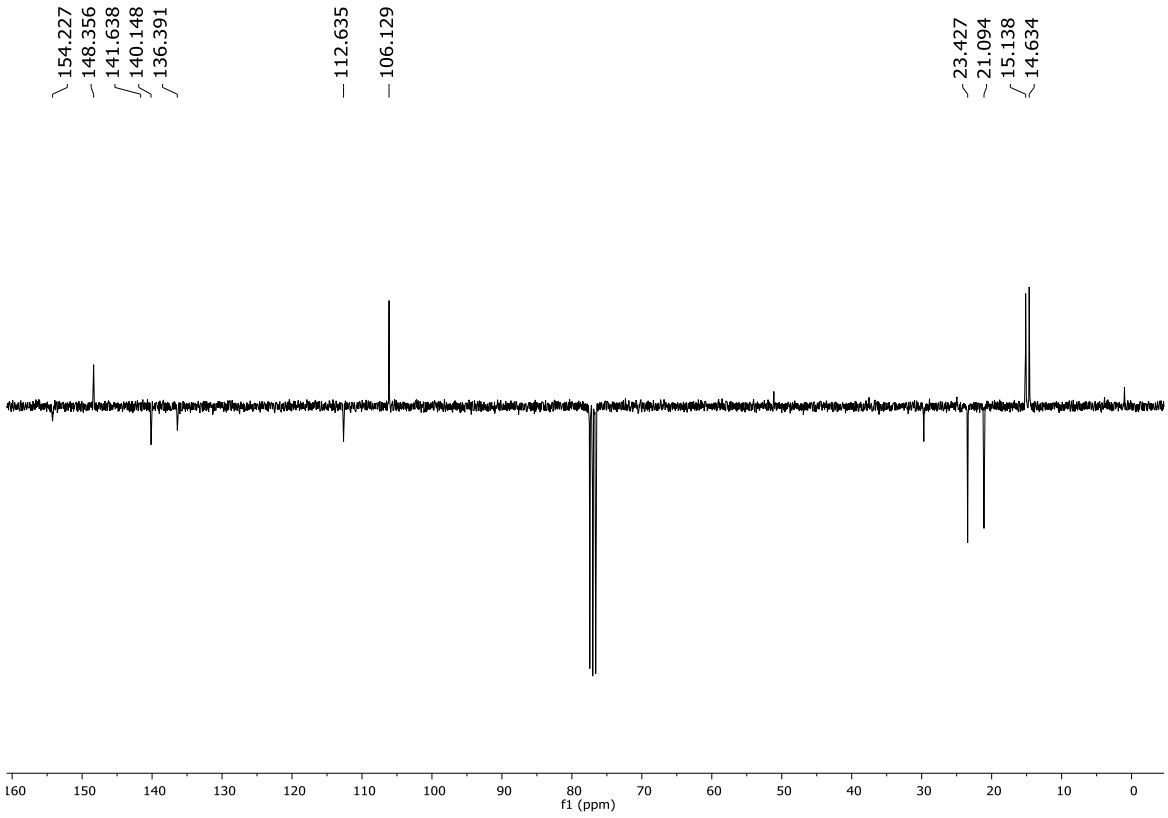


^{13}C(APT)-NMR spectrum of 3ea

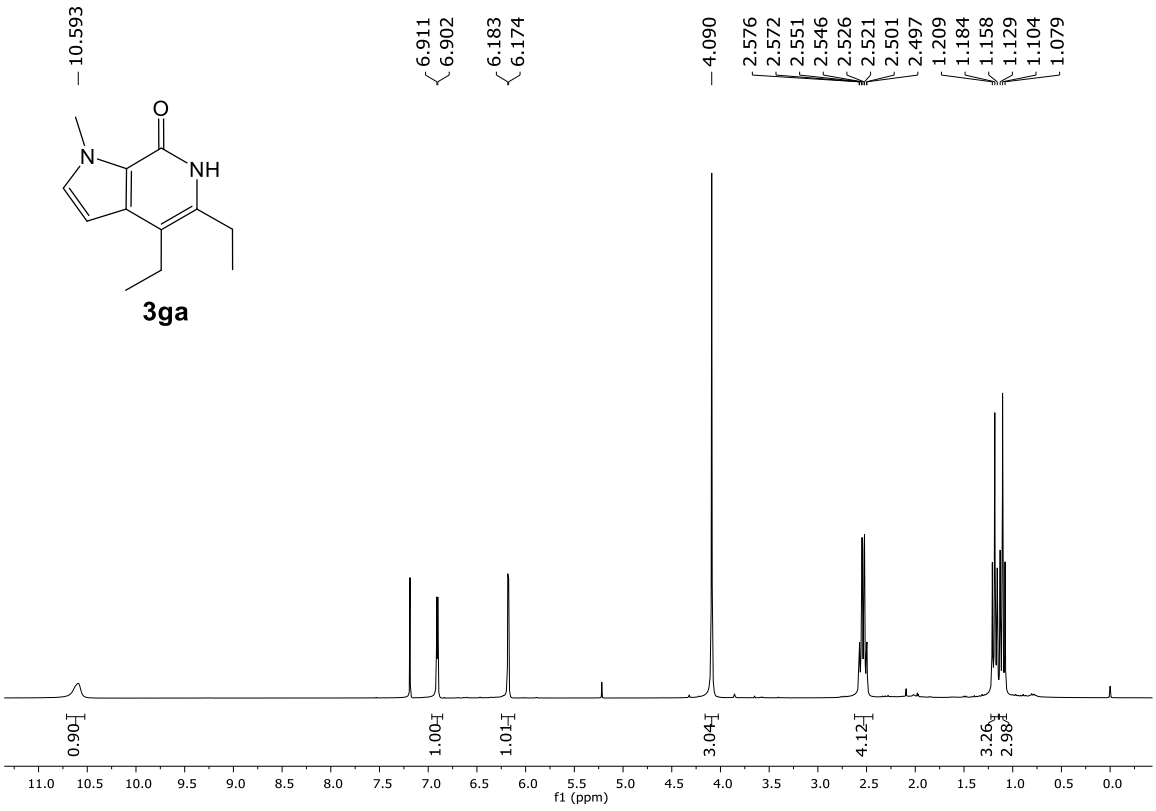


3fa

^{1}H-NMR spectrum of 3fa

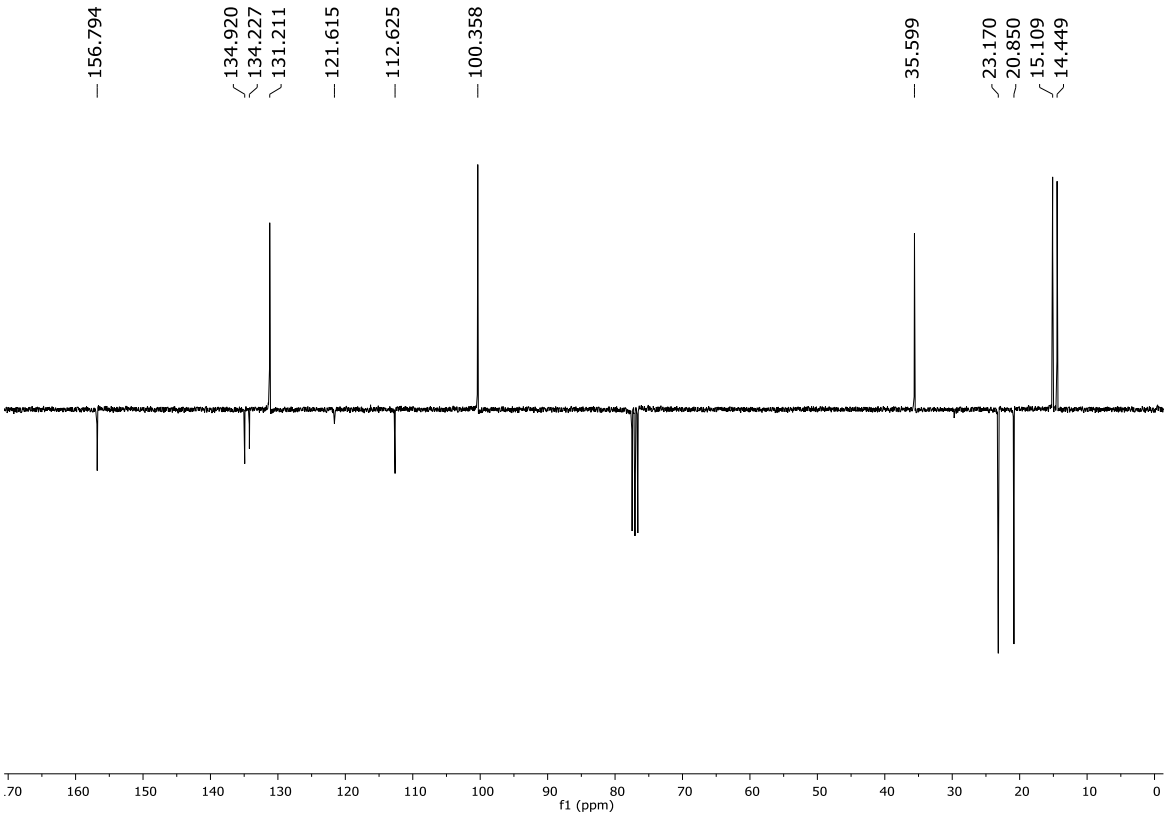


^{13}C(APT)-NMR spectrum of 3fa

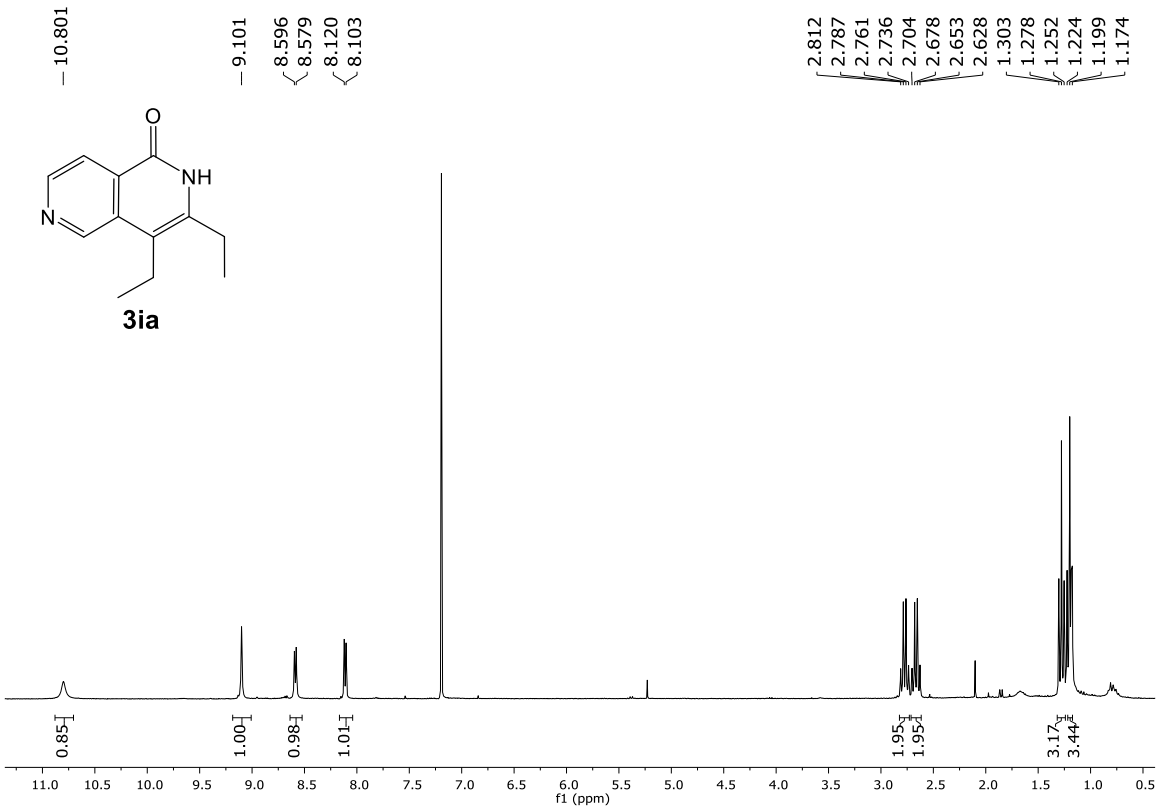


3ga

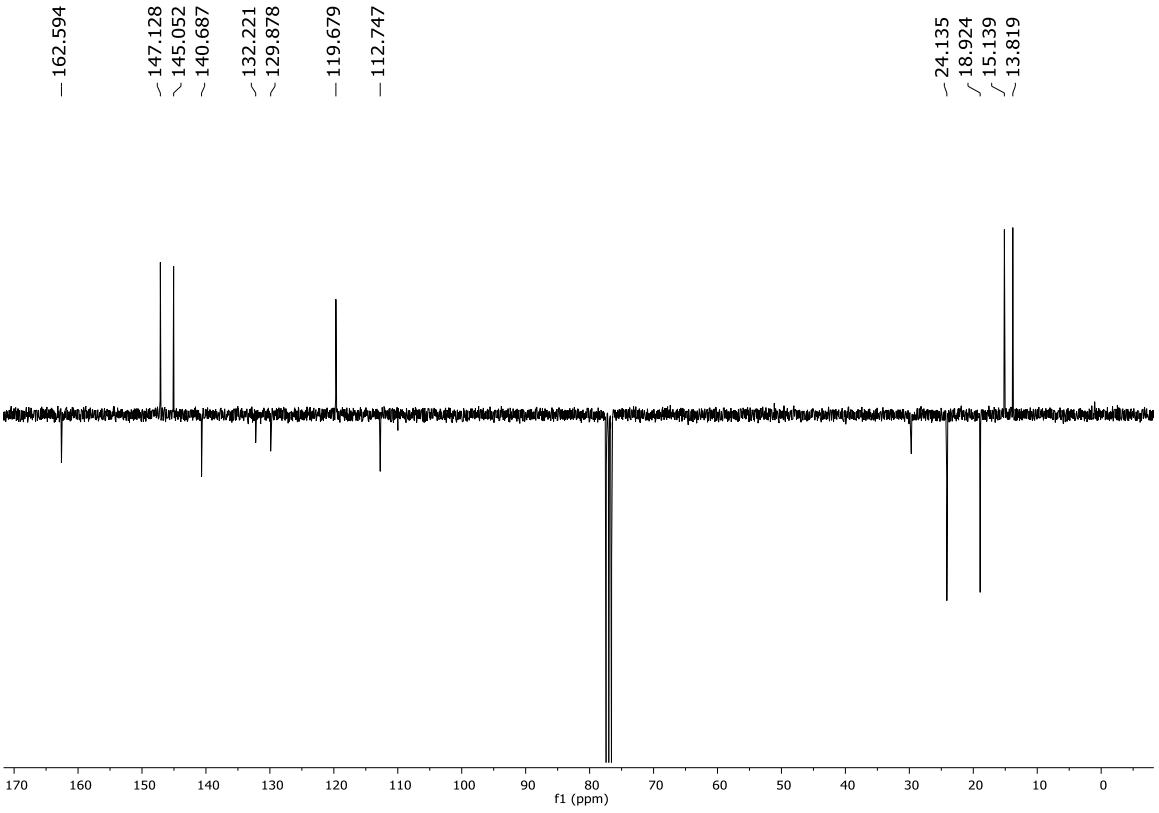
^{1}H-NMR spectrum of 3ga



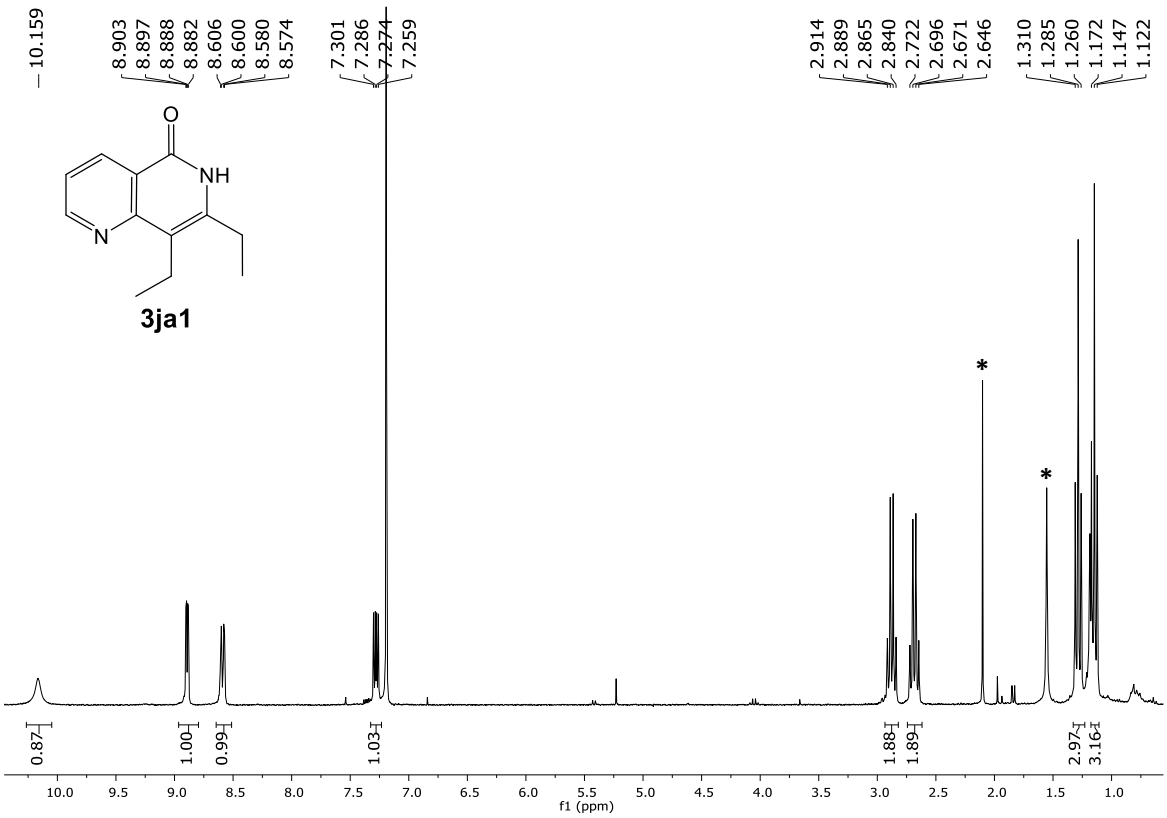
^{13}C(APT)-NMR spectrum of 3ga



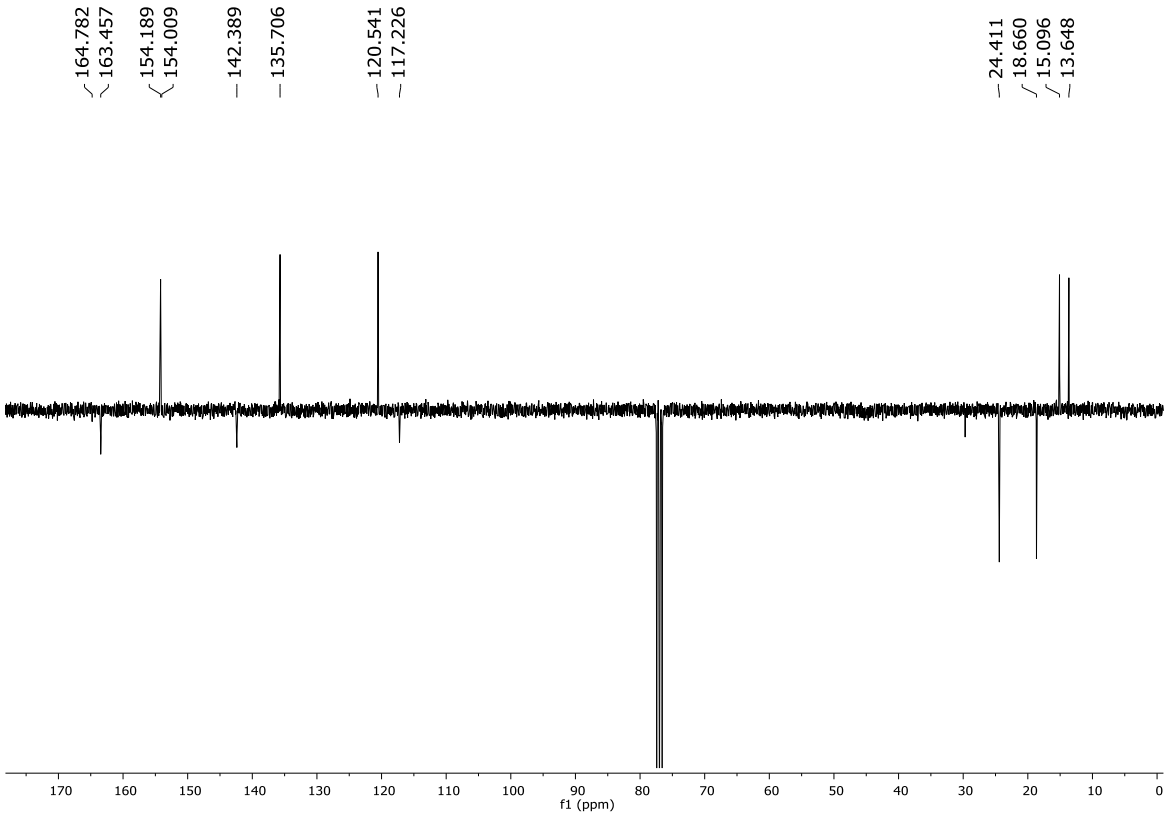
^{1}H-NMR spectrum of 3ia



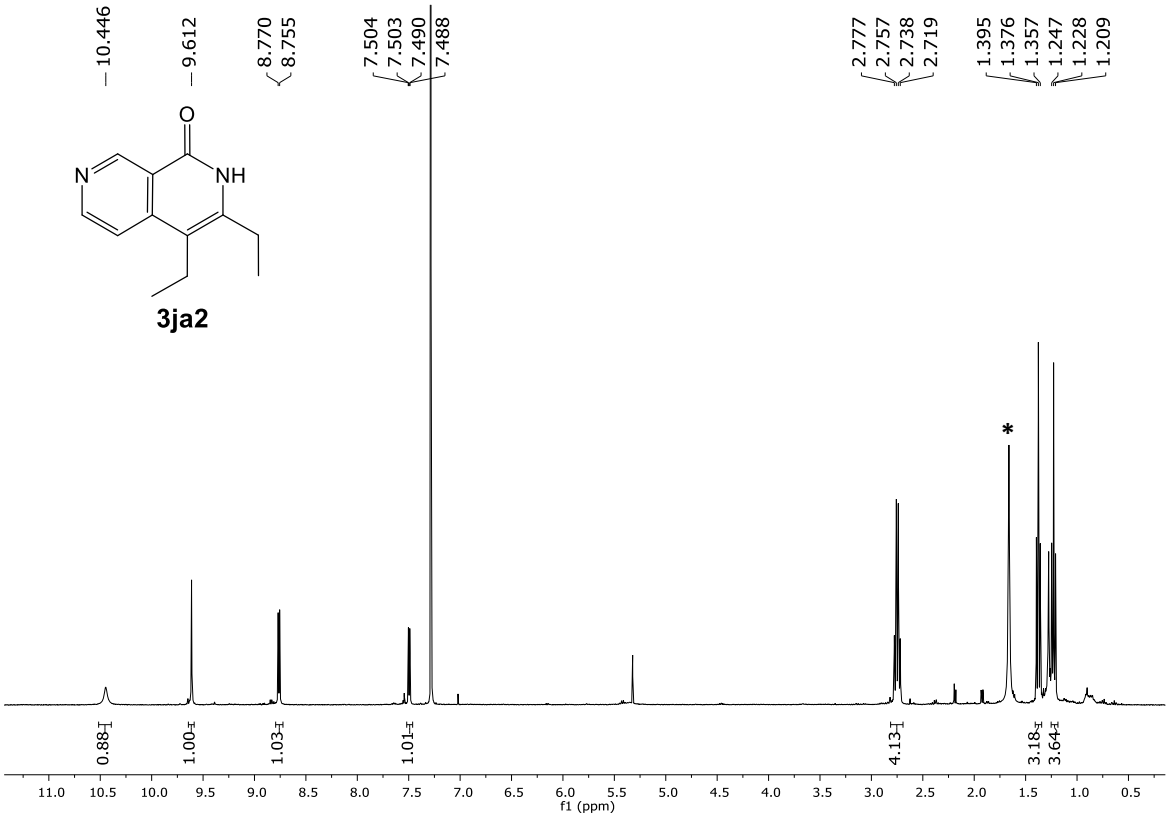
^{13}C(APT)-NMR spectrum of 3ia



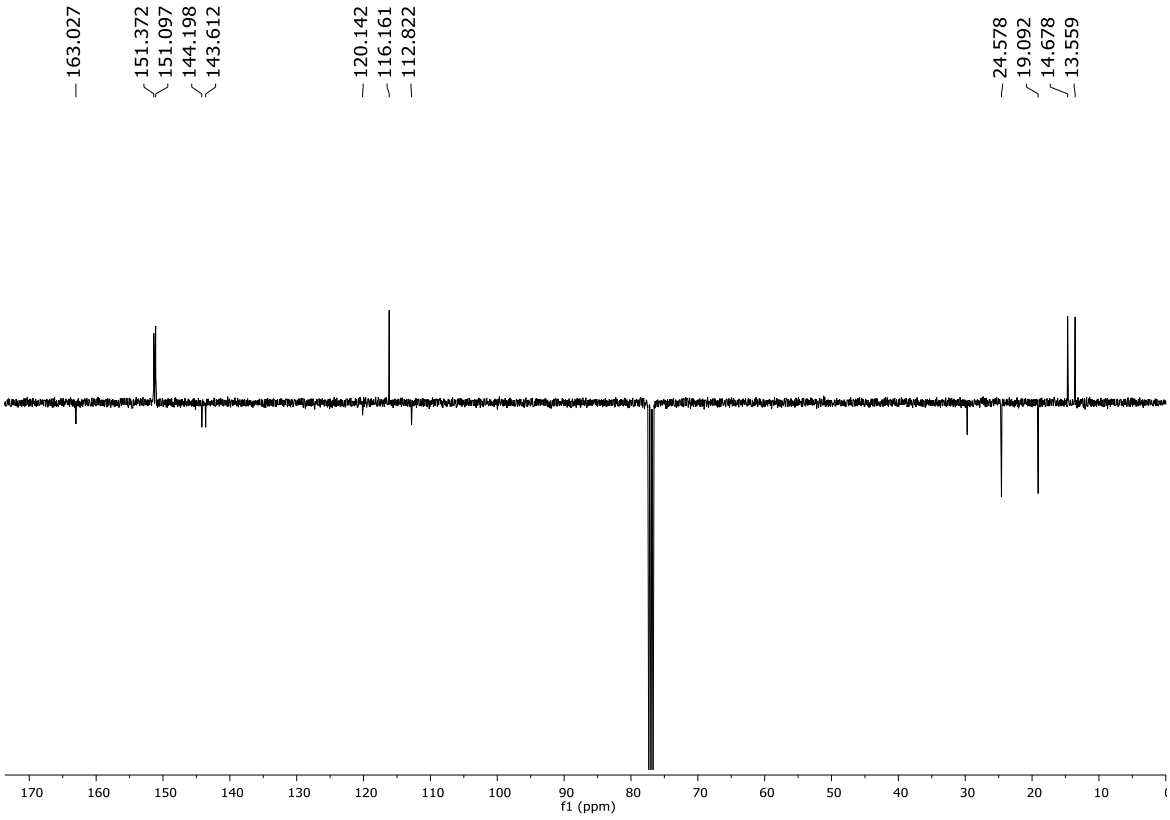
^{1}H-NMR spectrum of 3ja1 (* Solvent impurities)



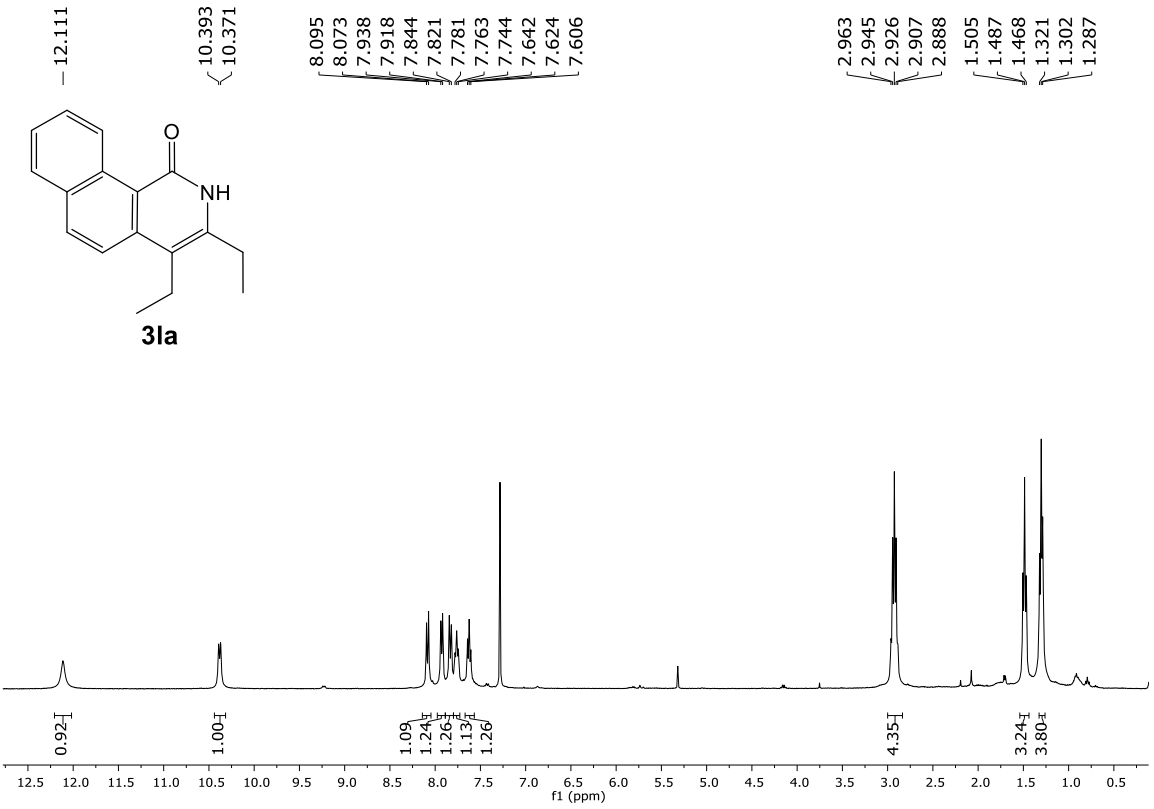
^{13}C(APT)-NMR spectrum of 3ja1



^{1}H-NMR spectrum of 3ja2 (*Solvent impurities)

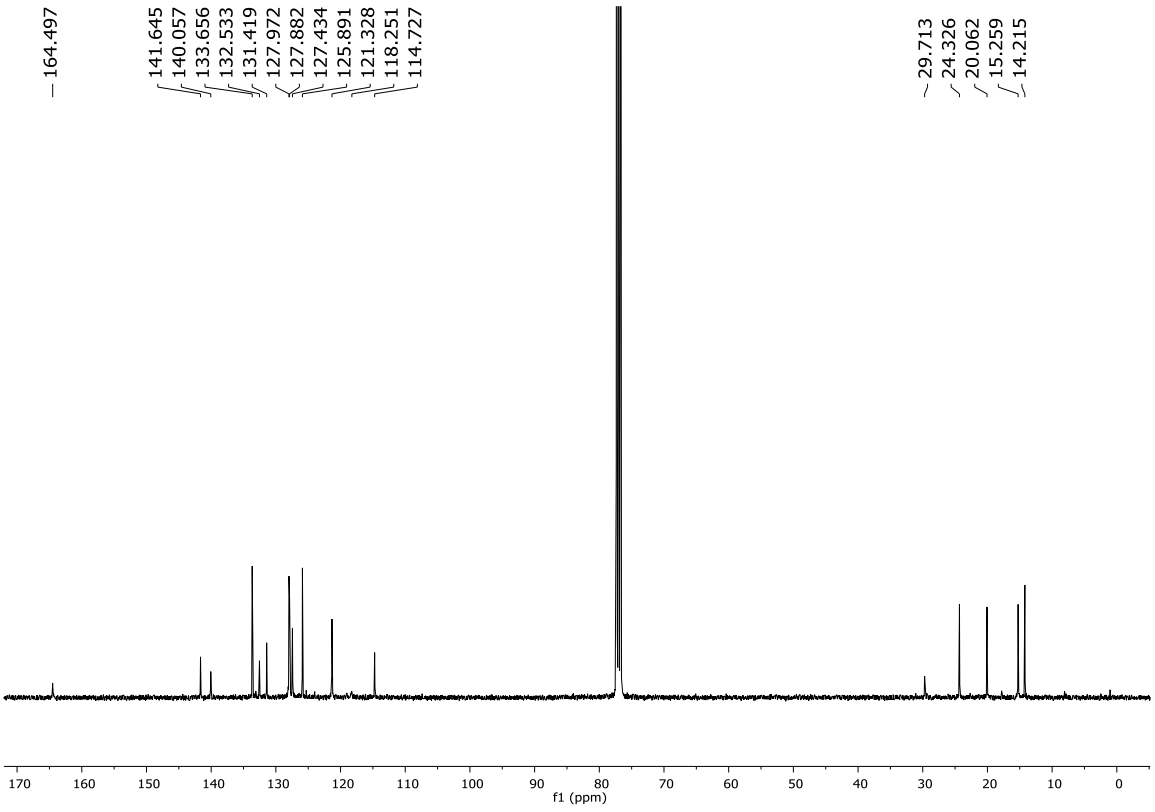


^{13}C(APT)-NMR spectrum of 3ja2

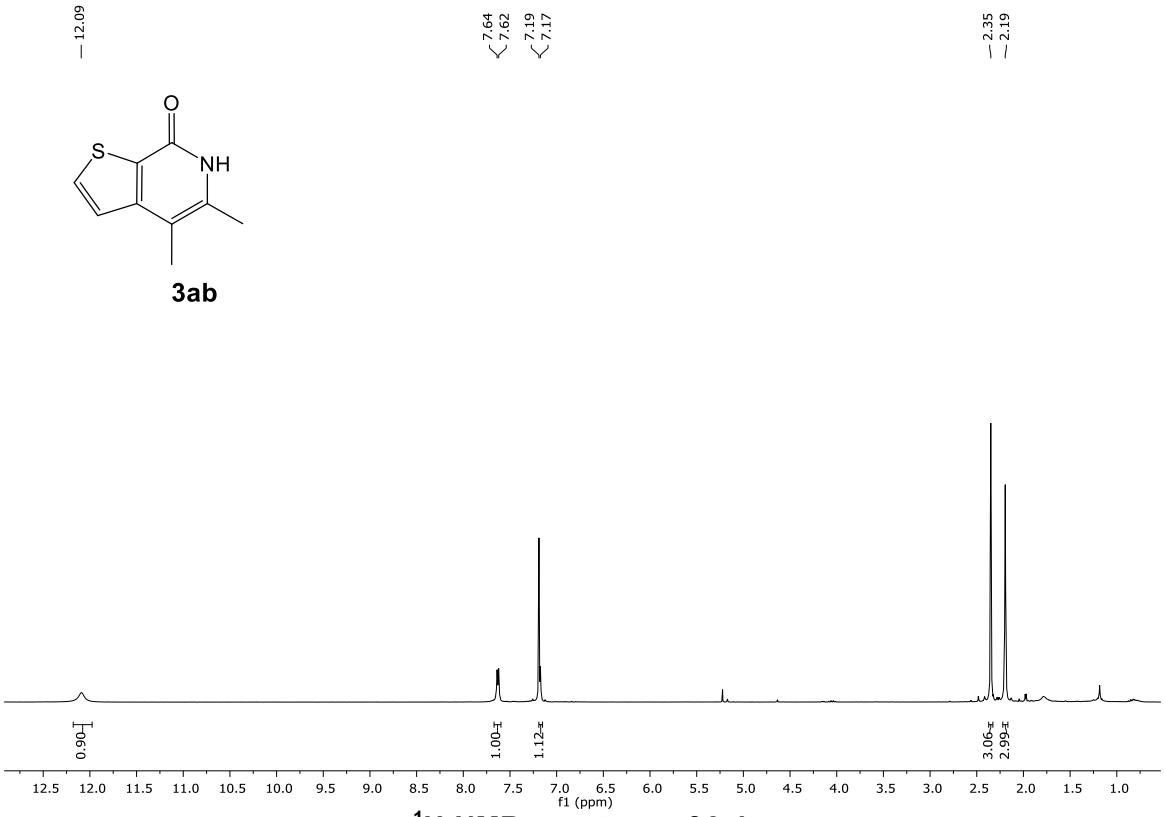


3la

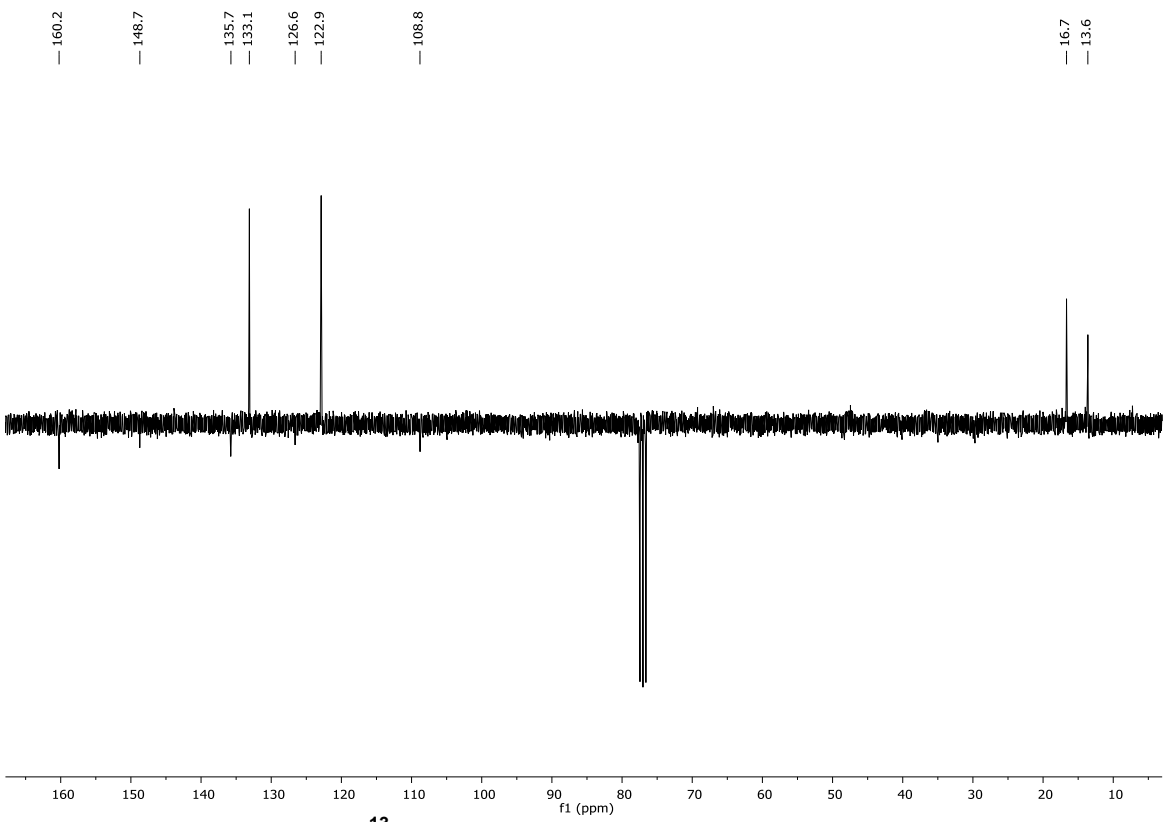
^{1}H-NMR spectrum of 3la



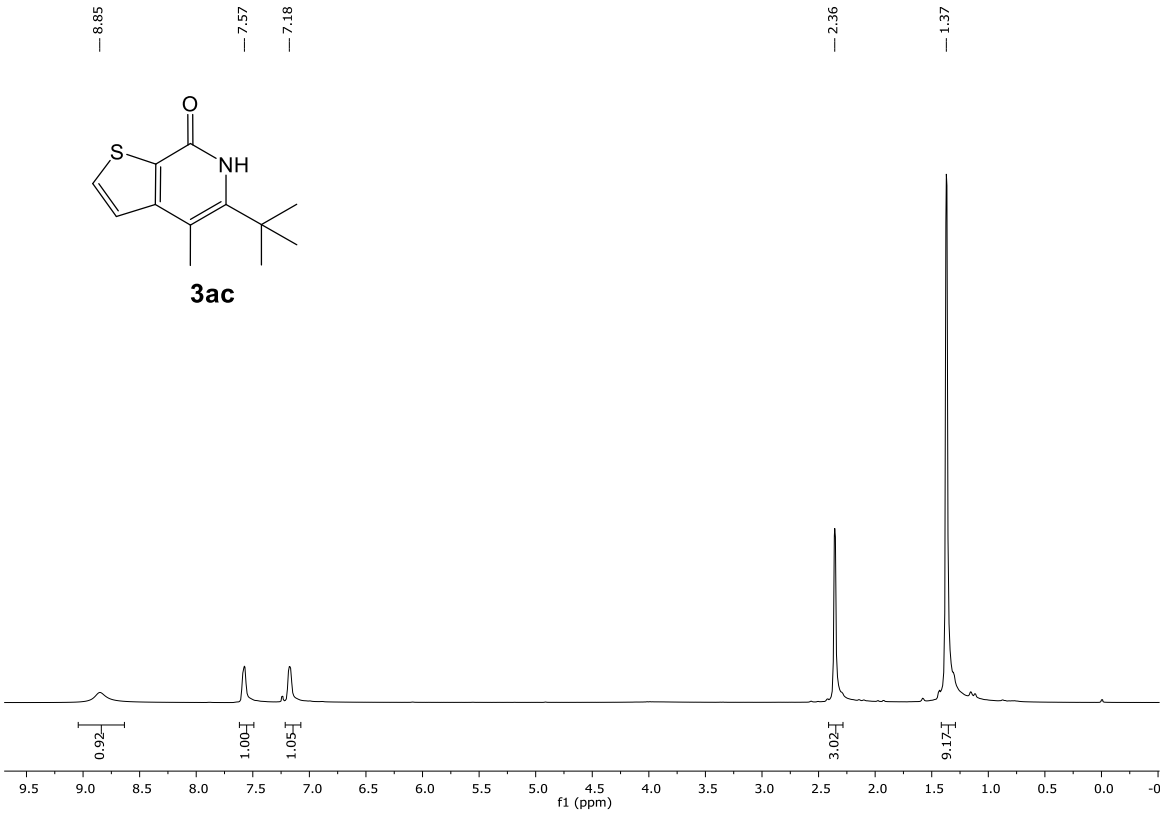
^{13}C{^{1}H}-NMR spectrum of 3la



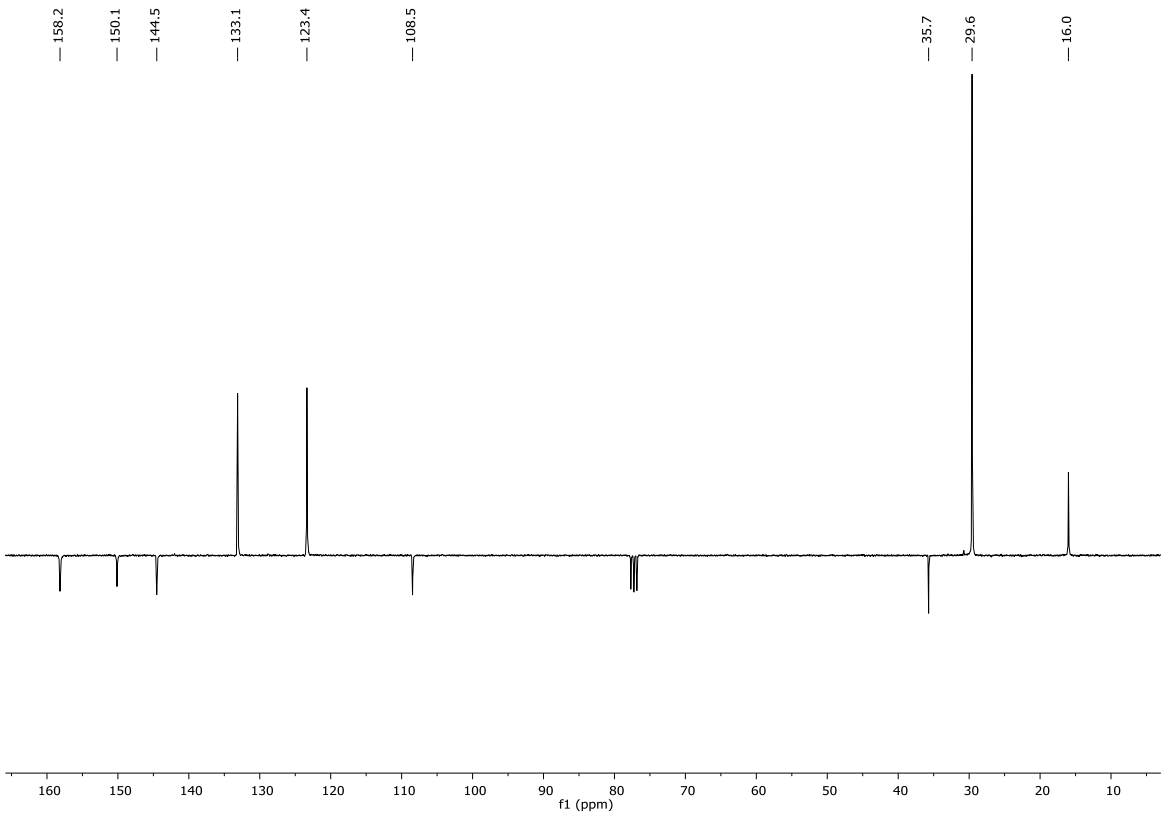
^{1}H-NMR spectrum of 3ab



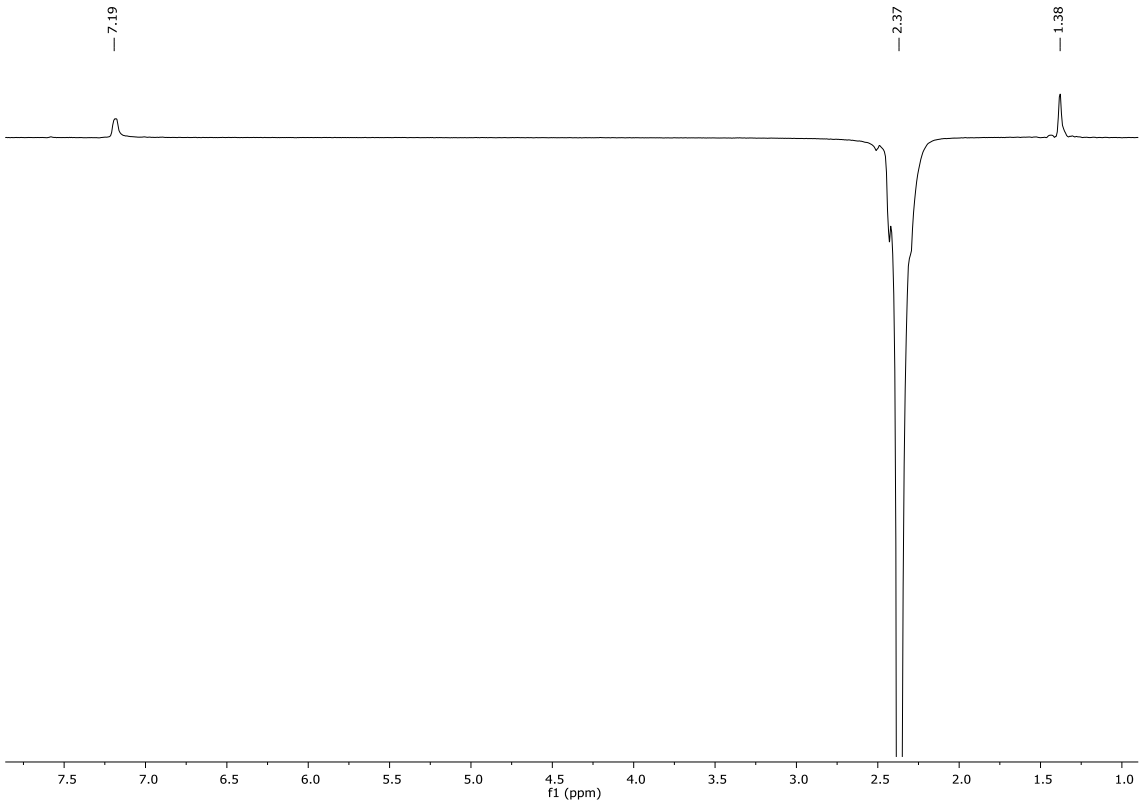
^{13}C(APT)-NMR spectrum of 3ab



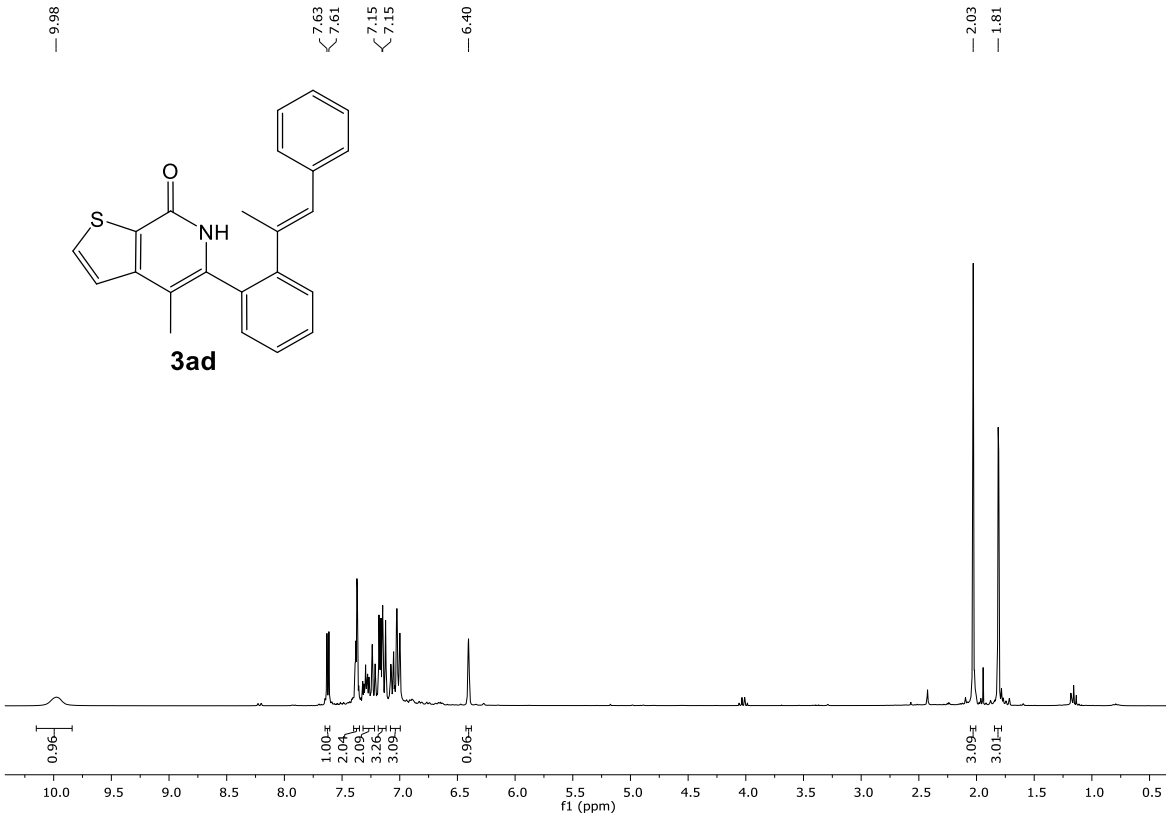
^{1}H-NMR spectrum of 3ac



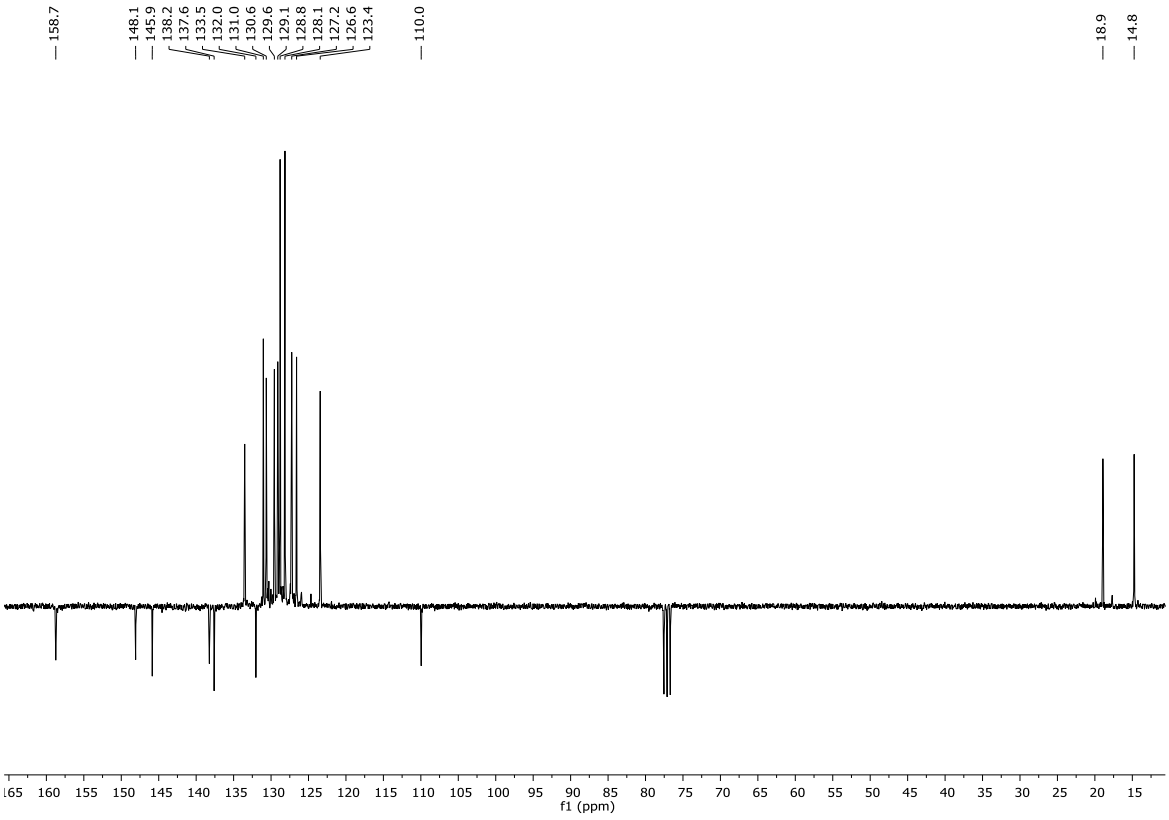
^{13}C(APT)-NMR spectrum of 3ac



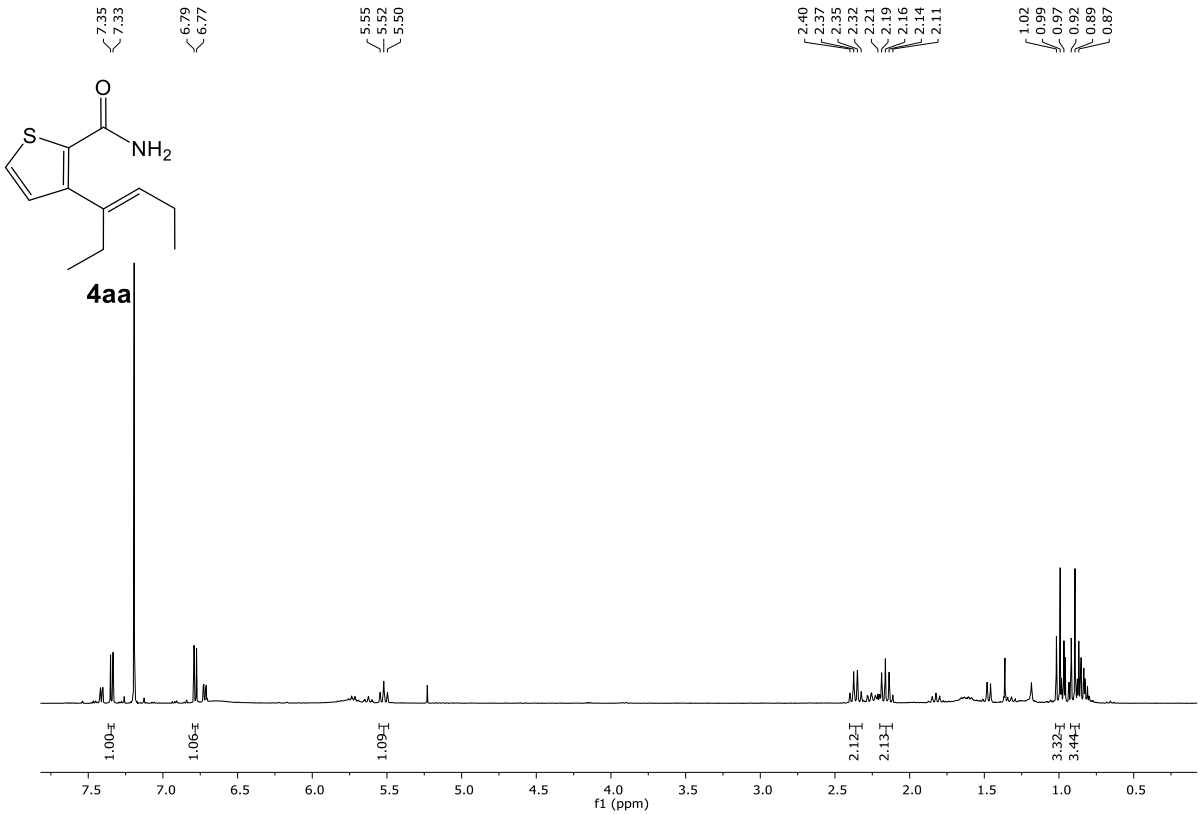
1D-NOESY-^{1}H-NMR spectrum of 3ac



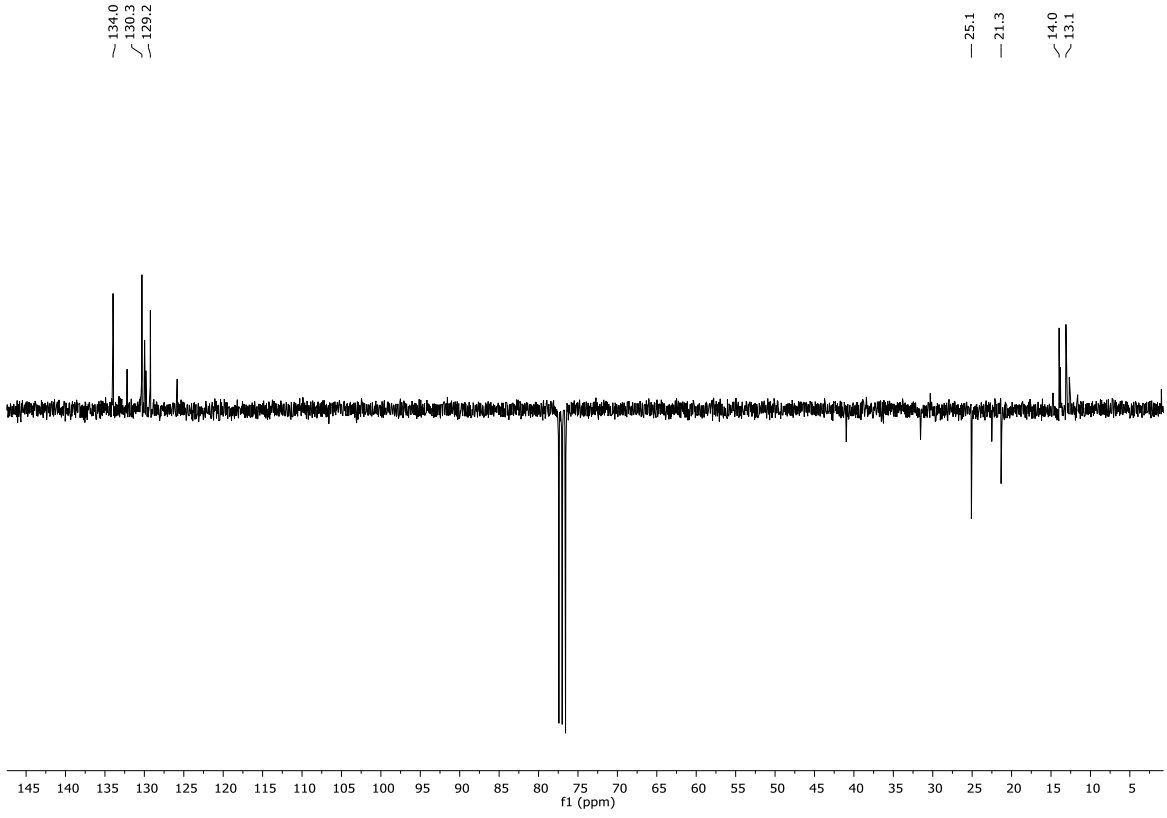
^{1}H-NMR spectrum of 3ad



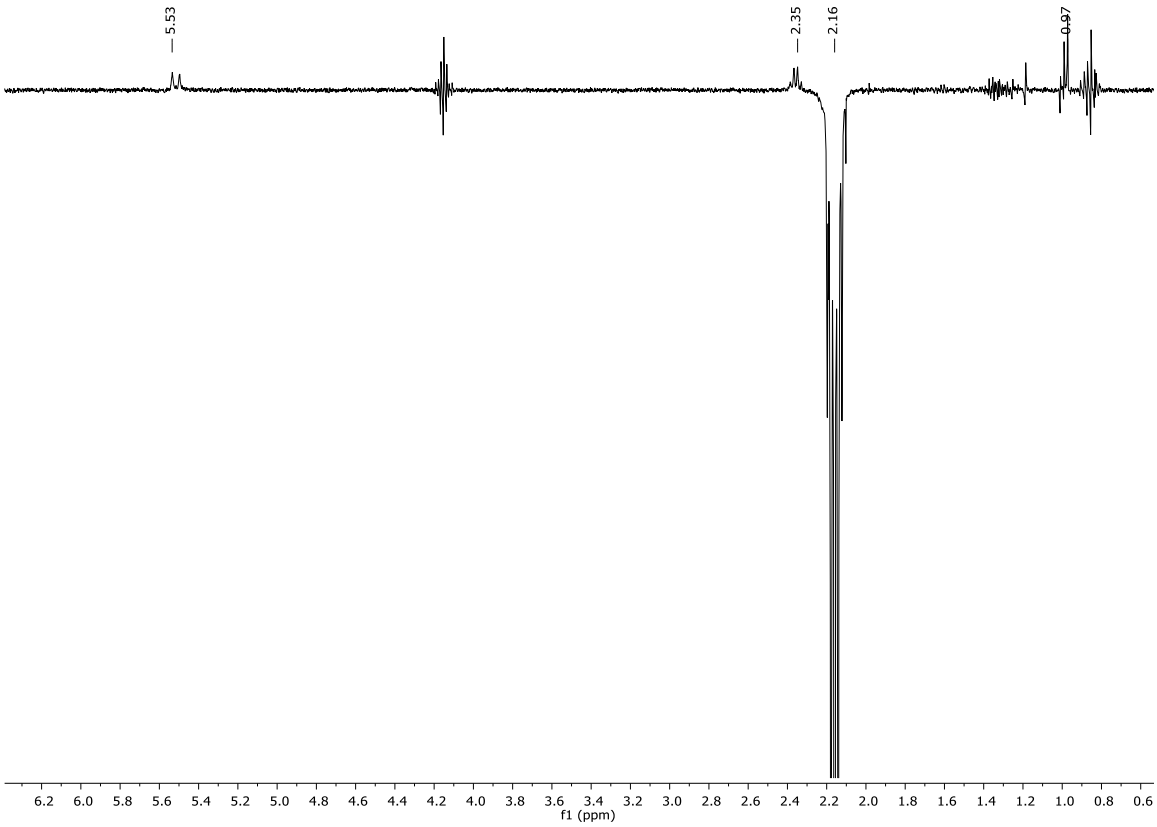
^{13}C(APT)-NMR spectrum of 3ad



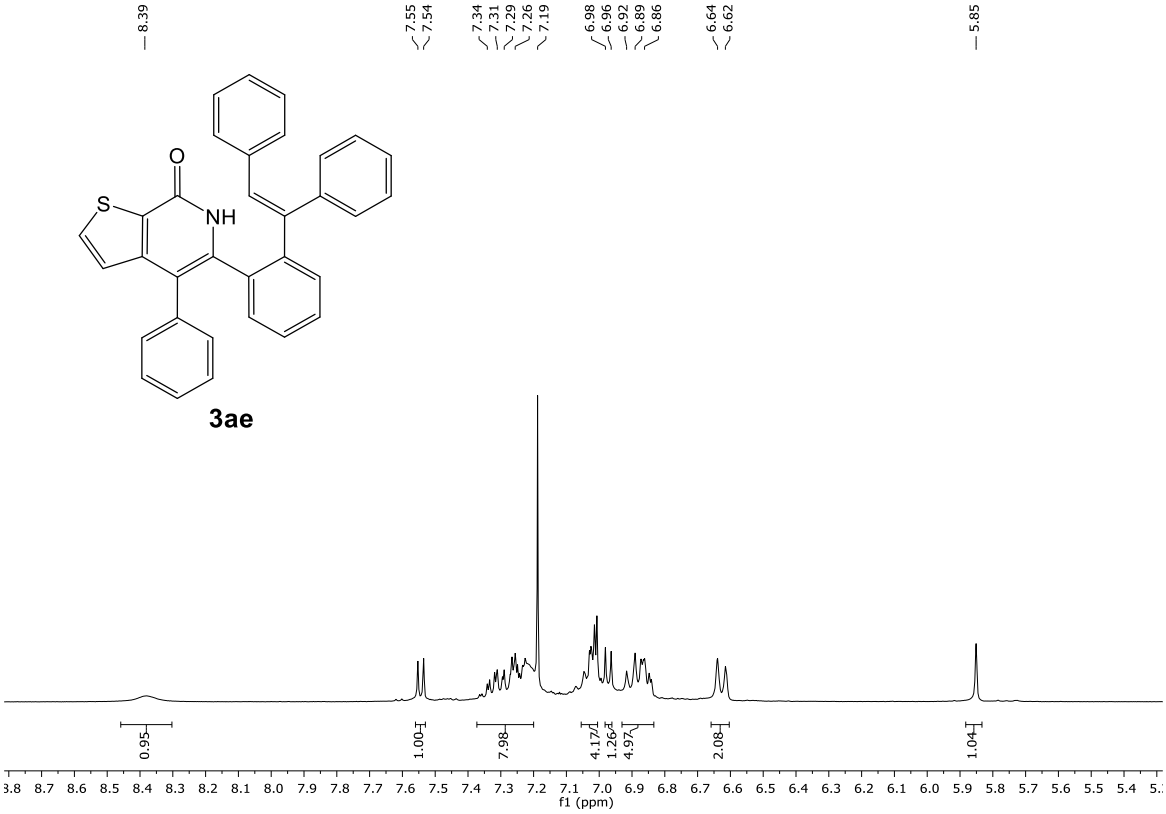
^{1}H-NMR spectrum of 4aa



^{13}C(APT)-NMR spectrum of 4aa

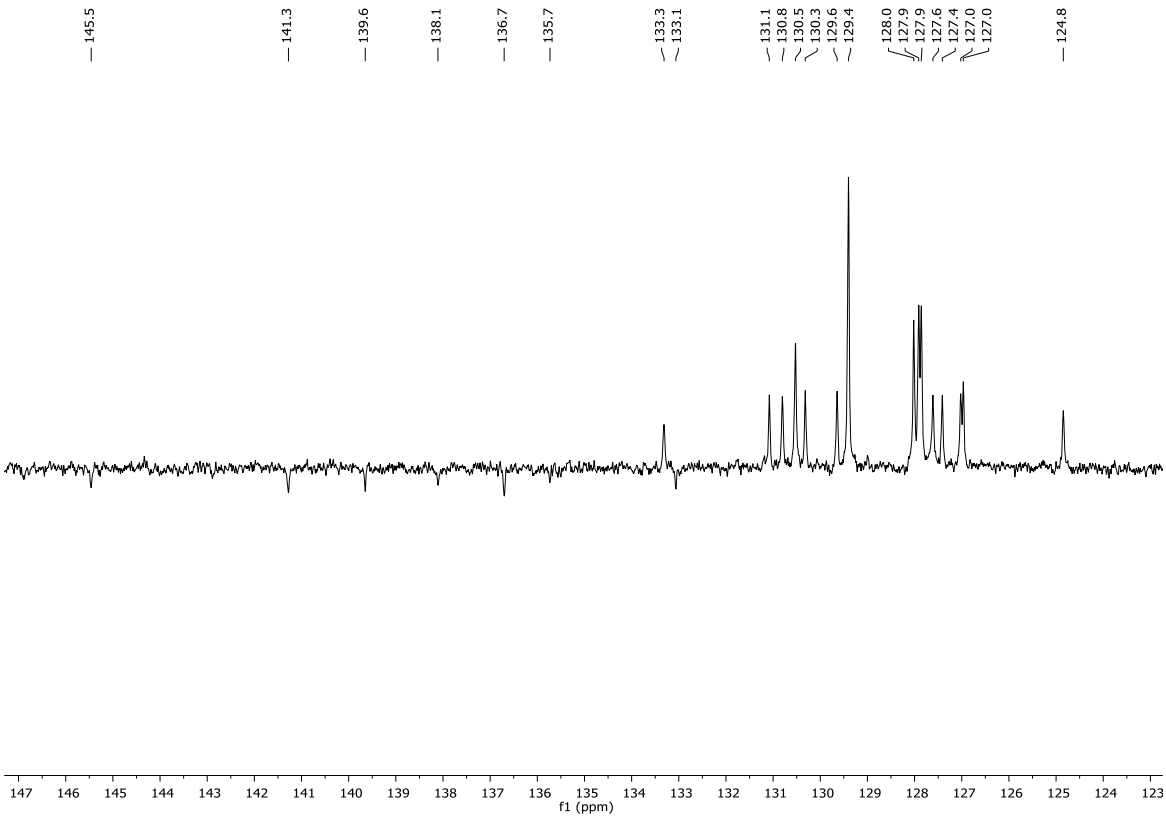


1D-NOESY-^{1}H-NMR spectrum of 4aa

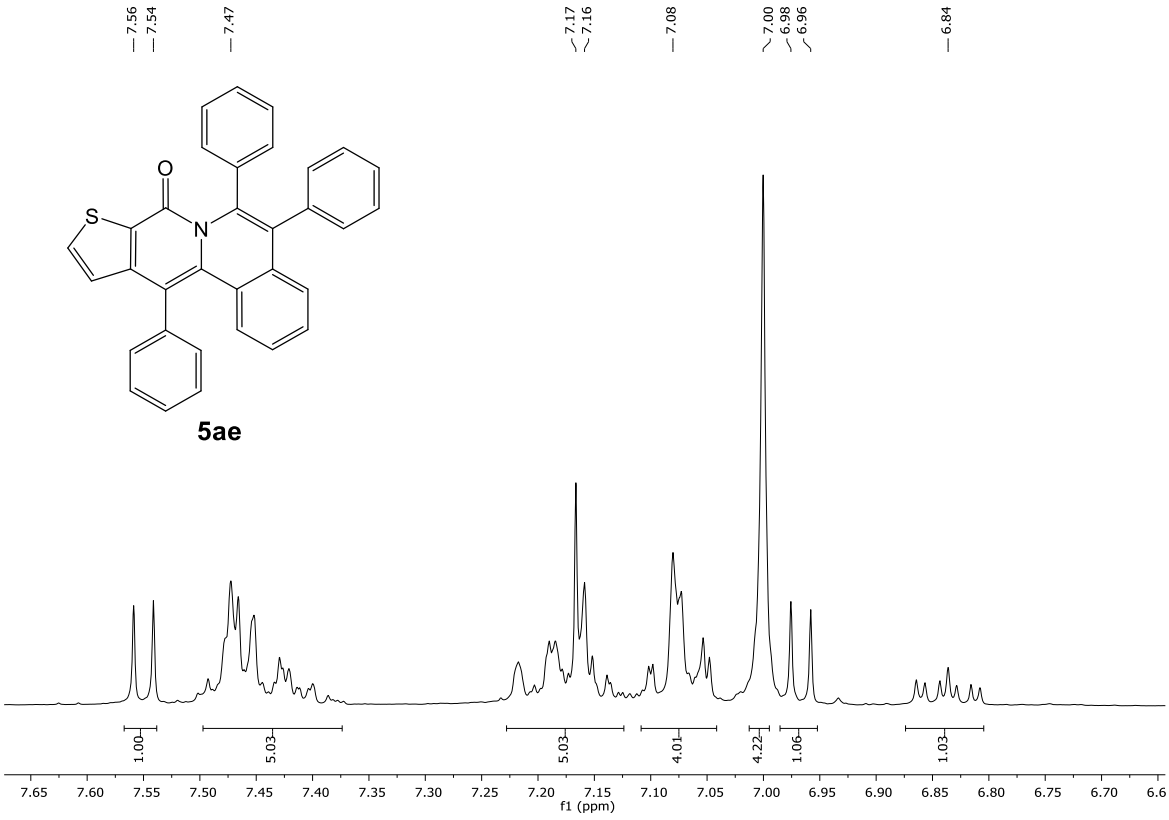


3ae

^{1}H-NMR spectrum of 3ae

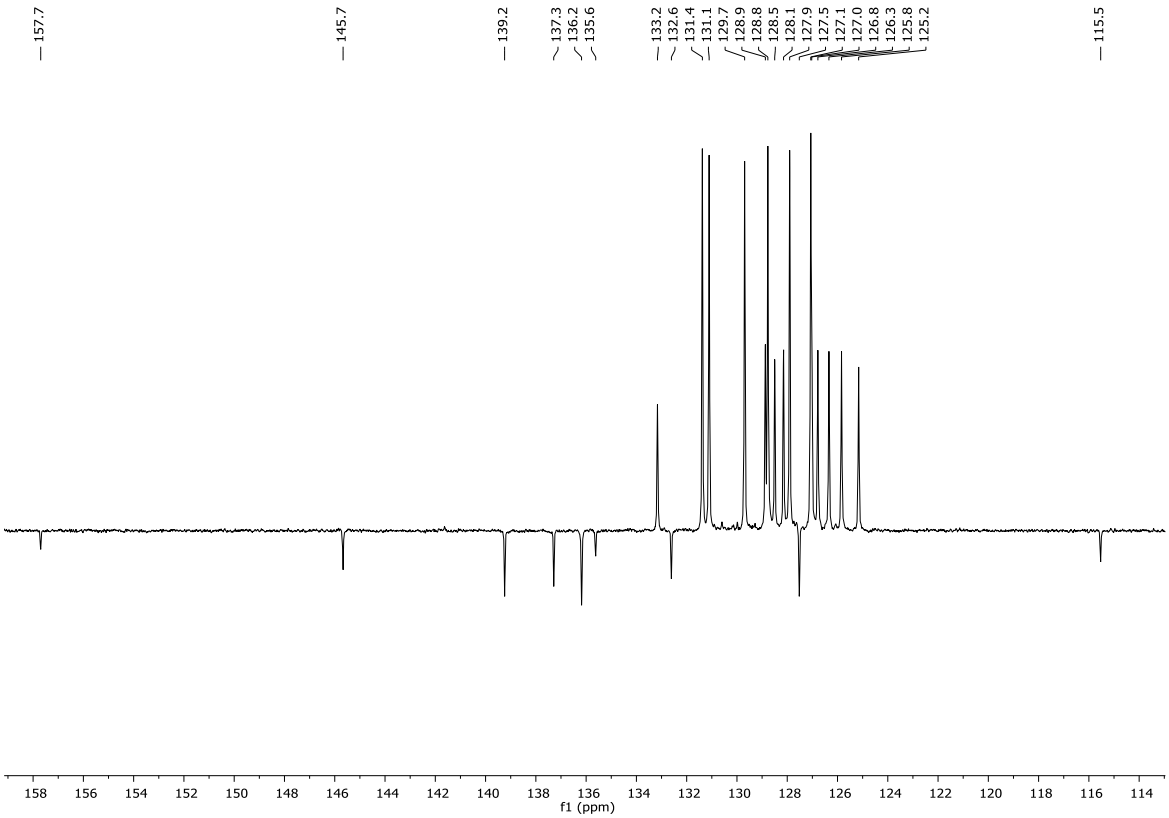


^{13}C(APT)-NMR spectrum of 3ae

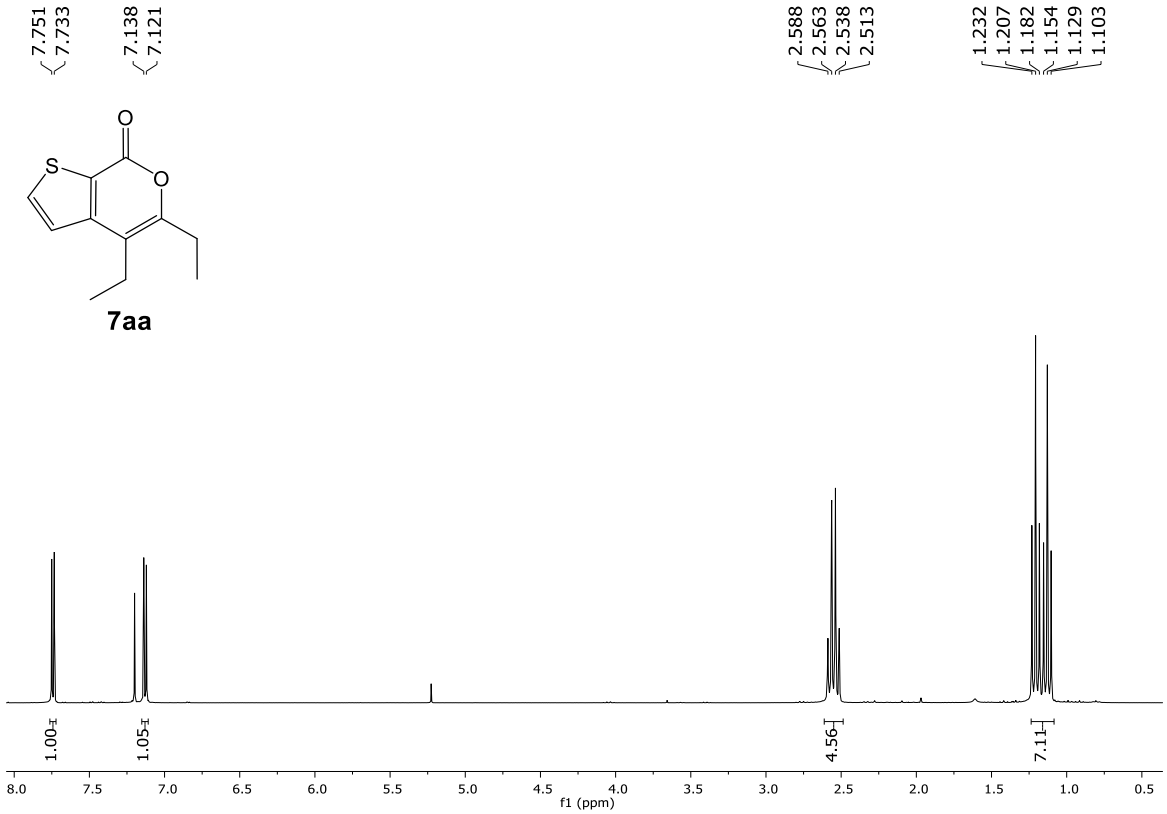


5ae

^{1}H-NMR spectrum of 5ae

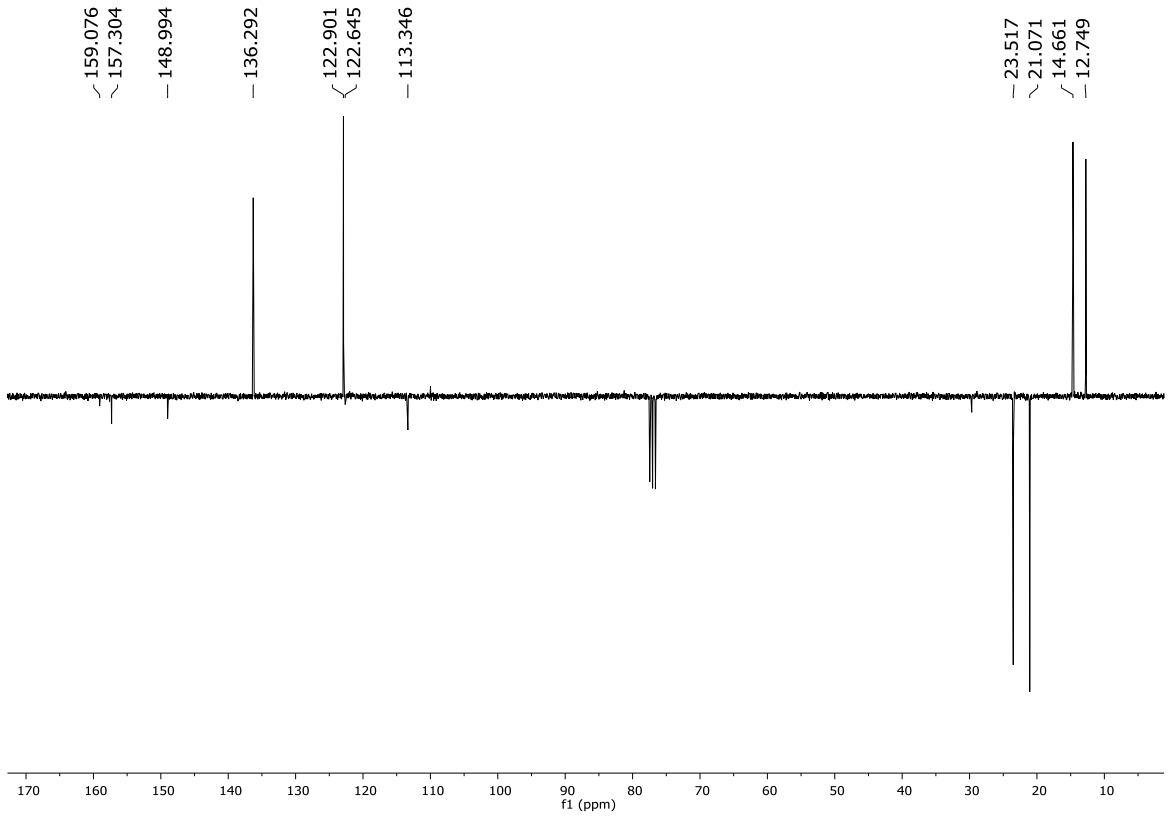


^{13}C(APT)-NMR spectrum of 5ae

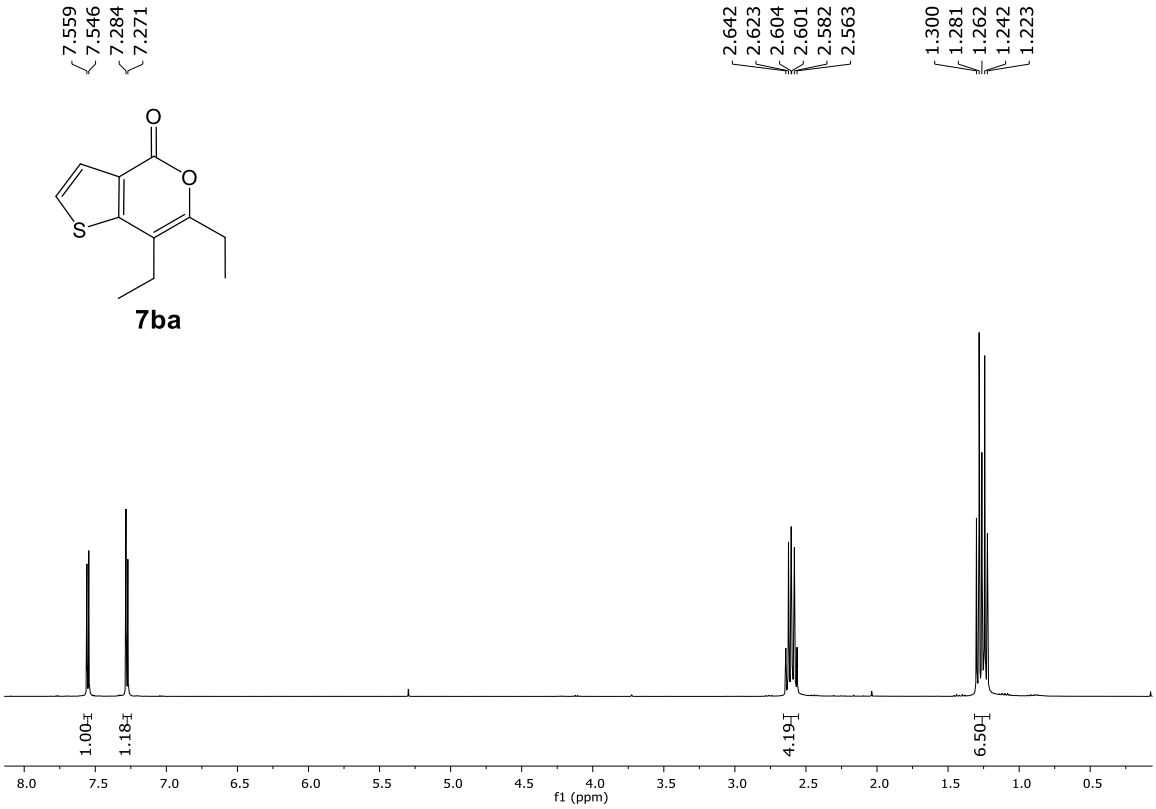


7aa

^{1}H-NMR spectrum of 7aa

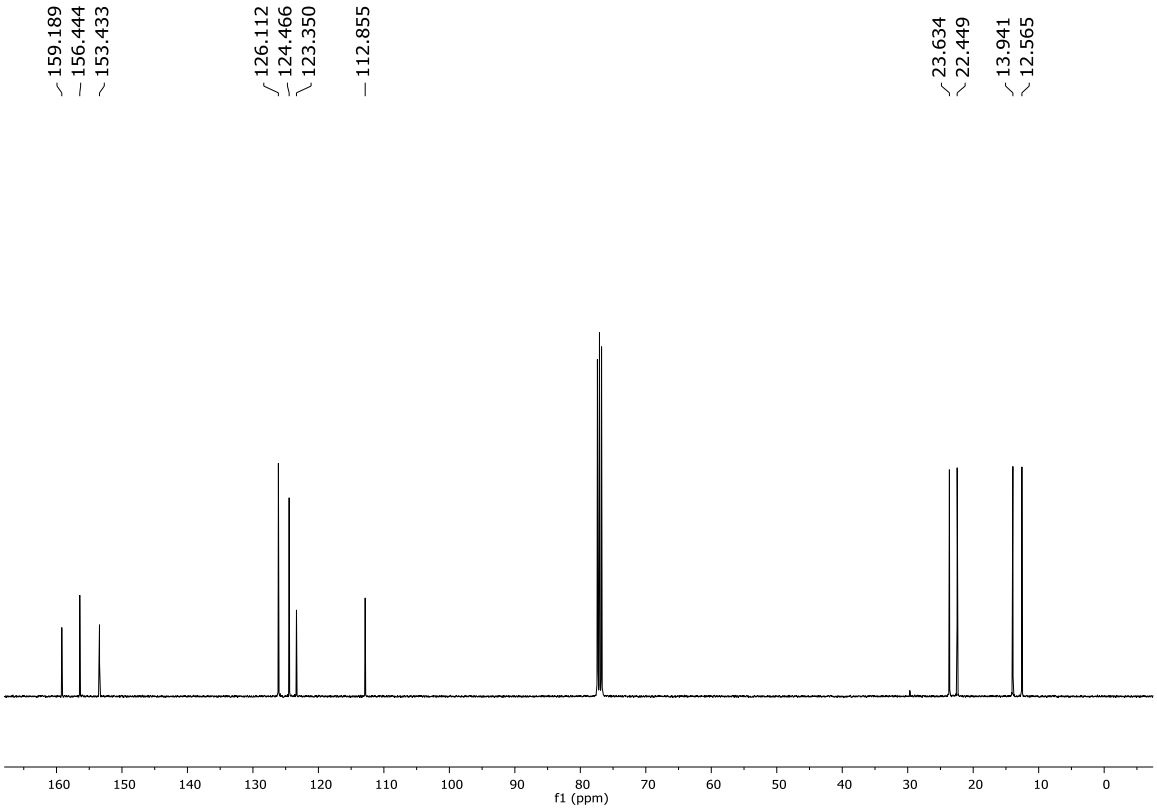


^{13}C(APT)-NMR spectrum of 7aa

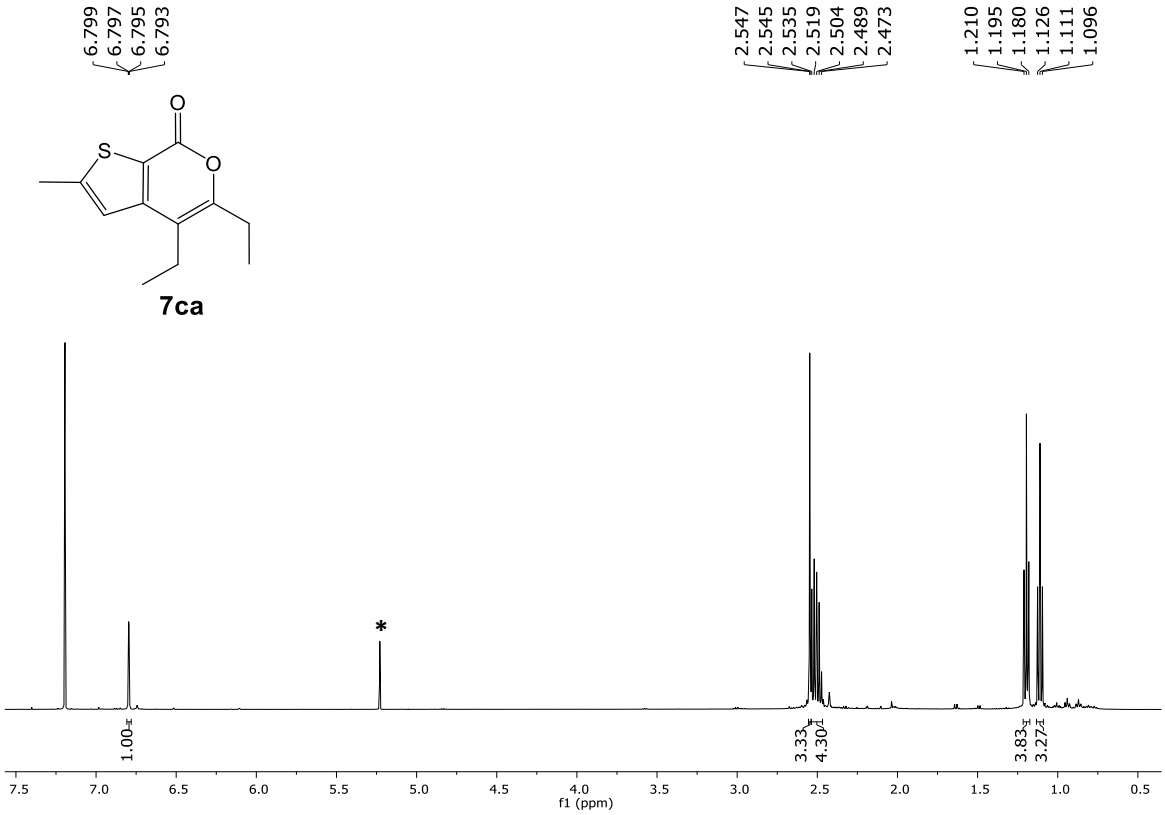


7ba

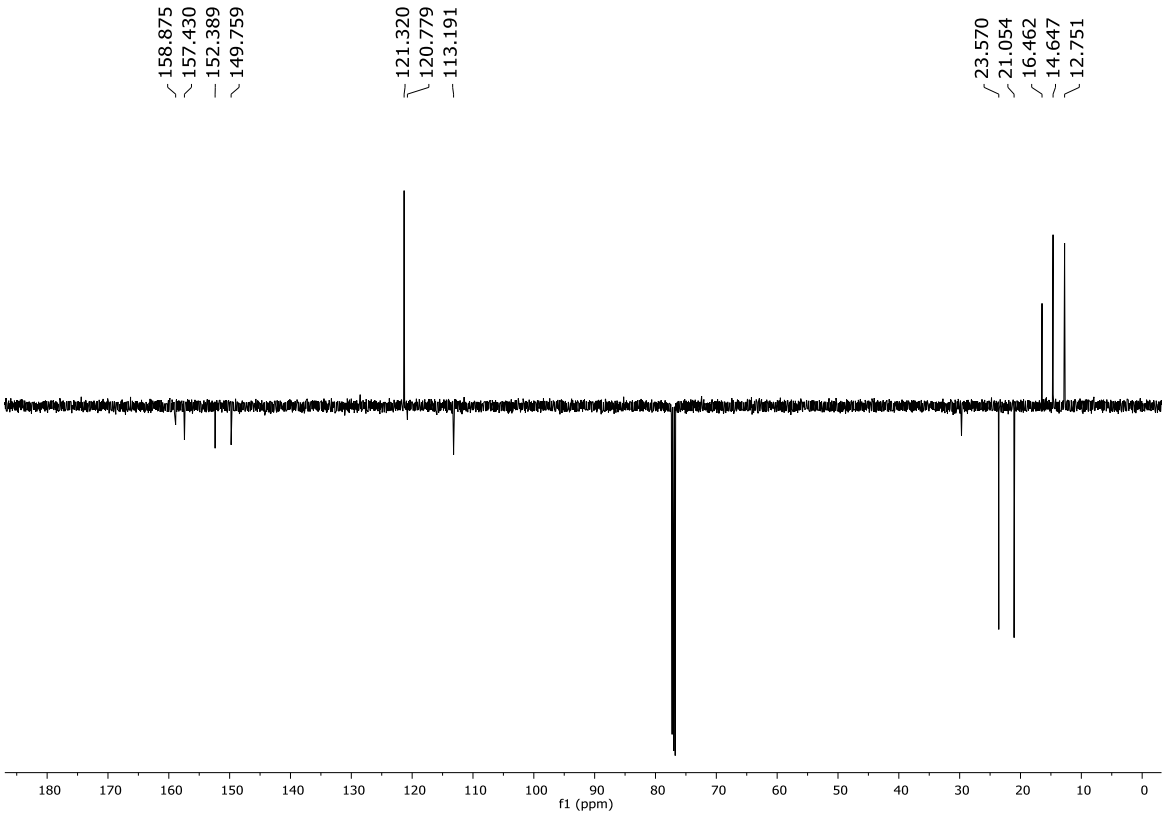
^{1}H-NMR spectrum of 7ba



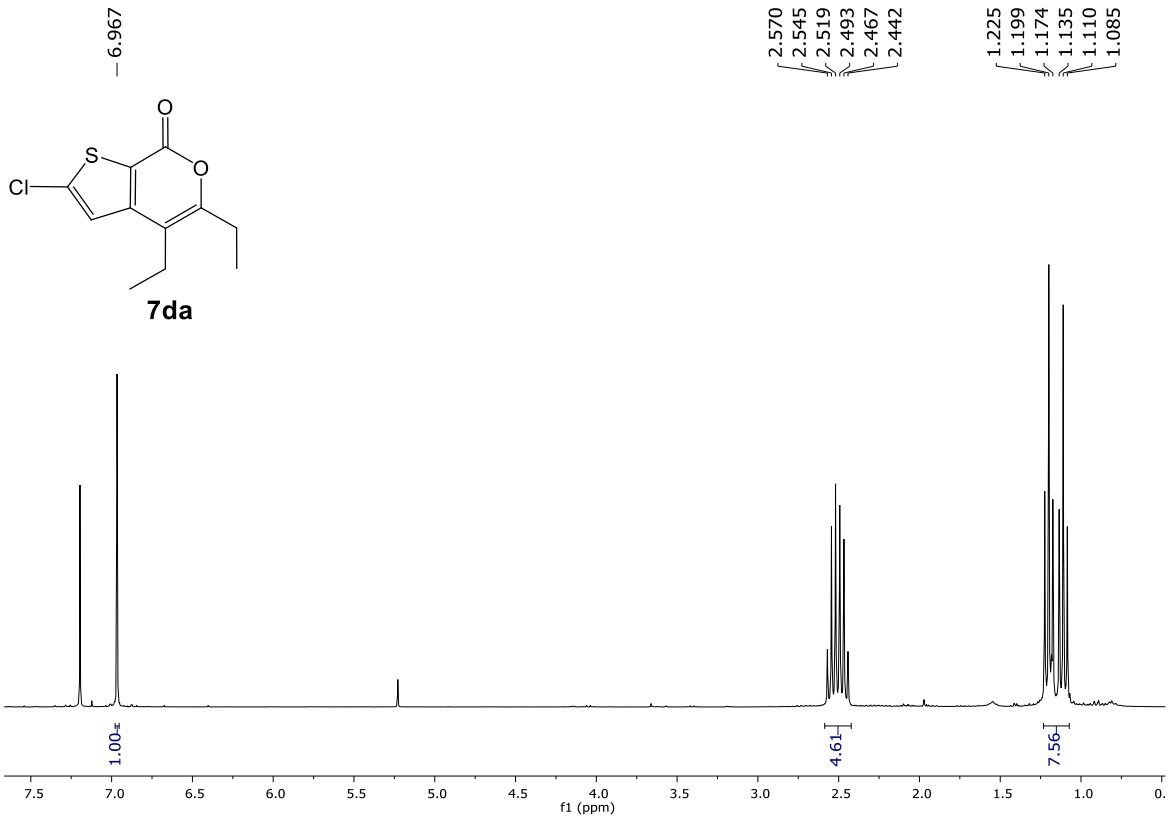
^{13}C{^{1}H}-NMR spectrum of 7ba



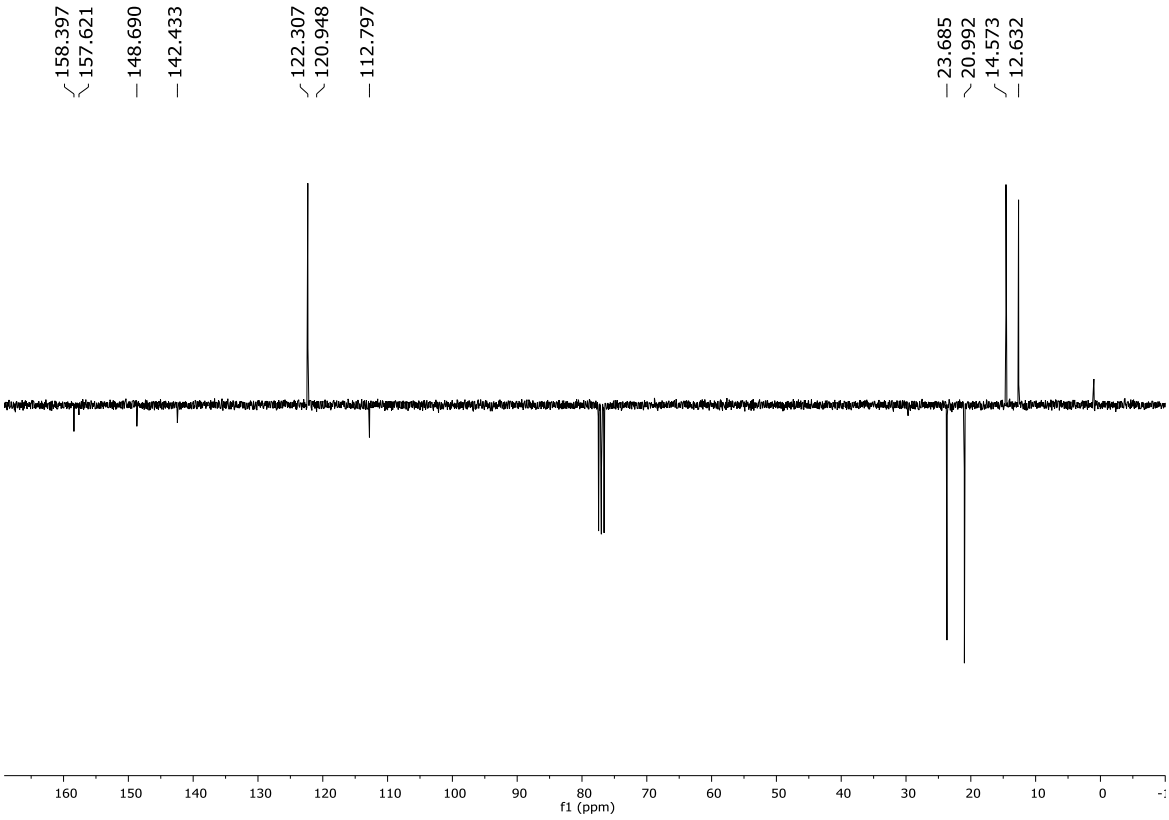
^{1}H-NMR spectrum of 7ca (*Solvent impurities)



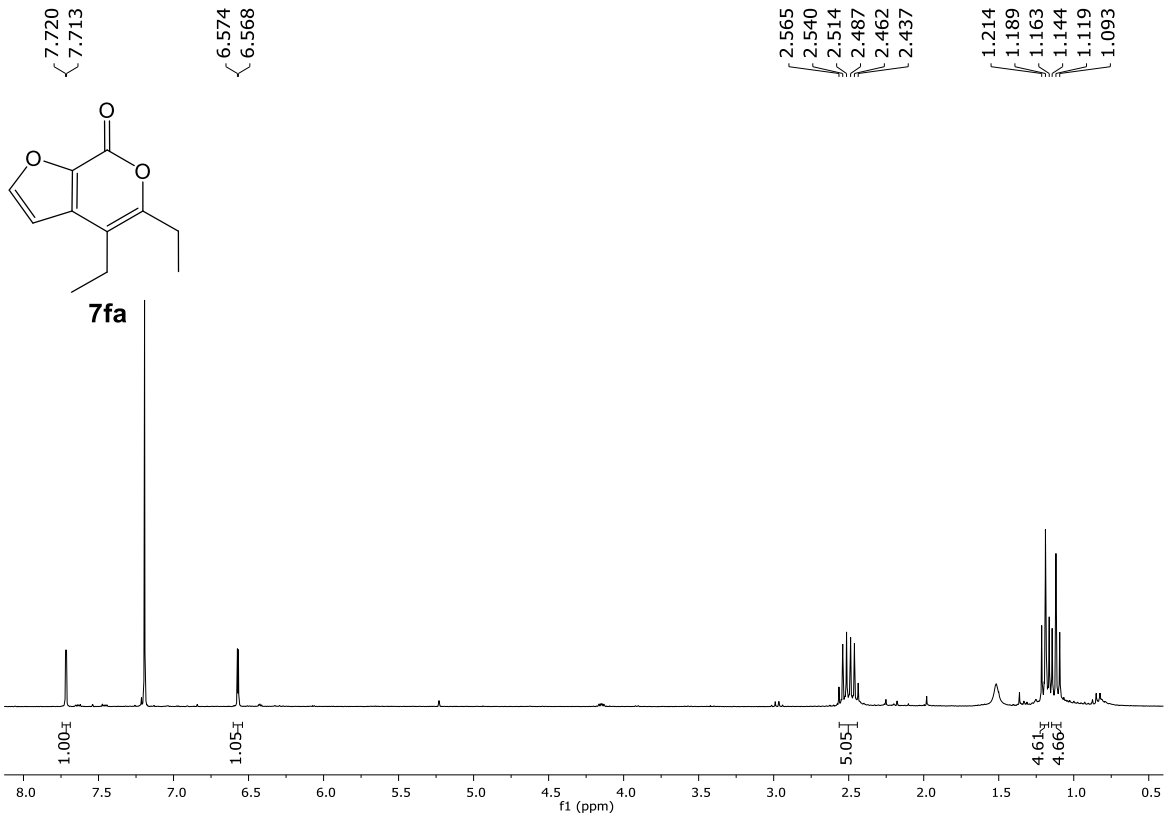
^{13}C(APT)-NMR spectrum of 7ca



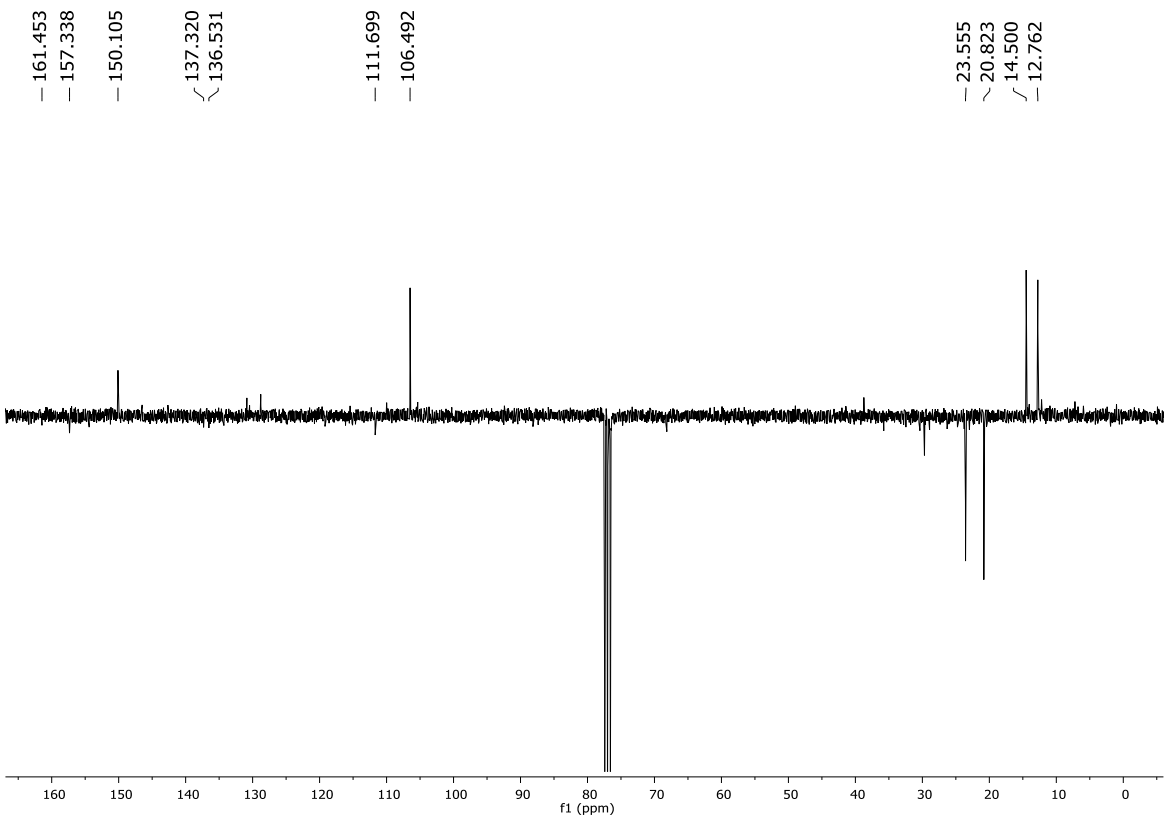
^{1}H-NMR spectrum of 7da



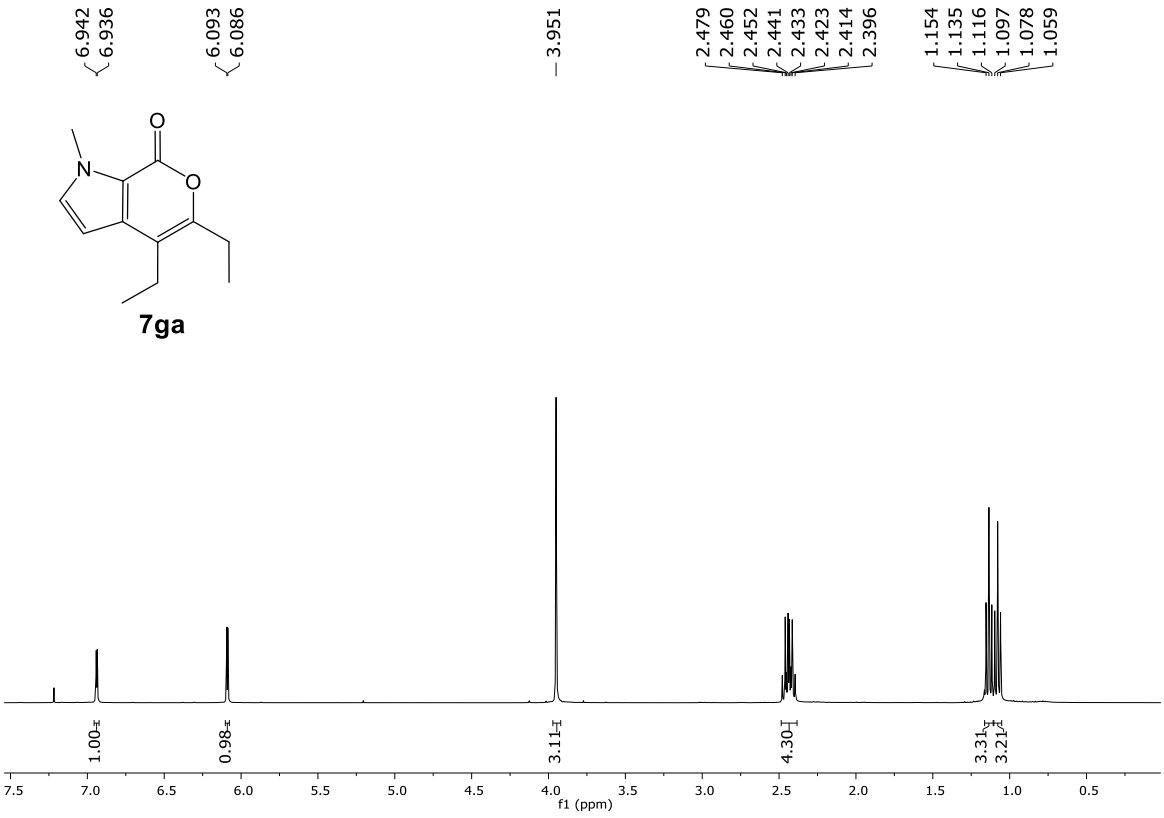
^{13}C(APT)-NMR spectrum of 7da



^{1}H-NMR spectrum of 7fa

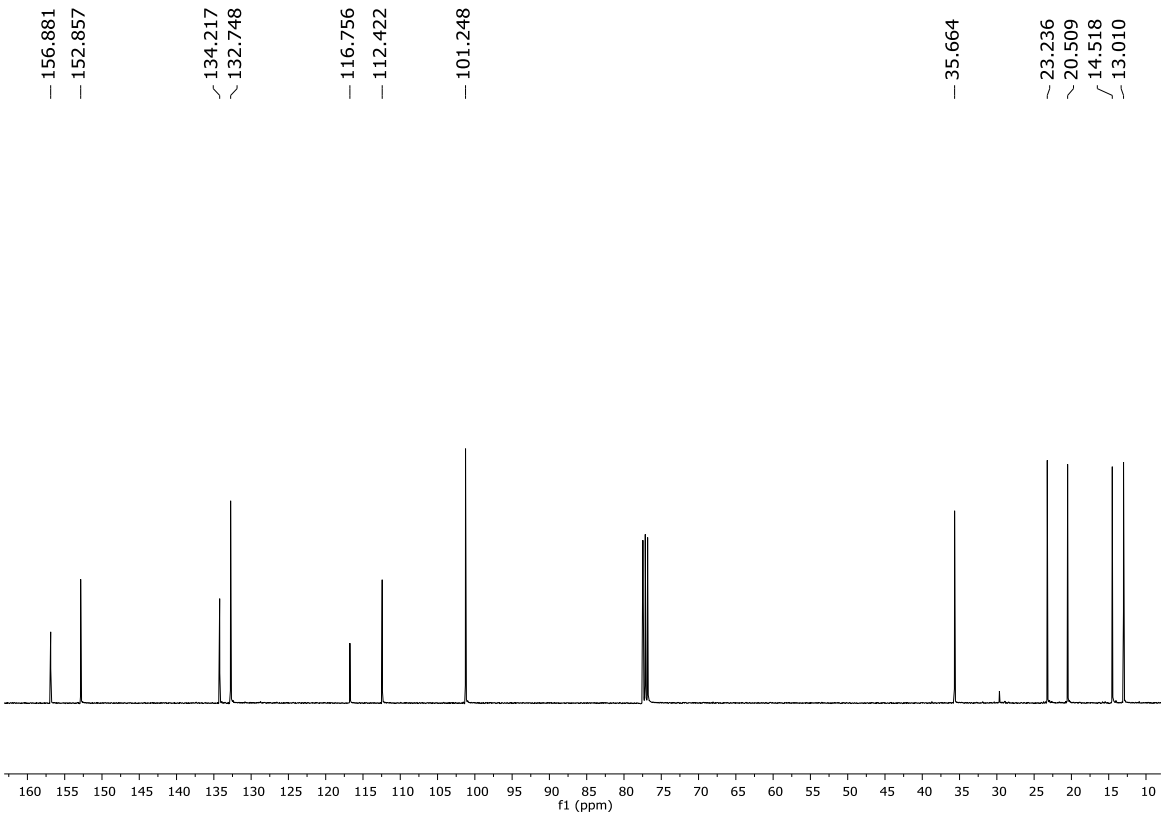


^{13}C(APT)-NMR spectrum of 7fa

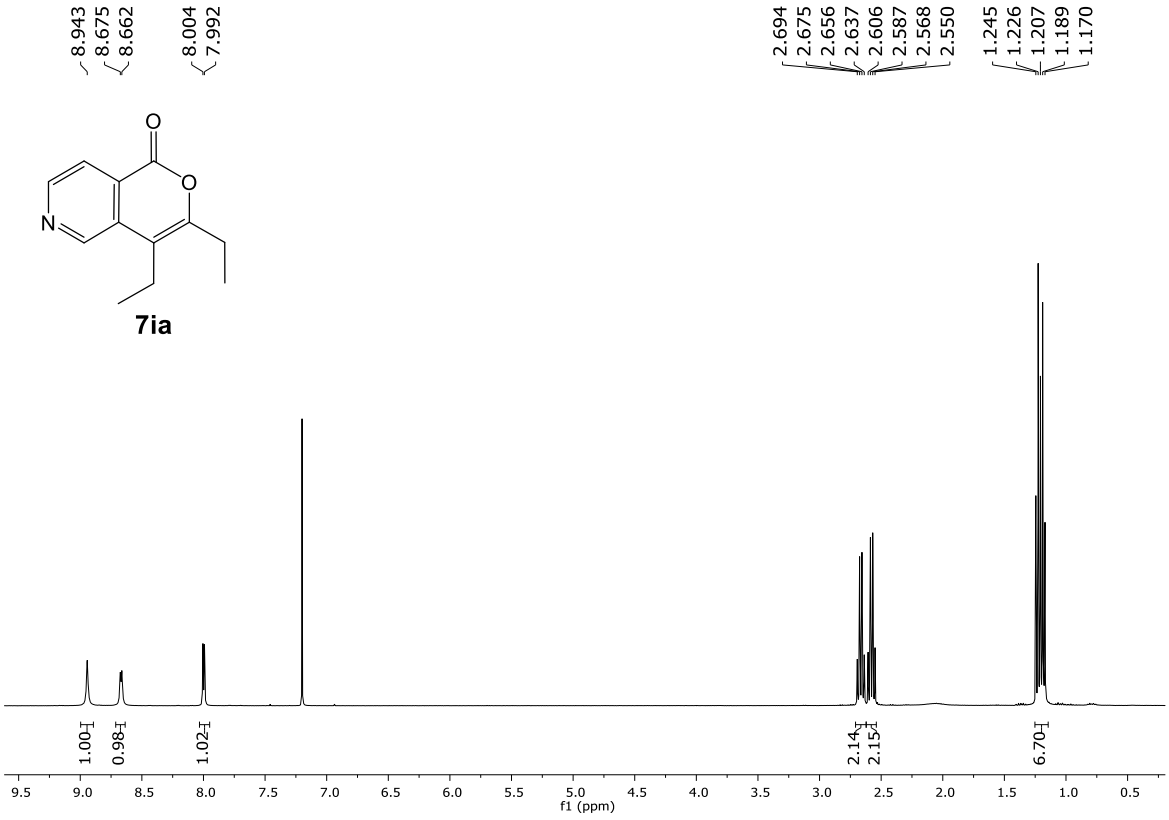


7ga

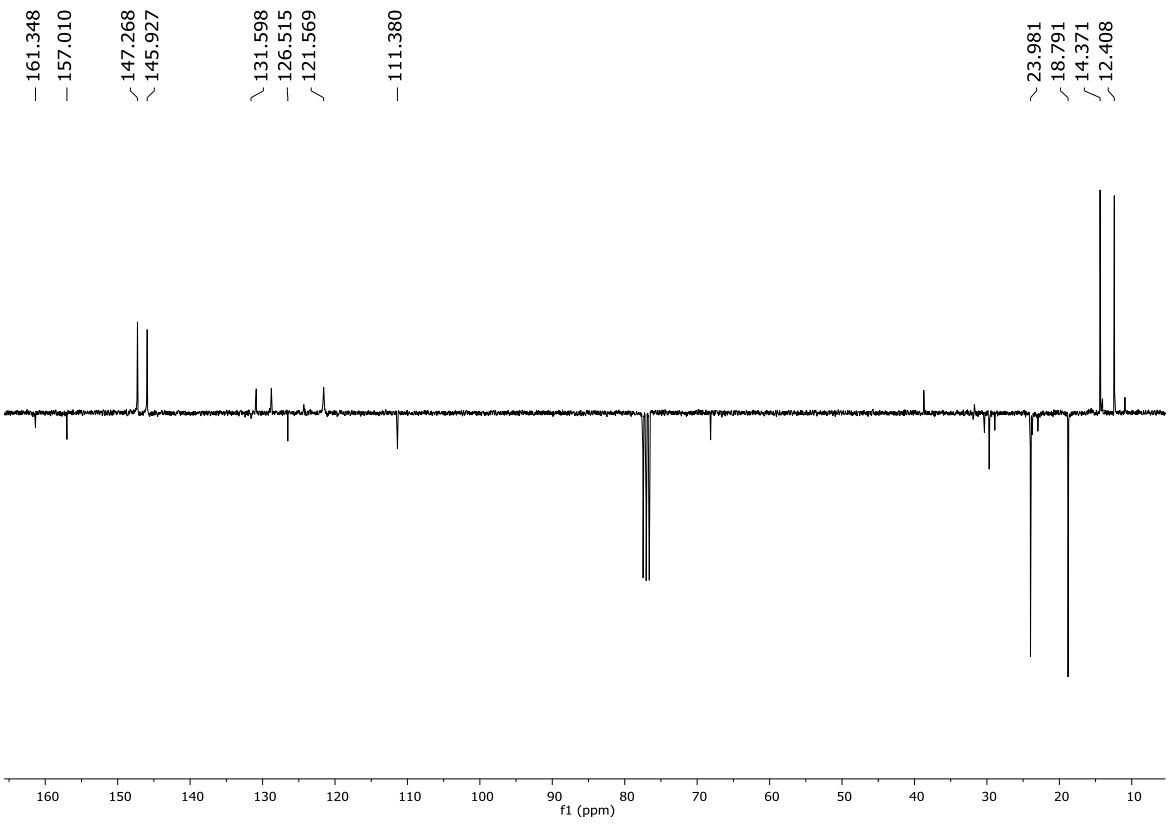
^{1}H-NMR spectrum of 7ga



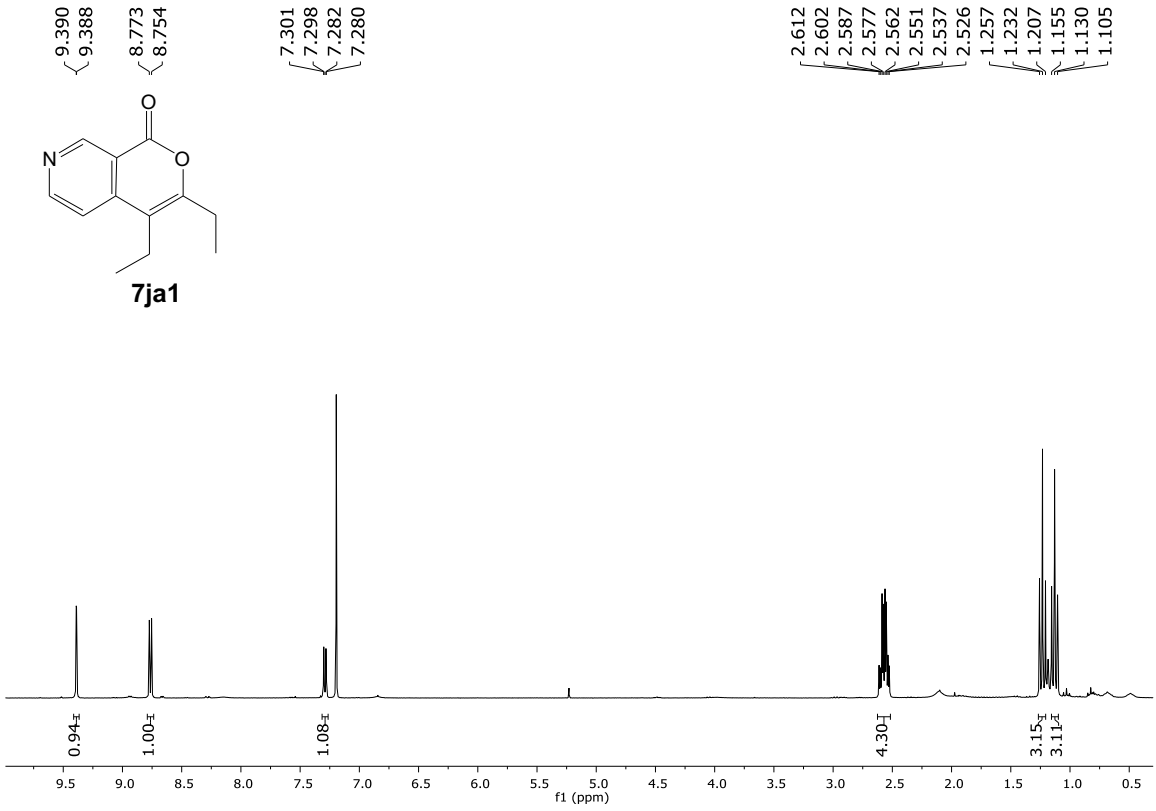
^{13}C{^{1}H}-NMR spectrum of 7ga



^{1}H-NMR spectrum of 7ia

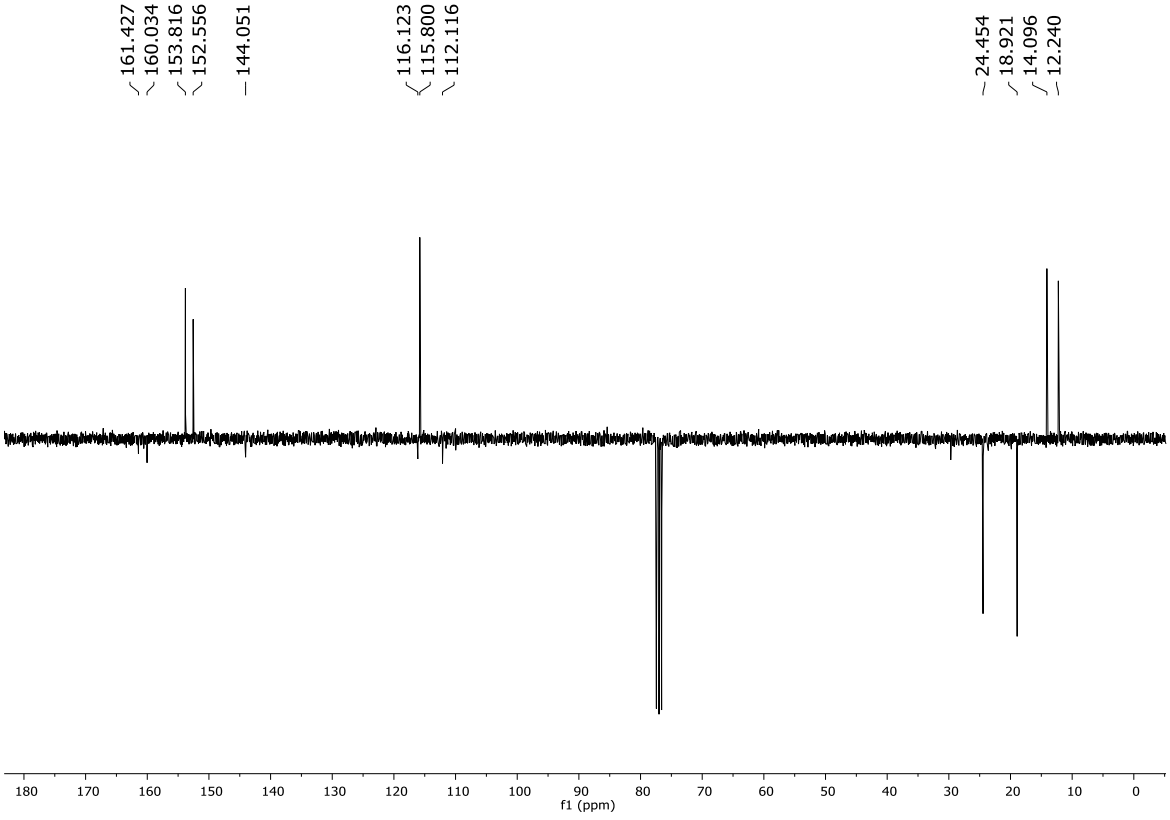


^{13}C(APT)-NMR spectrum of 7ia

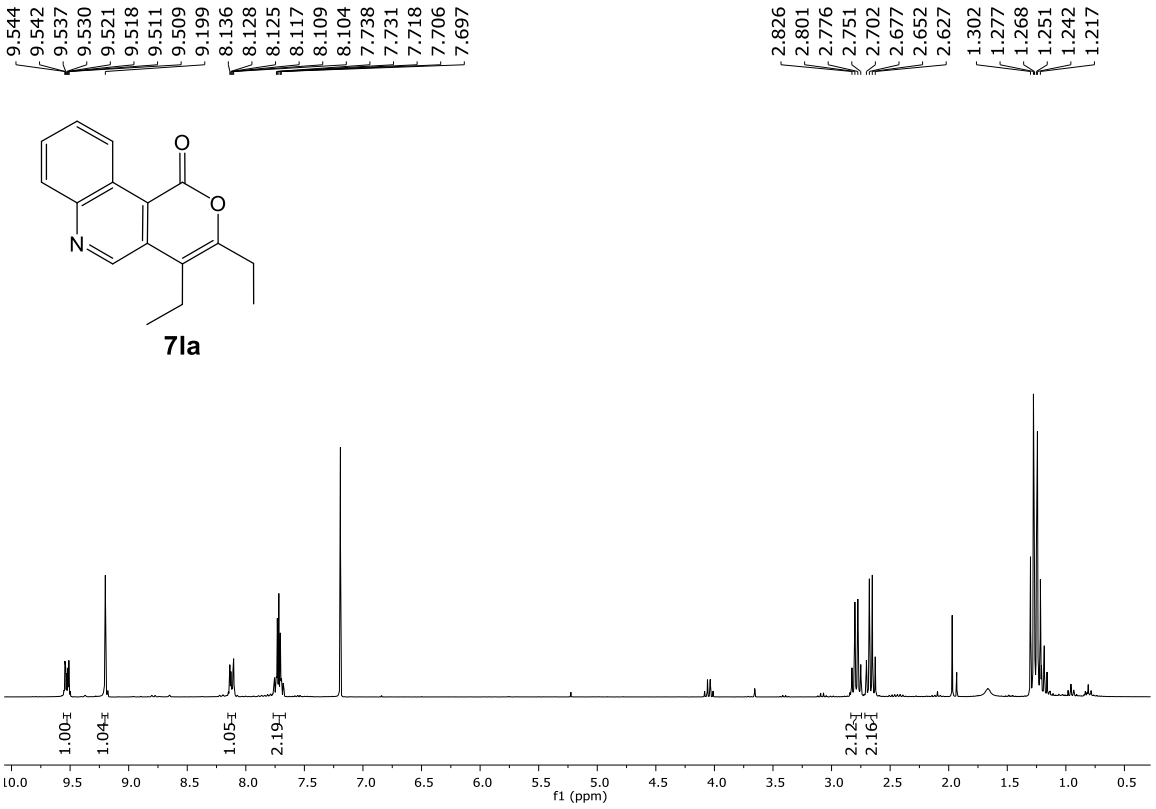


7ja1

^{1}H-NMR spectrum of 7ja1

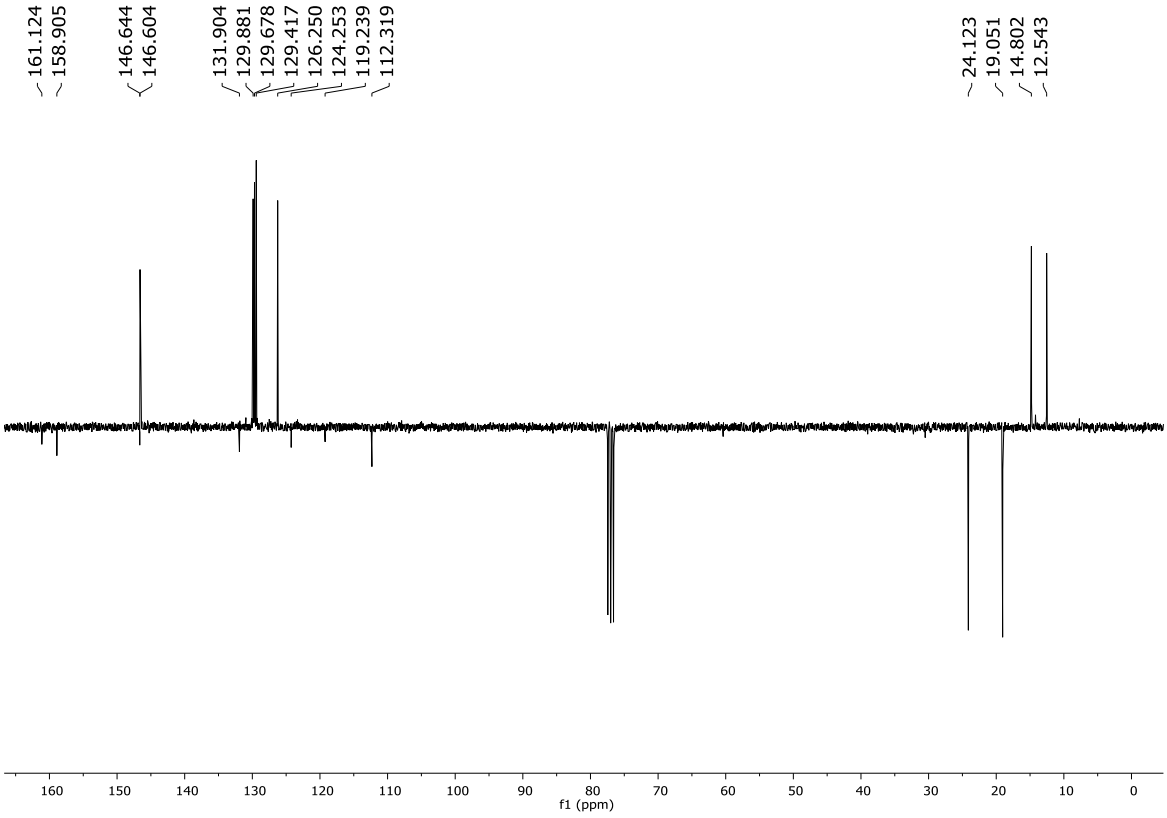


^{13}C(APT)-NMR spectrum of 7ja1

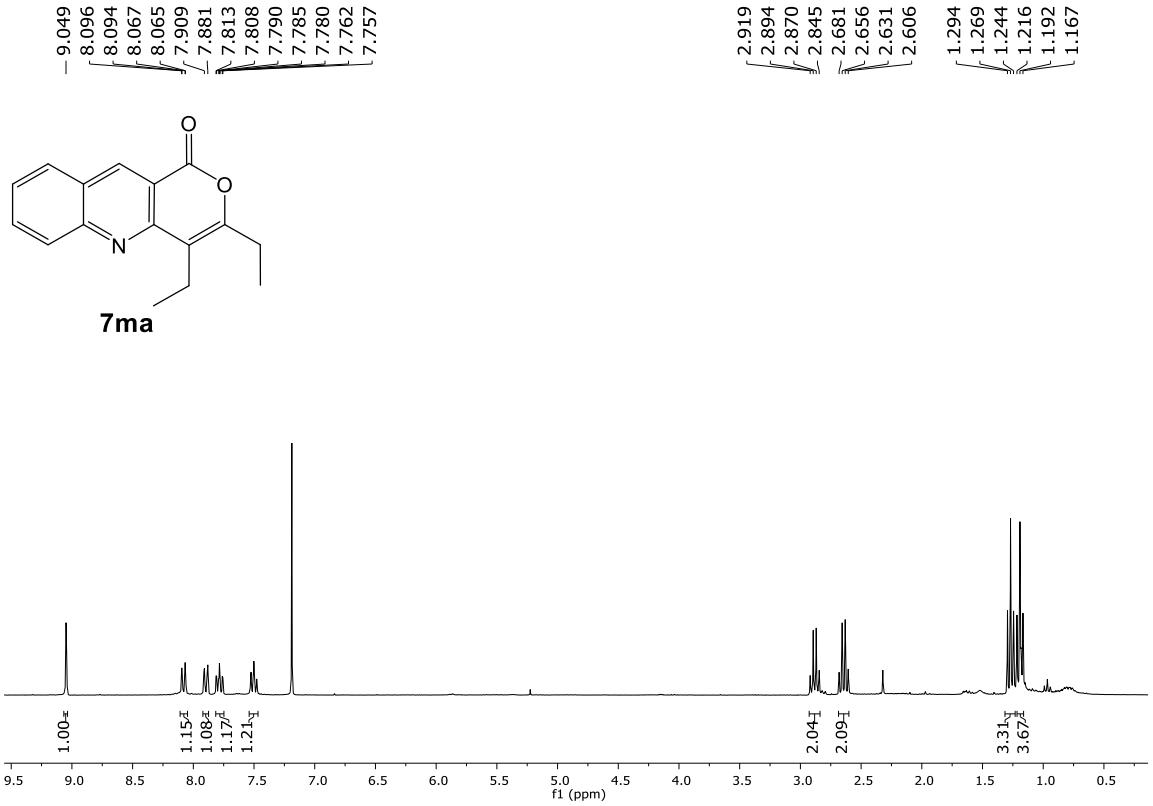


7la

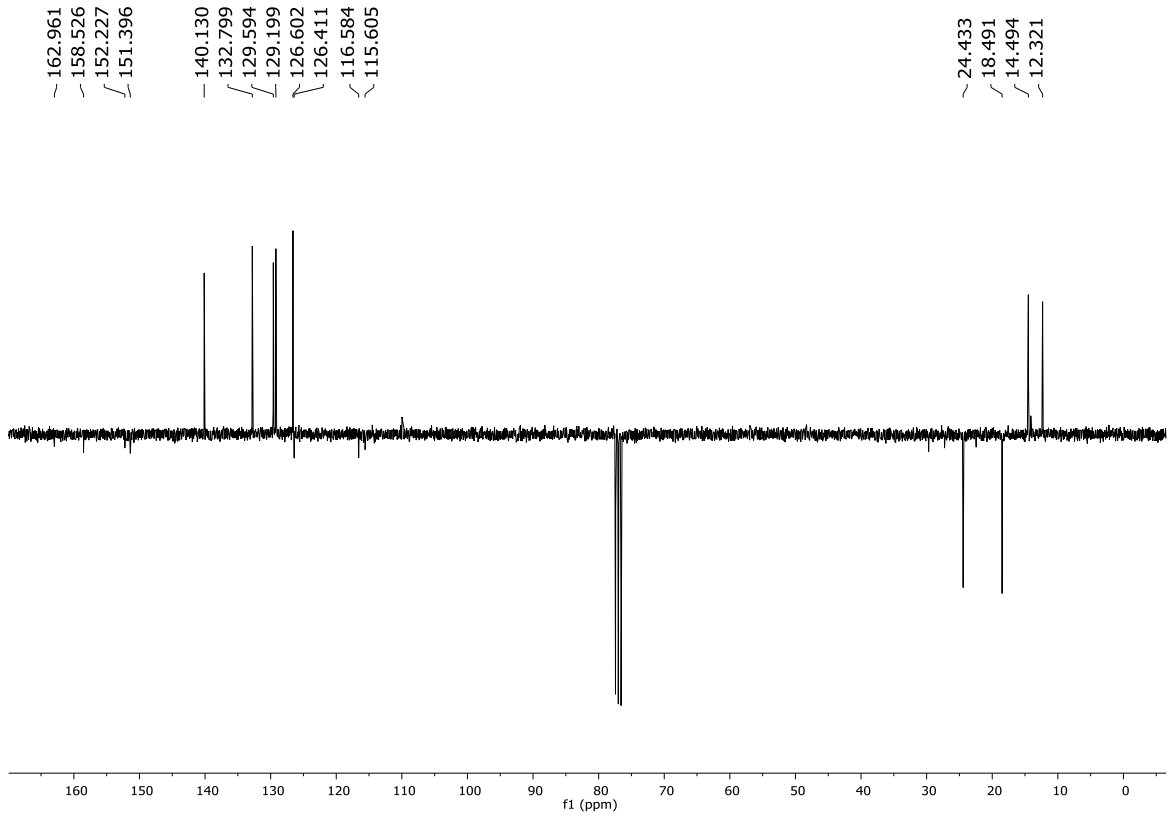
^{1}H-NMR spectrum of 7la



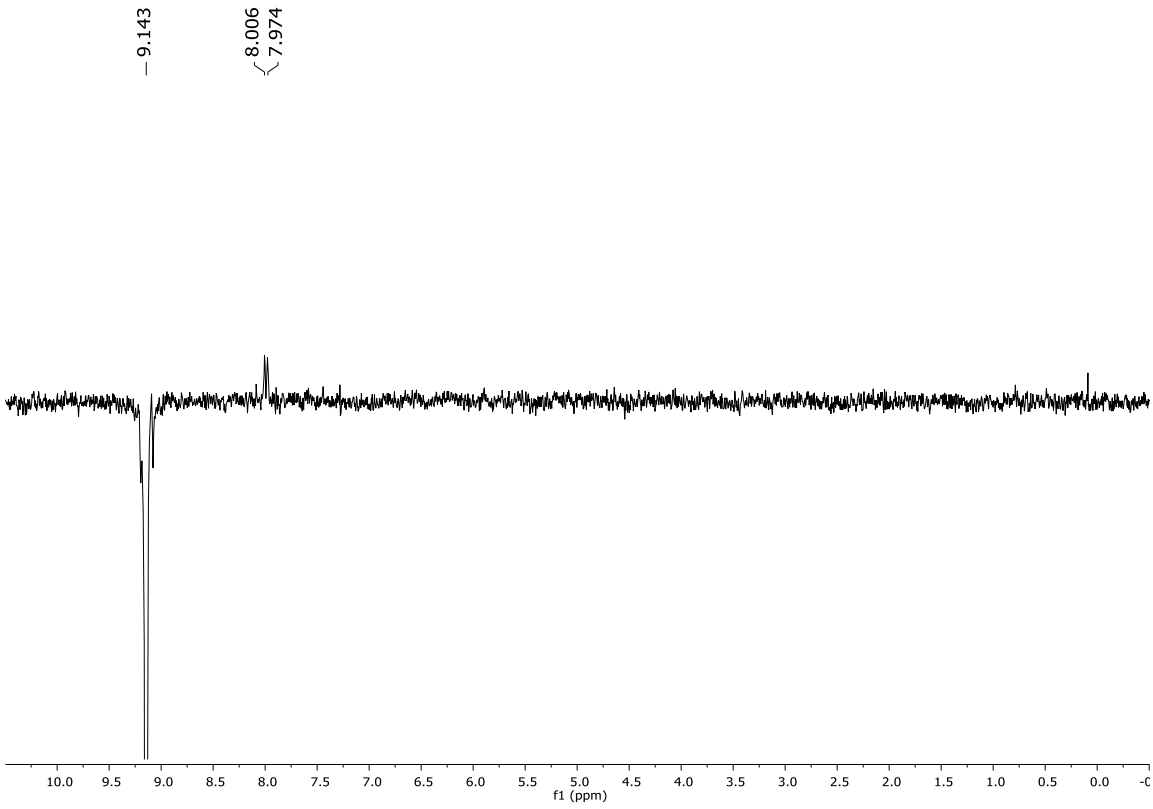
^{13}C(APT)-NMR spectrum of 7la



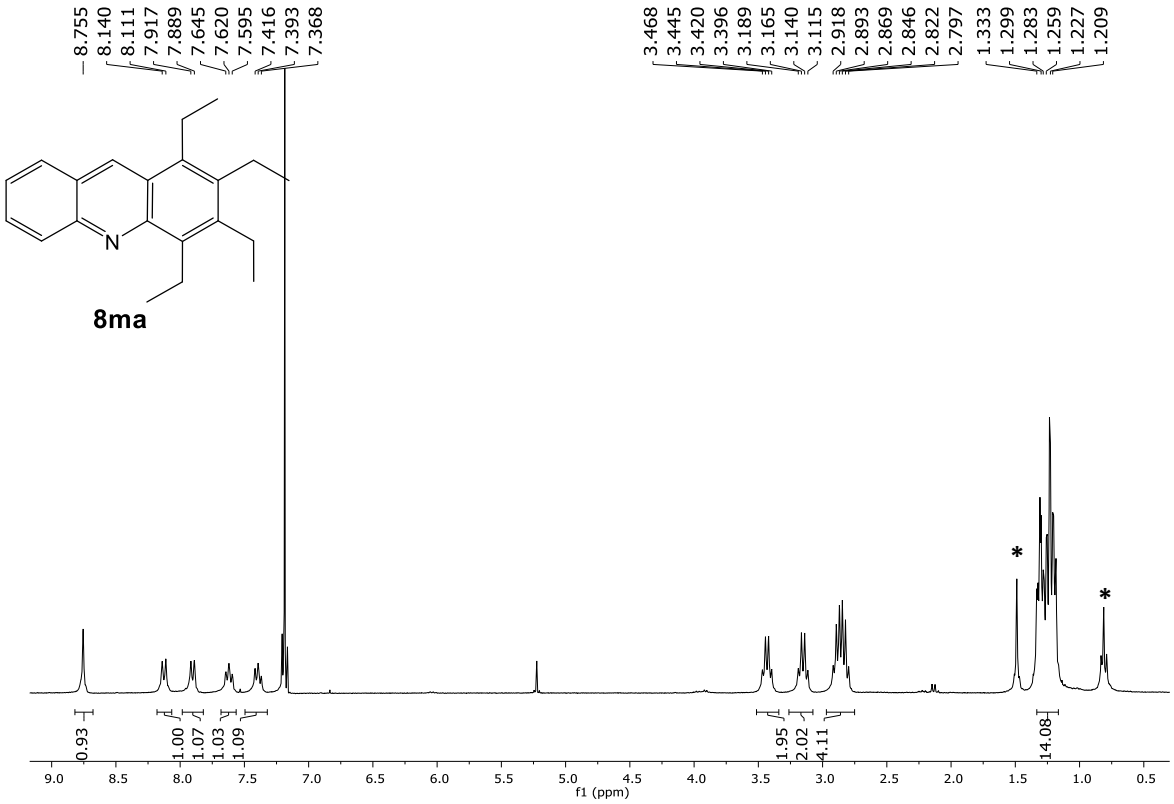
^{1}H-NMR spectrum of 7ma



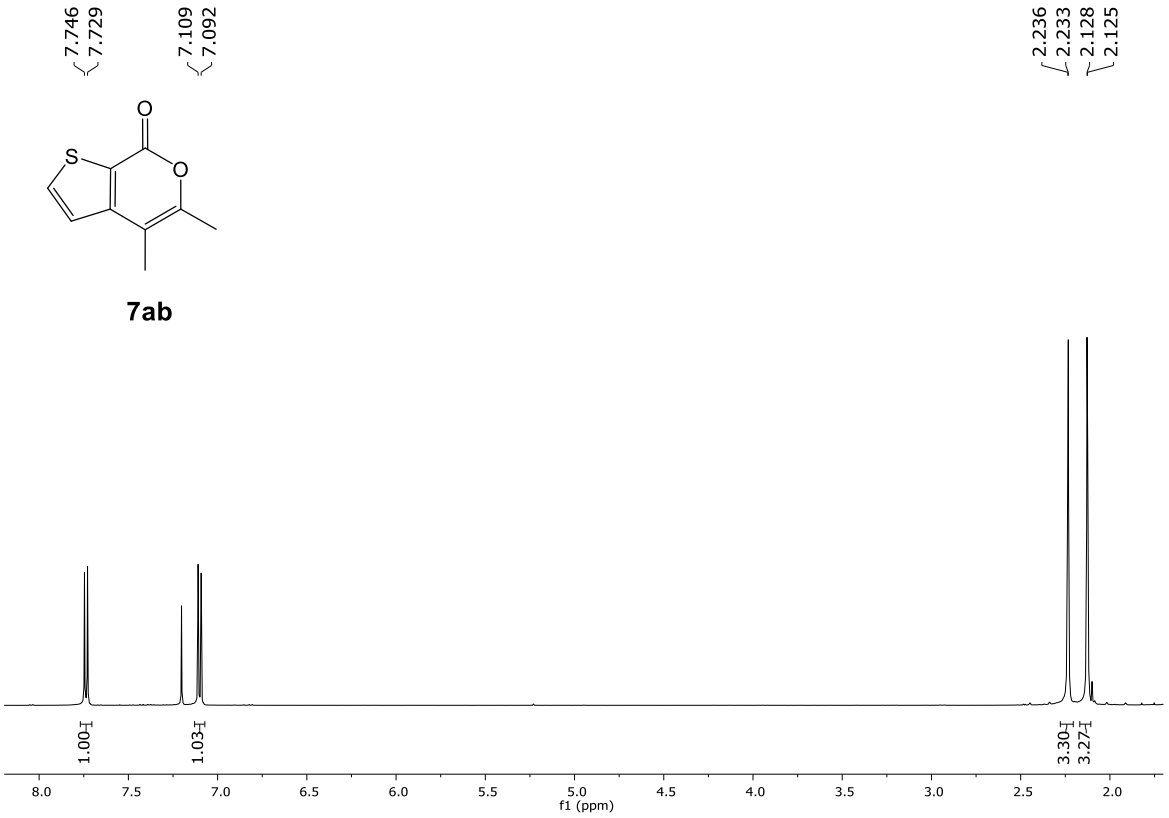
^{13}C(APT)-NMR spectrum of 7ma



1D-NOESY-^{1}H-NMR spectrum of 7ma

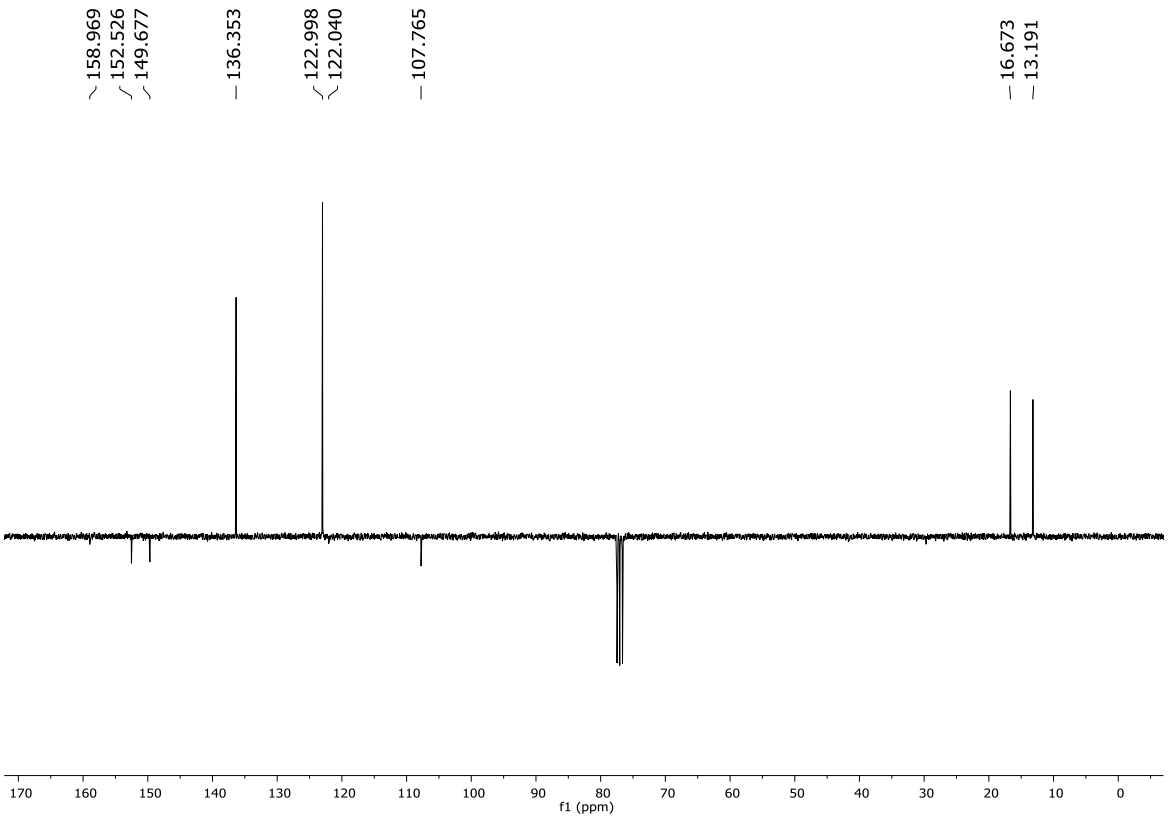


^{1}H-NMR spectrum of 8ma (* Solvent impurities)

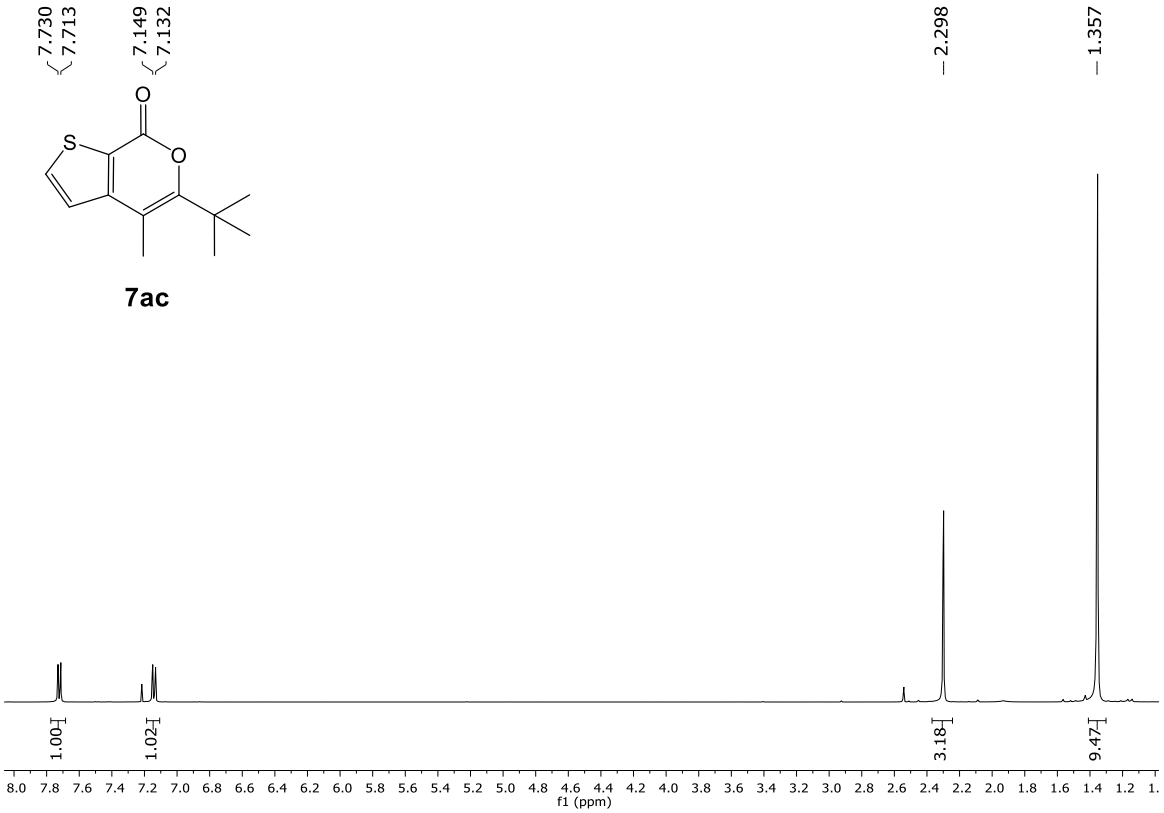


7ab

^{1}H-NMR spectrum of 7ab

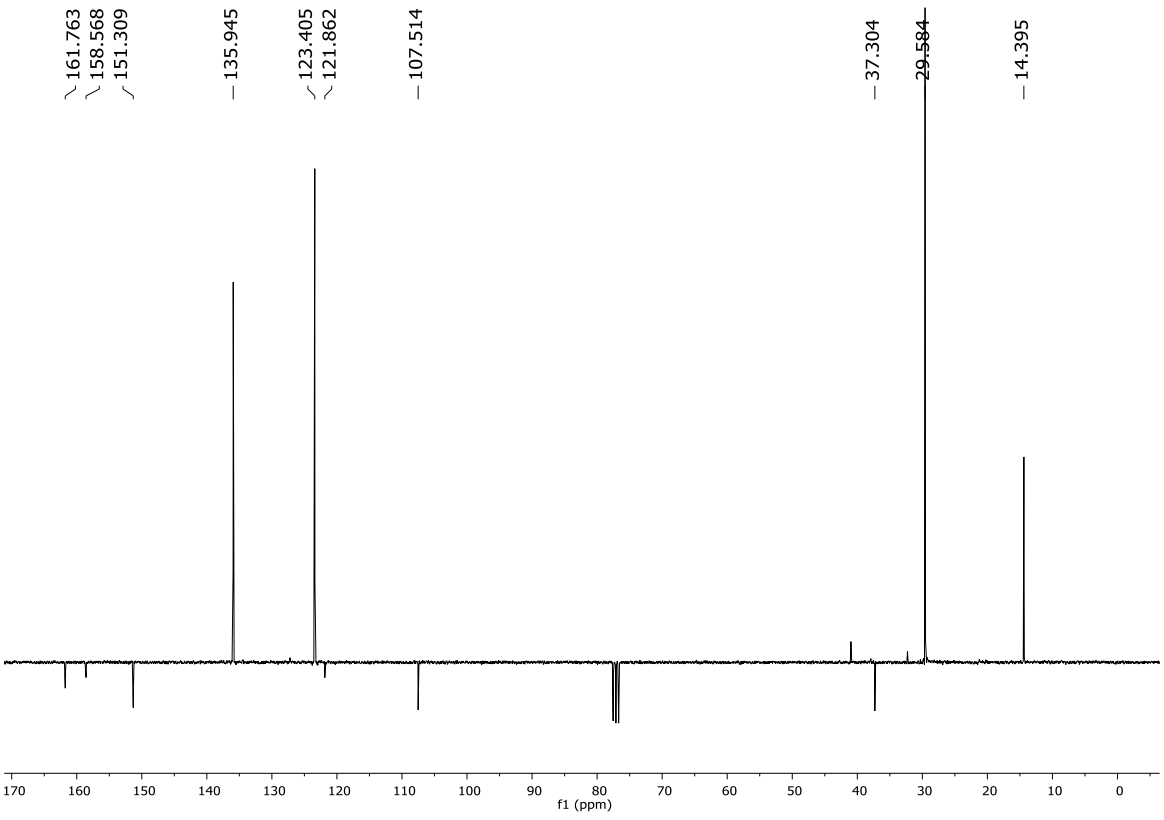


^{13}C(APT)-NMR spectrum of 7ab

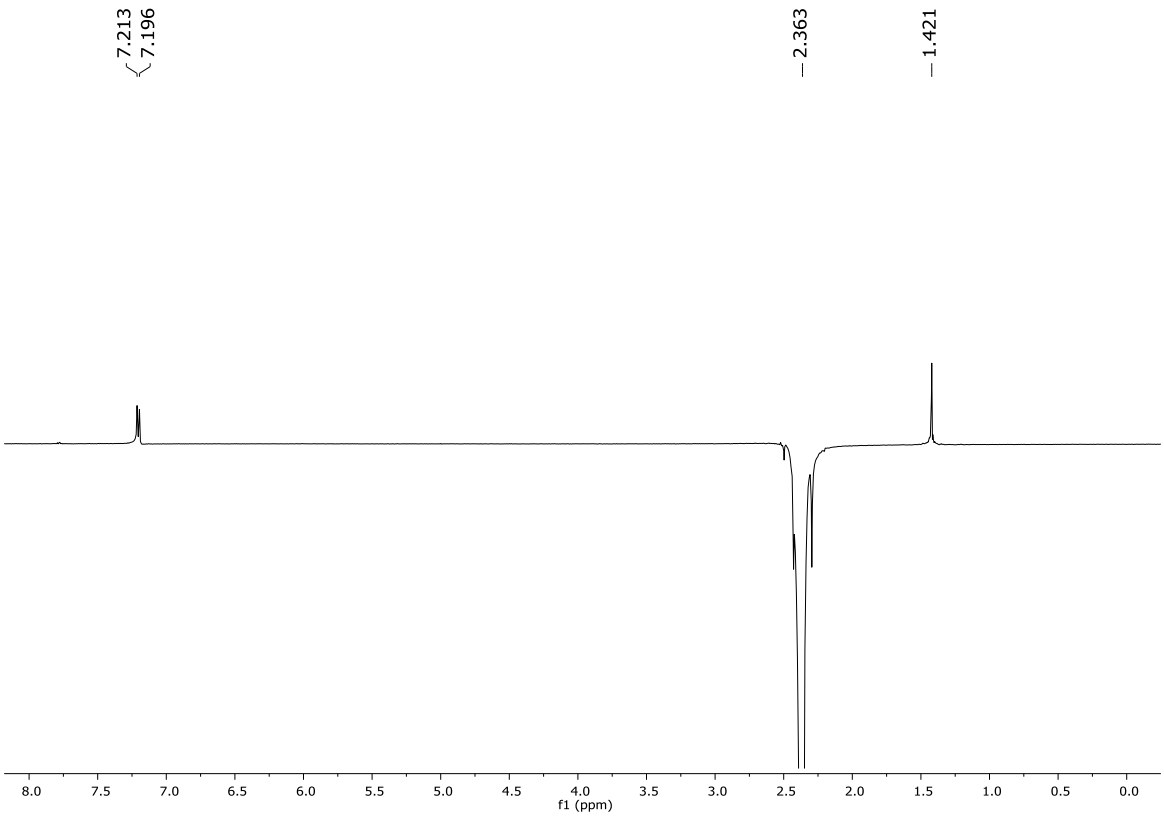


7ac

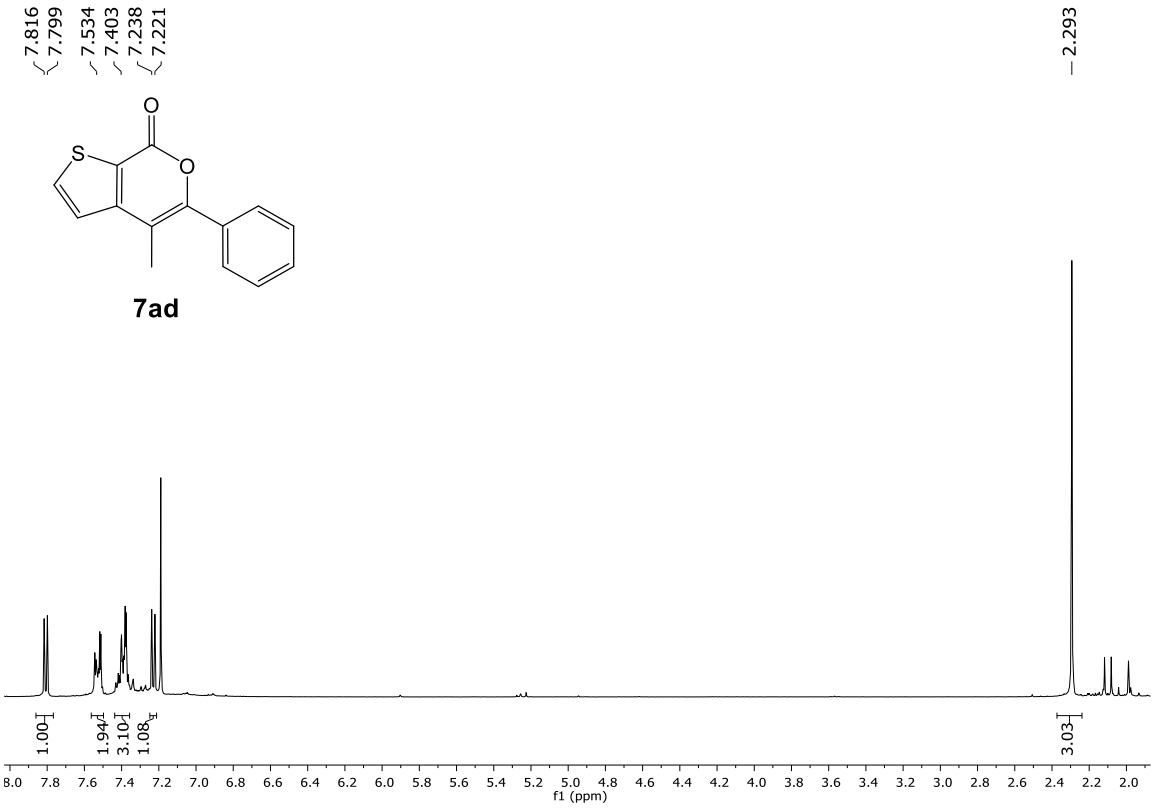
^{1}H-NMR spectrum of 7ac



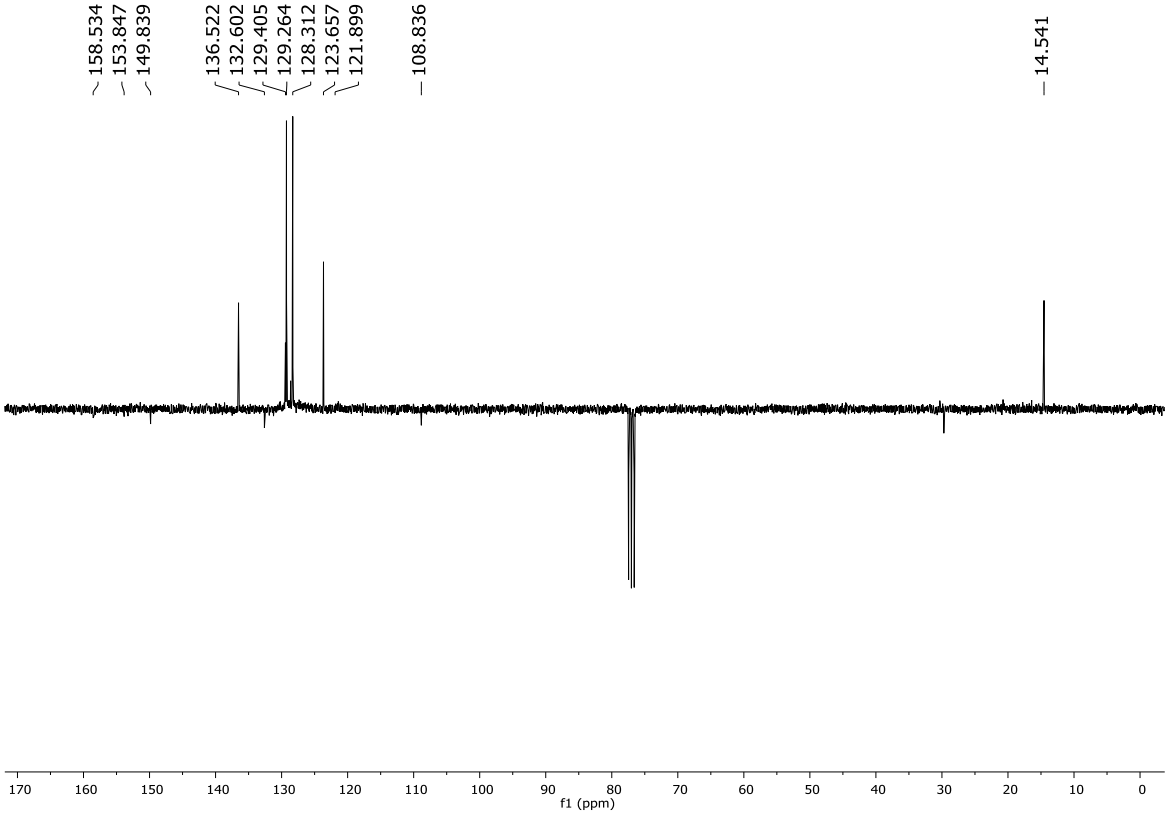
^{13}C(APT)-NMR spectrum of 7ac



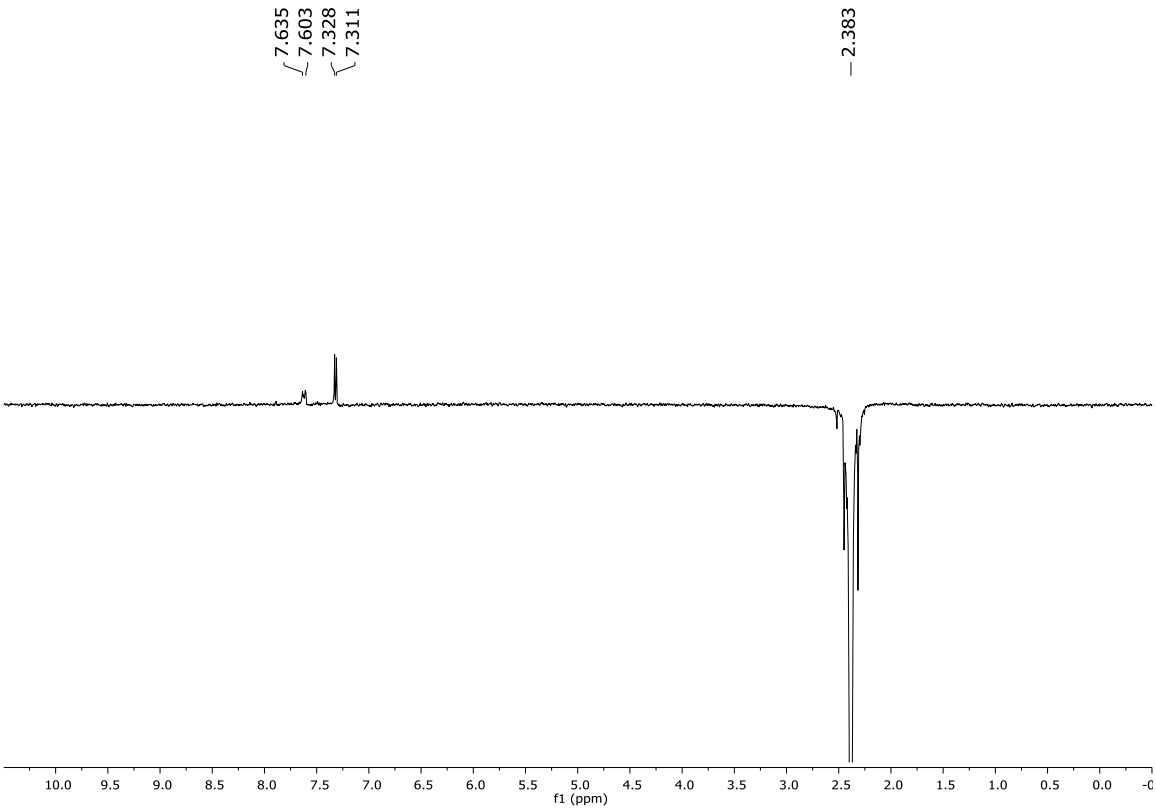
1D-NOESY-^{1}H-NMR spectrum of 7ac



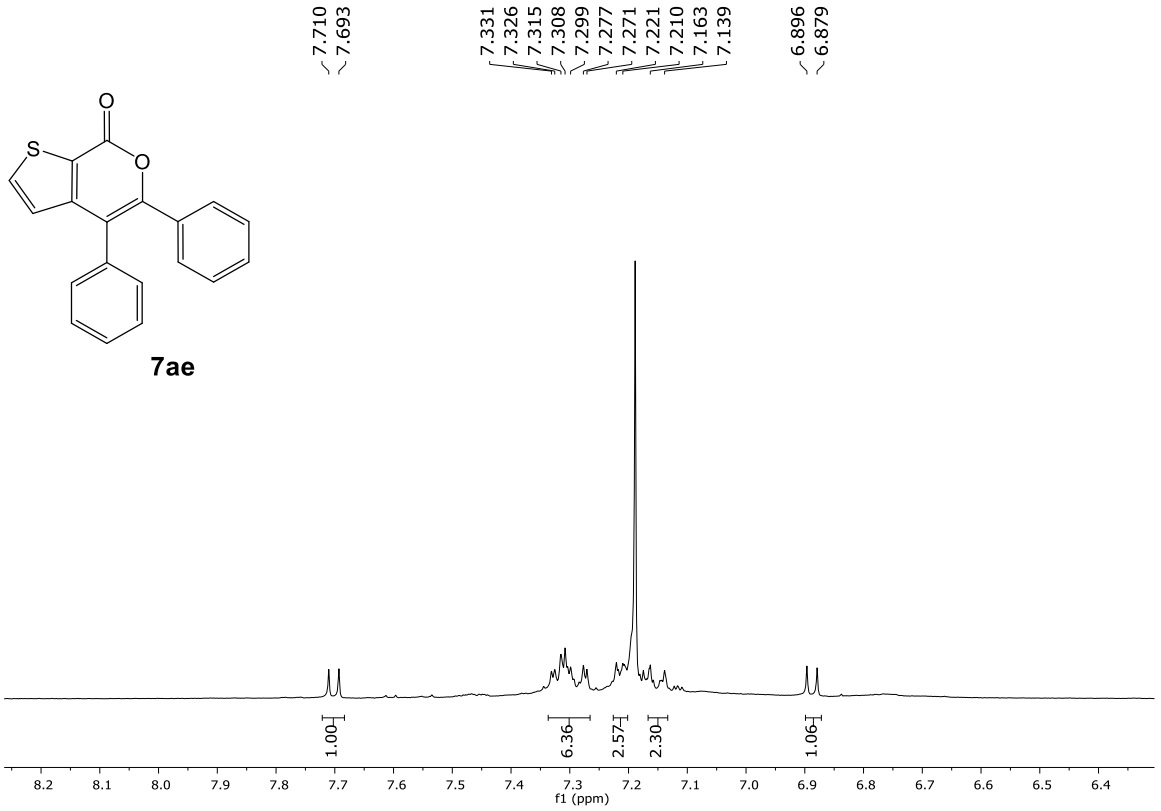
^{1}H-NMR spectrum of 7ad



^{13}C(APT)-NMR spectrum of 7ad

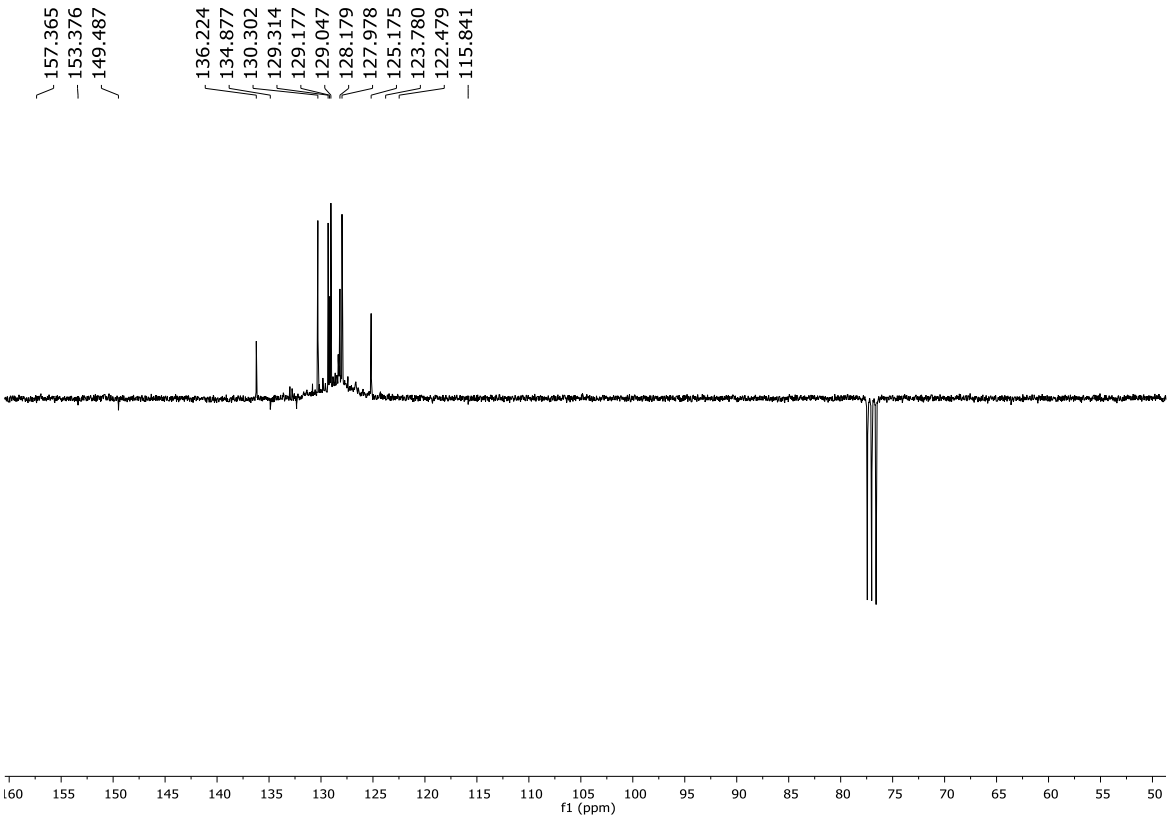


1D-NOESY-^{1}H-NMR spectrum of 7ad

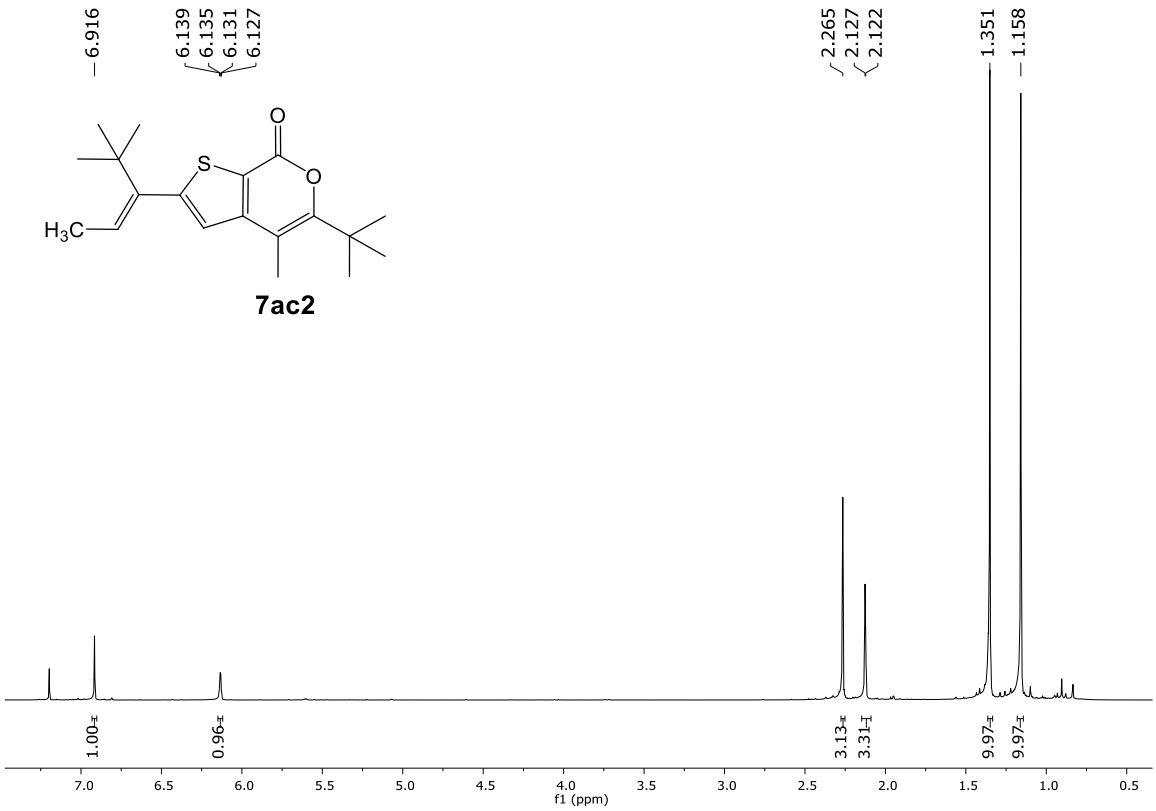


7ae

^{1}H-NMR spectrum of 7ae

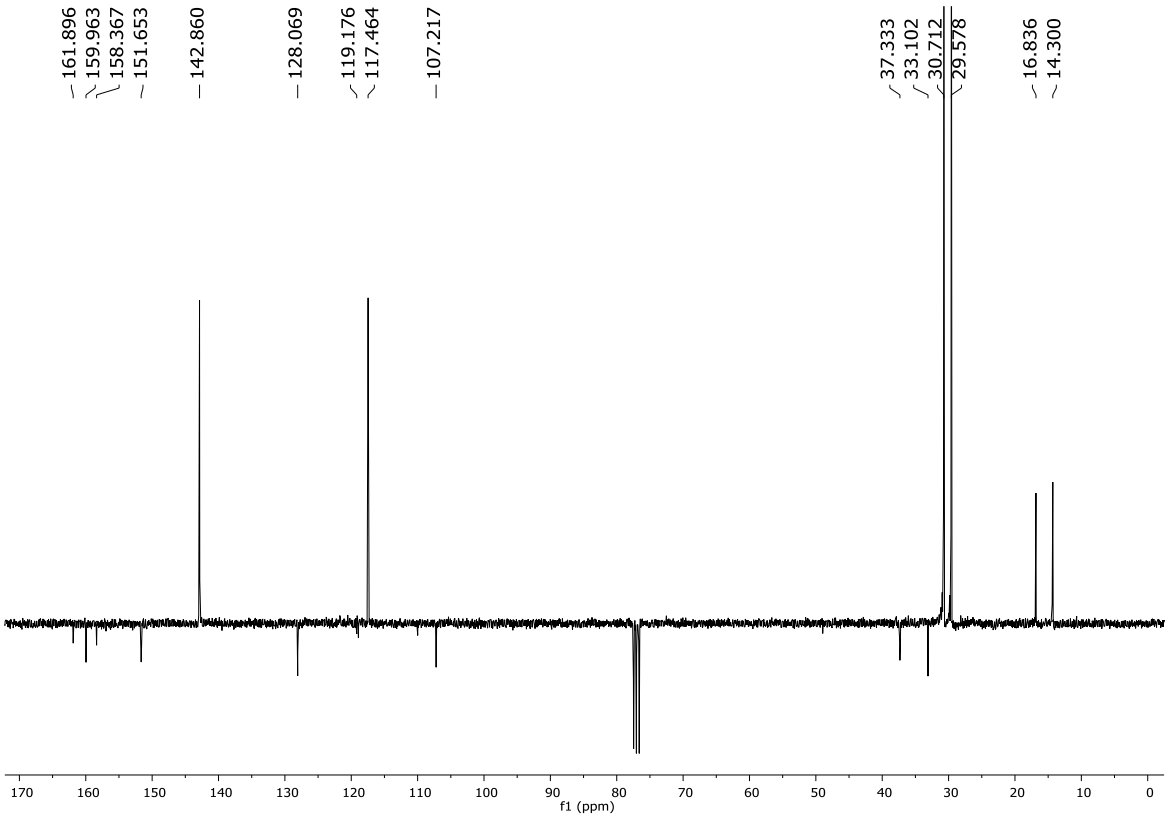


^{13}C(APT)-NMR spectrum of 7ae

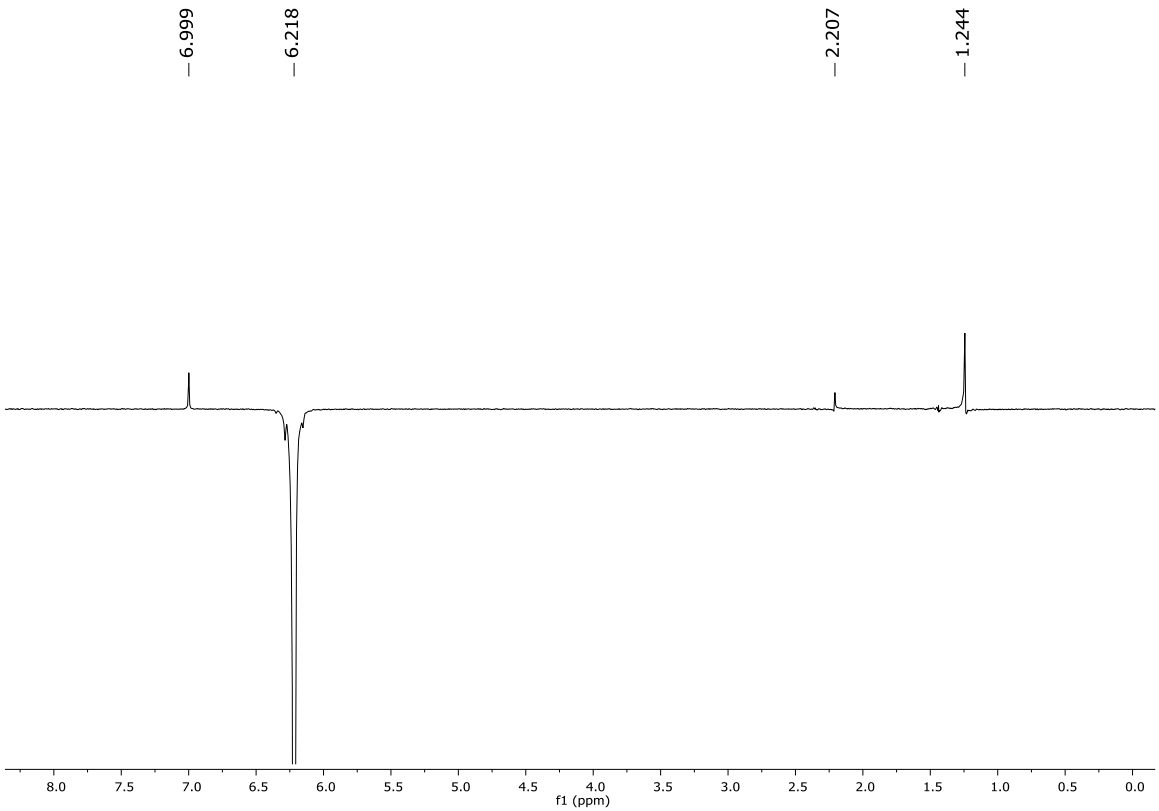


7ac2

^{1}H-NMR spectrum of 7ac2



^{13}C(APT)-NMR spectrum of 7ac2



1D-NOESY-^{1}H-NMR spectrum of 7ac2