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A straightforward access to 2-hydroxyoxazino[3,2-*f*]phenanthridines from phenanthridine, oxalylacetylenes and water

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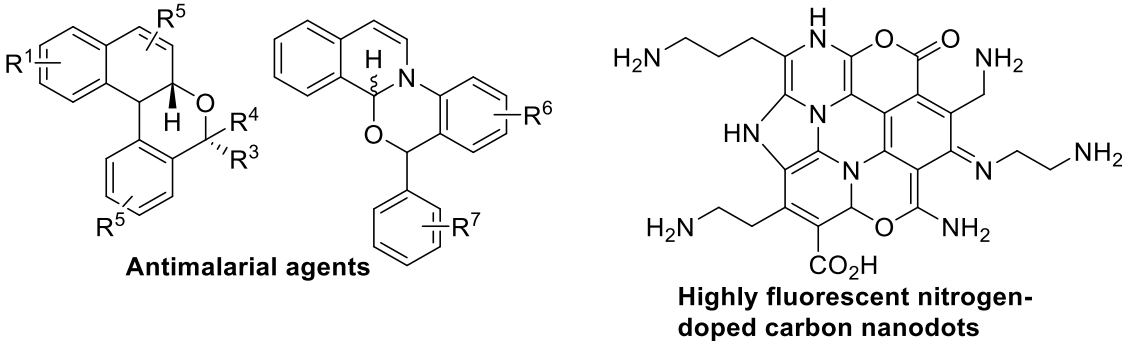


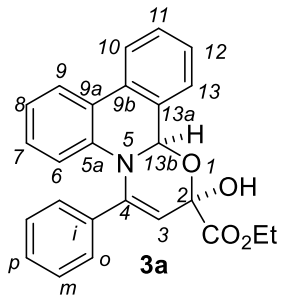
Figure S1. 1,3-Oxazinoazine moiety as platform in bio- and photoactive compounds

General

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded with an AV-400 Bruker BioSpin spectrometer. The internal standards were HMDS (for ^{1}H nuclei δ 0.05 ppm) or the residual solvent signals (for ^{13}C nuclei δ 77.16 ppm), and $CFCl_3$ (for ^{19}F nuclei δ 0.00 ppm) or C_6F_6 (for ^{19}F nuclei δ -162.90 ppm). IR spectra were recorded on a Bruker Vertex-70 instrument. Phenanthridine **1** is a commercial reagent. 1-Aryl-2-oxalylacetylenes **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

Ethyl (2R,13bR*)-2-hydroxy-4-phenyl-2H,13bH-[1,3]oxazino[3,2-f]phenanthridine-2-carboxylate (**3a**).* A mixture of phenanthridine **1** (90 mg, 0.5 mmol), acetylene **2a** (101 mg, 0.5 mmol) and H_2O (45 mg, 2.5 mmol) was stirred at 20-25 °C for 6 h. The solvents were removed under reduce pressure, column chromatography afforded oxazinophenanthridine **3a** (85 mg, 43%), as a light-yellow powder, mp 162-163 °C (MeCN). Initial phenanthridine (**1**) (44 mg, conversion was 51%) was recovered.



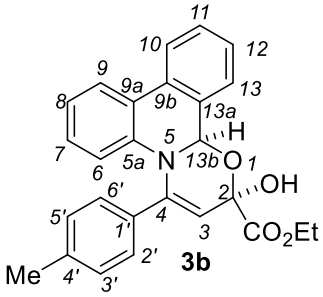
IR (microlayer): 1035, 1093, 1119, 1159, 1256 (C-O-C), 1606, 1636, (C=C), 1737 (C=O), 3453 (OH) cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.97 (d, $^3J_{H8,H9}$ = 7.9 Hz, 1H, H-9), 7.85 (m, 1H, H-10), 7.57 (m, 2H, H_o from Ph), 7.52 (m, 1H, H-13), 7.50 (m, 1H, H-11), 7.38 (m, 1H, H-12), 7.34 (m, 3H, $H_{m,p}$ from Ph), 6.94 (m, 2H, H-7, H-8), 6.54 (m, 1H, H-6), 6.09 (s, 1H, H-13b), 5.97 (s, 1H, H-3), 4.61 (s, 1H, OH), 4.02, 3.95 (m, 2H, C<u>H</u>$_2$ from OEt), 0.94 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, C<u>H</u>$_3$ from OEt) ppm.

^{13}C NMR (100.62 MHz, $CDCl_3$): δ 170.3 (C-14), 147.1 (C-4), 138.6 (C-9b), 135.5 (C_i from Ph), 131.2 (C-13a, C-5a), 129.9 (C_p from Ph), 129.6 (C-11), 129.3 (C-13), 129.2 (C_m from Ph), 128.4 (C-7), 127.9 (C-9), 126.2 (C_o from Ph), 123.8 (C-12), 122.3 (C-8), 121.8 (C-9a), 121.0 (C-10), 119.5 (C-6), 115.1 (C-3), 92.9 (C-2), 81.3 (C-13b), 62.8 (<u>C</u>H$_2$ from OEt), 13.7 (<u>C</u>H$_3$ from OEt) ppm.

$C_{25}H_{21}NO_4$ (399.45): calcd C 75.17, H 5.30, N 3.51; found C 75.23, H 5.27, N 3.49.

Ethyl (2R,13bR*)-2-hydroxy-4-(4-methylphenyl)-2H,13bH-[1,3]oxazino[3,2-f]phenanthridine-2-carboxylate (**3b**):* Analogously from phenanthridine **1** (90 mg, 0.5 mmol), acetylene **2b** (108 mg, 0.5 mmol) and H_2O (45 mg, 2.5 mmol), 20-25 °C, 24 h, oxazinophenanthridine **3b** was obtained (99 mg, 48%) as a light-yellow powder, mp 161-163 °C (MeCN). Initial phenanthridine (**1**) (17 mg, conversion was 81%) was recovered.



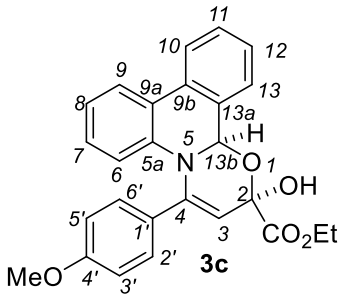
IR (thin layer): 1038, 1093, 1117, 1159, 1255 (C-O-C), 1609, 1642, (C=C), 1735 (C=O), 3444 (OH) cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.95 (d, $^3J_{H8,H9}$ = 7.6 Hz, 1H, H-9), 7.84 (m, 1H, H-10), 7.51 (m, 1H, H-13), 7.47 (m, 1H, H-11), 7.46 (m, 2H, $H_{2',6'}$ from Ar), 7.36 (m, 1H, H-12), 7.13 (m, 2H, $H_{3',5'}$ from Ar), 6.93 (m, 2H, H-7, H-8), 6.55 (d, $^3J_{H6,H7}$ = 7.2 Hz, 1H, H-6), 6.05 (s, 1H, H-13b), 5.96 (s, 1H, H-3), 4.64 (s, 1H, OH), 4.02, 3.91 (m, 2H, C<u>H</u>$_2$ from OEt), 2.32 (s, 3H, C<u>H</u>$_3$-4'), 0.92 (t, 3H, C<u>H</u>$_3$ from OEt) ppm.

^{13}C NMR (100.62 MHz, $CDCl_3$): δ 170.4 (C-14), 147.0 (C-4), 139.7 ($C_{4'}$ from Ar), 138.7 (C-9b), 132.6 ($C_{1'}$ from Ar), 131.2 (C-5a), 129.8 (C-11, $C_{3',5'}$ from Ar), 129.2 (C-13), 128.4 (C-13a), 128.3 (C-7), 127.8 (C-9), 126.1 ($C_{2',6'}$ from Ar), 123.7 (C-12), 122.2 (C-8), 121.8 (C-9a), 120.9 (C-10), 119.5 (C-6), 114.2 (C-3), 92.9 (C-2), 81.2 (C-13b), 62.7 (<u>C</u>H$_2$ from OEt), 21.4 (<u>C</u>H$_3$-4'), 13.7 (<u>C</u>H$_3$ from OEt) ppm.

$C_{26}H_{23}NO_4$ (413.47): calcd C 75.53, H 5.61, N 3.39; found C 75.55, H 5.63, N 3.36.

Ethyl (2R,13bR*)-2-hydroxy-4-(4-methoxyphenyl)-2H,13bH-[1,3]oxazino[3,2-f]-henanthridine-2-carboxylate (**3c**):* Analogously from phenanthridine **1** (90 mg, 0.5 mmol), acetylene **2c** (116 mg, 0.5 mmol), H_2O (45 mg, 2.5 mmol), and MeCN (0.5 ml), 20-25 °C, 24 h, oxazinophenanthridine **3c** was obtained (125 mg, 58%) as a light-yellow powder, mp 158-160 °C (MeCN). Initial phenanthridine (**1**) (7 mg, conversion was 92%) was recovered.



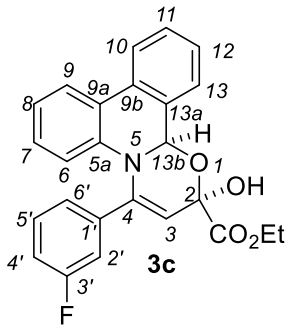
IR (microlayer): 1034, 1095, 1116, 1175, 1253 (C-O-C), 1608, 1646 (C=C), 1735 (C=O), 3442 (OH) cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.68 (m, 2H, $H_{3',5'}$ from Ar), 7.97 (d, $^3J_{H8,H9}$ = 7.6 Hz, 1H, H-9), 7.85 (m, 1H, H-10), 7.51 (m, 4H, H-11, H-13, $H_{2',6'}$ from Ar), 7.38 (m, 1H, H-12), 6.94 (m, 2H, H-7, H-8), 6.56 (d, $^3J_{H6,H7}$ = 7.2 Hz, 1H, H-6), 5.98 (s, 1H, H-13b), 5.96 (s, 1H, H-3), 4.59 (s, 1H, OH), 4.03, 3.92 (m, 2H, $C\underline{H}_2$ from OEt), 3.78 (s, 3H, $OC\underline{H}_3$-4'), 0.93 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, $C\underline{H}_3$ from OEt) ppm.

^{13}C NMR (100.62 MHz, $CDCl_3$): δ 170.5 (C-14), 160.8 ($C_{4'}$ from Ar), 146.8 (C-4), 138.8 (C-9b), 131.2 (C-5a), 128.0 ($C_{1'}$ from Ar), 129.8 (C-11), 129.3 (C-13), 128.4 (C-13a), 128.3 (C-7), 127.8 (C-9), 127.6 ($C_{2',6'}$ from Ar), 123.7 (C-12), 122.3 (C-8), 121.8 (C-9a), 120.9 (C-10), 119.6 (C-6), 114.5 ($C_{3',5'}$ from Ar), 113.2 (C-3), 93.0 (C-2), 81.2 (C-13b), 62.8 ($\underline{C}H_2$ from OEt), 55.4 ($O\underline{C}H_3$-4'), 13.7 ($\underline{C}H_3$ from OEt) ppm.

$C_{26}H_{23}NO_5$ (429.47): calcd C 72.71; H 5.40, N 3.26; found C 72.74; H 5.38, N 3.26.

Ethyl (2R,13bR*)-4-(3-fluorophenyl)-2-hydroxy-2H,13bH-[1,3]oxazino[3,2-f]phenanthridine-2-carboxylate (**3d**):* Analogously from phenanthridine **1** (90 mg, 0.5 mmol), acetylene **2d** (0.110 mg, 0.5 mmol), H_2O (45 mg, 2.5 mmol), and MeCN (0.5 ml), 20-25 °C, 24 h, oxazinophenanthridine **3d** was obtained (90 mg, 43%) as a light-beige powder, mp 170-172 °C (MeCN). Initial phenanthridine **1** (32 mg, conversion was 64%) was recovered.



IR (microlayer): 1036, 1093, 1140, 1197, 1265 (C-O-C), 1584, 1608, 1641 (C=C), 1737 (C=O), 3483 (OH) cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.98 (d, $^3J_{H8,H9}$ = 7.6 Hz, 1H, H-9), 7.87 (m, 1H, H-10), 7.52 (m, 1H, $H_{5'}$ from Ar), 7.50 (m, 1H, H-13), 7.40 (m, 1H, H-11), 7.38 (m, 1H, $H_{6'}$ from Ar), 7.32 (m, 1H, H-12), 7.27 (m, 1H, $H_{2'}$ from Ar), 7.04 (m, 1H, $H_{4'}$ from Ar), 6.97 (m, 2H, H-7, H-8), 6.50 (m, 1H, H-6), 6.11 (s, 1H, H-13b), 5.95 (s, 1H, H-3), 4.62 (s, 1H, OH), 4.03, 3.95 (m, 2H, $C\underline{H}_2$ from OEt), 0.95 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, $C\underline{H}_3$ from OEt) ppm.

^{13}C NMR (100.62 MHz, $CDCl_3$): δ 170.0 (C-14), 163.4 (d, $^1J_{C,F}$ = 245.0 Hz, $C_{3'}$ from Ar), 146.0 (C-4), 138.4 (C-9b), 137.9 (d, $^3J_{C,F}$ = 7.7 Hz, $C_{1'}$ from Ar), 131.1 (C-5a), 130.8 (d, $^3J_{C,F}$ = 8.0 Hz, $C_{5'}$ from Ar), 130.0 (C-11), 129.3 (C-13), 128.4 (C-7), 128.2 (C-13a), 127.9 (C-9), 123.9 (C-12), 122.3 (C-8), 121.9 (C-9a), 121.8 ($C_{6'}$ from Ar), 121.3 (C-10), 119.4 (C-6), 116.5 (d, $^2J_{C,F}$ = 21.2 Hz, $C_{4'}$ from Ar), 116.1 (C-3), 113.1 (d, $^2J_{C,F}$ = 22.8 Hz, $C_{2'}$ from Ar), 92.7 (C-2), 81.3 (C-13b), 62.9 ($\underline{C}H_2$ from OEt), 13.7 ($\underline{C}H_3$ from OEt) ppm.

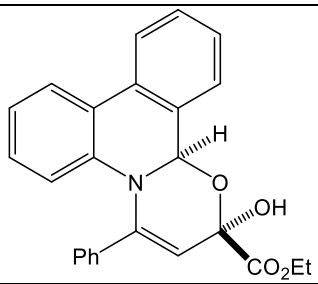
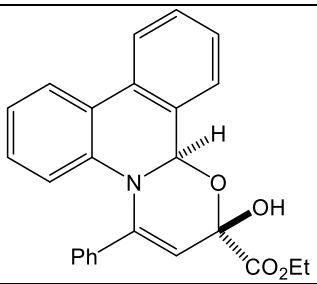
^{19}F NMR (376.5 MHz, $CDCl_3$): δ -111.9 (m, F-3') ppm.

$C_{25}H_{20}FNO_4$ (417.44): calcd C 71.93; H 4.83, F 4.55, N 3.36; found C 71.90; H 4.84, F 4.57, N 3.34.

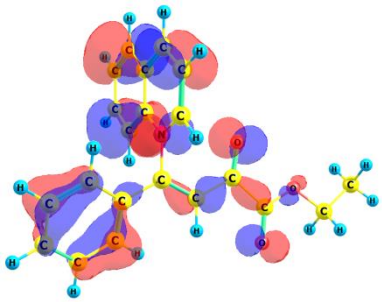
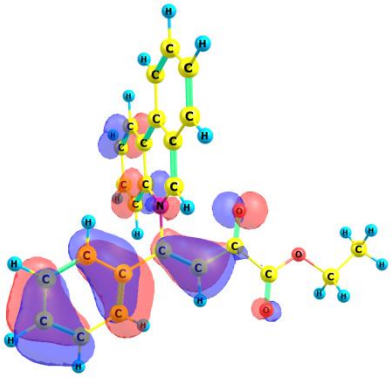
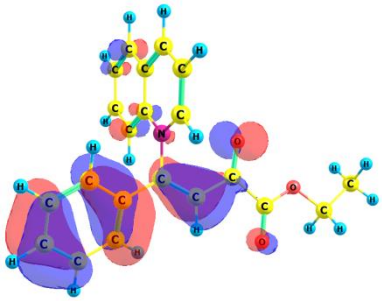
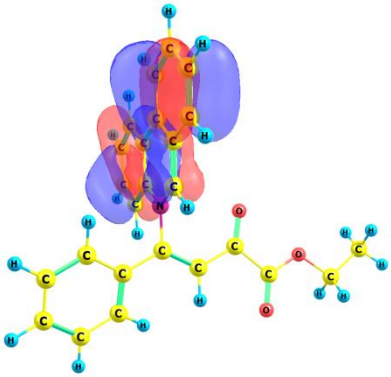
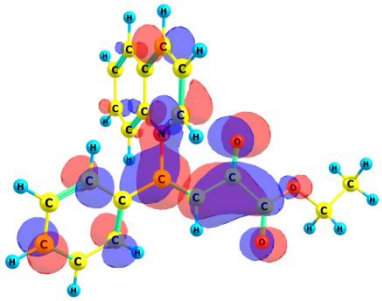
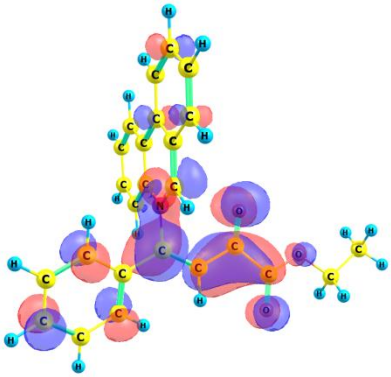
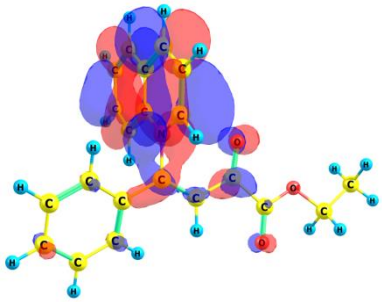
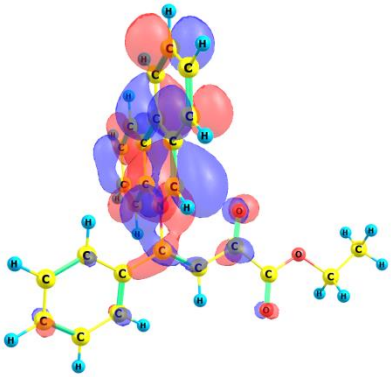
Computational details

All calculations were performed with full geometry optimization at the Becke's three-parameter hybrid exchange functional with the Lee-Yang-Parr correlation functional (B3LYP) [S2, S3] employing 6-311++G(d,p) basis set. Solvation effect on the mechanism was examined for acetonitrile, using the integral equation formalism polarizable continuum model (IEF-PCM) throughout the manuscript. For each stationary point, second derivatives of the energy with respect to the Cartesian nuclear coordinates were calculated to confirm whether these structures were local minima or transition states. To achieve more accurate total energies, MP2/6-311++G(d,p) single point calculation was performed utilizing optimized geometry at B3LYP/6-311++G(d,p). For comparison, the long-range corrected density functional with atom-atom dispersion correction ωB97X-D3 using the same basis set was also tested [S4]. Throughout the Results and Discussion section, if not stated otherwise, "energy" [taking into account ZPVE correction calculated at MP2/6-311++G(d,p)//B3LYP/6-311++G(d,p)] and "geometrical parameters" refer to the B3LYP/6-311++G(d,p) calculations. All calculations were performed using the Gaussian09 suite of programs [S5]. For structure visualization, ChemCraft 1.8 was employed [S6]. Charge model 5 (CM5) charges proposed by Truhlar et al. [S7], Laplacian bond orders (LBO) [S8] as well as condensed Fukui functions analysis were performed using Multiwfn 3.7. [S9].

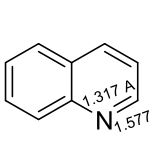
Table S1 Relative stability of 2-hydroxyoxazinophenanthridine (kcal mol^{-1})

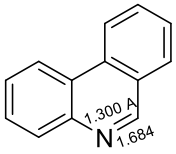
Energy parameter		
MP2//B3LYP/6-311++(d,p)		
ΔH^0	0.0	3.5
ΔG^0	0.0	3.4
ωB97X-D3/6-311++(d,p)		
ΔH^0	0.0	3.7
ΔG^0	0.0	3.5

The analysis of protonated 1,3-dipole B boundary orbitals on the HF/cc-pVTZ level

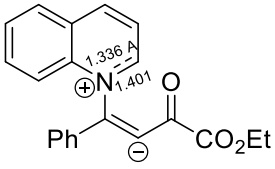
for quinoline	for phenanthridine
	
HOMO-1 (-0.2829 Eh)	HOMO-1 (-0.2721 Eh)
	
HOMO (-0.2725 Eh)	HOMO (-0.2693 Eh)
	
LUMO (-0.1364 Eh)	LUMO (-0.1362 Eh)
	
LUMO+1 (-0.1234 Eh)	LUMO+1 (-0.1213 Eh)

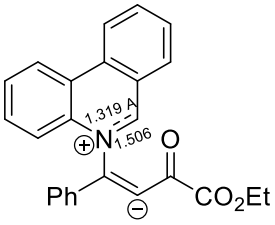
Lengths (Å) and LBO orders of C-N bond in quinoline and phenanthridine



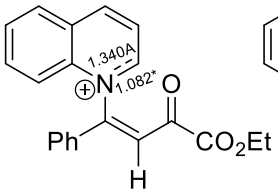


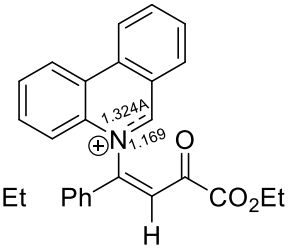
Lengths (Å) and LBO orders of C-N bond in 1,3-dipoles of quinoline or phenanthridine and phenyloxalylacetylene





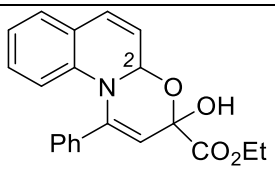
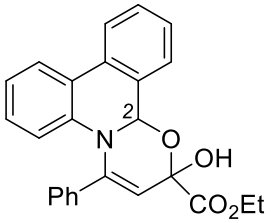
Lengths (Å) and LBO orders of C-N bond in protonated 1,3-dipoles of quinoline or phenanthridine and phenyloxalylacetylene

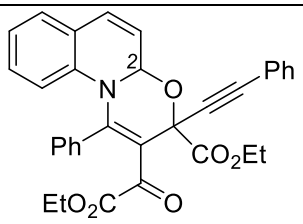
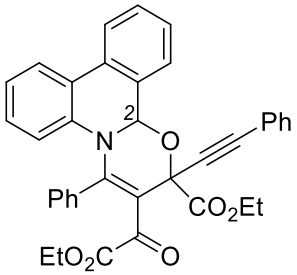




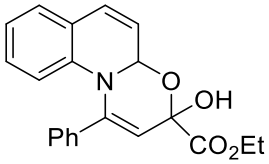
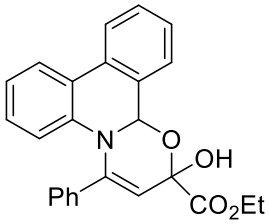
*The order is close to ordinary C-N bond.

Analysis of bond lengths and orders in oxazinoazines of the composition quinoline+acetylene+water (**1a**) and quinoline+2×acetylene (**2a**) for phenanthridine (**1b**) and (**2b**), respectively.

Compound	C2···O, Å	C2–O bond order	C2···N, Å	C2–N bond order
 **1a**	1.461	0.330	1.449	0.912
 **1b**	1.457	0.349	1.444	0.941

 **2a**	1.439	0.388	1.460	0.870
 **2b**	1.438	0.393	1.452	0.905

Relative stability of 2-hydroxyoxazinoazines with respect to nonreacting system [quinoline (phenanthridine) + acetylene + water] calculated at MP2//B3LYP/6-311++(d,p) and *ω*B97X-D3/6-311++(d,p) (in brackets)

Energy parameter		
ΔE^1	-38.2 (-39.2)	-46.3 (-45.3)
$\Delta E+ZPVE^2$	-31.0 (-31.7)	-39.0 (-37.8)
ΔH^0	-33.4 (-34.1)	-41.4 (-40.2)
ΔG^0	-4.9 (-5.7)	-12.8 (-11.7)

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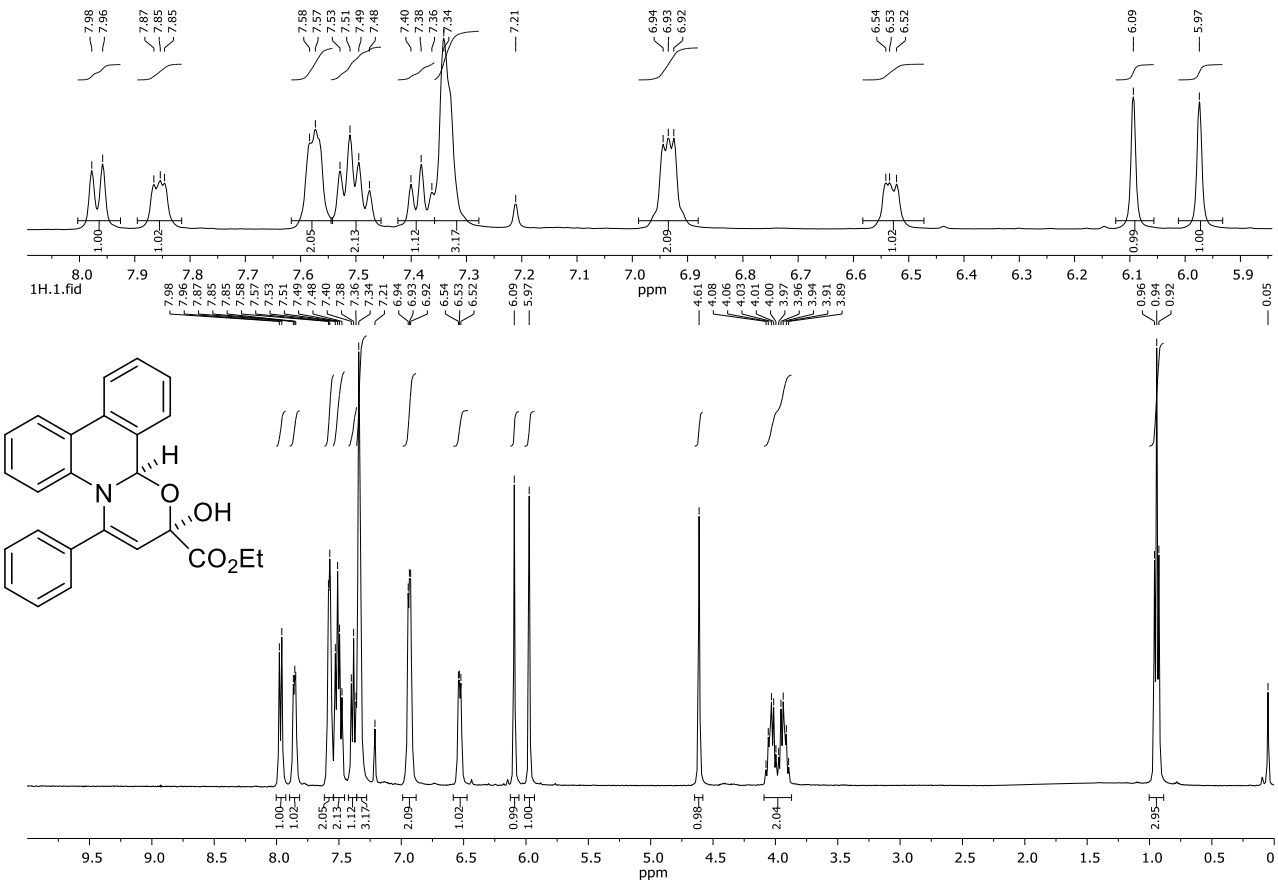
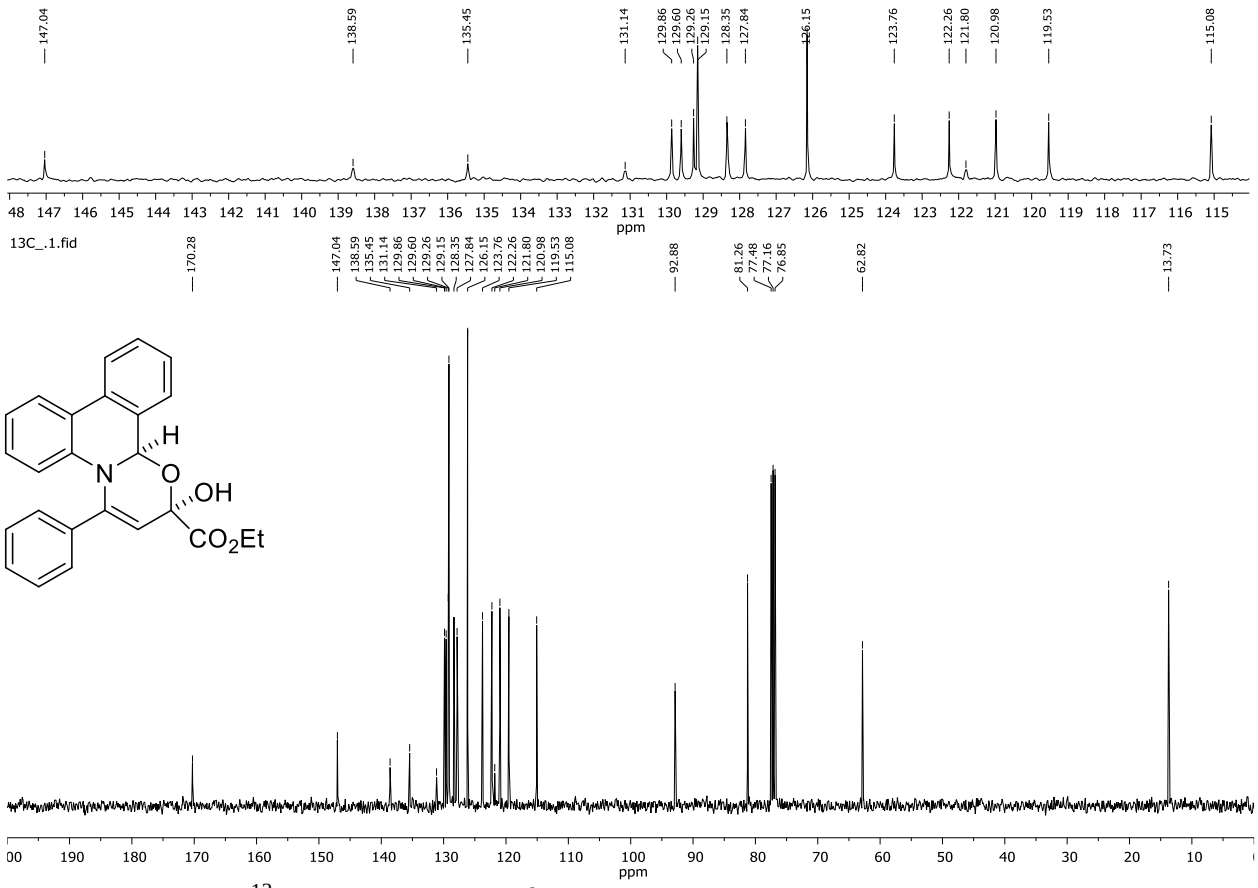
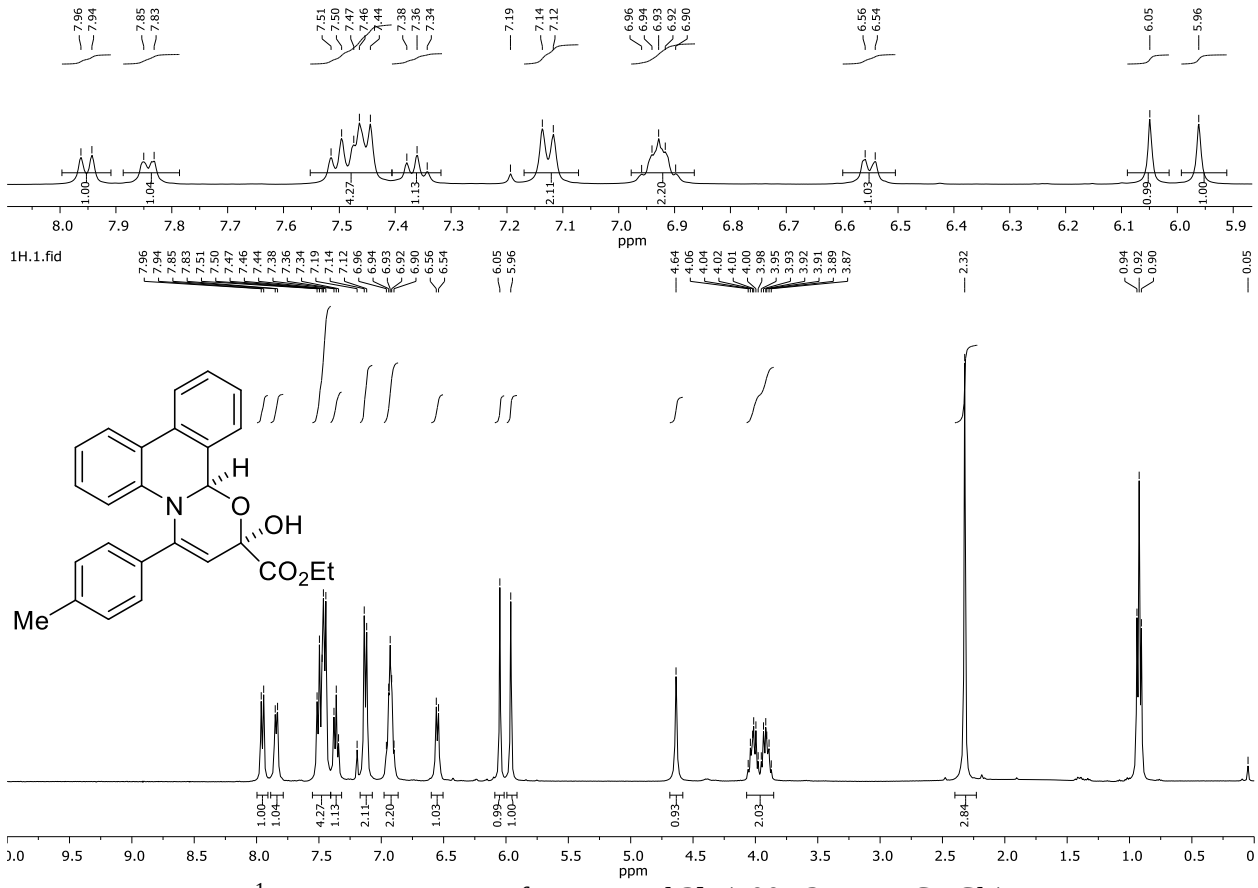
Copies of NMR Spectra



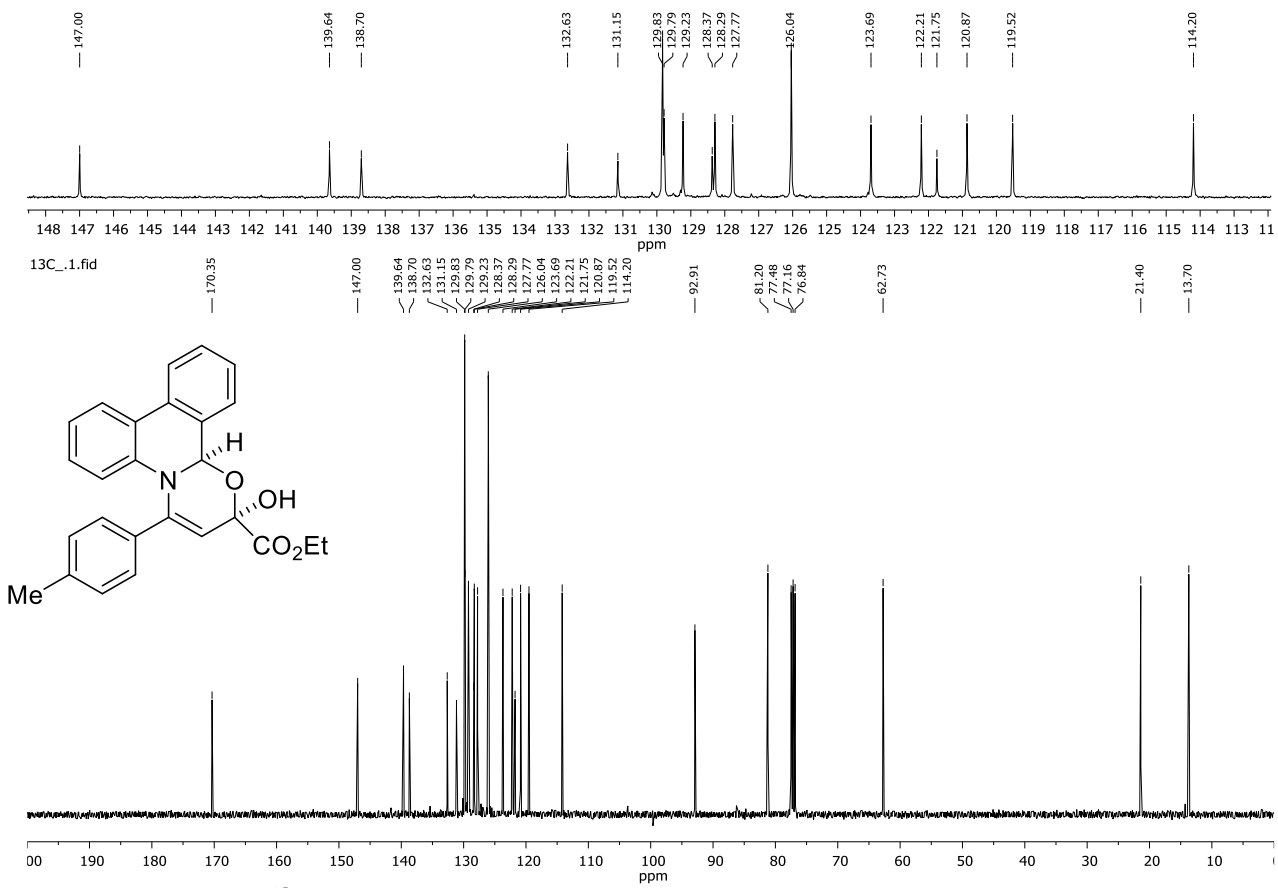
^{1}H NMR spectrum of compound **3a** (400.13 MHz, $CDCl_3$)



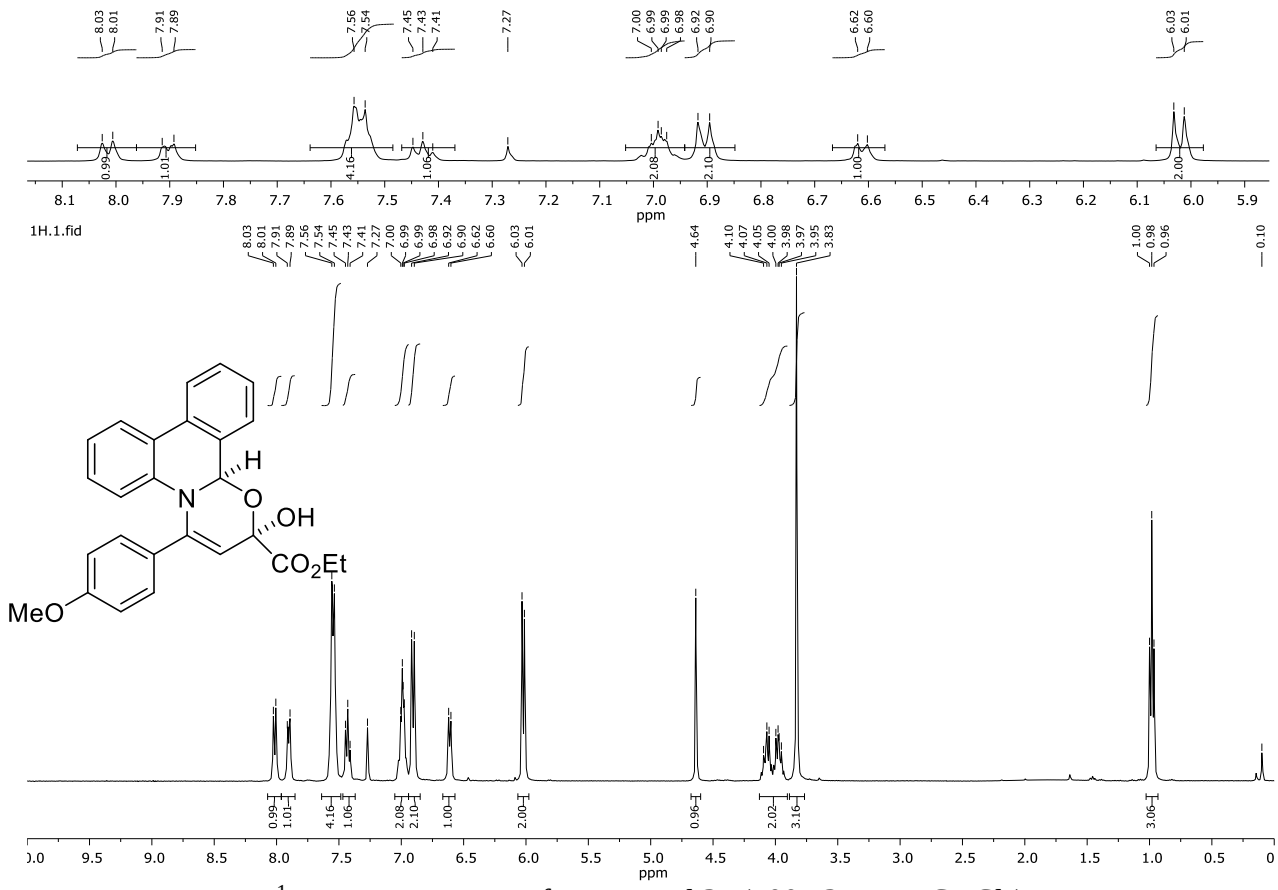
^{13}C NMR spectrum of compound **3a** (100.62 MHz, $CDCl_3$)



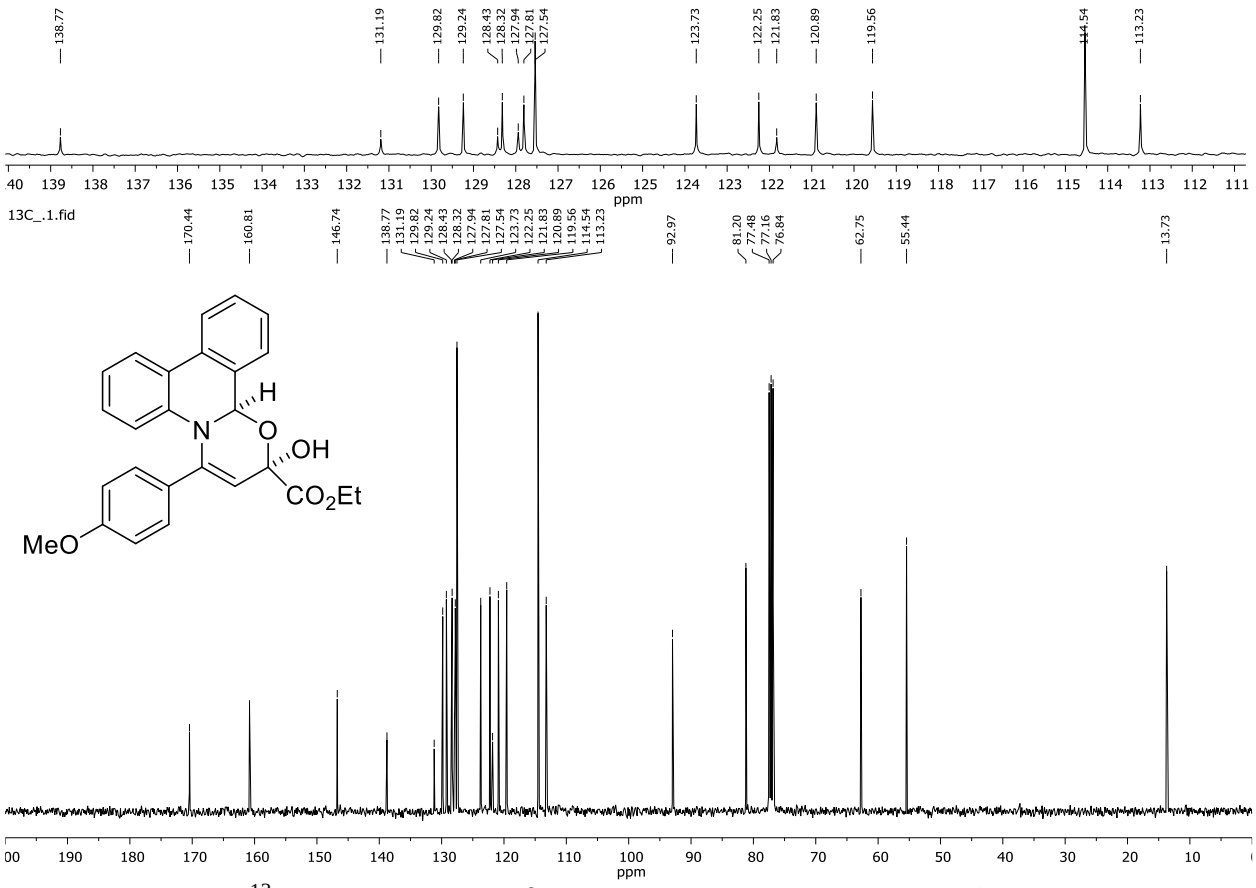
^{1}H NMR spectrum of compound **3b** (400.13 MHz, $CDCl_3$)



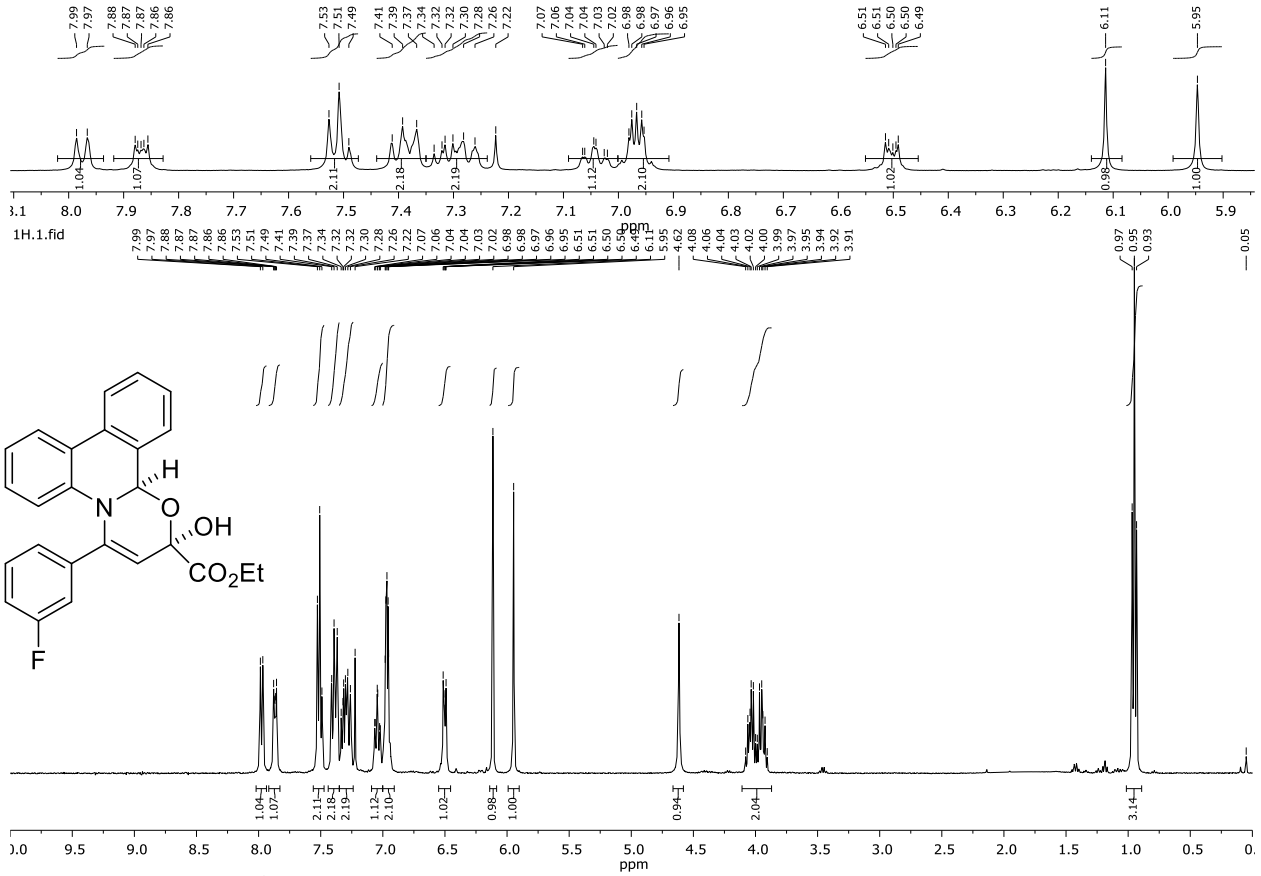
^{13}C NMR spectrum of compound **3b** (100.62 MHz, $CDCl_3$)



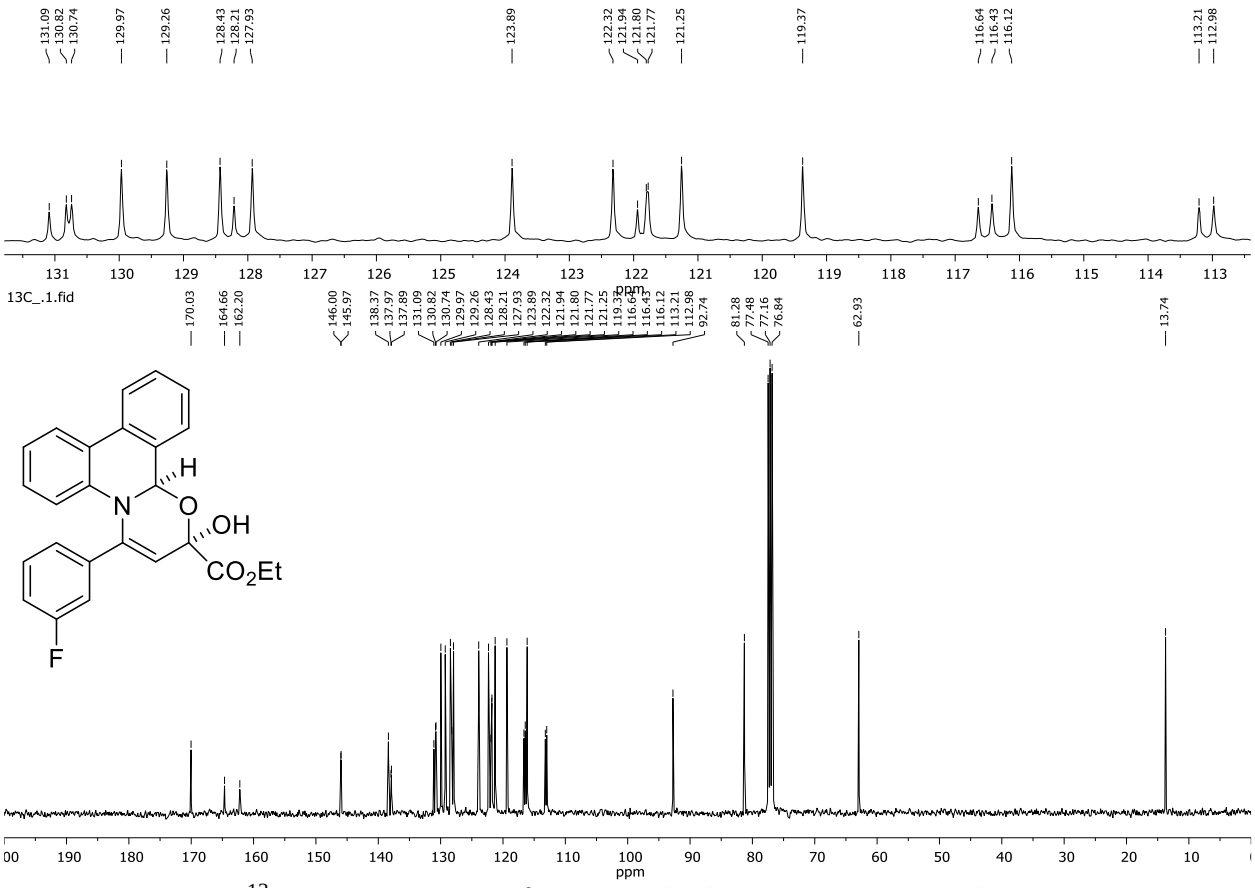
^{1}H NMR spectrum of compound **3c** (400.13 MHz, $CDCl_3$)



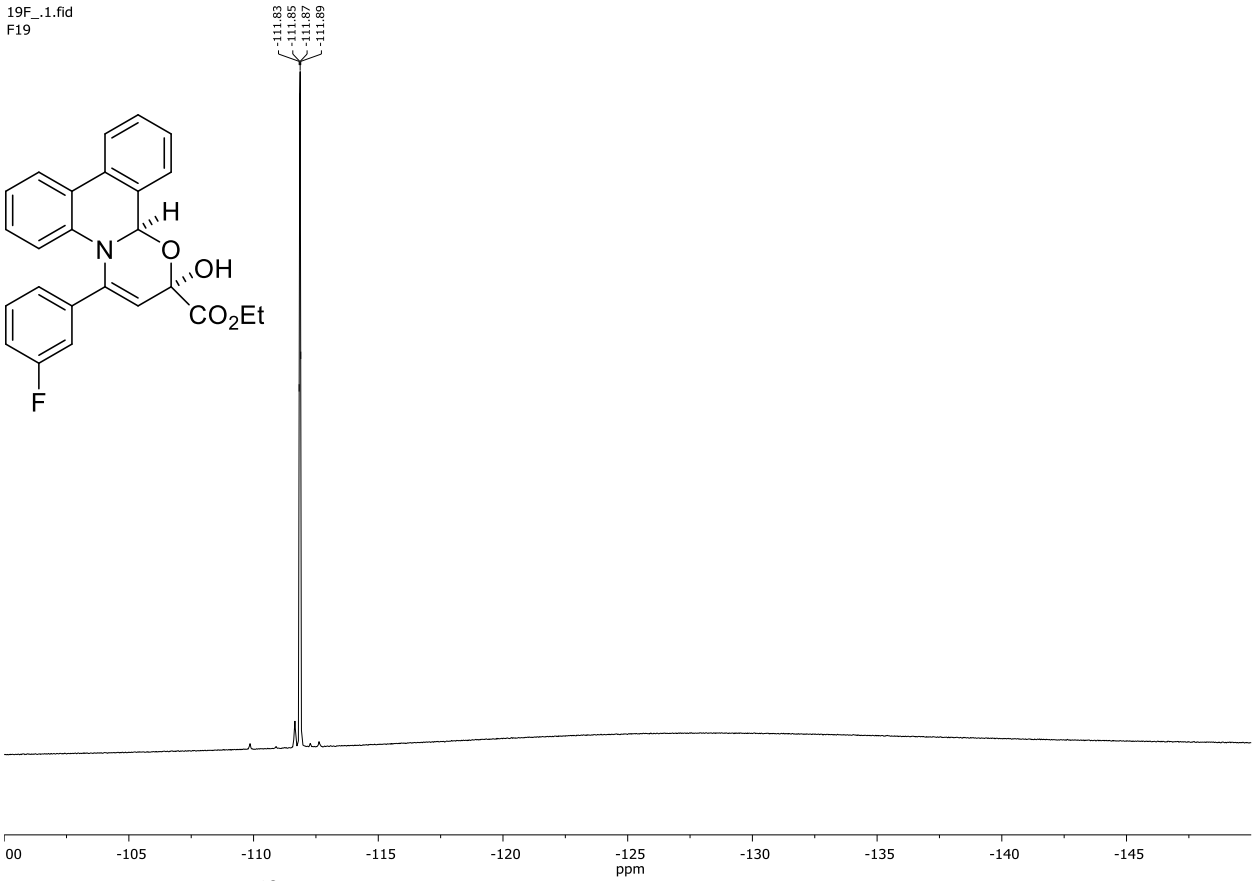
^{13}C NMR spectrum of compound **3c** (100.62 MHz, $CDCl_3$)



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



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



^{19}F NMR spectrum of compound **3d** (376.5 MHz, $CDCl_3$)