

SUPPORTING INFORMATION

Catalytic [4+n]-cycloaddition using furan-fused cyclobutanone as a privileged C4 synthon

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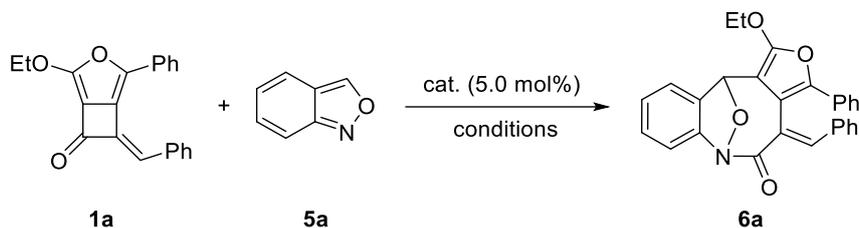
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General Information

All reactions were carried out in oven-dried glassware. Solvents were purified and distilled by following the standard methods. Flash column chromatography was performed using silica gel (300-400 mesh). Analytical thin-layer chromatography was performed using glass plates pre-coated with 200-300 mesh silica gel impregnated with a fluorescent indicator (254 nm). The ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded in CDCl_3 on 400 MHz and 500 MHz spectrometer; chemical shifts were reported in ppm with the solvent signal as reference, and coupling constants (J) were given in Hertz. The peak information was described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite. The enantioselectivity was determined on HPLC using Daicel Chiralpak IA and IC column. High-resolution mass spectra (HRMS) were recorded on a commercial apparatus (ESI Source). All substrates whose syntheses were not described herein were either obtained from commercial suppliers or prepared using the referenced literature procedures¹⁻⁴. Unless stated otherwise, all commercially available compounds were used as received.

Optimization of the Reaction Conditions

Table S1 | Condition optimization for the [4+4]-cycloaddition^a

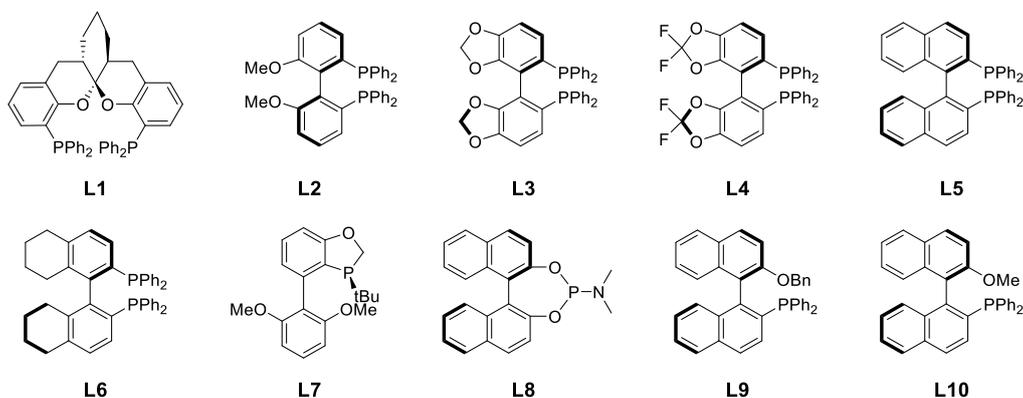
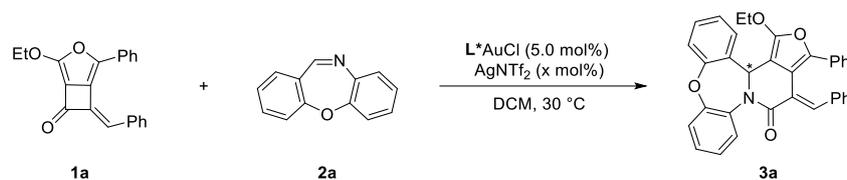


Entry	Cat. (5.0 mol%)	Solvent	<i>T</i> (°C)	Yield (%) ^b
1	Pd ₂ (dba) ₃	DCE	40	ND ^c
2	Rh(COD) ₂ BF ₄	DCE	40	NR ^d
3	Cu(OTf) ₂	DCE	40	36
4	Fe(OTf) ₃	DCE	40	21
5	Sc(OTf) ₃	DCE	40	17
6	AgSbF ₆	DCE	40	38
7	PPh ₃ AuNTf ₂	DCE	40	62
8	IPrAuNTf ₂	DCE	40	83
9	Me ₃ (OMe) <i>t</i> BuXPhosAuNTf ₂	DCE	40	61
10	JohnPhosAu(MeCN)SbF₆	DCE	40	98(93)^e
11	JohnPhosAu(MeCN)SbF ₆	DCM	40	86
12	JohnPhosAu(MeCN)SbF ₆	THF	40	37
13	JohnPhosAu(MeCN)SbF ₆	EtOAc	40	30
14	JohnPhosAu(MeCN)SbF ₆	<i>p</i> -xylene	40	19 ^f
15	JohnPhosAu(MeCN)SbF ₆	PhCF ₃	40	78
16	JohnPhosAu(MeCN)SbF ₆	DCE	60	90
17	JohnPhosAu(MeCN)SbF ₆	DCE	25	92

^aThe reaction was carried out on a 0.1 mmol scale. To a solution of **1a** (31.6 mg, 0.1 mmol) and **5a** (13.1 mg, 0.11 mmol, 1.1 equiv.) in 1.0 mL solvent, was added a solution of catalyst (5.0 mol%) in 1.0 mL same solvent *via* syringe under argon atmosphere at indicated temperature, and the reaction mixture was stirred for 18 h under these conditions.

^bDetermined by ¹H NMR analysis of the crude reaction mixture based on internal standard (1,3,5-trimethoxybenzene). ^cND = not detected. ^dNR = not reaction. ^eIsolated yield. ^fMost of the starting material **1a** and **5a** was recovered.

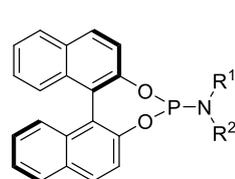
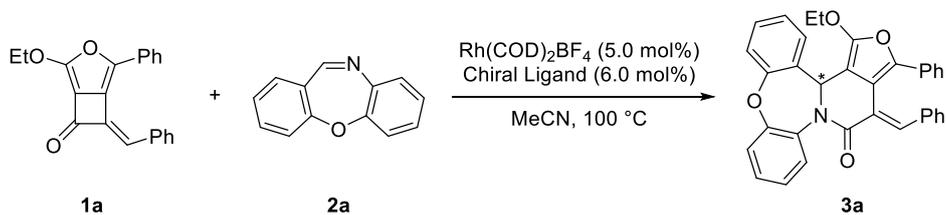
Table S2 | Screening of chiral gold catalysts for the [4+2]-cycloaddition^a



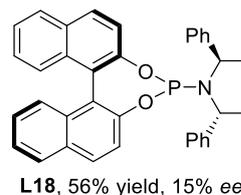
Entry	[Au]	$AgNTf_2$ (x mol%)	Yield (%) ^b	<i>ee</i> (%) ^c
1	L1 (AuCl) ₂	10	44	19
2	L2 (AuCl) ₂	10	18	5
3	L3 (AuCl) ₂	10	54	0
4	L4 (AuCl) ₂	10	61	5
5	L5 (AuCl) ₂	10	30	5
6	L6 (AuCl) ₂	10	39	0
7	L7 AuCl	5.0	27	5
8	L8 AuCl	5.0	13	22
9	L9 AuCl	5.0	36	40
10	L10 AuCl	5.0	41	13

^aThe reaction was carried out on a 0.1 mmol scale. To a solution of **1a** (31.6 mg, 0.1 mmol) and **2a** (19.5 mg, 0.11 mmol, 1.1 equiv.) in 1.0 mL DCM, was added a solution of gold catalyst (5.0 mol%) and $AgNTf_2$ (10 or 5.0 mol%) in 1.0 mL DCM *via* syringe under argon atmosphere at 30 °C, and the reaction mixture was stirred for 12 h under these conditions. ^bDetermined by ¹H NMR analysis of the crude reaction mixture based on limited reagent **2a** with mesitylene as internal standard. ^cDetermined by Chiral HPLC analysis with Chiralpak IC column.

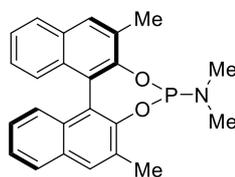
Table S3 | Screening of chiral ligands for the Rh-catalyzed enantioselective [4+2]-cycloaddition^a



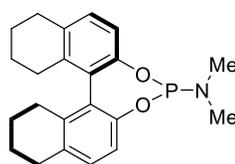
L11, R¹ = R² = Me, 91% yield, 73% ee
L12, R¹ = R² = Et, 89% yield, 20% ee
L13, R¹ = R² = *i*Pr, 68% yield, 53% ee
L14, R¹ = R² = *n*Pr, 60% yield, 55% ee
L15, R¹ = Ph, R² = Me, 57% yield, 0% ee
L16, R¹ = Bn, R² = Me, 55% yield, 55% ee
L17, R¹ = Allyl, R² = Me, 66% yield, 23% ee



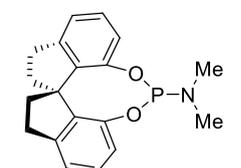
L18, 56% yield, 15% ee



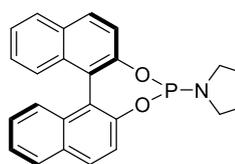
L19, 75% yield, 65% ee



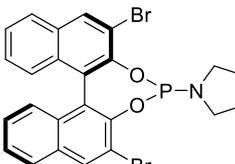
L20, 20% yield, 0% ee



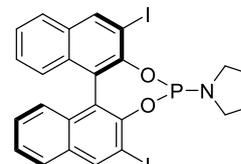
L21, 59% yield, 37% ee



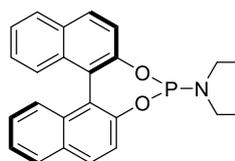
L22, 71% yield, 84% ee



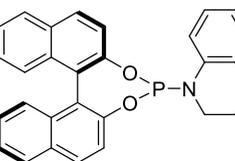
L23, 65% yield, -27% ee



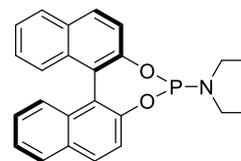
L24, 6% yield, 15% ee



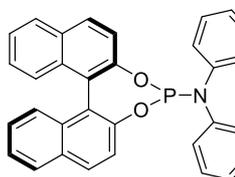
L25, 67% yield, 55% ee



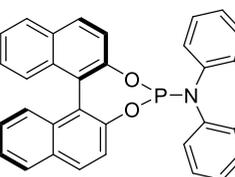
L26, 63% yield, -25% ee



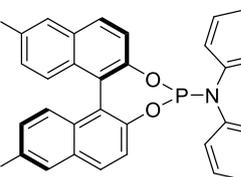
L27, 61% yield, 51% ee



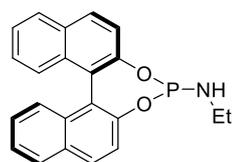
L28, 60% yield, -41% ee



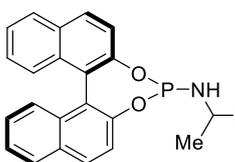
L29, 72% yield, -40% ee



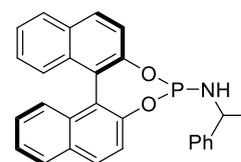
L30, 65% yield, -45% ee



L31, 61% yield, 55% ee

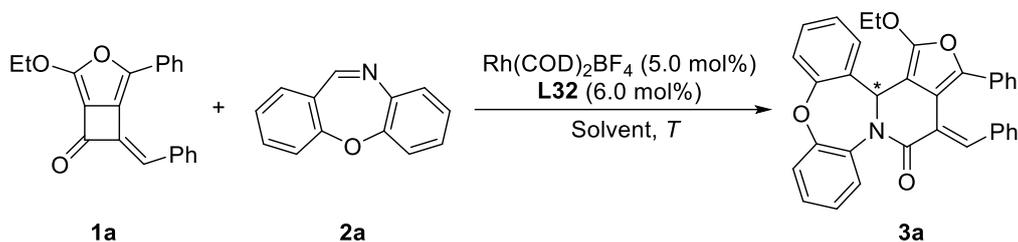


L32, 65% yield, 93% ee



L33, 70% yield, -83% ee

Table S4 | Condition optimization for the Rh-catalyzed enantioselective [4+2]-cycloaddition^a



Entry	Solvent	<i>T</i> (°C)	Yield (%) ^b	<i>ee</i> (%) ^c
1	THF	100	56	-75
2	toluene	100	35	-61
3	<i>p</i> -xylene	100	35	-65
4	MeNO ₂	100	45	0
5	1,4-dioxane	100	36	-75
6	PhCl	100	49	-55
7	PhCF ₃	100	20	0
8 ^d	MeCN	100	50	89
9 ^e	MeCN	100	65	93
10 ^f	MeCN	100	52	91
11 ^e	MeCN	100	51	94
12 ^e	MeCN	100	45	95
13 ^e	MeCN	80	28	91
14 ^e	MeCN	95	39	90
15 ^e	MeCN	100	65	93
16 ^e	MeCN	105	46	90
17 ^e	MeCN	120	17	81
18 ^e	MeCN	140	20	71
19 ^{d,e}	MeCN	100	67	93
20^{d,e,g}	MeCN	100	70	93
21 ^{d,e,h}	MeCN	100	69	93

^aThe reaction was carried out on a 0.1 mmol scale. To a solution of **1a** (31.6 mg, 0.1 mmol) and **2a** (21.5 mg, 0.11 mmol, 1.1 equiv.) in 1.0 mL solvent, was added a solution of Rh(COD)₂BF₄ (2.0 mg, 5.0 mol%) and **L32** (2.3 mg, 6.0 mol%) in 1.0 mL same solvent *via* syringe at 100 °C under argon atmosphere, and the reaction mixture was stirred for 12 h under these conditions.

^bDetermined by ¹H NMR analysis of the crude reaction mixture based on internal standard (1,3,5-trimethoxybenzene). ^cDetermined by chiral HPLC analysis with a Chiralpak IC column.

^dRh(COD)₂BF₄ (10 mol%) and **L32** (12 mol%) were added. ^e50.0 mg 4Å MS was used as additive.

^f50.0 mg 5Å MS was used as additive. ^g**1a** (0.12 mmol) and **2a** (0.1 mmol) was added. ^h**1a** (0.2 mmol and **2a** (0.1 mmol) was added.

Table S5 | Screening of chiral ligands for the enantioselective [4+4]-cycloaddition^a

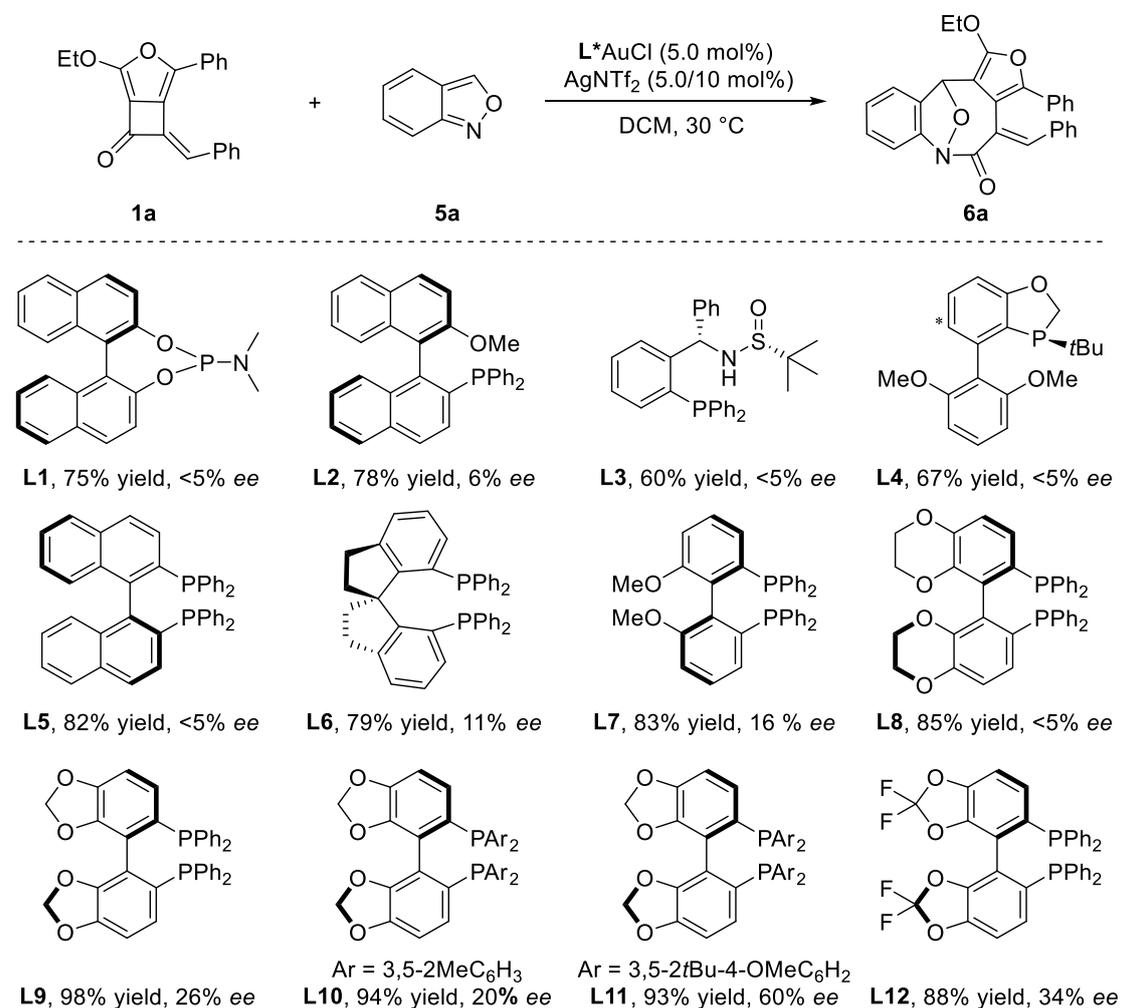
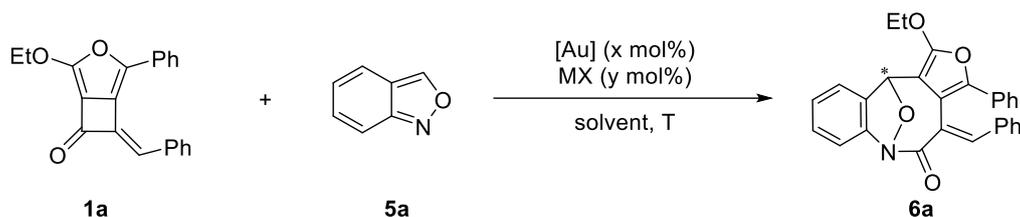


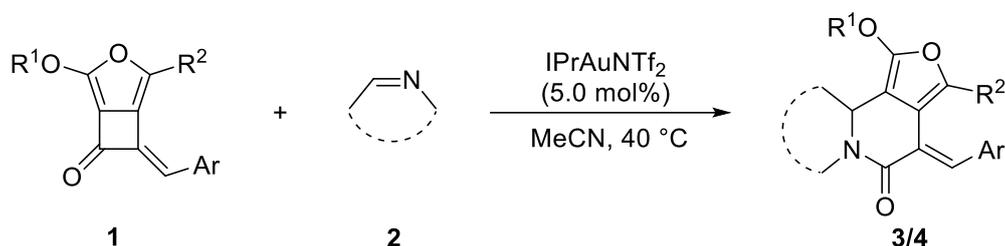
Table S6 | Condition optimization for the enantioselective [4+4]-cycloaddition^a

Entry	[Au] (x mol%)	MX (y mol%)	Solvent	Yield (%) ^b	ee (%) ^c
1	L11 (AuCl) ₂ (5.0)	AgOTf (10)	DCM	85	49
2	L11 (AuCl) ₂ (5.0)	AgSbF ₆ (10)	DCM	93	64
3	L11 (AuCl) ₂ (5.0)	AgBF ₄ (10)	DCM	82	57
4	L11 (AuCl) ₂ (5.0)	NaBARF (10)	DCM	83	57
5	L11 (AuCl) ₂ (5.0)	AgSbF ₆ (5.0)	DCM	80	60
6	L11 (AuSbF ₆) ₂ (5.0)	-	DCM	91	64
7	L11 (AuSbF ₆) ₂ (5.0)	-	DCE	87	56
8	L11 (AuSbF ₆) ₂ (5.0)	-	PhCF ₃	85	40
9	L11 (AuSbF ₆) ₂ (5.0)	-	EtOAc	60	49
10 ^d	L11 (AuSbF ₆) ₂ (5.0)	-	DCM	94	60
11 ^e	L11 (AuSbF ₆) ₂ (5.0)	-	DCM	93	62
12 ^f	L11 (AuSbF ₆) ₂ (5.0)	-	DCM	90	59
13 ^g	L11 (AuSbF ₆) ₂ (5.0)	-	DCM	trace	-
14	L11 (AuSbF ₆) ₂ (10)	-	DCM	91	68

^aTo a solution of gold catalyst (x mol%) in 1.0 mL indicated solvent, was added a solution of **1a** (22.8 mg, 0.072 mmol, 1.2 equiv.) and **5a** (7.1 mg, 0.06 mmol) in the same solvent (1.0 mL) *via* syringe under argon atmosphere at room temperature, and the reaction mixture was stirred under these conditions. ^bDetermined by ¹H NMR analysis of the crude reaction mixture based on limited reagent **5a** with mesitylene as internal standard. ^cDetermined by Chiral HPLC analysis with Chiralpak OD-H column. ^d50 mg 3 Å MS was added. ^e50 mg 4 Å MS was added. ^f50 mg 5 Å MS was added. ^gThe reaction was conducted at 0 °C and most of the starting material **1a** and **5a** was recovered.

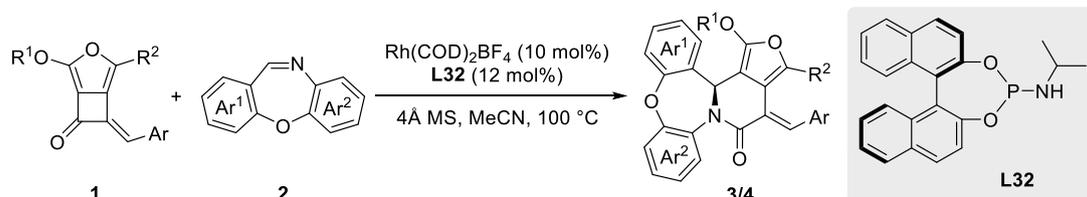
General Procedure for the [4+2] Cycloaddition Reaction

Condition A:

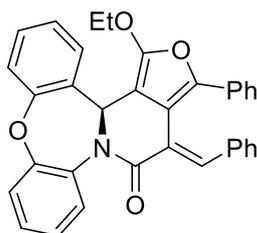


To a 10-mL oven-dried vial containing a magnetic stirring bar, cyclobutanone **1** (0.12 mmol, 1.2 equiv.), imine **2** (0.1 mmol, 1.0 equiv.), IPrAuNTf₂ (4.3 mg, 5.0 mol%), and MeCN (2.0 mL) were added sequentially under argon atmosphere. After addition, the reaction mixture was stirred overnight at 40 °C until consumption of the material (monitored by TLC). The solvent was evaporated in vacuo. Then, the residues was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 50:1 to 10:1) to give the pure products **3** or **4** in good to high yields.

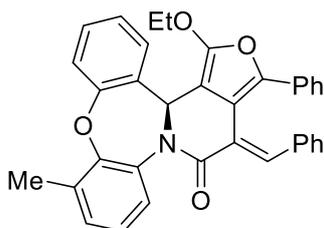
Condition B:



To a 10-mL oven-dried vial containing a magnetic stirring bar, cyclobutanone **1** (0.12 mmol, 1.2 equiv.), imine **2** (0.1 mmol, 1.0 equiv.), Rh(COD)₂BF₄ (4.0 mg, 10 mol%), 4 Å MS (50 mg), chiral ligand **L32** (4.6 mg, 12 mol%), and MeCN (2.0 mL) were added sequentially under argon atmosphere at 100 °C. After addition, the reaction mixture was stirred overnight under these conditions until consumption of the material (monitored by TLC). The solvent was evaporated in vacuo. Then the residues was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 50:1 to 10:1) to give the pure products **3** or **4** in good to high yields with generally excellent enantioselectivity.

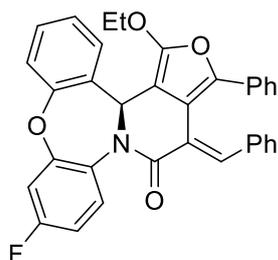


(*S,E*)-15-Benzylidene-3-ethoxy-1-phenyl-3*Bh*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3a). Condition A: 45.0 mg, 88% yield, Condition B: 35.8 mg, 70% yield; 93% *ee*, $[\alpha]_D^{20} = 413.0$ ($c = 0.033$, CH_2Cl_2); Yellow solid, m.p. = 105.3 - 107.2 °C; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.53 (s, 1H), 7.48 (d, $J = 8.0$ Hz, 1H), 7.32 - 7.28 (comp, 3H), 7.25 - 7.17 (comp, 5H), 7.14 - 7.07 (m, 2H), 6.99 - 6.91 (comp, 7H), 6.30 (s, 1H), 4.43 - 4.31 (m, 2H), 1.41 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 167.9, 154.7, 153.2, 149.9, 139.2, 135.8, 135.6, 131.4, 130.9, 130.8, 129.8, 129.3, 129.0, 128.8, 127.84, 127.80, 127.6, 127.0, 126.0, 125.0, 123.6, 123.1, 122.6, 121.3, 121.0, 115.3, 94.6, 68.7, 54.7, 15.4; HRMS (TOF MS ESI⁺) calculated for $\text{C}_{34}\text{H}_{25}\text{NO}_4\text{Na}[\text{M}+\text{Na}]^+$: 534.1676, found 534.1675; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 11.7$ min, $t_{\text{major}} = 17.9$ min.

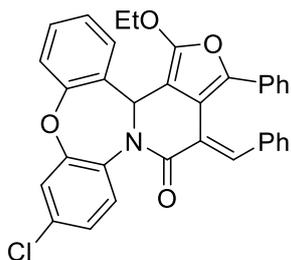


(*S,E*)-15-Benzylidene-3-ethoxy-9-methyl-1-phenyl-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3b). Condition A: 47.3 mg, 90% yield, Condition B: 32.6 mg, 62% yield; 96% *ee*, $[\alpha]_D^{20} = 570.1$ ($c = 0.033$, CH_2Cl_2); Yellow solid, m.p. = 100.6 - 102.5 °C; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.55 (s, 1H), 7.29 - 7.25 (comp, 3H), 7.21 - 7.16 (comp, 6H), 7.03 (t, $J = 6.5$ Hz, 1H), 6.96 - 6.90 (comp, 7H), 6.16 (s, 1H), 4.47 - 4.35 (m, 2H), 2.46 (s, 3H), 1.43 (t, $J = 5.6$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) (δ , ppm) 168.2, 154.4, 153.3, 149.5, 139.2, 135.63, 135.58, 132.4, 130.81, 130.78, 130.5, 129.7, 129.5, 129.0, 128.7, 127.8, 127.5, 126.90,

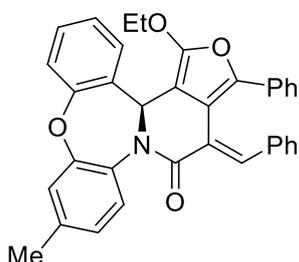
126.88, 126.7, 125.0, 123.4, 123.1, 122.8, 121.2, 115.3, 95.6, 68.6, 55.1, 17.2, 15.4; HRMS (TOF MS ESI⁺) calculated for C₃₅H₂₇NO₄Na[M+Na]⁺: 548.1832, found 548.1829; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, *t*_{minor} = 12.1 min, *t*_{major} = 14.0 min.



(*S,E*)-15-Benzylidene-3-ethoxy-10-fluoro-1-phenyl-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3c). **Condition A:** 45.5 mg, 86% yield, **Condition B:** 35.5 mg, 67% yield. 95% *ee*, [α]_D²⁰ = - 9.0 (c = 0.033, CH₂Cl₂); Yellow oil. ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.53 - 7.52 (m, 1H), 7.45 - 7.42 (m, 1H), 7.31 - 7.29 (m, 2H), 7.26 - 7.12 (comp, 5H), 7.01 - 6.95 (comp, 8H), 6.84 - 6.81 (m, 1H), 6.27 - 6.25 (m, 1H), 4.45 - 4.33 (m, 2H), 1.45 - 1.40 (m, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 168.0, 161.2 (d, *J* = 246.6 Hz), 154.2, 153.2, 150.6 (d, *J* = 12.0 Hz), 139.3, 135.9, 135.5, 131.3, 130.7, 130.4 (d, *J* = 9.8 Hz), 129.9, 129.0, 128.9, 127.9, 127.6, 127.1, 127.0, 126.1, 125.0, 123.9, 122.9, 120.9, 115.2, 109.9 (d, *J* = 22.4 Hz), 108.2 (d, *J* = 25.4 Hz), 94.3, 68.7, 54.6, 15.4; ¹⁹F NMR (376 MHz, CDCl₃) (δ, ppm) -113.94; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₄FNO₄Na[M+Na]⁺: 552.1582, found 552.1583; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, *t*_{minor} = 8.4 min, *t*_{major} = 10.9 min.

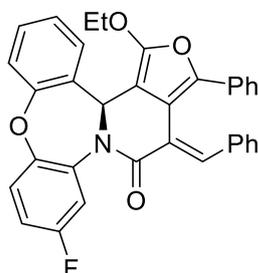


(E)-15-Benzylidene-10-chloro-3-ethoxy-1-phenyl-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (3d). Condition A: 42.5 mg, 78% yield; Yellow oil; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.52 (s, 1H), 7.42 (d, *J* = 10.0 Hz, 1H), 7.31 - 7.30 (comp, 3H), 7.25 - 7.14 (comp, 5H), 7.13 - 7.11 (m, 1H), 7.07 - 7.05 (m, 1H), 6.99 - 6.92 (comp, 6H), 6.28 (s, 1H), 4.44 - 4.31 (m, 2H), 1.42 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 167.8, 154.3, 153.2, 145.0, 139.4, 136.1, 135.5, 132.5, 131.6, 130.7, 130.2, 123.0, 129.4, 129.0, 128.9, 127.9, 127.6, 127.0, 125.9, 125.0, 124.1, 122.9, 122.7, 121.4, 121.0, 115.2, 94.1, 68.7, 54.4, 15.4; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₄ClNO₄Na[M+Na]⁺: 568.1286, found 568.1288.

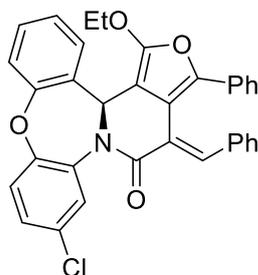


(S,E)-15-Benzylidene-10-chloro-3-ethoxy-1-phenyl-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (3e). Condition A: 44.7 mg, 85% yield, Condition B: 38.7 mg, 71% yield. 93% *ee*, [α]_D²⁰ = 162.0 (c = 0.033, CH₂Cl₂); Yellow oil. ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.53 (s, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.30 (d, *J* = 7.4 Hz, 2H), 7.21 - 7.20 (comp, 3H), 7.17 - 7.10 (comp, 3H), 6.98 - 6.90 (comp, 8H), 6.27 (s, 1H), 4.43 - 4.30 (m, 2H), 2.36 (s, 3H), 1.41 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 167.8, 154.7, 153.2, 149.5, 139.2, 138.0, 135.7, 135.6, 131.4, 130.8, 129.7, 129.0, 128.8, 128.7, 128.3, 127.8, 127.5, 126.9, 126.1, 125.0, 123.5, 123.2, 121.5, 120.9, 115.4, 94.7, 68.7, 54.7, 21.0, 15.4; HRMS (TOF MS ESI⁺) calculated for C₃₅H₂₇NO₄Na[M+Na]⁺: 548.1832, found 548.1828;

HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 12.4$ min, $t_{\text{major}} = 20.4$ min.

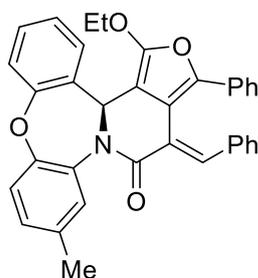


(*S,E*)-15-Benzylidene-3-ethoxy-11-fluoro-1-phenyl-3b*H*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3f). **Condition A:** 47.1 mg, 89% yield, **Condition B:** 38.7 mg, 70% yield; 90% *ee*, $[\alpha]_{\text{D}}^{20} = -3.0$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.54 (s, 1H), 7.32 - 7.30 (m, 2H), 7.26 - 7.11 (comp, 7H), 6.96 - 6.94 (comp, 8H), 6.31 (s, 1H), 4.45 - 4.31 (m, 2H), 1.44 - 1.40 (m, 3H); ^{13}C NMR (126 MHz, CDCl_3) (δ , ppm) 167.8, 157.3 (d, $J = 242.0$ Hz), 154.6, 153.2, 146.14 (d, $J = 2.6$ Hz), 139.3, 136.1, 135.4, 131.7, 130.7, 129.9, 129.0, 128.9, 127.9, 127.6, 127.0, 126.0, 125.0, 123.9, 122.9, 122.1 (d, $J = 8.9$ Hz), 120.9, 115.7 (d, $J = 25.6$ Hz), 115.1, 114.7 (d, $J = 23.3$ Hz), 94.2, 68.7, 54.3, 15.4; ^{19}F NMR (376 MHz, CDCl_3) (δ , ppm) -120.22; HRMS (TOF MS ESI $^+$) calculated for $\text{C}_{34}\text{H}_{24}\text{FNO}_4\text{Na}[\text{M}+\text{Na}]^+$: 552.1582, found 552.1580; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 11.4$ min, $t_{\text{major}} = 13.7$ min.

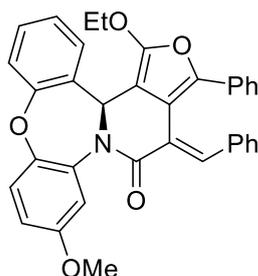


(*S,E*)-15-Benzylidene-11-chloro-3-ethoxy-1-phenyl-3b*H*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3g). **Condition A:** 45.3 mg, 83% yield,

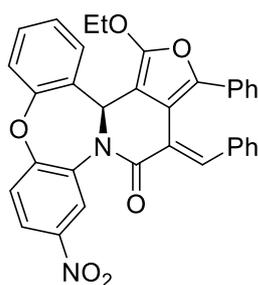
Condition B: 35.5 mg, 65% yield; 90% *ee*, $[\alpha]_D^{20} = 420.0$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.54 (s, 1H), 7.50 (d, $J = 2.1$ Hz, 1H), 7.31 - 7.29 (m, 2H), 7.25 - 7.17 (comp, 6H), 7.15 - 7.11(m, 1H), 7.00 - 6.91 (comp, 7H), 6.28 (s, 1H), 4.45 - 4.30 (m, 2H), 1.42 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 167.8, 154.4, 153.2, 148.5, 139.4, 136.2, 135.4, 131.5, 131.4, 130.7, 129.9, 129.0, 128.9, 127.9, 127.7, 127.6, 127.3, 127.1, 126.0, 125.0, 123.9, 122.8, 122.4, 120.9, 115.1, 94.0, 68.7, 54.5, 15.4; HRMS (TOF MS ESI^+) calculated for $\text{C}_{34}\text{H}_{24}\text{ClNO}_4\text{Na}[\text{M}+\text{Na}]^+$: 568.1286, found 568.1291; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 9.9$ min, $t_{\text{major}} = 12.5$ min.



(*S,E*)-15-Benzylidene-3-ethoxy-11-methyl-1-phenyl-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (3h). **Condition A:** 42.0 mg, 80% yield, **Condition B:** 36.3 mg, 69% yield; 91% *ee*, $[\alpha]_D^{20} = 123.0$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (500 MHz, CDCl_3) (δ , ppm) 7.55 (s, 1H), 7.30 - 7.29 (comp, 3H), 7.22 - 7.11 (comp, 5H), 7.12 (d, $J = 7.6$ Hz, 1H), 7.03 (d, $J = 8.3$ Hz, 1H), 6.98 - 6.91 (comp, 7H), 6.26 (s, 1H), 4.43 - 4.30 (m, 2H), 2.33 (s, 3H), 1.41 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) (δ , ppm) 167.8, 154.7, 153.2, 147.9, 139.2, 135.8, 135.6, 132.2, 131.2, 130.8, 130.6, 129.7, 129.3, 129.0, 128.8, 128.6, 127.8, 127.5, 126.9, 126.1, 125.0, 123.4, 123.1, 121.0, 120.9, 115.3, 94.7, 68.7, 54.8, 20.7, 15.4; HRMS (TOF MS ESI^+) calculated for $\text{C}_{35}\text{H}_{27}\text{NO}_4\text{Na}[\text{M}+\text{Na}]^+$: 548.1832, found 548.1824; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 10.3$ min, $t_{\text{major}} = 15.6$ min.

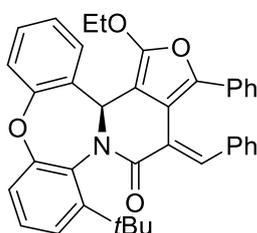


(*S,E*)-15-Benzylidene-3-ethoxy-11-methoxy-1-phenyl-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3i). **Condition A:** 48.2 mg, 89% yield, **Condition B:** 37.9 mg, 70% yield; 90% *ee*, $[\alpha]_{\text{D}}^{20} = -6.0$ ($c = 0.033$, CH_2Cl_2); Yellow oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) (δ , ppm) 7.56 (s, 1H), 7.30 (d, $J = 7.2$ Hz, 2H), 7.22 - 7.18 (comp, 4H), 7.17 - 7.12 (m, 2H), 7.01 (d, $J = 2.9$ Hz, 1H), 6.97 - 6.91 (comp, 7H), 6.81 (dd, $J = 9.0, 3.0$ Hz, 1H), 6.28 (s, 1H), 4.45 - 4.30 (m, 2H), 3.79 (s, 3H), 1.42 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) (δ , ppm) 168.0, 154.8, 154.6, 153.2, 144.2, 139.2, 135.9, 135.5, 131.4, 131.3, 130.8, 129.7, 129.0, 128.8, 127.8, 127.5, 127.0, 126.1, 125.0, 123.4, 123.0, 121.9, 120.9, 115.2, 115.1, 112.6, 94.7, 68.7, 55.9, 54.7, 15.4; HRMS (TOF MS ESI^+) calculated for $\text{C}_{35}\text{H}_{27}\text{NO}_4\text{Na}[\text{M}+\text{Na}]^+$: 564.1781, found 564.1785; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 21.5$ min, $t_{\text{major}} = 33.6$ min.

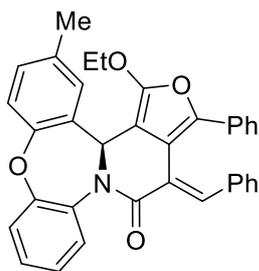


(*S,E*)-15-Benzylidene-3-ethoxy-11-nitro-1-phenyl-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3j). **Condition A:** 45.1 mg, 81% yield, **Condition B:** 45.1 mg, 81% yield; 90% *ee*, $[\alpha]_{\text{D}}^{20} = 147.0$ ($c = 0.033$, CH_2Cl_2); Yellow solid, m.p. = 242.3 - 244.2 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) (δ , ppm) 8.45 (d, $J = 2.5$ Hz, 1H), 8.09 - 8.07 (m, 1H), 7.55 (s, 1H), 7.35 (d, $J = 9.1$ Hz, 1H), 7.32 - 7.31 (m, 2H), 7.29 - 7.25 (m, 1H), 7.21 - 7.19 (comp, 3H), 7.15 (d, $J = 7.5$ Hz, 1H),

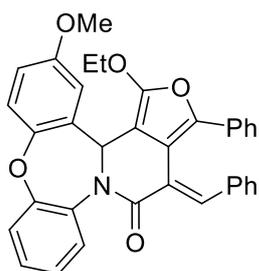
7.03 - 6.93 (comp, 7H), 6.34 (s, 1H), 4.46 - 4.33 (m, 2H), 1.42 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) (δ , ppm) 167.8, 154.3, 153.7, 153.2, 142.1, 139.6, 136.6, 135.2, 131.5, 130.6, 130.4, 130.2, 129.1, 129.0, 127.9, 127.6, 127.2, 125.9, 125.8, 125.0, 124.7, 122.7, 122.3, 122.0, 120.9, 114.8, 93.1, 68.7, 54.3, 15.3. HRMS (TOF MS ESI⁺) calculated for $\text{C}_{34}\text{H}_{24}\text{N}_2\text{O}_6\text{Na}[\text{M}+\text{Na}]^+$: 579.1527, found 579.1527; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, $t_{\text{minor}} = 25.5$ min, $t_{\text{major}} = 28.9$ min.



(*S,E*)-15-Benzylidene-12-(*tert*-butyl)-3-ethoxy-1-phenyl-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3k). **Condition A:** 53.9 mg, 95% yield, **Condition B:** 29.5 mg, 52% yield; 99% *ee*, $[\alpha]_{\text{D}}^{20} = 261.1$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (500 MHz, CDCl_3) (δ , ppm) 7.54 - 7.49 (m, 2H), 7.30 - 7.27 (m, 2H), 7.24 - 7.10 (comp, 8H), 6.95 - 6.92 (comp, 6H), 6.34 - 6.31 (m, 1H), 4.45 - 4.29 (m, 2H), 1.43 - 1.38 (m, 3H), 1.34 - 1.31 (m, 9H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 167.9, 154.8, 153.2, 147.4, 145.2, 139.2, 135.7, 135.6, 131.6, 130.8, 129.8, 129.7, 128.9, 128.8, 127.8, 127.5, 126.9, 126.2, 125.9, 125.0, 124.9, 123.5, 123.3, 120.9, 120.6, 115.4, 94.5, 68.7, 54.6, 34.5, 31.5, 15.4; HRMS (TOF MS ESI⁺) calculated for $\text{C}_{38}\text{H}_{33}\text{N}_1\text{O}_4\text{Na}[\text{M}+\text{Na}]^+$: 590.2302, found 590.2307; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, $t_{\text{minor}} = 8.1$ min, $t_{\text{major}} = 9.3$ min.

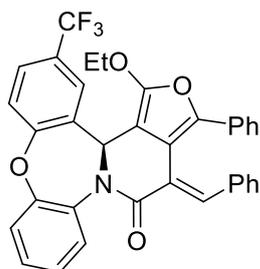


(*S,E*)-15-Benzylidene-3-ethoxy-5-methyl-1-phenyl-3b*H*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3l). **Condition A:** 48.4 mg, 92% yield, **Condition B:** 34.7 mg, 66% yield; 93% *ee*, $[\alpha]_D^{20} = 432.0$ ($c = 0.033$, CH_2Cl_2); Yellow oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) (δ , ppm) 7.51 (s, 1H), 7.47 - 7.45 (m, 1H), 7.33 (d, $J = 6.6$ Hz, 2H), 7.27 - 7.22 (comp, 4H), 7.09 - 7.05 (m, 2H), 7.00 - 6.90 (comp, 8H), 6.29 (s, 1H), 4.46 - 4.30 (m, 2H), 2.12 (s, 3H), 1.42 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) (δ , ppm) 167.9, 153.1, 152.5, 149.8, 139.2, 135.8, 135.7, 133.2, 131.4, 130.7, 130.6, 130.1, 129.3, 128.9, 128.8, 127.9, 127.7, 127.6, 127.0, 126.4, 124.9, 123.5, 122.3, 121.2, 120.6, 115.5, 94.5, 68.8, 54.5, 20.8, 15.4; HRMS (TOF MS ESI^+) calculated for $\text{C}_{35}\text{H}_{27}\text{NO}_4\text{Na}[\text{M}+\text{Na}]^+$: 548.1832, found: 548.1824; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 11.7$ min, $t_{\text{major}} = 18.1$ min.

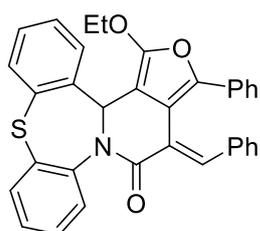


(*E*)-15-Benzylidene-3-ethoxy-5-methoxy-1-phenyl-3b*H*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3m). **Condition A:** 46.6 mg, 86% yield; Yellow oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) (δ , ppm) 7.58 - 7.57 (m, 1H), 7.49 - 7.47 (m, 1H), 7.36 - 7.34 (m, 2H), 7.26 - 7.21 (comp, 4H), 7.13 - 7.06 (m, 2H), 7.00 - 6.95 (comp, 6H), 6.74 - 6.65 (m, 2H), 6.31 (d, $J = 3.5$ Hz, 1H), 4.45 - 4.31 (m, 2H), 3.61 - 3.54 (m, 3H), 1.46 - 1.39 (m, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) (δ , ppm) 168.0,

154.8, 154.6, 153.2, 144.2, 139.2, 135.9, 135.5, 131.4, 131.3, 130.8, 129.7, 129.0, 128.8, 127.8, 127.5, 127.0, 126.1, 125.0, 123.4, 123.0, 121.9, 120.9, 115.2, 115.1, 112.6, 94.7, 68.7, 55.9, 54.7, 15.4; HRMS (TOF MS ESI⁺) calculated for C₃₅H₂₇NO₅Na[M+Na]⁺: 564.1781, found: 564.1785.

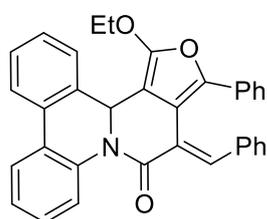


(*S,E*)-15-Benzylidene-3-ethoxy-1-phenyl-5-(trifluoromethyl)-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (3n). **Condition A:** 49.3 mg, 85% yield, **Condition B:** 34.8 mg, 60% yield; 90% *ee*, $[\alpha]_D^{20} = 363.0$ (*c* = 0.033, CH₂Cl₂); Yellow oil; ¹H NMR (400 MHz, CDCl₃) (δ , ppm) 7.53 - 7.52 (m, 1H), 7.49 - 7.46 (m, 2H), 7.39 (s, 1H), 7.28 - 7.22 (comp, 7H), 7.16 - 7.11 (m, 1H), 6.98 - 6.91 (comp, 6H), 6.25 (d, *J* = 2.2 Hz, 1H), 4.50 - 4.33 (m, 2H), 1.45 - 1.40 (m, 3H).; ¹³C NMR (101 MHz, CDCl₃) (δ , ppm) 167.8, 157.1, 153.3, 149.6, 139.5, 136.6, 135.3, 131.7, 131.0, 130.5, 129.4, 129.0, 128.8, 128.2, 127.9, 127.6, 127.1, 127.0 (q, *J* = 3.6 Hz), 125.3, 125.0, 123.8 (q, *J* = 3.4 Hz), 123.3, 122.7, 121.5, 121.3, 120.2 (q, *J* = 306.3 Hz), 114.9, 93.6, 68.6, 54.7, 15.3; ¹⁹F NMR (376 MHz, CDCl₃) (δ , ppm) -61.83; HRMS (TOF MS ESI⁺) calculated for C₃₅H₂₄F₃NO₄Na[M+Na]⁺: 602.1550, found: 602.1552; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, *t*_{minor} = 7.9 min, *t*_{major} = 12.5min.

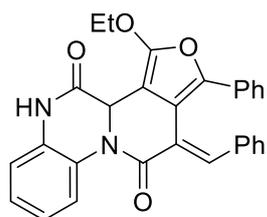


(*E*)-15-Benzylidene-3-ethoxy-1-phenyl-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-

***d*[[1,4]thiazepin-14(15*H*)-one (3o). Condition A:** 29.5 mg, 56% yield; Yellow oil; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.50 (s, 1H), 7.45 - 7.39 (comp, 3H), 7.35 - 7.33 (m, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 7.25 - 7.13 (comp, 6H), 7.06 (t, *J* = 7.5 Hz, 1H), 7.00 - 6.93 (comp, 6H), 6.37 (s, 1H), 4.45 - 4.30 (m, 2H), 1.42 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 169.0, 152.6, 142.0, 141.1, 139.1, 135.54, 135.48, 133.1, 130.7, 130.0, 129.4, 129.2, 129.1, 128.9, 128.7, 128.3, 127.9, 127.6, 127.1, 127.0, 126.9, 126.7, 126.2, 124.9, 124.1, 116.0, 96.3, 68.7, 55.9, 15.4; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₅NO₃SNa[M+Na]⁺: 550.1447, found: 550.1448.

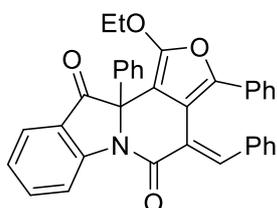


(*E*)-7-Benzylidene-10-ethoxy-8-phenyl-10*bH*-furo[3',4':3,4]pyrido[1,2-*f*]phenanthridin-6(7*H*)-one (3p). Condition A: 39.6 mg, 80% yield; Yellow oil. ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.90 (d, *J* = 7.7 Hz, 1H), 7.81 (d, *J* = 6.5 Hz, 2H), 7.62 (s, 1H), 7.49 - 7.39 (comp, 3H), 7.37 - 7.34 (m, 1H), 7.30 - 7.29 (m, 1H), 7.20 - 7.18 (comp, 4H), 6.96 - 6.90 (comp, 4H), 6.89 - 6.84 (m, 2H), 5.64 (s, 1H), 4.45 - 4.35 (m, 2H), 1.40 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 166.1, 154.8, 139.4, 138.9, 136.6, 135.8, 135.3, 132.7, 131.2, 129.6, 129.0, 128.6, 128.5, 128.2, 128.1, 127.6, 127.5, 126.9, 126.79, 126.76, 125.3, 124.4, 124.3, 123.8, 122.3, 114.4, 92.3, 68.5, 53.9, 29.9; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₅NO₃Na[M+Na]⁺: 550.1447, found: 550.1448.

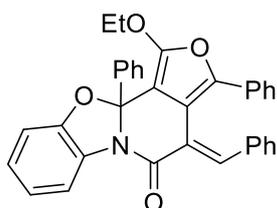


(*E*)-12-Benzylidene-3-ethoxy-1-phenyl-5*H*-furo[3',4':3,4]pyrido[1,2-*a*]quinoxalin-4,11(3*bH*,12*H*)-dione (3q). Condition A: 32.4 mg, 70% yield; Yellow oil; ¹H NMR

(400 MHz, CDCl₃) (δ, ppm) 8.53 (s, 1H), 7.81 - 7.78 (m, 1H), 7.76 (s, 1H), 7.24 - 7.18 (comp, 4H), 7.12 - 7.10 (m, 2H), 7.00 - 6.97 (m, 1H), 6.96 - 6.90 (comp, 4H), 6.88 - 6.83 (m, 2H), 5.10 (s, 1H), 4.49 - 4.37 (m, 2H), 1.43 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 166.7, 166.1, 155.7, 139.2, 136.3, 135.4, 131.2, 131.0, 129.3, 129.2, 128.8, 127.6, 127.5, 127.3, 126.9, 126.6, 125.4, 123.5, 121.2, 116.6, 113.7, 88.5, 68.9, 54.6, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₉H₂₂N₂O₄Na[M+Na]⁺: 485.1472, found: 485.1468.

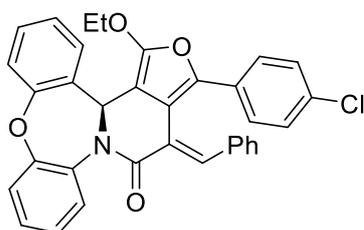


(E)-4-Benzylidene-1-ethoxy-3,11a-diphenylfuro[3',4':3,4]pyrido[1,2-*a*]indole-5,11(4H,11aH)-dione (3r). Condition A: 41.9 mg, 80% yield; Yellow oil; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 8.75 (d, *J* = 8.3 Hz, 1H), 7.82 - 7.77 (m, 2H), 7.49 (s, 1H), 7.44 - 7.42 (m, 2H), 7.30 - 7.24 (comp, 3H), 7.20 - 7.19 (m, 1H), 7.16 - 7.15 (m, 2H), 7.08 (d, *J* = 7.4 Hz, 2H), 6.96 - 6.88 (comp, 4H), 6.86 - 6.82 (m, 2H), 4.54 - 4.39 (m, 2H), 1.54 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 192.9, 166.8, 153.2, 152.2, 139.6, 138.7, 137.7, 136.2, 135.1, 130.5, 129.1, 128.5, 127.8, 127.6, 127.2, 125.6, 125.5, 125.1, 125.0, 124.3, 122.4, 117.3, 115.2, 97.6, 71.0, 70.0, 29.8, 15.5, 15.4; HRMS (TOF MS ESI⁺) calculated for C₃₅H₂₅NO₄Na[M+Na]⁺: 546.1676, found: 546.1672.

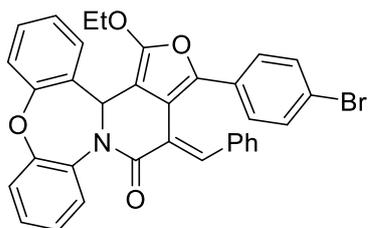


(E)-4-Benzylidene-1-ethoxy-3,11a-diphenyl-11aH-benzo[4,5]oxazolo[3,2-*a*]furo[3,4-*c*]pyridin-5(4H)-one (3s). Condition A: 20.5 mg, 40% yield; Yellow oil. ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 8.11 - 8.08 (m, 1H), 7.78 - 7.77 (m, 1H), 7.62 - 7.61 (m,

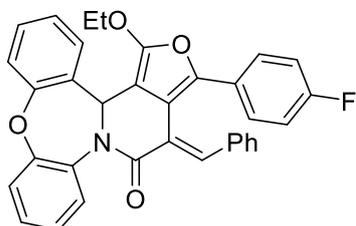
2H), 7.32 - 7.26 (comp, 3H), 7.19 - 7.18 (m, 2H), 7.11 - 7.10 (m, 2H), 7.07 - 7.04 (m, 1H), 7.02 - 7.00 (m, 1H), 6.98 - 6.95 (comp, 3H), 6.92 - 6.84 (comp, 4H), 4.53 - 4.44 (m, 2H), 1.56 - 1.51 (m, 3H); ^{13}C NMR (126 MHz, CDCl_3) (δ , ppm) 164.6, 152.5, 149.7, 141.9, 139.7, 136.3, 135.2, 130.7, 129.8, 129.12, 129.08, 129.0, 128.83, 127.75, 127.5, 127.3, 125.5, 125.4, 124.8, 122.5, 122.1, 116.6, 112.0, 109.7, 100.8, 96.4, 69.8, 15.4; HRMS (TOF MS ESI^+) calculated for $\text{C}_{34}\text{H}_{25}\text{NO}_4\text{Na}[\text{M}+\text{Na}]^+$: 534.1676, found: 534.1679.



(*S,E*)-15-Benzylidene-1-(4-chlorophenyl)-3-ethoxy-3b*H*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (4a). **Condition A:** 44.8 mg, 82% yield, **Condition B:** 38.7 mg, 71% yield; 90% *ee*, $[\alpha]_{\text{D}}^{20} = 33.0$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.54 (s, 1H), 7.46 (d, $J = 8.0$ Hz, 1H), 7.30 - 7.28 (comp, 3H), 7.25 - 7.17 (comp, 3H), 7.12 - 7.07 (comp, 4H), 7.02 - 6.95 (comp, 4H), 6.91 - 6.90 (m, 2H), 6.29 (s, 1H), 4.42 - 4.29 (m, 2H), 1.41 (t, $J = 6.3$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 167.5, 154.6, 153.2, 149.8, 137.9, 136.0, 135.3, 133.4, 132.5, 131.2, 130.7, 129.7, 129.1, 128.8, 128.0, 127.8, 127.6, 126.0, 125.8, 123.5, 123.0, 122.5, 121.4, 121.2, 120.9, 115.9, 94.6, 68.7, 54.5, 15.2; HRMS (TOF MS ESI^+) calculated for $\text{C}_{34}\text{H}_{24}\text{ClNO}_4\text{Na}[\text{M}+\text{Na}]^+$: 568.1286, found: 568.1290; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 12.6$ min, $t_{\text{major}} = 17.9$ min.

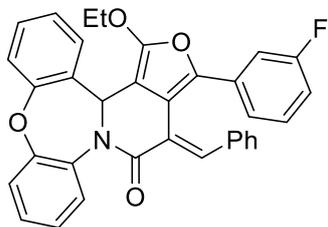


(E)-15-Benzylidene-1-(4-bromophenyl)-3-ethoxy-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (4b). Condition A: 41.3 mg, 70% yield; Yellow solid, m.p. = 203.2 - 204.6 °C; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.55 (s, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.30 - 7.28 (comp, 3H), 7.24 - 7.21 (m, 2H), 7.19 - 7.18 (m, 1H), 7.12 - 7.09 (m, 2H), 7.08 - 7.02 (comp, 5H), 7.00 - 6.94 (comp, 3H), 6.29 (s, 1H), 4.44 - 4.30 (m, 2H), 1.41 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 167.6, 154.7, 153.4, 149.9, 138.0, 136.1, 135.4, 131.3, 130.8, 130.7, 129.8, 129.6, 129.23, 129.20, 128.9, 128.1, 127.9, 126.4, 126.0, 123.6, 123.1, 122.6, 121.4, 121.0, 120.7, 116.1, 94.7, 68.8, 54.7, 15.4; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₄BrNO₄Na[M+Na]⁺: 612.0781, found: 612.0780.

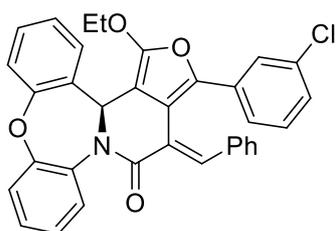


(E)-15-Benzylidene-3-ethoxy-1-(4-fluorophenyl)-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (4c). Condition A: 47.1 mg, 89% yield; Yellow solid, m.p. = 251.6 - 252.7 °C; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.54 (s, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.30 - 7.28 (comp, 3H), 7.25 - 7.21 (m, 2H), 7.19 - 7.15 (comp, 3H), 7.13 - 7.08 (m, 2H), 7.03 - 7.00 (m, 1H), 6.97 - 6.94 (comp, 3H), 6.64 (t, *J* = 8.7 Hz, 2H), 6.30 (s, 1H), 4.43 - 4.29 (m, 2H), 1.41 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 167.7, 161.8 (d, *J* = 247.8 Hz), 154.7, 153.1, 149.9, 138.4, 135.7, 135.4, 131.4, 130.9, 129.8, 129.2, 129.04, 128.96, 128.0, 127.8, 127.1 (d, *J* = 3.1 Hz), 126.8 (d, *J* = 8.2 Hz), 126.0, 123.6, 123.1, 122.6, 121.3, 121.0, 115.1, 114.6 (d, *J* = 21.9 Hz), 94.6, 68.8, 54.7, 15.4; ¹⁹F NMR (376 MHz, CDCl₃) (δ, ppm) -114.07; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₄FNO₄Na[M+Na]⁺: 552.1582,

found: 552.1582.

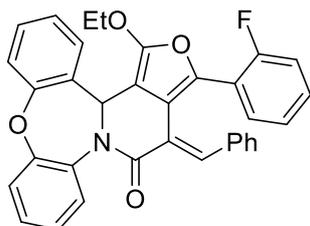


(E)-15-Benzylidene-3-ethoxy-1-(3-fluorophenyl)-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (4d). Condition A: 40.2 mg, 76% yield; Yellow solid, m.p. = 236.6 - 237.7 °C; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.57 (s, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.31 - 7.28 (comp, 3H), 7.26 - 7.18 (comp, 3H), 7.13 - 7.08 (m, 2H), 7.02 - 6.95 (comp, 5H), 6.89 - 6.86 (m, 2H), 6.66 (t, *J* = 8.0 Hz, 1H), 6.30 (s, 1H), 4.45 - 4.31 (m, 2H), 1.42 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 167.6, 162.1 (d, *J* = 244.6 Hz), 154.7, 153.4, 149.9, 137.7 (d, *J* = 3.1 Hz), 136.4, 135.6, 132.6 (d, *J* = 8.7 Hz), 131.3, 130.8, 129.8, 129.2, 129.1 (d, *J* = 8.4 Hz), 128.9, 128.8, 128.0, 127.9, 126.0, 123.6, 123.0, 122.6, 121.3, 121.0, 120.7 (d, *J* = 2.7 Hz), 116.4, 113.7 (d, *J* = 21.3 Hz), 111.8 (d, *J* = 23.7 Hz), 94.6, 68.7, 54.7, 15.3; ¹⁹F NMR (376 MHz, CDCl₃) (δ, ppm) -113.90; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₄FN₄O₄Na[M+Na]⁺: 552.1582, found: 552.1580.

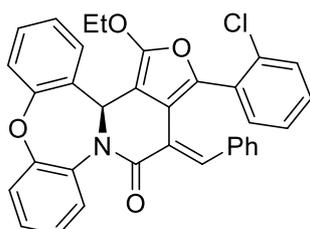


(S,E)-15-Benzylidene-1-(3-chlorophenyl)-3-ethoxy-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (4e). Condition B: 36.5 mg, 67% yield; 90% *ee*, [α]_D²⁰ = 33.00 (c = 0.033, CH₂Cl₂); Yellow oil; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.50 - 7.49 (m, 1H), 7.39 - 7.37 (m, 1H), 7.20 - 7.09 (comp, 7H), 7.02 - 7.00 (comp, 4H), 6.88 - 6.84 (comp, 4H), 6.82 - 6.78 (m, 1H), 6.21 - 6.20 (m, 1H), 4.34 - 4.23 (m, 2H), 1.34 - 1.30 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 167.5, 154.6, 153.5, 149.9, 137.4, 136.5, 135.5, 133.6, 132.3, 131.2, 130.8, 129.8, 129.2,

128.9, 128.71, 128.65, 128.0, 127.9, 126.8, 125.9, 124.9, 123.5, 122.9, 122.8, 122.6, 121.3, 121.0, 116.4, 94.6, 68.7, 54.6, 15.3; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₄ClNO₄Na[M+Na]⁺: 568.1286, found: 568.1285; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, t_{minor} = 11.9 min, t_{major} = 22.1 min.

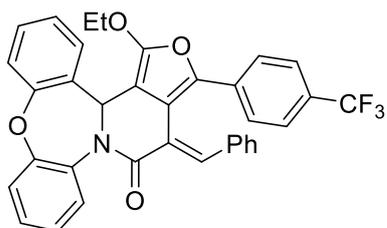


(E)-15-Benzylidene-3-ethoxy-1-(2-fluorophenyl)-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (4f). Condition A: 45.5 mg, 86% yield; Yellow solid, m.p. = 230.1 - 232.7 °C; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.62 (s, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.29 - 7.22 (comp, 4H), 7.19 - 7.18 (comp, 3H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.11 - 7.07 (m, 1H), 6.99 (t, *J* = 6.9 Hz, 2H), 6.90 - 6.88 (comp, 3H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.62 (t, *J* = 9.4 Hz, 1H), 6.32 (s, 1H), 4.43 - 4.28 (m, 2H), 1.40 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 167.2, 158.2 (d, *J* = 252.4 Hz), 154.7, 153.9, 150.0, 137.2 (d, *J* = 1.7 Hz), 135.5, 134.6, 131.7, 131.1, 129.8, 129.4, 129.3, 128.7, 128.6 (d, *J* = 1.6 Hz), 128.3, 127.8, 127.6, 126.1, 123.6, 123.3, 122.6 (d, *J* = 4.1 Hz), 121.3, 121.0, 120.0 (d, *J* = 13.7 Hz), 117.9, 115.6 (d, *J* = 20.1 Hz), 94.1, 68.6, 54.6, 15.4; ¹⁹F NMR (376 MHz, CDCl₃) (δ, ppm) -109.36; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₄FNO₄Na[M+Na]⁺: 552.1582, found: 552.1586.

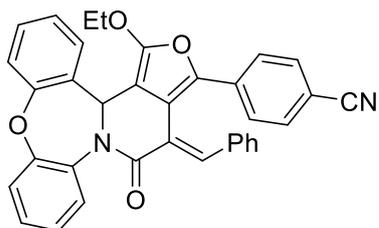


(S,E)-15-Benzylidene-1-(2-chlorophenyl)-3-ethoxy-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (4g). Condition B: 35.4 mg, 65% yield;

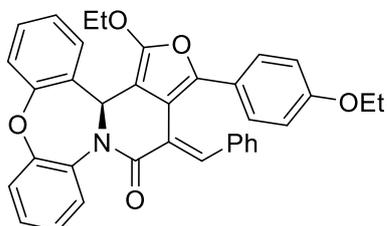
90% *ee*, $[\alpha]_{\text{D}}^{20} = 33.00$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (500 MHz, CDCl_3) (δ , ppm) 7.50 (s, 1H), 7.42 (d, $J = 8.0$ Hz, 1H), 7.22 - 7.15 (comp, 4H), 7.13 - 7.11 (m, 2H), 7.09 - 7.07 (m, 2H), 7.04 - 7.01 (m, 1H), 6.98 - 6.94 (m, 2H), 6.89 - 6.80 (comp, 5H), 6.25 (s, 1H), 4.35 - 4.20 (m, 2H), 1.34 - 1.31 (m, 3H); ^{13}C NMR (126 MHz, CDCl_3) (δ , ppm) 167.0, 154.7, 153.7, 149.9, 137.1, 136.9, 135.4, 132.5, 131.7, 131.0, 130.7, 130.5, 129.9, 129.8, 129.3, 129.1, 128.6, 128.2, 127.8, 127.7, 126.08, 126.05, 123.7, 122.6, 121.3, 121.0, 117.9, 93.6, 68.6, 54.7, 15.3; HRMS (TOF MS ESI^+) calculated for $\text{C}_{34}\text{H}_{24}\text{ClNO}_4\text{Na}[\text{M}+\text{Na}]^+$: 568.1286, found: 568.1283; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 12.1$ min, $t_{\text{major}} = 25.4$ min.



(*E*)-15-Benzylidene-3-ethoxy-1-(4-(trifluoromethyl)phenyl)-3b*H*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (4h). Condition A: 46.9 mg, 81% yield; Yellow solid, m.p. = 228.2 - 229.7 °C; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.59 (s, 1H), 7.47 (d, $J = 8.0$ Hz, 1H), 7.30 - 7.21 (comp, 7H), 7.19 - 7.08 (comp, 5H), 6.98 - 6.93 (comp, 4H), 6.31 (s, 1H), 4.48 - 4.33 (m, 2H), 1.43 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 167.4, 154.7, 153.9, 150.0, 137.5, 136.7, 135.5, 133.9, 131.2, 130.9, 129.9, 129.2, 129.1, 128.8, 128.4 (q, $J = 32.6$ Hz), 128.1, 128.0, 125.9, 124.8, 124.4 (q, $J = 3.4$ Hz), 124.2 (q, $J = 272.1$ Hz), 123.6, 123.0, 122.7, 121.4, 121.1, 117.5, 94.9, 68.7, 54.7, 15.4; ^{19}F NMR (376 MHz, CDCl_3) (δ , ppm) -62.55; HRMS (TOF MS ESI^+) calculated for $\text{C}_{35}\text{H}_{24}\text{F}_3\text{NO}_4\text{Na}[\text{M}+\text{Na}]^+$: 602.1550, found: 602.1545.

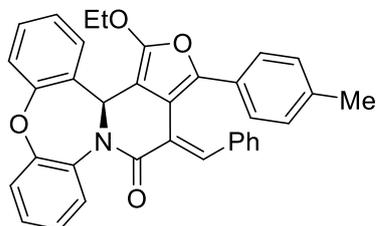


(*S,E*)-4-(15-Benzylidene-3-ethoxy-14-oxo-14,15-dihydro-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-1-yl)benzonitrile (4i). Condition A: 20.9 mg, 39% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.59 (s, 1H), 7.45 (d, $J = 8.0$ Hz, 1H), 7.30 - 7.29 (comp, 3H), 7.26 - 7.23 (comp, 5H), 7.21 - 7.19 (comp, 3H), 7.11 - 7.10 (m, 2H), 7.04 - 7.02 (m, 1H), 7.00 - 6.97 (m, 2H), 6.23 (s, 1H), 4.49 - 4.35 (m, 2H), 1.44 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 167.2, 154.7, 154.3, 149.9, 137.1, 136.7, 135.3, 134.4, 131.3, 131.0, 130.7, 130.0, 129.4, 129.1, 128.8, 128.3, 128.0, 125.8, 124.7, 123.6, 123.0, 122.7, 121.4, 121.1, 119.1, 118.9, 109.3, 95.1, 68.7, 54.6, 15.3; HRMS (TOF MS ESI $^+$) calculated for $\text{C}_{35}\text{H}_{24}\text{N}_2\text{O}_4\text{Na}[\text{M}+\text{Na}]^+$: 559.1628, found: 559.1619.

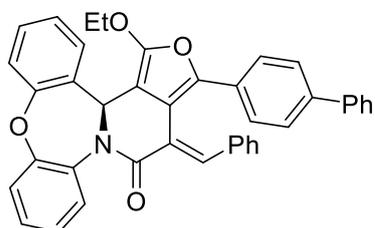


(*S,E*)-15-Benzylidene-3-ethoxy-1-(4-ethoxyphenyl)-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (4j). Condition A: 37.8 mg, 68% yield, Condition B: 40.6 mg, 73% yield; 95% *ee*, $[\alpha]_{\text{D}}^{20} = 579.1$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.51 (s, 1H), 7.48 (d, $J = 7.9$ Hz, 1H), 7.31 - 7.27 (comp, 3H), 7.23 - 7.16 (comp, 3H), 7.13 - 7.07 (comp, 4H), 7.00 - 6.94 (comp, 4H), 6.47 (d, $J = 8.6$ Hz, 2H), 6.29 (s, 1H), 4.42 - 4.27 (m, 2H), 3.95 - 3.84 (m, 2H), 1.40 (t, $J = 7.1$ Hz, 3H), 1.35 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 168.0, 158.2, 154.7, 152.7, 149.9, 139.6, 135.6, 135.1, 131.6, 131.0, 129.7, 129.3, 129.1, 128.8, 127.8, 126.5, 126.0, 123.7, 123.6, 123.3, 122.5, 121.3, 120.9, 113.7, 94.5, 68.8, 63.6, 54.7, 15.4, 14.8; HRMS (TOF MS ESI $^+$) calculated for $\text{C}_{36}\text{H}_{29}\text{NO}_5\text{Na}[\text{M}+\text{Na}]^+$: 578.1938, found: 578.1945; HPLC conditions for

determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 19.9$ min, $t_{\text{major}} = 33.2$ min.

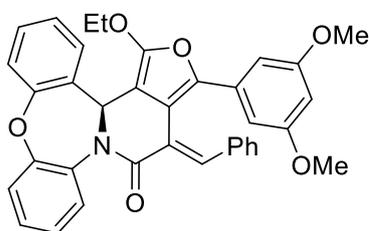


(S,E)-15-Benzylidene-3-ethoxy-1-(p-tolyl)-3bH-dibenzo[b,f]furo[3',4':3,4]pyrido[1,2-d][1,4]oxazepin-14(15H)-one (4k). **Condition A:** 45.2 mg, 86% yield, **Condition B:** 40.6 mg, 71% yield; 92% *ee*, $[\alpha]_{\text{D}}^{20} = 405.0$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.51 (s, 1H), 7.48 (d, $J = 8.0$ Hz, 1H), 7.31 - 7.27 (comp, 3H), 7.24 - 7.16 (comp, 3H), 7.13 - 7.06 (comp, 4H), 6.98 - 6.91 (comp, 4H), 6.76 - 6.74 (m, 2H), 6.29 (s, 1H), 4.41 - 4.29 (m, 2H), 2.18 (s, 3H), 1.40 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 168.0, 154.6, 152.9, 149.9, 139.6, 137.0, 135.6, 135.5, 131.5, 130.9, 129.7, 129.3, 129.0, 128.7, 128.2, 128.0, 127.82, 127.76, 126.0, 124.9, 123.6, 123.2, 122.5, 121.3, 120.9, 114.6, 94.5, 68.7, 54.6, 21.3, 15.4; HRMS (TOF MS ESI^+) calculated for $\text{C}_{35}\text{H}_{27}\text{NO}_4\text{Na}[\text{M}+\text{Na}]^+$: 548.1832, found: 548.1837; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 12.7$ min, $t_{\text{major}} = 21.3$ min.

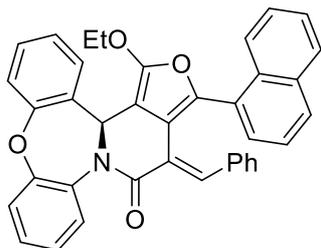


(S,E)-1-([1,1'-Biphenyl]-4-yl)-15-benzylidene-3-ethoxy-3bH-dibenzo[b,f]furo[3',4':3,4]pyrido[1,2-d][1,4]oxazepin-14(15H)-one (4l). **Condition A:** 48.1 mg, 82% yield, **Condition B:** 40.9 mg, 77% yield; 90% *ee*, $[\alpha]_{\text{D}}^{20} = 33.0$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.59 (s, 1H), 7.51 - 7.49 (m, 1H), 7.46 - 7.44 (m, 2H), 7.40 - 7.37 (m, 2H), 7.33 - 7.30 (comp, 3H), 7.27 - 7.22 (comp,

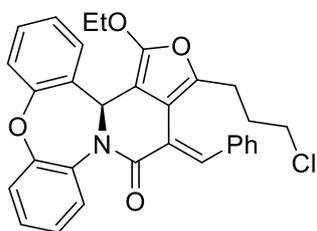
4H), 7.21 - 7.20 (m, 1H), 7.18 - 7.14 (comp, 4H), 7.10 - 7.07 (m, 1H), 6.96 - 6.92 (comp, 4H), 6.32 (s, 1H), 4.43 - 4.32 (m, 2H), 1.42 - 1.38 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 167.7, 154.6, 153.2, 149.8, 140.7, 139.6, 139.0, 135.8, 135.5, 131.4, 130.9, 129.72, 129.65, 129.2, 128.9, 128.8, 127.82, 127.76, 127.3, 126.9, 126.1, 126.0, 125.3, 123.5, 123.1, 122.5, 121.3, 120.9, 115.5, 94.6, 68.7, 54.6, 15.3; HRMS (TOF MS ESI⁺) calculated for C₄₀H₂₉NO₄Na[M+Na]⁺: 610.1989, found 610.1983; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 ml/min, *t*_{minor} = 20.8 min, *t*_{major} = 44.3min.



(*S,E*)-15-Benzylidene-1-(3,5-dimethoxyphenyl)-3-ethoxy-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (4m). **Condition A:** 45.2 mg, 79% yield, **Condition B:** 42.3 mg, 74% yield; 91% *ee*, [α]_D²⁰ = 414.0 (c = 0.033, CH₂Cl₂); Yellow solid, m.p. = 109.1 - 111.0 °C; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.46 (s, 1H), 7.40 - 7.38 (m, 1H), 7.24 (s, 1H), 7.21 - 7.19 (m, 1H), 7.16 - 7.08 (comp, 4H), 7.03 - 7.00 (m, 2H), 6.98 - 6.95 (m, 1H), 6.93 - 6.89 (m, 2H), 6.86 - 6.84 (m, 1H), 6.33 (d, *J* = 2.2 Hz, 2H), 6.21 (s, 1H), 6.04 (t, *J* = 2.1 Hz, 1H), 4.34 - 4.22 (m, 2H), 3.51 (s, 6H), 1.33 (t, *J* = 7.9 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 167.8, 160.0, 154.6, 153.0, 149.8, 139.1, 135.8, 135.4, 132.5, 131.3, 130.8, 129.7, 129.2, 129.0, 128.9, 127.8, 127.7, 125.9, 123.5, 123.0, 122.4, 121.2, 120.9, 115.8, 103.3, 100.1, 94.5, 68.6, 55.2, 54.5, 15.2. HRMS (TOF MS ESI⁺) calculated for C₃₆H₂₉NO₆Na[M+Na]⁺: 594.1887, found: 594.1880; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 85:15, flow rate = 1.0 mL/min, *t*_{minor} = 14.0 min, *t*_{major} = 24.8min.

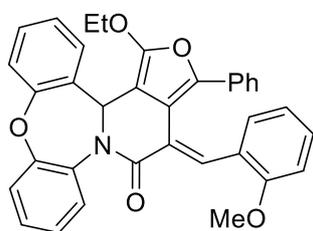


(*S,E*)-15-Benzylidene-3-ethoxy-1-(naphthalen-1-yl)-3b*H*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (4n). **Condition A:** 44.9 mg, 80% yield, **Condition B:** 44.9 mg, 80% yield; 95% *ee*, $[\alpha]_{\text{D}}^{20} = 363.0$ ($c = 0.033$, CH_2Cl_2); Yellow solid, m.p. = 135.8 - 137.2 °C; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.85 (d, $J = 8.3$ Hz, 1H), 7.63 (d, $J = 7.9$ Hz, 1H), 7.57 (d, $J = 7.9$ Hz, 1H), 7.52 - 7.47 (comp, 3H), 7.43 - 7.41 (m, 2H), 7.32 - 7.23 (comp, 3H), 7.21 - 7.19 (m, 2H), 7.15 - 7.11 (m, 2H), 7.02 (t, $J = 6.8$ Hz, 1H), 6.72 - 6.71 (m, 2H), 6.54 - 6.51 (m, 1H), 6.41 - 6.39 (comp, 3H), 4.46 - 4.29 (m, 2H), 1.43 - 1.40 (m, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 167.2, 154.7, 153.7, 150.0, 139.0, 137.0, 134.9, 133.4, 131.8, 131.1, 129.8, 129.7, 129.4, 129.3, 128.7, 128.5, 127.83, 127.80, 127.4, 127.2, 126.8, 126.3, 126.1, 125.9, 125.7, 124.5, 123.7, 122.6, 122.5, 121.4, 121.0, 117.4, 94.1, 68.7, 54.7, 15.4; HRMS (TOF MS ESI^+) calculated for $\text{C}_{38}\text{H}_{27}\text{NO}_4\text{Na}[\text{M}+\text{Na}]^+$: 584.1832, found: 584.1833; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 11.3$ min, $t_{\text{major}} = 21.5$ min.

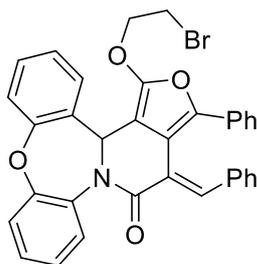


(*S,E*)-15-Benzylidene-1-(3-chloropropyl)-3-ethoxy-3b*H*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (4o). **Condition A:** 42.5 mg, 83% yield, **Condition B:** 40.9 mg, 80% yield; 93% *ee*, $[\alpha]_{\text{D}}^{20} = -72.0$ ($c = 0.033$, CH_2Cl_2); Yellow solid, m.p. = 172.4 - 174.2 °C; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.53 (s, 1H), 7.46 - 7.41 (comp, 3H), 7.36 (t, $J = 7.5$ Hz, 2H), 7.30 - 7.28 (m, 1H), 7.26 - 7.22

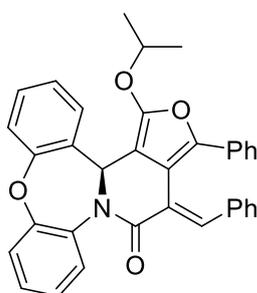
(comp, 3H), 7.20 - 7.16 (m, 1H), 7.13 - 7.12 (m, 1H), 7.09 - 7.04 (m, 1H), 7.01 (t, $J = 7.3$ Hz, 1H), 6.20 (s, 1H), 4.28 - 4.17 (m, 2H), 3.29 - 3.19 (m, 2H), 2.16 - 2.08 (m, 1H), 1.98 - 1.90 (m, 1H), 1.88 - 1.71 (m, 2H), 1.34 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 166.8, 154.5, 152.6, 149.9, 140.6, 136.5, 135.1, 131.4, 131.0, 129.8, 129.2, 128.9, 128.8, 128.5, 127.8, 126.1, 123.7, 123.4, 122.5, 121.3, 120.9, 115.2, 92.9, 68.8, 55.1, 44.2, 29.8, 26.1, 15.3; HRMS (TOF MS ESI^+) calculated for $\text{C}_{31}\text{H}_{26}\text{ClNO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 534.1443, found: 534.1447; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 15.0$ min, $t_{\text{major}} = 21.6$ min.



(E)-3-Ethoxy-15-(2-methoxybenzylidene)-1-phenyl-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (4p). Condition A: 42.2 mg, 78% yield; Yellow solid, m.p. = 259.6 - 260.8 °C; ^1H NMR (500 MHz, CDCl_3) (δ , ppm) 7.81 (s, 1H), 7.49 (d, $J = 8.0$ Hz, 1H), 7.28 - 7.15 (comp, 8H), 7.07 (t, $J = 7.5$ Hz, 1H), 6.99 - 6.95 (comp, 5H), 6.57 (d, $J = 8.2$ Hz, 1H), 6.40 (t, $J = 7.3$ Hz, 1H), 6.31 (s, 1H), 4.41 - 4.27 (m, 2H), 3.78 (s, 3H), 1.39 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) (δ , ppm) 167.6, 157.4, 154.7, 153.0, 149.8, 139.2, 132.3, 131.7, 130.9, 130.8, 130.3, 129.7, 129.4, 128.2, 127.6, 127.3, 126.7, 126.0, 125.1, 125.0, 123.5, 122.9, 122.4, 121.2, 120.9, 119.7, 115.6, 110.2, 94.5, 68.7, 55.3, 54.6, 15.3; HRMS (TOF MS ESI^+) calculated for $\text{C}_{35}\text{H}_{27}\text{NO}_5\text{Na}$ $[\text{M}+\text{Na}]^+$: 564.1781, found: 564.1778.

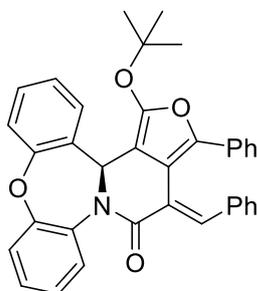


(E)-15-Benzylidene-3-(2-bromoethoxy)-1-phenyl-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (4q). Condition A: 41.3 mg, 70% yield; Yellow solid, m.p. = 172.4 - 174.2 °C; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.56 (s, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.29 - 7.28 (comp, 3H), 7.26 - 7.24 (m, 1H), 7.22 - 7.19 (comp, 4H), 7.12 - 7.09 (m, 2H), 7.00 - 6.91 (comp, 7H), 6.33 (s, 1H), 4.61 - 4.55 (m, 2H), 3.61 (t, *J* = 6.2 Hz, 2H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 167.7, 154.7, 152.0, 150.0, 139.8, 136.1, 135.5, 131.1, 131.0, 130.5, 129.8, 129.2, 129.0, 128.9, 127.91, 127.85, 127.6, 127.3, 126.0, 125.1, 123.6, 122.8, 122.7, 121.3, 121.0, 115.3, 96.0, 71.9, 54.5, 28.7; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₄BrNO₄Na [M+Na]⁺: 612.0781, found: 612.0787.

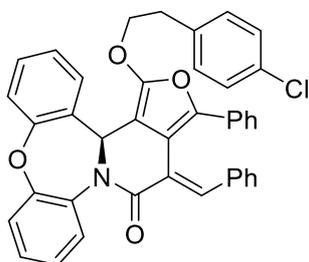


(S,E)-15-Benzylidene-3-isopropoxy-1-phenyl-3bH-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15H)-one (4r). Condition B: 32.6 mg, 62% yield; 91% *ee*, [α]_D²⁰ = 210.0 (c = 0.033, CH₂Cl₂); Yellow oil; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.46 - 7.45 (m, 1H), 7.41 - 7.39 (m, 1H), 7.23 - 7.20 (comp, 3H), 7.19 - 7.09 (comp, 5H), 7.08 - 7.00 (m, 2H), 6.88 - 6.86 (comp, 7H), 6.18 - 6.17 (m, 1H), 4.72 - 4.69 (m, 1H), 1.35 - 1.33 (m, 3H), 1.30 - 1.29 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 167.9, 154.7, 152.6, 149.9, 139.5, 135.7, 135.6, 131.5, 130.93, 130.85, 129.7, 129.2, 129.0, 128.8, 127.83, 127.77, 127.5, 127.0, 126.0, 125.0, 123.6, 123.2, 122.5, 121.3, 121.0, 115.2, 96.3, 54.7, 22.8, 22.6; HRMS (TOF MS ESI⁺) calculated for

C₃₅H₂₇NO₄Na [M+Na]⁺: 548.1832, found 548.1824; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, t_{minor} = 10.2 min, t_{major} = 16.2min.

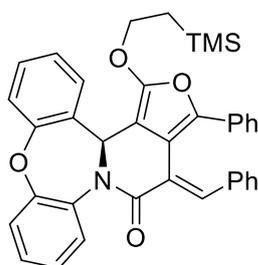


(*S,E*)-15-Benzylidene-3-(*tert*-butoxy)-1-phenyl-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (4s). Condition B: 32.6 mg, 58% yield; 90% *ee*, [α]_D²⁰ = -6.0 (c = 0.033, CH₂Cl₂); Yellow oil; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.51 (s, 1H), 7.48 - 7.45 (m, 1H), 7.31 - 7.27 (comp, 3H), 7.23 - 7.18 (comp, 4H), 7.11- 7.06 (m, 2H), 7.00 - 6.90 (comp, 8H), 6.22 (s, 1H), 1.46 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 168.1, 154.7, 151.6, 149.9, 140.4, 135.7, 135.5, 131.7, 131.00, 130.96, 129.7, 129.3, 129.0, 128.8, 127.9, 127.8, 127.6, 127.1, 126.1, 125.2, 123.6, 123.4, 122.6, 121.3, 121.0, 114.8, 100.7, 84.9, 54.8, 29.1. HRMS (TOF MS ESI+) calculated for C₃₆H₂₉NO₄Na [M+Na]⁺: 562.1989, found: 562.1990; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, t_{minor} = 10.2 min, t_{major} = 16.2min.



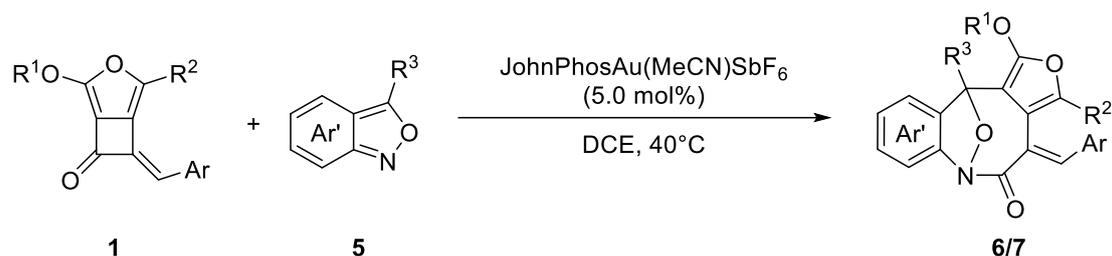
(*S,E*)-15-Benzylidene-3-(4-chlorophenoxy)-1-phenyl-3*bH*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*)-one (4t). Condition B: 43.5 mg, 70% yield; 90% *ee*, [α]_D²⁰ = 237.0 (c = 0.033, CH₂Cl₂); Yellow solid, m.p. = 136.7 - 138.2 °C; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.48 (s, 1H), 7.39 (d, *J* = 7.9 Hz, 1H),

7.22 - 7.20 (comp, 4H), 7.18 - 7.12 (comp, 7H), 7.04 - 7.02 (m, 2H), 6.92 - 6.83 (comp, 8H), 6.25 (s, 1H), 4.53 - 4.47 (m, 2H), 3.53 (t, $J = 6.2$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) (δ , ppm) 167.7, 154.7, 152.0, 150.0, 139.8, 136.1, 135.5, 131.1, 131.0, 130.5, 129.8, 129.2, 129.0, 128.9, 127.91, 127.85, 127.6, 127.3, 126.0, 125.1, 123.6, 122.8, 122.7, 121.3, 121.0, 115.3, 96.0, 71.9, 54.5, 28.7; HRMS (TOF MS ESI+) calculated for $\text{C}_{40}\text{H}_{28}\text{ClNO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 644.1599, found: 644.1597; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 15.4$ min, $t_{\text{major}} = 24.6$ min.

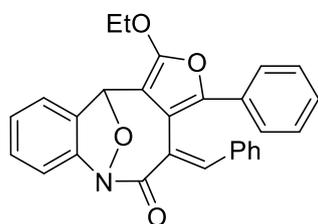


(*S,E*)-15-Benzylidene-1-phenyl-3-(2-(trimethylsilyl)ethoxy)-3b*H*-dibenzo[*b,f*]furo[3',4':3,4]pyrido[1,2-*d*][1,4]oxazepin-14(15*H*) (4u). Condition B: 39.5 mg, 68% yield; 90% *ee*, $[\alpha]_{\text{D}}^{20} = -33.0$ ($c = 0.033$, CH_2Cl_2); Yellow oil; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.52 (s, 1H), 7.47 - 7.45 (m, 1H), 7.29 - 7.25 (comp, 3H), 7.22 - 7.14 (comp, 5H), 7.11 - 7.04 (m, 2H), 6.96 - 6.88 (comp, 7H), 6.26 (s, 1H), 4.40 - 4.33 (m, 2H), 1.16 - 1.12 (t, $J = 8.0$ Hz, 3H), 0.00 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 167.9, 154.7, 153.3, 150.0, 139.3, 135.8, 135.6, 131.4, 131.1, 130.9, 129.7, 129.3, 129.0, 128.8, 127.8, 127.6, 126.9, 126.1, 125.0, 123.5, 123.2, 122.6, 121.3, 120.9, 115.4, 95.0, 71.4, 71.3, 54.8, 54.7, 18.6, -1.35, -1.37; HRMS (TOF MS ESI+) calculated for $\text{C}_{37}\text{H}_{33}\text{NO}_4\text{SiNa}$ $[\text{M}+\text{Na}]^+$: 606.2071, found: 606.2069; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, $\lambda = 254$ nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 8.9$ min, $t_{\text{major}} = 13.2$ min.

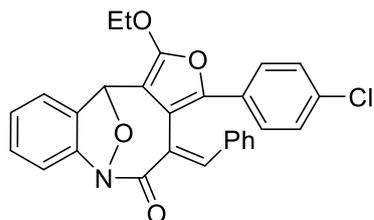
General Procedure for the [4+4] Cycloaddition Reaction



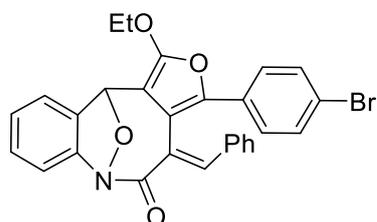
To a 10-mL oven-dried vial containing a magnetic stirring bar, cyclobutanone **1** (0.1 mmol, 1.0 equiv.), and anthranil **5** (0.11 mmol, 1.1 equiv.) in DCE (1.0 mL), was added a solution of JohnPhosAu(MeCN)SbF₆ (3.9 mg, 5.0 mol%) in DCE (1.0 mL) *via* syringe under argon atmosphere at 40 °C. After addition, the reaction mixture was stirred 12 h under these conditions until consumption of the material (monitored by TLC). The solvent was evaporated in vacuo. Then, the residues was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 30:1 to 10:1) to give the pure products **6** or **7** in good to high yields.



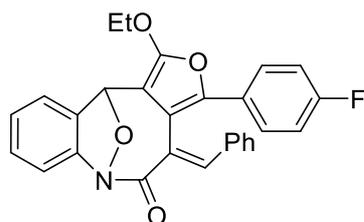
(E)-4-Benzylidene-1-ethoxy-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6a). Yellow solid, m.p. = 185.6 - 186.6 °C; 40.5 mg, 93% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.34 - 7.30 (m, 1H), 7.24 - 7.17 (comp, 5H), 6.95 - 6.93 (comp, 6H), 6.91 (s, 1H), 6.27 (s, 1H), 4.39 - 4.23 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.8, 152.6, 142.4, 141.1, 136.4, 135.2, 133.6, 130.4, 130.0, 128.80, 128.77, 128.2, 127.9, 127.3, 126.7, 125.7, 120.7, 115.8, 110.7, 99.7, 77.4, 68.2, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₂NO₄ [M+H]⁺: 436.1543, found 436.1546.



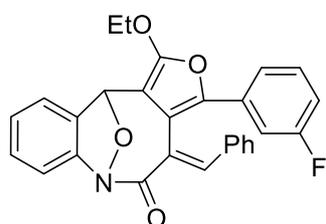
(E)-4-Benzylidene-3-(4-chlorophenyl)-1-ethoxy-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6b). Yellow solid, m.p. = 159.7 - 160.7 °C; 41.4 mg, 88% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.51 (d, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.5 Hz, 1H), 7.18 - 7.17 (m, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.00 - 6.99 (comp, 3H), 6.94 - 6.91 (comp, 3H), 6.26 (s, 1H), 4.39 - 4.24 (m, 2H), 1.46 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.6, 152.8, 142.4, 139.8, 136.3, 135.1, 133.9, 132.9, 130.0, 128.9, 128.84, 128.77, 128.6, 128.11, 128.08, 127.0, 126.8, 120.7, 115.8, 111.4, 99.8, 77.3, 68.3, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₁ClNO₄ [M+H]⁺: 470.1154, found 470.1156.



(E)-4-Benzylidene-3-(4-bromophenyl)-1-ethoxy-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6c). Yellow solid, m.p. = 179.1 - 180.5 °C; 46.3 mg, 90% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.51 (d, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.19 - 7.16 (m, 2H), 7.09 - 7.05 (comp, 4H), 7.00 - 6.99 (comp, 3H), 6.93 (s, 1H), 6.26 (s, 1H), 4.39 - 4.23 (m, 2H), 1.46 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.5, 152.8, 142.4, 139.8, 136.3, 135.1, 133.9, 131.0, 130.0, 129.3, 128.9, 128.8, 128.6, 128.1, 127.2, 126.8, 121.1, 120.7, 115.8, 111.5, 99.8, 77.3, 68.2, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₀BrNO₄Na [M+Na]⁺: 536.0468, found 536.0464.

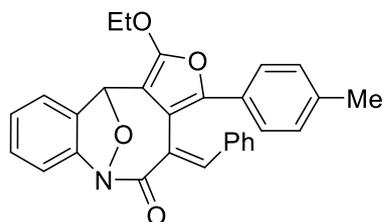


(E)-4-Benzylidene-1-ethoxy-3-(4-fluorophenyl)-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]jazocin-5(4H)-one (6d). Yellow solid, m.p. = 171.7 - 172.9 °C; 38.5 mg, 85% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 7.7 Hz, 1H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.18 - 7.15 (comp, 4H), 6.99 - 6.98 (comp, 3H), 6.91 (s, 1H), 6.66 (t, *J* = 8.7 Hz, 2H), 6.27 (s, 1H), 4.39 - 4.23 (m, 2H), 1.46 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.7, 162.0 (d, *J* = 247.6 Hz), 152.6, 142.4, 140.2, 136.4, 135.2, 133.7, 130.1, 128.9, 128.8, 128.4, 128.0, 127.8 (d, *J* = 8.2 Hz), 126.8, 126.7 (d, *J* = 3.3 Hz), 120.7, 115.8, 115.0 (d, *J* = 21.9 Hz), 110.7, 99.8, 77.3, 68.3, 15.4; ¹⁹F NMR (376 MHz, CDCl₃) (δ, ppm) -113.85; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₀FNO₄Na [M+Na]⁺: 476.1269, found 476.1272.

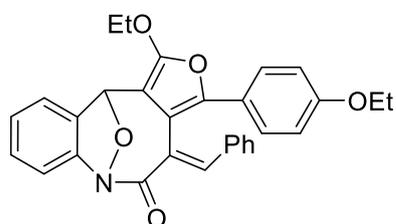


(E)-4-Benzylidene-1-ethoxy-3-(3-fluorophenyl)-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]jazocin-5(4H)-one (6e). Yellow solid, m.p. = 174.5 - 175.6 °C; 41.3 mg, 91% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.23 - 7.19 (comp, 3H), 7.02 - 6.98 (comp, 4H), 6.96 (s, 1H), 6.93 - 6.86 (m, 2H), 6.64 - 6.60 (m, 1H), 6.27 (s, 1H), 4.40 - 4.26 (m, 2H), 1.46 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.5, 162.3 (d, *J* = 244.5 Hz), 152.8, 142.4, 139.4 (d, *J* = 2.9 Hz), 136.3, 135.2, 134.2, 132.3 (d, *J* = 8.7 Hz), 129.9, 129.4 (d, *J* = 8.5 Hz), 128.9, 128.7, 128.5, 128.0, 126.8, 121.3 (d, *J* = 2.8 Hz), 120.7, 115.8, 113.9 (d, *J* = 21.3 Hz), 112.3 (d, *J* = 23.6 Hz), 111.9, 99.8, 77.3, 68.2, 15.4; ¹⁹F NMR (470 MHz, CDCl₃) (δ, ppm) -113.65; HRMS (TOF MS ESI⁺)

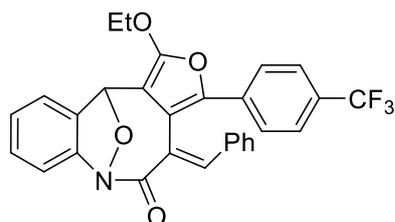
calculated for C₂₈H₂₀FNO₄Na [M+Na]⁺: 476.1269, found 476.1271.



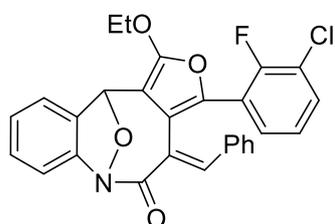
(E)-4-Benzylidene-1-ethoxy-3-(p-tolyl)-11H-6,11-epoxybenzo[b]furo[3,4-e]azocin-5(4H)-one (6f). Yellow solid, m.p. = 188.1 - 182.3 °C; 41.4 mg, 92% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.51 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 7.4 Hz, 1H), 7.34 - 7.30 (m, 1H), 7.23 - 7.17 (comp, 3H), 7.10 (d, *J* = 8.2 Hz, 2H), 6.96 - 6.95 (comp, 3H), 6.89 (s, 1H), 6.76 (d, *J* = 8.0 Hz, 2H), 6.26 (s, 1H), 4.38 - 4.22 (m, 2H), 2.14 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.9, 152.4, 142.5, 141.5, 137.2, 136.5, 135.3, 133.4, 130.2, 128.9, 128.8, 128.6, 128.2, 127.9, 127.6, 126.7, 125.7, 120.7, 115.8, 110.1, 99.7, 77.4, 68.2, 21.3, 15.5; HRMS (TOF MS ESI⁺) calculated for C₂₉H₂₃NO₄Na [M+Na]⁺: 472.1519, found 472.1521.



(E)-4-Benzylidene-1-ethoxy-3-(4-ethoxyphenyl)-11H-6,11-epoxybenzo[b]furo[3,4-e]azocin-5(4H)-one (6g). Yellow solid, m.p. = 196.8 - 197.9 °C; 43.6 mg, 91% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.23 - 7.18 (comp, 3H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.98 - 6.97 (comp, 3H), 6.89 (s, 1H), 6.49 (d, *J* = 8.5 Hz, 2H), 6.26 (s, 1H), 4.37 - 4.21 (m, 2H), 3.91 - 3.85 (m, 2H), 1.46 (d, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 180.0, 158.3, 152.2, 142.5, 141.4, 136.5, 135.3, 133.2, 130.2, 128.9, 128.8, 128.3, 127.9, 127.3, 126.7, 123.2, 120.7, 115.8, 114.1, 109.3, 99.7, 77.4, 68.3, 63.5, 15.5, 14.8; HRMS (TOF MS ESI⁺) calculated for C₃₀H₂₅NO₅Na [M+Na]⁺: 502.1625, found 502.1629.

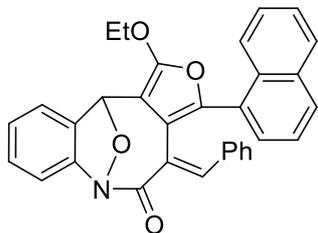


(E)-4-Benzylidene-1-ethoxy-3-(4-(trifluoromethyl)phenyl)-11H-6,11-epoxybenzo[b]furo[3,4-e]azocin-5(4H)-one (6h). Yellow solid, m.p. = 168.5 - 169.9 °C; 40.8 mg, 81% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.53 (d, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.15 - 7.13 (m, 2H), 6.97 - 6.94 (comp, 4H), 6.28 (s, 1H), 4.42 - 4.28 (m, 2H), 1.47 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.4, 153.3, 142.4, 139.2, 136.2, 135.1, 134.4, 133.7, 129.9, 129.0, 128.70 (q, *J* = 32.4 Hz), 128.68, 128.6, 128.1, 126.8, 125.8, 124.8 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 271.9 Hz), 120.7, 115.9, 112.8, 99.9, 77.3, 68.2, 15.4; ¹⁹F NMR (470 MHz, CDCl₃) (δ, ppm) -62.78; HRMS (TOF MS ESI⁺) calculated for C₂₉H₂₀F₃NO₄Na [M+Na]⁺: 526.1237, found 526.1233.

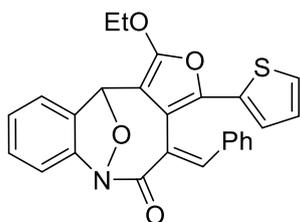


(E)-4-Benzylidene-3-(3-chloro-2-fluorophenyl)-1-ethoxy-11H-6,11-epoxybenzo[b]furo[3,4-e]azocin-5(4H)-one (6i). Yellow solid, m.p. = 166.8 - 167.9 °C; 38.5 mg, 79% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.06 - 6.96 (comp, 7H), 6.95 (s, 1H) 6.71 (t, *J* = 7.9 Hz, 1H), 6.28 (s, 1H), 4.38 - 4.24 (m, 2H), 1.45 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.3, 154.5 (d, *J* = 254.6 Hz), 153.4, 142.4, 136.2, 135.1, 135.0, 134.8, 130.0, 129.9, 128.9, 128.6, 128.5, 128.2, 128.00, 127.97, 126.7, 124.0 (d, *J* = 4.4 Hz), 121.4 (d, *J* = 17.7 Hz), 120.8, 120.3 (d, *J* = 13.8 Hz), 115.8, 114.3, 99.3, 77.3, 68.1, 15.4; ¹⁹F NMR (376 MHz, CDCl₃) (δ, ppm) -113.36; HRMS (TOF MS ESI⁺) calculated for C₂₈H₁₉ClFNO₄Na [M+Na]⁺: 510.0879,

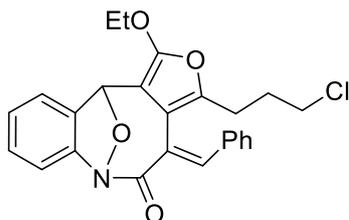
found 510.0882.



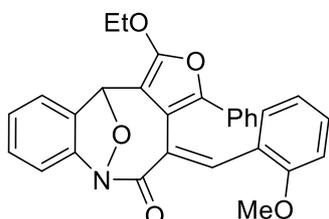
(E)-4-Benzylidene-1-ethoxy-3-(naphthalen-1-yl)-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6j). Yellow solid, m.p. = 169.7 - 170.6 °C; 43.2 mg, 89% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.62 - 7.56 (comp, 3H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.44 (d, *J* = 7.3 Hz, 1H), 7.39 - 7.34 (comp, 3H), 7.27 - 7.23 (m, 1H), 7.19 - 7.17 (m, 1H), 7.14 - 7.11 (m, 1H), 6.79 (s, 1H), 6.70 (d, *J* = 7.3 Hz, 2H), 6.53 (t, *J* = 7.5 Hz, 2H), 6.46 (t, *J* = 7.3 Hz, 1H), 6.33 (s, 1H), 4.38 - 4.21 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.7, 153.1, 142.6, 141.0, 136.4, 134.8, 134.5, 133.6, 130.2, 130.1, 128.9, 128.8, 128.3, 128.2, 127.74, 127.65, 127.4, 126.8, 126.7, 126.2, 125.8, 125.6, 124.9, 120.8, 115.9, 113.3, 99.5, 77.5, 68.2, 15.5; HRMS (TOF MS ESI⁺) calculated for C₃₂H₂₃NO₄Na [M+Na]⁺: 508.1519, found 508.1520.



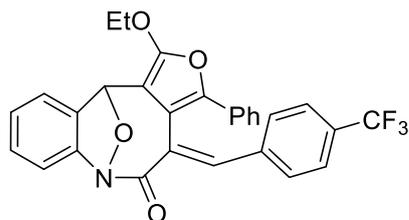
(E)-4-Benzylidene-1-ethoxy-3-(thiophen-2-yl)-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6k). Yellow oil; 26.9 mg, 61% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.50 (d, *J* = 7.7 Hz, 1H), 7.39 (d, *J* = 7.3 Hz, 1H), 7.34 - 7.31 (comp, 3H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.09 - 7.08 (comp, 3H), 6.97 (s, 1H), 6.94 (d, *J* = 5.0 Hz, 1H), 6.74 (d, *J* = 3.0 Hz, 1H), 6.61 - 6.59 (m, 1H), 6.26 (s, 1H), 4.39 - 4.25 (m, 2H), 1.46 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.5, 152.2, 142.4, 136.5, 136.3, 135.4, 133.9, 131.4, 129.5, 128.88, 128.85, 128.7, 128.2, 127.0, 126.7, 125.0, 124.7, 120.6, 115.8, 110.8, 99.7, 77.3, 68.4, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₉H₁₉NO₄SNa [M+Na]⁺: 464.0927, found 464.0931.



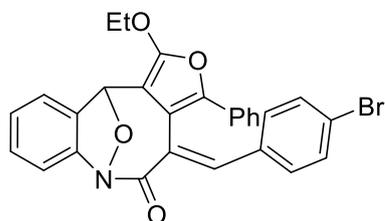
(E)-4-Benzylidene-3-(3-chloropropyl)-1-ethoxy-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6l). Yellow solid, m.p. = 132.6 - 133.6 °C; 26.2 mg, 60% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.46 (d, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 2H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.33 - 7.29 (comp, 3H), 7.27 - 7.24 (m, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.02 (s, 1H), 6.19 (s, 1H), 4.26 - 4.13 (m, 2H), 3.15 (t, *J* = 6.7 Hz, 2H), 2.04 - 1.98 (m, 1H), 1.94 - 1.88 (m, 1H), 1.67 - 1.61 (m, 1H), 1.47 - 1.43 (m, 1H), 1.41 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.4, 151.9, 142.4, 141.8, 136.4, 135.8, 132.4, 130.9, 129.0, 128.83, 128.75, 128.5, 126.6, 120.6, 115.8, 111.2, 98.6, 77.4, 68.3, 44.3, 29.4, 25.0, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₅H₂₂ClNO₄Na [M+Na]⁺: 458.1130, found 458.1134.



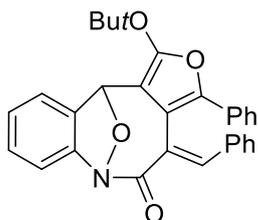
(E)-1-Ethoxy-4-(2-methoxybenzylidene)-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6m). Yellow solid, m.p. = 206.9 - 207.9 °C; 39.6 mg, 85% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 7.4 Hz, 1H), 7.34 - 7.30 (m, 1H), 7.26 - 7.25 (m, 1H), 7.22 - 7.16 (comp, 4H), 6.98 - 6.90 (comp, 4H), 6.52 (t, *J* = 7.5 Hz, 1H), 6.44 (d, *J* = 8.3 Hz, 1H), 6.27 (s, 1H), 4.37 - 4.21 (m, 2H), 3.67 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.8, 157.3, 152.5, 142.6, 141.0, 136.5, 130.6, 130.4, 129.9, 129.7, 128.9, 128.8, 127.7, 126.9, 126.6, 125.8, 124.2, 120.7, 119.7, 115.8, 111.1, 110.0, 100.0, 77.4, 68.2, 54.9, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₉H₂₃NO₅Na [M+Na]⁺: 488.1468, found 488.1469.



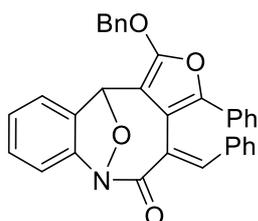
(E)-1-Ethoxy-3-phenyl-4-(4-(trifluoromethyl)benzylidene)-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6n). Yellow solid, m.p. = 171.8 - 172.6 °C; 37.3 mg, 74% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.53 (d, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 7.4 Hz, 1H), 7.37 - 7.33 (m, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.20 - 7.15 (comp, 4H), 7.09 - 7.07 (m, 2H), 6.98 - 6.95 (comp, 3H), 6.90 (s, 1H), 6.29 (s, 1H), 4.39 - 4.23 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.2, 152.8, 142.3, 141.7, 139.1, 136.2, 132.6, 131.8, 130.2, 129.5 (q, *J* = 32.7 Hz), 129.0, 128.9, 128.2, 127.7, 126.9, 126.4, 124.8 (q, *J* = 3.5 Hz), 121.3 (q, *J* = 274.0 Hz), 120.8, 115.8, 110.3, 99.6, 77.4, 68.3, 15.4; ¹⁹F NMR (376 MHz, CDCl₃) (δ, ppm) -62.99; HRMS (TOF MS ESI⁺) calculated for C₂₉H₂₀F₃NO₄Na [M+Na]⁺: 526.1237, found 526.1240.



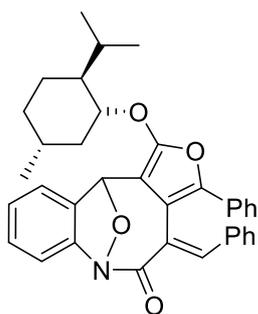
(E)-4-(4-Bromobenzylidene)-1-ethoxy-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6o). Yellow solid, m.p. = 191.6 - 192.8 °C; 45.8 mg, 89% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.35 - 7.32 (m, 1H), 7.24 - 7.21 (m, 1H), 7.18 - 7.16 (m, 2H), 7.07 - 7.05 (m, 2H), 7.03 - 6.99 (comp, 5H), 6.82 (s, 1H), 6.26 (s, 1H), 4.38 - 4.24 (m, 2H), 1.46 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.5, 152.8, 142.4, 141.3, 136.3, 134.2, 132.3, 131.1, 131.0, 130.3, 128.9, 128.1, 127.7, 126.8, 126.0, 122.2, 120.7, 115.8, 110.5, 99.6, 77.4, 68.2, 15.5; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₀BrNO₄Na [M+Na]⁺: 536.0468, found 536.0461.



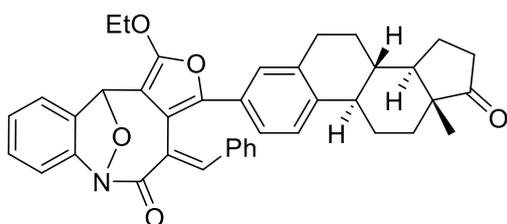
(E)-4-Benzylidene-1-(tert-butoxy)-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6p). Yellow solid, m.p. = 162.4 - 163.6 °C; 43.1 mg, 93% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 7.3 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.22 - 7.15 (comp, 5H), 6.95 - 6.91 (comp, 7H), 6.23 (s, 1H), 1.53 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.9, 151.2, 142.4, 142.0, 136.2, 135.3, 133.4, 130.5, 130.2, 128.9, 128.8, 128.2, 127.9, 127.3, 126.6, 125.8, 120.9, 115.8, 110.0, 104.6, 84.5, 77.7, 29.2; HRMS (TOF MS ESI⁺) calculated for C₃₀H₂₅NO₄Na [M+Na]⁺: 486.1676, found 486.1678.



(E)-4-Benzylidene-1-(benzyloxy)-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (6q). Yellow oil; 42.3 mg, 85% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.49 (d, *J* = 7.8 Hz, 1H), 7.46 - 7.43 (comp, 5H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.22 - 7.19 (comp, 3H), 7.15 - 7.12 (m, 3H), 6.99 - 6.93 (comp, 6H), 6.90 (s, 1H), 6.10 (s, 1H), 5.29 (d, *J* = 11.5 Hz, 1H), 5.23 (d, *J* = 11.5 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.8, 152.0, 142.3, 141.6, 136.2, 135.5, 135.2, 133.8, 130.3, 130.0, 129.2, 129.0, 128.8, 128.7, 128.2, 128.0, 127.9, 127.4, 126.7, 125.9, 120.8, 115.7, 110.7, 101.1, 77.3, 74.3; HRMS (TOF MS ESI⁺) calculated for C₃₃H₂₃NO₄Na [M+Na]⁺: 520.1519, found 520.1523.

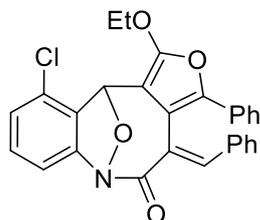


4-((*E*)-Benzylidene)-1-(((*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl)oxy)-3-phenyl-11*H*-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4*H*)-one (6r). Yellow solid, m.p. = 142.4 - 144.1 °C; 47.5 mg, 87% yield, 1:1 *dr*; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.63 - 7.61 (m, 2H), 7.56 - 7.50 (comp, 4H), 7.43 - 7.37 (m, 2H), 7.35 - 7.28 (comp, 4H), 7.22 - 7.20 (comp, 8H), 6.98 - 6.95 (comp, 8H), 6.92 - 6.91 (m, 2H), 6.26 (d, *J* = 2.7 Hz, 1H), 6.24 (d, *J* = 2.7 Hz, 1H), 4.38 - 4.33 (m, 2H), 2.42 - 2.35 (m, 1H), 2.27 - 2.24 (m, 1H), 2.21 - 2.17 (m, 1H), 1.95 - 1.92 (m, 1H), 1.78 - 1.67 (comp, 5H), 1.60 - 1.55 (m, 3H), 1.38 - 1.34 (m, 2H), 1.29 - 1.27 (m, 2H), 1.14 - 1.09 (m, 2H), 1.06 - 1.01 (comp, 6H), 0.97 (dd, *J* = 6.9, 2.8 Hz, 6H), 0.88 (dd, *J* = 6.3, 2.8 Hz, 3H), 0.81 (dd, *J* = 6.8, 2.9 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.9, 179.8, 156.1, 154.5, 152.3, 152.1, 142.4, 142.3, 140.9, 140.8, 136.2, 135.2, 135.2, 133.4, 130.9, 130.5, 130.4, 130.1, 130.0, 128.8, 128.73, 128.71, 128.7, 128.13, 128.07, 127.83, 127.79, 127.2, 127.1, 126.5, 126.3, 125.8, 125.5, 124.4, 121.1, 120.9, 119.7, 118.2, 115.7, 115.6, 115.1, 110.7, 110.6, 100.4, 100.0, 82.8, 82.7, 77.5, 77.3, 48.07, 48.05, 41.9, 41.6, 34.21, 34.17, 31.7, 31.5, 26.1, 23.5, 23.2, 22.3, 22.0, 21.0, 20.8, 16.3, 16.2; HRMS (TOF MS ESI⁺) calculated for C₃₆H₃₅NO₄Na [M+Na]⁺: 568.2458, found 568.2460.

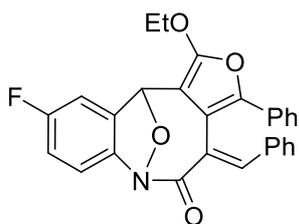


4-((*E*)-Benzylidene)-1-ethoxy-3-(((*8S,9R,13R,14R*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)-11*H*-6,11-epoxybenz

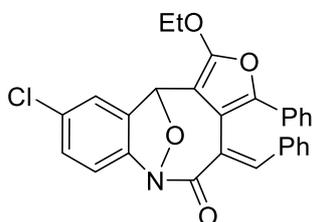
o[b]furo[3,4-*e*]azocin-5(4*H*)-one (6s). Yellow solid, m.p. = 158.9 - 160.1 °C; 53.8 mg, 88% yield, 1:1 *dr*; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 7.7 Hz, 1H), 7.39 (d, *J* = 7.3 Hz, 1H), 7.35 - 7.32 (m, 1H), 7.23 - 7.20 (m, 1H), 7.15 - 7.13 (m, 2H), 6.98 - 6.92 (comp, 4H), 6.89 - 6.88 (d, *J* = 5.9 Hz, 2H), 6.77 (d, *J* = 9.6 Hz, 1H), 6.26 (s, 1H), 4.37 - 4.23 (m, 2H), 2.62 - 2.56 (m, 2H), 2.49 (dd, *J* = 19.1, 8.8 Hz, 1H), 2.28 - 2.25 (m, 1H), 2.16 - 2.09 (m, 2H), 2.05 - 2.00 (m, 1H), 1.93 - 1.88 (m, 2H), 1.64 - 1.56 (m, 2H), 1.48 - 1.39 (comp, 7H), 0.89 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 180.01, 179.97, 152.41, 152.40, 142.5, 141.4, 141.2, 139.1, 138.9, 136.4, 135.7, 135.7, 135.54, 135.49, 133.39, 133.35, 130.2, 130.1, 128.8, 128.7, 128.6, 128.04, 127.99, 127.9, 127.8, 127.69, 127.65, 126.7, 126.6, 126.5, 124.9, 123.7, 123.6, 120.7, 115.8, 110.3, 110.2, 99.68, 99.65, 77.41, 77.36, 68.2, 50.53, 50.49, 48.0, 44.4, 38.1, 36.0, 31.6, 29.4, 26.5, 26.4, 25.8, 25.7, 21.69, 21.67, 15.4, 13.92, 13.90; HRMS (TOF MS ESI⁺) calculated for C₄₀H₃₇NO₅Na [M+Na]⁺: 634.2564, found 634.2567.



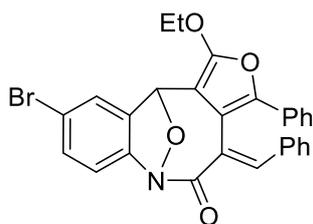
(*E*)-4-Benzylidene-10-chloro-1-ethoxy-3-phenyl-11*H*-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4*H*)-one (7a). Yellow solid, m.p. = 209.9 - 211.1 °C; 35.7 mg, 76% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.42 (d, *J* = 7.7 Hz, 1H), 7.29 - 7.25 (m, 1H), 7.21 - 7.17 (comp, 3H), 7.13 - 7.12 (m, 2H), 6.99 - 6.94 (comp, 6H), 6.90 (s, 1H), 6.41 (s, 1H), 4.43 - 4.36 (m, 1H), 4.28 - 4.22 (m, 1H), 1.45 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.5, 153.3, 144.0, 141.5, 135.2, 134.6, 134.3, 130.31, 130.25, 129.6, 128.7, 128.2, 128.0, 127.9, 127.44, 127.37, 127.2, 126.1, 114.2, 110.7, 97.7, 77.3, 68.3, 15.2; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₀ClNO₄Na [M+Na]⁺: 492.0973, found 492.0973.



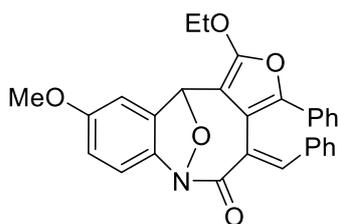
(E)-4-Benzylidene-1-ethoxy-9-fluoro-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (7b). Yellow solid, m.p. = 172.6 - 174.1 °C; 37.2 mg, 82% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.46 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.22 - 7.17 (comp, 4H), 7.09 (dd, *J* = 7.4, 2.4 Hz, 1H), 7.02 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.99 - 6.94 (comp, 6H), 6.91 (s, 1H), 6.24 (s, 1H), 4.42 - 4.27 (m, 2H), 1.47 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.8, 161.4 (d, *J* = 245.3 Hz), 152.8, 141.2, 138.50, 138.45 (d, *J* = 6.2 Hz), 135.1, 133.8, 130.3, 129.7, 128.8, 128.4, 128.0, 127.4, 125.8, 116.9 (d, *J* = 8.9 Hz), 115.3 (d, *J* = 24.2 Hz), 110.6, 108.8, 108.5, 98.6, 77.4, 68.1, 15.5; ¹⁹F NMR (376 MHz, CDCl₃) (δ, ppm) -115.52; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₀FNO₄Na [M+Na]⁺: 476.1269, found 476.1266.



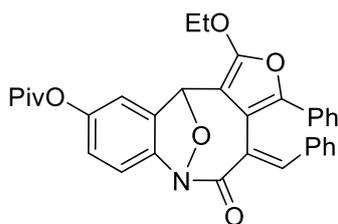
(E)-4-Benzylidene-9-chloro-1-ethoxy-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (7c). Yellow solid, m.p. = 175.6 - 176.9 °C; 39.5 mg, 84% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.52 (d, *J* = 1.5 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.21 - 7.16 (comp, 5H), 6.98 - 6.94 (comp, 6H), 6.92 (s, 1H), 6.25 (s, 1H), 4.40 - 4.25 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.3, 152.6, 143.6, 141.3, 135.11, 135.09, 134.6, 134.1, 130.3, 129.6, 128.8, 128.4, 128.0, 127.4, 126.8, 125.8, 121.4, 116.5, 110.5, 99.1, 77.3, 68.1, 15.5; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₀ClNO₄Na [M+Na]⁺: 492.0973, found 492.0977.



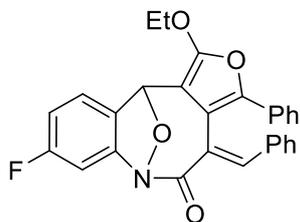
(E)-4-Benzylidene-9-bromo-1-ethoxy-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]jazocin-5(4H)-one (7d). Yellow oil; 33.9 mg, 66% yield; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.50 (d, $J = 1.3$ Hz, 1H), 7.46 - 7.44 (m, 1H), 7.40 - 7.38 (m, 1H), 7.21 - 7.16 (comp, 4H), 6.98 - 6.95 (comp, 6H), 6.91 (s, 1H), 6.24 (s, 1H), 4.42 - 4.28 (m, 2H), 1.47 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 179.4, 152.7, 141.6, 141.2, 138.7, 135.1, 134.0, 131.7, 130.3, 129.5, 128.8, 128.4, 127.9, 127.4, 125.8, 124.1, 119.6, 117.2, 110.5, 98.7, 77.2, 68.1, 15.4; HRMS (TOF MS ESI^+) calculated for $\text{C}_{28}\text{H}_{20}\text{BrNO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 536.0468, found 536.0465.



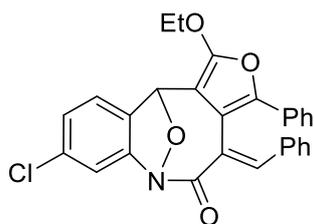
(E)-4-Benzylidene-1-ethoxy-9-methoxy-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]jazocin-5(4H)-one (7e). Yellow solid, m.p. = 142.1 - 143.6 °C; 36.8 mg, 79% yield; ^1H NMR (400 MHz, CDCl_3) (δ , ppm) 7.42 (d, $J = 8.5$ Hz, 1H), 7.23 - 7.17 (comp, 4H), 6.98 - 6.93 (comp, 7H), 6.89 (s, 1H), 6.81 (dd, $J = 8.5, 2.5$ Hz, 1H), 6.22 (s, 1H), 4.40 - 4.25 (m, 2H), 3.80 (s, 3H), 1.46 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) (δ , ppm) 180.3, 158.8, 152.7, 141.0, 138.1, 135.9, 135.3, 133.4, 130.4, 130.1, 128.8, 128.2, 127.9, 127.3, 125.8, 116.4, 112.7, 110.8, 107.7, 99.4, 77.5, 68.1, 56.0, 15.5; HRMS (TOF MS ESI^+) calculated for $\text{C}_{29}\text{H}_{23}\text{NO}_5\text{Na}$ $[\text{M}+\text{Na}]^+$: 488.1468, found 488.1470.



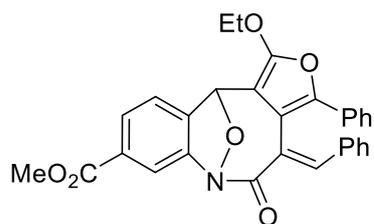
(E)-4-Benzylidene-1-ethoxy-5-oxo-3-phenyl-4,5-dihydro-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-9-yl pivalate (7f). Yellow solid, m.p. = 119.1 - 120.5 °C; 47.7 mg, 89% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.49 (d, *J* = 8.4 Hz, 1H), 7.22 - 7.16 (comp, 4H), 7.11 (d, *J* = 1.6 Hz, 1H), 7.01 - 6.95 (comp, 7H), 6.91 (s, 1H), 6.25 (s, 1H), 4.40 - 4.25 (m, 2H), 1.44 (t, *J* = 7.1 Hz, 3H), 1.35 (s, 9H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.7, 177.1, 154.7, 152.8, 149.6, 141.3, 139.8, 137.7, 135.2, 133.8, 130.4, 129.8, 128.8, 128.3, 127.9, 127.4, 125.9, 121.5, 116.3, 114.6, 110.6, 99.3, 77.4, 68.3, 39.3, 27.2, 15.4; HRMS (TOF MS ESI⁺) calculated for C₃₃H₂₉NO₆Na [M+Na]⁺: 558.1887, found 558.1889.



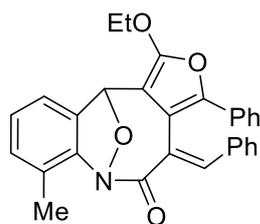
(E)-4-Benzylidene-1-ethoxy-8-fluoro-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (7g). Yellow solid, m.p. = 175.4 - 176.4 °C; 38.5 mg, 85% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.32 - 7.30 (m, 1H), 7.26 - 7.24 (m, 1H), 7.22 - 7.20 (m, 2H), 7.18 - 7.17 (m, 2H), 6.98 - 6.95 (comp, 6H), 6.92 - 6.88 (m, 2H), 6.24 (s, 1H), 4.39 - 4.25 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.3, 163.0 (d, *J* = 247.1 Hz), 152.6, 143.9 (d, *J* = 12.0 Hz), 141.2, 135.1, 134.0, 132.2 (d, *J* = 2.6 Hz), 130.3, 129.7, 128.8, 128.4, 127.9, 127.4, 125.8, 121.4 (d, *J* = 9.7 Hz), 113.3 (d, *J* = 23.1 Hz), 110.5, 104.6 (d, *J* = 27.5 Hz), 99.4, 77.2, 68.1, 15.4; ¹⁹F NMR (376 MHz, CDCl₃) (δ, ppm) -112.17; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₀FNO₄Na [M+Na]⁺: 476.1269, found 476.1273.



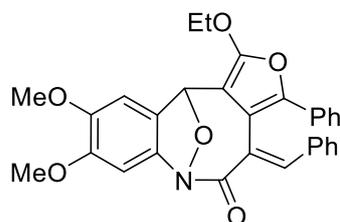
(E)-4-Benzylidene-8-chloro-1-ethoxy-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (7h). Yellow solid, m.p. = 198.6 - 199.9 °C; 38.1 mg, 81% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.44 (d, *J* = 8.2 Hz, 1H), 7.35 (s, 1H), 7.30 - 7.28 (m, 1H), 7.22 - 7.16 (comp, 4H), 6.96 - 6.95 (comp, 6H), 6.91 (s, 1H), 6.24 (s, 1H), 4.41 - 4.27 (m, 2H), 1.47 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.5, 152.7, 141.2, 141.1, 138.3, 135.1, 134.0, 132.0, 130.3, 129.6, 128.8, 128.4, 127.9, 127.4, 125.8, 121.2, 116.8, 110.5, 98.7, 77.3, 68.1, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₀ClNO₄Na [M+Na]⁺: 492.0973, found 492.0977.



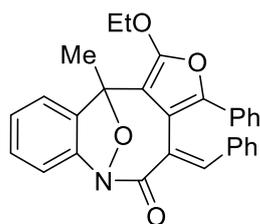
Methyl (E)-4-benzylidene-1-ethoxy-5-oxo-3-phenyl-4,5-dihydro-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocine-8-carboxylate (7i). Yellow solid, m.p. = 163.8 - 164.9 °C; 43.9 mg, 89% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 8.15 (s, 1H), 7.97 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.21 - 7.17 (comp, 4H), 6.97 - 6.94 (comp, 7H), 6.31 (s, 1H), 4.41 - 4.25 (m, 2H), 3.93 (s, 3H), 1.46 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.4, 166.2, 152.7, 142.8, 141.3, 141.1, 135.1, 134.0, 131.3, 130.3, 129.5, 128.9, 128.8, 128.4, 127.9, 127.4, 125.8, 120.6, 116.6, 110.6, 98.6, 77.3, 68.1, 52.5, 15.4; HRMS (TOF MS ESI⁺) calculated for C₃₀H₂₃NO₆Na [M+Na]⁺: 516.1418, found 516.1413.



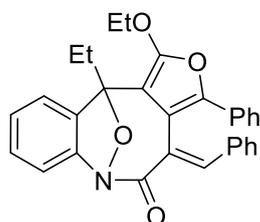
(E)-4-Benzylidene-1-ethoxy-7-methyl-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (7j). Yellow solid, m.p. = 169.8 - 171.2 °C; 40.9 mg, 91% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.25 - 7.23 (comp, 3H), 7.21 - 7.19 (m, 2H), 7.15 - 7.10 (m, 2H), 6.98 - 6.92 (comp, 6H), 6.86 (s, 1H), 6.20 (s, 1H), 4.39 - 4.32 (m, 1H), 4.31 - 4.25 (m, 1H), 2.66 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 181.0, 152.8, 141.9, 140.8, 137.0, 135.3, 132.4, 130.9, 130.54, 130.47, 128.8, 128.2, 127.9, 127.7, 127.2, 126.9, 125.7, 118.1, 111.1, 99.4, 77.6, 68.3, 19.1, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₉H₂₃NO₄Na [M+Na]⁺: 472.1519, found 472.1514.



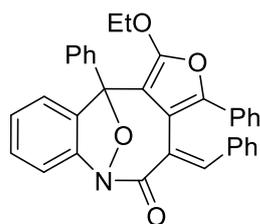
(E)-4-Benzylidene-1-ethoxy-8,9-dimethoxy-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (7k). Yellow solid, m.p. = 194.3 - 195.7 °C; 41.1 mg, 83% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.22 - 7.21 (m, 2H), 7.18 - 7.17 (m, 2H), 7.13 (s, 1H), 6.98 - 6.95 (comp, 6H), 6.92 (s, 1H), 6.90 (s, 1H), 6.21 (s, 1H), 4.40 - 4.33 (m, 1H), 4.32 - 4.27 (m, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 1.46 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 180.5, 152.4, 149.6, 148.0, 141.1, 136.0, 135.2, 133.5, 130.4, 130.2, 128.8, 128.2, 127.9, 127.4, 127.3, 125.8, 110.7, 104.3, 100.6, 100.1, 77.8, 68.1, 56.6, 56.6, 15.5; HRMS (TOF MS ESI⁺) calculated for C₃₀H₂₅NO₆Na [M+Na]⁺: 518.1574, found 518.1573.



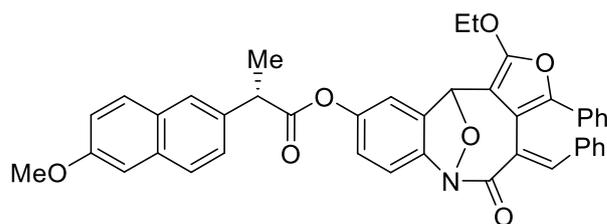
(E)-4-Benzylidene-1-ethoxy-11-methyl-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (7l). Yellow solid, m.p. = 209.6 - 210.7 °C; 40.0 mg, 89% yield; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.49 (d, *J* = 7.7 Hz, 1H), 7.32 - 7.29 (m, 2H), 7.22 - 7.18 (comp, 5H), 6.98 - 6.93 (comp, 6H), 6.90 (s, 1H), 4.36 - 4.30 (m, 1H), 4.28 - 4.22 (m, 1H), 2.11 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.2, 152.4, 142.9, 140.5, 139.6, 135.3, 133.1, 130.4, 130.3, 128.8, 128.5, 128.2, 127.92, 127.90, 127.3, 126.7, 125.8, 119.7, 115.7, 111.0, 103.6, 84.8, 68.1, 21.1, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₉H₂₃NO₄Na [M+Na]⁺: 472.1519, found 472.1516.



(E)-4-Benzylidene-1-ethoxy-11-ethyl-3-phenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (7m). Yellow solid, m.p. = 207.9 - 209.2 °C; 43.1 mg, 93% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.49 (d, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.26 - 7.16 (comp, 6H), 6.99 - 6.96 (comp, 6H), 6.90 (s, 1H), 4.36 - 4.20 (m, 2H), 2.68 - 2.59 (m, 1H), 2.49 - 2.41 (m, 1H), 1.43 (t, *J* = 7.0 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 179.2, 152.1, 143.2, 140.6, 138.4, 135.4, 132.9, 130.6, 130.4, 128.7, 128.4, 128.1, 127.9, 127.2, 126.6, 125.8, 119.9, 115.7, 111.6, 102.2, 88.1, 68.0, 26.8, 15.5, 8.2; HRMS (TOF MS ESI⁺) calculated for C₃₀H₂₅NO₄Na [M+Na]⁺: 486.1676, found 486.1679.

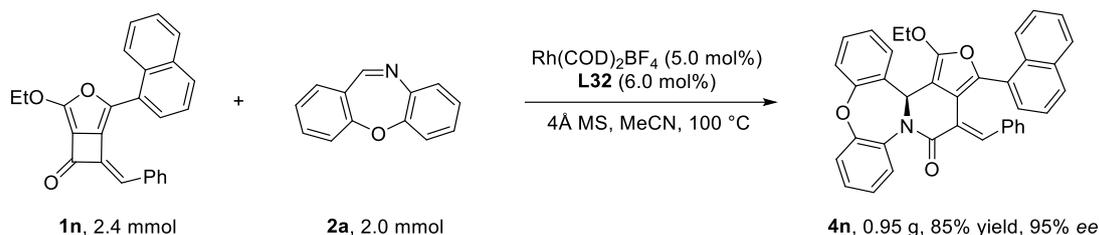


(E)-4-Benzylidene-1-ethoxy-3,11-diphenyl-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-5(4H)-one (7n). Yellow solid, m.p. = 197.2 - 198.5 °C; 43.5 mg, 85% yield; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.71 - 7.70 (m, 2H), 7.57 - 7.55 (m, 1H), 7.46 - 7.38 (comp, 3H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.30 - 7.23 (comp, 6H), 7.00 - 6.96 (comp, 6H), 6.93 (s, 1H), 4.21 - 4.07 (m, 2H), 1.19 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 178.7, 152.7, 144.1, 140.6, 138.2, 136.3, 135.3, 133.0, 130.4, 130.3, 129.8, 129.3, 128.8, 128.7, 128.5, 128.3, 128.0, 127.3, 126.7, 125.7, 121.8, 115.4, 111.9, 101.7, 90.0, 67.6, 15.3; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₅NO₄Na [M+Na]⁺: 534.1676, found 534.1674.

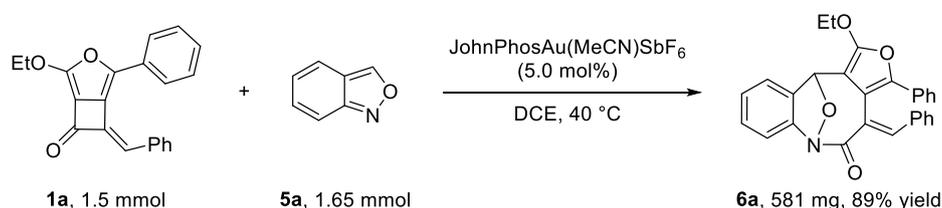


4-((E)-Benzylidene)-1-ethoxy-5-oxo-3-phenyl-4,5-dihydro-11H-6,11-epoxybenzo[*b*]furo[3,4-*e*]azocin-9-yl (2S)-2-(6-methoxynaphthalen-2-yl)propanoate (7o). Yellow solid, m.p. = 116.3 - 117.5 °C; 57.1 mg, 86% yield, 1:1 *dr*; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.75 - 7.71 (comp, 3H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.24 (s, 1H) 7.20 - 7.13 (comp, 6H), 7.01 - 6.99 (m, 1H), 6.94 - 6.91 (comp, 6H), 6.88 (s, 1H), 6.19 (s, 1H), 4.30 - 4.12 (m, 2H), 4.11 - 4.06 (m, 1H), 3.91 (s, 3H), 1.68 (d, *J* = 7.1 Hz, 3H), 1.28 - 1.24 (m, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 179.61, 179.60, 173.2, 157.9, 152.7, 149.32, 149.30, 141.19, 141.16, 139.87, 139.86, 137.70, 137.68, 135.1, 135.01, 134.99, 134.0, 133.8, 130.3, 129.8, 129.4, 129.1, 128.8, 128.3, 127.9, 127.5, 127.3, 126.3, 126.2, 126.1, 125.82, 125.80, 121.5, 121.4, 119.31, 119.29, 116.27, 116.25, 114.5, 110.6, 105.72, 105.71, 99.2, 99.1, 77.4, 77.3, 68.32, 68.27, 55.5, 45.6, 18.5, 15.3, 15.2; HRMS (TOF MS ESI⁺) calculated for C₄₂H₃₃NO₇Na [M+Na]⁺: 686.2149, found 686.2145.

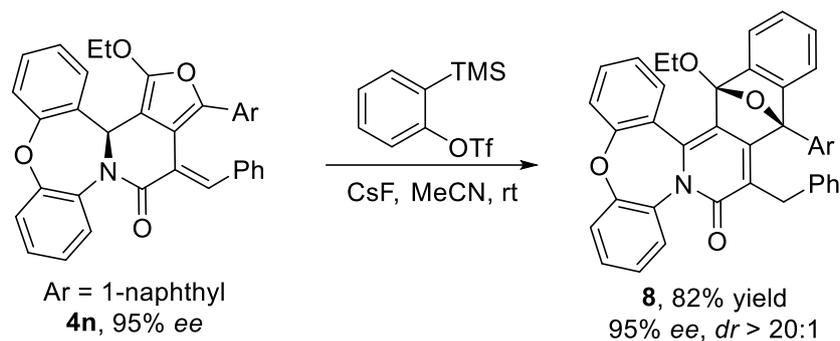
General Procedure for Scale Up and Synthetic Applications



Scale-up for the synthesis 4n: To a 50-mL oven-dried vial containing a magnetic stirring bar, cyclobutanone **1n** (879.4 mg, 2.4 mmol, 1.2 equiv.), imine **2a** (390.2 mg, 2.0 mmol, 1.0 equiv.), 4Å MS (1.0 g), Rh(COD)₂BF₄ (40.0 mg, 5.0 mol%), and chiral ligand **L32** (46.0 mg, 6.0 mol%) in 10 mL MeCN under argon atmosphere at 100 °C. After addition, the reaction mixture was stirred overnight under these conditions until consumption of the material (monitored by TLC). Then the solvent was evaporated under reduced pressure. The residues was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 50:1 to 20:1) to give 0.95 g pure product **4n** in 85% yield with 95% *ee*.

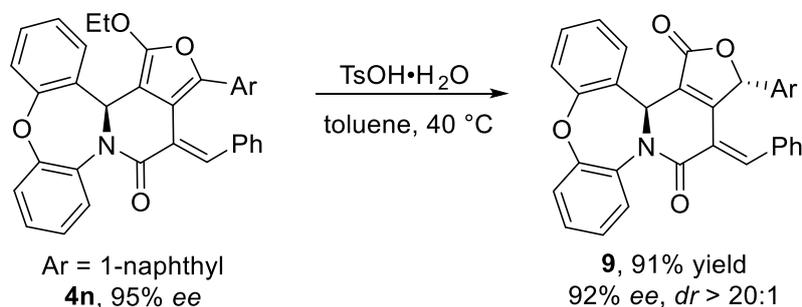


Scale up for the synthesis 6a: To a 25-mL oven-dried vial containing a magnetic stirring bar, cyclobutanone **1a** (474.5 mg, 1.5 mmol, 1.0 equiv.), and anthranil **5a** (196.6 mg, 1.65 mmol, 1.1 equiv.) in DCE (5.0 mL), was added a solution of JohnPhosAu(MeCN)SbF₆ (57.9 mg, 5.0 mol%) in dry DCE (5.0 mL) slowly *via* a syringe under argon atmosphere at 40 °C. After addition, the reaction mixture was stirred overnight under these conditions until consumption of the material (monitored by TLC). Then the solvent was evaporated under reduced pressure. The residues was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 30:1 to 10:1) to give 581 mg pure product **6a** in 89% yield.

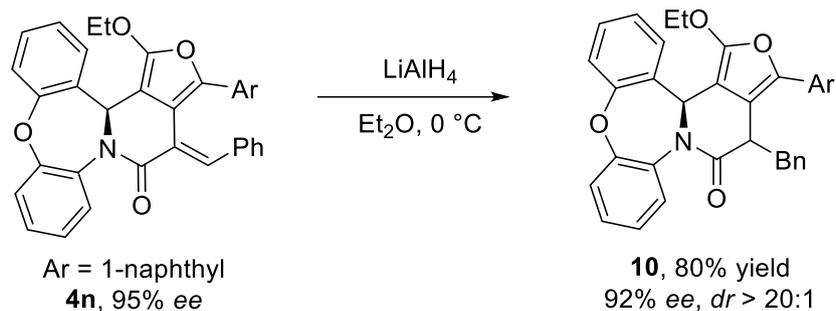


Synthesis of 8: To a 10-mL oven-dried round bottom flask containing a magnetic stirring bar, 2-(trimethylsilyl)phenyltrifluoromethanesulfonate (89.4 mg, 0.3 mmol, 1.5 equiv.) in dry MeCN (1.0 mL), was added CsF (91.1 mg, 0.6 mmol, 3.0 equiv.) at room temperature, and the reaction mixture was stirred for 15 min under these conditions. Then a solution of **4n** (112.2 mg, 0.2 mmol, 1.0 equiv.) in dry MeCN (1.0 mL) was added slowly *via* a syringe at room temperature. After stirring for additional 3.0 h, the reaction was quenched with saturated aqueous NH₄Cl solution (3.0 mL) and the organic phase was separated, and the aqueous phase was extracted with EtOAc (3 × 5.0 mL). The combined organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure after filtration. The obtained residues was purified by column chromatography on silica gel (Hexane/EtOAc = 20/1 - 10/1) to give the pure product **8** as white solid (104.5 mg, 82% yield). m.p. = 210.5 - 212.2 °C; *dr* > 20:1, 95% ee; $[\alpha]_D^{20} = 27.00$ (c = 0.033, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 8.30 (d, *J* = 7.2 Hz, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.56 - 7.48 (comp, 4H), 7.46 - 7.41 (m, 1H), 7.35 - 7.28 (comp, 4H), 7.23 (s, 1H), 7.19 (t, *J* = 7.5 Hz, 2H), 7.15 - 7.08 (comp, 5H), 6.62 - 6.60 (m, 2H), 3.88 - 3.84 (m, 1H), 3.73 (d, *J* = 14.8 Hz, 1H), 3.17 - 3.13 (m, 1H), 2.61 (d, *J* = 14.8 Hz, 1H), 0.80 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) (δ, ppm) 162.4, 162.2, 157.9, 155.8, 146.7, 145.7, 139.7, 135.1, 134.4, 132.5, 131.8, 131.2, 131.0, 129.7, 129.0, 128.92, 128.85, 128.0, 127.6, 127.2, 126.9, 126.3, 125.9, 125.8, 125.1, 124.9, 124.9, 124.8, 124.7, 124.6, 123.5, 121.1, 120.3, 119.7, 119.3, 110.6, 86.8, 62.4, 31.2, 14.8; HRMS (TOF MS ESI⁺) calculated for C₄₄H₃₁NO₄Na [M+Na]⁺: 660.2145, found: 660.2140; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol

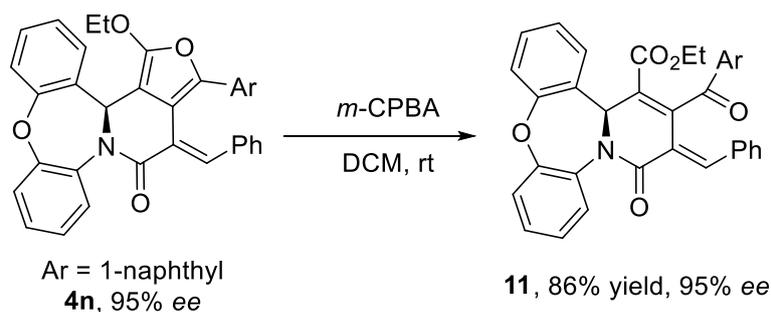
= 90:10, flow rate = 1.0 mL/min, $t_{\text{minor}} = 15.4$ min, $t_{\text{major}} = 22.5$ min.



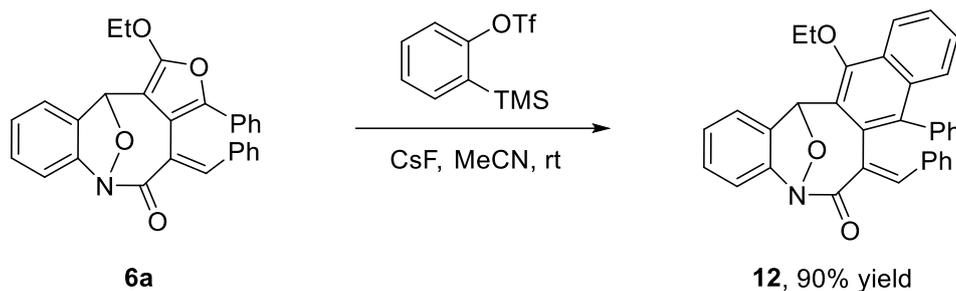
Synthesis of 9: To a 10-mL oven-dried vial containing a magnetic stirring bar, *p*-toluenesulfonic acid (TsOH·H₂O, 38.0 mg, 0.2 mmol, 2.0 equiv.), **4n** (56.1 mg, 0.1 mmol), and toluene (2.0 mL) were added in sequence, and the reaction mixture was stirred at 40 °C for 1.0 h. After the reaction was completed (reaction monitored by TLC), the reaction mixture was diluted with H₂O (3.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residues was purified by flash chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 10:1 to 5:1) to afford pure product **9** as white solid (48.5 mg, 91% yield). m.p. = 258.9 - 260.2 °C; *dr* > 20:1, 92% ee; $[\alpha]_{\text{D}}^{20} = 27.00$ (c = 0.033, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 8.12 (s, 1H), 7.75 - 7.71 (m, 2H), 7.52 - 7.48 (m, 2H), 7.44 - 7.42 (m, 1H), 7.40 - 7.37 (m, 1H), 7.35 - 7.21 (comp, 6H), 7.13 - 7.10 (m, 1H), 6.92 - 6.91 (m, 2H), 6.84 - 6.79 (m, 3H), 6.71 - 6.69 (m, 2H), 6.23 (s, 1H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 169.7, 163.4, 157.1, 154.6, 152.2, 146.2, 134.6, 133.5, 132.3, 131.5, 130.6, 130.0, 129.4, 129.3, 128.58, 128.55, 128.5, 128.4, 128.2, 127.6, 127.0, 126.5, 126.0, 125.8, 124.9, 124.5, 124.3, 123.1, 122.4, 121.8, 121.7, 79.1, 56.5; HRMS (TOF MS ESI⁺) calculated for C₃₆H₂₃NO₄Na [M+Na]⁺: 556.1519, found 556.1523; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 70:30, flow rate = 1.0 mL/min, $t_{\text{minor}} = 21.3$ min, $t_{\text{major}} = 16.7$ min.



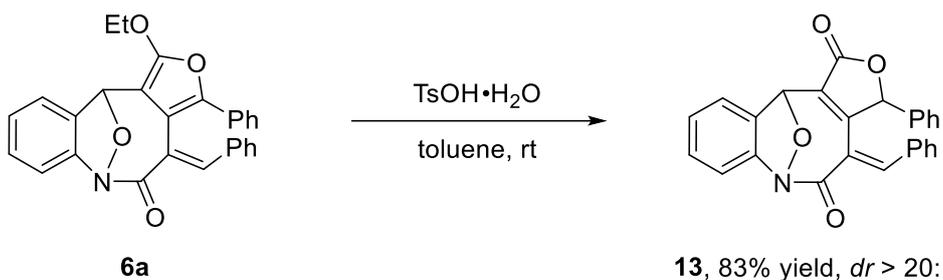
Synthesis of 10: To a 10-mL oven-dried round-bottom flask with a magnetic stirring bar, and **4n** (56.1 mg, 0.1 mmol) in dry Et₂O (2.0 mL), was added LiAlH₄ (3.8 mg, 0.1 mmol, 1.0 equiv.) at 0 °C, and the reaction mixture was stirred for 1.0 h under these conditions. After the reaction was completed (reaction monitored by TLC), the reaction mixture was quenched with saturated aqueous ammonium chloride (3.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residues was purified by flash chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 15:1) to give pure product **10** as colorless oil (45.1 mg, 80% yield). *dr* > 20:1, 92% *ee*; [α]_D²⁰ = 162.11 (c = 0.033, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.73 - 7.69 (m, 2H), 7.63 (d, *J* = 8.2 Hz, 1H), 7.40 - 7.34 (m, 3H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.27 - 7.22 (m, 3H), 7.19 - 7.07 (comp, 5H), 6.85 (d, *J* = 7.0 Hz, 1H), 6.48 - 6.45 (m, 2H), 6.40 - 6.39 (m, 2H), 6.00 (s, 1H), 4.35 - 4.22 (m, 2H), 4.03 (dd, *J* = 11.3, 5.2 Hz, 1H), 2.87 (dd, *J* = 13.0, 5.1 Hz, 1H), 2.22 - 2.11 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 171.8, 154.3, 153.7, 152.3, 139.3, 137.2, 134.3, 133.8, 131.5, 129.7, 129.1, 129.0, 128.9, 128.8, 128.72, 128.71, 128.2, 127.6, 127.5, 127.3, 126.2, 126.1, 125.8, 125.7, 125.1, 124.4, 123.2, 121.8, 121.3, 119.9, 94.8, 68.2, 57.1, 44.6, 39.5, 15.4.; HRMS (TOF MS ESI⁺) calculated for C₃₈H₂₉NO₄Na [M+Na]⁺: 586.1989, found 586.1990; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, *t*_{minor} = 14.9 min, *t*_{major} = 19.3 min.



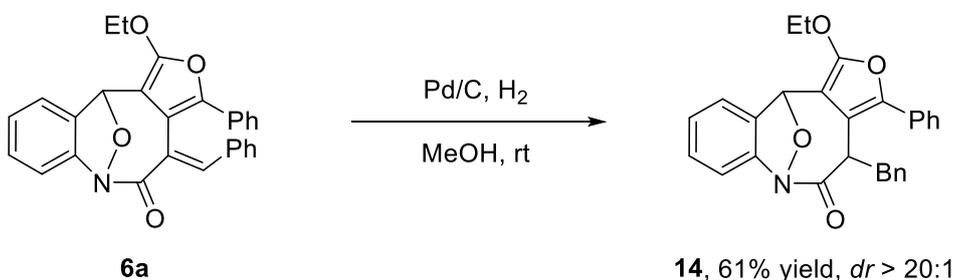
Synthesis of 11: To a 10-mL oven-dried vial containing a magnetic stirring bar, and **4n** (56.1 mg, 0.1 mmol) in DCM (2.0 mL), was added *m*-CPBA (25.9 mg, 0.15 mmol, 1.5 equiv.) at room temperature. The reaction mixture was stirred for 0.5 h under these conditions. After the reaction was completed (reaction monitored by TLC), the reaction mixture was treated with saturated aqueous NaHCO₃ (3.0 mL) and Na₂S₂O₃ (3.0 mL). The reaction mixture was extracted with EtOAc (3 × 5.0 mL). The combined organic extract was washed with brine, dried with anhydrous Na₂SO₄, and concentrated under reduced pressure after filtration. Then, the residue was purified by flash chromatography on silica gel (Hexanes : EtOAc = 5:1) to give 49.6 mg of pure product **11** as colorless oil (61.3 mg, 72% yield). 95% *ee*; [α]_D²⁰ = 156.01 (c = 0.033, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 8.04 (d, *J* = 8.6 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.84 (s, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.62 - 7.58 (m, 2H), 7.43 - 7.37 (m, 2H), 7.35 - 7.28 (comp, 4H), 7.26 - 7.22 (m, 2H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.15 - 7.13 (m, 1H), 7.08 (t, *J* = 7.1 Hz, 2H), 6.92 (d, *J* = 7.4 Hz, 2H), 6.26 (s, 1H), 4.12 - 4.08 (m, 2H), 0.99 - 0.96 (m, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 193.6, 165.0, 164.5, 155.1, 149.6, 148.1, 145.7, 134.3, 133.8, 133.6, 131.8, 131.6, 130.7, 130.5, 130.3, 130.1, 129.9, 129.1, 128.8, 128.2, 128.14, 128.11, 128.05, 126.4, 126.3, 125.9, 125.7, 124.2, 124.0, 122.4, 121.5, 121.2, 62.2, 58.8, 13.6; HRMS (TOF MS ESI⁺) calculated for C₃₈H₂₇NO₅Na [M+Na]⁺: 600.1781, found: 600.1783; HPLC conditions for determination of enantiomeric excess: Chiralpak IC, λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, *t*_{minor} = 18.5 min, *t*_{major} = 29.5 min.



Synthesis of 12: To a 10-mL oven-dried round bottom flask containing a magnetic stirring bar, and 2-(trimethylsilyl)phenyltrifluoromethanesulfonate (44.7 mg, 0.15 mmol, 1.5 equiv.) in dry MeCN (1.0 mL), was added CsF (45.6 mg, 0.3 mmol, 3.0 equiv.) at room temperature, and the reaction mixture was stirred for 15 min under these conditions. Then a solution of **6a** (43.5 mg, 0.1 mmol, 1.0 equiv.) in dry MeCN (1.0 mL) was added slowly *via* a syringe at room temperature. After stirring for additional 3.0 h, the reaction was quenched with saturated aqueous NH₄Cl solution (5.0 mL) and the organic phase was separated, and the aqueous phase was extracted with EtOAc (3 × 5.0 mL). The combined organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure after filtration. The obtained residues was purified by column chromatography on silica gel (Hexane/EtOAc = 20/1 - 10/1) to give the pure product **12** as white solid (44.6 mg, 90% yield). m.p. = 184.8 - 185.8 °C; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.49 (d, *J* = 6.2 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 2H), 7.19 - 7.12 (comp, 5H), 6.98 - 6.93 (comp, 6H), 6.91 - 6.86 (m, 2H), 6.75 (d, *J* = 7.1 Hz, 1H), 6.68 (t, *J* = 7.5 Hz, 1H), 6.60 (t, *J* = 7.4 Hz, 1H), 6.25 (s, 1H), 4.22 - 4.15 (m, 2H), 1.57 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 175.4, 150.3, 149.6, 145.1, 143.7, 143.5, 137.5, 134.9, 134.0, 129.8, 129.4, 128.9, 128.7, 128.3, 128.0, 127.7, 127.6, 125.9, 125.7, 125.3, 124.1, 122.4, 120.6, 119.4, 115.6, 113.0, 89.5, 80.5, 63.4, 16.1; HRMS (TOF MS ESI⁺) calculated for C₃₄H₂₅NO₃Na [M+Na]⁺: 518.1727, found: 518.1725.

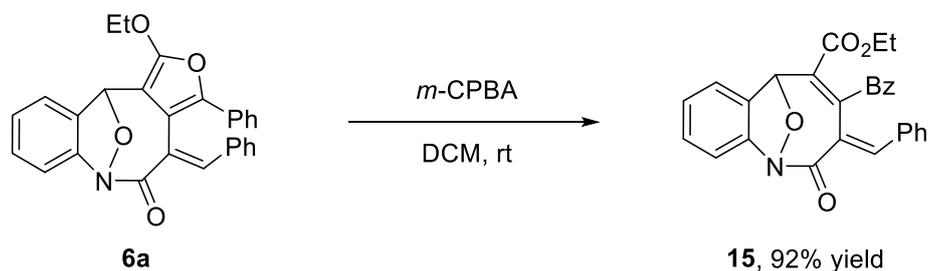


Synthesis of 13: To a 10-mL oven-dried vial containing a magnetic stirring bar, *p*-toluenesulfonic acid (TsOH·H₂O, 38.0 mg, 0.2 mmol, 2.0 equiv.), **6a** (43.5 mg, 0.1 mmol), and toluene (2.0 mL) were added in sequence, and the reaction mixture was stirred under 40 °C for 1.0 h. After the reaction was completed (reaction monitored by TLC), the reaction mixture was diluted with H₂O (3.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure after filtration. The residues was purified by flash chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 10:1 to 5:1) to afford pure product **13** as white solid (33.8 mg, 83% yield). m.p. = 119.1 - 120.2 °C; > 20:1 *dr*; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.63 (d, *J* = 7.4 Hz, 1H), 7.53 - 7.46 (comp, 4H), 7.41 (t, *J* = 7.7 Hz, 1H), 7.38 (s, 1H), 7.34 (d, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.04 (t, *J* = 7.7 Hz, 2H), 6.19 - 6.16 (m, 3H), 5.81 (d, *J* = 1.8 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 176.2, 169.6, 152.3, 143.9, 142.7, 134.2, 133.1, 133.0, 131.9, 130.8, 130.5, 130.0, 129.9, 129.7, 129.2, 128.8, 127.14, 127.06, 122.1, 115.9, 83.2, 78.7; HRMS (TOF MS ESI⁺) calculated for C₂₆H₁₇NO₄Na [M+Na]⁺: 430.1050, found 430.1050.



Synthesis of 14: To a 10-mL hydrogenation reactor containing a magnetic stirring bar, and **6a** (43.5 mg, 0.1 mmol) in 1.5 mL of MeOH, was added wet 10% Pd/C (10 mg, 20 %). The heterogeneous mixture was placed under 40-60 psi H₂ atmosphere

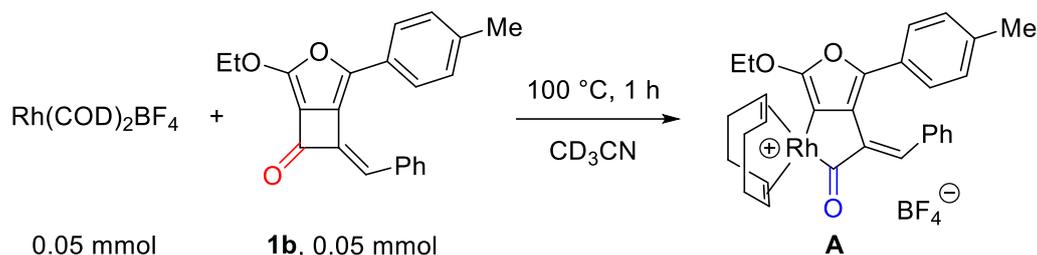
and stirred overnight at room temperature. After the reaction was completed, as indicated by LC-MS analysis. The mixture was filtered through a pad of Celite to remove Pd/C, and the solid was washed with MeOH. The combined filtrate was concentrated under vacuum. Then, the residues was purified by flash chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 15:1 to 5:1) to afford pure product **14** as white solid (26.7 mg, 61% yield). m.p. = 155.5 - 156.5 °C; > 20:1 *dr*; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.42 (d, *J* = 7.7 Hz, 1H), 7.38 - 7.32 (comp, 6H), 7.30 - 7.27 (m, 1H), 7.24 - 7.19 (comp, 3H), 7.16 - 7.13 (comp, 3H), 6.19 (s, 1H), 5.20 - 5.17 (m, 1H), 4.27 - 4.17 (m, 2H), 3.00 - 2.95 (m, 1H), 2.78 - 2.74 (m, 1H), 1.40 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) (δ, ppm) 181.5, 152.9, 143.0, 140.8, 140.1, 137.2, 131.8, 131.4, 129.2, 129.1, 128.4, 128.3, 128.0, 126.8, 126.3, 120.4, 117.2, 114.6, 97.8, 78.0, 67.7, 44.6, 33.5, 15.4; HRMS (TOF MS ESI⁺) calculated for C₂₈H₂₃NO₄Na [M+Na]⁺: 460.1519, found 460.1521.



Synthesis of 15: To a 10-mL oven-dried vial containing a magnetic stirring bar, and **6a** (56.1 mg, 0.1 mmol) in DCM (2.0 mL), was added *m*-CPBA (25.9 mg, 0.15 mmol, 1.5 equiv.) at room temperature. The reaction mixture was stirred for 0.5 h under these conditions, After the reaction was completed (reaction monitored by TLC), the reaction mixture was treated with saturated aqueous NaHCO₃ (3.0 mL) and Na₂S₂O₃ (3.0 mL) in sequence. The reaction mixture was extracted with EtOAc (3 × 5.0 mL). The combined organic extract was washed with brine, dried with anhydrous Na₂SO₄, and concentrated under reduced pressure after filtration. Then, the residues was purified by flash chromatography on silica gel (Hexanes : EtOAc = 5:1) to afford pure product **15** as white solid (41.8 mg, 92% yield). m.p. = 227.4 - 228.5 °C; ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.62 (d, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.37 (t,

$J = 7.3$ Hz, 1H), 7.31 - 7.27 (m, 2H), 7.25 - 7.20 (comp, 4H), 7.17 (t, $J = 7.7$ Hz, 2H), 7.13 - 7.10 (comp, 4H), 6.43 (s, 1H), 4.05 - 3.99 (m, 2H), 0.95 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) (δ , ppm) 193.1, 178.2, 164.7, 142.4, 142.0, 139.4, 138.9, 135.6, 134.0, 133.2, 132.9, 130.7, 130.0, 129.7, 128.8, 128.1, 128.0, 127.1, 121.7, 116.7, 82.1, 62.2, 13.4; HRMS (TOF MS ESI⁺) calculated for $\text{C}_{28}\text{H}_{21}\text{NO}_5\text{Na}$ [$\text{M}+\text{Na}$]⁺: 474.1312, found 474.1313.

Control Experiment



A solution of **1b** (16.5 mg, 0.05 mmol) in CD_3CN (0.7 mL) was added to an oven-dried NMR tube, and the mixture was subjected to ^{13}C NMR analysis (Fig. S1, bottom spectrum). The carbonyl signal of **1b** was observed in 174.7 ppm. Then, $\text{Rh}(\text{COD})_2\text{BF}_4$ (20.3 mg, 0.05 mmol) was added to the above NMR tube, and the NMR tube was subjected to a 100 °C oil bath for 1 h. Then, the reaction mixture was subjected to ^{13}C NMR analysis (Fig. S1, up spectrum). The carbonyl signal of possible C-C bond activation intermediate **A** was observed in 202.7 ppm. This intermediate is relatively stable under these conditons.

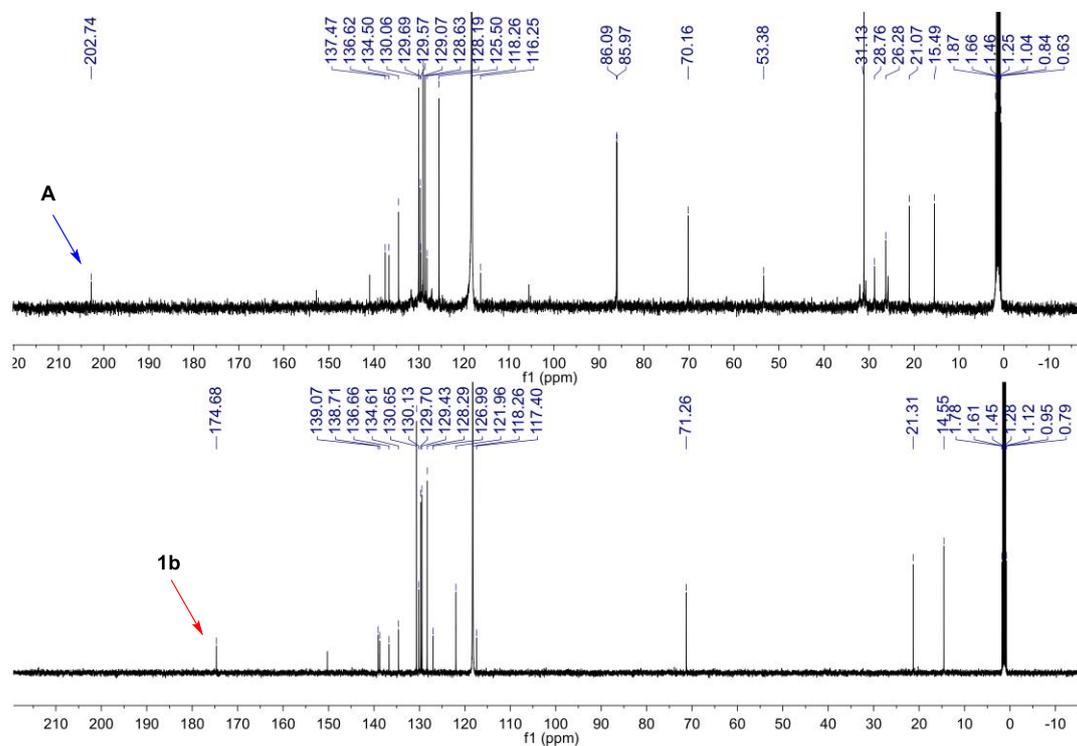
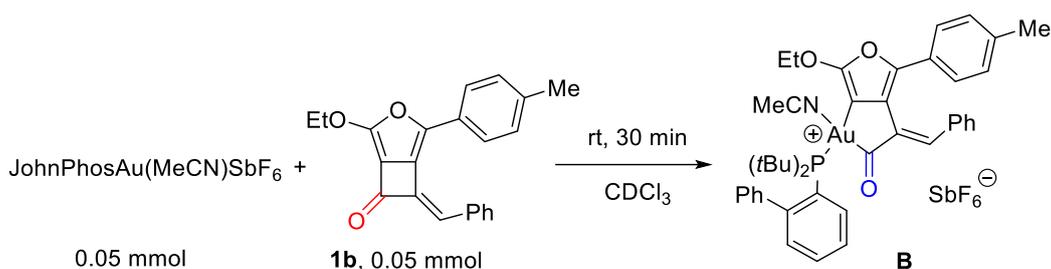


Fig. S1 | ^{13}C NMR Observation of compound **1b** and **1b** treated with rhodium complex in CD_3CN .



A solution of **1b** (16.5 mg, 0.05 mmol) in CDCl_3 (0.7 mL) was added to an oven-dried NMR tube, and the mixture was subjected to ^{13}C NMR analysis (Fig. S2, bottom spectrum). The carbonyl signal of **1b** was observed in 174.7 ppm. Then, $\text{JohnPhosAu(MeCN)SbF}_6$ (38.6 mg, 0.05 mmol) was added to the above NMR tube at room temperature. The reaction mixture was subjected to ^{13}C NMR analysis after 30 mins (Fig. S2, up spectrum). The carbonyl signal of possible C-C bond activation intermediate **B** was observed in 194.3 ppm. The material **1b** decomposed to complex mixture under these conditions within 5.0 mins.

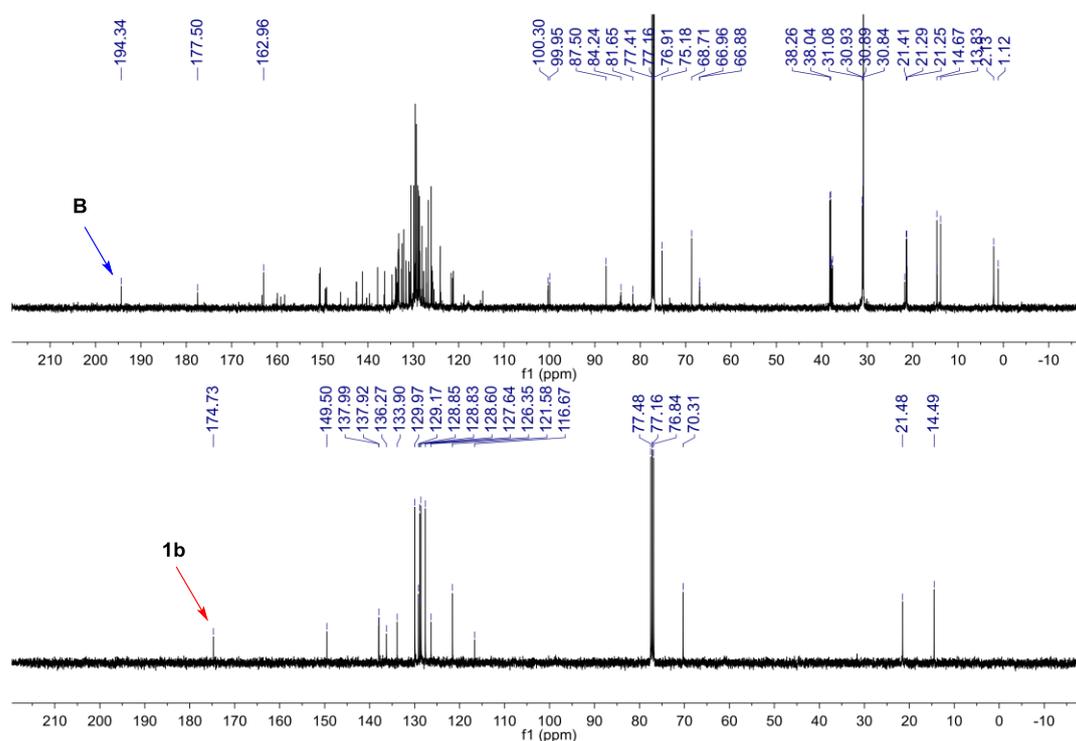
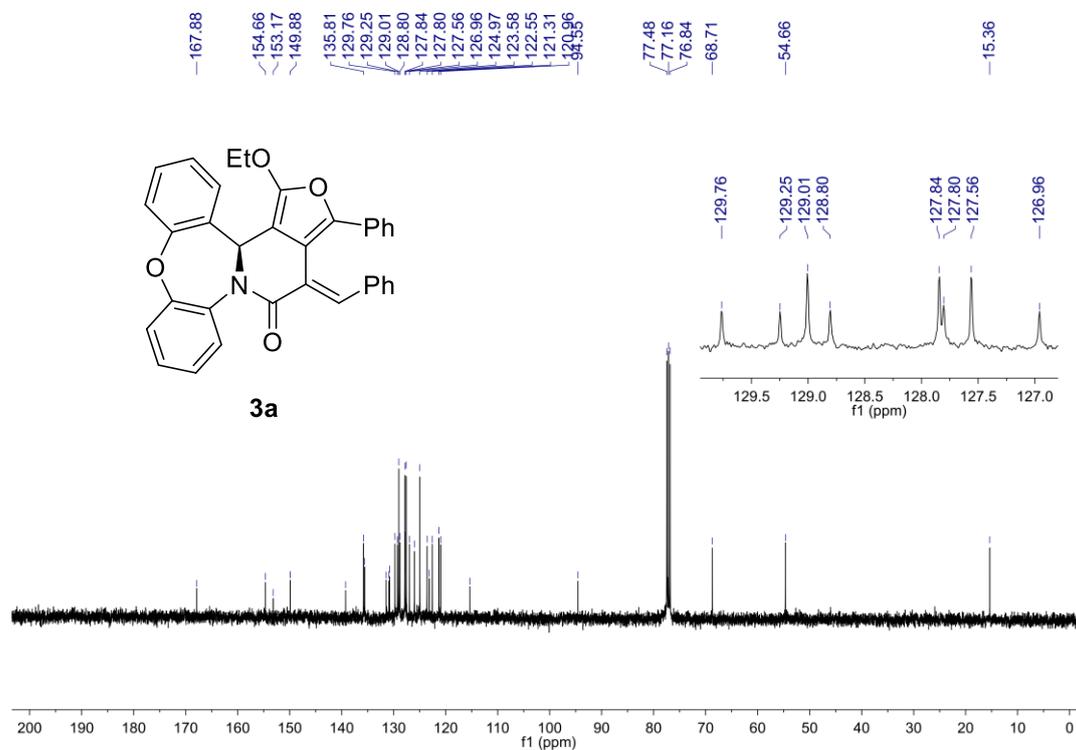
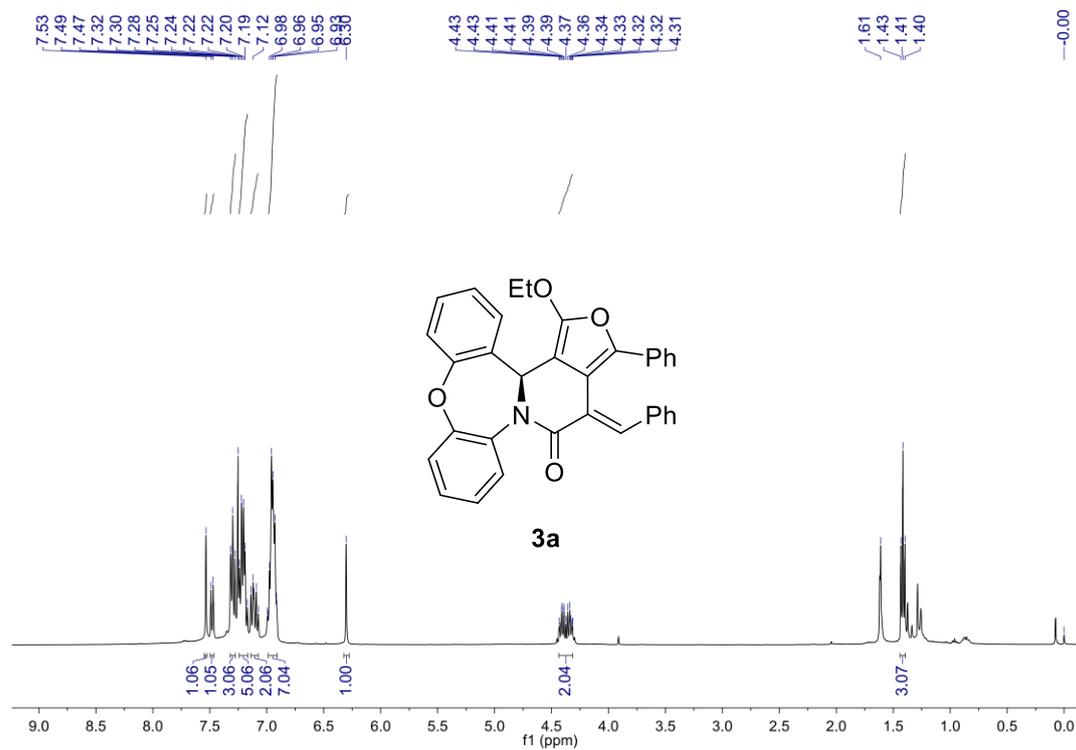
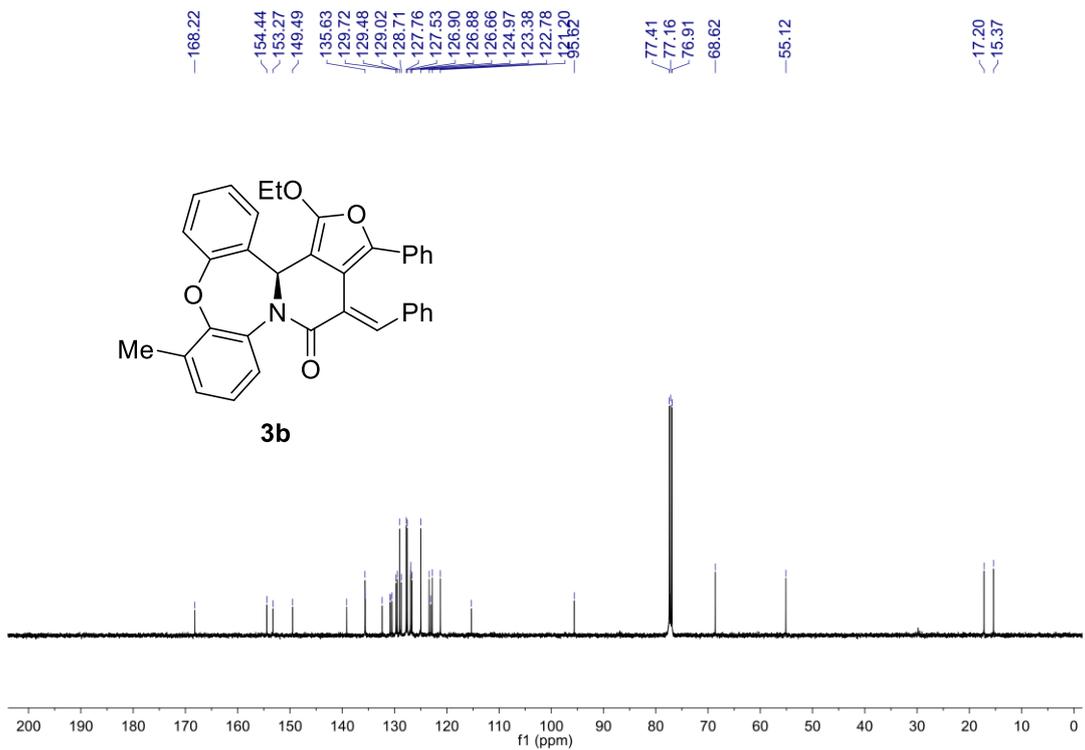
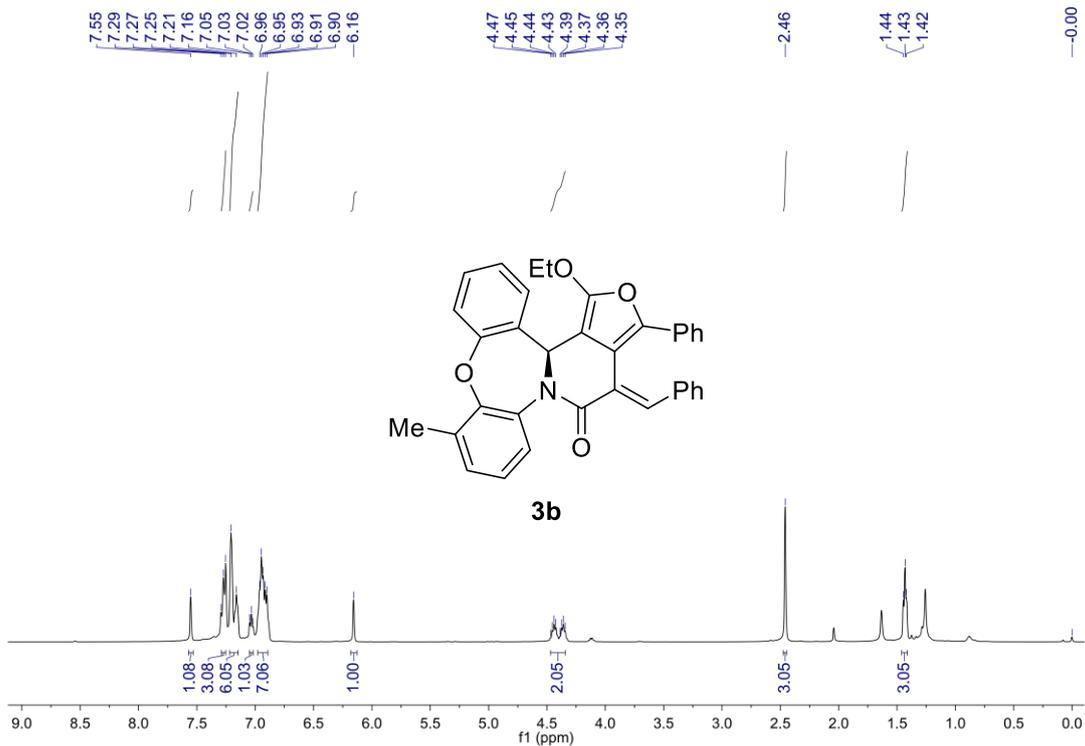
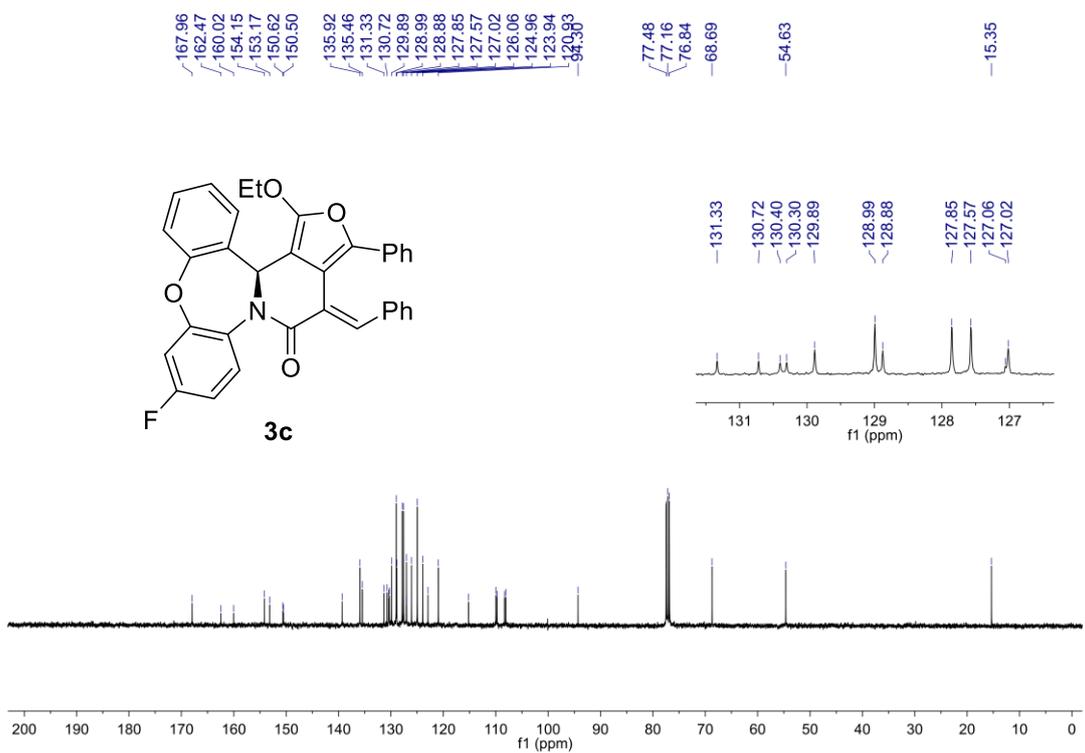
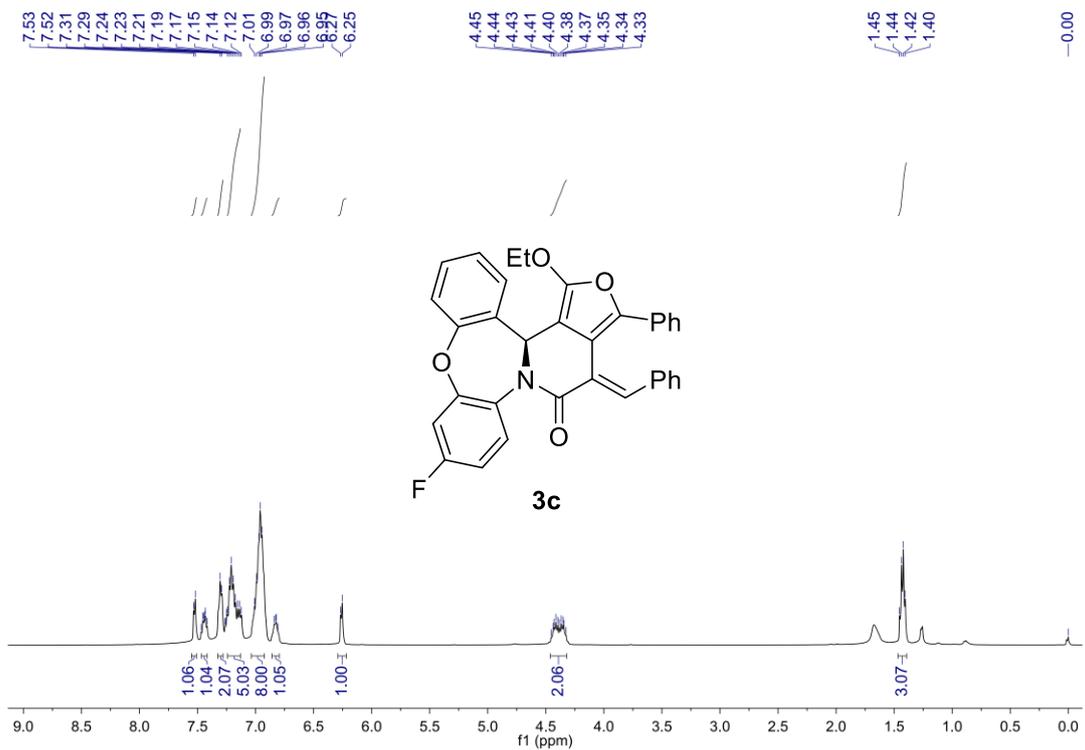


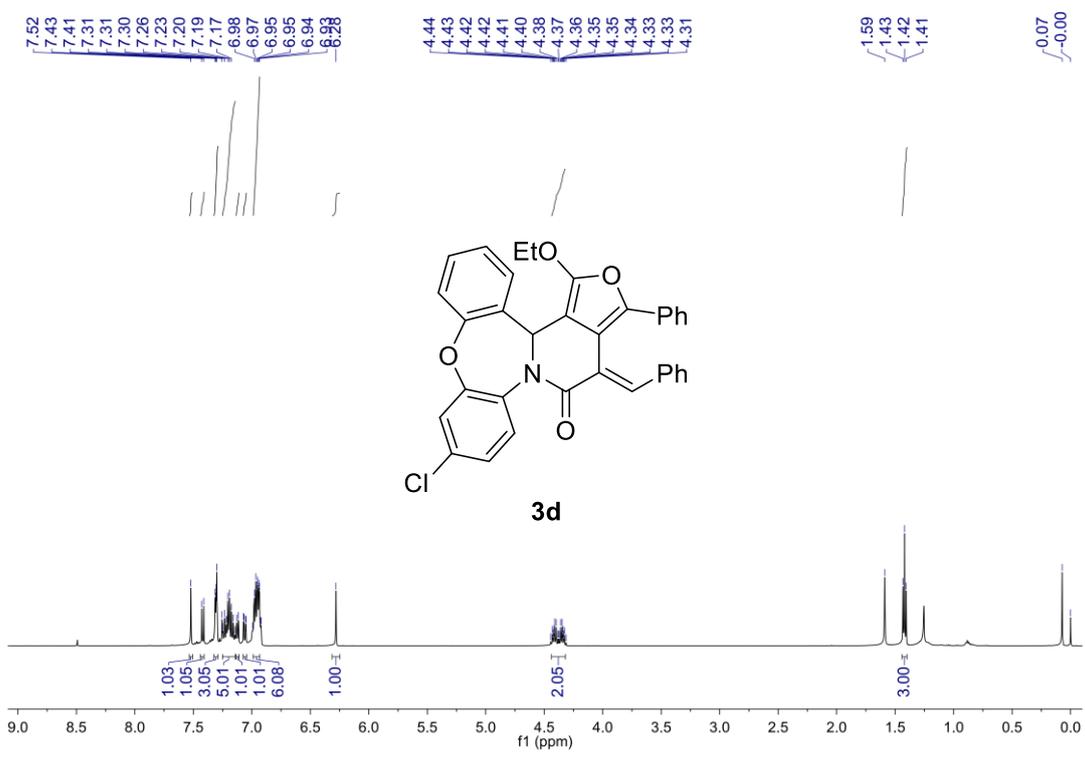
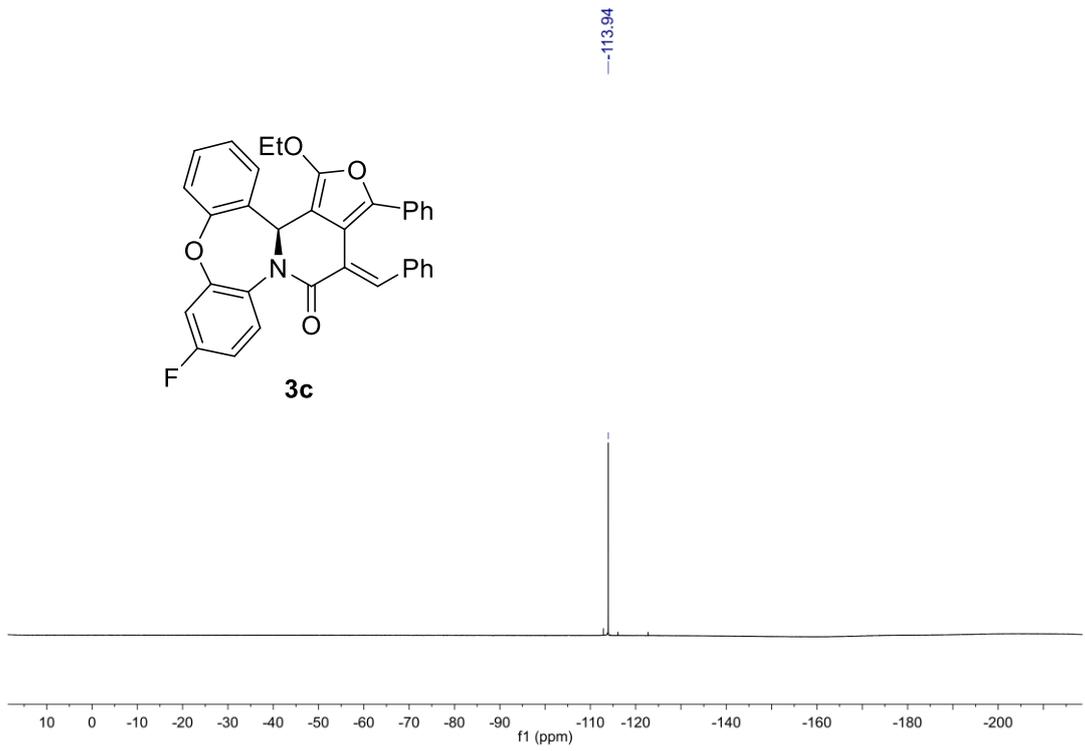
Fig. S2 | ^{13}C NMR Observation of compound **1b** and **1b** treated with gold complex in CDCl_3 .

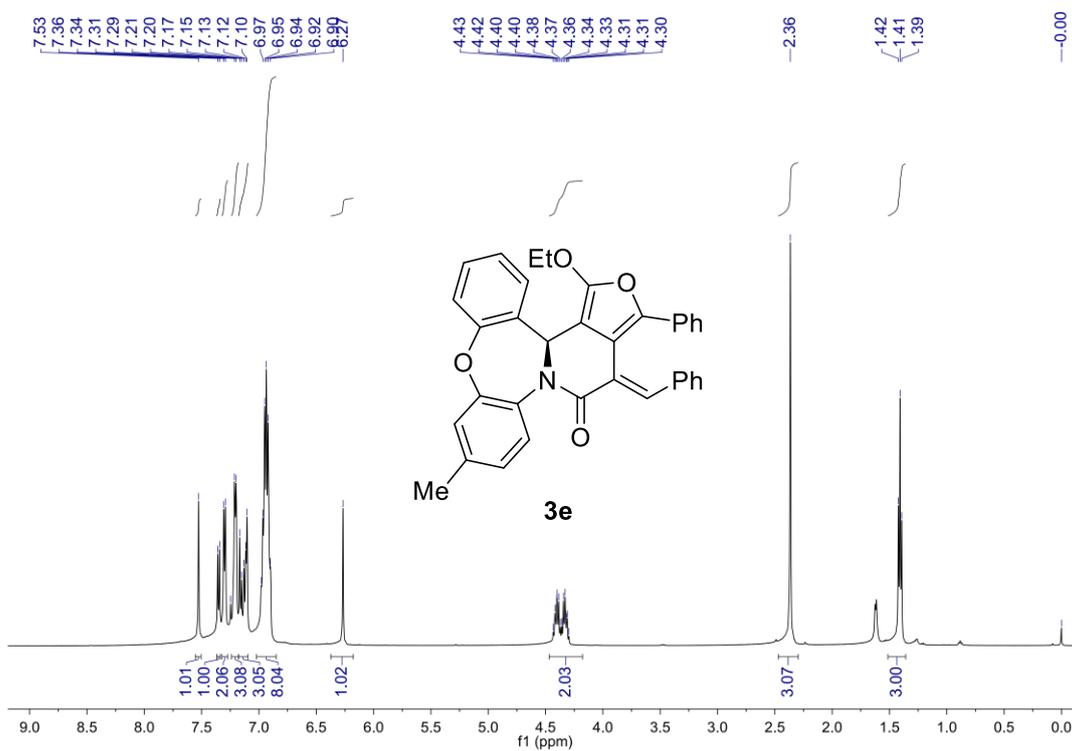
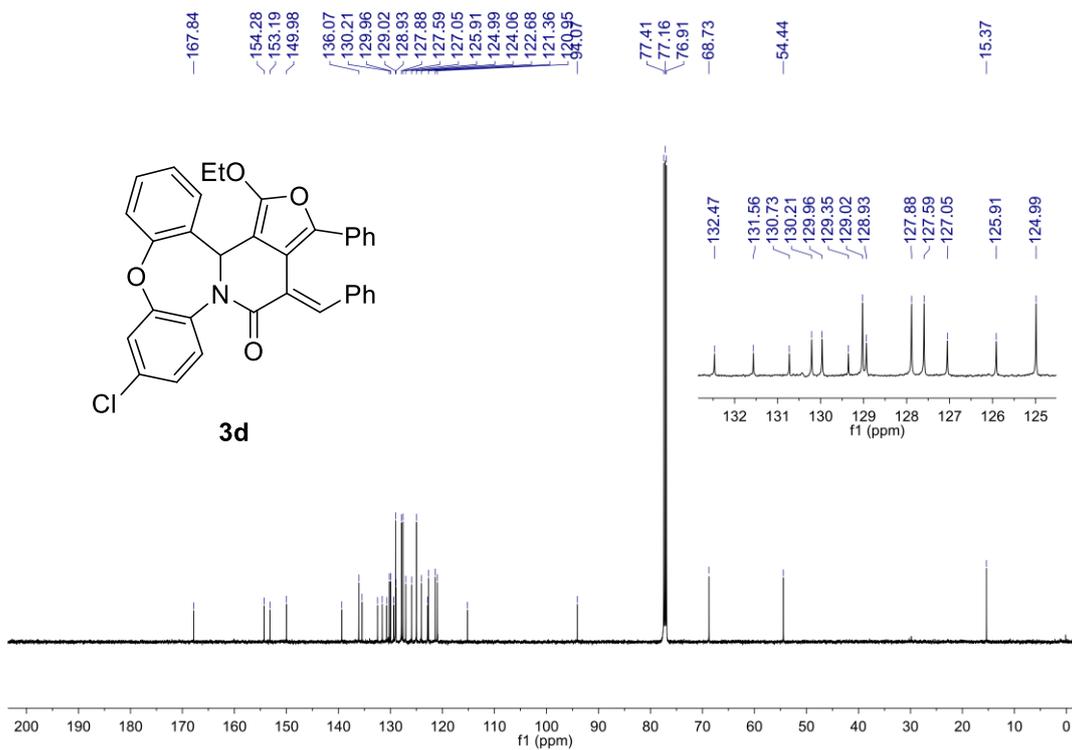
NMR Spectra of New Compounds 3, 4, and 6-15

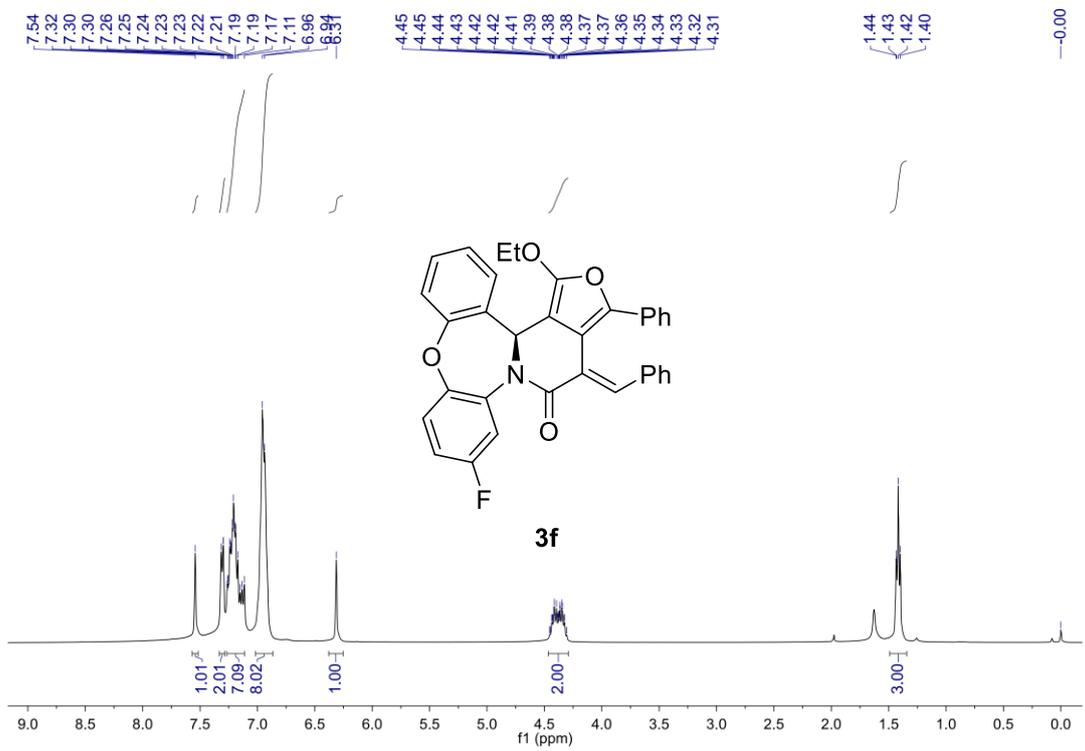
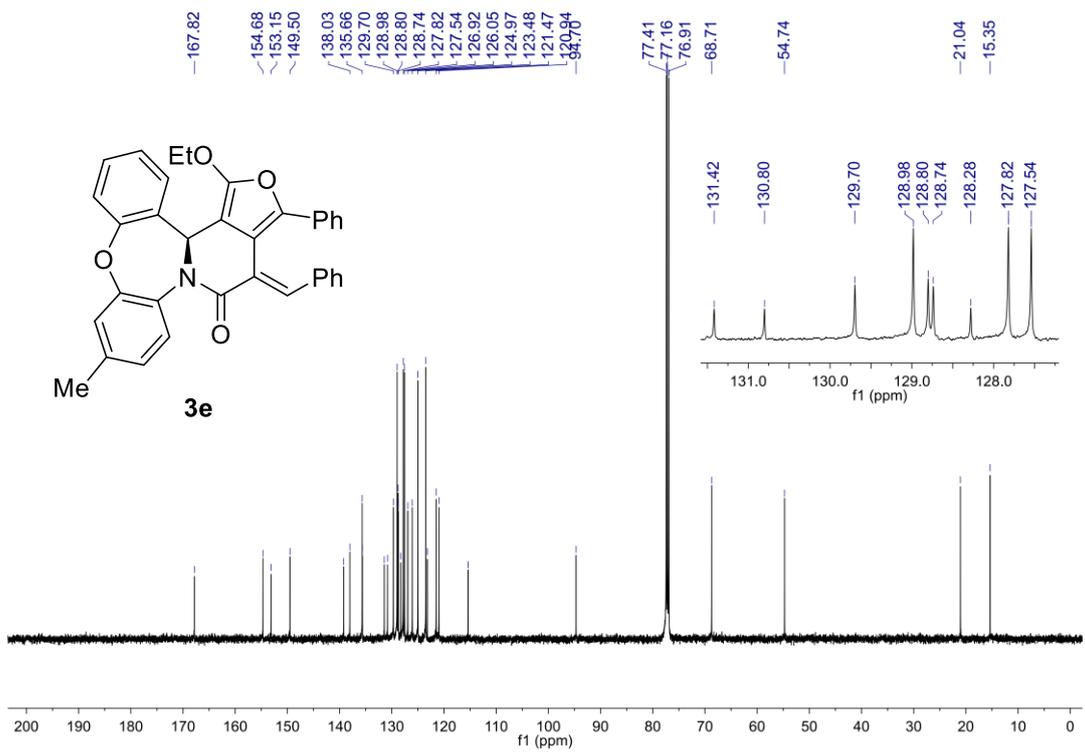


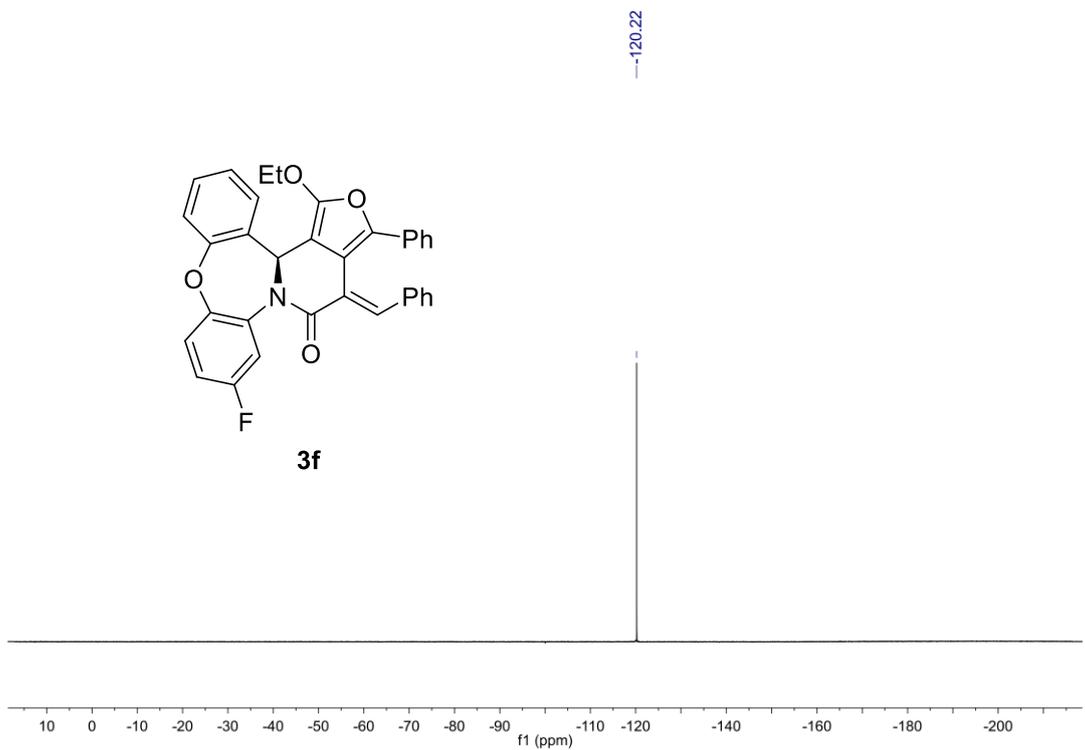
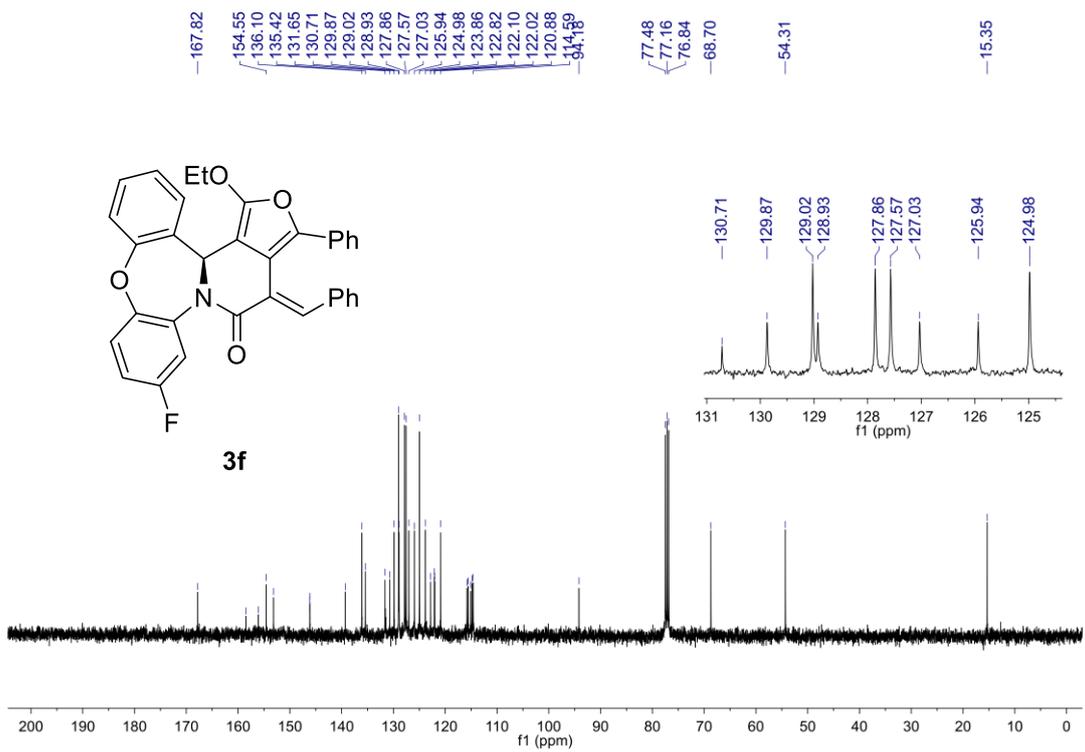


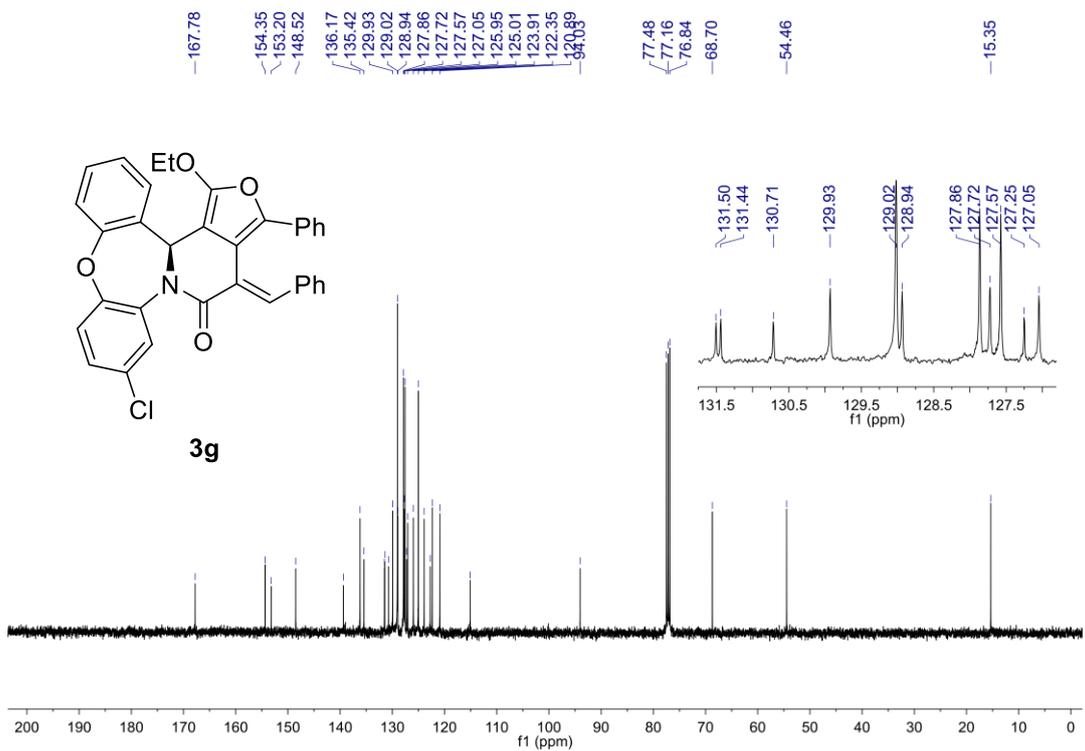
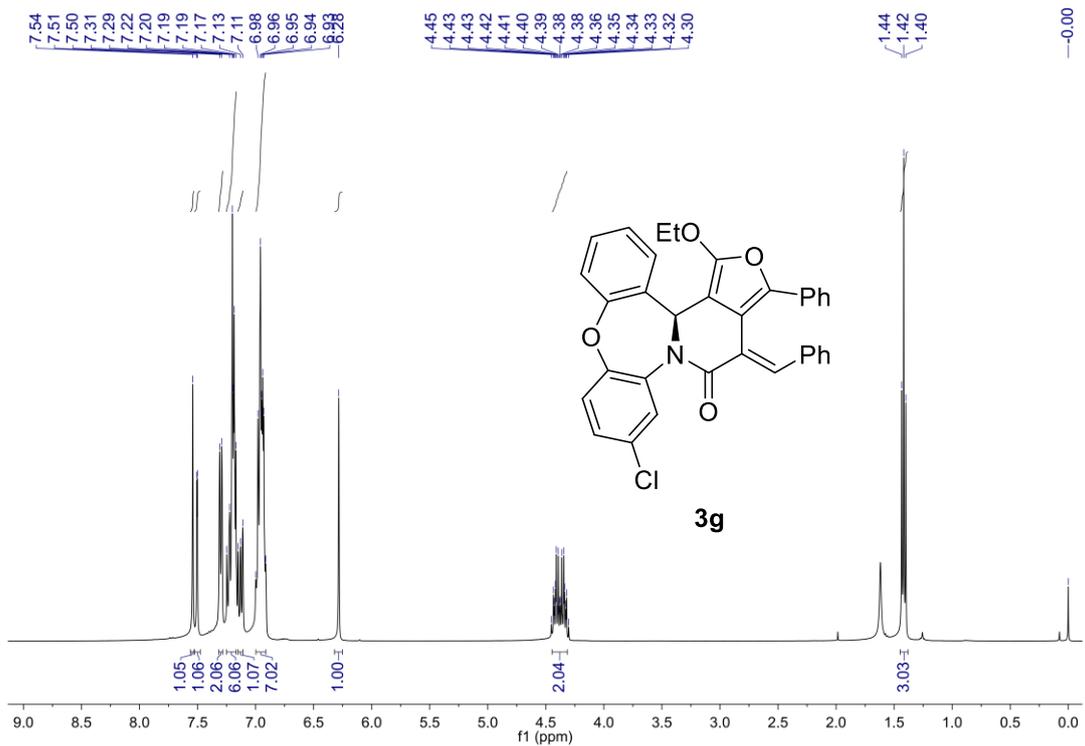


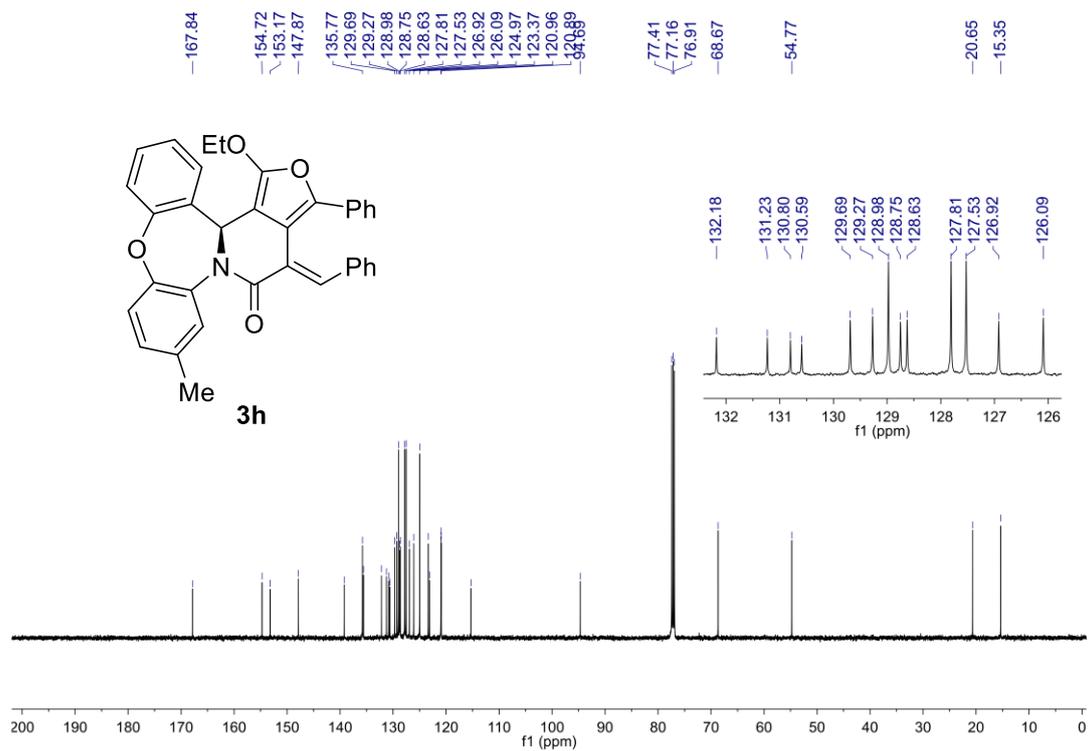
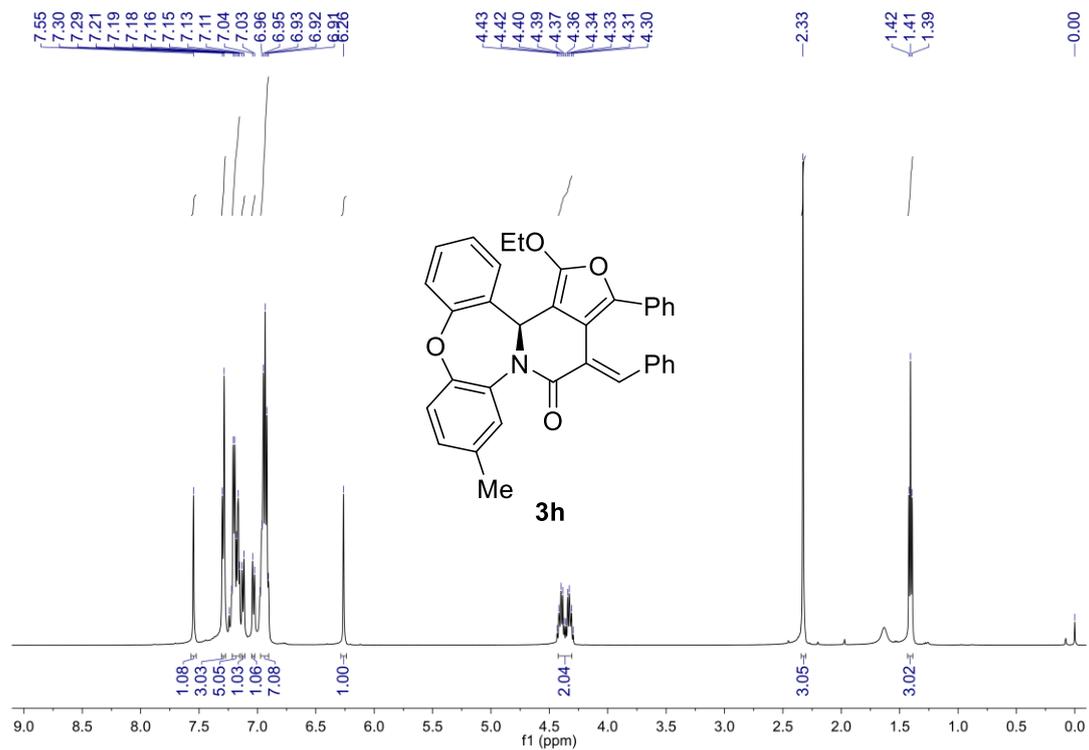


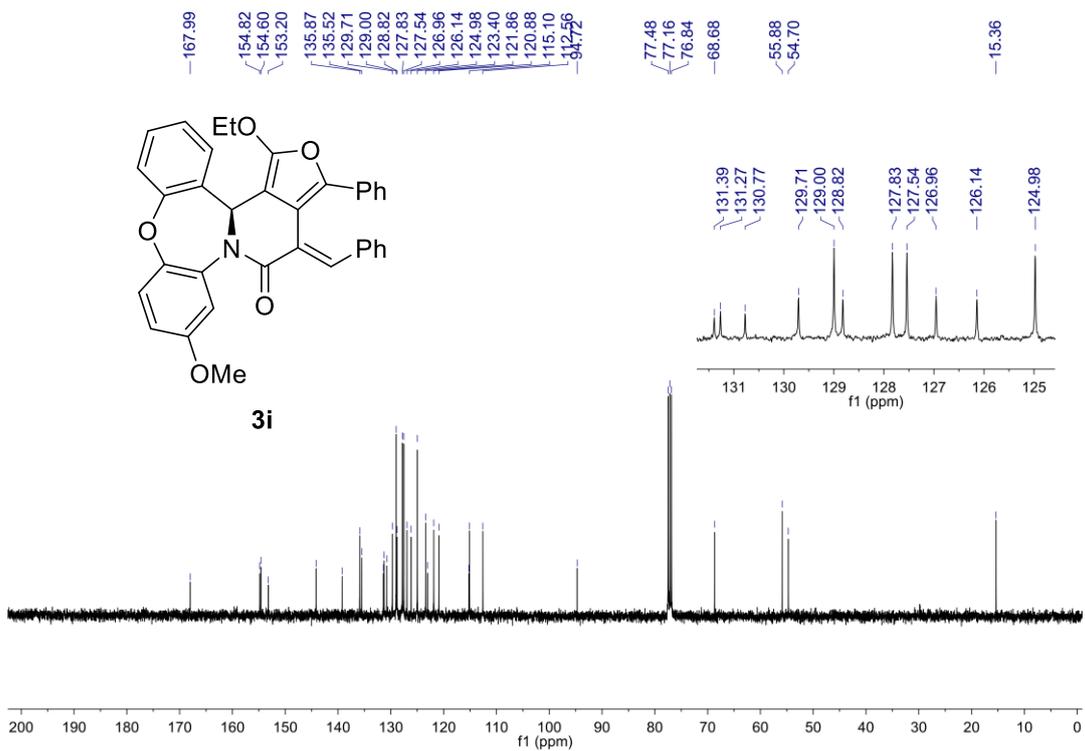
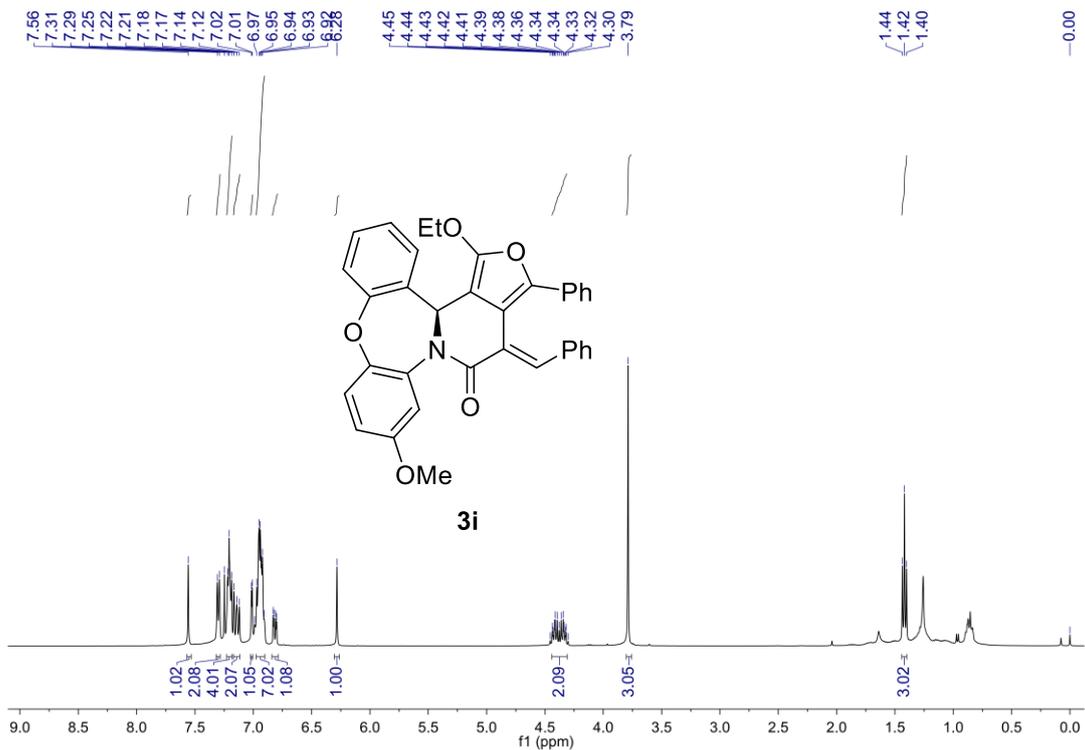


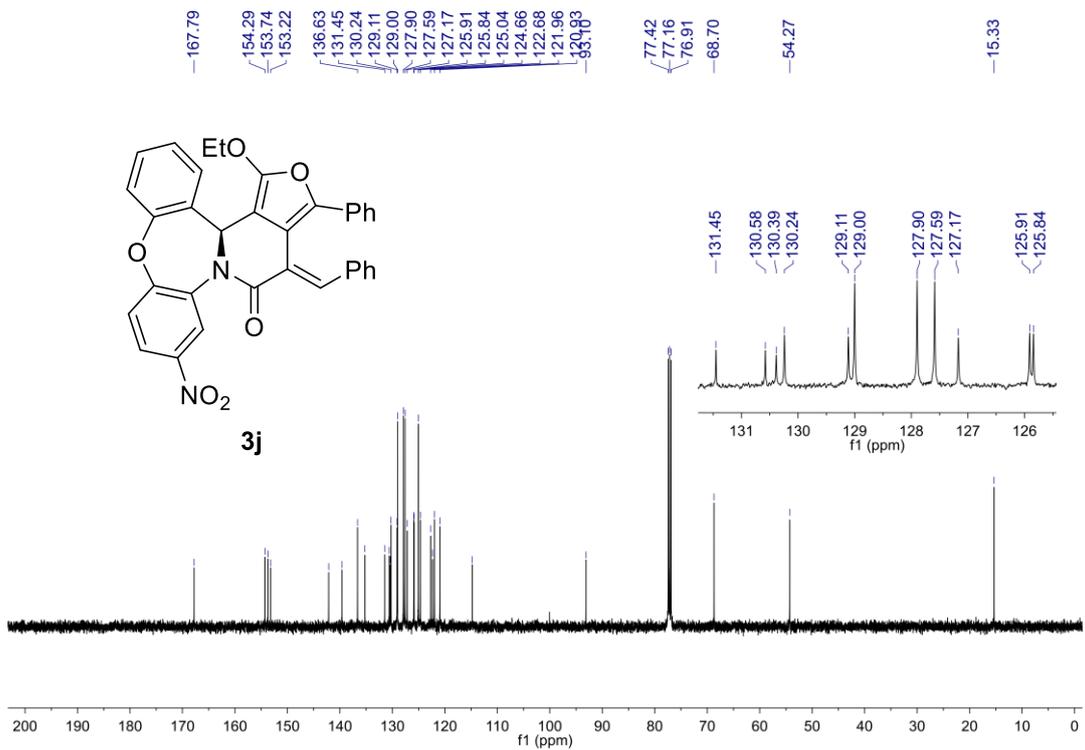
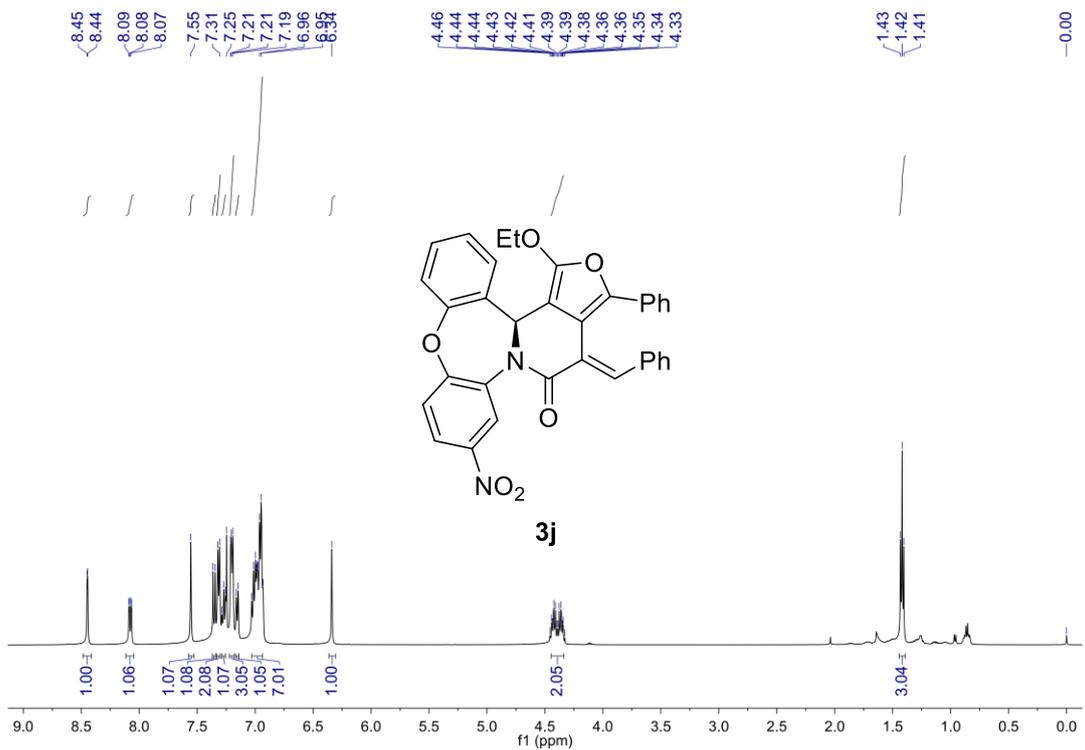


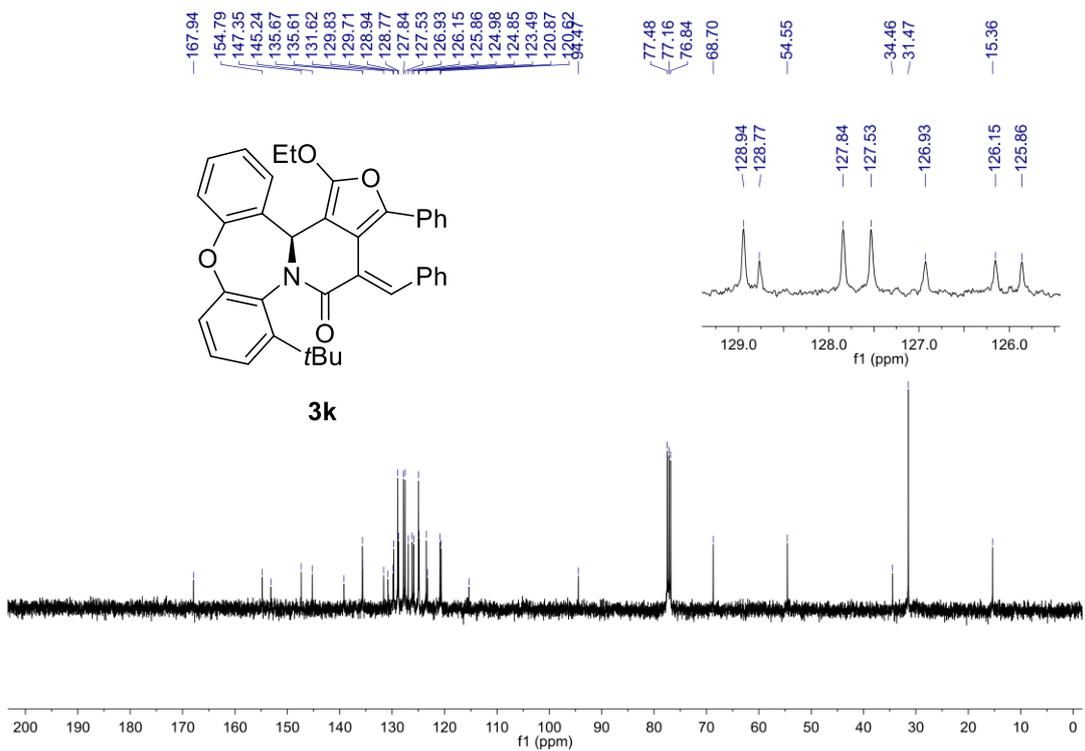
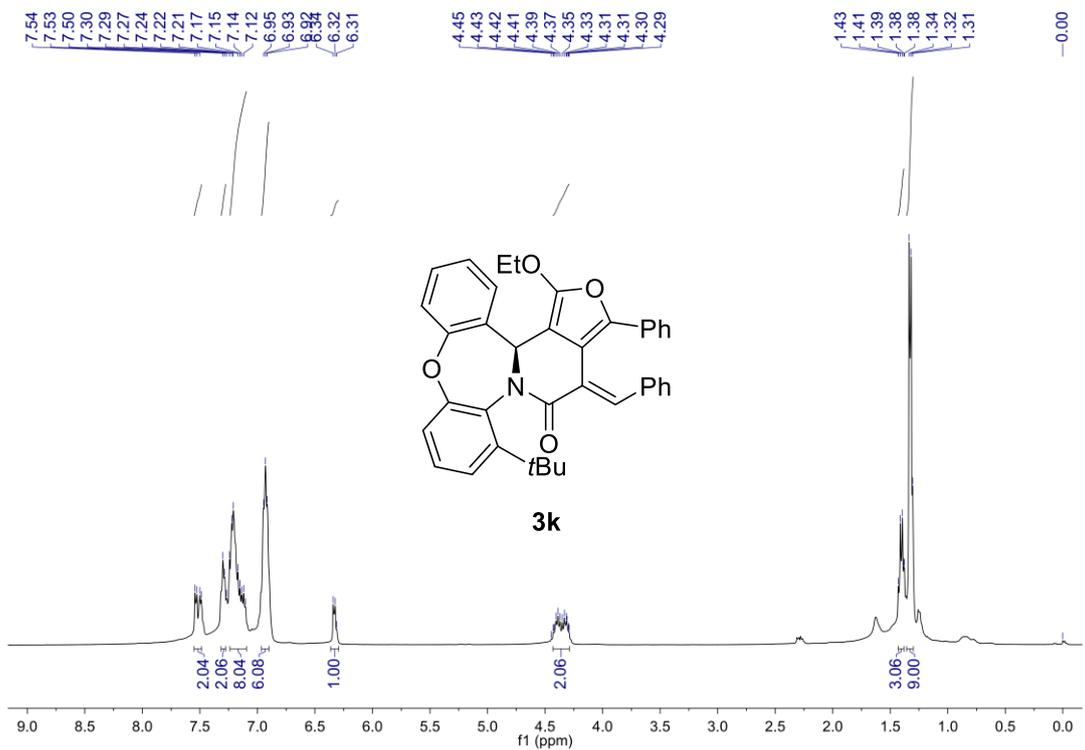


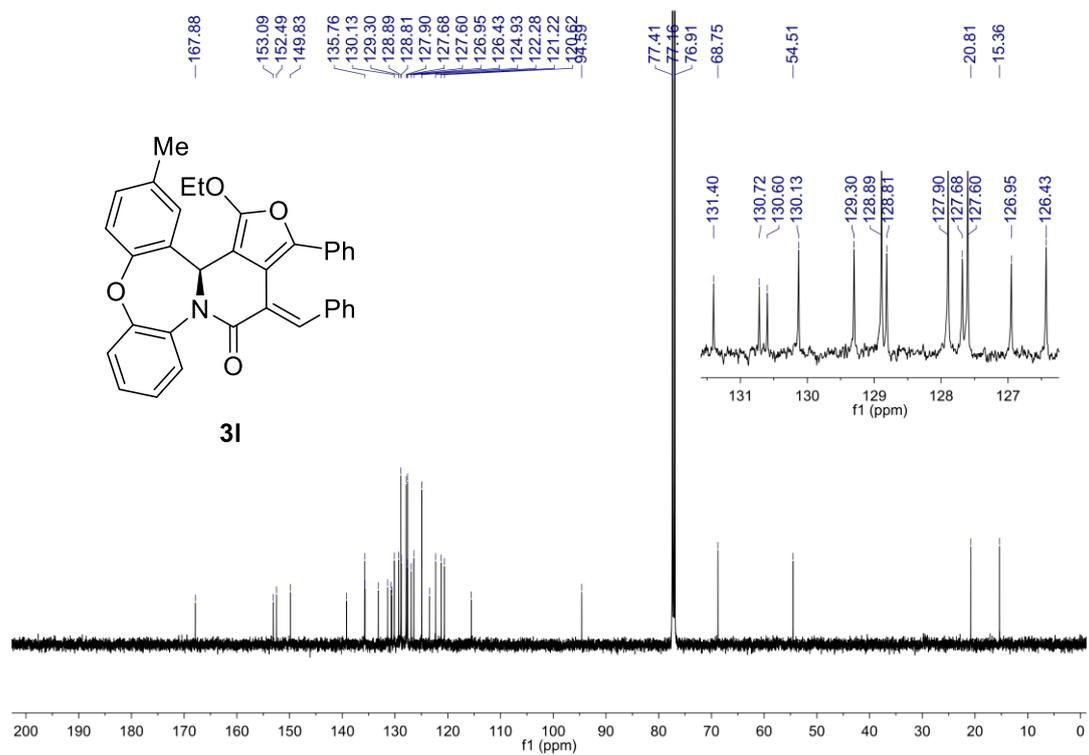
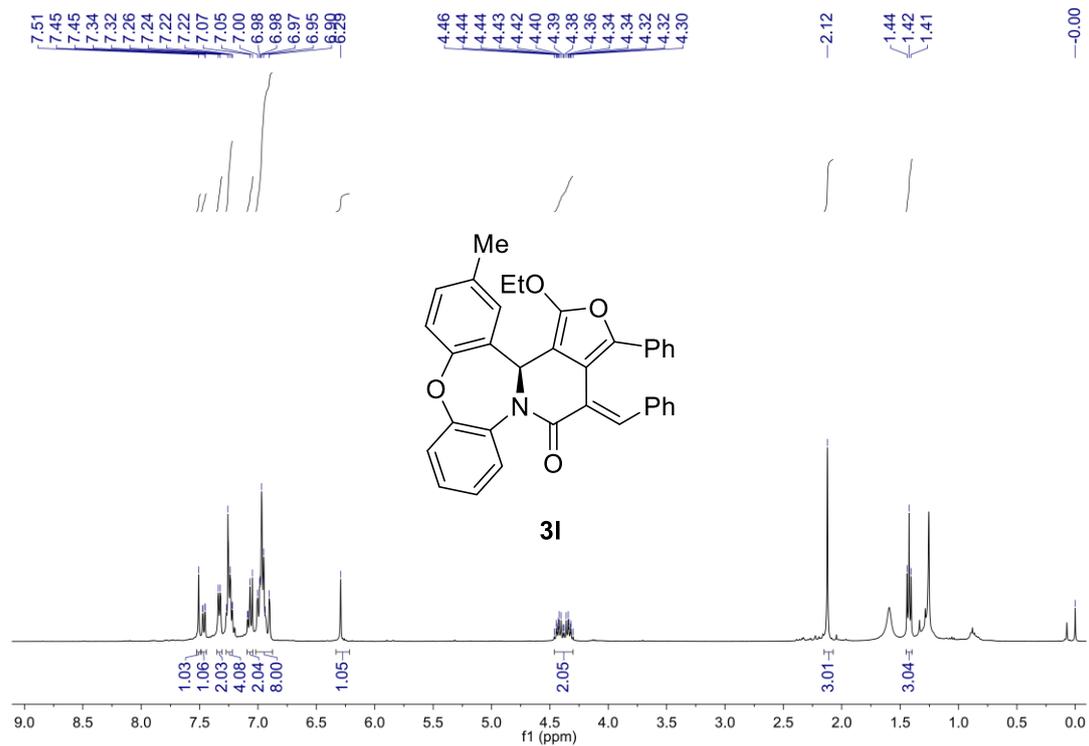


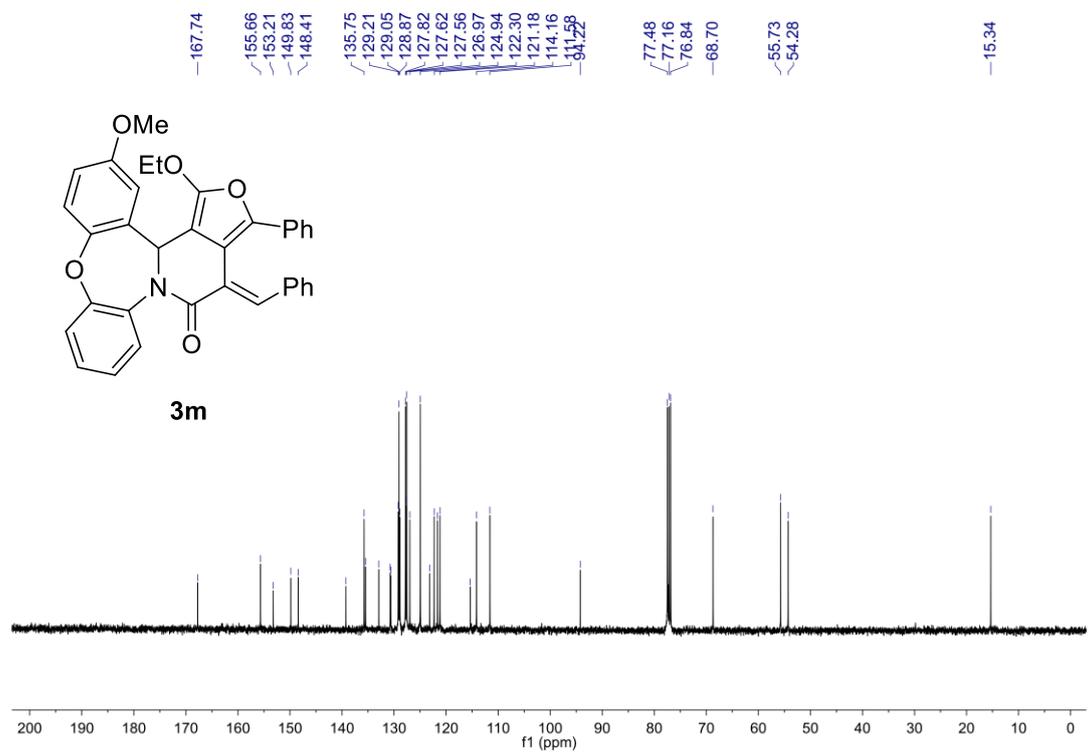
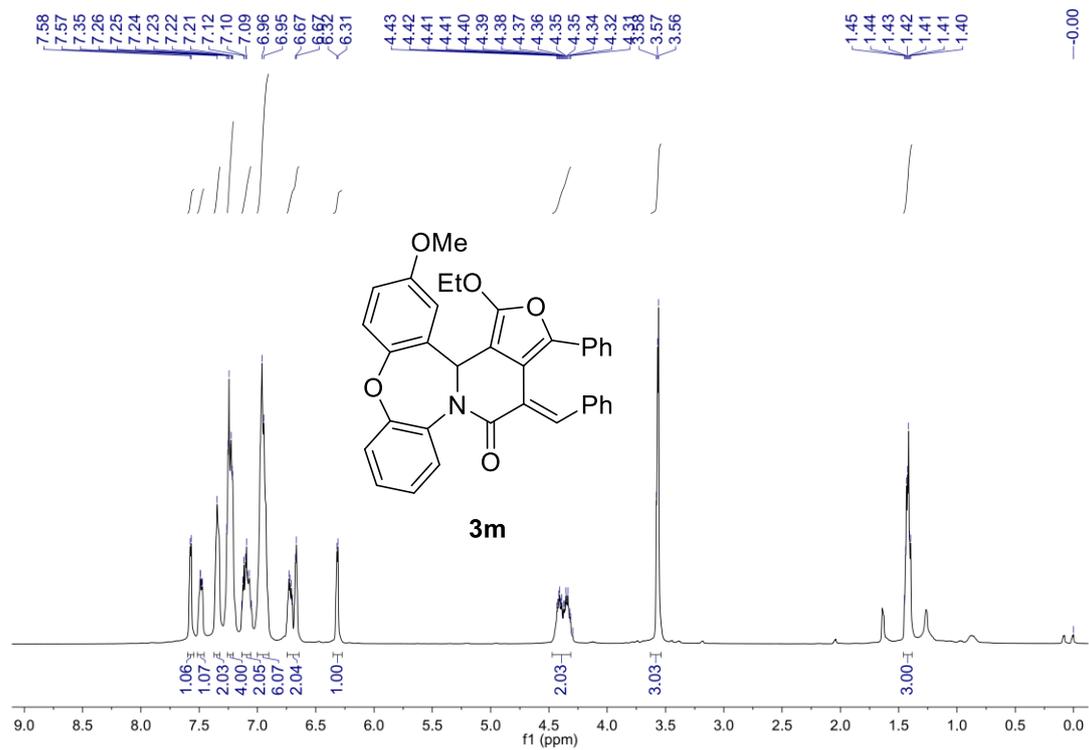


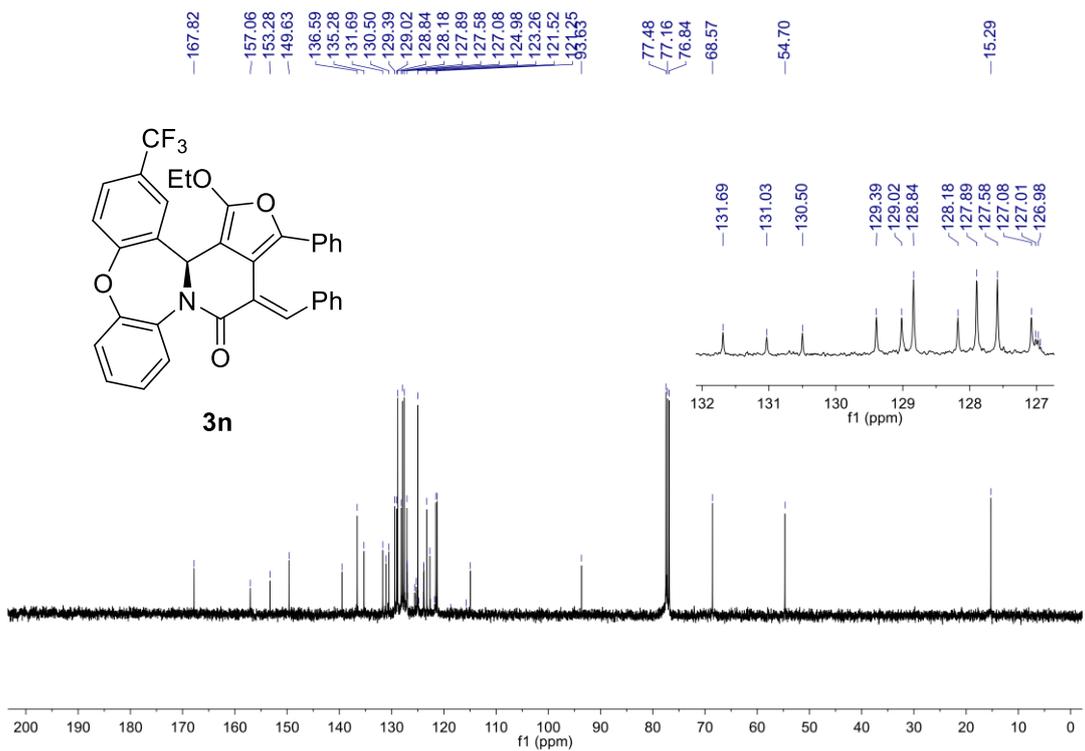
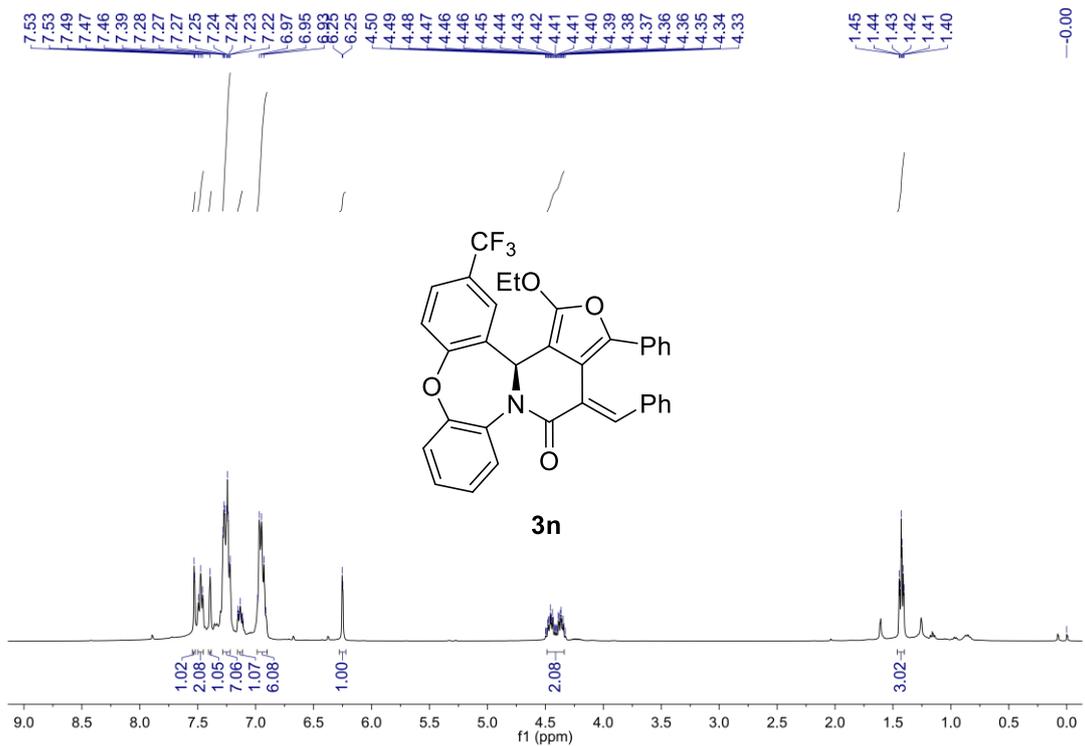


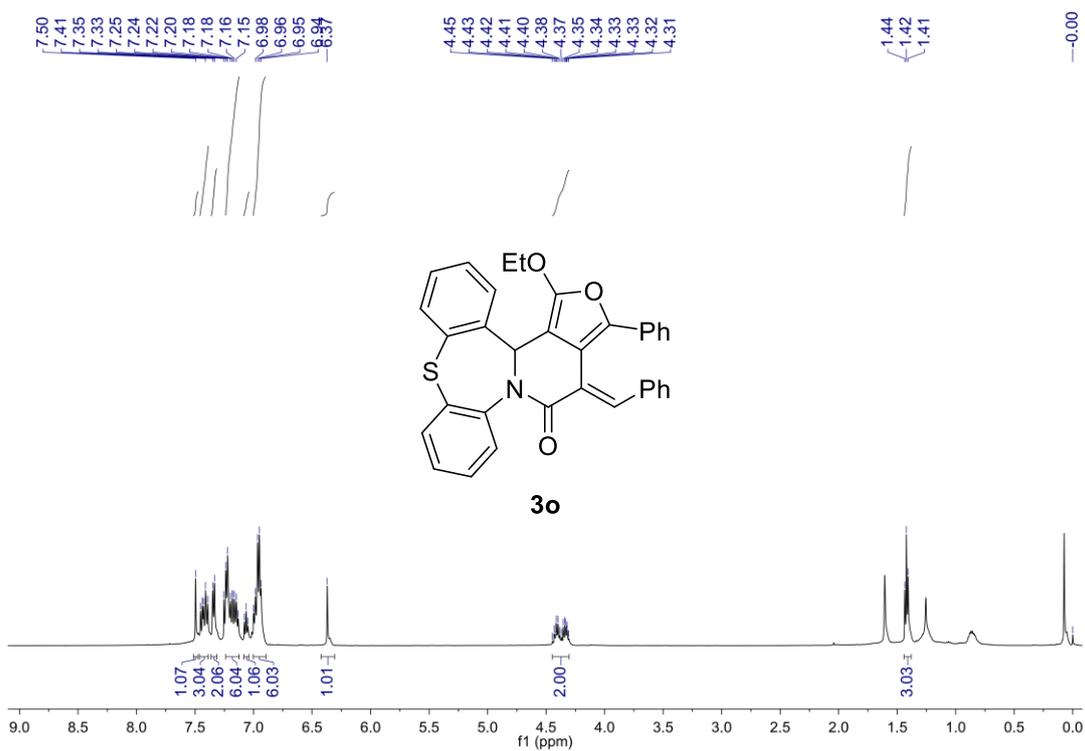
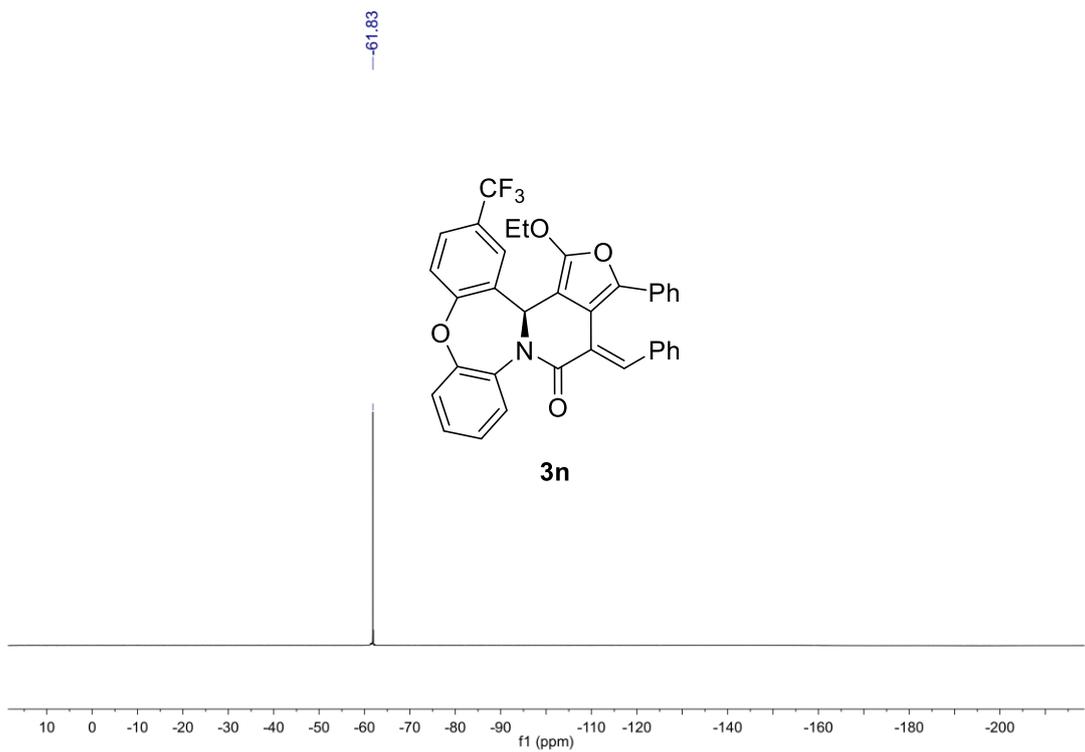


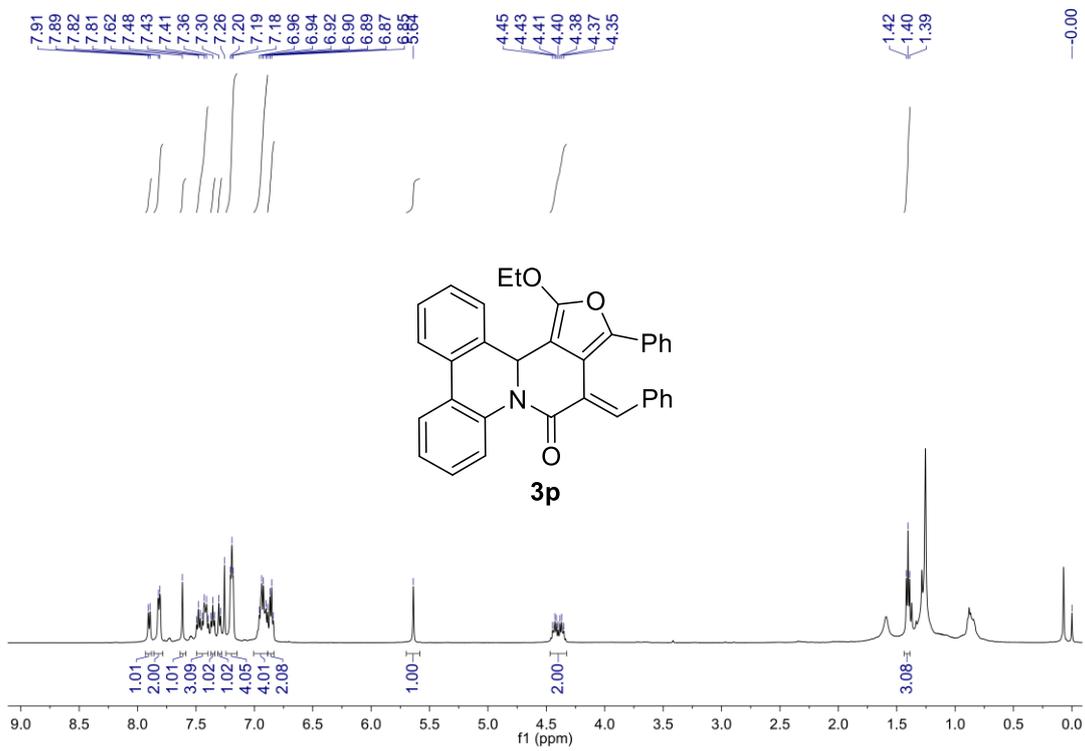
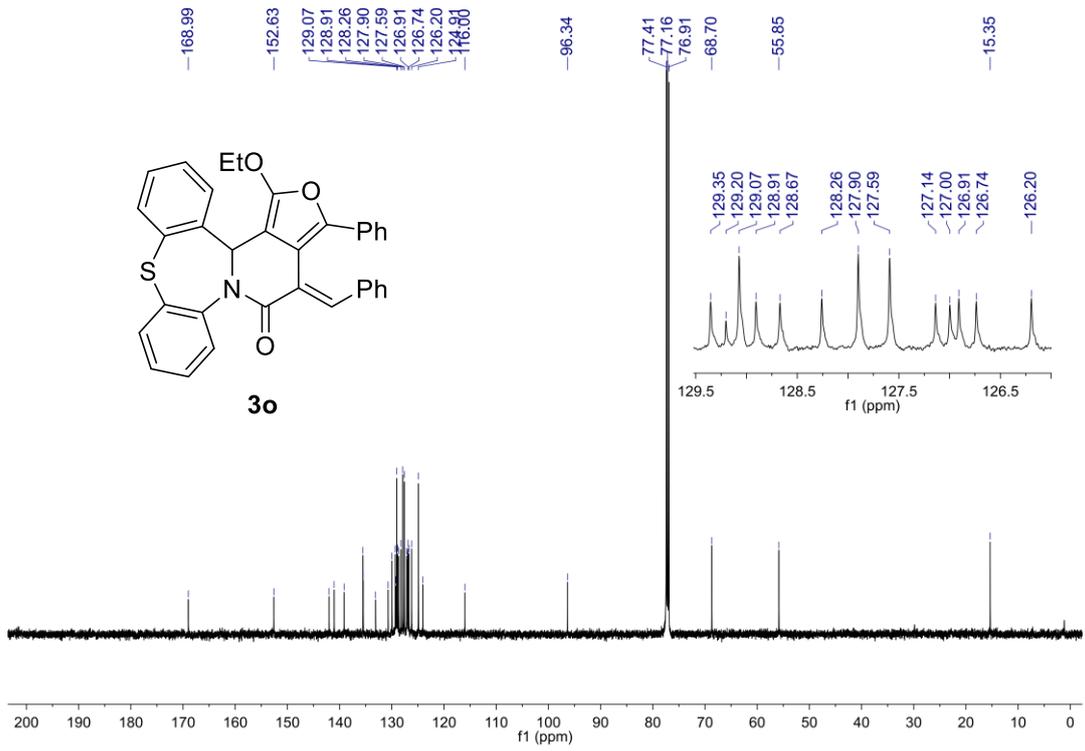


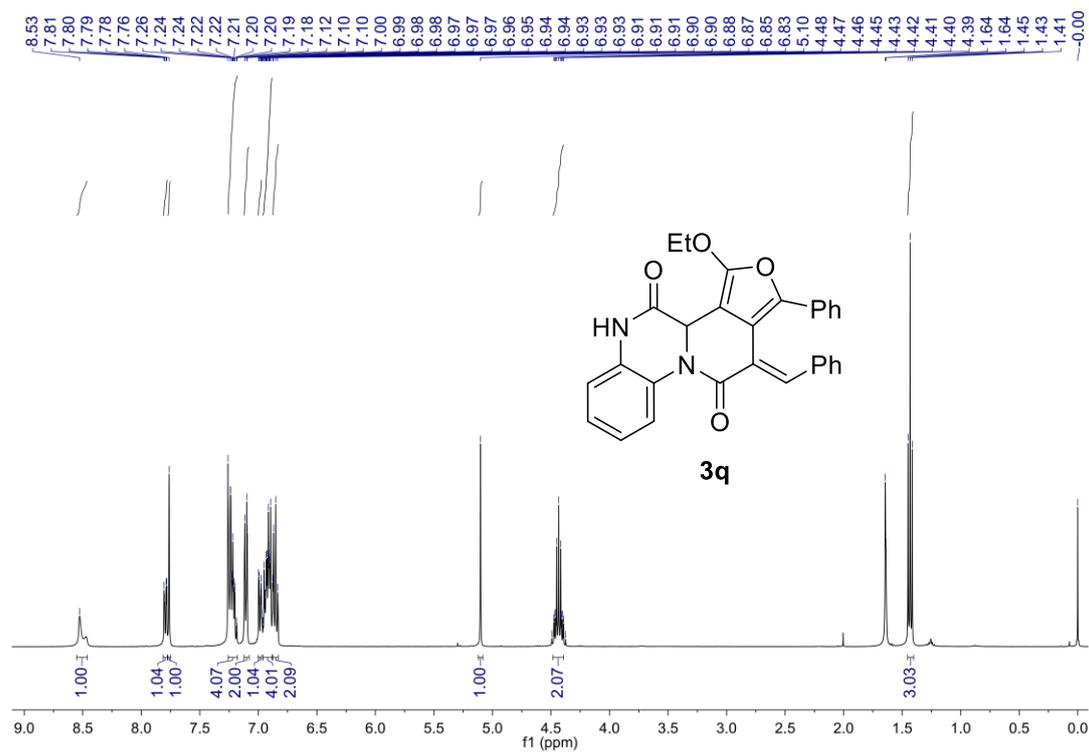
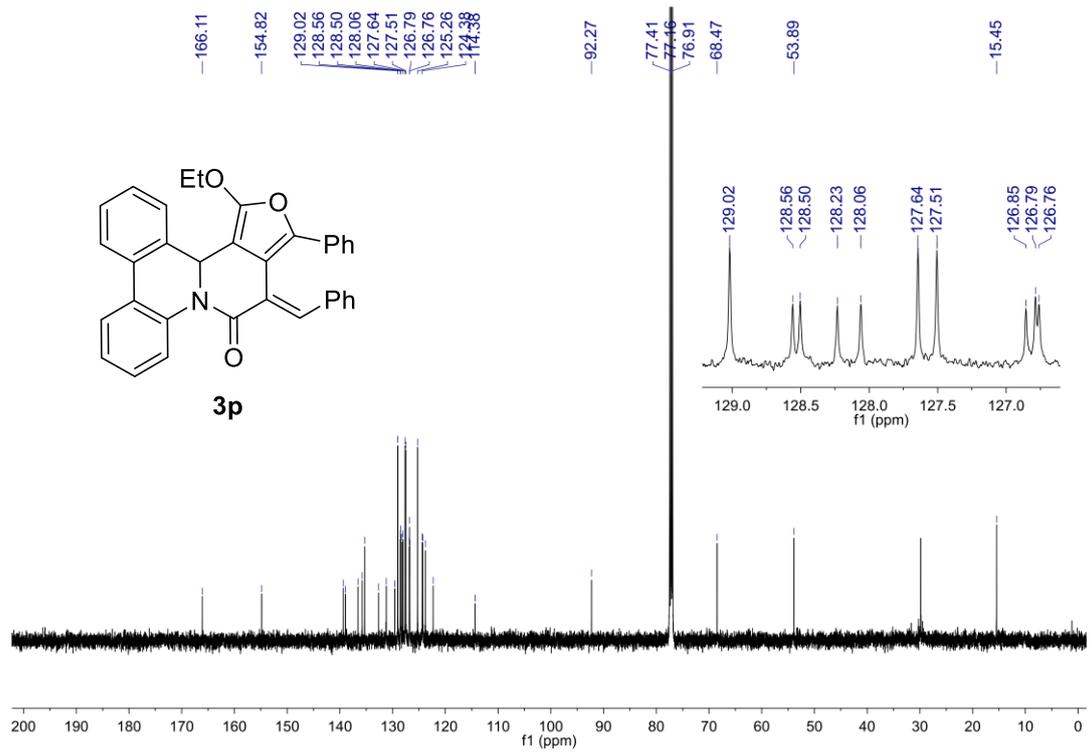


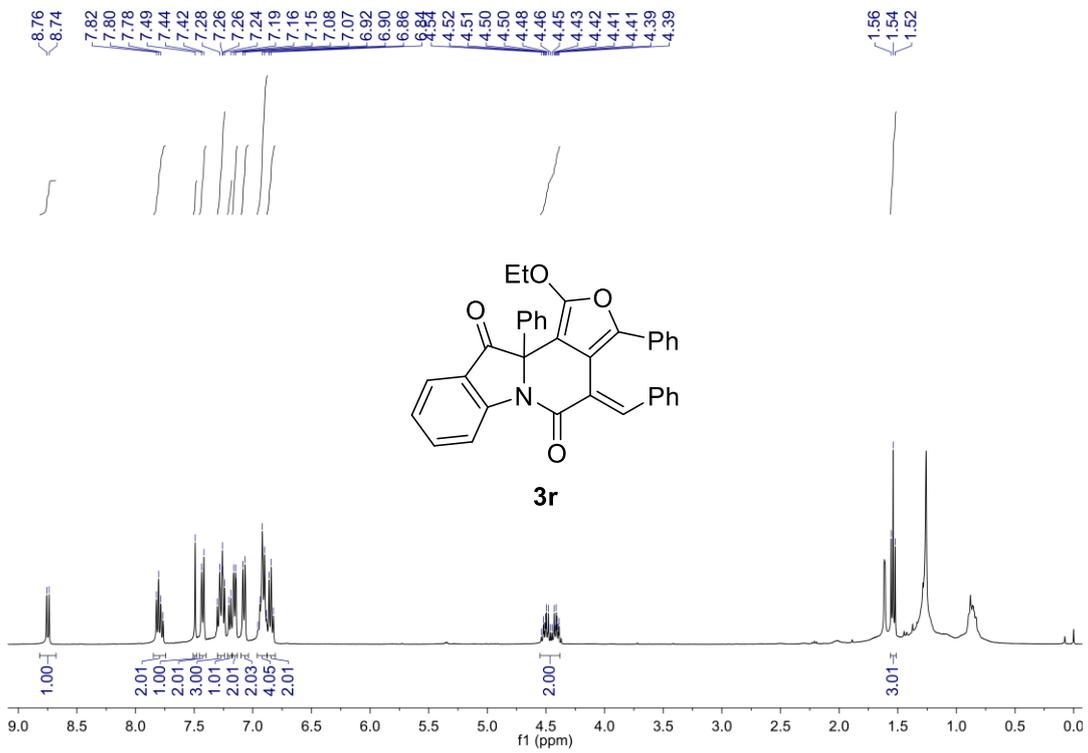
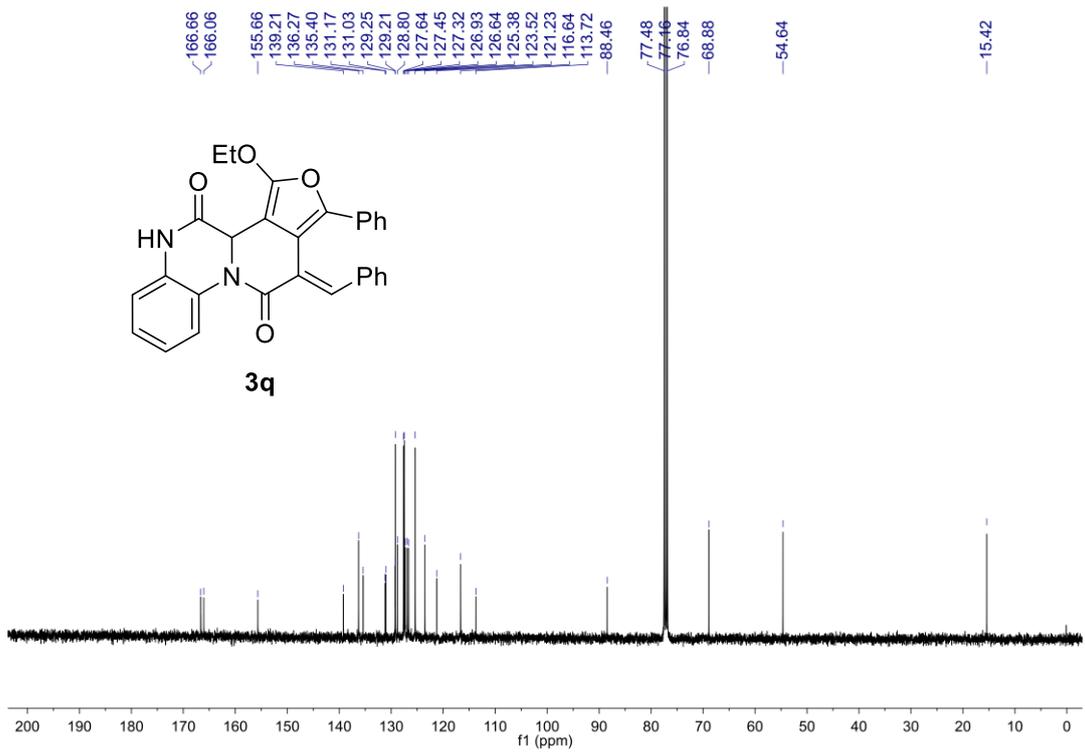


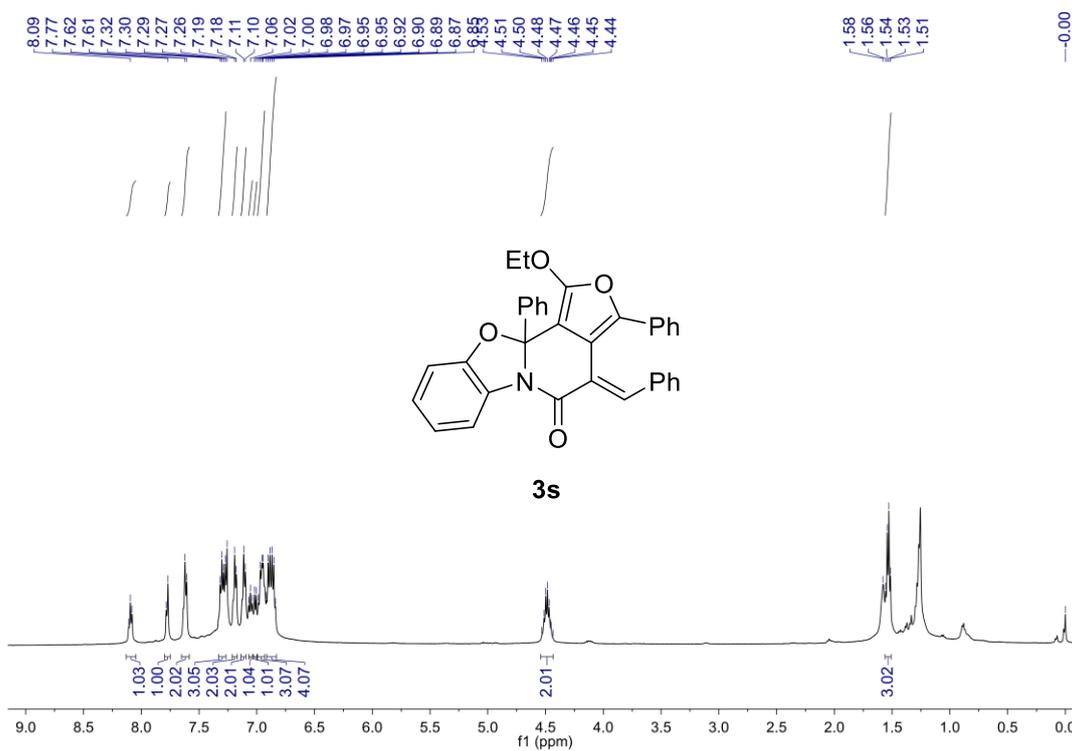
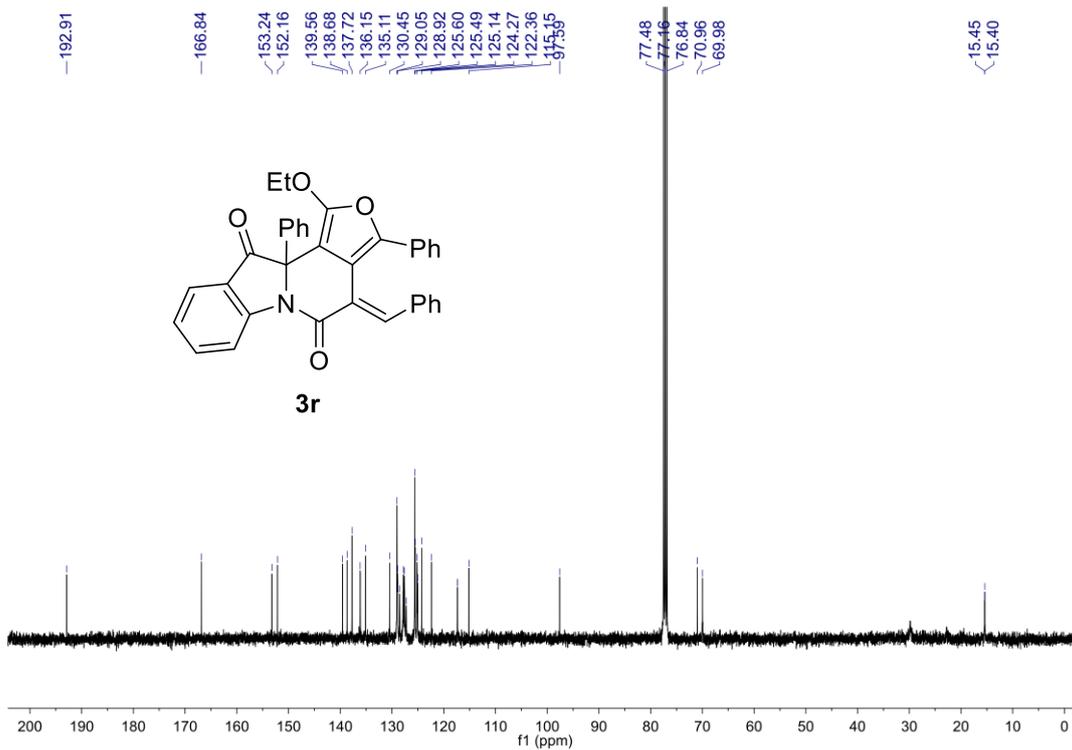


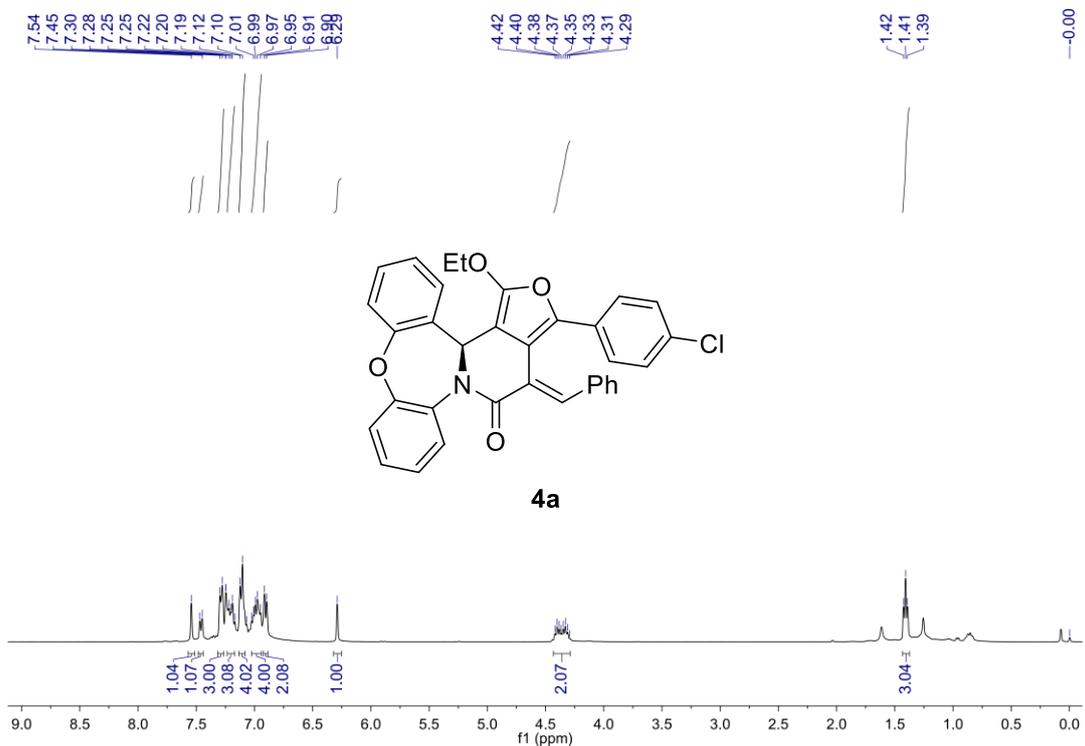
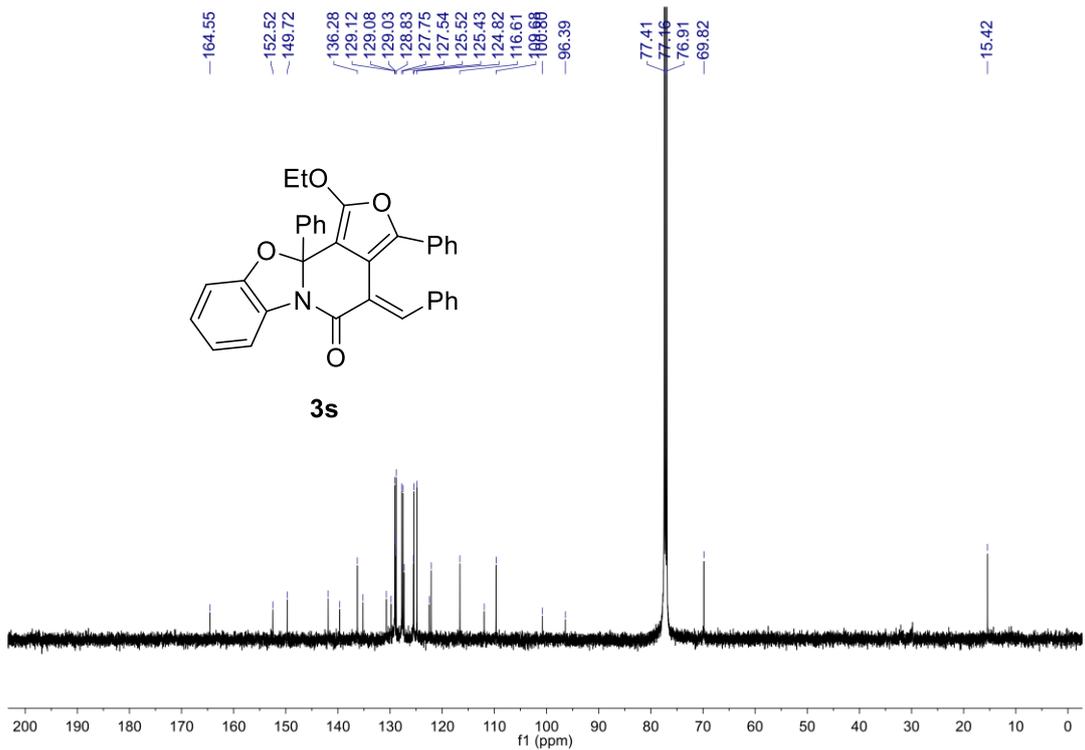


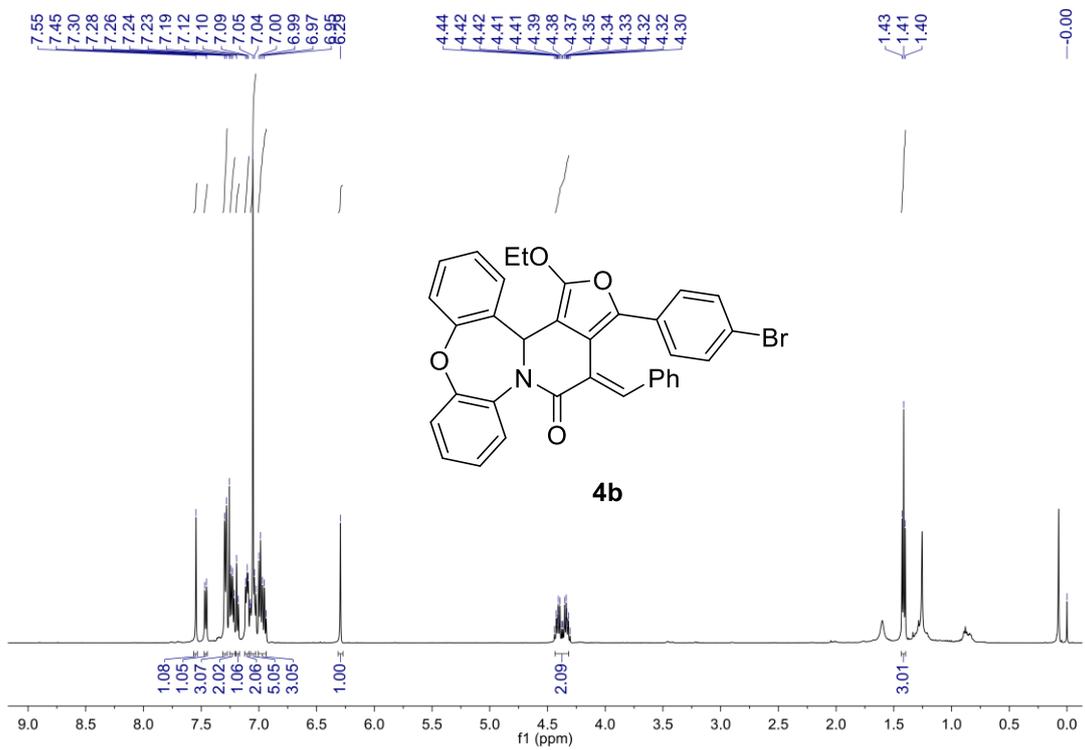
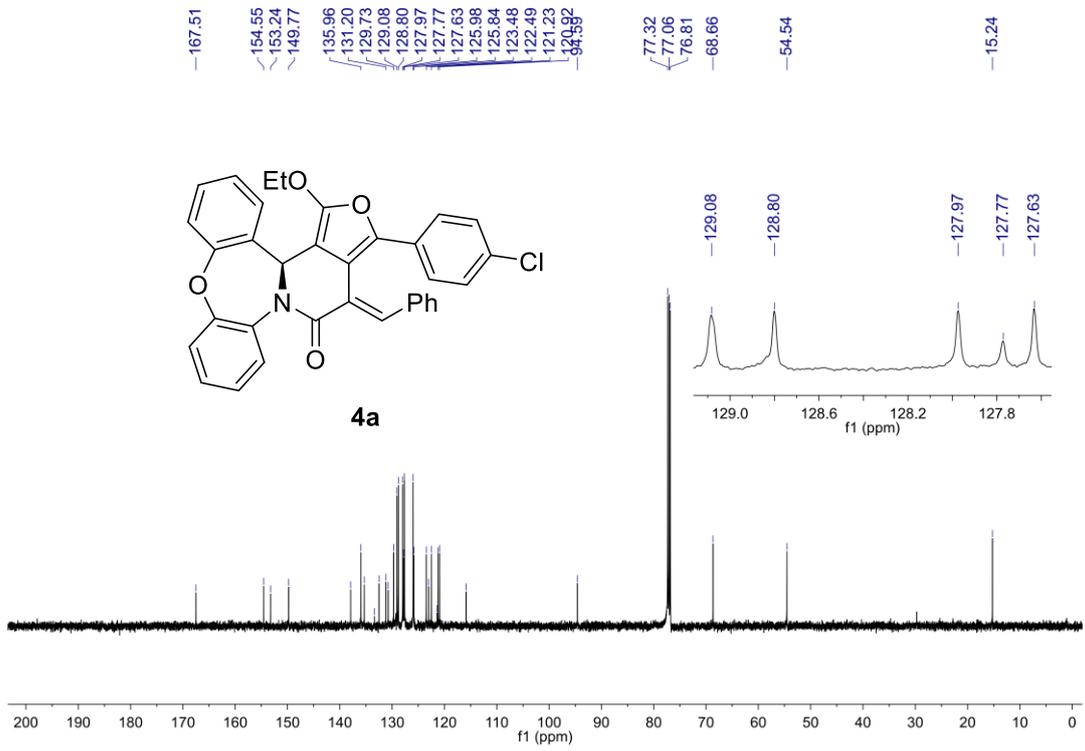


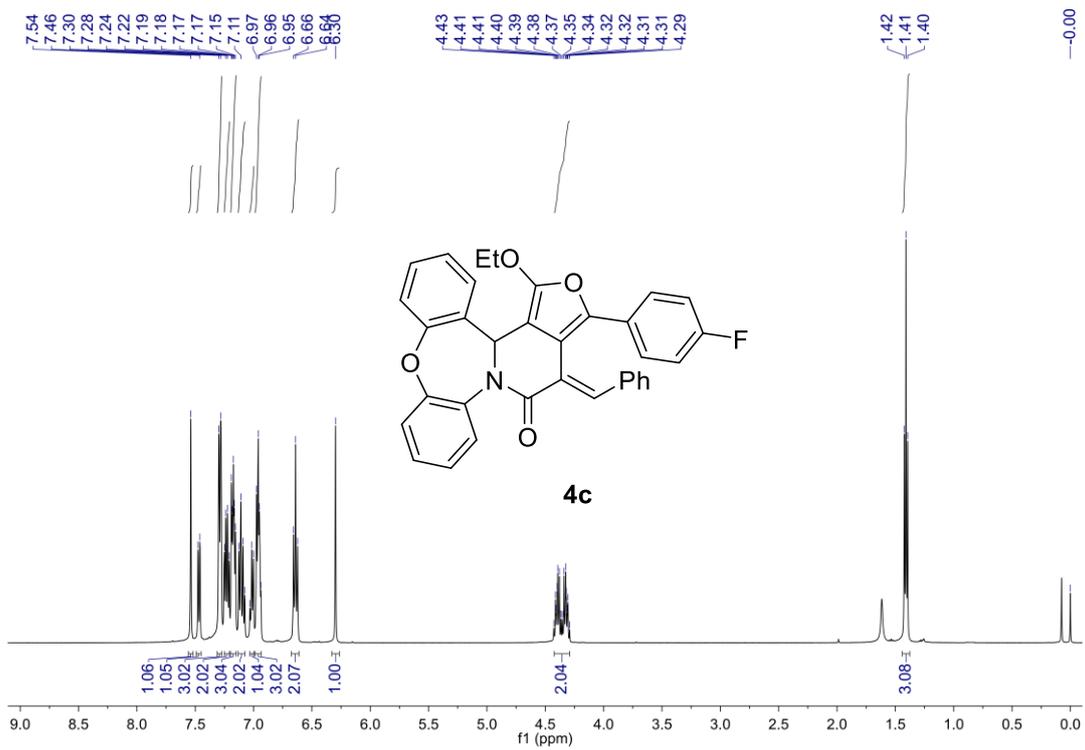
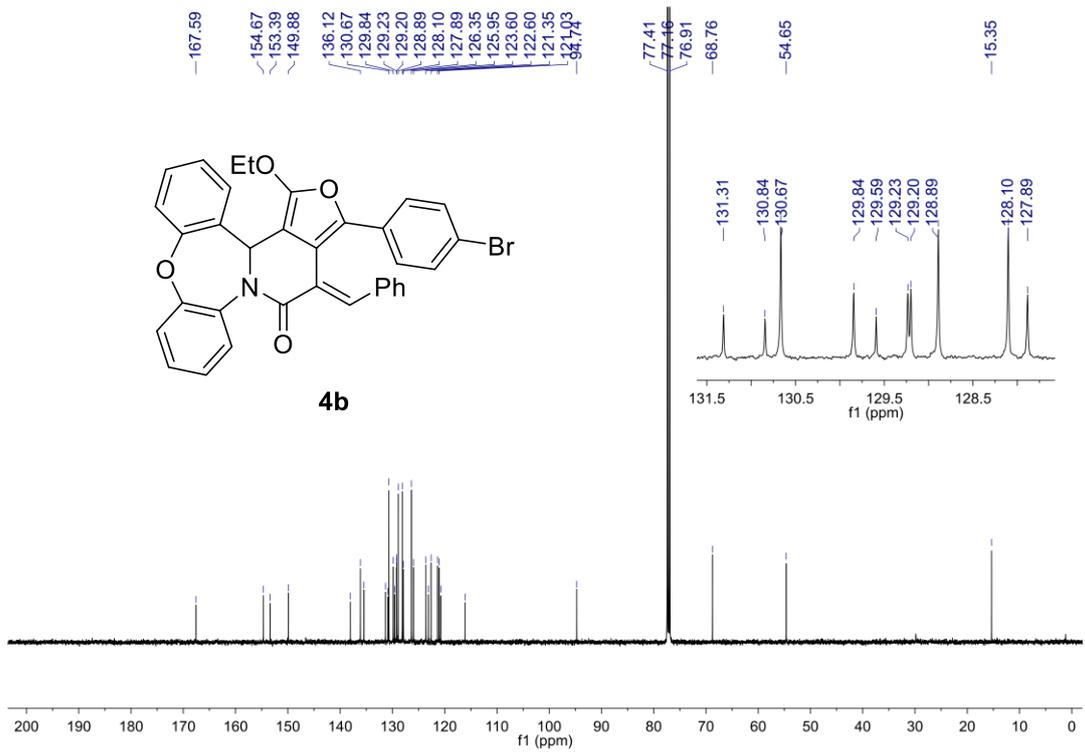


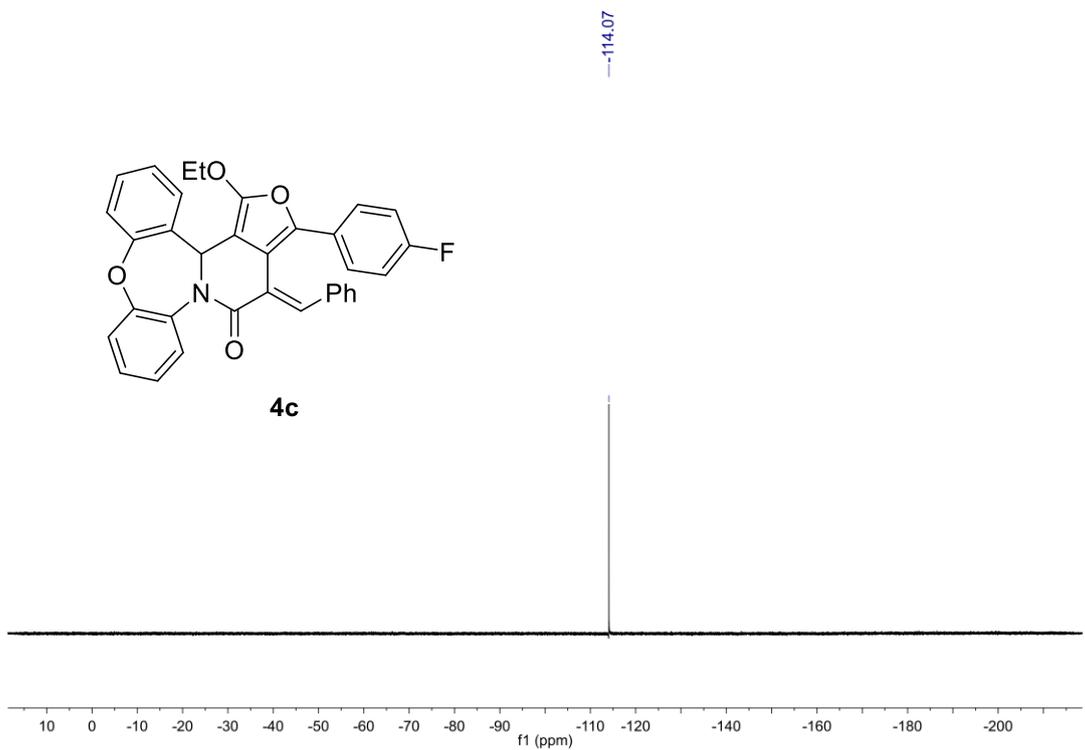
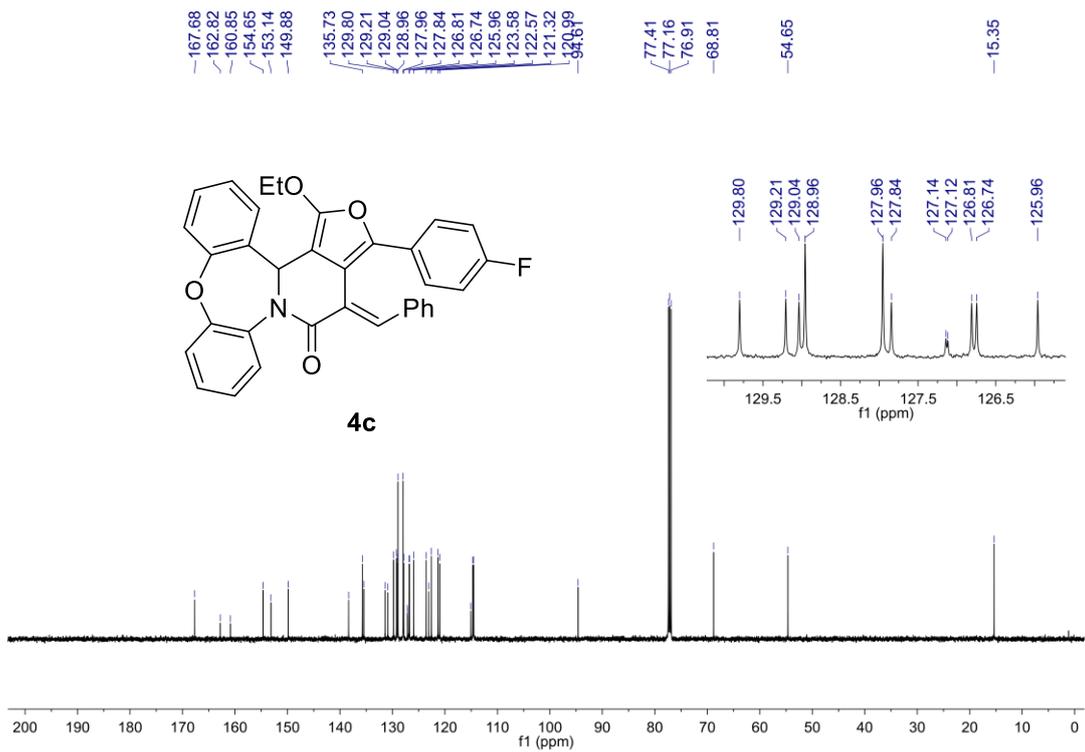


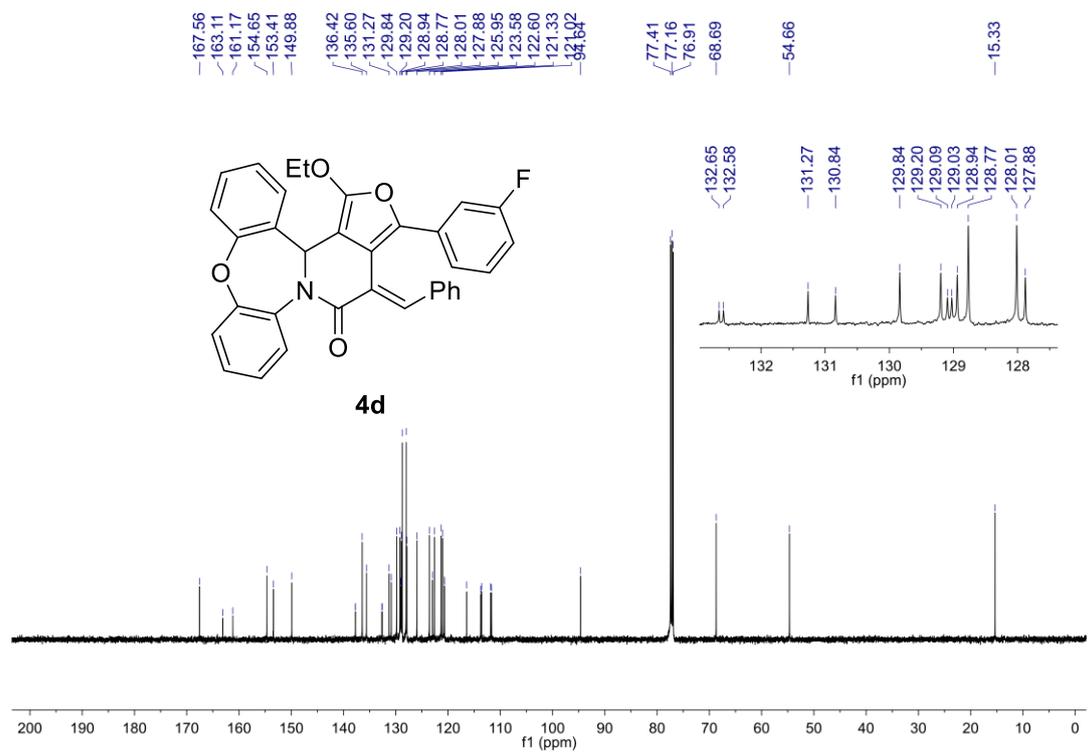
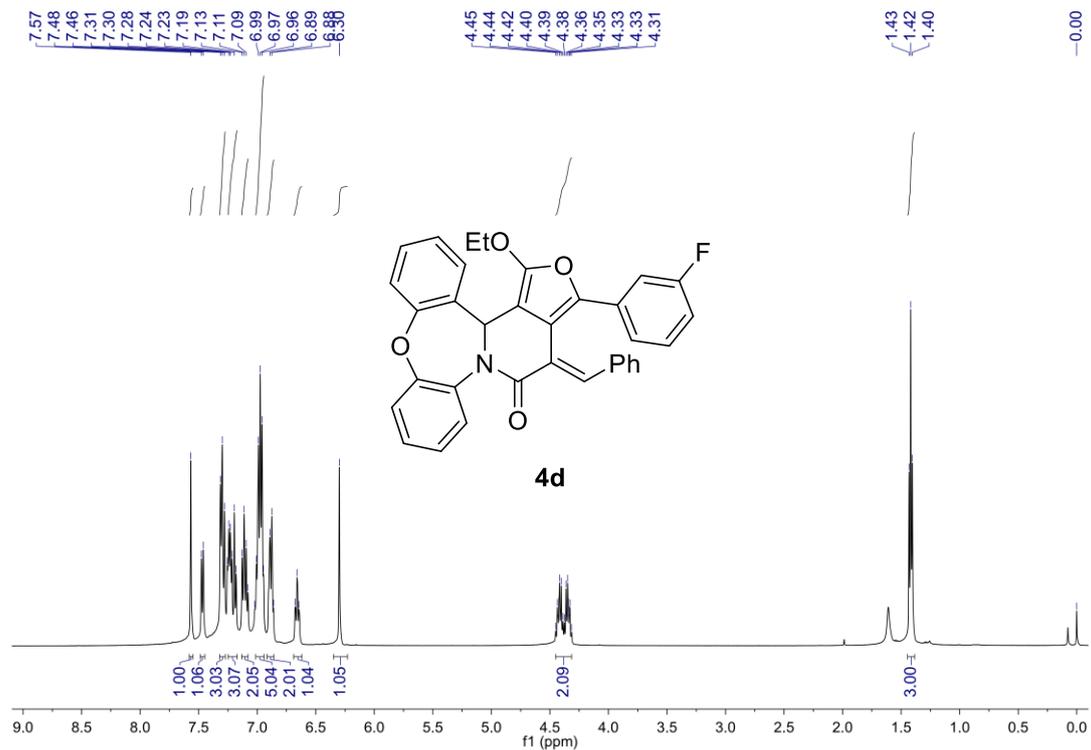


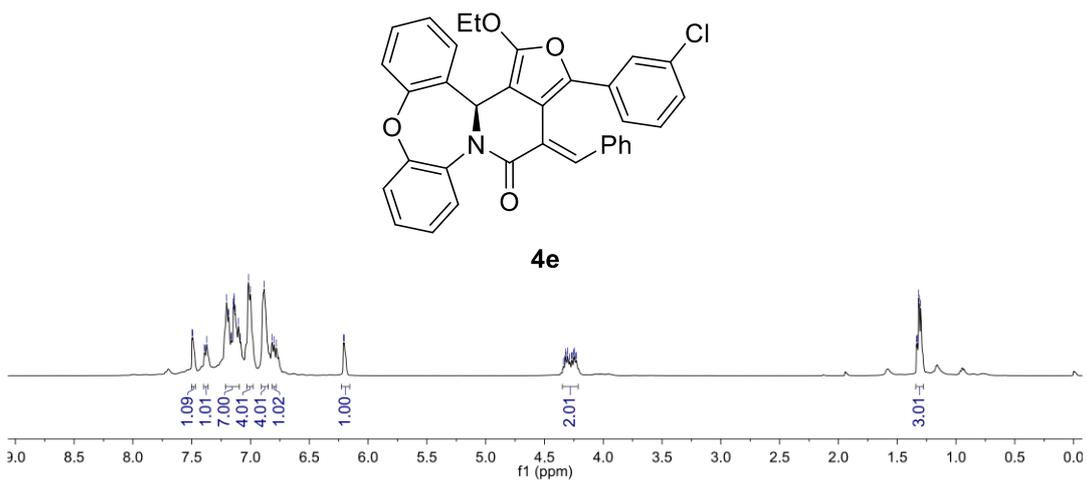
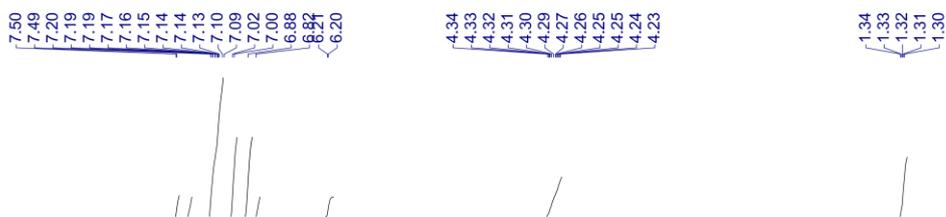
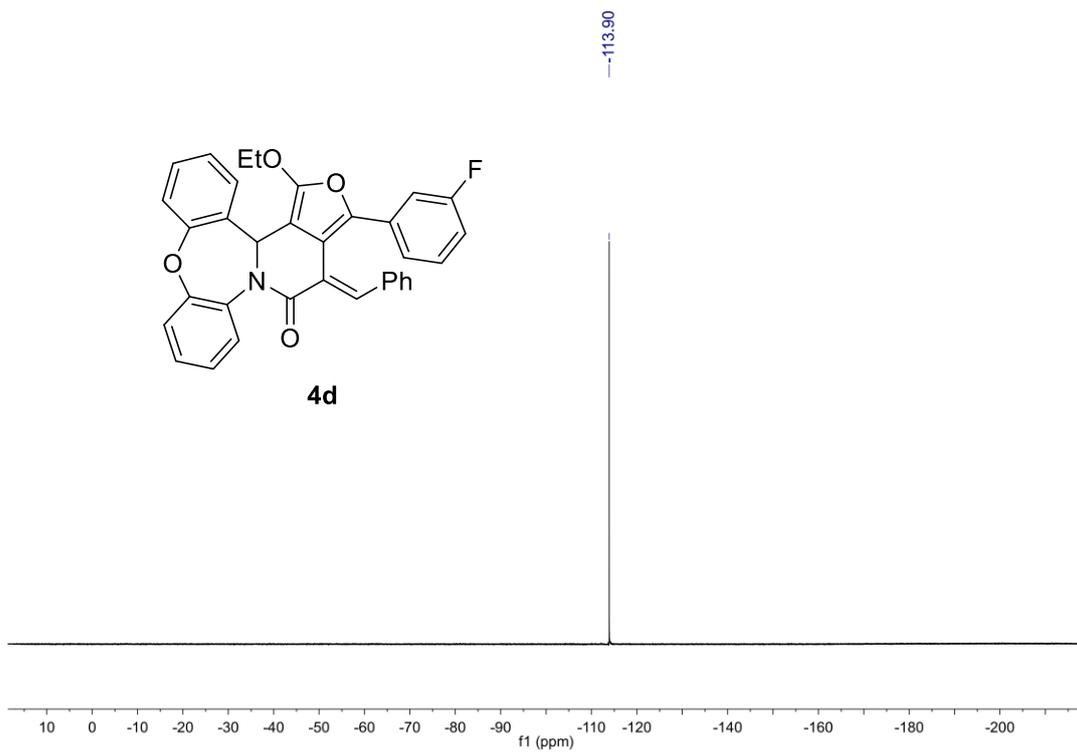


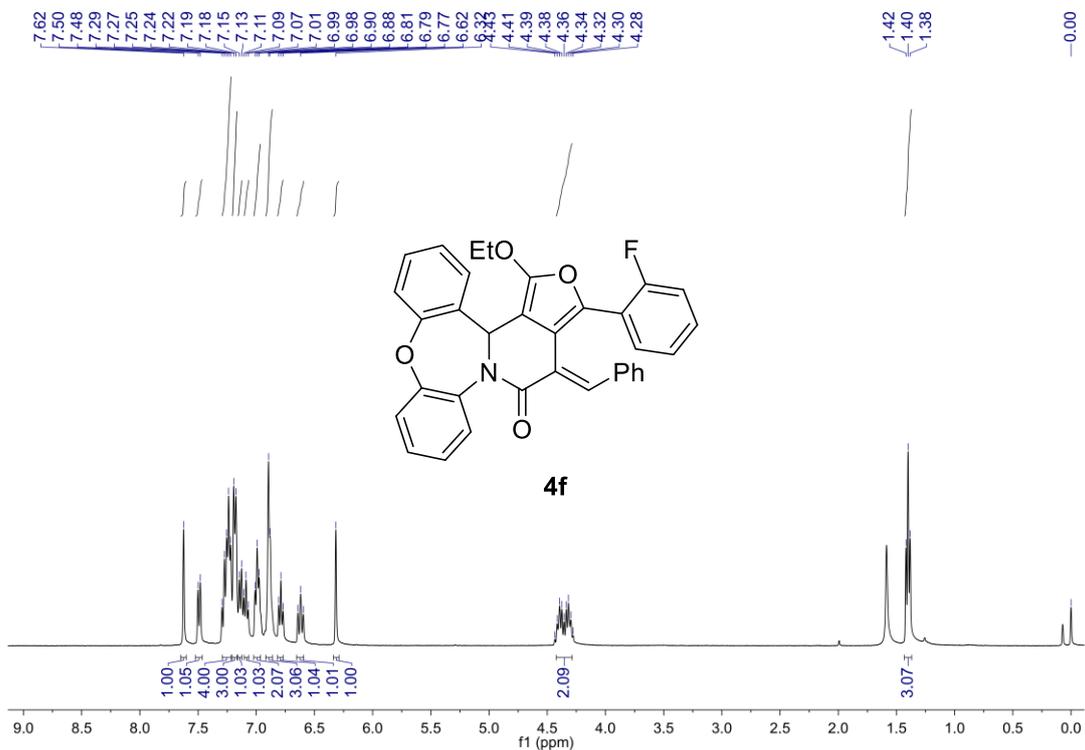
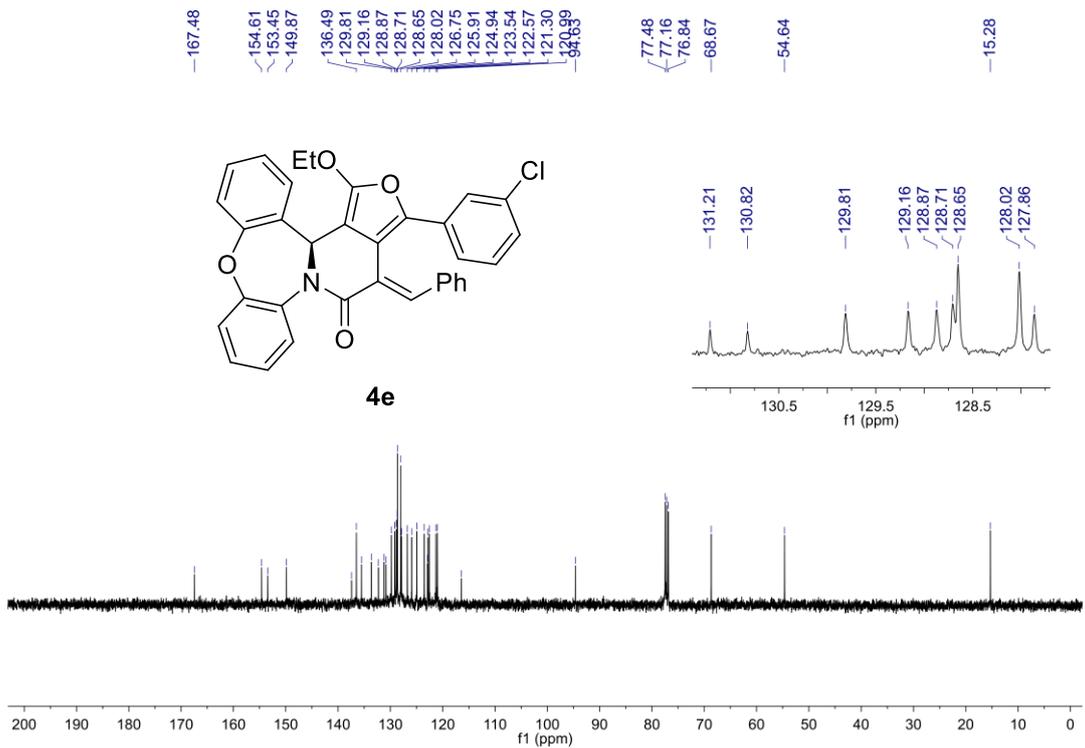


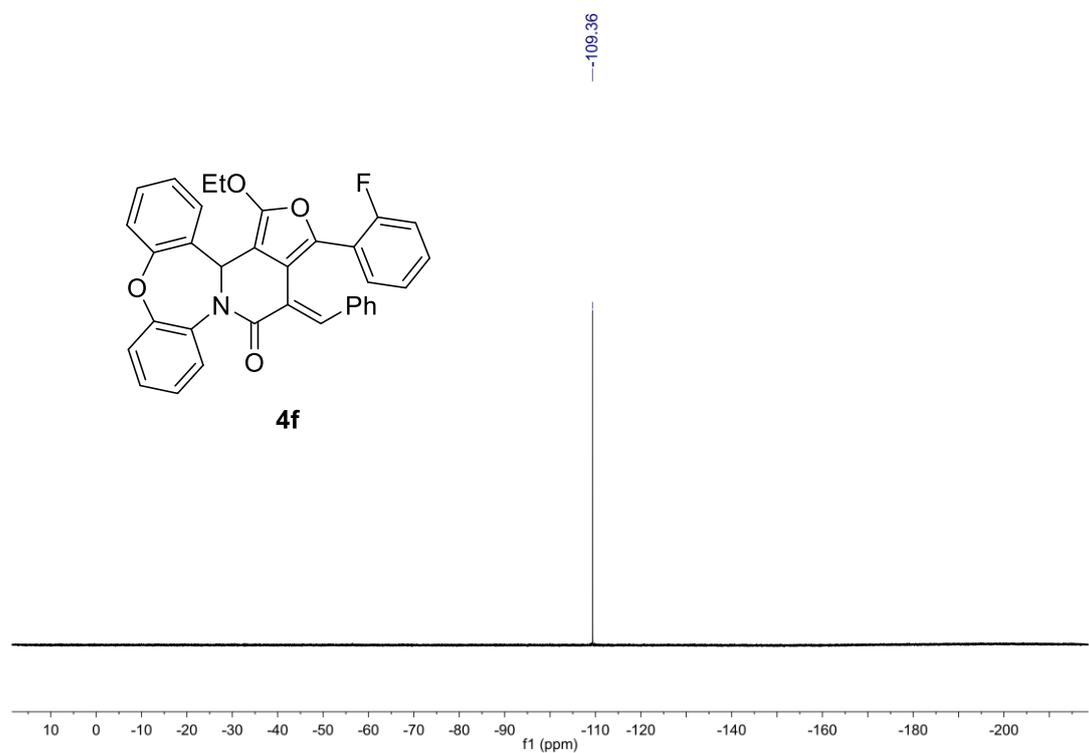
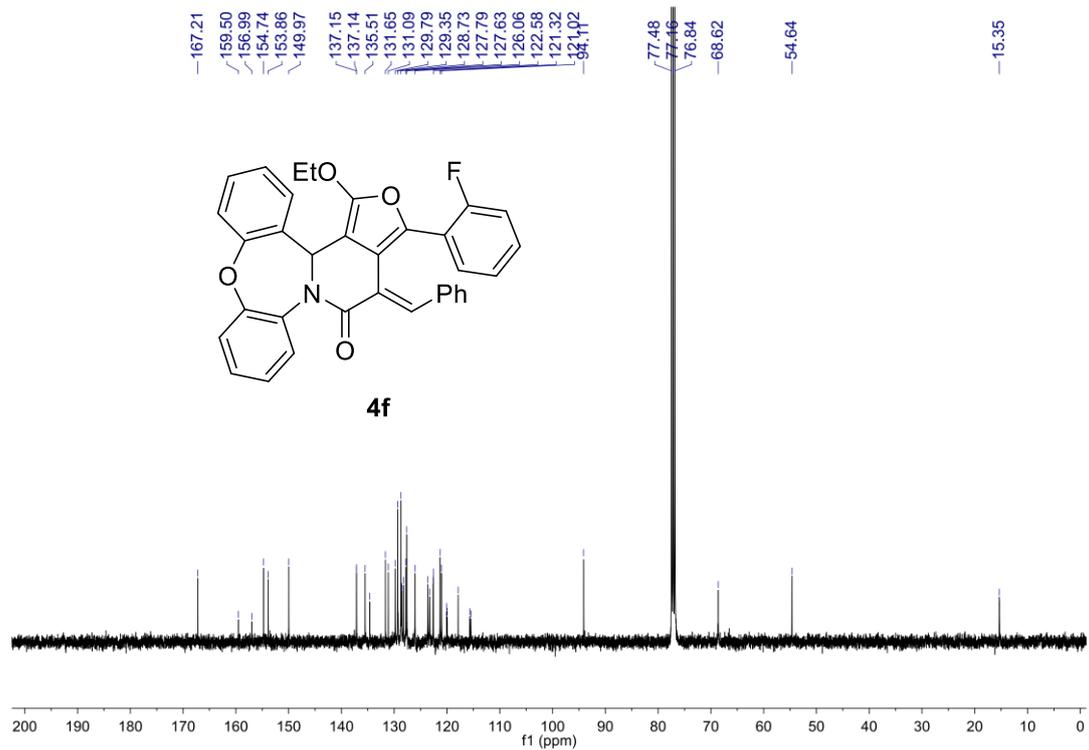


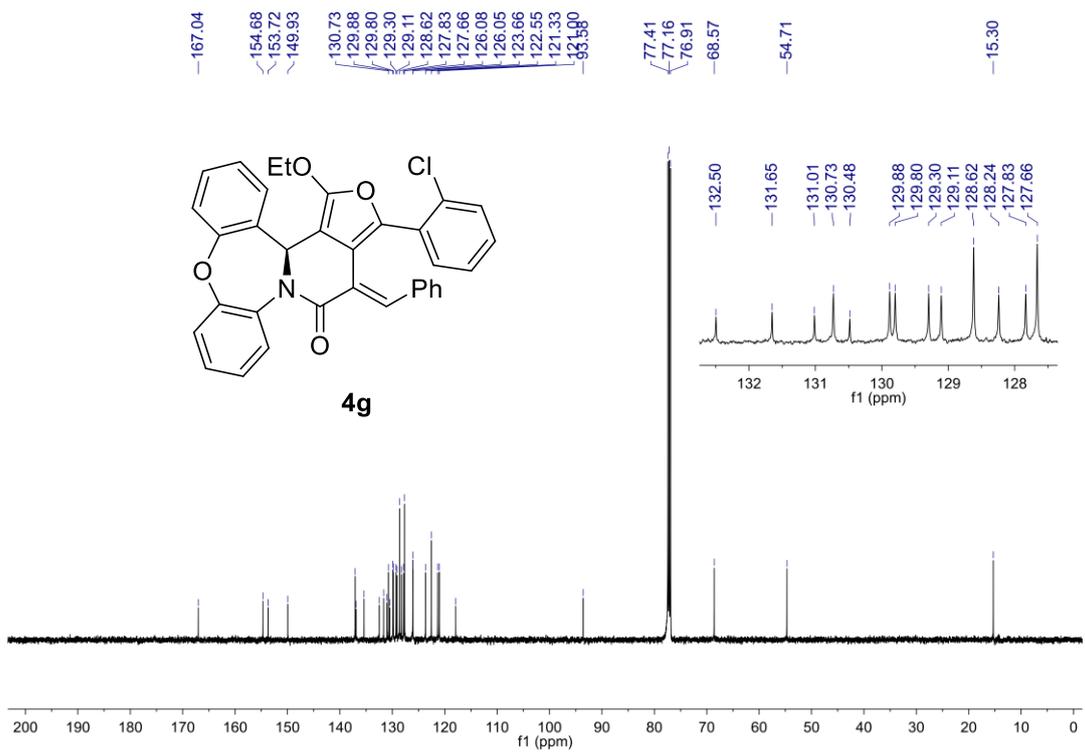
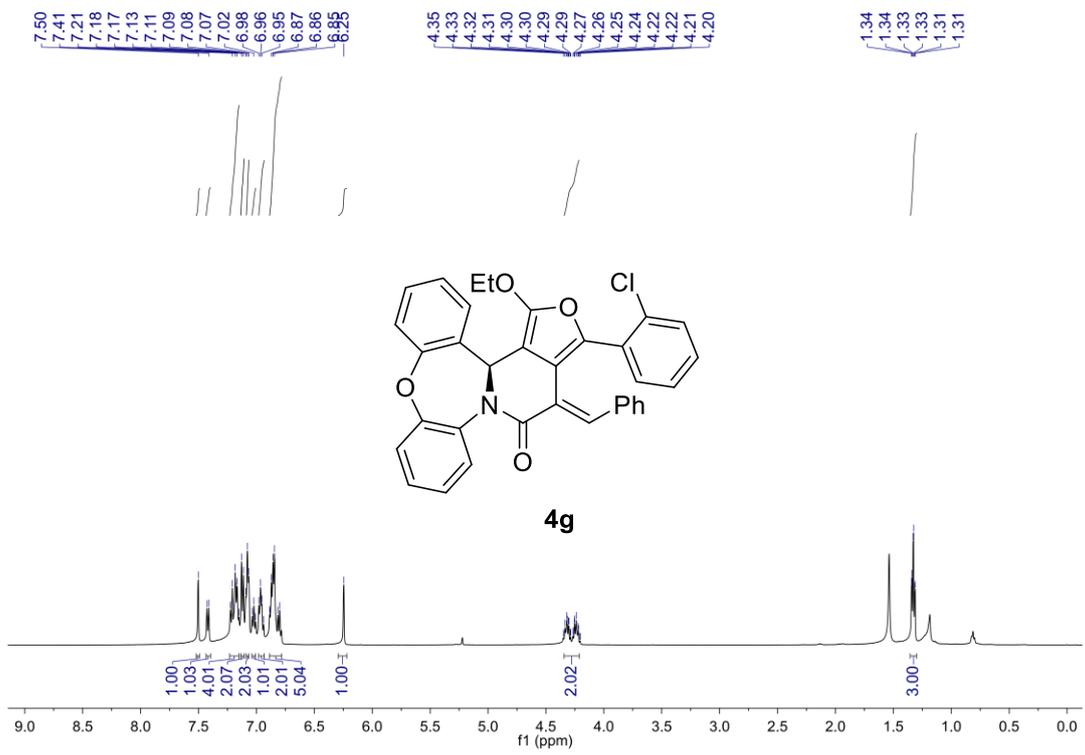


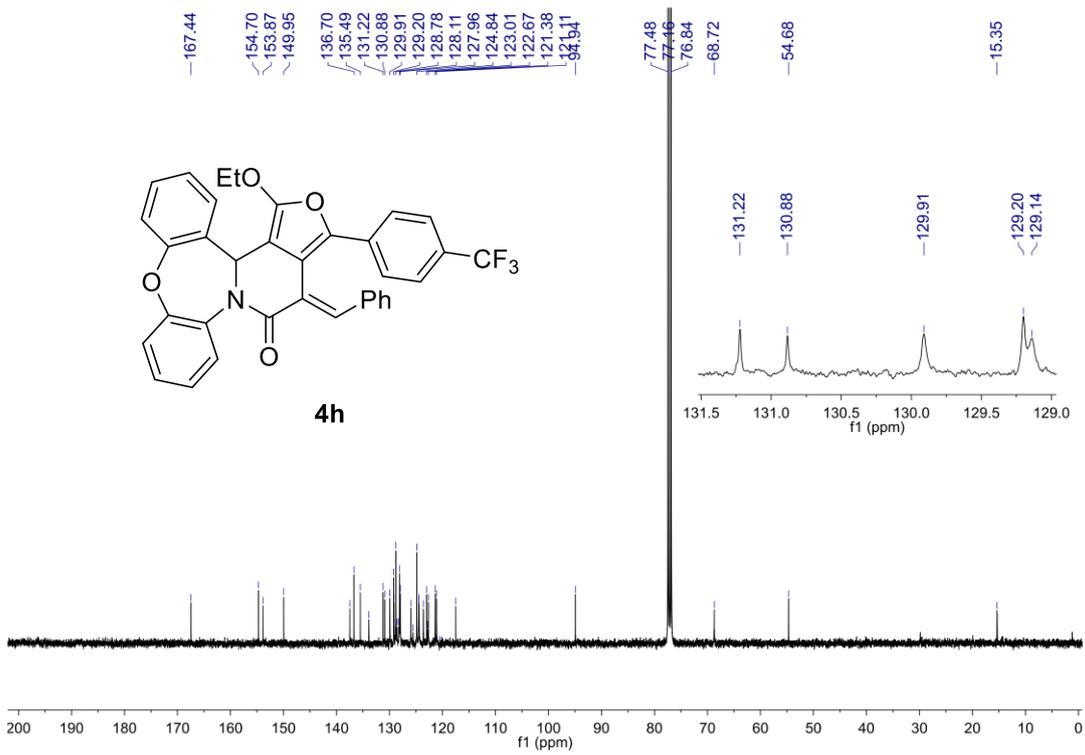
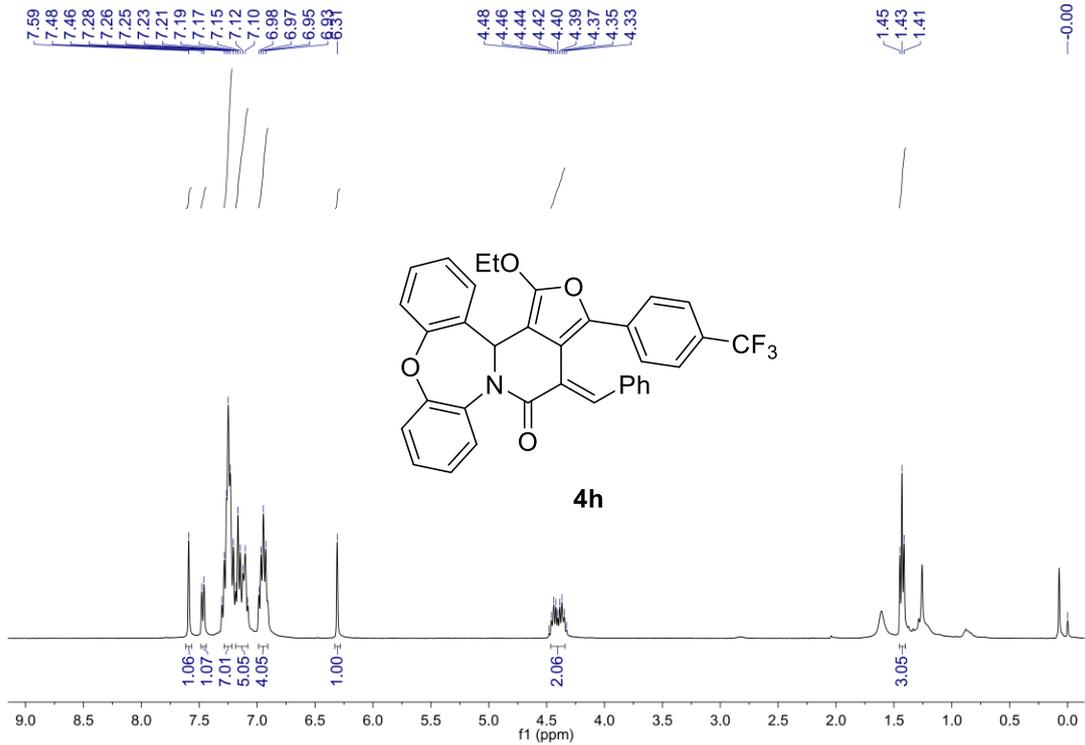


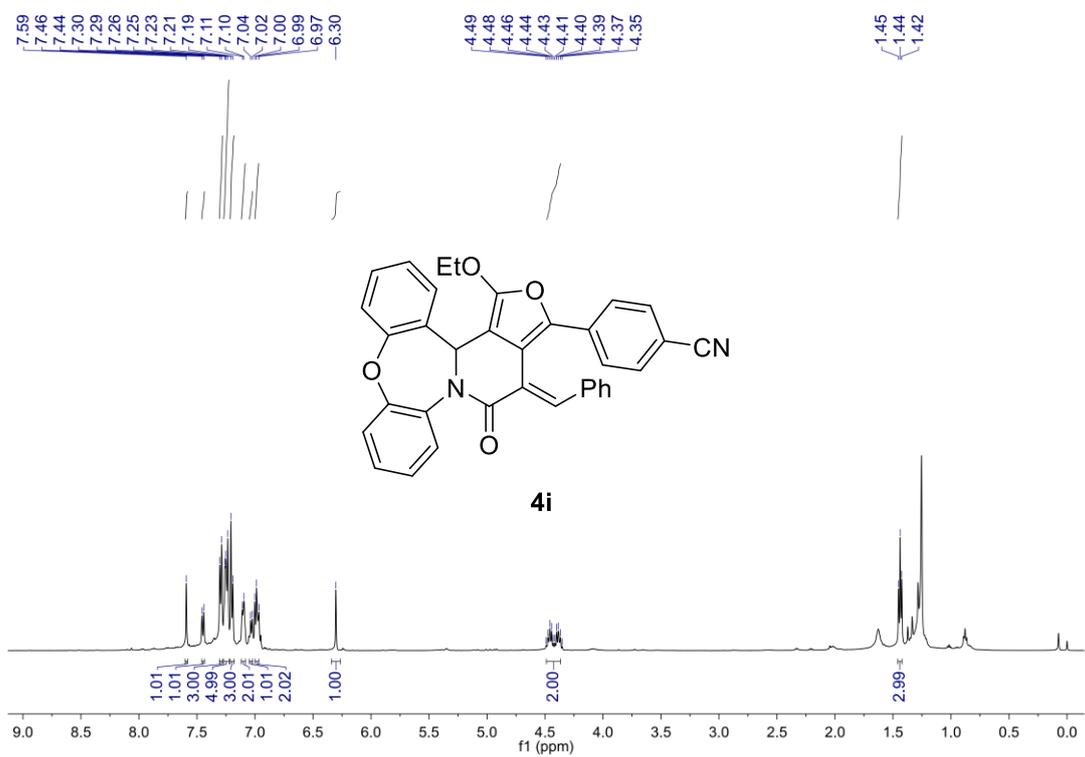
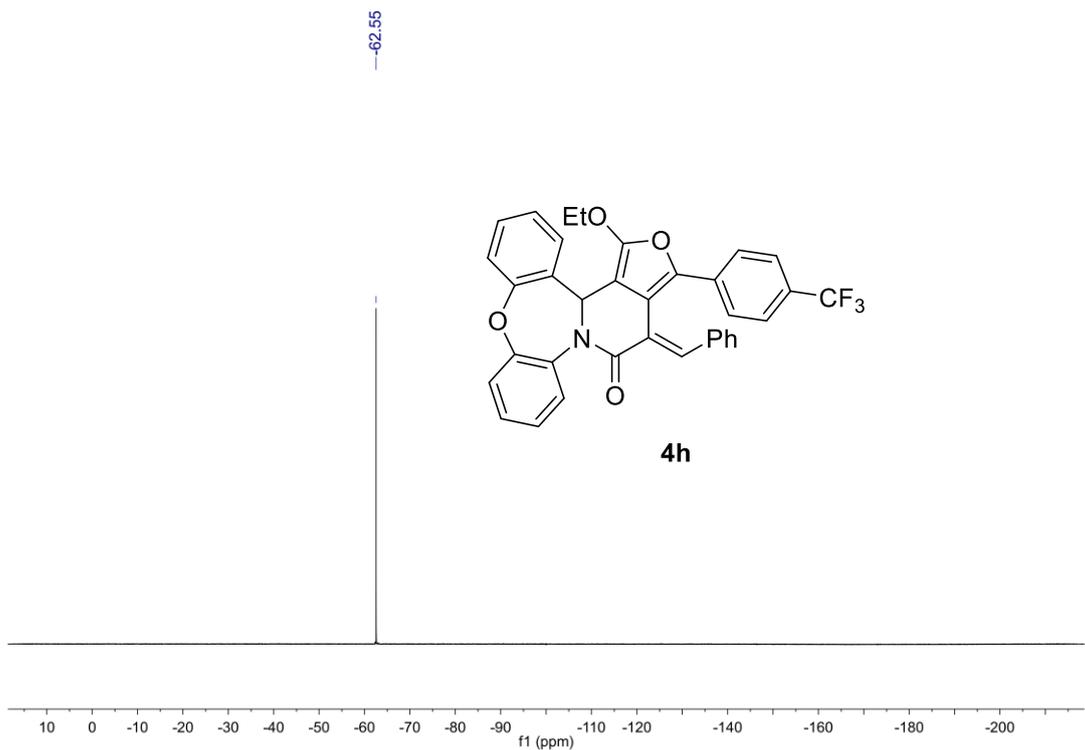


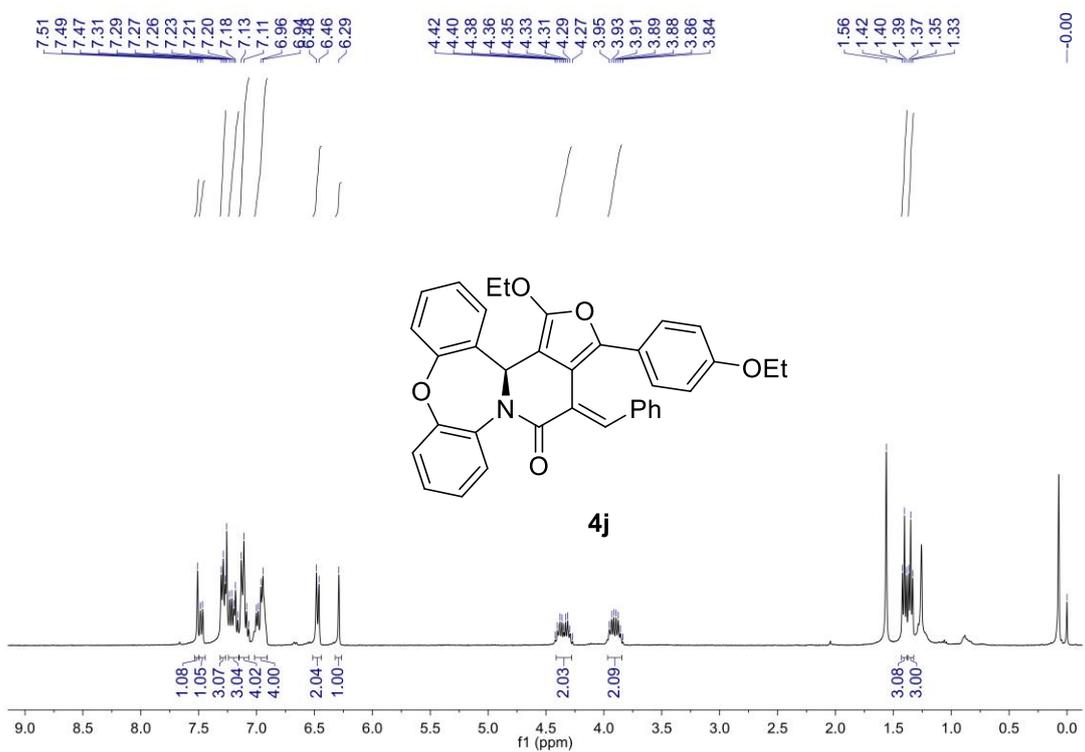
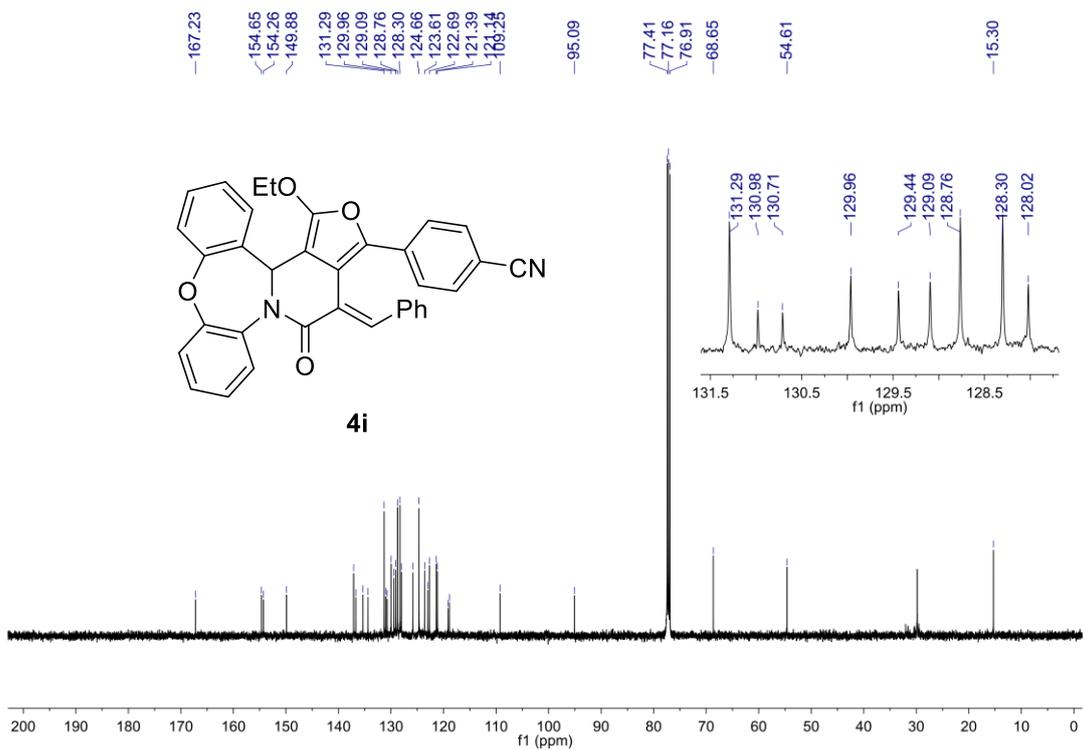


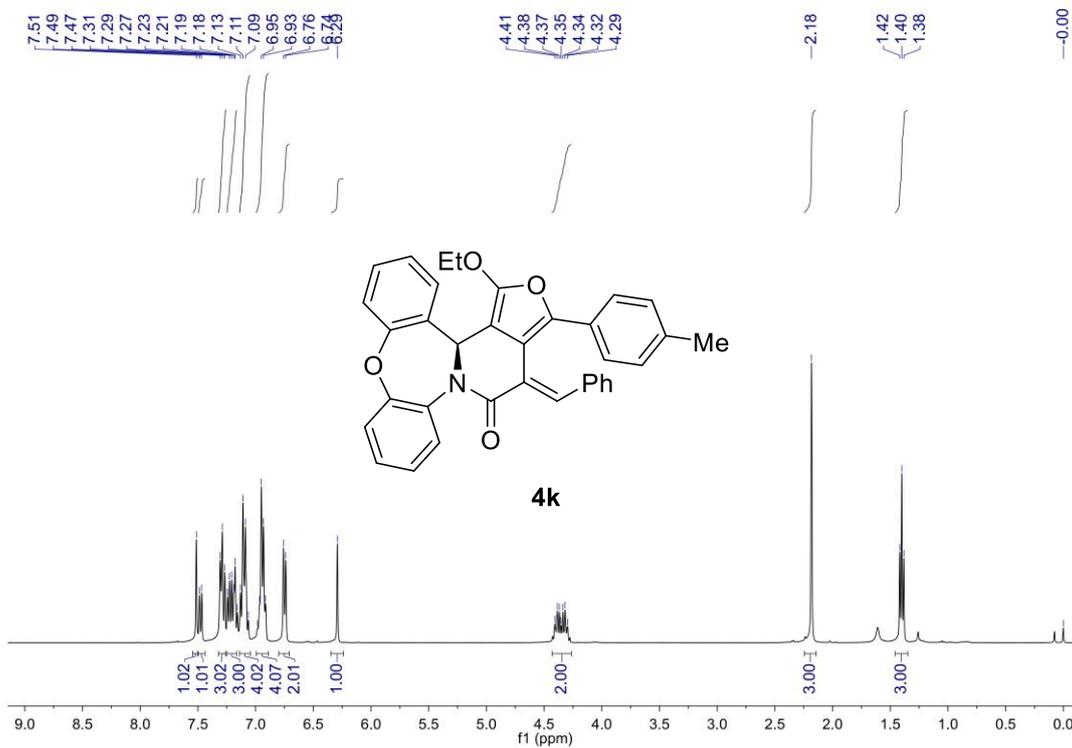
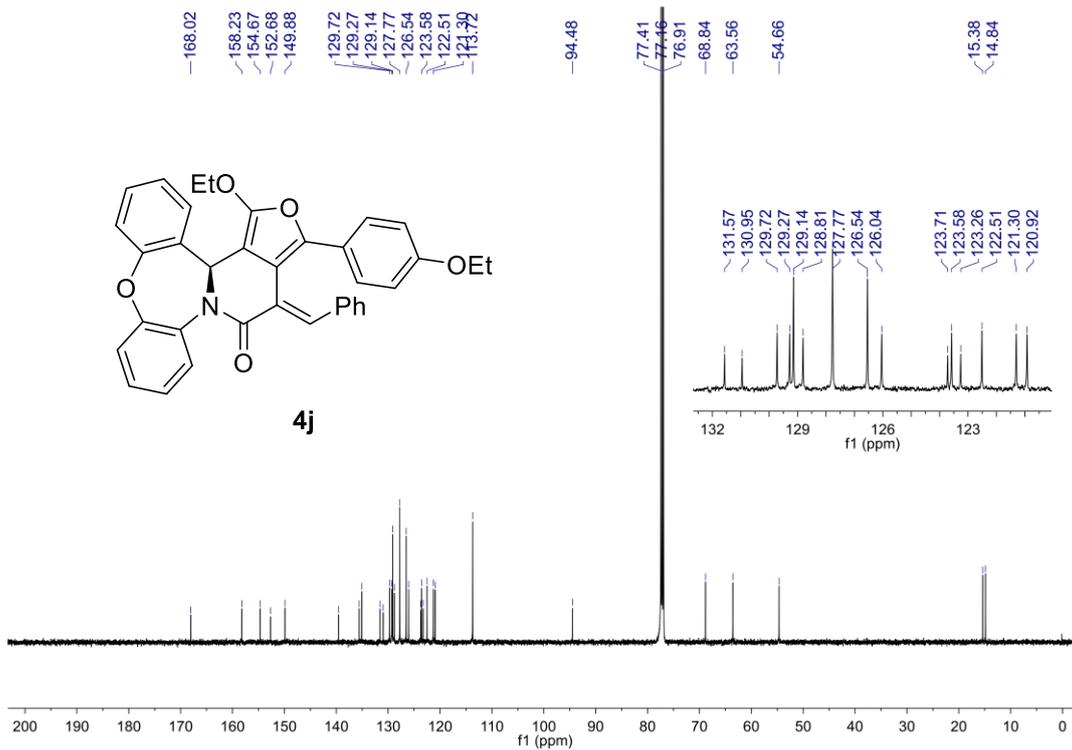


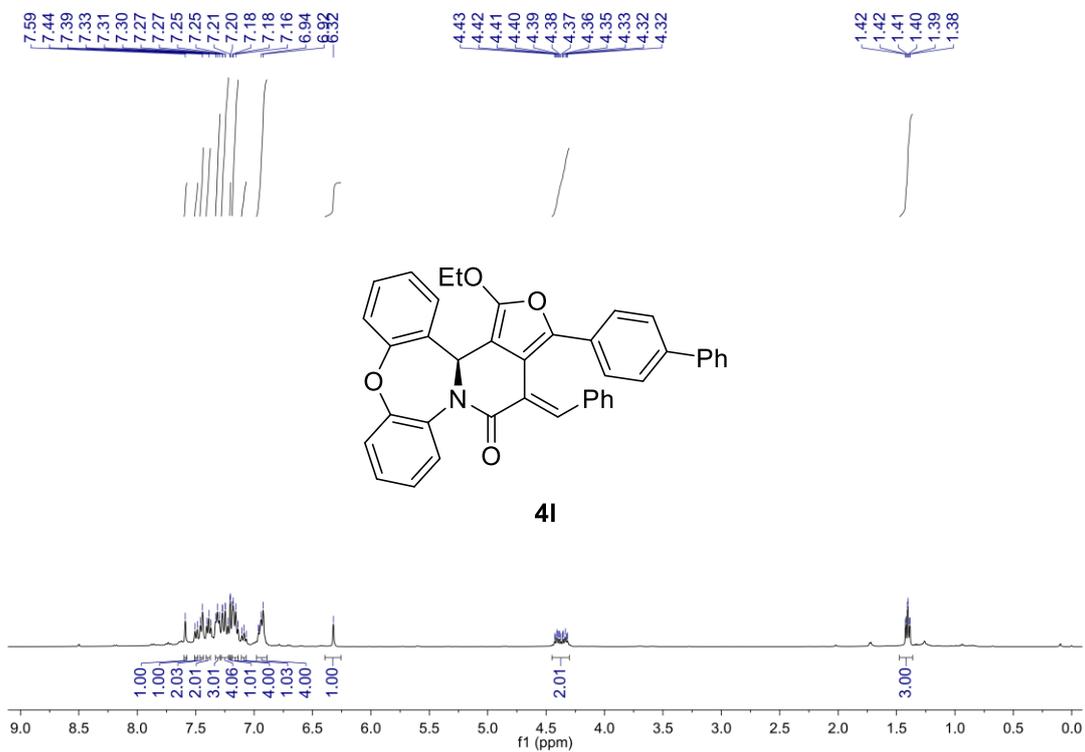
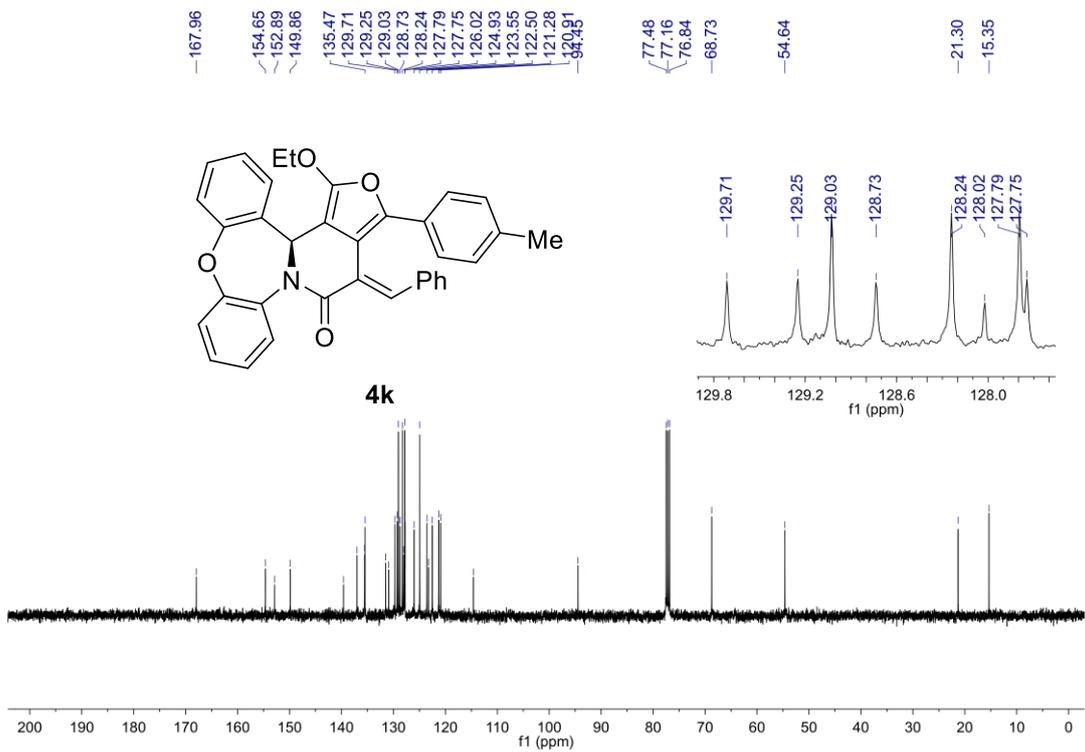


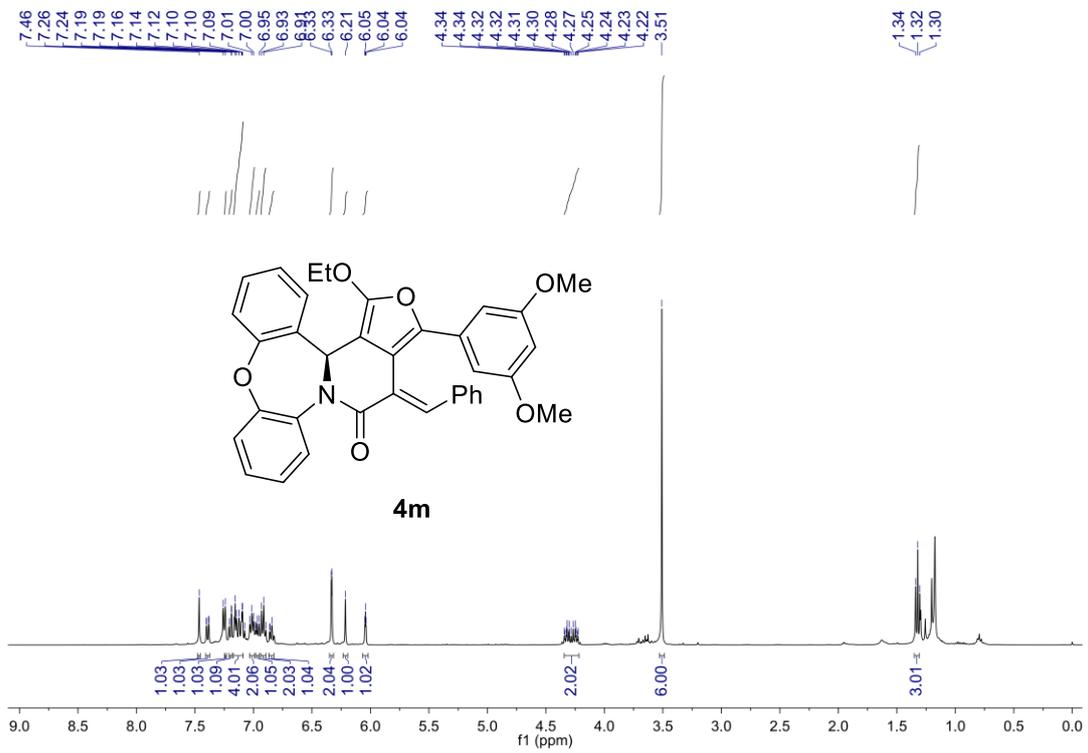
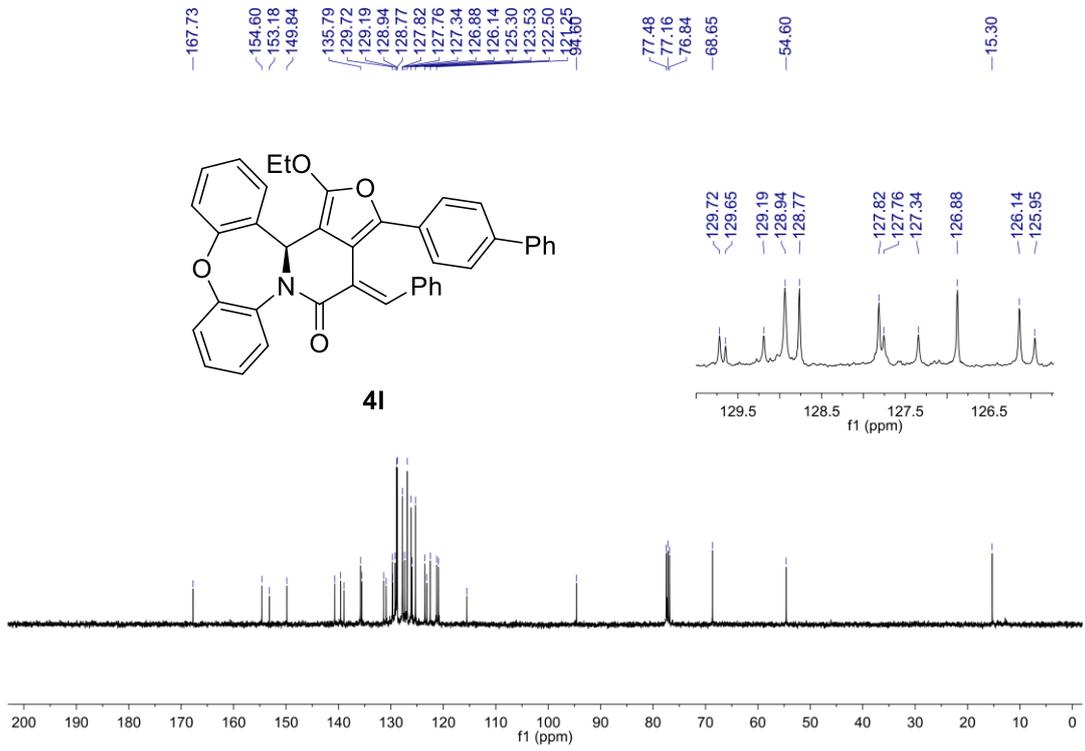


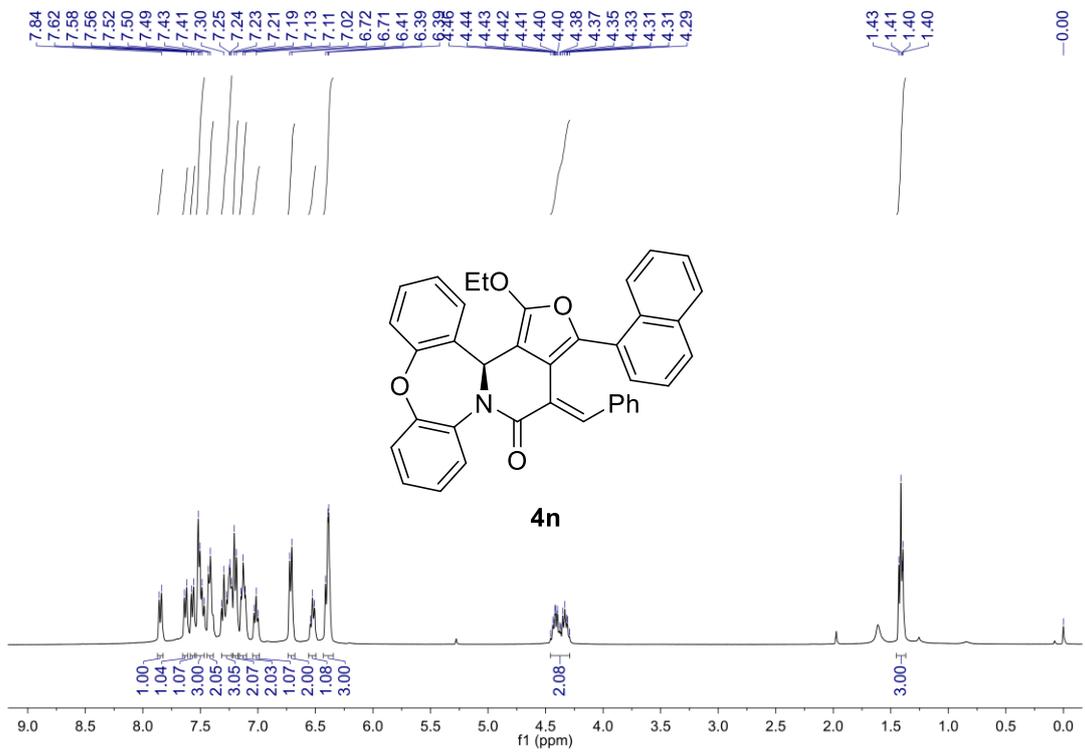
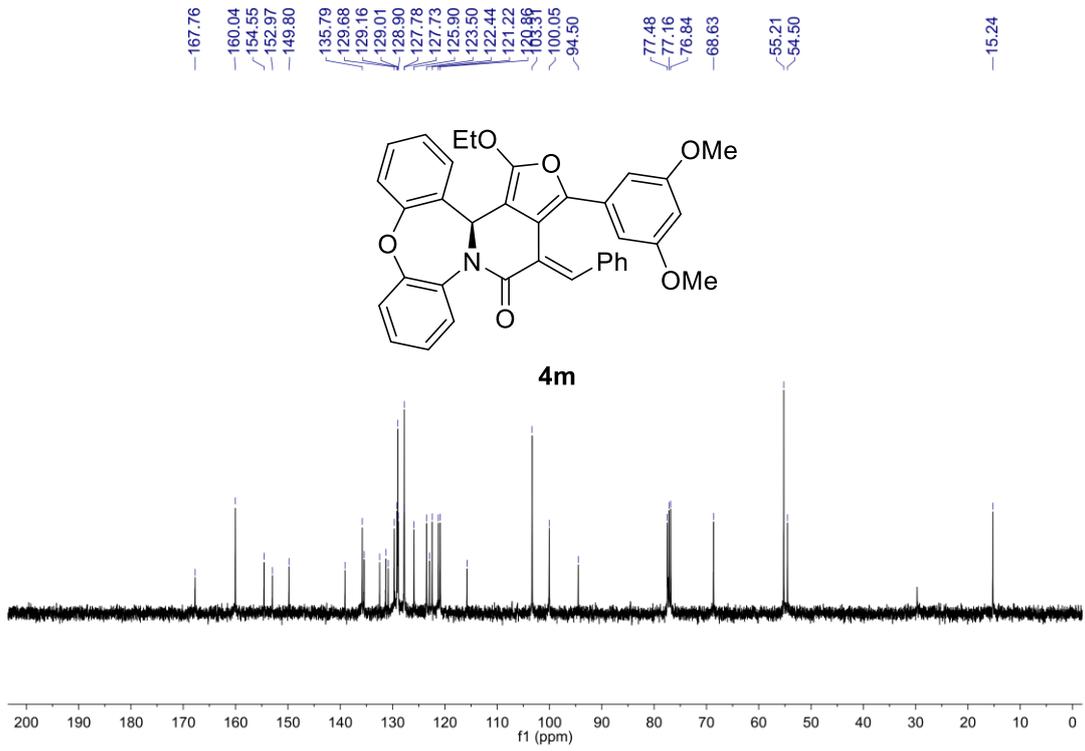


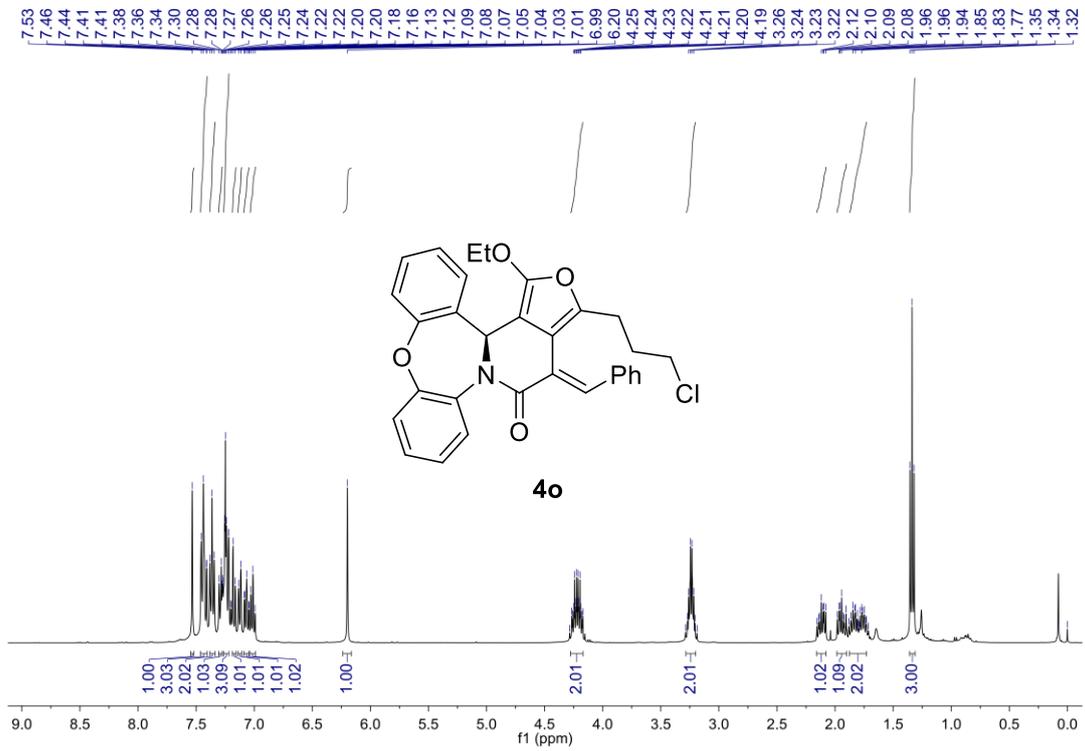
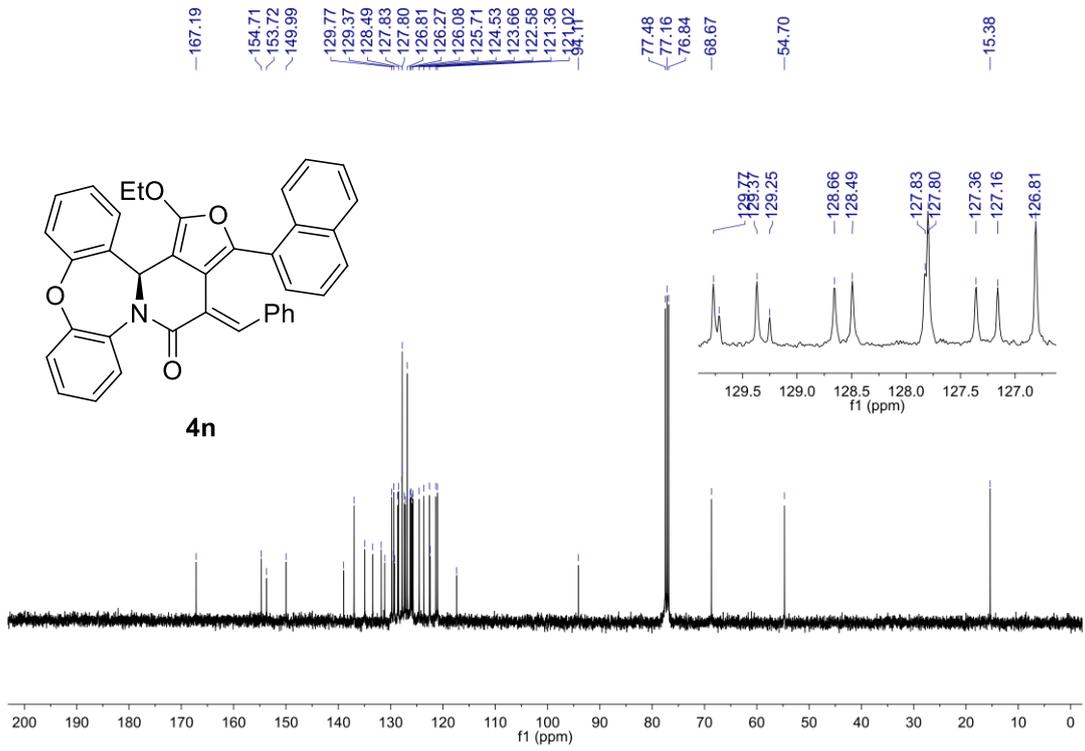


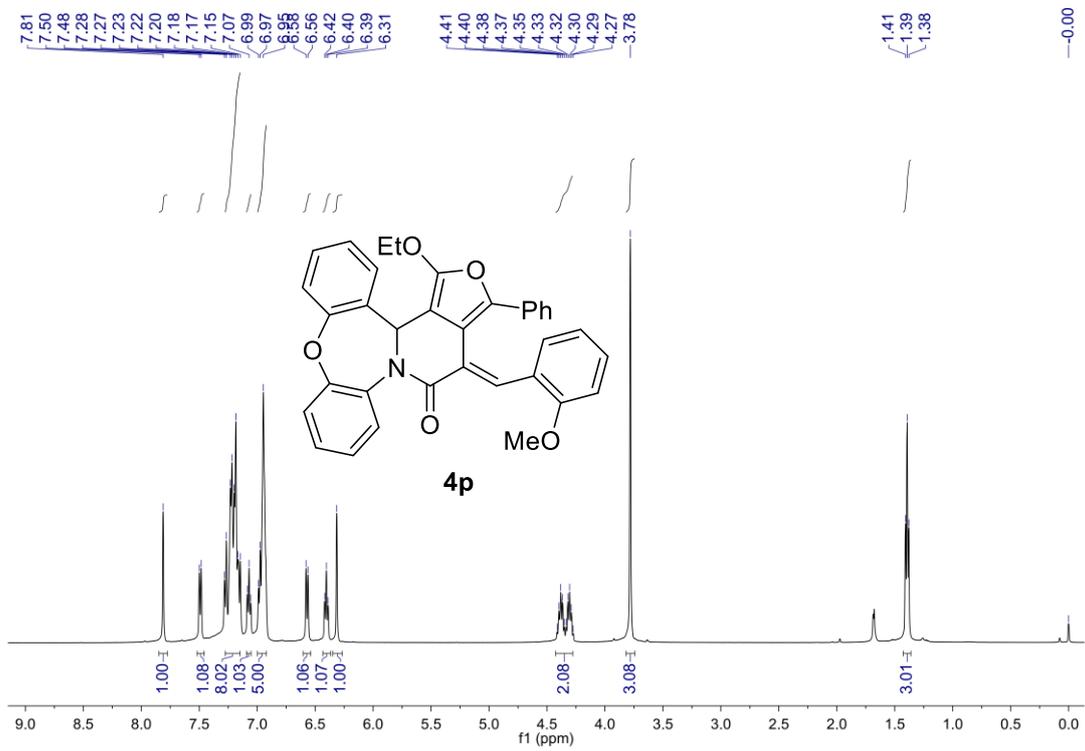
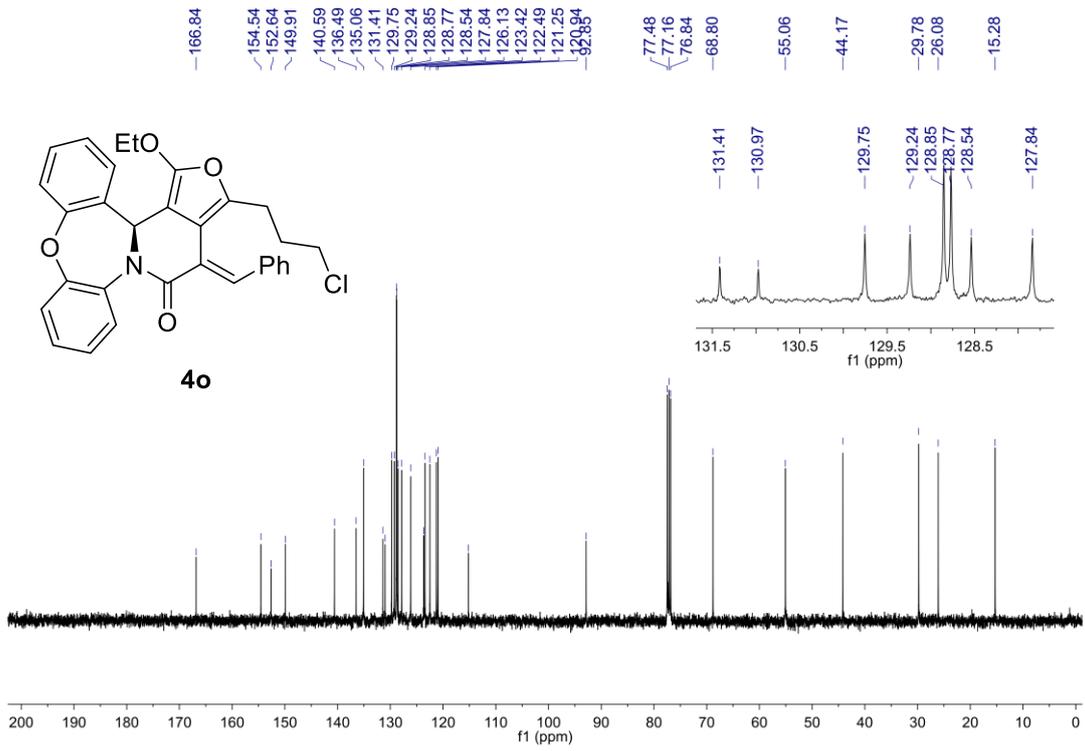


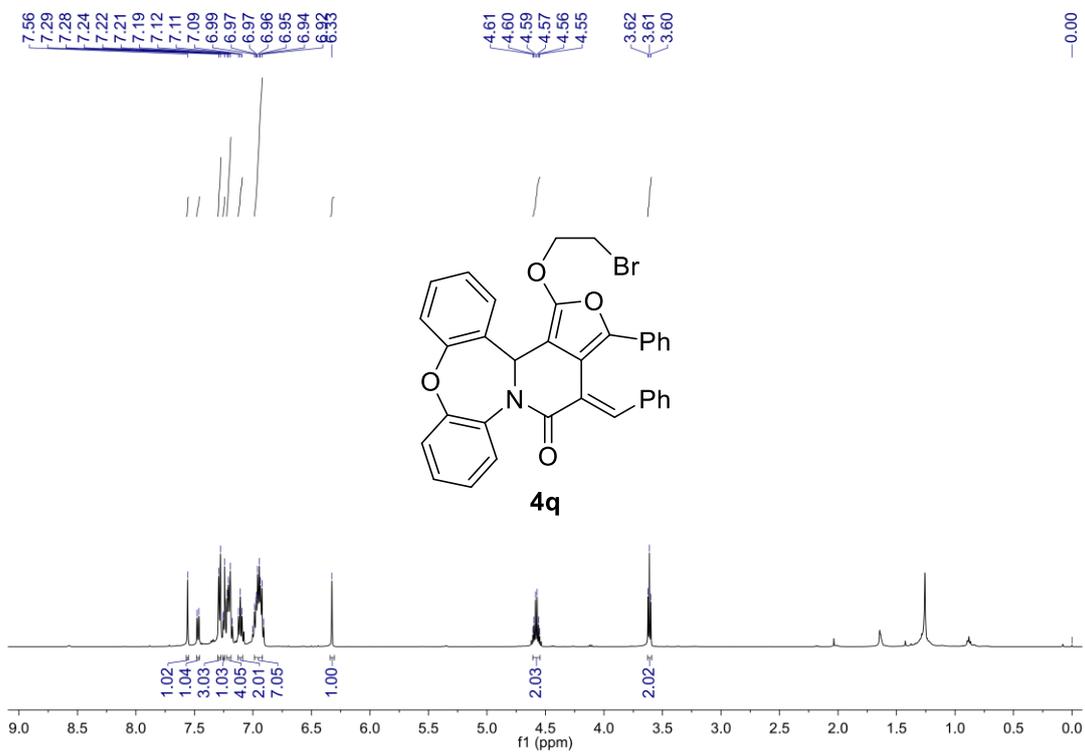
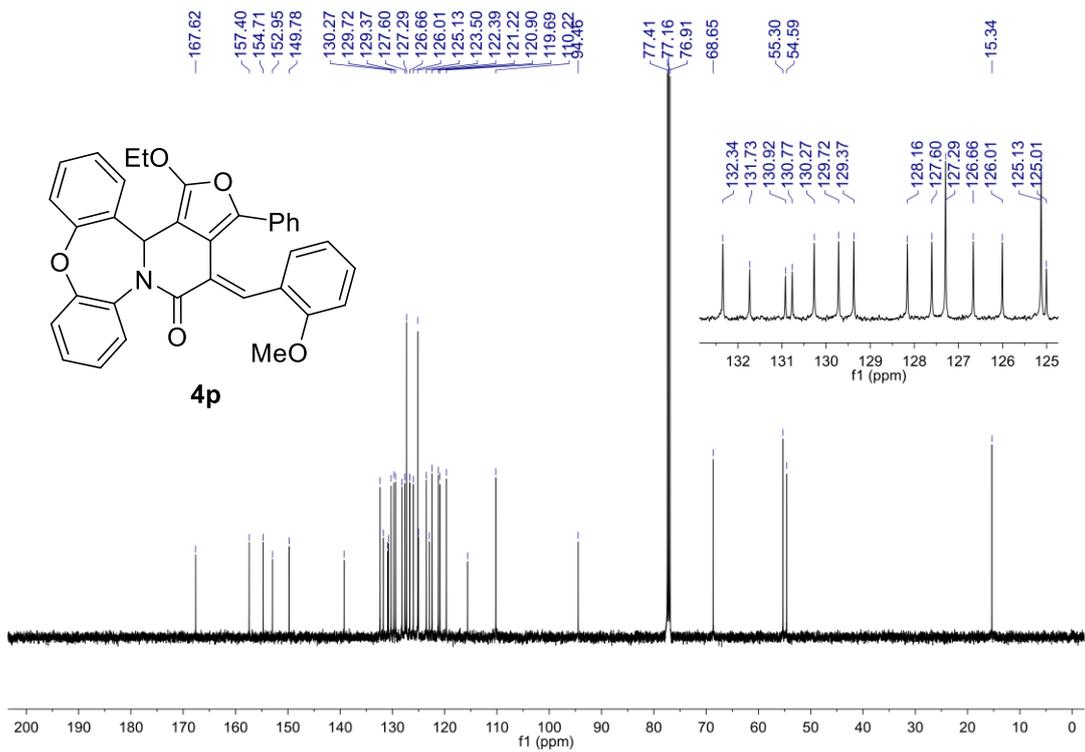


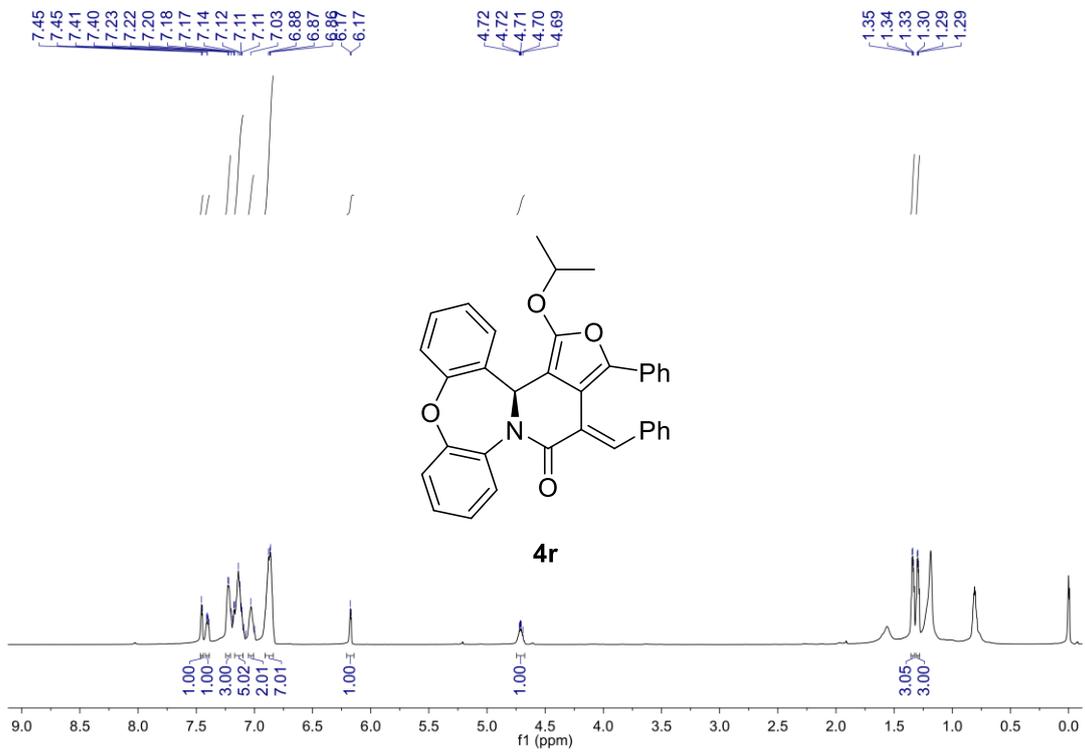
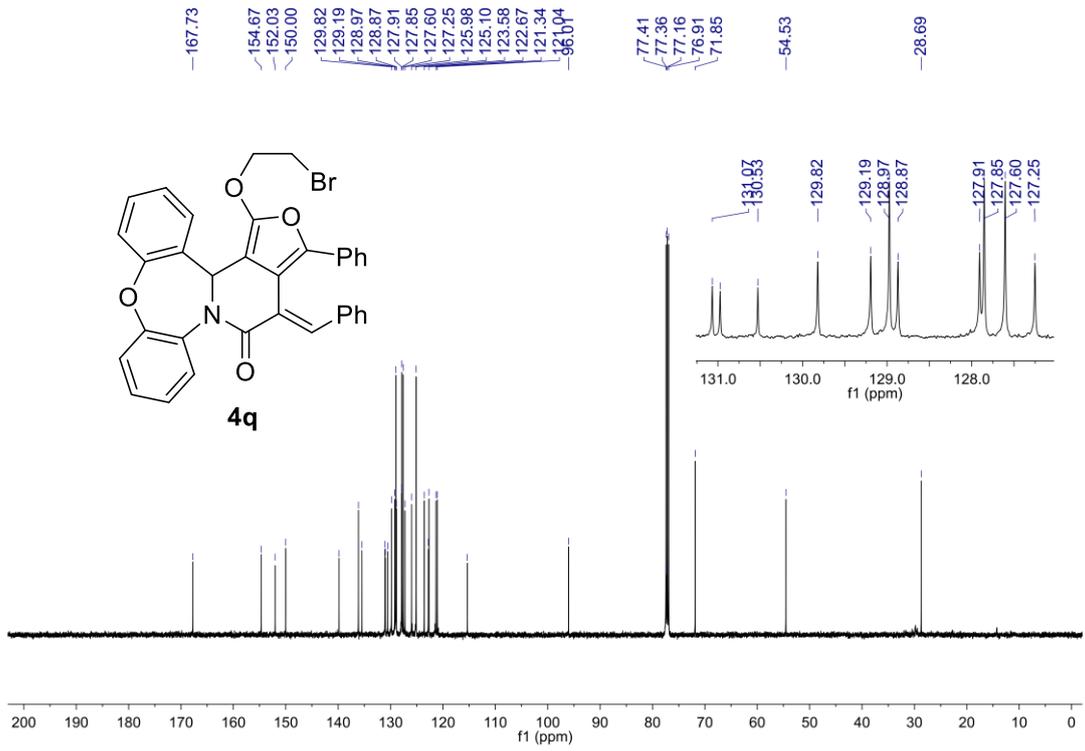


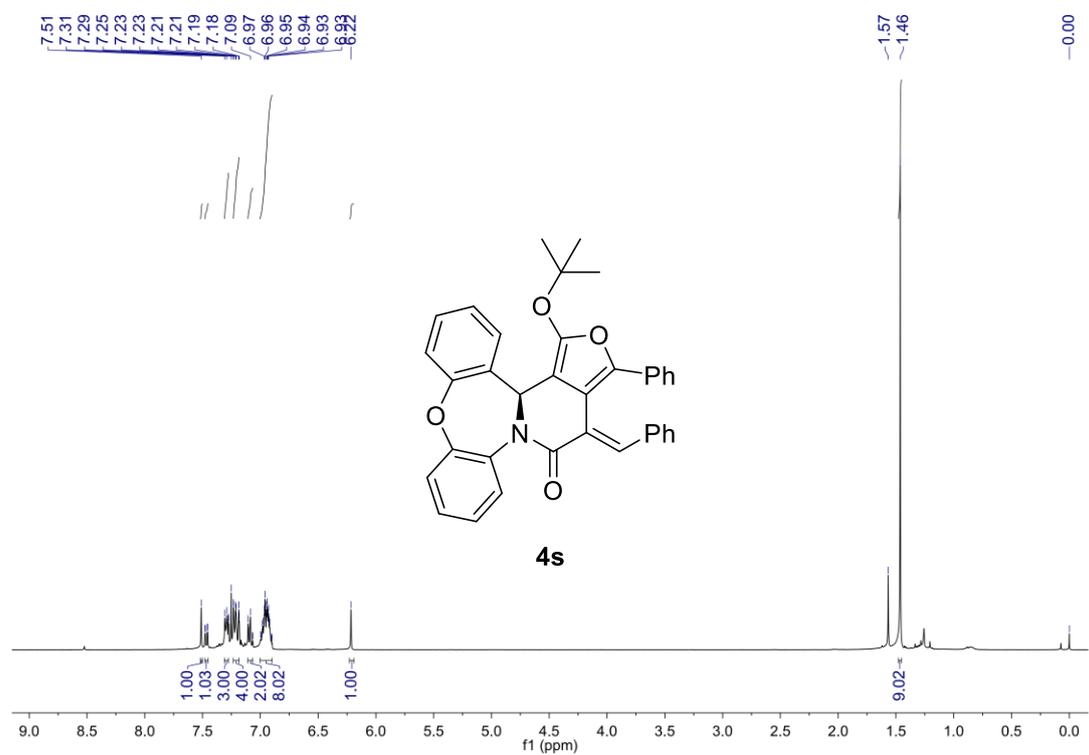
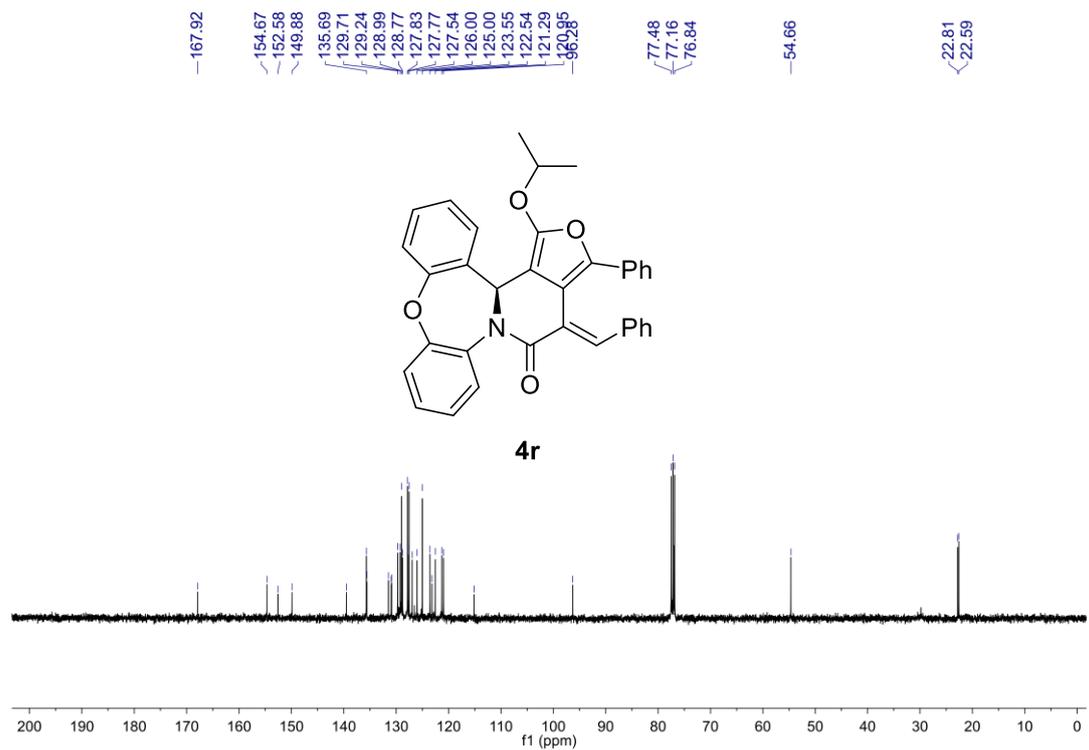


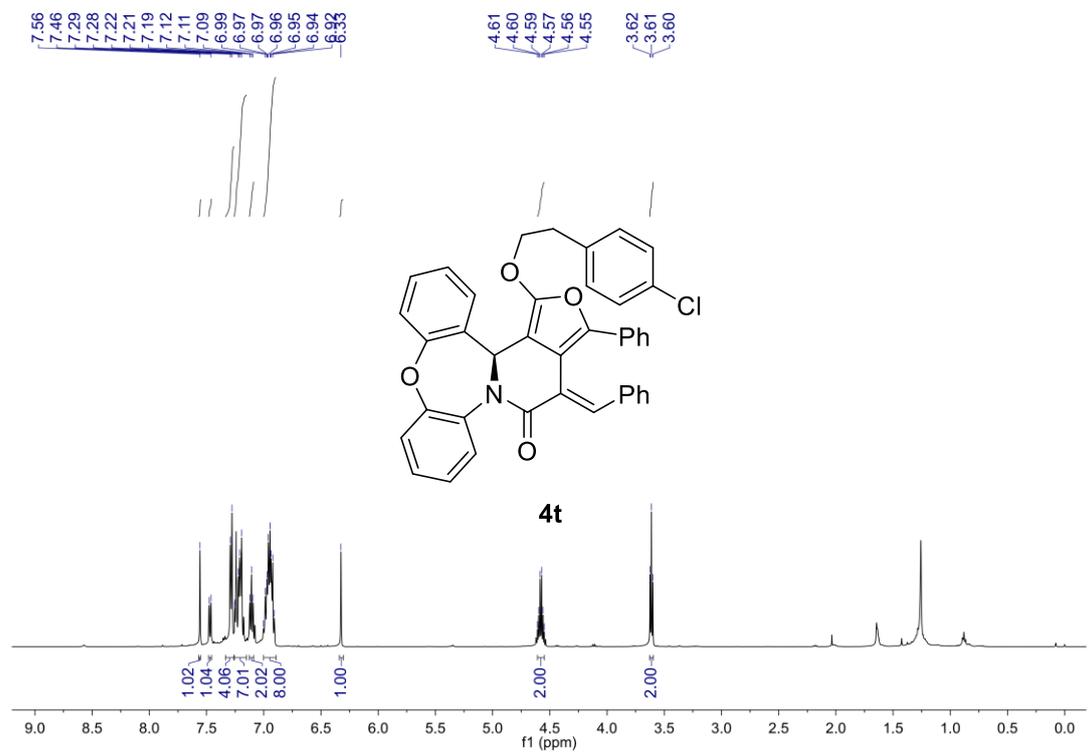
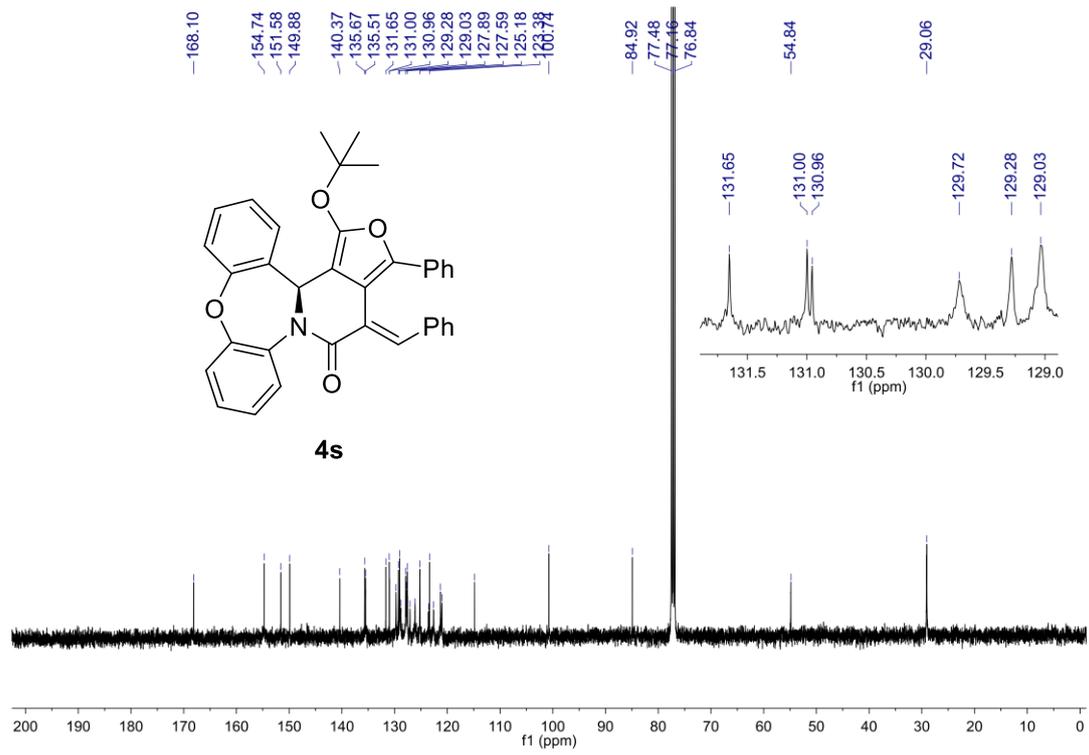


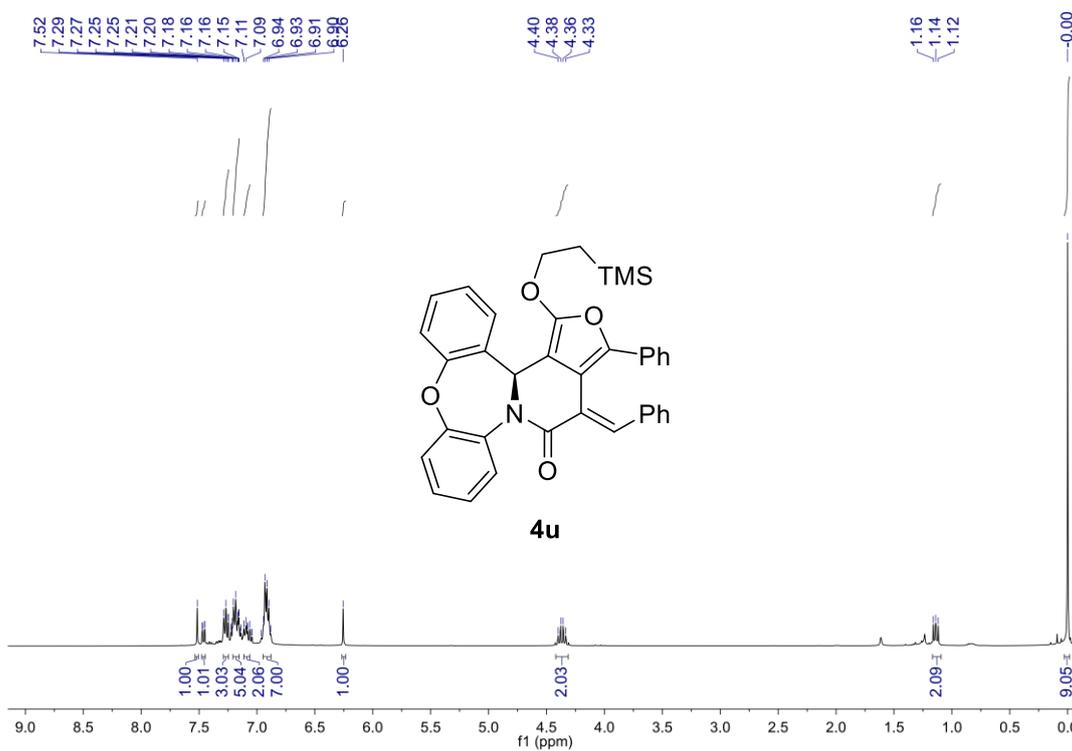
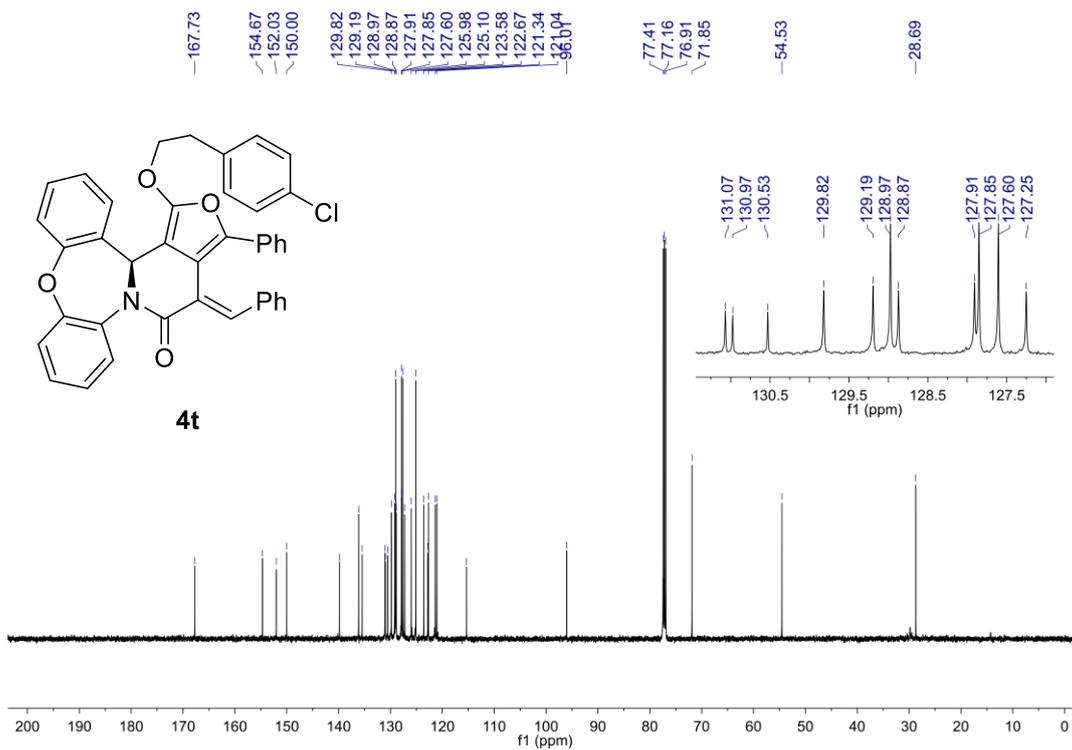


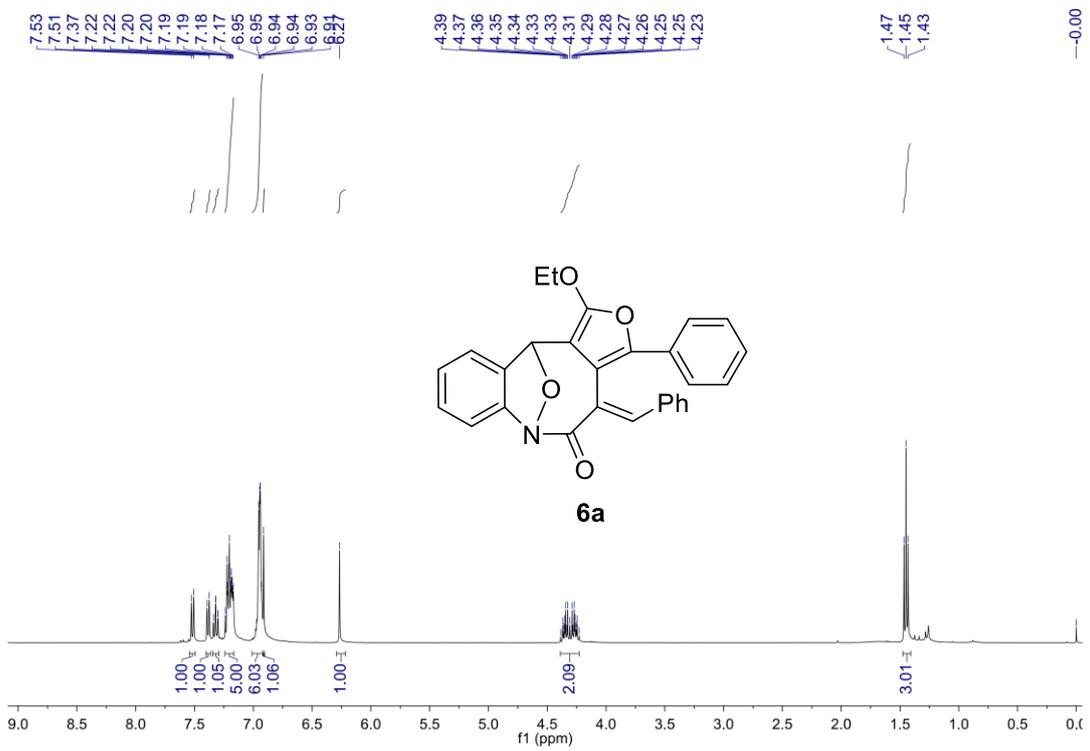
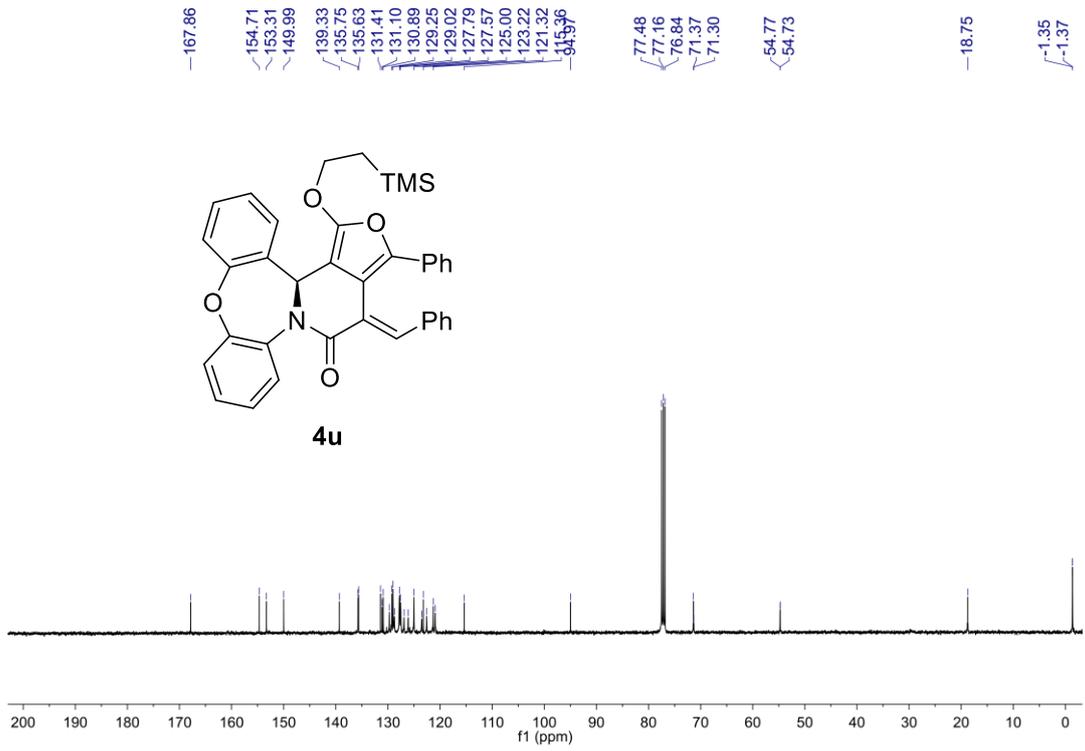


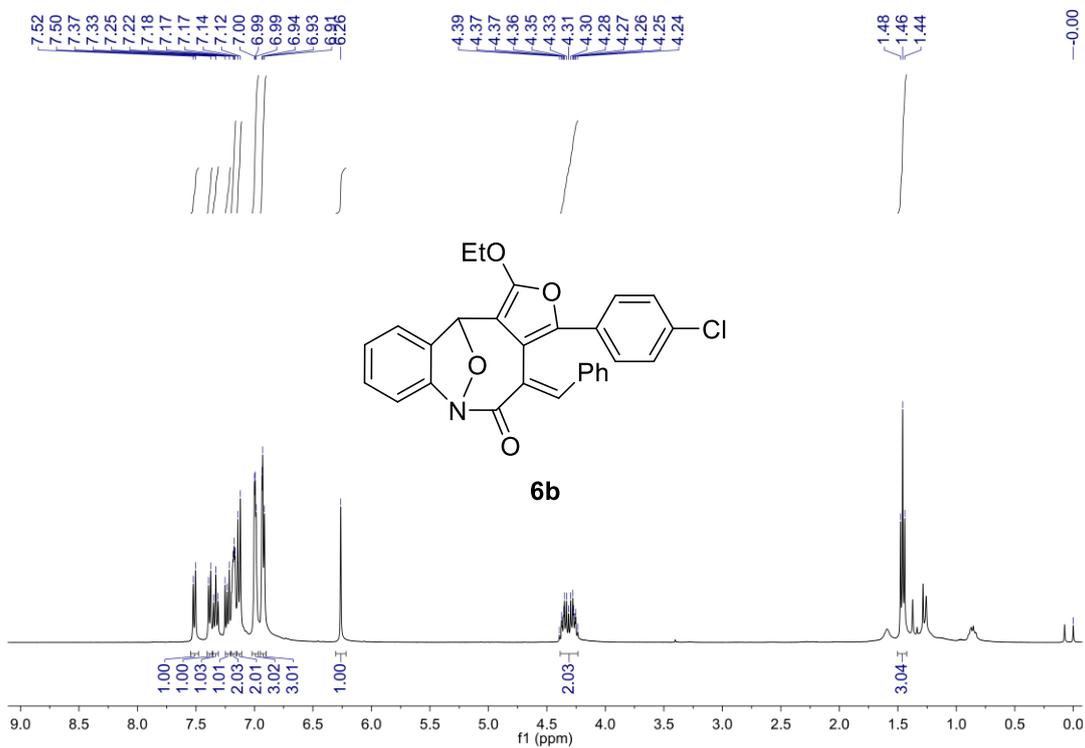
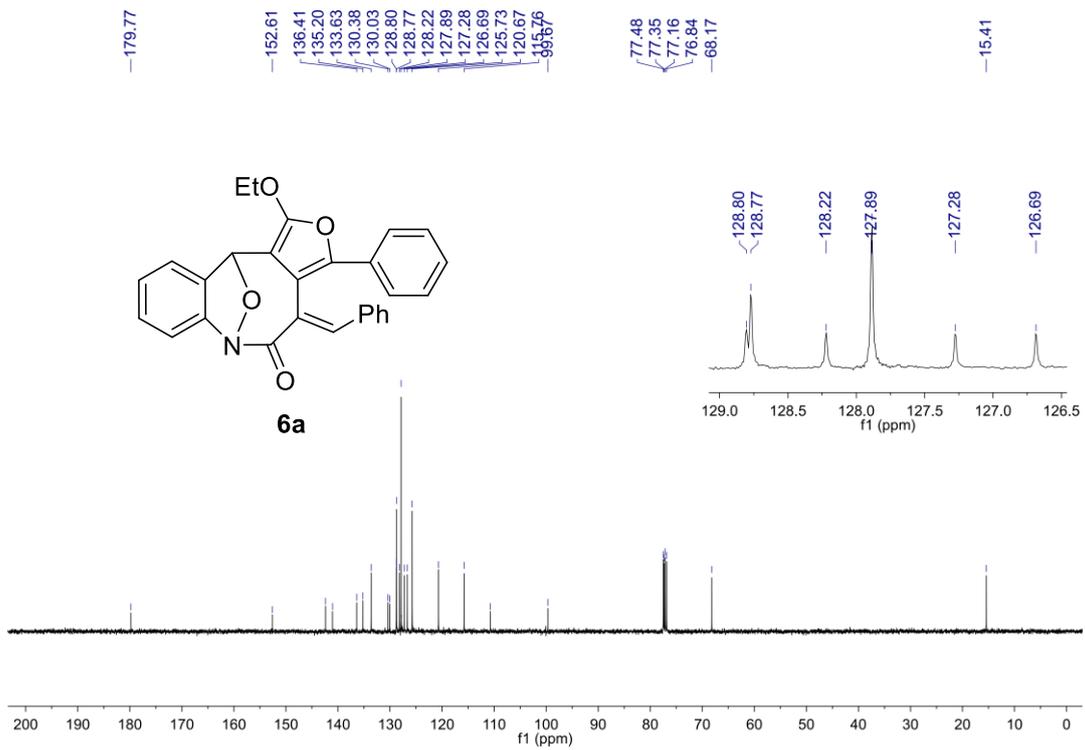


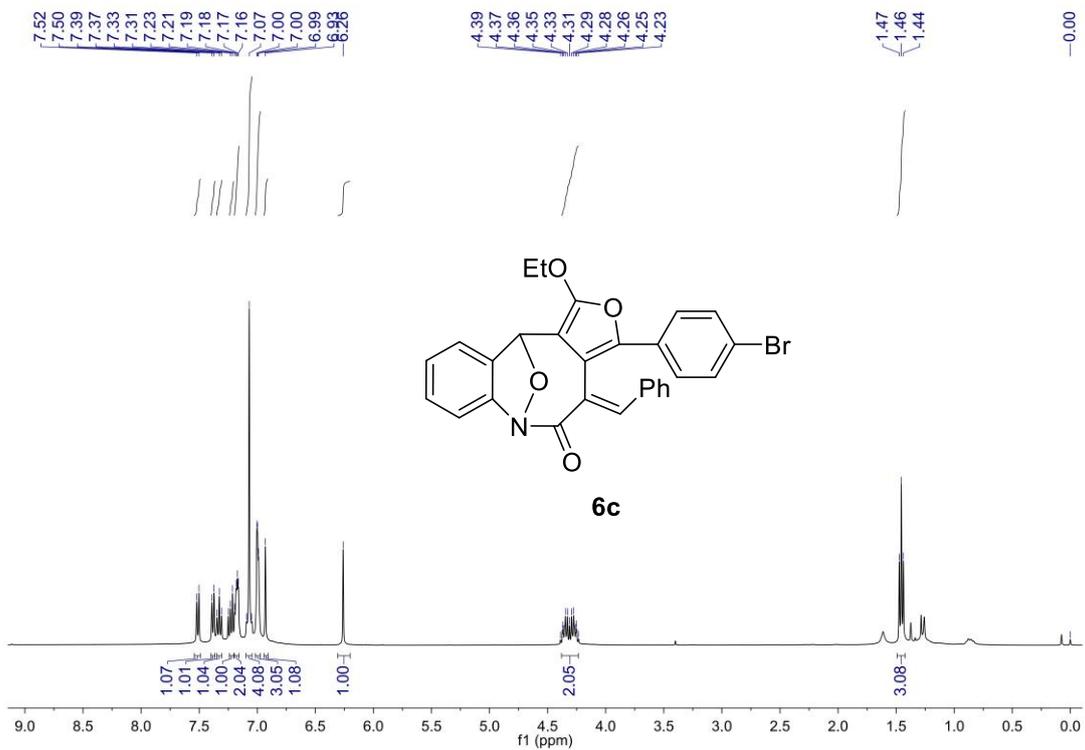
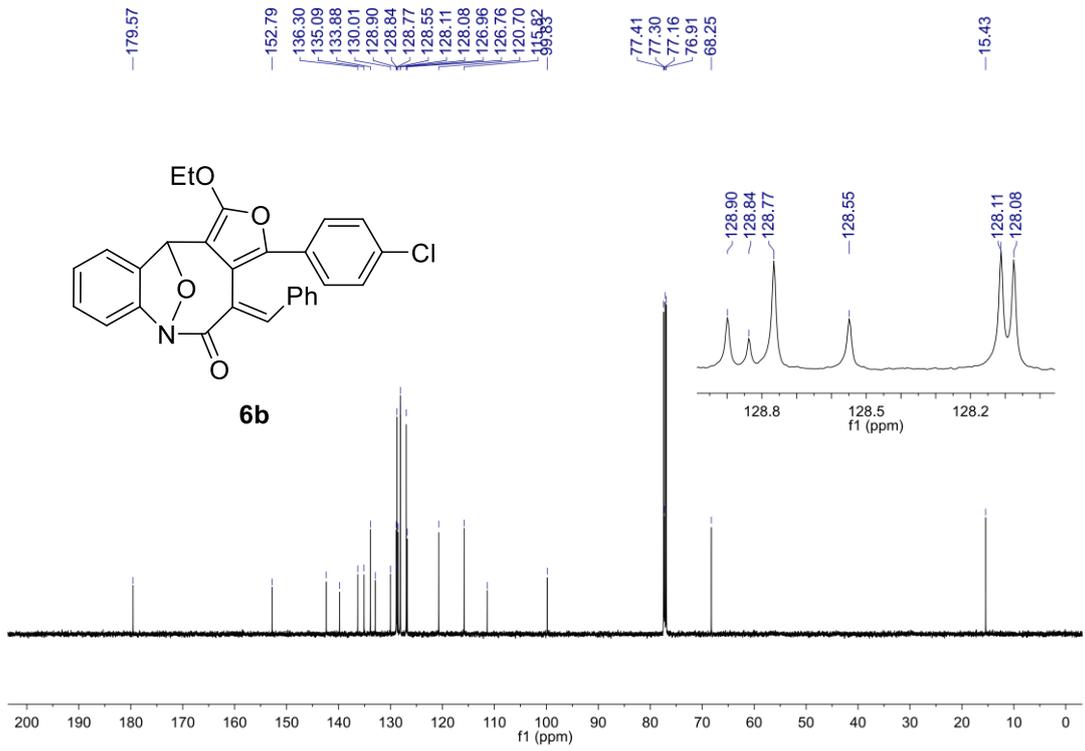


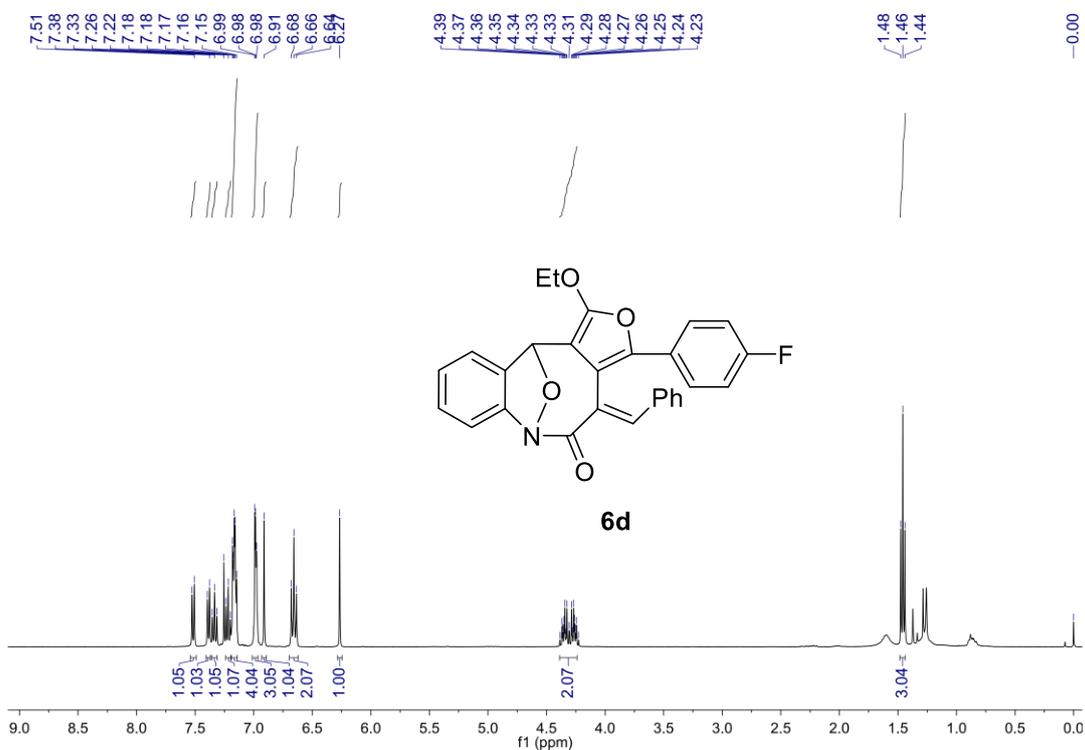
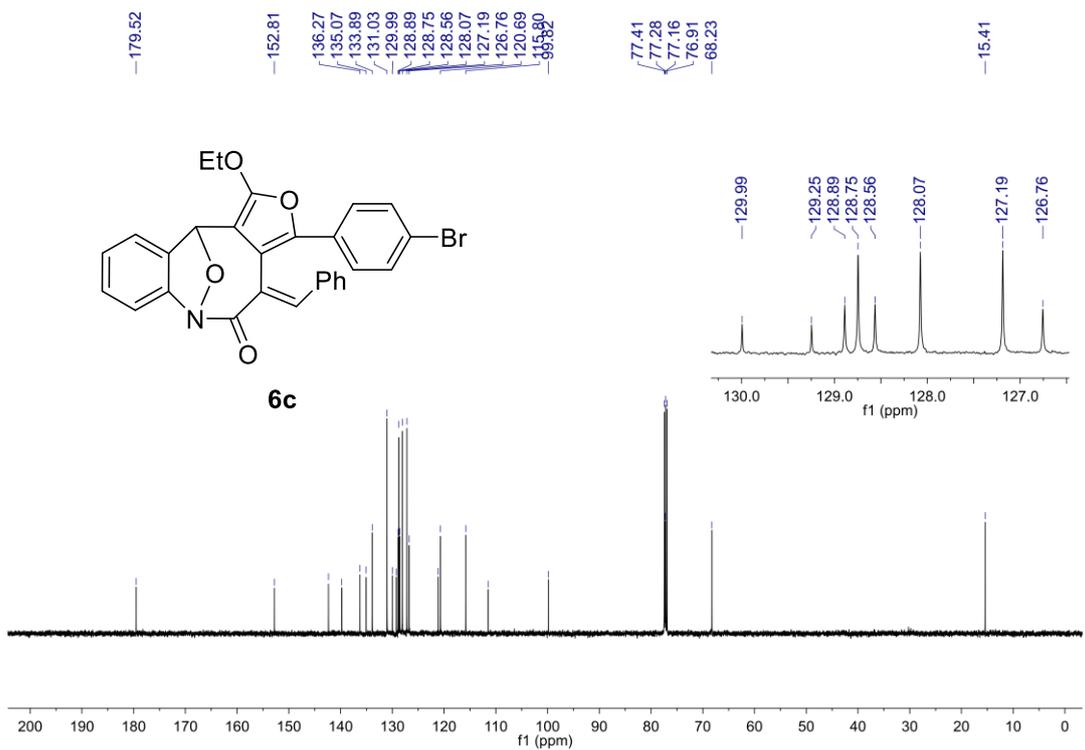


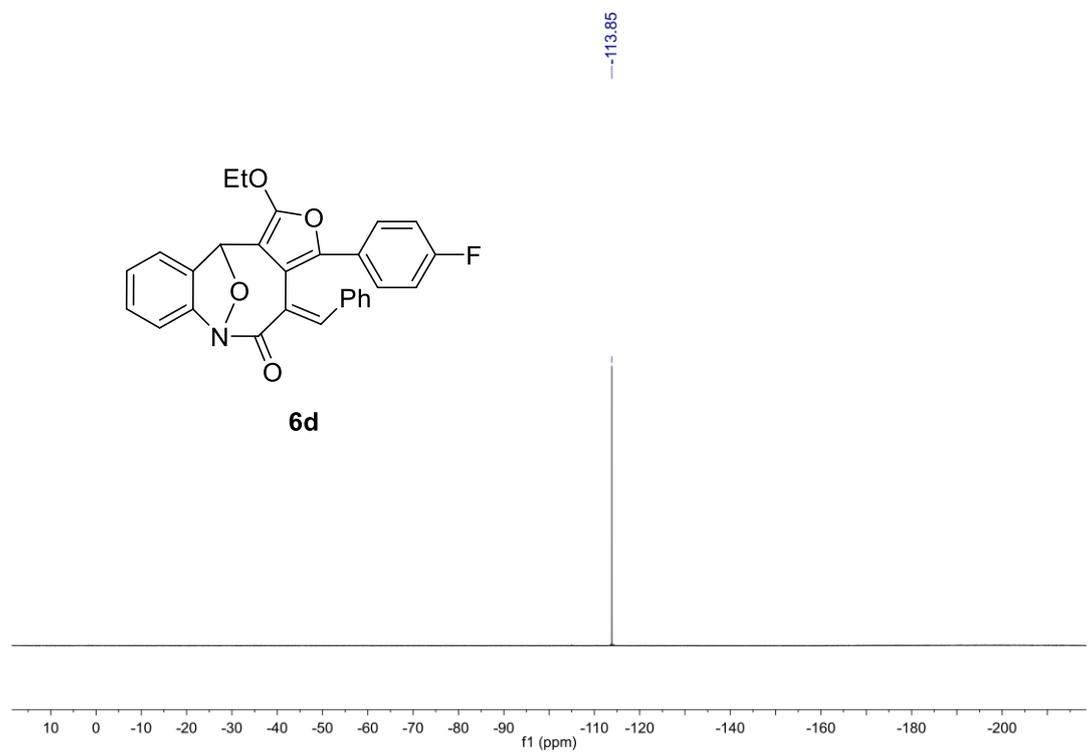
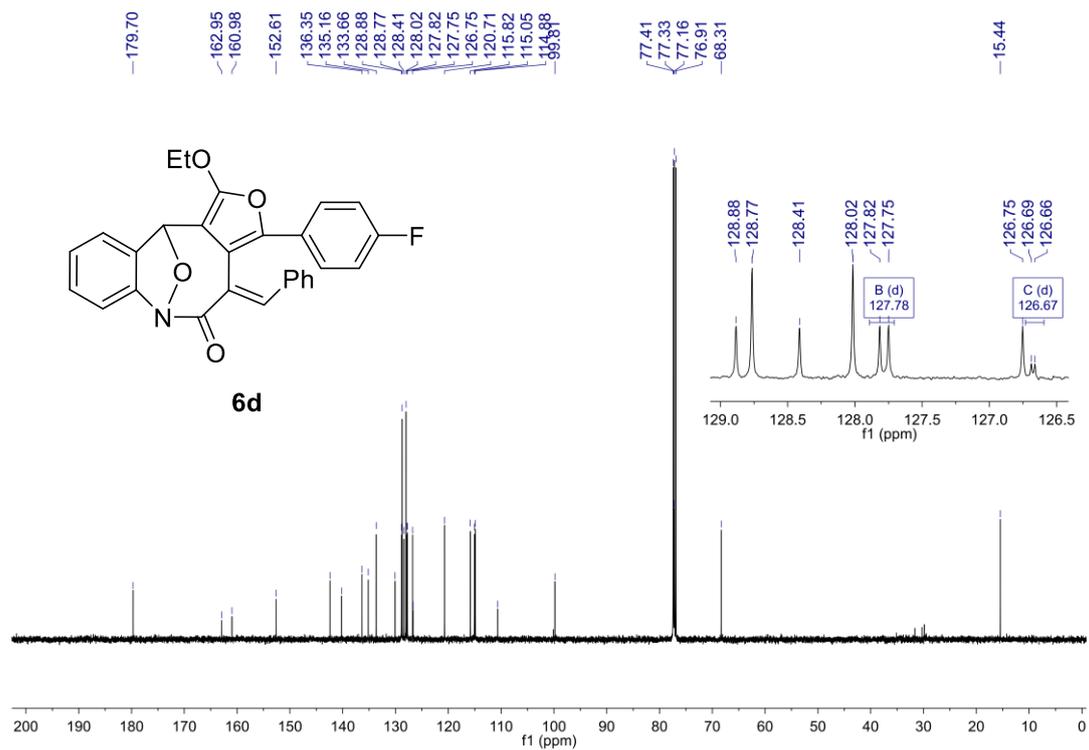


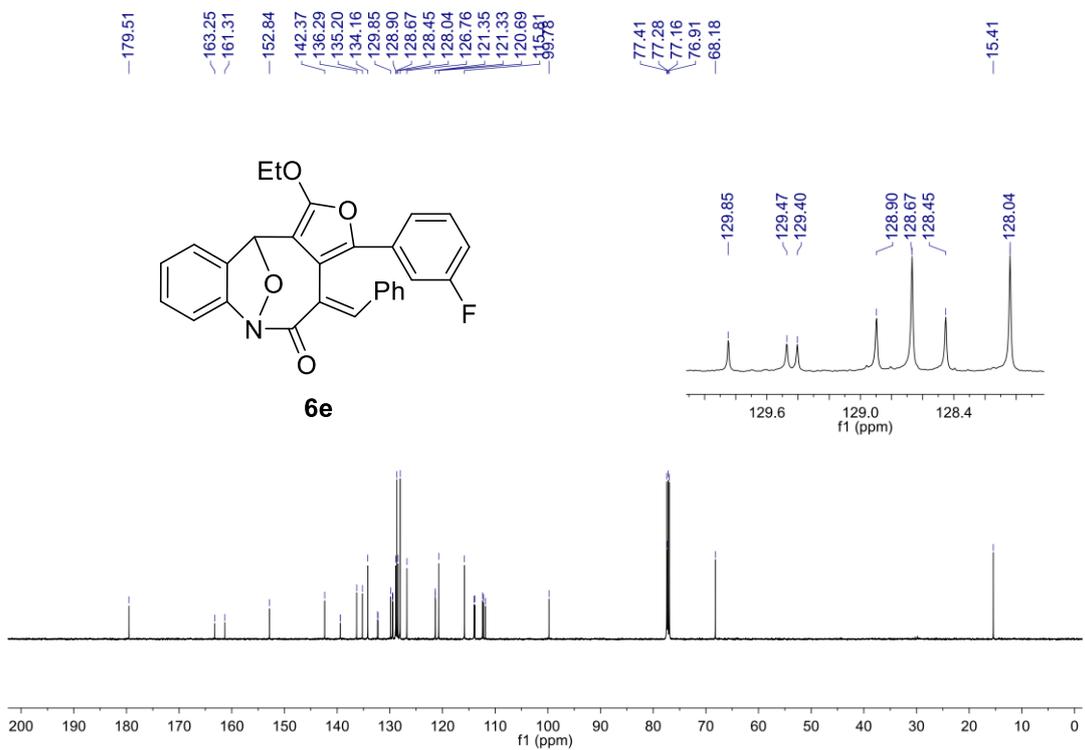
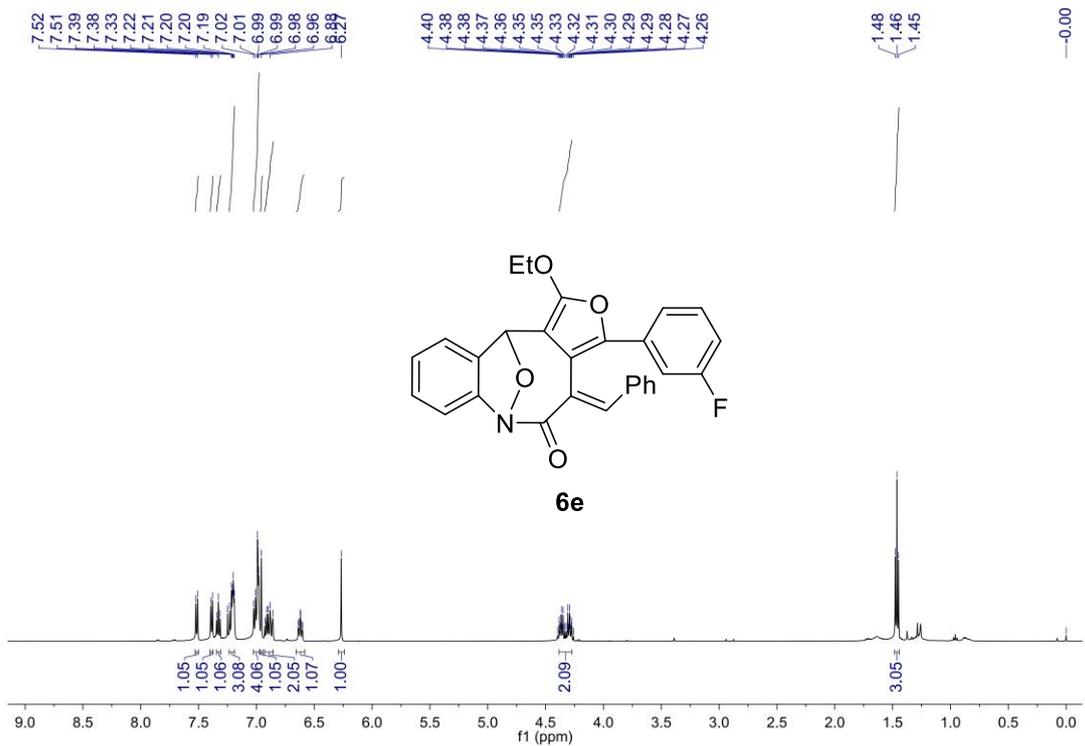


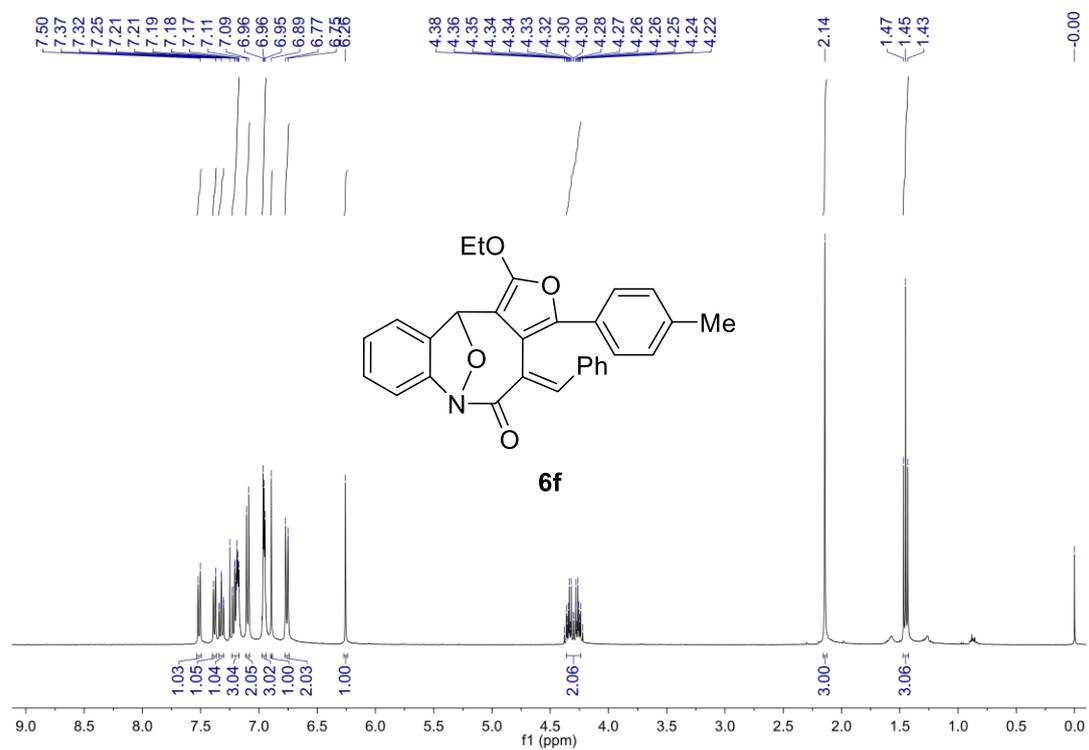
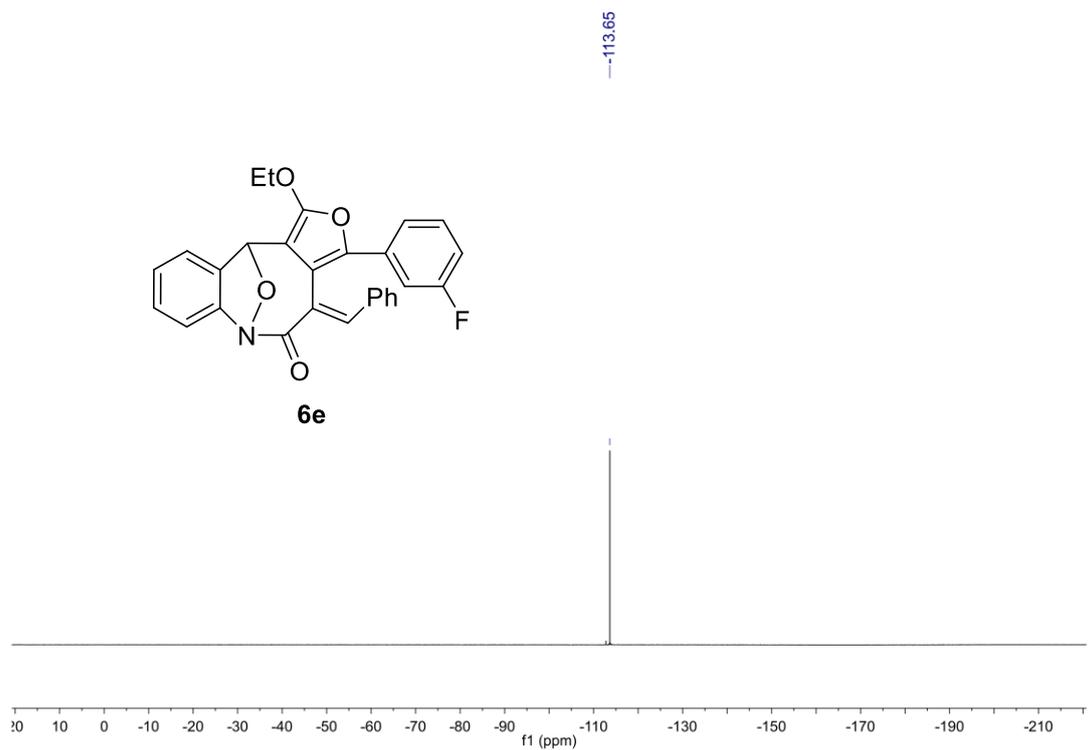


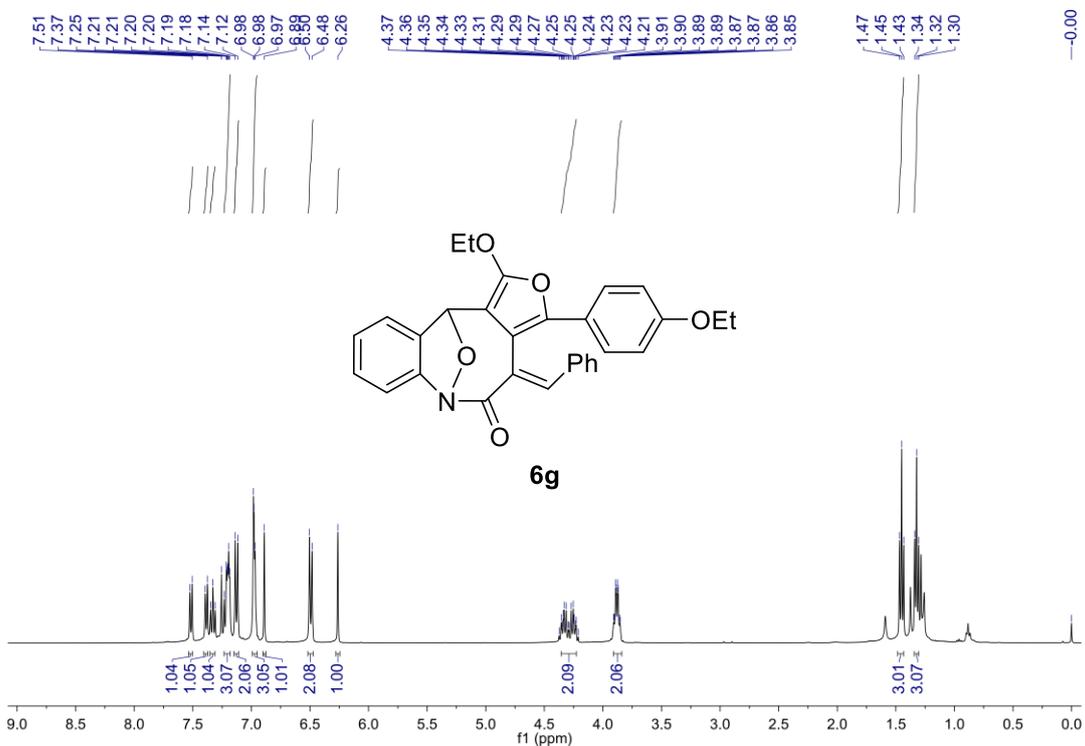
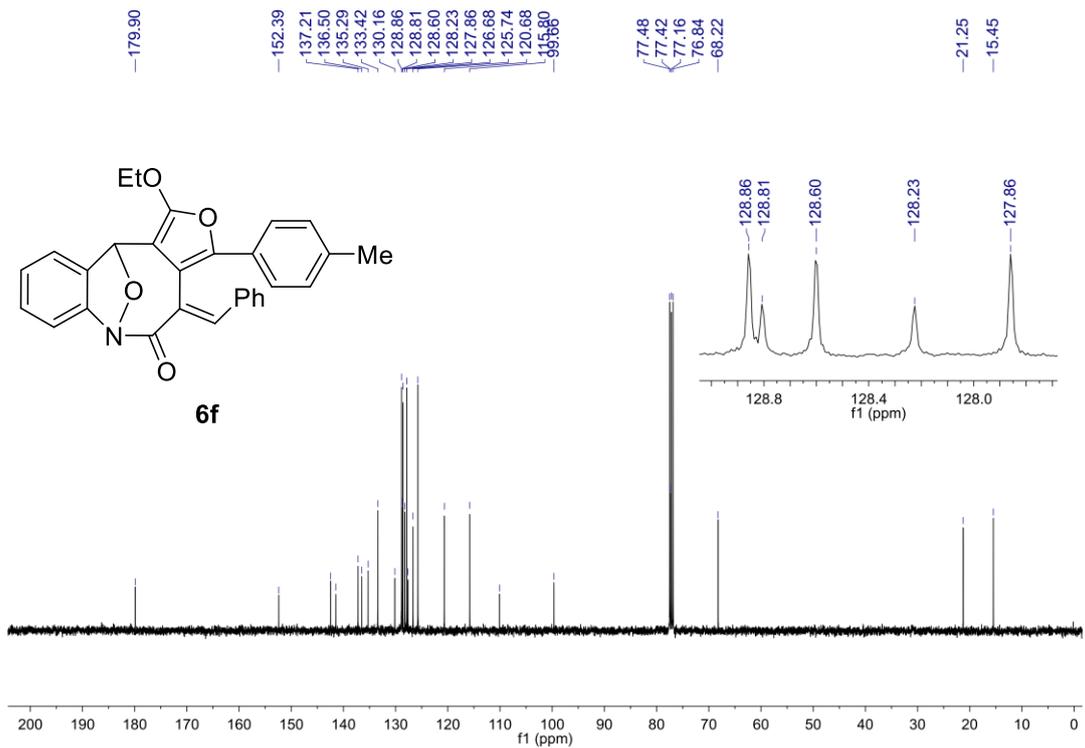


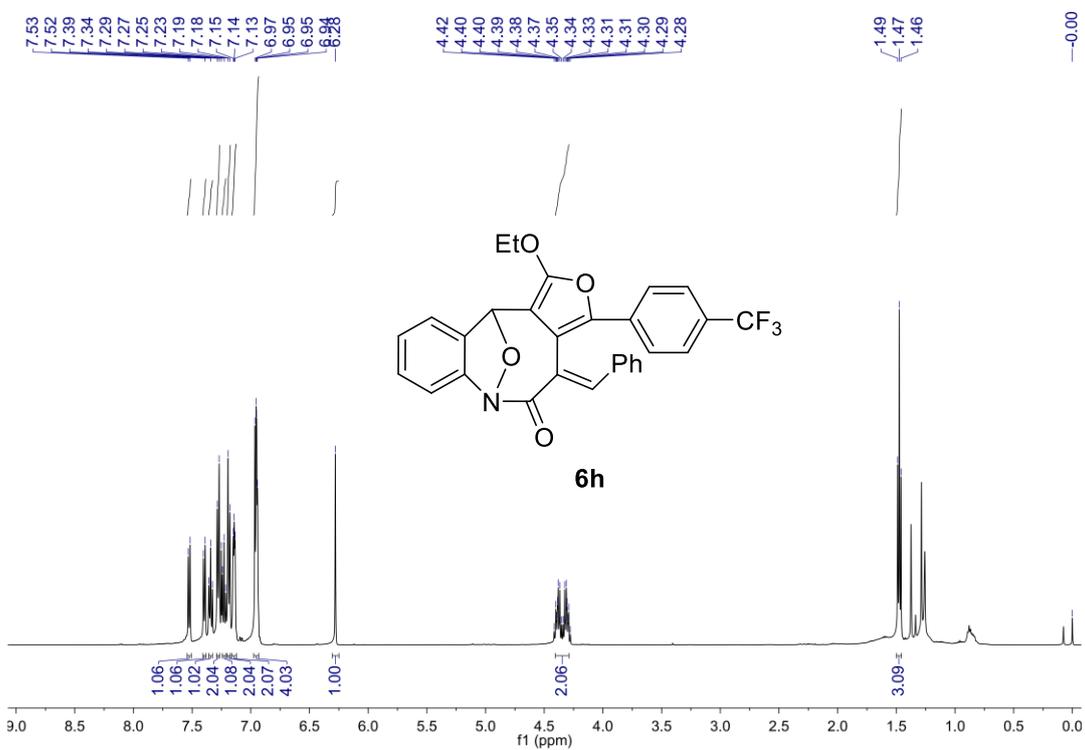
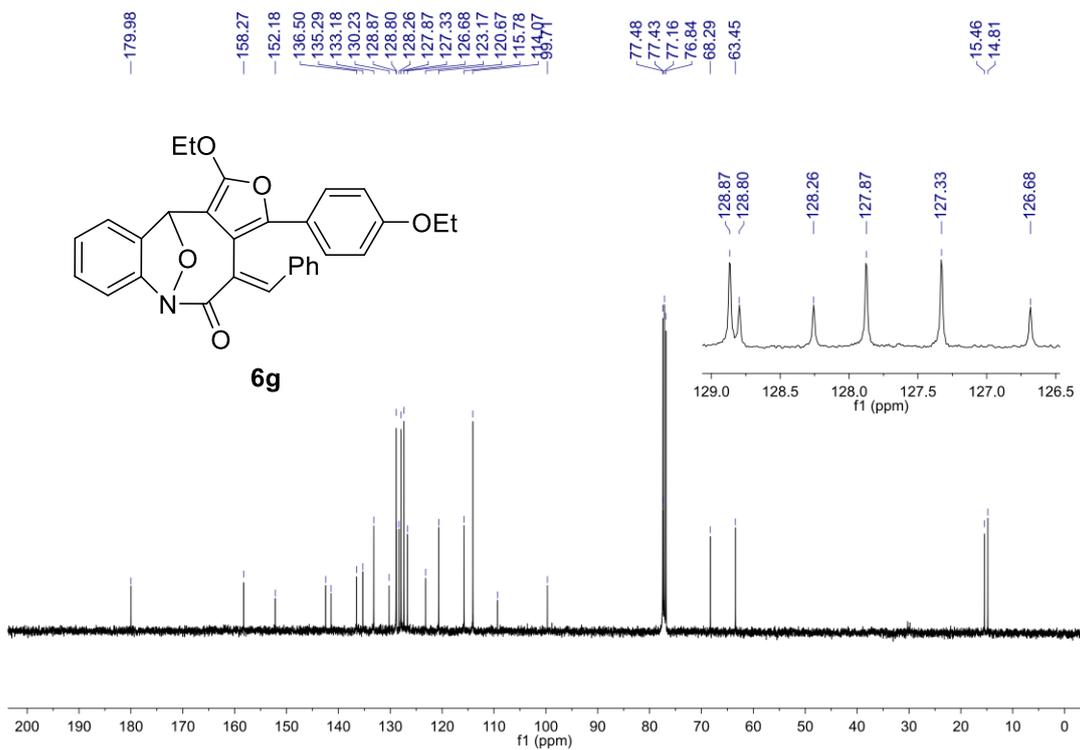


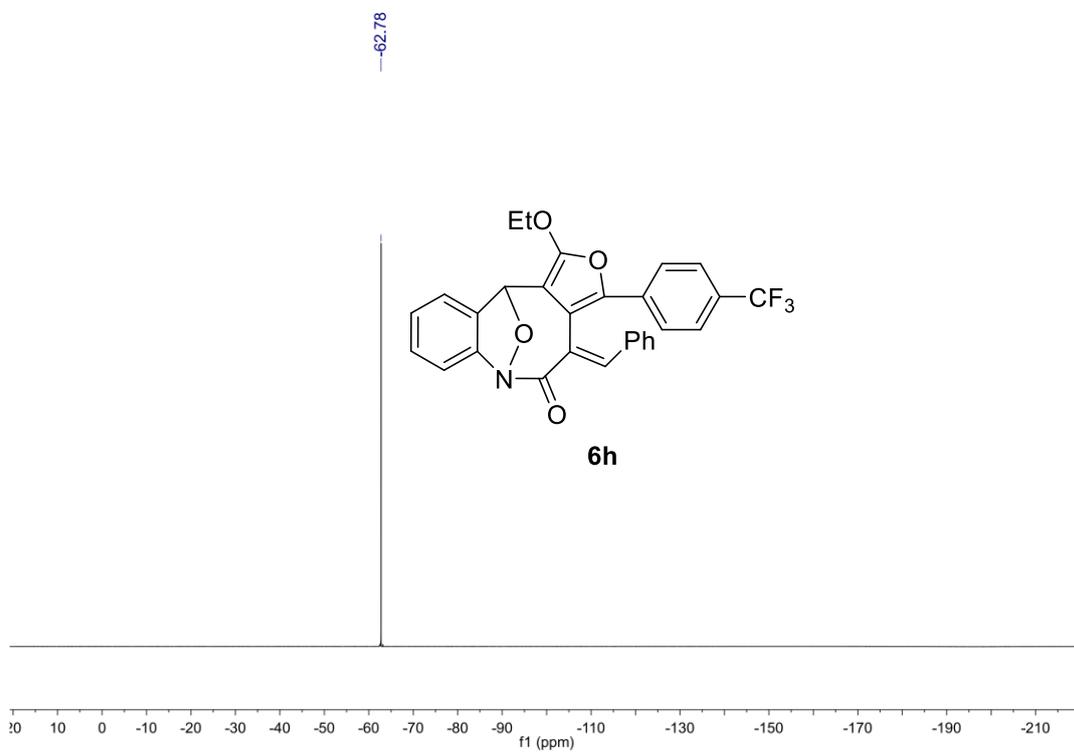
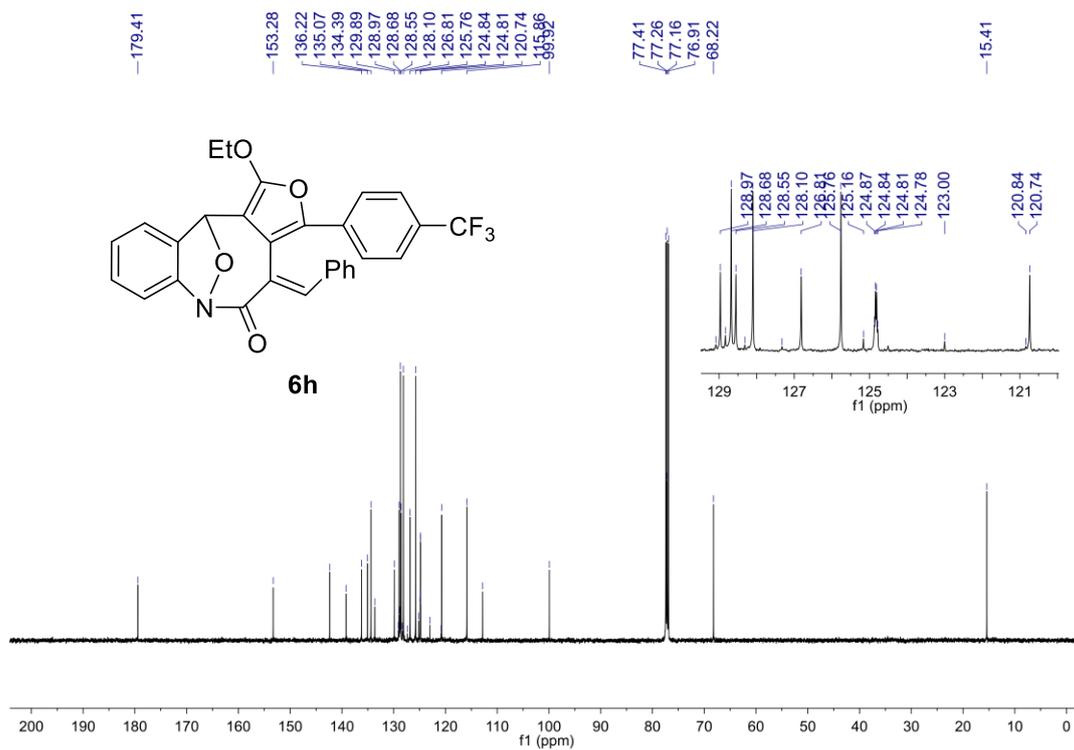


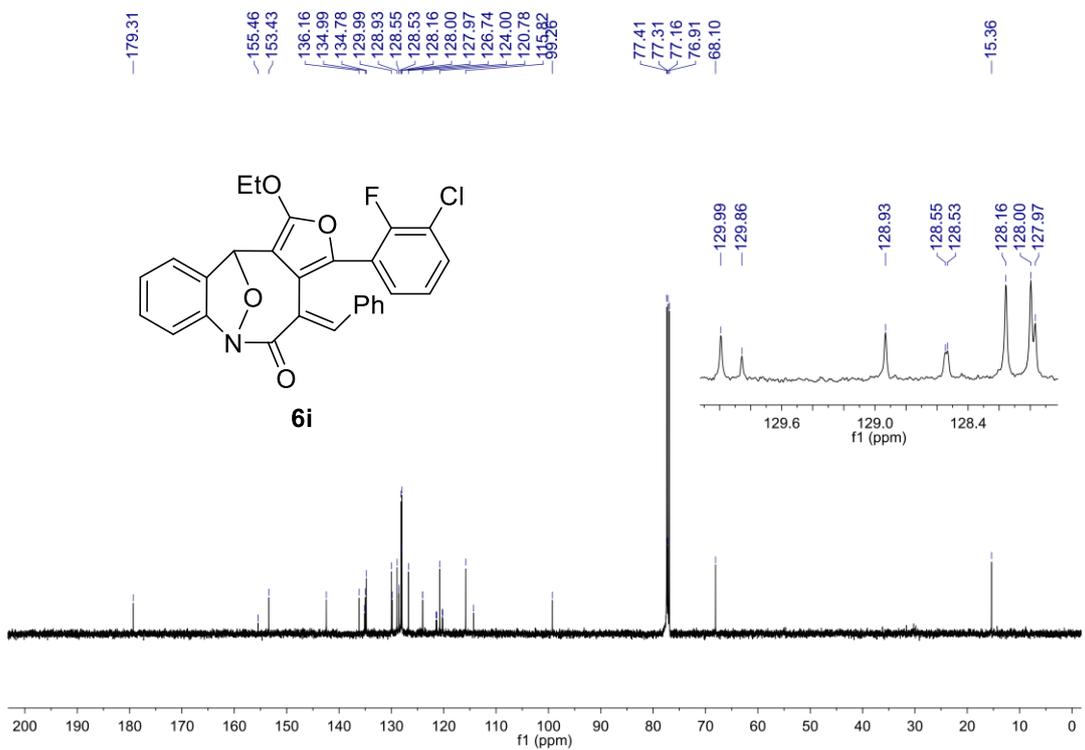
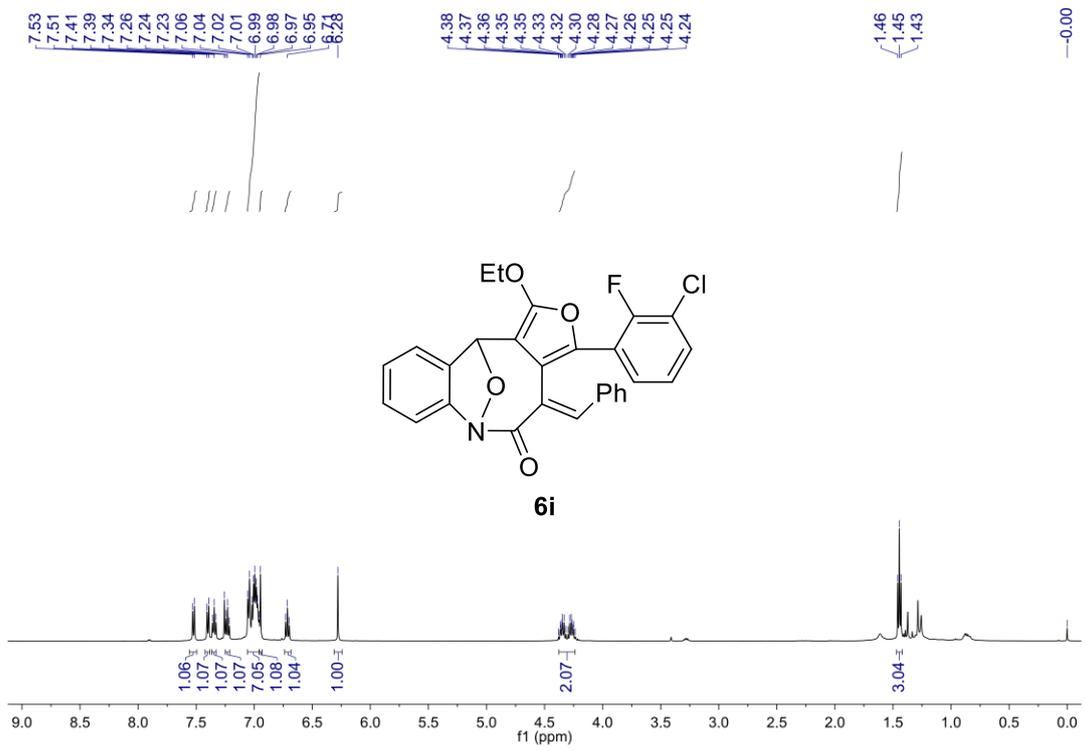


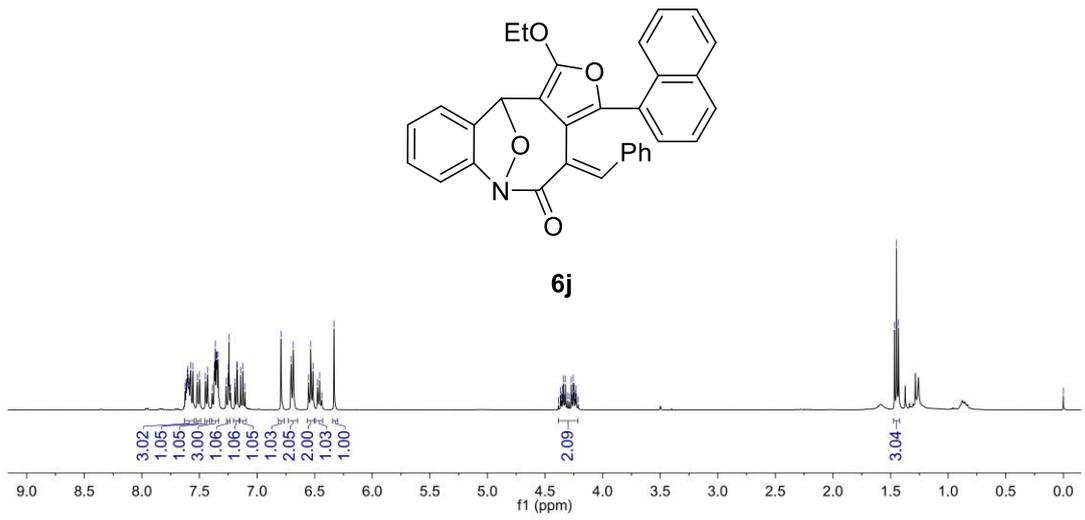
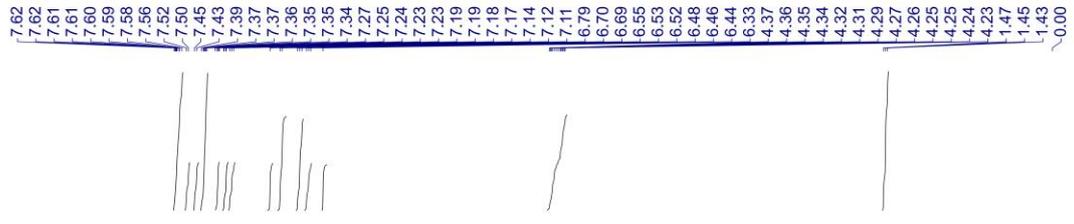
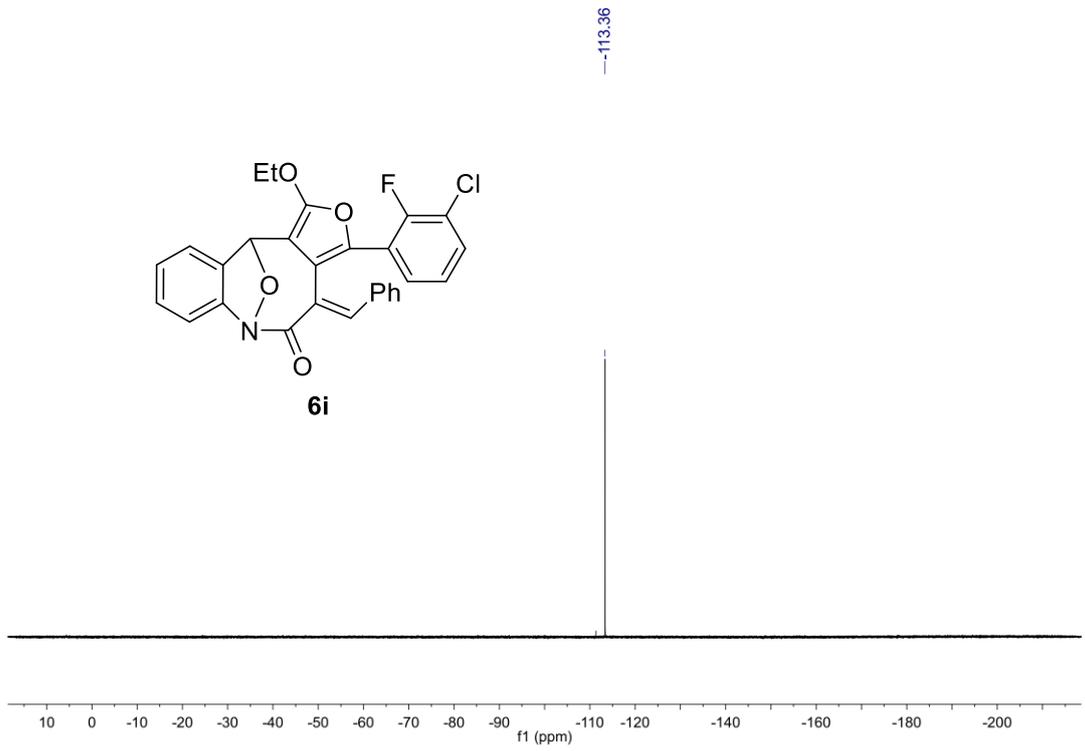


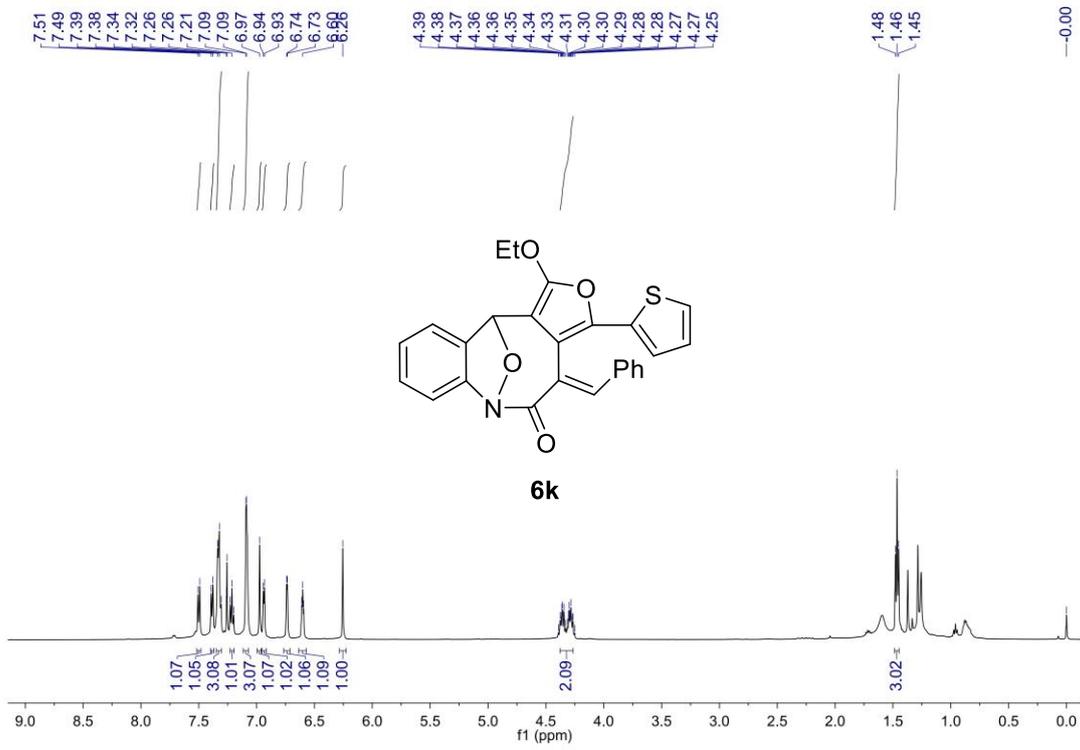
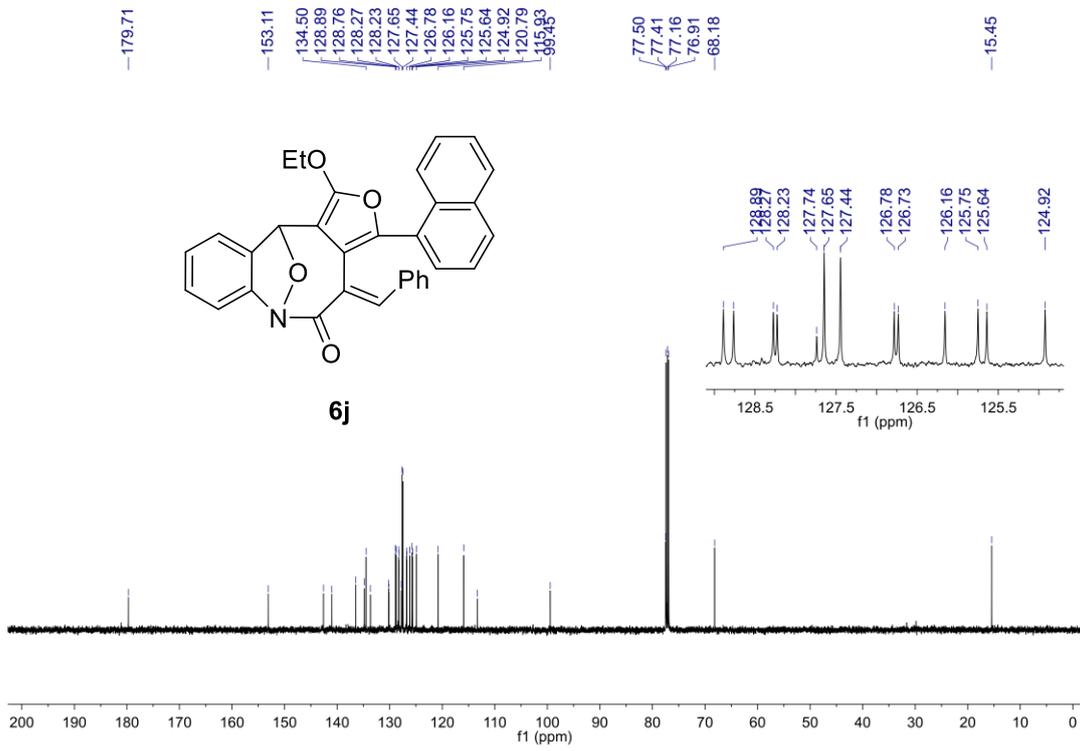


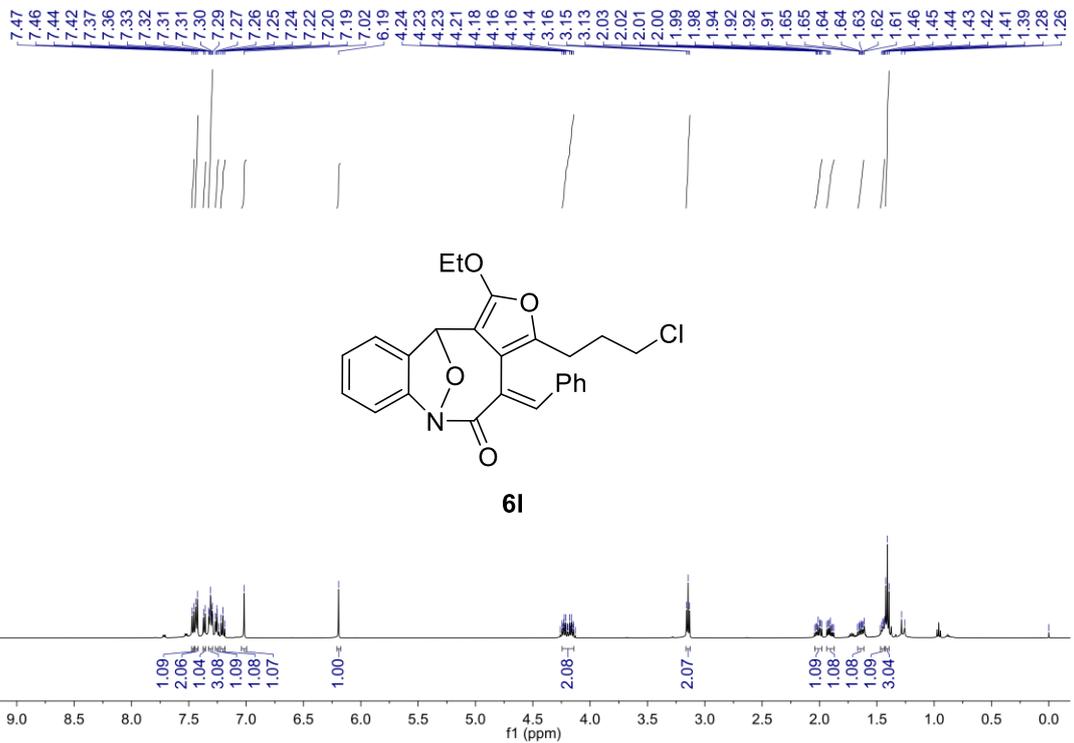
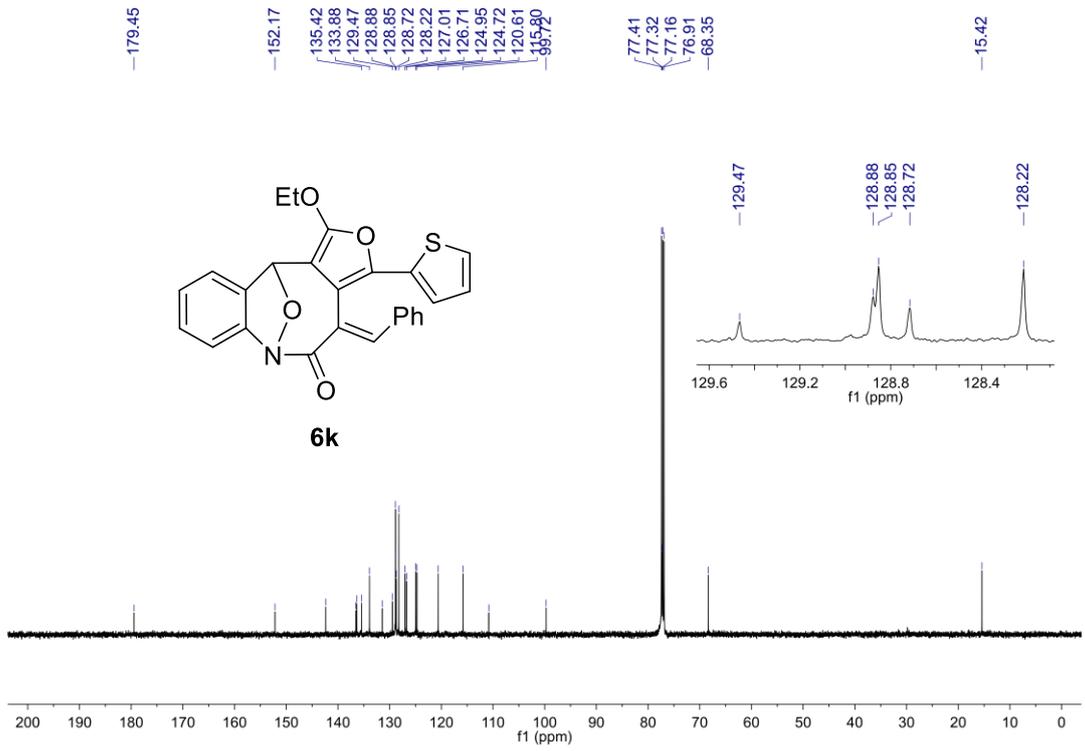


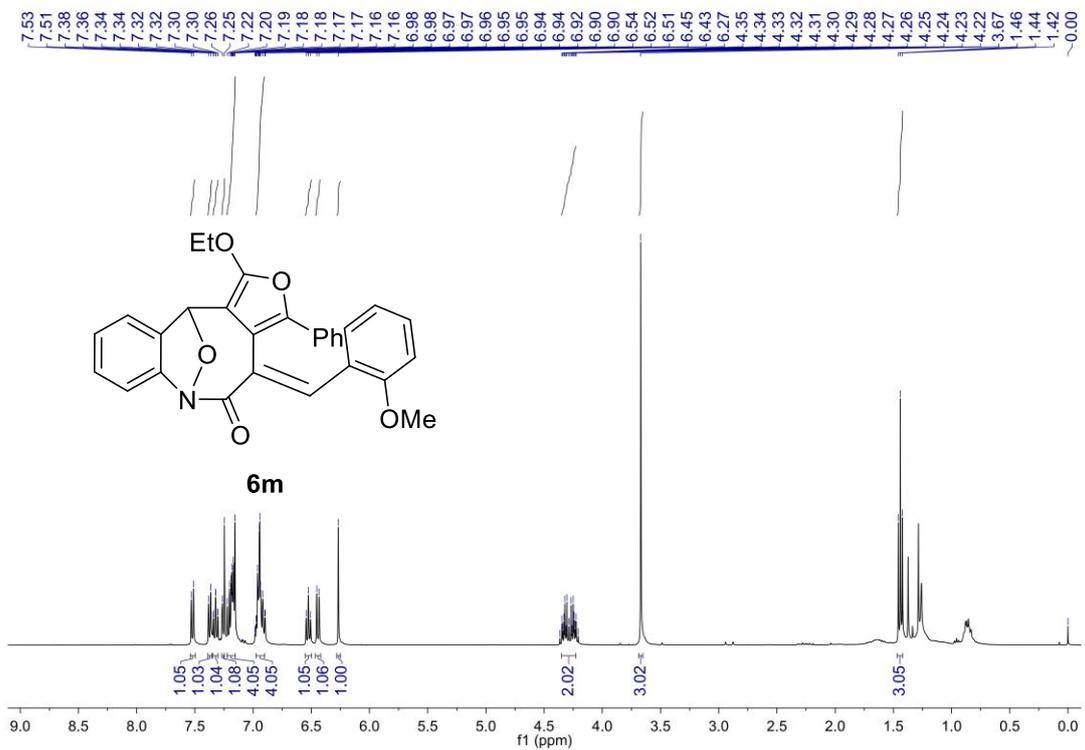
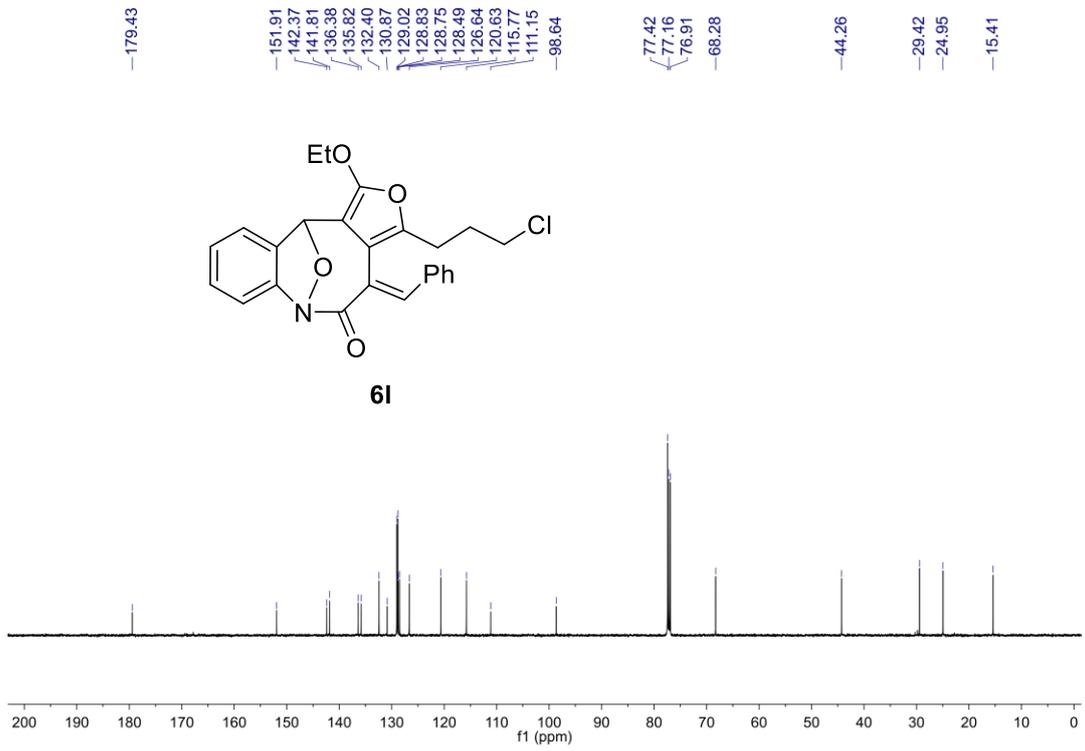


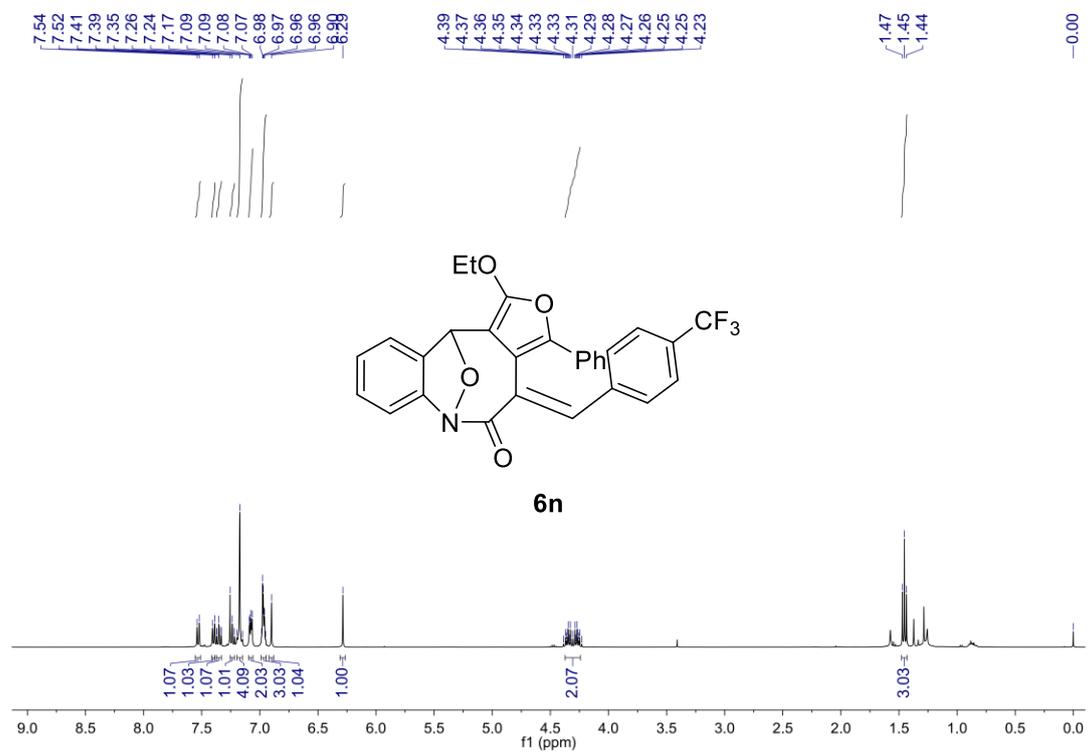
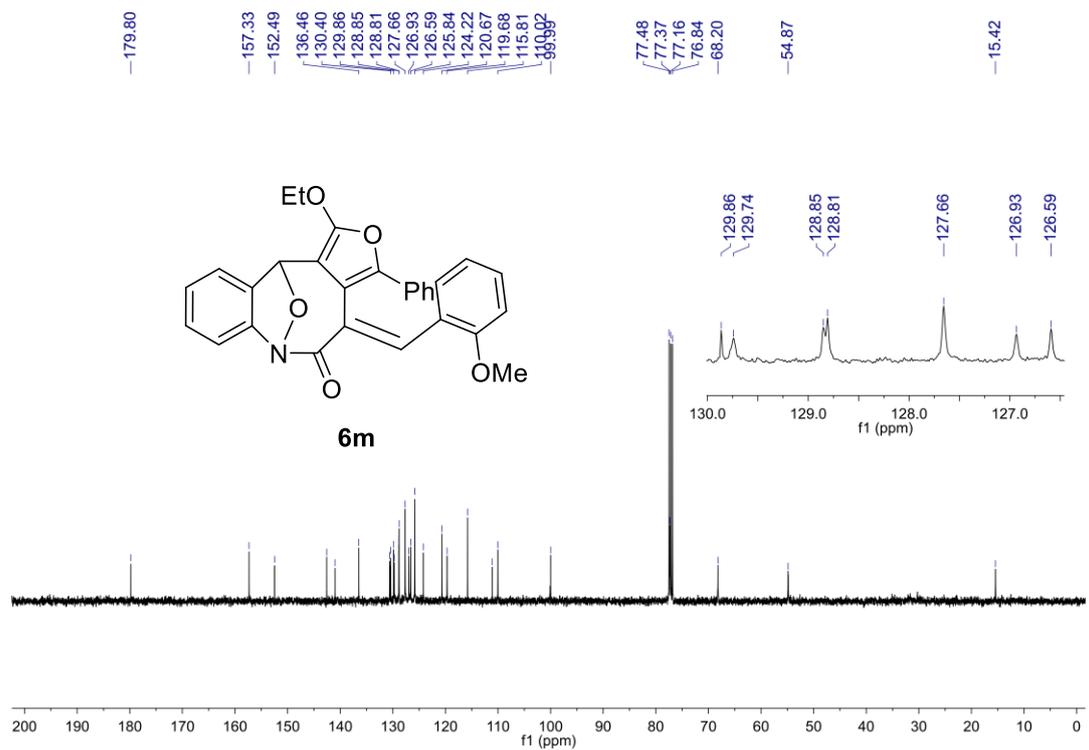


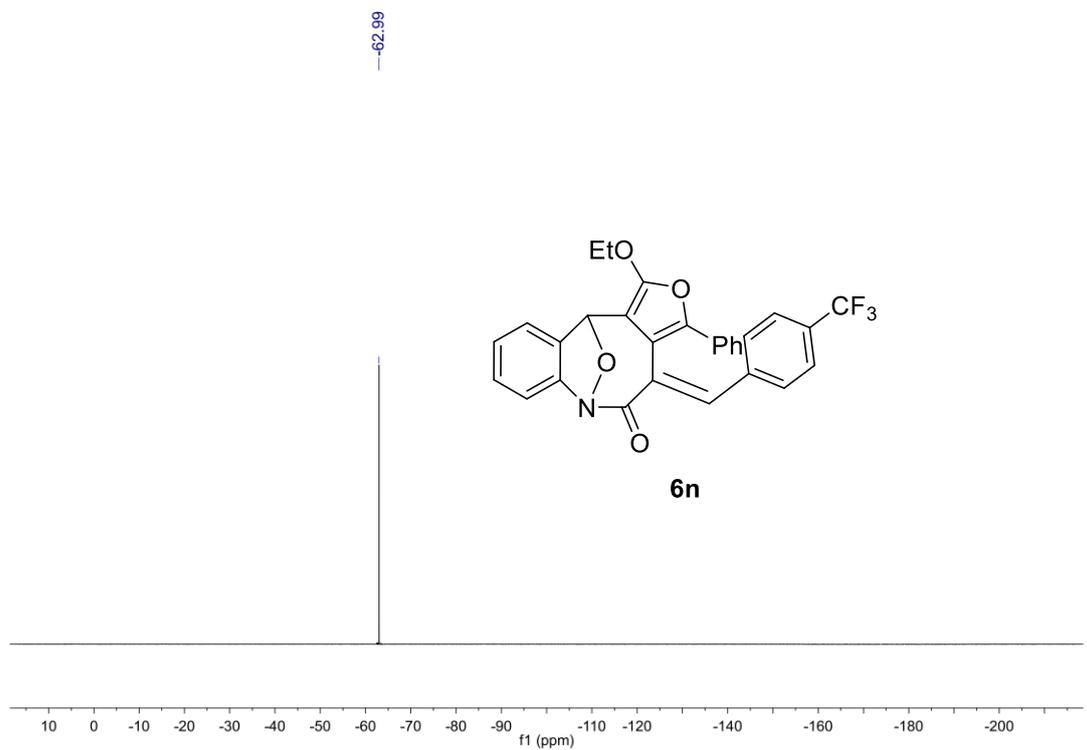
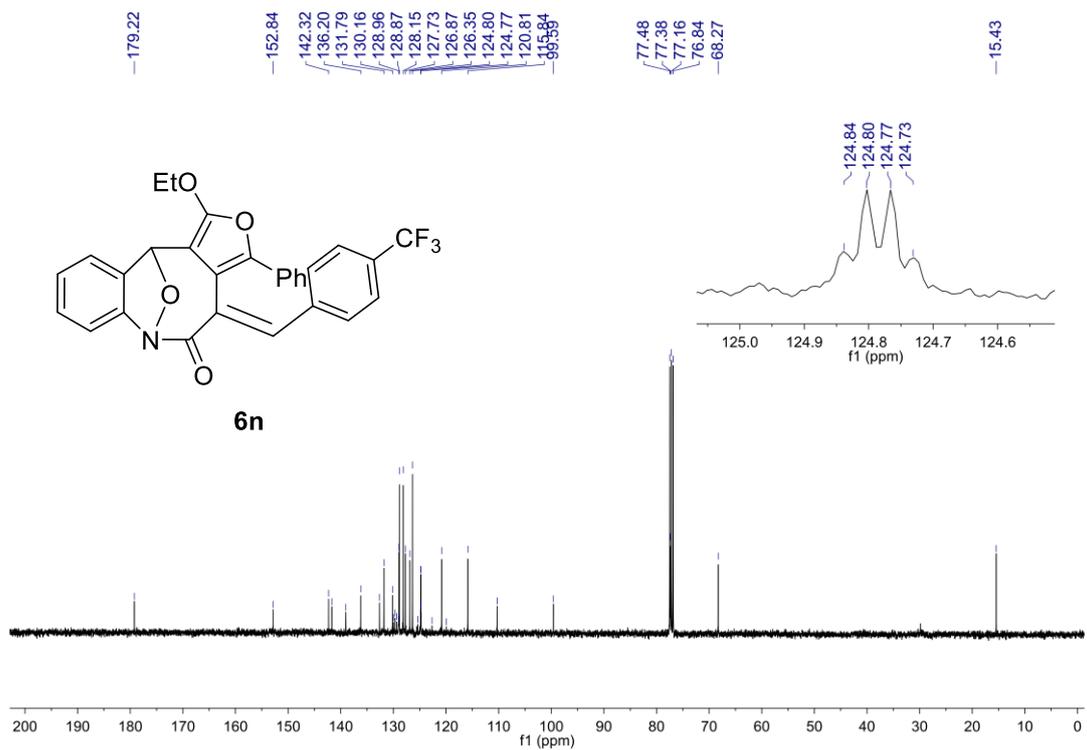


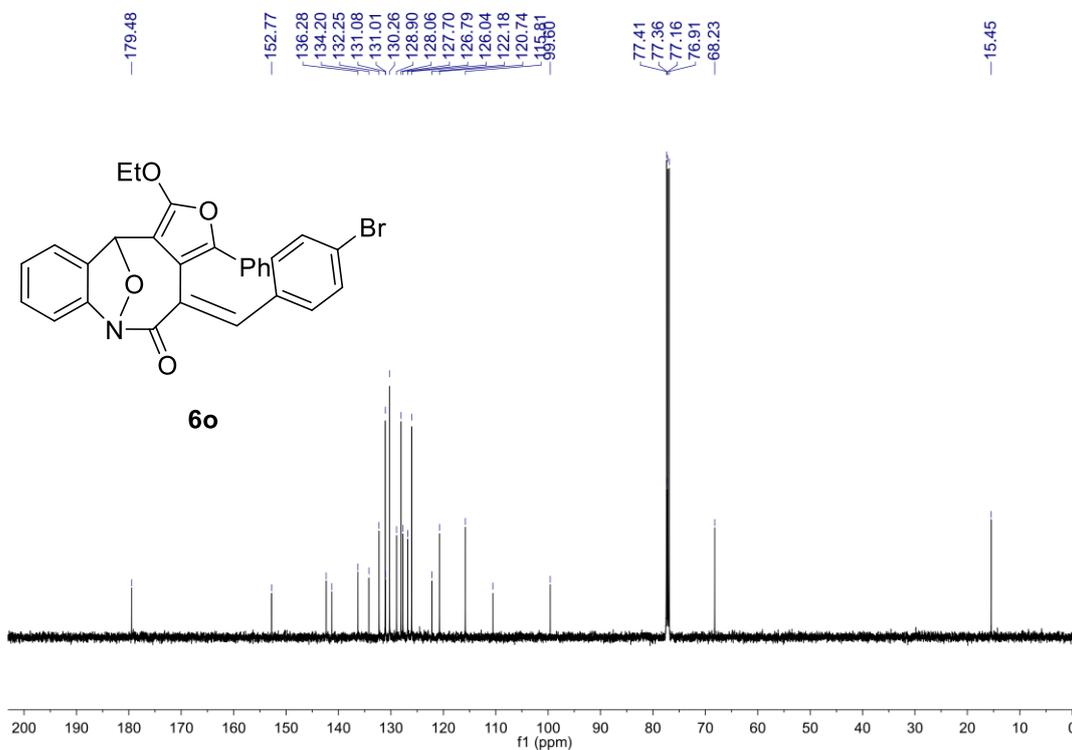
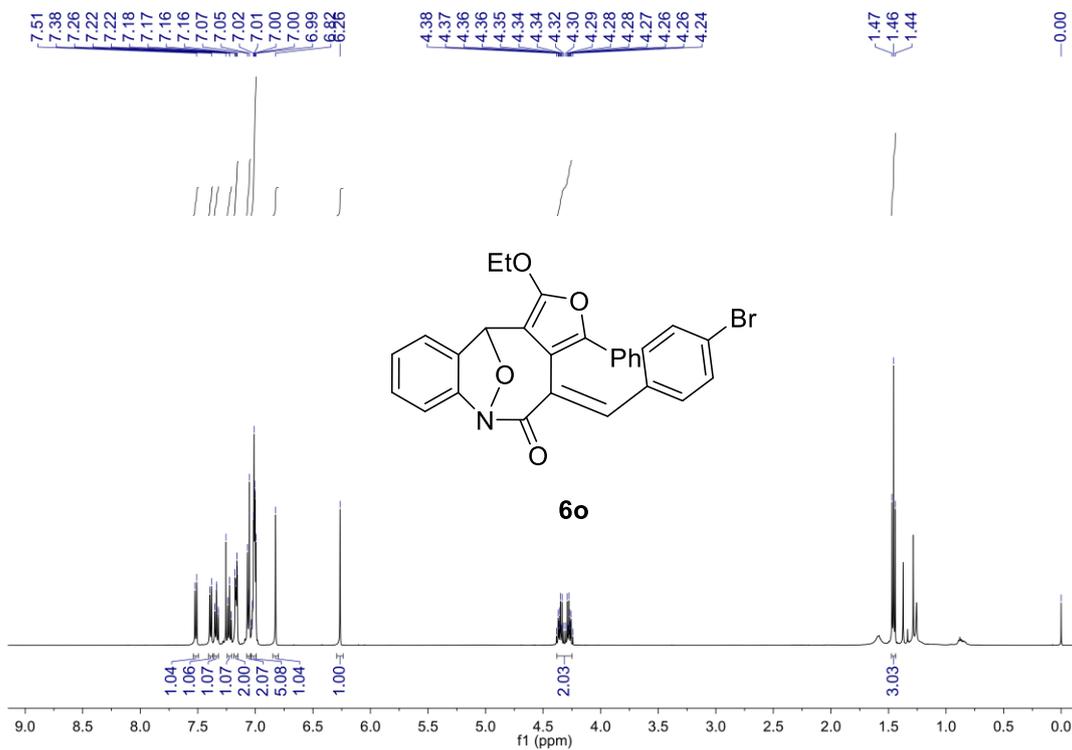


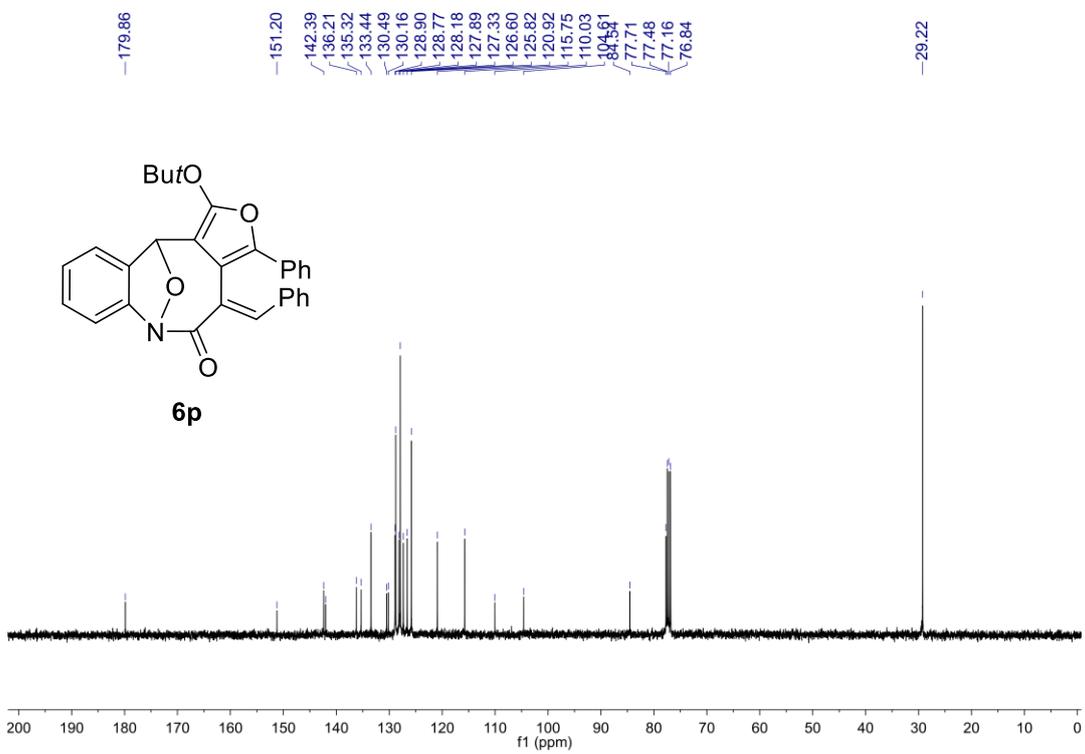
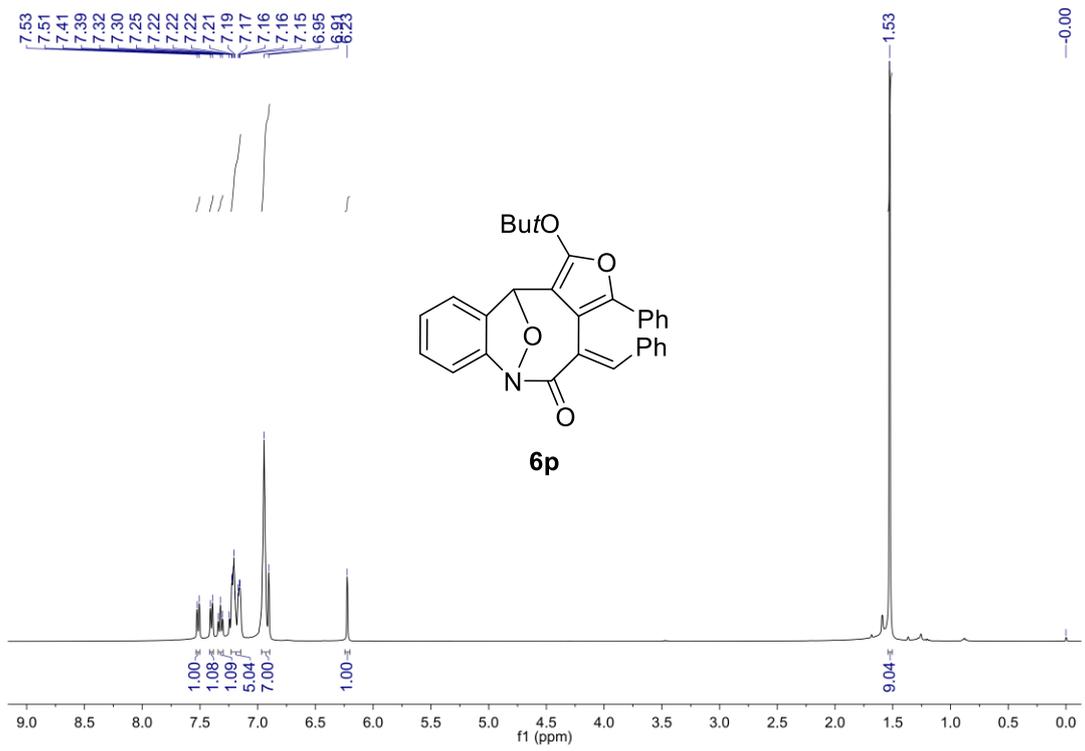


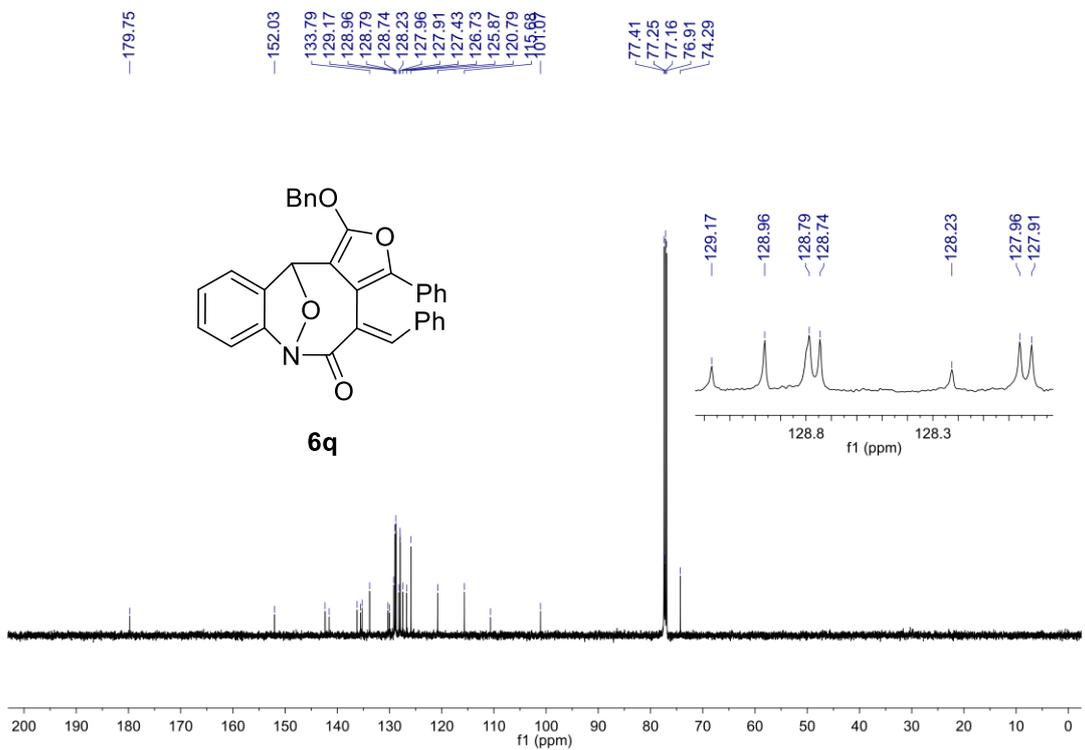
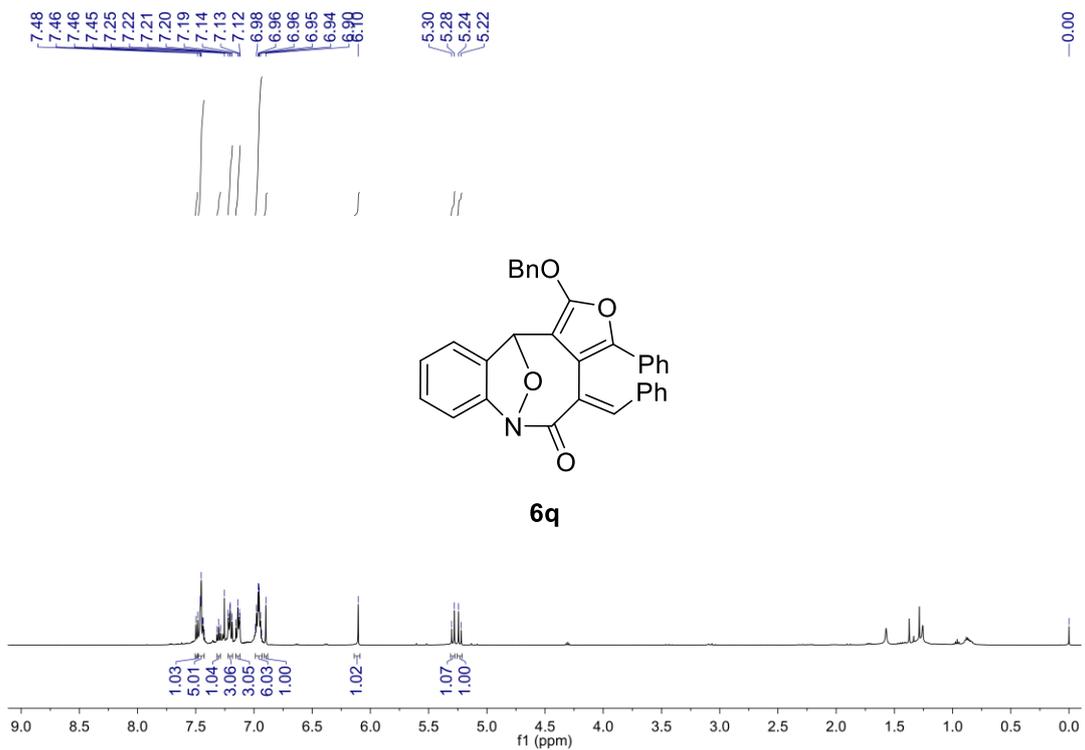


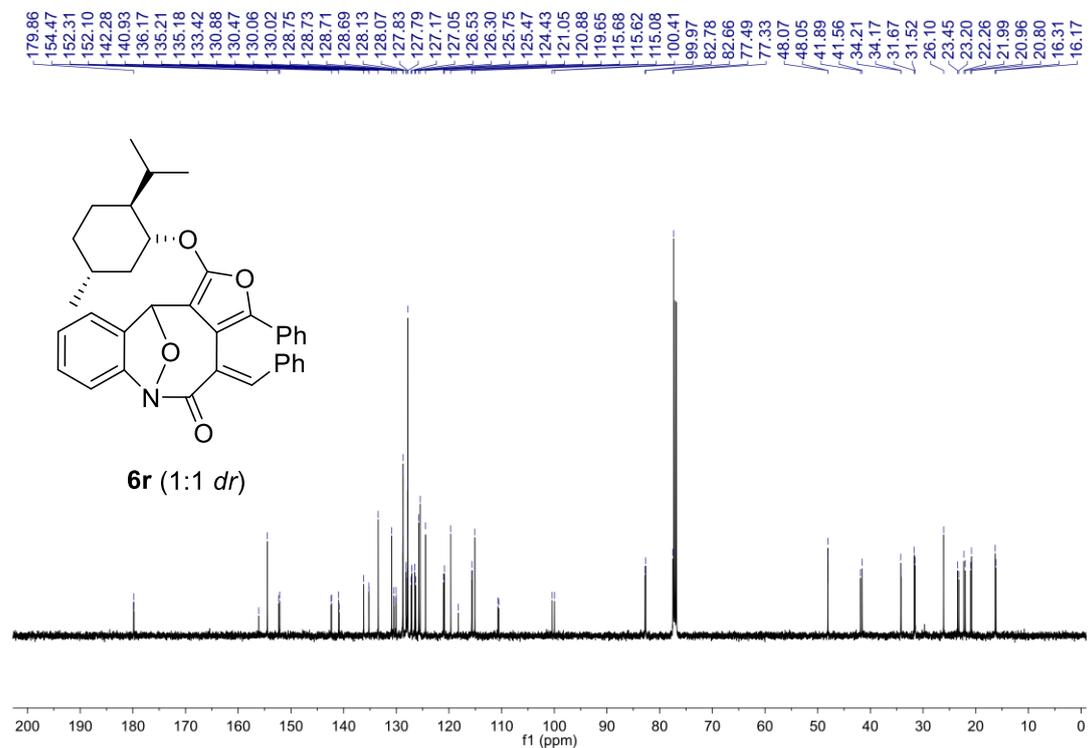
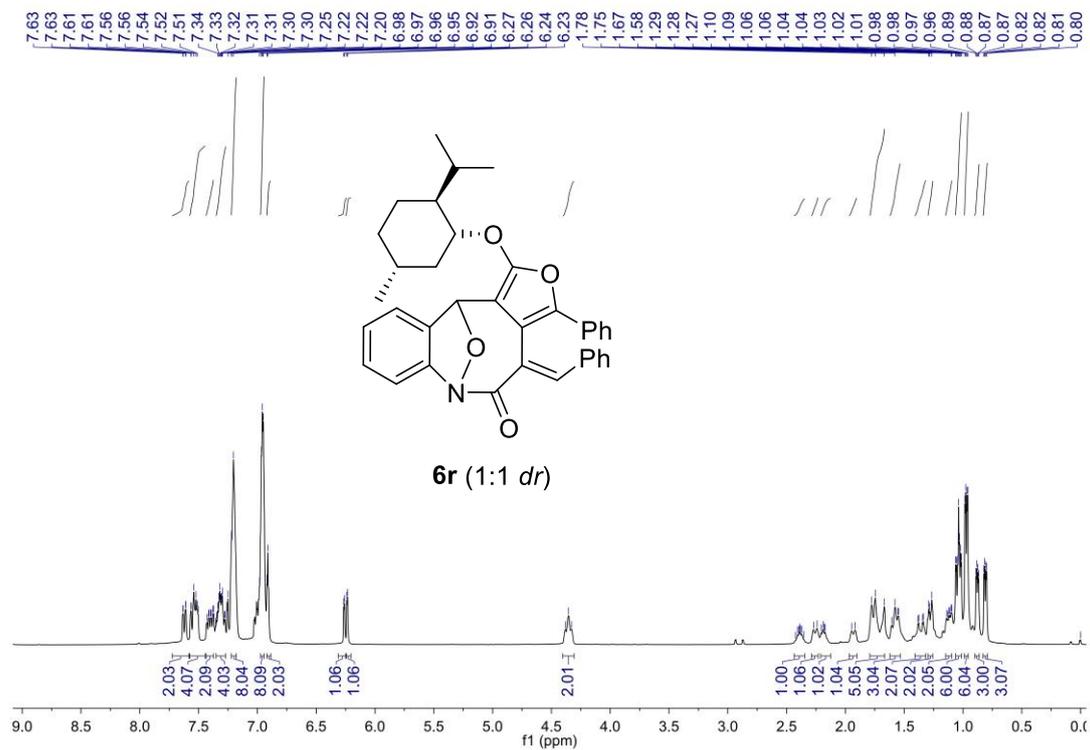


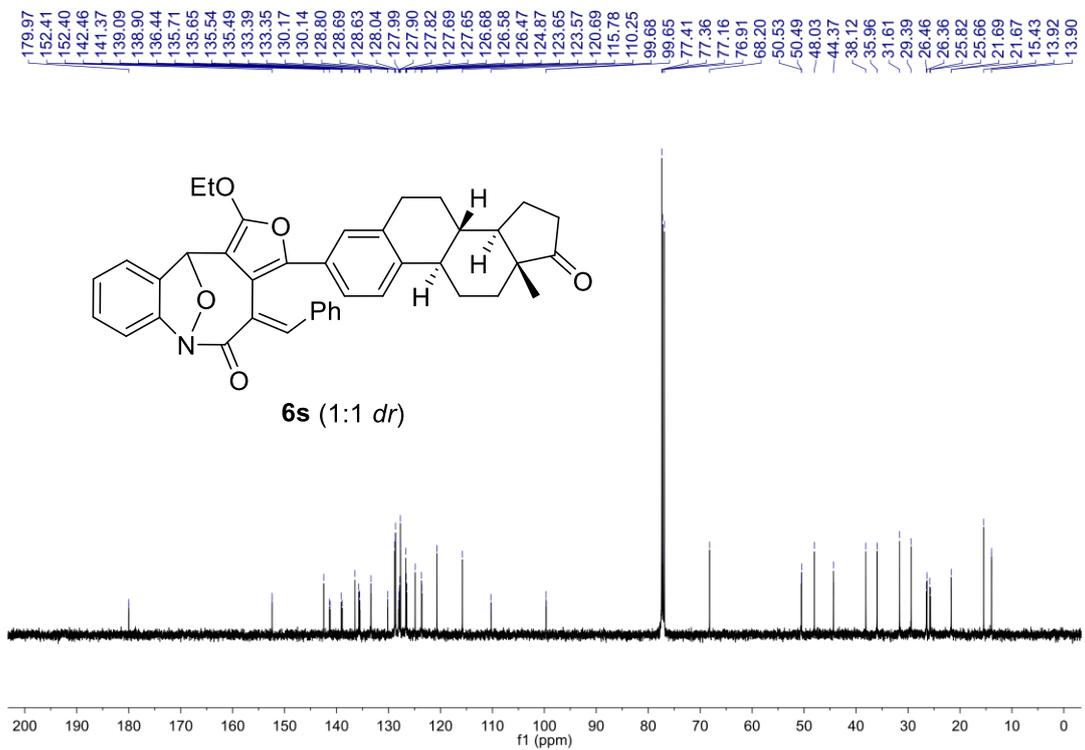
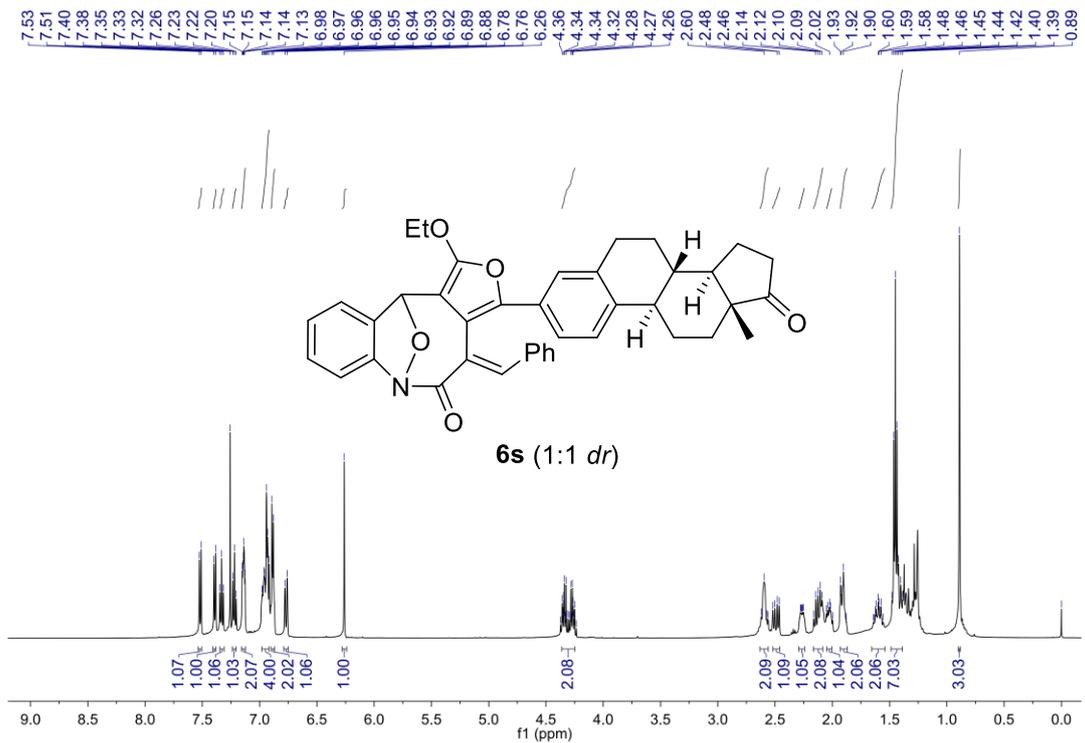


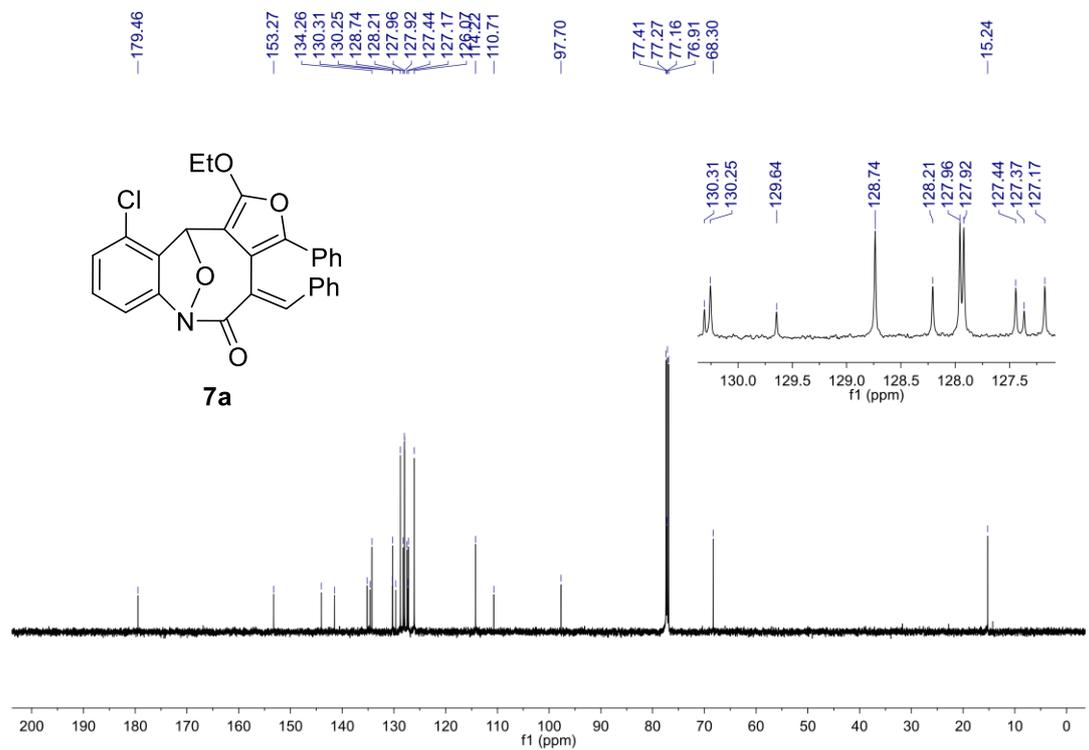
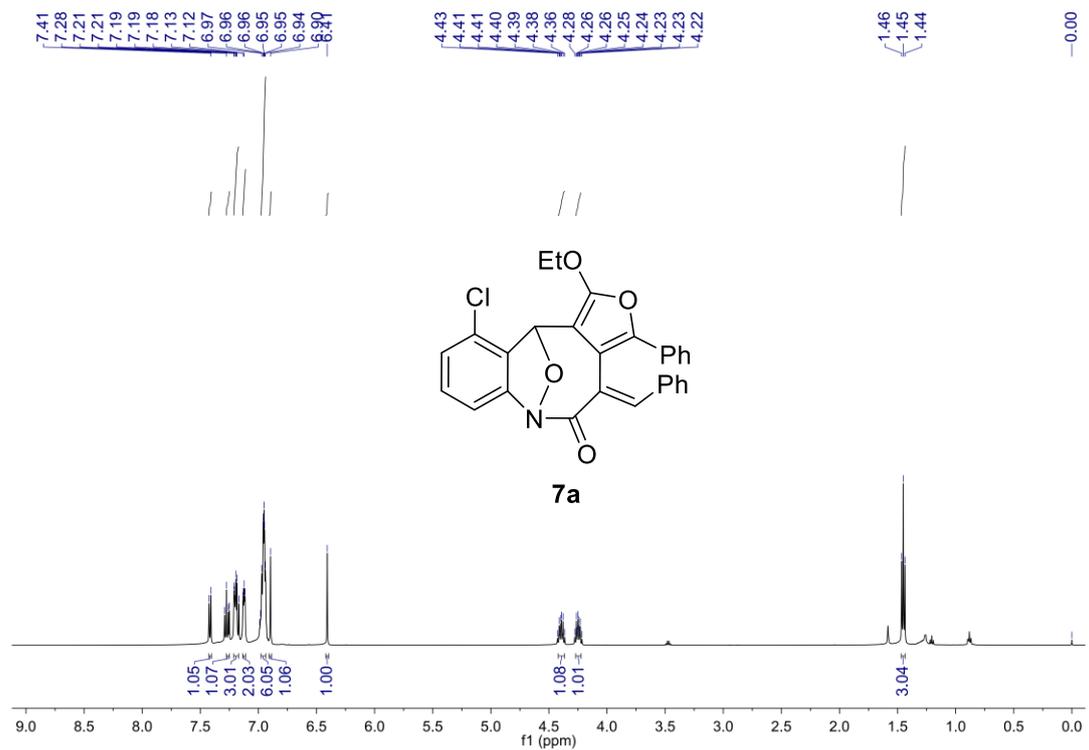


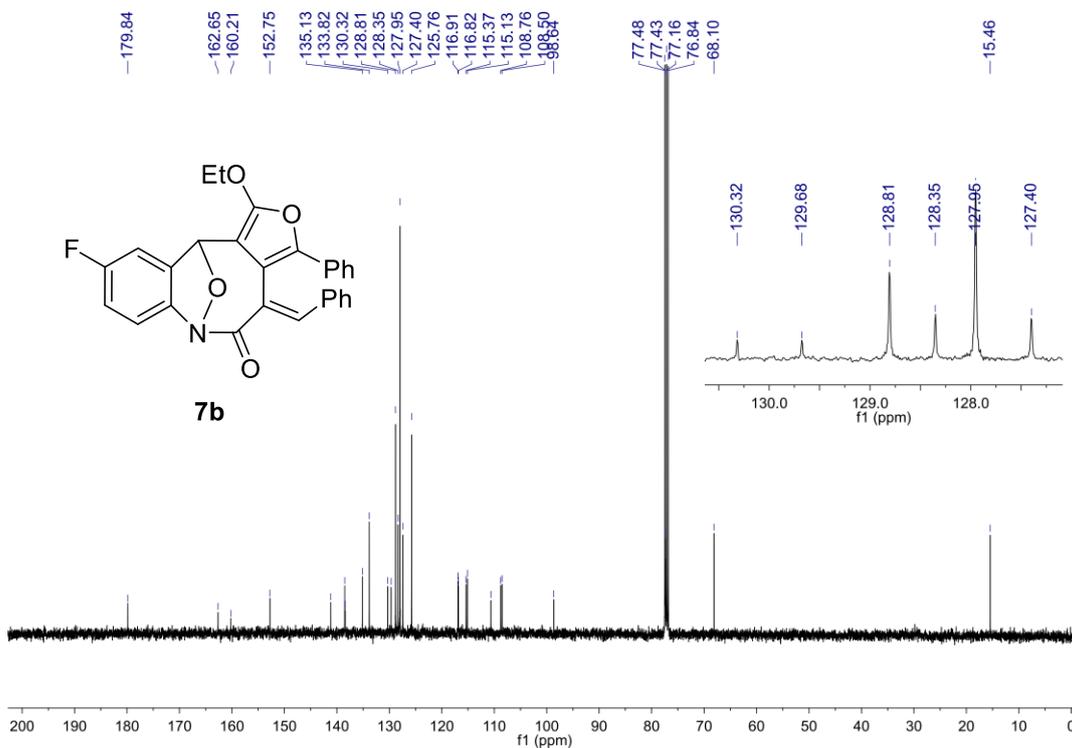
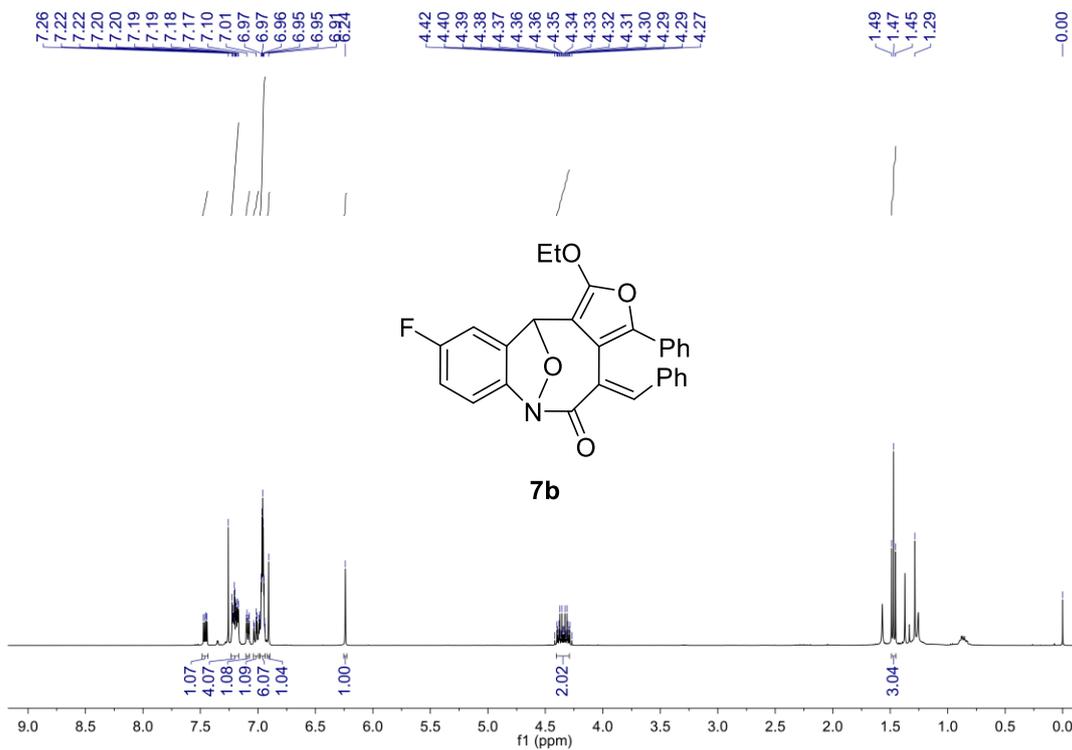


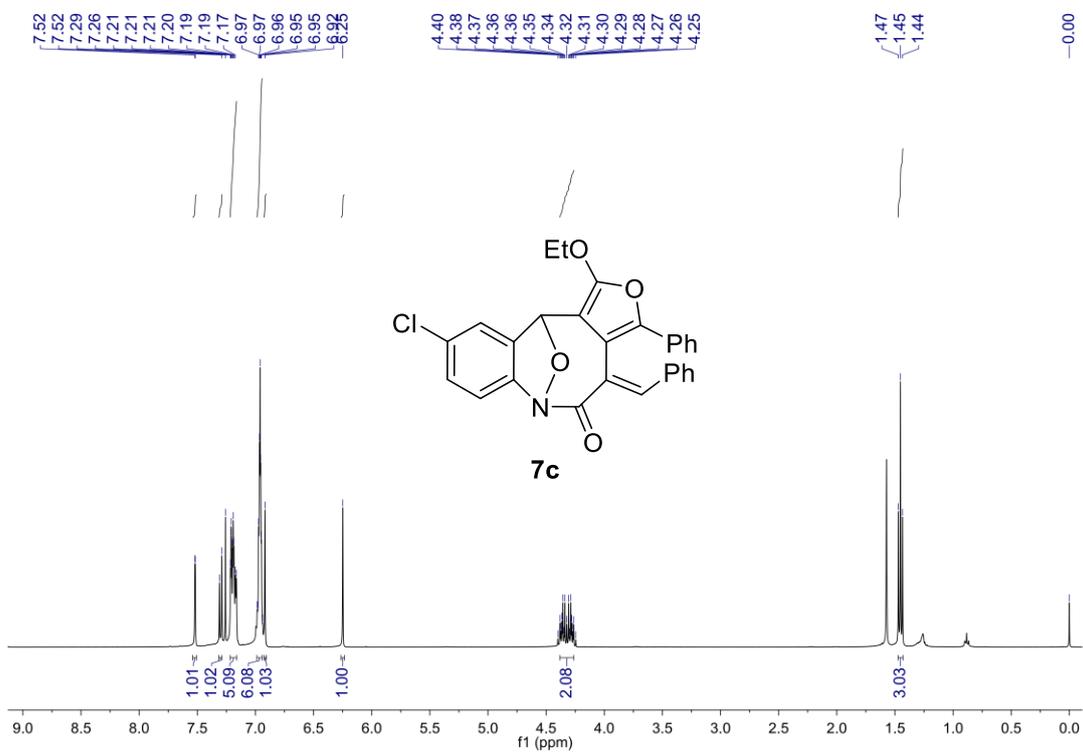
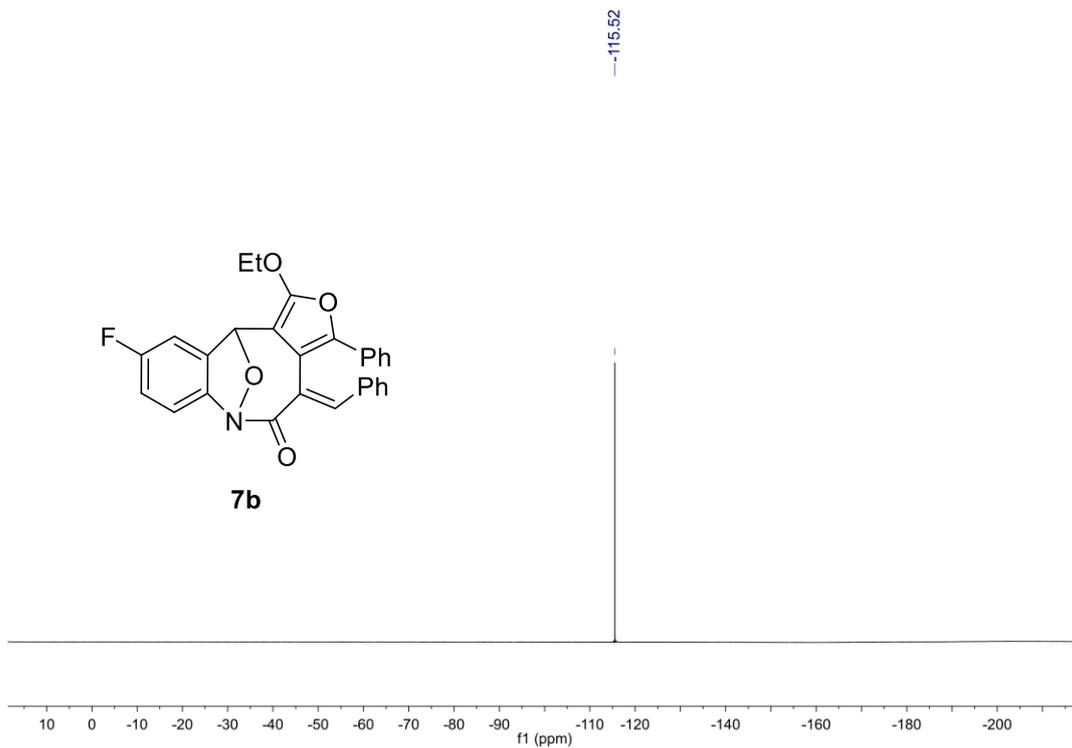


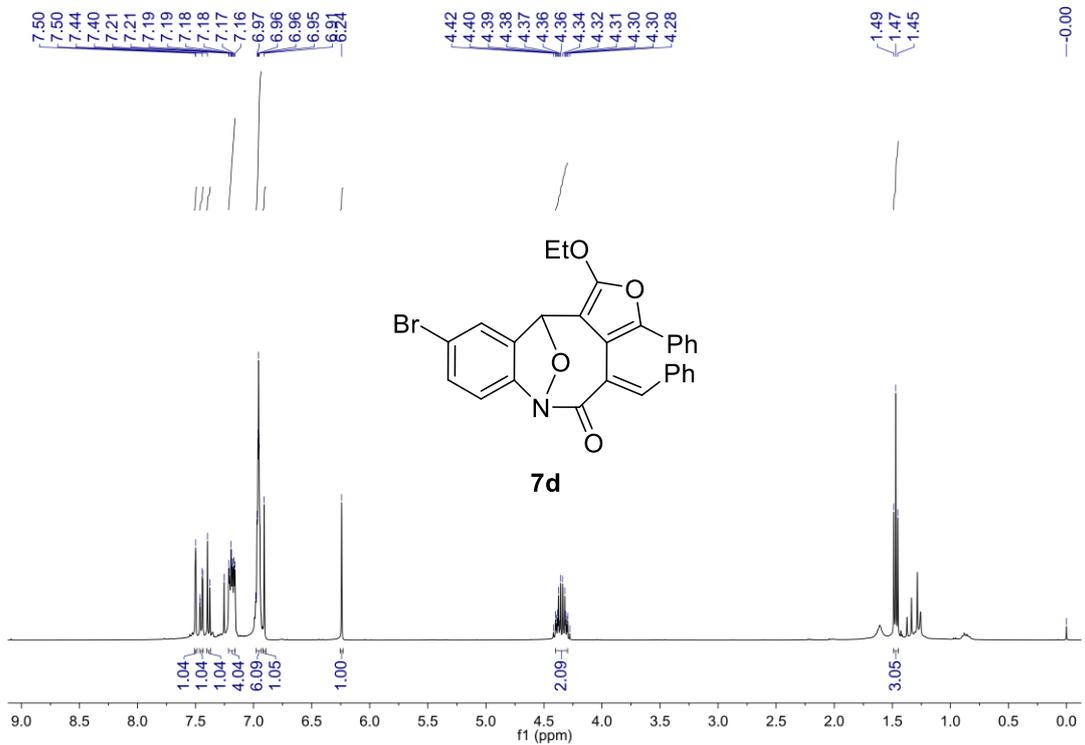
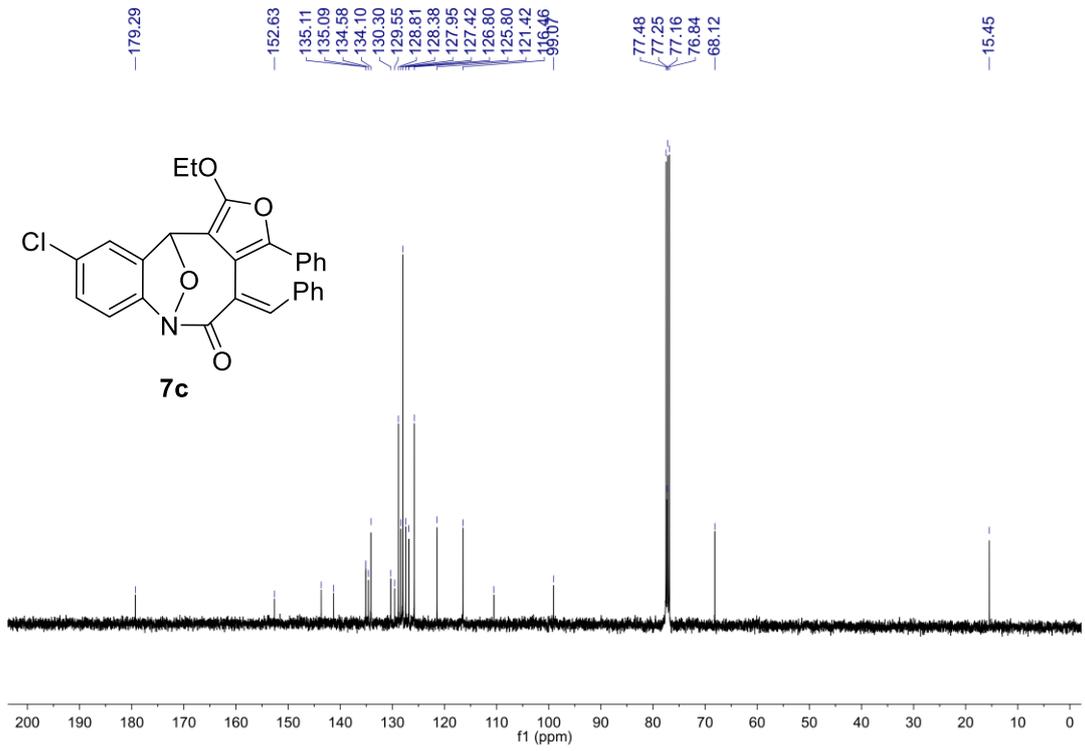


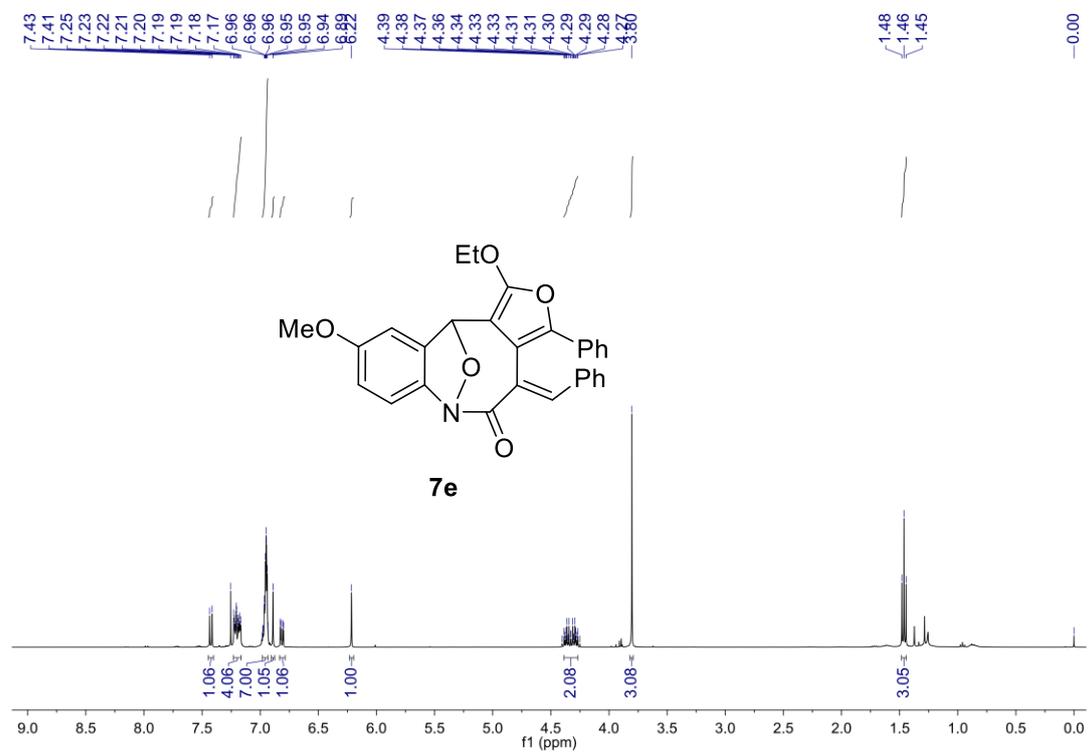
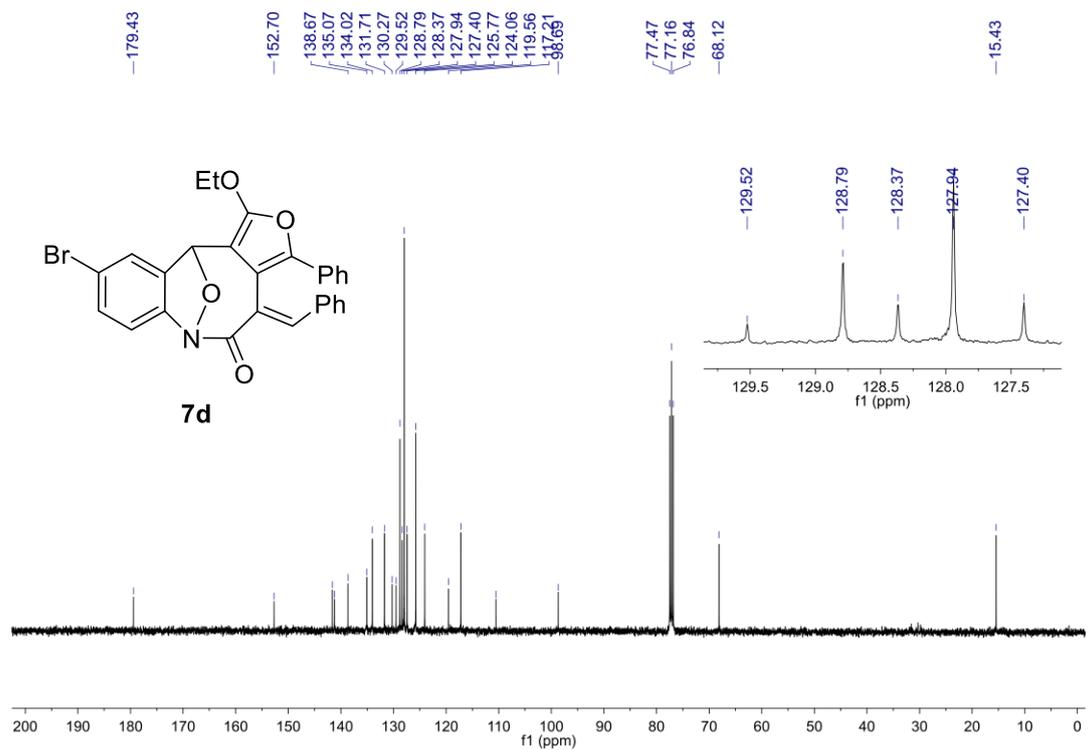


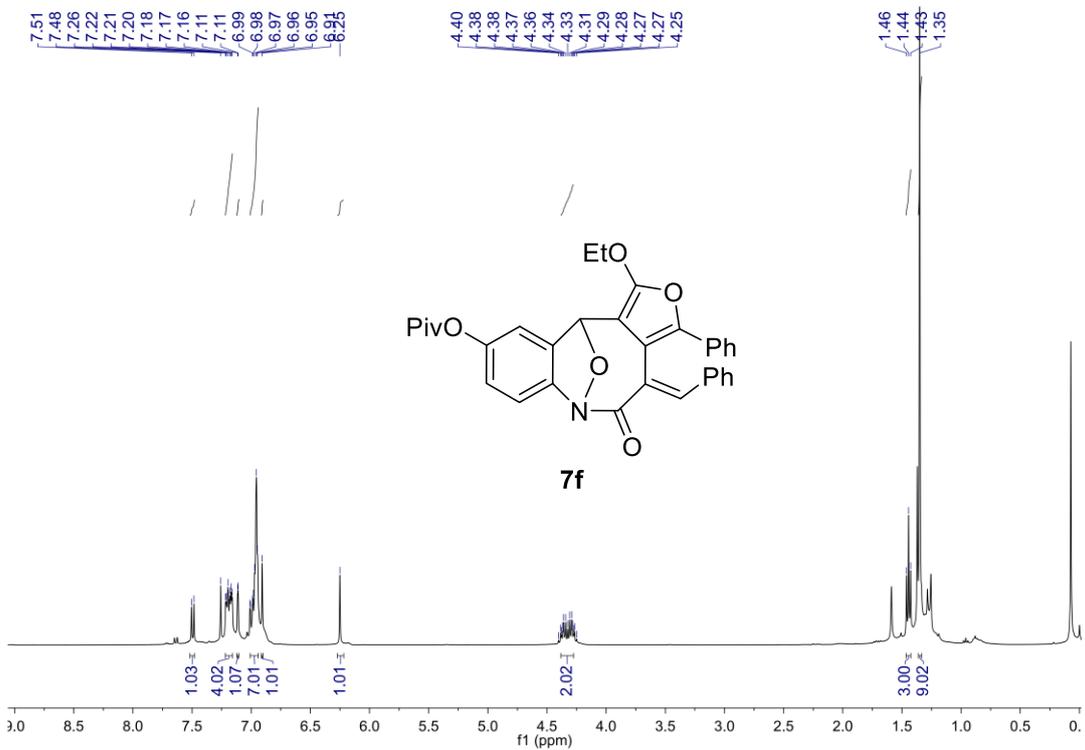
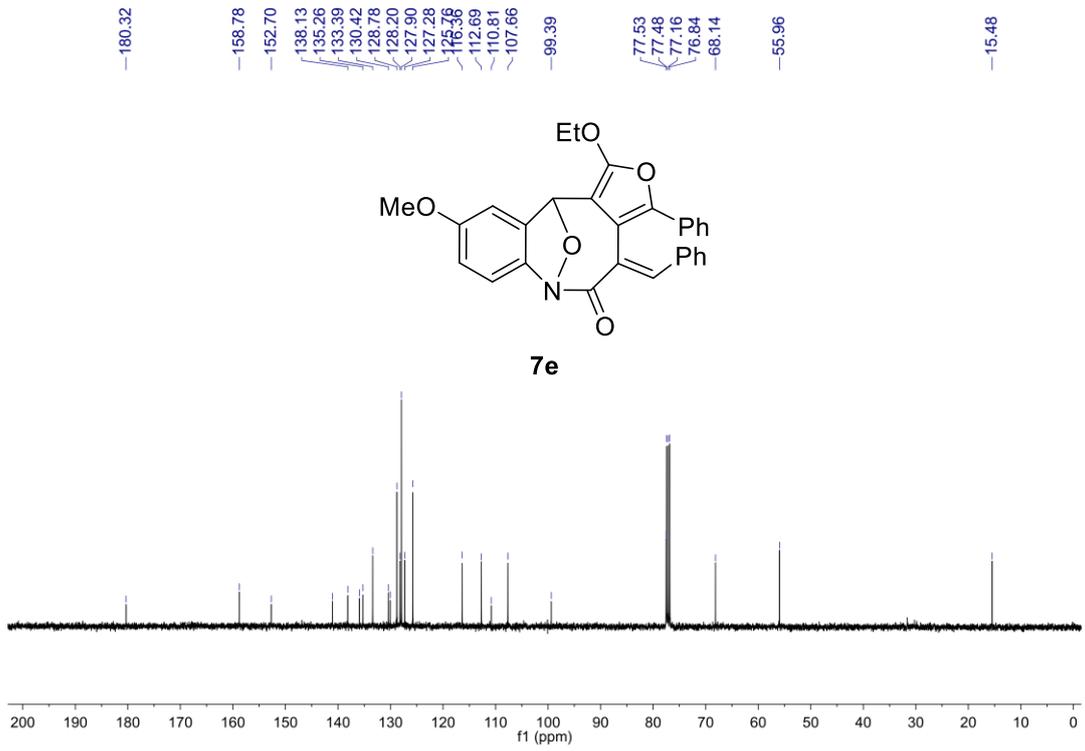


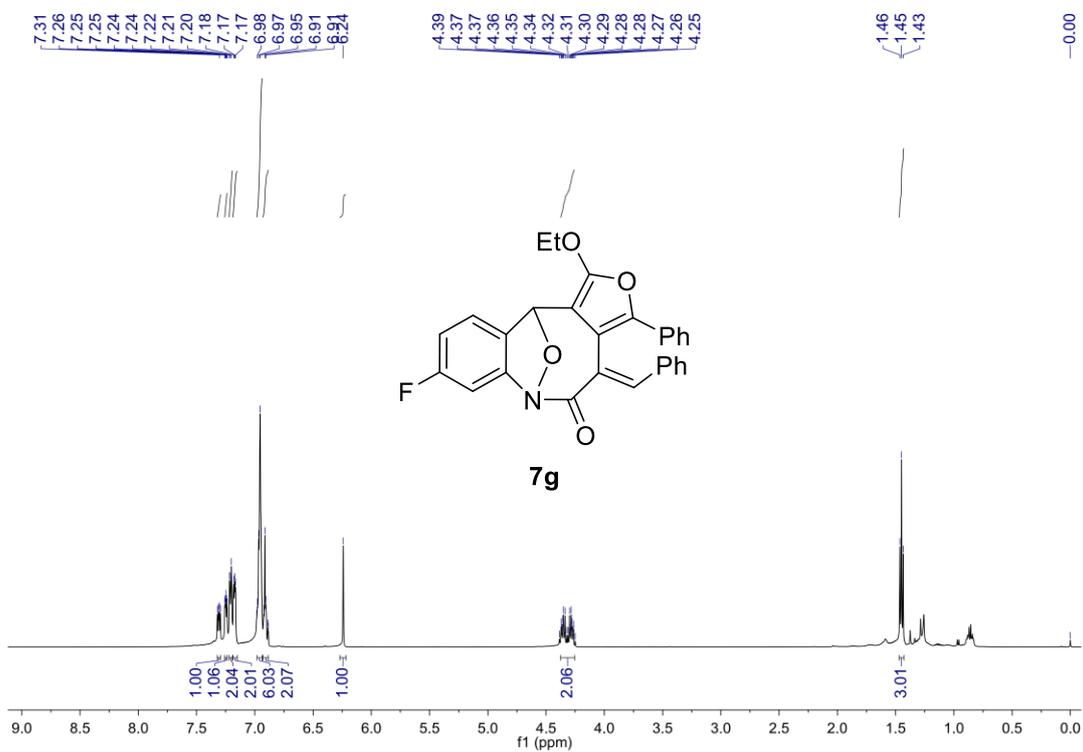
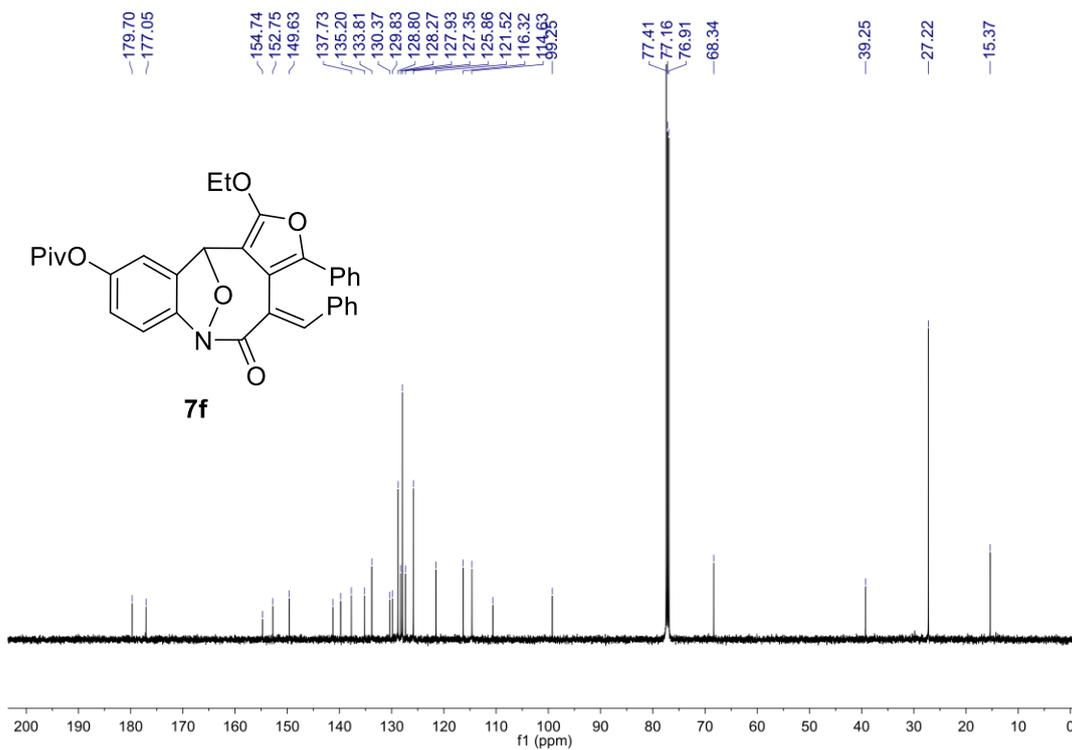


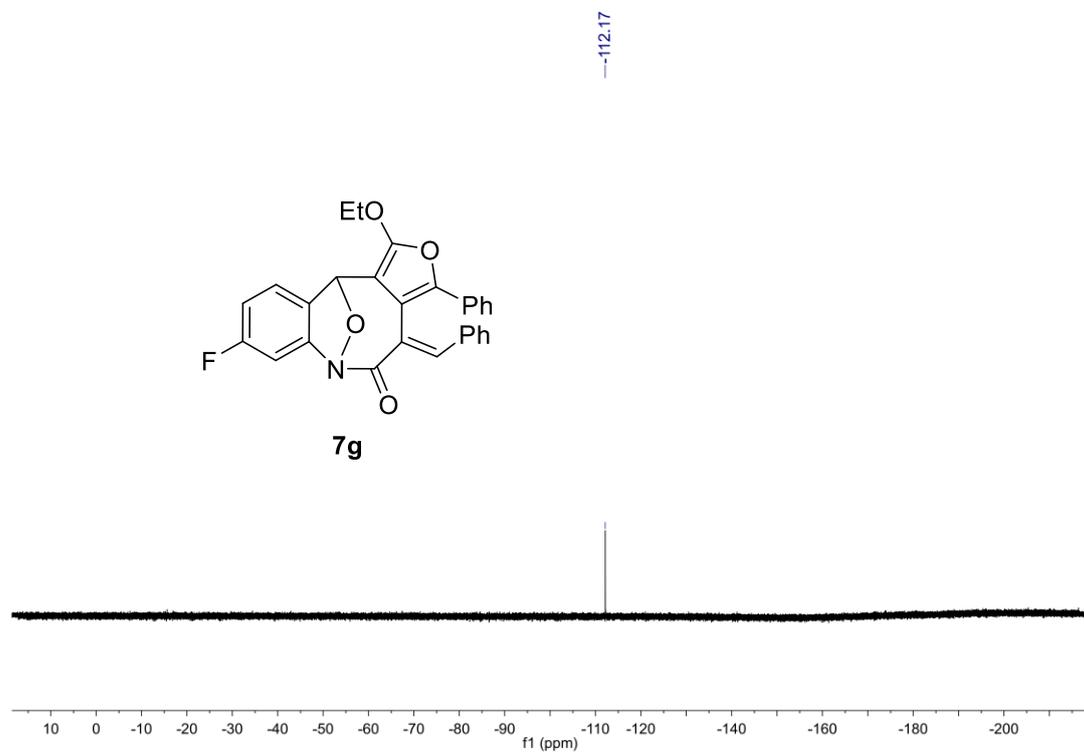
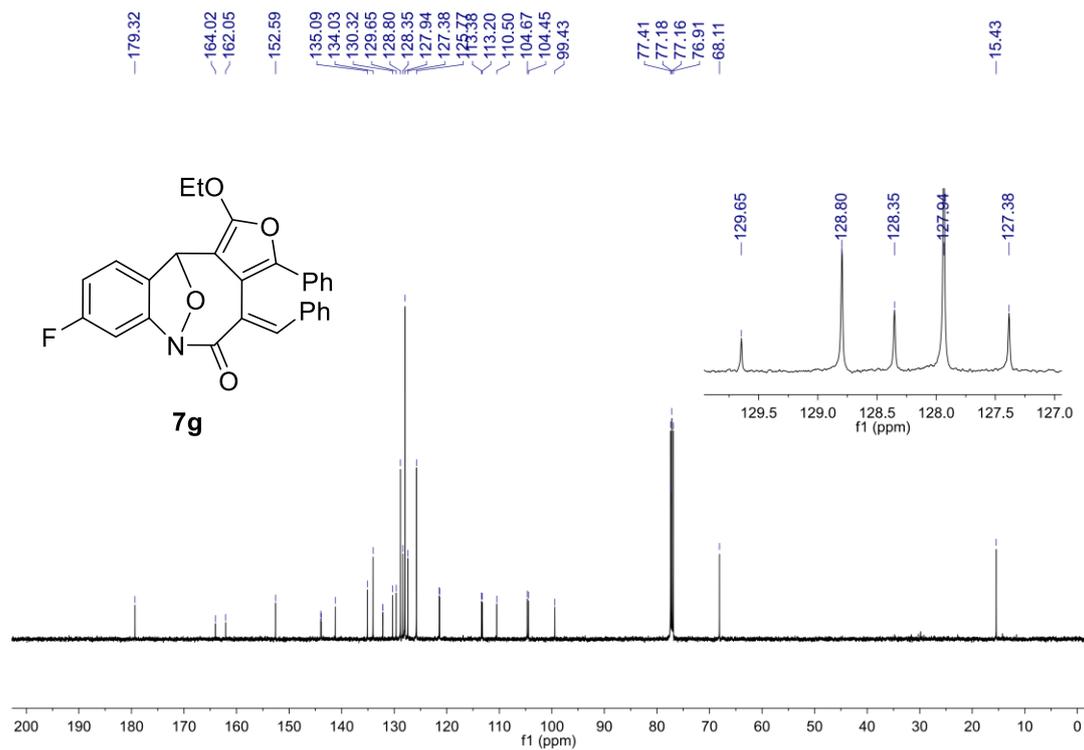


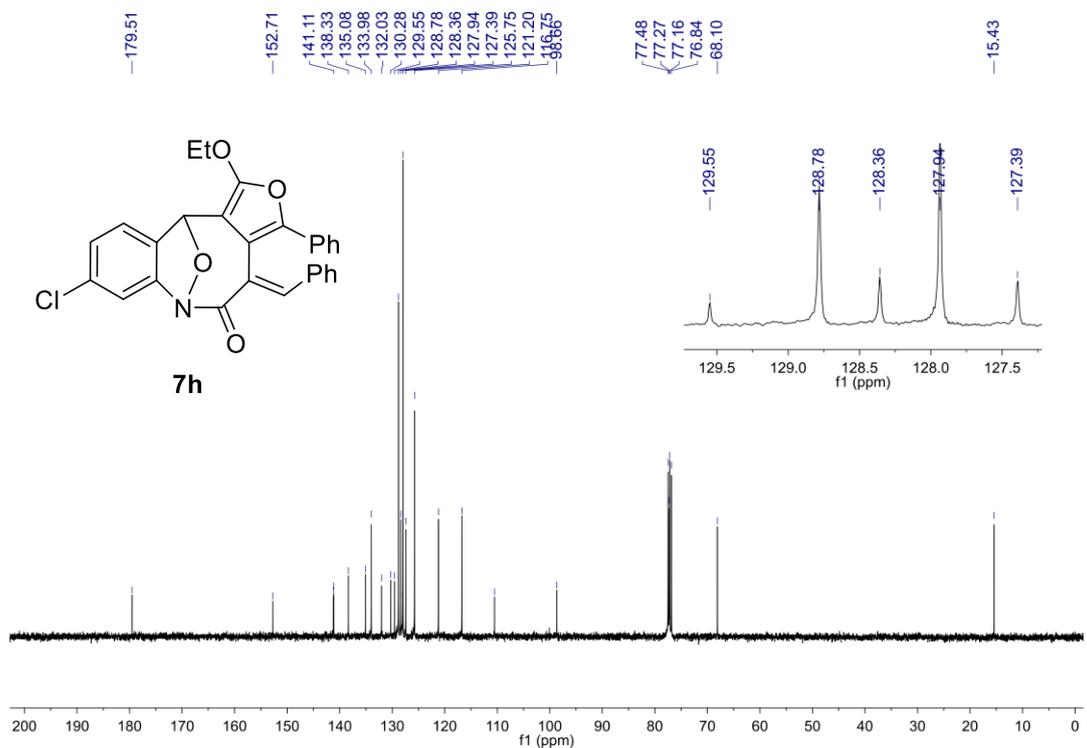
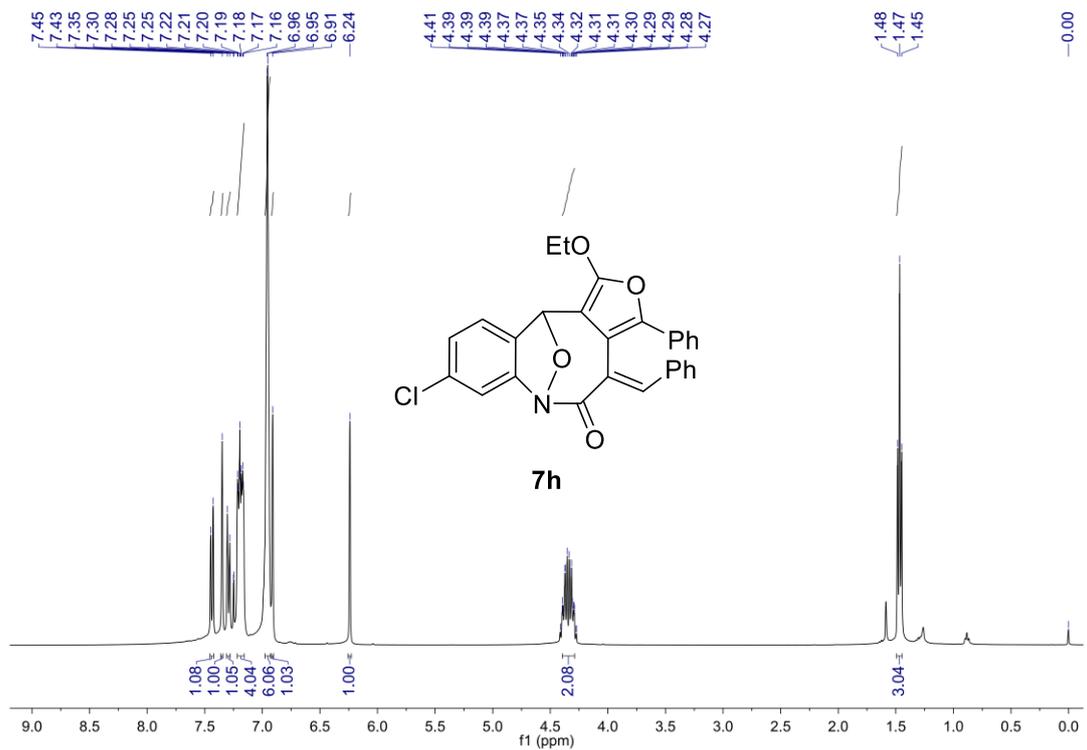


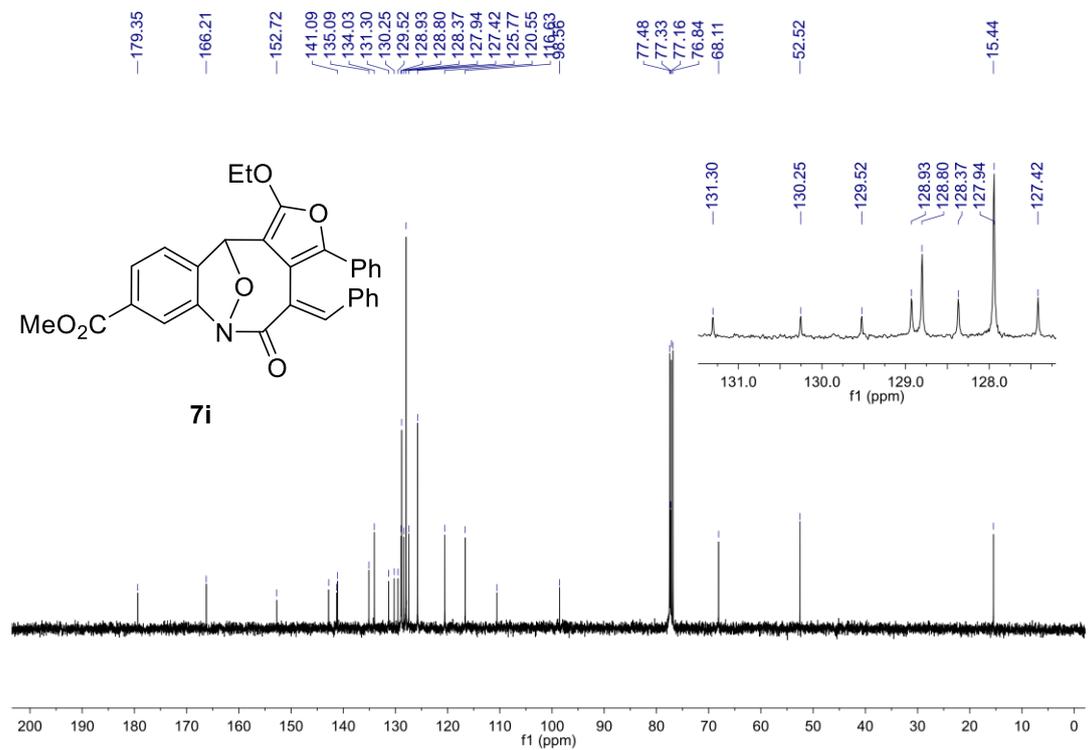
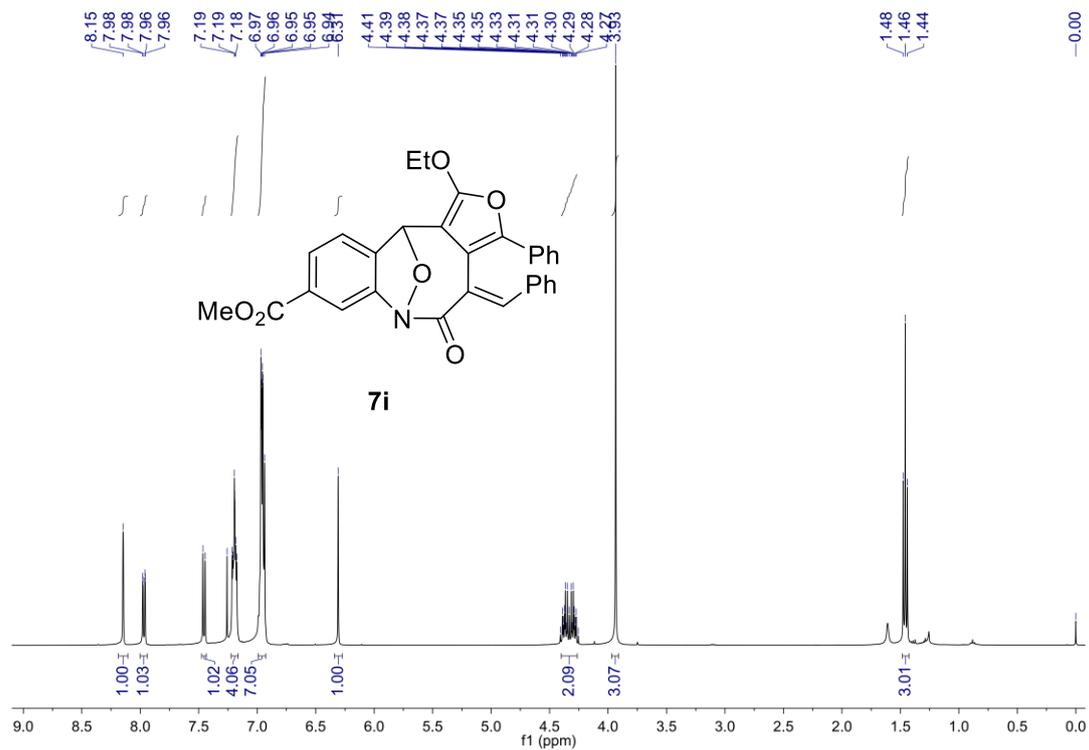


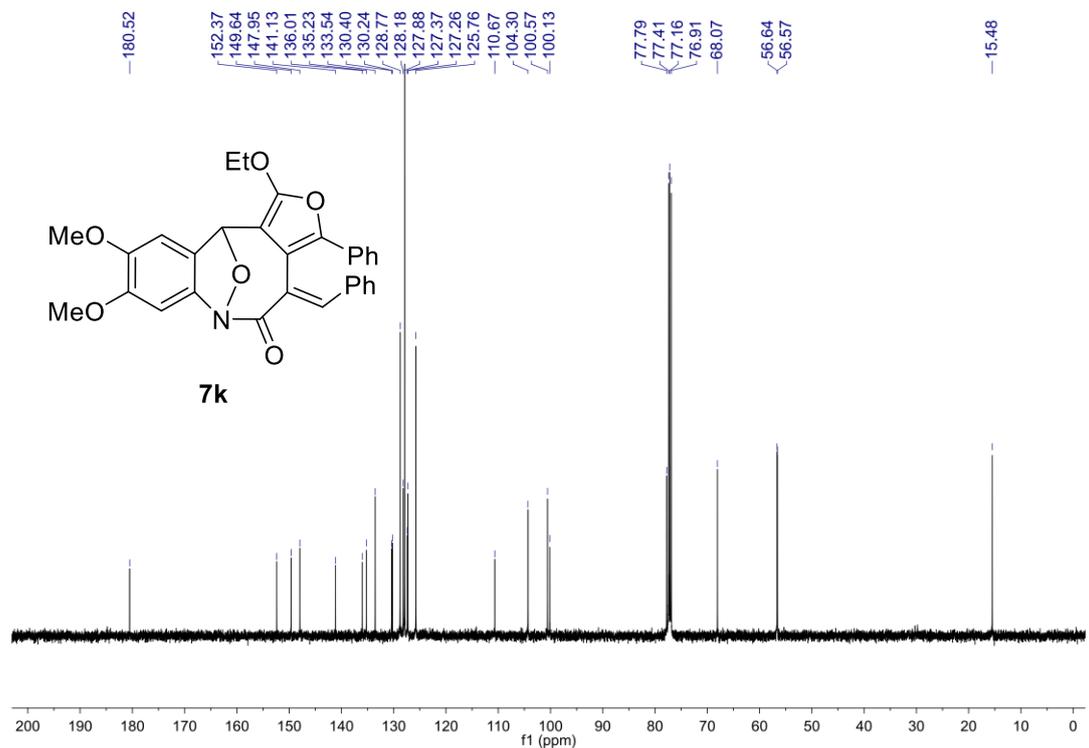
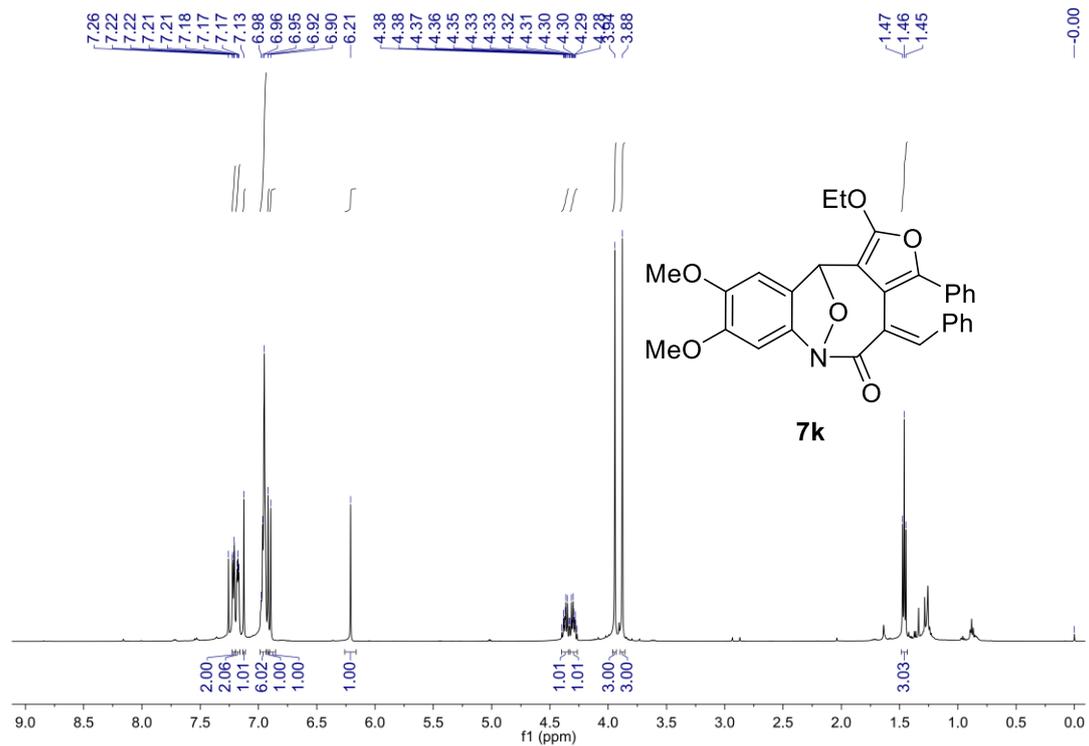


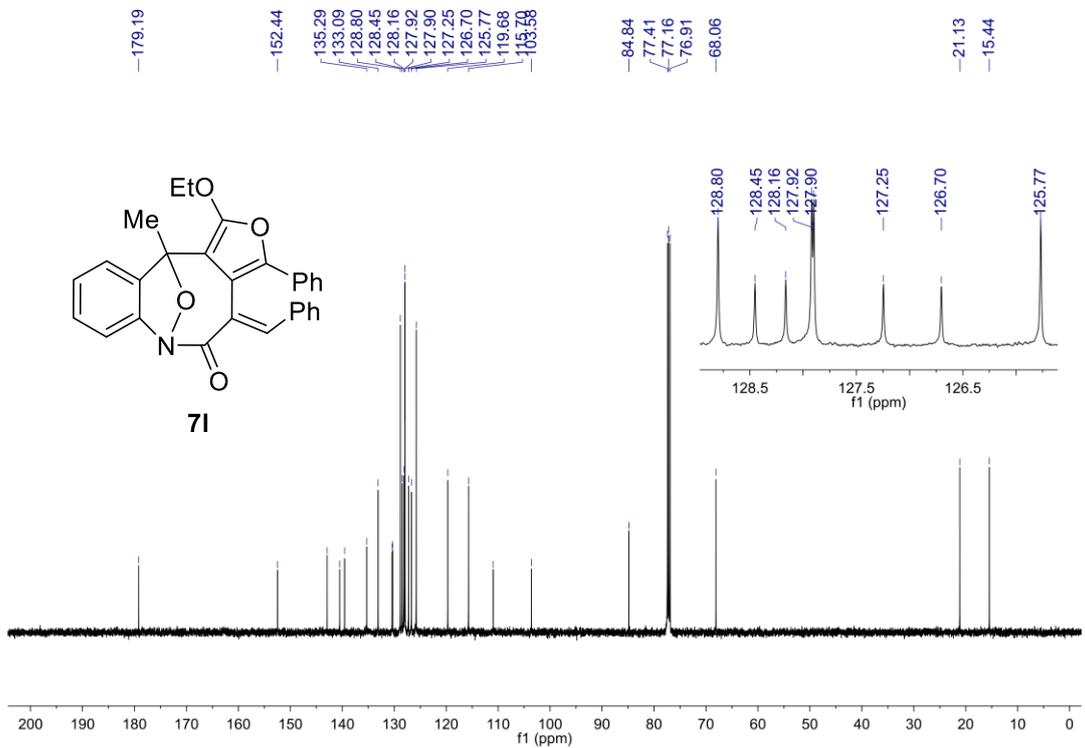
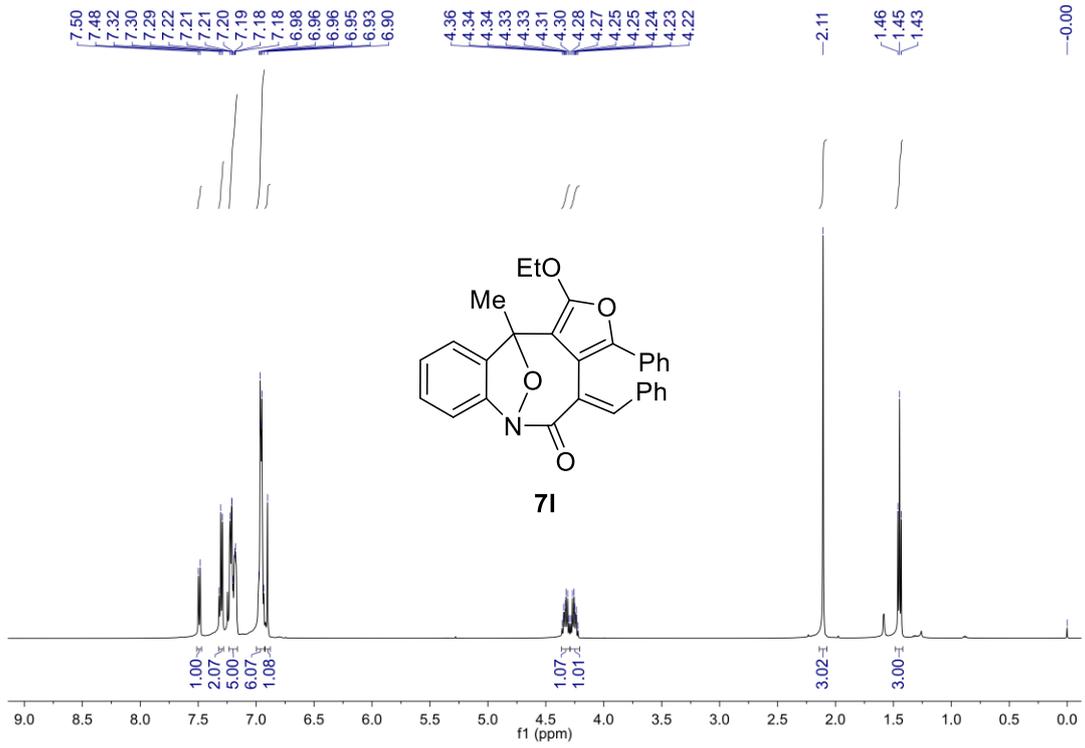


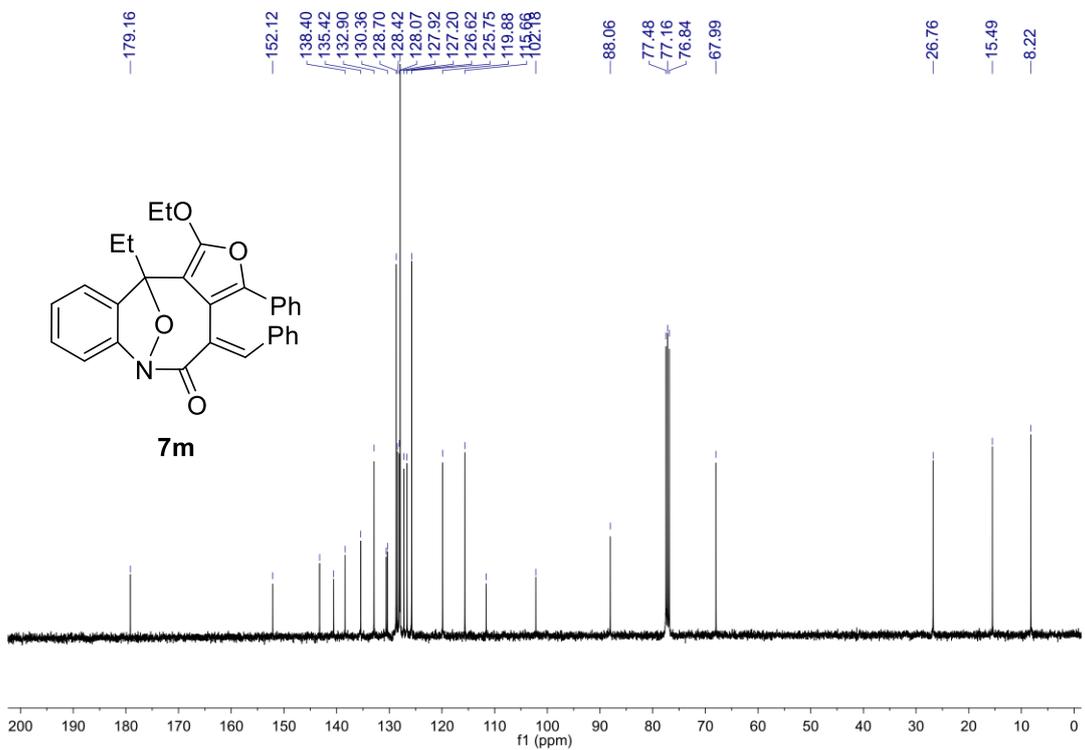
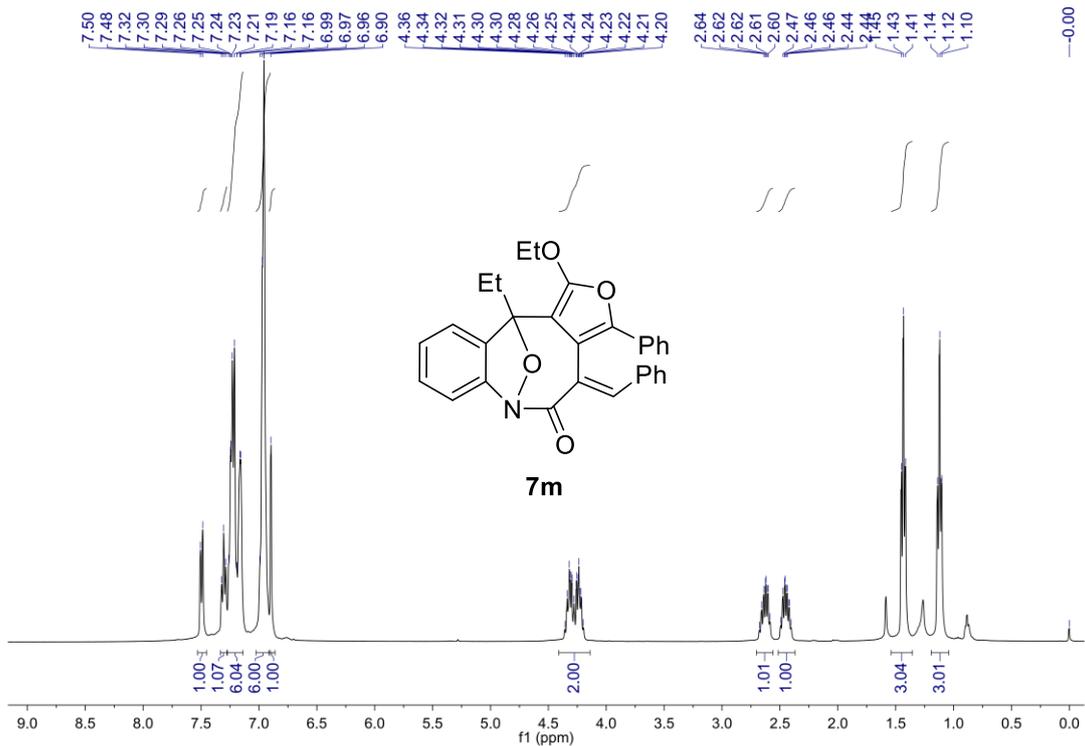


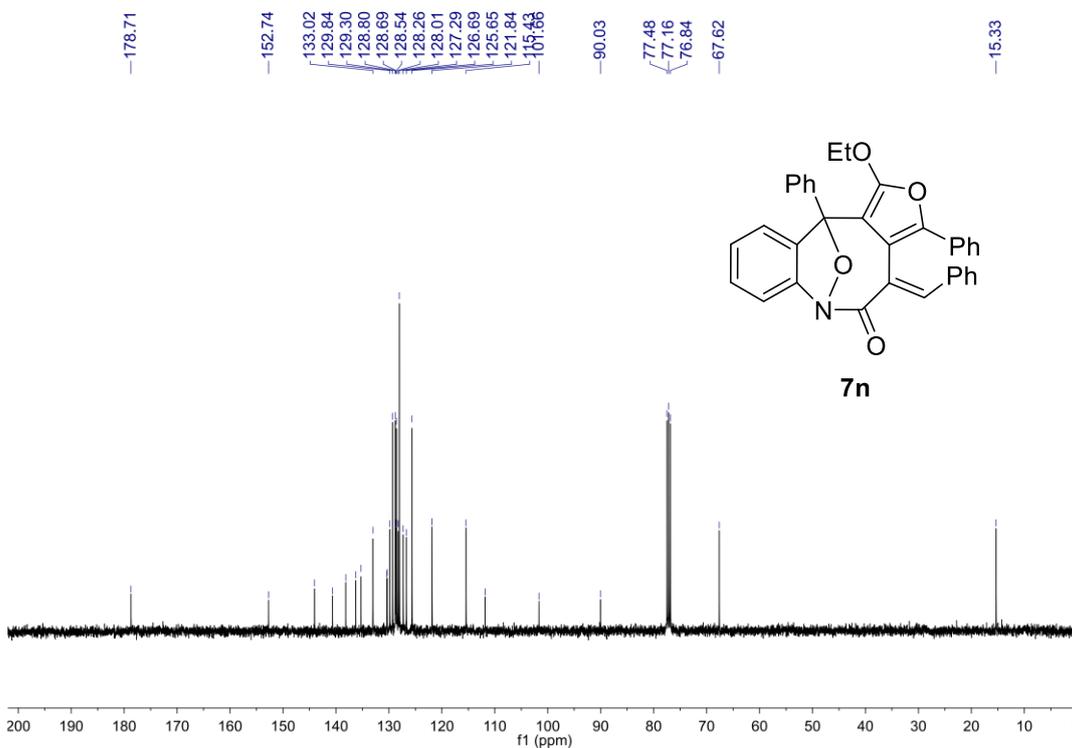
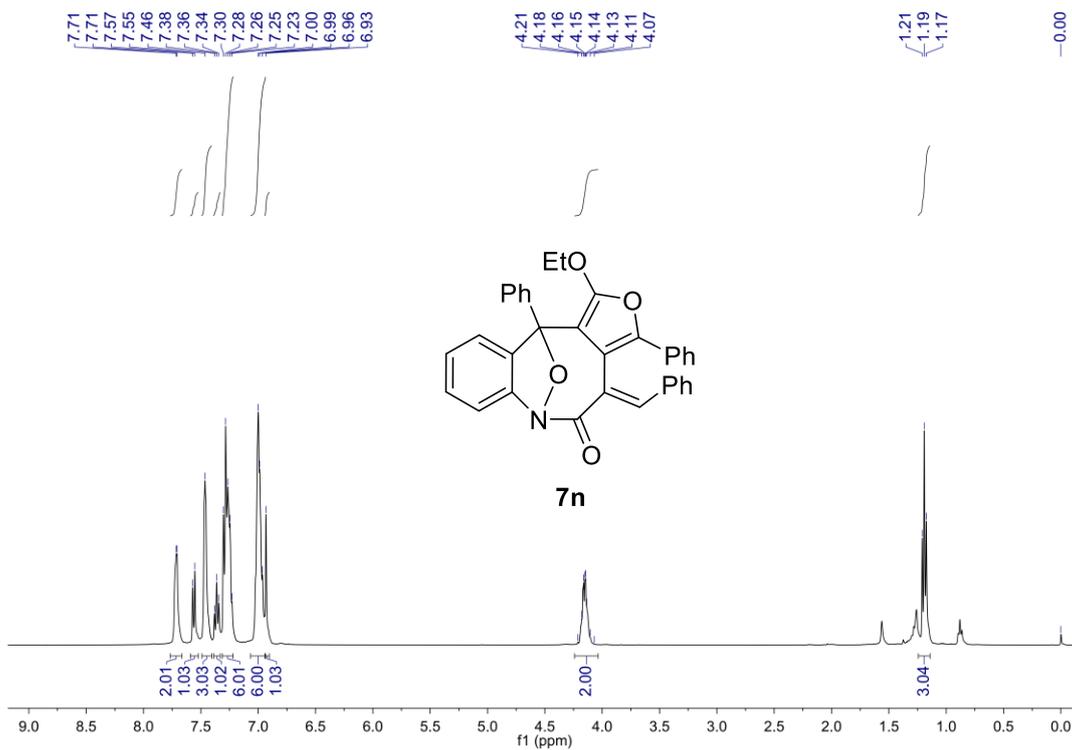


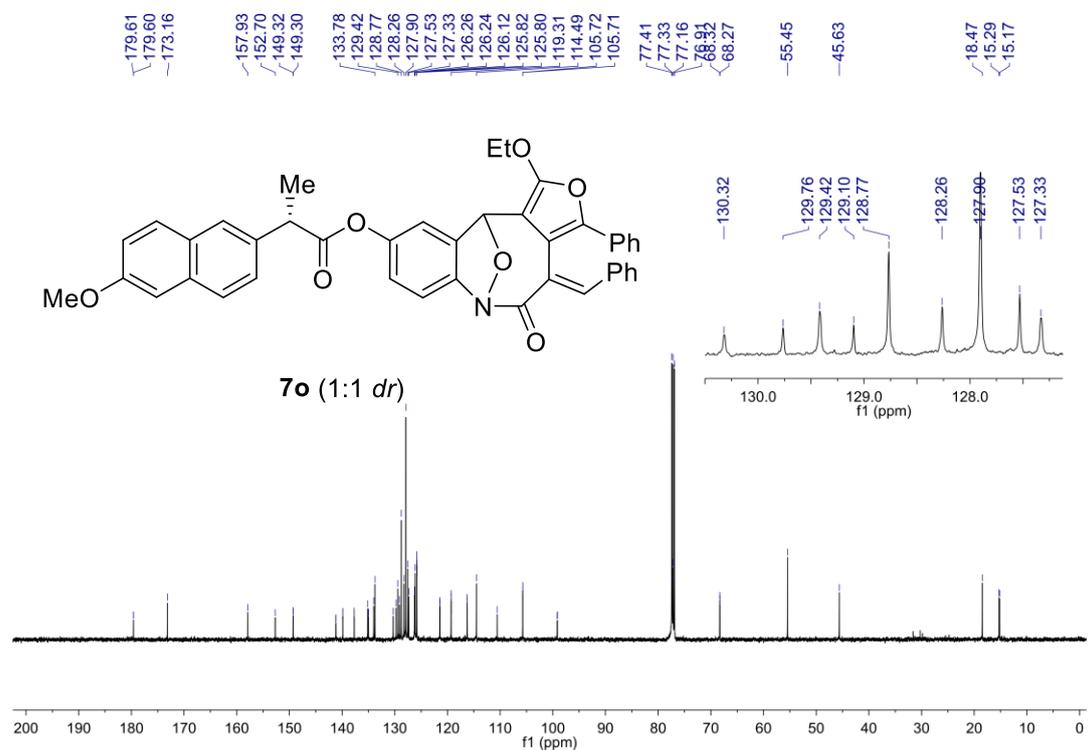
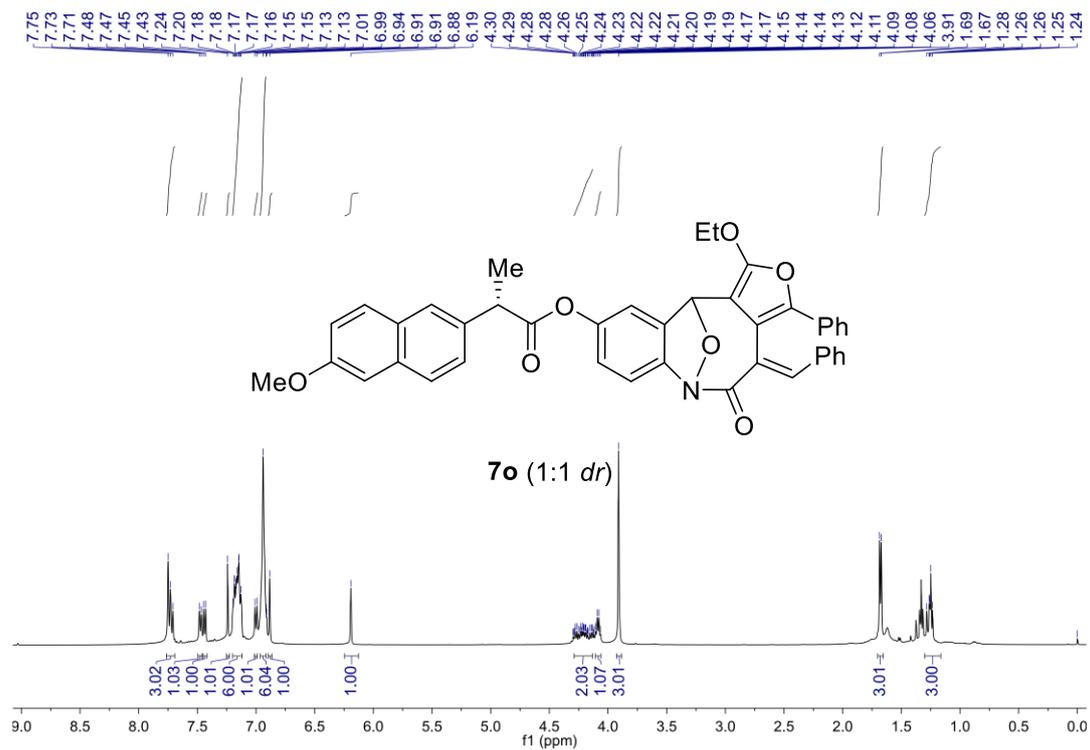


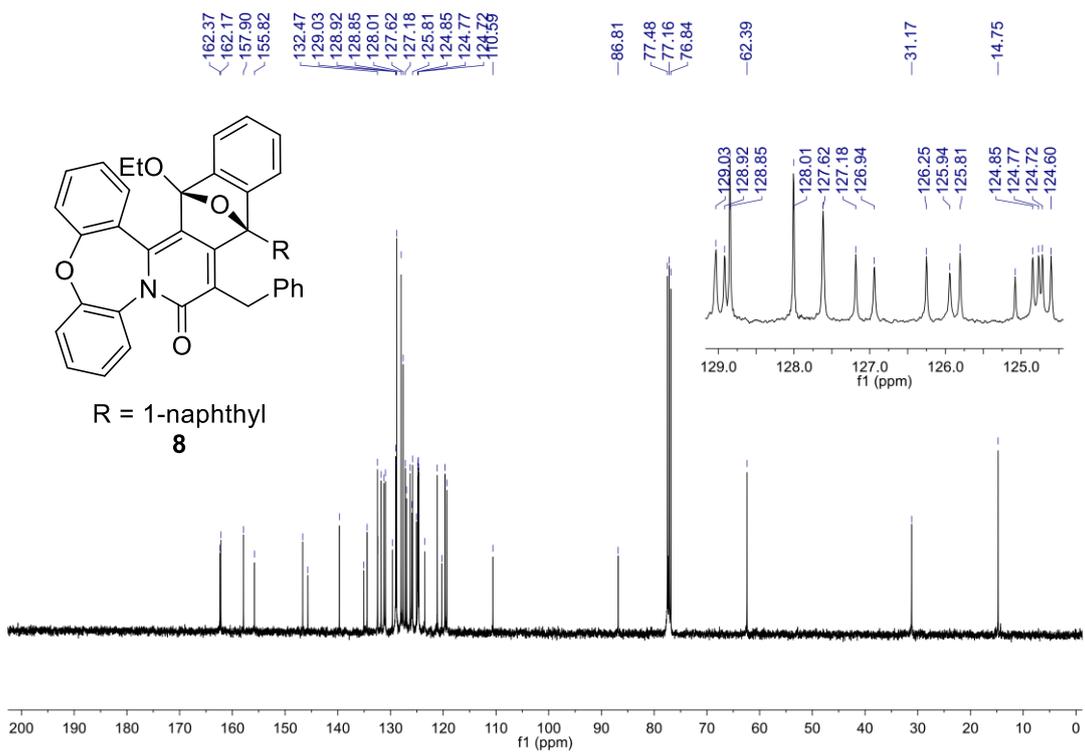
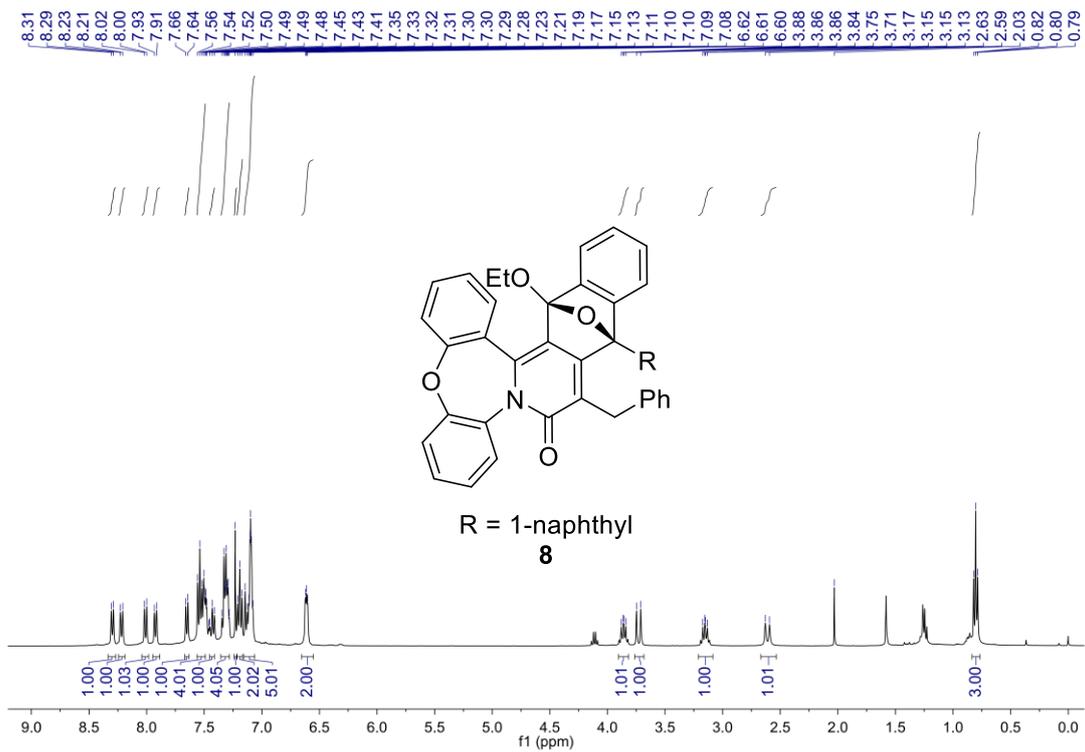


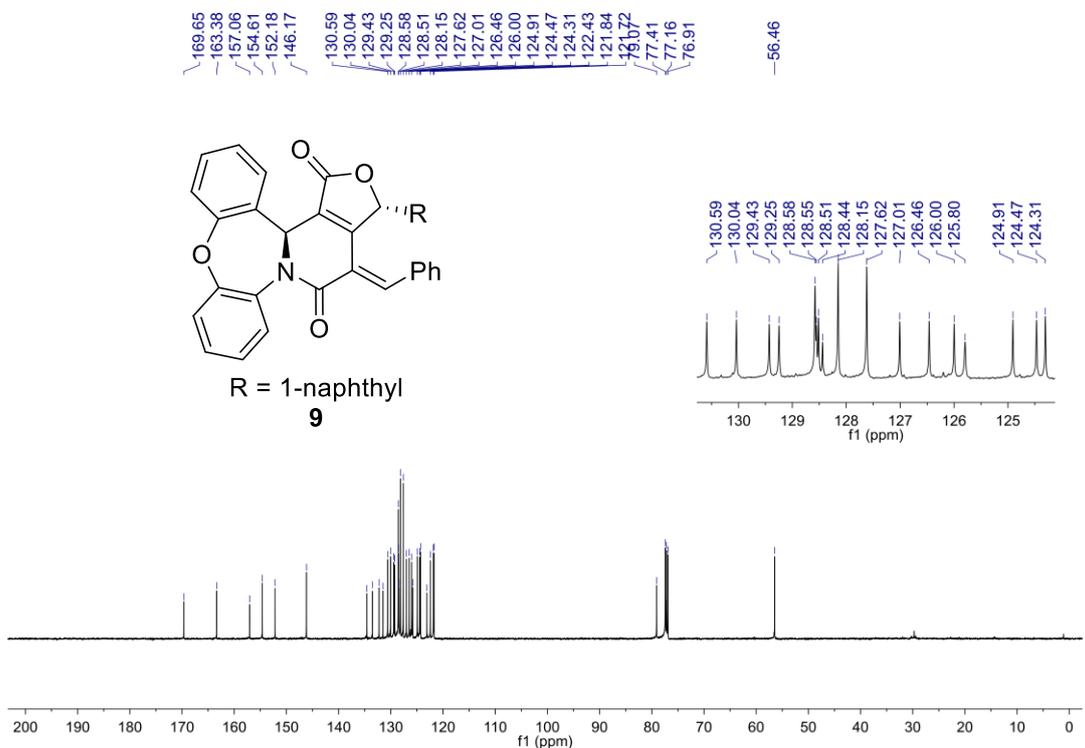
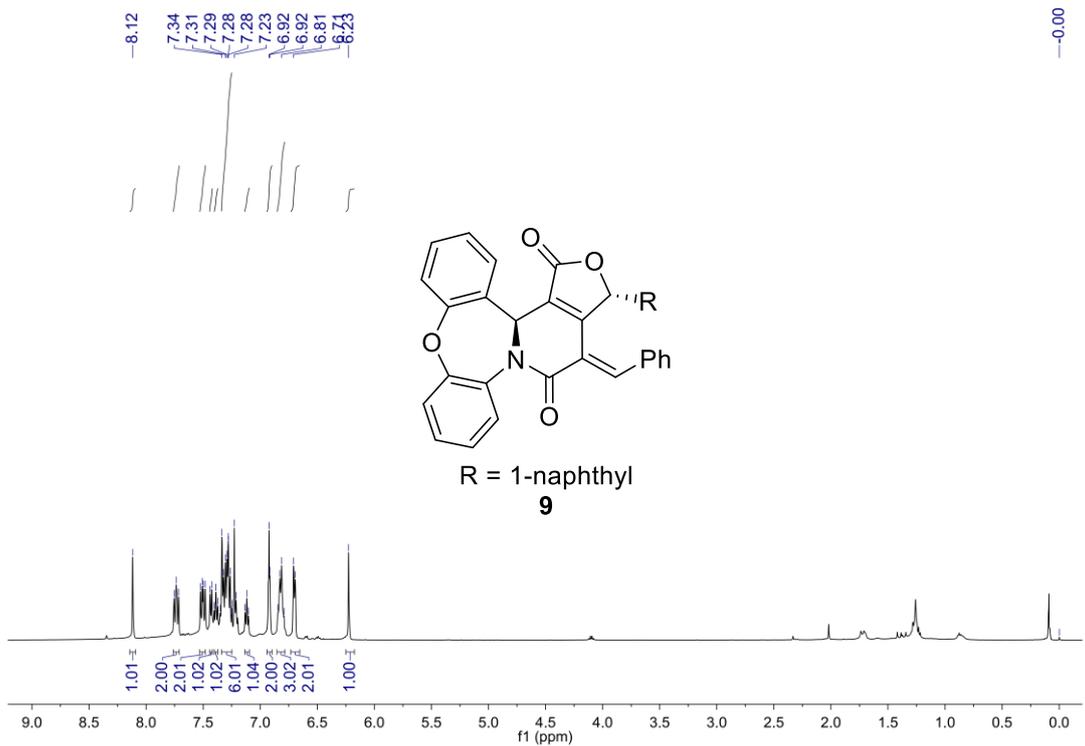


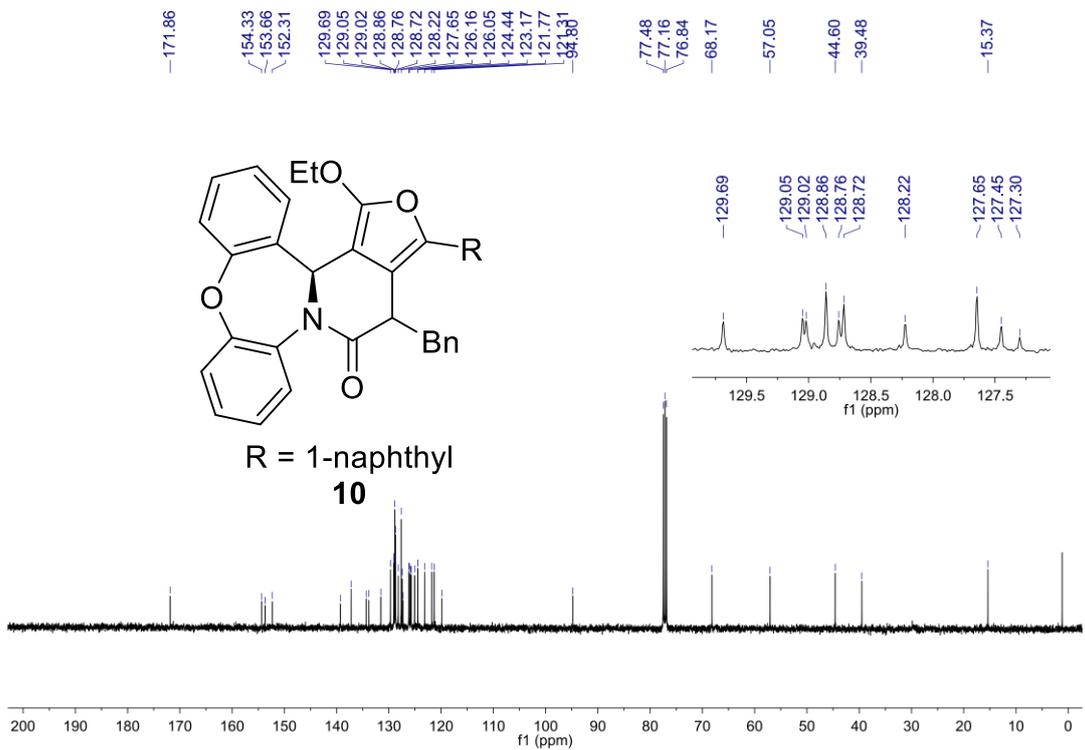
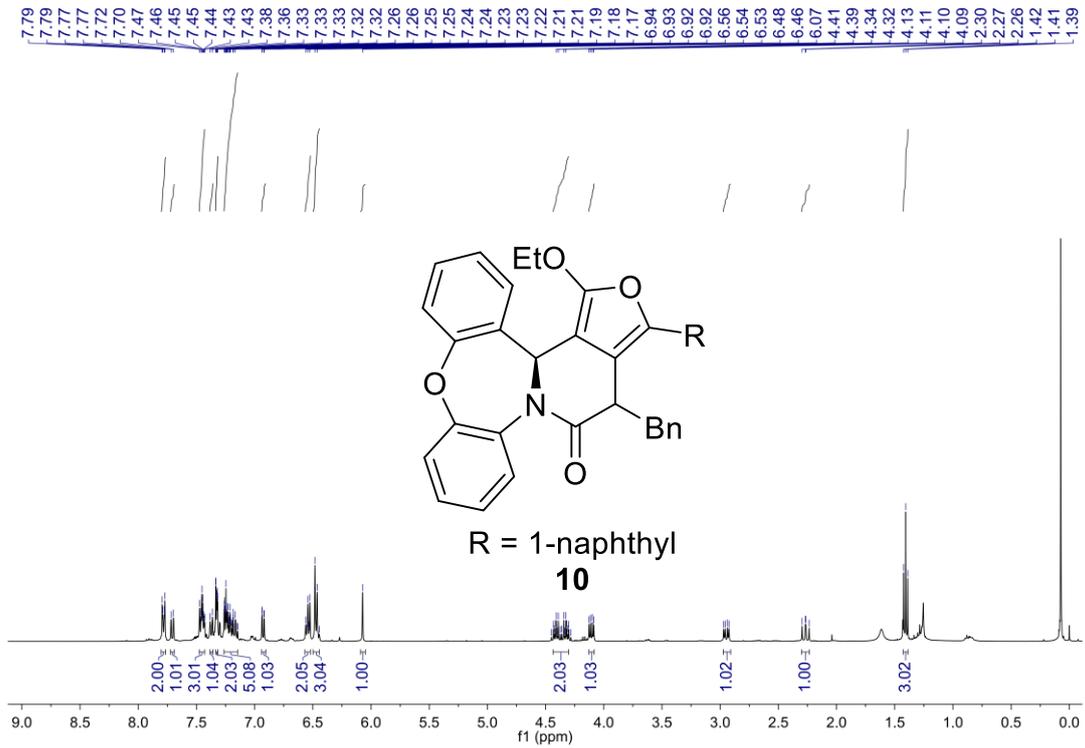


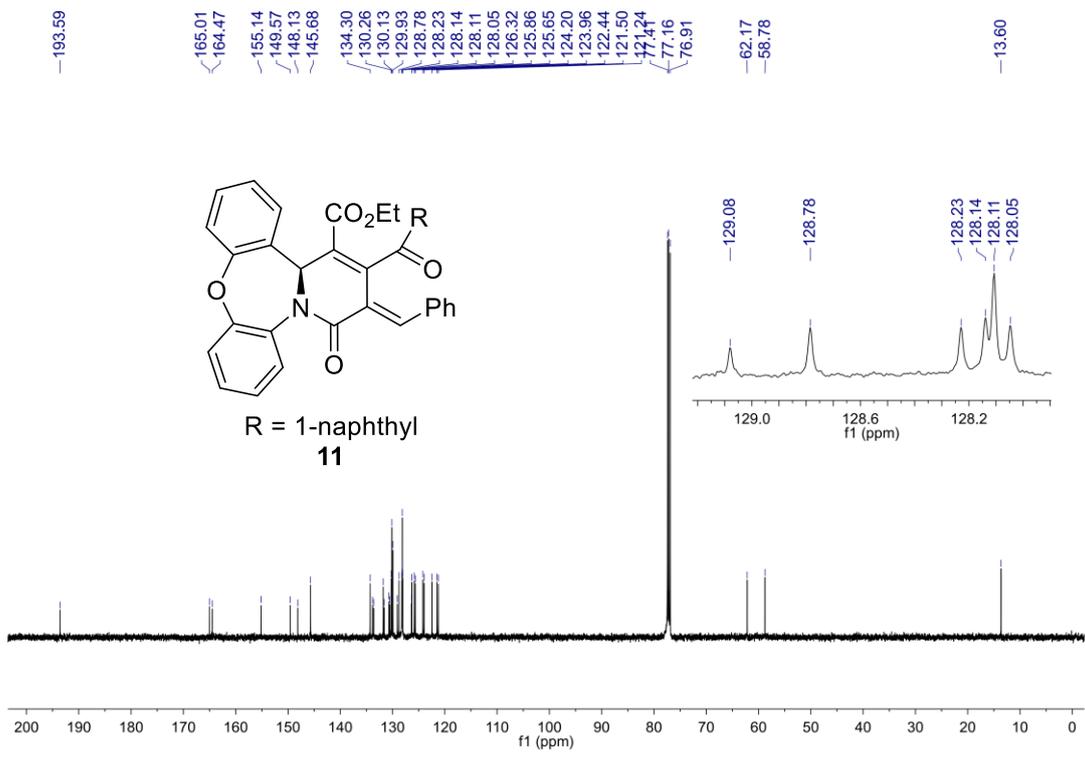
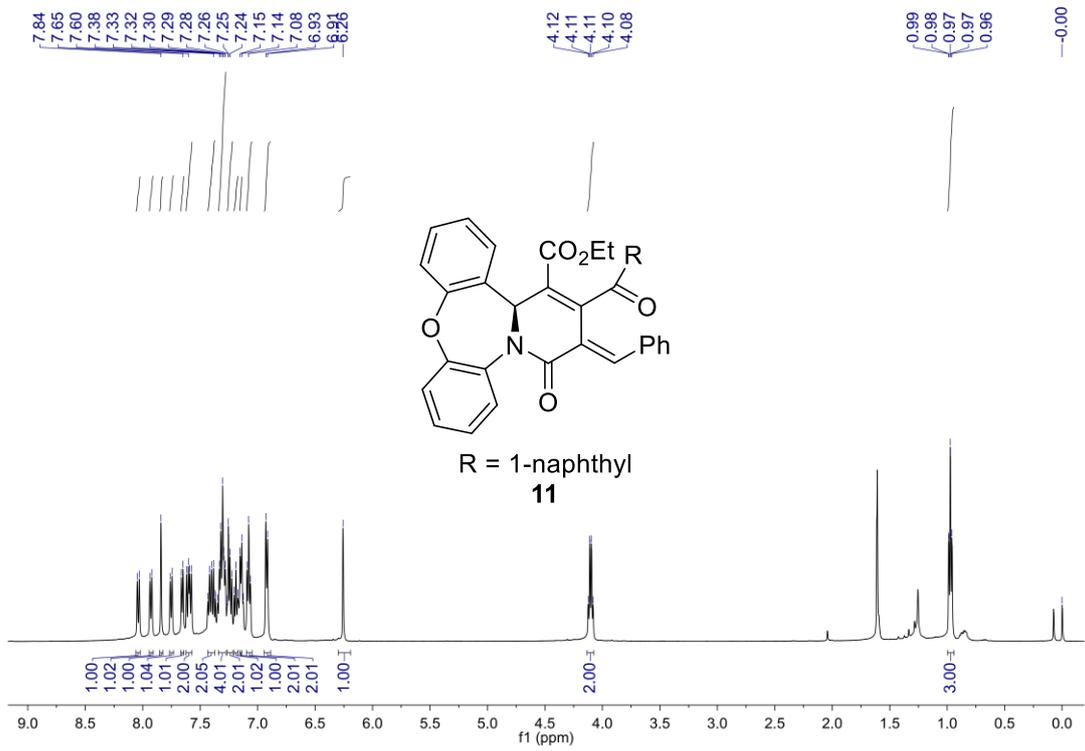


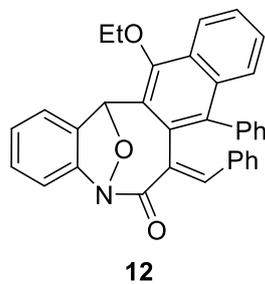
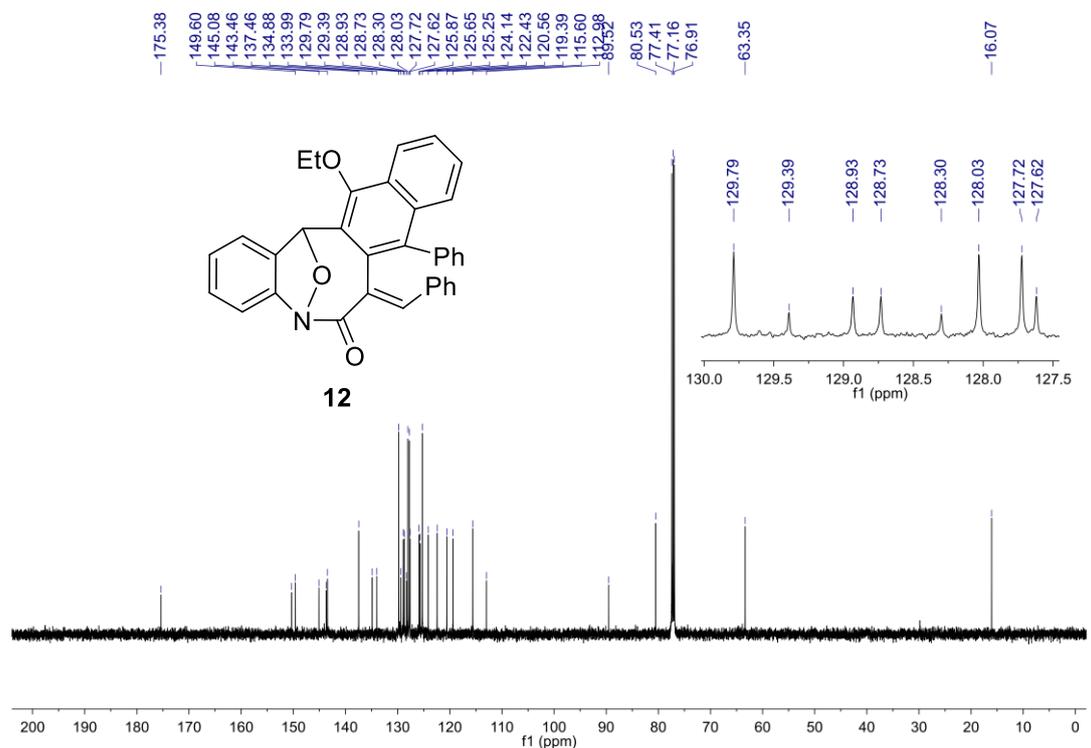
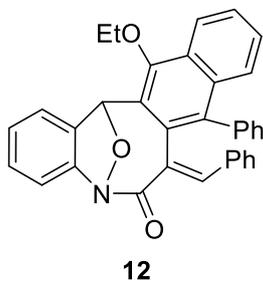
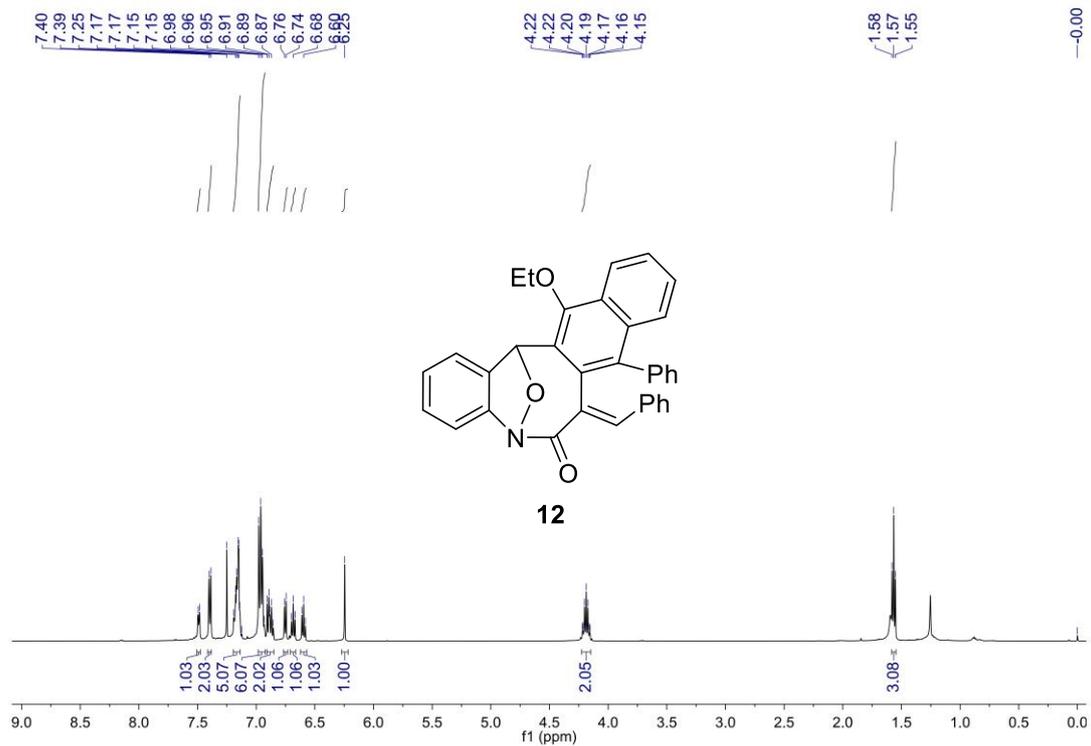


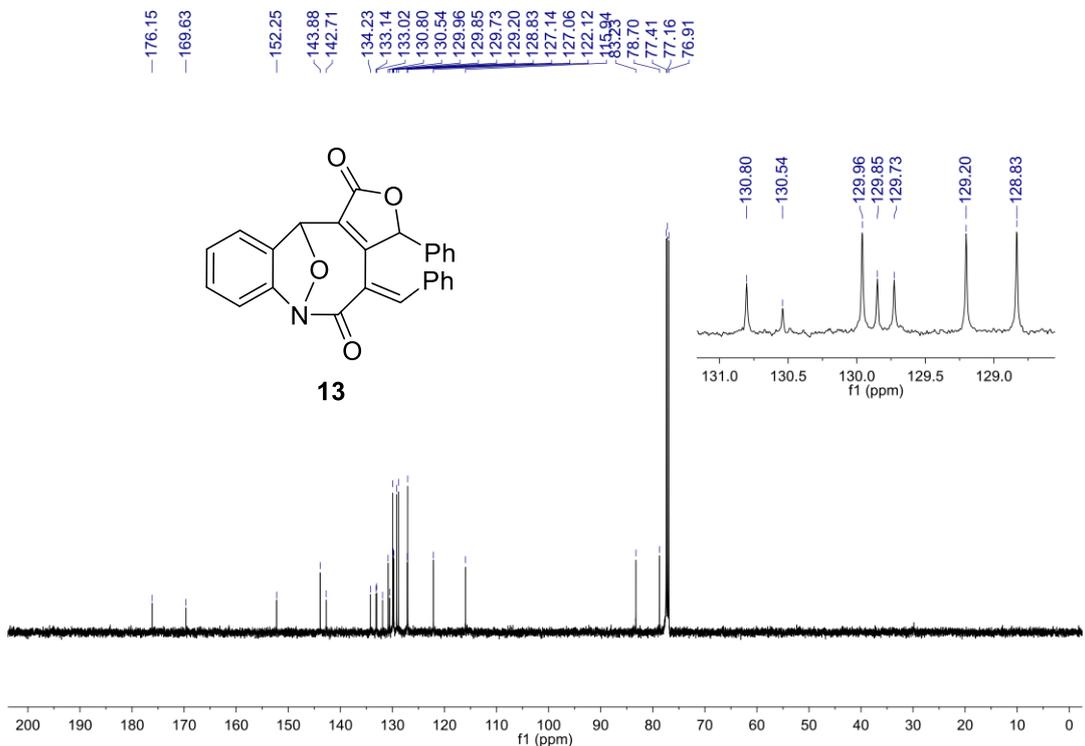
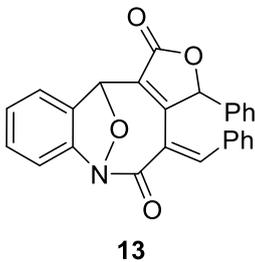
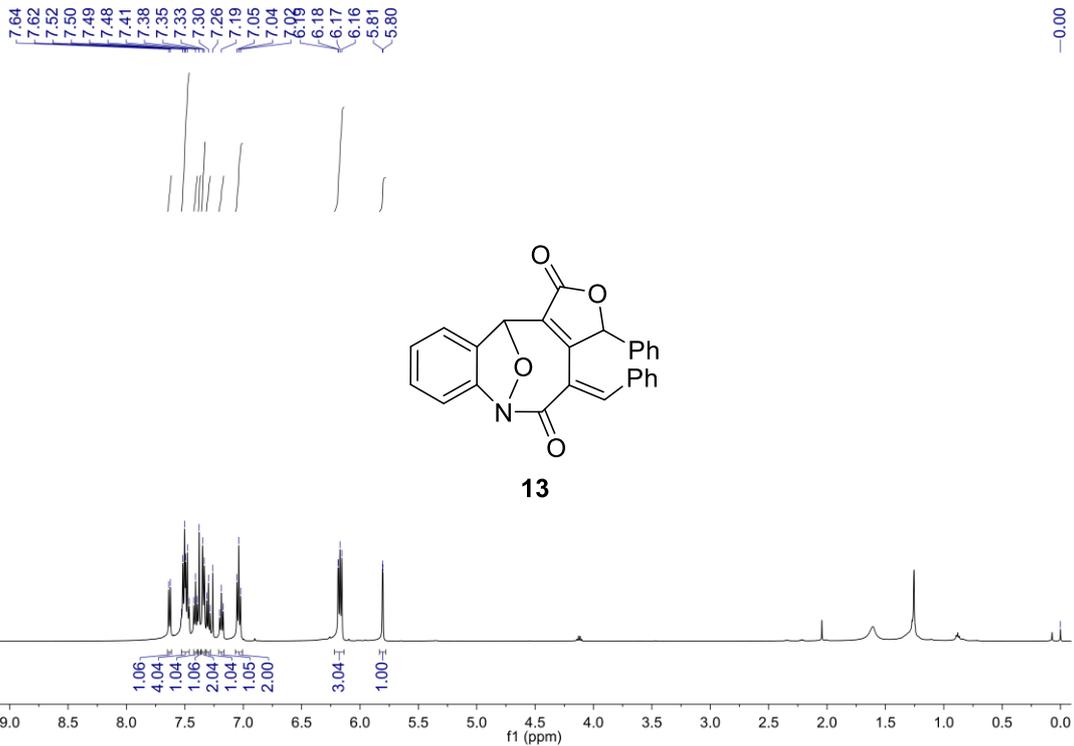


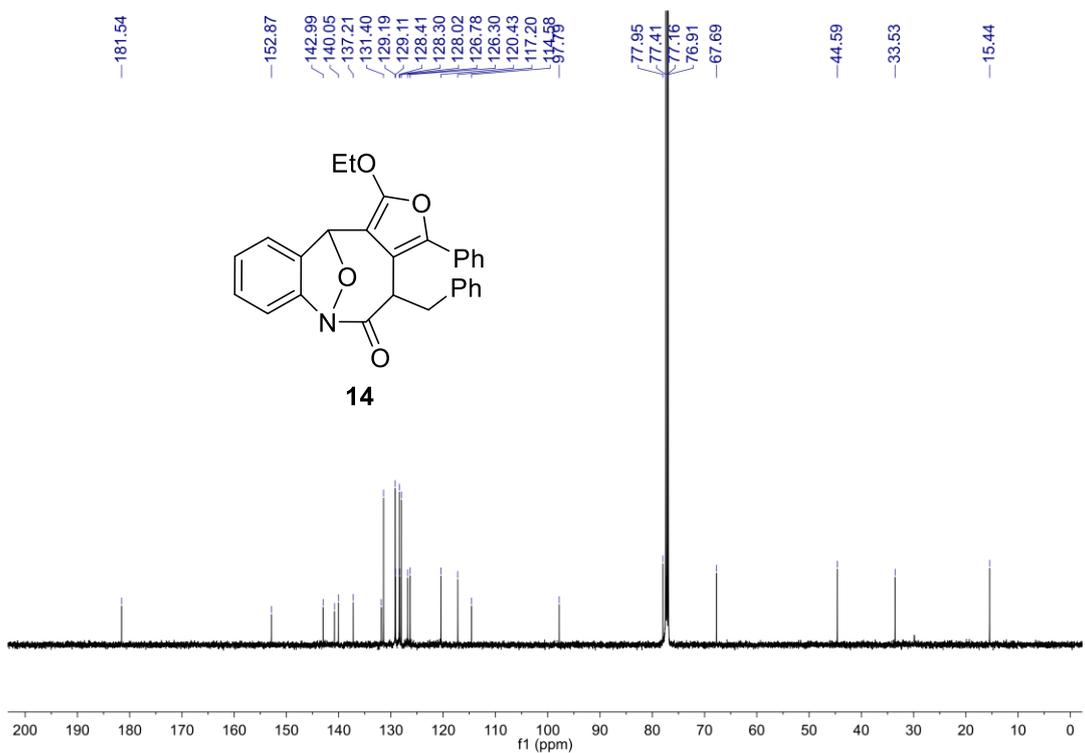
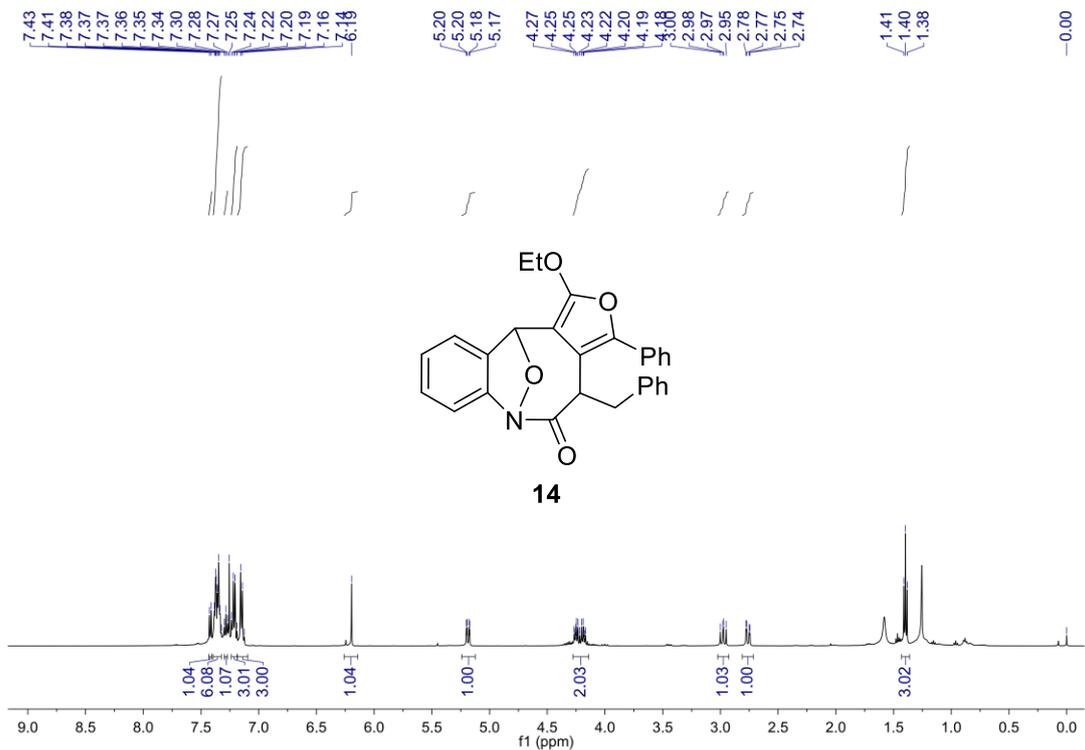


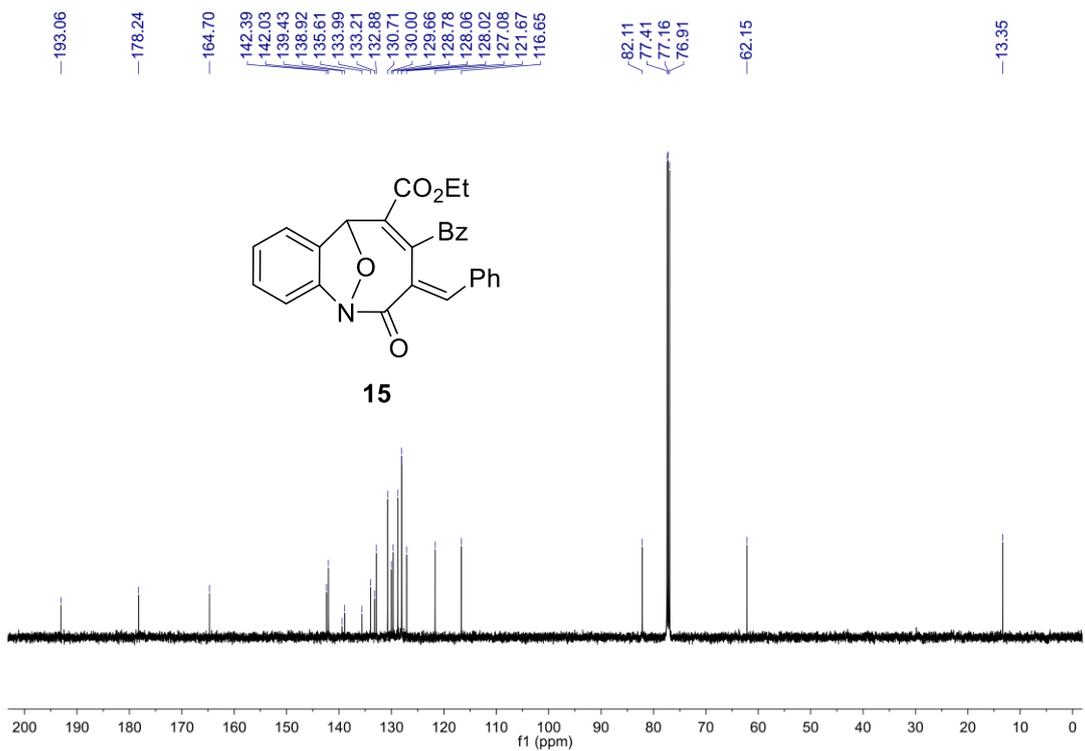
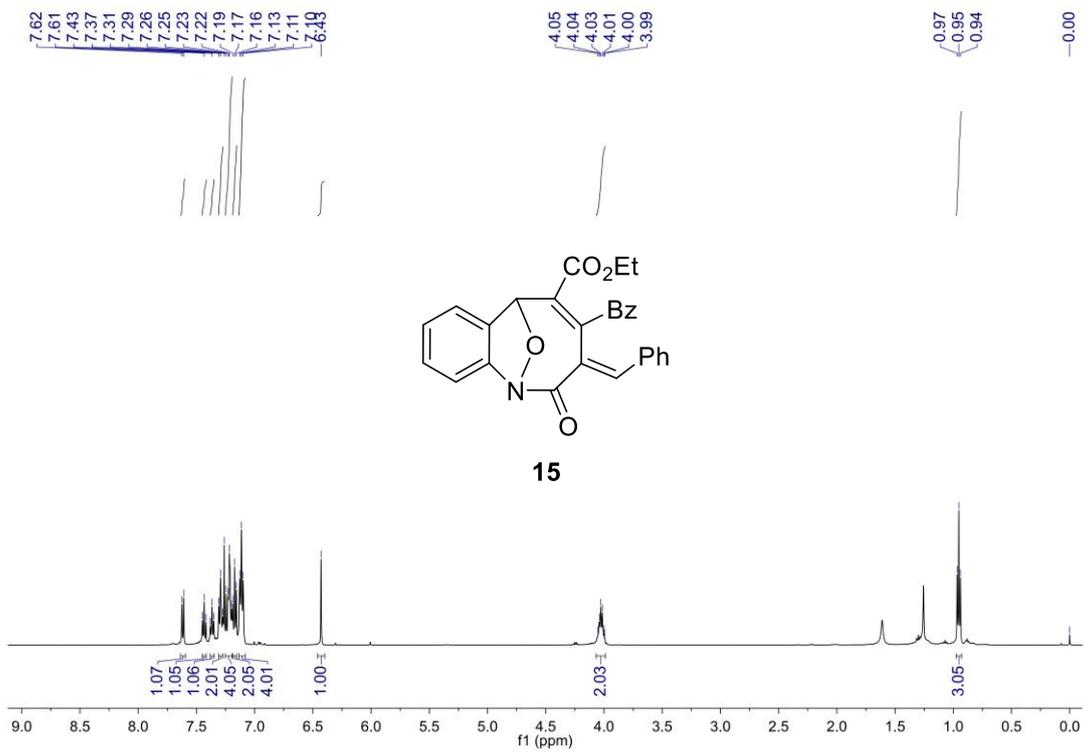








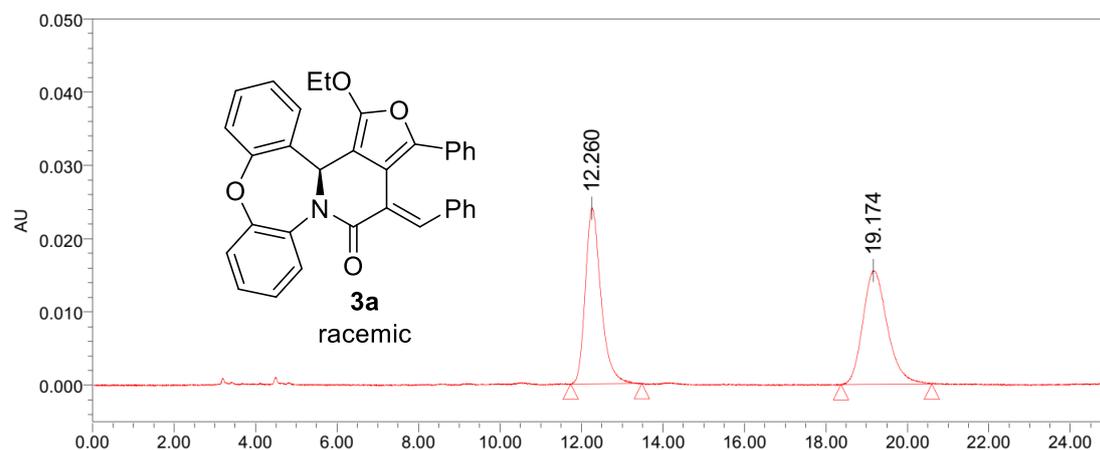




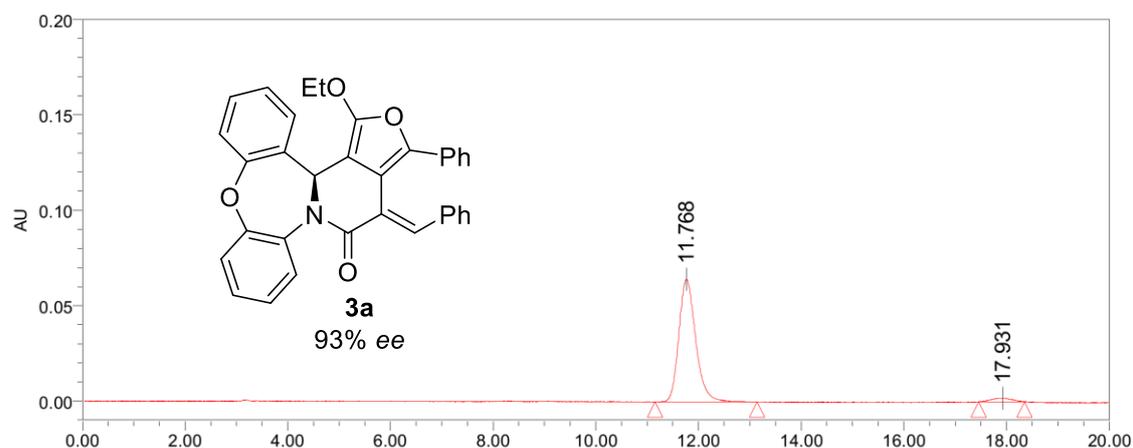
HPLC Analyses Figures of Compounds 3, 4, and 8-11

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



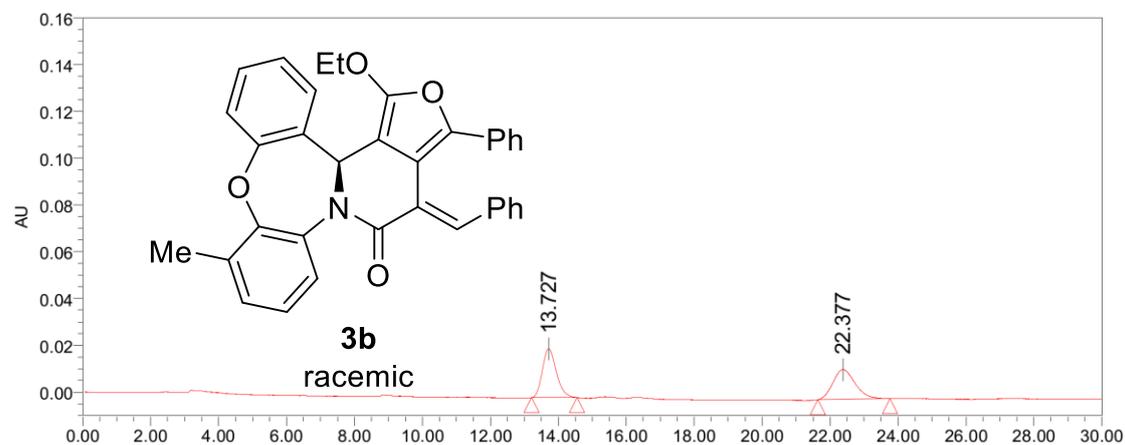
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1	12.260	648403	23985	49.99
2	19.174	648687	15513	50.01



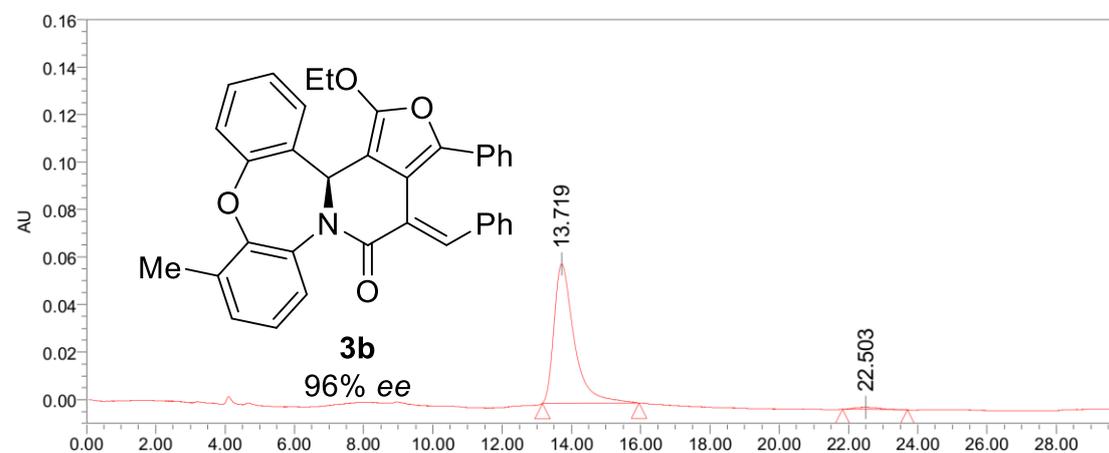
Entry	RT min	Height mV	Area mV.sec	% Area %
1	11.768	1479995	64378	96.27
2	17.931	57289	1991	3.73

Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



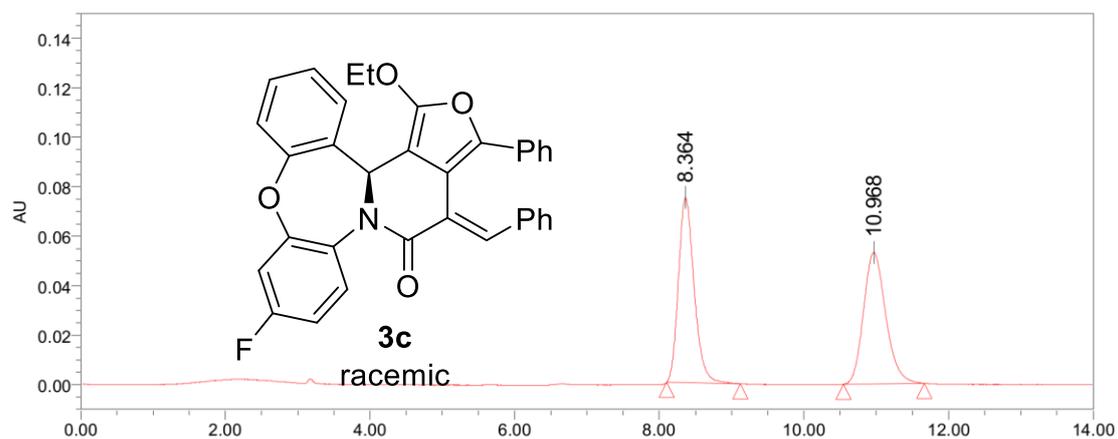
Entry	RT min	Height mV	Area mV.sec	% Area %
1	13.727	597058	20945	50.78
2	22.377	578710	12688	49.22



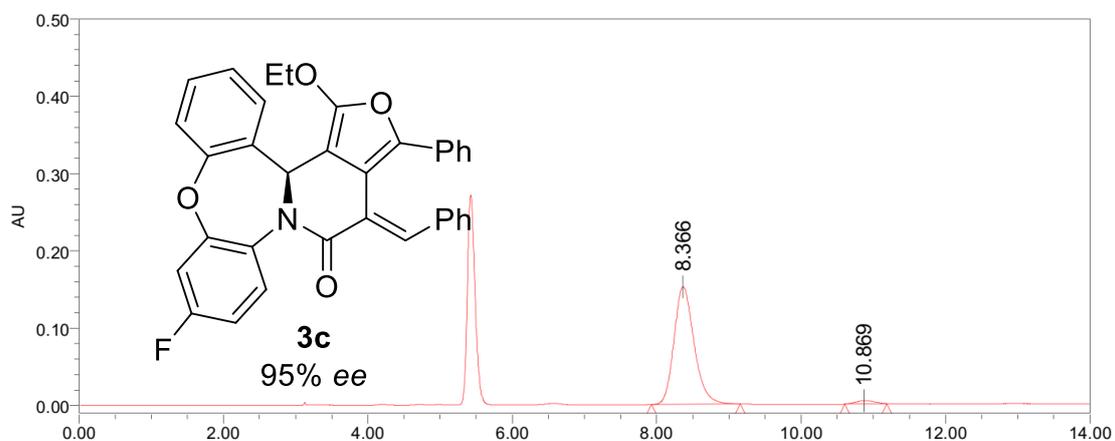
Entry	RT min	Height mV	Area mV.sec	% Area %
1	13.719	2361257	58608	97.84
2	22.503	52211	992	2.16

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



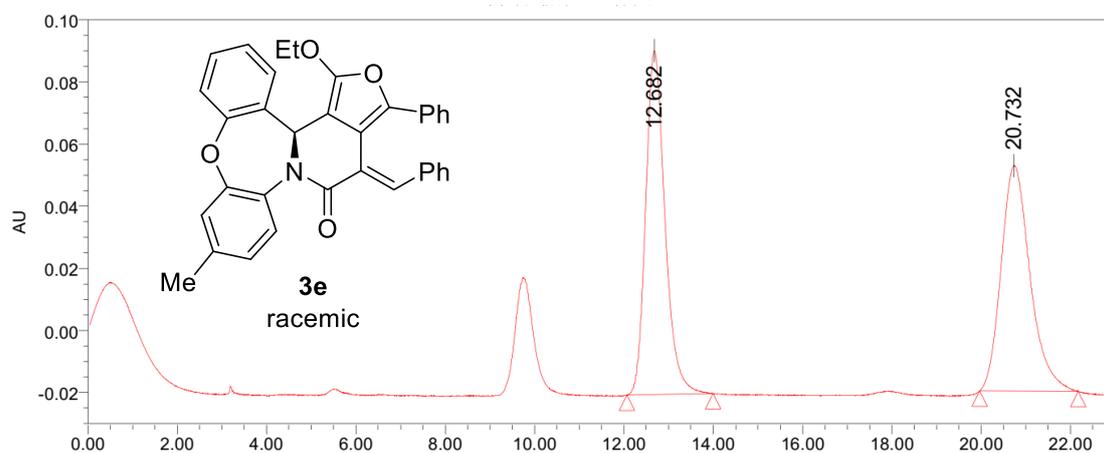
Entry	RT min	Height mV	Area mV.sec	% Area %
1	8.364	1135345	74812	50.00
2	10.968	1135518	53151	50.00



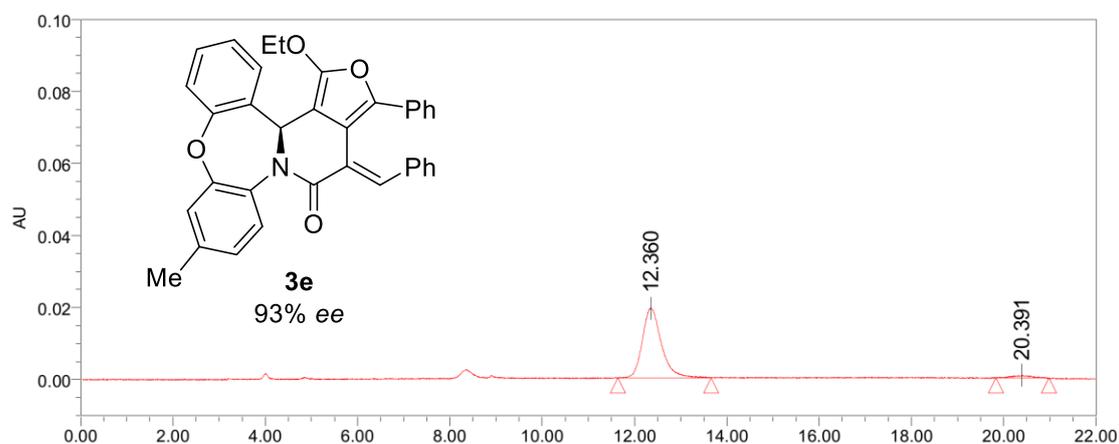
Entry	RT min	Height mV	Area mV.sec	% Area %
1	8.366	2951147	152297	97.47
2	10.869	76522	4092	2.53

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



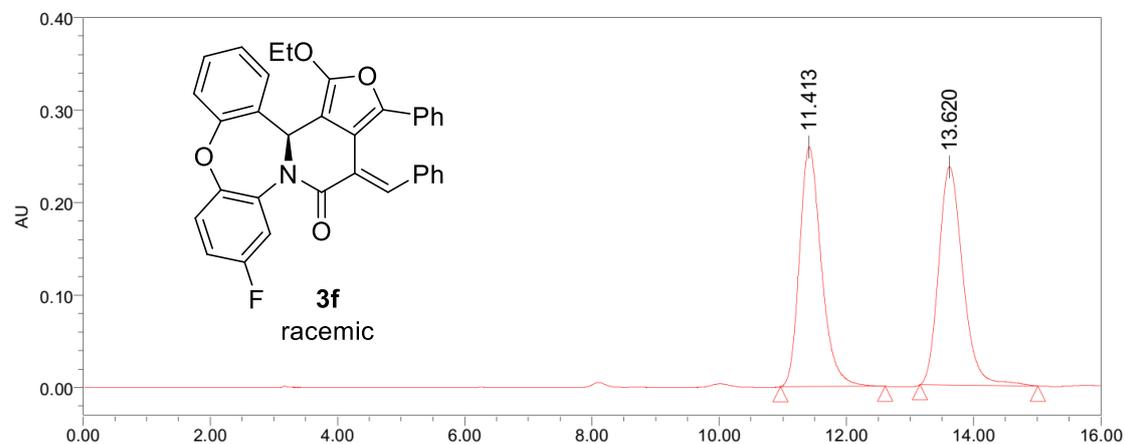
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1	12.682	3292371	110634	50.12
2	20.732	3276205	72592	49.88



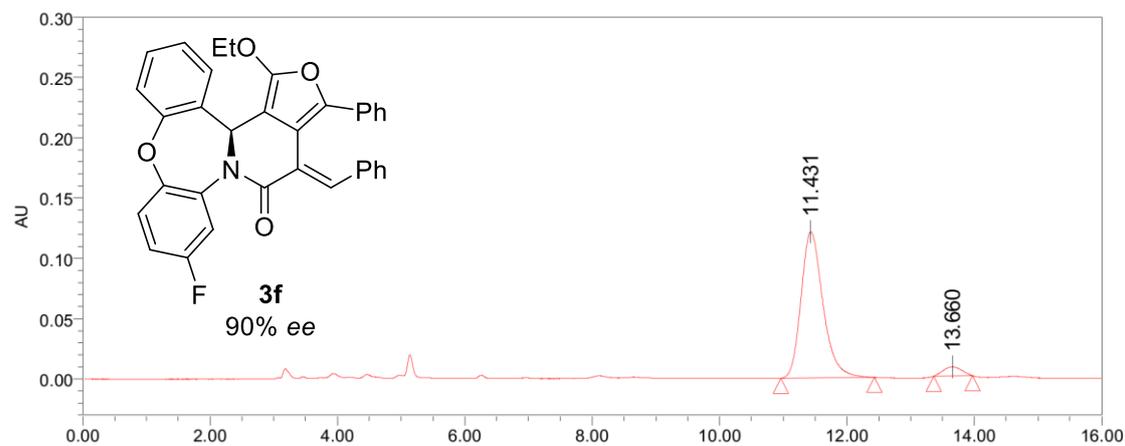
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.360	558796	19403	96.52
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Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



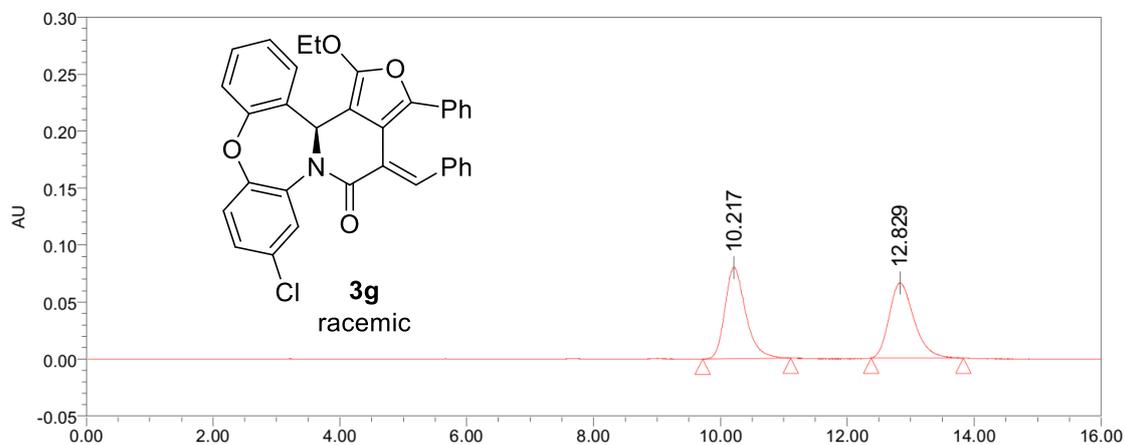
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1	11.413	6183908	259100	49.85
2	13.620	6221258	235868	50.15



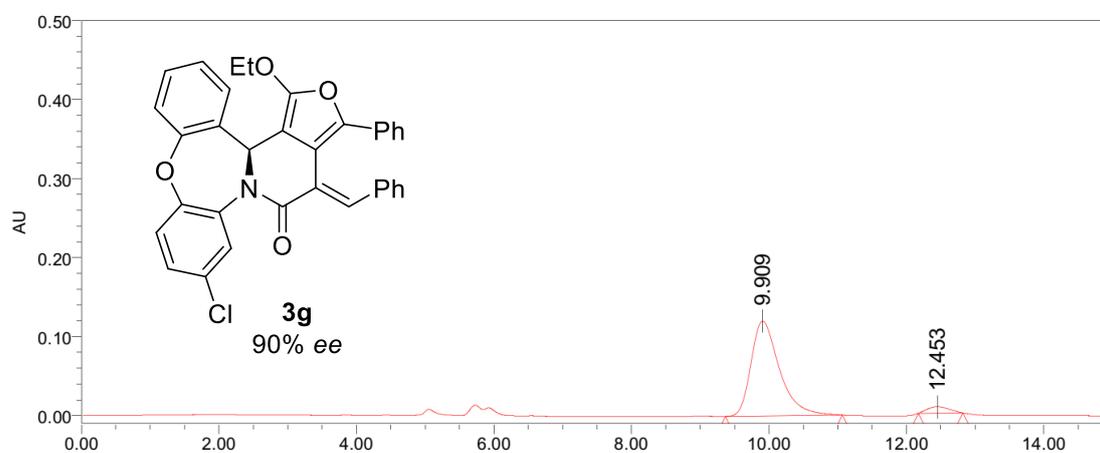
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1	11.431	2904457	121170	95.07
2	13.660	150587	7474	4.93

Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



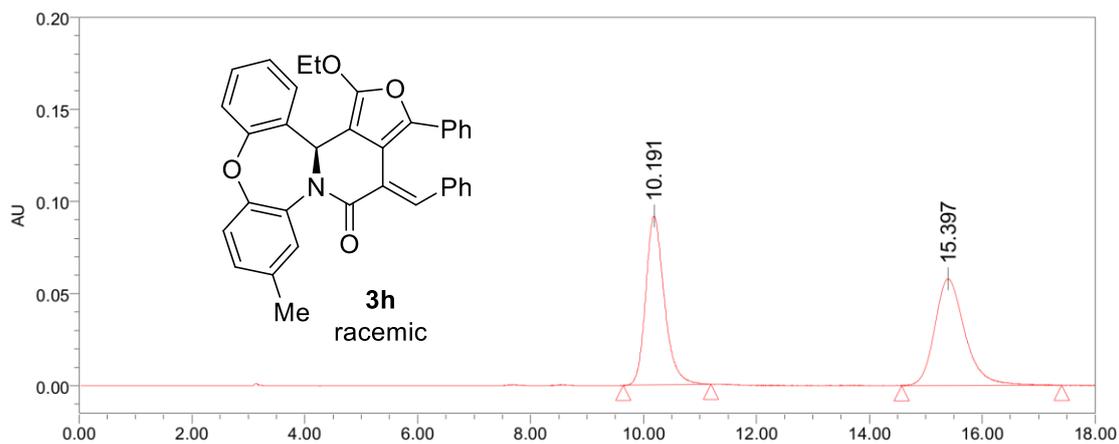
Entry	RT min	Height mV	Area mV.sec	% Area %
1	10.217	1836621	80072	50.45
2	12.829	1803558	66009	49.55



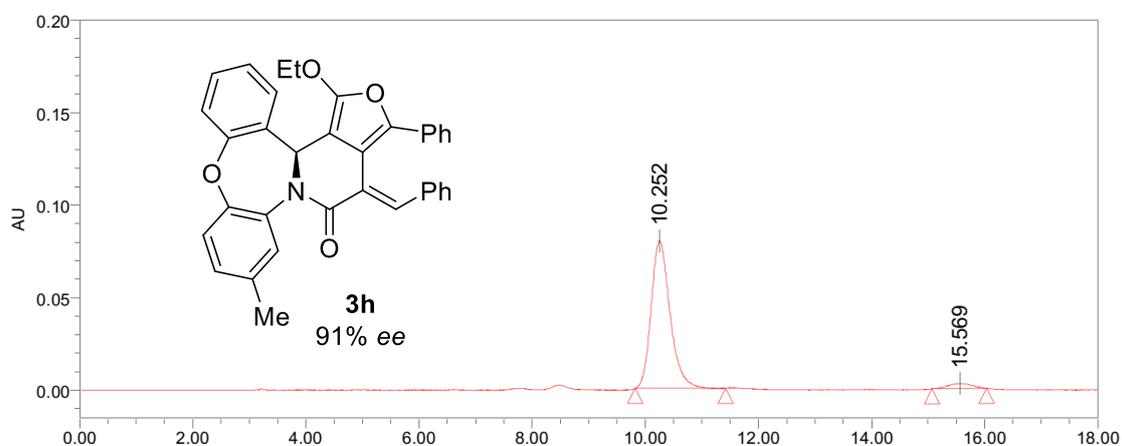
Entry	RT min	Height mV	Area mV.sec	% Area %
1	9.909	3438322	120178	95.02
2	12.453	180191	8085	4.98

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



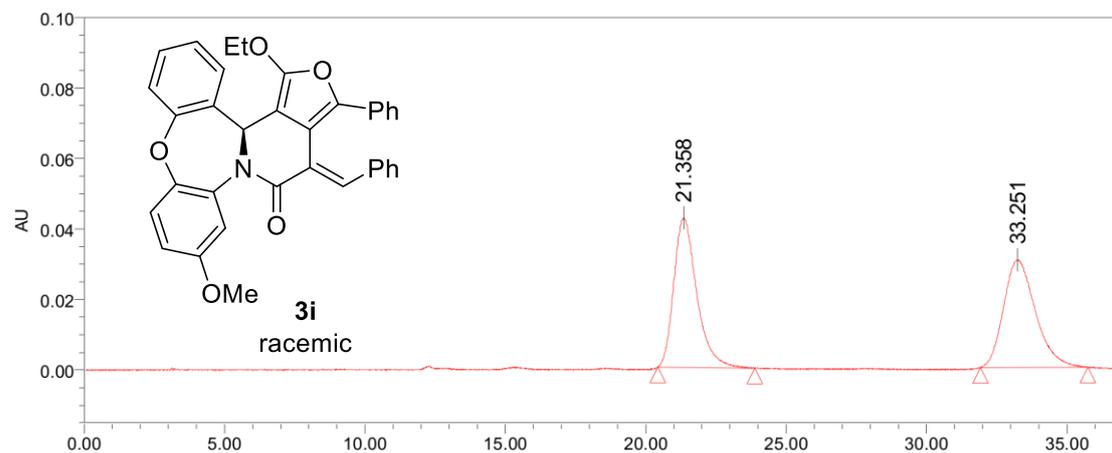
Entry	RT min	Height mV	Area mV.sec	% Area %
1	10.191	2114177	91730	49.66
2	15.397	2143216	57826	50.34



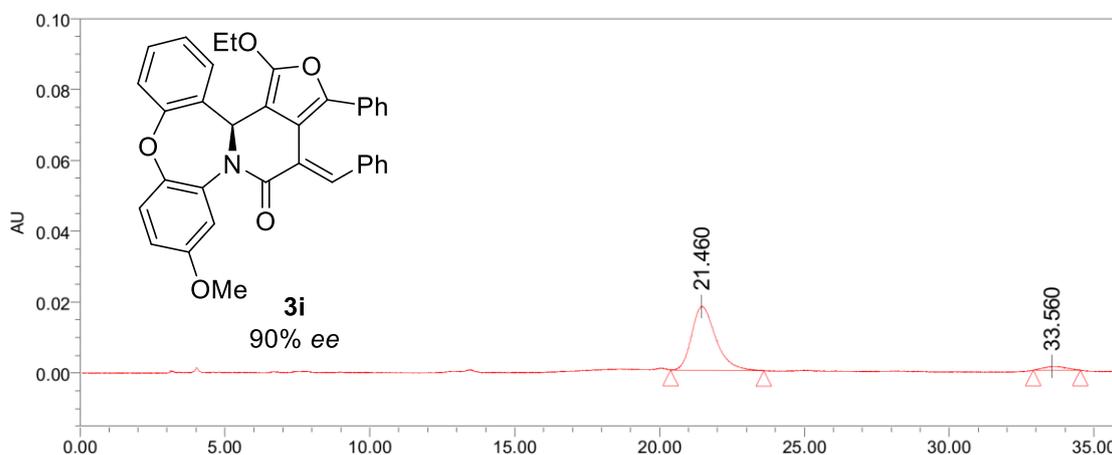
Entry	RT min	Height mV	Area mV.sec	% Area %
1	10.252	1849267	79607	95.67
2	15.569	83642	2791	4.33

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



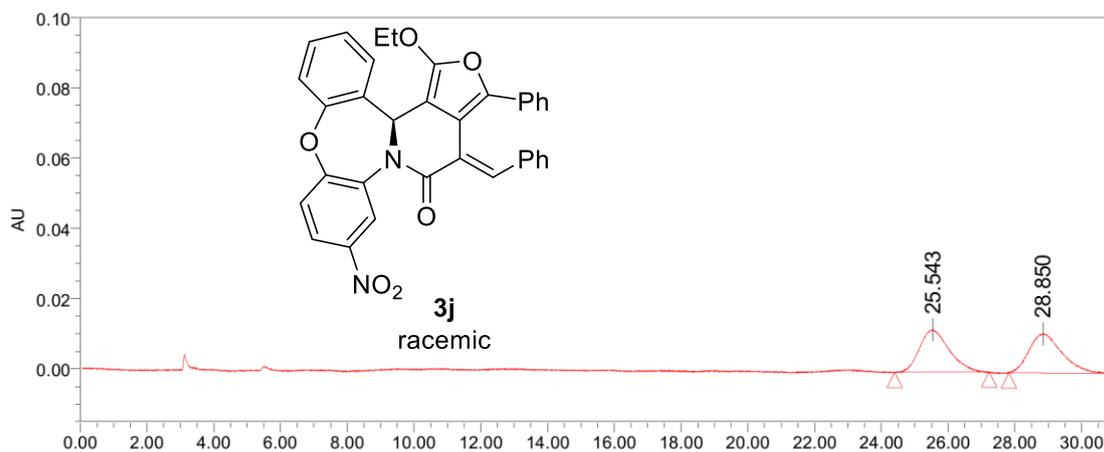
Entry	RT min	Height mV	Area mV.sec	% Area %
1	21.358	2417378	42369	50.00
2	33.251	2417164	30510	50.00



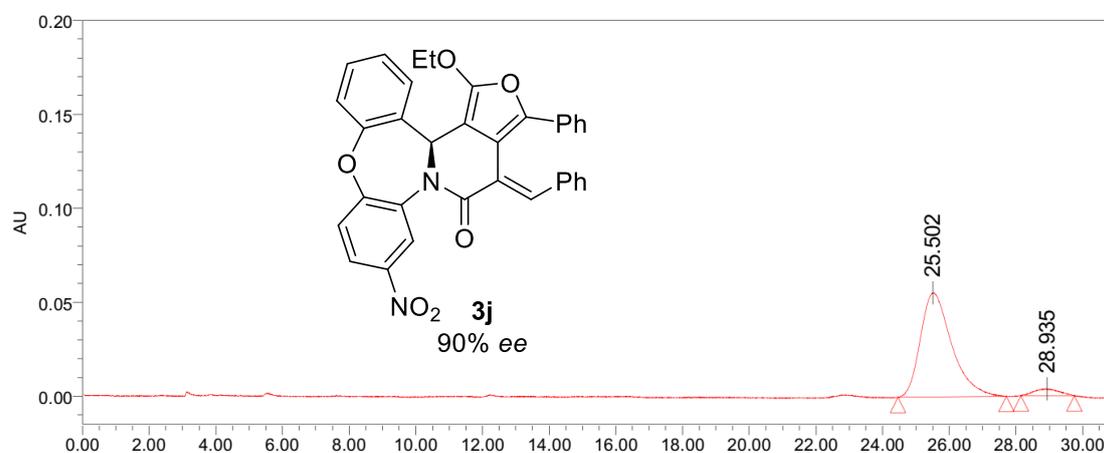
Entry	RT min	Height mV	Area mV.sec	% Area %
1	21.460	1044566	18033	95.01
2	33.560	54853	1070	4.99

Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



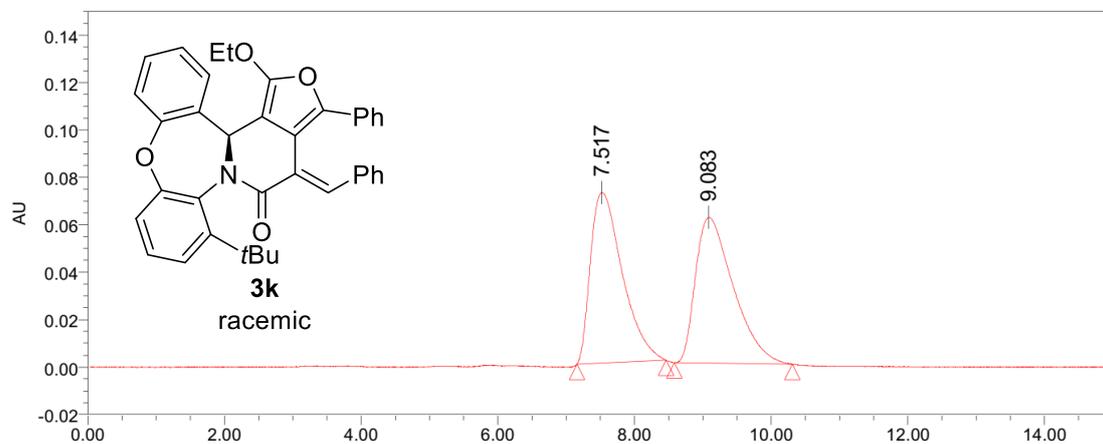
Entry	RT min	Height mV	Area mV.sec	% Area %
1	25.543	748184	12105	49.36
2	28.850	767736	11228	50.64



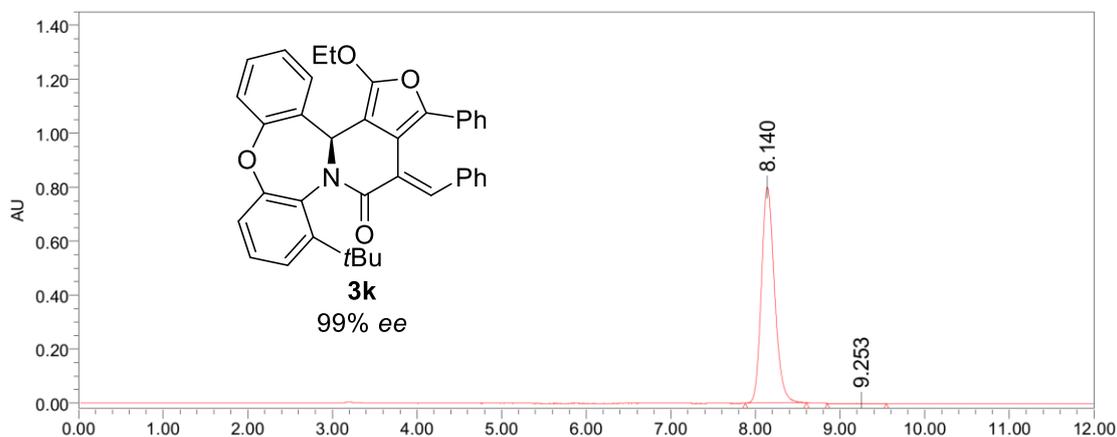
Entry	RT min	Height mV	Area mV.sec	% Area %
1	25.502	3592847	55368	95.06
2	28.935	186624	3654	4.94

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



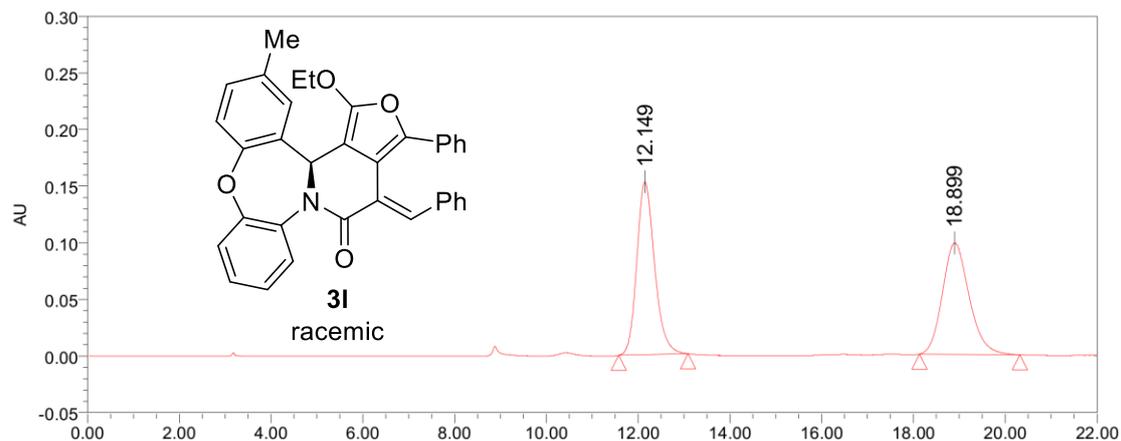
Entry	RT min	Height mV	Area mV.sec	% Area %
1	7.517	2329296	71949	49.53
2	9.083	2373674	61578	50.47



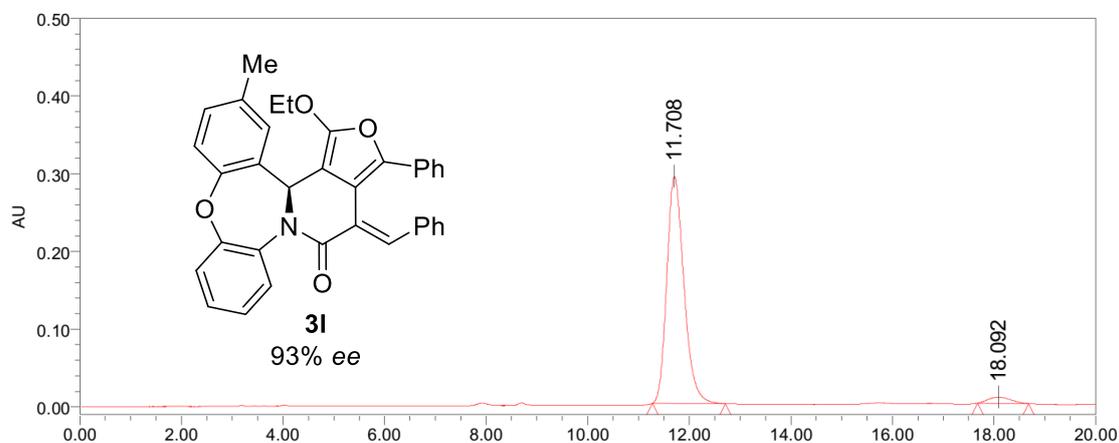
Entry	RT min	Height mV	Area mV.sec	% Area %
1	8.140	8613877	800077	99.96
2	9.253	3683	342	0.04

Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



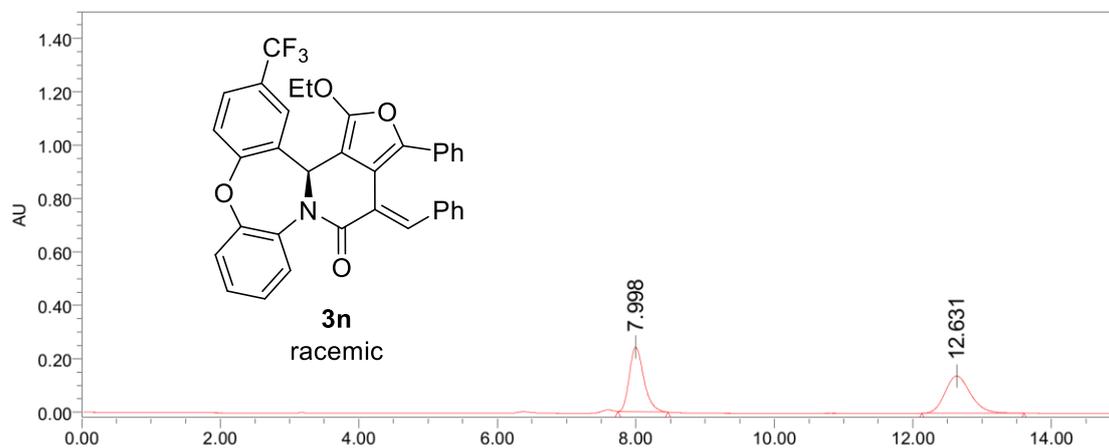
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.149	4070848	152667	50.41
2	18.899	4004064	98322	49.59



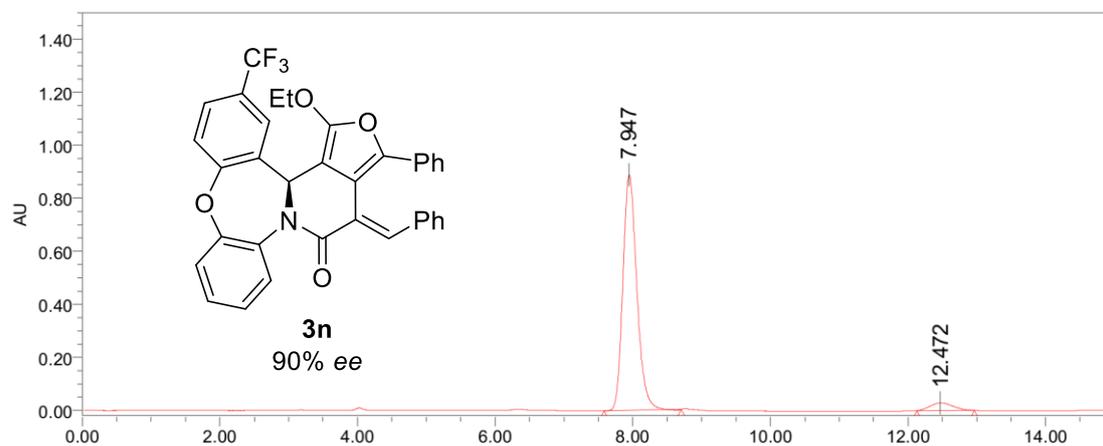
Entry	RT min	Height mV	Area mV.sec	% Area %
1	11.708	6873575	292048	96.55
2	18.092	245816	8004	3.45

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



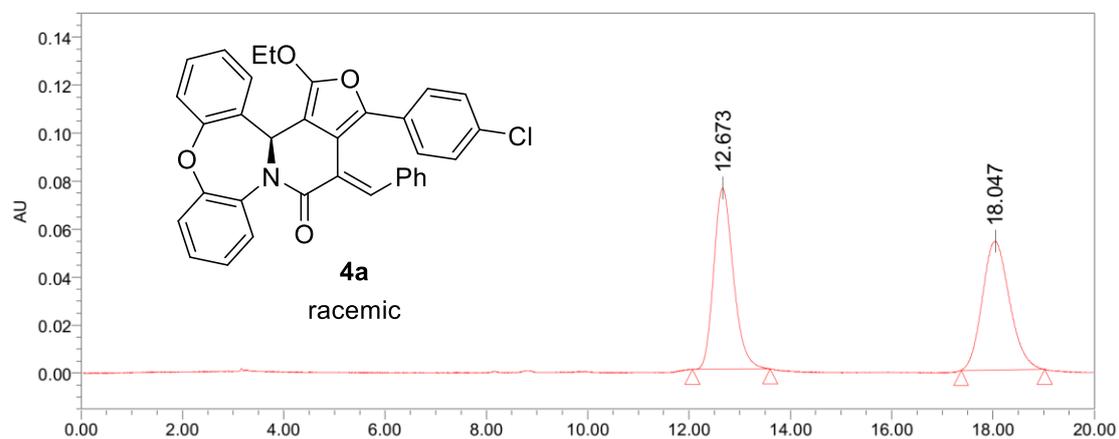
Entry	RT min	Height mV	Area mV.sec	% Area %
1	7.998	3528471	242351	49.67
2	12.631	3575101	139879	50.33



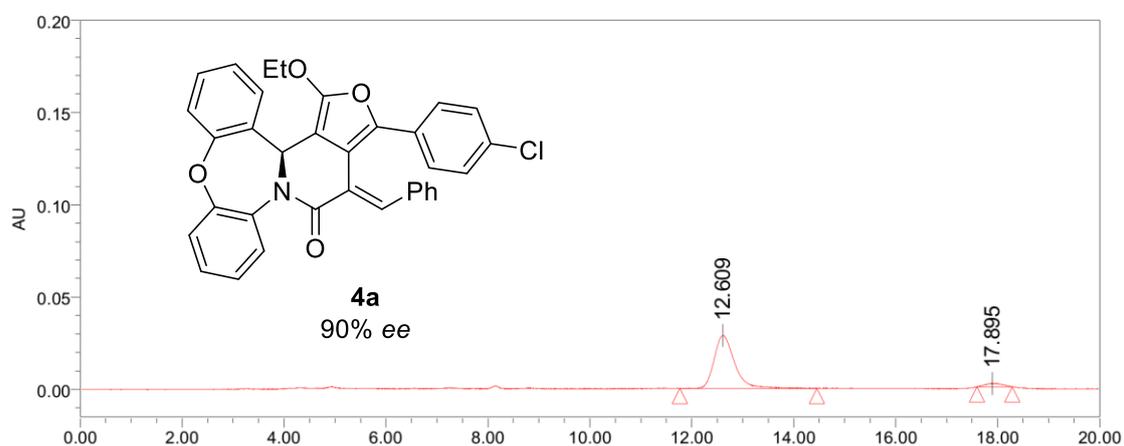
Entry	RT min	Height mV	Area mV.sec	% Area %
1	7.947	12497165	887654	95.01
2	12.472	656335	28586	4.99

Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



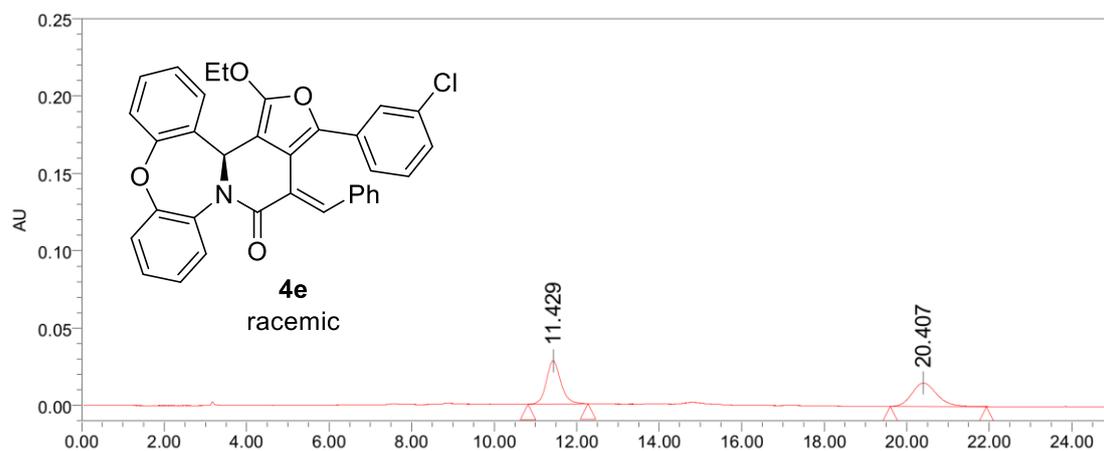
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.673	2026397	75422	50.16
2	18.047	2013535	53644	49.84



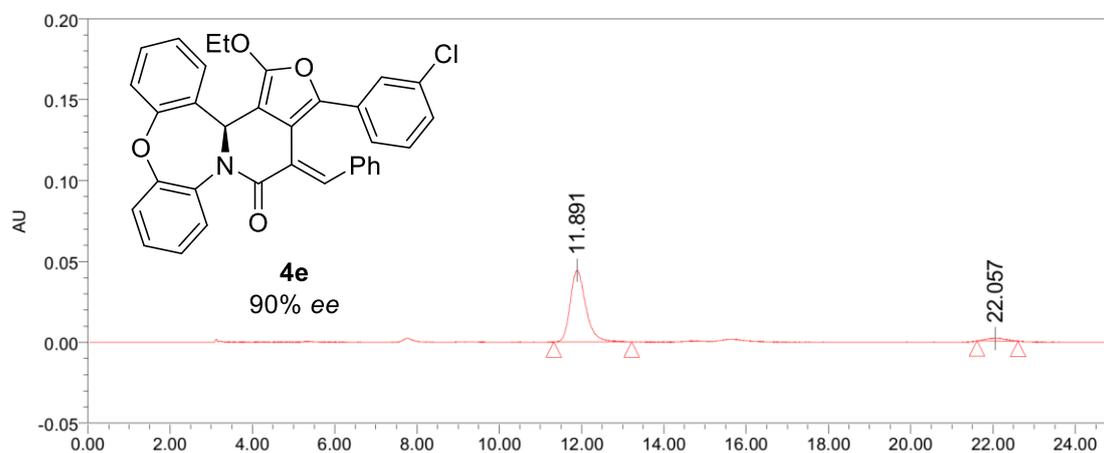
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.609	796689	28697	94.82
2	17.895	43491	1786	5.18

Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



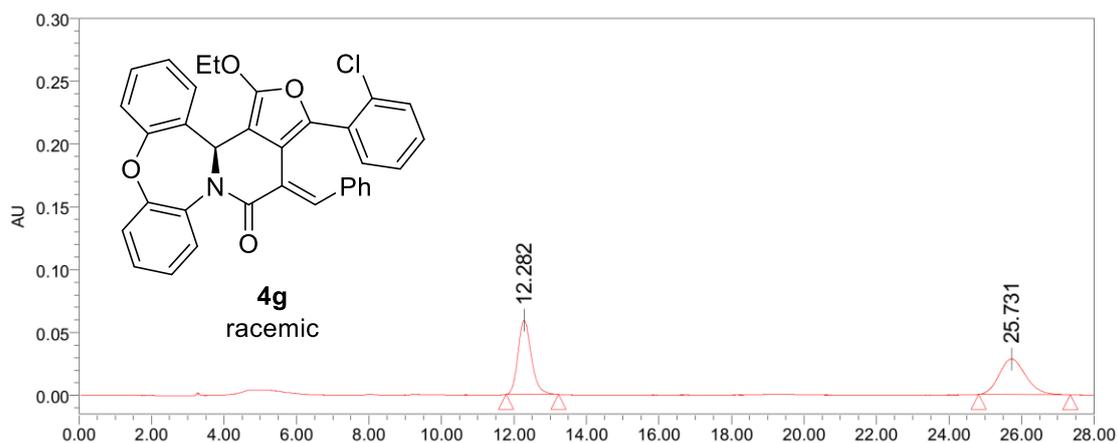
Entry	RT min	Height mV	Area mV.sec	% Area %
1	11.429	672583	27881	51.61
2	20.407	630724	15159	48.39



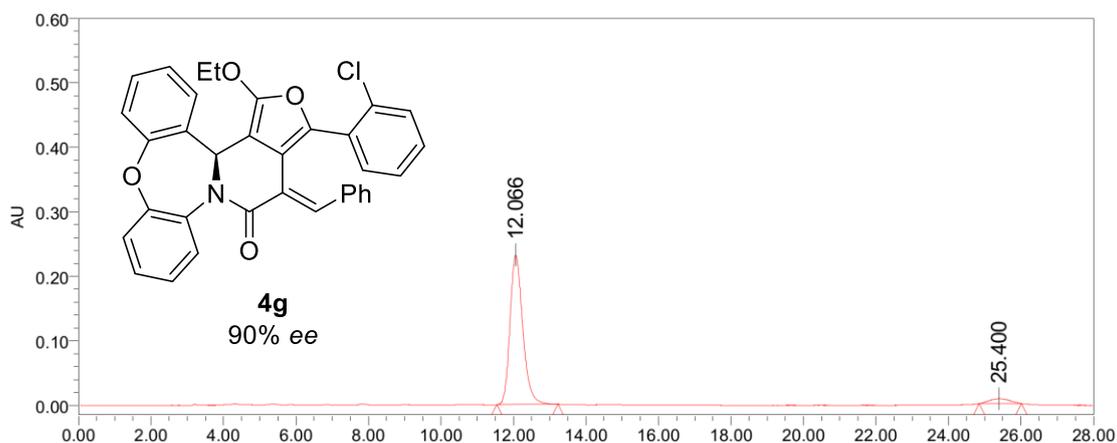
Entry	RT min	Height mV	Area mV.sec	% Area %
1	11.891	1171564	44222	95.00
2	22.057	61640	1837	5.00

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



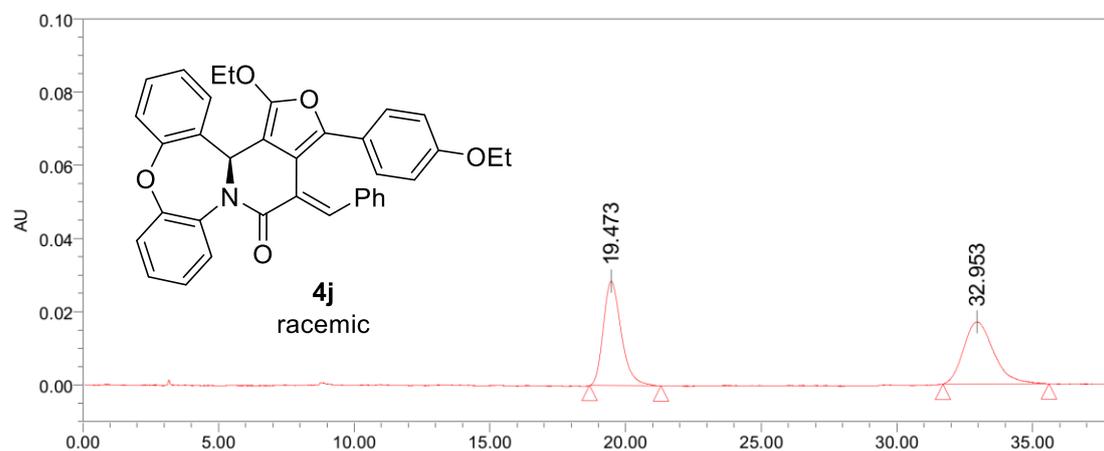
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.282	1504896	58945	50.91
2	25.731	1450853	28377	49.09



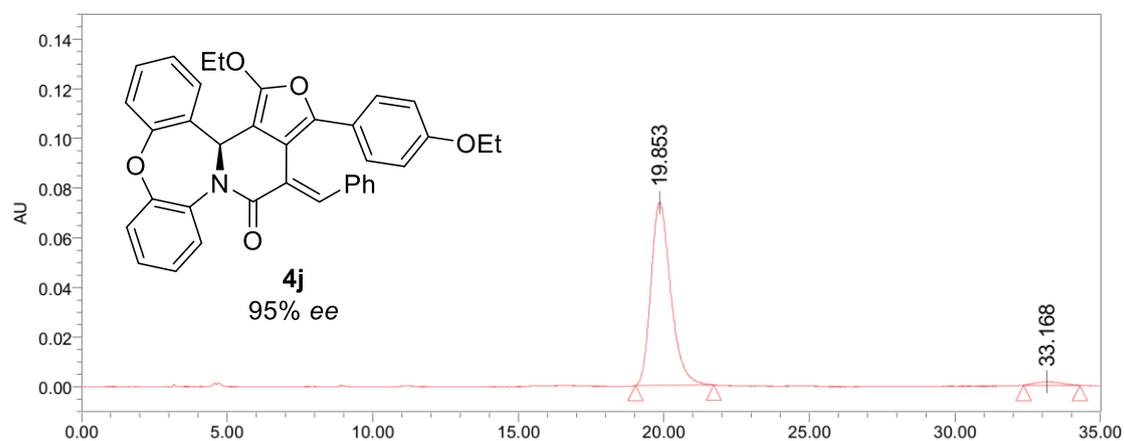
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.066	5708977	232318	95.11
2	25.400	293834	7522	4.89

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



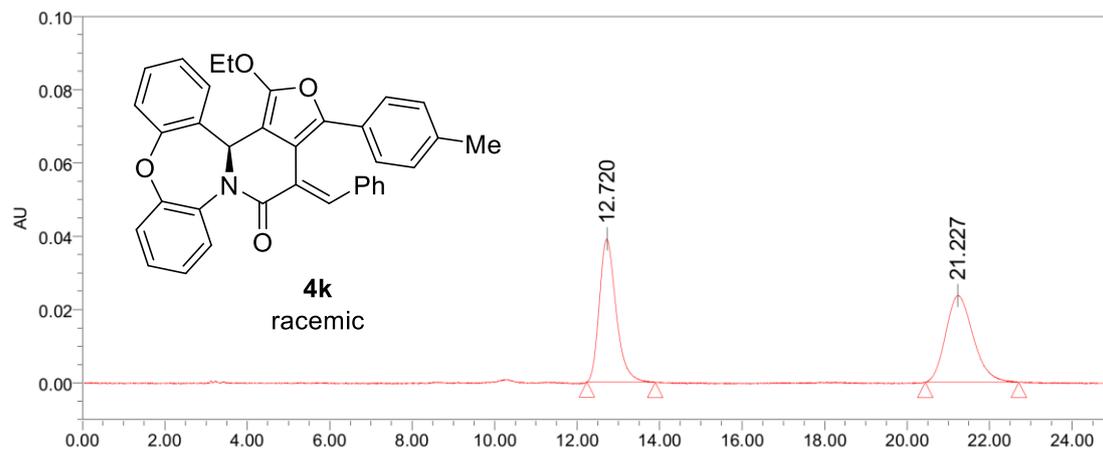
Entry	RT min	Height mV	Area mV.sec	% Area %
1	19.473	1309496	28540	49.97
2	32.953	1311163	16969	50.03



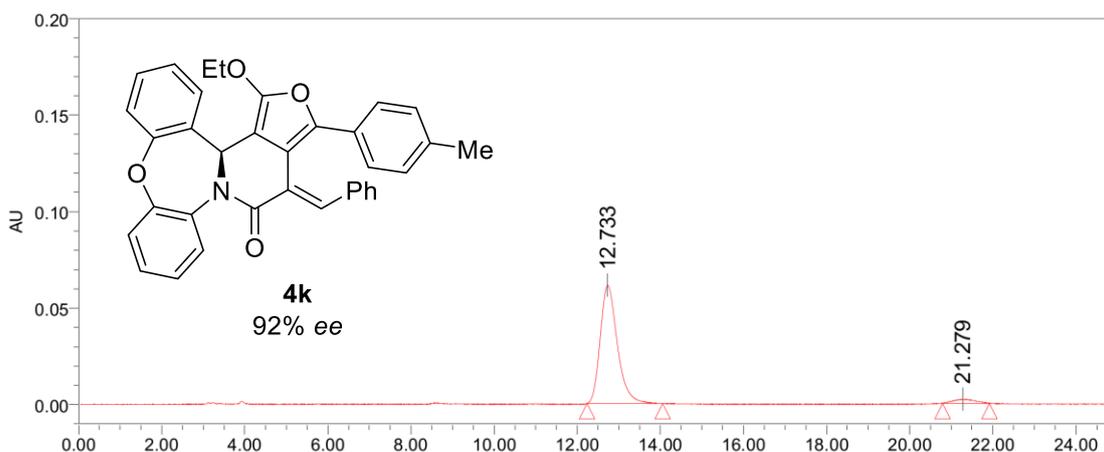
Entry	RT min	Height mV	Area mV.sec	% Area %
1	19.853	3487963	73671	97.59
2	33.168	86290	1415	2.41

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



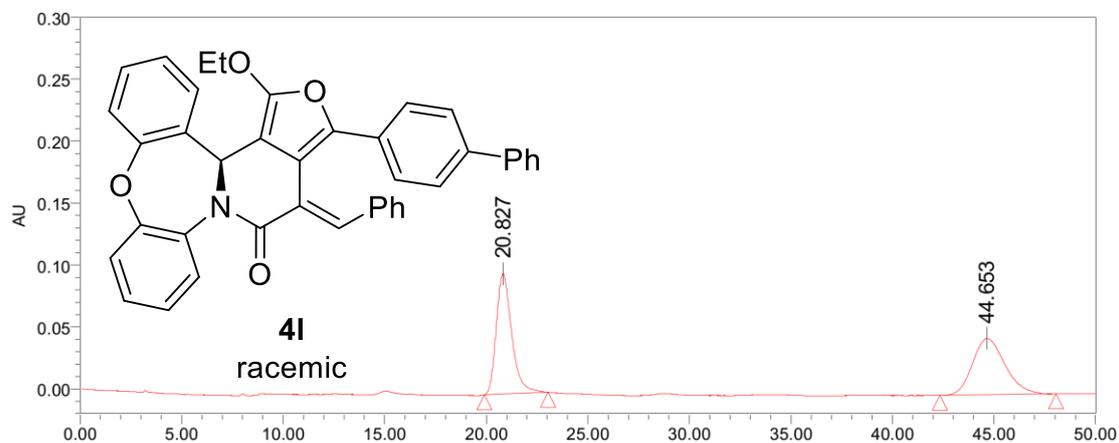
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.720	1093966	38996	50.17
2	21.227	1086568	23621	49.83



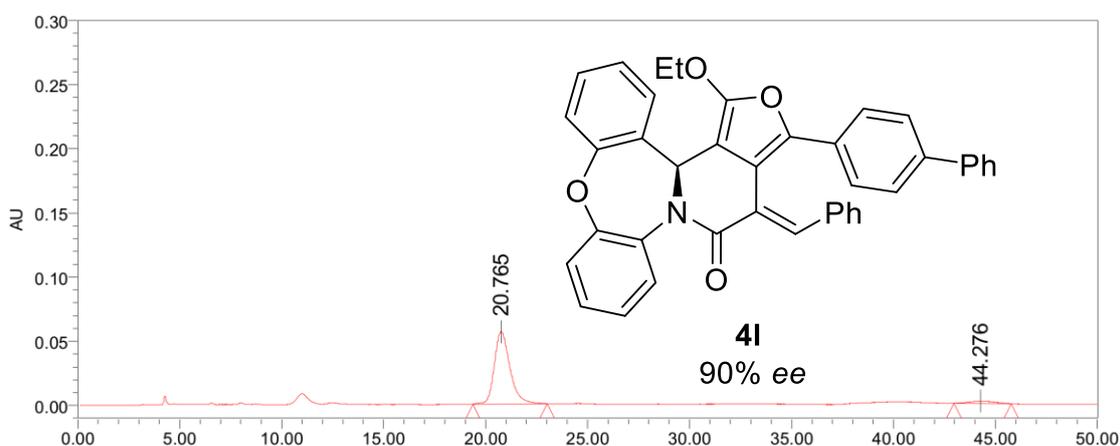
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.733	1746114	61286	96.05
2	21.279	71894	2043	3.95

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



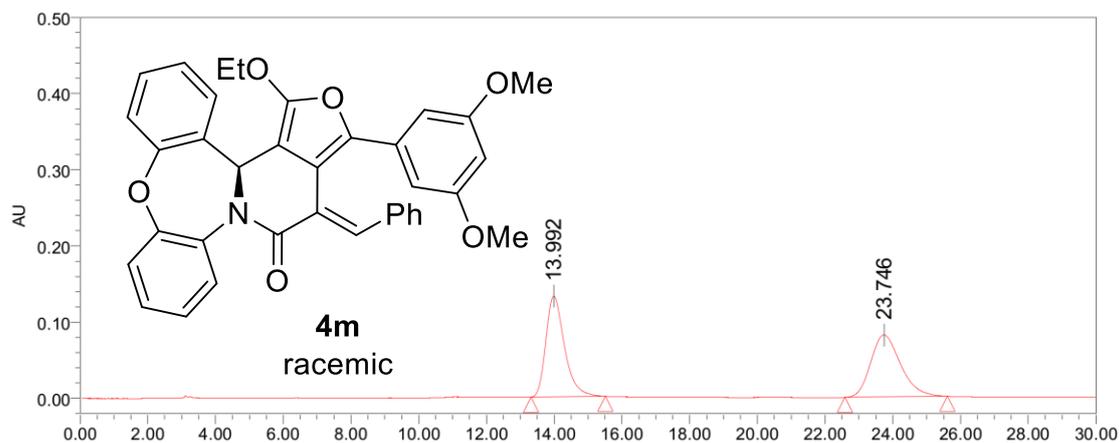
Entry	RT min	Height mV	Area mV.sec	% Area %
1	20.827	5141941	97075	50.51
2	44.653	5037317	45419	49.49



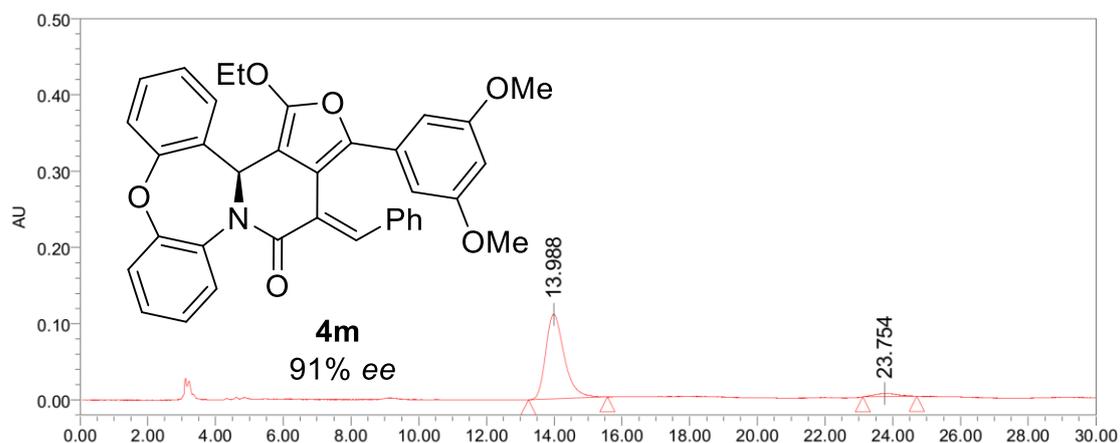
Entry	RT min	Height mV	Area mV.sec	% Area %
1	20.765	2994879	56318	95.02
2	44.276	157013	1771	4.98

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 85:15

flow rate = 1.0 mL/min



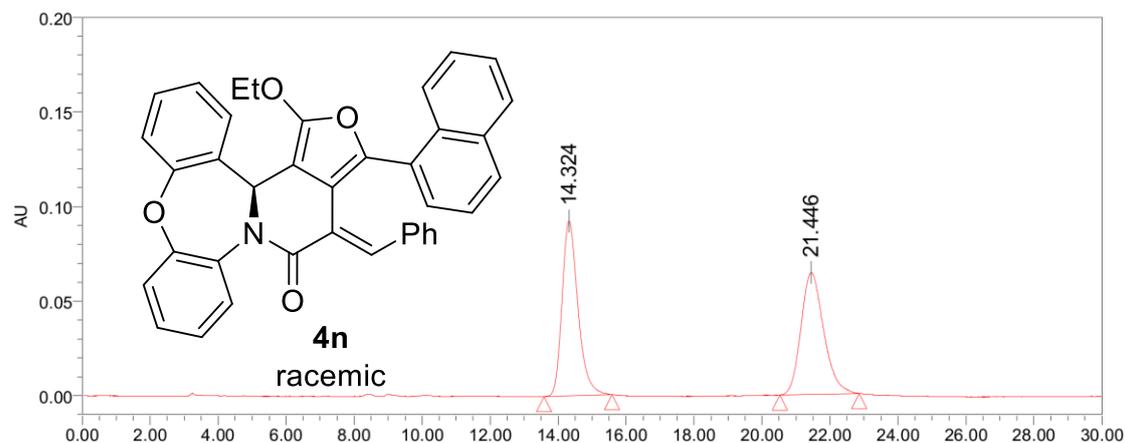
Entry	RT min	Height mV	Area mV.sec	% Area %
1	13.992	5031551	132139	50.32
2	23.746	4967807	81373	49.68



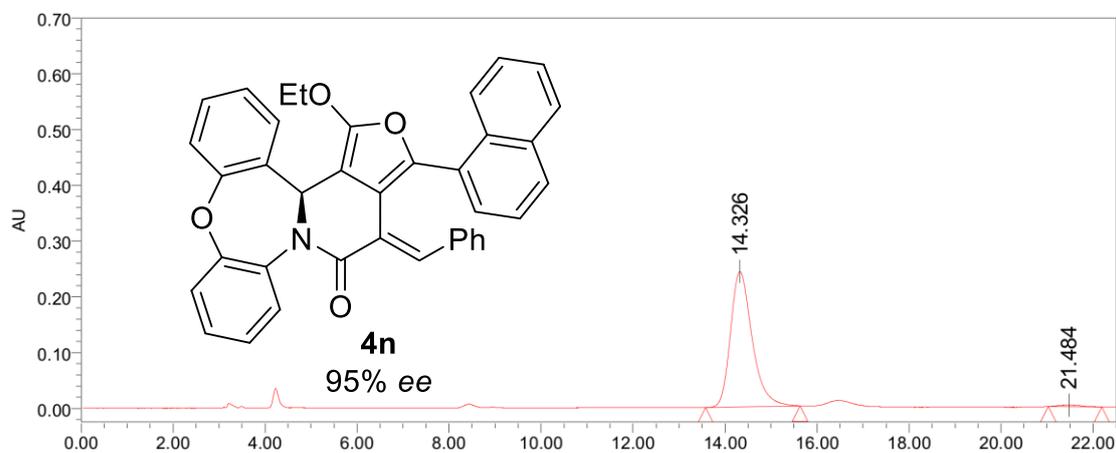
Entry	RT min	Height mV	Area mV.sec	% Area %
1	13.988	4228489	111042	95.61
2	23.754	194161	4028	4.39

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



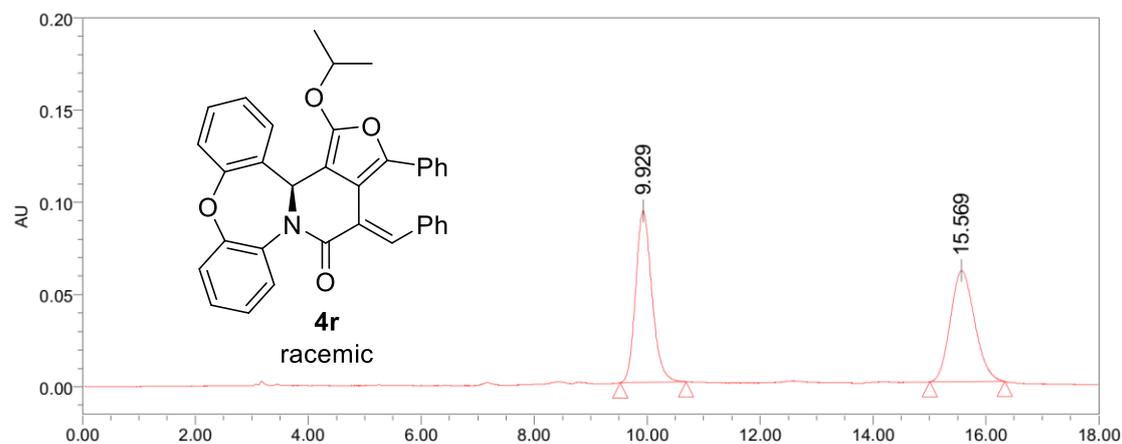
Entry	RT min	Height mV	Area mV.sec	% Area %
1	14.324	2998082	92426	49.48
2	21.446	2997939	64407	50.52



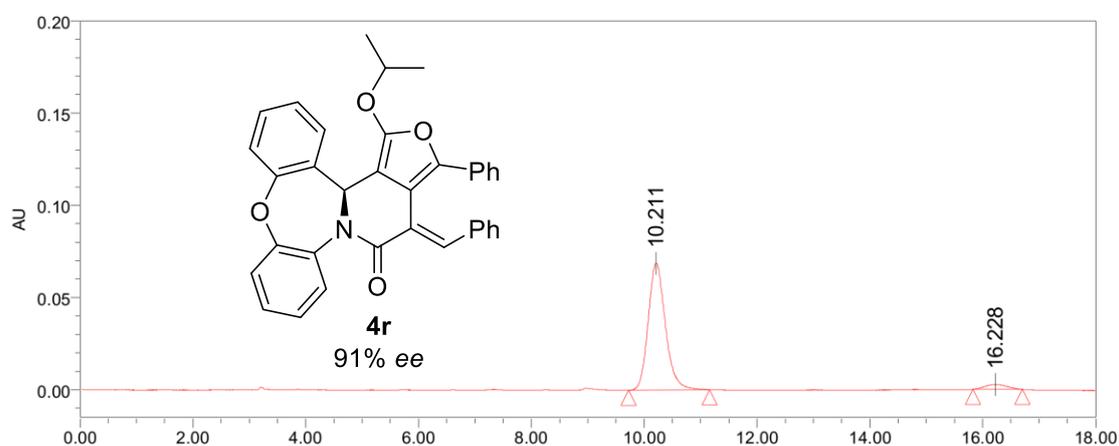
Entry	RT min	Height mV	Area mV.sec	% Area %
1	14.326	7889330	242801	97.53
2	21.484	104297	2912	2.47

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



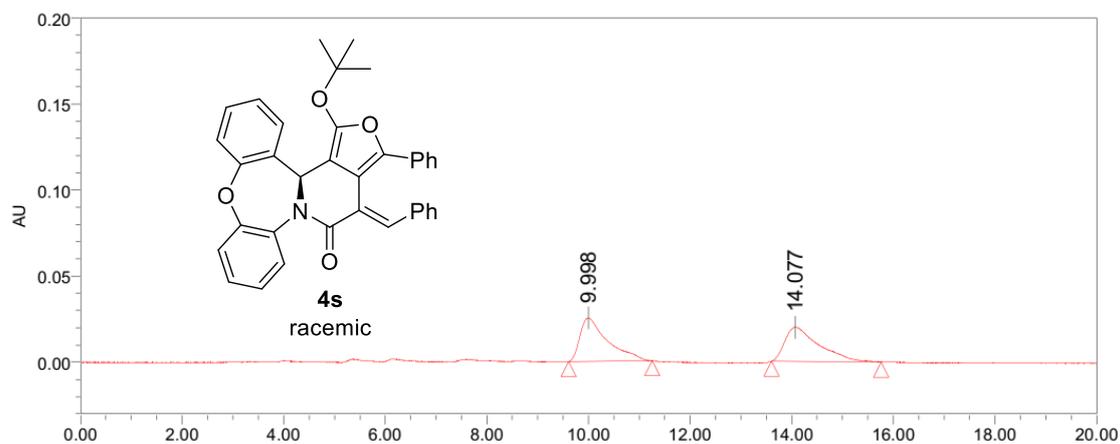
Entry	RT min	Height mV	Area mV.sec	% Area %
1	9.929	1861311	92999	50.84
2	15.569	1799573	60188	49.16



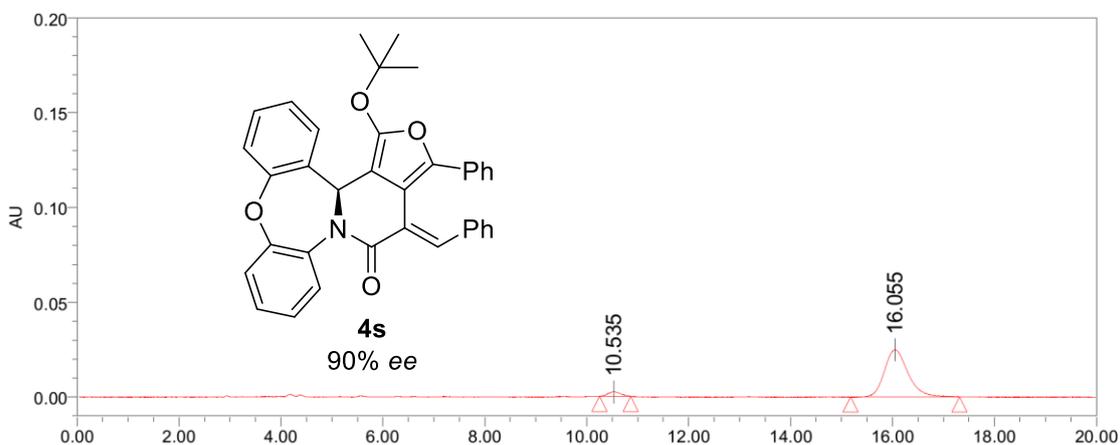
Entry	RT min	Height mV	Area mV.sec	% Area %
1	10.211	1463814	68812	95.33
2	16.228	71767	2665	4.67

Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 85:15

flow rate = 1.0 mL/min



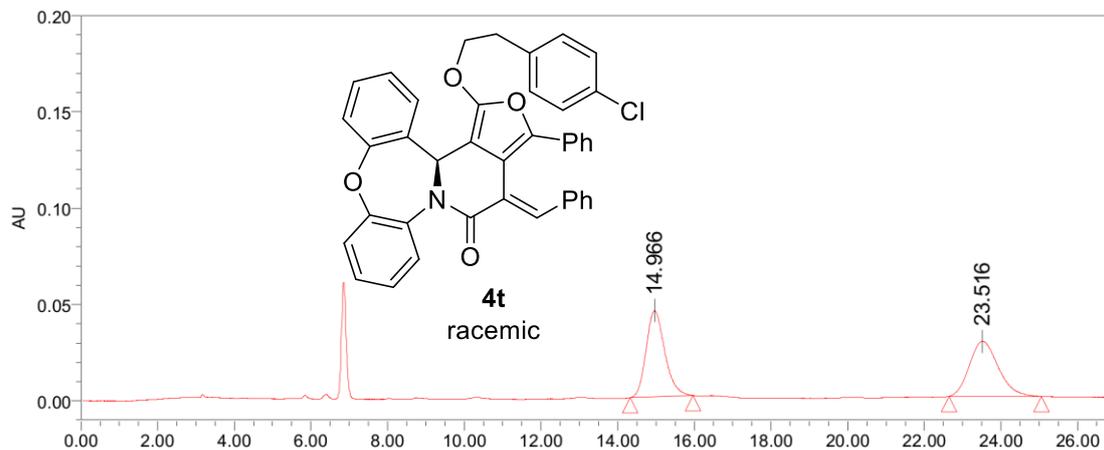
Entry	RT min	Height mV	Area mV.sec	% Area %
1	9.998	950869	25144	50.79
2	14.077	921302	19829	49.21



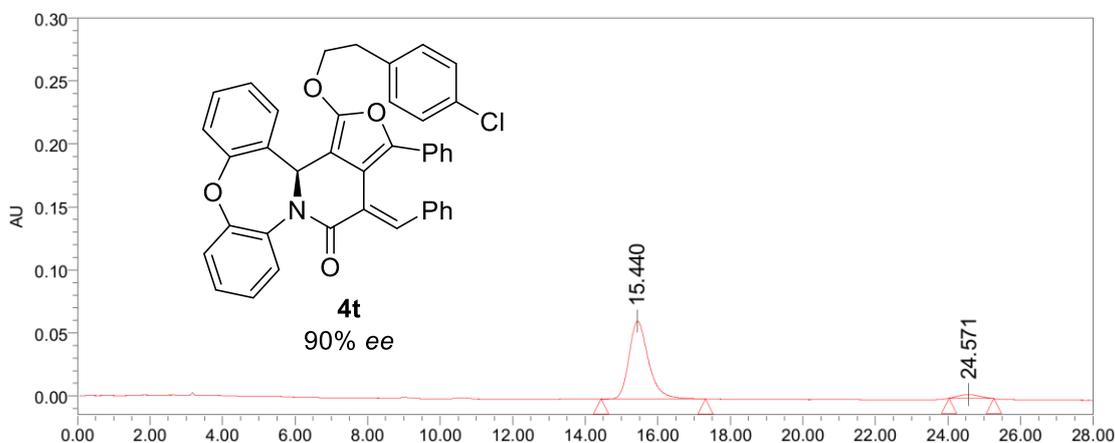
Entry	RT min	Height mV	Area mV.sec	% Area %
1	10.535	40761	2374	4.86
2	16.055	797235	24968	95.14

Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



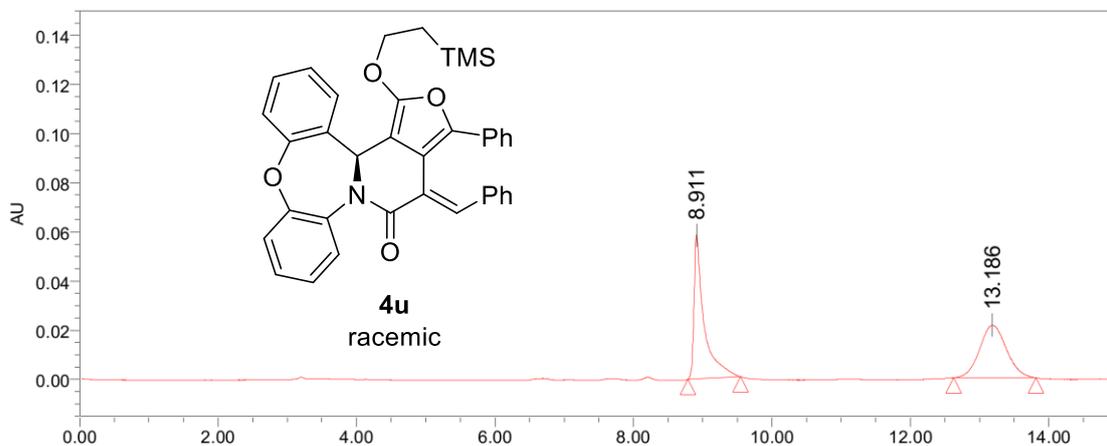
Entry	RT min	Height mV	Area mV.sec	% Area %
1	14.966	1520906	44740	50.48
2	23.516	1491785	28570	49.52



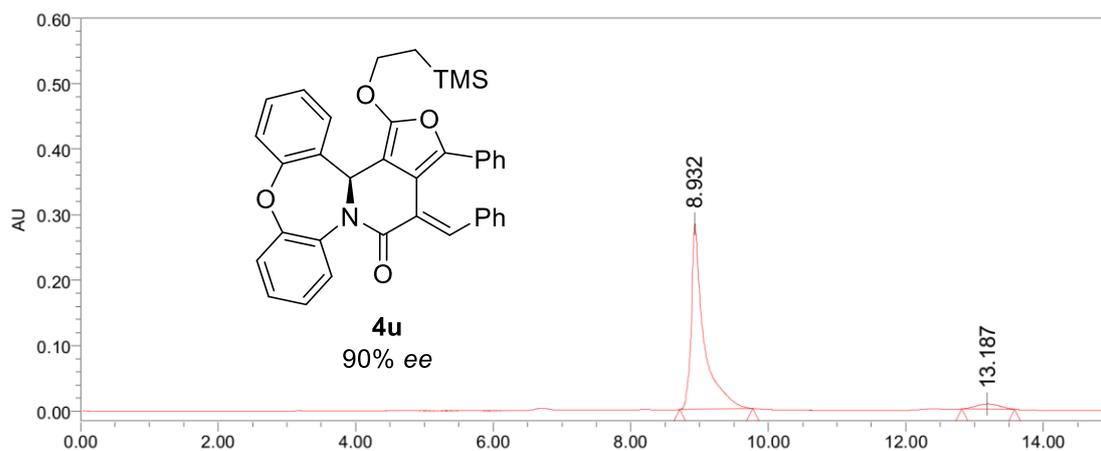
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.440	2308811	61750	95.09
2	24.571	119142	2869	4.91

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



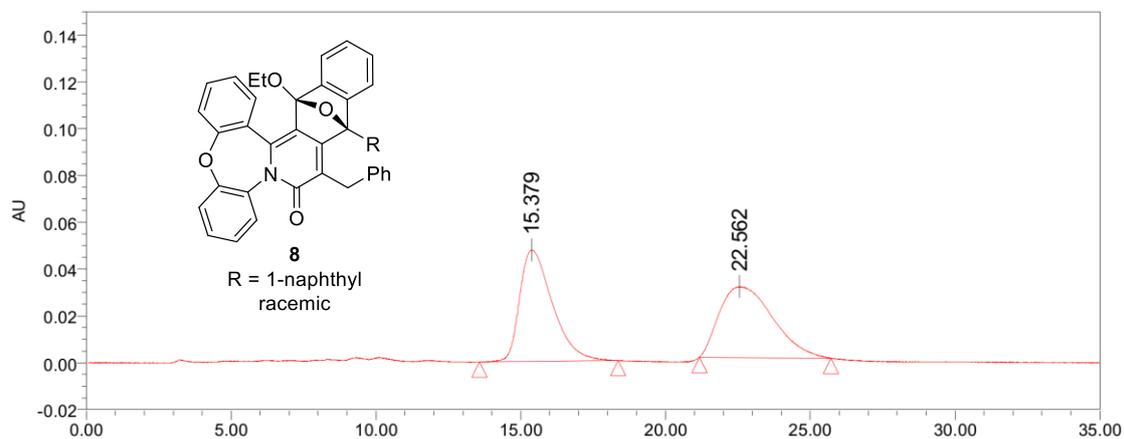
Entry	RT min	Height mV	Area mV.sec	% Area %
1	8.911	588359	58343	50.50
2	13.186	576653	21351	49.50



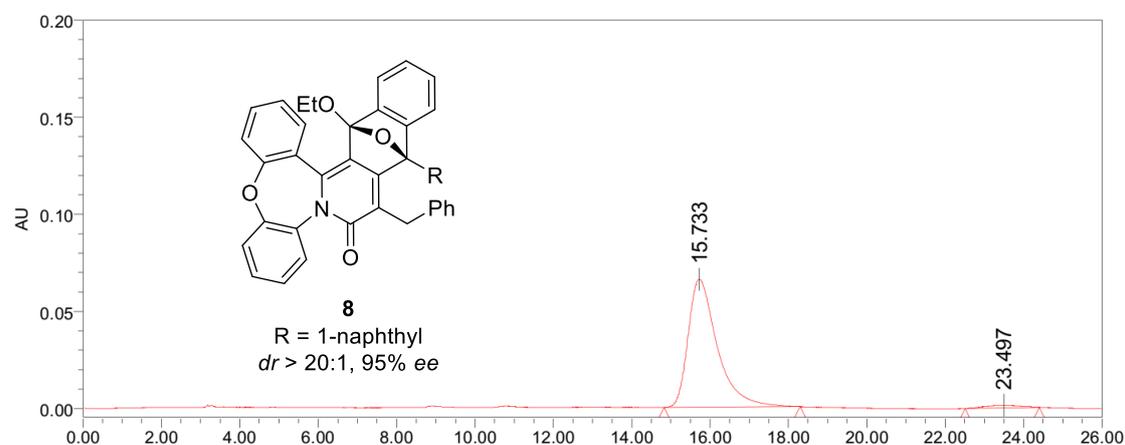
Entry	RT min	Height mV	Area mV.sec	% Area %
1	8.932	3581315	283032	95.02
2	13.187	187670	7769	4.98

Condition: Daicel Chiralpak IA, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 90:10

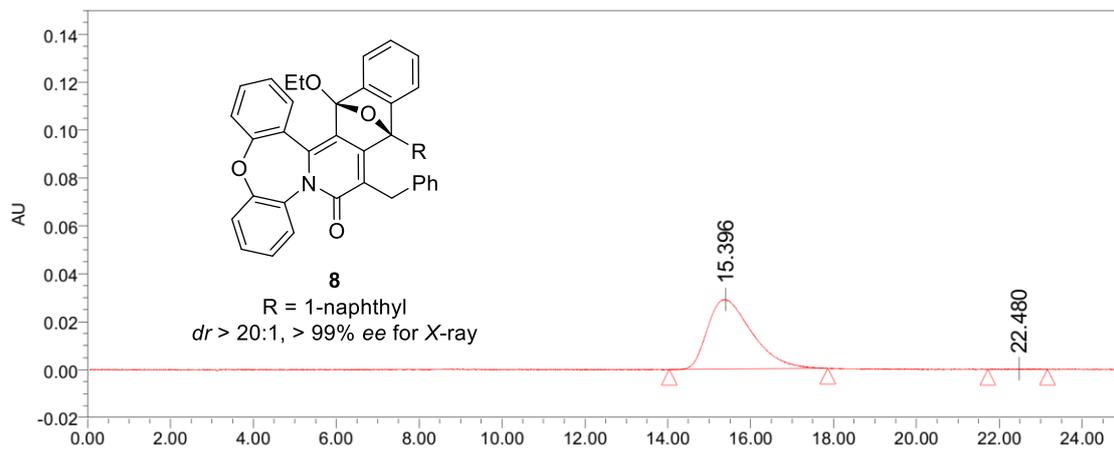
flow rate = 1.0 mL/min



Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.379	3750389	47631	49.04
2	22.562	3897353	30238	50.96



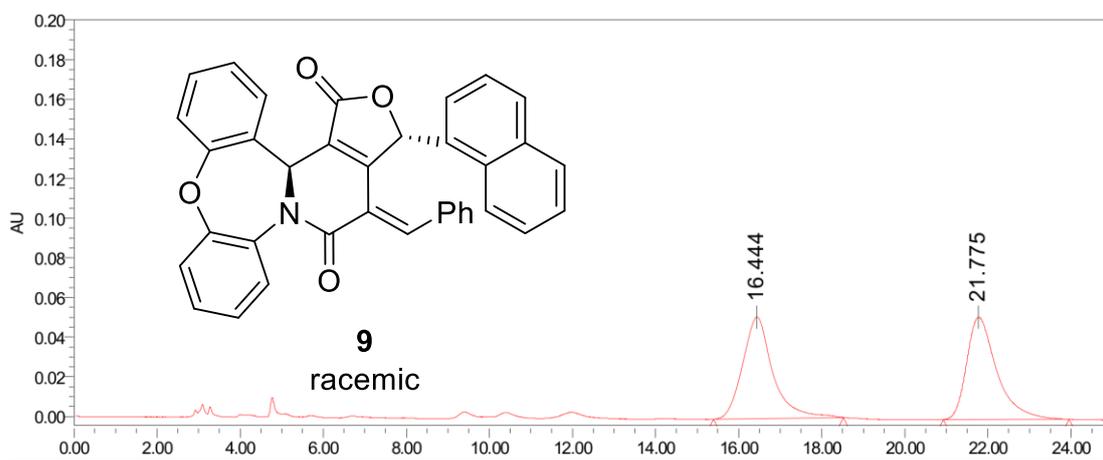
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.733	3406398	65869	97.61
2	23.497	83464	1307	2.39



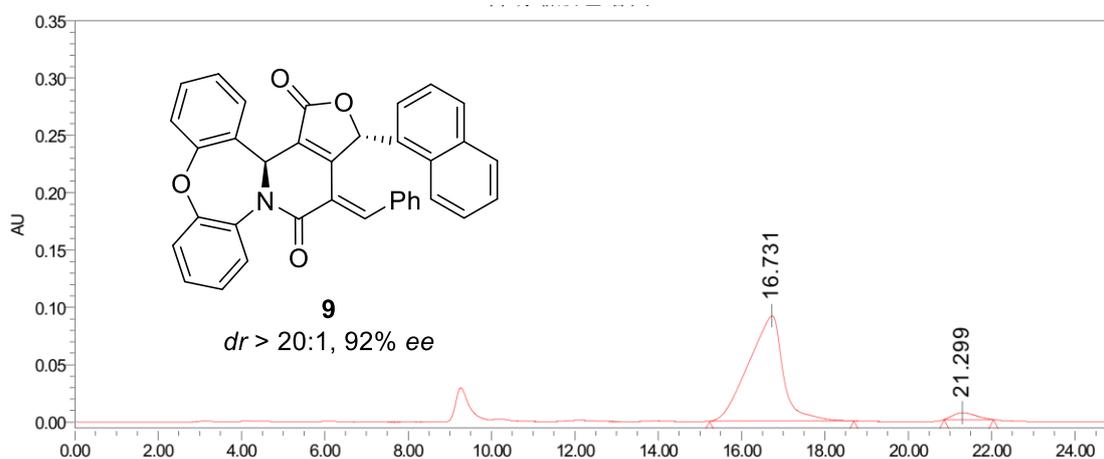
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.396	2153981	29061	99.79
2	22.480	4527	226	0.21

Condition: Daicel Chiralpak IA, $\lambda = 254$ nm, hexane/2-propanol = 70:30

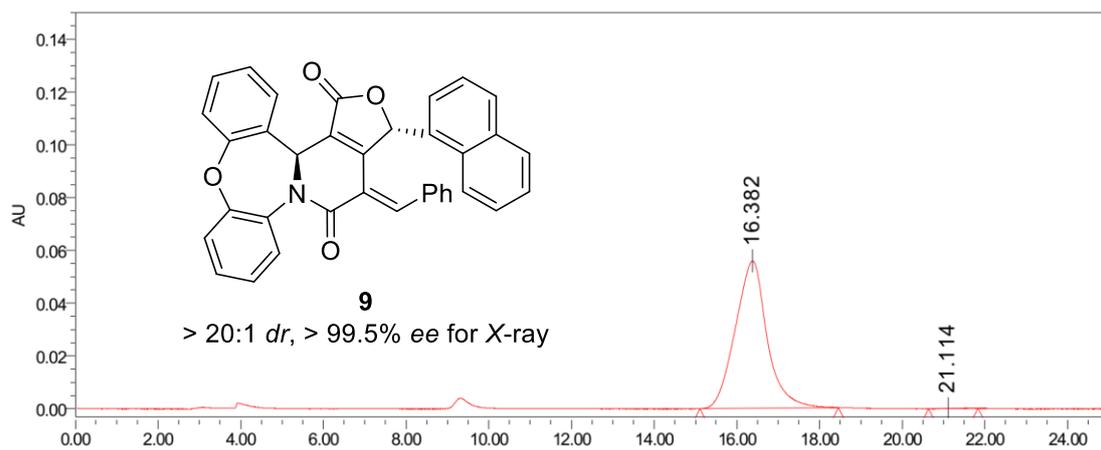
flow rate = 1.0 mL/min



Entry	RT min	Height mV	Area mV.sec	% Area %
1	16.444	2592524	51258	49.94
2	21.775	2598485	51586	50.06



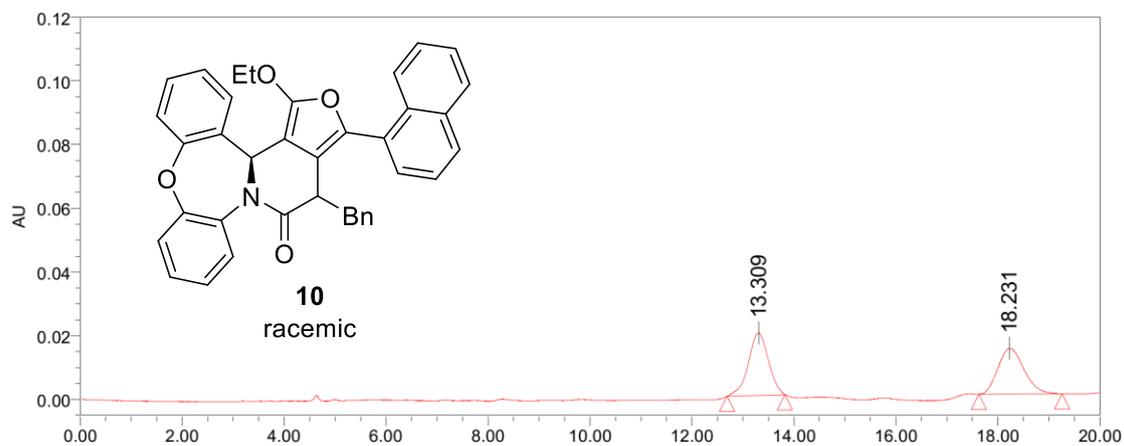
Entry	RT min	Height mV	Area mV.sec	% Area %
1	16.731	5303064	91934	95.94
2	21.299	224137	5974	4.06



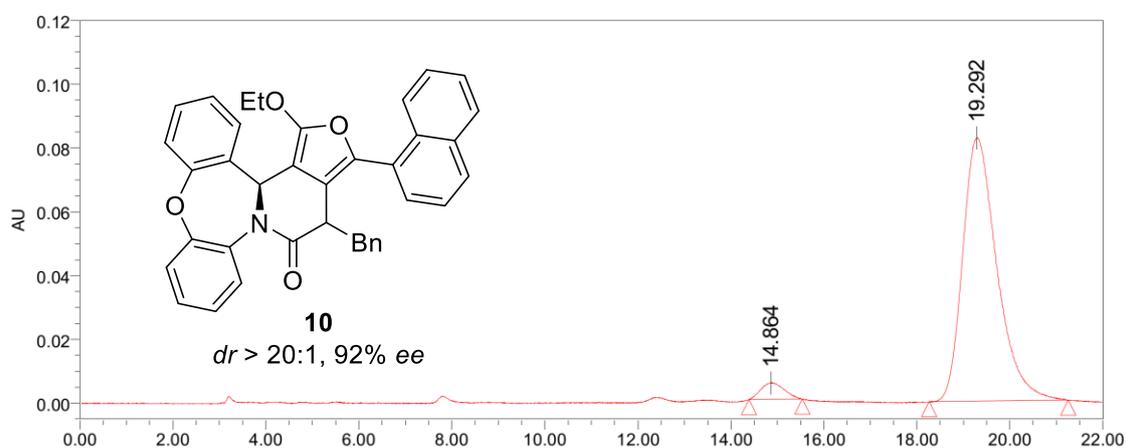
Entry	RT min	Height mV	Area mV.sec	% Area %
1	16.382	2978370	55741	99.94
2	21.114	1811	-62	0.06

Condition: Daicel Chiralpak IC, $\lambda = 254$ nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



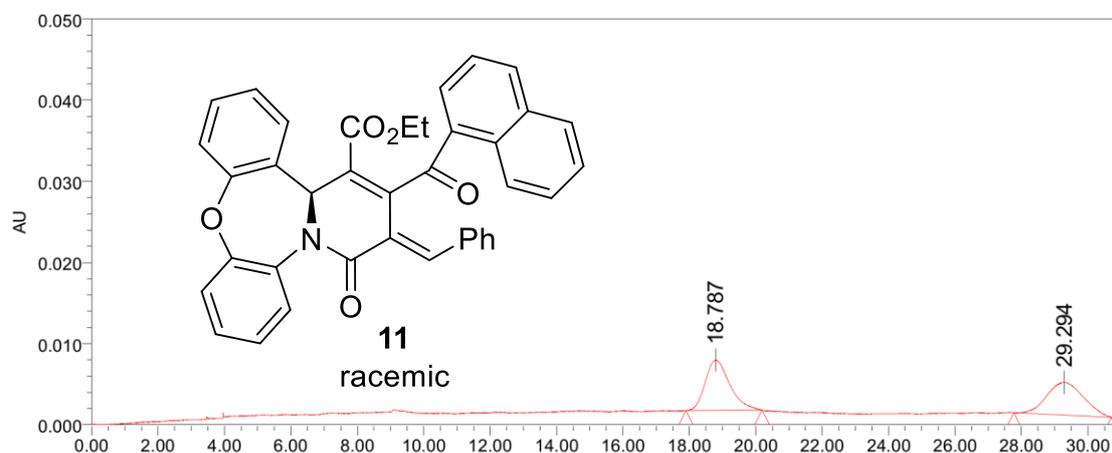
Entry	RT min	Height mV	Area mV.sec	% Area %
1	13.309	532967	19573	50.94
2	18.231	513295	14389	49.06



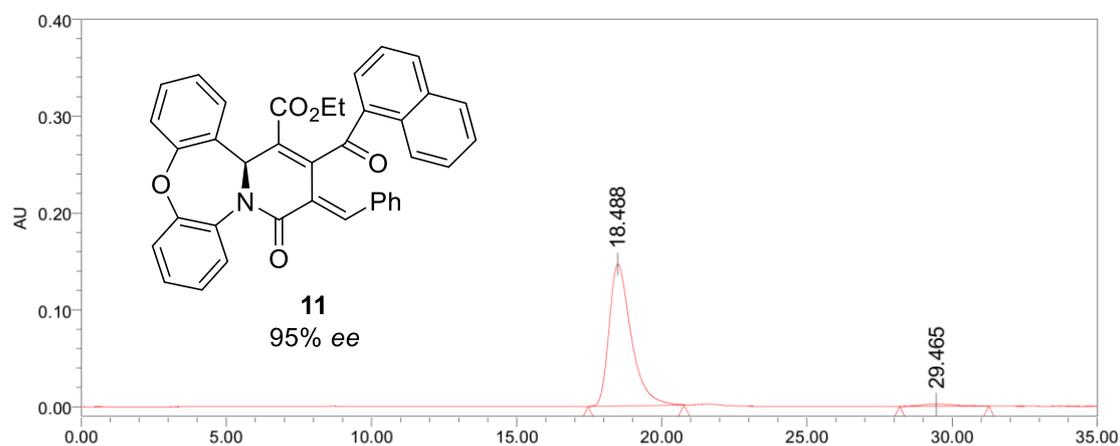
Entry	RT min	Height mV	Area mV.sec	% Area %
1	14.864	182582	5239	4.14
2	19.292	4228196	82562	95.86

Condition: Daicel Chiralpak IC, $\lambda = 254 \text{ nm}$, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min

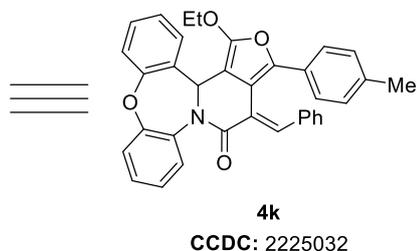
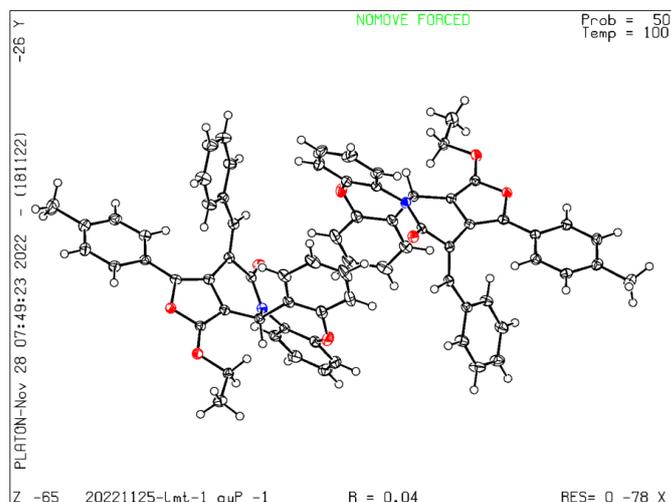


Entry	RT min	Height mV	Area mV.sec	% Area %
1	18.787	320074	6232	50.73
2	29.294	310823	4047	49.27



Entry	RT min	Height mV	Area mV.sec	% Area %
1	18.488	7708688	146423	97.64
2	29.465	186640	2289	2.36

Single-Crystal X-ray Diffraction of 4k



Bond precision: C-C = 0.0019 Å

Wavelength=1.54184

Cell: a=12.9766 (2) b=14.1296 (2) c=16.5741 (2)
 alpha=104.808 (1) beta=94.218 (1) gamma=111.857 (1)
 Temperature: 100 K

	Calculated	Reported
Volume	2678.18 (7)	2678.17 (7)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C ₃₅ H ₂₇ N O ₄	C ₃₅ H ₂₇ N O ₄
Sum formula	C ₃₅ H ₂₇ N O ₄	C ₃₅ H ₂₇ N O ₄
Mr	525.58	525.57
D _x , g cm ⁻³	1.304	1.303
Z	4	4
Mu (mm ⁻¹)	0.680	0.680
F ₀₀₀	1104.0	1104.0
F ₀₀₀ '	1107.30	
h, k, l _{max}	16, 17, 20	16, 17, 20
N _{ref}	11129	10733
T _{min} , T _{max}	0.783, 0.903	0.484, 1.000
T _{min} '	0.712	

Correction method= # Reported T Limits: T_{min}=0.484 T_{max}=1.000
 AbsCorr = MULTI-SCAN

Data completeness= 0.964

Theta(max)= 75.570

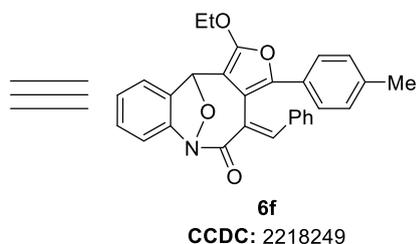
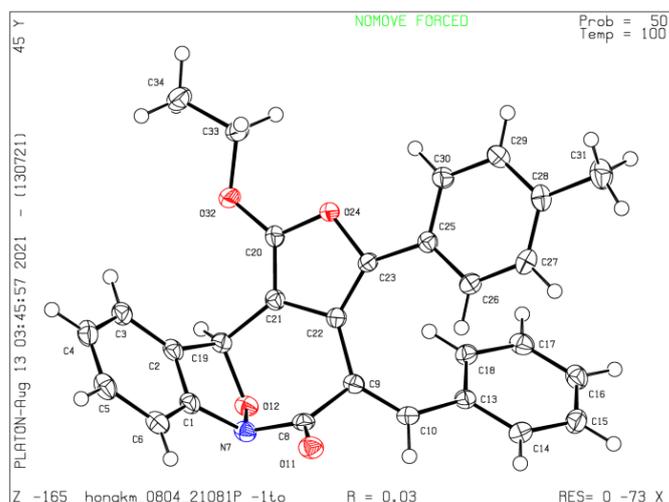
R(reflections)= 0.0403 (10396)

wR₂(reflections)=
0.1029 (10733)

S = 1.053

N_{par}= 725

Single-Crystal X-ray Diffraction of 6f



Bond precision: C-C = 0.0017 Å

Wavelength=1.54184

Cell: a=7.9086(2) b=11.3545(3) c=13.6401(3)
 alpha=70.485(2) beta=87.467(2) gamma=77.723(2)
 Temperature: 100 K

	Calculated	Reported
Volume	1127.61(5)	1127.61(5)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C ₂₉ H ₂₃ N O ₄	C ₂₉ H ₂₃ N O ₄
Sum formula	C ₂₉ H ₂₃ N O ₄	C ₂₉ H ₂₃ N O ₄
Mr	449.48	449.48
Dx, g cm ⁻³	1.324	1.324
Z	2	2
Mu (mm ⁻¹)	0.711	0.711
F000	472.0	472.0
F000'	473.44	
h, k, lmax	9, 14, 17	9, 14, 17
Nref	4688	4453
Tmin, Tmax	0.774, 0.808	0.964, 1.000
Tmin'	0.752	

Correction method= # Reported T Limits: Tmin=0.964 Tmax=1.000
 AbsCorr = MULTI-SCAN

Data completeness= 0.950

Theta(max)= 75.876

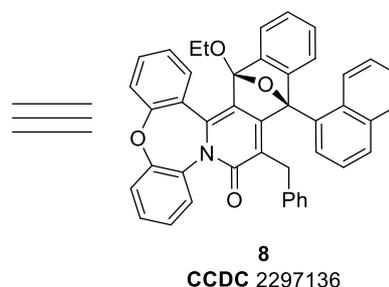
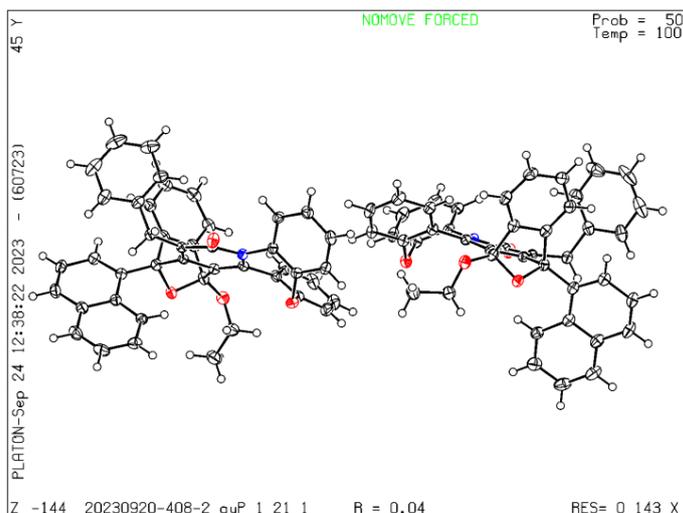
R(reflections)= 0.0342(4144)

wR2(reflections)= 0.0882(4453)

S = 1.045

Npar= 310

Single-Crystal X-ray Diffraction of 8



Bond precision: C-C = 0.0040 Å

Wavelength=1.54184

Cell: a=10.2322 (1)

b=16.3070 (1)

c=19.7132 (1)

alpha=90

beta=99.641 (1)

gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	3242.82 (4)	3242.82 (4)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C ₄₄ H ₃₁ N O ₄	2(C ₄₄ H ₃₁ N O ₄)
Sum formula	C ₄₄ H ₃₁ N O ₄	C ₈₈ H ₆₂ N ₂ O ₈
Mr	637.70	1275.39
Dx, g cm ⁻³	1.306	1.306
Z	4	2
Mu (mm ⁻¹)	0.662	0.662
F ₀₀₀	1336.0	1336.0
F ₀₀₀ '	1339.92	
h, k, lmax	12, 20, 24	12, 20, 24
Nref	13440 [6965]	12773
Tmin, Tmax	0.888, 0.936	0.766, 1.000
Tmin'	0.820	

Correction method= # Reported T Limits: Tmin=0.766 Tmax=1.000

AbsCorr = MULTI-SCAN

Data completeness= 1.83/0.95

Theta(max)= 75.453

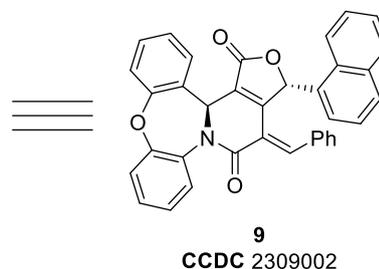
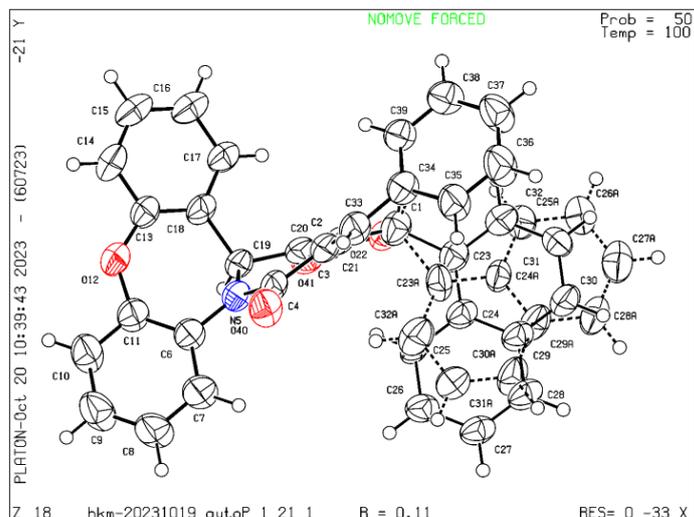
R(reflections)= 0.0352 (12487)

wR2(reflections)=
0.0843 (12773)

S = 1.108

Npar= 886

Single-Crystal X-ray Diffraction of 9



Bond precision: C-C = 0.0110 Å

Wavelength=1.54184

Cell: a=10.2145 (4)
alpha=90

b=9.5543 (4)
beta=103.071 (4)

c=13.9690 (4)
gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	1327.95 (9)	1327.95 (9)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C ₃₆ H ₂₃ N O ₄	C ₃₆ H ₂₃ N O ₄
Sum formula	C ₃₆ H ₂₃ N O ₄	C ₃₆ H ₂₃ N O ₄
Mr	533.55	533.55
Dx, g cm ⁻³	1.334	1.334
Z	2	2
Mu (mm ⁻¹)	0.699	0.699
F ₀₀₀	556.0	556.0
F ₀₀₀ '	557.68	
h, k, lmax	12, 11, 16	12, 11, 16
Nref	4697 [2504]	4571
Tmin, Tmax	0.920, 0.946	0.268, 1.000
Tmin'	0.900	

Correction method= # Reported T Limits: Tmin=0.268 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.83/0.97

Theta(max)= 66.580

R(reflections)= 0.1077 (3906)

wR2(reflections)=
0.2596 (4571)

S = 0.883

Npar= 389

General Procedure for the *in vitro* Anti-tumor Activity Study

Cell viability was measured by CCK-8 assay

Human cancer cell lines HCT116, A549, and KYSE-520 were obtained from Cell Cook. Cells were cultured in RPMI1640 medium containing 10% fetal bovine serum and 1% penicillin/streptomycin (Gibco) in a humidified incubator containing 5% CO₂ at 37 °C. Human cancer cell lines MCF-7 was obtained from Procell and cells were cultured in MEM medium containing 10% fetal bovine serum, 1% penicillin/streptomycin (Gibco) and 0.01 mg/mL insulin (Procell) in a humidified incubator containing 5% CO₂ at 37 °C. For cell viability, cells were seeded in 96-well plates at 5000 cells per well. After 24 hours, serially diluted compounds were added and cells were cultured for another 48 hours. Cell viability was measured using a Cell Counting Kit-8 (CCK-8) assay according to the manufacturer's instructions (Yeasen Biotechnology, China).

These representative products **6b - 6o**, **6s**, **7b - 7c**, **7e**, **7g - 7i**, and **7l - 7m** on cell viability was evaluated *via* CCK8 assay in HCT116 (colon cancer), MCF-7 (breast cancer), A549 (lung adenocarcinoma), and KYSE-520 (esophageal squamous cell carcinoma) human cancer cell lines, and the *in vitro* anti-tumor activity results are listed in **Table S7** and **Table S8**.

Most of these poly-substituted furan-fused eight-membered lactams, such as **6e**, **6f**, **6h**, and **6m** showed significant anti-cancer activity in comparison to the Paclitaxel (**Fig. S3-S6**). The results demonstrated that compound **6e** shows the highest anticancer potency against human colon cancer cells (HCT-116 cells, IC₅₀ = 0.50 ± 0.05 μM), compound **6f** possesses the highest anticancer potency against human esophageal squamous cell carcinoma cells (KYSE-520 cells, IC₅₀ = 0.89 ± 0.13 μM). These results were presented as percentages and vehicle-treated cells set at 5000.

Table S7 | Anti-tumor activities of compounds 6b - 6o, 6s, 7b - 7c, 7e, 7g - 7i, and 7l - 7m (inhibition rate at 20 μ M).

Compound	HCT-116 (%)	MCF-7 (%)	A549 (%)	KYSE-520 (%)
6b	97.34 \pm 0.22	62.14 \pm 2.77	53.19 \pm 0.31	96.89 \pm 0.75
6c	97.80 \pm 0.43	65.23 \pm 3.05	60.66 \pm 2.57	98.03 \pm 0.55
6d	90.14 \pm 1.38	58.58 \pm 3.78	55.30 \pm 5.05	92.29 \pm 2.70
6e	91.53 \pm 0.66	55.48 \pm 2.46	60.38 \pm 2.00	90.98 \pm 1.27
6f	96.40 \pm 0.41	68.24 \pm 0.30	62.86 \pm 3.89	96.30 \pm 1.40
6g	98.89 \pm 0.25	89.16 \pm 1.91	91.01 \pm 2.20	99.05 \pm 0.48
6h	92.05 \pm 0.63	53.63 \pm 6.02	59.68 \pm 3.08	96.04 \pm 0.75
6i	97.73 \pm 0.44	56.33 \pm 1.39	73.64 \pm 2.24	93.16 \pm 1.12
6j	97.44 \pm 0.96	61.57 \pm 3.15	51.09 \pm 0.39	96.16 \pm 0.10
6k	96.43 \pm 2.14	69.21 \pm 1.49	86.25 \pm 2.14	98.41 \pm 0.60
6l	80.04 \pm 3.16	49.54 \pm 2.68	37.76 \pm 7.13	99.28 \pm 0.73
6m	93.26 \pm 1.12	72.59 \pm 2.64	69.54 \pm 2.35	98.06 \pm 0.17
6n	98.52 \pm 0.42	75.28 \pm 4.57	76.32 \pm 1.51	98.42 \pm 0.49
6o	99.25 \pm 0.24	78.98 \pm 5.11	84.25 \pm 3.57	97.54 \pm 0.16
6s	77.14 \pm 1.40	53.30 \pm 3.42	48.82 \pm 0.39	73.00 \pm 1.98
7b	91.09 \pm 4.67	52.14 \pm 5.40	34.49 \pm 3.34	94.79 \pm 0.78
7c	98.03 \pm 0.77	72.28 \pm 3.47	65.95 \pm 1.10	99.05 \pm 0.27
7e	99.11 \pm 0.49	79.23 \pm 5.02	86.87 \pm 2.76	98.14 \pm 0.55
7g	91.03 \pm 0.61	59.55 \pm 1.37	38.90 \pm 3.54	97.91 \pm 0.46
7h	97.01 \pm 0.36	82.43 \pm 0.50	81.40 \pm 1.82	98.65 \pm 0.66
7i	96.91 \pm 0.51	69.24 \pm 4.45	66.90 \pm 2.48	98.57 \pm 0.09
7l	75.97 \pm 1.57	56.02 \pm 2.84	38.13 \pm 4.59	92.09 \pm 1.25
7m	69.85 \pm 4.21	43.67 \pm 3.16	32.93 \pm 2.45	79.34 \pm 4.51
Taxol	73.85 \pm 1.57	89.20 \pm 1.08	85.52 \pm 5.20	90.46 \pm 2.11

Table S8 | Anti-tumor activities of compounds 6b - 6o, 7b - 7c, 7e, 7g - 7i, and 7l (IC₅₀, μM)^a

Compound	HCT-116	MCF-7	A549	KYSE-520
6b	0.99±0.31	-	-	4.30±0.44
6c	0.89±0.07	-	-	3.61±0.32
6d	3.11±0.73	-	-	2.62±0.41
6e	0.50±0.05	-	-	2.03±0.28
6f	2.09±0.31	-	-	0.89±0.13
6g	1.00±0.07	7.54±1.05	-	9.69±0.49
6h	2.92±0.39	-	-	0.95±0.10
6i	0.77±0.07	-	-	11.32±0.58
6j	1.07±0.06	-	-	1.46±0.36
6k	1.18±0.11	-	-	5.23±0.74
6l	-	-	-	2.25±0.24
6m	1.34±0.25	-	-	1.53±0.30
6n	1.23±0.05	-	-	5.74±0.57
6o	0.69±0.09	-	-	12.09±0.67
7b	0.61±0.09	-	-	1.69±0.22
7c	2.81±0.58	-	-	9.16±0.92
7e	1.13±0.16	-	-	6.91±0.66
7g	1.86±0.12	-	-	1.76±0.21
7h	0.86±0.08	-	-	6.17±0.62
7i	0.93±0.07	-	-	1.19±0.21
7l	-	-	-	1.81±0.26

^aIC₅₀ is the half maximal inhibitory concentration.

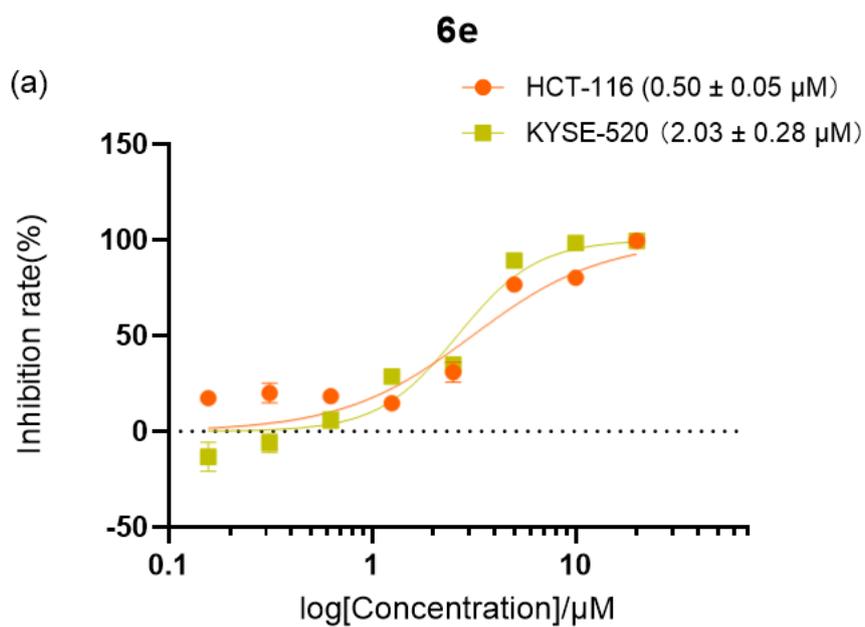


Fig. S3 | Compound 6e on the inhibition of HCT-116 and KYSE-520 cells.

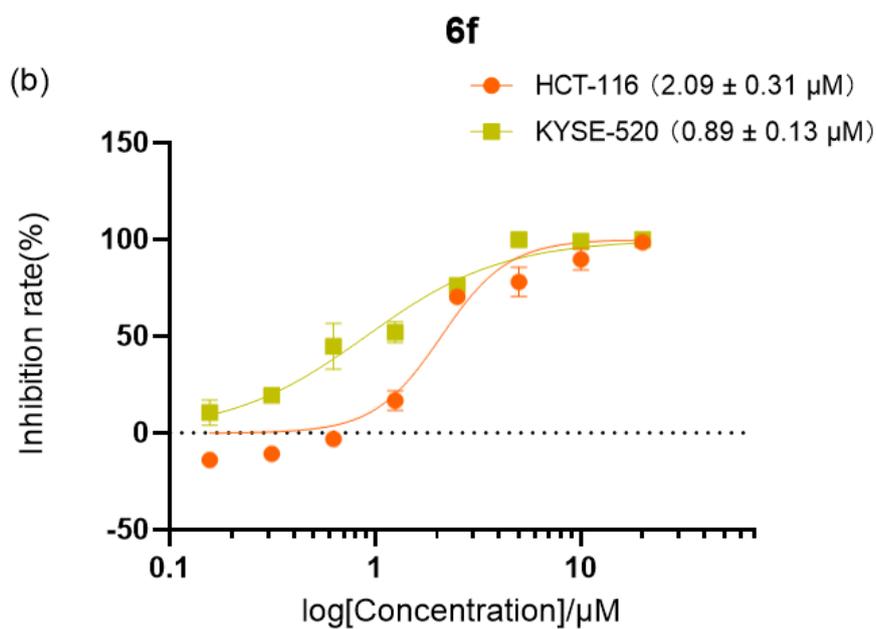


Fig. S4 | Compound 6f on the inhibition of HCT-116 and KYSE-520 cells.

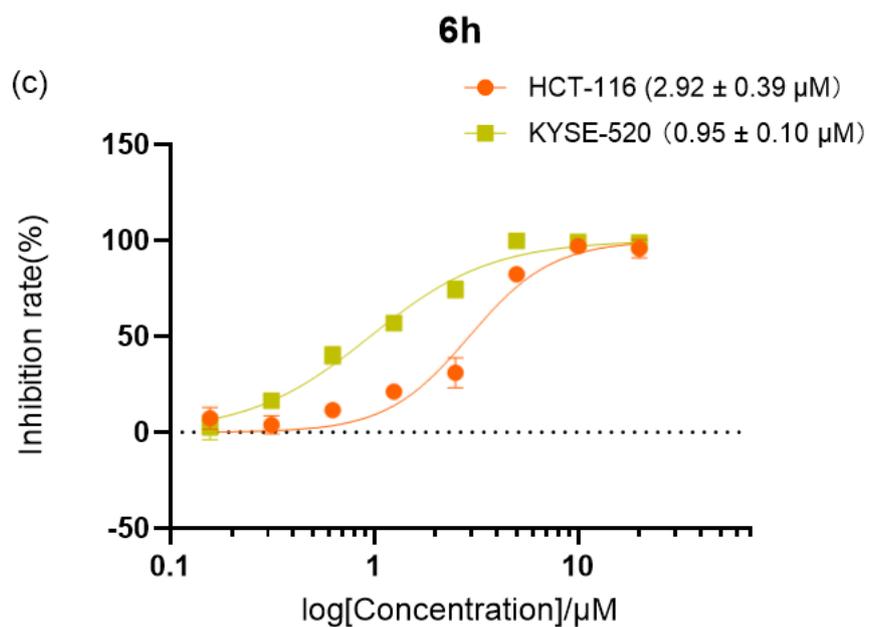


Fig. S5. | Compound 6h on the inhibition of HCT-116 and KYSE-520 cells.

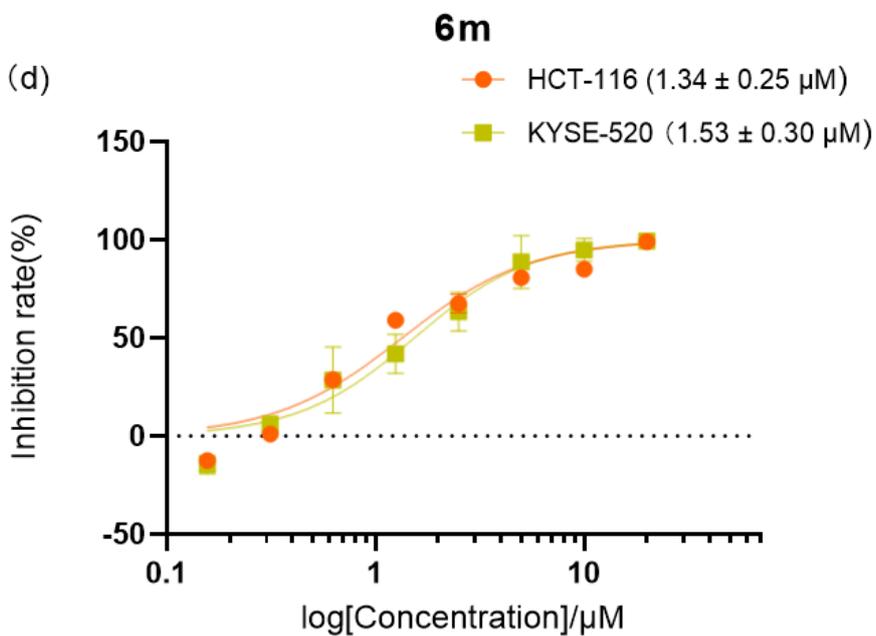


Fig. S6. | Compound 6m on the inhibition of HCT-116 and KYSE-520 cells.

References

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