Electronic Supplementary Material (ESI) for Chemical Science.

Dynamic kinetic resolution of γ,γ-disubstituted indole 2-carboxaldehydes via NHC-Lewis acid cooperative catalysis for the synthesis of tetracyclic *ε*-lactones

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Supporting Information

1. General Information

Unless otherwise specified, all reactions were carried out under an atmosphere of nitrogen in oven-dried reaction vessels with Teflon screw caps. 25 °C Corresponds to the room temperature (rt) of the lab when the experiments were performed. Dry toluene was purchased from commercial sources and stored under nitrogen over sodium wire, and dry $CHCl_3$ was purchased from commercial sources and stored under nitrogen over 4 Å molecular sieves. The 1*H*-indole-2-carbaldehyde **1a**, **1b-1u** were synthesised following the literature procedure.[1] The *p*-quinone methide **2a-2g** were synthesized by following the literature procedure.[2] The triazolium salt **4** was synthesized following the literature procedure.[3] The Kharasch oxidant **8** was synthesized following the literature procedure.[4] Cs_2CO_3 was purchased from Spectrochem and was activated before use. $Bi(OTf)_3$ and $Sc(OTf)_3$ were purchased from Sigma-Aldrich.

Analytical thin layer chromatography was performed on TLC Silica gel 60 F_{254}. Visualization was accomplished with short wave UV light or $KMnO_4$ staining solutions followed by heating. Flash chromatography was performed on silica gel (230-400 mesh) by standard techniques eluting with Pet. Ether-EtOAc solvent system.

All compounds were fully characterized. ^1H and ^{13}C NMR spectra were recorded on Bruker AV 400 and Bruker Ultrashield spectrometer in solvents as indicated. Chemical shifts (δ) are given in ppm. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: $\delta H = 7.26$ ppm, $\delta C = 77.16$ ppm and Acetone-D_6: $\delta H = 2.05$ ppm, $\delta C = 29.84, 206.26$ ppm). Infrared (FT-IR) spectra were recorded on a Bruker Alfa FT-IR, ν-max in cm^{-1}. Optical rotations were measured on JASCO P-2000 Polarimeter at room temperature using 50 mm cell of 1.0 mL capacity. HRMS (ESI) data were recorded on a Waters Xevo G2-XS Q-TOF instrument. HPLC analysis was performed on Agilent Technologies 1260 Infinity II with a Variable Wavelength Detector.

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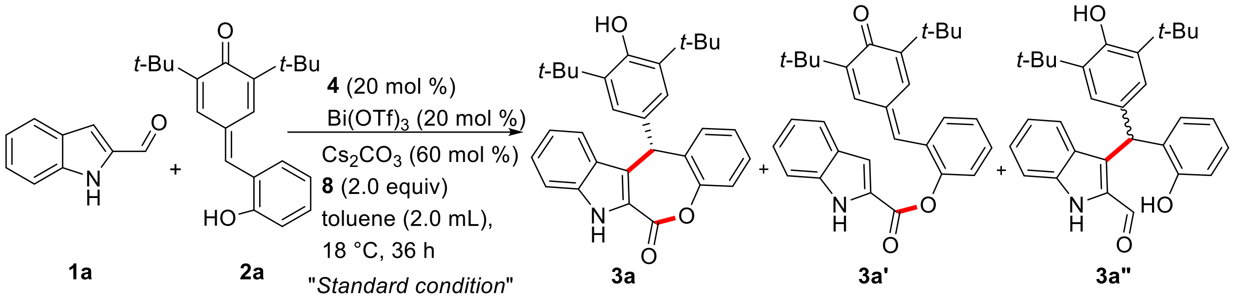
[1] Y. Liu, G. Luo, X. Yang, S. Jiang, W. Xue, Y. R. Chi and Z. Jin, *Angew. Chem., Int. Ed.*, 2020, **59**, 442.

[2] J.-P. Tan, P. Yu, J.-H. Wu, Y. Chen, J. Pan, C. Jiang, X. Ren, H.-S. Zhang and T. Wang, *Org. Lett.*, 2019, **21**, 7298.

[3] C.-G. Zhao, F.-Y. Li and J. Wang, *Angew. Chem., Int. Ed.*, 2016, **55**, 1820.

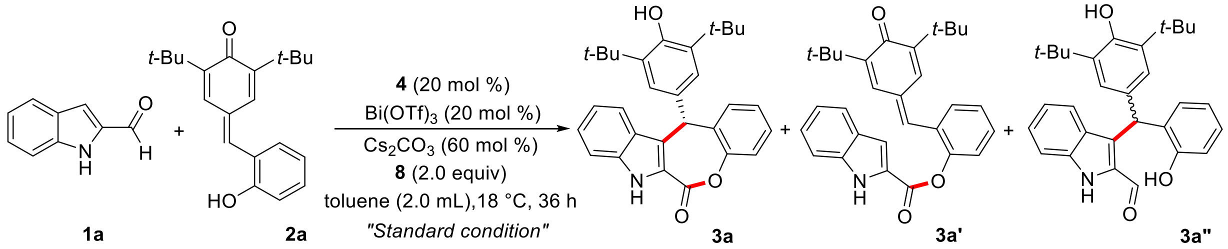
[4] M. S. Kharasch and B. S. Joshi, *J. Org. Chem.*, 1957, **22**, 1439.

2. General Procedure for the Optimization of the Reaction Conditions



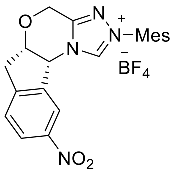
To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (5.6 mg, 0.012 mmol), Cs_2CO_3 (19.5 mg, 0.06 mmol) and $Bi(OTf)_3$ (15.6 mg, 0.024 mmol) inside a glove-box. Then 1*H*-indole-2-carbaldehyde **1a** (17.4 mg, 0.12 mmol), 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (52.1 mg, 0.168 mmol) and oxidant **8** (49.0 mg, 0.12 mmol) were added outside the glove-box at 18 °C under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (5.6 mg, 0.012 mmol), Cs_2CO_3 (4.0 mg, 0.012 mmol), and oxidant **8** (49.0 mg, 0.12 mmol) were added at 18 °C under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere. After the completion of the reaction, the solvent was evaporated, and the crude residue was purified by flash column chromatography on silica gel to afford the corresponding (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino [3,4-*b*] indol-6-one **3a.** The enantiomeric ratio was determined by HPLC analysis on a chiral stationary phase.

Optimization Studies



entry	Variation of the standard conditions^{a}	Yield of **3a** (%)^{b}	er of **3a**^{c}	Yield of **3a’** (%)^{b}	Yield of **3a”** (%)^{b}
Carbene Precursor Screening					
1	***none***	***69***	***95:5***	***<5***	***<5***
2	**5** instead of **4**	62	86:14	<5	<5
3	**6** instead of **4**	11	86:14	<5	66

4	**7** instead of **4**	19	81:19	<5	<5
	Base Screening				
5	K_2CO_3 instead of Cs_2CO_3	36	91:9	<5	25
6	KO*t*-Bu instead of Cs_2CO_3	<5	-nd-	<5	<5
7	DBU instead of Cs_2CO_3	<5	-nd-	<5	<5
8	DABCO instead of Cs_2CO_3	<5	-nd-	<5	<5
9	DMAP instead of Cs_2CO_3	<5	-nd-	<5	<5
	Acid Screening				
10	$Sc(OTf)_3$ instead of $Bi(OTf)_3$	52	92:8	<5	<5
11	$Sn(OTf)_3$ instead of $Bi(OTf)_3$	<5	-nd-	64	<5
12	$Mg(OTf)_2$ instead of $Bi(OTf)_3$	<5	-nd-	76	<5
13	$Eu(OTf)_3$ instead of $Bi(OTf)_3$	<5	-nd-	64	<5
14	Tl(OTf) instead of $Bi(OTf)_3$	<5	-nd-	72	<5
15	$AgNO_3$ instead of $Bi(OTf)_3$	<5	-nd-	88	<5
16	CF_3SO_3H instead of $Bi(OTf)_3$	60	91:9	<5	<5
	Solvent Screening				
17	THF instead of toluene	<5	-nd-	71	<5
18	DME instead of toluene	<5	-nd-	67	<5
19	DMSO instead of toluene	<5	-nd-	<5	<5
20	DCM instead of toluene	31	89:11	<5	52
21	DCE instead of toluene	14	90:10	<5	75
22	Mesitylene instead of toluene	22	91:9	<5	18
23	Chlorobenzene instead of toluene	16	86:14	<5	68
24	Trifluorotoluene instead of toluene	15	86:14	<5	70
	Temperature Screening				
25^{d}	50 °C instead of 18 °C	79	86:14	<5	<5
26^{d}	45 °C instead of 18 °C	63	88:12	<5	<5
27^{d}	40 °C instead of 18 °C	52	90:10	<5	07
28^{d}	30°C instead of 18 °C	37	91:9	<5	57
29^{d}	0 °C instead of 18 °C	<5	-nd-	<5	<5
	Stoichiometry variation				
30	10 mol % of **4** instead of 20 mol %	31	95:5	<5	48
31	15 mol % of **4** instead of 20 mol %	49	95:5	<5	22
32	25 mol % of **4** instead of 20 mol %	69	95:5	<5	<5
33	1.0 equiv of **8** instead of 2.0 equiv	39	94:6	<5	28
34	1.5 equiv of **8** instead of 2.0 equiv	58	94:6	<5	17
35	1.0 equiv of **2a** instead of 1.4 equiv	53	94:6	<5	<5
36	1.2 equiv of **2a** instead of 1.4 equiv	60	94:6	<5	<5
37	1.6 equiv of **2a** instead of 1.4 equiv	68	94:6	<5	<5
38	Reaction without **4**	<5	-nd-	<5	89
39	Reaction without $Bi(OTf)_3$	<5	-nd-	87	<5



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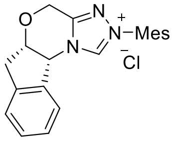

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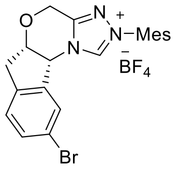

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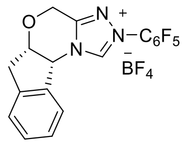

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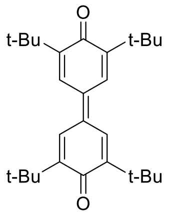

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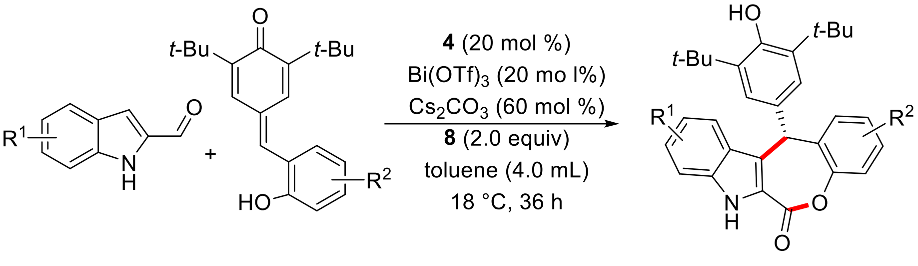
[a] Standard conditions: **1a** (0.12 mmol), **2a** (0.168 mmol), **4** (20 mol %), $Bi(OTf)_3$ (20 mol %), Cs_2CO_3 (60 mol %), **8** (2.0 equiv), toluene (2.0 mL), 18 °C and 36 h. [b] Yield of the column chromatography purified products are provided. [c] The er was established by HPLC analysis on a chiral stationary column. [d] Reaction performed upto12 h.

3. General Procedure for the Enantioselective Synthesis of Tetracyclic *ε*-Lactones



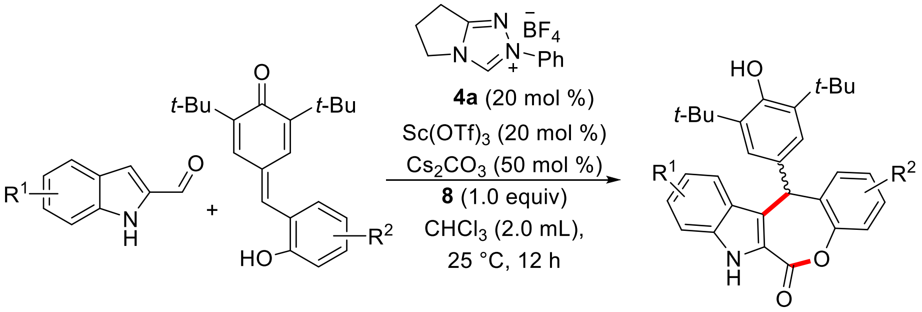
1 **2** **3**

To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (41.0 mg, 0.125 mmol) and $Bi(OTf)_3$ (33.0 mg, 0.05 mmol) in a glove-box. Then 1*H*-indole-2-carbaldehyde derivative **1** (36.3 mg, 0.25 mmol), 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one derivative **2** (108.6 mg, 0.35 mmol) and oxidant **8** (102.0 mg, 0.25 mmol) were added outside the glove-box at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (8.0 mg, 0.025 mmol), and oxidant **8** (102.0 mg, 0.25 mmol) were added at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere, after the completion of the reaction solvent was evaporated, and the crude residue was purified by flash column chromatography on silica gel to afford the corresponding tetracyclic *ε*-lactones **3.**

Procedure for the 1 mmol scale experiment

To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (46.4 mg, 0.1 mmol), Cs_2CO_3 (163.0 mg, 0.5 mmol) and $Bi(OTf)_3$ (130.0 mg, 0.2 mmol) in a glove-box. Then 1*H*-indole-2-carbaldehyde **1a** (145.0 mg, 1.0 mmol), 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (434.0 mg, 1.4 mmol) and oxidant **8** (408.0 mg, 1.0 mmol) were added outside the glove-box at 18 °C under nitrogen atmosphere followed by addition of toluene (4.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (46.4 mg, 0.1 mmol), Cs_2CO_3 (33.0 mg, 0.1 mmol), and oxidant **8** (408.0 mg, 1.0 mmol) were added at 18 °C under nitrogen atmosphere followed by addition of toluene (4.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere, after the completion of the reaction solvent was evaporated, and the crude residue was purified by flash column chromatography on silica gel to afford the corresponding (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo [6,7]oxepino[3,4-*b*]indol-6-one **3a** as a white solid (328.0 mg, 72 % yield with 95:5 er).

4. General Procedure for the Racemic Synthesis of Tetracyclic ε-Lactones



1 **2** **3**

To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4a** (6.5 mg, 0.024 mmol), Cs_2CO_3 (19.5 mg, 0.06 mmol) and $Sc(OTf)_3$ (11.8 mg, 0.024 mmol) in a glove-box. Then 1*H*-indole-2-carbaldehyde derivative **1** (17.4 mg, 0.12 mmol), 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one derivative **2** (52.1 mg, 0.168 mmol) and oxidant **8** (49.0 mg, 0.12 mmol) were added outside the glove-box at 25 °C under nitrogen atmosphere followed by addition of $CHCl_3$ (1.0 mL). The reaction mixture was stirred at 25 °C for 12 h under nitrogen atmosphere, after the completion of the reaction solvent was evaporated, and the crude residue was purified by flash column chromatography on silica gel to afford the corresponding tetracyclic ε-lactones **3.**

5. X-ray Data of 3d

X-ray intensity data measurements of compound **3d** was carried out on a Bruker D8 VENTURE Kappa Duo PHOTON II CPAD diffractometer equipped with Incoatec multilayer mirrors optics. The intensity measurements were carried out with Cu micro-focus sealed tube diffraction source (CuK_α= 1.54178 Å) at 100(2) K temperature. The X-ray generator was operated at 50 kV and 1.1 mA. A preliminary set of cell constants and an orientation matrix were calculated from two sets of 40 frames. Data were collected with ω scan width of 0.5° at different settings of φ and 2θ with a frame time of 15 secs keeping the sample-to-detector distance fixed at 5.00 cm. The X-ray data collection was monitored by APEX3 program (Bruker, 2016).[5] All the data were corrected for Lorentzian, polarization and absorption effects using SAINT[6] and SADABS programs (Bruker, 2016). Using APEX3 (Bruker) program suite, the structure was solved with the ShelXS-97[7] (Sheldrick, 2008) structure solution program, using direct methods. The model was refined with version of ShelXL-2014[8] (Sheldrick, 2014) using Least Squares minimisation. All the hydrogen atoms were placed in a geomerically idalized positions and constrained to ride on its parent atoms except H-atom attached to the hydroxy group of ethanol solvent molecule. The H-atom bound to the –OH group of ethanl solvent molecule has been located in the difference Fourier and refined isotropically. An *ORTEP* III[9] view of compound was drawn with 50% probability displacement ellipsoids and H atoms are shown as small spheres of arbitrary radii. The absolute configuration was established by anomalous dispersion effect (Flack parameter, 0.1(3)) in X-ray diffraction measurements carried out with Cu radiation. The single crystal X-ray diffraction data analysis clearly established that our synthesize compound has *S* configurations at C1 position.

Compound **3d** having molecular formula $C_{33}H_{39}NO_4$ with approximate crystal dimensions 0.050 mm × 0.120 mm × 0.140 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54178 Å). The integration of the data using a monoclinic unit cell yielded a total of 28158 reflections to a maximum θ angle of 72.24° (0.81 Å resolution), of which 5575 were independent (average redundancy 5.051, completeness = 99.3%, R_{int} = 4.82%, R_{sig} = 4.22%) and 5497 (98.60%) were greater than $2\sigma(F^2)$. The final cell constants of $\underline{a}$ = 9.2800(10) Å, $\underline{b}$ = 17.0143(19) Å, $\underline{c}$ =10.0461(10) Å, β = 115.351(5)°, volume = 1433.5(3) Å^3, are based upon the refinement of the XYZ-centroids of reflections above 20 $\sigma(I)$. The calculated minimum and maximum transmission coefficients (based on crystal size)

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[5] APEX3 suite for crystallographic software, Bruker axs, Madison, WI (Bruker (2016).

[6] SAINT - Software for the Integration of CCD Detector System Bruker Analytical X-ray Systems, Bruker axs, Madison, WI (Bruker, 2006 and Bruker, 2016)

[7] G. M. Sheldrick, A short history of ShelX, Acta Cryst., 2008, **A64**, 339.

[8] T. Gruene, H. W. Hahn, A. V. Luebben, F. Meilleur and G. M. Sheldrick, *J. Appl. Cryst.* 2014, **47**, 462.

[9] L. J. Farrugia, *J. Appl. Cryst.* 1997, **30**, 565.

are 0.6366 and 0.7536. The structure was solved and refined using the Bruker SHELXTL Software Package, using the Sohnke (chiral) space group *P*2(1), with *Z* = 2 for the formula unit, $C_{33}H_{39}NO_4$. The final anisotropic full-matrix least-squares refinement on F^2 with 357 variables converged at *R*1 = 4.33%, for the observed data and *wR*2 = 10.73% for all data. The goodness-of-fit was 1.066. The largest peak in the final difference electron density synthesis was 0.478 e^-/Å^3 and the largest hole was -0.460 e^-/Å^3 with an RMS deviation of 0.047 e^-/Å^3. On the basis of the final model, the calculated density was 1.190 g/cm^3 and *F*(000), 552 e^-.

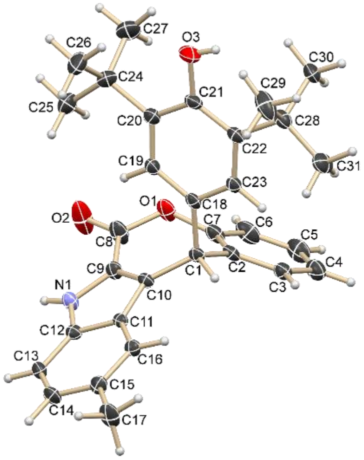


Figure 1. ORTEP view of compound **3d** showing the atom-numbering scheme. The displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres with arbitrary radii. The solvent ethanol molecule is omitted for clarity.

Sample and crystal data for 3d.

Identification code	**3d**
CCDC	2131951
Chemical formula	$C_{33}H_{39}NO_4$
Formula weight	513.65 g/mol
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal size	0.050 × 0.120 × 0.140 mm
Crystal system	monoclinic
Space group	P2(1)

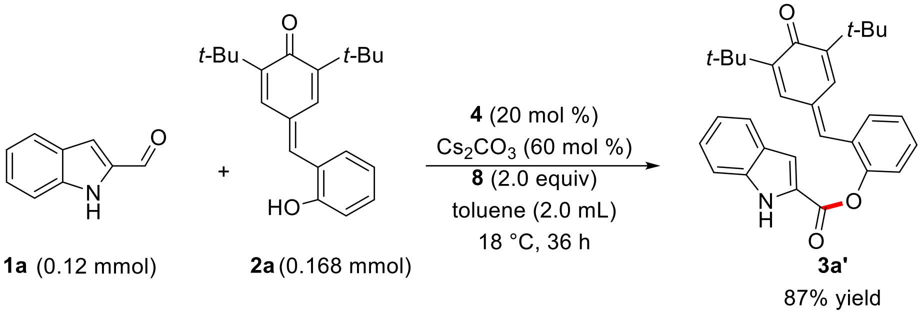
Unit cell dimensions	*a* = 9.2800(10) Å	*α* = 90°
	b = 17.0143(19) Å	*β* = 115.351(5)°
	c = 10.0461(10) Å	*γ* = 90°
Volume	1433.5(3) $Å^3$	
Z	2	
Density (calculated)	1.190 g/cm^3	
Absorption coefficient	0.611 mm^{-1}	
F(000)	552	

Data collection and structure refinement for 3d.

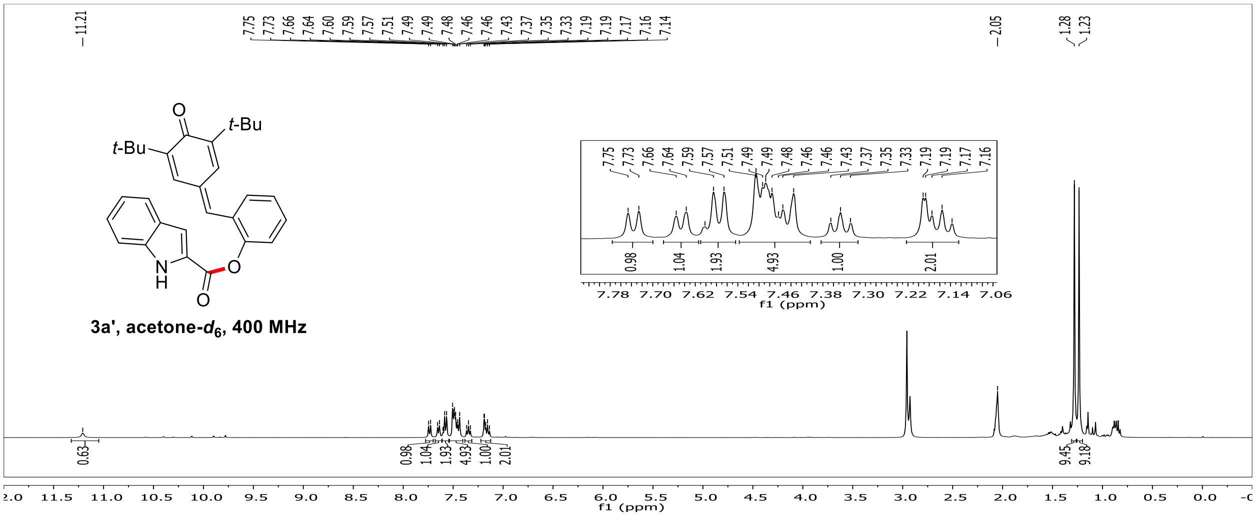
Theta range for data collection	4.87 to 72.24°	
Index ranges	-11<=h<=11, -20<=k<=21, -12<=l<=12	
Reflections collected	28158	
Independent reflections	5575 [R(int) = 0.0482]	
Max. and min. transmission	0.7536 and 0.6366	
Structure solution technique	direct methods	
Structure solution program	SHELXS-97 (Sheldrick 2008)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)	
Function minimized	Σ w(F_o^2 - F_c^2)^2	
Data / restraints / parameters	5575 / 1 / 357	
Goodness-of-fit on F^2	1.066	
Final R indices	5497 data; I>2σ(I)	R1 = 0.0433, wR2 = 0.1068
	all data	R1 = 0.0438, wR2 = 0.1073
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0408P)^2+0.6926P]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	0.1(3)	
Extinction coefficient	0.0121(15)	
Largest diff. peak and hole	0.478 and -0.460 $eÅ^{-3}$	
R.M.S. deviation from mean	0.047 $eÅ^{-3}$	

6. Mechanistic Experiments

(a) Reaction performed in the absence of $Bi(OTf)_3$

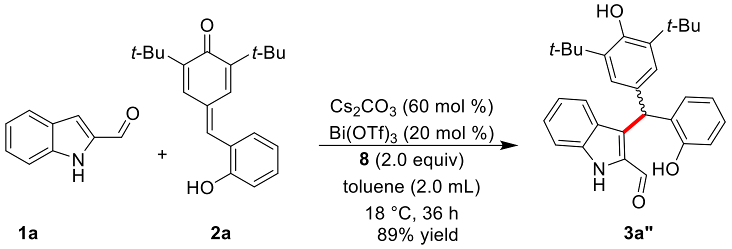


To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (5.6 mg, 0.012 mmol), and Cs_2CO_3 (19.5 mg, 0.06 mmol)) in a glove-box. Then 1*H*-indole-2-carbaldehyde **1a** (17.4 mg, 0.12 mmol), 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (52.1 mg, 0.168 mmol) and oxidant **8** (49.0 mg, 0.12 mmol) were added outside the glove-box under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, Cs_2CO_3 (3.9 mg, 0.012 mmol), triazolium salt **4** (5.6 mg, 0.012 mmol) and oxidant **8** (49.0 mg, 0.12 mmol) were added again under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere. After the completion of the reaction, the solvent was evaporated and the crude residue preadsorbed on silica gel and purified by flash column chromatography on silica gel to afford 2-((3,5-di-*tert*-butyl-4-oxocyclohexa-2,5-dien-1-ylidene)methyl)phenyl 1*H*-indole-2-carboxylate **3a'** as a orange solid (47.5 mg, 87% yield).



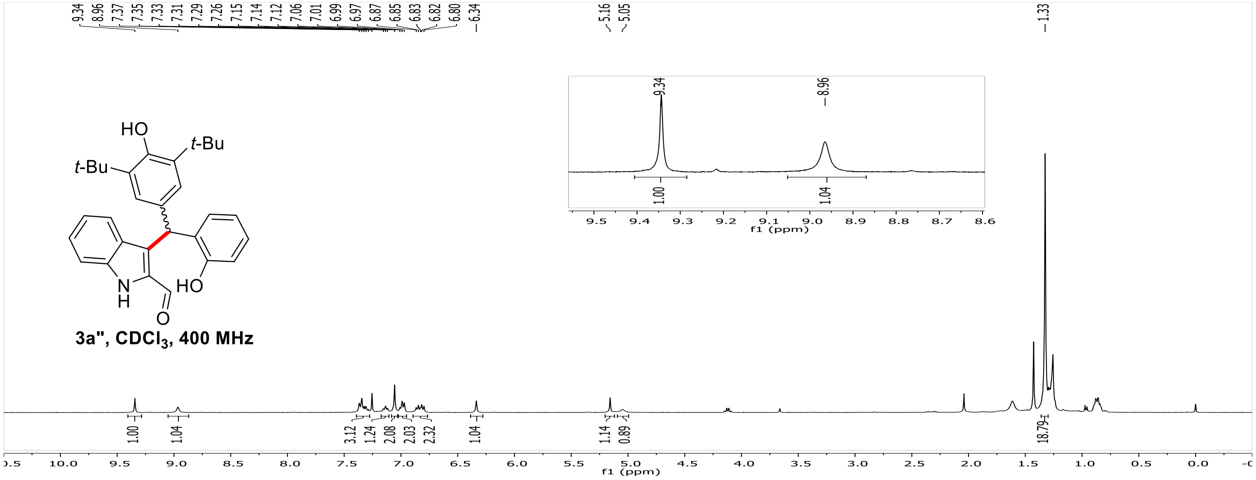
This experiment indicates the role of Bi(OTf)3 in the Friedel-Crafts alkylation step.

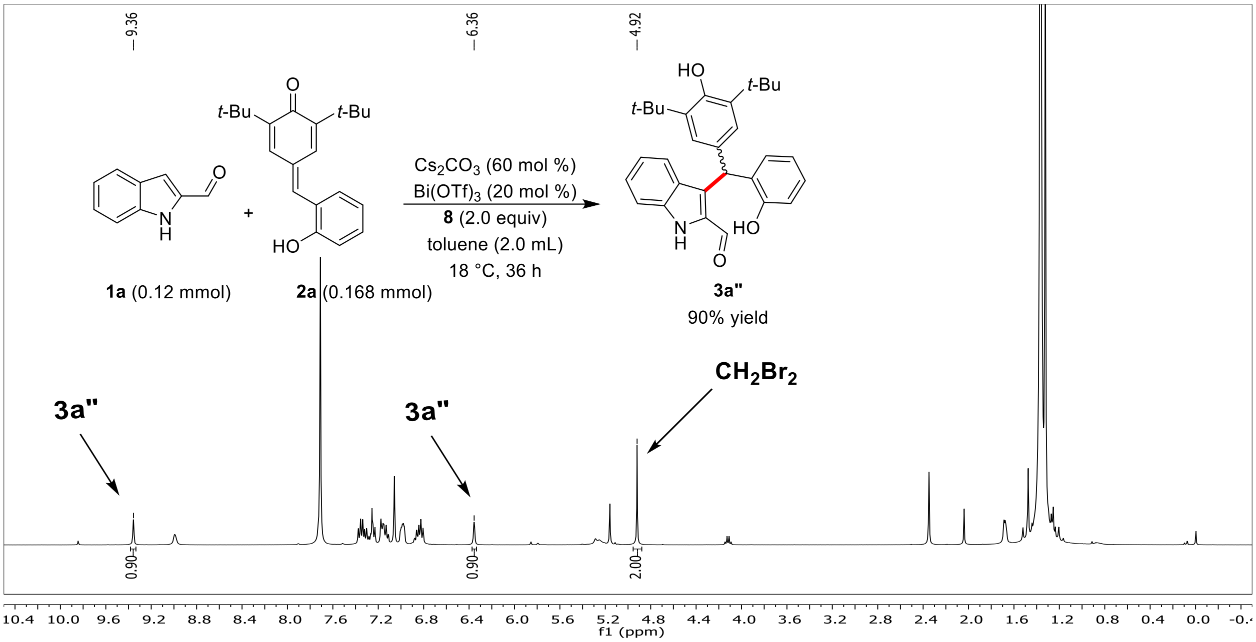
(b) Reaction performed in the absence of NHC



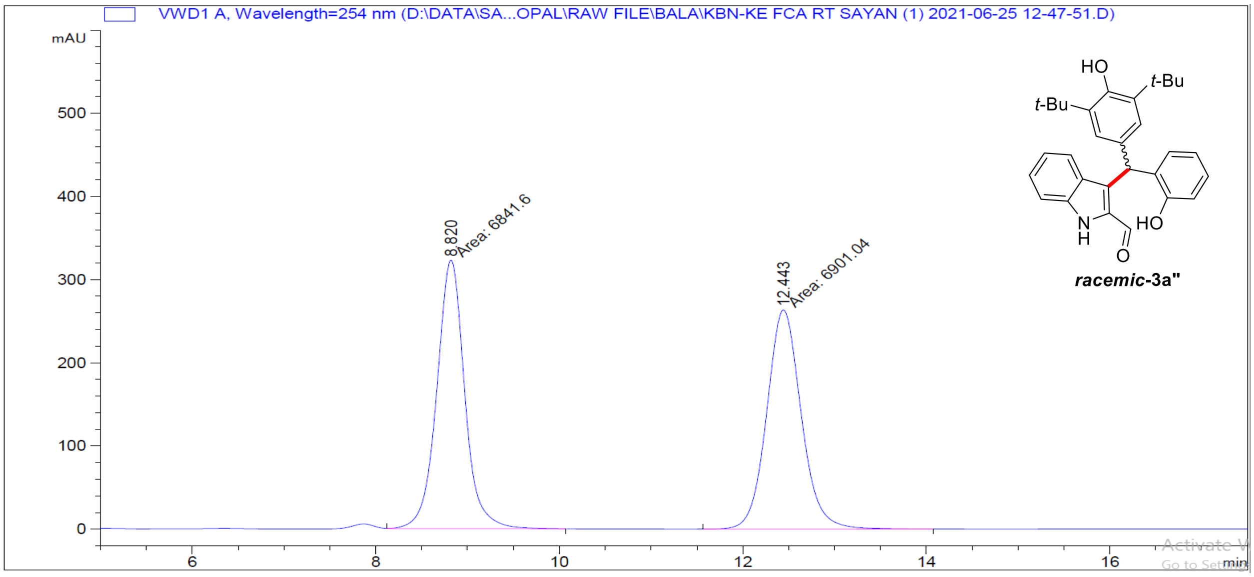
To an oven-dried Schlenk tube with a teflon screw cap was taken the Cs_2CO_3 (19.5 mg, 0.06 mmol) and $Bi(OTf)_3$ (15.6 mg, 0.024 mmol) in a glove-box. Then 1*H*-indole-2-carbaldehyde **1a** (17.4 mg, 0.12 mmol), 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (52.1 mg, 0.168 mmol) and oxidant **8** (49.0 mg, 0.12 mmol) were added outside the glove-box under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, Cs_2CO_3 (3.9 mg, 0.012 mmol), and oxidant **8** (49.0 mg, 0.12 mmol) were added again under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere. After the completion of the reaction, the solvent was evaporated to obtain the crude product, which was analyzed using ^1H NMR using CH_2Br_2 (8.5 µL, 0.12 mmol) as the internal standard. ^1H NMR analysis shows that the crude mixture contains the expected product **3a”** in 90% yield as well as the crude residue was further purified by flash column chromatography on silica gel to afford the corresponding 3-((3,5-di-*tert*-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)-1*H*-indole-2-carbaldehyde **3a”** as a white solid (48.5 mg, 89% yield).

^{1}H-NMR Spectrum of 3-((3,5-di-*tert*-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)-1*H*-indole-2-carbaldehyde 3a”





3-((3,5-di-*tert*-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)-1*H*-indole-2-carbaldehyde (3a”)



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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
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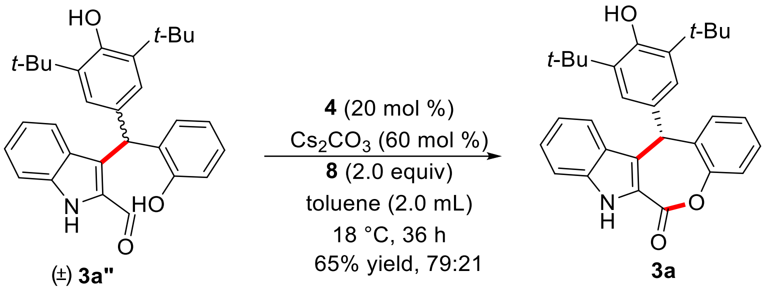
  2  12.443 MM    0.4365 6901.03857  263.52148  50.2163
```

```
Sample Info     : CHIRALPAK IA, 15 % IPA-HEXANE, 1.0 mL/min, 254 nM.M
```

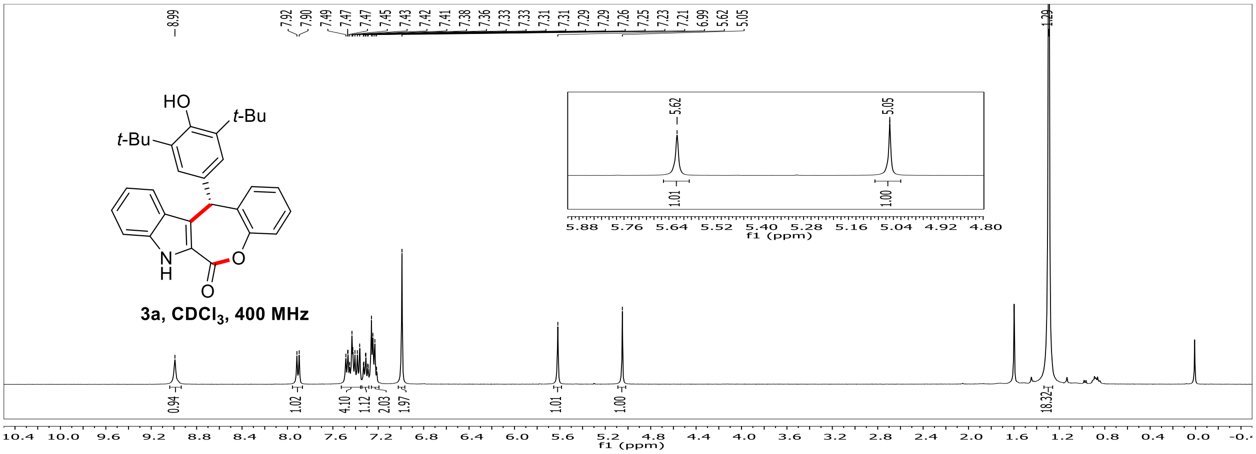
The above result indicates the role of NHC for the formation of the desired ε-lactone product.

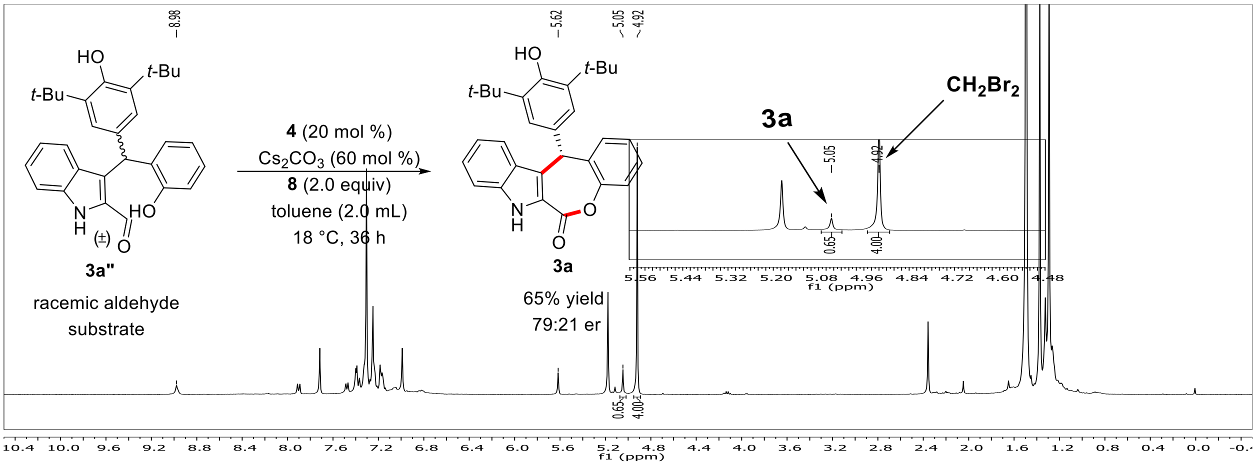
(c) Reaction performed in the absence of **Bi(OTf)₃**



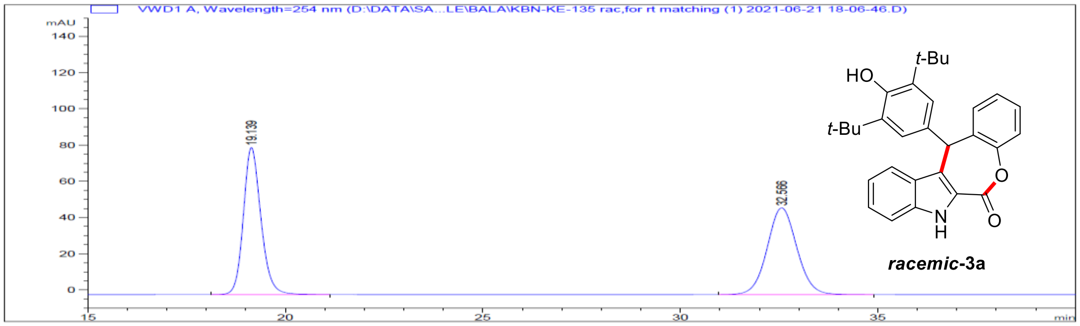
To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (5.6 mg, 0.012 mmol) and Cs_2CO_3 (19.5 mg, 0.06 mmol) in a glove-box. Then 3-((3,5-di-*tert*-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)-1*H*-indole-2-carbaldehyde **3a”** (54.6 mg, 0.12 mmol), and oxidant **8** (49.0 mg, 0.12 mmol) were added outside the glove-box under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (5.6 mg, 0.012 mmol), Cs_2CO_3 (3.9 mg, 0.012 mmol), and oxidant **8** (49.0 mg, 0.12 mmol) were added again under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere. After the completion of the reaction, the solvent was evaporated to obtain the crude product, which was analyzed using ^{1}H NMR using CH_2Br_2 (17.0 µL, 0.24 mmol) as the internal standard. ^{1}H NMR analysis shows that the crude mixture contains the expected product **3a** in 65% yield as well as the crude residue was further purified by flash column chromatography on silica gel to afford the corresponding (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino [3,4-*b*] indol-6-one **3a** as a white solid (35.0 mg, 65 % yield with 79:21 er).

^{1}H-NMR Spectrum of (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino [3,4-*b*] indol-6-one (3a)





(*S*)-12-(3, 5-Di-*tert*-butyl-4-hydroxyphenyl)-7, 12-dihydro-6*H*-benzo [6, 7] oxepino [3, 4-*b*] indol-6-one (3a)



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Peak RetTime Type  Width      Area       Height     Area
  #   [min]        [min]    [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
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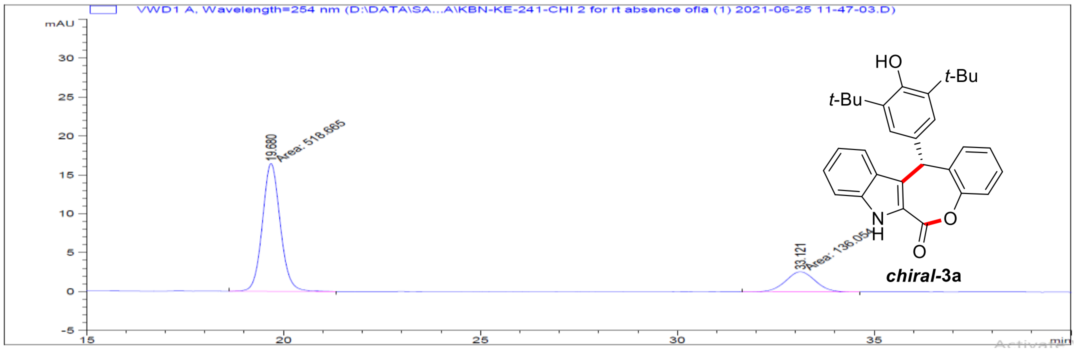
  2   32.566 BB    0.8066 2497.81885   47.80070  49.9696
```



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Peak RetTime Type  Width     Area      Height     Area
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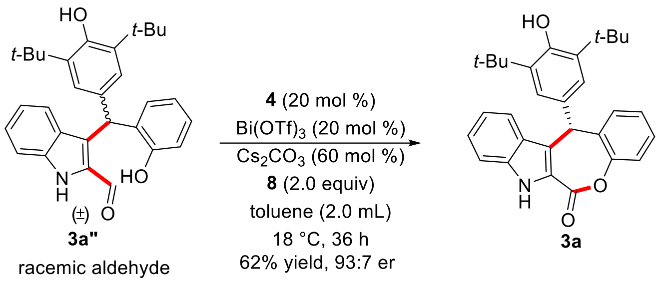
  1   19.680 MM    0.5263  518.66522   16.42613  79.2195
  2   33.121 MM    0.8778  136.05414    2.58312  20.7805
```

```
Sample Info      : CHIRALPAK IA, 10 % IPA-HEXANE, 1.0 mL/min, 254 nM.M
```

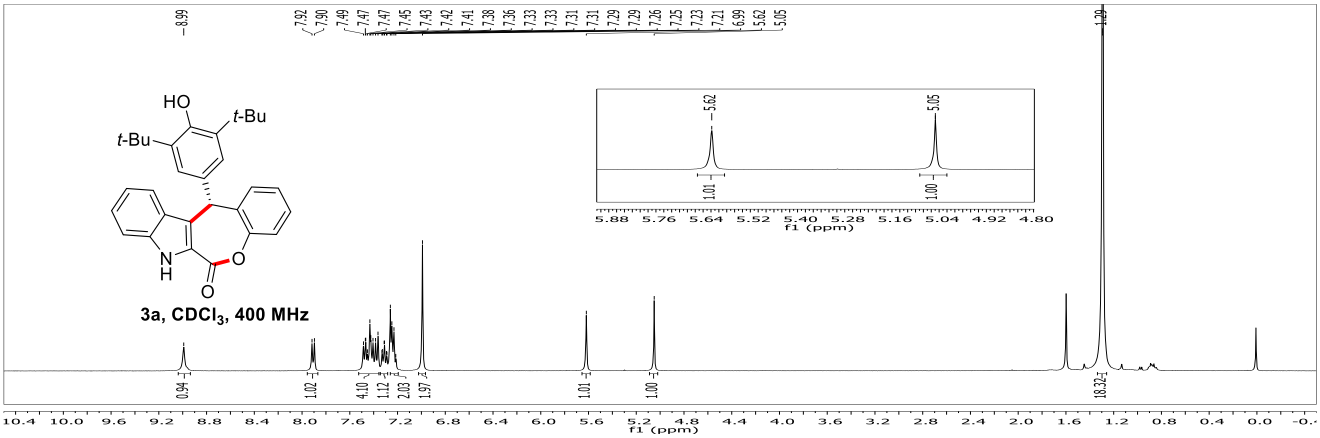
The above result indicates the role of Lewis acid in the present DKR process.

(d) Reaction performed in the presence of Bi(OTf)$_3$

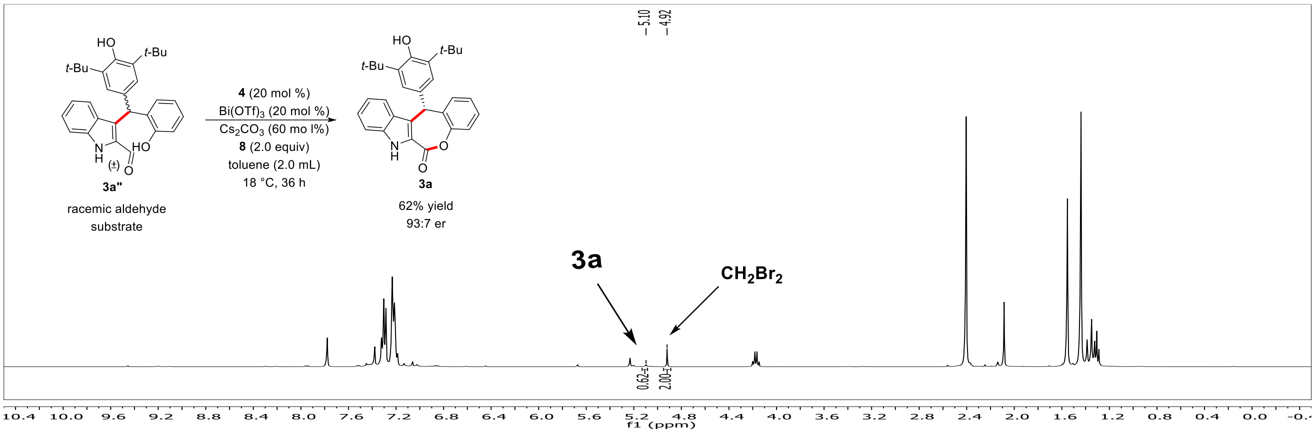


To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (5.6 mg, 0.012 mmol), Cs_2CO_3 (19.5 mg, 0.06 mmol) and Bi(OTf)$_3$ (15.6 mg, 0.024 mmol) in a glove-box. Then 3-((3,5-di-*tert*-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)-1*H*-indole-2-carbaldehyde **3a”** (54.6 mg, 0.12 mmol), and oxidant **8** (49.0 mg, 0.12 mmol) were added outside the glove-box under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (5.6 mg, 0.012 mmol), Cs_2CO_3 (3.9 mg, 0.012 mmol), and oxidant **8**(49.0 mg, 0.12 mmol) were added again under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere. After the completion of the reaction, the solvent was evaporated to obtain the crude product, which was analyzed using ^{1}H NMR using CH_2Br_2 (8.5 µL, 0.12 mmol) as the internal standard. ^{1}H NMR analysis shows that the crude mixture contains the expected product **3a** in 62% yield as well as the crude residue was further purified by flash column chromatography on silica gel to afford the corresponding (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino [3,4-*b*] indol-6-one **3a** as a white solid (33.5 mg, 62 % yield with 93:7 er).

^{1}H-NMR Spectrum of (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3a)

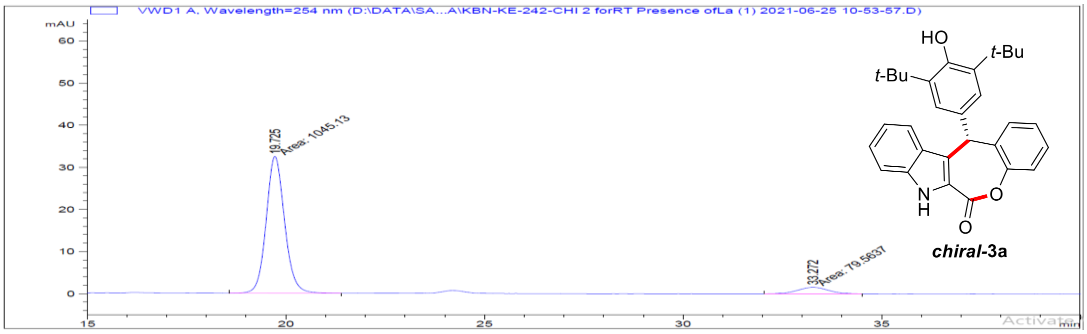


^{1}H-NMR Spectrum of the Reaction Mixture



(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3a)

```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1   19.139 BB    0.4718 2500.86304   81.08739  50.0304
  2   32.566 BB    0.8066 2497.81885   47.80070  49.9696
```



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Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
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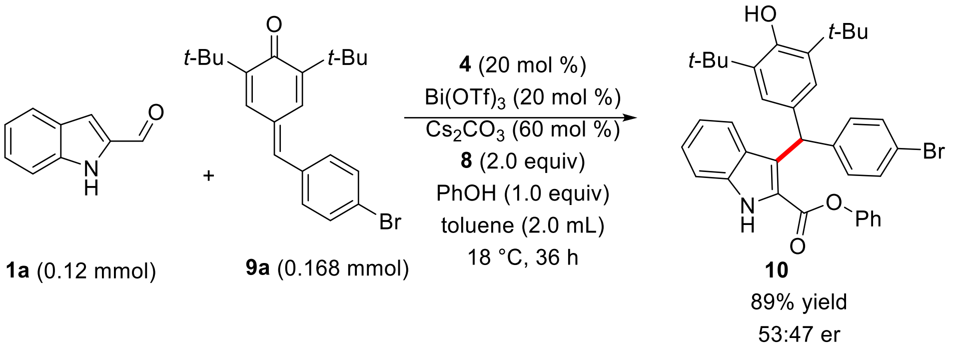
  1   19.725 MM    0.5369 1045.13416   32.44448   92.9258
  2   33.272 MM    0.8763   79.56369    1.51319    7.0742
```

```
Sample Info     : CHIRALPAK IA, 10 % IPA-HEXANE, 1.0 mL/min, 254 nM.M
```

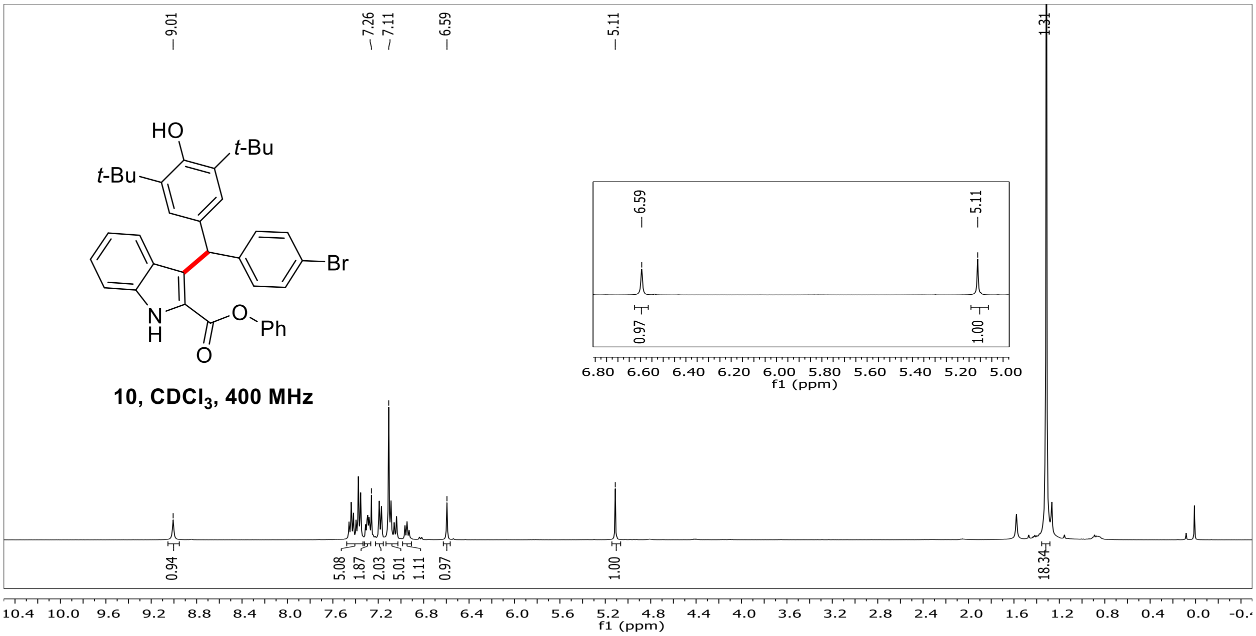
The above result indicates that the present reaction is NHC-Lewis acid cooperatively catalyzed dynamic kinetic resolution.

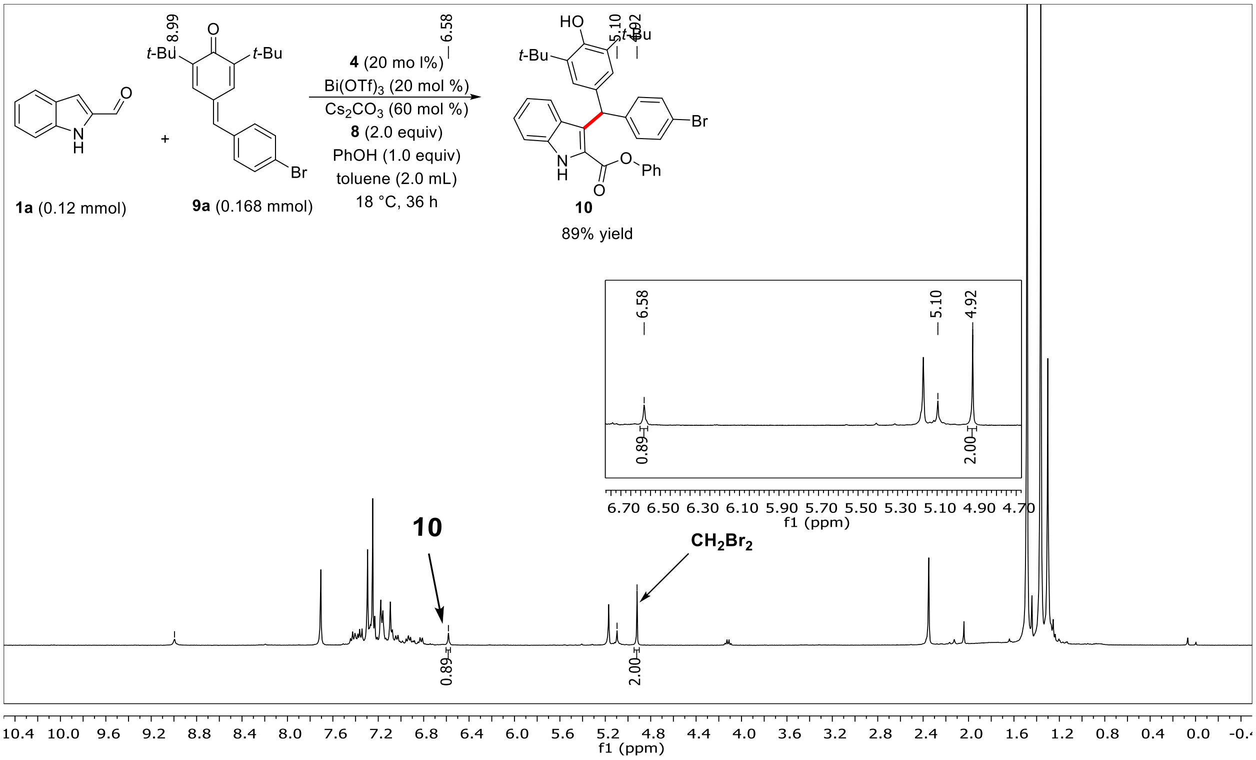
(e) Role of -OH group on PQM (one-pot reaction)



To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (5.6 mg, 0.012 mmol), Cs_2CO_3 (19.5 mg, 0.06 mmol) and $Bi(OTf)_3$ (15.6 mg, 0.024 mmol) in a glove-box. Then 1*H*-indole-2-carbaldehyde **1a** (17.4 mg, 0.12 mmol), 4-(4-bromobenzylidene)-2,6-di-*tert*-butylcyclohexa-2,5-dien-1-one **9a** (62.5 mg, 0.168 mmol), PhOH (11.3 mg, 0.12 mmol), and oxidant **8** (49.0 mg, 0.12 mmol) were added outside the glove-box under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, Cs_2CO_3 (3.9 mg, 0.012 mmol), and oxidant **8** (49.0 mg, 0.12 mmol) were added again under nitrogen atmosphere followed by addition of toluene (1.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere. After the completion of the reaction, the solvent was evaporated to obtain the crude product, which was analyzed using ^{1}H NMR using CH_2Br_2 (8.5 μL, 0.12 mmol) as the internal standard. ^{1}H NMR analysis shows that the crude mixture contains the expected product **10** in 89% yield as well as the crude residue was further purified by flash column chromatography on silica gel to afford the corresponding phenyl 3-((4-bromophenyl)(3,5-di-*tert*-butyl-4-hydroxyphenyl)methyl)-1*H*-indole-2-carboxylate **10** as a white solid (66.0 mg, 89% yield with 53:47 er).

^{1}H-NMR Spectrum of phenyl 3-((4-bromophenyl)(3,5-di-*tert*-butyl-4-hydroxyphenyl)methyl)-1*H*-indole-2-carboxylate (10)

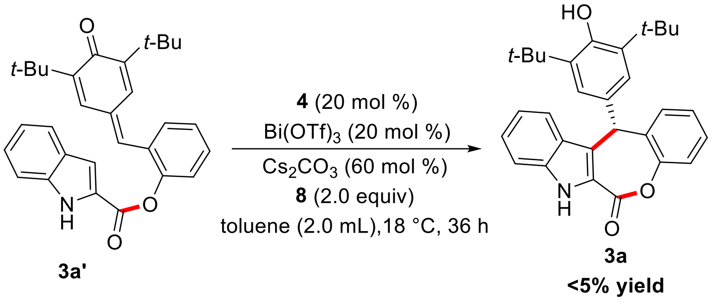




Reaction performed using phenol and paraquinone methide ***9a,*** *which does not contain -OH group afforded the acyclic ester product* ***10*** *in 89% yield with only 6% ee, which indicated that the presence of phenol group on PQM is crucial for getting enantioselectivity.*

(f) To test the feasibility of intramolecular Friedel-Crafts Reaction as the second step

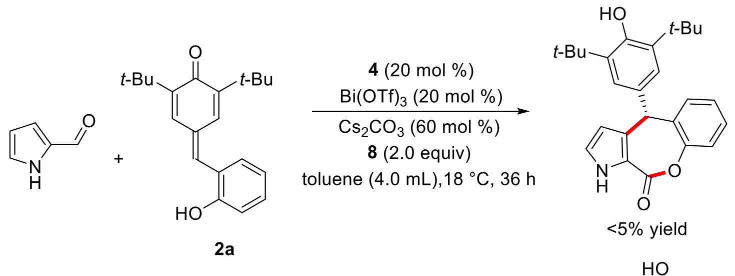
To an oven-dried Schlenk tube with a Teflon screw cap was taken the triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (41.0 mg, 0.125 mmol) and $Bi(OTf)_3$ (33.0 mg, 0.05 mmol) in a glove-box. Then 2-((3,5-di-*tert*-butyl-4-oxocyclohexa-2,5-dien-1-ylidene)methyl)phenyl 1*H*-indole-2-carboxylate **3a'** (113.4 mg, 0.25 mmol), oxidant **8** (102.0 mg, 0.25 mmol) were added outside the glove-box at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (8.0 mg, 0.025 mmol), and oxidant **8** (102.0 mg, 0.25 mmol) were added at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere. The present reaction did not afford the corresponding tetracyclic *ε*-lactone **3a.**

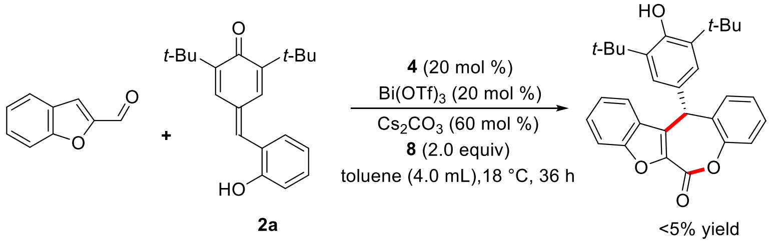


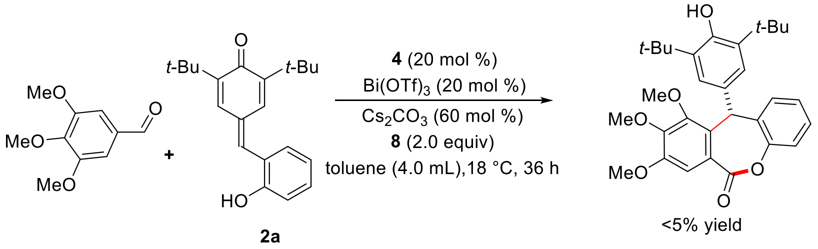
*This reaction did not work and the product **3a** was not formed under these conditions. This indicates that the Friedel-Crafts alkylation proceeds prior to the annulation, which is catalyzed by NHCs.*

(g) Attempted Reaction with other Electron-rich Aldehydes

To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (41.0 mg, 0.125 mmol) and $Bi(OTf)_3$ (33.0 mg, 0.05 mmol) in a glove-box. Then aromatic/heteroaromatic aldehyde derivatives (0.25 mmol), 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2** (108.6 mg, 0.35 mmol) and oxidant **8** (102.0 mg, 0.25 mmol) were added outside the glove-box at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (8.0 mg, 0.025 mmol), and oxidant **8** (102.0 mg, 0.25 mmol) were added at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere.



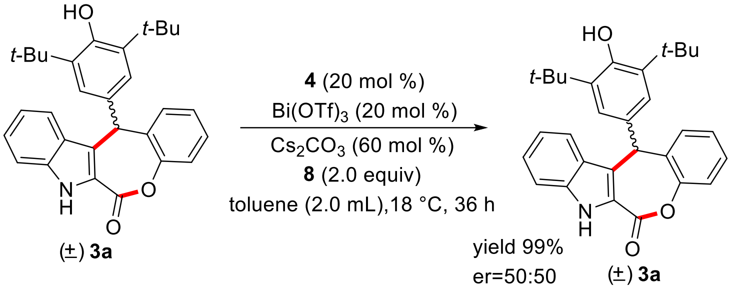




We used the indole 2-carboxaldehydes as nucleophiles because they are sufficiently nucleophilic at the 3-position despite the presence of -CHO moiety at the 2-position. The performed reactions with pyrrole 2-carboxaldehyde, benzofuran 2-carboxaldehyde and 3,4,5-trimethoxy benzaldehyde as nucleophiles did not afford the desired annulated products under the optimized conditions.

(h) Test for the Reversibility of Product Formation

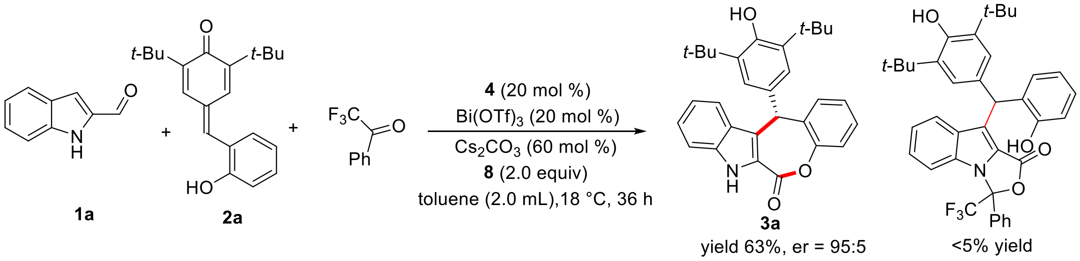
To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (41.0 mg, 0.125 mmol) and $Bi(OTf)_3$ (33.0 mg, 0.05 mmol) in a glove-box. Then 12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (+/-)**3a** (113.4 mg, 0.25 mmol), oxidant **8** (102.0 mg, 0.25 mmol) were added outside the glove-box at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (8.0 mg, 0.025 mmol), and oxidant **8** (102.0 mg, 0.25 mmol) were added at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere, after the completion of the reaction solvent was evaporated, and the crude residue was purified by flash column chromatography on silica gel to afford the corresponding tetracyclic ε-lactones (+/-)**3a** as a white solid (112.0 mg, 99% yield with 50:50 er). The enantiomeric ratio was determined by HPLC analysis on a chiral column.



*The performed a reaction of racemic (+/-)**3a** under the optimized reaction conditions did not afford the enantioenriched lactone **3a**. This indicates the irreversible nature of the present annulation.*

(i) Test the possibility of Indole N-H Functionalization

To an oven-dried Schlenk tube with a Teflon screw cap was taken the triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (41.0 mg, 0.125 mmol) and $Bi(OTf)_3$ (33.0 mg, 0.05 mmol) in a glove-box. Then 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25 mmol), 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol), oxidant **8** (102.0 mg, 0.25 mmol) were added outside the glove-box at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL) and 2,2,2-trifluoro-1-phenylethan-1-one (70.0 µL, 0.5 mmol). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (8.0 mg, 0.025 mmol), and oxidant **8** (102.0 mg, 0.25 mmol) were added at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere, after the completion of the reaction solvent was evaporated, and the crude mixture was passed through a pad of silica gel and eluted with EtOAc (3x10 mL). The reaction mixture was concentrated under reduced pressure and then the yield of **3a** was determined by the ^{1}H NMR analysis of the crude reaction products using CH_2Br_2 as the internal standard.

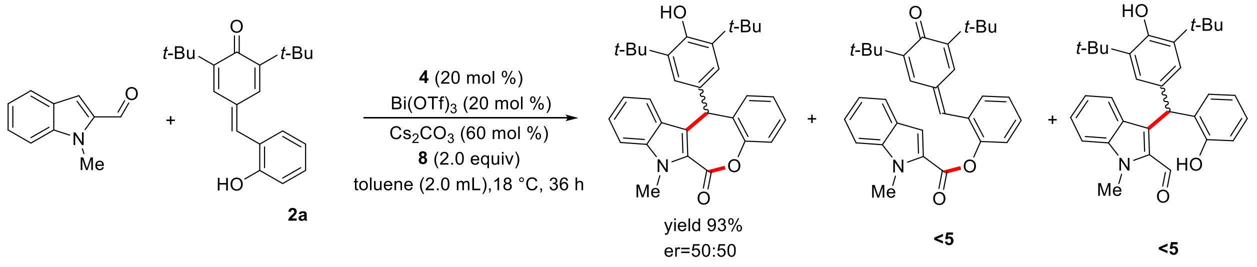


*The desired ε-lactone **3a** was formed in 63% yield and the product derived from NHC-aza-fulvene intermediate was not observed in this case. These results likely indicate that the initial Friedel-Crafts alkylation is faster than the formation of acylazolium intermediate from indole2-aldehyde.*

(j) Reaction Using N-Methyl Indole 2-Carboxaldehyde

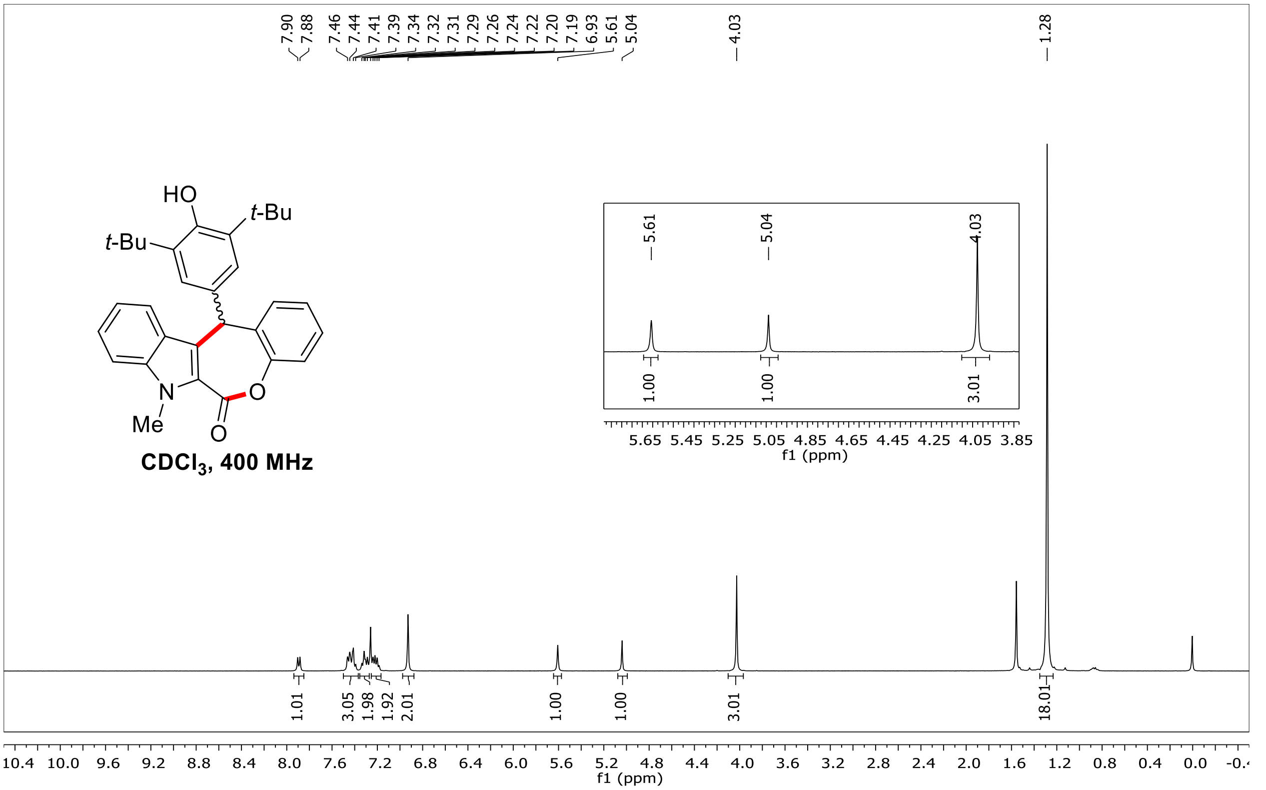
Following the general procedure, treatment of 1-methyl-1*H*-indole-2-carbaldehyde (39.8 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **5** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether - EtOAc: 98:2 to 90:10) to afford 12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-7-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*] indol-6-one as a white solid (117.0 mg, 93 % yield with 50:50 er). ***R_f*** (Pet. ether /EtOAc = 90/10): 0.42; er = 50:50, **HPLC** (Chiralpak IA, *n*-hexane/IPA = 98:2, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 5.1 min, 10.4 min.

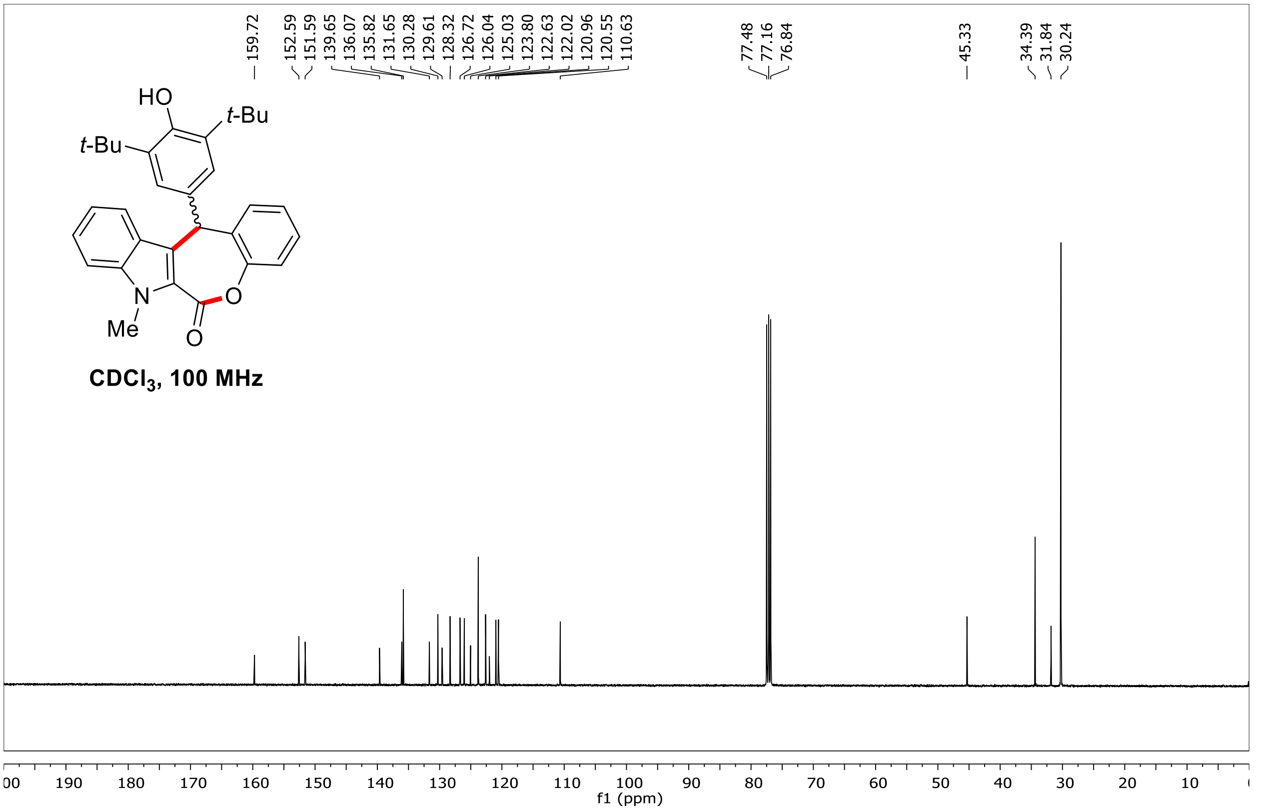
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 1H), 7.46-7.39 (m, 3H), 7.34-7.29 (m, 2H), 7.24-7.19 (m, 2H), 6.93 (s, 2H), 5.61 (s, 1H), 5.04 (s, 1H), 4.03 (s, 3H), 1.28 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 159.7, 152.6, 151.6, 139.6, 136.1, 135.8, 131.6, 130.3, 129.6, 128.3, 126.7, 126.0, 125.0, 123.8, 122.6, 122.6, 122.0, 121.0, 120.5, 110.6, 45.3, 34.4, 31.8, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{31}H_{34}NO_3$ 468.2533; found 468.2538. **FTIR (cm^{-1})** 3635, 2960, 2870,1713, 1488, 1434, 1236, 1177, 1070, 882.



*The reaction afforded the N-methyl ε-lactones in 93% yield and er 50:50; This result indicates that the free N-H is required for getting selectivity. It could be acylazolium **III** stabilized by intramolecular hydrogen bonding with the N-H moiety.*

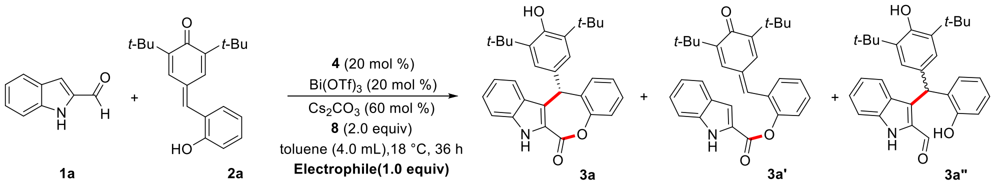
12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one

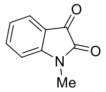
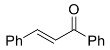
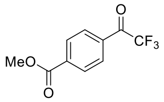
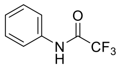
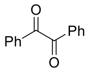
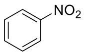




(k) Tolerance of the Reaction with Common Functional Groups

To an oven-dried Schlenk tube with a teflon screw cap was taken the triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (41.0 mg, 0.125 mmol) and $Bi(OTf)_3$ (33.0 mg, 0.05 mmol) in a glove-box. Then 1*H*-indole-2-carbaldehyde derivative **1** (36.3 mg, 0.25 mmol), 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one derivative **2** (108.6 mg, 0.35 mmol), oxidant **8** (102.0 mg, 0.25 mmol) and **electrophile** (0.25 mmol) were added outside the glove-box at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 12 h and then to the stirring solution, triazolium salt **4** (11.6 mg, 0.025 mmol), Cs_2CO_3 (8.0 mg, 0.025 mmol), and oxidant **8** (102.0 mg, 0.25 mmol) were added at 18 °C under nitrogen atmosphere followed by addition of toluene (2.0 mL). The reaction mixture was stirred at 18 °C for 24 h under nitrogen atmosphere, after the completion of the reaction solvent was evaporated, and the crude mixture was passed through a pad of silica gel and eluted with EtOAc (3x10 mL). The reaction mixture was concentrated under reduced pressure and then the yield of recovered electrophile and **3a** was determined by the ^{1}H NMR analysis of the crude reaction products using CH_2Br_2 as the internal standard.

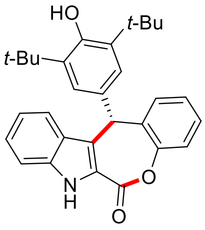


Entry	Electrophile	Electrophile remaining (%)^b	Yield of **3a** (%)^b	er of **3a** (%)^c	Yield of **3a'**(%)^b	Yield of **3a''**(%)^b
1	none	–	68	95:5	<5	<5
2		100	40	95:5	<5	49
3		100	68	95:5	<5	<5
4		92	67	95:5	<5	18
5		92	60	95:5	<5	<5
6		93	33	95:5	<5	55
7		94	66	95:5	<5	<5

^{a} Reaction conditions: **1** (0.25 mmol), **2** (1.4 equiv), Electrophile (0.25 mmol), **4** (20 mol %), $Bi(OTf)_3$ (20 mol %), Cs_2CO_3 (60 mol %), **8** (2.0 equiv), toluene (4.0 mL), 18 °C and 36 h. ^{b} Yield was determined on the basis of the ^{1}H NMR of the crude products using CH_2Br_2 as the internal standard. ^{c} The er was established by HPLC analysis on a chiral stationary phase.

7. Synthesis and Characterization of Tetracyclic *ε*-Lactones

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3a)



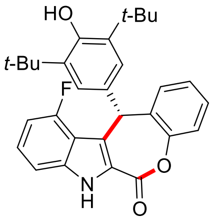
3a

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene) cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*t*er*t*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino [3,4-*b*]indol-6-one (**3a**) as a white solid (78.0 mg, 69 % yield with 95:5 er).

R_f (Pet. ether /EtOAc = 90/10): 0.40; er = 95:5, $[\alpha]_D^{25}$ = +83.98 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 19.0 min (major), 32.5 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.91 (d, *J* = 8.15 Hz, 1H), 7.49-7.36 (m, 4H), 7.33-7.29 (m, 1H), 7.25-7.21 (m, 2H), 6.99 (s, 2H), 5.62 (s, 1H), 5.05 (s, 1H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.7, 152.6, 151.4, 137.3, 135.9, 134.8, 132.0, 130.9, 129.0, 128.5, 127.2, 126.3, 126.2, 123.8, 123.0, 121.5, 121.2, 120.8, 112.4, 46.0, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd for $C_{30}H_{31}NO_3Na$ 476.2196; found 476.2192. **FTIR (cm^{-1})** 3630, 3334, 2960, 2869, 2335, 1690, 1433, 1233, 1094, 895.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-11-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3b)



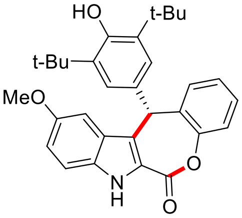
3b

Following the general procedure, treatment of 4-fluoro-1*H*-indole-2-carbaldehyde **1b** (41.0 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-11-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3b**) as a white solid (111.0 mg, 93 % yield with

96:4 er). ***R*_f** (Pet. ether /EtOAc = 90/10): 0.49; er = 96:4, $[\alpha]_D^{25}$ = +58.91 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 26.6 min (major), 33.2 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 7.84 (s, 1H), 7.47-7.46 (m, 1H), 7.36-7.30 (m, 2H), 7.24-7.24 (m, 1H), 7.13-7.11 (m, 1H), 7.04-6.96 (m, 3H), 5.56 (s, 1H), 5.07 (s, 1H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.9 (d, *J* = 244.9 Hz), 160.5, 152.7, 151.4, 137.5 (d, *J* = 12.9 Hz), 136.0, 134.6, 131.7, 130.9, 129.3, 128.7, 126.4, 123.8, 123.0, 122.2 (d, *J* = 10.7 Hz), 122.1 (d, *J* = 3.5 Hz), 111.08 (d, *J* = 24.9 Hz), 98.4 (d, *J* = 26.3 Hz), 46.1, 34.4, 30.2. **^{19}F-NMR (376 MHz, $CDCl_3$)** δ = -113.1. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{31}FNO_3$: 472.2282, found: 472.2288. **FTIR (cm^{-1})** 3614, 3322, 2959, 2333, 1691, 1628, 1433, 1317, 1235, 1082, 1024, 840.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-methoxy-7,12-dihydro-6*H*-benzo[6,7] oxepino[3, 4-b]indol-6-one (3c)

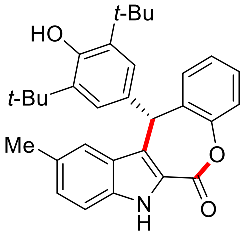


3c

Following the general procedure, treatment of 5-methoxy-1*H*-indole-2-carbaldehyde **1c** (43.8 mg, 0.25mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert* butyl-4-hydroxyphenyl)-10-methoxy-7, 12-dihydro-6*H*-benzo[6,7]oxepino[3, 4-b]indol-6-one **(3c)** as a white solid (87 mg, 72 % yield with 94:6 er). ***R*_f** (Pet. ether /EtOAc = 85/15): 0.41; er =94:6, $[\alpha]_D^{25}$ = +21.38 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 12.3 min (major), 24.1 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 7.49 (d, *J* = 6.41 Hz, 1H), 7.38-7.29 (m, 3H), 7.24-7.22 (m, 2H), 7.10-7.07 (m, 1H), 7.00 (s, 2H), 5.56 (s, 1H), 5.06 (s, 1H), 3.91 (s, 3H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.7, 155.1, 152.5, 151.5, 135.9, 134.9, 132.8, 132.1, 130.9, 128.5, 128.3, 126.5, 126.2, 123.8, 123.0, 121.9, 119.2, 113.5, 100.3, 55.9, 46.0, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{31}H_{34}NO_4$ 484.2482; found 484.2485. **FTIR (cm^{-1})** 3104, 3064, 2924, 2854, 2377, 2305, 1694, 1629, 1586, 1433, 1117, 1021, 900, 851.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-methyl-7,12-dihydro-6*H*benzo [6,7]oxepino[3,4-b]indol-6-one (3d)



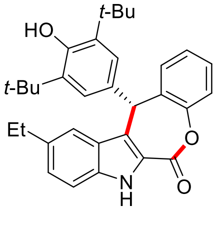
3d

Following the general procedure, treatment of 5-methyl-1*H*-indole-2-carbaldehyde **1d** (39.8 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-10-methyl-7,12-dihydro-6*H* benzo [6,7]oxepino[3,4-b]indol-6-one (**3d**) as a yellow solid (84.1 mg, 72 % yield with >99:1 er).

***R**_f_* (Pet. ether /EtOAc = 90/10): 0.24; er = >99:1, $[\alpha]_D^{25}$ = +32.65 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 11.2 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 7.65 (s, 1H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.36-7.19 (m, 5H), 6.99 (s, 2H), 5.58 (s, 1H), 5.04 (s, 1H), 2.48 (s, 3H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.8, 152.6, 151.4, 135.8, 135.0, 132.0, 130.8, 130.6, 129.2, 128.4, 128.3, 126.4, 126.2, 123.8, 123.0, 121.6, 119.9, 112.1, 46.0, 34.4, 30.2, 21.7. **HRMS (ESI)** calculated $[M+Na]^+$ for $C_{31}H_{33}NNaO_3$: 490.2353, found: 490.2355. **FTIR (cm^{-1})** 3635, 3325, 2959, 2867, 1690, 1433, 1232, 1076, 863.

(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-10-ethyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3e)



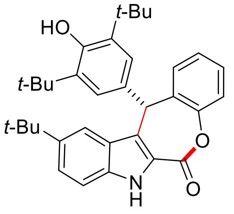
3e

Following the general procedure, treatment of 5-ethyl-1*H*-indole-2-carbaldehyde **1e** (43.3 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-10-ethyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3e) as a white solid (89.7 mg, 75 % yield with 98:2 er).

Rf (Pet. ether /EtOAc = 90/10): 0.29; er = 98:2, $[\alpha]_D^{25}$ = +28.4 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 11.4 min (major), 27.3 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99-8.98 (m, 1H), 7.70 (s, 1H), 7.50-7.48 (m, 1H), 7.38-7.35 (m, 2H), 7.33-7.26 (m, 2H), 7.25-7.21 (m, 1H), 7.02 (s, 2H), 5.62 (s, 1H), 5.06 (s, 1H), 2.80 (q, *J* = 7.4 Hz, 2H), 1.34-1.30 (m, 21H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.8, 152.6, 151.6, 137.3, 136.0, 135.9, 134.9, 132.2, 130.9, 128.7, 128.5, 128.3, 126.5, 126.3, 123.9, 123.0, 121.6, 118.7, 112.2, 46.0, 34.4, 30.3, 29.2, 16.3. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{32}H_{36}NO_3$: 482.2690, found: 482.2692. **FTIR (cm^{-1})** 3451, 3417, 2918, 2867, 1691, 1629, 1433, 1335, 1174.

(*S*)-10-(*Tert*-butyl)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H* benzo[6,7]oxepino[3,4-b]indol-6-one (3f)



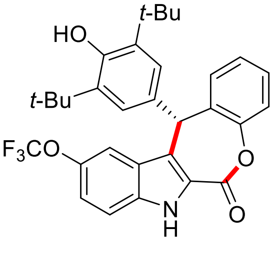
3f

Following the general procedure, treatment of 5-(*tert*-butyl)-1*H*-indole-2-carbaldehyde **1f** (52.6 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2 hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-10-(*tert*-butyl)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H* benzo[6,7]oxepino[3,4-b]indol-6-one (**3f**) as a white solid (81.4 mg, 64 % yield with 95:5 er).

Rf (Pet. ether /EtOAc = 90/10): 0.28; er = 95:5, $[\alpha]_D^{25}$ = +19.5 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 98:2, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 9.6 min (minor), 11.6 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.86 (s, 1H), 7.52-7.48 (m, 2H), 7.40-7.35 (m, 2H), 7.34-7.29 (m, 1H), 7.25-7.21 (m, 1H), 7.03 (s, 2H), 5.63 (s, 1H), 5.06 (s, 1H), 1.42 (s, 9H),1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.8, 152.6, 151.6, 144.2, 135.9, 135.6, 134.6, 132.3, 131.1, 129.3, 128.5, 126.3, 126.1, 126.0, 123.9, 123.0, 121.3, 115.9, 112.0, 45.9, 35.0, 34.4, 31.8. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{34}H_{40}NO_3$: 510.3003, found: 510.3008. **FTIR (cm^{-1})** 3189, 3069, 2960, 2868, 2362, 1690, 1433, 1232, 1067, 868.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-(trifluoromethoxy)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3g)



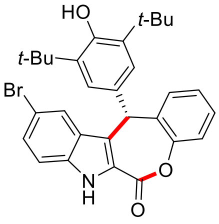
3g

Following the general procedure, treatment of 5-(trifluoromethoxy)-1*H*-indole-2-carbaldehyde **1g** (57.2 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-(trifluoromethoxy)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3g**) as a white solid (78.0 mg, 72 % yield with 91:9 er).

R_f (Pet. ether /EtOAc = 90/10): 0.25; er = 91:9, $[\alpha]_D^{25}$ = +4.30 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 6.4 min (major), 11.7 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.76 (s, 1H), 7.49-7.44 (m, 2H), 7.39-7.24 (m, 4H), 6.97 (s, 2H), 5.54 (s, 1H), 5.08 (s, 1H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.5, 152.8, 151.3, 143.9, 136.1, 135.4, 134.4, 131.7, 131.1, 129.2, 128.8, 126.6, 126.2, 123.7, 123.2, 123.0, 121.5, 120.8 (q, *J* = 256.2 Hz), 113.6, 112.9, 46.0, 34.4, 30.1. **^{19}F-NMR (376 MHz, $CDCl_3$)** δ = -58.1. **HRMS (ESI)** calculated $[M+Na]^+$ for $C_{31}H_{30}F_3NO_4Na$: 560.2019, found: 560.2025. **FTIR (cm^{-1})** 3640, 3402, 2963, 2854, 1692, 1434, 1265, 1078, 865.

(*S*)-10-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo [6,7]oxepino[3,4-*b*]indol-6-one (3h)

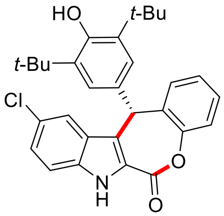


3h

Following the general procedure, treatment of 5-bromo-1*H*-indole-2-carbaldehyde **1h** (56.0 mg, 0.25mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-10-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo [6,7]oxepino[3,4-*b*]indol-6-one (**3h**) as a white solid (85 mg, 64 % yield with 91:9 er). ***R$_f$*** (Pet. ether /EtOAc = 90/10): 0.40; er = 91:9, $[\alpha]_D^{25}$ = +29.61 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 7.3 min (major), 14.0 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.03 (s, 1H), 7.49-7.47 (m, 2H), 7.36-7.29 (m, 3H), 7.24-7.23 (m, 1H), 6.96 (s, 2H), 5.52 (s, 1H), 5.07 (s, 1H), 1.30 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.4, 152.8, 151.2, 136.0, 135.7, 134.7, 131.5, 130.8, 130.1, 128.7, 127.9, 127.7, 126.5, 123.7, 123.4, 123.0, 122.7, 114.4, 114.0, 46.0, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{31}BrNO_3$ 532.1482; found 532.1487. **FTIR (cm^{-1})** 3633, 3298, 2959, 2868, 1691, 1432, 1368, 1213, 1159, 1083, 943, 860.

(*S*)-10-Chloro-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3i)



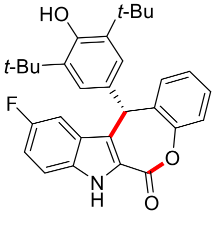
3i

Following the general procedure, treatment of 5-chloro-1*H*-indole-2-carbaldehyde **1i** (45.0 mg, 0.25mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-10-chloro-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3i**) as a white solid (87 mg, 71 % yield with 95:5 er).

R$_f$ (Pet. ether /EtOAc = 90/10): 0.41; er = 95:5, $[\alpha]_D^{25}$ = +7.92 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 8.4 min (major), 17.6 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.86 (s, 1H), 7.48-7.30 (m, 6H), 6.96 (s, 2H), 5.52 (s, 1H), 5.07 (s, 1H), 1.30 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.4, 152.8, 151.2, 136.0, 135.5, 134.7, 131.5, 130.8, 128.7, 128.0, 127.7, 127.1, 127.0, 126.5, 123.7, 123.0, 122.9, 120.2, 113.6, 46.0, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{31}ClNO_3$ 488.1987; found 488.1992. **FTIR (cm^{-1})** 3629, 3292, 2954, 2913, 2858, 1692, 1458, 1430, 1369, 1295, 1233, 1176, 1019, 949, 859.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3j)

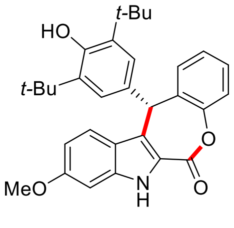


3j

Following the general procedure, treatment of 5-fluoro-1*H*-indole-2-carbaldehyde **1j** (41.0 mg, 0.25mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (**3j**) as a white solid (96 mg, 81 % yield with 99:1 er). ***R_f*** (Pet. ether /EtOAc = 90/10): 0.36; er = 99:1, $[\alpha]_D^{25}$ = +45.58 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 8.2 min (major), 24.1 min (minor).

^{1}H NMR (400 MHz, acetone-D6) δ 11.14 (s, 1H), 7.74-7.71 (m, 3H), 7.30-7.10 (m, 6H), 5.87 (s, 2H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, acetone-D6)** δ 160.1, 159.1 (d, *J* = 235.7 Hz), 153.5, 152.4, 138.2, 138.1, 136.9, 135.4, 133.6, 131.7, 129.3, 128.7 (d, *J* = 5.7 Hz), 127.1, 127.0, 124.4, 123.4, 116.4 (d, *J* = 27.2 Hz), 115.1 (d, *J* = 27.2 Hz), 105.6 (d, *J* = 23.7 Hz), 46.0, 35.2, 30.6. **^{19}F-NMR (376 MHz, $CDCl_3$)** δ = -121.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{31}FNO_3$ 472.2282; found 472.2286. **FTIR (cm^{-1})** 3632, 3294, 2959, 2870, 2332, 1693, 1628, 1547, 1433, 1359, 1231, 1149, 1075.

(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-9-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3k)



3k

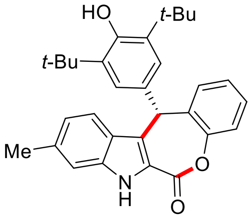
Following the general procedure, treatment of 6-methoxy-1*H*-indole-2-carbaldehyde **1k** (43.8 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-9-

methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (**3k**) as a white solid (73.5 mg, 61 % yield with 95:5 er).

R_f (Pet. ether /EtOAc = 90/10): 0.20; er = 95:5, $[\alpha]_D^{25}$ = +36.8 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 22.2 min (major), 48.4 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 7.79 (d, *J* = 8.9 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.35-7.32 (m, 1H), 7.29-7.24 (m, 1H), 7.03 (s, 2H), 6.95-6.92 (m, 1H), 6.87 (s, 1H), 5.60 (s, 1H), 5.10 (s, 1H), 3.90 (s, 3H),1.33 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.8, 160.3, 152.6, 151.6, 138.8, 135.8, 134.7, 132.0, 130.9, 129.7, 128.5, 126.2, 123.8, 123.0, 121.7, 120.7, 120.2, 113.3, 93.7, 55.7, 46.1, 34.4, 30.2. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{31}H_{34}NO_4$: 484.2482, found: 484.2483. **FTIR (cm^{-1})** 3635, 3318, 3071, 2961, 2870, 1683, 1627, 1433, 108, 759.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3l)

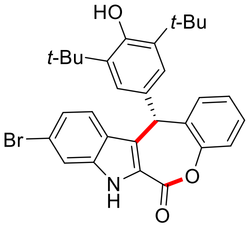


3l

Following the general procedure, treatment of 6-methyl-1*H*-indole-2-carbaldehyde **1l** (39.8 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-9-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3l**) as a white solid (89.0 mg, 78% yield with >99:1 er). ***R_f*** (Pet. ether /EtOAc = 90/10): 0.41; er = >99:1, $[\alpha]_D^{25}$ = +46.42 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 24.6 min (major), 42.9 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.77-7.75 (m, 1H), 7.47-7.45 (m, 1H), 7.30-7.30 (m, 1H), 7.21-7.21 (m, 3H), 7.08-7.06 (m, 1H), 6.98 (s, 2H), 5.57 (s, 1H), 5.04 (s, 1H), 2.49 (s, 3H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.8, 152.6, 151.5, 137.8, 137.7, 135.8, 134.8, 132.1, 130.9, 129.1, 128.5, 126.2, 124.3, 123.8, 123.4, 123.0, 120.9, 120.4, 111.9, 46.1, 34.4, 30.2, 22.2. **HRMS (ESI)** $[M+H]^+$ calcd for $C_{31}H_{34}NO_3$: 468.2533, found: 468.2535. **FTIR (cm^{-1})** 3583, 3322, 3077, 2923, 2852, 1716, 1544, 1433, 1326, 1233, 1081, 1022.

(*S*)-9-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3m)

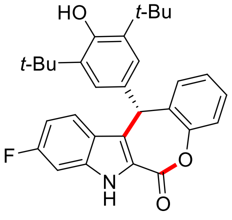


3m

Following the general procedure, treatment of 6-bromo-1*H*-indole-2-carbaldehyde **1m** (56.0 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-9-Bromo-12-(3,5-di-*t*er*t*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3m**) as a white solid (101.0 mg, 76% yield with 96:4 er). ***R**f* (Pet. ether /EtOAc = 90/10): 0.46; er = 96:4, $[\alpha]_D^{25}$ = +45.84 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 27.1 min (major), 33.8 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (s, 1H), 7.76 (d, *J* = 8.77 Hz, 1H), 7.62 (s, 1H), 7.46 (d, *J* = 7.51 Hz, 1H), 7.36-7.30 (m, 3H), 7.25-7.21 (m, 1H), 6.94 (s, 2H), 5.5 (s, 1H), 5.07 (s, 1H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.4, 152.8, 151.3, 137.7, 136.0, 134.6, 131.7, 130.9, 129.0, 128.7, 126.4, 125.1, 124.9, 123.7, 123.0, 122.2, 122.1, 121.2, 115.3, 45.9, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{31}BrNO_3$ 532.1482; found 532.1487. **FTIR (cm^{-1})** 3745, 3617, 3586, 3290, 2920, 2866, 2364, 1836, 1742, 1695, 1539, 1429, 1218, 1044.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3n)

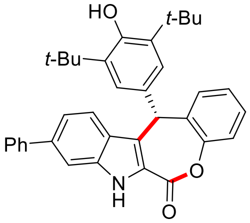


3n

Following the general procedure, treatment of 6-fluoro-1*H*-indole-2-carbaldehyde **1n** (40.8 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet.ether-EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-9-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3n**) as a white solid (86.0 mg, 72% yield with 83:17 er). ***R_f*** (Pet. ether /EtOAc = 90/10): 0.35; er = 83:17, $[\alpha]_D^{25}$ = +181.28 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 8.2 min (minor), 13.5 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 7.48 (d, *J* = 7.31 Hz, 1H), 7.38-7.27 (m, 3H), 7.24-7.18 (m, 2H), 7.10 (s, 2H), 6.88-6.84 (m, 1H), 5.92 (s, 1H), 5.06 (s, 1H), 1.31 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.5, 158.5 (d, *J* = 250.7 Hz), 152.7, 151.3, 139.2 (d, *J* =9.2 Hz), 135.9, 134.8, 132.4, 131.3, 128.6, 127.7 (d, *J* =4.4 Hz), 127.5 (d, *J* =8.3 Hz), 126.5, 124.0, 122.8, 121.7, 115.7 (d, *J* = 18.1 Hz), 108.6 (d, *J* = 4.1 Hz), 106.0 (d, *J* = 19.2 Hz), 47.2, 34.4, 30.2. **^{19}F-NMR (376 MHz, $CDCl_3$)** δ = -121.0. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{31}FNO_3$: 472.2282, found: 472.2289. **FTIR (cm^{-1})** 3631, 3295, 2912, 2009, 1692, 1608, 1428, 1239, 1110, 1051, 902, 733.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-phenyl-7,12-dihydro-6*H* benzo[6,7]oxepino[3,4-*b*]indol-6-one (3o)

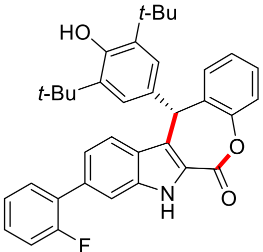


3o

Following the general procedure, treatment of 6-phenyl-1*H*-indole-2-carbaldehyde **1o** (55.3 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-9-phenyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3o**) as a white solid (98 mg, 74 % yield with 94:6 er). ***R_f*** (Pet. ether /EtOAc = 90/10): 0.41; er = 94:6, $[\alpha]_D^{25}$ = +25.48 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 24.8 min (major), 59.3 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 7.95 (d, *J* = 8.56 Hz, 1H), 7.68-7.63 (m, 3H), 7.53-7.45 (m, 4H), 7.39-7.30 (m, 3H), 7.24-7.22 (m, 1H), 7.03 (s, 2H), 5.64 (s, 1H), 5.06 (s, 1H), 1.31 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.6, 152.7, 151.5, 141.4, 140.6, 137.9, 136.0, 134.9, 132.0, 130.9, 129.0, 129.0, 128.6, 127.7, 127.6, 126.3, 125.6, 123.8, 123.0, 122.0, 121.4, 121.1, 110.5, 46.2, 34.4, 30.3. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{36}H_{36}NO_3$ 530.2690; found 530.2691. **FTIR (cm^{-1})** 3618, 3337, 2918, 2861, 2237, 1684, 1510, 1429, 1358, 1239, 1142, 904, 867.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-(2-fluorophenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino[3,4-*b*] indol-6-one (3p)



3p

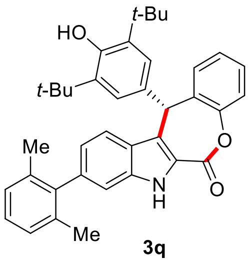
Following the general procedure, treatment of 6-(2-fluorophenyl)-1*H*-indole-2-carbaldehyde **1p** (59.8 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-9-(2-fluorophenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino[3,4-*b*] indol-6-one (**3p**) as a yellow solid (91.7 mg, 67 % yield with 95:5 er).

R$_f$ (Pet. ether /EtOAc = 90/10): 0.23; er = 95:5, $[\alpha]_D^{25}$ = +51.08 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 23.2 min (major), 43.4 (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.63 (s, 1H), 7.53-7.44 (m, 3H), 7.39-7.30 (m, 3H), 7.26-7.16 (m, 3H), 7.04 (s, 2H), 5.64 (s, 1H), 5.07 (s, 1H), 1.31 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.6, 159.9 (d, *J* = 248.0 Hz), 152.7, 151.4, 137.4, 135.9, 134.8, 131.9, 131.1(d, *J* = 3.6 Hz), 130.9, 129.4, 129.3, 129.2, 128.8, 128.6, 126.4, 125.6, 124.6 (d, *J* = 3.6 Hz), 123.8, 123.0, 122.8 (d, *J* = 2.2 Hz), 122.2, 120.7, 116.4 (d, *J* = 22.8 Hz), 112.8 (d, *J* = 3.0 Hz) 46.2, 34.4, 30.2. **^{19}F-NMR (376 MHz, $CDCl_3$)** δ = -117.5. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{36}H_{35}FNO_3$: 548.2595, found: 548.2601. **FTIR (cm^{-1})** 3635, 3329, 2961, 2870, 1686, 1435, 1236, 1080, 872.

(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-9-(2,6-dimethylphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3q)

Following the general procedure, treatment of 6-(2,6-dimethylphenyl)-1*H*-indole-2-carbaldehyde **1q** (62.3 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-

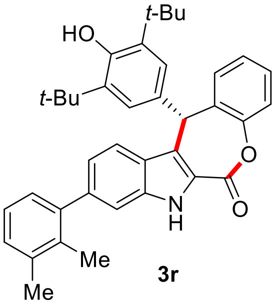

3q

one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether - EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-9-(2,6-dimethylphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3q**)as a white solid (93.1 mg, 67 % yield with 96:4 er).

R$_f$ (Pet. ether /EtOAc = 90/10): 0.25; er = 96:4, $[\alpha]_D^{25}$ = +19.8 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 13.9 min (minor), 24.0 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (s, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.48 (d, *J* = 7.3 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.23-7.11 (m, 5H), 7.04 (s, 3H), 5.66 (s, 1H), 5.07 (s, 1H), 2.02 (s, 6H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.8, 152.7, 151.5, 141.8, 140.5, 137.7, 136.2, 136.2, 135.9, 134.7, 132.1, 131.0, 129.2, 128.6, 127.5, 127.5, 127.4, 126.4, 125.1, 123.8, 123.0, 121.5, 120.9, 112.5, 46.2, 34.4, 30.2, 20.9, 20.9. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{38}H_{40}NO_3$: 558.3003, found: 558.3007. **FTIR (cm^{-1})** 3452, 3396, 2920, 2868, 1869, 1626, 1434, 1027, 898.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-(2,3-dimethylphenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino[3,4-*b*] indol-6-one (3r)

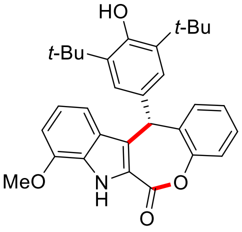

3r

Following the general procedure, treatment of 6-(2,3-dimethylphenyl)-1*H*-indole-2-carbaldehyde **1r** (62.3 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-9-(2,3-dimethylphenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino[3,4-*b*] indol-6-one (**3r**) as a white solid (94.7 mg, 68 % yield with 95:5 er).

Rf (Pet. ether /EtOAc = 90/10): 0.25; er = 95:5, $[\alpha]_D^{25}$ = +36.46 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 95:5, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 40.7 min (major), 47.7 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 7.3 Hz, 1H), 7.39-7.30 (m, 3H), 7.23-7.12 (m, 5H), 7.05 (s, 2H), 5.64 (s, 1H), 5.06 (s, 1H), 2.36 (s, 3H), 2.15 (s, 3H), 1.31 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.8, 152.7, 151.4, 142.3, 142.0, 137.4, 137.3, 135.9, 134.8, 134.2, 132.1, 130.9, 129.2, 129.0, 128.5, 127.8, 126.3, 125.4, 124.9, 123.9, 123.6, 123.0, 121.7, 120.1, 112.8, 46.3, 34.4, 30.2, 20.8, 17.2. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{38}H_{40}NO_3$: 558.3003, found: 548.3009. **FTIR (cm^{-1})** 3637, 3397, 2962, 2868, 1688, 1433, 1236, 1098, 870.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-8-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3s)

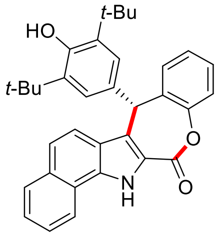


3s

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1s** (43.8 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene) cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-8-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3s**) as a white solid (74.0 mg, 61% yield with 96:4 er). ***Rf*** (Pet. ether /EtOAc = 85/15): 0.36; er = 96:4, $[\alpha]_D^{25}$ = +51.12 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 8.8 min (minor), 33.8 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.48-7.46 (m, 2H), 7.38-7.36 (m, 1H), 7.32-7.31 (m, 1H), 7.24-7.22 (m, 1H), 7.17-7.15 (m, 1H), 6.99 (s, 2H), 6.88 (d, *J* = 7.56 Hz, 1H) 5.58 (s, 1H), 5.04 (s, 1H), 3.97 (s, 3H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.5, 152.6, 151.5, 146.8, 135.9, 134.9, 132.1, 130.9, 129.1, 128.7, 128.5, 127.5, 126.2, 123.8, 123.0, 121.7, 121.2, 112.9, 105.6, 55.7, 46.3, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{31}H_{34}NO_4$ 484.2482, found: 484.2488. **FTIR (cm^{-1})** 3634, 3321, 3007, 2364, 1704, 2861, 1580, 1392, 1259, 1113, 983, 856.

(*S*)-7-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-7,14-dihydro-13*H*-benzo[*g*]benzo[6,7] oxepino[3,4-*b*]indol-13-one (3t)



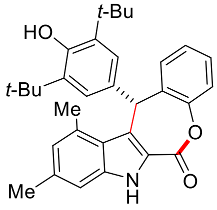
3t

Following the general procedure, treatment of 1H-benzo[*g*]indole-2-carbaldehyde **1t** (48.8 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-7-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-7,14-dihydro-13*H*-benzo[*g*]benzo[6,7]oxepino[3,4-*b*]indol-13-one (**3t**) as a white solid (77.6 mg, 62 % yield with 99:1 er).

R_f (Pet. ether /EtOAc = 90/10): 0.25; er = 99:1, $[\alpha]_D^{25}$ = +36.1 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 8.8 min (minor), 9.7 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19-10.12 (m, 1H), 8.24-8.20 (m, 1H), 7.93 (d, *J* = 7.9 Hz, 1H), 7.86 (d, *J* = 8.9 Hz, 1H), 7.62-7.51 (m, 4H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.27-7.24 (m, 1H), 7.02 (s, 2H), 5.70 (s, 1H), 5.06 (s, 1H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.6, 152.7, 151.7, 135.9, 134.8, 133.8, 132.9, 132.0, 131.0, 130.4, 129.2, 128.6, 126.7, 126.7, 126.3, 123.8, 123.1, 122.8, 122.4, 121.7, 121.0, 120.1, 118.9, 46.2, 34.4, 30.2. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{34}H_{34}NO_3$: 504.2533, found: 504.2535. **FTIR (cm^{-1})** 3618, 3442, 2958, 2921, 2886, 1686, 1431, 1035, 1027, 859.

(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-9,11-dimethyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3u)



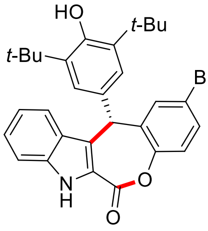
3u

Following the general procedure, treatment of 4,6-dimethyl-1*H*-indole-2-carbaldehyde **1u** (43.3 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene)cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford **(***S***)**-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-9,11-dimethyl-

7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (**3u**) as a white solid (84.1 mg, 70 % yield with 94:6 er). ***R**f* (Pet. ether /EtOAc = 90/10): 0.27; er = 94:6, $[\alpha]_D^{25}$ = +70.5 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 98:2, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 10.6 min (minor), 23.4 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 7.45 (d, *J* = 7.0 Hz, 1H), 7.33-7.26 (m, 2H), 7.24-7.20 (m, 1H), 7.06 (s, 1H) 6.87 (s, 2H), 6.76 (s, 1H), 5.94 (s, 1H), 5.04 (s, 1H), 2.79 (s, 3H), 2.42 (s, 3H), 1.28 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 161.1, 152.5, 151.2, 138.3, 137.3, 135.8, 135.7, 132.6, 132.0, 130.7, 129.6, 128.4, 126.2, 125.4, 123.8, 123.1, 122.8, 121.3, 110.0, 47.2, 34.4, 30.2, 21.9, 20.8. **HRMS (ESI)** calculated $[M+H]^+$ for $C_{32}H_{36}NO_3$: 482.2690, found: 482.2692. **FTIR (cm^{-1})** 3452, 3418, 2960, 2866, 1683, 1433, 1230, 1149, 837.

(S)-2-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3v)



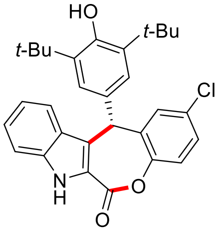
3v

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25mmol) and 4-(5-bromo-2-hydroxybenzylidene)-2,6-di-*tert*-butylcyclohexa-2,5-dien-1-one **2b** (136.3 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 10 °C for 48 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-2-bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo [6,7]oxepino[3,4-b]indol-6-one **(3v)** as a white solid (84 mg, 64 % yield with 94:6 er).

***R**f* (Pet. ether /EtOAc = 85/15): 0.37; er = 94:6, $[\alpha]_D^{25}$ = +73.95 (c 1.0, $CHCl_3$). **HPLC** (ChiralCell OD-H, *n*-hexane/IPA = 99:1, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 24.3 min (major), 38.7 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 7.88 (d, *J* = 8.16 Hz, 1H),7.62 (d, *J* =2.18 Hz,1H), 7.43-7.40 (m, 3H), 7.28-7.23 (m, 2H), 7.00 (s, 2H), 5.54 (s, 1H), 5.08 (s, 1H), 1.31 (s, 18H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.2, 152.9, 150.6, 137.4, 136.9, 136.1, 133.5, 131.4, 131.3, 128.4, 127.4, 126.0, 124.7, 123.7, 121.4, 121.1, 120.7, 119.1, 112.5, 45.9, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{31}BrNO_3$ 532.1482; found 532.1490. **FTIR (cm^{-1})** 3630, 3336, 2960, 2916, 2868, 2365, 2333, 1696, 1549, 1477, 1433, 1329, 1207, 1160, 1116, 885.

(*S*)-2-Chloro-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3w)

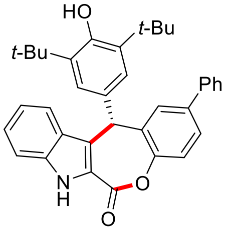


3w

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1** (36.3 mg, 0.25mmol) and 2,6-di-*tert*-butyl-4-(5-chloro-2-hydroxybenzylidene) cyclohexa-2,5-dien-1-one **2** (120.7 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 10 °C for 48 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-2-chloro-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7] oxepino [3,4-b] indol-6-one **(3w)** as a white solid (82 mg, 67 % yield with 91:9 er). ***R_f*** (Pet. ether/EtOAc = 90/10): 0.40; er = 91:9, $[\alpha]_D^{25}$ = +68.72 (c 1.0, $CHCl_3$). **HPLC** (ChiralCell OD-H, *n*-hexane/IPA = 99:1, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 23.9 min (major), 37.9 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 7.88 (d, *J* = 8.12 Hz, 1H), 7.48-7.42 (m, 3H), 7.31-7.24 (m, 3H), 7.01 (s, 2H), 5.55 (s, 1H), 5.08 (s, 1H), 1.31 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.2, 152.9, 150.0, 137.3, 136.5, 136.1, 131.4, 130.5, 128.4, 128.3, 127.4, 126.1, 124.4, 123.7, 121.4, 121.1, 120.7, 112.5, 46.0, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{31}ClNO_3$ 488.1987; found 488.1990. **FTIR (cm^{-1})** 3632, 3336, 2960, 2367, 1695, 1549, 1480, 1433, 1234, 1160, 1077, 870.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-phenyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3x)



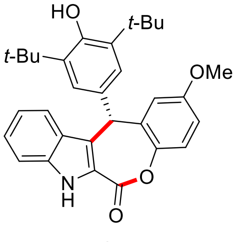
3x

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25mmol) and 2,6-di-*tert*-butyl-4-((4-hydroxy-[1,1'-biphenyl]-3-yl)methylene)cyclohexa-2,5-dien-1-one **2d** (135.3 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-Phenyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (**3x**) as a white solid (94 mg, 71 % yield with 93:7 er). ***R_f*** (Pet. ether /EtOAc = 85/115): 0.50; er = 93:7, $[\alpha]_D^{25}$ = +95.16 (c 1.0, $CHCl_3$). **HPLC**

(Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 16.8 min (minor), 25.4 min (major).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.98 (s, 1H), 7.93 (d, *J* = 7.93 Hz, 1H), 7.69-7.36 (m, 11H), 7.07 (s, 2H), 5.69 (s, 1H), 5.07 (s, 1H), 1.31 (s, 18H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 160.7, 152.7, 150.8, 140.0, 139.4, 137.3, 135.9, 135.0, 132.0, 129.5, 129.0, 128.9, 127.7, 127.2, 127.1, 126.2, 123.8, 123.4, 121.4, 121.3, 120.8, 112.4, 46.4, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{36}H_{36}NO_3$ 530.2690; found 530.2695, **FTIR (cm^{-1})** 3634, 3333, 2959, 2869, 2362, 2330, 1693, 1329, 1207, 1119, 1081, 889.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-methoxy-7,12-dihydro-6*H*-benzo [6,7]oxepino[3,4-b]indol-6-one (3y)

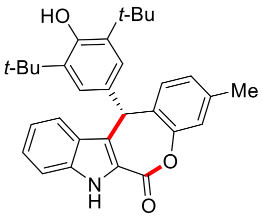


3y

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxy-5 methoxybenzylidene)cyclohexa-2,5-dien-1-one **2e** (119.2 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 95:15) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (**3y**) as a white solid (88 mg, 73% yield with 95:5 er). ***R_f*** (Pet. ether /EtOAc = 85/15): 0.45; er = 95:5, $[\alpha]_D^{25}$ = +80.66 (c 1.0, CHCl$_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 38.9 min (major), 52.6 min (minor).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.87 (s, 1H), 7.90 (d, *J* = 7.49 Hz, 1H), 7.42-7.38 (m, 2H), 7.30-7.28 (m, 2H), 7.02-6.97 (m, 3H), 6.82-6.80 (m, 1H), 5.53 (s, 1H), 5.05 (s, 1H), 3.82 (s, 3H), 1.30 (s, 18H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 161.1, 157.4, 152.7, 145.3, 137.1, 135.9, 135.8, 131.9, 128.7, 127.1, 126.2, 123.8, 121.5, 121.2, 120.7, 115.7, 113.1, 112.4, 55.8, 46.3, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{31}H_{34}NO_4$ 484.2482; found 484.2487. **FTIR (cm^{-1})** 2960, 2920, 2362, 1689, 1547, 1494, 1432, 1231, 1183, 1081, 1038, 871.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-3-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3z)



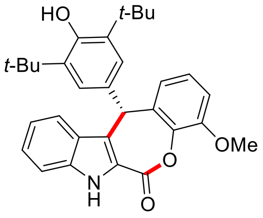
3z

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxy-4-methylbenzylidene)cyclohexa-2,5-dien-1-one **2f** (113.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-3-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (**3z**) as a white solid (77 mg, 66 % yield with 94:6 er).

R_f (Pet. ether /EtOAc = 85/15): 0.50; er = 94:6, $[\alpha]_D^{25}$ = +26.0 (c 1.0, $CHCl_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 15.1 min (major), 44.3 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.90 (d, *J* = 8.09 Hz, 1H), 7.45-7.34 (m, 3H), 7.26-7.19 (m, 2H), 7.04-7.02 (m, 3H), 5.58 (s, 1H), 5.05 (s, 1H), 2.36 (s, 3H) 1.30 (s, 18H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.9, 152.6, 151.2, 138.7, 137.2, 135.8, 132.3, 131.7, 130.6, 129.2, 127.1, 127.0, 126.2, 123.8, 123.4, 121.6, 121.2, 120.8, 112.4, 45.7, 34.4, 30.2, 20.9. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{31}H_{34}NO_3$ 468.2533; found 468.2542. **FTIR (cm^{-1})** 3635, 3333, 2959, 2913, 2869, 1688, 1547, 1433, 1236, 1210, 1117, 888.

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-4-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3, 4-b]indol-6-one (3aa)

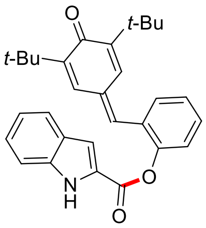


3aa

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxy-3 methoxybenzylidene)cyclohexa-2,5-dien-1-one **2g** (119.2 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49 mg, 0.15 mmol), oxidant **8** (204 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 85:15) to afford (*S*)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-4-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (**3aa**) as a white solid (83 mg, 69 % yield with 92:8 er). ***R**$_f$* (Pet. ether /EtOAc = 85/15): 0.32; er = 92:8, $[\alpha]_D^{25}$ = +108.74 (c 1.0, CHCl$_3$). **HPLC** (Chiralpak IA, *n*-hexane/IPA = 98:2, flow rate = 1.0 mL/min, λ = 254 nm) t$_R$ = 37.1 min (major), 41.7 min (minor).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.99 (s, 1H), 7.87 (d, *J* = 7.77 Hz, 1H), 7.43-7.40 (m, 2H), 7.23-7.14 (m, 2H), 7.07-7.05 (m, 1H), 6.99 (s, 2H), 6.92-6.90 (m, 1H), 5.60 (s, 1H), 5.04 (s, 1H), 3.91 (s, 3H), 1.29 (s, 18H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 160.7, 152.6, 152.3, 140.7, 137.3, 137.2, 135.8, 131.5, 128.9, 127.0, 126.4, 126.2, 123.8, 122.0, 121.8, 121.1, 120.7, 112.5, 111.4, 56.4, 45.9, 34.4, 30.2. **HRMS (ESI) m/z:** $[M+ Na]^+$ calcd for $C_{31}H_{33}NO_4Na$ 506.2302; found 506.2305. **FTIR (cm^{-1})** 3634, 33246, 2960, 2869, 2704, 2331, 1693, 1476, 1434, 1232, 1170, 1081, 886.

2-((3,5-Di-*tert*-butyl-4-oxocyclohexa-2,5-dien-1-ylidene)methyl)phenyl-1*H*-indole-2-carboxylate (3a')



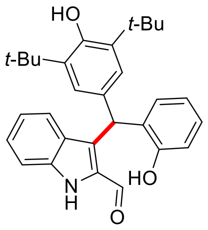
3a'

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene) cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs$_2$CO$_3$ (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford 2-((3,5-Di-*tert*-butyl-4-oxocyclohexa-2,5-dien-1-ylidene)methyl)phenyl-1*H*-indole-2-carboxylate **3a'** as a orange solid (98.0 mg, 87 % yield). ***R**$_f$* (Pet. ether /EtOAc = 90/10): 0.44

^{1}H NMR (400 MHz, Acetone-d6) δ 11.21 (s, 1H), 7.74 (d, *J* = 8.09 Hz, 1H), 7.66-7.64 (m, 1H), 7.60-7.57 (m, 2H), 7.51-7.43 (m, 5H), 7.37-7.33 (m, 1H), 7.19-7.14 (m, 2H), 1.28 (s, 9H), 1.23 (s, 9H). **^{13}C NMR (100 MHz, Acetone-d6)** δ 186.9, 160.2, 150.2, 149.7, 148.2, 139.0, 138.0, 135.7, 133.9, 132.6, 131.3, 130.0, 128.8, 128.1, 127.0, 126.4, 124.1, 123.2, 121.5, 113.3, 110.8, 35.9, 35.5, 29.6. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{32}NO_3$ 454.2377; found 454.2381 **FTIR (cm^{-1})** 3608, 3345, 2956, 2866, 1711, 1614, 1526, 1452, 1361, 1219, 1175, 1144, 1101, 1023, 949.

3-((3,5-Di-*tert*-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)-1*H*-indole-2-carbaldehyde (3a")

Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25 mmol) and 2,6-di-*tert*-butyl-4-(2-hydroxybenzylidene) cyclohexa-2,5-dien-1-one **2a** (108.6 mg, 0.35



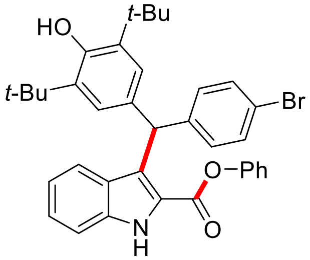
3a"

mmol) with Cs_2CO_3 (49.0 mg, 0.15 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether-EtOAc: 98:2 to 90:10) to afford 3-((3,5-Di-*tert*-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)-1*H*-indole-2-carbaldehyde (**3a”**) as a white solid (101.0 mg, 89 % yield with 50:50 er).

R$_f$ (Pet. ether /EtOAc = 85/15): 0.36; er = 50:50, **HPLC** (Chiralpak IA, *n*-hexane/IPA = 85:15, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 8.8 min, 12.4 min.

^{1}H NMR (400 MHz, Acetone-d6) δ 10.62 (s, 1H), 9.56 (s, 1H), 8.43 (s, 1H), 7.50-7.48 (m, 1H), 7.40-7.38 (m, 1H), 7.28-7.24 (m, 1H), 7.15 (s, 2H), 7.08-7.06 (m, 2H), 6.96-6.89 (m, 2H), 6.80-6.77 (m, 1H), 6.59 (s, 1H), 5.96 (s, 1H), 1.33 (s, 18H). **^{13}C NMR (100 MHz, Acetone-d6)** δ 183.1, 155.6, 153.7, 153.3, 138.7, 138.2, 134.5, 134.0, 131.5, 131.0, 128.5, 128.5, 127.1, 126.5, 123.7, 120.6, 120.3, 116.2, 113.5, 41.6, 35.2, 30.7. **HRMS (ESI) m/z:** $[M+H]^+$ calcd for $C_{30}H_{34}NO_3$ 456.2533; found 456.2539. **FTIR (cm^{-1})** 3630, 3419, 3198, 2954, 1619, 1506, 1426, 1318, 1245, 1196, 1147, 877.

Phenyl-3-((4-bromophenyl)(3,5-di-tert-butyl-4-hydroxyphenyl)methyl)-1*H*-indole-2-carboxylate (10)



10

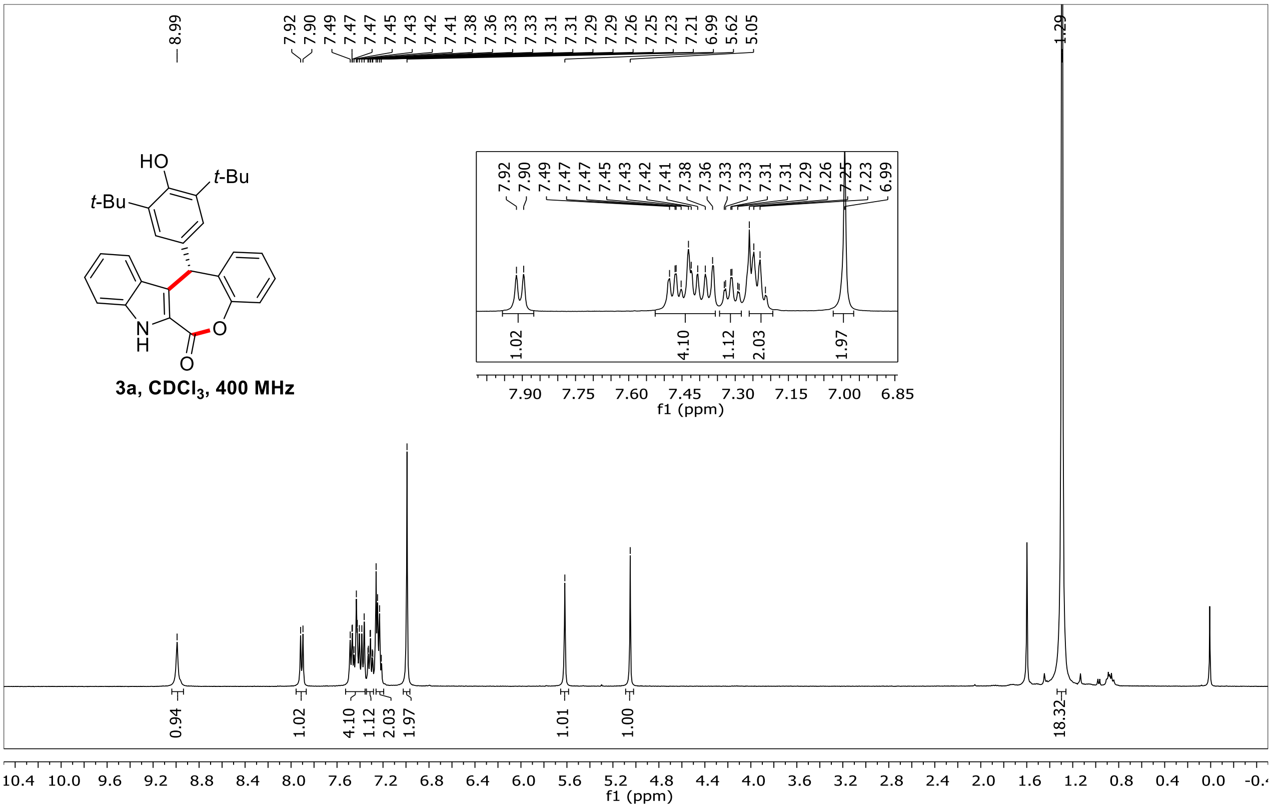
Following the general procedure, treatment of 1*H*-indole-2-carbaldehyde **1a** (36.3 mg, 0.25 mmol) and 4-(4-bromobenzylidene)-2,6-di-tert-butylcyclohexa-2,5-dien-1-one **9a** (130.2 mg, 0.35 mmol) with triazolium salt **4** (23.2 mg, 0.05 mmol), Cs_2CO_3 (49.0 mg, 0.15 mmol), PhOH (23.5 mg, 0.25 mmol), oxidant **8** (204.0 mg, 0.5 mmol), $Bi(OTf)_3$ (33.0 mg, 0.05mmol) in toluene (4.0 mL) and stirring the reaction mixture at 18 °C for 36 h followed by flash column chromatography (Pet. ether -EtOAc: 98:2 to 90:10) to afford Phenyl-3-((4-bromophenyl)(3,5-di-tert-butyl-4-hydroxyphenyl)methyl)-1*H*-indole-2-carboxylate (**10**) as a white solid (136.0 mg, 89 % yield with 53:47 er). ***R$_f$*** (Pet. ether /EtOAc = 90/10): 0.43; er = 53:47, **HPLC** (Chiralpak IA, *n*-hexane/IPA = 90:10, flow rate = 1.0 mL/min, λ = 254 nm) t_R = 6.85 min (major), 7.82 min (minor).

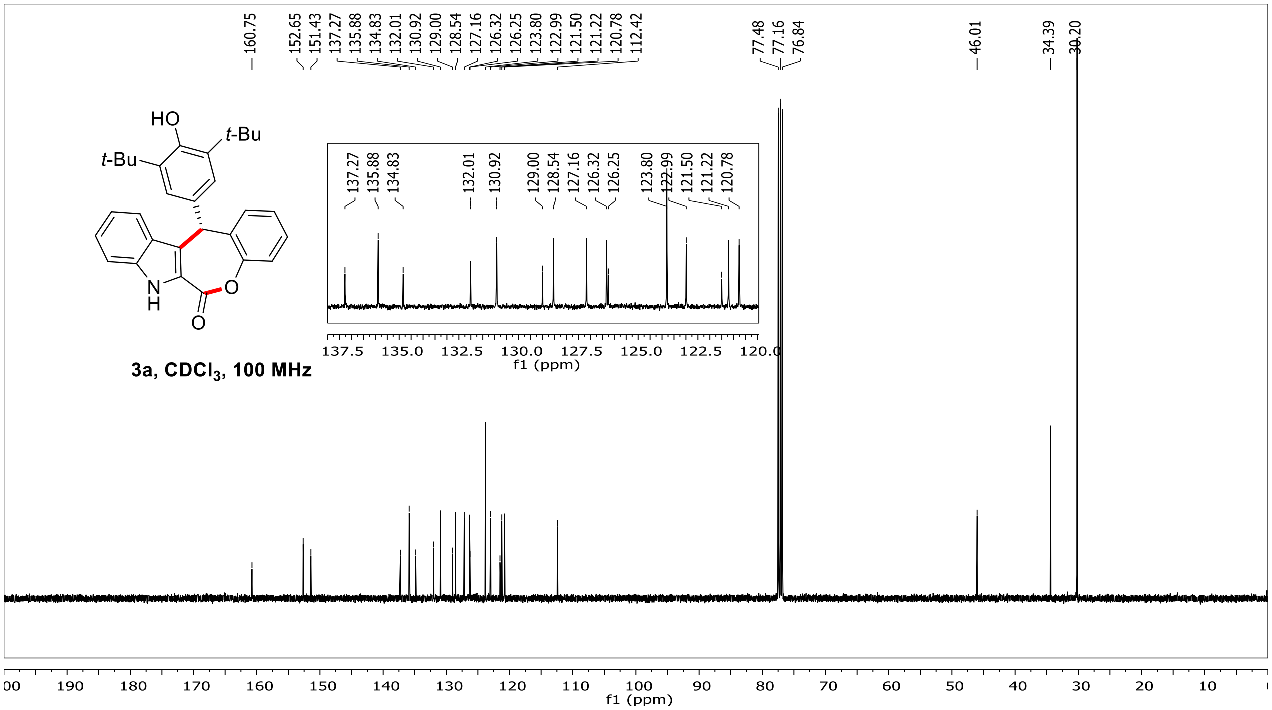
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 7.46-7.35 (m, 5H), 7.31-7.28 (m, 2H), 7.19-7.17 (m, 2H), 7.11-7.04 (m, 5H), 6.97-6.93 (m, 1H), 6.59 (s, 1H), 5.11 (s, 1H), 1.31 (s, 18H). **^{13}C NMR**

(100 MHz, CDCl$_3$) δ 160.6, 152.5, 150.3, 143.6, 136.8, 135.8, 133.0, 131.2, 131.0, 129.7, 128.3, 127.1, 126.3, 126.2, 126.0, 123.8, 122.8, 121.9 ,120.5, 120.0, 112.1, 46.9, 34.5, 30.4. **HRMS (ESI) m/z:** $[M+K]^+$ calcd for $C_{36}H_{36}BrNO_3K$ 648.1510; found 648.1514. **FTIR (cm^{-1})** 3634, 3582, 3348, 2957, 2924, 2871, 1695, 1593, 1487, 1434, 1233, 1193, 1160, 1070, 1010, 909.

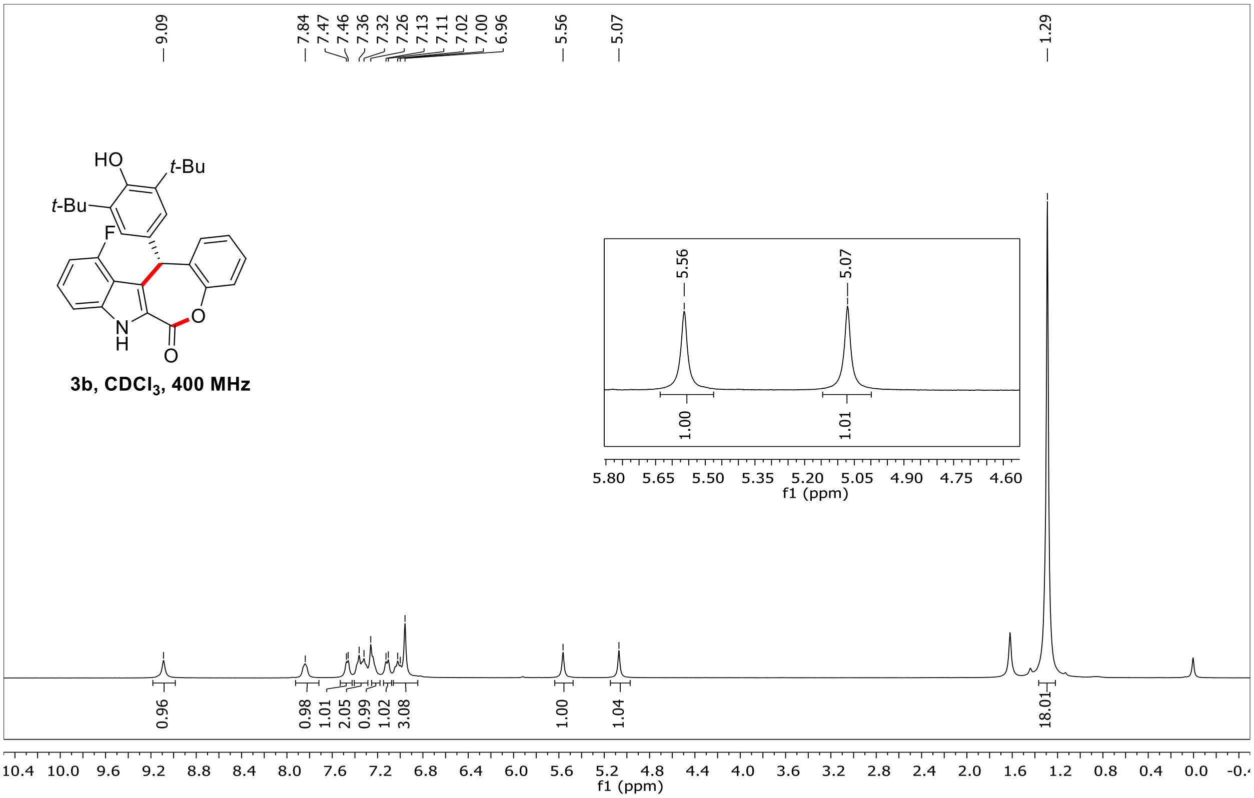
8. ^{1}H and ^{13}C NMR Spectra of Tetracyclic *ε*-Lactones

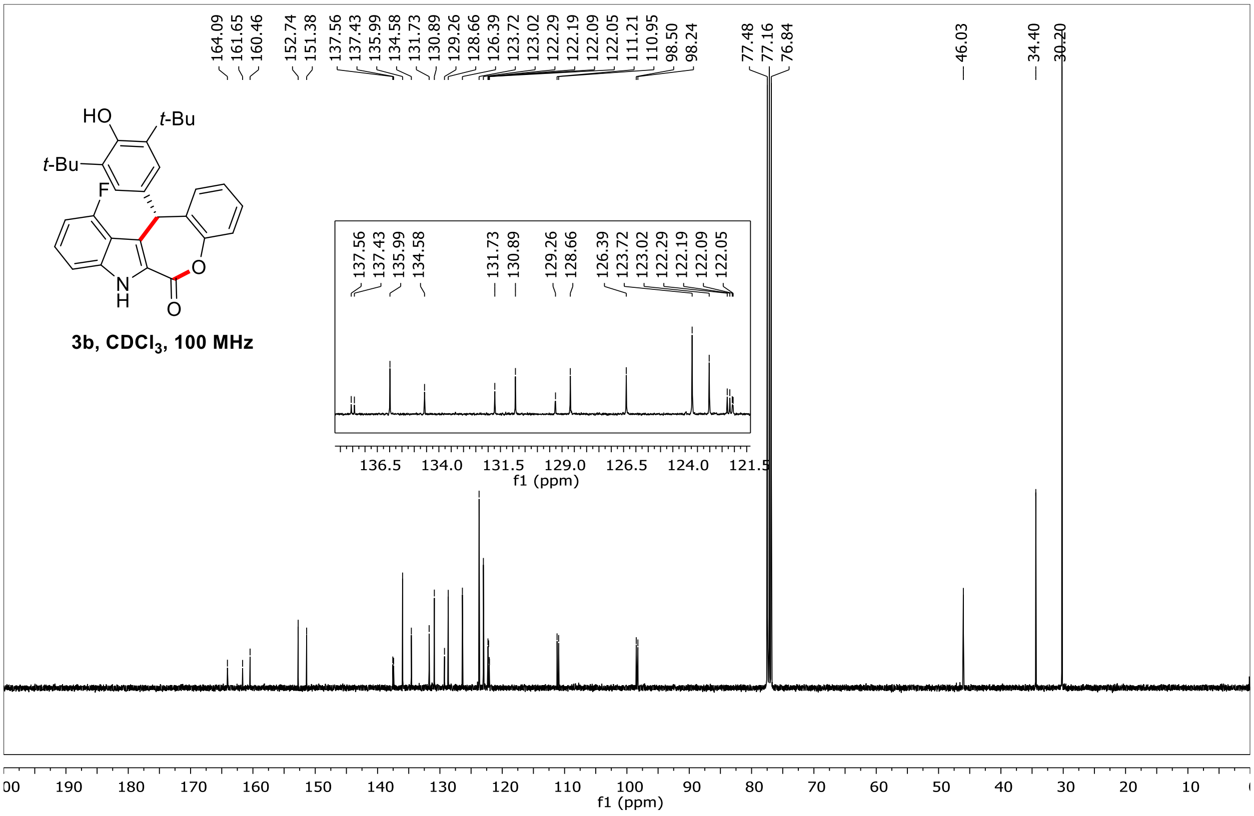
(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*] indol-6-one (3a)



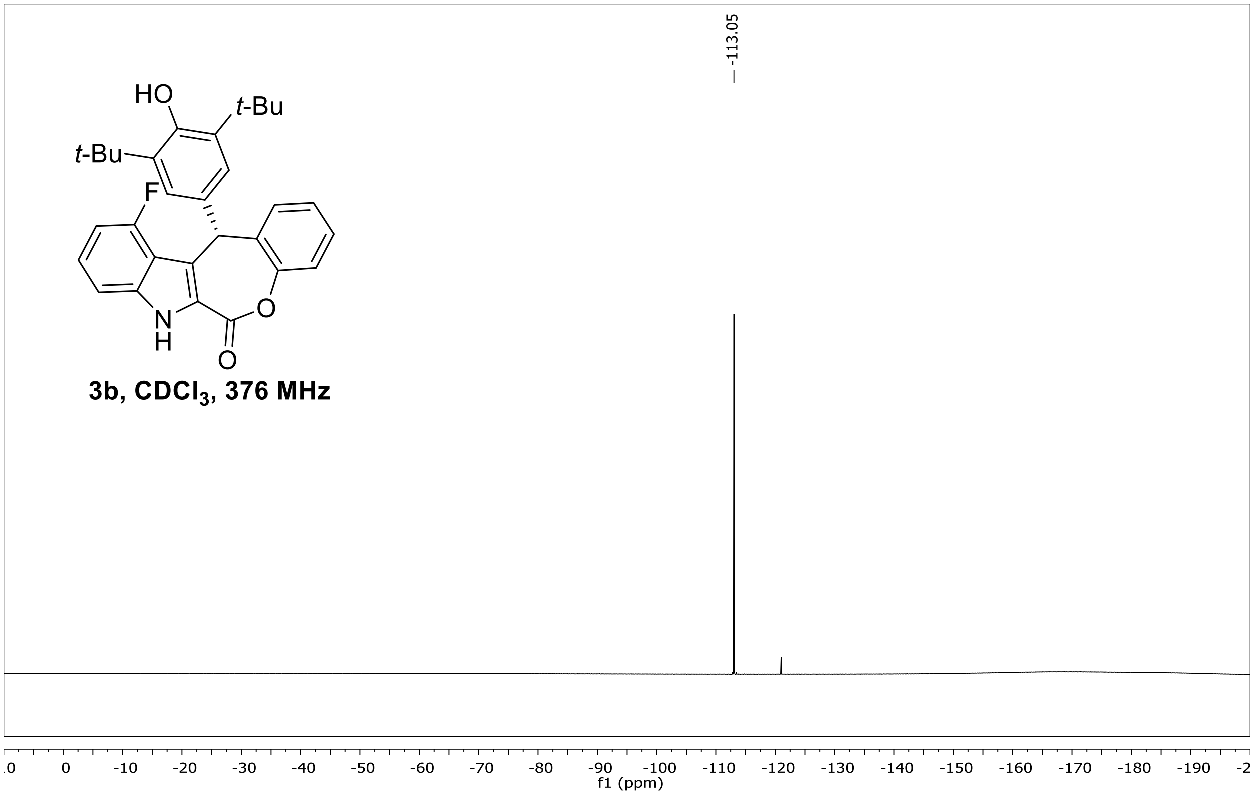


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-11-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3b)

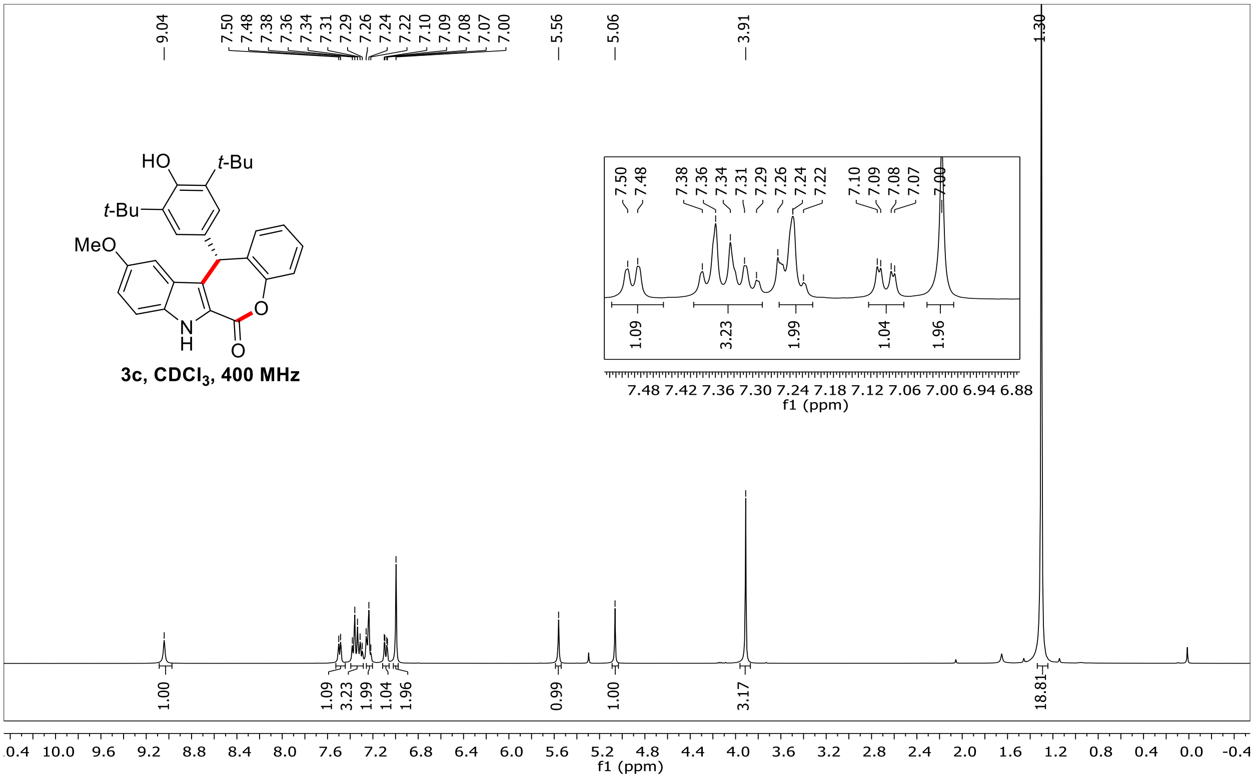


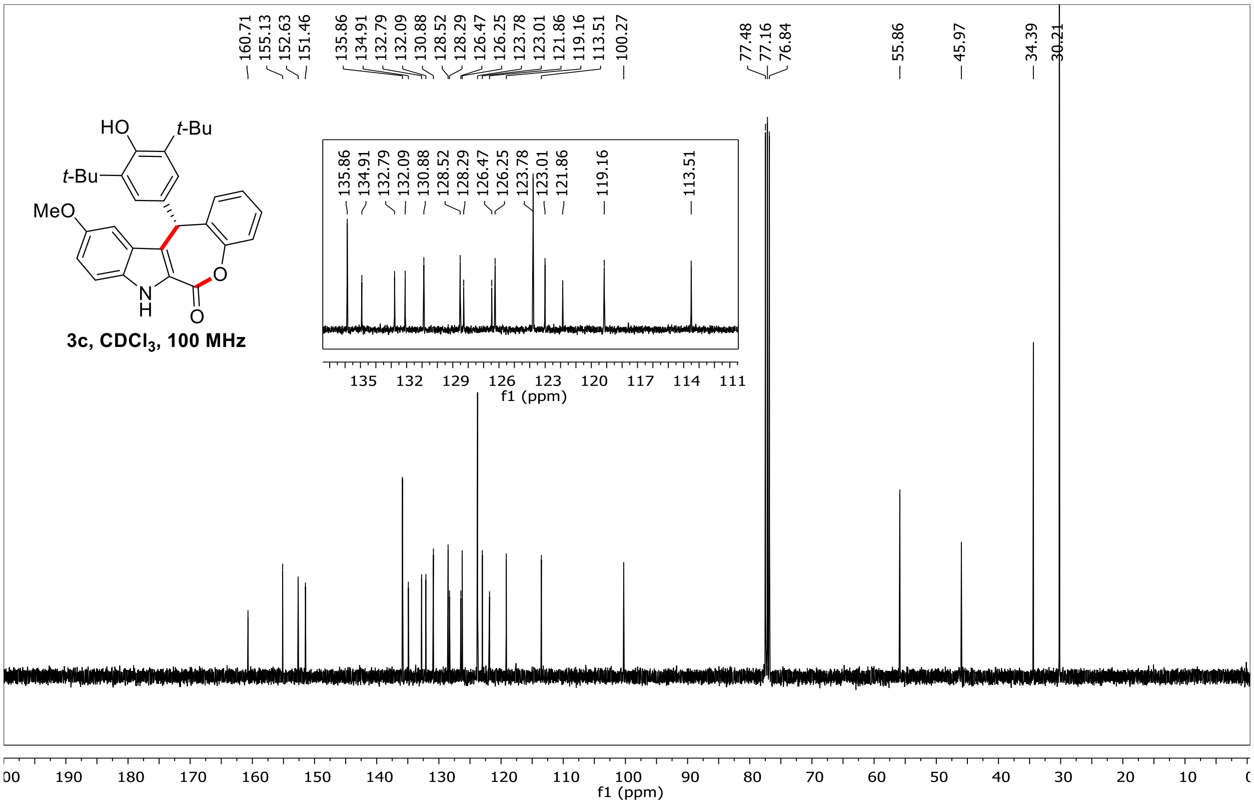


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-11-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3b)

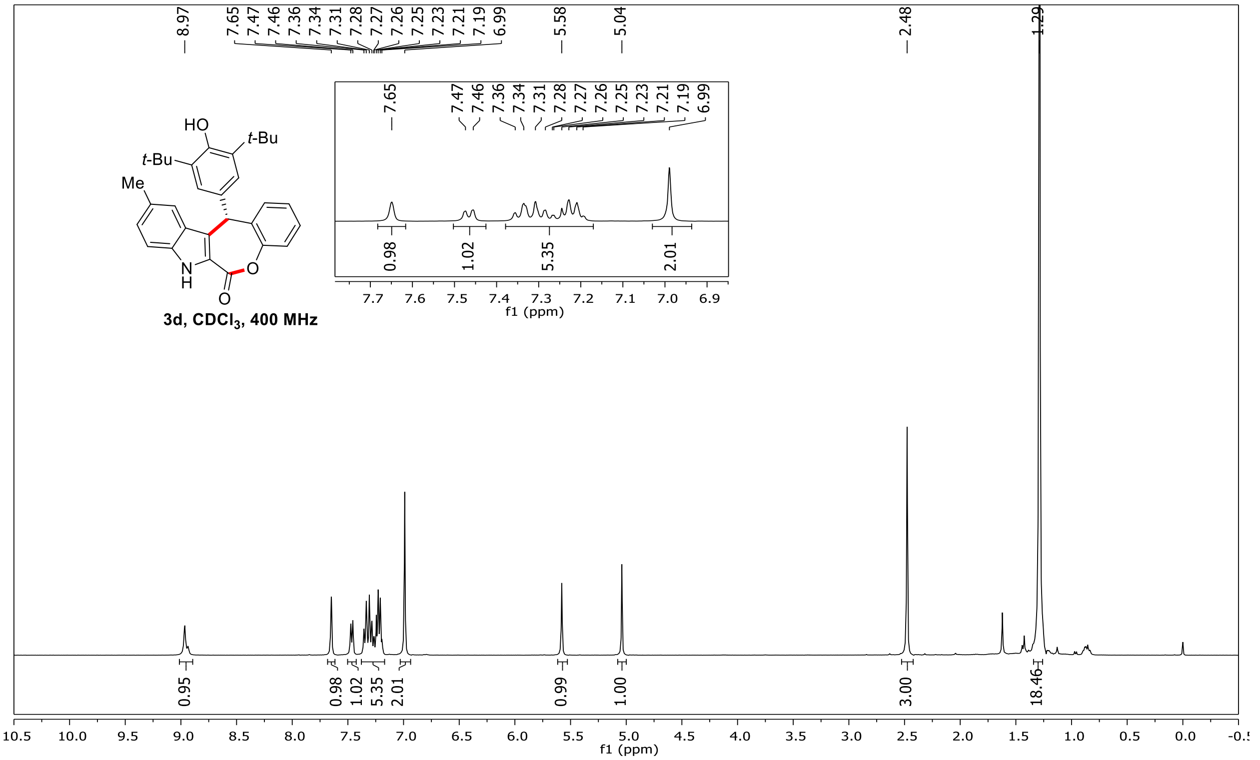


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3c)

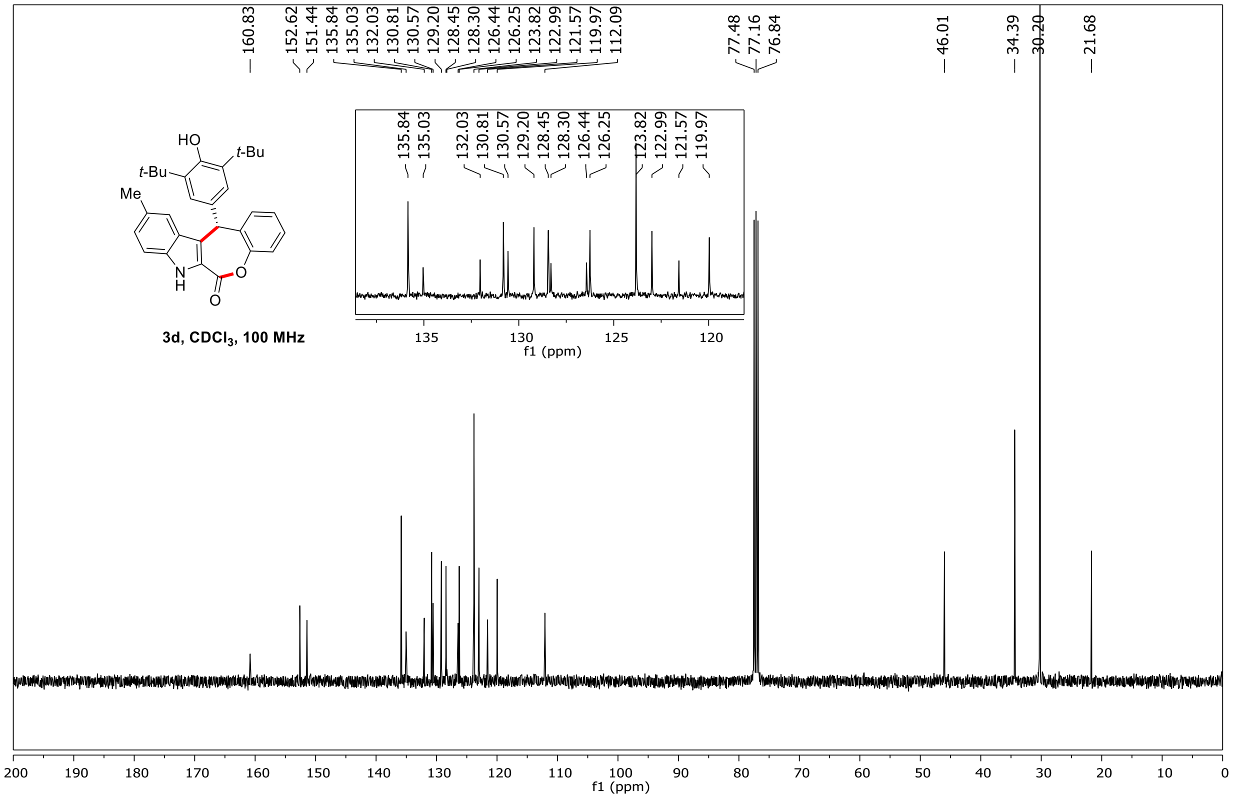




(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-methyl-7,12-dihydro-6*H* benzo [6,7]oxepino[3,4-b]indol-6-one (3d)

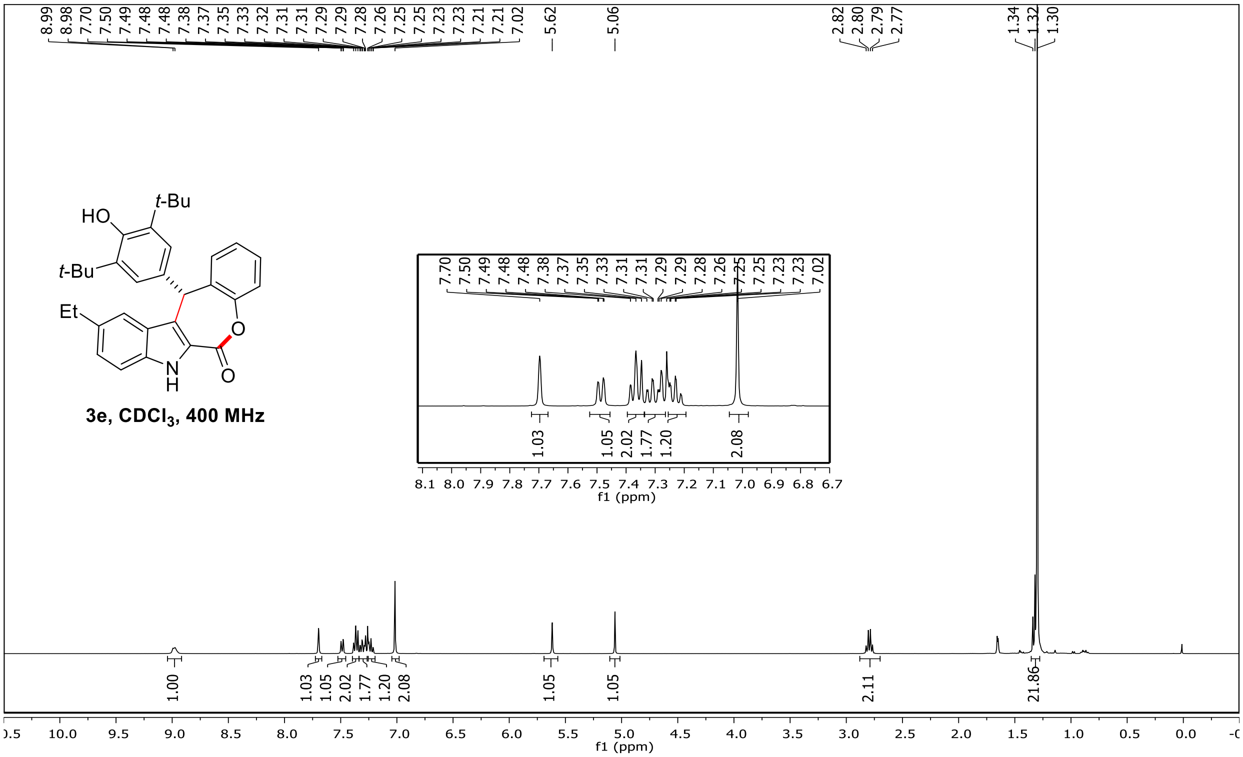


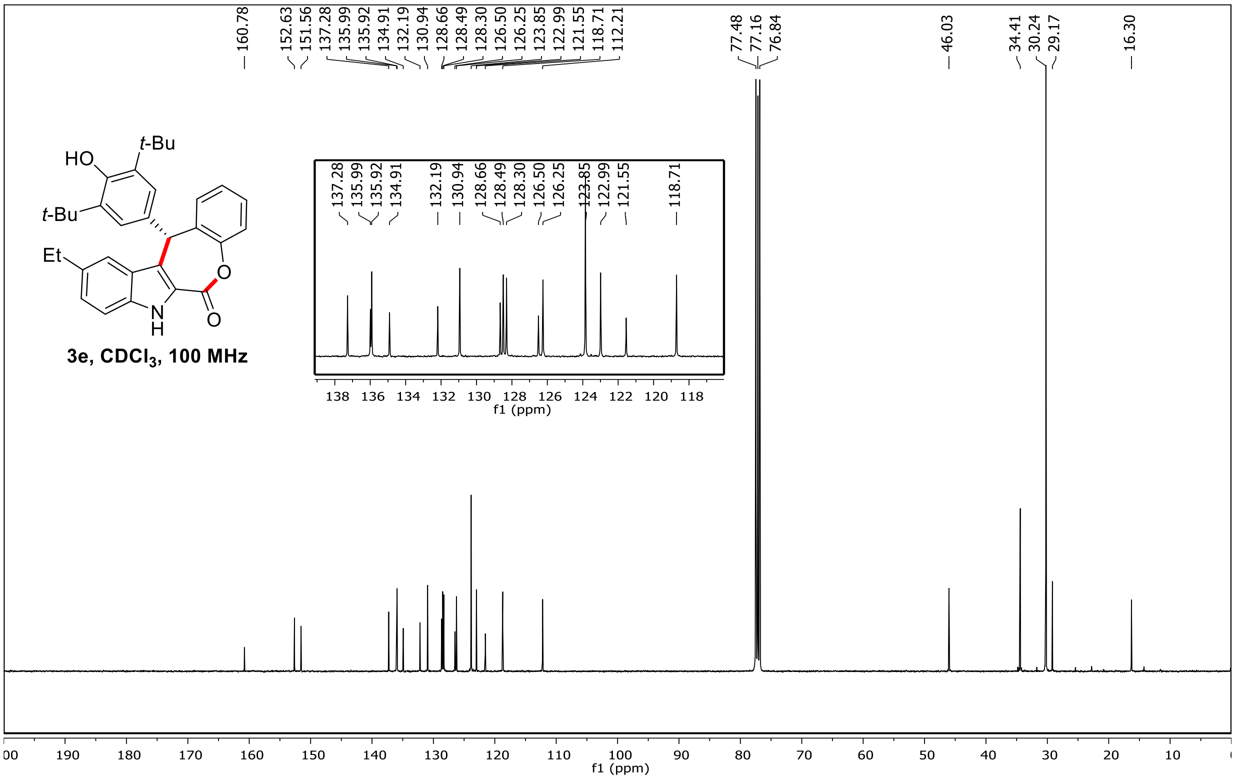
3d, CDCl$_3$, 400 MHz



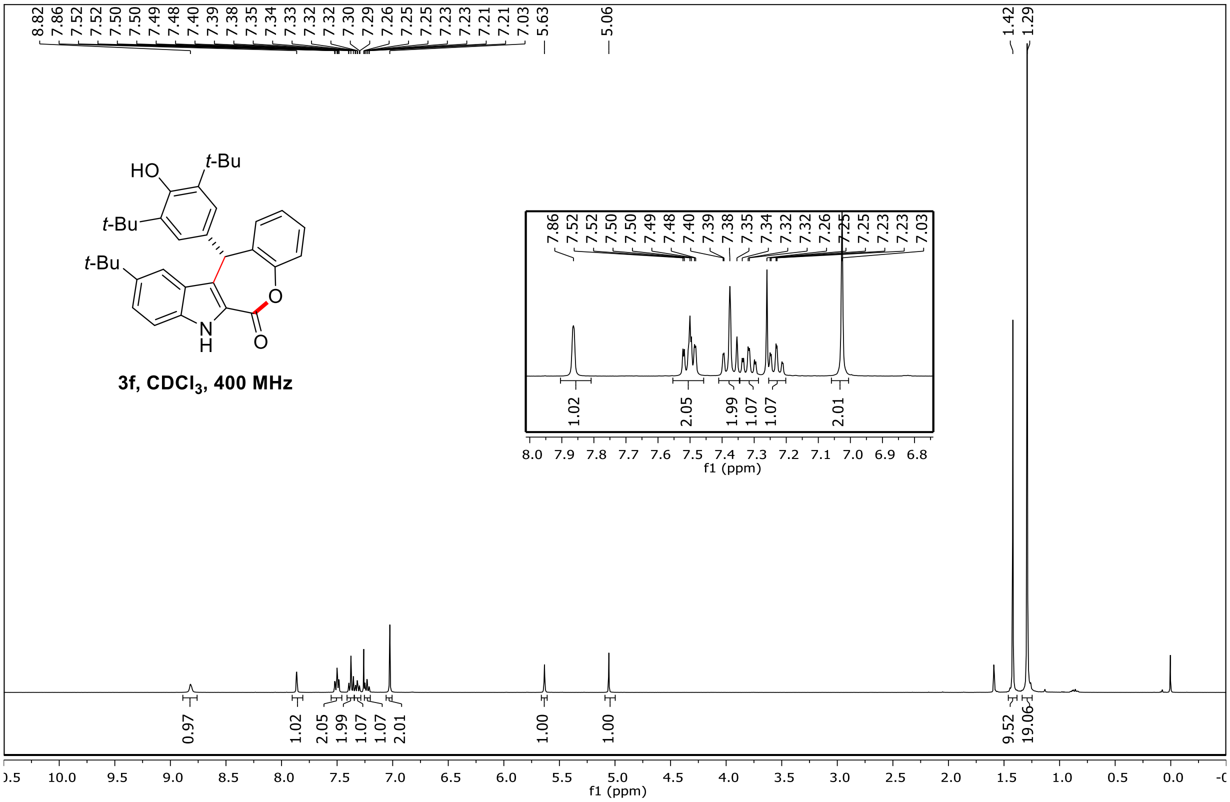
3d, CDCl$_3$, 100 MHz

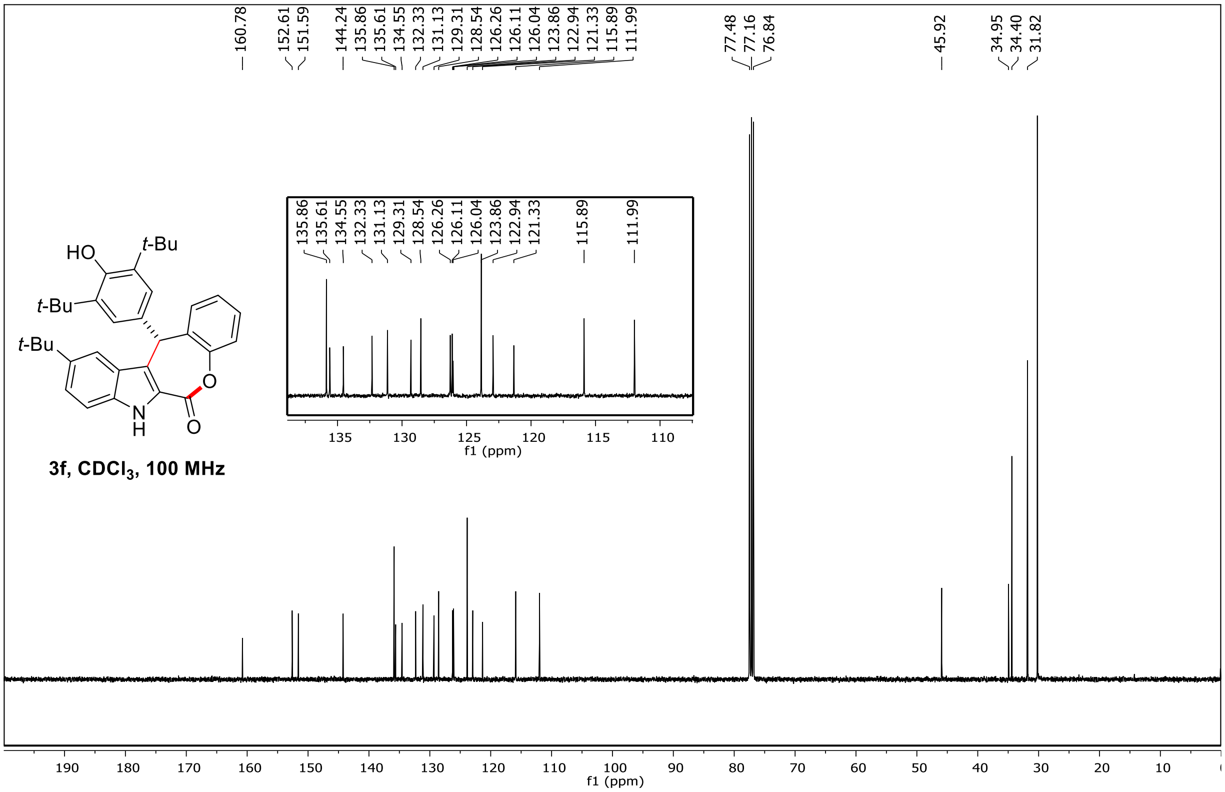
(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-10-ethyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3e)



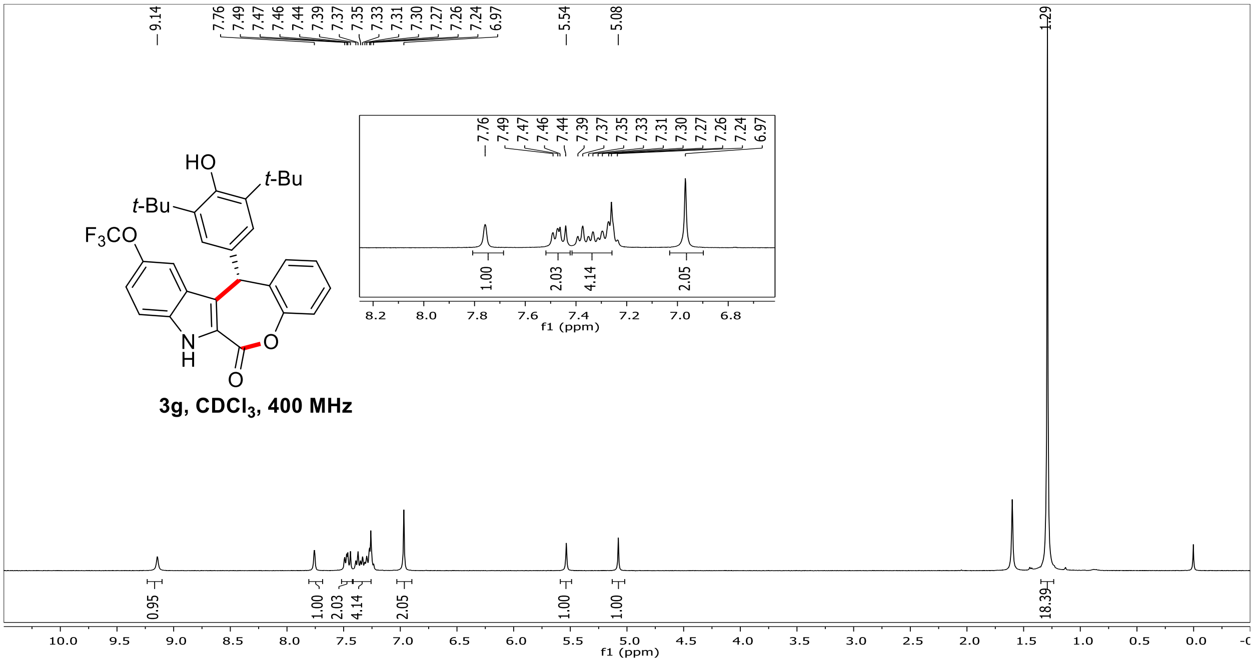


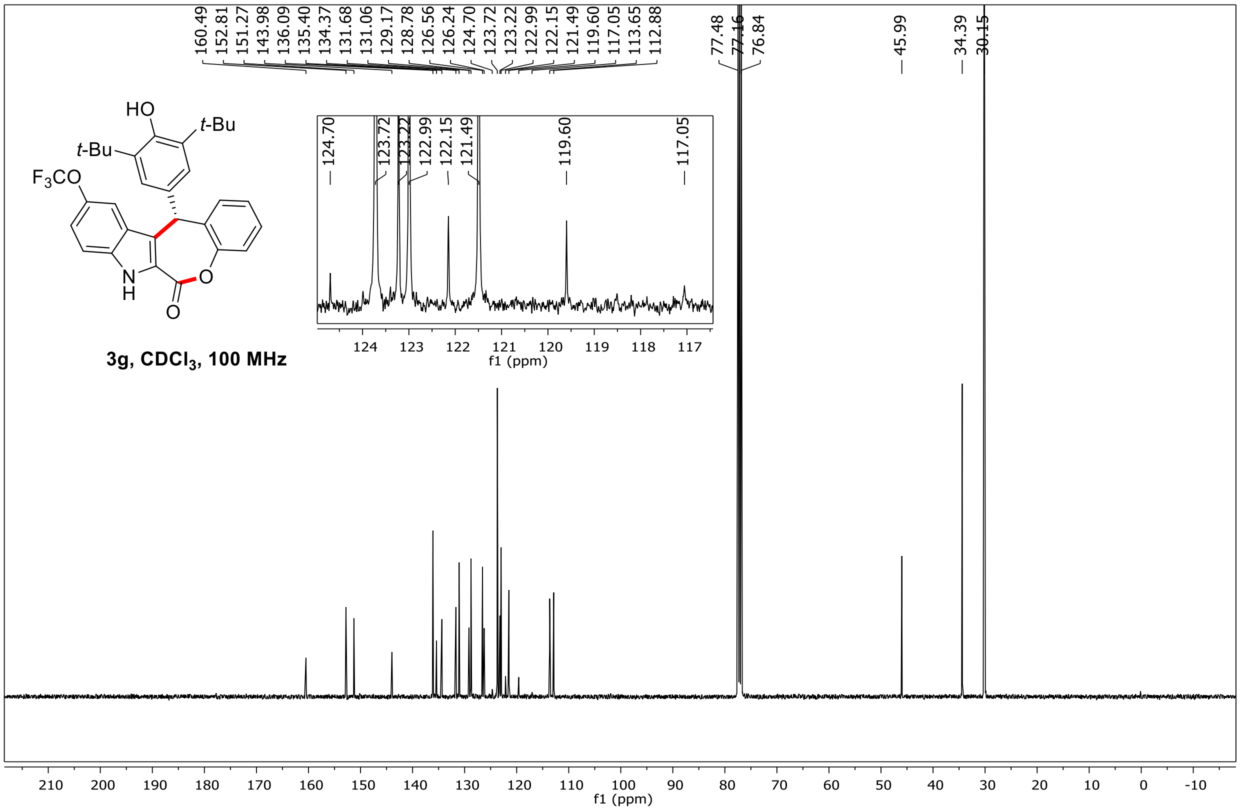
(*S*)-10-(*Tert*-butyl)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H* benzo[6,7]oxepino[3,4-b]indol-6-one (3f)



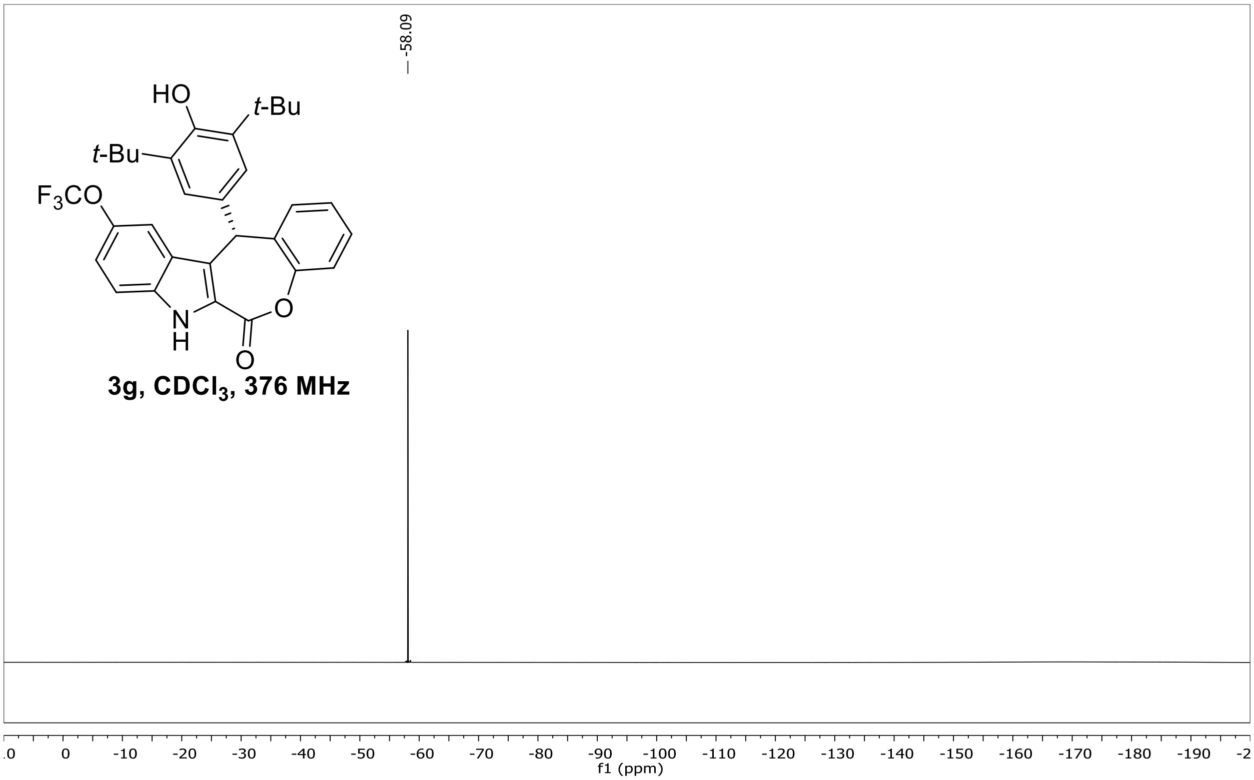


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-(trifluoromethoxy)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3g)

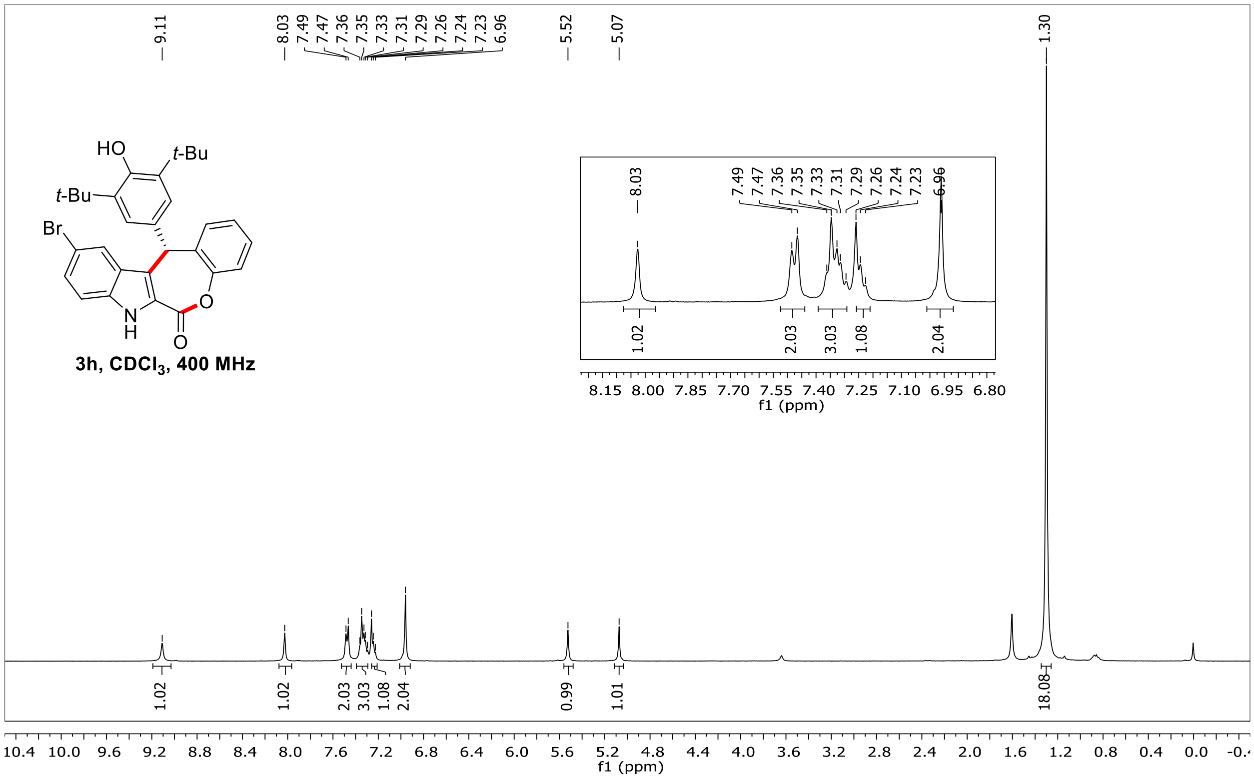


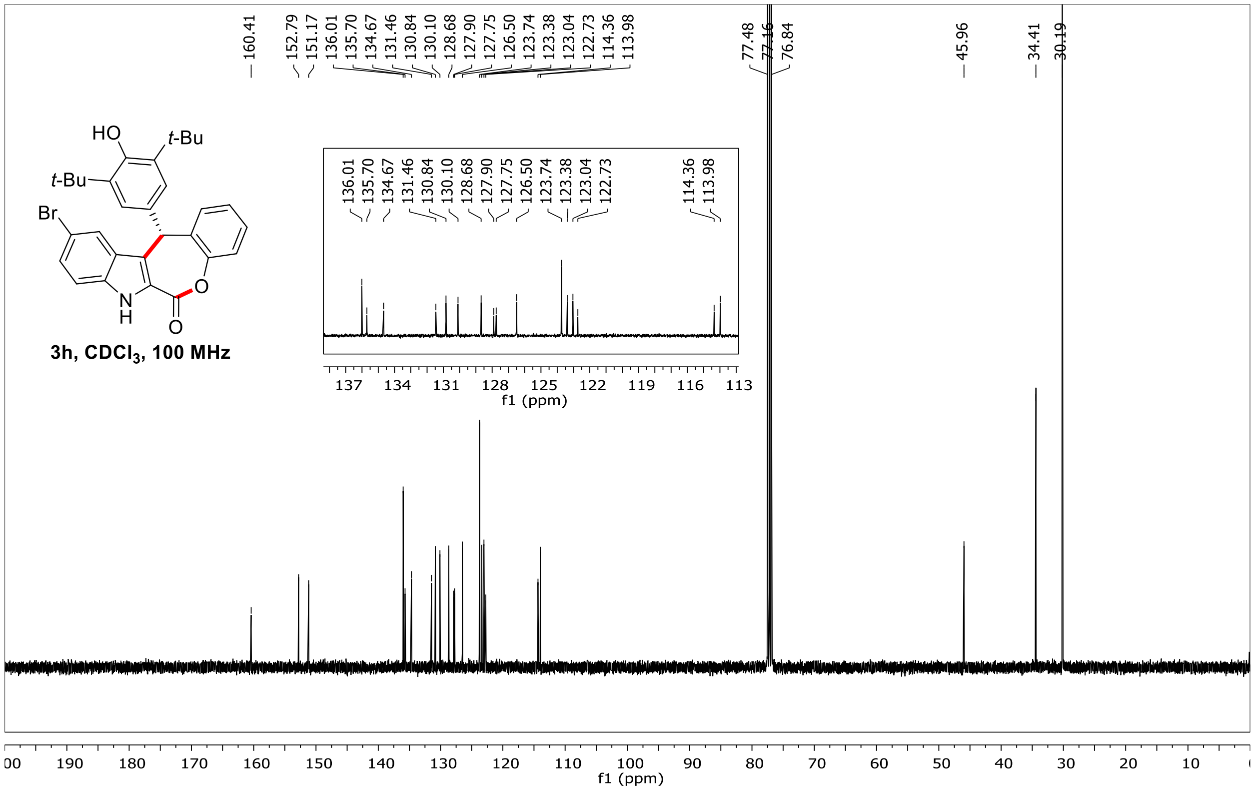


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-(trifluoromethoxy)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3g)

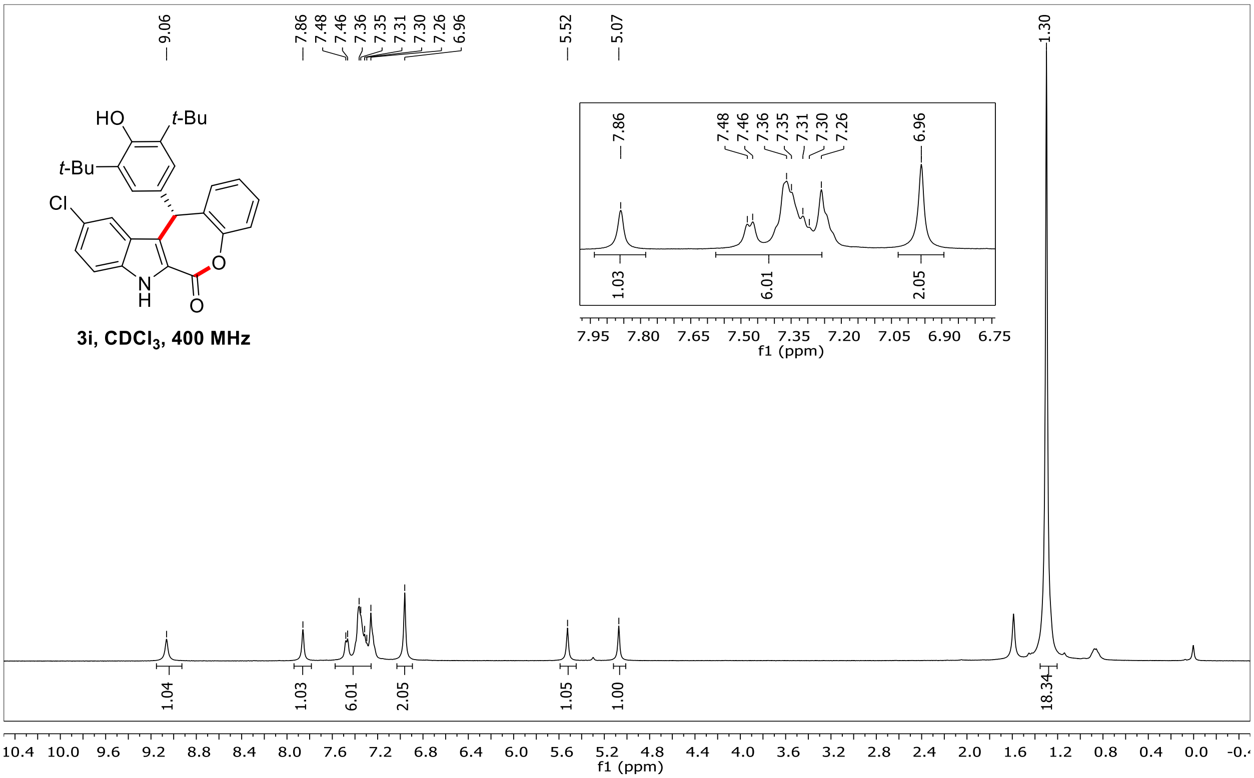


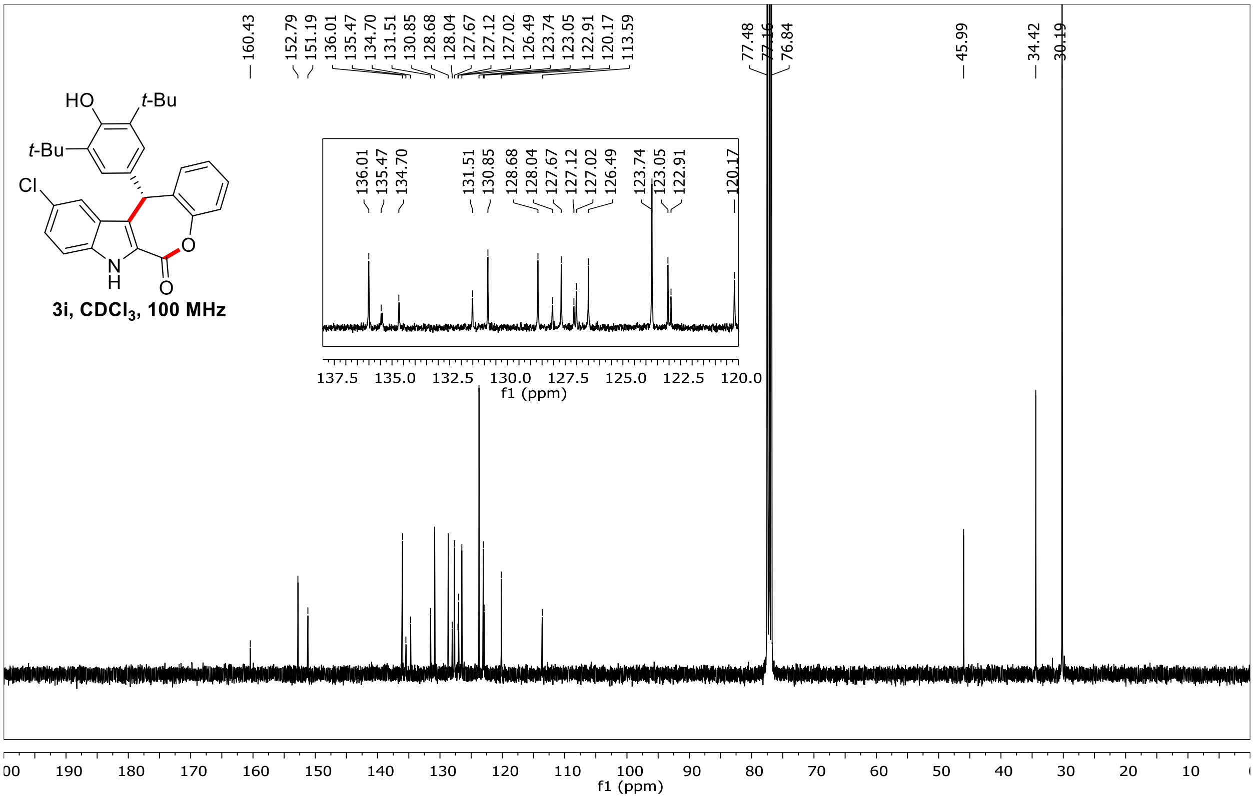
(*S*)-10-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3h)



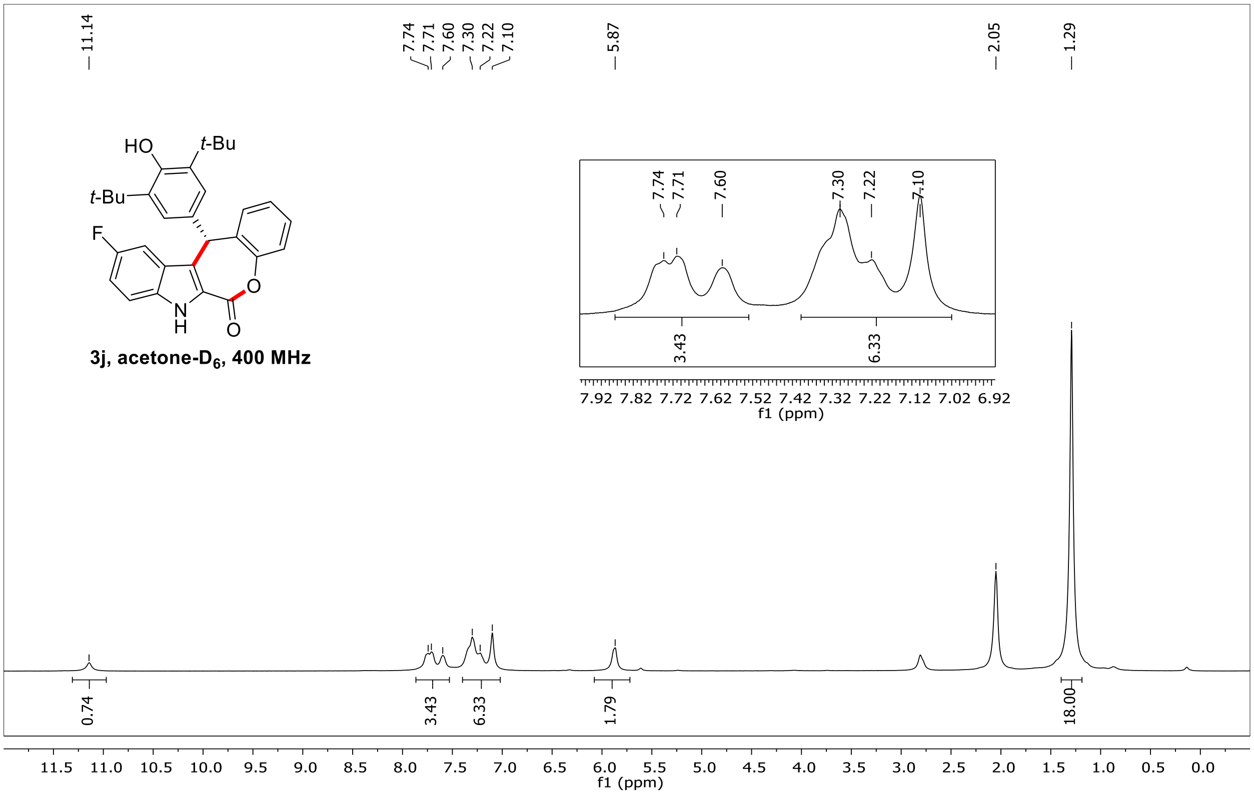


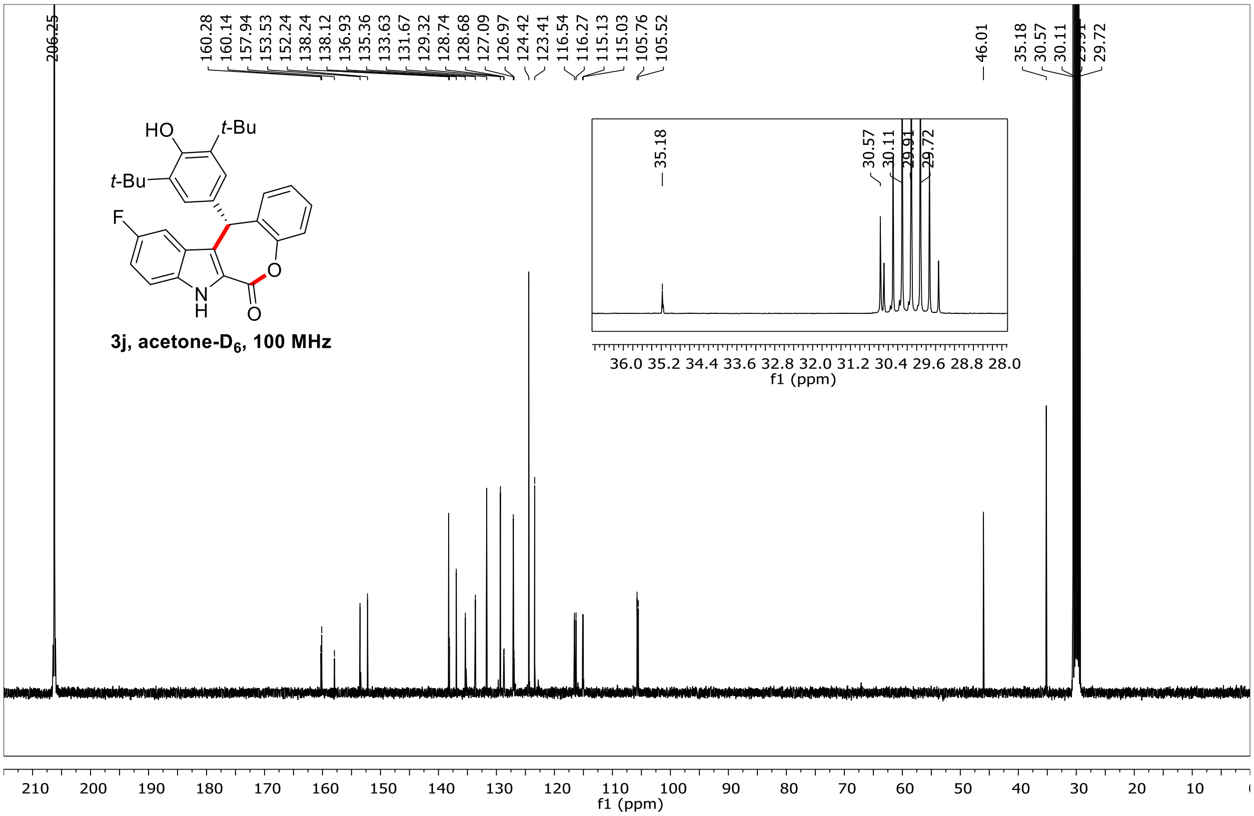
(*S*)-10-Chloro-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3i)



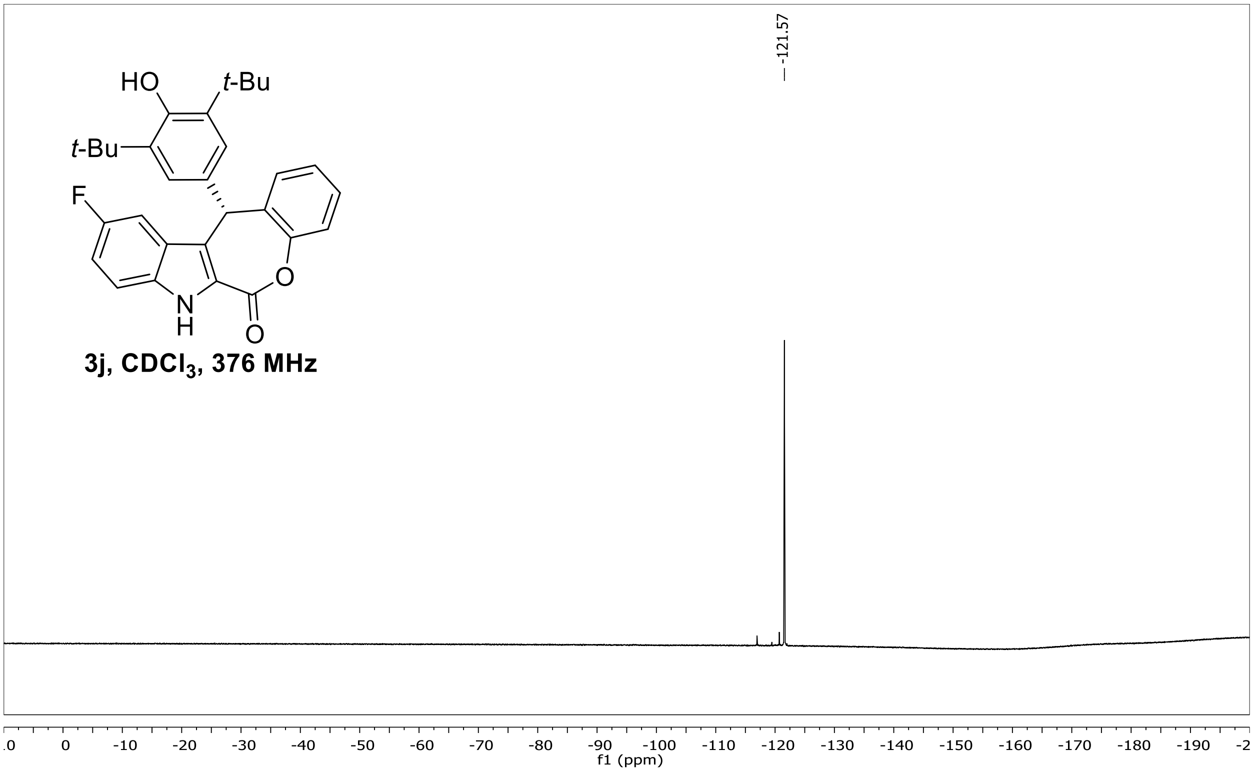


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3j)

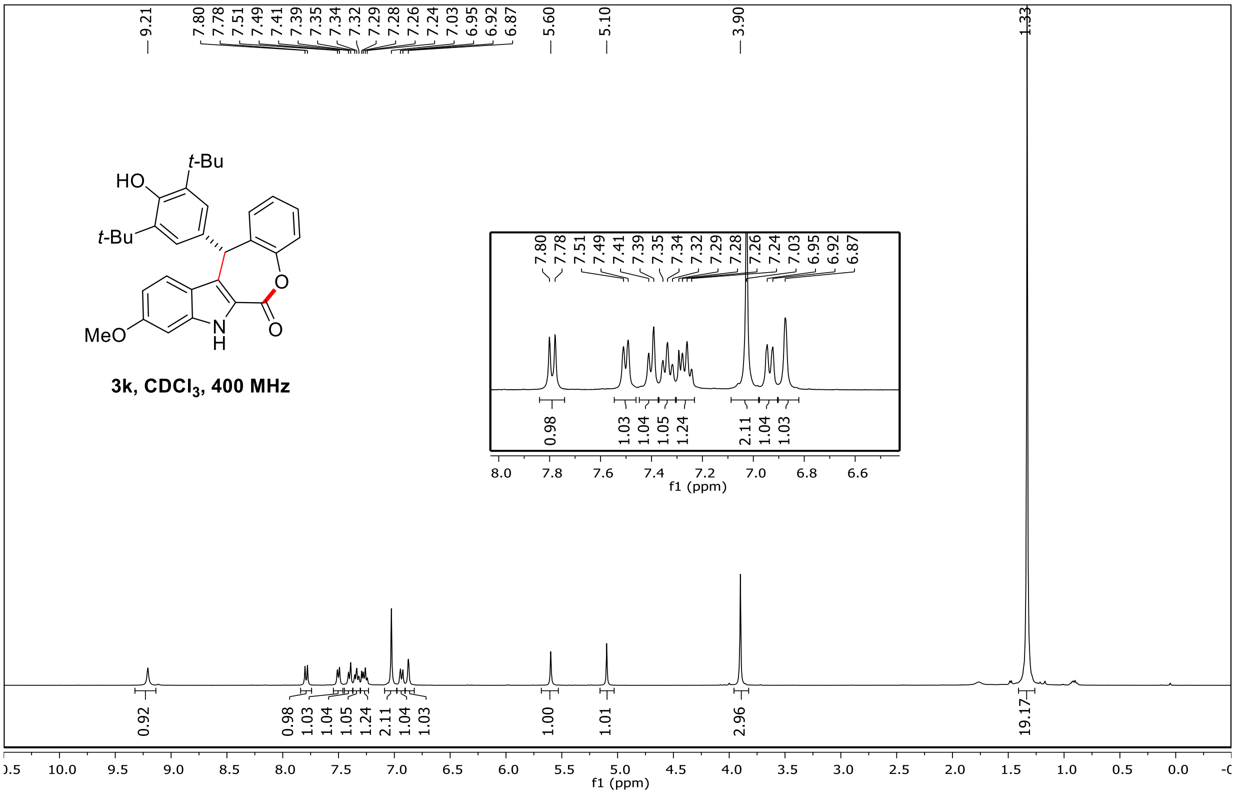


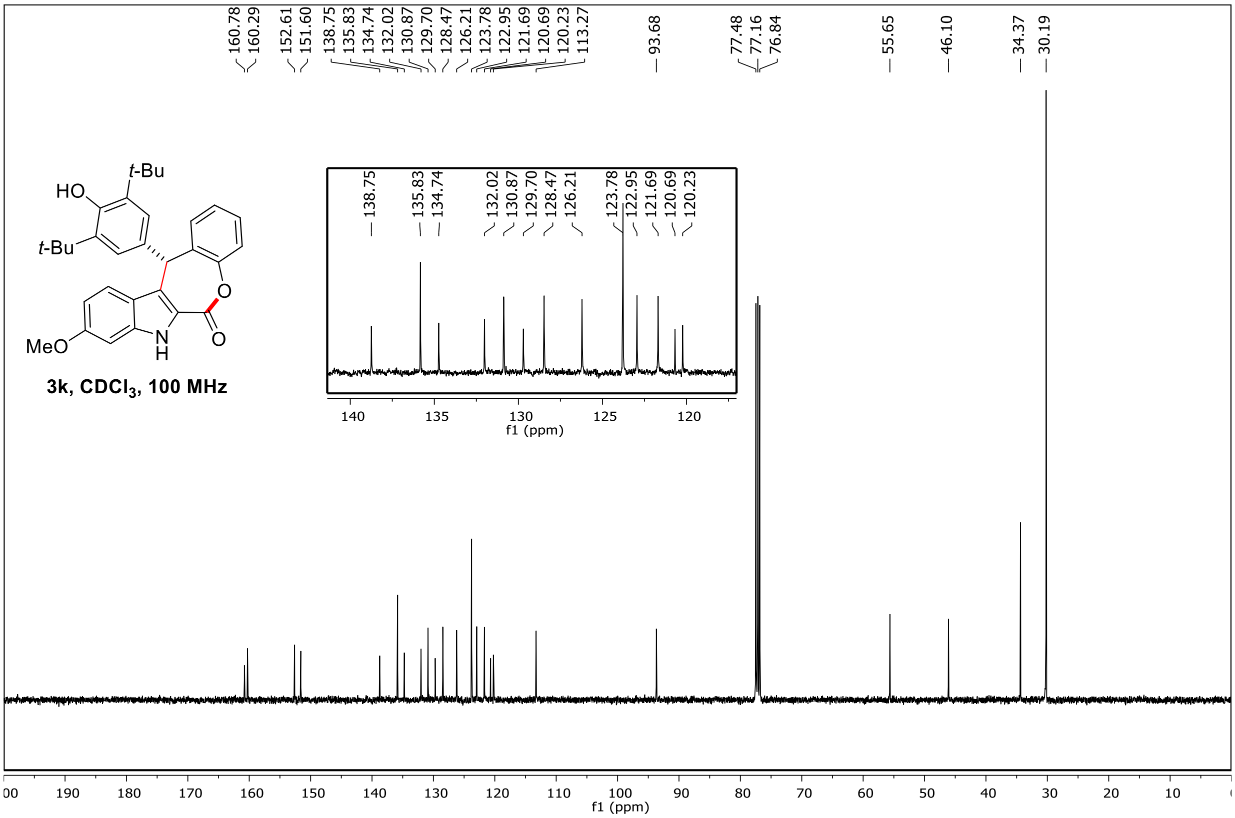


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3j)

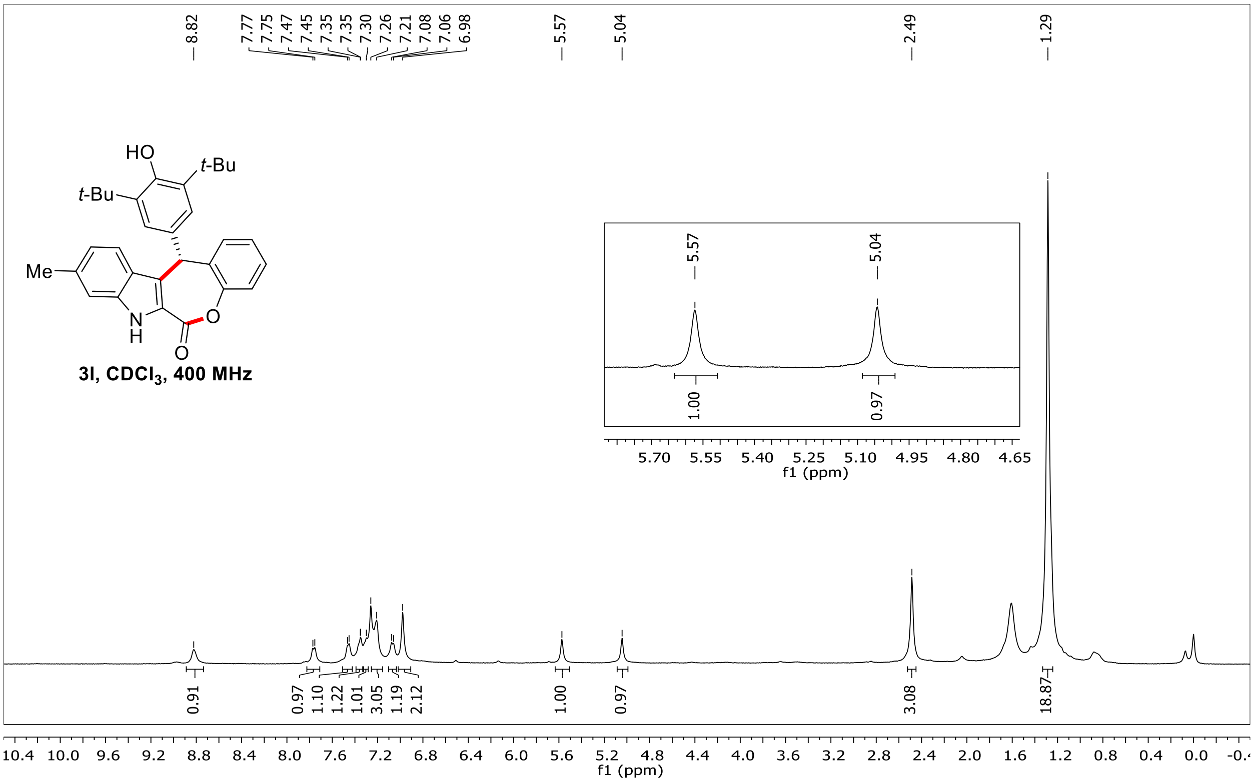


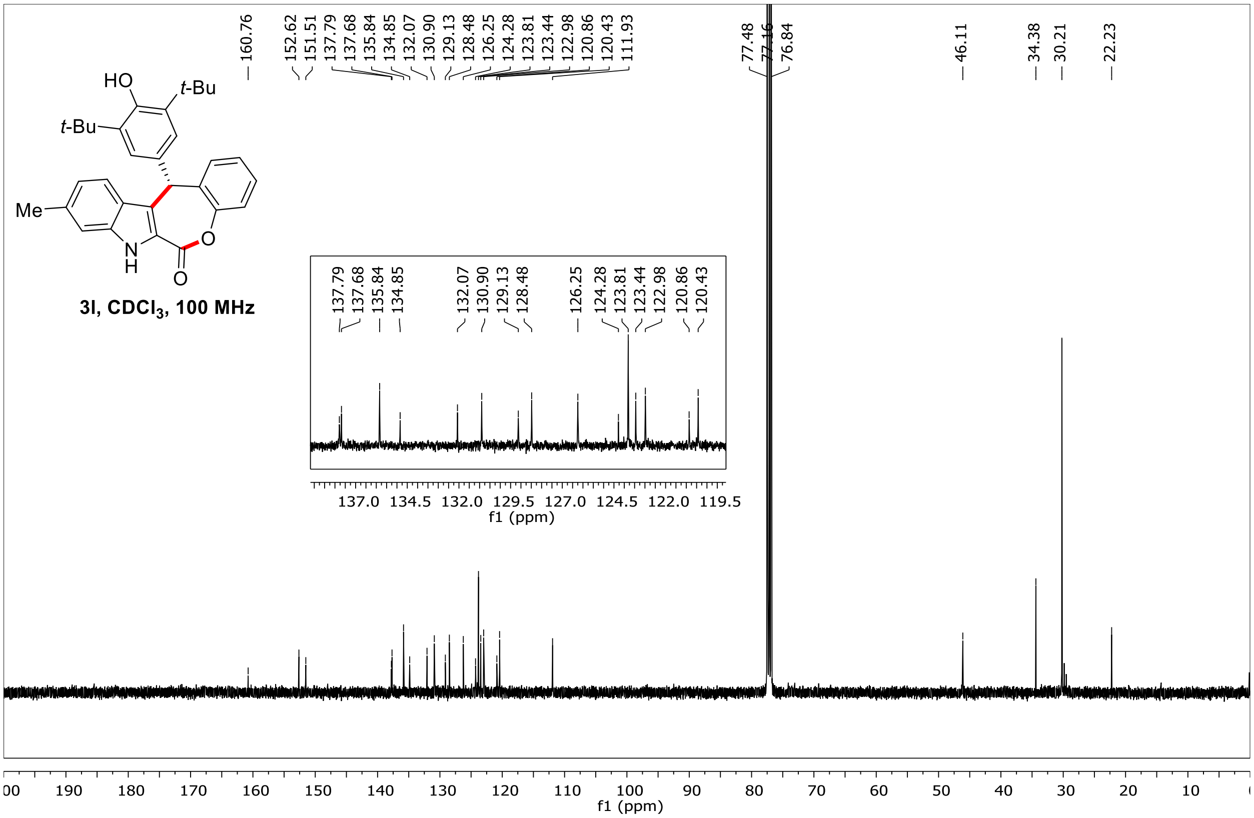
(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3k)



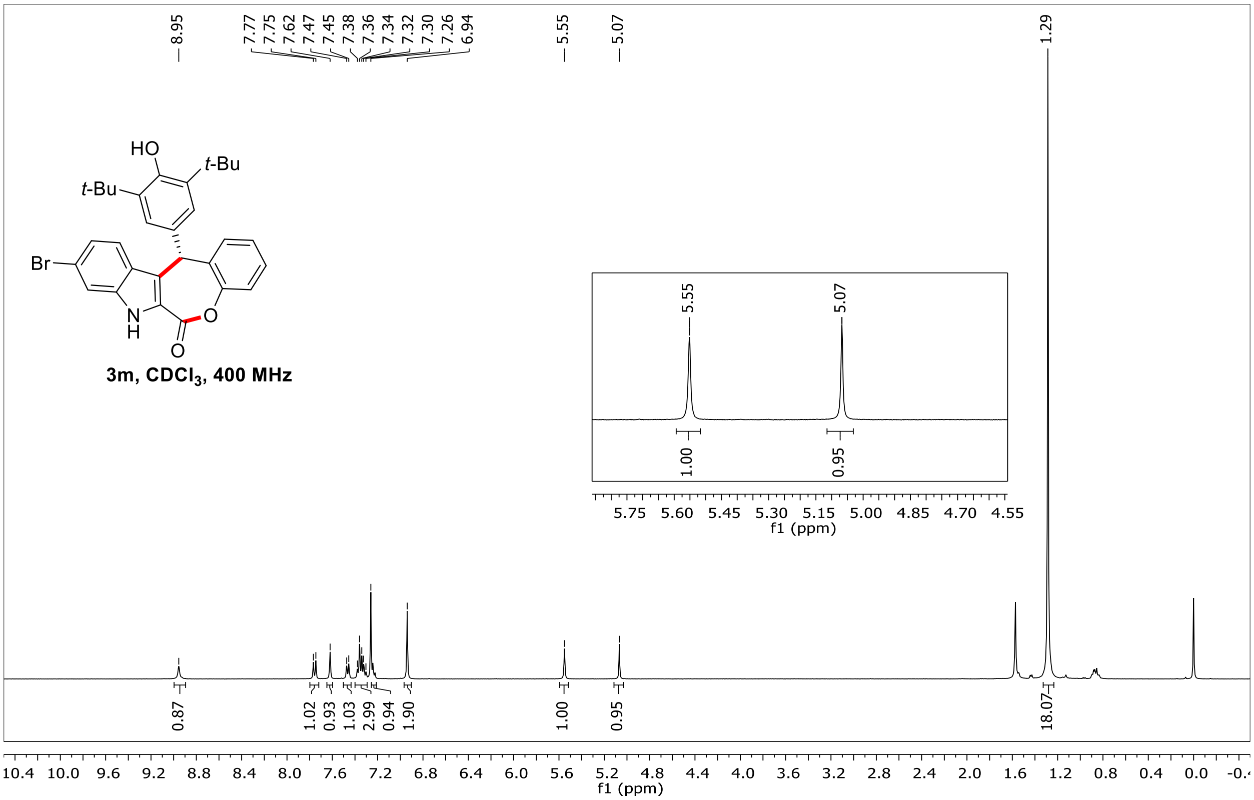


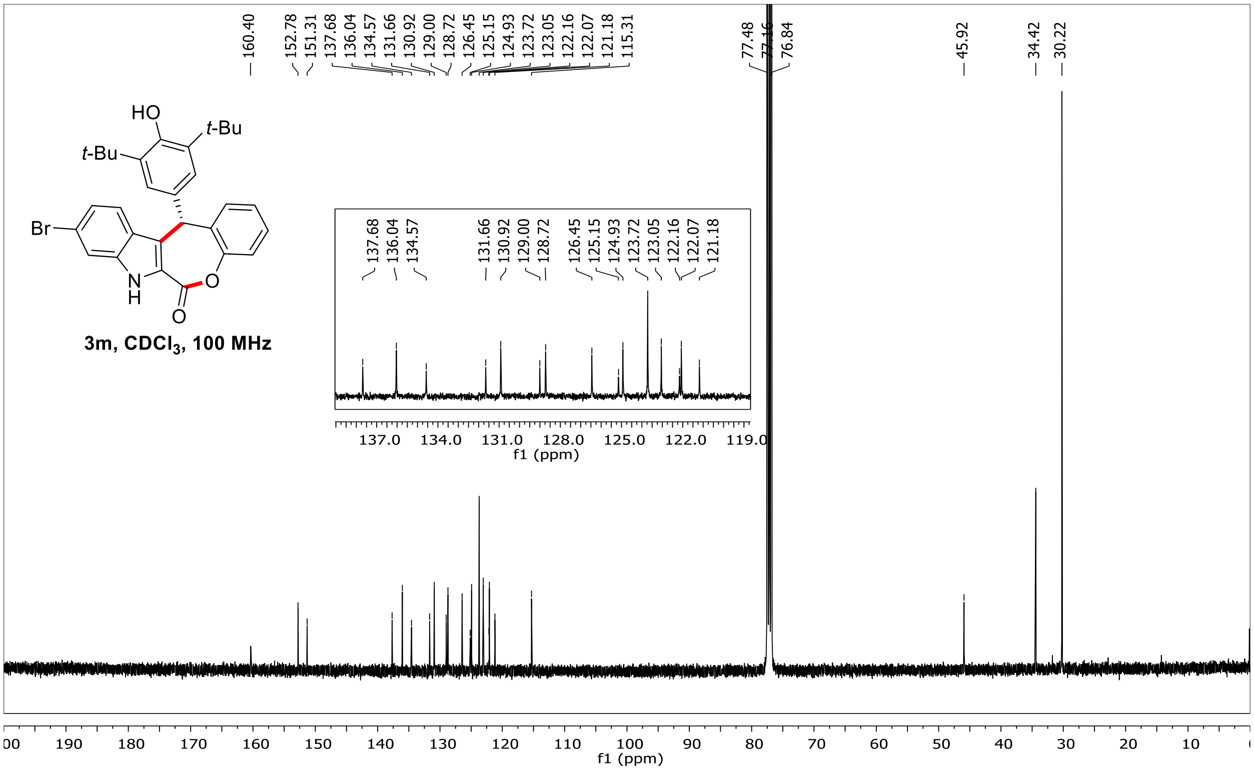
(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3l)



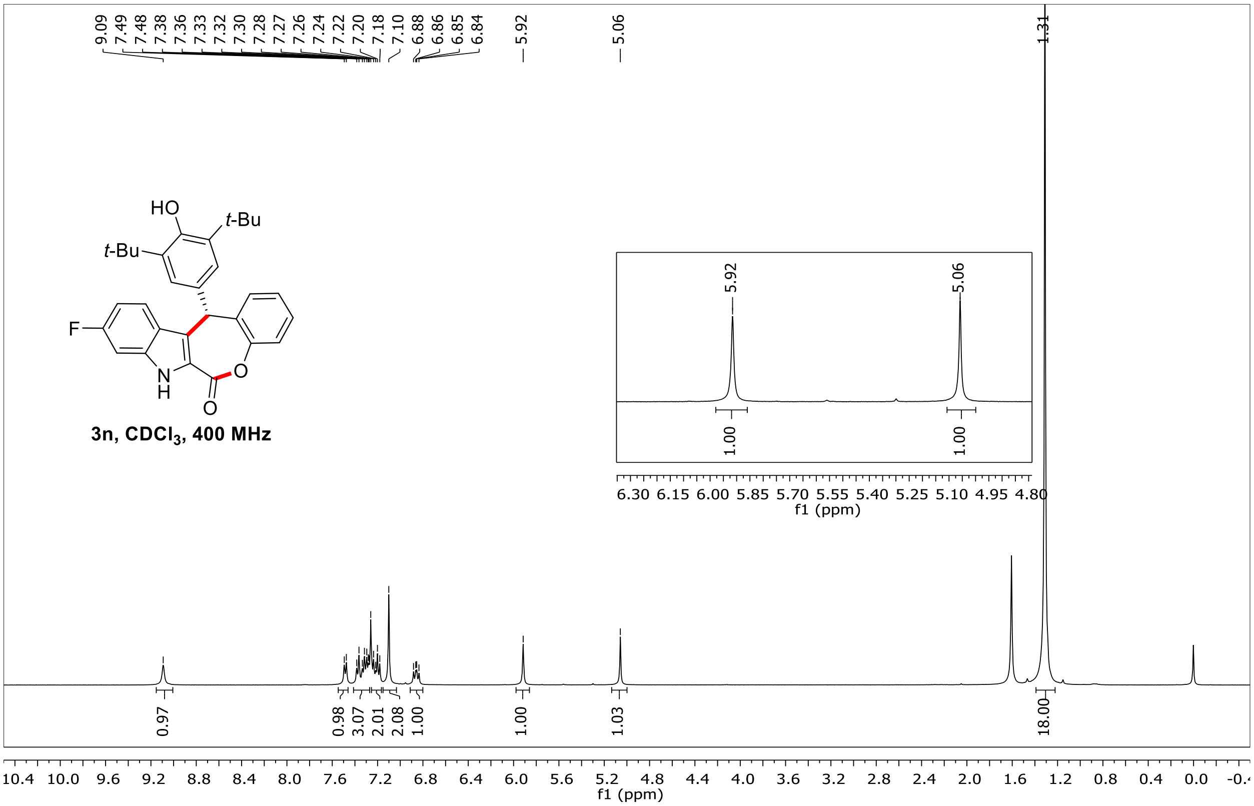


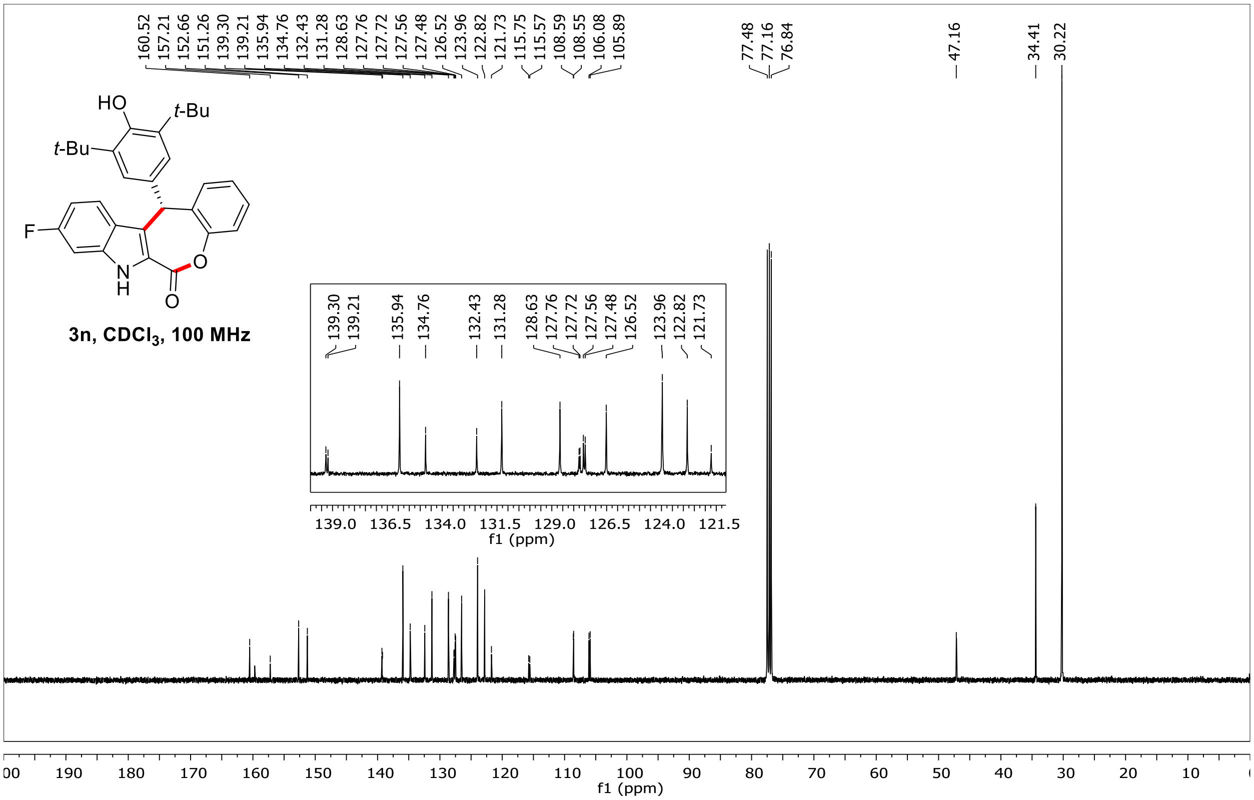
(*S*)-9-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3m)



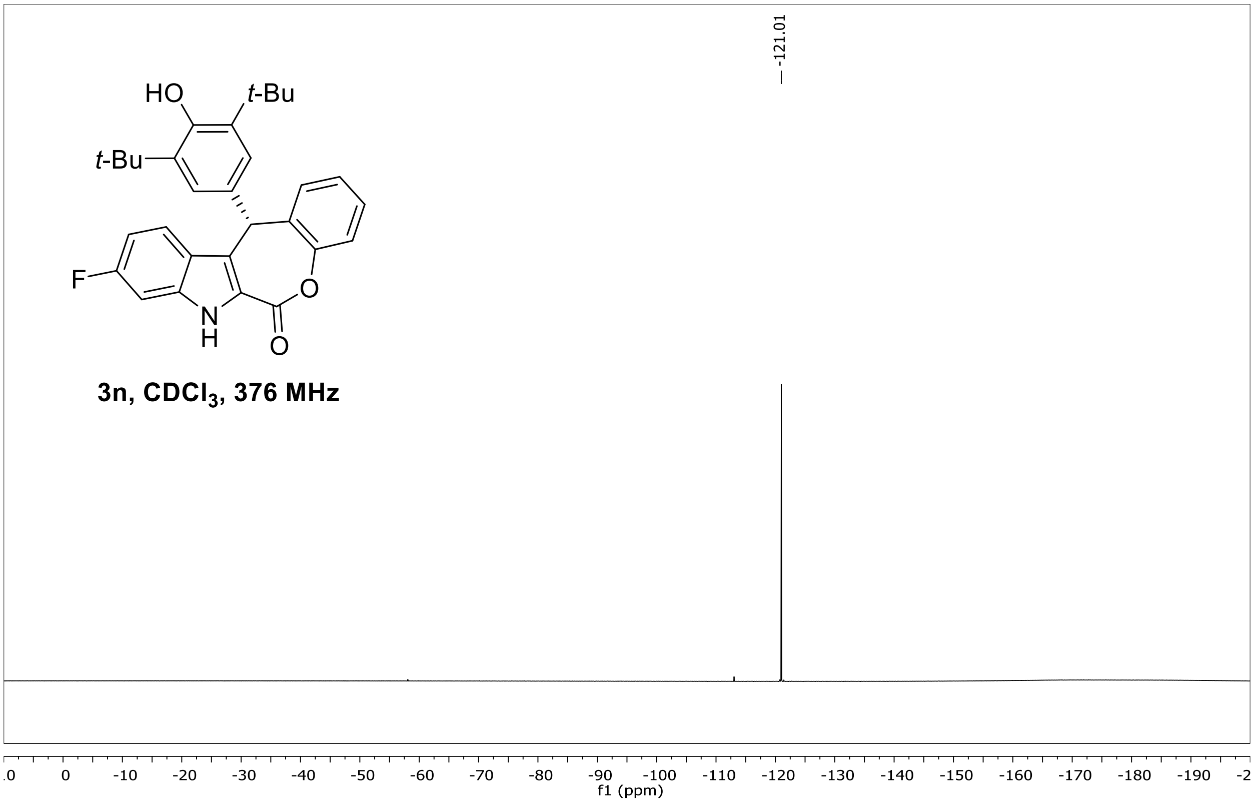


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3n)

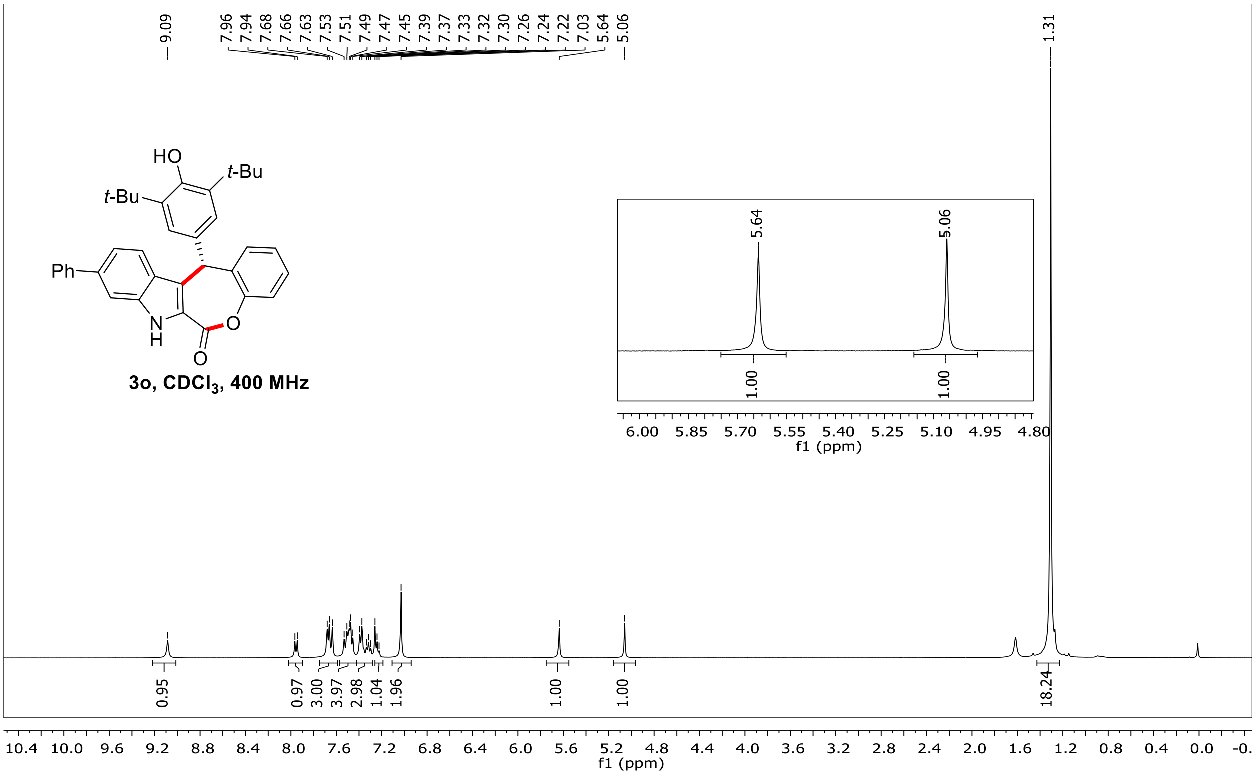


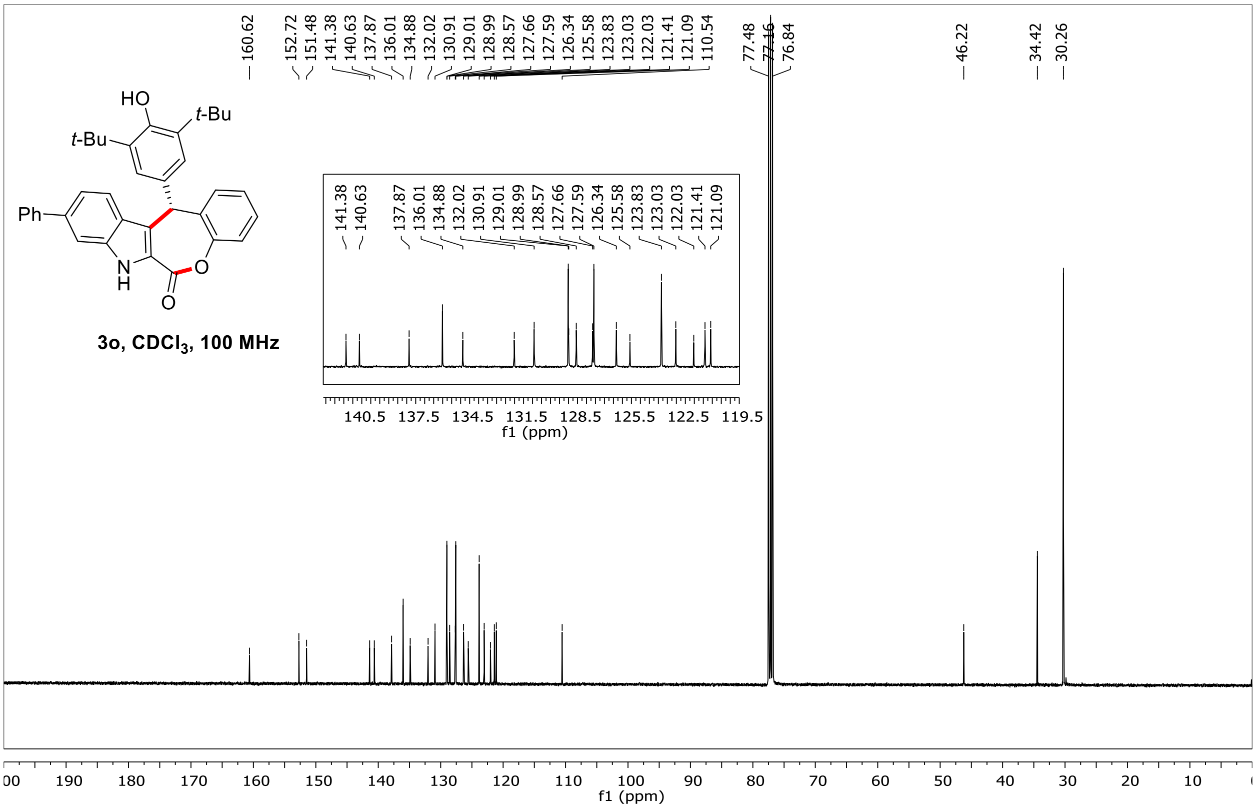


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3n)

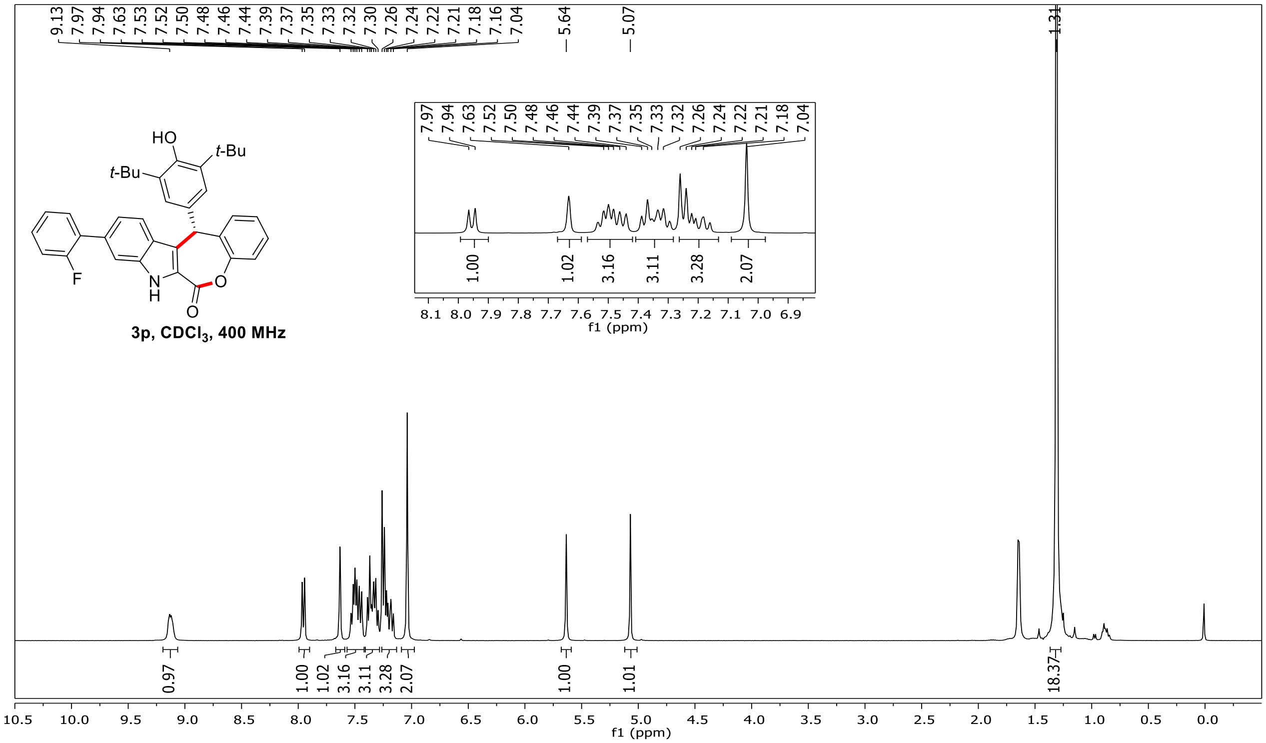


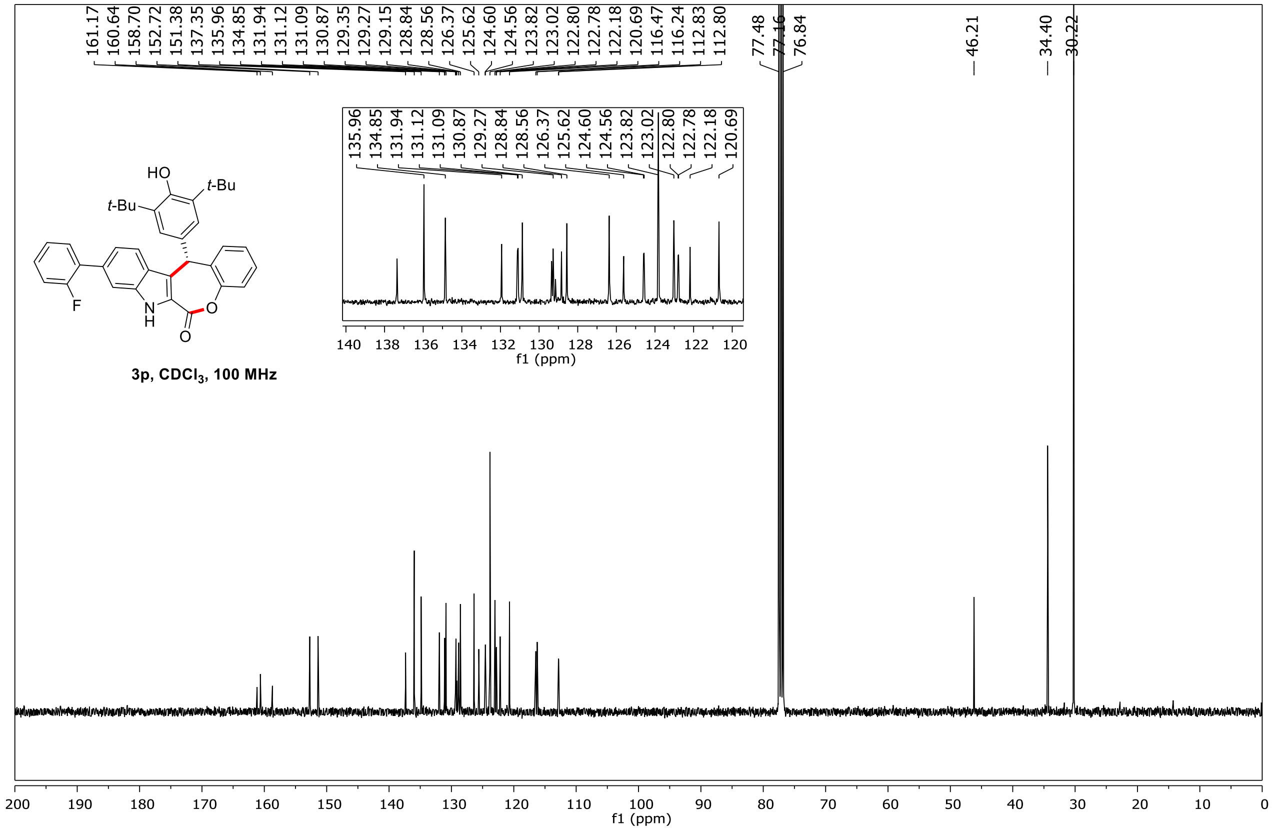
(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-phenyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3o)



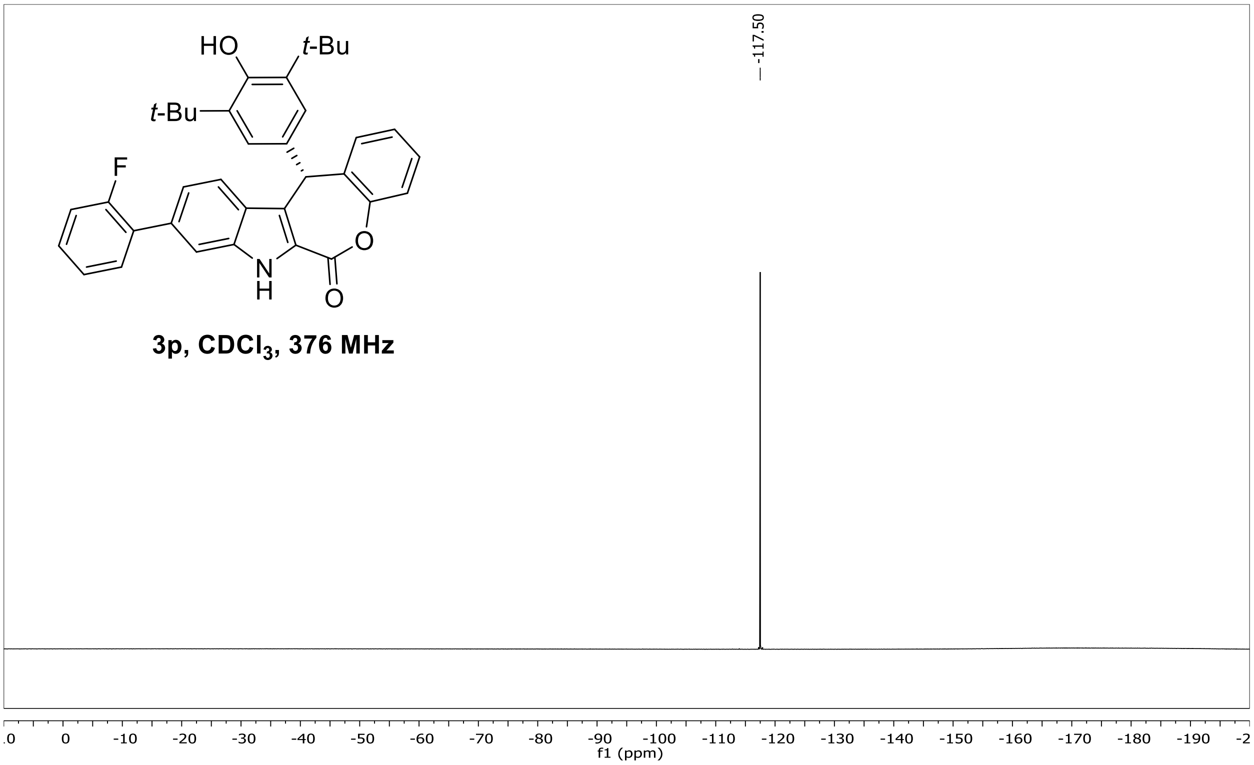


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-(2-fluorophenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino[3,4-*b*] indol-6-one (3p)

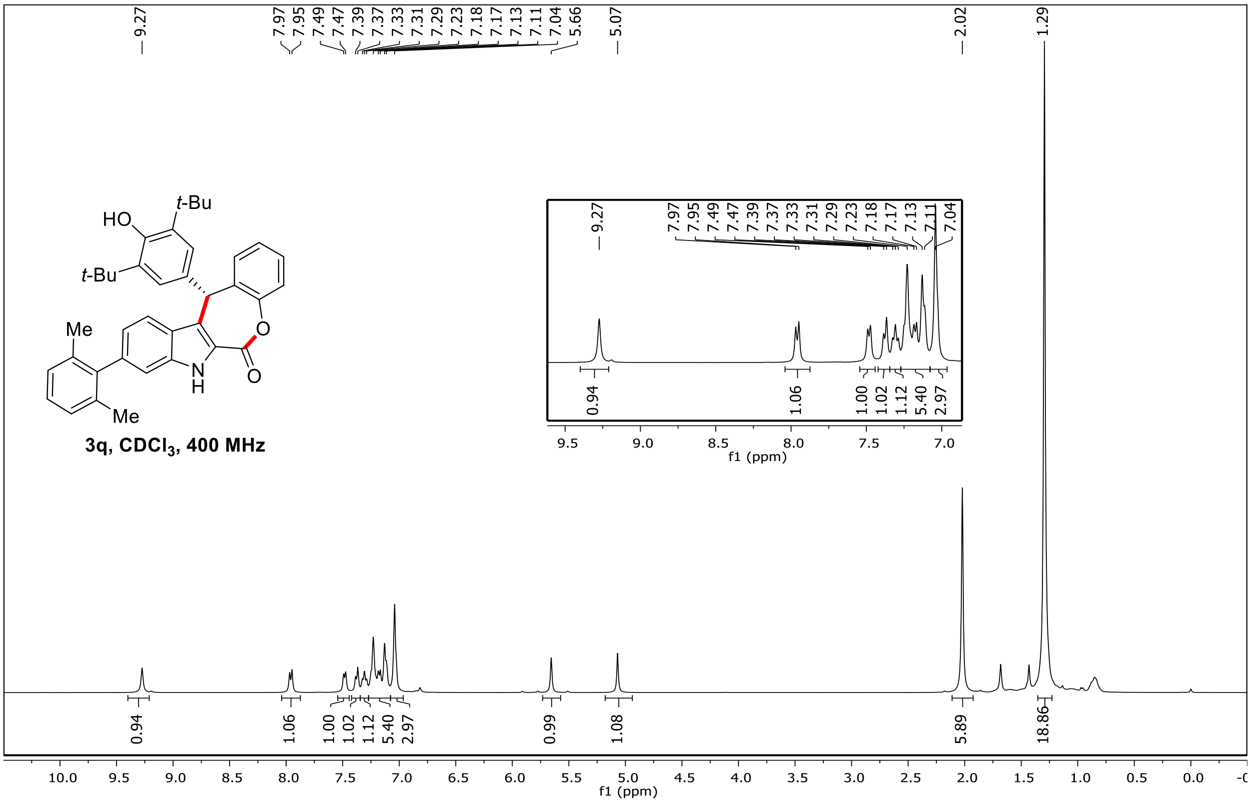


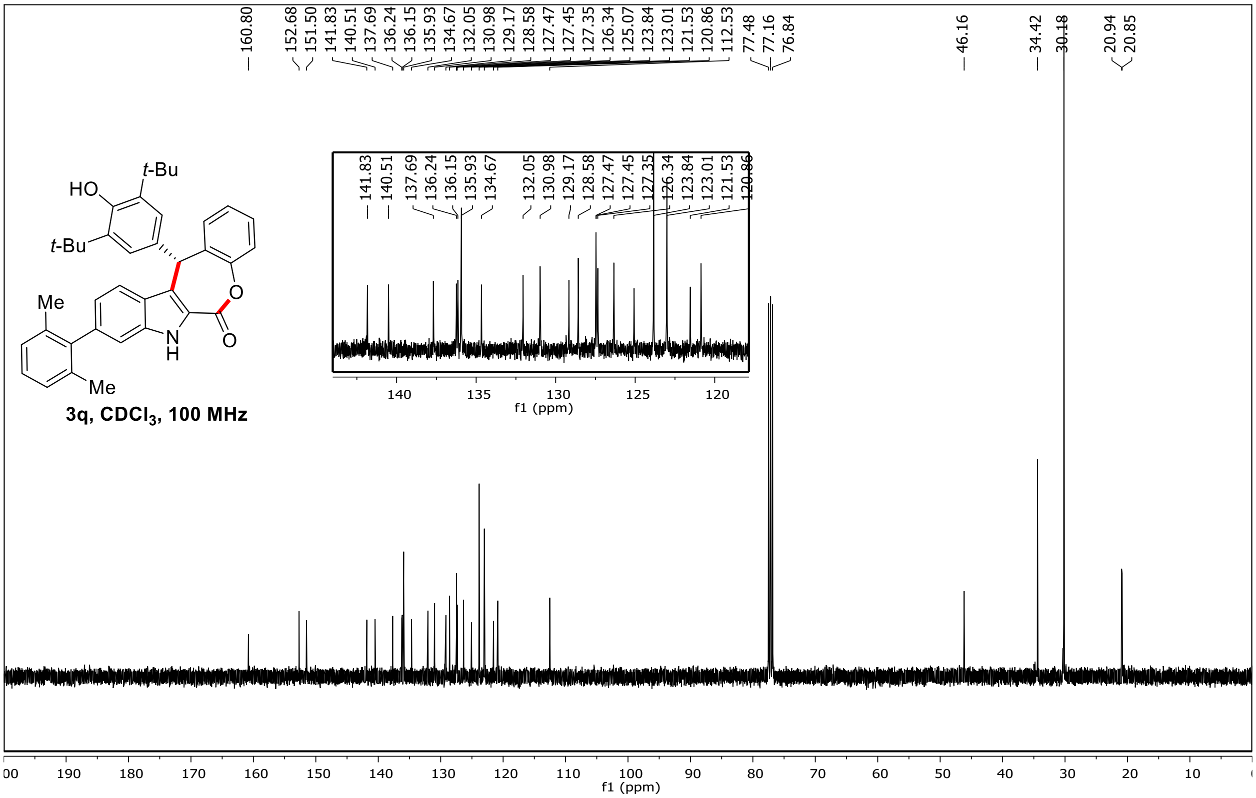


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-(2-fluorophenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino[3,4-*b*] indol-6-one (3p)

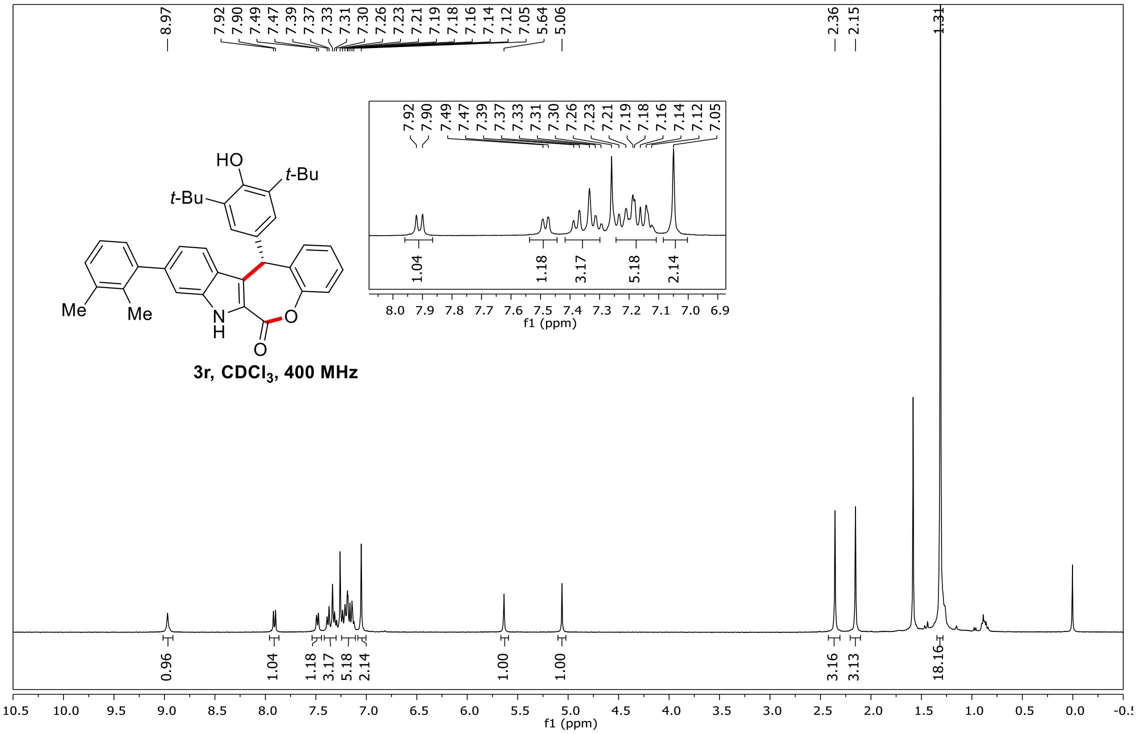


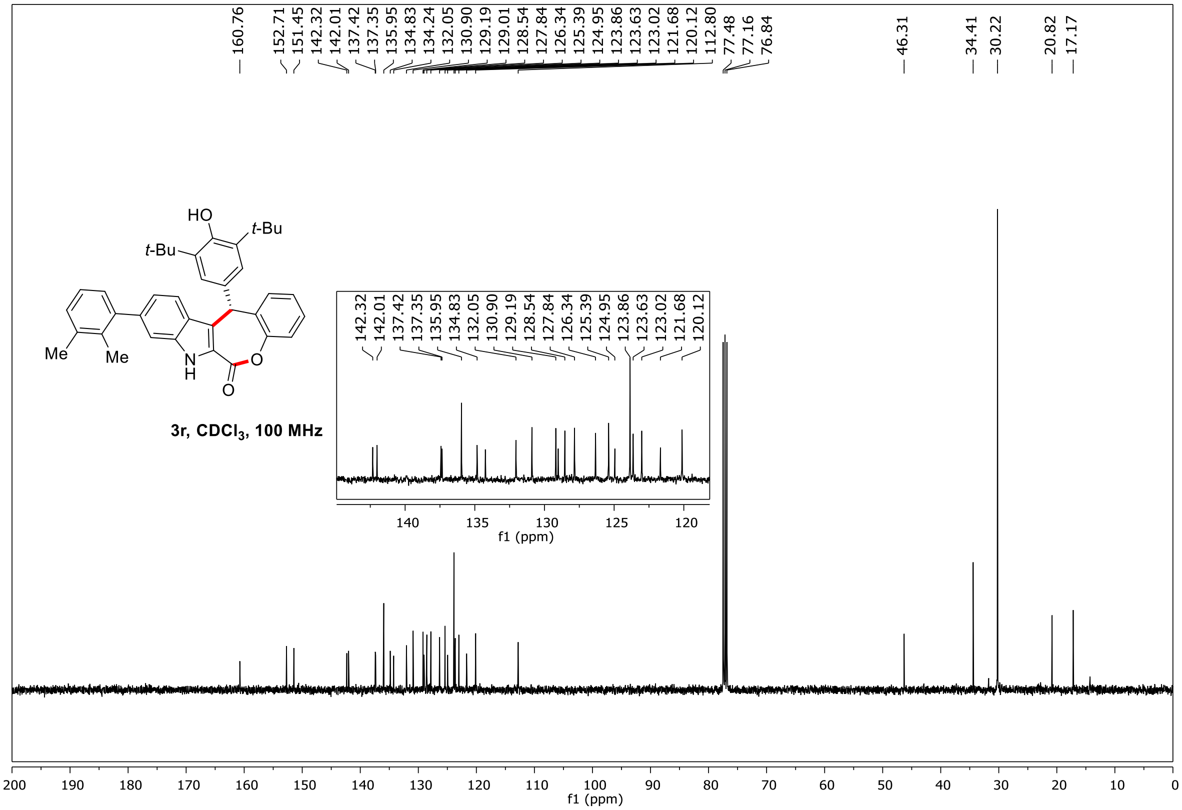
(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-9-(2,6-dimethylphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3q)



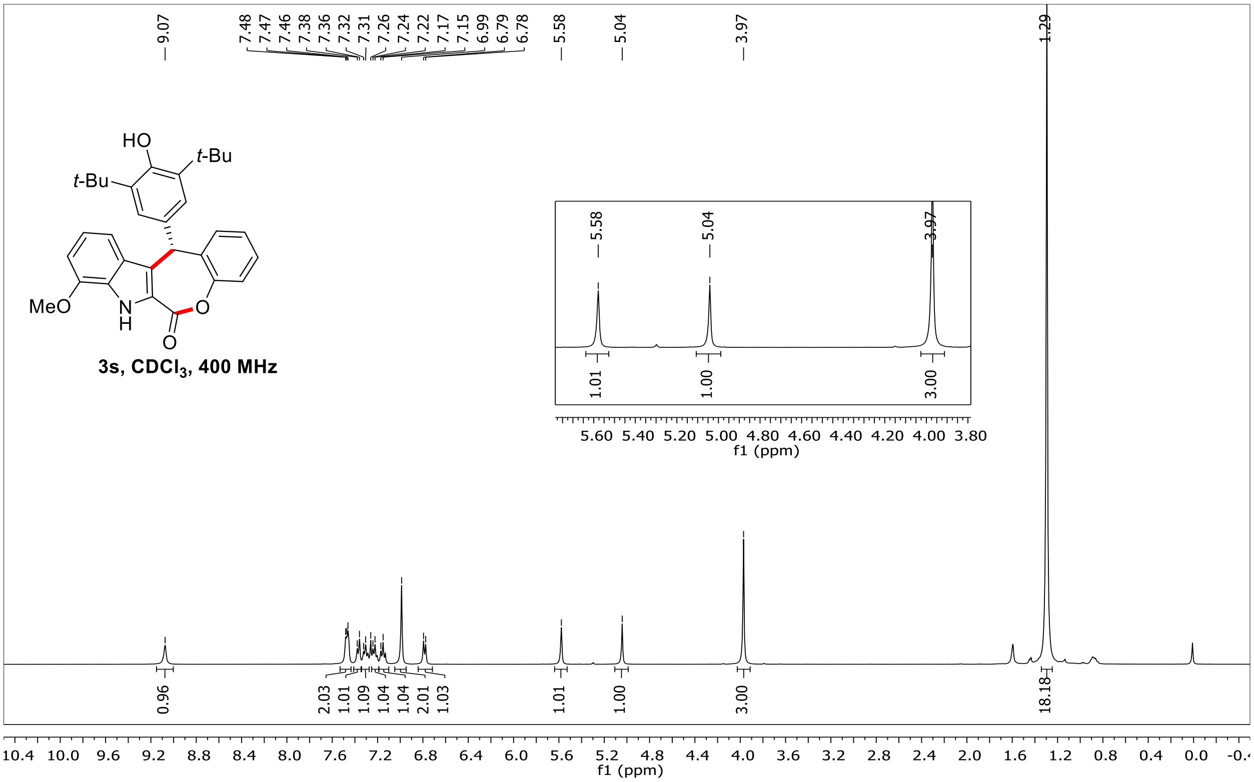


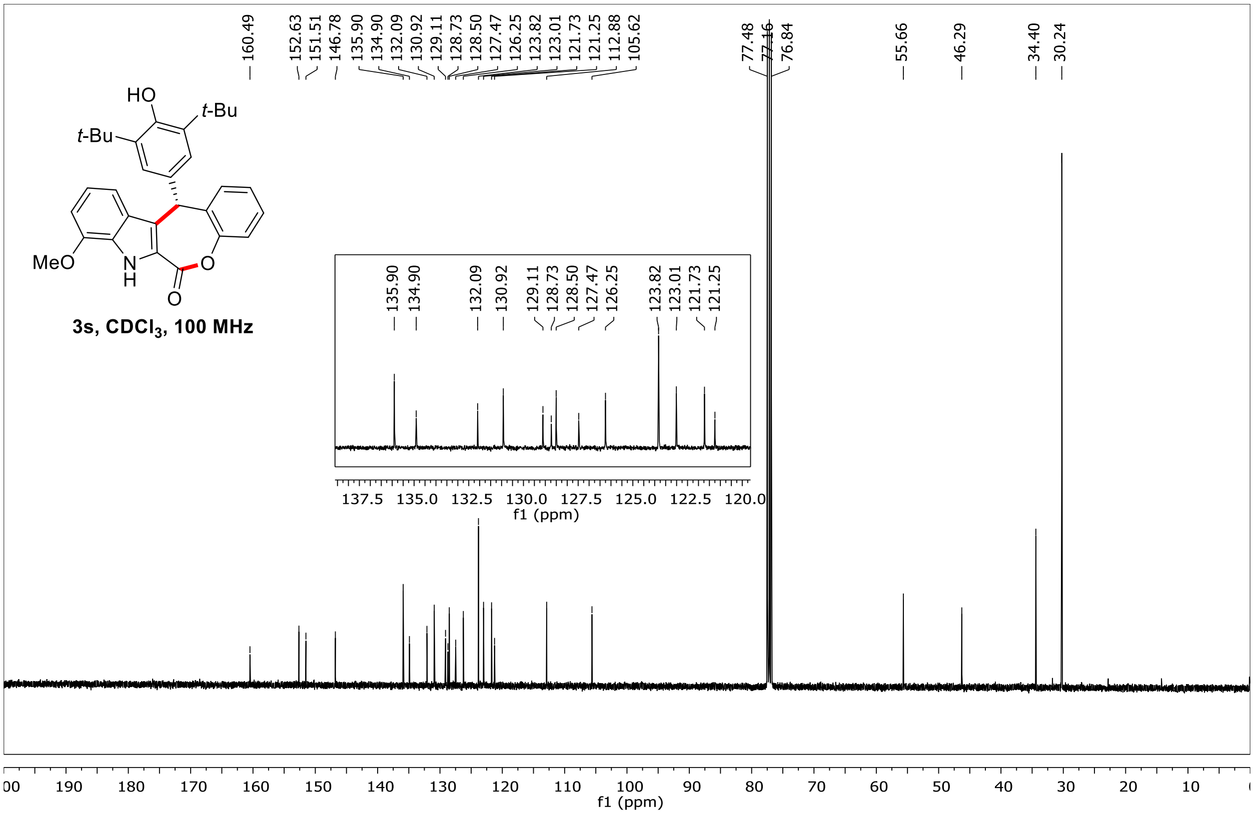
(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-(2,3-dimethylphenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino[3,4-*b*] indol-6-one (3r)



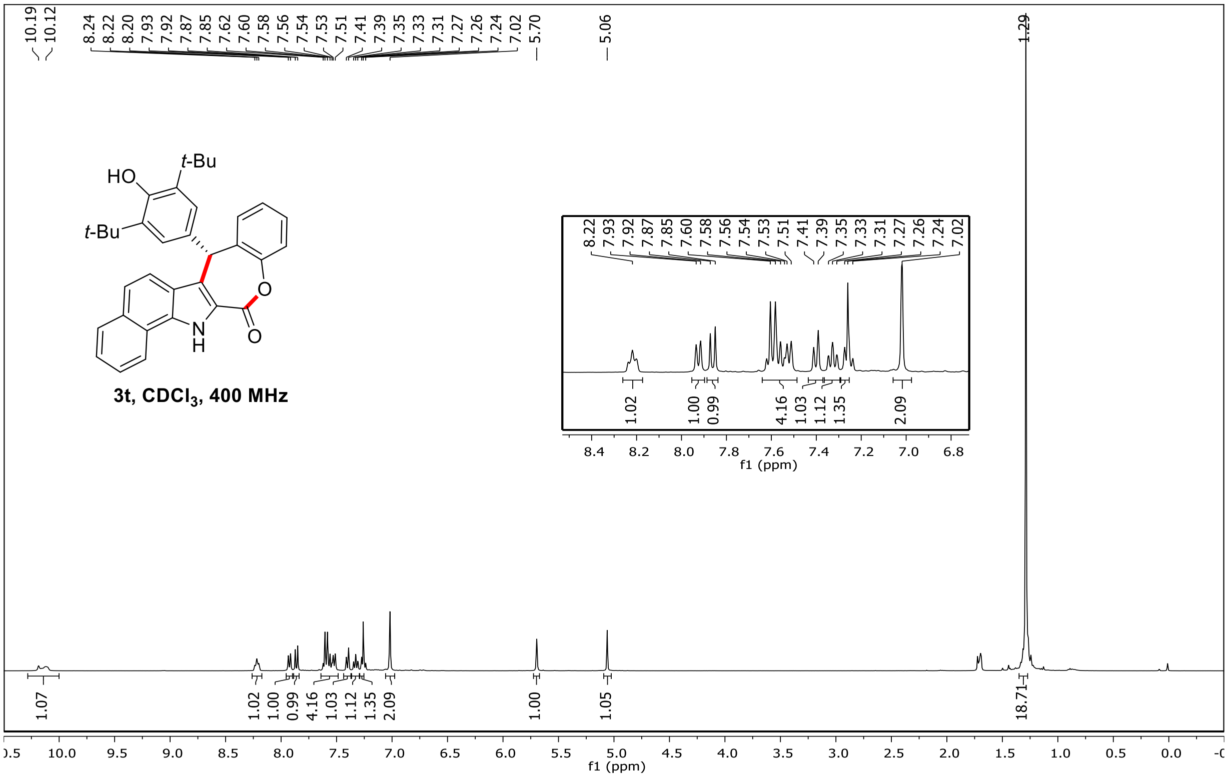


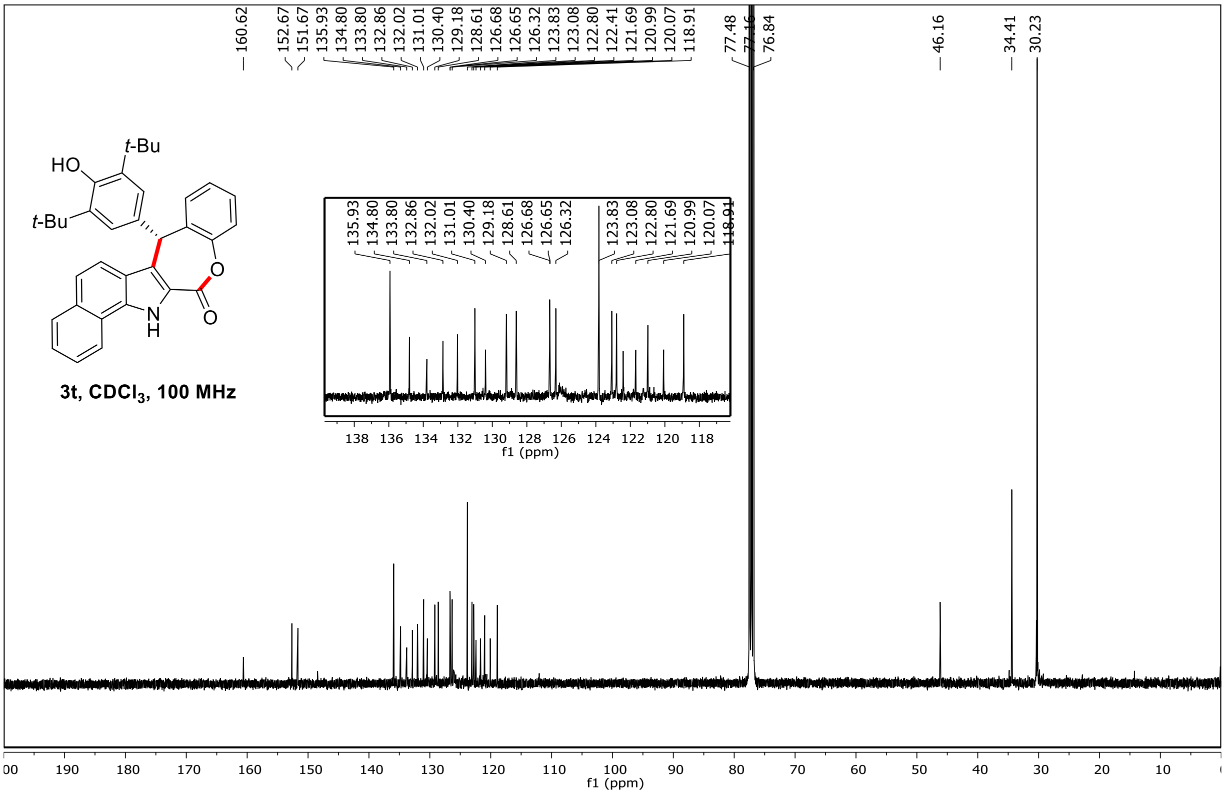
(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-8-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3s)



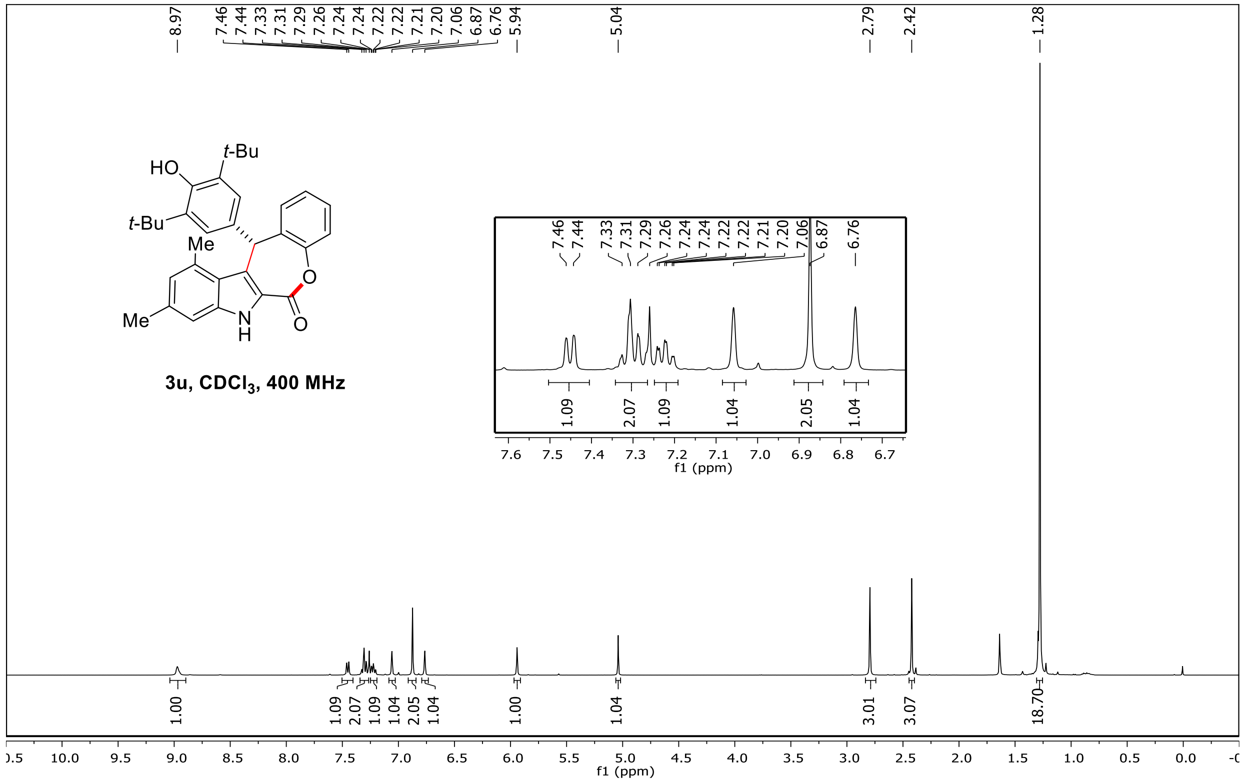


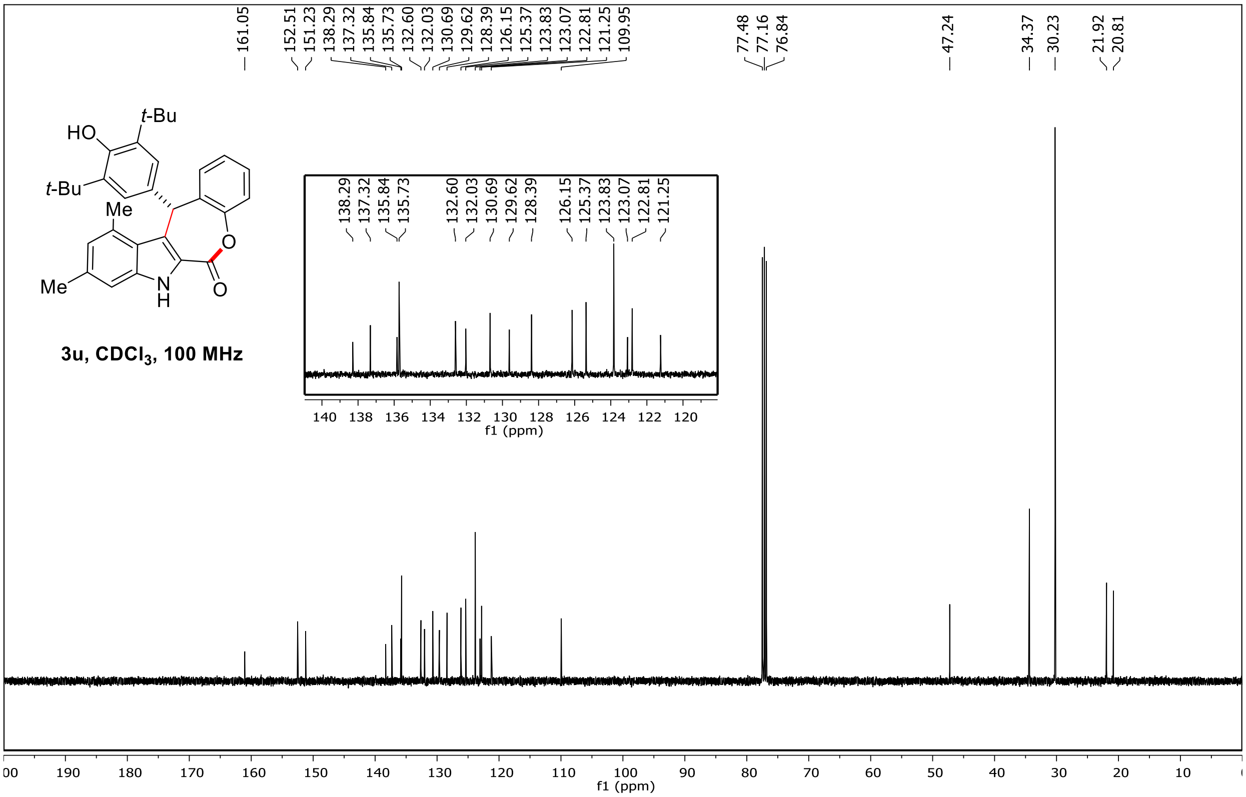
(*S*)-7-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-7,14-dihydro-13*H*-benzo[*g*]benzo[6,7]oxepino[3,4-*b*]indol-13-one (3t)



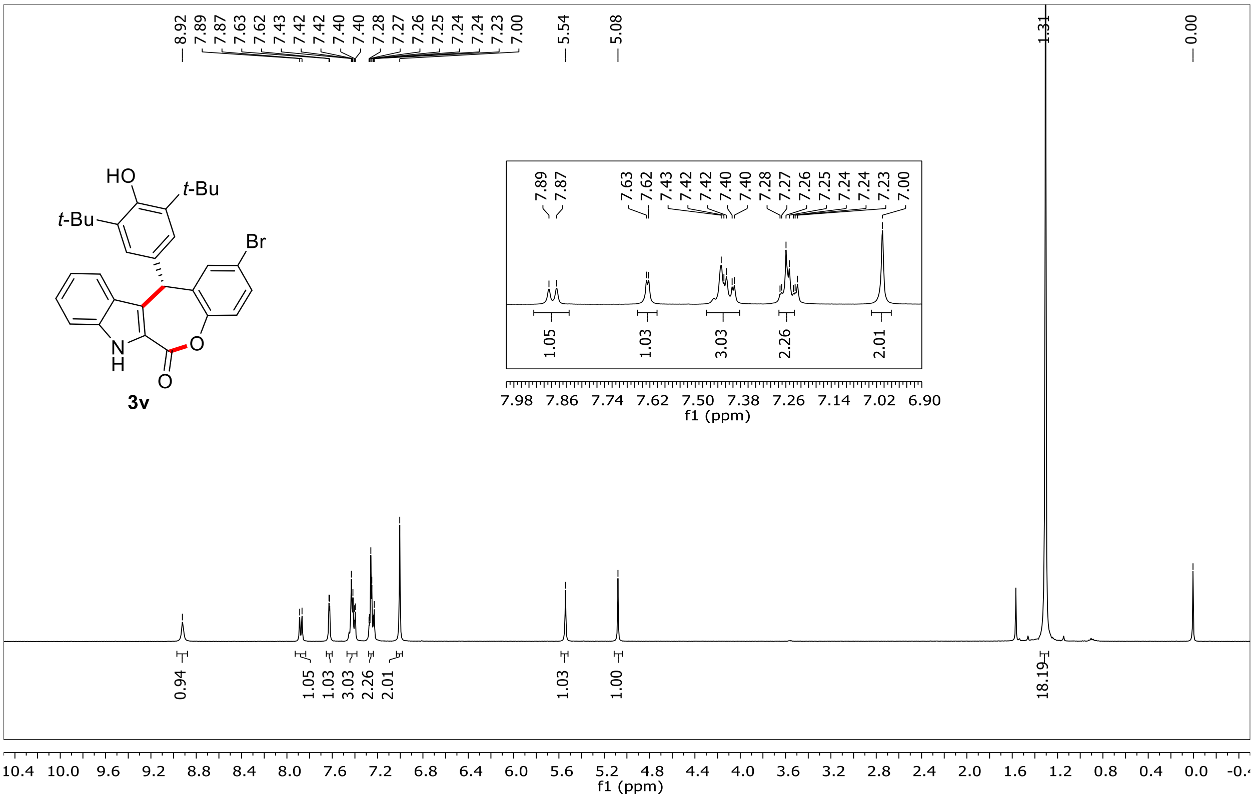


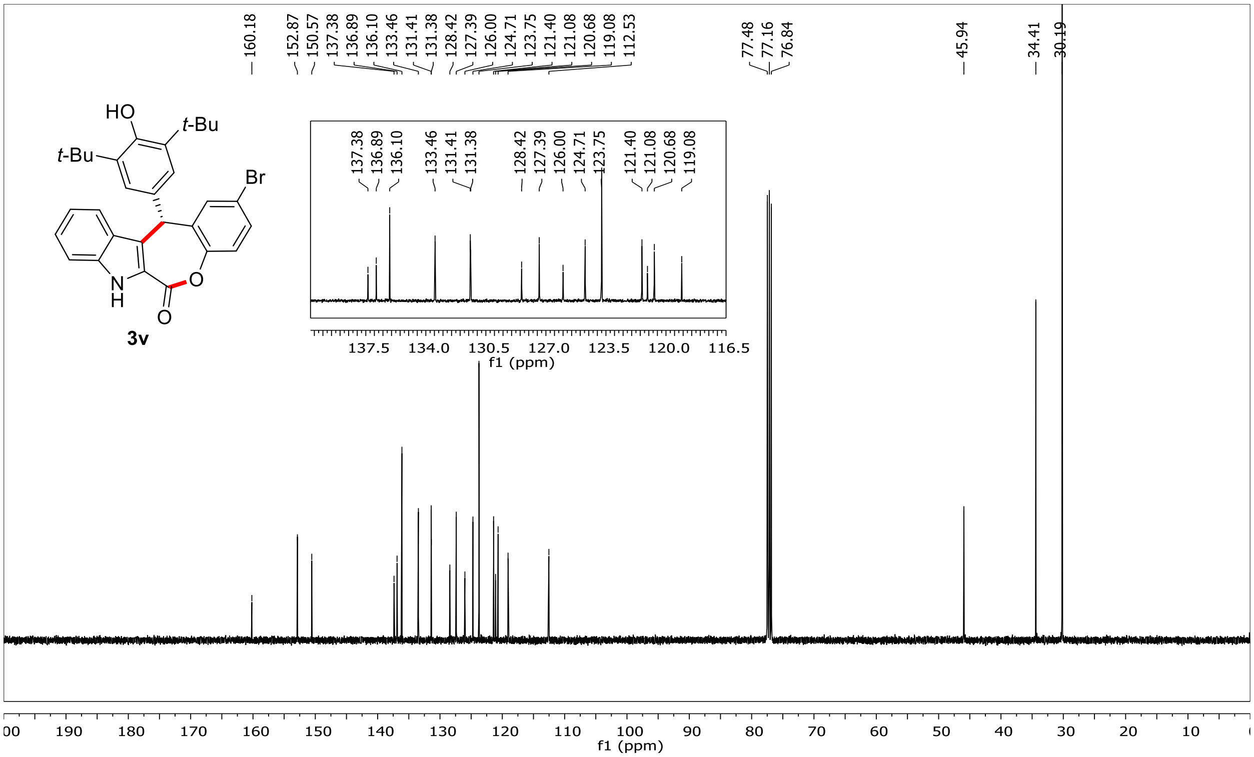
(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-9,11-dimethyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3u)



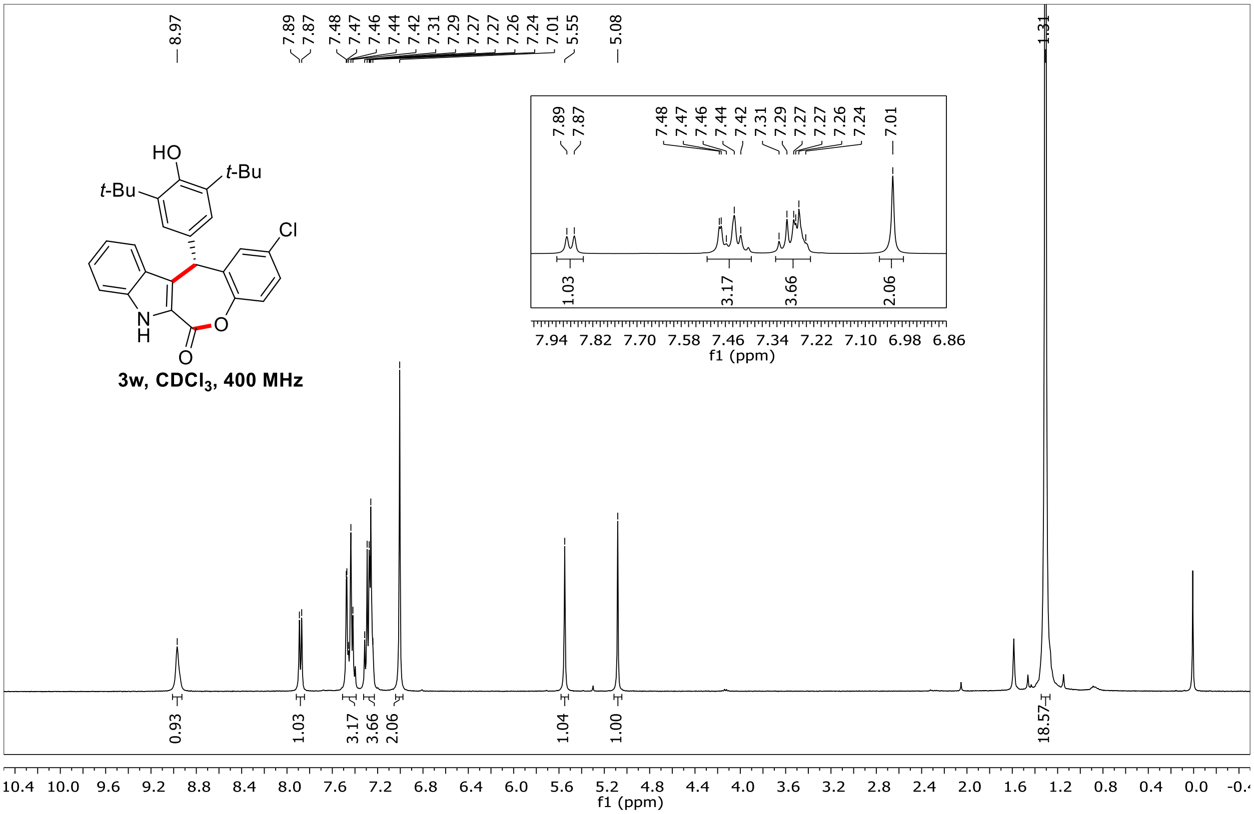


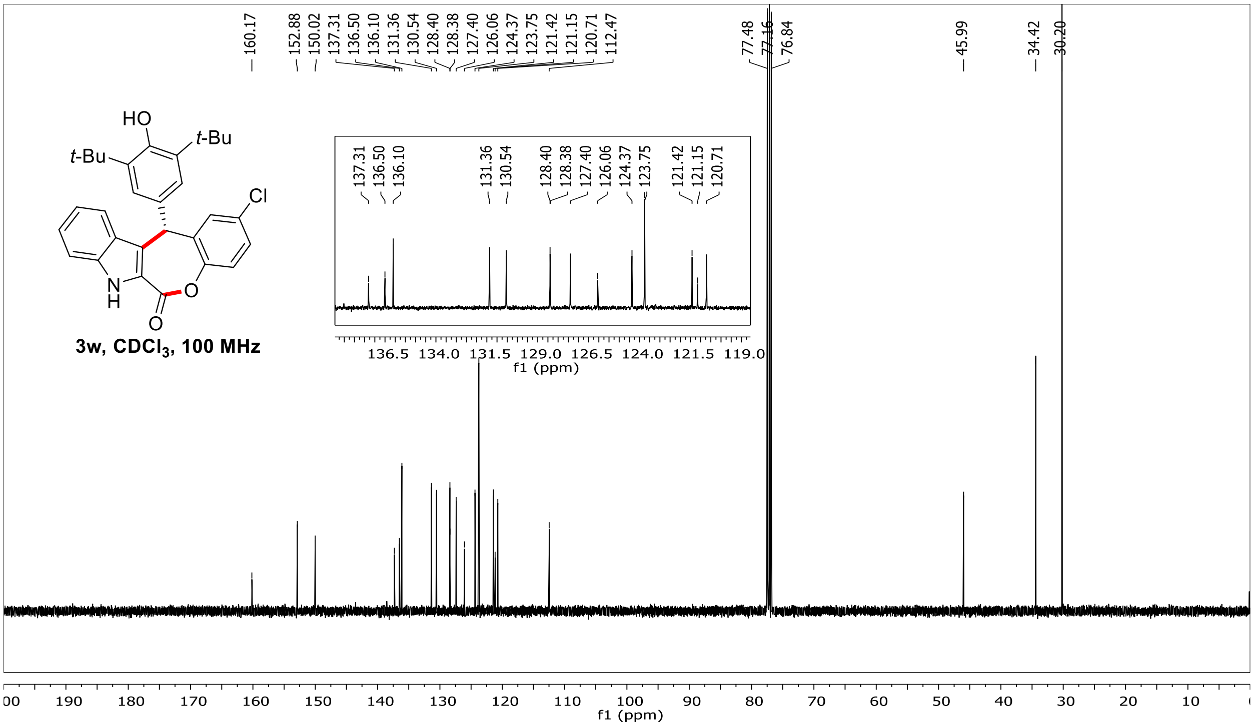
(*S*)-2-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3v)



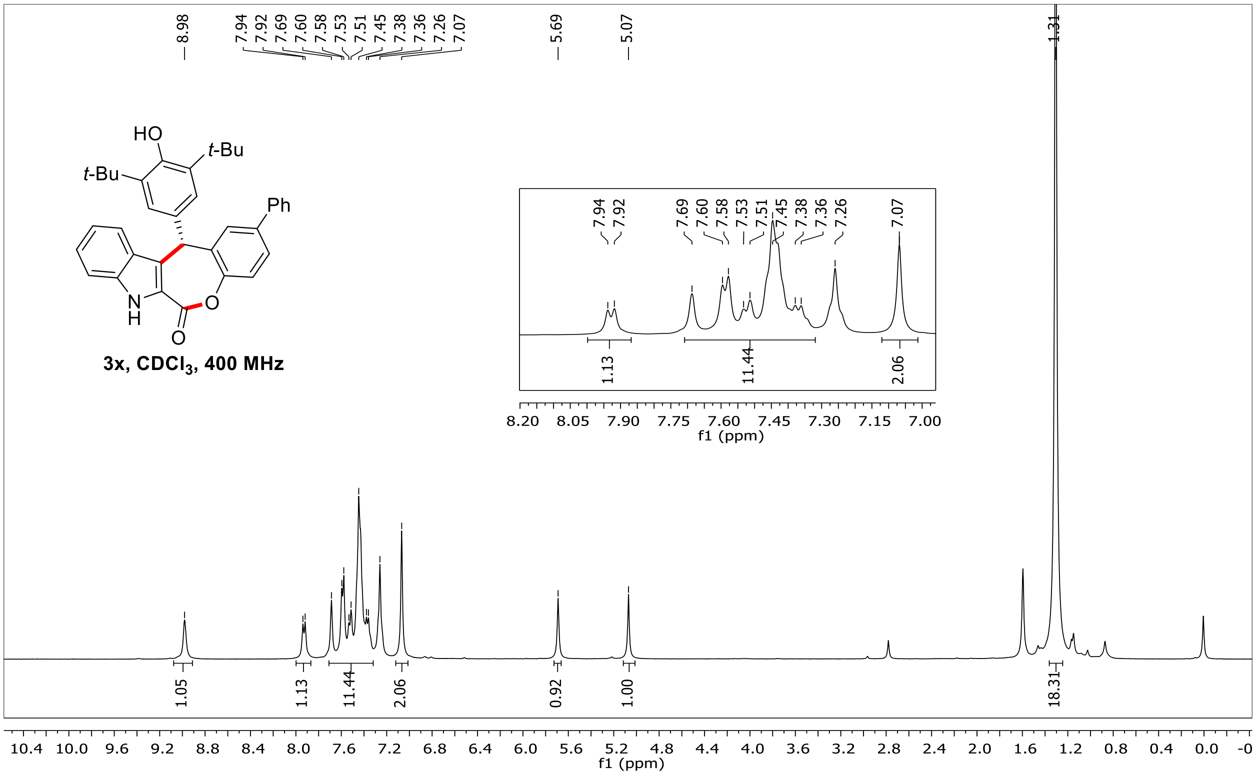


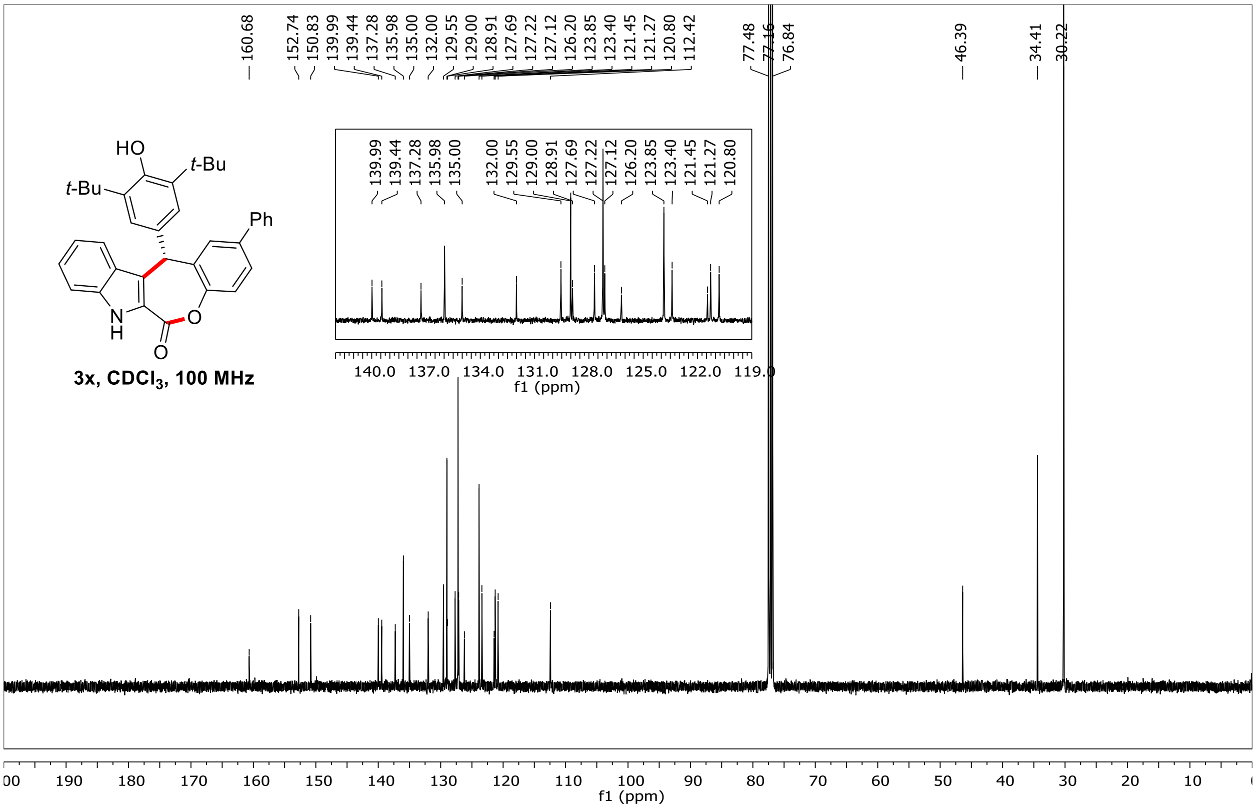
(*S*)-2-Chloro-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3w)



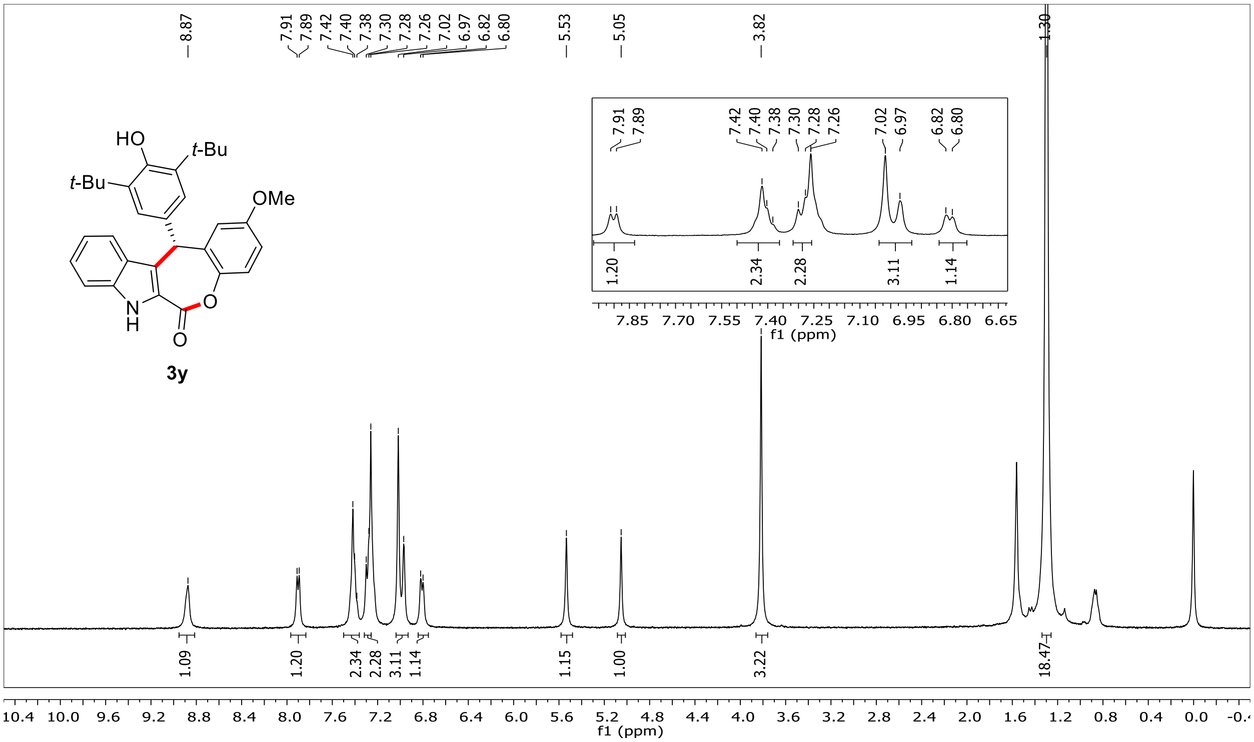


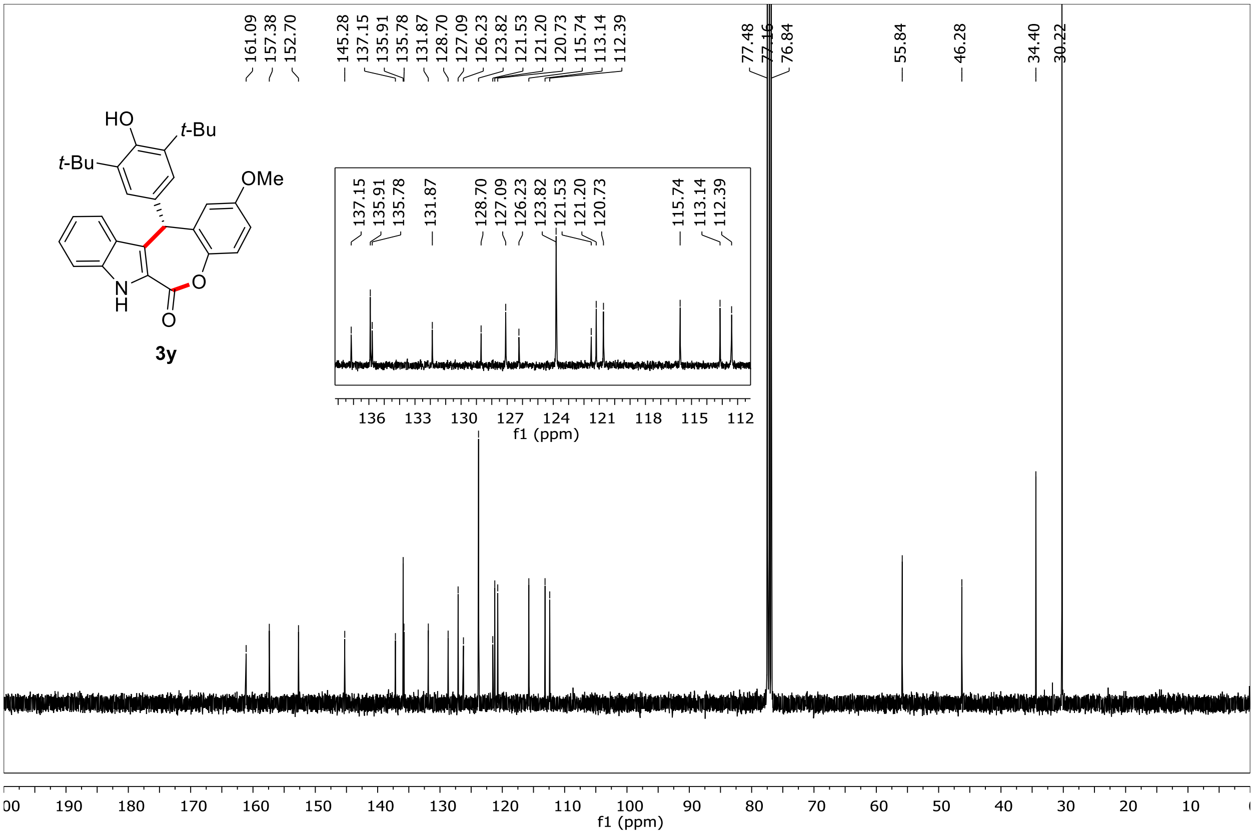
(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-phenyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3x)



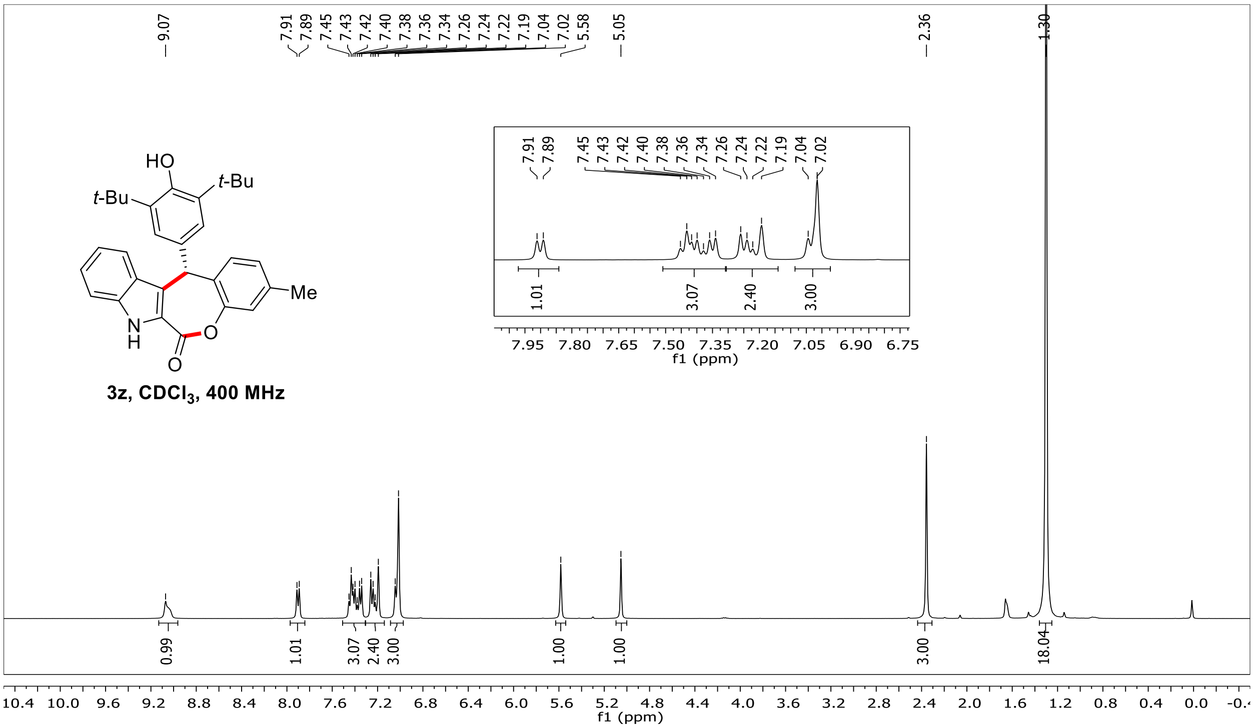


(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-methoxy-7,12-dihydro-6*H* benzo[6,7]oxepino[3, 4-b]indol-6-one (3y)

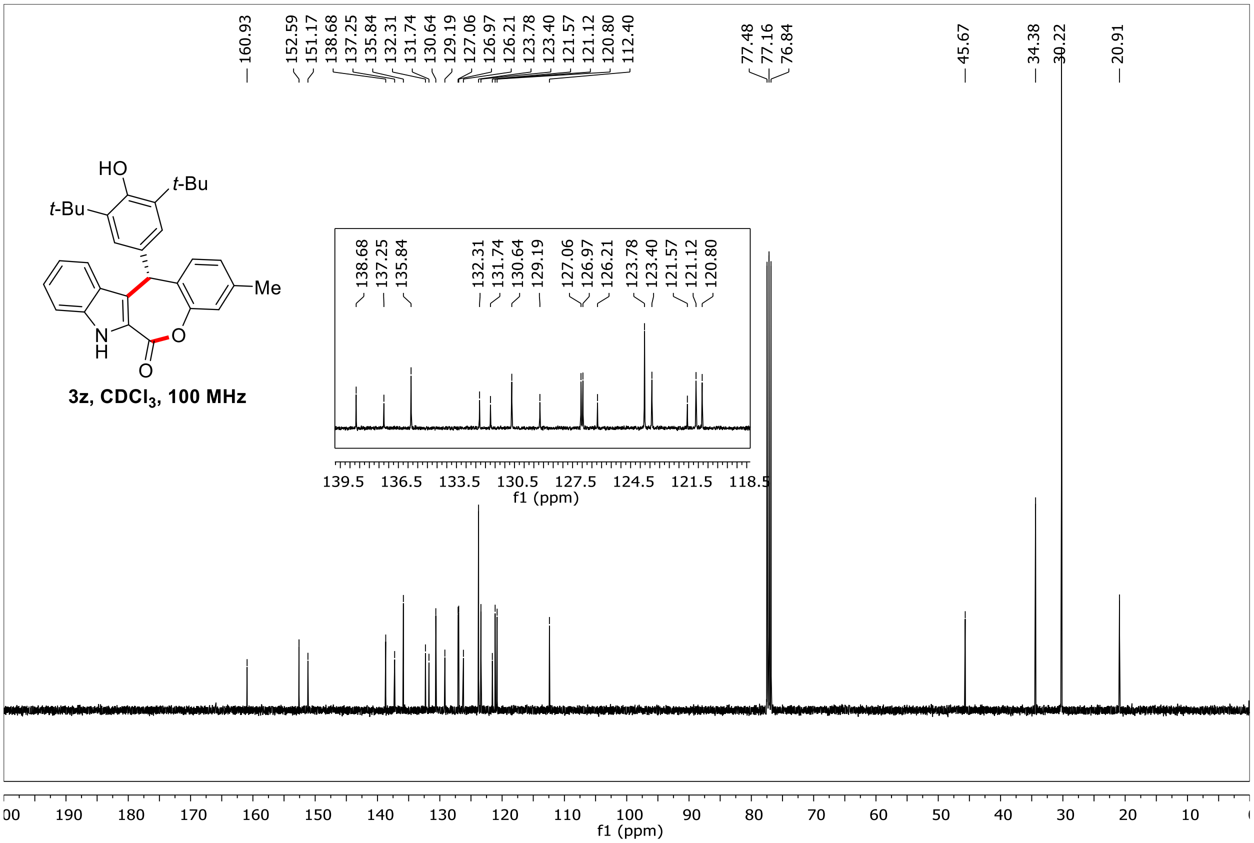




(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-3-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3z)

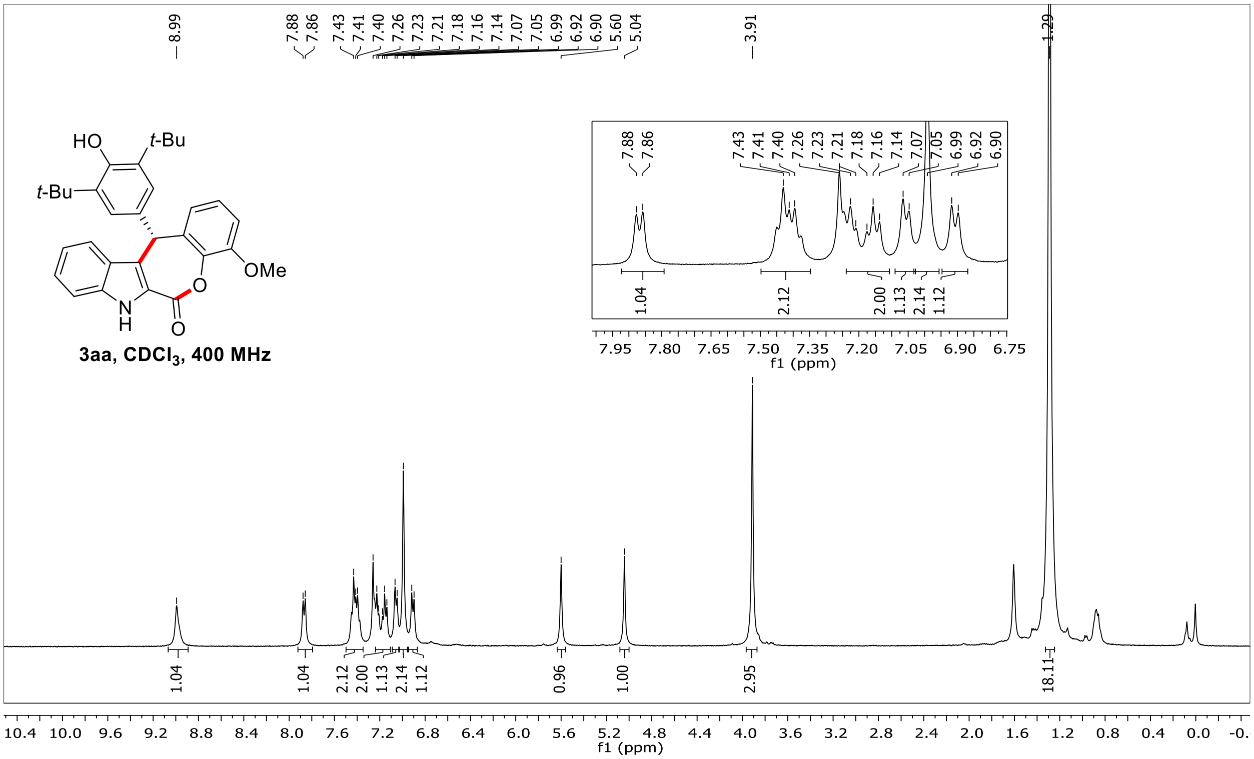


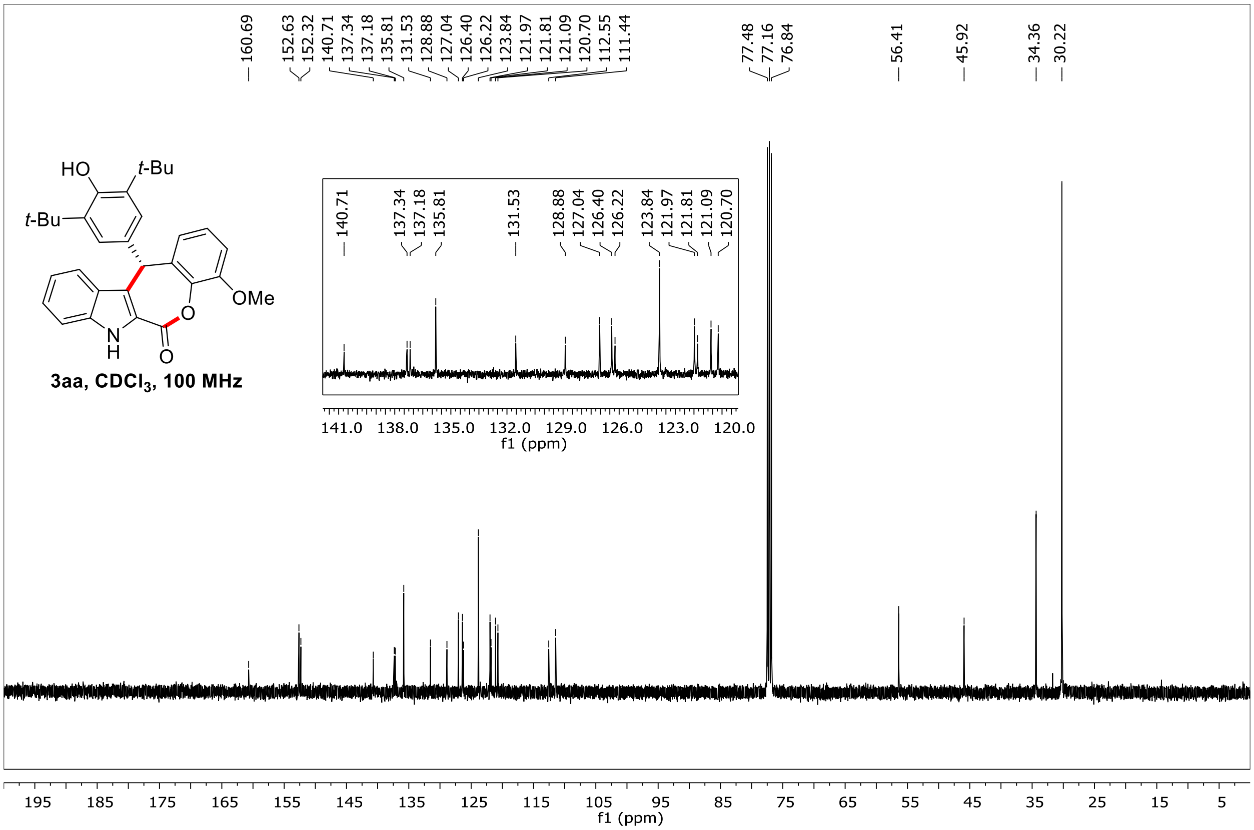
3z, CDCl$_3$, 400 MHz



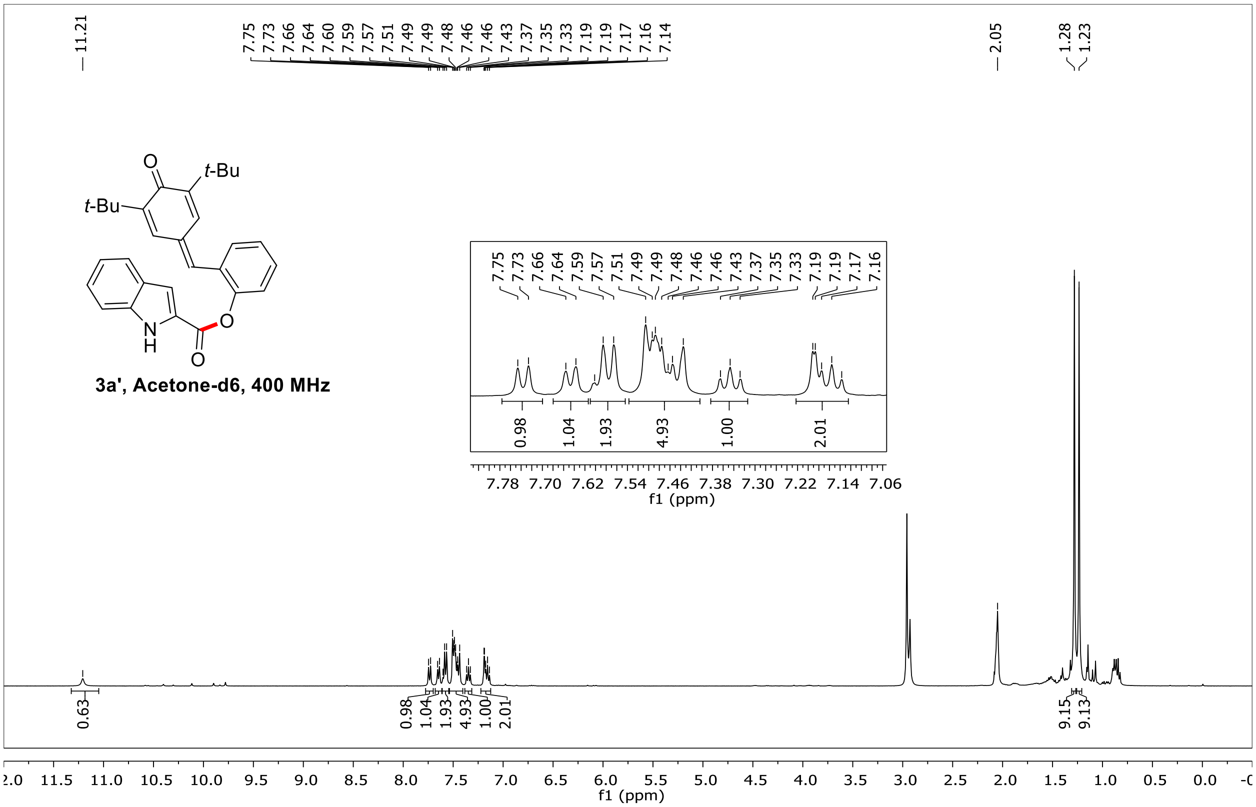
3z, CDCl$_3$, 100 MHz

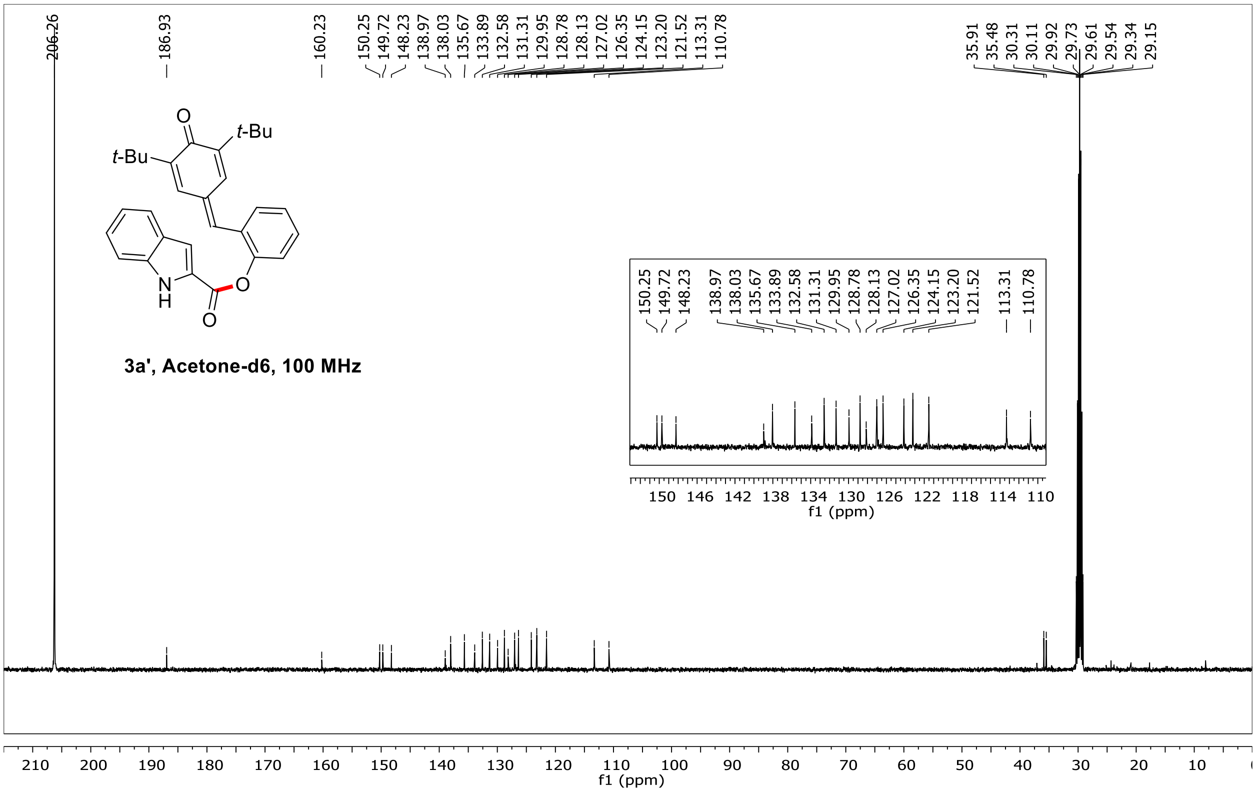
(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-4-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3, 4-b]indol-6-one (3aa)



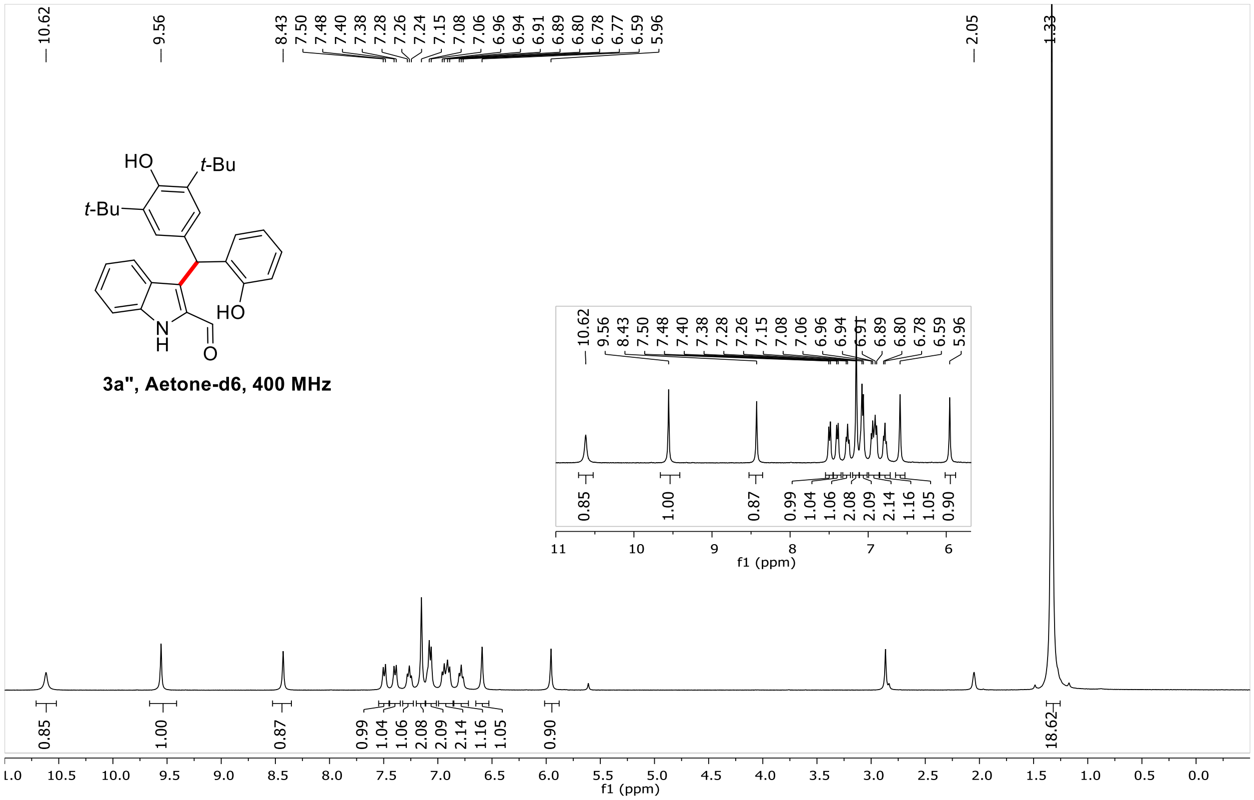


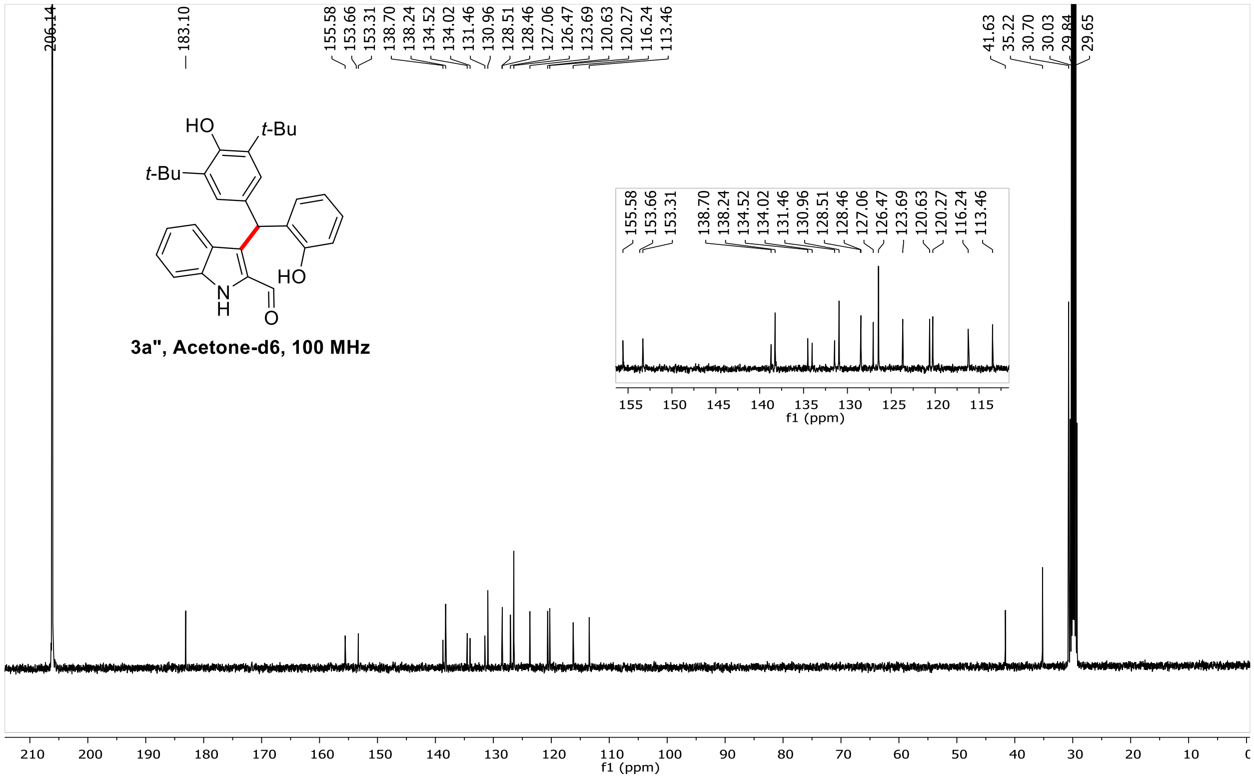
2-((3,5-Di-*tert*-butyl-4-oxocyclohexa-2,5-dien-1-ylidene)methyl)phenyl-1*H*-indole-2-carboxylate (3a’)



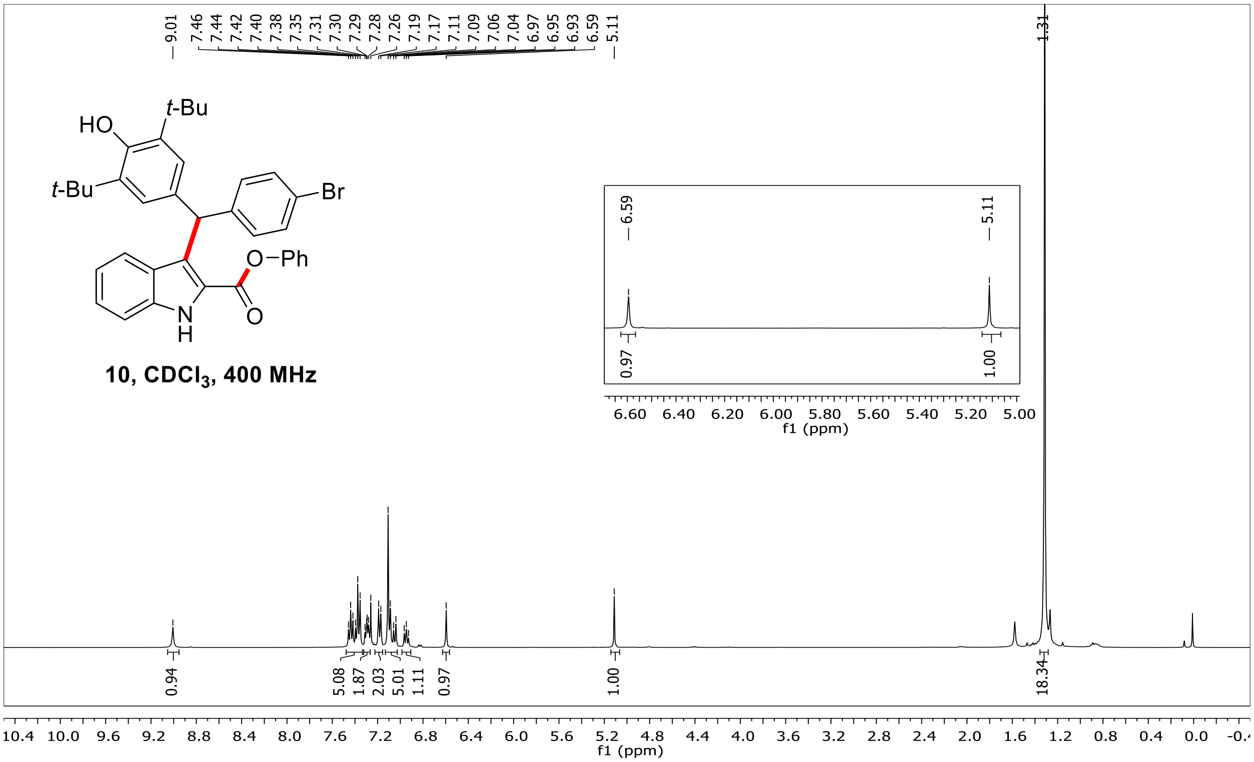


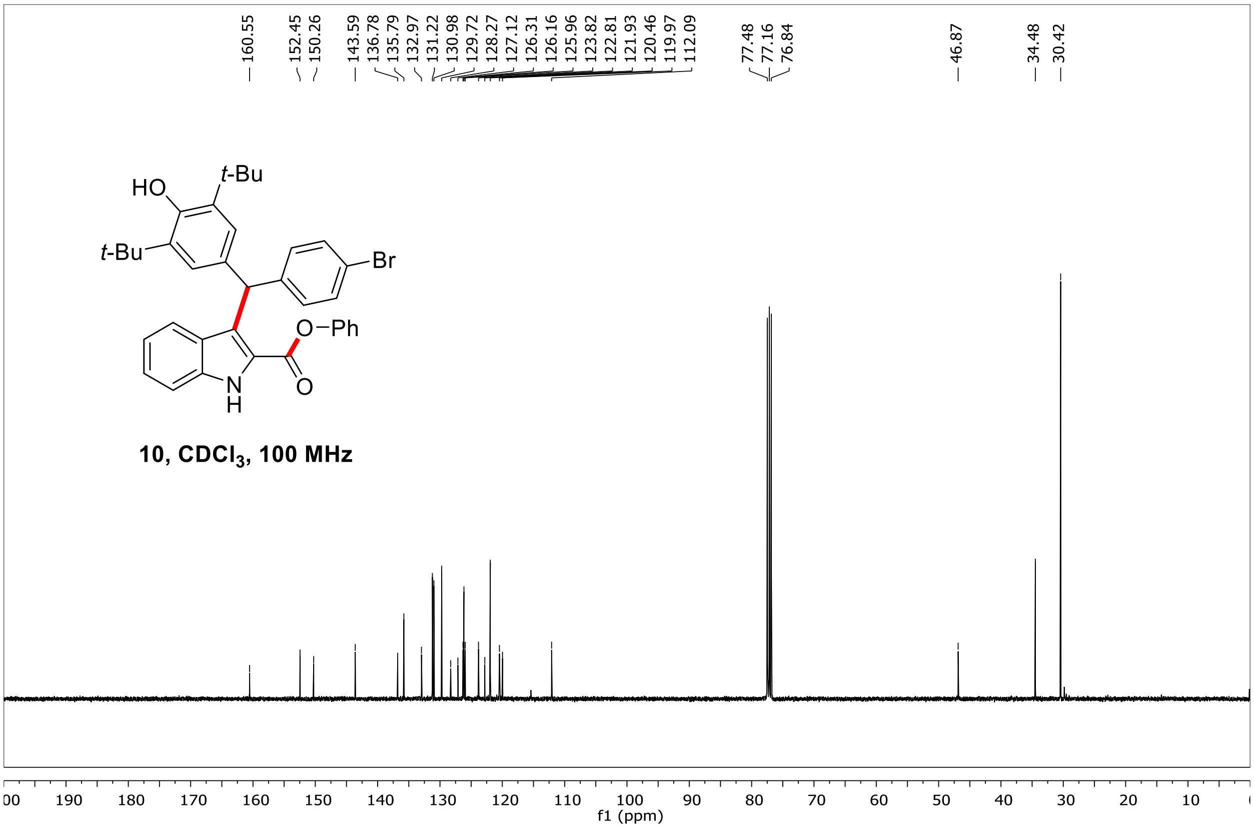
3-((3,5-Di-*tert*-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)-1*H*-indole-2-carbaldehyde (3a”)





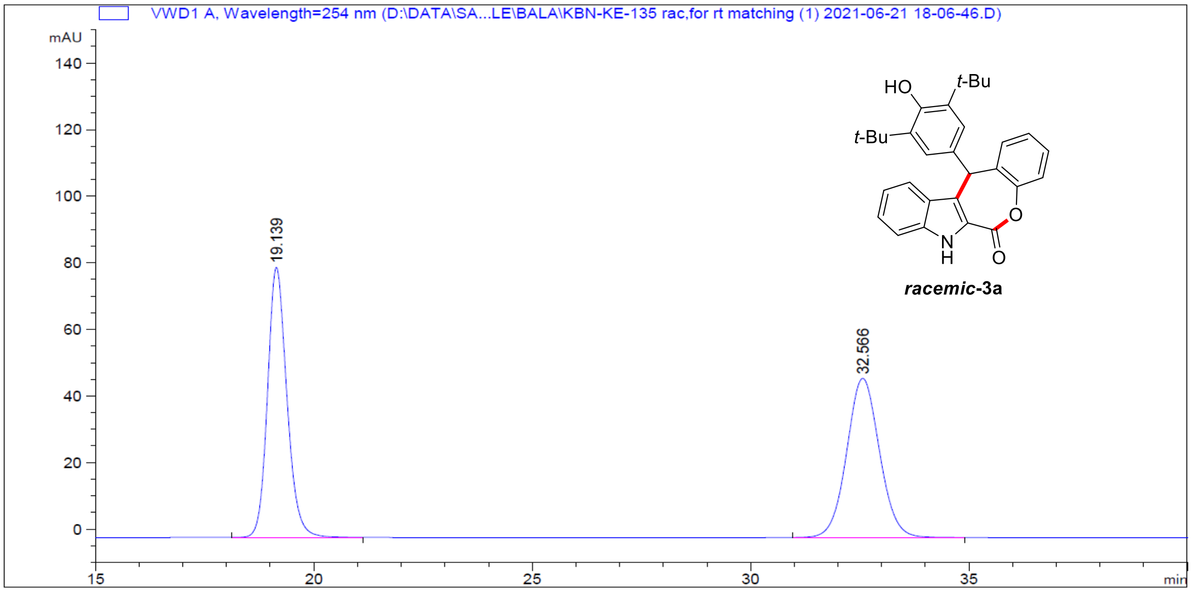
Phenyl-3-((4-bromophenyl)(3,5-di-tert-butyl-4-hydroxyphenyl)methyl)-1*H*-indole-2-carboxylate (10)



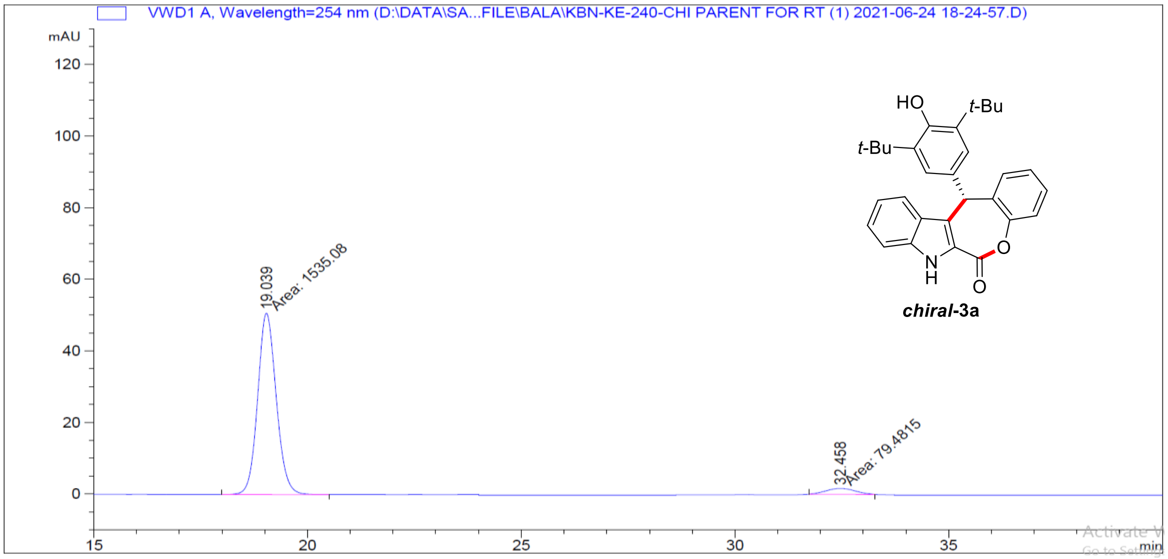


9. HPLC Data of Tetracyclic ε-Lactones

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*] indol-6-one (*chiral*-3a)



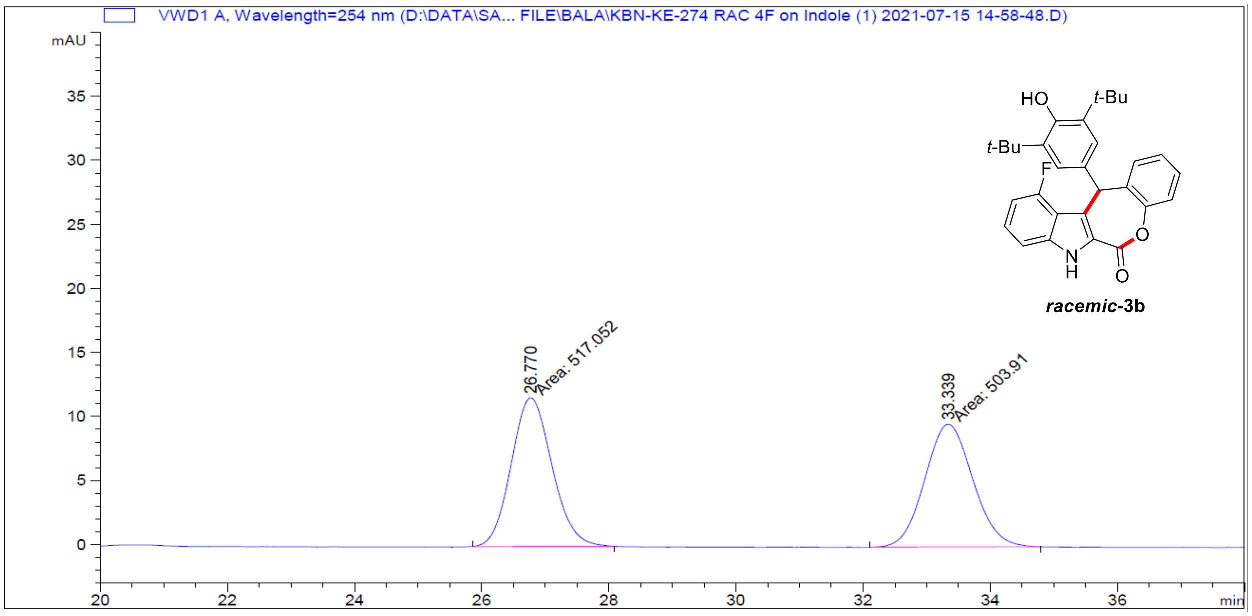
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  19.139 BB    0.4718 2500.86304   81.08739  50.0304
   2  32.566 BB    0.8066 2497.81885   47.80070  49.9696
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  19.039 MM    0.5049 1535.07922   50.66981  94.6130
   2  32.455 MM    0.8341   87.40266    1.74635   5.3870
```

```
Sample Info     : CHIRALPAK IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-11-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3b)



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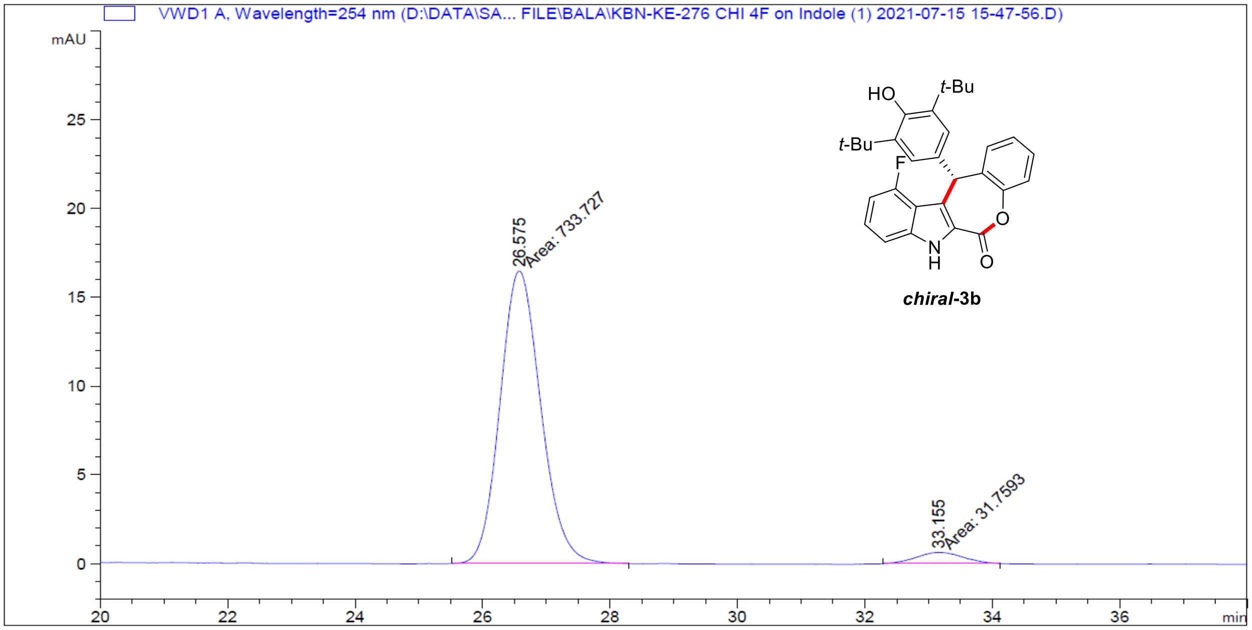
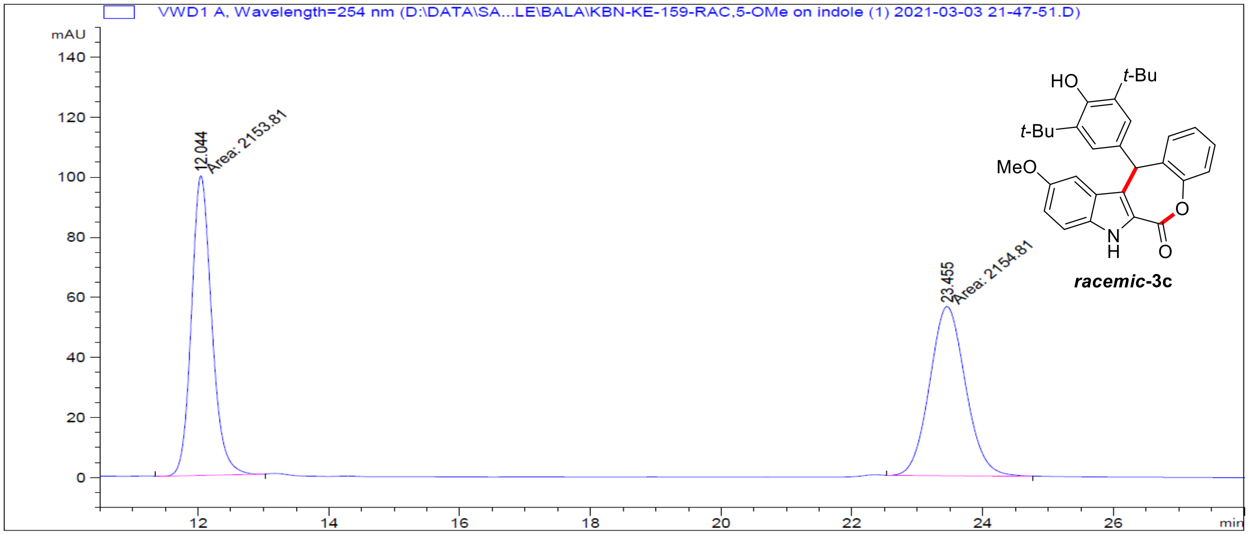
Peak  RetTime  Type   Width      Area        Height      Area
  #    [min]          [min]     [mAU*s]      [mAU]        %
----|--------|-----|--------|-----------|-----------|---------|
   1   26.770  MM     0.7427   517.05225    11.60322   50.6436
   2   33.339  MM     0.8759   503.91010     9.58895   49.3564
```



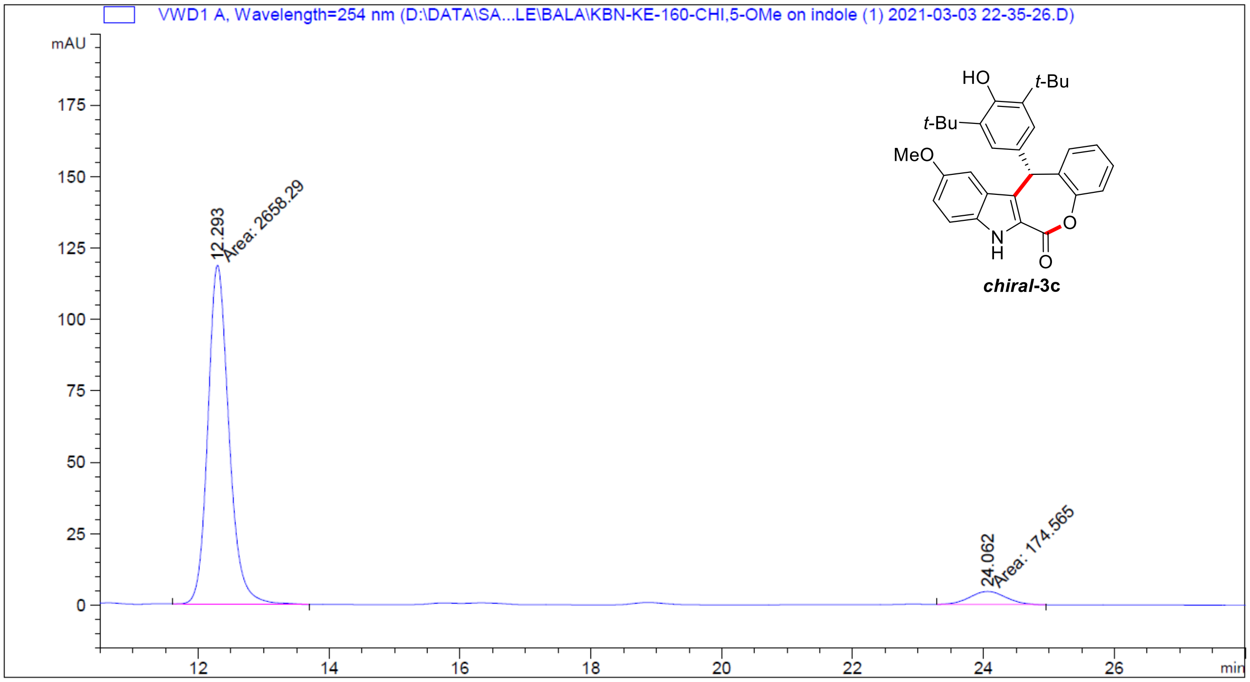
```
Peak  RetTime  Type   Width      Area        Height      Area
  #    [min]          [min]     [mAU*s]      [mAU]        %
----|--------|-----|--------|-----------|-----------|---------|
   1   26.575  MM     0.7419   733.72742    16.48237   95.8511
   2   33.155  MM     0.8507    31.75931 6.22197e-1    4.1489
```

Sample Info   : CHIRALPAK IA, 10 % IPA-HEXANE, 1.0 mL/min, 254 nM.M

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-methoxy-7,12-dihydro-6*H*-benzo[6,7] oxepino[3, 4-b]indol-6-one (3c)



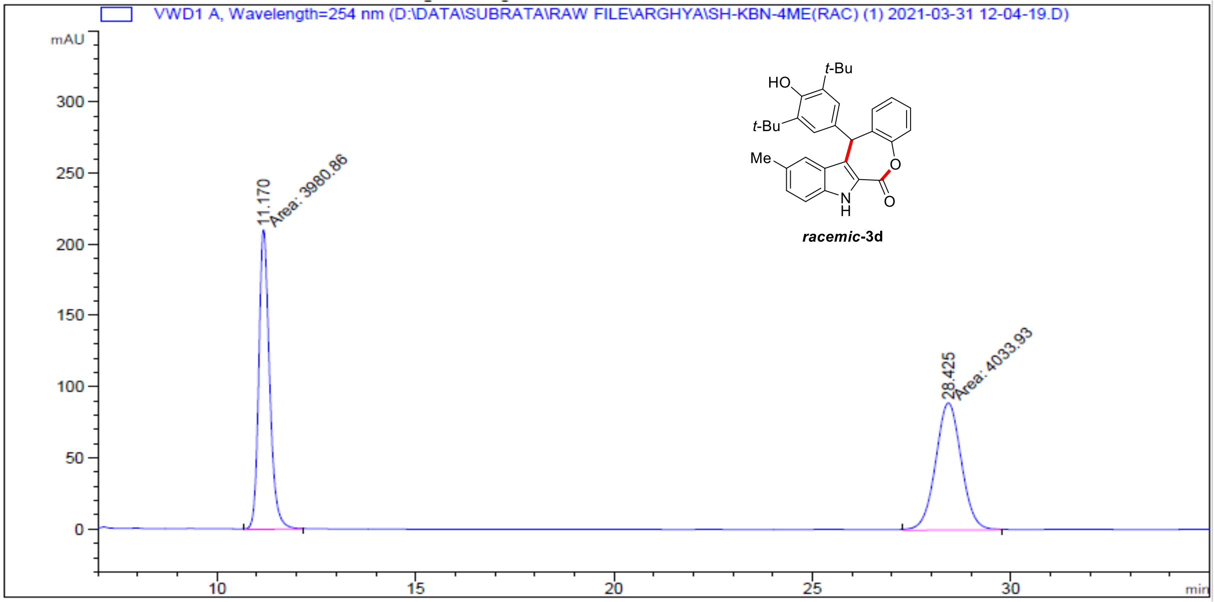
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1  12.044 MM    0.3599 2153.81470   99.75196  49.9884
  2  23.455 MM    0.6375 2154.81421   56.33720  50.0116
```



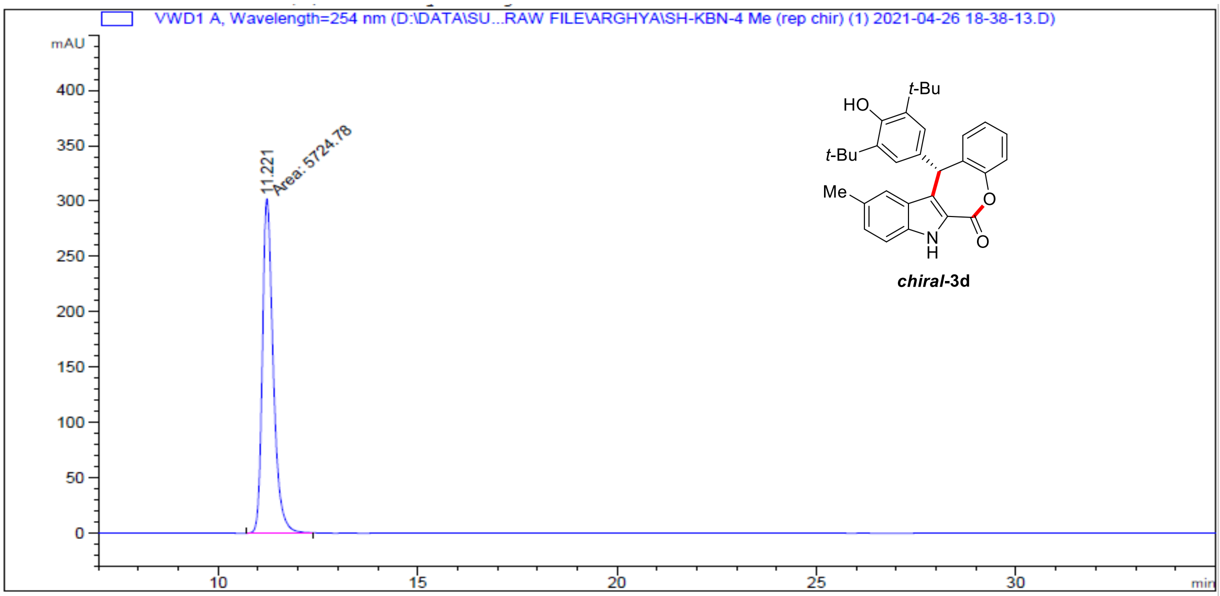
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1  12.293 MM    0.3736 2658.28613  118.58536  93.8378
  2  24.062 MM    0.6359  174.56494    4.57559   6.1622
```

```
Sample Info      : CHIRALPAK-IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-methyl-7,12-dihydro-6*H*benzo [6,7]oxepino[3,4-b]indol-6-one (3d)



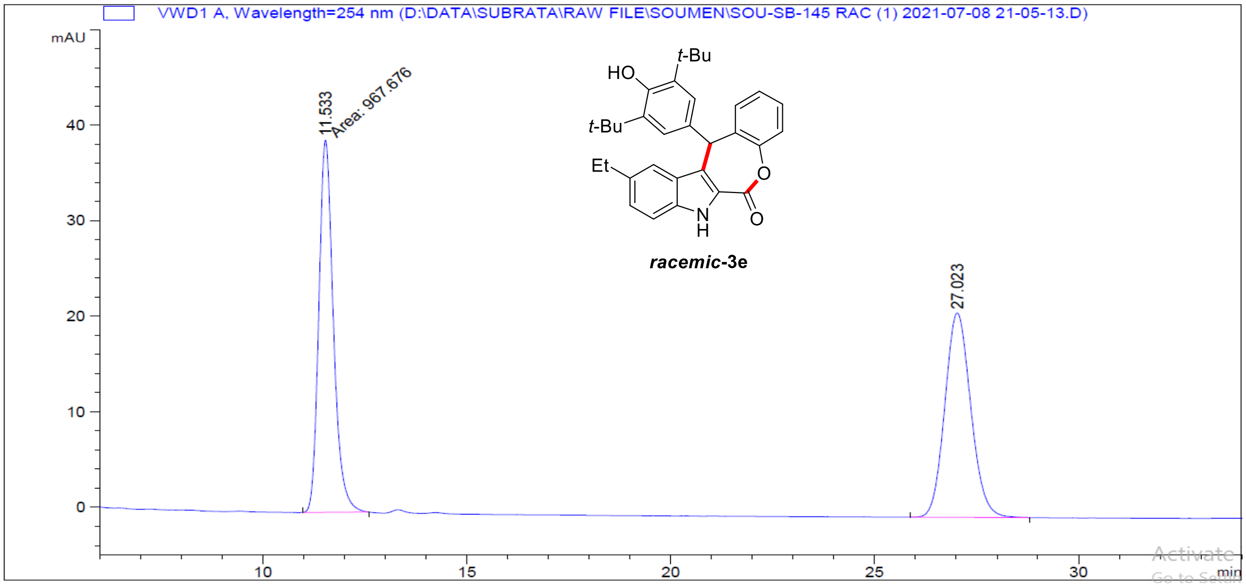
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.170 MM    0.3154 3980.85620  210.38341  49.6689
   2  28.425 MM    0.7531 4033.93091   89.27859  50.3311
```



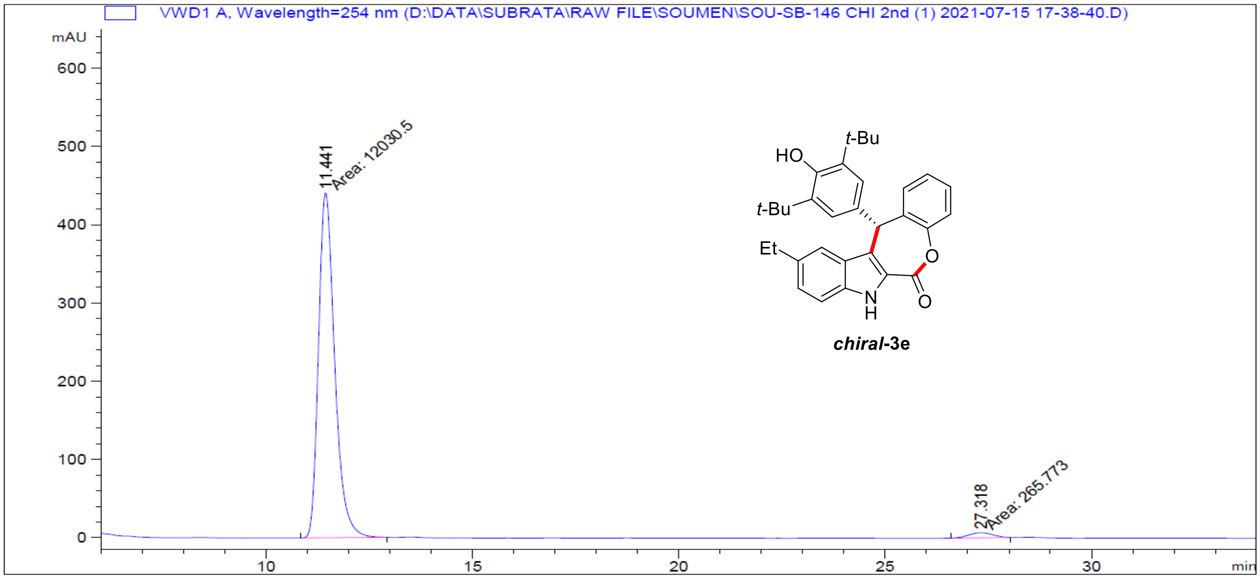
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.221 MM    0.3157 5724.78125  302.23056 100.0000
```

```
Sample Info     : CHIRALPAK IA, 10% IPA-HEXANE,1.0 mL/min, 254 nm
```

S)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-10-ethyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3e)



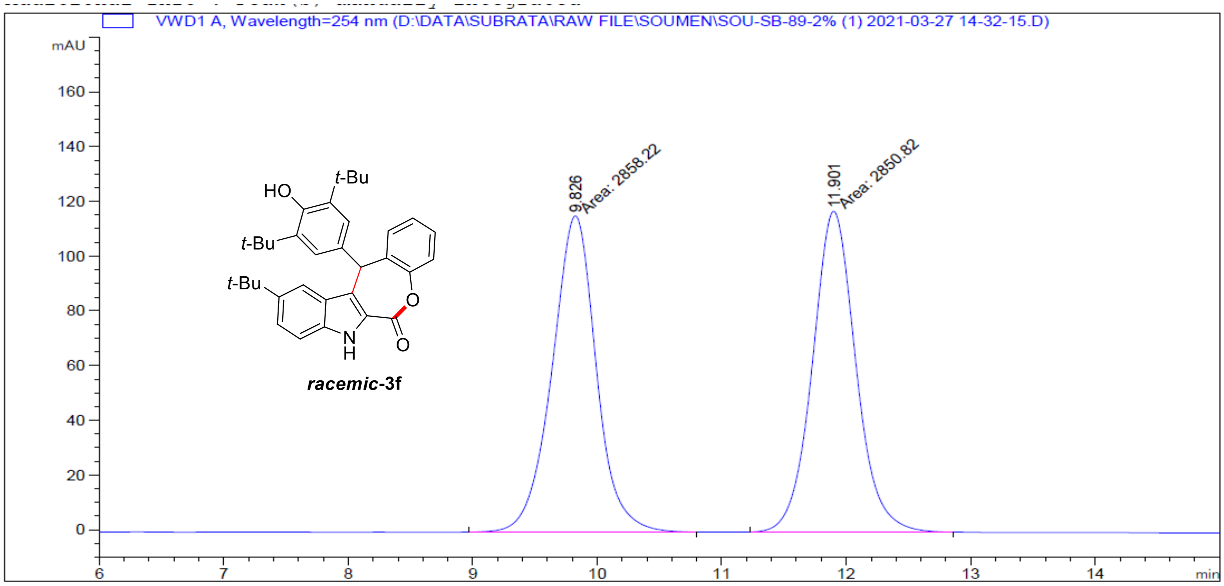
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.533 MM    0.4143  967.67603   38.92627  50.5375
   2  27.023 BB    0.6858  947.09058   21.38240  49.4625
```



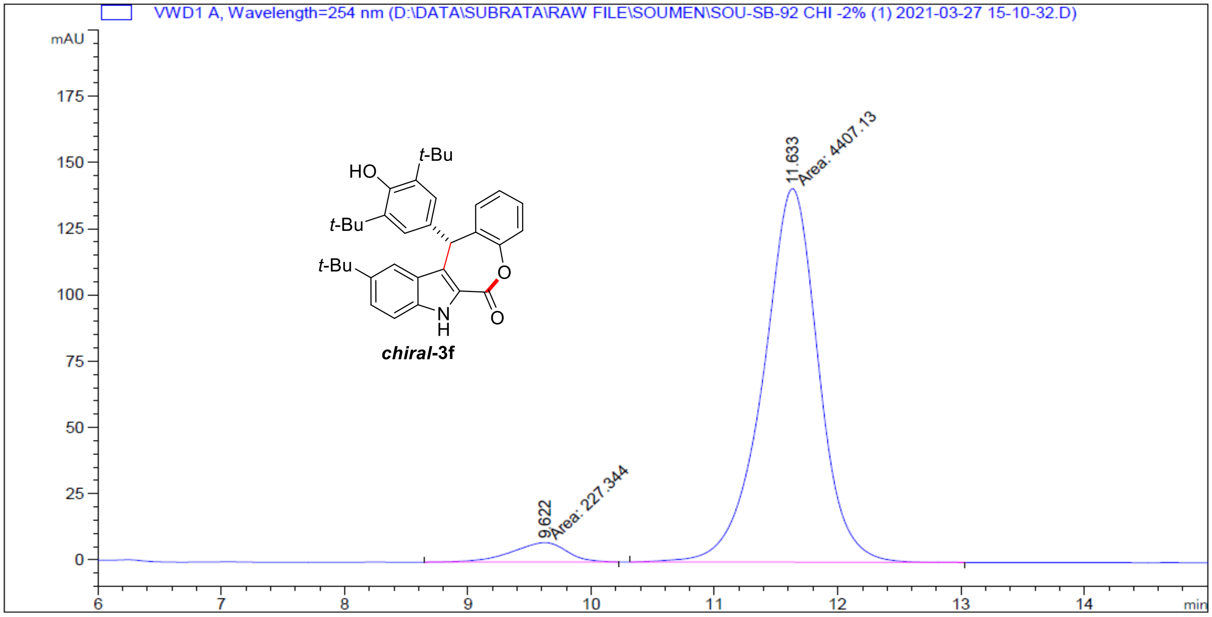
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.441 MM    0.4551 1.20305e4  440.59888  97.8386
   2  27.318 MM    0.6743  265.77267    6.56903   2.1614
```

```
Sample Info     : CHIRALPAK IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-10-(*Tert*-butyl)-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H* benzo[6,7]oxepino[3,4-b]indol-6-one (3f)



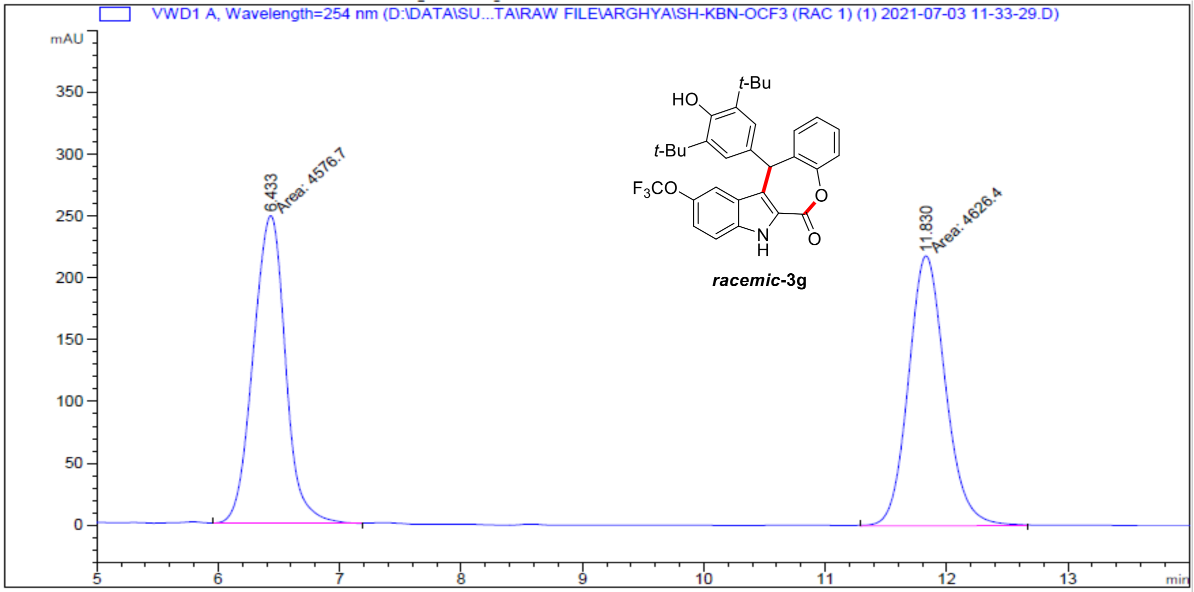
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1    9.622 MM    0.5192  227.34413    7.29850   4.9055
  2   11.633 MM    0.5209 4407.13135  141.01996  95.0945
```



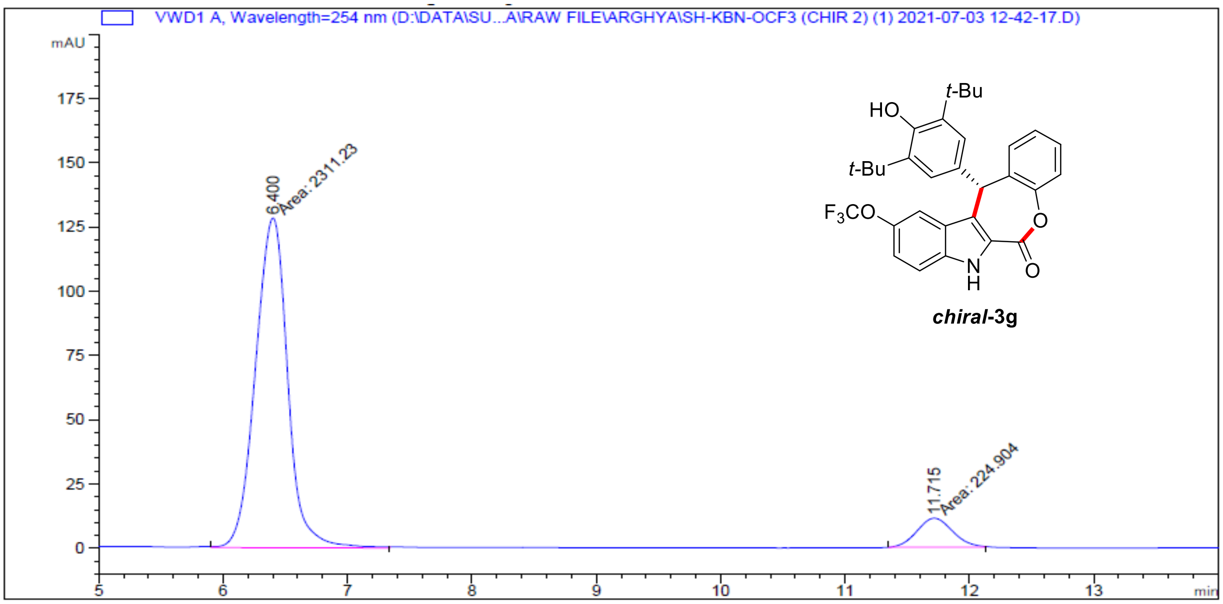
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1    9.622 MM    0.5192  227.34413    7.29850   4.9055
  2   11.633 MM    0.5209 4407.13135  141.01996  95.0945
```

```
Sample Info      : CHIRALPAK-IA, 2 % IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-(trifluoromethoxy)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3g)



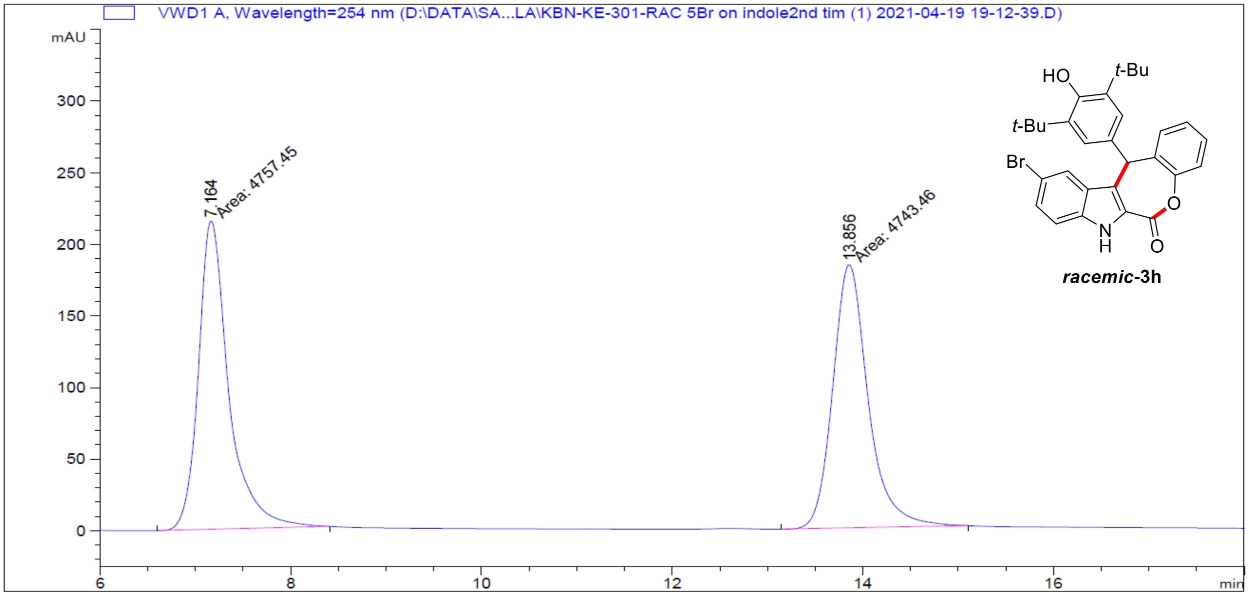
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.433 MM    0.3069 4576.70166  248.50728  49.7300
   2  11.830 MM    0.3534 4626.39746  218.18427  50.2700
```



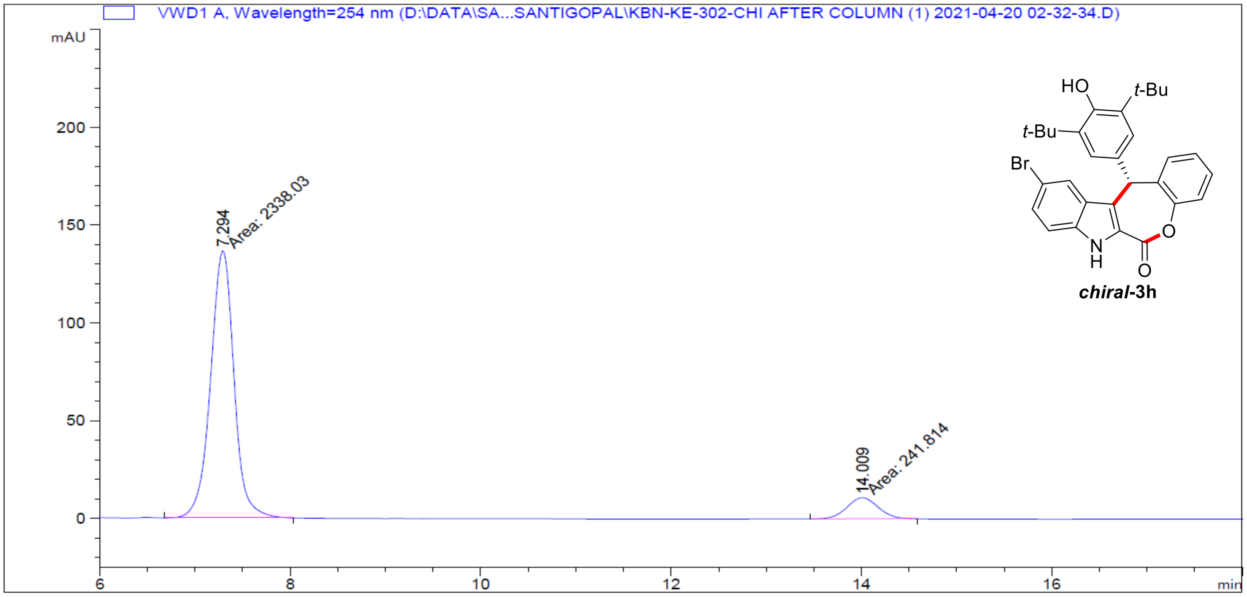
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.400 MM    0.3002 2311.22803  128.31041  91.1320
   2  11.715 MM    0.3318  224.90450   11.29724   8.8680
```

```
Sample Info     : CHIRALPAK IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-10-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3h)



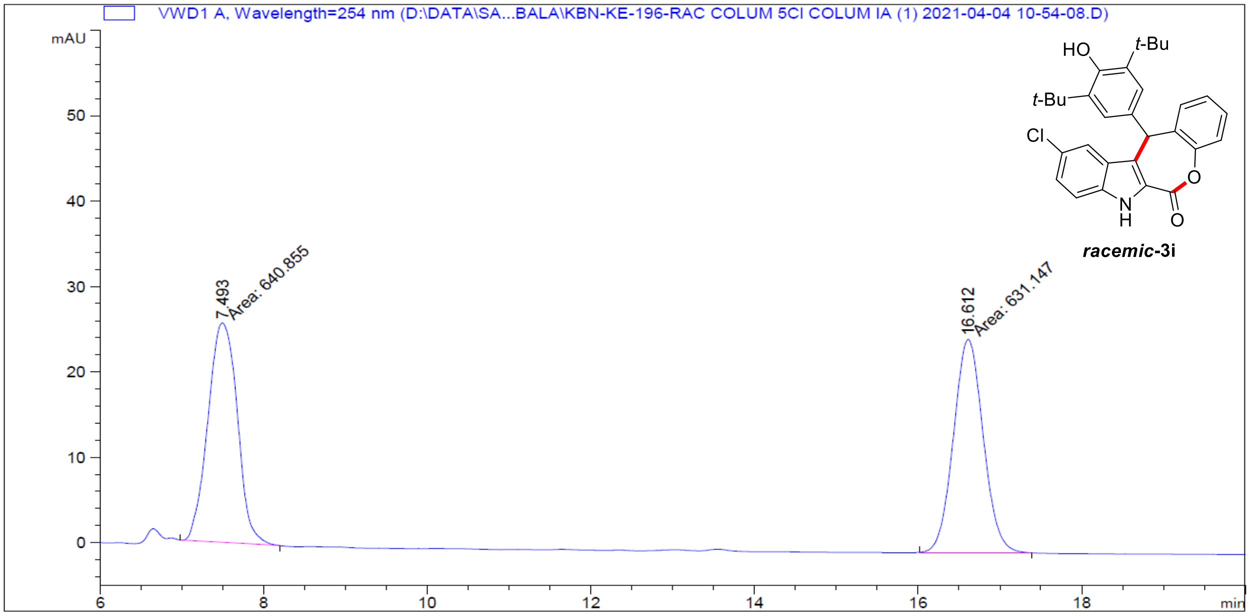
```
Peak RetTime Type  Width     Area      Height      Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    7.164 MM    0.3685 4757.44629  215.16971  50.0736
  2   13.856 MM    0.4304 4743.46094  183.66583  49.9264
```



```
Peak RetTime Type  Width     Area      Height      Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    7.294 MM    0.2855 2338.03467  136.48889  90.6268
  2   14.009 MM    0.3761  241.81406   10.71552   9.3732
```

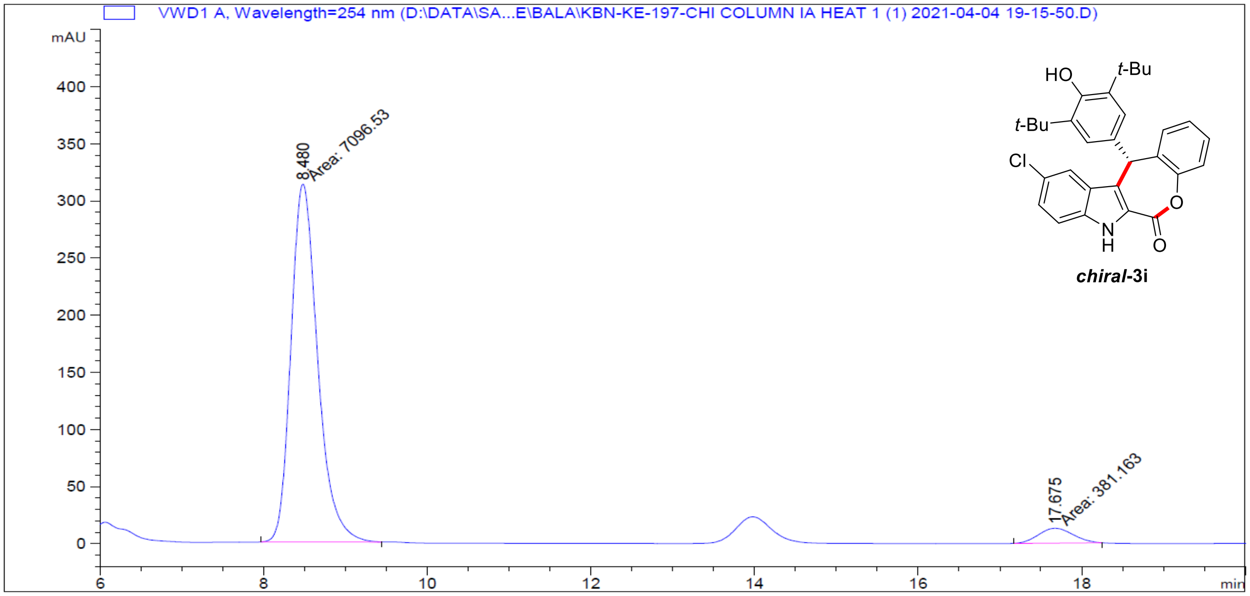
```
Sample Info      : CHIRALPAK-IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-10-Chloro-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3i)



***racemic*-3i**

```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]         %
----|-------|----|-------|----------|----------|--------|
  1    7.493 MM    0.4157  640.85535   25.69365   50.3816
  2   16.612 MM    0.4212  631.14740   24.97251   49.6184
```

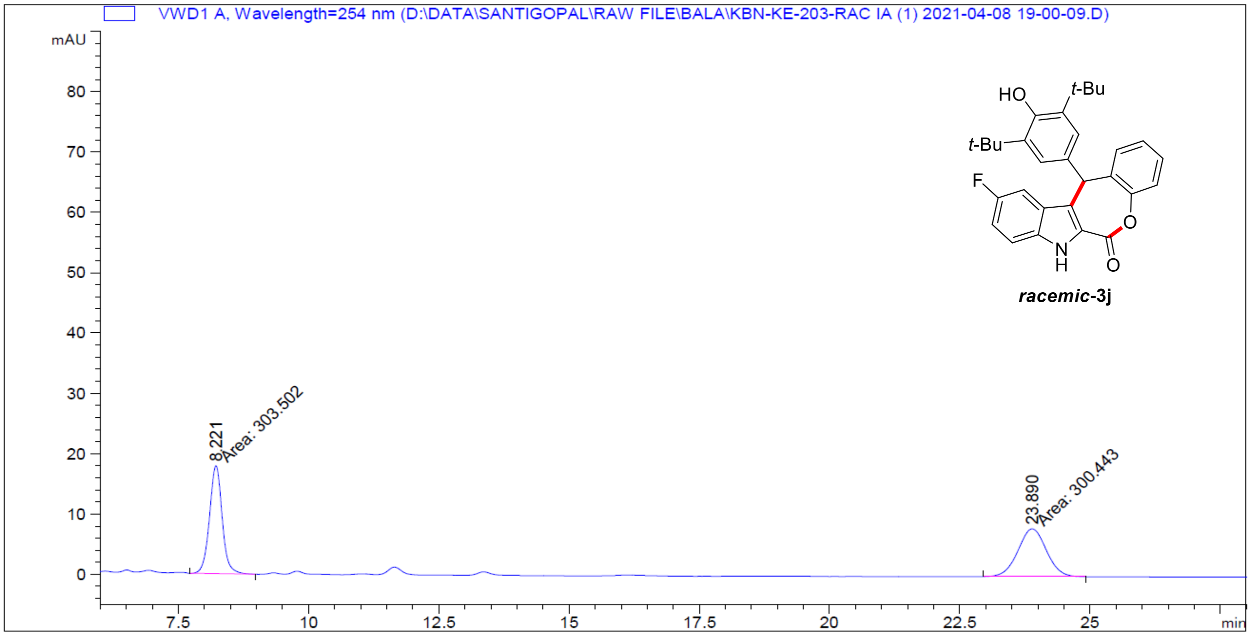


***chiral*-3i**

```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]         %
----|-------|----|-------|----------|----------|--------|
  1    8.480 MM    0.3779 7096.53027  312.97079   94.9027
  2   17.675 MM    0.4874  381.16318   13.03368    5.0973
```

Sample Info   : CHIRALPAK-IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-10-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3j)

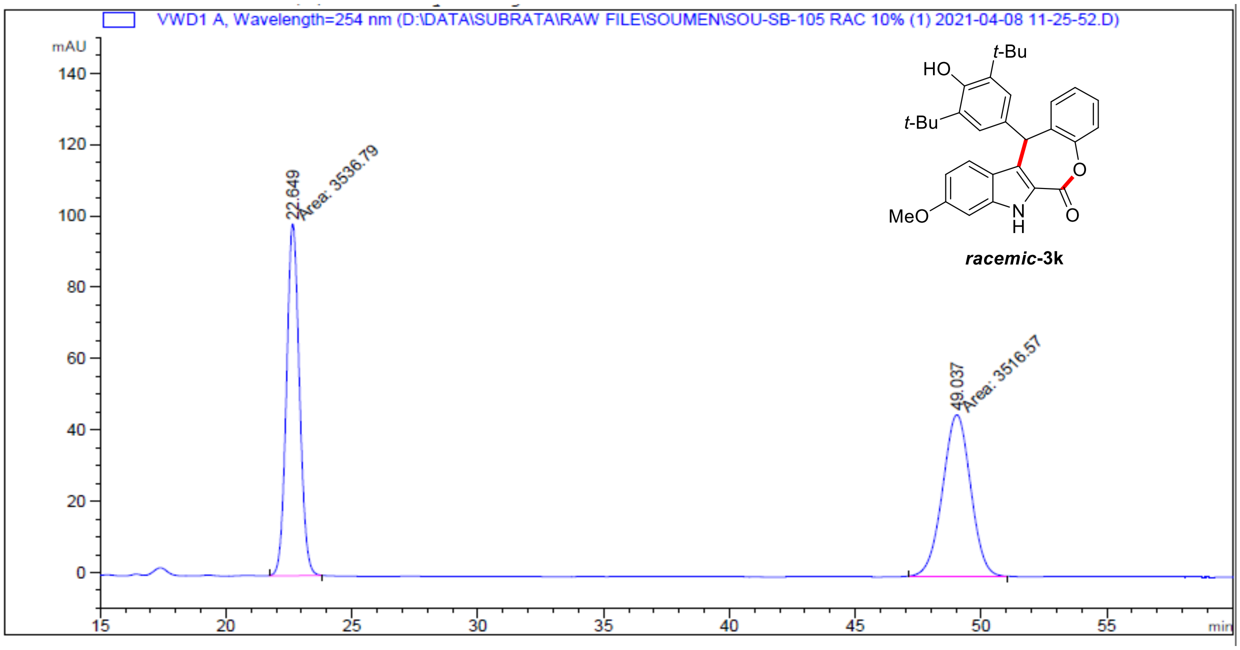


```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]         [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   8.221 MM    0.2826  303.50235   17.89635  50.2533
   2  23.890 MM    0.6332  300.44290    7.90804  49.7467
```

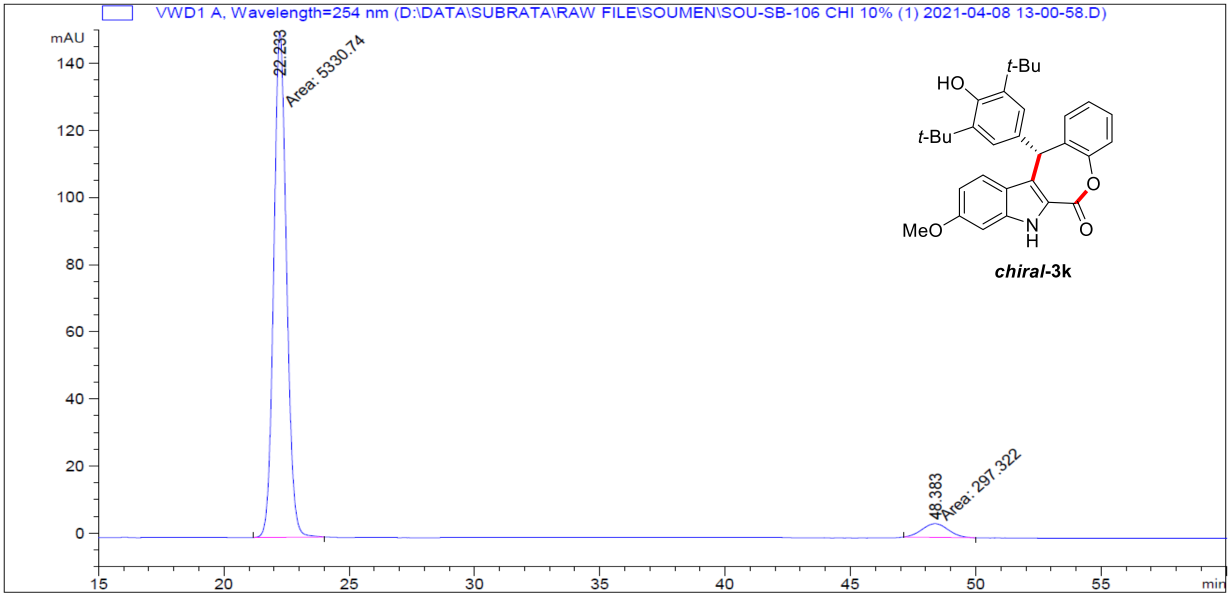
```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]         [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   8.254 MM    0.2876 3104.07861  179.85658  98.7705
   2  24.147 MM    0.5979   38.64014    1.07716   1.2295
```

Sample Info   : CHIRALPAK- IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm

(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-9-methoxy-7,12-dihydro-6*H* benzo[6,7]oxepino[3,4-b]indol-6-one(3k)



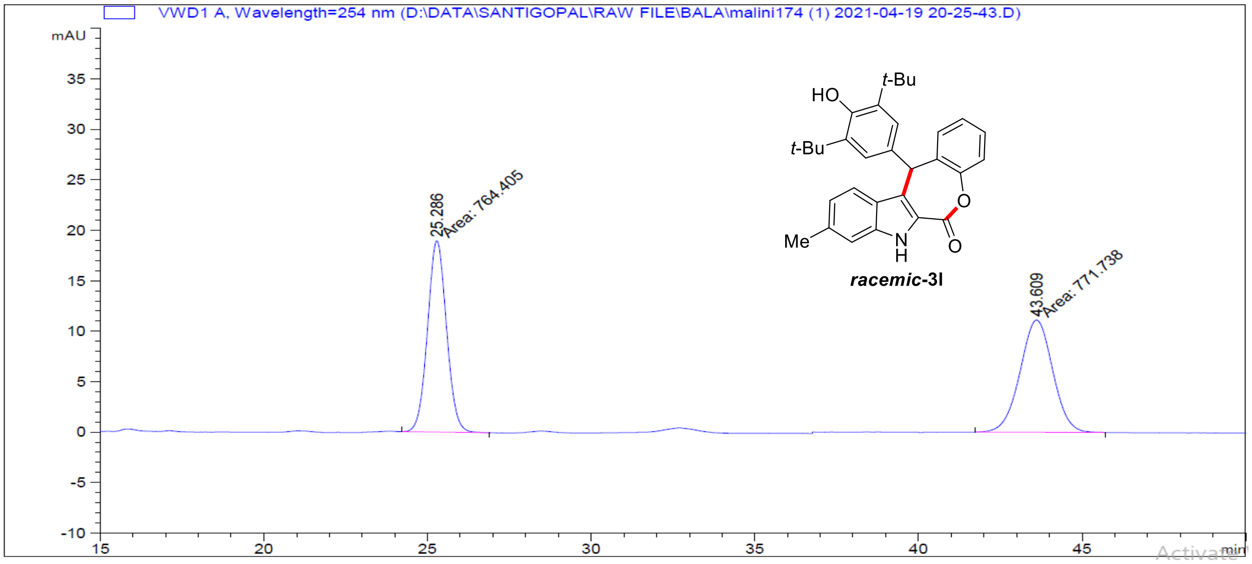
```
Peak RetTime Type  Width     Area       Height     Area
 #    [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1  22.649 MM    0.5979 3536.78931   98.59322  50.1433
  2  49.037 MM    1.2941 3516.57104   45.28960  49.8567
```



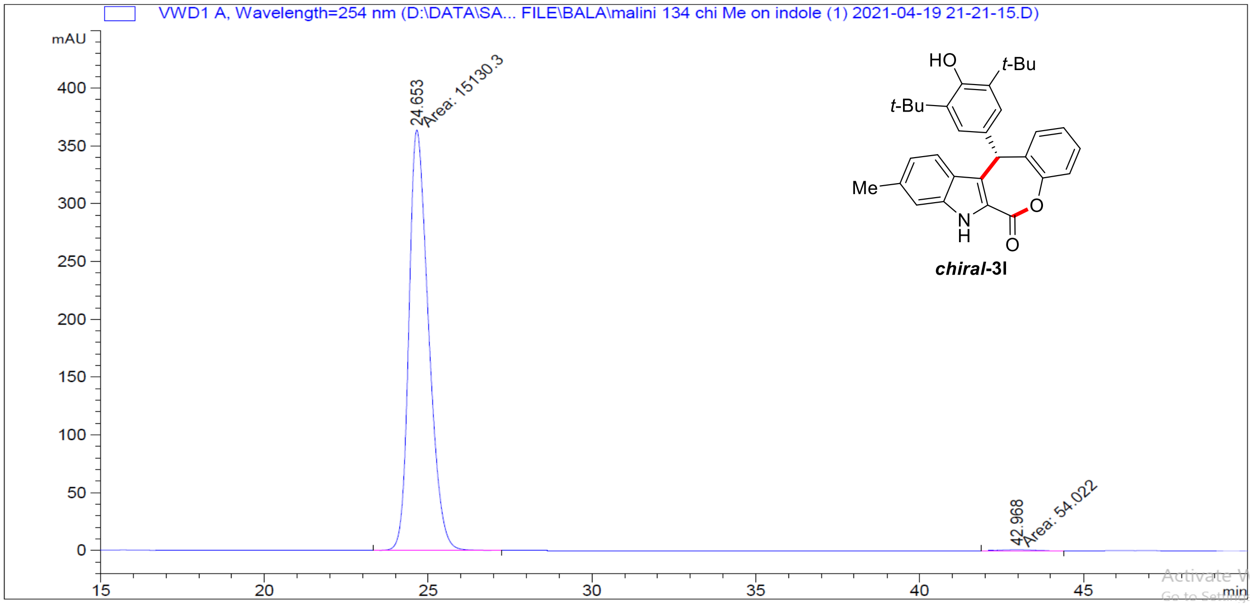
```
Peak RetTime Type  Width     Area       Height     Area
 #    [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1  22.233 MM    0.5918 5330.74023  150.12422  94.7171
  2  48.383 MM    1.2107  297.32248    4.09314   5.2829
```

```
Sample Info     : CHIRALPAK IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3l)



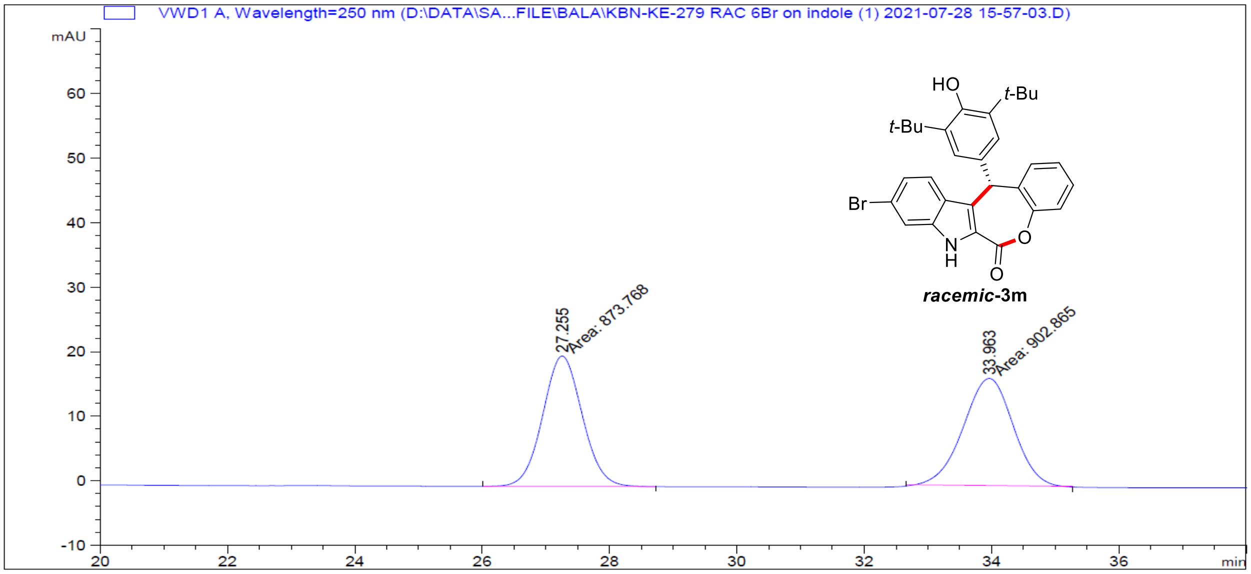
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  25.286 MM    0.6721  764.40466  18.95465  49.7613
  2  43.609 MM    1.1570  771.73798  11.11731  50.2387
```



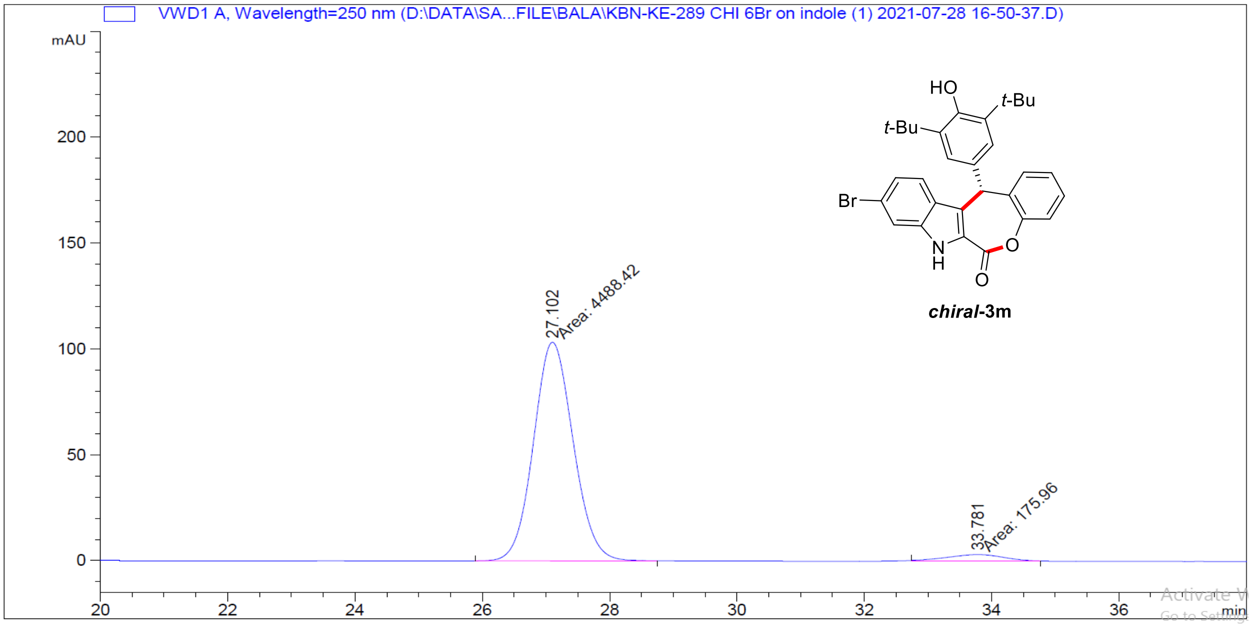
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  24.653 MM    0.6935 1.51303e4  363.61896  99.6442
  2  42.968 MM    1.0951  54.02200 8.22173e-1  0.3558
```

```
Sample Info     : CHIRALPAK-IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-9-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3m)



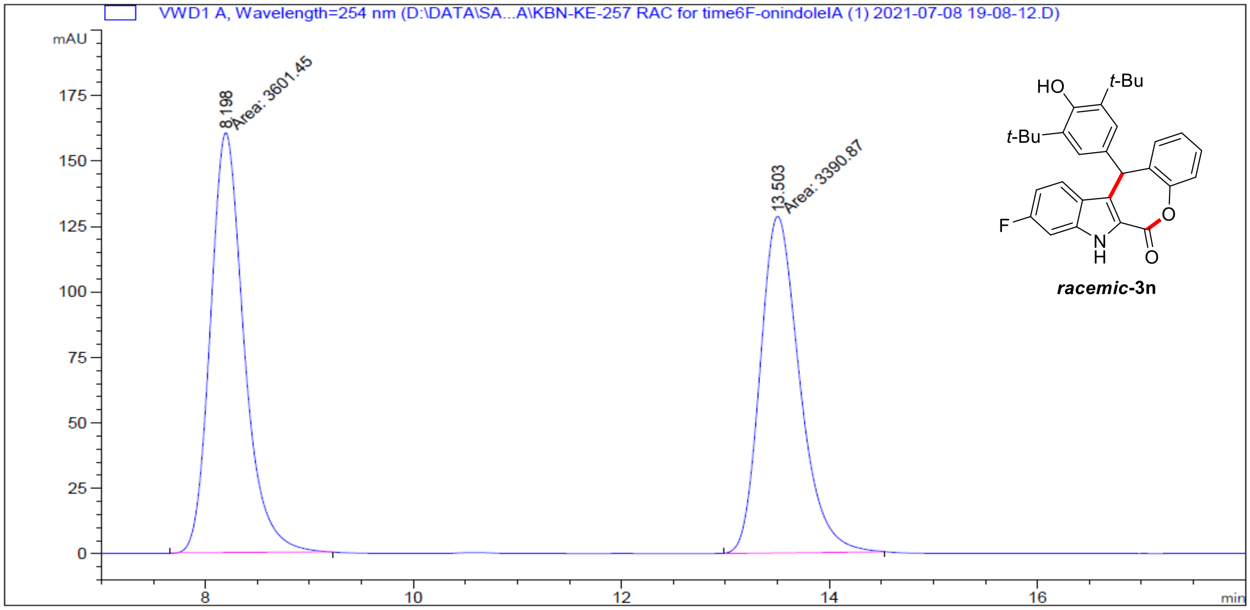
```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]         [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  27.255 MM    0.7209  873.76837   20.20135  49.1811
  2  33.963 MM    0.9076  902.86536   16.57979  50.8189
```



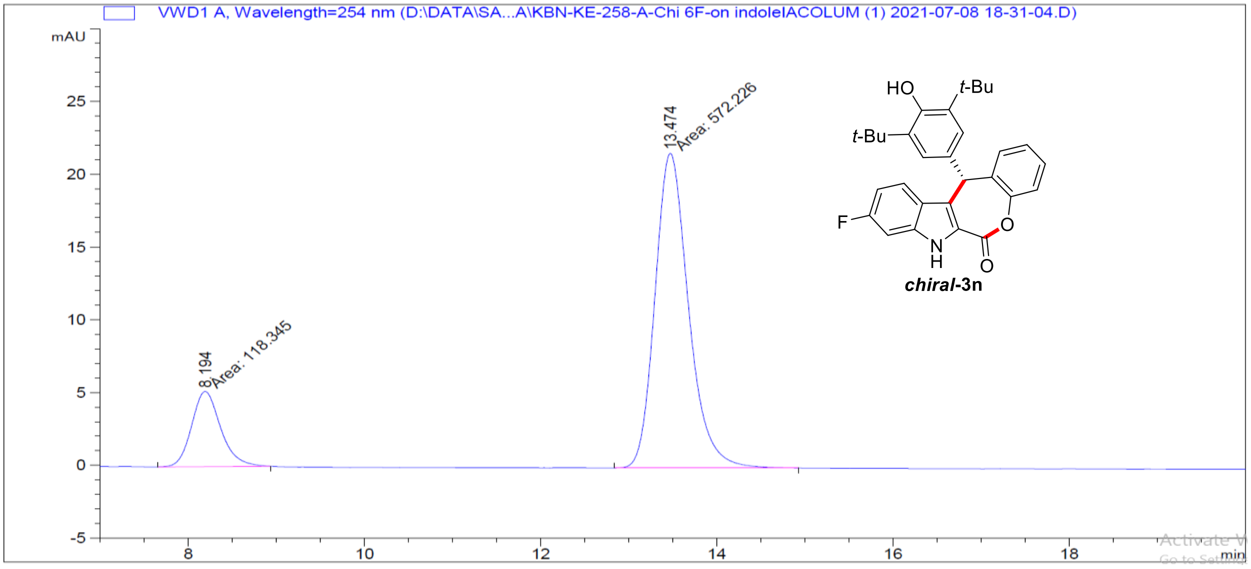
```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]         [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  27.102 MM    0.7243 4488.42285  103.28620  96.2276
  2  33.781 MM    0.9994  175.95998    2.93451   3.7724
```

```
Sample Info     : CHIRALPAK IA, 10 % IPA-HEXANE, 1.0 mL/min, 254 nM.M
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-fluoro-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3n)



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1   8.198 MM    0.3744 3601.45190  160.31020  51.5058
  2  13.503 MM    0.4395 3390.87061  128.58704  48.4942
```

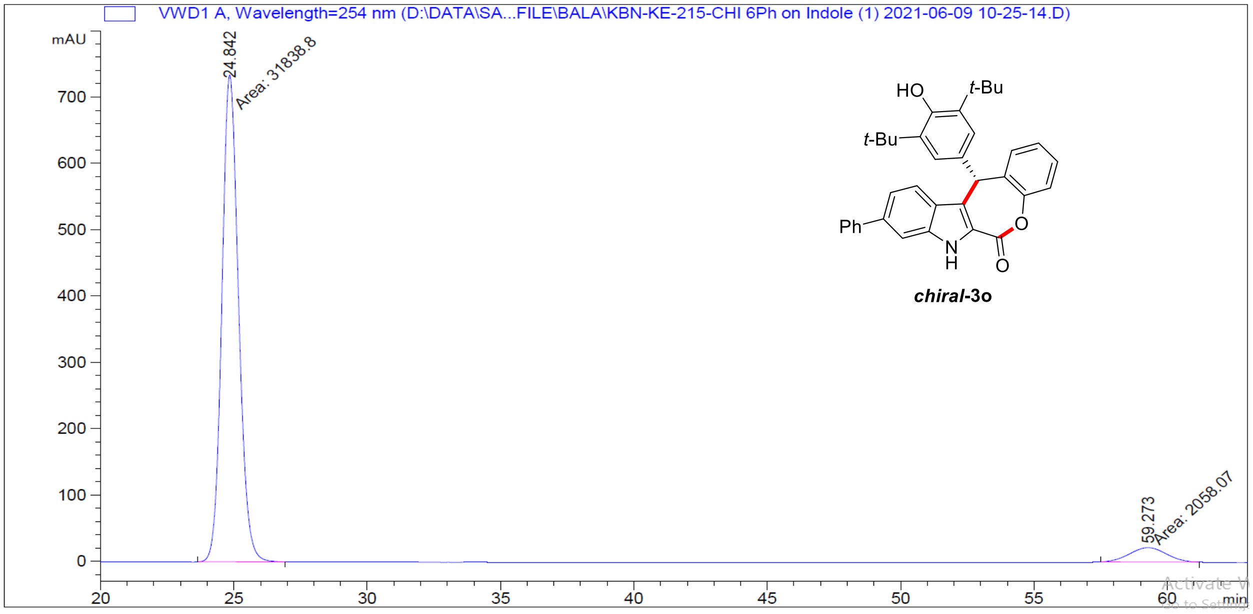


```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1   8.194 MM    0.3819  118.34513    5.16443  17.1373
  2  13.474 MM    0.4413  572.22565   21.61150  82.8627
```

```
Sample Info     : CHIRALPAK IA, 10 % IPA-HEXANE, 1.0 mL/min, 254 nM.M
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-phenyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3o)

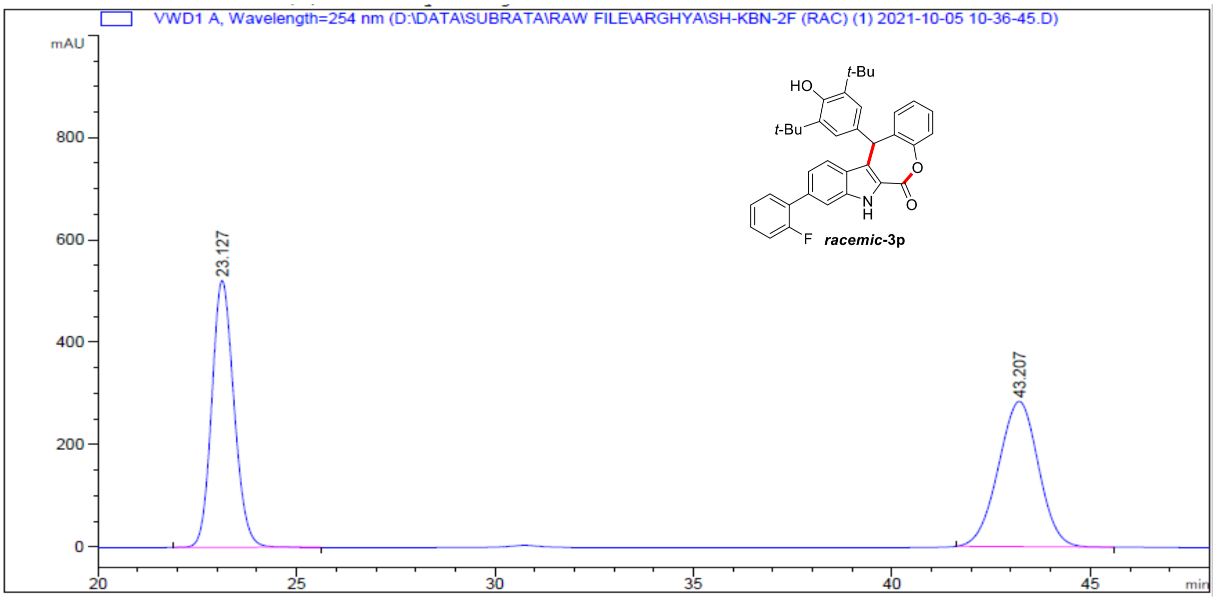
```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  24.528 MM    0.7014 9177.21191  218.07961  50.1196
   2  58.394 MM    1.6354 9133.39941   93.07738  49.8804
```



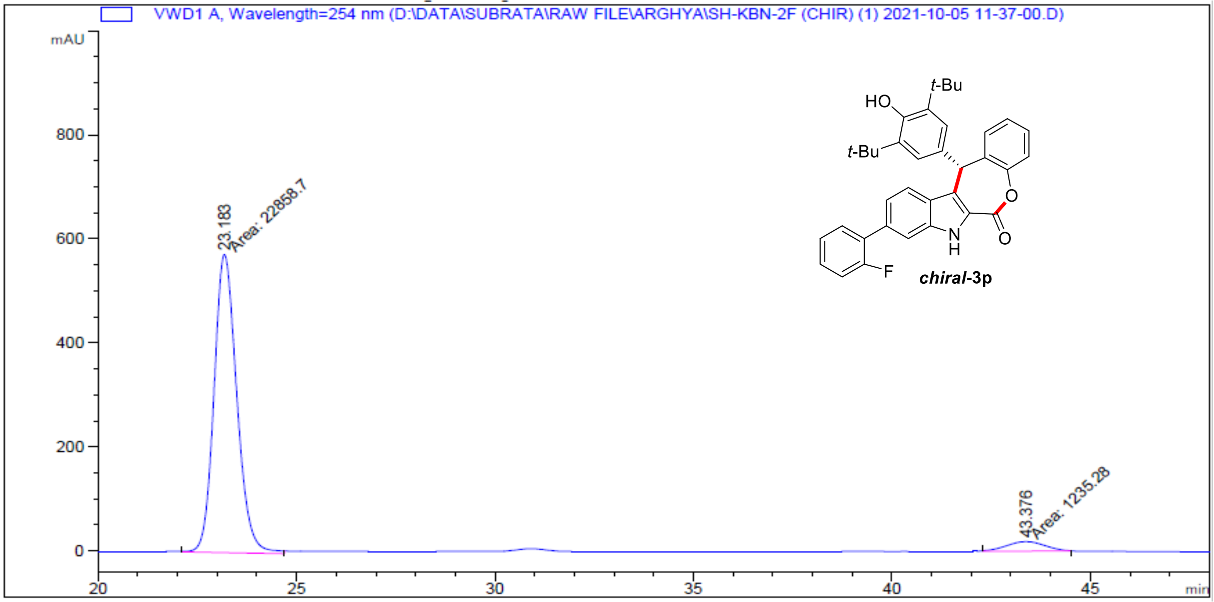
```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  24.842 MM    0.7232 3.18388e4  733.76428  93.9284
   2  59.273 MM    1.5853 2058.07251  21.63685   6.0716

Sample Info     : CHIRALPAK IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-(2-fluorophenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino[3,4-*b*] indol-6-one (3p)



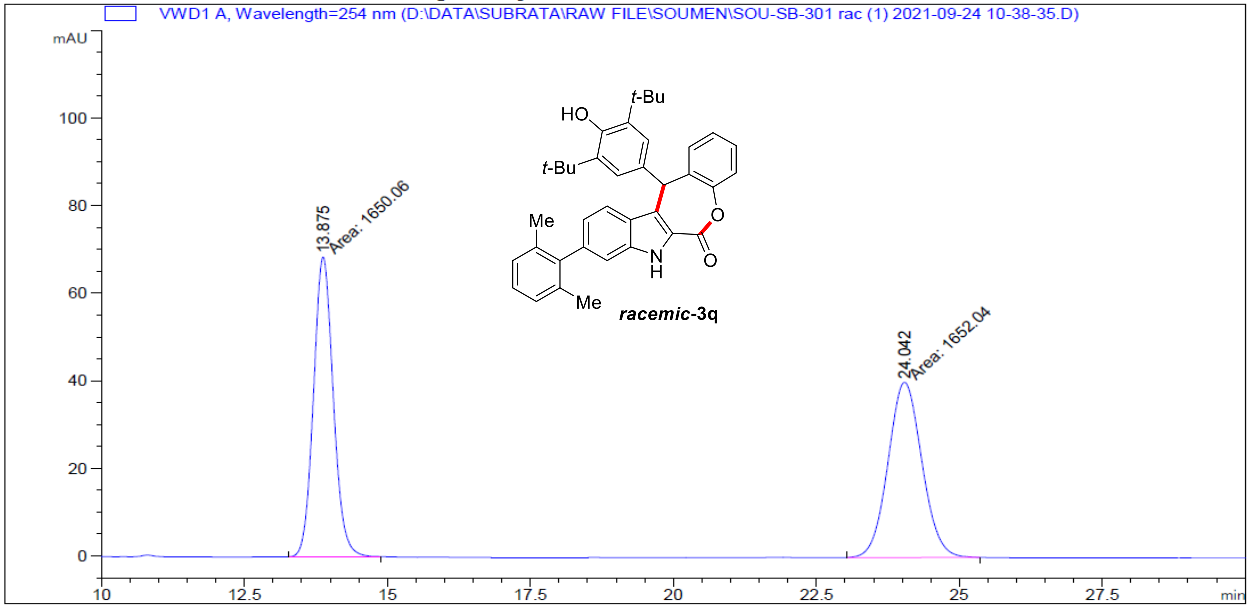
```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  23.127 MM    0.6492 2.03000e4  521.15692  49.7931
   2  43.207 MM    1.1927 2.04686e4  286.02219  50.2069
```



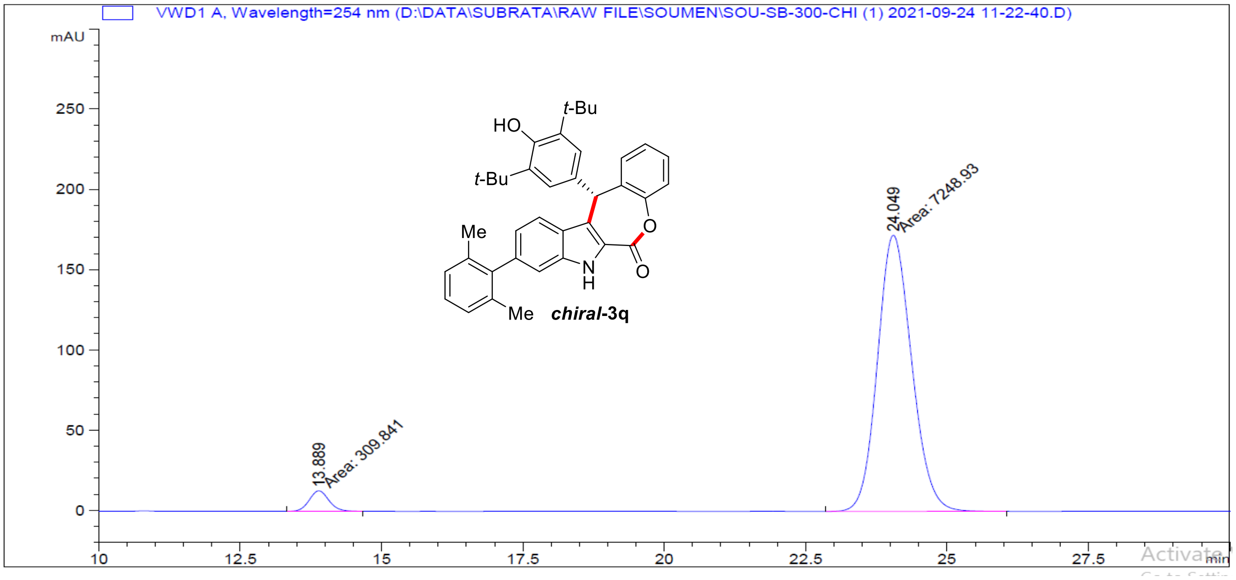
```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  23.183 MM    0.6647 2.28587e4  573.17816  94.8731
   2  43.376 MM    1.1191 1235.28381  18.39662   5.1269
```

```
Sample Info      : CHIRALPAK IA, 10% IPA-HEXANE,1.0 mL/min, 254 nm
```

(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-9-(2,6-dimethylphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3q)



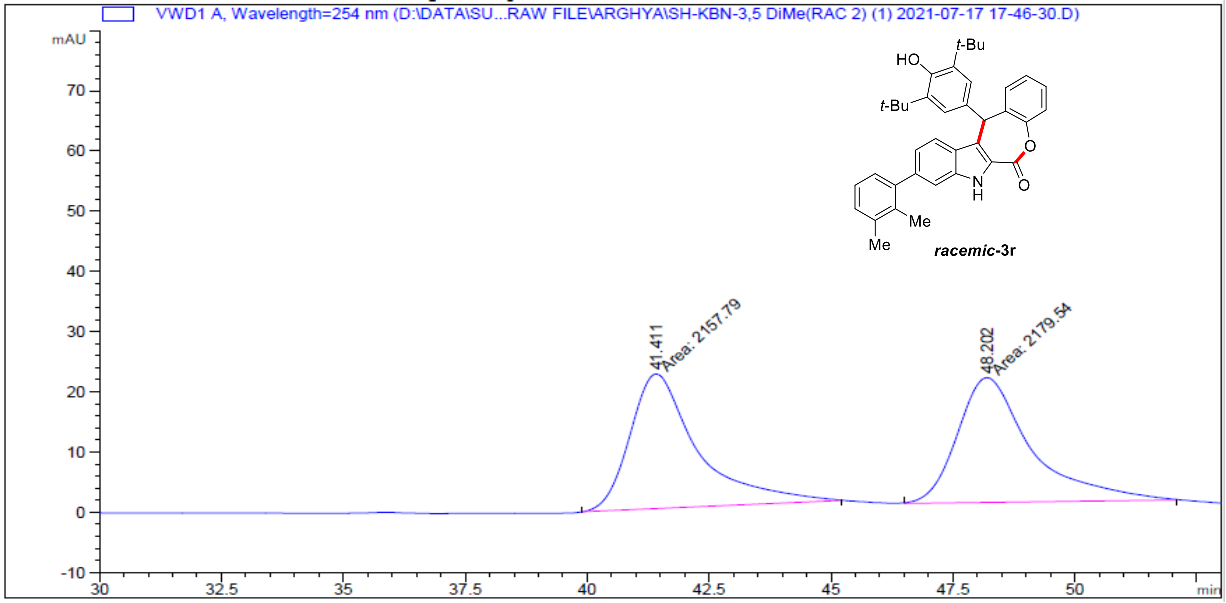
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]   [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1  13.875 MM    0.4017 1650.05579   68.45570  49.9699
   2  24.042 MM    0.6879 1652.04370   40.02373  50.0301
```



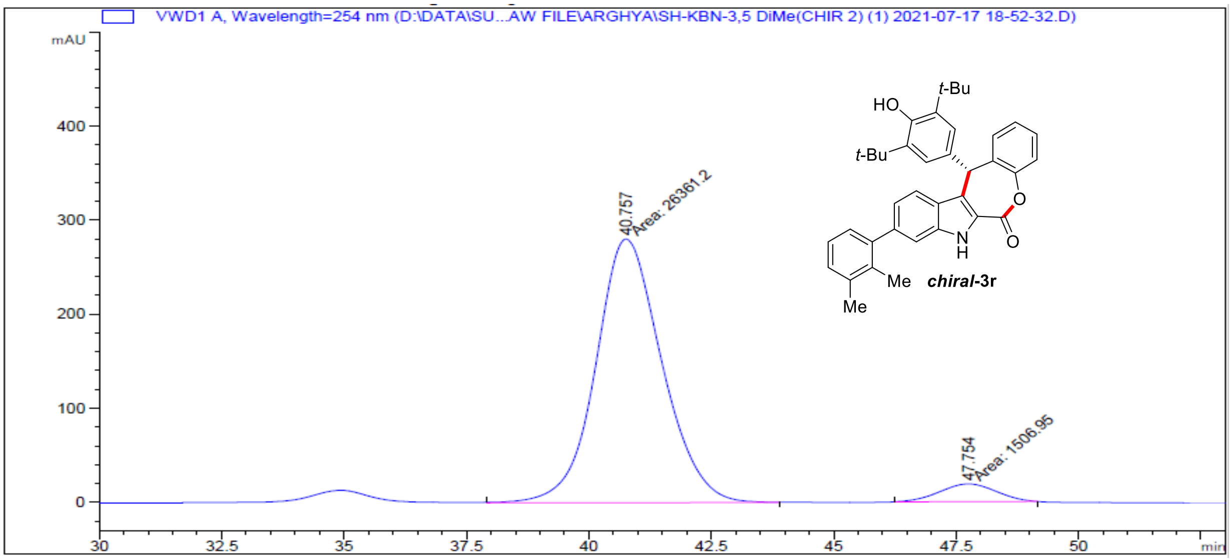
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]   [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1  13.889 MM    0.4039  309.84128   12.78569   4.0991
   2  24.049 MM    0.7022 7248.92920  172.06261  95.9009
```

```
Sample Info     : CHIRALPAK IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-9-(2,3-dimethylphenyl)-7,12-dihydro-6*H*-benzo [6,7] oxepino[3,4-*b*] indol-6-one (3r)



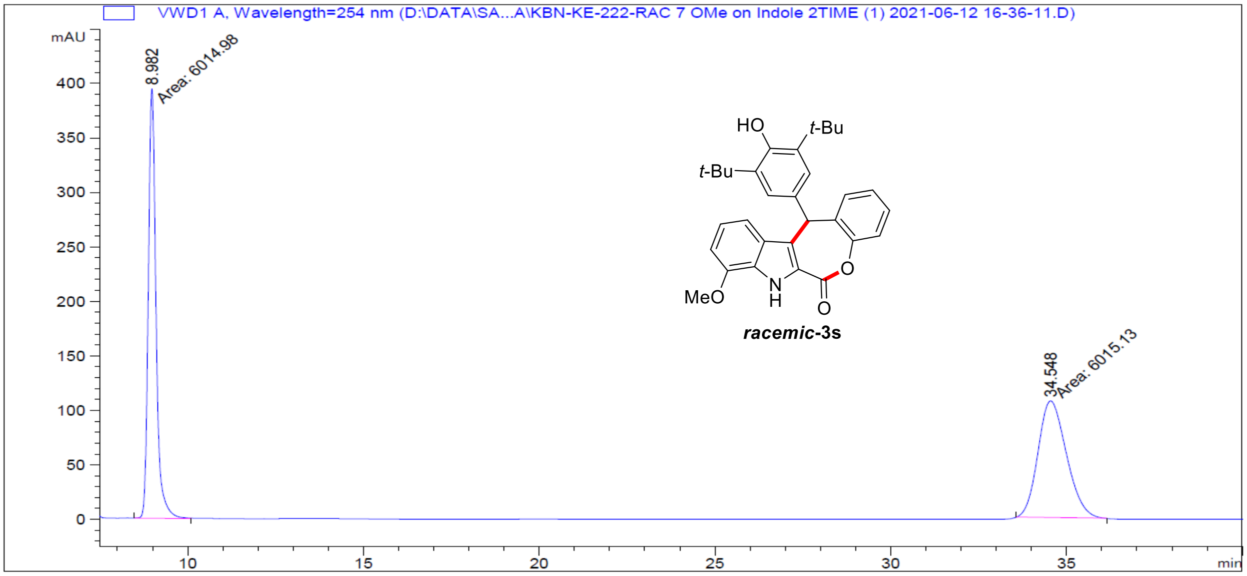
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  41.411 MM    1.6103 2157.79395   22.33299  49.7493
  2  48.202 MM    1.7548 2179.54419   20.70073  50.2507
```



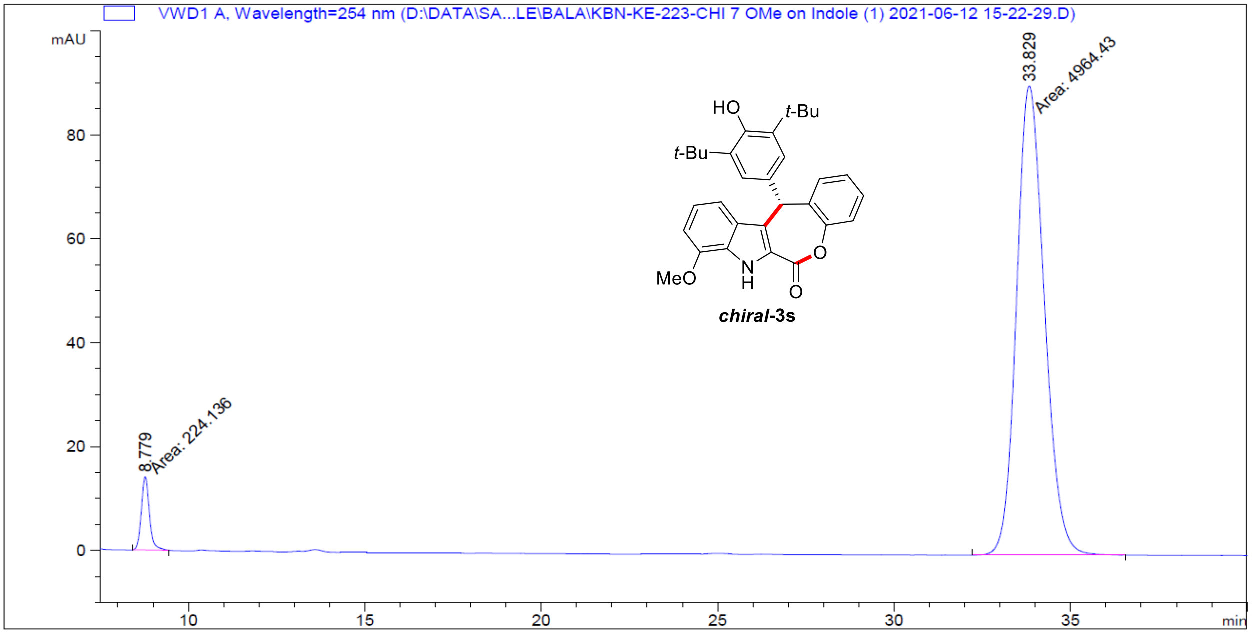
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  40.757 MM    1.5673 2.63612e4  280.31915  94.5926
  2  47.754 MM    1.3370 1506.94922  18.78528   5.4074
```

```
Sample Info      : CHIRALPAK IA, 5 % IPA-HEXANE, 1.0 mL/min, 254 nM.M
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-8-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-*b*]indol-6-one (3s)



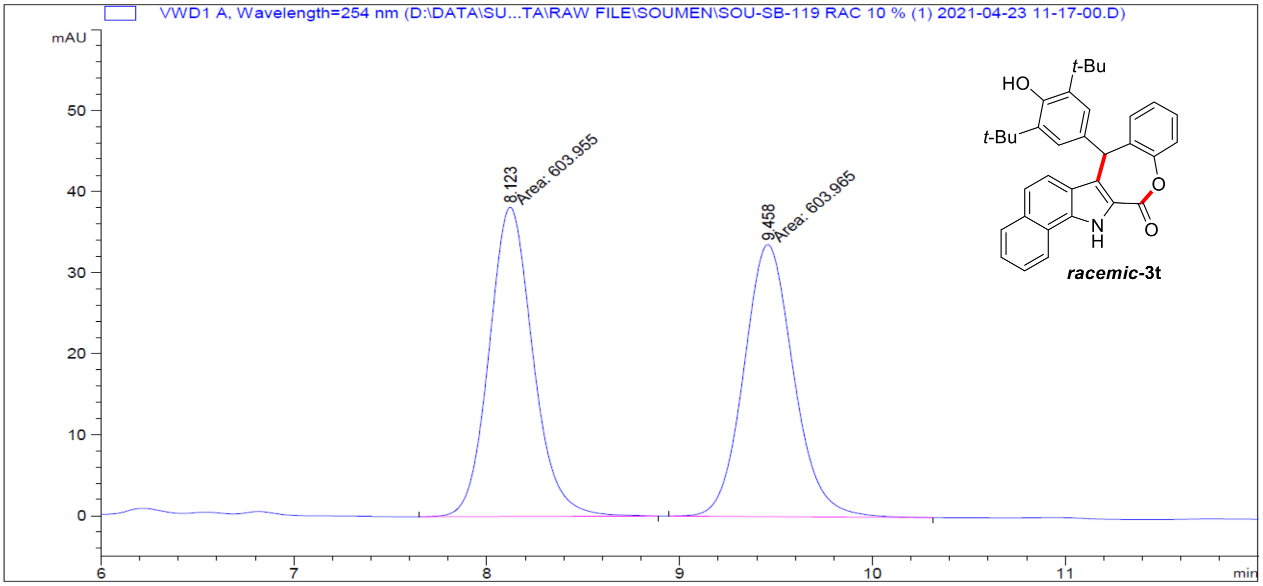
```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]         [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   8.982 MM    0.2543 6014.97803  394.17563  49.9994
   2  34.548 MM    0.9372 6015.12549  106.97084  50.0006
```



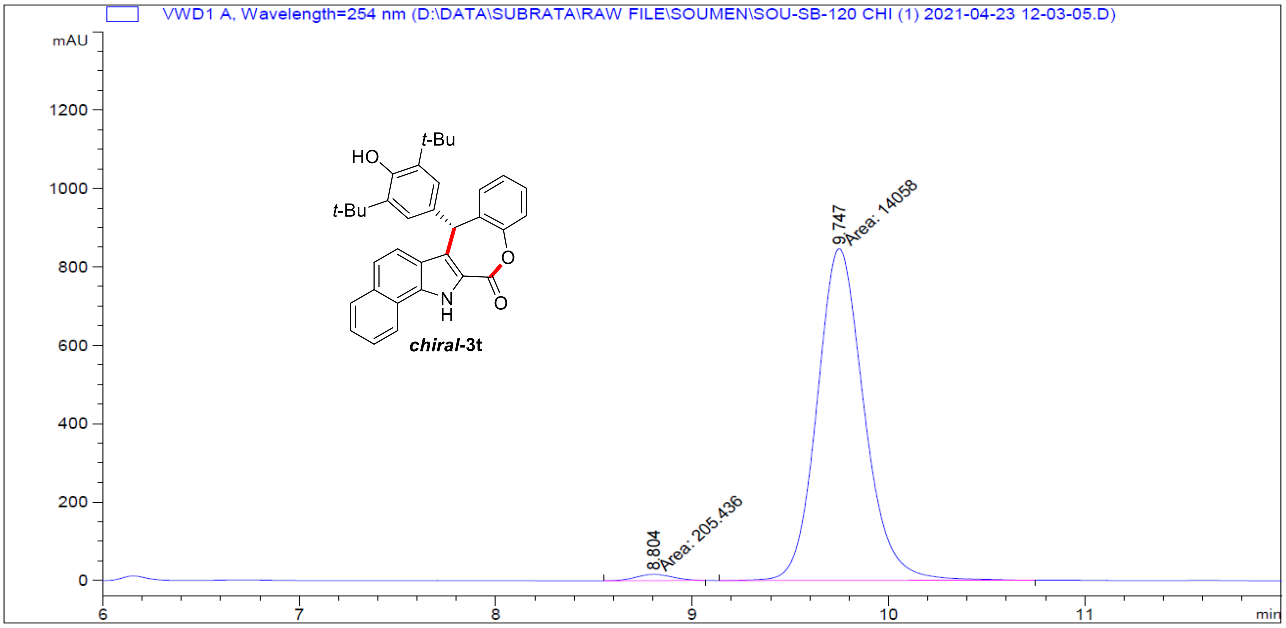
```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]         [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   8.779 MM    0.2650  224.13635   14.09578   4.3198
   2  33.829 MM    0.9163 4964.43311   90.29681  95.6802
```

```
Sample Info      : CHIRALPAK IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-7-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-7,14-dihydro-13*H*-benzo[*g*]benzo[6,7]oxepino[3,4-*b*]indol-13-one (3t)



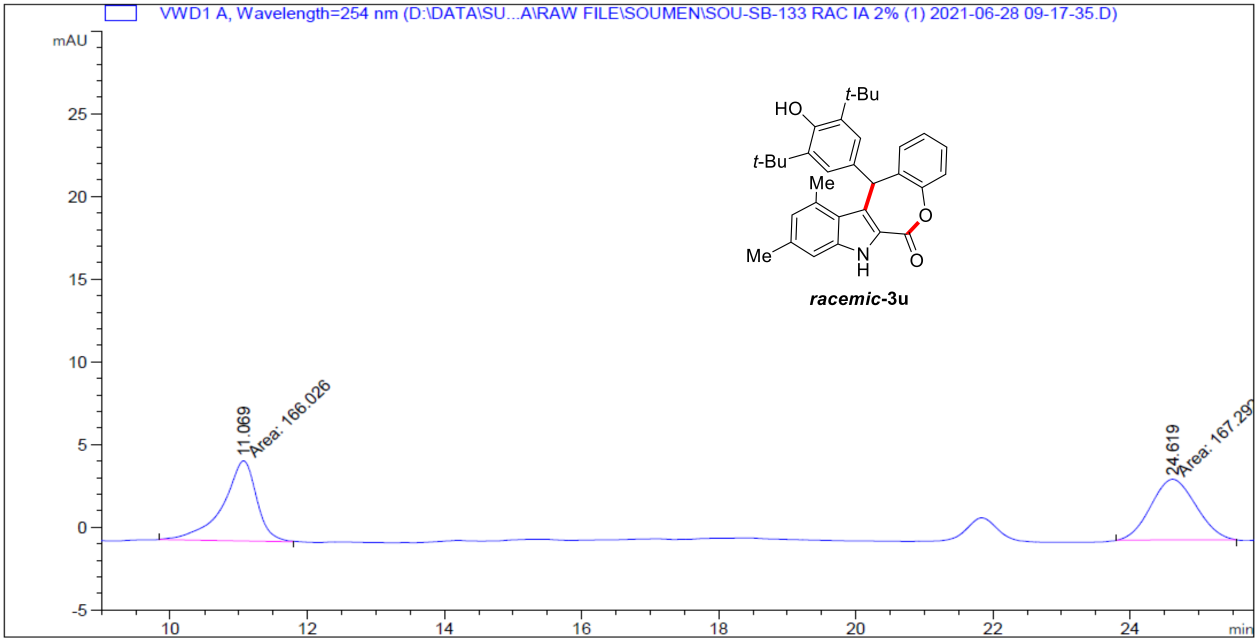
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.123 MM    0.2639  603.95520   38.14765  49.9996
   2   9.458 MM    0.2997  603.96454   33.58168  50.0004
```



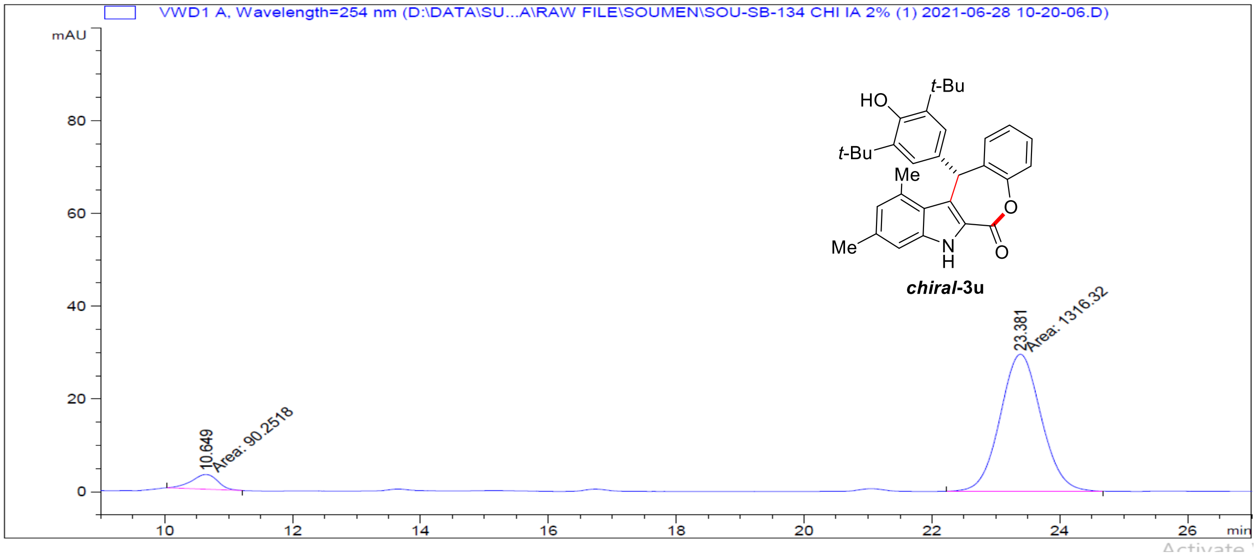
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.804 MM    0.2167  205.43631   15.79901   1.4403
   2   9.747 MM    0.2768 1.40580e4   846.43469  98.5597
```

Sample Info   : CHIRALPAK IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm

(*S*)-12-(3,5-di-*Tert*-butyl-4-hydroxyphenyl)-9,11-dimethyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3u)



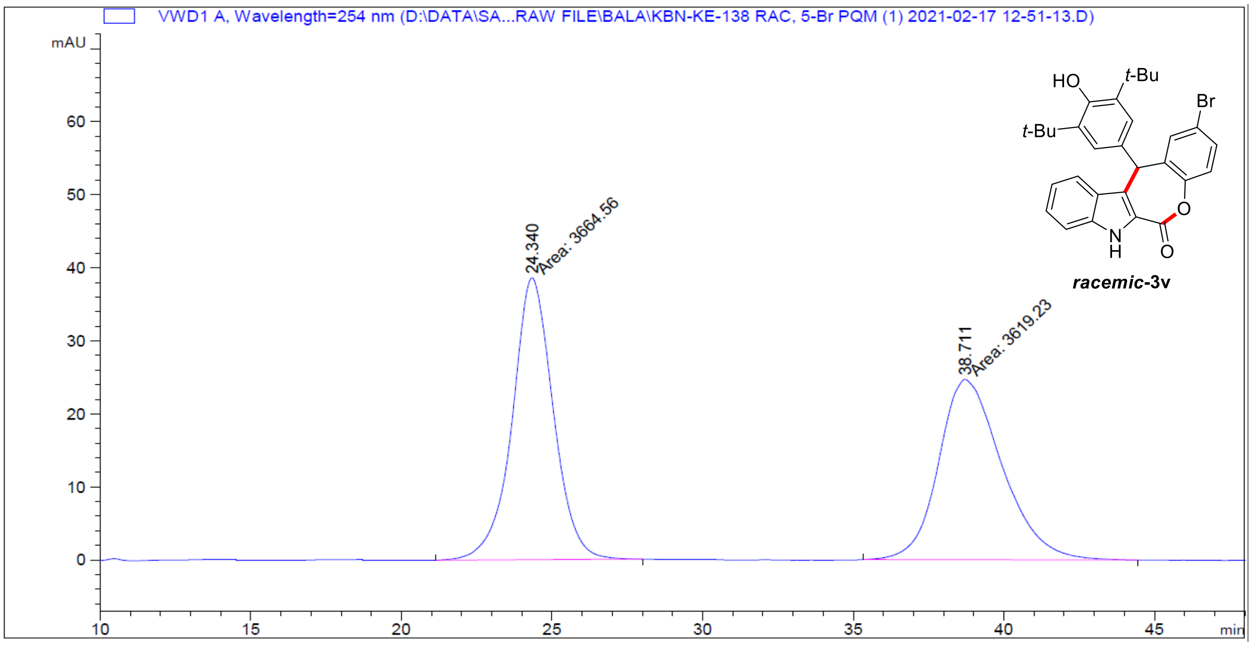
```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.069 MM    0.5708  166.02626    4.84737  49.8101
   2  24.619 MM    0.7601  167.29187    3.66826  50.1899
```



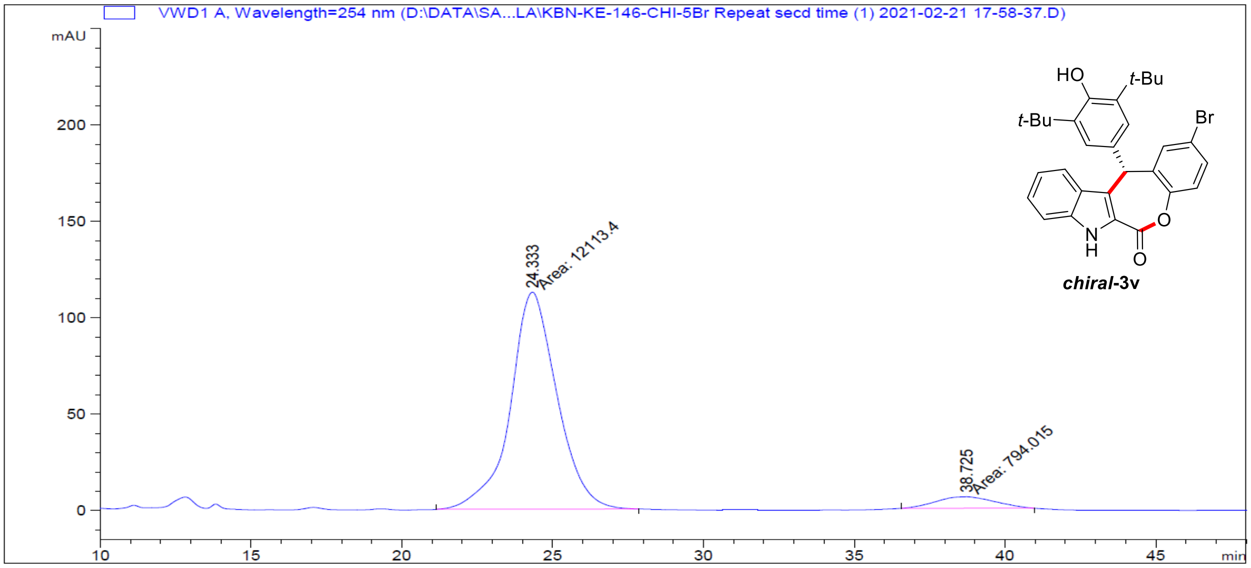
```
Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.649 MM    0.4747   90.25180    3.16868   6.4164
   2  23.381 MM    0.7430 1316.31995   29.52674  93.5836
```

```
Sample Info     : CHIRALPAK IA, 2 % IPA-HEXANE, 1.0 mL/min, 254 nM.M
```

(S)-2-Bromo-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3v)



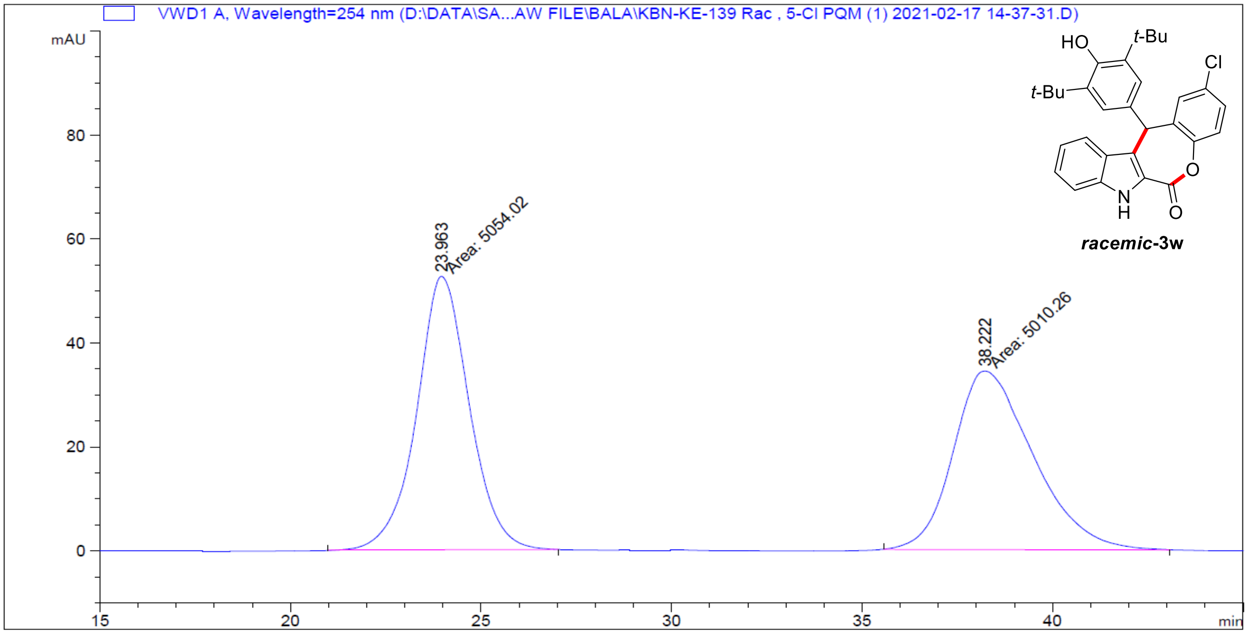
```
Peak RetTime Type  Width      Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  24.340 MM    1.5823 3664.55737   38.59905  50.3111
   2  38.711 MM    2.4427 3619.23145   24.69383  49.6889
```



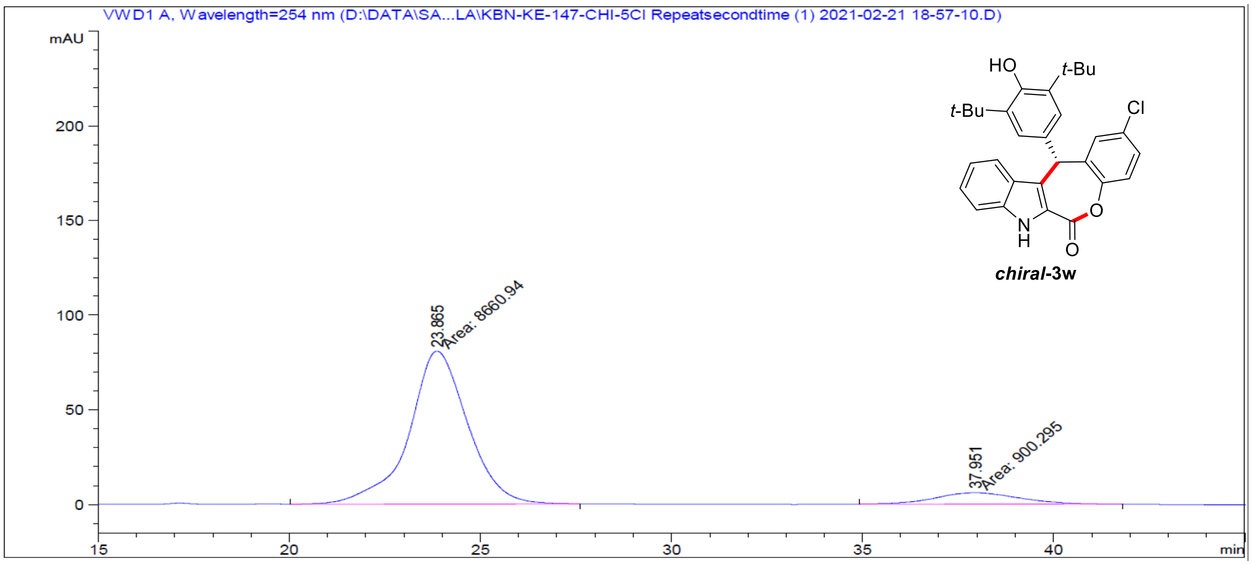
```
Peak RetTime Type  Width      Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  24.333 MM    1.7938 1.21134e4   112.54713  93.8484
   2  38.725 MM    2.2220  794.01489    5.95578   6.1516
```

```
Sample Info     : CHIRALCELL OD-H , 1% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-2-Chloro-12-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3w)



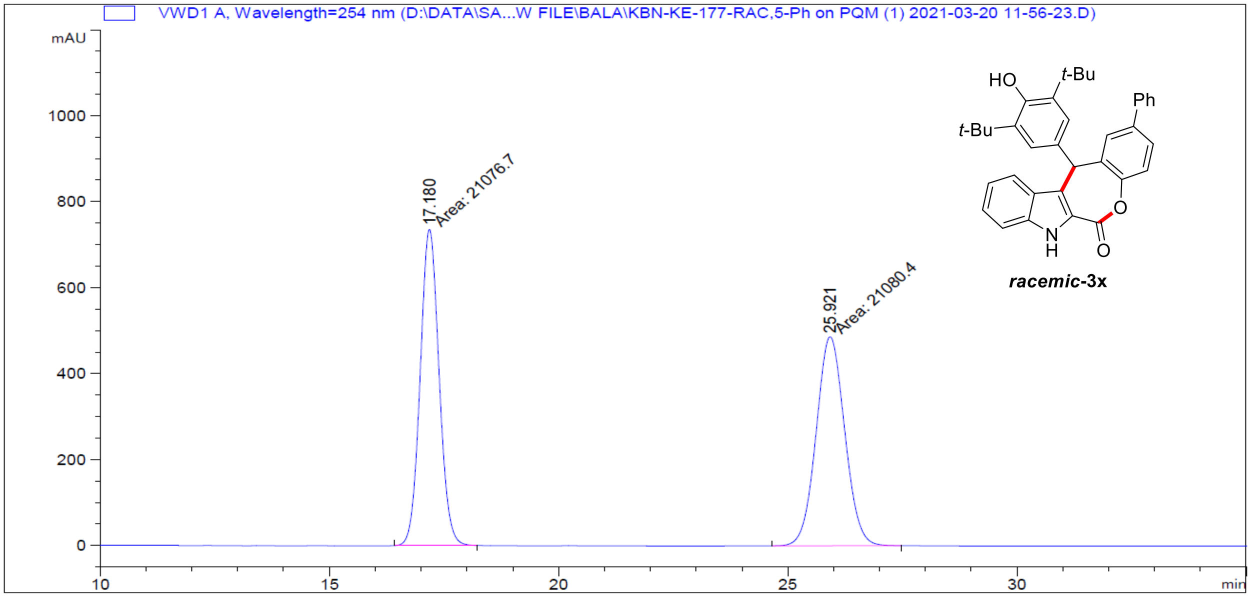
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  23.963 MM    1.6010 5054.01709   52.61432  50.2174
   2  38.222 MM    2.4320 5010.26367   34.33619  49.7826
```



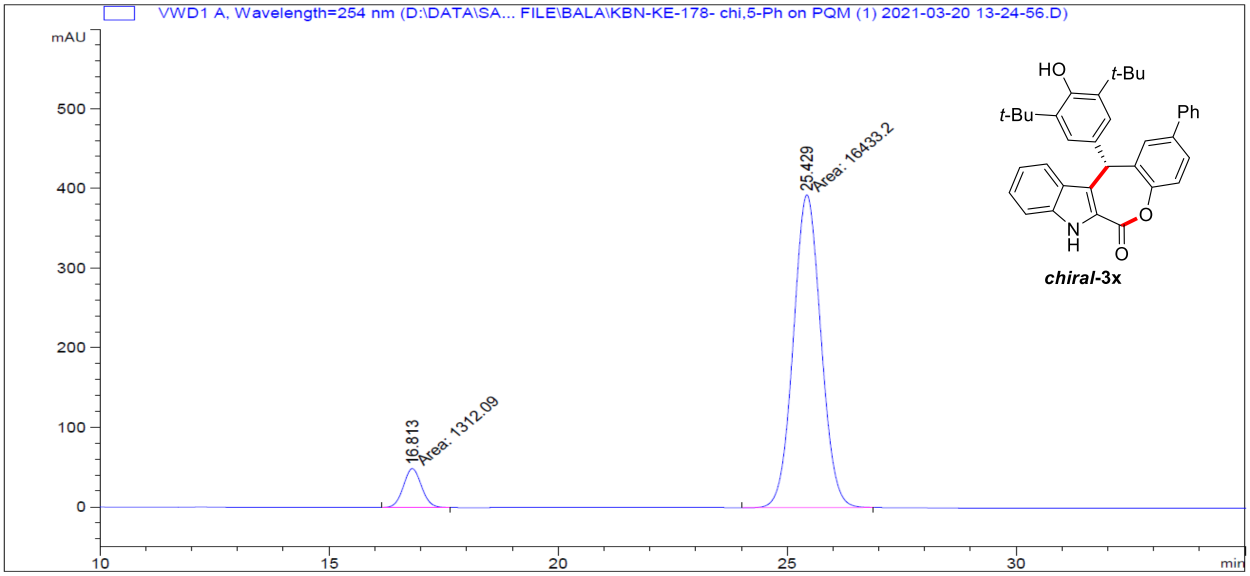
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  23.865 MM    1.7883 8660.93750   80.71883  90.5839
   2  37.951 MM    2.5025  900.29535    5.99599   9.4161
```

```
Sample Info      : CHIRALCELL OD-H , 1% IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-phenyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3x)



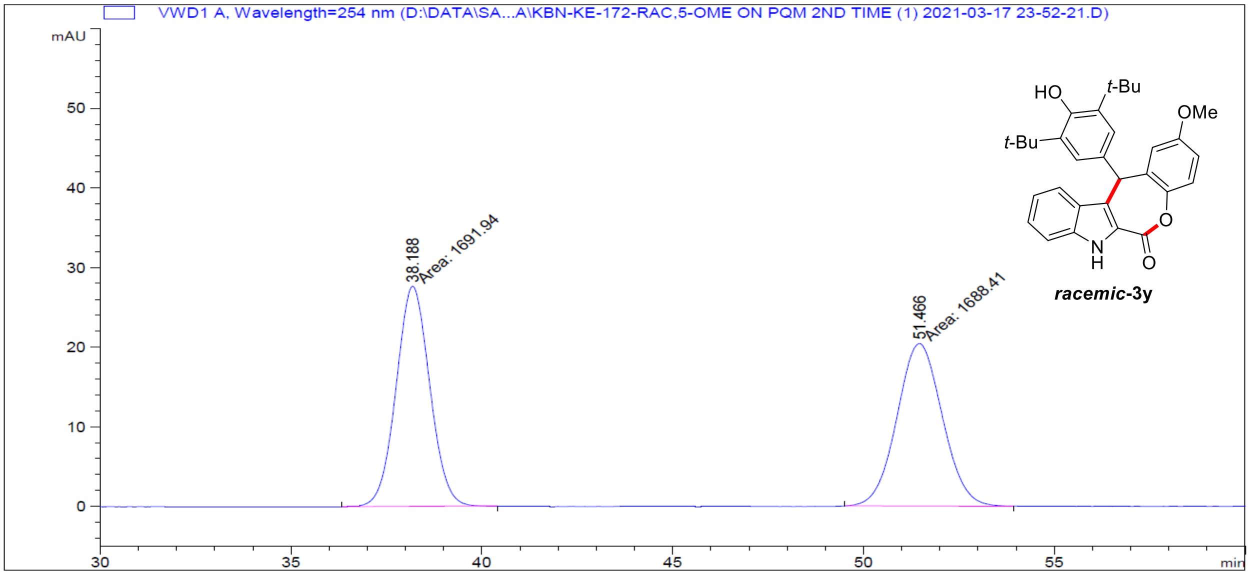
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  17.180 MM    0.4774 2.10767e4  735.84338  49.9957
   2  25.921 MM    0.7225 2.10804e4  486.27020  50.0043
```



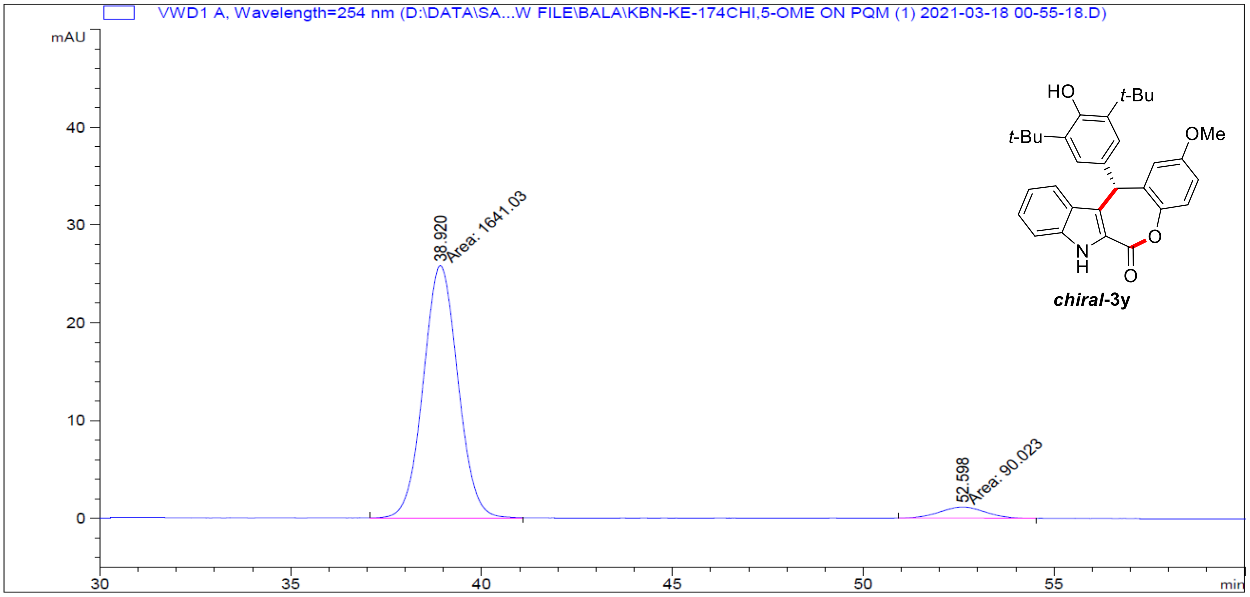
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  16.813 MM    0.4517 1312.08813   48.41216   7.3940
   2  25.429 MM    0.6974 1.64332e4  392.72919  92.6060

Sample Info     : CHIRALPAK IA, 10 % IPA-HEXANE, 1.0 mL/min, 254 nm
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3y)



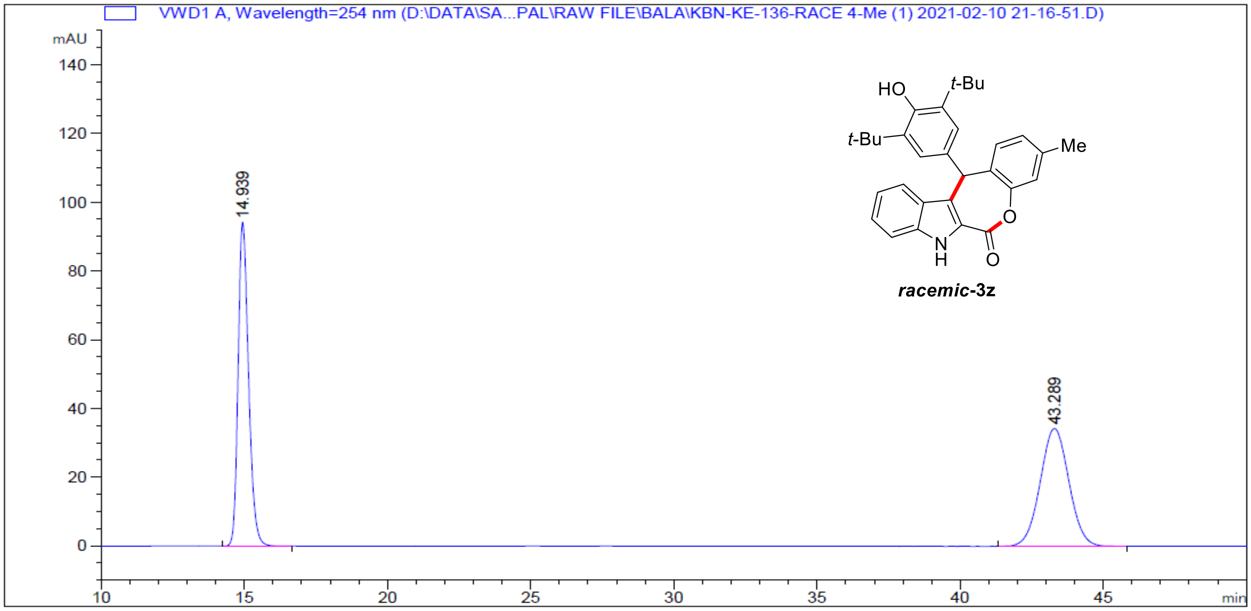
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]  [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1   38.188 MM    1.0206 1691.94189   27.62939  50.0522
  2   51.466 MM    1.3792 1688.41443   20.40334  49.9478
```



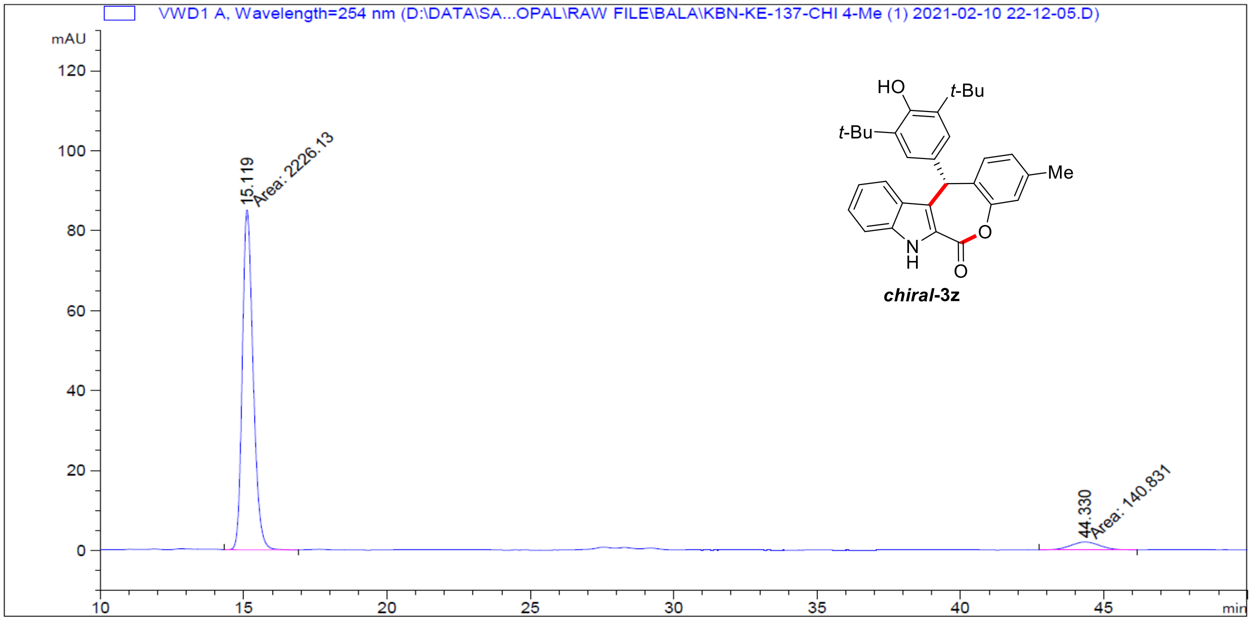
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]  [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1   38.920 MM    1.0574 1641.02502   25.86586  94.7995
  2   52.598 MM    1.3496   90.02300    1.11170   5.2005
```

```
Sample Info      : CHIRALPAK IA, 10 % IPA-HEXANE, 1mL/min, 254 nm
```

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-3-methyl-7,12-dihydro-6*H*-benzo[6,7]oxepino[3,4-b]indol-6-one (3z)



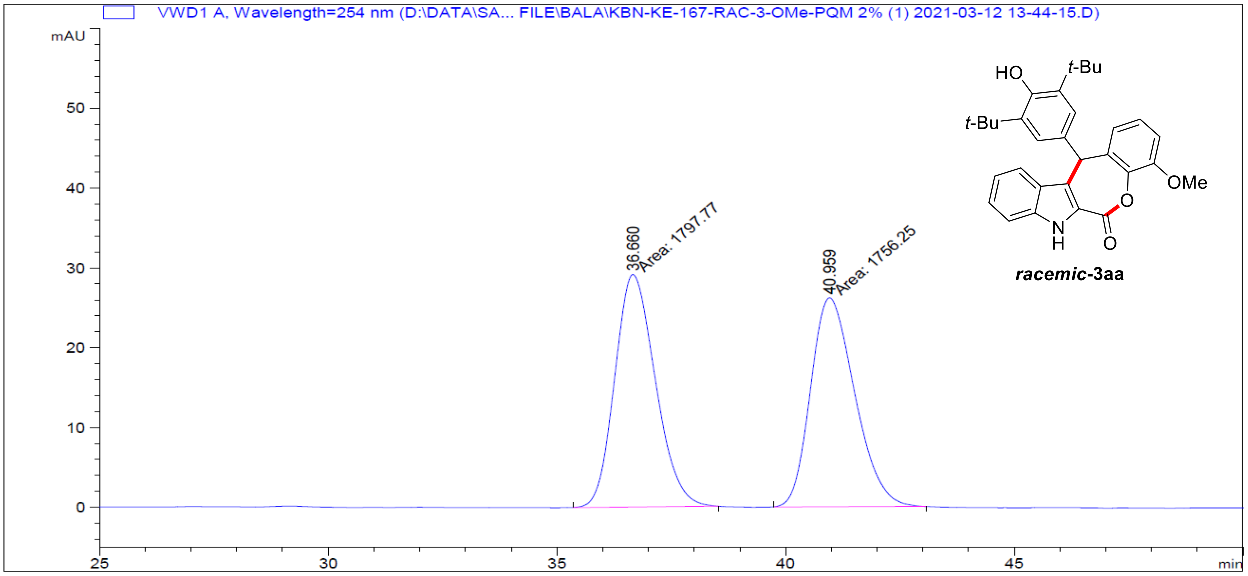
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.939 BB    0.3893 2386.49146   94.28596  49.8928
   2  43.289 BB    1.0722 2396.75098   34.29923  50.1072
```



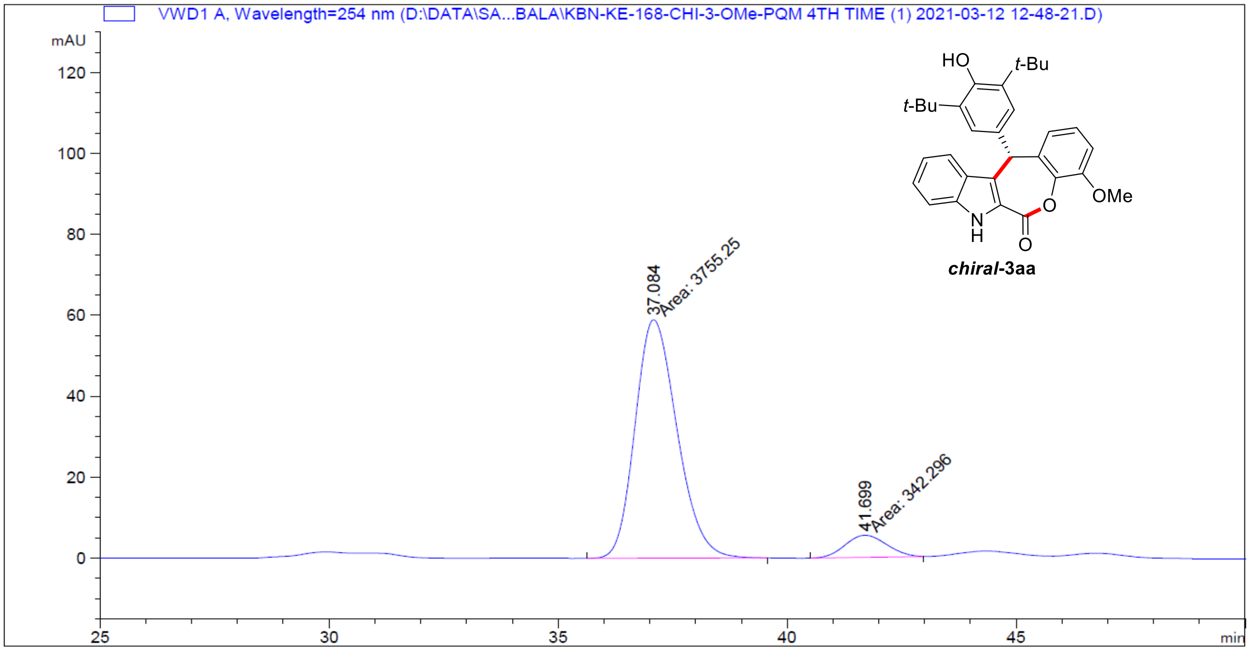
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------
   1  15.119 MM    0.4364 2226.13379   85.02112  94.0501
   2  44.330 MM    1.1957  140.83144    1.96308   5.9499
```

Sample Info : CHIRALPAK IA, 10% IPA-HEXANE, 1.0 mL/min, 254 nm

(*S*)-12-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-4-methoxy-7,12-dihydro-6*H*-benzo[6,7]oxepino[3, 4-b]indol-6-one (3aa)



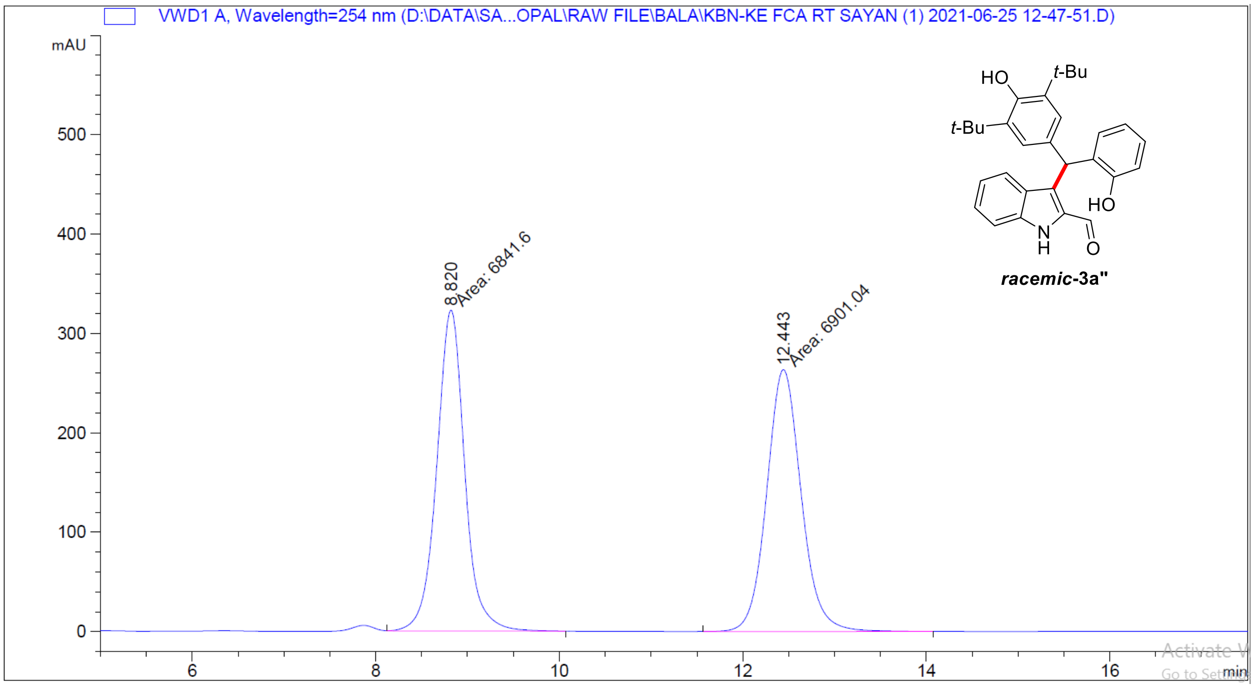
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  36.660 MM    1.0288 1797.76794   29.12329  50.5841
  2  40.959 MM    1.1185 1756.24951   26.17004  49.4159
```



```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  37.084 MM    1.0625 3755.25269   58.90541  91.6463
  2  41.699 MM    1.0507  342.29568    5.42984   8.3537
```

```
Sample Info     : CHIRAl PAK IA,2% IPA-HEXANE, 1.0 mL/min, 254 nm
```

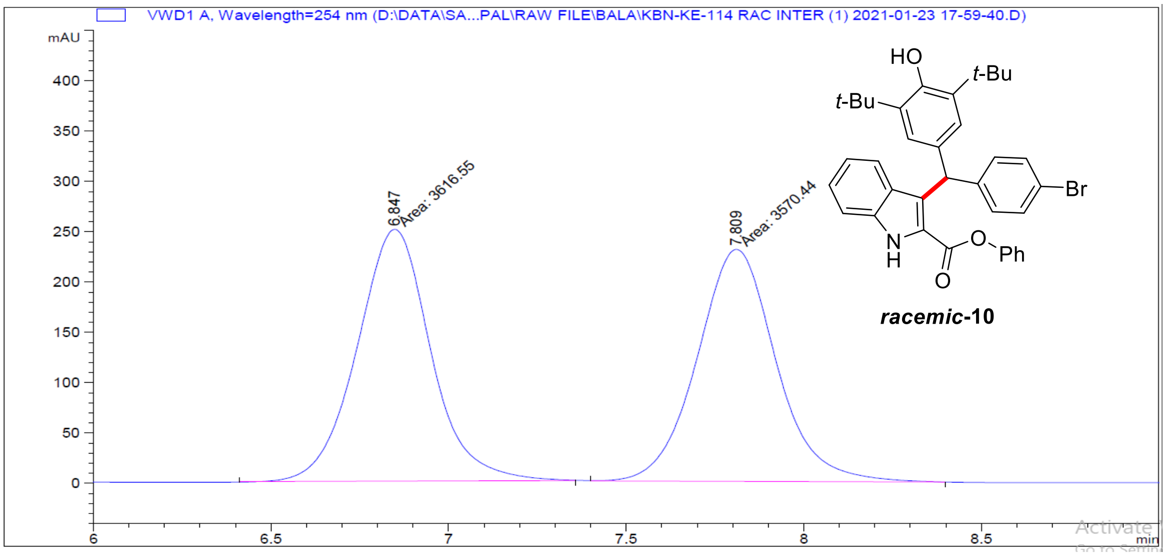
3-((3,5-Di-*tert*-butyl-4-hydroxyphenyl)(2-hydroxyphenyl)methyl)-1*H*-indole-2-carbaldehyde (3a”)



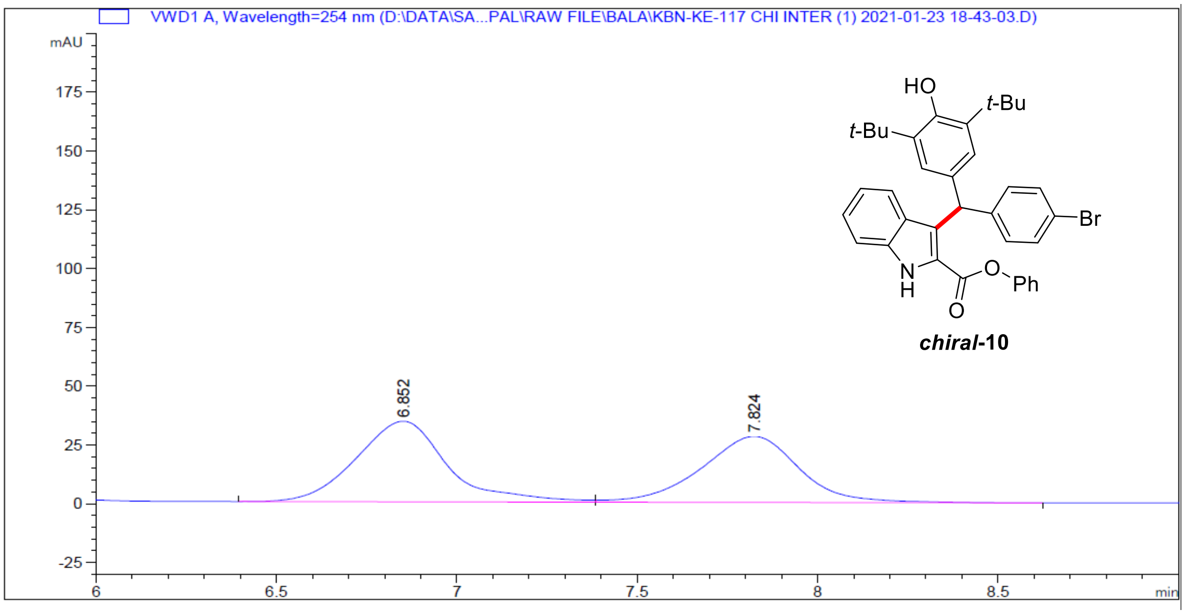
```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.820 MM    0.3533 6841.59912  322.76346  49.7837
   2  12.443 MM    0.4365 6901.03857  263.52148  50.2163

 Sample Info      : CHIRALPAK IA, 15 % IPA-HEXANE, 1.0 mL/min, 254 nM.M
```

Phenyl 3-((4-bromophenyl)(3,5-di-*tert*-butyl-4-hydroxyphenyl)methyl)-1*H*-indole-2-carboxylate (10)



```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.847 MM    0.2409 3616.55298  250.24260  50.3208
   2   7.809 MM    0.2579 3570.44287  230.69826  49.6792
```



```
Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.852 BV    0.2652  603.20142   34.30189  53.2210
   2   7.824 VB    0.2830  530.18756   28.11667  46.7790
```

```
Sample Info      : CHIRAL PAK IA,10% IPA-HEXANE, 1.0 mL/min.,254 nm
```