

Organocatalytic Asymmetric Spirocyclization Reactions of Cyclic 2,4-dienones with Cyanoketones: Synthesis of Spiro-Dihydropyrano Cyclohexanones

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1. General Information: Chemicals and solvents were purchased from commercial suppliers and used as received. ^1H NMR spectra were recorded on 400 MHz, 500 MHz and 600 MHz spectrometer. ^{13}C NMR spectra were recorded on 100 MHz, 125 MHz and 150 MHz. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.260), carbon (chloroform δ 77.23). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), brs (broad singlet). Coupling constants were reported in Hertz (Hz). High-resolution mass spectra (HRMS) were recorded in Q-TOF electron spray ionization (ESI). Enantiomeric ratios were determined by HPLC analysis using Dionex (Ultimate 3000) instrument with chiral columns using a Daicel Chiralpak IA Column, Daicel Chiralpak IB Column, Daicel Chiralpak IC Column, Daicel Chiralpak ID Column. For visualizing the products UV light and I_2 were used. Toluene was distilled over CaH_2 under argon and stored over 4A° molecular sieves. DCM was distilled over CaH_2 under argon and stored over 4A° molecular sieves. Silica gel (60-120 mesh size) was used for the column chromatography. Reactions were monitored by TLC on silica gel 60 F254 (0.25 mm).

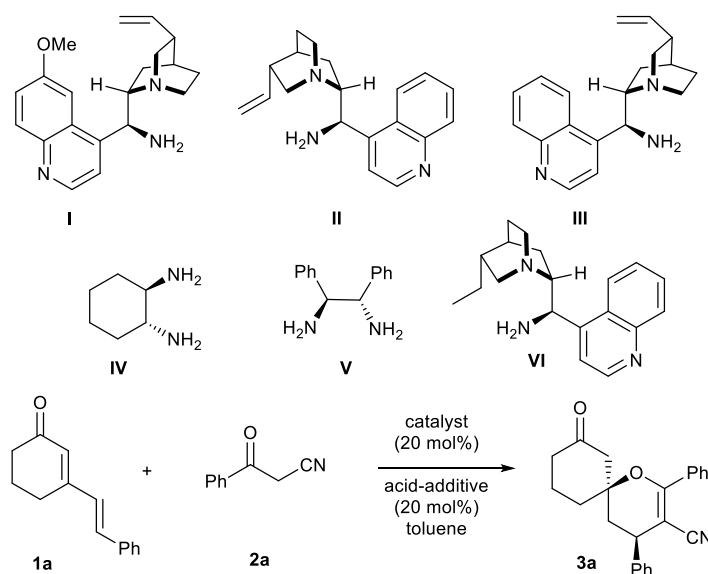
2. General procedure for the synthesis of Dienones:

Dienones **1a-1g** were prepared according to reported procedure.¹

3. General procedure for the synthesis of catalyst:

The catalyst (**I**, **II** and **III**) was prepared according to reported procedures.²

4. Catalyst optimization (Table S1):

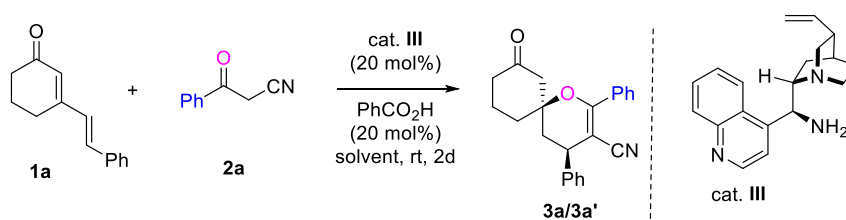


Scheme S1

entry ^a	catalyst	acid-additive	yield ^b	dr ^c	ee ^d
1	I	PhCO ₂ H	70	1.2:1	52/54
2	II	PhCO ₂ H	74	1.3:1	77/80
3	III	PhCO ₂ H	75	1.3:1	82/79
4	IV	PhCO ₂ H	66	1.1:1	18/20
5	V	PhCO ₂ H	68	1.1:1	42/36
6	VI	PhCO ₂ H	70	1.1:1	-77/-80

^aUnless otherwise mentioned, reactions were carried out with 0.06 mmol of **1a** with 0.05 mmol of **2a** in 0.5 ml solvent using 20 mol% catalyst and 20 mol% acid additive at room temperature for 2 days. ^bIsolated combined yield after silica gel column chromatography. ^cDetermined by ¹H NMR of crude reaction mixture. ^dDetermined by chiral HPLC.

5. Solvent optimization (Table S2):

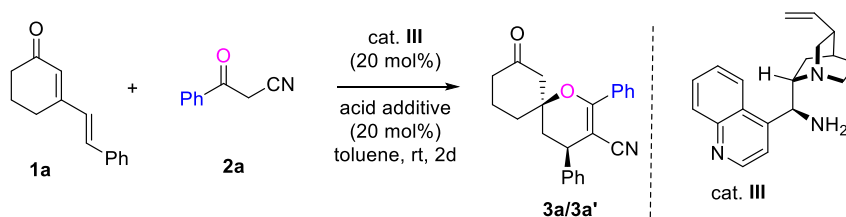


Scheme S2

entry ^a	solvent	yield (%) ^b	dr ^c	ee ^d
1	CHCl ₃	69	1.1:1	82/72
2	CH ₂ Cl ₂	58	1.1:1	76/20
3	PhCF ₃	73	1:1	78/78
3	MTBE	68	1.2:1	80/78
4	mesitylene	70	1.2:1	81/74
5	toluene	75	1.3:1	82/79

^aUnless otherwise mentioned, reactions were carried out with 0.06 mmol of **1a** with 0.05 mmol of **2a** in 0.5 ml solvent using 20 mol% cat. **III** and 20 mol% PhCO₂H at room temperature for 2 days. ^bIsolated combined yield after silica gel column chromatography. ^cDetermined by ¹H NMR of crude reaction mixture. ^dDetermined by chiral HPLC.

6. Acid-additive optimization (Table S3):

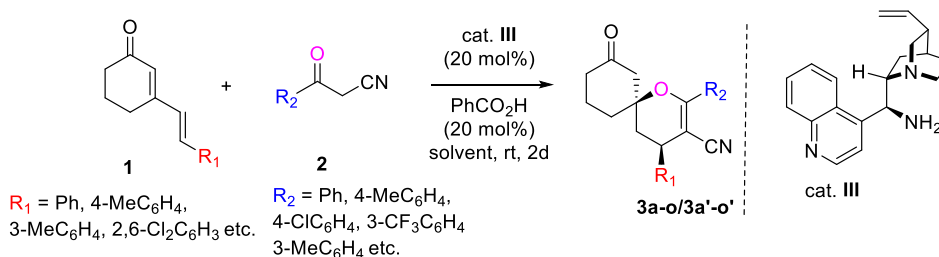


Scheme S3

entry ^a	acid-additive	yield (%) ^b	dr ^c	ee ^d
1	2-OHC ₆ H ₄ CO ₂ H	79	1:1	88/78
2	4-OMeC ₆ H ₄ CO ₂ H	70	1.1	80/71
3	(<i>R</i>)-3-Phenyllactic acid	68	1:1	87/77
4	<i>D</i> -CSA	73	1:1	88/79
5	<i>N</i> -Boc- <i>l</i> -leucine	80	1.1:1	90/88
6^e	<i>N</i>-Boc-<i>l</i>-leucine	85	1.2:1	95/92

^aUnless otherwise mentioned, reactions were carried out with 0.06 mmol of **1a** with 0.05 mmol of **2a** in 0.5 mL solvent using 20 mol% cat. **III** and 20 mol% acid additive at room temperature for 2 days. ^bIsolated combined yield after silica gel column chromatography. ^cDetermined by ¹H NMR of crude reaction mixture. ^dDetermined by chiral HPLC. ^eReaction was carried out at 0 °C and for 5 days.

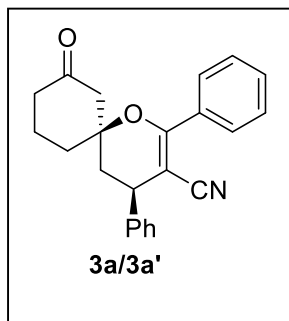
7. General procedure for the synthesis of compound **3**:



In an oven dried round bottom flask, **1** (0.24 mmol), **2** (0.2 mmol), 20 mol% of catalyst **III** and 20 mol% of *N*-Boc (*L*)-tert-leucine were taken. 2 mL of toluene was added to the reaction mixture and stirred at 0 °C for 5 days. Completion of reaction was checked by TLC. After the completion of reaction, solvent was concentrated and reaction mixture was directly purified by

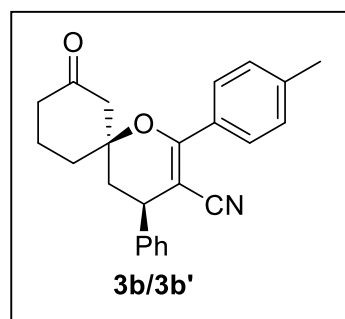
column chromatography on silica gel eluting with hexane/ethyl acetate (25-30 %) to afford desired product **3a-3o**.

8. Characterisation of the products:



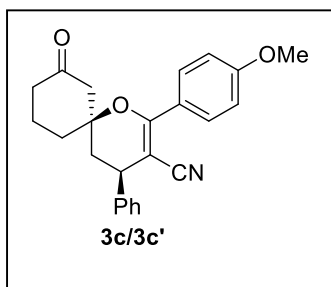
(4R,6R)-8-oxo-2,4-diphenyl-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3a): Light yellow sticky solid; 85% yield (58.4 mg); 1.2:1 dr. ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, *J* = 7.8 Hz, 2H), 7.64 (d, *J* = 6.5 Hz, 2H), 7.45 – 7.38 (m, 10H), 7.32 (d, *J* = 6.2 Hz, 6H), 3.78 (dd, *J* = 11.6, 6.5 Hz, 1H), 3.68 (dd, *J* = 11.9, 6.5 Hz, 1H), 2.98 (d, *J* = 14.3 Hz, 1H), 2.68 (d, *J* = 14.7 Hz, 1H), 2.62 – 2.46 (m, 4H), 2.46 – 2.32 (m, 3H), 2.22 (dt, *J* = 18.1, 9.1 Hz, 4H), 2.12 – 1.84 (m,

9H). ¹³C NMR (100 MHz, CDCl₃) δ 207.9, 207.3, 164.4, 164.2, 140.9, 140.8, 133.3, 133.1, 131.2, 131.1, 129.3, 128.6, 128.6, 128.4, 127.9, 127.9, 119.5, 119.3, 87.8, 87.3, 82.3, 82.0, 52.7, 47.6, 41.7, 41.2, 41.0, 40.7, 38.5, 38.1, 36.3, 30.9, 29.8, 20.8, 20.6. **HPLC Analysis:** 95% ee (*t*_{major} = 18.3 min, *t*_{minor} = 25.2 min) and 92% ee (*t*_{major} = 19.7 min, *t*_{minor} = 21.4 min); Chiralpak IA Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, λ = 254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₃H₂₂NO₂ [M+H]⁺ 344.1645, found 344.1650.

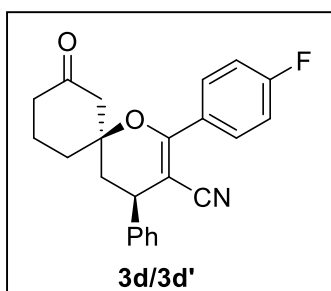


(4R,6R)-8-oxo-4-phenyl-2-(p-tolyl)-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3b): Colorless sticky solid; 78% (55.7 mg); 1.3:1 dr. ¹H NMR (600 MHz, CDCl₃) δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 4H), 7.36 – 7.28 (m, 7H), 7.21 (d, *J* = 7.1 Hz, 4H), 3.77 (dd, *J* = 11.7, 6.5 Hz, 1H), 3.67 (dd, *J* = 11.9, 6.5 Hz, 1H), 2.97 (d, *J* = 14.3 Hz, 1H), 2.66 (d, *J* =

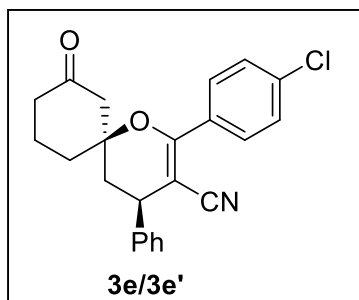
14.8 Hz, 1H), 2.54 (dd, *J* = 14.7, 10.2 Hz, 3H), 2.51 (t, *J* = 11.0 Hz, 3H), 2.47 – 2.39 (m, 3H), 2.38 (d, *J* = 2.5 Hz, 7H), 2.29 – 2.17 (m, 3H), 2.06 (dd, *J* = 12.8, 8.7 Hz, 3H), 2.03 – 1.96 (m, 2H), 1.96 – 1.84 (m, 4H). ¹³C NMR (151 MHz, CDCl₃) δ 208.0, 207.5, 164.5, 164.2, 141.6, 141.5, 141.0, 140.9, 130.4, 130.2, 129.2, 128.4, 128.3, 127.9, 127.8, 119.8, 119.5, 87.1, 86.5, 82.2, 81.9, 52.7, 47.5, 41.6, 41.2, 41.0, 40.7, 38.5, 38.0, 36.3, 30.8, 21.6, 21.6, 20.80, 20.6. **HPLC Analysis:** 89% ee (*t*_{major} = 18.7 min, *t*_{minor} = 24.4 min) and 97% ee (*t*_{major} = 21.4 min, *t*_{minor} = 23.7 min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, λ = 254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₄H₂₄NO₂ [M+H]⁺ 358.1802, found 358.1804.



(4R,6R)-2-(4-methoxyphenyl)-8-oxo-4-phenyl-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3c): Brown sticky solid; 73% (54.5 mg); 1:1 dr. ¹H NMR (600 MHz, CDCl₃) δ 7.72 (d, *J* = 8.9 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.41 – 7.35 (m, 4H), 7.31 (d, *J* = 7.3 Hz, 6H), 6.91 (d, *J* = 8.7 Hz, 4H), 3.82 (d, *J* = 3.3 Hz, 6H), 3.79 – 3.74 (m, 1H), 3.66 (dd, *J* = 11.9, 6.6 Hz, 1H), 2.97 (d, *J* = 14.2 Hz, 1H), 2.66 (d, *J* = 14.6 Hz, 1H), 2.58 – 2.37 (m, 7H), 2.28 – 2.15 (m, 3H), 2.10 – 1.97 (m, 4H), 1.95 – 1.83 (m, 4H). ¹³C NMR (150 MHz, CDCl₃) δ 208.2, 207.7, 164.0, 163.7, 161.7, 141.1, 141.0, 131.4, 130.1, 130.0, 129.2, 127.8, 125.6, 125.3, 120.1, 119.8, 113.9, 86.3, 85.6, 82.2, 81.9, 55.5, 52.7, 47.5, 41.7, 41.2, 41.0, 40.7, 38.5, 38.1, 36.3, 30.7, 29.8, 28.4, 26.6, 20.8, 20.7, 14.3. **HPLC Analysis:** 91% ee (*t*_{major} = 20.2 min, *t*_{minor} = 26.5 min) and 93% ee (*t*_{major} = 23.9 min, *t*_{minor} = 31.9 min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, λ = 254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₄H₂₄NO₃ [M+H]⁺ 374.1751, found 374.1761.

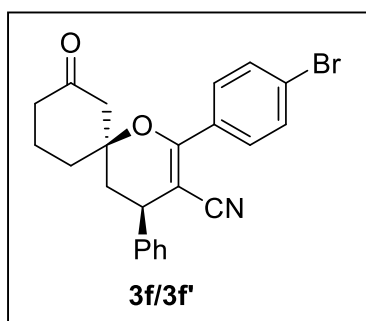


(4R,6R)-2-(4-fluorophenyl)-8-oxo-4-phenyl-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3d): Brown sticky solid; 69% (50.0 mg); 1.3:1 dr. ¹H NMR (600 MHz, CDCl₃) δ 7.77 – 7.72 (m, 2H), 7.64 – 7.61 (m, 2H), 7.39 (t, *J* = 6.8 Hz, 5H), 7.31 (t, *J* = 9.0 Hz, 7H), 7.11-7.07 (m, 5H), 3.77 (dd, *J* = 11.7, 6.5 Hz, 1H), 3.67 (dd, *J* = 12.0, 6.5 Hz, 1H), 2.97 (d, *J* = 14.2 Hz, 1H), 2.67 (d, *J* = 14.7 Hz, 1H), 2.54 (dd, *J* = 26.3, 14.2 Hz, 4H), 2.47 – 2.38 (m, 4H), 2.27 – 2.17 (m, 4H), 2.11 – 1.99 (m, 5H), 1.96 – 1.86 (m, 4H). ¹³C NMR (150 MHz, CDCl₃) δ 208.1, 207.4, 165.1, 163.4, 163.4, 163.3, 163.0, 140.7, 140.6, 130.8, 130.7, 130.6, 129.3, 128.0, 127.9, 127.8, 119.5, 119.2, 115.8, 115.7, 87.9, 87.2, 82.5, 82.3, 52.7, 47.6, 41.6, 41.1, 41.0, 40.7, 38.4, 38.0, 36.3, 30.9, 20.8, 20.7. **HPLC Analysis:** 90% ee (*t*_{major} = 20.3 min, *t*_{minor} = 16.1 min) and 83% ee (*t*_{major} = 52.8 min, *t*_{minor} = 19.0 min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, λ = 254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₃H₂₁FNO₂ [M+H]⁺ 362.1551, found 362.1559.



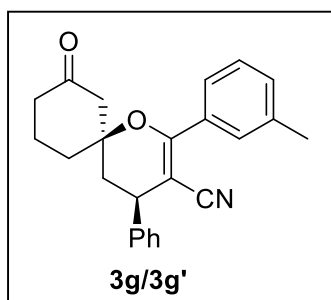
(4R,6R)-2-(4-chlorophenyl)-8-oxo-4-phenyl-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3e): White semi solid; 75% (56.7 mg); 2:1 dr. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.69 (d, $J = 8.6$ Hz, 2H), 7.57 (d, $J = 8.6$ Hz, 3H), 7.42 – 7.36 (m, 12H), 7.40 – 7.37 (m, 10H), 3.77 (dd, $J = 11.7, 6.5$ Hz, 1H), 3.67 (dd, $J = 12.0, 6.5$ Hz, 2H), 2.96 (d, $J = 14.2$ Hz, 2H), 2.67 (d, $J =$

14.7 Hz, 1H), 2.59 – 2.49 (m, 5H), 2.49 – 2.33 (m, 4H), 2.27 – 2.15 (m, 5H), 2.11 – 1.99 (m, 6H), 1.98 – 1.85 (m, 7H). $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 208.0, 207.3, 163.2, 162.9, 140.6, 140.5, 137.2, 131.7, 131.4, 129.9, 129.7, 129.3, 129.10 128.9, 128.0, 127.9, 127.8, 127.5, 119.3, 119.0, 88.3, 87.7, 82.6, 82.4, 52.7, 47.6, 41.5, 41.0, 40.7, 38.5, 38.0, 36.3, 20.8, 20.7. **HPLC Analysis:** 89% ee ($t_{\text{major}} = 21.3$ min, $t_{\text{minor}} = 19.9$ min) and 97% ee ($t_{\text{major}} = 26.5$ min, $t_{\text{minor}} = 24.5$ min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 $^\circ\text{C}$, $\lambda = 254$ nm. **HRMS (+ESI-TOF) m/z :** calcd. For $\text{C}_{23}\text{H}_{21}\text{ClNO}_2$ $[\text{M}+\text{H}]^+$ 378.1255, found 378.1268.



(4R,6R)-2-(4-bromophenyl)-8-oxo-4-phenyl-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3f): Brown sticky solid; 72% (60.6 mg); 1.3:1 dr. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.62 (d, $J = 8.6$ Hz, 2H), 7.55 – 7.53 (m, 4H), 7.49 (d, $J = 8.6$ Hz, 2H), 7.43 – 7.37 (m, 5H), 7.36 – 7.27 (m, 7H), 3.76 (dd, $J = 11.7, 6.5$ Hz, 1H), 3.66 (dd, $J = 11.9, 6.5$ Hz, 1H), 2.95 (d, $J = 14.2$ Hz, 1H), 2.67 (d, $J = 14.6$ Hz, 1H), 2.53 (dd, $J = 26.4, 14.0$ Hz, 4H),

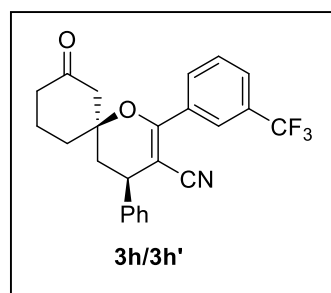
2.47 – 2.35 (m, 4H), 2.27 – 2.15 (m, 4H), 2.10 – 1.99 (m, 5H), 1.97 – 1.87 (m, 4H). $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 207.9, 207.3, 163.3, 163.0, 140.5, 132.1, 131.9, 130.1, 129.9, 129.3, 128.0, 127.9, 127.8, 125.6, 119.2, 119.0, 88.4, 87.8, 82.6, 82.4, 52.7, 47.6, 41.5, 41.0, 40.7, 38.5, 38.0, 36.3, 30.9, 20.8, 20.7. **HPLC Analysis:** 91% ee ($t_{\text{major}} = 27.1$ min, $t_{\text{minor}} = 33.1$ min) and 84% ee ($t_{\text{major}} = 20.0$ min, $t_{\text{minor}} = 24.1$ min); Chiralpak Lux cellulose-1 Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 $^\circ\text{C}$, $\lambda = 254$ nm. **HRMS (+ESI-TOF) m/z :** calcd. For $\text{C}_{23}\text{H}_{21}\text{BrNO}_2$ $[\text{M}+\text{H}]^+$ 422.0750, found 422.0749.



(4R,6R)-8-oxo-4-phenyl-2-(m-tolyl)-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3g): Light yellow sticky solid; 70% (50.0 mg);

1.4:1 dr. ¹H NMR (400 MHz, CDCl₃) δ 7.43 (d, *J* = 7.2 Hz, 2H), 7.33 (dd, *J* = 16.9, 8.5 Hz, 7H), 7.27 – 7.21 (m, 9H), 7.18 (dd, *J* = 7.9, 5.6 Hz, 4H), 3.68 (dd, *J* = 11.7, 6.5 Hz, 1H), 3.59 (dd, *J* = 11.9, 6.5 Hz, 1H), 2.89 (d, *J* = 14.3 Hz, 1H), 2.59 (d, *J* = 14.7 Hz, 1H),

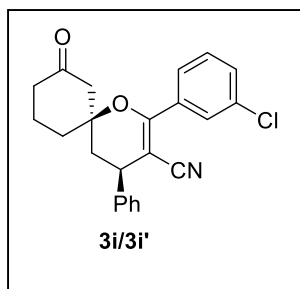
2.51 – 2.37 (m, 5H), 2.30 (s, 10H), 2.13 (dd, *J* = 14.0, 6.5 Hz, 4H), 2.01-1.76 (m, 10H). ¹³C NMR (150 MHz, CDCl₃) δ 208.0, 207.5, 164.3, 164.0, 140.8, 140.7, 138.9, 138.8, 133.3, 133.1, 131.1, 129.1, 128.7, 128.7, 128.6, 128.5, 128.4, 124.9, 119.6, 119.4, 87.9, 87.39 82.3, 82.0, 52.8, 47.6, 41.7, 41.2, 41.0, 40.7, 38.4, 38.0, 36.3, 30.8, 21.7, 20.8, 20.6. **HPLC Analysis:** 91% ee (*t*_{major} = 20.4 min, *t*_{minor} = 16.9 min) and 98% ee (*t*_{major} = 19.1 min, *t*_{minor} = 1.3 min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, λ = 254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₄H₂₄NO₂ [M+H]⁺ 358.1802, found 358.1800.



(4R,6R)-8-oxo-4-phenyl-2-(3-(trifluoromethyl)phenyl)-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3h): Brown sticky solid; 65% (53.4 mg); 1.5:1 dr. ¹H NMR (400 MHz, CDCl₃) δ

7.86 (s, 2H), 7.78 (d, *J* = 12.5 Hz, 3H), 7.64 (d, *J* = 7.7 Hz, 2H), 7.50 – 7.44 (m, 2H), 7.34 – 7.31 (m, 5H), 7.26 – 7.22 (m, 8H), 7.18 (s, 1H), 3.71 (dd, *J* = 11.7, 6.4 Hz, 1H), 3.63 (dd, *J* = 11.9, 6.5 Hz,

1H), 2.89 (d, *J* = 14.3 Hz, 1H), 2.63 (d, *J* = 14.7 Hz, 1H), 2.46 (dd, *J* = 14.4, 10.8 Hz, 4H), 2.40 – 2.29 (m, 4H), 2.18 (dd, *J* = 14.1, 6.5 Hz, 4H), 2.06 – 1.80 (m, 10H). ¹³C NMR (100 MHz, CDCl₃) δ 207.5, 206.9, 162.7, 162.6, 140.4, 140.3, 134.2, 134.0, 131.94 131.7, 131.4, 131.0, 129.4, 129.3, 129.1, 128.1, 127.9, 125.4, 125.2, 118.7, 118.5, 89.3, 88.9, 82.8, 82.6, 52.8, 47.8, 41.4, 40.9, 40.8, 40.6, 38.4, 38.1, 36.3, 31.1, 29.9, 20.7, 20.7. **HPLC Analysis:** 99% ee (*t*_{major} = 26.0 min, *t*_{minor} = 32.8 min) and 41% ee (*t*_{major} = 29.5 min, *t*_{minor} = 22.2 min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, λ = 254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₄H₂₁F₃NO₂ [M+H]⁺ 412.1519, found 412.1514.



(4R,6R)-2-(3-chlorophenyl)-8-oxo-4-phenyl-1-oxaspiro[5.5]undec-

2-ene-3-carbonitrile (3i): Light brown sticky solid; 71% (53.8 mg);

1.7:1 dr. ¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, *J* = 8.9 Hz, 2H),

7.58 – 7.52 (m, 3H), 7.48 – 7.27 (m, 19H), 3.76 (dd, *J* = 11.7, 6.5

Hz, 1H), 3.68 (dd, *J* = 11.9, 6.5 Hz, 2H), 2.95 (d, *J* = 14.2 Hz, 2H),

2.69 (d, *J* = 14.8 Hz, 1H), 2.62 – 2.48 (m, 5H), 2.48 – 2.33 (m, 4H),

2.23 (dd, *J* = 14.1, 6.6 Hz, 5H), 2.16 – 1.86 (m, 11H). ¹³C NMR (100 MHz, CDCl₃) δ 207.6,

162.9, 162.7, 140.5, 140.4, 135.0, 134.6, 131.2, 131.1, 129.9, 129.3, 128.5, 128.3, 128.1, 128.0,

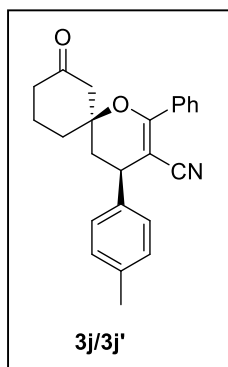
127.9, 126.8, 126.7, 118.9, 118.73 88.9, 82.6, 82.4, 52.7, 47.7, 41.4, 40.9, 40.6, 38.5, 38.1,

36.3, 20.7, 20.6. **HPLC Analysis:** 98% ee (*t*_{major} = 24.7 min, *t*_{minor} = 26.1 min) and 69% ee

(*t*_{major} = 28.6 min, *t*_{minor} = 20.0 min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate

1.0 mL/min, 25 °C, λ = 254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₃H₂₂ClNO₂ [M+H]⁺

378.1255, found 378.1264.



(4R,6R)-8-oxo-2-phenyl-4-(p-tolyl)-1-oxaspiro[5.5]undec-2-ene-3-

carbonitrile (3j): Colorless sticky solid; 79% (56.4 mg); 1.5:1 dr. ¹H NMR

(600 MHz, CDCl₃) δ 7.74 (d, *J* = 7.1 Hz, 2H), 7.63 (d, *J* = 7.0 Hz, 3H),

7.48 – 7.38 (m, 7H), 7.20 (d, *J* = 2.4 Hz, 9H), 3.74 (dd, *J* = 11.7, 6.5 Hz,

1H), 3.65 (dd, *J* = 12.0, 6.5 Hz, 1H), 2.98 (d, *J* = 14.3 Hz, 1H), 2.67 (d, *J*

= 14.7 Hz, 1H), 2.53 (dd, *J* = 33.4, 13.9 Hz, 5H), 2.48 – 2.39 (m, 4H), 2.35

(d, *J* = 2.0 Hz, 7H), 2.27 – 2.18 (m, 4H), 2.06 (d, *J* = 9.8 Hz, 5H), 1.98 –

1.84 (m, 5H). ¹³C NMR (150 MHz, CDCl₃) δ 208.0, 207.5, 164.2, 164.0, 137.8, 137.7, 137.6,

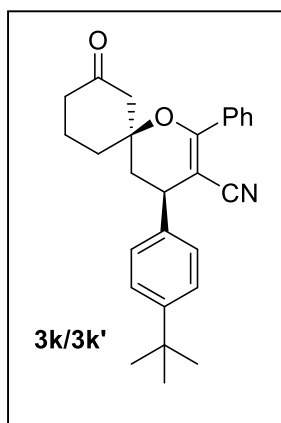
137.5, 133.3, 133.1, 131.1, 131.0, 129.9, 128.6, 128.5, 128.4, 127.7, 119.6, 119.4, 88.1, 87.5,

82.3, 82.0, 52.8, 47.6, 41.7, 41.2, 41.0, 40.7, 38.1, 37.6, 36.3, 30.9, 21.3, 20.8, 20.6. **HPLC**

Analysis: 92% ee (*t*_{major} = 12.2 min, *t*_{minor} = 13.8 min) and 95% ee (*t*_{major} = 18.4 min, *t*_{minor} =

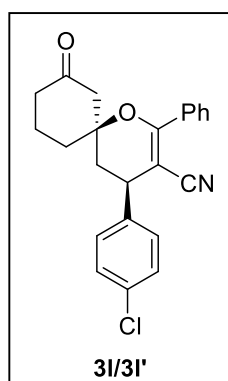
15.4 min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, λ =

254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₃H₂₄NO₂ [M+H]⁺ 358.1802, found 358.1811.



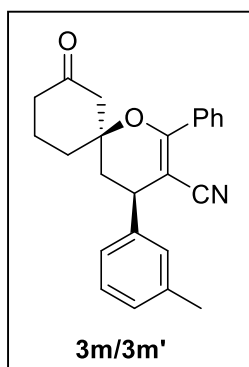
(4R,6R)-4-(4-(tert-butyl)phenyl)-8-oxo-2-phenyl-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3k): Off white semisolid; 80% (63.9 mg); 1.3:1 dr. **¹H NMR (600 MHz, CDCl₃)** δ 7.66 (d, *J* = 7.2 Hz, 2H), 7.55 (d, *J* = 7.1 Hz, 3H), 7.38 – 7.32 (m, 11H), 7.17 (dd, *J* = 8.3, 6.6 Hz, 5H), 3.68 (dd, *J* = 11.7, 6.5 Hz, 1H), 3.59 (dd, *J* = 11.9, 6.5 Hz, 1H), 2.91 (d, *J* = 14.3 Hz, 1H), 2.59 (d, *J* = 14.7 Hz, 1H), 2.45 (dt, *J* = 14.7, 9.9 Hz, 5H), 2.40 – 2.30 (m, 4H), 2.18 – 2.11 (m, 4H), 2.02 – 1.97 (m, 3H), 1.90 – 1.80 (m, 5H), 1.25 (d, *J* = 2.1 Hz, 21H).

¹³C NMR (150 MHz, CDCl₃) δ 208.0, 207.5, 164.3, 164.0, 140.8, 140.7, 138.9, 138.8, 133.3, 133.1, 131.1, 129.1, 128.7, 128.7, 128.6, 128.5, 128.4, 124.9, 119.6, 119.4, 87.9, 87.3, 82.3, 82.0, 52.8, 47.6, 41.7, 41.2, 41.0, 40.7, 38.4, 38.0, 36.3, 30.8, 21.7, 20.8, 20.6. **HPLC Analysis:** 95% ee (*t*_{major} = 16.3 min, *t*_{minor} = 17.9 min) and 98% ee (*t*_{major} = 12.6 min, *t*_{minor} = 9.4 min); Chiralpak ID Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, λ = 254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₇H₃₀NO₂ [M+H]⁺ 400.2271, found 400.2269.

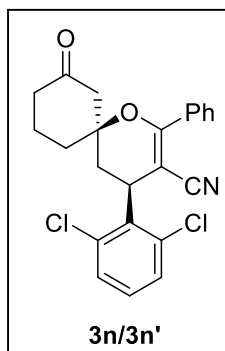


(4R,6R)-4-(4-chlorophenyl)-8-oxo-2-phenyl-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3l): Brown sticky solid; 76% (59.6 mg); 1.7:1 dr. **¹H NMR (600 MHz, CDCl₃)** δ 7.74 (d, *J* = 7.4 Hz, 2H), 7.65 – 7.61 (m, 2H), 7.50 – 7.45 (m, 3H), 7.44 – 7.41 (m, 6H), 7.38 – 7.36 (m, 5H), 7.29 – 7.25 (m, 6H), 3.78 (dd, *J* = 11.7, 6.5 Hz, 1H), 3.68 (dd, *J* = 11.9, 6.5 Hz, 2H), 2.97 (d, *J* = 14.3 Hz, 2H), 2.68 (d, *J* = 14.7 Hz, 1H), 2.62 – 2.49 (m, 5H), 2.48 – 2.36 (m, 4H), 2.30 – 2.18 (m, 5H), 2.14 – 1.99 (m, 5H), 1.98 – 1.82 (m, 5H). **¹³C NMR (150 MHz, CDCl₃)** δ 208.0, 207.5, 164.2, 164.0, 137.8,

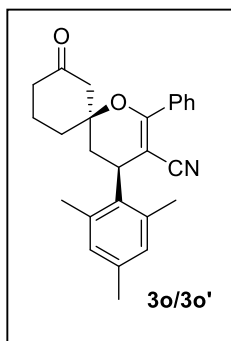
137.7, 137.6, 137.5, 133.3, 133.1, 131.0, 129.9, 128.6, 128.5, 128.4, 127.7, 119.6, 119.4, 88.1, 87.5, 82.3, 82.0, 52.8, 47.6, 41.7, 41.2, 41.0, 40.7, 38.1, 37.6, 36.3, 30.9, 21.3, 20.8, 20.6. **HPLC Analysis:** 92% ee (*t*_{major} = 13.1 min, *t*_{minor} = 11.0 min) and 72% ee (*t*_{major} = 19.2 min, *t*_{minor} = 21.0 min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, λ = 254 nm. **HRMS (+ESI-TOF) *m/z*:** calcd. For C₂₃H₂₁ClNO₂ [M+H]⁺ 378.1255, found 378.1263.



(4R,6R)-8-oxo-2-phenyl-4-(m-tolyl)-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3m): Colourless sticky solid; 73% (52.2 mg); 1.6:1 dr. ^1H NMR (600 MHz, CDCl_3) δ 7.75 (d, $J = 7.1$ Hz, 2H), 7.64 (d, $J = 7.0$ Hz, 3H), 7.47 – 7.39 (m, 8H), 7.30 – 7.26 (m, 3H), 7.15 – 7.10 (m, 7H), 3.74 (dd, $J = 11.7, 6.5$ Hz, 1H), 3.64 (dd, $J = 12.0, 6.5$ Hz, 2H), 2.98 (d, $J = 14.3$ Hz, 2H), 2.68 (d, $J = 14.7$ Hz, 1H), 2.54 (dd, $J = 33.5, 13.9$ Hz, 5H), 2.48 – 2.40 (m, 4H), 2.38 (s, 8H), 2.22 – 2.18 (m, 4H), 2.13 – 1.97 (m, 5H), 1.94 – 1.86 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ 208.0, 207.5, 164.3, 164.0, 140.8, 140.7, 138.9, 133.3, 133.1, 129.1, 128.7, 128.6, 128.5, 128.4, 124.9, 124.9, 119.6, 119.4, 87.9, 87.3, 82.3, 82.0, 52.8, 47.6, 41.7, 41.2, 41.0, 40.7, 38.4, 38.0, 36.3, 30.8, 21.72, 20.8, 20.6. **HPLC Analysis**: 94% ee ($t_{\text{major}} = 12.2$ min, $t_{\text{minor}} = 15.4$ min) and 92% ee ($t_{\text{major}} = 20.1$ min, $t_{\text{minor}} = 13.3$ min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, $\lambda = 254$ nm. **HRMS (+ESI-TOF) m/z** : calcd. For $\text{C}_{23}\text{H}_{24}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 358.1802, found 358.1813.



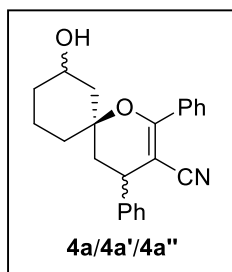
(4S,6R)-4-(2,6-dichlorophenyl)-8-oxo-2-phenyl-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3n): Off white semi solid; 65% (47.9 mg); 1.6:1 dr. ^1H NMR (400 MHz, CDCl_3) δ 7.73 (d, $J = 7.0$ Hz, 2H), 7.65 – 7.60 (m, 3H), 7.45 – 7.39 (m, 8H), 7.37 (t, $J = 8.9$ Hz, 5H), 7.20 (t, $J = 8.1$ Hz, 3H), 4.79 (dd, $J = 12.2, 6.7$ Hz, 1H), 4.70 (dd, $J = 12.2, 6.7$ Hz, 2H), 3.03 (d, $J = 14.3$ Hz, 2H), 2.73 (d, $J = 14.6$ Hz, 1H), 2.57 (dd, $J = 17.6, 14.6$ Hz, 5H), 2.51 – 2.36 (m, 5H), 2.36 – 2.22 (m, 3H), 2.13 (dd, $J = 17.5, 6.1$ Hz, 3H), 2.09 – 1.93 (m, 7H). ^{13}C NMR (150 MHz, CDCl_3) δ 207.9, 207.4, 163.5, 163.5, 136.3, 136.2, 135.2, 135.1, 134.3, 134.2, 133.4, 133.1, 131.0, 130.7, 129.5, 128.9, 128.6, 128.5, 128.3, 119.0, 118.8, 86.2, 85.7, 82.2, 82.0, 52.9, 47.6, 41.0, 40.7, 36.4, 34.6, 34.3, 34.2, 33.5, 30.9, 20.8, 20.6. **HPLC Analysis**: 96% ee ($t_{\text{major}} = 20.6$ min, $t_{\text{minor}} = 28.2$ min) and 96% ee ($t_{\text{major}} = 17.9$ min, $t_{\text{minor}} = 16.1$ min); Chiralpak ID Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, $\lambda = 254$ nm. **HRMS (+ESI-TOF) m/z** : calcd. For $\text{C}_{23}\text{H}_{20}\text{Cl}_2\text{NO}_2$ $[\text{M}+\text{H}]^+$ 412.0866, found 412.0869.



(4R,6R)-4-mesityl-8-oxo-2-phenyl-1-oxaspiro[5.5]undec-2-ene-3-carbonitrile (3o): Brown sticky solid; 67% (51.6 mg); 1.6:1 dr. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.76 (t, $J = 6.9$ Hz, 1H), 7.70 (d, $J = 8.1$ Hz, 1H), 7.59 – 7.57 (m, 3H), 7.47 – 7.35 (m, 8H), 7.21 – 7.14 (m, 1H), 6.84 (s, 4H), 4.24 (dd, $J = 11.4, 7.7$ Hz, 1H), 4.16 (dd, $J = 12.2, 7.0$ Hz, 2H), 2.98 (d, $J = 14.2$ Hz, 2H), 2.68 (d, $J = 14.6$ Hz, 1H), 2.60 – 2.48 (m, 5H), 2.42 (d, $J = 10.3$ Hz, 8H), 2.36 (d, $J = 5.3$ Hz, 6H), 2.33 (s, 6H), 2.23 (s, 9H), 2.15 – 1.91 (m, 12H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 207.9, 207.3, 162.6, 162.4, 137.0, 136.7, 136.5, 136.4, 136.3, 133.5, 133.2, 132.5, 131.9, 131.8, 131.0, 130.9, 129.9, 129.8, 128.7, 128.3, 128.1, 128.0, 119.3, 119.1, 88.8, 88.2, 82.4, 82.0, 53.1, 48.0, 41.0, 40.7, 36.7, 36.1, 35.7, 32.9, 32.5, 31.1, 29.9, 28.4, 22.9, 21.1, 21.0, 20.9, 20.6, 20.2, 20.1. **HPLC Analysis:** 96% ee ($t_{\text{major}} = 16.1$ min, $t_{\text{minor}} = 10.7$ min) and 75% ee ($t_{\text{major}} = 8.8$ min, $t_{\text{minor}} = 11.9$ min); Chiralpak IB Column, n-Hexane/EtOH = 90/10, flow rate 1.0 mL/min, 25 °C, $\lambda = 254$ nm. **HRMS (+ESI-TOF)** m/z : calcd. For $\text{C}_{26}\text{H}_{28}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 386.2115, found 386.2114.

General procedure for the preparation of derivatives 4:

To a solution of compound **3a** (68.6 mg, 0.2 mmol) in EtOH (0.4 mL) was added NaBH_4 (15 mg, 0.4 mmol) at 0 °C and the mixture was stirred for 5 h. The reaction mixture was diluted with DCM (3 mL), and the organic layer was washed with brine (2×2 mL). Then organic layer was dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography using EtOAc–hexane (30–40%) as eluent to afford the compound **4**.



4 (2S,3S)-5-amino-1'-benzyl-4'-(3-methoxyphenyl)-2'-oxo-3-phenyl-3H-spiro[furan-2,3'-indoline]-4-carbonitrile was obtained as a pale yellow sticky solid in 81% yield (20.2 mg) after column chromatography. $^1\text{H NMR}$ (400 MHz, DMSO-d_6) δ 8.02 (s, 4H), 7.67 (s, 3H), 7.40 – 7.33 (m, 10H), 7.31 – 7.22 (m, 6H), 7.19 – 7.11 (m, 4H), 7.04 (t, $J = 3.4$ Hz, 6H), 6.95 (d, $J = 7.0$ Hz, 3H), 6.89 (d, $J = 8.1$ Hz, 1H), 6.73 (d, $J = 7.8$ Hz, 1H), 6.53 – 6.48 (m, 2H), 5.23 (s, 0.8H), 4.96 (dd, $J = 35.3, 15.6$ Hz, 2H), 4.86 (s, 1H), 4.74 (d, $J = 16.0$ Hz, 0.8H), 4.29 (d, $J = 16.0$ Hz, 0.8H), 3.74 (s, 6.6H). $^{13}\text{C NMR}$ (150 MHz, DMSO-d_6) δ 174.1, 170.2, 168.2, 167.8, 158.5, 144.8, 144.1, 135.5, 135.3, 134.7, 134.4, 133.0,

132.0, 128.8, 128.7, 128.7, 128.4, 128.3, 128.1, 127.8, 127.8, 127.6, 127.4, 127.2, 127.0, 126.8, 126.5, 126.3, 125.2, 124.0, 123.8, 119.4, 119.1, 118.9, 118.7, 118.5, 115.7, 109.0, 108.9, 88.8, 88.7, 55.8, 54.8, 53.3, 51.6, 51.5, 43.3, 42.6. **HPLC Analysis:** 75% ee ($t_{\text{major}} = 80.3$ min, $t_{\text{minor}} = 89.8$ min) and 38% ee ($t_{\text{major}} = 72.5$ min, $t_{\text{minor}} = 104.5$ min); Daicel Chiralpak IF Column, n-Hexane/ i-PrOH = 90/10, flow rate 1.0 mL/min, 25 °C, $\lambda = 254$ nm. **FT-IR (thin film):** 3434, 2925, 2189, 1807, 1730, 1666, 1605, 1495, 1453, 1424, 1343, 1282, 1169, 1143, 1079, 1030, 863, 770, 700, 632, 580 cm^{-1} ; **ESI HRMS:** calcd. For $\text{C}_{32}\text{H}_{26}\text{N}_3\text{O}_3[\text{M}+\text{H}]^+$ 500.1969, found 500.1977.

9. Single crystal X-ray diffraction analysis of 3f:

CCDC No.	1903384
Empirical formula	$\text{C}_{23}\text{H}_{20}\text{BrNO}_2$
Formula weight	422.30
Crystal habit, colour	block/Colourless
Crystal size, mm^3	$0.33 \times 0.21 \times 0.11$
Temperature, T	296(2) K
Wavelength, λ (Å)	0.71073
Crystal system	orthorhombic
Space group	' $P 21 21 2$ '
Unit cell dimensions	$a = 13.351(4)$ Å $b = 25.715(7)$ Å $c = 5.7490(17)$ Å $\alpha = 90^\circ, \beta = 90^\circ, \gamma = 90^\circ$
Volume, V (Å ³)	1973.8(10)
Z	4
Calculated density, $\text{Mg} \cdot \text{m}^{-3}$	1.421
Absorption coefficient, μ (mm^{-1})	2.100
$F(000)$	864.0
θ range for data collection	1.584° to 25.048°
Limiting indices	$-15 \leq h \leq 15, -30 \leq k \leq 30, -6 \leq l \leq 6$
Reflection collected/unique	3497/ 1942
Max. and min. transmission	0.595/0.794
Refinement method	'SHELXT 2014/5 (Sheldrick, 2014)'
Data/restraints/parameters	3497/0/245

Goodness-of-fit on F^2	1.880
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.1147$, $wR2 = 0.2340$
R indices (all data)	$R1 = 0.1851$, $wR2 = 0.2477$
Ellipsoid contour % probability	40%

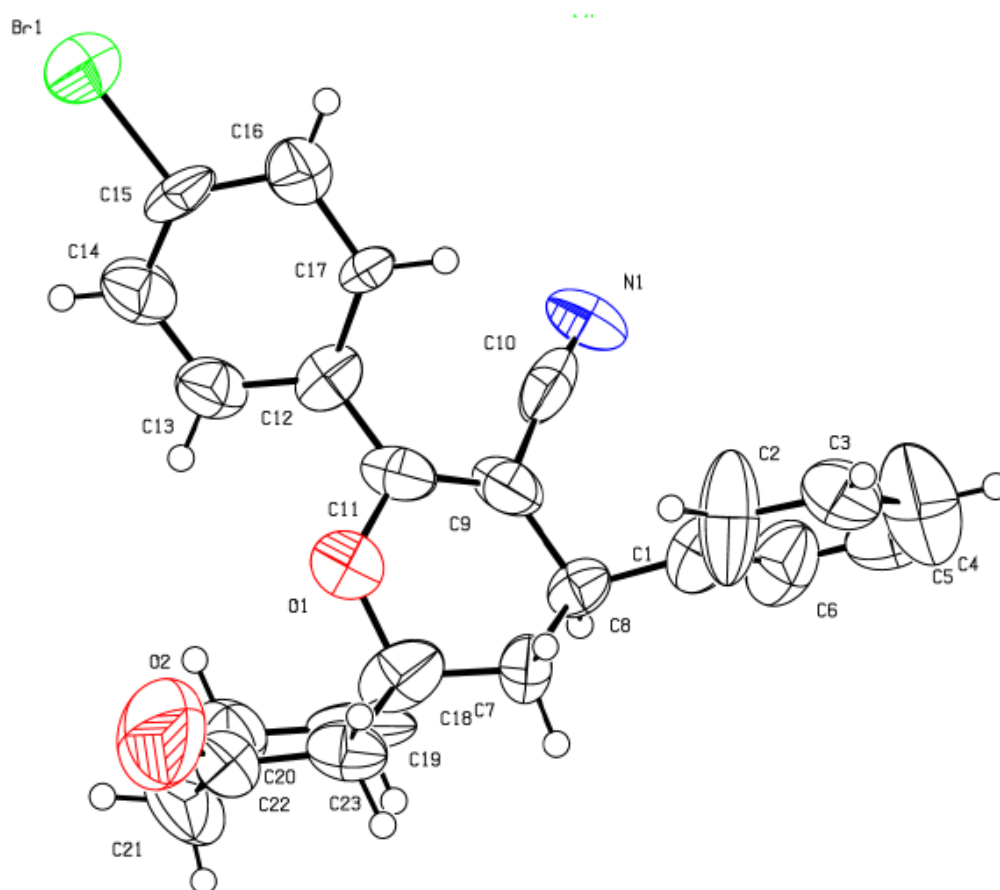
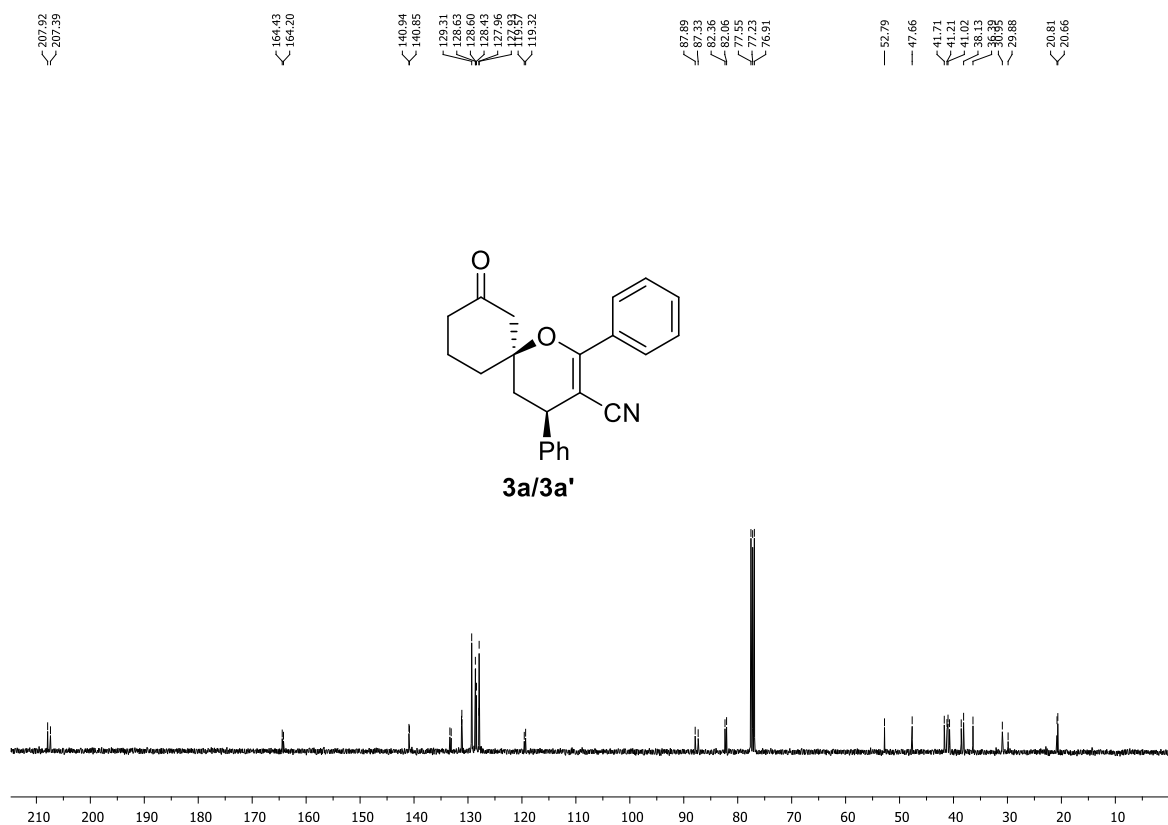
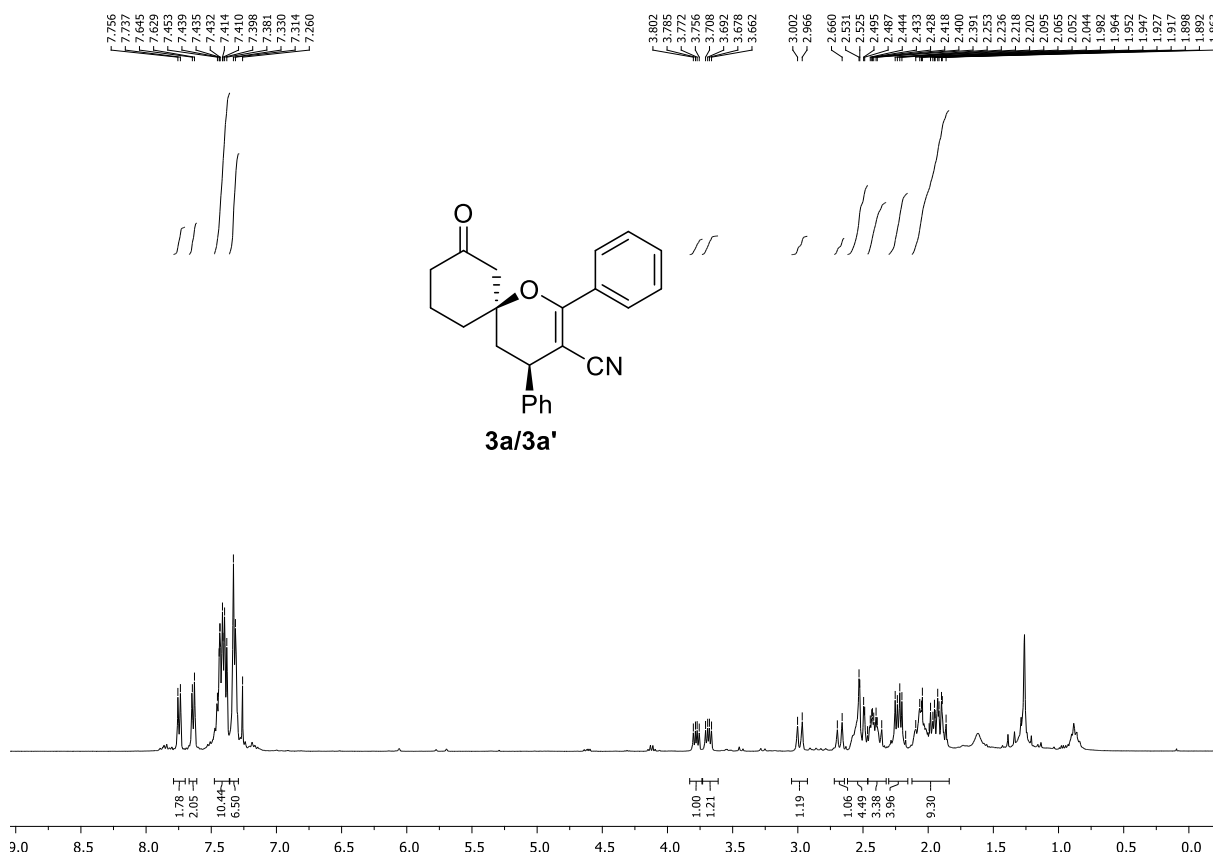
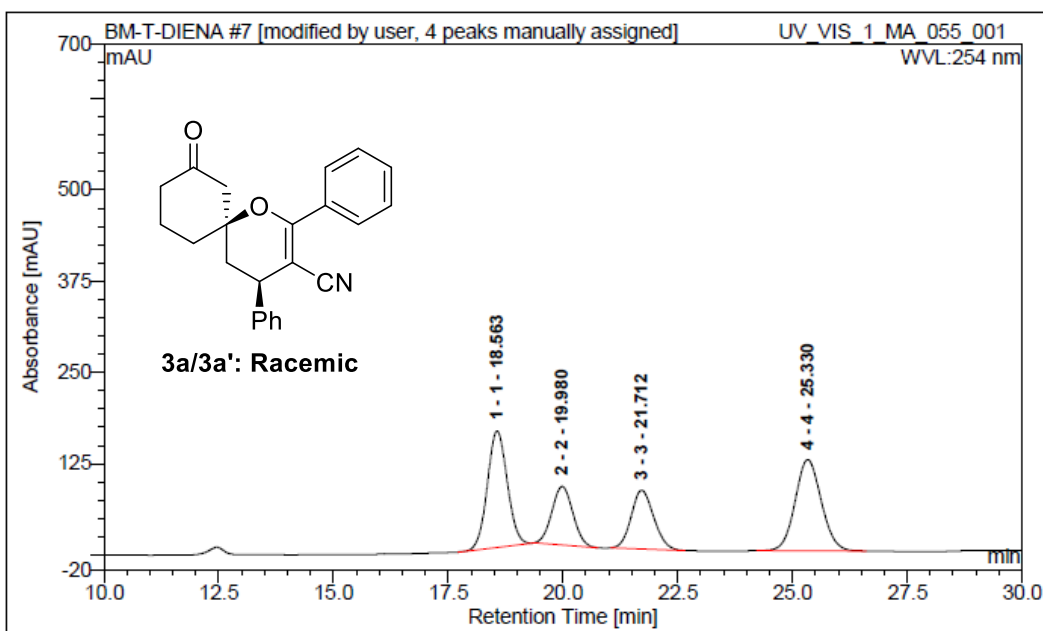


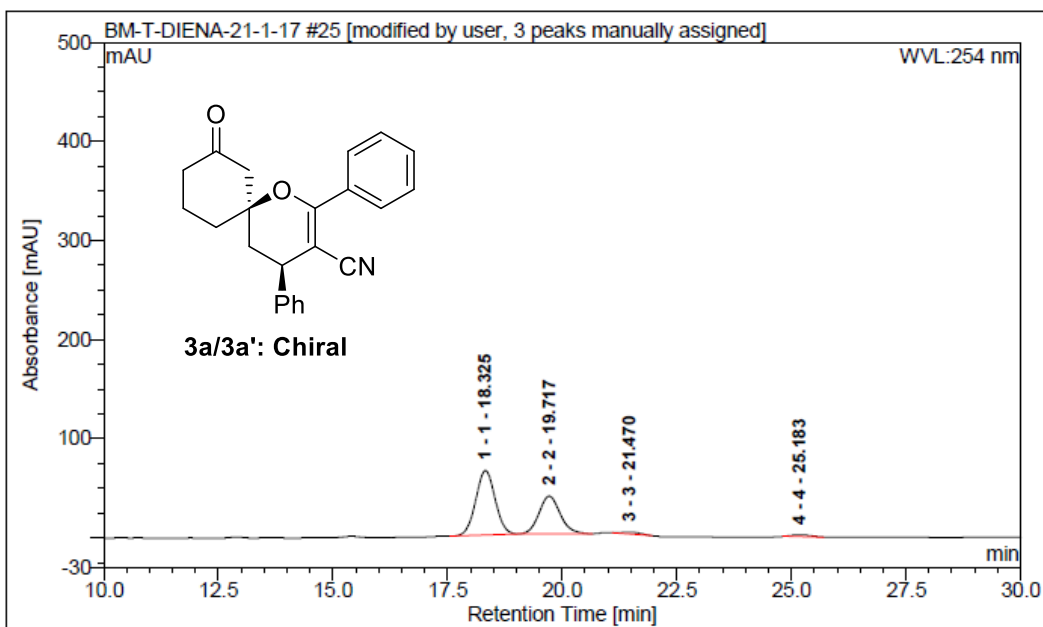
Figure S1: 3f (Ellipsoid contour % probability 40%)

10. NMR and HPLC spectra of the products:

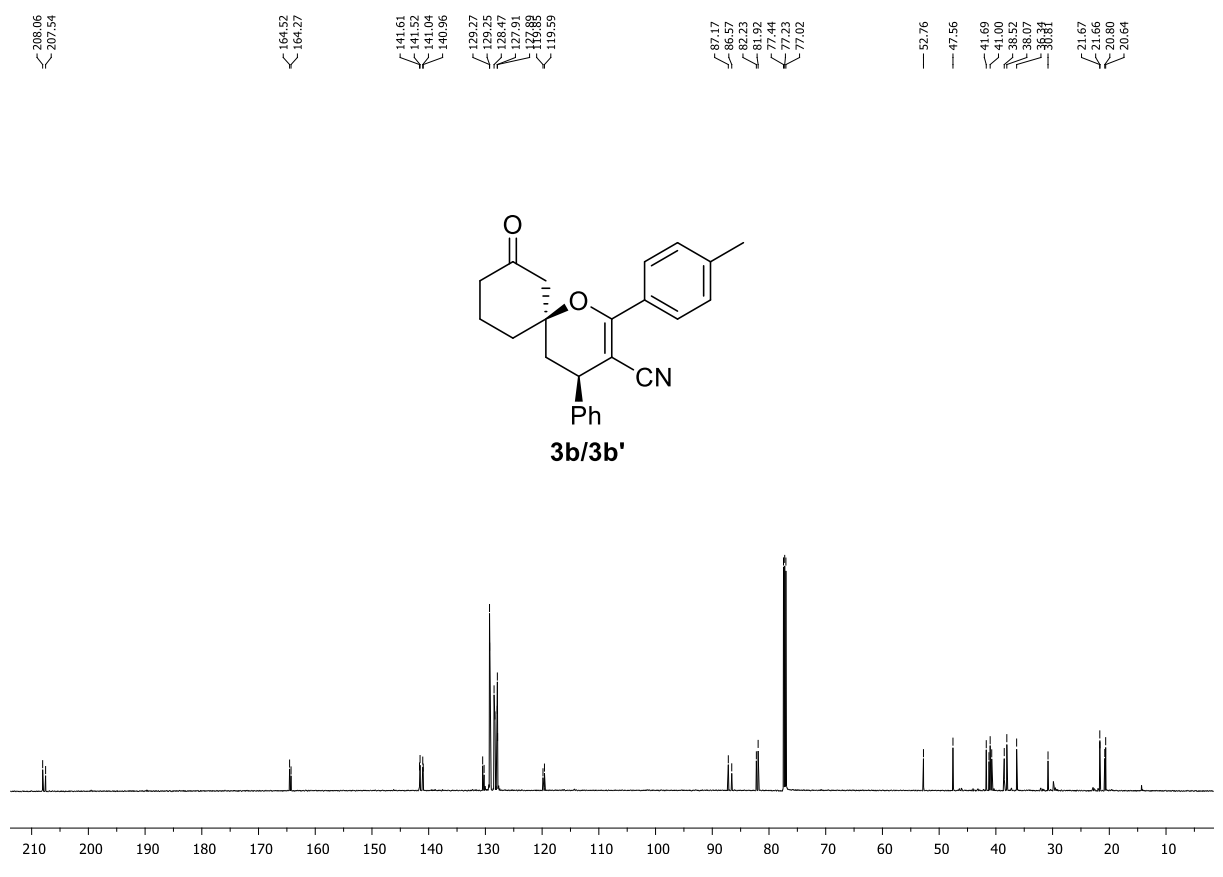
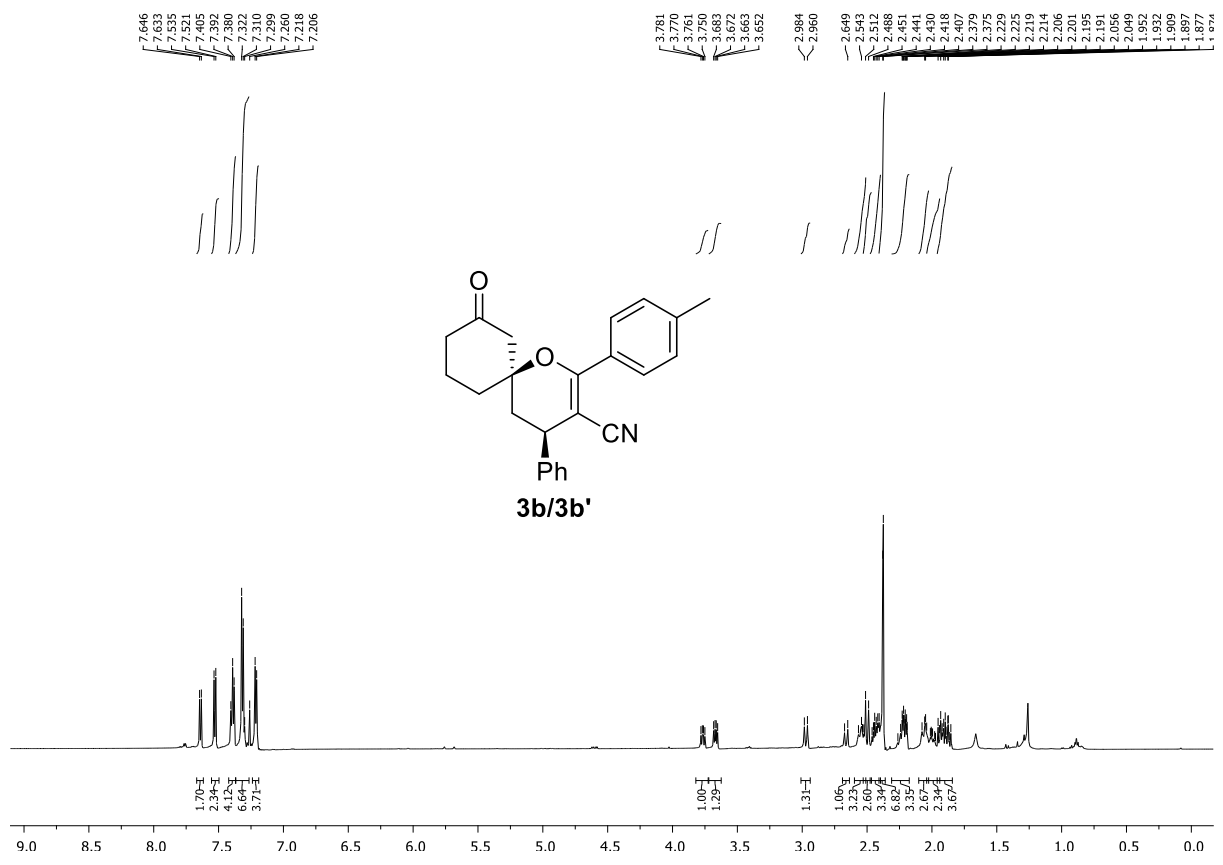


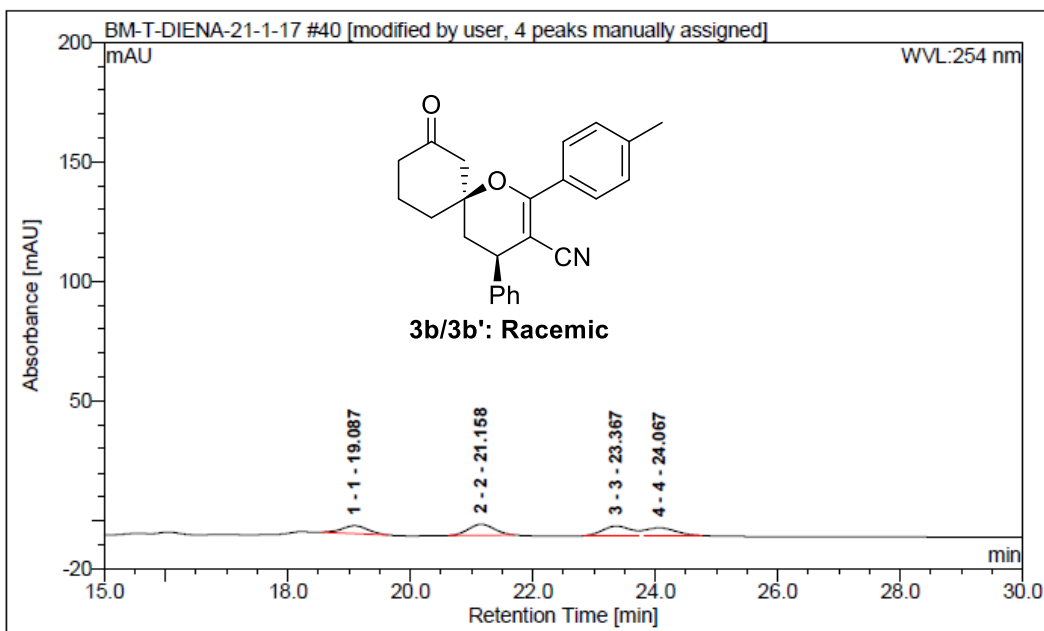


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	18.56	79.80707	31.85835223	159.2174	n.a.
2	2	19.98	42.30061	16.88606899	80.04608	n.a.
3	3	21.71	45.89463	18.32077239	80.48288	n.a.
4	4	25.33	82.504	32.93480638	124.775	n.a.

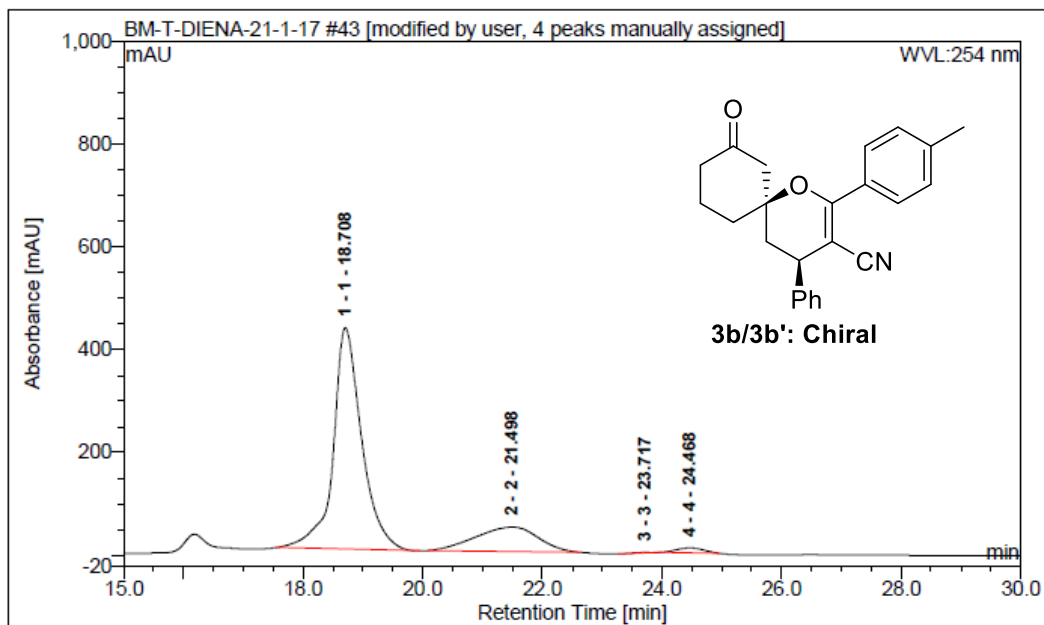


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	18.33	31.75854	59.07482984	64.96074	n.a.
2	2	19.72	20.23426	37.63824715	37.97543	n.a.
3	3	21.47	0.896025	1.666718432	1.8862	n.a.
4	4	25.18	0.871	1.620204579	1.770	n.a.

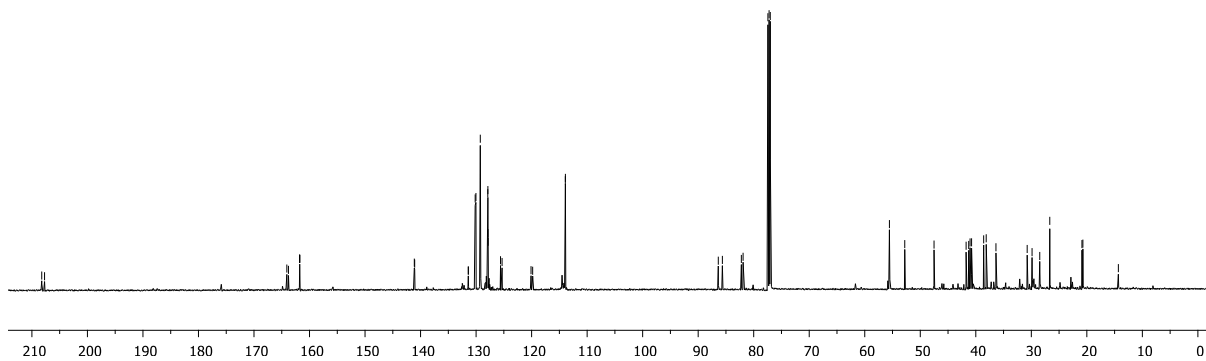
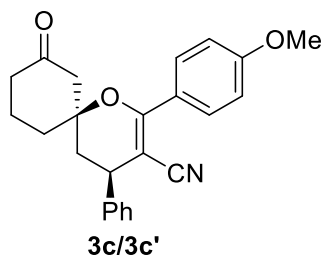
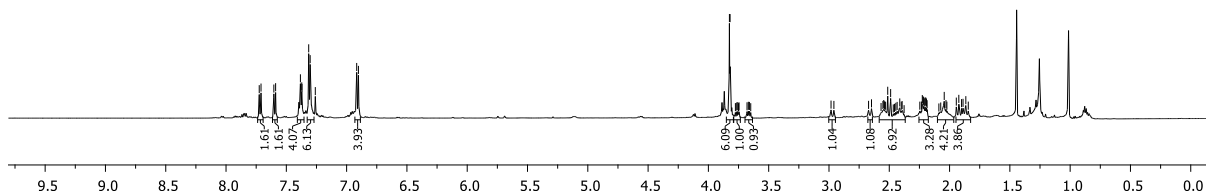
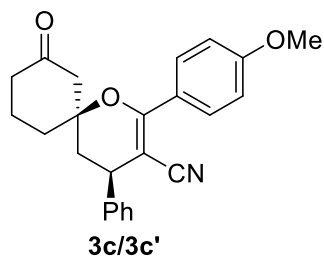
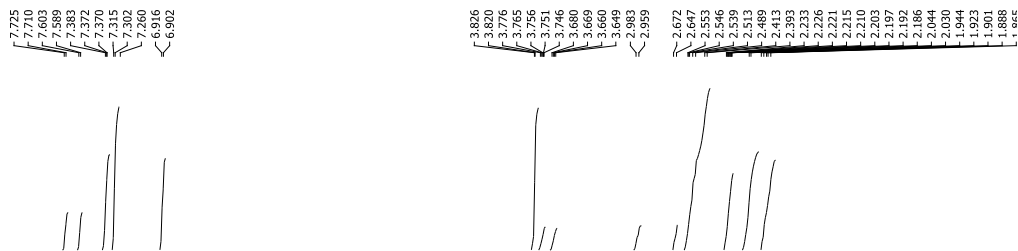


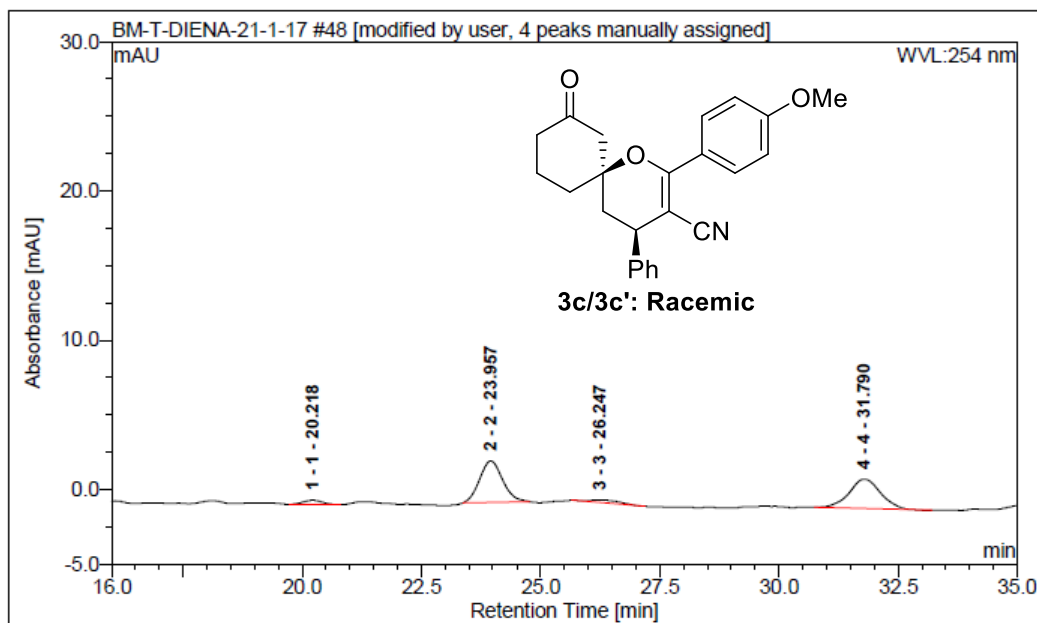


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	19.09	1.594548	20.98952367	3.25383	n.a.
2	2	21.16	2.194366	28.88511979	4.53413	n.a.
3	3	23.37	2.109307	27.76546296	3.9975	n.a.
4	4	24.07	1.699	22.35989358	3.217	n.a.

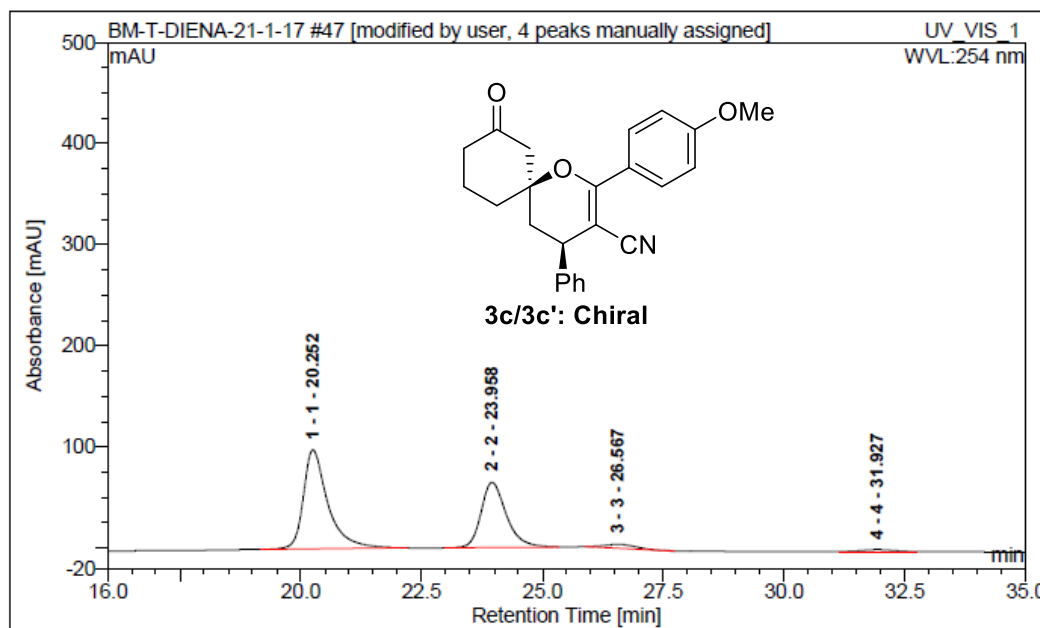


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	18.71	238.59	78.95456024	430.2533	n.a.
2	2	21.50	57.90265	19.16123058	47.77032	n.a.
3	3	23.72	0.379093	0.1254501005	1.04984	n.a.
4	4	24.47	5.315	1.758759084	9.818	n.a.

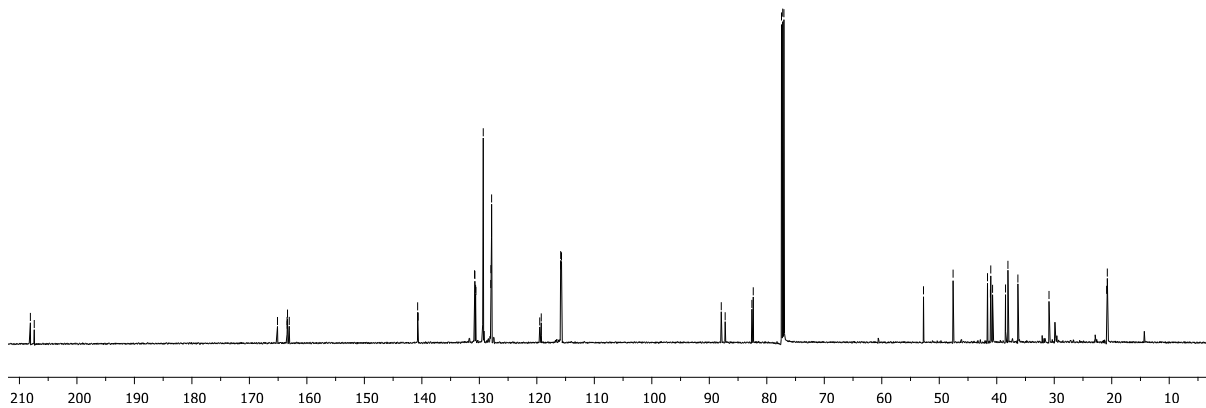
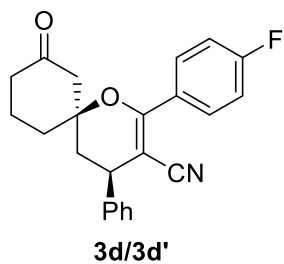
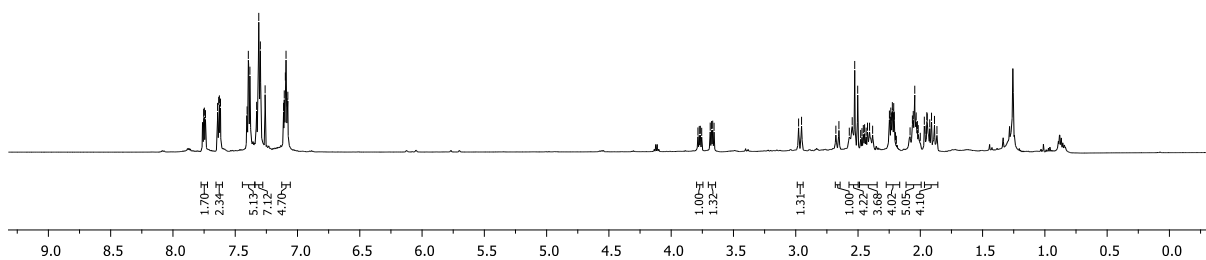
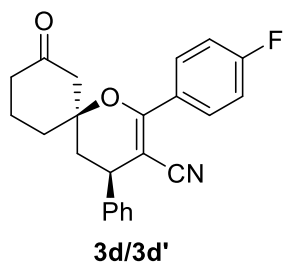
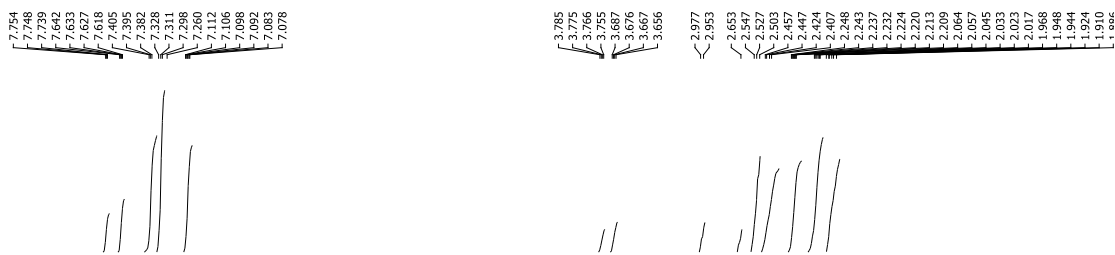


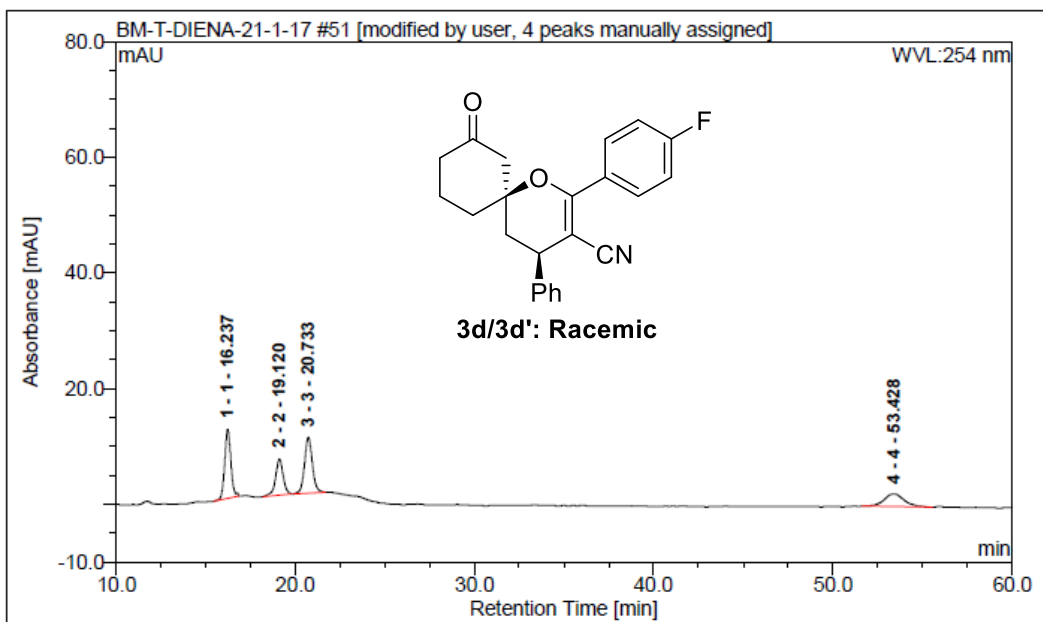


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	20.22	0.133987	4.024644474	0.28853	n.a.
2	2	23.96	1.547447	46.48156988	2.76799	n.a.
3	3	26.25	0.139169	4.180310237	0.18291	n.a.
4	4	31.79	1.509	45.31347541	1.969	n.a.

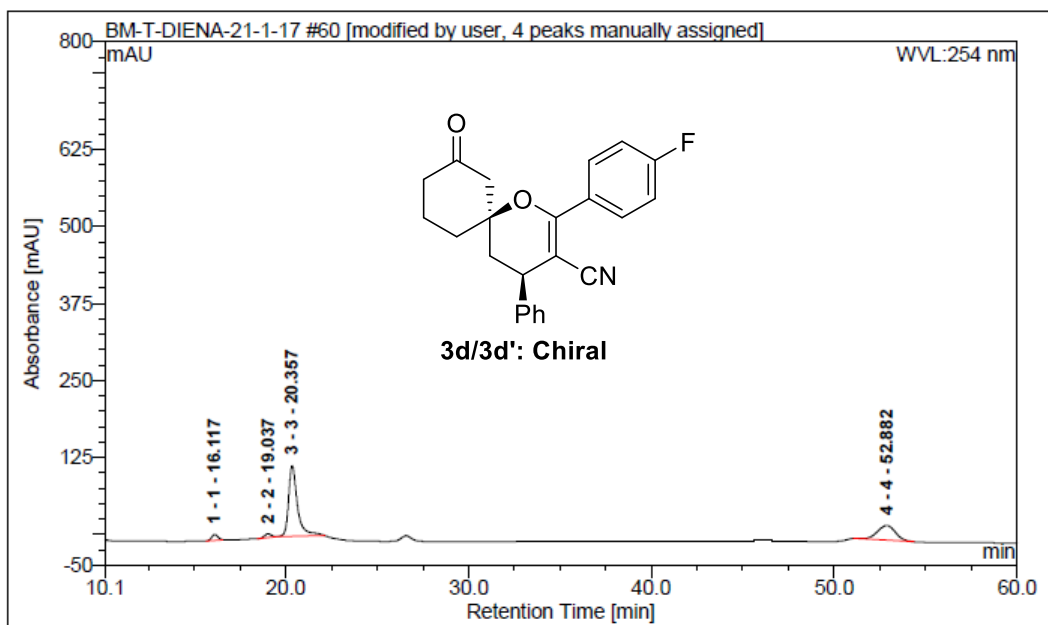


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	20.25	57.7782	57.11346864	97.95073	n.a.
2	2	23.96	39.06872	38.61924118	64.50036	n.a.
3	3	26.57	2.906363	2.872925355	3.91606	n.a.
4	4	31.93	1.411	1.394364821	1.912	n.a.

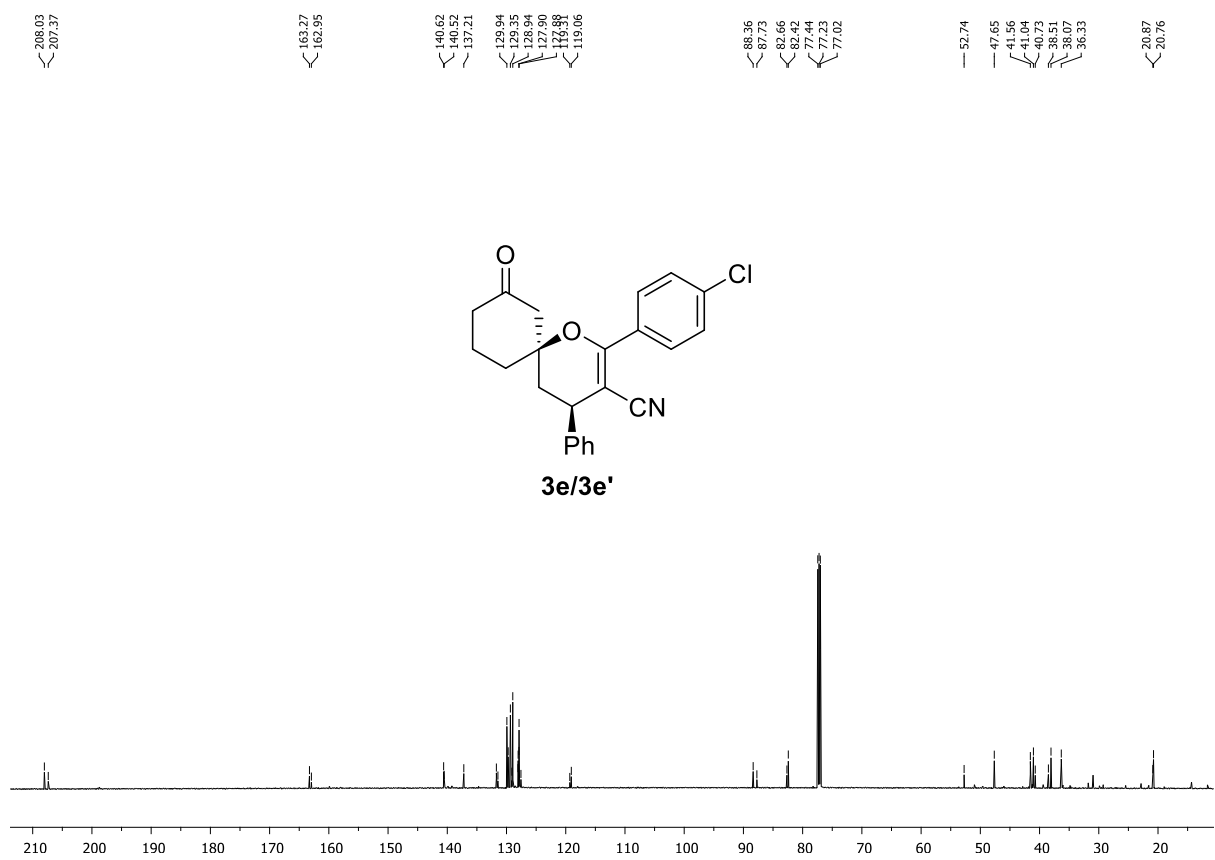
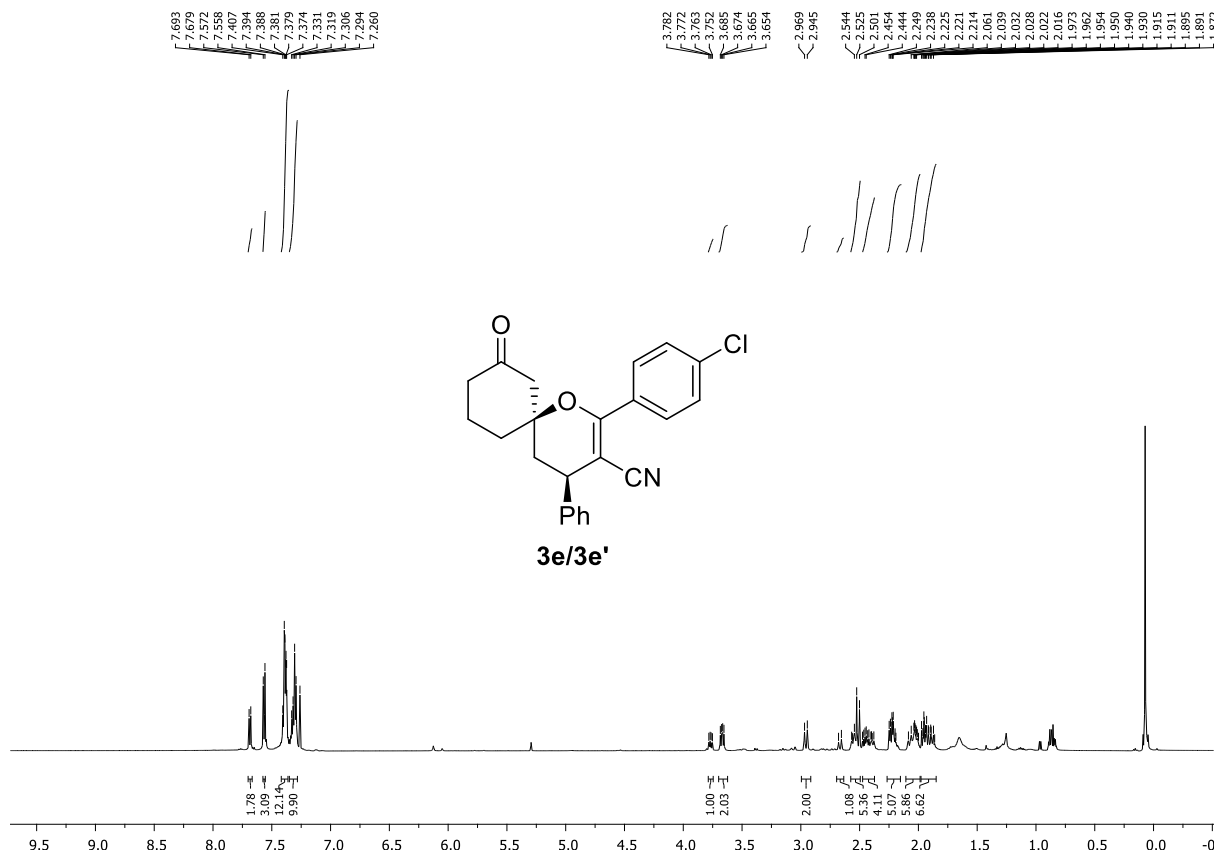


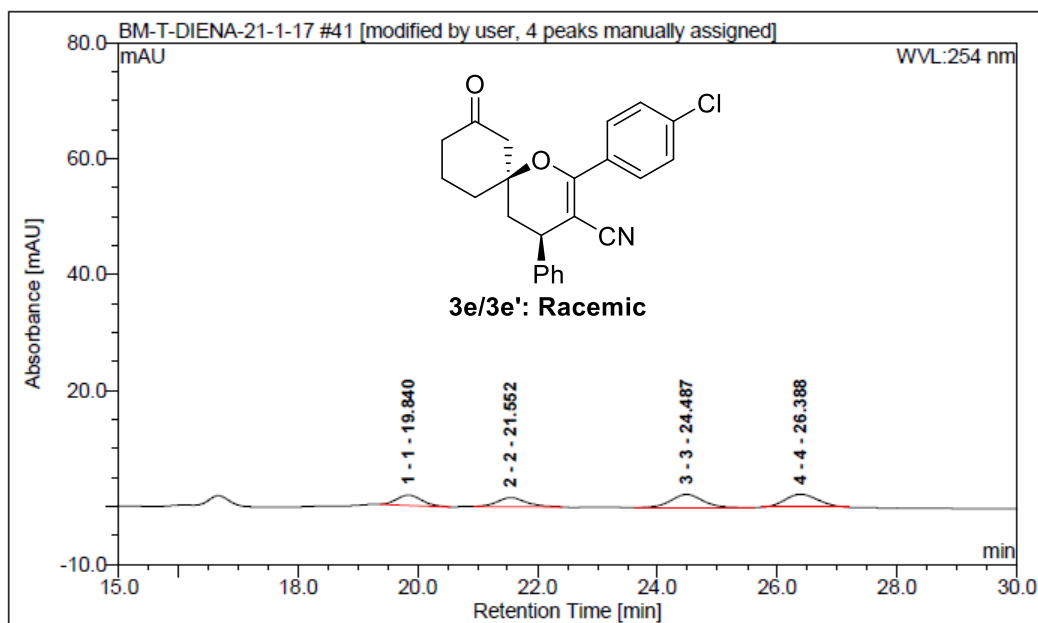


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 1		16.24	4.730537	30.52604994	11.92859	n.a.
2 2		19.12	3.047447	19.66510646	6.21168	n.a.
3 3		20.73	4.897125	31.60103996	9.6538	n.a.
4 4		53.43	2.822	18.20780364	2.217	n.a.

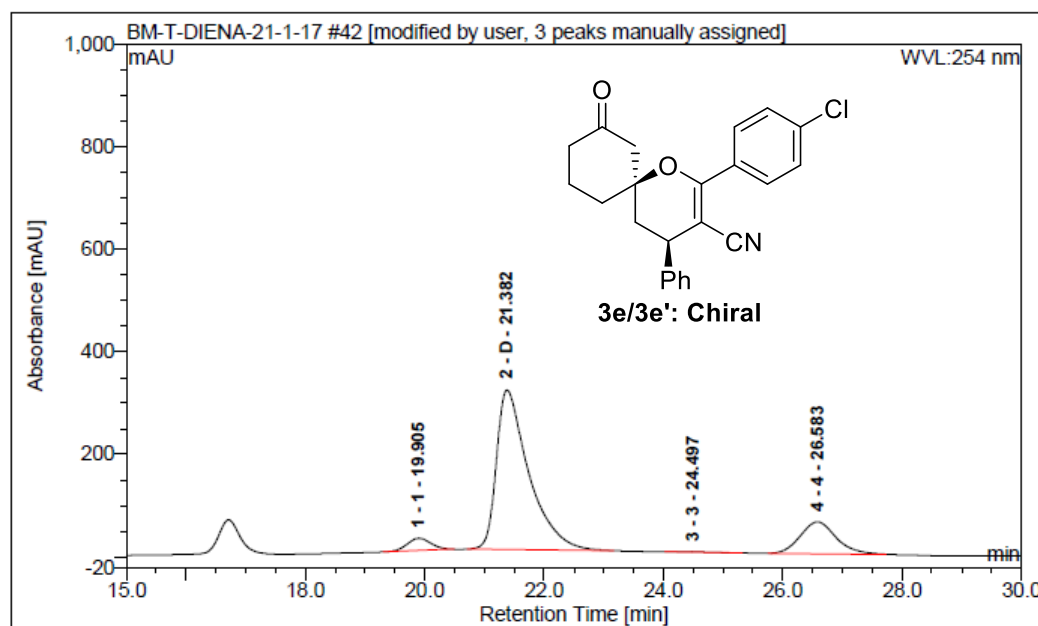


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 1		16.12	3.610299	3.66302283	9.66627	n.a.
2 2		19.04	2.520483	2.557291498	6.04261	n.a.
3 3		20.36	65.03682	65.98661086	114.5663	n.a.
4 4		52.88	27.393	27.79307481	24.041	n.a.

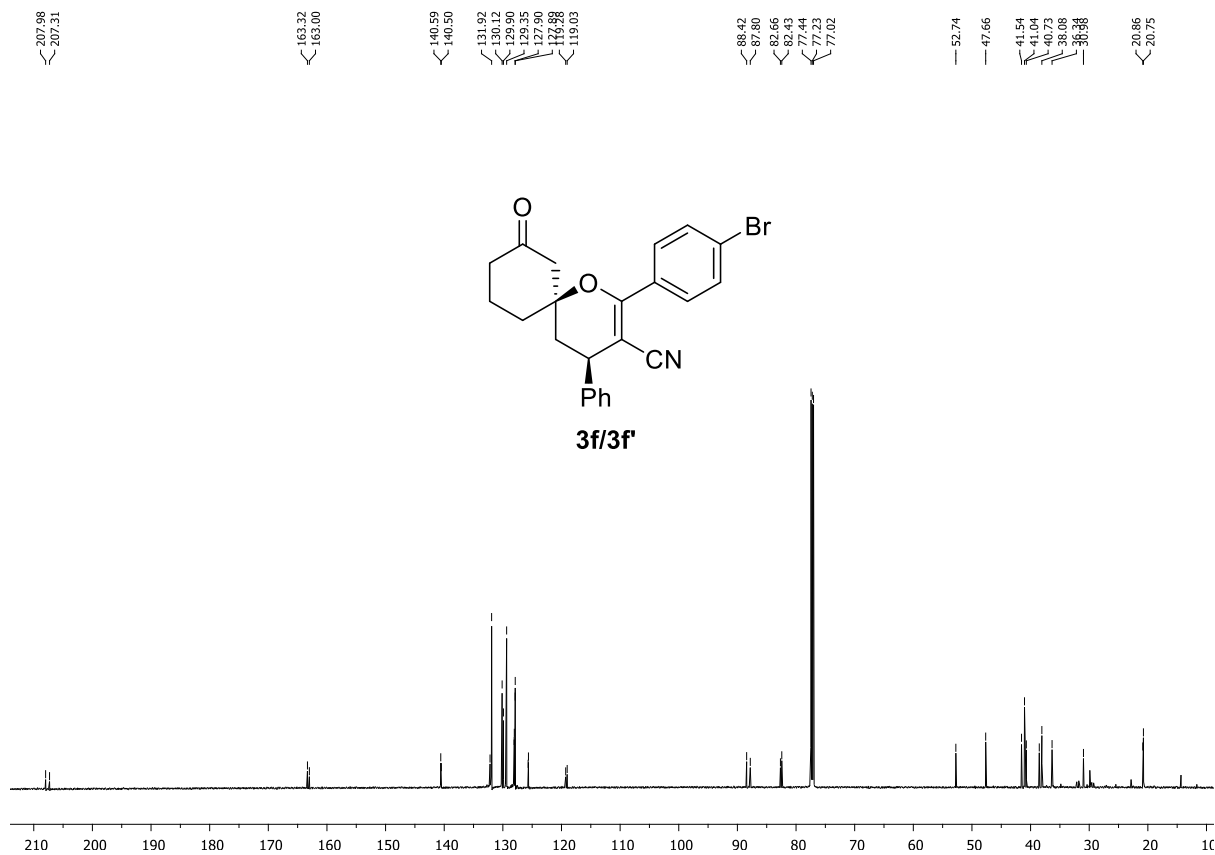
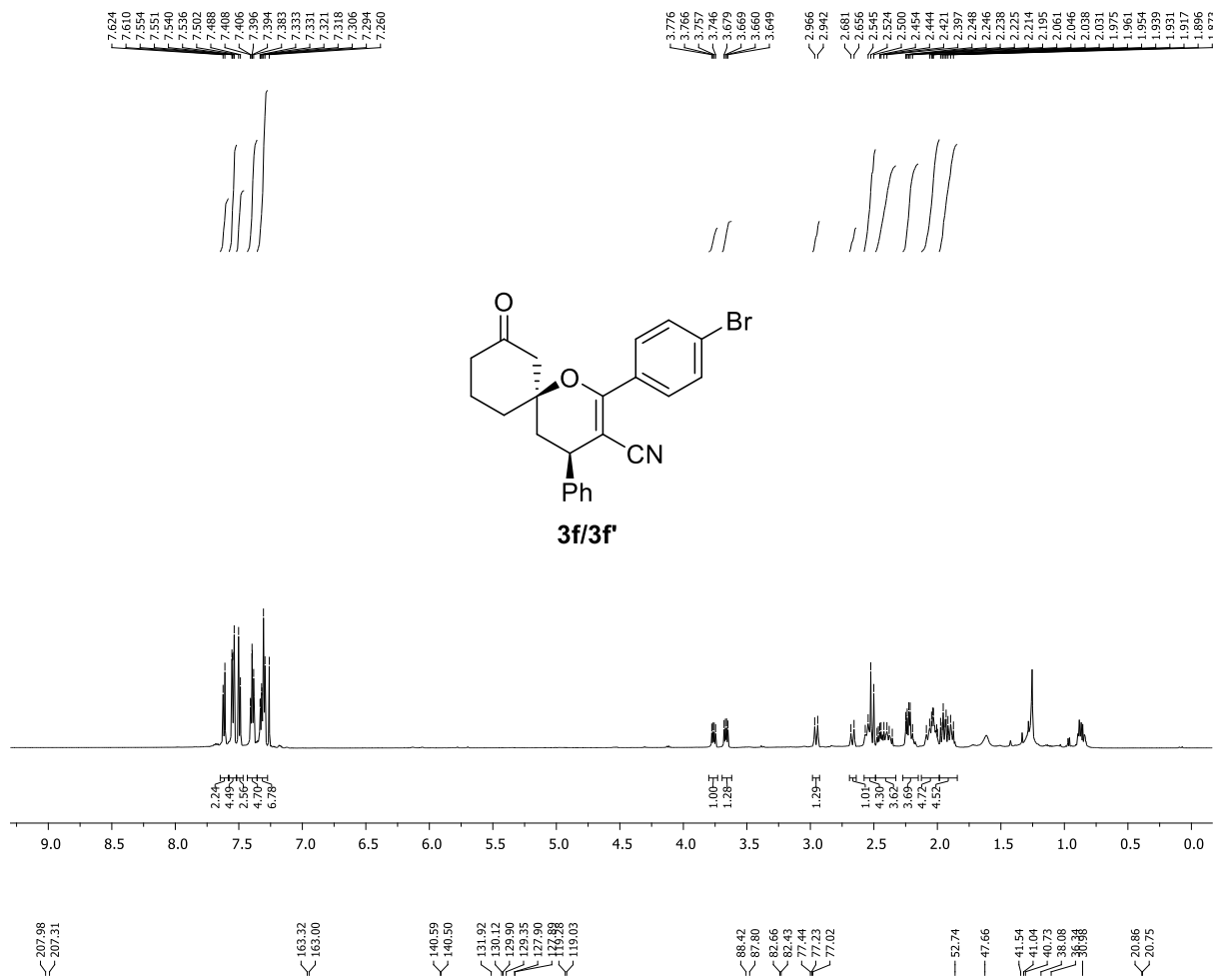


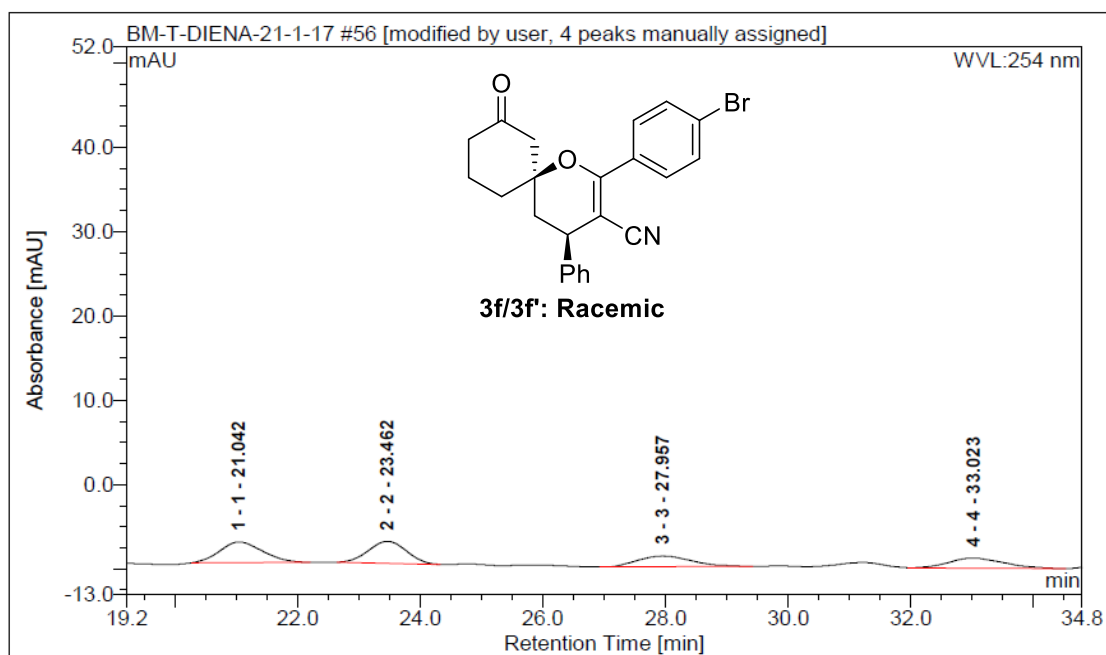


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 1		19.84	0.844403	18.418576	1.75928	n.a.
2 2		21.55	0.876887	19.12712469	1.5579	n.a.
3 3		24.49	1.407942	30.71078792	2.28438	n.a.
4 4		26.39	1.455	31.74351139	2.254	n.a.

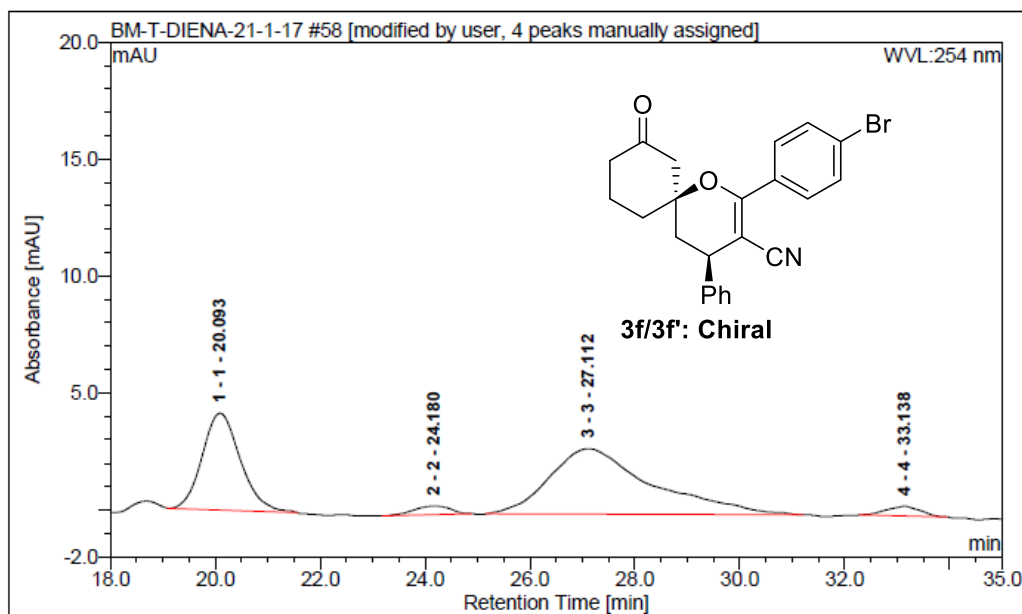


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 1		19.91	11.11645	4.439502408	24.00413	n.a.
2 D		21.38	195.4689	78.06310958	310.6909	n.a.
3 3		24.50	0.585916	0.2339932695	0.9088	n.a.
4 4		26.58	43.227	17.26339474	61.858	n.a.

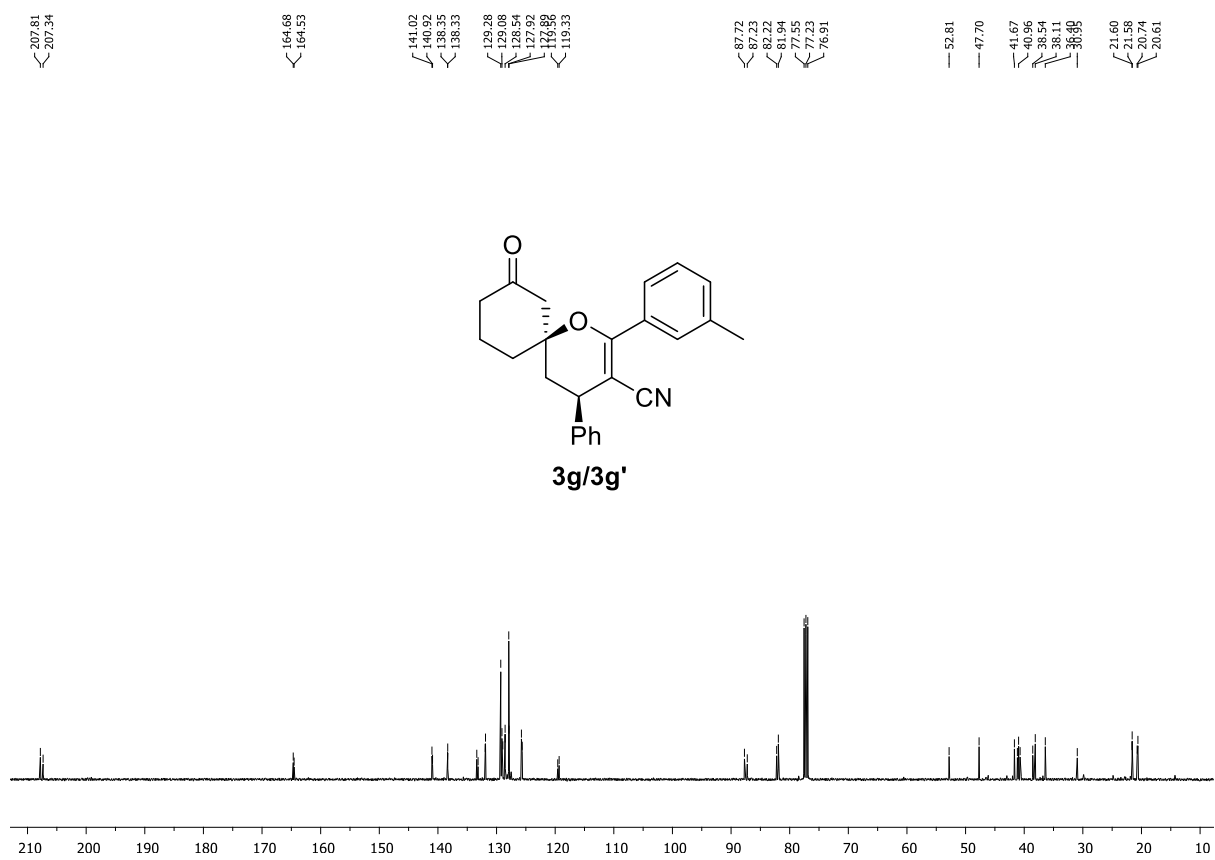
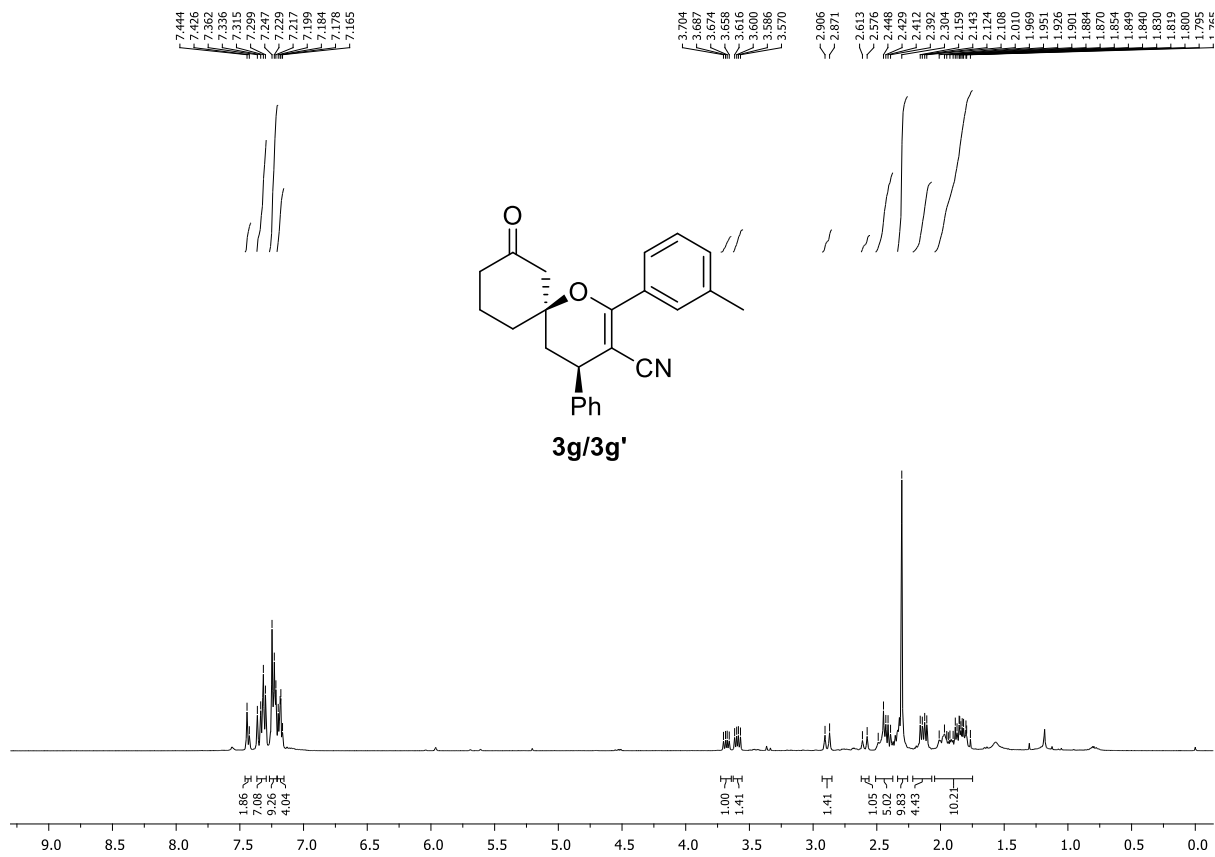


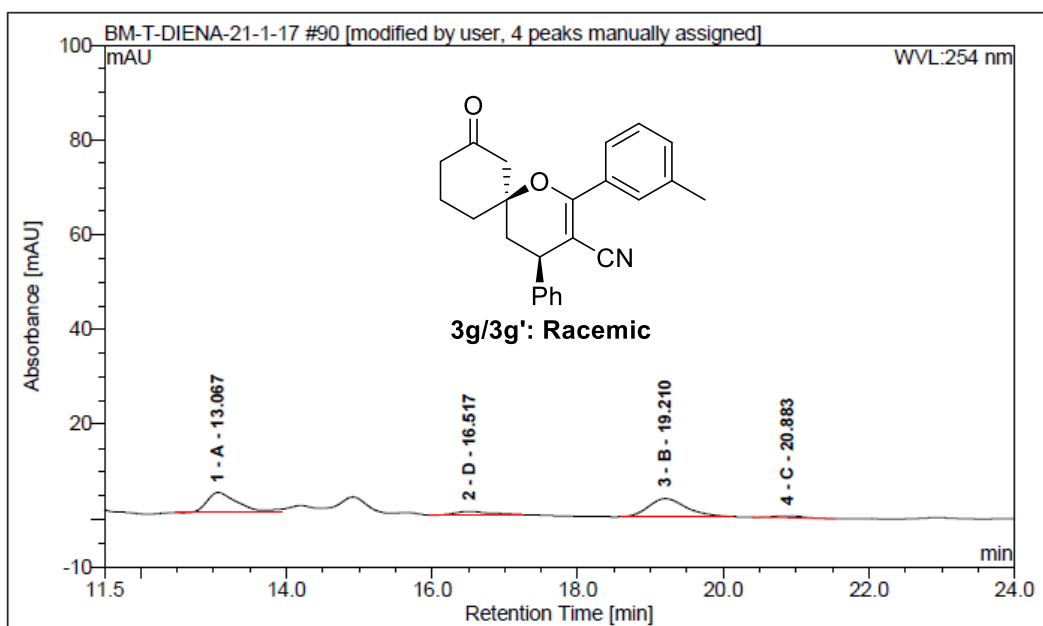


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	21.04	1.978355	30.93613704	2.45506	n.a.
2	2	23.46	1.8735	29.2964819	2.60797	n.a.
3	3	27.96	1.308113	20.45535746	1.25731	n.a.
4	4	33.02	1.235	19.3120236	1.207	n.a.

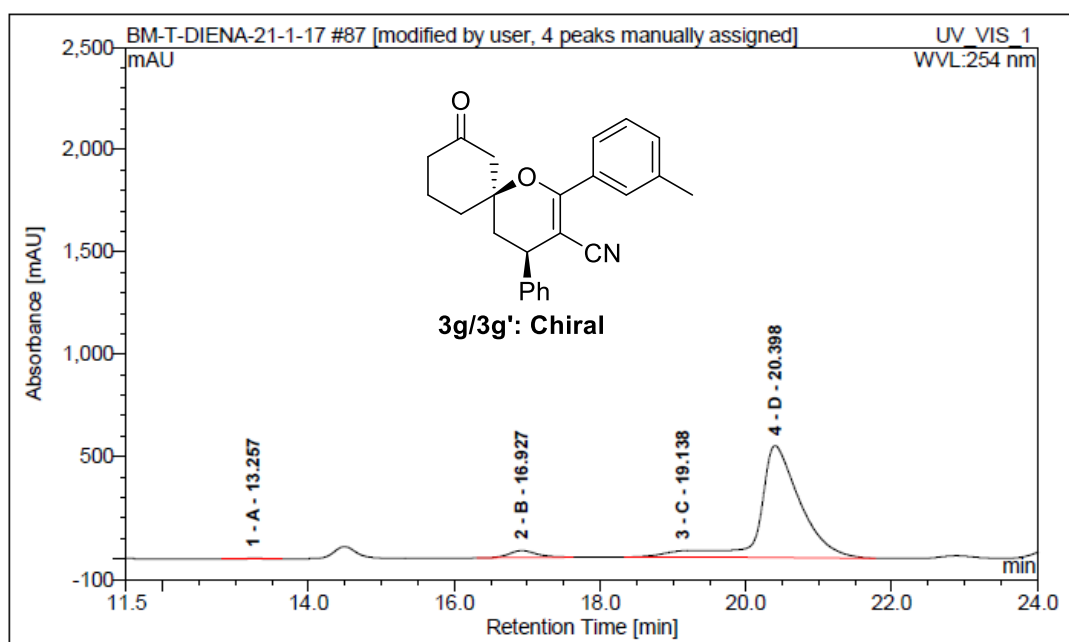


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	20.09	3.490626	33.56171739	4.13584	n.a.
2	2	24.18	0.299419	2.878860434	0.36728	n.a.
3	3	27.11	6.300948	60.58245081	2.79609	n.a.
4	4	33.14	0.310	2.976971365	0.412	n.a.





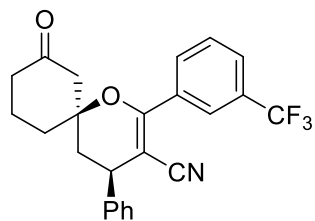
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	13.07	2.232972	43.54985386	4.29258	n.a.
2	D	16.52	0.395131	7.70626974	0.74232	n.a.
3	B	19.21	2.293397	44.72831933	3.81331	n.a.
4	C	20.88	0.206	4.015557074	0.461	n.a.



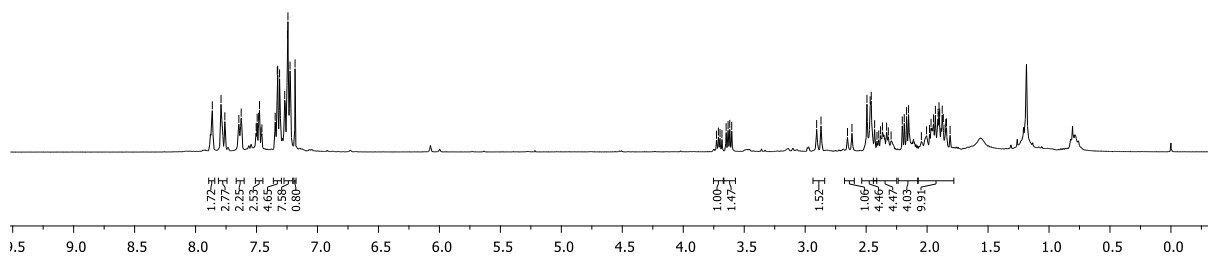
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	13.26	0.424038	0.1143335297	1.07083	n.a.
2	B	16.93	15.16459	4.08883479	34.24916	n.a.
3	C	19.14	36.71143	9.898517967	31.87549	n.a.
4	D	20.40	318.578	85.89831371	546.521	n.a.

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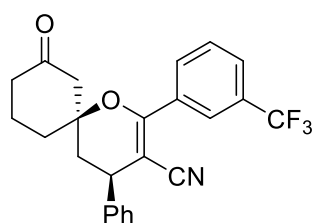
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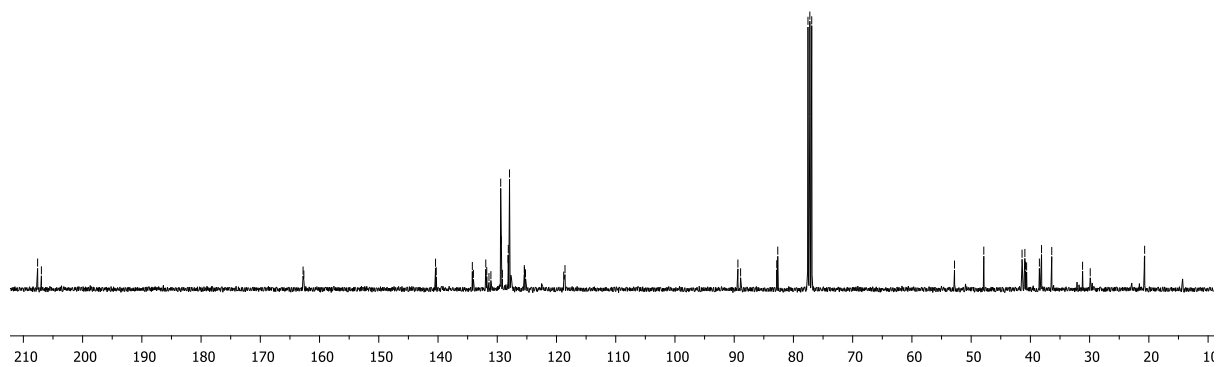
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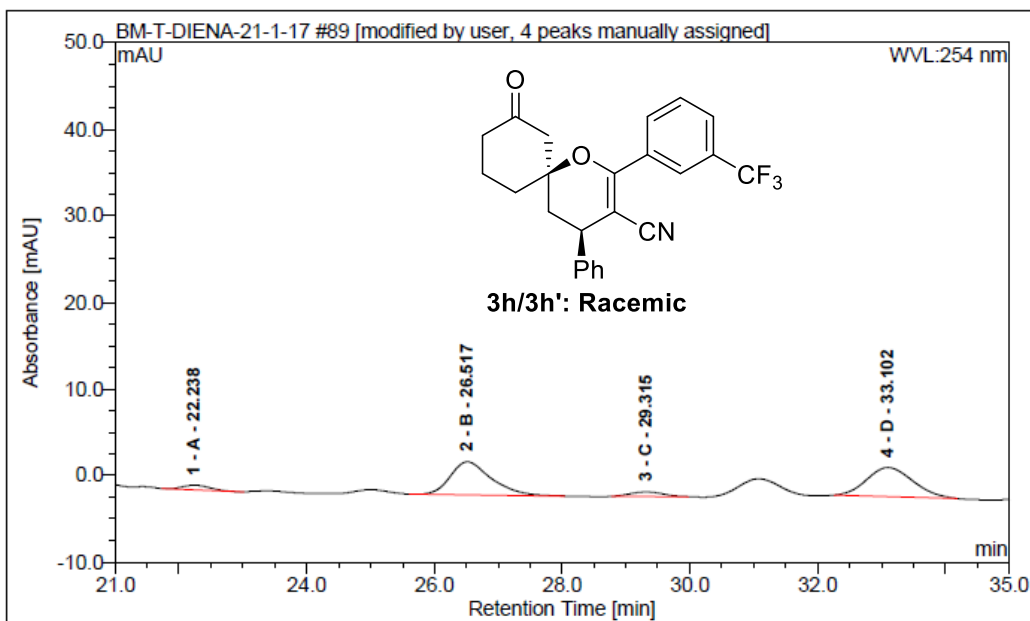
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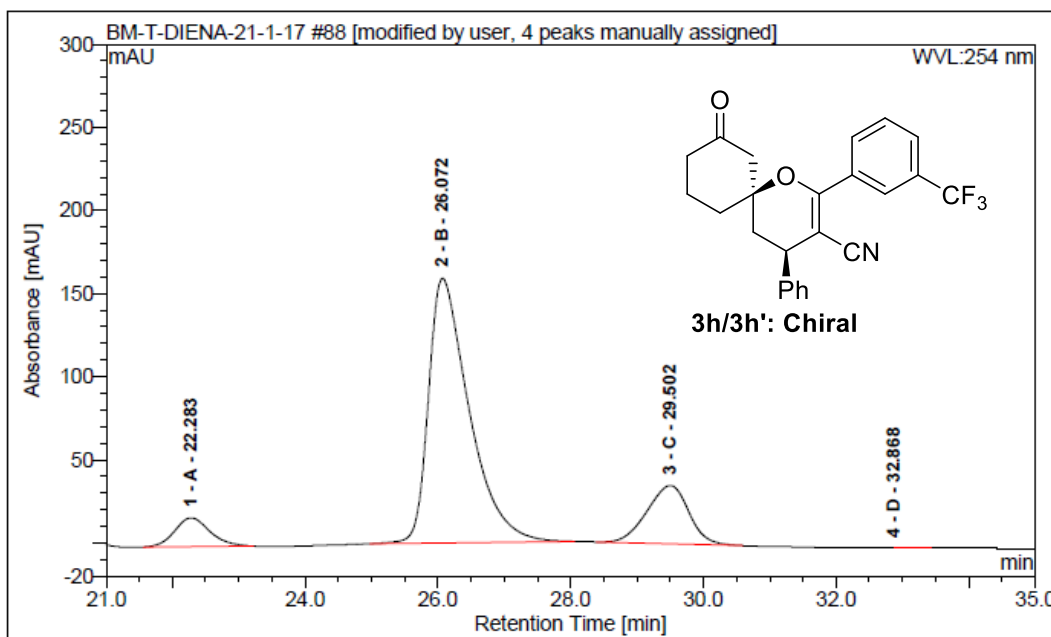


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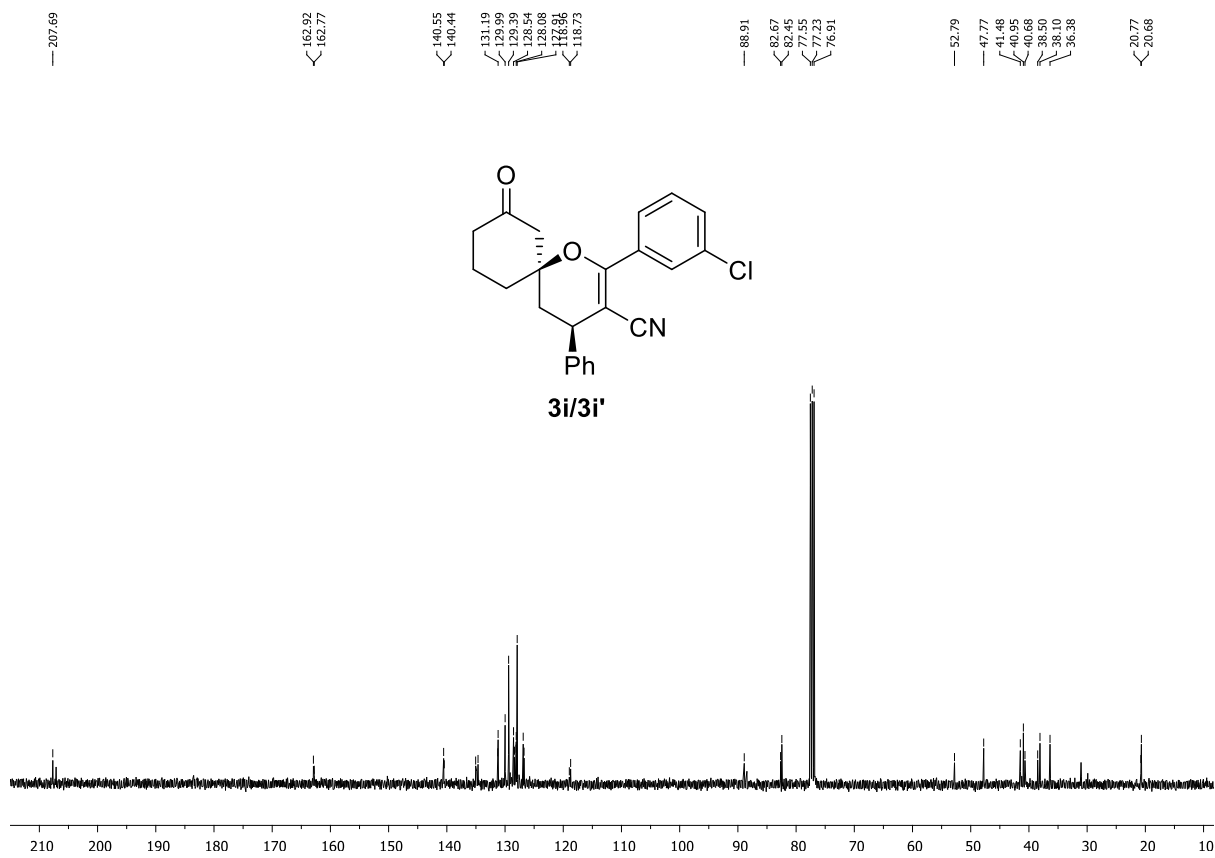
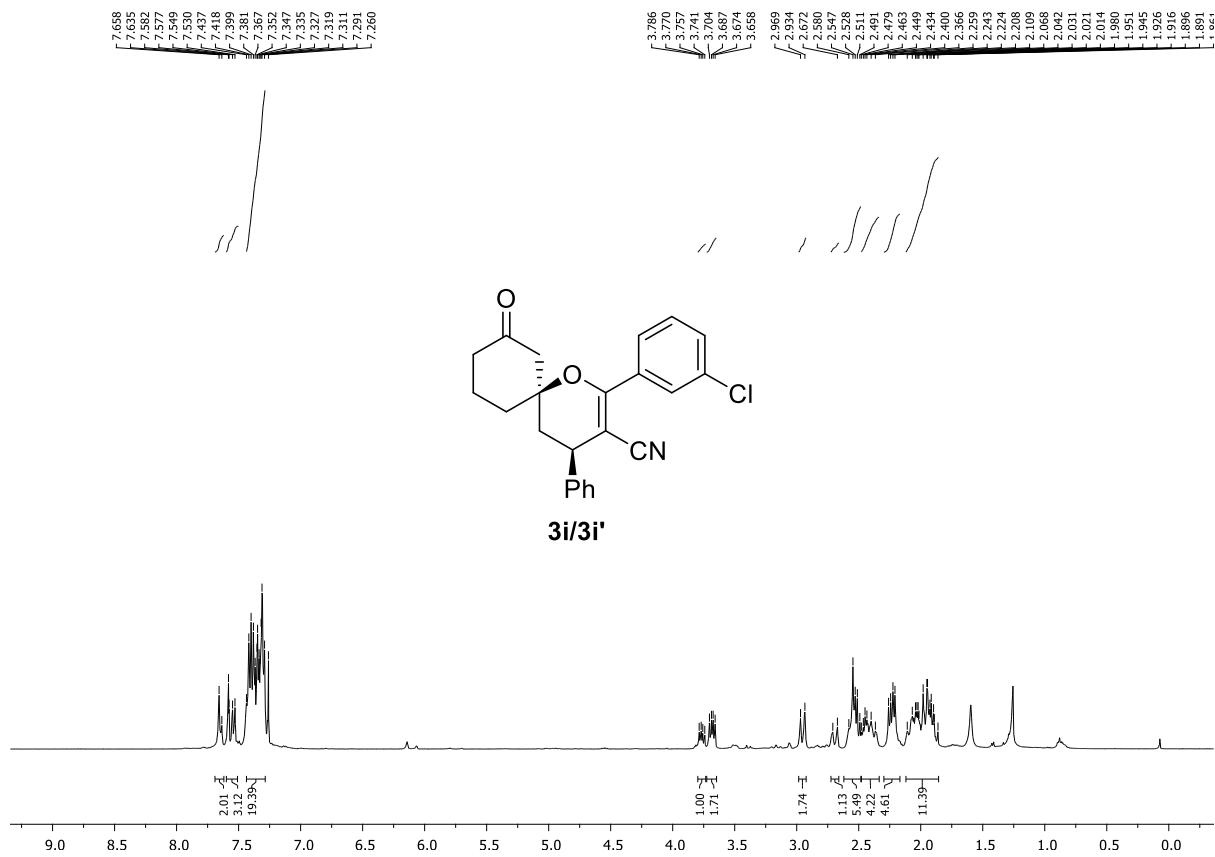


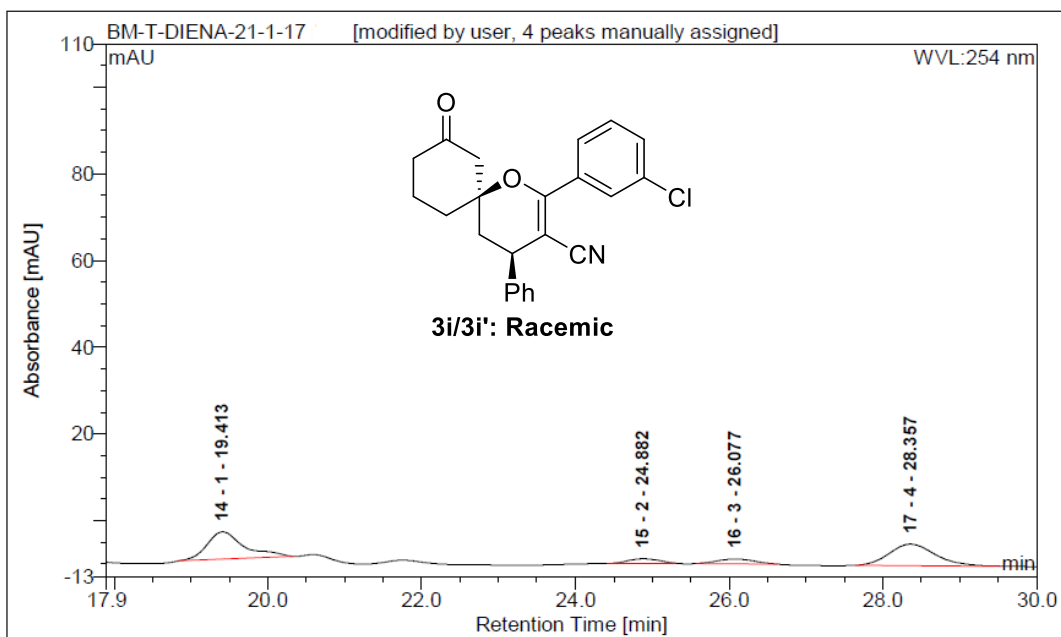


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 A		22.24	0.251598	4.06036797	0.52667	n.a.
2 B		26.52	2.834386	45.74221754	3.81369	n.a.
3 C		29.32	0.300653	4.852040259	0.50706	n.a.
4 D		33.10	2.810	45.34537423	3.350	n.a.

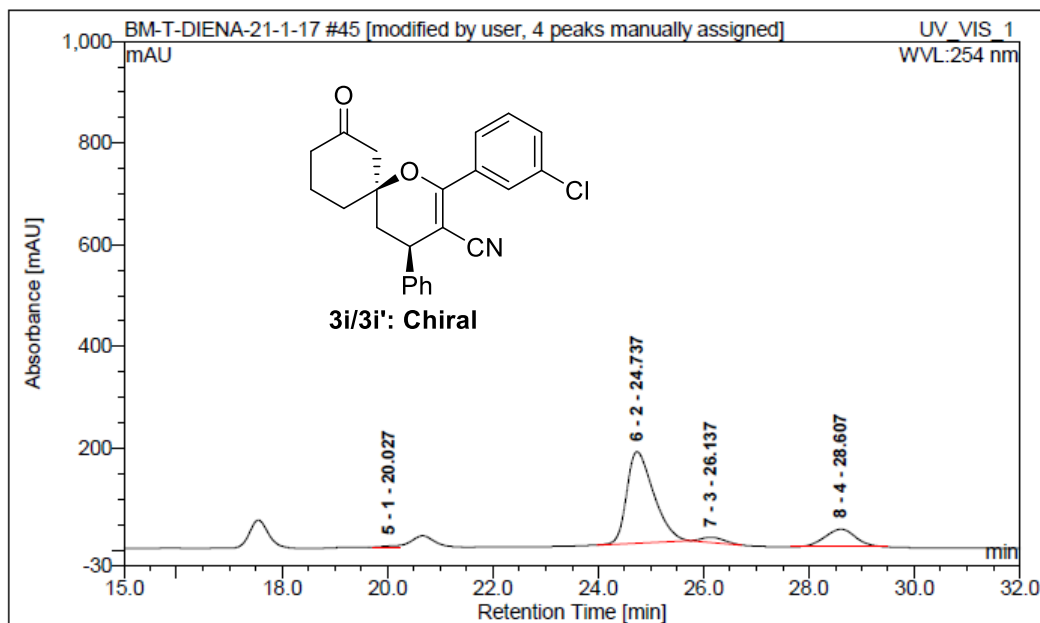


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 A		22.28	10.69295	7.163362427	17.32086	n.a.
2 B		26.07	112.9136	75.64240365	159.196	n.a.
3 C		29.50	25.66111	17.19074369	35.08944	n.a.
4 D		32.87	0.005	0.003490231114	0.000	n.a.

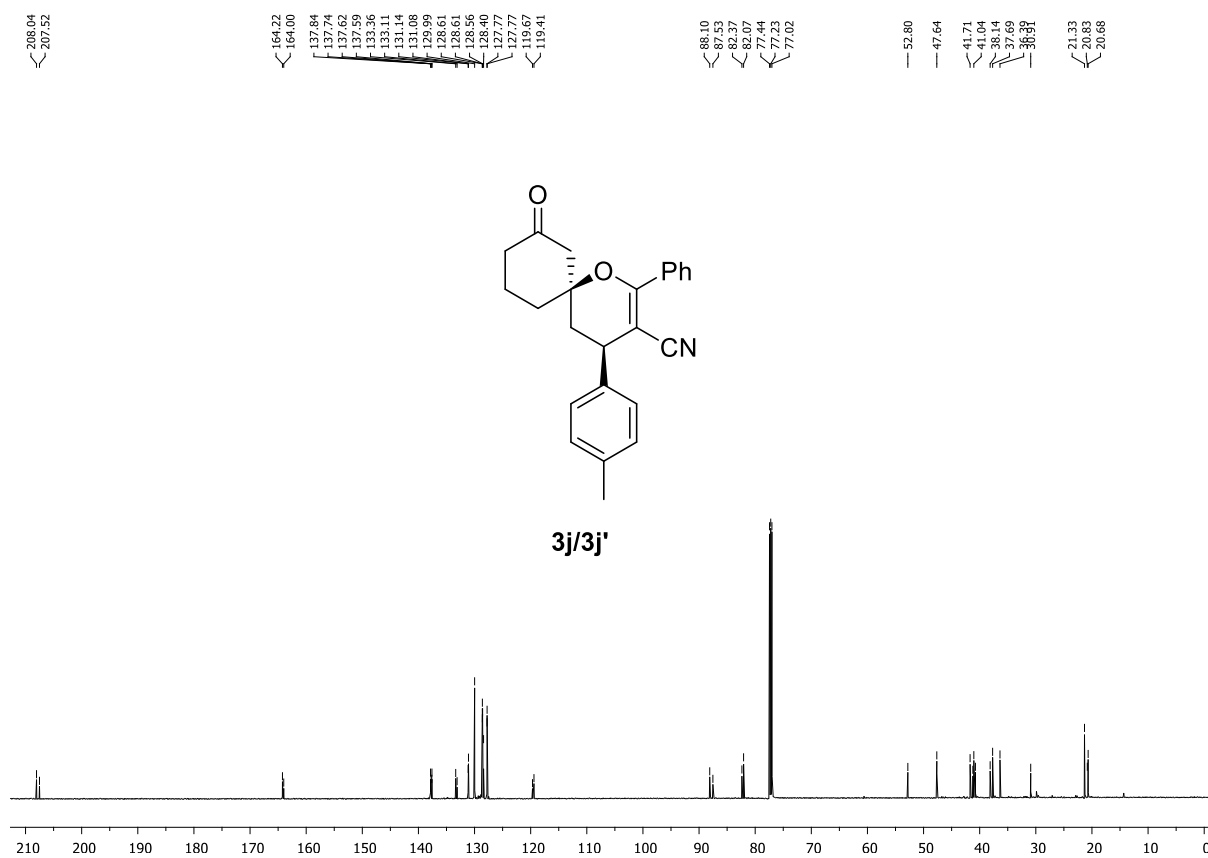
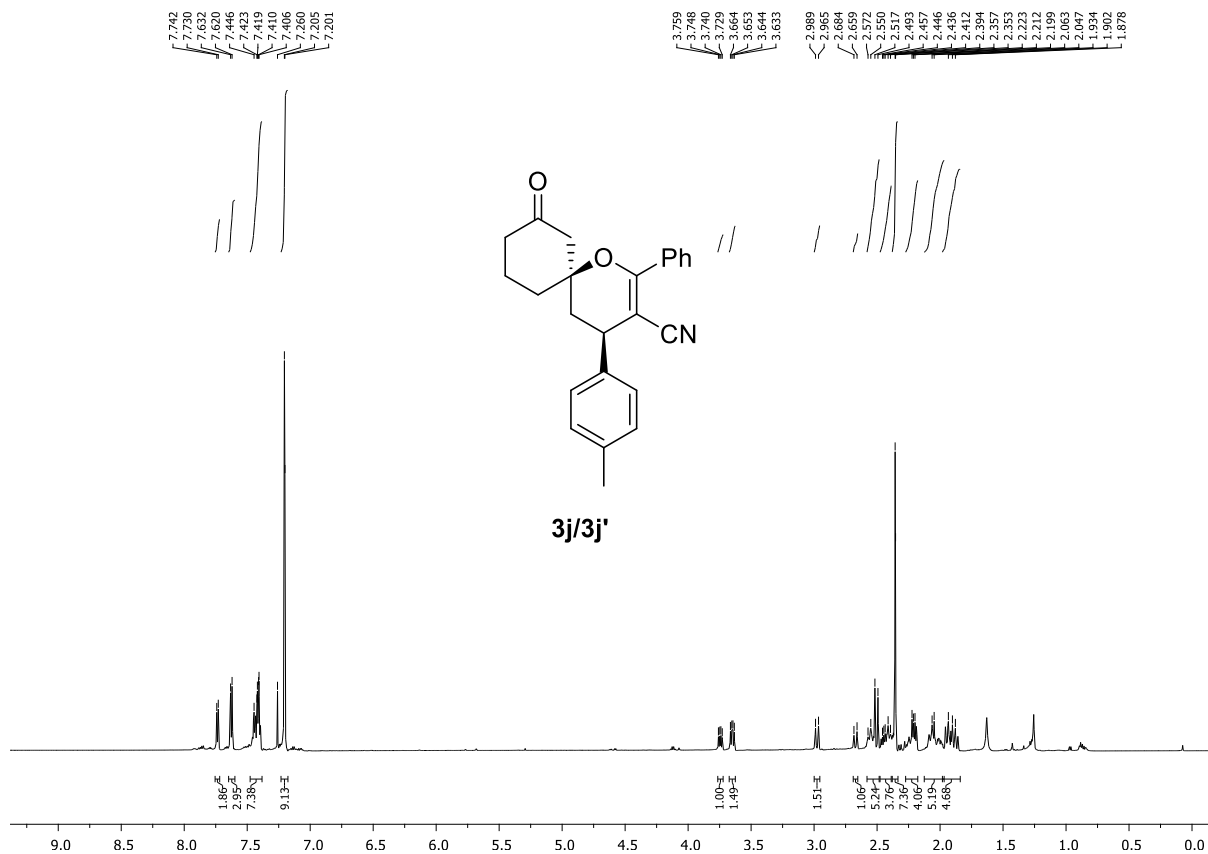


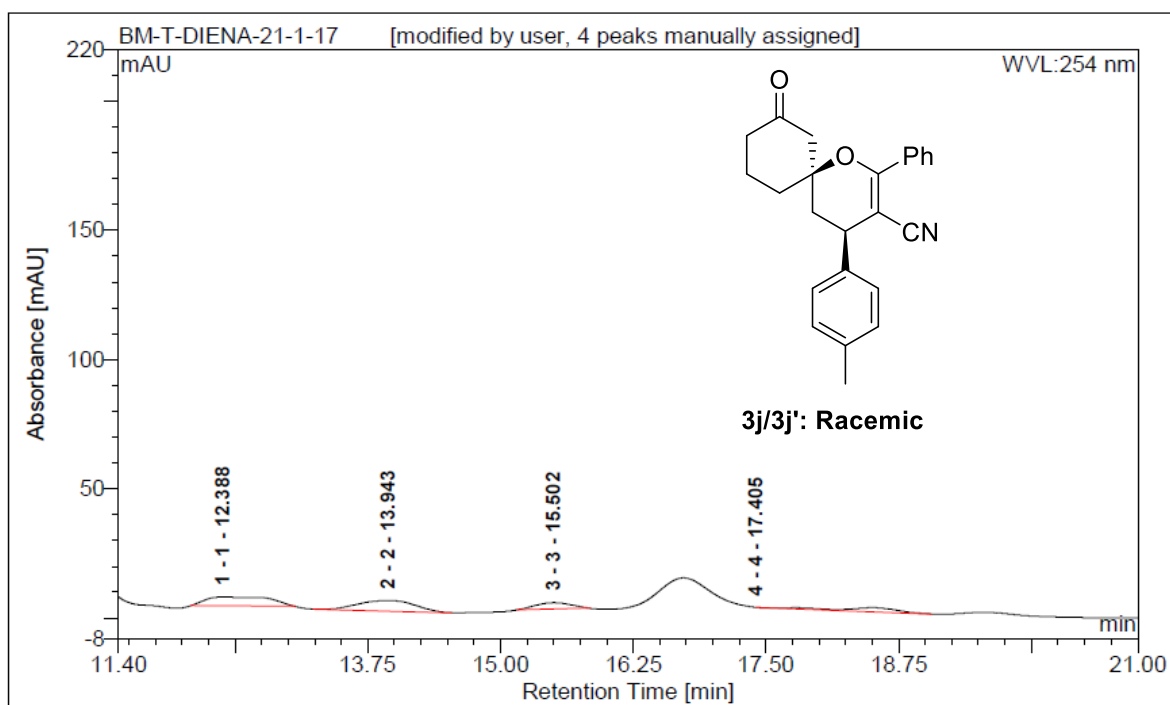


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
14 1		19.41	3.562404	43.73801024	6.31914	n.a.
15 2		24.88	0.522868	6.419601887	1.11104	n.a.
16 3		26.08	0.637827	7.831022772	1.15595	n.a.
17 4		28.36	3.422	42.0113651	4.941	n.a.

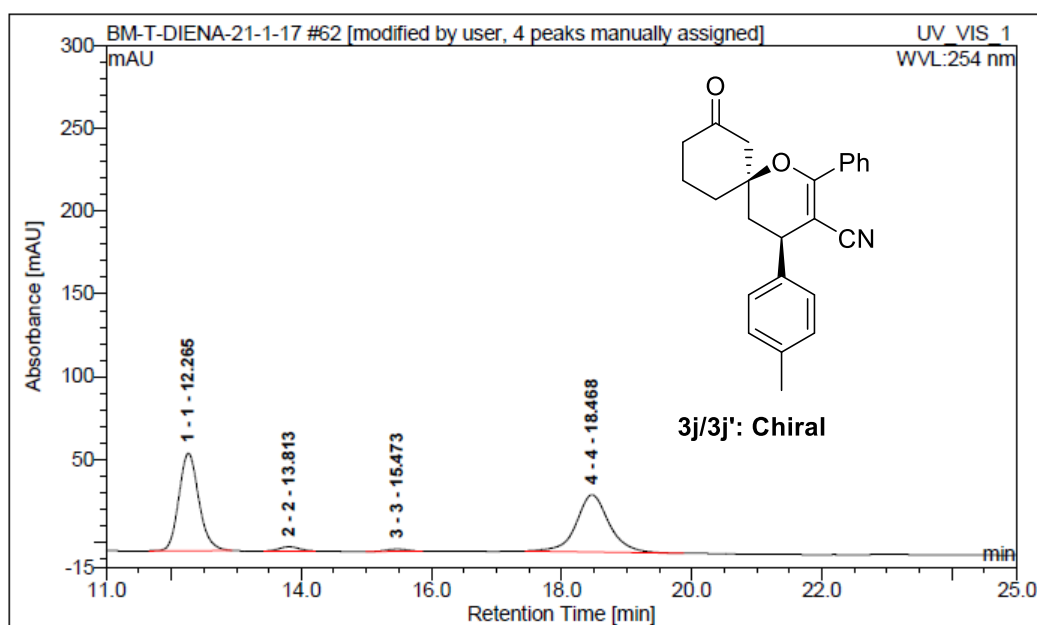


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
5 1		20.03	0.894412	0.6587112772	2.33277	n.a.
6 2		24.74	106.1595	78.18374177	179.5268	n.a.
7 3		26.14	4.904411	3.611971658	9.87111	n.a.
8 4		28.61	23.824	17.5455753	34.668	n.a.

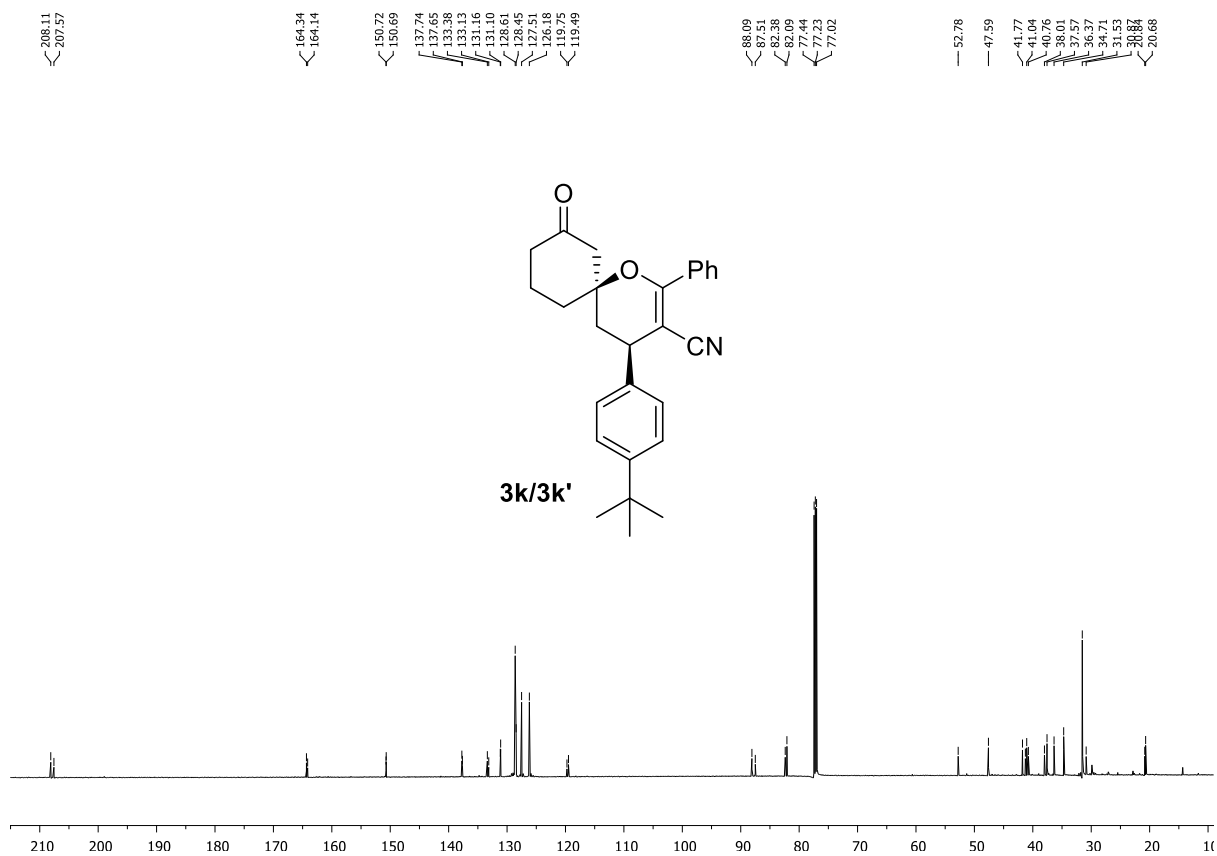
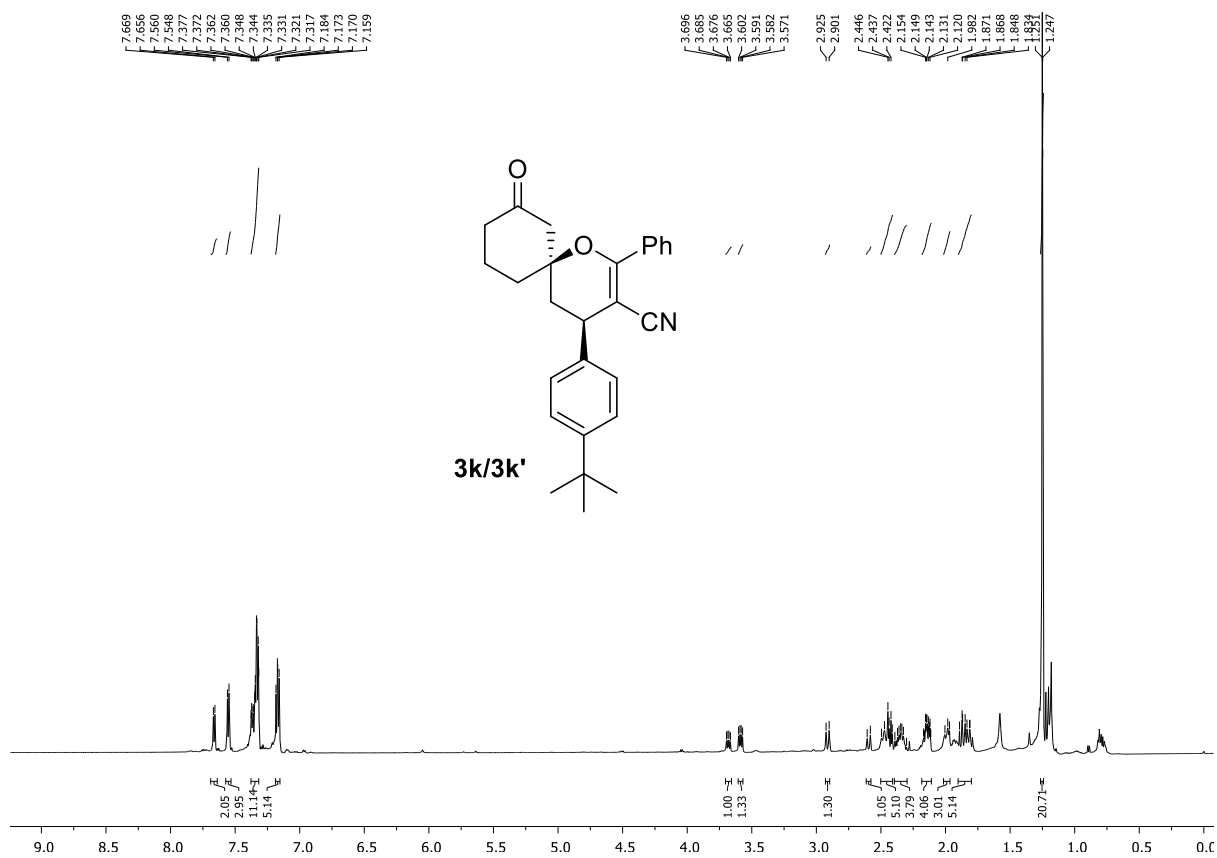


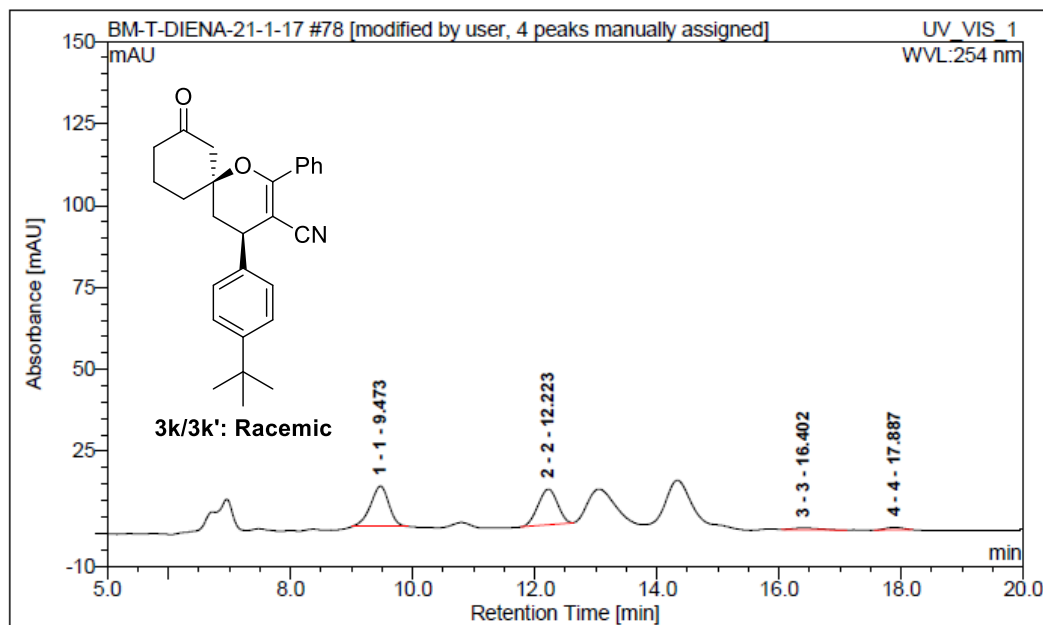


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 1		12.39	2.530226	36.43524941	3.53372	n.a.
2 2		13.94	2.51917	36.27604341	4.1084	n.a.
3 3		15.50	0.985709	14.19420428	2.48043	n.a.
4 4		17.41	0.909	13.0945029	0.004	n.a.

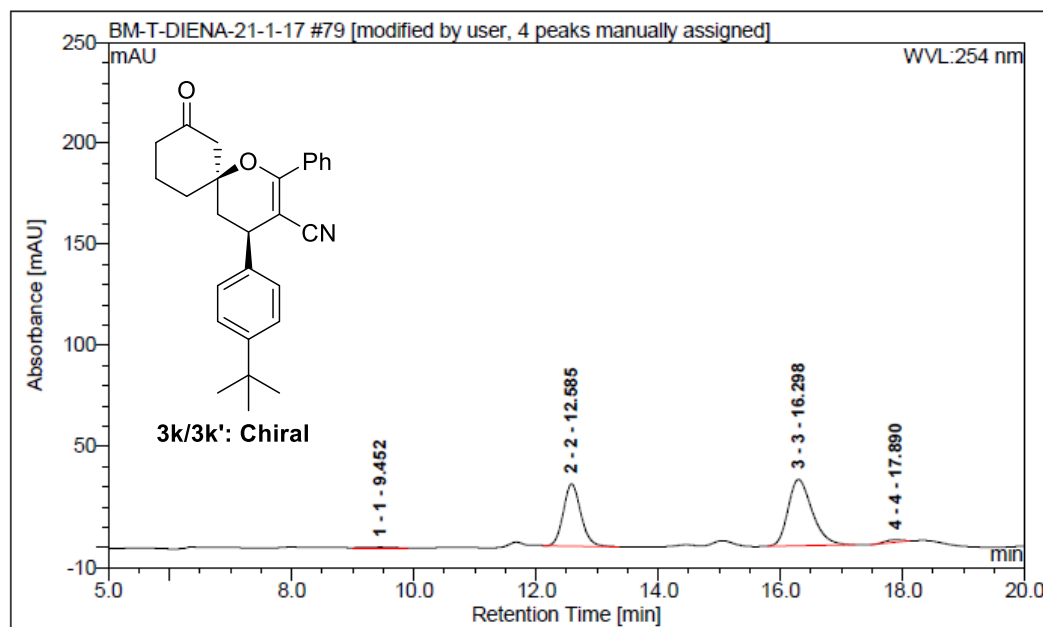


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 1		12.27	20.88991	49.02230559	58.80935	n.a.
2 2		13.81	0.884084	2.074678177	2.49281	n.a.
3 3		15.47	0.541877	1.271621003	1.41633	n.a.
4 4		18.47	20.297	47.63139523	34.484	n.a.

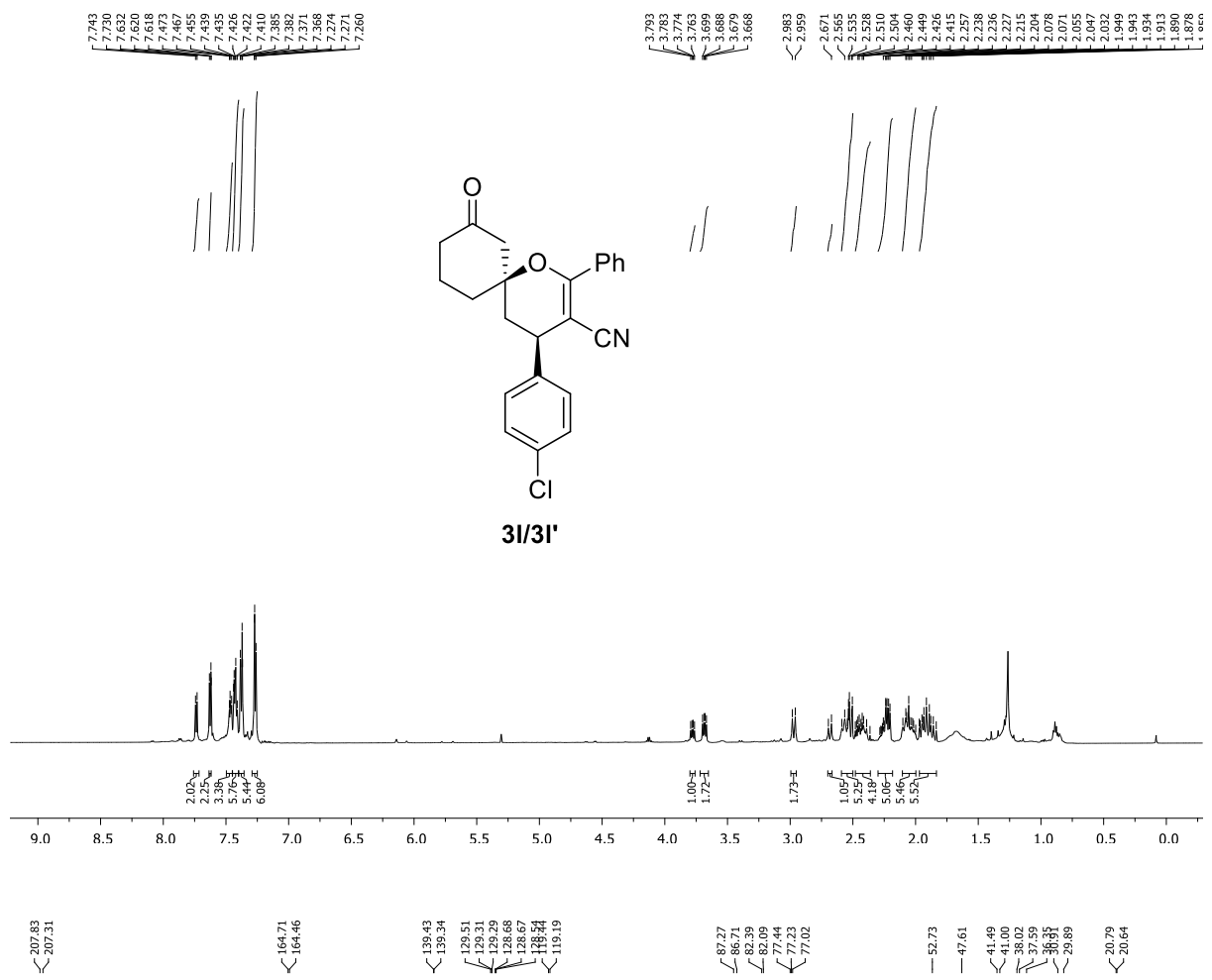


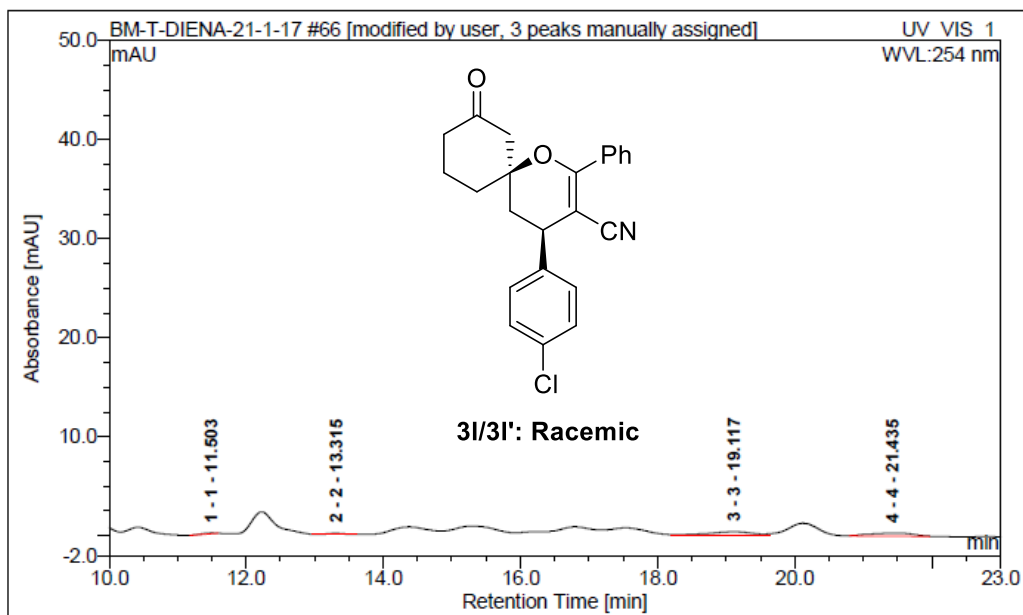


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 1		9.47	4.261071	48.67102725	12.24656	n.a.
2 2		12.22	4.004442	45.73974561	10.87258	n.a.
3 3		16.40	0.223642	2.554494911	0.52054	n.a.
4 4		17.89	0.266	3.034732225	0.808	n.a.

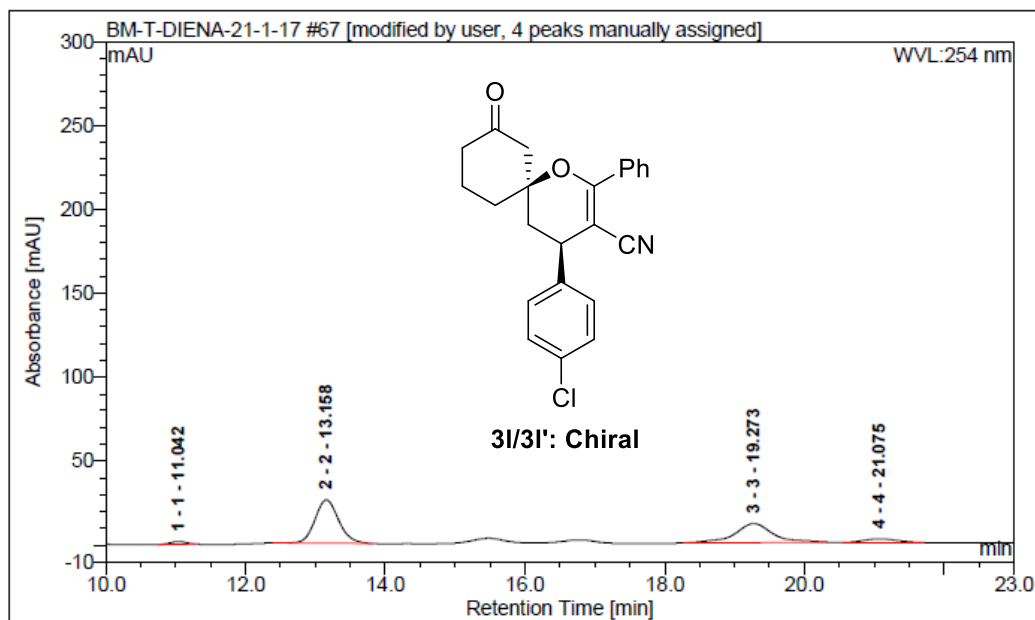


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1 1		9.45	0.112345	0.4375368061	0.30959	n.a.
2 2		12.59	10.22547	39.82406714	30.7818	n.a.
3 3		16.30	14.95458	58.24202817	32.78086	n.a.
4 4		17.89	0.384	1.496367886	1.171	n.a.

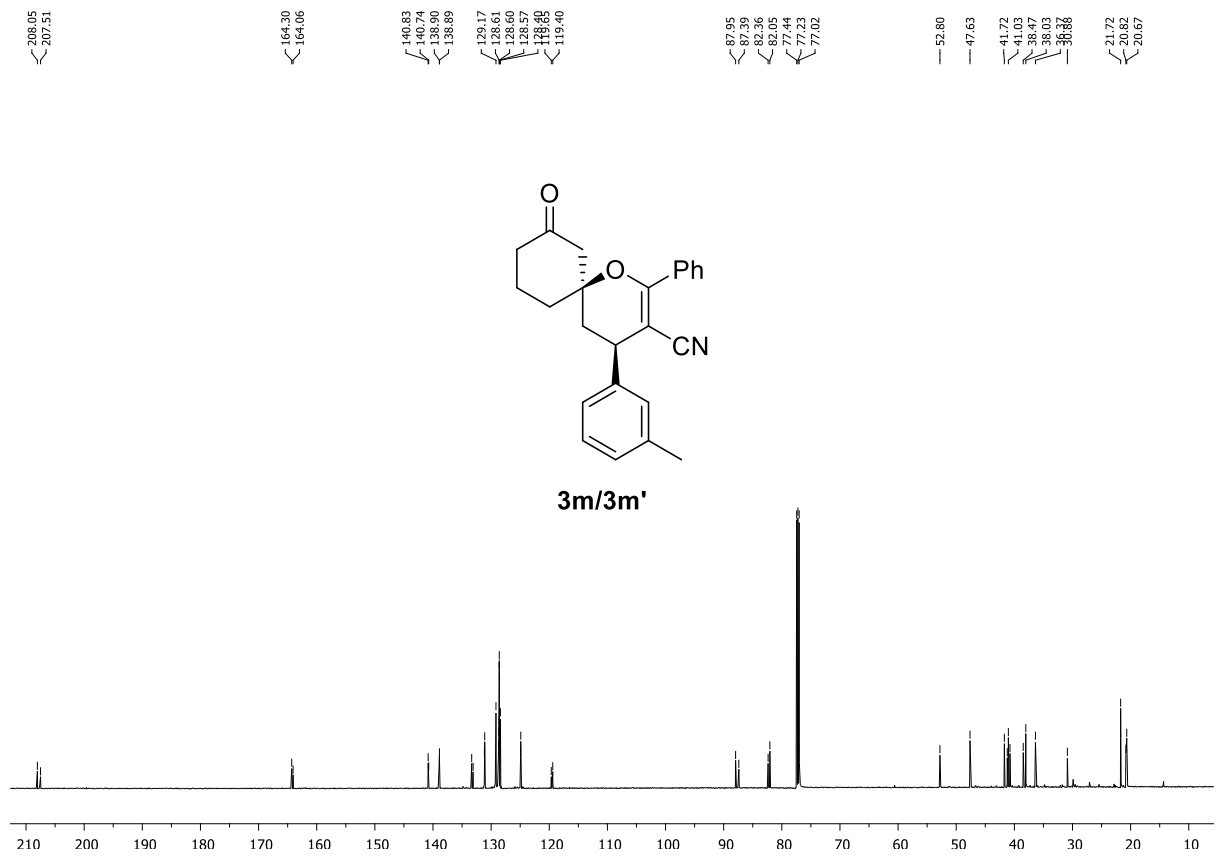
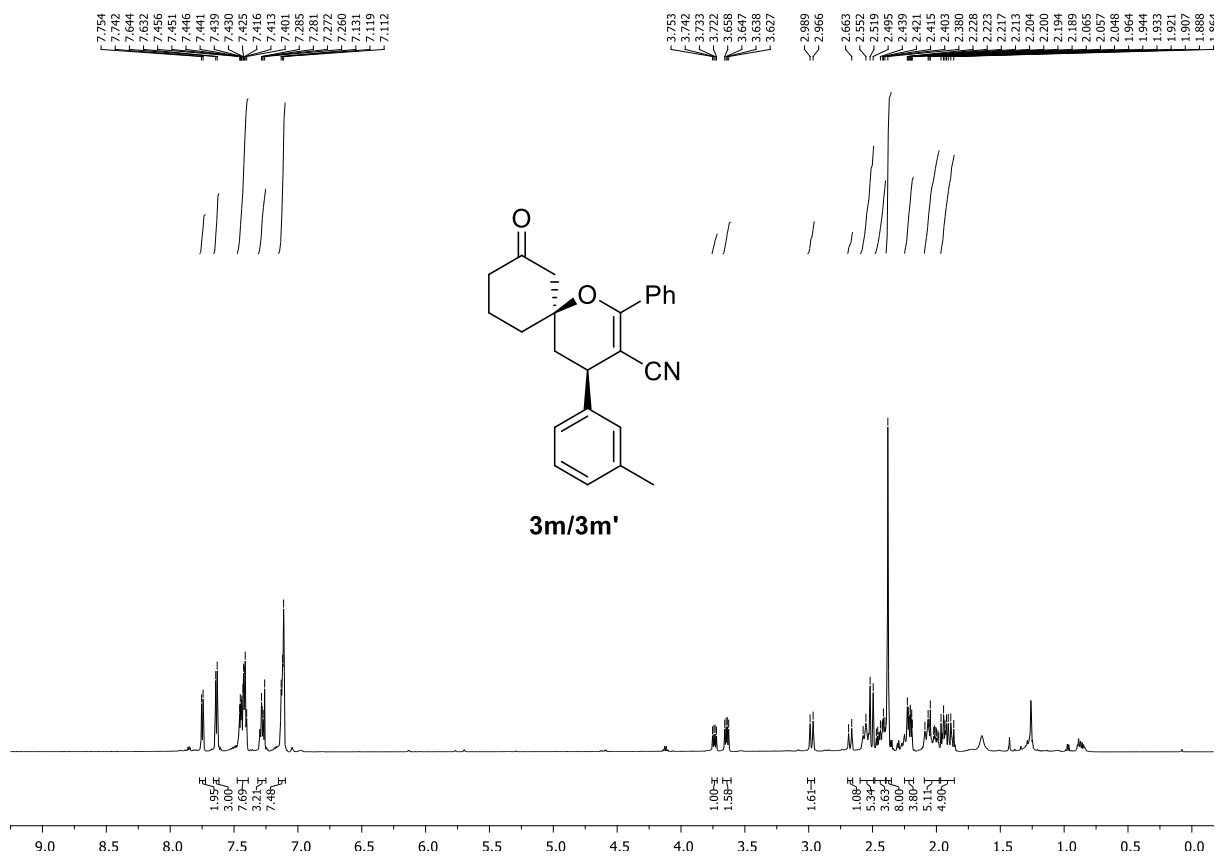


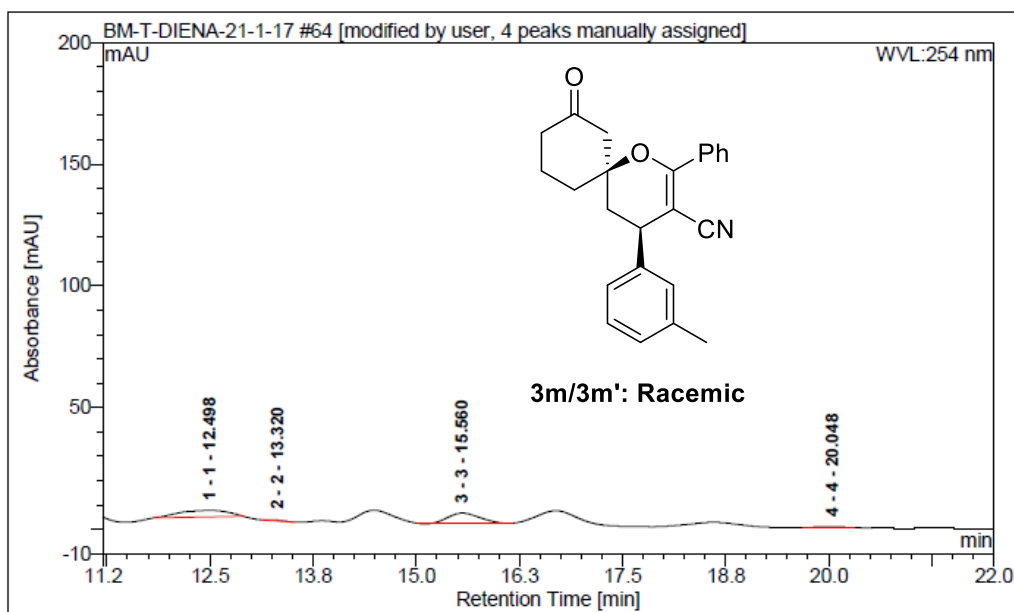


No.	Peak Name	Ret. Time (detected) min	Area mAU*min	Rel. Area (ident.) %	Height mAU	Amount
1	1	11.50	0.019053	4.281069062	0.08031	n.a.
2	2	13.32	0.019343	4.346202186	0.09331	n.a.
3	3	19.12	0.204909	46.0417186	0.31315	n.a.
4	4	21.44	0.202	45.33101015	0.298	n.a.

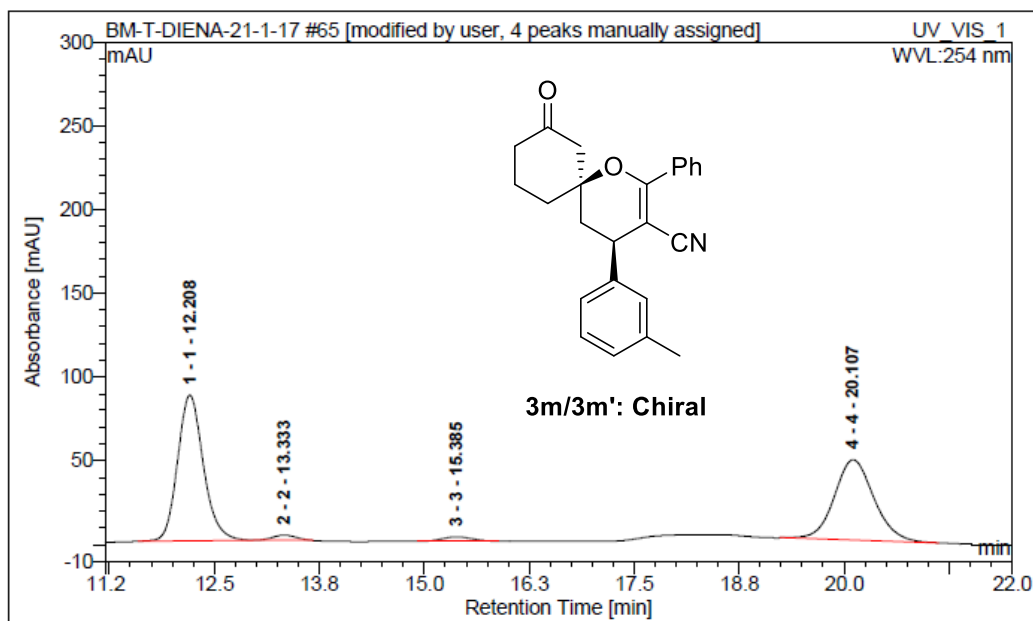


No.	Peak Name	Ret. Time (detected) min	Area mAU*min	Rel. Area (ident.) %	Height mAU	Amount
1	1	11.04	0.431483	2.280002384	1.62	n.a.
2	2	13.16	10.23206	54.06738018	25.87591	n.a.
3	3	19.27	7.099736	37.51580334	11.28491	n.a.
4	4	21.08	1.161	6.13681409	2.139	n.a.

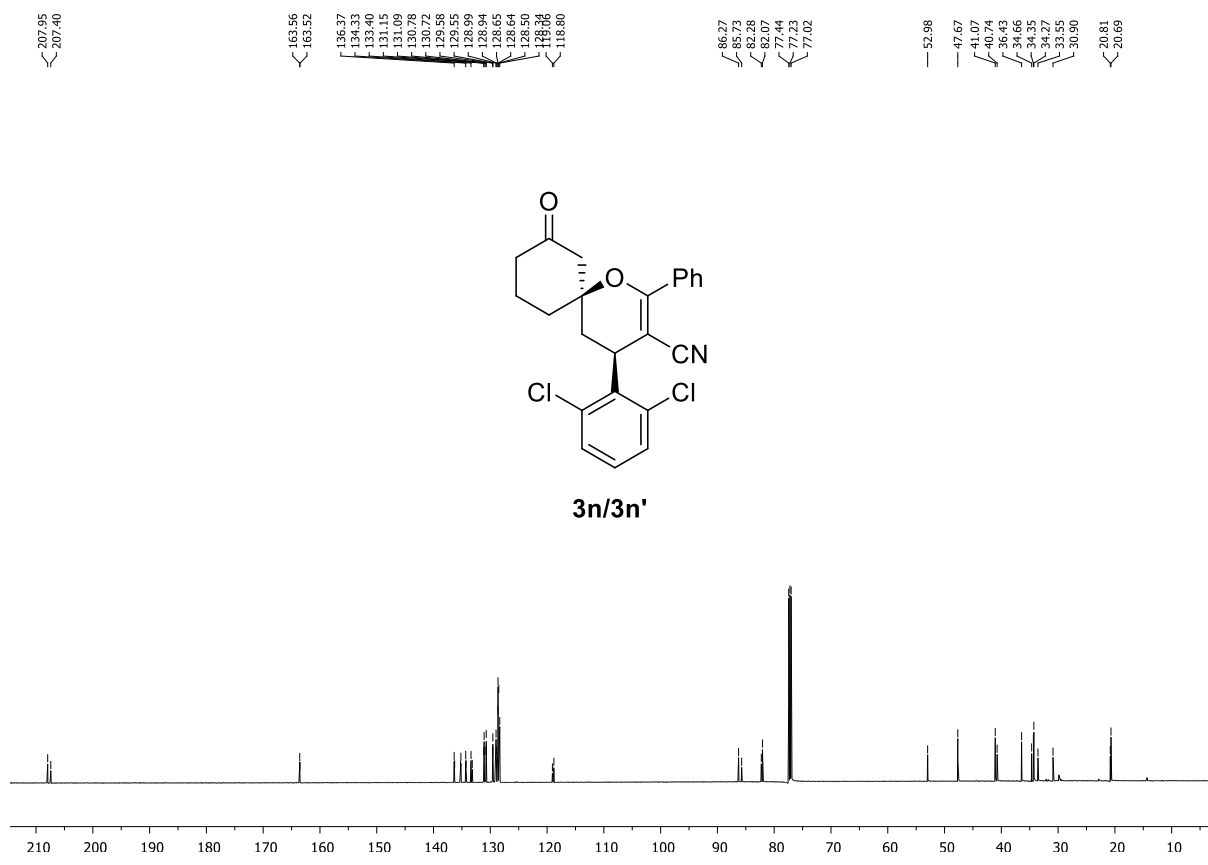
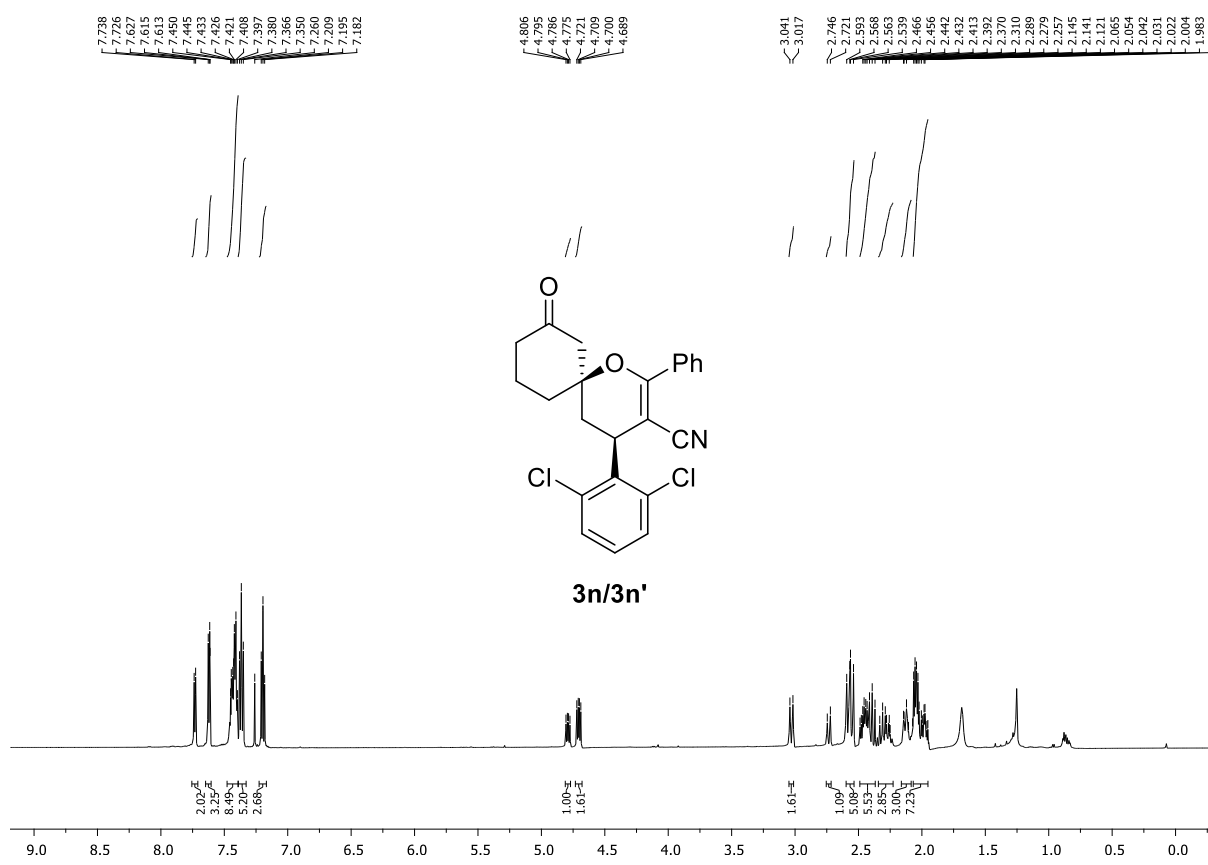


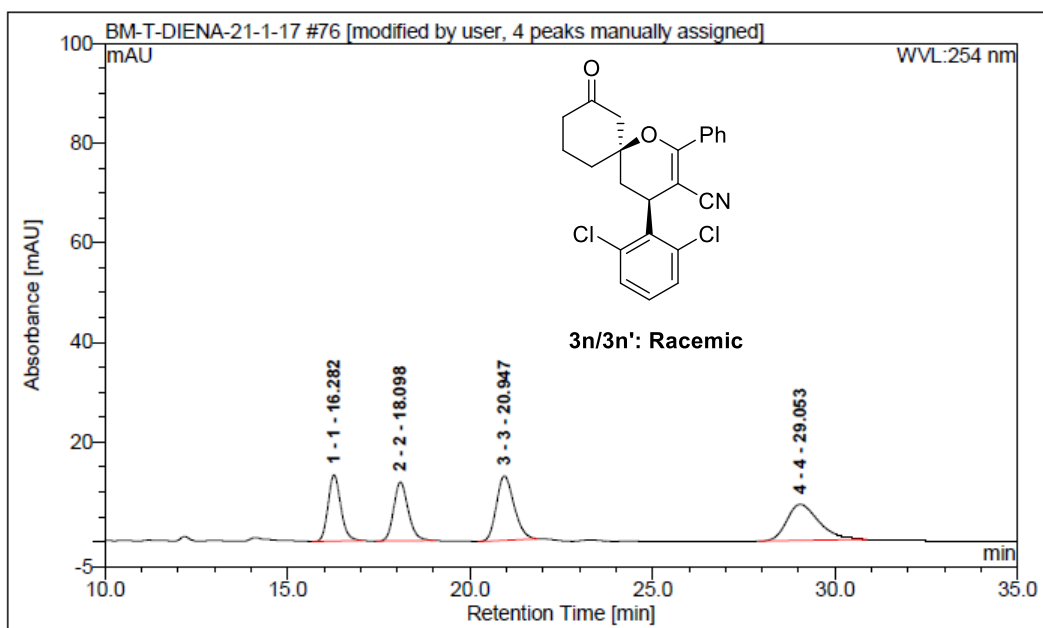


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	12.50	1.820015	48.68822407	2.6453	n.a.
2	2	13.32	0.064621	1.728712757	0.31565	n.a.
3	3	15.56	1.765341	47.22559716	4.11869	n.a.
4	4	20.05	0.088	2.357466012	0.220	n.a.

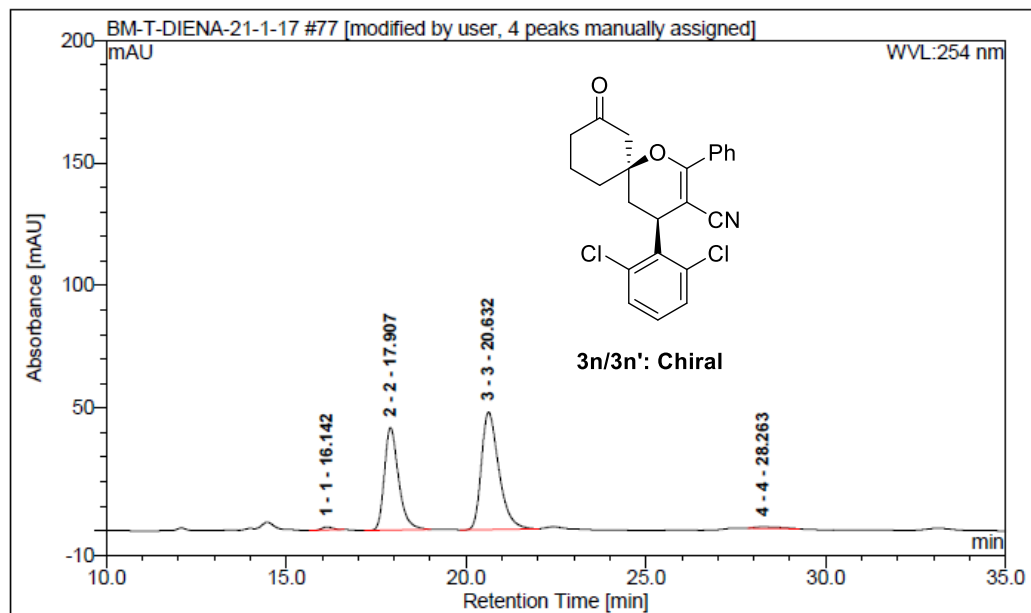


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	12.21	31.07365	52.23454485	86.98119	n.a.
2	2	13.33	1.020616	1.715646922	3.11022	n.a.
3	3	15.39	1.152092	1.936655992	2.7452	n.a.
4	4	20.11	26.242	44.11315223	47.984	n.a.

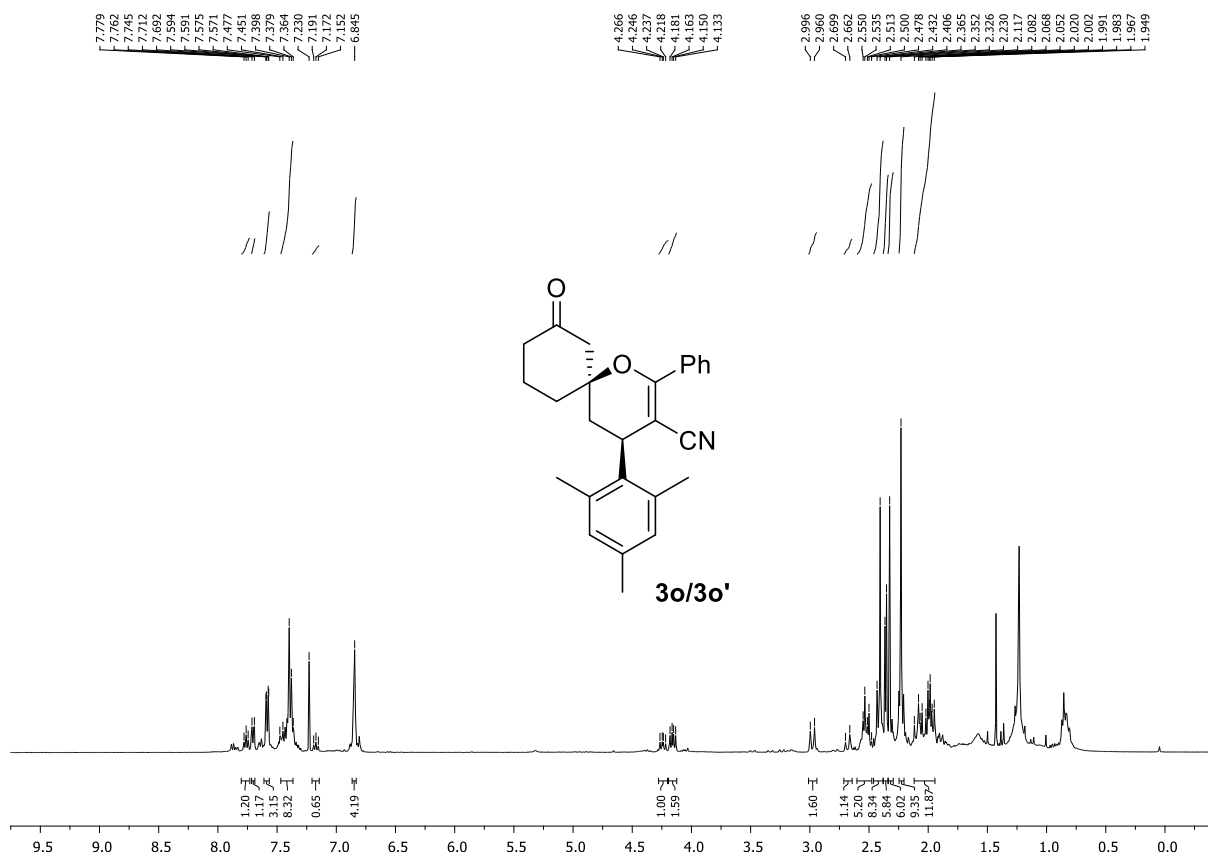


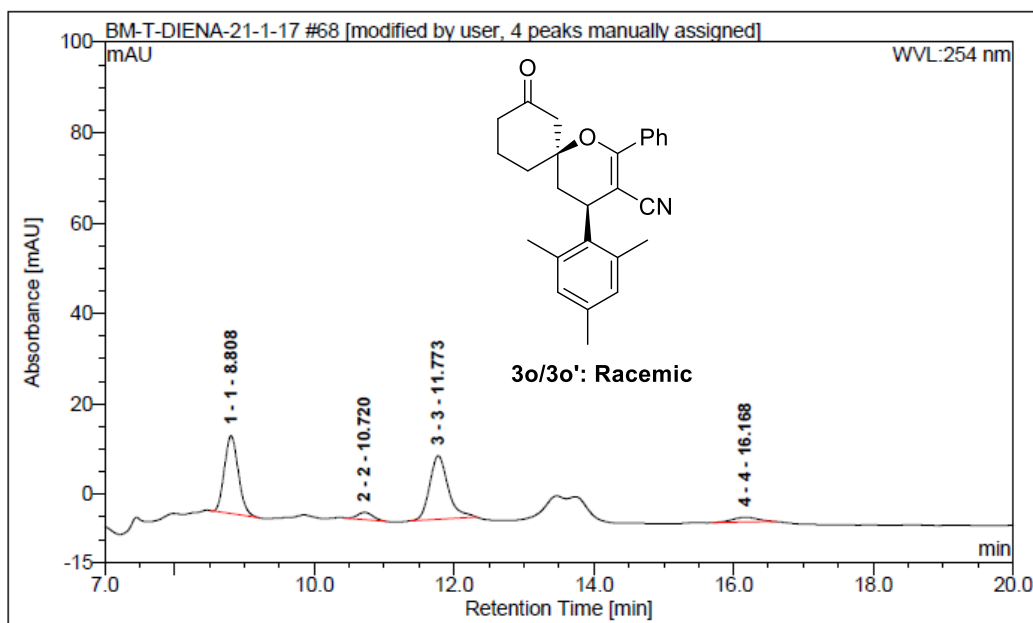


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	16.28	5.369914	21.05003086	13.27281	n.a.
2	2	18.10	5.474008	21.45808027	11.80687	n.a.
3	3	20.95	7.234977	28.36106751	12.92189	n.a.
4	4	29.05	7.431	29.13082136	7.275	n.a.

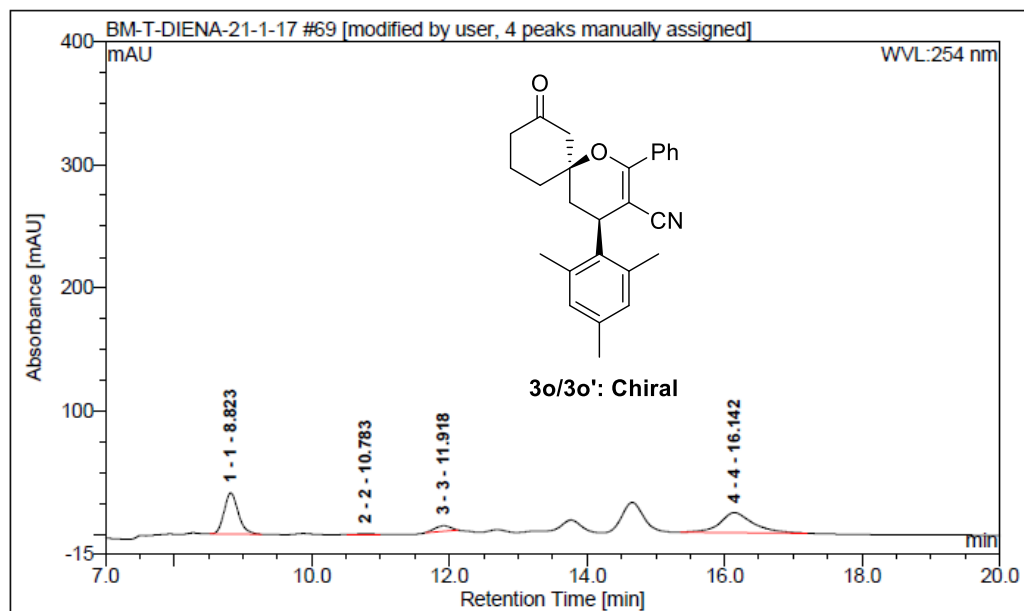


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	16.14	0.405991	0.8626425553	1.20091	n.a.
2	2	17.91	19.14793	40.68520265	41.82359	n.a.
3	3	20.63	26.94174	57.24534544	47.84936	n.a.
4	4	28.26	0.568	1.206809357	0.653	n.a.



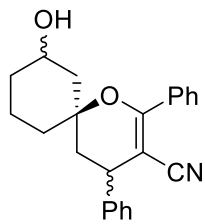


No.	Peak Name	Ret. Time (detected) min	Area mAU*min	Rel. Area (ident.) %	Height mAU	Amount
1	1	8.81	4.011835	43.78810173	17.2457	n.a.
2	2	10.72	0.399844	4.364191072	1.59406	n.a.
3	3	11.77	4.295888	46.88846891	14.04893	n.a.
4	4	16.17	0.454	4.959238281	1.054	n.a.

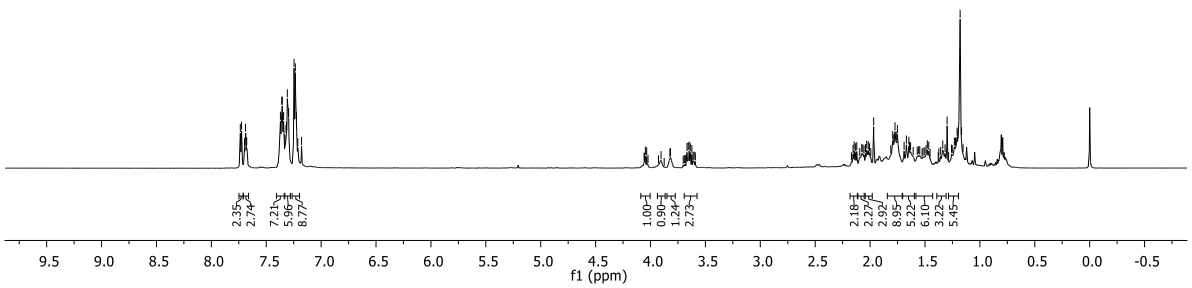


No.	Peak Name	Ret. Time (detected) min	Area mAU*min	Rel. Area (ident.) %	Height mAU	Amount
1	1	8.82	7.949954	43.23766986	33.30797	n.a.
2	2	10.78	0.171969	0.9352927514	0.74281	n.a.
3	3	11.92	1.126343	6.125875559	4.25539	n.a.
4	4	16.14	9.138	49.70116183	16.265	n.a.

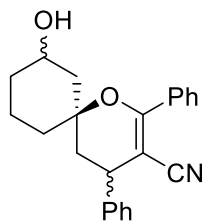
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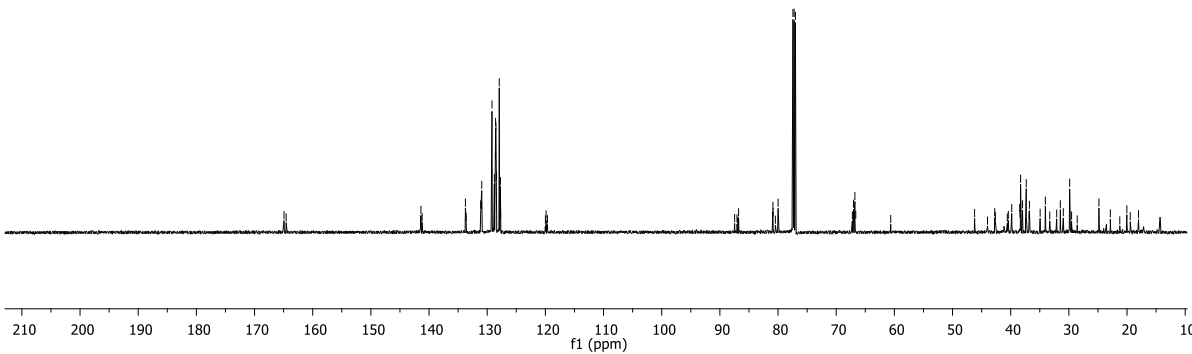
4a/4a'/4a''

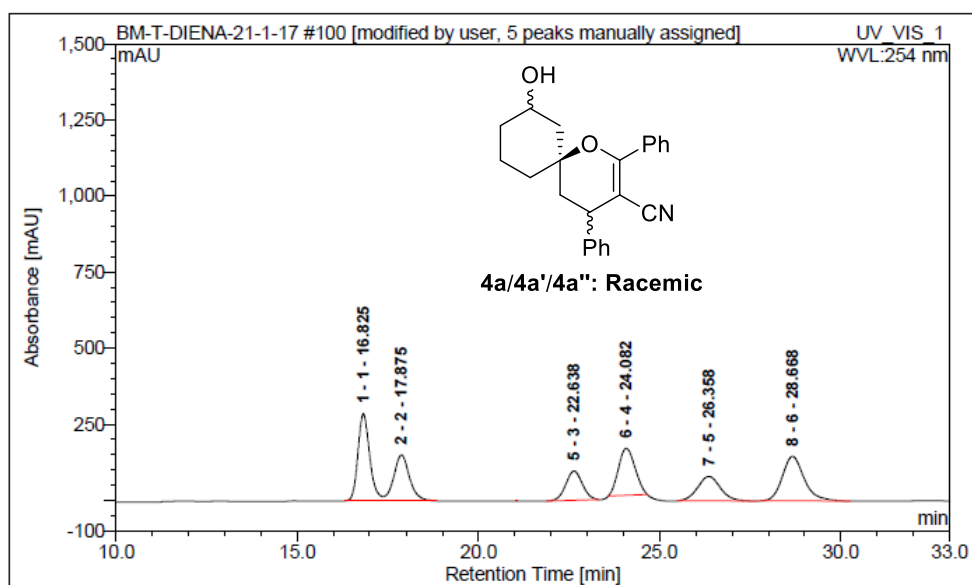


164.93, 164.57, 141.47, 141.45, 141.39, 141.18, 139.18, 128.58, 128.56, 128.50, 127.93, 127.88, 119.88, 119.84, 87.46, 87.05, 86.94, 86.78, 79.98, 77.44, 77.23, 77.02, 72.92, 67.02, 66.79, 66.63, 60.62, 46.21, 42.75, 42.62, 39.62, 38.40, 38.30, 37.97, 37.33, 36.83, 36.78, 34.94, 34.06, 33.04, 31.47, 30.96, 29.87, 24.84, 22.87, 20.03, 18.03

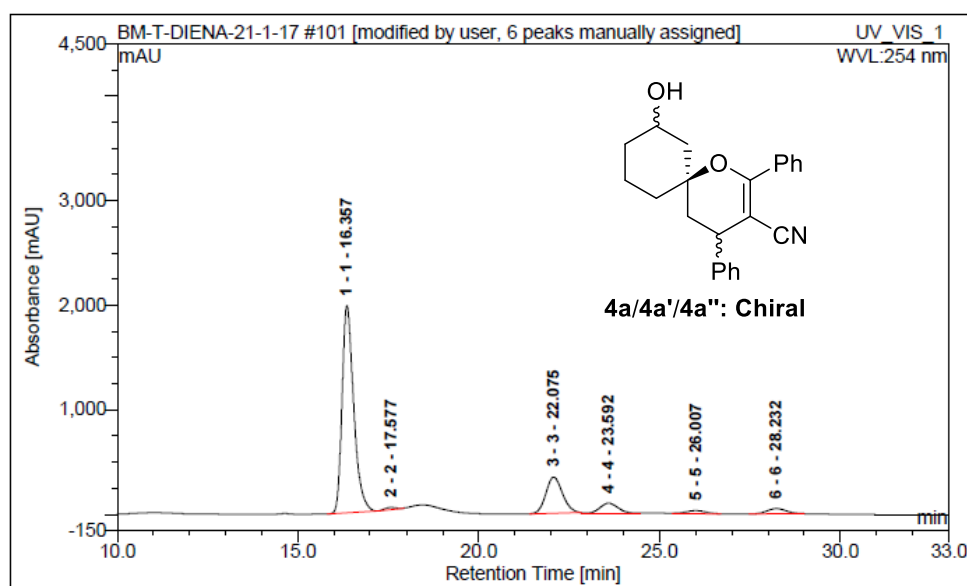


4a/4a'/4a''





No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	16.83	105.3329	22.08478598	286.2953	n.a.
2	2	17.88	78.25188	16.40679773	151.0108	n.a.
5	3	22.64	50.45645	10.57902753	95.56473	n.a.
6	4	24.08	81.62027	17.11303673	154.0356	n.a.
7	5	26.36	58.1882	12.20011648	80.28439	n.a.
8	6	28.67	103.098	21.61623556	146.334	n.a.



No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	16.36	740.0622	71.63109638	1981.99	n.a.
2	2	17.58	6.864653	0.6644342582	19.84202	n.a.
3	3	22.08	184.8126	17.88813357	346.5213	n.a.
4	4	23.59	50.99049	4.935402256	93.07691	n.a.
5	5	26.01	18.00049	1.742279269	29.07569	n.a.
6	6	28.23	32.427	3.138654268	51.481	n.a.

References:

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2. M. S. Manna and S. Mukherjee, *Chem. Eur. J.*, 2012, **18**, 15277.