Organocatalytic tandem Morita-Baylis-Hillman/Michael reaction for asymmetric synthesis of a drug-like oxa-spirocyclic indanone scaffold

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Supporting Information

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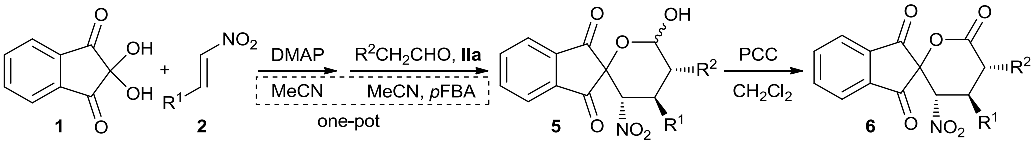
1. General methods

NMR data was obtained for ^1H at 400 MHz, and for ^{13}C at 100 MHz. Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard in $CDCl_3$ solution. ESI HRMS was recorded on a Waters SYNAPT G2. In each case, enantiomeric ratio was determined by HPLC analysis on chiral column in comparison with authentic racemates, using a Daicel Chiralpak AD-H Column (250 x 4.6 mm), Daicel Chiralpak OD-H Column (250 x 4.6 mm) or Kromasil CelluCoat Column (250 x 4.6 mm). UV detection was monitored at 220 nm or 254 nm. Optical rotation data were examined in CH_2Cl_2 solution at 20 ℃. Column chromatography was performed on silica gel (200-300 mesh) eluting with ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates. UV light and I_2 were used to visualize products. Melting points were determined on a Mel-Temp apparatus and are uncorrected. All chemicals were used without purification as commercially available unless otherwise noted. The catalysts **II** were synthesized according to the literature procedures. [1]

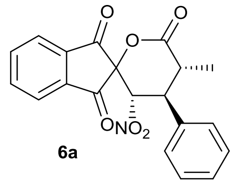
[1]. (a) Marigo, M.; Wabnitz, T. C.; Fielenbach, D.; Jøgensen, K. A. *Angew. Chem., Int. Ed*. **2005**, *44*, 794. (b) Hayashi, Y.; Gotoh, H.; Hayasi, T.; Shoji, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 4212.

2. General procedure for the asymmetric synthesis of spiroindanone δ-lactone 6



The reaction was carried out with ninhydrin **1** (89 mg, 0.5 mmol) and nitroolefin **2** (0.4 mmol) in the presence of DMAP (3.6 mg, 0.04 mmol) in MeCN (2.0 mL) at room temperature for 1 h to afford the MBH adduct **3**, after which aldehyde **4** (0.5 mmol), diphenyl prolinol TMS ether **IIa** (32.5 mg, 0.1 mmol) and 4-fluorobenzoic acid (14.0 mg, 0.1 mmol) were added in one-pot. The reaction mixture was stirred at room temperature for a specified reaction time (about 3h) until the reaction completed (monitored by TLC). Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give hemiacetal **5**.

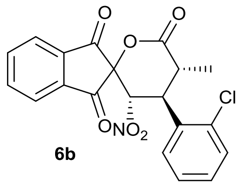
Hemiacetal **5** were oxidized to the stable corresponding spiroindanone δ-lactone **6**. To a solution of **5** in methylene chloride (5 mL) was added PCC (107.8 mg, 0.5 mmol). The mixture was stirred for 2 h at 50 °C. The solid was removed by filtration through celite. The filtrate was evaporated under reduced pressure and the residual was purified by column chromatography (petroleum ether/ethyl acetate = 15:1) to give spiroindanone δ-lactone **6**. The dr values of **6** were calculated by ^{1}H NMR analysis of the crude reaction mixture and the major diastereomers of **6** could be isolated in pure form for NMR, HRMS and HPLC analysis.



6a

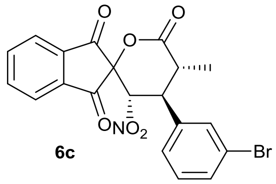
6a was obtained as a white solid in 76% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 93% by HPLC on Chiralpak OD-H column (30% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t_{minor} = 11.05 min, t_{major} = 12.11 min. m.p. 167-168 °C; $[\alpha]_D^{20}$ -129.4 (*c* = 0.12 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12-8.05 (m, 2H), 8.01-7.94 (m, 2H), 7.40-7.34 (m, 3H), 7.27-7.26 (m, 2H), 5.64 (d, *J* = 12.4 Hz, 1H), 4.16 (t, *J* = 12.0 Hz, 1H), 3.10-3.02 (m, 1H), 1.39 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.31, 190.03, 169.62, 141.15, 140.18, 138.00, 137.48, 135.43, 129.51, 129.05, 127.77, 124.99, 124.72, 87.28, 46.58, 41.42, 14.74 ppm; ESI HRMS: calcd. For $C_{20}H_{15}NO_6$+Na 388.0797, found 388.0795.

For the minor diastereomer of **6a**, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05-7.84 (m, 4H), 7.33-7.18 (m, 5H), 5.56 (d, *J* = 12.0 Hz, 1H), 4.09 (t, *J* = 11.6 Hz, 1H), 3.02-2.94 (m, 1H), 1.31 (d, *J* = 6.8 Hz, 3H) ppm; ESI HRMS: calcd. For $C_{20}H_{15}NO_6$+Na 388.0797, found 388.0796.



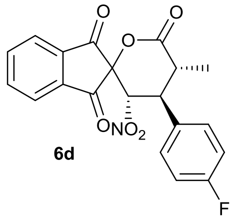
6b

6b was obtained as a white solid in 76% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 99% by HPLC on Kromasil CelluCoat column (10% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t_{minor} = 26.42 min, t_{major} = 28.33 min. m.p. 167-168 °C; $[\alpha]_D^{20}$ -126.2 (*c* = 0.18 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15-8.07 (m, 2H), 8.03-7.95 (m, 2H), 7.43-7.39 (m, 3H), 7.30-7.27 (m, 1H), 5.63 (d, *J* = 12.4 Hz, 1H), 5.19 (t, *J* = 12.0 Hz, 1H), 2.99-2.97 (m, 1H), 1.42 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.07, 190.04, 169.22, 141.15, 140.21, 137.90, 137.43, 135.66, 133.85, 130.44, 129.83, 128.10, 126.70, 124.99, 124.93, 86.23, 42.39, 40.71, 14.31 ppm; ESI HRMS: calcd. For $C_{20}H_{14}ClNO_6$+Na 422.0407, found 422.0409.



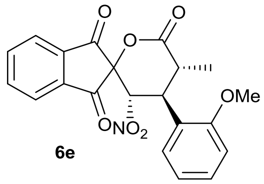
6c

6c was obtained as a white solid in 78% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 98% by HPLC on Chiralpak OD-H column (20% 2-propanol/n-hexane, 1 mL/min), UV 220 nm, t_{minor} = 13.62 min, t_{major} = 14.97 min. m.p. 168-169 ^oC; $[\alpha]_D^{20}$ -95.2 (*c* = 0.12 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.13-8.07 (m, 2H), 8.03-7.98 (m, 2H), 7.50-7.43 (m, 2H), 7.30-7.20 (m, 2H), 5.60 (d, *J* = 12.0 Hz, 1H), 4.15 (t, *J* = 11.6 Hz, 1H), 3.03-2.99 (m, 1H), 1.40 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.17, 189.80, 169.08, 141.07, 140.21, 138.01, 137.82, 137.57, 132.32, 131.06, 130.90, 126.44, 125.06, 124.78, 123.53, 86.78, 46.17, 41.30, 14.78 ppm; ESI HRMS: calcd. For $C_{20}H_{14}BrNO_6$+Na 465.9902, found 465.9905.



6d

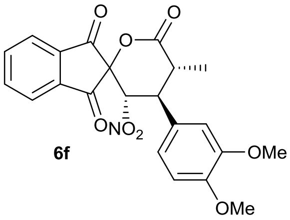
6d was obtained as a white solid in 72% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 97% by HPLC on Chiralpak OD-H column (20% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t_{minor} = 11.74 min, t_{major} = 13.13 min. m.p. 170-172 ^oC; $[\alpha]_D^{20}$ -107.6 (*c* = 0.12 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.13-8.06 (m, 2H), 8.03-7.96 (m, 2H), 7.26-7.23 (m, 2H), 7.11-7.07 (m, 2H), 5.57 (d, *J* = 12.4 Hz, 1H), 4.18 (t, *J* = 12.0 Hz, 1H), 3.02-2.97 (m, 1H), 1.39 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.25, 189.90, 169.29, 162.84 (d, J_{CF} = 248 Hz), 141.11, 140.17, 138.04, 137.55, 131.20, 129.49 (d, J_{CF} = 8 Hz), 125.04, 124.76, 116.65 (d, J_{CF} = 22 Hz), 99.99, 87.21, 45.87, 41.54, 14.70 ppm; ESI HRMS: calcd. For $C_{20}H_{14}FNO_6$+H 384.0883, found 384.0886.



6e

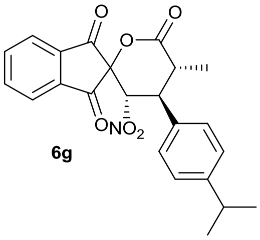
6e was obtained as a white solid in 70% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 99% by HPLC on Chiralpak OD-H column (20% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t_{minor} = 15.64 min, t_{major} = 17.68 min. m.p. 168-170 ^oC; $[\alpha]_D^{20}$ -125.8 (*c* = 0.08 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.12-8.05 (m, 2H), 8.01-7.93 (m, 2H), 7.34-7.30 (m, 1H), 7.08-7.06 (m, 1H), 6.95-6.89 (m, 2H), 6.14 (br s, 1H), 4.24 (br s, 1H), 3.93(s, 3H), 3.52 (br s, 1H), 1.39 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.67, 190.39, 170.38, 157.58, 141.32, 140.22, 137.72, 137.18, 130.31, 124.86, 124.61, 122.27, 122.21, 121.25, 111.62, 84.56, 55.59, 50.44, 38.60, 15.38 ppm; ESI HRMS: calcd. For $C_{21}H_{17}NO_6$+Na

418.0903, found 418.0901.



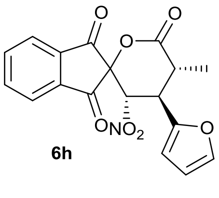
6f

6f was obtained as a white solid in 65% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 97% by HPLC on Chiralpak OD-H column (20% 2-propanol/n-hexane, 1 mL/min), UV 220 nm, t$_{minor}$ = 27.63 min, t$_{major}$ = 36.53 min. m.p. 171-172 ^{o}C; $[\alpha]_D^{20}$ -139.9 (*c* = 0.12 in CH$_2$Cl$_2$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.13-8.06 (m, 2H), 8.03-7.95 (m, 2H), 7.27 (s, 1H), 6.86-6.79 (m, 2H), 6.71-6.70 (m, 1H), 5.58 (d, *J* = 12.4 Hz, 1H), 4.09 (t, *J* = 12.0 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.06-2.98 (m, 1H), 1.41 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 192.36, 190.09, 169.64, 149.61, 149.43, 141.18, 140.17, 138.01, 137.47, 127.55, 124.99, 124.67, 120.08, 111.67, 110.36, 87.54, 56.07, 55.90, 46.35, 41.61, 14.77 ppm; ESI HRMS: calcd. For C$_{22}$H$_{19}$NO$_8$+Na 448.1008, found 448.1011.



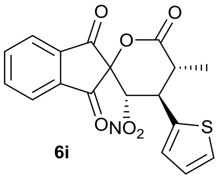
6g

6g was obtained as a white solid in 72% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 98% by HPLC on Chiralpak OD-H column (10% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t$_{minor}$ = 16.32 min, t$_{major}$ = 18.03 min. m.p. 156-158 ^{o}C; $[\alpha]_D^{20}$ -117.2 (*c* = 0.10 in CH$_2$Cl$_2$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.13-8.05 (m, 2H), 8.02-7.94 (m, 2H), 7.23-7.21 (m, 2H), 7.17-7.15 (m, 2H), 5.60 (d, *J* = 12.4 Hz, 1H), 4.11 (t, *J* = 12.0 Hz, 1H), 3.06-2.98 (m, 1H), 2.92-2.85 (m, 1H), 1.39 (d, *J* = 6.8 Hz, 3H), 1.23 (s, 3H), 1.22 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 192.31, 190.08, 169.74, 149.73, 141.17, 140.20, 137.95, 137.43, 132.58, 127.63, 127.54, 124.98, 124.70, 87.36, 77.23, 77.10, 46.21, 41.52, 33.75, 23.81, 14.78 ppm; ESI HRMS: calcd. For C$_{23}$H$_{21}$NO$_6$+H 408.1447, found 408.1450.



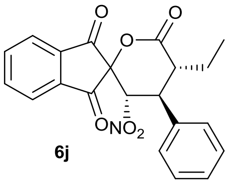
6h

6h was obtained as a white solid in 66% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 95% by HPLC on Chiralpak OD-H column (20% 2-propanol/n-hexane, 1 mL/min), UV 220 nm, t$_{major}$ = 8.85 min, t$_{minor}$ = 18.05 min. m.p. 152-154 ^{o}C; $[\alpha]_D^{20}$ -106.2 (*c* = 0.09 in CH$_2$Cl$_2$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.13-8.06 (m, 2H), 8.02-7.95 (m, 2H), 7.45 (s, 1H), 6.33-6.28 (m, 2H), 5.69 (d, *J* = 12.0 Hz, 1H), 4.34 (t, *J* = 11.6 Hz, 1H), 3.28-3.20 (m, 1H), 1.45 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 192.48, 189.77, 169.22, 147.41, 143.68, 141.09, 140.27, 137.88, 137.47, 125.03, 124.76, 110.77, 110.70, 84.91, 76.18, 40.69, 38.95, 14.94 ppm; ESI HRMS: calcd. For $C_{18}H_{13}NO_7$+Na 378.0590, found 378.0593.



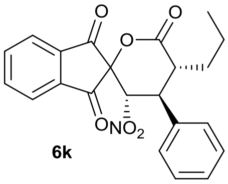
6i

6i was obtained as a white solid in 69% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 97% by HPLC on Chiralpak OD-H column (10% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t_{minor} = 21.08 min, t_{major} = 27.83 min. m.p. 156-158 ^{o}C; $[\alpha]_D^{20}$ -125.8 (*c* = 0.14 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13-8.06 (m, 2H), 8.01-7.94 (m, 2H), 7.33 (s, 1H), 6.97 (s, 2H), 5.54 (d, *J* = 12.0 Hz, 1H), 4.52 (t, *J* = 11.6 Hz, 1H), 3.07-3.05 (m, 1H), 1.49 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.26, 189.65, 168.82, 141.09, 140.20, 138.35, 138.02, 137.54, 127.78, 127.48, 126.32, 125.03, 124.73, 88.19, 76.78, 42.82, 42.36, 14.92 ppm; ESI HRMS: calcd. For $C_{18}H_{13}NO_6S$+Na 394.0361, found 394.0357.



6j

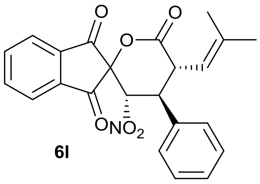
6j was obtained as a white solid in 78% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 99% by HPLC on Kromasil CelluCoat column (20% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t_{minor} = 8.15 min, t_{major} = 13.39 min. m.p. 169-171 ^{o}C; $[\alpha]_D^{20}$ -94.7 (*c* = 0.09 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12-8.05 (m, 2H), 8.01-7.93 (m, 2H), 7.40-7.32 (m, 3H), 7.28-7.26 (m, 2H), 5.61 (d, *J* = 12.0 Hz, 1H), 4.44 (t, *J* = 12.0 Hz, 1H), 3.12-3.08 (m, 1H), 2.08-2.02 (m, 1H), 1.56-1.48 (m, 1H), 1.12 (t, *J* = 7.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.19, 190.11, 168.56, 141.20, 140.11, 137.96, 137.41, 135.30, 129.52, 129.02, 127.69, 124.96, 124.67, 87.75, 77.23, 46.68, 42.77, 21.08, 9.71 ppm; ESI HRMS: calcd. For $C_{21}H_{17}NO_6$+Na 402.0954, found 402.0955.



6k

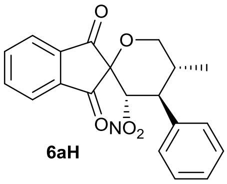
6k was obtained as a white solid in 75% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 99% by HPLC on Chiralpak AD-H column (10% 2-propanol/n-hexane, 1 mL/min), UV 220 nm, t_{major} = 11.22 min, t_{minor} = 12.98 min. m.p. 155-156 ^{o}C; $[\alpha]_D^{20}$ -91.8 (*c* = 0.08 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12-8.05 (m, 2H), 8.02-7.94 (m, 2H), 7.41-7.33 (m, 3H), 7.27-7.26 (m, 2H), 5.59 (d, *J* = 12.4 Hz, 1H), 4.39 (t, *J* = 12.0 Hz, 1H), 3.13-3.08 (m, 1H), 1.92-1.85 (m, 1H), 1.69-1.46 (m, 3H), 0.87 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$):

δ = 191.23, 189.06, 167.79, 140.16, 139.10, 136.93, 136.39, 134.37, 128.47, 127.98, 126.69, 123.92, 123.63, 86.76, 76.21, 44.71, 42.57, 29.46, 17.86, 13.05 ppm; ESI HRMS: calcd. For $C_{22}H_{19}NO_6$+Na 416.1110, found 416.1113.



6l

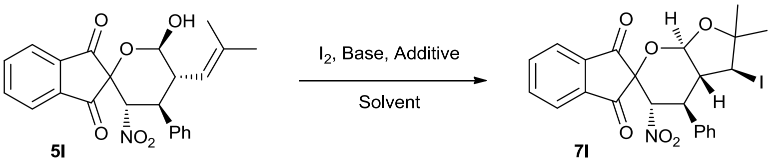
6l was obtained as a white solid in 60% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 99% by HPLC on Chiralpak OD-H column (15% 2-propanol/n-hexane, 1 mL/min), UV 220 nm, t_{minor} = 14.76 min, t_{major} = 15.86 min. m.p. 162-164 °C; $[\alpha]_D^{20}$ -125.2 (*c* = 0.10 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.13-8.06 (m, 2H), 8.02-7.94 (m, 2H), 7.36-7.27 (m, 3H), 7.24-7.22 (m, 2H), 5.75 (d, *J* = 12.4 Hz, 1H), 5.36 (d, *J* = 9.2 Hz, 1H), 4.24 (t, *J* = 12.0 Hz, 1H), 3.81 (dd, *J* = 10.8 Hz, *J* = 9.2 Hz, 1H), 1.68 (s, 3H), 1.14 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.31, 189.98, 168.32, 141.18, 140.23, 139.57, 137.95, 137.47, 135.32, 129.13, 128.69, 127.97, 124.98, 124.72, 117.60, 86.67, 77.22, 46.55, 46.03, 25.53, 17.78 ppm; ESI HRMS: calcd. For $C_{23}H_{19}NO_6$+Na 428.1110, found 428.1107.



6aH

6aH was obtained as a white solid in 75% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 97% by HPLC on Chiralpak AD-H column (10% 2-propanol/n-hexane, 1 mL/min), UV 220 nm, t_{major} = 12.75 min, t_{minor} = 23.03 min. m.p. 183-184 °C; $[\alpha]_D^{20}$ -145.8 (*c* = 0.08 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.06-8.01 (m, 2H), 7.93-7.86 (m, 2H), 7.37-7.28 (m, 5H), 5.41 (d, *J* = 12.0 Hz, 1H), 4.25 (t, *J* = 12.0 Hz, 1H), 3.93 (dd, *J* = 12.0 Hz, *J* = 5.2 Hz, 1H), 3.85 (t, *J* = 12.0 Hz, 1H), 2.35-2.27 (m, 1H), 0.78 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.83, 193.66, 141.50, 140.09, 137.09, 137.04, 136.60, 128.94, 127.99, 124.49, 124.16, 88.45, 73.97, 69.77, 47.58, 36.19, 13.93 ppm; ESI HRMS: calcd. For $C_{20}H_{17}NO_5$+Na 374.1004, found 374.1007.

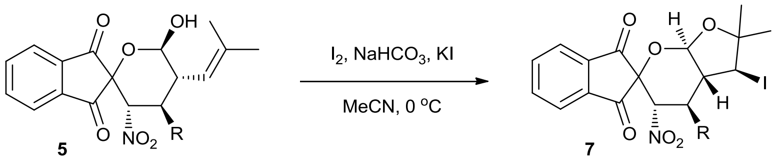
3. Screening studies to improve the yield of hexahydrofuro[2,3-*b*]pyran derivatives 7[a]



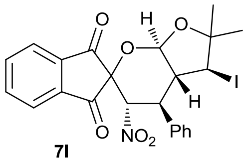
entry	Base	additive	Solvent[b]	Time (h)	Yield[c] (%)	ee[d]
1	Na_2CO_3	-	THF	12	49	82
2	K_2CO_3	**-**	THF	12	45	78
3	$NaHCO_3$	-	THF	12	48	95
4	$NaHCO_3$	KI	THF	6	53	96
5	$NaHCO_3$	KI	Dioxane	8	31	95
6	$NaHCO_3$	KI	DCM	8	38	96
7	$NaHCO_3$	KI	MeCN	2	61	97
8	**$NaHCO_3$**	**KI**	**MeCN[e]**	**2**	**71**	**97**

[a] Unless noted otherwise, reactions were performed with allylic hemiacetal **5X** (0.4 mmol), I_2 (1.2 mmol), Base (1.2mmol), and additive (0.04 mmol) at 0°C in 4 mL solvent for the times specified (TLC monitoring). [b] The commercially available solvent was used without distillation or drying. [c] Isolated yield. [d] By chiral HPLC analysis. [e] The anhydrous acetonitrile was used.

4. General procedure for the asymmetric synthesis of 7

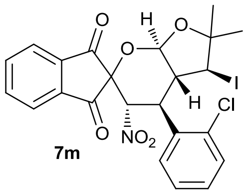


To a solution of allylic hemiacetal **5** (0.4 mmol) in 4 mL anhydrous MeCN were added I_2 (304.8 mg, 1.2 mmol), $NaHCO_3$ (100.8 mg, 1.2 mmol), and KI (6.6 mg, 0.04 mmol). The mixture was stirred for the times specified (TLC monitoring) at 0 °C. Ethyl acetate (20 mL) was added and the resulting mixture washed with saturated aqueous sodium thiosulfate (30 mL). The separated aqueous phase was extracted with ether (3×10 mL) and the combined organic solution dried and evaporated. The residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20:1) to give tetracyclic hexahydrofuro[2,3-*b*]pyran-based compounds **7**. For the reason that the major and minor diastereomers of compounds **7** could not be isolated in pure form by column chromatography, the dr values of **7** were calculated by chiral HPLC analysis.



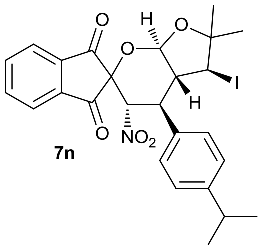
7l

7l was obtained as a white solid in 71% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 97% by HPLC on Chiralpak AD-H column (20% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t_{major} = 10.09 min, t_{minor} = 12.14 min. m.p. 194-196 ^{o}C; $[\alpha]_D^{20}$ -124.2 (*c* = 0.08 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.09-8.01 (m, 2H), 7.92-7.90 (m, 2H), 7.44-7.31 (m, 5H), 5.66 (d, *J* = 8.0 Hz, 1H), 5.56 (d, *J* = 10.8 Hz, 1H), 4.18 (t, *J* = 11.6 Hz, 1H), 3.94 (d, *J* = 12.4 Hz, 1H), 2.53 (td, *J* = 12.0 Hz, *J* = 8.0 Hz, 1H), 1.51 (s, 3H), 1.36 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.71, 171.25, 140.76, 140.41, 137.01, 136.99, 131.77, 129.03, 128.86, 128.66, 124.82, 124.60, 100.20, 85.95, 85.75, 52.08, 45.90, 30.61, 26.68, 25.22 ppm; ESI HRMS: calcd. For $C_{23}H_{20}INO_6$+Na 556.0233, found 556.0231.



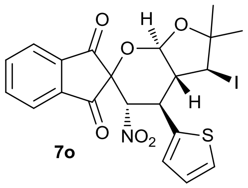
7m

7m was obtained as a white solid in 69% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 94% by HPLC on Chiralpak AD-H column (20% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t_{major} = 6.56 min, t_{minor} = 12.24 min. m.p. 206-207 ^{o}C; $[\alpha]_D^{20}$ -149.5 (*c* = 0.32 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.10-8.02 (m, 2H), 7.93-7.92 (m, 2H), 7.51-7.47 (m, 2H), 7.38-7.25 (m, 2H), 5.65-5.62 (m, 2H), 5.05 (t, *J* = 11.6 Hz, 1H), 4.07 (d, *J* = 12.4 Hz, 1H), 2.41 (td, *J* = 12.0 Hz, *J* = 8.0 Hz, 1H), 1.49 (s, 3H), 1.38 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.44, 191.14, 140.73, 140.41, 136.98, 136.94, 136.21, 132.80, 130.14, 129.25, 127.31, 126.78, 124.88, 124.68, 100.26, 85.95, 84.30, 81.83, 53.04, 40.26, 30.59, 26.72, 24.99 ppm; ESI HRMS: calcd. For $C_{23}H_{19}ClINO_5$+Na 589.9843, found 589.9841.



7n

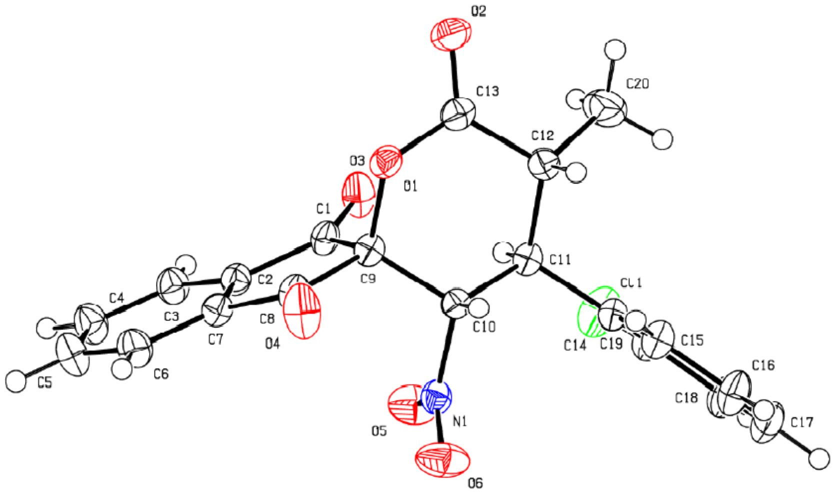
7n was obtained as a white solid in 65% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 98% by HPLC on Kromasil CelluCoat column (5% 2-propanol/n-hexane, 1 mL/min), UV 220 nm, t_{minor} = 9.09 min, t_{major} = 10.13 min. m.p. 171-173 ^{o}C; $[\alpha]_D^{20}$ -139.6 (*c* = 0.18 in CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.09-8.01 (m, 2H), 7.93-7.90 (m, 2H), 7.34-7.24 (m, 4H), 5.66 (d, *J* = 8.0 Hz, 1H), 5.55 (d, *J* = 11.2 Hz, 1H), 4.15 (t, *J* = 11.6 Hz, 1H), 3.92 (d, *J* = 12.4 Hz, 1H), 2.94-2.87 (m, 1H), 2.50 (td, *J* = 12.4 Hz, *J* = 8.0 Hz, 1H), 1.51 (s, 3H), 1.36 (s, 3H), 1.24 (s, 3H), 1.22 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.76, 191.37, 149.66, 140.78, 140.42, 137.00, 131.32, 126.88, 125.38, 124.81, 124.58, 100.21, 86.08, 85.73, 52.11, 45.53, 33.75, 30.60, 26.68, 25.20, 24.00 ppm; ESI HRMS: calcd. For $C_{26}H_{26}INO_6$+H 576.0883, found 576.0886.

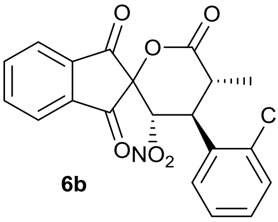


7o

7o was obtained as a white solid in 61% yield for two steps after flash chromatography and the enantiomeric excess was determined to be 97% by HPLC on Kromasil CelluCoat column (5% 2-propanol/n-hexane, 1 mL/min), UV 254 nm, t_{minor} = 14.13 min, t_{major} = 28.33 min. m.p. 188-190 °C; $[\alpha]_D^{20}$ -157.6 (*c* = 0.06 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10-8.00 (m, 2H), 7.95-7.90 (m, 2H), 7.30 (d, *J* = 5.2 Hz, 1H), 7.13 (d, *J* = 3.2 Hz, 1H), 7.02 (dd, *J* = 4.8 Hz, *J* = 3.6 Hz, 1H), 5.65 (d, *J* = 8.0 Hz, 1H), 5.46 (d, *J* = 10.8 Hz, 1H), 4.51 (t, *J* = 11.6 Hz, 1H), 3.98 (d, *J* = 12.4 Hz, 1H), 2.50 (td, *J* = 12.0 Hz, *J* = 8.0 Hz, 1H), 1.53 (s, 3H), 1.38 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.61, 190.93, 140.71, 140.42, 137.13, 137.06, 127.18, 125.12, 124.86, 124.63, 100.06, 89.88, 87.07, 85.84, 53.34, 30.60, 26.71, 24.91 ppm; ESI HRMS: calcd. For $C_{21}H_{18}INO_6S$+Na 561.9797, found 561.9798.

5. Crystal data of 6b



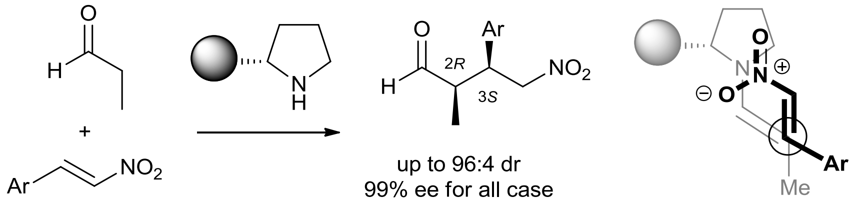


6b

Empirical formula	$C_{20}H_{14}ClNO_6$
Formula weight	399.77
Temperature/K	143(2)
Crystal system	orthorhombic
Space group	P212121
a/Å	8.1843(16)
b/Å	10.679(2)
c/Å	21.790(4)
α/°	90.00
β/°	90.00
γ/°	90.00
Volume/Å3	1904.4(6)
Z	4
ρcalcmg/mm3	1.394
m/mm-1	0.238
F(000)	824.0
Crystal size/mm3	0.4 × 0.38 × 0.37
2Θ range for data collection	5.34 to 58.28 °
Index ranges	$-11 \le h \le 11$, $-14 \le k \le 13$, $-29 \le l \le 29$
Reflections collected	16915
Independent reflections	5110[R(int) = 0.0281]
Data/restraints/parameters	5110/0/254
Goodness-of-fit on F2	1.000
Final R indexes [I>=2σ (I)]	R1 = 0.0340, wR2 = 0.0802
Final R indexes [all data]	R1 = 0.0363, wR2 = 0.0819
Largest diff. peak/hole / e Å-3	0.23/-0.30
Flack parameter	0.03(5)

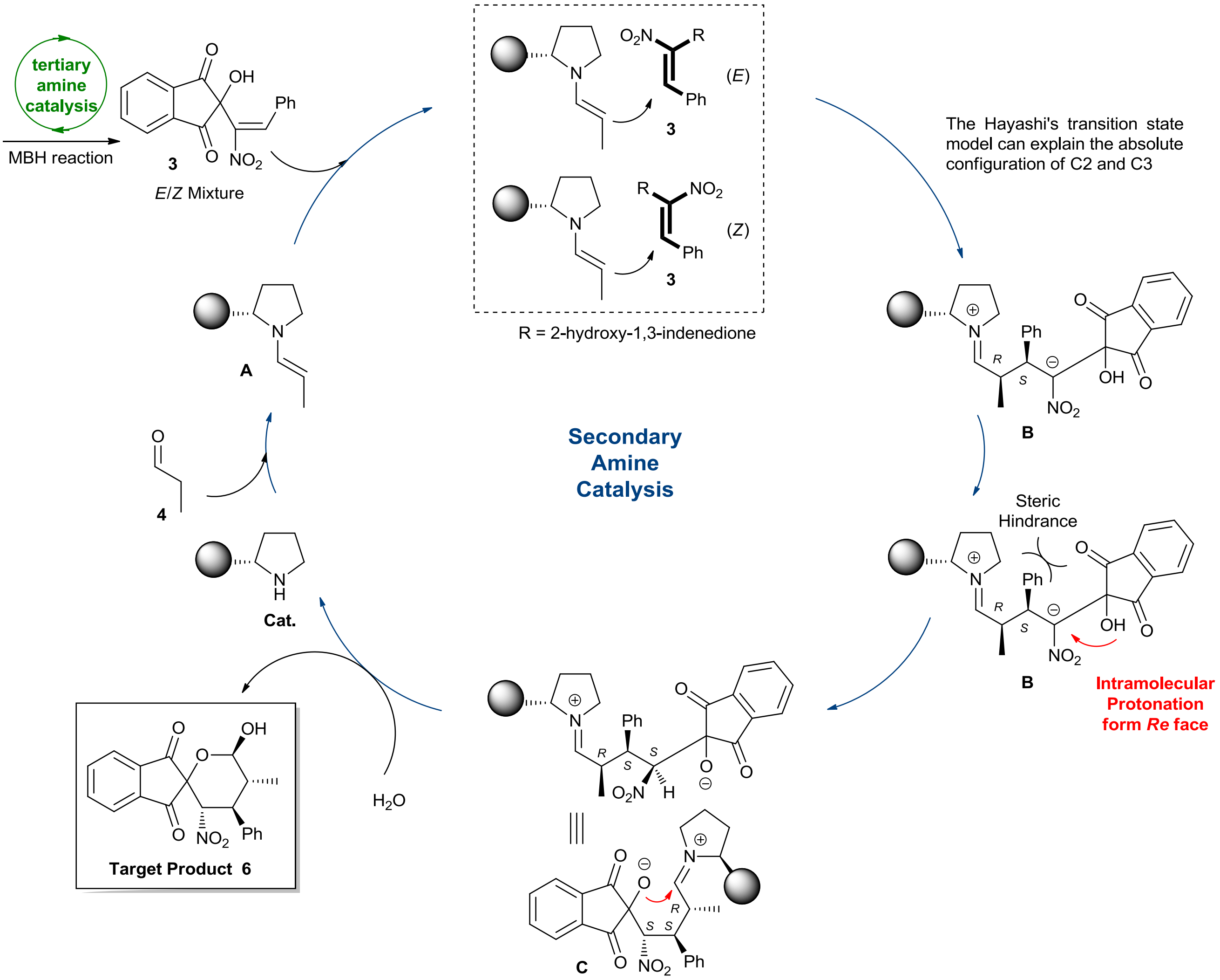
6. Proposed catalytic cycles for the enantioselective transformation

※ In 2005, Yujiro Hayashi demonstrated that diphenylprolinol silyl ethers were efficient chiral secondary amine catalyst in the asymmetric Michael reaction of aldehydes and nitroalkenes. A reasonable transition state model has been proposed to explain the high diastereoselectivities and excellent enantioselectivities of this reaction. The Hayashi's transition state model can explain the absolute configuration of C2 (α-position of CHO) and C3 (β-position of NO_2). (ACIE. 2005, 44, 4212)



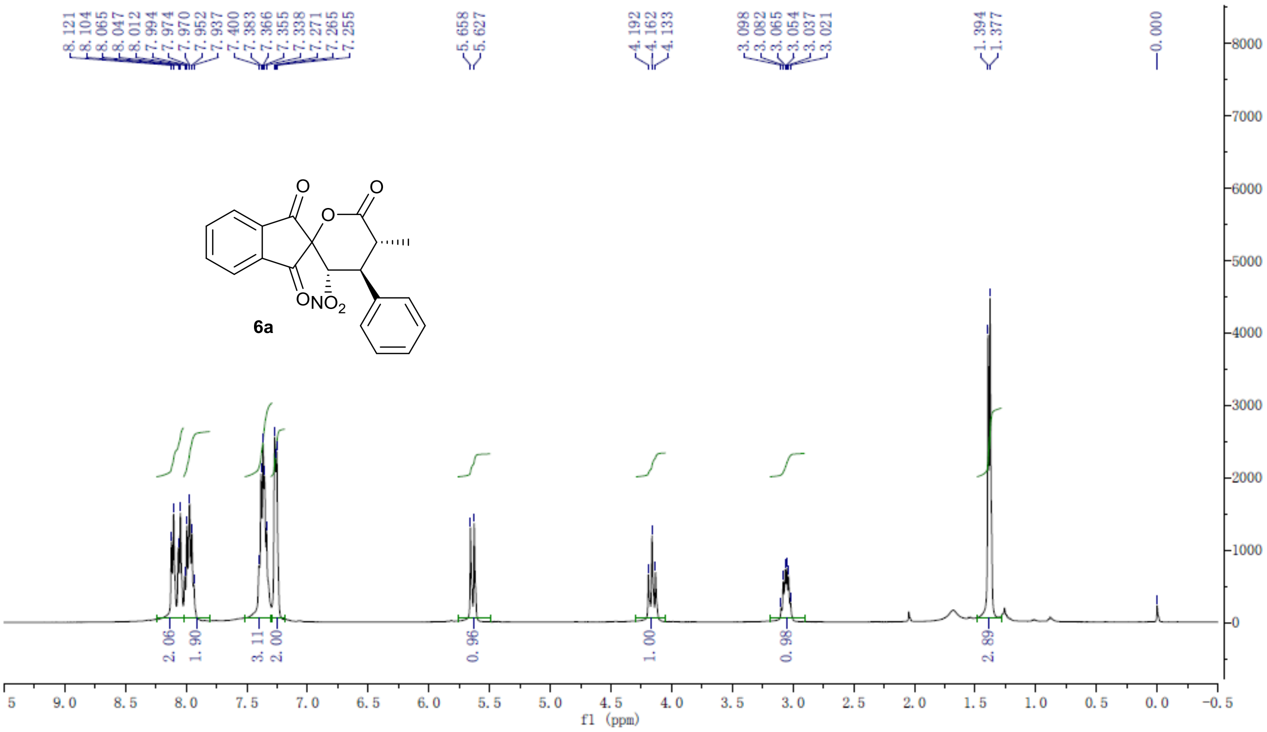
Angew. Chem. Int. Ed. **2005**, *44*, 4212

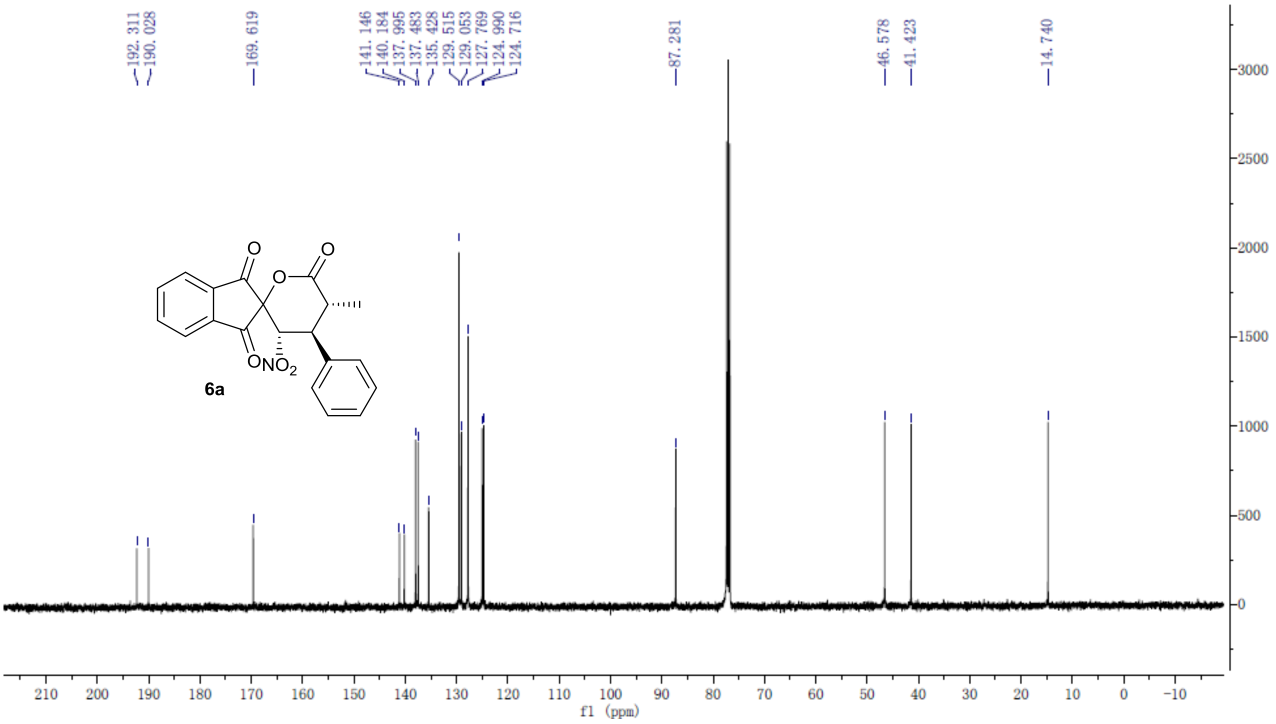
Based on Hayashi's transition state model, we proposed the plausible catalytic cycles and transition-state structures which were responsible for the enantioselective transformation:



The plausible mechanism includes two catalytic cycles: tertiary amine catalysis and secondary amine catalysis. In the first catalytic cycle, the tertiary amine-catalyzed MBH reaction of conjugated nitroalkene with ninhydrin can provide tertiary alcohol intermediate **3** (E/Z mixtures), which then participates directly in the second catalytic cycle by serving as the receptor in an asymmetric Michael addition. The activated nucleophilic enamine specie **A** would be generated from aldehyde **4** and secondary amine catalyst. The transition state structure of asymmetric Michael addition between enamine **A** and nitroalkene derivative **3** is similar to Hyashi's model. Therefore, Zwitterion intermediate **B** could be obtained with good stereoselectivities at C2 (α-position of CHO) and C3 (β-position of NO$_2$). It is noteworthy that the E/Z configuration of MBH tertiary alcohol **3** will not affect the chirality of C4 (α-position of NO$_2$), owing to the generation of achiral carbanion at this position. Influenced by the steric hindrance effect of benzene ring at C3 position, intramolecular C4 protonation form *Re* face will afford Zwitterion intermediate **C** with high diastereoselectivity. Subsequent hydrolysis and hemi-acetalization provides the desired oxa-spirocyclic indanone **6** with excellent ee and good dr value, and the catalyst is regenerated.

7. NMR spectra and HPLC chromatograms





Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	10.86	100.687	50.30	250.073	n.a.
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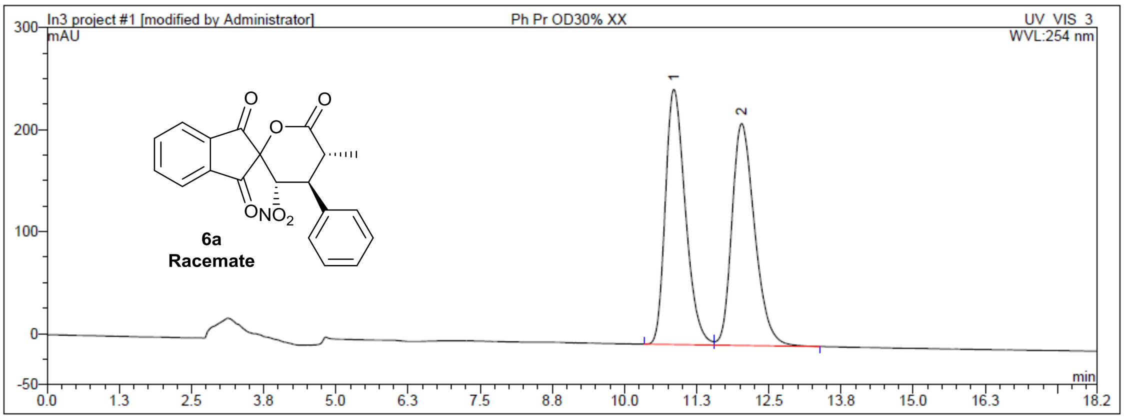
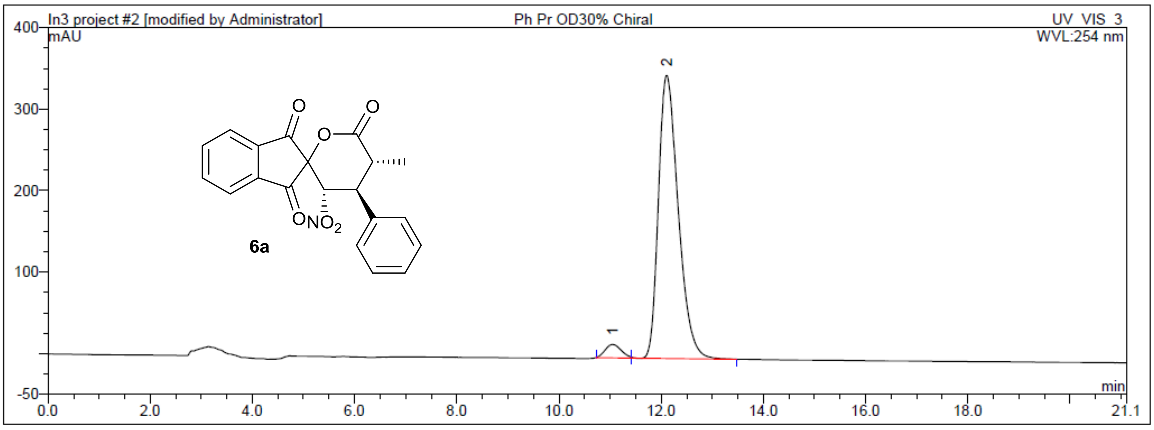
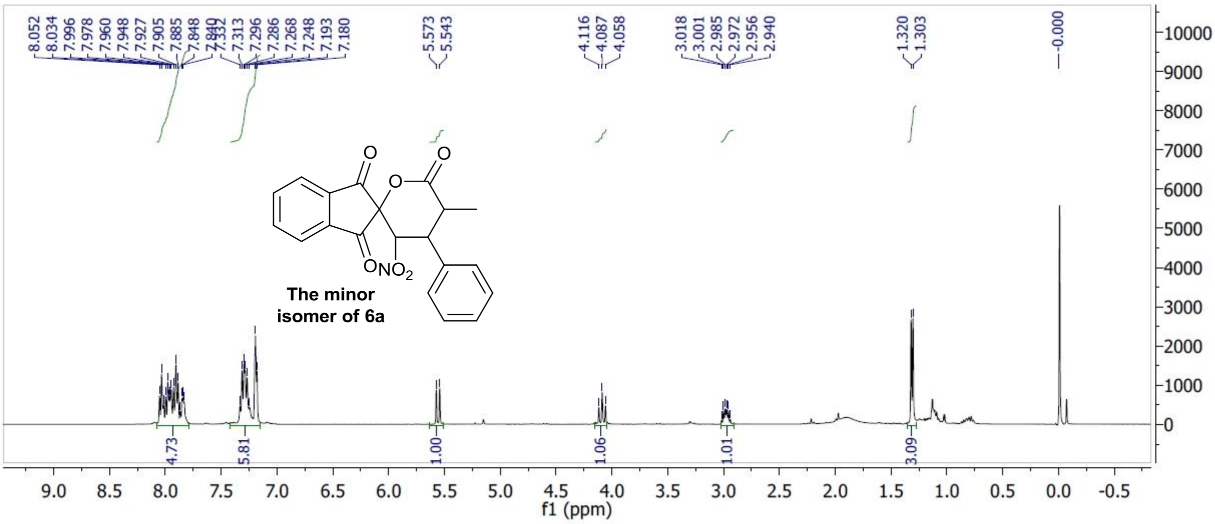
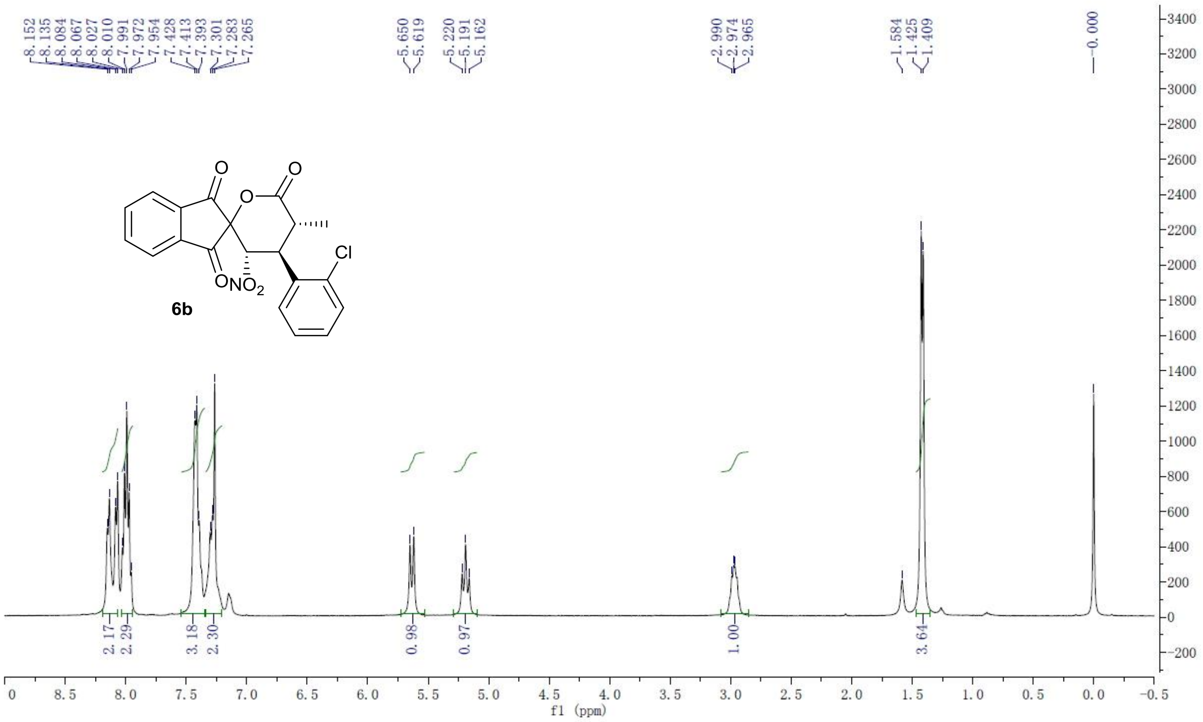


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.05	5.913	3.66	16.395	n.a.
2	n.a.	12.11	155.766	96.34	347.363	n.a.



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8.027
8.010
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7.972
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7.428
7.413
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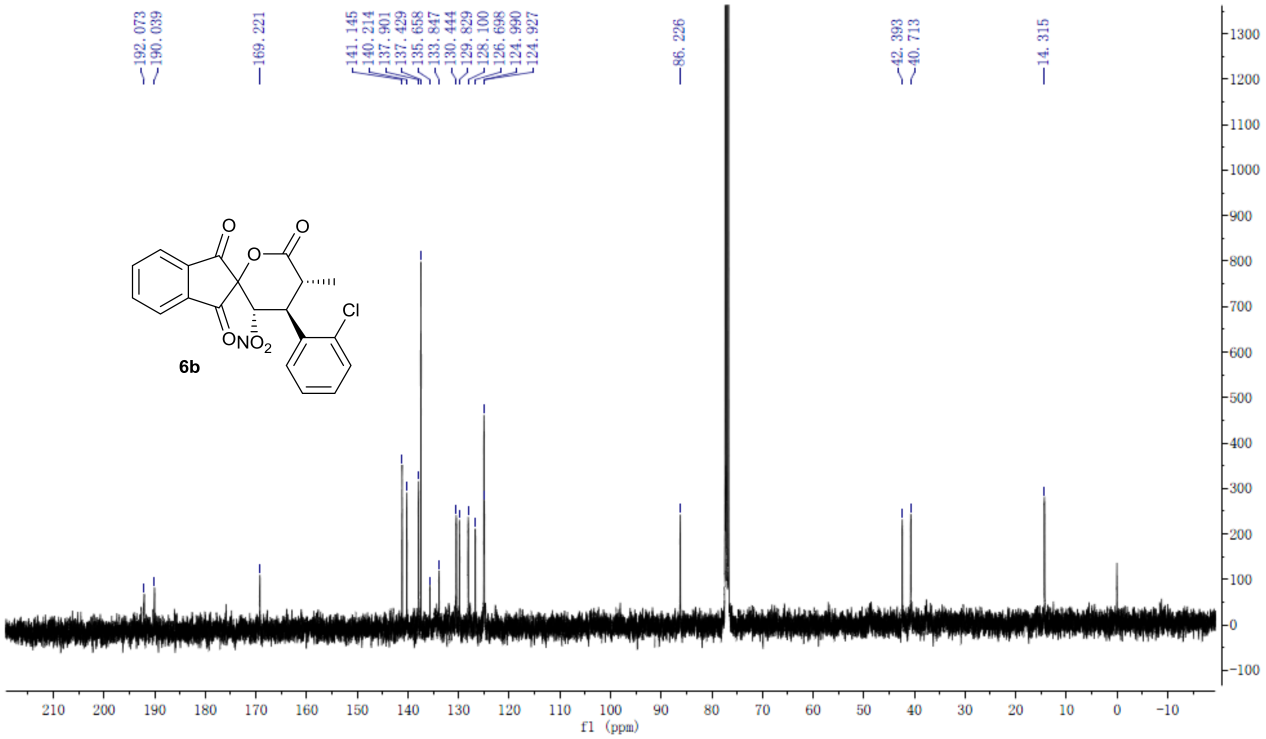
7.283
7.265
5.650
5.619
5.220
5.191
5.162
2.990
2.974
2.965
1.584
1.425
1.409
0.000
O
O
O
Cl
O
NO2
6b
2.17
2.29
3.18
2.30
0.98
0.97
1.00
3.64
f1 (ppm)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141.145
140.214
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137.429
135.658
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130.444
129.829
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124.927
86.226
42.393
40.713
14.315
O
O
O
Cl
O
NO2
6b
f1 (ppm)

Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	26.53	376.848	49.53	301.463	n.a.
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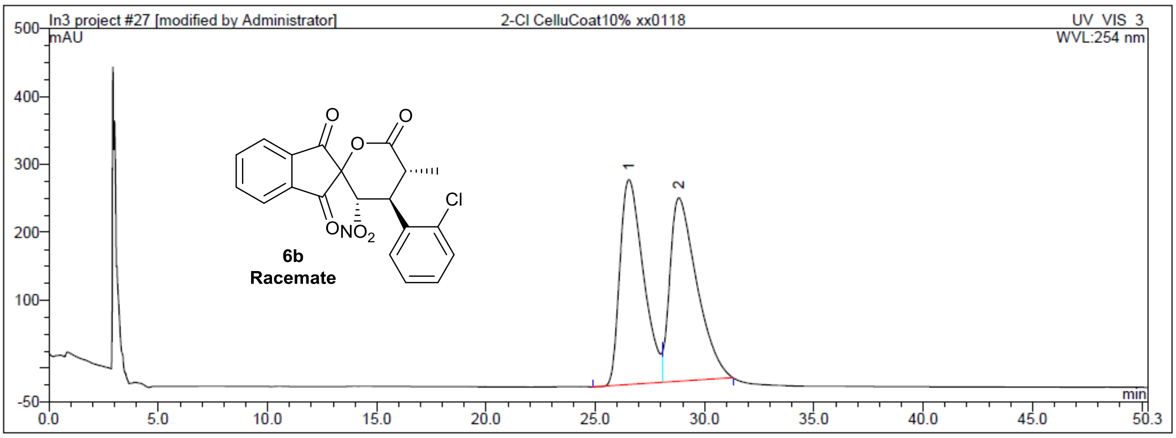

Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
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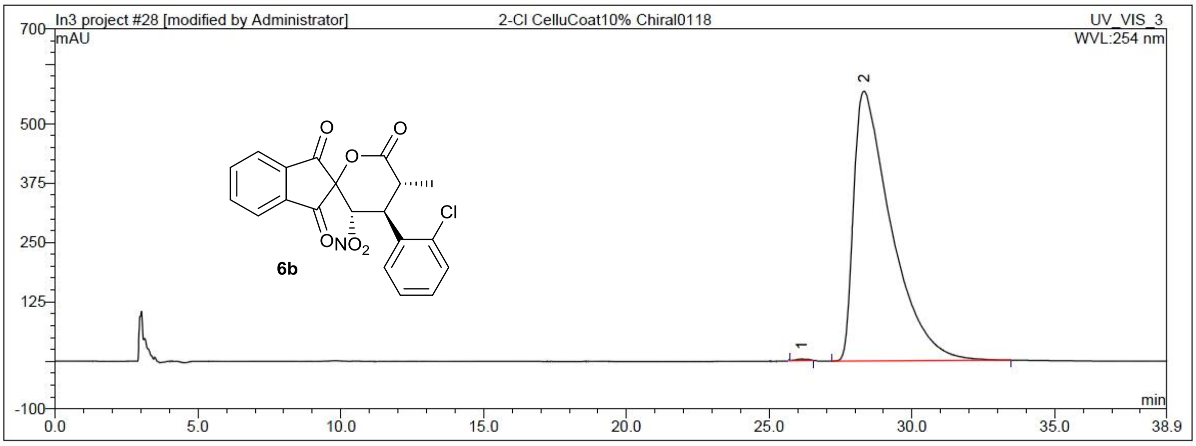
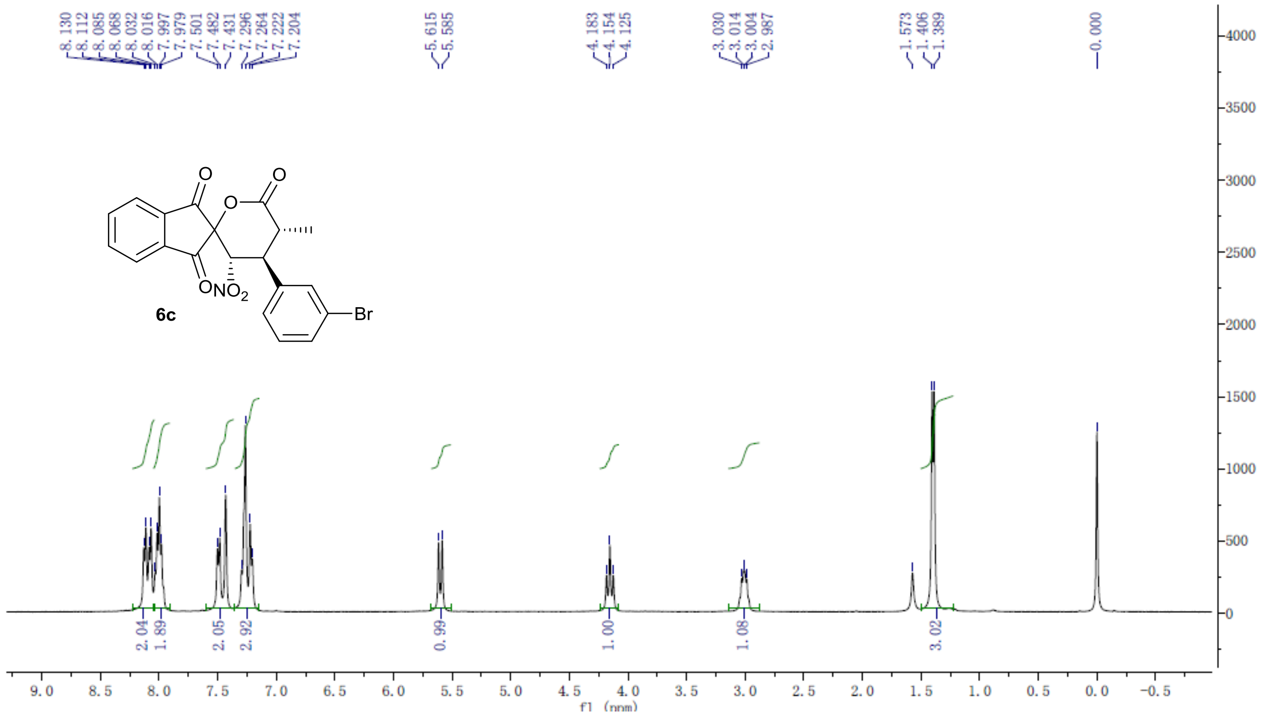
2	n.a.	28.33	865.230	99.83	567.553	n.a.

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8.068
8.032
8.016
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7.979
7.501
7.482
7.431
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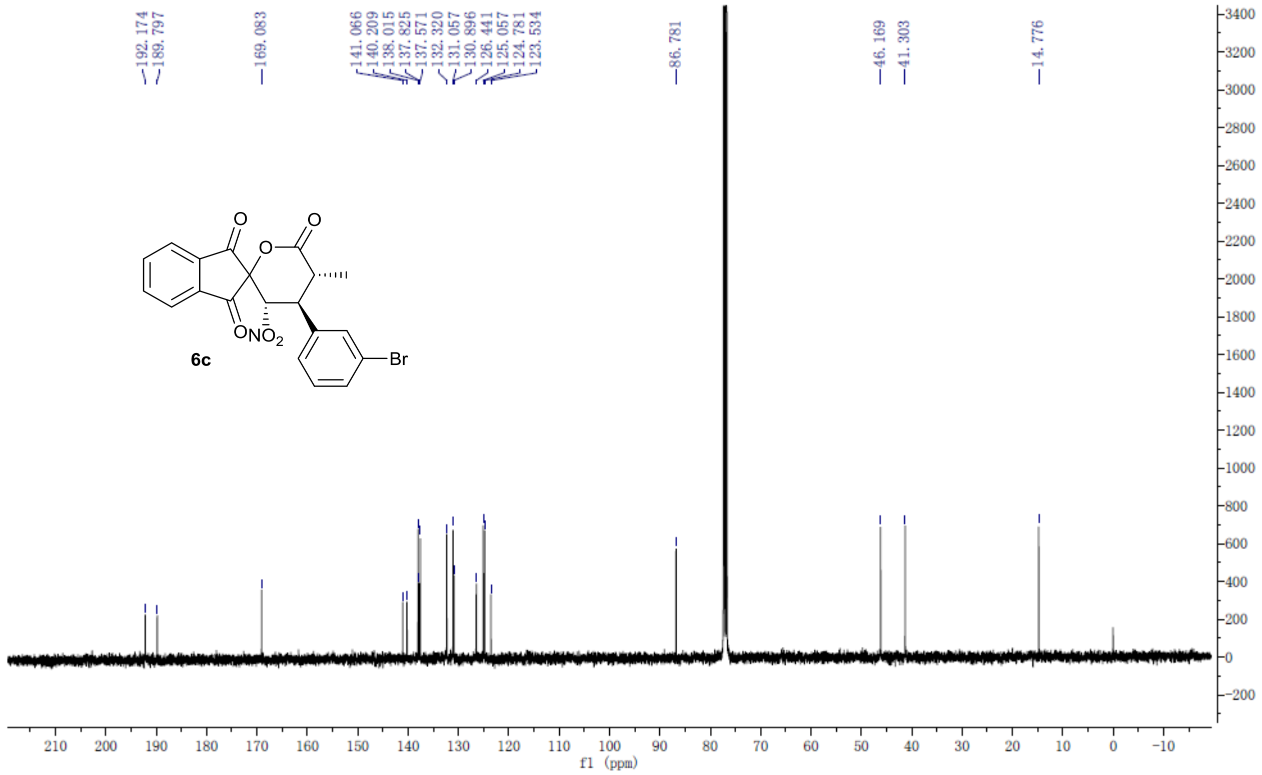
7.222
7.204
5.615
5.585
4.183
4.154
4.125
3.030
3.014
3.004
2.987
1.573
1.406
1.389
0.000
O
O
O
O
NO2
Br
6c
2.04
1.89
2.05
2.92
0.99
1.00
1.08
3.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)
4000
3500
3000
2500
2000
1500
1000
500
0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131.057
130.896
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125.057
124.781
123.534
86.781
46.169
41.303
14.776
O
O
O
O
NO2
Br
6c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
−200

Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
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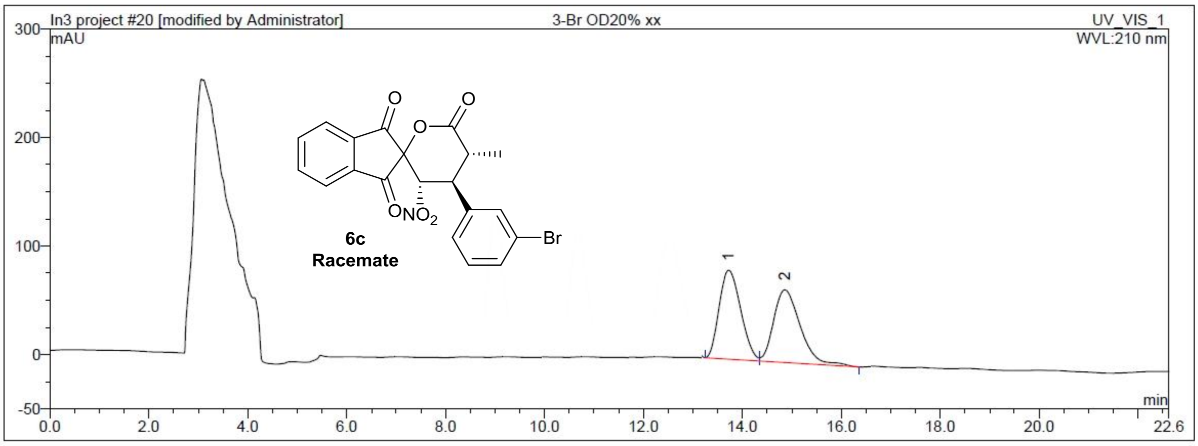

Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
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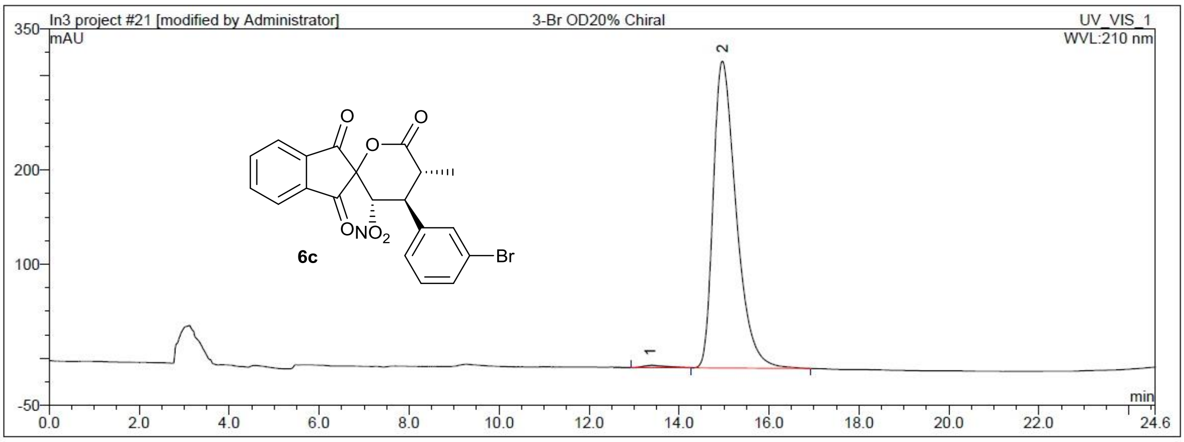
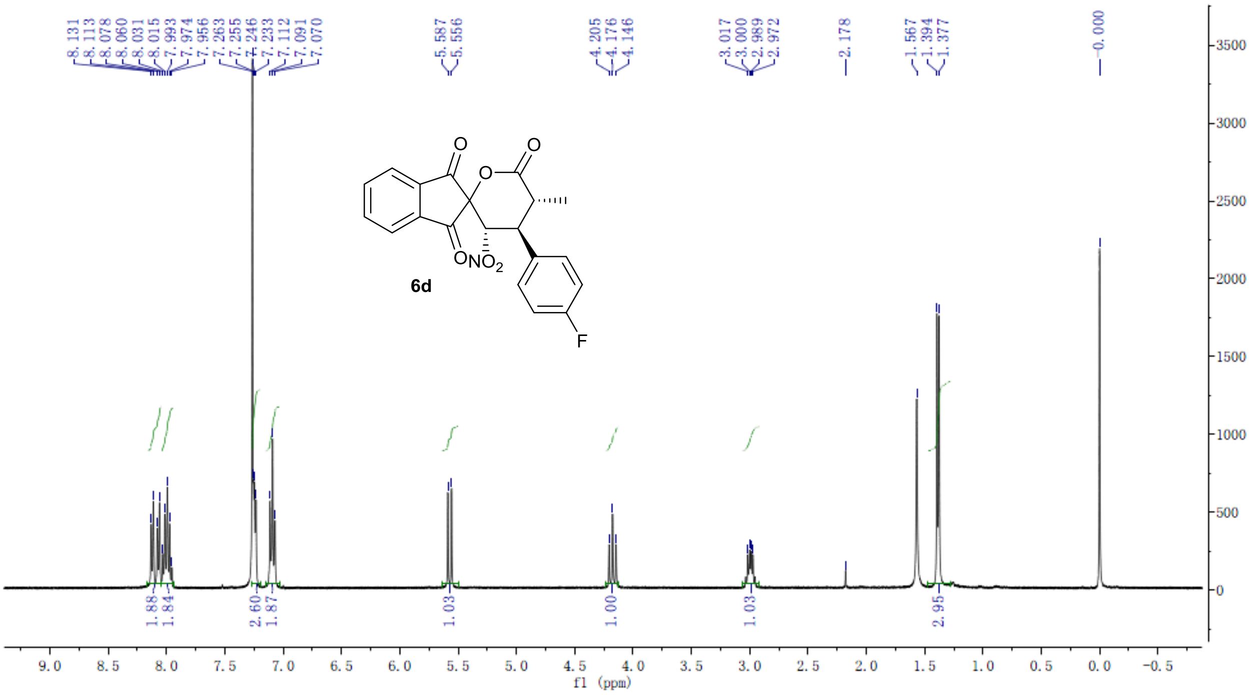
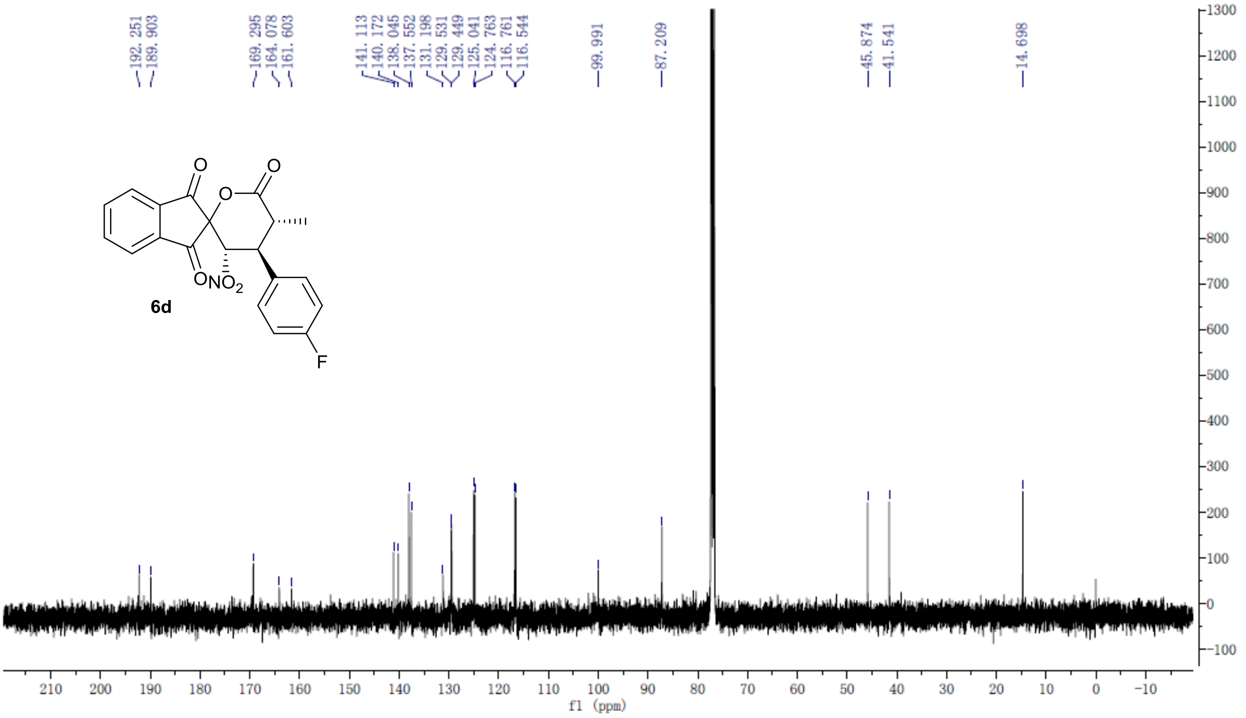
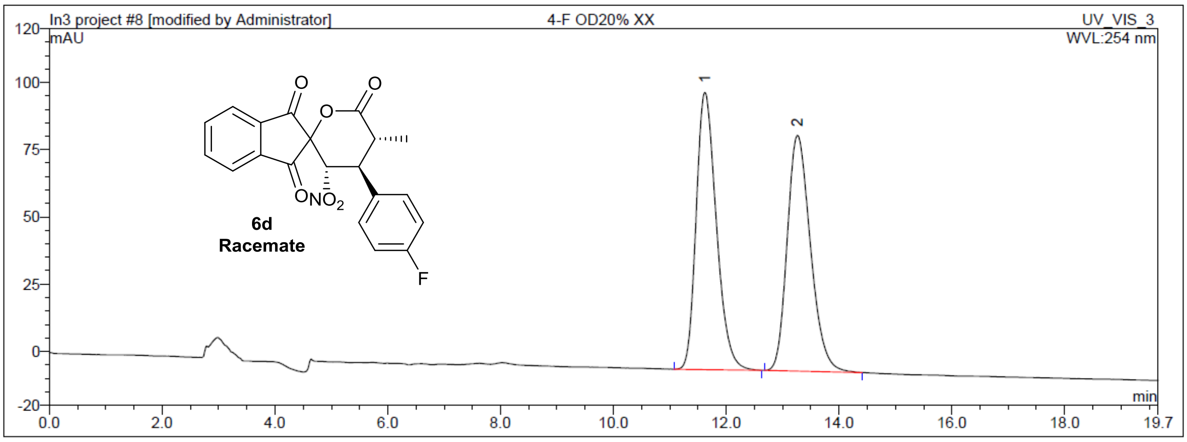



8.131 8.113 8.078 8.060 8.031 8.015 7.993 7.974 7.956 7.263 7.255 7.246 7.233 7.112 7.091 7.070
5.587 5.556
4.205 4.176 4.146
3.017 3.000 2.989 2.972
2.178
1.567 1.394 1.377
0.000
1.88 1.84 2.60 1.87 1.03 1.00 1.03 2.95
6d
O
O
O
O
NO2
F
3500 3000 2500 2000 1500 1000 500 0
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


192.251 189.903
169.295 164.078 161.603
141.113 140.172 138.045 137.552 131.198 129.531 129.449 125.041 124.763 116.761 116.544
99.991
87.209
45.874 41.541
14.698
6d
O
O
O
O
NO2
F
1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

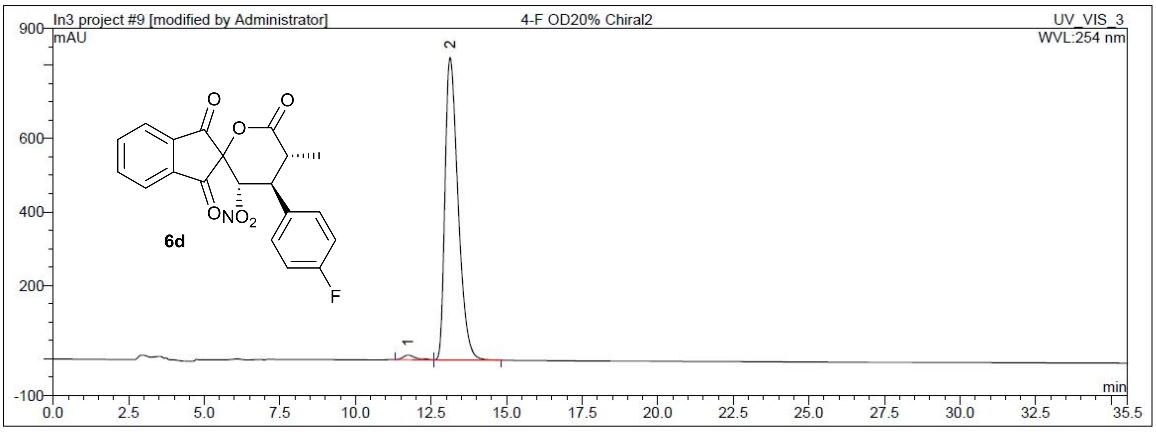
Peak Analysis Report

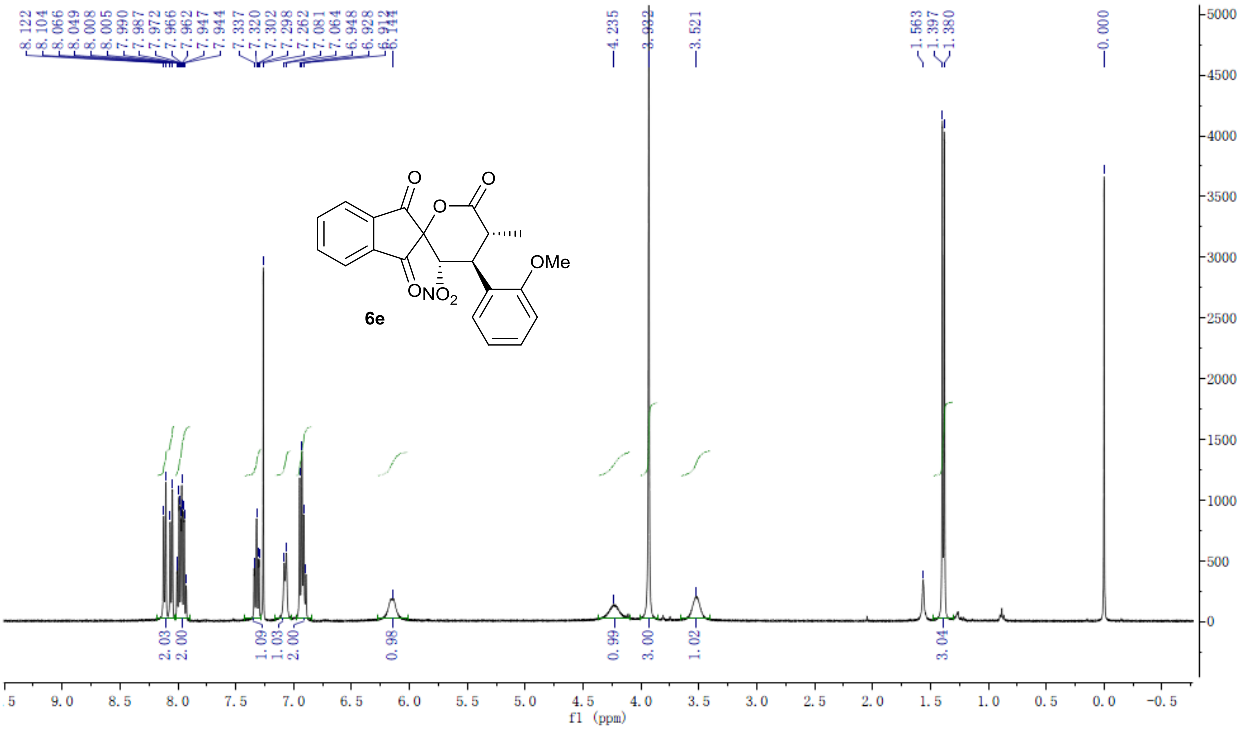
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.63	42.711	50.47	103.008	n.a.
2	n.a.	13.27	41.908	49.53	87.620	n.a.

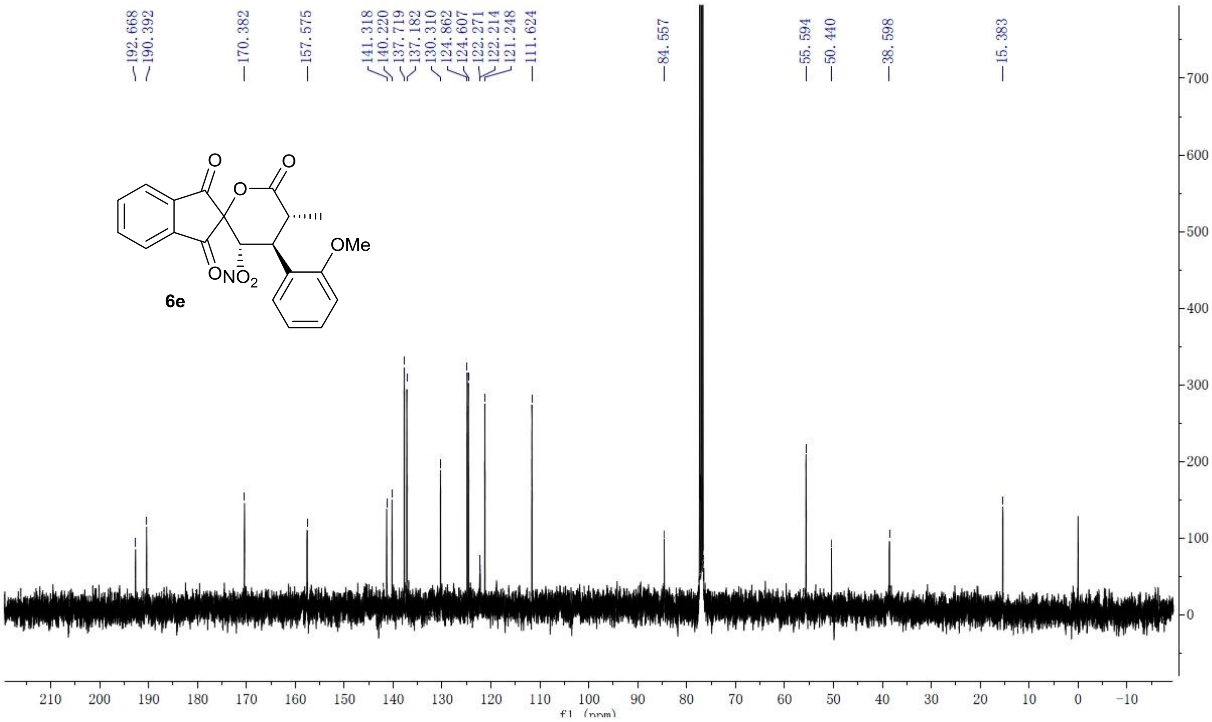


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.74	5.833	1.40	12.197	n.a.
2	n.a.	13.13	412.027	98.60	823.225	n.a.

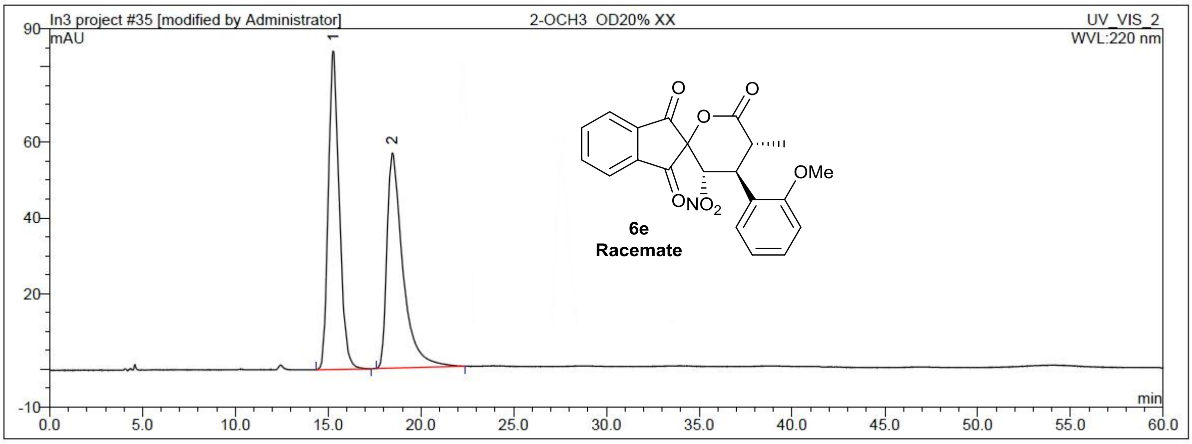



8.122
8.104
8.066
8.049
8.008
8.005
7.990
7.987
7.972
7.966
7.962
7.947
7.944
7.337
7.320
7.302
7.298
7.262
7.081
7.064
6.948
6.928
6.912
6.144
4.235
3.932
3.521
1.563
1.397
1.380
0.000
O
O
O
OMe
NO2
O
6e
2.03
2.00
1.09
1.03
2.00
0.98
0.99
3.00
1.02
3.04
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


192.668
190.392
170.382
157.575
141.318
140.220
137.719
137.182
130.310
124.862
124.607
122.271
122.214
121.248
111.624
84.557
55.594
50.440
38.598
15.383
O
O
O
OMe
NO2
O
6e
700
600
500
400
300
200
100
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Peak Analysis Report

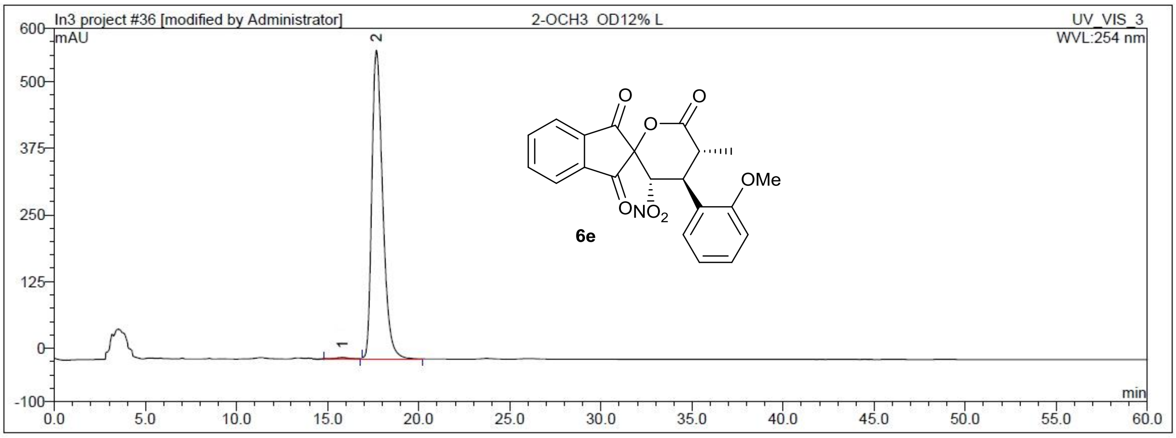
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	15.62	39.256	50.28	84.166	n.a.
2	n.a.	17.55	38.824	49.72	56.744	n.a.



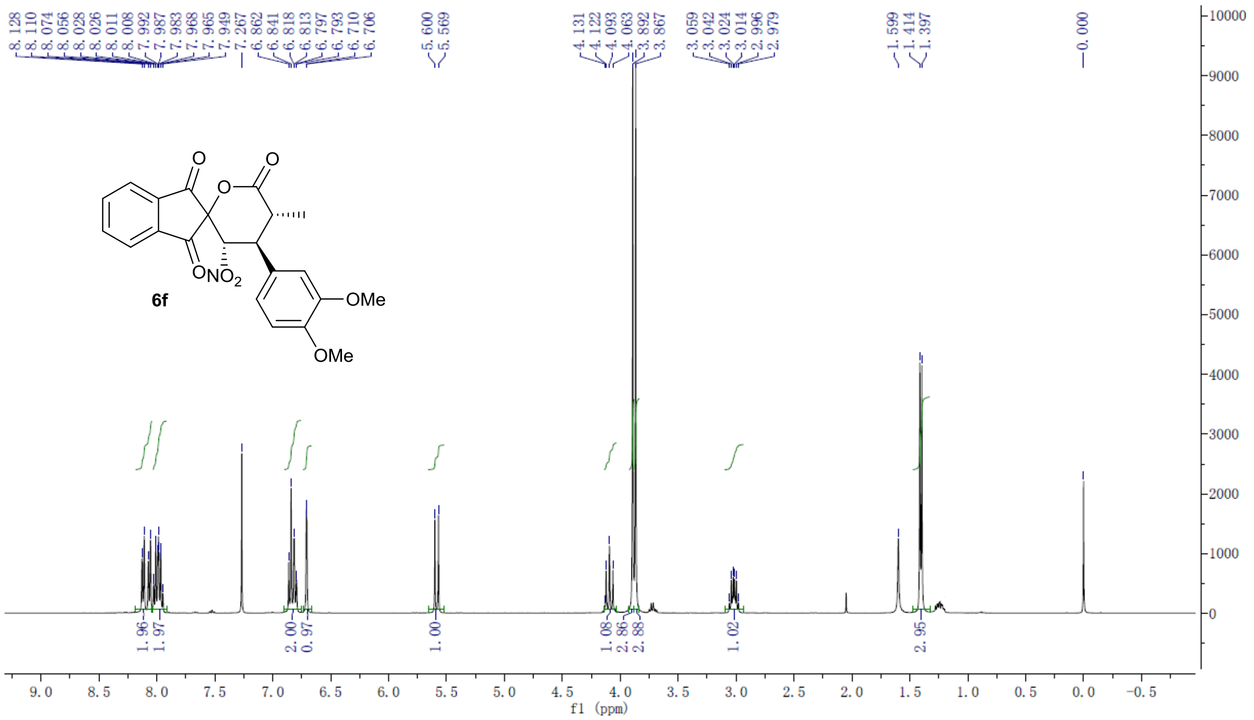
6e
Racemate

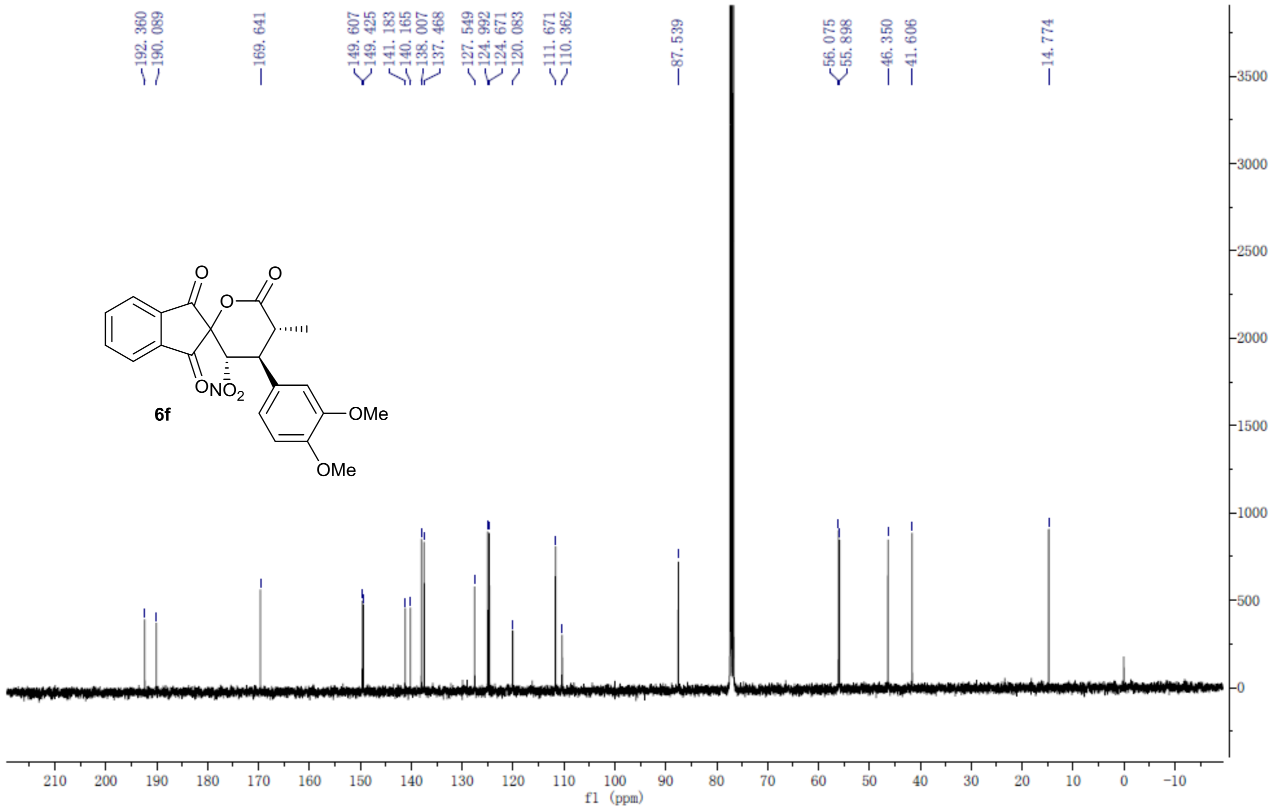
Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	15.64	1.939	0.48	2.615	n.a.
2	n.a.	17.68	400.824	99.52	578.678	n.a.



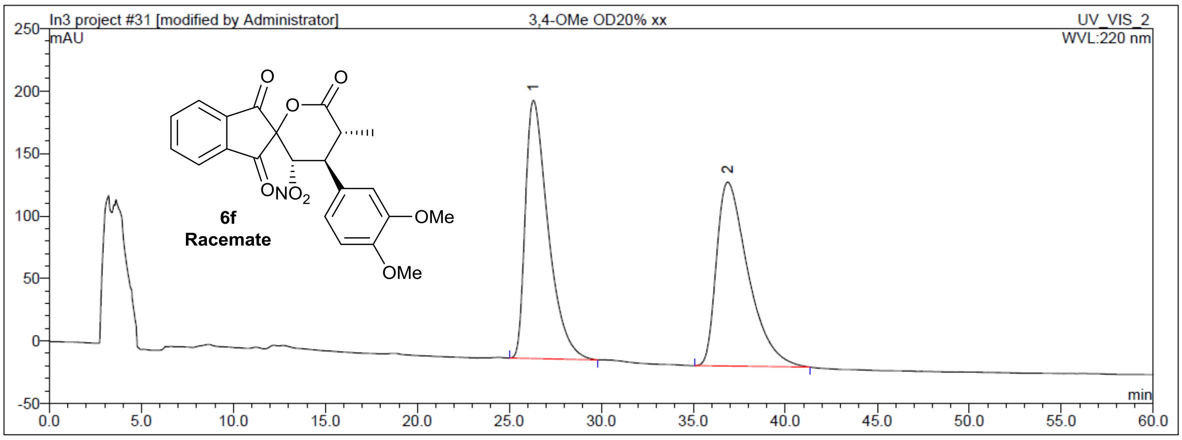
6e


8.128
8.110
8.074
8.056
8.028
8.026
8.011
8.008
7.992
7.987
7.983
7.968
7.965
7.949
7.267
6.862
6.841
6.818
6.813
6.797
6.793
6.710
6.706
5.600
5.569
4.131
4.122
4.093
4.063
3.892
3.867
3.059
3.042
3.024
3.014
2.996
2.979
1.599
1.414
1.397
0.000
O
O
O
O
NO2
OMe
OMe
6f
1.96
1.97
2.00
0.97
1.00
1.08
2.86
2.88
1.02
2.95
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


192.360
190.089
169.641
149.607
149.425
141.183
140.165
138.007
137.468
127.549
124.992
124.671
120.083
111.671
110.362
87.539
56.075
55.898
46.350
41.606
14.774
O
O
O
O
NO2
OMe
OMe
6f
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

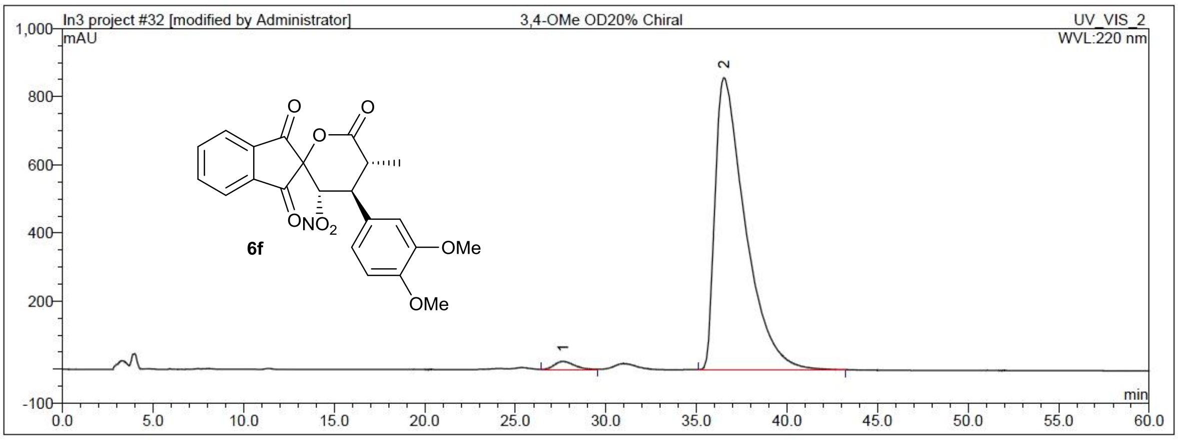
Peak Analysis Report

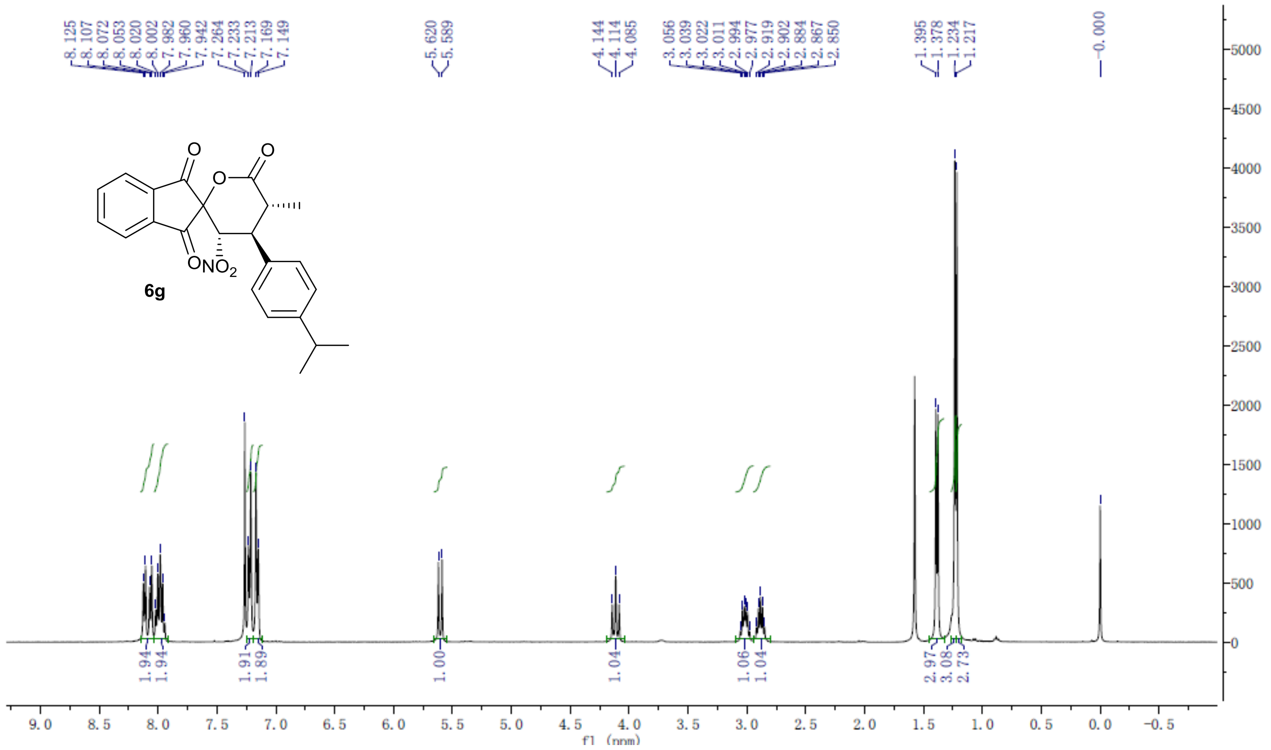
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	26.31	295.694	50.12	206.502	n.a.
2	n.a.	36.88	294.240	49.88	147.219	n.a.

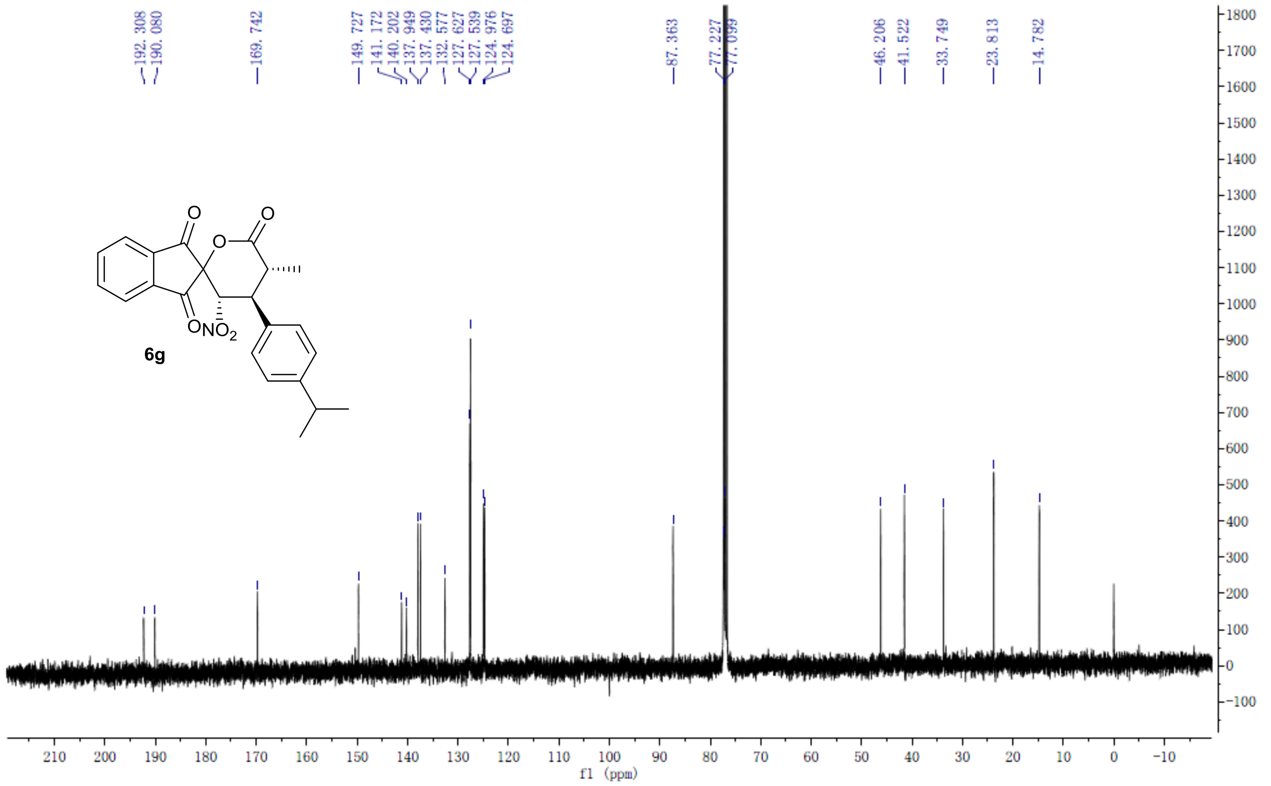


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	27.63	28.594	1.70	23.184	n.a.
2	n.a.	36.53	1655.628	98.30	856.754	n.a.

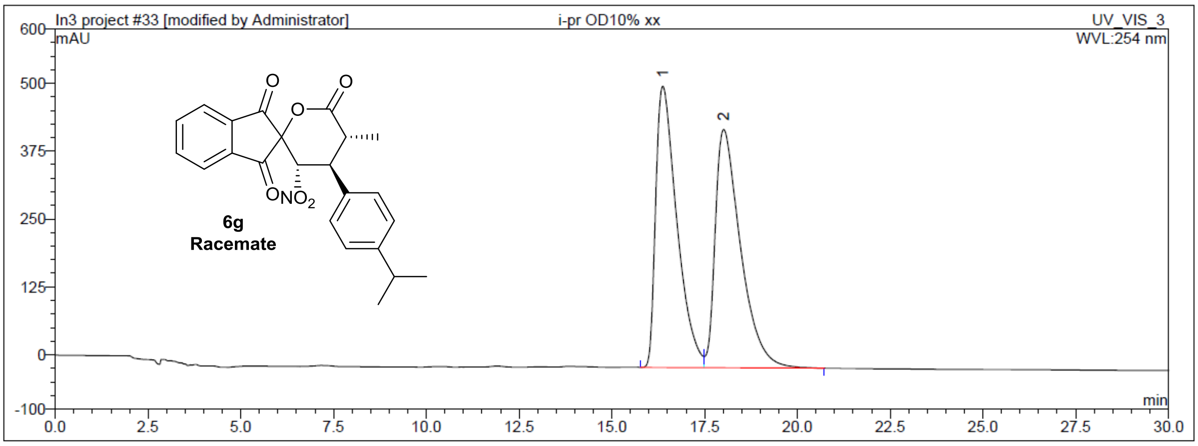



8.125
8.107
8.072
8.053
8.020
8.002
7.982
7.960
7.942
7.264
7.233
7.213
7.169
7.149
5.620
5.589
4.144
4.114
4.085
3.056
3.039
3.022
3.011
2.994
2.977
2.919
2.902
2.884
2.867
2.850
1.395
1.378
1.234
1.217
0.000
6g
O
O
O
O
NO2
1.94
1.94
1.91
1.89
1.00
1.04
1.06
1.04
2.97
3.08
2.73
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0


192.308
190.080
169.742
149.727
141.172
140.202
137.949
137.430
132.577
127.627
127.539
124.976
124.697
87.363
77.227
77.099
46.206
41.522
33.749
23.813
14.782
6g
O
O
O
O
NO2
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

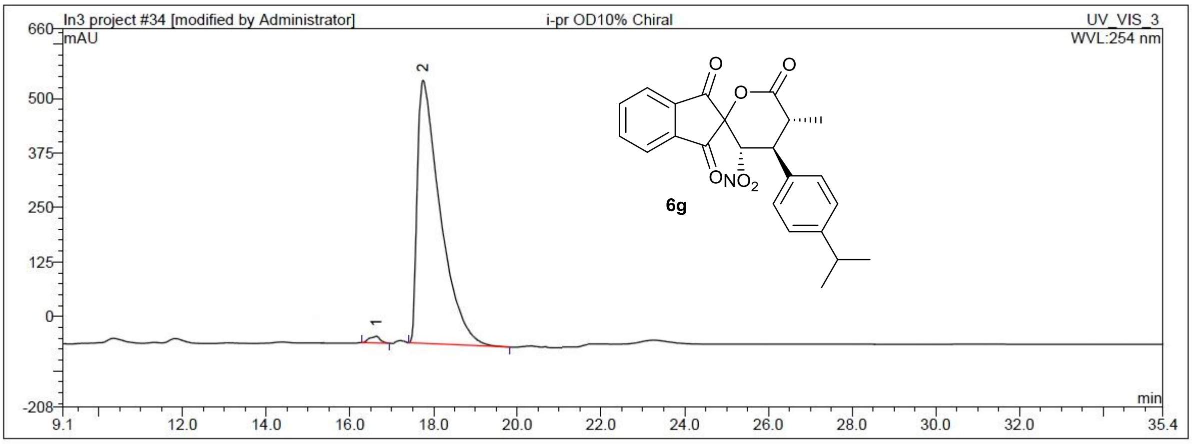
Peak Analysis Report

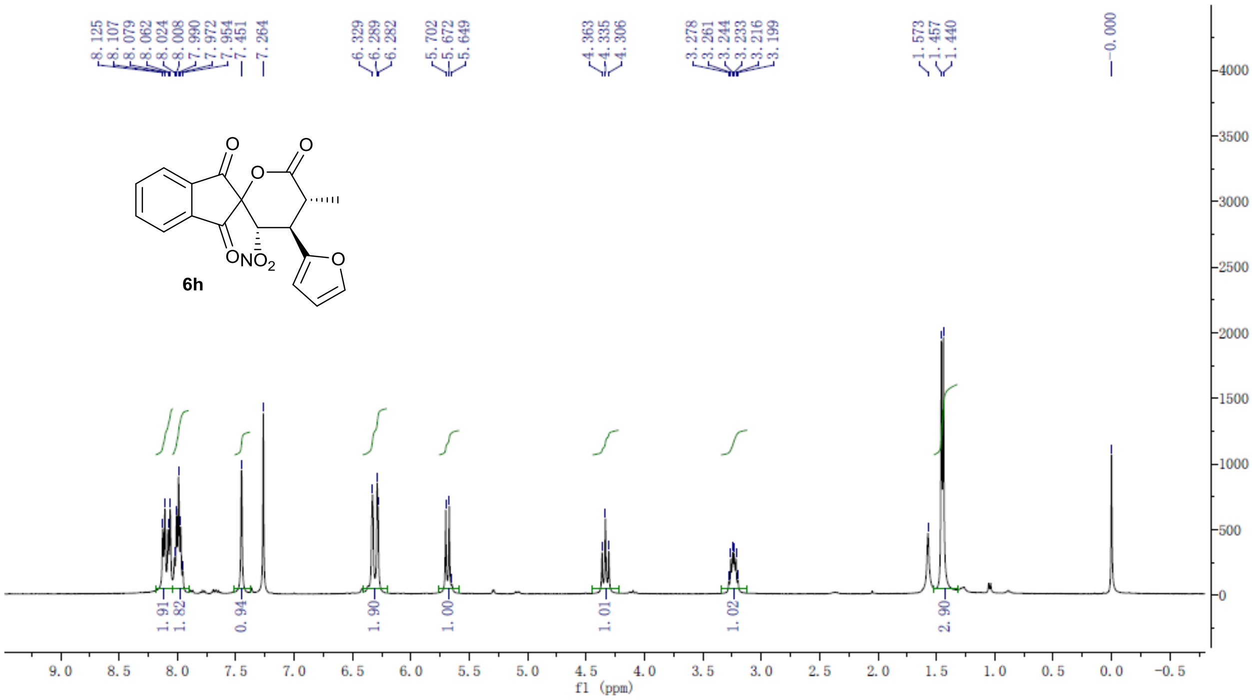
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	16.38	342.639	49.63	517.674	n.a.
2	n.a.	18.02	347.684	50.37	438.691	n.a.

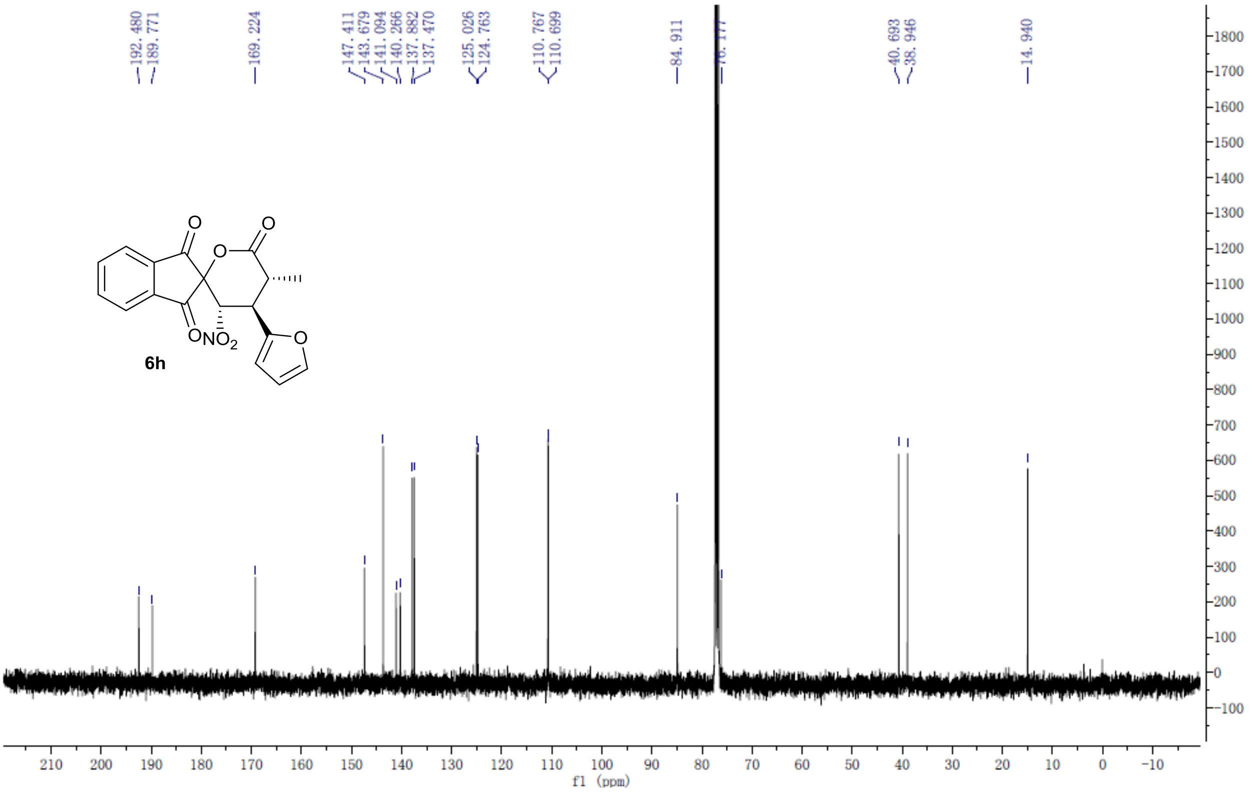


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	16.32	6.123	1.18	15.217	n.a.
2	n.a.	18.03	512.026	98.82	602.632	n.a.

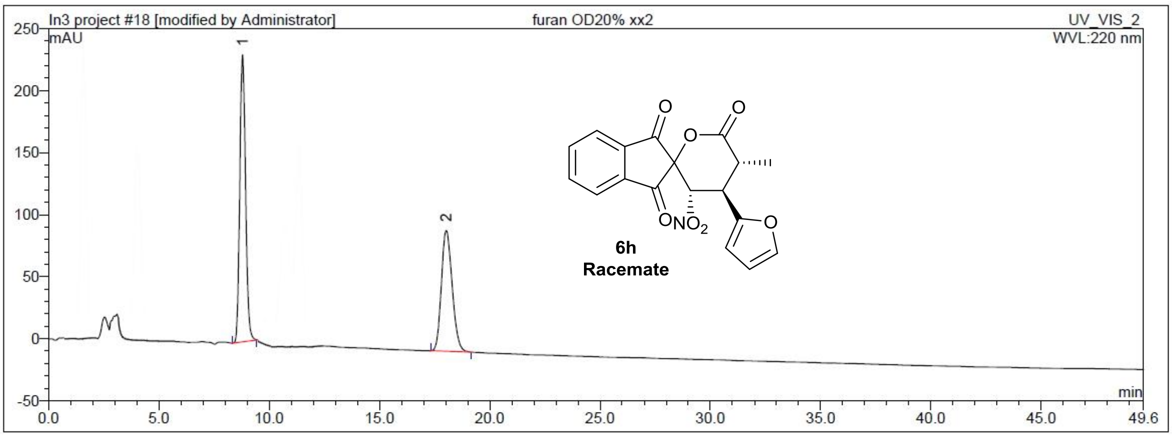



8.125
8.107
8.079
8.062
8.024
8.008
7.990
7.972
7.954
7.451
7.264
6.329
6.289
6.282
5.702
5.672
5.649
4.363
4.335
4.306
3.278
3.261
3.244
3.233
3.216
3.199
1.573
1.457
1.440
0.000
O
O
O
O
NO2
O
6h
4000
3500
3000
2500
2000
1500
1000
500
0
1.91
1.82
0.94
1.90
1.00
1.01
1.02
2.90
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


192.480
189.771
169.224
147.411
143.679
141.094
140.266
137.882
137.470
125.026
124.763
110.767
110.699
84.911
76.177
40.693
38.946
14.940
O
O
O
O
NO2
O
6h
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

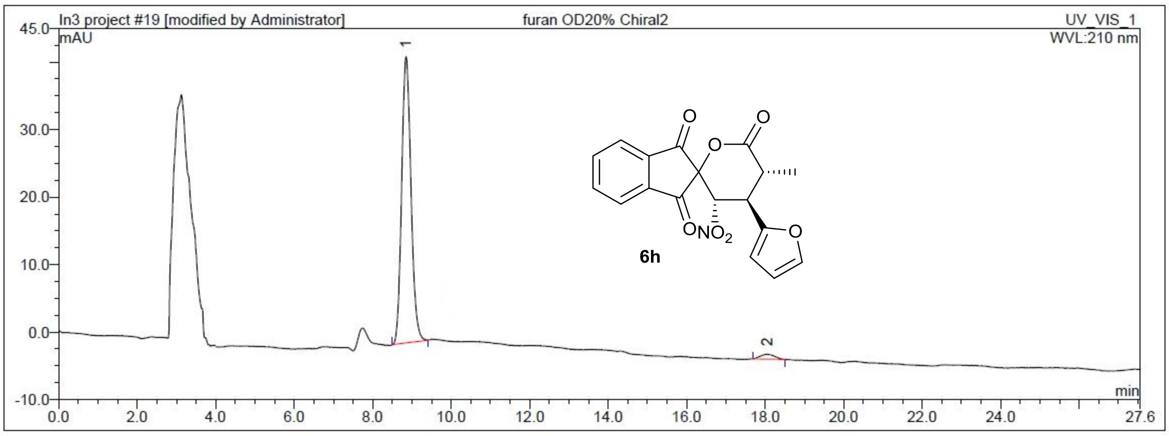
Peak Analysis Report

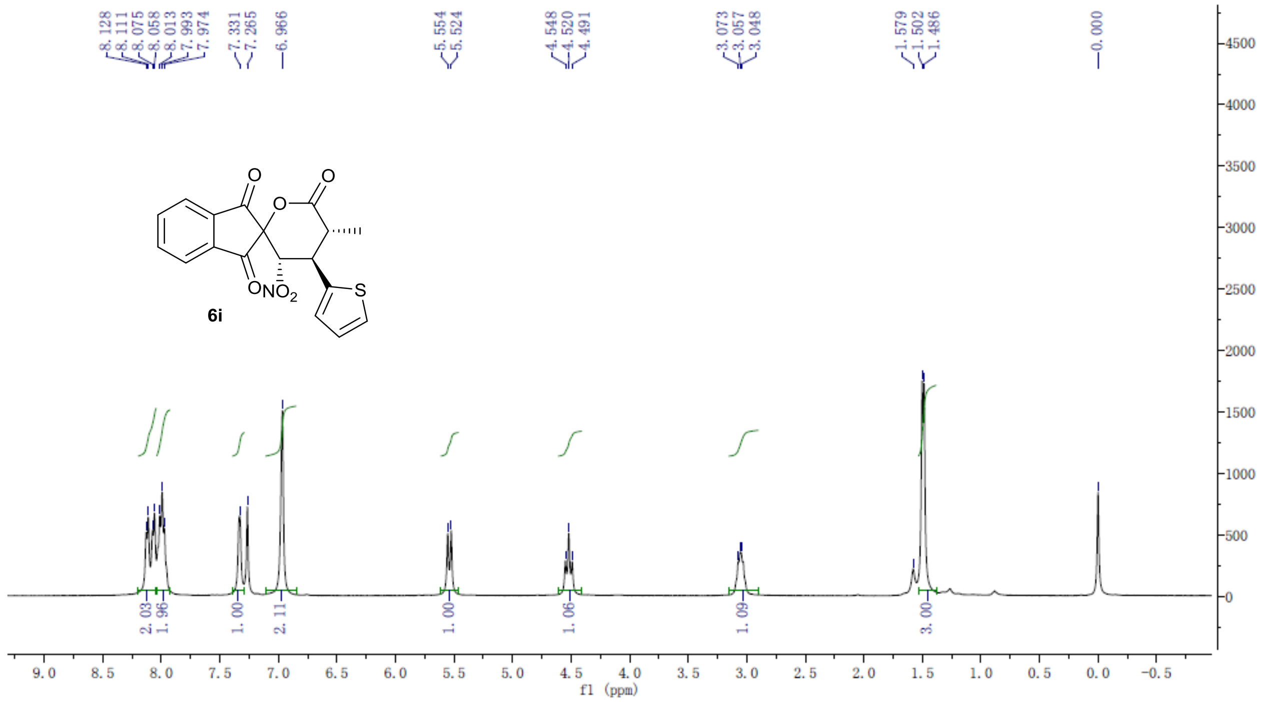
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.79	77.142	50.91	231.274	n.a.
2	n.a.	18.03	74.372	49.09	97.405	n.a.

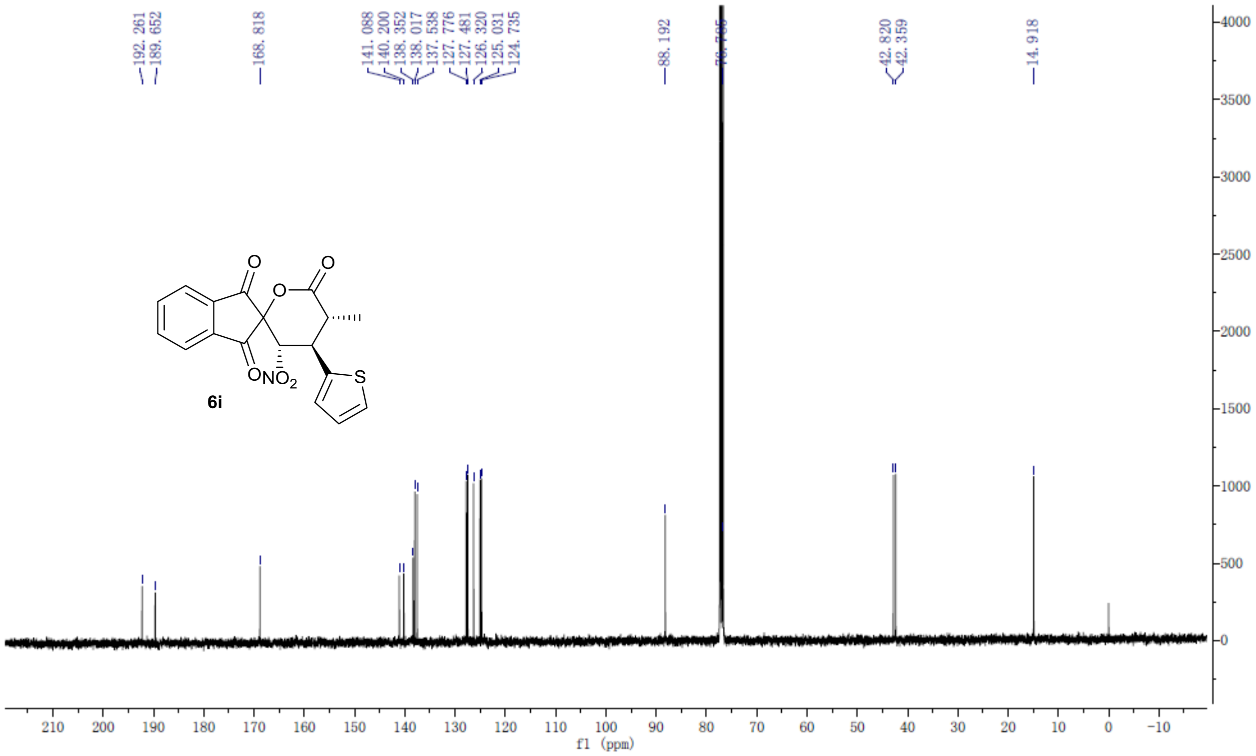


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.85	11.711	97.50	42.418	n.a.
2	n.a.	18.05	0.301	2.50	0.716	n.a.

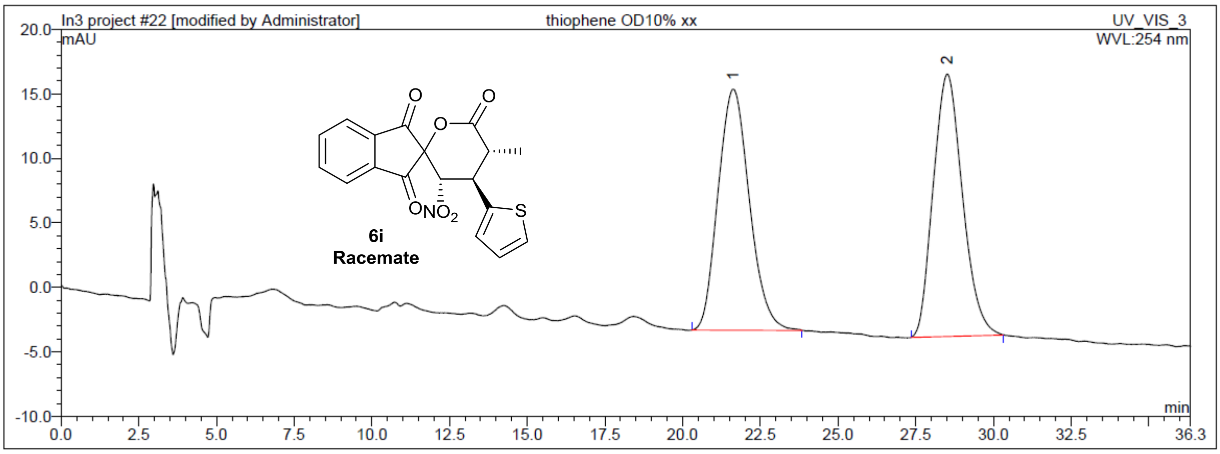



8.128
8.111
8.075
8.058
8.013
7.993
7.974
7.331
7.265
6.966
5.554
5.524
4.548
4.520
4.491
3.073
3.057
3.048
1.579
1.502
1.486
0.000
6i
O
O
O
NO2
S
2.03
1.96
1.00
2.11
1.00
1.06
1.09
3.00
4500
4000
3500
3000
2500
2000
1500
1000
500
0
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


192.261
189.652
168.818
141.088
140.200
138.352
138.017
137.538
127.776
127.481
126.320
125.031
124.735
88.192
76.785
42.820
42.359
14.918
6i
O
O
O
NO2
S
4000
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

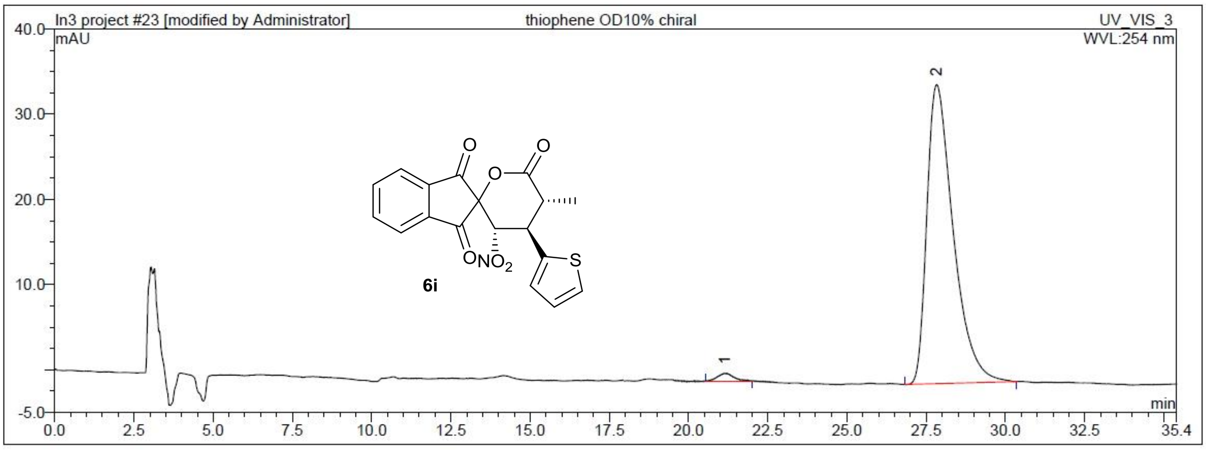
Peak Analysis Report

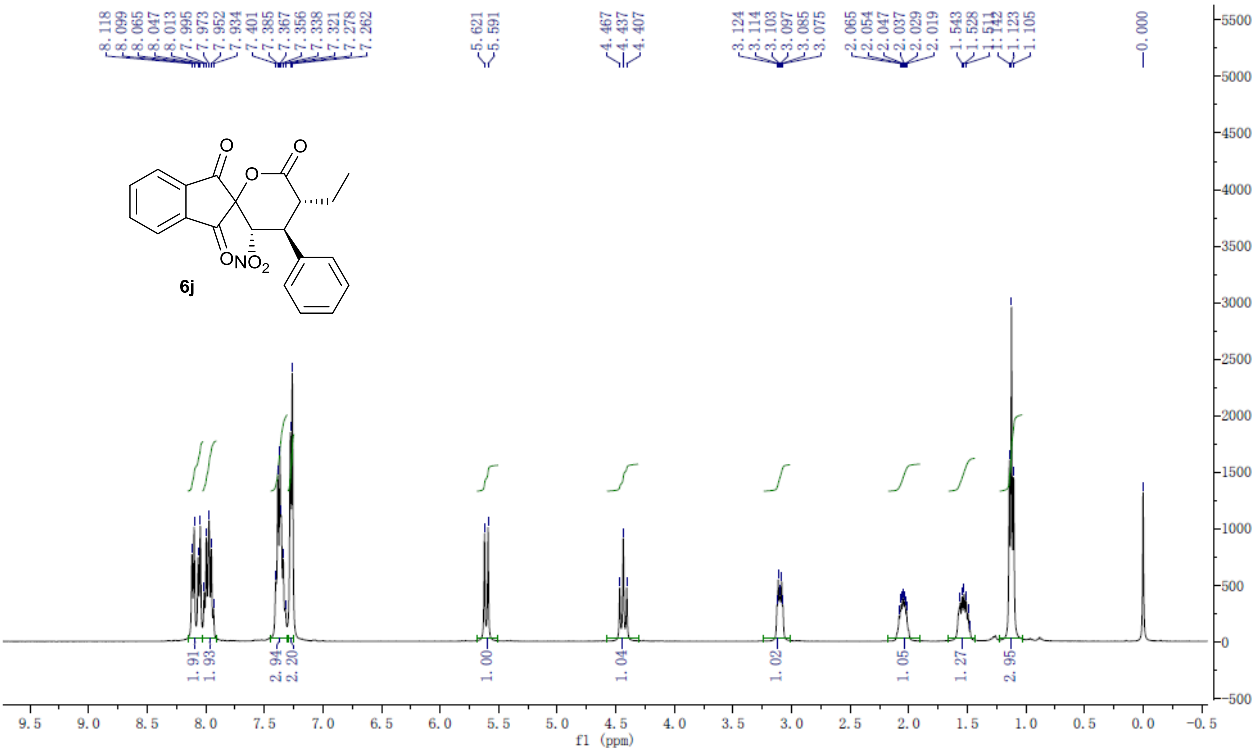
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	21.63	21.863	49.59	18.674	n.a.
2	n.a.	28.51	22.221	50.41	20.334	n.a.

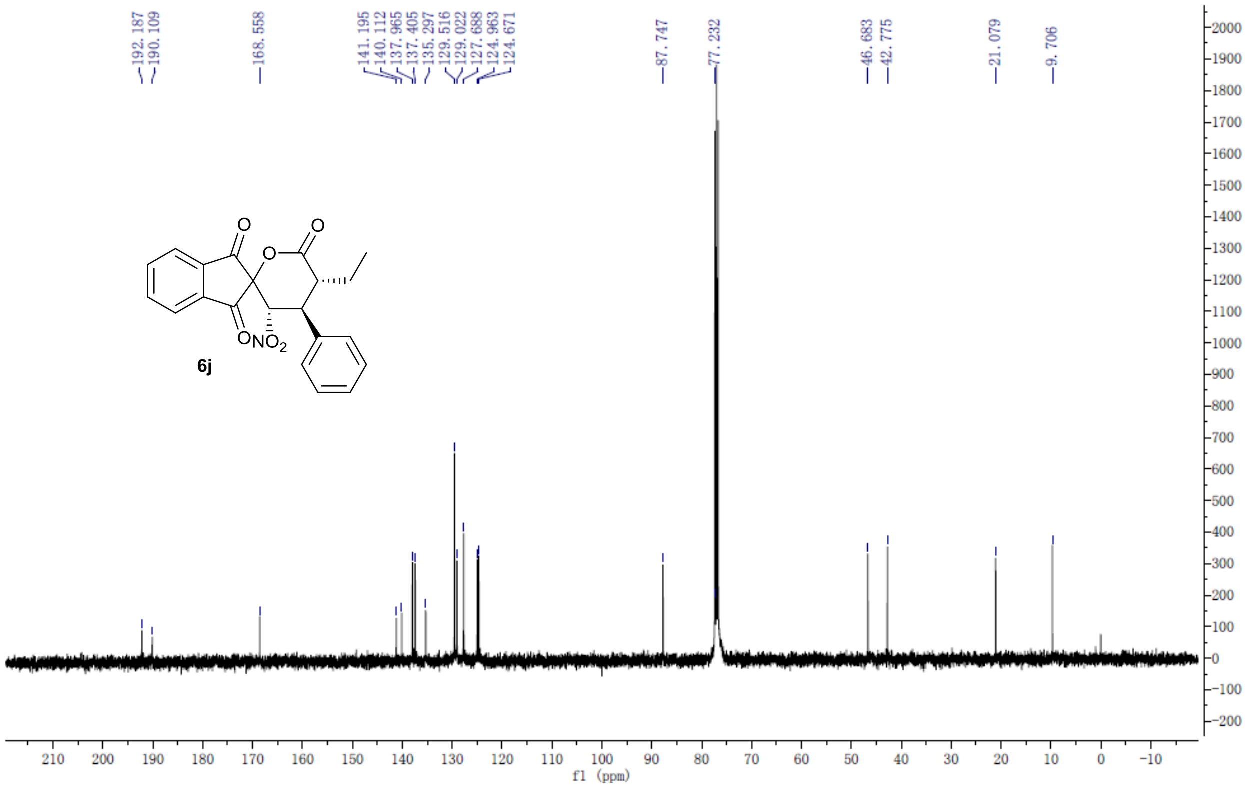


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	21.08	0.533	1.55	0.902	n.a.
2	n.a.	27.83	33.889	98.45	35.105	n.a.




8.118
8.099
8.065
8.047
8.013
7.995
7.973
7.952
7.934
7.401
7.385
7.367
7.356
7.338
7.321
7.278
7.262
5.621
5.591
4.467
4.437
4.407
3.124
3.114
3.103
3.097
3.085
3.075
2.065
2.054
2.047
2.037
2.029
2.019
1.543
1.528
1.511
1.142
1.123
1.105
0.000
O
O
O
O
NO2
6j
1.91
1.93
2.94
2.20
1.00
1.04
1.02
1.05
1.27
2.95
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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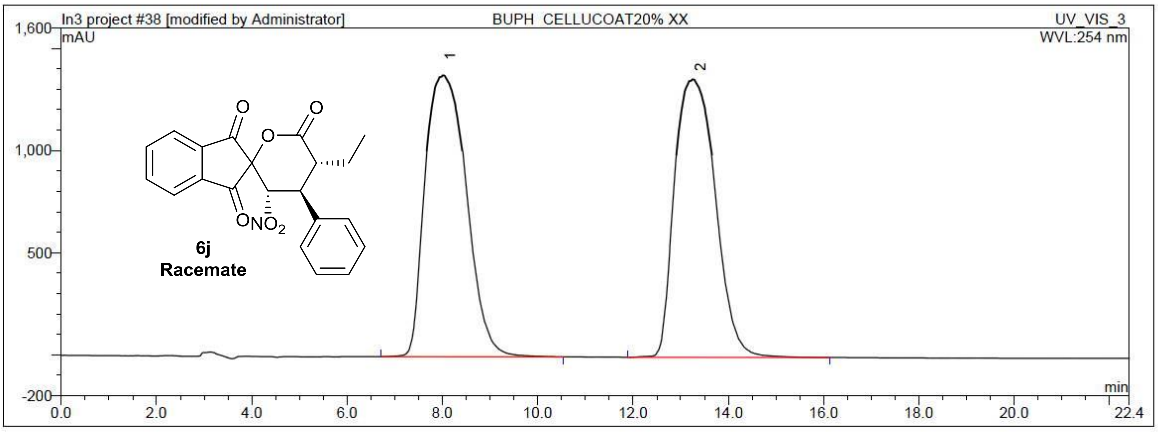
168.558
141.195
140.112
137.965
137.405
135.297
129.516
129.022
127.688
124.963
124.671
87.747
77.232
46.683
42.775
21.079
9.706
O
O
O
O
NO2
6j
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

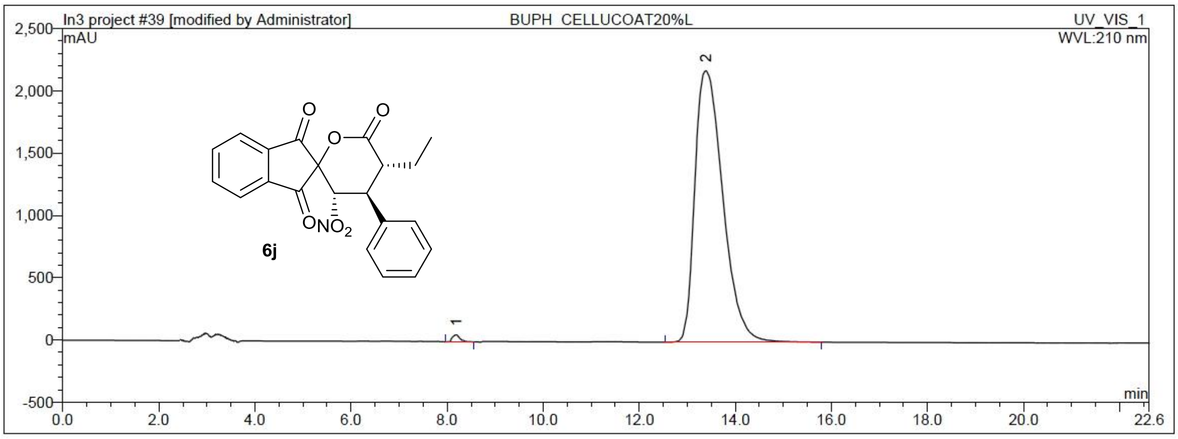
Peak Analysis Report

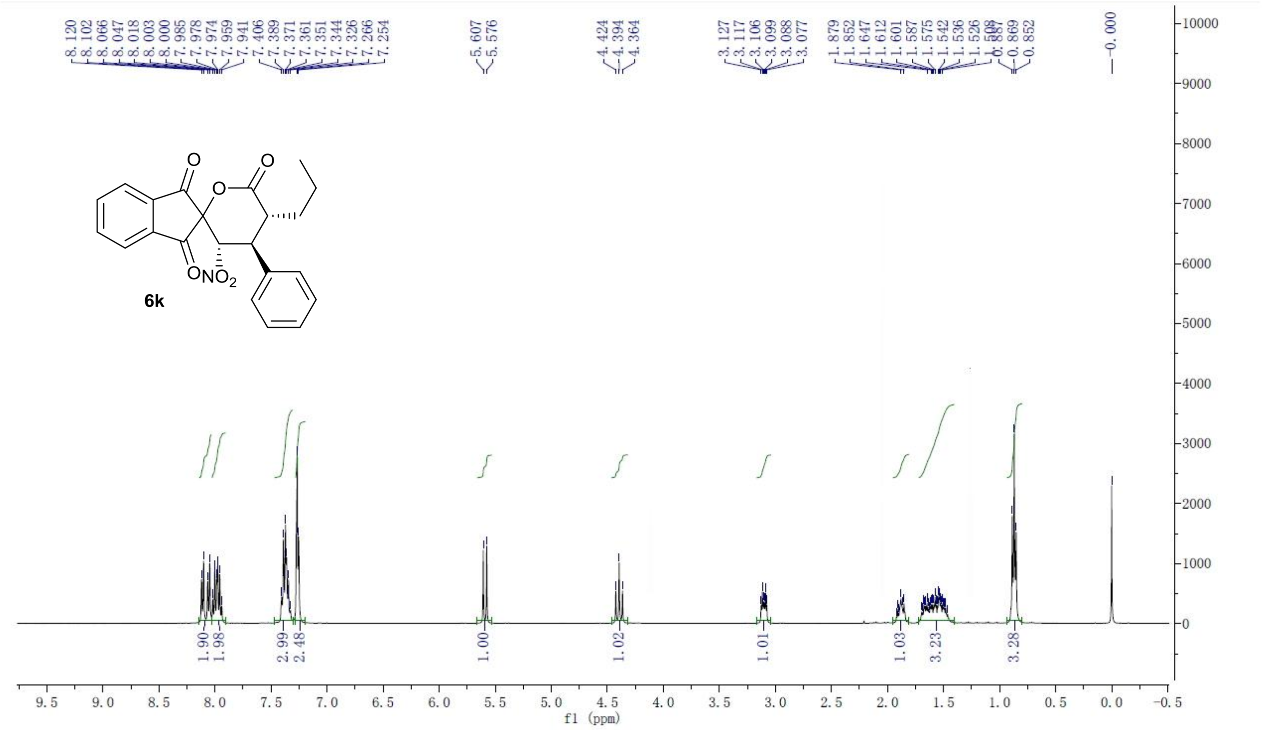
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.17	1380.660	51.10	1407.284	n.a.
2	n.a.	13.42	1321.286	48.90	1359.002	n.a.

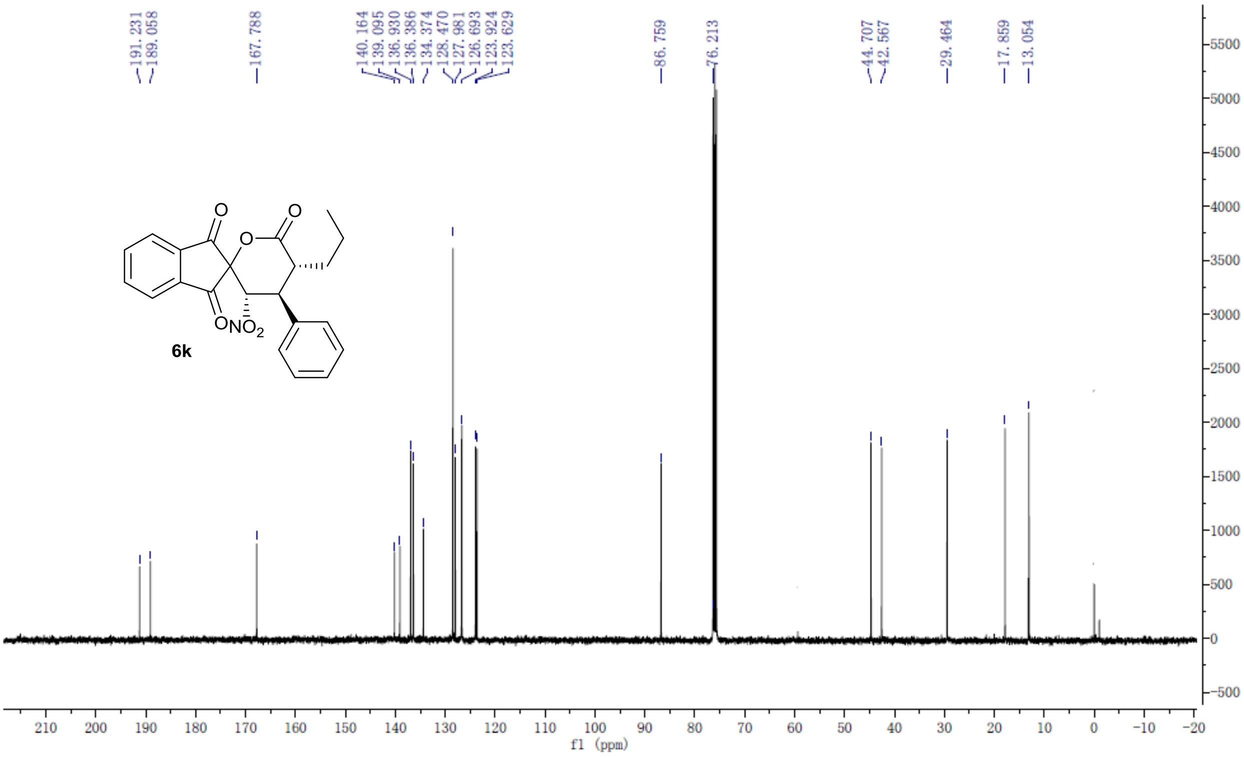


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.15	10.085	0.69	55.658	n.a.
2	n.a.	13.39	1462.010	99.31	2176.358	n.a.

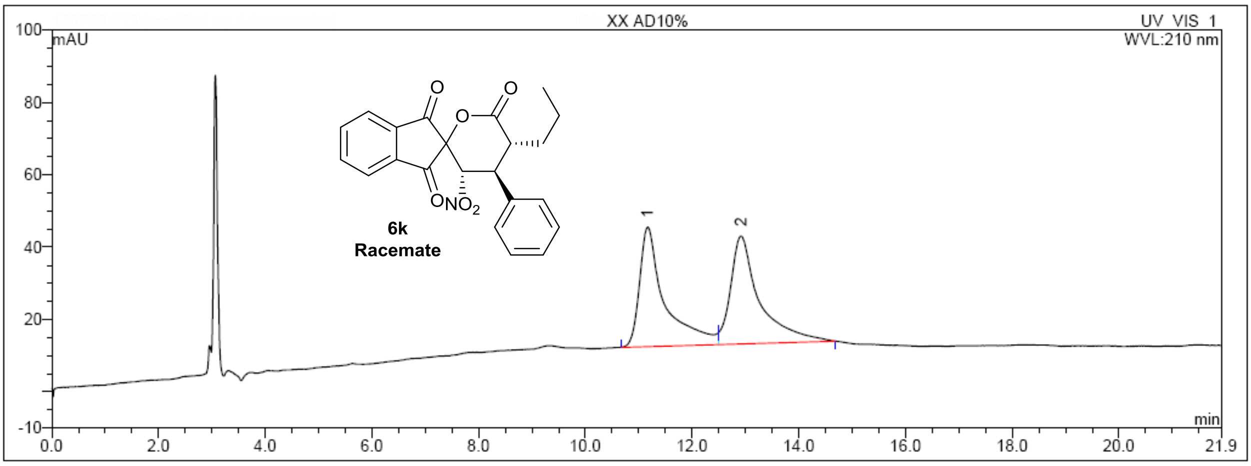



8.120 8.102 8.066 8.047 8.018 8.003 8.000 7.985 7.978 7.974 7.959 7.941 7.406 7.389 7.371 7.361 7.351 7.344 7.326 7.266 7.254
5.607 5.576
4.424 4.394 4.364
3.127 3.117 3.106 3.099 3.088 3.077
1.879 1.852 1.647 1.612 1.601 1.587 1.575 1.542 1.536 1.526 1.508 0.887 0.869 0.852
-0.000
6k
1.90 1.98 2.99 2.48 1.00 1.02 1.01 1.03 3.23 3.28
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0


191.231 189.058
167.788
140.164 139.095 136.930 136.386 134.374 128.470 127.981 126.693 123.924 123.629
86.759
76.213
44.707 42.567
29.464
17.859 13.054
6k
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)
5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0 -500

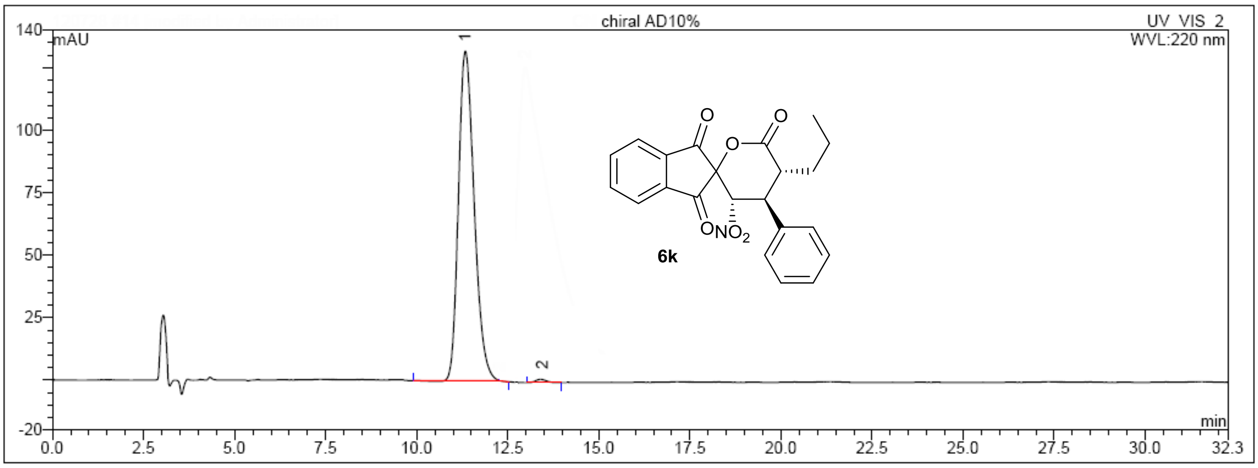
Peak Analysis Report

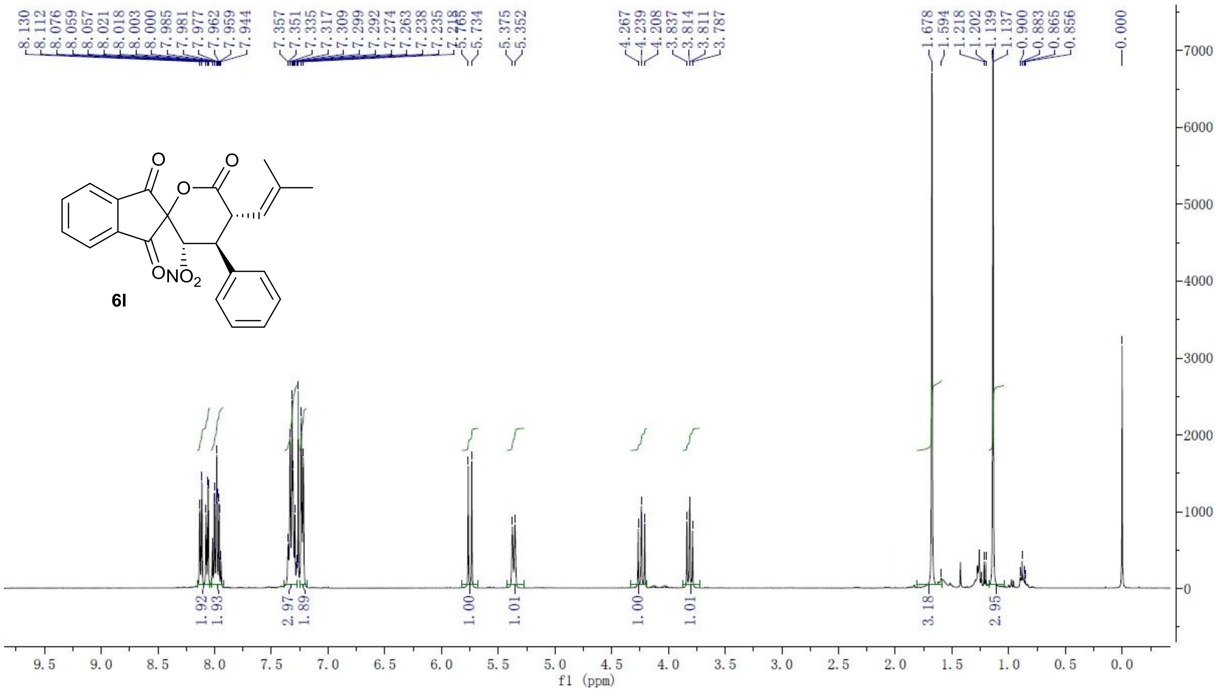
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.17	18.054	49.04	33.008	n.a.
2	n.a.	12.92	18.759	50.96	29.807	n.a.

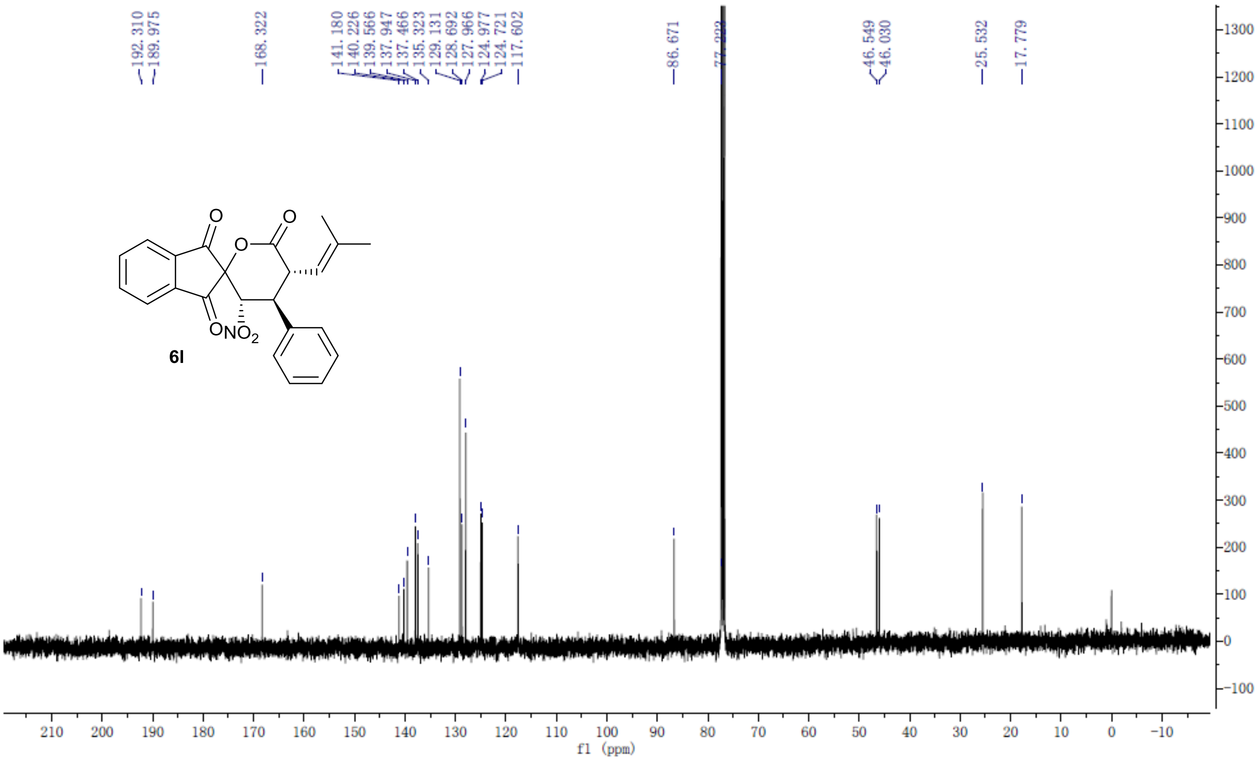


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.22	76.891	99.37	124.374	n.a.
2	n.a.	12.98	0.485	0.63	1.403	n.a.

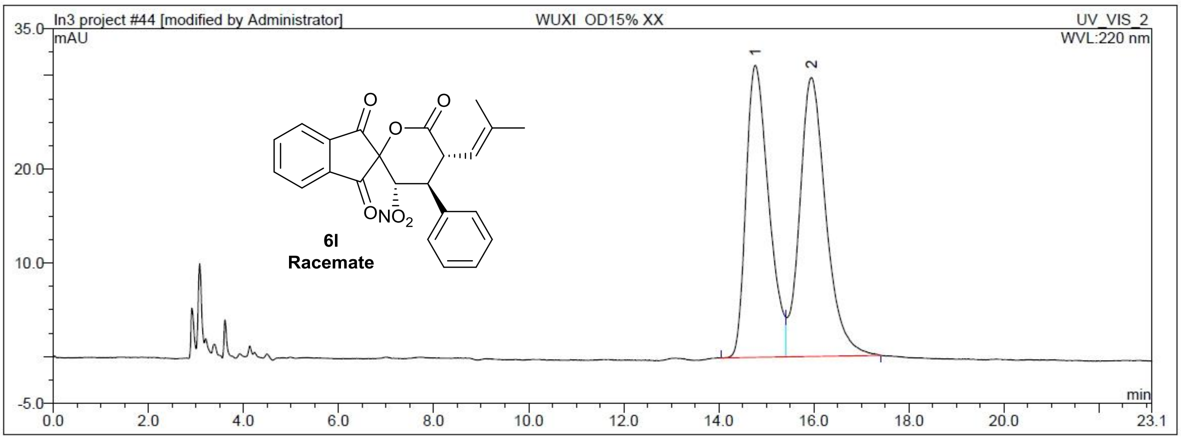



8.130
8.112
8.076
8.059
8.057
8.021
8.018
8.003
8.000
7.985
7.981
7.977
7.962
7.959
7.944
7.357
7.351
7.335
7.317
7.309
7.299
7.292
7.274
7.263
7.238
7.235
7.218
5.765
5.734
5.375
5.352
4.267
4.239
4.208
3.837
3.814
3.811
3.787
1.678
1.594
1.218
1.202
1.139
1.137
0.900
0.883
0.865
0.856
0.000
O
O
O
O
O
NO_2
6l
1.92
1.93
2.97
1.89
1.00
1.01
1.00
1.01
3.18
2.95
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
7000
6000
5000
4000
3000
2000
1000
0


192.310
189.975
168.322
141.180
140.226
139.566
137.947
137.466
135.323
129.131
128.692
127.966
124.977
124.721
117.602
86.671
77.229
46.549
46.030
25.532
17.779
O
O
O
O
O
NO_2
6l
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

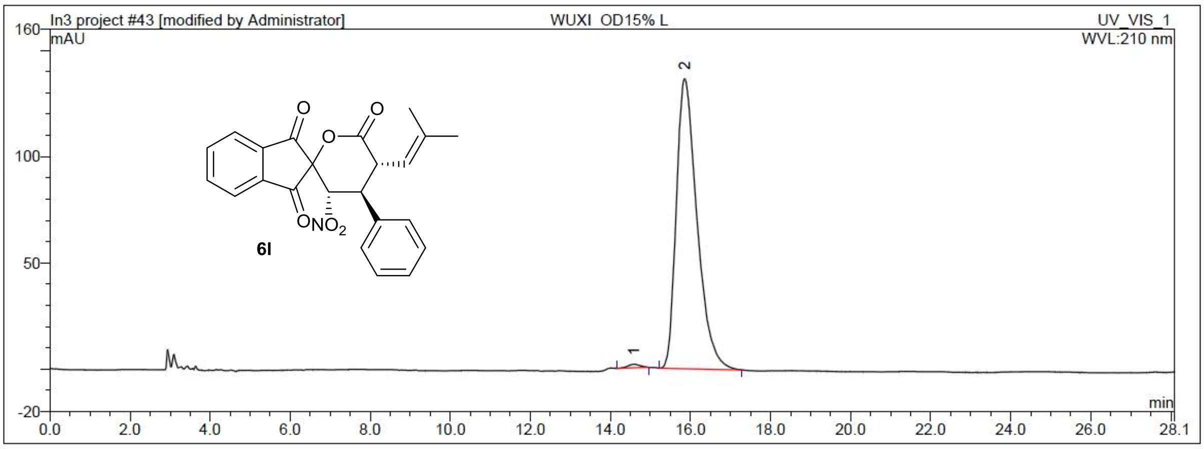
Peak Analysis Report

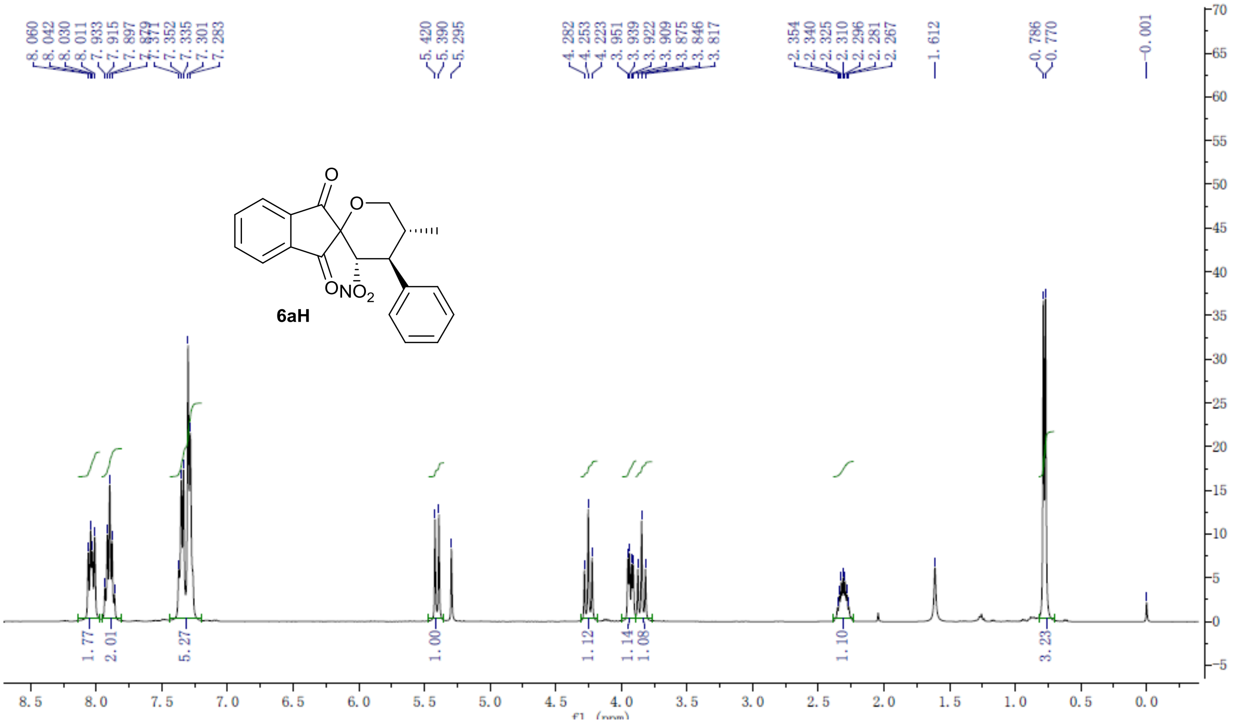
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	14.78	16.762	49.06	30.809	n.a.
2	n.a.	15.95	17.403	50.94	28.831	n.a.

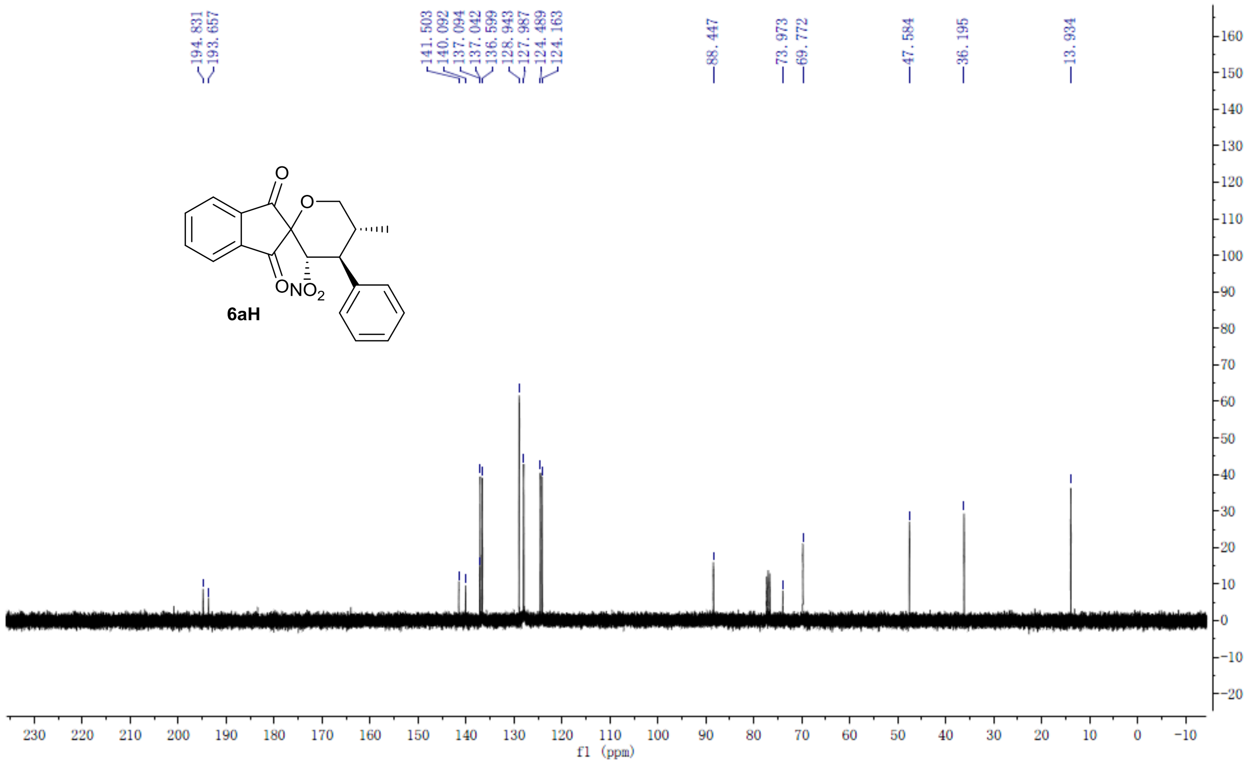


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	14.76	0.570	0.70	1.620	n.a.
2	n.a.	15.86	81.387	99.30	136.373	n.a.

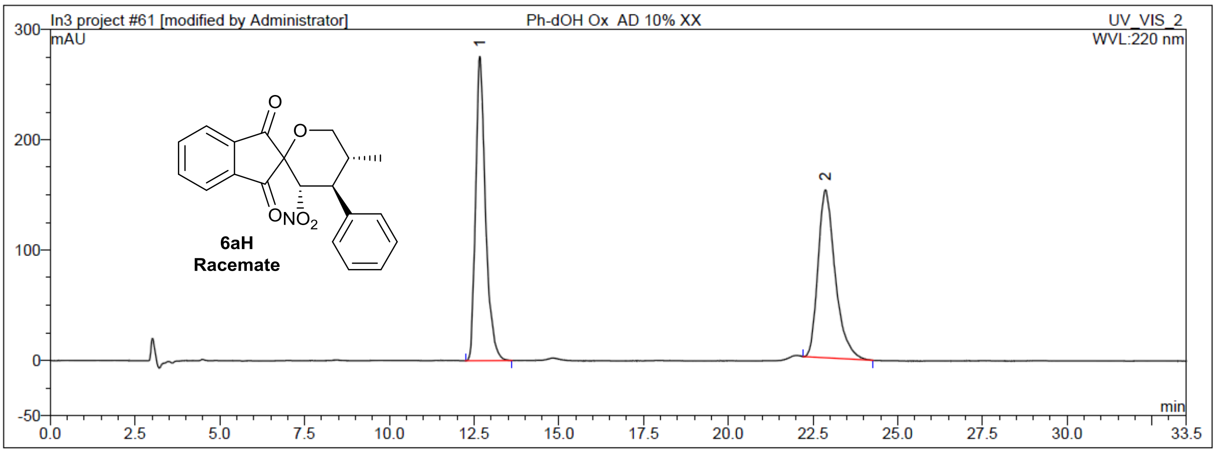



8.060
8.042
8.030
8.011
7.933
7.915
7.897
7.879
7.371
7.352
7.335
7.301
7.283
5.420
5.390
5.295
4.282
4.253
4.223
3.951
3.939
3.922
3.909
3.875
3.846
3.817
2.354
2.340
2.325
2.310
2.296
2.281
2.267
1.612
0.786
0.770
-0.001
O
O
NO2
O
6aH
1.77
2.01
5.27
1.00
1.12
1.14
1.08
1.10
3.23
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5


194.831
193.657
141.503
140.092
137.094
137.042
136.599
128.943
127.987
124.489
124.163
88.447
73.973
69.772
47.584
36.195
13.934
O
O
NO2
O
6aH
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

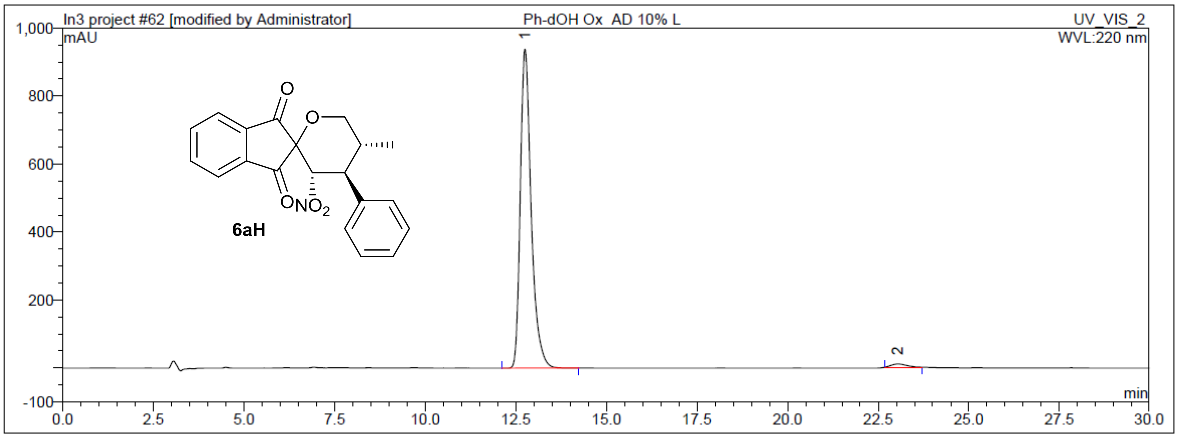
Peak Analysis Report

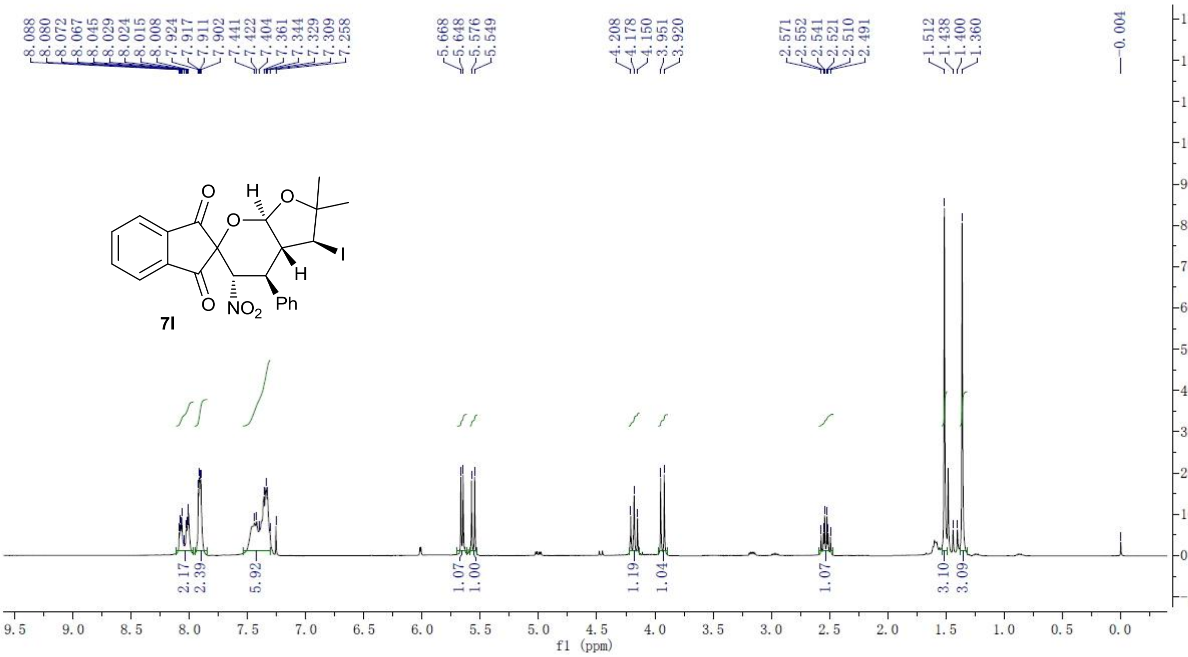
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	12.68	92.147	50.87	275.469	n.a.
2	n.a.	22.87	89.002	49.13	151.869	n.a.

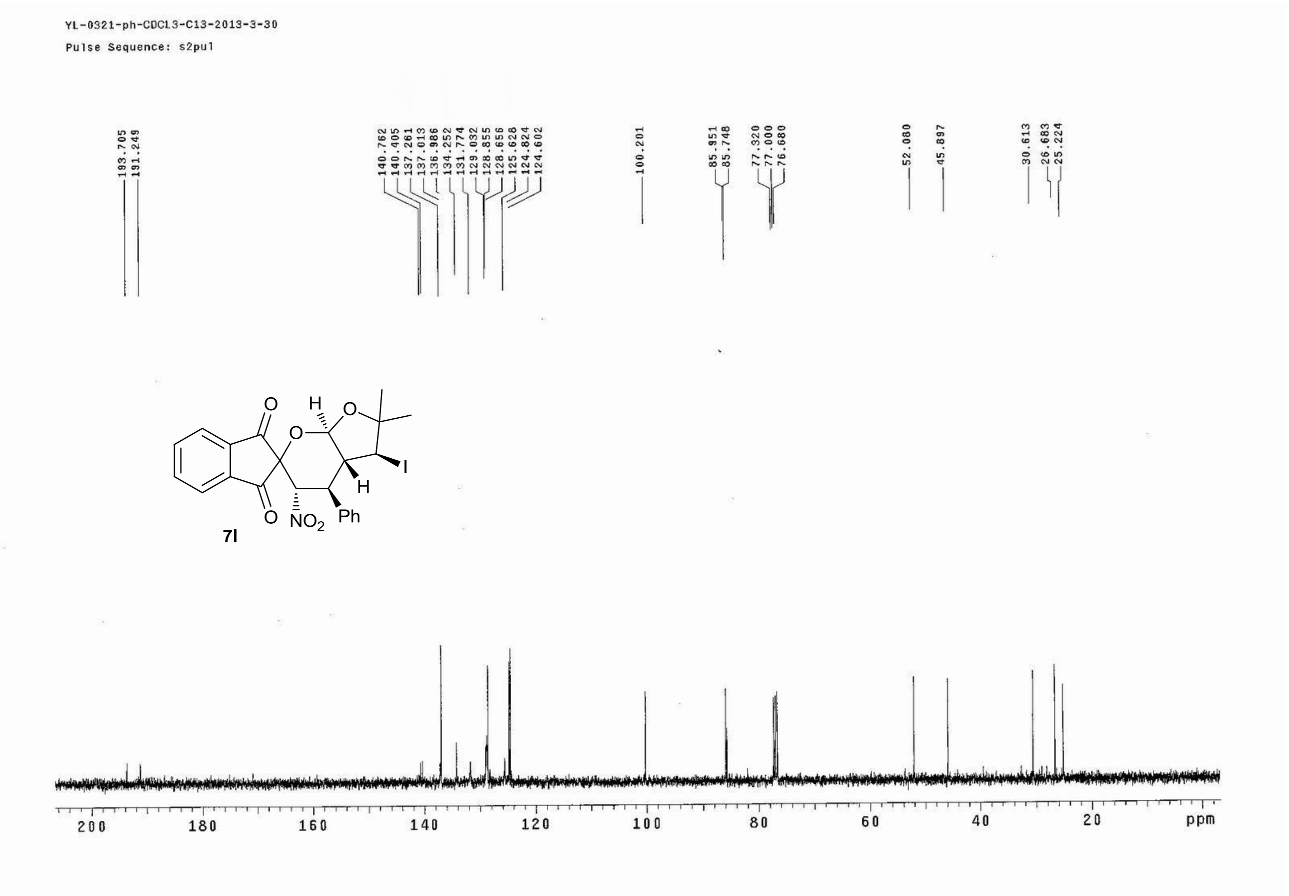


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	12.75	326.697	98.55	938.310	n.a.
2	n.a.	23.03	4.814	1.45	9.684	n.a.

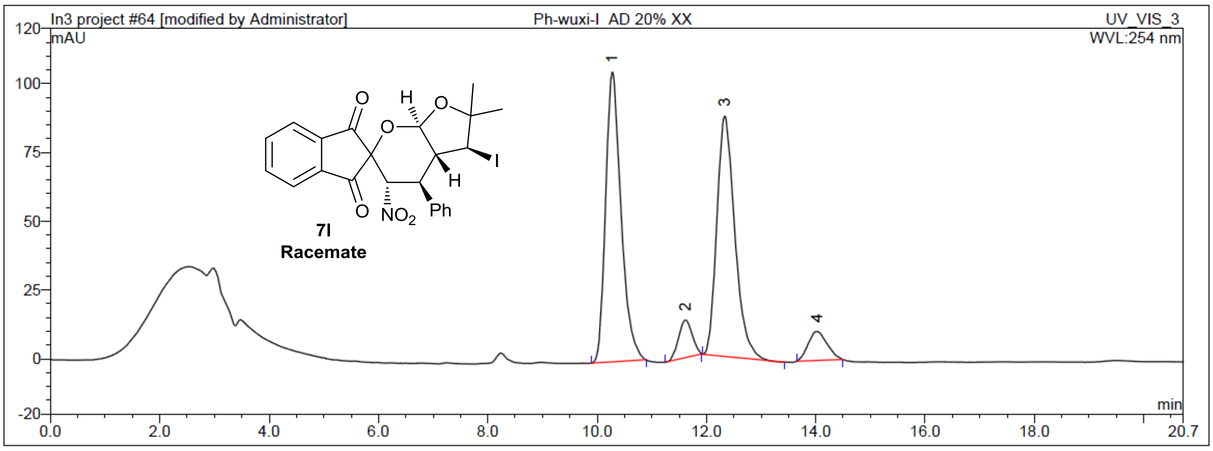



8.088
8.080
8.072
8.067
8.045
8.029
8.024
8.015
8.008
7.924
7.917
7.911
7.902
7.441
7.422
7.404
7.361
7.344
7.329
7.309
7.258
5.668
5.648
5.576
5.549
4.208
4.178
4.150
3.951
3.920
2.571
2.552
2.541
2.521
2.510
2.491
1.512
1.438
1.400
1.360
-0.004
O
H
O
O
I
H
O
NO2
Ph
7l
2.17
2.39
5.92
1.07
1.00
1.19
1.04
1.07
3.10
3.09
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


YL-0321-ph-CDCL3-C13-2013-3-30
Pulse Sequence: s2pul
193.705
191.249
140.762
140.405
137.261
137.013
136.986
134.252
131.774
129.032
128.855
128.656
125.628
124.824
124.602
100.201
85.951
85.748
77.320
77.000
76.680
52.080
45.897
30.613
26.683
25.224
O
H
O
O
I
H
O
NO2
Ph
7l
200
180
160
140
120
100
80
60
40
20
ppm

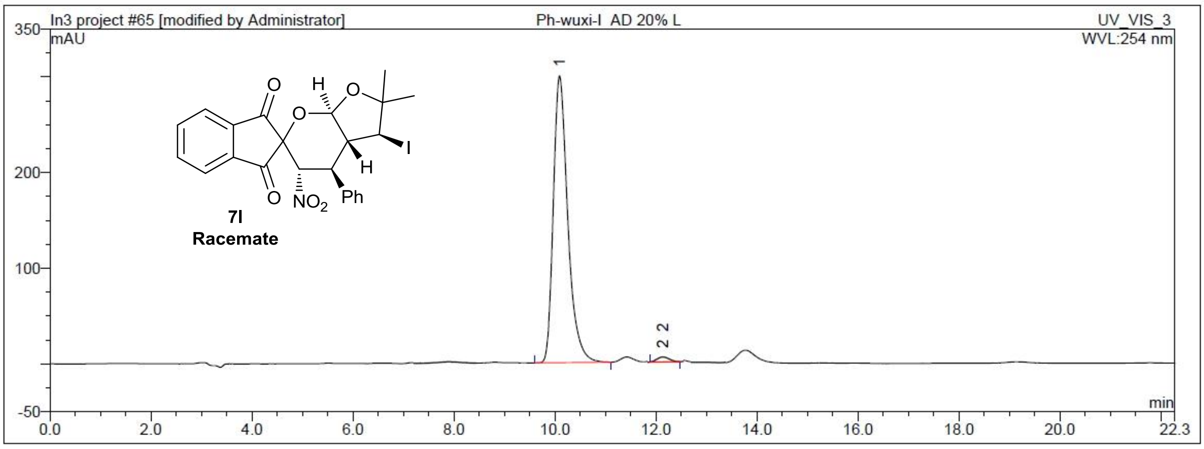
Peak Analysis Report

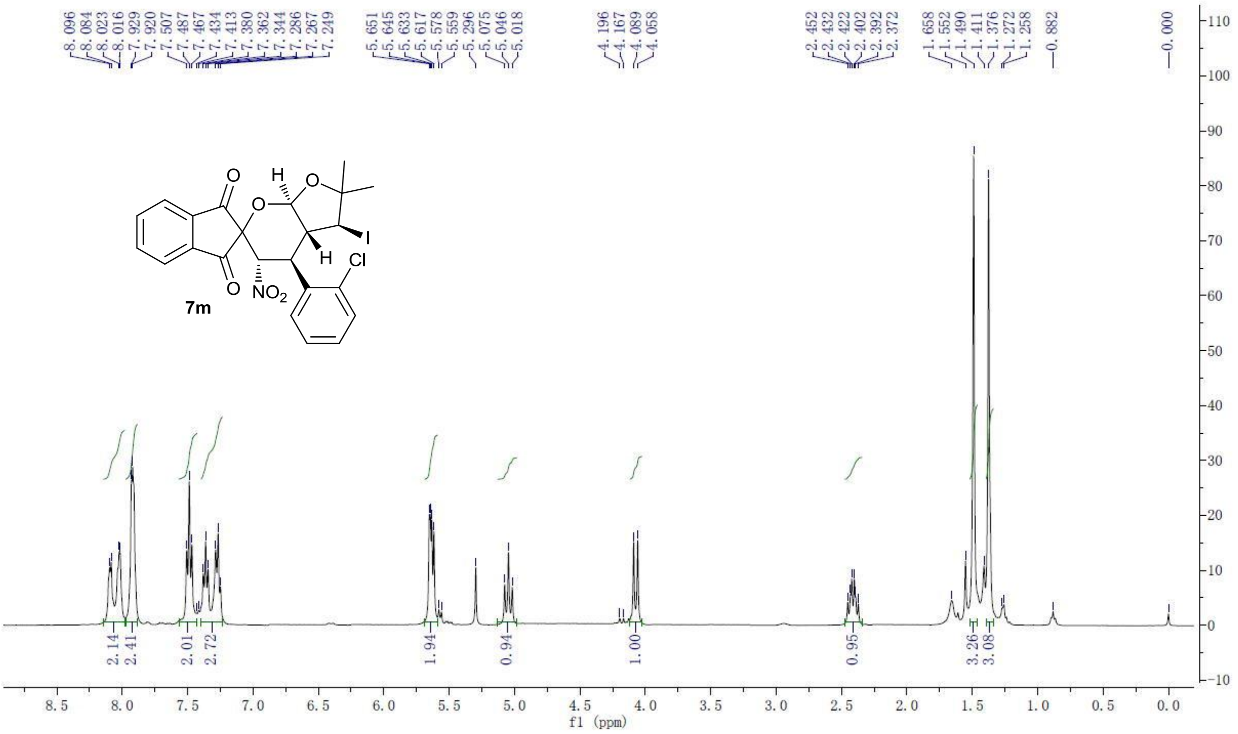
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	10.28	34.496	45.46	105.150	n.a.
2	n.a.	11.62	3.930	5.18	13.560	n.a.
3	n.a.	12.33	33.259	43.83	87.219	n.a.
4	n.a.	14.03	4.202	5.54	10.503	n.a.

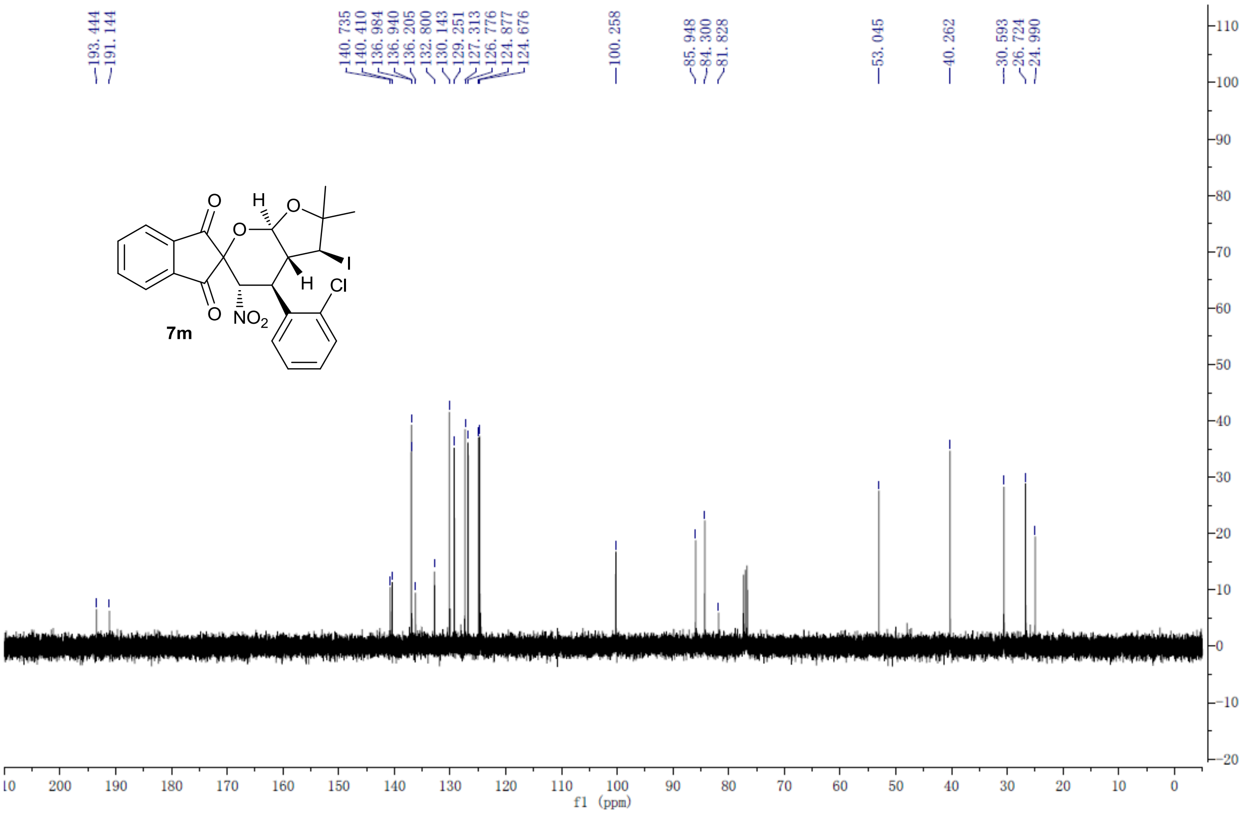


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	10.09	99.440	98.59	299.955	n.a.
2	n.a.	12.14	1.425	1.41	5.103	n.a.

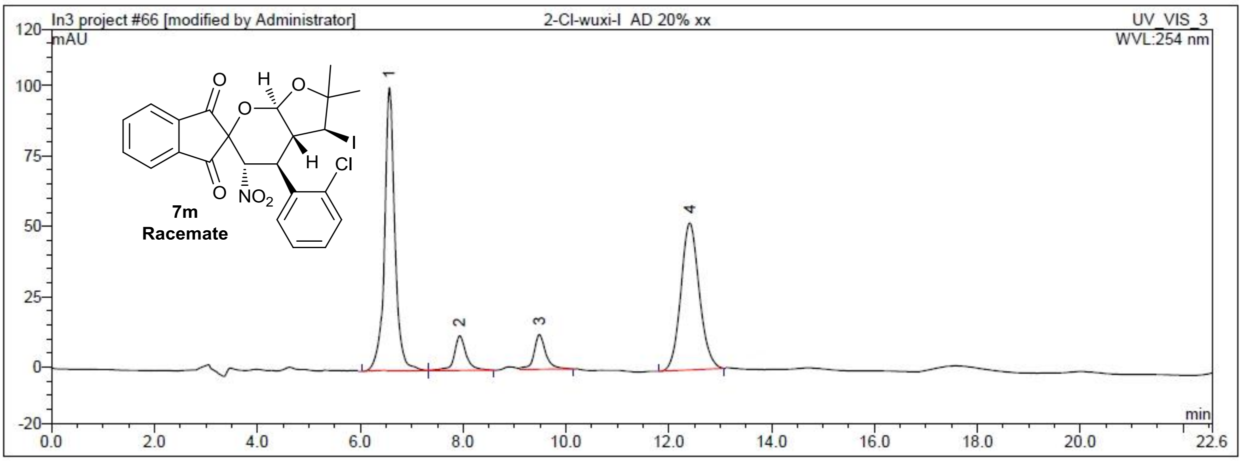



8.096
8.084
8.023
8.016
7.929
7.920
7.507
7.487
7.467
7.434
7.413
7.380
7.362
7.344
7.286
7.267
7.249
5.651
5.645
5.633
5.617
5.578
5.559
5.296
5.075
5.046
5.018
4.196
4.167
4.089
4.058
2.452
2.432
2.422
2.402
2.392
2.372
1.658
1.552
1.490
1.411
1.376
1.272
1.258
0.882
0.000
2.14
2.41
2.01
2.72
1.94
0.94
1.00
0.95
3.26
3.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
110
100
90
80
70
60
50
40
30
20
10
0
-10
O
H
O
O
I
H
Cl
O
NO2
7m


193.444
191.144
140.735
140.410
136.984
136.940
136.205
132.800
130.143
129.251
127.313
126.776
124.877
124.676
100.258
85.948
84.300
81.828
53.045
40.262
30.593
26.724
24.990
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
O
H
O
O
I
H
Cl
O
NO2
7m

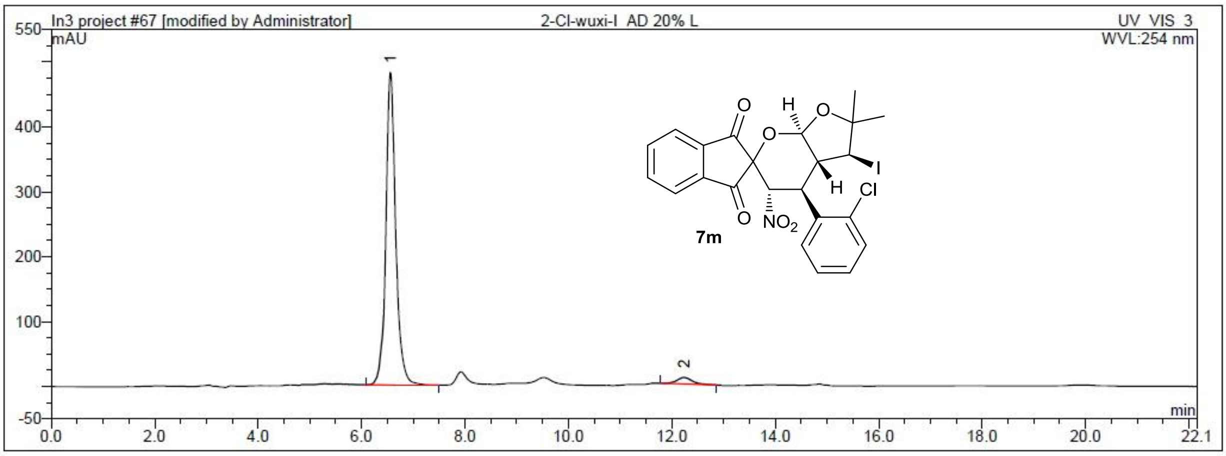
Peak Analysis Report

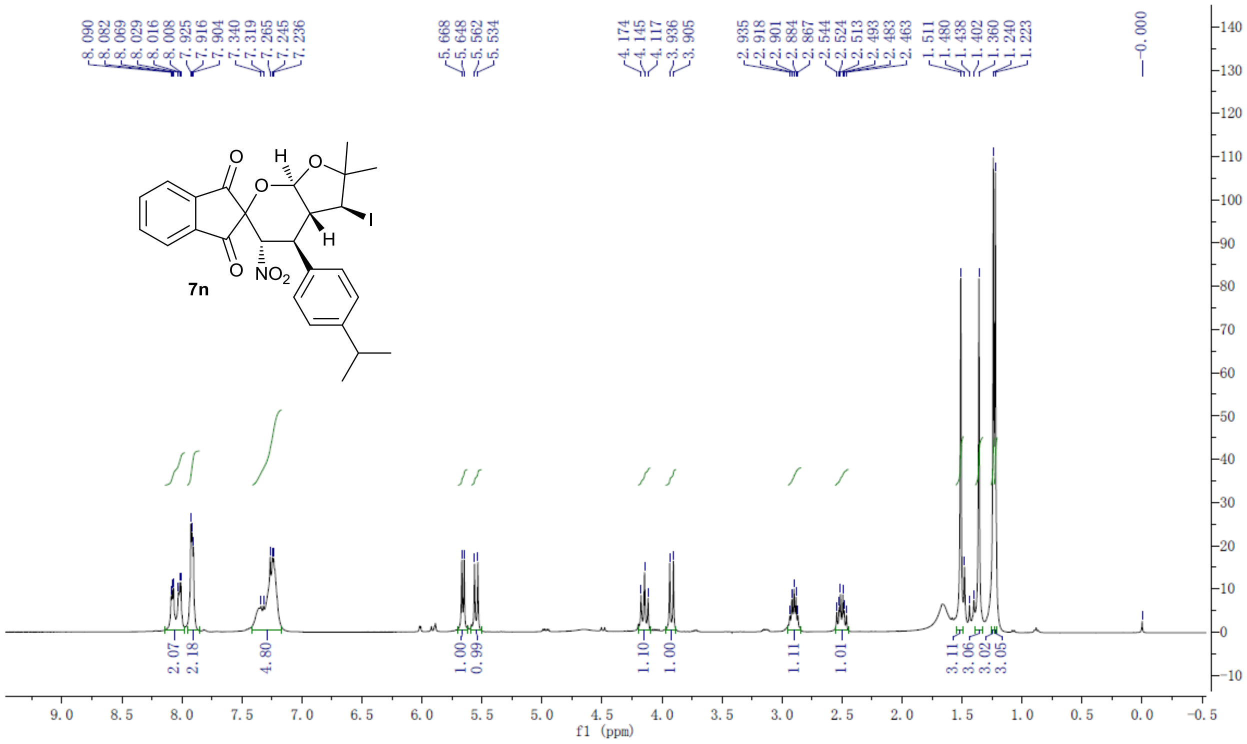
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	6.57	23.919	43.89	100.246	n.a.
2	n.a.	7.93	3.326	6.10	11.981	n.a.
3	n.a.	9.51	3.285	6.03	11.763	n.a.
4	n.a.	12.41	23.971	43.98	51.902	n.a.

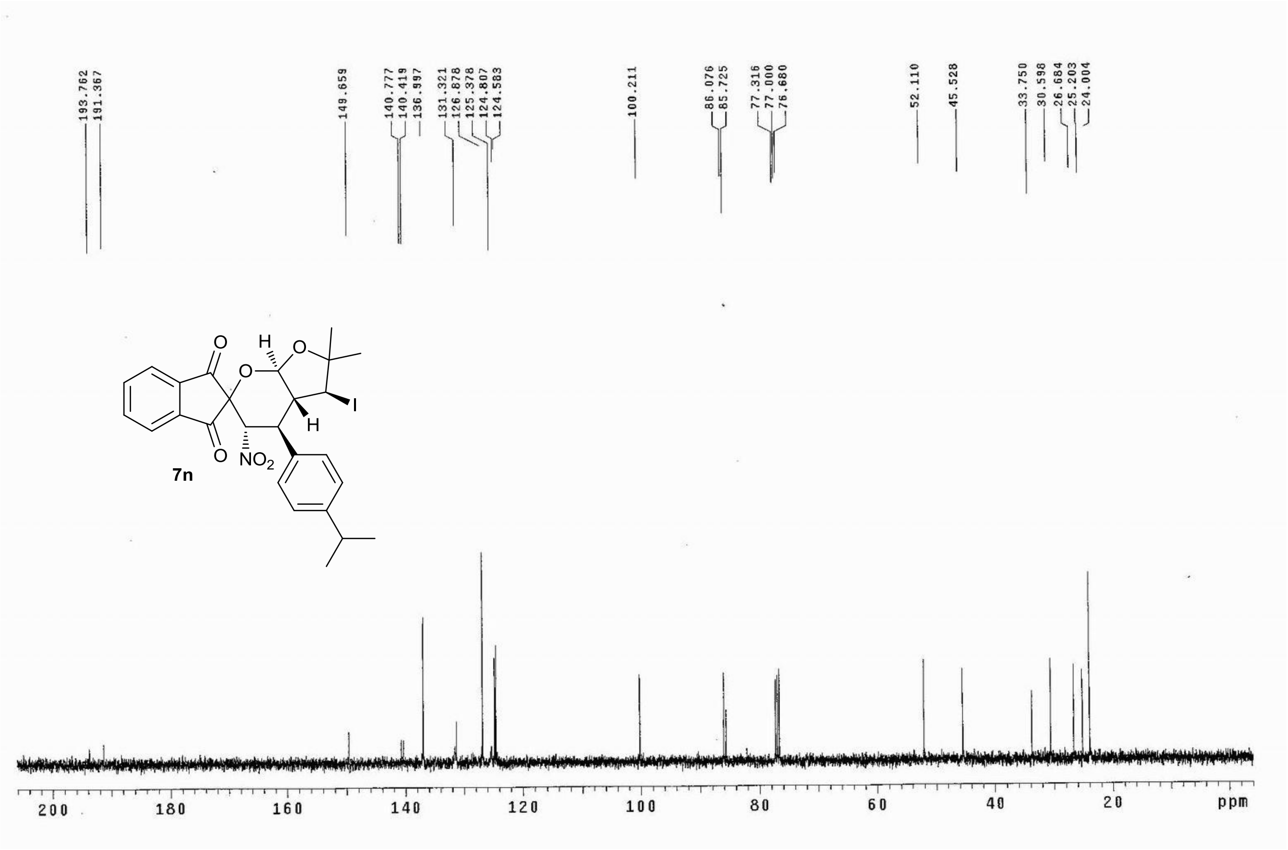


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	6.56	108.420	96.92	482.328	n.a.
2	n.a.	12.24	3.450	3.08	10.118	n.a.

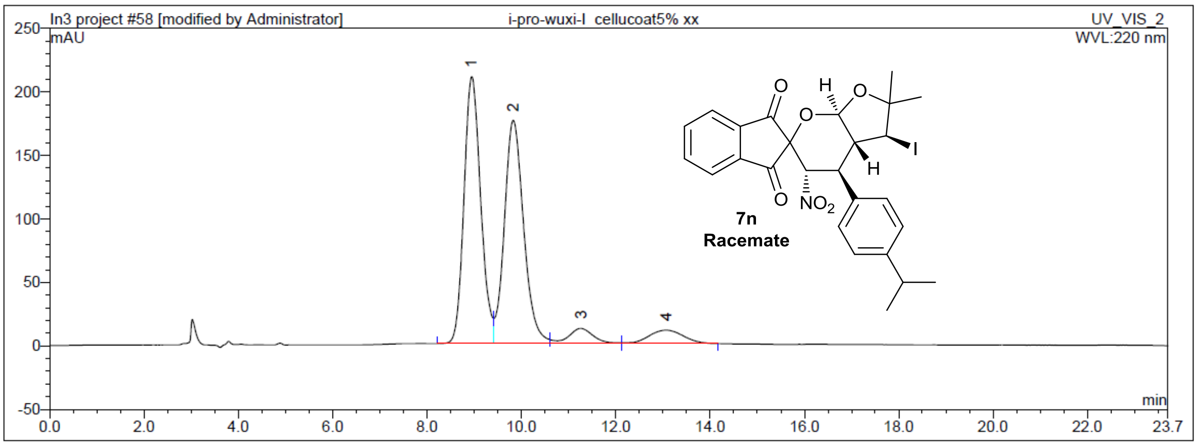



8.090 8.082 8.069 8.029 8.016 8.008 7.925 7.916 7.904 7.340 7.319 7.265 7.245 7.236
5.668 5.648 5.562 5.534
4.174 4.145 4.117 3.936 3.905
2.935 2.918 2.901 2.884 2.867 2.544 2.524 2.513 2.493 2.483 2.463
1.511 1.480 1.438 1.402 1.360 1.240 1.223
0.000
7n
O
O
H
O
O
I
H
NO2
2.07 2.18 4.80 1.00 0.99 1.10 1.00 1.11 1.01 3.11 3.06 3.02 3.05
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


193.762 191.367
149.659
140.777 140.419 136.997
131.321 126.878 125.378 124.807 124.583
100.211
86.076 85.725
77.316 77.000 76.680
52.110
45.528
33.750 30.598 26.684 25.203 24.004
7n
O
O
H
O
O
I
H
NO2
200 180 160 140 120 100 80 60 40 20 ppm

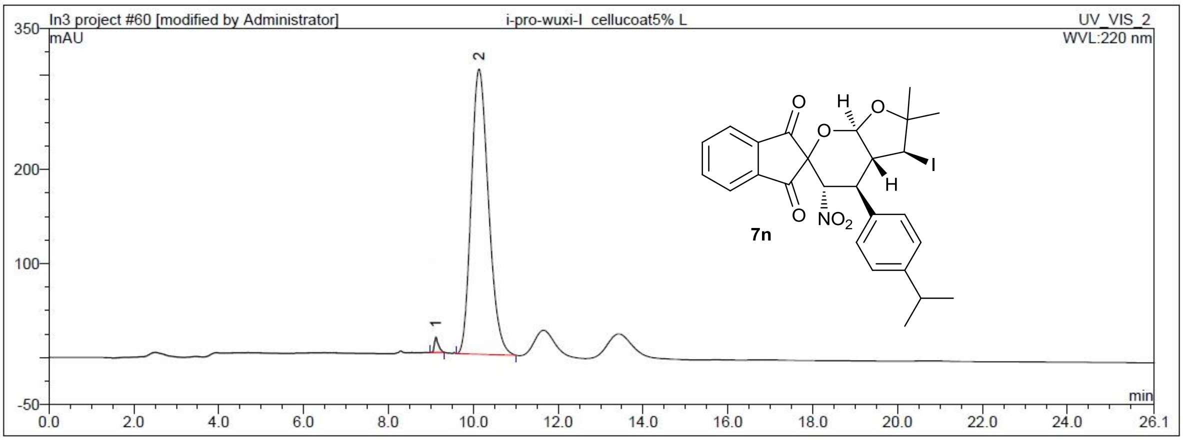
Peak Analysis Report

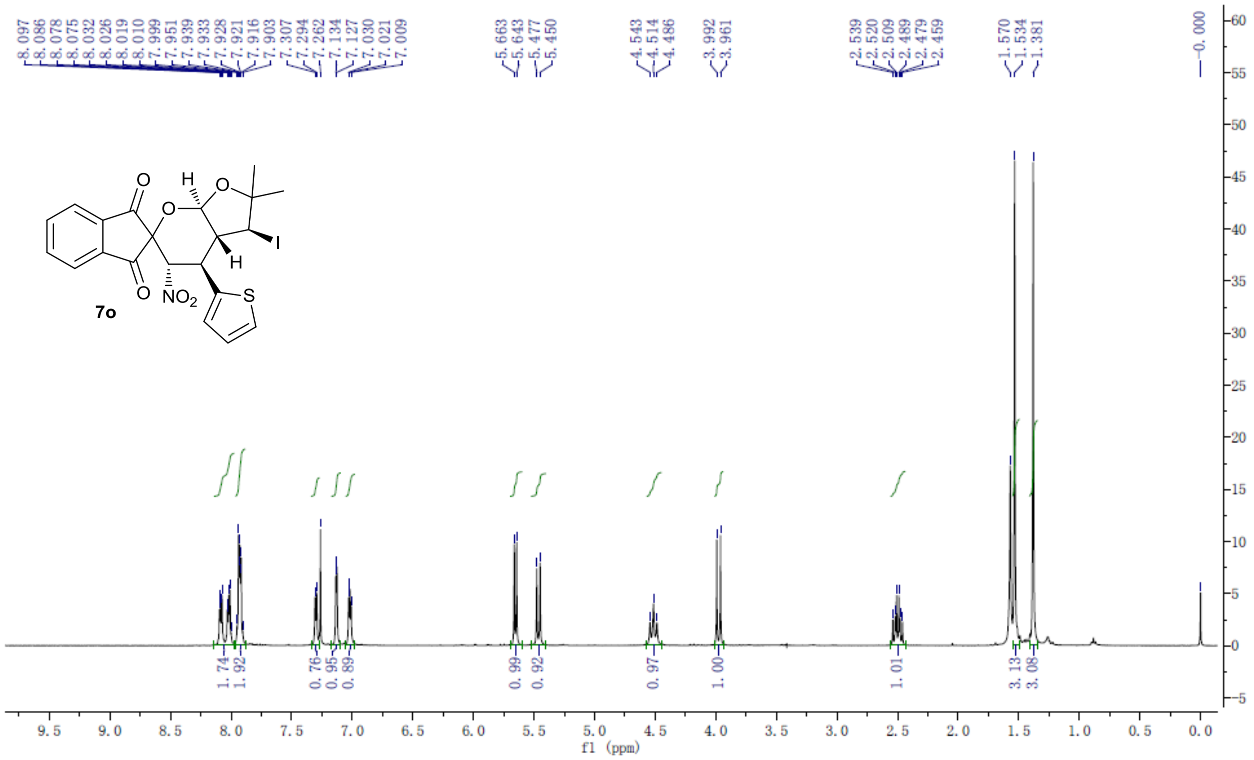
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.94	86.329	46.41	210.160	n.a.
2	n.a.	9.83	83.154	44.70	175.807	n.a.
3	n.a.	11.27	7.444	4.00	11.983	n.a.
4	n.a.	13.07	9.092	4.89	10.634	n.a.

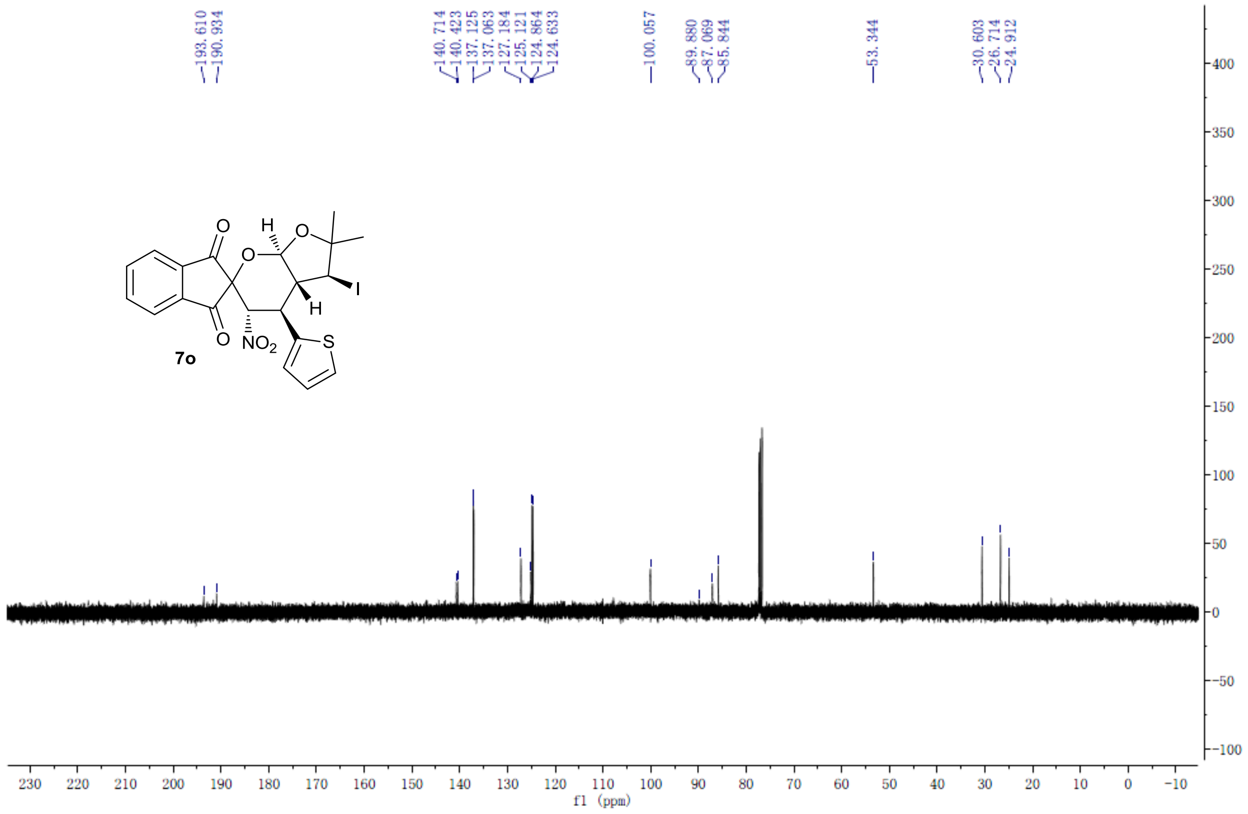


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.09	1.761	1.22	16.901	n.a.
2	n.a.	10.13	142.786	98.78	303.280	n.a.

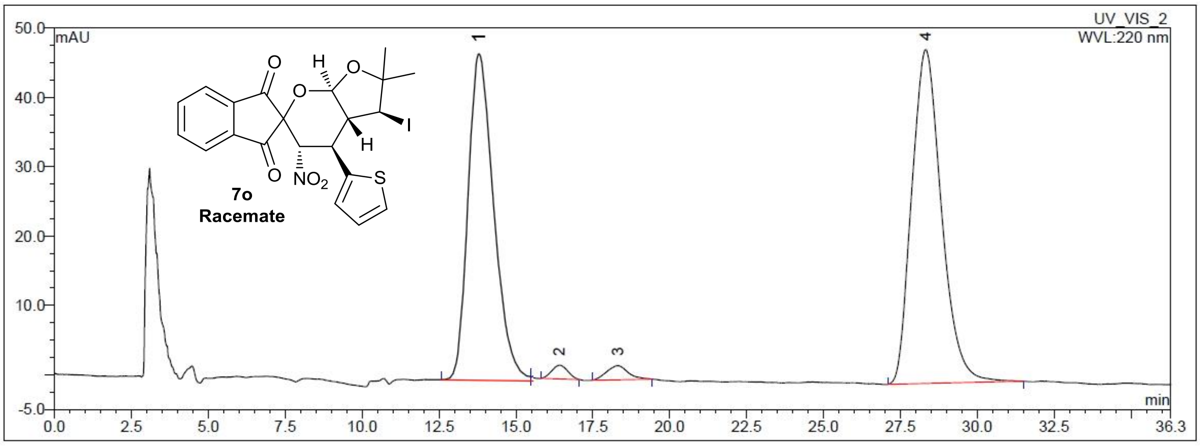



8.097
8.086
8.078
8.075
8.032
8.026
8.019
8.010
7.999
7.951
7.939
7.933
7.928
7.921
7.916
7.903
7.307
7.294
7.262
7.134
7.127
7.030
7.021
7.009
5.663
5.643
5.477
5.450
4.543
4.514
4.486
3.992
3.961
2.539
2.520
2.509
2.489
2.479
2.459
1.570
1.534
1.381
0.000
7o
1.74
1.92
0.76
0.95
0.89
0.99
0.92
0.97
1.00
1.01
3.13
3.08
f1 (ppm)


193.610
190.934
140.714
140.423
137.125
137.063
127.184
125.121
124.864
124.633
100.057
89.880
87.069
85.844
53.344
30.603
26.714
24.912
7o
f1 (ppm)

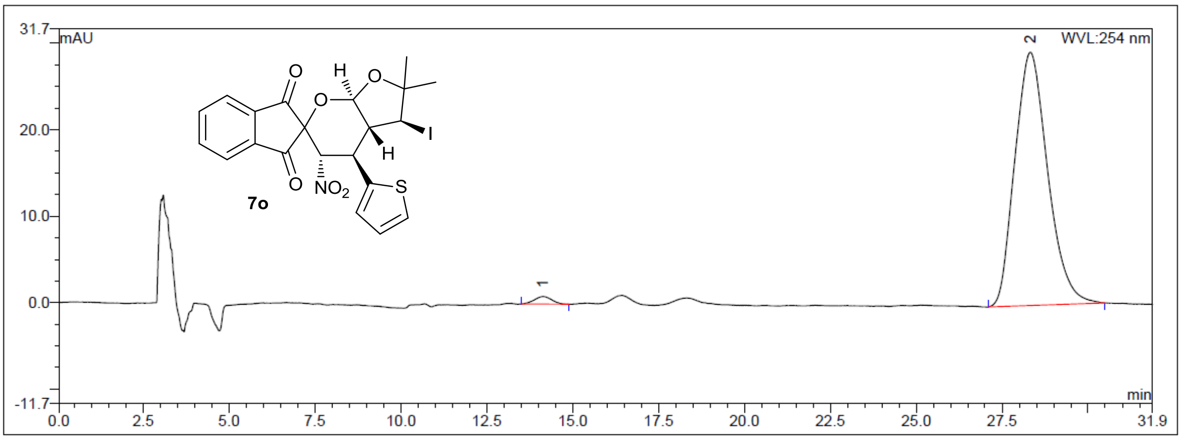
Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	14.13	13.453	46.07	46.062	n.a.
2	n.a.	16.41	1.187	4.06	1.972	n.a.
3	n.a.	18.32	1.206	4.13	1.787	n.a.
4	n.a.	28.32	13.353	45.73	48.365	n.a.



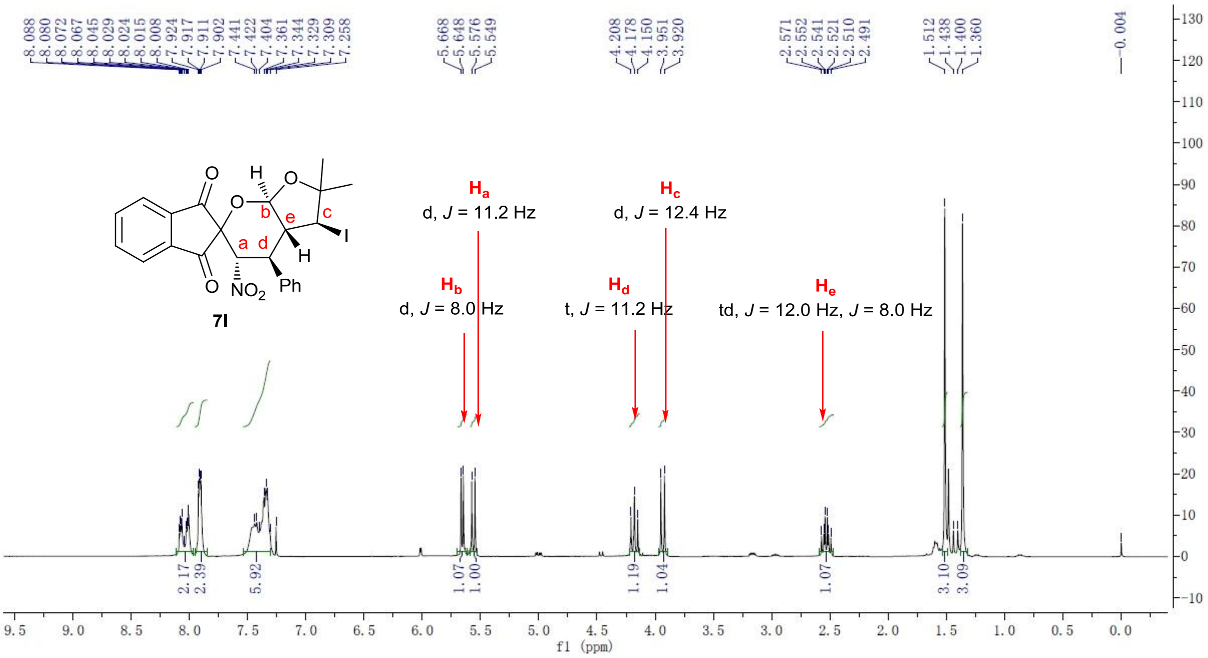
Peak Analysis Report

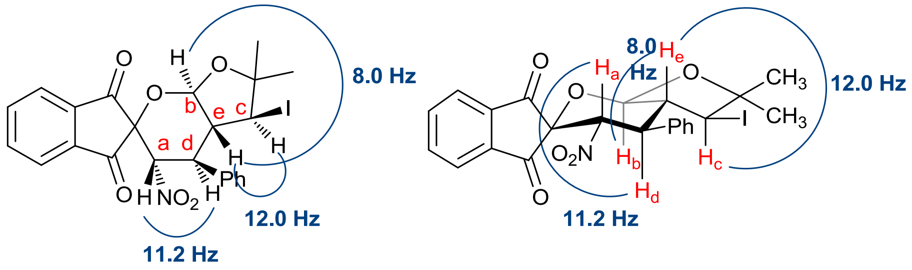
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	14.13	0.514	1.56	0.894	n.a.
2	n.a.	28.33	32.543	98.44	29.291	n.a.



8. The confirmation of the absolute configuration of 7l

The absolute configuration of **7l** was determined by selected NOESY spectra and the products **7m-7o** were assigned by analogy.

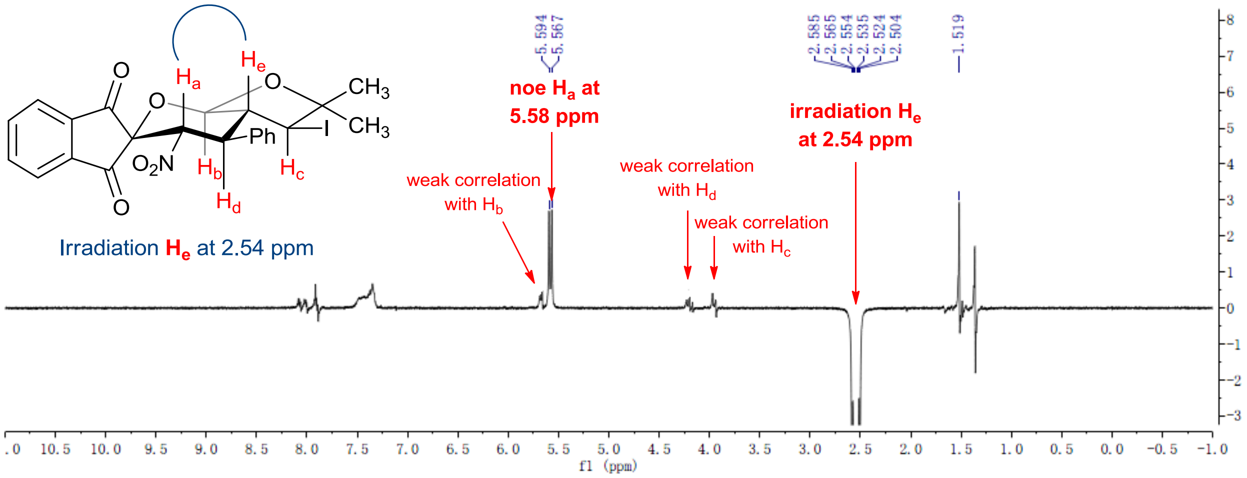


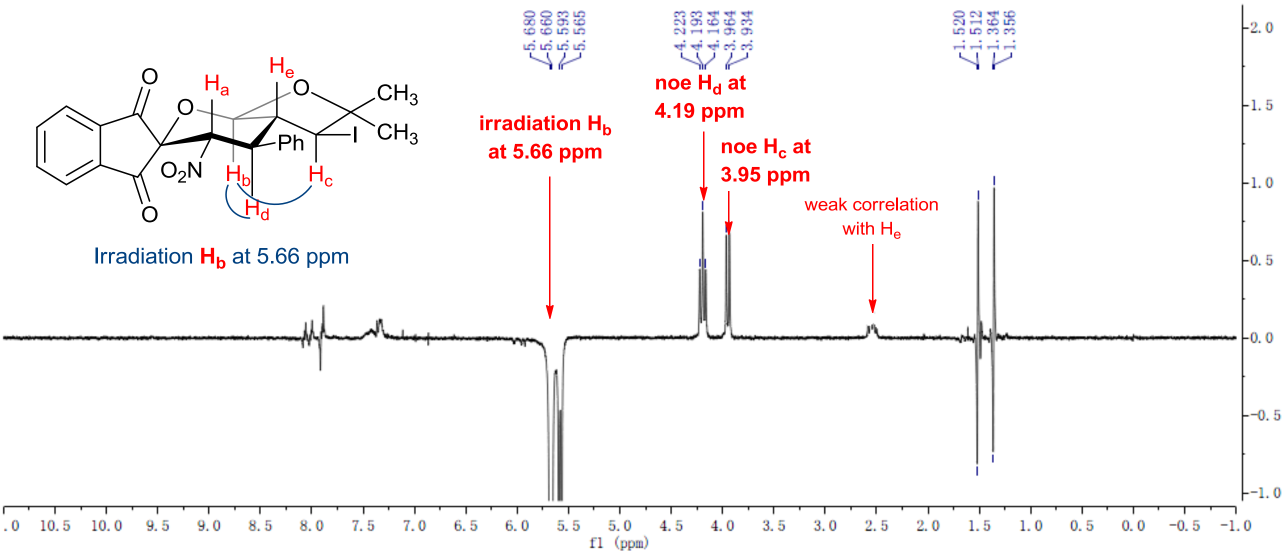


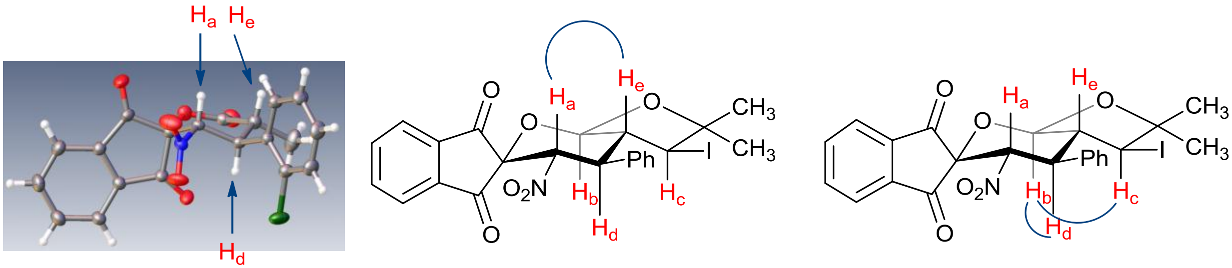
Coupling Constants of 7l

◇ The ^{1}H NMR spectrum of **7l** exhibited five proton signals ascribable to H_a, H_b, H_c, H_d and H_e on the hexahydrofuro[2,3-*b*]pyran framework. Other signals observed in the ^{1}H NMR spectrum included nine aromatic protons and two methyl singlets (δ 1.51, 1.36 ppm).

◇ Three doublets could be assigned as H_a, H_b and H_c by chemical shifts and coupling constants. H_d appeared as a triplet at δ 4.18 (t, *J* = 11.2 Hz, 1H) and H_e appeared as a triple doublet at δ 2.53 (td, *J* = 12.0, 8.0 Hz, 1H).


O
O
O
O
H_a
H_e
CH_3
CH_3
Ph
I
O_2N
H_b
H_c
H_d
Irradiation H_e at 2.54 ppm
5.594
5.567
noe H_a at 5.58 ppm
weak correlation with H_b
weak correlation with H_d
weak correlation with H_c
2.585
2.565
2.554
2.535
2.524
2.504
irradiation H_e at 2.54 ppm
1.519
8
7
6
5
4
3
2
1
0
-1
-2
-3
.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


O
O
O
O
H_a
H_e
CH_3
CH_3
Ph
I
O_2N
H_b
H_c
H_d
Irradiation H_b at 5.66 ppm
5.680
5.660
5.593
5.565
irradiation H_b at 5.66 ppm
4.223
4.193
4.164
3.964
3.934
noe H_d at 4.19 ppm
noe H_c at 3.95 ppm
weak correlation with H_e
1.520
1.512
1.364
1.356
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)



Irradiation $\mathbf{H_e}$ at 2.54 ppm

Irradiation $\mathbf{H_b}$ at 5.66 ppm

Selected NOESY Analysis

◇ The absolute configuration of H_a, H_d and H_e could be confirmed by analogy from X-ray crystal structure of **6b** and the conformation of the three C-H bonds could be determined as axial.

◇ Irradiation $\mathbf{H_e}$ at 2.54 ppm: The strong NOESY correlation between H_e and H_a indicated that H_e and H_a were on the same side of the ring which was consistent with the X-ray crystal structure.

◇ Irradiation $\mathbf{H_b}$ at 5.66 ppm: The strong NOESY correlations of H_b with H_d and H_c indicated that H_b, H_d and H_c were on the same side of the ring.