α-Regioselective [3 + 2] Annulations with Morita–Baylis–Hillman Carbonates of Isatins and 2-Nitro-1,3-enynes

Guang-Yao Ran,[a] Pan Wang,[a] Wei Du,[a] and Ying-Chun Chen*[a,b]

[a]*Key Laboratory of Drug-Targeting and Drug Delivery System of the Ministry of Education, West China School of Pharmacy, Sichuan University, Chengdu 610041, China,*

[b]*College of Pharmacy, Third Military Medical University, Shapingba, Chongqing 400038, China*

E-mail: ycchen@scu.edu.cn

Supplementary Information

Table of Contents

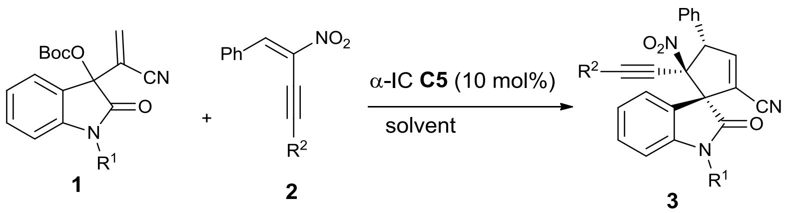
1. General methods

NMR data were obtained for ^{1}H at 400 MHz and for ^{13}C at 100 MHz. Chemical shifts were given in parts per million (δ) 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 a chiral column in comparison with authentic racemate, using a Daicel Chiralpak IA Column (250 × 4.6 mm), Chiralpak ID Column (250 × 4.6 mm), Chiralpak OD Column (250 × 4.6 mm) or Chiralpak AD Column (250 × 4.6 mm). UV detection was monitored at 220 nm or 254 nm. Optical rotation data were examined in $CHCl_3$ or EtOAc 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. All chemicals were used without purification as commercially available unless otherwise noted. THF, ethyl acetate (EA), petroleum ether (PE), methylene chloride (CH_2Cl_2), toluene, and CH_3CN were distilled before use. Cinchona alkaloids catalysts β-ICD **C3**, **C4**, and α-IC **C5** were prepared according to the literature procedures.[1] 2-Nitro-1,3-enynes and α-phenyl- or styryl-nitroolefins were synthesized based on the reported method.[2]

1 (*a*) Y. Iwabuchi, M. Nakatani, N. Yokoyama and S. Hatakeyama, *J. Am. Chem. Soc.*, 1999, **121**, 10219; (*b*) Y. Nakamoto, F. Urabe, K. Takahashi, J. Ishihara and S. Hatakeyama, *Chem. Eur. J.*, 2013, **19**, 12653.

2 (*a*) G. Bharathiraja, S. Sakthivel, M. Sengoden and T. Punniyamurthy, *Org. Lett.*, 2013, **15**, 4996; (*b*) M. Ganesh and I. N. N. Namboothiri, *Tetrahedron*, 2007, **63**, 11973.

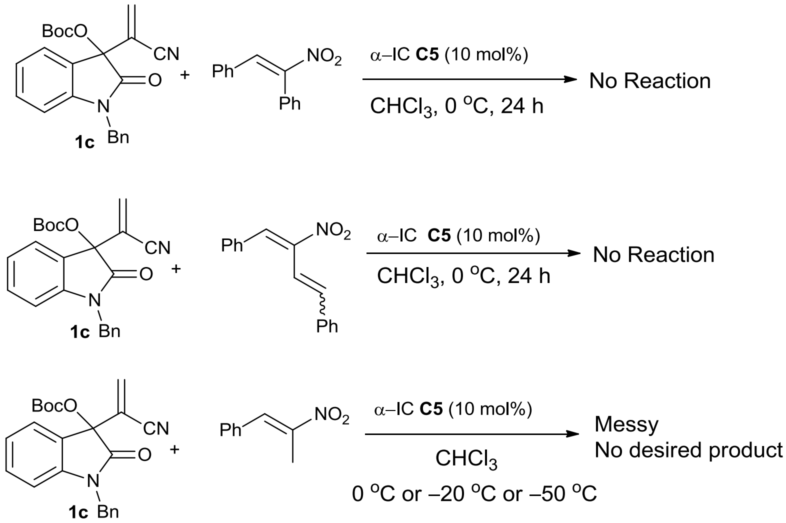
2. Additional screening studies[a]



Entry	R^1	R^2	Solvent	*t* (min)	Yield (%)[b]	dr[c]	ee (%)[d]
1	Me	Ph	$CHCl_3$	120	71	> 19:1	55
2	Me	$BocOCH_2$-	$CHCl_3$	50	77	> 19:1	74
3	Bn	$BnOCH_2$-	$CHCl_3$	25	88	> 19:1	86
4	Bn	$BnOCH_2$-	DCM	25	88	> 19:1	85
5	Bn	$BnOCH_2$-	Toluene	300	71	> 19:1	84

6	Bn	$BnOCH_2$-	EtOAc	60	68	> 19:1	85
7	Bn	$BnOCH_2$-	CH_3CN	40	43	> 19:1	83

[a] Reactions were performed with 0.1 mmol of **1**, 0.11 mmol of **2**, 10 mol% of **C5** in 1 mL solvent. [b] Isolated yield. [c] Determined by ^{1}H NMR analysis. [d] Based on chiral HPLC analysis.



Scheme S1. The reactions of MBH carbonate and other α-substituted nitroalkenes

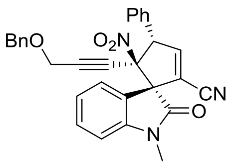
As shown in Scheme S1, α-phenyl and α-styryl nitroalkenes exhibited very poor reactivity with the MBH carbonate under the optimised conditions; while α-methyl nitroalkene did not provide the desired product even at low temperature (–20 °C or –50 °C). These results demonstrated that the α-alkynyl group is vital to the reaction. Actually, the alkynyl group had been proven to be more electron negative than vinyl group.[3] It could stabilize the carboanion of the intermediate, resulting in higher reactivity than the phenyl, vinyl or methyl substituted nitroolefins. In addition, the α-alkynyl substituent provided extra steric hindrance, rendering the γ-selective transition state congested.[4] Thus it led to α-selectivity for the [3 + 2] annulation.

3. S.-J. Min, G. O. Jones, K. N. Houk and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2007, **129**, 10078.

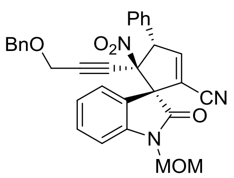
4 (*a*) K.-K. Wang, T. Jin, X. Huang, Q. Ouyang, W. Du and Y.-C. Chen, *Org. Lett.*, 2016, **18**, 872; (*b*) G. Zhan, M.-L. Shi, Q. He, W.-J. Lin, Q. Ouyang, W. Du and Y.-C. Chen, *Angew. Chem., Int. Ed.,* 2016, **55**, 2147.

3. General procedure for [3 + 2] annulation reaction

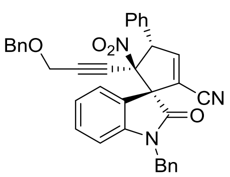
A solution of MBH carbonate **1** (0.1 mmol) and (*E*)-2-nitro-1,3-enyne **2** (0.11 mmol) in $CHCl_3$ (1.0 mL) was cooled to 0 °C and α-IC **C5** (10 mol%) was added in one portion. The reaction was stirred for a few minutes at the same temperature. Upon workup, product **3** was obtained by flash chromatography on silica gel (EtOAc/petroleum ether = 1:8).



3a, colorless oil, 36.2 mg, 74% yield; $[\alpha]^{20}_{D}$ = −183 (*c* = 0.19 in $CHCl_3$); 80% ee, determined by HPLC analysis [Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 6.52 min, t (major) = 10.21 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.49 (d, *J* = 6.8 Hz, 2H), 7.44-7.29 (m, 7H), 7.25-7.19 (m, 3H), 7.14-7.07 (m, 2H), 6.86 (d, *J* = 8.0 Hz, 1H), 5.42 (d, *J* = 2.4 Hz, 1H), 4.08 (d, *J* = 1.6 Hz, 2H), 3.91, 3.90 (ABq, *J* = 16.8 H, 2H), 3.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 152.0, 144.9, 137.5, 135.4, 132.2, 130.9, 129.3, 128.9, 128.8, 128.7, 128.3, 124.5, 124.3, 122.5, 115.9, 113.1, 109.6, 100.1, 94.8, 71.5, 69.9, 61.1, 57.0, 27.42. ESI-HRMS: calcd. for $C_{30}H_{23}N_3O_4$+Na^+ 512.1581, found 512.1580.

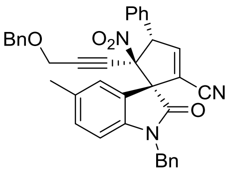


3b, white solid, 36.9 mg, 71% yield; $[\alpha]^{20}_{D}$ = −249 (*c* = 0.13 in $CHCl_3$); 80% ee, determined by HPLC analysis [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major) = 16.36 min, t (minor) = 27.98 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.48-7.09 (m, 15H), 5.53 (d, *J* = 2.0 Hz, 1H), 5.18, 5.09 (ABq, *J* = 11.2 Hz, 2H), 4.08 (s, 2H), 3.90 (s, 2H), 3.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 171.7, 151.2, 142.7, 137.0, 134.8, 131.8, 130.3, 128.9, 128.5, 128.3, 128.1, 127.9, 124.2, 124.0, 121.8, 115.6, 112.5, 110.7, 99.7, 94.5, 72.0, 71.1, 69.4, 60.1, 56.5, 56.3; ESI-HRMS: calcd. for $C_{31}H_{25}N_3O_5$+Na^+ 542.1686, found 542.1680.

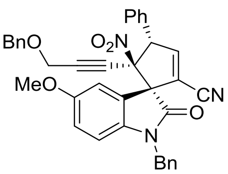


3c, white semisolid, 49.7 mg, 88% yield; $[\alpha]^{20}_{D}$ = −195 (*c* = 0.12 in $CHCl_3$); 87% ee, determined by HPLC analysis: [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major) = 27.93 min, t (minor) = 40.32 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.51 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.32-7.20 (m, 12H), 7.15 (d, *J* = 7.6 Hz, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 5.52 (d, *J* = 2.4 Hz, 1H), 5.04 (d, *J* = 16.0 Hz, 1H), 4.82 (d, *J* = 16.0 Hz, 1H), 4.06, 4.01 (ABq, J_{AB} = 12.0 Hz, 2H), 3.89, 3.79 (ABq, J_{AB} = 16.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 171.5, 151.3, 143.7, 135.0, 134.6, 131.7, 130.4, 128.9, 128.9, 128.5, 128.3, 128.1, 127.8, 126.9, 124.1, 123.8, 115.8, 112.7, 110.2, 99.7, 94.5, 71.1, 69.2, 60.6, 56.5, 44.5; ESI-HRMS: calcd. for $C_{36}H_{27}N_3O_4$+Na^+ 588.1894, found 588.1894.

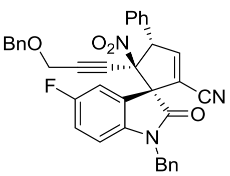
Enantiomer of **3c**, white semisolid, 40.1 mg, 71% yield; $[\alpha]_D^{20}$ = 203 (*c* = 0.12 in $CHCl_3$); −92% ee, determined by HPLC analysis: [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor)= 29.57 min, t (major) = 40.24 min].



3d, white solid, 48.1 mg, 83% yield; $[\alpha]_D^{20}$ = –256 (*c* = 1.12 in $CHCl_3$); 86% ee, determined by HPLC analysis: [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major) = 16.20 min, t (minor) = 27.06 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.51 (d, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 6.8 Hz, 2H), 7.32-7.15 (m, 12H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 5.52 (d, *J* = 2.4 Hz, 1H), 5.02 (d, *J* = 16.0 Hz, 1H), 4.81 (d, *J* = 16.0 Hz, 1H), 4.09, 4.00 (ABq, *J* = 11.6 Hz, 2H), 3.90, 3.80 (ABq, *J* = 16.4 Hz, 2H). 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 171.4, 151.1, 141.2, 134.9, 132.0, 130.4, 128.9, 128.5, 128.3, 128.1, 127.8, 127.7, 126.8, 124.7, 115.9, 112.7, 109.9, 99.8, 94.4, 71.1, 69.3, 60.4, 56.6, 44.5, 21.1; ESI-HRMS: calcd. for $C_{37}H_{29}N_3O_4$+Na^+ 602.2050, found 602.2048.

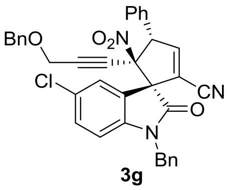


3e, white semisolid, 52.4 mg, 88% yield; $[\alpha]_D^{20}$ = –246 (*c* = 0.29 in $CHCl_3$); 95% ee, determined by HPLC analysis: [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 11.13 min, t (major) = 24.96 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.51 (d, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.32-7.15 (m, 12H), 6.80 (dd, *J* = 8.4 Hz, 2.4 Hz, 1H), 3.75 (d, *J* = 2.4 Hz, 1H), 6.61 (d, *J* = 8.8 Hz, 1H), 5.49 (d, *J* = 2.8 Hz, 1H), 5.01 (d, *J* = 16.0 Hz, 1H), 4.80 (d, *J* = 16.0 Hz, 1H), 4.06, 4.01 (ABq, *J* = 11.6 Hz, 2H), 3.90, 3.80 (ABq, *J* = 16.4 Hz, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 171.3, 156.5, 151.4, 137.0, 136.8, 134.9, 134.7, 130.5, 128.9, 128.5, 128.3, 128.2, 126.9, 116.0, 115.8, 112.7, 111.5, 110.6, 99.8, 94.5, 71.1, 69.5, 60.7, 56.5, 55.9, 44.5; ESI-HRMS: calcd. for $C_{37}H_{29}N_3O_5$+Na^+ 618.1999, found 618.1998.



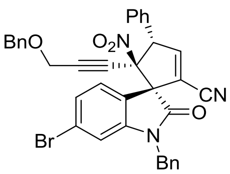
3f, white solid, 42.0 mg, 72% yield; $[\alpha]_D^{20}$ = –201 (*c* = 0.24 in $CHCl_3$); 86% ee, determined by HPLC analysis: [Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 5.91 min, t (major) = 17.67 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.50 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.33-7.15 (m, 12H), 7.01 (td, *J* = 8.4 Hz, 2.4 Hz, 1H), 6.92 (dd, *J* = 8.0 Hz, 2.8 Hz, 1H), 6.64

(dd, J = 8.4 Hz, 4.0 Hz, 1H), 5.47 (d, J = 2.4 Hz, 1H), 5.02 (d, J = 16.4 Hz, 1H), 4.80 (d, J = 16.0 Hz, 1H), 4.06, 4.01 (ABq, J = 11.6 Hz ,2H), 3.90, 3.81 (ABq, J = 16.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.4, 160.6, 158.2, 151.9, 139.7, 139.7, 137.0, 134.7, 134.2, 130.5, 129.0, 128.5, 128.4, 128.2, 128.0, 127.9, 126.9, 123.7, 118.4, 118.2, 115.3, 112.6, 112.5, 112.4, 110.9, 110.9, 99.6, 94.8, 71.1, 69.3, 60.8, 56.5, 44.6; ESI-HRMS: calcd. for $C_{36}H_{26}FN_3O_4$+Na^+ 606.1800, found 606.1804.



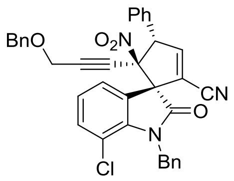
3g

3g, white solid, 48.6 mg, 81% yield; $[\alpha]^{20}_{D}$ = –250 (c = 0.28 in $CHCl_3$); 84% ee, determined by HPLC analysis: [Daicel Chiralpak AD, n-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 5.51 min, t (major) = 15.82 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.49 (d, J = 6.8 Hz, 2H), 7.38 (t, J = 6.8 Hz, 2H), 7.33-7.13 (m, 14H), 6.64 (d, J = 8.4 Hz, 1H), 5.51 (d, J = 2.8 Hz, 1H), 5.02 (d, J = 16.0 Hz, 1H), 4.82 (d, J = 16.0 Hz, 1H), 4.07, 4.03 (ABq, J = 12.0 Hz , 2H), 3.89, 3.82 (ABq, J = 16.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.0, 151.8, 142.2, 134.1, 131.7, 130.4, 129.3, 129.0, 128.5, 128.3, 128.1, 128.0, 127.9, 126.9, 124.5, 115.2, 112.5, 111.2, 99.7, 94.9, 71.2, 68.9, 60.4, 56.5, 44.6; ESI-HRMS: calcd. for $C_{36}H_{26}ClN_3O_4$+Na^+ 622.1504, found 622.1504.



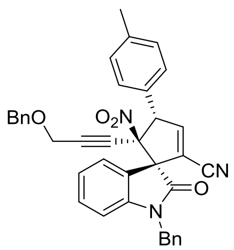
3h, white solid, 55.4 mg, 86% yield; $[\alpha]^{20}_{D}$ = –199 (c = 0.60 in $CHCl_3$); 82% ee, determined by HPLC analysis: [Daicel Chiralpak AD, n-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 7.22 min, t (major) = 15.30 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.49 (d, J = 7.2 Hz, 2H), 7.37 (t, J = 7.2 Hz, 2H), 7.33-7.21 (m, 11H), 7.17-7.15 (m, 2H), 7.01 (d, J = 8.0 Hz, 1H), 6.88 (d, J = 1.6 Hz, 1H), 5.47 (d, J = 2.4 Hz, 1H), 5.01 (d, J = 16.0 Hz, 1H), 4.80 (d, J = 8.0 Hz, 1H), 4.05, 3.99 (ABq, J = 11.6 Hz, 2H), 3.88, 3.78 (ABq, J = 16.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.4, 151.8, 145.0, 130.4, 129.1, 129.0, 128.5, 128.4, 128.1, 128.1, 127.9, 126.9, 126.8, 125.3, 121.1, 115.1, 113.6, 112.4, 99.5, 94.9, 71.1, 68.9, 60.8, 56.5, 44.6; ESI-HRMS: calcd. for $C_{36}H_{26}BrN_3O_4$+Na^+ 666.0999, found 666.0996

3i, white solid, 48.6 mg, 81% yield; $[\alpha]^{20}_{D}$ = –153 (c = 0.25 in $CHCl_3$); 86% ee, determined by HPLC analysis: [Daicel Chiralpak IA, n-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 7.07 min, t (major) = 31.25 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.47 (d, J = 7.2 Hz, 2H),

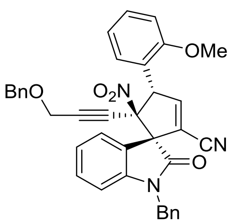


7.37-7.01 (m, 17H), 5.52 (d, J = 2.4 Hz, 1H), 5.35 (d, J = 2.4 Hz, 2H), 4.02, 3.92 (ABq, J = 11.6 Hz, 2H), 3.84, 3.68 (ABq, J = 16.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.1, 151.8, 137.0, 136.4, 134.7, 134.4, 130.4, 129.0, 128.7, 128.6, 128.3, 128.1 127.8, 127.2, 126.1, 125.2, 124.6, 122.6, 116.3, 115.2, 112.5, 100.0, 95.0, 71.1, 68.8, 60.5, 56.5, 45.8; ESI-HRMS: calcd. for $C_{36}H_{26}ClN_3O_4$+Na^+ 622.1504, found 622.1506.

Enantiomer of **3i**, white solid, 37.8 mg, 63% yield; $[\alpha]_D^{20}$ = 146 (c = 0.23 in $CHCl_3$); −84% ee, determined by HPLC analysis: [Daicel Chiralpak IA, n-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor)= 7.07 min, t (major) = 39.98 min].

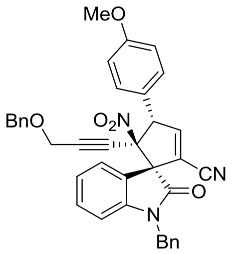


3j, white solid, 49.3 mg, 85% yield; $[\alpha]_D^{20}$ = –209 (c = 0.22 in $CHCl_3$); 86% ee, determined by HPLC analysis: [Daicel Chiralpak OD, n-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 25.12 min, t (major) = 34.64 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39 (d, J = 8.0 Hz, 2H), 7.32-7.15 (m, 15H), 7.07 (t, J = 7.6 Hz, 1H), 5.46 (d, J = 1.6 Hz, 1H), 5.05 (d, J = 16.0 Hz, 1H), 4.82 (d, J = 16.0 Hz, 1H), 4.05, 4.00 (ABq, J = 12.0 Hz, 2H), 3.93, 3.81 (ABq, J = 16.4 Hz, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.6, 151.7, 143.7, 138.8, 134.6, 131.8, 131.7 , 130.3, 129.2, 128.9, 128.3, 128.1, 127.8, 126.9, 124.1, 123.8, 115.4, 112.7, 110.2, 99.7, 94.3, 71.0, 69.2, 60.3, 56.6, 44.5, 21.1; ESI-HRMS: calcd. for $C_{37}H_{29}N_3O_4$+Na^+ 602.2050, found 602.2051.

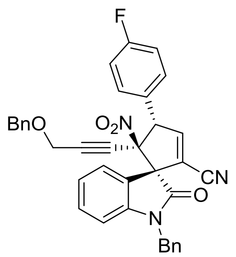


3k, white semisolid, 54.2 mg, 91% yield; $[\alpha]_D^{20}$ = –84 (c = 0.39 in $CHCl_3$); 93% ee, determined by HPLC analysis: [Daicel Chiralpak OD, n-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 8.78 min, t (major) = 16.81 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, J = 7.2 Hz, 1H), 7.32-7.13 (m, 14H), 7.08 (t, J = 7.6 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H), 6.71 (d, J = 7.6 Hz, 1H), 5.71 (d, J = 6.8 Hz, 1H), 4.94 (d, J = 8.0 Hz, 1H), 4.74 (d, J = 8.0 Hz, 1H), 4.00, 3.81 (ABq, J = 12.0 Hz, 2H), 3.82, 3.63 (ABq, J = 19.6 Hz, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.4, 157.4, 152.5, 144.0, 137.1, 131.6, 130.5, 130.1, 128.9, 128.3, 128.1, 127.8, 127.7, 126.8, 124.5, 124.4, 120.4, 115.4, 112.8, 110.1, 110.0, 98.3, 91.6, 70.8, 70.5, 56.4, 55.5, 44.4; ESI-HRMS: calcd. for $C_{37}H_{29}N_3O_5$+Na^+ 618.1999, found 618.2002.

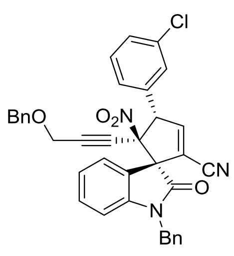
Enantiomer of **3k**, white semisolid, 41.7 mg, 70% yield; $[\alpha]^{20}_{D}$ = 88 (*c* = 0.13 in $CHCl_3$); −94% ee, determined by HPLC analysis: [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major)= 8.62 min, t (minor) = 17.14 min].



3l, white solid, 48.2 mg, 81% yield; $[\alpha]^{20}_{D}$ = –379 (*c* = 0.21 in $CHCl_3$); 85% ee, determined by HPLC analysis: [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 29.07 min, t (major) = 60.68 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.43 (d, *J* = 8.8 Hz, 2H), 7.32-7.14 (m, 13H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 5.44 (d, *J* = 2.8 Hz, 1H), 5.05 (d, *J* = 16.0 Hz, 1H), 4.82 (d, *J* = 16.0 Hz, 1H), 4.09, 4.03 (ABq, J_{AB} = 11.6 Hz, 2H), 3.98, 3.78 (ABq, *J* = 11.6 Hz, 2H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.7, 156.0, 151.8, 143.7, 137.1, 134.6, 131.7, 128.9, 128.3, 128.1, 127.8, 126.9, 124.1, 123.9, 115.3, 113.8, 112.8, 110.2, 99.8, 94.4, 71.1, 69.2, 60.2, 56.7, 55.2, 44.5; ESI-HRMS: calcd. for $C_{37}H_{29}N_3O_5+Na^+$ 618.1999, found 618.9998.

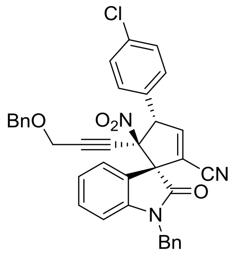


3m, white semisolid, 46.1 mg, 79% yield; $[\alpha]^{20}_{D}$ = –154 (*c* = 0.23 in $CHCl_3$); 72% ee, determined by HPLC analysis: [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 10.93 min, t (major) = 16.15 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.51-7.48 (m, 2H), 7.32-7.21 (m, 10H), 7.17-7.13 (m, 4H), 7.09-7.03 (m, 3H), 6.73 (d, *J* = 8.0 Hz, 1H), 4.46 (d, *J* = 2.8 Hz, 1H), 5.03 (d, *J* = 12.0 Hz, 1H), 4.82 (d, *J* = 16.0 Hz, 1H), 4.15, 4.08 (ABq, *J* = 11.6 Hz, 2H), 3.90, 3.81 (ABq, *J* = 12.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.6, 164.3, 161.8, 151.0, 143.7, 134.5, 132.3, 132.2 , 131.8, 130.7, 129.0, 128.4, 128.0, 127.8, 126.9, 124.1, 123.9, 115.9, 115.6, 115.3, 112.6, 110.3, 99.5, 94.7, 71.2, 69.3, 60.1, 56.5, 44.5; ESI-HRMS: calcd. for $C_{36}H_{26}FN_3O_4+Na^+$ 606.1800, found 606.1798.

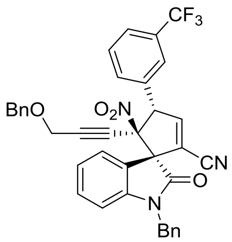


3n, white solid, 46.8 mg, 78% yield; $[\alpha]^{20}_{D}$ = –91 (*c* =0.36 in $CHCl_3$); 87% ee, determined by HPLC analysis: [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major) = 16.38 min, t (minor) = 29.07 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.55 (s, 1H), 7.42-7.41 (m, 1H), 7.33-7.13 (m, 15H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 5.46 (d, *J*

= 2.4 Hz, 1H), 5.04 (d, *J* = 16.0 Hz, 1H), 4.82 (d, *J* = 16.0 Hz, 1H), 4.10 (d, *J* = 2.4 Hz, 2H), 3.93, 3.84 (ABq, *J* = 16.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.4, 150.4, 143.7, 131.8, 130.6, 129.7, 129.1, 128.9, 128.6, 128.3, 128.1, 127.8, 126.8, 124.0, 123.9, 116.4, 112.5, 110.3, 99.4, 94.9, 71.2, 69.1, 60.1, 56.6, 44.5; ESI-HRMS: calcd. for $C_{36}H_{26}ClN_3O_4+Na^+$ 622.1504, found 622.1503.

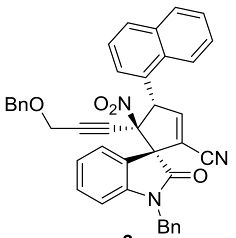


3o, white solid, 51.0 mg, 85% yield; $[\alpha]_D^{20}$ = –202 (*c* = 0.23 in $CHCl_3$); 74% ee, determined by HPLC analysis: [Daicel Chiralpak OD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 15.59 min, t (major) = 23.81 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.46 (d, *J* = 8.4 Hz, 2H), 7.36-7.21 (m, 11H), 7.18-7.13 (m, 3H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 5.44 (d, *J* = 2.8 Hz, 1H), 5.02 (d, *J* = 16.0 Hz, 1H), 4.82 (d, *J* = 16.0 Hz, 1H), 4.14, 4.06 (ABq, *J* = 12.0 Hz, 2H), 3.91, 3.82 (ABq, *J* = 16.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.6, 150.8, 143.7, 134.5, 131.9, 131.8, 128.9, 128.7, 128.4, 128.1, 127.8, 128.8, 126.8, 124.1, 124.0, 116.2, 112.5, 110.2, 99.3, 94.8, 71.2, 69.3, 60.1, 56.5, 44.5; ESI-HRMS: calcd. for $C_{36}H_{26}ClN_3O_4+Na^+$ 622.1504, found 622.1508.



3p, colorless oil, 45.0 mg, 71% yield; $[\alpha]_D^{20}$ = –210 (*c* = 0.14 in $CHCl_3$); 79% ee, determined by HPLC analysis: [Daicel Chiralpak ID, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 6.38 min, t (major) = 12.05 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.77 (d, *J* = 6.4 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.33-7.13 (m, 13H), 7.08 (t, *J* = 3.6 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 5.53 (d, *J* = 2.4 Hz, 1H), 5.03 (d, 8.0 Hz, 1H), 4.82 (d, *J* = 8.0 Hz, 1H), 4.05 (d, *J* = 3.6 Hz, 2H), 3.84 (d, *J* = 4.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.0 , 150.0, 143.6, 134.3, 133.8, 131.8, 129.0, 128.9, 128.3, 128.3, 127.9, 127.8, 127.8, 126.8, 123.9, 123.9, 116.7, 112.2, 110.3, 99.0, 95.0, 71.1, 69.1, 60.1, 56.4, 44.4; ESI-HRMS: calcd. for $C_{36}H_{26}F_3N_3O_4+Na^+$ 656.1768, found 656.1765.

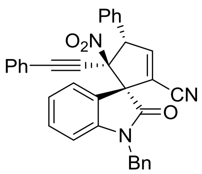
3q, white solid, 52.3 mg, 85% yield; $[\alpha]_D^{20}$ = –75 (*c* = 0.23 in $CHCl_3$); 90% ee, determined by HPLC analysis: [Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (minor) = 9.70 min, t (major) = 21.99 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.92 (d, *J* = 6.8 Hz, 1H),



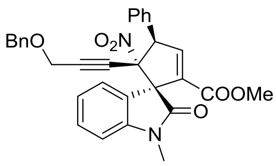
3q

7.83 (dd, J = 7.6 Hz, 3.2 Hz, 2H), 7.68 (d, J = 8.4 Hz, 1H), 7.58-7.52 (m, 2H), 7.47 (t, J = 7.2 Hz, 1H), 7.41 (d, J = 2.8 Hz, 1H), 7.34 (dt, J = 7.6 Hz, 0.8 Hz, 1H), 7.23-7.18 (m, 10 Hz), 7.13 (dt, J = 7.6 Hz, 0.8 Hz, 1H), 6.93-6.91 (m, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.18 (d, J = 2.8 Hz, 1H), 4.99 (d, 16.0 Hz, 1H), 4.74 (d, J = 16.0 Hz, 1H), 3.42-3.35 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.3, 152.6, 144.0, 136.9, 129.6, 129.3, 128.9, 128.1, 128.1, 127.7, 126.9, 125.9, 125.3, 124.3, 124.3, 124.3, 115.6, 112.7, 110.1, 98.9, 93.1, 70.7, 70.5, 57.7, 56.0, 44.5; ESI-HRMS: calcd. for $C_{40}H_{29}N_3O_4+Na^+$ 638.2050, found 638.2090.

Enantiomer of **3q**, white solid, 40.0 mg, 65% yield; $[\alpha]_D^{20}$ = 72 (c = 0.12 in $CHCl_3$); −90% ee, determined by HPLC analysis: [Daicel Chiralpak AD, n-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major)= 9.42 min, t (minor) = 21.52 min].

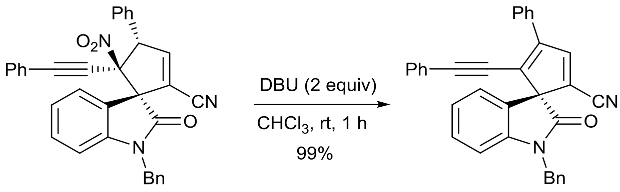


3r, white solid, 43.8 mg, 84% yield; $[\alpha]_D^{20}$ = –326 (c = 0.62 in $CHCl_3$); 88% ee, determined by HPLC analysis [Daicel Chiralpak OD, n-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major) = 12.35 min, t (minor) = 21.09 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.54-7.55 (m, 2H), 7.42-7.41 (m, 3H), 7.31-7.05 (m, 11H), 7.07 (t, J = 8.0 Hz, 1H), 6.95 (d, J = 7.2 Hz, 2H), 6.73 (d, J = 8.0 Hz, 1H), 5.61 (d, J = 2.4 Hz, 1H), 5.15 (d, J =15.6 Hz, 1H), 4.77 (d, J = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.4, 151.3, 143.7, 134.7, 132.0, 131.6, 130.4, 129.6, 128.9, 128.7, 128.4, 128.1, 127.7, 127.1, 124.1, 123.7, 115.9, 112.8, 110.2, 100.5, 97.6, 79.2, 69.0, 60.6, 44.6; ESI-HRMS: calcd. for $C_{34}H_{23}N_3O_3+Na^+$ 544.1632, found 544.1624.



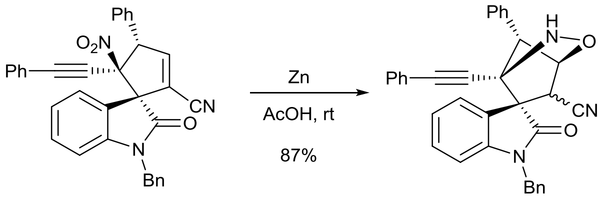
3s, white solid, 28.3 mg , 54% yield; $[\alpha]_D^{20}$ = 327 (c = 0.52 in $CHCl_3$); −98% ee, determined by HPLC analysis: [Daicel Chiralpak ID, n-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major) = 8.89 min, t (minor) = 11.55 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.50 (d, J = 7.2 Hz, 2H), 7.38-7.22 (m, 10H), 7.10 (d, J = 6.8 Hz, 1H), 7.02 (t, J = 7.2 Hz, 1H), 6.86 (d, J = 8.0 Hz, 1H), 5.61 (d, J = 2.0 Hz, 1H), 4.24, 4.16 (ABq, J = 5.2 Hz, 2H), 3.98 (d, J = 1.2 Hz, 2H), 3.64 (s, 3H), 3.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.6, 162.0, 145.9, 144.6, 137.2, 135.7, 135.4, 130.6, 130.2, 128.5, 128.3, 128.2, 127.8, 125.1, 123.2, 122.7, 108.6, 100.8, 93.7, 71.0, 66.9, 58.4, 56.6, 52.2, 26.9; ESI-HRMS: calcd. for $C_{37}H_{30}N_2O_6+Na^+$ 545.1683, found 545.1683.

4. Synthetic transformations of product 3r



3r 88% ee   **4** 86% ee

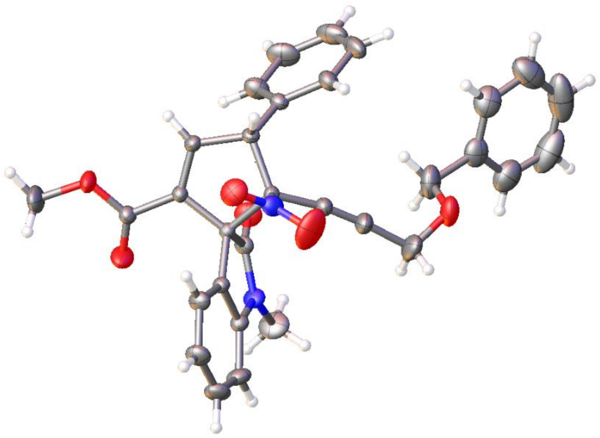
To a stirred solution of **3r** (26 mg, 0.05 mmol) in 1 mL of $CHCl_3$ was added DBU (0.1 mmol) at room temperature. The mixture was stirred until **3r** was consumed (1 h). Then evaporation of solvent under reduced pressure followed by purification by silica gel column chromatography using EtOAc/petroleum ether (1:8) afforded the compound **4** in a quantitative yield (99%). light yellow oil, 23.7 mg, 99% yield; $[\alpha]_D^{20}$ = 20 (*c* = 0.12 in EtOAc); 86% ee, determined by HPLC analysis: [Daicel Chiralpak ID, *n*-hexane/*i*-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major) = 14.78 min, t (minor) = 29.86 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.98 (d, *J* = 7.2 Hz, 2H), 7.90 (s, 1H), 7.49 (t, *J* = 7.2 Hz, 2H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.37 (d, *J* = 7.2 Hz, 2H), 7.32-7.27 (m, 2H), 7.22 (t, *J* = 7.2 Hz, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.10-7.01 (m, 6H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.30 (d, *J* = 15.6 Hz, 1H), 4.78 (d, *J* = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 169.6, 150.3, 147.1, 144.2, 131.8, 130.1, 129.7, 129.2, 128.9, 128.8, 128.4, 127.7, 127.4, 127.1, 124.1, 123.7, 117.8, 114.1, 110.2, 102.4, 83.8, 73.3, 44.7; ESI-HRMS: calcd. for $C_{34}H_{22}N_2O+Na^+$ 497.1624, found 497.1628.

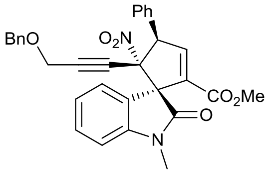


3r 88% ee   **5** 1:0.9 dr

To a stirred suspension of product **3r** (70 mg, 0.13 mmol) in CH_3COOH (1 mL) was added Zn dust (87 mg, 1.3 mmol, 10 equiv) in one portion at room temperature. The mixture was stirred for 1.5 hours. Upon completion, the mixture was diluted by EtOAc and saturated $NaHCO_3$ was added carefully. The aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography (petroleum ether/EtOAc = 4:1) to afford bridged heterocycle **5** as a diastereomeric mixture (59.1 mg, 87% yield). 1:0.9 dr, determined by ^{1}H NMR analysis. The diastereomeric mixture could not be isolated very well on a chiral column by HPLC analysis, the enantioselectivity almost remained unchanged compared with **3r**. 86% ee, determined by HPLC analysis: [Daicel Chiralpak ID, *n*-hexane/*i*-PrOH = 70/30, 1.0 mL/min, λ = 254 nm, t_1 (major) = 9.66 min, t_1 (minor) = 14.62 min]; 86% ee, determined by HPLC analysis: [t_2 (minor) = 20.47 min, t_2 (major) = 32.43 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 9.37-9.16 (m, 1.66H), 7.50-7.28 (m, 33.91H), 7.22-7.14 (m, 5.93H), 7.00 (t, *J* = 7.6 Hz, 1.81H), 6.91 (t, *J* = 7.6 Hz, 1.18H), 6.70 (t, *J* = 7.6 Hz, 2.40H), 6.57 (d, *J* = 7.2 Hz, 0.93H), 5.25 (d, *J* = 9.6 Hz, 1.11H), 5.12 (d, *J* = 8.8 Hz, 1.00H), 5.03 (d, *J* = 6.4 Hz, 1.08H), 4.99 (d, *J* = 6.0 Hz, 1.33H), 4.88- 4.78 (m, 4.49H), 4.67 (s, 0.96H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 173.1, 172.9, 149.7, 149.5, 143.4, 143.4, 142.8, 142.2, 138.4, 136.8, 134.9, 132.2, 132.1, 123.0, 129.8, 129.5, 129.3, 129.0, 128.9, 128.8, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.2, 127.2, 124.9, 124.6, 124.5, 124.4, 123.5, 123.3, 121.1, 120.9, 116.7, 116.7, 112.6, 112.4, 109.8, 103.2, 102.8, 78.6, 78.5, 49.2, 48.7, 46.3, 46.1, 44.3; ESI-HRMS: calcd. for $C_{34}H_{25}N_3O_2+Na^+$ 530.1839, found 530.1847.

5. Crystal data and structure refinement for enantiopure 3s

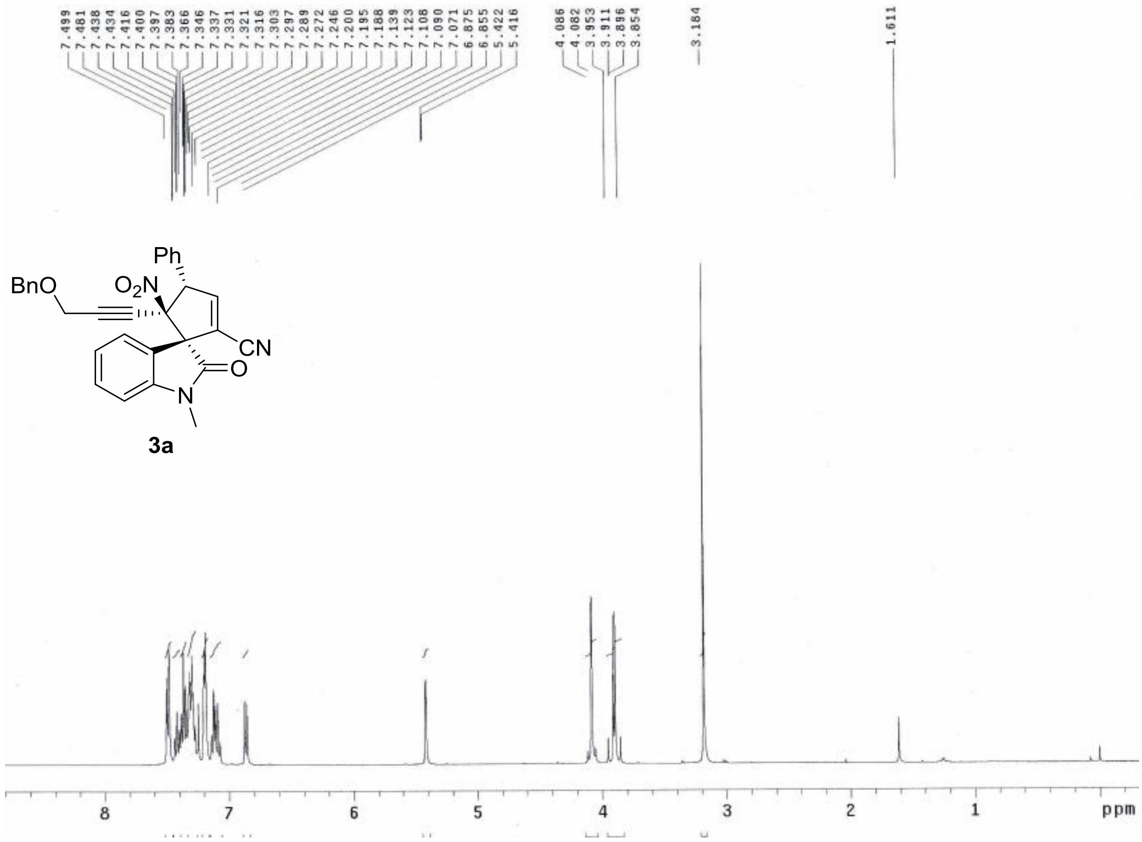




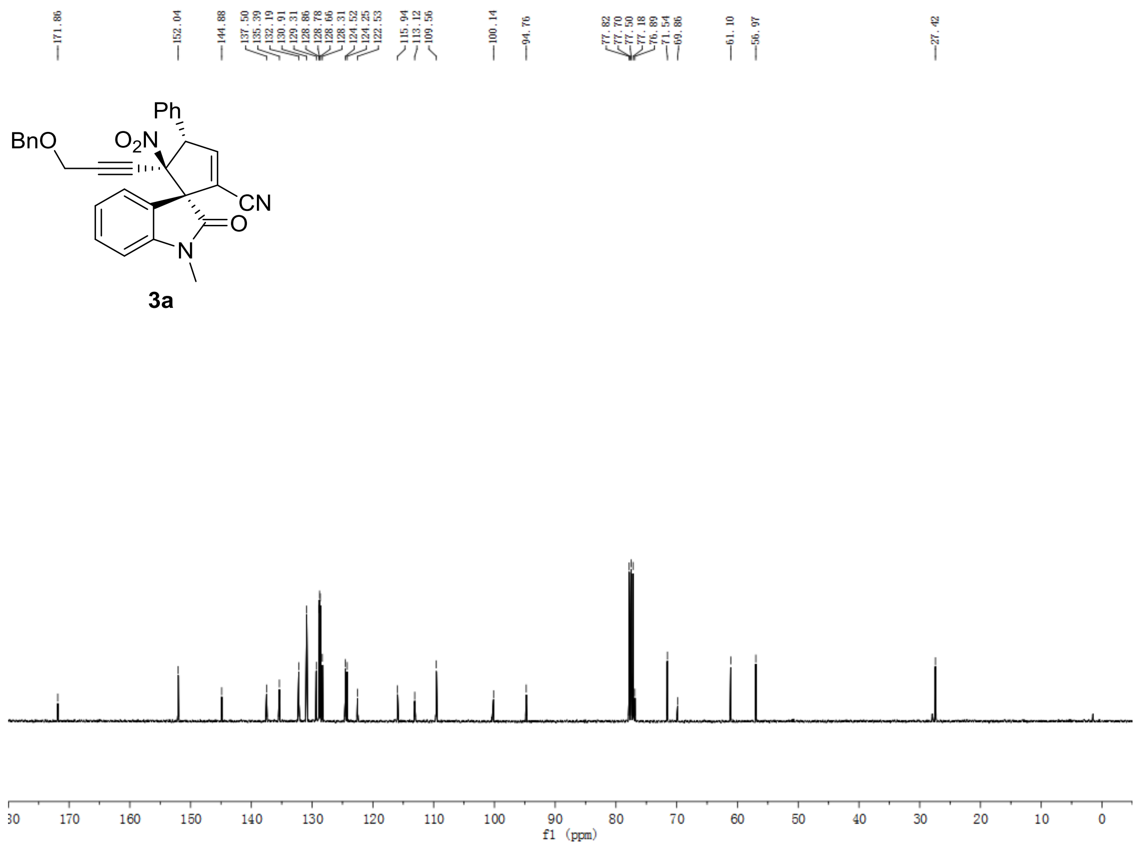
3s

Identification code	**3s**
Empirical formula	$C_{31}H_{26}N_2O_6$
Formula weight	521.53
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.02156(13)
b/Å	9.44417(11)
c/Å	30.9480(4)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2636.81(6)
Z	4
ρ_{calc}g/cm^3	1.314
μ/mm^{-1}	0.754
F(000)	1092.0
Crystal size/mm^3	0.14 × 0.13 × 0.13
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.792 to 142.754
Index ranges	$-7 \leq h \leq 10$, $-11 \leq k \leq 11$, $-33 \leq l \leq 37$
Reflections collected	13769
Independent reflections	4592 [R_{int} = 0.0290, R_{sigma} = 0.0224]
Data/restraints/parameters	4592/0/354
Goodness-of-fit on F^2	1.055
Final R indexes [I>=2σ (I)]	R_1 = 0.0494, wR_2 = 0.1341
Final R indexes [all data]	R_1 = 0.0498, wR_2 = 0.1347
Largest diff. peak/hole / e Å^{-3}	0.47/-0.28
Flack parameter	-0.09(10)

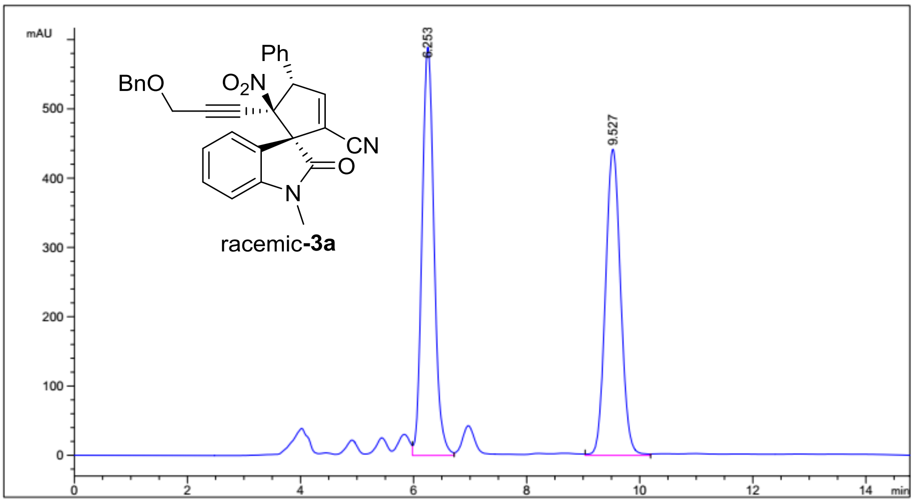
6. NMR spectra and HPLC chromatograms



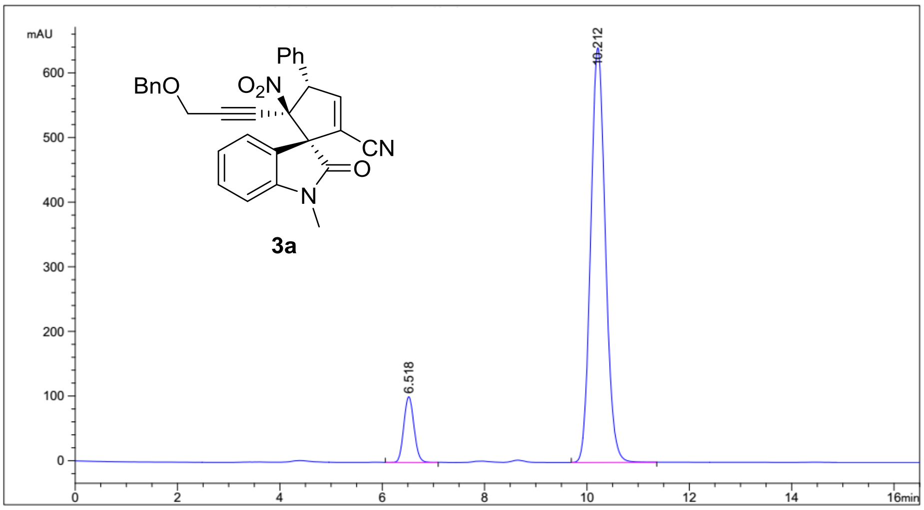
3a



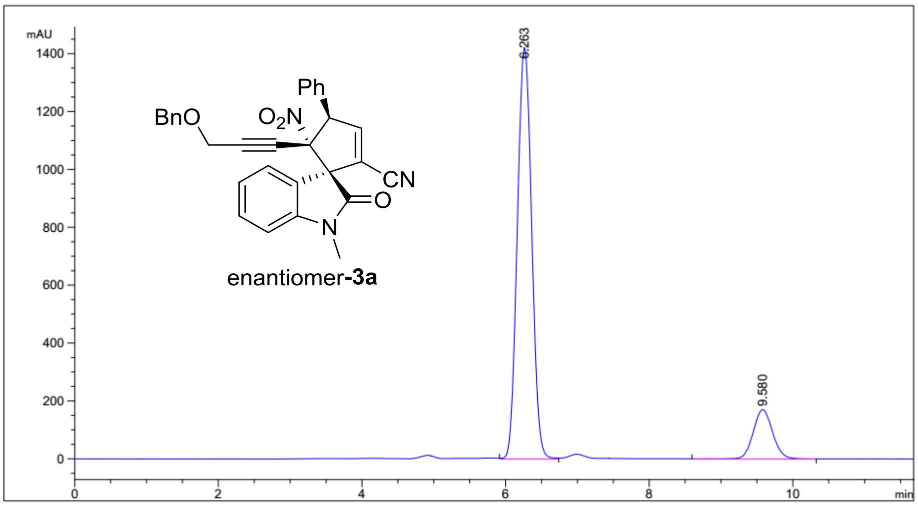
3a



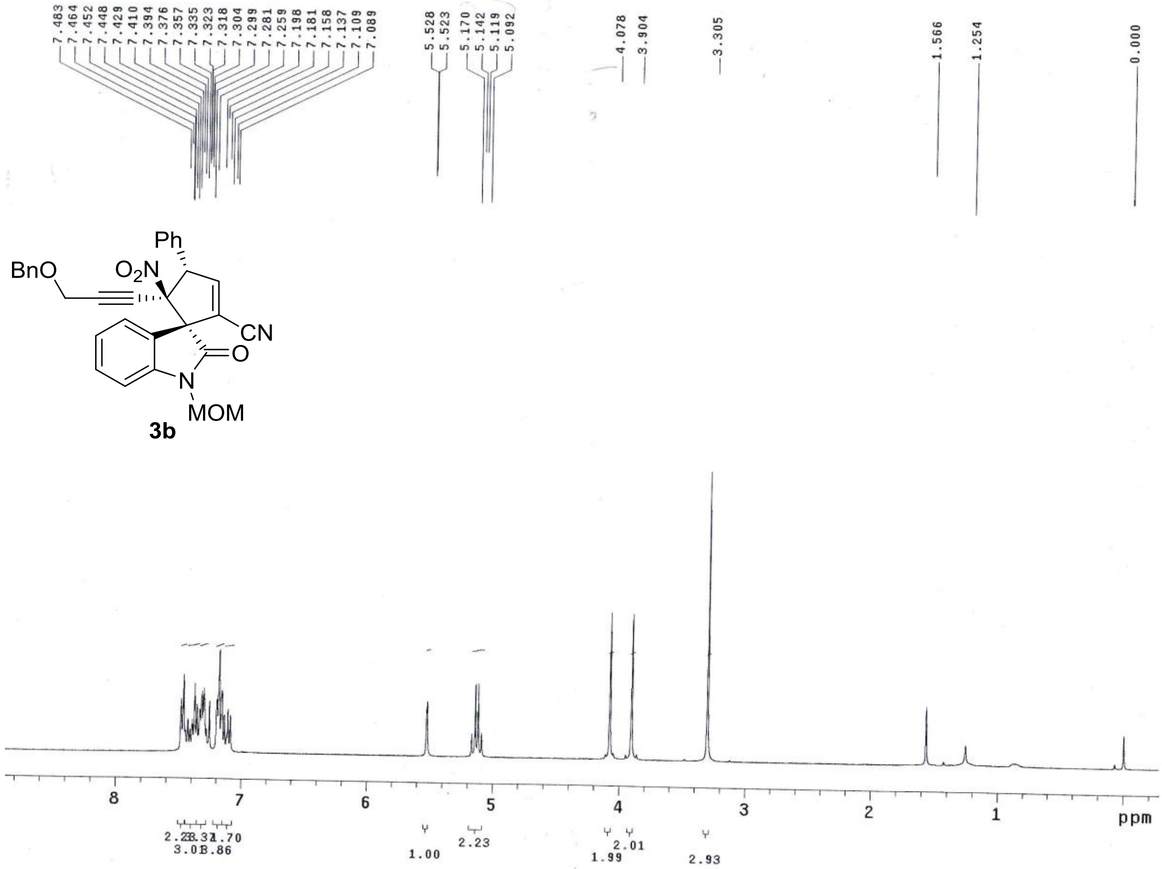
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.253	VV	0.2303	8677.76953	588.50793	51.4421
2	9.527	VV	0.2922	8191.22119	441.50714	48.5579

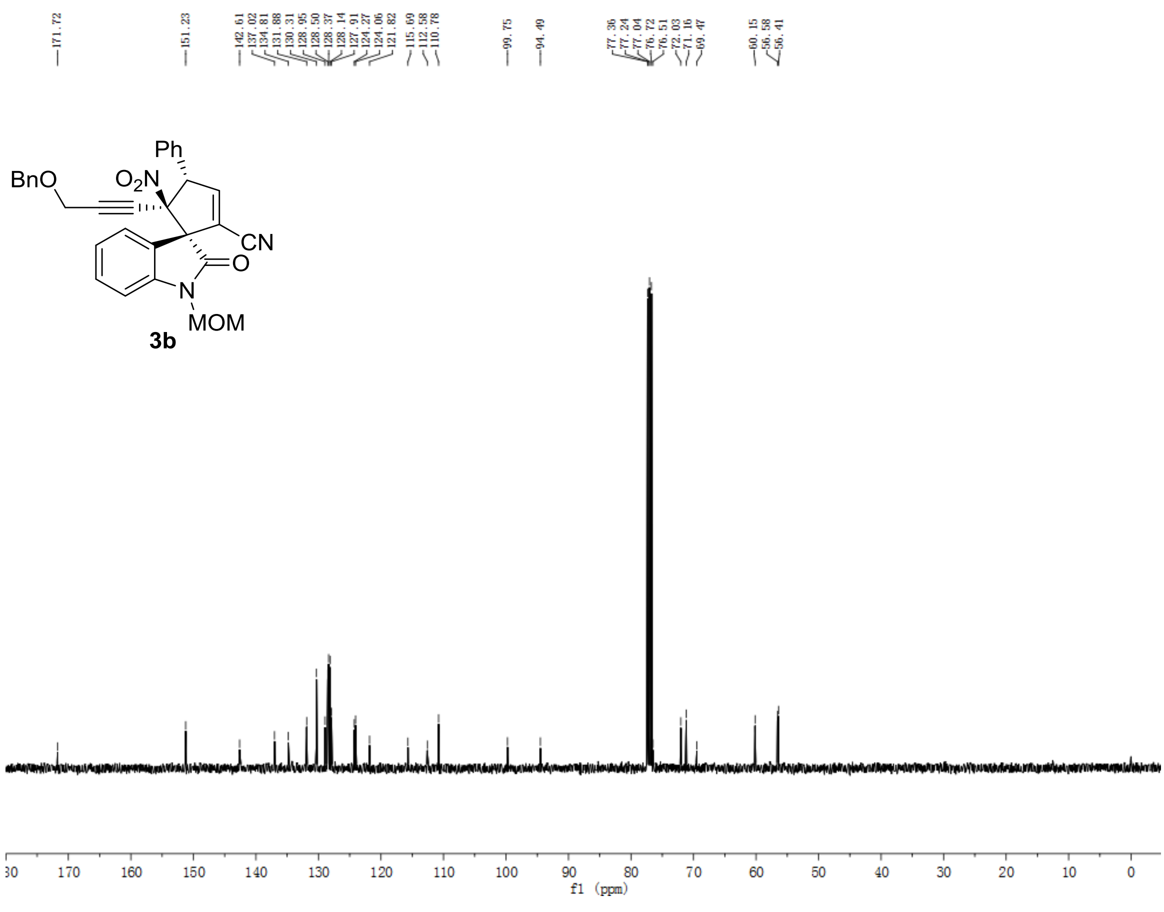


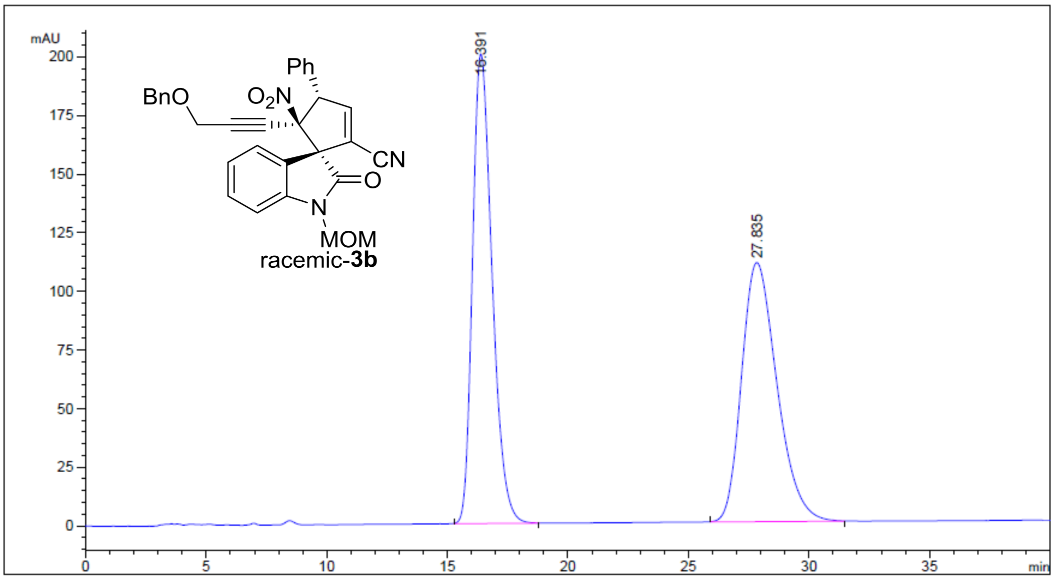
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.518	VB	0.2205	1411.11707	101.48647	9.9642
2	10.212	BB	0.3136	1.27507e4	640.98602	90.0358



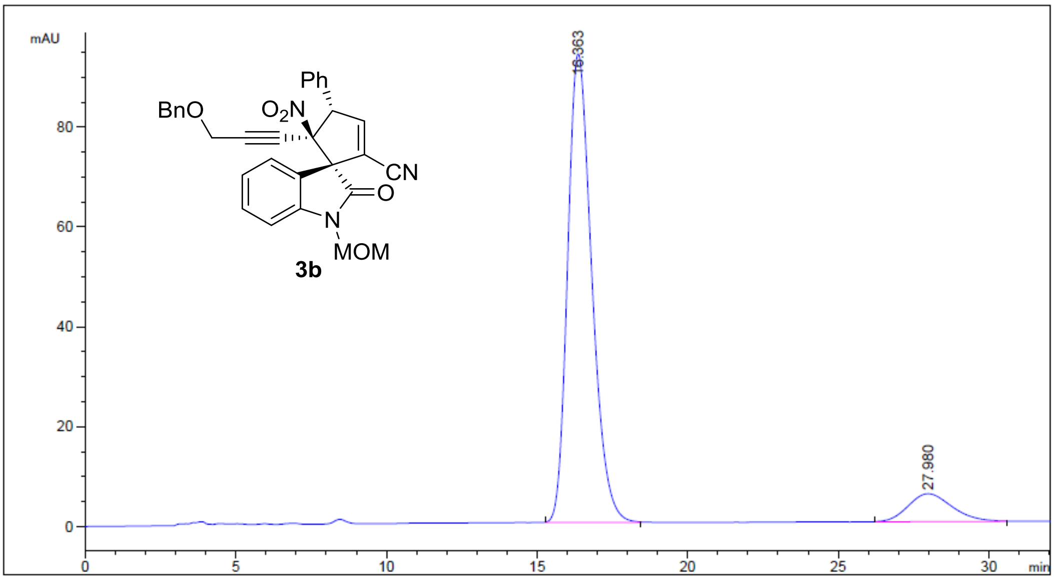
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.263	VV	0.2207	1.97651e4	1419.51978	86.0286
2	9.580	VV	0.2957	3209.94116	170.23338	13.9714


7.483
7.464
7.452
7.448
7.429
7.410
7.394
7.376
7.357
7.335
7.323
7.318
7.304
7.299
7.281
7.259
7.198
7.181
7.158
7.137
7.109
7.089
5.528
5.523
5.170
5.142
5.119
5.092
4.078
3.904
3.305
1.566
1.254
0.000
Ph
BnO
O2N
CN
O
N
MOM
3b
8
7
6
5
4
3
2
1
ppm
2.28
3.31
1.70
3.01
3.86
1.00
2.23
1.99
2.01
2.93

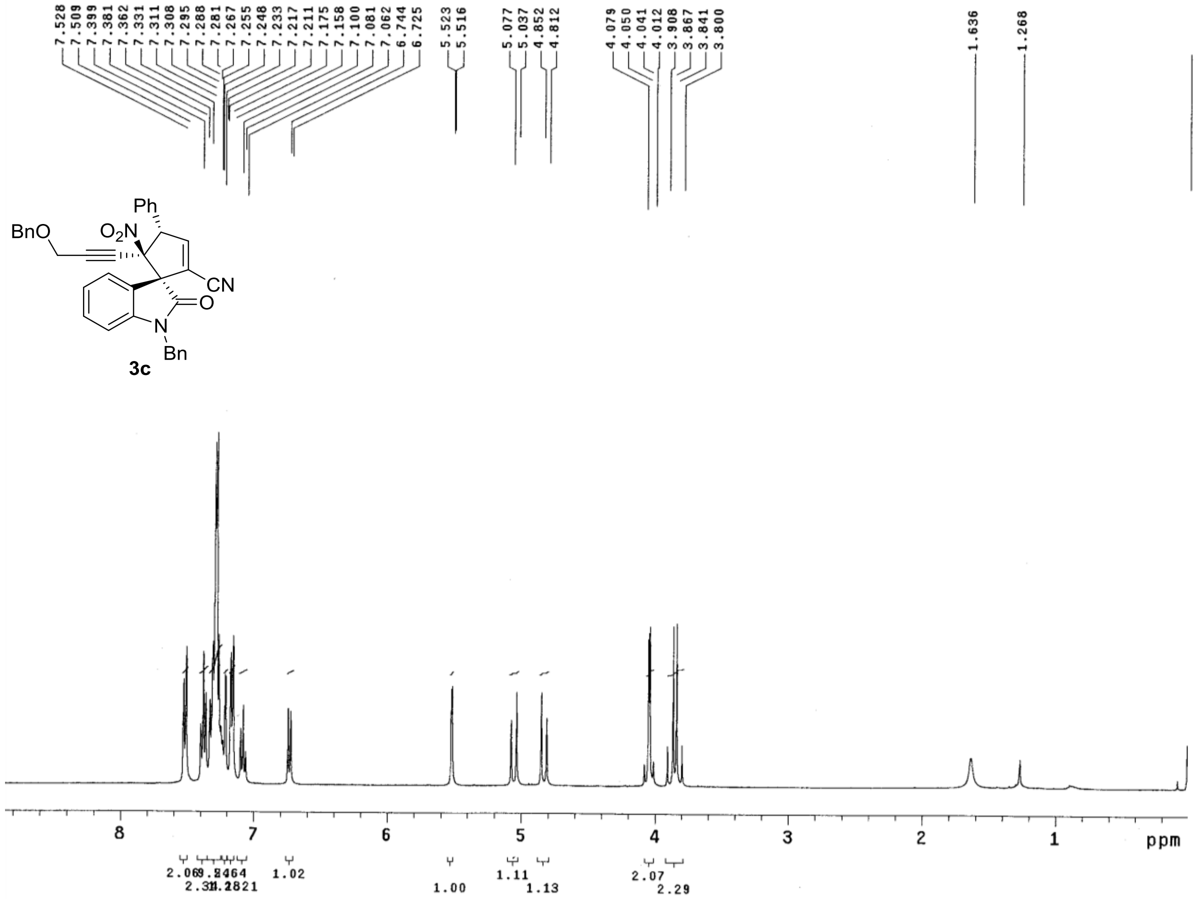

171.72
151.23
142.61
137.02
134.81
131.88
130.31
128.95
128.50
128.37
128.14
127.91
124.27
124.06
121.82
115.69
112.58
110.78
99.75
94.49
77.36
77.24
77.04
76.72
76.51
72.03
71.16
69.47
60.15
56.58
56.41
Ph
BnO
O2N
CN
O
N
MOM
3b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



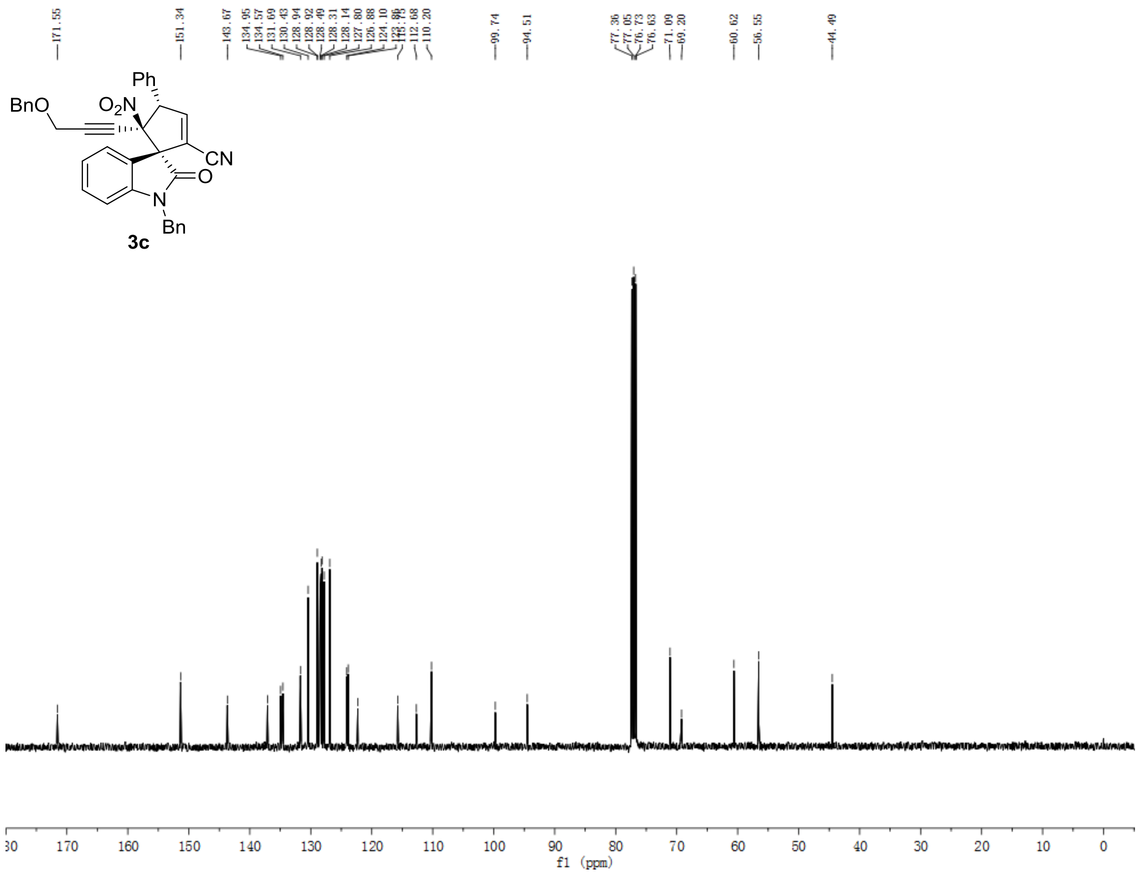
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.391	BB	0.8749	1.13190e4	200.25632	50.1143
2	27.835	BB	1.5740	1.12674e4	110.49579	49.8857



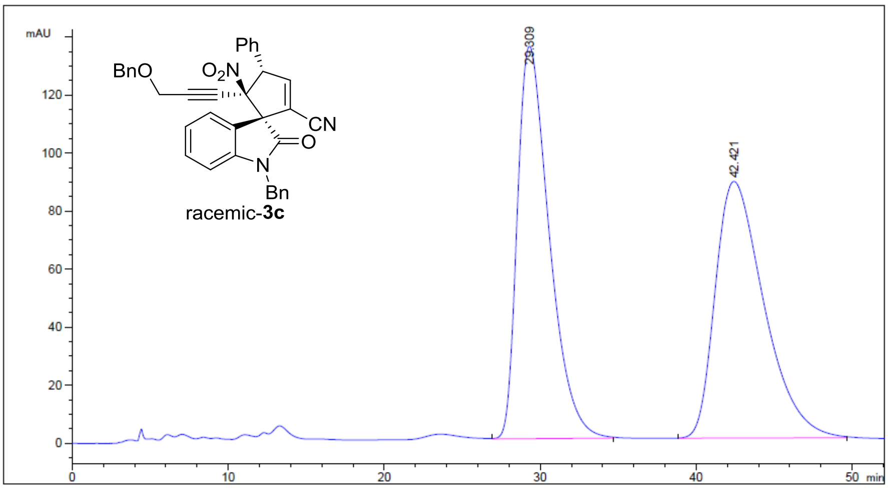
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.363	BB	0.8594	5225.41992	93.83466	90.1911
2	27.980	BB	1.5712	568.30328	5.58675	9.8089



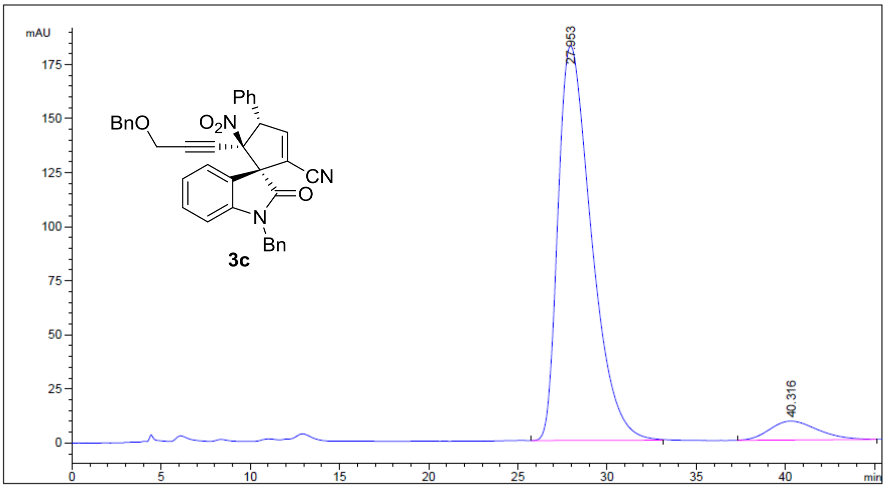
7.528 7.509 7.399 7.381 7.362 7.331 7.311 7.308 7.295 7.288 7.281 7.267 7.255 7.248 7.233 7.217 7.211 7.175 7.158 7.100 7.081 7.062 6.744 6.725
5.523 5.516
5.077 5.037 4.852 4.812
4.079 4.050 4.041 4.012 3.908 3.867 3.841 3.800
1.636
1.268
BnO
O2N
Ph
CN
O
N
Bn
3c
ppm



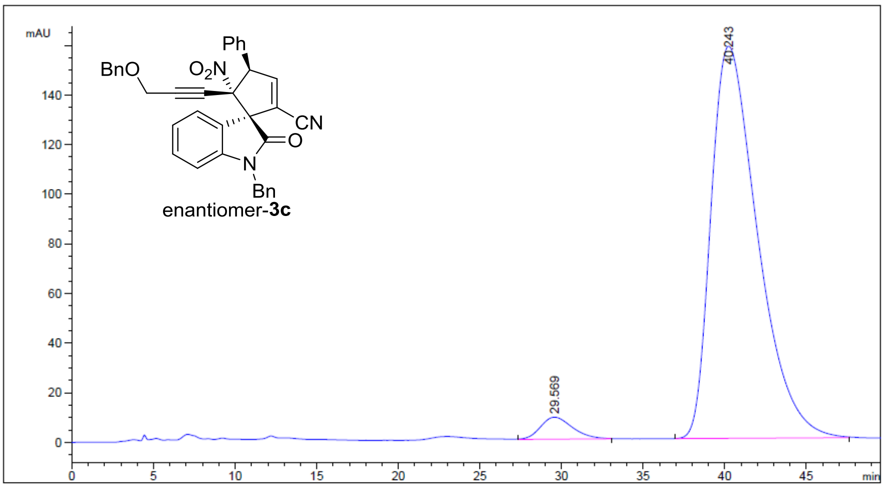
171.55
151.34
143.67
134.95 134.57 131.69 130.43 128.94 128.92 128.49 128.31 128.14 127.80 126.88 124.10
112.68 110.20
99.74
94.51
77.36 77.05 76.73 76.63
71.09 69.20
60.62
56.55
44.49
BnO
O2N
Ph
CN
O
N
Bn
3c
f1 (ppm)



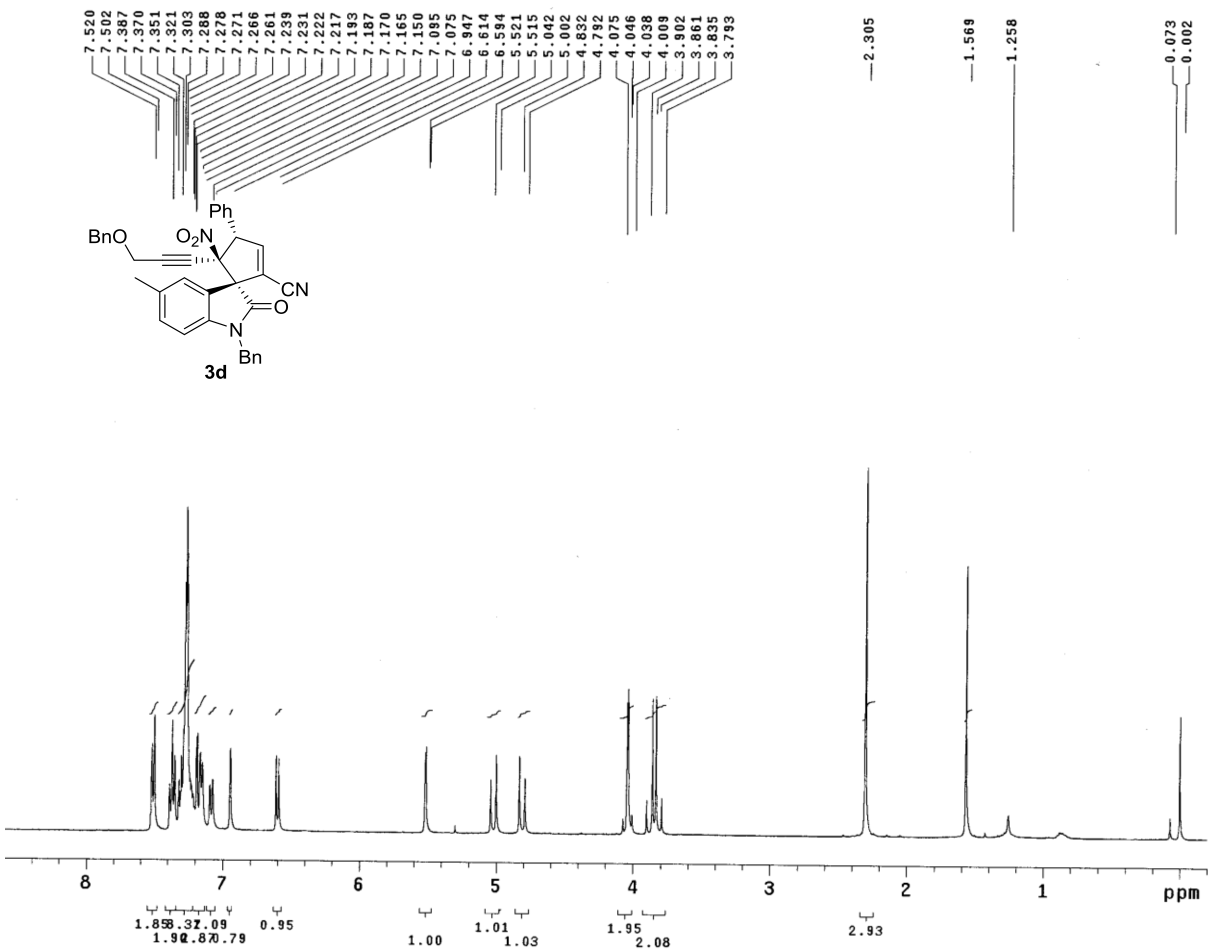
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	29.309	BB	2.1826	1.92209e4	135.21243	50.0011
2	42.421	BB	3.3225	1.92200e4	88.41209	49.9989



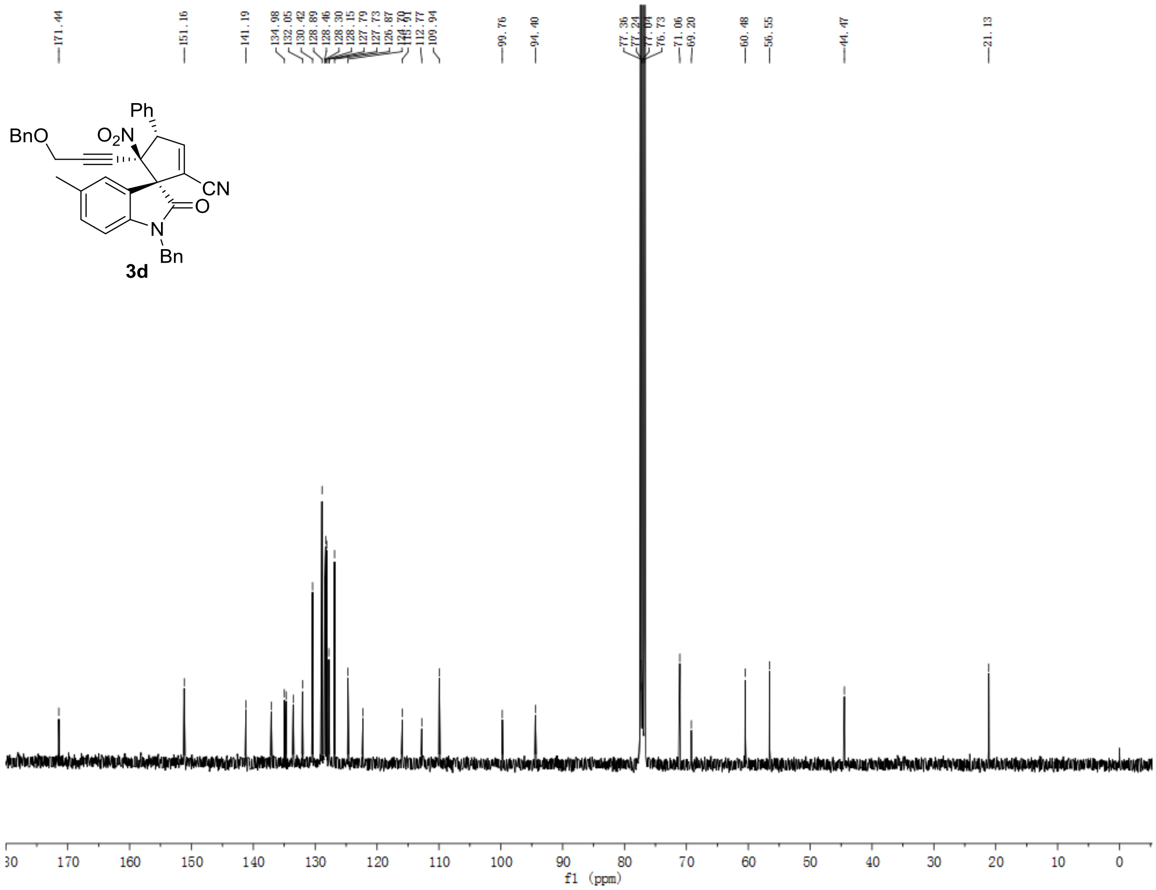
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	27.953	BB	1.9889	2.37326e4	182.49559	93.5484
2	40.316	BB	2.8205	1636.72607	8.73638	6.4516



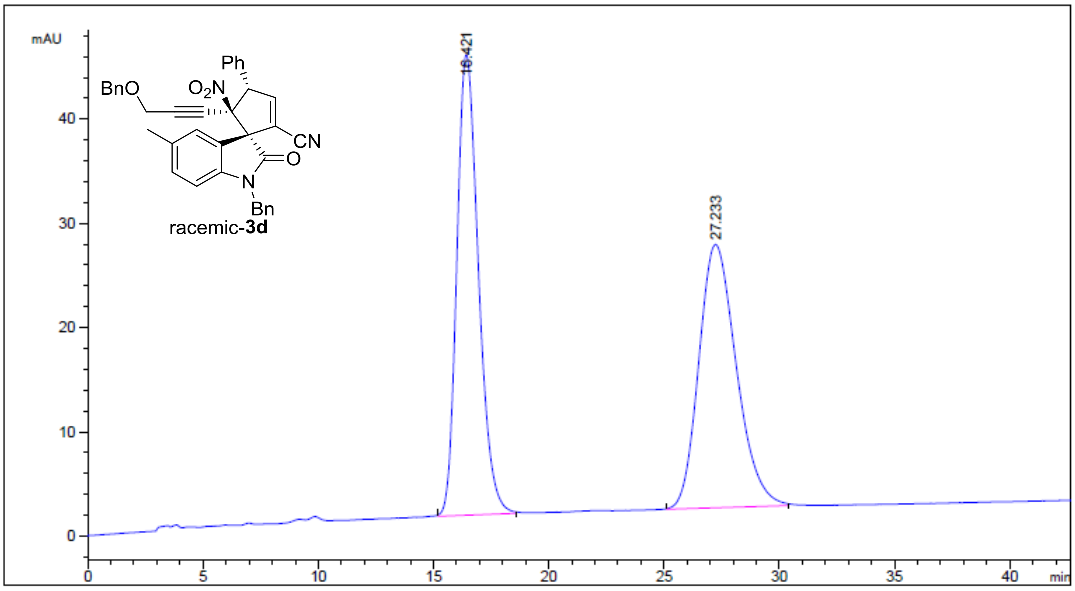
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	29.569	BB	2.0955	1213.23425	8.87603	3.7235
2	40.243	BB	3.0266	3.13698e4	158.02118	96.2765



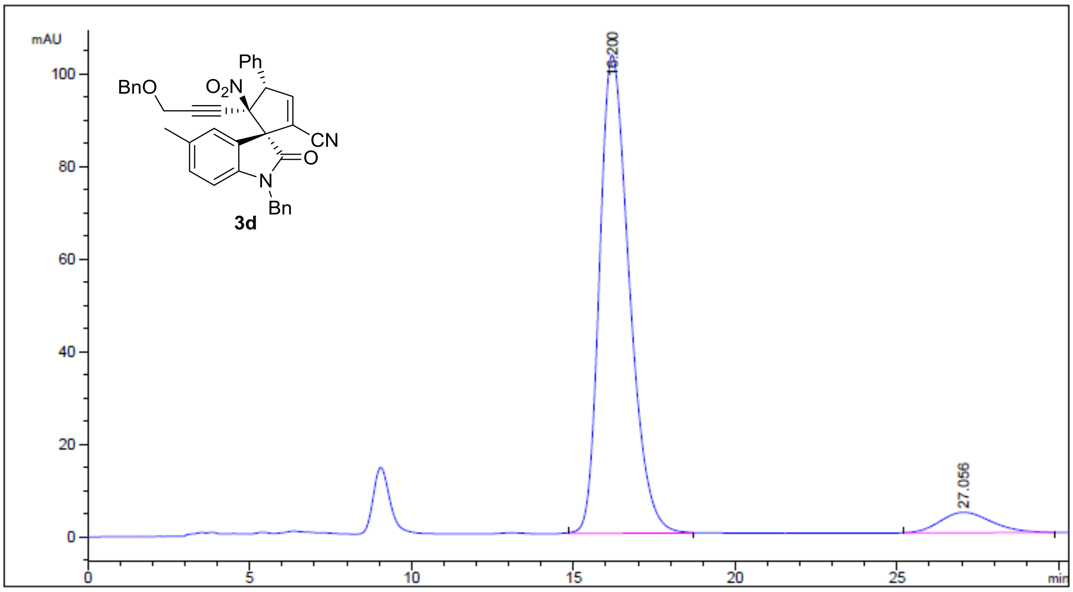
7.520
7.502
7.387
7.370
7.351
7.321
7.303
7.288
7.278
7.271
7.266
7.261
7.239
7.231
7.222
7.217
7.193
7.187
7.170
7.165
7.150
7.095
7.075
6.947
6.614
6.594
5.521
5.515
5.042
5.002
4.832
4.792
4.075
4.046
4.038
4.009
3.902
3.861
3.835
3.793
2.305
1.569
1.258
0.073
0.002
Ph
BnO
O2N
CN
O
N
Bn
3d
ppm
0.95
1.00
1.01
1.03
1.95
2.08
2.93



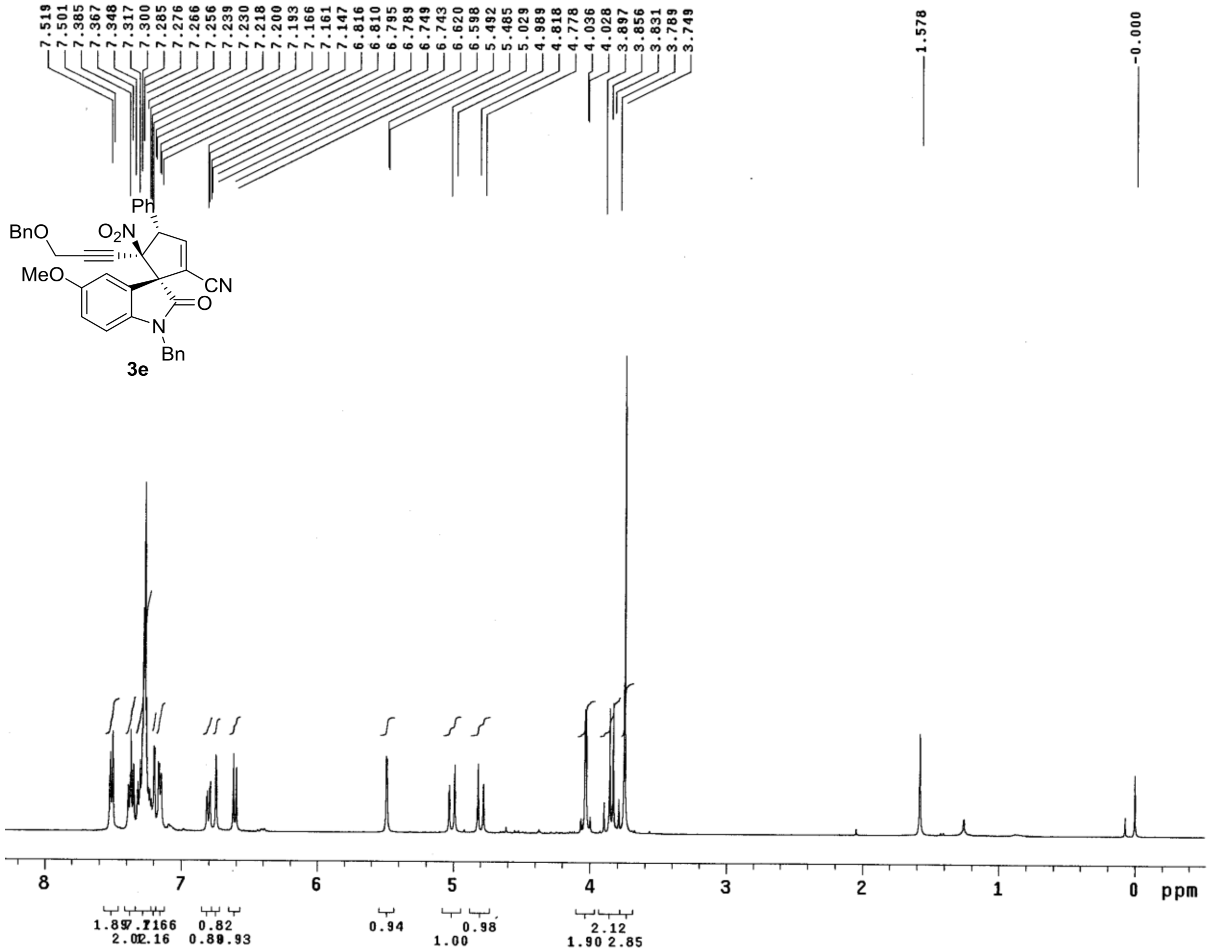
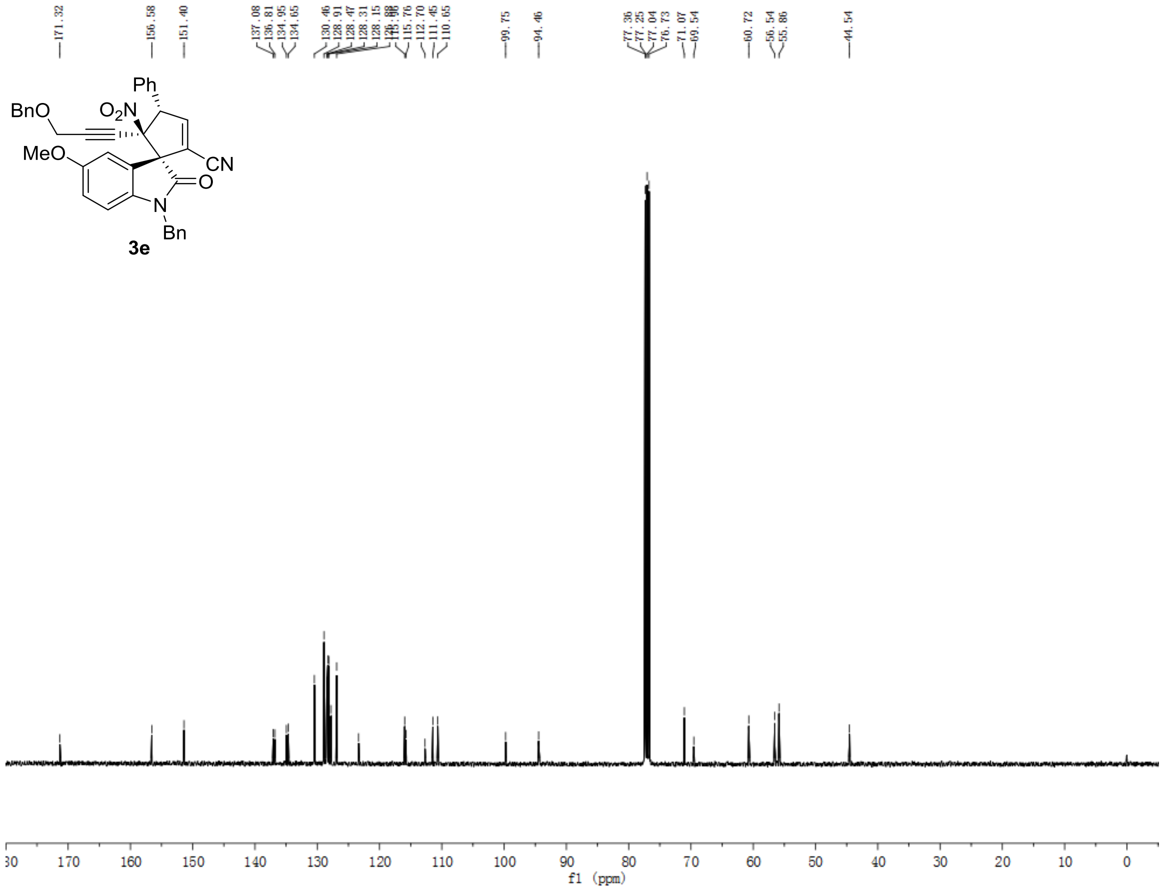
171.44
151.16
141.19
134.98
132.05
130.42
128.89
128.46
128.30
128.15
127.79
127.73
126.87
112.77
109.94
99.76
94.40
77.36
76.73
71.06
69.20
60.48
56.55
44.47
21.13
Ph
BnO
O2N
CN
O
N
Bn
3d
f1 (ppm)

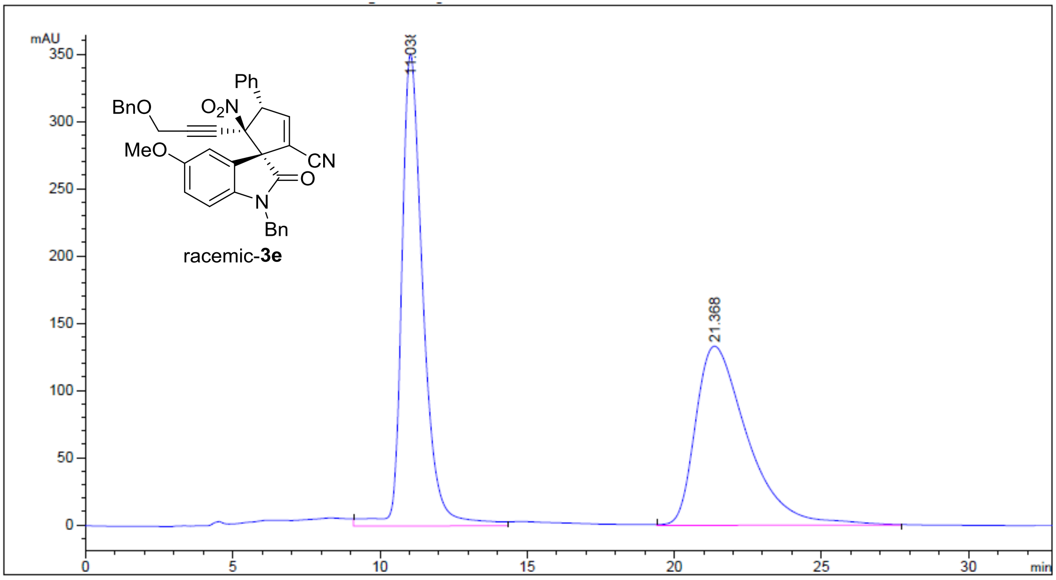


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.421	BB	1.0033	2873.47290	44.18745	50.1545
2	27.233	BB	1.7559	2855.76685	25.25754	49.8455

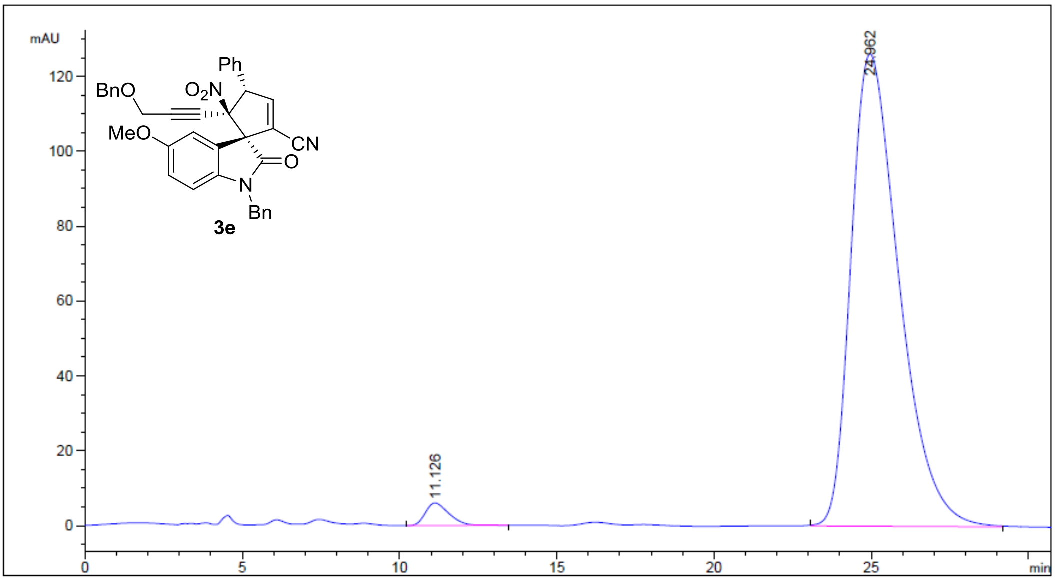


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.200	BB	0.9815	6576.28027	103.29659	93.0683
2	27.056	BB	1.7097	489.79822	4.40845	6.9317

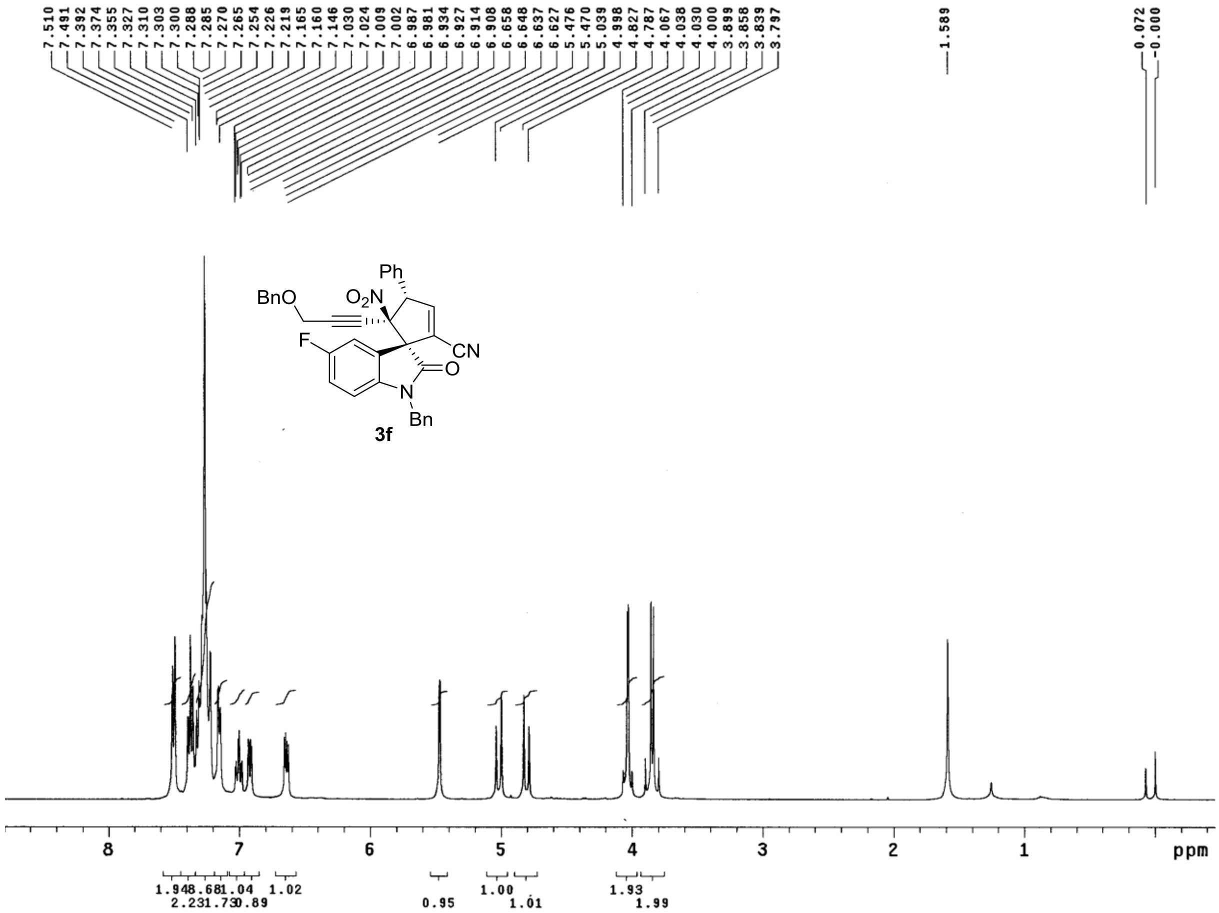

7.519 7.501 7.385 7.367 7.348 7.317 7.300 7.285 7.276 7.266 7.256 7.239 7.230 7.218 7.200 7.193 7.166 7.161 7.147 6.816 6.810 6.795 6.789 6.749 6.743 6.620 6.598 5.492 5.485 5.029 4.989 4.818 4.778 4.036 4.028 3.897 3.856 3.831 3.789 3.749
1.578
-0.000
Ph
BnO
O2N
MeO
CN
O
N
Bn
3e
ppm
1.00
0.94
0.98
0.82
2.12
1.90
2.85

171.32
156.58
151.40
137.08 136.81 134.95 134.65
130.46 128.91 128.47 128.31 128.15
115.76 112.70 111.45 110.65
99.75
94.46
77.36 77.25 77.04 76.73 71.07 69.54
60.72 56.54 55.86
44.54
Ph
BnO
O2N
MeO
CN
O
N
Bn
3e
f1 (ppm)

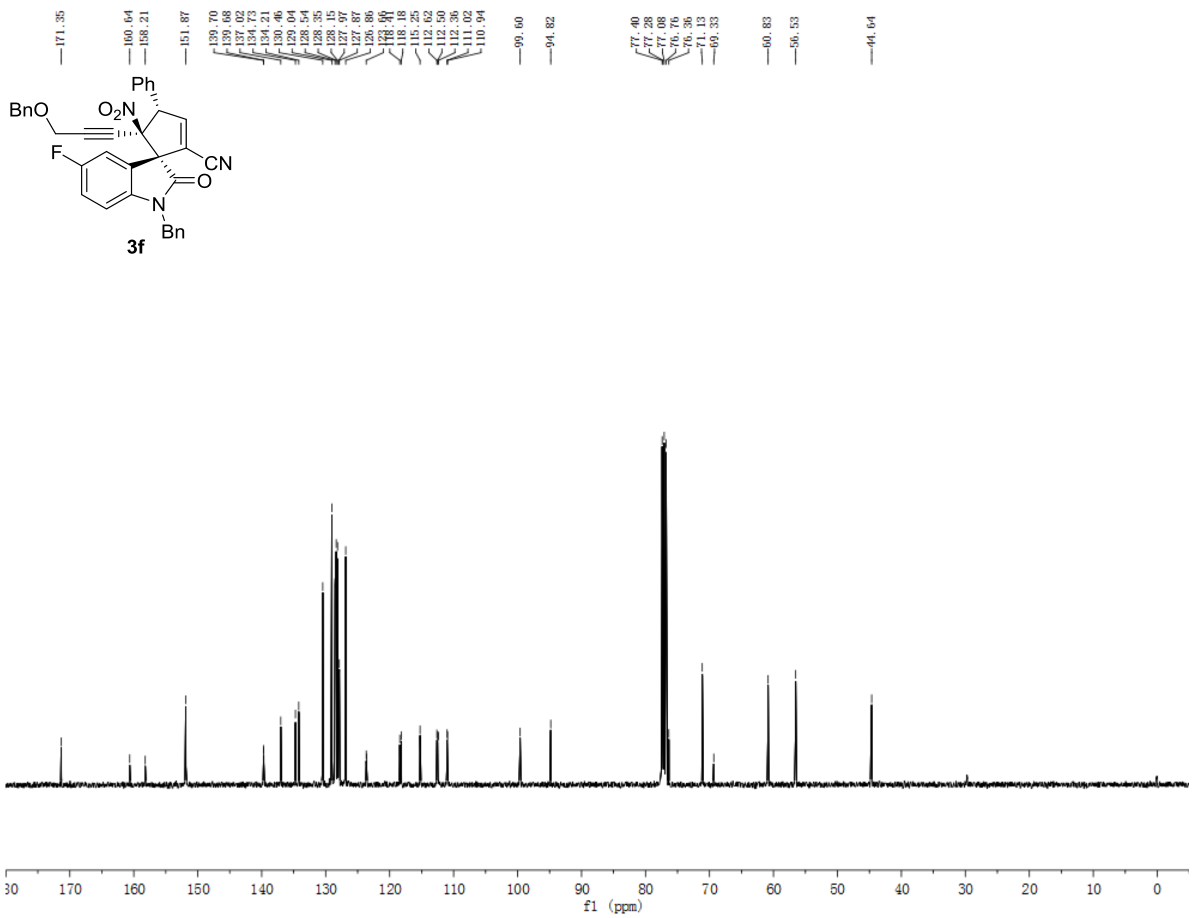


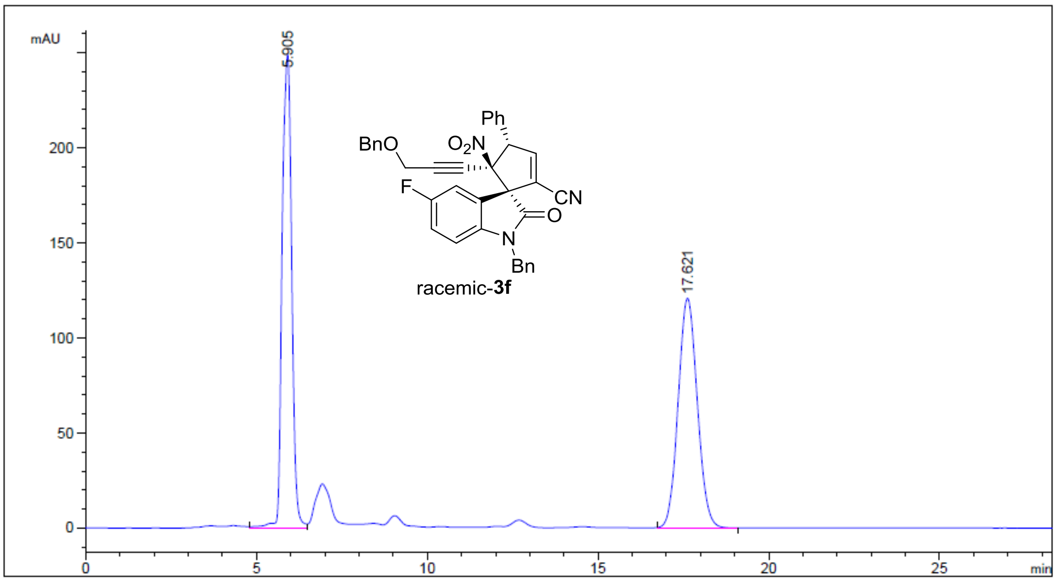
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.038	VB	0.7676	1.78317e4	350.88116	52.0892
2	21.368	BB	1.8676	1.64013e4	133.19142	47.9108



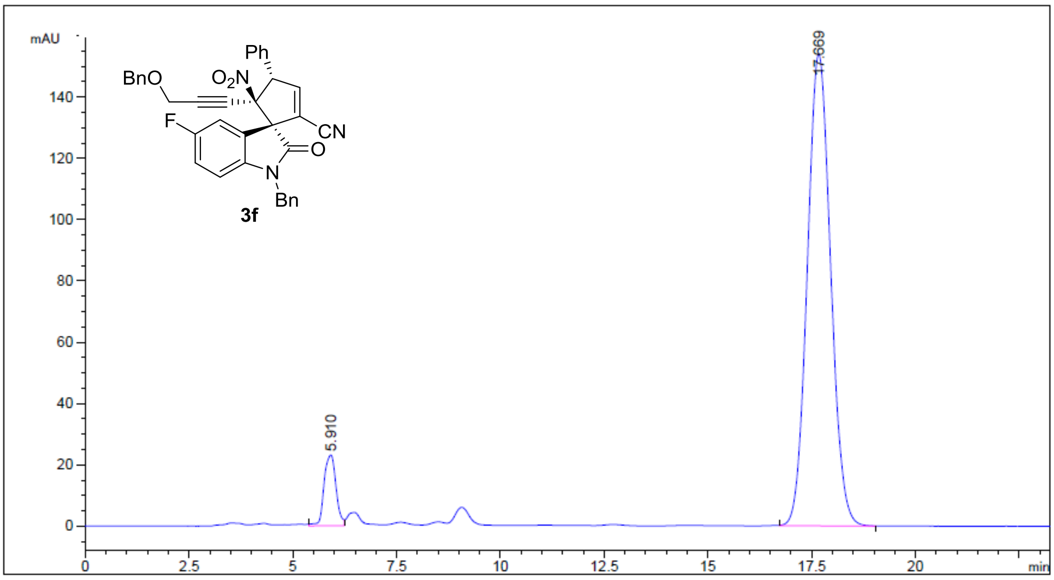
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.126	VB	0.8008	317.86523	6.03598	2.3134
2	24.962	BB	1.6371	1.34221e4	126.17245	97.6866


BnO
O2N
Ph
CN
F
O
N
Bn
3f
ppm

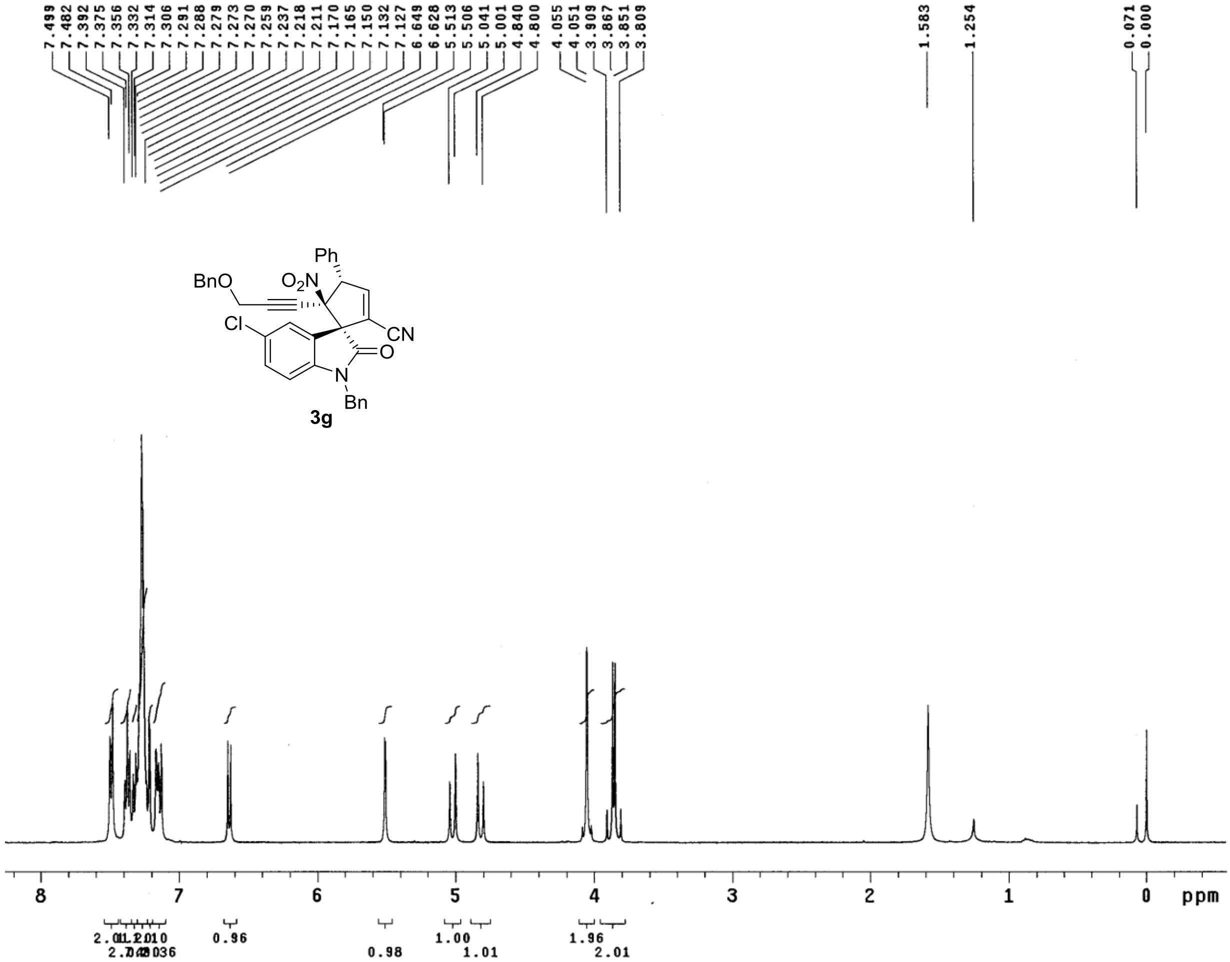

BnO
O2N
Ph
CN
F
O
N
Bn
3f
f1 (ppm)



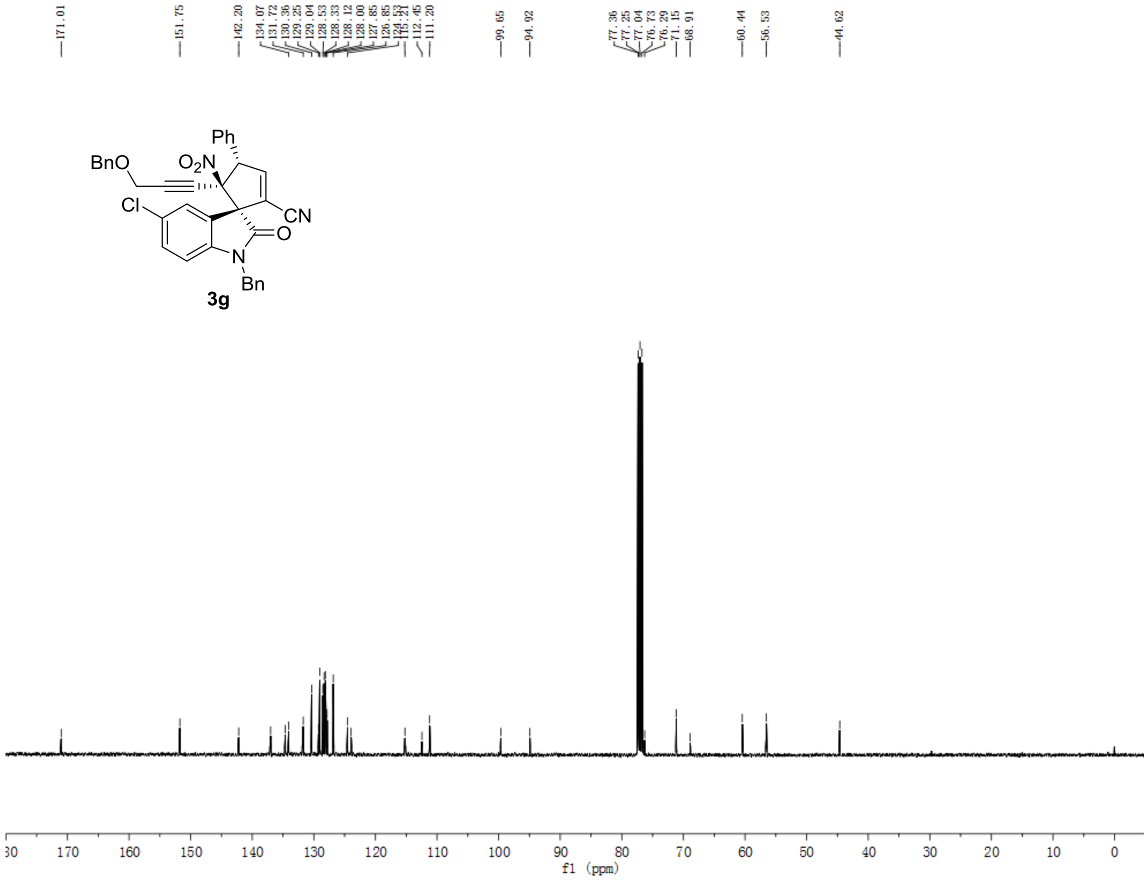
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.905	VV	0.3155	4870.72900	249.04913	50.8625
2	17.621	BB	0.6060	4705.53467	120.77073	49.1375



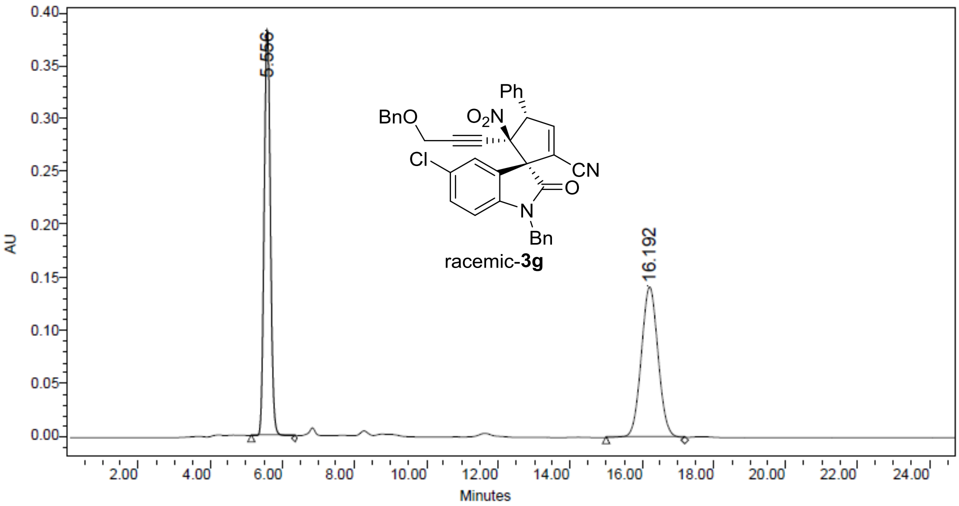
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.910	BV	0.3212	463.70474	23.13674	7.1710
2	17.669	BB	0.6064	6002.72852	153.91989	92.8290


7.499
7.482
7.392
7.375
7.356
7.332
7.314
7.306
7.291
7.288
7.279
7.273
7.270
7.259
7.237
7.218
7.211
7.170
7.165
7.150
7.132
7.127
6.649
6.628
5.513
5.506
5.041
5.001
4.840
4.800
4.055
4.051
3.909
3.867
3.851
3.809
1.583
1.254
0.071
0.000
Ph
BnO
O_2N
Cl
CN
O
N
Bn
ppm
0.96
0.98
1.00
1.01
1.96
2.01

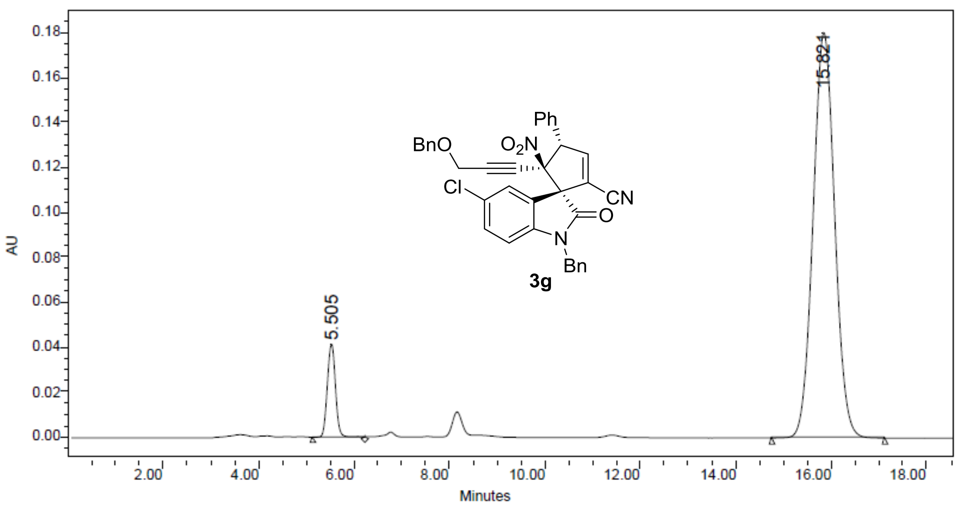
3g


171.01
151.75
142.20
134.07
131.72
130.36
129.25
129.04
128.53
128.33
128.12
128.00
127.85
126.85
124.53
115.21
112.45
111.20
99.65
94.92
77.36
77.25
77.04
76.73
76.29
71.15
68.91
60.44
56.53
44.62
Ph
BnO
O_2N
Cl
CN
O
N
Bn
f1 (ppm)

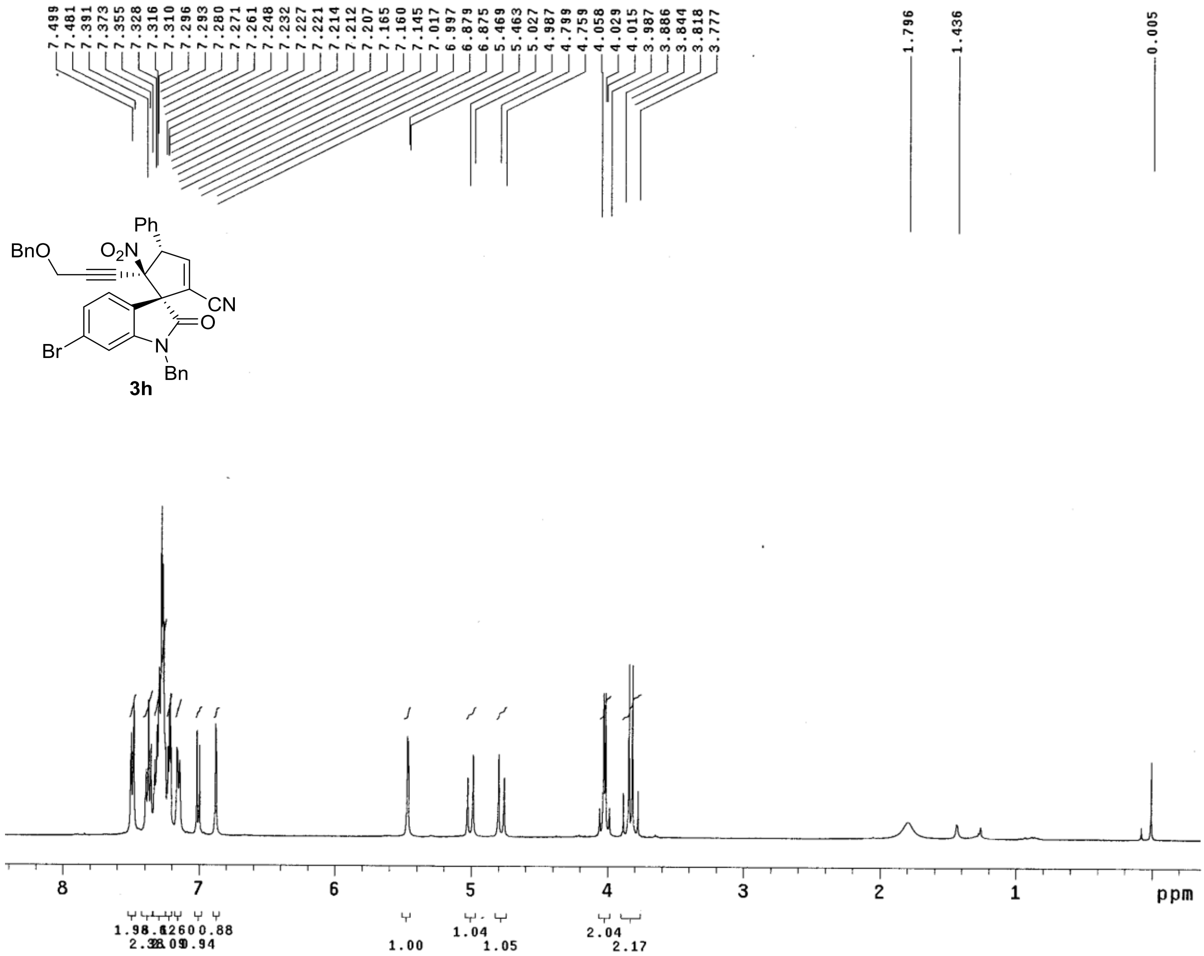
3g



	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	5.556	4615173	49.98	383509	72.97
2	16.192	4618960	50.02	142048	27.03

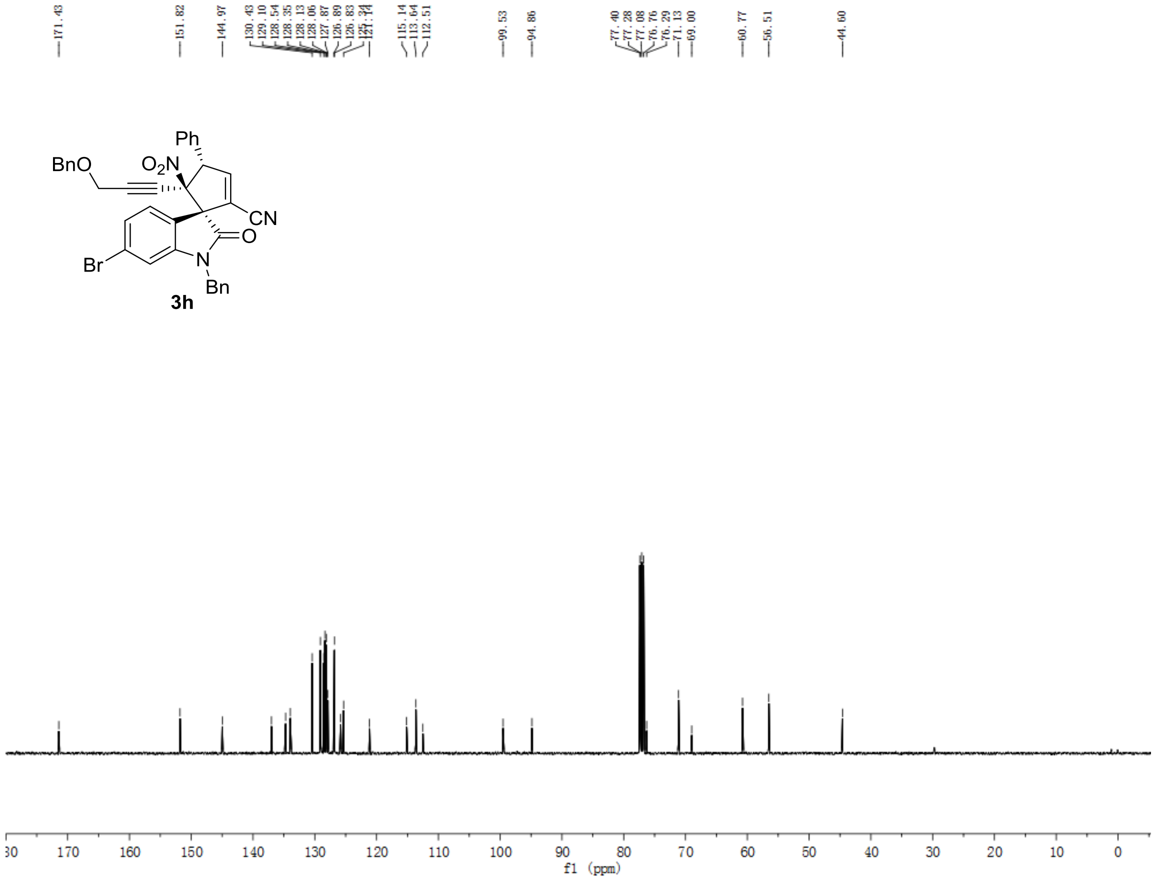


	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	5.505	492946	8.01	41442	18.67
2	15.821	5661250	91.99	180484	81.33



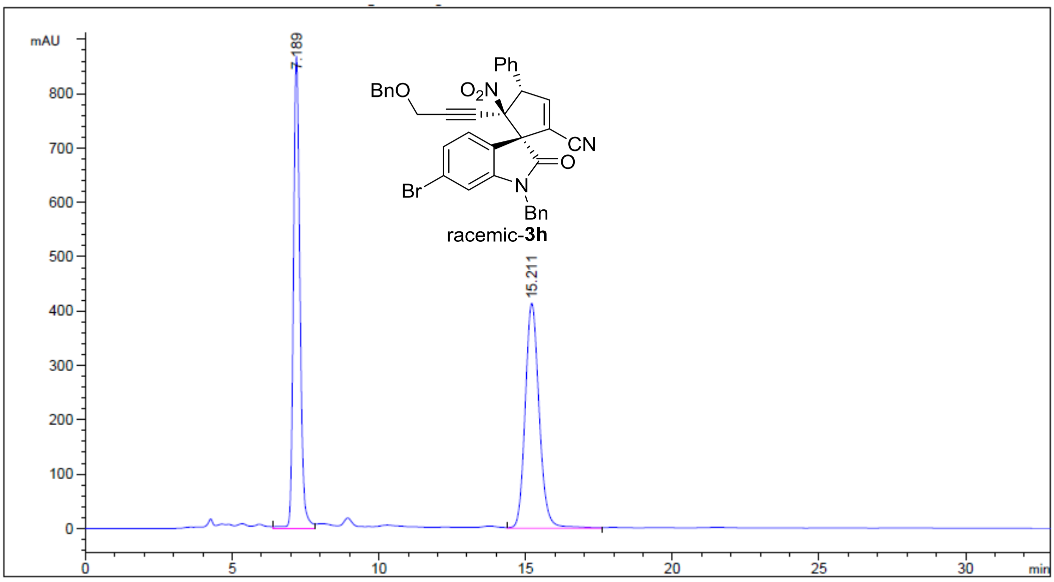
7.499
7.481
7.391
7.373
7.355
7.328
7.316
7.310
7.296
7.293
7.280
7.271
7.261
7.248
7.232
7.227
7.221
7.214
7.212
7.207
7.165
7.160
7.145
7.017
6.997
6.879
6.875
5.469
5.463
5.027
4.987
4.799
4.759
4.058
4.029
4.015
3.987
3.886
3.844
3.818
3.777
1.796
1.436
0.005
BnO
O2N
Ph
CN
O
N
Br
Bn
ppm
1.00
1.04
1.05
2.04
2.17
0.88
0.94

3h

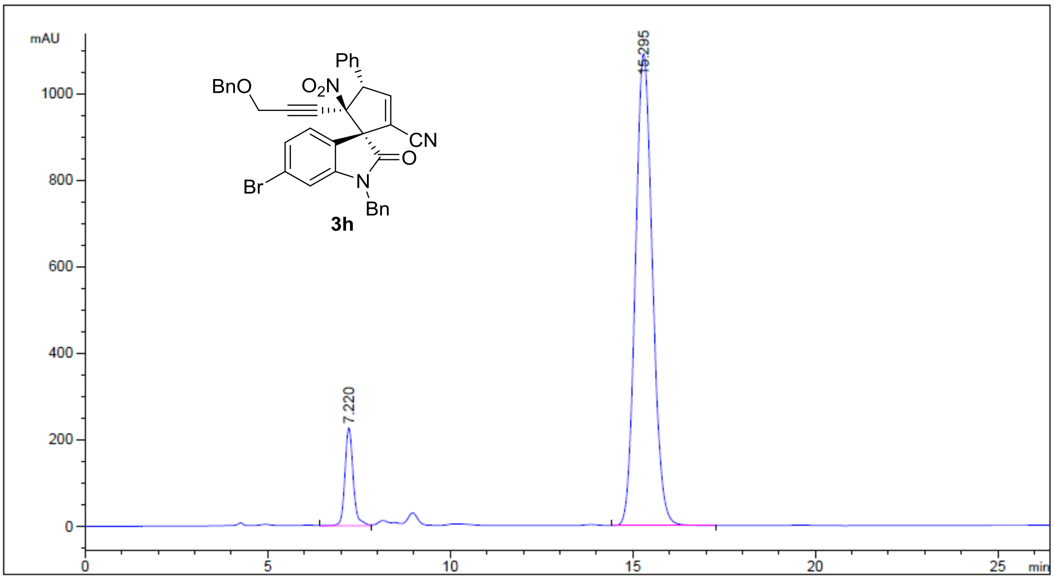


171.43
151.82
144.97
130.43
129.10
128.54
128.35
128.13
128.06
127.87
126.89
126.83
115.14
113.64
112.51
99.53
94.86
77.40
77.28
77.08
76.76
76.29
71.13
69.00
60.77
56.51
44.60
BnO
O2N
Ph
CN
O
N
Br
Bn
f1 (ppm)

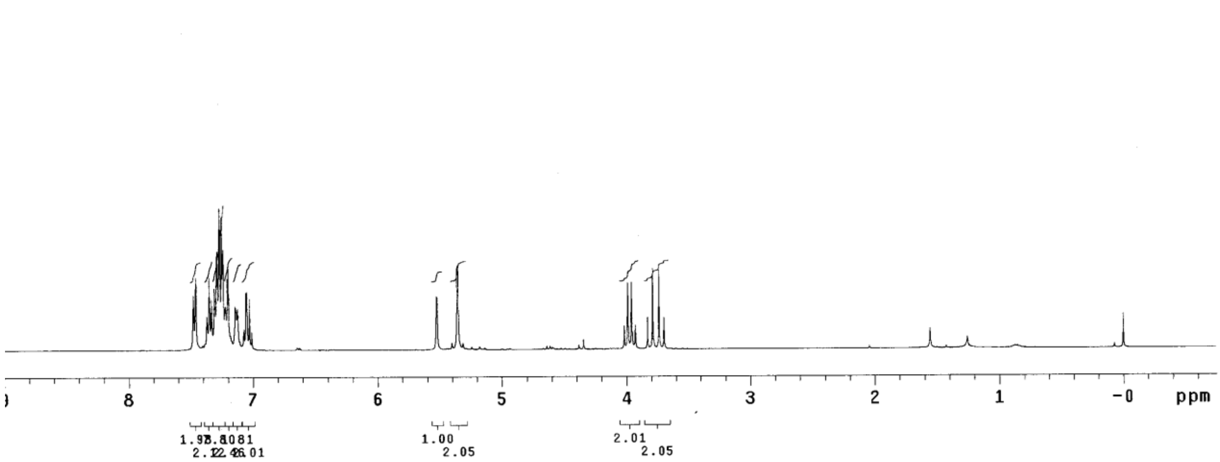
3h



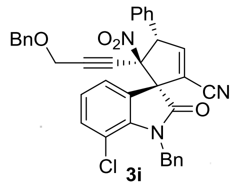
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.189	VV	0.2443	1.33978e4	867.38934	49.4286
2	15.211	VB	0.5087	1.37076e4	413.84927	50.5714



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.220	VV	0.2437	3597.09033	226.33247	9.2196
2	15.295	VB	0.5070	3.54185e4	1090.76428	90.7804

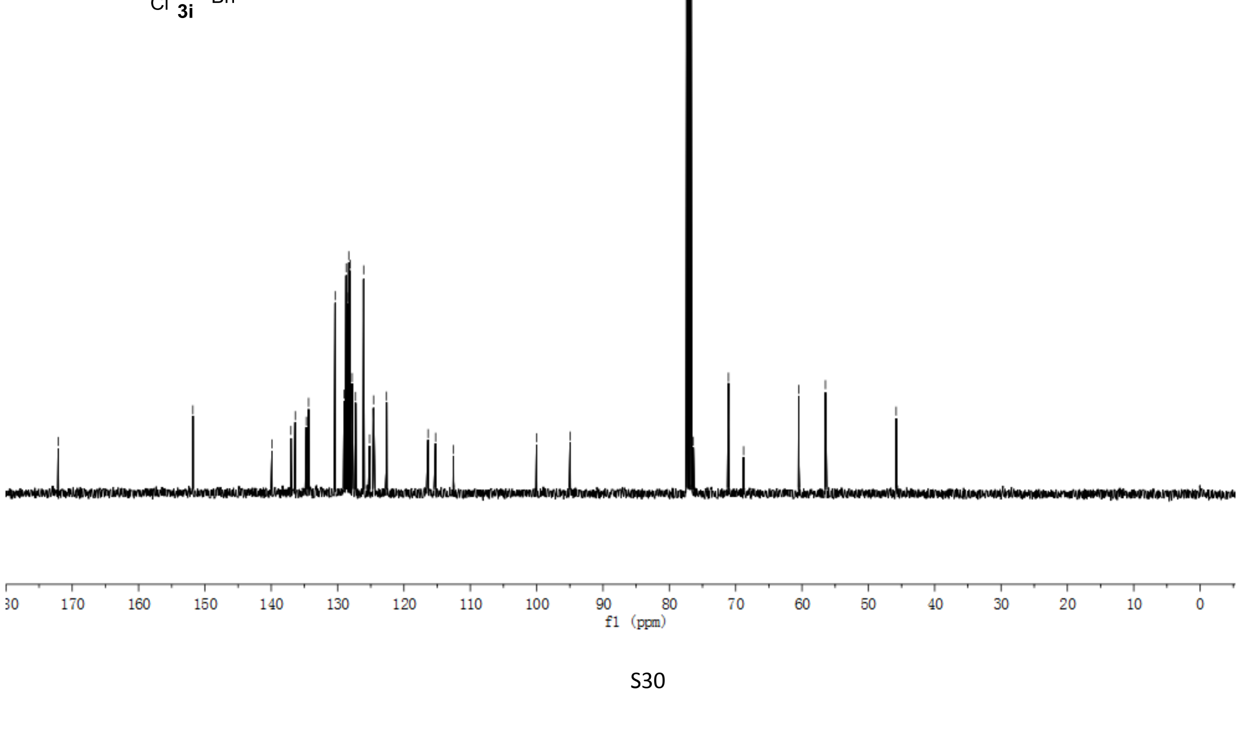


7.478
7.460
7.368
7.351
7.332
7.313
7.308
7.293
7.287
7.268
7.251
7.238
7.218
7.203
7.197
7.142
7.137
7.124
7.071
7.056
7.052
7.047
7.027
5.525
5.519
5.358
5.352
4.017
3.988
3.958
3.929
3.829
3.788
3.738
3.696
1.555
0.000
8
7
6
5
4
3
2
1
-0
ppm
1.00
2.05
2.01
2.05

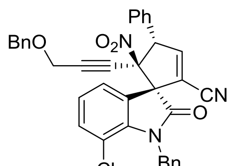


Ph
BnO
O_2N
CN
O
N
Cl
Bn

3i

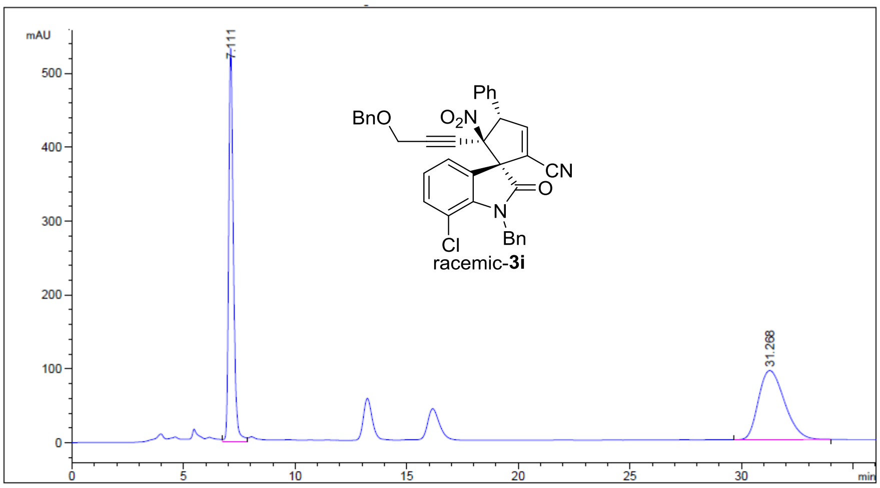


172.10
151.82
137.04
136.38
134.71
134.37
130.37
129.01
128.70
128.55
128.32
128.11
127.82
127.29
126.07
125.18
124.58
115.23
112.54
100.00
94.95
77.38
77.26
77.06
76.74
76.37
71.09
68.81
60.48
56.47
45.81
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

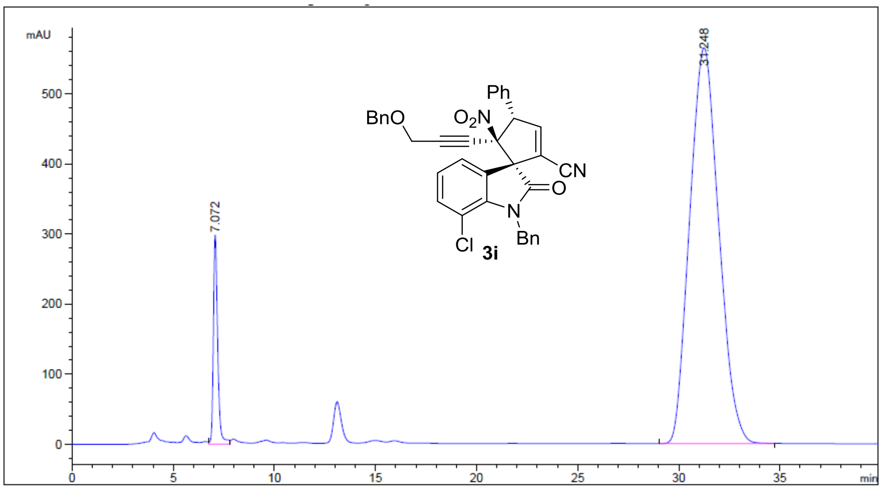


Ph
BnO
O_2N
CN
O
N
Cl
Bn

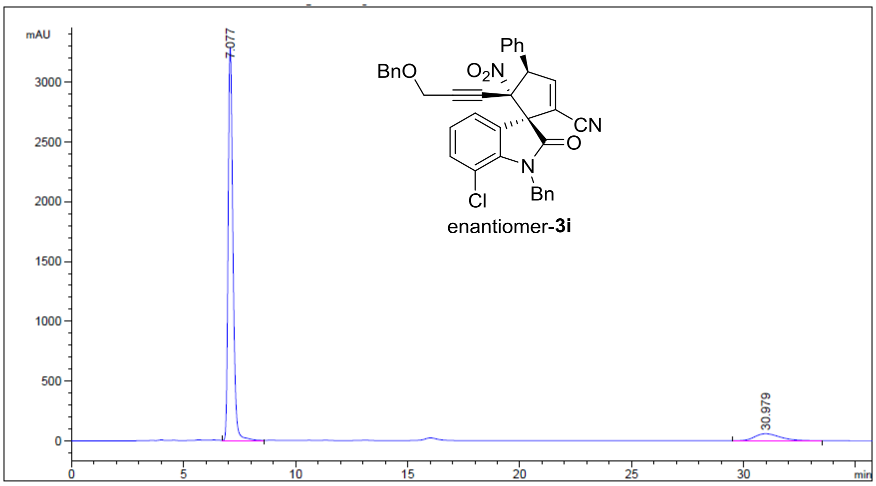
3i



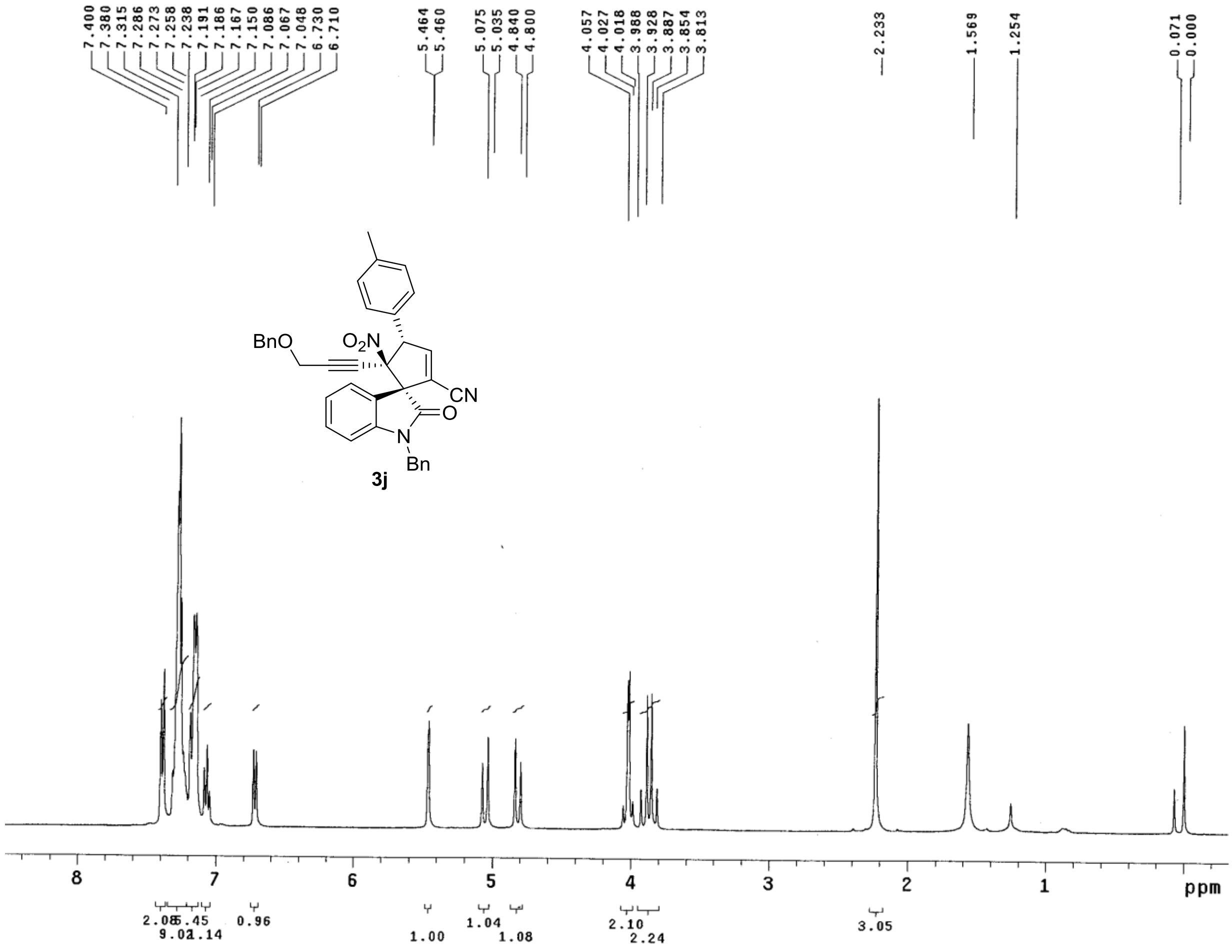
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.111	VV	0.2232	7787.90039	532.05328	50.6248
2	31.268	BB	1.2789	7595.66455	93.58517	49.3752

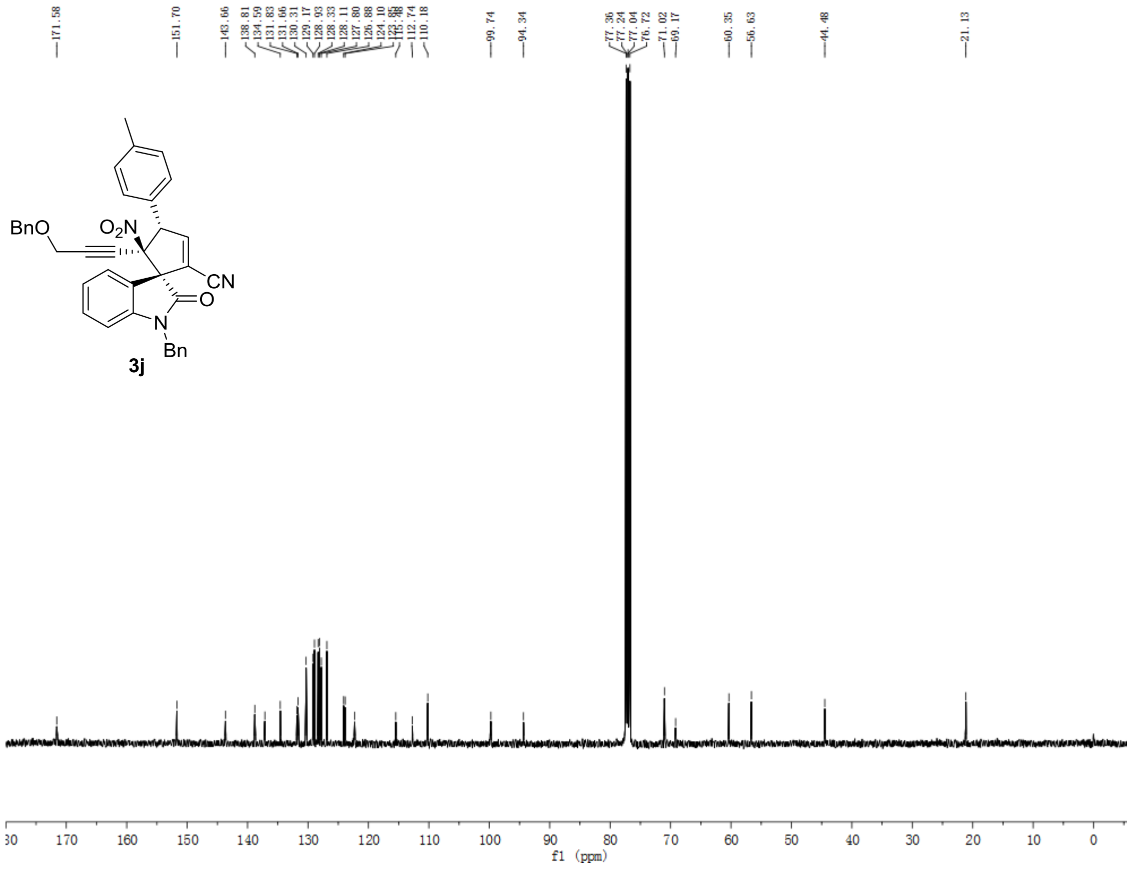


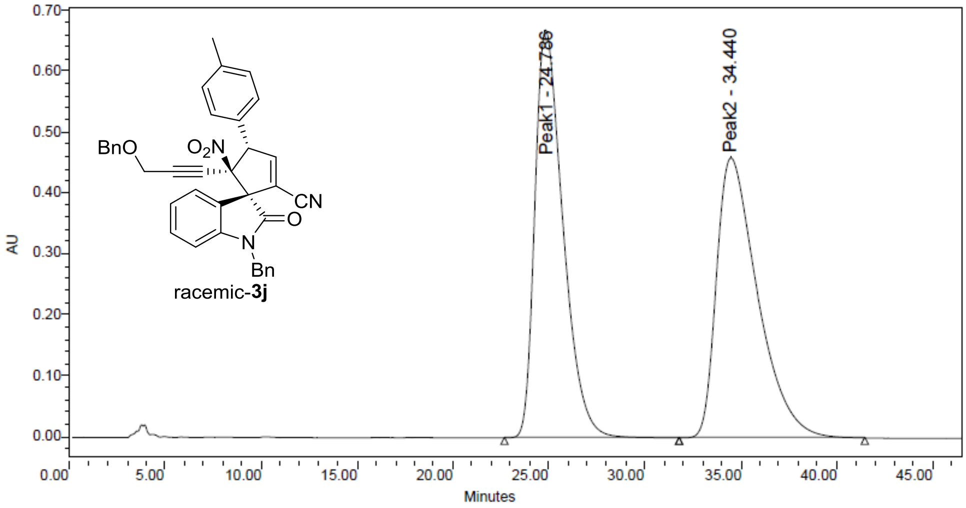
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.072	VV	0.2247	4396.73975	297.76468	7.2296
2	31.248	BB	1.5438	5.64192e4	564.86444	92.7704



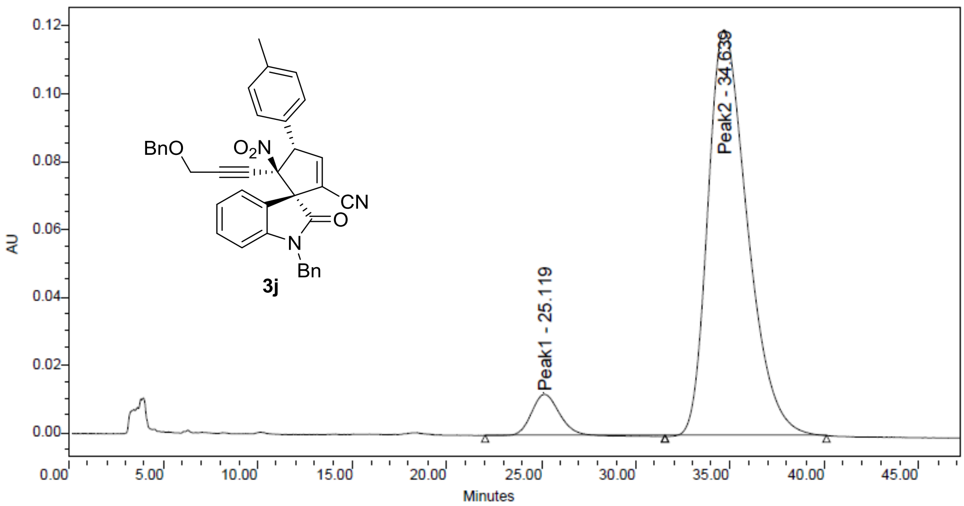
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.077	VV	0.2277	4.93668e4	3286.48535	91.8360
2	30.979	BB	1.1953	4388.57910	57.37062	8.1640


7.400 7.380 7.315 7.286 7.273 7.258 7.238 7.191 7.186 7.167 7.150 7.086 7.067 7.048 6.730 6.710
5.464 5.460
5.075 5.035 4.840 4.800
4.057 4.027 4.018 3.988 3.928 3.887 3.854 3.813
2.233
1.569
1.254
0.071 0.000
BnO
O_2N
CN
O
N
Bn
3j
8 7 6 5 4 3 2 1 ppm
2.08 5.45 9.02 1.14 0.96 1.00 1.04 1.08 2.10 2.24 3.05

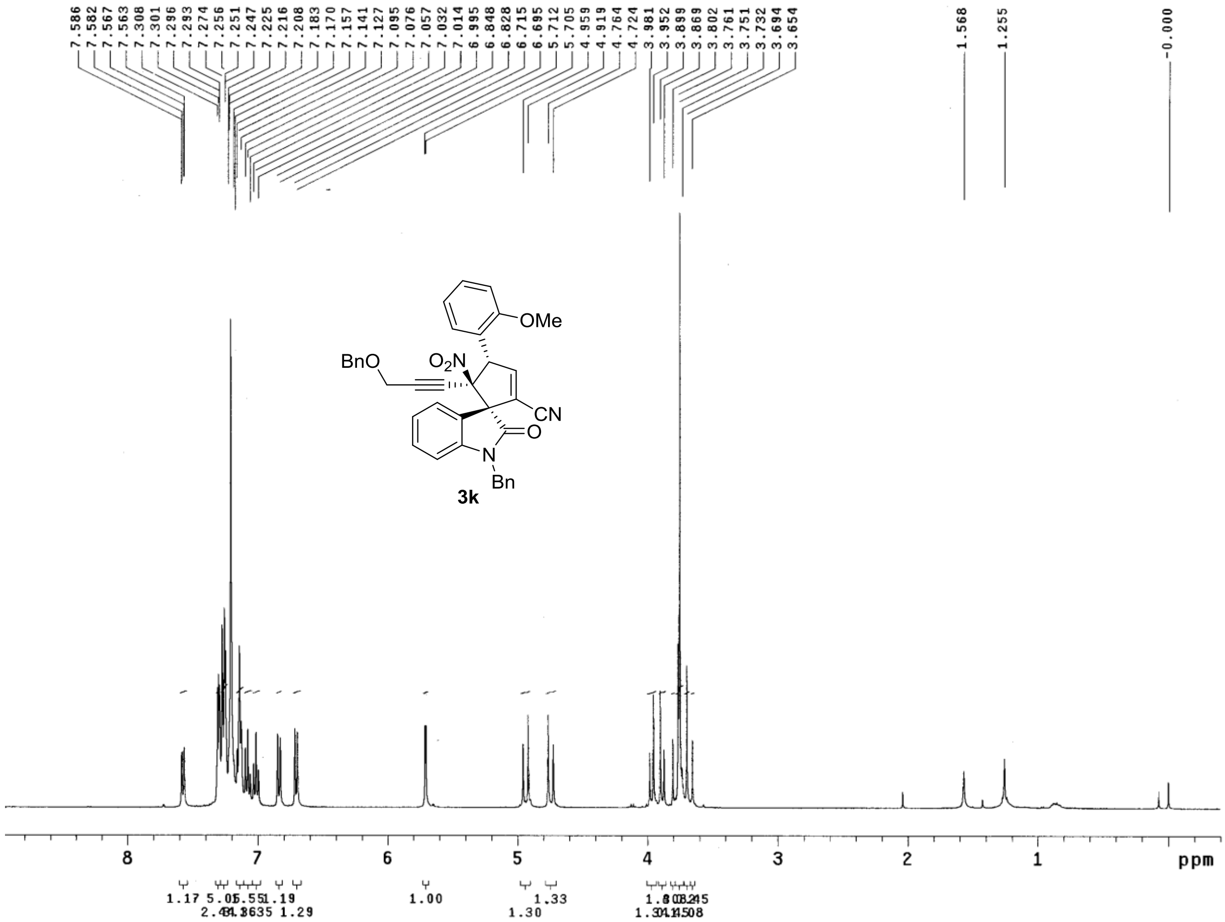

171.58
151.70
143.66 138.81 134.59 131.83 131.66 130.31 129.17 128.93 128.33 128.11 127.80 126.88 124.10 112.74 110.18
99.74
94.34
77.36 77.24 77.04 76.72 71.02 69.17
60.35 56.63
44.48
21.13
BnO
O_2N
CN
O
N
Bn
3j
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

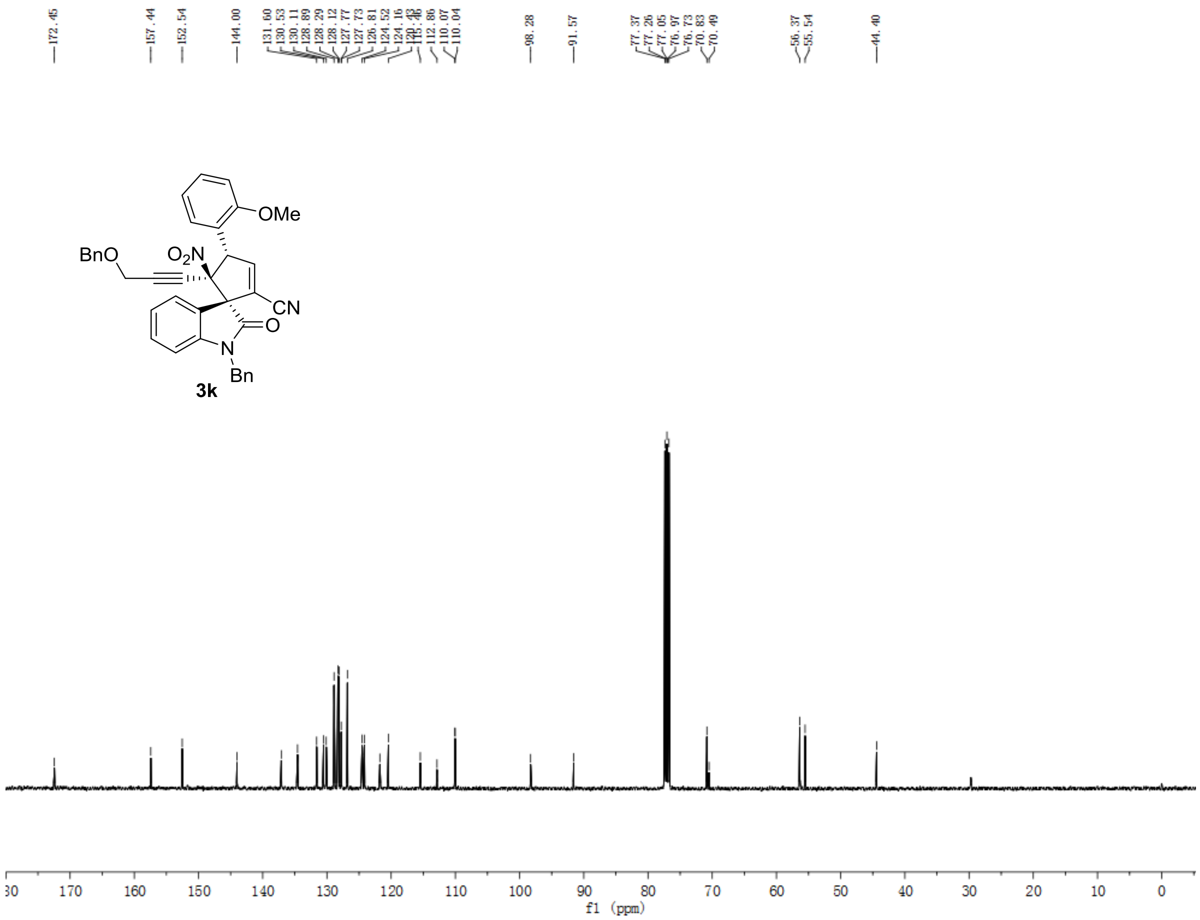


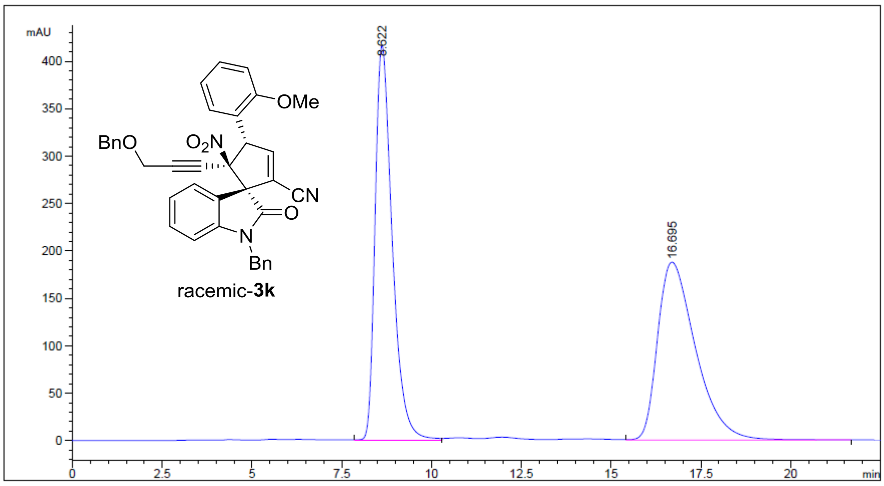
	Peak Name	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	Peak1	24.786	68355933	49.97	669626	59.28
2	Peak2	34.440	68443851	50.03	459927	40.72



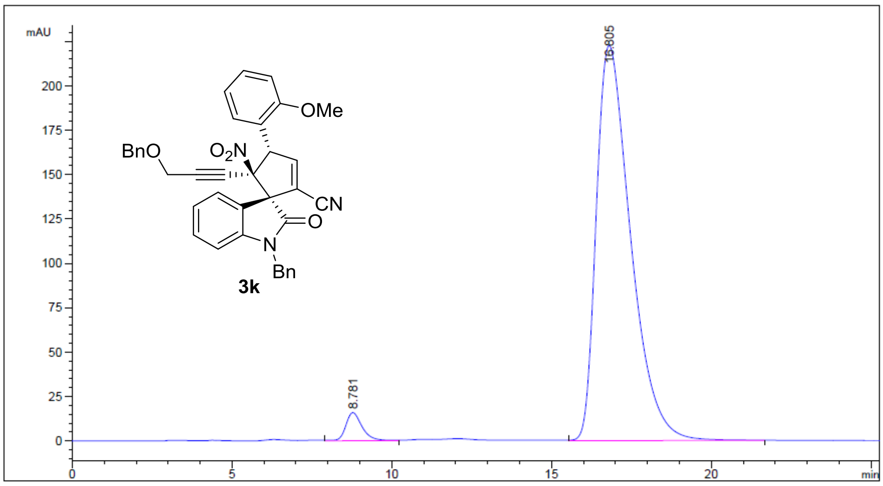
	Peak Name	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	Peak1	25.119	1301768	6.95	12277	9.30
2	Peak2	34.639	17424820	93.05	119736	90.70



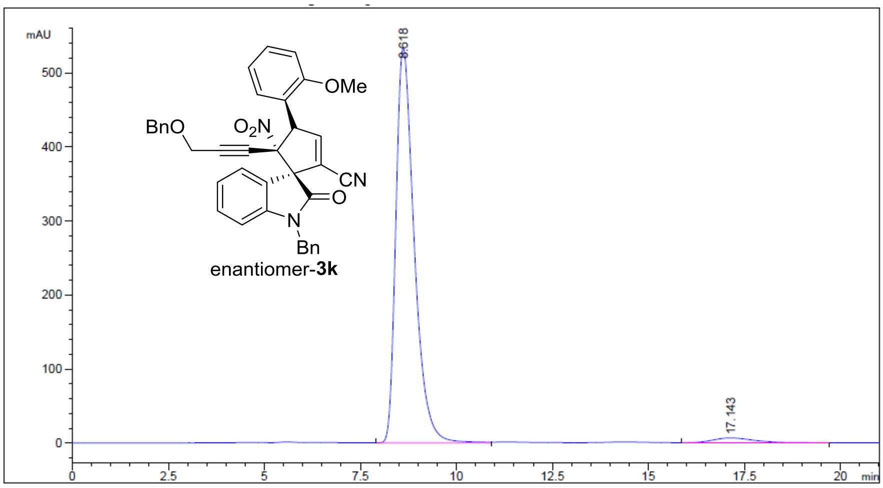




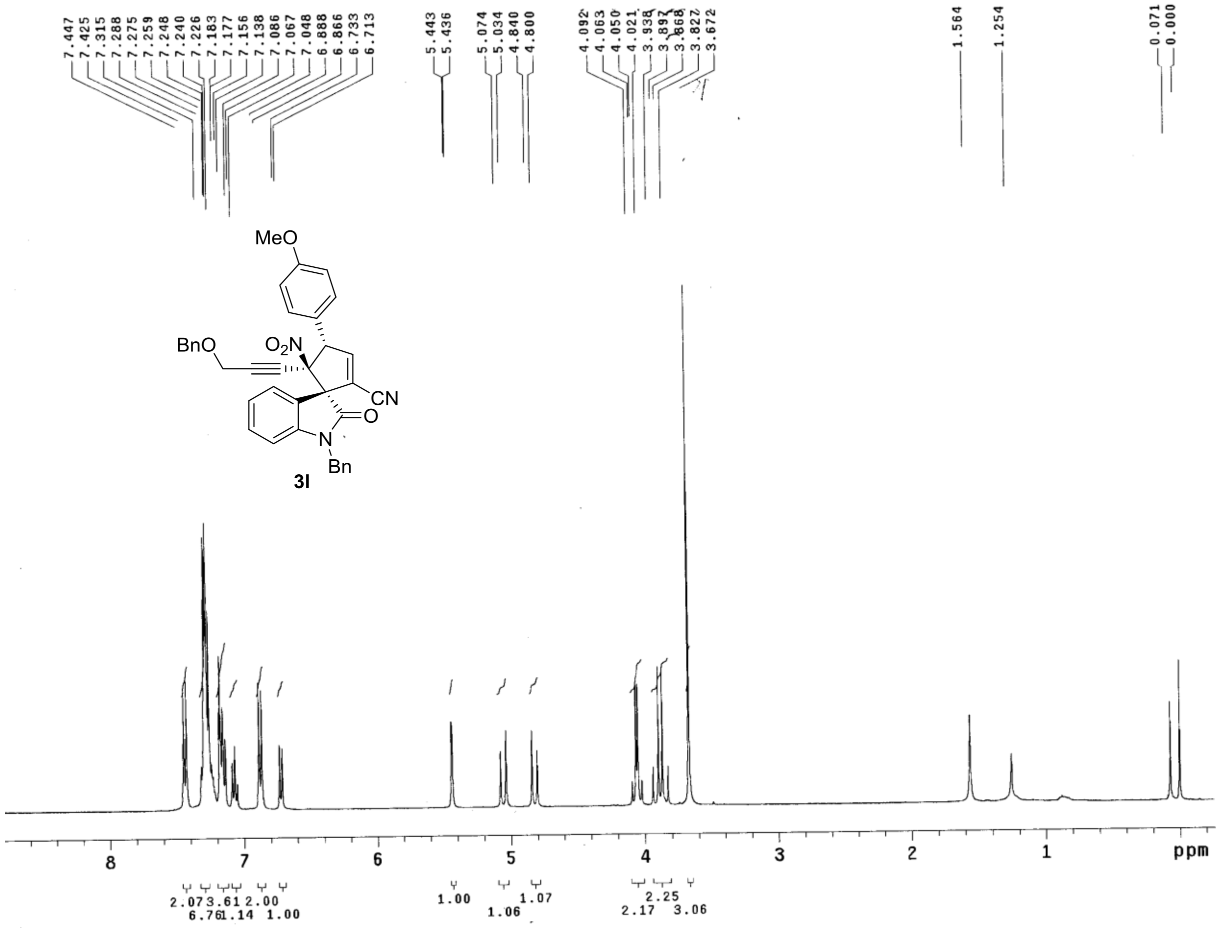
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.622	VV	0.5103	1.38352e4	416.03738	50.0648
2	16.695	VB	1.1261	1.37994e4	187.60307	49.9352

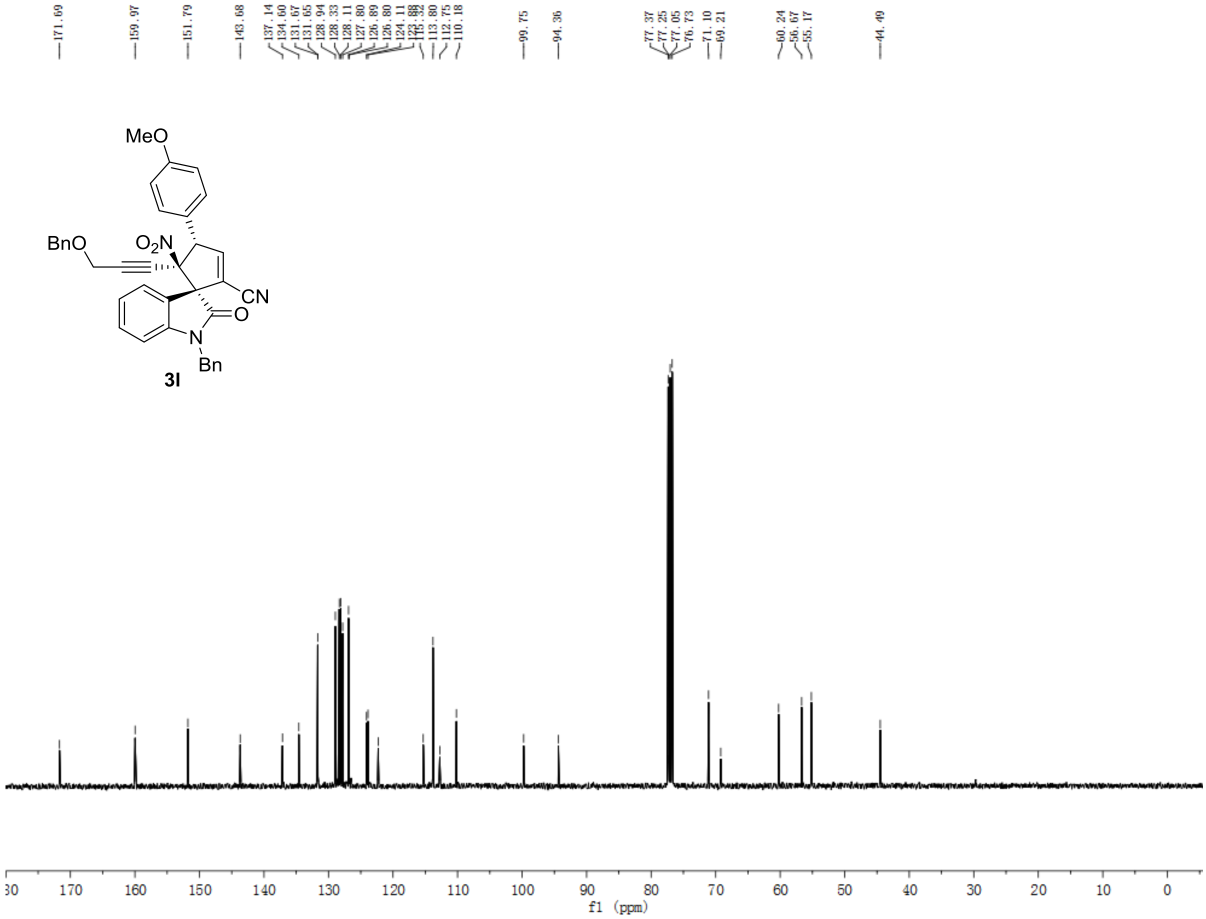


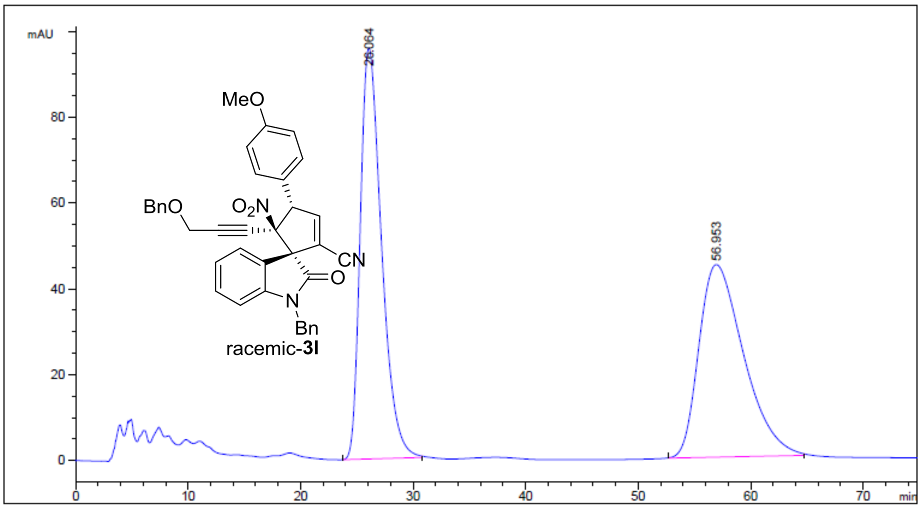
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.781	VB	0.5432	572.45154	15.86849	3.3313
2	16.805	BB	1.1507	1.66115e4	222.47063	96.6687



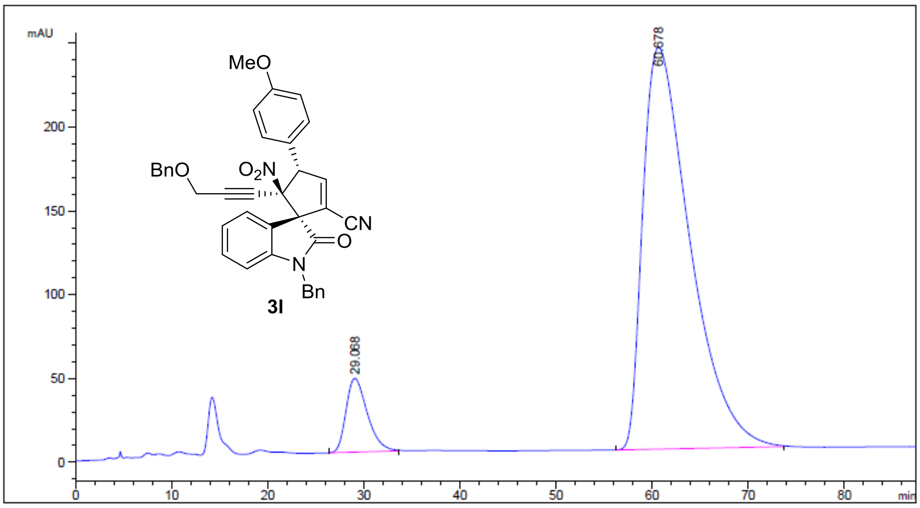
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.618	VV	0.5106	1.77406e4	532.98291	97.2539
2	17.143	VB	1.1521	500.92450	6.60936	2.7461



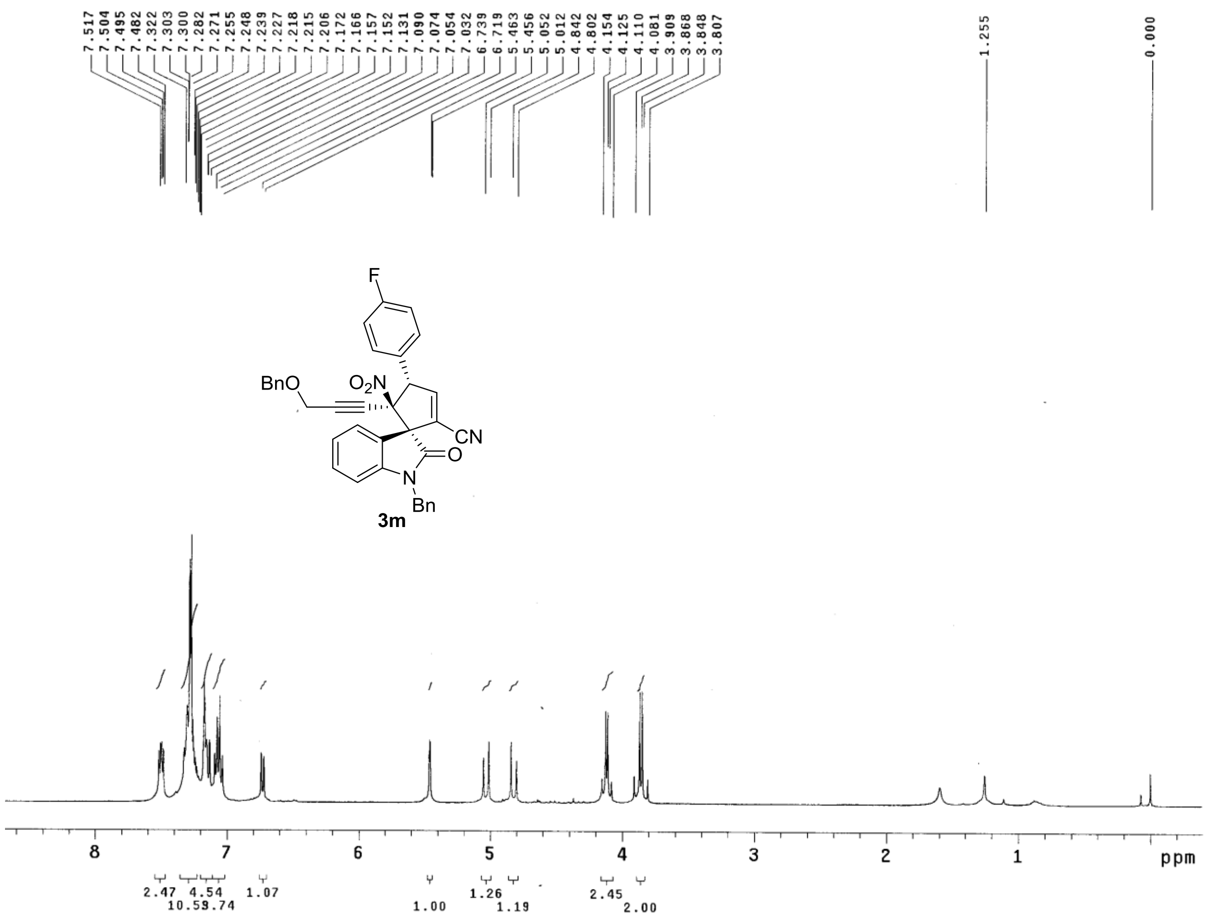


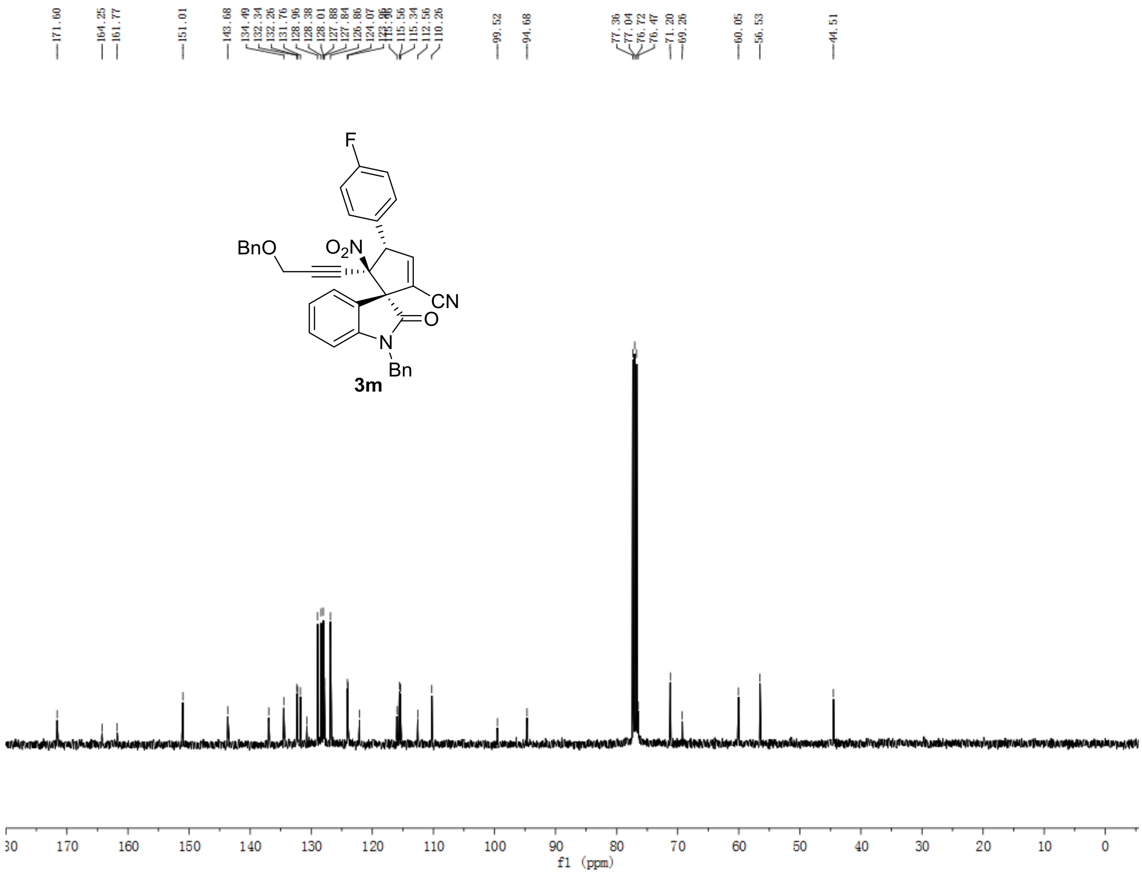


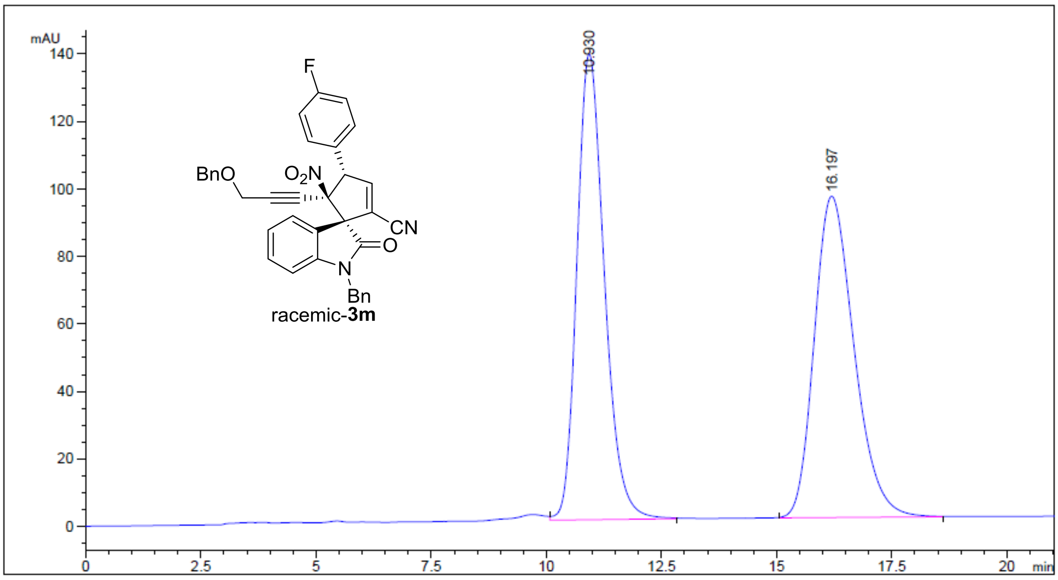
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	26.064	BB	2.0134	1.25589e4	95.76397	50.3056
2	56.953	BB	4.0224	1.24063e4	44.88697	49.6944



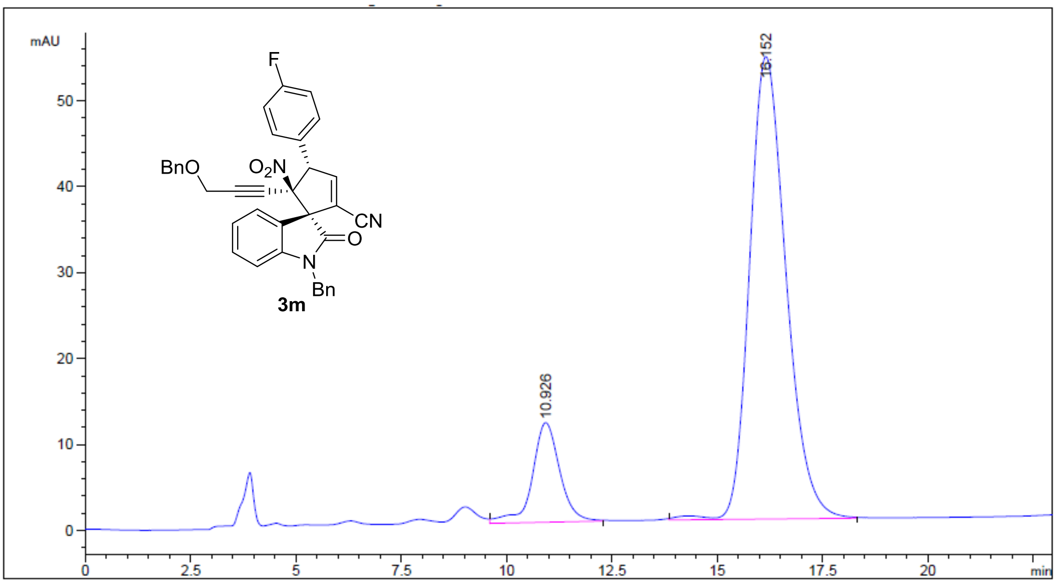
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	29.068	BB	2.3478	6768.31787	44.00336	7.6427
2	60.678	BB	5.2232	8.17912e4	239.59181	92.3573


7.517
7.504
7.495
7.482
7.322
7.303
7.300
7.282
7.271
7.255
7.248
7.239
7.227
7.218
7.215
7.206
7.172
7.166
7.157
7.152
7.131
7.090
7.074
7.054
7.032
6.739
6.719
5.463
5.456
5.052
5.012
4.842
4.802
4.154
4.125
4.110
4.081
3.909
3.868
3.848
3.807
1.255
0.000
F
BnO
O_2N
CN
O
N
Bn
3m
ppm
2.47
4.54
10.53
9.74
1.07
1.00
1.26
1.19
2.45
2.00

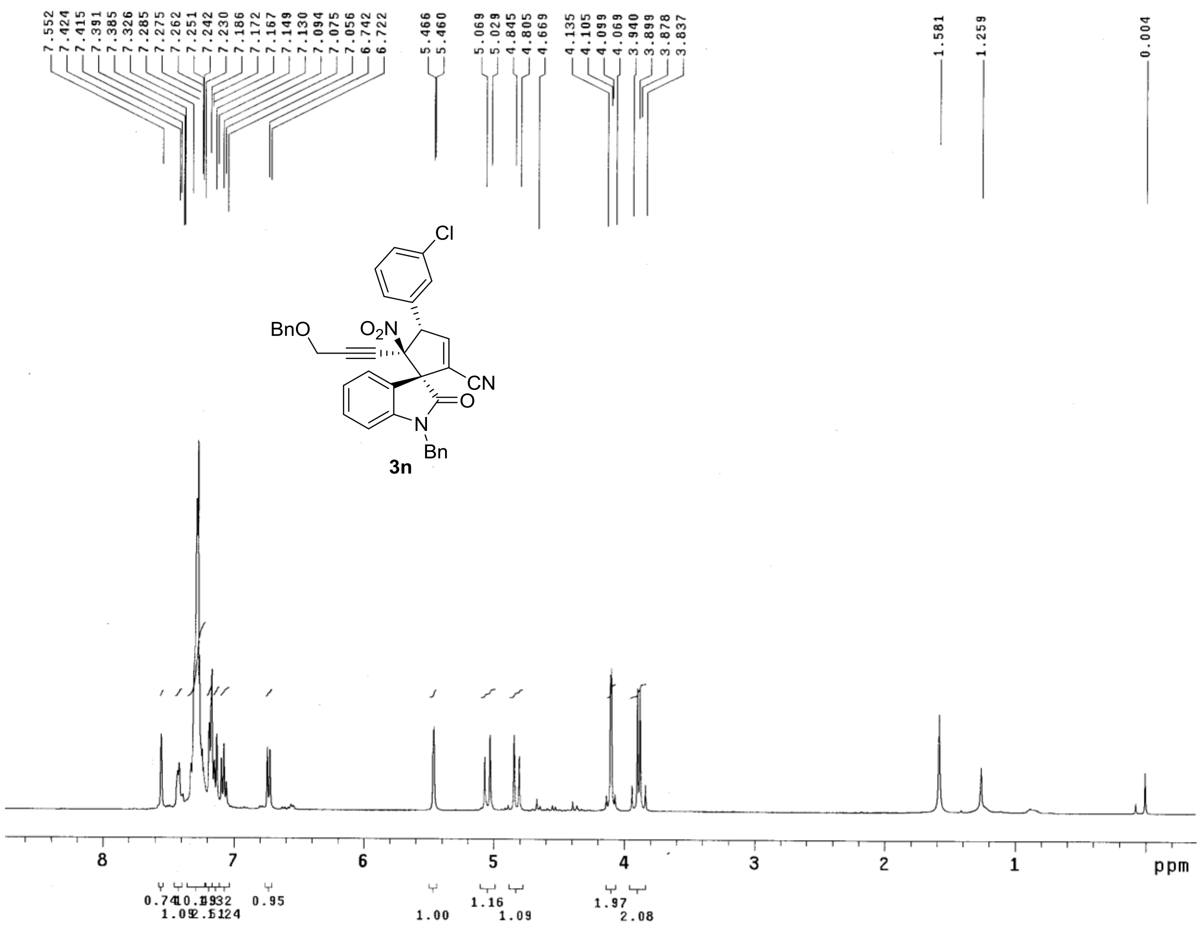

171.60
164.25
161.77
151.01
143.68
134.49
132.34
132.26
131.76
128.96
128.38
128.01
127.88
127.84
126.86
124.07
115.56
115.34
112.56
110.26
99.52
94.68
77.36
77.04
76.72
76.47
71.20
69.26
60.05
56.53
44.51
F
BnO
O_2N
CN
O
N
Bn
3m
f1 (ppm)



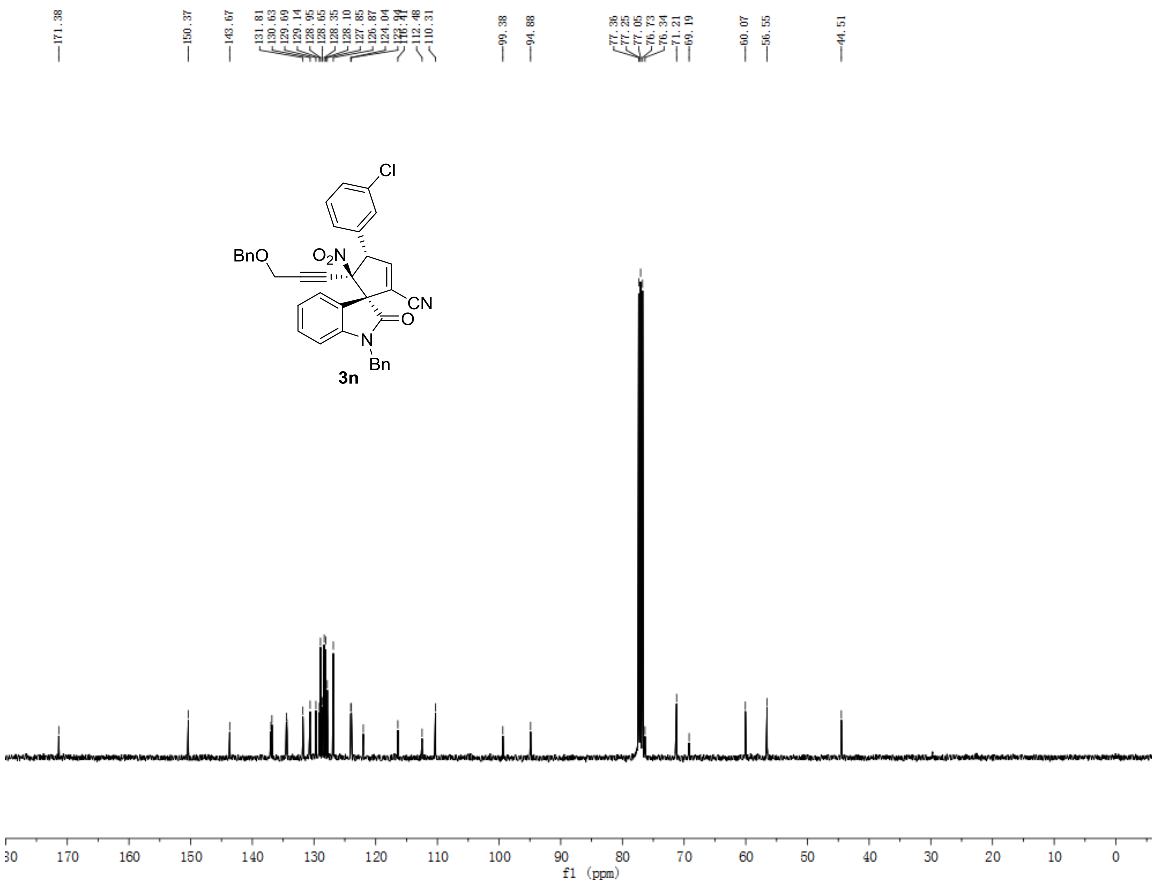
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.930	VB	0.6420	5734.80859	138.01170	50.0846
2	16.197	BB	0.9277	5715.44580	95.17852	49.9154



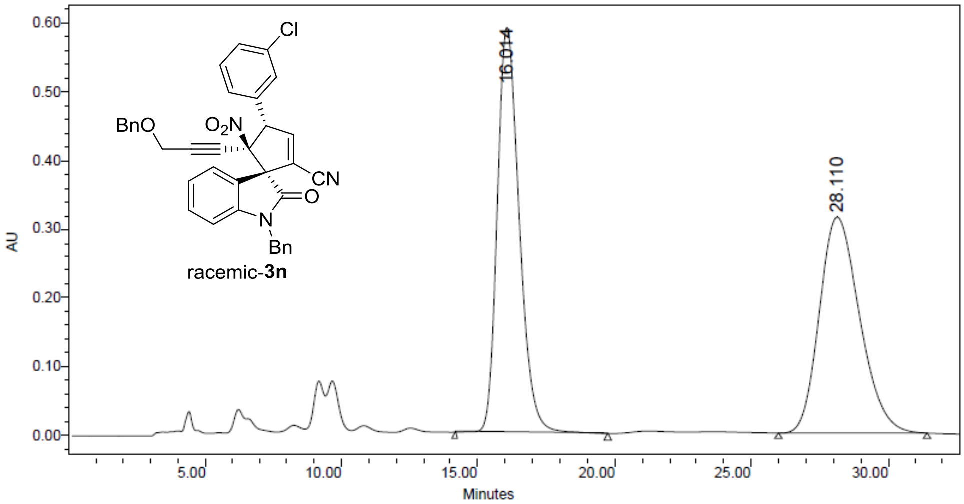
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.926	VB	0.6885	527.43433	11.58362	13.9921
2	16.152	BB	0.9304	3242.07202	53.78559	86.0079



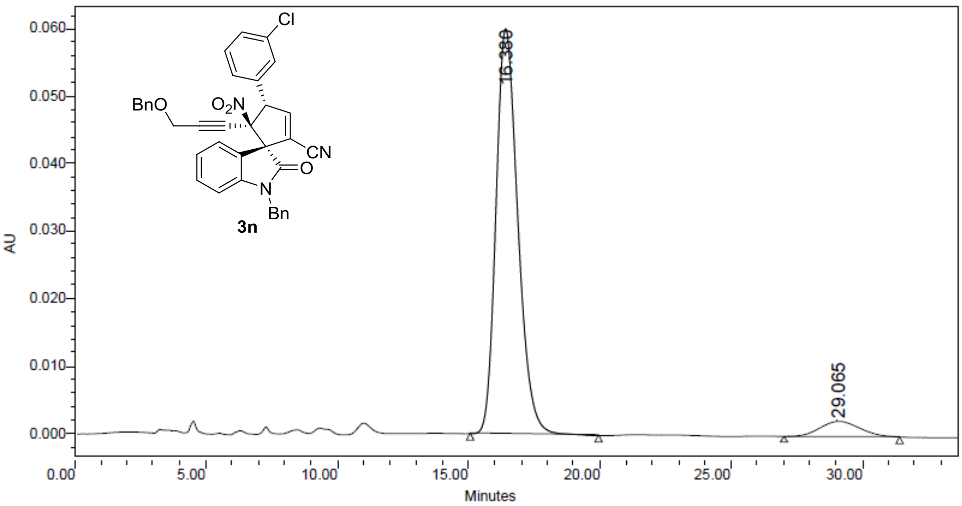
7.552
7.424
7.415
7.391
7.385
7.326
7.285
7.275
7.262
7.251
7.242
7.230
7.186
7.172
7.167
7.149
7.130
7.094
7.075
7.056
6.742
6.722
5.466
5.460
5.069
5.029
4.845
4.805
4.669
4.135
4.105
4.099
4.069
3.940
3.899
3.878
3.837
1.581
1.259
0.004
Cl
BnO
O_2N
CN
O
N
Bn
3n
0.95
1.00
1.16
1.09
1.97
2.08
ppm



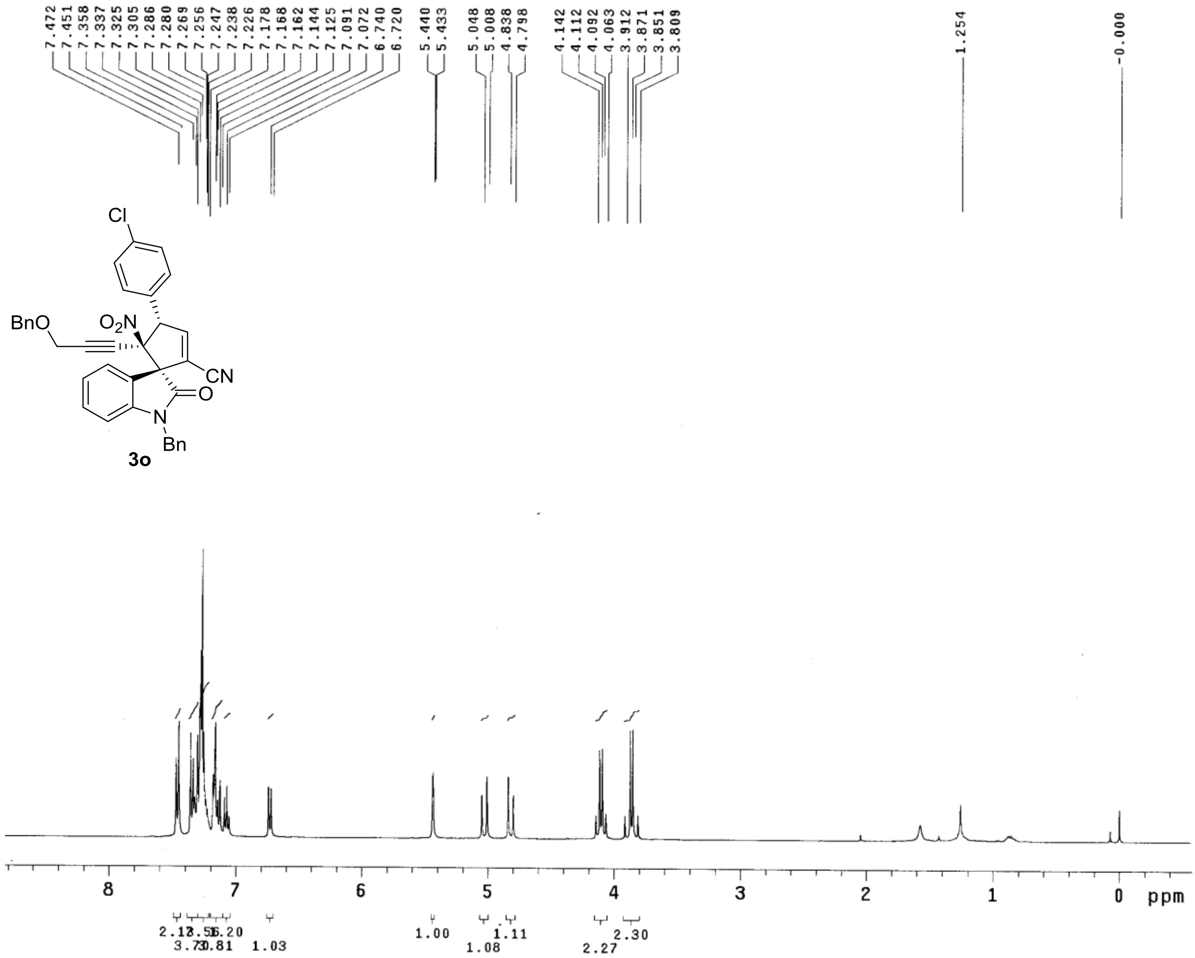
171.38
150.37
143.67
131.81
130.63
129.69
129.14
128.95
128.65
128.35
128.10
127.85
126.87
124.04
112.48
110.31
99.38
94.88
77.36
77.25
77.05
76.73
76.34
71.21
69.19
60.07
56.55
44.51
Cl
BnO
O_2N
CN
O
N
Bn
3n
f1 (ppm)



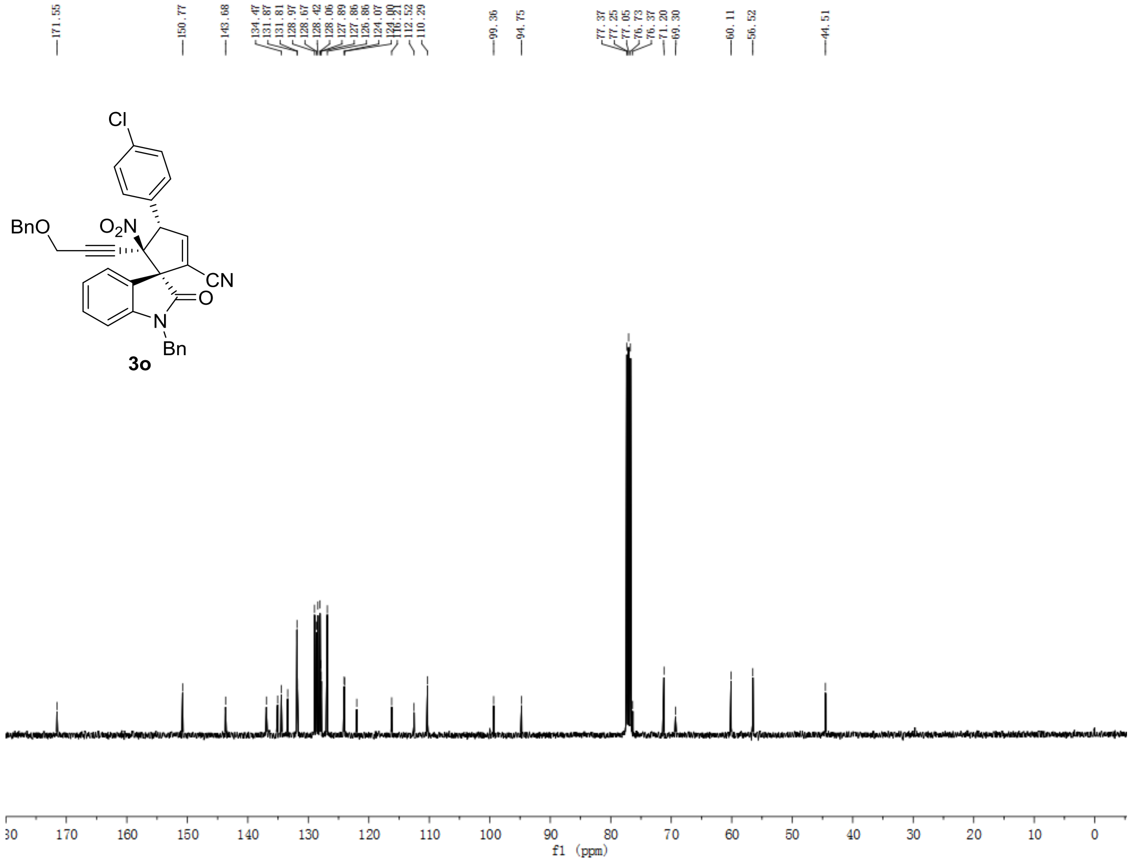
	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	16.014	33102757	50.59	590521	65.23
2	28.110	32334155	49.41	314761	34.77



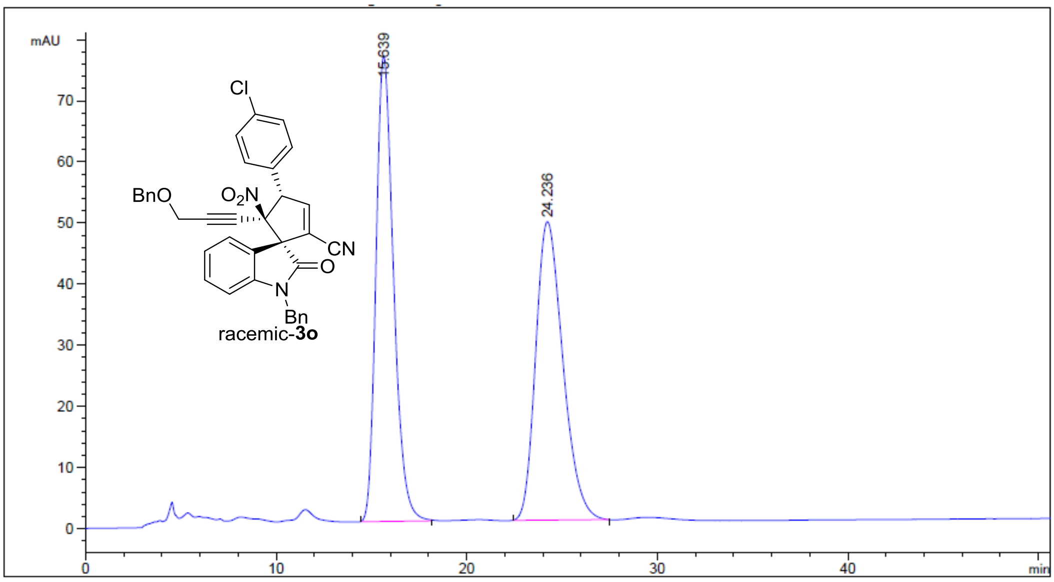
	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	16.380	3490405	93.47	60091	96.35
2	29.065	243822	6.53	2275	3.65


7.472 7.451 7.358 7.337 7.325 7.305 7.286 7.280 7.269 7.256 7.247 7.238 7.226 7.178 7.168 7.162 7.144 7.125 7.091 7.072 6.740 6.720
5.440 5.433
5.048 5.008 4.838 4.798
4.142 4.112 4.092 4.063 3.912 3.871 3.851 3.809
1.254
-0.000
Cl
BnO
O_2N
CN
O
N
Bn
8 7 6 5 4 3 2 1 0 ppm
2.17 3.56 6.20 3.73 0.81 1.03 1.00 1.08 1.11 2.27 2.30

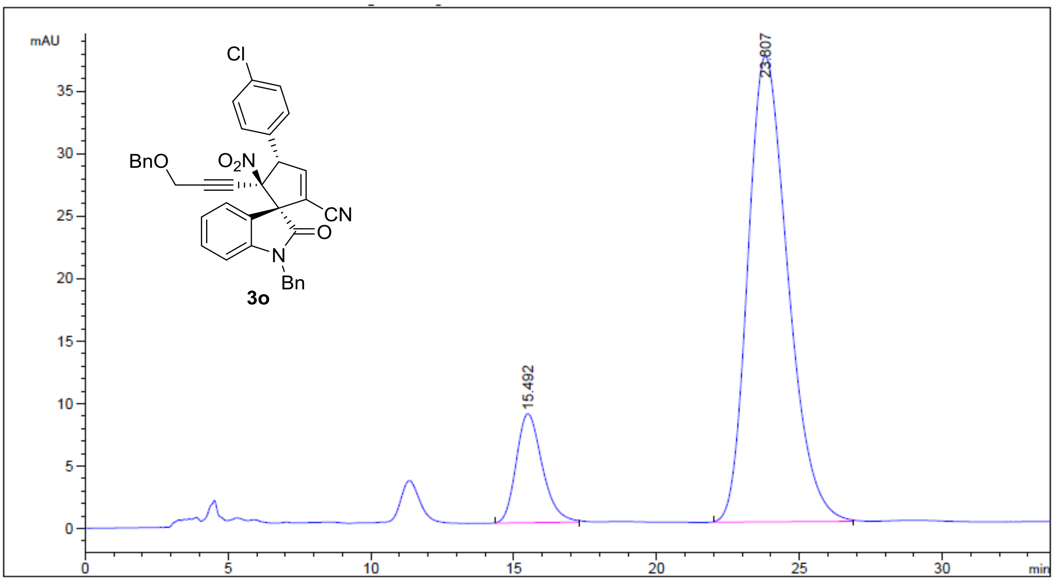
3o


171.55
150.77
143.68
134.47 131.87 131.81 128.97 128.67 128.42 128.06 127.89 127.86 126.86 124.07 122.21 116.21 112.52 110.29
99.36
94.75
77.37 77.25 77.05 76.73 76.37 71.20 69.30
60.11
56.52
44.51
Cl
BnO
O_2N
CN
O
N
Bn
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

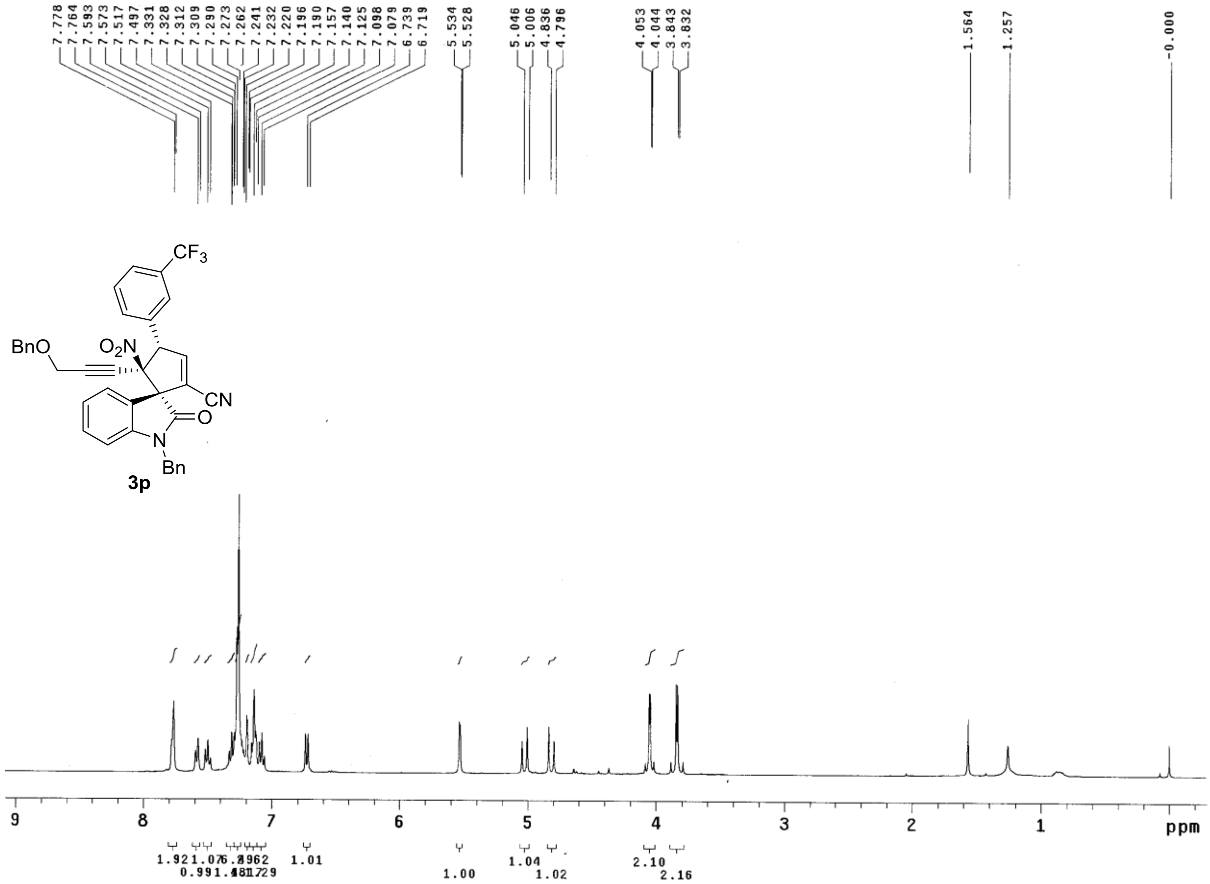
3o

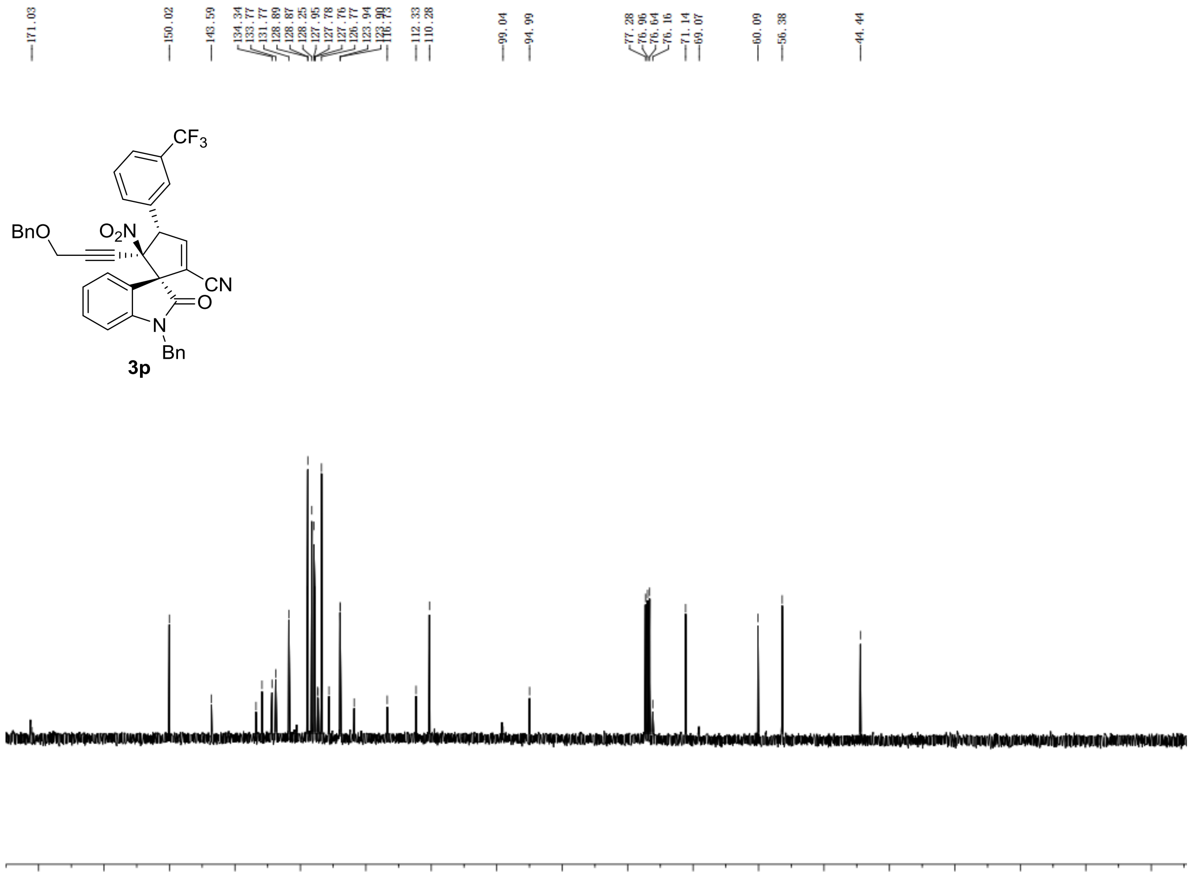


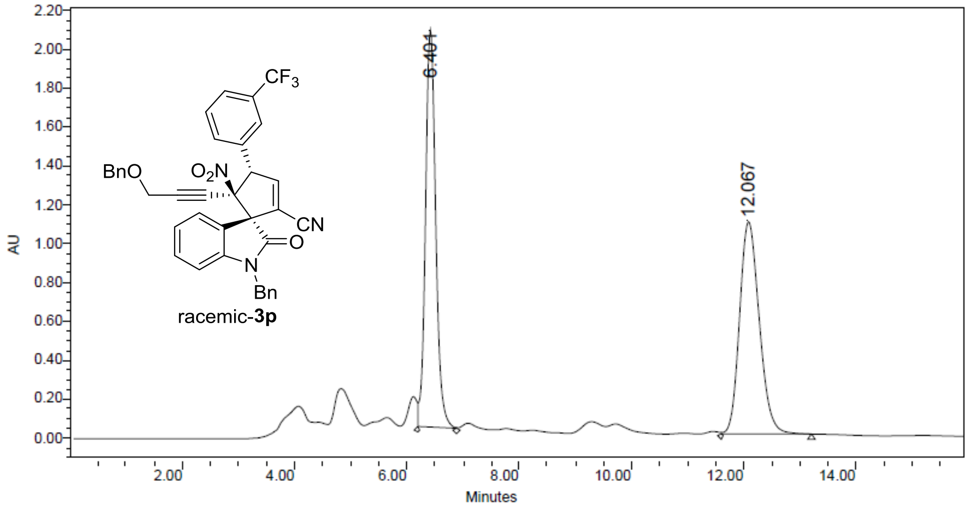
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.639	BB	0.9910	4869.78125	76.11813	50.1441
2	24.236	BB	1.5357	4841.79590	48.81699	49.8559



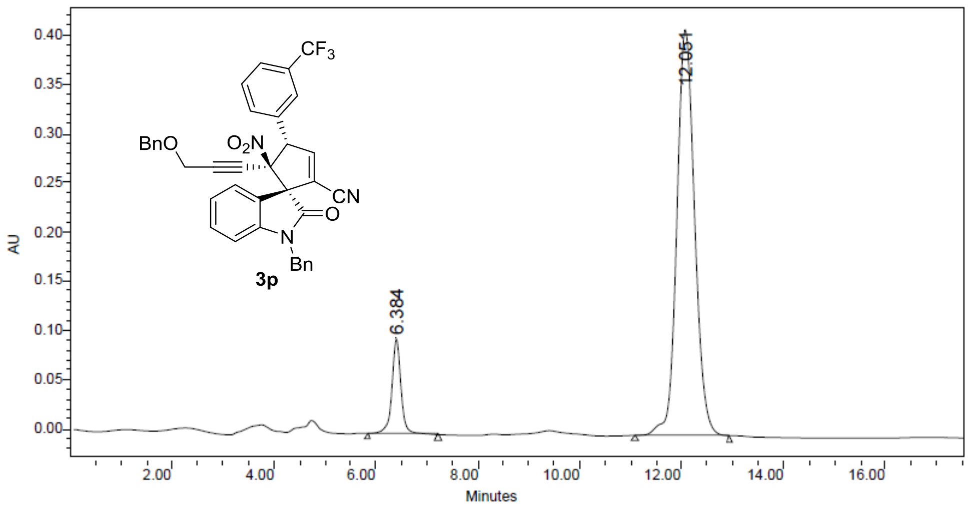
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.492	BB	0.9800	554.19824	8.72305	13.2396
2	23.807	BB	1.5030	3631.69995	37.29377	86.7604


7.778
7.764
7.593
7.573
7.517
7.497
7.331
7.328
7.312
7.309
7.290
7.273
7.262
7.241
7.232
7.220
7.196
7.190
7.157
7.140
7.125
7.098
7.079
6.739
6.719
5.534
5.528
5.046
5.006
4.836
4.796
4.053
4.044
3.843
3.832
1.564
1.257
-0.000
CF3
BnO
O2N
CN
O
N
Bn
3p
1.01
1.00
1.04
1.02
2.10
2.16
ppm

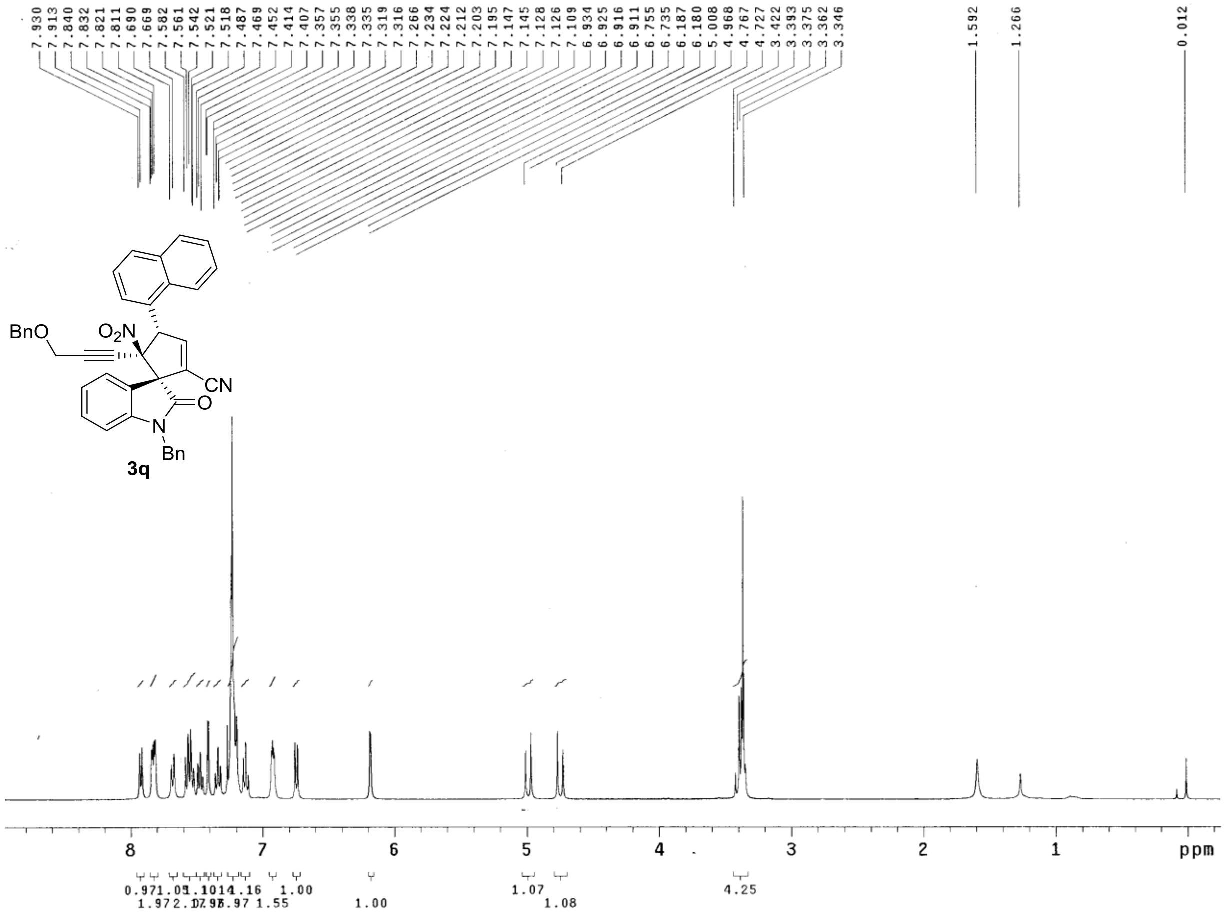

171.03
150.02
143.59
134.34
133.77
131.77
128.89
128.87
128.25
127.95
127.78
127.76
126.77
123.94
112.33
110.28
99.04
94.99
77.28
76.96
76.64
76.16
71.14
69.07
60.09
56.38
44.44
CF3
BnO
O2N
CN
O
N
Bn
3p
f1 (ppm)



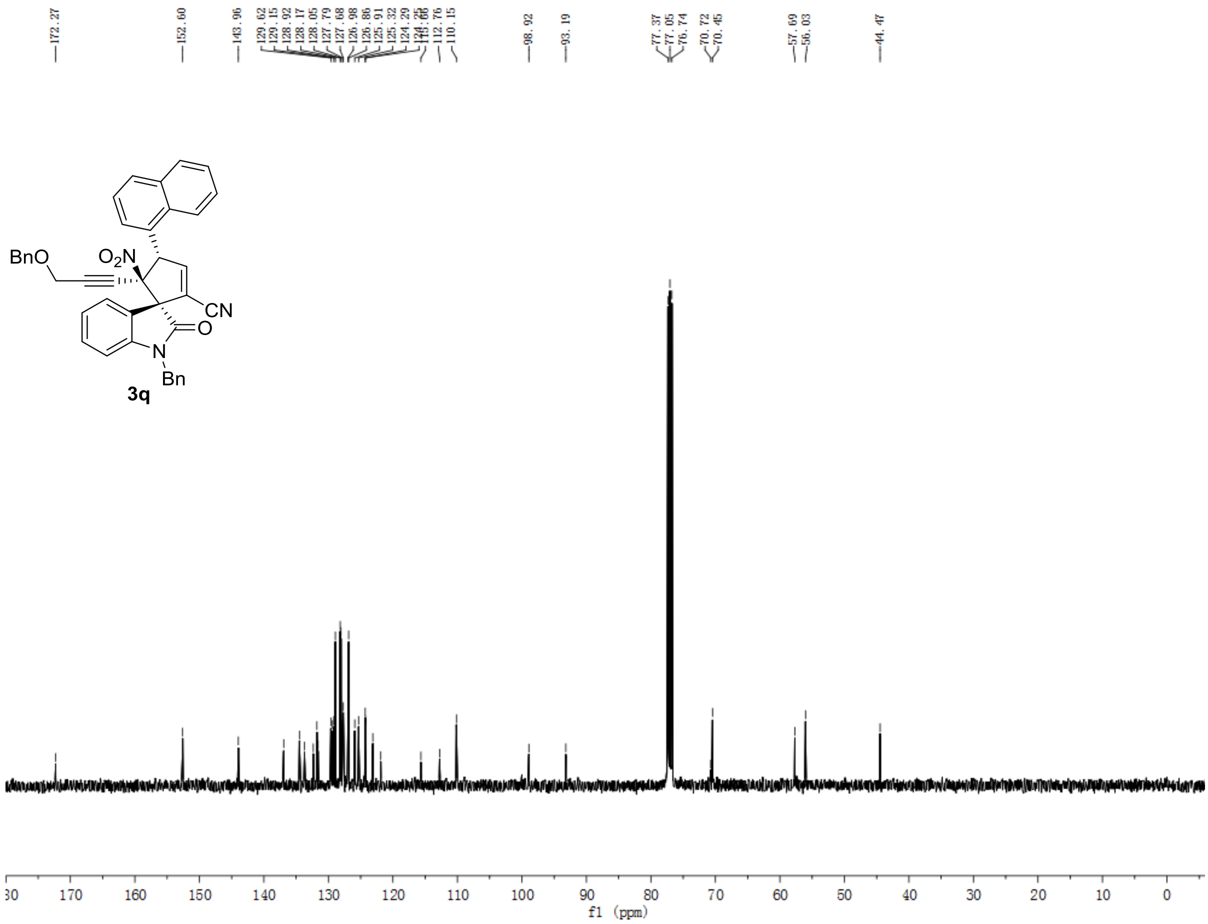
	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	6.401	25780249	49.19	2044871	65.17
2	12.067	26628300	50.81	1092999	34.83



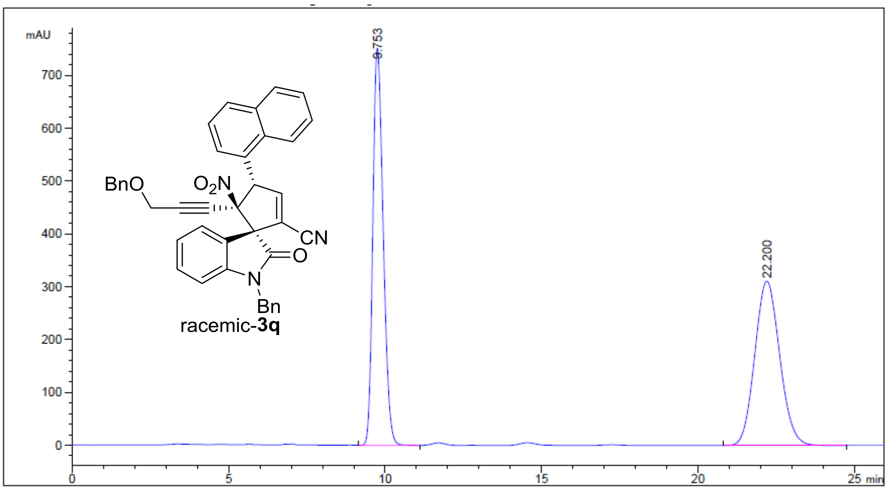
	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	6.384	1197374	10.67	96185	18.93
2	12.051	10027796	89.33	411957	81.07



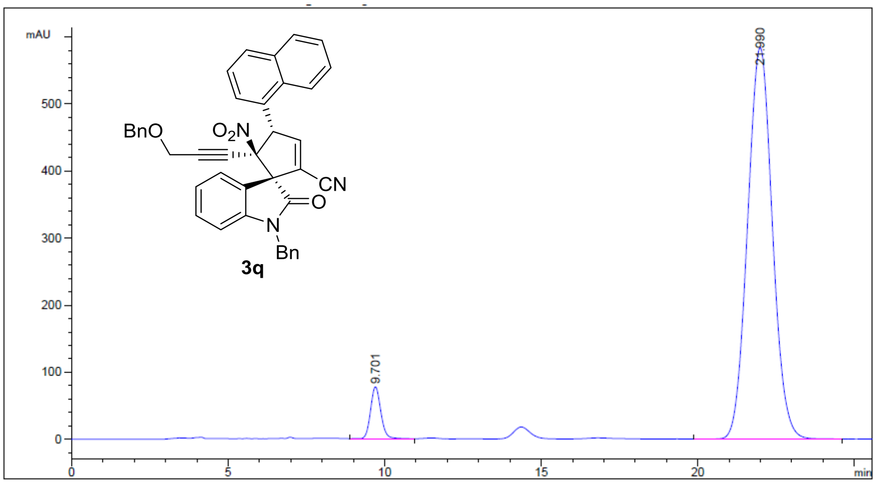
7.930
7.913
7.840
7.832
7.821
7.811
7.690
7.669
7.582
7.561
7.542
7.521
7.518
7.487
7.469
7.452
7.414
7.407
7.357
7.355
7.338
7.335
7.319
7.316
7.266
7.234
7.224
7.212
7.203
7.195
7.147
7.145
7.128
7.126
7.109
6.934
6.925
6.916
6.911
6.755
6.735
6.187
6.180
5.008
4.968
4.767
4.727
3.422
3.393
3.375
3.362
3.346
1.592
1.266
0.012
BnO
O2N
CN
O
N
Bn
3q
8
7
6
5
4
3
2
1
ppm
1.00
1.55
1.00
1.07
1.08
4.25



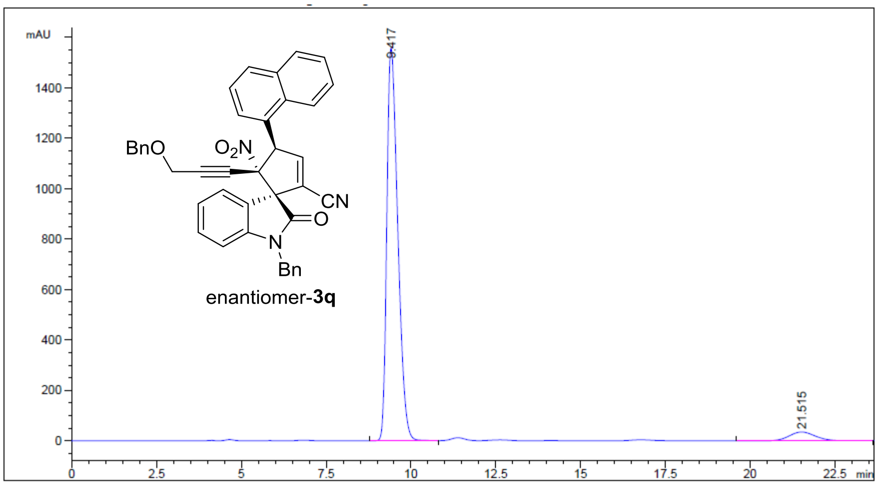
172.27
152.60
143.96
129.62
129.15
128.92
128.17
128.05
127.79
127.68
126.98
126.86
125.91
125.32
124.29
112.76
110.15
98.92
93.19
77.37
77.05
76.74
70.72
70.45
57.69
56.03
44.47
BnO
O2N
CN
O
N
Bn
3q
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



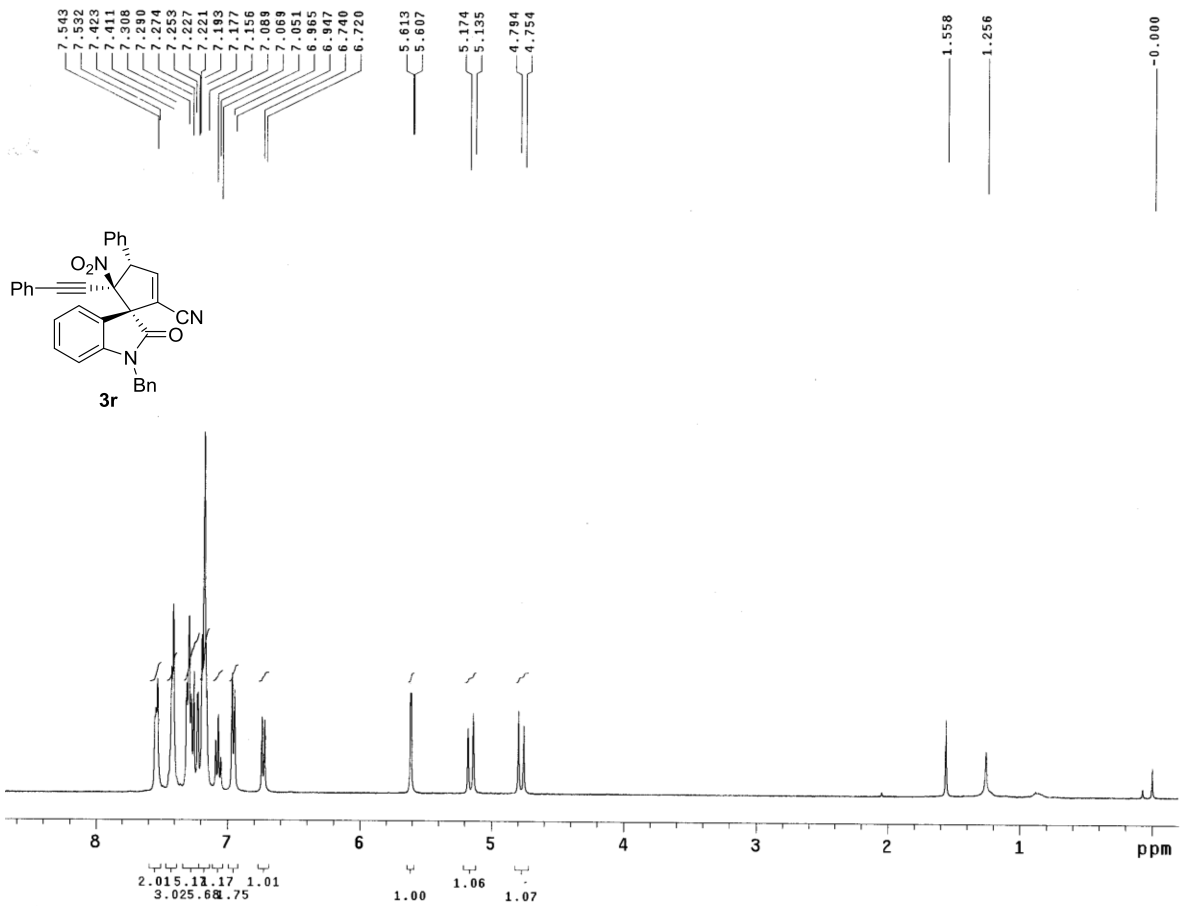
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.753	VV	0.3610	1.72428e4	750.99896	50.0120
2	22.200	BB	0.8616	1.72346e4	311.21744	49.9880

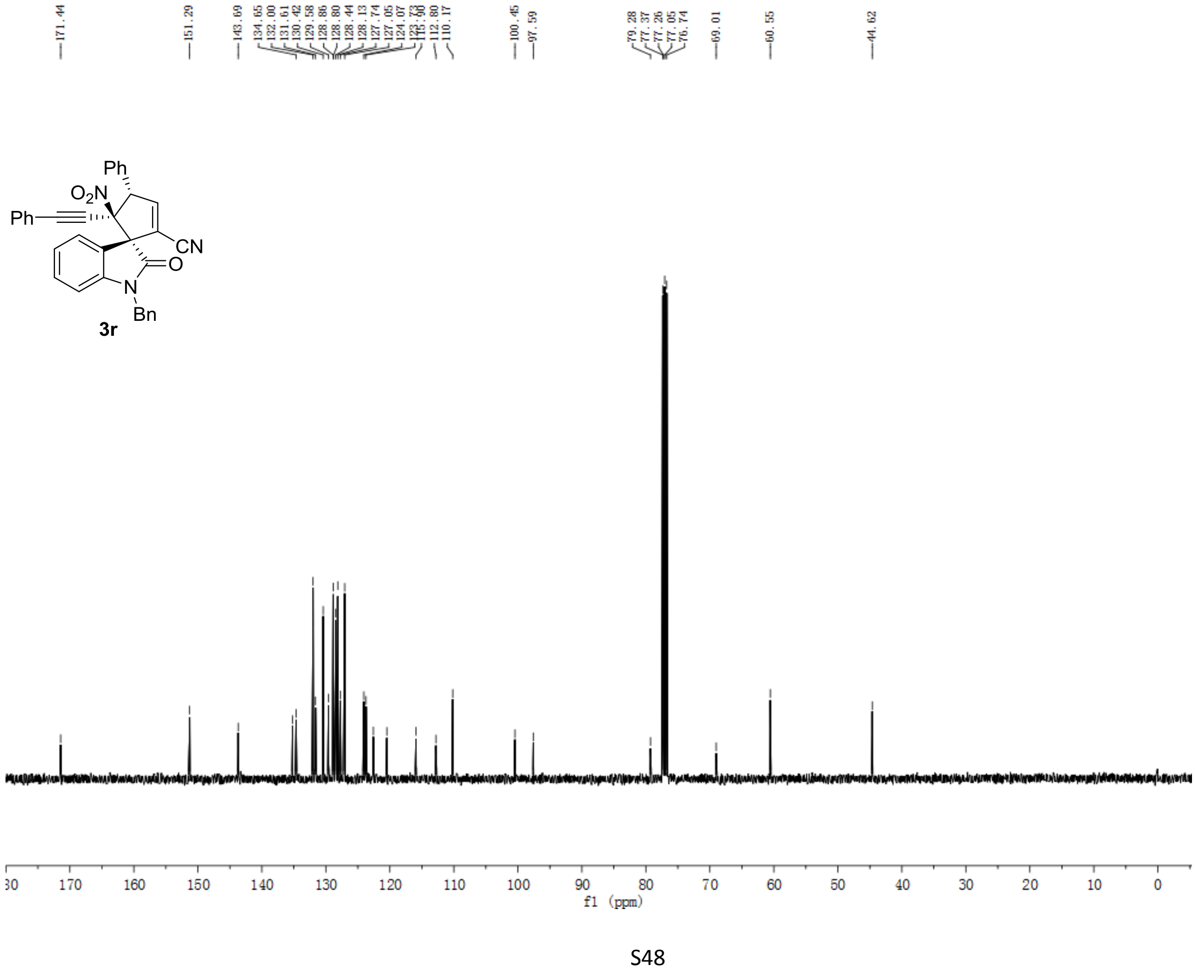


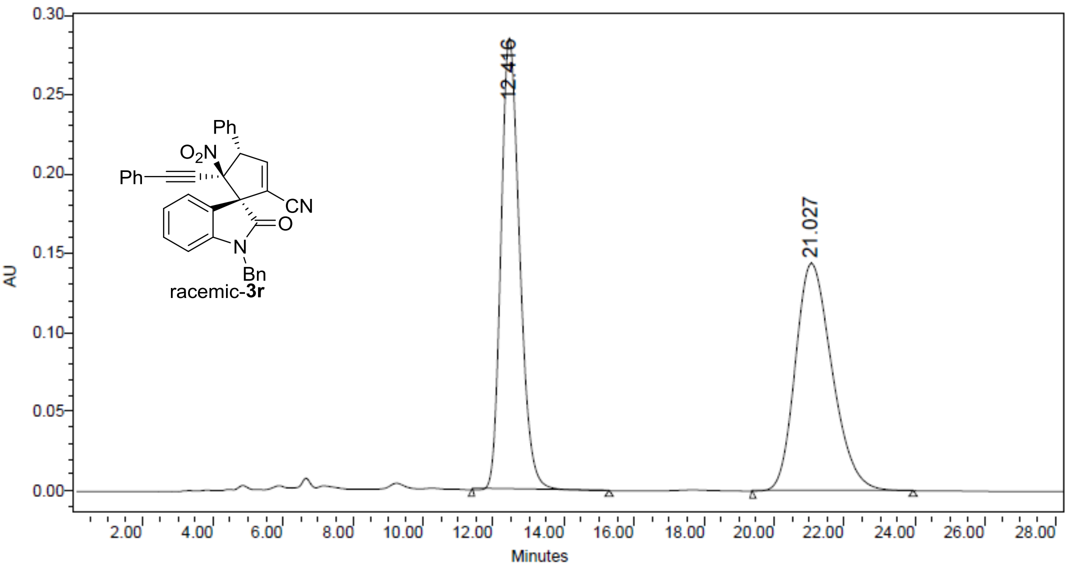
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.701	VV	0.3671	1875.56079	78.22633	5.4988
2	21.990	VB	0.8538	3.22330e4	583.84595	94.5012



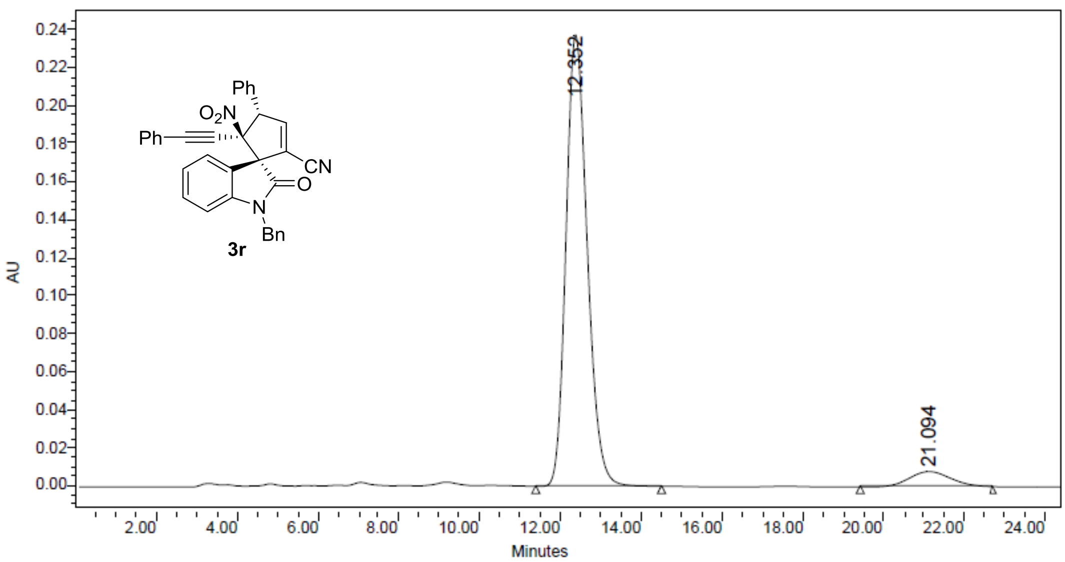
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.417	VV	0.3497	3.49691e4	1555.32178	94.8537
2	21.515	BBA	0.8408	1897.23730	35.07074	5.1463


7.543
7.532
7.423
7.411
7.308
7.290
7.274
7.253
7.227
7.221
7.193
7.177
7.156
7.089
7.069
7.051
6.965
6.947
6.740
6.720
5.613
5.607
5.174
5.135
4.794
4.754
1.558
1.256
-0.000
Ph
O_2N
Ph
CN
O
N
Bn
3r
ppm
2.01
3.02
5.11
5.68
1.17
1.75
1.01
1.00
1.06
1.07

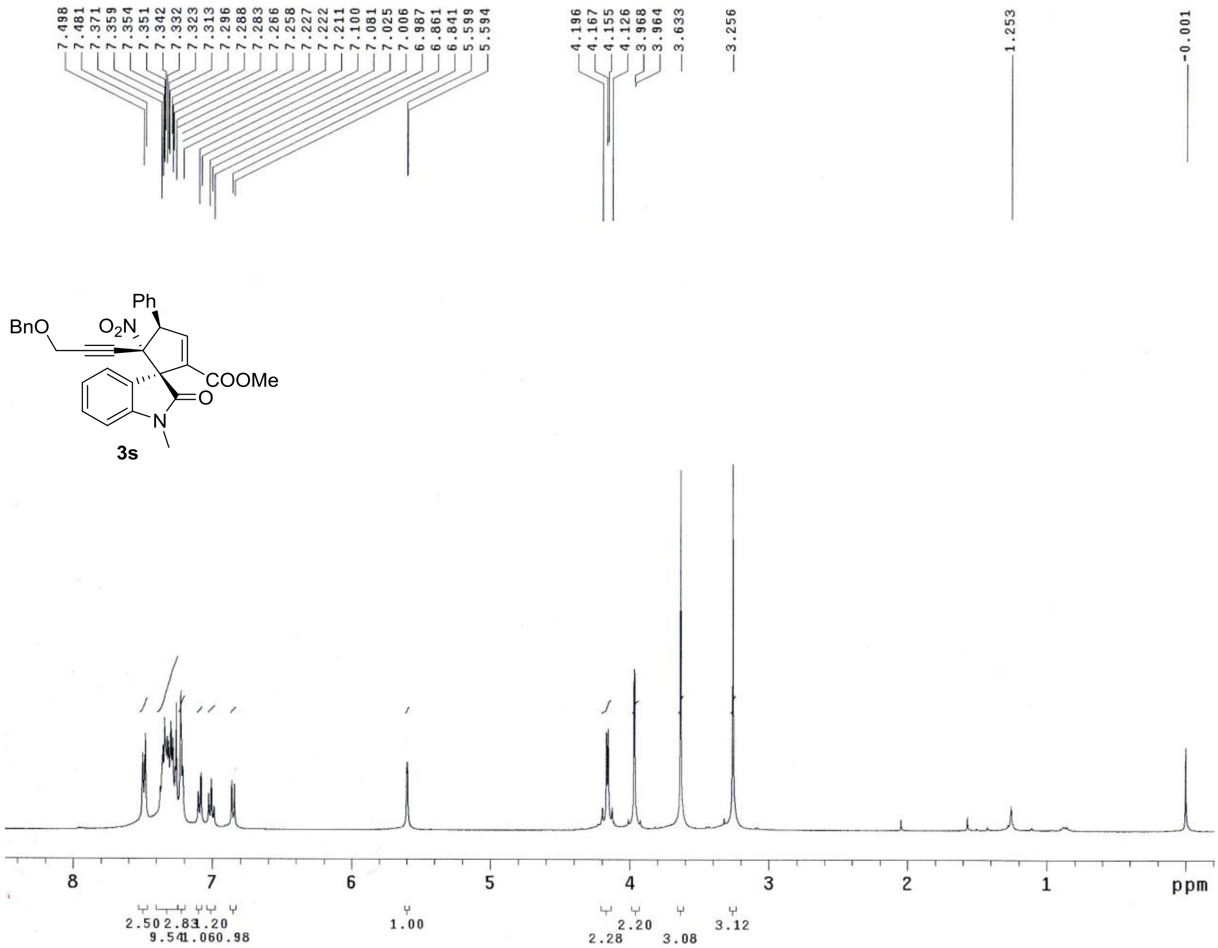

171.44
151.29
143.69
134.65
132.00
131.61
130.42
129.58
128.86
128.80
128.44
128.13
127.74
127.65
124.07
112.80
110.17
100.45
97.59
79.28
77.37
77.26
77.05
76.74
69.01
60.55
44.62
Ph
O_2N
Ph
CN
O
N
Bn
3r
f1 (ppm)

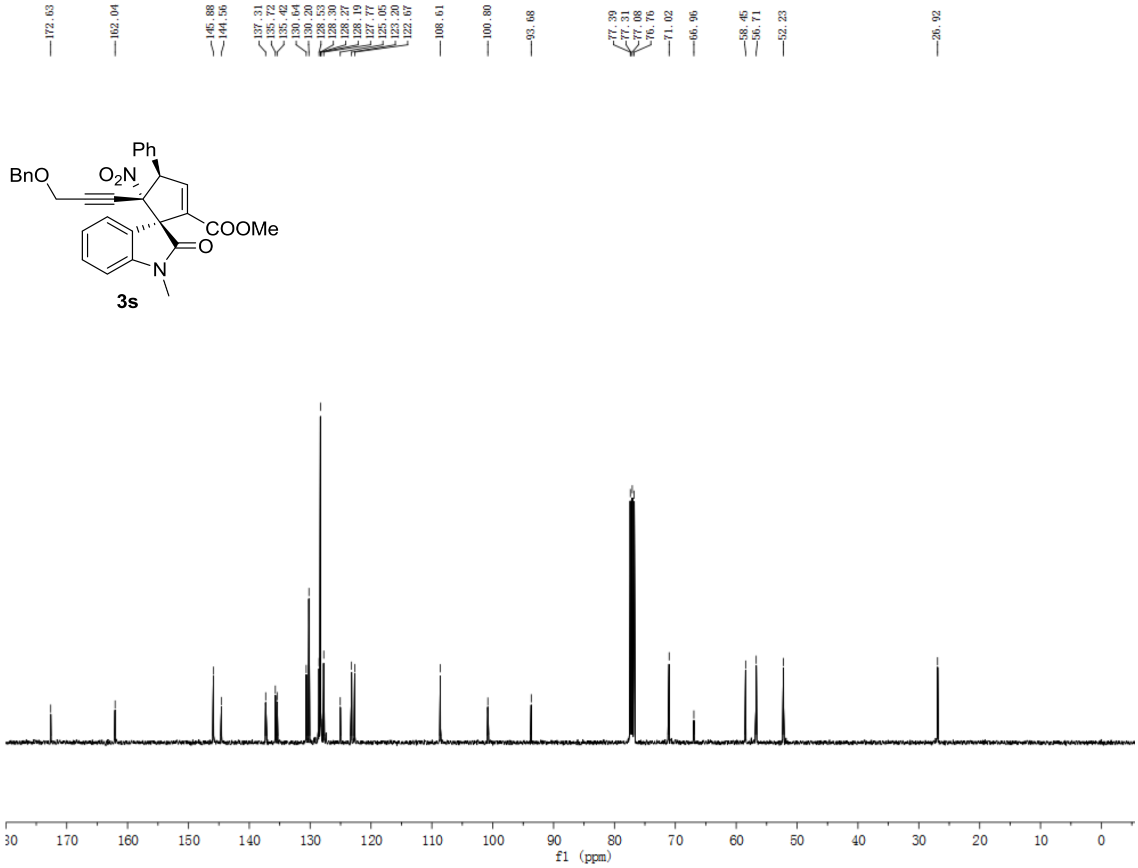


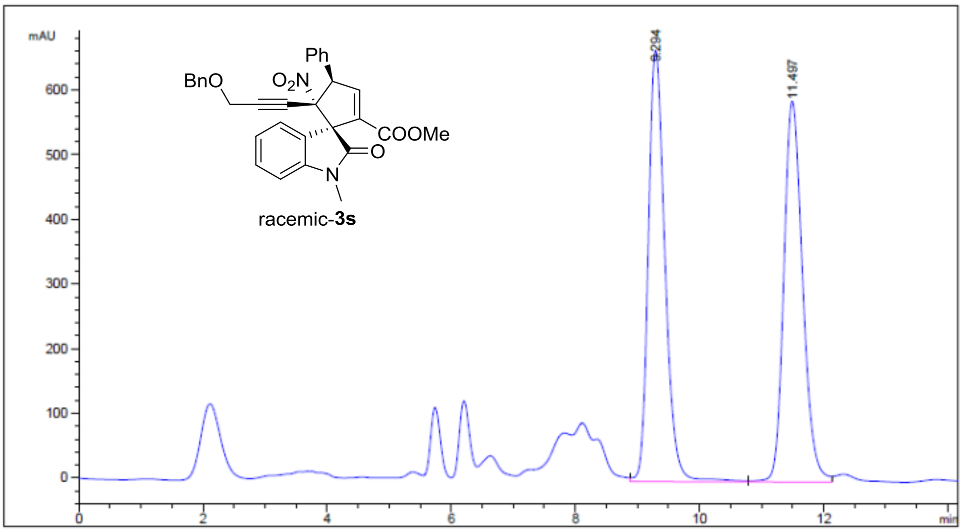
	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	12.416	10606392	50.33	285491	66.52
2	21.027	10467560	49.67	143684	33.48



	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	12.352	8643170	93.77	237211	96.74
2	21.094	574192	6.23	8006	3.26

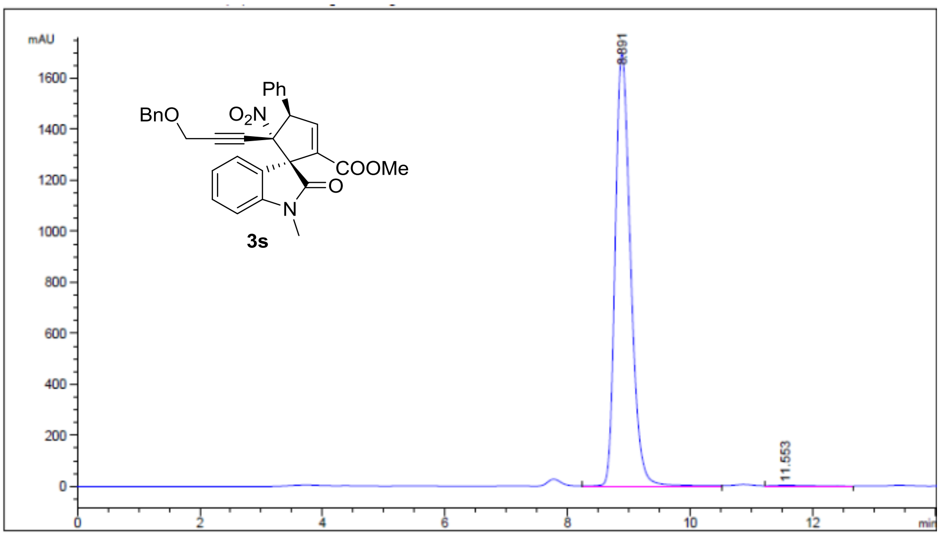

7.498
7.481
7.371
7.359
7.354
7.351
7.342
7.332
7.323
7.313
7.296
7.288
7.283
7.266
7.258
7.227
7.222
7.211
7.100
7.081
7.025
7.006
6.987
6.861
6.841
5.599
5.594
4.196
4.167
4.155
4.126
3.968
3.964
3.633
3.256
1.253
-0.001
Ph
BnO
O_2N
COOMe
O
N
3s
ppm
2.50
2.83
1.20
9.54
1.06
0.98
1.00
2.20
2.28
3.08
3.12


172.63
162.04
145.88
144.56
137.31
135.72
135.42
130.64
130.20
128.53
128.30
128.27
128.19
127.77
125.05
123.20
122.67
108.61
100.80
93.68
77.39
77.31
77.08
76.76
71.02
66.96
58.45
56.71
52.23
26.92
Ph
BnO
O_2N
COOMe
O
N
3s
f1 (ppm)



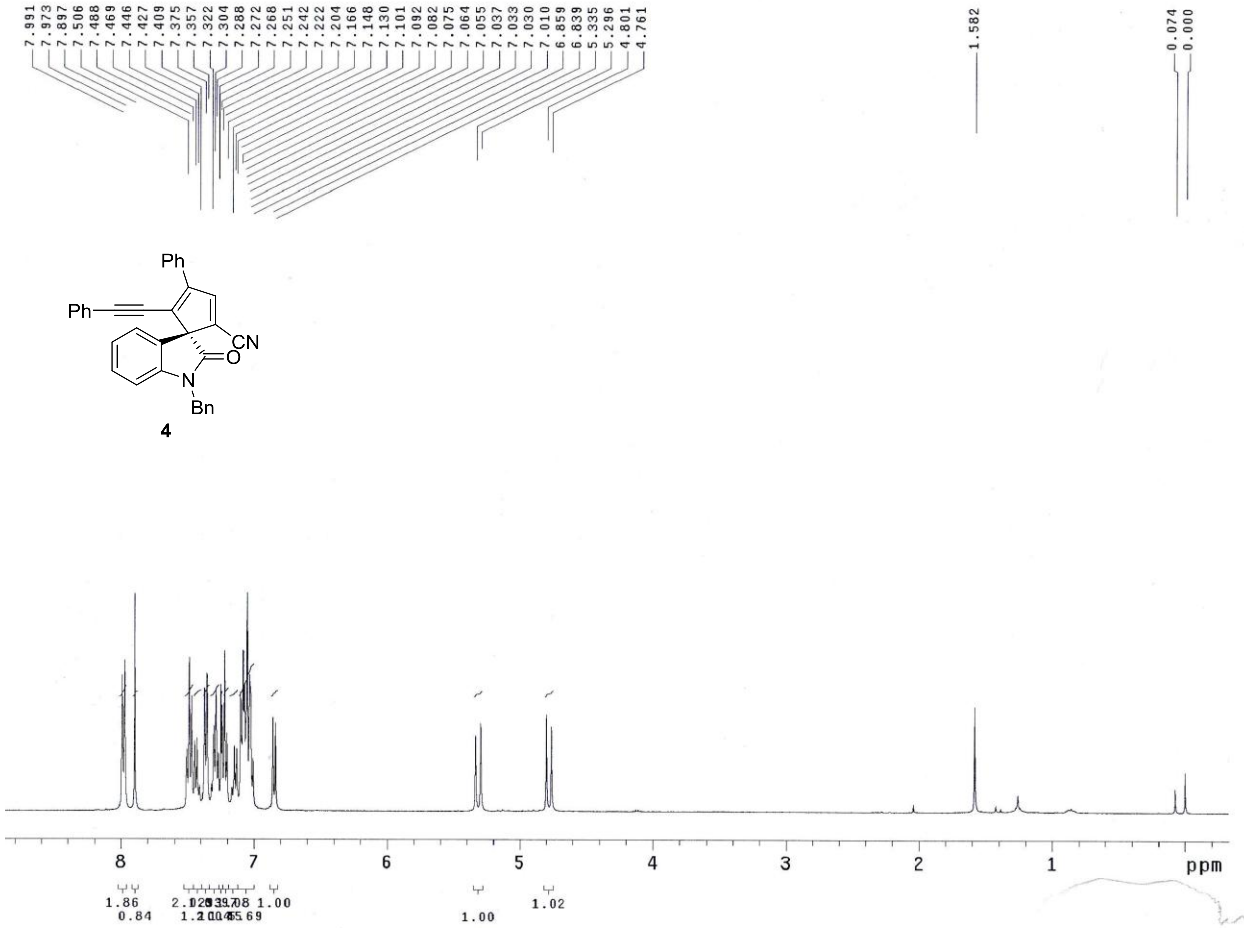
Signal 1: VWD1 A, Wavelength=254 nm

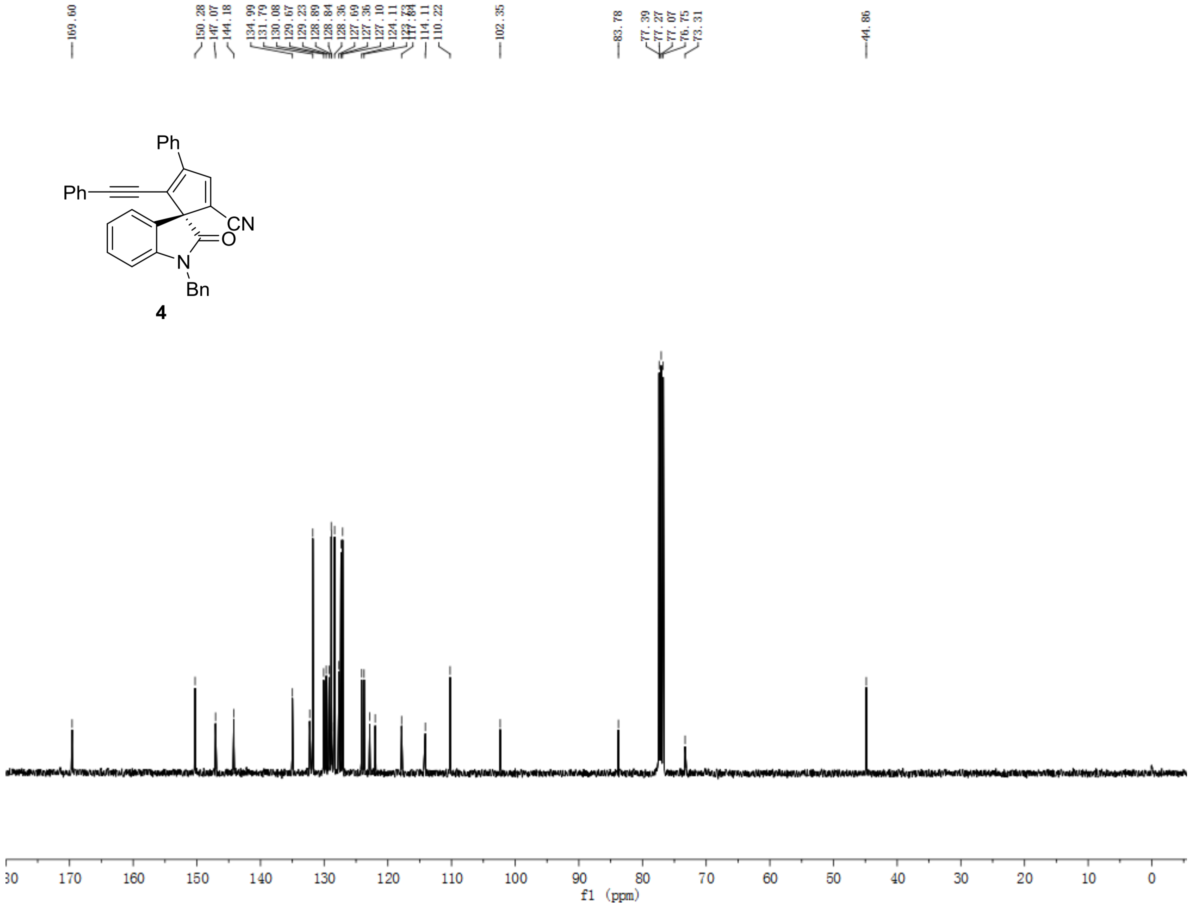
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.294	VV	0.3010	1.24897e4	663.96277	50.1527
2	11.497	VV	0.3287	1.24137e4	585.95331	49.8473

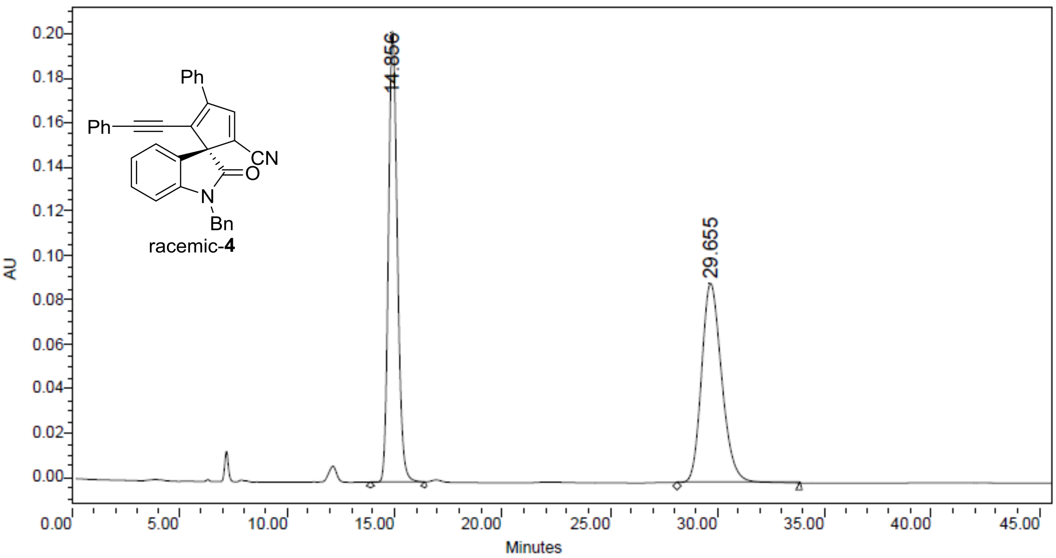


Signal 1: VWD1 A, Wavelength=254 nm

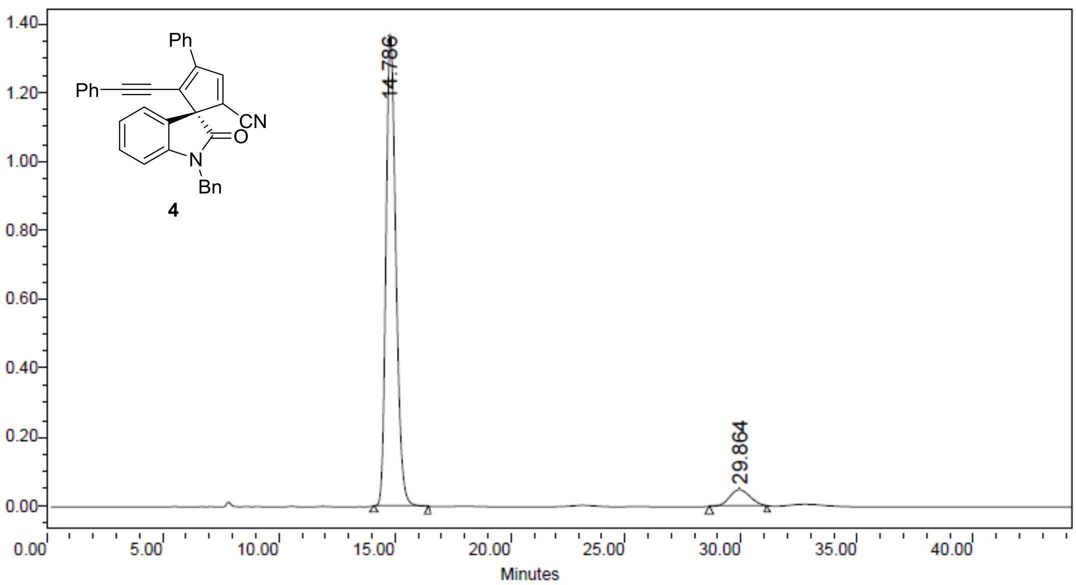
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.891	VV	0.2765	2.97280e4	1679.03918	99.2202
2	11.553	VV	0.7938	233.64839	4.09496	0.7798


7.991 7.973 7.897 7.506 7.488 7.469 7.446 7.427 7.409 7.375 7.357 7.322 7.304 7.288 7.272 7.268 7.251 7.242 7.222 7.204 7.166 7.148 7.130 7.101 7.092 7.082 7.075 7.064 7.055 7.037 7.033 7.030 7.010 6.859 6.839 5.335 5.296 4.801 4.761
1.582
0.074 0.000
Ph
Ph
CN
O
N
Bn
4
8 7 6 5 4 3 2 1 ppm
1.86 0.84 1.00 1.00 1.02

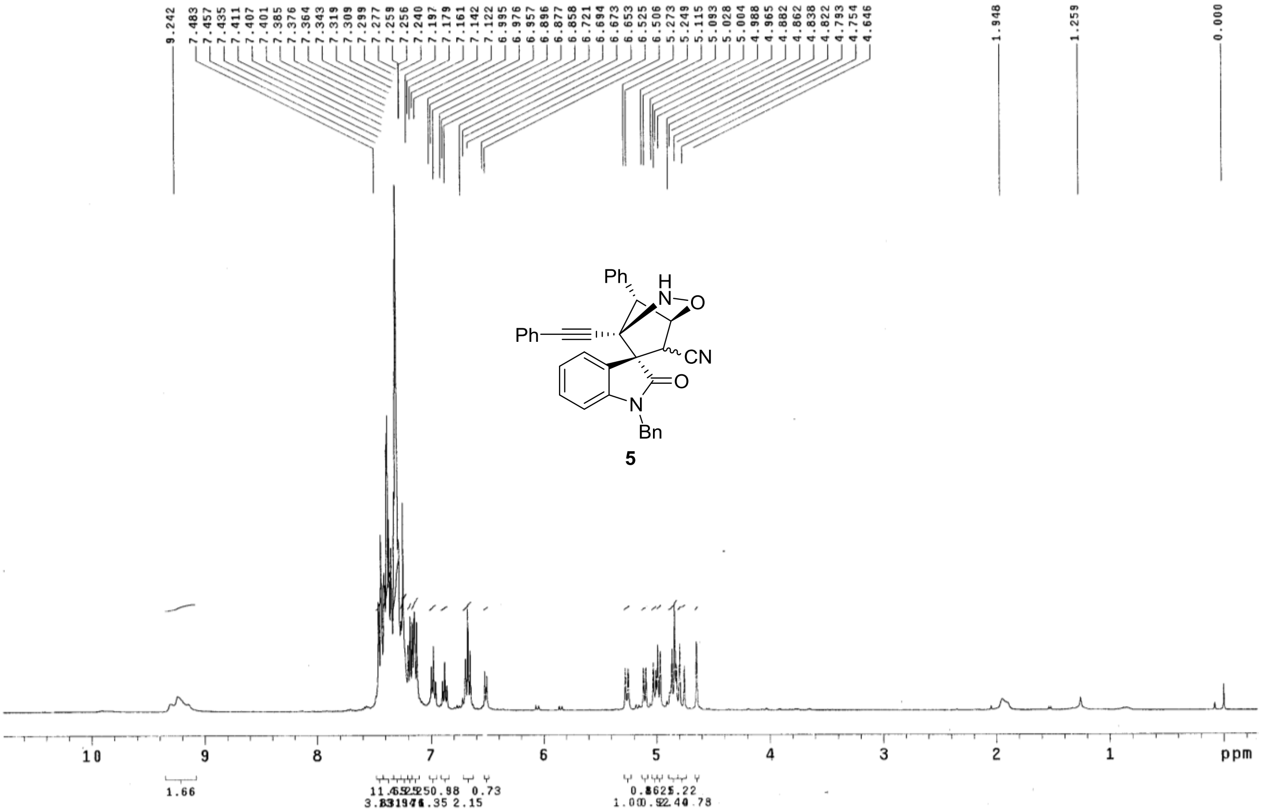

169.60
150.28 147.07 144.18
134.99 131.79 130.08 129.67 129.23 128.89 128.84 128.36 127.69 127.36 127.10 124.11
114.11 110.22
102.35
83.78
77.39 77.27 77.07 76.75 73.31
44.86
Ph
Ph
CN
O
N
Bn
4
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

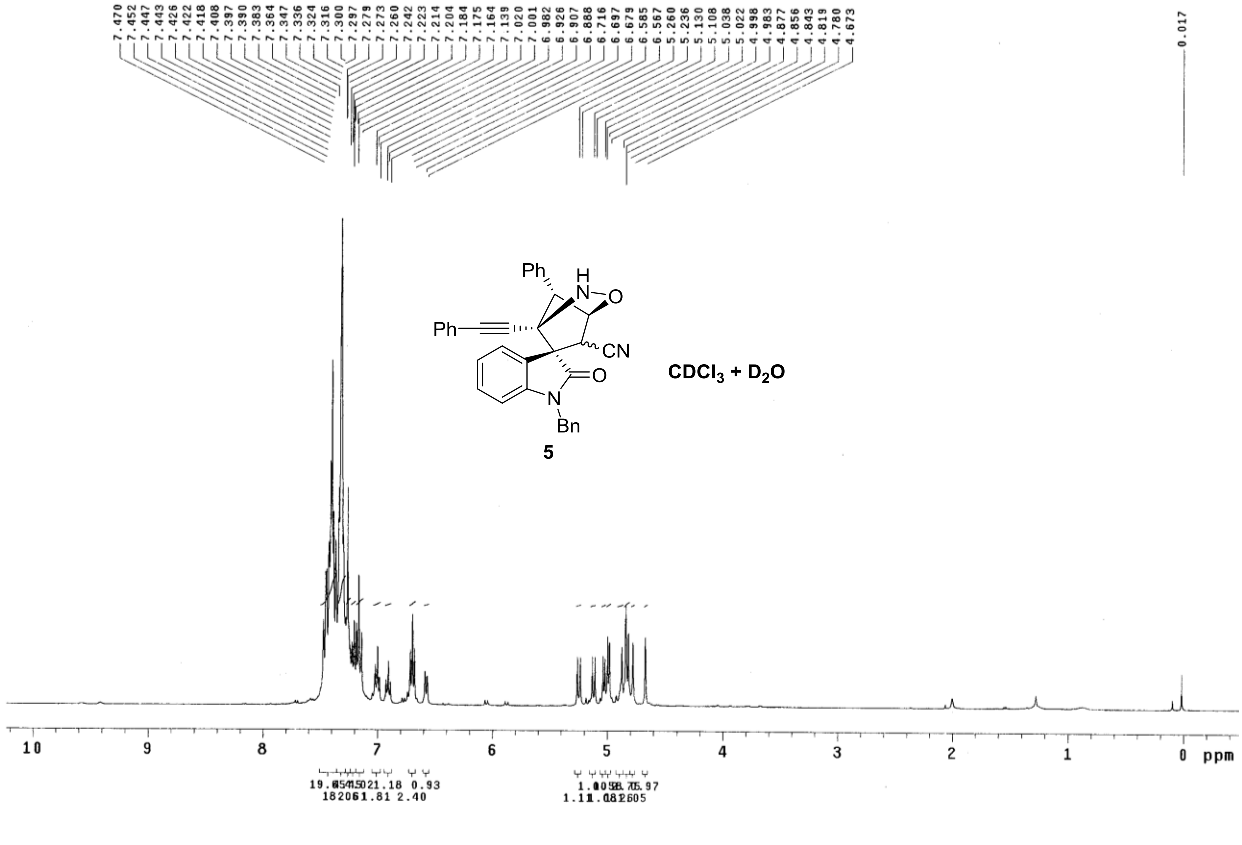


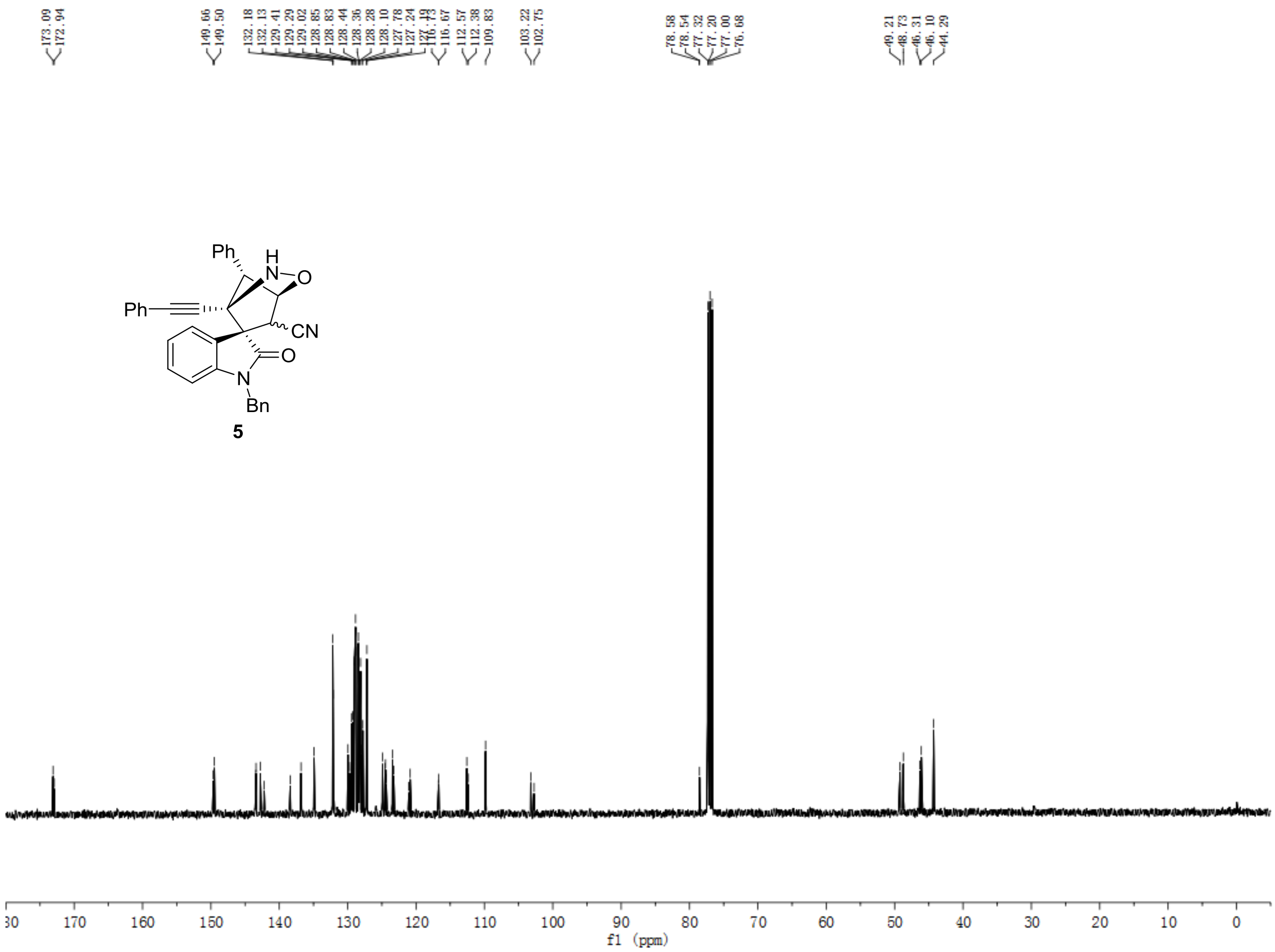
	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	14.856	5869992	49.88	202889	69.29
2	29.655	5898840	50.12	89912	30.71

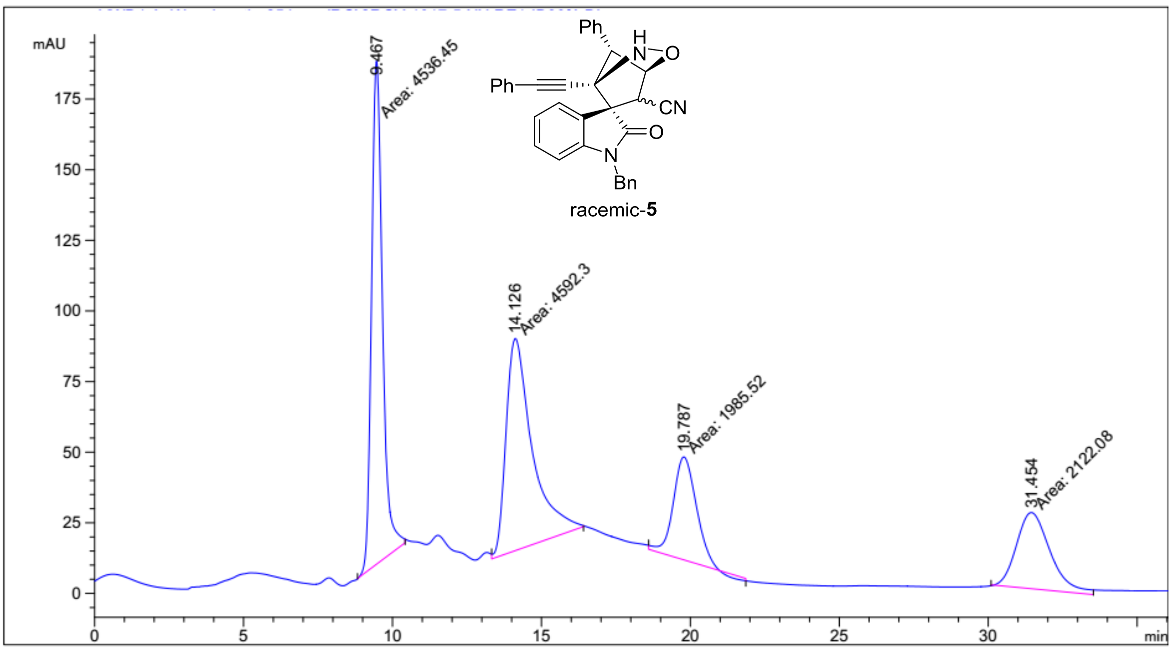


	RT (min)	Area (*sec)	% Area	Height ( )	% Height
1	14.786	40609924	93.17	1366951	96.62
2	29.864	2975102	6.83	47873	3.38

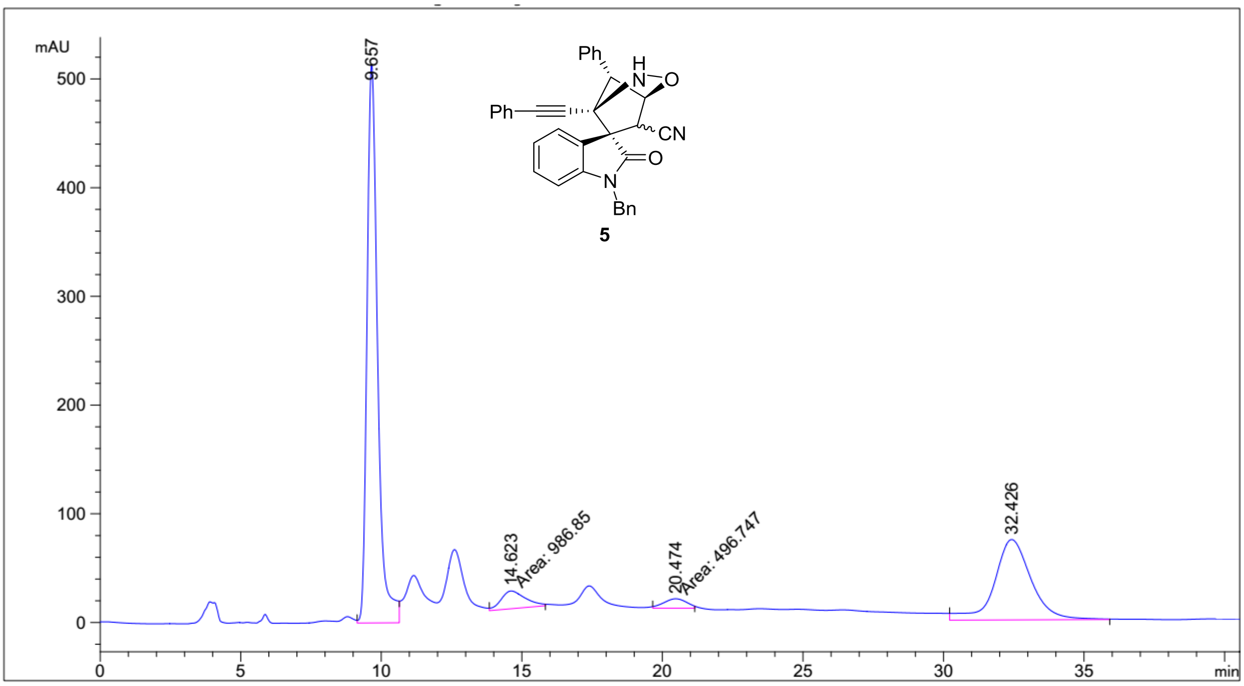

Ph
H
N
O
Ph
CN
O
N
Bn
5
ppm


Ph
H
N
O
Ph
CN
O
N
Bn
5
$CDCl_3 + D_2O$
ppm





Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.467	MM	0.4240	4536.45264	178.30330	34.2727
2	14.126	MM	1.0189	4592.29932	75.12148	34.6946
3	19.787	MM	0.9084	1985.52026	36.42939	15.0005
4	31.454	MM	1.3119	2122.08081	26.96021	16.0322



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.657	VV	0.4038	1.33904e4	512.61932	61.9293
2	14.623	MM	1.0064	986.84979	16.34323	4.5641
3	20.474	MM	0.9490	496.74673	8.72362	2.2974
4	32.426	VB	1.3677	6748.06250	73.93297	31.2092