Asymmetric [4 + 2] Cycloadditions with 3-Furfural Derivatives and α-Cyano-α,β-Unsaturated Ketones

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Supplementary Information

1. General Methods

NMR spectra were recorded with tetramethylsilane as the internal standard. ^{1}H NMR spectra were recorded at 400 or 600 MHz and ^{13}C NMR spectra were recorded at 100 or 150 MHz. Chemical shifts are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) for ^{13}C NMR spectroscopy. Coupling constants are given in Hz. ESI-HRMS was recorded on a Waters SYNAPT G2. In each case, diastereomeric ratio was determined by ^{1}H NMR analysis and enantiomeric ratio was determined by HPLC analysis on a chiral stationary phase in comparison with authentic racemate, using a Daicel Chiralpak AD-H Column (250 × 4.6 mm), Chiralpak ID Column (250 × 4.6 mm). TLC was performed on glass-backed silica plates. UV light and I_2 were used to visualize products. Column chromatography was performed using silica gel (200-300 mesh) eluting with EtOAc/petroleum ether. Optical rotations were measured at 589 nm at 25 ℃. Unless otherwise noted, commercial reagents were used as received and all reactions were carried out directly in air atmosphere. Furfural derivatives **1**[1] and **4**[2] and α-cyano-α,β-unsaturated ketones **2**[3] were obtained according to the literature procedures.

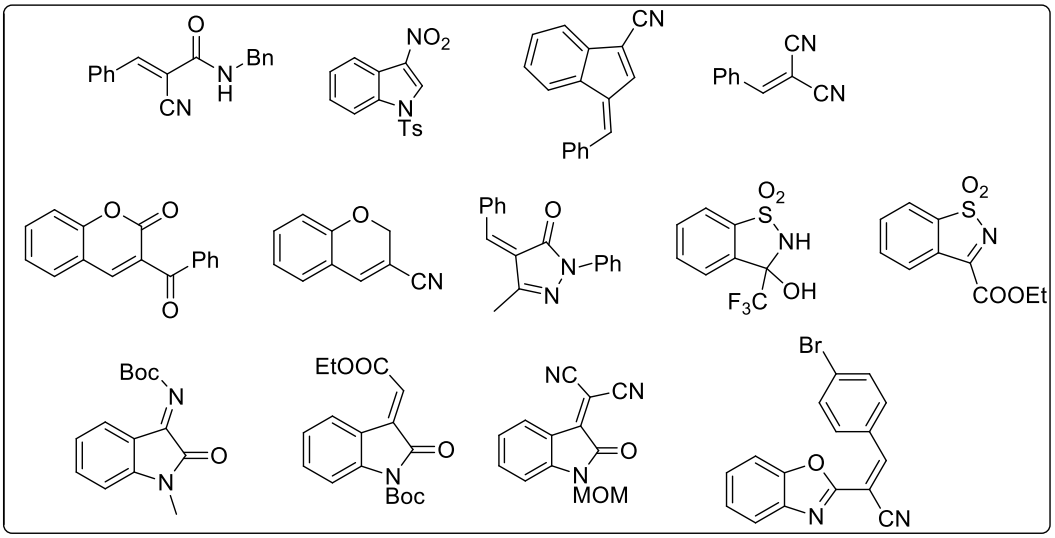
References

1 (*a*) A. R. Kelly, M. H. Kerrigan and P. J. Walsh, *J. Am. Chem. Soc*., 2008, **130**, 4097; (*b*) X.-L. He, H.-R. Zhao, C.-Q. Duan, X. Han, W. Du and Y.-C. Chen, *Chem. Eur. J*., 2018, **24**, 6277.

2 M. Raghu, J. Grover and S. S. V. Ramasastry, *Chem. Eur. J*., 2016, **22**, 18316.

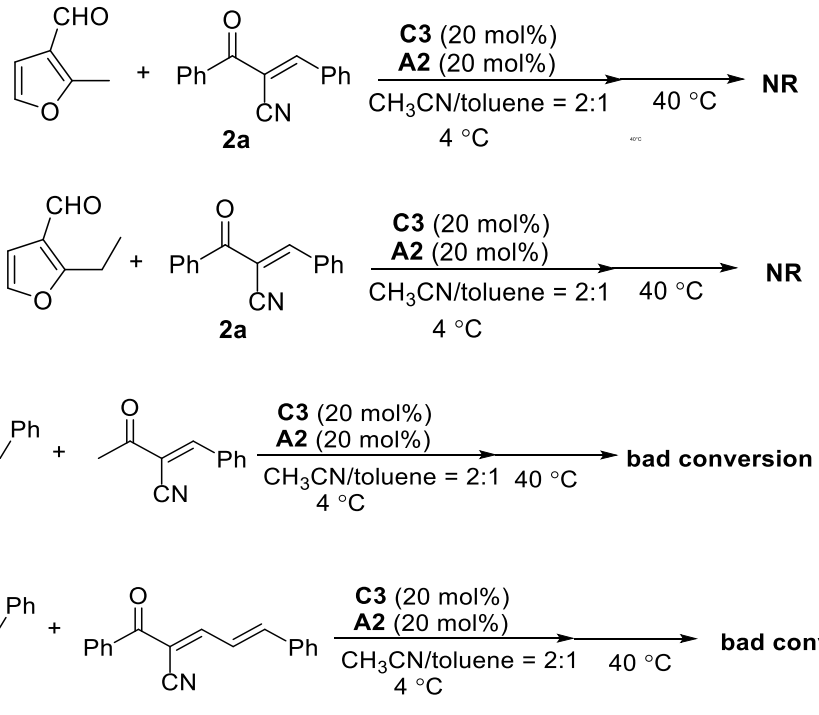
3 (*a*) W.-Q. Yu, Y.-F. Du and K. Zhao, *Org. Lett*., 2009, **11**, 2417; (*b*) P. K. Amanch, Y.-C. Lai, I.-C. Chen, H.-J. Liu and J.-L. Zhu, *Tetrahedron*, 2010, **66**, 871.

2. More screening studies on different electrophiles



To further expand the utility of this strategy, more electron-deficient electrophiles were explored in the reactions with 3-furfural derivative **1a** under the similar catalytic conditions. Unfortunately, the electrophiles outlined in the above scheme did not react with **1a** and failed to give the desired [4 + 2] cycloadducts.

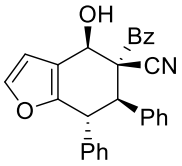
3. Failed attempts on the asymmetric [4 + 2] cycloaddition reactions



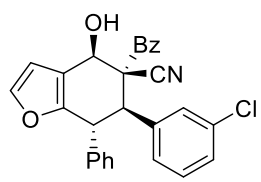
Some substrates with different substituents at the benzylic position were also applied to the standard conditions but failed to give the desired cycloadducts.

4. Typical procedure for the asymmetric [4 + 2] cycloadditions of 3-furfural derivatives

The reaction was carried out with furfural derivative **1** (0.12 mmol), α-cyano-α,β-unsaturated ketone **2** (0.10mmol), catalyst **C3** (0.02 mmol) and **A2** (0.02 mmol) in acetonitrile/toluene (0.67 mL/0.33 mL) at 4 °C for the indicated time. After completion, the solution was purified by flash chromatography on silica gel (THF/petroleum ether = 1/15) to afford the pure chiral product **3**, usually as a mixture of inseparable diastereomers.

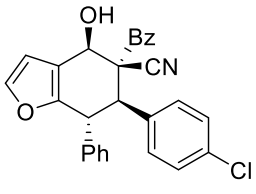


(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-4-hydroxy-6,7-diphenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3a): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-phenylacrylonitrile **2a** (23.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3a** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (38.1 mg) in 91% yield; $[\alpha]_D^{25}$ = –211.75 (*c* = 0.80 in $CHCl_3$); >19:1 dr, 97% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 19.42 min, t (major) = 21.87 min]; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.47– 7.32 (m, 2H), 7.30–7.19 (m, 6H), 7.20–7.06 (m, 6H), 6.96–6.83 (m, 2H), 6.56 (d, *J* = 1.7 Hz, 1H), 5.69 (s, 1H), 4.70 (d, *J* = 10.9 Hz, 1H), 3.77 (d, *J* = 10.9 Hz, 1H), 2.83 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): *δ* (ppm) 198.0, 150.6, 143.6, 137.9, 137.7, 135.4, 134.9, 132.2, 129.5, 128.6, 128.5, 128.4, 128.2, 127.8, 127.4, 120.0, 118.9, 108.2, 72.8, 64.3, 55.7, 45.5; ESI-HRMS: calcd. for $C_{28}H_{21}NO_3$+Na^+ 442.1414, found 442.1415.

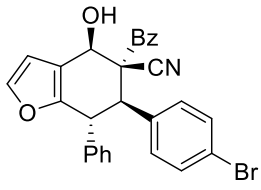


(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-6-(3-chlorophenyl)-4-hydroxy-7-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3b): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(3-chlorophenyl)acrylonitrile **2b**

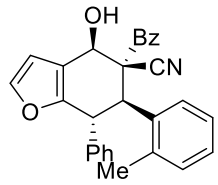
(26.7 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 60 h. Upon workup, product **3b** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (41.2 mg) in 91% yield; $[\alpha]_D^{25}$ = –235.2 (*c* = 0.50 in $CHCl_3$); >19:1 dr, 92% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 16.42 min, t (major) = 18.32 min]; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.44 (t, *J* = 7.4 Hz, 1H), 7.41–7.33 (m, 3H), 7.33–7.23 (m, 5H), 7.22–7.15 (m, 3H), 7.15–7.05 (m, 1H), 6.87 (m, 2H), 6.56 (d, *J* = 1.8 Hz, 1H), 5.64 (s, 1H), 4.61 (d, *J* = 10.9 Hz, 1H), 3.76 (d, *J* = 11.0 Hz, 1H), 2.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 197.5, 150.2, 143.7, 143.6, 137.6, 137.2, 137.0, 134.4, 132.5, 129.8, 129.7, 128.6, 128.5, 128.4, 127.9, 127.6, 127.6, 119.9, 118.7, 108.2, 72.8, 63.8, 55.2, 45.5; ESI-HRMS: calcd. for $C_{28}H_{20}{}^{35}ClNO_3$+$Na^+$ 476.1024, found 476.1025; $C_{28}H_{20}{}^{37}ClNO_3$+$Na^+$ 478.0994, found 478.1005.



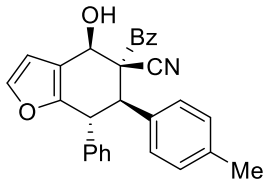
(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-6-(4-chlorophenyl)-4-hydroxy-7-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3c): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(4-chlorophenyl)acrylonitrile **2c** (26.7 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 60 h. Upon workup, product **3c** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (40.8 mg) in 90% yield; $[\alpha]_D^{25}$ = –265.8 (*c* = 0.33 in $CHCl_3$); 17:1 dr, 92% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 24.57 min, t (major) = 21.05 min]; ^{1}H NMR (600 MHz, $CDCl_3$): *δ* (ppm) 7.48–7.31 (m, 4H), 7.31–7.22 (m, 2H), 7.12 (m, 7H), 6.94–6.80 (m, 2H), 6.55 (s, 1H), 5.64 (s, 1H), 4.61 (d, *J* = 10.1 Hz, 1H), 3.77 (d, *J* = 11.0 Hz, 1H), 2.90 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): *δ* (ppm) 197.7, 150.2, 143.7, 137.7, 137.3, 135.3, 134.1, 133.6, 132.5, 130.7, 128.8, 128.5, 128.5, 127.9, 127.5, 120.0, 118.8, 108.2, 72.8, 63.9, 55.0, 45.6; ESI-HRMS: calcd. for $C_{28}H_{20}{}^{35}ClNO_3$+$Na^+$ 476.1024, found 476.1025; $C_{28}H_{20}{}^{37}ClNO_3$+$Na^+$ 478.0994, found 478.1003.



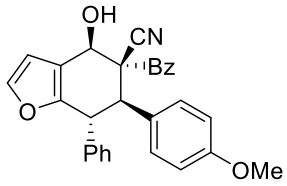
(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-6-(4-bromophenyl)-4-hydroxy-7-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3d): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(4-bromophenyl)acrylonitrile **2d** (31.1 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 60 h. Upon workup, product **3d** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (45.7 mg) in 92% yield; $[\alpha]_D^{25}$ = –261.3 (*c* = 0.95 in $CHCl_3$); 16:1 dr, 96% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 ml/min, λ = 254 nm, t (minor) = 11.64 min, t (major) = 10.11 min]; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.48–7.40 (m, 1H), 7.40–7.32 (m, 3H), 7.32–7.23 (m, 4H), 7.21–7.05 (m, 5H), 6.93–6.82 (m, 2H), 6.56 (d, *J* = 1.8 Hz, 1H), 5.64 (s, 1H), 4.61 (d, *J* = 10.9 Hz, 1H), 3.76 (d, *J* = 11.0 Hz, 1H), 2.76 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 197.6, 150.3, 143.8, 137.6, 137.3, 134.1, 132.6, 131.8, 128.6, 128.5, 128.4, 128.0, 127.6, 127.6, 122.3, 119.9, 118.8, 108.1, 72.8, 63.8, 55.1, 45.5; ESI-HRMS: calcd. for $C_{28}H_{20}{}^{79}BrNO_3$+$Na^+$ 520.0519, found 520.0520; $C_{28}H_{20}{}^{81}BrNO_3$+$Na^+$ 522.0498, found 522.05008.



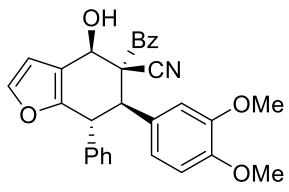
(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-4-hydroxy-7-phenyl-6-(*o*-tolyl)-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3e): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(*o*-tolyl)acrylonitrile **2e** (24.7 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3e** was obtained by flash chromatography on silica gel (THF /petroleum ether = 1/15) as a white solid (38.8 mg) in 90% yield; $[\alpha]_D^{25}$ = –334.1 (*c* = 1.50 in $CHCl_3$); 17:1 dr, >99% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 10.69 min, t (major) = 14.80 min]; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.97 (d, *J* = 7.6 Hz, 1H), 7.46–7.32 (m, 2H), 7.24 (t, *J* = 7.2 Hz, 4H), 7.18–6.96 (m, 5H), 6.82 (m, 3H), 6.60 (s, 1H), 5.71 (s, 1H), 4.58 (d, *J* = 10.3 Hz, 1H), 4.06 (d, *J* = 10.7 Hz, 1H), 1.70 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 197.8, 150.7, 143.6, 138.0, 137.8, 137.7, 134.0, 132.0, 130.6, 128.6, 128.2, 128.0, 127.7, 127.4, 127.2, 126.9, 126.3, 120.7, 119.5, 108.2, 73.1, 63.9, 49.5, 46.8, 19.15; ESI-HRMS: calcd. for $C_{29}H_{23}NO_3$+Na^+ 456.1570, found 456.1572.



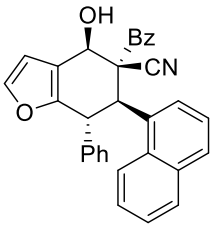
(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-4-hydroxy-7-phenyl-6-(*p*-tolyl)-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3f): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(*p*-tolyl)acrylonitrile **2f** (24.7 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3f** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (36.7 mg) in 85% yield; $[\alpha]_D^{25}$ = –223.0 (*c* = 0.33 in $CHCl_3$); >19:1 dr, 95% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 18.38 min, t (major) = 20.55 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.42–7.30 (m, 2H), 7.30–7.18 (m, 4H), 7.13 (s, 5H), 7.03–6.82 (m, 4H), 6.54 (s, 1H), 5.67 (s, 1H), 4.67 (d, *J* = 10.6 Hz, 1H), 3.75 (d, *J* = 10.9 Hz, 1H), 3.14 (s, 1H), 2.18 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 198.06, 150.57, 143.47, 143.45, 137.95, 137.83, 137.81, 132.09, 131.70, 129.24, 128.54, 128.34, 127.70, 127.41, 127.29, 119.94, 118.95, 108.16, 72.74, 64.40, 55.24, 45.41, 20.94; ESI-HRMS: calcd. for $C_{29}H_{23}NO_3$+Na^+ 456.1570, found 456.1572.



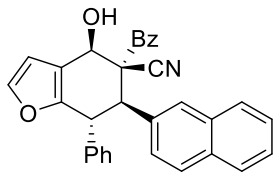
(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-4-hydroxy-6-(4-methoxyphenyl)-7-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3g): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12mmol), (*E*)-2-benzoyl-3-(4-methoxyphenyl) acrylonitrile **2g** (26.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 96 h. Upon workup, product **3g** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (38.6 mg) in 86% yield; $[\alpha]_D^{25}$ = –288.8 (*c* = 0.50 in $CHCl_3$); >19:1 dr, 97% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20,1.0 ml/min, λ =254 nm, t (minor) = 12.11 min, t (major) = 13.26 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41–7.27 (m, 2H), 7.27–7.15 (m, 4H), 7.15–6.99 (m, 5H), 6.89–6.72 (m, 2H), 6.60 (d, *J* = 8.4 Hz, 2H), 6.50 (d, *J* = 1.4 Hz, 1H), 5.61 (d, *J* = 9.8 Hz, 1H), 4.58 (d, *J* = 9.3 Hz, 1H), 3.67 (d, *J* = 11.0 Hz, 1H), 3.62 (s, 3H), 2.65 (d, *J* = 9.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.0, 159.2, 150.7, 143.6, 138.0, 137.8, 132.2, 130.5, 128.6, 128.4, 127.8, 127.5, 127.4, 126.8, 119.9, 119.0, 114.0, 108.1,72.7, 64.5, 55.2, 55.0, 45.6; ESI-HRMS: calcd. for $C_{29}H_{23}NO_4$+Na^+ 472.1519, found 472.1520.



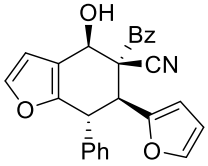
(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-6-(3,4-dimethoxyphenyl)-4-hydroxy-7-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3h): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(3,4-dimethoxy phenyl)acrylonitrile **2h** (29.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 96 h. Upon workup, product **3h** was obtained by flash chromatography on silica gel (THF /petroleum ether = 1/15) as a white solid (38.3 mg) in 80% yield; $[\alpha]_D^{25}$ = –276.1 (*c* = 1.35 in $CHCl_3$); >19:1 dr, 91% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 70/30, 1.0 ml/min, λ = 254 nm, t (minor) = 7.07 min, t (major) = 9.25 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.45–7.29 (m, 4H), 7.25 (t, *J* = 7.3 Hz, 2H), 7.16 (s, 3H), 6.89 (s, 2H), 6.74 (s, 2H), 6.65–6.48 (m, 2H), 5.66 (s, 1H), 4.61 (d, *J* = 10.8 Hz, 1H), 3.75 (s, 3H), 3.70 (d, *J* = 11.1 Hz, 1H), 3.63 (s, 3H), 3.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.0, 150.5, 148.6, 148.6, 143.5,143.5, 137.9, 137.8, 132.2, 128.5, 128.4, 127.8, 127.5, 127.3, 127.2, 121.8, 120.0, 119.2,110.9, 108.1, 72.6, 64.2, 55.8, 55.7, 55.4, 45.8; ESI-HRMS: calcd. for $C_{30}H_{25}NO_5$+ Na^+ 502.1625, found 502.1627.



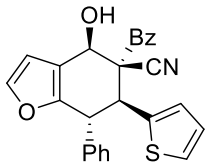
(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-4-hydroxy-6-(naphthalen-1-yl)-7-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3i): 2-Benzylfuran-3-carbaldehyde**1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(naphthalen-1-yl)acrylonitrile **2i** (28.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3i** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (36.6 mg) in 78% yield; $[\alpha]_D^{25}$ = –242.4 (*c* = 0.75 in $CHCl_3$); 8:1 dr, 98 % ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 ml/min, λ = 254 nm, t (minor) = 9.19 min, t (major) =13.63 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.24 (d, *J* = 7.2 Hz, 1H), 7.77–7.53 (m, 3H), 7.47– 7.23 (m, 6H), 7.18–7.06 (m, 2H), 7.05–6.81 (m, 7H), 6.71–6.58 (m, 1H), 5.87 (s, 1H), 4.81 (s, 2H), 3.13 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 196.8, 150.9, 143.6, 137.7, 137.3, 133.5, 132.0, 131.9, 131.8, 128.9, 128.3, 128.2, 128.2, 127.6, 127.3, 127.2, 126.2, 125.6, 125.4, 124.8, 122.5, 120.3, 119.4, 108.3, 73.0, 64.2, 47.5, 47.2; ESI-HRMS: calcd. for $C_{32}H_{23}NO_3$+Na^+492.1570, found 492.1572.



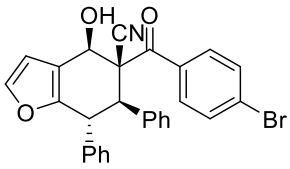
(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-4-hydroxy-6-(naphthalen-2-yl)-7-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3j): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(naphthalen-2-yl) acrylonitrile **2j** (28.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3j** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (35.2 mg) in 75% yield; $[\alpha]_D^{25}$ = –284.0 (*c* = 1.20 in $CHCl_3$); 14:1 dr, 97% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 ml/min, λ= 254 nm, t (minor) = 27.49 min, t (major) = 23.99 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm)7.75–7.56 (m, 4H), 7.47–7.32 (m, 4H), 7.33–7.15 (m, 3H), 7.14–7.01 (m, 5H), 6.96–6.81 (m, 2H), 6.58 (s, 1H), 5.73 (s, 1H), 4.82 (d, *J* = 10.5 Hz, 1H), 3.97 (d, *J* = 10.9 Hz, 1H), 3.06 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): *δ* (ppm)197.8, 150.6, 143.6, 143.6, 137.8, 137.6, 132.9, 132.8, 132.3, 132.2, 128.5, 128.4, 128.4, 128.3, 128.0, 127.7, 127.4, 127.4, 127.4, 126.2, 126.2, 120.0, 119.1, 108.2, 72.9, 64.2, 55.7, 45.6; ESI-HRMS: calcd. for $C_{32}H_{23}NO_3$+Na^+492.1570, found 492.1568.



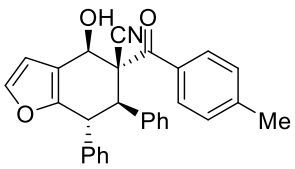
(4*R*,5*S*,6*S*,7*R*)-5-Benzoyl-6-(furan-2-yl)-4-hydroxy-7-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3k): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(furan-2-yl)acrylonitrile **2k** (22.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3k** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (35.2 mg) in 86% yield; $[\alpha]_D^{25}$ = –194.8 (*c* = 0.50 in $CHCl_3$); 13:1 dr, 85% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 17.19 min, t (major) = 20.49 min]; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.58–7.43 (m, 2H), 7.41–7.28 (m, 4H), 7.27–7.17 (m, 4H), 6.99–6.86 (m, 2H), 6.55 (s, 1H), 6.10 (s, 1H), 5.95 (d, *J* = 2.9 Hz, 1H), 5.67 (s, 1H), 4.81 (d, *J* = 10.6 Hz, 1H), 3.90 (d, *J* = 10.9 Hz, 1H), 2.56 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): *δ* (ppm) 197.1, 149.9, 148.5, 143.7, 142.6, 137.7, 137.3, 132.7, 128.5, 128.3, 128.0, 127.9, 127.7, 120.0, 118.3, 110.7, 110.5, 108.2, 72.2, 62.7, 49.8, 43.9; ESI-HRMS: calcd. for $C_{26}H_{19}NO_4$+Na^+ 432.1206, found 432.1209.



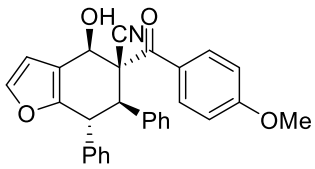
(4*R*,5*S*,6*S*,7*R*)-5-Benzoyl-4-hydroxy-7-phenyl-6-(thiophen-2-yl)-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3l): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-(thiophen-2-yl)acrylonitrile **2l** (23.9 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3l** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (35.3 mg) in 83% yield; $[\alpha]_D^{25}$ = –253.3 (*c* = 0.45 in $CHCl_3$); 17:1 dr, 88% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 18.63 min, t (major) = 22.15 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.42 (d, *J* = 12.6 Hz, 2H), 7.38–7.13 (m, 7H), 7.06 (d, *J* = 4.9 Hz, 1H), 7.02–6.92 (m, 2H), 6.86 (s, 1H), 6.80–6.68 (m, 1H), 6.55 (s, 1H), 5.64 (s, 1H), 4.61 (d, *J* = 10.7 Hz, 1H), 4.12 (d, *J* = 10.8 Hz, 1H), 2.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 197.8, 150.1, 143.6, 137.8, 137.5, 137.3, 135.3, 132.5, 128.5, 128.1, 127.9, 127.6, 127.5, 126.7, 125.4, 120.0, 118.6, 108.2, 72.4, 64.8, 51.3, 47.3; ESI-HRMS: calcd. for $C_{26}H_{19}NO_3S+Na^+$ 448.0978, found 448.0980.



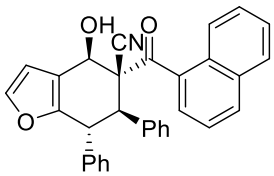
(4*R*,5*S*,6*R*,7*R*)-5-(4-Bromobenzoyl)-4-hydroxy-6,7-diphenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3m): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-(4-bromobenzoyl)-3-phenylacrylonitrile **2m** (31.1 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 60 h. Upon workup, product **3m** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (38.7 mg) in 78% yield; $[\alpha]_D^{25}$ = –207.2 (*c* = 0.50 in $CHCl_3$); >19:1 dr, 98% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH= 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 20.15 min, t (major) = 18.88 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.45–7.33 (m, 2H), 7.31–7.20 (m, 2H), 7.20–7.06 (m, 9H), 6.96–6.79 (m, 2H), 6.58 (d, *J* = 1.6 Hz, 1H), 5.68 (d, *J* = 9.7 Hz, 1H), 4.70 (d, *J* = 10.9 Hz, 1H), 3.75 (d, *J* = 10.9 Hz, 1H), 2.68 (d, *J* = 9.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 197.1, 150.6, 143.8, 143.8, 137.5, 136.6, 134.7, 131.2, 129.5, 129.0, 128.8, 128.5, 128.5, 128.4, 127.5, 119.8, 118.8, 108.0, 72.8, 64.4, 55.7, 45.4; ESI-HRMS: calcd. for $C_{28}H_{20}{}^{79}BrNO_3+Na^+$ 520.0519, found 520.0521; $C_{28}H_{20}{}^{81}BrNO_3+Na^+$ 522.0498, found 522.0510.



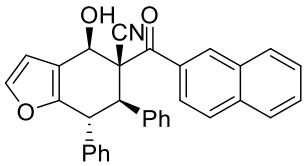
(4*R*,5*S*,6*R*,7*R*)-4-Hydroxy-5-(4-methylbenzoyl)-6,7-diphenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3n)： 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-(4-methylbenzoyl)-3-phenylacrylonitrile **2n** (24.7 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3n** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (38.1 mg) in 88% yield; $[\alpha]_D^{25}$ = –210.5 (*c* = 0.65 in $CHCl_3$); 17:1 dr, 90% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 18.46 min, t (major) = 15.78 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41–7.29 (m, 1H), 7.28–7.19 (m, 4H), 7.18–7.06 (m, 6H), 7.03 (d, 2H), 6.94–6.80 (m, 2H), 6.56 (s, 1H), 5.68 (s, 1H), 4.70 (d, *J* = 10.8 Hz, 1H), 3.78 (d, *J* = 10.9 Hz, 1H), 2.95 (s, 1H), 2.28 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 197.3, 150.5, 143.5, 143.5, 143.1, 137.8, 135.2, 134.9, 128.6, 128.5, 128.5, 128.4, 128.1, 127.8, 127.3, 120.0, 119.1, 108.2, 72.8, 64.0, 55.6, 45.4, 21.5; ESI-HRMS: calcd. for $C_{29}H_{23}NO_3$ +Na^+ 456.1570, found 456.1571.



(4*R*,5*S*,6*R*,7*R*)-4-Hydroxy-5-(4-methoxybenzoyl)-6,7-diphenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (**3o**): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-(4-methoxybenzoyl)-3-phenylacrylonitrile **2o** (26.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3o** was obtained by flash chromatography on silica gel (THF /petroleum ether = 1/15) as a white solid (35.5 mg) in 79% yield; $[\alpha]_D^{25}$ = –296.9 (*c* = 0.65 in $CHCl_3$); 14:1 dr, 99% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 36.94 min, t (major) = 30.10 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 (d, *J* = 8.4 Hz, 1H), 7.35 (s, 1H), 7.25 (s, 2H), 7.19–7.00 (m, 7H), 6.92 (d, *J* = 16.0 Hz, 2H), 6.70 (d, *J* = 8.3 Hz, 2H), 6.54 (d, *J* = 17.4 Hz, 1H), 5.70 (s, 1H), 4.71 (d, *J* = 10.6 Hz, 1H), 3.84 (d, *J* = 37.2 Hz, 1H), 3.75 (s, 3H), 3.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 195.3, 163.0, 150.5, 143.5, 137.9, 135.0, 130.5, 130.5, 129.4, 128.6, 128.5, 128.4, 128.1, 127.3, 120.0, 119.4, 113.1, 108.3, 72.7, 63.6, 55.6, 55.3, 45.4; ESI-HRMS: calcd. for $C_{29}H_{23}NO_4$+Na^+ 472.1519, found 472.1521.

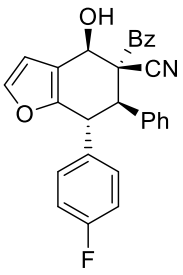


(4*R*,5*S*,6*R*,7*R*)-5-(1-Naphthoyl)-4-hydroxy-6,7-diphenyl-4,5,6,7-tetrahydro benzofuran-5-carbonitrile (3p): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-(1-naphthoyl)-3-phenylacrylonitrile **2p** (28.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3p** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (35.6 mg) in 76% yield; $[\alpha]_D^{25}$ = –135.3 (*c* = 0.90 in $CHCl_3$); >19:1 dr, 95% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 ml/min, λ = 254 nm, t (minor) = 12.76 min, t (major) = 16.99 min]; ^{1}H NMR (400 MHz, $CDCl_3$):*δ* (ppm) 7.87 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.57 (d, *J* = 7.1 Hz, 1H), 7.37 (m, 4H), 7.29–7.01 (m, 9H), 6.86 (s, 2H), 6.55 (s, 1H), 5.74 (d, *J* = 8.7 Hz, 1H), 4.64 (d, *J* = 10.5 Hz, 1H), 3.92 (d, *J* = 10.9 Hz, 1H), 3.01 (d, *J* = 9.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 198.7, 150.8, 143.6, 143.6, 137.6, 135.3,134.7, 133.5, 132.2, 129.4, 128.9, 128.6, 128.4, 128.4, 128.0, 127.4, 127.3, 126.6, 126.1,124.6, 123.5, 120.1, 119.0, 108.1, 73.7, 64.9, 55.7, 46.4; ESI-HRMS: calcd. for $C_{32}H_{23}NO_3$ +Na^+ 492.1570, found 492.1569.

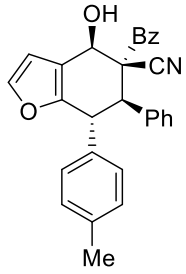


(4*R*,5*S*,6*R*,7*R*)-5-(2-Naphthoyl)-4-hydroxy-6,7-diphenyl-4,5,6,7-tetrah ydrobenzofuran-5-carbonitrile (3q): 2-Benzylfuran-3-carbaldehyde **1a** (22.3 mg, 0.12 mmol), (*E*)-2-(2-naphthoyl)-3-phenylacrylonitrile **2q** (28.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3q** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (36.1 mg) in 77% yield; $[\alpha]_D^{25}$ = –340.0 (*c* = 0.75 in $CHCl_3$); >19:1 dr, 99% ee, determined by HPLC analysis [Daicel chiralpak ID, *n*-hexane/*i*-PrOH= 80/20, 1.0 ml/min, λ = 254 nm, t (minor) = 20.22 min, t (major) = 9.33 min];^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.82 (d, *J* = 13.4 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.6 Hz, 1H), 7.48 (m, 2H), 7.40–7.21 (m, 4H), 7.20–7.07 (m, 6H), 6.95–6.84 (m, 2H), 6.56 (s, 1H), 5.76 (s, 1H), 4.73 (d, *J* = 10.5 Hz, 1H), 3.83 (d, *J* = 10.9 Hz, 1H), 3.14 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): *δ* (ppm) 197.8, 150.5, 143.6, 143.6, 137.7, 135.2, 134.9, 134.7, 131.6, 129.5, 129.1, 128.7,128.6, 128.4, 128.4, 128.2, 127.7, 127.6, 127.4, 126.7, 123.3, 120.0, 119.0, 108.2, 72.8, 64.4, 55.8, 45.4; ESI-HRMS:

calcd. for $C_{32}H_{23}NO_3$ +Na^+ 492.1570, found 492.1571.

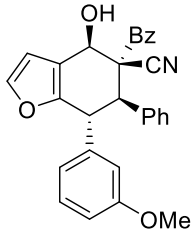


(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-7-(4-fluorophenyl)-4-hydroxy-6-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3r): 2-(4-Fluorobenzyl)furan-3-carbaldehyde **1b** (24.5 mg, 0.12 mmol), (*E*)-2-benzoyl-3-phenylacrylonitrile **2a** (23.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 60 h. Upon workup, product **3r** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (38.5 mg) in 88% yield; $[\alpha]_D^{25}$ = –240.0 (*c* =0.70 in $CHCl_3$); >19:1 dr, 95% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 19.59 min, t (major) = 17.77 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.46–7.31 (m, 2H), 7.31–7.19 (m, 6H), 7.15 (s, 3H), 6.82 (d, J = 12.8 Hz, 4H), 6.57 (s, 1H), 5.67 (s, 1H), 4.69 (d, *J* = 10.7 Hz, 1H), 3.71 (d, *J* = 10.9 Hz, 1H), 2.82 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 197.8, 161.9 (d, *J* = 244.6 Hz), 150.2, 143.7, 143.7, 137.9, 134.6, 133.4 (d, *J* = 3.1 Hz), 132.3, 130.0 (d, *J* = 8.1 Hz), 128.7, 128.3, 127.8, 127.4, 120.1, 118.9, 115.4 (d, *J* = 21.4 Hz), 108.2, 72.8, 64.2, 55.8, 44.8; ESI-HRMS: calcd. for $C_{28}H_{20}FNO_3$ +Na^+ 460.1319, found 460.1320.

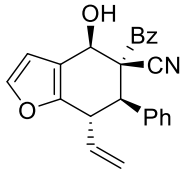


(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-4-hydroxy-6-phenyl-7-(p-tolyl)-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3s):2-(4-Methylbenzyl)furan-3-carbaldehyde **1c** (24.0 mg, 0.12 mmol), (*E*)-2-benzoyl-3-phenylacrylonitrile **2a** (23.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3s** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (38.6 mg) in 89% yield; $[\alpha]_D^{25}$ = –278.8 (*c* = 0.85 in $CHCl_3$); >19:1 dr, 98% ee, determined by HPLC analysis [Daicel chiralpak ID, *n*-hexane/*i*-PrOH= 60/40, 1.0 ml/min, λ = 254 nm, t (minor) = 10.02 min, t (major) = 5.69 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.46–7.31 (m, 2H), 7.31–7.18 (m, 6H), 7.13 (s, 3H), 6.95 (d, *J* = 7.6 Hz, 2H), 6.79 (d, *J* = 7.7 Hz, 2H), 6.55 (s, 1H), 5.68 (s, 1H), 4.67 (d, *J* = 10.6 Hz, 1H), 3.77 (d, *J* = 10.9 Hz, 1H), 2.94 (s, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 198.0, 150.8, 143.5, 138.0, 137.0, 135.0, 134.5, 132.2, 129.5, 129.2, 128.6, 128.4, 128.2, 127.8, 127.4, 119.8, 118.9, 108.1, 72.8, 64.4, 55.6, 45.0, 21.0;

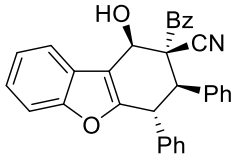
ESI-HRMS: calcd. for $C_{29}H_{23}NO_3$+Na^+ 460.1570, found 456.1567.



(4*R*,5*S*,6*R*,7*R*)-5-Benzoyl-4-hydroxy-7-(3-methoxyphenyl)-6-phenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3t): 2-(3-Methoxybenzyl)furan-3-carbaldehyde **1d** (25.9 mg, 0.12 mmol), (*E*)-2-benzoyl-3-phenylacrylonitrile **2a** (23.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3t** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (38.2 mg) in 85% yield; $[\alpha]_D^{25}$ = –117.1 (c = 0.55 in $CHCl_3$); >19:1 dr, 99% ee, determined by HPLC analysis [Daicel chiralpak ID, *n*-hexane/*i*-PrOH = 60/40, 1.0 ml/min, λ = 254 nm, t (minor) = 17.49 min, t (major) = 8.73 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.43–7.31 (m, 2H), 7.31–7.18 (m, 5H), 7.18–7.00 (m, 5H), 6.68 (d, *J* = 7.7 Hz, 1H), 6.61–6.36 (m, 3H), 5.68 (s, 1H), 4.67 (d, *J* = 10.6 Hz, 1H), 3.77 (d, *J* = 10.9 Hz, 1H), 3.62 (s, 3H), 2.95 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 198.0, 159.4, 150.3, 143.6, 143.6, 139.2, 137.9, 134.9, 132.2, 129.4, 128.6, 128.2, 127.8, 127.4, 120.9, 120.0, 118.9, 114.5, 112.7, 108.1, 72.8, 64.3, 55.5, 55.1, 45.5; ESI-HRMS: calcd. for $C_{29}H_{23}NO_4$+Na^+ 472.1519, found 472.1521.

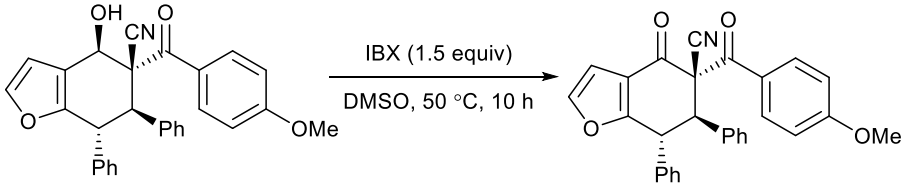


(4*R*,5*S*,6*R*,7*S*)-5-Benzoyl-4-hydroxy-6-phenyl-7-vinyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (3u): 2-Allylfuran-3-carbaldehyde **1e** (16.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-phenylacrylonitrile **2a** (23.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 72 h. Upon workup, product **3u** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (25.1 mg) in 68% yield; $[\alpha]_D^{25}$ = –141.4 (*c* = 0.78 in $CHCl_3$); >19:1 dr, 72% ee, determined by HPLC analysis [Daicel chiralpak ID, *n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm, t (minor) = 26.61 min, t (major) = 20.72 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.44 (s, 1H), 7.42–7.31 (m, 3H), 7.30–7.14 (m, 7H), 6.55 (d, *J* = 1.7 Hz, 1H), 5.69–5.44 (m, 2H), 5.20–4.96 (m, 2H), 4.30–4.09 (m, 1H), 3.59 (d, *J* = 10.9 Hz, 1H), 2.67 (d, *J* = 9.9 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 1978.0, 149.8, 143.6, 137.9, 135.2, 133.5, 132.2, 129.6, 128.8, 128.4, 127.8, 127.4, 120.3, 118.8, 118.7, 108.4, 72.8, 64.0, 53.0, 43.4; ESI-HRMS: calcd. for $C_{24}H_{19}NO_3$+Na^+ 392.1263, found 392.1262.



(1*R*,2*S*,3*R*,4*R*)-2-Benzoyl-1-hydroxy-3,4-diphenyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-2-carbonitrile (5)： 2-Benzylbenzofuran-3-carbaldehyde **4** (28.3 mg, 0.12 mmol), (*E*)-2-benzoyl-3-phenylacrylonitrile **2a** (23.3 mg, 0.10 mmol), catalyst **C3** (10.2 mg, 0.02 mmol) and acid **A2** (2.8 mg, 0.02 mmol) were dissolved in acetonitrile/toluene (0.67 mL/0.33 mL) and stirred at 4 °C for 96 h. Upon workup, product **5** was obtained by flash chromatography on silica gel (THF/petroleum ether = 1/15) as a white solid (33.3 mg) in 71% yield; $[\alpha]_D^{25}$ = –130.3 (*c* = 0.80 in $CHCl_3$); 17:1 dr, 76% ee, determined by HPLC analysis [Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 ml/min, λ = 254 nm, t (minor) = 18.29 min, t (major) = 13.93 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.88–7.74 (m, 1H), 7.46–7.37 (m, 2H), 7.36–7.29 (m, 2H), 7.29–7.21 (m, 5H), 7.16 (s, 7H), 6.99–6.80 (m, 2H), 5.97 (d, *J* = 7.3 Hz, 1H), 4.63 (d, *J* = 10.8 Hz, 1H), 3.81 (d, *J* = 10.9 Hz, 1H), 3.24 (d, *J* = 9.9 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 197.7, 155.5, 153.5, 137.9, 137.3, 134.7, 134.7, 132.3, 128.7, 128.5, 128.5, 128.3, 127.8, 127.5, 127.4, 126.2, 124.7, 123.1, 120.4, 118.7, 114.9, 111.9, 73.4, 64.4, 55.5, 45.4; ESI-HRMS: calcd. for $C_{32}H_{23}NO_3$+Na^+ 492.1570, found 492.1571.

5. Synthetic transformations of [4 + 2] products

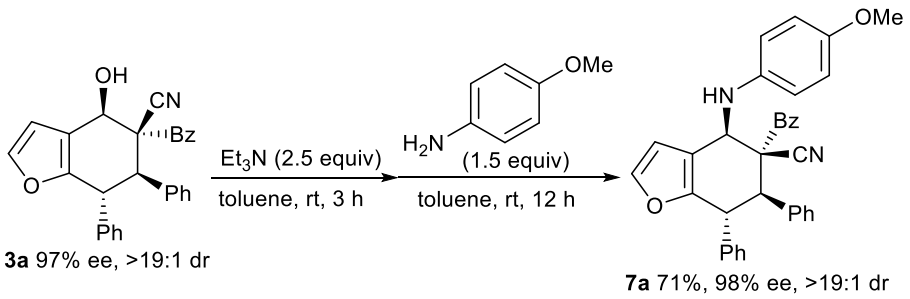


3o 99% ee, 14:1 dr　　**6** 78%, 99% ee, >19:1 dr

To a solution of adduct **3o** (44.9 mg, 0.1 mmol) in DMSO (1 mL) was added IBX (42 mg, 0.15 mmol), The reaction was stirred at 50 °C for 10 h. Upon workup, extraction with EtOAc and purification by flash chromatography on silica gel (THF/petroleum ether = 1/15) to give the product **6** as a white solid (34.9 mg, 78% yield).

(5*R*,6*R*,7*R*)-5-(4-Methoxybenzoyl)-4-oxo-6,7-diphenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (6)： 34.9 mg, white solid, 78% yield; $[\alpha]_D^{25}$= –105.1 (*c* = 1.30 in $CHCl_3$); >19:1 dr, 99% ee, determined by HPLC analysis[Daicel chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, t (minor) = 26.62 min, t (major) = 19.69 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)

7.66–7.52 (m, 2H), 7.43 (d, *J* = 1.9 Hz, 1H), 7.29–7.15 (m, 5H), 7.15–7.08 (m, 3H), 7.06–6.98 (m, 2H), 6.92–6.75 (m, 3H), 4.94 (d, *J* = 11.3 Hz, 1H), 4.50 (d, *J* = 11.3 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 182.4, 167.7, 163.5, 144.9, 144.9, 135.6, 133.7, 132.7, 131.4, 129.2, 128.8, 128.7, 128.5, 128.4, 127.9, 119.7, 116.3, 113.6, 107.5, 65.6, 55.7, 55.5, 45.5; ESI-HRMS: calcd. for $C_{29}H_{21}NO_4$+Na^+ 470.1363, found 470.1361.

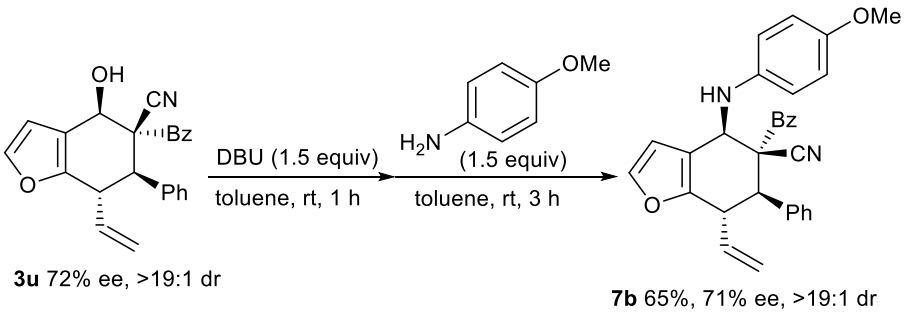


3a 97% ee, >19:1 dr

7a 71%, 98% ee, >19:1 dr

To a solution of adduct **3a** (62 mg, 0.148 mmol) in toluene (1 mL) was added Et_3N (37.4 mg, 0.37 mmol). The reaction was stirred at room temperature for 3 h. Then 4-methoxyaniline (27.3 mg, 0.22 mmol) was added in one pot and the solution was stirred at room temperature for 12 h. Purification by flash chromatography on silica gel (THF/petroleum ether = 1/30) gave the product **7a** as a white solid (55 mg, 71% yield).

(4*R*,5*R*,6*R*,7*R*)-5-Benzoyl-4-((4-methoxyphenyl)amino)-6,7-diphenyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (7a): 55 mg, white solid, 71% yield; $[\alpha]_D^{25}$= –223.0 (*c* = 0.58 in $CHCl_3$); >19:1 dr, 98% ee, determined by HPLC analysis [Daicel chiralpak ID, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, t (minor) = 33.63 min, t (major) = 38.26 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.36–7.23 (m, 4H), 7.23–7.07 (m, 8H), 7.06–6.88 (m, 4H), 6.76 (s, 4H), 6.38 (d, *J* = 1.9 Hz, 1H), 5.67 (dd, *J* = 11.5, 2.5 Hz, 1H), 4.74 (dd, *J* = 11.0, 2.3 Hz, 1H), 3.87 (d, *J* = 11.1 Hz, 2H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.6, 153.7, 150.4, 143.2, 139.8, 137.9, 137.9, 135.1, 131.9, 129.6, 128.7, 128.6, 128.4, 128.2, 127.5, 127.4, 127.2, 120.1, 119.4, 116.97, 114.9, 108.7, 77.3, 77.0, 76.7, 63.5, 59.7, 56.6, 55.7, 45.3; ESI-HRMS: calcd. for $C_{35}H_{28}N_2O_3$+H^+ 525.2173, found 525.2174.



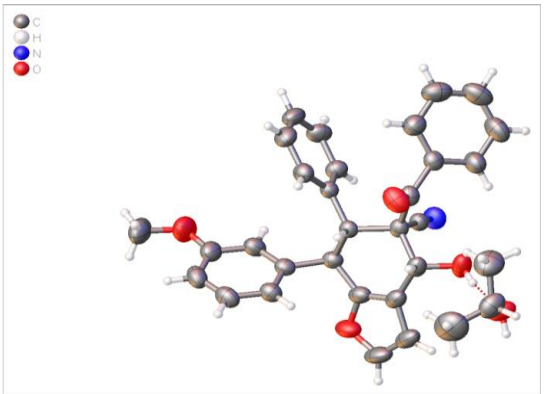
3u 72% ee, >19:1 dr

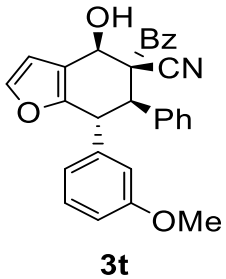
7b 65%, 71% ee, >19:1 dr

To a solution of adduct **3u** (36.9 mg, 0.1 mmol) in toluene (1 mL) was added DBU (22.8 mg, 0.15 mmol). The reaction was stirred at room temperature for 1 h. Then 4-methoxyaniline (18.5 mg, 0.15 mmol) was added in one pot and the solution was stirred at room temperature for 3 h. Upon workup, purification by flash chromatography on silica gel (THF/petroleum ether = 1/30) gave the product **7b** as a white solid (30.8 mg, 65% yield).

(4*R*,5*R*,6*R*,7*S*)-5-Benzoyl-4-((4-methoxyphenyl)amino)-6-phenyl-7-vinyl-4,5,6,7-tetrahydrobenzofuran-5-carbonitrile (7b)： 30.8 mg, white solid, 65% yield; $[\alpha]_D^{25}$ = –187.5 (*c* = 0.68 in $CHCl_3$); >19:1 dr; 71% ee, determined by HPLC analysis [Daicel chiralpak ID, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, t (minor) = 19.36 min, t (major) = 29.71 min]; ^{1}H NMR (600 MHz, $CDCl_3$) : *δ* (ppm) 7.37 (d, *J* = 14.1 Hz, 2H), 7.33–7.25 (m, 4H), 7.25–7.18 (m, 1H), 7.11 (t, *J* = 7.5 Hz, 2H), 6.98 (d, *J* = 7.7 Hz, 2H), 6.73 (q, *J* = 8.5 Hz, 4H), 6.34 (s, 1H), 5.66–5.45 (m, 2H), 5.20–4.99 (m, 2H), 4.24 (t, *J* = 9.5 Hz, 1H), 3.79 (d, *J* = 11.4 Hz, 1H), 3.73 (s, 3H), 3.69 (d, *J* = 10.9 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): *δ* (ppm) 198.6, 153.7, 149.5, 143.1, 139.8, 137.9, 135.4, 133.8, 131.9, 128.9, 128.4, 127.5, 127.2, 120.2, 119.2, 119.1, 117.0, 114.9, 112.5, 109.0, 63.1, 59.6, 55.6, 53.8, 43.2; ESI-HRMS: calcd. for $C_{31}H_{26}N_2O_3$+H^+ 475.2016, found 475.2026.

6. Crystal data and structural refinement for enantiopure 3t

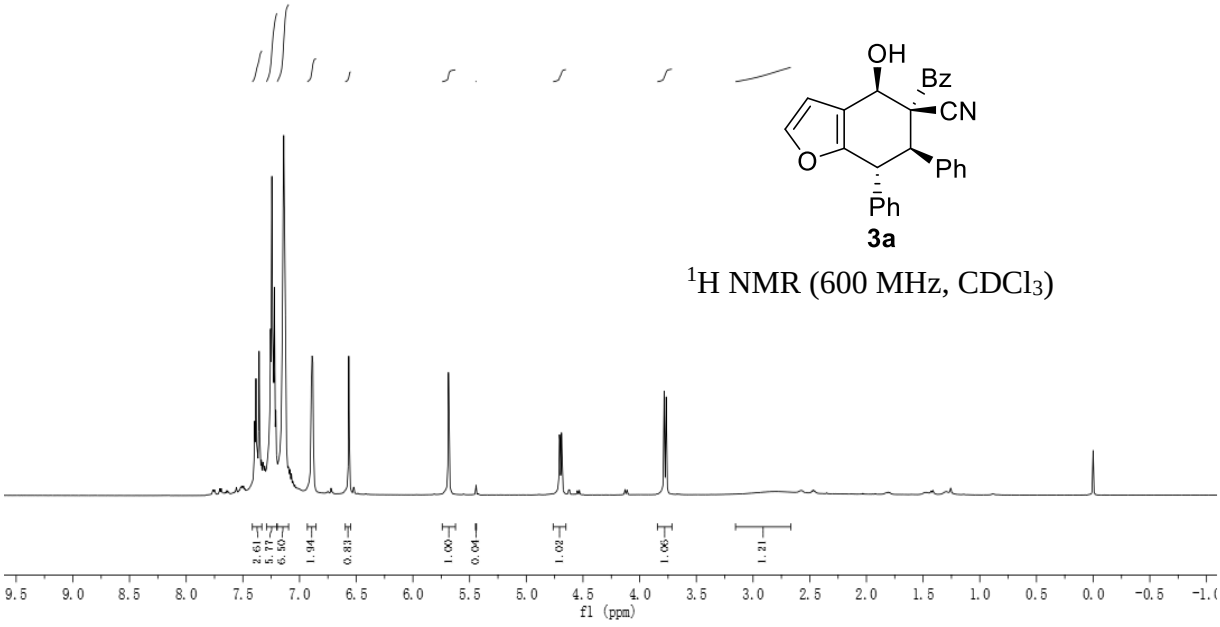




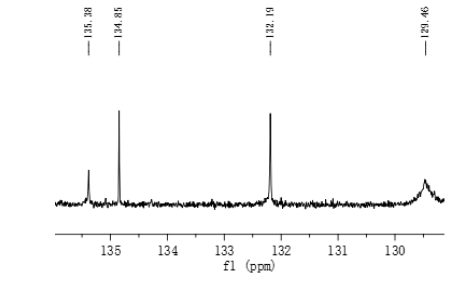
3t

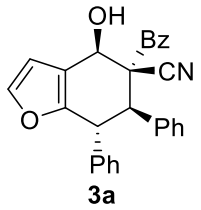
Identification code	**3t**
Empirical formula	$C_{32}H_{31}NO_5$
Formula weight	509.61
Temperature/K	297.6(8)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	10.1535(2)
b/Å	10.5316(2)
c/Å	25.5650(6)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2733.73(10)
Z	4
ρ_{calc}g/cm^3	1.2381
μ/mm^{-1}	0.672
F(000)	1083.5
Crystal size/mm^3	0.65 × 0.5 × 0.4
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.08 to 145.64
Index ranges	-12 ≤ h ≤ 12, -12 ≤ k ≤ 12, -30 ≤ l ≤ 30
Reflections collected	24296
Independent reflections	5334 [R_{int} = 0.0318, R_{sigma} = 0.0188]
Data/restraints/parameters	5334/0/347
Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0432, wR_2 = 0.1184
Final R indexes [all data]	R_1 = 0.0447, wR_2 = 0.1208
Largest diff. peak/hole / e Å^{-3}	0.14/-0.21
Flack parameter	-0.06(16)

7. NMR spectra and HPLC chromatograms

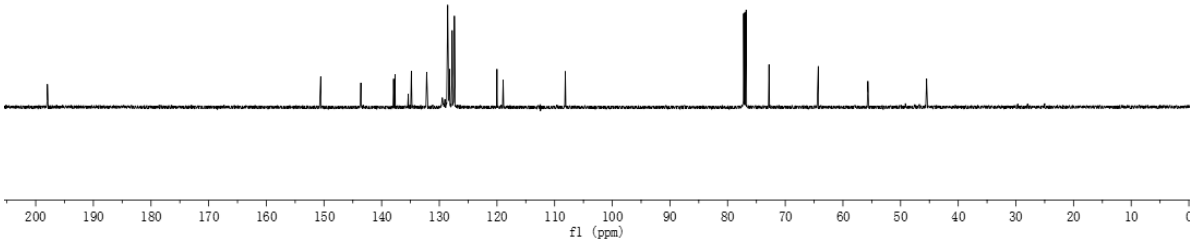


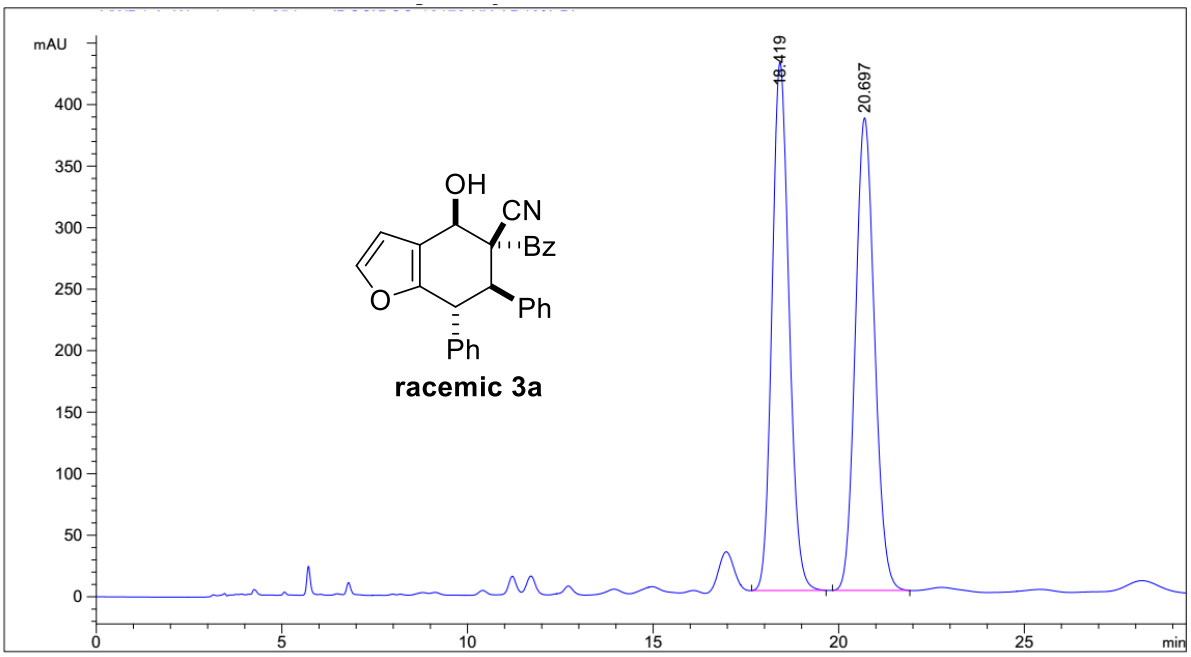
^{1}H NMR (600 MHz, $CDCl_3$)





^{13}C NMR (150 MHz, $CDCl_3$)





Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
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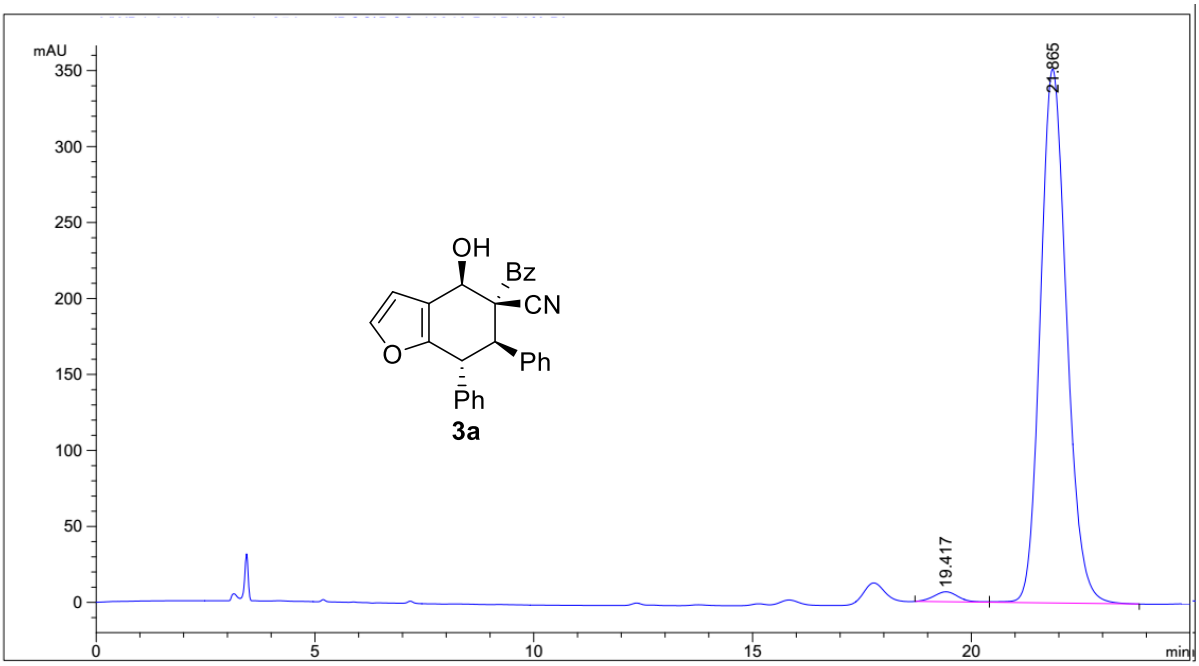
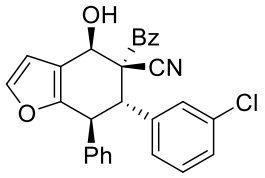
2	20.697	BB	0.5586	1.37883e4	384.10623	50.1837

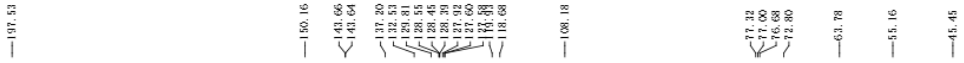


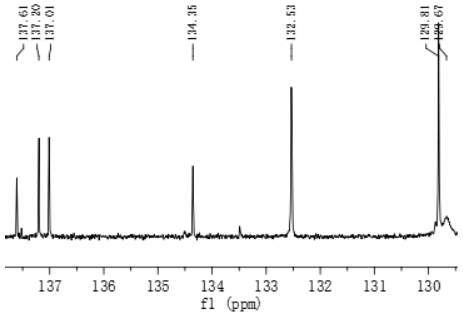
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.417	BV	0.6529	255.01956	6.37681	1.7063
2	21.865	VB	0.6810	1.46904e4	346.50735	98.2937

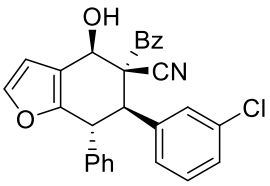


3b

^{1}H NMR (600 MHz, $CDCl_3$)

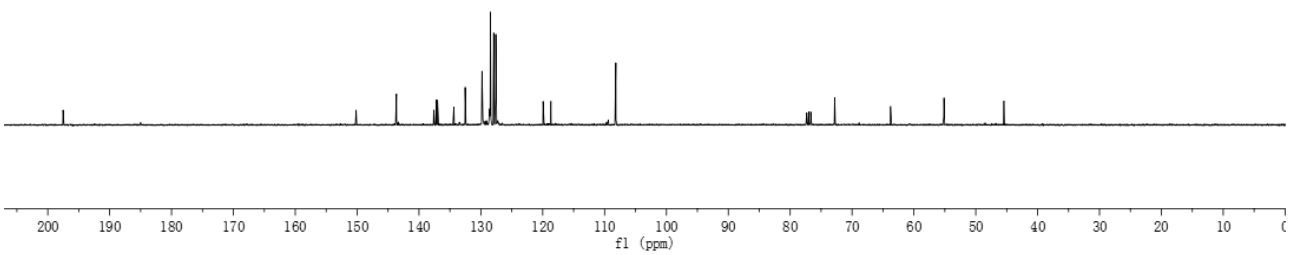


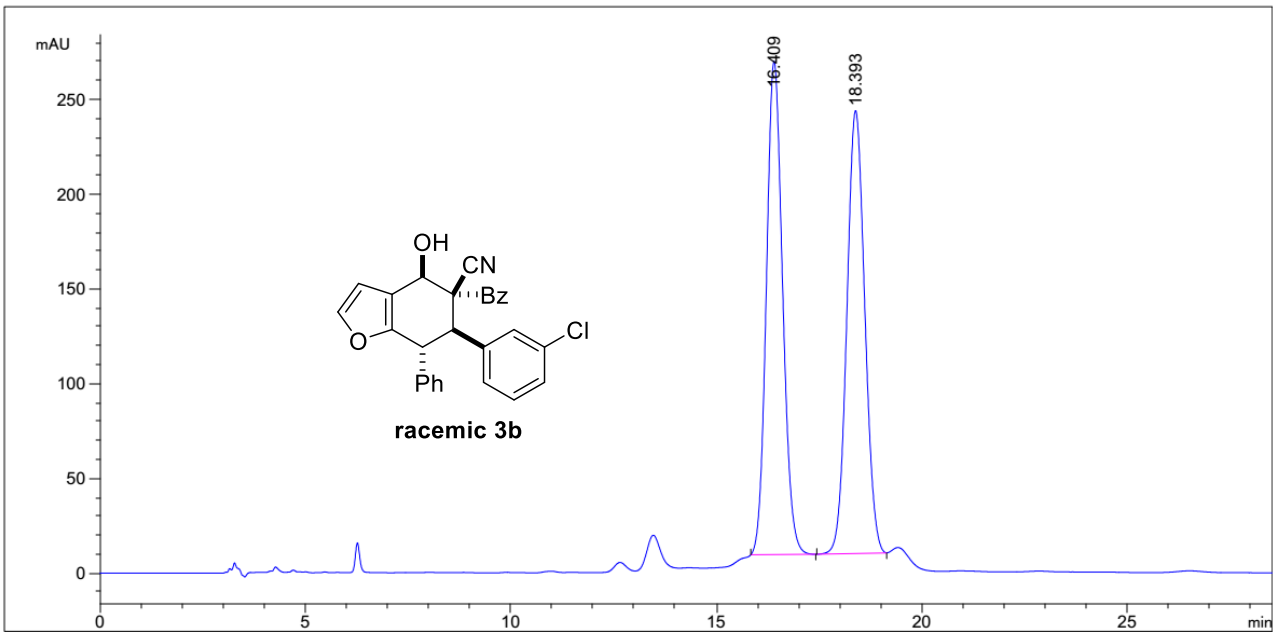




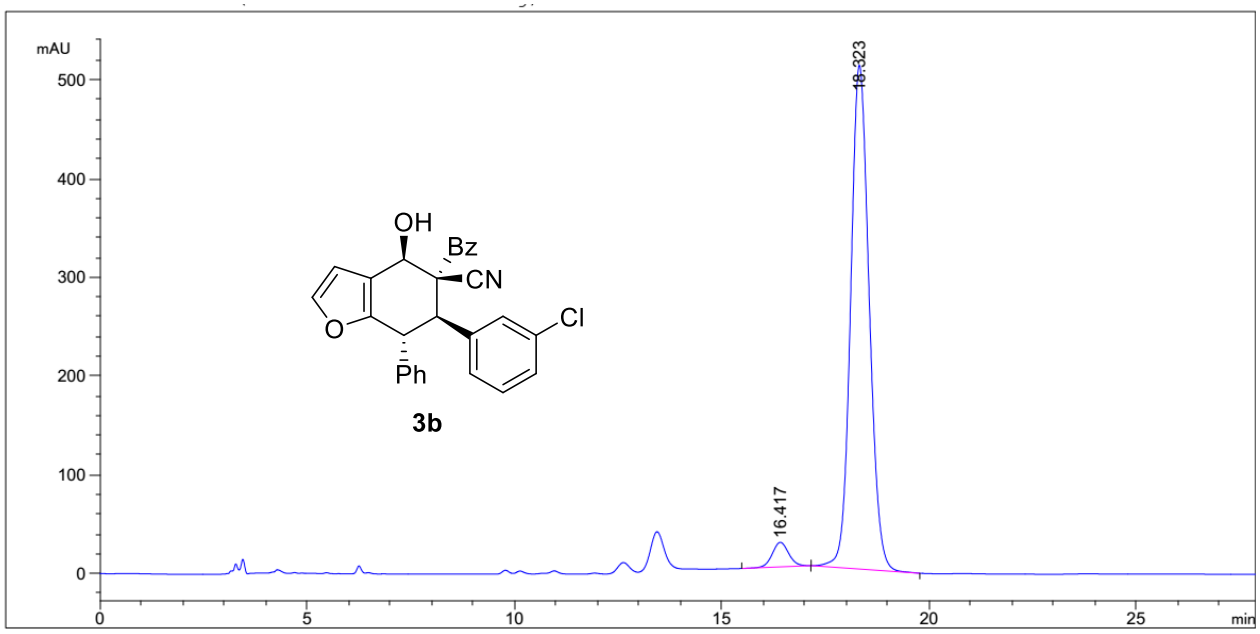
3b

^{13}C NMR (100 MHz, $CDCl_3$)

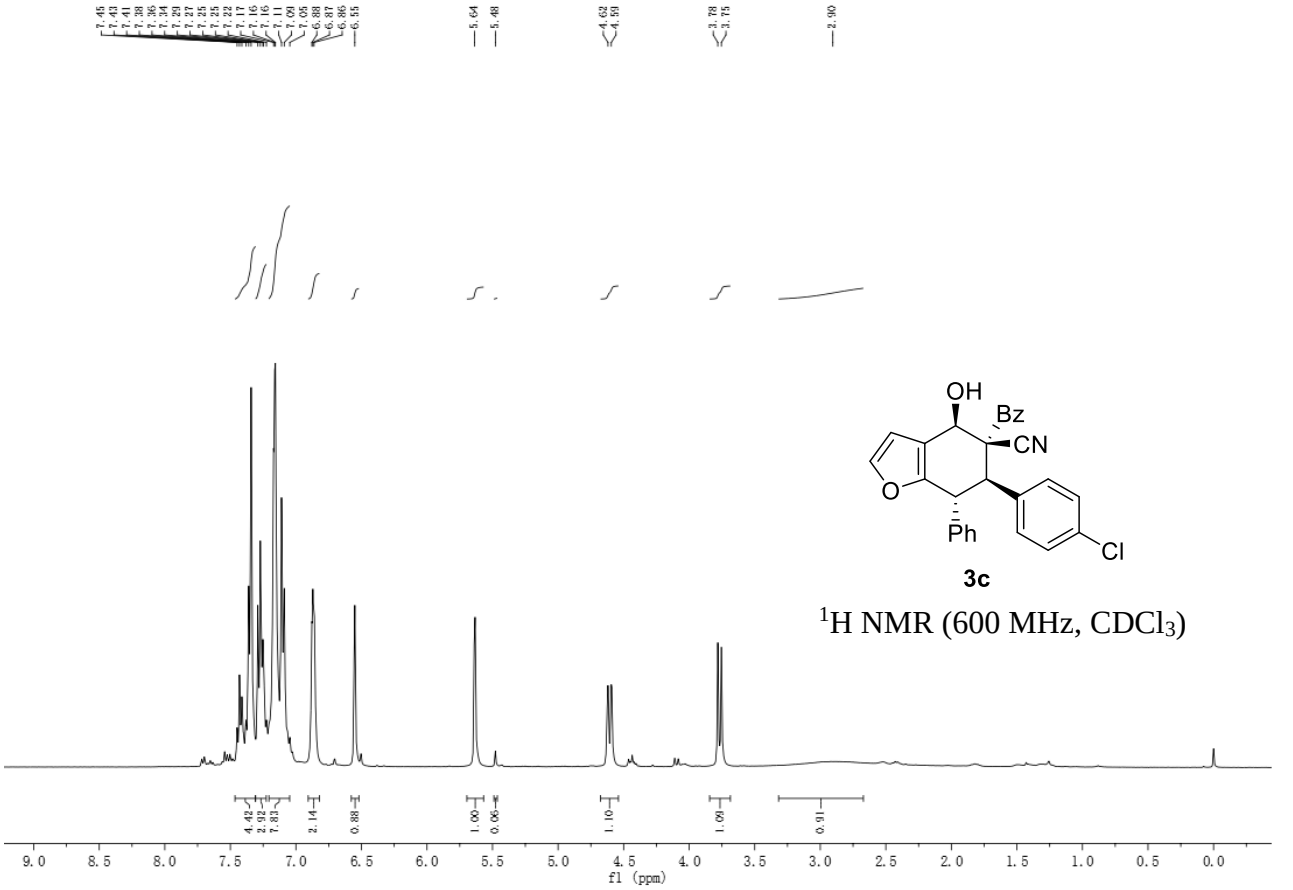




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.409	BB	0.4248	7144.32227	260.52994	50.2486
2	18.393	BB	0.4709	7073.62354	233.78799	49.7514

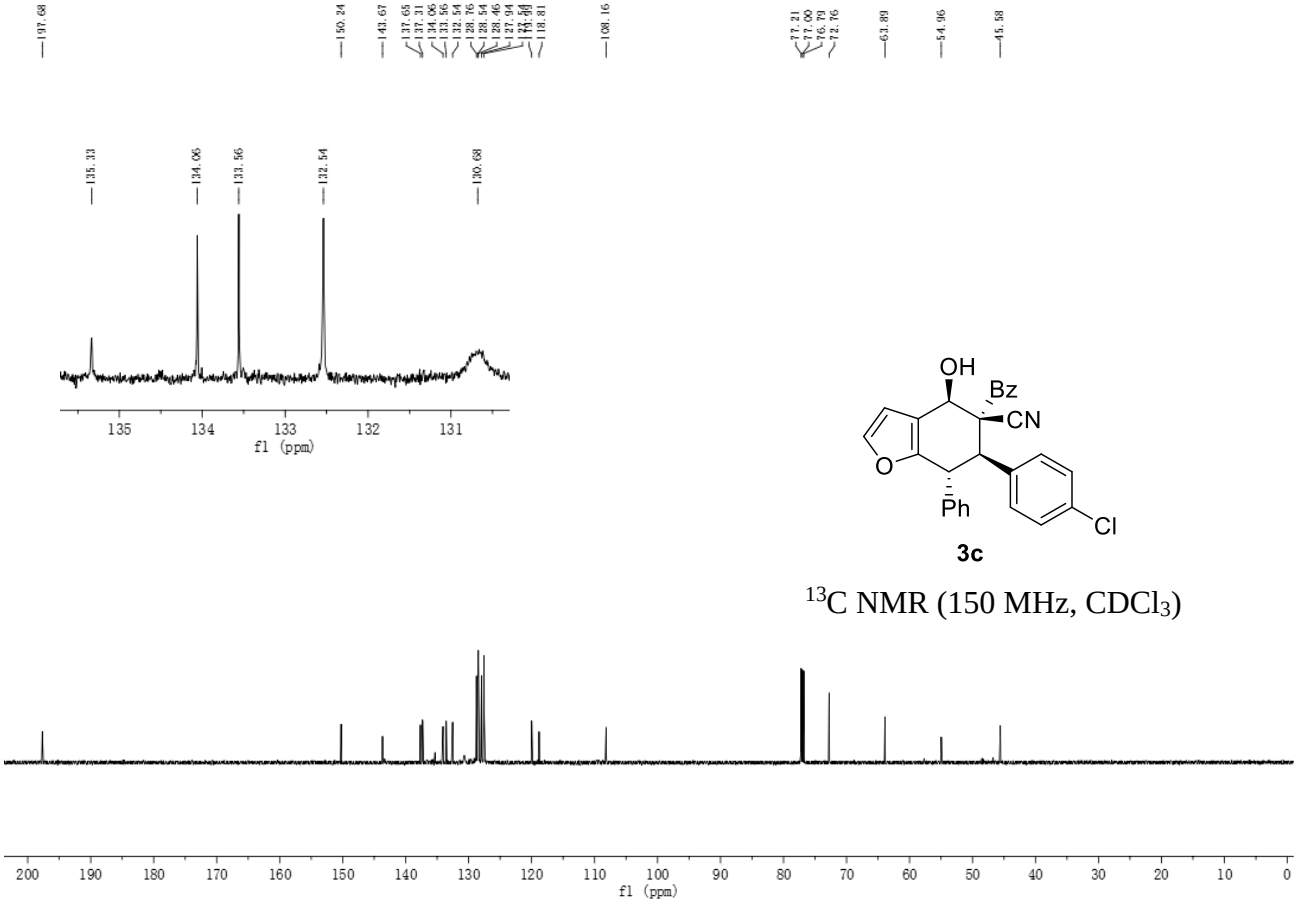


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.417	BB	0.4282	687.95923	24.93551	4.1601
2	18.323	BB	0.4804	1.58493e4	510.19644	95.8399



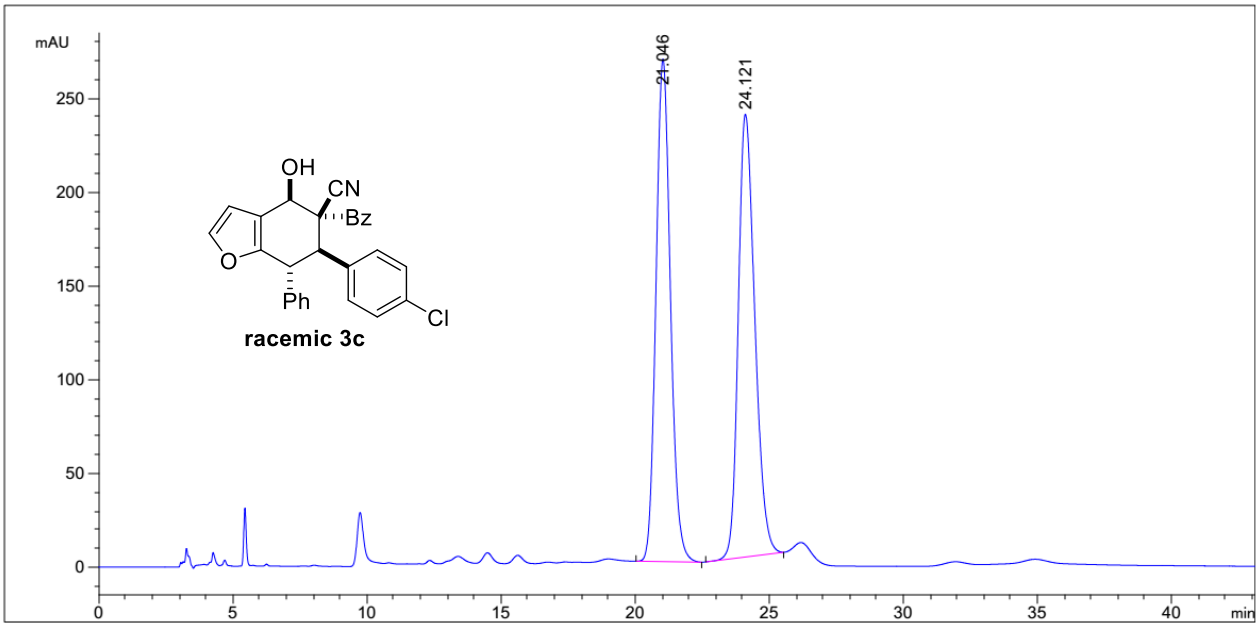
3c

^{1}H NMR (600 MHz, $CDCl_3$)

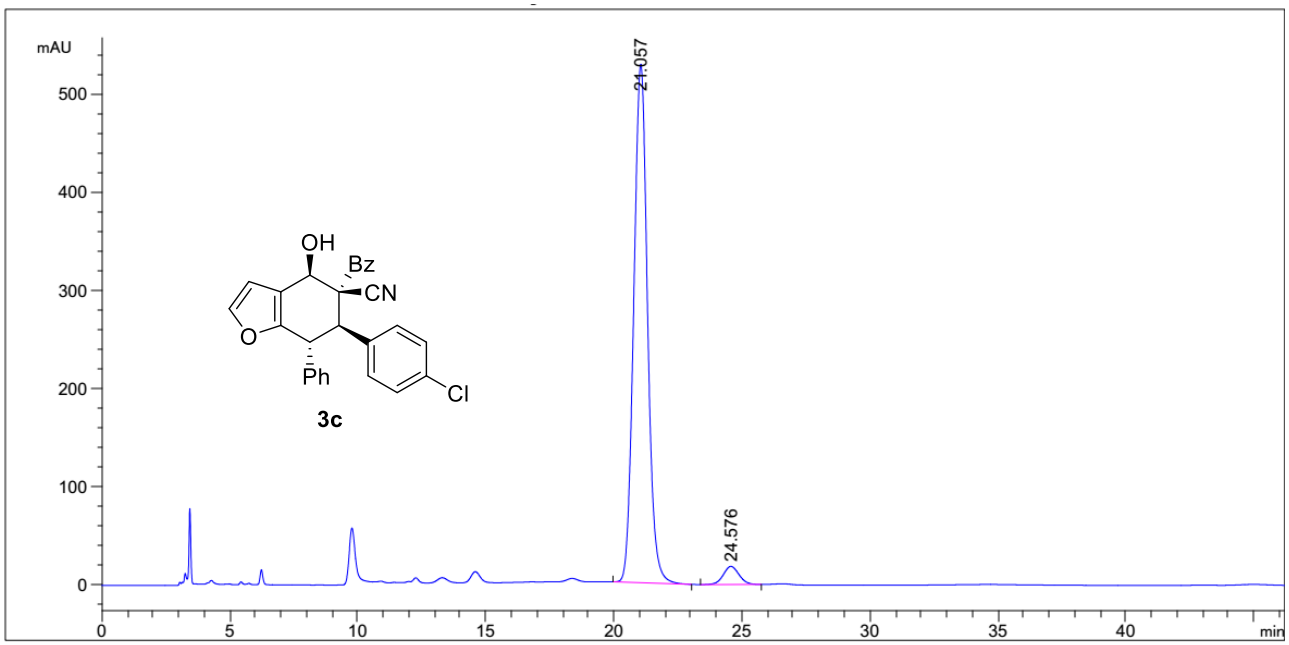


3c

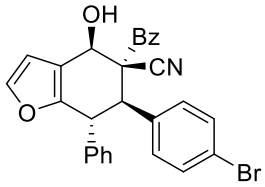
^{13}C NMR (150 MHz, $CDCl_3$)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.046	BB	0.5793	1.00302e4	268.01495	49.7708
2	24.121	BB	0.6632	1.01226e4	236.12740	50.2292

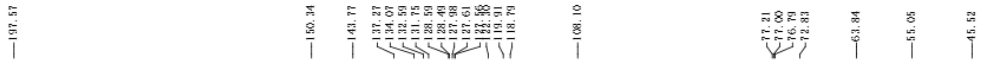


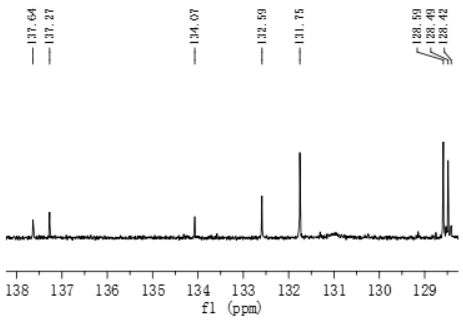
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.057	BB	0.5752	1.96334e4	527.82922	96.1309
2	24.576	BB	0.6499	790.21405	18.49384	3.8691

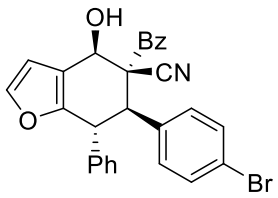


3d

^{1}H NMR (600 MHz, $CDCl_3$)

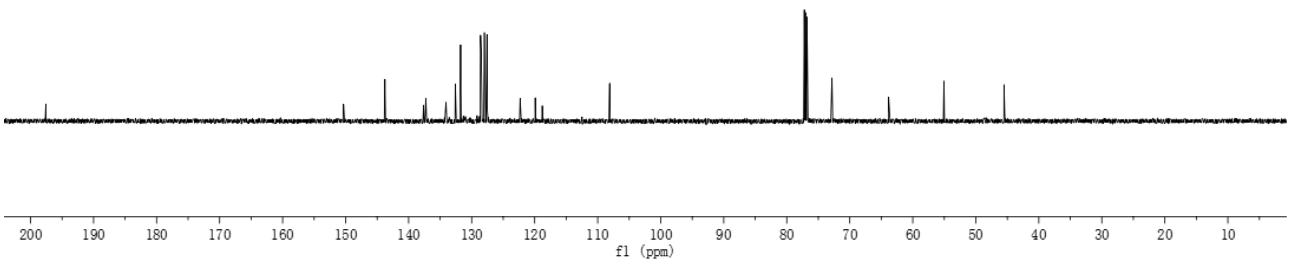


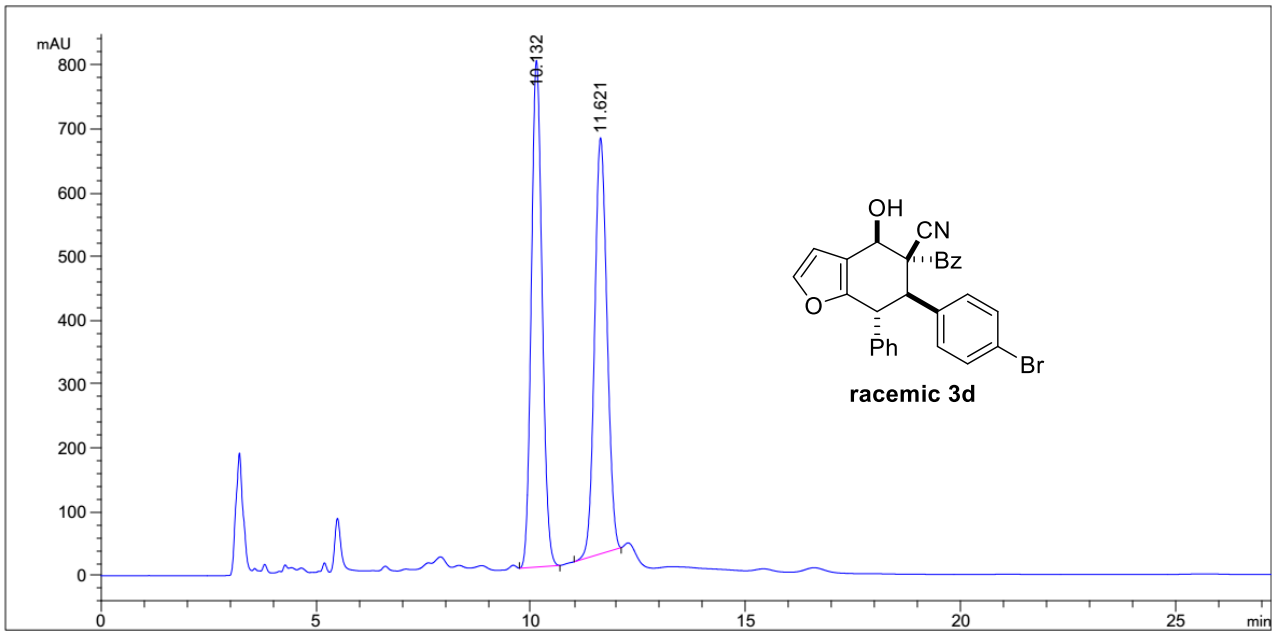




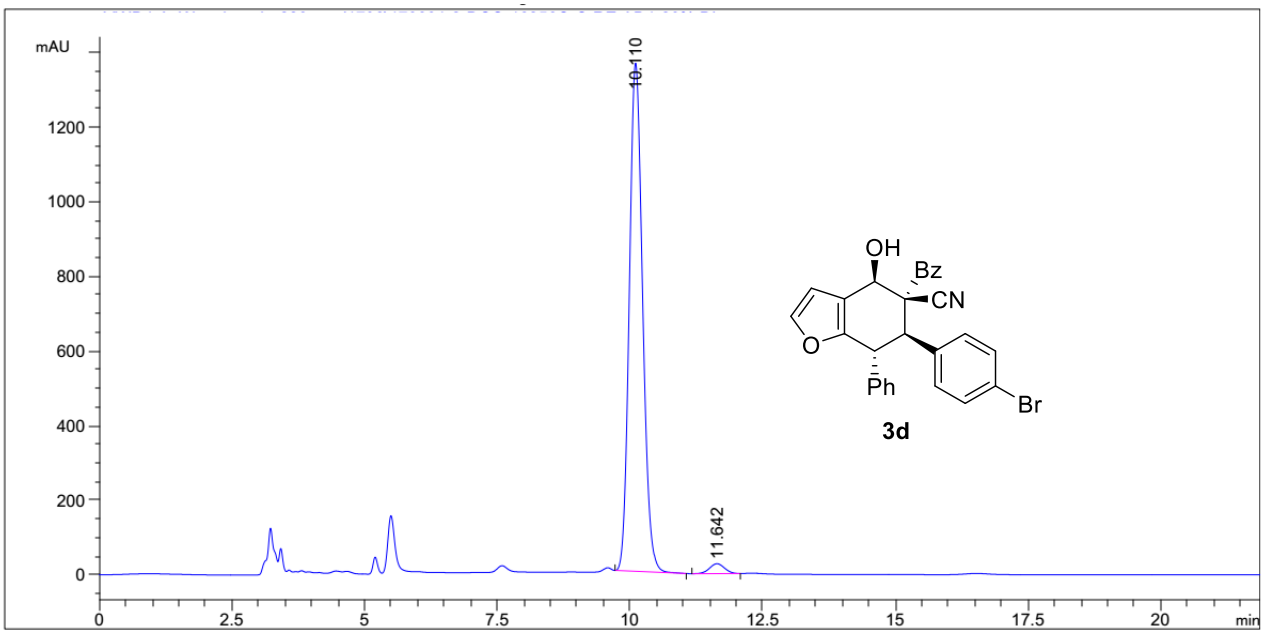
3d

^{13}C NMR (150 MHz, $CDCl_3$)

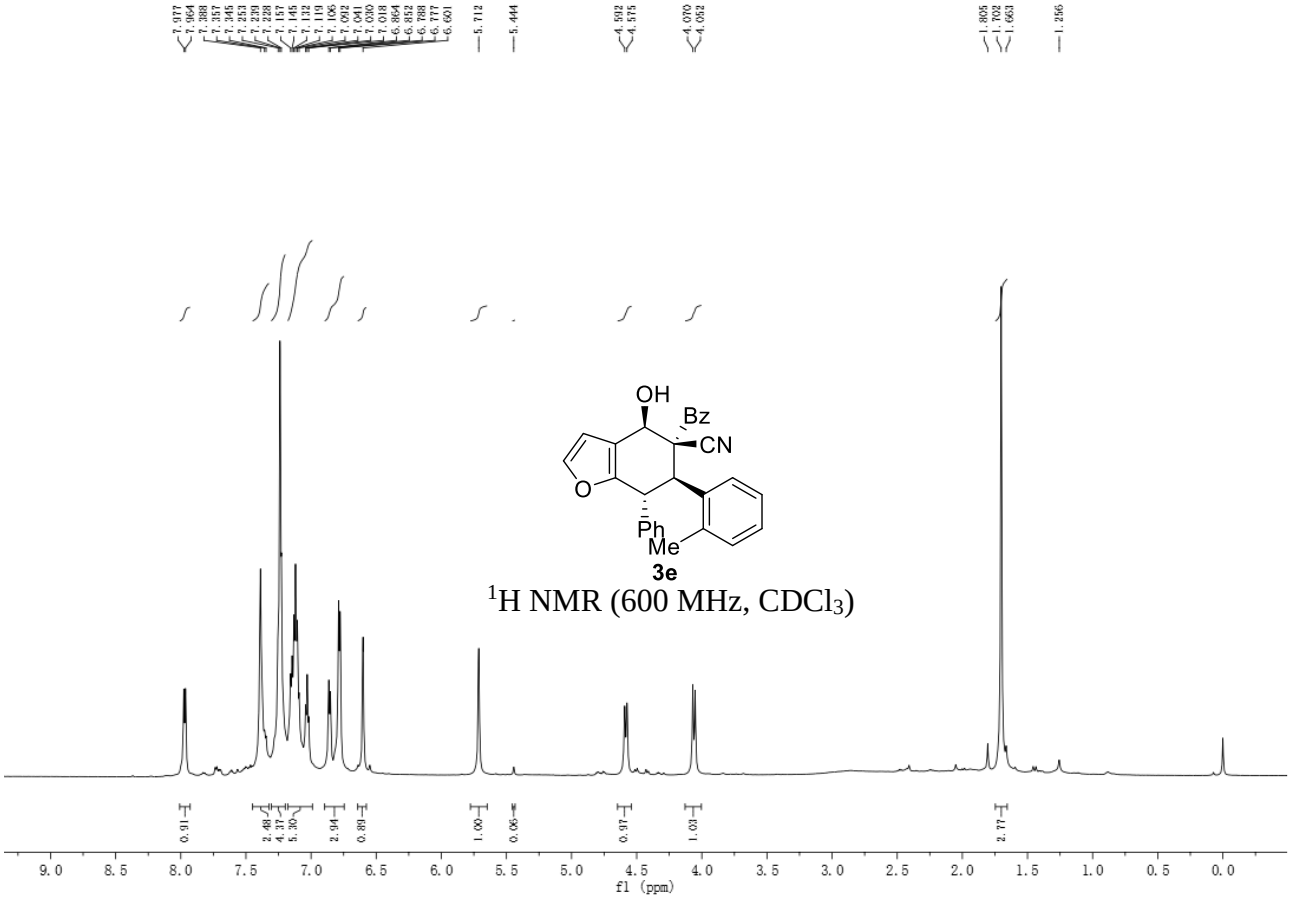




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.132	BB	0.2709	1.38702e4	793.66132	51.4740
2	11.621	BB	0.3112	1.30759e4	651.88141	48.5260

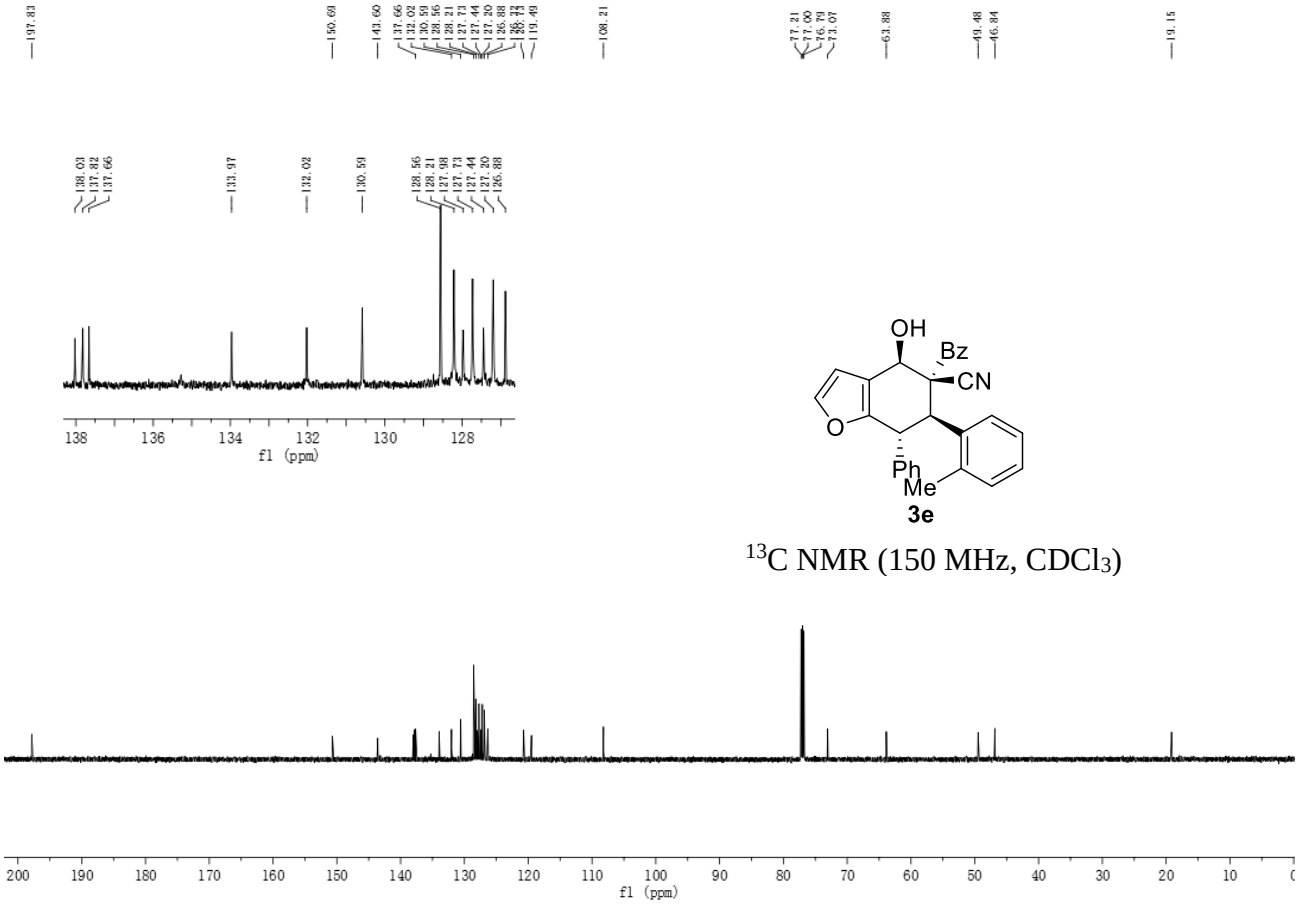


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.110	BB	0.2704	2.37462e4	1362.15295	97.8644
2	11.642	BB	0.3060	518.19788	26.42245	2.1356



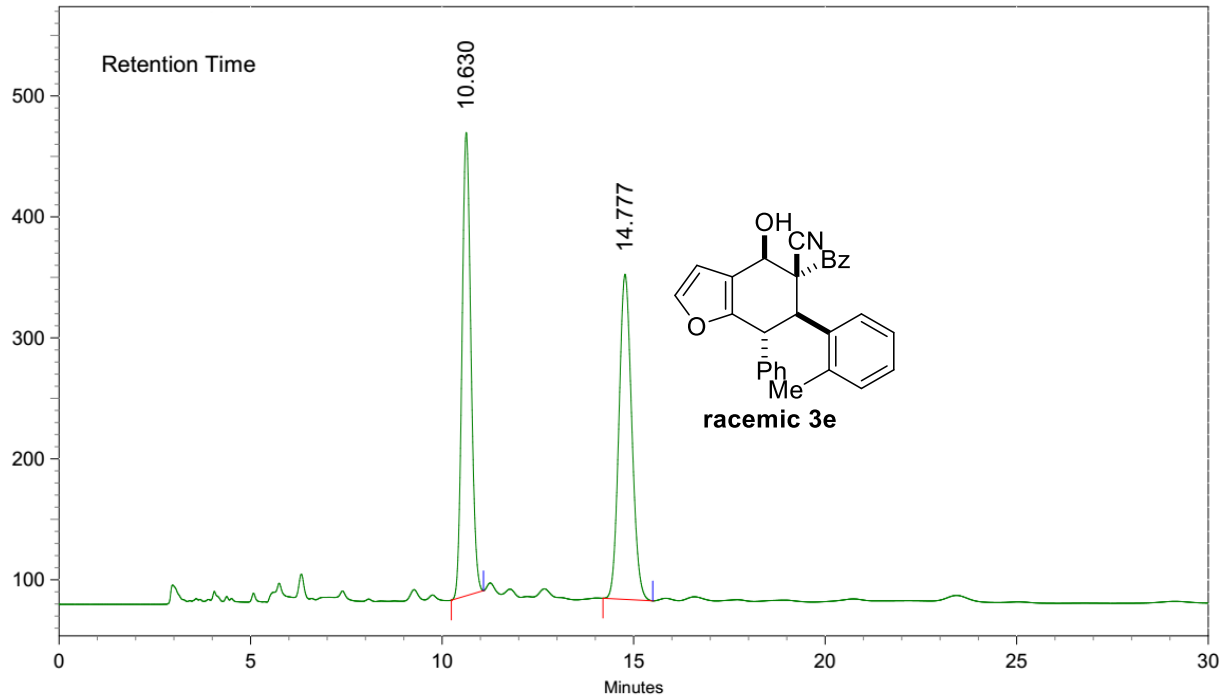
3e

^{1}H NMR (600 MHz, $CDCl_3$)

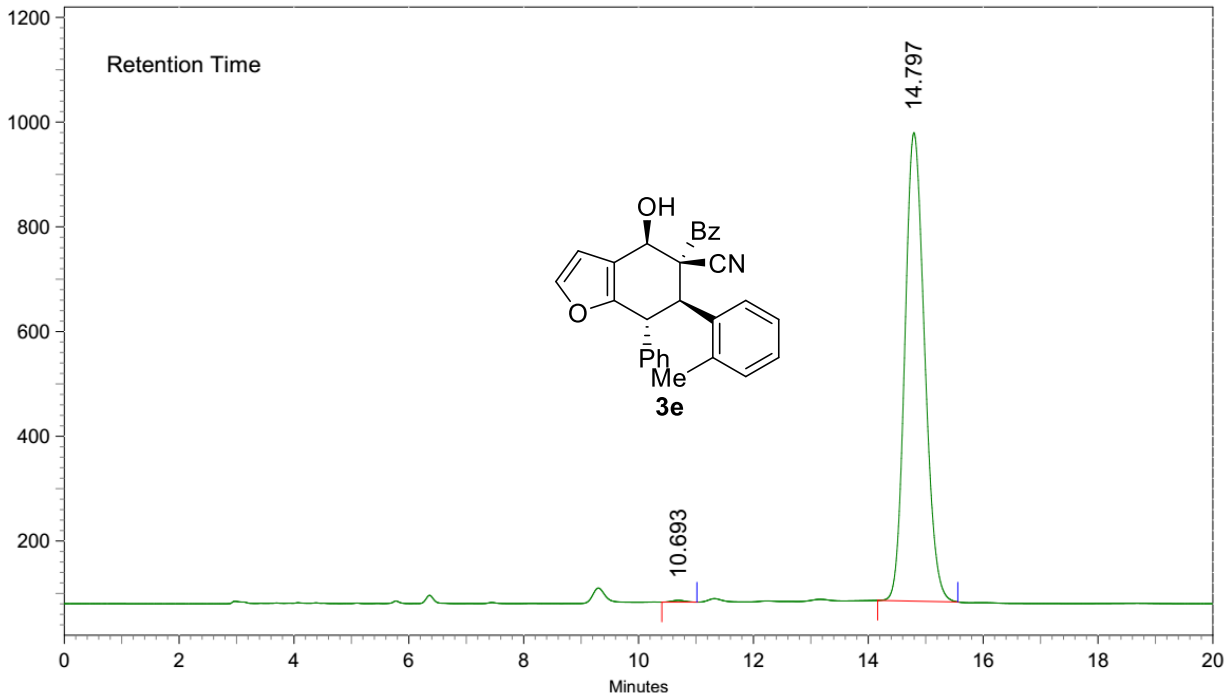


3e

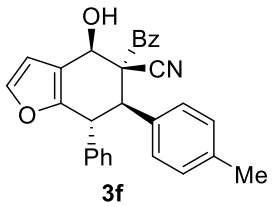
^{13}C NMR (150 MHz, $CDCl_3$)



Peak No.	Ret Time	Width	Height	Area	Area [%]
1	10.630	0.840	6426337	103560928	49.7053
2	14.777	1.300	4510474	104788882	50.2947

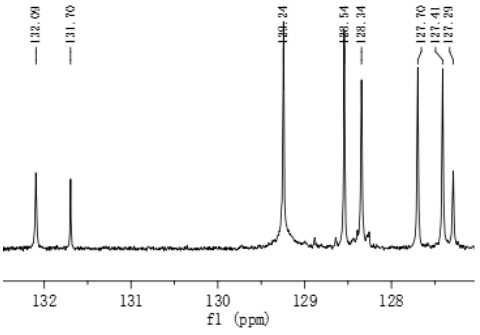


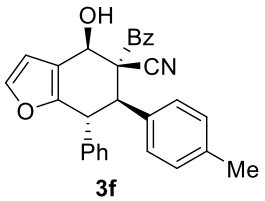
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	10.693	0.610	56883	863890	0.2413
2	14.797	1.397	15008999	357180798	99.7587



3f

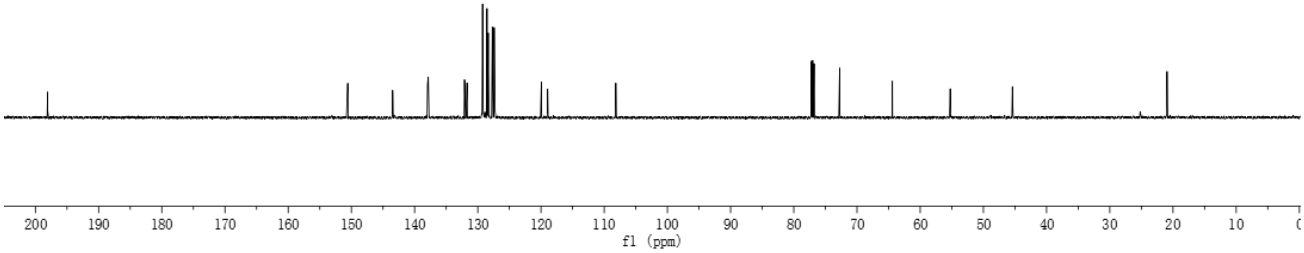
^{1}H NMR (400 MHz, $CDCl_3$)

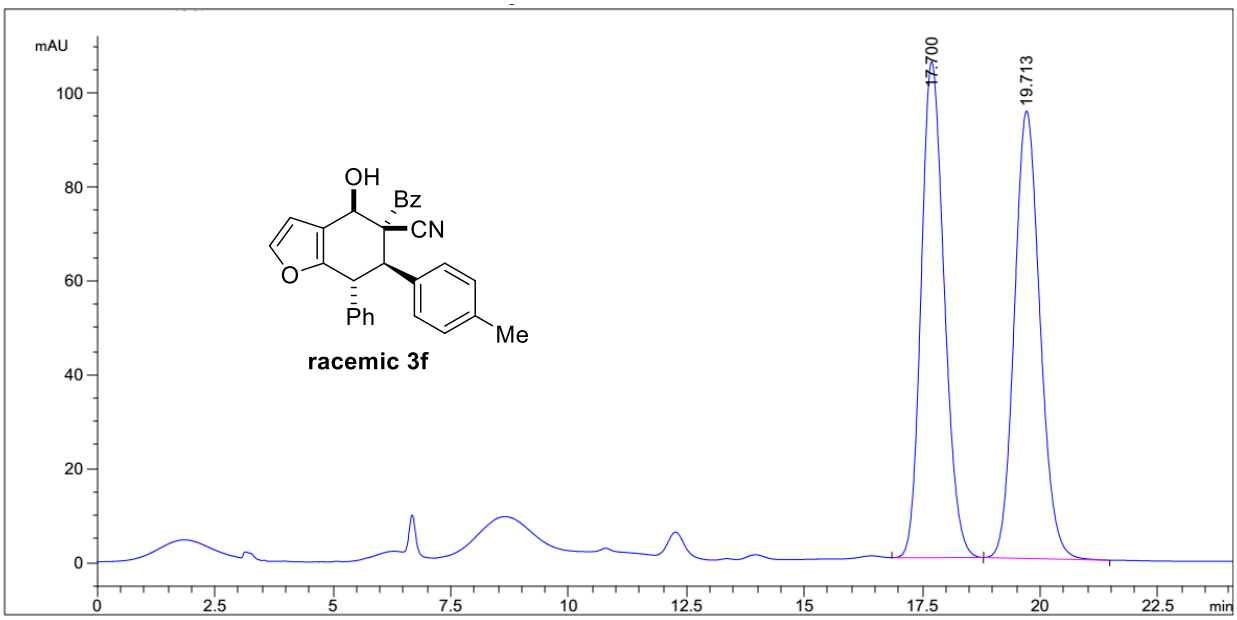




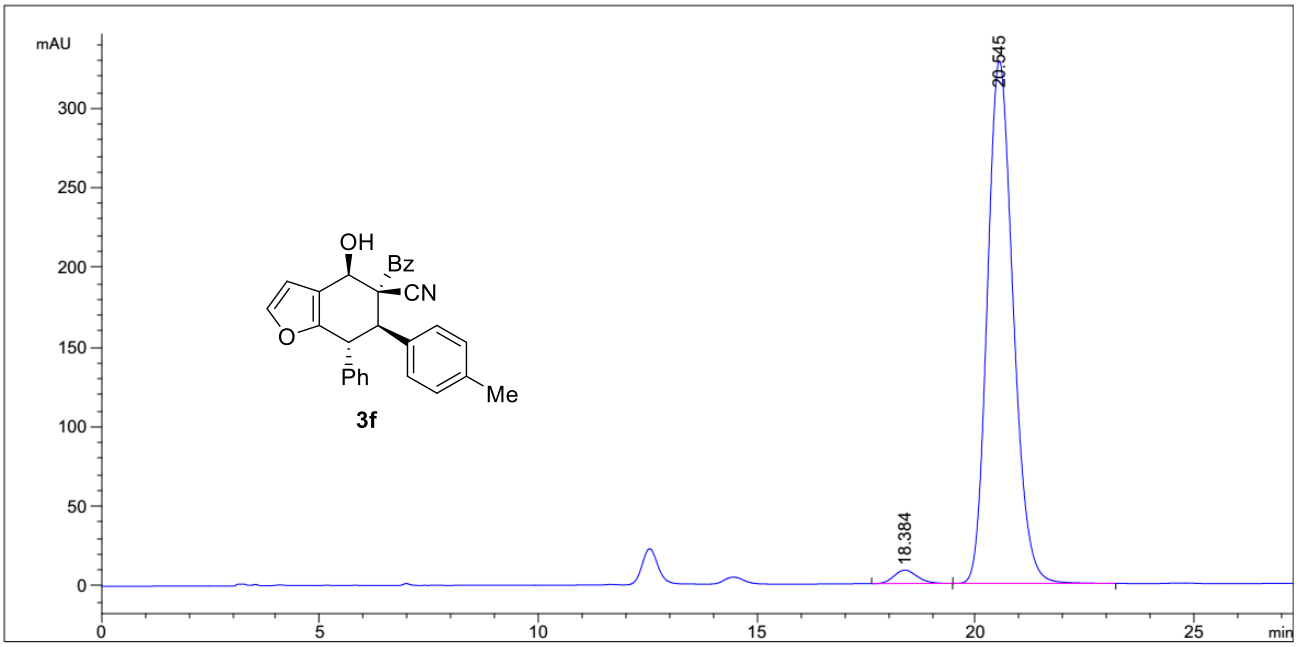
3f

^{13}C NMR (150 MHz, $CDCl_3$)

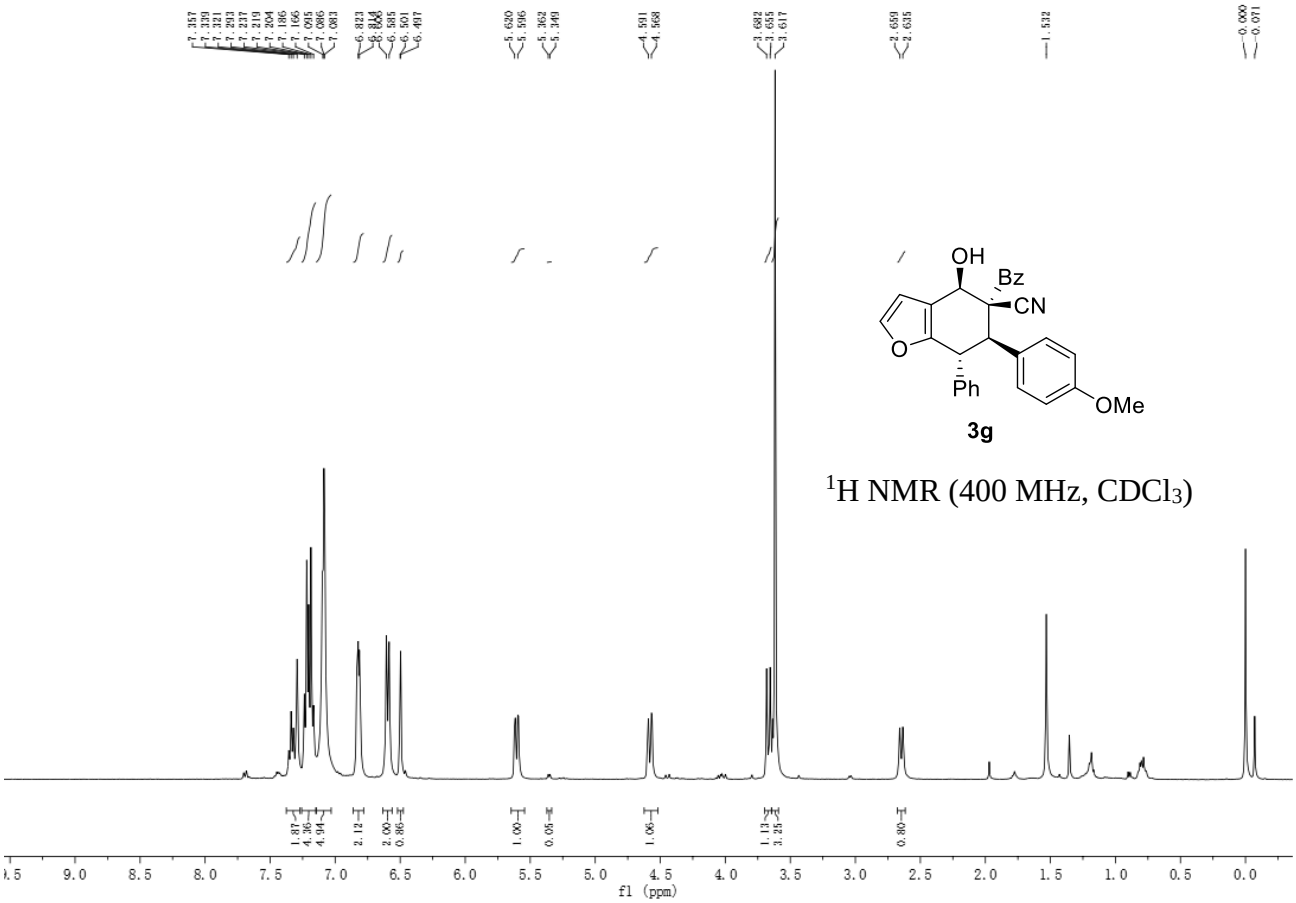




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	17.700	BB	0.5261	3591.09546	105.64939	49.9668
2	19.713	BB	0.5842	3595.87158	95.34259	50.0332

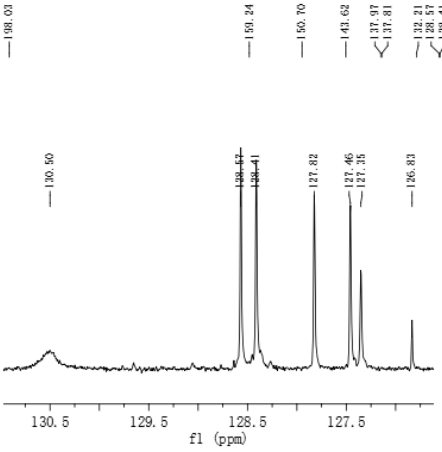


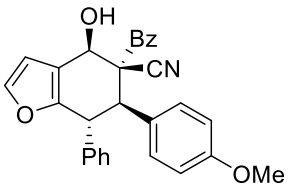
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.384	BB	0.5710	316.37616	8.50246	2.2958
2	20.545	BB	0.6347	1.34640e4	327.97440	97.7042



3g

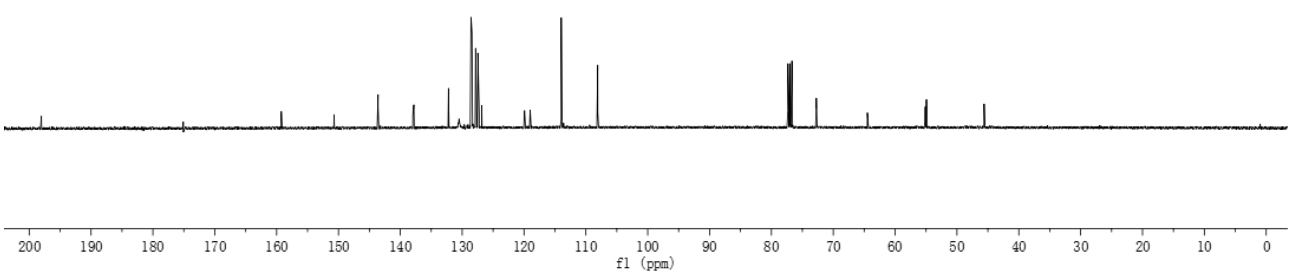
^{1}H NMR (400 MHz, $CDCl_3$)

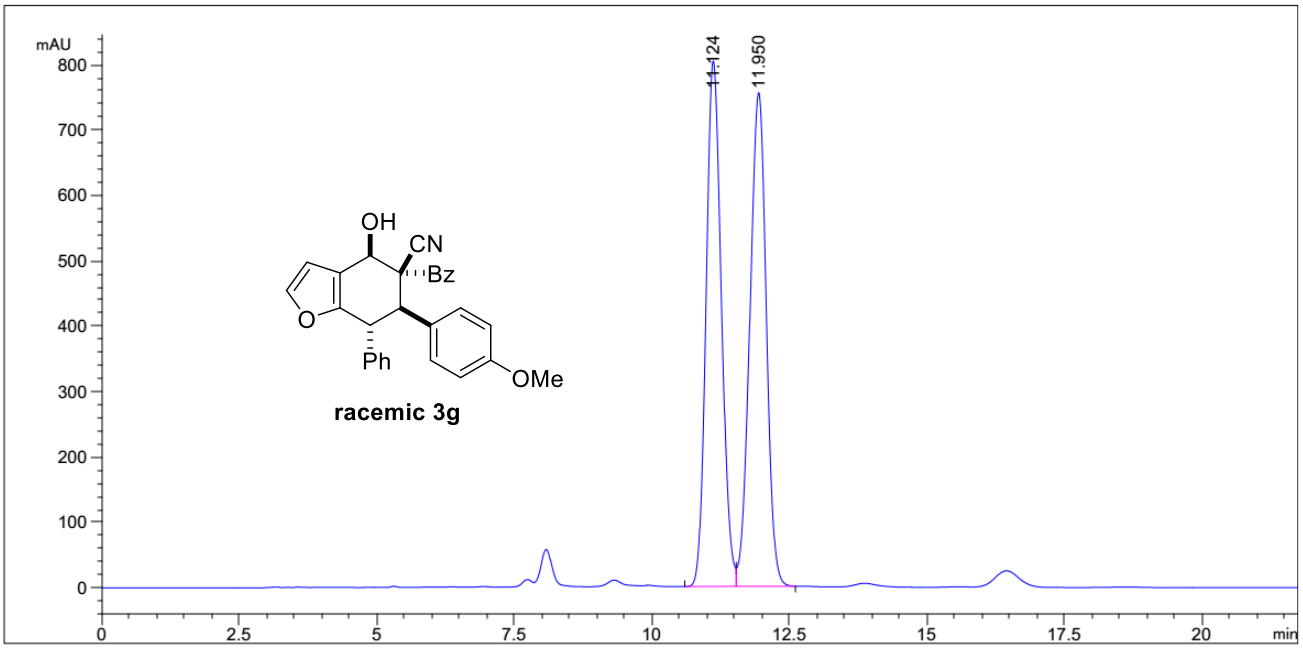




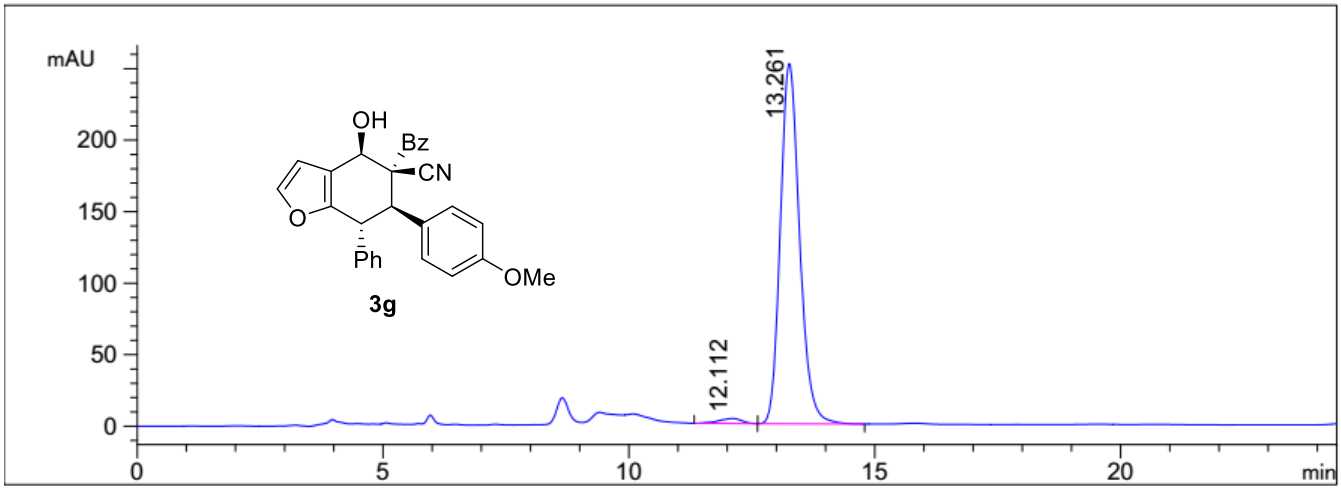
3g

^{13}C NMR (100 MHz, $CDCl_3$)

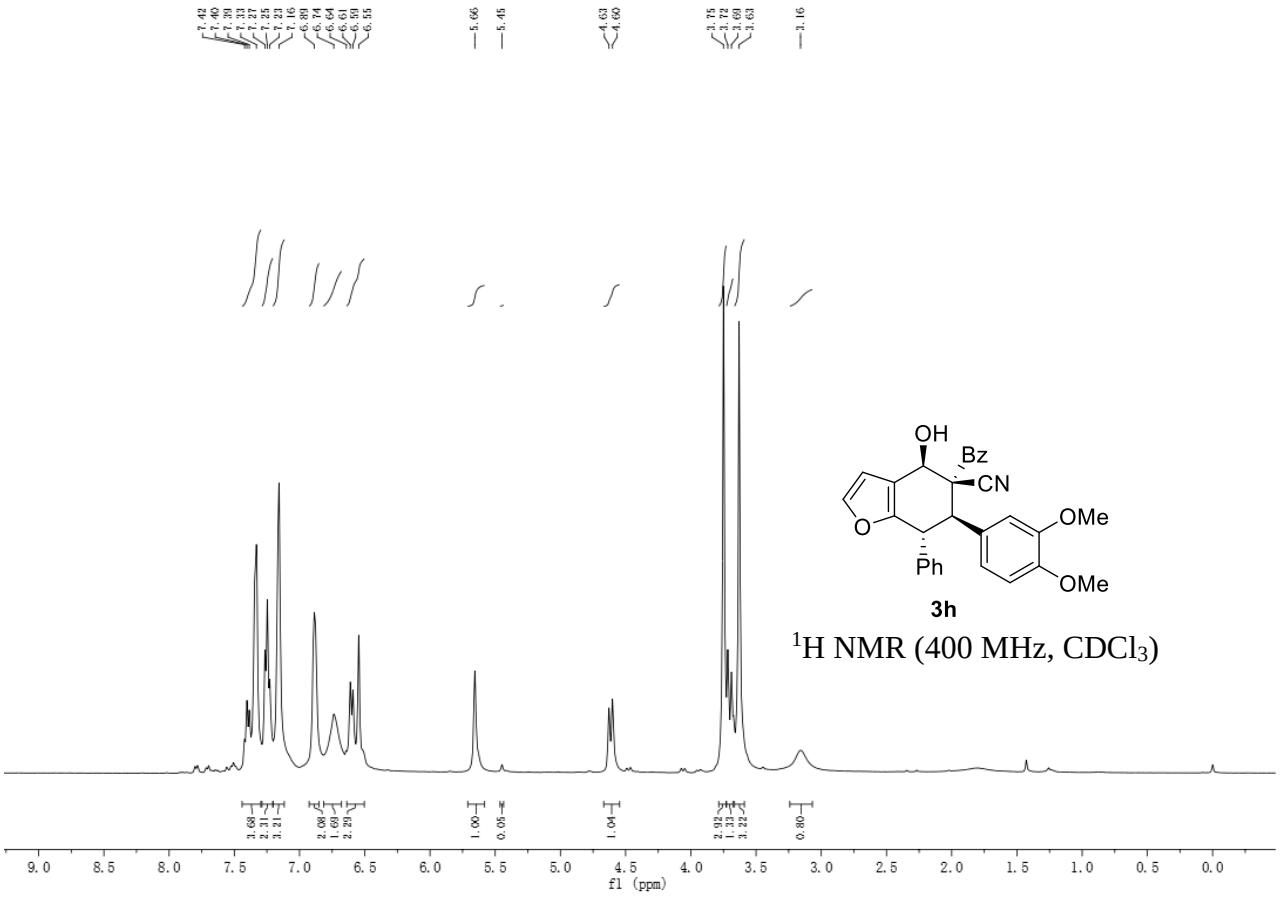


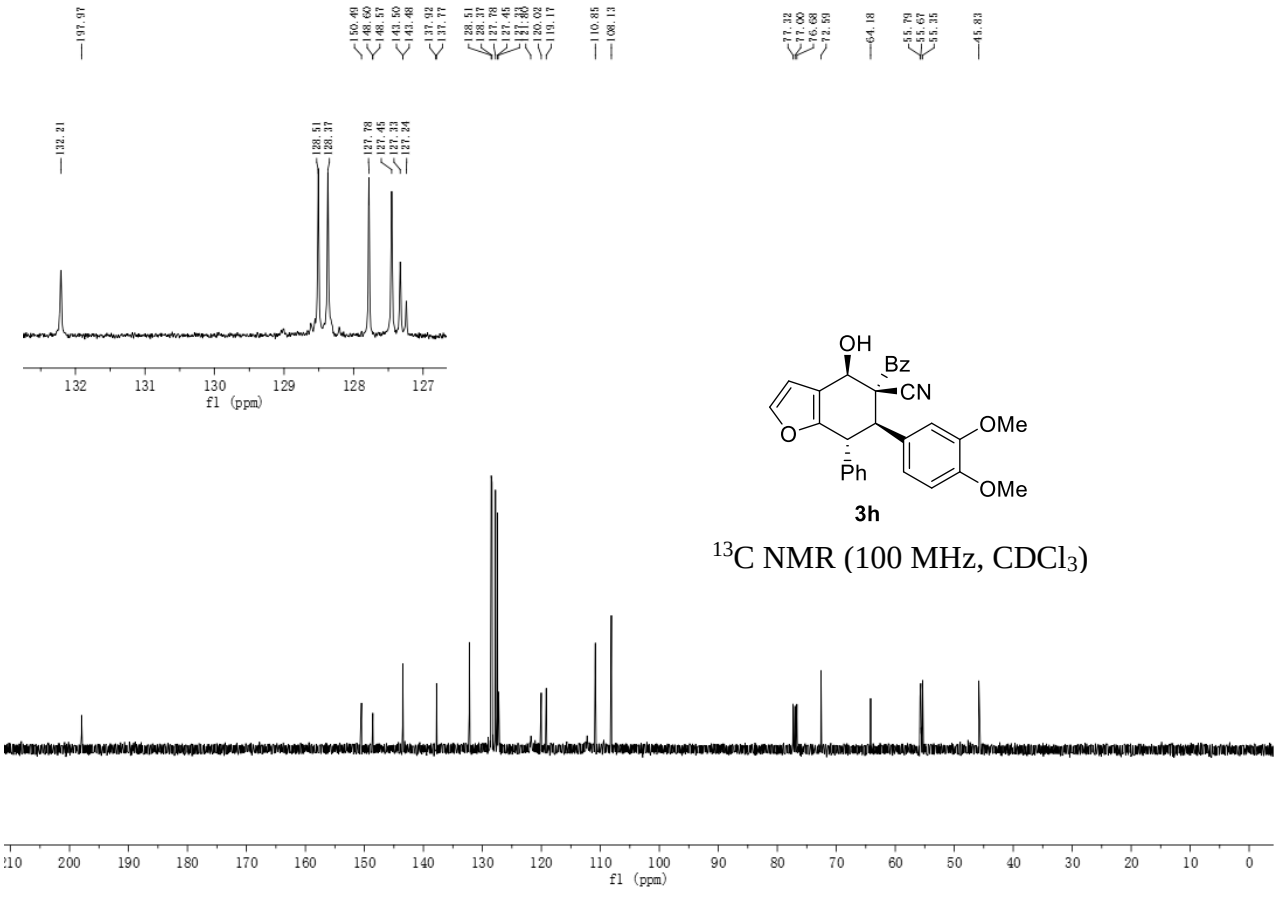


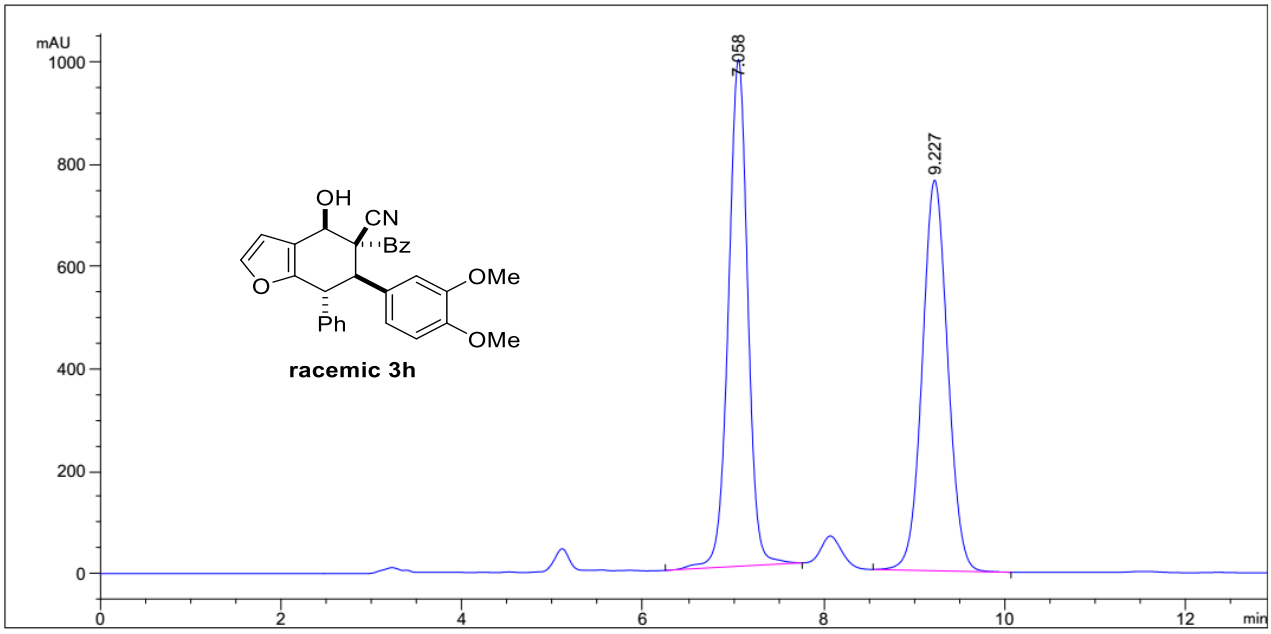
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.124	BV	0.3017	1.55665e4	803.67456	49.7801
2	11.950	VBA	0.3242	1.57040e4	754.91724	50.2199



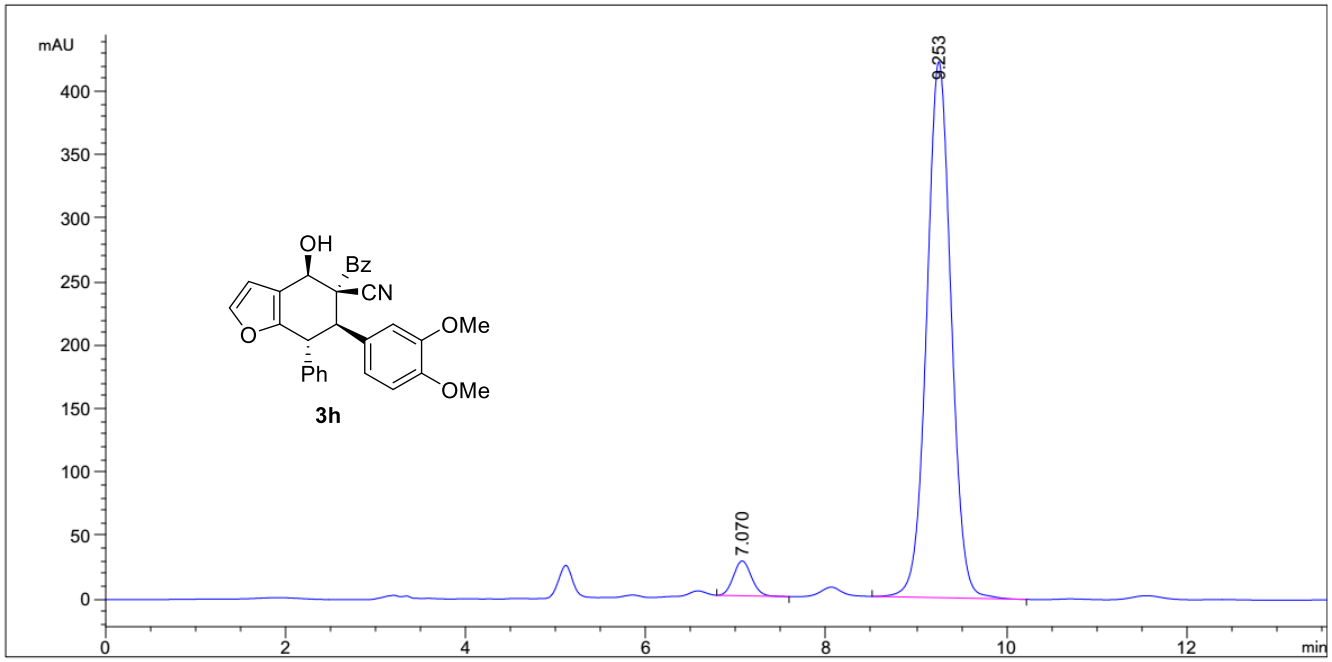
Meas.RT min	Area mAU*sec	Height mAU	Area %
12.11	112.6	3.5	1.6
13.26	6843.5	251.7	98.4


OH
Bz
CN
O
OMe
OMe
Ph
3h
1H NMR (400 MHz, CDCl3)
fl (ppm)

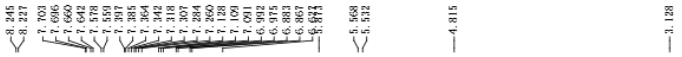

OH
Bz
CN
O
OMe
OMe
Ph
3h
13C NMR (100 MHz, CDCl3)
fl (ppm)

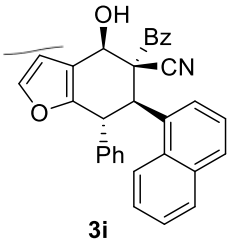


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.058	BB	0.2290	1.47734e4	992.29779	49.7531
2	9.227	BB	0.3005	1.49200e4	764.35229	50.2469



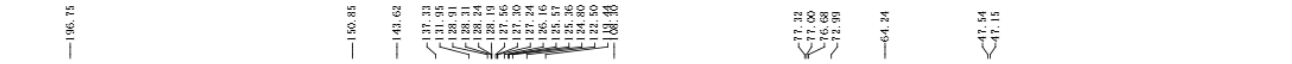
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.070	BB	0.2180	382.32651	27.42797	4.5832
2	9.253	BB	0.2912	7959.64502	422.38986	95.4168

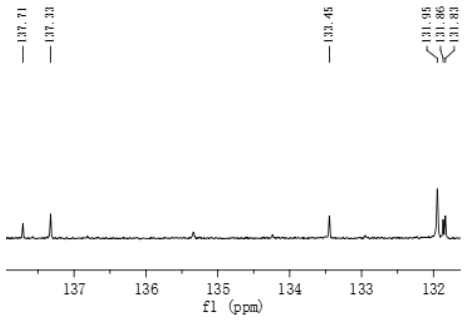


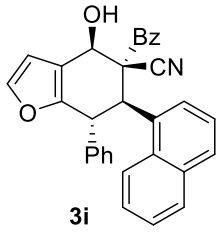


3i

^{1}H NMR (400 MHz, $CDCl_3$)

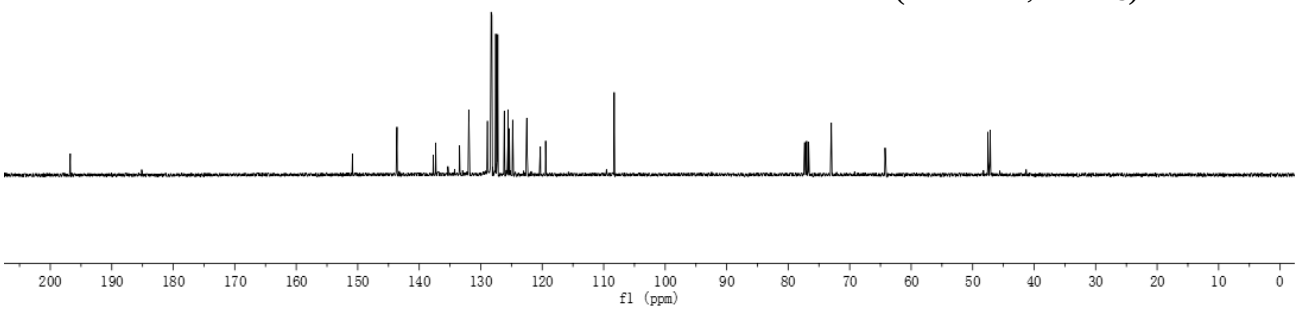


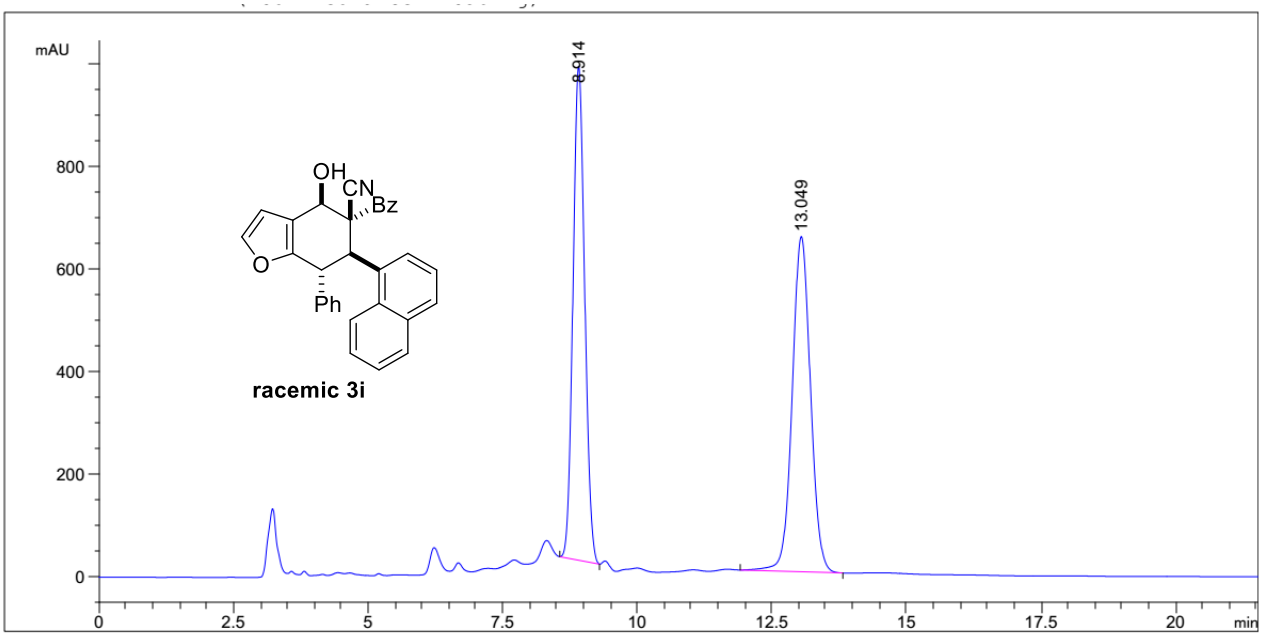




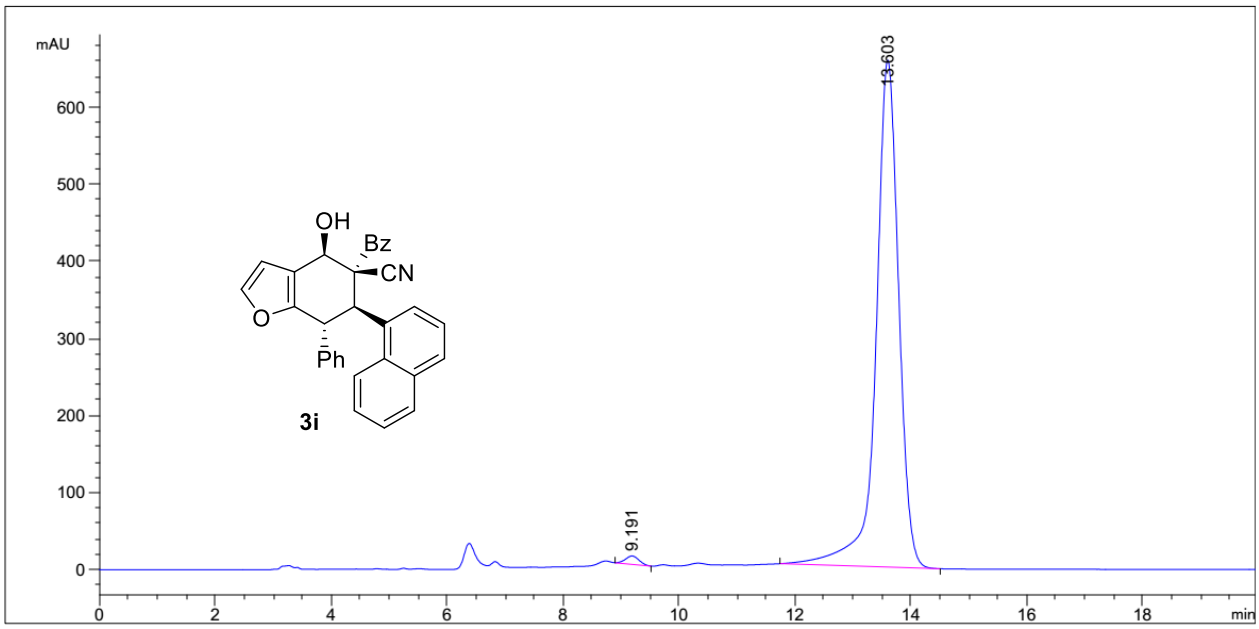
3i

^{13}C NMR (100 MHz, $CDCl_3$)

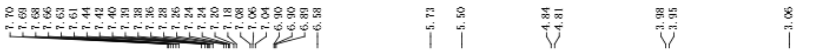


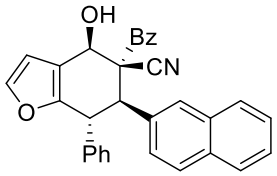


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.914	BB	0.2344	1.45202e4	961.87347	48.4650
2	13.049	BBA	0.3662	1.54400e4	652.88184	51.5350



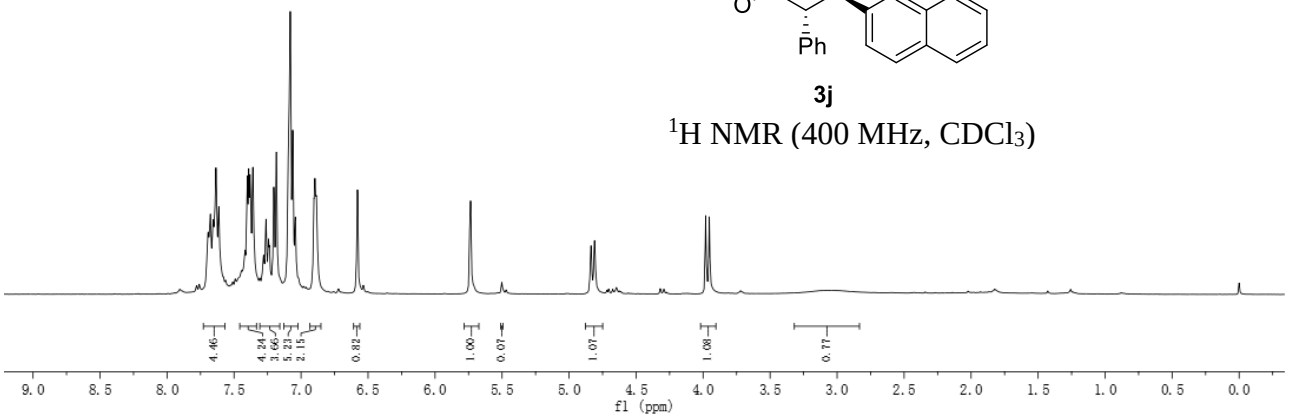
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.191	BB	0.2502	172.99916	10.75985	0.9564
2	13.603	BB	0.4124	1.79162e4	657.80676	99.0436

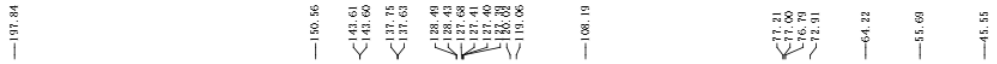


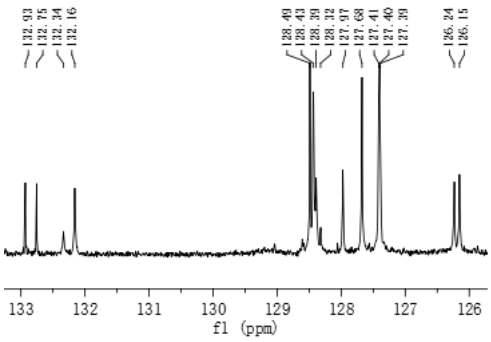


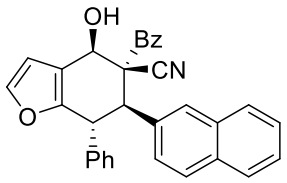
3j

^{1}H NMR (400 MHz, $CDCl_3$)



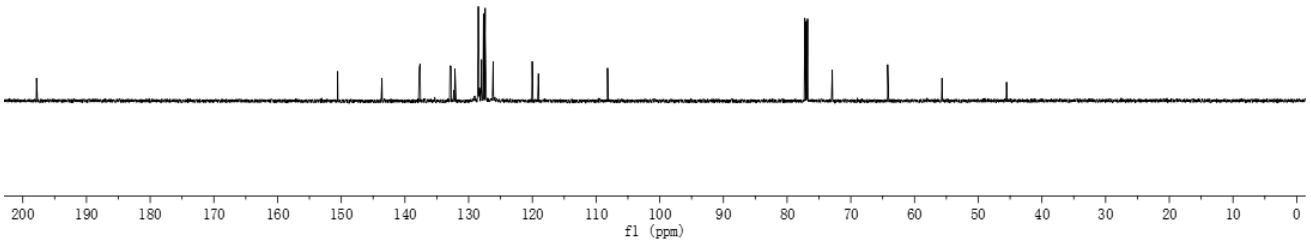


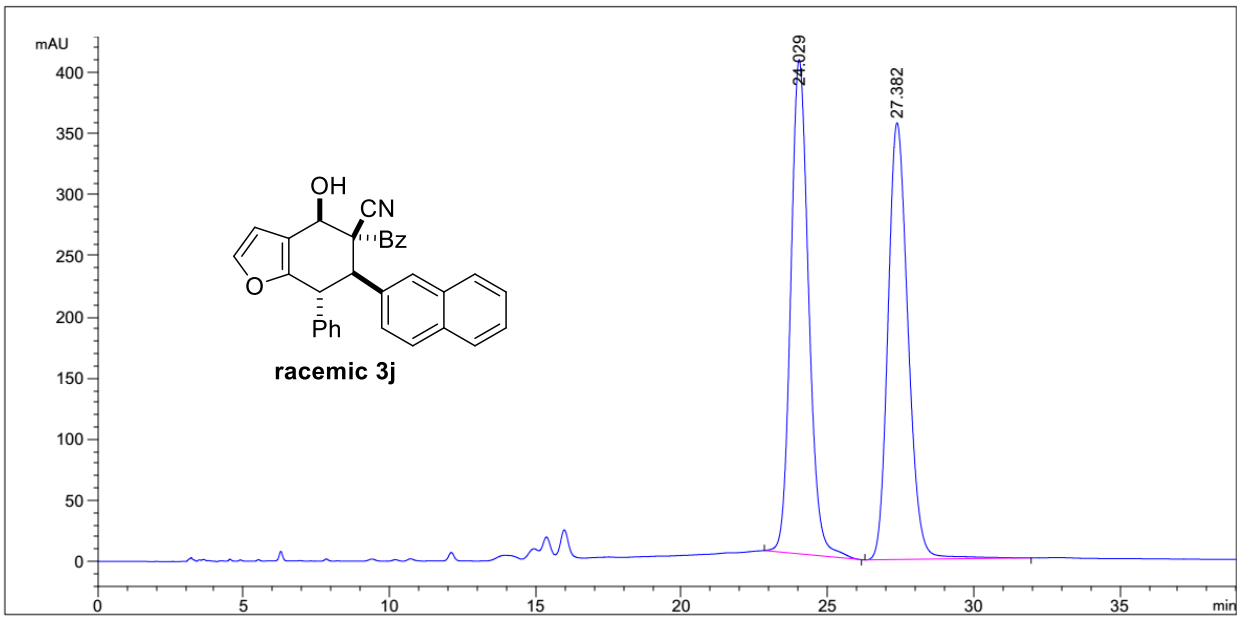




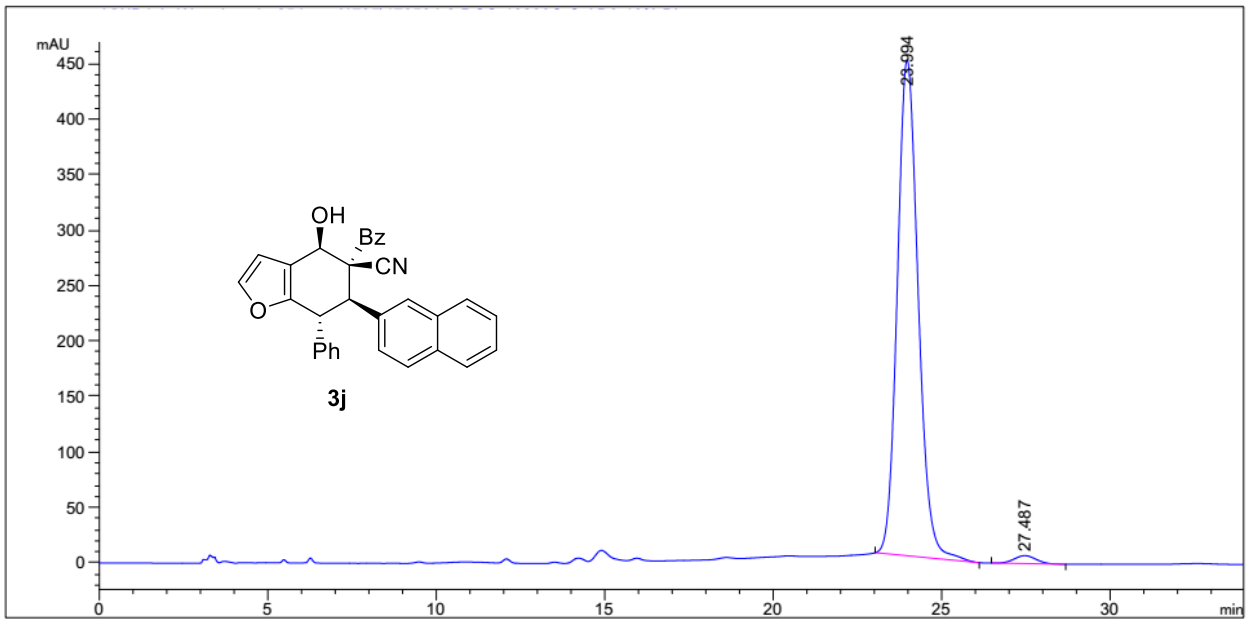
3j

^{13}C NMR (150 MHz, $CDCl_3$)

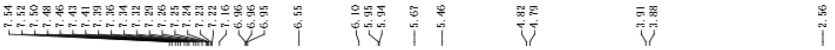


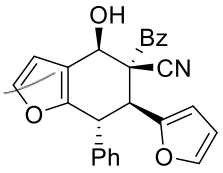


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	24.029	BB	0.6486	1.72379e4	404.49954	50.2518
2	27.382	BB	0.7389	1.70652e4	357.50055	49.7482



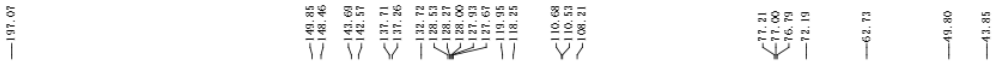
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	23.994	BB	0.6416	1.92091e4	446.59363	98.3387
2	27.487	BB	0.6997	324.51236	7.15254	1.6613

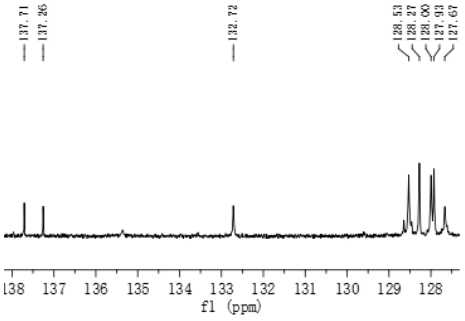


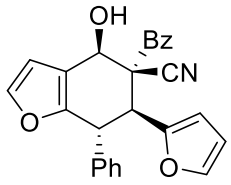


3k

^{1}H NMR (600 MHz, $CDCl_3$)

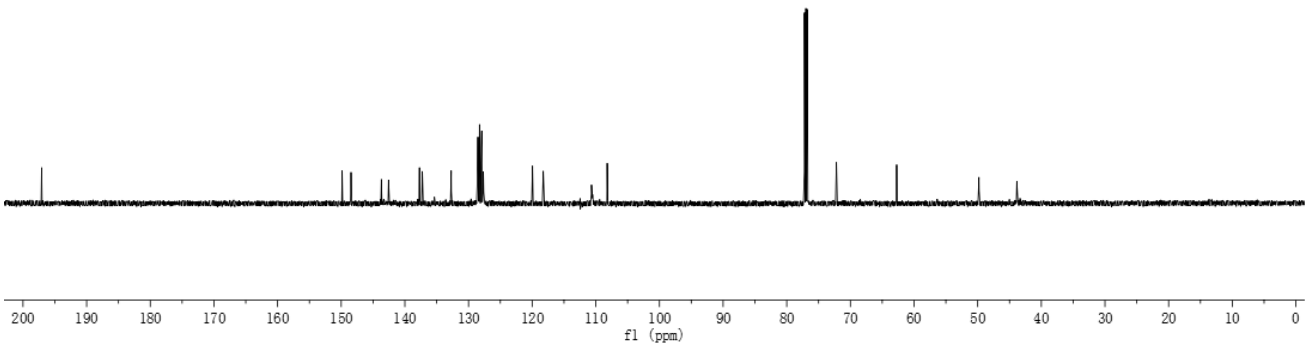


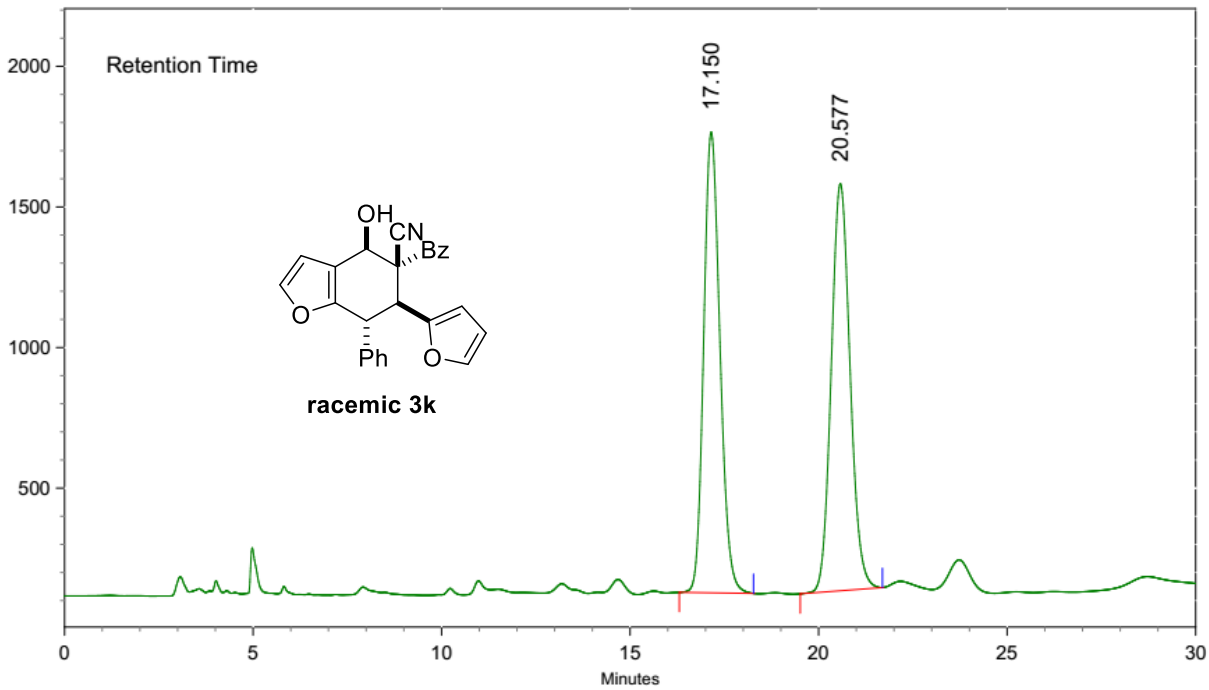




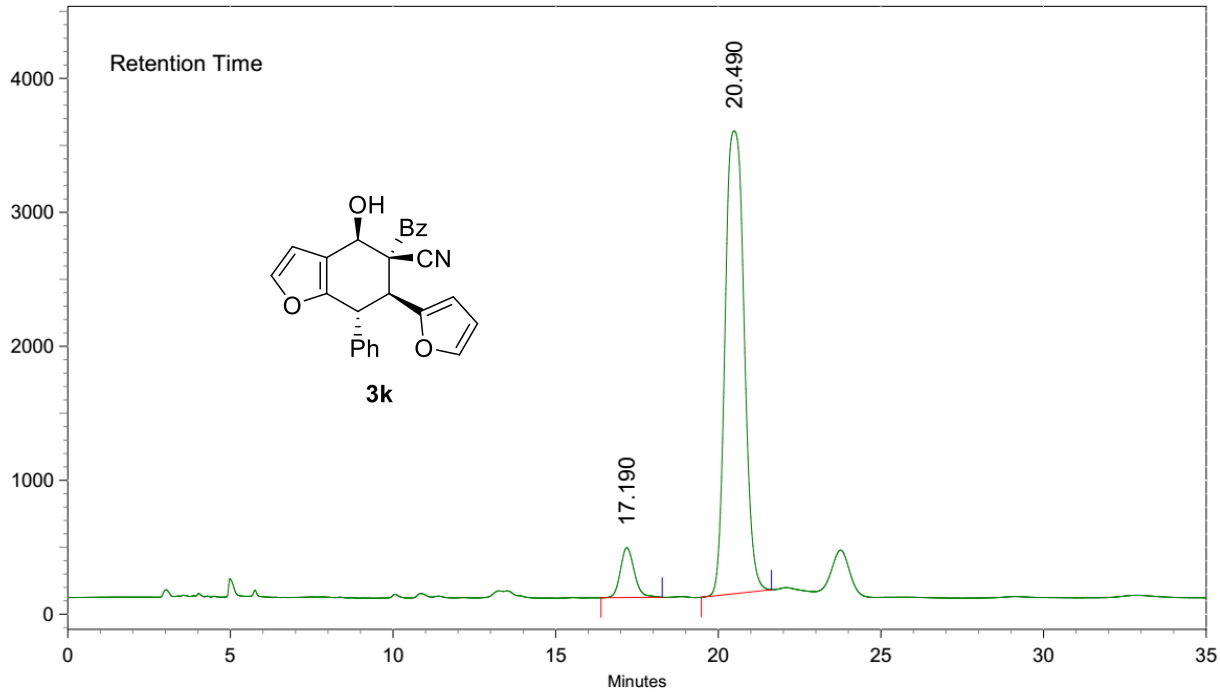
3k

^{13}C NMR (150 MHz, $CDCl_3$)

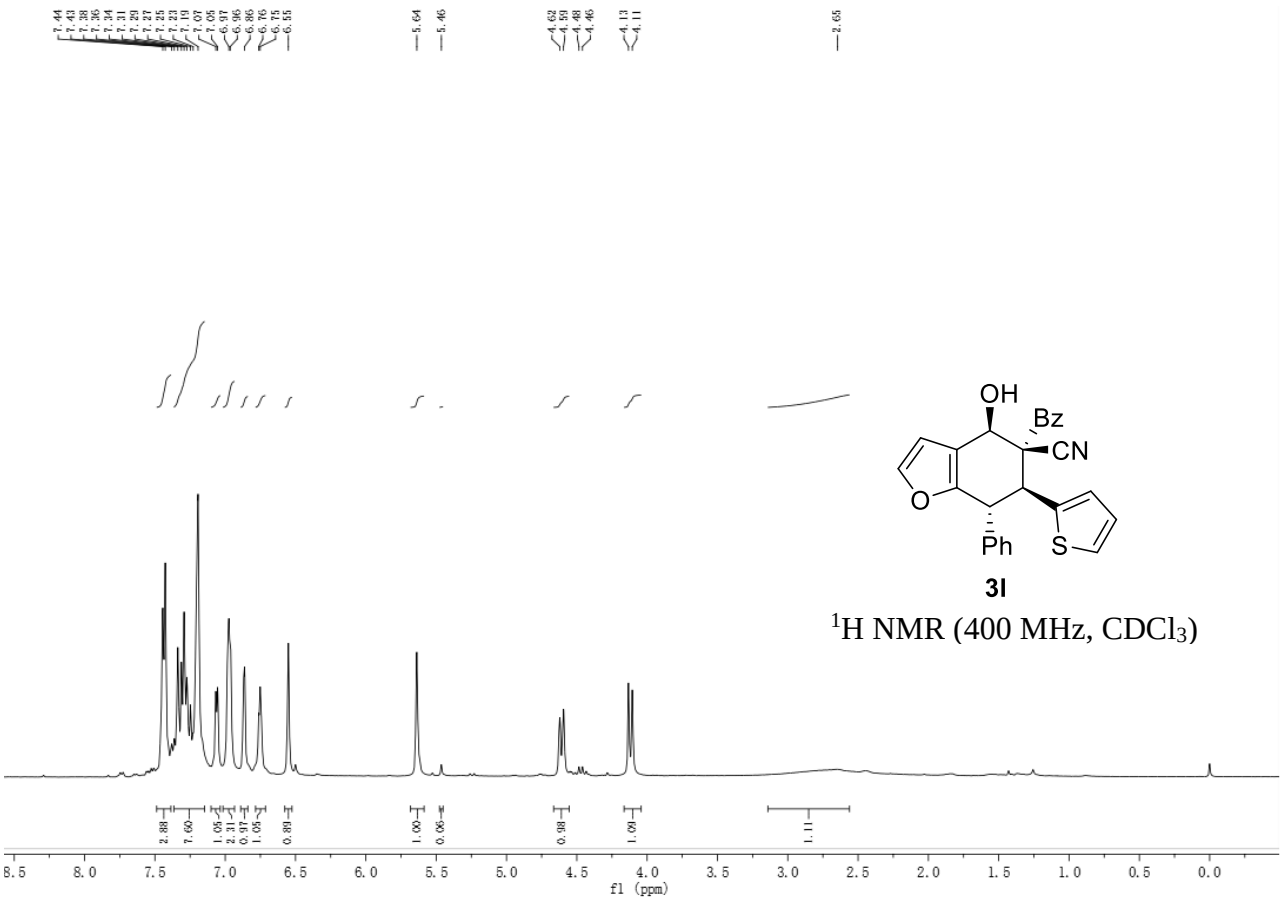




Peak No.	Ret Time	Width	Height	Area	Area [%]
1	17.150	1.967	27477500	823400836	49.3948
2	20.577	2.180	24281243	843577478	50.6052

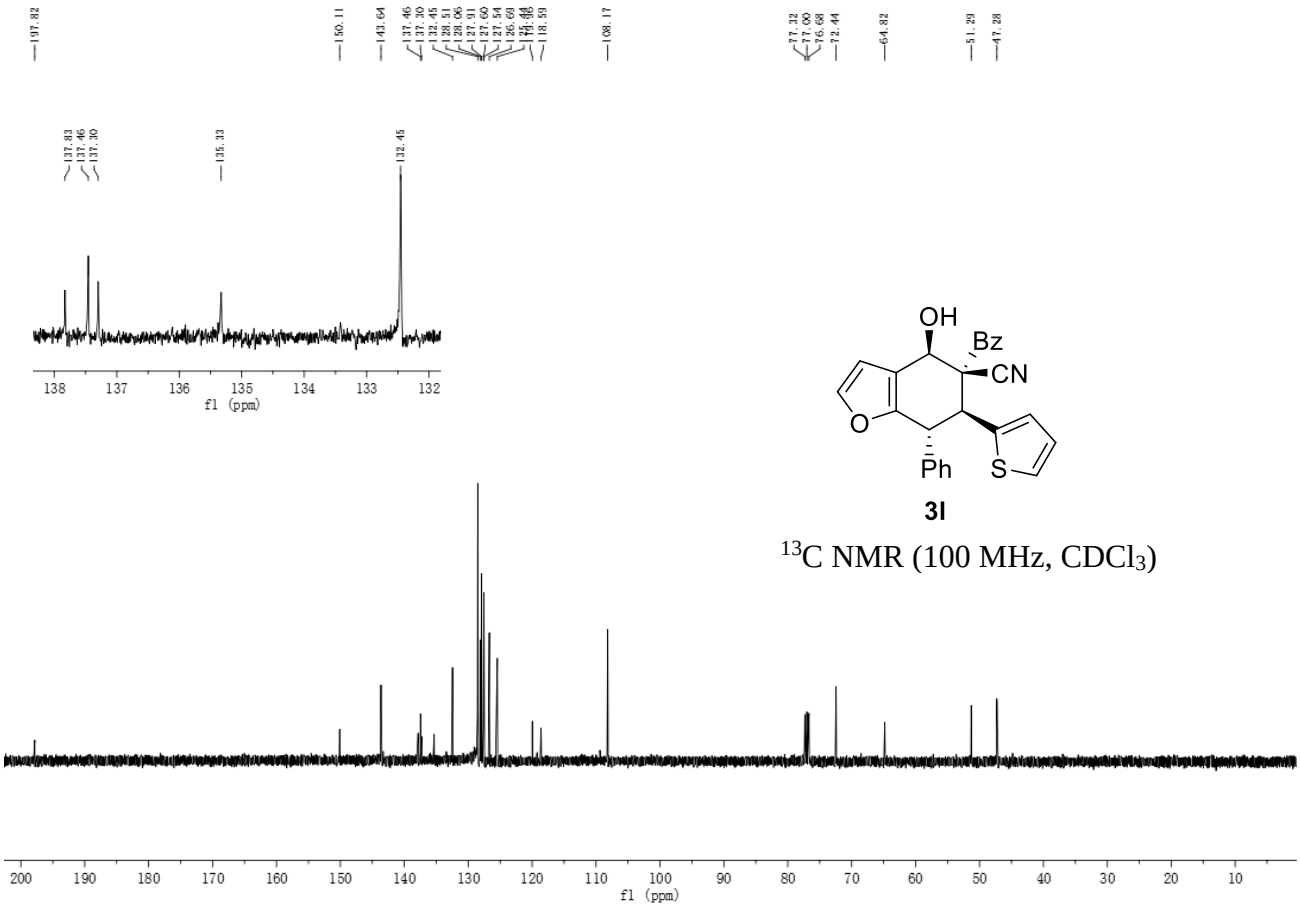


Peak No.	Ret Time	Width	Height	Area	Area [%]
1	17.190	1.883	6250065	185480407	7.3126
2	20.490	2.157	57967141	2350978250	92.6874



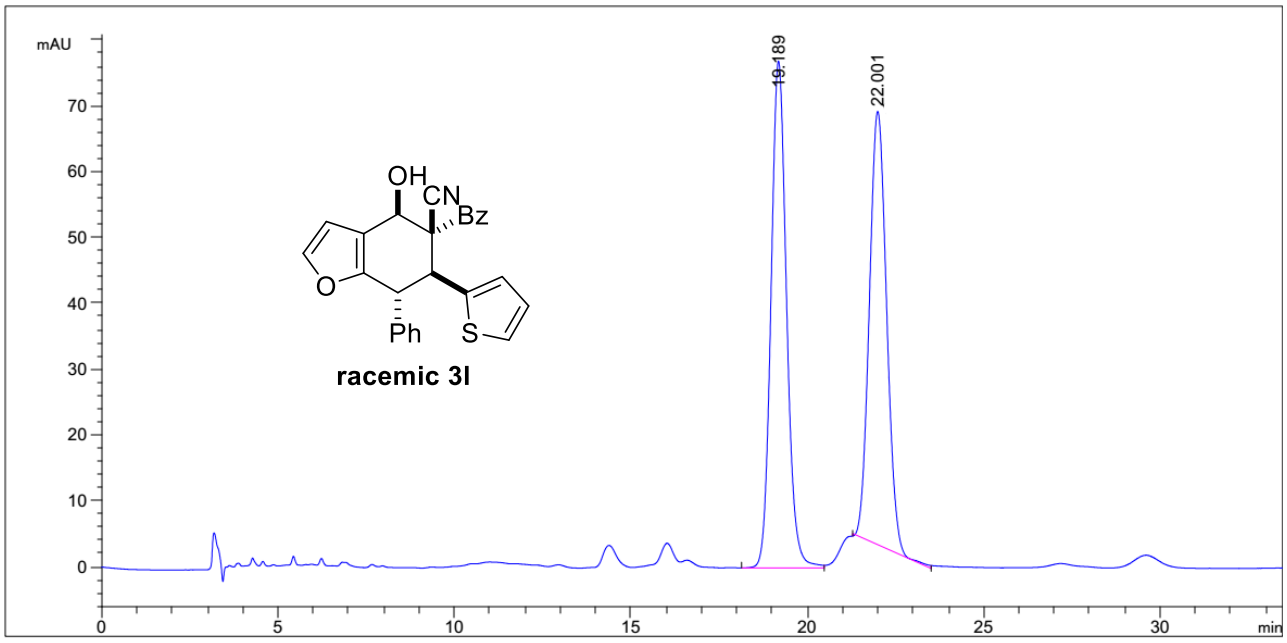
3l

^{1}H NMR (400 MHz, $CDCl_3$)

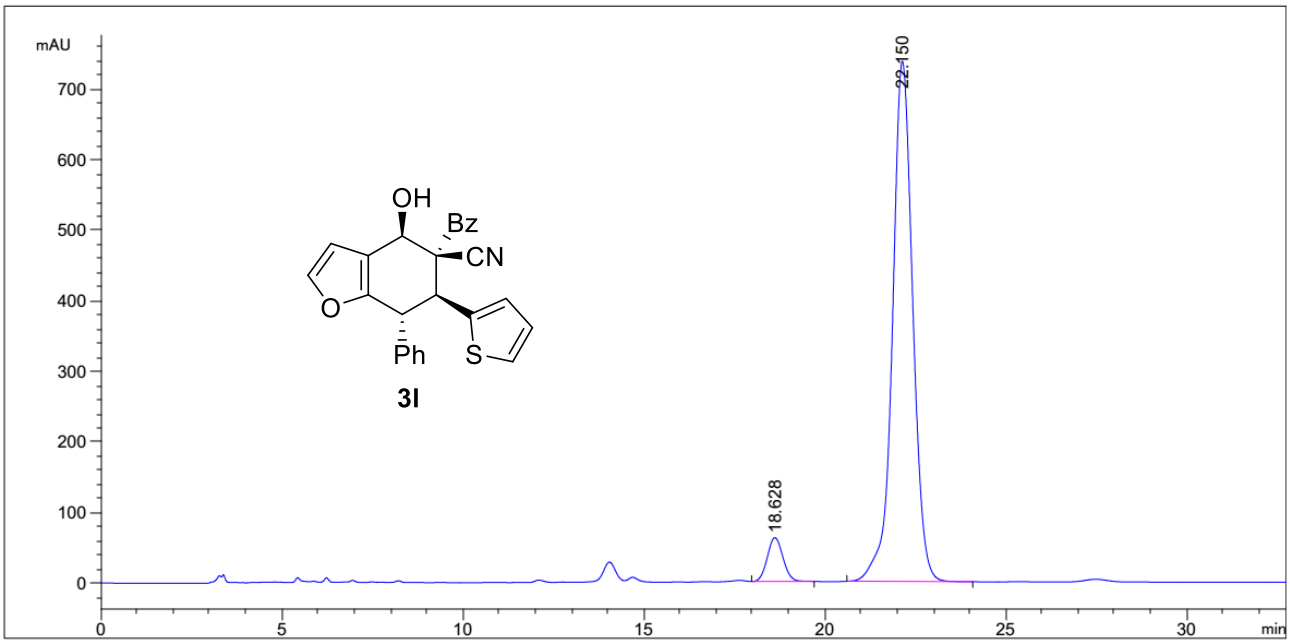


3l

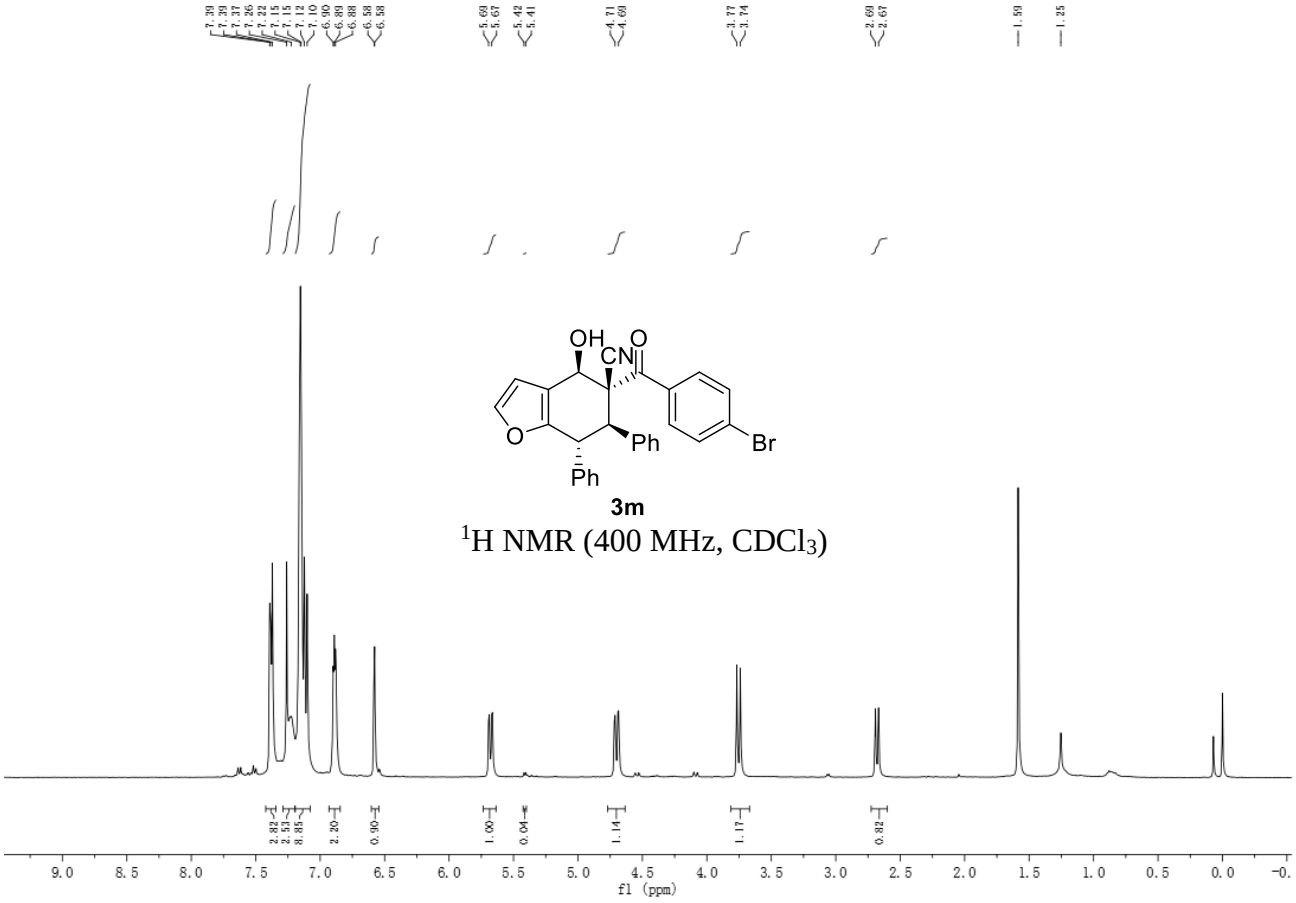
^{13}C NMR (100 MHz, $CDCl_3$)

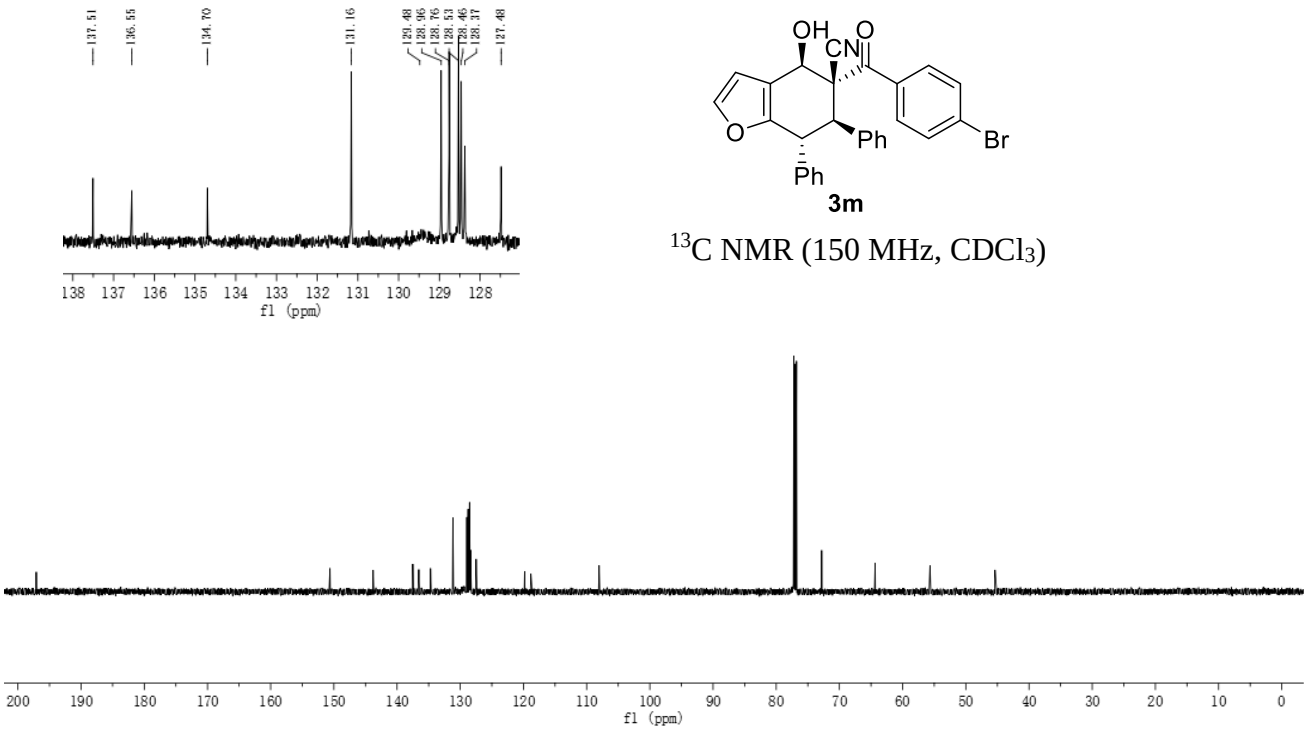


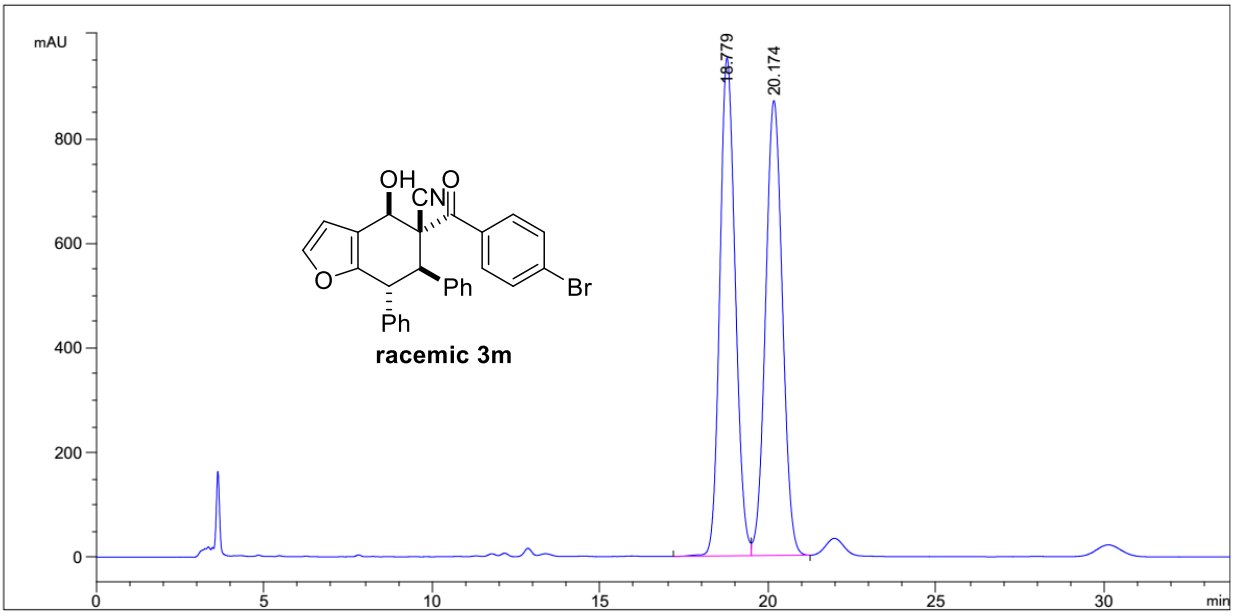
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.189	BV	0.4680	2356.93872	76.96023	51.3490
2	22.001	MM	0.5656	2233.09961	65.79971	48.6510



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.628	BBA	0.4685	1869.03198	62.20608	6.1255
2	22.150	BBA	0.5957	2.86434e4	737.70801	93.8745

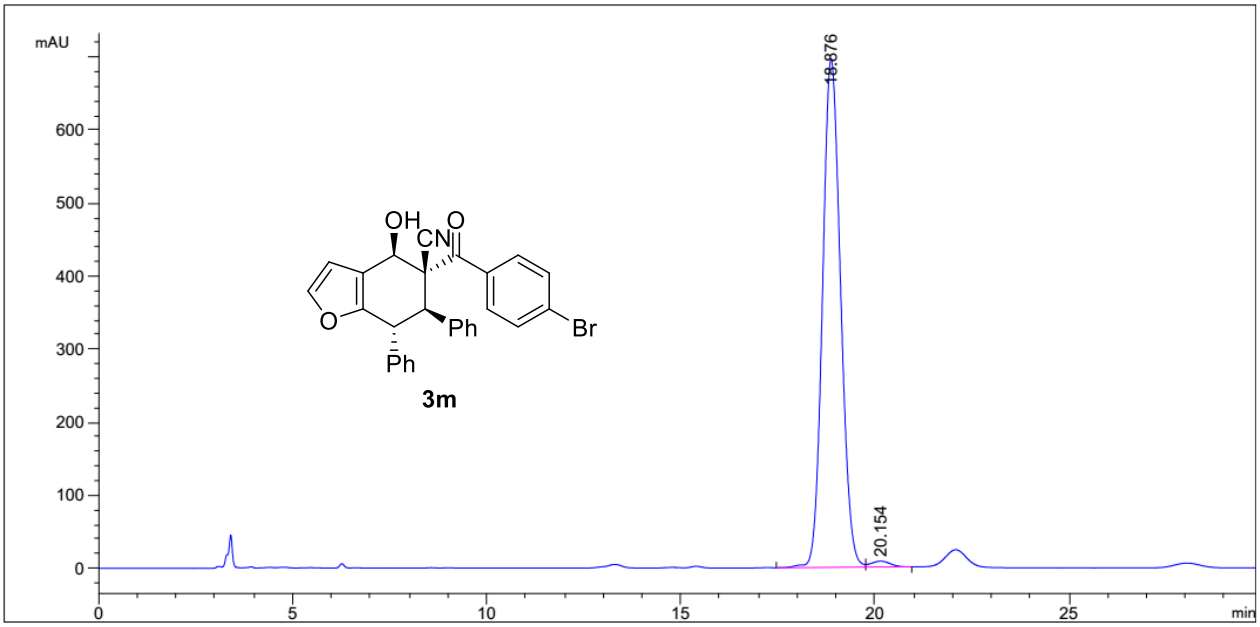

OH
CN
O
O
Ph
Ph
Br
3m
1H NMR (400 MHz, CDCl3)
f1 (ppm)


OH
CN
O
O
Ph
Ph
Br
3m
13C NMR (150 MHz, CDCl3)
f1 (ppm)



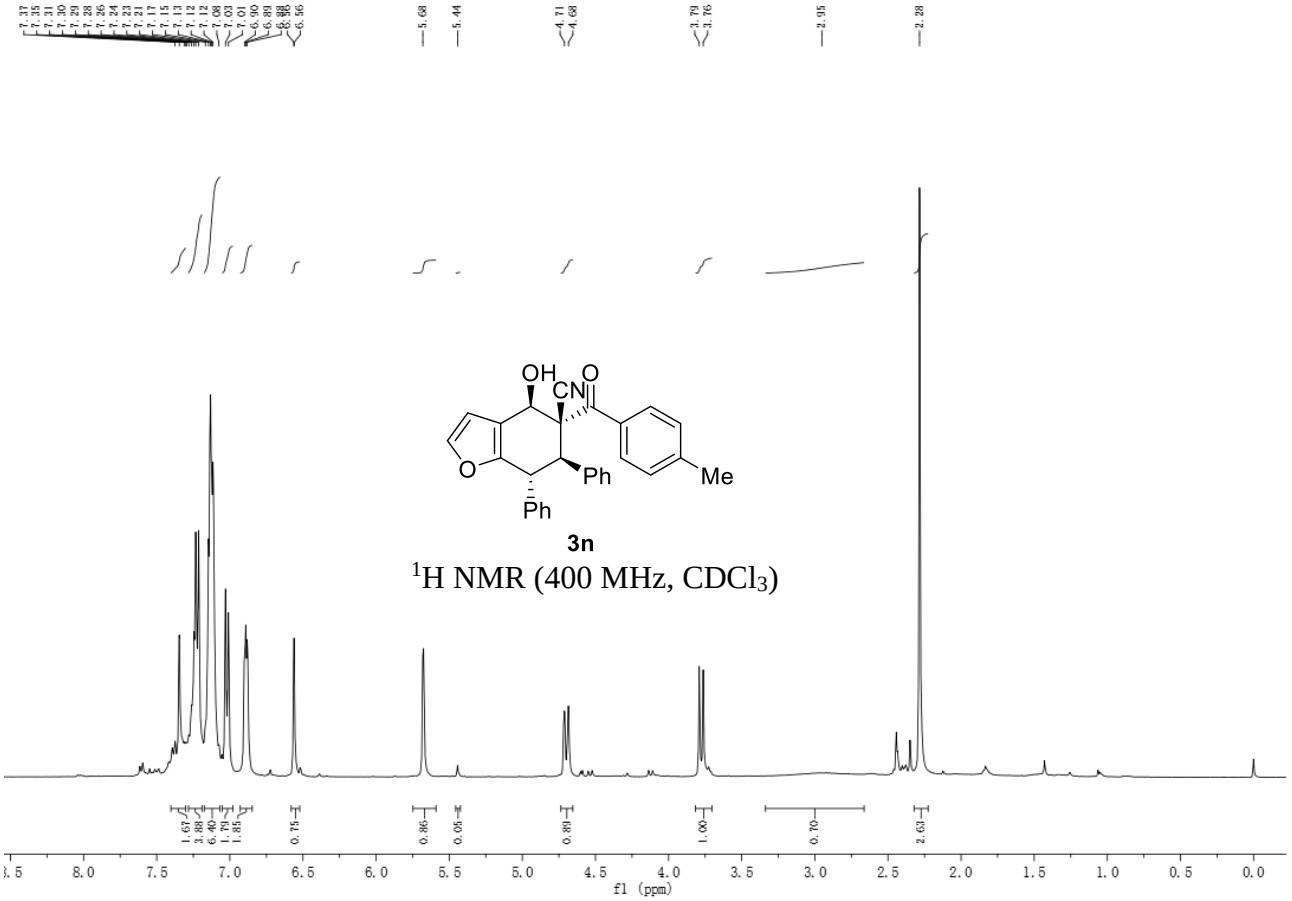
racemic 3m

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.779	BV	0.4991	3.05157e4	952.25824	50.0879
2	20.174	VB	0.5462	3.04086e4	869.87469	49.9121



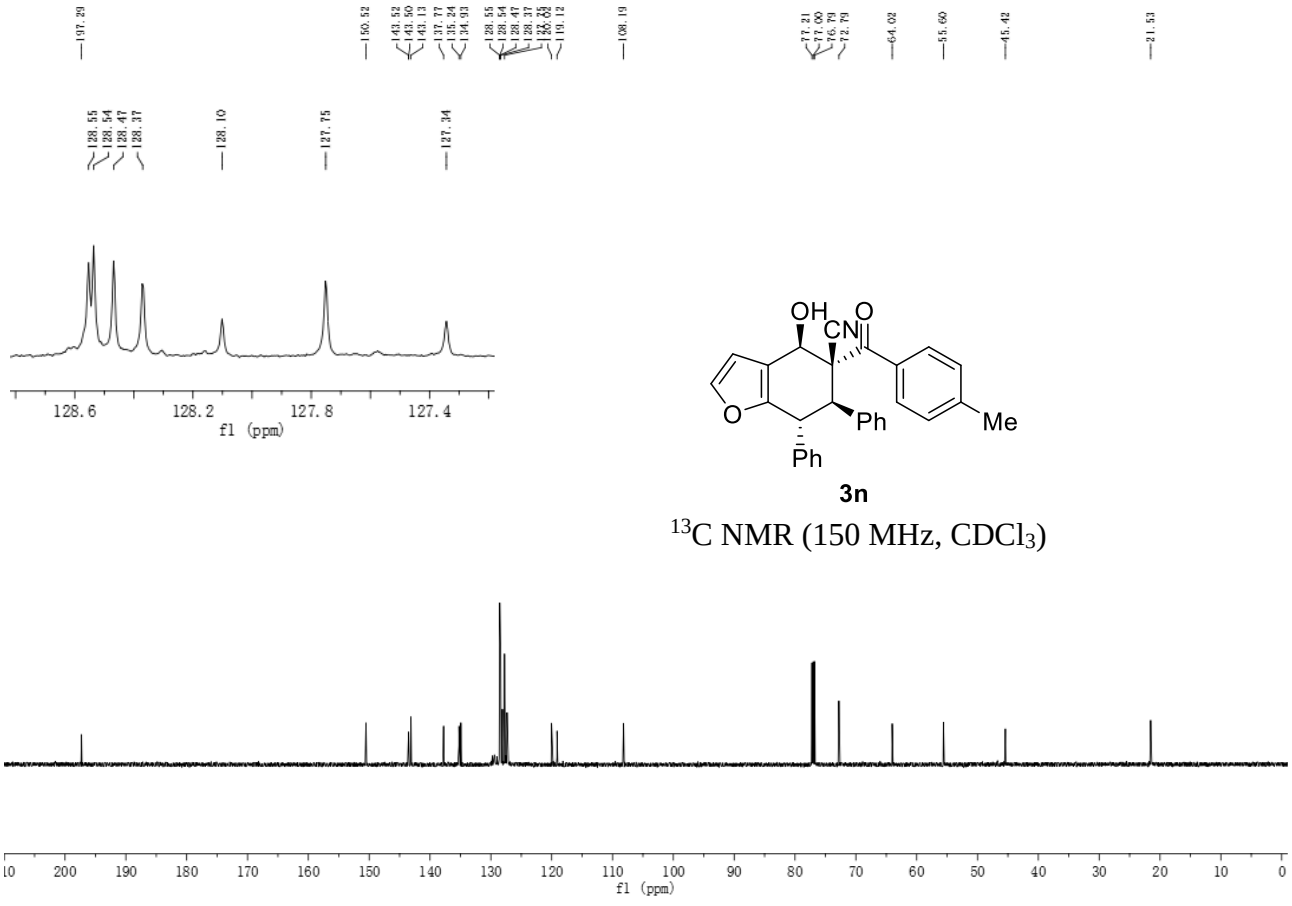
3m

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.876	BV	0.5026	2.24442e4	696.58429	98.7770
2	20.154	VBA	0.5321	277.90131	8.11284	1.2230



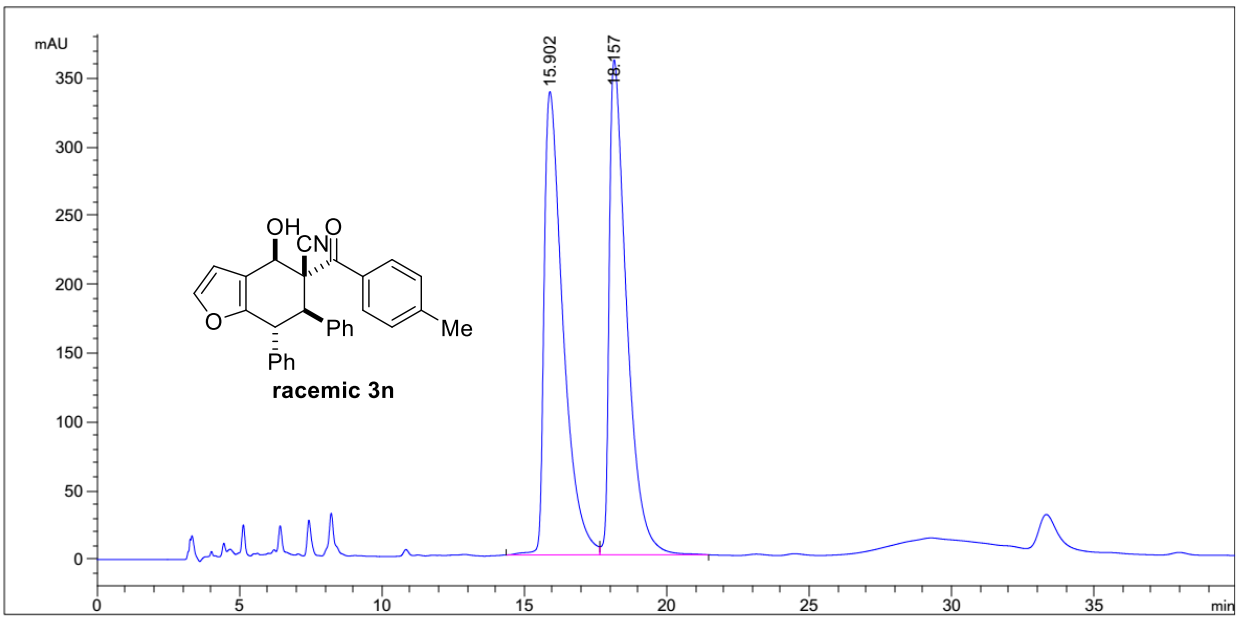
3n

^{1}H NMR (400 MHz, $CDCl_3$)

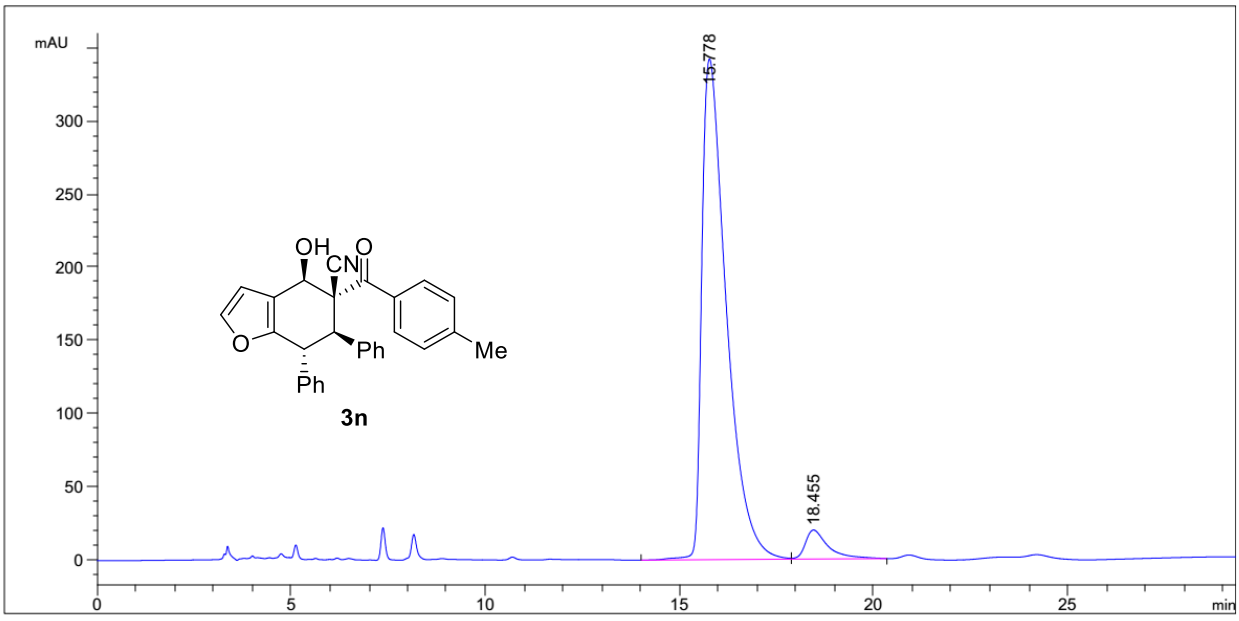


3n

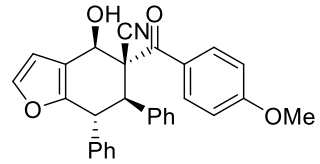
^{13}C NMR (150 MHz, $CDCl_3$)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.902	BV	0.6937	1.55613e4	336.57605	50.4044
2	18.157	VBA	0.6351	1.53116e4	359.59912	49.5956

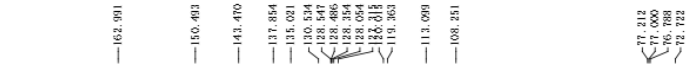


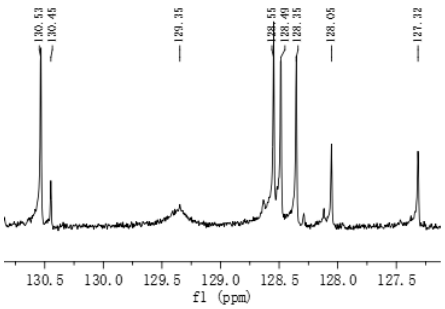
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.778	BV	0.6639	1.50436e4	341.51941	94.8793
2	18.455	VBA	0.6020	811.92175	19.80806	5.1207

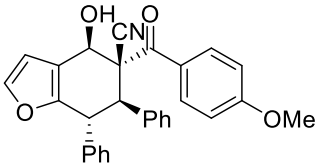


3o

^{1}H NMR (400 MHz, $CDCl_3$)

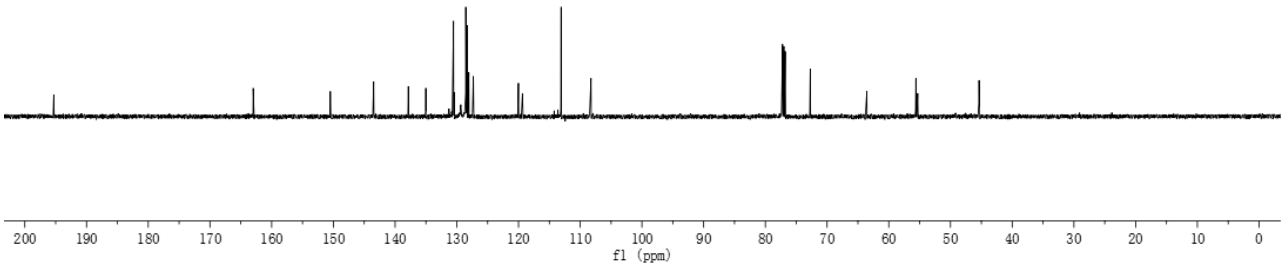


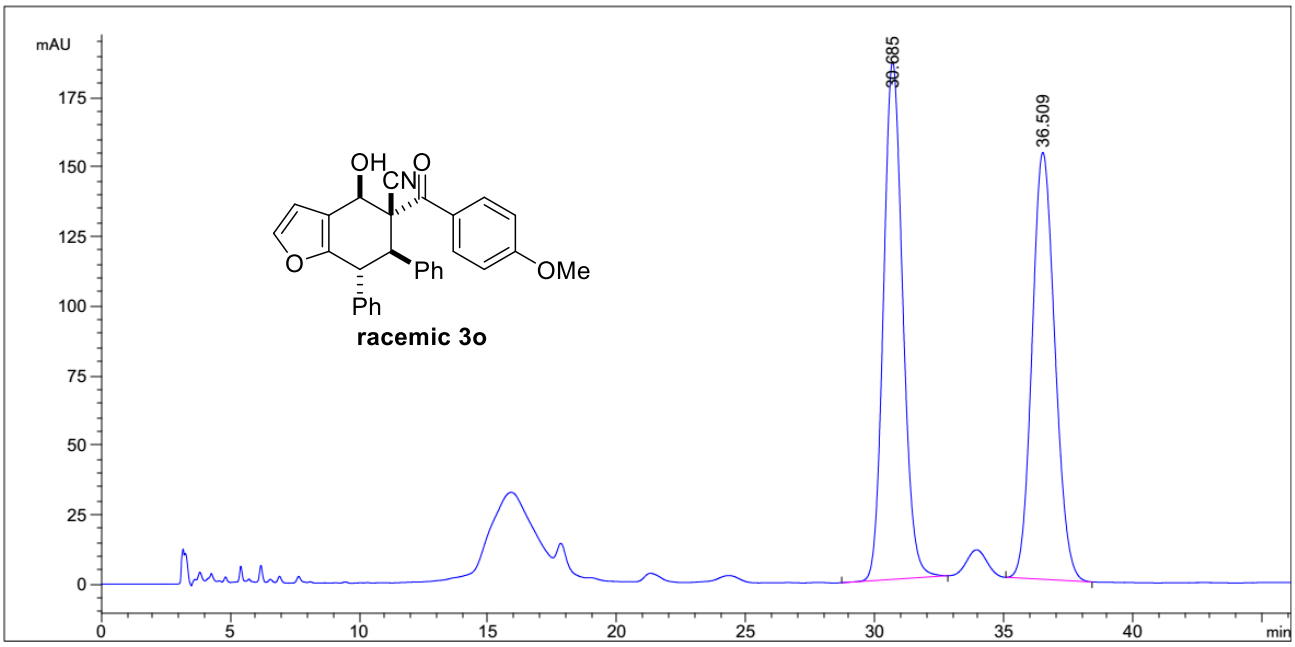




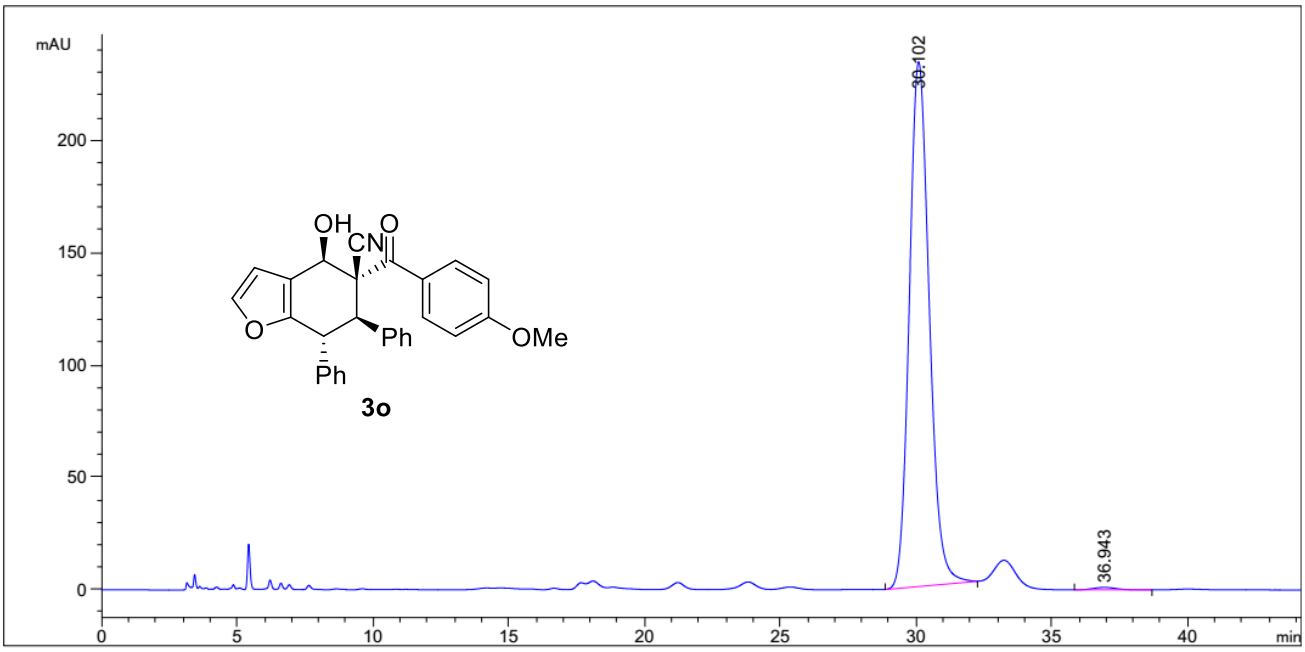
3o

^{13}C NMR (150 MHz, $CDCl_3$)

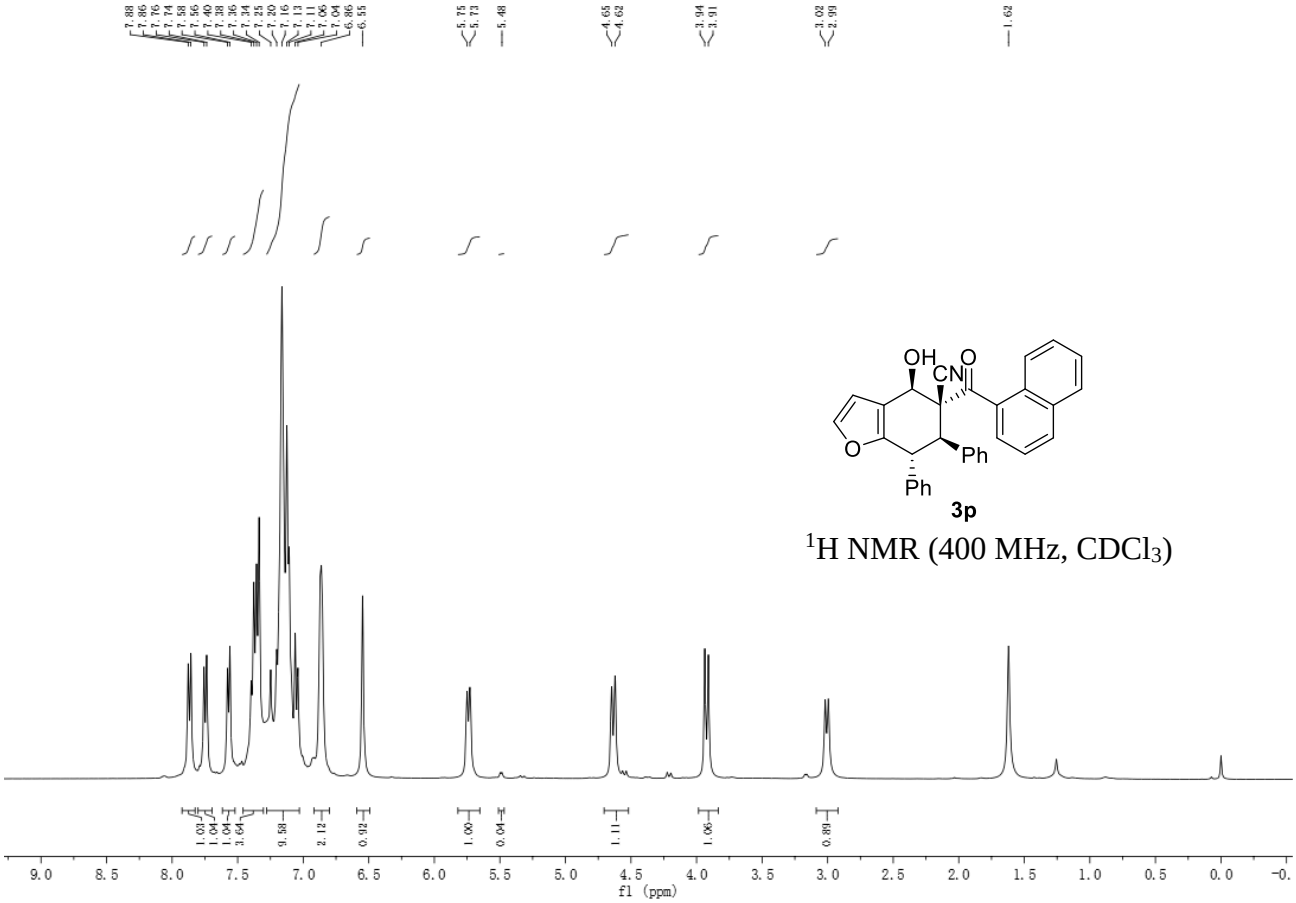




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	30.685	BBA	0.8070	9673.30371	186.20090	50.5998
2	36.509	BBA	0.9577	9443.97461	153.57173	49.4002

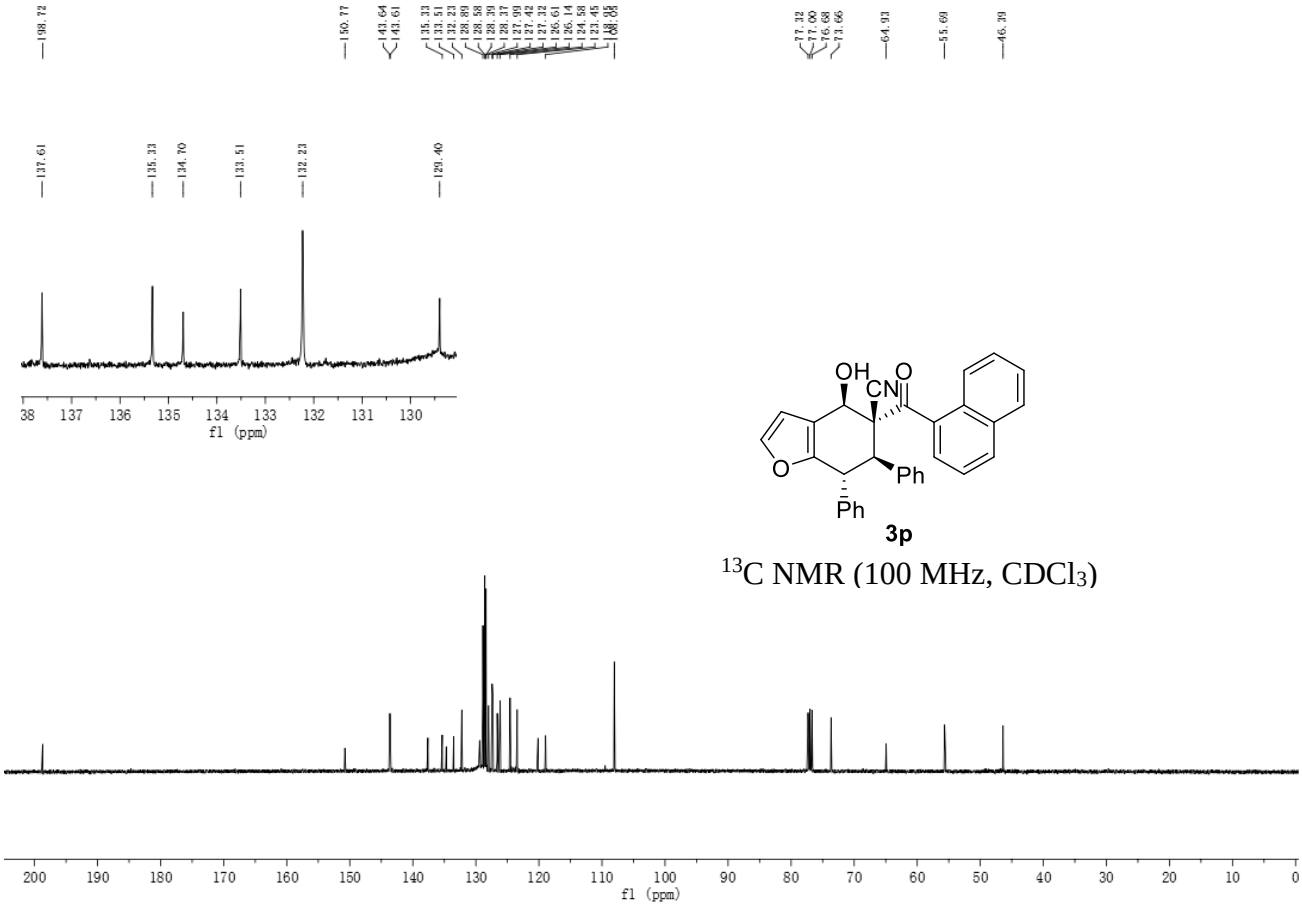


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	30.102	BBA	0.7917	1.19075e4	233.43832	99.4554
2	36.943	BBA	0.7054	65.20788	1.09423	0.5446



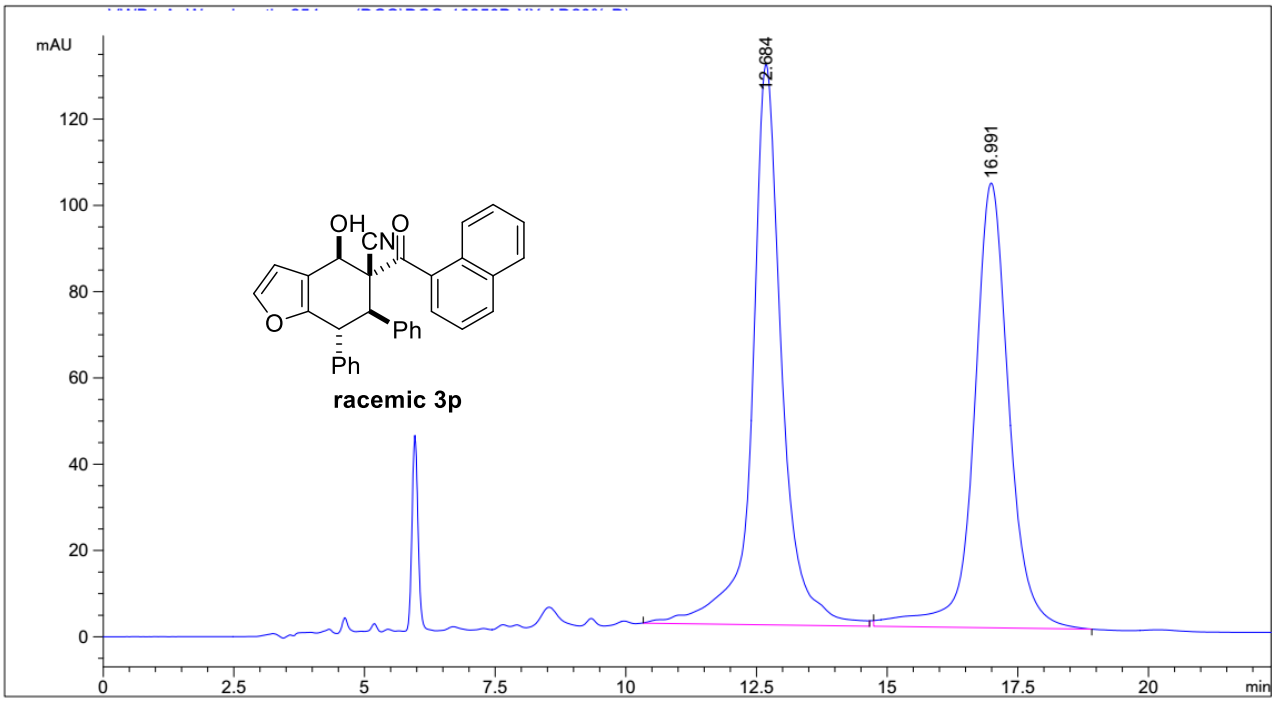
3p

^{1}H NMR (400 MHz, $CDCl_3$)

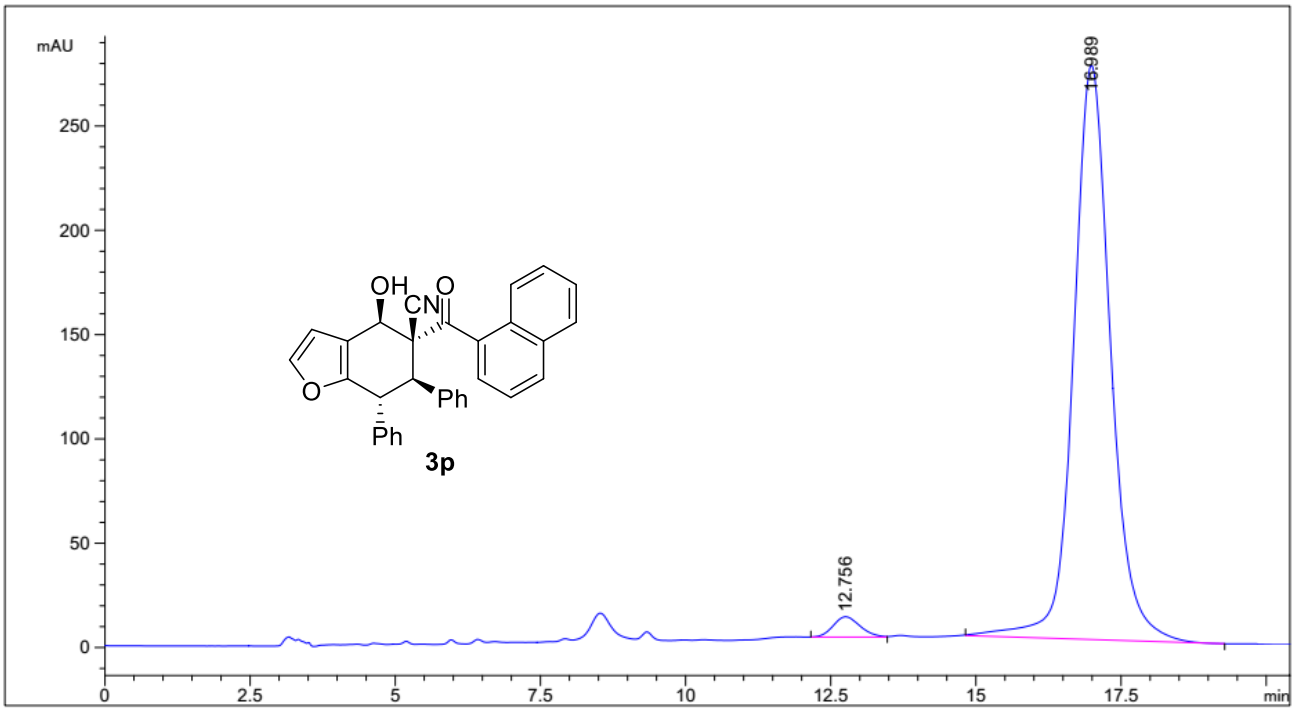


3p

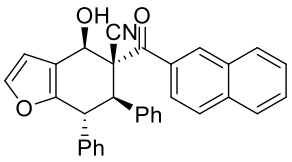
^{13}C NMR (100 MHz, $CDCl_3$)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.684	BB	0.5807	5166.98389	129.85204	51.7505
2	16.991	BBA	0.7025	4817.43896	103.07568	48.2495

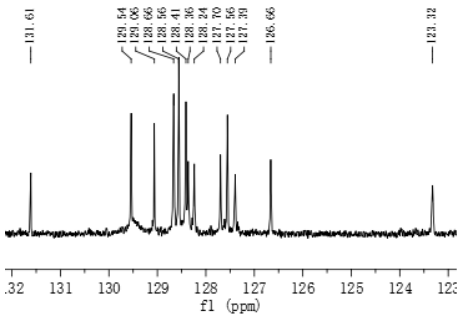


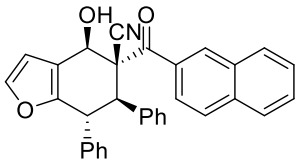
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.756	BV	0.4918	312.46356	9.71351	2.4829
2	16.989	BBA	0.6775	1.22721e4	275.21460	97.5171



3q

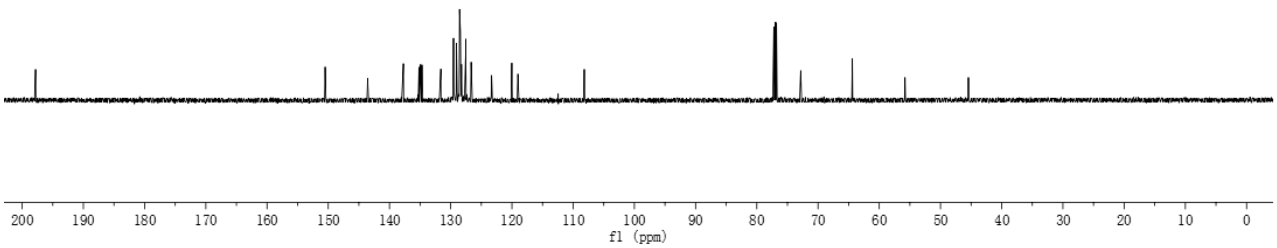
^{1}H NMR (400 MHz, $CDCl_3$)

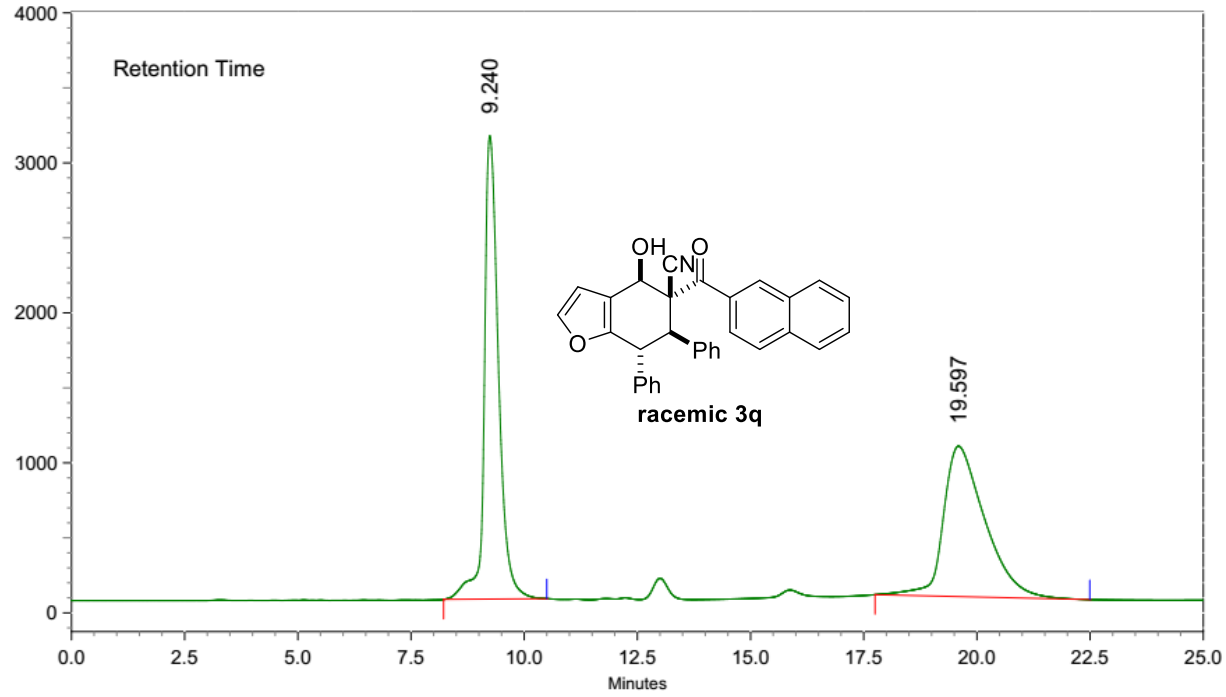




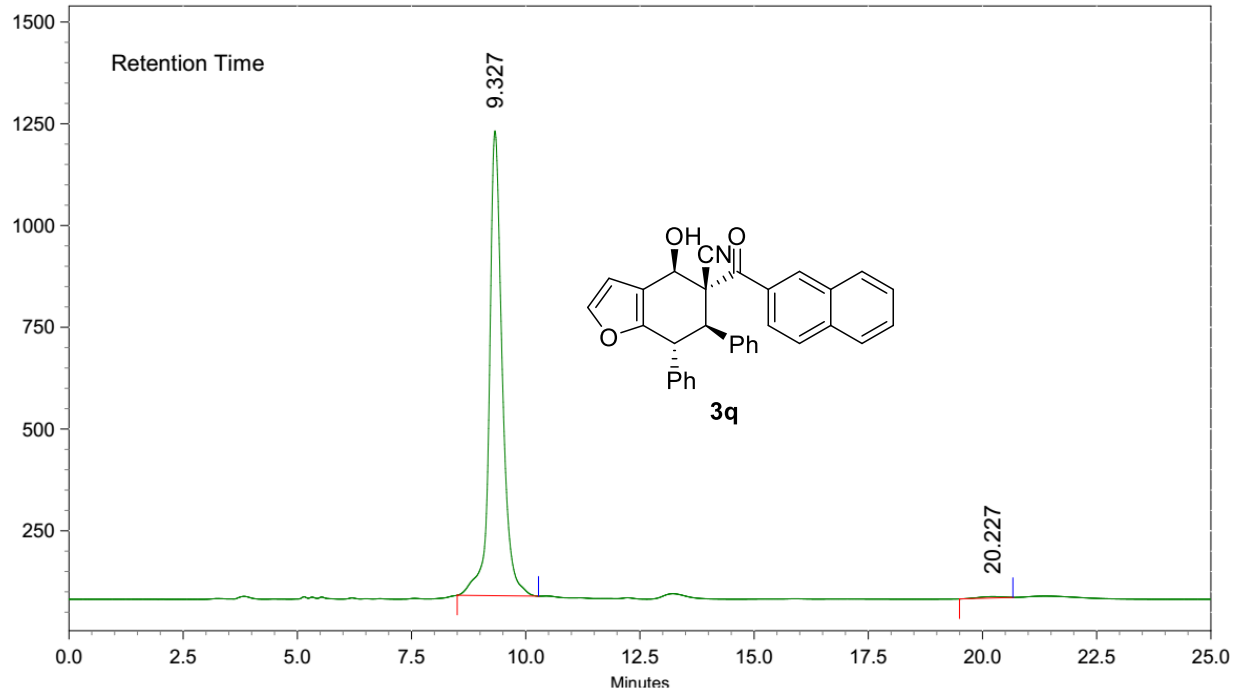
3q

^{13}C NMR (150 MHz, $CDCl_3$)

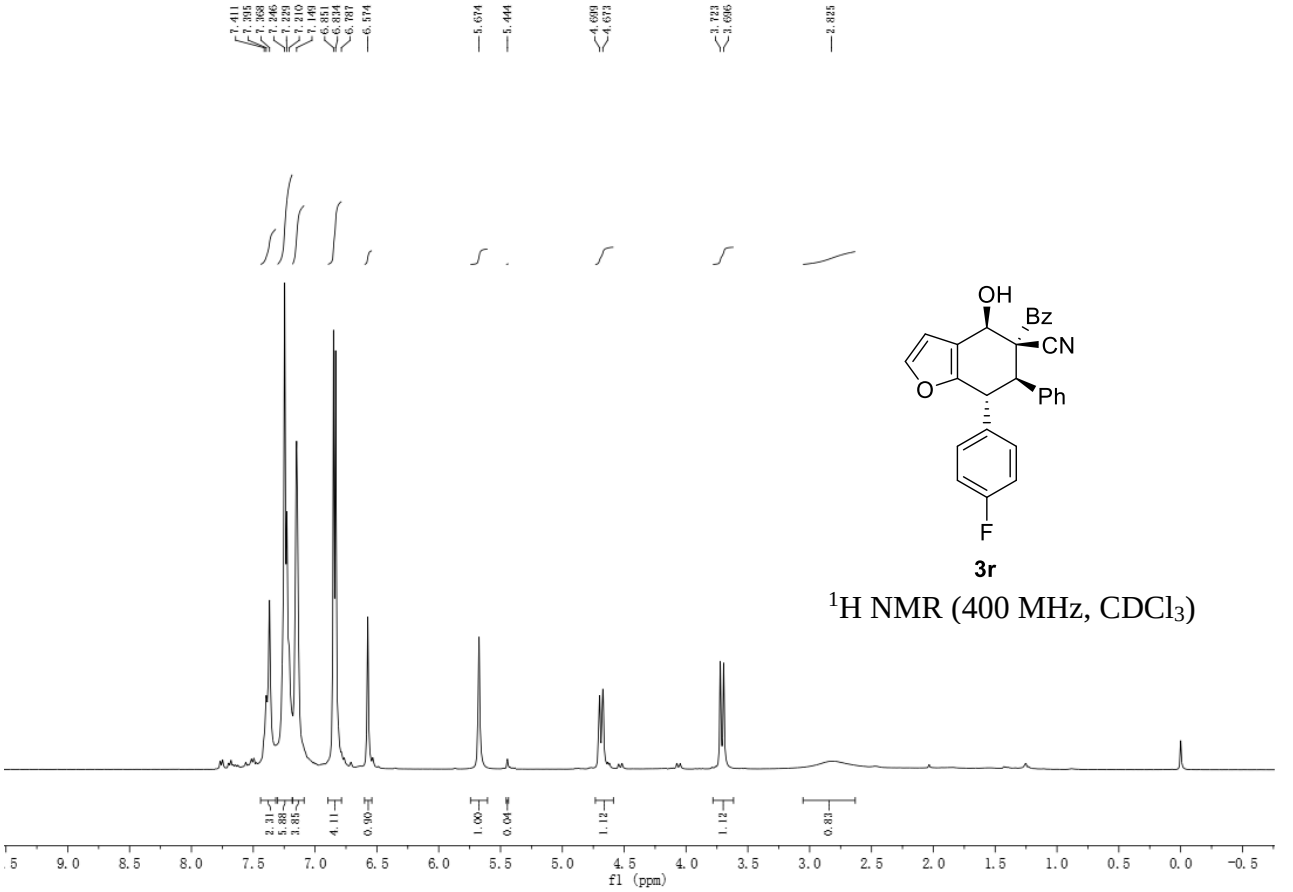


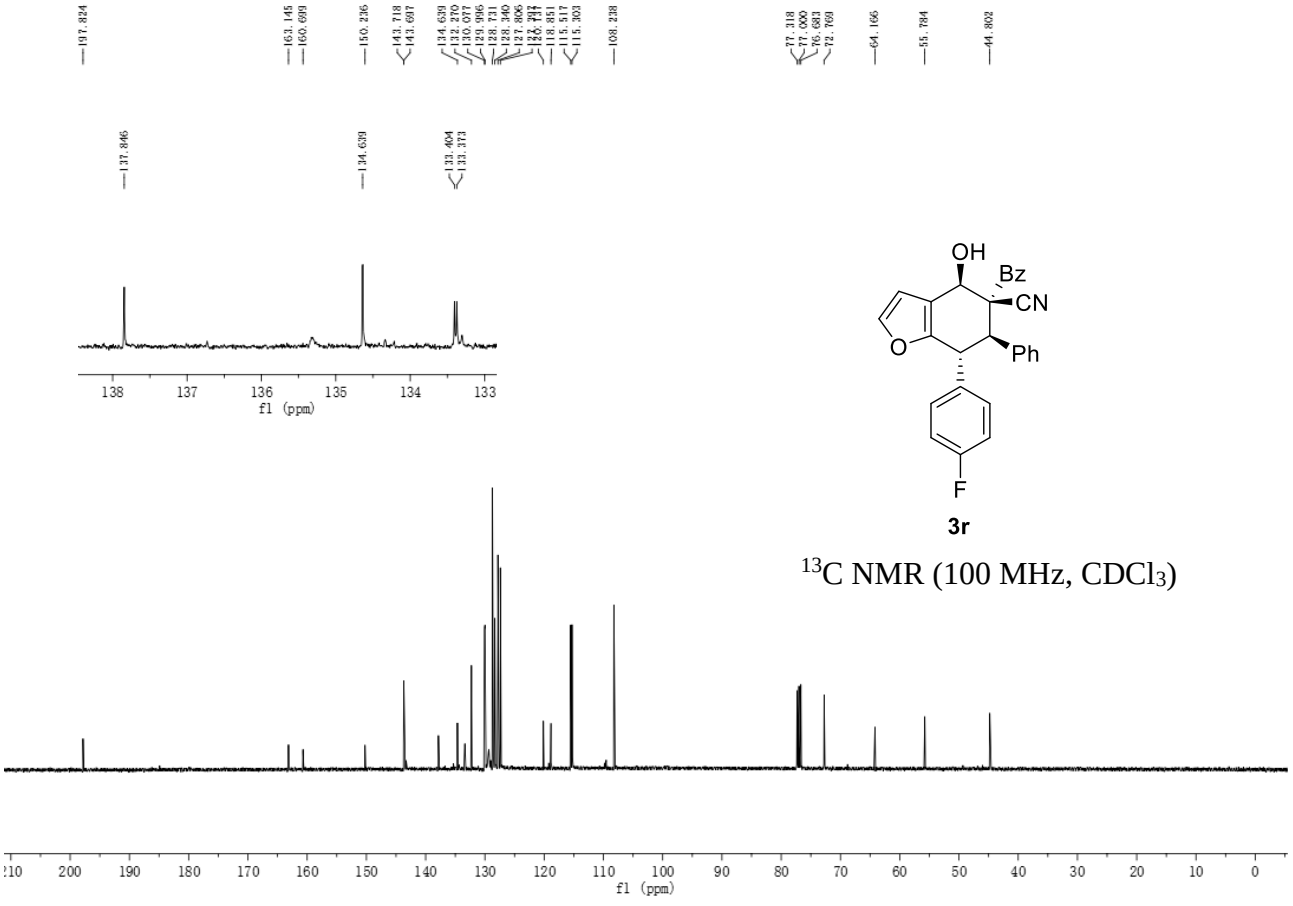


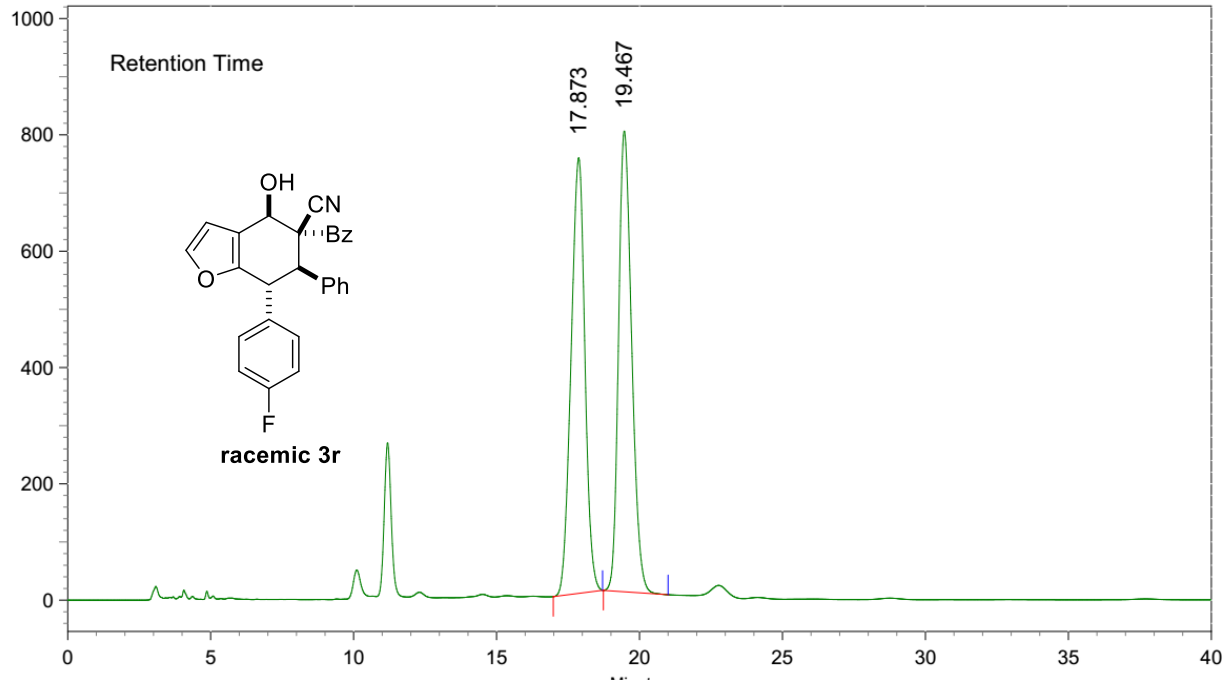
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.240	2.280	51810791	1136836427	51.4296
2	19.597	4.743	16827750	1073636683	48.5704



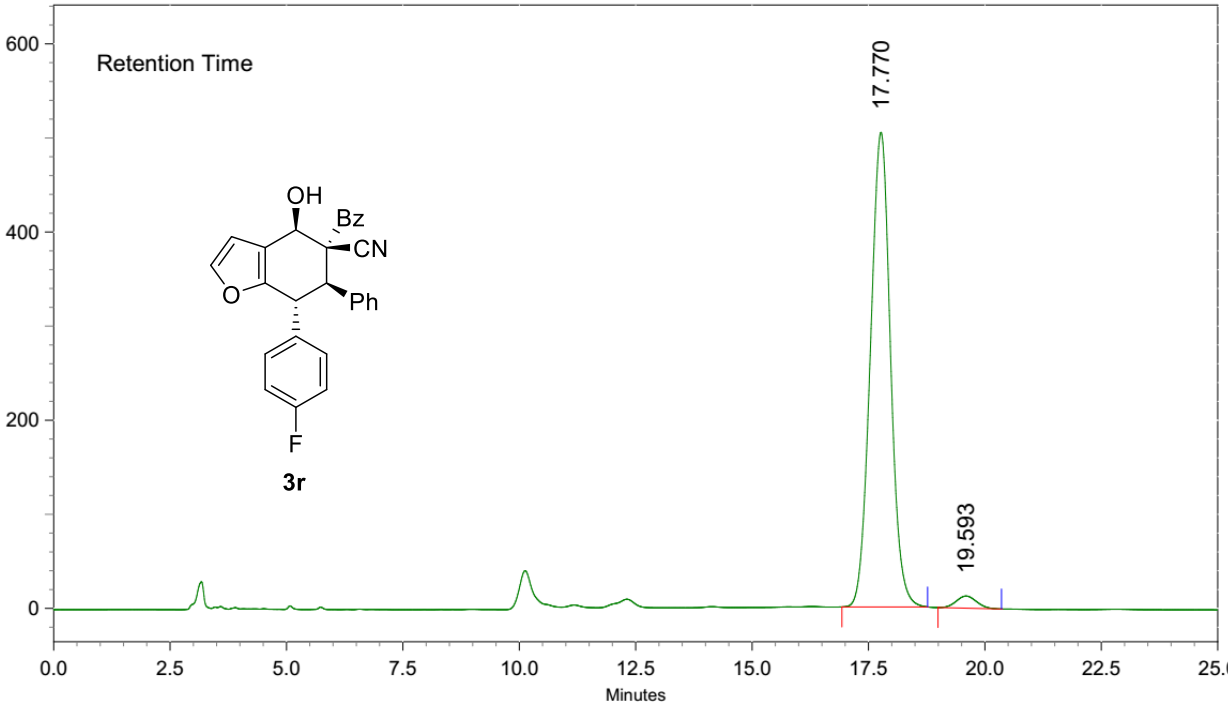
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.327	1.780	19157237	375137938	99.4700
2	20.227	1.170	55471	1998860	0.5300


OH
Bz
CN
Ph
O
F
3r
^{1}H NMR (400 MHz, $CDCl_3$)
f1 (ppm)

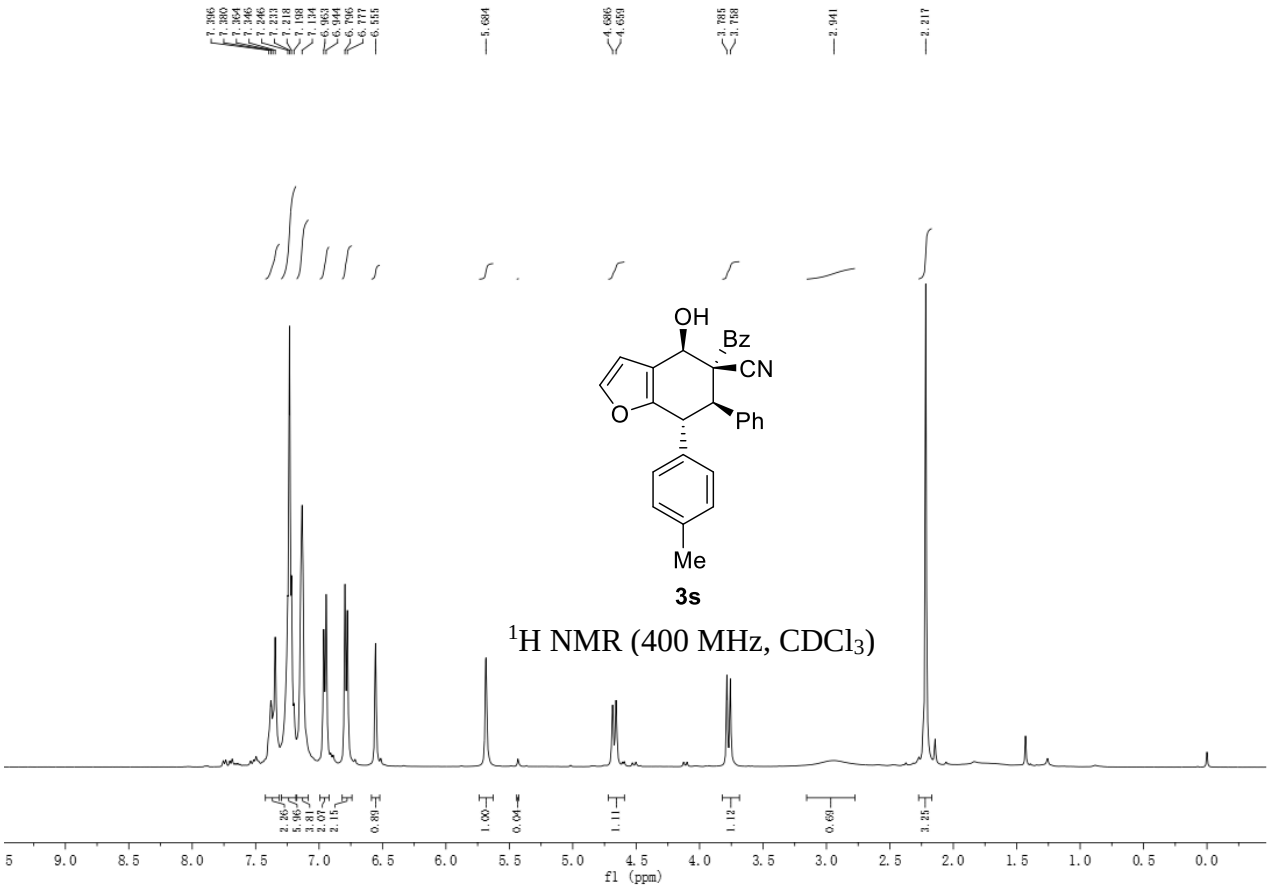

OH
Bz
CN
Ph
O
F
3r
^{13}C NMR (100 MHz, $CDCl_3$)
f1 (ppm)

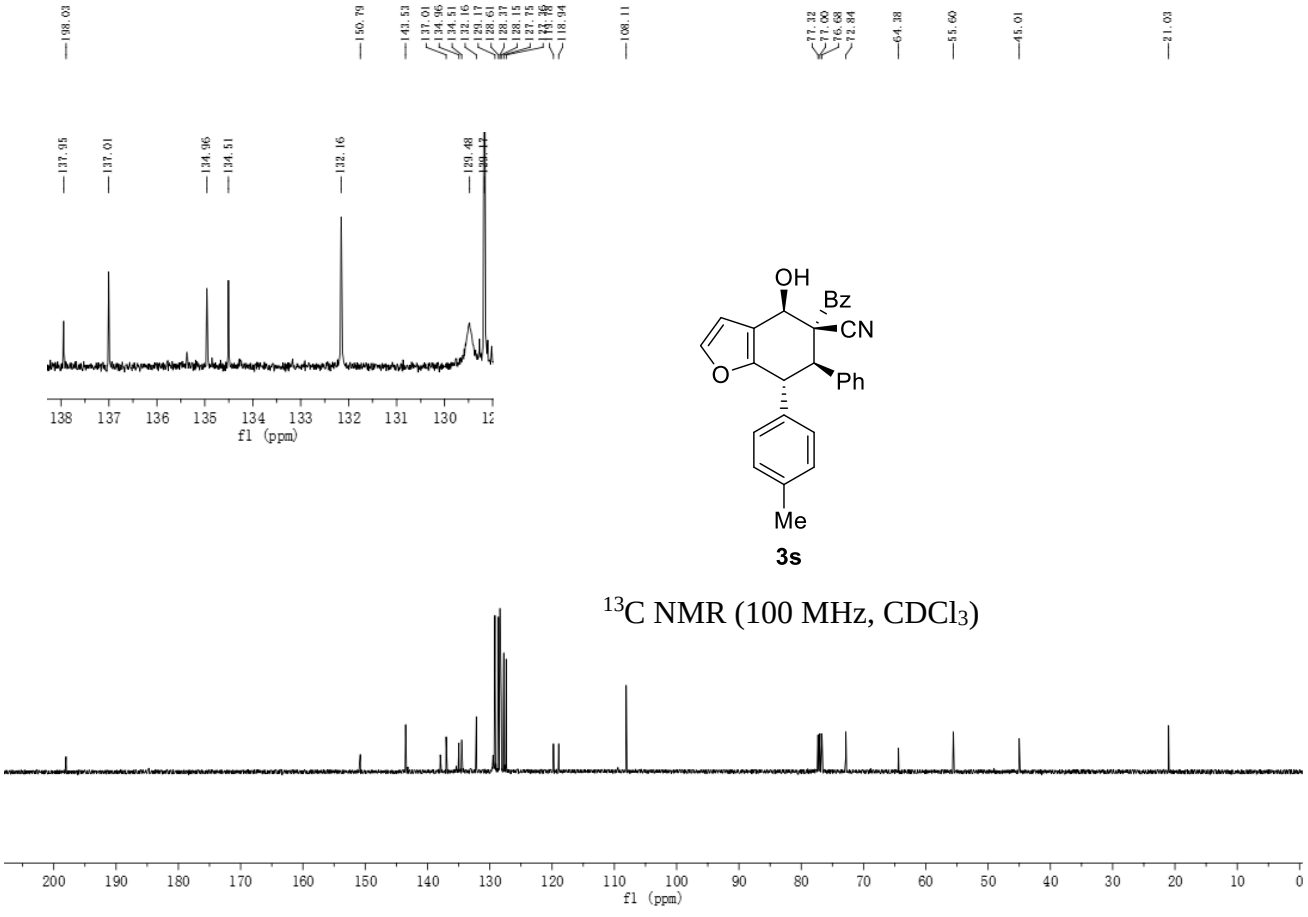


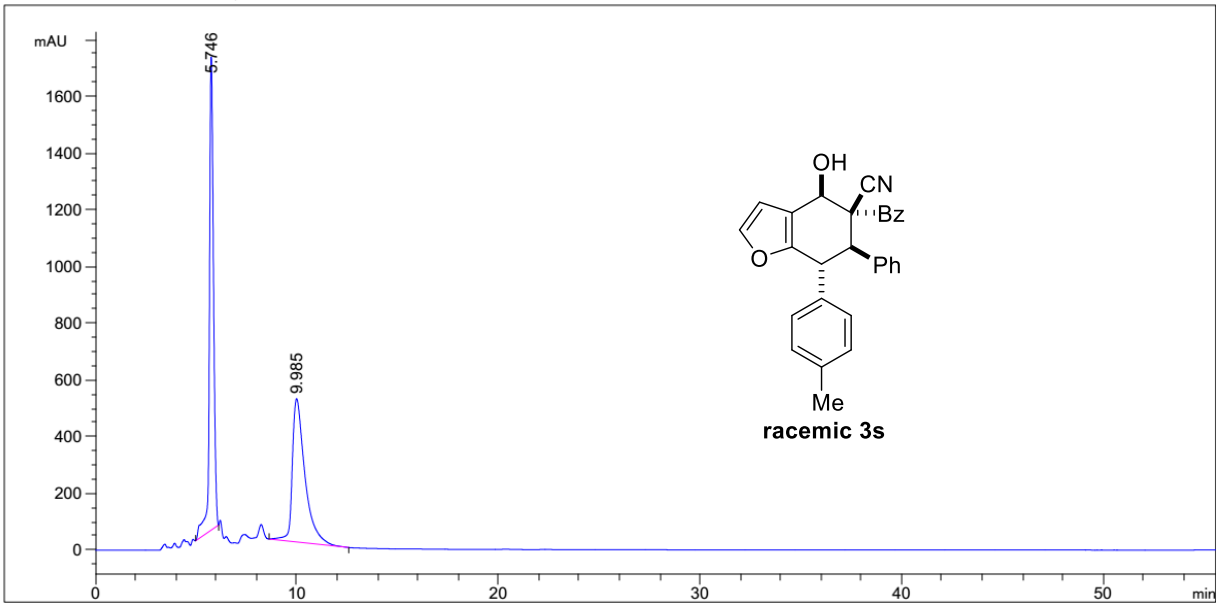
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	17.873	1.723	12569507	421953462	49.8056
2	19.467	2.263	13291551	425247450	50.1944



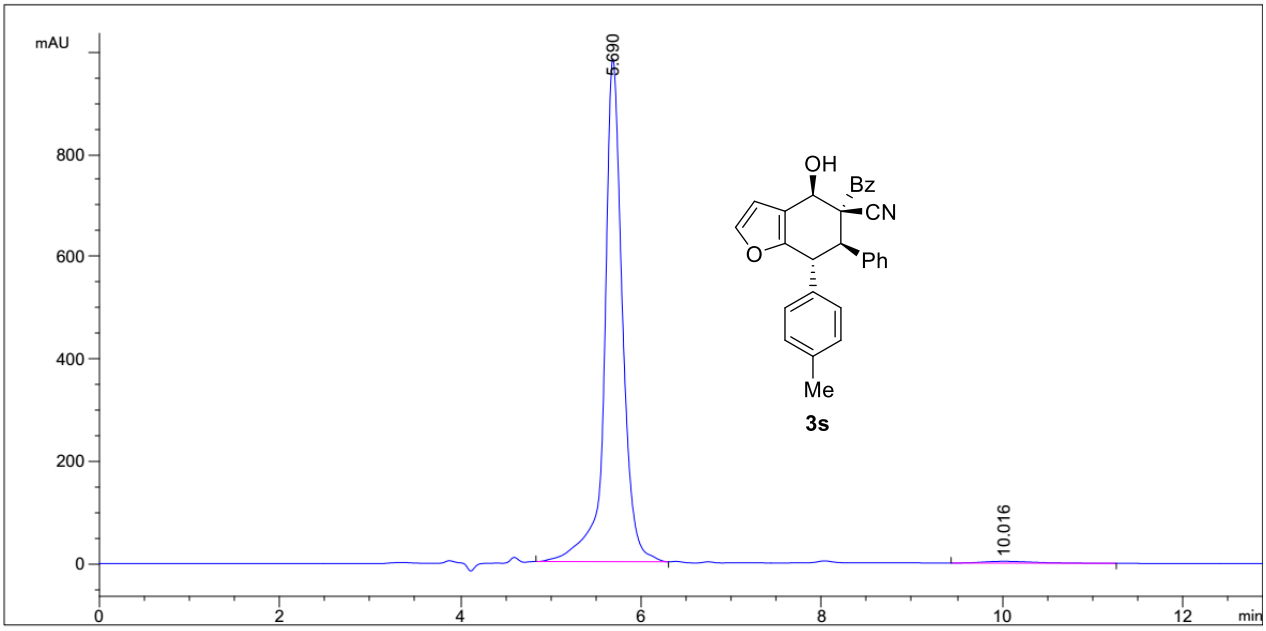
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	17.770	1.840	8462994	253442266	97.4616
2	19.593	1.363	216975	6600922	2.5384


OH
Bz
CN
O
Ph
Me
3s
1H NMR (400 MHz, CDCl3)
f1 (ppm)

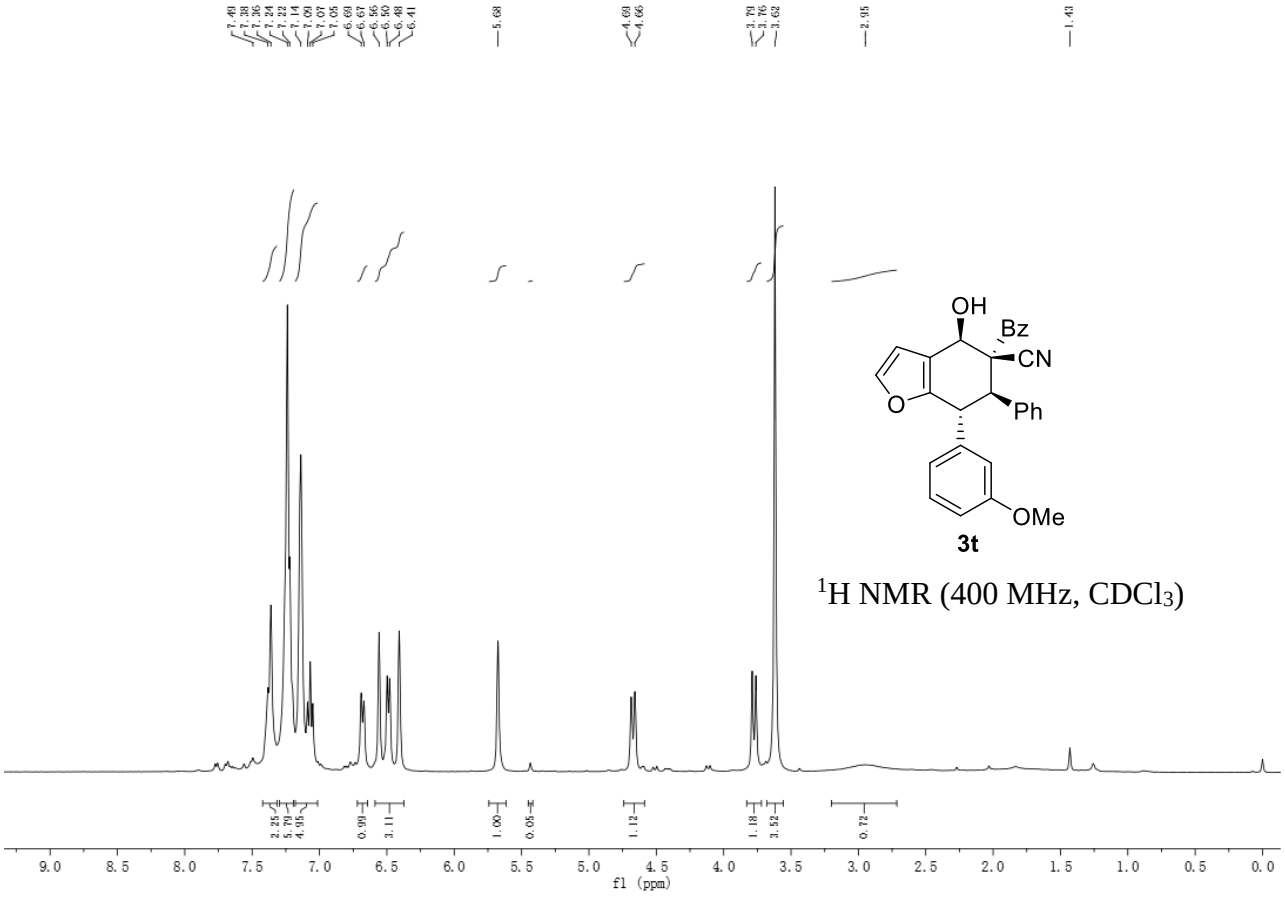

OH
Bz
CN
O
Ph
Me
3s
13C NMR (100 MHz, CDCl3)
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.746	BB	0.2183	2.37096e4	1667.41797	51.8269
2	9.985	BB	0.6427	2.20381e4	505.35608	48.1731

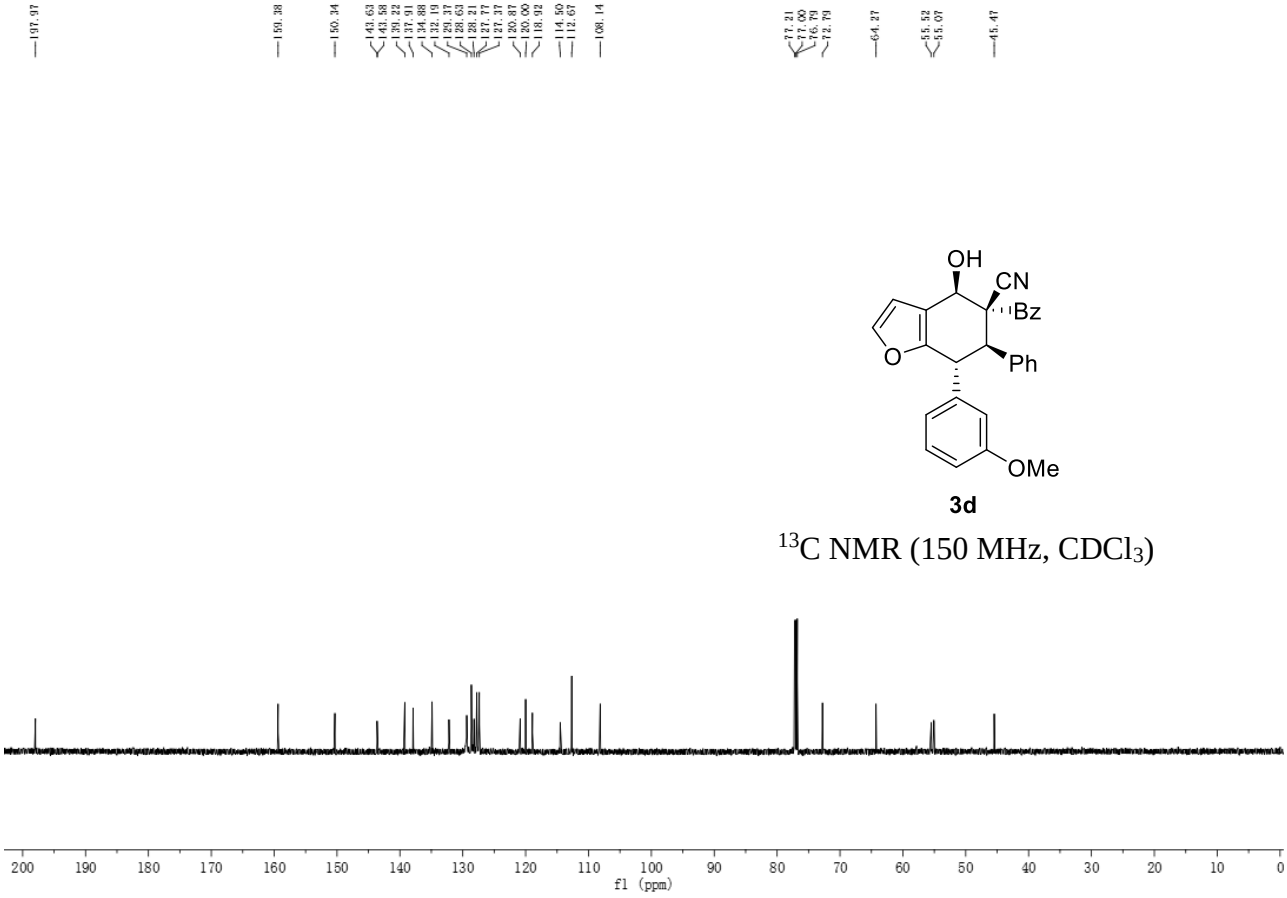


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.690	BB	0.2050	1.35971e4	983.42096	98.9948
2	10.016	BBA	0.5855	138.06299	3.48819	1.0052



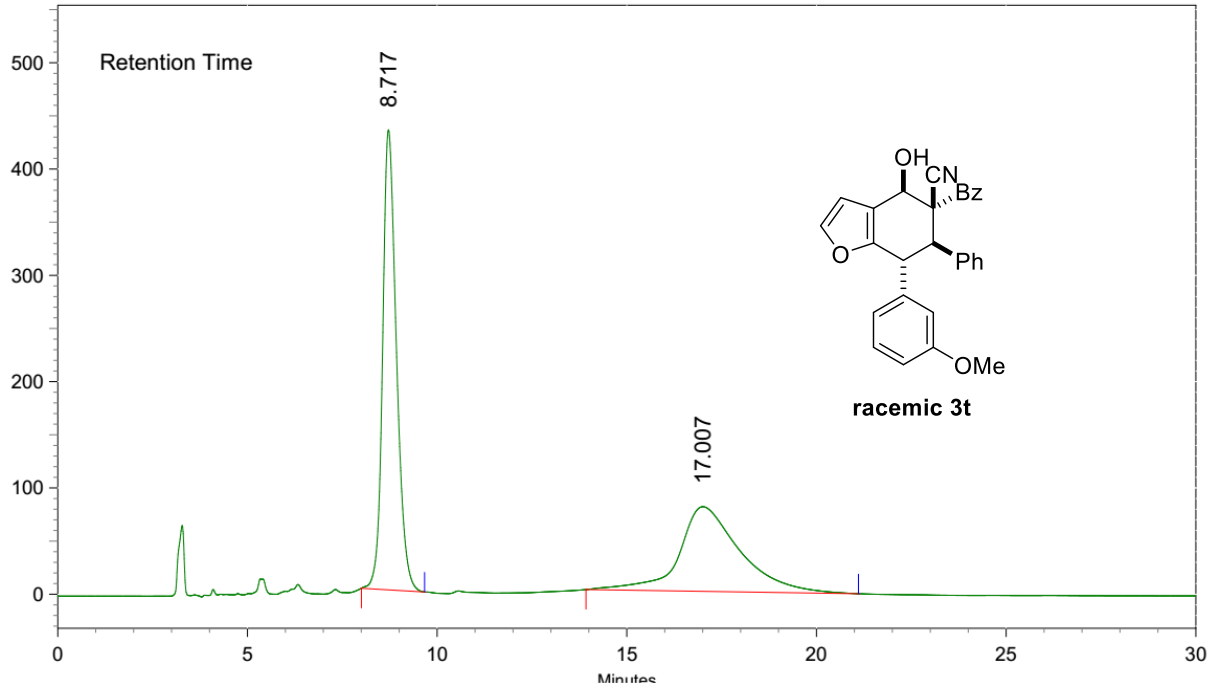
3t

^{1}H NMR (400 MHz, $CDCl_3$)

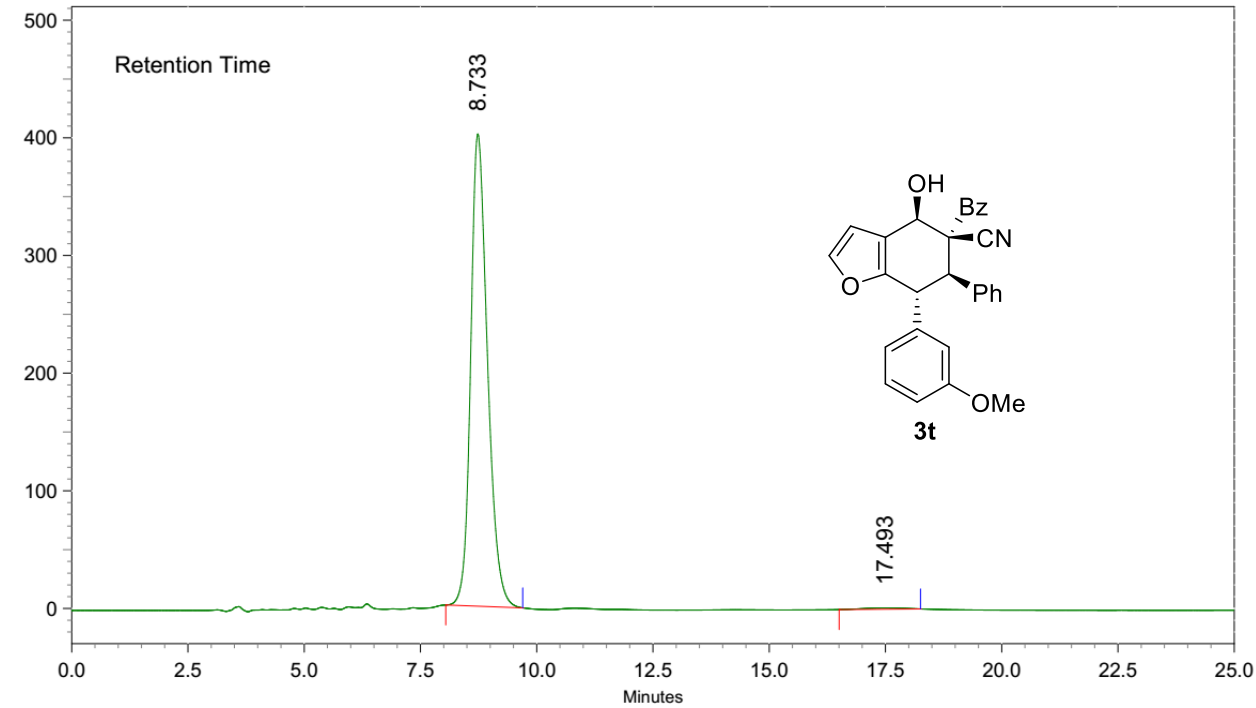


3d

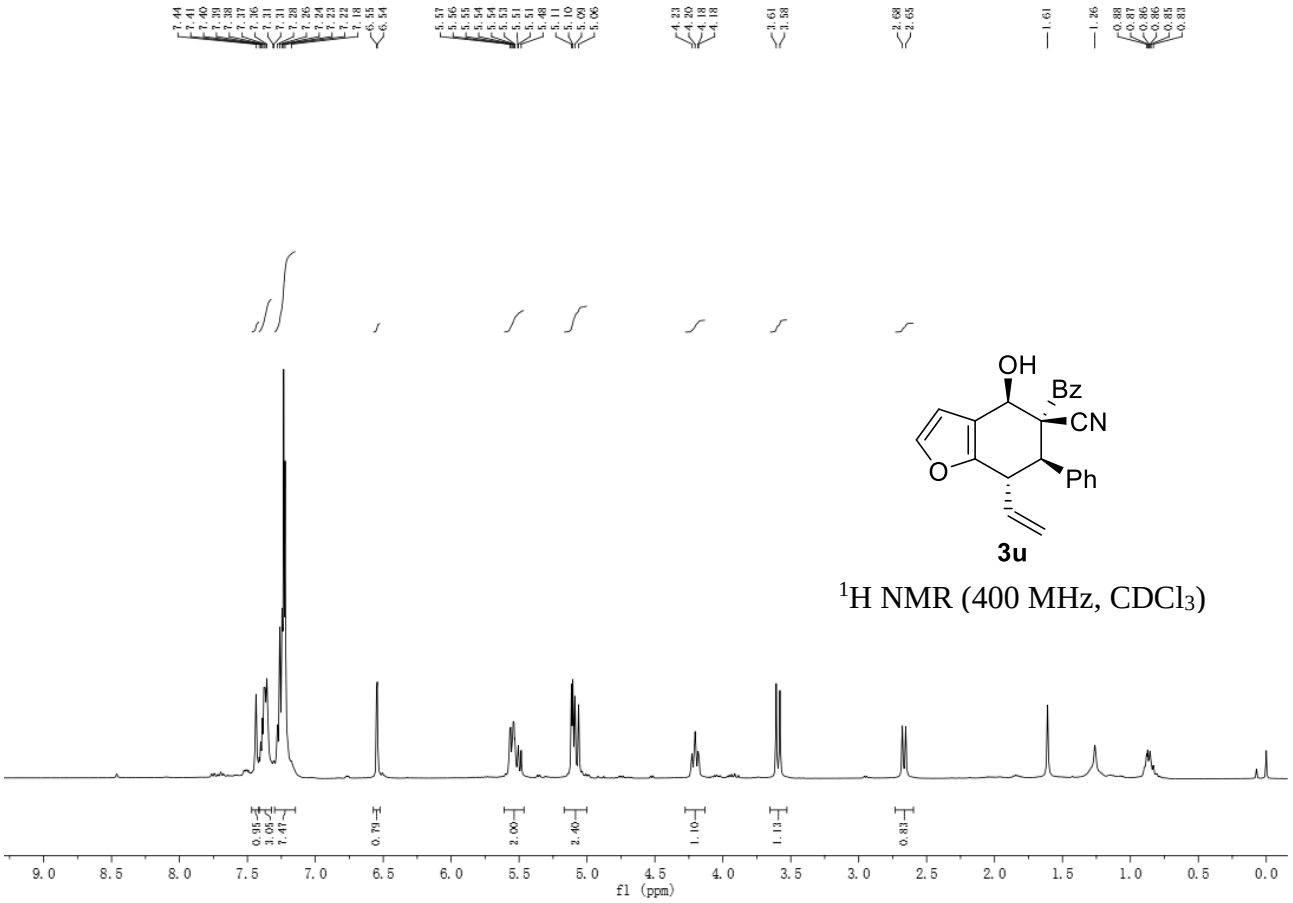
^{13}C NMR (150 MHz, $CDCl_3$)



Peak No.	Ret Time	Width	Height	Area	Area [%]
1	8.717	1.667	7260950	183526233	55.1926
2	17.007	7.183	1335875	148993496	44.8074

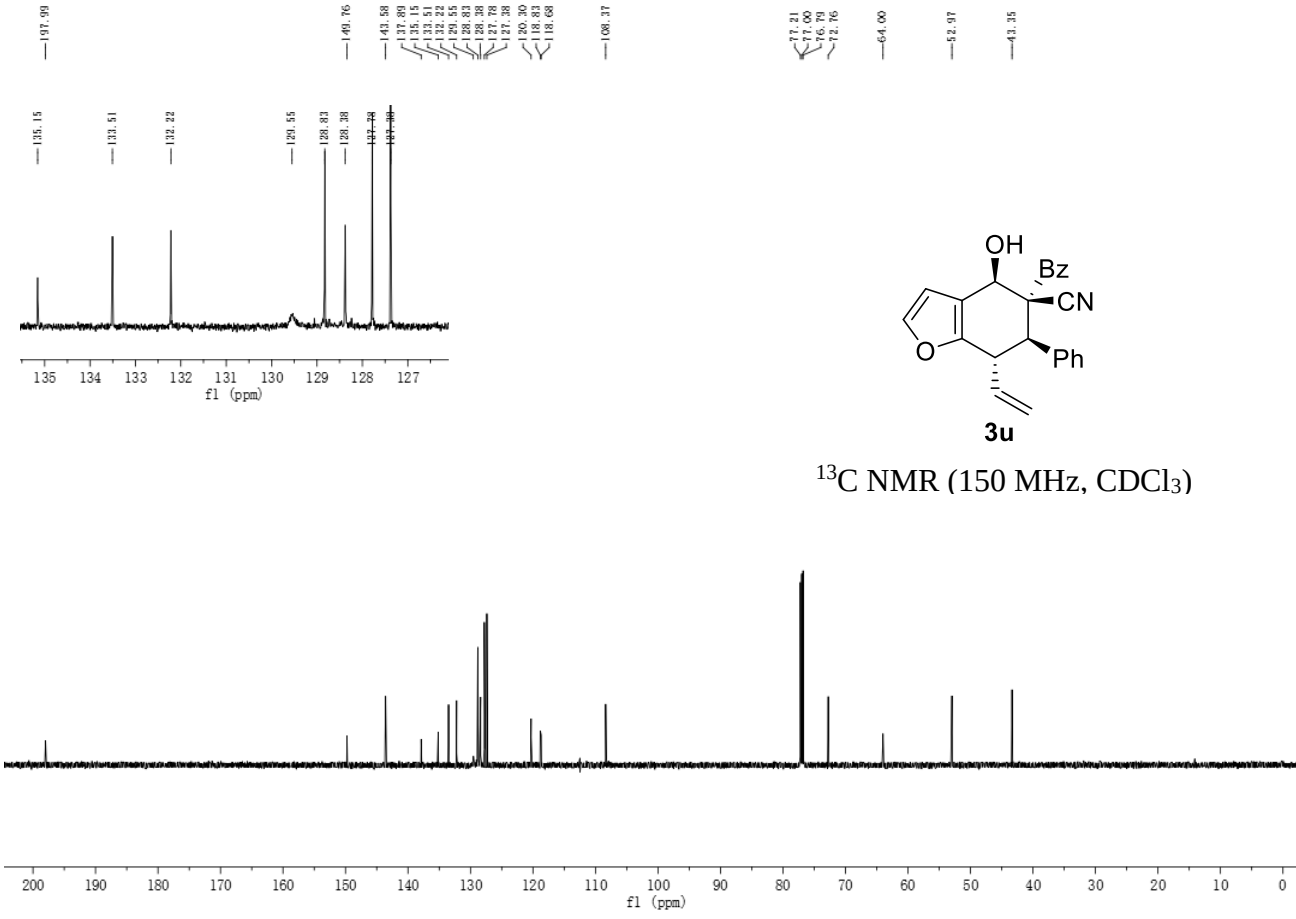


Peak No.	Ret Time	Width	Height	Area	Area [%]
1	8.733	1.657	6733817	169294283	99.3683
2	17.493	1.750	17768	1076232	0.6317



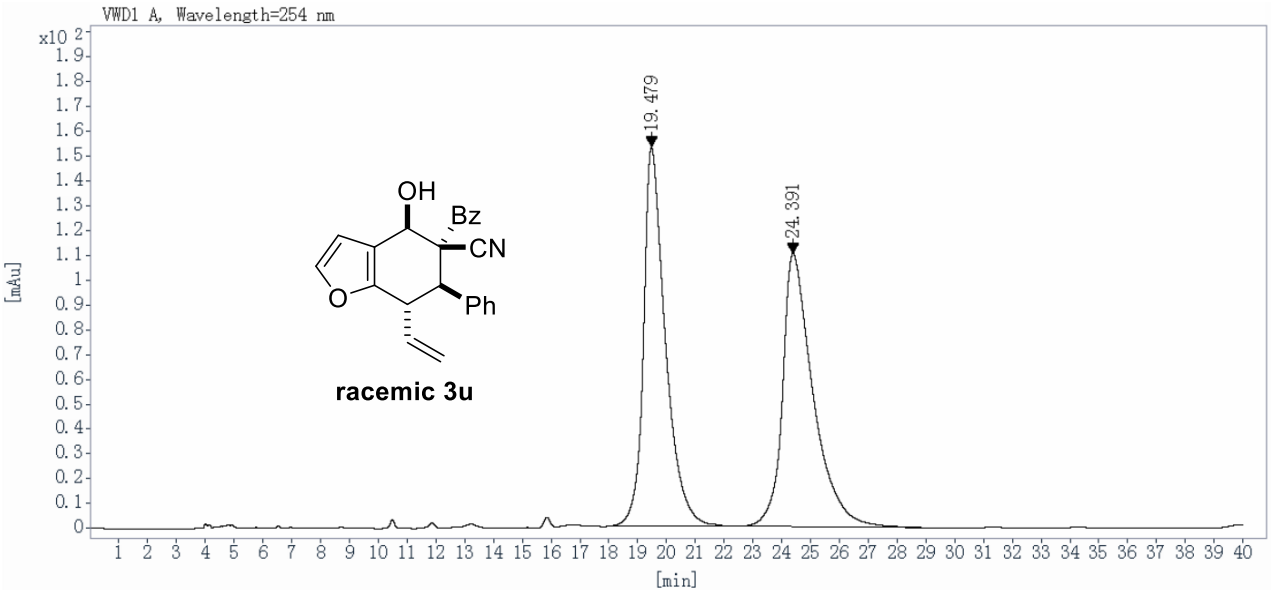
3u

^{1}H NMR (400 MHz, $CDCl_3$)

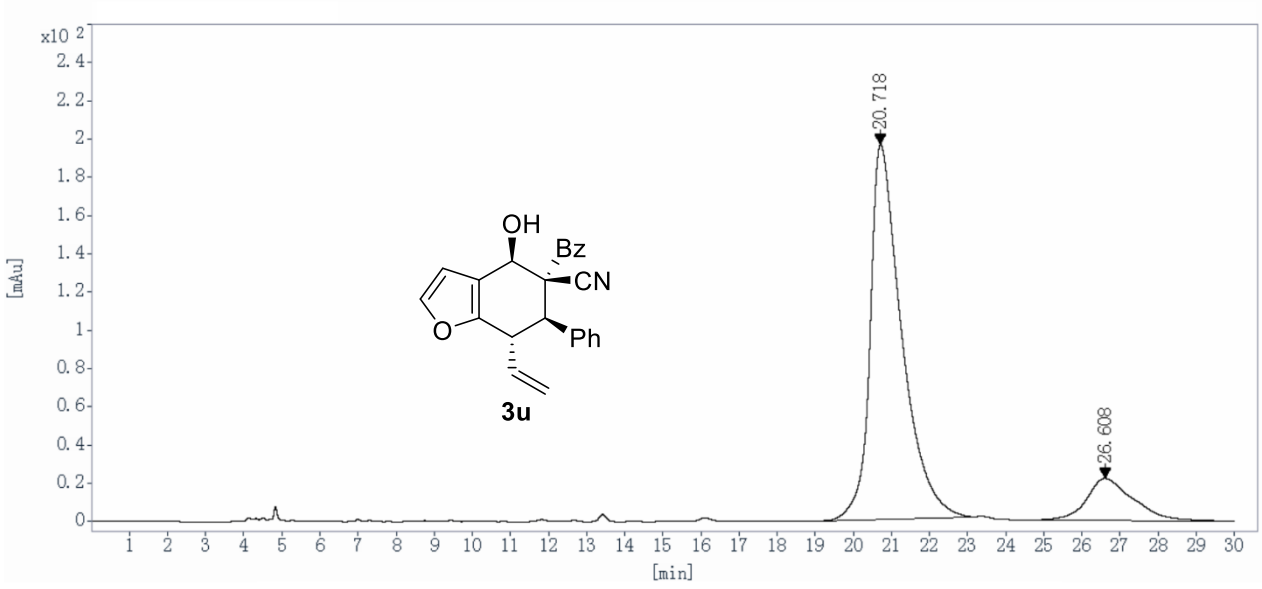


3u

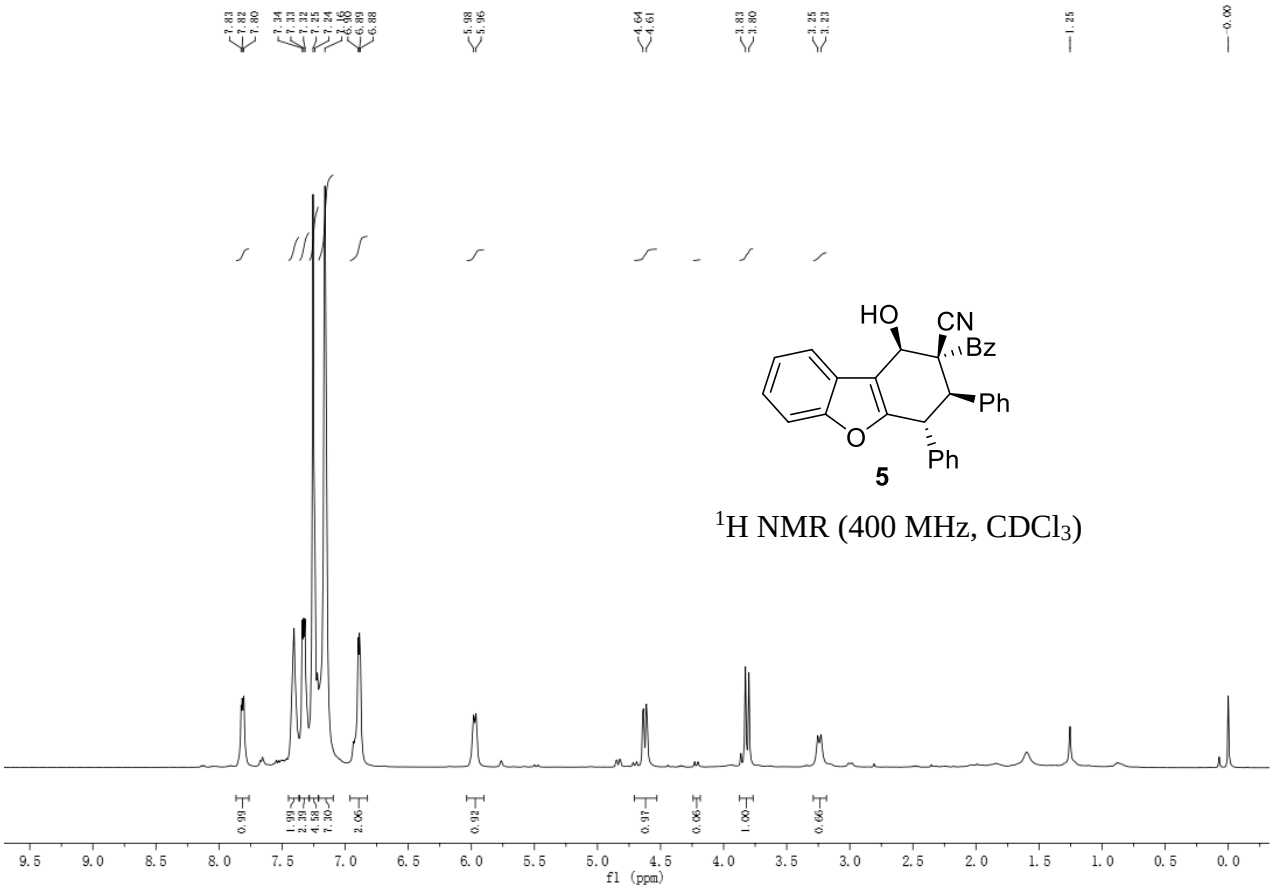
^{13}C NMR (150 MHz, $CDCl_3$)

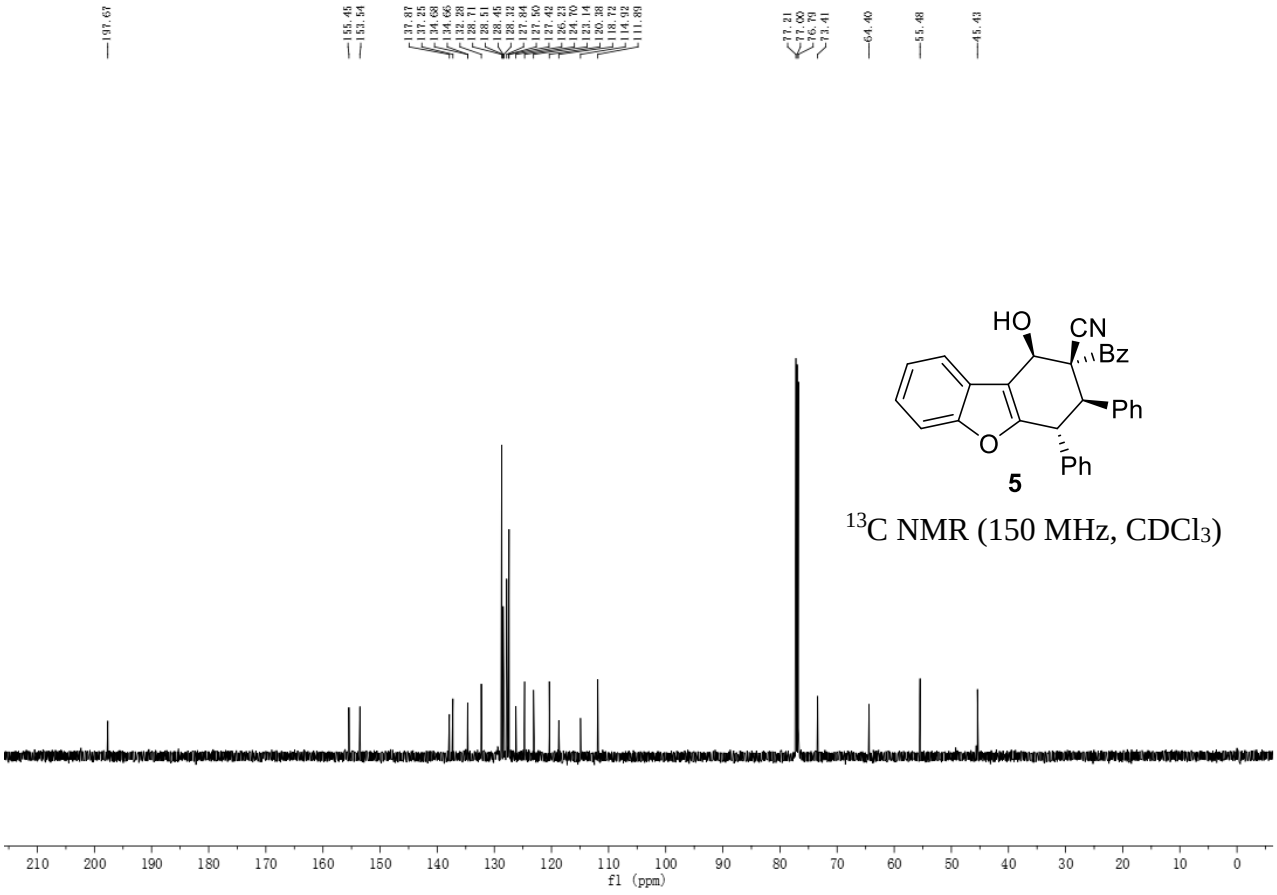


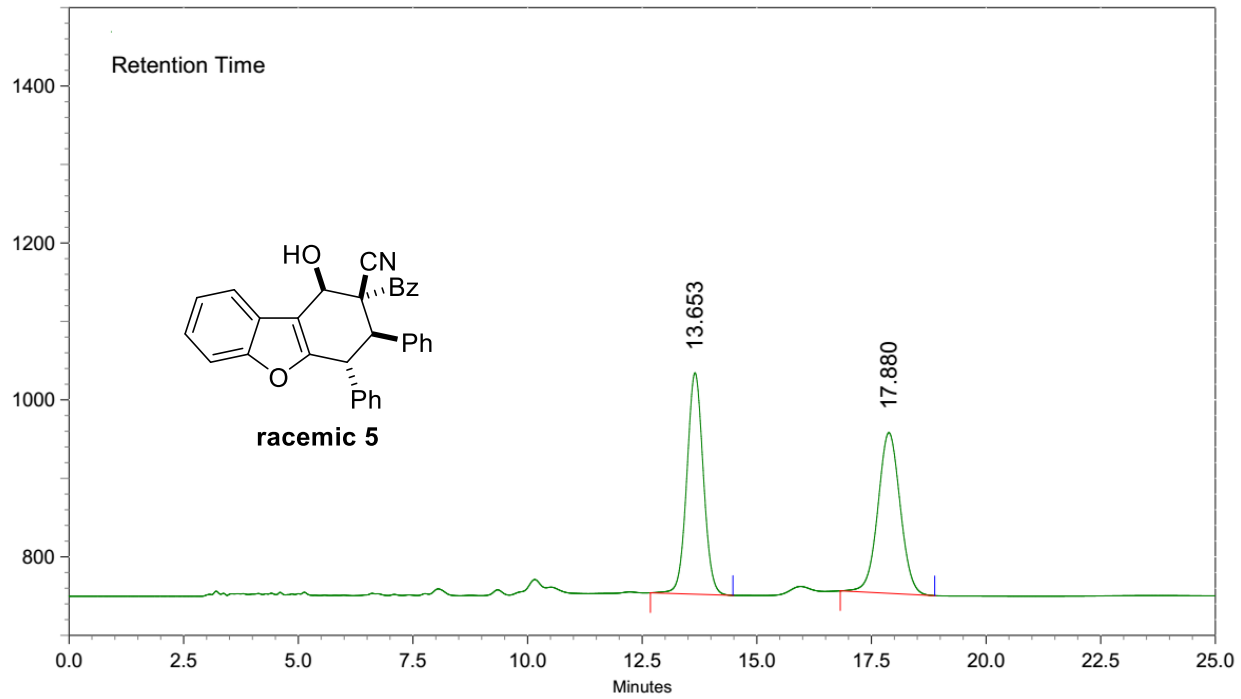
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
19.479	BB	0.76	152.5386	8031.4390	49.5923
24.391	BB	1.07	110.0788	8163.4902	50.4077



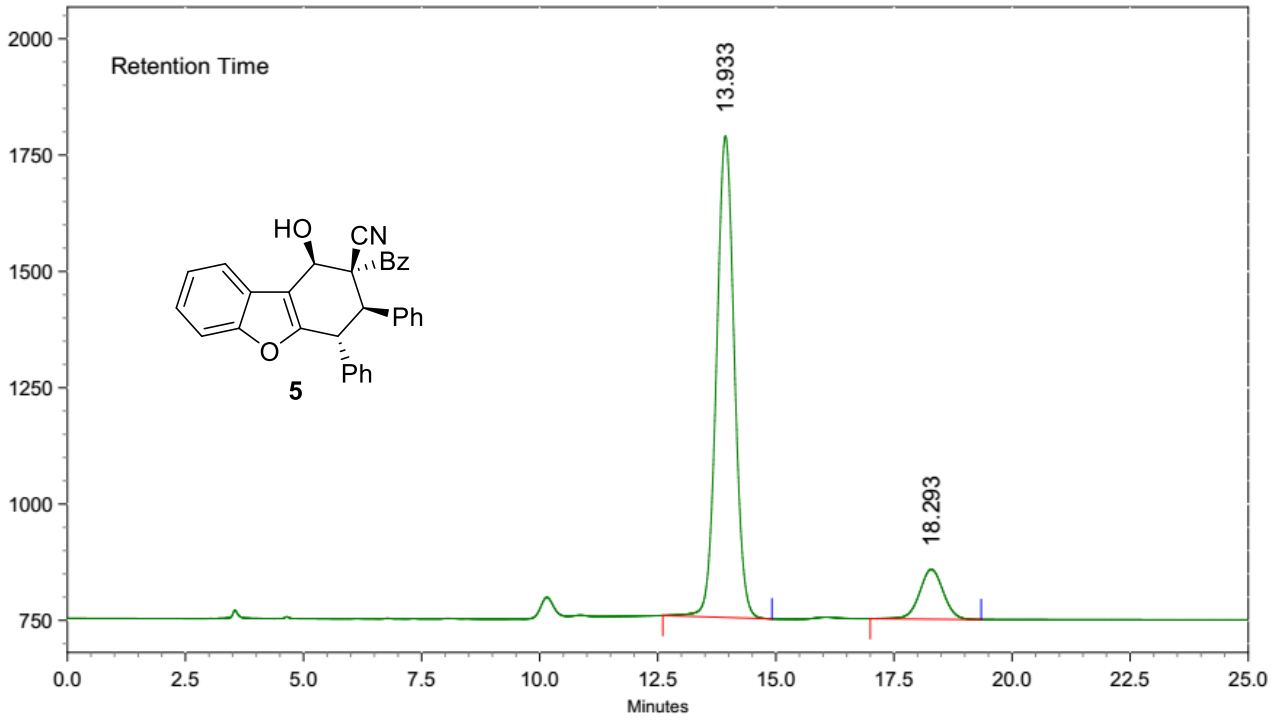
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
20.718	BB	0.83	195.9273	11300.0742	85.7882
26.608	BBA	1.19	21.9459	1871.9857	14.2118


HO
CN
Bz
Ph
O
Ph
5
1H NMR (400 MHz, CDCl3)
f1 (ppm)

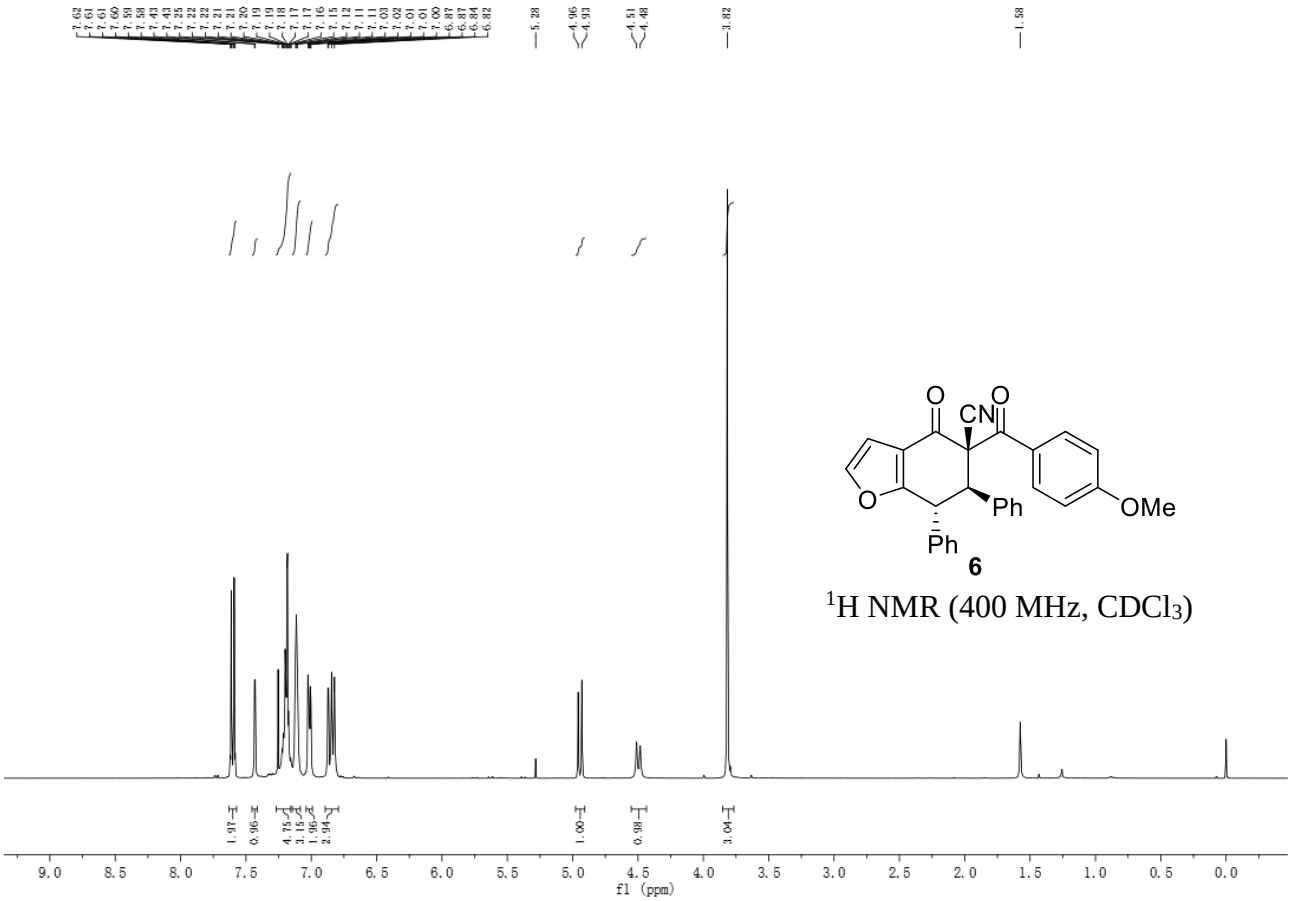

HO
CN
Bz
Ph
O
Ph
5
13C NMR (150 MHz, CDCl3)
f1 (ppm)



Peak No.	Ret Time	Width	Height	Area	Area [%]
1	13.653	1.800	4733045	118316890	50.4482
2	17.880	2.060	3435392	116214534	49.5518

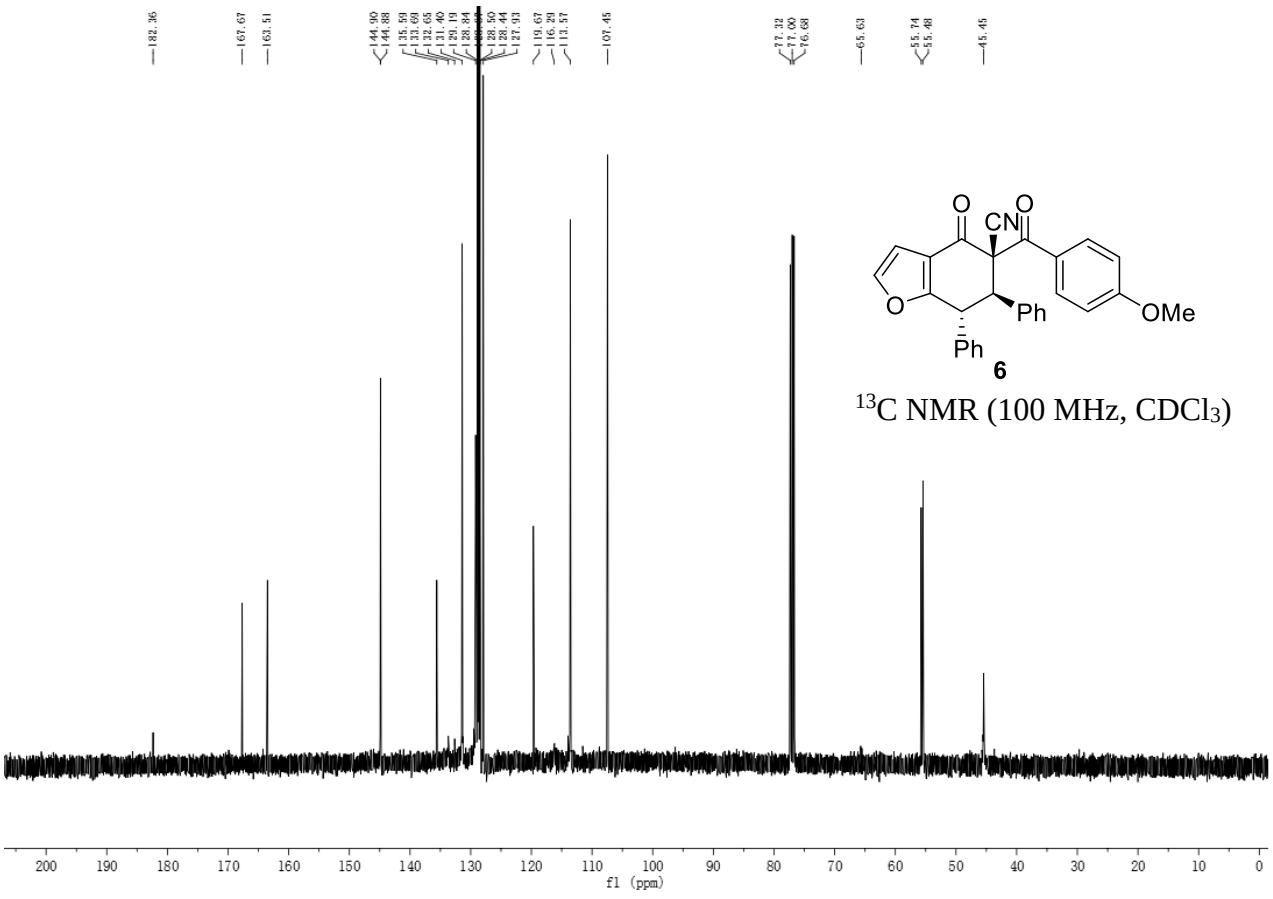


Peak No.	Ret Time	Width	Height	Area	Area [%]
1	13.933	2.310	17355913	454936464	87.8631
2	18.293	2.347	1797300	62842274	12.1369



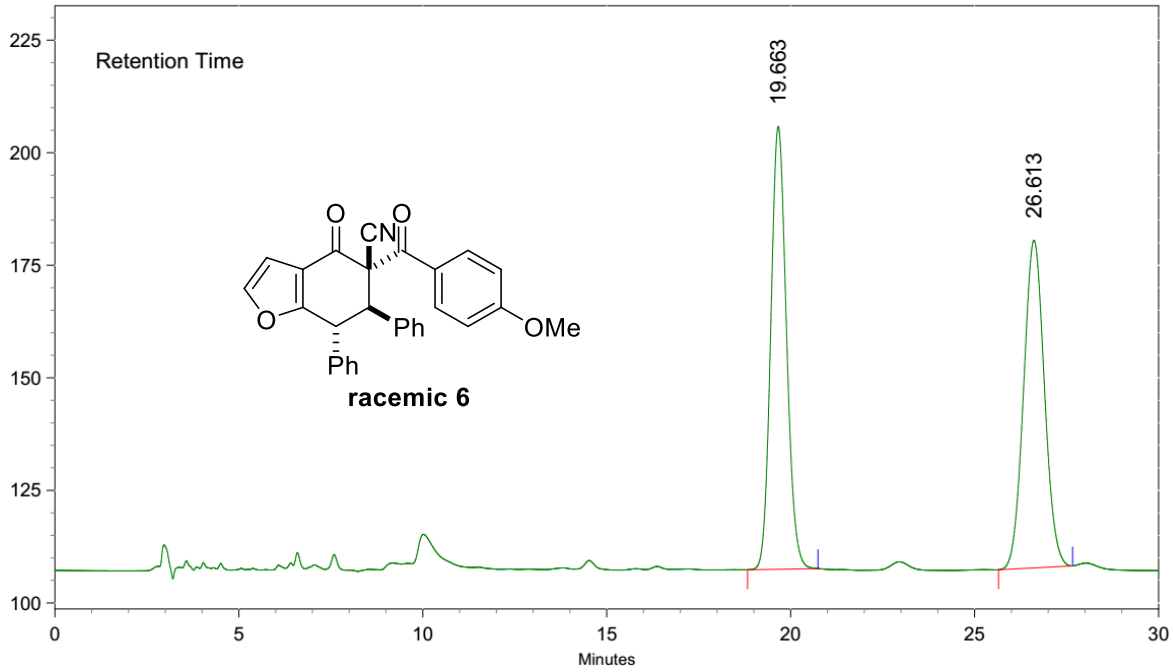
6

^{1}H NMR (400 MHz, $CDCl_3$)

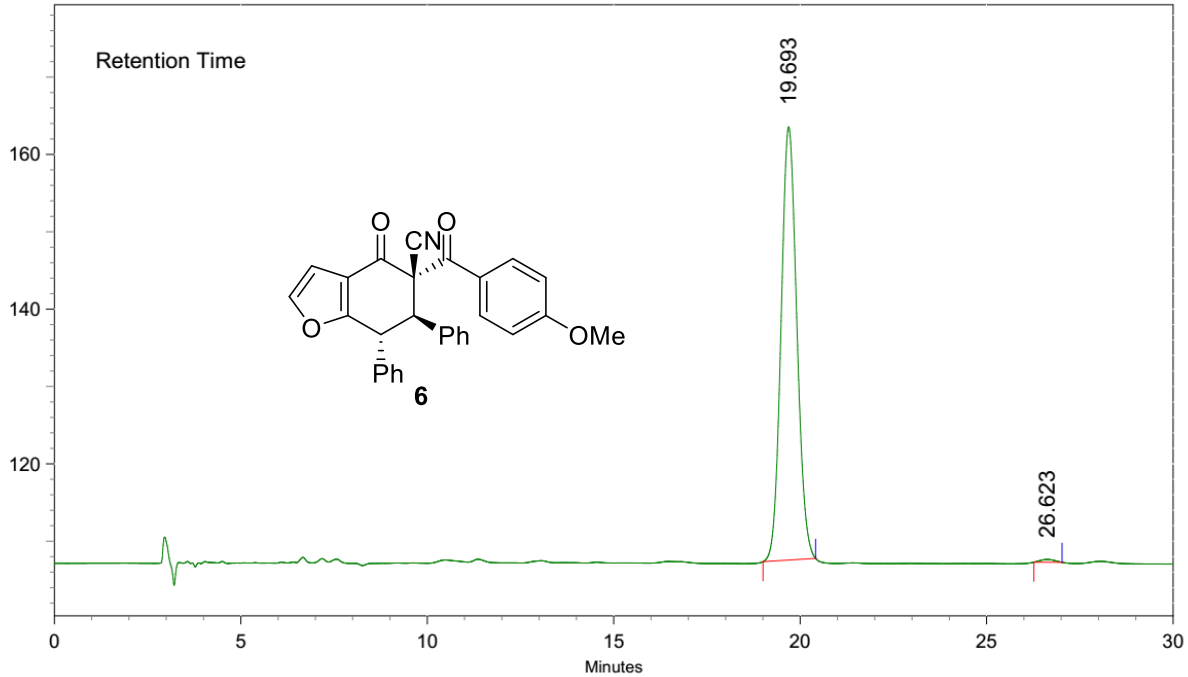


6

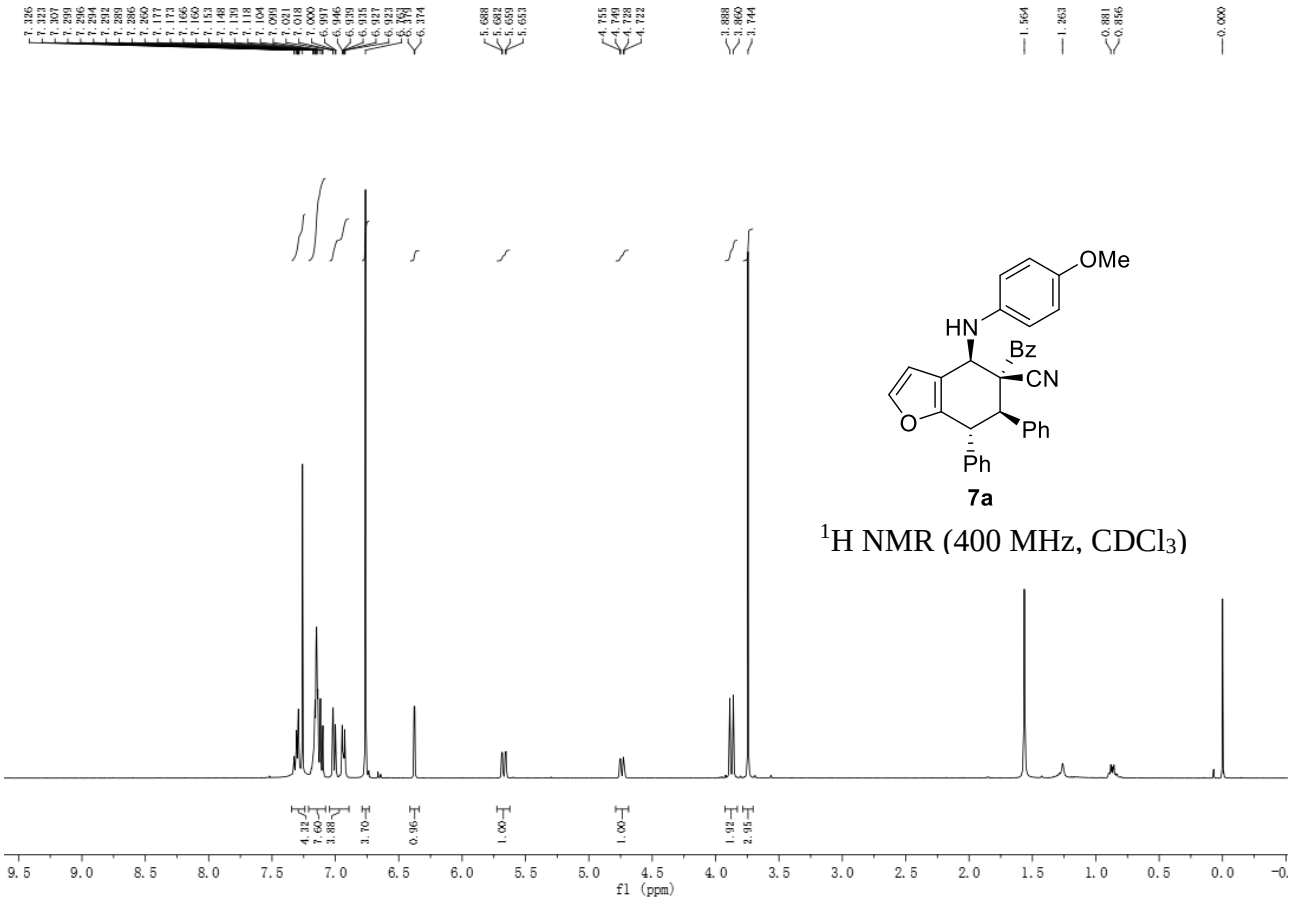
^{13}C NMR (100 MHz, $CDCl_3$)



Peak No.	Ret Time	Width	Height	Area	Area [%]
1	19.663	1.917	1650567	48931799	50.4522
2	26.613	2.013	1221236	48054748	49.5478

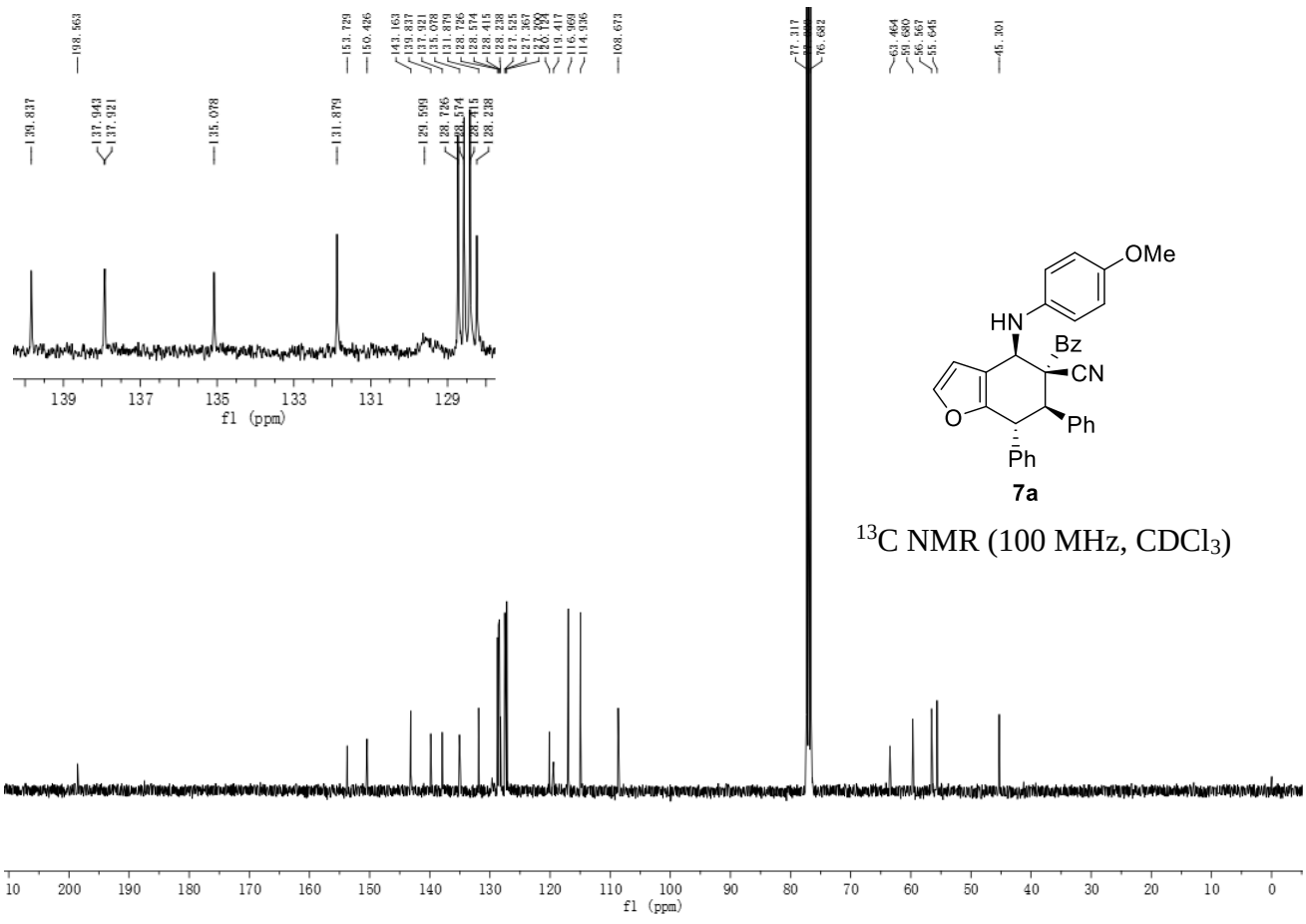


Peak No.	Ret Time	Width	Height	Area	Area [%]
1	19.693	1.410	939509	27551296	99.4196
2	26.623	0.757	5976	160853	0.5804



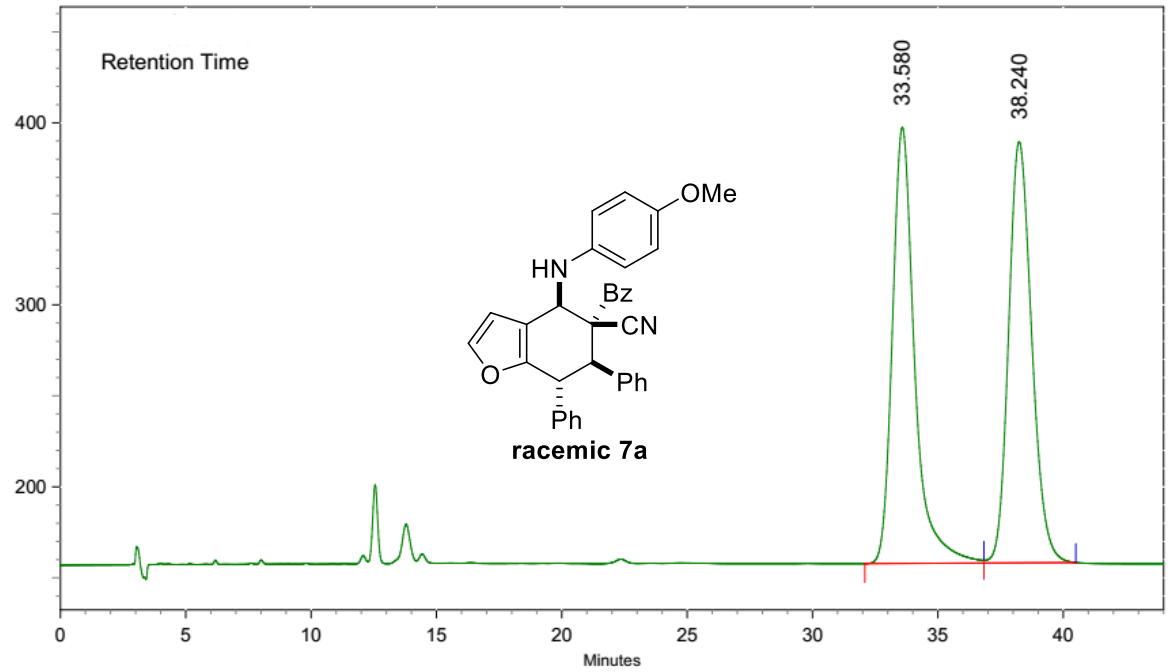
7a

^{1}H NMR (400 MHz, $CDCl_3$)

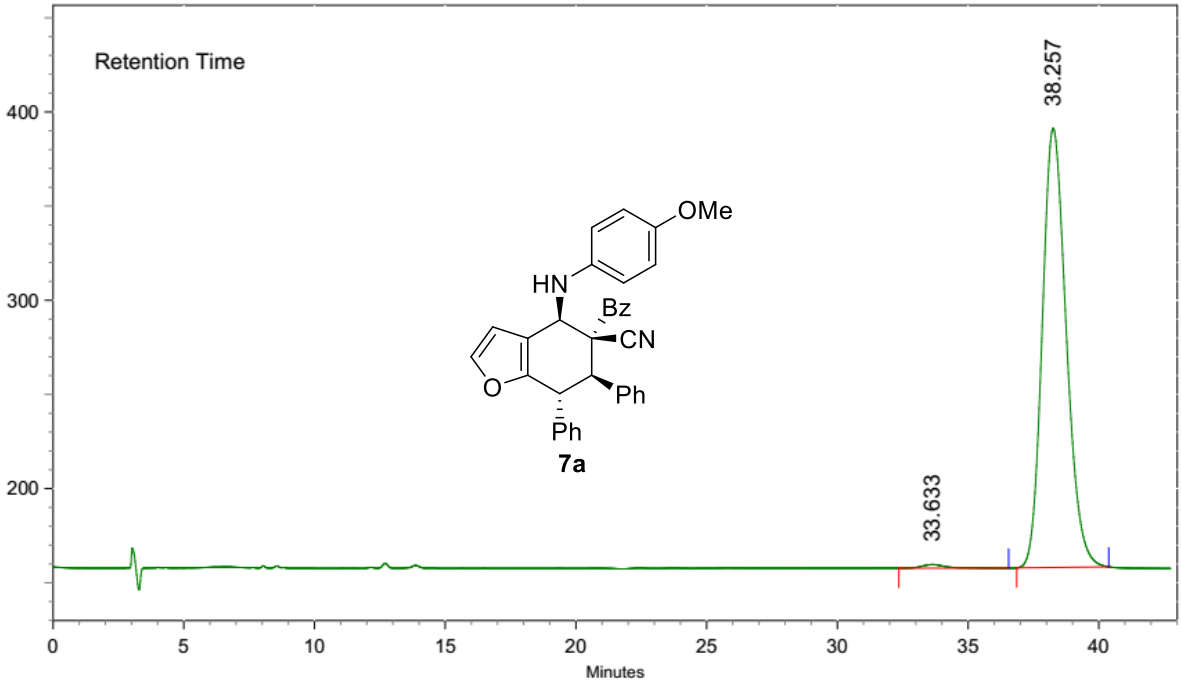


7a

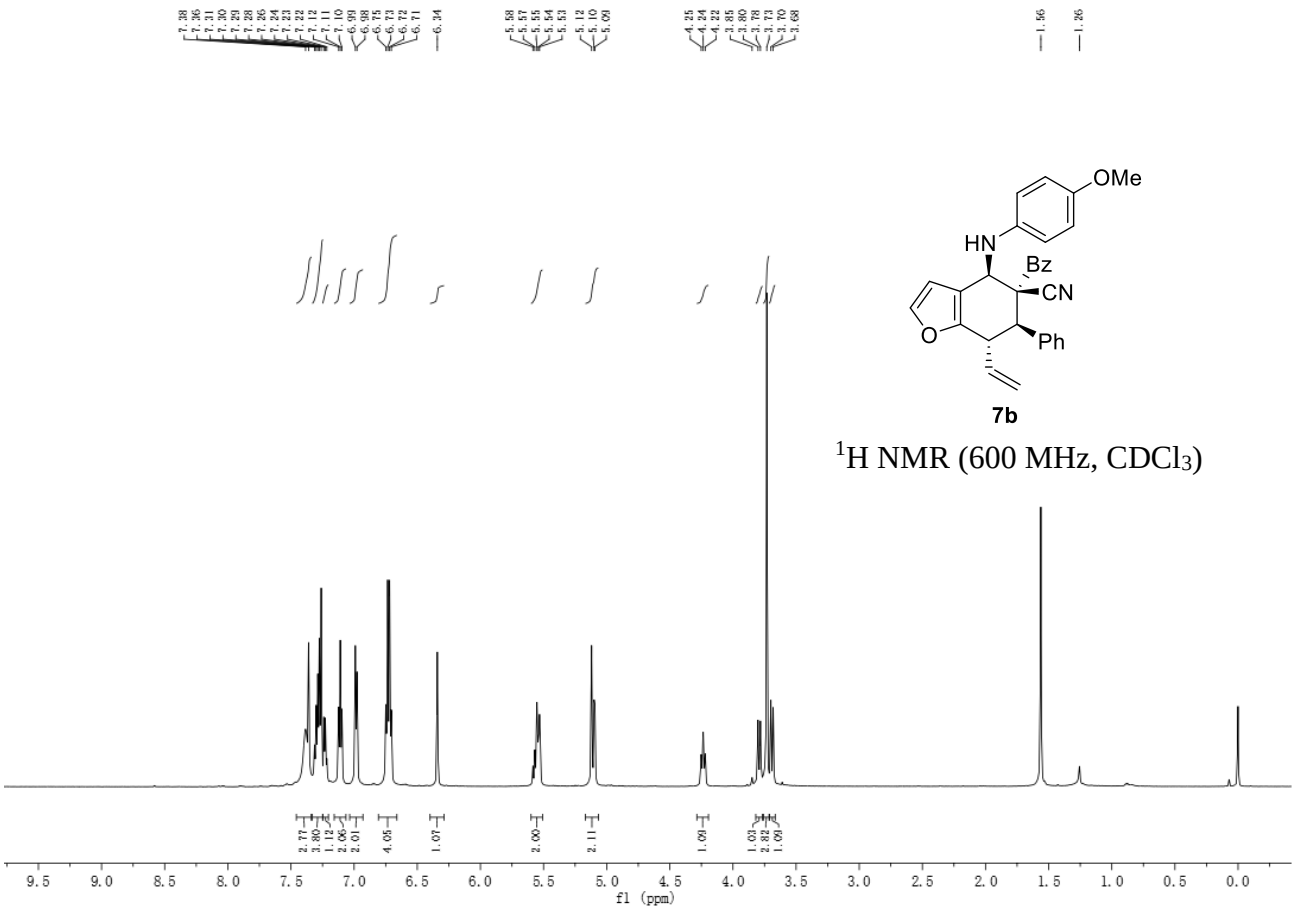
^{13}C NMR (100 MHz, $CDCl_3$)

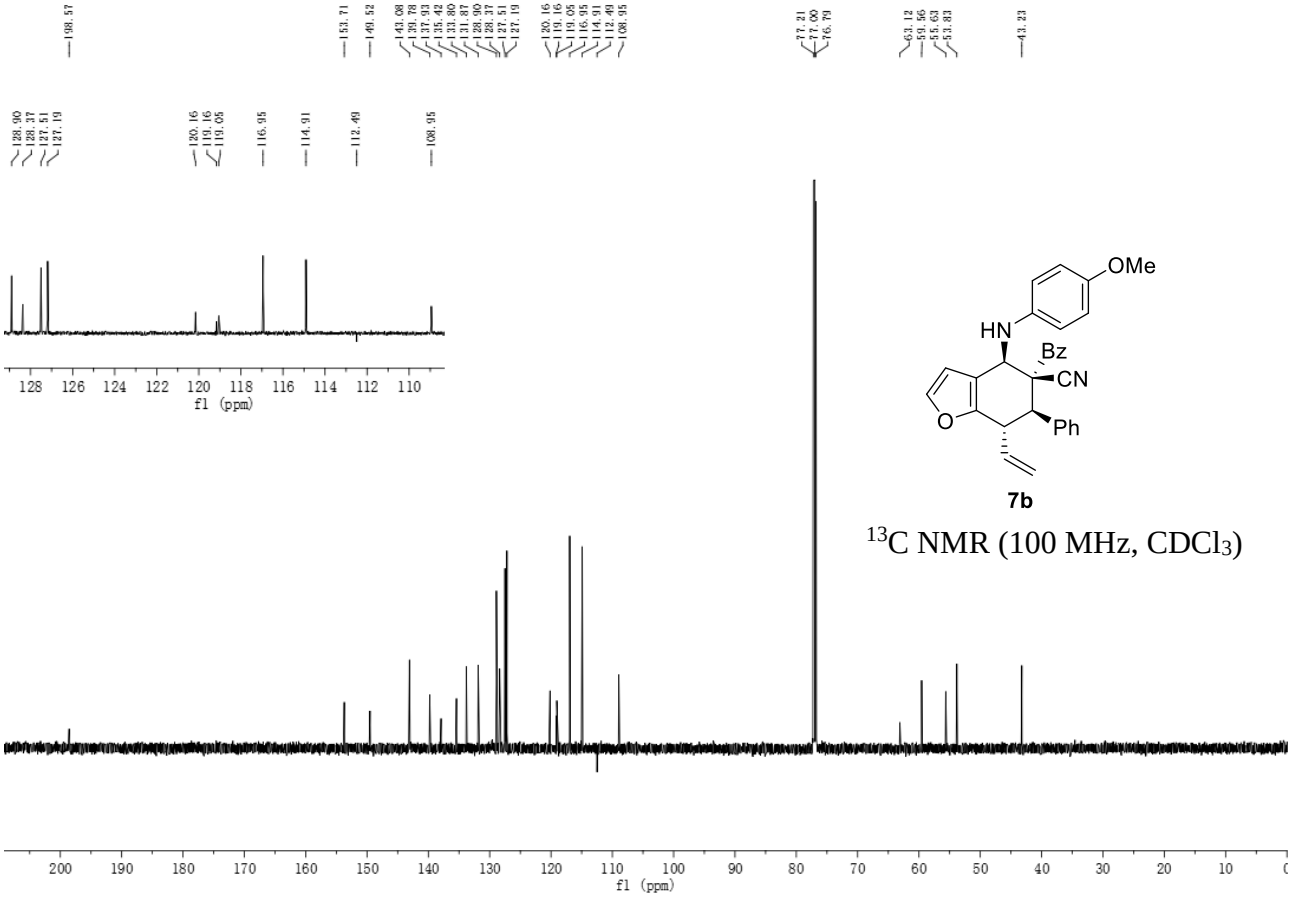


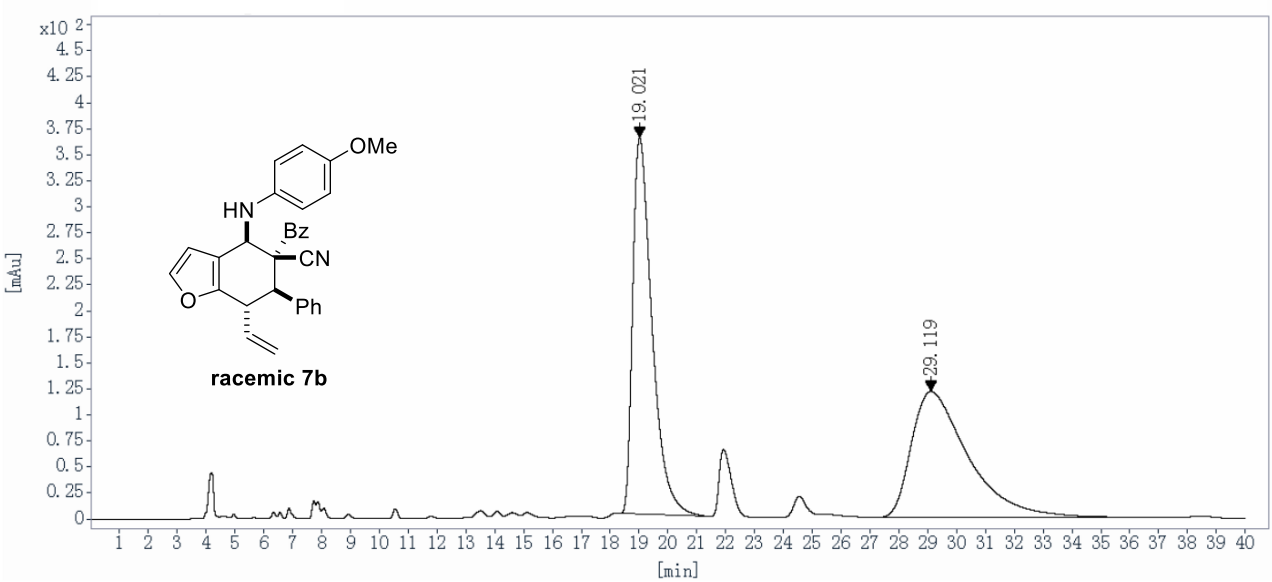
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	33.580	4.747	4019355	247748652	49.8261
2	38.240	3.667	3882693	249477824	50.1739



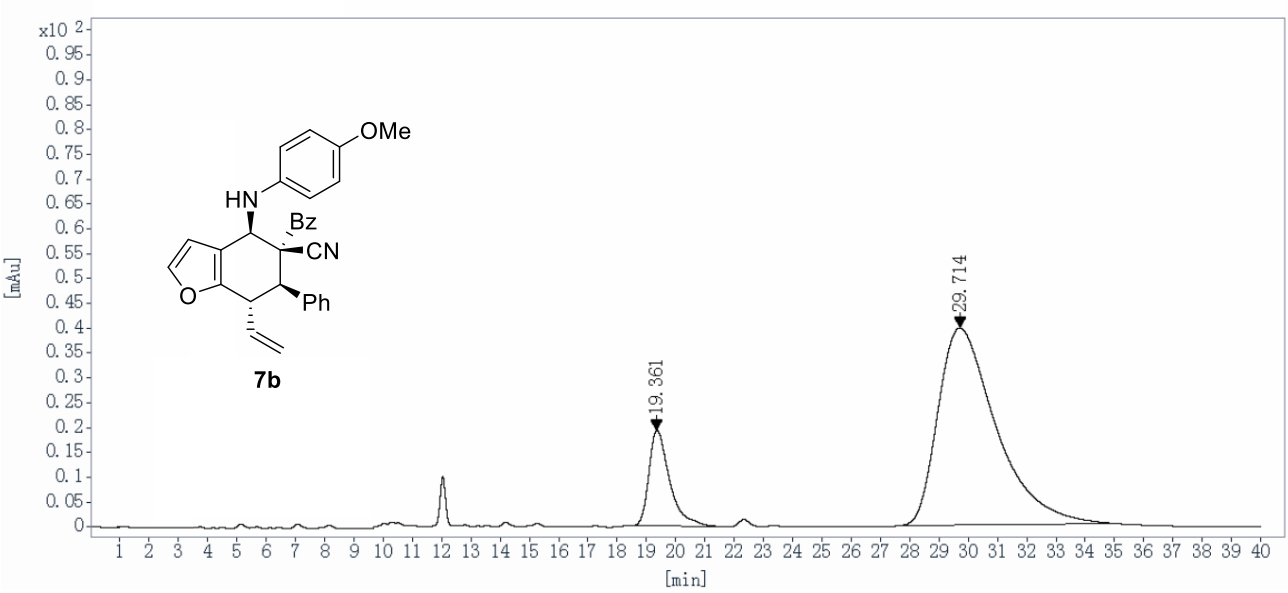
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	33.633	4.200	32287	2035246	0.8101
2	38.257	3.523	3912629	249203840	99.1899


OMe
HN
Bz
CN
O
Ph
7b
1H NMR (600 MHz, CDCl3)
f1 (ppm)


OMe
HN
Bz
CN
O
Ph
7b
13C NMR (100 MHz, CDCl3)
f1 (ppm)

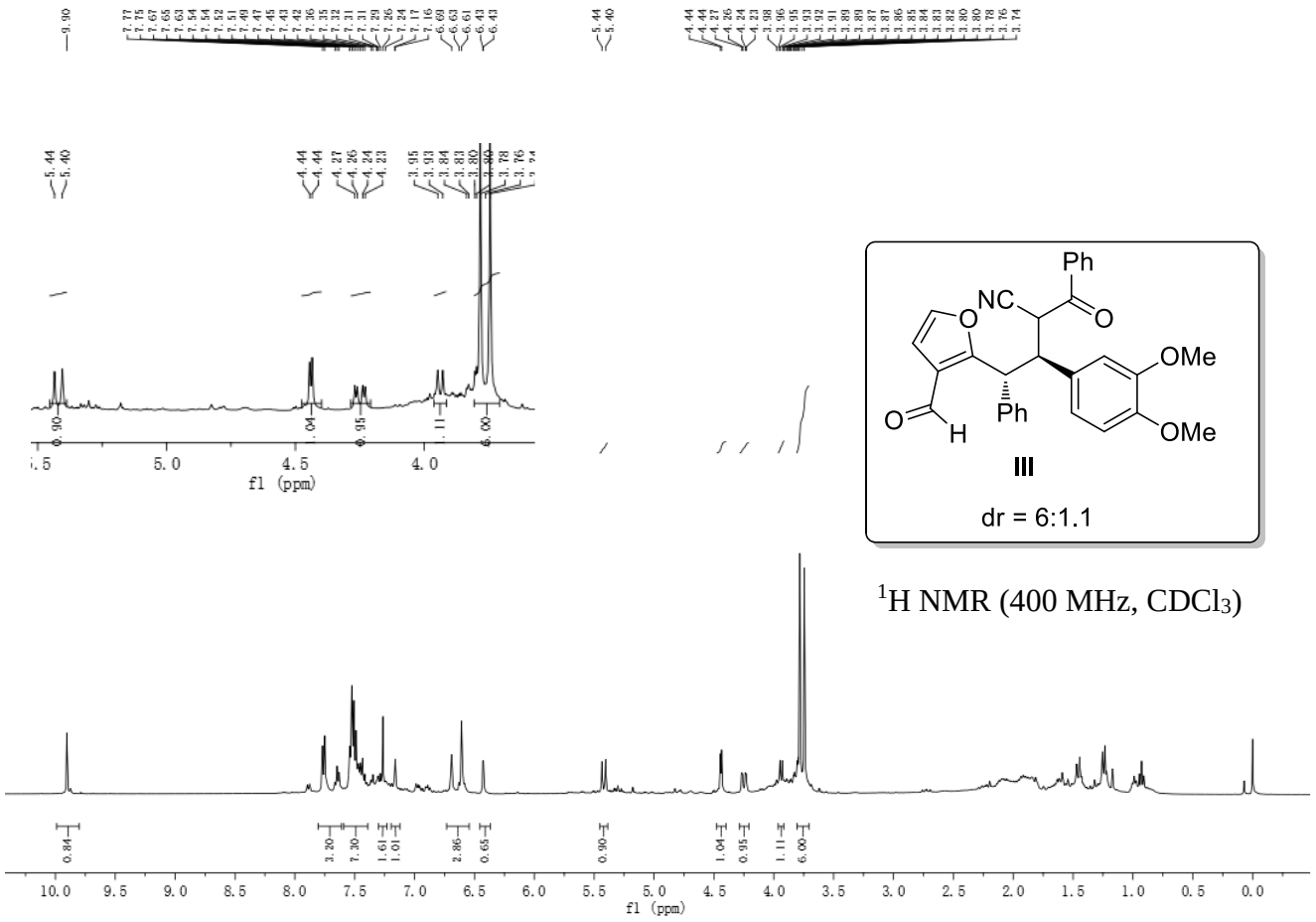


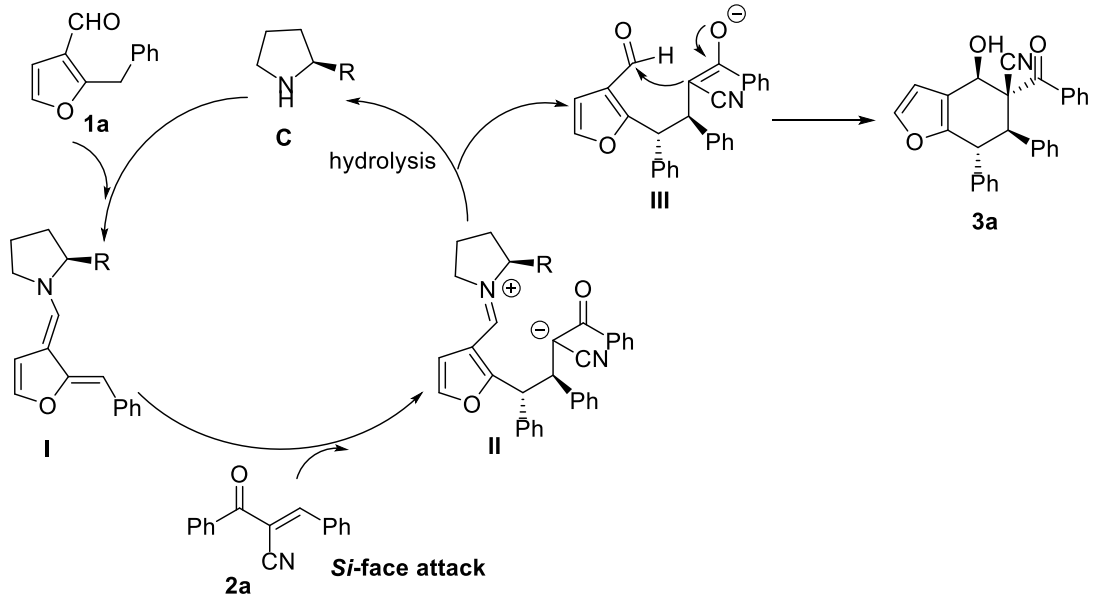
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
19.021	BBA	0.71	361.7579	16885.4883	50.5218
29.119	BBA	2.02	121.1952	16536.6953	49.4782



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
19.361	BBA	0.74	19.3182	948.8295	14.6780
29.714	BBA	2.00	39.7010	5515.4463	85.3220

8. ^{1}H NMR spectrum of the Michael intermediate of 3h





Proposed mechanism for the [4 + 2] formal cycloaddition reaction