Supporting Information

Facile Asymmetric Hydrogenation of γ-Butenolides and γ-Hydroxybutenolides to Prepare Chiral γ-Butyrolactones

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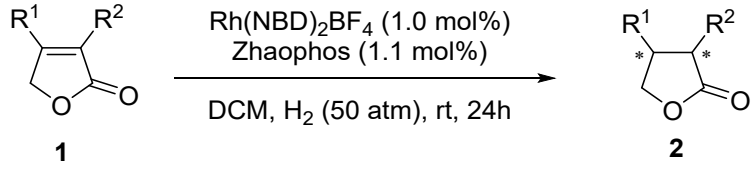
Content

1. General Information

All anhydrous reactions were performed in oven-dried round-bottomed flasks under a positive pressure of dry argon. Air- and moisture-sensitive compounds were introduced via syringes or cannula using standard inert atmosphere techniques. Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers without further purification. Anhydrous solvents were purchased from J&K. γ-Butenolides **1a-n**, **1n'** and γ-hydroxybutenolides **3** were purchased from Bide pharm or prepared according to literature reports.[1-5] γ-Butenolide **1o** was purchased from Energy Chemical, and **1p** was purchased from Chemsky Shanghai. For heating, an oil bath was used. Reactions were monitored by thin-layer chromatography (TLC) using Yantai Huayang silica gel plates, T-HSGF5025025, with a 0.23 mm thickness. Components were visualized by illumination with short-wavelength ultraviolet light and/or staining. Nylon-66 membrane syringe filters were purchase from Tianjin Jinteng. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 300-400 mesh). The NMR spectra were recorded in $CDCl_3$ (calibrated at $\delta = 7.26$ ppm for ^1H and $\delta = 77.16$ ppm for ^{13}C) with tetramethylsilane (TMS) as an internal standard, at an ambient temperature on a Bruker Avance 600 operating at 600 MHz for ^1H NMR, and at 150 MHz for ^{13}C NMR. ^1H NMR was designated as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sep =

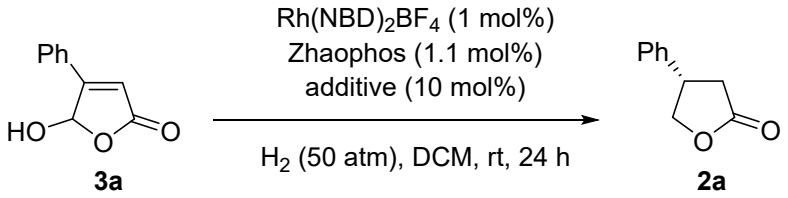
septet, dd = doublet of doublets, m = multiplet, br = broad), coupling constants (Hz), and integration. ^{13}C NMR was designated as ppm. Optical rotations were measured using a 1 mL cell with a 1 dm path length on a Rudolph Autopol I polarimeter at 589 nm. HPLC analyses were performed using Daicel chiral columns on an Agilent 1260 Series HPLC instrument. GC analyses were carried out on Angilent 1200 Series instrument using assigned chiral capillary columns. Melting points were accessed on a SGWX-4A melting point apparatus, and only the data of suitable crystal products were given. High resolution mass spectra (HRMS) were obtained on Thermo Scientific Q Exactive hybrid quadrupole-Orbitrap mass spectrometer. PE refers to petroleum ether; EA refers to ethyl acetate; DCM refers to dichloromethane.

2. General Procedure A of Hydrogenation of γ-Butenolides 1



In the argon-filled glovebox, a solution of ZhaoPhos (9.7 mg, 11 μmol) and $Rh(NBD)_2BF_4$ (3.7 mg, 10 μmol) in 1.0 mL anhydrous DCM was stirred at room temperature for 40 min. A specified volume of the resulting solution (0.1 mL, 1.0 mol% Rh-Zhaophos catalyst) was transferred by syringe to a score-break ampule charged with substrate (0.1 mmol in 0.9 mL dichloromethane). The ampule was placed into an autoclave, which was then purged with H_2 and charged with desired H_2 pressure (50 atm). The reaction mixture was stirred at room temperature for 24 h. After release of H_2 carefully, the reaction mixture was passed through a short column of silica gel (about 1.0 cm in height) in 1.0 ml syringe (equipped with Nylon-66 membrane syringe filter, pore size 0.22 μm, diam. 13 mm) to remove the metal residue, and then rinsed with PE/EA (3:1, 1 mL). The combined filtrates were concentrated, and the obtained products were pure enough for NMR and HPLC analysis.

3. Additive Screening for Hydrogenation of γ-Hydroxybutenolides 3a

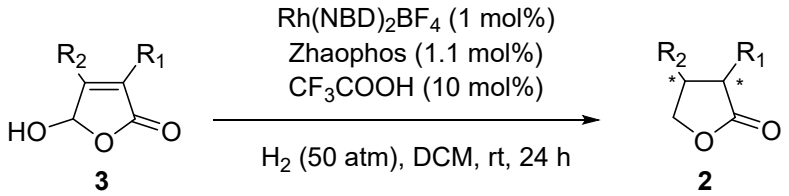


In the argon-filled glovebox, a solution of ZhaoPhos (9.7 mg, 11 μmol) and $Rh(NBD)_2BF_4$ (3.7 mg, 10 μmol) in 1.0 mL anhydrous DCM was stirred at room temperature for 40 min. A specified volume of the resulting solution (0.1 mL, 1.0 mol% Rh-Zhaophos catalyst) was transferred by syringe to a score-break ampule charged with substrate **3a** (18 mg, 0.1 mmol in 0.9 mL dichloromethane), and then additive (0.01 mmol, 10 mol%) was added. The ampule was placed into an autoclave, which was then purged with H_2 and charged with desired H_2 pressure (50 atm). The reaction mixture was stirred at room temperature for 24 h. After release of H_2 carefully, the reaction mixture was directly analyzed by ^1H NMR and HPLC analysis.

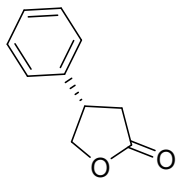
entry	additive	conv. (%)[a]	ee (%)[b]
1	-	91	94
2	AcOH	67	94
3	H_3PO4	100	94
4	CF_3COOH	100	96
5	HCl	85	94
6	$BF_3{\cdot}Et_2O$	93	92
7	TMSOTf	100	90
8	AgOTf	100	92

[a]Determined by ^1H NMR. [b]Determined by HPLC analysis.

4. General Procedure B of Hydrogenation of γ-Hydroxybutenolides 3



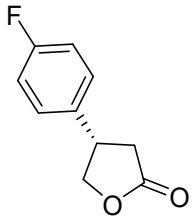
In the argon-filled glovebox, a solution of ZhaoPhos (9.7 mg, 11 μmol) and $Rh(NBD)_2BF_4$ (3.7 mg, 10 μmol) in 1.0 mL anhydrous DCM was stirred at room temperature for 40 min. A specified volume of the resulting solution (0.1 mL, 1.0 mol% Rh-Zhaophos catalyst) was transferred by syringe to a score-break ampule charged with substrate **3** (0.1 mmol in 0.9 mL dichloromethane), and then CF_3COOH (1.2 mg, 10 μmol, 10 mol%) was added. The ampule was placed into an autoclave, which was then purged with H_2 and charged with desired H_2 pressure (50 atm). The autoclave was stirred at room temperature for 24 h. After release of H_2 carefully, the reaction mixture was passed through a short column of silica gel (about 1.0 cm in height) in 1.0 ml syringe (equipped with Nylon-66 membrane syringe filter, pore size 0.22 μm, diam. 13 mm) to remove the metal residue, and then rinsed with PE/EA (3:1, 1 mL). The combined filtrates were concentrated, and the obtained products were pure enough for NMR and HPLC analysis.



2a

(S)-4-phenyldihydrofuran-2(3H)-one (**2a**): Compound **2a** was

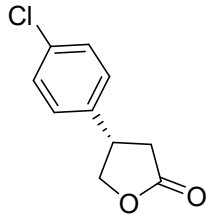
obtained as a white solid (15.7 mg, 97% yield, 98% ee) according to general procedure A using **1a**; Compound **2a** was also obtained as a white solid (15.9 mg, 98% yield, 96% ee) according to general procedure B using **3a**. $[\alpha]_D^{23}$ = + 42.5 (*c* 0.84, $CHCl_3$) for isomer with 98% ee; The spectral data were consistent with literature;[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.39 – 7.35 (m, 2H), 7.30 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.25 – 7.21 (m, 2H), 4.69 – 4.64 (m, 1H), 4.29 – 4.25 (m, 1H), 3.79 (p, *J* = 8.4 Hz, 1H), 2.92 (dd, *J* = 17.5, 8.8 Hz, 1H), 2.68 (dd, *J* = 17.5, 9.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 176.5, 139.5, 129.2, 127.8, 126.8, 74.1, 41.2, 35.8; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AS-3 column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 85:15, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 17.730 min (*S*) (major), 19.896 min (*R*) (minor).



2b

(S)-4-(4-fluorophenyl)dihydrofuran-2(3H)-one (**2b**): Compound **2b** was obtained as a white solid (17.8 mg, 99% yield, 98% ee) according to general procedure A using **1b**; Compound **2b** was also obtained as a white solid (17.7 mg, 98% yield, 96% ee) according to general procedure B using **3b**. $[\alpha]_D^{23}$ = + 46.6 (*c* 0.57, $CHCl_3$) for isomer with 98% ee; The spectral data were consistent with literature;[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]

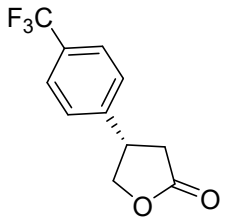
= 7.23 – 7.17 (m, 2H), 7.06 – 7.00 (m, 2H), 4.66 – 4.61 (m, 1H), 4.24 – 4.18 (m, 1H), 3.77 (p, J = 8.7 Hz, 1H), 2.90 (dd, J = 17.7, 8.7 Hz, 1H), 2.61 (dd, J = 17.8, 9.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 176.27, 162.1 (d, $J_{C\text{-}F}$ = 244.8 Hz), 135.3 (d, $J_{C\text{-}F}$ = 3.2 Hz), 128.4 (d, $J_{C\text{-}F}$ = 7.7 Hz), 116.0 (d, $J_{C\text{-}F}$ = 21.5 Hz), 74.0, 40.4, 35.8; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AS-3 column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 80:20, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 16.737 min (*S*) (major), 17.838 min (*R*) (minor).



2c

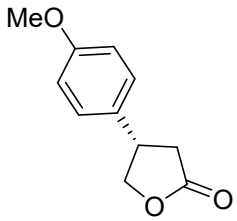
(S)-4-(4-chlorophenyl)dihydrofuran-2(3H)-one (**2c**): Compound **2c** was obtained as a white solid (19.1 mg, 97% yield, 98% ee) according to general procedure A using **1c**; Compound **2c** was also obtained as a white solid (19.1 mg, 97% yield, 94% ee) according to general procedure B using **3c**. $[\alpha]_D^{23}$ = + 57.6 (*c* 0.75, $CHCl_3$) for isomer with 98% ee; The spectral data were consistent with literature;[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.33 (d, J = 9.0 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 4.67 – 4.63 (m, 1H), 4.25 – 4.20 (m, 1H), 3.76 (p, J = 8.3 Hz, 1H), 2.92 (dd, J = 17.5, 8.8 Hz, 1H), 2.62 (dd, J = 17.5, 8.9 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 176.1, 138.1, 133.7, 129.4, 128.2, 73.9, 40.6, 35.7; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB N-3

column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 85:15, flow rate = 1.0 mL/min, λ = 220 nm, t_R: 16.840 min (*S*) (major), 17.754 min (*R*) (minor).



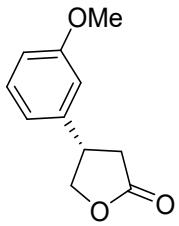
2d

(S)-4-(4-(trifluoromethyl)phenyl)dihydrofuran-2(3H)-one (**2d**): Compound **2d** was obtained as a white solid (21.9 mg, 95% yield, 97% ee) according to general procedure A using **1d**; Compound **2d** was also obtained as a white solid (22.6 mg, 98% yield, 98% ee) according to general procedure B using **3d**. $[\alpha]_D^{23}$ = + 62.0 (*c* 0.58, $CHCl_3$) for isomer with 97% ee; The spectral data were consistent with literature;[7] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.63 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 4.72 – 4.66 (m, 1H), 4.31 – 4.25 (m, 1H), 3.86 (p, J = 8.2 Hz, 1H), 2.97 (dd, J = 17.5, 8.8 Hz, 1H), 2.67 (dd, J = 17.5, 8.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 175.9, 143.8, 130.2 (q, $J_{C\text{-}CF3}$ = 32.6 Hz), 127.3, 124.0 (q, $J_{C\text{-}CF3}$ = 270.8 Hz), 126.2 (q, $J_{C\text{-}CF3}$ = 3.5 Hz), 73.6, 41.0, 35.6; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IF-3 column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 90:10, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 12.683 min (*R*) (minor), 13.506 min (*S*) (major).



2e

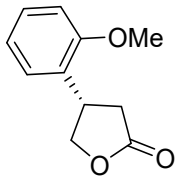
(S)-4-(4-methoxyphenyl)dihydrofuran-2(3H)-one (**2e**): a white solid, 18.3 mg, 95% yield, 98% ee, $[\alpha]_D^{23}$ = + 42.9 (*c* 0.57, $CHCl_3$); The spectral data were consistent with literature;[7] ^1H NMR (400 MHz, $CDCl_3$) δ [ppm] = 7.17 – 7.11 (m, 2H), 6.91 – 6.86 (m, 2H), 4.65 – 4.58 (m, 1H), 4.24 – 4.16 (m, 1H), 3.79 (s, 3H), 3.72 (p, J = 8.1 Hz, 1H), 2.92 – 2.83 (m, 1H), 2.66 – 2.56 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 176.6, 159.0, 131.3, 127.8, 114.4, 74.2, 55.3, 40.4, 35.8; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB N-3 column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 85:15, flow rate = 1.0 mL/min, λ = 230 nm, t_R: 16.449 min (*S*) (major), 17.499 min (*R*) (minor).



2f

(S)-4-(3-methoxyphenyl)dihydrofuran-2(3H)-one (**2f**): Compound **2f** was obtained as a white solid (18.5 mg, 96% yield, 98% ee) according to general procedure A using **1f**; Compound **2f** was also obtained as a white solid (18.6 mg, 97% yield, 95% ee) according to general procedure B using **3f**. $[\alpha]_D^{23}$ = + 45.0 (*c* 1.0, $CHCl_3$) for isomer with 98% ee; The spectral data

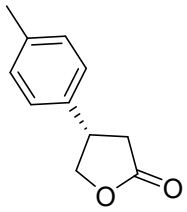
were consistent with literature;[8] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.30 – 7.26 (m, 1H), 6.85 – 6.80 (m, 2H), 6.76 – 6.74 (m, 1H), 4.67 – 4.62 (m, 1H), 4.28 – 4.23 (m, 1H), 3.80 (s, 3H), 3.75 (p, J = 8.4 Hz, 1H), 2.90 (dd, J = 17.5, 8.7 Hz, 1H), 2.66 (dd, J = 17.5, 9.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 176.5, 160.2, 141.1, 130.3, 118.9, 113.0, 112.7, 74.0, 55.4, 41.2, 35.7; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AS-3 column (0.46 x 25 cm), the gradient elution was *n*-hexane / *i*-propanol as 95:5~50:50 for 0-20min, 50:50 for 20-25min, 95:5 for 25-30min, flow rate = 1.0 mL/min, λ = 220 nm, t_R: 18.456 min (*S*) (major), 19.425 min (*R*) (minor).



2g

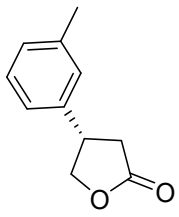
(S)-4-(2-methoxyphenyl)dihydrofuran-2(3H)-one (**2g**): Compound **2g** was obtained as a white solid (18.6 mg, 97% yield, 97% ee) according to general procedure A using **1g**; Compound **2g** was also obtained as a white solid (18.8 mg, 98% yield, 96% ee) according to general procedure B using **3g**. $[\alpha]_D^{23}$ = + 42.7 (*c* 0.93, $CHCl_3$) for isomer with 97% ee; The spectral data were consistent with literature;[9] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.31 – 7.25 (m, 1H), 7.14 (d, J = 7.5 Hz, 1H), 6.97 – 6.88 (m, 2H), 4.68 – 4.63 (m, 1H), 4.30 – 4.26 (m, 1H), 3.96 (p, J = 8.3 Hz, 1H), 3.84 (s, 3H), 2.83 (dd, J = 17.5, 9.2 Hz, 1H), 2.77 (dd, J = 17.5, 8.4 Hz, 1H); ^{13}C NMR

(150 MHz, $CDCl_3$) δ [ppm] = 177.2, 157.2, 128.7, 127.6, 120.7, 110.7, 72.9, 55.2, 36.6, 33.8; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AS-3 column (0.46 x 25 cm), the gradient elution was *n*-hexane / *i*-propanol as 95:5~50:50 for 0-20min, 50:50 for 20-25min, 95:5 for 25-30min, flow rate = 1.0 mL/min, λ = 220 nm, t_R: 14.748 min (*S*) (major), 17.428 min (*R*) (minor).



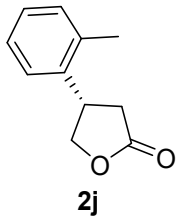
2h

(S)-4-(p-tolyl)dihydrofuran-2(3H)-one (**2h**): Compound **2h** was obtained as a white solid (16.9 mg, 96% yield, 98% ee) according to general procedure A using **1h**; Compound **2h** was also obtained as a white solid (16.7 mg, 95% yield, 91% ee) according to general procedure B using **3h**. $[\alpha]_D^{23}$ = + 39.4 (*c* 0.58, $CHCl_3$) for isomer with 98% ee; The spectral data were consistent with literature;[6] ^1H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.18 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 7.7 Hz, 2H), 4.67 – 4.62 (m, 1H), 4.26 – 4.21 (m, 1H), 3.75 (p, J = 8.7 Hz, 1H), 2.93 – 2.87 (m, 1H), 2.69 – 2.62 (m, 1H), 2.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 176.7, 137.6, 136.4, 129.9, 126.7, 74.3, 40.9, 35.9, 21.1; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB N-3 column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 90:10, flow rate = 1.0 mL/min, λ = 220 nm, t_R: 15.021 min (*S*) (major), 15.915 min (*R*) (minor).



2i

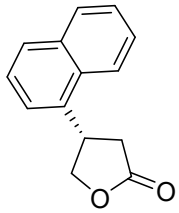
(S)-4-(m-tolyl)dihydrofuran-2(3H)-one (**2i**): Compound **2i** was obtained as a white solid (16.9 mg, 96% yield, 98% ee) according to general procedure A using **1i**; Compound **2i** was also obtained as a white solid (17.1 mg, 97% yield, 94% ee) according to general procedure B using **3i**. $[\alpha]_D^{23}$ = + 38.2 (*c* 0.60, $CHCl_3$) for isomer with 98% ee; The spectral data were consistent with literature;[10] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.27 – 7.24 (m, 1H), 7.11 (d, J = 7.5 Hz, 1H), 7.06 – 7.00 (m, 2H), 4.67 – 4.63 (m, 1H), 4.28 – 4.24 (m, 1H), 3.75 (p, J = 8.4 Hz, 1H), 2.90 (dd, J = 17.5, 8.7 Hz, 1H), 2.67 (dd, J = 17.5, 9.1 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 176.6, 139.5, 139.0, 129.1, 128.5, 127.5, 123.8, 74.2, 41.1, 35.8, 21.5; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AS-3 column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 90:10, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 16.363 min (*S*) (major), 19.173 min (*R*) (minor).



2j

(S)-4-(o-tolyl)dihydrofuran-2(3H)-one (**2j**): Compound **2j** was obtained as a white solid (16.9 mg, 96% yield, 98% ee) according to

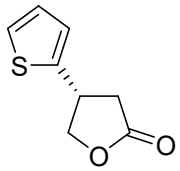
general procedure A using **1j**; Compound **2j** was also obtained as a white solid (17.4 mg, 99% yield, 99% ee) according to general procedure B using **3j**. $[\alpha]_D^{23}$ = + 40.8 (*c* 0.45, $CHCl_3$) for isomer with 98% ee; The spectral data were consistent with literature;[7] ^1H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.25 – 7.22 (m, 2H), 7.21 – 7.18 (m, 2H), 4.67 – 4.63 (m, 1H), 4.32 – 4.28 (m, 1H), 3.99 (p, J = 7.8 Hz, 1H), 2.91 (dd, J = 17.5, 8.7 Hz, 1H), 2.65 (dd, J = 17.5, 8.1 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 176.6, 137.7, 135.9, 131.1, 127.6, 127.0, 125.0, 73.5, 37.2, 35.4, 19.8; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IC column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 80:20, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 17.024 min (*R*) (minor), 19.168 min (*S*) (major).



2k

(S)-4-(naphthalen-1-yl)dihydrofuran-2(3H)-one (**2k**): Compound **2k** was obtained as a white solid (20.2 mg, 95% yield, 98% ee) according to general procedure A using **1k**; Compound **2k** was also obtained as a white solid (21.0 mg, 99% yield, 99% ee) according to general procedure B using **3k**. $[\alpha]_D^{23}$ = + 56.1 (*c* 0.89, $CHCl_3$) for isomer with 98% ee; The spectral data were consistent with literature;[6] ^1H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.96 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.82 (d, J = 8.1 Hz,

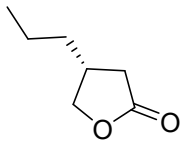
1H), 7.60 – 7.56 (m, 1H), 7.56 – 7.53 (m, 1H), 7.50 – 7.46 (m, 1H), 7.43 (d, J = 7.1 Hz, 1H), 4.83 (dd, J = 9.2, 7.3 Hz, 1H), 4.57 (p, J = 7.3 Hz, 1H), 4.46 (dd, J = 9.2, 6.3 Hz, 1H), 3.08 (dd, J = 17.4, 8.5 Hz, 1H), 2.86 (dd, J = 17.4, 7.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 176.5, 135.2, 134.2, 131.3, 129.5, 128.5, 126.9, 126.2, 125.7, 122.6, 122.5, 73.5, 36.9, 35.3; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak IB N-3 column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 70:30, flow rate = 1.0 mL/min, λ = 220 nm, t_R: 17.423 min (*S*) (major), 19.427 min (*R*) (minor).



2l

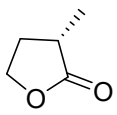
(R)-4-(thiophen-2-yl)dihydrofuran-2(3H)-one (**2l**): a white solid, 16.7 mg, 99% yield, 98% ee, $[\alpha]_D^{23}$ = + 43.2 (*c* 0.73, $CHCl_3$); The spectral data were consistent with literature;[11] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.24 (dd, J = 5.1, 1.2 Hz, 1H), 6.98 (dd, J = 5.1, 3.5 Hz, 1H), 6.92 (dt, J = 3.5, 1.0 Hz, 1H), 4.65 (dd, J = 9.0, 7.6 Hz, 1H), 4.27 (dd, J = 9.1, 7.8 Hz, 1H), 4.05 (p, J = 8.3 Hz, 1H), 2.96 (dd, J = 17.4, 8.5 Hz, 1H), 2.70 (dd, J = 17.3, 9.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 175.7, 142.3, 127.4, 124.64, 124.60, 74.2, 37.0, 36.8; The enantiomeric excess was determined by HPLC analysis on Daicel Chiralpak AD-3 column (0.46 x

25 cm), *n*-hexane / *i*-propanol = 95:5, flow rate = 1.0 mL/min, λ = 230 nm, t_R: 13.919 min (*S*) (minor), 15.073 min (*R*) (major).



2m

(R)-4-propyldihydrofuran-2(3H)-one (**2m**): Compound **2m** was obtained as a colorless liquid (12.4 mg, 97% yield, 95% ee) according to general procedure A using **1m**; Compound **2m** was also obtained as a colorless liquid (12.4 mg, 97% yield, 96% ee) according to general procedure B using **3m**. $[\alpha]_D^{23}$ = + 7.9 (*c* 1.5, $CHCl_3$) for isomer with 95% ee; The spectral data were consistent with literature;[12] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm] = 4.40 (dd, J = 8.9, 7.3 Hz, 1H), 3.91 (dd, J = 9.0, 7.2 Hz, 1H), 2.64 – 2.51 (m, 2H), 2.16 (dd, J = 16.8, 7.8 Hz, 1H), 1.47 – 1.42 (m, 2H), 1.38 – 1.30 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 177.4, 73.5, 35.6, 35.4, 34.6, 20.7, 14.0; The enantiomeric excess was determined by GC analysis on γ-DEX™ 225 L × I.D. 30 m × 0.25 mm, d_f 0.25 μm, oven program (120 °C for 2 min, then 1 °C/min to 127 °C for 22 min, then 20 °C/min to 200 °C for 3 min), detector FID 250 °C, t_R: 20.282 min (*S*) (minor), 20.501 min (*R*) (major).



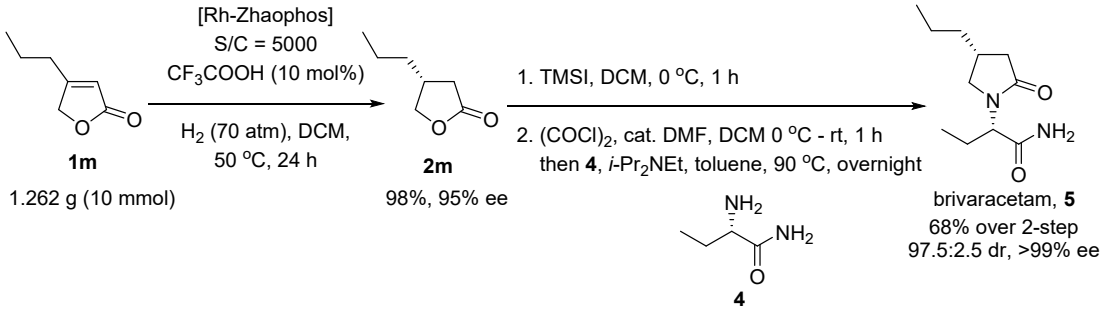
2n

(S)-3-methyldihydrofuran-2(3H)-one (**2n**): Compound **2n** was obtained as a colorless liquid (9.8 mg, 98% yield, 84% ee) according to

general procedure A using **1n**; Compound **2n** was also obtained as a colorless liquid **(**9.8 mg, 98% yield, 82% ee) according to general procedure A using **1n'**; $[\alpha]_D^{23}$ = – 16.4 (*c* 0.58, $CHCl_3$) for isomer with 84% ee; The spectral data were consistent with literature;[13] ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm] = 4.29 (td, J = 8.7, 2.7 Hz, 1H), 4.14 (td, J = 9.4, 6.6 Hz, 1H), 2.60 – 2.52 (m, 1H), 2.44 – 2.36 (m, 1H), 1.92 – 1.84 (m, 1H), 1.23 (d, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ [ppm] = 180.2, 66.3, 34.2, 30.7, 15.2; The enantiomeric excess was determined by GC analysis on β-DEX™ 225 L × I.D. 30 m × 0.25 mm, d_f 0.25 μm, oven program (105 °C for 0 min, then 1 °C/min to 113 °C for 18 min, then 20 °C/min to 200 °C for 4 min), detector FID 250 °C, t_R: 13.663 min (*R*) (minor), 13.845 min (*S*) (major).

5. Synthetic Applications

Gram-scale hydrogenation of 3m (S/C = 5000) and application in brivaracetam synthesis

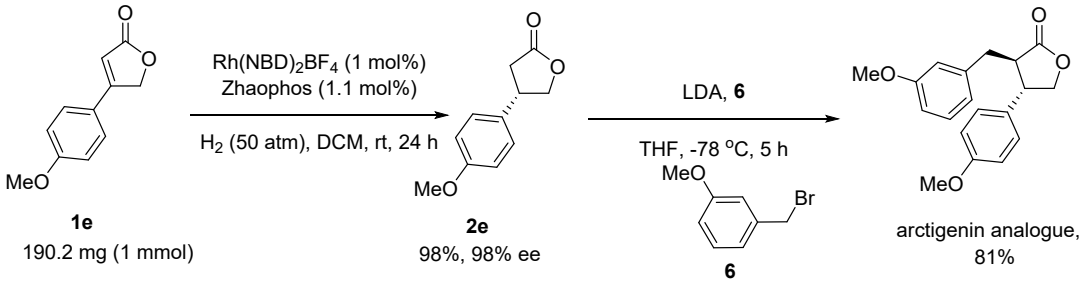


In the argon-filled glovebox, a solution of ZhaoPhos (9.7 mg, 11 μmol) and $Rh(NBD)_2BF_4$ (3.7 mg, 10 μmol) in 1.0 mL anhydrous DCM was stirred at room temperature for 40 min. A specified volume of the resulting solution (0.2 mL, 0.02 mol% Rh-Zhaophos catalyst) was transferred by syringe to a score-break ampule charged with substrate **1m** (10 mmol in 10 mL dichloromethane), and then CF_3COOH (0.11 g, 1.0 mmol, 10 mol%) was added. The ampule was placed into an autoclave, which was then purged with H_2 and charged with desired H_2 pressure (50 atm). The autoclave was stirred at room temperature for 24 h. After release of H_2 carefully, the reaction mixture was passed through a short column of silica gel (about 1.0 cm in height) in 10 ml syringe (equipped with Nylon-66 membrane syringe filter, pore size 0.22 μm, diam. 13 mm) to remove the metal residue, and then rinsed with PE/EA (3:1, 1 mL). The combined filtrates were concentrated, and the obtained products **2m** (1.3 g) were pure enough for the next step.

To a 50 mL round-bottomed flask containing α,β-unsaturated lactone **2m** (0.77 g, 6.0 mmol, 1.0 equiv.) under ambient atmosphere was added dry DCM (20 mL) at room temperature. The mixture was cooled down to 0 ℃, and TMSI (1.3 mL, 9.0 mmol, 1.5 equiv.) was added. After the reaction was stirred at 0 ℃ for 1 h, 1 M HCl (30 mL) was added at 0 ℃, and then the layers were separated. The aqueous layer was extracted with DCM (3 × 20 mL). The combined organic layers were washed with water (30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$, and concentrated. The crude product (1.7 g) was directly used in the next step without further purification. The crude acid was then dissolved in dry DCM (30 mL) with two drops of DMF and cooled to 0 ℃. Oxalyl chloride (0.78 mL, 9.0 mmol, 1.5 equiv.) was added slowly via syringe over 5 min. The reaction was allowed to warm to room temperature, and then stirred for 5 hours. The reaction mixture was concentrated to afford the crude acid chloride (1.6 g) which was used in the next step without further purification. The crude acid chloride was dissolved in dry toluene (20 mL), and (*S*)-2-aminobutyramide (0.67 g, 6.6 mmol, 1.1 equiv.) and *i*-Pr_2NEt (1.6 g, 12 mmol, 2.0 equiv.) were added at room temperature. The reaction mixture was heated to 90 ℃, and stirred for overnight at the same temperature. After cooling to 0 ℃, water was added, and then the layers were separated. The aqueous layer was extracted with DCM (3 × 20 mL). The combined organic layers were washed with water (30 mL) and brine

(30 mL), dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel eluting with DCM/MeOH (10:1) to give brivaracetam **5** as a white solid (0.87 g, 68% yield over 3 steps, 96.9:3.1 dr, >99% ee). The spectroscopic data were identical to previous literature reports.[14] $[\alpha]_D^{23} = -57.8$ (*c* 1.0, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ [ppm] = 6.31 (s, 1H), 5.56 (s, 1H), 4.44 (dd, *J* = 8.8, 6.8 Hz, 1H), 3.48 (dd, *J* = 9.8, 7.9 Hz, 1H), 3.02 (dd, *J* = 9.8, 7.1 Hz, 1H), 2.57 (dd, *J* = 16.8, 8.7 Hz, 1H), 2.32 (hept, *J* = 7.7 Hz, 1H), 2.07 (dd, *J* = 16.8, 8.0 Hz, 1H), 1.93 (dp, *J* = 14.4, 7.3 Hz, 1H), 1.68 (dp, *J* = 14.9, 7.5 Hz, 1H), 1.40 (q, *J* = 7.4 Hz, 2H), 1.36 – 1.27 (m, 2H), 0.90 (q, *J* = 7.1 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.8, 172.2, 56.1, 49.7, 38.0, 36.7, 32.0, 21.0, 20.7, 14.1, 10.6; The enantiomeric excess and diastereomeric excess was determined by HPLC on Chiracel IC-3 column (0.46 x 25 cm), *n*-hexane / *i*-propanol = 45:55, flow rate = 1.0 mL/min, λ = 210 nm, t_R: 10.619 min (2*S*, 4*R*) (major), 15.755 min (2*S*, 4*S*) (minor).

Synthesis of arctigenin analogue



In the argon-filled glovebox, a solution of ZhaoPhos (9.7 mg, 0.011 mmol) and $Rh(NBD)_2BF_4$ (3.7 mg, 0.010 mmol) in 1.0 mL anhydrous

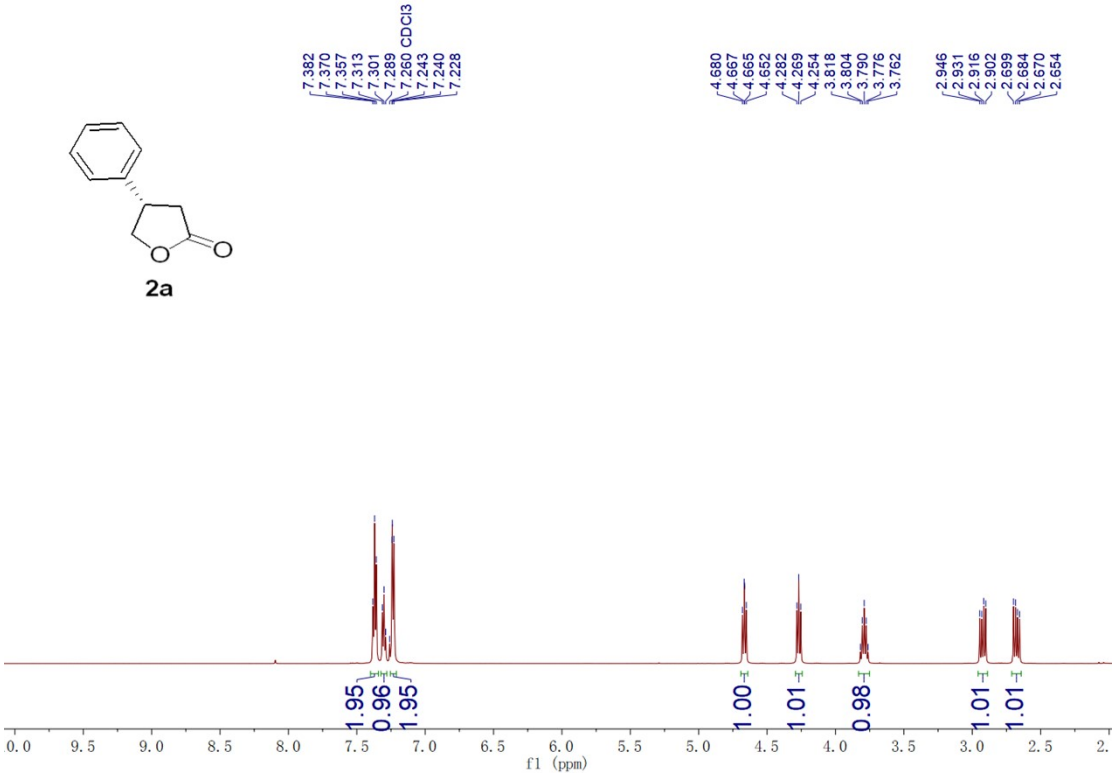
DCM was stirred at room temperature for 40 min, and the resulting solution was then transferred by syringe to a score-break ampule charged with substrate (1.0 mmol in 4.0 mL dichloromethane). The ampule was placed into an autoclave, which was then purged with H_2 and charged with desired H_2 pressure (50 atm). The autoclave was stirred at room temperature for 24 h. After release of H_2 carefully, the reaction mixture was passed through a short column of silica gel (about 1.0 cm in height) in 10 ml syringe (equipped with Nylon-66 membrane syringe filter, pore size 0.22 μm, diam. 13 mm) to remove the metal residue, and then rinsed with PE/EA (3:1, 1 mL). The combined filtrates were concentrated, and the obtained products **2e** (189 mg, 98% ee) were pure enough for the next step.

To a 10 mL round-bottomed flask containing lactone **2e** (96 mg, 0.5 mmol, 1.0 equiv.) under argon atmosphere was added dry THF (2 mL) at room temperature. The mixture was cooled down to -78 ℃, and LDA (0.3 mL, 0.6 mmol, 2.0 mol/L in THF, 1.2 equiv.) was added dropwise. After the reaction was stirred at same temperature for 30 min, 1-(bromomethyl)-3-methoxybenzene **6** (0.12 g, 0.6 mmol, 1.2 equiv.) in THF (1 mL) was added dropwise, and the resulting solution was further stirred for 5 h at -78 ℃. Water (4 mL) was added, and the mixture was allowed to warm up to room temperature. DCM (4 mL) was added, and then the layers were separated. The aqueous layer was extracted with DCM (3 × 4 mL). The combined organic layers were washed with water (10 mL) and brine (10

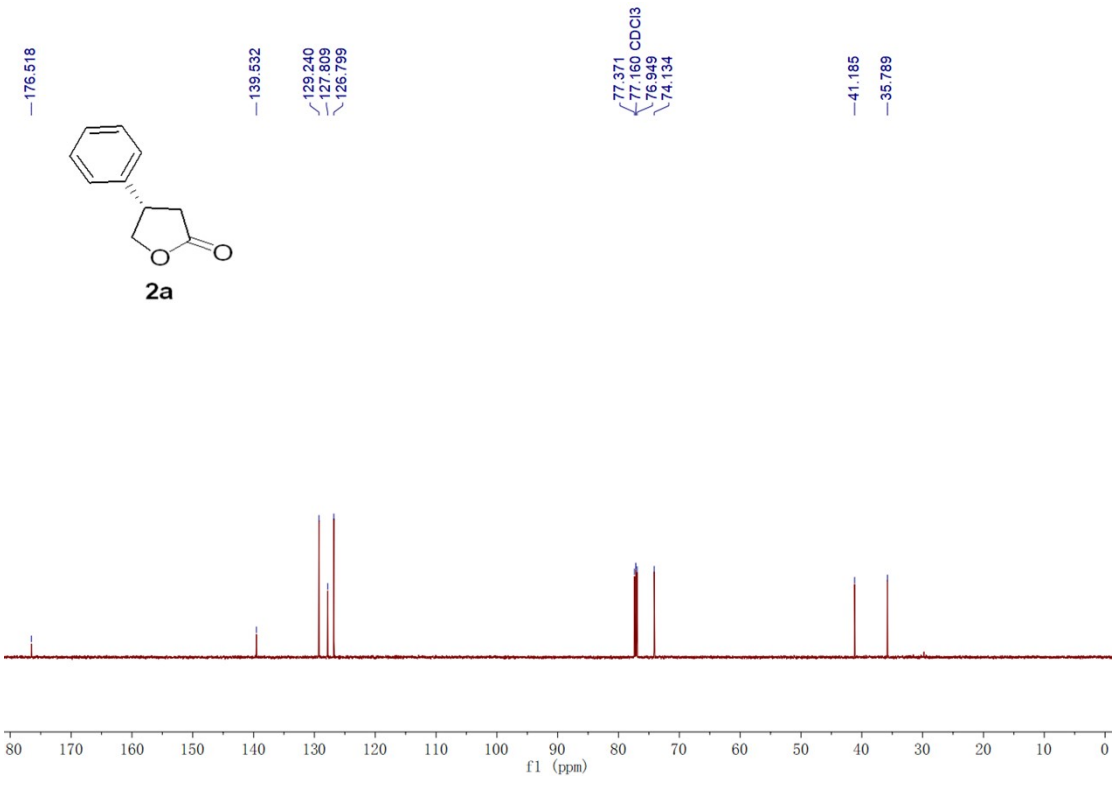
mL), dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel eluting with PE/EA (4:1) to obtain **7** as a colorless oil (0.12 g, 81% yield). The spectroscopic data were identical to previous literature reports.[8] $[\alpha]_D^{23}$ = + 4.7 (*c* 0.5, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ [ppm] = 7.15 (t, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.75 – 6.71 (m, 2H), 6.69 (s, 1H), 4.38 (t, *J* = 8.6 Hz, 1H), 4.04 (t, *J* = 9.5 Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H), 3.31 (q, *J* = 10.1 Hz, 1H), 3.12 (dd, *J* = 14.0, 5.1 Hz, 1H), 3.02 (dt, *J* = 10.9, 5.4 Hz, 1H), 2.93 (dd, *J* = 14.0, 5.6 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm] = 177.8, 159.8, 159.2, 138.9, 129., 128.5, 127.9, 122.2, 115.2, 114.6, 112.6, 72.6, 55.4, 55.2, 48.0, 45.0, 33.7.

6. NMR Spectra

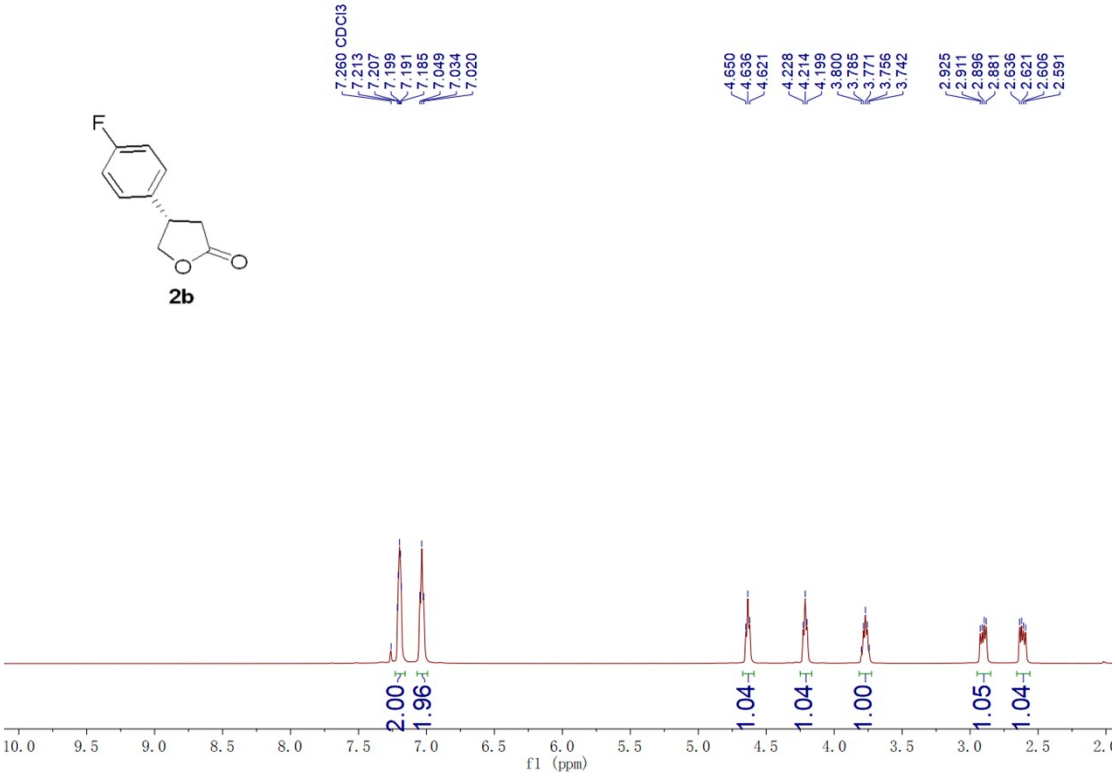
^{1}H NMR (600 MHz, $CDCl_3$)



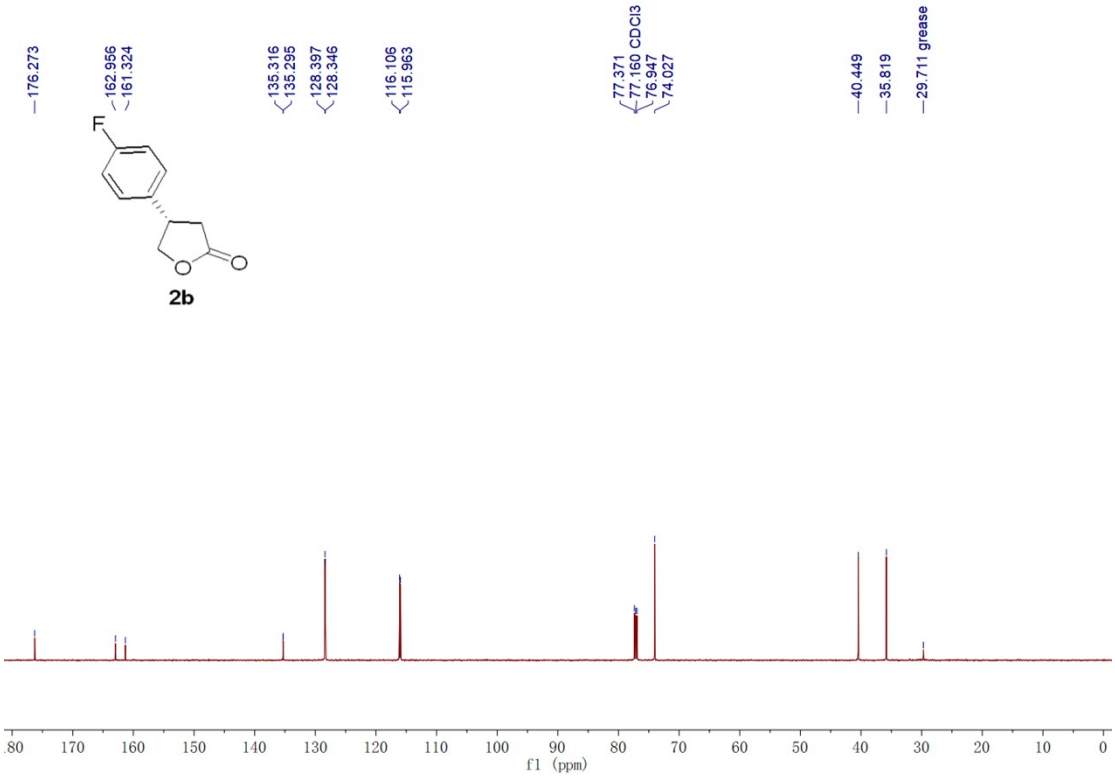
^{13}C NMR (150 MHz, $CDCl_3$)



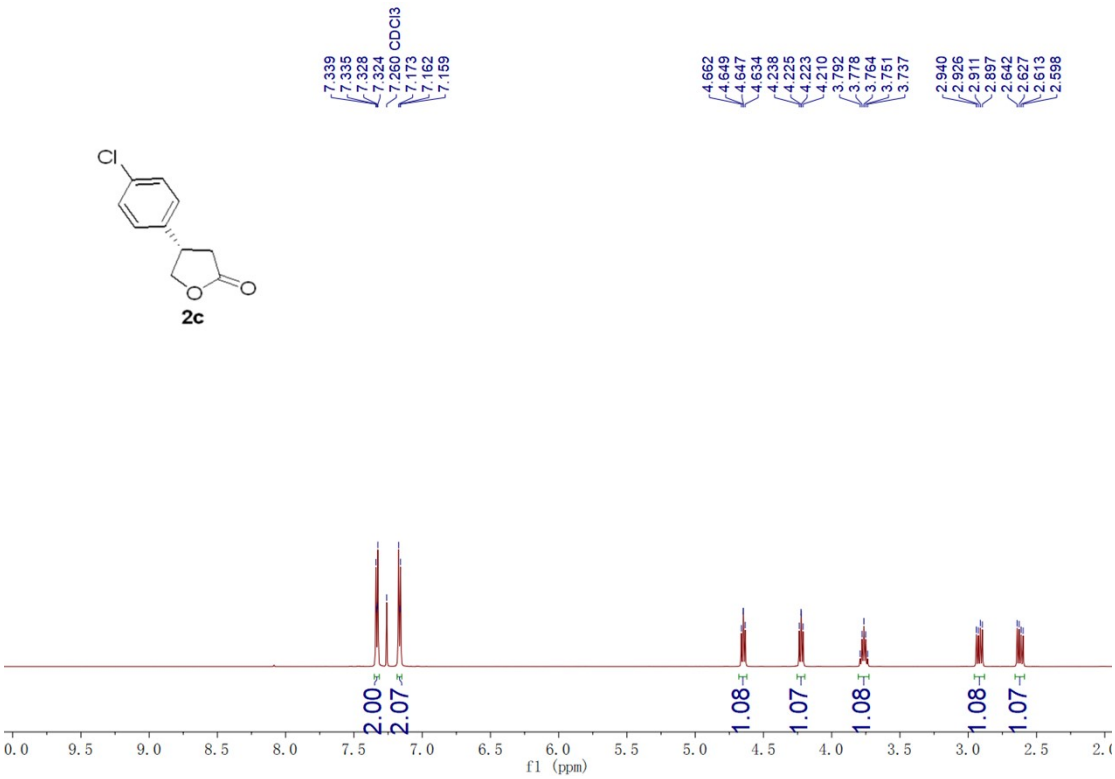
^{1}H NMR (600 MHz, $CDCl_3$)



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



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



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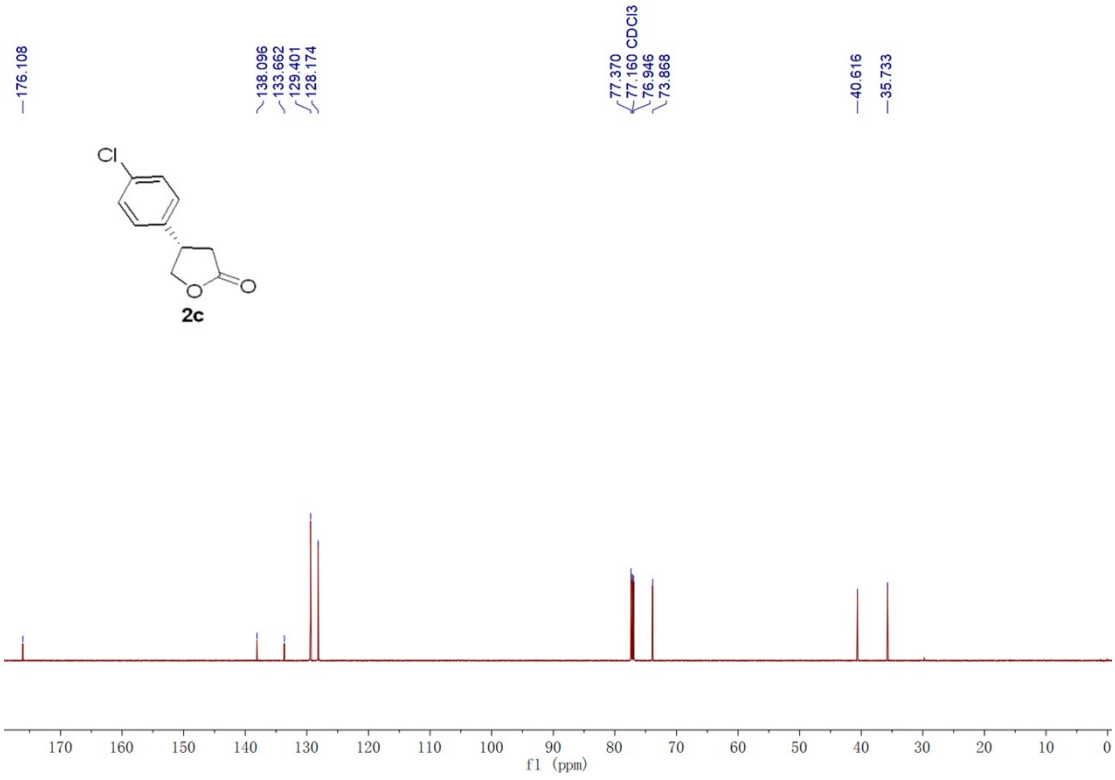

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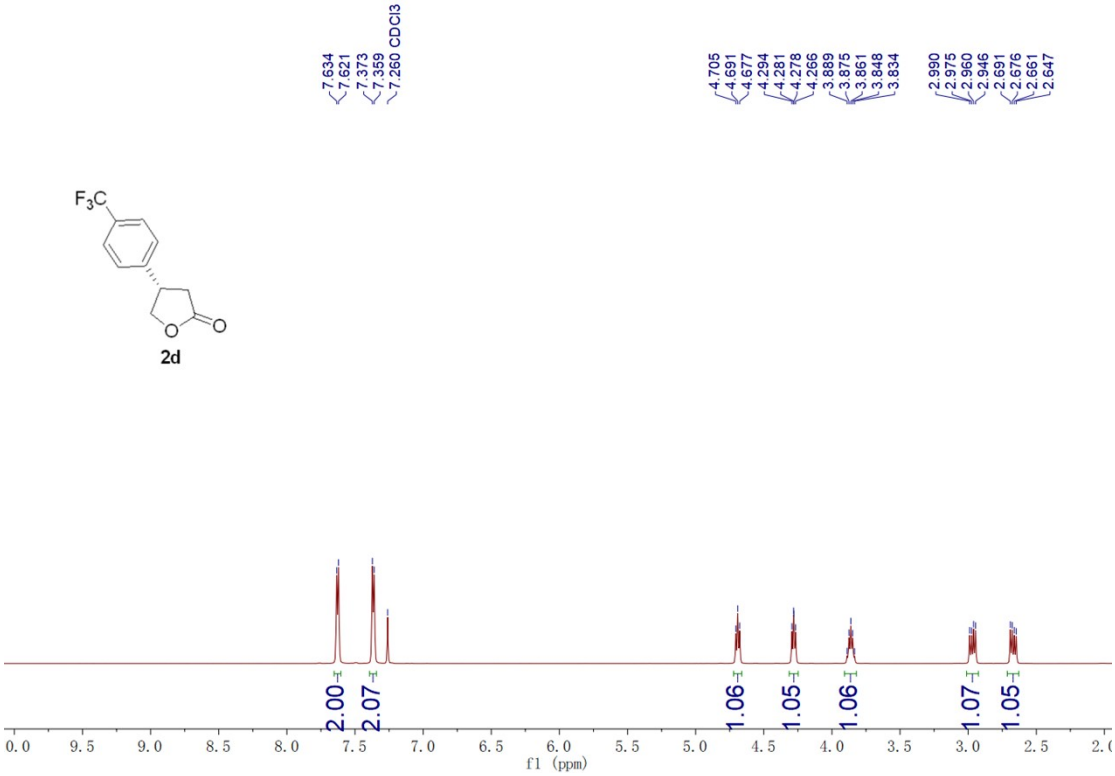

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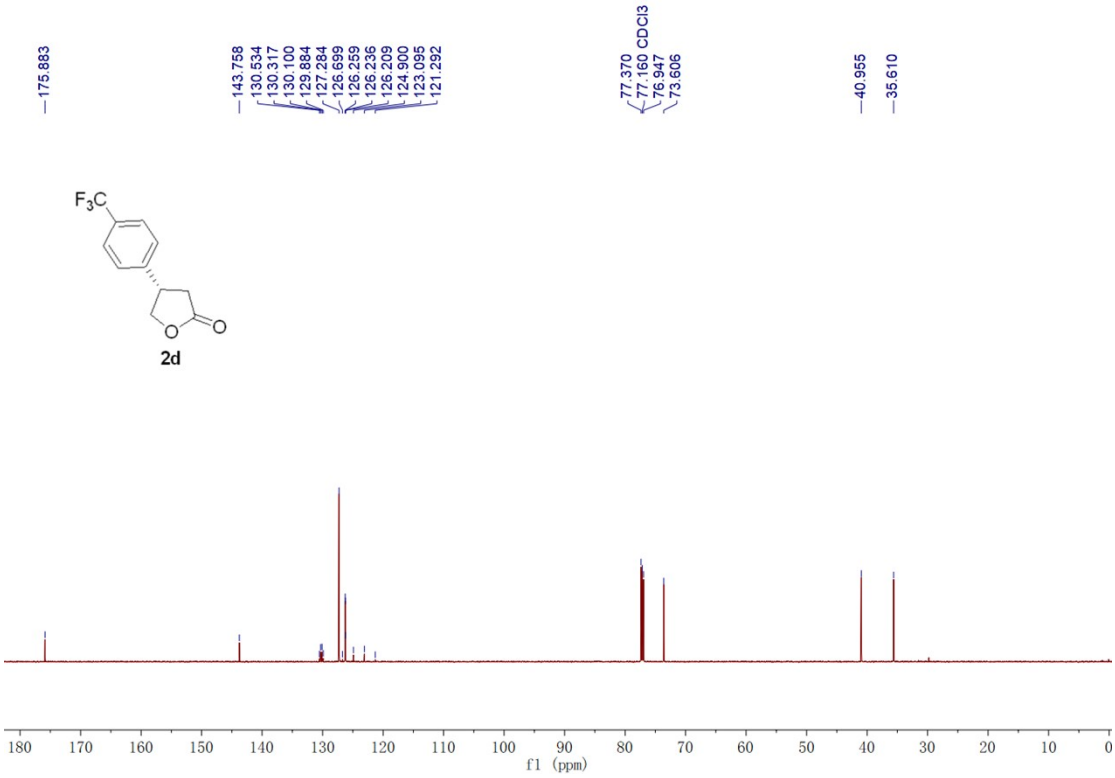

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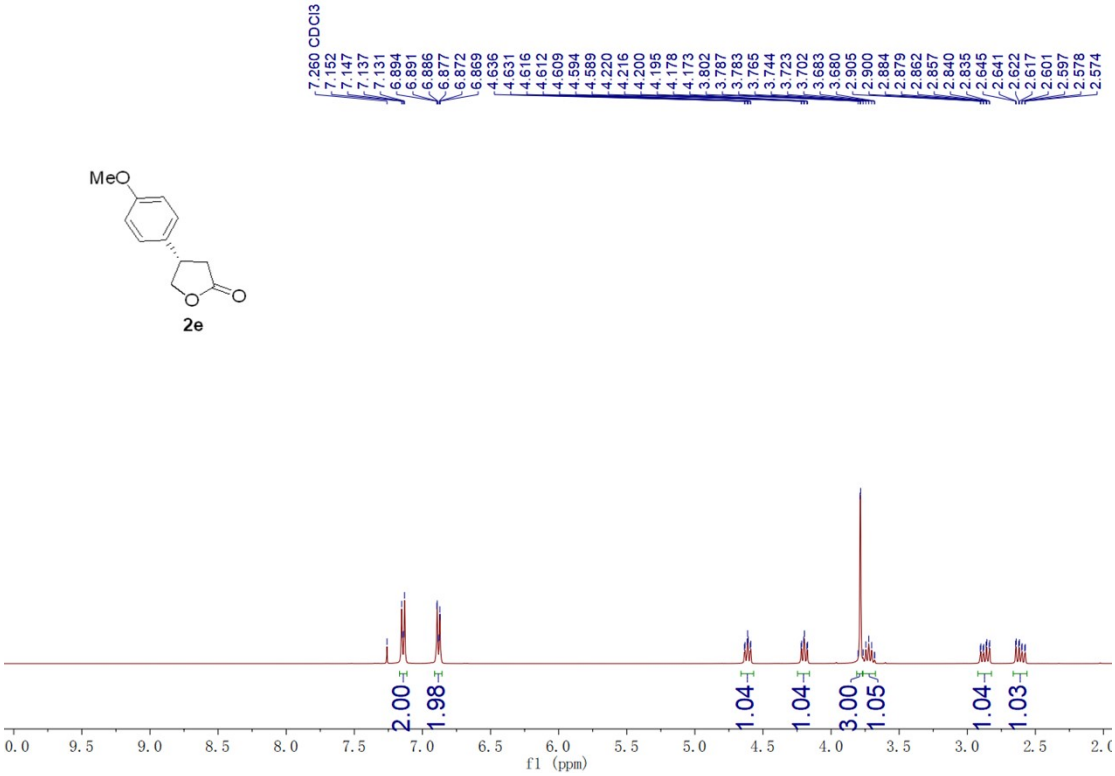

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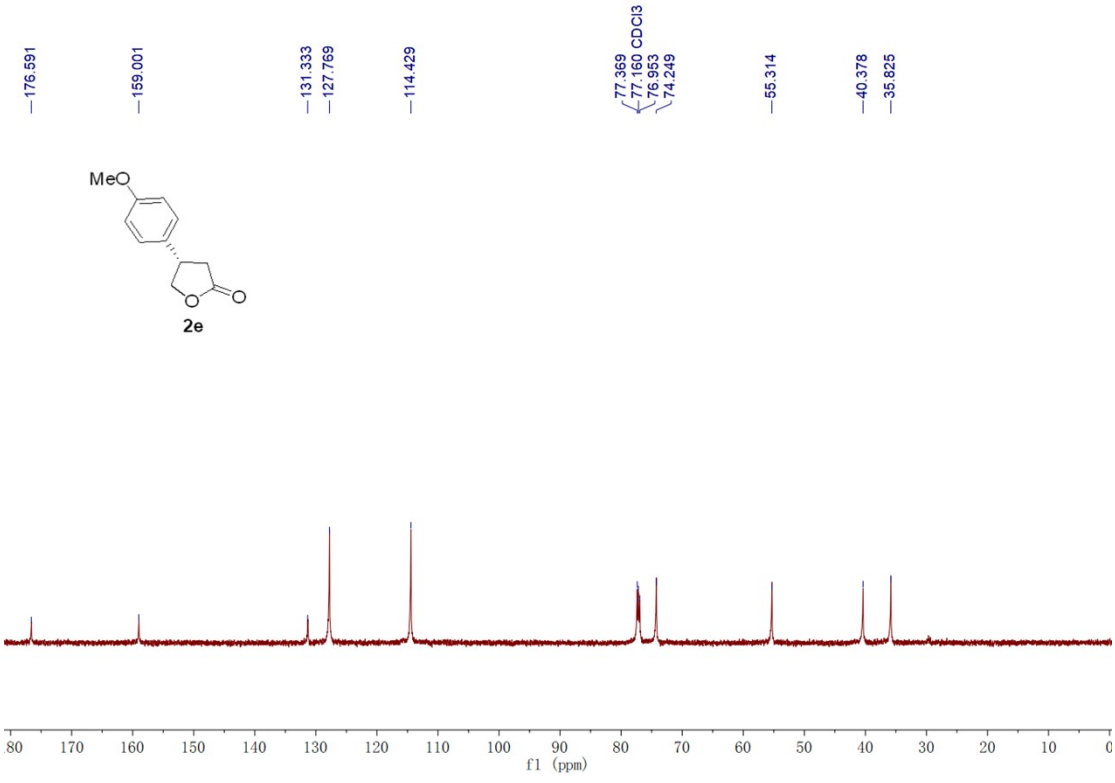

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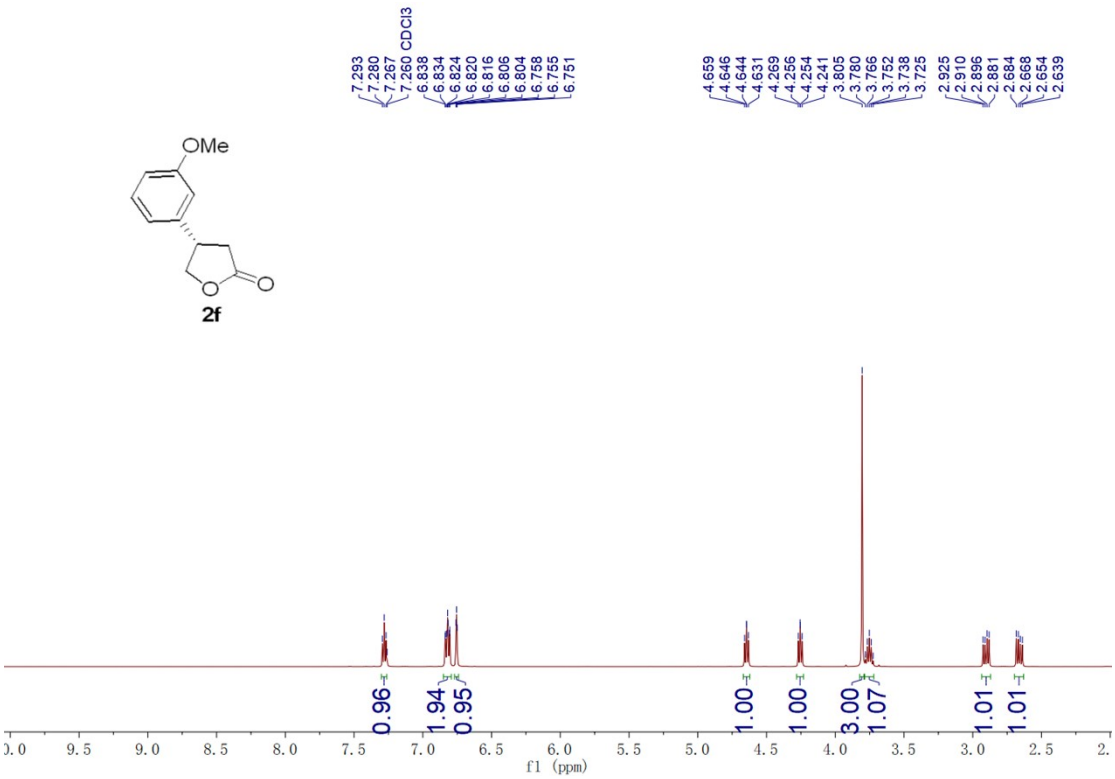
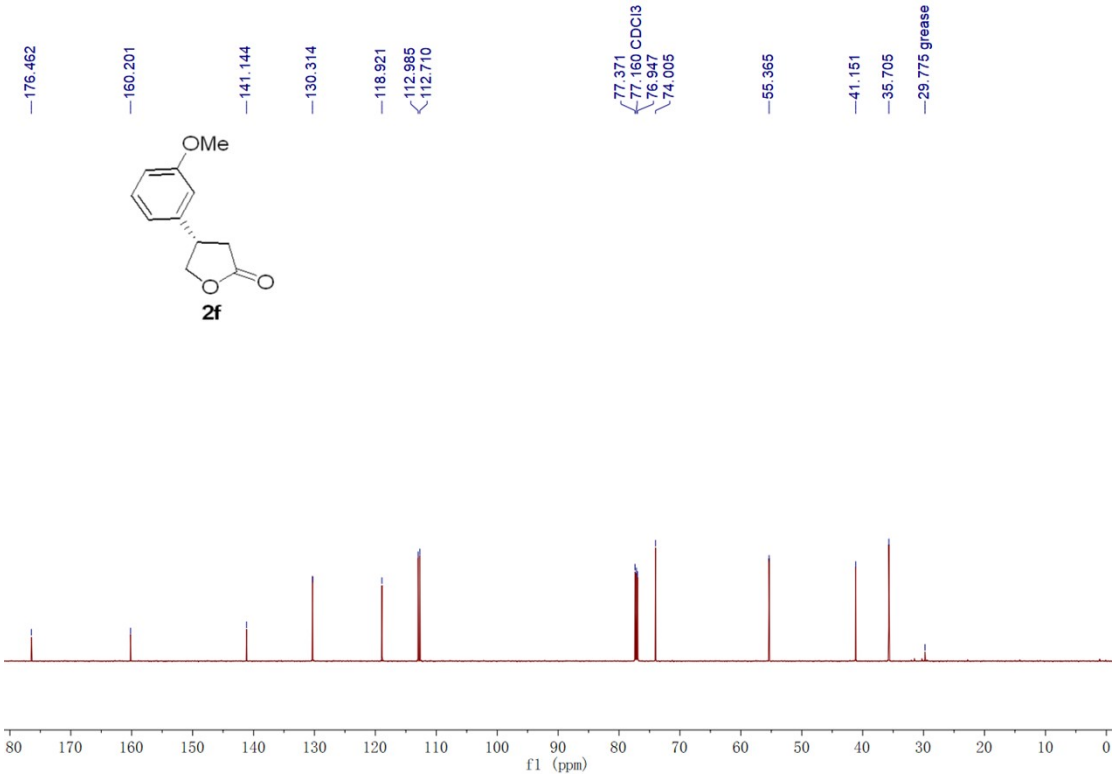


^{13}C NMR (150 MHz, $CDCl_3$)



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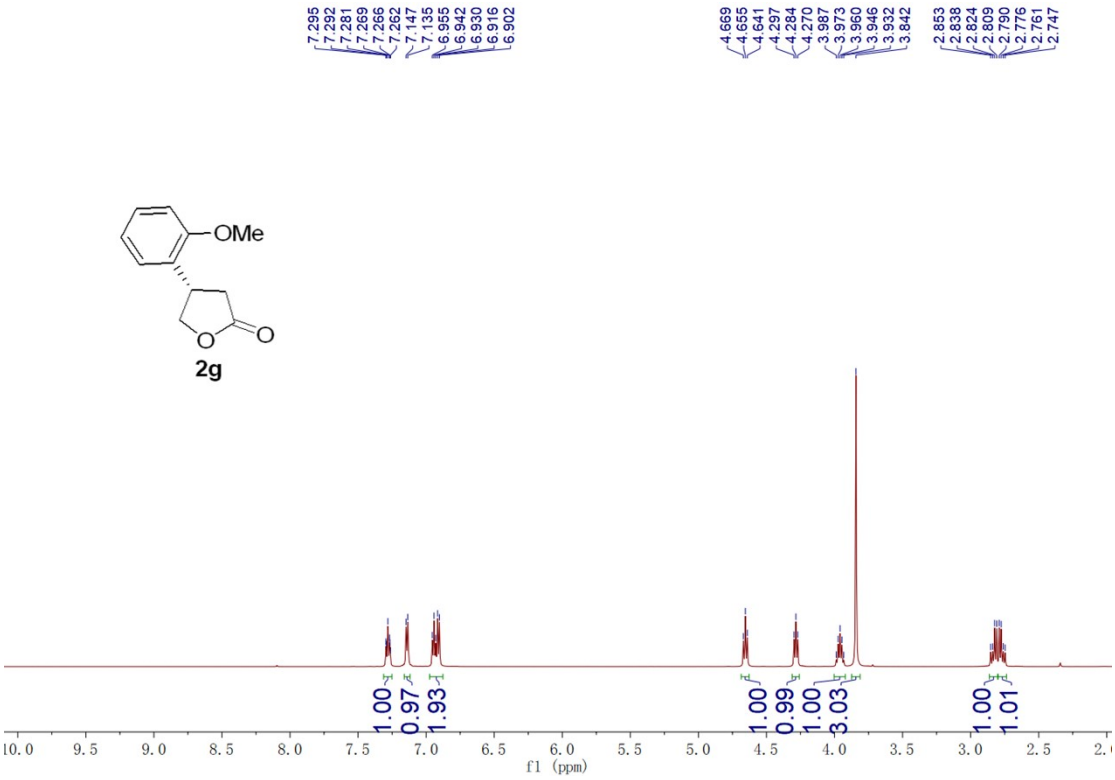

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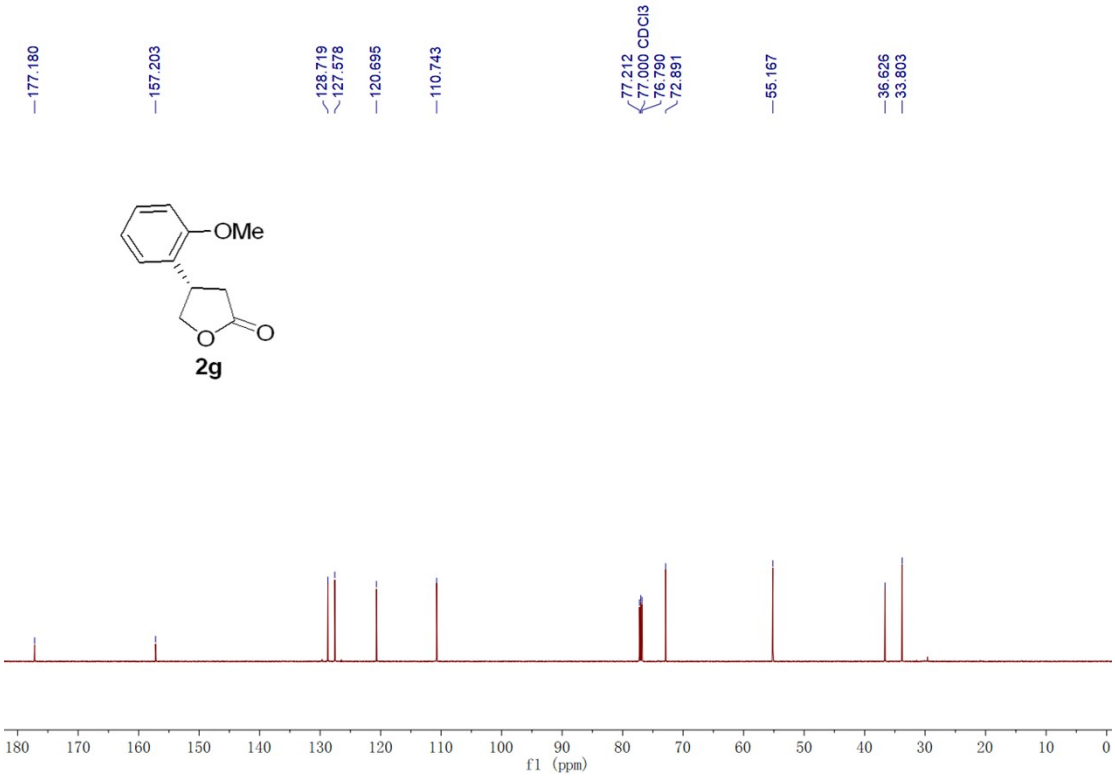

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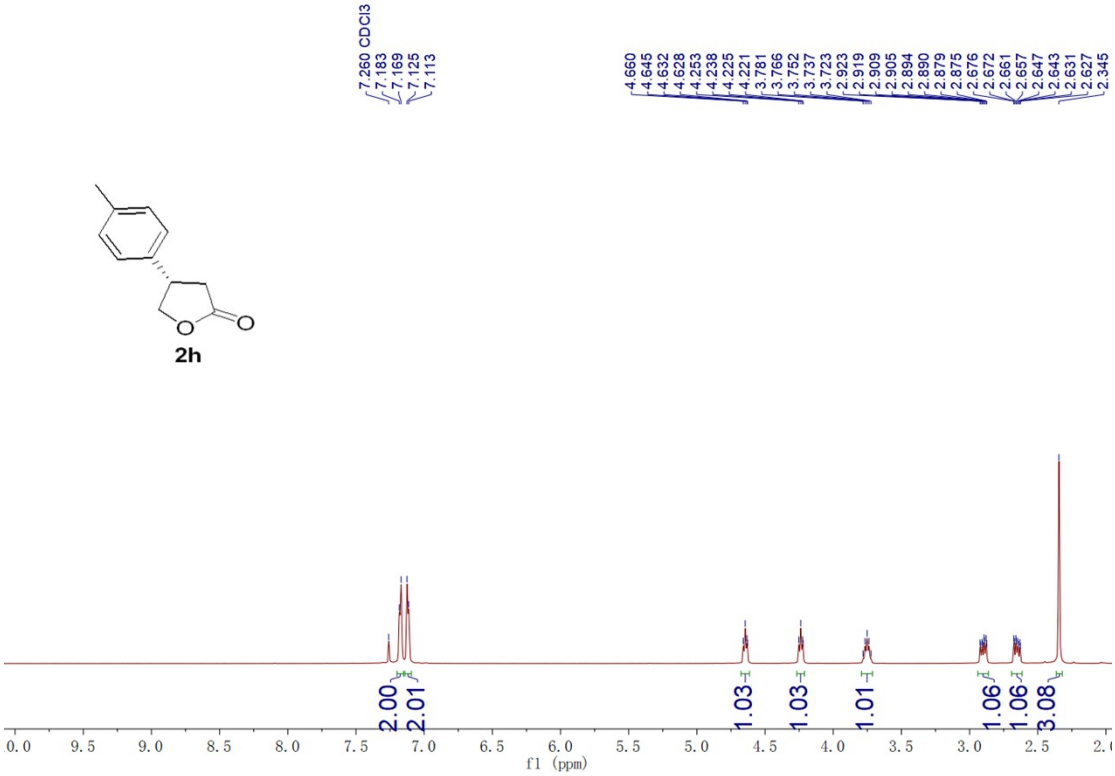

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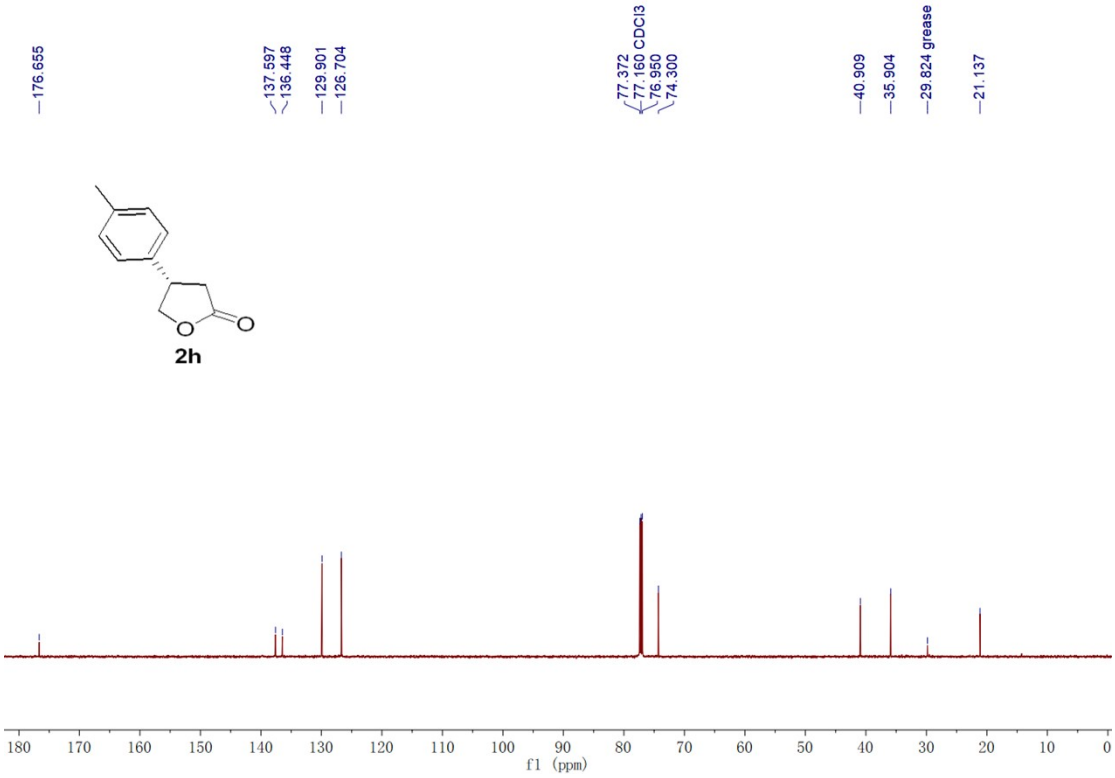

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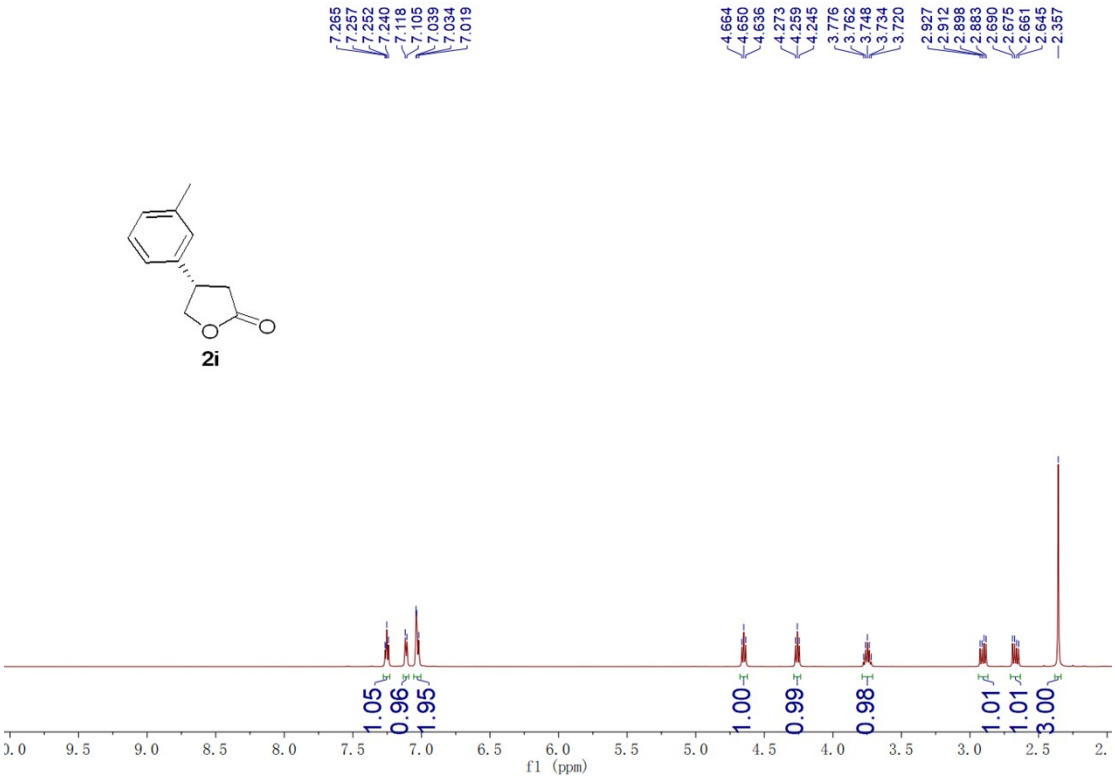

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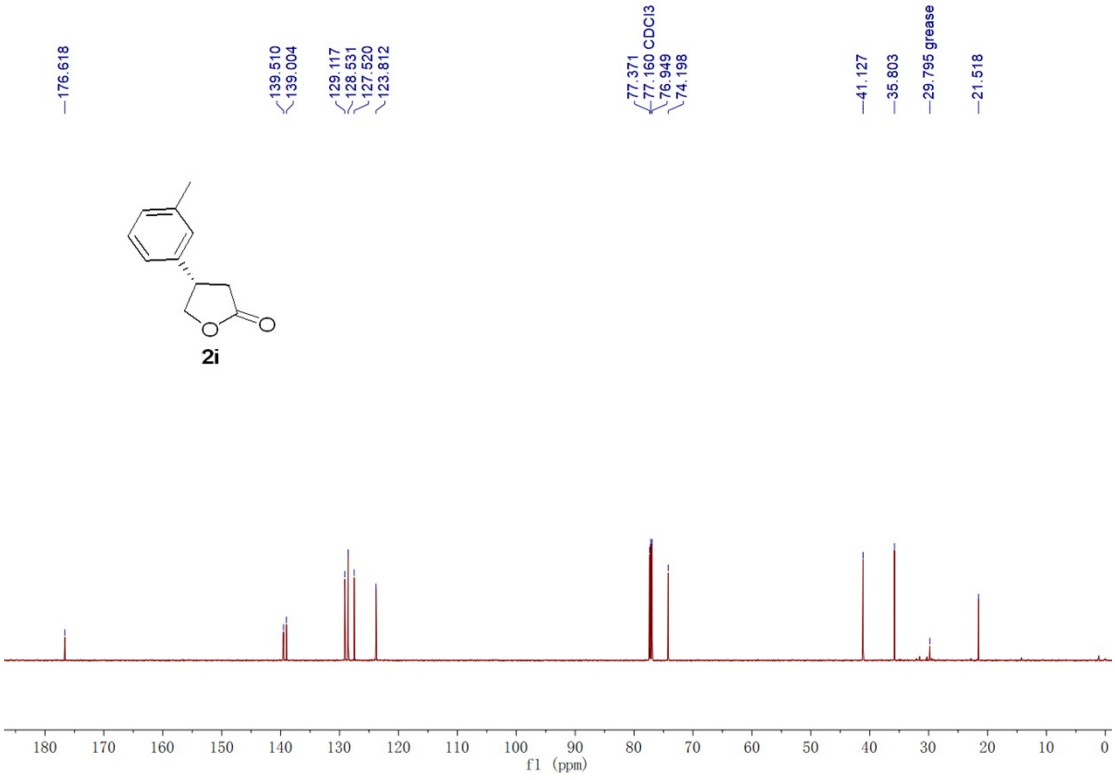

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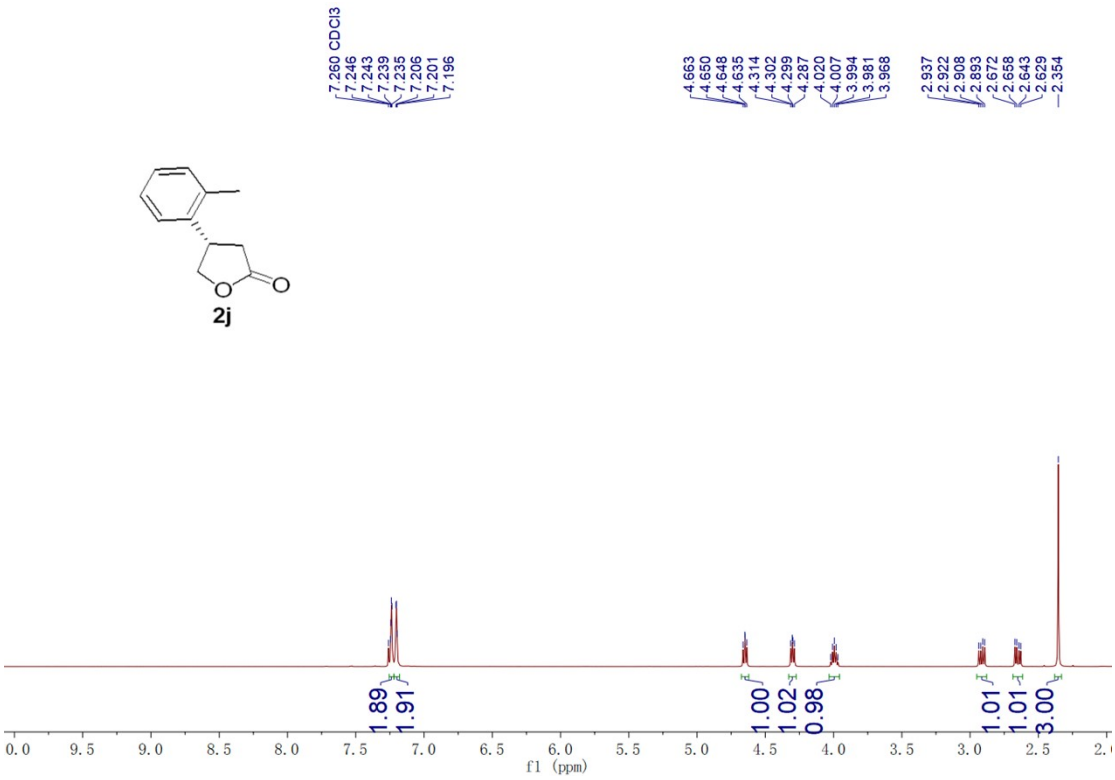

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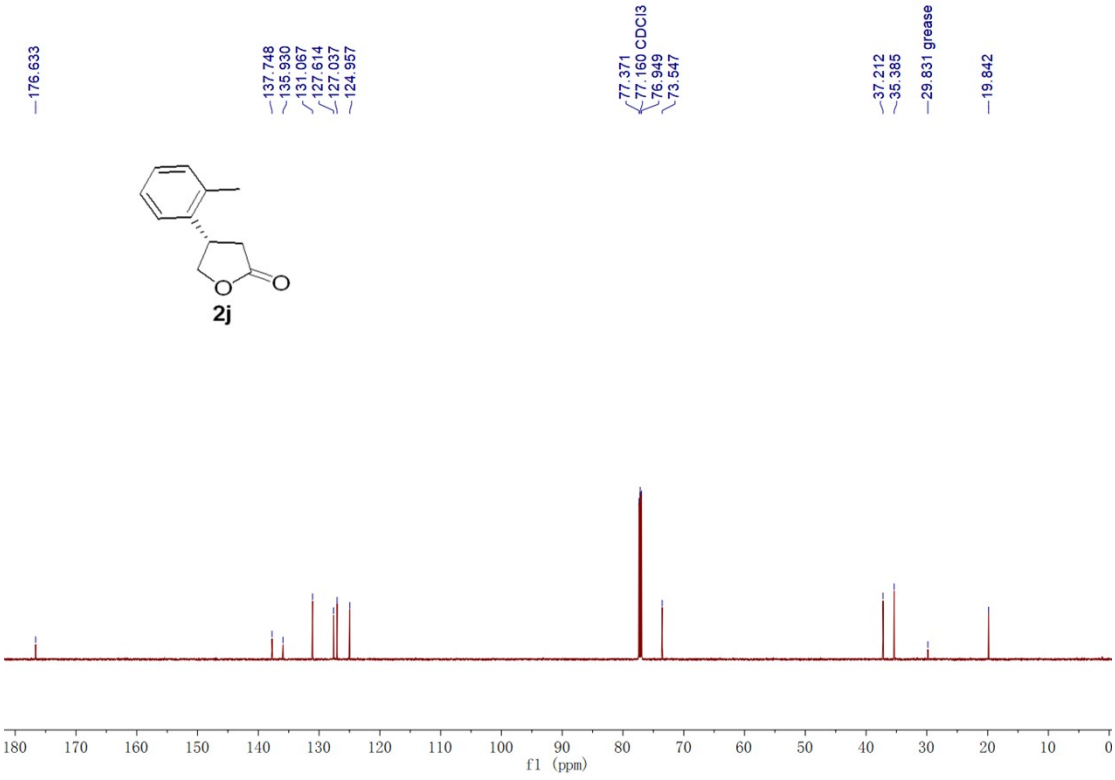

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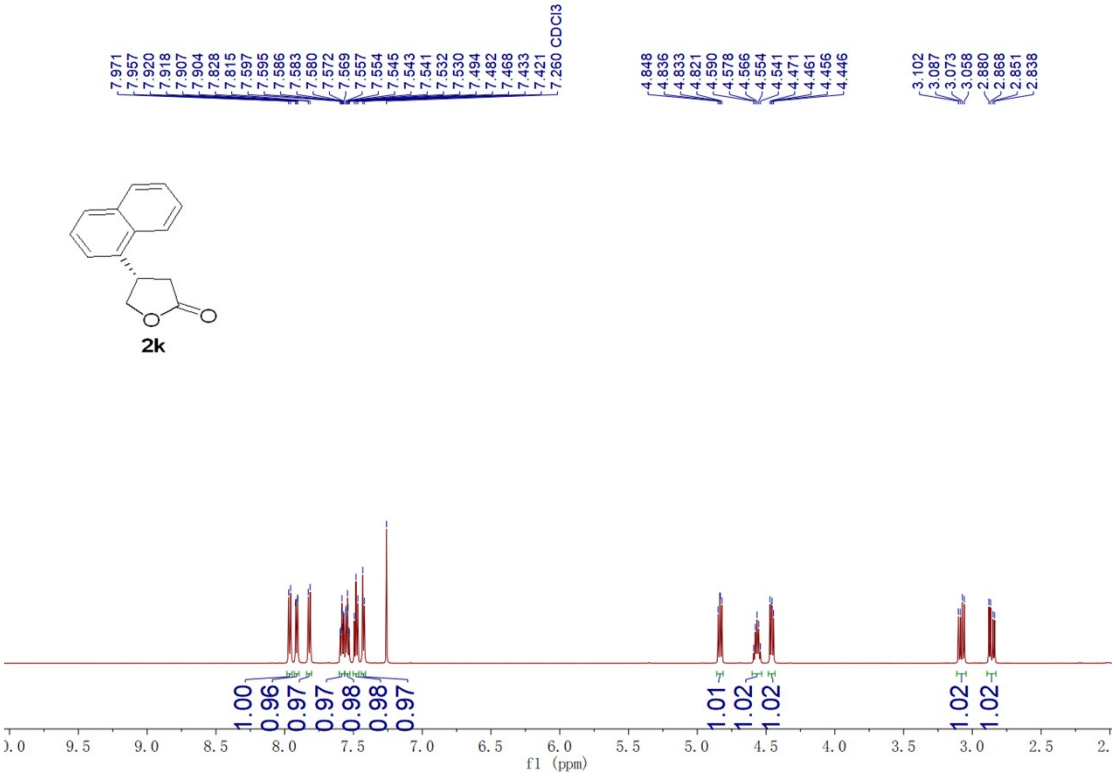

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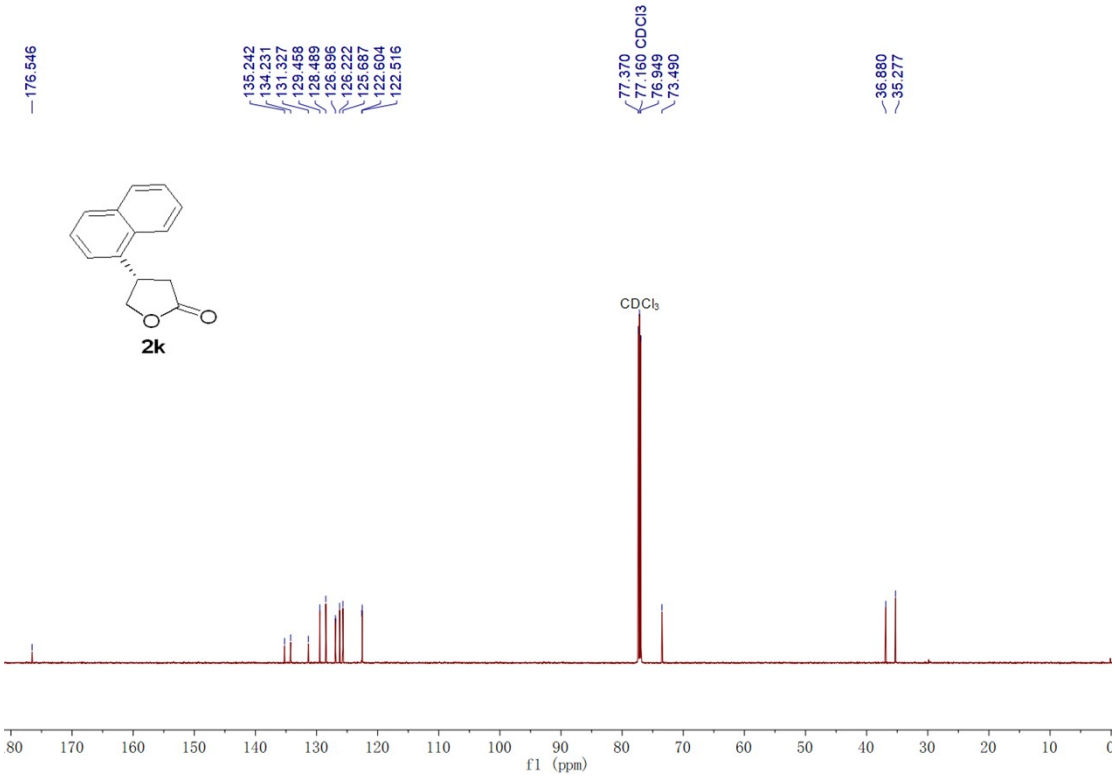
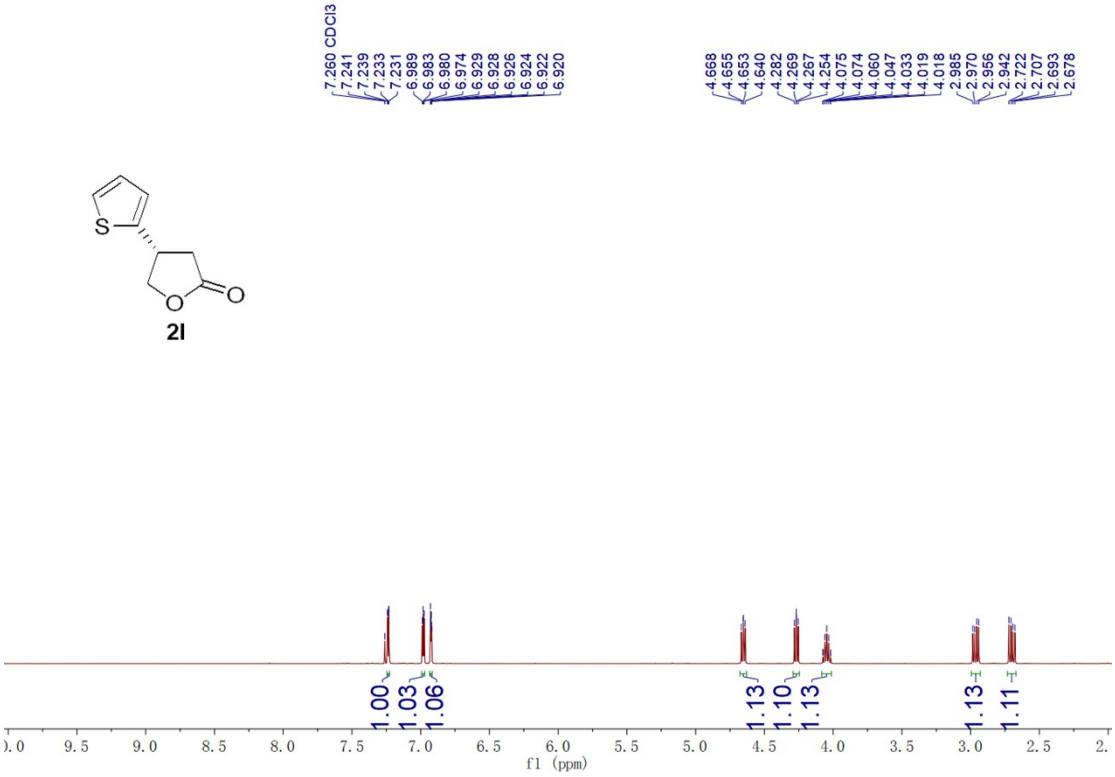
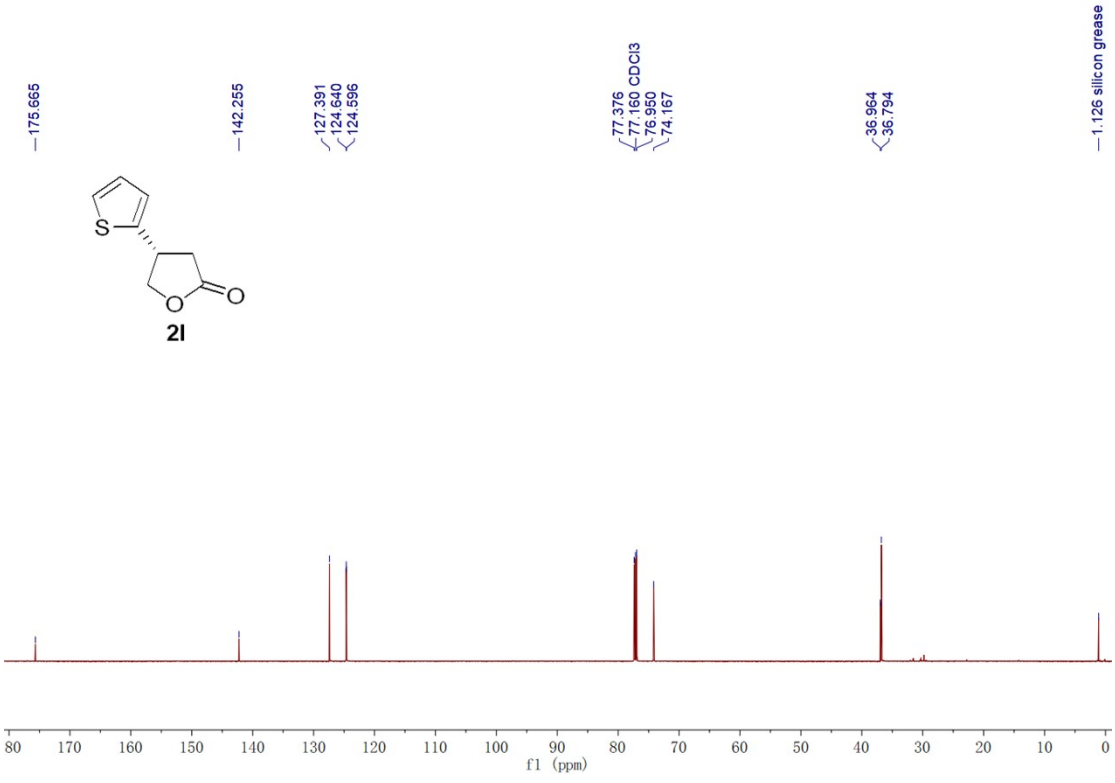


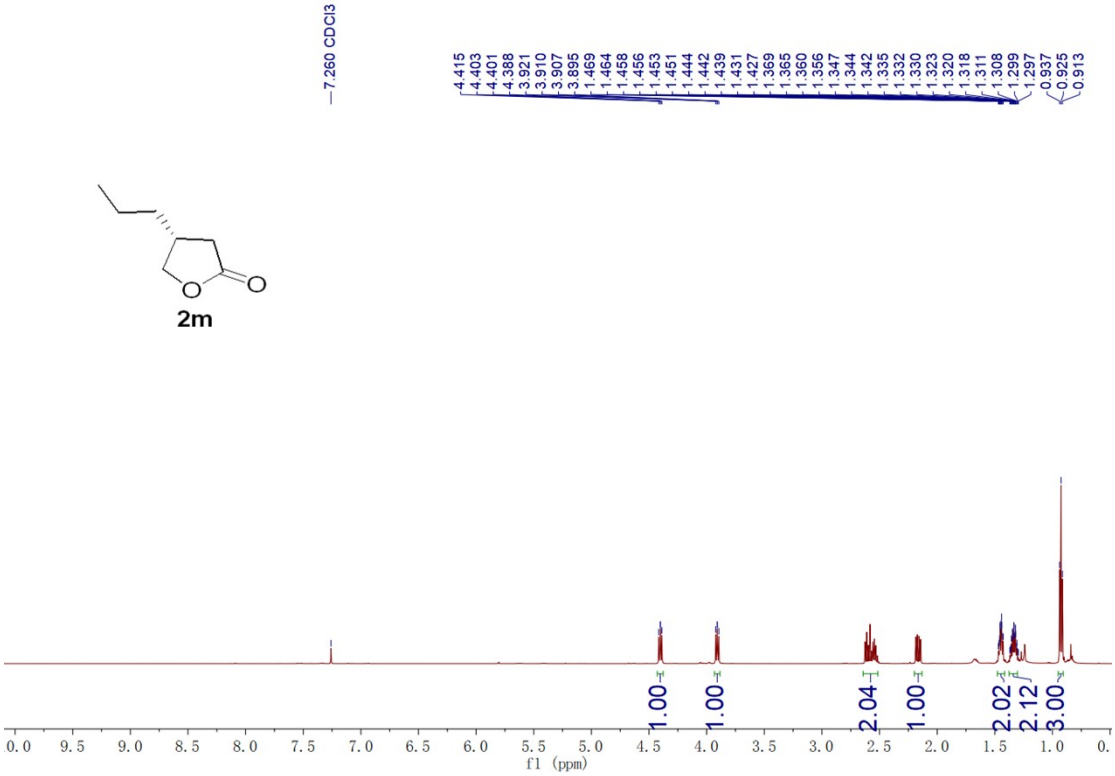
^{1}H NMR (600 MHz, $CDCl_3$)



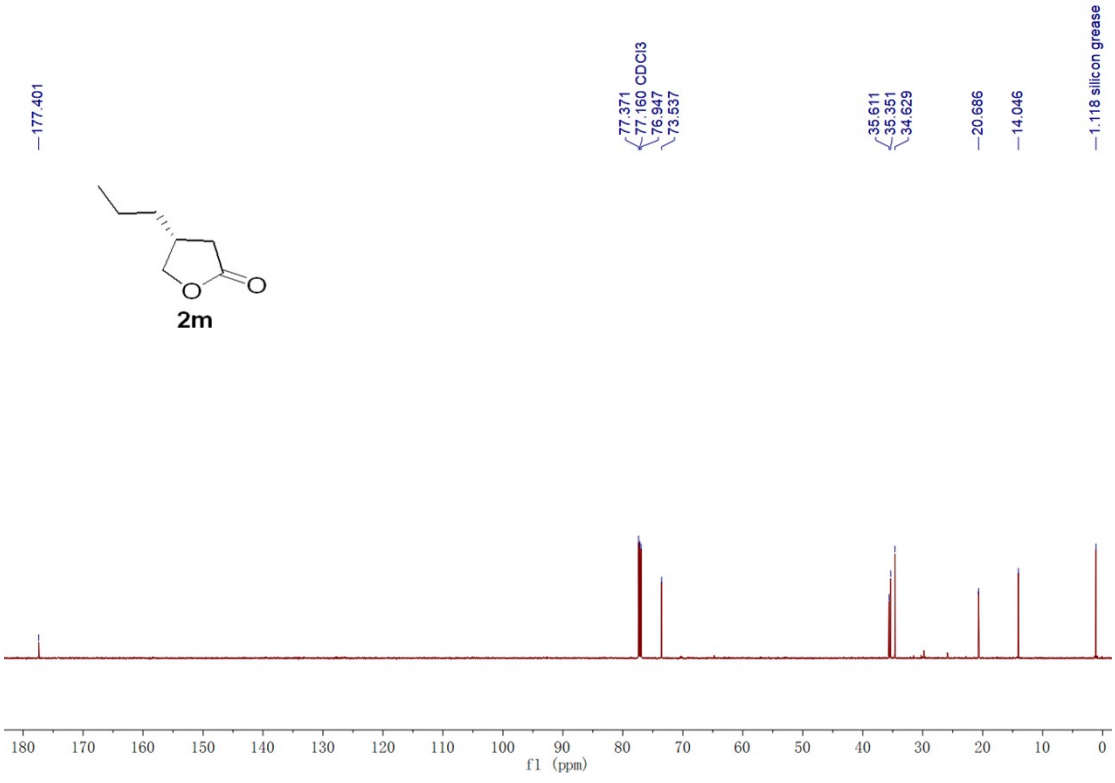
^{13}C NMR (150 MHz, $CDCl_3$)



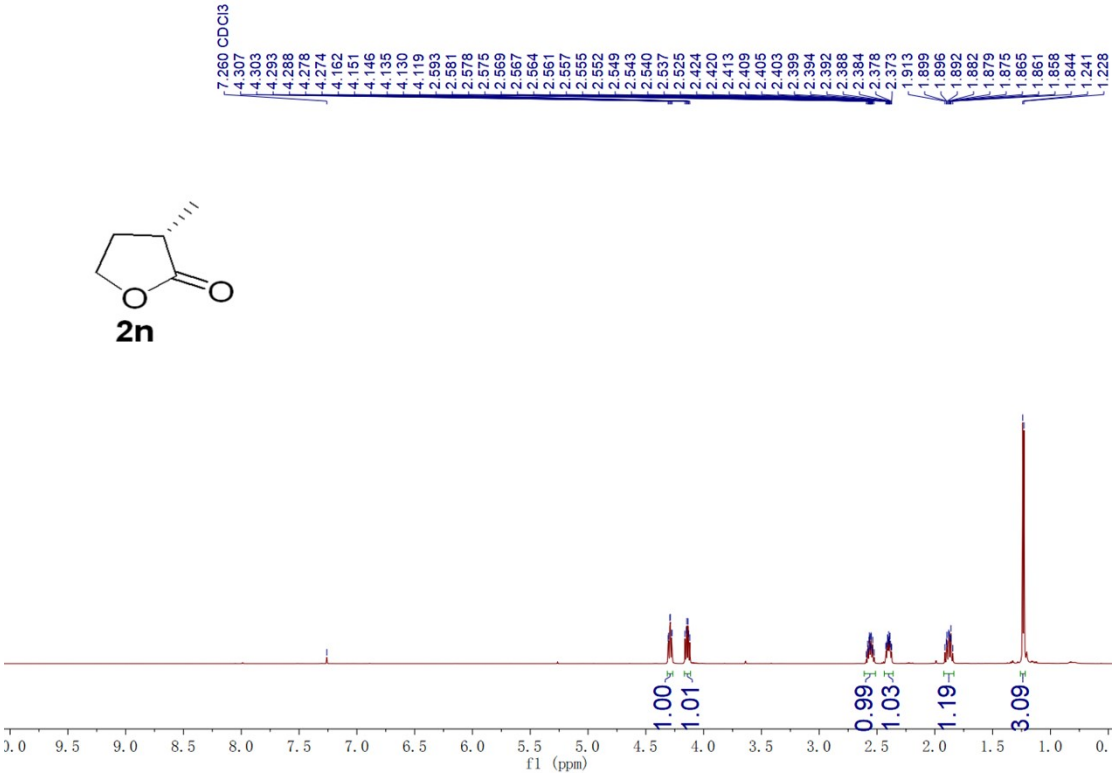
^{1}H NMR (600 MHz, $CDCl_3$)



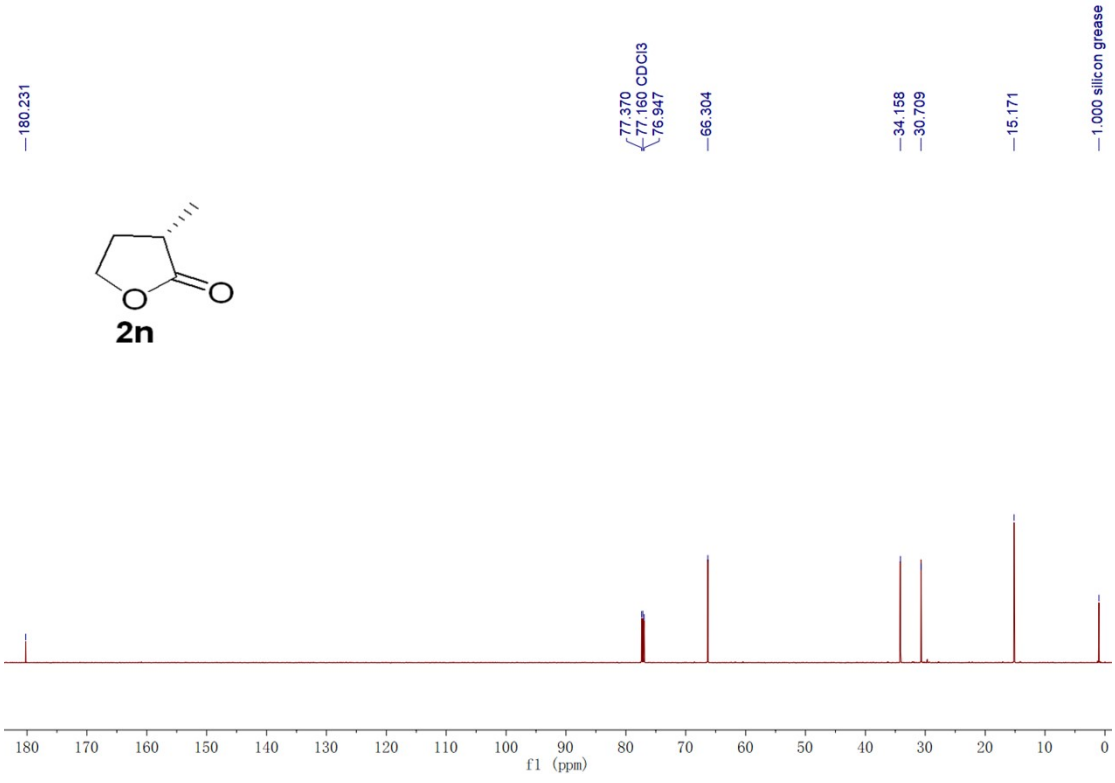
^{13}C NMR (150 MHz, $CDCl_3$)



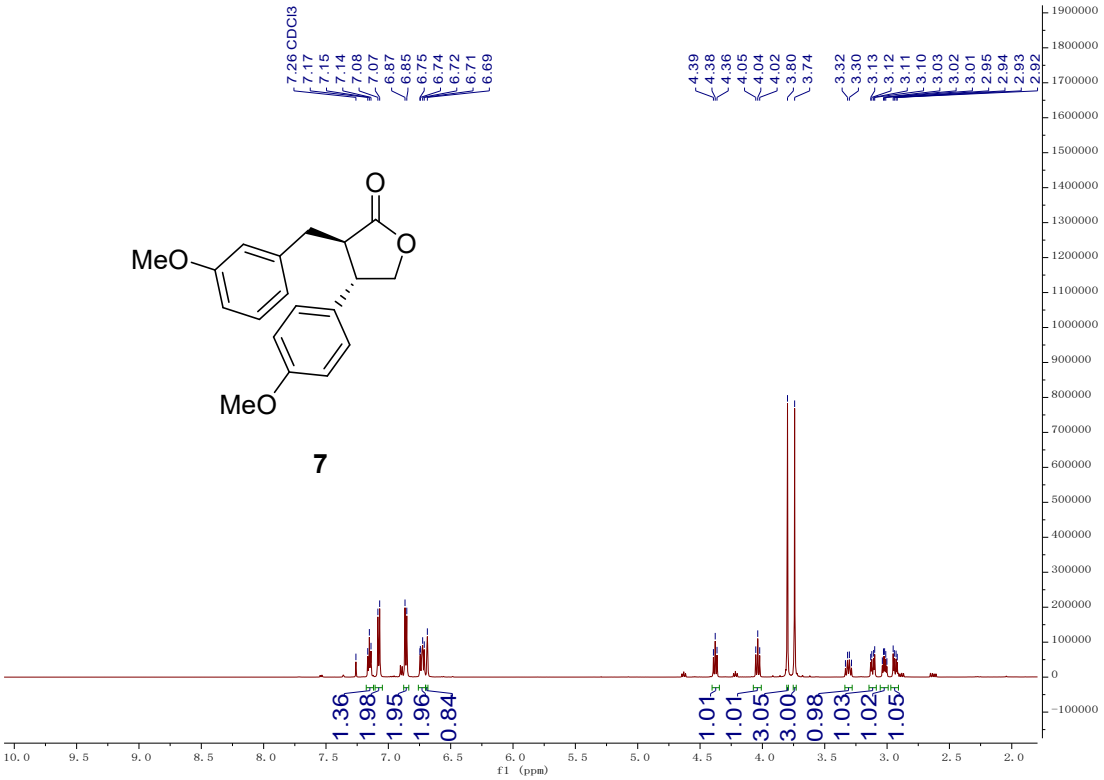
^{1}H NMR (600 MHz, $CDCl_3$)



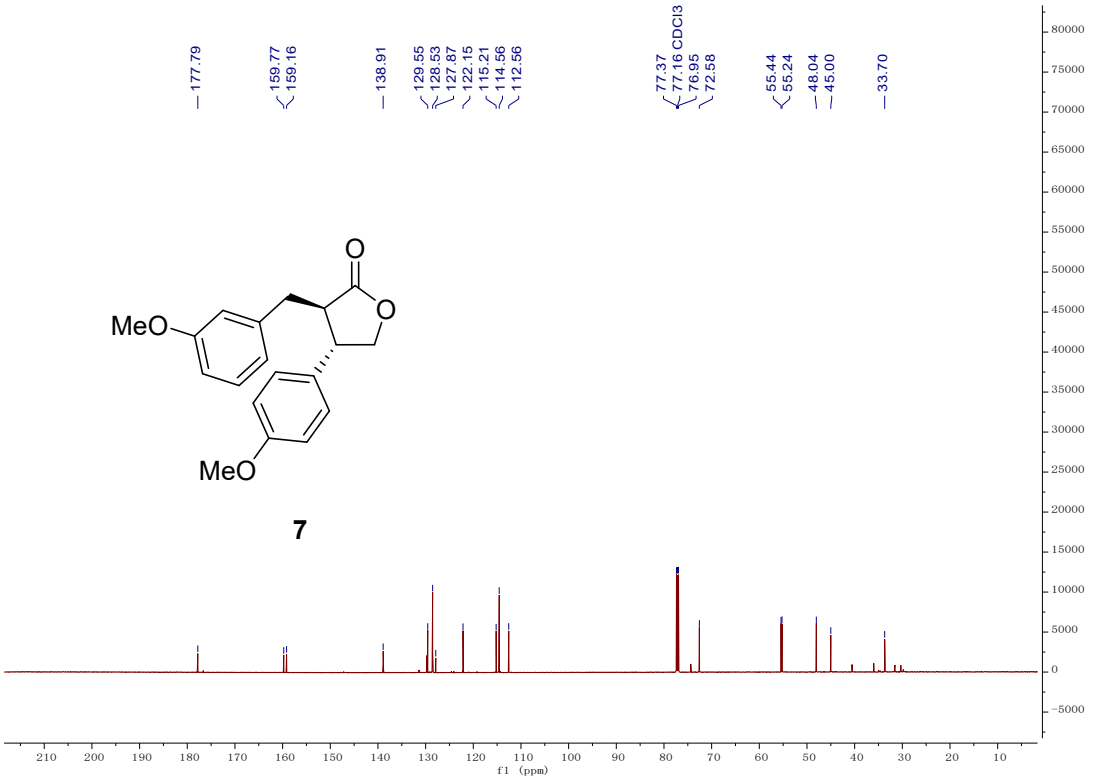
^{13}C NMR (150 MHz, $CDCl_3$)



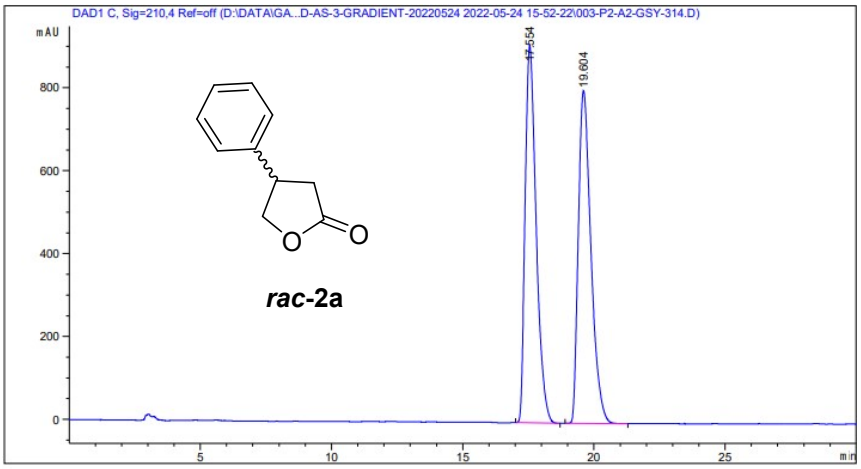
^{1}H NMR (600 MHz, $CDCl_3$)



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



7. HPLC Spectra



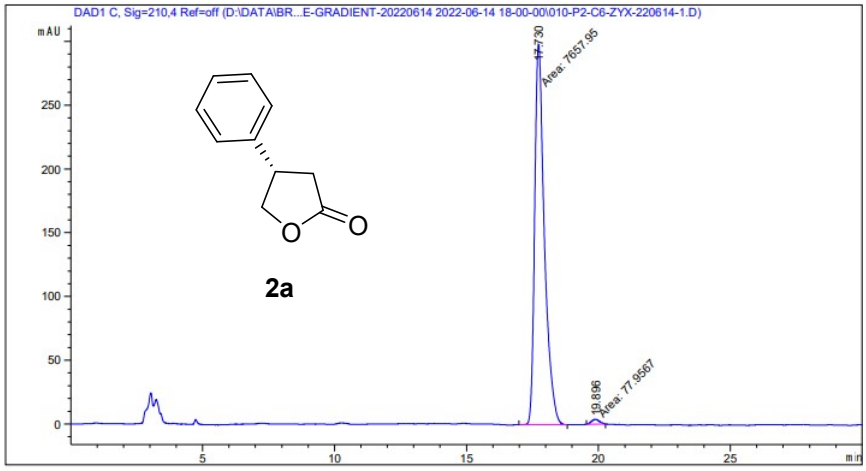

```
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.554 BB    0.4583 2.65900e4   911.65179  49.8375
   2  19.604 BB    0.5249 2.67634e4   802.97314  50.1625

Totals :                  5.33534e4  1714.62494
```



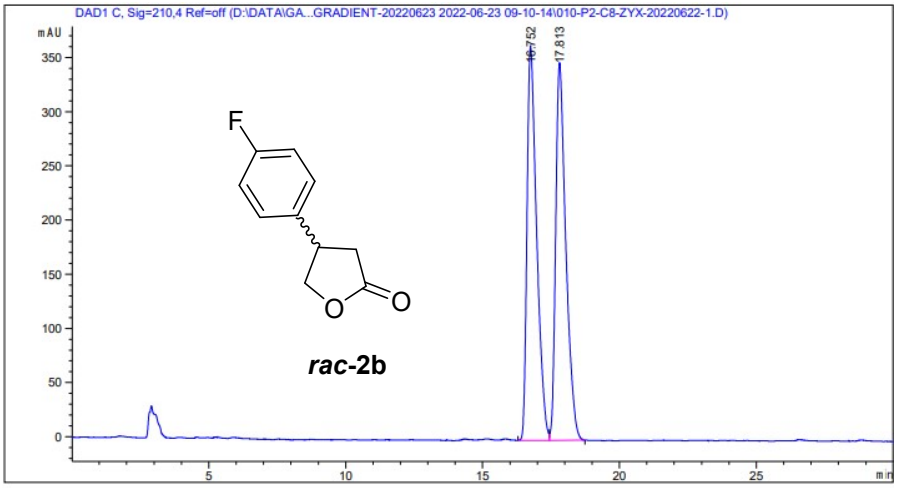

```
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.730 MM    0.4278 7657.94775  298.33279  98.9923
   2  19.896 MM    0.3520   77.95670    3.69120   1.0077

Totals :                  7735.90446  302.02400
```



***rac*-2b**

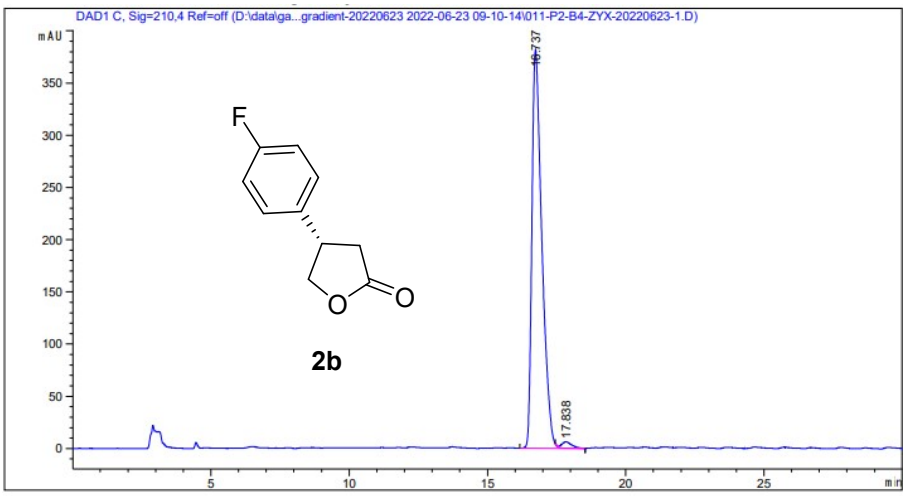
```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.752 BV    0.3642 8928.54395  363.90018  49.9102
   2  17.813 VB    0.3821 8960.68359  348.40439  50.0898

Totals :                  1.78892e4   712.30457
```



2b

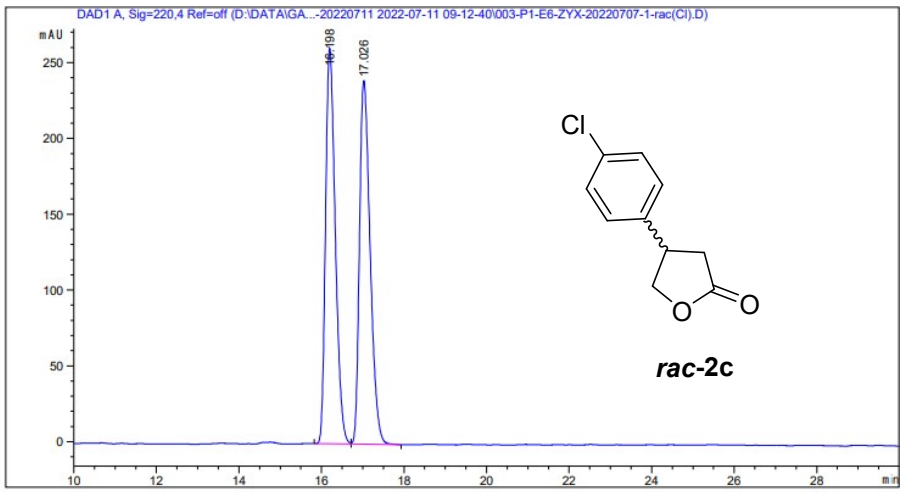
```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.737 BV R  0.3715 9537.99414  381.70267  98.3777
   2  17.838 VB E  0.3653  157.28676    6.25718   1.6223

Totals :                  9695.28090  387.95985
```

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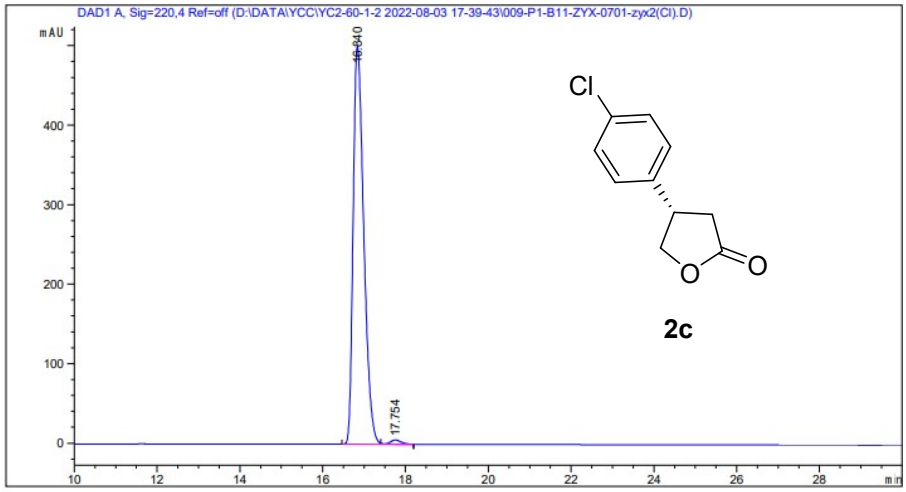
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.198 BV    0.2533 4278.80371  260.94119  49.9156
   2  17.026 VB    0.2769 4293.26758  239.82726  50.0844

Totals :                  8572.07129  500.76845
```



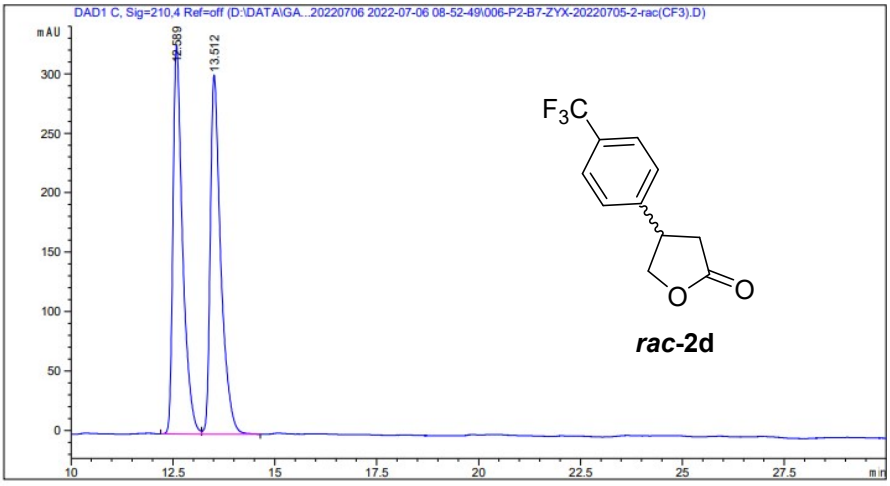

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.840 BV R  0.2732 8892.00293  500.57700  98.9318
   2  17.754 VB E  0.2755   96.00578    5.39840   1.0682

Totals :                  8988.00871  505.97540
```



***rac*-2d**

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=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.589 BV    0.2439 5373.98926  326.77206  49.7840
   2  13.512 VB    0.2677 5420.62207  301.64206  50.2160

Totals :                  1.07946e4   628.41412
```
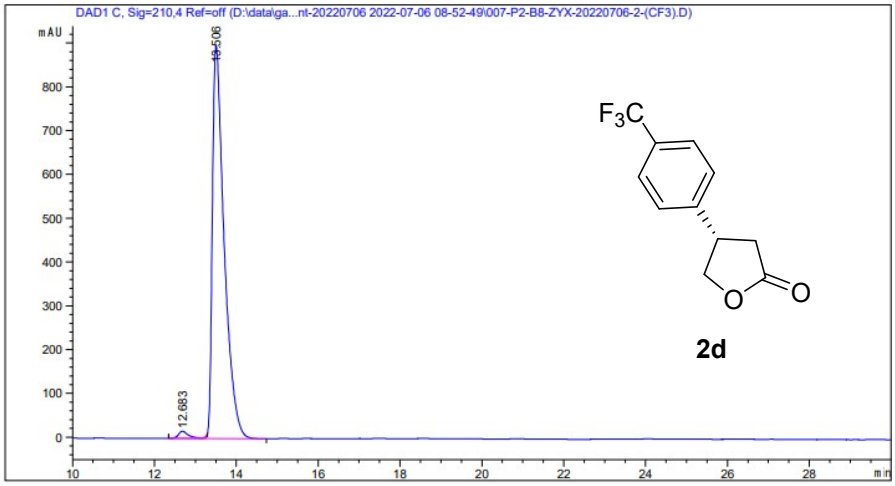
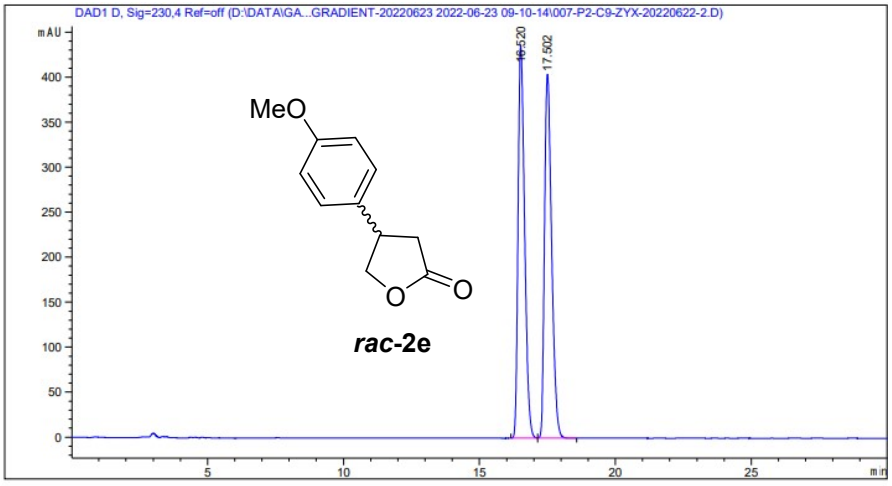
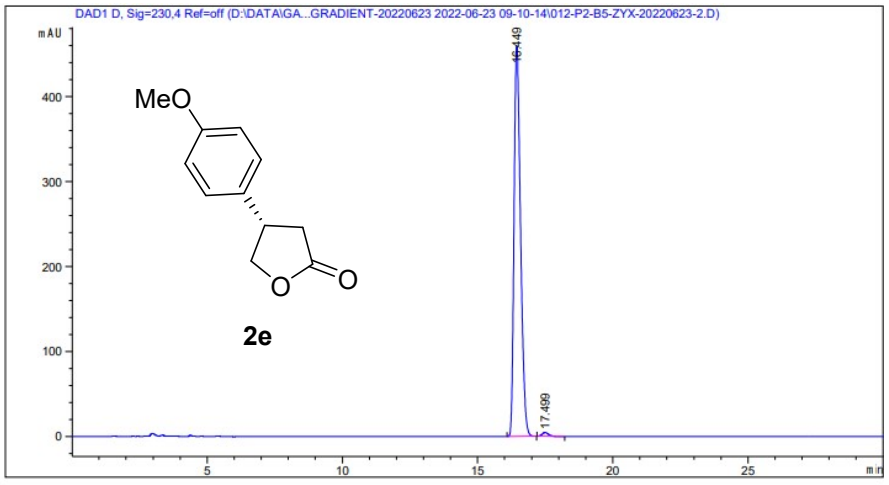



2d

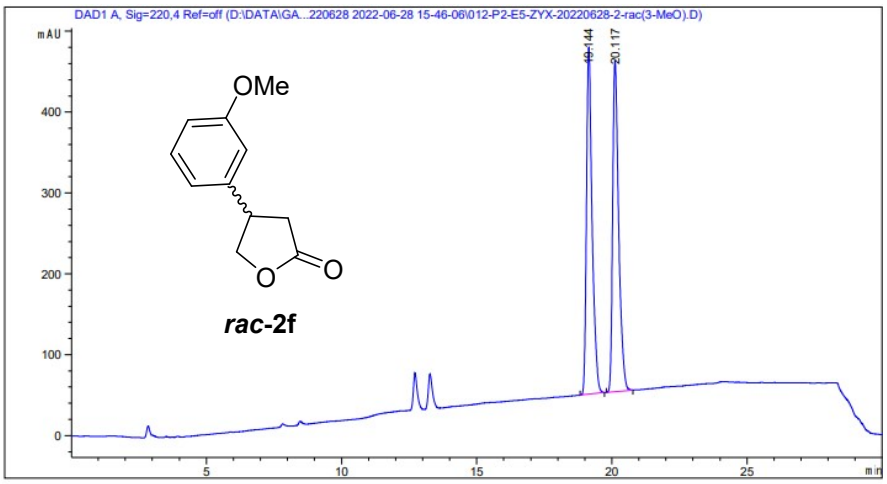
```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.683 BV E  0.2486  280.90237   16.33854   1.5400
   2  13.506 VB R  0.2956 1.79598e4   896.89978  98.4600

Totals :                  1.82407e4   913.23833
```



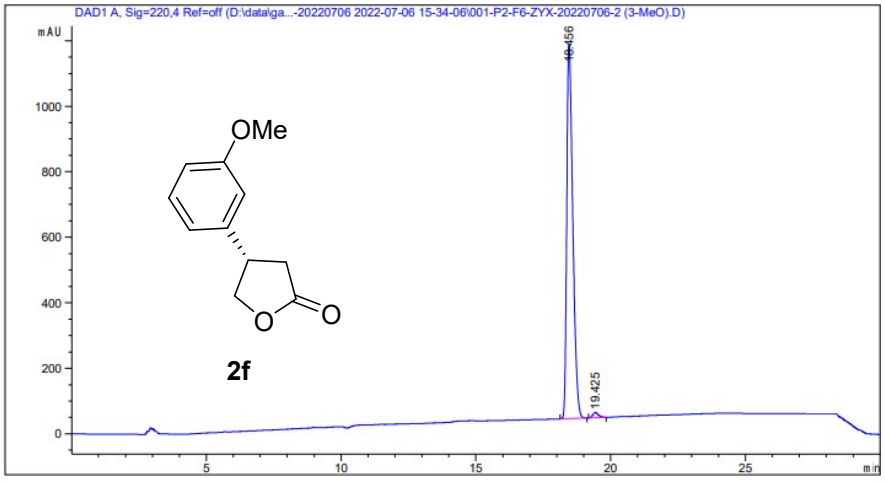

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=230,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.520 BB    0.2617 7315.36670  436.05536  49.9025
   2  17.502 BB    0.2822 7343.96191  403.75708  50.0975

Totals :                  1.46593e4   839.81244
```



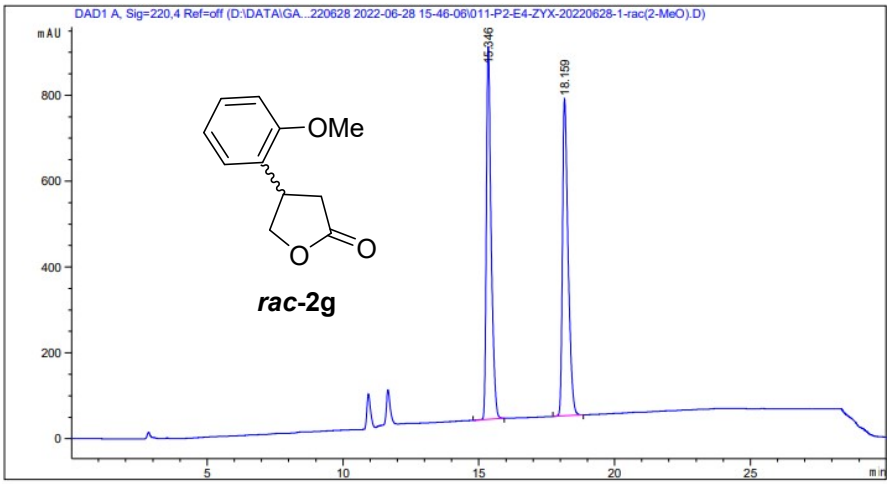

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=230,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.449 BB    0.2607 7658.74561  458.85324  99.0379
   2  17.499 BB    0.2533   74.40300    4.49002   0.9621

Totals :                  7733.14861  463.34326
```




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  19.144 BB    0.2151 6219.23535  428.97073  49.8616
   2  20.117 BB    0.2263 6253.76221  409.12857  50.1384

Totals :                  1.24730e4   838.09930
```

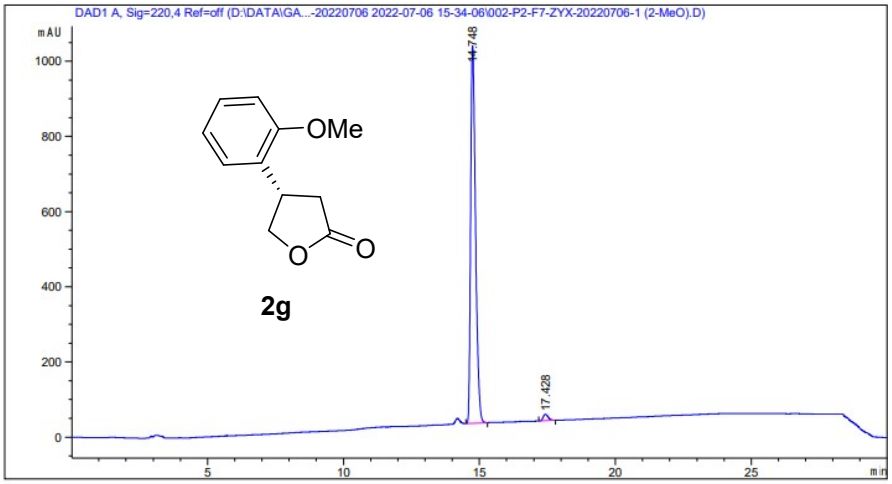



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  18.456 BB    0.2384 1.78153e4  1139.32507  98.7563
   2  19.425 BB    0.2143  224.36044   15.73641   1.2437

Totals :                  1.80396e4  1155.06148
```



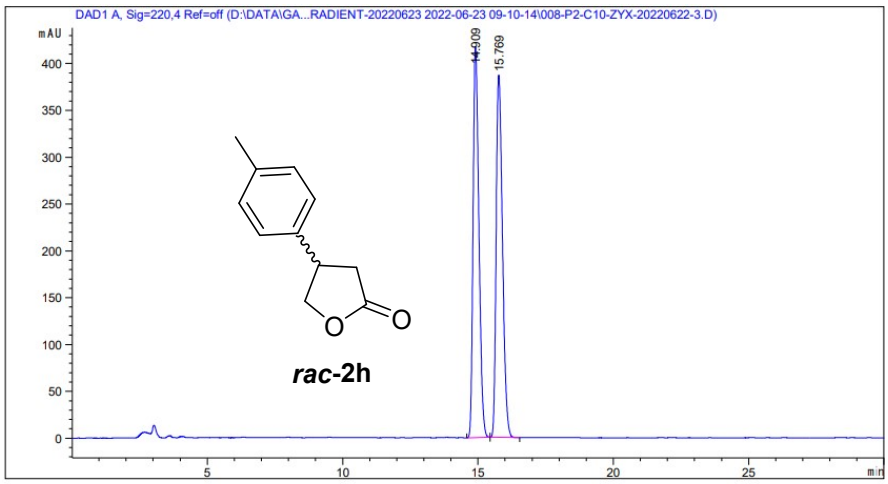
***rac*-2g**

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.346 BB    0.1813 1.06753e4   869.00891  49.9941
   2  18.159 BB    0.2168 1.06778e4   738.21930  50.0059
Totals :                  2.13531e4  1607.22821
```

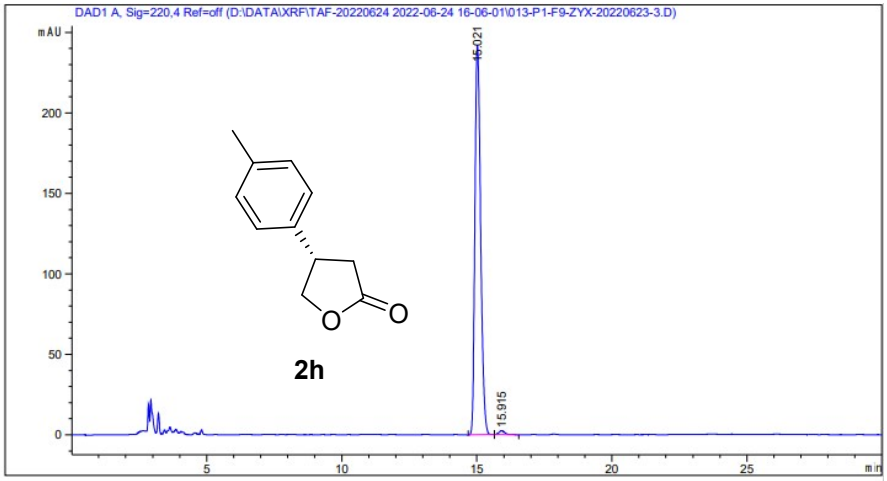


2g

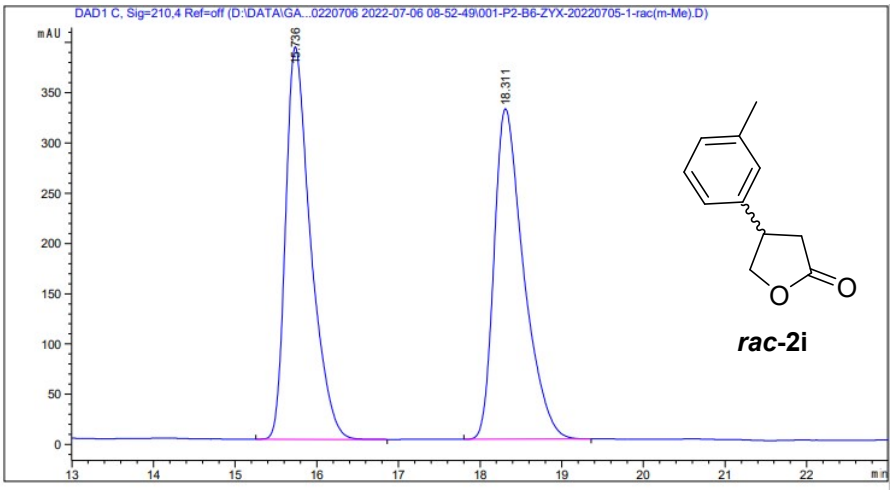
```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.748 BB    0.1877 1.23867e4  1005.42017  98.2339
   2  17.428 BB    0.1947  222.69682   17.23898   1.7661

Totals :                  1.26094e4  1022.65915
```




```
====================================================================
                        Area Percent Report
====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.909 BB    0.2334 6269.33398  416.94226  49.9810
   2  15.769 BB    0.2512 6274.09180  386.96332  50.0190

Totals :                  1.25434e4   803.90558
```

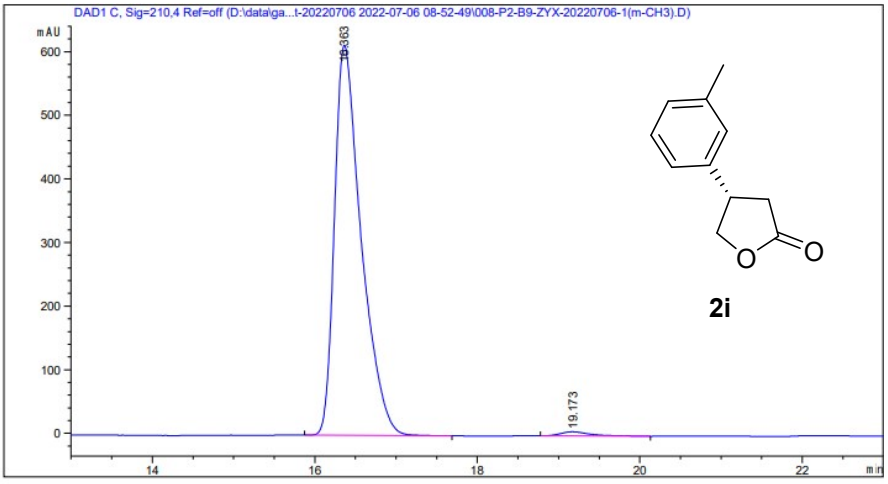



```
====================================================================
                        Area Percent Report
====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.021 BB    0.2267 3544.67700  242.23021  98.9285
   2  15.915 BB    0.2237   38.39378    2.49202   1.0715

Totals :                  3583.07079  244.72223
```



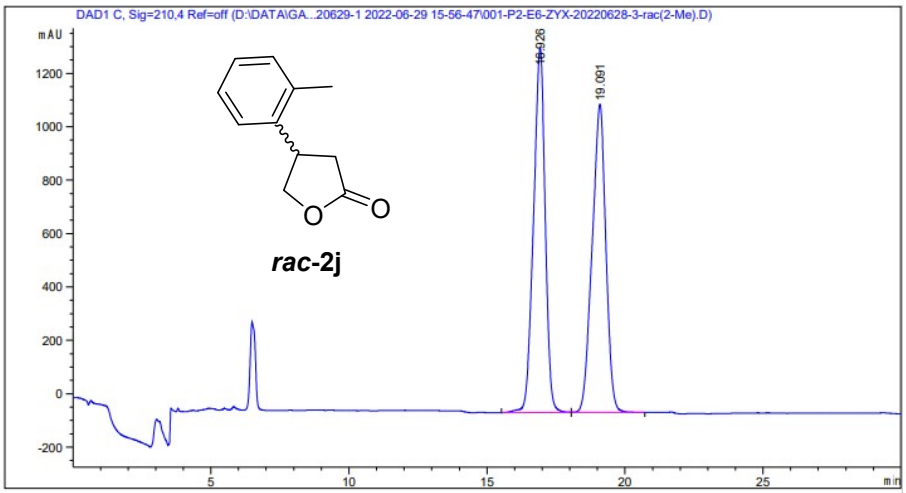
***rac*-2i**

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.736 BB    0.3180 8296.78125  390.32135  50.0429
   2  18.311 BB    0.3759 8282.54004  328.78058  49.9571

Totals :                  1.65793e4   719.10193
```

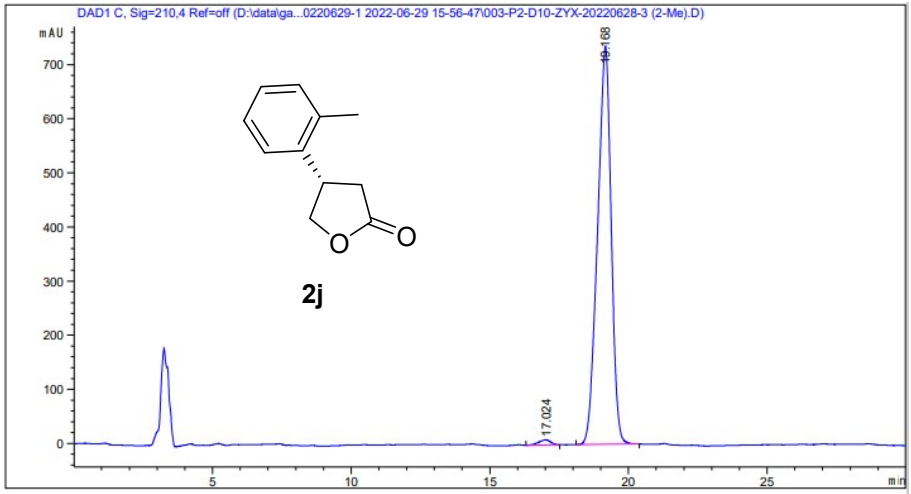


2i

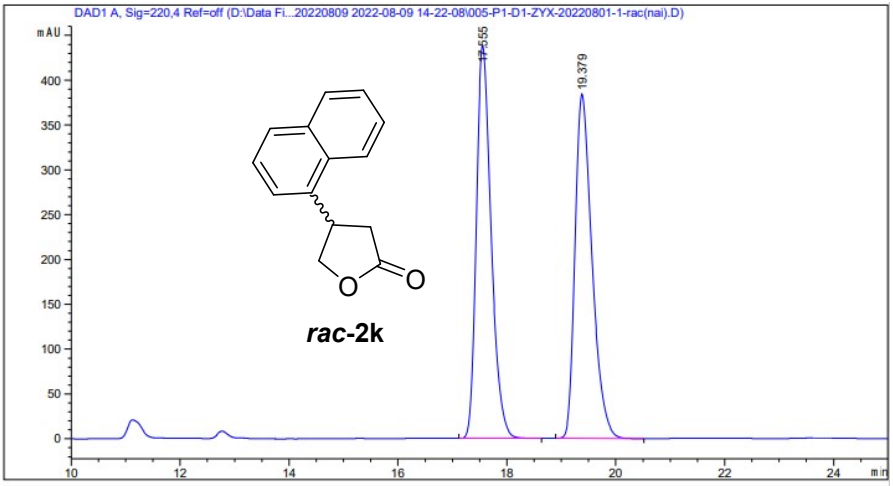
```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.363 BB    0.3364 1.40025e4   613.20581  98.7841
   2  19.173 BB    0.3788  172.35622    6.55392   1.2159

Totals :                  1.41749e4   619.75973
```



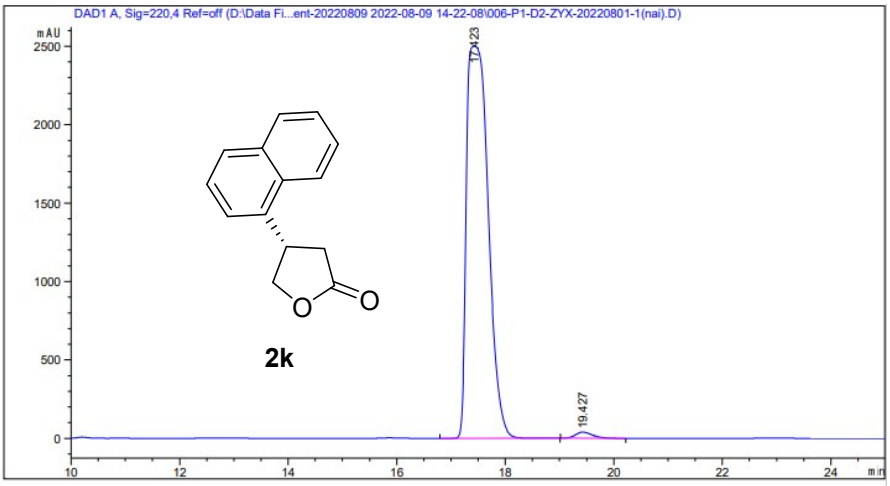

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.926 BB    0.4296 3.99824e4  1365.42834  50.1658
   2  19.091 BB    0.4932 3.97180e4  1154.93848  49.8342
Totals :                  7.97004e4  2520.36682
```



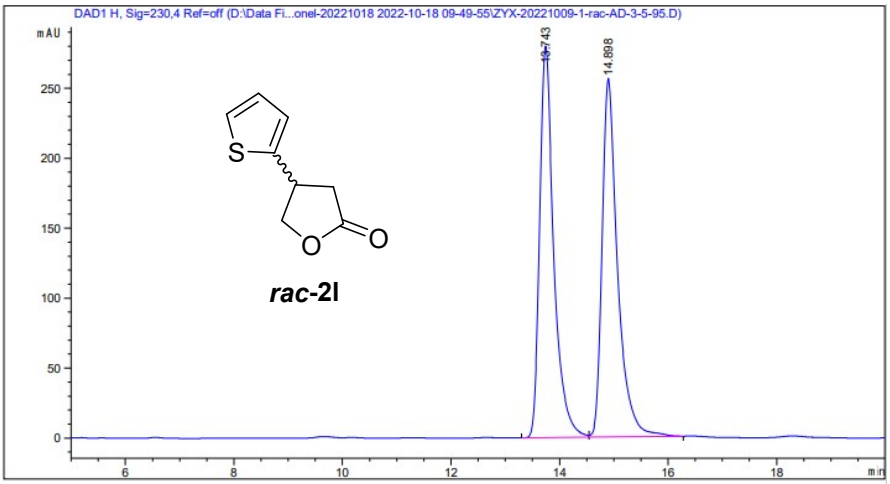

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.024 BB    0.3902  283.76025    9.50735   1.1205
   2  19.168 BB    0.4972 2.50407e4   735.41461  98.8795
Totals :                  2.53245e4   744.92196
```




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.555 BB    0.2880 8259.22754  438.08722  49.7994
   2  19.379 BB    0.3329 8325.76270  384.14825  50.2006

Totals :                  1.65850e4   822.23547
```

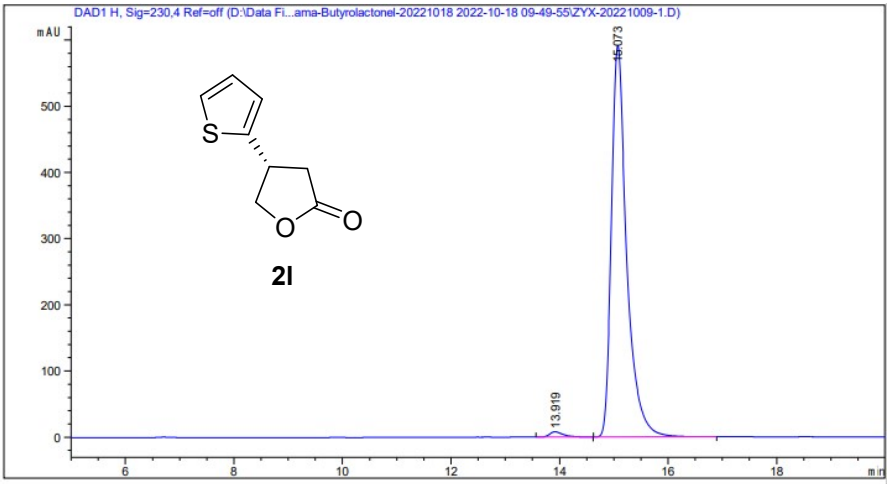



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=220,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.423 BB    0.4395 6.92752e4  2498.67554  98.7940
   2  19.427 BB    0.3259  845.62933   39.47557   1.2060

Totals :                  7.01208e4  2538.15111
```



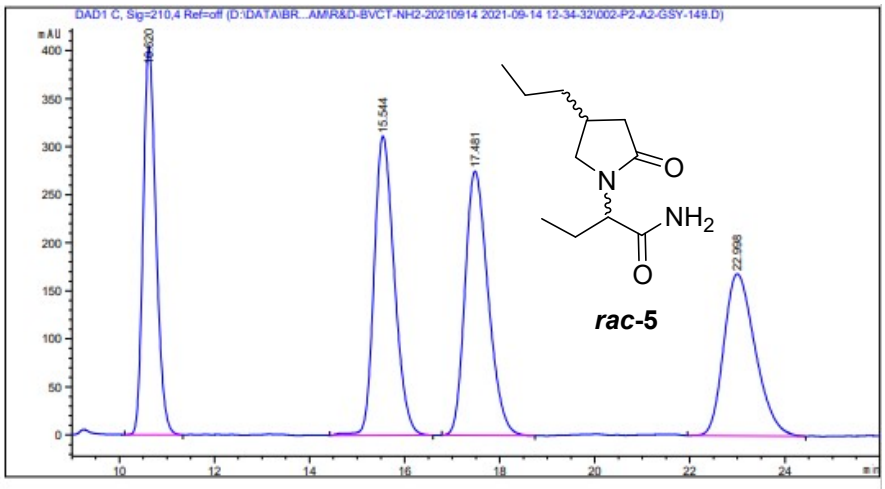
***rac*-2l**

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 H, Sig=230,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  13.743 BV    0.2682 5039.24170  279.63739  49.8086
   2  14.898 VB    0.2953 5077.97314  256.12122  50.1914

Totals :                  1.01172e4   535.75861
```



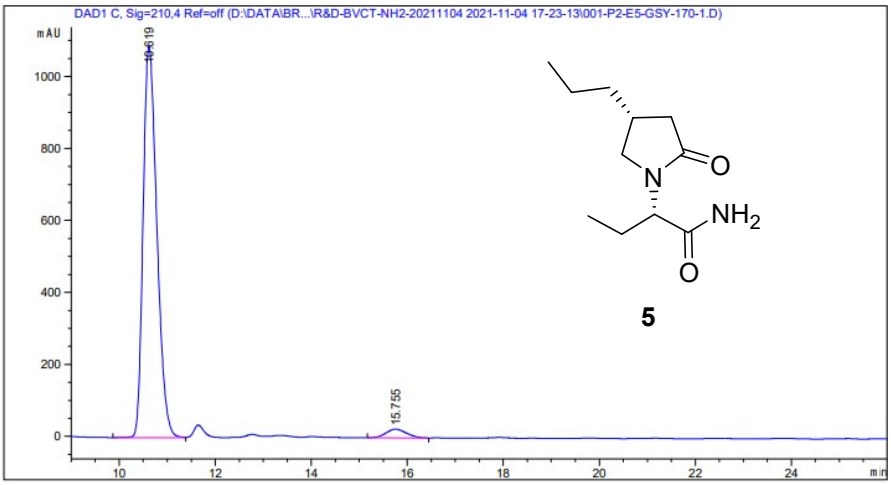
2l

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 H, Sig=230,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  13.919 BB    0.2597  139.02673    7.96188   1.1913
   2  15.073 BB    0.2895 1.15308e4   591.36938  98.8087

Totals :                  1.16698e4   599.33126
```



***rac*-5**

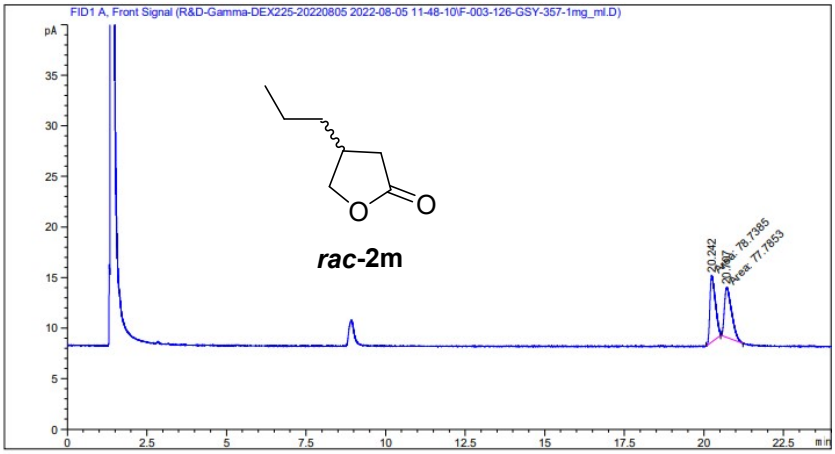
```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.620 BB    0.2917 7583.06348  402.76846  22.4521
   2  15.544 BB    0.4560 9170.25000  310.97925  27.1515
   3  17.481 BB    0.5269 9304.79492  274.87088  27.5499
   4  22.998 BB    0.7125 7716.27051  168.41872  22.8465
Totals :                  3.37744e4  1157.03731
```



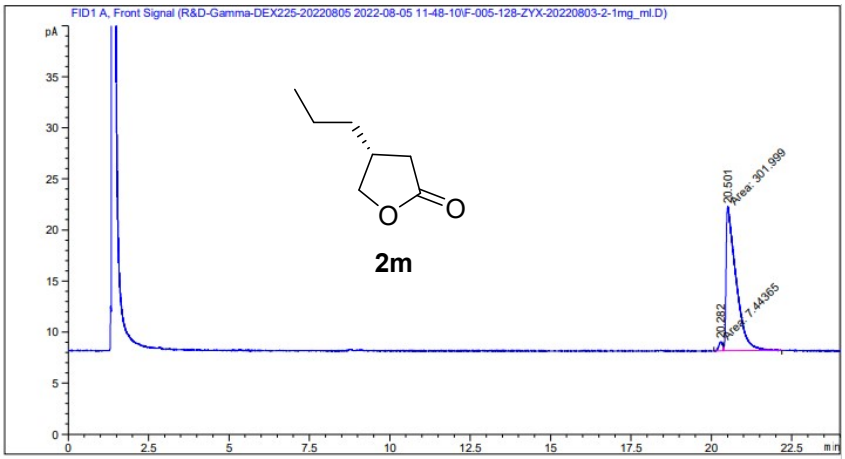
5

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.619 BV    0.3102 2.16361e4  1086.85876  96.8609
   2  15.755 BB    0.4509  701.19250   23.85451   3.1391

Totals :                  2.23373e4  1110.71328
```

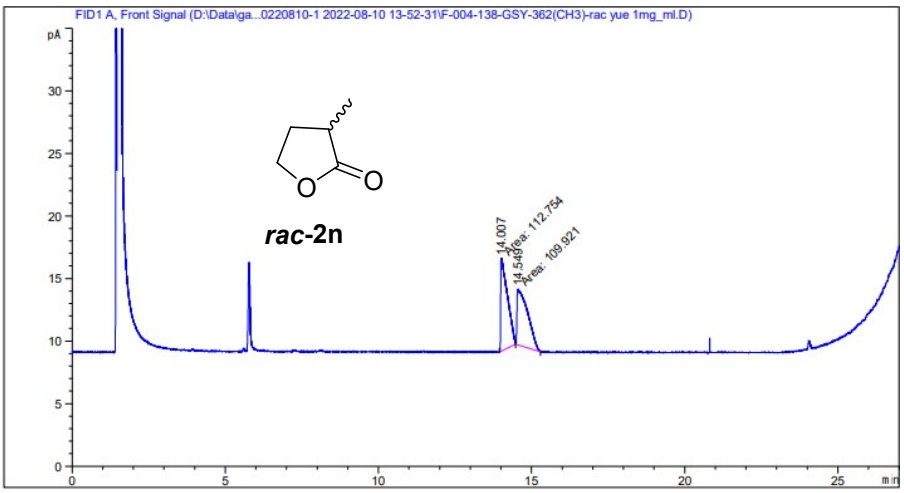
8. GC Spectra



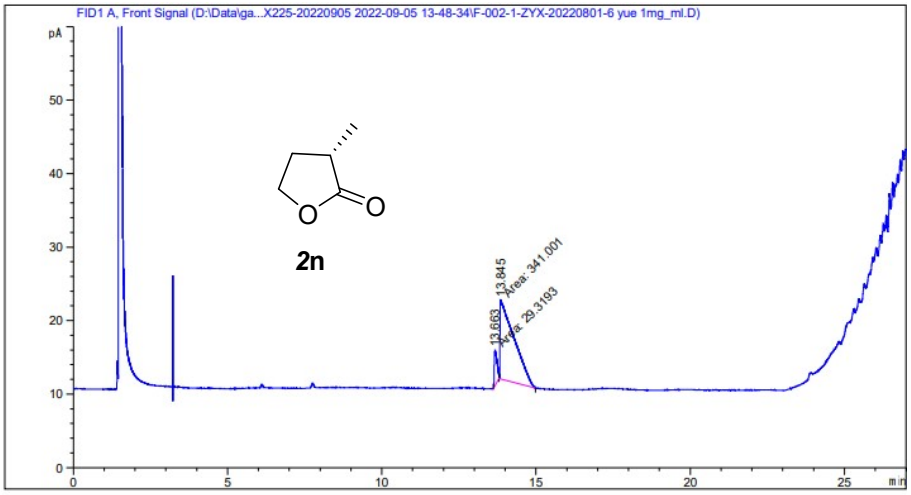

```
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  20.242 MM    0.1994   78.73846    6.58091 50.30449
   2  20.707 MM    0.2629   77.78526    4.93058 49.69551

Totals :                   156.52372   11.51149
```




```
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  20.282 MF    0.1396    7.44365 8.88958e-1  2.40550
   2  20.501 FM    0.3572  301.99921   14.09239 97.59450

Totals :                   309.44285   14.98135
```




```
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  14.007 MM    0.2517  112.75397    7.46495 50.63622
   2  14.549 MM    0.4096  109.92059    4.47262 49.36378

Totals :                   222.67456   11.93757
```




```
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  13.663 MM    0.0996   29.31932    4.90778  7.91728
   2  13.845 MM    0.5261  341.00116   10.80254 92.08272

Totals :                   370.32048   15.71032
```

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