Versatile Enantioselective Synthesis of Functionalized Lactones via Copper-Catalyzed Radical Oxyfunctionalization of Alkenes

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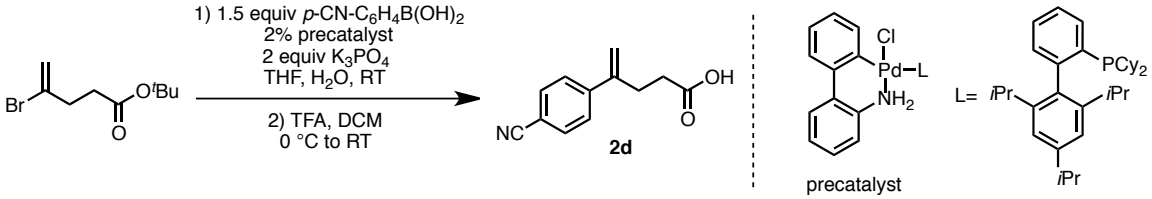
SUPPORTING INFORMATION

General considerations. All reactions were carried out with dry solvents under anhydrous conditions, unless otherwise noted. Anhydrous ethyl acetate (EtOAc), methyl *tert*-butyl ether (MTBE) and 2,2′-isopropylidenebis[(4*S*)-4-*tert*-butyl-2-oxazoline] (99%) were purchased from Aldrich and used as received. Tetrakis(acetonitrile)copper(I) hexafluorophosphate was purchased from Strem and stored in a dry box. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. All chemicals were weighed on the bench top, in the air. Reactions were monitored by ^{1}H NMR spectroscopy and thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as a visualizing agent and phosphomolybdic acid in ethanol or iodine on silica gel as developing agents. Flash silica gel chromatography was performed using Silicycle SiliaFlashP60 (230-400 mesh) silica gel. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 400 spectrometer and were calibrated using residual solvent as an internal reference ($CDCl_3$: 7.26 ppm for ^{1}H NMR and 77.16 ppm for ^{13}C NMR). ^{19}F NMR spectra were recorded on a Varian 300 MHz spectrometer or a Bruker AMX 400 spectrometer and were calibrated using $CFCl_3$ as an external reference (0 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad, at = apparent triplet, ad = apparent doublet. IR spectra were recorded on a Thermo Scientific Nicolet iS5 FT-IR spectrometer (iD5 ATR). HPLC analyses were performed on an Angilent 1100 series system with Daicel Chiralcel® columns (4.6 mm x 250 mm) in hexanes/*i*-PrOH mixtures. Melting points (m.p.) were obtained on a Mel-Temp capillary melting point apparatus. Optical rotations were measured on Jacsco P-1010 polarimeter with a sodium lamp (589 nm) at 24 °C. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA. HRMS (DART or ESI)

spectra were recorded on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS).

Synthesis and Characterization of non-Commercial Substrates

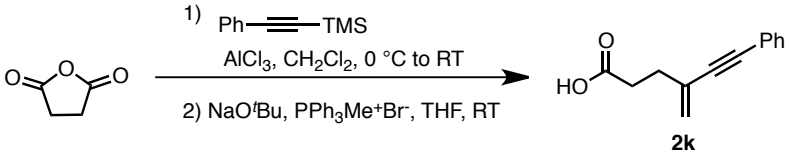
4-Phenylpent-4-enoic acid (**2a**),[1] 4-(4-bromophenyl)pent-4-enoic acid (**2b**),[1] 4-(4-chlorophenyl)pent-4-enoic acid (**2c**),[1] 4-(4-trifluoromethylphenyl)pent-4-enoic acid (**2e**),[1] 4-(4-methoxyphenyl)pent-4-enoic acid (**2f**),[2] 4-(3-thienyl)pent-4-enoic acid (**2g**),[1] 4-(3-acetylphenyl)pent-4-enoic acid (**2h**),[1] 5-phenylhex-5-enoic acid (**2i**),[1] 3,3-dimethyl-5-phenylhex-5-enoic acid (**2j**),[1] (*Z*)-5-phenylhept-5-enoic acid ((*Z*)-**2m**, *Z*:*E* = 14:1 as determined by ^{1}H NMR analysis),[1] (*E*)-5-phenylhept-5-enoic acid ((*E*)-**2m**, *Z*:*E* < 1:20 as determined by ^{1}H NMR analysis),[1] were prepared according to literature procedures.



4-(4-Cyanophenyl)pent-4-enoic acid (**2d**) : An oven-dried 100 mL round-bottom-flask equipped with a magnetic stir bar was charged with 4-cyanophenyl boronic acid (1.5 equiv, 0.96 g, 6.5 mmol) and precatalyst (80 mg, 0.02 equiv). The flask was sealed with a rubber septum and connected to a Schlenk line though a needle. The flask was then evacuated and backfilled with argon (This sequence was repeated a total of three times). *tert*-Butyl 4-bromopent-4-enoate (1.02 g, 4.3 mmol, 1.0 equiv),[3] followed by anhydrous tetrahydrofuran (10 mL) and potassium phosphate aqueous solution (2 equiv, 1.84 g in 17 mL degassed water) was added via syringe. The resulting mixture was stirred at room temperature for 48 h before diluted with water (50 mL) and ethyl ether (50 mL). The aqueous phase was separated and extracted with ethyl ether (50 mL × 3). The combined organic layers was concentrated *in vacuo*. The residue was passed through a short plug of silica gel (1 cm × 4 cm) and eluted with hexanes/ethyl ether until all the coupling product was eluted as detected by TLC. The elute was concentrated *in vacuo* and redissolved in dichloromethane (20 mL), to which at 0 °C was added 6.5 mL (20 equiv) trifluoroacetic acid slowly. The resulting mixture was stirred at room temperature for 48 h before

concentrating *in vacuo* to remove the solvents and excess trifluoroacetic acid. The residue was purified by silica gel flash column chromatography (hexanes: ethyl acetate = 5:1 to 1:1) followed by one recrystallization to afford **2d** (0.35 g, 40% yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.8 Hz, 2 H), 7.51 (d, *J* = 8.8 Hz, 2 H), 5.42 (s, 1 H), 5.25 (s, 1 H), 2.84 (t, *J* = 7.6 Hz, 2 H), 2.53 (t, *J* = 7.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 145.2, 145.2, 132.4, 126.9, 118.9, 116.0, 111.4, 32.8, 29.7; IR (film) ν_{max} 2970, 2232, 1739, 1699, 1627, 1365, 1217, 905, 839 cm^{-1}; R_f(hexanes: ethyl acetate = 1:1)= 0.25; m. p. 101 °C. HRMS: $[M+NH_4]^+$ Calcd. For $C_{12}H_{15}N_2O_2$: 219.1128; Found: 219.1128.



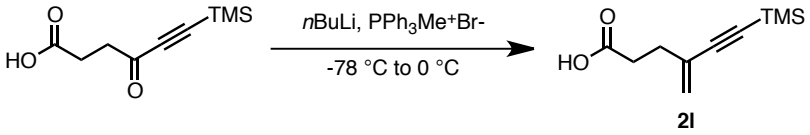
2k

4-Methylene-6-phenylhex-5-ynoic acid (**2k**): Adapted from a previously reported procedure:[4] Powered anhydrous $AlCl_3$ (3.7 g, 28 mmol, 1.75 equiv) was added in portions to an ice-cold mixture of succinic anhydride (2.4 g, 24 mmol, 1.5 equiv) and 1-phenyl-2-trimethylsilylacetylene (3.1 mL, 16 mmol, 1.0 equiv) in 200 mL anhydrous CH_2Cl_2. The mixture was stirred at 0 °C for 2 h and then at room temperature for 16 h. The dark brown mixture was carefully quenched with 1 N HCl at 0 °C. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (100 mL × 2). The combined organic phase was washed with 1 N HCl, water and brine, and dried over sodium sulfate. The solvent was removed *in vacuo* and the residue was purified by passing through a short silica gel column to afford the crude product 4-oxo-6-phenylhex-5-ynoic acid as a brown solid (1.6 g, 50 % yield) which was used in the next reaction without further purification.

An oven-dried 200 mL round-bottom-flask equipped with a magnetic stir bar was charged with methyltriphenylphosphonium bromide (3.7 g, 10.4 mmol, 1.3 equiv) and anhydrous THF (100 mL). The mixture was stirred at 0 °C and sodium *tert*-butoxide (2.0 g, 20.6 mmol, 2.6 equiv) was added in portions. The resulting yellow slurry was stirred at room temperature for 45 min before being cooled to 0 °C. At 0 °C, 4-oxo-6-phenylhex-5-ynoic acid (1.6 g, 8 mmol, 1.0 equiv) was added slowly to the reaction mixture. The resulting mixture was stirred at room temperature for 16 h before concentrating *in vacuo*. The residue was diluted with 200 mL 0.5 N

aqueous sodium hydroxide and washed with CH_2Cl_2 (30 mL × 3). The aqueous layer was cooled to 0 °C, acidified (pH < 2), and extracted with Et_2O (100 mL × 3). The combined organic layers were washed with water (30 mL × 3) and brine (30 mL), dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography to afford **2k** as a yellow solid (0.77 g, 54% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.43 (m, 2 H), 7.31 (m, 3 H), 5.47 (s, 1 H), 5.38 (d, *J* = 1.2 Hz, 1 H), 2.68 (t, *J* = 7.6 Hz, 2 H), 2.59 (t, *J* = 7.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.2, 131.8, 129.6, 128.5, 128.4, 123.1, 122.3, 90.2, 88.7, 33.0, 32.2; IR (film) ν_{max} 2970, 1737, 1706, 1610, 1489, 1442, 1373, 1217, 901, 754, 689 cm^{-1}; R_f(hexanes: ethyl acetate = 2:1)= 0.50; m. p. 74 °C. Anal. Calcd. For $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.81; H, 6.05.



2l

4-Methylene-6-(trimethylsilyl)hex-5-ynoic acid (**2l**): An oven-dried 200 mL round-bottom-flask equipped with a magnetic stir bar was charged with methyltriphenylphosphonium bromide (12.8 g, 36 mmol, 2.4 equiv). The flask was sealed with a rubber septum and connected to a Schlenk line though a needle. The flask was briefly evacuated and backfilled with argon (this sequence was repeated a total of 3 times). Anhydrous THF (100 mL) was added via syringe. At -78 °C to the stirring mixture was added *n*-butyl lithium solution (2.5 M in hexane, 22 mL, 54 mmol, 3.6 equiv) dropwise. The reaction mixture was moved to a 0 °C bath and stirred at the same temperature for 0.5 h before being cooled to -78 °C. At -78 °C, a solution of 4-oxo-6-(trimethylsilyl)hex-5-ynoic acid[5] (3.1 g, 15 mmol, 1.0 equiv) in anhydrous THF (2 M) was added slowly to the reaction mixture via syringe. The resulting mixture was stirred at -78 °C for 0.5 h, then 0 °C for 2 h, and finally warmed to room temperature and stirred overnight. The reaction mixture was quenched at 0 °C by the addition of 70 mL 1 M HCl, 50 mL saturated aqueous NH_4Cl and 50 mL brine. The aqueous layer was separated and extracted with ethyl ether. The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography to afford **2l** as a colorless oil. (1.34 g, 42% yield)

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.67 (br, 1 H), 5.41 (s, 1 H), 5.32 (s, 1 H), 2.61 (t, *J* = 7.6 Hz, 2 H), 2.48 (t, *J* = 7.6 Hz, 2 H), 0.19 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.3, 129.6, 123.1, 104.4, 95.2, 32.8, 31.9, 0.0; IR (film) ν_{max} 2960, 2145, 1709, 1608, 1411, 1250, 904, 838, 759 cm^{-1}; R_f(hexanes: ethyl acetate = 2:1)= 0.70; HRMS: $[M-H]^-$ Calcd. For $C_{10}H_{15}O_2Si$: 195.0847; Found: 195.0854.

General Procedure and Characterization for the Copper-Catalyzed Enantioselective Oxyfunctionalization of Alkenes

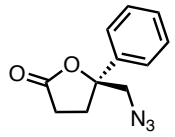
Enantioselective Oxyazidation:

General procedure A for the Cu-catalyzed enantioselective oxyazidation (Table 1):

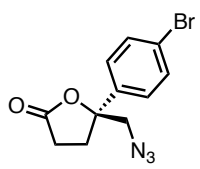
Caution: Proper safety precautions should be followed. This reaction should be carried out behind a blast shield and only on a small scale. It should be noted that while no incident occurred during this study, azides are potentially hazardous compounds and adequate safety measures should be taken.

An oven-dried 100 mL round bottom flask equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (9.3 mg, 0.025 mmol, 0.05 equiv), 2,2'-isopropylidenebis[(4*S*)-4-*tert*-butyl-2-oxazoline] (**L**) (7.4 mg, 0.025 mmol, 0.05 equiv) and unsaturated carboxylic acid **2** (0.50 mmol, 1.0 equiv). The flask was sealed with a rubber septum and connected to a Schlenk line though a needle. The flask was briefly evacuated and backfilled with argon (this sequence was repeated a total of two times). The septum was removed, (diacetoxyiodo)benzene (403 mg, 1.25 mmol, 2.5 equiv, dried under high vacuum for 2 h in advance.) was quickly added into the flask and the flask was sealed again with the septum. The flask was connected to a Schlenk line though a needle. The reaction flask was then briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). The reaction flask was cooled to -78 °C. At the same temperature, without stirring, anhydrous diethyl ether (30 mL) was added to the flask via syringe followed by trimethylsilyl azide (158 μL, 1.20 mmol, 2.4 equiv). After cooled at -78 °C for 2 min, the argon pressure was removed. A venting needle was inserted. The reaction mixture was moved to a -10 °C bath and

stirred at the same temperature for 16 h. The reaction mixture was quenched carefully with saturated aqueous sodium bicarbonate solution (20 mL). The aqueous layer was separated and extracted with diethyl ether (15 mL×3). The combined organic layers was concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (EtOAc/hexanes/toluene, using UV light as a visualizing agent and phosphomolybdic acid in ethanol or iodine on silica gel as developing agents) to afford the oxyazidation product **4**.



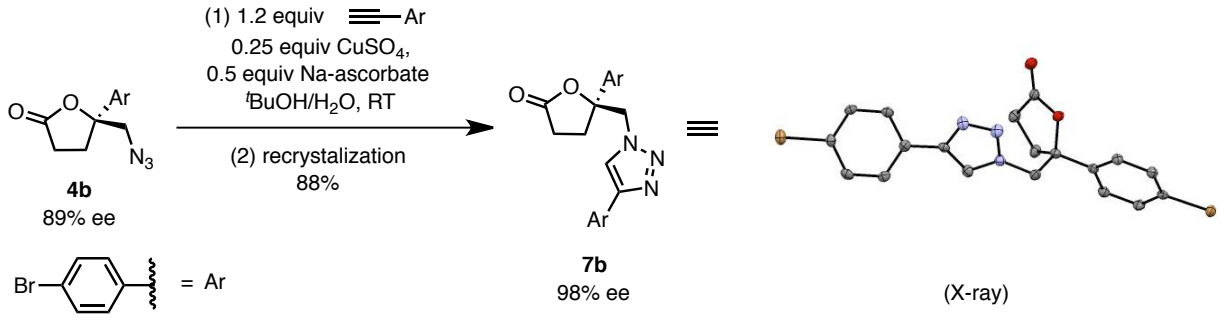
(*S*)-5-(azidomethyl)-5-phenyldihydrofuran-2(3H)-one (4a) Following general procedure A, the title compound was synthesized from 4-phenyl-4-pentenoic acid (**2a**) (88.0 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene: ethyl acetate = 1:0:0 to 0:1:0 to 0:12:1 to 0:8:1) to afford **4a** (66.9 mg, 62% yield, 89% ee) as a pale yellow sticky oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.33 (m, 5 H), 3.67 (d, *J* = 13.2 Hz, 1 H), 3.53 (d, *J* = 13.2 Hz, 1 H), 2.78-2.65 (m, 2 H), 2.55-2.40 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 140.6, 128.9, 128.6, 124.7, 87.7, 60.0, 31.4, 28.7; IR (film) ν_{max} 2096, 1772, 1739, 1448, 1365, 1196, 1062, 935 cm^{-1}; R_f(toluene: ethyl acetate = 4:1)= 0.6; Anal. Calcd. For $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10. Found: C, 61.11; H, 5.18. $[\alpha]_D^{24}$ = -28.1 (c= 0.8, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm, t_R = 20.6 min (major) and 26.3 min (minor).



(*S*)-5-(azidomethyl)-5-(4-bromophenyl)dihydrofuran-2(3H)-one (4b) Following general procedure A, the title compound was synthesized from 4-(4-bromophenyl)pent-4-enoic acid (**2b**) (127.5 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene: ethyl acetate = 1:0:0 to 10:0:1 to 6:1:1 to 4:2:1) to afford **4b** (82.6 mg, 56% yield, 89% ee) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 2 H), 7.26 (d, *J* = 8.4 Hz, 1 H), 3.65 (d, *J* = 13.2 Hz, 1 H), 3.51 (d, *J* = 13.2 Hz, 1 H), 2.80-2.64 (m, 2 H), 2.52 (m, 1 H), 2.39 (m, 1 H), ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 139.7, 132.1, 126.6, 122.9, 87.2, 59.9, 31.5, 28.7; IR (film) ν_{max} 2097, 1738, 1365, 1229, 1217, 1007cm^{-1}; R_f(hexanes: toluene: ethyl acetate = 2:2:1)= 0.4; Anal. Calcd. For $C_{11}H_{10}N_3O_2Br$: C, 44.62; H, 3.40. Found: C, 44.90; H, 3.54. $[\alpha]_D^{24}$ = + 4.8 (c= 1, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis:

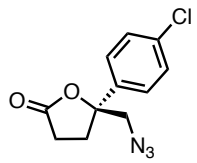
Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 230 nm, t_R = 24.6 min (major) and 31.4 min (minor).

***SI-Scheme 1**. Synthesis and ORTEP presentation of **7b**. (thermal ellipsoids shown at 50% probability. Hydrogen atoms are omitted for clarity.)*



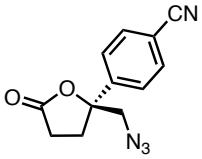
Derivatization of 4b: **(*S*)-5-(4-bromophenyl)-5-((4-(4-bromophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)dihydrofuran-2(3H)-one** (**7b**) To a mixture of **4b** (1.0 equiv, 25 mg, 0.08 mmol), 4-bromophenylacetylene (1.2 equiv, 18 mg, 0.10 mmol) in H_2O/^{t}BuOH (1 mL/1 mL) was added $CuSO_4$•$5H_2O$ (0.25 equiv, 5 mg) and sodium ascorbate (0.5 equiv, 8 mg). The resulting mixture was stirred at room temperature for 20 h before diluted with ethyl acetate (5 mL), saturated aqueous EDTA solution (0.2 mL) and water (5 mL). The aqueous layer was extracted with ethyl acetate (5 mL×3). The combined organic layers were dried over Na_2SO_4, filtered through a short silica gel plug, and concentrated *in vacuo*. The residue was triturated with hexanes, and then recrystallized in CH_2Cl_2/EtOAc to afford **7b** as a colorless crystalline solid (35.4 mg, 88% yield, 98% ee). ^{1}H NMR (400 MHz, $CDCl_3$,) δ 7.86 (s, 1 H), 7.68 (d, *J* = 8.8 Hz, 2 H), 7.57 (m, 4 H), 7.31 (d, *J* = 8.8 Hz, 2 H), 4.84 (d, *J* = 14.8 Hz, 1 H), 4.68 (d, *J* = 14.8 Hz, 1 H), 2.71 (ddd, *J* = 13.2, 9.6, 8.0 Hz, 1 H), 2.50 (ddd, *J* = 13.2, 10.0, 5.2 Hz, 1 H), 2.40 (ddd, *J* = 17.2, 9.6, 8.0 Hz, 1 H), 2.12 (ddd, *J* = 17.2, 9.6, 5.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 147.6, 138.6, 132.5, 132.2, 129.1, 127.5, 126.6, 123.4, 122.6, 121.5, 86.5, 58.3, 31.4, 28.0; IR (film) ν_{max} 1738, 1455, 1365, 1229, 1217, 1000, 922, 831, 817 cm^{-1}; R_f (hexanes : ethyl acetate = 1:1) = 0.5; Anal. Calcd. For $C_{19}H_{15}N_3O_2Br_2$: C, 47.83; H, 3.17. Found: C, 47.78; H, 3.09. $[\alpha]_D^{24}$ = +51.0 (c= 0.5, CH_2Cl_2). m. p. 235-236 °C. The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel IA 4.6 mm x 250 mm, hexanes:*i*-PrOH = 80:20, 1.0 mL/min, 254 nm, t_R =

37.0 min (major) and 21.6 min (minor). The absolute stereochemistry of **7b** was assigned by X-ray crystallography, based on which the absolute stereochemistry of **4b** was assigned. The absolute stereochemistry of **4a**, **4c**-**n**, **8a**-**c**, **9a**-**d**, **13**, **14** and **15** were assigned based on analogy to **4b**.



(*S*)-5-(azidomethyl)-5-(4-chlorophenyl)dihydrofuran-2(3H)-one (4c)

Following general procedure A, the title compound was synthesized from 4-(4-chlorophenyl)pent-4-enoic acid (**2c**) (105 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene: ethyl acetate = 1:0:0 to 0:1:0 to 0:12:1 to 0:7:1) to afford **4c** (65.7 mg, 52% yield, 89% ee) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 9.0 Hz, 2 H), 7.32 (d, *J* = 9.0 Hz, 2 H), 3.65 (d, *J* =12.8 Hz, 1 H), 3.52 (d, *J* =12.8 Hz, 1 H), 2.80-2.65 (m, 2 H), 2.52 (m, 1 H), 2.39 (m, 1 H), ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 139.2, 134.7, 129.2, 126.2, 87.2, 59.9, 31.5, 28.7; IR (film) ν_{max} 2097, 1774, 1492, 1277, 1175, 1068, 1011, 935 cm^{-1}; R_f(toluene: ethyl acetate = 4:1)= 0.3; Anal. Calcd. For $C_{11}H_{10}N_3O_2Cl$: C, 52.50; H, 4.01. Found: C, 52.35; H, 4.11. $[\alpha]_D^{24}$ = +1.3 (c= 0.9, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 230 nm, t_R = 20.0 min (major) and 24.6 min (minor).

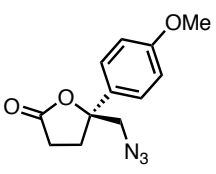


(*S*)-5-(azidomethyl)-5-(4-cyanophenyl)dihydrofuran-2(3H)-one (4d)

Following a slightly modified general procedure A in which the combined organic layers after ethyl ether extraction was briefly washed with Na_2CO_3 aqueous solution (0.02 M, 10 mL×2) before concentrating *in vacuo*, the title compound was synthesized from 4-(4-cyanophenyl)pent-4-enoic acid (**2d**) (100 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene: ethyl acetate = 1:0:0 to 0:1:0 to 0:10:1 to 0:6:1) to afford **4d** (56.5 mg, 47% yield, 90% ee) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.4 Hz, 2 H), 7.52 (d, *J* = 8.4 Hz, 2 H), 3.66 (d, *J* =13.2 Hz, 1 H), 3.57 (d, *J* = 13.2 Hz, 1 H), 2.84-2.69 (m, 2 H), 2.53 (m, 1 H), 2.40 (m, 1 H), ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 145.8, 132.8, 125.8, 118.2, 112.8, 86.8, 59.7, 31.5, 28.5; IR (film) ν_{max} 2229, 2102, 1778, 1176, 1070, 937, 838, 729 cm^{-1}; R_f(toluene: ethyl acetate = 3:1)= 0.4; Anal. Calcd. For $C_{12}H_{10}N_4O_2$: C, 59.50; H, 4.16. Found: C, 59.57; H, 4.42. $[\alpha]_D^{24}$ = + 10.8 (c= 0.5, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H

4.6 mm x 250 mm, hexanes:*i*-PrOH = 85:15, 1.0 mL/min, 230 nm, t_R = 30.6 min (major) and 34.3 min (minor).

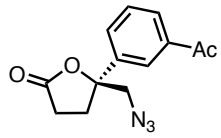
(*S*)-5-(azidomethyl)-5-(4-trifluoromethylphenyl)dihydro furan-2(3H)-one (4e) Following a slightly modified general procedure A in which (1) tetrakis(acetonitrile)copper(I) hexafluorophosphate (14.9 mg, 0.04 mmol, 0.08 equiv) and 2,2'-isopropylidenebis[(4*S*)-4-*tert*-butyl-2-oxazoline] (**L**) (11.8 mg, 0.04 mmol, 0.08 equiv) were used; (2) the combined organic layers after ethyl ether extraction was briefly washed with Na_2CO_3 aqueous solution (0.02 M, 10 mL×2) before concentrating *in vacuo*, the title compound was synthesized from 4-(4-trifluoromethylphenyl)pent-4-enoic acid (**2e**) (122 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene: ethyl acetate = 1:0:0 to 0:1:0 to 0:12:1 to 0:8:1) to afford **4e** (65.5 mg, 46% yield, 90% ee) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 2 H), 7.53 (d, *J* = 8.4 Hz, 1 H), 3.68 (d, *J* = 13.2 Hz, 1 H), 3.57 (d, *J* = 13.2 Hz, 1 H), 2.84-2.70 (m, 2 H), 2.54 (m, 1 H), 2.43 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 144.7, 131.1 (q, J_{CF} = 32 Hz), 126.1 (q, J_{CF} = 4 Hz), 125.4, 123.9 (q, J_{CF} = 270 Hz), 87.1, 59.9, 31.6, 28.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.8 (s); IR (film) ν_{max} 2102, 1738, 1365, 1229, 1217, 1115, 1077cm^{-1}; R_f (toluene: ethyl acetate = 6:1)= 0.2; HRMS: $[M+NH_4]^+$ Calcd. For $C_{12}H_{14}N_4F_3O_2$: 303.1063; Found: 303.1050. $[\alpha]_D^{24}$ = -11.6 (c = 0.4, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm, t_R = 19.8 min (major) and 25.6 min (minor).



(*S*)-5-(azidomethyl)-5-(4-methoxyphenyl)dihydrofuran-2(3H)-one (4f) Following general procedure A, the title compound was synthesized from 4-(4-methoxyphenyl)pent-4-enoic acid (**2f**) (103 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene: ethyl acetate = 1:0:0 to 0:1:0 to 0:12:1 to 0:7:1) to afford **4f** (79.6 mg, 65% yield, 75% ee) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* =8.8 Hz, 1 H), 6.91 (d, *J* =8.8 Hz, 1 H), 3.80 (s, 3 H), 3.64 (d, *J* = 13.2 Hz, 1 H), 3.48 (d, *J* = 13.2 Hz, 1 H), 2.76-2.61 (m, 2 H), 2.51 (m, 1 H), 2.40 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 159.7, 132.4, 126.1, 114.2, 87.6, 60.1, 55.4, 31.3, 28.8; IR (film) ν_{max} 2098, 1772, 1611, 1513, 1247, 1175, 1068, 934 cm^{-1}; R_f(toluene: ethyl acetate = 4:1)= 0.5; Anal. Calcd. For $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30. Found: C, 58.44; H, 5.49.

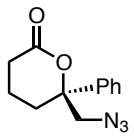
$[\alpha]_D^{24}$ = +1.6 (c= 0.6, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 230 nm, t_R = 23.2 min (major) and 27.6 min (minor).

(*S*)-5-(azidomethyl)-5-(thiophen-3-yl)dihydrofuran-2(3H)-one (4g) Following a slightly modified general procedure A in which additional 2,6-di-*tert*-butylpyridine (120 mL, 0.55 mmol, 1.1 equiv) was added via syringe after the addition of trimethylsilyl azide, the title compound was synthesized from 4-(3-thiophenyl)pent-4-enoic acid (**2g**) (91 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene: ethyl acetate = 10:0:1 to 6:1:1) to afford **4g** (76.1 mg, 68% yield, 82% ee) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, *J* =5.2 Hz, 3.0 Hz. 1 H), 7.31 (dd, *J* =3.0 Hz, 1.2 Hz. 1 H), 7.02 (dd, *J* =5.2 Hz, 1.2 Hz. 1 H), 3.71 (d, *J* = 13.0 Hz, 1 H), 3.53 (d, *J* = 13.0 Hz, 1 H), 2.77-2.52 (m, 3 H), 2.40 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 141.7, 127.6, 124.7, 121.9, 86.4, 59.3, 31.3, 28.8; IR (film) ν_{max} 2102, 1775, 1181, 1070, 1040, 942, 847 cm^{-1}; R_f(toluene: ethyl acetate = 4:1)= 0.6; Anal. Calcd. For $C_9H_9N_3O_2S$: C, 48.42; H, 4.06. Found: C, 48.34; H, 3.97. $[\alpha]_D^{24}$ = -9.0 (c= 0.5, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 230 nm, t_R = 29.0 min (major) and 36.9 min (minor).

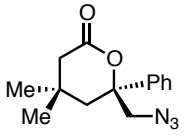


(*S*)-5-(azidomethyl)-5-(3-acetylphenyl)dihydrofuran-2(3H)-one (4h) Following a slightly modified general procedure A in which tetrakis(acetonitrile)copper(I) hexafluorophosphate (14.9 mg, 0.04 mmol, 0.08 equiv) and 2,2'-isopropylidenebis[(4*S*)-4-*tert*-butyl-2-oxazoline] (**L**) (11.8 mg, 0.04 mmol, 0.08 equiv) were used, the title compound was synthesized from 4-(3-acetylphenyl)pent-4-enoic acid (**2h**) (109 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene: ethyl acetate = 1:0:0 to 0:1:0 to 0:10:1 to 0:5:1) to afford **4h** (67.7 mg, 52% yield, 90% ee) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (m ,2 H), 7.62 (m, 1 H), 7.51 (m, 1 H), 3.67 (d, *J* = 13.2 Hz, 1 H), 3.57 (d, *J* = 13.2 Hz, 1 H), 2.81-2.69 (m, 2 H), 2.61 (s, 3 H), 2.56-2.42 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 175.4, 141.5, 137.7, 129.5, 129.4, 128.7, 124.4, 87.3, 60.0, 31.5, 28.7, 26.8; IR (film) ν_{max} 2101, 1773, 1682, 1365, 1217, 1069, 938 cm^{-1}; R_f(toluene: ethyl acetate = 4:1)= 0.3; Anal. Calcd. For $C_{13}H_{13}N_3O_3$: C, 60.22; H, 5.05. Found: C, 60.38; H, 5.12. $[\alpha]_D^{24}$ = -12.8 (c= 0.5, $CHCl_3$). m. p. 80-81 °C. The

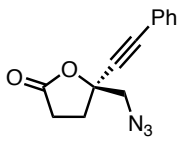
enantiomeric excess was determined by chiral HPLC analysis: Chiralcel IA 4.6 mm x 250 mm, hexanes:*i*-PrOH = 90:10, 1.0 mL/min, 230 nm, t_R = 20.5 min (major) and 18.7 min (minor).



(*S*)-6-(azidomethyl)-6-phenyltetrahydro-2H-pyran-2-one (4i) Following general procedure A, the title compound was synthesized from 5-phenylhex-5-enoic acid (**2i**) (95 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene: ethyl acetate = 1:0:0 to 0:1:0 to 0:12:1 to 0:8:1) to afford **4i** (69.8 mg, 60% yield, 89% ee) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.32 (m, 5 H), 3.61 (d, *J* = 12.8 Hz, 1 H), 3.42 (d, *J* = 12.8 Hz, 1 H), 2.50 (ddd, *J* = 18 Hz, 9.6 Hz, 7.2 Hz, 1 H), 2.45 (ddd, *J* = 18 Hz, 7.2 Hz, 4 Hz, 1 H), 2.31-2.22 (m, 2 H), 1.83 (m, 1 H), 1.60 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 140.4, 129.2, 128.5, 125.3, 86.9, 60.8, 29.3, 29.1, 16.2; IR (film) ν_{max} 2096, 1736, 1447, 1232, 1187, 1048, 934 cm^{-1}; R_f(toluene: ethyl acetate = 4:1) = 0.6; Anal. Calcd. For $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67. Found: C, 62.51; H, 5.78. $[\alpha]_D^{24}$ = +24.9 (c= 0.5, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm, t_R = 19.5 min (major) and 26.5 min (minor).

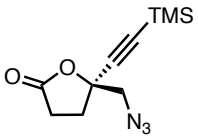


(*S*)-6-(azidomethyl)-4,4-dimethyl-6-phenyltetrahydro-2H-pyran-2-one (4j) Following general procedure A, the title compound was synthesized from 3,3-dimethyl-5-phenylhex-5-enoic acid (**2j**) (109 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene : ethyl acetate = 1:0:0 to 0:1:0 to 0:20:1 to 0:15:1 to 0:10:1) to afford **4j** (83.0 mg, 64% yield, 92% ee) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.30 (m, 5 H), 3.50 (d, *J* = 12.8 Hz, 1 H), 3.29 (d, *J* = 12.8 Hz, 1 H), 2.33-2.17 (m, 4 H), 1.09 (s, 3 H), 0.78 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 141.6, 129.0, 128.3, 125.1, 85.8, 62.0, 43.8, 41.7, 31.9, 30.7, 29.1; IR (film) ν_{max} 2970, 2097, 1739, 1447, 1365, 1217, 1060, 759, 702 cm^{-1}; R_f(toluene: ethyl acetate = 5:1) = 0.7; HRMS: $[M+Na]^+$ Calcd. For $C_{14}H_{17}N_3O_2Na$: 282.1213; Found: 282.1205. $[\alpha]_D^{24}$ = +35.9 (c= 0.8, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm, t_R = 13.0 min (major) and 15.0 min (minor).

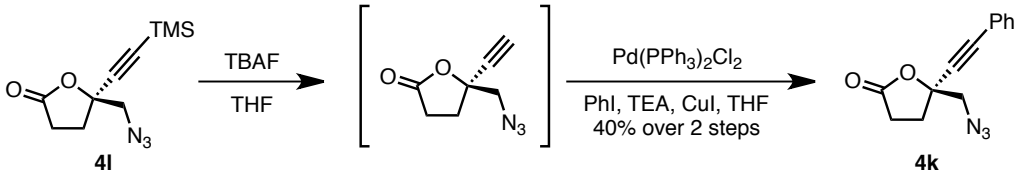


(*S*)-5-(azidomethyl)-5-(phenylethynyl)dihydrofuran-2(3H)-one (4k) Following a slightly modified general procedure A in which tetrakis(acetonitrile)copper(I)

hexafluorophosphate (14.9 mg, 0.04 mmol, 0.08 equiv) and 2,2'-isopropylidenebis[(4*S*)-4-*tert*-butyl-2-oxazoline] (**L**) (11.8 mg, 0.04 mmol, 0.08 equiv) were used, the title compound was synthesized from 4-methylene-6-phenylhex-5-ynoic acid (**2k**) (100 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene : ethyl acetate = 1:0:0 to 0:1:0 to 0:15:1 to 0:8:1) to afford **4k** (61.4 mg, 51% yield, 72% ee) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.44 (m, 2 H), 7.38-7.31 (m, 3 H), 3.77 (d, *J* = 13.2 Hz, 1 H), 3.61 (d, *J* = 13.2 Hz, 1 H), 2.83 (ddd, *J* = 17.6 Hz, 9.6 Hz, 9.2 Hz, 1 H), 2.71 (ddd, *J* = 17.6 Hz, 7.6 Hz, 6.4 Hz, 1 H), 2.53-2.49 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 132.0, 129.5, 128.6, 121.1, 88.1, 85.3, 80.0, 57.9, 32.2, 28.7; IR (film) ν_{max} 2990, 2099, 1738, 1365, 1228, 1217, 918, 756 cm^{-1}; R_f(hexanes: ethyl acetate = 2:1) = 0.5; HRMS: $[M+NH_4]^+$ Calcd. For $C_{13}H_{15}N_4O_2$: 259.1190; Found: 259.1183. $[\alpha]_D^{24}$ = +35.7 (c= 1, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 230 nm, t_R = 17.0 min (major) and 19.7 min (minor).



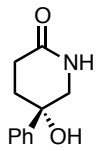
(*S*)-5-(azidomethyl)-5-((trimethylsilyl)ethynyl)dihydrofuran-2(3H)-one (4l) Following a slightly modified general procedure A in which tetrakis(acetonitrile)copper(I) hexafluorophosphate (14.9 mg, 0.04 mmol, 0.08 equiv) and 2,2'-isopropylidenebis[(4*S*)-4-*tert*-butyl-2-oxazoline] (**L**) (11.8 mg, 0.04 mmol, 0.08 equiv) were used, the title compound was synthesized from 4-methylene-6-(trimethylsilyl)hex-5-ynoic acid (**2l**) (96 mg, 0.50 mmol). The product was purified by silica gel flash column chromatography (hexanes: toluene : ethyl acetate = 1:0:0 to 0:1:0 to 0:20:1 to 0:15:1 to 0:10:1) to afford **4l** (52.9 mg, 45% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (d, *J* = 13.2 Hz, 1 H), 3.49 (d, *J* = 13.2 Hz, 1 H), 2.75 (ddd, *J* = 17.6 Hz, 9.6 Hz, 9.2 Hz, 1 H), 2.63 (ddd, *J* = 17.6 Hz, 7.2 Hz, 6.8 Hz, 1 H), 2.43-2.39 (m, 2 H), 0.18 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 101.2, 94.0, 79.4, 57.7, 32.1, 28.6, -0.4; IR (film) ν_{max} 2103, 1784, 1739, 1365, 1249, 1174, 1056, 841 cm^{-1}; R_f(toluene: ethyl acetate = 10:1) = 0.6; HRMS: $[M+NH_4]^+$ Calcd. For $C_{10}H_{19}N_4O_2Si$: 255.1272; Found: 255.1275. $[\alpha]_D^{24}$ = +28.6 (c= 1, $CHCl_3$).



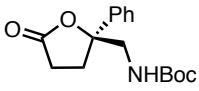
Enantiomeric excess determination of **4l** by converting to **4k**: To a solution of **4l** (15 mg, 0.06 mmol) in anhydrous THF (0.5 mL) was added tetrabutylammonium fluoride (1 M in THF, 0.12

mL) slowly at 0 °C. The yellow mixture was stirred at the same temperature for 0.5 h before diluted with saturated aqueous NH_4Cl (1 mL). The aqueous layer was separated and extracted with ethyl ether (1 mL × 2). The combined organic layers was dried over Na_2SO_4, passed through a silica gel plug, and concentrated *in vacuo* to afford the crude product. Under an Ar atmosphere, a mixture of this crude product, $PdCl_2(PPh_3)_2$ (3.5 mg), iodobenzene (24 mg), and triethylamine (20 mg) in anhydrous THF (1 mL) was stirred at room temperature (25 °C) for 5 min before CuI (1.9 mg) was added. The reaction vessel was briefly evacuated and backfilled with argon. The reaction mixture was stirred at 70 °C for 2 h before diluted with ethyl ether (2 mL), saturated aqueous NH_4Cl (1 mL) and 1 M aqueous HCl (1 mL). The aqueous layer was separated and extracted with ethyl ether (1 mL × 2). The combined organic layers was concentrated *in vacuo*. The residue was purified by preparative thin-layer-chromatography to afford **4k** (6 mg, *ca*. 40% yield over 2 steps, 82% ee). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 230 nm, t_R = 17.0 min (major) and 19.7 min (minor).

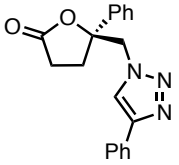
*Derivatization of Oxyazidation Product **4a** (Scheme 3)*



(*S*)-5-hydroxy-5-phenylpiperidin-2-one (5) A mixture of **4a** (32 mg, 0.15 mmol, 1.0 equiv, 89% ee) and 5% Pd/C (6 mg) in methanol (1 mL) was stirred at room temperature (25 °C) under H_2 atmosphere for 16 h. 4-Dimethylaminopyridine (2 mg, 0.015 mmol, 0.1 equiv) was added to the reaction mixture and the resulting mixture was stirred at room temperature for 8 h before concentrating *in vacuo*. The residue was purified by silica gel flash column chromatography (ethyl acetate: methanol = 1:0 to 5:1) to afford **5** (22 mg, 78% yield, 89% ee) as a colorless solid. ^{1}H NMR (400 MHz, CD_3OD) δ 7.55 (m, 2 H), 7.37 (m, 2 H), 7.28 (m, 1 H), 3.60 (d, *J* =12.8 Hz, 1 H), 3.28 (dd, *J* =12.8 Hz, 2.8 Hz, 1 H), 2.67 (m, 1 H), 2.48-2.33 (m, 2 H), 2.01 (m, 1 H); ^{13}C NMR (100 MHz, CD_3OD) δ 174.6, 146.6, 129.4, 128.5, 126.1, 70.8, 54.2, 33.5, 28.9; IR (film) ν_{max} 3225, 2917, 2384, 1633, 1494, 1233, 978, 768 cm^{-1}; R_f(methanol: ethyl acetate = 5:1)= 0.40; HRMS: $[M+H]^+$ Calcd. For $C_{11}H_{14}NO_2$: 192.1019; Found: 192.1026. $[\alpha]_D^{24}$ = -2.2 (c= 0.9, MeOH). m. p. 198-199 °C. The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel IA 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm, t_R = 67.5 min (major) and 80.1 min (minor).



(*S*)-*tert*-butyl((5-oxo-2-phenyltetrahydrofuran-2-yl)methyl)carbamate (6) A mixture of **4a** (56 mg, 0.26 mmol, 1.0 equiv, 89% ee), di-*tert*-butyl dicarbonate (84 mg, 0.39 mmol, 1.5 equiv) and 5% Pd/C (5 mg) in THF (1.5 mL) was stirred at room temperature (25 °C) under H_2 atmosphere for 15 h. The reaction mixture was then concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (hexanes: ethyl acetate = 10:1 to 1:1) to afford **6** (66 mg, 88% yield, 89% ee) as a colorless sticky oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.29 (m, 5 H), 4.91 (br, 1 H), 3.71 (dd, *J* =14.8 Hz, 7.6 Hz, 1 H), 3.42 (dd, *J* =14.8 Hz, 5.2 Hz, 1 H), 2.67-2.33 (m, 4 H), 1.39 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 156.2, 141.1, 128.8, 128.2, 124.8, 89.1, 80.0, 49.3, 31.2, 28.8, 28.3; IR (film) ν_{max} 1774, 1709, 1508, 1365, 1245, 1163, 1115, 1092, 1069, 912, 730, 700 cm^{-1}; R_f(hexanes: ethyl acetate = 2:1)= 0.2; Anal. Calcd. For $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27. Found: C, 65.84; H, 7.31. $[\alpha]_D^{24}$ = -36.1 (c= 1, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OJ-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 90:10, 1.0 mL/min, 210 nm, t_R = 8.2 min (major) and 7.3 min (minor).

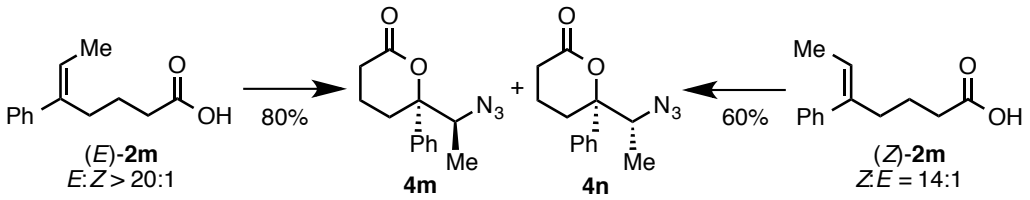


(*S*)-5-phenyl-5-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)dihydrofuran-2(3H)-one (**7**) To a mixture of **4a** (1.0 equiv, 22 mg, 0.1 mmol), phenyl acetylene (1.1 equiv, 11 mg, 0.11 mmol) in H_2O/^{t}BuOH (1 mL/1 mL) was added $CuSO_4$•$5H_2O$ (0.4 equiv, 10 mg) and sodium ascorbate (0.8 equiv, 16 mg). The resulting mixture was stirred at room temperature for 17 h before diluted with ethyl acetate (5 mL), saturated aqueous EDTA solution (0.2 mL) and water (5 mL). The aqueous layer was extracted with ethyl acetate (5 mL×3). The combined organic layers were dried over Na_2SO_4, filtered through a short silica gel plug, and concentrated *in vacuo*. The residue was triturated with hexanes to afford **7** as a white solid (31 mg, 96% yield, 89% ee). ^{1}H NMR (400 MHz, $CDCl_3$,) δ 7.85 (s, 1 H), 7.81 (d, *J* = 7.2 Hz, 1 H), 7.45-7.32 (m, 8 H), 4.88 (d, *J* = 14.8 Hz, 1 H), 4.69 (d, *J* = 14.8 Hz, 1 H), 2.70 (ddd, *J* = 13.2, 9.6, 8.0 Hz, 1 H), 2.52 (ddd, *J* = 13.2, 10.0, 5.6 Hz, 1 H), 2.39 (ddd, *J* = 17.6, 9.6, 8.0 Hz, 1 H), 2.09 (ddd, *J* = 17.6, 10.0, 5.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 148.4, 139.7, 130.2, 129.2, 129.1, 129.0, 128.5, 126.0, 124.8, 121.4, 87.0, 58.5, 31.3, 28.1; IR (film) ν_{max} 1777, 1738, 1449, 1365, 1228, 1217, 1147, 931, 764, 697 cm^{-1}; R_f(hexanes: ethyl acetate = 2:1)= 0.1; HRMS: $[M+H]^+$ Calcd. For $C_{19}H_{18}N_3O_2$: 320.1394; Found: 320.1373. $[\alpha]_D^{24}$ = -0.6 (c= 0.5, $CHCl_3$). m. p. 151-152 °C. The enantiomeric excess was

determined by chiral HPLC analysis: Chiralcel IA 4.6 mm x 250 mm, hexanes:*i*-PrOH = 85:15, 1.0 mL/min, 210 nm, t_R = 27.1 min (major) and 20.5 min (minor).

Trisubstituted Alkene Substrates as Mechanistic Probes (Scheme 4)

Caution: Proper safety precautions should be followed. This reaction should be carried out behind a blast shield and only on a small scale. It should be noted that while no incident occurred during this study, azides are potentially hazardous compounds and adequate safety measures should be taken.



(*E*)-**2m**
E:*Z* > 20:1

4m

4n

(*Z*)-**2m**
Z:*E* = 14:1

substrate	d.r.[b]	**4m**	**4n**	ratio of stereoisomers
		ee [%][b]	ee [%][b]	**4m** : *ent*-**4m** : **4n** : *ent*-**4n**
(*E*)-**2m**	10 : 1	12	93	51.1 : 40.0 : 8.6 : 0.3
(*Z*)-**2m**	10 : 1	11	93	50.6 : 40.3 : 8.8 : 0.3

Reaction with (*Z*)-2m: An oven-dried 20 × 125 mm re-sealable test tube (Fisher Scientific, Cat. #1495937) equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (3.8 mg, 0.01 mmol, 0.1 equiv), 2,2'-isopropylidenebis[(4*S*)-4-*tert*-butyl-2-oxazoline] (**L**) (3.0 mg, 0.01 mmol, 0.1 equiv) and (*Z*)-**2m** (0.10 mmol, 1.0 equiv). The reaction tube was sealed with a septum screw-cap (10/90, Teflon/SIL, National Scientific) and connected to a Schlenk line. The reaction tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of two times). The septum screw-cap was removed, (diacetoxyiodo)benzene (80 mg, 0.25 mmol, 2.5 equiv, dried under high vacuum for 2 h in advance.) was added into the tube quickly and the tube was sealed again with the septum screw-cap. The reaction tube was connected to a Schlenk line. The reaction tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). The reaction tube was cooled to -78 °C. At the same

temperature, without stirring, anhydrous diethyl ether (6 mL) was added to the tube via syringe followed by trimethylsilyl azide (32 μL, 0.24 mmol, 2.4 equiv). After cooled at -78 °C for 2 min, argon pressure was removed. A venting needle was inserted. The reaction mixture was moved to a -10 °C bath and stirred at the same temperature for 16 h. The reaction was quenched with saturated aqueous sodium bicarbonate solution (6 mL). The aqueous layer was separated and extracted with diethyl ether (5 mL × 3). The combined organic layers was concentrated *in vacuo*. Phenanthrene (9.0 mg) was added and the crude product was analyzed by ^{1}H NMR spectroscopy. The total yield of **4m** and **4n** was 60% as determined by ^{1}H NMR spectroscopy.

A small portion of the crude product was then subjected to a rapid TLC purification to remove the non-polar components (internal standard and iodobenzene) as well as the polar carboxylic acid derivatives. The residue (R_f (toluene: ethyl acetate = 5:1) between 0.4 and 0.8) was analyzed by chiral HPLC. Chiralcel OD-H/OD-H 4.6 mm x 250 mm, pentane: EtOH = 97:3, 0.8 mL/min, 210 nm. **4m** (11% ee): t_R = 35.5 min (major) and 37.6 min (minor). **4n** (93% ee): t_R = 33.5 min (major) and 44.8 min (major). d.r.(**4m**: **4n**) = 10:1. Stereoisomer ratio calculated: (**4m** + *ent*-**4m**):(**4n** + *ent*-**4n**) = 51:49.

The rest of the crude material was purified by preparative thin-layer chromatography to afford an inseparable mixture of **4m** and **4n**. IR (film) ν_{max} 2094, 1739, 1447, 1365, 1230, 1217, 1033, 760, 702 cm^{-1}; HRMS: $[M+NH_4]^+$ Calcd. For $C_{13}H_{19}N_4O_2$: 263.1503; Found: 263.1507. $[\alpha]_D^{24}$ = +1.2 (c= 0.8, $CHCl_3$).

Major diastereomer: **(*S*)-6-((*S*)-1-azidoethyl)-6-phenyltetrahydro-2H-pyran-2-one** (**4m**) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.31 (m, 5 H), 3.78 (q, *J* = 6.8 Hz, 1 H), 2.56 (dtd, *J* =14.4 Hz, 4.4 Hz, 0.8 Hz, 1 H), 2.46 (ddd, *J* = 18.4 Hz, 9.2 Hz, 7.6 Hz, 1 H), 2.37 (dddd, *J* =18.4 Hz, 7.2 Hz, 3.6 Hz, 0.8 Hz, 1 H), 2.06 (ddd, *J* = 14.4 Hz, 12.4 Hz, 4.4 Hz, 1 H), 1.85 (m, 1 H), 1.62 (m, 1 H), 1.11 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 138.8, 128.8, 128.5, 126.5, 88.5, 65.0, 28.3, 28.0, 16.2, 14.0.

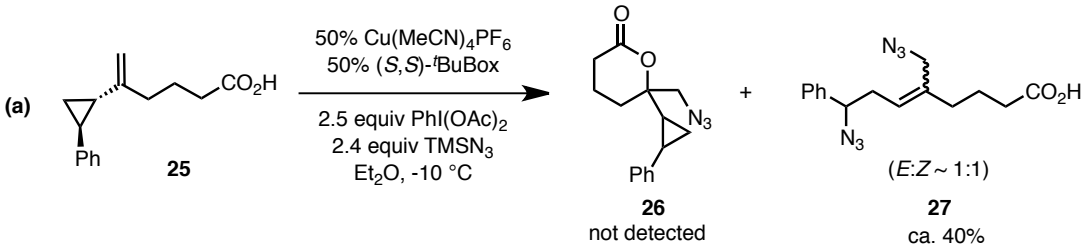
Minor diastereomer: **(*S*)-6-((*R*)-1-azidoethyl)-6-phenyltetrahydro-2H-pyran-2-one** (**4n**) ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.57 (q, *J* = 6.8 Hz, 1 H), 2.22 (td, *J* =13.6 Hz, 3.6 Hz, 1 H), 1.17 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 140.6, 129.1, 128.2, 125.5, 88.8, 64.1, 29.8, 29.6, 16.2, 13.0.

The relative stereochemistry of **4m** and **4n** were assigned based on comparison with known compounds.[6]

Reaction with (*E*)-2m: Following the same procedure for the reaction with (*E*)-**2m** described above, an over-dried 20 × 125 mm re-sealable test tube (Fisher Scientific, Cat. #1495937) equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (3.8 mg, 0.01 mmol, 0.1 equiv), 2,2'-isopropylidenebis[(4S)-4-tert-butyl-2-oxazoline] (**L**) (3.0 mg, 0.01 mmol, 0.1 equiv) and (*E*)-**2m** (0.10 mmol, 1.0 equiv). The reaction tube was sealed with a septum screw-cap (10/90, Teflon/SIL, National Scientific) and connected to a Schlenk line. The reaction tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of two times). The septum screw-cap was removed, (diacetoxyiodo)benzene (80 mg, 0.25 mmol, 2.5 equiv, dried under high vacuum for 2 h in advance.) was added into the tube quickly and the tube was sealed again with the septum screw-cap. The reaction tube was connected to a Schlenk line. The reaction tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). The reaction tube was cooled to -78 °C. At the same temperature, without stirring, anhydrous diethyl ether (6 mL) was added to the tube via syringe followed by trimethylsilyl azide (32 µL, 0.24 mmol, 2.4 equiv). After cooled at -78 °C for 2 min, argon pressure was removed. A venting needle was inserted. The reaction mixture was moved to a -10 °C bath and stirred at the same temperature for 16 h. The reaction was quenched with saturated aqueous sodium bicarbonate solution (6 mL). The aqueous layer was separated and extracted with diethyl ether (5 mL × 3). The combined organic layers was concentrated *in vacuo*. Phenanthrene (9.0 mg) was added and the crude product was analyzed by ^{1}H NMR spectroscopy. The total yield of **4m** and **4n** was 80% as determined by ^{1}H NMR spectroscopy.

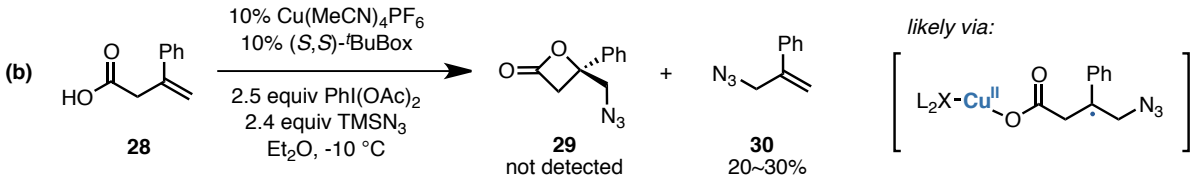
A small portion of the crude product was then subjected to a rapid TLC purification to remove the non-polar components (internal standard and iodobenzene) as well as the polar carboxylic acid derivatives. The residue (R_f (toluene: ethyl acetate = 5:1) between 0.4 and 0.8) was analyzed by chiral HPLC. **4m**:12% ee; **4n**: 93% ee; d.r.(**4m**: **4n**) = 10:1. Stereoisomer ratio calculated: (**4m** + *ent*-**4m**):(**4n** + *ent*-**4n**) = 51:49.

Additional Evidence Consistent with the Proposed Mechanism (footnote 13)

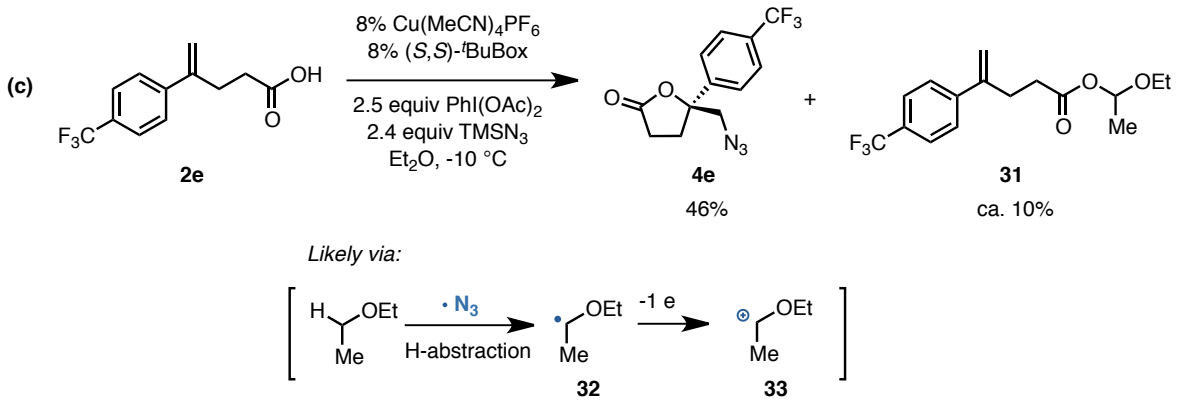


(a) Radical clock substrate **25** was treated with $PhI(OAc)_2$ and $TMSN_3$ in the presence of 0.5 equiv of the copper catalyst and the ligand using a protocol similar to the general procedure A described before. The oxyazidation product **26** was not observed. Cyclopropane ring-opening product **27** (1:1 mixture of alkene geometric isomers, chromatographically inseparable from other carboxylic acid derivatives in the crude reaction mixture) was detected by ^1H NMR analysis of the crude reaction mixture.

8-azido-5-(azidomethyl)-8-phenyloct-5-enoic acid (27) ^1H NMR (400 MHz, $CDCl_3$): δ 5.48 and 5.46 (t, *J* = 7.2 Hz, 1 H), 4.50 and 4.48 (t, *J* = 6.8 Hz, 1 H), 3.73 and 3.69 (s, 2 H), 2.64-2.50 (m, 2 H), 2.32 (m, 2 H), 2.17-2.09 (m, 2 H), 1.79-1.62 (m, 2 H); HRMS (DART, Negative): $[M-H]^-$ Calcd. for $C_{15}H_{17}N_6O_2$: 313.1418; Found: 313.1420.



(b) 3-Phenylbut-3-enoic acid (**28**) was treated with $PhI(OAc)_2$ and $TMSN_3$ in the presence of 0.1 equiv of the copper catalyst and the ligand using a protocol similar to the general procedure described before. The oxyazidation product **29** was not observed, while (3-azidoprop-1-en-2-yl)benzene (**30**)[7] was detected by ^1H NMR analysis of the crude reaction mixture. It is likely that **30** was formed via the copper-mediated decarboxylative elimination of the *β*-radical-carboxylate intermediate[8] derived from the azidyl radical addition.



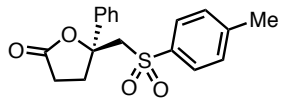
(c) In the oxyazidation reaction of an electron-deficient styrene derivative **2e**, side product **31** was identified by ^{1}H NMR analysis of the crude reaction mixture. (characteristic ^{1}H NMR signals (400 MHz, $CDCl_3$): δ 5.97 (q, *J* = 5.2 Hz, 1 H); chromatographically inseparable from other acetal derivatives in the crude reaction mixture) It is likely that **31** was formed via the nucleophilic trapping of a cationic intermediate **33** derived from the hydrogen-abstraction of a solvent molecule by an azidyl radical followed by one-electron oxidation.[9]

Enantioselective Oxysulfonylation:

General procedure B for optimization (Table 2): An oven-dried Fisher Scientific 13×100 mm re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (3.7 mg, 0.010 mmol, 0.10 equiv), 2,2'-isopropylidenebis[(4*S*)-4-tert-butyl-2-oxazoline] (**L**) (2.9 mg, 0.010 mmol, 0.10 equiv), *p*-tosyl chloride **10a** (0.11 mmol, 1.1 equiv), base and **2a** (0.10 mmol, 1.0 equiv). The reaction tube was sealed with a septum screw-cap (Thermo Scientific ASM PHN CAP w/PTFE/SIL, cat. #03378316). The reaction tube was connected to a Schlenk line though a needle. The reaction tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). Anhydrous EtOAc (2 mL) was added to the tube via syringe and the argon pressure was removed. The reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with saturated aqueous sodium bicarbonate solution (4 mL) and ethyl acetate (2 mL). The aqueous layer was separated and extracted with ethyl acetate (4 mL×3). The combined organic layers was concentrated *in vacuo*. The residue was analyzed by ^{1}H NMR spectroscopy using phenanthrene as an internal standard. The residue was purified by

thin-layer chromatography to afford the oxysulfonylation product **8a**, which was analyzed by chiral HPLC.

General procedure C for substrate scope (Scheme 4): An oven-dried Fisher Scientific 20×150 mm re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (18.7 mg, 0.05 mmol, 0.10 equiv), 2,2'-isopropylidenebis[(4*S*)-4-tert-butyl-2-oxazoline] (**L**) (14.7 mg, 0.05 mmol, 0.10 equiv), arylsulfonyl chloride **10** (0.55 mmol, 1.1 equiv), silver carbonate (82.8 mg, 0.30 mmol, 0.60 equiv) and **2** (0.50 mmol, 1.0 equiv). The reaction tube was sealed with a septum screw-cap (10/90, Teflon/SIL, National Scientific) and connected to a Schlenk line. The reaction tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). Anhydrous EtOAc (8 mL) was added to the tube via syringe and the argon pressure was removed. The reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with saturated aqueous sodium bicarbonate solution (8 mL) and ethyl acetate (4 mL). The aqueous layer was separated and extracted with ethyl acetate (8 mL×3). The combined organic layers was concentrated *in vacuo*. The residue was then purified by silica gel flash column chromatography (Et_2O/Hexanes or EtOAc/Hexanes) to afford the oxysulfonylation product **8**.



(*S*)-5-phenyl-5-(tosylmethyl)dihydrofuran-2(3H)-one (8a) Following general procedure C, the title compound was synthesized from 4-phenylpent-4-enoic acid (**2a**) (0.50 mmol, 88 mg) and tosyl chloride (**10a**) (0.55 mmol, 105 mg). The product was purified by silica gel flash column chromatography (Et_2O/hexanes = 1:1 to 3:1) to afford **8a** (149.8 mg, 91% yield, 74% ee).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* =8.0 Hz, 2 H), 7.35-7.28 (m, 7 H), 3.77 (d, *J* =14.8 Hz, 1 H), 3.72 (d, *J* =14.8 Hz, 1 H), 3.35 (ddd, *J* =12.8 Hz, 10.0 Hz, 8.0 Hz, 1 H), 2.84 (ddd, *J* =17.6 Hz, 10.0 Hz, 4.8 Hz, 1 H), 2.63 (ddd, *J* =12.8 Hz, 10.0 Hz, 4.8 Hz, 1 H), 2.48 (ddd, *J* =17.6 Hz, 8.0 Hz, 10.0 Hz, 1 H), 2.42 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 145.0, 142.0, 137.6, 128.9, 128.0, 124.6, 4.8, 65.1, 32.6, 28.3, 21.7; IR (film) ν_{max} 1776, 1596, 1449, 1318, 1285, 1173, 1137, 1084, 1049, 841 cm^{-1}; R_f(hexanes: ethyl ether = 1:2)= 0.3; HRMS: $[M+NH_4]^+$ Calcd. For $C_{18}H_{22}NO_4S$: 348.1264; Found: 348.1248. $[\alpha]_D^{24}$ = -3.2 (c = 1.5, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel IA 4.6 mm x 250 mm, hexanes:*i*-PrOH = 90:10, 1.0 mL/min, 230 nm, t_R = 34.5 min (minor) and 36.9 min (major).

(*S*)-5-(((4-bromophenyl)sulfonyl)methyl)-5-(4-chlorophenyl)dihydrofuran-2(3*H*)-one (8b) Following general procedure C, the title compound was synthesized from 4-(4-chlorophenyl) pent-4-enoic acid (**2c**) (0.50 mmol, 105 mg) and 4-bromobenzenesulfonyl chloride (**10b**) (0.55 mmol, 140.5 mg). The product was purified by silica gel flash column chromatography (Et_2O/hexanes = 3:1 to 7:1 to EtOAc/hexanes = 1:1) to afford **8b** (204.8 mg, 95% yield, 78% ee).[1]H NMR (400 MHz, $CDCl_3$) δ 7.65 (m, 4 H), 7.31 (d, *J* =8.4 Hz, 2 H), 7.23 (d, *J* =8.4 Hz, 2 H), 3.73 (m, 2 H), 3.27 (ddd, *J* =12.8 Hz, 9.6 Hz, 8.4 Hz, 1 H), 2.82 (ddd, *J* =17.6 Hz, 9.6 Hz, 4.4 Hz, 1 H), 2.61 (ddd, *J* =12.8 Hz, 9.6 Hz, 4.4 Hz, 1 H), 2.49 (ddd, *J* =17.6 Hz, 8.4 Hz, 9.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 139.8, 139.3, 135.0, 132.7, 129.6, 129.2, 126.3, 84.1, 65.1, 33.1, 28.1; IR (film) ν_{max} 1776, 1572, 1326, 1140, 1067, 1137, 997, 812 cm^{-1}; R_f(hexanes: ethyl acetate = 1:1)= 0.2; HRMS: $[M+NH_4]^+$ Calcd. For $C_{17}H_{18}ClBrNO_4S$: 447.9808; Found: 447.9827. $[\alpha]_D^{24}$ = +12.9 (c = 1, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel IA 4.6 mm x 250 mm, hexanes:*i*-PrOH = 85:15, 1.0 mL/min, 230 nm, t_R = 35.0 min (minor) and 68.4 min (major).

(*S*)-5-(3-acetylphenyl)-5-(((4-(trifluoromethyl)phenyl)sulfonyl)methyl)dihydrofuran-2(3*H*)-one (8c) An oven-dried Fisher Scientific 20×150 mm re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (18.7 mg, 0.05 mmol, 0.10 equiv), 2,2'-isopropylidenebis[(4*S*)-4-tert-butyl-2-oxazoline] (**L**) (14.7 mg, 0.05 mmol, 0.10 equiv), silver carbonate (82.8 mg, 0.60 mmol, 1.2 equiv) and **2h** (109 mg, 0.50 mmol, 1.0 equiv). The reaction tube was sealed with a septum screw-cap (10/90, Teflon/SIL, National Scientific) and connected to a Schlenk line. The reaction tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). A solution of 4-trifluoromethylbenzenesulfonyl chloride (**10c**) (134 mg, 0.55 mmol, 1.1 equiv) in anhydrous EtOAc (8 mL) was added to the tube via syringe under argon. The argon pressure was removed and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with saturated aqueous sodium bicarbonate solution (8 mL) and ethyl acetate (4 mL). The aqueous layer was separated and extracted with ethyl acetate (8 mL×3). The combined organic layers was concentrated *in vacuo*. The residue purified by silica gel flash column chromatography (Et_2O/hexanes = 3:1 to

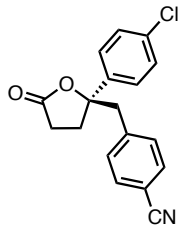
EtOAc/hexanes = 1:1) to afford **8c** (142.2 mg, 67% yield, 81% ee).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* =8.4 Hz, 2 H), 7.84 (m, 2 H), 7.75 (d, *J* =8.4 Hz, 2 H), 7.56 (m, 1 H), 7.45 (m, 1 H), 3.86 (d, *J* =15.2 Hz, 1 H), 3.83 (d, *J* =15.2 Hz, 1 H), 3.28 (ddd, *J* =12.8 Hz, 9.6 Hz, 8.0 Hz, 1 H), 2.85 (ddd, *J* =17.6 Hz, 9.6 Hz, 4.8 Hz, 1 H), 2.66 (ddd, *J* =12.8 Hz, 9.6 Hz, 4.8 Hz, 1 H), 2.57 (s, 3 H), 2.50 (ddd, *J* =17.6 Hz, 8.0 Hz, 9.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 174.8, 143.7, 142.1, 137.7, 135.6 (q, J_{CF} = 33 Hz), 129.5, 129.3, 128.9, 128.8, 126.5 (q, J_{CF} = 4 Hz), 124.3, 123.1 (q, J_{CF} = 272 Hz), 84.1, 64.9, 33.4, 28.0, 26.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3 (s); IR (film) ν_{max} 1782, 1683, 1403, 1320, 1167, 1132, 1061, 914, 844 cm^{-1}; R_f(hexanes: ethyl acetate = 1:1)= 0.2; HRMS: $[M+NH_4]^+$ Calcd. For $C_{20}H_{21}F_3NO_5S$: 444.1087; Found: 444.1090. $[\alpha]_D^{24}$ = -0.8 (c = 0.9, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel IA 4.6 mm x 250 mm, hexanes:*i*-PrOH = 85:15, 1.0 mL/min, 230 nm, t_R = 51.6 min (minor) and 55.5 min (major).

Enantioselective oxyarylation

Caution: Proper safety precautions should be followed. This reaction should be carried out behind a blast shield and only on a small scale. It should be noted that while no incident occurred during this study, aryldiazonium salts are potentially hazardous compounds and adequate safety measures should be taken.

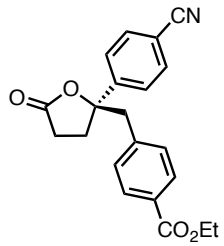
General procedure D for the enantioselective oxyarylation (Scheme 5): An oven-dried Fisher Scientific 20×150 mm re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (22.4 mg, 0.06 mmol, 0.12 equiv), 2,2-isopropylidenebis[(4*S*)-4-tert-butyl-2-oxazoline] (**L**) (14.7 mg, 0.05 mmol, 0.1 equiv), aryldiazonium tetrafluoroborate **11** (1.0 mmol, 2.0 equiv) and **2** (0.50 mmol, 1.0 equiv). The tube was then sealed with a septum screw-cap (10/90, Teflon/SIL, National Scientific) and connected to a Schlenk line. The vessel was briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). Anhydrous EtOAc (8 mL) was added to the tube via syringe followed by 2,6-di-*tert*-butylpyridine (224 μL, 2.0 equiv). Argon pressure was removed. A venting needle was inserted. The reaction mixture was stirred at room temperature (25 °C) for 16 h. The reaction mixture was carefully diluted with saturated aqueous sodium bicarbonate solution (8 mL) and EtOAc (4 mL). The aqueous layer was separated and extracted with EtOAc (8 mL×3).

The combined organic layers were concentrated *in vacuo*. The residue was then purified by silica gel flash column chromatography (Et_2O/Hexanes or EtOAc/Hexanes) to afford the oxyarylation product **9**.



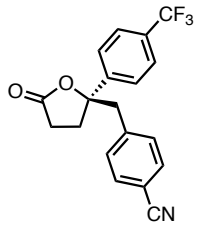
(R)-4-((2-(4-chlorophenyl)-5-oxotetrahydrofuran-2-yl)methyl)benzonitrile (9a) Following general procedure D, the title compound was synthesized from 4-(4-chlorophenyl)pent-4-enoic acid (**2c**) (105 mg, 0.50 mmol) and 4-cyanophenyldiazonium tetrafluoroborate (217 mg). The product was purified by silica gel flash column chromatography (Et_2O/hexanes = 2:1 to EtOAc/hexanes = 2:1) to afford **9a** (115.1 mg, 74% yield, 73% ee) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* =8.4 Hz, 2 H), 7.30 (d, *J* =8.8 Hz, 2 H), 7.16 (d, *J* =8.8 Hz, 2 H), 7.11 (d, *J* =8.4 Hz, 2 H), 3.26 (d, *J* =14.4 Hz, 1 H), 3.22 (d, *J* =14.4 Hz, 1 H), 2.55-2.50 (m, 2 H), 2.42-2.38 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 140.6, 140.3, 134.2, 132.1, 131.4, 128.9, 126.4, 118.7, 111.3, 87.9, 48.6, 34.3, 28.5; IR (film) v_{max} 1742, 1434, 1366, 1229, 1217 cm^{-1}; R_f(hexanes: ethyl acetate = 1:1)= 0.3; HRMS: $[M+NH_4]^+$ Calcd. For $C_{18}H_{18}ClN_2O_2$: 329.1051; Found: 329.1071. $[\alpha]_D^{24}$ = +48.8 (c = 1.1, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 90:10, 1.0 mL/min, 230 nm, t_R = 34.5 min (major) and 39.5 min (minor).

(*R*)-ethyl-4-((2-(4-cyanophenyl)-5-oxotetrahydrofuran-2-yl)methyl)benzoate (9b) Following general procedure D, the title compound was synthesized from 4-(4-cyanophenyl)pent-4-enoic acid (**2d**) (100 mg, 0.50 mmol) and 4-ethoxycarbonylphenyldiazonium tetrafluoroborate (264 mg). The product was purified by silica gel flash column chromatography (Et_2O/hexanes = 2:1 to EtOAc/hexanes = 1:1) to afford **9b** (132.0 mg, 76% yield, 71% ee) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* =8.0 Hz, 2 H), 7.64 (d, *J* =8.8 Hz, 2 H), 7.40 (d, *J* =8.8 Hz, 2 H), 7.11 (d, *J* =8.0 Hz, 2 H), 4.36 (q, *J* =7.2 Hz, 2 H), 3.27 (d, *J* =14.0 Hz, 1 H), 3.21 (d, *J* =14.0 Hz, 1 H), 2.62 (ddd, *J* =12.8 Hz, 10.0 Hz, 7.2 Hz, 1 H), 2.51-2.33 (m, 2 H), 2.26 (ddd, *J* =17.2 Hz, 9.6 Hz, 6.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 166.4, 148.1, 139.3 132.6, 130.6, 129.9, 129.7, 125.8, 118.4, 112.2, 87.9, 61.2, 48.5, 33.6, 28.5, 14.5; IR (film) v_{max} 2228, 1774, 1738, 1717, 1365, 1277, 128, 1217, 1104, 1021 cm^{-1}; R_f(hexanes: ethyl acetate = 1:1)= 0.1; HRMS: $[M+NH_4]^+$ Calcd. For $C_{21}H_{23}N_2O_4$: 367.1652;

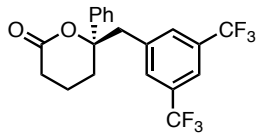


Found: 367.1665. $[\alpha]_D^{24}$ = +11.3 (c = 1, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel AD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 85:15, 1.0 mL/min, 230 nm, t_R = 20.3 min (major) and 29.1 min (minor).

(R)-4-((5-oxo-2-(4-(trifluoromethyl)phenyl)tetrahydrofuran-2-yl)methyl)benzonitrile (9c)



Following general procedure D, the title compound was synthesized from 4-(4-trifluoromethylphenyl)pent-4-enoic acid (**2e**) (122 mg, 0.50 mmol) and 4-cyanophenyldiazonium tetrafluoroborate (217 mg). The product was purified by silica gel flash column chromatography (Et_2O/hexanes = 2:1 to EtOAc/hexanes = 1:1) to afford **9c** (90.4 mg, 52% yield, 76% ee) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* =8.4 Hz, 2 H), 7.51 (d, *J* =8.4 Hz, 2 H), 7.37 (d, *J* =8.4 Hz, 2 H), 7.14 (d, *J* =8.4 Hz, 2 H), 3.30 (d, *J* =14.4 Hz, 1 H), 3.26 (d, *J* =14.4 Hz, 1 H), 2.63-2.51 (m, 2 H), 2.47-2.33 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 146.2, 140.0, 132.2, 131.4, 130.6 (q, J_{CF} = 32 Hz), 125.8 (q, J_{CF} = 3 Hz), 125.4, 123.9 (q, J_{CF} = 270 Hz), 118.7, 111.5, 87.8, 48.5, 34.2, 28.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.7 (s); IR (film) ν_{max} 1738, 1434, 1365, 1229, 1217, 1163 cm^{-1}; R_f(toluene: ethyl acetate = 5:1)= 0.3; HRMS: $[M+NH_4]^+$ Calcd. For $C_{19}H_{18}F_3N_2O_2$: 363.1315; Found: 363.1332. $[\alpha]_D^{24}$ = +8.0 (c = 0.9, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 90:10, 1.0 mL/min, 230 nm, t_R = 30.3 min (major) and 37.6 min (minor).



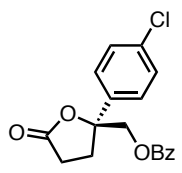
(*R*)-6-(3,5-bis(trifluoromethyl)benzyl)-6-phenyltetrahydro-2*H*-pyran-2-one (9d) Following general procedure D, the title compound was synthesized from 5-phenylhex-5-enoic acid (**2i**) (95 mg, 0.50 mmol) and 3,5-bis(trifluoromethyl)phenyldiazonium tetrafluoroborate (328 mg). The product was purified by silica gel flash column chromatography (hexanes: ethyl acetate = 10:1 to 4:1) to afford **9d** (164.9 mg, 82% yield, 56% ee) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1 H), 7.36-7.30 (m, 5 H), 7.19-7.178 (m, 2 H), 3.28 (d, *J* =14.0 Hz, 1 H), 3.26 (d, *J* =14.0 Hz, 1 H), 2.47-2.33 (m, 3 H), 1.97 (ddd, *J* =14.4, 12.8, 4.8 Hz, 1 H), 1.80 (m, 1 H), 1.63 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 141.3, 137.7, 131.1 (q, J_{CF} = 33 Hz), 130.9, 129.0, 128.2, 125.3, 123.3 (q, J_{CF} = 271 Hz), 120.9 (m), 86.7, 49.9, 31.7, 29.1, 16.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.9 (s); IR (film) ν_{max} 1736, 1378, 1275, 1235, 1167, 1125, 1044, 894 cm^{-1}; R_f(toluene: ethyl acetate = 5:1)= 0.6; $[M+NH_4]^+$ Calcd. For $C_{20}H_{20}F_6NO_2$: 420.1393; Found: 420.1370. $[\alpha]_D^{24}$ = +2.3 (c= 0.7,

$CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 90:10, 1.0 mL/min, 230 nm, t_R = 7.1 min (major) and 10.6 min (minor).

Enantioselective diacyloxylation *(Scheme 7)*

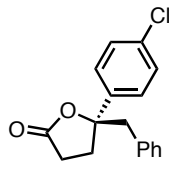
Caution: Proper safety precautions should be followed. This reaction should be carried out behind a blast shield and only on a small scale. It should be noted that while no incident occurred during this study, peroxides are potentially hazardous compounds and adequate safety measures should be taken.

An oven-dried Fisher Scientific 20×150 mm re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (18.7 mg, 0.05 mmol, 0.10 equiv), 2,2'-isopropylidenebis[(4*S*)-4-tert-butyl-2-oxazoline] (**L**) (14.7 mg, 0.05 mmol, 0.10 equiv), dibenzoyl peroxide (75%) (244 mg, 0.75 mmol, 1.5 equiv), manganese powder (55 mg, 1.0 mmol, 2.0 equiv) and **2c** (105 mg, 0.50 mmol, 1.0 equiv). The tube was then sealed with a Teflon screw-cap septum (10/90, Teflon/SIL, National Scientific) and connected to a Schlenk line. The vessel was briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). Anhydrous EtOAc (8 mL) was added to the tube via syringe and the argon pressure was removed. A venting needle was inserted. The reaction mixture was stirred at room temperature (25 °C) for 16 h. The reaction mixture was carefully diluted with saturated aqueous sodium bicarbonate solution (8 mL) and EtOAc (4 mL). Internal standard (phenanthrene) was added. The aqueous layer was separated and extracted with EtOAc (8 mL×3). The combined organic layers were concentrated *in vacuo*. The residue was analyzed by ^{1}H NMR spectroscopy (^{1}H NMR yield: **13**: 29%; **14**: 40%). The residue was then purified by silica gel flash column chromatography (hexanes: ethyl acetate = 10:1 to 4:1 to toluene: ethyl acetate = 4:1) to afford **13** (42.5 mg, 26% yield, 65% ee) and **14** (50.8 mg, 35% yield, 66% ee).



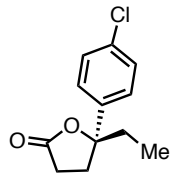
(*S*)-(2-(4-Chlorophenyl)-5-oxotetrahydrofuran-2-yl)methyl benzoate (13) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (m, 2 H), 7.59 (m, 1 H), 7.47-7.41 (m, 6 H), 4.64 (d, *J* =12.4 Hz, 1 H), 4.45 (d, *J* =12.4 Hz, 1 H), 2.82-2.71 (m, 2 H), 2.63-2.45 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 166.0, 138.7, 134.8, 133.73, 129.8, 129.3, 129.2, 128.8, 126.6, 86.6, 69.9, 31.5, 28.9; IR (film) ν_{max} 1779, 1720, 1264, 1111,

1093, 1012, 910 cm^{-1}; R_f(toluene: ethyl acetate = 5:1)= 0.4; $[M+H]^+$ Calcd. For $C_{18}H_{16}ClO_4$: 331.0732; Found: 331.0750. $[\alpha]_D^{24}$ = -16.4 (c= 0.4, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 90:10, 1.0 mL/min, 230 nm, t_R = 16.8 min (major) and 31.9 min (minor).



(*R*)-5-Benzyl-5-(4-chlorophenyl)dihydrofuran-2(3*H*)-one (14) ^1H NMR (400 MHz, $CDCl_3$) δ 7.33-7.23 (m, 7 H), 7.08 (m, 2 H), 3.22 (d, *J* =14.0 Hz, 1 H), 3.10 (d, *J* =14.0 Hz, 1 H), 2.57 (ddd, *J* =12.8, 10.4, 7.2 Hz, 1 H), 2.44-2.28 (m, 2 H), 2.11 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 142.1, 134.8, 133.8, 130.8, 128.7, 128.5, 127.4, 126.4, 88.6, 48.8, 33.2, 28.8; IR (film) ν_{max} 1772, 1492, 1163, 1003, 926, 808, 701 cm^{-1}; R_f(toluene: ethyl acetate = 5:1)= 0.6; $[M+NH_4]^+$ Calcd. For $C_{17}H_{19}ClNO_2$: 304.1099; Found: 304.1105. $[\alpha]_D^{24}$ = +4.1 (c= 1, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OD-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 230 nm, t_R = 19.5 min (major) and 18.2 min (minor).

Enantioselective Oxyalkylation *(Scheme 8)*



(*S*)-5-(4-chlorophenyl)-5-ethyldihydrofuran-2(3*H*)-one (15) (Scheme 7) An oven-dried Fisher Scientific 20×150 mm re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (37.3 mg, 0.10 mmol, 0.20 equiv), 2,2'-isopropylidenebis[(4*S*)-4-tert-butyl-2-oxazoline] (**L**) (29.4 mg, 0.10 mmol, 0.20 equiv), (diacetoxyiodo)benzene (320 mg, 1.0 mmol, 2.0 equiv), potassium fluoride (15 mg, 0.25 mmol, 0.50 equiv) and **2c** (105 mg, 0.50 mmol, 1.0 equiv). The tube was then sealed with a Teflon screw-cap septum (10/90, Teflon/SIL, National Scientific) and connected to a Schlenk line. The vessel was briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). Anhydrous MTBE (8 mL) was added to the tube via syringe and the argon pressure was removed. The reaction mixture was stirred at room temperature (25 °C) for 16 h. The reaction mixture was carefully diluted with saturated aqueous sodium bicarbonate solution (8 mL) and Et_2O (4 mL). The aqueous layer was separated and extracted with Et_2O (8 mL×3). The combined organic layers were concentrated *in vacuo*. The residue was then purified by

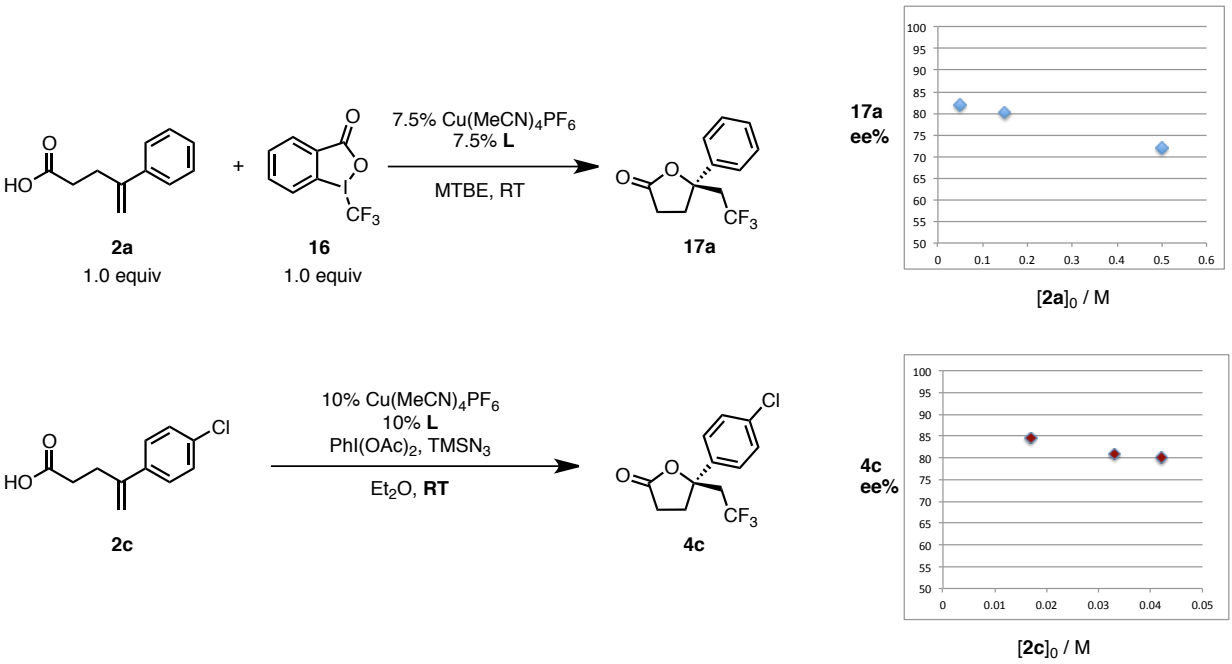
silica gel flash column chromatography (hexanes: ethyl acetate = 10:1 to 4:1) to afford **15** (22.0 mg, 20% yield, 60% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* =8.4 Hz, 2 H), 7.27 (d, *J* =8.4 Hz, 2 H), 2.60 (m, 1 H), 2.51-2.39 (m, 3 H), 1.97 (q, *J* =7.2 Hz, 2 H), 0.82 (t, *J* =7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 141.5, 133.6, 128.8, 126.4, 89.5, 35.4, 34.7, 28.8, 8.3; IR (film) ν_{max} 1739, 1365, 1229, 1217, 1091; R_f(hexanes: ethyl acetate = 2:1)= 0.5; $[M+H]^+$ Calcd. For $C_{12}H_{14}ClO_2$: 225.0677; Found: 225.0683. The enantiomeric excess was determined by chiral HPLC analysis: Chiralcel OJ-H 4.6 mm x 250 mm, hexanes:*i*-PrOH = 90:10, 1.0 mL/min, 230 nm, t_R = 14.7 min (major) and 11.3 min (minor).

Effect of concentration on enantioselectivity

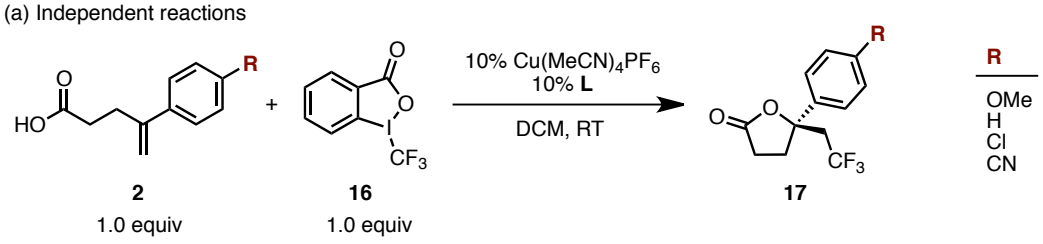
The enantioselectivity slightly decreases as the system gets more concentrated, as shown by the following chart using oxytrifluoromethylation as an example (SI-Scheme 2). The enantiomeric excess of the product **17a** dropped to 72% from 82% as the concentration increased from 0.05 M to 0.5 M. Concentrations lower than 0.05 M did not afford significant ee improvement but resulted in much lower conversion of **2a** as well as lower yield of **17a** (~10% yield at 0.005M). Similar trend was observed with the oxyazidation reaction, where the product **4c**'s ee increased from 80% to 85% as the reaction concentration decreased from 0.042 M to 0.017 M (at RT). However <10% yield was obtained at 0.005 M.

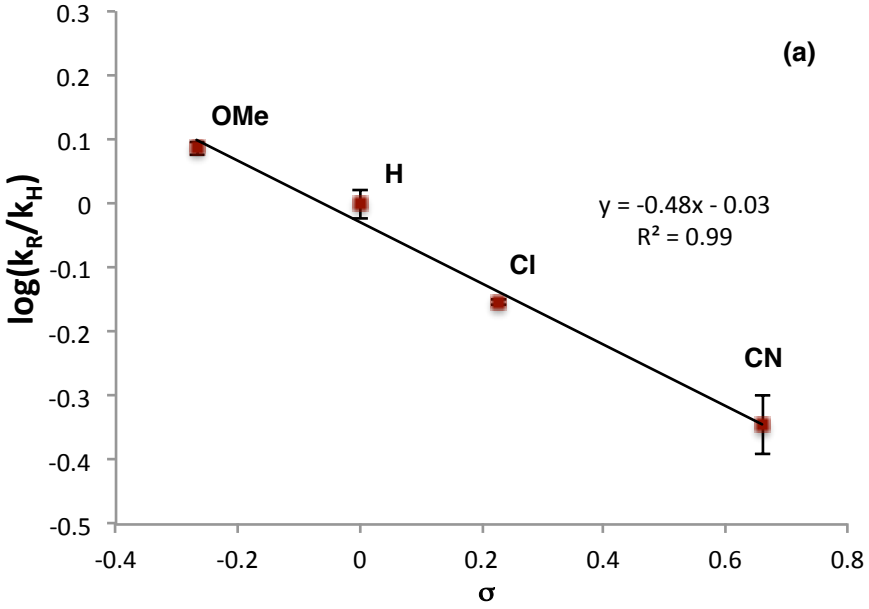
***SI-Scheme 2**. Concentration effect.*



Hammett plot (Scheme 9)

Independent reactions: An oven-dried screw-cap NMR tube was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (1.9 mg, 0.0050 mmol, 0.10 equiv) and sealed with a Teflon screw-cap septum. The tube was connected to a Schlenk line. The tube was briefly evacuated and backfilled with argon (this sequence was repeated a total of two times). The argon pressure was removed. 0.60 mL of a stock solution in anhydrous methylene chloride under argon containing **16** (0.083 mol/L), **2** (0.083 mol/L), **L** (0.0083 mol/L) and internal standard (α,α,α-trifluorotoluene) was added to the tube via syringe. The reaction progress was monitored by ^{19}F NMR spectroscopy. The initial reaction rate was determined and used for the calculation of $\log(k_R/k_H)$.



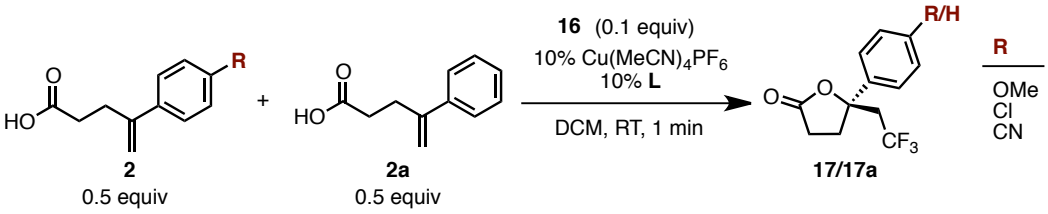


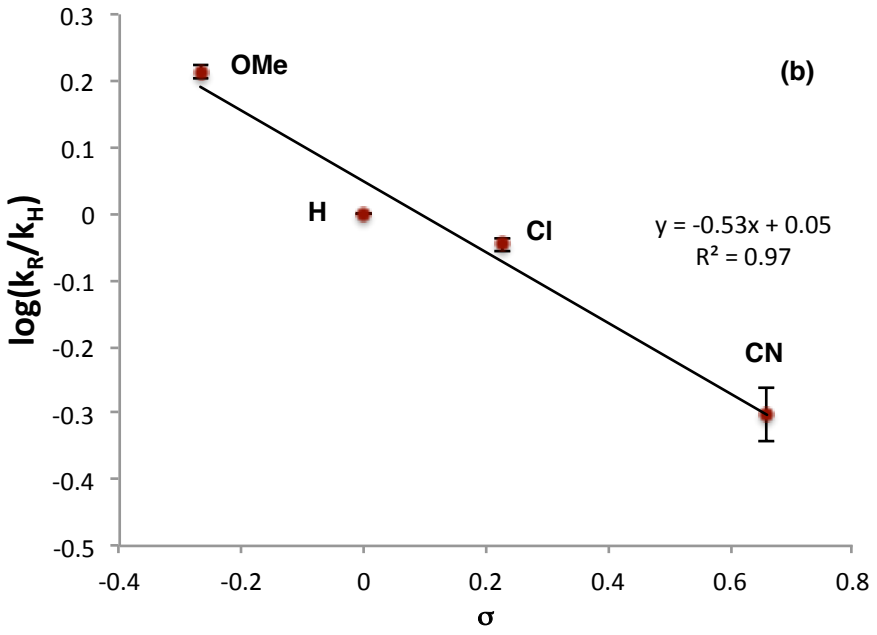
R	log(k_R/k_H)		
	run 1	run 2	ave
OMe	0.098	0.076	0.087 ± 0.011
H	-0.023	0.022	0.000 ± 0.022
Cl	-0.15	-0.16	-0.154 ± 0.006
CN	-0.30	-0.39	-0.343 ± 0.047

One-pot competition experiments: An oven-dried Fisher Scientific 13×100 mm re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (3.7 mg, 0.010 mmol, 0.10 equiv), 2,2'-isopropylidenebis[(4*S*)-4-tert-butyl-2-oxazoline] (**L**) (2.9 mg, 0.010 mmol, 0.10 equiv) and **16** (3.2 mg, 0.010 mmol, 0.10 equiv). The reaction tube was sealed with a septum screw-cap (Thermo Scientific ASM PHN CAP w/PTFE/SIL, cat. #03378316). The reaction tube was connected to a Schlenk line though a needle. The reaction tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). The argon pressure was removed and 1.2 mL of a stock solution in anhydrous methylene chloride under argon containing **2** (0.042 mol/L, 0.50 equiv) and **2a** (0.042 mol/L, 0.50 equiv) was added to the tube via syringe. The

reaction mixture was stirred at room temperature for 1 min. The reaction mixture was diluted with saturated aqueous sodium bicarbonate solution (4 mL) and ethyl ether (2 mL). The aqueous layer was separated and extracted with ethyl acetate (2 mL×3). The combined organic layers was concentrated *in vacuo*. The residue was redissolved in $CDCl_3$ and internal standard (α,α,α-trifluorotoluene) was added. The resulting mixture was analyzed by ^{19}F NMR spectroscopy (proton decoupled). The product ratio **17**/**17a** was determined and used for the calculation of $\log(k_R/k_H)$.

(b) Competition reactions

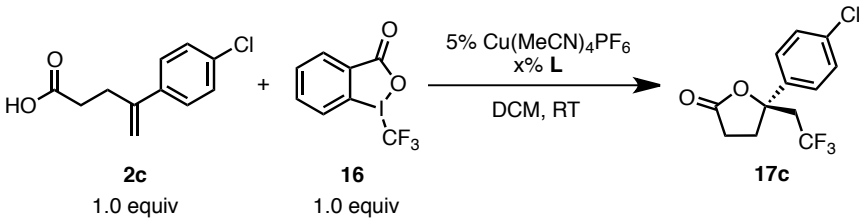




R	product ration (**17**:**17a**)					$\log(k_R/k_H)$
	# 1	# 2	#3	#4	#5	
OMe	1.60	1.64	1.70	1.58	1.66	0.21 ± 0.01
Cl	0.89	0.90	0.87	0.93	0.92	-0.046 ± 0.01
CN	0.55	0.54	0.46	0.44	-	-0.30 ± 0.04

Effect of ligand stoichiometry (Figure 1)

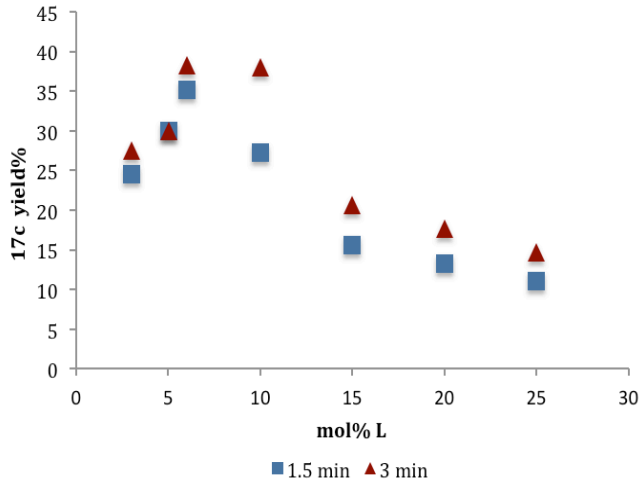
An oven-dried Fisher Scientific 13×100 mm re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with tetrakis(acetonitrile)copper(I) hexafluorophosphate (3.7 mg, 0.010 mmol, 0.10 equiv). The reaction tube was sealed with a septum screw-cap (Thermo Scientific ASM PHN CAP w/PTFE/SIL, cat. #03378316). The reaction tube was connected to a Schlenk line though a needle. The reaction tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). The argon pressure was removed. 20***x*** μL of stock solution of 2,2'-isopropylidenebis[(4*S*)-4-tert-butyl-2-oxazoline] (**L**) (0.050 mol/L in anhydrous methylene chloride) was added via syringe followed by additional (600-20***x***) μL anhydrous methylene chloride. The resulting mixture was stirred at RT for 1 min, to which 0.60 mL of a stock solution in anhydrous methylene chloride under argon containing **2c** (0.16 mol/L, 1.0 equiv), **16** (0.16 mol/L, 1.0 equiv) and internal standard (α,α,α-trifluorotoluene) was added via syringe. The reaction mixture was stirred at room temperature for y min (y = 1.5 or 3.0). The reaction mixture was diluted with saturated aqueous sodium bicarbonate solution (4 mL) and $CHCl_3$ (2 mL). The organic layer was separated and analyzed by ^{19}F NMR spectroscopy.



2c
1.0 equiv

16
1.0 equiv

17c



Experimental References and Notes

[1] Zhu, R.; Buchwald, S. L. *Angew. Chem. Int. Ed*. **2013**, *52*, 12655.

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[5] Jian, Y.-J.; Tang, C.-J.; Wu, Y. *J. Org. Chem*. **2007**, *72*, 4851.

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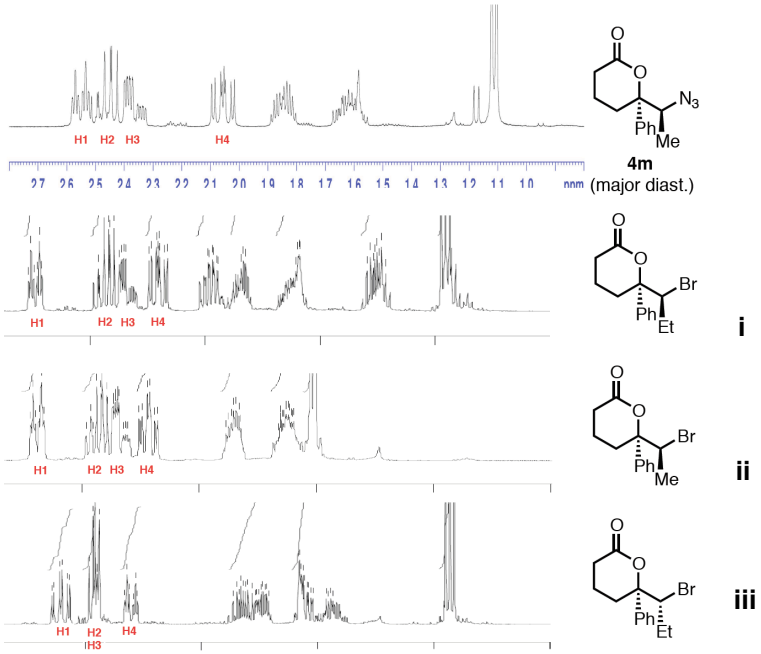

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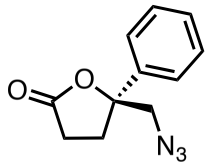
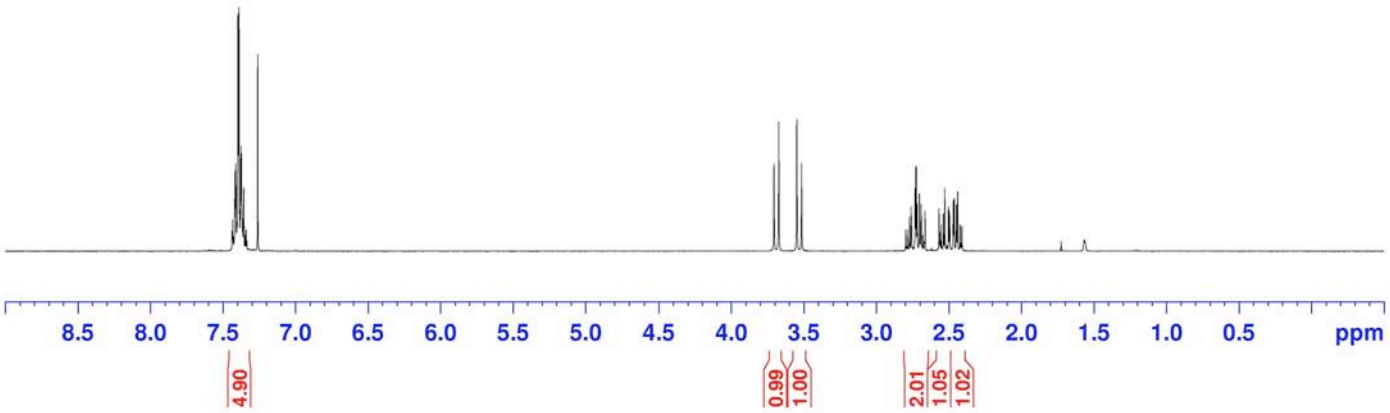
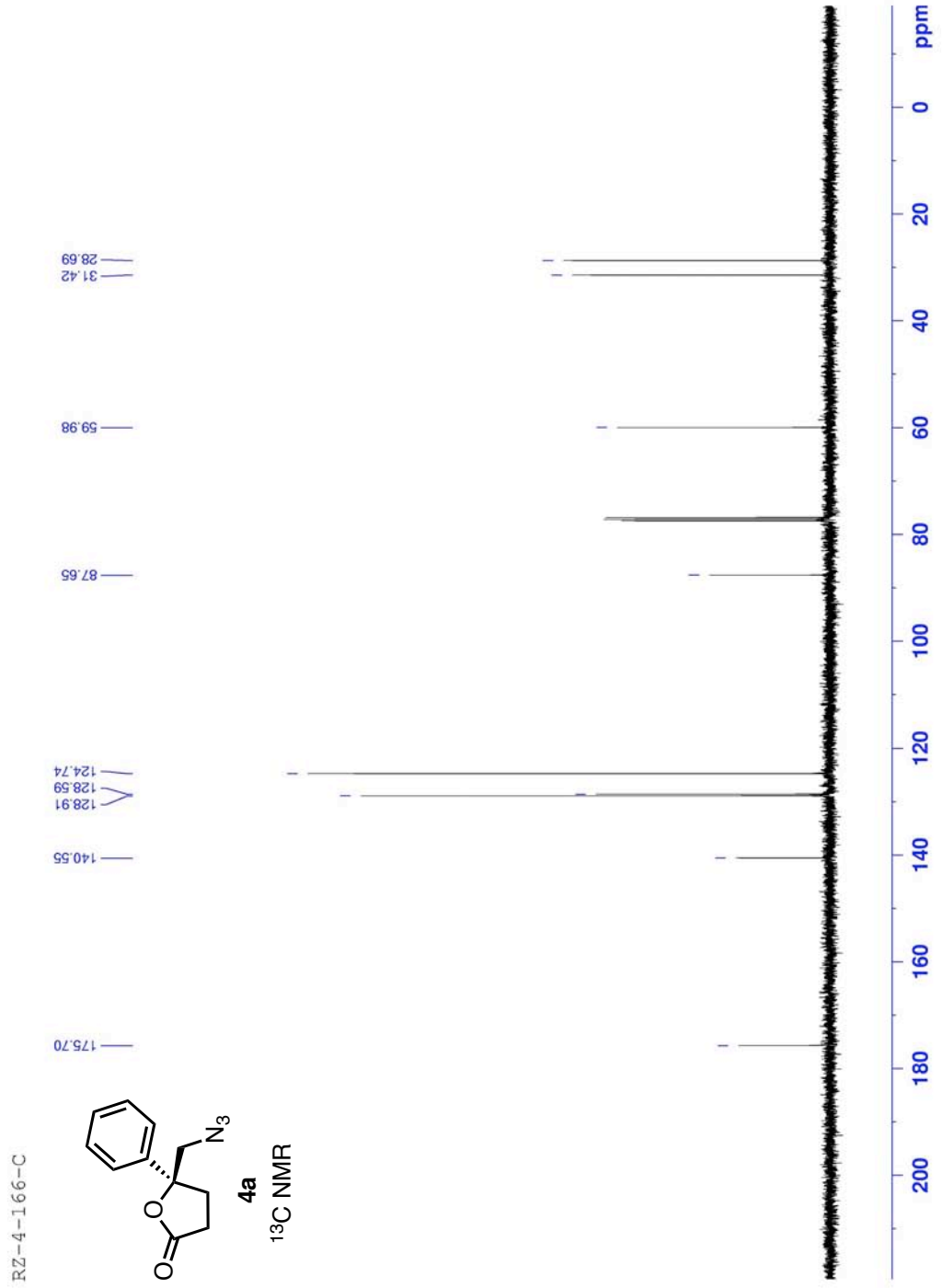
RZ-4-166-H



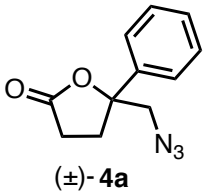
4a

^{1}H NMR




RZ-4-166-C
175.70
140.55
128.91
128.59
124.74
87.65
59.98
31.42
28.69
ppm
0
20
40
60
80
100
120
140
160
180
200
N3
O
O
4a
13C NMR

HPLC traces for 4a:



(±)-**4a**

Sample Name: RZ-4-166-RAC

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    Acq. Instrument : Instrument 1                     Location : Vial 17
    Injection Date  : 7/22/2014 8:52:16 AM                  Inj :   1
                                                     Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-22 08-08-53\RZ-5IPA-1ML-2013-.M
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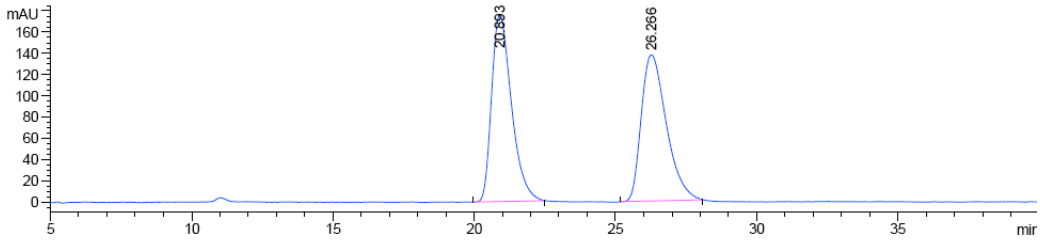
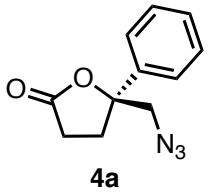
DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-22 08-08-53\RZ-4-166-RAC.D)



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.893	BB	0.7269	8601.23047	175.76074	50.1902
2	26.266	BB	0.7623	8536.03516	137.86684	49.8098
Totals :				1.71373e4	313.62758	

Sample Name: RZ-4-166



4a

```
    ======================================================================
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    Acq. Instrument : Instrument 1                     Location : Vial 16
    Injection Date  : 7/22/2014 8:11:08 AM                  Inj :   1
                                                     Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-22 08-08-53\RZ-5IPA-1ML-2013-.M
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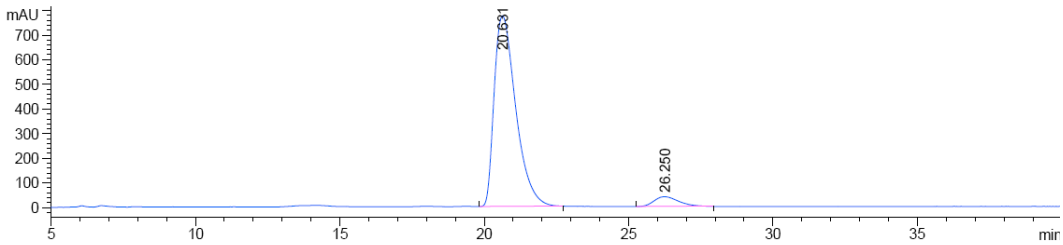
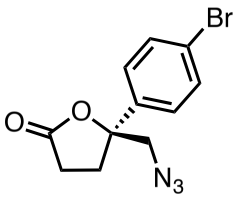
DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-22 08-08-53\RZ-4-166.D)



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

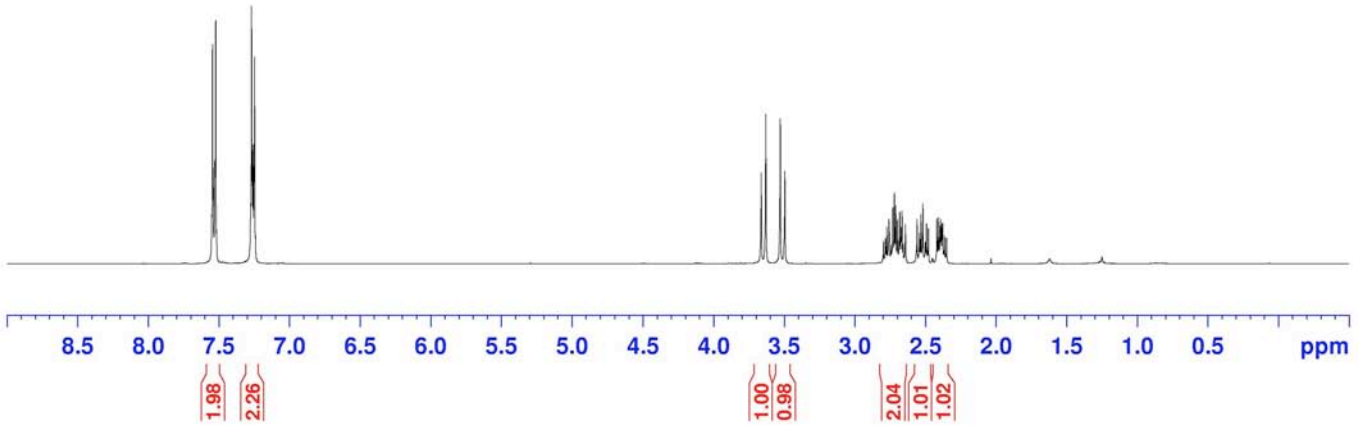
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.631	BV	0.7812	4.02596e4	773.55682	94.3599
2	26.250	VB	0.7156	2406.40234	40.01611	5.6401
Totals :				4.26660e4	813.57293	

RZ-4-182-H

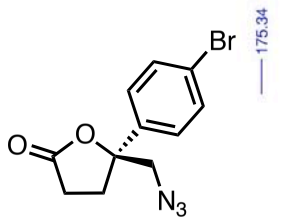


4b

^{1}H NMR



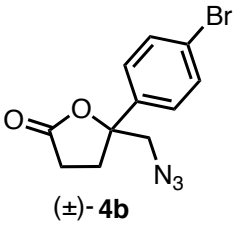
RZ-4-182-C



4b

^{13}C NMR

HPLC traces for 4b:



(±)-**4b**

Sample Name: RZ-4-182-RAC

```
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                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
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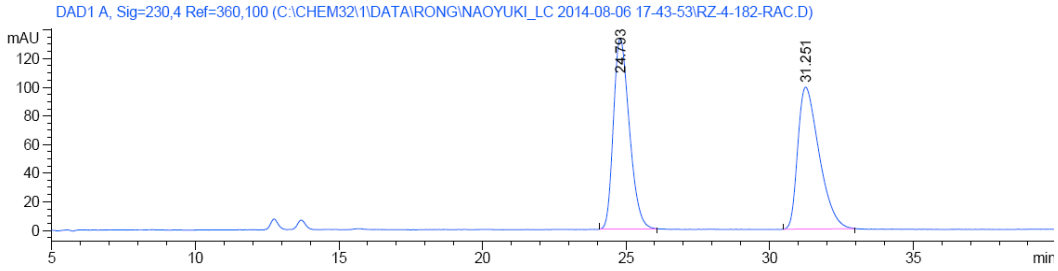
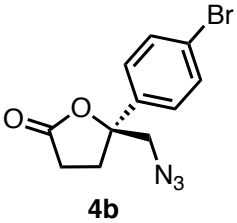


Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.793	BB	0.6001	5160.43164	133.17227	49.9961
2	31.251	BB	0.7904	5161.24463	99.30509	50.0039
Totals :				1.03217e4	232.47736	



4b

Sample Name: RZ-4-182

```
    ======================================================================
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    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 8/1/2014 7:17:52 AM                      Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
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```
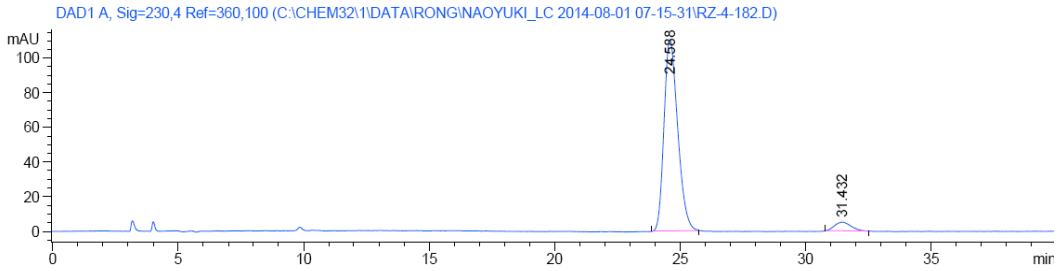
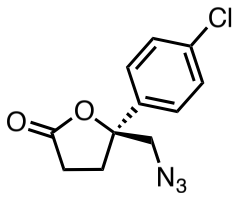



Signal 1: DAD1 A, Sig=230,4 Ref=360,100

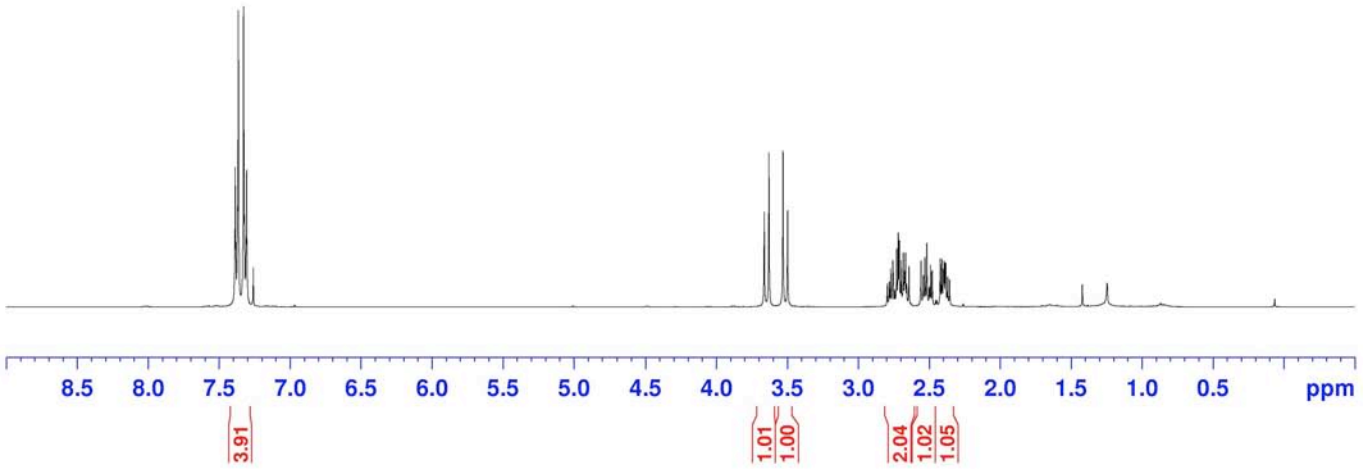
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.588	BB	0.5745	4195.15039	110.60049	94.5795
2	31.432	BB	0.5531	240.42851	5.16516	5.4205
Totals :				4435.57890	115.76566	

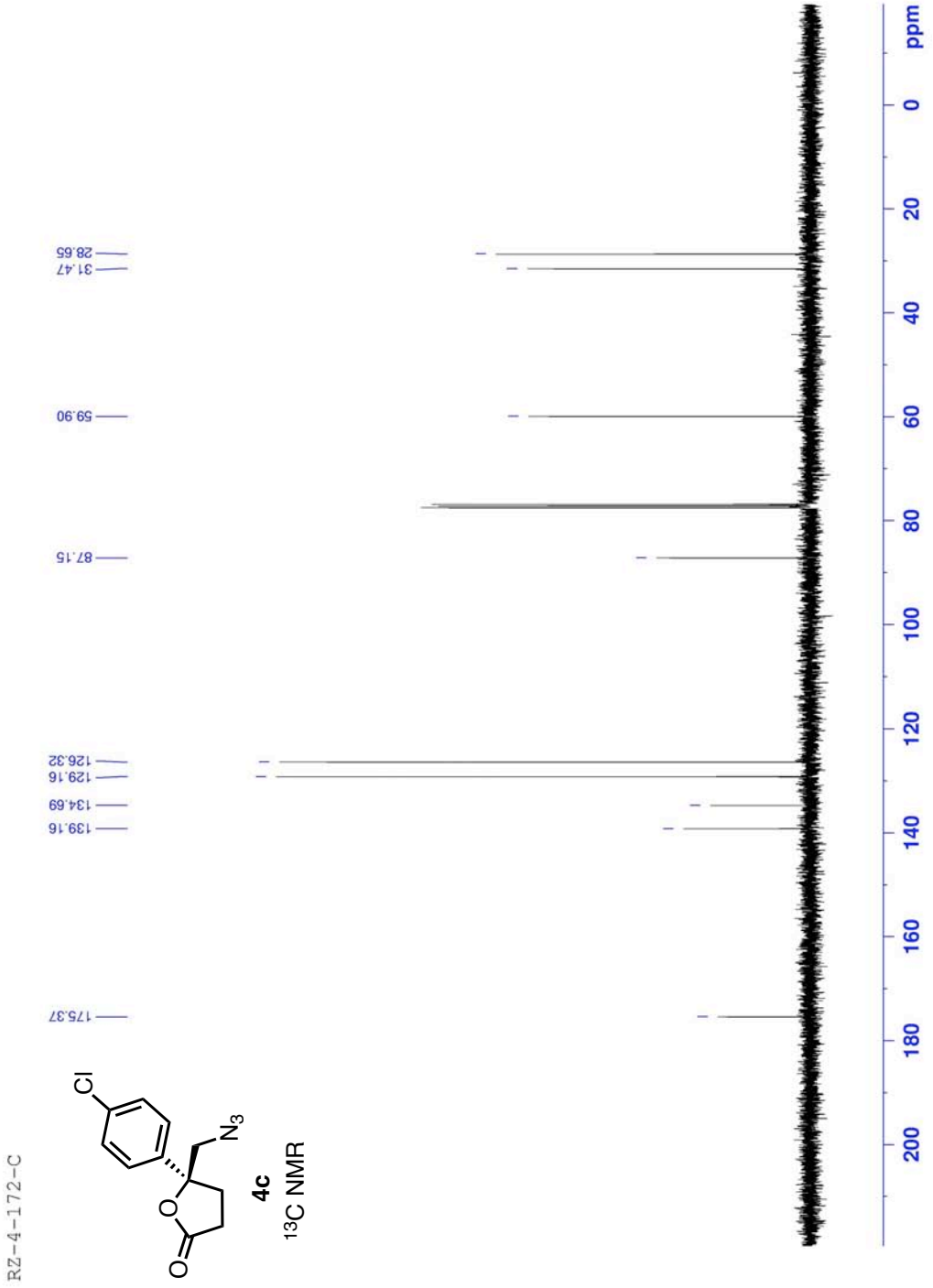
RZ-4-172-H



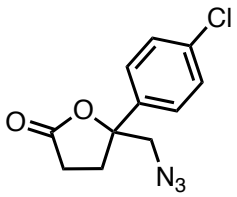
4c

^{1}H NMR




RZ-4-172-C
Cl
N3
O
O
4c
13C NMR
175.37
139.16
134.69
129.16
126.32
87.15
59.90
31.47
28.65
ppm
0
20
40
60
80
100
120
140
160
180
200

HPLC traces for 4c:



(±)-**4c**

Sample Name: RZ-4-172-RAC

```
    ============================================================================
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    Acq. Instrument : Instrument 1                        Location : Vial 18
    Injection Date  : 7/22/2014 10:50:36 AM                    Inj :   1
                                                       Inj Volume : 1 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-22 08-08-53\RZ-5IPA-1ML-2013-.M
```
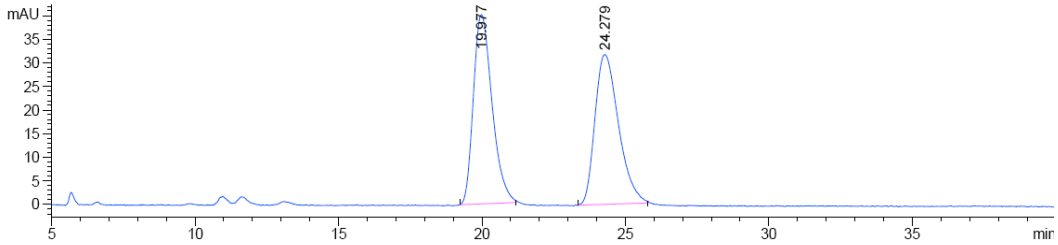
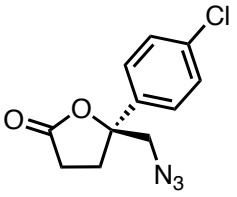

DAD1 A, Sig=230,4 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-22 08-08-53\RZ-4-172-RAC.D)



Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.977	BB	0.6513	1820.84253	40.13295	50.0045
2	24.279	BB	0.7439	1820.51843	31.80194	49.9955
Totals :				3641.36096	71.93489	

Sample Name: RZ-4-172



4c

```
    ============================================================================
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    Acq. Instrument : Instrument 1                        Location : Vial 17
    Injection Date  : 7/22/2014 10:09:30 AM                    Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 2 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-22 08-08-53\RZ-5IPA-1ML-2013-.M
```
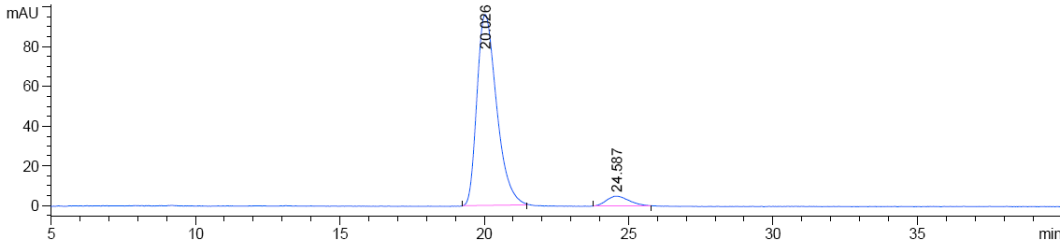
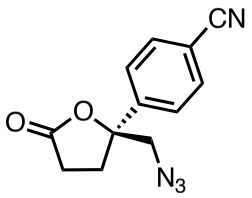

DAD1 A, Sig=230,4 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-22 08-08-53\RZ-4-172.D)



Signal 1: DAD1 A, Sig=230,4 Ref=360,100

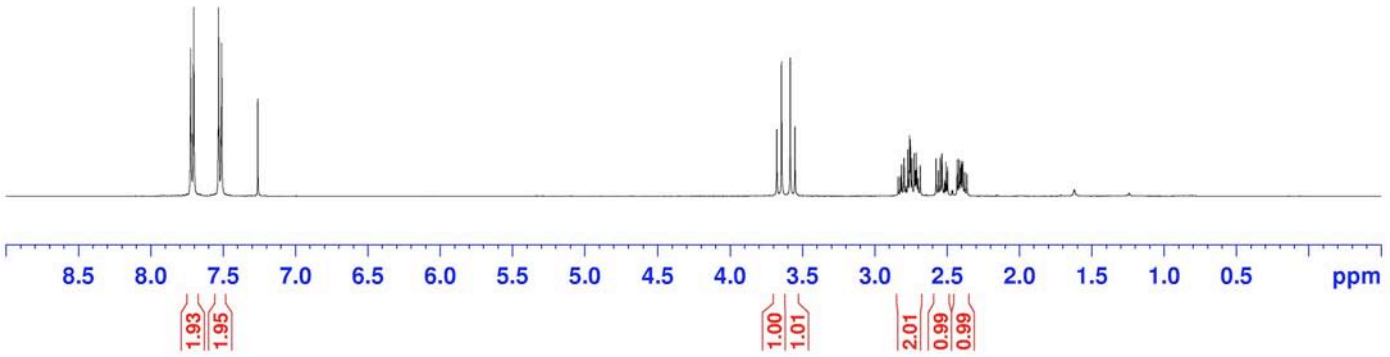
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.026	BB	0.7173	4562.40234	96.20024	94.4555
2	24.587	BB	0.6477	267.80951	4.91480	5.5445
Totals :				4830.21185	101.11505	

RZ-4-190-H

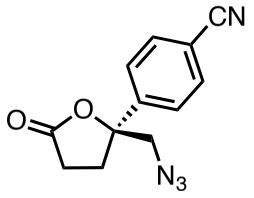


4d

^{1}H NMR



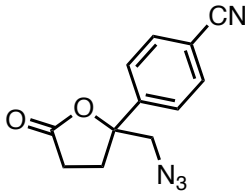
RZ-4-190-C



4d

^{13}C NMR

HPLC traces for 4d:



(±)-**4d**

Sample Name: RZ-4-190-RAC

```
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    Acq. Instrument : Instrument 1                        Location : Vial 17
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                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
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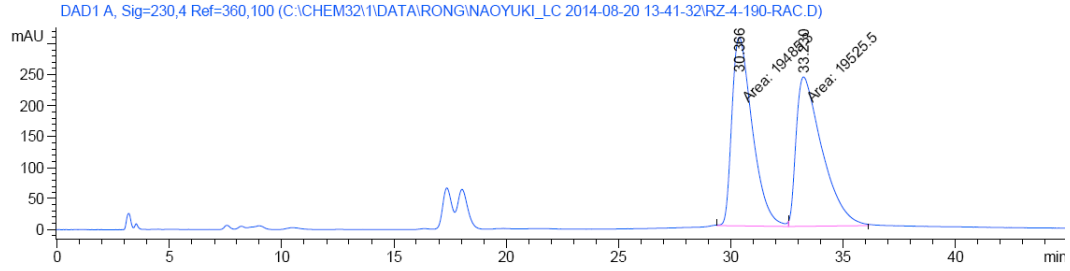


```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  30.366 MM    1.0648 1.94853e4   304.99750  49.9484
   2  33.230 MM    1.3457 1.95255e4   241.82451  50.0516

Totals :                  3.90108e4   546.82201
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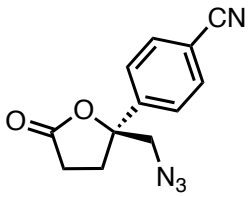
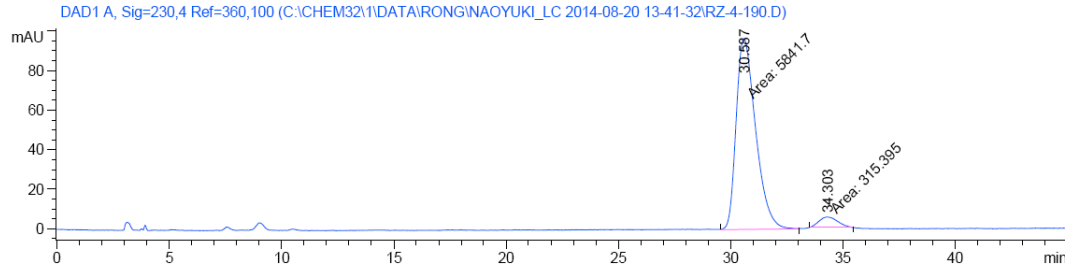
Sample Name: RZ-4-190



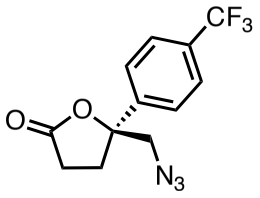
4d

```
    ======================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 8/20/2014 2:30:02 PM                    Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-20 13-41-32\RZ-15IPA-2014.M
```



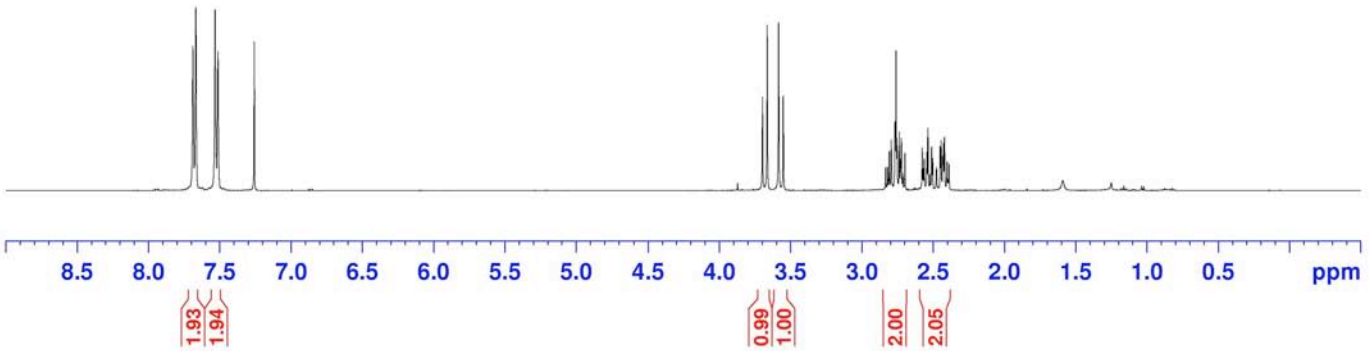

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  30.587 MM    1.0066 5841.70020   96.71944  94.8775
   2  34.303 MM    0.9822  315.39474    5.35182   5.1225

Totals :                  6157.09494  102.07127
```

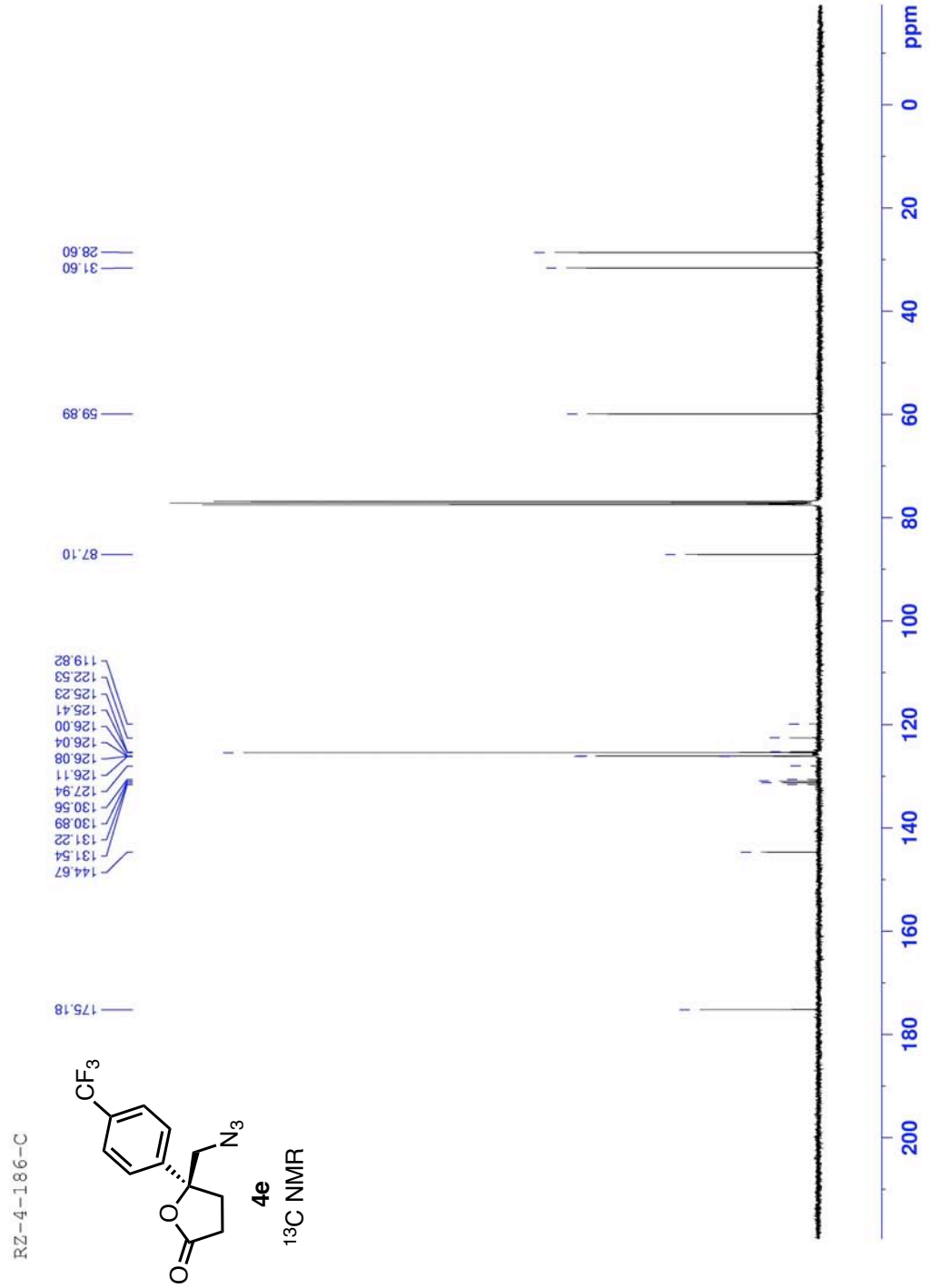
RZ-4-186-H



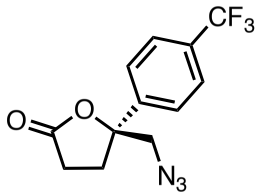
4e

^{1}H NMR



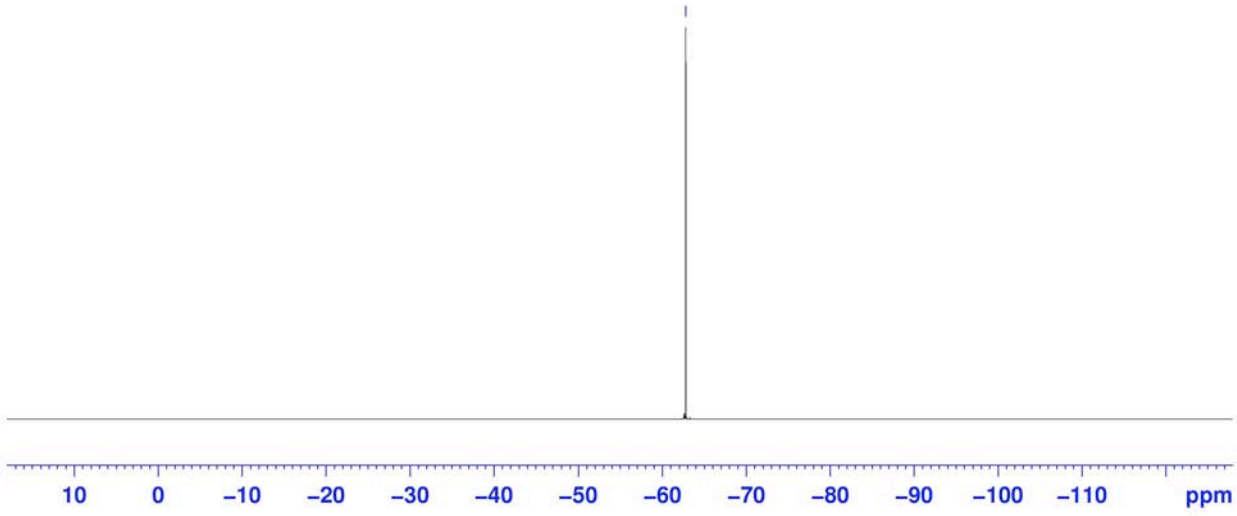

RZ-4-186-C
CF3
N3
O
O
4e
13C NMR
175.18
144.67
131.54
131.22
130.89
130.56
127.94
126.11
126.08
126.04
126.00
125.41
125.23
122.53
119.82
87.10
59.89
31.60
28.60
ppm
0
20
40
60
80
100
120
140
160
180
200

RZ-4-186-F

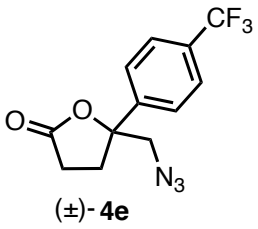


4e

^{19}F NMR



HPLC traces for 4e:

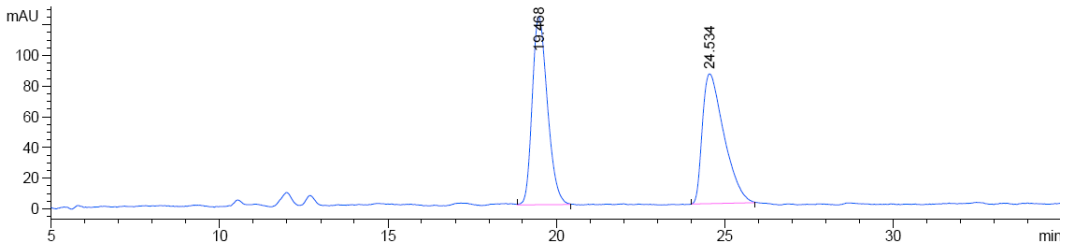


(±)-**4e**

Sample Name: RZ-4-186-RAC

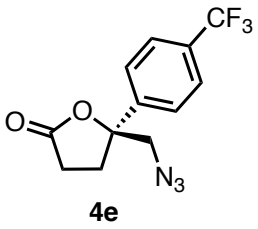
```
    ======================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 17
    Injection Date  : 8/19/2014 8:53:02 AM                     Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-19 08-50-48\RZ-5IPA-1ML-2013-.M
```

DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-19 08-50-48\RZ-4-186-RAC.D)



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.468	VB	0.4645	3856.93750	122.78101	50.3897
2	24.534	BB	0.6219	3797.28760	84.88390	49.6103
Totals :				7654.22510	207.66491	

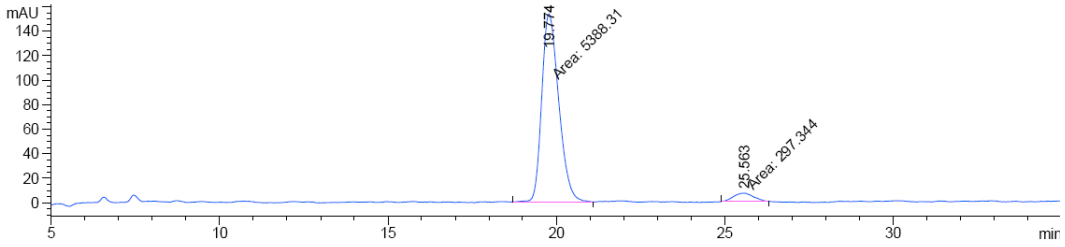


4e

Sample Name: RZ-4-186

```
    ======================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 8/19/2014 2:53:19 PM                     Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 12 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-19 14-50-59\RZ-5IPA-1ML-2013-.M
```

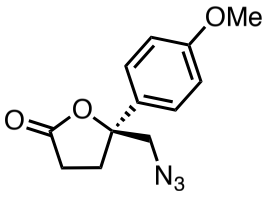
DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-19 14-50-59\RZ-4-186.D)



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

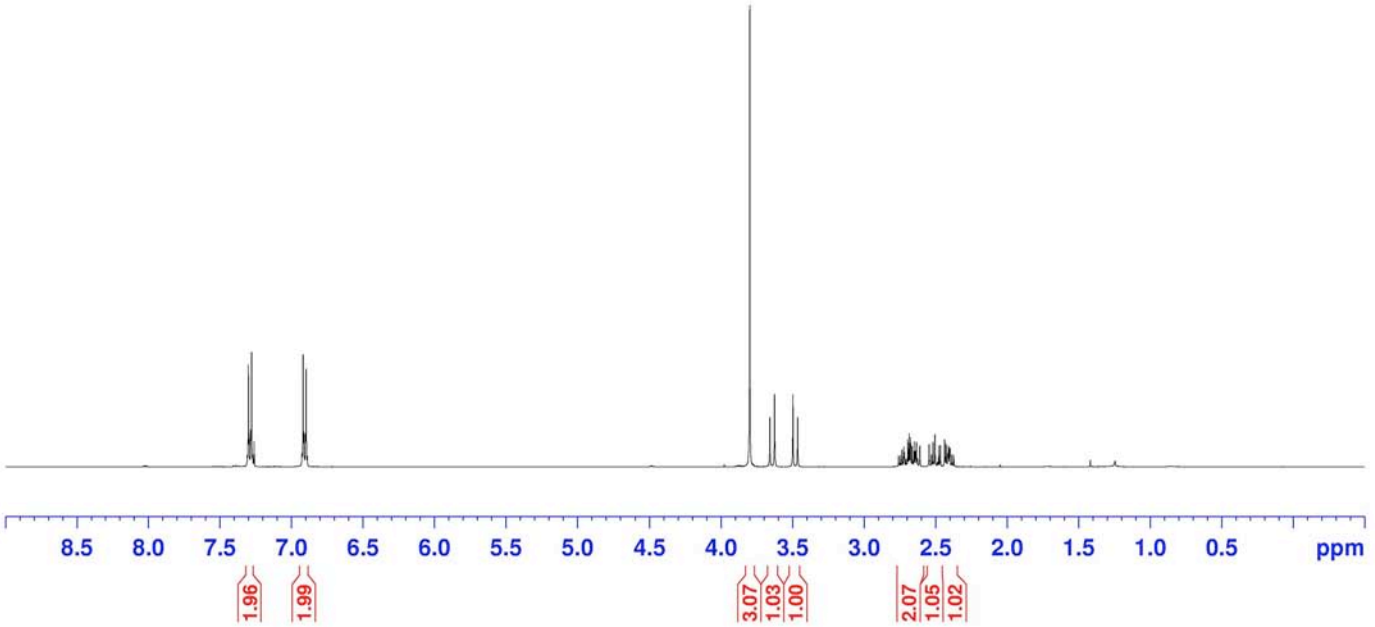
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.774	MM	0.5860	5388.30957	153.24788	94.7703
2	25.563	MM	0.7042	297.34396	7.03758	5.2297
Totals :				5685.65353	160.28546	

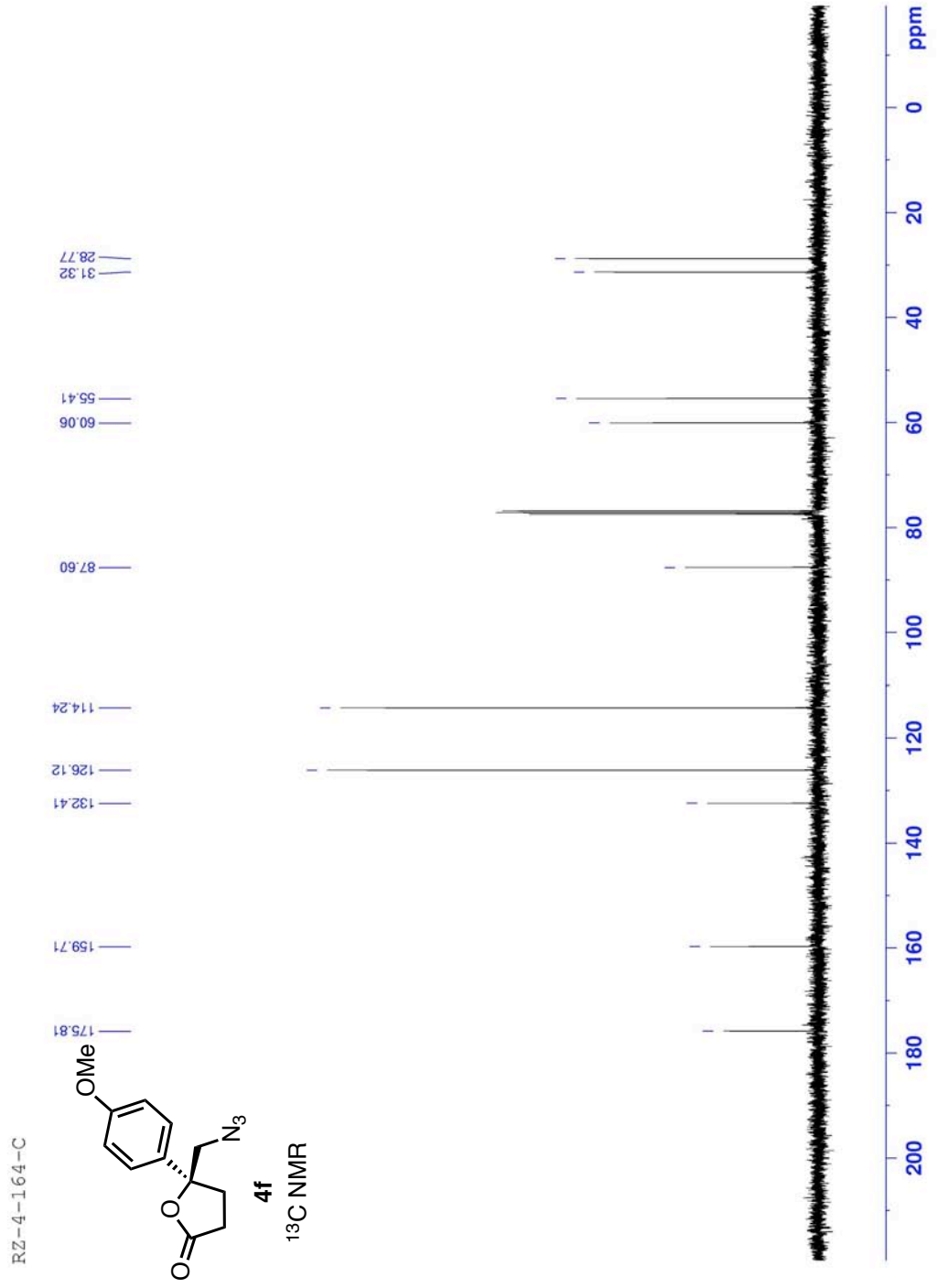
RZ-4-164-H



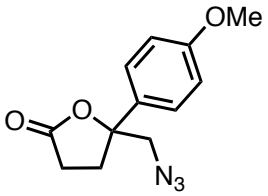
4f

^{1}H NMR



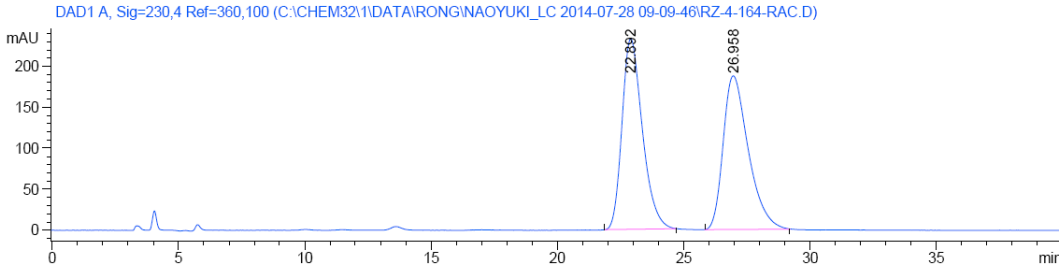

RZ-4-164-C
OMe
N3
O
O
4f
13C NMR
175.81
159.71
132.41
126.12
114.24
87.60
60.06
55.41
31.32
28.77
ppm
200
180
160
140
120
100
80
60
40
20
0

HPLC traces for 4f:

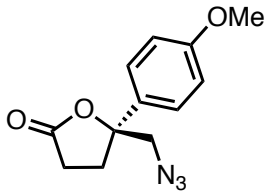


(±)- **4f**

```
Sample Name: RZ-4-164-RAC

    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 1                        Location : Vial 17
    Injection Date  : 7/28/2014 9:53:18 AM                    Inj :   1
                                                        Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-28 09-09-46\RZ-5IPA-1ML-2013-.M
```

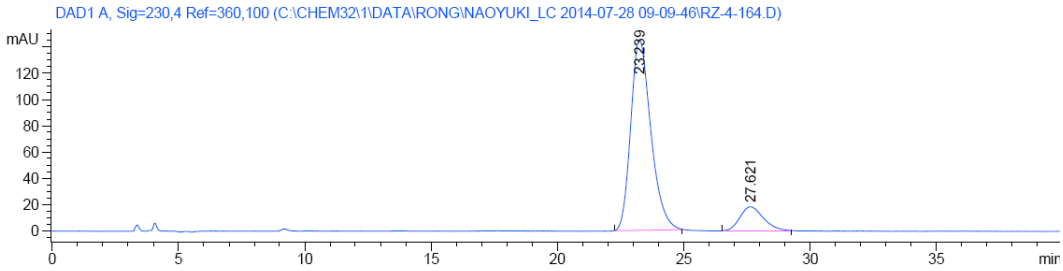



```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  22.892 BB    0.8382 1.31085e4   233.07202  50.1893
   2  26.958 BB    0.9848 1.30096e4   187.66890  49.8107

Totals :                  2.61181e4   420.74092
```



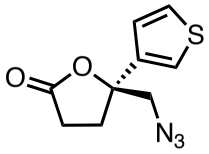
4f

```
Sample Name: RZ-4-164

    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 7/28/2014 9:12:06 AM                    Inj :   1
                                                        Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-28 09-09-46\RZ-5IPA-1ML-2013-.M
```



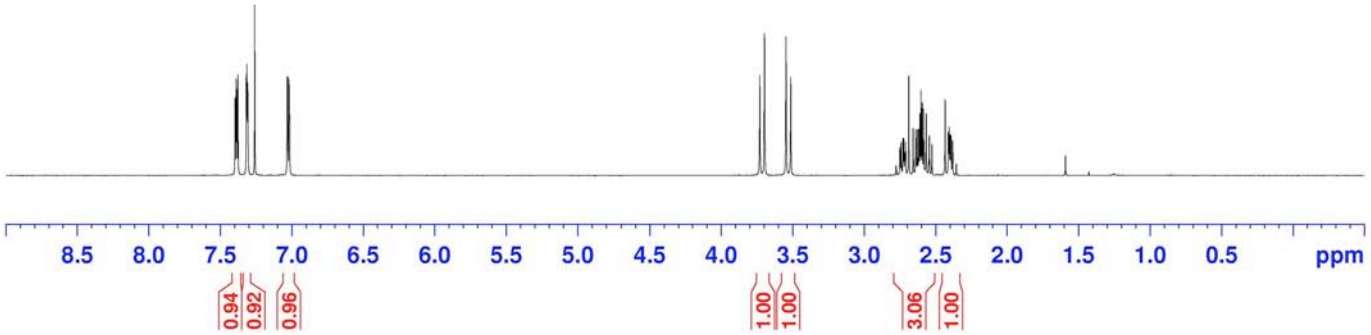

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  23.239 BB    0.8258 8031.23877  145.08575  87.2371
   2  27.621 BB    0.7676 1174.97656   18.23970  12.7629

Totals :                  9206.21533  163.32545
```

RZ-4-218A-H

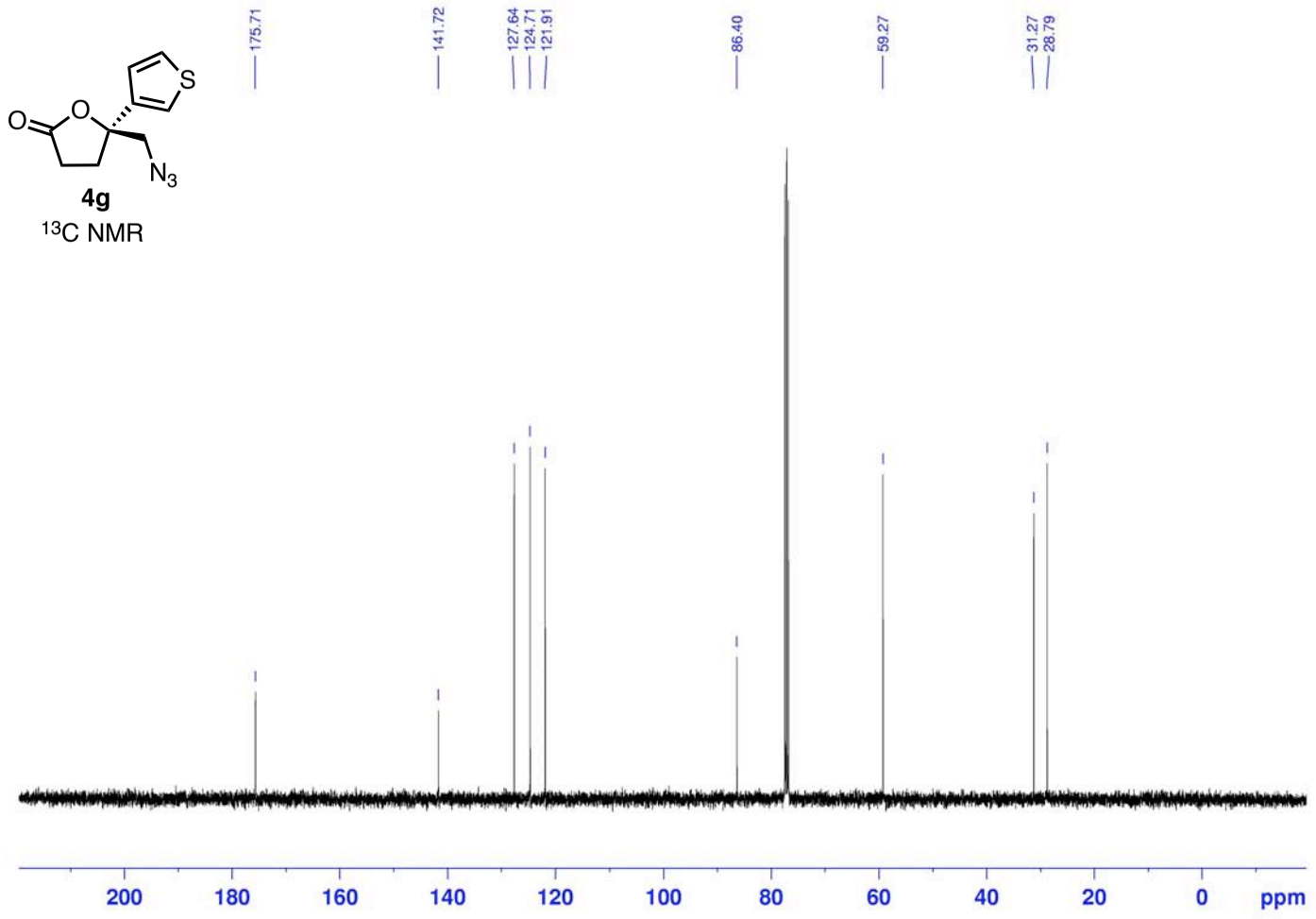


4g

^{1}H NMR



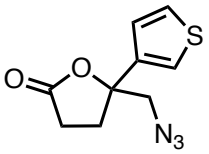
RZ-4-218A-C



4g

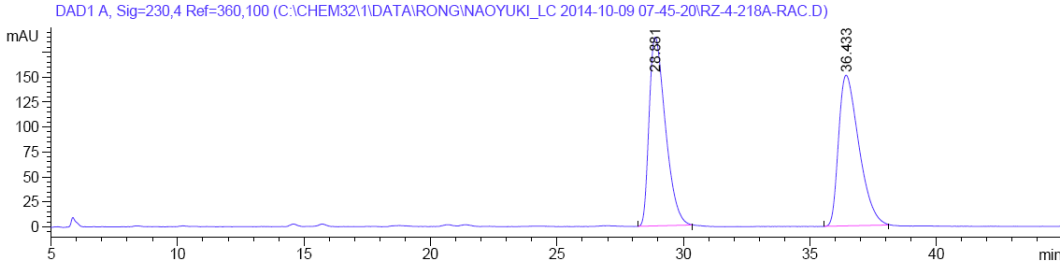
^{13}C NMR

HPLC traces for 4g:



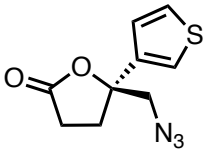
(±)-**4g**

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-10-09 07-45-20\RZ-4-218A-RAC.D
Sample Name: RZ-4-218A-RAC

    ======================================================================
    Acq. Operator   : RZ                              Seq. Line :   6
    Acq. Instrument : Instrument 1                     Location : Vial 19
    Injection Date  : 10/9/2014 11:09:11 AM               Inj :   1
                                                    Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-10-09 07-45-20\RZ-5IPA-1ML-2013-.M
```

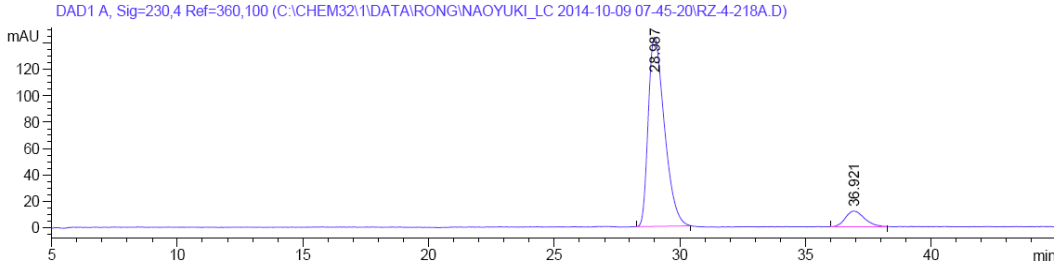



```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  28.881 BB    0.6575 8484.71289  189.09726  50.0582
   2  36.433 BB    0.7776 8464.98535  151.09933  49.9418

Totals :                  1.69497e4   340.19659
```

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-10-09 07-45-20\RZ-4-218A.D
Sample Name: RZ-4-218A

    ======================================================================
    Acq. Operator   : RZ                              Seq. Line :   4
    Acq. Instrument : Instrument 1                     Location : Vial 17
    Injection Date  : 10/9/2014 9:36:43 AM                Inj :   1
                                                    Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 12 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-10-09 07-45-20\RZ-5IPA-1ML-2013-.M
```

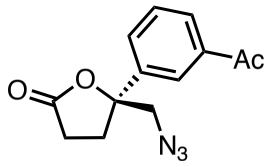


4g



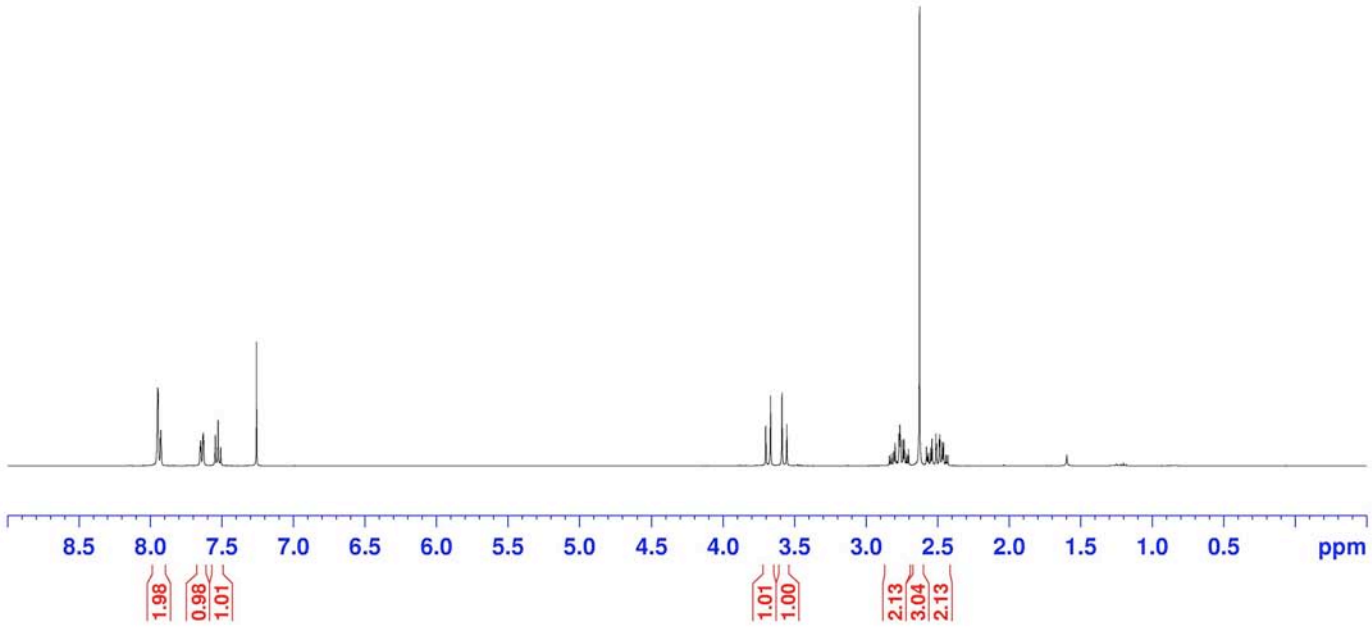

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  28.987 BB    0.6492 6429.18652  143.35242  91.1065
   2  36.921 BB    0.6312  627.59711   11.86257   8.8935

Totals :                  7056.78363  155.21498
```

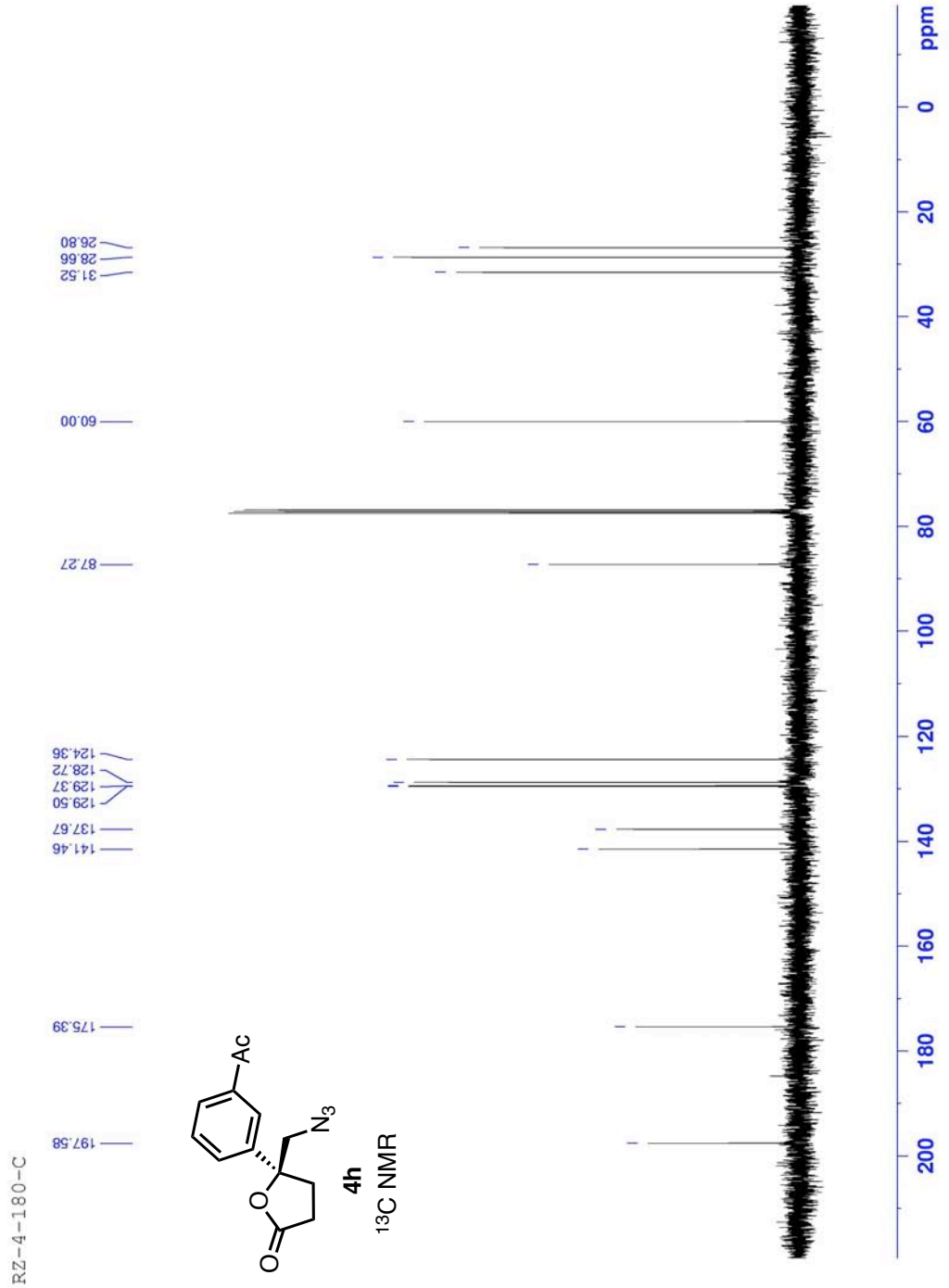
RZ-4-180-H



4h

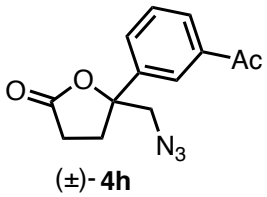
^{1}H NMR




RZ-4-180-C
197.58
175.39
141.46
137.67
129.50
129.37
128.72
124.36
87.27
60.00
31.52
28.66
26.80
Ac
N3
O
O
4h
13C NMR
ppm
0
20
40
60
80
100
120
140
160
180
200

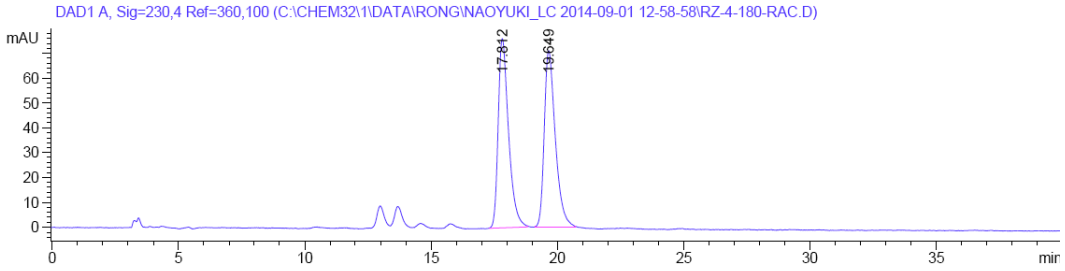
HPLC traces for 4h:

Sample Name: RZ-4-180-RAC



(±)-**4h**

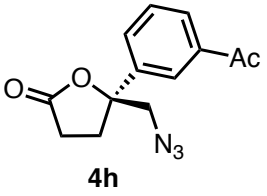
```
    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 9/1/2014 1:01:22 PM                      Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-09-01 12-58-58\RZ-SHUTDOWN.M
```



Signal 1: DAD1 A, Sig=230,4 Ref=360,100

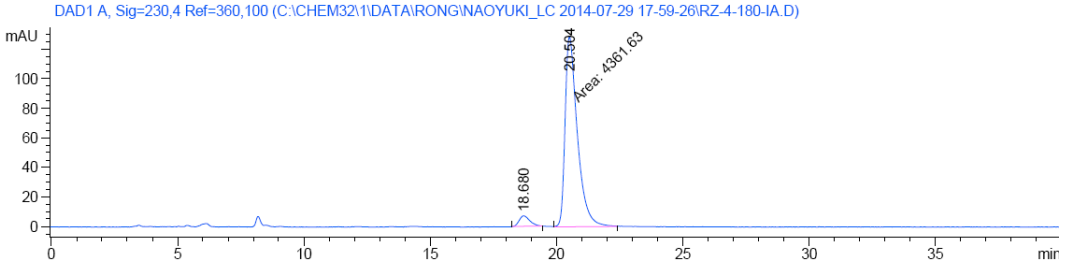
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.812	BB	0.4240	2168.58911	76.19683	50.0957
2	19.649	BB	0.4531	2160.30054	70.98513	49.9043
Totals :				4328.88965	147.18196	

Sample Name: RZ-4-180



4h

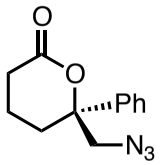
```
    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 7/29/2014 6:01:45 PM                     Inj :   1
                                                       Inj Volume : 1 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-29 17-59-26\RZ-SHUTDOWN.M
```



Signal 1: DAD1 A, Sig=230,4 Ref=360,100

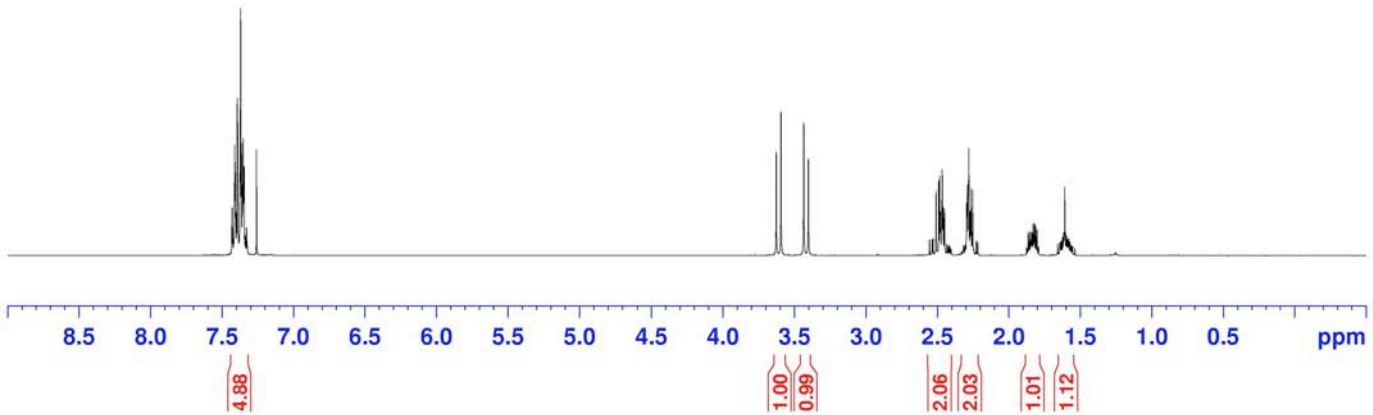
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.680	BB	0.3921	219.16219	7.26251	4.7844
2	20.504	MM	0.5649	4361.62939	128.67712	95.2156
Totals :				4580.79158	135.93964	

RZ-4-158-H

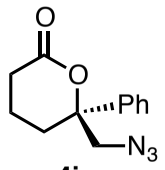


4i

^{1}H NMR



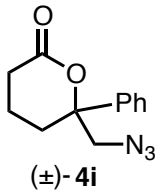
RZ-4-158-C



4i

^{13}C NMR

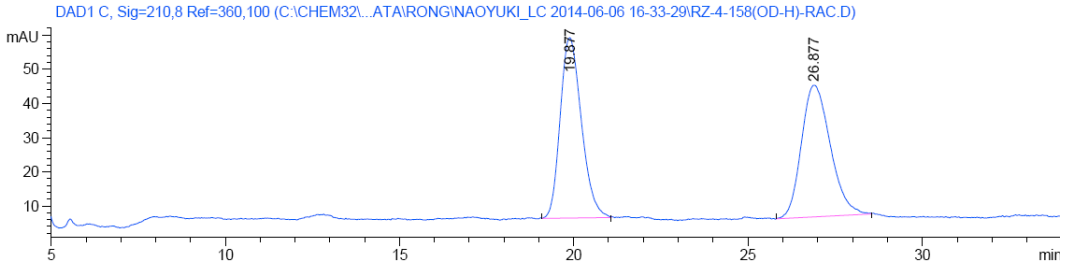
HPLC traces for 4i:



(±)-**4i**

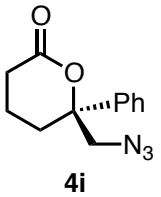
Sample Name: RZ-4-158-rac

```
    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 17
    Injection Date  : 6/6/2014 4:34:38 PM                     Inj :   1
                                                        Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-06-06 16-33-29\RZ-5IPA-1ML-2013-.M
```



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

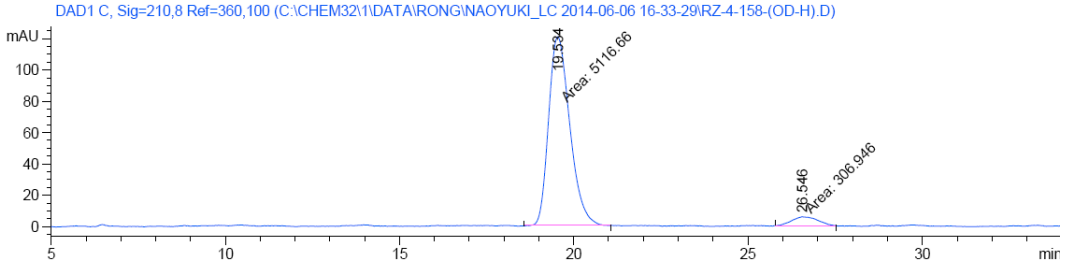
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.877	VB	0.5830	2242.23364	52.84458	50.1395
2	26.877	BB	0.6945	2229.76001	38.56628	49.8605
Totals :				4471.99365	91.41086	



4i

Sample Name: RZ-4-158

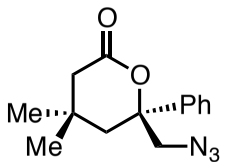
```
    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   3
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 6/6/2014 5:45:50 PM                     Inj :   1
                                                        Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 0.8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-06-06 16-33-29\RZ-5IPA-1ML-2013-.M
```



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

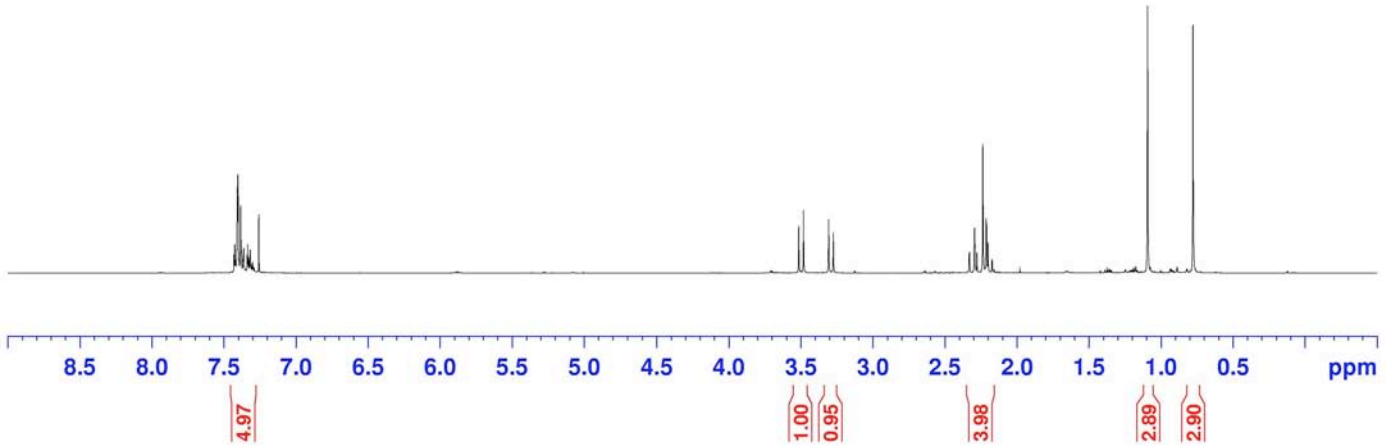
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.534	MM	0.7066	5116.65674	120.68810	94.3405
2	26.546	MM	0.8724	306.94647	5.86426	5.6595
Totals :				5423.60321	126.55235	

RZ-4-208-H

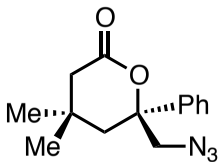


4j

^{1}H NMR



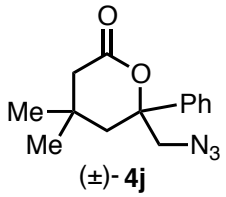
RZ-4-208-C



4j

^{13}C NMR

HPLC traces for 4j:

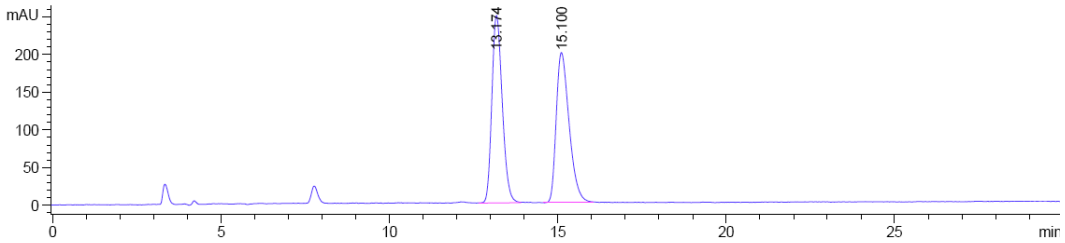


(±)-**4j**

Sample Name: RZ-4-208-RAC

```
    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 9/16/2014 3:33:43 PM                    Inj :   1
                                                        Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\ZY 2014-09-16 15-31-25\RZ-5IPA-1ML-2013-.M
```

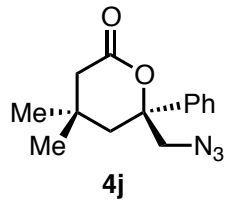
DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\ZY 2014-09-16 15-31-25\RZ-4-208-RAC.D)



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.174	VV	0.3313	5349.82373	248.41367	50.0666
2	15.100	VV	0.4024	5335.59473	199.26160	49.9334
Totals :				1.06854e4	447.67526	

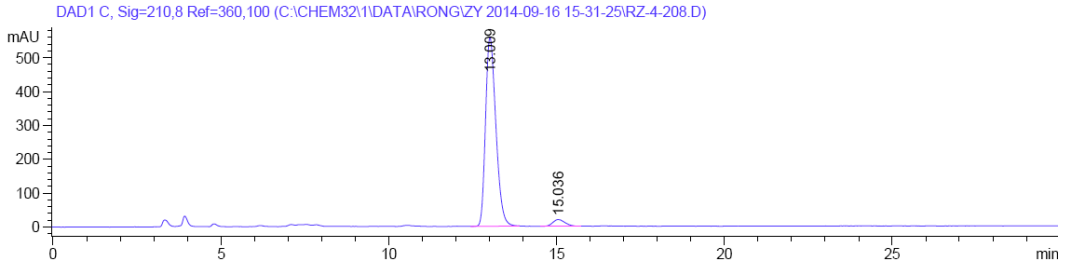
Sample Name: RZ-4-208



4j

```
    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 1                        Location : Vial 17
    Injection Date  : 9/16/2014 4:05:01 PM                    Inj :   1
                                                        Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\ZY 2014-09-16 15-31-25\RZ-5IPA-1ML-2013-.M
```

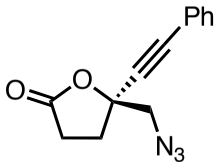
DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\ZY 2014-09-16 15-31-25\RZ-4-208.D)



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

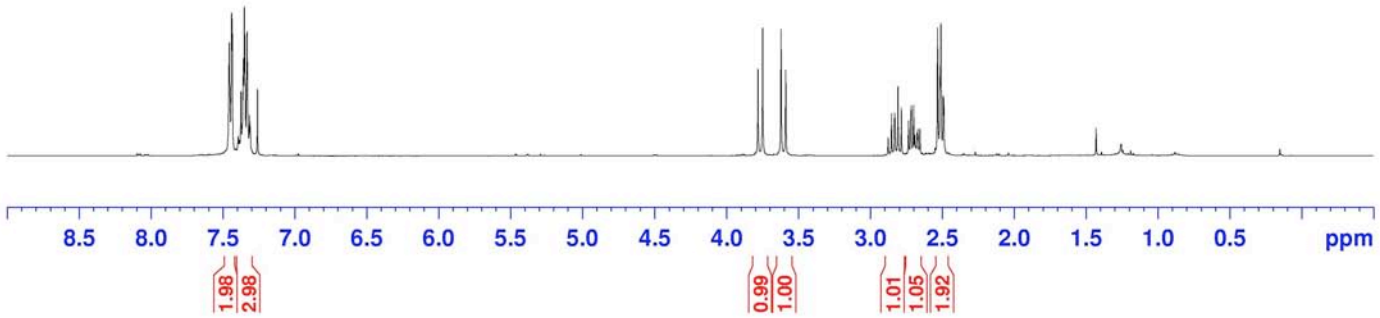
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.009	VB	0.3308	1.19998e4	558.26044	95.8692
2	15.036	BV	0.3174	517.04474	20.01099	4.1308
Totals :				1.25169e4	578.27143	

RZ-4-188-H

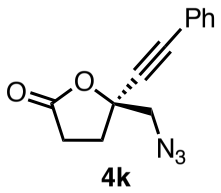


4k

^{1}H NMR



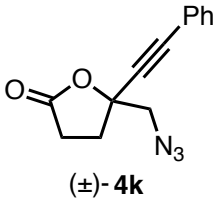
RZ-4-188-C



4k

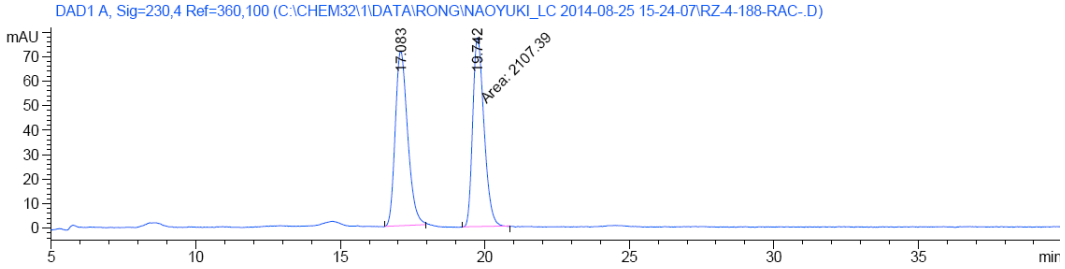
^{13}C NMR

HPLC traces for 4k:



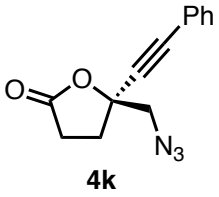
(±)- **4k**

```
Sample Name: RZ-4-188-RAC

    ============================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 8/25/2014 4:07:52 PM                     Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 16 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-25 15-24-07\RZ-5IPA-1ML-2013-.M
```

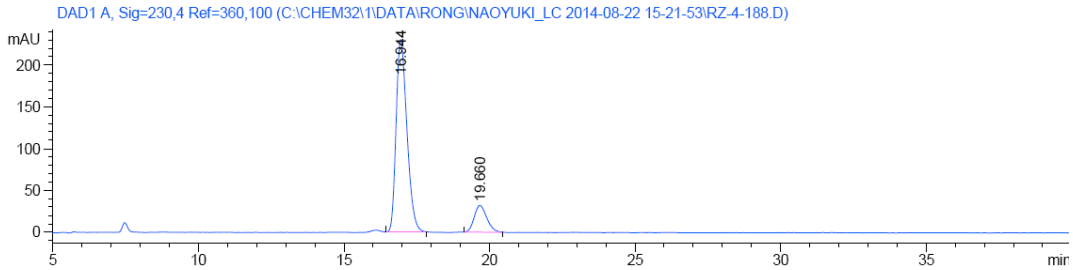



```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.083 BB    0.4547 2134.21069   71.40211  50.3162
   2  19.742 MM    0.4543 2107.38574   77.31142  49.6838

Totals :                  4241.59644  148.71352
```

```
Sample Name: RZ-4-188

    ============================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 8/22/2014 3:24:11 PM                     Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-22 15-21-53\RZ-5IPA-1ML-2013-.M
```

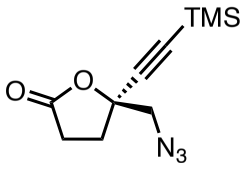


4k



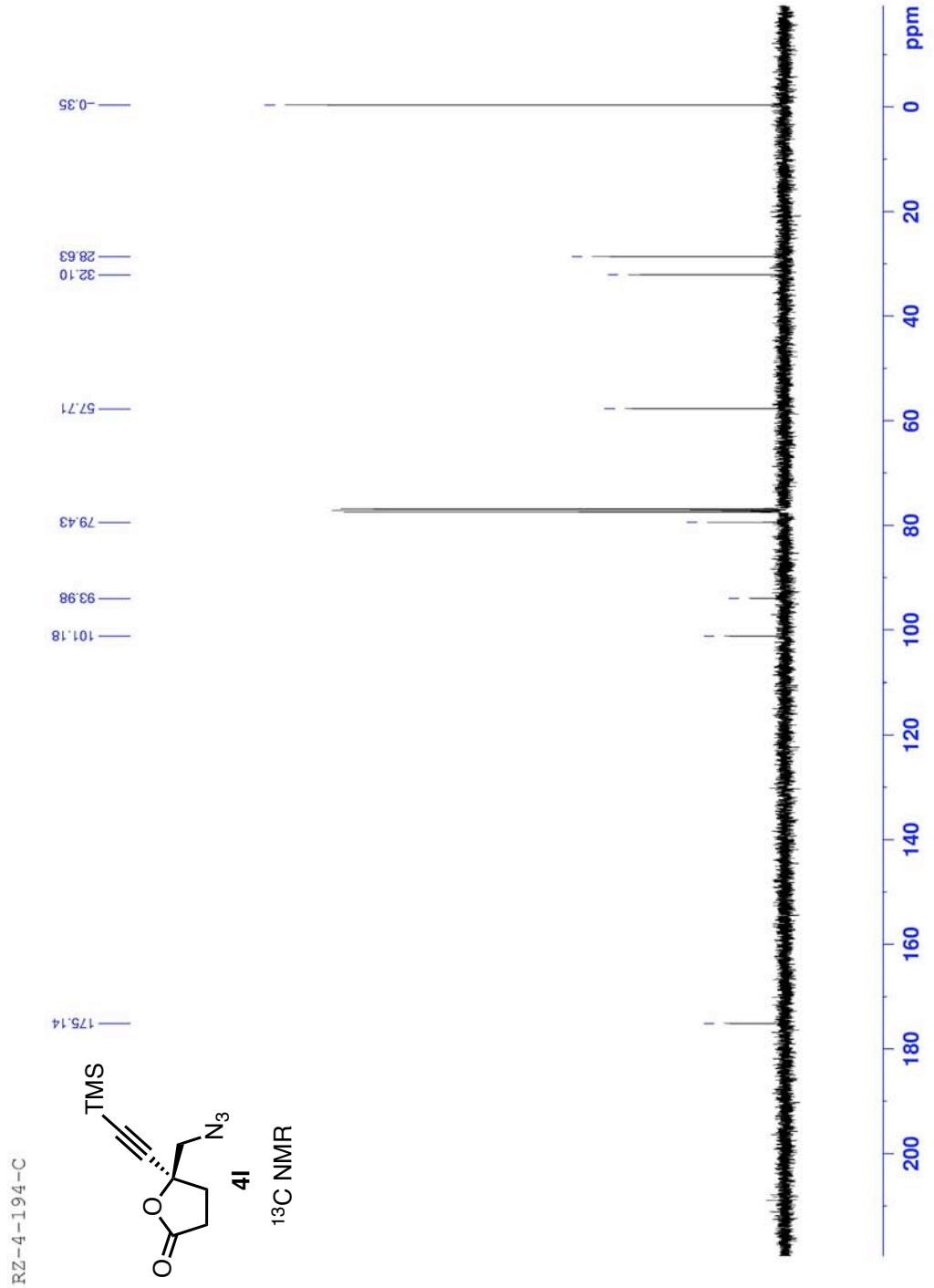

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.944 VB    0.4069 5986.67236  230.57608  85.8726
   2  19.660 BB    0.4423  984.89868   32.43007  14.1274

Totals :                  6971.57104  263.00615
```

RZ-4-194-H

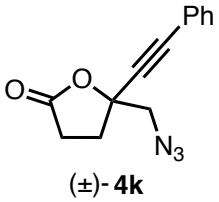


4l

^{1}H NMR


RZ-4-194-C
TMS
N3
O
O
4l
13C NMR
175.14
101.18
93.98
79.43
57.71
32.10
28.63
-0.35
ppm
200
180
160
140
120
100
80
60
40
20
0

HPLC traces for compound 4k derived from 4l:

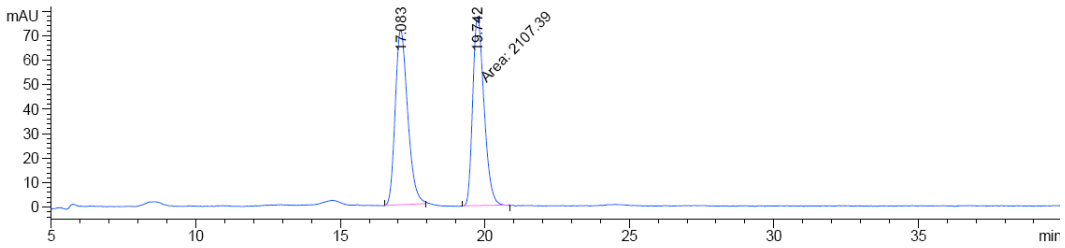


(±)- **4k**

Sample Name: RZ-4-188-RAC

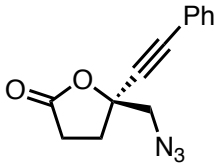
```
==========================================================================
Acq. Operator   : RZ                                Seq. Line :   2
Acq. Instrument : Instrument 1                      Location : Vial 16
Injection Date  : 8/25/2014 4:07:52 PM                   Inj :   1
                                                  Inj Volume : 1 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 16 µl
Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-25 15-24-07\RZ-5IPA-1ML-2013-.M
```

DAD1 A, Sig=230,4 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-25 15-24-07\RZ-4-188-RAC-.D)



Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.083	BB	0.4547	2134.21069	71.40211	50.3162
2	19.742	MM	0.4543	2107.38574	77.31142	49.6838
Totals :				4241.59644	148.71352	

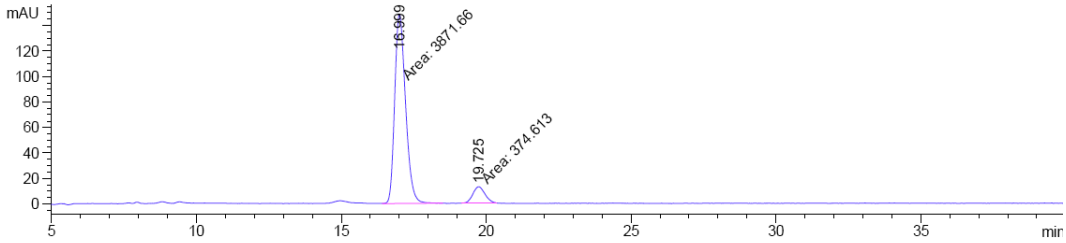


4k
(derived from **4l**)

Sample Name: RZ-4-195

```
==========================================================================
Acq. Operator   : RZ                                Seq. Line :   2
Acq. Instrument : Instrument 1                      Location : Vial 16
Injection Date  : 9/2/2014 6:38:01 PM                    Inj :   1
                                                  Inj Volume : 1 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
Acq. Method     : C:\CHEM32\1\DATA\RONG\ZY 2014-09-02 17-54-08\RZ-5IPA-1ML-2013-.M
```

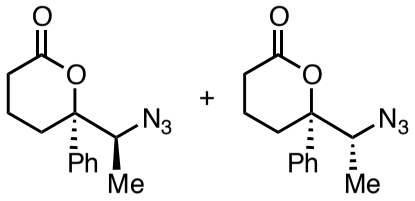
DAD1 A, Sig=230,4 Ref=360,100 (C:\CHEM32\1\DATA\RONG\ZY 2014-09-02 17-54-08\RZ-4-195-.D)



Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.999	MM	0.4347	3871.66455	148.43346	91.1778
2	19.725	MM	0.4853	374.61334	12.86601	8.8222
Totals :				4246.27789	161.29947	

RZ-4-202-H

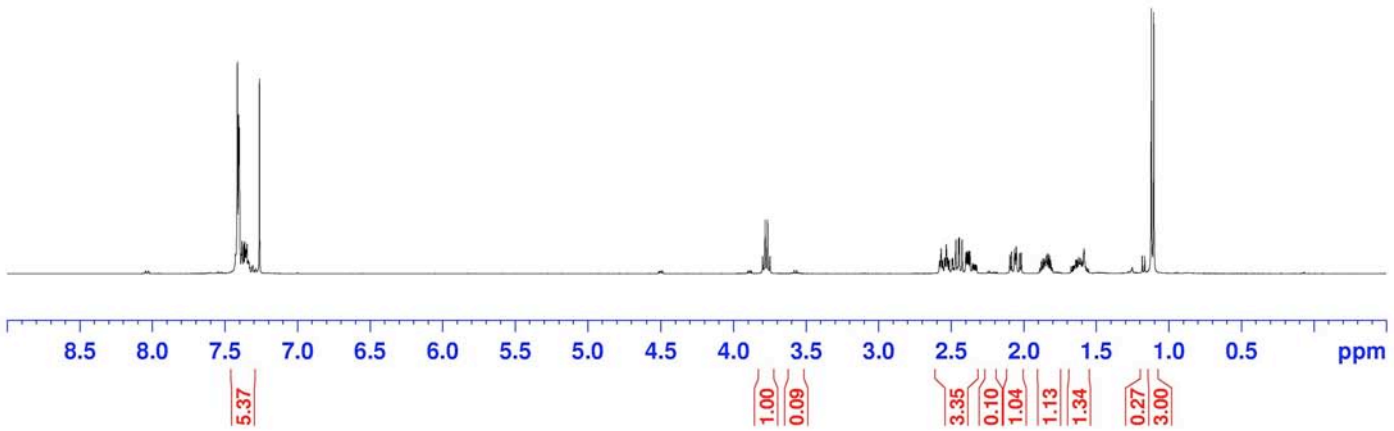


+

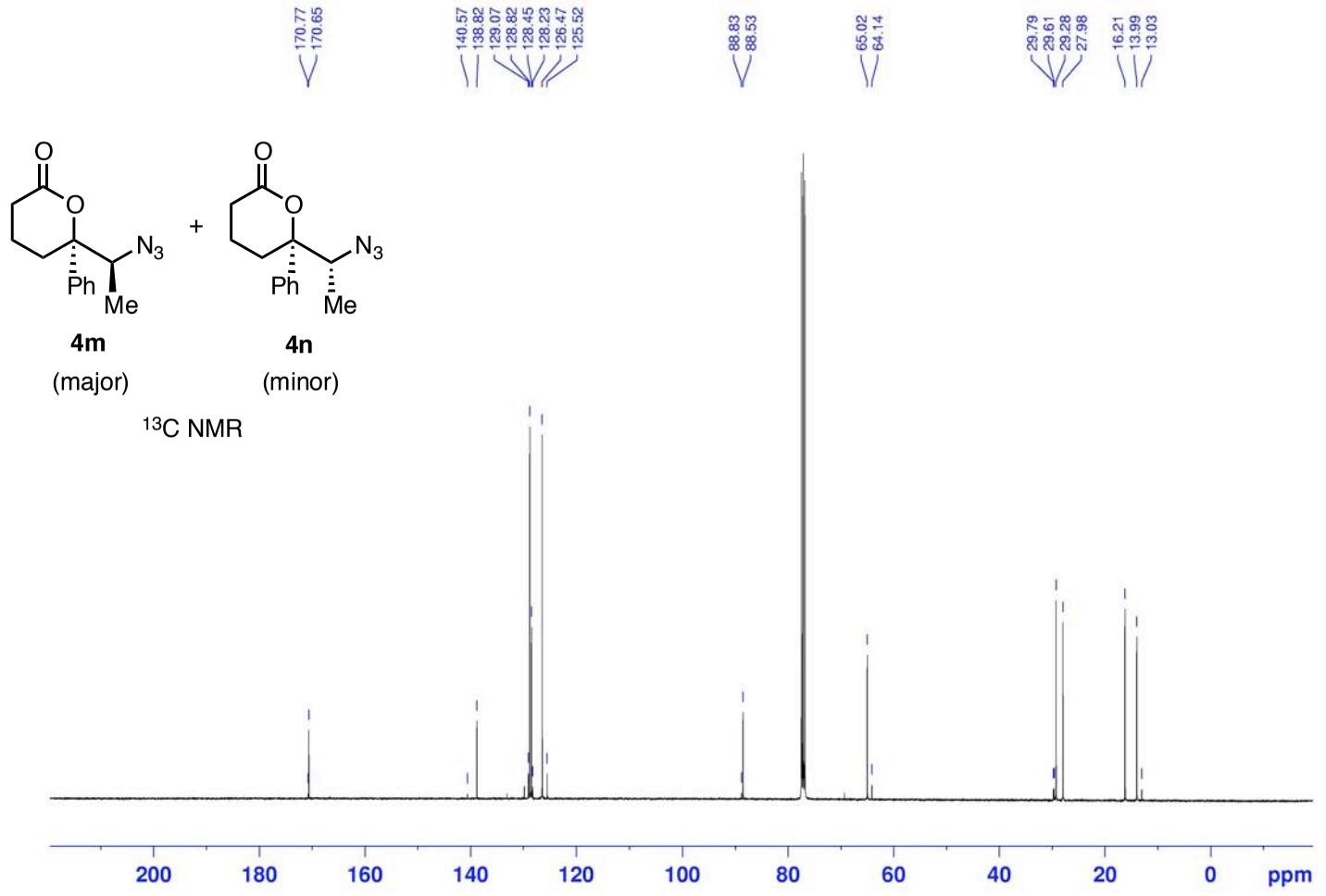
4m
(major)

4n
(minor)

^{1}H NMR

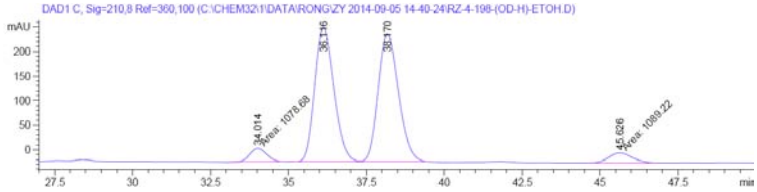


RZ_4-202-C


170.77
170.65
140.57
138.82
129.07
128.82
128.45
128.23
126.47
125.52
88.83
88.53
65.02
64.14
29.79
29.61
29.28
27.98
16.21
13.99
13.03
O
O
N3
Ph
Me
+
O
O
N3
Ph
Me
4m
(major)
4n
(minor)
13C NMR
200
180
160
140
120
100
80
60
40
20
0
ppm

HPLC traces for 4m and 4n:

```
Sample Name: RZ-4-198

================================================================
Acq. Operator   : RZ                          Seq. Line :  1
Acq. Instrument : Instrument 1                 Location : Vial 15
Injection Date  : 9/5/2014 2:42:58 PM             Inj :  1
                                             Inj Volume : 1 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
Acq. Method     : C:\CHEM32\1\DATA\RONG\ZY 2014-09-05 14-40-24\RZ-3-IPA-08ML-ETOH.M
```

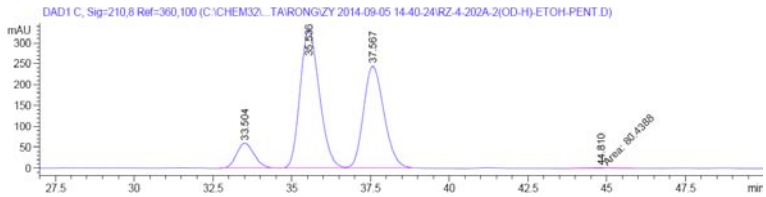


(±)-**4m** (major) + (±)-**4n** (minor)

```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  34.014 MM   0.6350 1078.68335   28.31096   4.1476
   2  36.116 BB   0.6560 1.18816e4   275.04449  45.6854
   3  38.170 BB   0.6922 1.19579e4   262.13486  45.9789
   4  45.626 MM   0.8747 1089.22266   20.75443   4.1881

Totals :                2.60074e4   586.24474
```

from (*E*)-**2m**

```
Sample Name: RZ-4-202A

================================================================
Acq. Operator   : RZ                          Seq. Line :  2
Acq. Instrument : Instrument 1                 Location : Vial 16
Injection Date  : 9/5/2014 3:39:26 PM             Inj :  1
                                             Inj Volume : 1 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 14 µl
Acq. Method     : C:\CHEM32\1\DATA\RONG\ZY 2014-09-05 14-40-24\RZ-3-IPA-08ML-ETOH.M
```



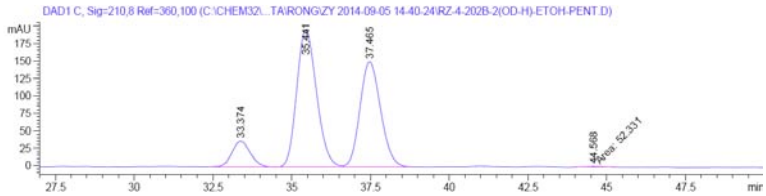
4m + **4n**

d.r. = 10 : 1

```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  33.504 BB   0.5563 2393.19165   59.87408   8.6433
   2  35.536 BV   0.6450 1.41347e4   329.12018  51.0492
   3  37.567 VB   0.6900 1.10800e4   243.89116  40.0169
   4  44.810 MM   1.0080   80.43877    1.32999   0.2905

Totals :                2.76884e4   634.21541
```

from (*Z*)-**2m**

```
Sample Name: RZ-4-202B

================================================================
Acq. Operator   : RZ                          Seq. Line :  3
Acq. Instrument : Instrument 1                 Location : Vial 17
Injection Date  : 9/5/2014 4:34:11 PM             Inj :  1
                                             Inj Volume : 1 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 20 µl
Acq. Method     : C:\CHEM32\1\DATA\RONG\ZY 2014-09-05 14-40-24\RZ-3-IPA-08ML-ETOH.M
```

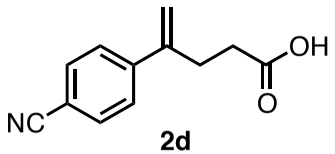


4m + **4n**

d.r. = 10 : 1

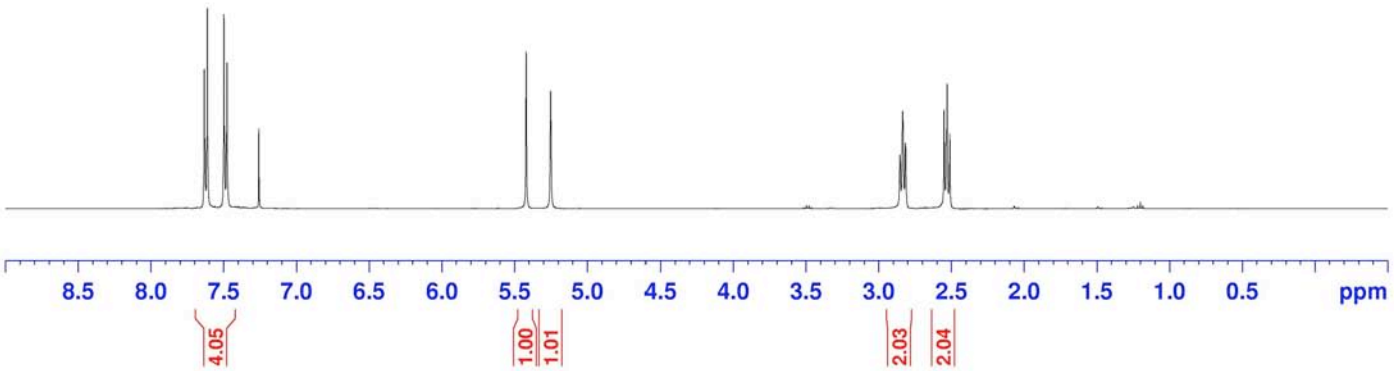
```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  33.374 BB   0.4942 1512.04651   37.04641   8.8356
   2  35.441 BB   0.6560 8655.40430  197.23421  50.5775
   3  37.465 BB   0.6805 6893.37061  151.03995  40.2811
   4  44.568 MM   0.6933   52.33103    1.25798   0.3058

Totals :                1.71132e4   386.57854
```

RZ-4-84-H

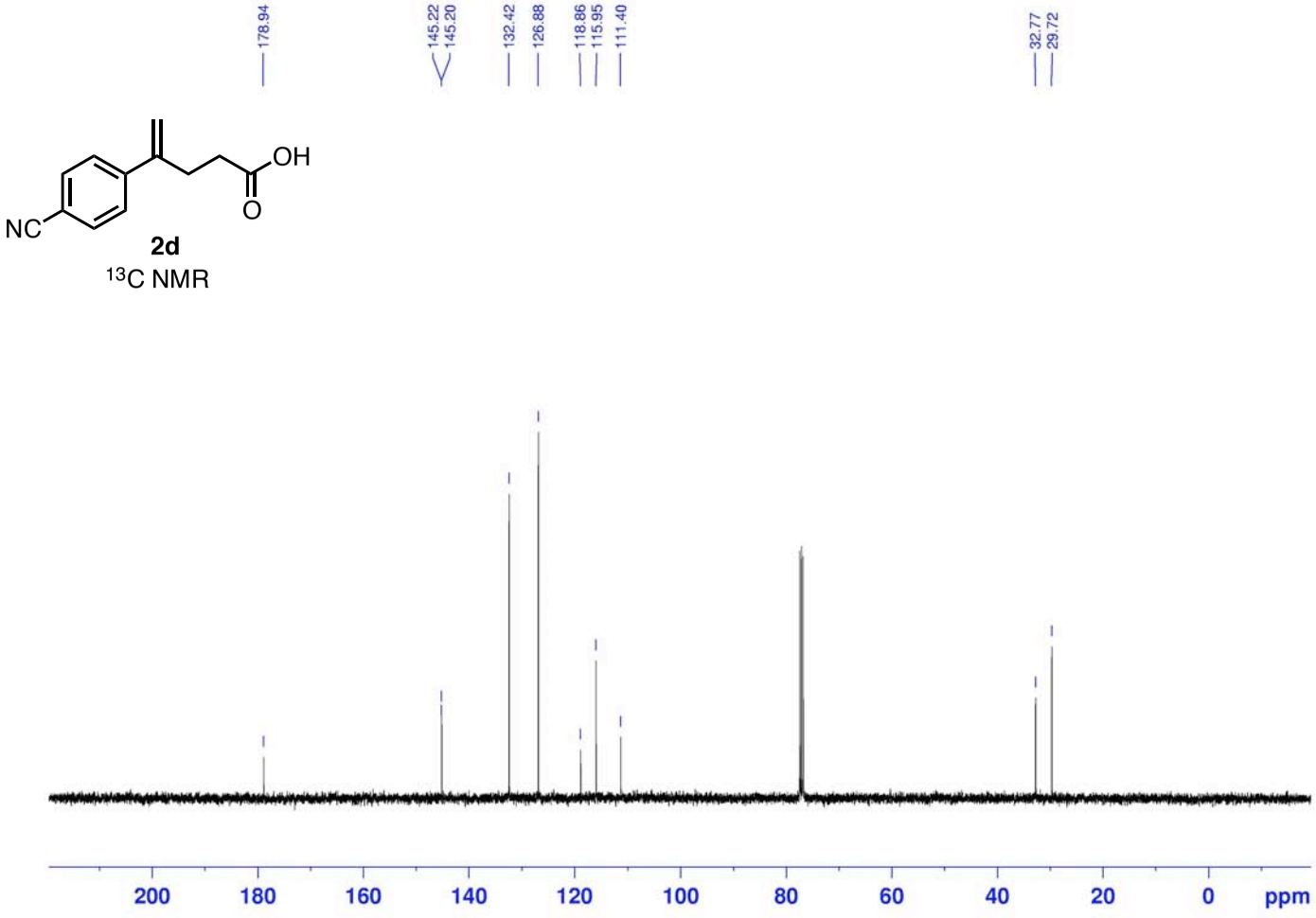


2d

^{1}H NMR



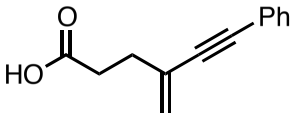
RZ-4-84-C



2d

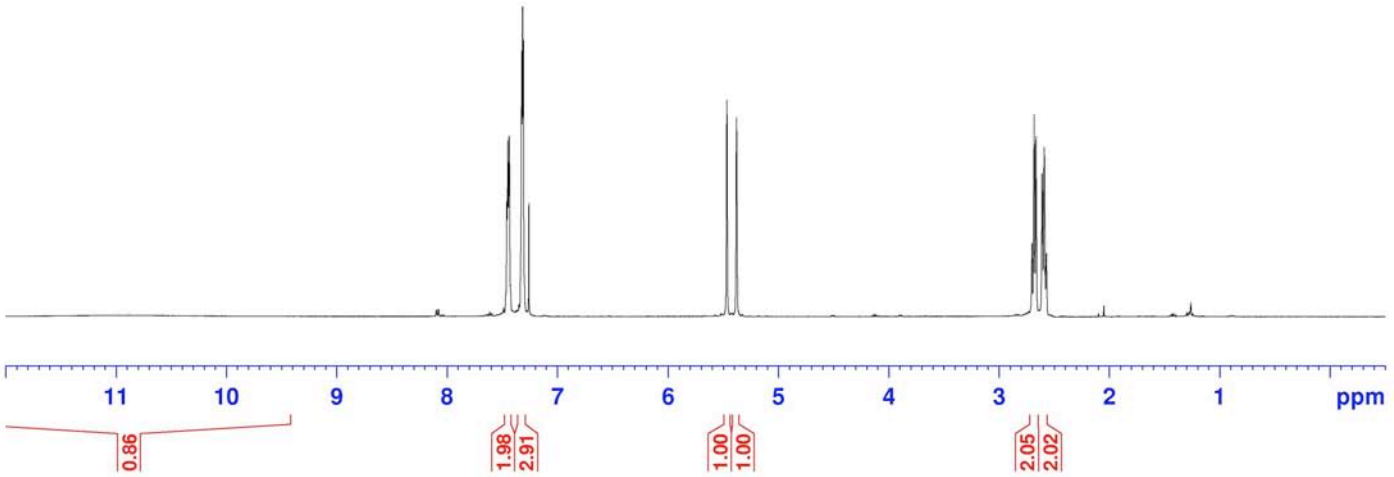
^{13}C NMR

RZ-4-162r2-H

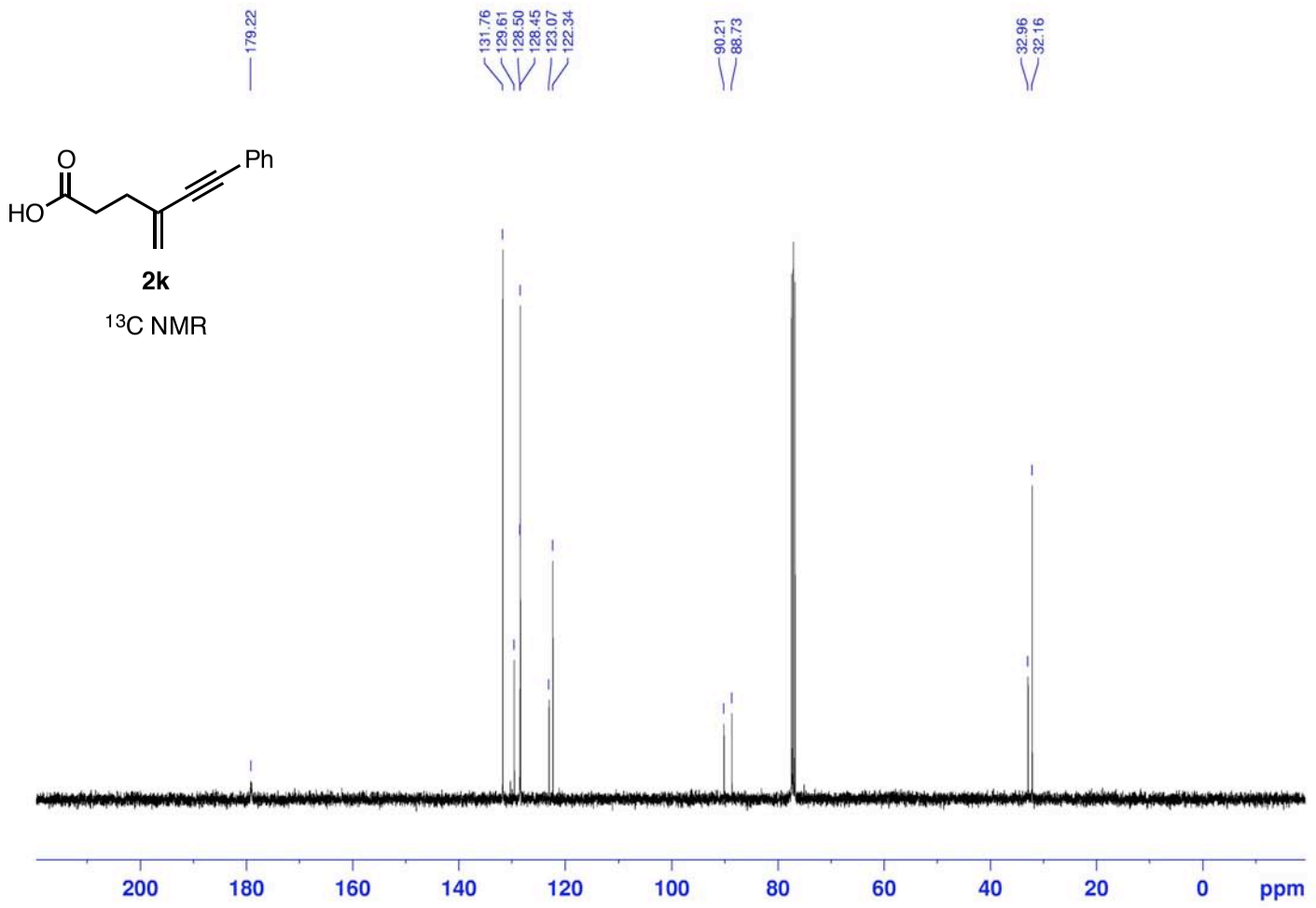


2k

^{1}H NMR



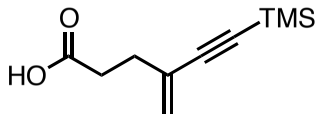
RZ-4-162r2-C



2k

^{13}C NMR

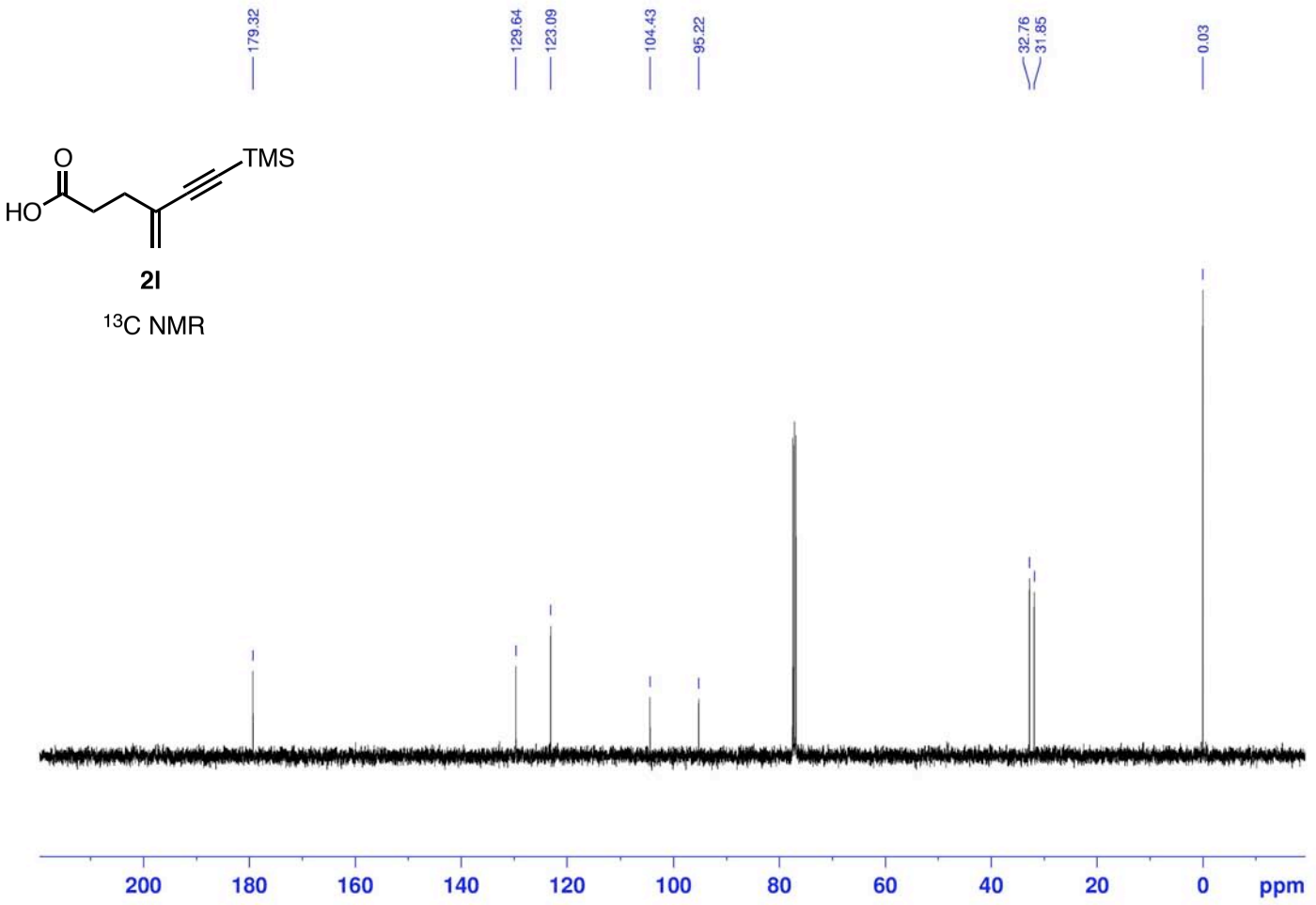
RZ-4-135-H



2l

^{1}H NMR

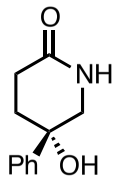
RZ-4-135-C



2l

^{13}C NMR

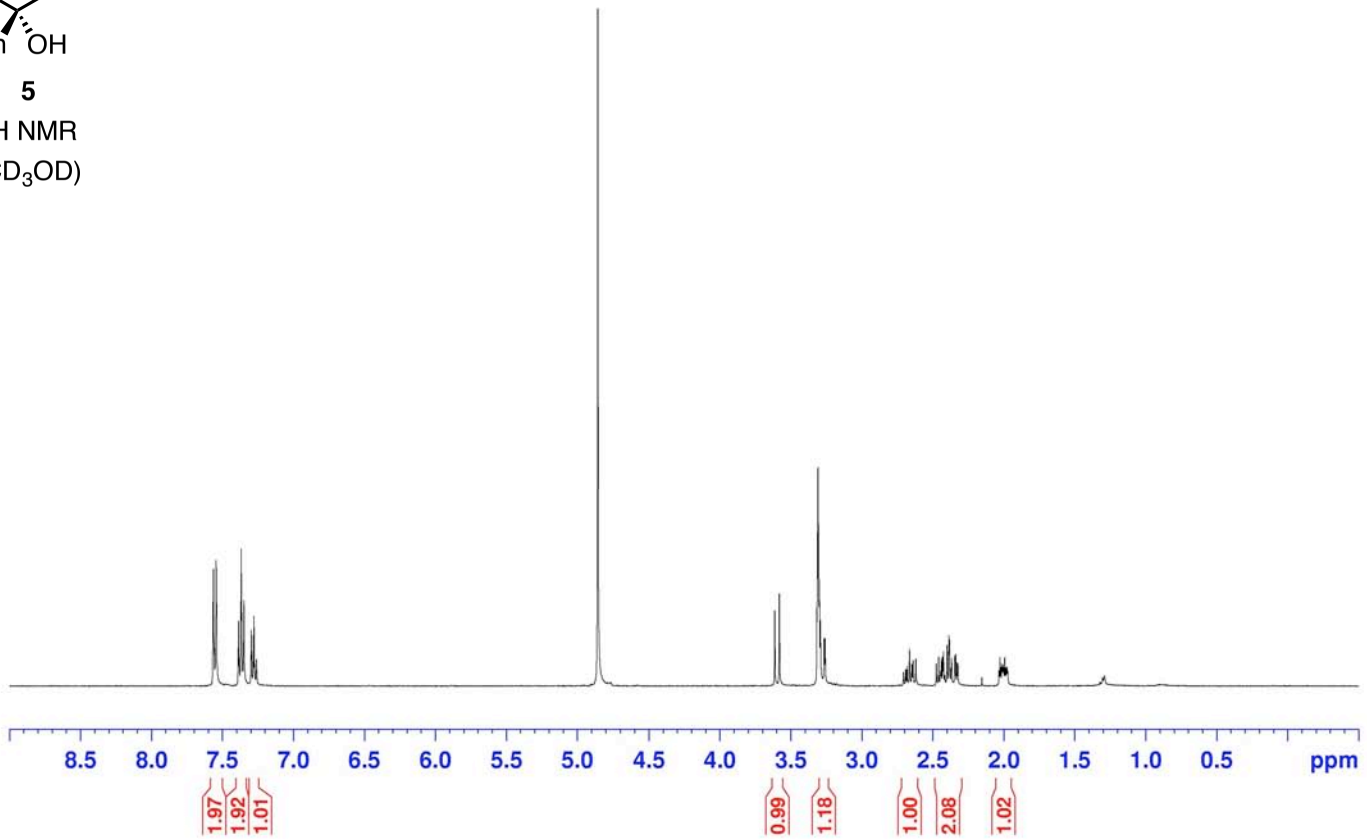
RZ-4-174-H (methanol-d4)



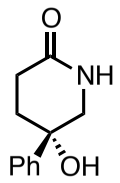
5

^{1}H NMR

(CD_3OD)



RZ-4-174-C (CD3OD)

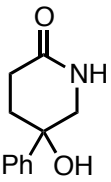


5

^{13}C NMR

(CD_3OD)

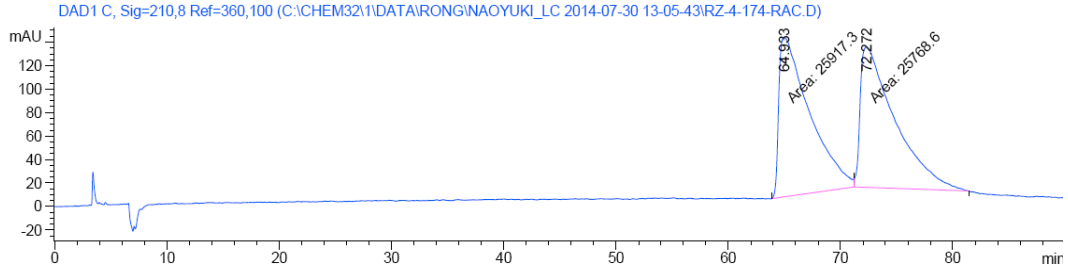
HPLC traces for 5:



(±)-**5**

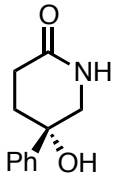
Sample Name: RZ-4-174-RAC

```
    ======================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 7/30/2014 1:08:06 PM                     Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-30 13-05-43\RZ-5IPA-2014-70MIN.M
```



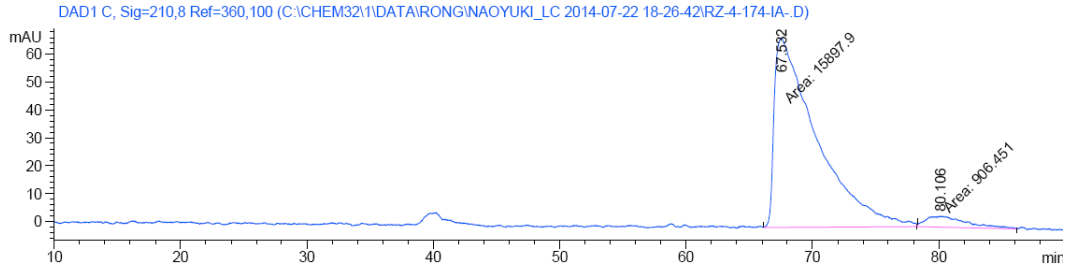

```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  64.933 MM    3.1716 2.59173e4   136.19344  50.1438
   2  72.272 MM    3.5883 2.57686e4   119.68867  49.8562

Totals :                  5.16859e4   255.88211
```

Sample Name: RZ-4-174



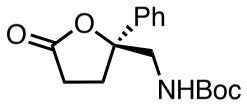
5

```
    ======================================================================
    Acq. Operator   : RZ                                 Seq. Line :   3
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 7/22/2014 9:31:20 PM                     Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-07-22 18-26-42\RZ-5IPA-2014-70MIN.M
```




```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  67.532 MM    3.8921 1.58979e4    68.07827  94.6059
   2  80.106 MM    3.7487  906.45111    4.03003   5.3941

Totals :                  1.68044e4    72.10830
```

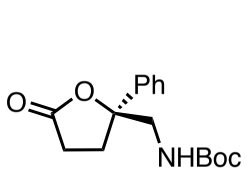
RZ-4-220-H



6

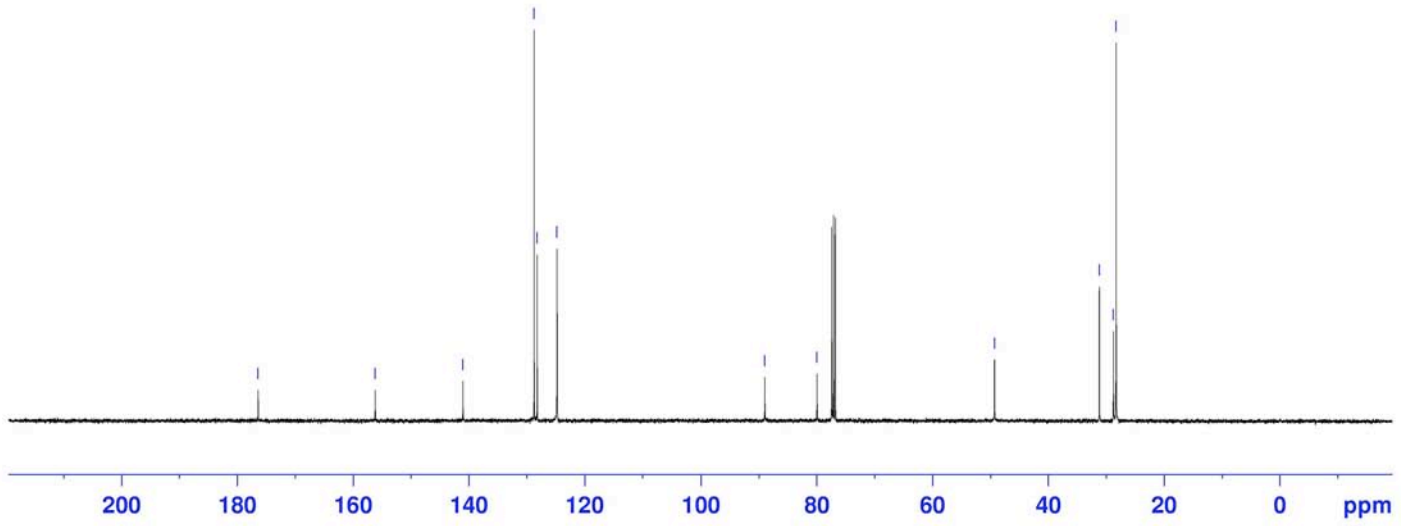
^{1}H NMR

RZ-4-220-C



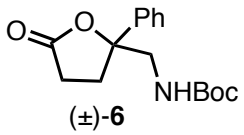
6

^{13}C NMR



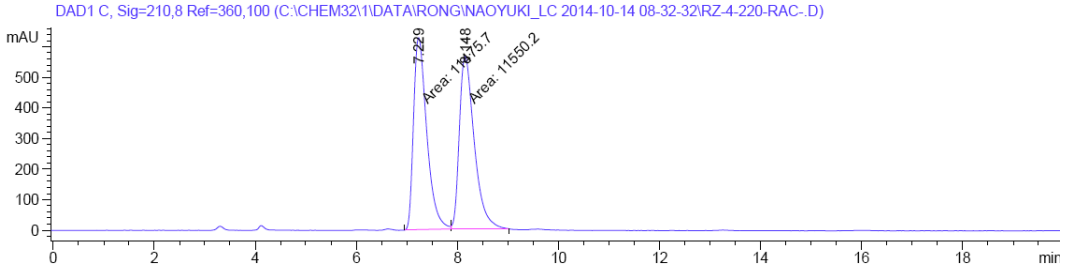
HPLC traces for 6:

Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-10-14 08-32-32\RZ-4-220-RAC-.D
Sample Name: RZ-4-220-RAC



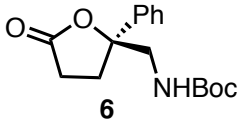
(±)-6

```
    ==================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 10/14/2014 8:56:28 AM                    Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-10-14 08-32-32\RZ-SHUTDOWN.M
```



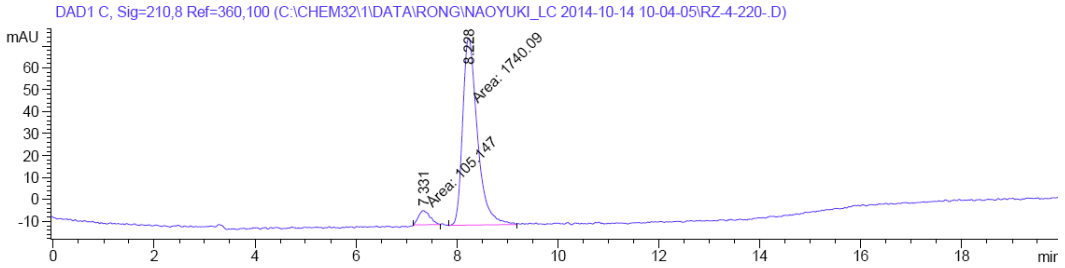

```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.229 MM    0.3042 1.14757e4   628.67841  49.8381
   2   8.148 MM    0.3413 1.15502e4   564.09924  50.1619

Totals :                  2.30259e4  1192.77765
```

Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-10-14 10-04-05\RZ-4-220-.D
Sample Name: RZ-4-220



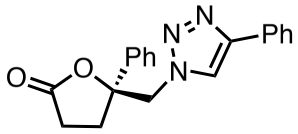
6

```
    ==================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 17
    Injection Date  : 10/14/2014 10:06:08 AM                   Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 0.2 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-10-14 10-04-05\RZ-SHUTDOWN.M
```



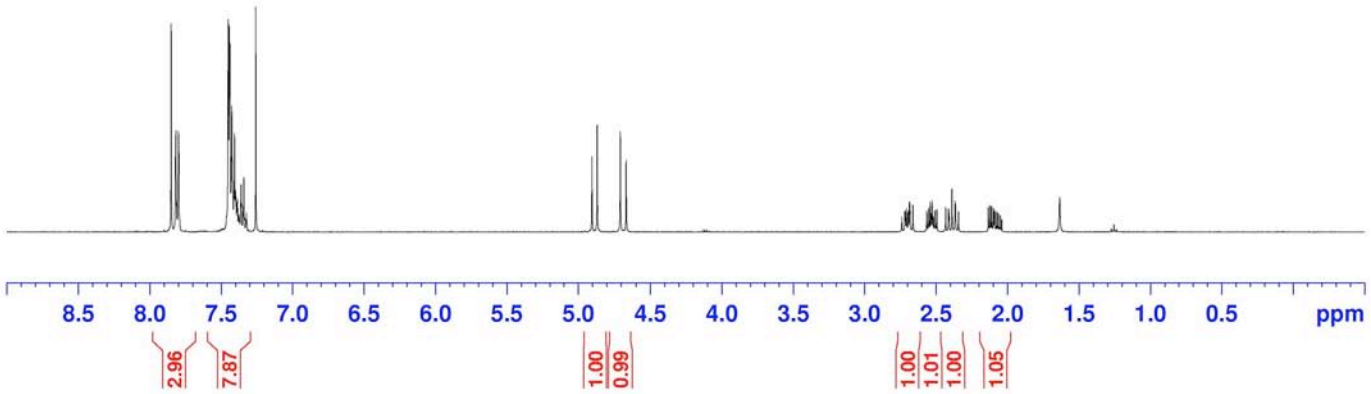

```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.331 MM    0.2658  105.14742    6.59191   5.6983
   2   8.228 MM    0.3391 1740.08972   85.52530  94.3017

Totals :                  1845.23714   92.11721
```

RZ-4-184-H

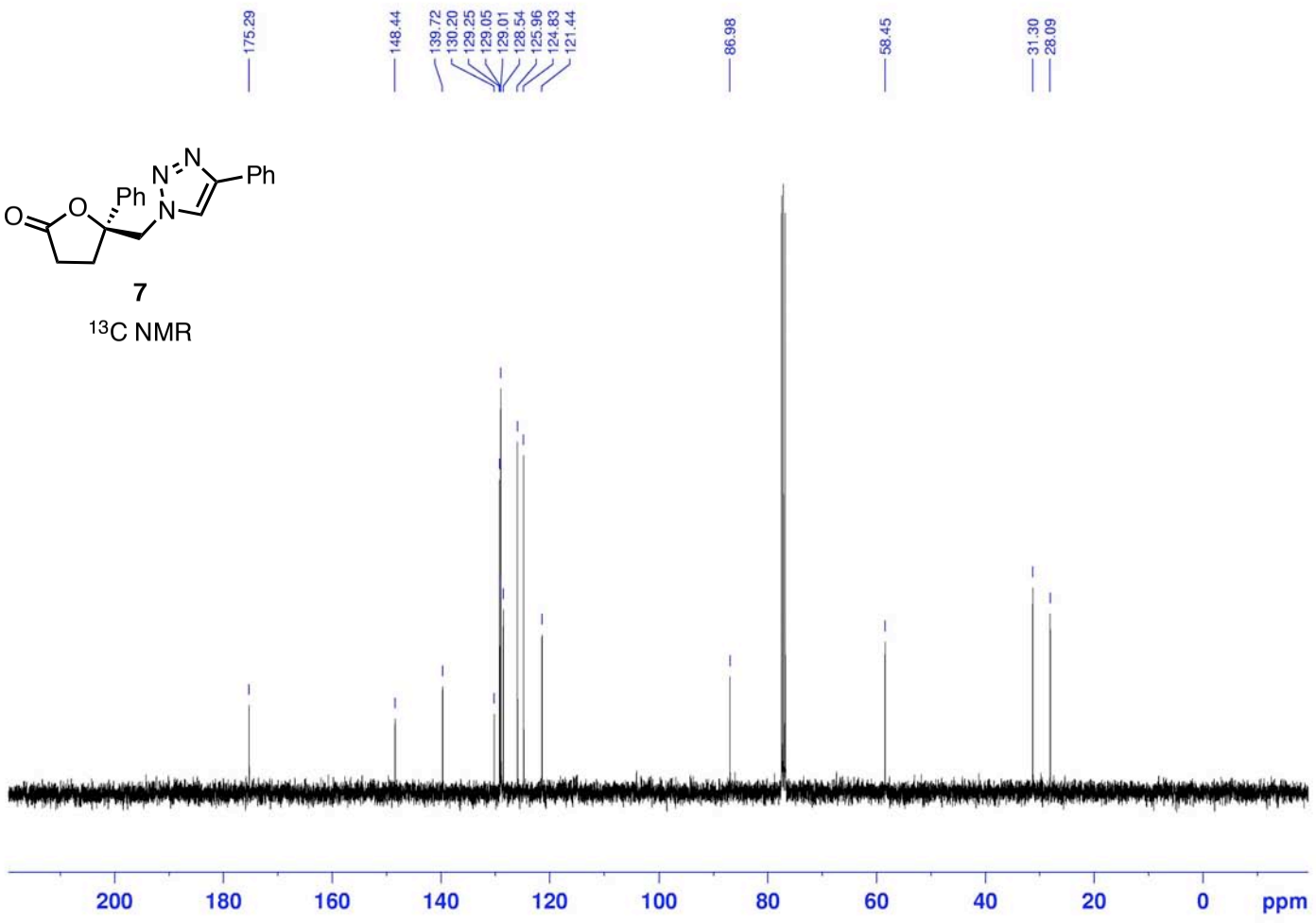


7

^{1}H NMR



RZ-4-184-C

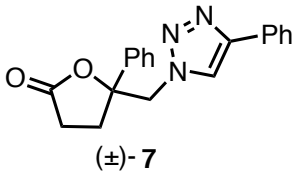


7

^{13}C NMR

HPLC traces for 7:

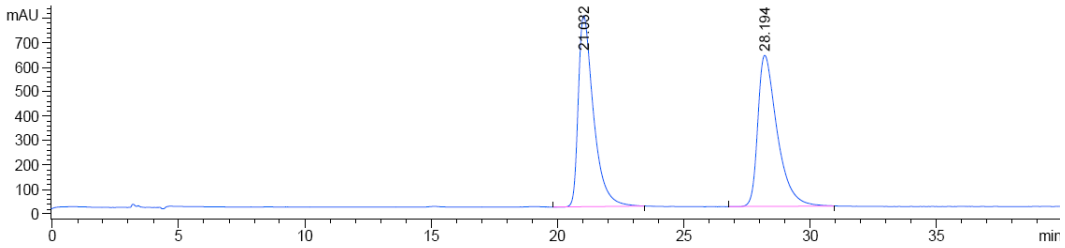
Sample Name: RZ-4-184-RAC



(±)- **7**

```
    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 19
    Injection Date  : 8/7/2014 9:24:47 AM                      Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-07 09-22-20\RZ-15IPA-2014.M
```

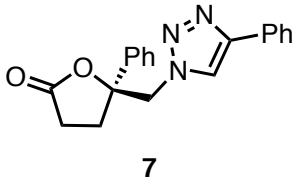
DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-07 09-22-20\RZ-4-184-RAC.D)



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.032	VB	0.6184	3.28333e4	781.09888	49.6663
2	28.194	VB	0.8013	3.32746e4	618.87622	50.3337
Totals :				6.61078e4	1399.97510	

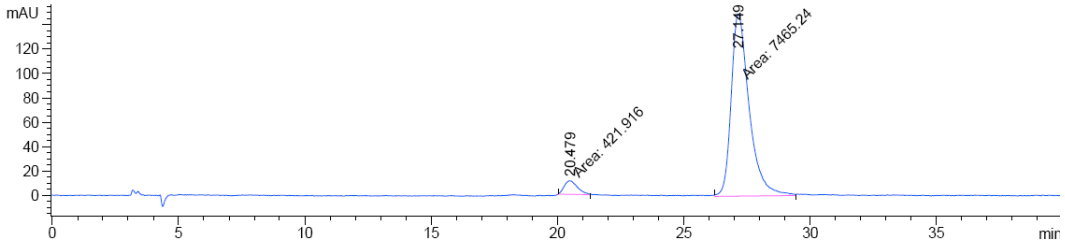
Sample Name: RZ-4-184



7

```
    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 8/19/2014 11:13:39 AM                    Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 2 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-19 10-30-20\RZ-15IPA-2014.M
```

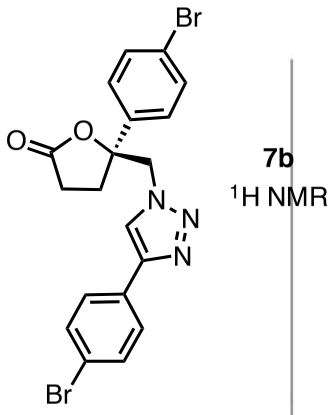
DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-08-19 10-30-20\RZ-4-184-.D)



Signal 3: DAD1 C, Sig=210,8 Ref=360,100

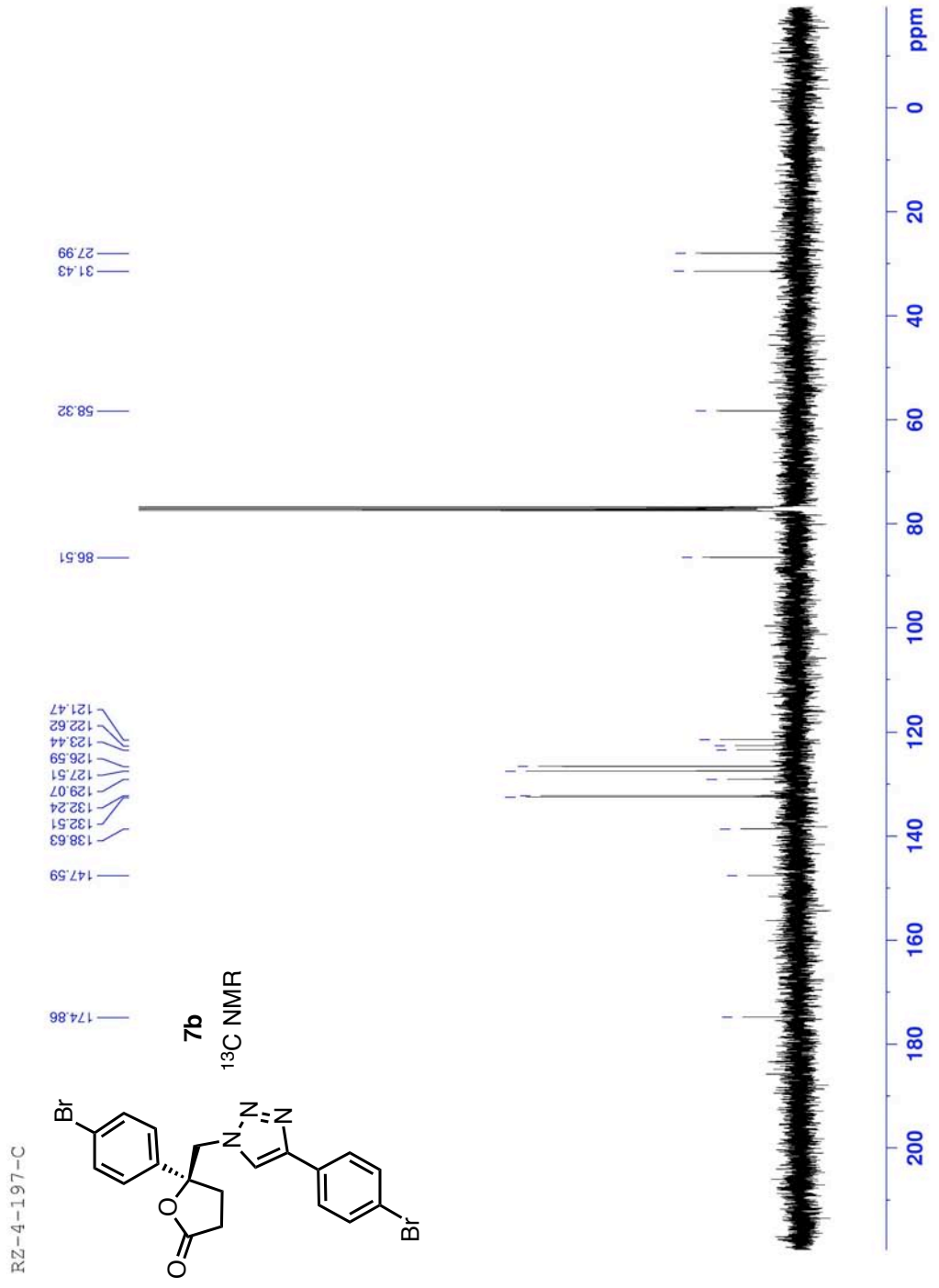
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.479	MM	0.6195	421.91553	11.35162	5.3494
2	27.149	MM	0.8317	7465.23828	149.60146	94.6506
Totals :				7887.15381	160.95307	

RZ-4-197-H

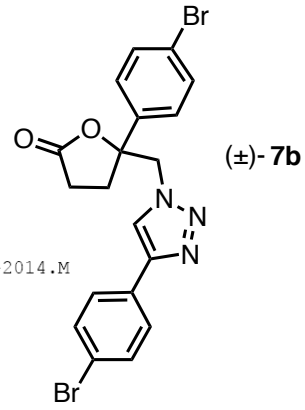


7b

^{1}H NMR


RZ-4-197-C
7b
^{13}C NMR
Br
Br
O
O
N
N
N
174.86
147.59
138.63
132.51
132.24
129.07
127.51
126.59
123.44
122.62
121.47
86.51
58.32
31.43
27.99
ppm
0
20
40
60
80
100
120
140
160
180
200

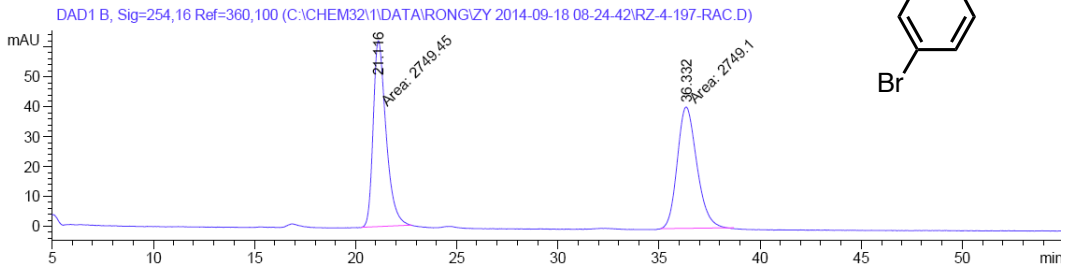
HPLC traces for 7b:



(±)-**7b**

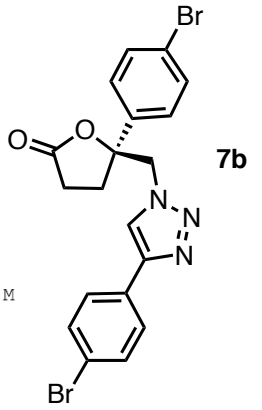
Sample Name: RZ-4-197-RAC

```
    ======================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 17
    Injection Date  : 9/18/2014 8:27:14 AM                    Inj :   1
                                                        Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 20 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\ZY 2014-09-18 08-24-42\RZ-20IPA-2014.M
```



Signal 2: DAD1 B, Sig=254,16 Ref=360,100

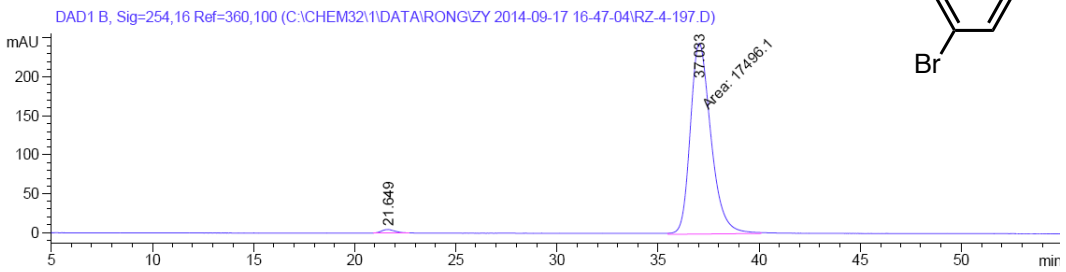
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.116	MM	0.7375	2749.44751	62.13118	50.0031
2	36.332	MM	1.1271	2749.10229	40.65299	49.9969
Totals :				5498.54980	102.78416	



7b

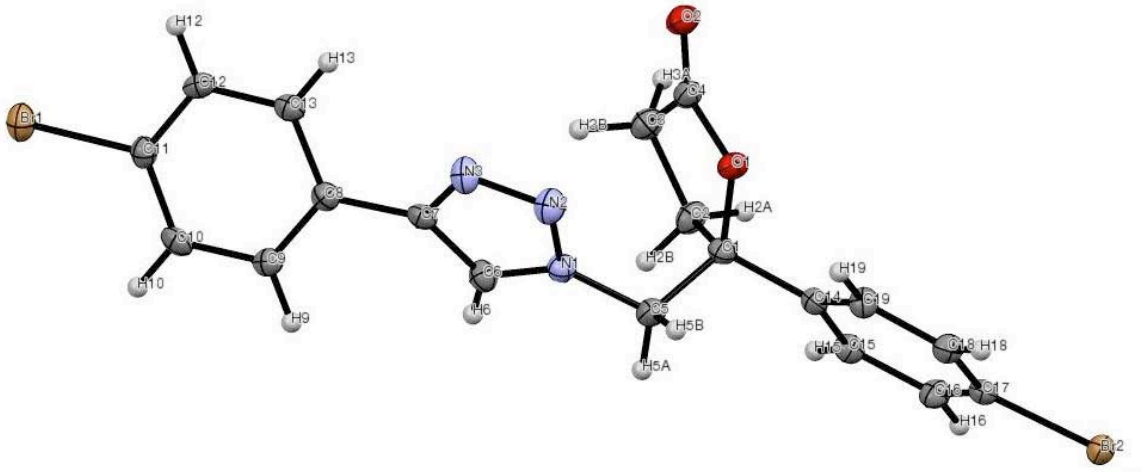
Sample Name: RZ-4-197

```
    ======================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 9/17/2014 5:41:02 PM                    Inj :   1
                                                        Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\ZY 2014-09-17 16-47-04\RZ-20IPA-2014.M
```



Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.649	BB	0.5420	202.84988	4.48220	1.1461
2	37.033	MM	1.1893	1.74961e4	245.18356	98.8539
Totals :				1.76989e4	249.66576	



SI-Table 1. Crystal data and structure refinement for compound 7b.

Identification code	X14147	
Empirical formula	C19 H15 Br2 N3 O2	
Formula weight	477.16	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.1816(11) Å	$\alpha = 90°$.
	b = 11.0851(15) Å	$\beta = 90°$.
	c = 21.848(3) Å	$\gamma = 90°$.
Volume	1739.3(4) $Å^3$	
Z	4	
Density (calculated)	1.822 Mg/m^3	
Absorption coefficient	4.681 mm^{-1}	
F(000)	944	
Crystal size	0.110 x 0.065 x 0.015 mm^3	
Theta range for data collection	1.864 to 30.032°.	
Index ranges	-10<=h<=10, -13<=k<=14, -30<=l<=30	
Reflections collected	37176	
Independent reflections	4912 [R(int) = 0.0502]	
Completeness to theta = 25.242°	98.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.5645 and 0.4825	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4912 / 387 / 235	
Goodness-of-fit on F^2	1.028	
Final R indices [I>2sigma(I)]	R1 = 0.0326, wR2 = 0.0653	
R indices (all data)	R1 = 0.0428, wR2 = 0.0683	
Absolute structure parameter	-0.004(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.709 and -0.727 $e.Å^{-3}$	

SI-Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for compound 7b. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	6633(1)	3221(1)	6294(1)	25(1)
Br(2)	3532(1)	3581(1)	-1120(1)	21(1)
O(1)	3070(4)	5450(3)	1809(1)	19(1)
O(2)	1516(5)	6548(3)	2496(1)	26(1)
N(1)	5840(5)	4282(3)	2562(2)	19(1)
N(2)	6068(5)	5455(4)	2731(2)	23(1)
N(3)	6239(5)	5470(3)	3326(2)	21(1)
C(1)	3546(6)	4187(4)	1698(2)	18(1)
C(2)	2072(6)	3470(4)	2061(2)	22(1)
C(3)	1444(7)	4348(4)	2556(2)	22(1)
C(4)	1948(6)	5565(4)	2307(2)	19(1)
C(5)	5561(6)	3982(4)	1919(2)	19(1)
C(6)	5890(6)	3557(4)	3056(2)	20(1)
C(7)	6148(5)	4324(4)	3542(2)	17(1)
C(8)	6304(6)	4042(4)	4198(2)	18(1)
C(9)	7070(5)	2967(4)	4406(2)	19(1)
C(10)	7208(6)	2726(4)	5029(2)	20(1)
C(11)	6522(6)	3566(4)	5446(2)	19(1)
C(12)	5762(6)	4647(4)	5251(2)	20(1)
C(13)	5660(6)	4886(4)	4629(2)	19(1)
C(14)	3539(6)	4001(4)	1009(2)	17(1)
C(15)	2885(6)	2952(4)	744(2)	19(1)
C(16)	2884(6)	2812(4)	105(2)	19(1)
C(17)	3586(6)	3731(4)	-255(2)	16(1)
C(18)	4325(6)	4768(4)	0(2)	19(1)
C(19)	4289(6)	4905(4)	633(2)	18(1)

SI-Table 3. Bond lengths [Å] and angles [°] for compound 7b.

Br(1)-C(11)	1.895(4)	C(2)-C(3)	1.524(6)
Br(2)-C(17)	1.898(4)	C(2)-H(2A)	0.9900
O(1)-C(4)	1.360(5)	C(2)-H(2B)	0.9900
O(1)-C(1)	1.461(5)	C(3)-C(4)	1.498(6)
O(2)-C(4)	1.206(5)	C(3)-H(3A)	0.9900
N(1)-C(6)	1.346(6)	C(3)-H(3B)	0.9900
N(1)-N(2)	1.361(5)	C(5)-H(5A)	0.9900
N(1)-C(5)	1.457(5)	C(5)-H(5B)	0.9900
N(2)-N(3)	1.306(5)	C(6)-C(7)	1.372(6)
N(3)-C(7)	1.357(6)	C(6)-H(6)	0.9500
C(1)-C(14)	1.518(6)	C(7)-C(8)	1.471(6)
C(1)-C(5)	1.543(6)	C(8)-C(9)	1.389(6)
C(1)-C(2)	1.543(6)	C(8)-C(13)	1.406(6)

C(9)-C(10)	1.390(6)	N(1)-C(5)-H(5A)	108.9
C(9)-H(9)	0.9500	C(1)-C(5)-H(5A)	108.9
C(10)-C(11)	1.394(6)	N(1)-C(5)-H(5B)	108.9
C(10)-H(10)	0.9500	C(1)-C(5)-H(5B)	108.9
C(11)-C(12)	1.383(6)	H(5A)-C(5)-H(5B)	107.7
C(12)-C(13)	1.387(6)	N(1)-C(6)-C(7)	104.7(4)
C(12)-H(12)	0.9500	N(1)-C(6)-H(6)	127.7
C(13)-H(13)	0.9500	C(7)-C(6)-H(6)	127.7
C(14)-C(15)	1.382(6)	N(3)-C(7)-C(6)	108.6(4)
C(14)-C(19)	1.404(6)	N(3)-C(7)-C(8)	122.3(4)
C(15)-C(16)	1.404(6)	C(6)-C(7)-C(8)	129.2(4)
C(15)-H(15)	0.9500	C(9)-C(8)-C(13)	118.8(4)
C(16)-C(17)	1.381(6)	C(9)-C(8)-C(7)	122.1(4)
C(16)-H(16)	0.9500	C(13)-C(8)-C(7)	119.1(4)
C(17)-C(18)	1.383(6)	C(8)-C(9)-C(10)	120.9(4)
C(18)-C(19)	1.391(6)	C(8)-C(9)-H(9)	119.5
C(18)-H(18)	0.9500	C(10)-C(9)-H(9)	119.5
C(19)-H(19)	0.9500	C(9)-C(10)-C(11)	119.1(4)
		C(9)-C(10)-H(10)	120.4
C(4)-O(1)-C(1)	111.2(3)	C(11)-C(10)-H(10)	120.4
C(6)-N(1)-N(2)	110.5(4)	C(12)-C(11)-C(10)	121.1(4)
C(6)-N(1)-C(5)	129.8(4)	C(12)-C(11)-Br(1)	119.6(3)
N(2)-N(1)-C(5)	119.7(4)	C(10)-C(11)-Br(1)	119.3(3)
N(3)-N(2)-N(1)	107.0(4)	C(11)-C(12)-C(13)	119.3(4)
N(2)-N(3)-C(7)	109.2(4)	C(11)-C(12)-H(12)	120.4
O(1)-C(1)-C(14)	107.1(3)	C(13)-C(12)-H(12)	120.4
O(1)-C(1)-C(5)	108.0(3)	C(12)-C(13)-C(8)	120.8(4)
C(14)-C(1)-C(5)	107.1(4)	C(12)-C(13)-H(13)	119.6
O(1)-C(1)-C(2)	104.3(3)	C(8)-C(13)-H(13)	119.6
C(14)-C(1)-C(2)	115.9(4)	C(15)-C(14)-C(19)	119.0(4)
C(5)-C(1)-C(2)	114.0(3)	C(15)-C(14)-C(1)	122.1(4)
C(3)-C(2)-C(1)	103.8(4)	C(19)-C(14)-C(1)	118.9(4)
C(3)-C(2)-H(2A)	111.0	C(14)-C(15)-C(16)	120.7(4)
C(1)-C(2)-H(2A)	111.0	C(14)-C(15)-H(15)	119.6
C(3)-C(2)-H(2B)	111.0	C(16)-C(15)-H(15)	119.6
C(1)-C(2)-H(2B)	111.0	C(17)-C(16)-C(15)	118.9(4)
H(2A)-C(2)-H(2B)	109.0	C(17)-C(16)-H(16)	120.5
C(4)-C(3)-C(2)	104.2(3)	C(15)-C(16)-H(16)	120.5
C(4)-C(3)-H(3A)	110.9	C(16)-C(17)-C(18)	121.6(4)
C(2)-C(3)-H(3A)	110.9	C(16)-C(17)-Br(2)	119.6(3)
C(4)-C(3)-H(3B)	110.9	C(18)-C(17)-Br(2)	118.8(3)
C(2)-C(3)-H(3B)	110.9	C(17)-C(18)-C(19)	118.9(4)
H(3A)-C(3)-H(3B)	108.9	C(17)-C(18)-H(18)	120.5
O(2)-C(4)-O(1)	120.7(4)	C(19)-C(18)-H(18)	120.5
O(2)-C(4)-C(3)	128.8(4)	C(18)-C(19)-C(14)	120.8(4)
O(1)-C(4)-C(3)	110.5(4)	C(18)-C(19)-H(19)	119.6
N(1)-C(5)-C(1)	113.4(3)	C(14)-C(19)-H(19)	119.6

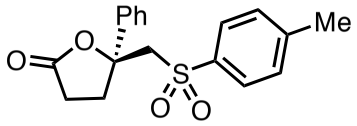
SI-Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for compound 7b. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	27(1)	30(1)	19(1)	4(1)	-2(1)	-3(1)
Br(2)	22(1)	26(1)	16(1)	-1(1)	-1(1)	3(1)
O(1)	20(2)	17(2)	18(1)	-2(1)	4(1)	0(1)
O(2)	31(2)	24(2)	22(1)	-2(1)	5(1)	4(2)
N(1)	18(2)	19(2)	19(2)	0(1)	-1(1)	0(1)
N(2)	23(2)	23(2)	24(2)	-2(2)	-3(1)	-5(1)
N(3)	22(2)	21(2)	21(2)	3(1)	-4(1)	-6(1)
C(1)	21(2)	15(2)	19(2)	0(1)	1(2)	2(2)
C(2)	25(2)	22(2)	18(2)	1(2)	4(2)	-4(2)
C(3)	22(2)	24(2)	21(2)	-1(2)	4(2)	-3(2)
C(4)	18(2)	24(2)	16(2)	-1(2)	1(2)	1(2)
C(5)	20(2)	22(2)	17(2)	-1(2)	1(2)	2(2)
C(6)	19(2)	20(2)	21(2)	0(2)	-2(2)	-1(2)
C(7)	12(2)	17(2)	21(2)	0(1)	-1(1)	1(1)
C(8)	13(2)	21(2)	19(2)	-2(1)	-1(2)	-2(2)
C(9)	15(2)	19(2)	22(2)	-5(2)	-1(1)	-1(1)
C(10)	13(2)	20(2)	27(2)	1(2)	-4(2)	1(2)
C(11)	17(2)	22(2)	17(2)	2(2)	-1(2)	-2(2)
C(12)	17(2)	20(2)	21(2)	-4(2)	4(2)	1(2)
C(13)	16(2)	19(2)	22(2)	0(2)	-1(2)	2(2)
C(14)	16(2)	16(2)	18(2)	0(1)	-1(2)	2(2)
C(15)	18(2)	17(2)	21(2)	1(2)	1(2)	-1(2)
C(16)	22(2)	15(2)	21(2)	-2(2)	0(2)	-2(2)
C(17)	14(2)	15(2)	19(2)	0(1)	1(2)	2(2)
C(18)	18(2)	18(2)	20(2)	1(2)	2(2)	-1(2)
C(19)	19(2)	16(2)	19(2)	0(2)	-1(2)	-3(2)

SI-Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for compound 7b.

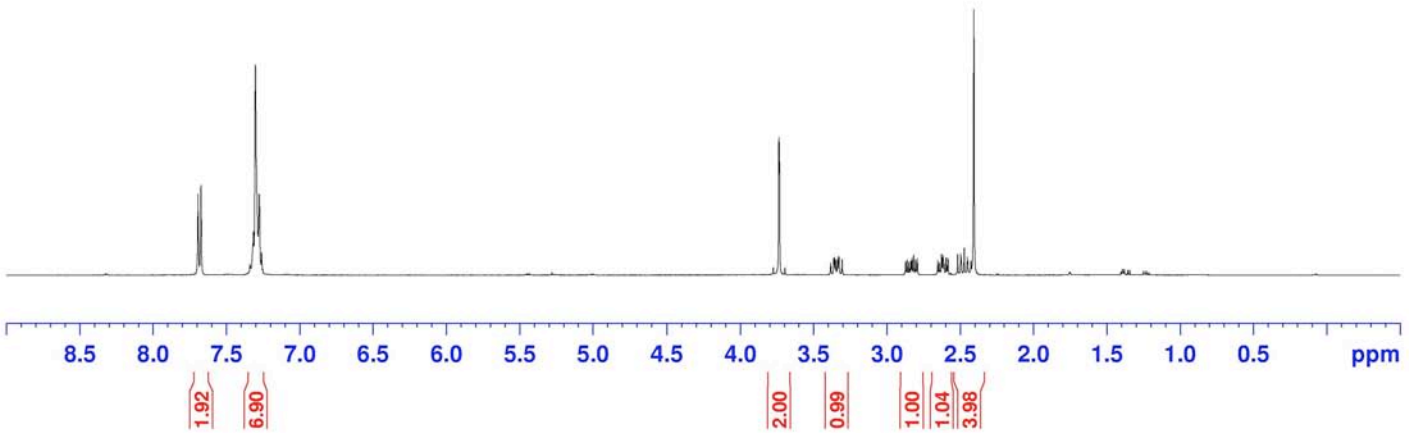
	x	y	z	U(eq)
H(2A)	1016	3236	1795	26
H(2B)	2621	2734	2243	26
H(3A)	85	4286	2626	27
H(3B)	2101	4190	2946	27
H(5A)	5895	3125	1855	23
H(5B)	6413	4479	1668	23
H(6)	5772	2704	3066	24
H(9)	7506	2389	4119	23
H(10)	7763	1998	5168	24
H(12)	5316	5218	5540	23
H(13)	5148	5629	4492	23
H(15)	2432	2319	996	22
H(16)	2407	2098	-77	23
H(18)	4848	5376	-253	23
H(19)	4779	5618	812	21

RZ-4-234-H

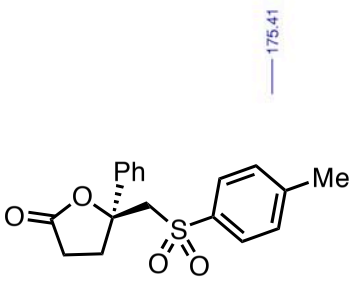


8a

^{1}H NMR



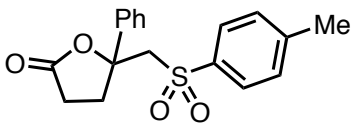
RZ-4-234-C



8a

^{13}C NMR

HPLC traces for 8a:



racemic

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Sample Name: RZ-4-234-RAC

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    Acq. Instrument : Instrument 1                     Location : Vial 17
    Injection Date  : 12/5/2014 12:12:25 PM                Inj :   1
                                                     Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\MTP1\NAOYUKI_LC 2014-12-05 10-43-13\RZ-SHUTDOWN.M
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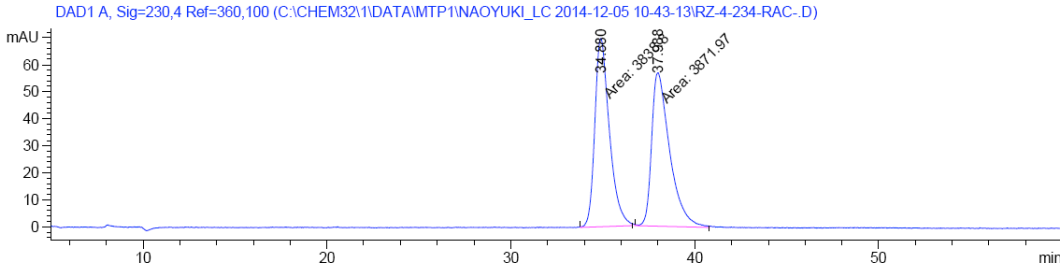


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Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  34.880 MM    0.9182 3838.79614   69.67712  49.7849
   2  37.988 MM    1.1363 3871.97144   56.78994  50.2151

Totals :                  7710.76758  126.46707
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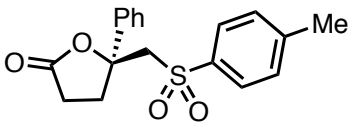

8a

```
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Sample Name: RZ-4-234

    ========================================================================
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    Acq. Instrument : Instrument 1                   Location : Vial 16
    Injection Date  : 12/13/2014 3:02:05 PM              Inj :   1
                                                   Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
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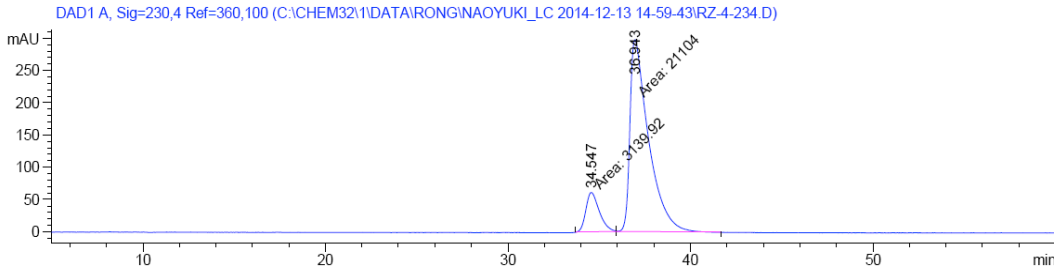


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Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
   1  34.547 MM    0.8546 3139.91797   61.23563  12.9514
   2  36.943 MM    1.1830 2.11040e4   297.32425  87.0486

Totals :                  2.42439e4   358.55988
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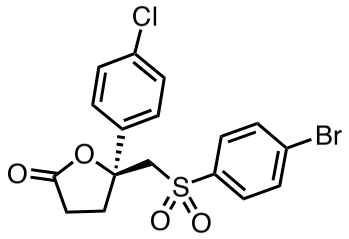
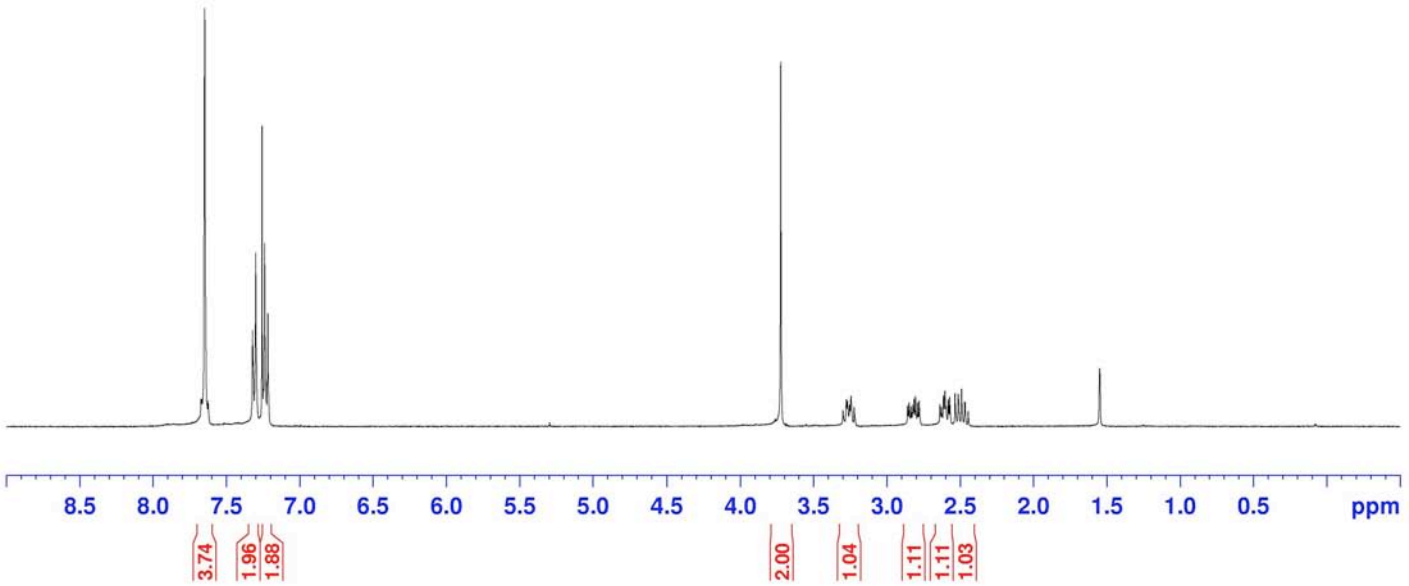
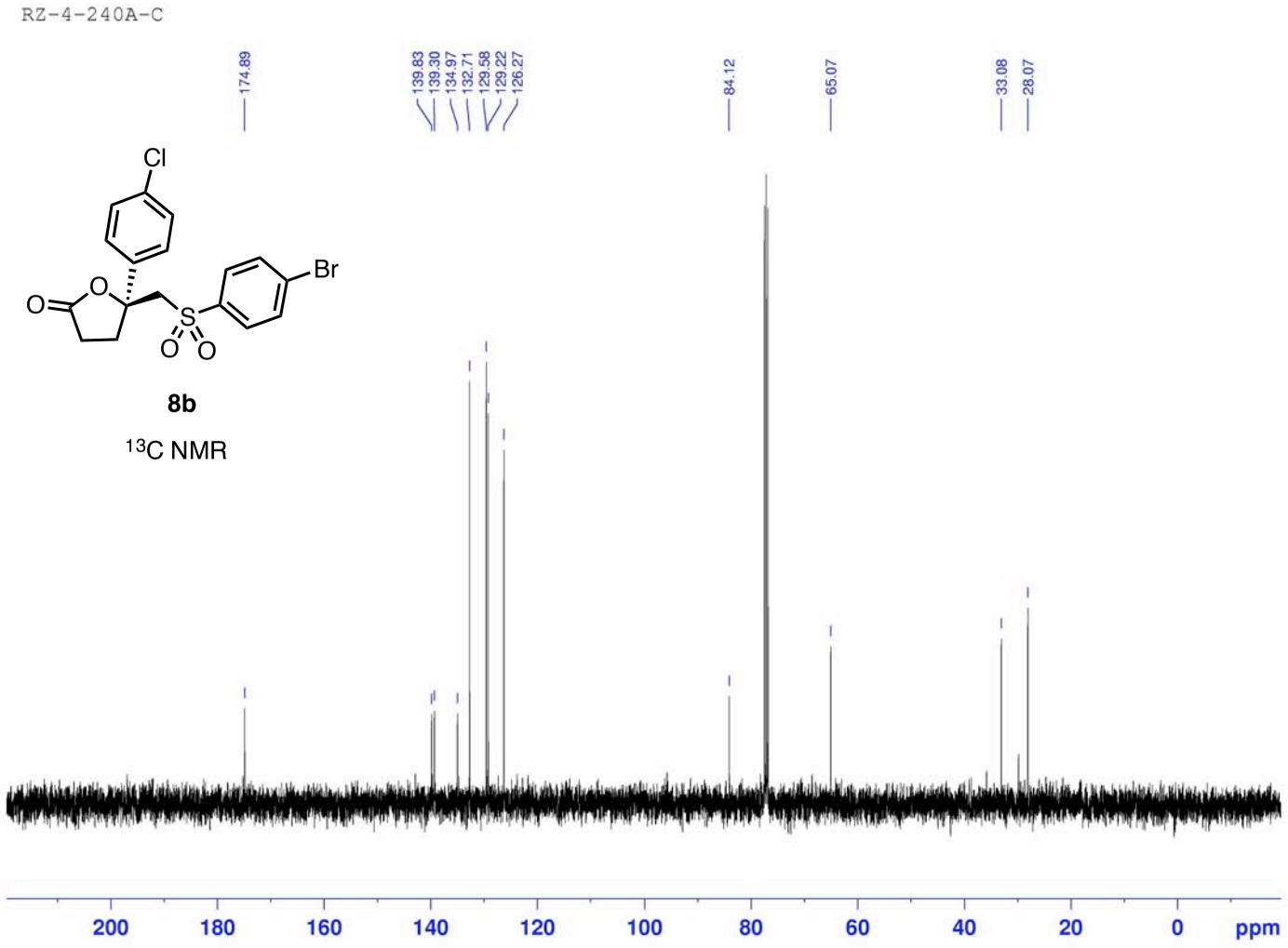
RZ-4-240A-H



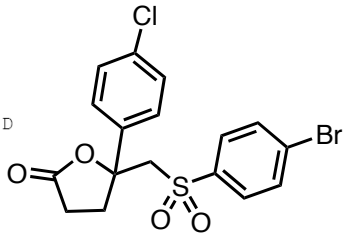
8b

^{1}H NMR




RZ-4-240A-C
174.89
139.83
139.30
134.97
132.71
129.58
129.22
126.27
84.12
65.07
33.08
28.07
Cl
Br
O
O
S
O
O
8b
^{13}C NMR
200
180
160
140
120
100
80
60
40
20
0
ppm

HPLC traces for 8b:



racemic

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Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-09 09-03-14\RZ-4-240A-RAC.D
Sample Name: RZ-4-240A-RAC

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    Acq. Instrument : Instrument 1                     Location : Vial 20
    Injection Date  : 12/9/2014 12:57:27 PM                Inj :   1
                                                    Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 12 µl
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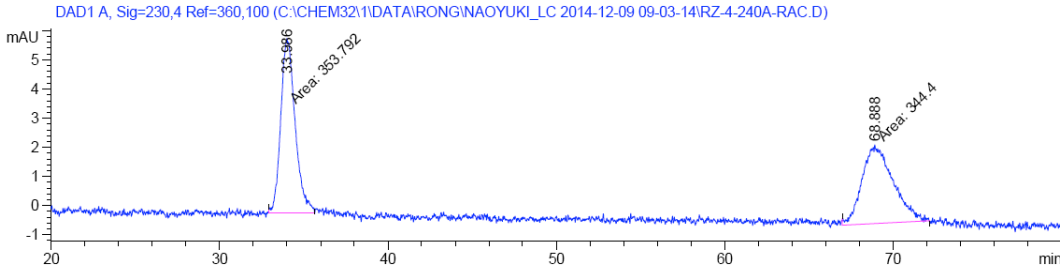


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Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  33.986 MM    0.9849  353.79236    5.98674  50.6726
   2  68.888 MM    2.1221  344.40015    2.70483  49.3274

Totals :                   698.19250    8.69158
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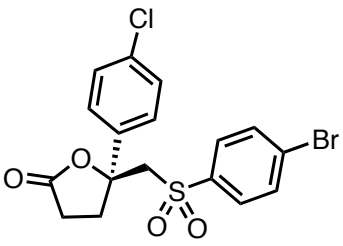

8b

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-09 17-16-57\RZ-4-240A.D
Sample Name: RZ-4-240A

    ========================================================================
    Acq. Operator   : RZ                              Seq. Line :   1
    Acq. Instrument : Instrument 1                     Location : Vial 28
    Injection Date  : 12/9/2014 5:19:13 PM                 Inj :   1
                                                    Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
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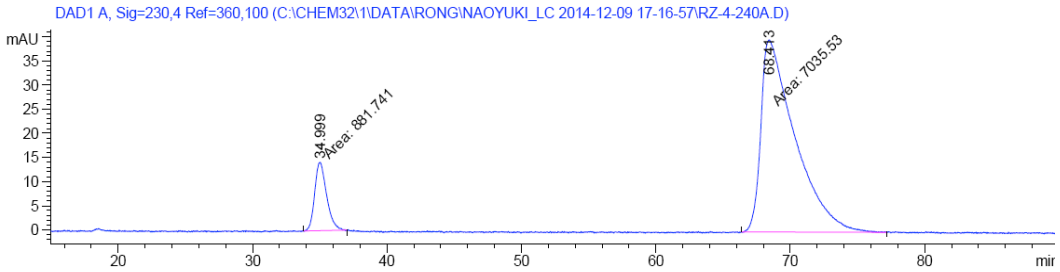
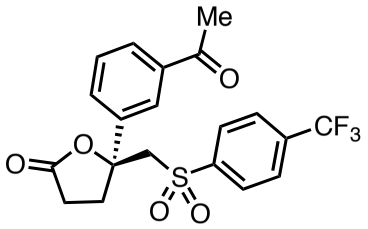


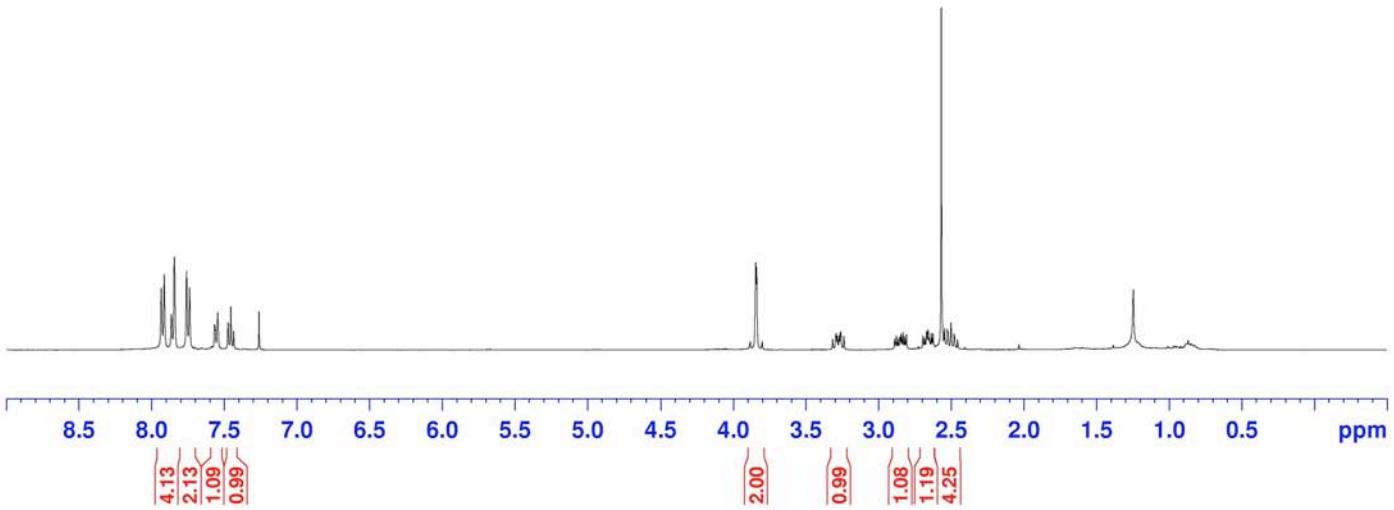

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  34.999 MM    1.0348  881.74060   14.20121  11.1369
   2  68.413 MM    2.9414 7035.52930   39.86550  88.8631

Totals :                  7917.26990   54.06671
```

RZ-4-240B-H



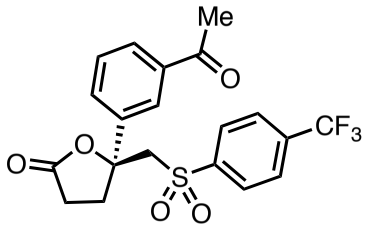
8c

^{1}H NMR



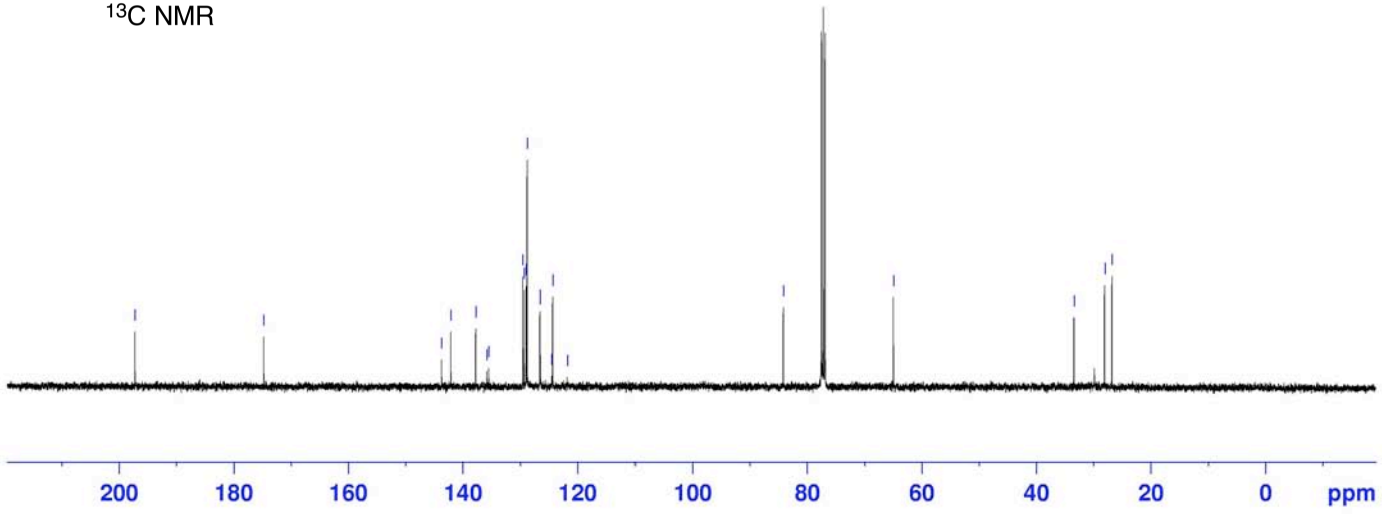
RZ-4-240B-C

197.25
174.77
143.72
142.09
137.74
135.81
135.48
129.53
129.27
128.92
128.77
126.55
126.51
124.48
124.31
121.76
84.14
64.93
33.39
28.02
26.76

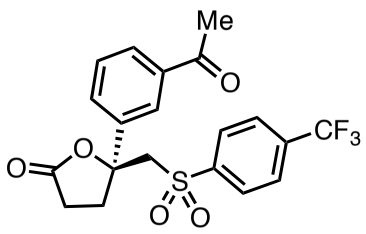


8c

^{13}C NMR



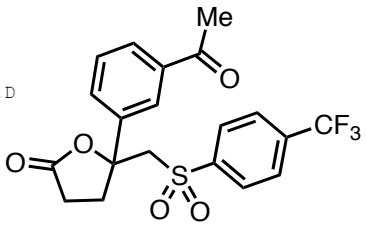
RZ-4-240B-F



8c

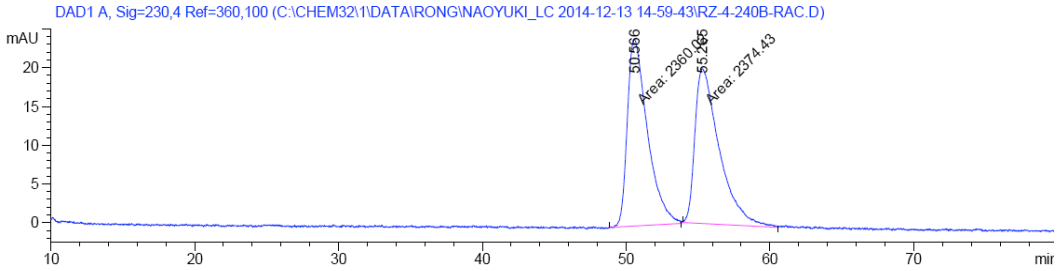
^{19}F NMR

HPLC traces for 8c:

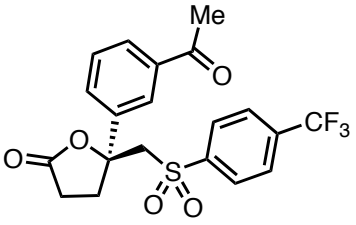


racemic

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-13 14-59-43\RZ-4-240B-RAC.D
Sample Name: RZ-4-240B-RAC

    ==========================================================================
    Acq. Operator   : RZ                                Seq. Line :   5
    Acq. Instrument : Instrument 1                       Location : Vial 19
    Injection Date  : 12/13/2014 9:06:58 PM                 Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-13 14-59-43\RZ-SHUTDOWN.M
```

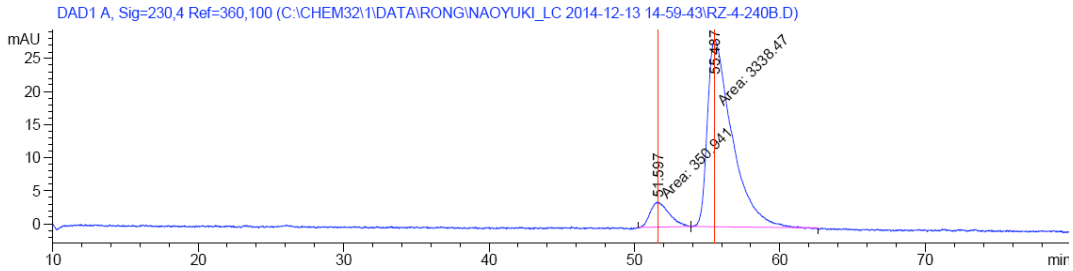



```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  50.566 MM    1.6244 2360.01953   24.21427  49.8479
   2  55.265 MM    1.9716 2374.42505   20.07225  50.1521

Totals :                  4734.44458   44.28651
```



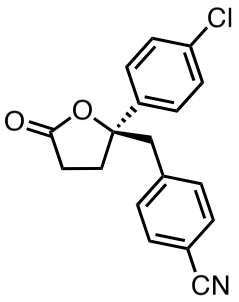
8c

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-13 14-59-43\RZ-4-240B.D
Sample Name: RZ-4-240B

    ==========================================================================
    Acq. Operator   : RZ                                Seq. Line :   3
    Acq. Instrument : Instrument 1                       Location : Vial 17
    Injection Date  : 12/13/2014 6:04:25 PM                 Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-13 14-59-43\RZ-SHUTDOWN.M
```



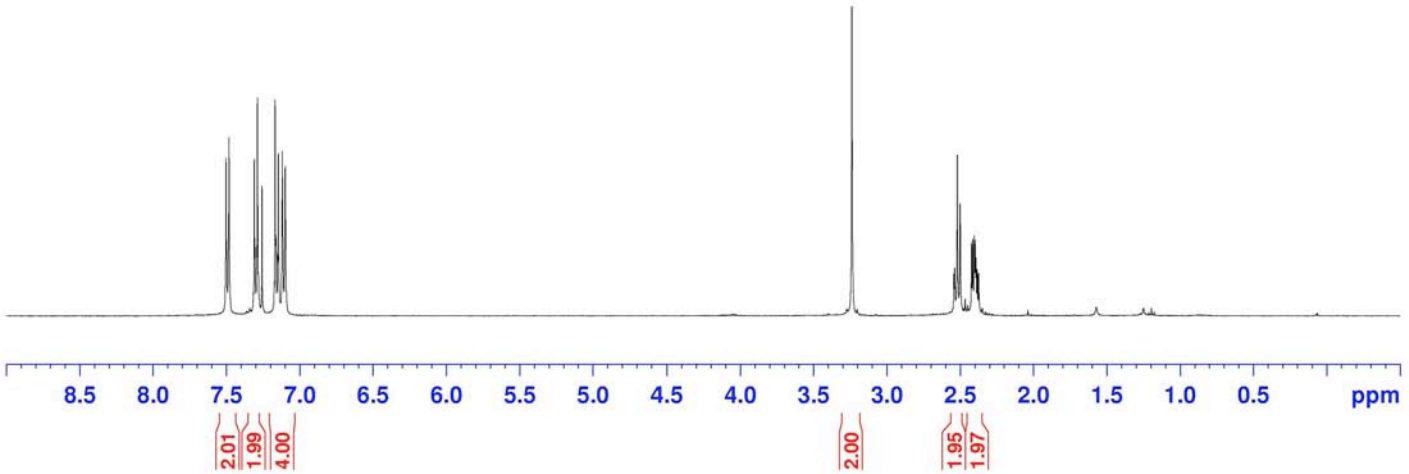

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  51.597 MM    1.5154  350.94086    3.85978   9.5121
   2  55.487 MM    1.9667 3338.47388   28.29182  90.4879

Totals :                  3689.41473   32.15160
```

RZ-4-242A-H

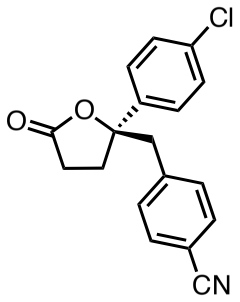


9a

^{1}H NMR



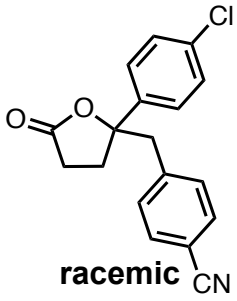
RZ-4-242A-C



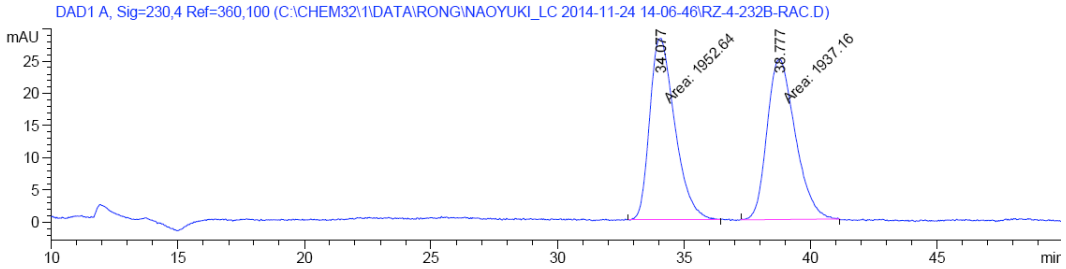
9a

^{13}C NMR

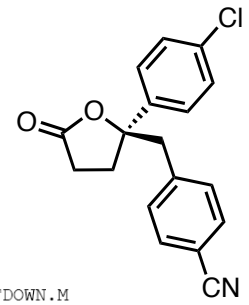
HPLC traces for 9a:




```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-11-24 14-06-46\RZ-4-232B-RAC.D
Sample Name: RZ-4-232B-RAC

    ========================================================================
    Acq. Operator   : RZ                              Seq. Line :   7
    Acq. Instrument : Instrument 1                     Location : Vial 27
    Injection Date  : 11/24/2014 6:26:06 PM                Inj :   1
                                                     Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-11-24 14-06-46\RZ-SHUTDOWN.M
```

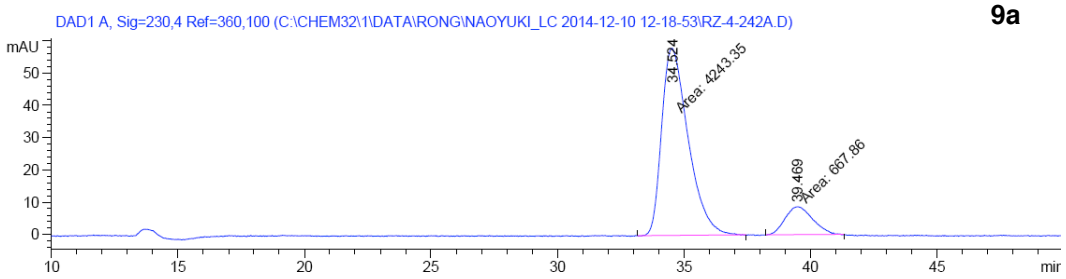



```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  34.077 MM    1.1550 1952.64087   28.17696  50.1990
   2  38.777 MM    1.2941 1937.16296   24.94906  49.8010

Totals :                  3889.80383   53.12602
```



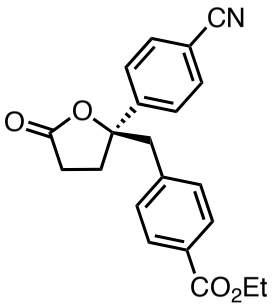
9a

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 12-18-53\RZ-4-242A.D
Sample Name: RZ-4-242A

    ========================================================================
    Acq. Operator   : RZ                              Seq. Line :   1
    Acq. Instrument : Instrument 1                     Location : Vial 18
    Injection Date  : 12/10/2014 12:21:12 PM               Inj :   1
                                                     Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 12-18-53\RZ-SHUTDOWN.M
```



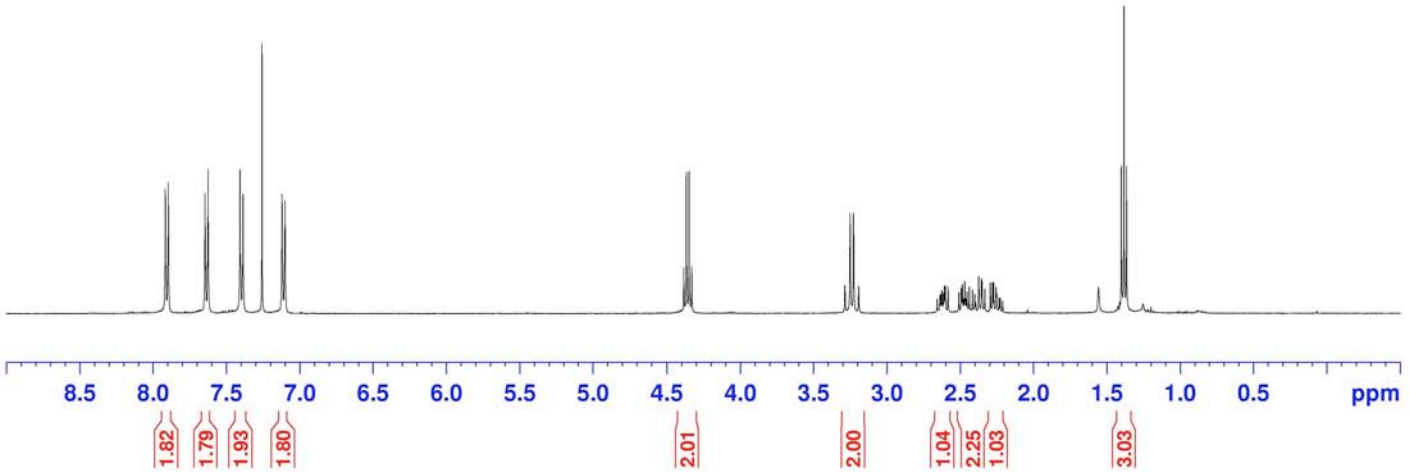

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  34.524 MM    1.2181 4243.34570   58.05779  86.4013
   2  39.469 MM    1.2756  667.85956    8.72598  13.5987

Totals :                  4911.20526   66.78376
```

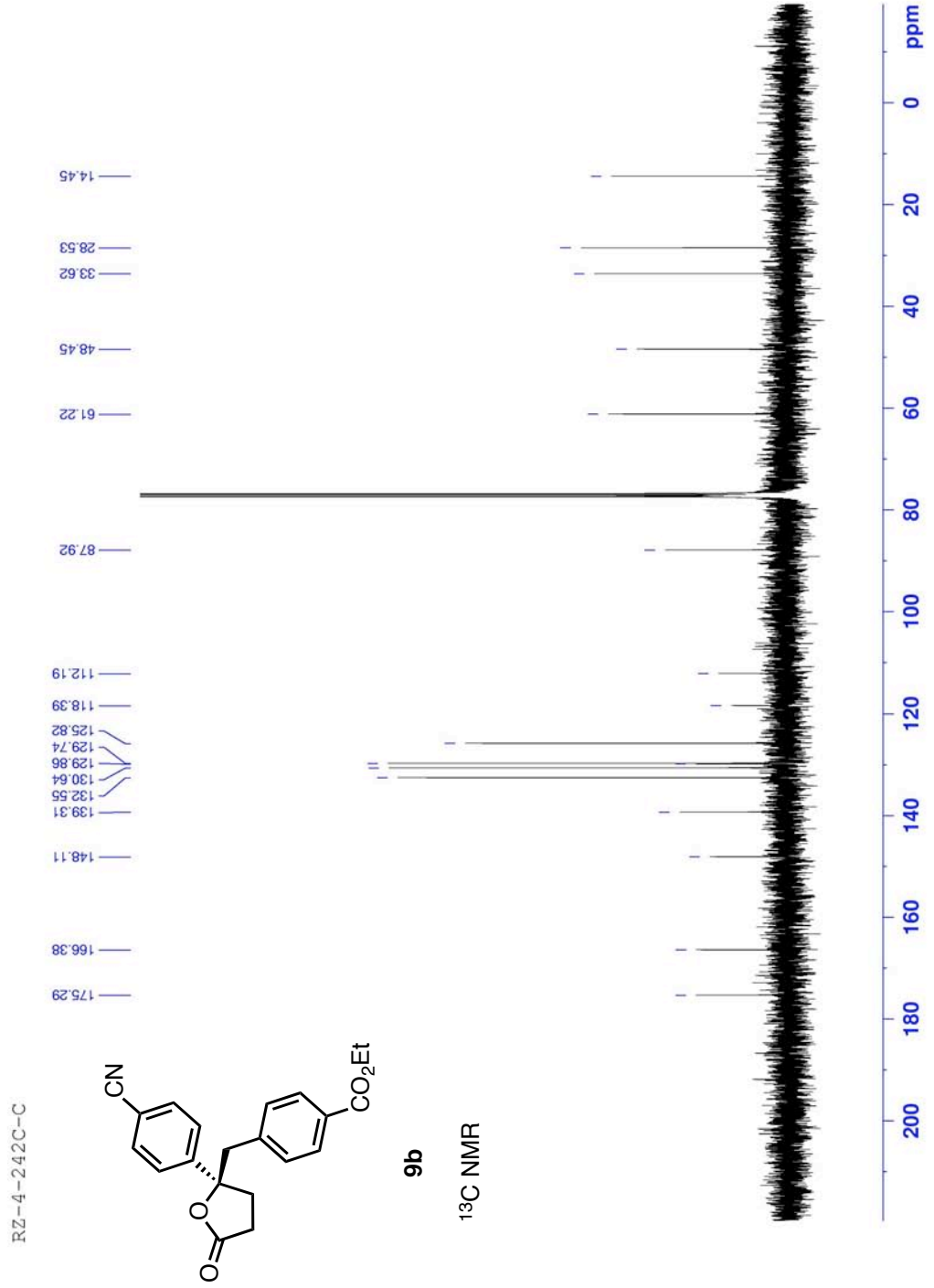
RZ-4-242C-H



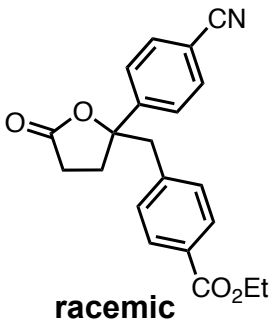
9b

^{1}H NMR




RZ-4-242C-C
CN
CO2Et
O
O
9b
13C NMR
175.29
166.38
148.11
139.31
132.55
130.64
129.86
129.74
125.82
118.39
112.19
87.92
61.22
48.45
33.62
28.53
14.45
ppm
0
20
40
60
80
100
120
140
160
180
200

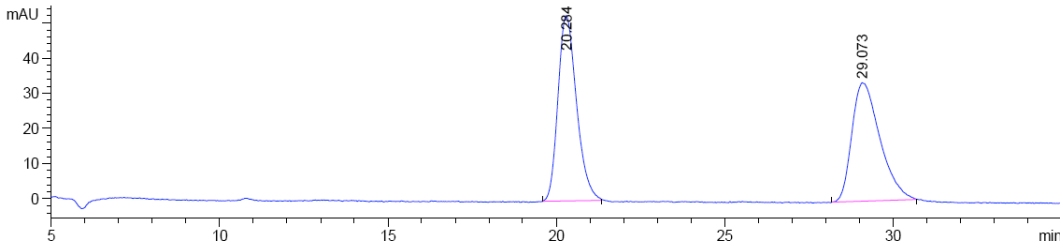
HPLC traces for 9b:



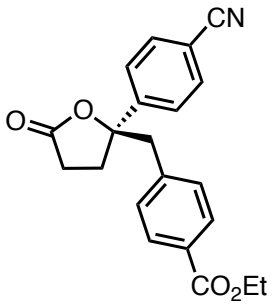
racemic

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 17-59-20\RZ-4-242C-RAC.D
Sample Name: RZ-4-242C-RAC

    ======================================================================
    Acq. Operator   : RZ                              Seq. Line :   2
    Acq. Instrument : Instrument 1                     Location : Vial 19
    Injection Date  : 12/10/2014 6:53:21 PM                Inj :   1
                                                    Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 20 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 17-59-20\RZ-15IPA-2014.M
```

DAD1 A, Sig=230,4 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 17-59-20\RZ-4-242C-RAC.D)



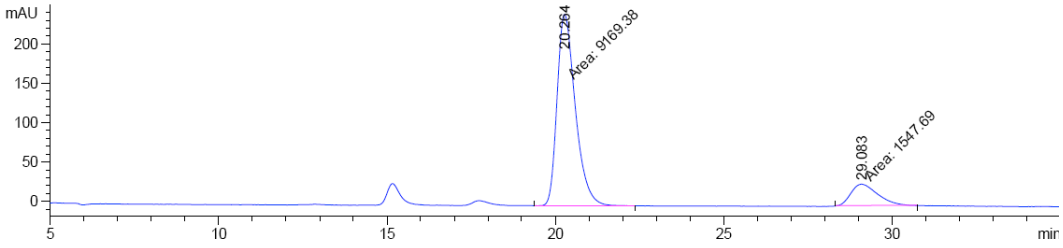

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  20.284 BB    0.5581 2026.92505   52.77429  50.8526
   2  29.073 BB    0.6995 1958.96021   33.73444  49.1474

Totals :                  3985.88525   86.50873
```



9b

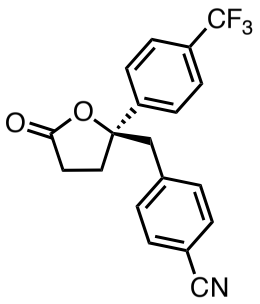
```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 17-59-20\RZ-4-242C.D
Sample Name: RZ-4-242C

    ======================================================================
    Acq. Operator   : RZ                              Seq. Line :   1
    Acq. Instrument : Instrument 1                     Location : Vial 17
    Injection Date  : 12/10/2014 6:01:47 PM                Inj :   1
                                                    Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 17-59-20\RZ-15IPA-2014.M
```

DAD1 A, Sig=230,4 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 17-59-20\RZ-4-242C.D)



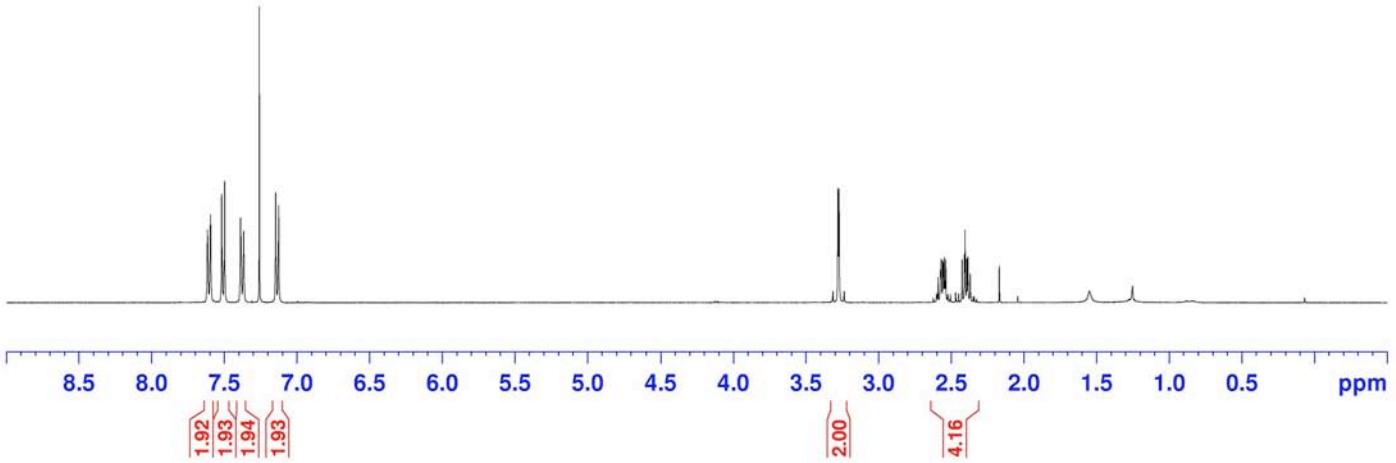

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  20.264 MM    0.6281 9169.38184  243.29703  85.5586
   2  29.083 MM    0.9316 1547.69482   27.68975  14.4414

Totals :                  1.07171e4   270.98678
```

RZ-4-242E-H

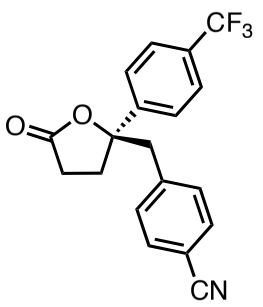


9c

^{1}H NMR



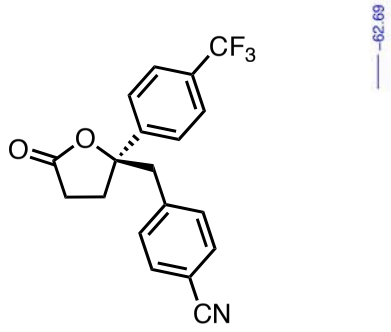
RZ-4-242E-C



9c

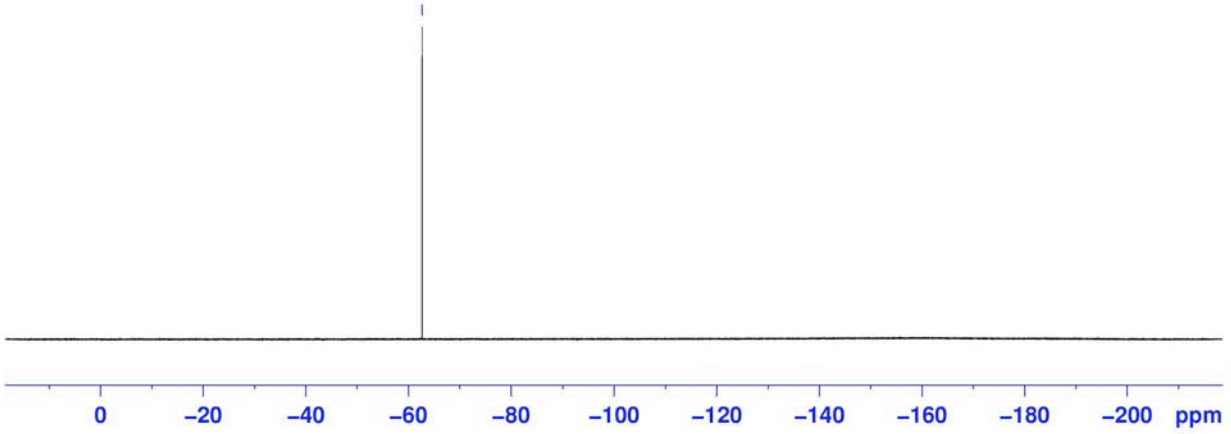
^{13}C NMR

RZ-4-242E-F

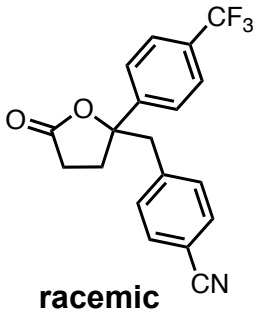


9c

^{19}F NMR

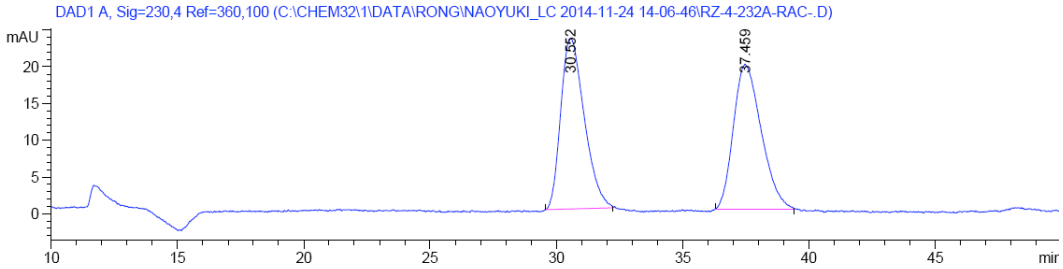


HPLC traces for 9c:

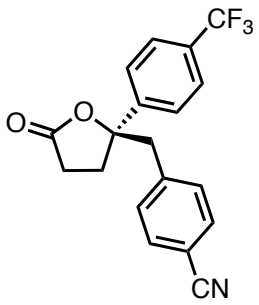


racemic

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-11-24 14-06-46\RZ-4-232A-RAC-.D
Sample Name: RZ-4-232A-RAC

    ======================================================================
    Acq. Operator   : RZ                                 Seq. Line :  10
    Acq. Instrument : Instrument 1                        Location : Vial 26
    Injection Date  : 11/24/2014 8:59:39 PM                    Inj :   1
                                                         Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 15 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-11-24 14-06-46\RZ-SHUTDOWN.M
```

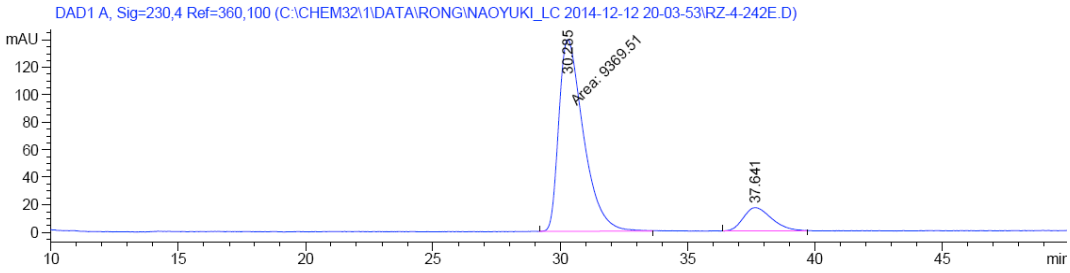



```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  30.552 BB    0.7657 1511.29687   23.27001  49.9620
   2  37.459 BB    0.9065 1513.59387   19.78445  50.0380

Totals :                  3024.89075   43.05446
```



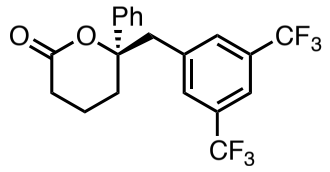
9c

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-12 20-03-53\RZ-4-242E.D
Sample Name: RZ-4-242E

    ======================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 1                        Location : Vial 17
    Injection Date  : 12/12/2014 9:07:15 PM                    Inj :   1
                                                         Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-12 20-03-53\RZ-SHUTDOWN.M
```



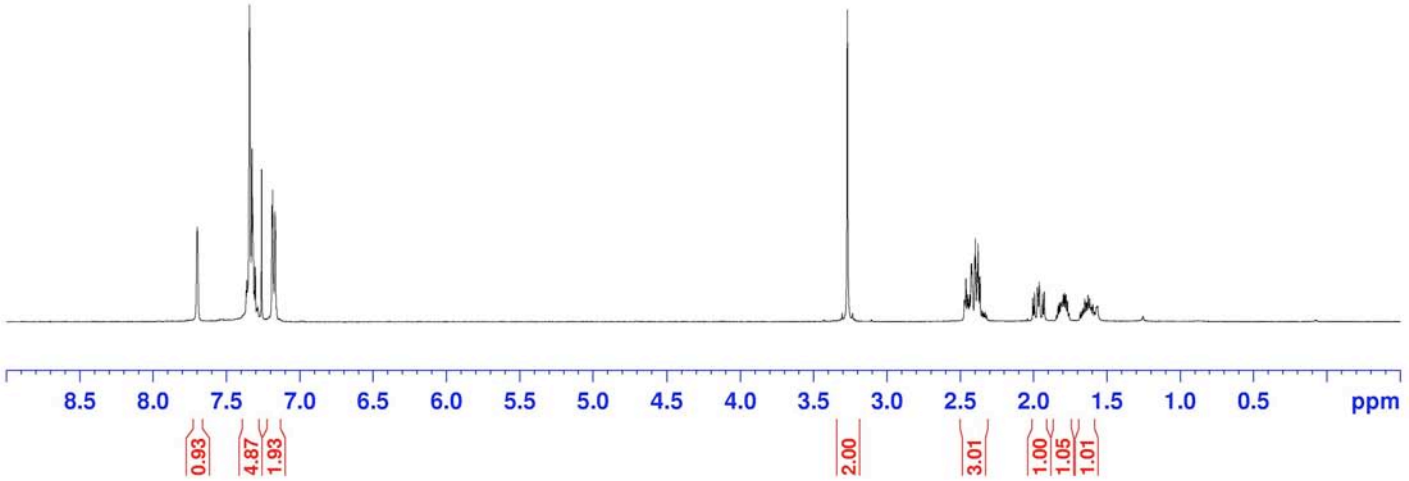

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  30.285 MM    1.1201 9369.51172  139.41949  87.8881
   2  37.641 BB    0.9050 1291.21948   16.83233  12.1119

Totals :                  1.06607e4   156.25183
```

RZ-4-242B-H

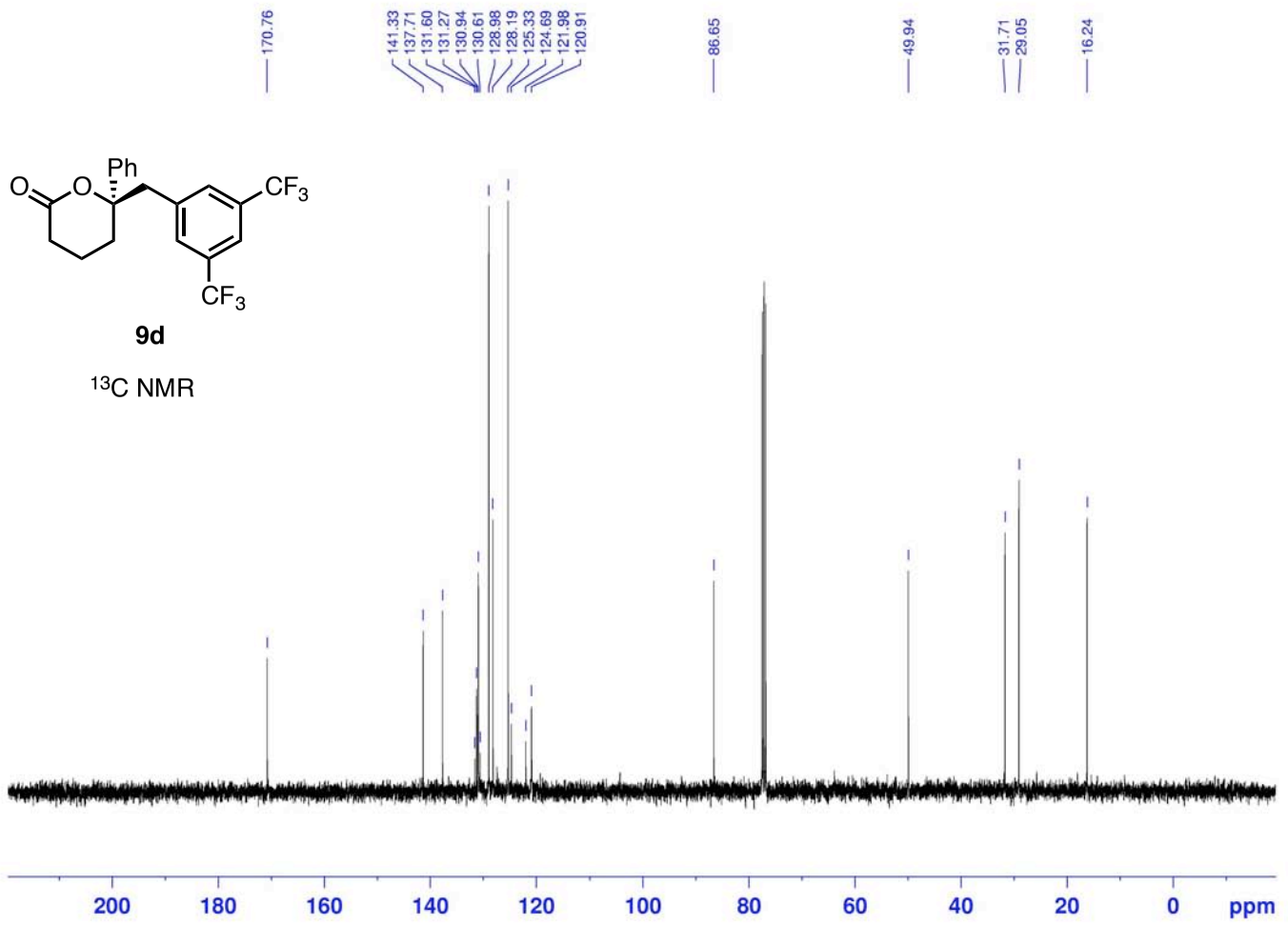


9d

^{1}H NMR



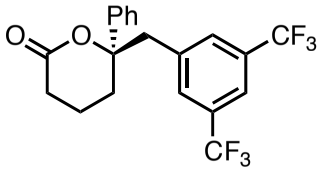
RZ-4-242B-C



9d

^{13}C NMR

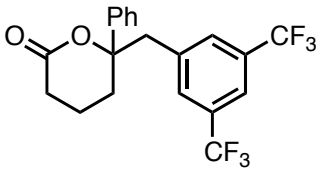
RZ-4-242B-F



9d

^{19}F NMR

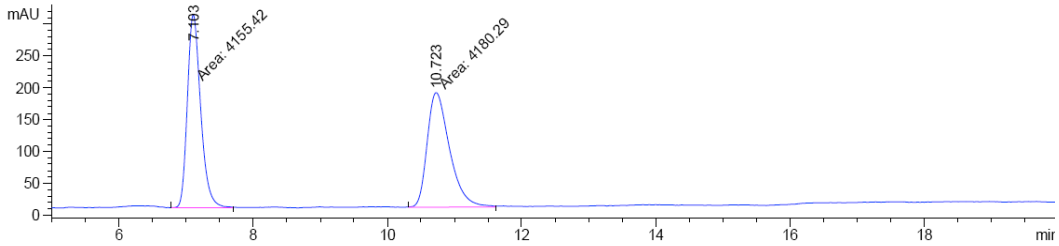
HPLC traces for 9d:



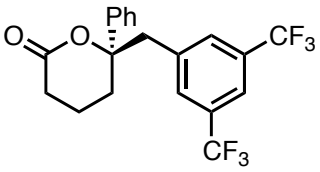
racemic

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-14 08-09-11\RZ-4-242B-RAC.D
Sample Name: RZ-4-242B-RAC

    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 12/14/2014 8:11:37 AM                    Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-14 08-09-11\RZ-SHUTDOWN.M
```

DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-14 08-09-11\RZ-4-242B-RAC.D)



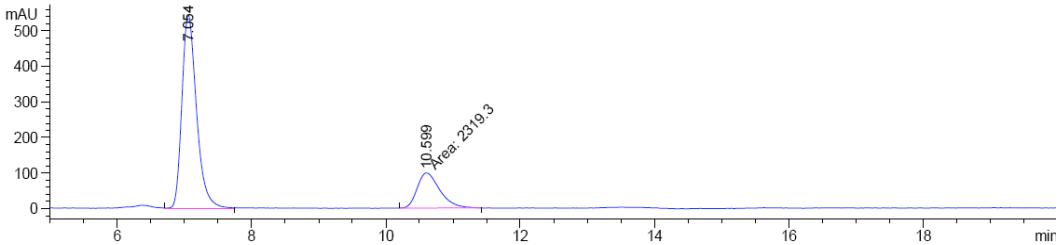

```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1   7.103 MM    0.2288 4155.41895  302.69006  49.8508
   2  10.723 MM    0.3872 4180.28613  179.91805  50.1492

Totals :                  8335.70508  482.60811
```



9d

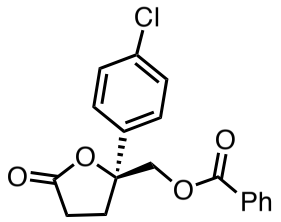
```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 09-18-36\RZ-4-242B.D
Sample Name: RZ-4-242B

    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 12/10/2014 9:20:55 AM                    Inj :   1
                                                       Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 09-18-36\RZ-SHUTDOWN.M
```

DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-10 09-18-36\RZ-4-242B.D)



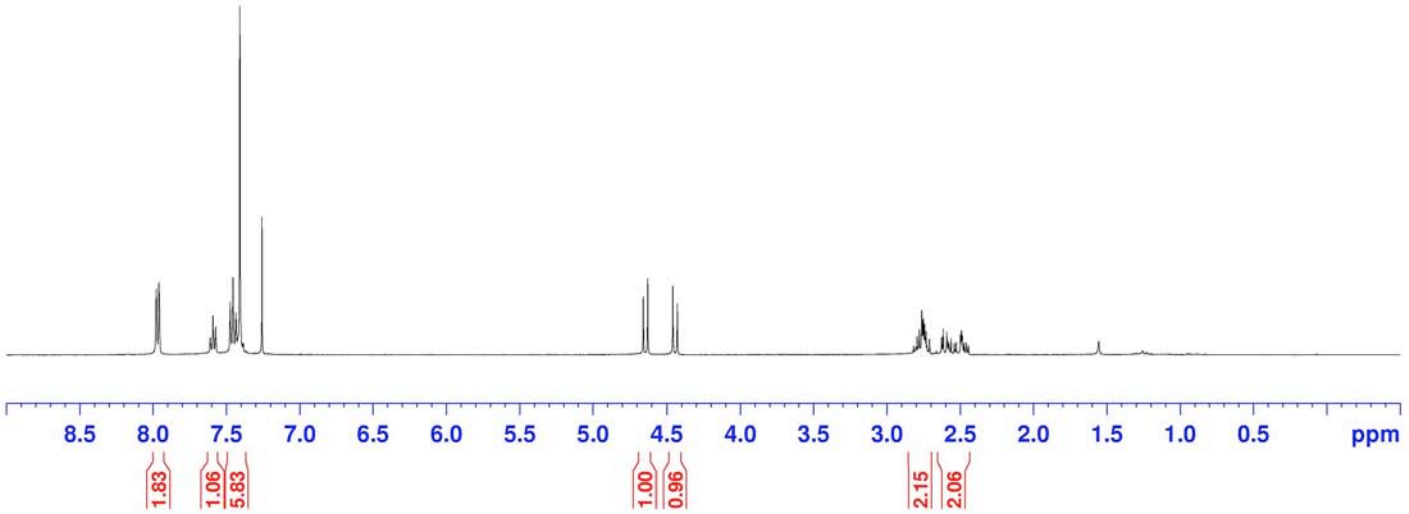

```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1   7.054 VB    0.2347 8238.34180  543.82831  78.0320
   2  10.599 MM    0.3910 2319.30396   98.86506  21.9680

Totals :                  1.05576e4   642.69337
```

RZ-4-235P1-H

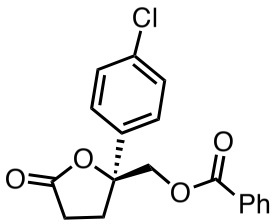


13

^{1}H NMR



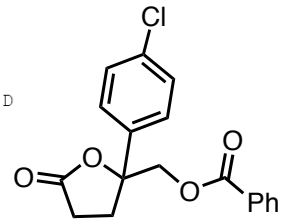
RZ-4-235P1-C



13

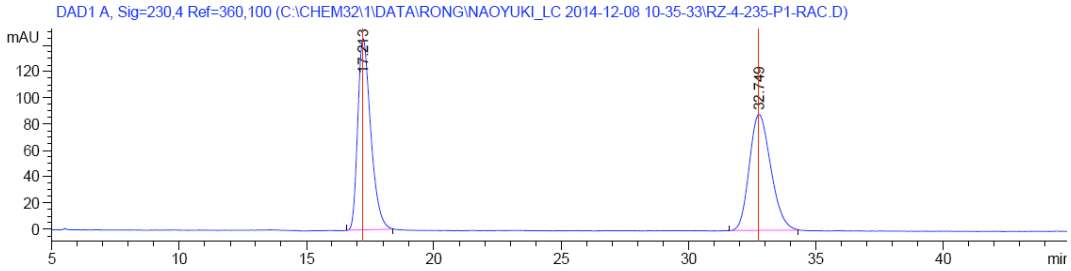
^{13}C NMR

HPLC traces for 13:

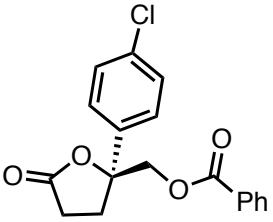


racemic

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-08 10-35-33\RZ-4-235-P1-RAC.D
Sample Name: RZ-4-235-P1-RAC

    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 1                        Location : Vial 18
    Injection Date  : 12/8/2014 11:29:03 AM                    Inj :   1
                                                         Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-08 10-35-33\RZ-SHUTDOWN.M
```

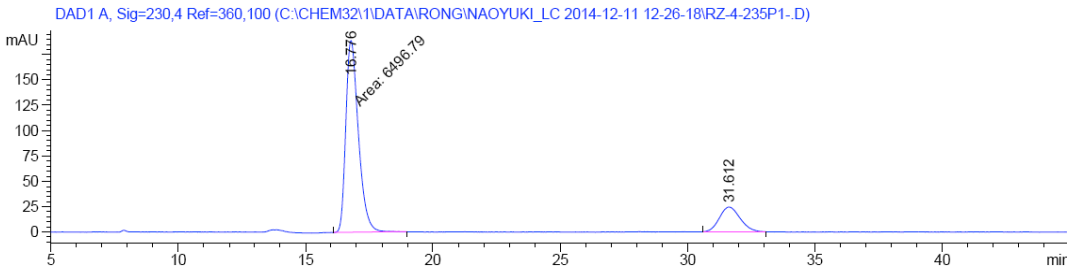



```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.213 BB    0.5263 5178.36182  145.83827  49.9535
   2  32.749 BB    0.8232 5187.99316   88.32819  50.0465

Totals :                  1.03664e4   234.16647
```



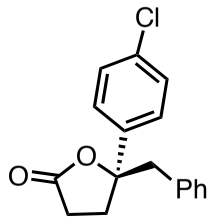
13

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-11 12-26-18\RZ-4-235P1-.D
Sample Name: RZ-4-235P1

    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   3
    Acq. Instrument : Instrument 1                        Location : Vial 16
    Injection Date  : 12/11/2014 2:10:58 PM                    Inj :   1
                                                         Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-11 12-26-18\RZ-SHUTDOWN.M
```



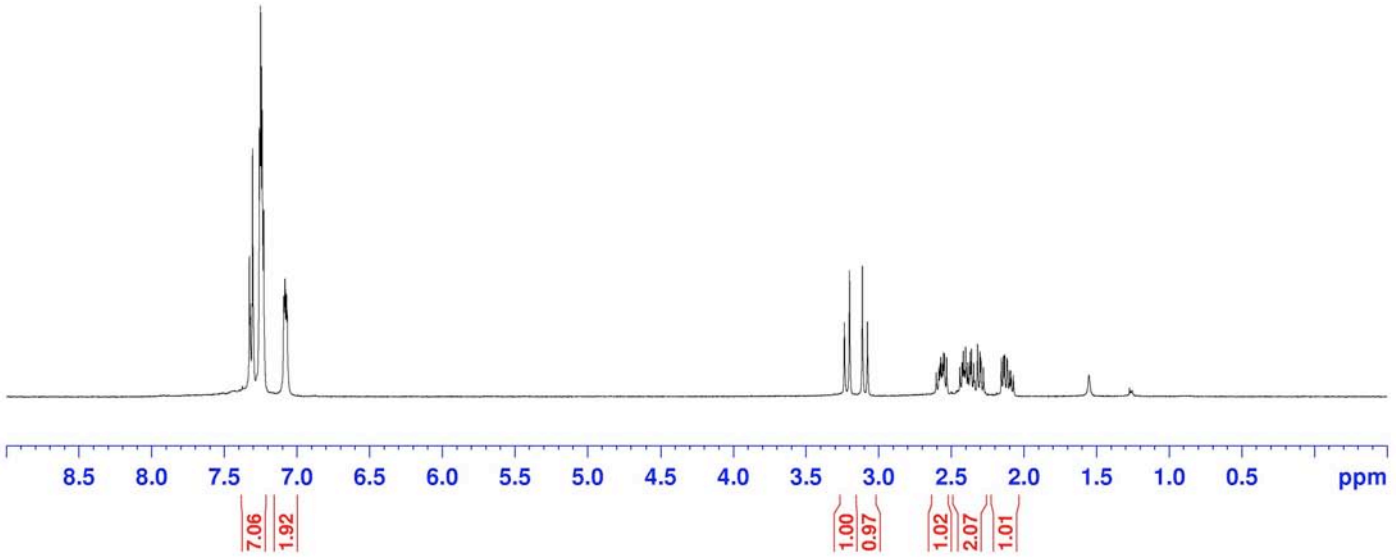

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.776 MM    0.5730 6496.78809  188.96053  82.4137
   2  31.612 BB    0.6725 1386.35205   24.48735  17.5863

Totals :                  7883.14014  213.44787
```

RZ-4-235P2-H

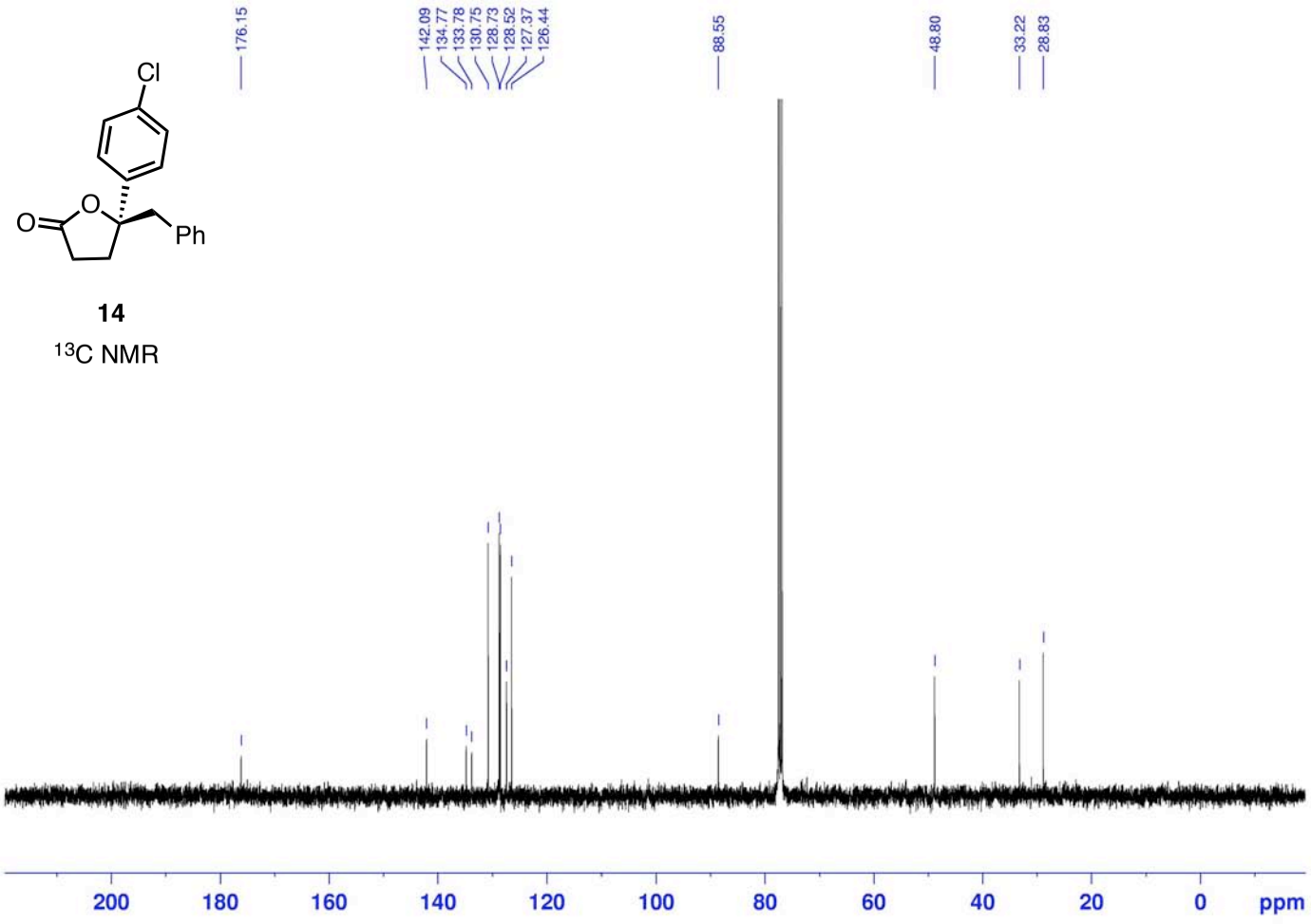


14

^{1}H NMR



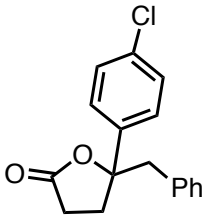
RZ-4-235P2-C



14

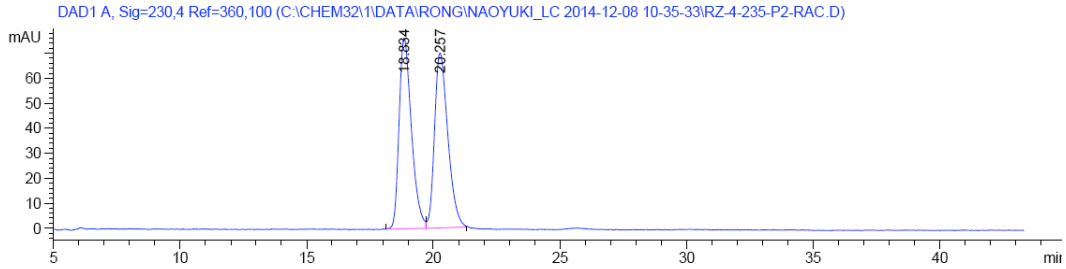
^{13}C NMR

HPLC traces for 14:

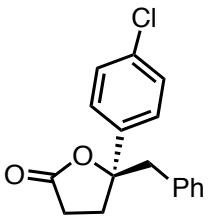


racemic

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-08 10-35-33\RZ-4-235-P2-RAC.D
Sample Name: RZ-4-235-P2-RAC

    ========================================================================
    Acq. Operator   : RZ                              Seq. Line :   4
    Acq. Instrument : Instrument 1                     Location : Vial 19
    Injection Date  : 12/8/2014 12:33:32 PM               Inj :   1
                                                     Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-08 10-35-33\RZ-5IPA-1ML-2013-.M
```

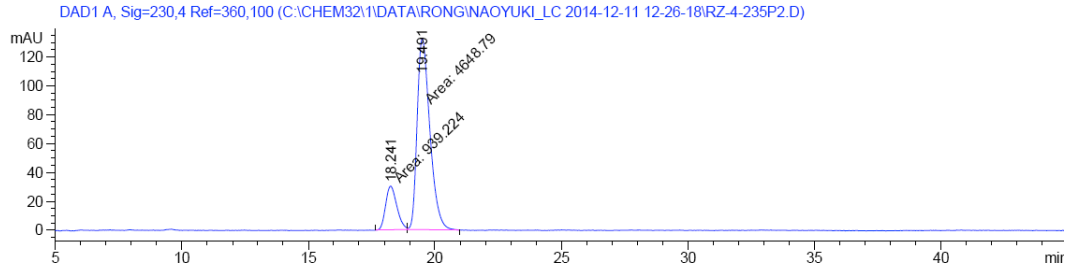



```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  18.834 BV    0.4962 2589.89990   76.26014  50.2433
   2  20.257 VB    0.5213 2564.81323   70.02714  49.7567

Totals :                  5154.71313  146.28728
```



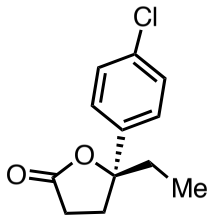
14

```
Data File C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-11 12-26-18\RZ-4-235P2.D
Sample Name: RZ-4-235P2

    ========================================================================
    Acq. Operator   : RZ                              Seq. Line :   5
    Acq. Instrument : Instrument 1                     Location : Vial 17
    Injection Date  : 12/11/2014 3:54:28 PM               Inj :   1
                                                     Inj Volume : 1 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\1\DATA\RONG\NAOYUKI_LC 2014-12-11 12-26-18\RZ-5IPA-1ML-2013-.M
```



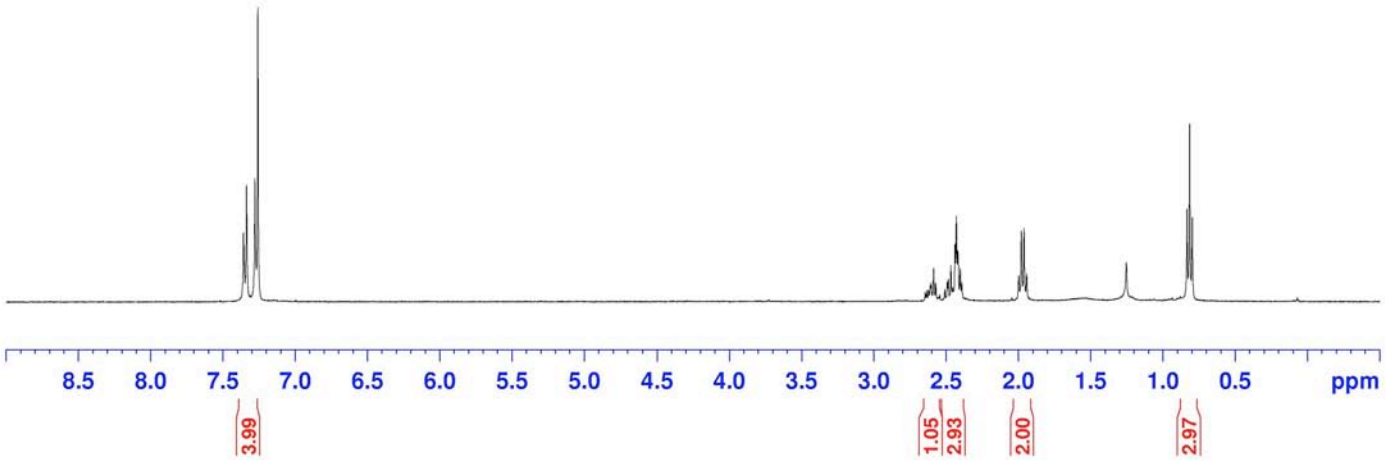

```
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  18.241 MM    0.5151  939.22388   30.39110  16.8078
   2  19.491 MM    0.5848 4648.78662  132.48862  83.1922

Totals :                  5588.01050  162.87972
```

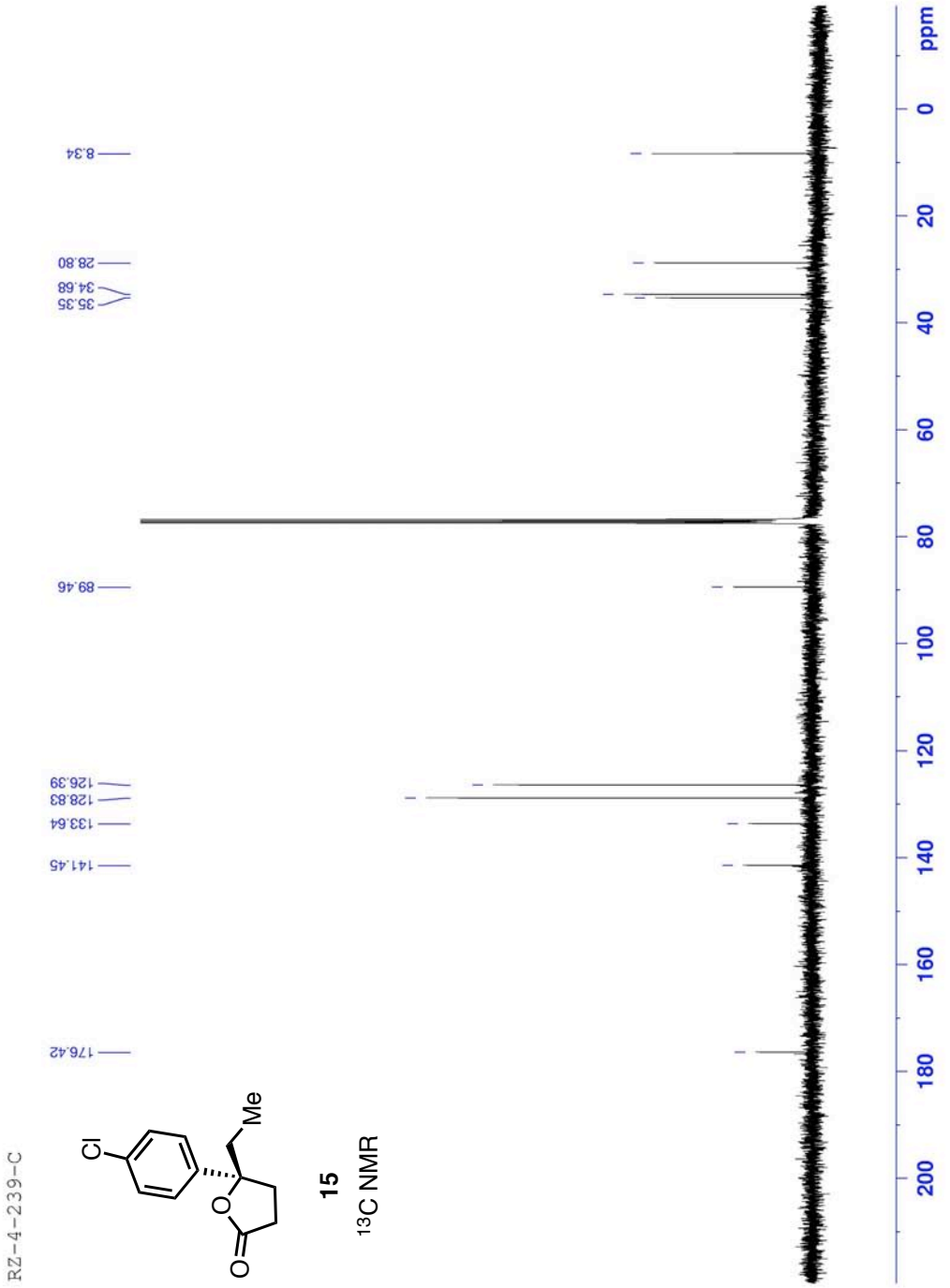
RZ-4-239-H



15

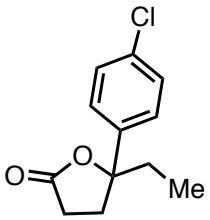
^{1}H NMR



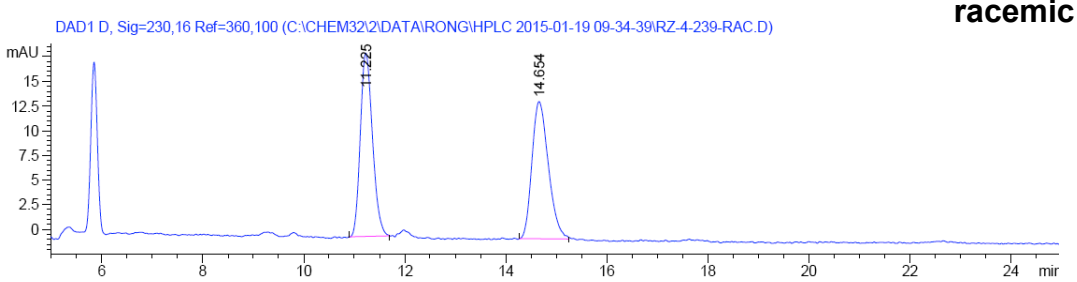

RZ-4-239-C
Cl
Me
O
O
15
^{13}C NMR
176.42
141.45
133.64
128.83
126.39
89.46
35.35
34.68
28.80
8.34
ppm
0
20
40
60
80
100
120
140
160
180
200

HPLC traces for 15:

```
Data File C:\CHEM32\2\DATA\RONG\HPLC 2015-01-19 09-34-39\RZ-4-239-RAC.D
Sample Name: RZ-4-239-RAC

    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   2
    Acq. Instrument : Instrument 2                        Location : Vial 17
    Injection Date  : 1/19/2015 10:06:27 AM                    Inj :   1
                                                         Inj Volume : 5 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 12 µl
    Acq. Method     : C:\CHEM32\2\DATA\RONG\HPLC 2015-01-19 09-34-39\RZ-SHUTDOWN2013.M
```

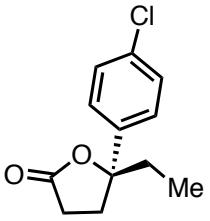


racemic

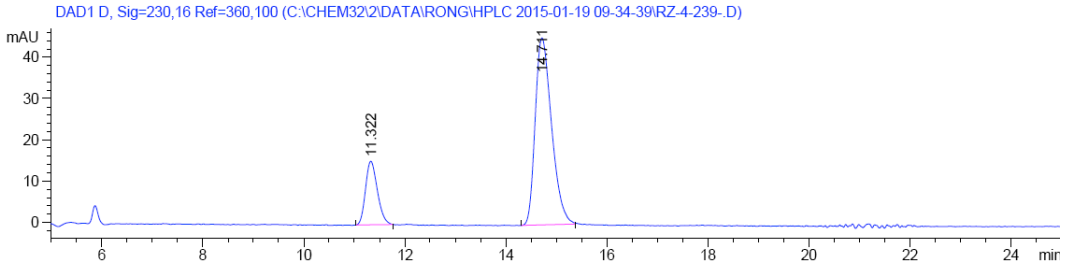



```
Signal 4: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.225 BB    0.2635  311.88034   18.60761  49.7788
   2  14.654 BB    0.3397  314.65201   13.91962  50.2212

Totals :                   626.53235   32.52723
```

```
Data File C:\CHEM32\2\DATA\RONG\HPLC 2015-01-19 09-34-39\RZ-4-239-.D
Sample Name: RZ-4-239-

    ========================================================================
    Acq. Operator   : RZ                                 Seq. Line :   1
    Acq. Instrument : Instrument 2                        Location : Vial 16
    Injection Date  : 1/19/2015 9:36:52 AM                     Inj :   1
                                                         Inj Volume : 5 µl
    Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
    Acq. Method     : C:\CHEM32\2\DATA\RONG\HPLC 2015-01-19 09-34-39\RZ-SHUTDOWN2013.M
```



15




```
Signal 4: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.322 BB    0.2515  253.43941   15.44407  19.8738
   2  14.711 BB    0.3512 1021.80634   45.29997  80.1262

Totals :                  1275.24574   60.74404
```