Intramolecular, Nucleophile-Catalyzed Aldol-Lactonization (NCAL) Reactions: Catalytic, Asymmetric Synthesis of Bicyclic β-Lactones[†]

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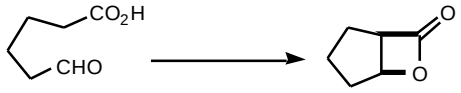
Supporting Information Available. General procedures for the intramolecular NCAL reactions and characterization data (including ^{1}H and ^{13}C NMR spectra) for bicyclic β-lactones **10a-10h** and cyclopentenes **18** and **19**. This material is available free of charge via the Internet at http://pubs.acs.org

[†] Dedicated to my mentor and friend Prof. A. I. Meyers, a father of asymmetric synthesis, on the occasion of his retirement

General. All reactions were carried out under N_2 in oven-dried or flame-dried glassware. Mukaiyama's reagent (2-chloro-1-methylpyridinium iodide) and keto-acid **8f** were purchased from Acros and used as received. Triethylamine, diisopropylethyl amine, and acetonitrile were distilled from CaH_2. All other commercially available reagents were purchased from Acros or Aldrich and were used as received. *O*-Acetylquinidine,[1] *O*-benzoylquinidine,[2] and *O*-acetylquinine[2] were prepared according to literature procedures. Aldehyde acid substrates were obtained by $NaIO_4$ cleavage of α-hydroxy cyclic ketones (**8a**)[3] or by ozonolysis of the corresponding trimethylsilylenol ethers (**8b**, **8c**, **8e**, **8f**)[4] or alkene acids (**8d**, **8g**).[5] Chiral GC analyses were performed using a 30 m Chiraldex β-DA column or a 2,3-di-OAc-6-TBS β-cyclodextrin column at the indicated oven temperatures and H_2 carrier pressures. All NMR spectra were obtained in $CDCl_3$ using tetramethylsilane (TMS) as internal standard, unless noted otherwise. Elemental analyses were conducted by Atlantic Micro Labs, Inc. In some cases, satisfactory HRMS or elemental analysis could not be obtained on the bicyclic-β-lactones (**10a**, **10c**, **10e**, **10f**, and **13**) due to apparent instability and/or volatility and therefore HRMS were obtained after β-lactone ring opening with *N*-benzyloxy amine to provide the corresponding benzyl hydroxamic acids.

General Procedure for the Racemic NCAL Reaction as Described for Bicyclic β-lactone (+/-)-10a.



8a (+/-)-**10a**

1) Waddell, T.G.; Woods, L.A.; Harrison, W.; Meyer, G.M. *J. Tennessee Acad. Sci.* **1984**, *59*, 48-50.

2) Pracejus, H.; Matje, H. *J. Prak. Chem.* **1964**, 195-205.

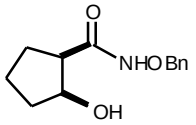
3) Floresca, R.; Kurihara, M.; Watt, D.S.; Demir, A. *J. Org. Chem.* **1993**, *58*, 2196-2200.

4) Padwa, A.; Brodney, M.A.; Marino, J.P., Jr.; Sheehan, S.M. *J. Org. Chem.* **1997**, *62*, 78-87.

5) Bailey, P.S. *Ozonation in Organic Chemistry*; Academic: San Diego, CA, **1982**; Vol. 2.

To a solution of 2.95 g of Mukaiyama's reagent (11.53 mmol, 3.0 equiv) and 2.15 mL of triethylamine (15.37 mmol, 4.0 equiv) in 45.0 mL of acetonitrile at 25 °C was added via syringe pump a solution of aldehyde-acid **8a**[3] (500 mg, 3.84 mmol) in 31.9 mL of acetonitrile over 10 h (final concentration: 0.05 M). The resulting dark red solution was stirred for another 12 h, at which point the volatiles were removed under reduced pressure to give a brown residue. The crude reaction mixture was then partitioned between diethyl ether and water (100 mL each). The phases were separated, and the aqueous layer was extracted with diethyl ether (2 x 100 mL). The combined organic phases were washed with saturated NH_4Cl (3 x 200 mL), and then brine (100 mL), dried over $MgSO_4$, filtered, and concentrated to afford a faint-orange residue that was purified by flash chromatography on SiO_2 (1:1 → 1:0, Et_2O/hexanes) to afford β-lactone **10a**[6] (240 mg, 55%) as a light yellow oil: R_f 0.57 (Et_2O); IR (thin film)ν_{max} 1818 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.00 (app t, *J* = 3.9 Hz, 1H), 3.90 (dd, *J* = 3.9, 7.8 Hz, 1H), 2.20 (dd, *J* = 6.3, 14.4 Hz, 1H), 2.13 (dd, *J* = 7.2, 12.6 Hz, 1H), 1.89-1.98 (m, 1H), 1.69-1.85 (m, 1H), 1.45-1.65 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 77.4, 55.5, 30.5, 26.1, 22.0.

FAB HRMS Calcd for $C_{13}H_{17}O_3N$: 236.1287. Found: 236.1277 (for the corresponding benzyl hydroxamic acid derivative).



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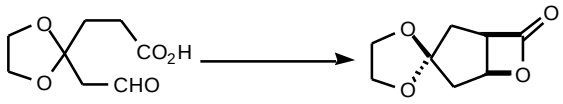

8b **10b**

β-Lactone 10b. This β-lactone was prepared from aldehyde-acid **8b** (200.0 mg, 1.06 mmol). Purification by flash chromatography (3:7 → 2:3, EtOAc/hexanes) gave β-lactone **10b** as a faint-yellow solid (118 mg, 66%): R_f 0.62 (4:1, EtOAc/hexanes); IR

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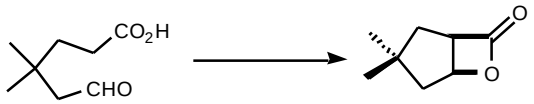
6) This compound has been prepared as a racemate from *cis*-hydroxycyclopentanecarboxylic acid upon treatment with cold tosyl chloride-pyridine, see: Philp, R. P.; Robertson, A. V. *Aust. J. Chem.* **1977**, *30*, 123-130.

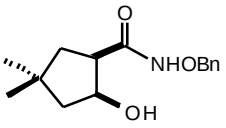
($CHCl_3$)ν_{max} 1832 cm^{-1}; ^{1}H NMR (300 MHz, benzene-d_6) δ 3.98 (app t, *J* = 4.7 Hz, 1H), 3.23-3.34 (m, 2H), 3.16-3.21 (m, 2H), 3.02 (dd, *J* = 4.3, 8.5 Hz, 1H), 1.98 (dd, *J* = 1.2, 14.9 Hz, 1H), 1.96 (ddd, *J* = 1.5, 2.3, 14.0 Hz, 1H), 1.37-1.41 (m, 1H), 1.31-1.36 (m, 1H); ^{13}C NMR (75 MHz, benzene-d_6) δ 169.8, 115.6, 73.4, 64.7, 64.5, 53.9, 39.5, 36.4. Anal. Calcd for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 56.67; H, 5.91.



8c **10c**

β-**Lactone 10c.** This β-lactone was prepared from aldehyde-acid **8c** (160.0 mg, 1.01 mmol). Purification by flash chromatography (1.5:8.5, Et_2O/hexanes) afforded β-lactone **10c** (100 mg, 68%) as a faint-yellow oil: R_f 0.60 (2:3, EtOAc/hexanes); IR ($CHCl_3$)ν_{max} 1815 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.02 (app t, *J* = 4.6 Hz, 1H), 3.90 (ddd, *J* = 1.2, 4.4, 9.5 Hz, 1H), 2.07 (app t, *J* = 15.6 Hz, 2H), 1.67 (dd, *J* = 9.2, 13.9 Hz, 1H), 1.64 (dd, *J* = 5.0, 15.4 Hz, 1H), 1.21 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 79.7, 56.6, 44.4, 40.6, 40.4, 31.3, 29.2.

FAB HRMS Calcd for $C_{13}H_{17}O_3N$: 264.1599. Found: 264.1594 (for the corresponding benzyl hydroxamic acid derivative).



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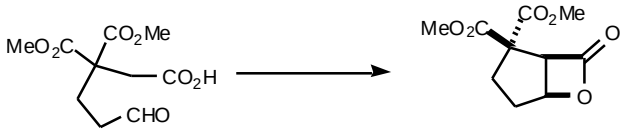
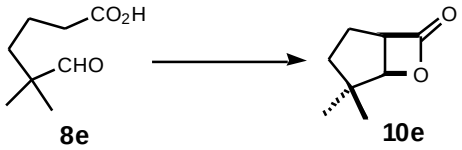


8d **10d**

β-**Lactone 10d.** This β-lactone was prepared from aldehyde-acid **8d** (250 mg, 1.01 mmol). Purification by flash chromatography (3:7, EtOAc/hexanes) afforded β-lactone **10d** (144 mg, 62%) as a white solid: R_f 0.64 (3:2, EtOAc/hexanes); IR ($CHCl_3$)ν_{max} 1831, 1737 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.09 (app t, *J* = 3.9 Hz, 1H), 4.44 (dd, *J* = 1.2, 3.9 Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 2.65 (ddd, *J* = 6.9, 14.0, 14.0 Hz, 1H), 2.39

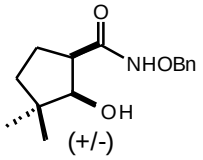
(dd, *J* = 7.3, 14.3 Hz, 1H), 2.27 (dd, *J* = 6.7, 15.1 Hz, 1H), 1.76 (dddd, *J* = 3.9, 7.2, 13.6, 19.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 167.5, 166.9, 77.3, 60.6, 60.2, 53.4, 53.1, 29.9, 28.8. Anal. Calcd for $C_{10}H_{12}O_6$: C, 52.63; H, 5.30. Found: C, 52.64; H, 5.36.



8e **10e**

β-**Lactone 10e.** This β−lactone was prepared from aldehyde-acid **8e**[7] (150 mg, 0.95 mmol). Purification by flash chromatography (1:1 → 1:0, Et_2O/hexanes) gave β-lactone **10e** (82.8 mg, 62%) as a light yellow oil: R_f 0.73 (Et_2O); IR (thin film)ν_{max} 1824 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.36 (app d, *J* = 3.6, 1H), 3.86 (dd, *J* = 3.9, 7.7 Hz, 1H), 2.04 (dd, *J* = 6.6, 13.2 Hz, 1H), 1.85 (ddd, *J* = 7.5, 12.6, 14.9 Hz, 1H), 1.72 (dd, *J* = 6.9, 12.3 Hz, 1H), 1.60 (dd, *J* = 6.3, 12.0 Hz, 1H), 1.17 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 83.7, 55.1, 40.3, 35.5, 24.2, 22.6, 21.9.

FAB HRMS Calcd for $C_{15}H_{21}O_3N$: 264.1560. Found: 264.1608 (for the corresponding benzyl hydroxamic acid derivative).



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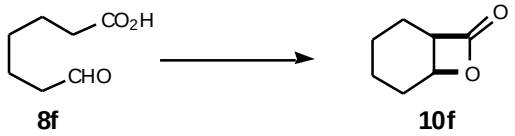

8f **10f**

β-**Lactone 10f.** This β-lactone was prepared from aldehyde-acid **8f** (180 mg, 1.25 mmol). Purification by flash chromatography (1.5:8.5, Et_2O/hexanes) afforded β-lactone **10f** (56.4 mg, 36%) as a faint-yellow oil: R_f 0.49 (1:1, Et_2O/hexanes); IR ($CHCl_3$)ν_{max} 1813 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.71 (ddd, *J* = 2.8, 4.4, 7.3 Hz, 1H), 3.67 (ddd, *J* = 3.4, 6.6, 9.8 Hz, 1H), 2.09 (dddd, *J* = 2.9, 4.9, 7.8, 14.7 Hz, 1H) 1.46-1.98 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 70.8, 47.0, 25.7, 19.6, 19.3, 16.7.

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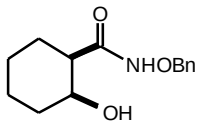
7) Batty, D.; Crich, D. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3193-3203.

FAB HRMS Calcd for $C_{14}H_{20}O_3N$: 250.1443. Found: 250.1454 (for the corresponding benzyl hydroxamic acid derivative).



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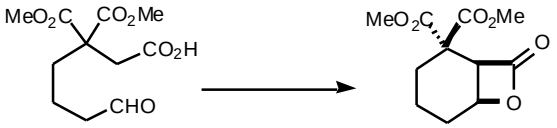
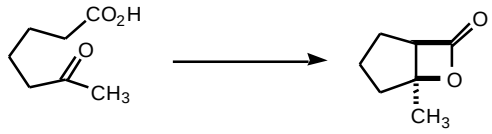


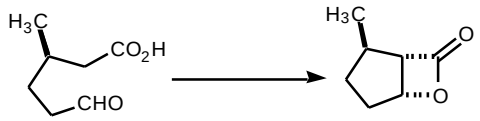
8g **10g**

β-**Lactone 10g.** This β-lactone was prepared from aldehyde-acid **8g** (360 mg, 1.38 mmol). Purification by flash chromatography (1:1 → 1:0, Et_2O/hexanes) gave β−lactone **10g** (190 mg, 57%) as a clear oil: R_f 0.67 (Et_2O); IR (thin film)ν_{max} 1829, 1737 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$) δ 4.96-5.02 (m, 1H), 4.43 (m, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 2.24-2.38 (m, 1H), 1.98-2.20 (m, 2H), 1.75-1.96 (m, 2H), 1.44-1.60 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 168.4, 168.2, 70.9, 53.2, 52.9, 51.9, 51.3, 25.7, 24.2, 14.6. Anal. Calcd for $C_{11}H_{14}O_6$: C, 54.54; H, 5.83. Found: C, 54.81; H, 5.93.



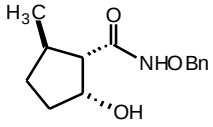
8h **10h**

β-**Lactone 10h.** This β−lactone was prepared from commercially available keto-acid **8h** (500 mg, 3.47 mmol). Purification by flash chromatography (1.4:1 → 1:0, Et_2O/hexanes) gave β−lactone **10h** (12.2 mg, 3%) as a light yellow oil: R_f 0.73 (Et_2O); IR (thin film)ν_{max} 1824 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.43 (app d, *J* = 7.5 Hz, 1H), 2.17 (dd, *J* = 5.4, 14.4 Hz, 1H), 2.09 (dd, *J* = 4.5, 12.0 Hz, 1H), 1.71-1.95 (m, 2H), 1.68 (s, 3H), 1.44-1.64 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 87.3, 59.1, 40.3, 36.2, 27.2, 23.9, 21.5.



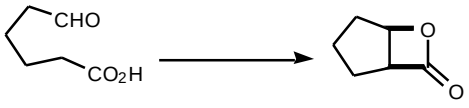
12 **13**

β-Lactone 13. This β-lactone was prepared from aldehyde-acid **12**, derived from (*R*)-citronellic acid[8] (100 mg, 0.64 mmol). Purification by flash chromatography (1:1 → 1:0, Et_2O/hexanes) gave β-lactone **13** (35.3 mg, 40%) as a faint-yellow oil: R_f 0.72 (Et_2O); $[\alpha]_D^{25}$ +30.2 (*c* 0.04, MeOH); IR (thin film)ν_{max} 1813 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.02 (app t, *J* = 3.9 Hz, 1H), 3.57 (app d, *J* = 3.9 Hz, 1H), 2.59 (ddd, *J* = 7.2, 7.2, 14.1 Hz, 1H), 2.15 (dd, *J* = 6.9, 14.4 Hz, 1H), 2.04 (ddd, *J* = 6.0, 11.7, 17.9 Hz, 1H), 1.72-1.86 (m, 1H), 1.66 (dd, *J* = 7.5, 12.3 Hz, 1H), 0.93 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 77.8, 62.6, 33.5, 29.3, 28.1, 18.9.



FAB HRMS Calcd for $C_{14}H_{19}O_3N$: 250.1443. Found: 250.1455 (for the corresponding benzyl hydroxamic acid derivative).

General procedure for the Catalytic, Asymmetric NCAL Reaction as Described for Bicyclic β-lactone (+)-(1*R*, 2*S*)-10a.



8a **(+)-10a**

O-Acetyl quinidine[1] (136 mg, 0.384 mmol), Mukaiyama's reagent (2.95 g, 11.53 mmol), and 2.70 ml of Hunig's base (15.4 mmol) were placed in a 100 mL round-bottomed flask and dissolved in 45 mL of CH_3CN. To this slurry was added a solution of aldehyde-acid **8a** (500 mg, 3.84 mmol) in 32 mL of CH_3CN via syringe pump over 12 h. After the addition was complete, the reaction was stirred an additional 96 h at 25 °C. The solvent was removed in vacuo, and the orange residue was partitioned between Et_2O (100 mL) and water (100 mL). The phases were separated, and the aqueous layer was extracted

8) Overberger, C. G.; Kage, H. *J. Am. Chem. Soc.* **1967**, *22*, 5640-5645.

with Et_2O (2 x 100 mL). The combined organic phases were washed with saturated NH_4Cl solution (3 x 200 mL), and then brine (1 x 200 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography on SiO_2 (1:1 → 1:0, Et_2O/hexanes) to give β-lactone (+)-**10a** (233 mg, 54%) as a light yellow oil: $[\alpha]_D^{25}$ +85.0 (*c* 0.02, MeOH). Enantiomeric excess was determined to be 92% by chiral GC analysis using a 2,3-di-OAc-6-TBS β-CD[9] column (130 °C, 11 psi); $t_{(1S,2R)}$ = 20.68 min (minor), $t_{(1R,2S)}$ = 21.32 min (major). All other spectroscopic data matched that displayed by the same compound prepared using Et_3N as nucleophile.

(–)-(1*S*, 2*R*)-β-lactone 10a. 51% yield; Prepared according to the general asymmetric NCAL procedure using Mukaiyama's reagent (1.53 g, 5.99 mmol), 1.40 mL of Hünig's base (7.99 mmol), and 73.2 mg of *O*-acetyl quinine (0.199 mmol) in 24.0 mL of CH_3CN, and 260.0 mg of aldehyde-acid **8a** (1.98 mmol) in 16.6 mL of CH_3CN. This gave β-lactone **10a** in 51% yield and 86% ee (chiral GC analysis using a 2,3-di-OAc-6-TBS β-CD column, 130 °C, 11 psi); $t_{(1S,2R)}$ = 20.49 min (major), $t_{(1R,2S)}$ = 22.40 min (major). $[\alpha]_D^{25}$ –48.1 (*c* 0.77, MeOH). All other spectroscopic data matched that displayed by the same compound prepared using Et_3N as nucleophile.

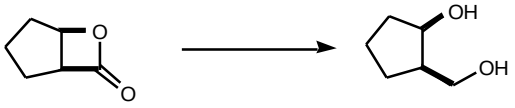
(+)-(3*R*, 4*S*)-β-lactone 10b. Prepared according to the general asymmetric NCAL procedure using Mukaiyama's reagent (2.03 g, 7.97 mmol), 1.80 mL of Hunig's base (4.03 mmol), and 97.0 mg of *O*-acetyl quinidine (0.100 mmol, 0.1 equiv.) in 32.0 mL of CH_3CN, and 500.0 mg of aldehyde-acid **8b** (2.66 mmol) in 22.2 mL of CH_3CN. This gave β-lactone **10b** in 37% yield and 92% ee (chiral GC analysis using a 30 m Chiraldex β–DA® column; 120 °C, 10 psi H_2); $t_{(3S,4R)}$ = 73.25 min (minor), $t_{(3R,4S)}$ = 73.59 min

9) We thank Prof. Vigh for providing this column for our studies. Shitangkoon, A.; Vigh, G. *J. Chromatogr. A* **1996**, 31-42.

(major). $[\alpha]_D^{25}$ +62.6 (*c* 0.95, $CHCl_3$). All other spectroscopic data matched that displayed by the same compound prepared using Et_3N as nucleophile.

(+)-(1*R*, 2*S*)-β-lactone 10c. Prepared according to the general asymmetric NCAL procedure using Mukaiyama's reagent (1.55 g, 6.07 mmol), 1.40 mL of Hunig's base (8.08 mmol), and 74.0 mg of *O*-acetyl quinidine (0.202 mmol, 0.1 equiv.) in 24.4 mL of CH_3CN, and 320.0 mg of aldehyde-acid **8c** (2.02 mmol) in 17.0 mL of CH_3CN. This gave β-lactone **10c** in 45% yield and 90% ee (chiral GC analysis using a 2,3-di-OAc-6-TBS β-CD[9] column; 130 °C, 11 psi); $t_{(1R,2S)}$ = 11.37 min, $t_{(1S,2R)}$ = 14.13 min. $[\alpha]_D^{25}$ +45 (*c* 0.6, $CHCl_3$). All other spectroscopic data matched that displayed by the same compound prepared using Et_3N as nucleophile.

Reduction of (+)-β-Lactone 10a to (–)-Diol 14.

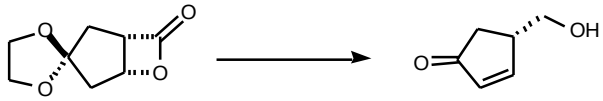


(+)-10a (92% ee) **(–)-14**

A solution of DIBAl-H (238 μL in 0.78 mL of CH_2Cl_2, 0.45 mmol) was added dropwise to a solution of β-lactone (+)-**10a** (53 mg, 0.47 mmol) in 5.3 mL of CH_2Cl_2 cooled to 0 °C. After stirring for 5 min, the solution was warmed to 25 °C and stirred for 1.0 h. The reaction mixture was then cooled to 0 °C, diluted with 2.4 mL of ethyl acetate and quenched with acetone (1.5 mL) and Rochelle's salt (4.0 mL). The mixture was vigorously stirred at 25 °C for 10 h. The layers were separated and the aqueous layer was extracted with ethyl acetate (2 x 4 mL). The combined organic layers were washed with brine (1 x 8 mL), dried over $MgSO_4$, filtered, and concentrated to give diol **14** as a colorless oil (26.1 mg, 48% yield). Purification by flash chromatography on SiO_2 (100%

EtOAc) gave an analytically pure sample: $[\alpha]_D^{25}$ –33.0° (*c* 0.02, MeOH; lit $[\alpha]_D^{25}$ –37.7° (*c* 0.68, MeOH.) All other spectroscopic data matched that previously reported.[10]

Conversion of (+)-β-lactone 10b to carbocyclic intermediate 20.



10b **18**

A solution of (+)-β-lactone **10b** (101.8 mg, 0.598 mmol) in 6.0 mL of anhydrous THF was cooled to 0 °C and treated with 850 μL of BH_3•DMS (15 equiv., 8.97 mmol). After stirring for 18 h at 25 °C, excess borane was quenched by careful addition of 5% Et_3N in anhydrous MeOH (8 mL). The volatiles were removed under reduced pressure to give a residue that was dissolved in 8 mL of 5% Et_3N/MeOH. The solvent was again removed, repeating this operation a total of five times. The crude diol was dissolved in 12.0 mL of THF and treated with 2.5 mL of 1.0 N aq. HCl. The yellow solution was stirred at 25 °C for 20 h, at which point the reaction mixture was poured onto 10 mL of brine and 20 mL of CH_2Cl_2. The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (4 x 20 mL). The organic phases were combined, and then washed with brine, dried over $MgSO_4$, filtered, and concentrated to afford a light yellow residue that was purified by flash chromatography on SiO_2 (EtOAc) to afford cyclopentenol **18** (34.2 mg, 51% yield for the two steps) as a colorless oil: R_f 0.45 (1:9, MeOH/EtOAc); $[\alpha]_D^{25}$ –15.9° (*c* 0.34, MeOH); IR ($CHCl_3$)ν_{max} 3435 (broad), 1703, 1670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 2.4, 5.6 Hz, 1H), 6.22 (dd, *J* = 2.0, 5.6 Hz, 1H), AB of ABX (δ_A = 3.74, δ_B = 3.69, J_{AB} = 10.5 Hz, J_{AX} = 6.1 Hz, J_{BX} = 5.9 Hz, 2H), 3.12-3.22 (m, 1H), 2.47 (dd, *J* = 6.6, 18.9 Hz, 1H), 2.16 (dd, *J* = 2.1, 18.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.8, 165.5, 135.2, 64.4, 44.1, 37.6.

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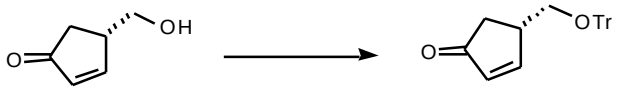
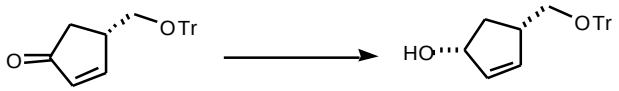
10) Inoguchi, K.; Fujie, N.; Yoshikawa, K.; Achiwa, K. *Chem. Pharm. Bull.* **1991**, *40*, 2921-2926.



18 **19**

4-Trityloxymethyl-cyclopent-2-enone (19). A solution of alcohol **18** (34.0 mg, 0.303 mmol) in 3.40 mL of anhydrous CH_2Cl_2 at ambient temperature was treated with 126.0 mg of triphenylmethyl chloride (0.453 mmol), 60 μL of anhydrous pyridine (0.727 mmol) and a catalytic amount of DMAP. After 18 h, the clear mixture was partitioned between saturated NH_4Cl (20 mL) and EtOAc (20 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated to afford a cloudy residue that was purified by flash chromatography on SiO_2 (3:7, Et_2O/hexanes) to provide trityl ether **19** (96.6 mg, 90% yield) as a colorless residue that solidifies upon standing: R_f 0.68 (1:1, EtOAc/hexanes); $[\alpha]_D^{25}$ –17° (*c* 0.5, MeOH); IR ($CHCl_3$)ν_{max} 1709, 1601 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 2.4, 5.9 Hz, 1H), 7.38-7.42 (m, 7H), 7.28-7.33 (m, 8H), 6.22 (dd, *J* = 2.0, 5.4 Hz, 1H), 3.27 (dd, *J* = 5.9, 8.3 Hz, 1H), 3.20 (dddd, *J* = 1.9, 4.4, 8.3, 10.7 Hz, 1H), 3.12 (dd, *J* = 6.3, 8.3 Hz, 1H), 2.46 (dd, *J* = 6.3, 18.6 Hz, 1H), 2.10 (dd, *J* = 1.9, 18.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.5, 166.0, 143.7, 134.9, 128.6, 127.9, 127.1, 86.6, 65.2, 42.1, 38.0; FAB HRMS calcd for $C_{25}H_{24}O_2$ [M + Na] 379.1674, found 379.1670.



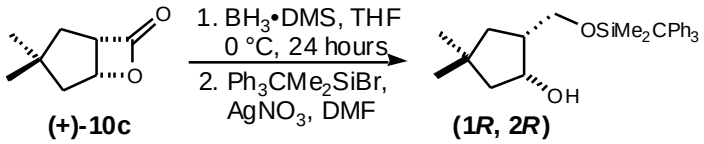
19 **20**

4-Trityloxylmethy-cyclopent-2-enol (20). Enone **19** (80.0 mg, 0.225 mmol) was dissolved in 11.5 mL of anhydrous THF, cooled to –78 °C, and treated with 240 μL of DIBAL-H (1.0 M in $PhCH_3$, 1.04 equiv.). After 30 minutes, an additional 0.70 equiv. of DIBAl-H was added. The reaction mixture was quenched by addition of 100 μL of water

and 600 mg of silica gel. The resulting slurry was allowed to warm to ambient temperature and was stirred vigorously for 1 h. The mixture was then filtered through a pad of anhydrous Na_2SO_4, washing with EtOAc. The solvent was removed under reduced pressure to give a residue (>19:1 dr, ^{1}H NMR) that was purified by flash chromatography to afford the desired cis-hydroxypentenol **20** (70 mg, 87% yield) as a colorless residue that crystallizes upon standing: R_f 0.63 (4:1, Et_2O/hexanes); $[\alpha]_D^{25}$ –66.3° (*c* 1.0, $CHCl_3$); literature $[\alpha]_D^{25}$ –72.1° (*c* 1.2, $CHCl_3$);[11] IR ($CHCl_3$)ν_{max} 3682, 3598, 3495, 1596, 1489 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-7.42 (m, 6H), 7.22-7.38 (m, 9H), 5.94-6.02 (m, 2H), 4.68-4.78 (m, 1H), 3.29 (dd, *J* = 4.7, 9.0 Hz, 1H), 3.07 (dd, *J* = 5.0, 9.0 Hz, 1H), 2.80-2.90 (m, 1H), 2.38 (ddd, *J* = 7.5, 8.6, 14.0 Hz, 1H), 2.12 (d, *J* = 8.7 Hz, 1H, OH), 1.44 (dt, *J* = 3.3, 14.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 135.7, 134.8, 128.8, 127.8, 127.0, 86.9, 76.6, 65.9, 44.8, 37.4; FAB HRMS calcd for $C_{25}H_{22}O_2$ [M + Na] 377.1517, found 377.1517.

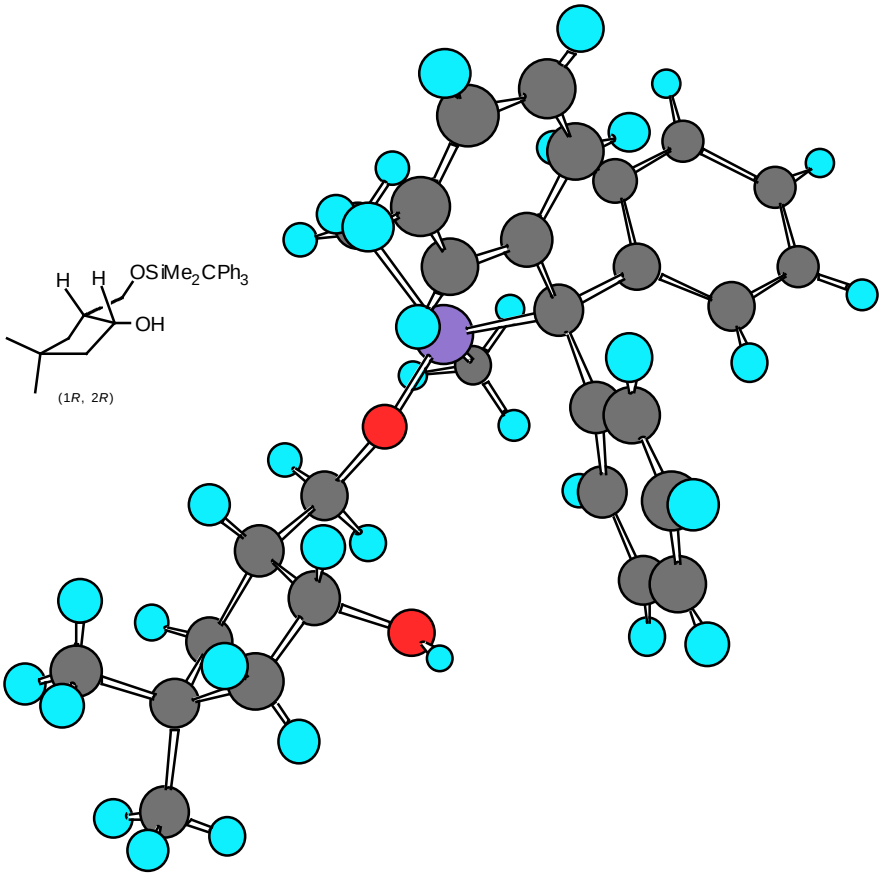
11) Roberts, S. M.; Shoberu, K. A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2605.

Proof of absolute configuration of (+)-**10c** was obtained via x-ray analysis of a crystalline derivative prepared as shown below.

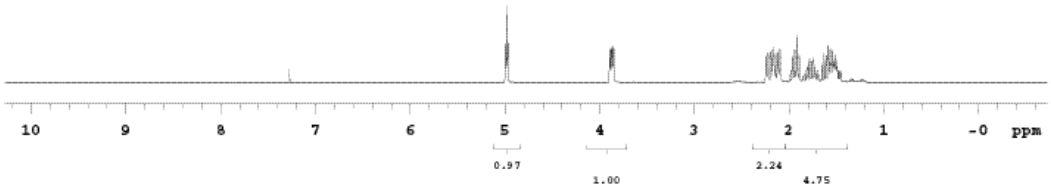


(+)-10c **(1*R*, 2*R*)**

The silicon atom was sufficient for anomalous dispersion techniques allowing assignment of the absolute configuration. The Chem3D representation of the x-ray structure is provided below.



10a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9
8
7
6
5
4
3
2
1
-0
ppm
0.97
1.00
2.24
4.75

10a

171.299
77.441
77.000
76.573
55.517
30.535
26.108
21.954
180
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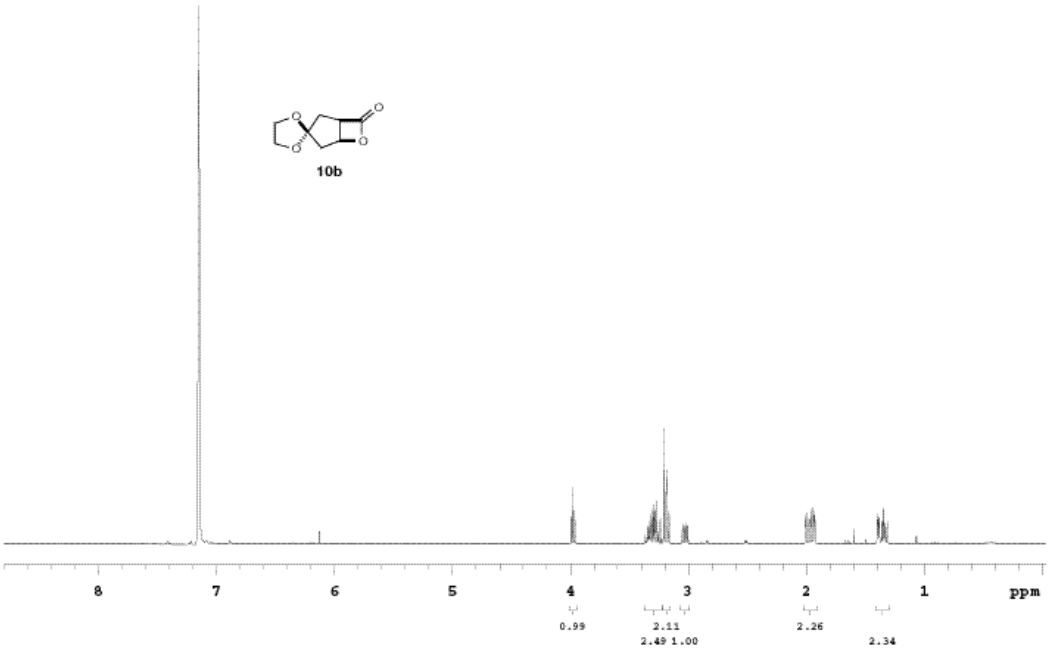
140
120
100
80
60
40
20
ppm


10b
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7
6
5
4
3
2
1
ppm
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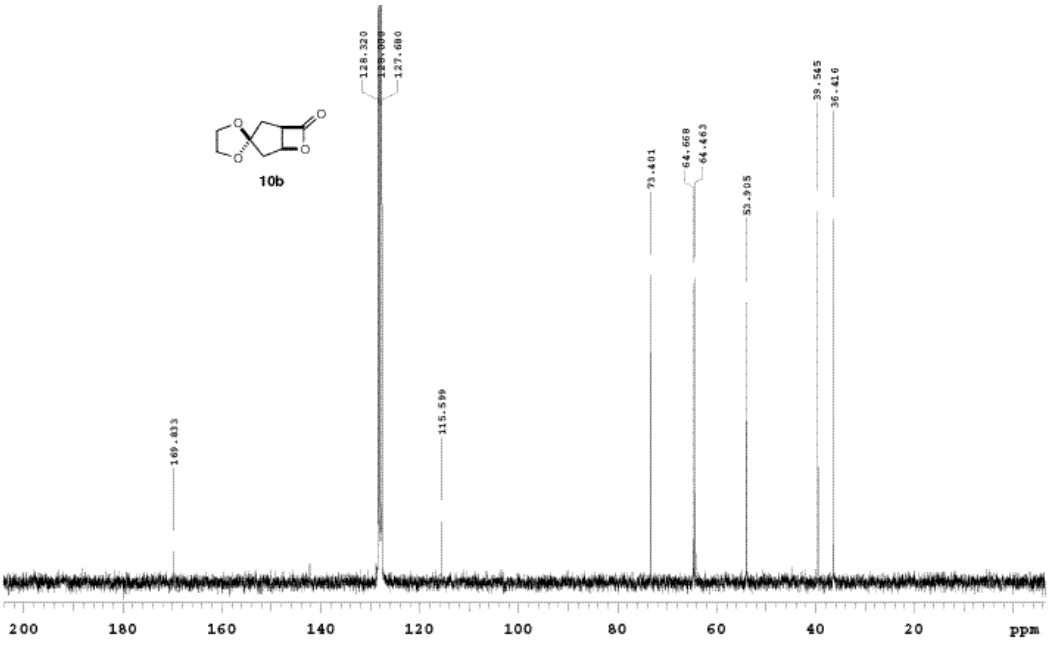
2.11
2.49
1.00
2.26
2.34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128.320
128.000
127.680
115.599
73.401
64.668
64.463
53.905
39.545
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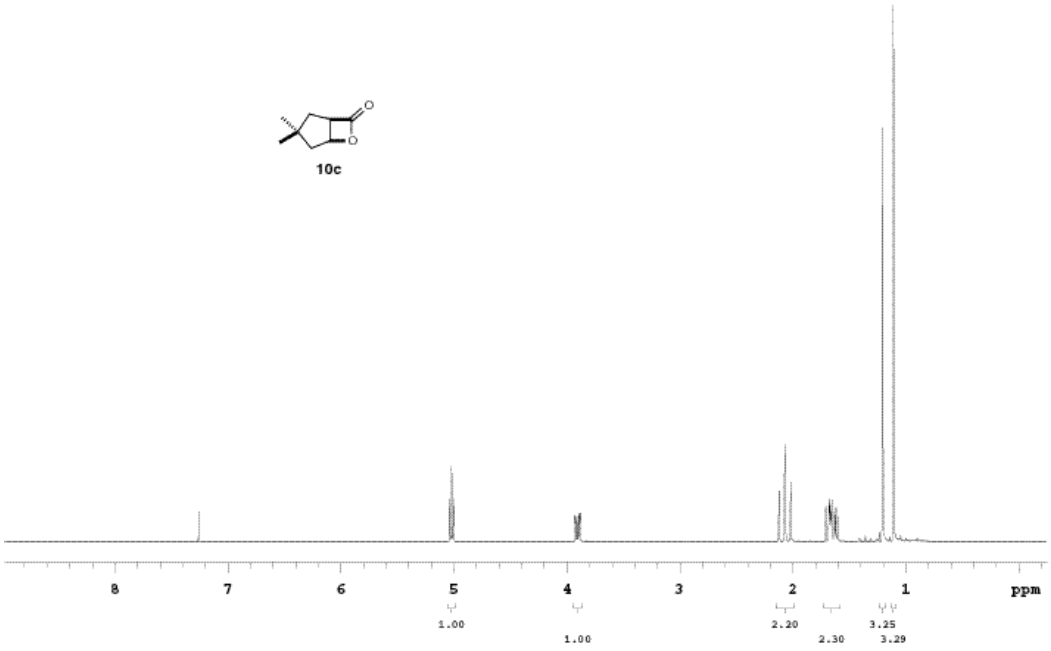
160
140
120
100
80
60
40
20
ppm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4
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2
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1.00
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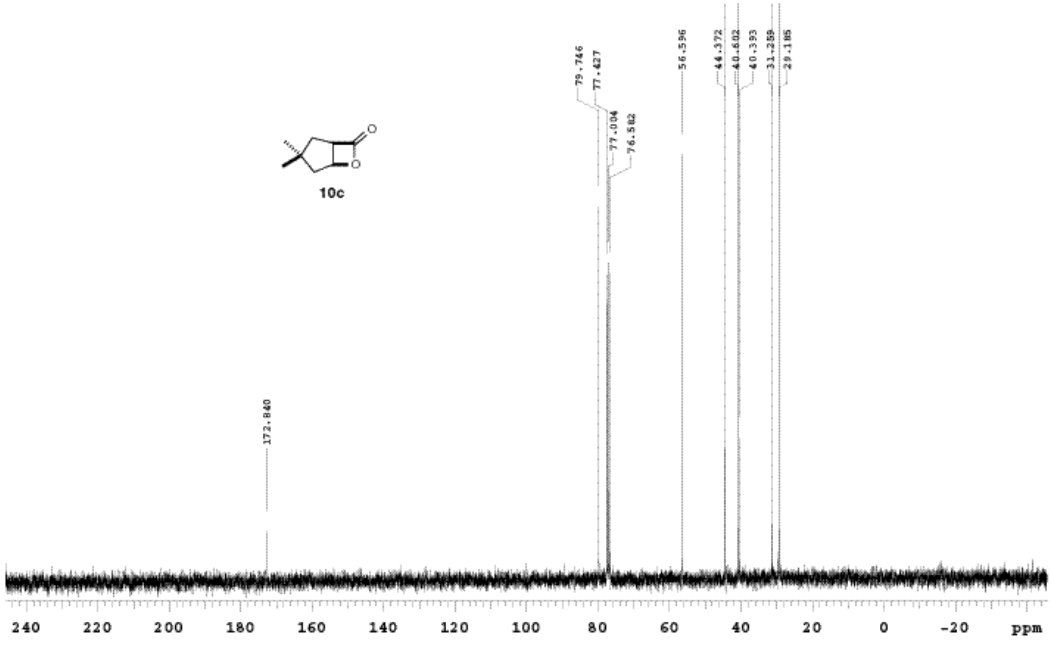
3.25
3.29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77.004
76.582
56.596
44.372
40.602
40.393
31.259
29.185
172.840
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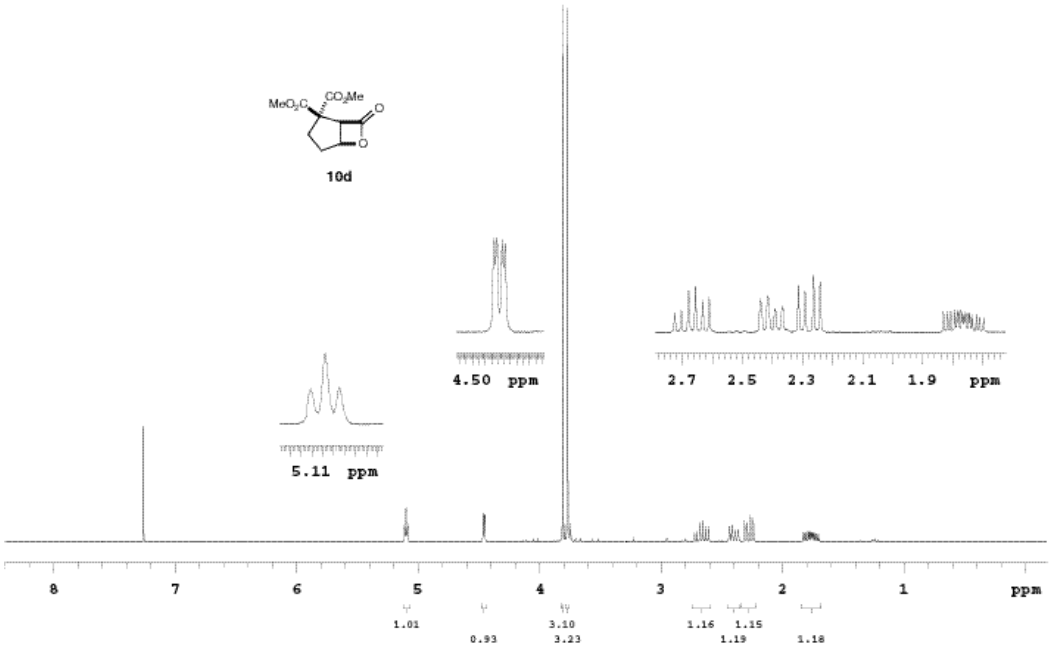
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm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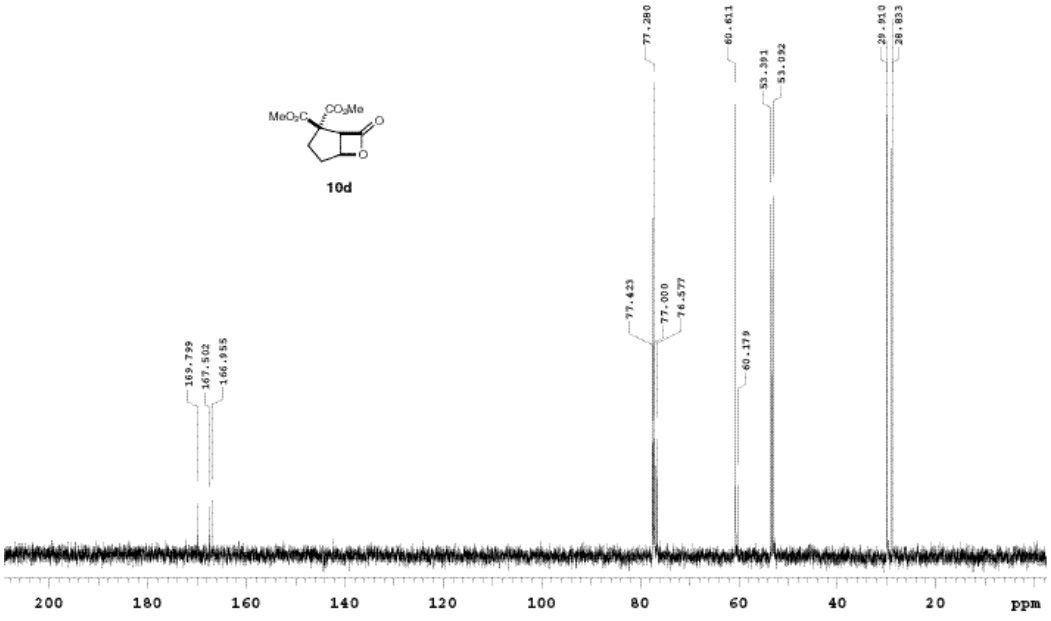
5.11 ppm
2.7 2.5 2.3 2.1 1.9 ppm
8 7 6 5 4 3 2 1 ppm
1.01 0.93 3.10 3.23 1.16 1.15 1.19 1.18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53.391
53.092
29.910
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77.423
77.000
76.577
60.179
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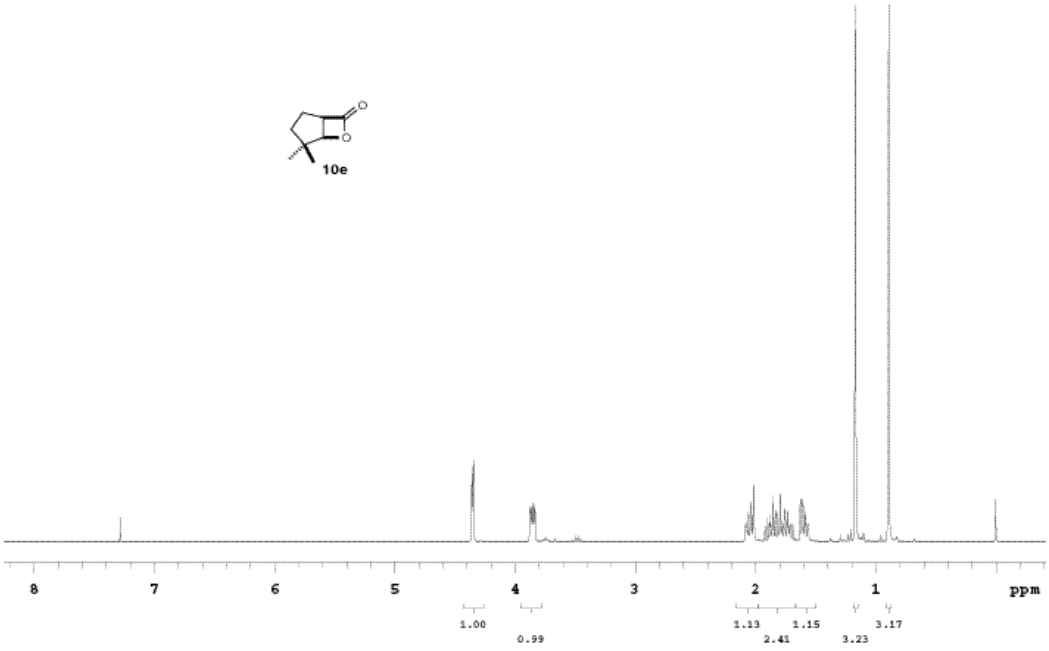
167.502
166.955
200 180 160 140 120 100 80 60 40 20 ppm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7
6
5
4
3
2
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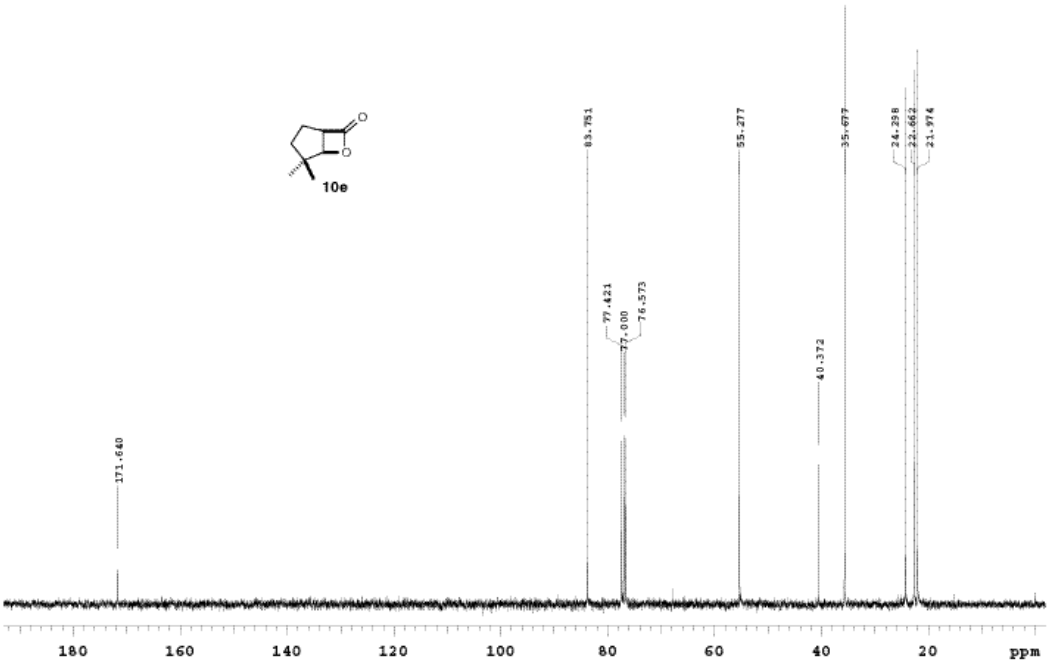
2.41
3.23
3.17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77.000
76.573
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120
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80
60
40
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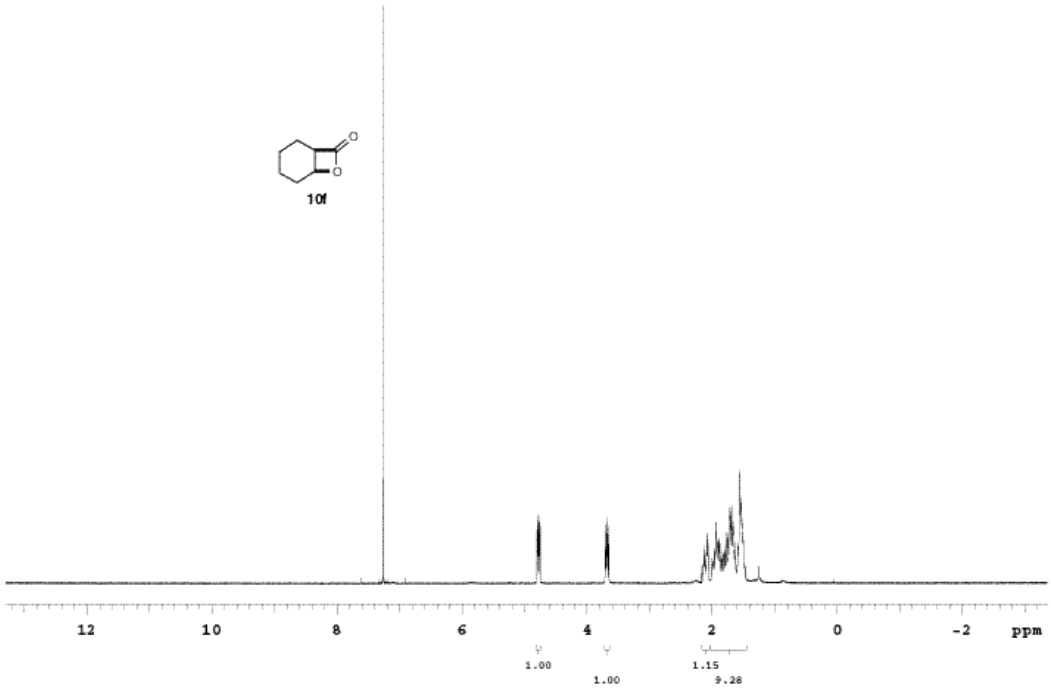
ppm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6
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2
0
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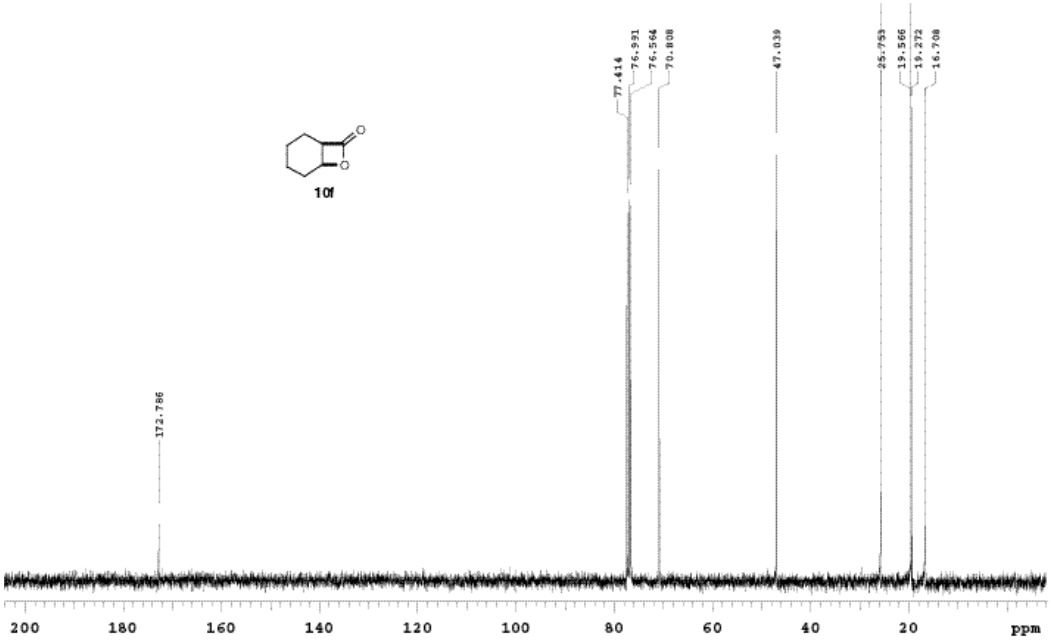
1.00
1.15
9.28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76.564
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172.786
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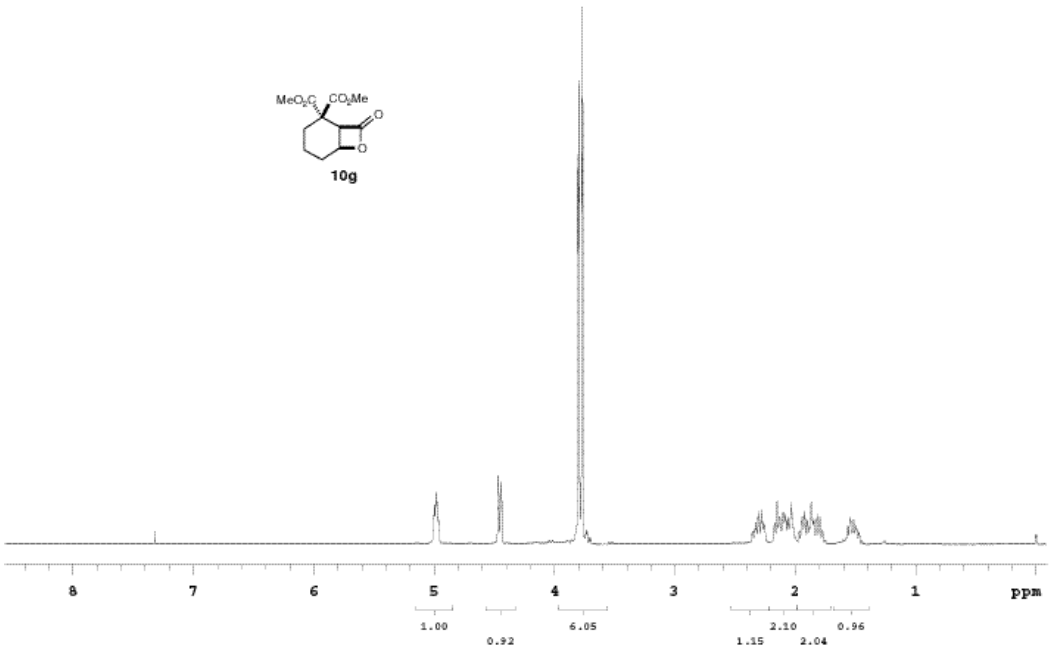
40
20
ppm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CO2Me
O
O
10g
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7
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2.10
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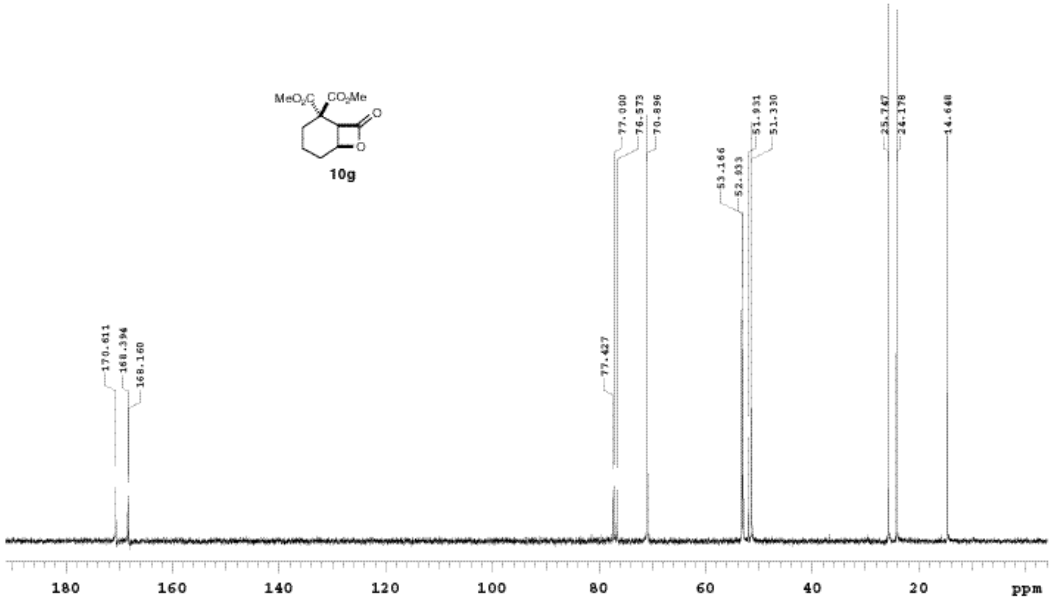
MeO2C
CO2Me
O
O
10g
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77.000
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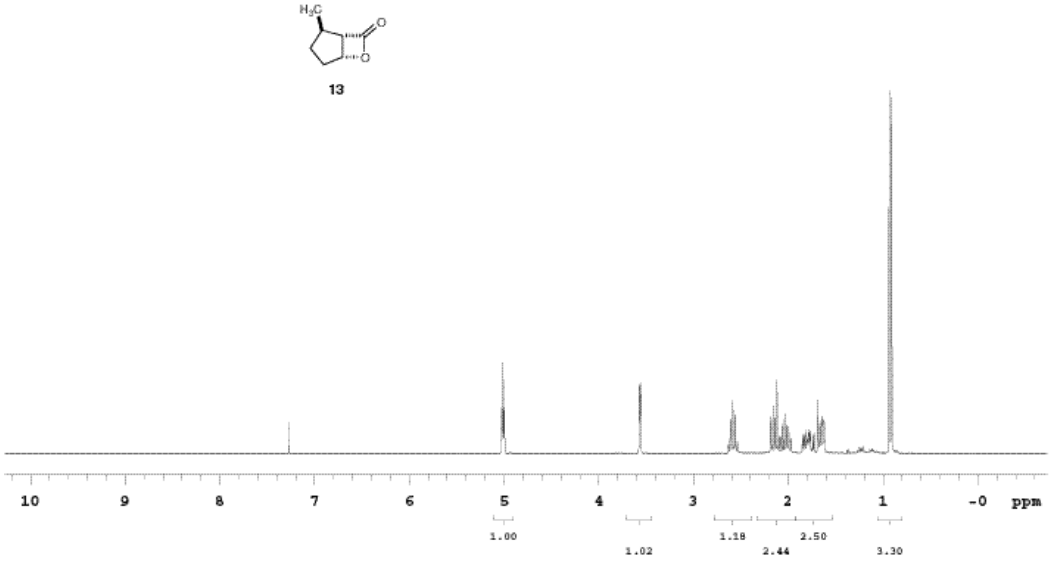
13
10
9
8
7
6
5
4
3
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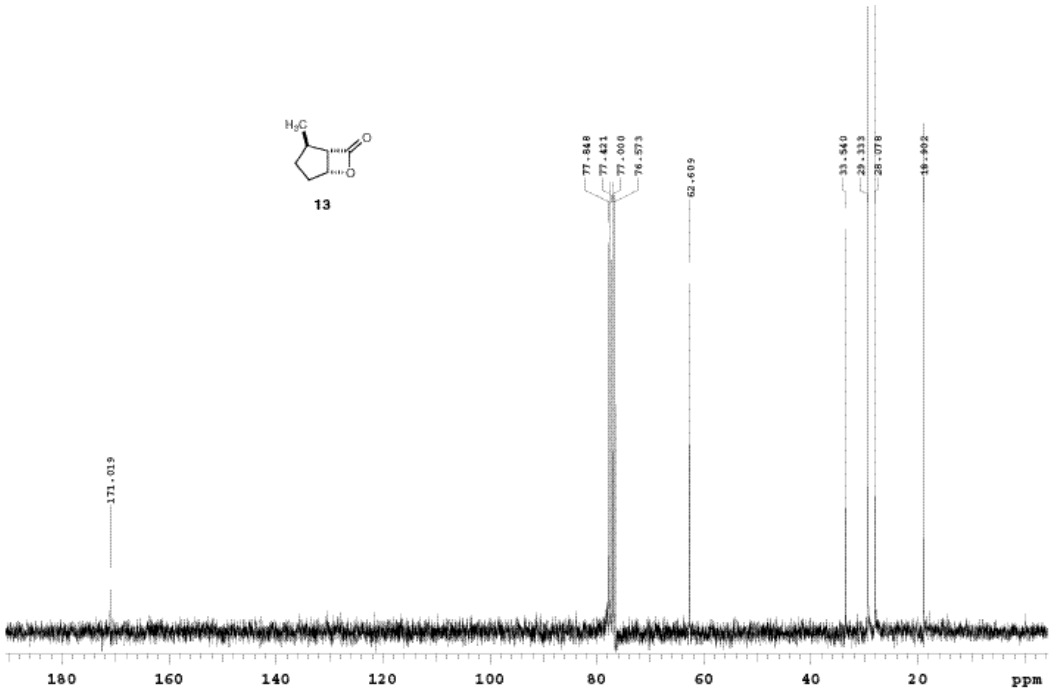
1.02
1.18
2.44
2.50
3.30


13
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77.000
76.573
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29.333
28.078
19.902
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160
140
120
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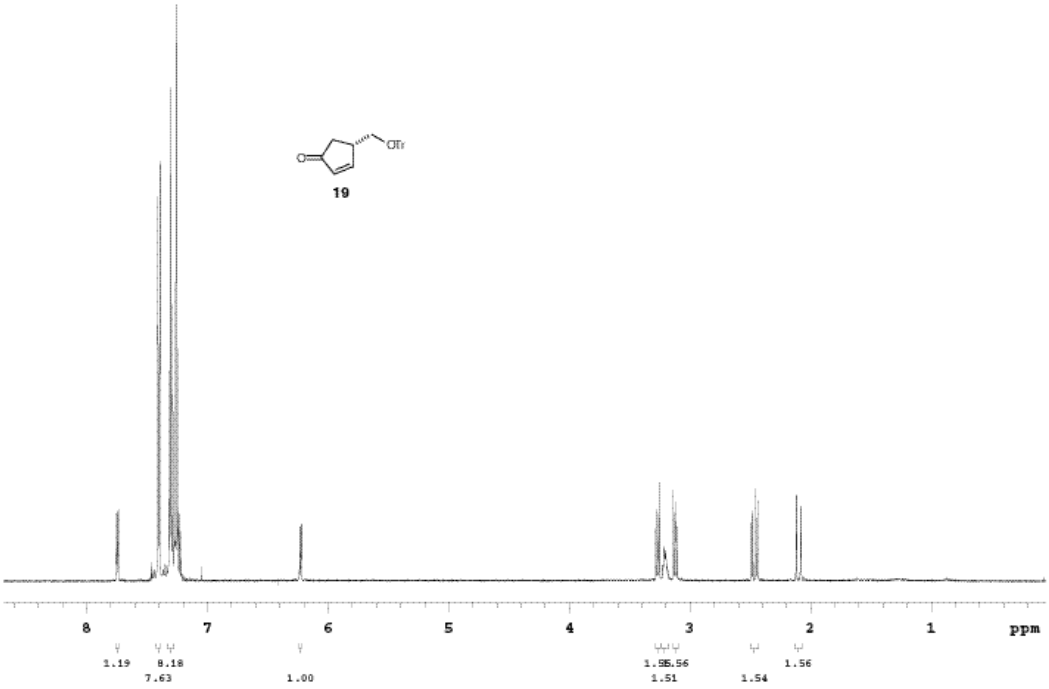
80
60
40
20
ppm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8
7
6
5
4
3
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ppm
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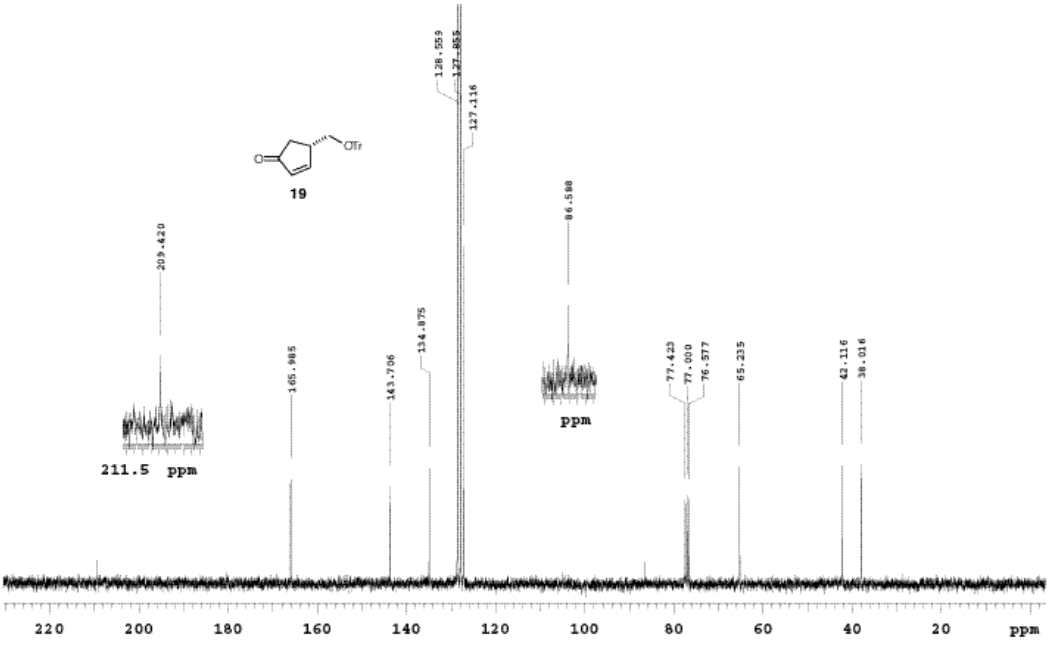
7.63
1.00
1.55
5.56
1.51
1.54
1.56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76.577
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ppm
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200
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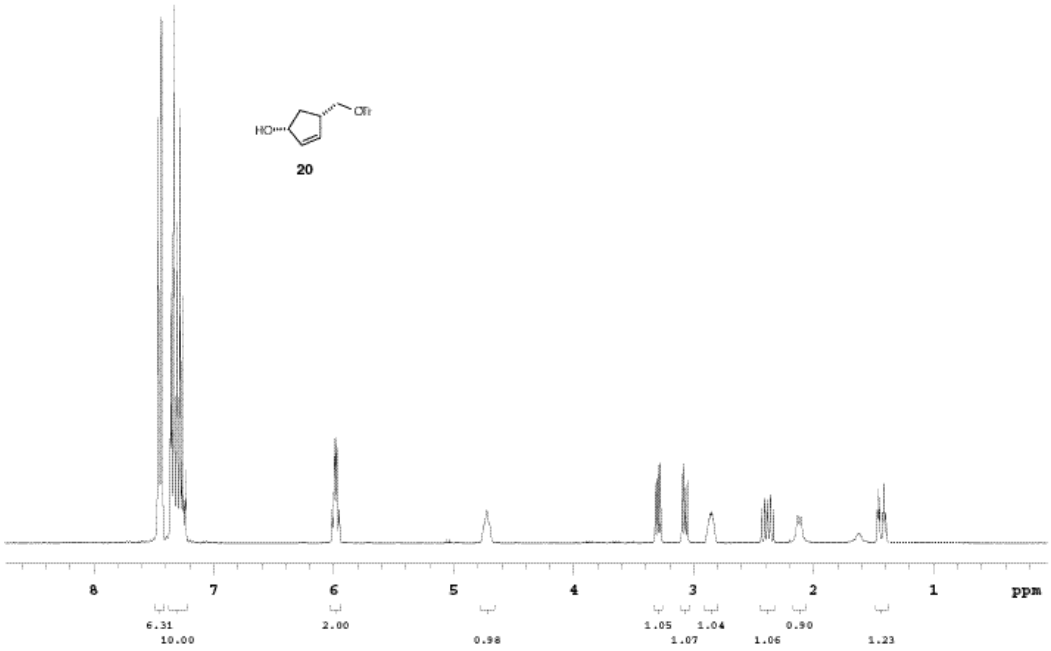
20
ppm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OTr
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6
5
4
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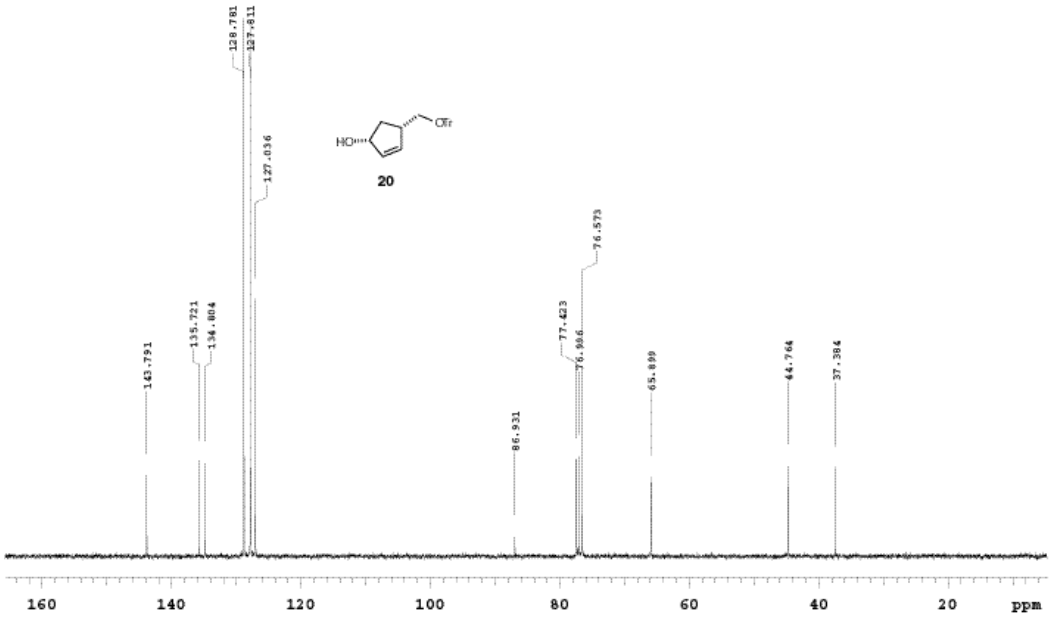
1.07
1.04
1.06
0.90
1.23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76.986
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65.899
44.764
37.384
160
140
120
100
80
60
40
20
ppm