SYNTHESIS OF 1-DECENE-2-^{13}C

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SUMMARY

A four-step synthesis of 1-decene-2-^{13}C starting with 1-bromooctane (57% overall yield) is described.

Key Words: Synthesis, Site-Specific 2-^{13}C Labelled Terminal Alkenes

INTRODUCTION

As part of an ongoing study of alkene oligomerizations, it became necessary for us to prepare 1-decene specifically isotopically enriched with ^{13}C in the 2-position. Retrosynthetically, this could be accomplished by the method indicated below:

$$R\text{-}{}^{*}CH{=}CH_2 \Longleftarrow R\text{-}{}^{*}CH{=}O \Longleftarrow R\text{-}{}^{*}CO_2H \Longleftarrow R\text{-}Br$$

where R = $\underline{n}$-C_8H_{17}, and the asterisk indicates the position of the carbon-13 label. Initially, we envisioned that 1-decene-2-^{13}C could be prepared by a Wittig reaction of triphenylphosphonium methylide with pelargonaldehyde-1-^{13}C. The aldehyde in turn could be synthesized via Grignard reaction of 1-octylmagnesium bromide with $^{13}CO_2$.

DISCUSSION

All synthetic operations were first performed on nonisotopically enriched materials, and the yield of each step was optimized. In practice, we found that while the synthesis of pelargonic acid using the Grignard procedure described above was straightforward, its reduction to pelargonaldehyde proved somewhat troublesome. Attempted reduction of pelargonic acid methyl ester with diisobutylaluminum hydride[1] afforded only mixtures of the desired pelargonaldehyde plus starting material. Increased reaction times did not markedly improve the yield of aldehyde, nor did this action result in an improved ratio of aldehyde

0362-4803/84/090793-05$01.00

Received April 2, 1984

to starting material in the product. Consequently, an alternative methods was sought for the reduction of pelargonic acid to pelargonaldehyde. Of the various methods that were considered and attempted, the best procedure proved to be (i) reduction of pelargonic acid to 1-nonanol using borane-THF complex[2] followed by (ii) careful oxidation of the alcohol to pelargonaldehyde with pyridinium chlorochromate.[3]

Our four-step synthesis of 1-decene-2-^{13}C from 1-bromooctane is outlined in the Scheme. This synthetic sequence provides the desired labelled 1-decene in 57% overall yield. Our method should be applicable generally to the synthesis of terminal alkenes which are site-specifically ^{13}C-labelled in the 2-position.

SCHEME

$$R\text{-}Br \xrightarrow[(76\%)]{(a\text{-}c)} R\text{-}{}^{*}CO_2H \xrightarrow[(98\%)]{(d)} R\text{-}{}^{*}CH_2OH \xrightarrow[(91\%)]{(e)} R\text{-}{}^{*}CH{=}O \xrightarrow[(84\%)]{(f)} R\text{-}{}^{*}CH{=}CH_2$$

R = $\underline{n}$-C_8H_{17}; asterisk indicates position of ^{13}C label.

(a) Mg, dry Et_2O; (b) CO_2, 90 mol-% ^{13}C isotopic enrichment; (c) Aqueous acidic workup; (d) Borane-THF complex, 0 °C; (e) Pyridinium chlorochromate, dry CH_2Cl_2, room temperature; (f) methyltriphenylphosphonium bromide, dimethyl sulfoxide, room temperature.

EXPERIMENTAL METHODS

Proton NMR spectra (60 MHz) were obtained with a Hitachi-Perkin Elmer Model R-24B NMR spectrometer. ^{13}C NMR spectra were recorded on a JEOL FX-90Q NMR spectrometer. In all cases, signals are reported in parts per million (δ) downfield from internal tetramethylsilane. Infrared spectra were obtained with a Perkin-Elmer model 1330 infrared spectrophotometer. Isotopically ^{13}C-enriched carbon dioxide (90 mol-%) was purchased from Amersham Corporation, Chicago, IL. The reaction products (i.e., pelargonic acid, 1-nonanol, pelargonaldehyde, and 1-decene) are well known compounds which have been fully characterized in the chemical literature; the boiling points of these materials (unlabelled and ^{13}C-labelled) as synthesized in the present study agree with the corresponding literature values.

Synthesis of Pelargonic Acid-1-^{13}C. A modification of the procedure described by Marshall and coworkers[4] was employed. A 250 mL three-necked flask was fitted with a condenser, thermometer, magnetic stirring bar, and addition funnel, and an argon inlet-outlet tube was placed at the top of the condenser. The system was flame dried and maintained under argon throughout the reaction. The reaction flask was then charged with magnesium metal (2.67 g, 0.11 mol), and 1-octylmagnesium bromide was prepared in the usual manner by reaction of the magnesium with a 1 M solution of 1-bromooctane in dry tetrahydrofuran

(THF, 100 mL, 0.1 mol). After the formation of the Grignard reagent had been completed, the thermometer and the addition funnel were replaced with glass stoppers, and the reaction flask was placed on a volume-calibrated (mol CO_2 vs. mm Hg) vacuum line. The stopcock which connects the reaction flask to the vacuum line remained closed. The Grignard solution was then frozen via application of external cooling (liquid nitrogen bath), and the reaction flask was evacuated to 0.01 mm Hg. The stopcock which connects the reaction flask to the vacuum line was again closed, and the requisite amount of $^{13}CO_2$ was bled into the pre-calibrated vacuum line. The stopcock was then opened, allowing CO_2 to diffuse into the cooled reaction flask. The liquid nitrogen bath was replaced by a dry ice-acetone bath; once the reaction solution became liquified, magnetic stirring was initiated, and the reaction mixture was stirred overnight. At the conclusion of the reaction, the mixture was quenched with 18% aqueous hydrochloric acid solution (50 mL). Water (100 mL) was then added, and the organic layer was separated from the aqueous layer. The aqueous layer was extracted with ether. The combined organic layers were stirred vigorously with 5% aqueous potassium hydroxide solution (300 mL) for 30 minutes. The organic layer was separated and then extracted with 5% aqueous potassium hydroxide solution (2 x 50 mL). The combined aqueous layers were acidified with concentrated aqueous hydrochloric acid solution and then extracted with ether. The combined organic layers were dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo to afford pure pelargonic acid-1-^{13}C (12.0 g, 76%); ^1H NMR ($CDCl_3$) δ0.93 (t, J = ca. 7 Hz, 3H), 1.04-1.75 (m, 12H), 2.33 (t, J = ca. 7 Hz, 2H), 11.54 (s, 1H); ^{13}C NMR ($CDCl_3$) δ180.36 (s), 34.04 (s), 31.77 (t), 29.16 (t), 29.16 (t), 29.06 (t), 24.67 (t), 22.56 (t), 13.89 (q); IR (neat) 2500-3400 (br, vs), 1677-1730 (br, vs), 1390-1472 (br, s), 1160-1350 (br, s), 1112 (m), 942 (s), 728 cm^{-1} (m).

Synthesis of 1-Nonanol-1-^{13}C. A modification of the procedure described by Brown and coworkers[2] was employed. A 1 M solution of borane-THF complex in dry THF (100 mL, 0.1 mol) under nitrogen was cooled to -10 °C. A solution of pelargonic acid-1-^{13}C (11.87 g, 0.075 mol) in dry THF (60 mL) was added to the borane-THF complex under nitrogen in such a manner that the temperature of the solution never exceeded 0 °C. After the addition of the pelargonic acid had been completed, the reaction mixture was stirred at 0 °C (15 minutes). The resulting mixture was warmed to room temperature and stirred for an additional 3 h. The reaction mixture was then poured into water (150 mL), stirred (10 minutes), and then 5% aqueous sodium bicarbonate solution was added (200 mL), whereupon stirring was continued for an additional 30 minutes. The organic layer was separated, and the aqueous layer was extracted with ether. Combined ether layers were

dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo to afford pure 1-nonanol-1-^{13}C (0.70 g, 98%); ^{1}H NMR ($CDCl_3$) δ1.42 (t, J = ca. 6 Hz, 3H), 1.63-2.4 (m, 15H), 4.17 (t, J = ca. 7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ62.78 (t), 32.88 (t), 32.07 (t), 29.80 (t), 29.63 (t), 29.47 (t), 26.00 (t), 22.81 (t), 14.14 (q); IR (neat) 3360 (br, s), 2930 (s), 2858 (s), 1470 (s), 1422 (s), 1338 (s), 1058 cm^{-1} (s).

Synthesis of Pelargonaldehyde-1-^{13}C. A modification of the procedure of Corey and Suggs[3] was employed. To a vigorously stirred solution of pyridinium chlorochromate (27.91 g, 0.13 mol) in dry methylene chloride (175 mL) was added all at once a solution of 1-nonanol-1-^{13}C (10.67 g, 0.074 mol) in methylene chloride (20 mL). The resulting mixture was stirred at room temperature (3 h) and then diluted with ether (200 mL). The reaction mixture was then filtered through a short pad of Fuller's earth; the pad was washed thoroughly with ether, and the wasings were added to the filtrate. The filtrate was then concentrated in vacuo to afford pelargonaldehyde-1-^{13}C (9.62 g, 91%); ^{1}H NMR ($CDCl_3$) δ0.88 (t, J = 5.5 Hz, 3H), 1.17-1.86 (m, 12H), 2.37 (q, J = 7 Hz, 2H), 9.74 (t, J = 2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ202.45 (d), 43.99 (t), 31.96 (t), 29.47 (t), 29.25 (t), 29.25 (t), 22.75 (t), 22.26 (t), 14.09 (q); IR (neat) 2928 (s), 2865 (s), 2718 (w), 1722 (s), 1472 (m), 1418 (w), 1395 (w), 1382 (w), 730 cm^{-1} (w).

Synthesis of 1-Decene-2-^{13}C. A modification of the procedure of Corey and Chaykovsky[5] was employed. Commercial sodium hydride (50% dispersion in oil, 11.04 g, 0.21 mol) was washed with dry hexane (3 x 100 mL); after the final washing, the last traces of hexane were removed in vacuo. To the remaining dry sodium hydride was added dry dimethyl sulfoxide (150 mL), and the resulting mixture was heated gently (70-75 °C) until evolution of hydrogen ceased. The mixture was then cooled to 15 °C. To this mixture was added a solution of methyltriphenylphosphonium bromide (76.17 g, 0.21 mol, which had previously been dried by heating overnight in vacuo at 110 °C) in dry dimethyl sulfoxide (220 mL) during 15 minutes. The reaction mixture was then stirred at room temperature (15 minutes). To the reaction mixture was then added a solution of pelargonaldehyde-1-^{13}C (22.76 g, 0.16 mol) in dry dimethyl sulfoxide (15 mL). The resulting mixture was stirred at room temperature (3 h) and then poured into a mixture of pentane (200 mL) and water (800 mL). This mixture was stirred (10 minutes), and the layers were then separated. The aqueous layer was extracted with pentane, and the combined pentane layers were washed sequentially with water (3 x 200 mL) and with brine (200 mL). The organic layer was then dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo to afford crude 1-decene-2-^{13}C (22.5 g, 97%). The crude product was purified via column chromatography on silica gel (pentane eluent) to afford

pure 1-decene-2-^{13}C (18.85 g, 84%); ^{1}H NMR ($CDCl_3$) δ0.88 (t, 3H), 1.28 (br s, 12H), 1.77-2.17 (m, 2H), 4.81-5.11 (complex m, 2H), 5.57-6.05 (complex m, 1H); ^{13}C NMR ($CDCl_3$) δ139.17 (d), 114.09 (t), 33.91 (t), 32.02 (t), 29.58 (t), 29.42 (t), 29.25 (t), 29.09 (t), 22.75 (t), 14.09 (q); IR (neat) 3082 (w), 2961 (sh, vs), 2929 (vs), 2861 (vs), 1614 (w), 1468 (m), 1383 (w), 993 (m), 912 (s), 730 cm^{-1} (w).

ACKNOWLEDGMENT

Financial support of this study by the United States Air Force (contract number F33615-81-C-5058, to Suntech Group, division of Sun Company), The Robert A. Welch Foundation (Grant B-963), and The North Texas State University Faculty Research Committee is gratefully acknowledged.

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