SYNTHESES OF 1-DODECYL-d_{25} PHOSPHATE

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SUMMARY

1-Dodecyl-d_{25} phosphate was prepared from commercially available 1-dodecanol-d_{26}. The 1-dodecanol-d_{26} reacted with diphenyl phosphorochloridate to produce 1-dodecyl-d_{25} diphenyl phosphate, which was reduced with hydrogen in the presence of Adams catalyst to give a 58.9 percent yield of 1-dodecyl-d_{25} phosphate with 99.4 atom percent deuterium.

Key Words: 1-dodecyl-d_{25} phosphate, synthesis, deuterium labeling, mass spectrometry, gas chromatography

INTRODUCTION AND DISCUSSION

1-Dodecyl-d_{25} phosphate was synthesized from commercially available 1-dodecanol-d_{26} for use as an internal standard in the Environmental Protection Agency's "Master Analytical Scheme" for the analysis of organic compounds in water (1). This scheme is intended to yield qualitative and quantitative analyses of organic compounds in water by gas chromatography/mass spectrometry (GC/MS). The purity of the product was established by elemental analysis and by gas chromatography (GC) and electron impact mass spectrometry of the trimethylsilyl (TMS) derivative.

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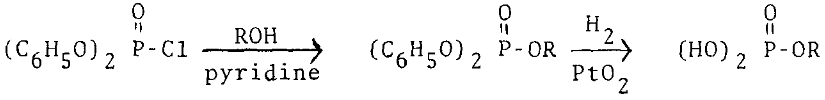
Diphenyl phosphorochloridate is a reagent for preparing a monoalkyl phosphate from an alcohol (2-4). The reagent was used by Brown and Maliphant (5) to synthesize monoalkyl phosphates of even-numbered alcohols in the C_{12} to C_{18} range. We have used their method on a smaller scale in the synthesis of the labeled 1-dodecyl-d_{25} phosphate.

Diphenyl phosphorochloridate (I) reacts with an alcohol in pyridine solution to give a triester (II), from which the phenyl groups can readily be removed by hydrogenation in the presence of Adams catalyst (6) to yield the monoalkyl phosphate (III).



$$(C_6H_5O)_2\overset{\overset{O}{\|}}{P}\text{-Cl} \xrightarrow[\text{pyridine}]{\text{ROH}} (C_6H_5O)_2\overset{\overset{O}{\|}}{P}\text{-OR} \xrightarrow[PtO_2]{H_2} (HO)_2\overset{\overset{O}{\|}}{P}\text{-OR}$$

(I) (II) (III)

Since a product of high isotopic purity was needed, a check was made to determine if any of the deuterium of the alkyl group in 1-dodecanol-d_{26} would exchange with hydrogen under the conditions to be used in the reduction. After 1 1/2 hours reduction, analysis of recovered 1-dodecanol-d_{26} by GC/MS of the trimethylsilyl derivative showed less than 0.01 atom percent loss of deuterium.

Gas chromatography and gas chromatography/mass spectrometry were used to follow the progress of each reaction and to determine the purity of the product. For example, in the hydrogenation to form the labeled 1-dodecyl-d_{25} phosphate, these analyses showed the presence of unreduced material in the second crop and in the mother liquor, and a second reduction was run on these materials to improve the yield. Gas chromatographic analysis also showed that some crops of the 1-dodecyl-d_{25} phosphate contained phosphoric acid, which was removed by extraction with water of a solution of the 1-dodecyl-d_{25} phosphate in 2:1 ethyl ether:toluene, according to a modification of the method used by Nelson and Toy (7).

A yield of 58.9 percent of crystalline 1-dodecyl-d_{25} phosphate with an isotopic purity of 99.4 atom percent and satisfactory elemental analysis was obtained. Further confirmation of the structure was obtained by GC/MS of the trimethylsilyl derivative. The mass spectrum is shown in figure 1. A molecular ion at m/z 435 and an $(M-CH_3)^+$ ion at m/z 420 (characteristic of trimethylsilyl derivatives) confirm the molecular weight. An isotopic purity of 99.4 atom percent deuterium was calculated from both the molecular ion and the $(M-CH_3)^+$ ion clusters. The most intense ions in the spectrum, m/z 245, 228, and 211, do not include the dodecyl-d_{25} group and are characteristic of the trimethylsilyl derivatives of phosphates (8).

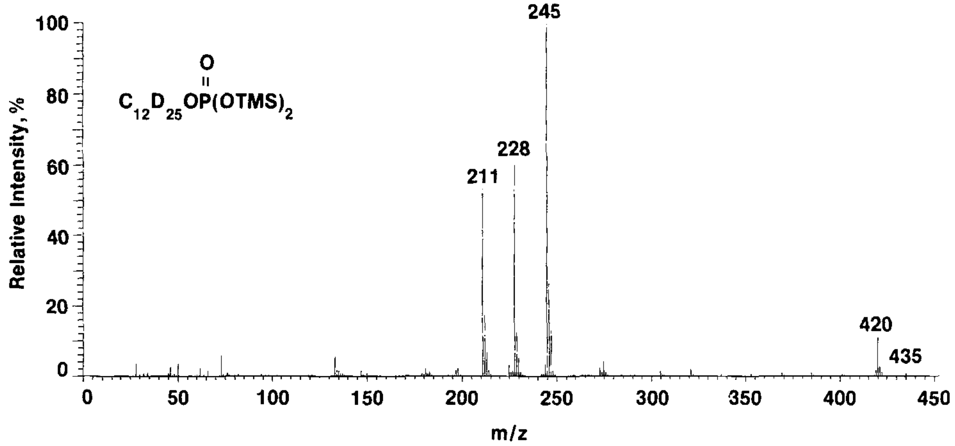


Figure 1. Mass Spectrum of the TMS Derivative of 1-Dodecyl-d_{25} Phosphate.

EXPERIMENTAL

Exchange of 1-Dodecanol-d_{26} with Hydrogen in the Presence of Adams Catalyst

To a 1-μL sample of 1-dodecanol-d_{26} in 5 mL of acetic acid were added a few mg of Adams catalyst, platinum(IV) oxide monohydrate, and hydrogen was bubbled through the mixture for 1 1/2 h. The catalyst was removed by filtration, and the acetic acid removed by concentration of the solution under reduced pressure. The material was converted to the trimethylsilyl derivative with N,O-bis(trimethylsilyl)acetamide (BSA), and analysis by GC/MS showed less than 0.01 atom percent loss of deuterium.

Synthesis of 1-Dodecyl-d_{25} Phosphate

Diphenyl phosphorochloridate (4.04 g, 0.0141 moles) was added slowly with swirling to a solution of 1-dodecanol-d_{26} (2.00 g, 0.0094 moles) in 5 mL of dry pyridine in a small standard-tapered flask. The flask was stoppered and set aside for 68 h. Then the contents of the flask were poured into 100 mL of cold (4 °C) 1 mol/L hydrochloric acid. The solution was extracted with 75 mL of diethyl ether, and the aqueous layer was extracted again with 25 mL of diethyl ether. The ether extracts were combined and washed three times with 50 mL of 1 mol/L hydrochloric acid, five times with 40 mL of 0.6 mol/L sodium bicarbonate, and five times with 40 mL of distilled water. The ether solution was dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The resulting syrup, containing 1-dodecyl-d_{25} diphenyl phosphate, was stored in a desiccator over anhydrous calcium sulfate.

A suspension of 0.41 g of Adams catalyst in 10 mL of glacial acetic acid was shaken with hydrogen (9) until absorption of hydrogen ceased (20 min). The catalyst was then washed with 2 mol/L hydrochloric acid, water, and finally with glacial acetic acid by decantation. The crude 1-dodecyl-d_{25} diphenyl phosphate was dissolved in 50 mL glacial acetic acid and was added to the catalyst. The mixture was shaken with hydrogen at 17 psi for 6 1/2 h. The catalyst was removed by filtration through a fine porosity sintered glass funnel, and washed with glacial acetic acid. The combined acetic acid solutions were concentrated under reduced pressure to a syrup, and added to 60 mL of 2:1 diethyl ether:toluene in a separatory funnel. The organic layer was extracted twice with 25 mL portions of distilled water to remove phosphoric acid, then concentrated to a syrup under reduced pressure. Hexane was added, the solution cooled to 5 °C, and crystals of 1-dodecyl-d_{25} phosphate (0.774 g) were obtained. A second crop was obtained from the mother liquor. GC and GC/MS showed the presence of unreduced material in the second crop and in the mother liquor. This material was concentrated to a syrup, taken up in acetic acid, and reduced with Adams catalyst as before. The two crops of crystals obtained from this second reduction were combined with the material from the first reduction and recrystallized. Since GC showed the presence of some phosphoric acid, the material was dissolved in 2:1 ether:toluene, washed with water, and then crystallized from hexane to yield 1.617 g (58.9%) of white crystals. Mp found 55.5-57.0 °C, lit value for unlabeled material 58 °C (7), 59.5 °C (5). Anal. Calculated for $C_{12}D_{25}O_4PH_2$, 99.4 atom percent deuterium on the alkyl group:

C, 49.47 percent; apparent H, 10.30 percent; P, 10.63 percent. Found: C, 50.11 percent; H, 10.39 percent; P, 10.66 percent.

Gas Chromatography

Gas chromatographic conditions were as follows: the column was a 2 m x 6 mm glass column containing three percent SE-30, on 100/120 mesh Chromosorb*. The initial column temperature was 75 °C, and it was programmed at 15 °C/min to 290 °C. Injection port and flame ionization detector were at 270 °C. The carrier gas was helium at a flow rate of 15 mL/min.

All compounds were treated with BSA to form trimethylsilyl derivatives. Analyte concentrations were generally 1 µg/µL. Retention times for the trimethylsilyl derivatives were: dodecyl-d_{25} phosphate 11.8 min, 1-dodecanol-d_{25} 7.7 min, phenol 2.9 min, phosphoric acid 5.0 min, unreduced products (higher molecular weight impurities) 14.6 and 17.3 min.

Mass Spectrometry

Electron impact mass spectra were recorded at 70 eV and a source temperature of 250 °C. The spectrum of the trimethylsilyl derivative of 1-dodecyl-d_{25} phosphate obtained by GC/MS is shown in figure 1. 1-Dodecyl-d_{25} phosphate did not give a mass spectrum representative of intact material when heated on a direct probe.

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*Identification of any commercial product does not imply recommendation, or endorsement by the National Bureau of Standards, nor does it imply that the material or equipment identified is necessarily the best available for the purpose.

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