SYNTHESIS OF [^{18}O]THIONYL CHLORIDE

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Summary

A new synthesis of [^{18}O]thionyl chloride has been developed which, for the first time, allows the product to be isolated in pure form.

INTRODUCTION

During the investigation of the stereochemical course of chemical and enzyme catalysed sulphuryl transfer reactions, a general synthetic approach to chiral [^{16}O, ^{17}O, ^{18}O]sulphate monoesters[1] and a method for their analysis was developed.[2] A specific application of this methodology is represented by the preparation of R_S and S_S phenyl [^{16}O, ^{17}O, ^{18}O]sulphate.[3] In this synthetic strategy, the [^{17}O] isotope is introduced *via* the stereospecific ruthenium [$^{17}O_4$]tetraoxide oxidation of enantiomerically pure [^{18}O]sulphite diesters. The [^{18}O] isotope in the sulphite diesters originates from sulphur [$^{18}O_2$]dioxide and is incorporated into the sulphite diesters in the form of [^{18}O]thionyl chloride. We now report a new synthesis and the first isolation of [^{18}O]thionyl chloride.

EXPERIMENTAL

Sulphur [$^{18}O_2$]dioxide (99%) was obtained from Ventron Alfa Products, Zeppelinstrasse 7, Postfach 6540, D-7500 Karlsruhe 1, West Germany.

1,4-Bis-(trichloromethyl)-benzene was purchased from Aldrich Chemical Co., Dorset.

[^{18}O]Thionyl Chloride

A Carius tube was charged with 1,4-bis-(trichloromethyl)-benzene (1.00 g, 3.20 mmol) and anhydrous ferric chloride (0.082 g, 0.51 mmol) and attached to the vacuum manifold represented in Figure 1. With all of the taps open, the system was evacuated to

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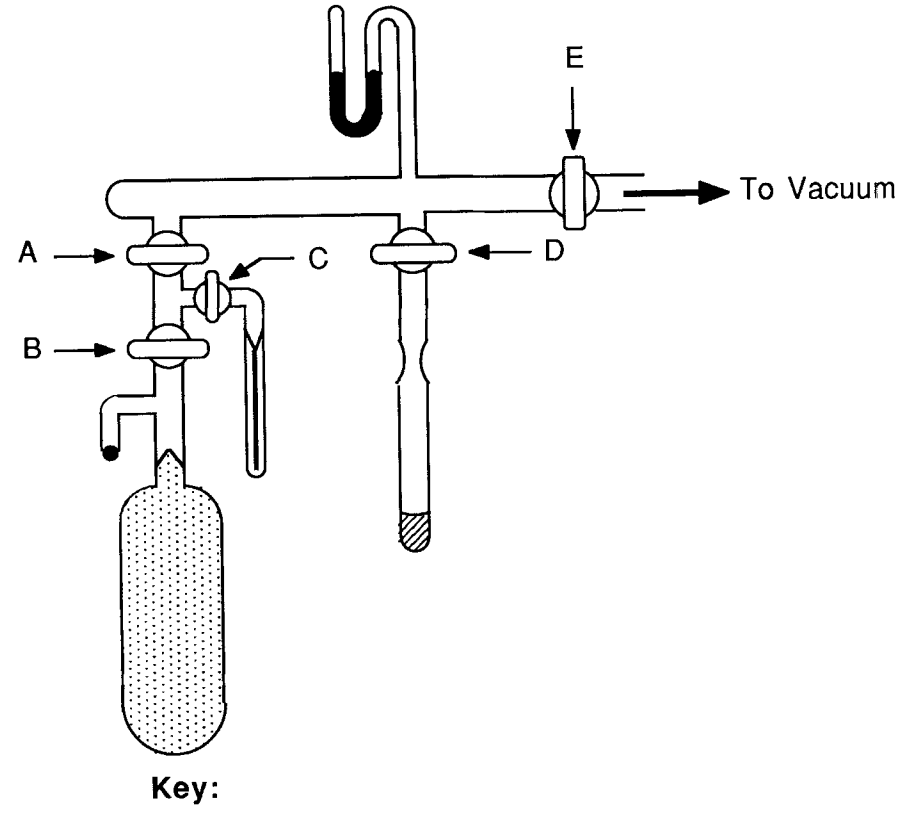

Figure 1

0.05 mm Hg for 1h. After closing taps B and E, the steel ball in the side arm of the sulphur [$^{18}O_2$]dioxide bottle was manipulated magnetically and used to break the glass seal in the neck of the container. Tap A was then closed, and the tip of the graduated capillary was cooled with liquid nitrogen. Tap B was slowly opened to release the sulphur [$^{18}O_2$]dioxide, so that it slowly distilled into the capillary tube. The level of the liquid nitrogen was adjusted as needed to facilitate the distillation. When 250 ml (5.32 mmol) had been collected, tap B was closed and tap A was opened. The liquid nitrogen bath was removed from the capillary and applied to the Carius tube to just below the point of

constriction, causing the sulphur [$^{18}O_2$]dioxide to distil out of the capillary tube into the Carius tube. After the distillation was complete (15 min.), the Carius tube was sealed with an air/gas flame while continuing the application of the liquid nitrogen bath. The tube was then allowed to warm to 20 °C in a protective container and maintained at that temperature for 3 d. The tube was cooled in liquid nitrogen, scored and opened. The reaction products were warmed to 20 °C under a dry nitrogen atmosphere and transferred to a 10 ml round bottom flask. The [^{18}O]thionyl chloride was subsequently distilled (100 °C, 1 atm.) into a preweighed, 25 ml receiving bulb cooled to -78 °C, giving 340 mg (53%) of [^{18}O]thionyl chloride; $\nu_{max.}$ (CCl_4): 1192 cm^{-1}(S=^{18}O).

RESULTS AND DISCUSSION

In the course of ongoing work concerning the application of chiral [^{16}O, ^{17}O, ^{18}O] sulphate monoesters to the study of chemical and enzymic sulphuryl transfer reactions we required [^{18}O]thionyl chloride as a precursor for our stereochemical probes. A method for preparing [^{18}O]thionyl chloride from sulphur [$^{18}O_2$]dioxide and phosphorus pentachloride had been previously developed.[1] Although this preparation is very convenient, the product is a mixture of [^{18}O]thionyl chloride and [^{18}O]phosphoryl chloride. [^{18}O]Thionyl chloride in this form has proved to be quite satisfactory for the preparation of cyclic [^{18}O]sulphites, but we found that the presence of phosphoryl chloride results in low yields and a number of side products when used in the synthesis of acyclic sulphite esters. Despite the difference in boiling points between thionyl chloride (79 °C) and phosphoryl chloride (105.8 °C), attempts to separate the mixture of these compounds by distillation were unsuccessful. Similar difficulties in the separation of thionyl chloride and phosphoryl chloride have been noted in the literature.[4] We therefore required an alternatative synthesis of [^{18}O]thionyl chloride which would allow us to isolate the product in a pure state as well as to retain the attributes of our previous methodology.

A particularly facile method of converting sulphur [$^{18}O_2$]dioxide to [^{18}O]thionyl chloride has been developed based on a reaction patented by Burk and Turnquest.[5] In this method we were able to preserve the simple technology utilised in the previous [^{18}O]thionyl chloride synthesis, by using 1,4-bis-(trichloromethyl)-benzene in the presence of a catalytic amount of ferric chloride (rather than phosphorus pentachloride), as the chlorinating agent.

The desired amount of sulphur [$^{18}O_2$]dioxide is distilled into a calibrated capillary tube and subsequently transferred via the vacuum system shown in Figure 1 to a Carius tube containing the 1,4-bis-(trichloromethyl)-benzene and ferric chloride. The Carius tube is then sealed and the reaction is allowed to proceed 3 d at 20 °C, giving [^{18}O]thionyl chloride and [^{18}O]terephthaloyl-1,4-chloride as products. Since the organic product is much less volatile, the [^{18}O]thionyl chloride is easily isolated from the product mixture by distillation.

The S=O stretching frequency of thionyl chloride (in CCl_4) is 1238 cm^{-1} whereas that for [^{18}O]thionyl chloride (in CCl_4) is 1192 cm^{-1}, an isotope shift of 46 cm^{-1}. This is similar to the isotope shift of 49 cm^{-1} observed when thionyl fluoride (gas phase, 1339 cm^{-1}) is substituted with ^{18}O (gas phase, 1285 cm^{-1}).[6]

Acknowledgements

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