NOTES

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SYNTHESES OF 2-CHLORO-2-METHYLPROPANE-1,1,1,3,3,3-D_6, 2-CHLORO-2-METHYLPROPANE-D_9, 2,2-DIMETHYL-D_6-PROPANE-1,1,1-D_3 AND 2,2-DIMETHYL-PROPANE-D_{12}.

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In connection with our studies of NMR line shapes for tunneling methyl groups and nuclear relaxation in solids, it was desirable to synthesize partial and fully deuterated 2-chloro-2-methylpropane and 2,2-dimethylpropane. The method described here is based on the reduction of acetone with methylmagnesium iodide to the alcohol (1). After a chlorination of the alcohol (2), it is coupled with methylmagnesium iodide to give 2,2-dimethylpropane.

$$CD_3COCD_3 \xrightarrow{CD_3MgI} (CD_3)_3COMgI \xrightarrow{aq.\ NH_4Cl}$$

$$(CD_3)_3COH \xrightarrow{Conc.\ HCl} (CD_3)_3CCl \xrightarrow{CD_3MgI} (CD_3)_4C$$

The chlorination of a small quantity of 2-chloro-2-methylpropane by bubbling hydrogen chloride gas through the solution has been reported (1). We found that the method was time consuming and the hydrogen chloride gas carried away some of the volatile product, 2-chloro-2-methylpropane (bp, 52°), even though the reaction vessel cooled in an ice-water bath. Thus concentrated hydrochloric acid was used in this step (2).

The coupling reaction between 2-halo-2-methyl-propane and methylmagnesium halides has been reported by several authors. A toluene solution of 2-bromo-2-methylpropane was added to the methylmagnesium iodide in ether and toluene at 40-49° (3). The yield was found to be 18.2% (4). Whitmore and Fleming treated 2-chloro-2-methylpropane in toluene with methylmagnesium chloride in toluene at 45-50° to give 42-50% yield (4). The coupling between 2-chloro-2-methylpropane and methyl-d_3-magnesium iodide (5) or methyl-d_3- magnesium bromide (6) in refluxing toluene was reported, but without details and yield. Compared to methyl-d_3 bromide (bp, 2.8°) and methyl-d_3 chloride (bp, -24.6°), methyl-d_3 iodide is cheaper and easier to handle because it has a higher boiling point (bp, 41.4°). The method adopted for this preparation was to add methyl-d_3-magnesium iodide to the corresponding chloride, both in toluene, at 64°-110°. This gave 55% yield. However, the preparation of the Grignard, methyl-d_3-magnesium iodide, in toluene was not successful unless a small quantity of ether (10% by volume) was added to the solution. Ether was removed by distillation before the coupling reaction. A glass apparatus consisting of two traps and three U tubes was attached to the reaction vessel to remove impurities such as isobutylene and to collect the product.

Experimental

2-Methyl-2-propanol-1,1,1,3,3,3-d_6

A three-necked round-bottomed flask equipped with a dropping funnel, a gas inlet and a reflux condenser attached to an oil bubbler was flushed with dry nitrogen. To the stirred suspension of 6.23 g of magnesium dust in 200 ml of dry ether was added dropwise a solution of 34 g of methyl iodide in 40 ml of ether to maintain at reflux. The solution was held at reflux for 1.5 hr, cooled and 15 g of acetone-d_6 (99.5 atom % D, Merck Sharp & Dohme of Canada Ltd., Canada) in 35 ml of ether was added dropwise to maintain at reflux. After the addition, the mixture was heated at reflux for 40 min, cooled and 50 ml of saturated ammonium chloride solution was added dropwise and left overnight. To this mixture was added 250 ml more of saturated ammonium chloride, separated, and extracted with ether (85 ml x 10). The combined ether layer was dried over anhydrous sodium sulfate and distilled to give 15.5 g of 2-methyl-2-

propanol-1,1,1,3,3,3-d_6 (99 atom % D, bp 79-81°).

The alcohol obtained above was used for the next step of preparation without further drying. It is difficult to be free from water by distillation (2).

2-Chloro-2-methylpropane-1,1,1,3,3,3-d_6

In a separatory funnel was placed 15.5 g of 2-methyl-2-propanol-1,1,1,3,3,3-d_6 and 49 ml of conc. hydrochloric acid (Sp. gr. 1.19) (2). After vigorous shaking, it was allowed to stand for 1 hr. The upper layer was drawn off, dried over anhydrous calcium chloride, degassed under vacuum and vacuum transferred twice to give 13.4 g of 2-chloro-2-methylpropane-1,1,1,3,3,3-d_6 (99 atom % D) with 58.4% yield based on acetone-d_6.

2-Chloro-2-methylpropane-d_9

2-Chloro-2-methylpropane-d_9 (99 atom % D) was made via a Grignard reaction and a chlorination similar to that described before, but starting with methyl-d_3 iodide (99.5 atom % D, Stohler Isotope Chemicals, Inc., New Jersey).

2,2-Dimethyl-d_6-propane-1,1,1-d_3

A three-necked round-bottomed flask fitted with a dropping funnel, a gas inlet and a Graham condenser which was attached to an oil bubbler and cooled with 0° water. To a stirred suspension of 2.51 g of magnesium dust in 60 ml of dry toluene and 5 ml of dry ether was added a solution of 15 g of methyl-d_3 iodide in 50 ml of dry toluene and 5 ml of dry ether dropwise at 35-45° (bath temperature) for 3 hr. In 5 hr, the mixture was gradually heated to 80°. The ether was then removed by distillation. The top of the Graham condenser was attached to a glass apparatus consisting of two traps (A, B), three U tubes (C, D, E), one sample tube (F) and one oil bubbler (G) in sequence. Trap A and B were filled with 85% sulfuric acid and cooled with ice-water mixture, U tube C was cooled with ice-salt mixture (at about -5°), U tube D and E with dry ice-acetone mixture and the condenser with 0° water. A solution of 10 g of 2-chloro-2-methylpropane-1,1,1,3,3,3-d_6 in 50 ml of dry toluene was added dropwise to the stirred residual mixture at 64° for 2.5 hr. The stirred mixture was heated at 64°-78° for 4.5 hr. A slow stream of dry nitrogen was introduced and the mixture was held at 78° for 4 hr. While being slowly flushed with nitrogen, the mixture was gradually heated to 110° and the condenser was warmed slowly from 0° to 10° in 2 hr. The valve between C and D and the valve between F and G were closed. The product collected in D was distilled into E by warming D to room temperature and cooling E with a dry ice-acetone mixture. Then the valve between D and E was closed and the product was distilled into F by warming E and cooling F with liquid nitrogen. It gave 4.4 g of 2,2-dimethyl-d_6-propane-1,1,1-d_3 (98 atom % D) with 55% yield based on 2-chloro-2-methylpropane-1,1,1,3,3,3-d_6 and identified by NMR.

2,2-Dimethylpropane-d_{12}

2,2-Dimethylpropane-d_{12} (99 atom % D) was prepared in a manner similar to the method described above, but using 2-chloro-2-methylpropane-d_9.

The deuterium contents were analyzed with a Jeolco C-60HL NMR spectrometer using internal standards.

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