

PREPARATION OF METHYLCYCLOPENTANE-1-d₁

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KEYWORDS

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deutero-tributylstannane
tertiary alkyl chloride, conversion to hydrocarbons

SUMMARY

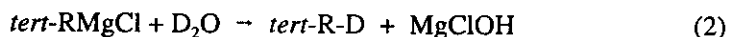
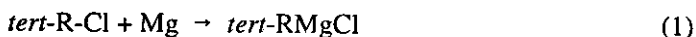
The title compound has been prepared in 70% yield by the reaction between 1-chloro-1-methylcyclopentane and deuterotributylstannane, without solvent. Small amounts (0.7-3.5%) of unreacted starting material remained after the reaction and were removed by solvolytic HCl elimination with water or aqueous sodium hydroxide, followed by oxidation with potassium permanganate or bromine addition at low temperature, which form products of low volatility. Small amounts of a by-product, deuterobutane, resulting from the cleavage of the carbon-tin bond in the reactant were also observed in the product.

INTRODUCTION

Intermolecular hydride shifts constitute an essential step in carbocationic reactions of saturated hydrocarbons.¹ It was reported that hydride transfer can be the rate-determining step of a carbocationic alkane isomerization^{2a} and it is the product-determining step (possibly also the rate-determining step) in alkane-alkene alkylation.^{2b} It was also found that there is very little intrinsic barrier for hydride transfer (less than 1 kcal/mol for the identity reaction of isobutane with t-butyl cation in solution).³ At the same time, it was reported that hydride transfers can be catalyzed by molecules with reactive

tertiary C-H bonds, especially adamantane⁴ but also branched alkanes and cycloalkanes.⁵ For a reinvestigation of hydride transfer in alkane isomerizations by rate and isotope effect measurements, we needed a branched hydrocarbon specifically deuterated at a tertiary position. Earlier studies showed that addition of methylcyclopentane (MCP) to a solution of tertiary alkyl cations (acyclic) in superacid leads to the methylcyclopentyl cation and the branched alkanes corresponding to the initial carbocations.⁶ Therefore, we chose MCP-1-d as deuteride donor.

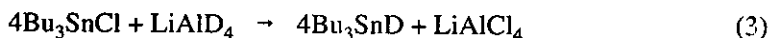
Hydrocarbons *tert*-R-D had been prepared from the corresponding chloro derivatives, by the Grignard reaction (Eq. 1-2).⁷ The procedure suffered from a tedious separation of the product from the large quantity of diethyl ether needed in the first step, but use of a high-boiling solvent like triglyme and distillation of the volatile hydrocarbon at the end of the reaction might remove this difficulty. More troublesome, however, was the finding that the product contained over 20% olefin and 18-25% unlabelled hydrocarbon, *tert*-R-H.⁷



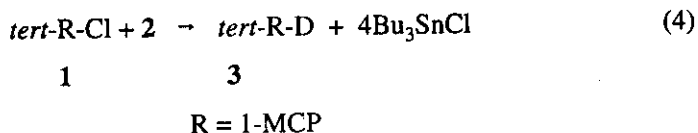
Addition of deuterium to methylcyclopentene was also attempted, because a β -D should introduce only a small secondary isotope effect in the hydride transfer reactions, but dideuteration was not specific; instead, the deuterium in C₆H₁₀D₂ was statistically distributed in all positions even at low temperature (with a Pd/C catalyst). As other possibilities, solvolysis of *tert*-R-Cl, or *tert*-R-OCO-C₃F₇,⁸ in the presence of NaBD₄ is a pathway to *tert*-R-D,⁹ but solvent removal is a problem there, too, whereas reaction of *tert*-R⁺ with D₂,¹⁰ even though specific,¹¹ is not easy to develop into a synthetic procedure.

RESULTS AND DISCUSSION

We chose for our synthesis the free-radical reduction of 1-chloro-1-methylcyclopentane (1) with deuterotributylstannane (2),¹² in which the source of deuterium is lithium aluminum deuteride (Eq. 3 and 4).^{12d,e,13}



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To simplify the isolation of the product, we ran the reaction without using a solvent. Methylcyclopentane-1-d (**3**) was isolated by distillation from the mixture with tributyltin chloride by-product and excess of reagent **2**, both much less volatile than **3**. The reaction was run photochemically, with α,α' -azobis(cyclohexanecarbonitrile) (ACHN) as photoinitiator.¹⁴ For high conversions, an excess of **2** had to be used, but the mixture of unreacted **2** and tributyltin chloride remaining after the distillation of the hydrocarbon product was vacuum-distilled and used for the reaction with lithium aluminum deuteride in the next batch.

The product contained small amounts (0.5-2%) of unreacted **1**, even though the reaction mixture was heated for 90 min after the exothermic reaction subsided. Longer periods of heating led to losses of the volatile product **3**. For purification, the crude **3** was stirred with water or dilute aqueous sodium hydroxide overnight and the methylcyclopentene formed was converted to less volatile products either by addition of bromine with cooling,⁷ or by oxidation with aqueous potassium permanganate. The purified product was dried in the same flask and recovered by bulb to bulb distillation.

GLC and GC-MS analyses have revealed deuterobutane (6-10% in the crude reaction mixture, 2.5-5% in the purified **3**) as a side product. It is most likely that butane is generally formed in dehalogenations with tributyltin hydride, by the homolytical cleavage of a tin-carbon bond, but it is usually removed with the solvent. As it did not interfere with the intended use of **3**, the removal of this impurity was not attempted, to avoid losses.

The method can be applied for the synthesis of any *tert*-R-D compound.

EXPERIMENTAL

Materials. The reagents and solvents used in the experiments were reagent-grade chemicals and were used as purchased.

Analyses. For NMR analyses, a 5-mm tube was placed coaxially inside a 10-mm tube with CDCl₃ as lock solvent, at 300.13 MHz (¹H) and 111.973 MHz (¹¹⁹Sn). For the latter, the

spectrum width was 45,000 Hz and external (coaxial) tetramethyltin¹⁵ (1 M in CH₂Cl₂) the reference. The procedures for GLC and GC-MS analyses were reported before.¹⁶

Preparation of reagents. Chloride **1** was obtained by the reaction of 1-methylcyclopentanol with hydrogen chloride at room temperature.¹⁷ The deuterated reagent, **2**, was prepared by the addition of 48.8 g (150 mmol) of tributyltin chloride dissolved in dry ether (75 mL) to an ice-cooled, stirred suspension of 3 g (71 mmol) lithium aluminum deuteride in 200 mL of anhydrous ether over a 50 min period; 50 mL of ether was then used to rinse the dropping funnel. The mixture was stirred for another 20 min with cooling and for 100 min at room temperature. A dry nitrogen atmosphere was maintained throughout these operations. The stoppered flask was left at room temperature overnight, then it was ice-cooled again and water (95 mL) was added dropwise, with vigorous stirring, after which 10% sulfuric acid (375 mL) was added dropwise. The layers were separated and the water layer was extracted three times with ether. The combined ether solution was washed once with saturated aqueous NaCl, dried on MgSO₄, and concentrated under vacuum on a rotary evaporator at room temperature. The residue was distilled under vacuum on an oil bath preheated at 115–120°C. A main fraction of 34.4 g (78.5% yield) was collected at 76–84°C/0.7 mmHg. A second cut (3.7 g, 8.4%) was collected to 88°C. The proton-decoupled ¹¹⁹Sn NMR signal of **2** (neat) had δ -92 ppm (t, J(Sn-D) = 245 Hz). The starting Bu₃SnCl exhibited a somewhat broadened singlet at δ +140 ppm.

Preparation of 3. The reactants **1** (5.89 g., 49.7 mmol), **2** (23.3 g., 79.3 mmol), and ACHN (0.266 g., 1.09 mmol) were placed in a 150 mL round-bottomed flask, provided with reflux condenser, immersed thermometer and Teflon-coated magnetic stirring bar. The flask was irradiated with a 140W Hanovia 30620 ultraviolet quartz lamp, while maintained at 90–95°C with a heating mantle, for 90 min. The product which was distilled from the mixture at the end of the reaction (3.68 g), consisted of 88.9 mole % **3** (i.e., 39.3 mmol, 79% yield), 1.8 mole % unreacted **1**, and 9.1 mole % deuterobutane (parent ion in GC-MS at m/z = 59).

For purification, the crude **3** was stirred for 2 h with 1.3 mL 1N NaOH in the stoppered flask, at room temperature. The flask was then cooled below 0°C and treated with bromine in small drops, until the light yellow color did not disappear immediately after addition of one drop. Solid sodium sulfite was added to remove the excess bromine,

most of the water layer was removed with a pipet, and calcium chloride was added to the hydrocarbon layer, which was then kept stoppered for 30 min. Bulb to bulb distillation at 50°C under vacuum (*ca* 150 torr) gave 3.30 g of product containing 93.5 mole % **3** (34.8 mmol, 70% yield), 5.4 mole % deuterobutane, and 1.1 mole % **1**. GC-MS of **3** gave *m/z* 84 (12.4), 85 (1000) and 86 (76), whereas the unlabelled methylcyclopentane (*M* = 84) gave no measurable *m/z* 83 peak. Thus, the product was deuterated to the same extent as the starting LiAlD₄, 98.8%.

In the alternative purification, the crude product (1.11 g; 94.1 mole % **3**, 1.0 mole % **1**, and 4.9 mole % deuterobutane) was stirred in the capped flask with a few drops of water for 16 hours, after which KMnO₄ (0.1 g, 0.6 mmol) was added, the flask was capped again, and stirring was continued for another 10 hours. Removal of the aqueous layer, treatment with CaCl₂, and bulb to bulb distillation as described above, gave 0.68g product, which was 96.2 mole % (7.8 mmol, 63% recovery) **3**, and 3.8% deuterobutane.

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