A Simple and Inexpensive Method for the Preparation of RCD₂·CO₂H and RCD₂·OH

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Summary The oxidation of α -deuteriated ketones, followed by hydrolysis, provides a simple and inexpensive method for the preparation of α -deuteriated acids and alcohols.

In connection with some mass spectral studies, it was necessary to prepare as starting materials the labelled compounds RCD₂·OH (I) and RCD₂·CO₂H (II) in relatively large quantities (>10 g). Previous methods require the use of relatively expensive deuteriated reagents (e.g. $LiAlD_4$ or $NaBD_4$)¹ for (I), and exchanges in sealed tubes [for (II)];² these factors usually limit the scale of the preparation. The procedure outlined in the Scheme is inexpensive and is capable of large-scale preparation.

The ease of base-catalysed deuteriation of the α -positions of ketones is well known. Three successive exchanges (12-24 h) with D₂O give deuteriated compounds with > 90% deuteriation.³ High yields (70-90%) are obtained for the oxidation of these ketones to the esters via the Baeyer-Villiger oxidation, using reagents such as commercially available trifluoroacetic anhydride and hydrogen peroxide.4 Hydrolysis with base, followed by the usual

$$(\text{RCH}_{2})_{2}\text{C}=\text{O} \xrightarrow{i} (\text{RCD}_{2})\text{C}=\text{O} \xrightarrow{ii} \text{RDC}_{2} \cdot \text{CO}_{2} \cdot \text{CD}_{2}\text{R}$$

$$\downarrow^{jii}$$

$$\text{RCD}_{2} \cdot \text{CO}_{2}\text{K} + \text{RCD}_{2} \cdot \text{OH}$$

$$\downarrow^{iv} \qquad (I)$$

$$\text{V}$$

$$\text{RCD}_{2} \cdot \text{CH}_{2} \cdot \text{OH} \leftarrow \text{RCD}_{2} \cdot \text{CO}_{2}\text{H}$$

(III)

work-up, gives (I) and (II). Alternatively, the ester can be

reduced with LiAlH₄ to give the deuteriated alcohols (I) and

SCHEME. Reagents: i, Base-D₃O (3 exchanges); ii, $(CF_3 \cdot CO)_2 - O-H_2O_2$; iii, KOH; iv, H⁺; v, a, CH_2N_2 ; b, $LiAlH_4$.

(III). In our hands, 43 g (0.5 mol) of pentan-3-one gave 24 g (0.32 mol) of CH₃·CD₂·CO₂H, and 15 g (0.31 mol) of CH₃·CD₂·OH, an overall yield of 64% and 62%, respectively. I thank Christ's College, Cambridge, for a fellowship

(Class B).

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(II)

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