Hydroxylation of Cyclohexane, Octan-1-ol, and Palmitic Acid by Trifluoroperoxyacetic Acid

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Summary The hydroxylation of cyclohexane, octan-1-ol, and palmitic acid by trifluoroperoxyacetic acid occurs in high yield without further oxidation.

Trifluoroperoxyacetic acid (per TFA) has the property of oxidizing alkanes rapidly while being totally inert to the alcohols and alkyl trifluoroacetates that are produced. The conversion of alkanes into alcohols occurs in high yield providing tertiary hydrogen atoms are absent. Also successful are hydroxylations of alkyl chains at positions remote from an alcohol group and other electronegative groups.

After 24 h at 25 °C, the n.m.r. spectra of a mixture of 0·78 g of cyclohexane (9·3 mmol), 1·2 g of 30% aqueous H_2O_2 (10·7 mmol), and 20 ml of CF_3CO_2H showed only the multiplets of cyclohexyl trifluoroacetate at δ 5·11 and 1·2—2·3 and the cyclohexane resonance at δ 1·46. Peak areas indicated a 73% yield of the cyclohexanol derivative. The 2·55 α-CH_2 peak of cyclohexanone and the 2·8 and 4·4 peaks of ϵ-caprolactone were absent. These results were confirmed by g.l.c. which showed cyclohexyl trifluoroacetate (78), cyclohexane (17·7), cyclohexanol (0·3), and two minor products (2·7 and 1·3%), and no trace of cyclohexanone or ϵ-caprolactone. Similar yields were obtained in experiments conducted for 20 min at reflux (83 °C).

Hydroxylation remote from electronegative substituents has been demonstrated with octan-1-ol and palmitic acid. After 1 h at 83 °C, octan-1-ol gave 59% of octanediols as their bis trifluoroacetates. Analysis by g.l.c. as described[1] showed relative percentages as: 3% for 1,8-, 51 for 1,7-, 25 for 1,6-, 14 for 1,5-, and 7 for 1,4-diol. No trifluoroacetates of octanetriols, or any ketones were detected. The 59% total yield shown by g.l.c. was confirmed by n.m.r. spectroscopy by comparing areas of the secondary trifluoroacetate peak at δ 5·22 relative to the primary trifluoroacetate peak at 4·48. The selectivity for hydroxylation remote from electronegative substituents is a result of the electrophilic (HO^+) nature of the reagent.[2]

Similar treatment of palmitic acid gave a 70% yield of hydroxypalmitic acids as estimated from the n.m.r. peak areas of the secondary trifluoroacetates (5·2) relative to the acidic H, α-CH_2, and terminal CH_3 peaks. The distribution of the OH groups was estimated by oxidizing 1·0 g of the hydroxypalmitic acids with 2 ml of 70% HNO_3 in 5 ml of acetic acid for 1 h at 100 °C. The dicarboxylic acids were converted into dimethyl esters and analysed by g.l.c. The C_{10} diacid was the most abundant. Relative to $C_{10}=1$ the molar ratios ranged from 0·4 for C_{14} diacid and 0·6 for C_{11}—C_{13} diacids to 0·8—0·9 for C_5—C_9 diacids. These ratios indicate a near random distribution of the position of the hydroxy substituent from C_5 to C_{15}. This method of determining the position of the hydroxy substituent was tested on 12-hydroxystearic acid which gave diacids in the ratio 9:9:2 for $C_{12}:C_{11}:C_{10}$.

Per TFA has been used previously to oxidize pentane.[3] A 100:1 ratio of pentane to per TFA was used and treatment with $LiAlH_4$ was used in the isolation procedure. It is clear from the present work that there was no need for the large excesses of pentane. The reaction of per TFA with alkanes containing tertiary hydrogen atoms is far more complex and large excesses of alkane are needed to obtain good yields of the t-alkyl trifluoroacetates. Such excesses were used in hydroxylating isopentane, methylcyclohexane,[3] and *cis*- and *trans*-1,2-dimethylcyclohexane.[4]

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