Regioselective Oxidation of Adsorbed Alkyl Hydrogen Succinates by Ozone in Freon 11

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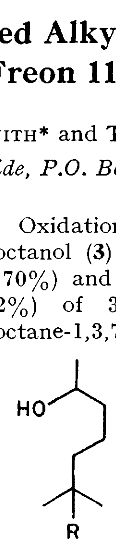
Summary The hydrogen succinates of 6-methylheptan-2-ol (**1**), 3,7-dimethyloctanol (**3**), adamantan-2-ol (**6**), cyclododecanol, undecanol, and the isomeric decalols, (**8**) and (**10**), when adsorbed on silica-gel, undergo regioselective oxidation at positions remote from the binding site when treated with ozone in Freon 11.

TREATMENT with gaseous ozone of alcohols adsorbed as their acetates on silica-gel and other suitable solid supports has been shown[1–3] to provide a useful method for the selective oxidation of saturated C–H positions remote from existing functionality. However, application of this technique to synthesis presents difficulties: the progress of the reaction is not easily monitored, yields are sometimes erratic, and there are technical limitations to the scale of the experiment. The use of ozone in solution is not usually practicable because the adsorbed monolayer, on the stability of which the regioselectivity of the method depends, is disrupted by the solvent.

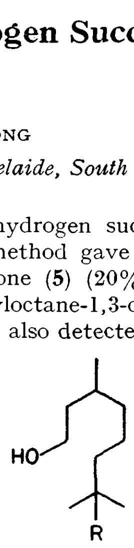
We now report that these difficulties can be overcome by the use of alkyl hydrogen succinates, which are strongly bound to silica-gel, as substrates, together with a solution of ozone in Freon 11 as oxidizing agent. The technique is simple, reliable, and applicable on a moderate scale. The following example of the hydroxylation of 6-methylheptan-2-ol (**1**) is illustrative.

A sample (5·8 g) of the hydrogen succinate of (**1**) was adsorbed on Sorbsil (36 g) by stirring the adsorbent with a solution of the ester in light petroleum for 1 h. A suspension of the dried solid in Freon 11 (600 ml) was then stirred at −25 °C while a stream of ozone in oxygen (24 l h^{-1}; 3% O_3) was bubbled in for 2 h. The resultant deep blue mixture was allowed to warm up to ambient temperature during 3 h at the end of which time all the ozone had been consumed. The treatment with ozone was repeated. The mixture was then filtered and the crude product was isolated by extraction from the silica-gel with ethyl acetate. Alkaline hydrolysis of the product gave an oil which was shown by g.l.c. to comprise the 2,6-diol (**2**) (92%), 6-oxoheptan-2-ol (4%), and starting material (4%). Distillation gave the pure diol (3·3 g, 88%), b.p. 72—74 °C at 0·3 mmHg.

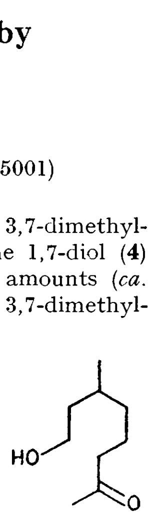
Oxidation of the hydrogen succinate of 3,7-dimethyloctanol (**3**) by this method gave mainly the 1,7-diol (**4**) (70%) and the 7-ketone (**5**) (20%). Small amounts (*ca.* 2%) of 3,7-dimethyloctane-1,3-diol and 3,7-dimethyloctane-1,3,7-triol were also detected.



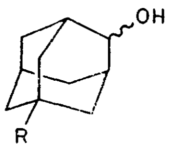
(1) R = H
(2) R = OH



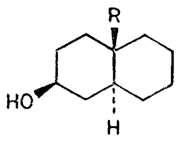
(3) R = H
(4) R = OH



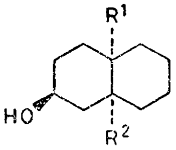
(5)



(6) R = H
(7) R = OH



(8) R = H
(9) R = OH



(10) R^1 = R^2 = H
(11) R^1 = H, R^2 = OH
(12) R^1 = OH, R^2 = H

Although the oxidation of methylene groups by ozone in Freon 11 proceeds slowly and requires prolonged treatment of the adsorbed substrate at ambient temperatures, the regioselectivity previously observed in the reaction with gaseous ozone[2] is preserved. Thus, the hydrogen succinate of cyclododecanol gave, after acetylation, 5-, 6-, and 7-oxocyclododecyl acetate (17, 28, and 10%, respectively). Oxidation of undecanol proceeded with 42% specificity at the 10-position.

Oxidation of the hydrogen succinate of adamantan-2-ol (**6**) affords 4-hydroxyadamantan-2-one (10%), adamantane-1,2-diol (6%), and adamantane-1,4-diol (**7**) (*cis,* 55%; *trans,* 15%).

Oxidation of the hydrogen succinates of the decalols (**8**) and (**10**) provides further evidence of the remarkable similarity between the results of ozonation and microbiological oxidation.[2] Thus the hydrogen succinate of the *trans*-decalol (**8**) undergoes regio- and stereo-specific attack to afford the diol (**9**), whereas the *cis*-decalol (**10**) gives approximately equal quantities of (**11**) and (**12**). Incubation of the *cis*- and *trans*-isomers of 2-decalone with *Curvularia falcata* has been shown to give very similar results.[4]

These results indicate that oxidation with ozone in Freon 11 solution retains the regio- and stereo-selectivity of the dry ozonation technique[1–3,5] whilst offering practical advantages.

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