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A CONVENIENT PROCEDURE FOR THE CIS-HYDROXYLATION OF OLEFINS

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The reaction of olefins with iodine and silver acetate in moist acetic acid (Woodward's procedure) is the best method for the preparation of cis-diols with the hydroxyl groups on the more hindered side of the molecule.[1]

In the Woodward's procedure the silver carboxylate is assumed to have a double function: i) to give an acyl hypoiodite that serves as a source of electrophilic iodine; ii) to facilitate the conversion of the acetylated trans--iodohydrin, formed in the addition step, into a dioxolenium ion that then leads to the cis-diol.[2]

We have now found that silver salt is not essential both for i) and ii) and have therefore developed a modified procedure that does not require this expensive reagent.

By making use of a method analogous to a recently reported one,[3] 5α-cholest-2-ene was converted in an 86% yield to 2β-acetoxy-3α-iodo-5α--cholestane m.p. 95-97° (lit.:[4] 96-97°), by reaction with iodine (0.50 moles) and potassium iodate (0.25 moles) in acetic acid solution at 60° (2 hours).[5]

When refluxed (1 hour) with silver acetate (1.1 moles) in moist acetic acid and then hydrolysed with alkali the acetylated trans-iodohydrin smoothly gave 5α-cholestan-2β,3β-diol m.p. 177.5-179° (lit.:[6] 177-179°) in an 84% yield (lit.:[6] 82%). However, the diol could be also obtained by replacing silver acetate with an equivalent amount of either cupric acetate (87% yield) or potassium acetate (76% yield) and even simply refluxing (10 hours) the acetylated trans-iodohydrin in acetic acid-water (1:1) (76% yield). Obviously, the isolation of this intermediate is not necessary, as it may be seen from the following procedure, that leads to cis-diol directly from 5α-cholest-2-ene :

5α-cholest-2-ene (0.5 g, 1.35 mmoles), glac. AcOH (20 ml), KJO_3 (70 mg, 0.34 mmoles) and iodine (170 mg, 0.675 mmoles) were stirred at 60° for 3 hr. AcOK (133 mg, 1.35 mmoles) was added and the reaction mixture was refluxed for

3 hr. After cooling, water was added and the mixture was extracted thrice with n-hexane. The extracts were washed with water and evaporated to give a solid which was refluxed in benzene (10 ml) with KOH (2 ml of a 10% MeOH soln.). Usual work up gave a solid which by chromatography afforded pure 5α-cholestan-2β,3β-diol (390 mg, 70%) besides 60 mg of unreacted olefin.

The above procedure was essayed on two other representative olefins too. Thus, when reacted with iodine and potassium iodate in acetic acid at r.t. for 5 hr. and then refluxed with potassium acetate for 7 hr. cyclohexene gave (after hydrolysis with alkali) *cis*-1,2-cyclohexandiol m.p. 97.5° (86% yield; lit.:[7] 70%), gas chromatographically free from the *trans*-isomer. Analogously, from oleic acid (24 hr. at r. t. and then 6 hr. reflux) a 63.5% yield (lit.:[7] 56%) of *erythro*-9,10-dihydroxystearic acid m.p. 126-129° (lit.:[8] 127-129°) was obtained after hydrolysis with alkali.

Owing to its simplicity and to the yields more than comparable with those of the classical Woodward's reaction the present procedure should be the method of choice for the olefins *cis*-hydroxylation.

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