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IODOHYDRINS AND IODOHYDRIN ESTERS. V.[1] A NOVEL ALKENE EPOXIDATION PROCEDURE

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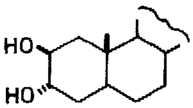
The reaction of 5α-cholest-2-ene with iodine and water in the presence of KIO_3/H_2SO_4 according to Cornforth and Green[2] has been recently[1] reported to give the trans-diaxial diol 1 in high yield. It has been shown that the expected iodohydrin 2 is actually formed (eqq. 1 and 2) but, owing to the favourable anticoplanar arrangement of the involved groups, it is converted into the epoxide 3 (eq. 3) by removal of hydrogen iodide (eq. 2) as soon as this is formed in the oxirane ring closure. However, the rather highly acidic medium causes 3 to be easily hydrolyzed to the observed 1.



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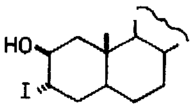

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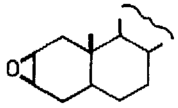

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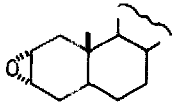

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We conceived that the reaction of 5α-cholest-2-ene with iodine and water in the presence of a reagent capable **of removing** hydrogen iodide in a non acidic medium, though not allowing the iodohydrin 2 to be isolated, might suppress the acid-catalyzed hydrolysis of the epoxide 3 and thus **provide** a convenient procedure to obtain this latter compound.

$$C{=}C + I_2 + H_2O \longrightarrow \overset{OH}{C}-\underset{I}{C} + I^- + H^+ \qquad \text{(eq. 1)}$$

$$5\,I^- + 6\,H^+ + IO_3^- \longrightarrow 3\,I_2 + 3\,H_2O \qquad \text{(eq. 2)}$$

$$\overset{OH}{C}-\underset{I}{C} \longrightarrow C\overset{O}{\triangle}C + H^+ + I^- \qquad \text{(eq. 3)}$$

In practice, this could be achieved by use of silver oxide as iodide removing agent. When 5α-cnolest-2-ene was treated with iodine and silver oxide in water/dioxane, smooth epoxidation occurred:

5α-cholest-2-ene (1 mmole) was treated with I_2 (1.5 mmoles) and Ag_2O (1.5 mmoles) in 12:1 dioxane-water (25 ml) at room temperature for 7 hours. Usual work up and chromatography on silica gel (9 g) with 95:5 hexane-ether afforded a mixture of the epoxides 3 and 4 (345 mg). Further elution with ether yielded the diol 1 (30 mg). TLC on silica gel (98:2 hexane-ether, 3 runs) of the epoxide mixture gave pure 3 (284 mg) and 4 (58 mg).

The above procedure was then tested with other olefins. The results obtained are shown in the table.

Reaction of olefins (1 mmole) with I_2 (1.5 mmoles) and Ag_2O (1.5 mmoles) in 12:1 dioxane-water (25 ml/mmole) at r.t. for 7 hours

	Products and yields[a]		*Epoxidation yields*
5α-cholest-2-ene	β-*epoxide*	*71%*	*86%*
	α-*epoxide*	*15%*	
	2β,3α-diol	*8%*	
3-methyl-5α-cholest-2-ene	α-*epoxide*	*70%*	*70%*
	2β,3α-diol	*10%*	
2-methyl-5α-cholest-2-ene	β-*epoxide*	*70%*	*70%*
	2β,3α-diol	*8%*	
cholesterol	α-*epoxide*	*54%*	*82%*
	β-*epoxide*	*28%*	
	3β,5α,6β-triol	*7%*	
cyclohexene	*epoxide*	*80%*	*80%*

(a) *All products have been identified by comparison (TLC, NMR, m.p.) with authentical samples. All yields are of pure, isolated products.*

The stereochemical results of the reaction deserve some comment. It is well known[3] that the nucleophilic step of the addition (opening of iodonium ion by H_2O) strongly affects the stereochemical outcome of the reaction of trisubstituted cyclic olefins. This accounts for the stereoselective formation of α-epoxide from 3-methyl-5α-cholest-2-ene and of β-epoxide from 2-methyl-5α-cholest-2-ene. On the same grounds, an highly prevailing production of α-epoxide was to be expected in the case of cholesterol. However, a rather low value (2:1) of the α-/β-epoxide ratio was found. The electronic acceleration due to the tertiary nature of the axial attack site of 5β, 6β-iodonium ion is in this case partially balanced by the steric hindrance to the entry of nucleophile towards the 5α-position.[4]

In our opinion, because of the satisfactory yields obtained and the very mild conditions employed, the present procedure represents an useful alternative to the current epoxidation methods. As an example, it is noteworthy that the reaction of 2-methyl-5α-cholest-2-ene with NBA/$HClO_4$, the only reported[5] procedure for direct epoxidation of steroidal olefins from the more hindered β-side, was found to occur in very low yield (<20%).

REFERENCES

1. Part IV: M.Parrilli, M.Adinolfi, G.Barone, G.Laonigro, L.Mangoni, Gazz.Chim.It.,in press (1975)
2. J.W. Cornforth, D.T. Green, J. Chem. Soc. (C), 846 (1970).
3. M. Parrilli, G. Barone, M. Adinolfi, L. Mangoni, Gazz. Chim. It., 104 835 (1974) and references therein.
4. A.S. Hallsworth, H.B. Henbest, J. Chem. Soc., 3571 (1960).
5. C.R. Eck, P. Kullberg, B. Green, Chem. Comm., 539 (1972).