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IODOHYDRINS AND IODOHYDRIN ESTERS. VI.[1] A GENERAL PROCEDURE FOR THE PREPARATION OF *trans*-1,2-IODOCARBOXYLATES

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trans-1,2-Iodoacetates have been shown to be easily obtained by reaction of alkenes with I_2/KIO_3 in acetic acid. The process is assumed to occur through the *anti* attack of AcOH on an iodonium ion, the role of KIO_3 being to favour the formation of this latter by the continous reoxidation of the iodide ion produced in the electrophilic addition step.[2]

N-iodosuccinimide (NIS) has now been found to be a very convenient alternative to the I_2/KIO_3 system as a source of positive iodine. In fact, *trans*-2-iodocyclohexyl acetate and 3α-iodo-5α-cholestanyl 2β-acetate were obtained in near quantitative yield when cyclohexene (1 hr, r.t.) and 5α-cholest-2-ene (1 hr, 60°), respectively, were reacted with NIS in AcOH.

More interestingly, the reaction with NIS and a carboxylic acid in an aprotic solvent could be imagined to be a general procedure for the obtaining of *trans*-1,2-iodocarboxylates other than *trans*-1,2-iodoacetates. The I_2/KIO_3 system, indeed, cannot be used with a carboxylic acid not suitable as the solvent (e.g., benzoic acid) or very prone to add to double bonds (e.g., trifluoroacetic acid).[+]

As a matter of fact, chloroform was found to be a good solvent for the reaction. The carboxylic acids tested and the results obtained are shown in the Table. A typical procedure follows:

To a solution of 5α-cholest-2-ene (1 mmole) in chloroform (10 ml, filtered on Al_2O_3*), benzoic acid (2 mmoles) and NIS (1.3 mmoles) are added. After 3 hr stirring at 60°, the cooled reaction mixture was diluted with ether (30 ml), washed with 2N* Na_2CO_3*, 5N* $Na_2S_2O_3$*, water and dried. Evaporation of the solvent and chromatography on silica gel with 98:2 hexane-ether gave 3α-iodo-5α-cholestanyl 2β-benzoate (82%).*

(+) The reaction of 5α-cholest-2-ene in CF_3COOH with I_2/KIO_3 at 60° gives only a mixture of 5α-cholestanyl 2- and 3-trifluoroacetates (our unpublished result).

Table

Reaction of olefins (1 mole) with NIS (1.3 moles) and
carboxylic acid (2 moles) in $CHCl_3$

	Acid	Time, temperature	Product and yield[a]
Cyclohexene	AcOH	1 hr, r.t.	*trans*-2-iodo-cyclohexyl acetate,[3] >95%
"	BzCOOH	1 hr, r.t.	*trans*-2-iodo-cyclohexyl benzoate,[3] >95%
"	CF_3COOH	1 hr, r.t.	*trans*-2-iodo-cyclohexyl trifluoroacetate,[3] >95%
5α-cholest-2-ene	AcOH	2 hr, 60°	3α-iodo-5α-cholestanyl 2β-acetate,[b,4] >90%
"	BzCOOH	3 hr, 60°	3α-iodo-5α-cholestanyl 2β-benzoate,[b,c] 82%
"	CF_3COOH	1 hr, 60°	3α-iodo-5α-cholestanyl 2β-trifluoroacetate,[b,5] >95%
"	HCOOH	1 hr, 60°	3α-iodo-5α-cholestanyl 2β-formate,[b,d] >95%
"	p-Cl-BzCOOH	3 hr, 60°	3α-iodo-5α-cholestanyl 2β-p-clorobenzoate,[b,e] 73%
"	$p\text{-}NO_2\text{-}BzCOOH$[f]	3 hr, 60°	3α-iodo-5α-cholestanyl 2β-p-nitrobenzoate,[b,g] 70%

(a) All yields are of pure, isolated products. All known products have been identified by comparison (NMR, TLC, m.p.) with authentical samples. (b) In addition to 3α-iodo-5α-cholestanyl 2β-carboxylate, a <5% yield of the isomeric 2β-iodo-5α-cholestanyl 3α-carboxylate was obtained. (c) M.p. 74-5°; $[\alpha]_D$ (CCl_4) +83°; $\delta(CCl_4)$ 4.60 (3β-H) and 5.35 (2α-H). (d) M.p. 110-1°; $[\alpha]_D(CCl_4)$ +99°; $\delta(CCl_4)$ 4.48 (3β-H), 5.12 (2α-H) and 7.84 (-OCO*H*). (e) M.p. 82-4°; $[\alpha]_D$ (CCl_4) +78°; $\delta(CCl_4)$ 4.60 (3β-H) and 5.32 (2α-H). (f) Solvent: $CHCl_3$ with 3% dioxane. (g) M.p. 146-8°; $[\alpha]_D$ (CCl_4) +68°; $\delta(CCl_4)$ 4.65 (3β-H) and 5.40 (2α-H).

When this work was completed, a paper[6] appeared reporting the use of the reaction of olefins with NBS and AcOAg in AcOH to obtain *cis*-diols through *trans*-1,2-bromoacetates, not isolated. This *cis*-hydroxylation method is analogous to that reported by us some years ago.[4] However, our method , of which the French Authors seem to be not aware, very advantageously avoids the use of expensive silver acetate.

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