

PROSTAGLANDINS : BY-PRODUCTS IN BBr_3 -CLEAVAGE OF COREY'S METHYLEETHER INTERMEDIATE

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The cleavage of the methoxyalkanes $\text{CH}_3\text{O}-(\text{CH}_2)_n-\text{CH}_3$, ($n = 2-17$), by means of BBr_3 is a very complicated reaction whose mechanism probably depends upon the extension and the conformation of the aliphatic chain (¹); this reaction gave mixtures of variable composition of alcohols and of corresponding alkyl bromides (¹).

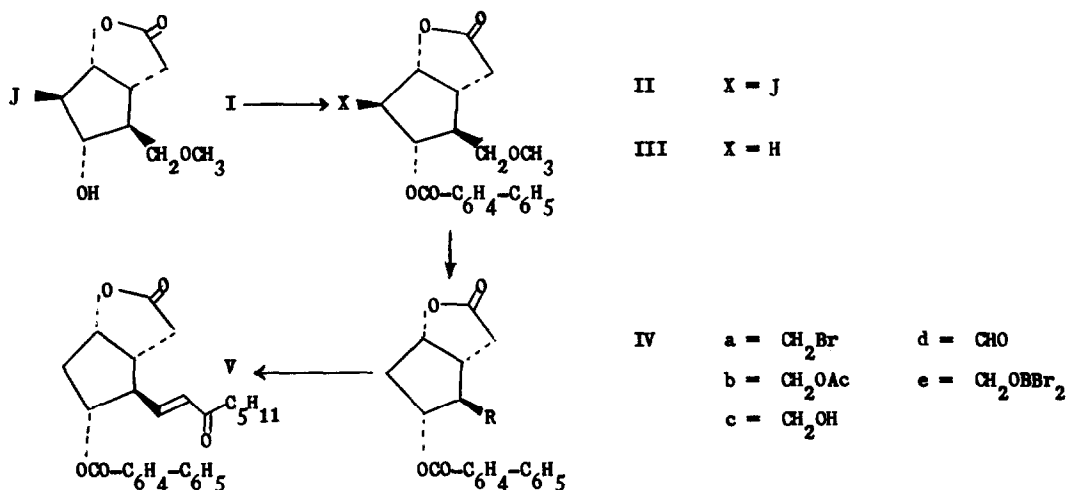
Treatment of 3 α -methoxy or 3 β -methoxy-cholestanes with BBr_3 , at 25°, gave complete cleavage in 10 minutes to the corresponding 3-bromo-cholestanes only (²).

In our turn, on repeating Corey's synthesis of prostaglandins, we observed that the cleavage of lactone methylether III with BBr_3 (4.4 equiv) in methylene chloride at 0° always affords the 5 β -bromomethyl derivative IVa, m.p. 119-122° (from methanol), $[\alpha]_D^{25} = -91.4^\circ$ (found for IVa C : 61.32, H : 4.39, Br : 15.26) in 10-30% yield as by-product, in addition to alcohol IVc.

Esterification of iodo lactone (I), as colorless oil, $[\alpha]_D^{25} = -43.7^\circ$ ($c = 2.53$) (³) with p-phenylbenzoyl chloride (2.5 equiv) in pyridine, at 90°, for 3 hr gave the iodo lactone-p-phenylbenzoate (II), m.p. 155.5-157°, $[\alpha]_D^{25} = +10.1^\circ$ (found for II C : 53.85, H : 4.23, J : 25.68), which was reduced with tributyltin hydride (⁴), at 55°, nitrogen atmosphere, to deiodinated lactone III, m.p. 74-75°, $[\alpha]_D^{25} = -104.8^\circ$ (found for III C : 72.60, H : 5.92, O : 21.74).

In following large-scale experiments of cleavage of the methylether III with BBr_3 , after anhydrous potassium acetate addition to destroy the excess of reactive, we obtained a mixture of three compounds: bromo derivative IVa, acetoxy-p-phenylbenzoate IVb and p-phenylbenzoate alcohol IVc, in a ratio 1 : 1 : 2 after column separation.

The acetoxy derivative IVb probably originates from a non-isolated bromo boronite compound



(IVe) (¹) through a substitution reaction.

Treatment of bromo derivative (IVa) in dimethylformamide with acetic acid and potassium acetate, at reflux temperature, produced (90% yield) the same crystalline acetoxy-*p*-phenylbenzoate (IVb), m.p. 111–113° (from ethyl ether), $[\alpha]_D = -97.7^\circ$ (found for IVb C : 70.32, H : 5.58, O : 24.46), which by selective cleavage of the acetoxy ester group by means of perchloric acid in methanol gave the *p*-phenylbenzoate alcohol IVc, m.p. 129.5–131°, $[\alpha]_D = -87.5^\circ$ (c = 1.563) (found for IVc C : 71.65, H : 5.62, O : 22.79).

The following oxidation of the alcohol IVc with dicyclohexylcarbodiimide in benzene-dimethylsulfoxide (75 : 25) in the presence of pyridine trifluoroacetate (⁵) allowed us to obtain the *p*-phenylbenzoate aldehyde IVd, which, without purification, was treated with the sodio derivative of dimethyl-2-oxoheptylphosphonate in dimethoxyethane (⁶) to form the trans-enone lactone V, as a crystalline product, m.p. 80–82° (from isopropyl alcohol), $[\alpha]_D = -146^\circ$ (c = 1.02), with 70% yield from IVc, reported: 81–82.5°, $[\alpha]_D^{25} = -146^\circ$, 80% yield (⁷).

Experimental: Unless otherwise stated, specific rotations were measured in chloroform solution (1% concentration), at 20°, with P-141 Perkin-Elmer polarimeter.

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References and Footnotes

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