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REACTION OF SOME TRISUBSTITUTED STEROID EPOXIDES WITH TRIPHENYLPHOSPHINE - IODINE COMPLEX. DEOXYGENATION OF EPOXIDES

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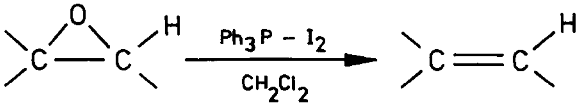
Summary: Triphenylphosphine - iodine complex was found to be an effective reagent for deoxygenation of trisubstituted steroidal epoxides. The mechanism of the reaction is proposed.

In connection with our work on carbocationic rearrangements of steroids and triterpenes, we required iodohydrins with hydroxy group attached to a tertiary carbon of the alicyclic steroidal skeleton. Examination of the triphenylphosphine - iodine complex[1] as a reagent for converting the appropriate epoxide into iodohydrin gave negative results.

In view of a recent communication[2] in which an Italian group reports an efficient and general synthesis of halohydrins from epoxides using this reagent, we present our results concerning deoxygenation of some steroidal epoxides with triphenylphosphine - iodine complex. Since the Italian worker's experiments can be repeated by us, results presented here suggest that the mode of reaction is sensitive to the degree of substitution of the epoxide ring.

In the preliminary experiment, 3β-acetoxy-5α,6α-epoxycholestane upon treatment with triphenylphosphine and iodine in dichloromethane at room temperature gave a product of lower polarity then the starting epoxide. It was shown by comparison with an authentic sample to be 3β-acetoxycholest-5-ene. Similarly, reaction of a series of trisubstituted steroidal epoxides gave olefins as sole or major products (Table).



Deoxygenation of epoxides into olefins is an important reaction and a great variety of reagents, which are effective in this transformation, has been reported.[3] Among them several phosphorus compounds[4] were found to be useful. For many cases, however, expensive reagents are required and yields are moderate.

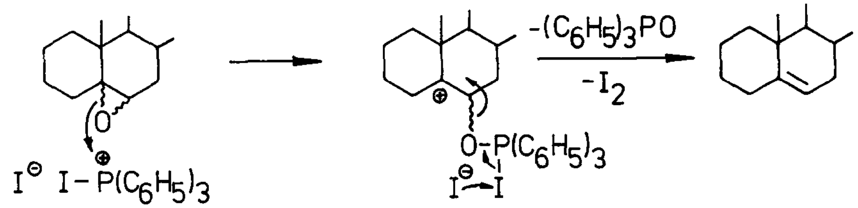
Table

Entry	Epoxide	Yield of olefin (%)[a]	Olefin[b]
1.	3β-acetoxy-5α,6α-epoxycholestane[5]	93	3β-acetoxycholest-5-ene
2.	3β-acetoxy-5β,6β-epoxycholestane[5]	95	3β-acetoxycholest-5-ene
3.	3β-acetoxy-5α,6α-epoxypregnan-20-one[6]	50	3β-acetoxypregn-5-en-20-one
4.	3β-acetoxy-5β,6β-epoxypregnan-20-one[7]	76	3β-acetoxypregn-5-en-20-one
5.	3β-acetoxy-5α,6α-epoxyandrostan-17-one[8]	98	3β-acetoxyandrost-5-en-17-one
6.	3β-acetoxy-5β,6β-epoxyandrostan-17-one[8]	75	3β-acetoxyandrost-5-en-17-one
7.	5,6-epoxycholestane	73[c]	cholest-5-ene[9]
8.	3β-chloro-5,6-epoxycholestane	95[c]	3β-chlorocholest-5-ene[10]
9.	spiro-[5α-cholestane-3,2'-oxiran][11]	28[d]	3-methyl-5α-cholest-2-ene[12]
10.	3β-acetoxy-8α,9α-epoxy-5α-lanostane[13]	95	3β-acetoxy-5α-lanosta-7,9(11)-diene[14]
11.	3β-acetoxy-9α,11α-epoxy-5α-lanostane[13]	100	3β-acetoxy-5α-lanosta-7,9(11)-diene

[a] Yield of isolated product is given.
[b] Olefins were compared with authentic samples by their m.p., R_f, ^{1}H NMR, and IR spectra.
[c] A mixture of α- and β-epoxides was employed.
[d] A mixture of (3R)- and (3S)-epoxides was employed.

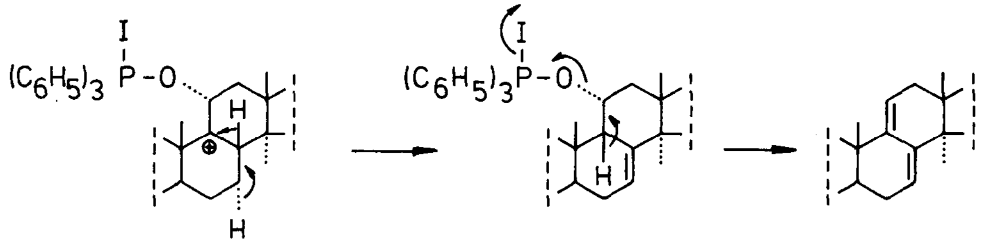
Our procedure is a new, simple and inexpensive reaction, in which trisubstituted steroidal epoxides may be converted into the respective olefins. The typical procedure is as follows: iodine and triphenylphosphine (1:1 molar ratio) are dissolved in dichloromethane followed by addition of a solution of an epoxide (0.9 mole equiv.) in the same solvent. The reaction is followed on t.l.c. plates and after disappearance of the substrate (0.5 to 6 hrs) the reaction mixture is worked up by washing with sodium thiosulfate. The crude reaction product in benzene solution is filtered through a silica column (25:1) to give the respective olefin. The yield of olefin in most cases is in the range 70-100%. Interestingly, the deoxygenation reaction appears to be not remarkably influenced by the configuration of the starting epoxide (α or β). Some polar products were observed on t.l.c. plates and are most probably iodohydrins.

It is suggested that the crucial role of iodine is to enhance the electrophilicity of the phosphorus atom in triphenylphosphine to effect the rupture of the tertiary carbon-oxygen bond. The tentative mechanism of this reaction is presented:



Intermediacy of a tertiary carbocation not readily accessible for nucleophilic attack seems to be responsible for triphenylphosphine oxide elimination rather than formation of a carbon-iodine bond according to S_N2 mechanism.[2] This interpretation is supported by the reaction of spiro-[5α-cholestane-3,2'-oxiran] (Table, entry 9). This epoxide, which on opening of the oxirane ring can possibly form a tertiary carbocation, also gives the product of oxygen elimination, albeit in lower yield (28%), most probably due to the competitive nucleophilic attack of iodide anion on primary carbocation.

Examination of the title reaction of 8α,9α- and 9α,11α-epoxylanostane derivatives revealed (Table, entry 10 and 11), however, that in these two cases 3β-acetoxy-5α-lanosta-7,9(11)-diene[14] was formed as the only product. This result resembles the ready conversion of these epoxides to the 7,9(11)-diene upon treatment with various electrophilic reagents.[14,15] In these examples it can be assumed that opening of the oxirane ring similarly occurs with initial formation of a tertiary carbocation, which undergoes rearrangement and elimination to the diene:



It would be expected, that opposite opening of the oxirane ring in 3β-acetoxy-9α,11α-epoxy-5α-lanostane, for example, should give either the respective iodohydrin i.e. 3β-acetoxy-11β-iodo-5α-lanostan-9α-ol or the 9,11-olefin instead of the diene.

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