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MERCURY SALTS AS INITIATORS FOR ELECTROPHILIC CYCLIZATION OF ISOPRENOIDS

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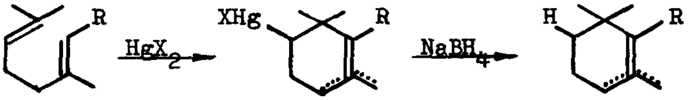
In the course of systematic investigation of the isoprenoid cyclization reaction under the action of "external" electrophiles such as H^+ (see, for instance [1]) and acyl- or alkyl-cations generated from complexes of type $R^+ BF_4^-$ [2], our attention was turned to electrophilic mercury salts.

As was anticipated the interaction of $Hg(OCOCH_3)_2$ with isopenoid compounds did not lead to the formation of cyclic compounds. Since the use of such mercury salts as $Hg(OCOCF_3)_2$ or $Hg(NO_3)_2$ in solvomercuration reactions is well-documented for many examples [3], we tried these salts as initiators of electrophylic cyclization. We examined the interaction of these salts with isoprenoid compounds of different structure and found that in all cases the main course of the reaction can be represented schematically as follows [4]



The intermediate organo mercurials were immediately reduced by $NaBH_4$ and no attempt was made to isolate them. In general the reaction was carried out by the addition of 1,2-2,0 equivalents of HgX_2 [5] in CH_3NO_2 or CH_3CN to the solution of isoprenoid compound at temperatures of -20°C to 0°C. After 5-30 min the reaction mixture was treated with the solution of two equivalents of $NaBH_4$ in 3M NaOH solution at 0° for 30 min. The products were then isolated as usual and indentified by g.l.c. and n.m.r. comparison with auten-

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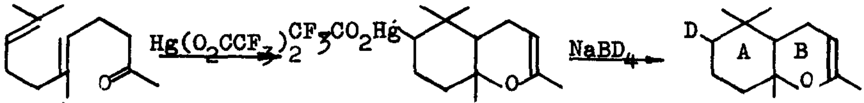
tical samples. The results are summarised in the table I.

Table I

No	Starting compound	$Hg(CF_3COO)_2$ (moles) per 1 mole of starting compound.	Solvent	Ml of solvent per 1 g of starting compound	t °C	Time of reaction, min.	Yield of cyclic product % •)
1.	trans-Geranylacetone (Ia)	1,2	CH_3NO_2	5	-20	10	62
2.	cis-Geranylacetone (Ib)	-"-	-"-	5	-20	10	65
3.	trans-Geranylacetone ethyleneketal (VI)	1,5	CH_3CN	8	-20	5	65
4.	cis-Geranylacetone ethyleneketal (IV)	-"-	-"-	8	-20	5	60
5.	Geranic acid Meester (mixtur of cis- and trans-isomers)	2,0	CH_3NO_2	8	0	30	30
6.	trans-6,7-trans-10,11-Farnesylic acid, Et-ester	1,2	CH_3NO_2	8	0	30	60

•) Yields are given for isolated products.

As can be seen geranylacetone (I) under the condition mentioned above gives rise to 2,5,5,9-tetramethylhexahydrochromene (III) with a good yield. This reaction was shown to proceed in stereospecific manner and the trans-fused product (IIIa) is formed from trans-Ia whereas cis-IIIb is formed from cis-Ib as it was found earlier for the acid-catalysed reaction [6].

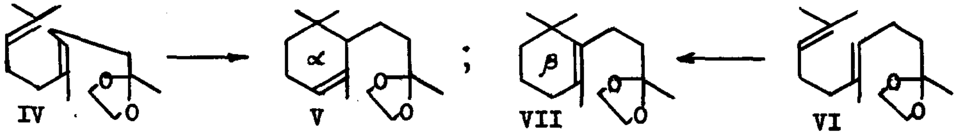


I a) trans-6,7 II III a) trans-A/B

b) cis-6,7 b) cis-A/B

Reduction of II with $NaBD_4$ resulted in the product III shown above which contained one D-atom (mass-spectrum), and proved to be identical to the sample obtained by the cyclization of I with D_2SO_4 [7]. The fragmentation patterns of the samples under electron impact were identical and indicated the presence of a D-atom in the ring A of III. This fact is consistent with the reaction scheme shown above.

Examples No3 and 4 in table I show the advantages of the proposed cyclization method, its mildness allowing operation with acid-labile protecting groups. It is worthwhile to note that the preferential formation of α-dihydroionone derivatives (V) from the cis-isomer (IV) and β-dihydroionone derivatives (VI) from the trans-isomer (VII) correspounds to the stereochemistry of the acid-catalysed cyclization reported earlier [8].



The cyclization of geranic ester (mixture of cis + trans isomers) under the conditions described proceeded less successfully, giving only 30% of α-cyclogeranic ester [9] after 30 min. at 0°C. As much as 46% of the reaction mixture was the starting geranic ester and 24% comprised of an unknown substance which had a retention time substantially higher than that of geranic ester (both isomers) and the α- or β-cyclogeranic ester. This result probably reflects the comparatively low reactivity (for electrophylic attack) of a conjugated 6,7-double bond. At the same time the cyclization of trans-6,7-, trans-10,11-farnesylic ester proceeds quite smoothly, giving, as in the case of H^+-promoted cyclization [10], trans-α-bicyclofarnesylic ester with equatorial orientation of the COOR-group. The cyclization of other isomers of farnesilic ester proceeds in a different manner and demands more thorough investigation.

Thus the proposed method of the cyclization of isoprenoid compounds under the action of electrophylic mercury salts appears to have general applicability. Because of its mildness this procedure might prove to be the method of choice for the cyclization of complex molecules. One may also expect the increased structural selectivity of mercury-induced cyclization due to the higher steric demands of mercury-cations in comparison with proton . An additional interesting feature of the reported reaction is connected with the possibility of substitution of theXHg-group in the intermediate organo mercurial for another one (i.e. Br).

Further studies of the scope and limitation of the method, its mechanism and preparative applications are in progress in this laboratory.

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