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HOMOALLYLIC INTERACTION IN STEROIDAL CYCLODECENYL SYSTEMS[1]

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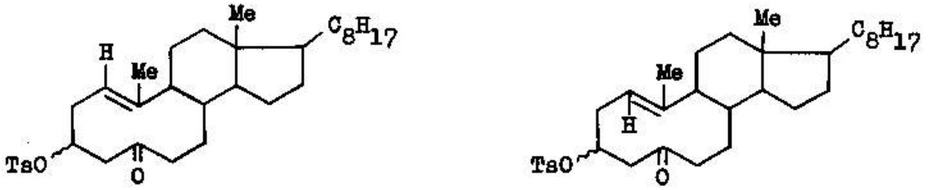
In continuation of our studies on the structure-reactivity relationship in medium-sized rings forming part of steroidal systems, we have now investigated the homoallylic interaction in the course of solvolysis of the configurationally and conformationally different (Z)-3α- and (Z)-3β- and (E)-3α- and (E)-3β-tosyloxy-5,10-seco-1(10)-cholesten-5-ones (Ia-Id, Figure 1).[**] The different degree of π-participation in the solvolysis of the four diastereomeric



Ia (Z)-3α-OTs
Ib (Z)-3β-OTs

Ic (E)-3α-OTs
Id (E)-3β-OTs

Figure 1

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[**] The affixes (Z) and (E) correspond to the *cis*- and *trans*-configuration, respectively, of the system (1)C-H/(10)C-(19)CH_3 around the 1(10)-double bond.[2]

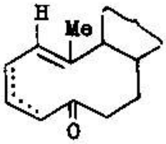
1(10)-unsaturated 3-tosylates should reflect the difference in the spatial orientation of the reacting centers and might therefore provide useful information regarding the conformations of the ten-membered ring system examined, in both ground state and transistion state.[3]

The solvolysis of the esters Ia-Id was carried out in acetone-water (90:10 v/v) solution at 80° and 90°, in the presence of one molar equivalent of sodium acetate. The results are summarized in Table 1.

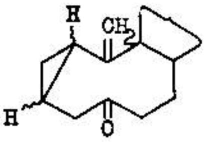
Table 1

Compound	$\underline{T}$ (°C)	$\underline{k}_1$ (sec^{-1})	$\Delta\underline{H}$ (kcal/mol)	$\Delta\underline{S}$ (eu)
Ia ($\underline{Z}$)-3α	80°	1.22×10^{-4}	20.4	-18.2
	90°	2.83×10^{-4}		
Ib ($\underline{Z}$)-3β	80°	very slow reaction		
	90°			
Ic ($\underline{E}$)-3α	80°	4.00×10^{-4}	19.8	-18.3
	90°	8.93×10^{-4}		
Id ($\underline{E}$)-3β	80°	1.07×10^{-3}	18.5	-20.0
	90°	2.26×10^{-3}		

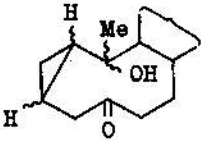
For the esters Ia, Ic and Id first order rate constants were obtained, the relative rates at 90° being approximately 1:3:8, while the kinetic data for the ester Ib, which reacted very slowly, indicate that solvolysis proceeds by a mixed mechanism. Assuming similar ground state energies for all four isomeric compounds, the rate enhancement observed in the reaction of the tosylates Ia, Ic and Id, as compared to the tosylate Ib, may be attributed to an increase of π-participation in the former three esters. These results were further substantiated by product analysis, the [7.1.0]-cyclopropane derivatives being formed only when intramolecular displacement was strongly favoured due to proximity and orientational factors, i.e. in both ($\underline{E}$)-isomers. Partial structures of the solvolysis products[4] are presented in Figure 2.



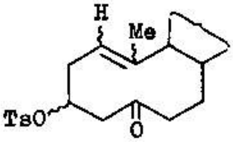
II



IIIe 3α-H
IIIf 3β-H



IVe 3α-H
IVf 3β-H



Va (Z)-3α-OAc, VIa (Z)-3α-OH
Vb (Z)-3β-OAc, VIb (Z)-3β-OH
Vd (E)-3β-OAc, VIc (E)-3α-OH
VId (E)-3β-OH

Figure 2

Thus, the (E)-3β-tosylate Id solvolyses to give the cyclopropane derivatives IIIe (32%) and IVe (2%) (which can be dehydrated to IIIe), and, with retention of configuration at C-3, the acetate Vd (35%) and alcohol VId (30%). The solvolysis of the (E)-3α-tosylate Ic also proceeds with cyclopropane ring formation, affording the 10-hydroxy product IVf in 64% yield. However, in contrast to the epimeric 3β-tosylate Id, in this case stabilization is taking place by nucleophilic substitution at C-10 rather than elimination, probably due to the greater accessibility of the configurationally different homoallylic cation intermediate.[*] The only other product formed in this reaction is the alcohol VIc with unchanged configuration at C-3 (34% yield). The

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[*] The fact that product IVf is smoothly dehydrated to the isomeric cyclopropane derivative IIIf, which is configurationally different from the isomeric cyclopropane IIIe, allows a safe assumption that both IVf and IIIe are formed from the corresponding substrates Ic and Id, respectively, by intramolecular displacement with inversion at C-3.

(Z)-3α-tosyl ester Ia solvolyses to give the following products: a mixture of two elimination products, i.e. the 1(10),2- and 1(10),3-dienones II (overall yield 4%), about 90% of the hydroxy compound VIa with unchanged configuration at C-3, and only 2% of the epimeric alcohol VIb with the 3β-configuration. The (Z)-3β-tosyl ester Ib, under the same reaction conditions, affords several products: the same mixture of the two elimination products II as found in the solvolysis of Ia (overall yield of 64%), a 1:4 mixture of 3α- and 3β-acetates Va and Vb (overall yield 20%), and a 1:1.5 mixture of 3α- and 3β-alcohols VIa and VIb (overall yield 7.5%). In the last case the reaction is very slow and probably proceeds without homoallylic assistance.

The results obtained in this study are in accordance with our earlier findings regarding the conformations and reactivity of 5,10-seco-steroid derivatives.[1] A detailed presentation of all stereochemical features of these reactions, particularly with respect to conformational analysis of the cyclopropane-containing products, will be published elsewhere.

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REFERENCES

1. Part X in the series "Synthesis, structure and reactions of seco-steroids containing a medium-sized ring". For part IX see: M. Lj. Mihailović, Lj. Lorenc, Z. Maksimović, and J. Kalvoda, Tetrahedron, **29**, 2583 (1973).
2. IUPAC Information Bull., **35**, 36 (1969).
3. For leading references on stereoelectronic requirements in homoallylic interaction see: P. D. Bartlett, "Nonclassical Ions", W. A. Benjamin, Inc. New York (1965), Papers 8, 22, 40, 51. See also: (a) M. Gašić, D. Whalen, B. Johnson, and S. Winstein, J. Amer. Chem. Soc., **89**, 6382 (1967); (b) D. Whalen, M. Gašić, B. Johnson, H. Jones, and S. Winstein, ibid., **89**, 6384 (1967); C. D. Poulter and S. Winstein, ibid., **92**, 4282 (1970), and references cited therein.
4. Satisfactory elemental analyses and physical data were obtained for all new compounds.