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TRANSANNULAR SOLVOLYSIS REACTIONS IN SECO-STEROIDS CONTAINING A TEN-MEMBERED RING (1).

M. Lj. Mihailović *, M. Dabović, Lj. Lorenc and M. Gašić

Department of Chemistry, Faculty of Sciences, University
of Belgrade and Institute for Chemistry, Technology and
Metallurgy, Belgrade, Yugoslavia

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5,10-Seco-steroids containing a ten-membered ring (2) (instead of the two fused six-membered rings A and B) (e.g. I and II on Scheme 1) represent a suitable substrate for the study of transannular reactivity in a medium-sized ring system, because of the relative rigidity of the general steroid framework still present. In view of the limited data available in the literature (1,2,3), the investigation of the solvolytic behaviour of such systems seemed to be of particular interest.

It was reported previously that the solvolysis of *cis*- and *trans*-5-cyclodecen-1-yl *p*-nitrobenzoates is accompanied by substantial double bond participation (4). A similar anchimeric assistance has now also been observed in the solvolysis of both

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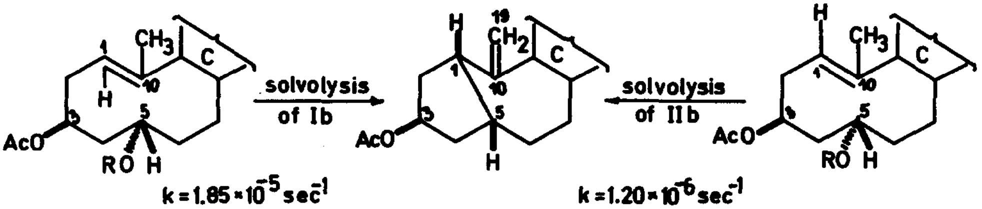
* Correspondence to: Department of Chemistry, Faculty of Sciences, Studentski Trg 16, P.O. Box 550, Belgrade, Yugoslavia

isomeric *trans*- and *cis*-3β-acetoxy-5,10-seco-1(10)-cholesten-5*S*-yl *p*-nitrobenzoates, (Ib) and (IIb), respectively (Scheme 1) [*].

Scheme 1



trans
(I)

(III)

cis
(II)

(a) R = H
(b) R = PNB (*p*-nitrobenzoate)
(c) R = Ac

The solvolysis of (Ib) and (IIb) was carried out in 90% aqueous acetone at 125°, and in both cases the only product isolated (in over 90% yield) was the compound formed by transannular cyclization, namely 5(10→1βH)*abeo*-5β-cholest-10(19)-en-3β-ol acetate (III) (1); no substitution by solvent or elimination at C-5 could be detected [**]. By kinetic measurements, first order rate constants for both (Ib) and (IIb) were obtained, the values being 1.85×10^{-5} sec^{-1} for the *trans*-isomer (Ib) and 1.20×10^{-6} sec^{-1} for the *cis*-isomer (IIb). The *p*-nitrobenzoate of the 1,10-saturated alcohol, obtained by catalytic hydrogenation of the 1,10-*trans*-unsaturated alcohol (Ia), solvolyses at a rate of $k \sim 10^{-9}$ sec^{-1}. These results indicate a considerable degree of

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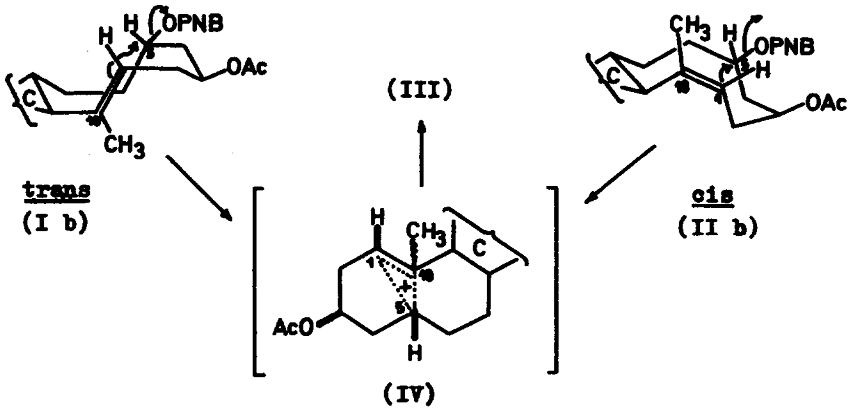
[*] Definite proof of configuration at C-5 for compounds (I) and (II) could not be obtained. However, spectral and other evidence (1) suggest the configurations shown in Scheme 1. Moreover, photochemical double bond isomerisation of the parent alcohols in the form of their 3,5-diacetates (IIc $\xrightarrow{h\nu}$ Ic) indicates that (Ib) and (IIb) have the same configuration at C-5.

[**] The corresponding C-5 tosylates of (Ia) and (IIa) are too reactive to be isolated, and in the course of their preparation they are transformed into the cyclization product (III).

anchimeric assistance in the former two cases, the relative rates being 18500 (Ib):1200 (IIb):1 (PNB of the 1,10-saturated alcohol). The relatively small difference in the solvolytic reactivity of (Ib) and (IIb) (factor of about 15 in favour of the *trans*-isomer Ib), as compared to that of the "free" cyclodecenyl system (factor of about 300) (4), can be rationalized by inspection of Dreiding models, on the basis of conformational factors (Scheme 2). Namely, in the *cis*-isomer (IIb) the unchanged part of the steroid framework and the substituents "lock" the ten-membered ring in such a way as to provide more anchimeric assistance, whereas, on the other hand, this effect should be somewhat retarded in the solvolysis of the *trans*-isomer (Ib), since maximum π-overlap during the reaction is possible only if the molecules take an energetically less favourable conformation than that which is believed to be the preferred one for such *trans*-unsaturated 5,10-seco-steroid systems (1). The probable conformations of (Ib) and (IIb) in the course of the solvolytic reaction and the pathways leading to the formation of the same cyclization product (III) from either of the isomers are shown on Scheme 2.

Scheme 2



Although on the basis of experimental data available so far it is not possible to present a precise picture of the structure of the reaction intermediate(s), it seems reasonable to assume that, due to the presence of the methyl group attached to C-10 of the double bond (in Ib and IIb), an unsymmetrical distribution of the positive charge at the three reacting centers C-1, C-5 and C-10 (i.e. structure (IV) on Scheme 2, with most of the positive charge at C-10) occurs in the rate determining step; the reaction pathway thus leads to the consecutive formation of the tertiary carbonium ion at C-10, which further undergoes hydrogen elimination yielding (III) as the sole transannular solvolytic product.

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