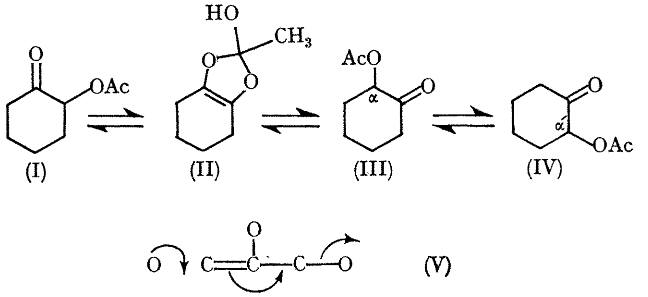
Degenerate Rearrangement of Acyloxycycloalkanones

By IRIS S.-Y. WANG and E. W. WARNHOFF*

(*Department of Chemistry, University of Western Ontario, London, Ontario, Canada*)

Summary Secondary α-ketol acetates in the presence of acetic acid–acetate ion or acetic acid alone undergo two reactions: (a) interchange of the functional groups at *ca.* 150° and (b) transfer of the acetate from the α- to the α′-position of the ketone at *ca.* 220°.

As the result of a re-investigation of the long known transformation of 2α-bromo-3-oxo-steroids into Δ^5-4-oxo-steroids in the presence of acetic acid and acetate ion,[1] we have encountered a hitherto unrecognised, and potentially useful, general reaction of secondary α-ketol acetates. When these compounds are heated in the presence of carboxylic acids with or without carboxylate ion, a rearrangement occurs in two stages. At *ca.* 150° *interchange* of the acyloxy and ketone functions occurs, presumably *via* an enediol intermediate[2] (*e.g.* I ⇄ II ⇄ III), and at a higher temperature (220—240°) *transfer* of acylate from the α- to the α′-position of the ketone (*e.g.* III ⇄ IV) takes place. The simultaneous operation of these two processes in unsubstituted acetoxycycloalkanones causes the ketone and acetate groups to pirouette around the carbocyclic ring in a degenerate rearrangement which is readily revealed by deuterium exchange since every hydrogen atom eventually



TABLE

$OC\cdot[CH_2]_{n-2}\cdot CHOAc$	Temp.	Time, hr.	$\overset{+}{OC\cdot[CH_2]_{n-2}CHO}$ $d_{no.D}$ (% of ions)†
$n=6$	220°	14	d_{12} (32), d_{11} (37), d_{10} (22), d_9 (6), d_8 (1·5)‡
7	240°	20	d_{11} (1·4), d_{10} (2·5), d_9 (4·8), d_8 (8), d_7 (16), d_6 (13), d_5 (31), d_4 (18), d_3 (4·7)
8	240°	24	d_7 (5), d_6 (3), d_5 (50), d_4 (27), d_3 (7)
9	240°	40	d_{14} (0·5), d_{13} (1), d_{12} (1), d_{11} (3·8), d_{10} (3·4), d_9 (13·5), d_8 (9·8), d_7 (25), d_6 (14), d_5 (12), d_4 (5), d_3 (2·7), d_2 (1·5)
12	240°	57	d_{21} (10), d_{20} (16), d_{19} (15), d_{18} (11), d_{17} (11), d_{16} (8), d_{15} (8), d_{14} (7), d_{13} (6)

† D analyses by mass spectroscopy. The subscripts refer to the number of D atoms in the $M-43$ ion shown.

‡ Molecular ion used for D analysis for $n = 6$.

becomes labile after successive rearrangements. The results of heating a series of cyclic ketol acetates with [$^2H_4$]acetic acid and [$^2H_3$]acetate in sealed tubes are given in the Table.

The various possible mechanisms for the transfer reaction are in essence intra- or inter-molecular allylic rearrangements of an enolic intermediate (in general terms, V). All of these mechanisms require three adjacent carbon atoms of the ring (α-C, C=O, α'-C) to approach trigonal hybridisation at the transition state, and the ease of deuteriation in this series of ketones correlates generally with the ease of introduction of three adjacent trigonal centres into carbocycles.[3] Whether the correlation is the result solely of the changing rate of the transfer reaction ($6 > 7 > 8 < 9 < 12$), or whether the acetoxy-ketone is drained off into the side-reaction products for $n = 7$, 8, and 9 is not yet established. When acetoxycyclohexanone is rearranged in propionic acid, the acetate group is exchanged for propionate at the temperature required for the transfer reaction, and hence it is not known whether the transfer reaction is intra- or inter-molecular. The transfer reaction may be related to two recently described acyloxy-rearrangements.[4,5] If the complete rearrangement cycle is blocked by a tertiary carbon atom in the ring, the ketol acetate is diverted mainly to $\alpha\beta$-unsaturated ketone by elimination at the tertiary position when it becomes adjacent to the keto-group in the course of rearrangement.

Suitable application of this two-stage rearrangement should prove useful in the preparation of deuterium and carbon labelled cyclic compounds.

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