Acid-catalysed Rearrangement of Derivatives of Blocked 2-Oxocycloheptaneacetic Acids to Spiro-αβ-butenolides

By BRYAN W. ROBERTS*

(*Department of Chemistry, University of Pennsylvania, Philadephia, Pennsylvania* 19104)

and STEVEN C. WELCH and DOUGLAS A. STEED

(*Department of Chemistry, University of Southern California, Los Angeles, California* 90007)

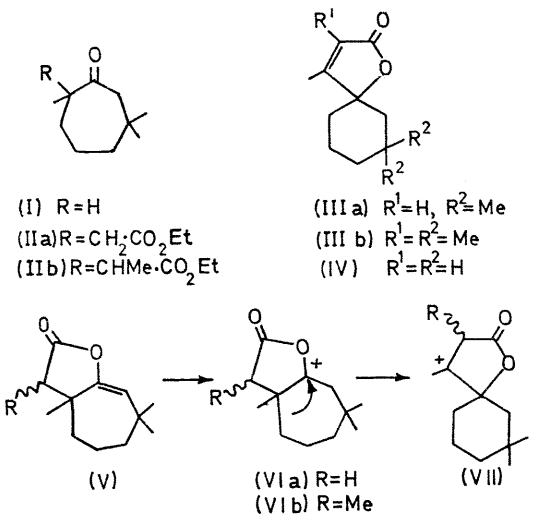
Summary Derivatives of some blocked 2-oxocycloheptaneacetic acids have been found to rearrange on treatment with boron trifluoride etherate, acetic acid, and acetic anhydride to spiro-αβ-butenolides.

RECENTLY we explored a synthetic route to sesquiterpenes related to longifolene and longiborneol, the first stage of which called for construction of an intermediate bicyclo-[4,2,1]nonane appropriately substituted for introduction of remaining skeletal features and functionality of the desired natural product.[1] Toward this end, the keto-ester (IIa), which was prepared by base-catalysed alkylation of tetrahydroeucarvone (I)[2] with ethyl bromoacetate,† was treated with a mixture of boron trifluoride etherate, acetic acid, and acetic anhydride at 85—100° for 18—24 hr. in an attempt to induce intramolecular acylation[3] to the requisite bicyclic intermediate. While the reaction was disappointing in affording none of the desired product, it did produce in yields of up to 90% a crystalline material, m.p. 63—64°, which we have identified as spiro-αβ-butenolide (IIIa) on the basis of the following evidence.

Compositional and mass spectral analyses indicated the molecular formula $C_{12}H_{18}O_2$. I.r. [λ_{max} ($CHCl_3$) 5·75(s) and 6·06 μm.(m)] and n.m.r. spectra (relative to Me_4Si) [δ (CCl_4) 0·94(s,3H), 1·10 (s,3H), 1·25—1·90 (m, 8H), 2·01(d, 3H, *J* 1·6 c./sec.), and 5·61 (q, 1H, *J* 1·6 c./sec.)] revealed the presence of an olefinic bond of the type ·MeC:CH·, a carbonyl group, and two nonequivalent quaternary methyl groups. This information, together with consideration of reasonable reaction paths open to keto-ester (IIa) under the

† An extensive study of base-catalysed alkylation and acylation of tetrahydroeucarvone has shown that substitution takes place exclusively at the α-methine position as shown by formation in all cases of a single product exhibiting in its n.m.r. spectrum an AB quartet for methylene protons α to the ketone carbonyl group. A similar quartet appears in the spectrum of tetrahydroeucarvone. S. C. Welch and B. W. Roberts, unpublished results.

reaction conditions (*vide infra*), immediately pointed toward spirobutenolide (IIIa) as the product. Further evidence strongly supported this assignment. Thus, the u.v. spectrum of our material [λ_{max} (95% EtOH) 211 nm. (ϵ 13,200)] was essentially identical with that of spirobutenolide (IV) recently prepared by Lehmann [λ_{max} (EtOH) 211 nm. (ϵ 13,300)].[4] Also, chemical degradation of the supposed butenolide functionality by sequential treatment with ozone, lithium aluminium hydride, and lead tetra-acetate afforded 3,3-dimethylcyclohexanone, which was identified by comparison with an authentic sample.[5] The latter result proved that ring contraction had occurred and established the nature of the carbocyclic portion of the compound.



Analogous results were obtained with keto-ester (IIb), which was available *via* base-catalysed alkylation of tetrahydroeucarvone (I) with ethyl α-bromopropionate. Treatment of (IIb) under conditions comparable to those used for rearrangement of (IIa) produced spirobutenolide (IIIb) as a colourless oil in 37% yield. Interestingly, the n.m.r. spectrum of this material revealed homoallylic coupling[6] of about 0·8 c./sec. within the *cis*-but-2-ene moiety. Other spectral data were in complete accord with the assigned structure.

Rearrangement of keto-esters (IIa) and (IIb) probably proceeds through the derived enol-lactones (V) and thence *via* protonation, 1,2-shift, and deprotonation (V→VI→VII) to the observed products. Consistent with this hypothesis is the fact that subjection of independently prepared enol-lactones (Va) and Vb) to rearrangement conditions led to (IVa) and (IVb) in yields of 85% and 62%, respectively. The results thus show that within the sequence of interconversions relating a γ-keto-acid or ester with its derived αβ- and βγ-butenolides and γδ-enollactone, a 1,2-shift may take place when β-proton loss is impossible.

We thank the National Institute of General Medical Sciences of the Public Health Service for financial support of this research. S.C.W. acknowledges fellowship and traineeship support from the National Science Foundation and the National Institutes of Health.

(*Received, March* 31*st*, 1969; *Com.* 464.)

[1] For example, culmorin: D. H. R. Barton and N. H. Werstiuk, *J. Chem. Soc.* (C), 1968, 148; and longicyclene: U. R. Nayak and S. Dev, *Tetrahedron*, 1968, **24**, 4099.
[2] O. Wallach, *Annalen*, 1911, **381**, 51; Y. Naves and P. Ardizio, *Helv. Chim. Acta*, 1949, **32**, 329.
[3] C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, 1954, **8**, ch. 3.
[4] H. G. Lehmann, *Angew. Chem.*, 1965, **77**, 808; H. G. Lehmann, *Ger. P.*, 1,218,440 (1966); *Chem. Abs.*, 1966, **65**, 7250.
[5] H. O. House and W. L. Fischer, *J. Org. Chem.*, 1968, **33**, 949.
[6] R. K. Harris and B. R. Howes, *J. Mol. Spectroscopy*, 1968, **28**, 191.