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HOMOKETONIZATION IN A HOMOCUBANE SYSTEM

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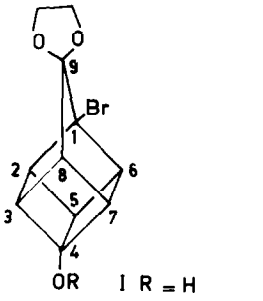
We wish to report a base-catalyzed transformation of a homocubane bridgehead alcohol (I) and its acetate (II) to the half-cage ketone III.

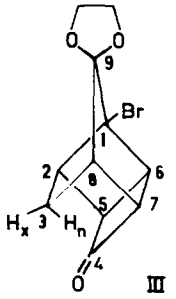
Treatment of the acetate[1] II with sodium methoxide (0.2 M) in methanol at room temperature for one hour gave a ketone, mp 75.5-77°, in almost quantitative yield. No trace of the alcohol[1] I which would be expected in a transesterification reaction[2], could be detected. The bridgehead alcohol I gave upon treatment with sodium methoxide in methanol in a fast reaction (5 min.) the same ketone. The isolated product[3] was isomeric with the alcohol I. On basis of spectral evidence described below structure III was assigned to the ketone. Apparently, exclusive cleavage of the C_3-C_4 bond (or the equivalent C_4-C_7 bond) has taken place, while scission of the C_4-C_5 bond to ketone IV does not occur.

This formation of the half-cage ketone III represents a new example of a homoketonization[4] reaction in a strained system.

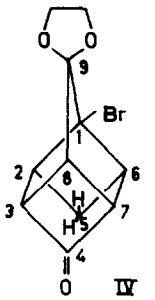


I R = H

II R = $-\overset{\overset{O}{\|}}{C}CH_3$



III



IV

The IR spectrum of III shows a carbonyl absorption at 1765 cm^{-1} which is typical for a cyclobutanone. The PMR spectrum in C_6D_6[5] displays an absorption for one proton as a doublet of doublets (one half of an AB pattern) centered at δ 1.30 ppm attributed to the carbonyl shielded proton[6] H_n, coupled with H_x ($J \sim 13$ Hz) and H_2 ($J \sim 2$ Hz). The coupling with H_8 is probably close to zero since the dihedral angle as shown in models is about 90°. The lowfield half of the AB pattern for H_x appears as a broad multiplet centered at δ 2.1 ppm. This absorption coincides with that of H_8. The ethylene ketal protons at C_9 appear as an unsymmetrical multiplet between δ 3.41 and 4.0 ppm. The bridgehead protons H_5 and H_7 absorb[7] as a complex multiplet at δ 2.4-3.0; H_2 and H_6 are found as a multiplet at δ 3.10-3.40 ppm.

This PMR spectrum is consistent with structure III but not with that of IV since: i. for the endo proton H_n in IV a doublet of triplets resulting from coupling with H_x and the equivalent protons H_2 and H_6, would be expected, ii. in the symmetrical ketone IV the ethylene ketal protons are expected[8] to appear as a symmetrical AA'BB' absorption, iii. the upfield shift for H_8 as compared[1] with Ia is in accordance with the relief of strain around C_8 in III (in IV the congestion around C_8 has hardly changed).

Treatment of II with sodium methoxide in CH_3OD gave the monodeuterated ketone III in quantitative yield. The PMR spectrum of this product showed the unchanged signals of the ketal group and the bridgehead protons H_2, H_5, H_6 and H_7, the absence of the AB pattern at δ 1.3 and a simplified two proton absorption for H_x and H_8 at $\delta \sim 2.1$ ppm. Thus, the endo proton H_n has been replaced by deuterium. Treatment of ketone III with sodium methoxide in CH_3OD at room temperature for 24 hrs or at 60° for 8 hrs did not lead to any H/D exchange in III. Therefore, we may conclude that the homoketonization process proceeds with a high stereospecificity (> 96%) introducing a hydrogen (or D) exclusively in the endo position.

The homoketonization is initiated by base giving the alkoxide anion of I. This homoenolate anion then ketonizes by C-C bond cleavage and stereospecific proton capture. Molecular models suggest that ketone III is less

strained than IV. We propose that because of the greater relief of strain homoketonization proceeds preferably in the direction of the least strained ketone III. Also for birdcage alcohols predominant formation of the least congested half-cage ketone was observed.[4c]

In our case proton uptake occurs specifically from the endo side (virtual retention of configuration at C_3, Fig. 1), whereas for the homoketonization of 1-hydroxynortricyclene[4b] in alkaline media stereospecific exo protonation was found (inversion of configuration at C_6, Fig. 2).

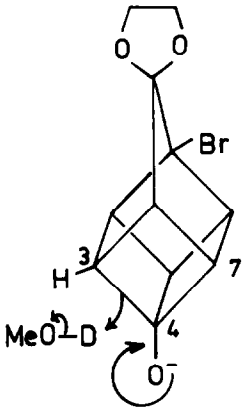


Fig. 1

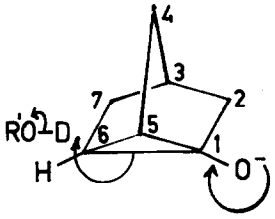


Fig. 2

Factors that govern the differences in these mechanisms require a more detailed study. The steric influence of the ethylene ketal group might play a role in the approach of a methanol molecule, as is suggested by molecular models.

Further studies on homoketonization and homoenolization in the homocubane and similar cage compounds are in progress.

REFERENCES AND NOTES

1. B. Zwanenburg and A.J.H. Klunder, Tetrahedron Letters 1971, preceding paper.
2. With ethanol/HCl a normal transesterification takes place, see ref. 1.
3. The product gave a correct elemental analysis for C, H and Br.

4. β-Homoketonization of 1-hydroxynortricyclene to norbornan-2-one: a. A. Nickon, J.H. Hammons, J.L. Lambert and R.O. Williams, J. Amer. Chem. Soc., 85, 3713 (1963); b. A. Nickon, J.L. Lambert, R.O. Williams and N.H. Werstiuk, ibid., 88, 3354 (1966); γ-homoketonization of birdcage alcohols: c. R. Howe and S. Winstein, ibid., 87, 915 (1965); d. T. Fukunaga, ibid., 87, 916 (1965).
5. The PMR spectrum in $CDCl_3$ has a similar pattern.
6. Cf. the inside proton absorption in half-birdcage ketones, ref. 4c and 4d.
7. In cage compounds protons at positions α to the carbonyl group appear at higher field than the main cage protons. R.J. Stedman and L.D. Davis, Tetrahedron Letters, 1968, 1871; G.L. Dunn, V.J. DiPasquo and J.R.E. Hoover, ibid., 1966, 3737; N.B. Chapman, J.M. Key and K.J. Toyne, J. Org. Chem., 35, 3860 (1970). Apparently, this is also true for a half-cage ketone.
8. However, when a symmetrical absorption is observed it does not necessarily imply that the ketal containing compound has a plain of symmetry. See for instance N.B. Chapman, J.M. Key and K.J. Toyne, Tetrahedron Letters, 1970, 5211.