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SOME REACTIONS OF 2-AZA- AND 2-OXA-BICYCLO[2,1,1]HEXANES

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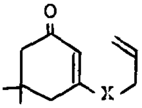
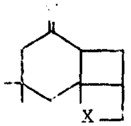
In an earlier communication[1] we reported the first example of a photochemical generation of 2-aza- and 2-oxa-bicyclo[2,1,1]hexane derivatives (IIIa and IV) from 3-allylamino- and 3-allyloxy-cyclohex-2-enones (I and II). The structural assignment of IIIa and IV was made mainly on the basis of the spectral evidence, which does not absolutely eliminate the alternative ring systems III' and IV'. To obtain further support for the ring structure and stereochemistry of these photoproducts, and to explore the chemistry of these new classes of heterocycles, we have investigated the chemical behavior of IIIa and IV.

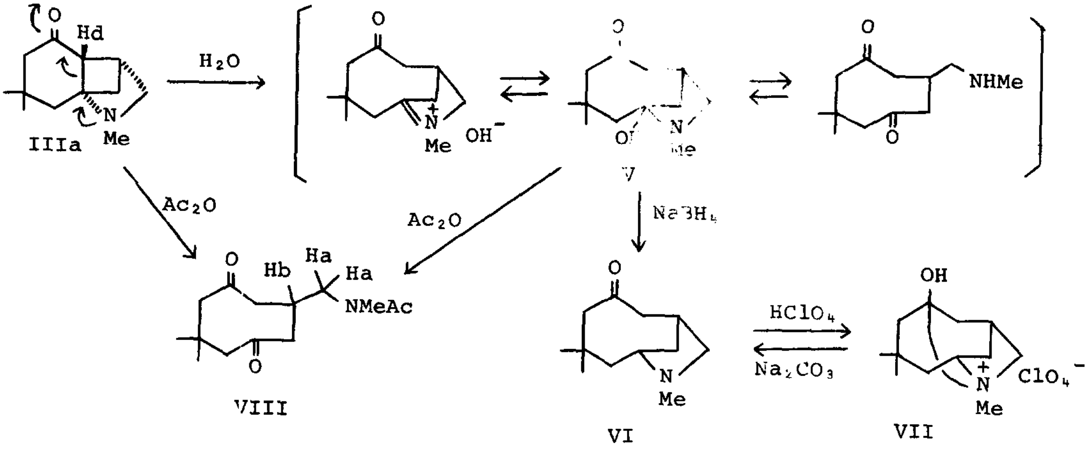
2-Azabicyclo[2,1,1]hexane derivative IIIa was found to be very labile in a protic solvent such as water, although it is stable in refluxing toluene. Thus, on refluxing in water IIIa yielded a crystalline compound, mp 79.5-80.5°, in 94% yield. On the basis of the elemental analysis and spectral data, taken along with the following chemical evidence, this compound was shown to exist in tautomeric forms (V).[2] Reduction of V with sodium borohydride afforded a new aminoketone, VI, mp 61-62°, [ir($CHCl_3$) 1680 cm^{-1}], which formed the perchlorate (VII), mp 280° (decomp). The ir spectrum of VII shows no carbonyl absorption, indicating the occurrence of a transannular cyclization reaction between the nitrogen and the carbonyl group.[3] Acetylation of V with acetic anhydride gave the N-acetate VIII, mp 130° [ir($CHCl_3$) 1700, 1640 cm^{-1}; Mass m/e 253 (2%, M^+), 86 (100%, $CH_2=N^+(CH_3)COCH_3$)]. Later this compound was found to be formed directly from IIIa upon treatment with acetic anhydride. The N-acetate under-

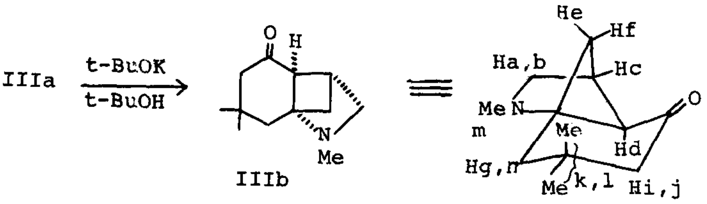


I, X=NMe
II, X=O



III', X=NMe
IV', X=O



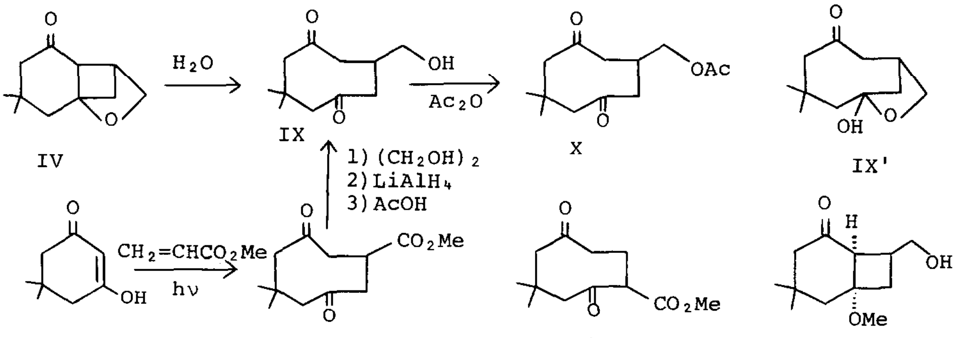


went facile incorporation of deuterium atoms α to the carbonyl group upon heating with deuterium oxide in the presence of sodium deuteroxide (the reaction was monitored by nmr spectroscopy), and a doublet at τ 6.65 ($J_{Ha,Hb}$=7 Hz) ascribable to Ha proton remained unchanged, in accordance with structure VIII. These results could establish the structure of IIIa except for the stereochemistry of Hd proton.

Treatment of IIIa with potassium t-butoxide in t-butanol gave an oily new basic substance (IIIb) [its hydrochloride, mp 139-140°], shown to be epimeric with IIIa on the basis of the following spectral [ir($CHCl_3$) 1705 cm^{-1}] and chemical evidence. Comparison of the nmr spectrum of IIIb (100 Mc, $CDCl_3$) with that of IIIa and decoupling experiments permitted the following assignment of the nmr signals; Ha or Hb (split doublet, τ 7.07), Hb or Ha (split doublet, τ 7.50), Hc (doublet, τ 7.03), Hd (doublet, τ 7.60), He (triplet, τ 8.51), Hf (multiplet, τ 8.16), Hg,h (AB quartet centered at τ 8.29), Hi,j (AB quartet centered at τ 7.85), Hk,l (two singlets, τ 8.87 and 8.94), Hm (singlet, τ 7.62); Jef=8.5 Hz, Jed=8.5 Hz, Jab=8 Hz, Jcf=3 Hz, Jgh=14 Hz, Jij=13.5 Hz. The long-range coupling constant between He and Hd (J=8.5 Hz; the corresponding coupling was not observed in the nmr spectrum of IIIa[1]) is consistent with that reported for bicyclo[2,1,1]hexanes.[4] Moreover, IIIb was transformed to V and VIII on treatment with water and acetic anhydride, respectively. The above data support the exo configuration of Hd proton in the photoproduct IIIa.

Previously the irradiation of II was shown to produce an inseparable mixture of two compounds in a ratio of ca. 4:1 and the major component was tentatively assigned structure IV on the basis of spectral comparison with IIIa.[1] The chemical evidence presented below firmly confirmed the proposed structure IV to be correct.

On gentle warming in water the mixture of the photoproduct provided 53% yield of a ketoalcohol, IX,[5] mp 110-111° [ir(CHCl$_3$) 3600, 3450, 1700 cm^{-1}; dioxime, mp 219-220°], accompanied by several minor products. Acetylation of IX with acetic anhydride in pyridine gave the acetate (X), mp 99.5-100°.



IV IX X IX' XI XI' XII

Decisive evidence for the assigned structure IX was provided by an independent four step synthesis. According to the method of de Mayo, et al.,[6] photoirradiation of dimedone and a large excess of methyl acrylate in cyclohexane gave in poor yield the desired ketoester (XI), mp 103.5-105°, whose ir spectrum [($CHCl_3$) 1735, 1705 cm^{-1}] precluded the alternative structure XI'. Ketalization of XI followed by lithium aluminum hydride reduction and treatment with 90% acetic acid gave the ketoalcohol which was identical to IX in all respects.[7]

These ring opening reactions also provide a convenient preparative method for medium-ring 1,5-dione derivatives.

Footnotes and References

1. Y. Tamura, Y. Kita, H. Ishibashi, and M. Ikeda, *Chem. Commun.*, **1971**, 1167.
2. O. Cervinka in "Enamines: Synthesis, Structure and Reactions", (A.G. Cook, ed.), Marcel Deker, Inc., New York, 1969, p 270.
3. ref. 2, p 272.
4. J. Meinwald and A. Lewis, *J. Am. Chem. Soc.*, **83**, 2769 (1961); K.B. Wiberg, B.R. Lowry, and B.J. Nist, *ibid.*, **84**, 1594 (1962).
5. It should be noted that the hemiacetal structure IX' is not so important, as suggested by the nmr spectral data.
6. B.D. Challand, H. Hikino, G. Kornis, G. Lange, and P. de Mayo, *J. Org. Chem.*, **34**, 794 (1969).
7. An attempt to epimerize IV (used as a mixture) under the similar reaction conditions used for IIIa failed, giving a complex mixture. Treatment of IV (as a mixture) with sodium methoxide in methanol resulted in the addition of methanol to give 52% yield of an oily compound (XII) [Mass m/e 212 (M^+); ir ($CHCl_3$) 3420, 1690 cm^{-1}; nmr ($CDCl_3$) τ 6.35 (doublet, 2H, $-CH\underline{CH_2}O-$, J=5 Hz), τ 6.85 (singlet, 3H, OCH_3)].