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X-RAY STRUCTURE DETERMINATION OF AN INTERESTING REARRANGEMENT PRODUCT, $C_{19}H_{21}O_2N$, ENCOUNTERED IN DITERPENE ALKALOID SYNTHESIS.

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In a recent paper(1) we have described a simple and stereospecific synthesis of the tetracyclic compound I. An analogue of this material with a suitably placed methoxy group in the benzene ring will be an excellent starting material for the synthesis of various hexacyclic diterpene alkaloids. Our first attempt to complete the nitrogen ring of I was based on a procedure which we have previously successfully elaborated in the synthesis of compound V.(2) In the present paper it will be shown that with compound I this procedure leads to an entirely different, and from the point of view of our objective undesirable, result.

Treatment of I with alkali and potassium cyanide in alcohol yielded the lactamol II to which we have ascribed(1) on the basis of our previous experience(2)** and an incorrect interpretation of subsequent transformations the stereochemistry IIb.

Prolonged treatment of II with alcoholic alkali gave(1) a compound m.p. 228°C to which we have ascribed(1) the structure IIIb. It showed in the infrared spectrum an unexpectedly low carbonyl peak at 1726 cm^{-1} and ultraviolet maxima at λ_{max} = 228 mμ (logε = 4.38) and 292 mμ (logε = 4.30). <u>It did not show</u>***, however, an aldehyde hydrogen in the N.M.R. spectrum and all other spectral and analytical data were in agreement with the formula IIIb. We have consequently explained the unexpected (on the basis of formula IIIb) infrared maximum and ultraviolet spectrum by a homo-conjugation effect of the carbonyl group and the strained benzene ring.

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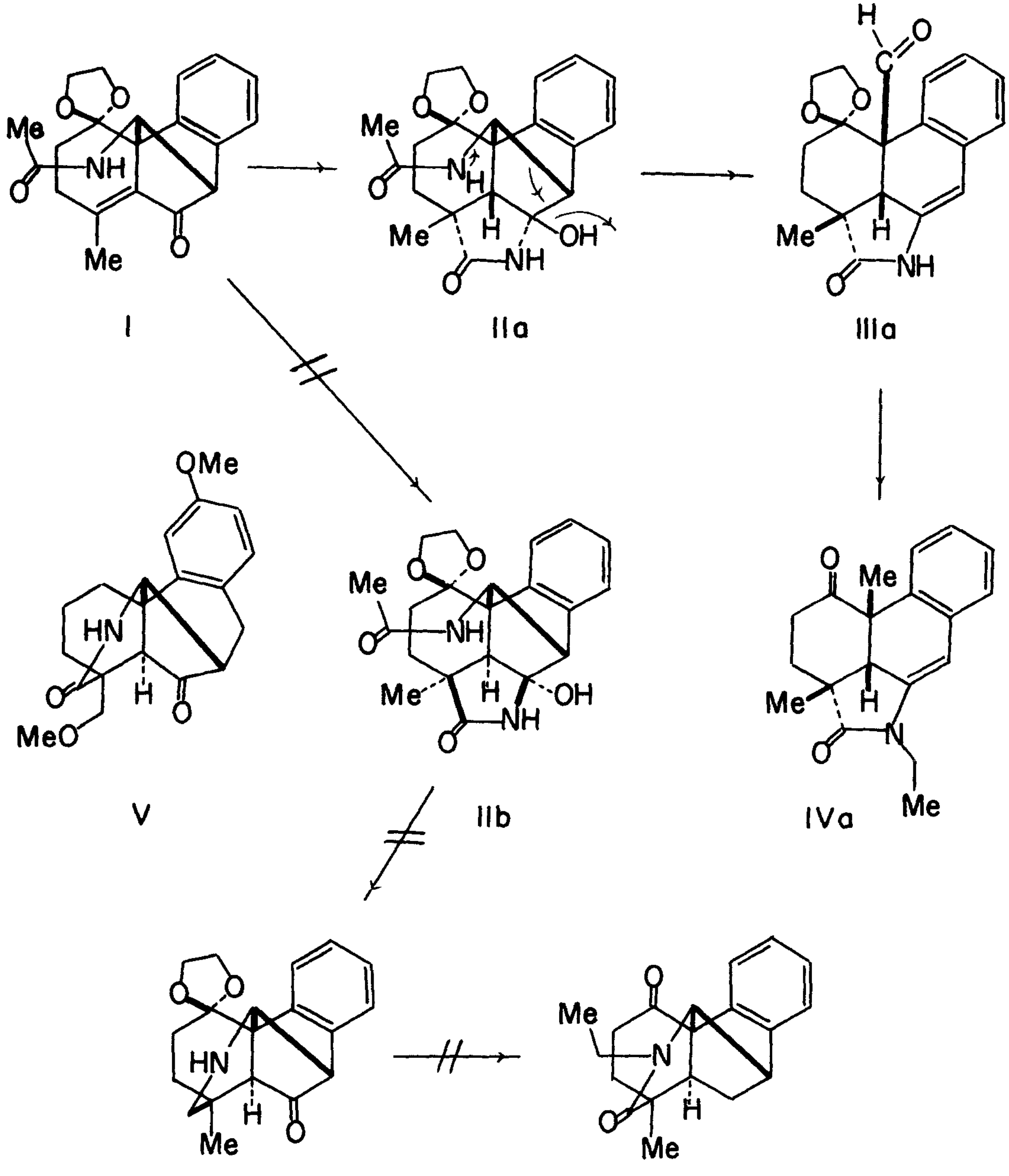
** It should be pointed out that the present work does in no way invalidate or affect our previous(2) results which have since been corroborated by a series of further transformations.(3)

*** A reinvestigation of the N.M.R. spectrum of III has corroborated this finding.



I IIa IIIa

V IIb IVa

IIIb IVb

Compound III was subjected to N-ethylation, Wolff-Kishner reduction and deketalization and by these processes the product IV was obtained in good yield. This material (m.p. 139°C) gave a correct elemental analysis and molecular ion in mass spectrography. In the infrared spectrum it showed a ketonic carbonyl peak at 1725 cm^{-1} and a lactam carbonyl at 1670 cm^{-1}. In the N.M.R. spectrum it showed, however, two tertiary methyl group singlets (3 H each) at τ = 8.45 and 8.23 p.p.m. The product IV showed moreover the same ultraviolet spectrum as compound III in spite of the fact that the "homo-conjugated" carbonyl group was now absent.

Thus it became clear that the structure IVb for the product was very dubious and that an X-ray crystal structure determination was desirable. The X-ray analysis is described below and revealed the structure to be IVa (and its enantiomer).

It is now clear that the lactamol II must possess the steric arrangement IIa and that treatment of II with alcoholic alkali gave the product IIIa and not IIIb. The mechanisms of all the transformations are clear. The lactamol IIa loses the N-acetyl group by hydrolysis and undergoes a 1,3-cleavage portrayed by the arrows in the formula IIa. A hydrolytic loss of ammonia completes the conversion into IIIa. The transformation of IIIa to IVa does not require any comment.

Suitable crystals for the X-ray analysis were obtained from an ethyl acetate : n-pentane solution. The crystals are monoclinic, space group $P2_1/c$, and there are four molecules in the unit cell of dimensions a = 10.901, b = 9.738, c = 16.389Å, and β = 117.17° (measured at -160°C). Low-temperature data were collected with a General Electric XRD5 manual diffractometer and of the 3439 independent reflections within the range of the diffractometer ($2\theta \leqslant 165°$) 3090 were observed.

The structure was solved by the symbolic addition procedure(4) which determined the signs of 452 normalized structure factors with values of $E \geqslant 1.5$. An E-map computed with these terms revealed the entire structure except hydrogen atoms. Initially the atomic coordinates and isotropic temperature parameters were refined by the block-diagonal least-squares method to a discrepancy factor ($R = \sum (|F_o| - |F_c|)/\sum|F_o|$) of 10%. All the hydrogen atoms were then located from a difference Fourier map and included in the subsequent refinement. With anisotropic temperature parameters for the non-hydrogen atoms and isotropic ones for the hydrogen atoms the R-factor is now 4.3% for all observed reflections. Further refinement is in progress.

The stereochemistry and conformation of the structure can be seen from Figure 1. The ring junctions A/B and A/D are both cis. Ring A occurs in a "twist boat" conformation with C(3) and C(5) on opposite sides of the mean plane through the other ring atoms. The conformation of ring B is "half boat" since the atoms C(5), C(6), C(7), and C(8) are coplanar and C(9) and C(10) are both displaced to the same side of this plane. However, the distance of C(10) to the plane is more than twice the displacement of C(9) and the "half boat" is thus distorted. Ring D is envelope shaped, C(5) being out of the plane defined by the other ring atoms.

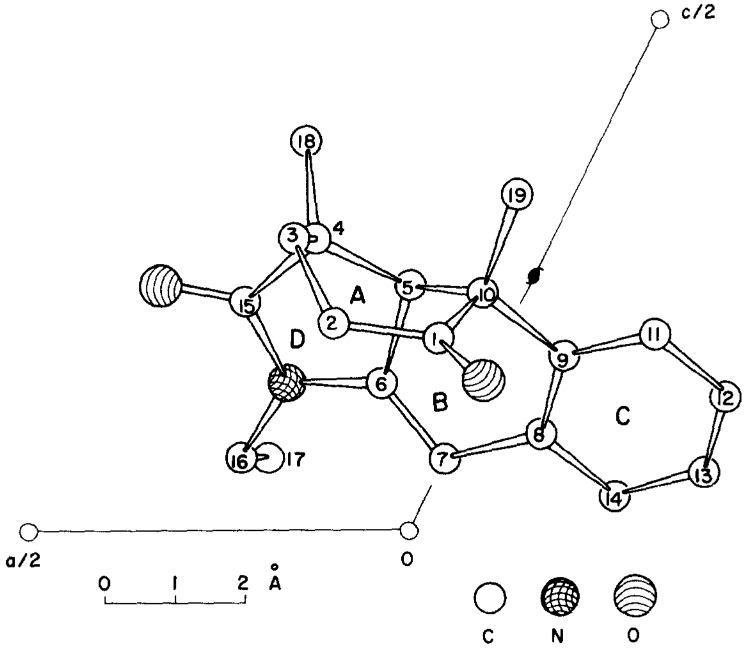


Fig. 1. View of the molecule along the b-axis.

Complete results of the X-ray analysis will be published elsewhere.

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