Tetrahedron Letters No.24, pp. 2711-2716, 1966. Pergamon Press Ltd.
Printed in Great Britain.

d,l-1-OXOCRINANE

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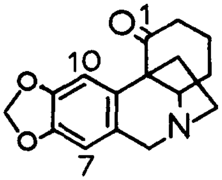
(Received 2 April 1966)

We wish to report the synthesis and characterization of both diastereoisomers of the title compound 1. This work



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offers confirmation of the assigned (1) stereochemistry and oxygenation pattern (2) of those Amaryllidaceae alkaloids possessing the 5,10b-ethanophenanthridine ring system. The synthesis is an extension of our previously reported (3) rearrangement of N-vinylazindines and is outlined in the figure.

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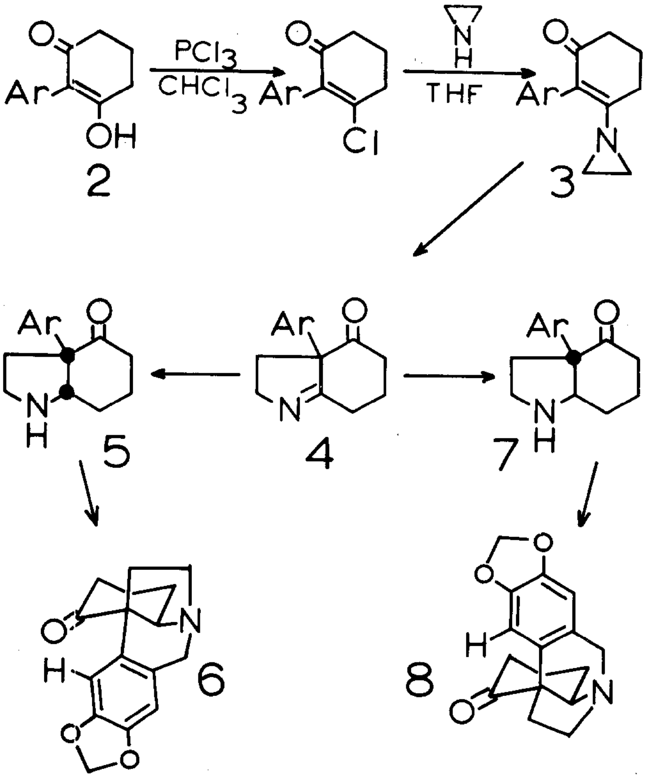
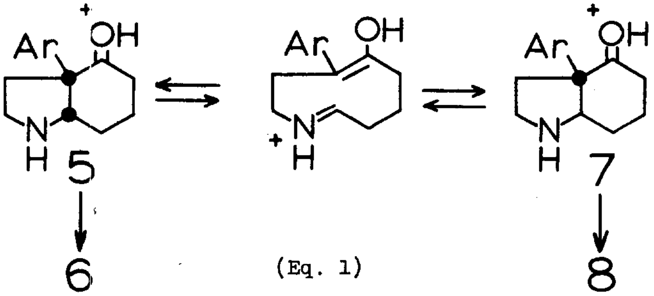


fig.

The synthesis of 2-(3',4'-methylenedioxyphenyl)-1,3-cyclohexanedione (2) (4), m.p. 203-205° was achieved by the general procedure of Born *et al*. (5). Heating enamine 3 (m.p. 120-121.5°) with an excess of sodium iodide in diglyme at 145° for 2.5 hr. afforded iminoketone 4 ($\lambda_{max}^{CHCl_3}$ 5.85 u, 6.05 u; mol. wt. (6) 257; m.p. 119.5-121.5°) in 55% yield. Catalytic hydrogenation of 4, using platinum oxide in ethanol and hydrochloric acid, was sufficiently stereopromiscuous (7) to afford both *cis*-aminoketone 5 (m.p. 100-101.5°; $\lambda_{max}^{CHCl_3}$ 5.85; mol. wt., 259) in 60% yield and *trans*-aminoketone 7 (m.p. 119.5-120.5°; $\lambda_{max}^{CHCl_3}$ 5.85 u; Mol. wt., 259) in 5.2% yield. As discussed in our previous communication (3), we feel confident in assigning a *cis* ring fusion to the major product (5) and a *trans* ring fusion to the minor product (7) of the hydrogenation. NMR spectra (8) of the N-acetyl derivatives of 5 (5a) and 7 (7a) are in agreement with this assignment, the methine hydrogen of 5a being appreciably more deshielded (τ 5.2) than that of 7a (τ 6.4).

Reaction of 5 with an excess of formalin for 3 min. followed by dilution with a large excess of 6M HCl gave, after 2 hr. at room temperature, a 79% yield of *dl*-1-oxocrinane (6), m.p. 123-125°. Comparison of its infrared (chloroform) and mass spectra with those of the naturally derived material, "oxodemethoxydihydrobuphanamine", which has been assigned structure 6 (9), showed them to be identical.

The possibility of a retro-Mannich reaction's causing epimerization (eq. 1) during the transformation 5 → 6



(Eq. 1)

was eliminated by the demonstration that reaction of 7 with formaldehyde under the above conditions gave d,l-4a-epi-1-oxocrinane (8), m.p. 165.5-166.5°, mol. wt. 271) in 80% yield (10). The NMR spectra of 6 and 8 are consistent with the proposed structures (11) and differ mainly in that the aromatic hydrogens of 6 appear as singlets at τ 3.6 and 2.3 while those of 8 appear as singlets at τ 3.5 and 3.75. The broad short singlet (τ 3.6 in 6, τ 3.5 in 8) in each spectrum is assigned to the hydrogens at C-7 (benzylic coupling)(11,12) and the large chemical shift difference between the hydrogens at C-10 (τ 2.3 in 6, τ 3.75 in 8) is ascribed tc their different positioning with respect to the carbonyl oxygen at C-1, as is apparent from the drawings.

Thus our experimental work, besides offering a facile synthesis of the basic 5,10b-ethanophenanthridine ring system, affords conclusions that are in complete accord with the proposed stereochemistry (as in 6) and oxygenation pattern of these alkaloids.

Acknowledgment. We wish to thank Dr. H. M. Fales of N.I H. for an authentic sample of 6; Professor W. C. Wildman for a solution infrared spectrum of 6, and Mr. S. Weiss for technical assistance. Partial support by the National Science Foundation and National Institutes of Health is also acknowledged.

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(4) All new compounds were adequately characterized by spectra and, except for 8, elemental analysis.

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(6) Molecular weights were determined from mass spectra, using a CEC-103C instrument equipped with an all-glass inlet system held at 200-250°. All spectra were run at 70 v. ionizing voltage.

(7) Palladium-on-carbon in acidic ethanol gave only the *cis* aminoketone, but in very poor yield.

(8) NMR spectra were determined in deuterochloroform at 60 mc, using a Varian A60 spectrometer.

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