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THE SELF-TRAPPING OF ENAMINE-ALDEHYDE CONDENSATION PRODUCTS: A NEW XANTHONE SYNTHESIS (1)

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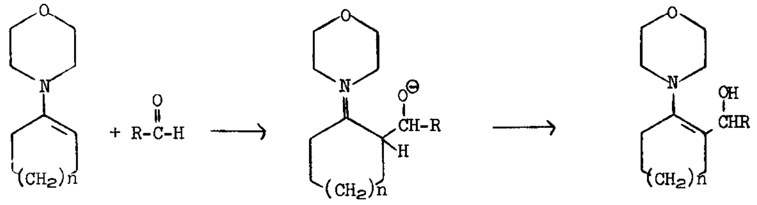
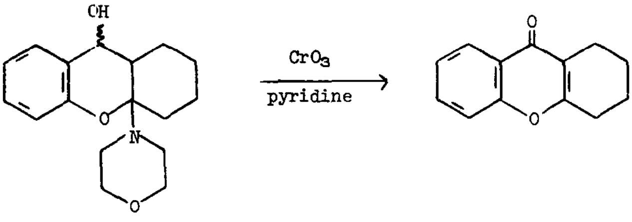
Dipolar species of generalized formula I are believed to be formed as intermediates in the reaction of enamines with aldehydes (2). Little is known about the properties of these unusual alkoxide ions other than that they can proceed to the hydroxy enamines II (2). We wish to describe a novel cyclization reaction which is based upon the well-known relative basicities of alkoxide and phenoxide ions and which appears to occur through the cyclization of zwitterions derived from I by intramolecular proton transfer. In addition, we seek to demonstrate that subsequent conversions of the condensation products suggest a new general approach to the synthesis of xanthones (3).



I

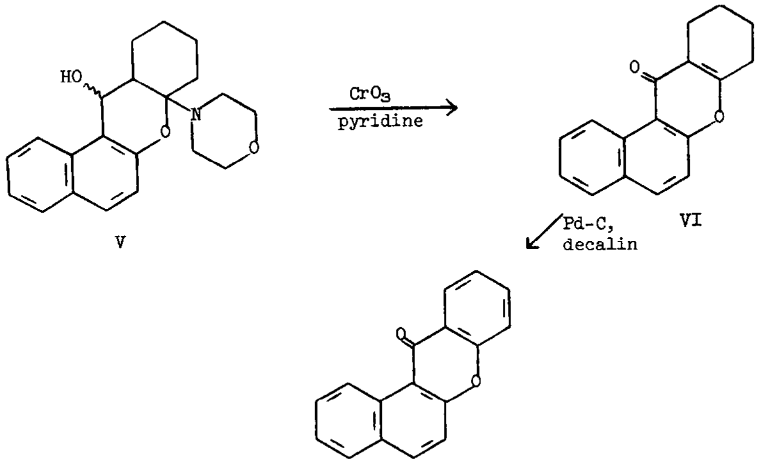
II

It has been found that 1-morpholinocyclohexene reacts exothermically with salicylaldehyde in an inert solvent such as benzene or hexane to give in very high yield a non-crystalline viscous oil formulated as III. Chemical confirmation of the gross structure of III was realized by Sarett oxidation (4) of this complex alcohol to the known 1,2,3,4-tetrahydroxanthone (IV), m.p. 102-103° (5), in 55% yield. IV was further characterized by nitration to the known 7-nitro derivative, m.p. 202° (5).



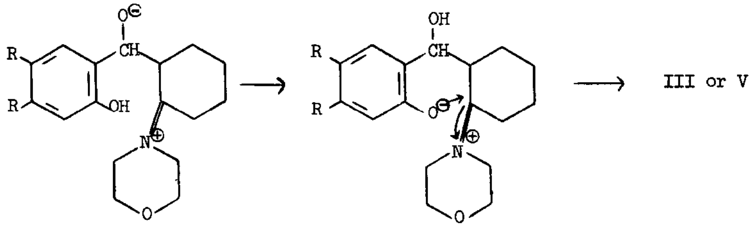
III IV

When equimolar quantities of 2-hydroxy-1-naphthaldehyde and 1-morpholinocyclohexene were allowed to stand in benzene solution overnight at room temperature, the crystalline adduct V, m.p. 89-90° (6), was obtained in 91.5% yield after recrystallization from acetone. Chromium trioxide-pyridine oxidation of V again proceeded with β-elimination of the morpholino moiety to give rise to VI, m.p. 155.5° (6), in 75% yield. Palladium-on-charcoal dehydrogenation of VI in refluxing decalin led quantitatively to the known 1,2-benzoxanthone (VII), m.p. 142-142.5° (7).



V VI VII

The simplest mechanism for the formation of III and V involves initial bimolecular combination of the reaction components to give a species such as I (see VIII). A subsequent intramolecular acid-base reaction can afford the isomeric zwitterion IX which can undergo facile ring closure (as depicted by the arrows) (8).



VIII R = H or benzo IX

The generality of this reaction is presently under investigation and our observations will be reported in due course.

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(1) Part XV of the series on Unsaturated Heterocyclic Systems. Paper XIV: L. A. Paquette, J. Am. Chem. Soc., **87**, in press.

(2) L. Birkhofer, S. M. Kim, and H. D. Engels, Chem. Ber., **95**, 1495 (1962).

(3) For a recent survey of xanthones of biological origin, see F. M. Dean, ''Naturally Occurring Oxygen Ring Compounds,'' Butterworth and Co., Ltd., London, England, Chapter 9; J. C. Roberts, Chem. Revs., **61**, 591 (1961).

(4) G. I. Pocs, G. E. Arth, R. E. Beyler and L. H. Sarett, J. Am. Chem. Soc., **75**, 422 (1953).

(5) H. I. Hall and S. G. P. Plant [J. Chem. Soc., 232 (1933)] report m.p. 104° for IV and m.p. 203° for its 7-nitro derivative.

(6) All new compounds gave acceptable microanalytical results.

(7) N. P. Buu-Hoi and N. D. Xuong [J. Org. Chem., **16**, 1633 (1951)] report m.p. 143° for VII.

(8) This entire process may also be concerted and not mediated by species VIII: