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CAPTURE OF MUNCHNONE IMINE INTERMEDIATES IN ACID-CATALYZED REACTIONS OF REISSERT COMPOUNDS

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A mechanism for the acid-catalyzed hydrolysis of a Reissert compound (a 1-acyl-1,2-dihydroquinaldonitrile or a 2-acyl-1,2-dihydroisoquinaldonitrile) has been proposed (1) in which a mesoionic compound is postulated to be an intermediate. Since such a mesoionic intermediate is essentially a munchnone imine, and since munchnones, sydnones and sydnone imines are known to undergo 1,3-dipolar addition reactions readily (2), it was anticipated that a 1,3-dipolarophile might be used to capture the intermediate. Also, it was felt that the reactions might lead to useful methods of synthesis of some complex heterocyclic compounds. These expectations were realized as described below.

When 2-benzoyl-1,2-dihydroisoquinaldonitrile was treated with fluoroboric acid in glacial acetic acid, a yellow precipitate of the hydrofluoroborate salt (I) of the Reissert compound was obtained. Reaction of this salt with dimethyl acetylenedicarboxylate in methylene chloride-ethanol (95%) solution afforded dimethyl 3-phenylpyrrolo[2,1-a]isoquinoline-1,2-dicarboxylate (V), m.p. 106-107°, in 90% yield. Thus, the anticipated reaction had taken place, and the proposed munchnone imine intermediate (II) had been captured.

The structure of the product, dimethyl 3-phenylpyrrolo[2,1-a]isoquinoline-1,2-dicarboxylate (V), was established in two different ways. First of all, the ester was subjected to hydrolysis and the resulting acid to decarboxylation to give 3-phenylpyrrolo[2,1-a]isoquinoline, m.p. 98.5-99.0°. The latter compound was also prepared by cyclodehydration of β-(1-isoquinolyl)-propiophenone (3) in the presence of polyphosphoric acid. In the second proof of structure, dimethyl 2-(1-isoquinolyl)-3-benzoylmaleate, m.p. 176-178°, was prepared by the reaction of the lithium salt of 2-benzoyl-1,2-dihydroisoquinaldonitrile with dimethyl acetylenedicarboxylate (4). Treatment of dimethyl 2-(1-isoquinolyl)-3-benzoylmaleate with 100% phosphoric acid at 120° gave dimethyl 3-phenylpyrrolo[2,1-a]isoquinoline-1,2-dicarboxylate (V), identical in every regard with the product of the 1,3-dipolar addition reaction.

In another example of a 1,3-dipolar addition reaction of the munchnone imine (II), the hydrofluoroborate salt (I) of 2-benzoyl-1,2-dihydroisoquinaldonitrile was caused to react with ethyl phenylpropiolate in methylene chloride-ethanol (95%). This reaction was noteworthy in that both 2-carbethoxy-1,3-diphenyl-3-hydroxy-13-cyano-3,13-dihydropyrrocoline-3,13-lactim (IV), m.p. 217-218°, the primary 1,3-dipolar addition product, and ethyl 1,3-diphenylpyrrolo[2,1-a]isoquinoline-2-carboxylate (VI), m.p. 101-102°, the completely aromatic product formed by elimination of isocyanic acid from IV, were isolated. Furthermore, the product of m.p. 217-218° could be converted to the product of m.p. 101-102° by pyrolysis at 220°, isocyanic acid being evolved.

The proof of structure of ethyl 1,3-diphenylpyrrolo[2,1-a]isoquinoline-2-carboxylate (VI) consisted of its hydrolysis and decarboxylation to 1,3-diphenylpyrrolo[2,1-a]isoquinoline, m.p. 136-138°. In an independent synthesis, 1,3-diphenylpyrrolo[2,1-a]isoquinoline-2-carboxamide, m.p. 225-227°, was prepared by the condensation of the lithium salt of 2-benzoyl-1,2-dihydroisoquinaldonitrile with cinnamonitrile (5). Hydrolysis of the amide and decarboxylation of the resulting acid gave the compound of m.p. 136-138°.

Benzaldehyde and quinaldic acid are obtained by the action of polyphosphoric acid, then water, on 1-benzoyl-1,2-dihydroquinaldic acid (VII). It has been suggested (6) that an intermediate (VIII), which is the conjugate acid of a munchnone (IX), is the precursor of the hydrolysis products. In an attempt to capture the munchnone (IX) we have caused 1-benzoyl-1,2-dihydroquinaldic acid to undergo reaction with dimethyl acetylenedicarboxylate in acetic anhydride solution. There was obtained a compound of m.p. 161-162°, which has been shown to be the expected product of a 1,3-dipolar addition reaction, namely dimethyl 1-phenylpyrrolo[1,2-a]quinoline-2,3-dicarboxylate (X). In an independent synthesis, the same compound was obtained by the condensation of 1-benzylquinolinium bromide with dimethyl acetylenedicarboxylate in dimethylformamide solution in the presence of potassium carbonate (7). Furthermore, the same compound was produced by the reaction of 1-benzoyl-1,2-dihydroquinaldonitrile hydrochloride with dimethyl acetylenedicarboxylate in dimethylformamide solution.

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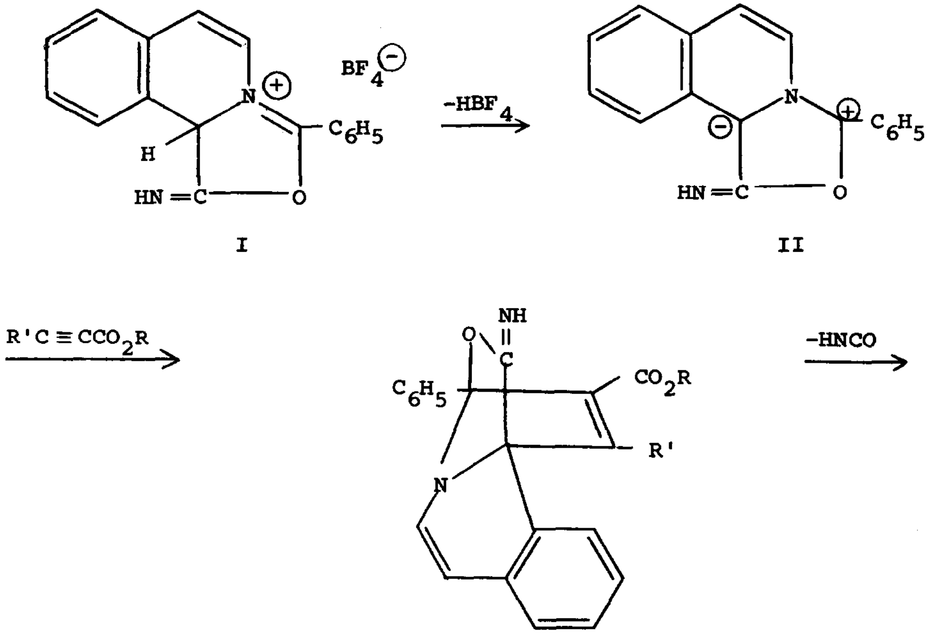
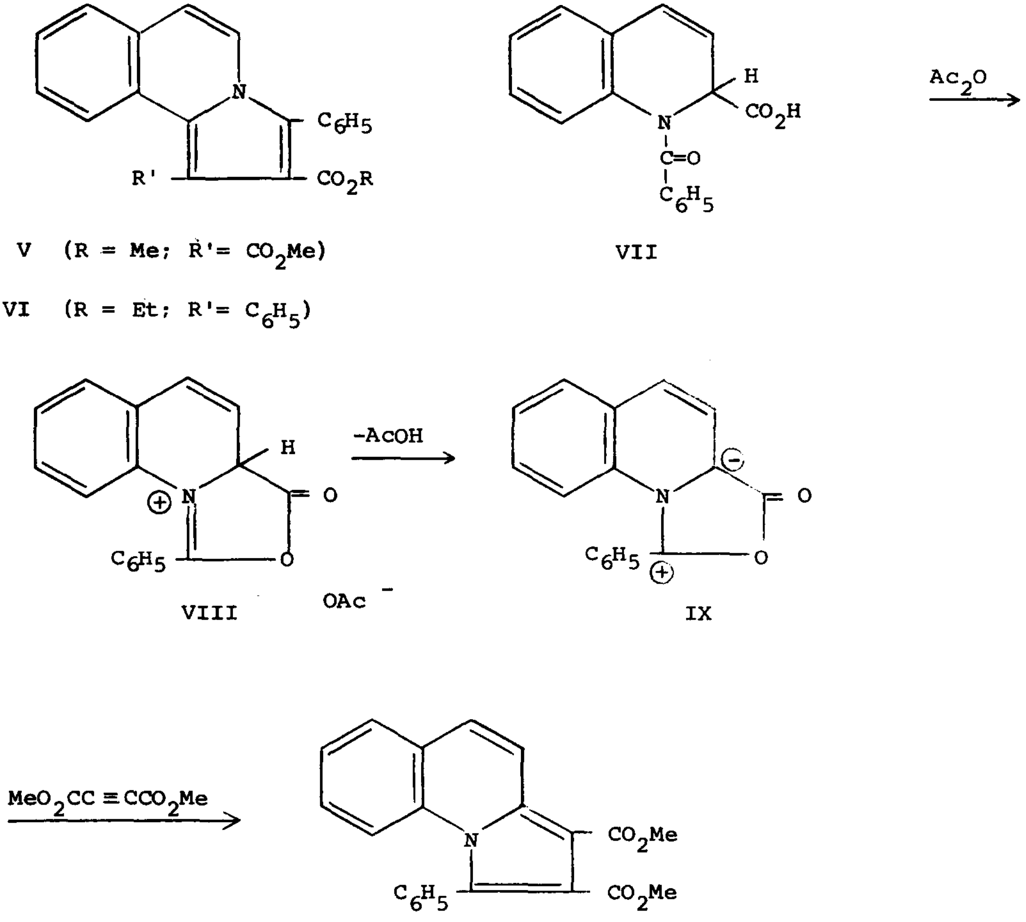


I

II

III (R = Me; R' = CO_2Me)

IV (R = Et; R' = C_6H_5)



V (R = Me; R'= CO_2Me)

VI (R = Et; R'= C_6H_5)

VII

VIII

IX

X

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