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SYNTHESIS OF 2-QUINOLONES FROM ISATINS AND DIKETENE

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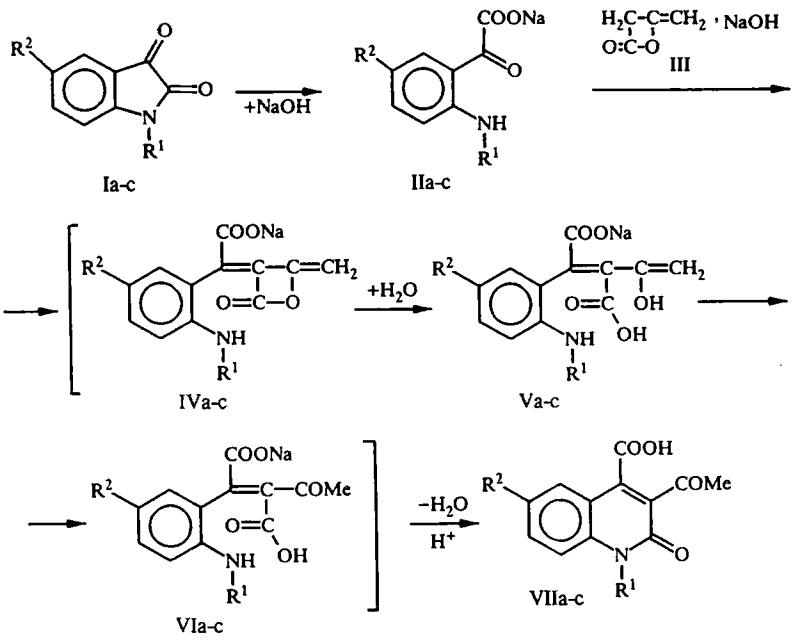
3-Acetyl-2-oxo-1,2-dihydroquinoline-4-carboxylic acid and its substitutes were synthesized by condensation of sodium isatates with diketene. The reaction takes place by a different mechanism than Pfitzinger synthesis of quinolines.

We briefly described condensation of isatins with diketene in [1]. More detailed data for this reaction are reported here. It probably begins with opening of the 5-member ring of isatins I by NaOH with formation of salts II, which react with diketene by crotonic condensation. Opening of the 4-member ring in intermediates IV formed yields intermediate compounds VI, cyclized in acid medium into 2-quinolone derivatives VII (Scheme 1).

Scheme 1



The described condensation is more general in character than Halberkann synthesis [2], since it makes it possible to synthesize 2-quinolones with an acetyl group at the $C_{(3)}$ atom and an alkyl substituent at the nitrogen atom.

The structure of products VIIa-c is confirmed by their mass spectra taken at 50 and 17 eV. Typical fragmentation of the molecular ion of acid VIIa with loss of CH_3, CO, and CO_2 is shown below (Scheme 2).

The mass spectra were taken on an MX-1320 instrument with direct introduction of the substances in the ion source. The melting points were determined on a Boetius instrument and were not corrected. Freshly distilled diketene was used.

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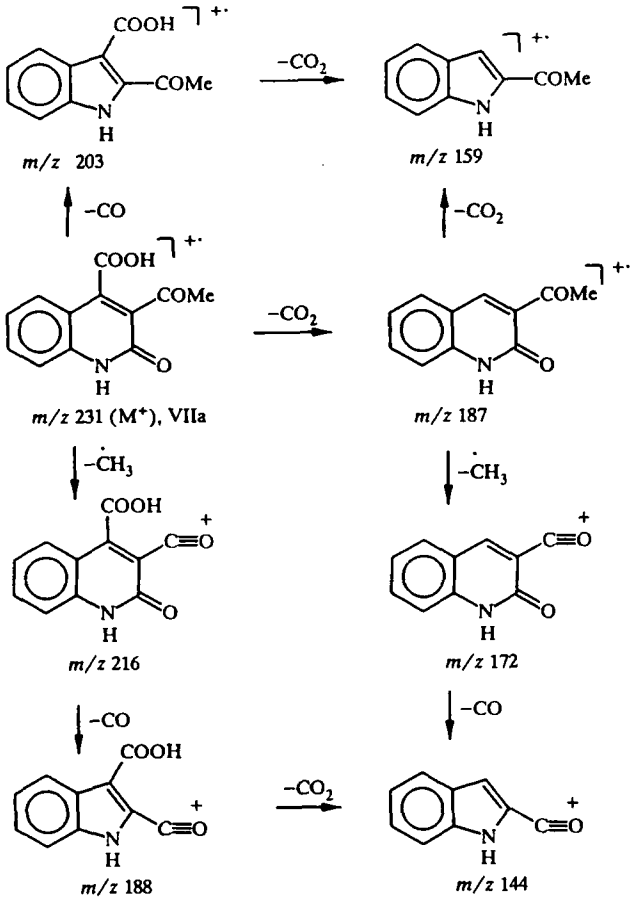
Scheme 2



3-Acetyl-2-oxo-1,2-dihydroquinoline-4-carboxylic Acid (VIIa). A solution of 7.35 g (50 mmole) of isatin in 20 ml of aqueous NaOH (2.4 g, 60 mmole) was stirred for 30 min and 5.04 g (60 mmole) of diketene was added at such a rate that the temperature did not exceed 30°C. The reaction mass was stirred for another 2 h, the sediment of product VIIa was separated and successively washed with 10 ml of 5% aqueous solution of hydrochloric acid, water, and alcohol. Yield of 5.8 g (43%) of acid VIIa; mp = 288-289°C (from methanol). Found, %: C 62.3; H 3.8; N 6.0. $C_{12}H_9NO_4$. Calculated, %: C 62.3; H 3.9; N 6.1.

Compounds VIIb, c were similarly synthesized from 5-methylisatin and 1-methylisatin.

3-Acetyl-6-methyl-2-oxo-1,2-dihydroquinoline-4-carboxylic Acid (VIIb). Yield of 47%; mp = 280-281°C (from *n*-isopropyl alcohol). Found, %: C 63.5; H 4.4; N 5.8. $C_{13}H_{11}NO_4$. Calculated, %: C 63.7; H 4.5; N 5.7.

3-Acetyl-1-methyl-2-oxo-1,2-dihydroquinoline-4-carboxylic Acid (VIIc). Yield of 8%; mp = 245-247°C (from ethyl acetate–hexane mixture). Found, %: C 63.4; H 4.6; N 5.6. $C_{13}H_{11}NO_4$. Calculated, %: C 63.7; H 4.5; N 5.7.

REFERENCES

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2. J. Halberkann, *Ber.*, **54**, 3090 (1921).