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A Simple Method for the Synthesis of 5-Methyloxazolo-[4,5-*c*]quinolin-4(5*H*)-ones

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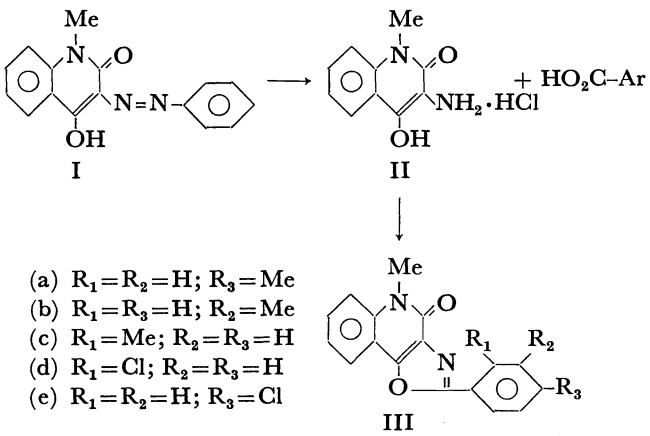
Synopsis. A general and simple method for the synthesis of oxazolo[4,5-*c*]quinoline-4(5*H*)-ones by heating 3-amino-4-hydroxy-2-quinolone hydrochloride with aromatic acids in the presence of PPA has been described. The structures are based on spectral and analytical data.

In recent years, a number of 1-methyl-2-quinolone derivatives have been synthesised since many of them have been reported to show antiseptic properties and also exhibit fungicidal activity.[1] Also, 4-hydroxy-3-nitro-2-quinolone derivatives have been reported[2] to possess antihistaminic action. The work on 1-methyl-2-quinolone also has received importance due to the isolation of 1-methyl-4,7,8-trimethoxy-2-quinolone from the plant *Spathelia sorbifolia* L and its subsequent synthesis.[3] Further, the antibiotics nybomycin and deoxynybomycin which have also been synthesised[4] possess an oxazolo[4,5-*c*]quinoline-2-one structure.

In view of this interesting data it was thought of interest to prepare 5-methyloxazolo[4,5-*c*]quinolin-4-(5*H*)-ones (III) since the latter would also be related to the antibiotic novobiocin.[5] We describe here a simple method to synthesise these compounds by heating 3-amino-4-hydroxy-1-methyl-2-quinolone hydrochloride (II), prepared from 4-hydroxy-1-methyl-3-phenylazo-2-quinolone[6] (I), with aromatic acids in the presence of PPA at 170—180 °C for 4 h. The required new oxazole derivatives were obtained as crystalline solids from ethyl acetate in 40—50% yields.



It is evident that in the reaction first an amide is formed which then cyclizes to an oxazole derivative.

TABLE 1. 5-METHYLOXAZOLO[4,5-*c*]QUINOLIN-4(5*H*)-ONES

Compound No.	Formula	Mp (°C)	Found (%) (Calcd) (%) C	H	N
IIIa	$C_{18}H_{14}N_2O_2$	235—236	74.6 (74.5)	5.0 (4.8)	9.7 (9.6)
IIIb	$C_{18}H_{14}N_2O_2$	189—191	74.5 (74.5)	5.0 (4.8)	9.8 (9.6)
IIIc	$C_{18}H_{14}N_2O_2$	205—206	74.4 (74.5)	4.5 (4.8)	9.9 (9.6)
IIId	$C_{17}H_{11}N_2O_2Cl$	196—198	65.6 (65.8)	3.7 (3.5)	9.4 (9.1)
IIIe	$C_{17}H_{11}N_2O_2Cl$	264—266	65.7 (65.8)	3.4 (3.5)	9.3 (9.1)

Experimental

All the meltng points are uncorrected. IR spectra were recorded by means of a Perkin Elmer spectrometer, while NMR spectra were obtained by Varian NMR spectrometer at 60 MHz, using tetramethylsilane as an internal standard.

Preparation of IIIa. A typical procedure is shown for IIIa. 3-Amino-4-hydroxy-1-methyl-2-quinolone (550 mg) and *p*-toluic acid (350 mg) were added to a mixture of phosphorus pentaoxide (5.5 g) and phosphoric acid (2.5 ml) preheated at 100 °C for 30 min. The heating was continued for 4 h at 170—180 °C. The mixture was cooled and decomposed with ice. The solid which separated was filtered, treated with aq sodium hydrogencarbonate solution and washed with water. It was crystallised from ethyl acetate in colourless needles, mp 235—236 °C (IIIa).

The spectral data of a typical compound (IIIa) are as follows: λ_{max}^{MeOH} nm (log ε): 210 (4.74), 255 (4.59), 310 (4.64), and 340 (4.53); IR (KBr): 1700 (C=O), 1625, 1590, and 1570 (heteroaromatic system) cm^{-1}. The position of the carbonyl band rules out the alternate 4-quinolone structure; NMR ($CDCl_3$): δ 2.43 (3H, s, Ar-$\underline{CH_3}$), 3.8 (3H, s, N-$\underline{CH_3}$), 7.0 and 8.3 (8H, m, aromatic protons). MS: *m/e* 290 (M^+).

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