Novel Approach to Pyrrolo[1,2-*a*]quinoline-1,5-diones

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J. Chem. Research (S), 1992, 260–261
J. Chem. Research (M), 1992, 1984–1996

The 4-quinolone ring system continues to attract attention because of its interesting biological activities, with a large number of derivatives exhibiting a range of antibacterial activities.[6–8] In continuation of our interest in the synthesis of 4-quinolone derivatives,[9] we report here a one-step synthesis of various pyrrolo[1,2-*a*]quinoline-1,5-diones.

Condensation of 2-aminoacetophenone with various acid anhydrides under basic conditions led in general to the formation of two types of compounds **2** and **3** (Scheme 1). The product (or ratio of products) was found to be dependent both on the type of acid anhydride and on the reaction conditions (Table 2).

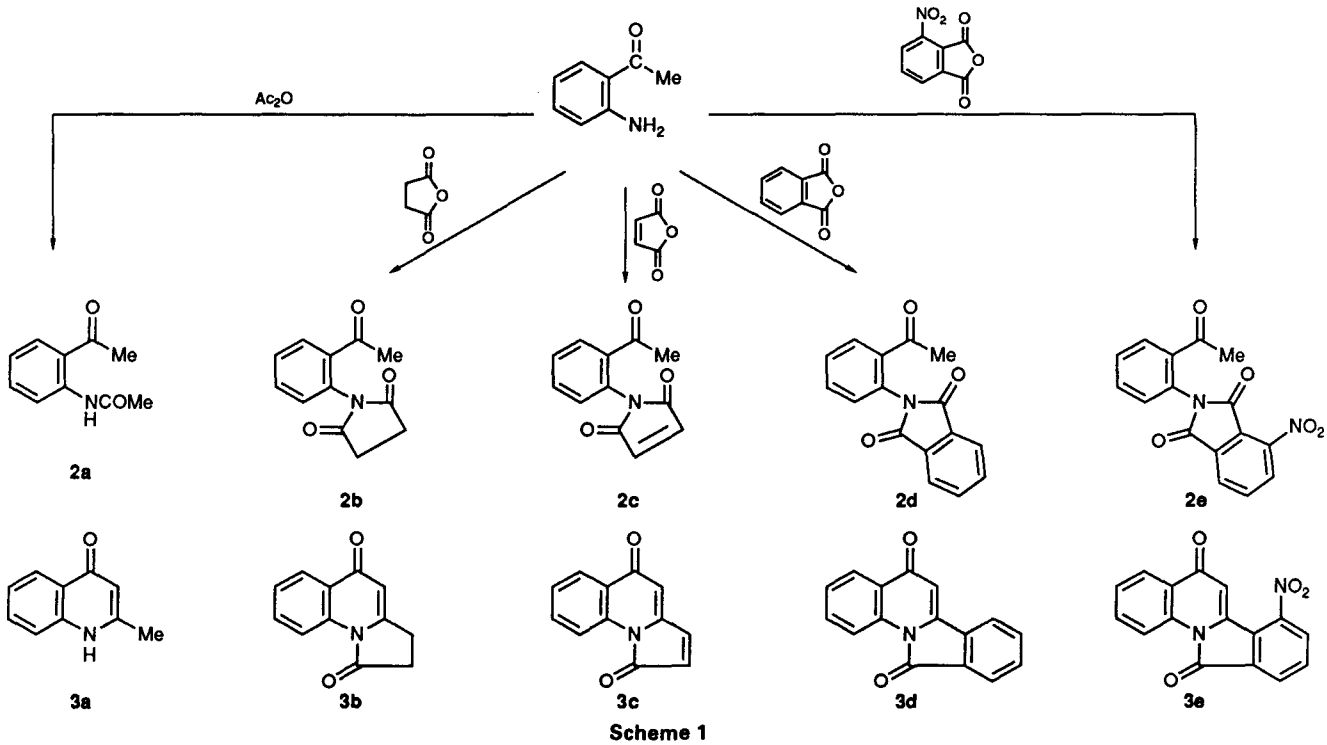
Acetic and succinic anhydrides gave the amide and imide derivatives **2a** and **2b**, respectively, with none or only a trace of the corresponding heterocycles **3a** and **3b**. In contrast, both imides (**2c** and **2d**) and heterocycles (**3c** and **3d**) were obtained from maleic and phthalic anhydrides, respectively, depending upon the reaction conditions. Thus increases in temperature and the amount of base led directly to the formation of the heterocyclic compounds **3c** and **3d**. Maleic anhydride was found to be more sensitive to the reaction conditions.

The situation with 3-nitrophthalic anhydride was far less complicated. The heterocyclic compound **3e** was the major compound under the two different sets of conditions used. Identification of the single isomer obtained was based upon

Table 2 Ratios of products obtained under different conditions

Acid anhydride	Reaction conditions	Products (relative % yields)[a]
Acetic	Xylene, Et_3N (5 ml), 140 °C	**2a** (100), **3a** (–)
Succinic	Xylene, Et_3N (5 ml), 140 °C	**2b** (~90), **3b** (traces)
Maleic	Toluene, Et_3N (2 ml), 110 °C	**2c** (~90), **3c** (traces)
	Xylene, Et_3N (2 ml), 120–140 °C	**2c** (~30), **3c** (~70)
	Xylene, Et_3N (5 ml), 120–140 °C	**2c** (traces), **3c** (~90)
	Toluene, Et_3N (4 drops), 120 °C	[b]
Phthalic	Xylene, Et_3N (1 ml), 130 °C	**2d** (~90), **3d** (traces)
	Xylene, Et_3N (5 ml), 140 °C	**2d** (~15), **3d** (~85)
3-Nitrophthalic	Xylene, Et_3N (1 ml), 130 °C	**2e** (~15), **3e** (~85)
	Xylene, Et_3N (5 ml), 140 °C	**2e** (traces), **3e** (~90)

[a]Based upon the amounts of each compound isolated from the reaction mixture. [b]Sole product was *N*-(2-acetylphenyl)maleamic acid.



Scheme 1

the ^1H and ^{13}C NMR spectra. Downfield shifts for the 5-H and C-5 absorbances were observed in the ^1H and ^{13}C NMR spectra of **3e** compared with those of its analogue **3d**. Thus in the ^1H NMR spectra, 5-H absorbed at δ 7.25 in **3e** and at δ 6.8 in **3d**, while in the ^{13}C spectrum, C-5 absorbed at δ 113.8 in **3e** but at δ 106.8 in **3d**. This is consistent with previous reports on the NMR spectra of 4-quinolone derivatives.[10] The downfield shift is large enough to be attributed only to the resonance present between the nitro group of **3e** and C-5. The other possible isomer, which was not observed, would not have this kind of resonance.

The products obtained under the various conditions shown in Table 2 strongly suggest that compounds of type **2** are intermediates in the cyclization to **3**. In fact when they were prepared and treated with a suitable base they did indeed cyclize to compounds of type **3** (Table 3).