Studies on the Reaction of Substituted 6-Nitrocoumarin with Anilines

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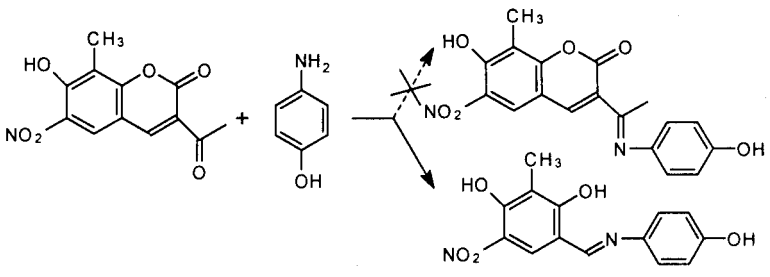
Abstract: 3-Acetyl-7-hydroxy-8-methyl-6-nitrocoumarin reacted with substituted anilines, and fission of the heterocyclic ring occurred.

Keyword: 6-Nitrocoumarin, heterocyclic ring fission, Schiff base, hydrazone.

Great attention has been paid to coumarins for their multi-activity against several diseases such as cancer, AIDS. In order to obtain some more effective anti-tumor compounds, we designed a series of coumarin derivatives with a novel retinoids structure. When we attempted to synthesis a Schiff base of nitro substituted 3-acetylcoumarins, however, it is surprisingly found that a new reaction occurred and a smaller sized Schiff base was obtained. ^{1}H-NMR, ^{13}C-NMR, MS and elemental analysis showed that the new compound was a heterocyclic ring fission product **I** (**Scheme 1**). Other substituted anilines (p-COOH...but not p-NO_2) behaved similarly with modest to excellent yields (46.9-100%).

Scheme 1

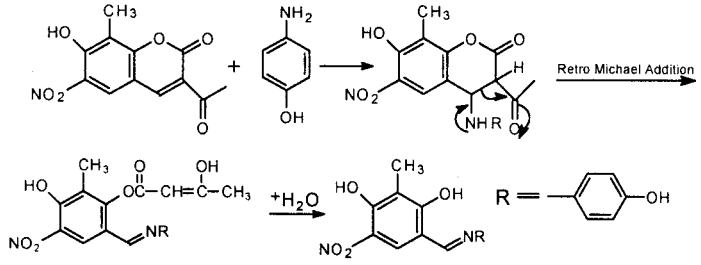


(**I**)

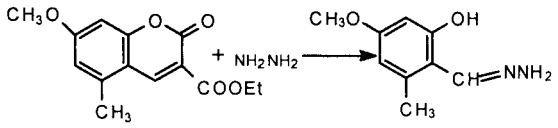
The possible reaction mechanism is as follows (**Scheme 2**). The 6-nitro group has strong electron-withdrawing power. Reinforcing the electron-withdrawing carbonyl, the charge of the 4-position of the nitrocoumarin is made even more positive. The stronger is the positive charge in the 4-position, the easilier proceeds the neucleophilic attack at

this position. Proving whether an aldehyde was formed at first (the possible reaction mechanism), the test in the above condition but without aniline was carried out. After two days, 3-acetyl-7-hydroxy-8-methyl-6-nitrocoumarin did not change at all.

Scheme 2



Furthermore, experiments showed, if coumarins have no nitro substitute in 6-position, they did not react with substituted anilines under the same condition. A similar ring-fission reaction occurs when 3-ethoxycarbonyl-5-methyl-7-methoxy coumarin reacts with hydrazine hydrate to obtain hydrazone **II**, the structure of which is elucidated through MS, elemental analysis. It was reported that when 3-(ethoxycarbonyl) benzodipyrone reacts with hydrazine hydrate, fission of the heterocyclic ring also happens[1]



(II)

From above results we can conclude that the 4--position of coumarin is easy to be attacked either by the strong nucleophilic reagent or when a strong electron-withdrawing group such as the nitro group was present in 6-position.

Acknowledgments

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Reference

1. Nadia A. M. M. , Shmeiss ; Nadia M. , Saleh ; *et al. Al-Azhar Bull. Sci.* **1996**, *7* (2), 1109.

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