Synthesis of 3-Aryl-9-chlorobenzo[e]-Δ^3-indoline-2,8-diones

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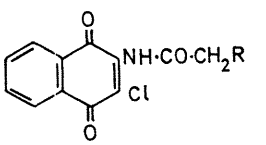
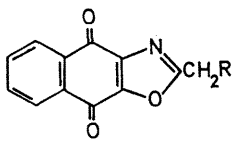
Summary Treatment of 2-arylacetamino-3-chloro-1,4-naphthoquinones with alkaline reagents or hot dimethyl sulphoxide gives 3-aryl-9-chlorobenzo[*e*]-Δ^3-indoline-2,8-dione.

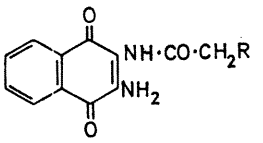
THE presence of the 2-acylamino-moiety in 2-acylamino-3-chloro 1,4-naphthoquinones (I) increases the activity of the



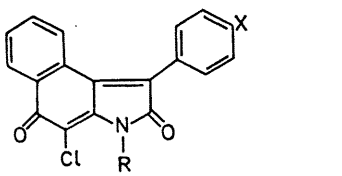
(I)



(II)



(III)



(IV) R=H

(V) R=PhCH$_2$, X=NO$_2$

halogen atom and both intramolecular displacement to give the corresponding 2-alkylnaphth[2,3-*d*]oxazole-4,9-dione (II) and intermolecular displacement with ammonia to give the corresponding 2-acylamino-3-amino-1,4-naphthoquinone (III) have been reported.[1,2] We report a third type of reaction of (I) which takes place when the methylene group next to the amide carbonyl has additional activation. For example, treatment of 2-(*p*-nitrophenylacetamino)-3-chloro-1,4-naphthoquinone (I; R = *p*-NO_2·C_6H_4) with ammonia in dioxan or nitrobenzene gave no detectable amount of 2-(*p*-nitrophenylacetamino)-3-amino-1,4-naphthoqu none (III; R = *p*-NO_2·C_6H_4). Instead, a product that analysed for $C_{18}H_9ClN_2O_4$ [λ_{max} (MeOH) 261, 327 and 370 nm. ($\epsilon \times 10^{-3}$ = 17·3, 18·7, and 14·5)] and showed absence of the methylene resonance in the n.m.r. spectrum [$(CD_3)_2SO$] was obtained. On the basis of this information the product has been assigned the structure 3-(*p*-nitrophenyl)-9-chlorobenzo[*e*]-Δ^3-indoline-2,8-dione (IV; X = NO_2). The product (IV; X = NO_2) has been formulated as the 2-oxo- rather than the 2-hydroxy-product on the basis of the i.r. spectrum (KBr) which showed a strong carbonyl absorption at 1730 cm.$^{-1}$ and NH absorption at 3115 cm.$^{-1}$. Apparently the increased acidity of the methylene group between the carbonyl and *p*-nitrophenyl group affords a base catalysed intramolecular condensation between this methylene group and the quinone carbonyl function to the complete exclusion of displacement of chloride by the ammonia. Treatment of (IV; X = NO_2) with benzyl bromide in the presence of anhydrous potassium carbonate in *NN*-dimethylformamide (DMF) gave 1-benzyl-3-(*p*-nitrophenyl)-9-chlorobenzo[*e*]-Δ^3-indoline-2,8-dione. The i.r. spectrum (KBr) which showed the absence of NH absorption and showed a strong carbonyl peak at 1715 cm.$^{-1}$ is in accord with this assignment. In contrast to (I; R = *p*-NO_2·C_6H_4), treatment of (I; R = Ph[2] or *p*-Cl·C_6H_4) with ammonia gave no cyclized product and the corresponding amino compounds (III; R = Ph and *p*-Cl·C_6H_4) were obtained in high yield. However, treatment of (I; R = Ph or *p*-Cl·C_6H_4 as well as *p*-NO_2·C_6H_4) with anhydrous potassium carbonate in DMF followed by acidification gave the corresponding 3-aryl-9-chlorobenzo-[*e*]-Δ^3-indoline-2,8-diones in good yield. The conversion of (III; R = *p*-NO_2·C_6H_4) to (IV; X = NO_2) could also be effected by warming a solution of (III; R = *p*-NO_2·C_6H_4) in anhydrous dimethyl sulphoxide (DMSO). The progress of the reaction could be followed by the disappearance of the methylene resonance in the n.m.r. spectrum. On cooling, a quantitative yield of (IV; X = NO_2) was obtained. The conversion of (III; R = Ph and *p*-Cl·C_6H_4) to (IV; X = H and Cl) in DMSO was also observed. However a higher

temperature and longer reaction time was required. As a result considerable decomposition accompanied the cyclization and the yields were considerably inferior to the K_2CO_3–DMF cyclization.

When (I; R = H) was treated with alkaline reagents, including sodium hydride in benzene or DMF, no cyclization to (IV) was observed. Apparently the methylene group next to the carbonyl in (I) requires additional activation for conversion into (IV).

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