SYNTHESIS OF 5-AMINOINDOLE DERIVATIVES FROM N-ARYLSULFONYLQUINONE DIIMINES

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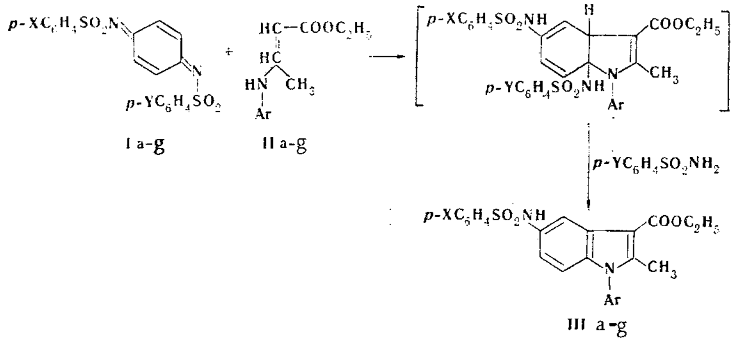
The reaction of N-arylsulfonyl-1,4-quinone diimines with 3-aryl-aminocrotonates gives 1-aryl-2-methyl-3-carbethoxy-5-arenesulfonamidoindoles, i.e., the enamine nitrogen atom participates in the formation of the pyrrole ring; in the case of quinone diimines with two different arylsulfonyl substituents, the arenesulfonamide with the more electronegative substituent is cleaved.

The reaction of p-quinone diimines with 1,3-dicarbonyl compounds described by Adams and Reifchneider [1] gives adducts that undergo prototropic cyclization to give 1-acyl-5-aminoindole derivatives. Domschke [2] used enamines in the reaction with p-quinone diimines to obtain 1-acyl-5-aminoindoles. Thus, the pyrrole ring in both cases arose through the nitrogen atom of the quinone diimine rather than through the nitrogen atom of the enamine; this limits the synthetic possibilities.

We have shown that the reaction of N-aryl-3-aminocrotonates (II) at room temperature in acetone proceeds with cleavage of an arenesulfonamide to give 1-aryl-2-methyl-3-carbethoxy-5-arenesulfonamidoindoles (III). Thus, in contrast to the previously described synthesis [1, 2], the enamine nitrogen atom participates in the formation of the pyrrole ring.



I—III a Ar=C_6H_5, X=Y=H, b Ar=C_6H_5, X=Y=CH_3, c Ar=p-$CH_3OC_6H_4$, X=Y=H, d Ar=p-$CH_3OC_6H_4$, X=Y=Cl, e Ar=p-$CH_3OC_6H_4$, X=CH_3, Y=H, f Ar=p-$CH_3OC_6H_4$, X=H, Y=Cl, g Ar=p-$CH_3C_6H_4$, X=Y=H

This made it possible to obtain a series of compounds of the III type by varying substituents X and Y. When X differs from Y, the sulfonamide grouping with the stronger electron-acceptor substituent is cleaved, i.e., the more acidic sulfonamide is eliminated. The addition of an enamine to the quinone imine apparently commences with the addition of a proton to the nitrogen atom of quinone imine I that has the highest electron density, after which the β-carbon atom of the enamine attacks the resulting carbonium ion with subsequent stabilization of the system through cyclization and elimination of an arenesulfonamide.

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The IR spectra of indoles III contain absorption bands at 3255, 1366, 1179, and 1280 cm^{-1} that confirm the presence of NH, SO_2, and $COOC_2H_5$ groups [3]. The PMR spectrum of a solution of indole IIIa in pyridine contains a singlet (2.2 ppm) of the protons of a methyl group attached to the pyrrole ring and a triplet (0.74 ppm) and quartet (4.08 ppm) of an ethyl group. Characteristic absorption maxima for an indole chromophore [4] at 223, 245, and 290 nm are observed in the UV spectrum of IIIa. The molecular ion peak with m/e 448 in the mass spectrum of a sample of IIIg constitutes 17% of the maximum peak. The primary process in the disintegration of the molecular ion is successive splitting out of a phenylsulfonyl radical (M-141) and ethylene to give ions F_1 (m/e 307, 100%) and F_2 (m/e 279, 9%). This disintegration is confirmed by peaks of metastable transitions. In addition, the spectrum contains peaks of ions with m/e 403 (1.1%, $M-C_2H_5O$), 263 (6%, $F_1-CO_2-C_2H_4$), and 91 (5.5%, C_7H_7), the combination of which corresponds to structure IIIg.

EXPERIMENTAL

The IR spectra of KBr pellets were recorded with a UR-20 spectrometer. The UV spectra of methanol solutions of the compounds were recorded with a Specord spectrophotometer. The PMR spectra were recorded by V. A. Budylin with an RS-60 spectrometer with hexamethyldisiloxane as the external standard. The mass spectrum was obtained by P. A. Sharbatyan with an MKh 1303 spectrometer at 170°, an ionizing voltage of 50 eV, and an emission current of 150 mA.

N-Phenylsulfonyl-N'-(p-tolylsulfonyl)-1,4-phenylenediamine. This compound was obtained by acylation of N-phenylsulfonyl-1,4-phenylenediamine (IV) with p-toluenesulfonyl chloride in pyridine [3]. A product with mp 243°(from glacial acetic acid) was obtained in 90% yield. Found : N 6.8; S 15.8%. $C_{19}H_{18}\cdot N_2O_4S_2$. Calculated: N 6.9; S 15.9%.

N-Phenylsulfonyl-N'-(p-chlorophenylsulfonyl)-1,4-phenylenediamine. This compound was similarly synthesized from IV and p-chlorobenzenesulfonyl chloride. A product with mp 237° (from glacial acetic acid) was obtained in 86% yield. Found, %: Cl 8.5; N 6.6. $C_{18}H_{15}ClN_2O_4S_2$. Calculated, %: Cl 8.4; N 6.6.

N-Arylsulfonyl-1,4-quinone Diimines (I). These compounds were obtained by oxidation of the corresponding N-arylsulfonyl-1,4-phenylenediamines with lead tetraacetate in glacial acetic acid [3].

N-Phenylsulfonyl-N'-(p-tolylsulfonyl)-1,4-quinone Diimine (Ie). This compound, with mp 176° (from benzene), was obtained in 92% yield. Found, %: N 6.9; S 15.7. $C_{19}H_{16}N_2O_4S_2$. Calculated, %: N 6.9; S 15.9.

N-Phenylsulfonyl-N"-(p-chlorophenylsulfonyl)-1,4-quinone Diimine (If). This compound, with mp 174° (from benzene) was obtained in 85% yield. Found, %: Cl 8.3; N 6.5. $C_{18}H_{13}ClN_2O_4S_2$. Calculated, %: Cl 8.4; N 6.6.

1-Aryl-2-methyl-3-carbethoxy-5-arenesulfonamidoindoles (III). A 0.011-mole sample of arylaminocrotonate II was added at room temperature with mechanical stirring to a suspension of 0.01 mole of quinone diimines I in 100 ml of acetone. Quinone diimine I dissolved slowly, and the solution became dark-red. Stirring was continued for 1 h until the indophenol reaction for the starting quinonimine imine was negative [5]. The acetone was evaporated in a stream of air, the residue was treated with chloroform, and the arenesulfonamide was separated by a filter. Methanol was added to the oil that was obtained after evaporation of the chloroform from the filtrate, and the resulting crystalline precipitate was removed by filtration, washed on the filter with methanol, and air dried.

In some cases better results were obtained when the oily residue was dissolved in glacial acetic acid and the solution was poured into water. The yields of indoles IIIa-g were 30, 20, 70, 66, 52, 75, and 68%, respectively. The identical character of IIIa-g and the samples obtained in [6] was established by mixed-melting-point determinations and by comparison of the IR spectra.

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