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The Condensation of Isatin with *o*-Phenylenediamine

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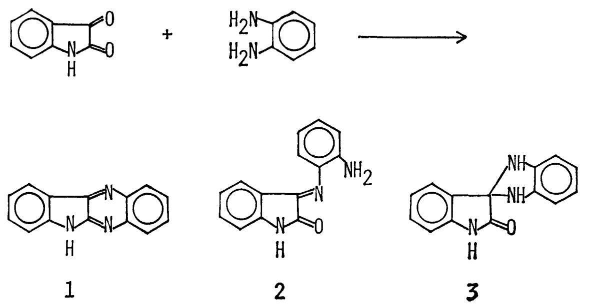
Synopsis. The condensation of isatin with *o*-phenylenediamine has been studied in various kinds of solvents. The reaction gave pure indolo[2,3-*b*]quinoxaline (**1**) in acidic solvents, while it gave a mixture containing at least two out three compounds, **1**, an anil and a spiro compound, in neutral or basic organic solvents. The anil and spiro compounds were converted to **1** in the presence of acid or by heating them above their melting points. The mechanism of the formation of these compounds and the conversion could be explained by the presence of the intermediate of the adduct formed between the amino groups of *o*-phenylenediamine and the β-carbonyl of isatin.

o-Phenylenediamine reacts with both carbonyl groups of isatin to form indolo[2,3-*b*]quinoxaline (**1**) in acetic acid.[1,2] It has been reported that spiro compounds were obtained by the reaction of a variety of isatin with aromatic *o*-diamines.[3,4] However, the formation of an anil compound has not been reported. In the present study, it was found that reaction of isatin with *o*-phenylenediamine gave **1**, anil **2**, and spiro **3** compounds, depending upon the reaction conditions. The present paper is also concerned with the conversion of the anil and spiro compounds to **1**.

Results and Discussion

o-Phenylenediamine was allowed to react with isatin in various kinds of solvents (Scheme 1).



Scheme 1.

When the reaction was carried out in acidic solvents, **1** was obtained exclusively. When polar amide solvents, such as *N*,*N*-dimethylacetamide (DMA) and *N*-methyl-2-pyrrolidone (NMP), were used, the spiro compound (**3**) was obtained in a high yield. The anil compound (**2**) was prepared at a low reaction temperature. The reaction conditions and the yields of the products are summarized in Table 1.

The IR spectra of **3** show characteristic absorptions around 1710 cm^{-1}, they are in good agreement with those observed in the similar spiro compounds prepared by Popp.[3] The carbonyl absorption of **2** was found at 1670 cm^{-1}. Figure 1 shows the infrared spectra of these compounds.

Table 1. The reaction of isatin with *o*-phenylenediamine

Reaction conditions			Yields/%[a]		
Solvents	Temp/°C	Time/h	**1**	**2**	**3**
THF	60	24	—	78	Tr
Benzene	80	7	Tr	76	Tr
Methanol	65	3	39	30	Tr
Pyridine	115	4	41	35	—
DMA	135	3	23	38	27
HMP	180	3	Tr	Tr	89
HMP	200	5	Tr	—	96
Water (HCl)	90	2	79	—	—
Acetic acid	118	3	85	—	—
PPA	140	5	91	—	—

a) Tr: The infrared spectrum of the crude products indicated a trace of the products.

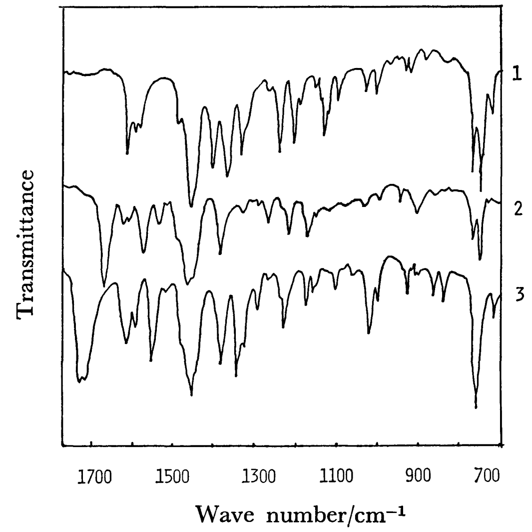


Fig. 1. Infrared spectra of **1**, **2**, and **3**.

As may be seen in Table 1, the reaction gave a mixture containing at least two products out of **1**, **2**, and **3** in neutral or basic organic solvents, while that gave **1** exclusively in acidic solvents. It is well known that ammonia reacts with the β-carbonyl of isatin at a low temperature to give the adduct **4**.[5] The analogous intermediate, **5**, would offer a reasonable explanation of the formation of **1**, **2**, and **3** in the organic solvents. The initial reaction of the amino group with the α-carbonyl of the intermediate, **5**, followed by the removal of two molecules of water would give **1**. The

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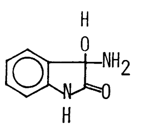

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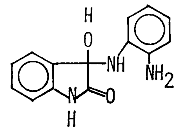

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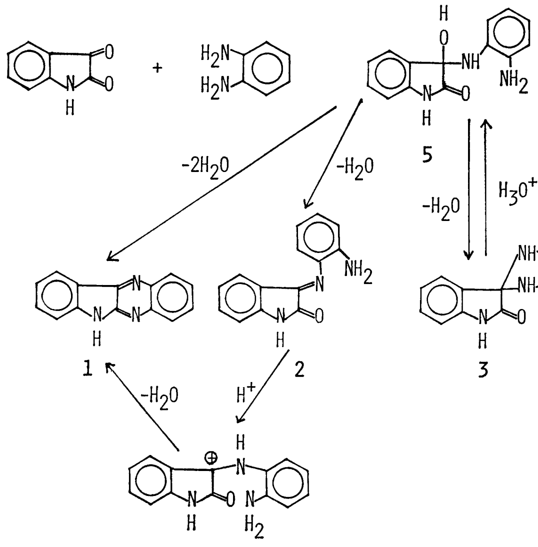
removal of one molecule of water from **5** appears to give **2**. The nucleophilic attack of the amino group on the β-carbon would lead to the formation of **3**.

Under acidic conditions, the reaction gave **1** exclusively, as has been mentioned previously, and **2** was easily converted to **1** by heating it in acetic acid, acetic anhydride, and polyphosphoric acid (PPA). The facile conversion in the presence of acid is accounted for by the *syn-anti* isomerism of the Schiff base. Apparently, **2** takes the *anti* form preferably, but it would be required to isomerize to the *syn* form, which provides the geometry necessary for the cyclodehydration. Under acidic conditions, the C–N double bond is protonated and the *anti-syn* interconversion is facilitated *via* the conjugated acid of the Schiff base.

In contrast to **2**, **3** was recovered unchanged after heating in acetic anhydride, formic acid, and PPA. However, it was easily converted to **1** by heating it in dilute hydrochloric acid. These results show that the conversion of **3** to **1** also proceeded *via* the intermediate, **5**, which was formed by the hydrolysis of the midazoline ring.

The formation of **1**, **2**, and **3**, and the rearrangements are summarized in Scheme 2.

It was also found out that **2** and **3** were rearranged into **1** by heating. The conversion of **2** proceeded very rapidly above its melting point. Figure 2 shows the TG-DSC curves for **2**. The conversion of **3** is a dehydration reaction involving the C–N bond cleavage, and the reaction proceeds slowly upon heating at a higher temperature than 280 °C.



Scheme 2.

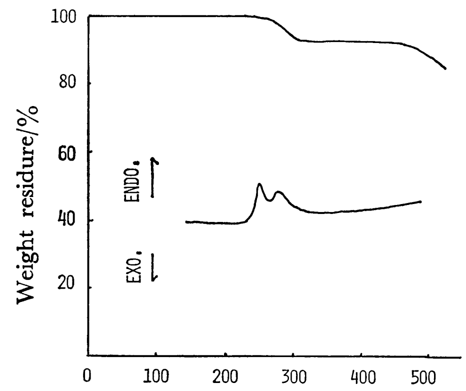


Fig. 2. TG-DSC for the conversion of **2** under nitrogen.

Experimental

*3-(*o*-Aminophenylimino)indolin-2-one (2).* A 1.47 g (0.01 mol) of isatin and 1.08 g (0.01 mole) of *o*-phenylenediamine were dissolved in 70 ml of benzene. The solution was refluxed for 7 h and then allowed to stand at room temperature overnight to give orange needles, which were subsequently collected by filtration and washed with water. The spectrum of the crude product indicated the presence of small quantity of **1**. Recrystallization from methanol gave 1.85 g (78%) of **2** as orange needles; mp 249.5—250 °C. Found: C, 70.15; H, 4.87; N, 17.61%. Calcd for $C_{14}H_{11}N_{13}O$: C, 70.87; H, 4.67; N, 17.71%.

*1,3-Dihydrospiro[benzimidazole-2(3*H*),3′-indolin]-2′-one (3).* A solution of a 1.47 g (0.01 mol) of isatin and 1.08 g (0.01 mol) of *o*-phenylenediamine in 40 ml of NMP was heated at 200 °C for 5 h. After cooling, the solution was poured into 500 ml of water to give a yellow precipitate, which was collected by filtration, washed with water, and dried. The IR spectrum of the crude product indicated the presence of a trace of **1**. Recrystallization from methanol gave 2.3 g (96%) of **3** as yellow crystals; mp 285—287 °C. Found: C, 70.87; H, 4.71; N, 17.62%. Calcd for $C_{14}H_{11}N_3O$: C, 70.87; H, 4.67; N, 17.71%.

References

1) E. Schunck and L. Marchlewski, *Ber.*, **28**, 2528 (1895).
2) I. Schopov and N. Popov, *J. Polym. Sci.*, *A-1*, **7**, 1803 (1969).
3) F. D. Popp, *J. Heterocycl. Chem.*, **6**, 125 (1969).
4) G. Henske and W. Lemke, *Chem. Ber.*, **91**, 101 (1958).
5) A. Reissert and H. Hoppmann, *Ber.*, **57B**, 972 (1924).