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ELECTROPHILIC SUBSTITUTION IN INDOLES, PART 18[1] HAMMETT CORRELATIONS OF THE COUPLING OF ARYL DIAZONIUM TETRAFLUOROBORATES WITH INDOLE

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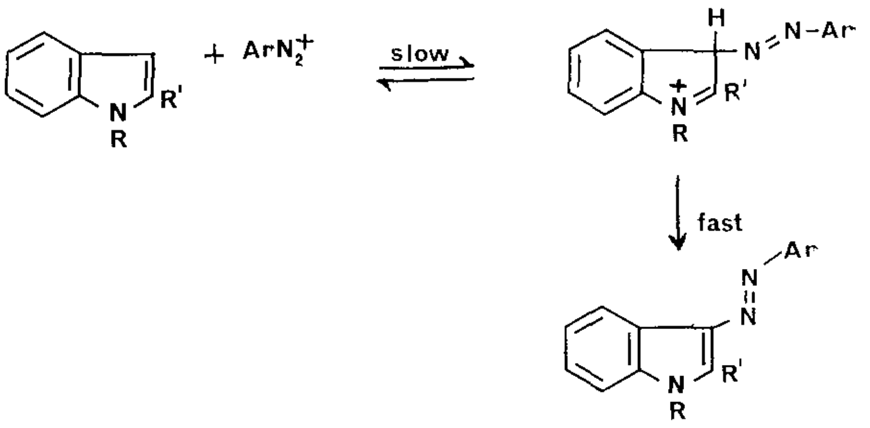
Abstract——Hammett plots for the coupling of a series of substituted aryldiazonium salts with indole and 3-methylindole show linear relationships thus confirming that the reactions are typical aromatic electrophilic substitutions.

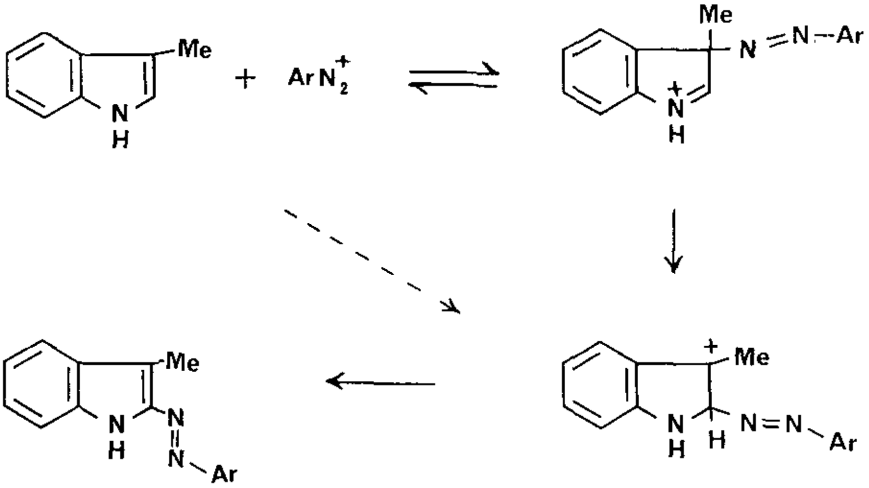
In previous studies,[1] we have investigated a variety of electrophilic substitution reactions in indoles. One of the most useful reactions for kinetic investigations was the coupling of indoles with *p*-nitrobenzenediazonium tetrafluoroborate in acetonitrile solution.[2] Under these conditions, the reactions can be readily followed spectrophotometrically as the arylazoindoles formed are yellow or orange dyes, and in this solvent the diazonium salts are presumably fully ionised. Moreover, in contrast to reactions carried out in aqueous or ethanolic solutions,[3] any decomposition or other side reactions which occur are appreciably slower in acetonitrile than the coupling reactions with indole.

Our initial studies[2] of the coupling of *p*-nitrobenzenediazonium tetrafluoroborate with indole and its 1- and 2-methyl derivatives in acetonitrile showed that the reactions were typical electrophilic substitutions in which the rate-determining step is the attack of the diazonium ion upon the indole (Scheme 1). There is no primary isotope effect with the 3-deuterioindoles, as shown both by our own work,[2] and previous studies on the coupling of *p*-nitrobenzenediazonium chloride with indole and 3-deuterioindole in aqueous ethanol.[4]



Scheme 1

The coupling of 3-methylindole with *p*-nitrobenzenediazonium tetrafluoroborate is more complex,[2] as it involves initial *ipso*-substitution at the 3-position of the indole nucleus followed by rearrangement of the arylazo group to the 2-position (Scheme 2).[2,5] Overall the formation of the 2-arylazo-3-methylindole followed essentially second order kinetics but a small deuterium isotope effect was observed for 2-deuterio-3-methylindole, and the reaction was also sensitive to base catalysis.[2]



Scheme 2

Stimulated by the classical studies of Zollinger[6] on the azo-coupling reactions of 2-naphthol- and 2-naphthylamine-6-sulphonic acids, we have now extended our kinetic studies of the azo-coupling of indole by using a range of substituted benzenediazonium salts in dry acetonitrile solution (see Figure). The reactions outlined in this paper were carried out in most cases in presence of a large excess of diazonium salt, although in a few cases an excess of indole was used. The formation of the arylazoindoles (λ_{max} ca. 360-430nm) was followed spectrophotometrically and the second order rate constants calculated in the usual manner.[2]

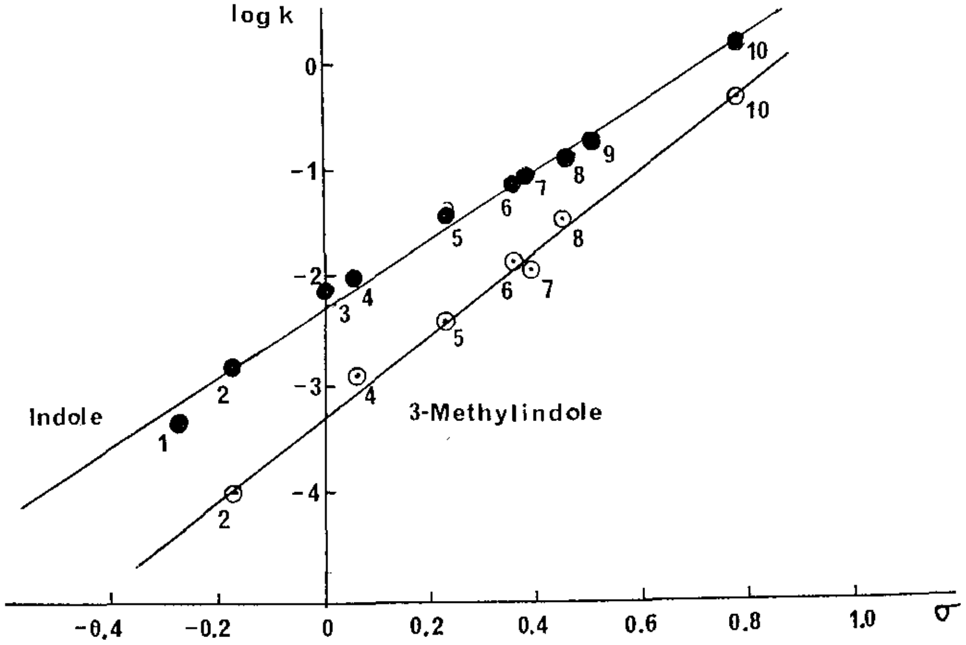


Figure: Hammett Plots for the Coupling of Substituted Benzenediazonium Tetrafluoroborates with Indole and 3-Methylindole
Substituents : **1**, *p*-OMe; **2**, *p*-Me; **3**, none; **4**, *p*-F; **5**, *p*-Cl; **6**, *m*-Cl; **7**, *p*-CO_2Me; **8**, *p*-CO_2Et; **9**, *p*-COMe; **10**, *p*-NO_2.

A Hammett plot of the rates of coupling of the various diazonium salts with indole is shown in the Figure, and as can be seen this is a straight line with a ρ-value ca. +3.4 This clearly confirmed the correctness of our earlier conclusions concerning the mechanism of the reactions (*cf.* Scheme 1) i.e. that it was a typical aromatic electrophilic substitution reaction in which the rate determining step is the attack of the electrophile.

Preliminary studies of the coupling of 3-methylindole with several of the diazonium salts were also carried out and afforded 2-arylazo-3-methylindoles. As with the reaction of *p*-nitrobenzenediazonium tetrafluoroborate[2] with 3-methylindole the reactions all showed essentially second order kinetics, even though the mechanism is slightly more complex (*cf.* Scheme 2) than that with indole (Scheme 1). The rates of the reaction with 3-methylindole were about an order of magnitude slower than those with indole and a good Hammett correlation was obtained (see Figure) with a ρ-value of +3.8. The relatively high positive ρ-values for both indole and 3-methylindole are comparable with those observed by Zollinger[6] for the azo-coupling of 2-naphthol-6-sulphonic acid (+3.4) and 2-naphthylamine-6-sulphonic acid (+4.3).

Further studies of the coupling reactions of a variety of substituted indoles are in progress and the results will be described in later papers.

Dedication

This paper is dedicated to the memory of Professor Tetsuji Kametani, one of the world's most notable and prolific organic chemists.

ACKNOWLEDGEMENTS

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