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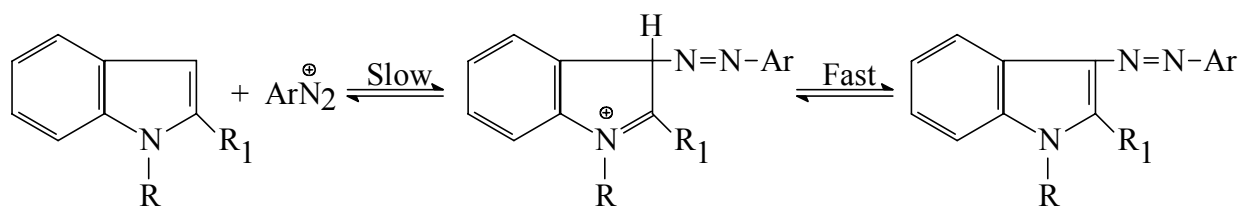
ELECTROPHILIC SUBSTITUTION IN INDOLES, PART 20' HAMMETT CORRELATIONS OF THE COUPLING OF ARYLDIAZONIUM TETRAFLUOROBORATES WITH INDOLE AND ITS 1-, 2- AND 3-METHYL DERIVATIVES

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Abstract - Hammett plots for the coupling of a range of substituted aryldiazonium tetrafluoroborate salts in dry acetonitrile with indole and its 1-, 2- and 3-methyl derivatives gave linear relationships, with ρ values *ca.* of +2.60, +2.54, +2.40 and +3.60 respectively.

As we have reported earlier,¹ electrophilic substitution reaction of indoles with aryldiazonium salts was found to be one of the most useful reactions for kinetic investigations. In this work, aryldiazonium tetrafluoroborate salts of aniline, fluoroanilin, *m*-chloroaniline, *p*-aminoacetophenone, *p*-anisidine, and ethyl *p*-aminobenzoate have been synthesized and their azo-coupling reactions with indole and its, 1-, 2- and 3-methyl derivatives in acetonitrile have been followed spectrophotometrically. First and second order rate constants were calculated. The Hammett plot of the rates of coupling of these salts with indole and its methyl derivatives gave a linear relationship with reasonable ρ values, thus confirming that the reactions are typical aromatic electrophilic substitutions, and reaction rates are in the following order: 3-methylindole < indole < *N*-methylindole < 2-methylindole.

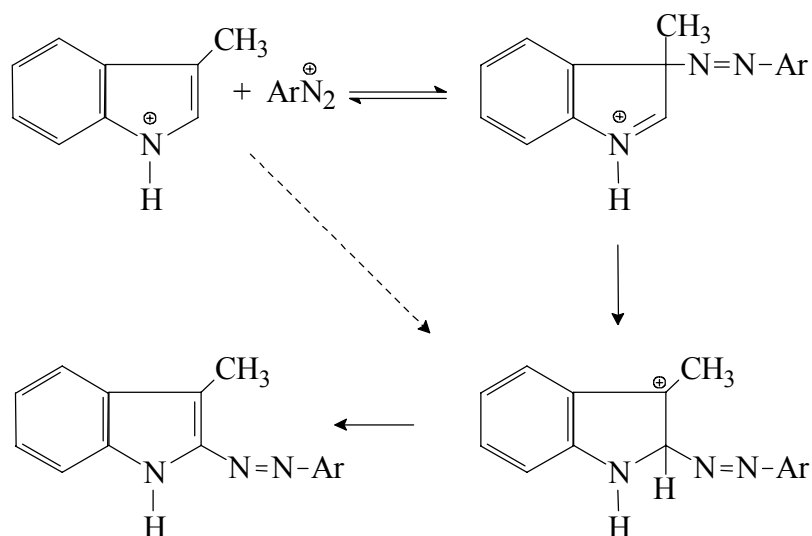
A variety of electrophilic substitution reactions of indoles have been previously reported.²⁻⁷ However, in our previous investigation¹ we reported a typical electrophilic substitution reaction of indoles with diazonium tetrafluoroborate salts in aqueous, ethanol,⁶ and in acetonitrile⁸ in which the rate determining step was the attack of the diazonium ion upon the indole (Scheme 1).



Scheme 1

Since arylazoindoles formed were colored dyes and diazonium salts are presumably fully ionized in acetonitrile, the coupling reactions in this solvent were far better than in aqueous or ethanolic solutions. The decomposition or side reactions which occur were much slower in acetonitrile than the coupling reactions with indole.^{8,9}

The coupling of 3-methylindole with diazonium tetrafluoroborate salts is more complex because it involves initial *ipso* attack at the 3-position of the pyrrole followed by rearrangement of the arylazo group to the 2-position (Scheme 2). The formation of the 2-arylo-3-methylindole follows an overall second order kinetics with small deuterium isotope effect and some sensitivity to base catalysis.⁸



Scheme 2

In this work, kinetic studies of the azo-coupling of *N*-methyl- and 2-methylindole were carried out by using a series of *para* and *meta* substituted benzenediazonium tetrafluoroborate salts in dry acetonitrile. In most cases a large excess of the diazonium salt, and in a few cases an excess of indole, was used and the formation of the colored arylazoindoles was followed spectrophotometrically (λ_{max} ca. 300-550 nm) and the second rate constants were calculated and compared with those of indole and 3-methylindole studied previously.¹

The Hammett equation, $\log(k/k^{\circ}) = \rho\sigma$, has provided a quantitative approach to the correlation of a large number of side chain reactions of aromatic derivatives. Here, ρ is the reaction constant (the slope of the straight line) and σ is the substituent constant.

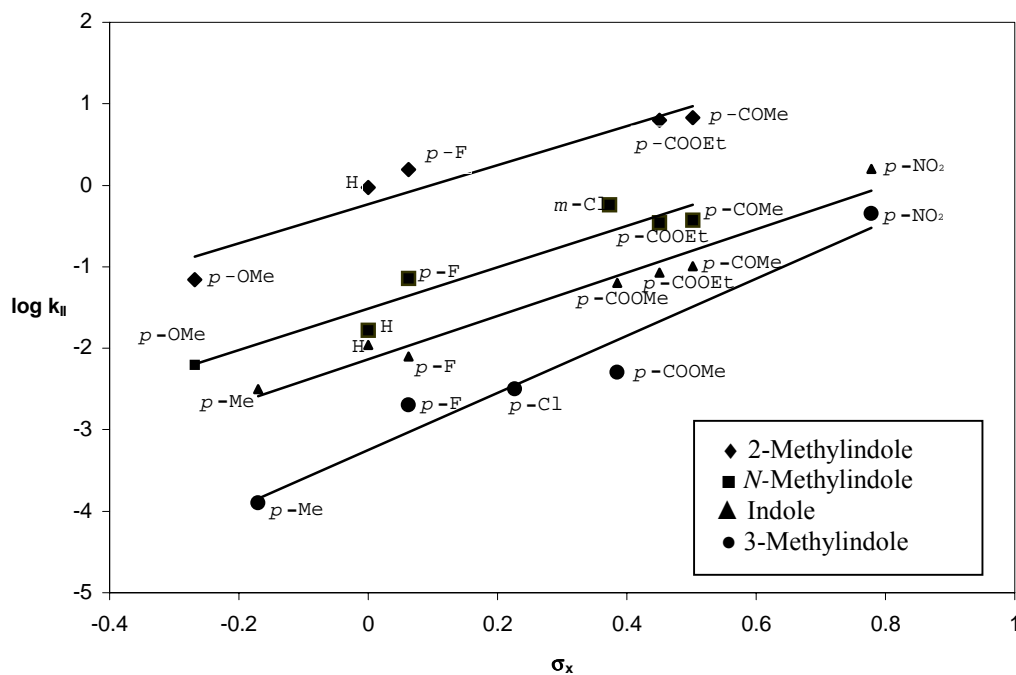


Figure 1. Hammett plots for coupling of *para* and *meta* substituted benzenediazonium salts with indole, *N*-, 2- and 3-methylindole.

Hammett plots for the coupling of the series of diazonium salts with indole and its methyl-derivatives gave a linear relationship, as shown in Figure 1, thus confirming that the reactions are classical aromatic electrophilic substitution reaction in which the rate-determining step is the attack of the diazonium upon the indoles. Values of ρ for indole, *N*-methylindole, 2-methylindole and 3-methylindole were found to be 2.60, 2.54, 2.40 and 3.60, respectively, as shown in Table 1.

Compound	ρ	Correlation coefficient
Indole	2.60	0.9617
<i>N</i> -Methylindole	2.54	0.9174
2-Methylindole	2.40	0.9150
3-Methylindole	3.60	0.9534

Table 1. ρ and correlation coefficients of indole, *N*-, 2-, and 3-methylindoles.

The rate of the reaction with 3-methylindole was an order of magnitude slower than that of the indole. 2-Methylindole was the fastest while 3-methylindole was the slowest. However, from ρ values we could see that a good Hammett correlation was obtained and that they were comparable with those values observed previously for analogous compounds.⁹

EXPERIMENTAL

Most of the kinetic runs in this study were followed from the concentration of the product azo-indole or its derivative but a few were followed from the disappearance of diazonium ion. UV spectra were determined with Carey-17 spectrophotometer. 1.3 mg of indole was dissolved in dry acetonitrile (250 mL). The concentration of the diazonium salt was approximately 50 times that of the indole. Baseline was obtained using diazonium salt in both reference and sample cells. UV cells containing diazonium salt in dry acetonitrile solution (2 mL) were placed in a water-jacketed cell holder in the spectrophotometer that was maintained at 30°C by the circulation of water from the thermostat bath. Then 0.7-1 mL of indole solution was added, mixed well and the timing started. The first order rate constant K_1 is thus calculated from the slope of the plot $\log(D_\infty - D_t)/t$ where D_t and D_∞ are the optical densities of the indole at time t and at the end of the reaction, respectively. The second order rate constant K_{11} was obtained by dividing the first order coefficient by the diazonium or indole concentration depending on which reagent was in excess.

Dedication

This paper is dedicated to the memory of Professor A. H. Jackson, one of the world's most distinguished and prolific organic chemists.

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