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**The Kinetics and Mechanism of the Condensation
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Disubstituted Benzils**

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The Kinetics and Mechanism of the Condensation Reaction Between *o*-Phenylene Diamine and *p*'*p*'-Disubstituted Benzils*

by

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ABSTRACT

The condensation reaction between *o*-phenylene diamine and para-disubstituted benzils has been studied kinetically. The reaction has been followed spectrophotometrically, at constant temperature 20°C, in strong and weak acidic media. The reaction mixture consists of 36 % water and 64 % methanol. The reaction was found to be second order in strong and weak acidic media. The rate-profile has been determined and the top of it was chosen as a common point for the study of the effect of different substituents (e.g. CH₃, CH₃O, Br, NO₂) on the reaction rate. The rate constants of the condensation reactions between *o*-phenylene diamine and different disubstituted benzils have been obtained, the ρ value is estimated as + 2.11.

The reaction mechanism has been found in accordance with the imine formation reaction.

INTRODUCTION

The quinoxaline formation from the *o*-phenylene diamine and 1,2-dicarboniles was first discovered by Körner(1) and Hinsberg(2) in 1884.

The chemistry of quinoxalines or benzopyrazines has been reviewed in three major references (3,4,5), also an outline of the

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progress in quinoxaline chemistry since 1955 up to 1963 has been reported in the review of G.W.H. Cheesman (6). Haley and Mitland studied the effect of pH on the yield of dimethyl quinoxaline formation(7), which was a preparative work.

Despite, a very large number of compounds which have been prepared by direct condensation between o-phenylene diamine and para-disubstituted benzils, several cases are on the record in which the reaction has either failed completely or has proceeded through an abnormal course. Some attempts have been made to correlate the failure of certain benzils to give quinoxalines by steric hinderance, the formation of hydrogen bond, or with their colour and the reactivity of the corresponding benzaldehydes (3,8); but non of these correlations gave a clear solution.

The authors of this article did not come across to any publication concerning the kinetics and mechanism of the quinoxaline formation. For these reasons it was thought that studying the kinetics, mechanism and the effect of substituents on the formation of 2,3-(p,p-substituted diphenyl) quinoxalines would be interesting.

In this paper the authors, studied the kinetics of the quinoxaline formation reaction between different p,p-substituted benzils and o-phenylene diamine in acidic and weak acidic aqueous methanolic (64 % MeOH, 36 % H₂O) media, the effect of the p,p-substituents on the formation rates, the correlation of Hammett substituent constants and suggested a new mechanism.

The unreactive benzils which do not condense directly with o-phenylene diamine to form quinoxalines will be dealt with in another paper.

RESULTS

The rate of the formation reaction of 2,3-diphenyl quinoxaline from direct condensation between benzil and o-phenylene diamine was determined spectrophotometrically and was found to be overall second order rate constant when kinetic runs were affected with equivalent concentrations of the reactants; and of

pseudo first order with respect to every reactant when it was taken at least 10 folds more concentrated than the other reactant. These series of kinetic runs have been carried out in weak acidic and acidic media i.e. pH 5.75 and pH 3.3 respectively (Tables 1.1 and 1.2).

TABLES 1.1 and 1.2

Rate constants of the formation of 2,3-diphenyl quinoxaline at $\lambda = 345\text{nm}$ and 20°C , produced in situ from the reaction of o-phenylene diamine.

Table 1.1: at pH=5.7 ^b			Table 1.2: at pH=3.3 ^b		
[A] ^c /M	[B] ^d /M	k/M ⁻¹ s ⁻¹	[A] ^c /M	[B] ^d /M	k/M ⁻¹ s ⁻¹
1.43 10 ⁻⁴	1.43 10 ⁻⁴	1.319 ^e	1.43 10 ⁻⁴	1.43 10 ⁻⁴	1.366 ^e
1.43 10 ⁻³	1.43 10 ⁻⁴	1.341 ^f	2.14 10 ⁻³	1.43 10 ⁻⁴	1.394 ^f
1.79 10 ⁻³	1.43 10 ⁻⁴		2.50 10 ⁻³	1.43 10 ⁻⁴	
2.14 10 ⁻³	1.43 10 ⁻⁴		2.86 10 ⁻³	1.43 10 ⁻⁴	
1.43 10 ⁻⁴	1.43 10 ⁻³	1.337 ^f	1.43 10 ⁻⁴	1.43 10 ⁻³	1.371 ^f
1.43 10 ⁻⁴	1.79 10 ⁻³		1.43 10 ⁻⁴	1.79 10 ⁻³	
1.43 10 ⁻⁴	2.14 10 ⁻³		1.43 10 ⁻⁴	2.14 10 ⁻³	

a- Characteristic wave length of the 2,3-diphenyl quinoxaline.

b- pH 5.75 was maintained by using buffer (NaOH + Na Citrate) and pH 3,3 by (HCl + Na Citrate).

c) Total concentration of o-phenylene diamine.

d) Total concentration of Benzil.

e) Second order rate constant determined directly from the application of the integrated rate equation.

f) Second order rate constant determined by the application of pseudo first order technique.

To figure out the rate-profile of the 2,3-diphenyl quinoxaline a series of kinetic runs were made in the pH range from 2 to 7 using different buffers, and keeping the reacting medium at the proportion of 36 % H₂O and 64 % MeOH (Table 2). Bell shaped rate-profile was obtained (Fig.1).

It was thought that the maximum point of the rate-profile would provide a good common point for comparing the effect of the different p,p' -bis substituted benzils on the formation rates of the corresponding quinoxalines. Any other point would have been subject to large errors since any slight change in pH of media will give rise to a big error in the k' values due to the steep slope of the right-hand left-hand parts of the rate-profile. As it will be

TABLE 2

Pseudo first order rate constants k' for the formation of 2,3-diphenyl quinoxaline at $\lambda_q=345^a$ nm and 20°C , produced in situ from reaction of o-phenylene diamine^b, with benzil^c.

pH	$10^3 k' / \text{s}^{-1}$	pH	$10^3 k' / \text{s}^{-1}$
2.00 (d)	0.176	5.48 (e)	2.493
2.88 (d)	0.870	5.75 (e)	1.632
3.55 (d)	2.339	5.88 (e)	1.673
4.00 (d)	3.253	5.98 (e)	1.003
4.81 (d)	3.286	6.22 (f)	0.948
5.02 (e)	2.947	7.00 (f)	0.274
5.05 (e)	3.023		

- a) Wave length of the characteristic peak of 2,3-diphenyl quinoxaline.
 b) Total concentration of o-phenylene diamine = $1.43 \cdot 10^{-4} \text{M}$.
 c) Total concentration of benzil = $1.43 \cdot 10^{-3} \text{M}$.
 d) (HCl + Na Citrate) buffer.
 e) (NaOH + Acetic acid) buffer.
 f) (NaOH + Na Citrate) buffer.

seen from the following results that changing substituents changes the location of the peak of the rate-profile, so any constant pH value will never correspond to the same point on the rate-profile of the other compounds.

A series of kinetic runs for 2,3-diphenylquinoxaline formation reaction were made at its maximum point (pH=4.5) of the rate profile (Table 3), and the second order rate constant was found to be $2.27 \text{ M}^{-1} \text{S}^{-1}$ at 20°C .

In studying the condensation reactions of the p,p'-disubstituted benzils with o-phenylene diamine a common procedure was followed: A series of kinetic runs within limited pH range were done to figure the upper part of the rate-profile and hence to point out the pH (pH_{max}) value where the formation rate reaches its maximum. Afterwards a series of pseudo first order reactions were made to determine the overall second order rate constant at pH value for every substituent. Values and rates for the formation of 2,3-(di-p-methylphenyl); 2,3-(di-p-bromophenyl) and 2,3-(di-p-nitrophenyl) quinoxalines from the corresponding p,p'-disubstituted benzils and o-phenylene diamine are listed in table 4.

In studying the condensation of 4,4'-dimethoxybenzil with o-phenylene diamine, the benzil compound was precipitated at the

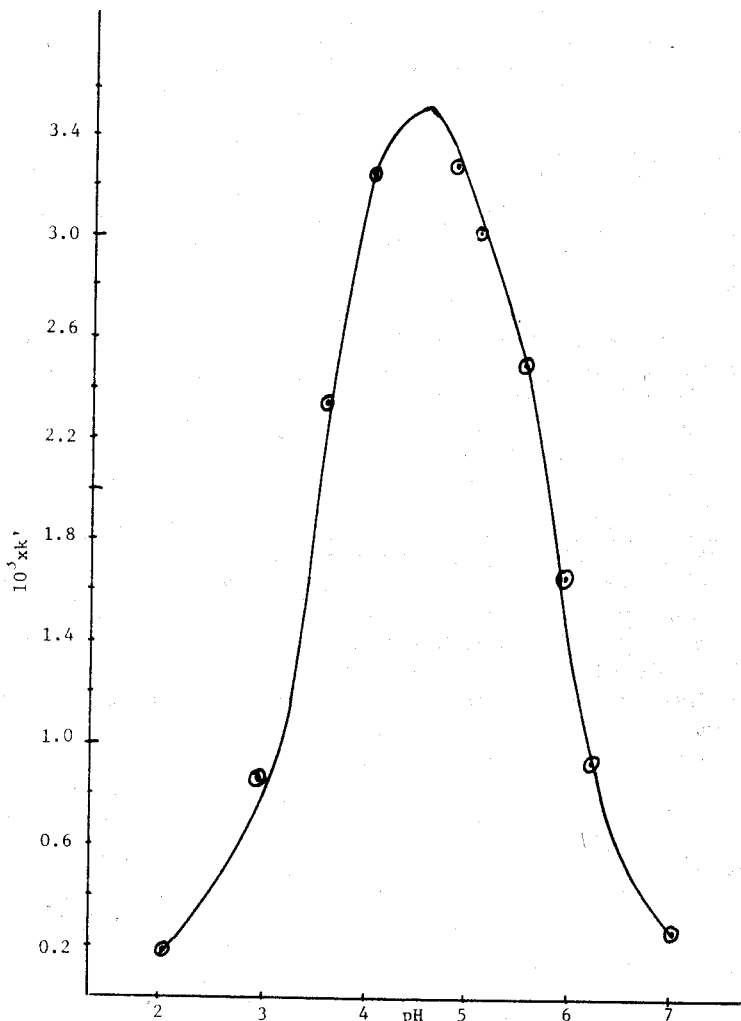


FIGURE 1. Rate-profile for the formation of 2,3-diphenyl quinoxaline from the condensation reaction of o-phenylene diamine and benzil.

TABLE 3

First order rate k' for the formation of 2,3-diphenyl quinoxaline at λ_q 345^anm, and 20°C, produced in situ from the reaction of $1.43 \cdot 10^{-4}$ M o-phenylene diamine and benzil at $\text{pH}=4.5^b$.

$10^3 [\text{Benzil}] / \text{M}$	$10^3 k' / \text{s}^{-1}$
1.43	3.556
1.57	3.777
1.71	4.155
1.86	4.548
2.00	4.753
2.14	5.161

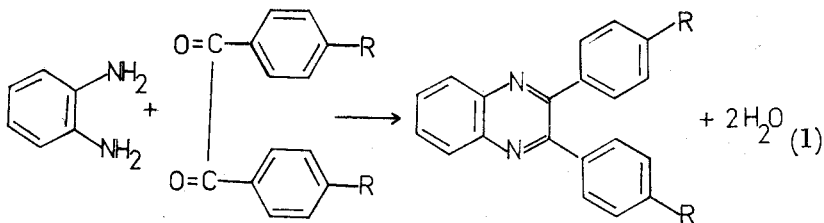
- a- Wavelength of the characteristic peak of the 2,3-diphenyl quinoxaline.
b- (NeOH + Na citrate) buffer.

TABLE 4

Second order overall rate constants (k), for the formation of some 2,3 (di-p-substituted phenyl) quinoxalines produced in situ from the reaction of o-phenylene diamine with corresponding p,p' disubstituted benzils at 20°.

R	λ_q^a / nm	pH_{max}^c	$k / \text{M}^{-1} \text{s}^{-1}$
CH ₃	354	4.68 ^c	0.648
Br ^b	349	4.1 ^d	3.95 ^e
No ₂	344	3.5 ^d	115

- a- Characteristic wave length of the formed quinoxaline
b- p,p'disubstituted benzil's concentration was kept below $0.5 \cdot 10^{-3}$ M to avoid its precipitation in the reaction medium.
c- By using (NaOH + Na Citrate) buffer.
d- By using (HCl + Citrate) buffer.
e- k' values (pseudo first order rate constants) were calculated by Guggenheim method because of the uncertainty observed in A_∞ values.



working concentration (at 20°C) and the reaction was found to be very slow. To avoid the precipitation problem and to speed up the reaction to a reasonable limit, it was thought that the application

of Arrhenius equation and working at high temperature; the required rate constant could be estimated. pH_{max} was found to be 4.75 (Table 5.1).

TABLE 5.1

First order rate k' value^a for the formation of 2,3-(di-*p*-methoxy phenyl) quinoxaline at 370 nm and 40°C, produced in situ from the reaction of *o*-phenylene diamine^b with anisil^c.

pH	$10^4 k' / \text{s}^{-1}$
4.38 d	3.45
4.48 d	3.95
4.7 d	4.11 (4.108) ^f
5.1 e	3.57

a- k' values were estimated according to Guggenheim method.

b- The total concentration of *o*-phenylene diamine = $1.43 \cdot 10^{-4}$ M.

c- The total concentration of Anisil = $1.43 \cdot 10^{-3}$ M.

d- (HCl + Na Citrate) buffer.

e- (NaOH + Na Citrate) buffer.

f- This value was determined after fixing the A_{∞} for a long period (15 hrs), for the sake of comparison.

Two series of kinetic runs to determine the second order rate constant at pH_{max} were carried at 30° and 40° (Table 5.2). The second order rate constant at these temperatures were calculated and the estimated k value corresponding to 20°C was calculated by application of Arrhenius equation, to be $0.055 \text{ M}^{-1}\text{s}^{-1}$ (Table 5.3 Figure 2).

TABLE 5.2

First order rate constants (k') for the formation of 2,3-(di-*p*-methoxyphenyl) quinoxaline at λ_q 370 nm, 30°C and 40°C; produced in situ from the reaction of Anisil and *o*-phenylene diamine^a at pH_{max} ^b 4.75.

$10^3 [\text{Anisil}] / \text{M}$	$10^4 k' / \text{s}^{-1} (\text{Temp. } 30^\circ\text{C})$	$10^4 k' / \text{s}^{-1} (\text{temp. } 40^\circ\text{C})$
1.25	3.14	4.11
1.07	2.88	3.45
0.893	2.69	2.76

a- Total concentration of *o*-phenylene diamine = $1.43 \cdot 10^{-4}$ M

b- (HCl + Na Citrate) buffer.

DISCUSSION: The comparison of the overall k values determined at the pH_{max} of the 2,3 (*p,p'*-disubstituted phenyl) quino-

TABLE 5.3

Second order rate constants at $\text{pH}_{\text{max}} = 4.75$ for the formation of 2,3-(di-p-methoxyphenyl) quinoxaline.

Temperetue	$10^3 1/T$	$k/M^{-1}s^{-1}$	logk
40°	3.195	0.367	0.435
30°	3.30	0.144	0.841
20°	3.413	0.055	1.26

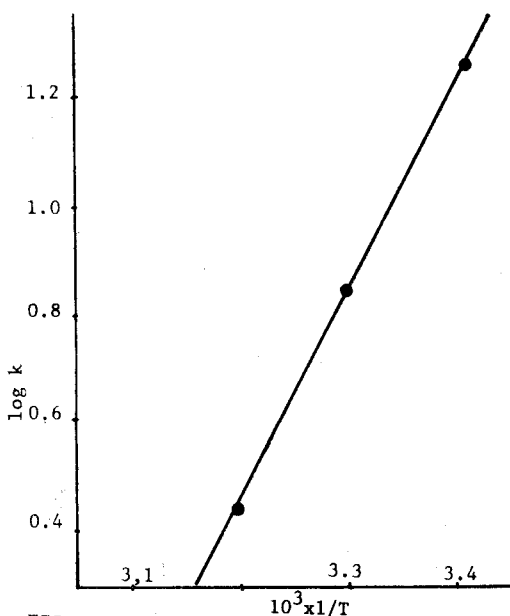


FIGURE 2. Second order rate constants for the formation reaction of 2,3-(p,p'-dimethoxy phenyl) quinoxaline at different temperatures.

xalines shows that electron releasing groups like methyl and methoxy groups slow down the formation reaction whereas, the electron withdrawing groups like bromo and nitro groups increase the reaction rate. Meanwhile it was observed that the electron releasing groups gave rise to a shift of the rate-profile and hence the pH_{max} to less acidic side and the electron withdrawing groups to the more acidic side.

It was found that $\log k$ values gave a satisfactory linear Hammett substituent effect correlation when it was plotted against

σ^+ values of the different substituents and ρ value was calculated to be 2.11 (Table 6, Fig. 3).

TABLE 6

Second order rate constants of the formation reaction of the different 2,3-(p,p') disubstituted diphenyl) quinoxalines, at 20°C, produced in situ from the corresponding benzils and o-phenylene diamine.

Substituent	ρH_{\max}	$\sigma^+(9)$	$k/M^{-1}s^{-1}$	log k
CH ₃ O-	4.75	-0.78	0.055	-1.26
CH ₃ -	4.68	-0.31	0.65	-0.19
H-	4.5	0.0	2.27	0.356
Br-	4.1	0.15	3.95	0.604
NO ₂ -	3.5	0.79	115.0	2.06

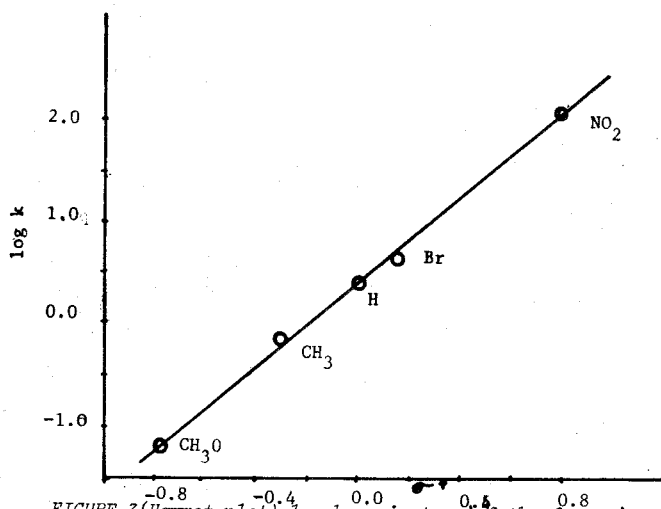
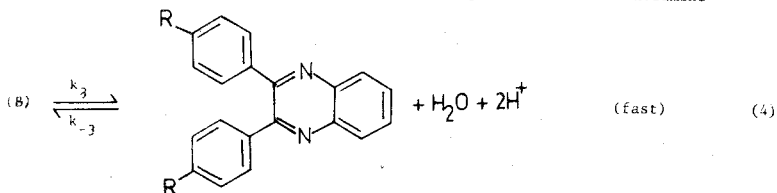
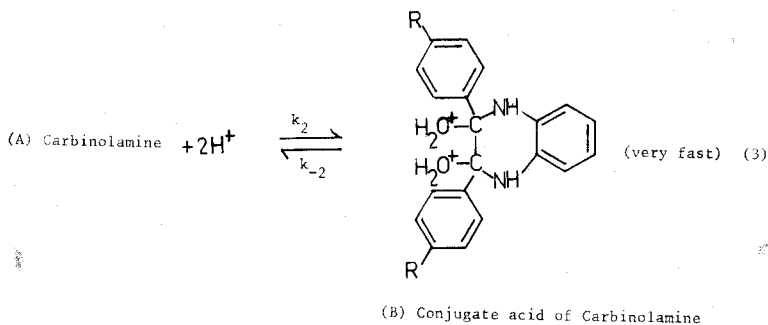
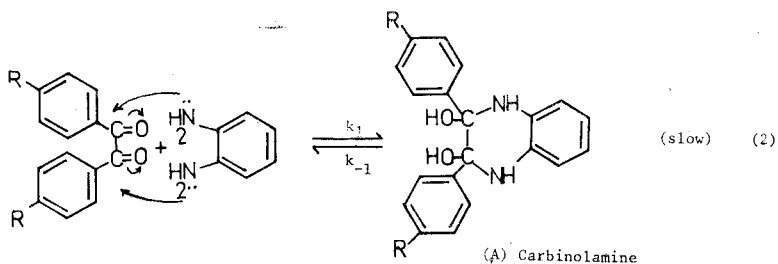


FIGURE 3 (Hammett plot) $\log k$ against σ^+ of the formation reactions of different 2,3-(p,p') disubstituted diphenyl) quinoxalines from the condensation reactions of o-phenylene diamine and corresponding benzils.

The proposed formation mechanism (equations 2,3 and 4) which proceeds through three steps, suggests that the electron withdrawing substituents on the p and p' positions of the reacting benzil would increase its electrophilicity by increasing the positive charge on the carbon atoms of the carbonyl groups so that amino groups of o-phenylene diamine attack them readily and hence it

would increase the overall reaction rate, since the first step considered as the rate determining step. Meanwhile it would decrease the protonation affinity of the formed carbinolamine and consequently the rate profile will be shifted to the more acidic pH region to compensate this decrease. The increase of the polar effect of the withdrawing substituent will increase the partial positive charge on the carbonyl group carbon atoms and hence will speed up the formation reaction and will shift the pH_{max} value to the more acidic region.



On the otherhand the electron donating groups would decrease the partial positive charge and expectedly will exert an oposit

effect on the formation overall rate and hence will shift the pH_{max} . value to less acidic pH regions.

The linear Hammett correlation shows that there is no change in the rate-determining step and that the quinoxaline formation in acidic and weak acidic media is of the same character of the general imine formation.

EXPERIMENTAL

Materials : The chemicals used in this study were puriss grade of Fluka Ag. Buchs g. Company. Benzils used in the kinetic study have been prepared by two methods: The benzil itself, p,p'- and p,p'-dimethoxy derivatives have been prepared from the corresponding benzoin which was obtained respectively from the condensation of the corresponding aldehydes. p,p'-dibromo and p,p'-dinitrobenzil have been prepared by the action of HNO_3 and HBr on 4,5-diphenyl glyoxalone respectively (10).

The corresponding diphenyl quinoxalines have been prepared by direct condensation of benzils and o-phenylene diamine in acetic acid medium under reflux (11).

The obtained benzils and quinoxalines and their uncorrected m.p.'s are listed in tables 7.1 and 7.2.

TABLE 7.1

Benzil	Lit. m.p.	Obtained m.p.
Benzil	94-6° (12)	95-6°
p,p'-dimethyl benzil	104-5° (13)	105-6°
p,p'-dimethoxy benzil	133° (13)	133°
p,p'-dinitro benzil	213° (14)	212°
p,p'-dibromo benzil	228-9° (15)	229°

TABLE 7.2

Quinoxaline	Lit. m.p.	Obtained m.p.
2,3-diphenyl	124° (16)	124° (Et OH)
2,3-di-p-methylphenyl	144-5° (17)	150-2° (Et OH)
2,3-di-p-methoxyphenyl	145-6° (16)	147.5-148° (EtOH)
2,3-di-p-nitrophenyl	203-4° (11)	203-203.5° (AcOH)
2,3-di-p-bromophenyl	188-9° (18)	190-2° (EtOH)

KINETIC METHOD

The kinetic measurements were made with a Beckman DB-G Grating spectrophotometer equipped with a jacketed cell holder maintained generally at 20° ($\pm 0.01^\circ$). Solutions were equilibrated at this temperature prior to mixing and the reaction was initiated by the addition of freshly prepared o-phenylene diamine to the reaction mixture containing the benzil and the buffer solutions. The pH of the solutions was measured with glass and Calomel electrodes using Beckman's H 3 pH meter.

The reactions were followed spectrophotometrically at the characteristic peak of the formed quinoxaline (λ_q) where no other component gave any observable absorbance.

For calculating the pseudo first order rate constants, Wiberg's (19) programme for single first order kinetic runs written in Fortran II, was modified for calculating first order k' values for many kinetic runs at different concentrations and to give the corresponding second order constant simultaneously, using the least squares method for calculating each k' value, and transmittance values instead of the absorbance values for the sake of accuracy.

A minor modification was made for the programme prepared by Wiberg (19) for calculating the second order rate constant, written in Fortran II by replacing the absorbance input values by transmittance ones. These modified programmes will be published elsewhere.

Both programmes were rewritten in Fortran IV and run by B 3500 Burroughs Computer with 120 KB type memory.

REFERENCES

- 1- G. Körner, Ber. 17, ref. 573 (1884).
- 2- O. Hinsberg, Ber. 17, 318 (1884).
- 3- J.C.E. Simpson, "Condensed Pyrazine and Pyrazine Rings", Interscience, Newyork, 1953.
- 4- Y.T. Pratt, in "Heterocyclic Compounds" (Ed. R.C. Elderfield), Vol. 6, chapter 10, Wiley, Newyork, 1956.
- 5- G.R. Ramage and J.K. Landquist, in "Chemistry of Carbon Compounds" (E.H. Rodd, ed.), Vol. IV B, Chapter XV, Elvesier, Amesterdam, 1959.

- 6- G.W.H. Cheesman, "Recent Advances in Quinoxaline Chemistry", Advanced Heterocyclic Chemistry", (C.A.R. Katritzky, ed.) Academic press, Vol 2, pp 203-44 (1963).
- 7- C.A.C. Haley and P. Maitland, J. Chem. Soc; 1951, 3158.
- 8- R.C. Fuson and Q.F. Soper, J. Org. Chem., 9, 193 (1944).
- 9- J.E. Lefler and E. Grunwald, "Rates and Equilibria of Organic Reactions" Jonh Wiley 1963, table 7.7.
- 10- H. Biltz, Ann., 368, 173 (1909).
- 11- H. Gilman and H.S. Broadbent, J. Am. Chem. Soc., 70, 2619-21 (1948).
- 12- A.I. Vogel, A "Text Book of Practical Organic Chemistry" part I, 3rd edition, Longmans, 1967, P. 714.
- 13- B. Klein, J. Am. Chem. Soc., 63, 1474 (1941).
- 14- F.D. Chattaway and E.A. Coulson, J. Chem. Soc., 1928, 1361.
- 15- H. Biltz, Ber., 41, 1761 (1908).
- 16- R.W. Bost and E.E. Towell, J. Am. Chem. Soc., 70, 903 (1948).
- 17- G. Derfahl and K. Winnfeld, J. Prakt. Chem., 28, (5-6), 236-41 (1965).
- 18- O. Buchardt and B. Jensen, Acta. Chem. Scand., 22, 877-82 (1968).
- 19- K.B. Wiberg, "Computer Programming for Chemists", W. A. Benjamin Inc., 1965.

ÖZET

Bu çalışmada o-fenilen diamin ile p,p'-disübstitüe benzillerin kondensasyon reaksiyonu incelenmiş, metanol ve su karışımında, zayıf asidik ve asidik ortamda 20°C de incelenen bu reaksiyonun ikinci mertebeden cereyan ettiği tesbit edilmiştir. Reaksiyon spektrofotometrik metotla izlenmiş, k'psöydo 1. mertebe ile k ikinci mertebe hız sabitleri hesaplanmıştır. Reaksiyonun Hız-Profilini tayin edilmiş, Hız-Profilinin zirve noktası bütün substratlar için ortak inceleme noktası seçilmiş ve CH₃, CH₃O, Br, NO₂; gruplarının benzilin p,p'-yerlerine girmeleriyle reaksiyon hızında meydana gelen hız değişiklikleri tesbit edilmiş, Hız-Profilinin zirve noktasında 2. mertebe hız sabitleri incelenmiştir. Elde edilen k değerlerinin logaritmaları σ^+ ya karşı çizilerek Hammett korrelasyonuna uygunluğu tesbit edilmiş ρ değeri + 2,11 olarak hesaplanmıştır. Reaksiyon yürüyüşünün imin formasyon reaksiyonlarının mekanizmasına benzer şekilde cereyan ettiği tesbit edilmiştir.

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