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A LA MEMOIRE D'ATATÜRK AU CENTENAIRE DE SA NAISAANCE

Kinetic Study on the Effect of Substituents on the Base-catalysed Darzens' like Condensations.

by

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DEDICATION TO ATATÜRK'S CENTENNIAL

Holding the torch that was lift by Atatürk in the hope of advancing our Country to a modern level of civilization, we celebrate the one hundredth anniversary of his birth. We know that we can only achieve this level in the fields of science and technology that are the wealth of humanity by being productive and creative. As we thus proceed, we are conscious that, in the words of Atatürk, "the truest guide" is knowledge and science.

As members of the Faculty of Science at the University of Ankara we are making every effort to carry out scientific research, as well as to educate and train technicians, scientists, and graduates at every level. As long as we keep in our minds what Atatürk created for his Country, we can never be satisfied with what we have been able to achieve. Yet, the longing for truth, beauty, and a sense of responsibility toward our fellow human beings that he kindled within us gives us strength to strive for even more basic and meaningful service in the future.

From this year forward, we wish and aspire toward surpassing our past efforts, and with each coming year, to serve in greater measure the field of universal science and our own nation.

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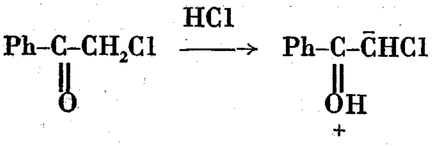
SUMMARY

The kinetics of the base-catalysed condensation of phenacyl chloride, p-methoxy-, p-methyl and p-chlorophenacyl chlorides with phenanthrenequinone were followed potentiometrically at different temperatures. The condensations follow overall third order kinetics, first with respect to each constituent. The rate of condensation increases with increasing electron-withdrawing power of the substituents. The rate also increases as the dielectric constant of the solvent increases. The attempts to achieve acid-catalysed Darzens' condensations failed with phenanthrenequinone and with p-nitrobenzaldehyde.

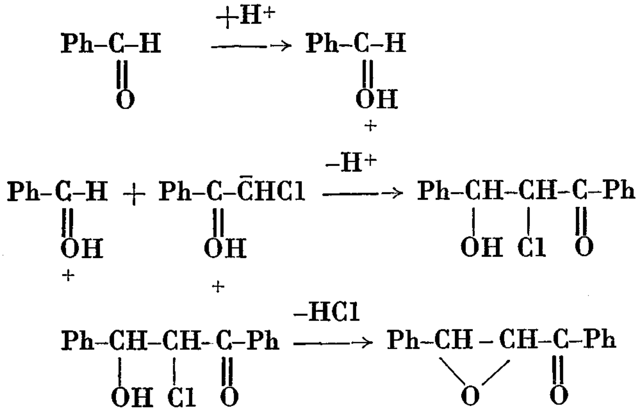
INTRODUCTION

The mechanism of the base-catalysed Darzens' condensation of phenacyl halides with benzaldehyde is generally regarded as being established by Ballester and Bartlett[1], who reported the absence of any appreciable results in attempted acid-catalysed Darzens' condensations. However, Sipos et al(2–6). claimed that the condensation of substituted phenacyl halides with substituted benzaldehydes was successfully carried out in different acid media. They reported a mechanism analogous to that of acid-catalysed aldol condensations[7]:



$$\mathrm{Ph{-}\underset{\underset{O}{\|}}{C}{-}CH_2Cl} \xrightarrow{\mathrm{HCl}} \mathrm{Ph{-}\underset{\underset{\underset{+}{OH}}{\|}}{C}{-}\bar{C}HCl}$$

(a)



$$\mathrm{Ph{-}\underset{\underset{O}{\|}}{C}{-}H} \xrightarrow{+H^+} \mathrm{Ph{-}\underset{\underset{\underset{+}{OH}}{\|}}{C}{-}H}$$

$$\mathrm{Ph{-}\underset{\underset{\underset{+}{OH}}{\|}}{C}{-}H} + \mathrm{Ph{-}\underset{\underset{\underset{+}{OH}}{\|}}{C}{-}\bar{C}HCl} \xrightarrow{-H^+} \mathrm{Ph{-}\underset{\underset{OH}{|}}{CH}{-}\underset{\underset{Cl}{|}}{CH}{-}\underset{\underset{O}{\|}}{C}{-}Ph} \qquad \text{(b) rate limiting}$$

$$\mathrm{Ph{-}\underset{\underset{OH}{|}}{CH}{-}\underset{\underset{Cl}{|}}{CH}{-}\underset{\underset{O}{\|}}{C}{-}Ph} \xrightarrow{-HCl} \mathrm{Ph{-}\underbrace{CH{-}CH}_{O}{-}\underset{\underset{O}{\|}}{C}{-}Ph} \qquad \text{(c)}$$

Since the formation of the carbanion in the first step of Darzens' condensation cannot be visualized in acid medium, we doubted the correctness of the results reported by Sipos et al[2–6]. In view of this controversy, we thought it is important to re-investigate the kinetics of Darzens'-like condensations, both in acid and in alkaline media. It is informative to try the condensation between substituted phenacyl chlorides and phenanthrenequinone, which is as reactive as p-nitrobenzaldenhyde[8].

Our study of the effect of substituents in phenacyl chloride on the rate of condensation was stimulated by our objection to the conclusion reached by Sipos et al([5–6]). They claimed that the rate was decreased by electron drawing substituents in phenacyl chloride.

EXPERIMENTAL

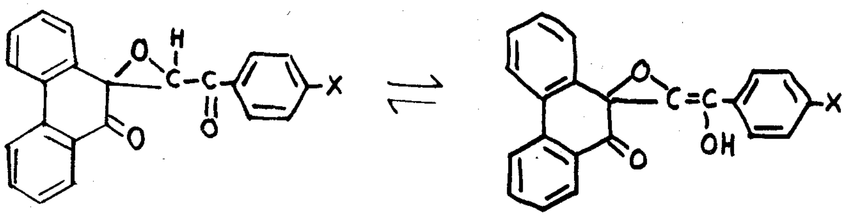
Materials: Phenacyl chloride of analytical reagent grade (m.p. 56–57 °)[9] was used. p-methoxyphenacyl chloride (m.p. 98–99 °)[10], p-methyl phenacyl chloride (m.p. 56–57 °)[11], p-chlorophenacyl chloride (m.p. 101–102 °)[12] and phenanthrenequinone (m.p. 207–208 °)[13] were prepared pure. Peroxide-free dioxan[14] and doubly distilled water were used throughout the study.

Kinetic measurements: The methods adopted for rate measurements were similar to those of Hine et al[15]. and Hanna et al[16]. involving potentiometric titration of the liberated halide ions at different intervals, against $AgN0_3$ using Ag/AgCl-quinhydrone electrode. CARL ZEISS (JENA, D.D.R.) moving scale sensitive galvanometer was employed.

The condensation reactions were carried out in 50, 60 and 70 % (v/v) dioxan-water mixtures at 1 ° (for investigating the effect of the solvent). The runs in 50 % aq. dioxan were carried out, in addition,at -3, -7 and -10 ° (for investigating the effect of the substituents). EIN (Germany) ultrathermostat (-20 ° to + 50 °, ∓0.1 °C.) was employed. The reaction was initiated by rapid addition of:

(A) concentrated solution of phenantherenequinone and phenacyl chloride (or derivative) in dioxan-water mixtures previuosly cooled to the desired temperature, to (B) a solution of sodium hydroxide in distilled water enough to adjust tc the desired molarities, also previously cooled to the desired temperature. At suitable time intervals, equal aliquots of the reaction mixture were pipetted out, quenched with 20 20 ml 0.1 N $H_2 S0_4$ and analysed for free halide ions. The reaction rates were found to be too fast to be followed accurately at temperatures above 1 °. In all runs, the reactions were followed up to 75 %. Each run was repeated 3 times to check reproducibility.

Isolation of products: The constituents were dissolved in one liter of 50 % aq. dioxan previously cooled to 1 °. The reaction mixture was kept at 1 ° for two hours, then at room temperature overnight. Crystalline solids were separated afterslow evaporation of the solvent at room temperature, washed with water and crystallized from the suitable solvent to give enol derivatives (i.r. υ 0H 3230 cm^{-1}) of spiro (oxirane--2,9'-phenanthrene)[17], of the general form:



X = H, Cl, CH_3 or $0CH_3$

The product obtained from the p-chloro derivative was an exception, where it gave a mixture of 50 % keto form and 40 % enol from at -3 °. Table (1) includes a full survey of the different products obtained.

Table 1

Products from Darzens' reactions of Chrysenequinone with p-substituted Phenacyl cçhlorides in alkaline medium.

Compound	Formula	Yield %	m.p. °C.	Found			Required			max cm⁻¹	
				C	H	Cl	C	H	Cl	OH⁻	C=0
X = H	$C_{26}H_{15}0_3$	84	238	82.55	4.61	—	82.98	4.25	11	32352	1680
X = Cl	$C_{26}H_{15}0_3Cl$	83	234	76.20	3.9	8.2	76.0	3.7	8.6	3250	1675
X = CH_3	$C_{27}H_{12}0_3$	83	220	82.70	4.8	—	83.07	4.62	—	3420	1700
X = OCH_3	$C_{27}H_{18}0_3$	79	210	79.70	4.7	—	79.83	4.43	—	3420	1673

All products crystallized from benzene

Acid-catalysed experiments: We repeated the reactions reported by Sipos et al[5,6]. for Darzens' condensation of phenacyl chloride, and its derivatives, with p-nitrobenzaldehyde in acidic media. We tried out the reaction between phenacyl chloride and its derivatives with phenanthrenequinone and with p-nitrobenzaldehyde in 50 % aq. dioxan at 1° in presence of sulphuric or phosphoric acids of concentration ranges from 3–30 %. We also attempted the phenanthrenequinone and p-nitrobenzaldehyde condensations in absolute ethanol, using 10 % and 30 % HCl gas as a catalyst, since Sipos et al. reported that they obtained the best yield in case of 30 % HCl.

In all the above cases, no reaction took place, as indicated by the isolation of the reactants unchanged. This is in clear contradicition to the results obtained by Sipos et al[5,6].When the reaction solution was neutralized, however, solid epoxides separated. These solidis were identified by melting points and mixed melting points to be the same the products obtained from the corresponding base-catalysed condensations. This might indicate that the produtcs obtained by Sipos were not formed in acid medium, but rather, only during neutralization.

RESULTS AND DISCUSSION

Kinetics: To permit accurate and reliable determinations of the rates, the molar concentrations of the reactants were not more than 0.001: 0.001: 0.01 M of phenanthrenequinone (A): phenacyl chloride (or substituted phenacyl) (B): sodium hydroxide, respectively. When higher concentrations were used, the reactions were too fast to follow accurately.

The kinetic results showed that the condensation reaction is an overall third order, first with respect to each component A, B and $0H^-$. Table (2) includes the rate constants obtained for the different molar ratios employed. Fig. 1 shows the graphical representation of pseudo-second order reactions, using excess of sodium hydroxide (1:1:10). Fig. 2 shows true third order representation when equimolar initial concentrations were used (1:1:1).

Solvent Effect: (Effect of dielectric constant): It was found that the rate of the reaction increases as the dielectric constant ofthe solvent increases, by increasing the dioxan: water (v/v) ratio. Fig. 3 shows a

Table 2

Rate constants for condensation reactions at -3° in 50 % aq. dioxan.

substituted phenacyl chloride	molar ratio of A: B: OH^-		
	1: 1: 1	1: 1: 10	1: 1: 10
(0.001 M)	k_3 l^2/mole^2. sec	k_1 l/mole. sec	k_3 l^2/mole^2. sec
p- chloro	1.25×10^2	3.33	3.33×0^2
unsubstituted	0.833×10^2	2.08	2.08×10^2
p-methyl	0.694×10^2	1.37	1.37×10^2
p-methoxy	0.463×10^2	1.14	1.14×10^2

plot of log k_3 vs. 1 /D for phenacyl chloride and its derivatives. The negative slope indicates that the reaction takes place between a negative ion and a dipolar molecule[18]. The employed compositions of the solvent were chosen on the basis that in 40 %, or less, aq. dioxan, precipitaion took place; and in 80 % or higher, aq. dioxan, the solvent became partially immiscible. Hence, only 50, 60 and 70 % aq. dioxan mixtures were used.

Effect of Substituents: Table (2) includes calculated values of k_3 at different temperatures. Table (4) includes the different activation thermodynamic parameters calculated from the temperature dependence of the rate constants, and related thermodynamic equations, for the

Table 3

Rate constants at different temperatures in 50 % aq. dioxan

Temp. °C.	k_3 l^2/mole^2. sec.			
	p-chloro	unsubstituted	p-methyl	p-methoxy
-10	2.08×10^2	1.14×10^2	0.80×10^2	0.667×10^2
-7	2.50×10^2	1.43×10	1.07×10^2	0.864×10^2
-3	3.33×10^2	2.08×10^2	1.37×10^2	1.14×10^2
+1	4.67×10^2	2.67×10^2	1.80×10^2	1.67×10^2

Table 4

Thermodynamic activation parameters

substituted phenacyl chloride	E^* K. cal /mole	ΔH^* K. cal.	ΔS^* e.u.	ΔG^*_{274} K. cal.
p-chloro	9.15	8.61	-31.70	17.29
unsubstituted	11.44	10.90	-24.46	17.60
p-methyl	12.58	12.40	-21.09	17,82
p-methoxy	13.07	12.53	-19.44	17.85

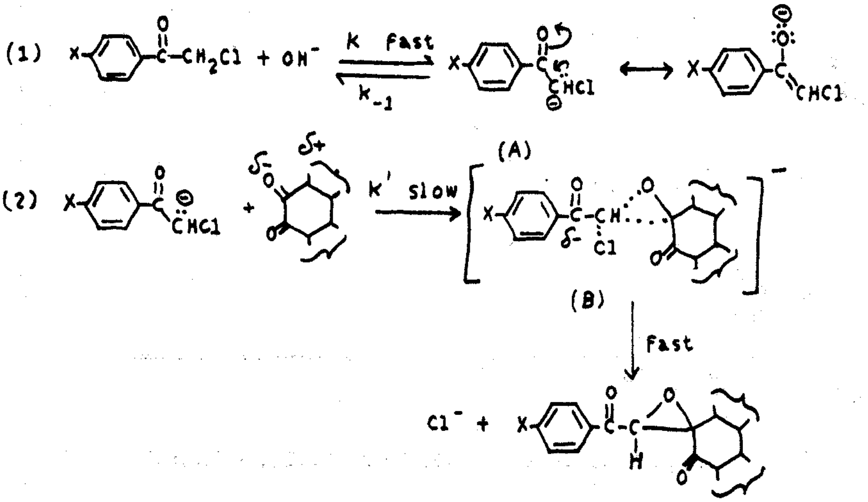
different substituted phenacyl chlorides investigated. It is clear from examination of the values in Table (4) that the order of accelerating the reaction is:

$$Cl > H > -CH_3 > -OCH_3$$

This conclusion is also substantiated by the linear relationship of log k vs. σ, showing conformity to the Hammett equation (Fig. 4) A positive value of ρ shows that the rate is enhanced by withdrawal of electron density from the reaction center, and vice versa.

This order of acceleration by the substituents is in clear contradiction to the order claimed by Sipos et al(5,5). who reported the exact opposite order, with no justification.

Mechanism: Based on all the foregoing discussion of the results, we can propose the following mechanism, which is similar to that given by Ballester[1]:



X = Cl, H, $-CH_3$ or $-OCH_3$

Since the reaction was found to be third order, hence, step (2) is considered to be the rate-limiting step. It can seen that the formation of the product in step (1) is favoured by electron withdrawal in the indicated direction, thus facilitating the removal of the H^+ by the OH^- group, and stabilizing the developed negative charge. This can explain the order of reaction acceleration of the different substituents that we report.

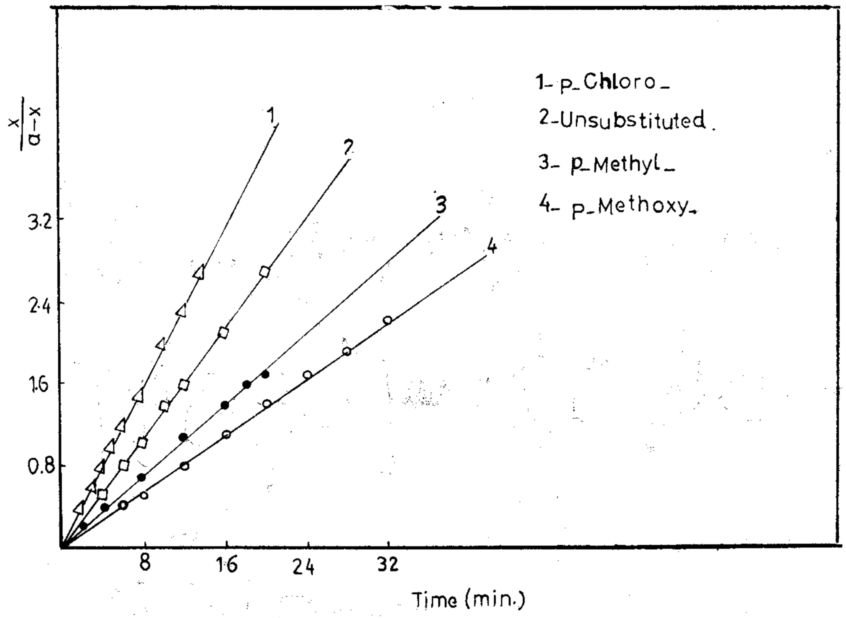


Fig. 1 Pseudo second order kinetics at − 3 . Molar ratios 1:1:10

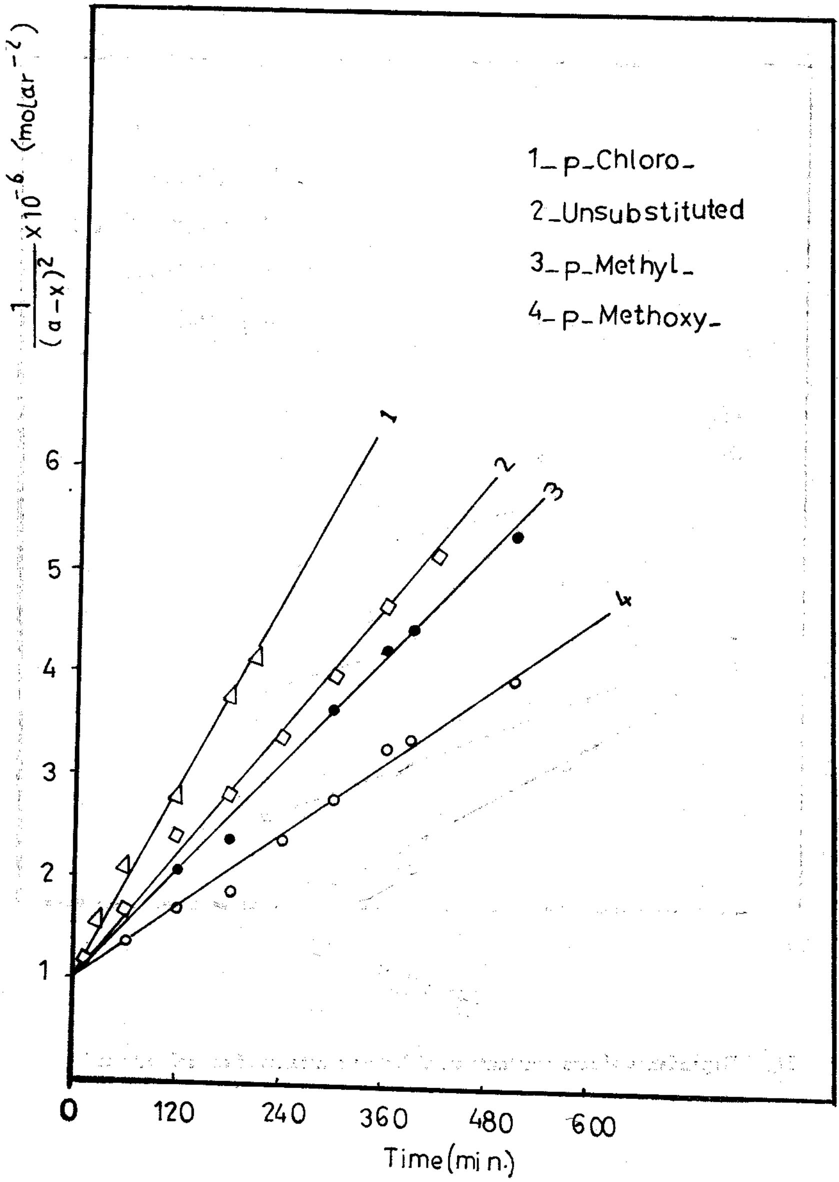


Fig. 2 True third order kinetics at – 3 . Molar ratios 1:1:1

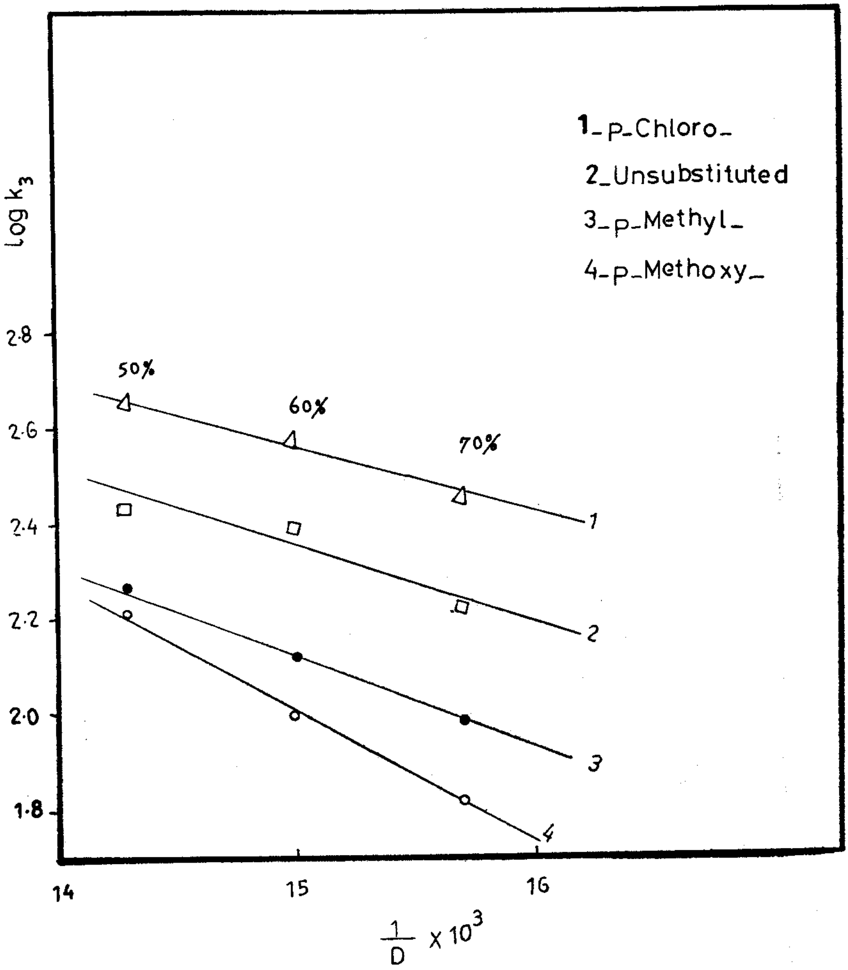


Fig. 3 Dependence of rate constants on dielectric constants of the solvents at 1° C

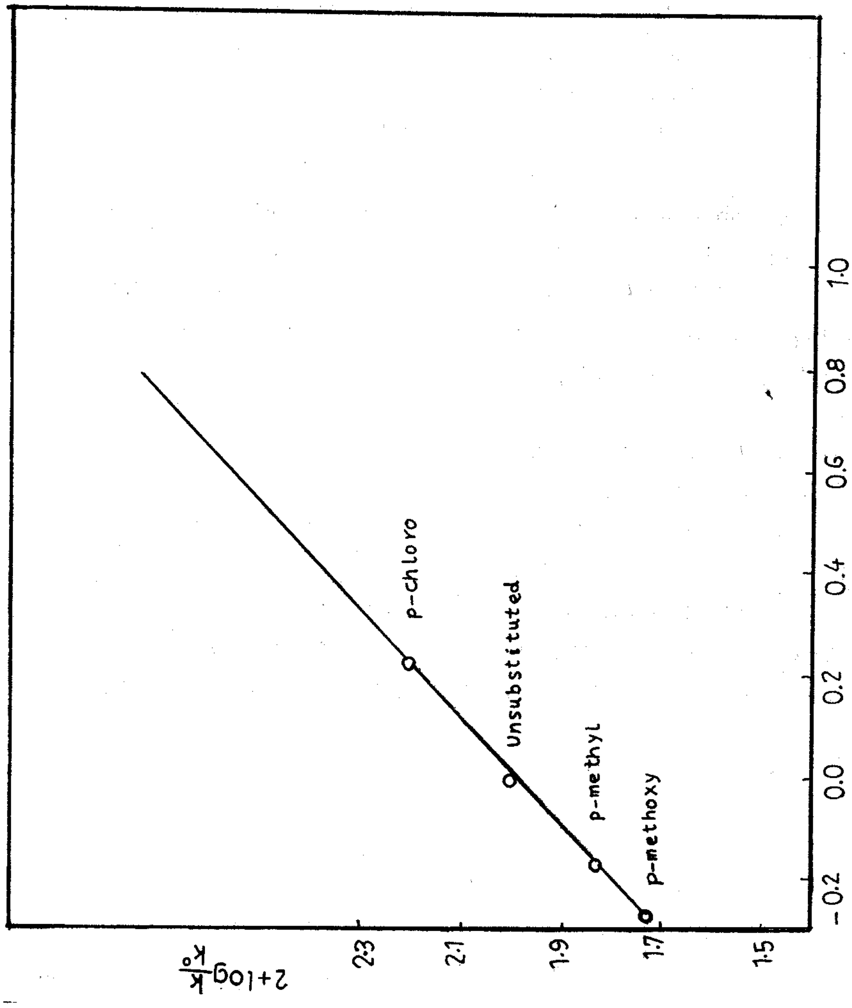


Fig. 4 Validity of the Hammett equation for the different substituents

Figures for manuscript entitled "Kinetic Study for the Effect of Substituents on the Base-catalyzed Darzens'-like Condensatins" by Awad et al.

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