

## Kinetics and Mechanistic Studies of the Bromination of some Substituted 2-Benzylidene-1,3-indandione

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### ABSTRACT

The rate of bromination of 2-benzylidene-1,3-indandione (I1) and its derivatives p-NO<sub>2</sub> (I2), p-Cl (I3), furan ring (I4), and p-OCH<sub>3</sub> (I5) have been studied in chloroform by means of U.V spectroscopy technique. The study indicated first order dependence on each of reactants with order of rates I2 > I3 > I4 > I1 > I5 at any temperature. The effect of substituents on the rate showed that electronic factors, inductive and resonance effects play reasonable role on the stability of the intermediates. Moreover, bromination processes showed a good free energy relationship with Hammett ρ value of greater than "1.0" at 298 K. The kinetic studies for these reactions revealed that these reactions are of nucleophilic addition type which characterized by the formation of intermediates that transformed to the desired products (II). Suggested mechanisms, which are consistent with the results, have been postulated and suitable rate laws in consonance with the suggested mechanisms have been derived.

**Keywords:** 2-arylidene-1,3-indandione, bromination, pseudo first order, Hammett equation

-3,1-      -2

الملخص

(I1)      -3,1-      -2

(I5)      (I4)      (I3)      (I2)

I5 < I1 <

I4 < I3 < I2

298

(1)

(ρ)

-3,1- -2 :

## INTRODUCTION

$\alpha,\beta$ -Unsaturated ketones play an important role in heterocyclic chemistry *via* the formation of dibromide intermediates which are derived from the addition of molecular bromine to these moieties such as 2-arylidene-1,3-indandiones (El Shehry *et al.*, 2010). These dibromide intermediates could be used as a synthon of other compounds, e.g., pyrazolines, benzodiazepines ..... etc (Karthikeyan *et al.*, 2007). These compounds, have biological and pharmacological activities as antimicrobial, anti-inflammatory, anticancer (Prasad *et al.*, 2008).

Although the exothermic addition of bromine to carbon-carbon double bonds has been studied extensively for many years, there are only a few published data on the bromination of exocyclic  $\alpha,\beta$ -unsaturated ketones (Dabbagh *et al.*, 2004). In general, there is not enough information to permit a thorough assessment of the factors influencing the bromination processes and the mechanism has still remained somewhat obscure.

Moreover, it is interesting to note that the kinetic data for the bromination of exocyclic  $\alpha,\beta$ -unsaturated ketones that contain two carbonyl groups are those reported in the present work, which provide, for the first time, detailed and reliable information about these systems.

Mechanisms for the reaction process were proposed on the basis of the experimental observed rate laws and products formed with the aim of analyzing the influence of substituents (X) in the phenyl ring on the stability of the expected transition state and intermediate.

## EXPERIMENTAL

### Materials

The bromine used was of annular grade as supplied by Fluka Company. The chloroform, (BDH) was pure enough for use. All 2-arylidene-1,3-indandiones were prepared in the department by standard procedure (Al-Sabawi, 2012). All organic compounds used for the synthesis were purified before use.

### Kinetic Measurements

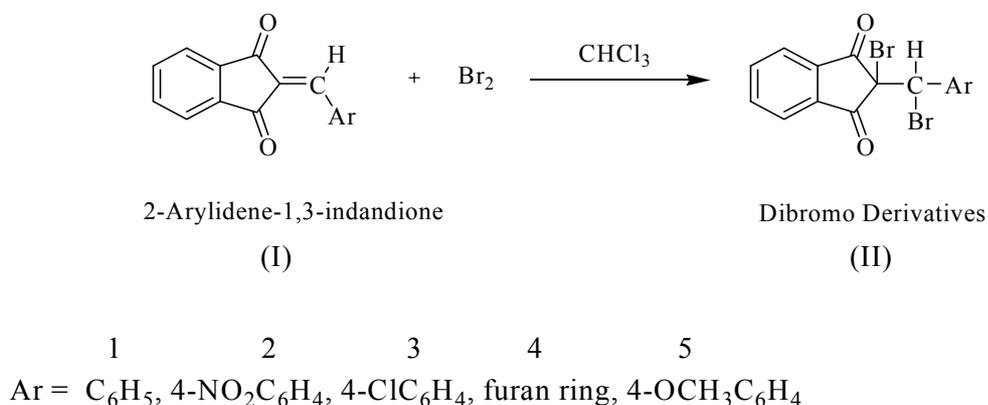
Kinetics was followed by U.V spectrophotometry on a Shimadzu UV-1800 spectrophotometer, monitoring the disappearance of the charge transfer complex, which was formed by addition of bromine to reactants, at a fixed wave length (444-488 nm) depending on the used substituent.

Stock solutions of 2-arylidene-1,3-indandiones I (1-5) in chloroform, ( $4.5 \times 10^{-2}$  M), 2 ml of this solution was transferred to a U.V cell at the appropriate temperature, 1 ml of

( $0.9 \times 10^{-2}$  M) bromine in chloroform was added to start the kinetic run. A reference cell containing 2 ml of the stock solution was always used. The instrument was programmed to take absorbance at different intervals. All kinetic runs were carried out, at least, in duplicate.

### RESULTS AND DISCUSSION

Preliminary experiments showed that reasonable rates of bromination were obtained at a temperature range between 283-313 K. No compounds other than reactants I and products II were detected in the product of these reactions as shown by their U.V analyses under kinetic conditions; IR and NMR analyses also confirmed (II) as the only product. Typical runs of reaction toward completion demonstrated very clearly how the absorbance of the charge transfer complex at infinite time  $A_{\infty}$  goes almost to zero and does not change its value even when the temperature is arisen indicating that the reaction is completely forward and no equilibrium between reactants and product is ever existed. These observations suggest the addition reaction proceeds clearly according to the simple stoichiometry of reaction:



Since 2-arylidene-1,3-indandiones I (1-5) were used in large quantities compared to bromine (10 mole ratio), the results were analyzed as a pseudo-first order reaction for which the rate equation is:

$$\ln \left( \frac{A_0 - A_{\infty}}{A_T - A_{\infty}} \right) = k_{obs} t \quad \dots \dots \dots (1)$$

Where A refers to the absorbance of the charge transfer complex and the subscript 0 refers t = 0.  $k_{obs}$  represents the observed rate constant and is a function of 2-arylidene-1,3-indandiones (reactant) concentration i.e  $k_{obs} = k$  [reactant]. Accepted straight lines were obtained with zero intercepts and slopes corresponding to the observed rate constant,  $k_{obs}$ . Such plots were linear for a period of more than three halves confirming the pseudo-first order kinetics and proving a first order kinetics with respect to bromine. At a range of temperatures between 283-313 K, runs were carried out for reactants at constant concentrations, the observed rate constants,  $k_{obs}$ , were calculated from the slopes of the plots as shown in Table (1). The standard error  $\sigma$  of the slope of a plot, shown in Table (1), simply represents the uncertainty due to the scatter of the points about the regression line, and is thus a measure of the reproducibility of the results rather than its absolute accuracy. Typical plots for the reactants I (1-5) at 298 K are exhibited in Fig. (1). On the other hand,

tests were made for the order of the reactants I (1-5). Kinetic runs, at different concentrations of I (1-5) were performed. Linear plots were obtained when the functions of  $\text{Log } k_{\text{obs}}$  vs  $\text{Log} [\text{reactant}]$  were demonstrated with slopes of unity proving, according to equation (2), a first order kinetics with respect to reactant I (1-5).

$$\text{Log } k_{\text{obs}} = \text{Log } k + n \text{Log} [\text{reactant}] \quad \dots\dots\dots (2)$$

Hence total second order kinetics was confirmed.

Arrhenius plots of  $\text{Ln } k_{\text{obs}}$  versus the reciprocal of absolute temperature between (283-313 K) were performed. The plots were excellent straight lines as shown in Fig. (2). Arrhenius parameters and entropies of activation are tabulated in Table (2).

**Table 1: Rate constants for reactions of I (1-5) with bromine at different temperatures.**

Temp. / K	$10^3 k_{\text{obs}}/ \text{s}^{-1} \pm 10^3 \sigma/\text{s}^{-1}$				
	1 H	2 p-NO <sub>2</sub>	3 p-Cl	4 Furan ring	5 p-OCH <sub>3</sub>
283	.....	.....	0.902 ± 0.034	.....	.....
288	.....	9.673 ± 0.229	1.252 ± 0.036	0.708 ± 0.017	.....
293	0.830 ± 0.032	12.670 ± 0.227	1.777 ± 0.107	1.025 ± 0.035	0.381 ± 0.004
298	1.202 ± 0.032	16.287 ± 0.927	2.560 ± 0.040	1.530 ± 0.076	0.543 ± 0.015
303	1.756 ± 0.053	.....	3.447 ± 0.110	2.158 ± 0.059	0.818 ± 0.020
308	.....	.....	.....	.....	1.236 ± 0.046
313	.....	.....	.....	.....	1.880 ± 0.068

- $\sigma$  is the standard error, see text.

**Table 2: Arrhenius parameters and entropies of activation for the reaction of I (1-5) with bromine.**

Compounds	Ea/kJ.mol <sup>-1</sup>	R <sup>2</sup>	A-factor/ s <sup>-1</sup>	$\Delta S^\ddagger/\text{JK}^{-1}\text{mol}^{-1}$ at 298 K
1. H	55.272	0.999	$5.953 \times 10^6$	- 123.467
2. p-NO <sub>2</sub>	37.184	0.999	$5.360 \times 10^4$	- 162.627
3. Cl	48.428	0.999	$7.793 \times 10^5$	- 140.371
4. Furan ring	54.331	0.999	$5.042 \times 10^6$	- 124.848
5. p-OCH <sub>3</sub>	61.180	0.997	$3.102 \times 10^7$	- 109.742

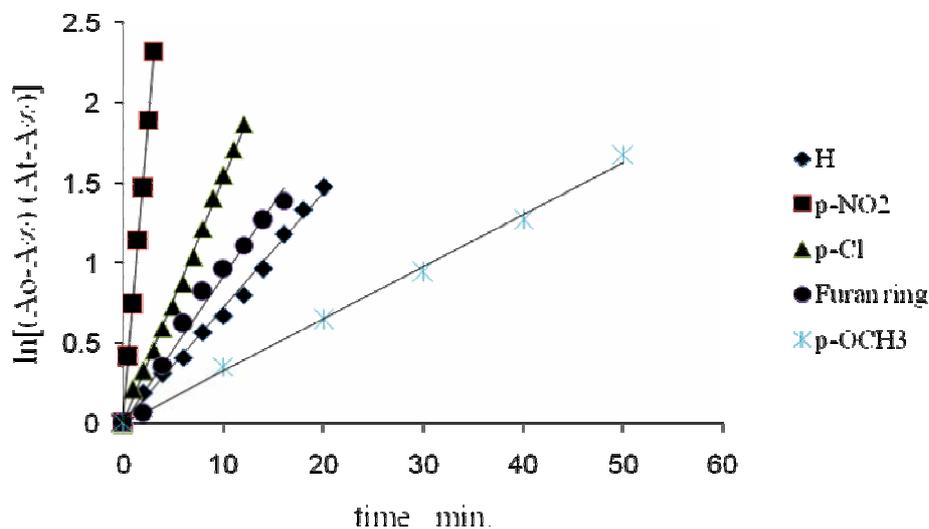


Fig. 1: Pseudo first order plot for the reaction of 2-benzylidene-1,3-indandiones and its derivatives I (1-5) with bromine in chloroform at 298 K.

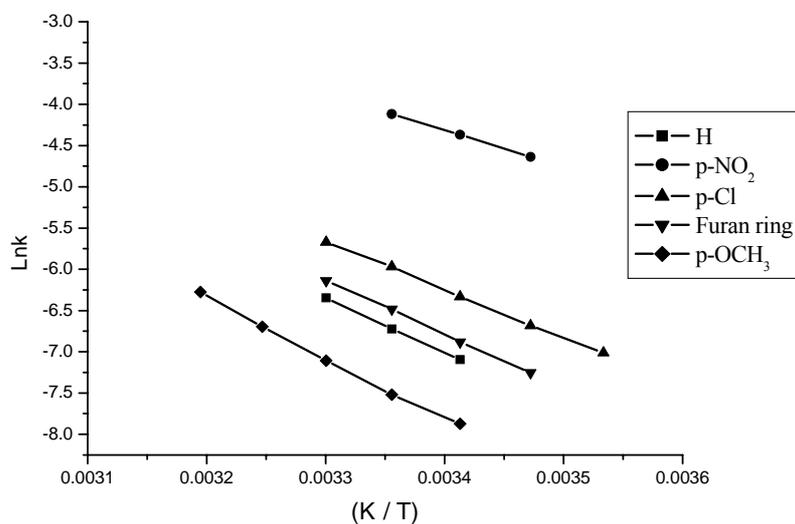


Fig. 2: Arrhenius plot for the reaction of 2-benzylidene-1,3-indandiones and its derivatives I (1-5) with bromine in chloroform.

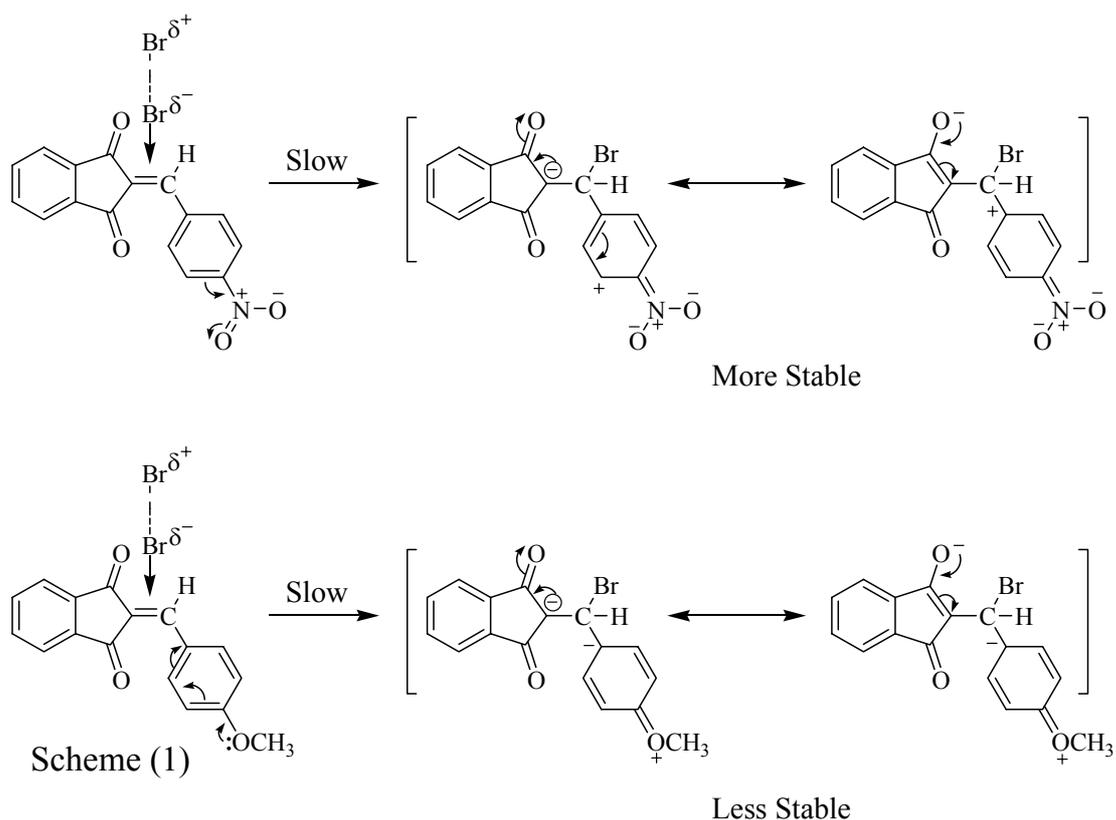
### Activation Parameters

The value of the activation parameters Table (2) is of great importance to discern the mechanisms under all circumstances of the study. In our present work, the bromination

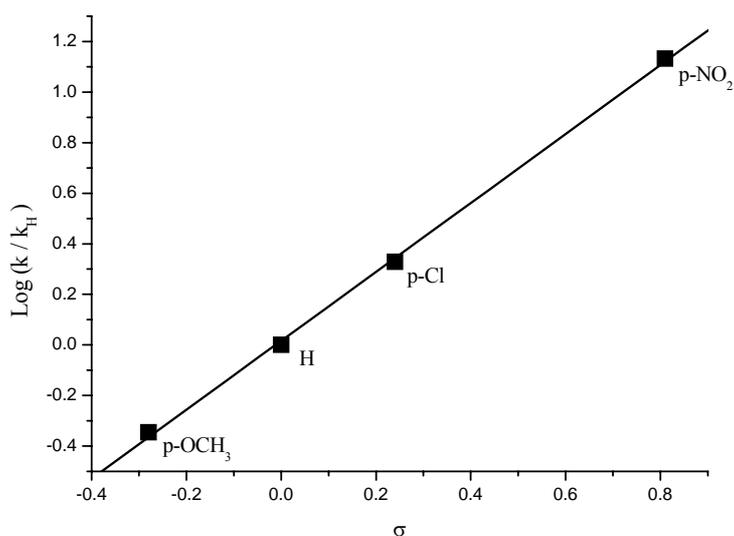
processes of all reactants I (1-5) were of small activation energies which vary within 37 - 61  $\text{kJ mol}^{-1}$ . The variation of their values may be attributed to the electron donating or withdrawing capabilities of the attached substituent that can affect on the formation of intermediate and its decay to the product. It is expected that electron withdrawing substituents enhance the nucleophilic reaction, whereas electron donating ones reduce it. These factors, as well as, the combined inductive and conjugative effects of the substituents (X) result in differences in rates according to the following order:



At first sight, the reaction may occur by initial  $\pi$ -interaction of the  $\text{C}=\text{C}$  double bond in I with bromine to form a stabilized charge transfer complex. The electron withdrawing substituents at the phenyl ring, such as  $p\text{-NO}_2$ ,  $p\text{-Cl}$ , furan ring, play important role in stabilizing this complex leading to the formation of the  $\beta$ -bromocarbanion, thus enhances the reaction rates, Table (1), as compared with the corresponding hydrogen analogue.



Such a fast reaction is supported by its lower activation energy, than the unsubstituted (H) analogue Table (2). This value is fairly reasonable for reactions having highly polar transition state (Atkinson and Bell, 1963).



**Fig. 3: Hammett free energy relationship for bromination of 2-arylidene-1,3-indandione using the substituent constants  $\sigma$  at 298 K.**

On the other hand, p-chloro substituent possesses a lower electron withdrawing ability than the p-NO<sub>2</sub> group (March, 2007). Hence its ability to enhance the bromination process is less, as shown in Table (1), since it exhibits two opposite types of electronic effects, resonance (donating) and predominant inductive (withdrawing) effects (March, 2007). The furan ring also increased the rate of reaction as compared with corresponding unsubstituted analogue (H), due to the oxygen contained furan ring.

In contrast, electron donating substituent such as p-OCH<sub>3</sub> results in regular decrease of bromination rate, as compared with the corresponding hydrogen analogue. In fact this group destabilizes the charge transfer complex by enhancing the electron density at the reaction center, thus reduces the reaction rate; hence higher activation energy is required for the process, Table (2).

The entropies of activation  $\Delta S^\ddagger$ , which are tabulated in Table (2), are all largely negative values indicating the formation of a restricted high polar transition state which suffers from lack of certain degrees of freedom as compared to the reactants (Dabbagh and Al-Hamadany, 1987). The decrease in the values of A-factor provides an important indication about the stability of the transition state and hence gives good support for explaining the reason of the differences in the values of rate constants. Again, it can be clearly discerned the effect of electronic properties of the different substituents on the transition state by noting the differences in  $\Delta S^\ddagger$  value for the p-nitro I (2) which is much lower than others due to the decrease of electron density at the reaction center leading to the formation of a highly oriented stable  $\beta$ -bromocarbanion. In contrast, the highest  $\Delta S^\ddagger$  value for the methoxy I (5) may be attributed to destabilized transition state since it enriches the reaction center with electron density. This confirms the formation of a  $\beta$ -bromocarbanion in the transition state.

On the other hand, the correlation between the structure of compounds and their chemical reactivity is one of the most instigating objectives to clarify the finer details of many individual reactions. The quantitative relation between the nature of the substituent

and the reactivity of the side chain are also considered in our study using Hammett equation (Connors, 1990).

$$\text{Log} \left[ \frac{k}{k_0} \right] = \sigma \rho$$

Where  $\sigma$ , the substituent constant, is a measure of the electron-donating or electron-withdrawing power of the substituent; and  $\rho$ , the reaction constant, is a measure of sensitivity of the rate constant due to change in the  $\sigma$  value of the substituent.

Correlation plots of  $\text{Log} (k/k_H)$  at 298 K against the available ordinary Hammett  $\sigma$  constants (March, 2007) are performed. Table (3) shows the values of  $\rho$ , R (correlation coefficient) and s (standard error), as shown in Fig. (3).

**Table 3: Reaction constant for bromination of 2-arylidene-1,3-indandiones at 298 K.**

Substituents	$\rho$	R	S
H, p-NO <sub>2</sub> , p-Cl, p- OCH <sub>3</sub>	1.363	0.999	0.028

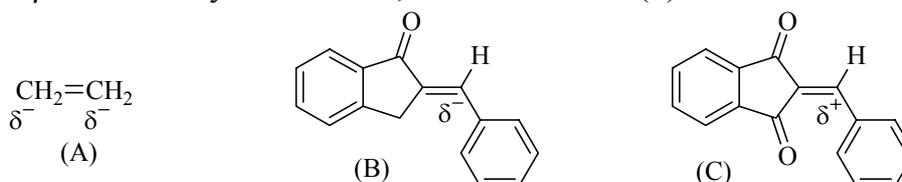
Excellent correlations are obtained for the bromination process. The positive sign of  $\rho$  value, as expected for nucleophilic attack, indicates that the substituent action in a site that generates a negative charge in the transition state and accordingly the reaction is facilitated by decreasing the electron density at the reaction center, i.e., the reaction is accelerated by electron withdrawing groups and reduced by electron donating ones. The high  $\rho$  value indicates to form full negative charge in transition state, which is stabilized *via* conjugation with carbonyl groups. This result is consistent with the idea of formation of open anionic ( $\beta$ -bromocarbanion) transition state and not carbocation or brominium ion (Al-Iraqi, 1998).

### Mechanism and Rate Equation

The carbon-carbon double bond is well known to undergo electrophilic addition of acids, halogens and hydrogen. The properties of (C=C) may be modified by the presence of another group.

If electron withdrawing groups, such as (- CN, - CO<sub>2</sub>R, - CO<sub>2</sub>H, - COR), are attached to carbon-carbon double bond, they will lead to a decrease in the electron density on the (C=C) bond, thus cause deactivation towards electrophilic addition. At the same time, these groups will activate the (C=C) bond towards the nucleophilic addition which is not common for ordinary alkenes (Fesenden, 1982).

Further evidence was obtained from the minimized geometry of compounds (A, B and C). The theoretical data for these compounds show that the atomic charges and electron densities at the  $\beta$ -carbon vary in the order, shown in Table (4).

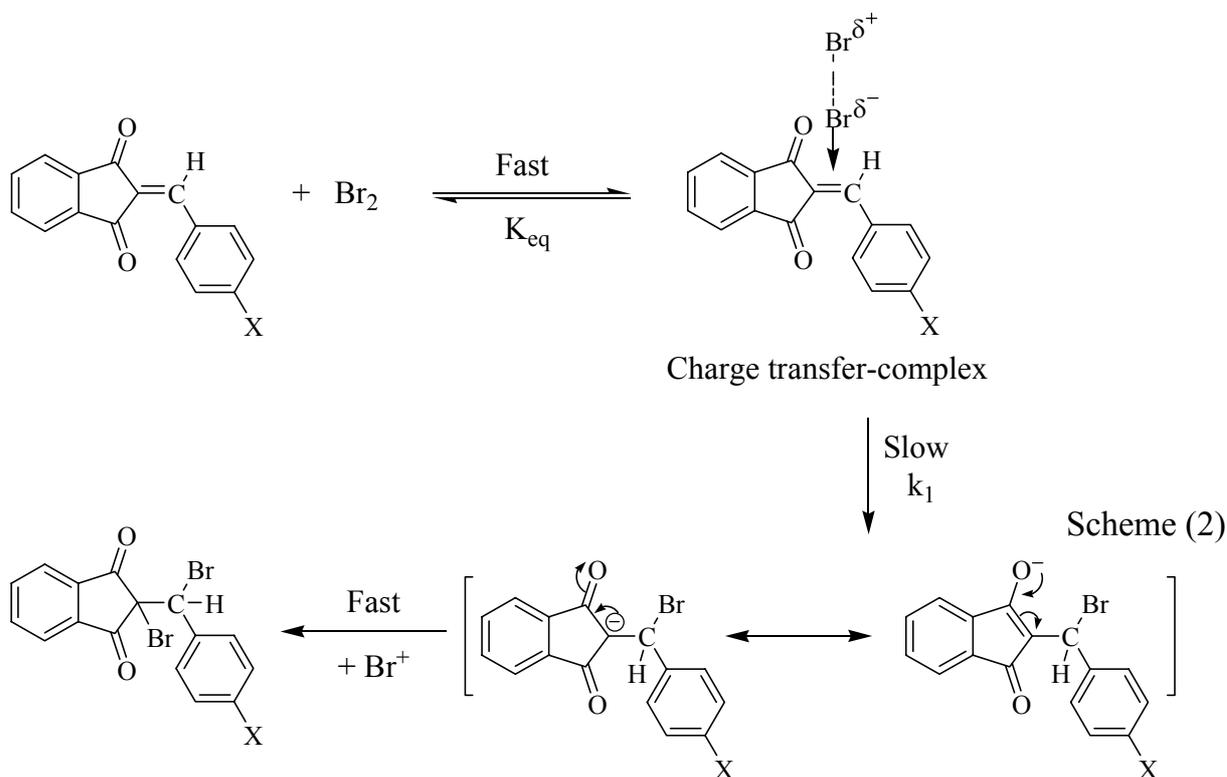


**Table 4: Atomic charges and electron densities of compounds (A, B and C).**

Compound	Atom	Charge	Atom Electron Density
A	C	-0.217961	4.2180
B	( $\beta$ -C)	-0.044562	4.0446
C	( $\beta$ -C)	0.048846	3.9512

It is worth to mention, in the above table, that compound (A) undergoes electrophilic addition more than compound (B), while compound (C) deactivates toward such addition, i.e. activates towards nucleophilic one.

It is implied that a rapid pre-equilibrium formation of a 1:1 transitory charge transfer complex between 2-arylidene-1,3-indandiones I (1-5) and bromine soon they mix together (Reichardt and Welton, 2011). Presumably this complex may lead, by a slow step, to the formation of the  $\beta$ -bromocarbanion, which attacks in a subsequent rapid step the bromide ion ( $\text{Br}^-$ ) to form the dibromo product.



This fact is confirmed by the second order equation with unit order to each of the reactants.

$$r = k [\text{Chalcone}][\text{Bromine}] \quad \dots\dots\dots (3)$$

Where  $k = K_{\text{eq}} k_1$

The mechanism is also confirmed by the pseudo first order rate equation when high concentrations of 2-arylidene-1,3-indandiones (10:1 mole ratio), are used.

$$r = k_{\text{obs}} [\text{Bromine}] \dots\dots\dots (4)$$

Where  $k_{\text{obs}} = K_{\text{eq}}k_1 [\text{Chalcone}]$

The above two equations are in quite good agreement with the experimental results obtained from our present studies.

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