KINETIC STUDIES OF SOME REACTIONS OF CARBANION INTERMEDIATES

Presented By

Wafy Nasla Wasf

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A C K N O W L E D G E M E N T

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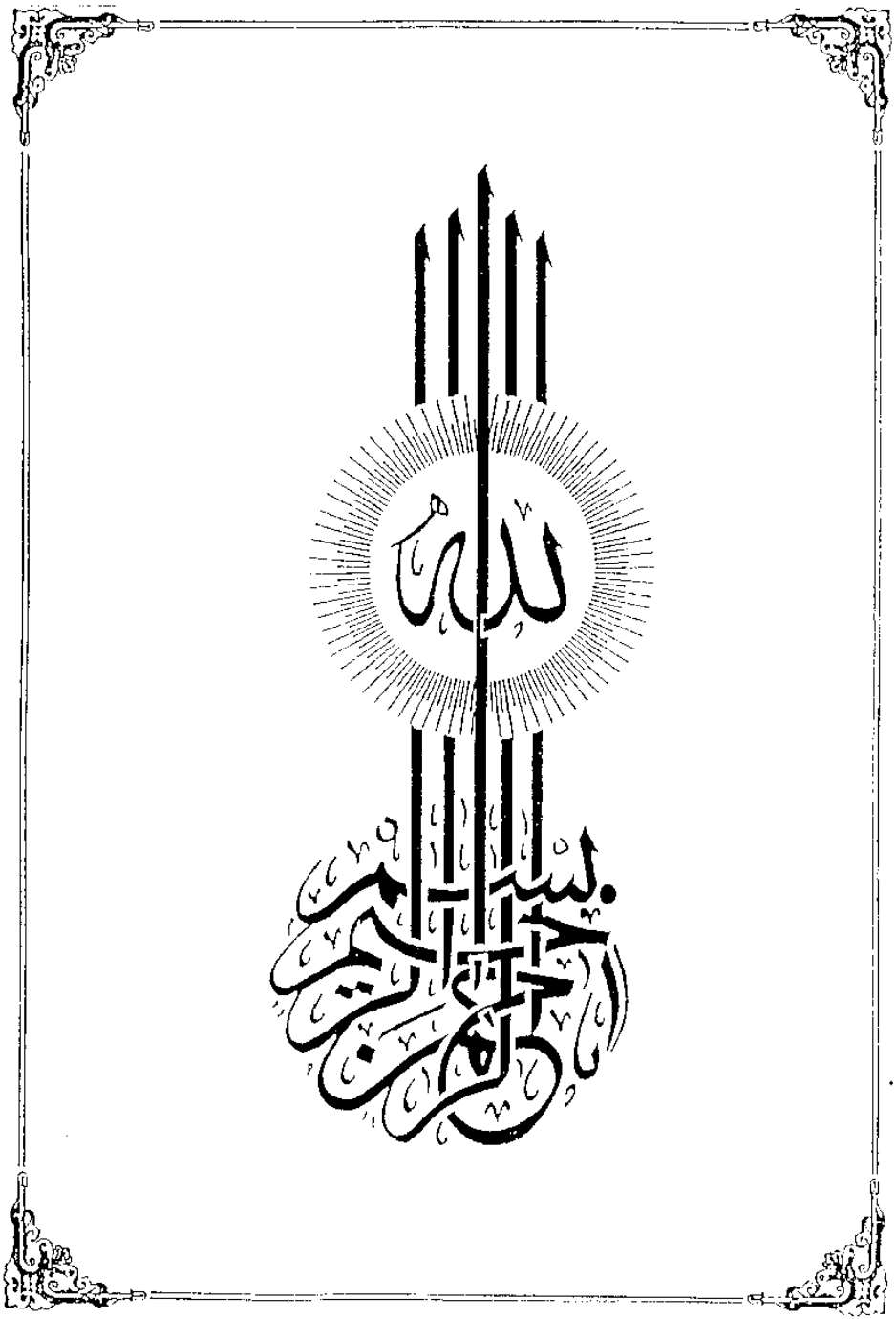


C O N T E N T S

Summary

The base-catalysed condensation of chloroacetone with sodium carbonate is found to be an overall third- order reaction, first with respect to the alkali and second with respect to chloroacetone. This third order kinetics makes it convenient that enolisation is not the rate determining step, and it is possible that the mechanism is involving self alkylation of the organic halide to form the dimeric halide in the rate-determining step followed by dehydrohalogenation (β-elimination) to give the dimeric olefin which is actually isolated in our investigation. The suggested mechanism for this reaction involves three steps, in the first step enolisation of chloroacetone takes place to form a carbanion which in turn acts as a powerfull nucleophile and attacks the positively charged carbonyl carbon of another molecule to form a transition state (cf. p 152). This structure is supported by the negative value of the entropy of activation i.e. with less degress of freedom (cf. p 149).

Finally, in the third step deprotonation of the carbon takes place which is accompanied by chloride ion liberation, leading to the formation of diacetylethylene which has been isolated and identified (cf.p 45).

The increase of the reaction rate by decreasing the polarity of the medium indicates that the transition state is less polar than the reactants and the negative charge is dispersed on it. Such a dispersion of charge stabilises the transition state and favours its formation. The linear isokinetic plots of $\Delta S^{\ddagger}$ vs. $\Delta E^{\ddagger}$ and $\Delta G^{\ddagger}$ vs. $\Delta E^{\ddagger}$ for all these reactions supports the suggested carbanion mechanism for the mentioned reaction.

I N T R O D U C T I O N

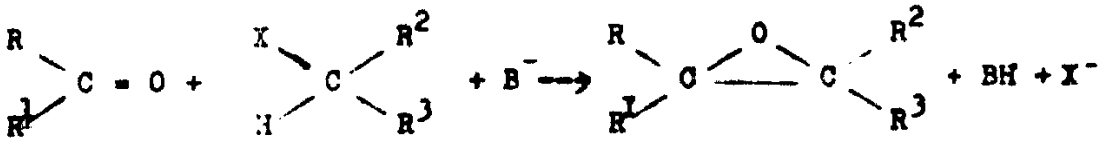
alkyl chloroacetates and chloropropionates gave yields comparable to those obtained with methyl and ethyl esters propyl and isopropyl, allyl, cyclohexyl, n-amyl, benzyl, and 2-ethyl hexyl. There is some evidence that better yields of condensation products may be obtained with halogamides . A 80% yield of glycidicamide is obtained from acetone and the diethylamide of chloroacetic acid[21] whereas with ethyl chloroacetate[3,15,22] much lower yield results. However, it has not been shown that the glycidic amides can be hydrolysed and decarboxylated to give aldehydes or ketones.

More complex haloesters , such as ethyl-β hydroxy-chloropropionate, ethyl α, β-dichloropropionate[23], and ethyl α-bromo-β, β-diethoxy propionate[24], failed to undergo the glycidic ester condensation.

Recently, a rather general definition of the Darzens condensation is accepted, including all the base-catalysed condensations of carbonyl compounds with halogenomethylene substances yielding, with the separation of halide ions, compounds having oxirane rings formed by the carbonyl and the halogenomethylene carbon atoms.

Accordingly, besides esters of α-halogenoacids, the condensation can be carried out with amides of these acids[25],

with α-halogenketones [26], with halogenomethyl sulphones and even with some aryl-substituted methyl halides [27,28]



The base is used up by the reaction and acts therefore as a third reactant, nevertheless it is also the catalyst for the condensation.

This condensation is greatly affected by the conditions under which this reaction takes place, such as temperature, solvent and the basic condensing agent. The solvent may be of the aprotic non-polar type, like anhydrous benzene or anhydrous ethyl ether, but ethyl alcohol and even aqueous dioxane have been used. Wislicenus[29] studied the interaction of ethyl sodioacetoacetate with different alkyl halides and found that dry ethyl alcohol is a poor ionising solvent for the alkyl halides. The selection of the solvent has been determined in many cases by the nature of the condensing agent. For example, when sodium amide, is used, an anhydrous solvent of the inert type must be employed.

As far as the condensing agent is concerned, sodium has been used in addition to sodium ethoxide or sodium amide.

In the condensations with arylmethyl halides potassium carbonate has been preferred[27], and with phenacyl halides sodium hydroxide has been used with excellent results[30,31]. It has been recently reported that sodium tert-butoxide gives good results in the condensations with α-halogeno-acids[32].

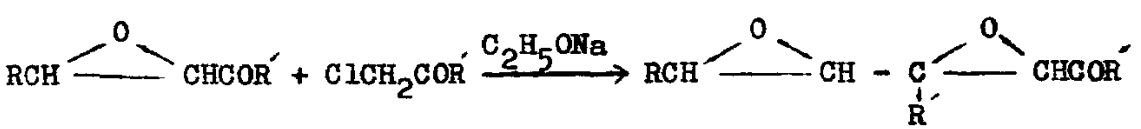
Using the terminology generally accepted for formally similar condensations, the carbonyl and halogenomethylene parts will be called the (A) and (B) components, respectively[33]. As a general rule, the condensation can occur only when the (B) component has an "activated" hydrogen atom attached to the halogenomethylene carbon atom. If no activation of the hydrogen atom on the halogenated carbon occurs, the condensation will not take place. Thus, in the reaction of esters of β-halogeno-acids with enolisable ketones, alkylation reactions occured giving esters of δ - keto acids[34,35]. However, in the condensation with enolisable (A) components with which a competing alkylation reaction is possible, the most favourable halogen for the (B) component is chlorine. In fact, in certain conditions, while the esters of the α-chloro-acids yield glycidic esters, those of α-iodo and also of α-bromoacids, although to a lesser extent give esters of δ - ketoacids[34,35].

These results may be ascribed to the greater ease with which bromine or iodine is displaced by an S_N2 mechanism. It has been shown that a p-toluene-sulphonate group may be substituted for a halogen atom in the (B) component[19].

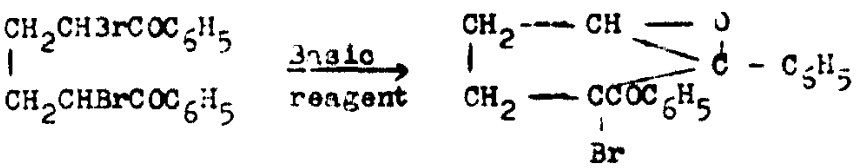
The (A) component may be an aldehyde or a ketone, The former being, as usual, more active than the latter. Some ketones are reported to react sluggishly or to be inactive so that it failled to give the Darzens condensation.

Unsuccessful attempts have been made to perform condensations with Michler's thioketone as an (A) component. In the cases reported the ethylene, corresponding to the expected thiirane was isolated; being formed probably through the latter[27]. This result could be explained in view of the well known oxidising character of some epoxides, especially those which may be prepared by a Darzens condensation[9,36].

The epoxyketones formed from Darzens reaction may condense with a second molecule of haloketone to yield $\alpha, \beta, \gamma, \delta$ -diepoxyketones[36].

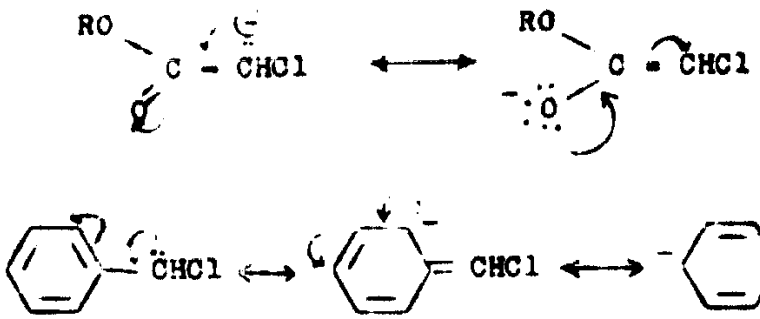


when 1,4-dibromo-,1,4-dibenzoyl butane is treated with sodium cyanide, diethylamine, sodium acetate[37], or the sodium derivative of malonic ester[38], a cyclic epoxyketone is produced; with molecular silver the debrominated analogy is obtained[38].



Bartlett[39,40] assumed that the basic catalyst activates the (B) component, i.e., the halogenomethylene compound, besides, the inductive effect of its halogen atoms, as has been shown in the haloform reaction, and in the halogenation of ketones[41], must facilitate the separation of the proton. Furthermore, it is well known that some of the most remarkable reactions of the α-halogenoketones (halogenation, self-condensation) are base-catalysed, and so the probability of the preliminary reaction of these halogenomethylene compounds with the base in their condensation reactions, is quite reasonable.

The stability of the anion formed from the (B) component is due to its resonance :



In the case of phenylmethyl halides the contribution of electronic structures to the resonance will be increased with ring-substitution by electron-attracting groups in the places where the negative charge is located, i.e., in the ortho or para position. Accordingly, in such condensations p-nitrobenzyl chloride has been the preferred (B) component[27]. It is doubtful whether the unsubstituted benzyl chloride is able to undergo condensation[42].

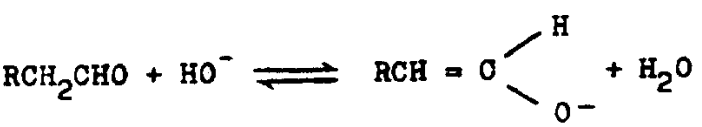
It is reasonable to assume that halogen atom in the anion is more disposed to separate as halide ion than in the unionised (B) from which it comes.

(II) General Consideration of the Mechanism of Darzens Condensation

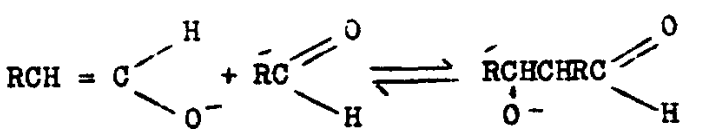
It is generally agreed that aldol and related condensations like the Perkin, Knoevenagel, or Claisen condensation, proceed by formation of the enolate ion of

the (B) component as a first step[43]. The (B) component has a hydrogen atom (bonded to a carbon atom) whose removal as a proton is favoured to a varying extent by structural features such as a carbonyl group in the α-position. The separation of that proton is essential as far as the enolisation is concerned.

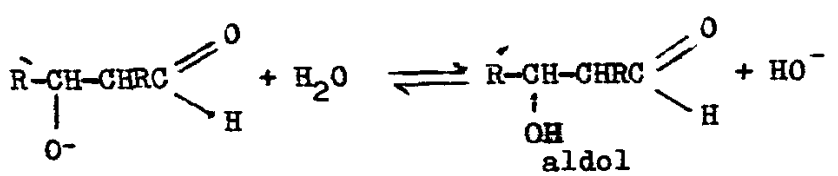
The anion resulting from the attack of the base on the (B) component is provided with a strong nucleophilic character, and therefore is much more reactive than the (B) component itself towards the (A) component (carbonyl component). The accepted general aldol mechanism is the following :



(B) component enolate ion



(A) component



aldol

The alternative assumption suggested by some authors[44,45] of a preliminary addition of the base to the (A) component seems not to be adequate, for it would imply that the reaction takes place between two molecular species of comparatively reduced activity than the component from which it comes. Therefore, the possibility exists that the anion would reorganise itself with halide ion separation. This is equivalent to elimination of a molecule of hydrogen halide, both atoms coming from the same carbon, i.e., what has been referred to by Ingold and Jessop as 1,1-elimination.[46] Consequently, a so-called "bivalent radical" would be formed. Such radicals were used liberally by Nef in the interpretation of organic reactions around the end of the last century[47], but the disproof of such mechanisms in some cases has led to bivalent radicals falling into general disfavour.

In spite of that, Hine[48] has recently proposed that the kinetics of the hydrolysis of chloroform may be ascribed to the formation of a transient bivalent radical, (CCl_2) formed through the following sequence:

$$Cl_3CH + HO^- \underset{\text{rapid}}{\rightleftharpoons} Cl_3C^- + H_2O$$

$$Cl_3C^- \xrightarrow{\text{slow}} Cl_2C + Cl^-$$