KINETIC STUDIES ON THE REACTION OF CARBANIONS WITH CARBONYL CONTAINING COMPOUNDS

Presented by

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B.Sc.

For

The Degree of M.Sc.

University College for Women
Ain Shams University
Heliopolis, A.R.E.

1990

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ACKNOWLEDGEMENT

The author wishes to express his thanks to **Prof. Dr. Ahmed A. Taha,** Dean of the University College and Head of Chemistry Department, University College for Women, Ain Shams University, for the facilities at his disposal, help and encouragement.

The author should like to express his gratitude to **Dr. Wasfy N. Wassef,** Chemistry Department, University College for Women, Ain Shams University, not only for suggesting the problems investigated but also for his continuous advice and help.

The author also wishes to express his deepest gratitude to his parents for their encouragement and great support.

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SUMMARY

SUMMARY

α-chlorocyclohexanone generates an α-carbanion in alkaline medium, faster than the α'-carbanion, the former has been trapped by active aromatic aldehydes to afford spiro [ethyleneoxide-α-(cyclohexane-2-one)-β-(Aryl)]18-23 in dimethyl sulphoxide (DMSO).

While in 50% aqueous dioxane the reaction yeilds the α-hydroxycyclohexanone (24) which was isolated and identified as its dimer (Adipoin) along with the unreacted aldehyde, except when p-nitrobenzaldehyde is used the corresponding epoxide is formed.

For comparison the base-catalyzed condensation of chloroacetone, phenacyl chloride, and ethylchloroacetate with diformylbenzene were studied in aqueous dioxane. Both phenacyl chloride and ethylchloroacetate afford the mono-and bis-oxirane compounds whereas chloroacetone yields the mono-oxirane only, also the reaction of α-chlorocyclohexanone with diformylbenzene in DMSO affords the mono-oxirane only.

It appears that the presence of α'-protons in the α-halogenomethylene compound reduces its ability to undergo Darzens condensation and that the α-anion, which is formed prior to the α'-anion, needs an active

species in the medium to trap it quickly, otherwise, interamolecular attack by the α'-anion might results in the displacement of the halide ion leading to a cyclopropanone intermediate (C.F. Scheme II), which is the generally accepted intermediate in Favorsky rearrangement kinetics show that the base-catalysed condensation of α-chlorocyclohexanone with aromatic aldehydes in diemthyl sulphoxide follows third-order kientics overall, first with respect to each of the halogenomethylene compound, the aldehyde and the base.

The energies of activation $\Delta E^{\ddagger}$ measured in DMSO are small (Ca.2-5 K. Cal. mal^{-1}) showing that the use of DMSO facilitates the attack of the α-carbanion on the carbon atom in the carbonyl group of the aldehyde.

The suggested mechanism for this reaction involves three steps: the first is the formation of the carbanion which is fast, the second is slower and rate-determining in which the attack of the carbanion on the carbonyl carbon takes place to form a transition state that looses the chloride ion to form the epoxides in the third step. The epoxidation step is the rate-determining step since the vilocity constants for these reactions fall in the following order:

$P\text{-}NO_2 > m\text{-}NO_2 > P\text{-}CHO > P\text{-}Cl > P\text{-}H$

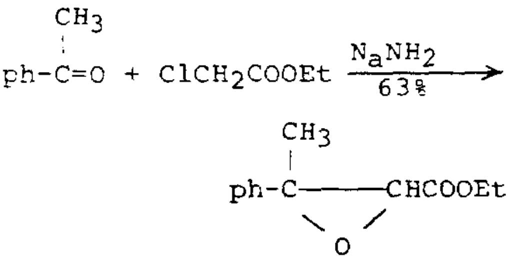
and since doubling the aldehyde concentration results in doubling the pesudo second-order rate constant.

In aqueous dioxan media the measured energies of activation for the reaction of α-chlorocyclohexanone with p-nitrobenzaldehyde in presence of sod. hydroxide are higher (a 10-12 K. Cal. mol^{-1}) than in DMSO. The increase of the reaction rate by decreasing the polarity of the medium (as dioxane ratio-increases), indicates that the transition state is less polar than the reactants and the negative charge is dispersed on it.

The activation parameters ΔH and ΔS of the reactions in DMSO and in aqueous dioxane are calculated.

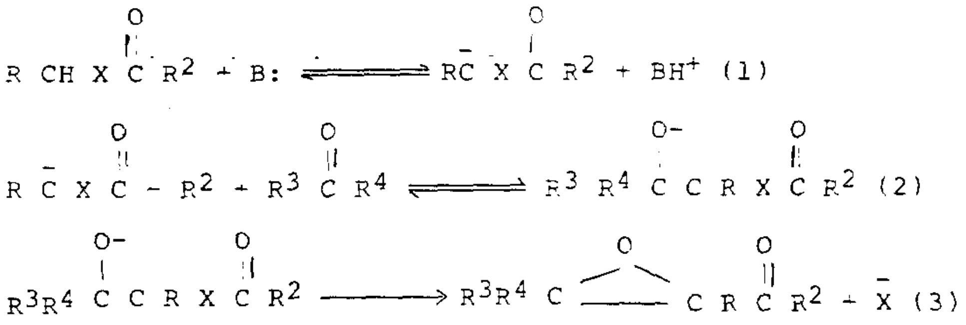
I. History and Scope of the Darzens Condensation *

The French Chemist George Darzens in the years 1905 - 1912 exploited the base-catalyzed condensation of α-haloesters with aldehydes and ketons. He showed that the products were free of halogen and were α, β-expoxyesters[1], commonly known as glycidic esters. Example of the Darzens condensation is shown in the following equation:-



$$ph\text{-}\overset{CH_3}{\overset{|}{C}}{=}O + ClCH_2COOEt \xrightarrow[63\%]{NaNH_2} ph\text{-}\overset{CH_3}{\overset{|}{C}}\text{—}CHCOOEt$$

A satisfactory mechanism postulated for this reaction which explains all Darzens and Darzens-like condensations is the sequence of reactions generally accepted to be as shown in the following[2] equations.



$$R\,CH\,X\,\overset{O}{\overset{\|}{C}}\,R^2 + B: \rightleftharpoons R\bar{C}\,X\,\overset{O}{\overset{\|}{C}}\,R^2 + BH^+ \quad (1)$$

$$R\,\bar{C}\,X\,\overset{O}{\overset{\|}{C}} - R^2 + R^3\,\overset{O}{\overset{\|}{C}}\,R^4 \rightleftharpoons R^3\,R^4\,\overset{O^-}{\overset{|}{C}}\,C\,R\,X\,\overset{O}{\overset{\|}{C}}\,R^2 \quad (2)$$

$$R^3R^4\,\overset{O^-}{\overset{|}{C}}\,C\,R\,X\,\overset{O}{\overset{\|}{C}}\,R^2 \longrightarrow R^3R^4\,C\overset{O}{\text{—}}C\,R\,\overset{O}{\overset{\|}{C}}\,R^2 + \bar{X} \quad (3)$$

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*In the preparation of this introduction the author consulted:
(a) M.S. Newman and B.J. Magerlein, Organic Reactions, 1949, 5, 413.
(b) M. Ballester, Chem. Rev., 1955, 55, 283.

The reaction has been conclusively demonstrated to be nocarbenoid[3]

The first synthesis of a glycidic ester was performed by Erlenmeyer[4], who obtained ethyl β-phenyl-α, β-epoxy propionate by condensing benzaldehyde with ethyl chloroacetate using sodium metal as condensing agent. It remained for Darzens however to develop and generalise this reaction[5-16]. He preferred sodium ethoxide as the condensing agent. Shortly after the appearance of Darzens first paper, Claisen[17] reported that sodium amide could be used as condensing agent. The glycidic ester condensation has not been applied as widely as one would expect in view of the number and variety of compounds that can be prepared by its use.

Darzens[18-20] has described another procedure which involves the reaction of aldehydes and ketones with ethyl dichloroacetate and magnesium amalgam. The first product of this reaction is a β-hydroxy α-chloroester (1) which is quantitatively converted to the glycidic ester (2) by treatment with sodium ethoxide. Alternatively, the hydroxy chloroesters may be dehydrated to yield α-chloro unsaturated ester (3).