12-1965

Rearrangements in the Synthesis of β-Ketoallyl Amines

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REARRANGEMENTS IN THE SYNTHESIS OF β-KETOALLYL AMINES

by

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A THESIS

Presented to the Faculty of

The Graduate College in the University of Nebraska

In Partial Fulfillment of Requirements

For the Degree of Master of Science

Department of Chemistry

Under the Supervision of Professor Norman H. Cromwell

Lincoln, Nebraska

December 3, 1965

ACKNOWLEDGMENTS

The author wishes to express his gratitude to Professor N. H. Cromwell at whose suggestion this investigation was undertaken. His guidance, encouragement, and patience have been greatly appreciated.

Many thanks go to his mother and to his wife both of whom gave encouragement and financial support over a period of many years.

The author also wishes to thank the National Science Foundation and the U. S. Public Health Service for their grants in support of this research.

Also greatly appreciated is the contribution of Goodrich-Gulf Chemicals, who greatly facilitated the publication of this work.

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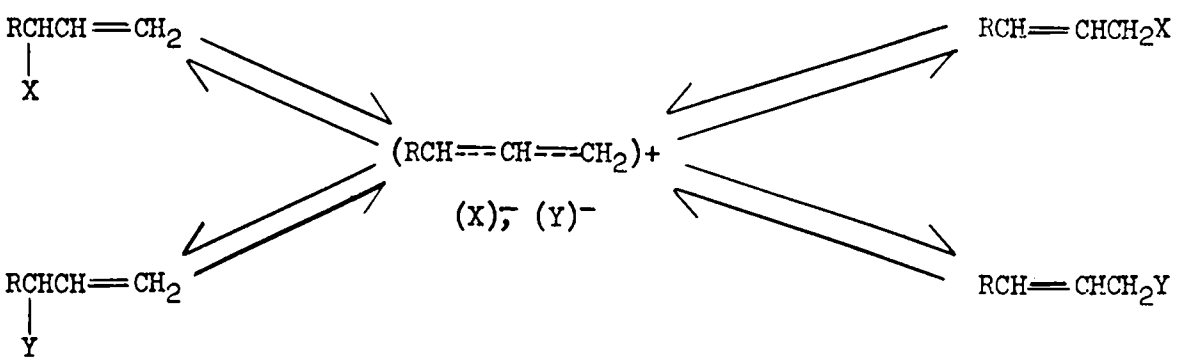
I. INTRODUCTION

A. Types of Allylic Rearrangement Mechanisms

In addition to the SN1, SN2, and SNi mechanisms[1] available to saturated systems, allylic compounds may undergo nucleophilic substitution by other mechanisms, all of which involve rearrangement of the allylic system. The consensus among most writers[1-6] is that the mechanisms of the rearrangement reactions in the three-carbon allylic system can be considered to be of three types, designated SN1', SN2', and SNi'.

1. The SN1' mechanism --- The unimolecular mechanism of nucleophilic substitution in allylic compounds is similar to the SN1 mechanism of substitution in that its rate-determining step involves the formation of a cationic intermediate, the process being assisted by the solvent. The SN1' intermediate, however, is resonance-stabilized and may react at either of the two electron-deficient carbon atoms with any available nucleophilic species, including solvent, to give an even greater mixture of products than the SN1 mechanism. A representation of the general mechanism, assuming reversibility and the presence of two nucleophilic species, is shown.



The SN' mechanism was suggested by Burton and Ingold[7] in 1928 and has been well established[1] by the accumulation of much evidence:

(a) The mobility of the system increases as the strength of the conjugate base decreases;

(b) The mobility increases as the electronic stabilization of the carbonium ion increases;

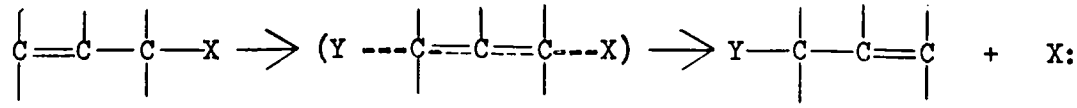
(c) The effects of both general acid catalysis and solvents are easily interpreted;

(d) The reaction may be diverted by the addition of other nucleophiles;

(e) The mechanism is in agreement with kinetic and product studies;

(f) The reactions are accompanied by racemization of optically active substrates.

2. The SN2' mechanism --- The bimolecular mechanism of substitution in allylic compounds is similar to the SN2 mechanism of substitution in that bond-making and bond-breaking are syncronous or nearly so. In the SN2' mechanism, however, the nucleophilic reagent attacks the unsaturated γ-carbon atom of the allyl substrate, displacing the α-substituent in a concerted process. A representation of the general mechanism is shown.



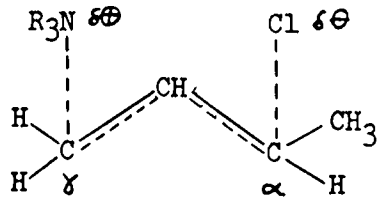
The SN2' mechanism was suggested as being theoretically possible by both Winstein[8] and Hughes[9] in 1938. During the next decade, attempts to demonstrate the mechanism in an unambiguous manner led to failure. In 1948, Catchpole, Hughes and Ingold,[10] based on a consideration of the steric and polar factors involved in the allylic system, concluded

that the SN2' mechanism rarely, if ever, occurs. Dewar,[11] in 1949, also concluded that it was unlikely that any example of the SN2' mechanism would be found. The basis for this conclusion was an erroneous consideration of the hybridization geometry involved, the consequences of which led to a linear and planar transition state, which was, of course, discounted as being highly inprobable.

The same year, Kepner, Winstein and Young[12] reported that the displacement by malonic ester anion on α-ethylallyl chloride led to 23% yield of the rearranged product. The reactions were found to be second order and the rearrangement was explained in terms of an SN2' mechanism.

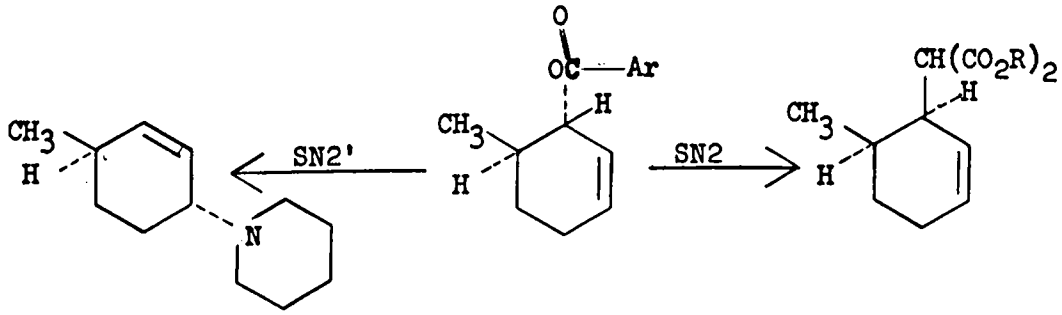
In 1951, Young, Webb and Goering[13] reported the displacement by diethylamine on either α- or γ-methylallyl chloride as leading to only N-diethyl- γ-methylallyl amine. Finding second-order kinetics, they proposed a SN2' mechanism for the displacement on α-methylallyl chloride.

The transition state suggested involved a triangle, formed by the carbon atoms of the allylic system. The p-orbitals of the α- and γ-carbon atoms, whose long axes are perpendicular to the plane of the carbon triangle, are used to form the bonds with the nucleophiles, which enter and leave on the same side of the trigonal plane, in a cis configuration.

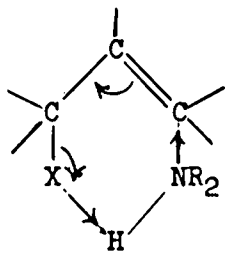


Stork and White[14] have since demonstrated that the entering and leaving nucleophiles are in fact in a cis configuration. Using

piperidine or malonic ester anion to displace 2,6-dichlorobenzoate anion from trans-6-alkyl-2-cyclohexenyl-1-2,6-dichlorobenzoate, they found that whenever allylic rearrangement occurred, the resulting product was trans, showing retention of configuration. However, if no rearrangement occurred, the resulting product was cis, indicating inversion of the 1-carbon by the SN2 mechanism.



It was suggested[13] that internal hydrogen bonding, available in reactions involving primary and secondary amines, may be assisting in the operation of the SN2' mechanism.



Ingold, in 1953,[1] proposed that on the basis of the existing evidence, the rearrangement reactions involving amines should be considered as proceeding by cyclic transformations of addition compounds, not as examples of SN2' mechanisms.

Young, et al.,[15,16] reported evidence concerning the importance of a hydrogen-bonded interaction in the SN2' displacement by amines on allylic systems. They found that the displacement by trimethylamine on α-methylallyl chloride gave 70% rearranged product while the corres-

ponding displacement by dimethylamine gave 100% rearranged product. From this it was concluded that the SN2' displacement by amines on allylic halides does not require the operation of a hydrogen-bonded interaction but the interaction may promote SN2' displacement. It was suggested that the relative steric requirements and nucleophilicities of the two classes of amines may also play a part in the increased susceptibility of the allylic chloride to rearrangement in the case of the secondary amines.

Dittmer and Marcantonio,[17] trying to assess the importance of a hydrogen-bonded interaction, followed the kinetics of two secondary amines, both deuterated and non-deuterated, in their displacements on α-methylallyl chloride. Finding no kinetic isotope effects, they concluded that the hydrogen (deuterium) of the secondary amine is not stretched in going from the initial state to the transition state and therefore rules out any considerable amount of hydrogen participation in the transition state.

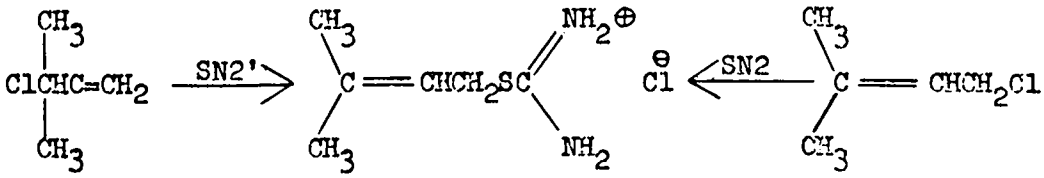
In order to realize SN2' rearrangement, inhibition of SN2 attack, either by steric or polar effects, seems to be desirable, even necessary, especially in the case of anionic nucleophiles.

In this connection, England[18] has reported the reaction of α- and γ-methylallyl bromide with radioactive bromide ion. The data shows that in the α-methylallyl system, SN2 proceeds only 60 times faster than SN2', being sterically hindered by the methyl group, while in the γ-methylallyl system, SN2 proceeds 28,000 times faster than SN2'. Further, it is seen that SN2' is not nearly as subject to steric hindrance as is SN2, as the SN2' reactions in the α-methylallyl system proceeds only 3 times faster than in the γ-methylallyl system.

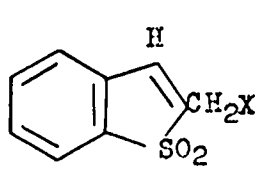
Other nucleophilic species, under the proper conditions, may also participate in SN2' reactions to the exclusion of SN2. De la Mare,

et al.[19] found that ethoxide ion displacement on either ∝- or ɣ-t-butylallyl chloride results in ɣ-t-butylallyl ethyl ether exclusively.

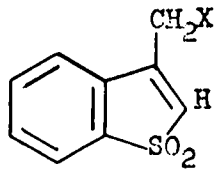
Rule, et al.[20] reported that the thiourea displacement on ∝, ∝ -dimethylallyl chloride leads to only rearranged product, the same product as that formed by the SN2 displacement by thiourea on ɣ, ɣ -dimethylallyl chloride.



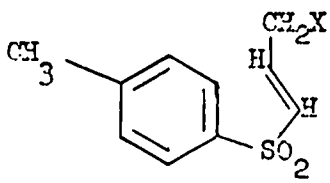
Bordwell, et al.[21] has investigated nucleophilic displacements by amines and thiourea on 2-(halomethyl)-benzothiophene-1, 1-dioxide (1), 3-(halomethyl)-benzothiophene-1, 1-dioxide (2), and 3-halo-1-p-toluenesulfonyl-1-propene (3).



(1)

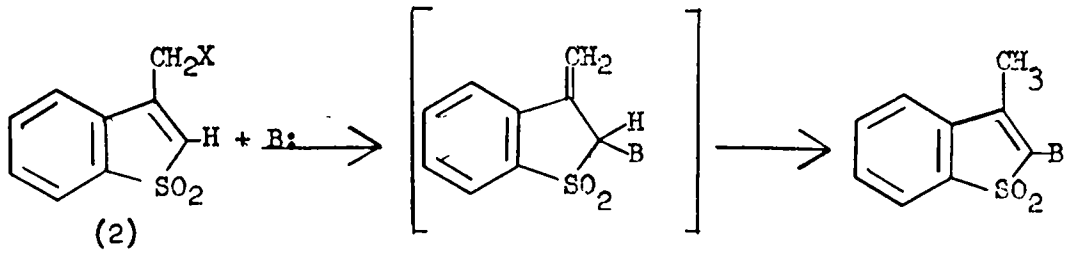


(2)



(3)

(1) and (3) give SN2 displacements while (2) gives a rearranged product formed, Bordwell suggests, by SN2' displacement followed by a tautomeric rearrangement.



(2)

The results were rationalized by assuming that both ρ- and ɣ- electrons are delocalized by the sulfonyl (benzenesulfonyl) group in

(1), (2), and (3) tending to promote SN2' displacement over SN2. But disruption of the conjugation of the allyl group with the benzene-sulfonyl group in (1) and with the sulfonyl group alone in (3) would lead to too high SN2' activation energies for these compounds. In (2), however, only direct conjugation with the sulfonyl group is lost(later restored by tautomeric rearrangement), the loss being relatively unimportant energetically compared to the conjugation with the benzenesulfonyl group.

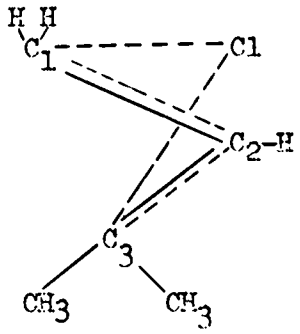
Bordwell claimed these to be the only known examples whereby primary allylic halides (chloride, bromide and iodide) had been found to react with nucleophilic reagents by an SN2' mechanism.

3. The SNi' mechanism --- The intramolecular mechanism of rearrangement and isomerization in allylic compounds as initially proposed [9,22] involved a cyclic-concerted process with little or no charge separation in the transition state. However, much evidence has been presented to support the view that there is a second intramolecular process involving an intimate ion-pair with considerable charge separation in the transition state.

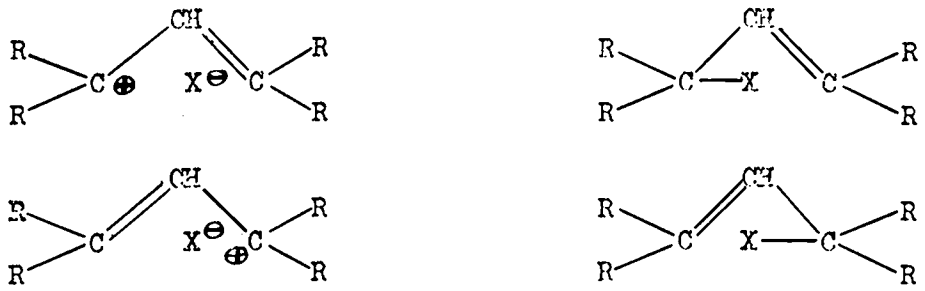
In 1951, Young, Winstein and Goering[23] reported the rearrangement of α, α-dimethylallyl chloride to γ, γ-dimethylallyl chloride. The rate of rearrangement was found to be independent of added chloride ion, indicating that the rearrangement was intramolecular. A mechanism, termed "internal return", embodying an intimate ion-pair in the transition state was proposed:

The planar pentenyl carbonium ion with sp^2 hybridization at carbon atoms C_1, C_2, and C_3 has electron deficient p orbitals at carbon C_1 and C_3, whose long axes are perpendicular to the carbon plane. The chloride ion is located above the plane of the carbonium ion, intermediate between carbon C_1 and C_3, the atomic orbitals of chloride over-

lapping the p orbitals of carbon C_1 and C_3.



It has been suggested[23, 24] that all SNi' reactions may be considered as proceeding by various mechanisms intermediate in the broad spectrum between the two extremes, the cyclic-concerted and the intimate ion-pair mechanisms. The transition state for all these mechanisms, intermediate and extreme, could be described by two pairs of "contributing structures";



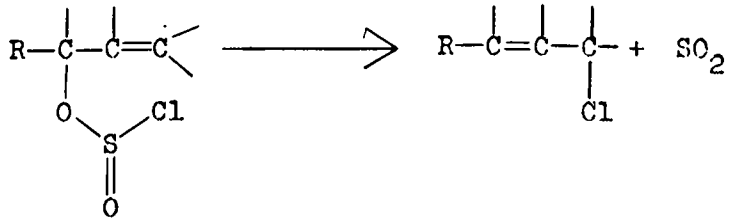
where the relative "contributions" of the hybrids may be assigned to some extent by various experimental evidence such as noting the effect, if any, on the rate of rearrangement by changing the ionizing power of the solvent or by substituting polar groups on the substrate.

The rearranging nucleophile (X) may be monodentate such as chloride ion or it may be ambidentate, such as carboxylate or thiocyanate ion. Thus a unique feature of the intimate ion-pair mechanism is the possibility of ion "scrambling"[25] in which an ambident anion is rotated °180, as contrasted to the stereospecificity of the concerted-cyclic mechanism.

Goering, et al.[25] has studied the intramolecular rearrangements of allylic esters and has concluded that the geometry of the SNi' transition state as proposed by Young also seems to be valid for rearrangements of allylic esters.

Braude has studied[26] and reviewed[27] the SNi' rearrangements of allylic esters, alcohols and ethers.

Young, et al.[28-30] in a series of papers have reported the isolation of several allylic chlorosulfinates and have studied their decomposition.

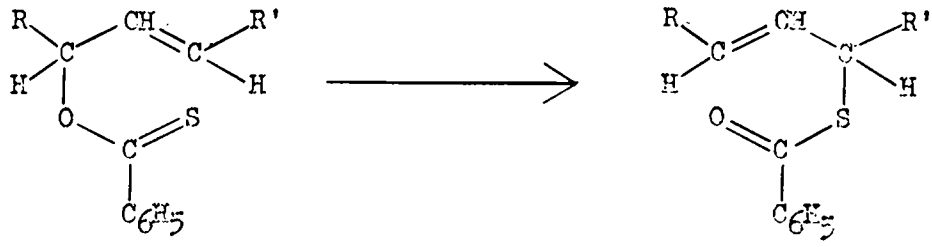


Postulating a SNi' mechanism for the decomposition reaction, they studied solvent polarity and substrate-substitution effects on rate of allylic rearrangement. They concluded that in the series, allyl chlorosulfinate, α-methylallyl chlorosulfinate, γ-methylallyl chlorosulfinate, and α-(trifluoromethyl)-allyl chlorosulfinate, the mechanism shifts from essentially intimate ion-pair to essentially cyclic-concerted.

The rearrangements of allylic thiocyanates to allylic isothiocyanates have been studied by Iliceto, et al.[31] and by Smith and Emerson.[32] The rearrangement of allyl thiocyanate and several of its methyl and dimethyl derivitives are reported to proceed by an essentially cyclic-concerted mechanism. γ-Phenyallyl thiocyanate shows no allylic rearrangement, however, giving only γ-phenylallyl isothiocyanate and shows great sensitivity to solvent ionizing power. It is suggested that the rearrangement proceeds by an intimate ion-pair mechanism in which the

ion is "scrambled", thus preserving the conjugated cinnamyl system.

Allylic thionbenzoates have been shown to rearrange to allylic thiolbenzoates. In contrast to the corresponding allylic oxo-benzoates, allyl-, α-methylallyl-, and γ-methylallyl thionbenzoates showed very little sensitivity to substrate substitution or solvent change in their rate of rearrangement, and Smith[33] has concluded that the transition state involves very little charge separation.

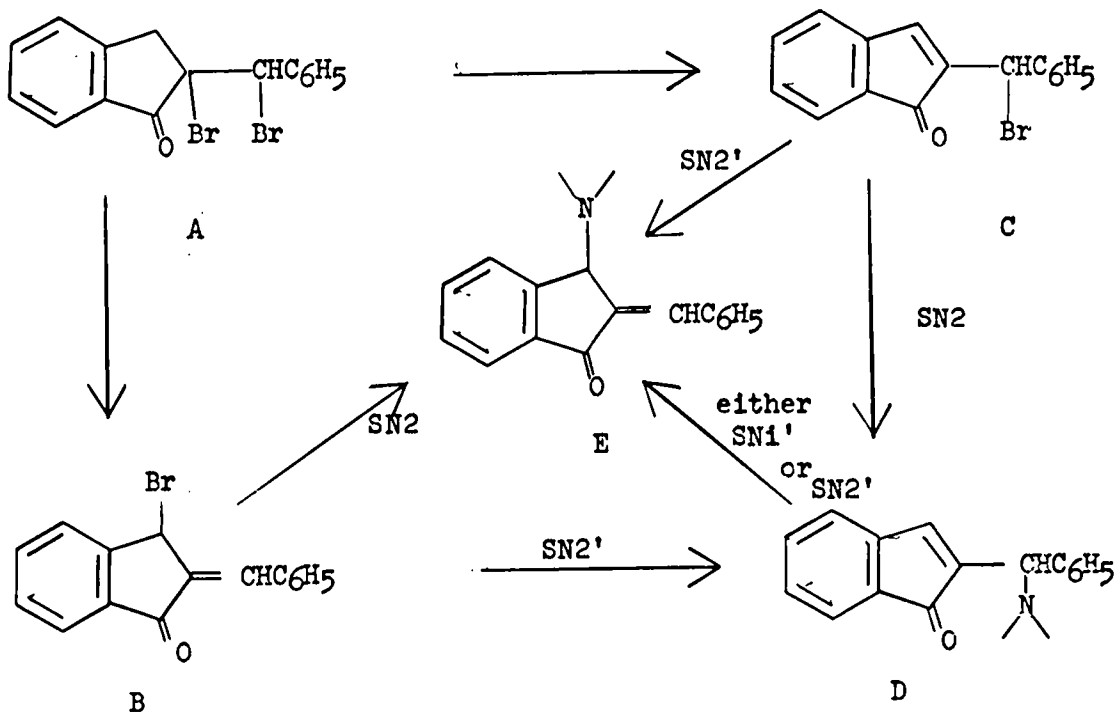


Gagneux, Winstein and Young[34] have found that the rate of equilibration between α, α-dimethylallyl azide and γ, γ-dimethylallyl azide and between α-methylazide and γ-methylallyl azide shows little sensitivity to either methyl substitution or to change of solvent.

B. Reactions of β-Keto-pherylallyl Bromides with Amines

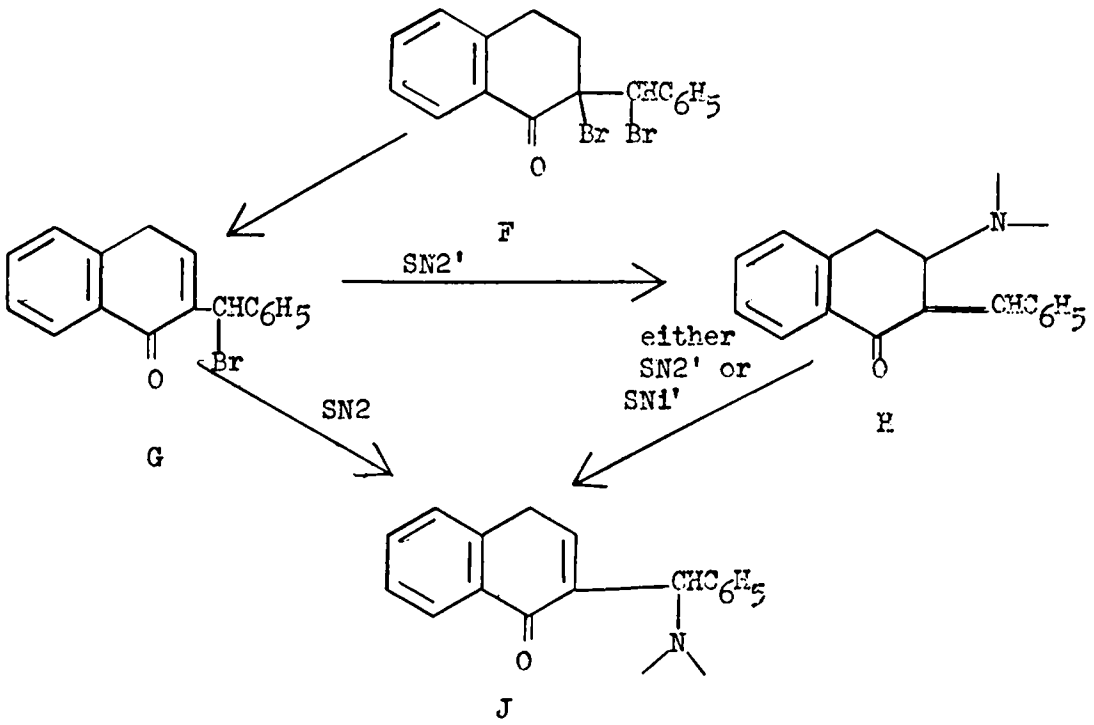
1. Reactions in the 2-benzal-1-indanone system --- In a series of studies on the elimination reactions of α-halogenated ketones, Cromwell, et al.[35,36] found that 2-bromo-2-(α-bromobenzyl)-1-indanone (A) reacts with piperidine or morpholine to give a 3-amino-2-benzal-1-indanone (E). Thermal elimination of A gives 3-bromo-2-benzal-1-indanone (B) which also reacts with piperidine or morpholine to give E.

Several reaction mechanisms seemed possible and even though an SNi' mechanism involving amines had never been reported in the literature, it could not be positively eliminated on this basis.



2. Reactions in the 2-Benzal-1-tetralone system --- In a series of studies on the chemistry of the derivatives of 2-benzal-1-tetralone, Hassner and Cromwell[37] found that 2-bromo-2-(∝-bromobenzyl)-4,4-dimethyl-1-tetralone (F) reacts with piperidine or morpholine to give a 2-(∝-aminobenzyl)-4,4-dimethyl-1-keto-1,4-dihydronaphthalene (J). Thermal elimination of F was found to give 2-(∝-bromobenzyl)-4,4-dimethyl-1-keto-1,4-dihydronaphthalene (G) which also reacts with piperidine or morpholine to give J.

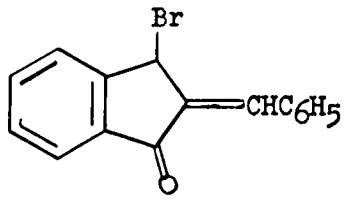
Here again, the positive assignment of a mechanism to the reaction was not possible, even though it was obvious that G must be an intermediate in the amine-promoted elimination of F, as well as the product from the thermal elimination.



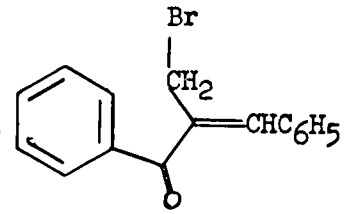
In both the indanone and the tetralone systems, two reaction courses are possible, one of which may involve a SNi' mechanism. In order to more seriously consider this latter mechanism, the existence of the SNi' mechanism must be demonstrated by isolation of an intermediate such as D or H and by obtaining kinetic and product data showing in an unambiguous manner evidence for an intramolecular rearrangement in that particular allylic amine.

A possible difficulty in the choice of an intermediate such as D, is that the indone ring system is highly strained, thus decreasing the probability both of its formation and of its rearrangement via SNi'.

A better choice may be the non-cyclic keto-analog of B, α-(bromomethyl)-chalcone (K). A possible disadvantage arises, however, in that K would be expected, a priori, to have a higher SN2/SN2' reaction rate ratio than B due to decreased steric hindrance to SN2 displacement at the bromine carbon atom.



B



K

II. STATEMENT OF PROBLEM

The work reported in this thesis is part of an integrated research program in progress at the University of Nebraska dealing with the mechanisms of addition, elimination, and substitution in α,β-unsaturated ketones and their halogen derivatives.

The essential scope of this research is the investigation of the mechanism(s) of substitution by amines on α-(bromomethyl)-chalcone. A knowledge of the mechanism(s) involved would be useful in elucidating some of the factors determining the structure of reaction products observed in other similar systems.

This work involves the following objectives:

(1) To synthesize α-(bromomethyl)-chalcone.

(2) To study the structure of the products formed by the reaction of α-(bromomethyl)-chalcone with amines in a variety of solvents.

(3) To study the effect of the differing steric requirements and nucleophilicities of various amines on the structure of the reaction products.

(4) To study the kinetics of the amine substitution reactions.

(5) To determine, from the foregoing studies, the mechanism(s) of substitution involved in this system.

III. EXPERIMENTAL

The uncorrected capillary melting points reported were obtained using an electrically-heated silicone oil-bath.

Infrared spectra were determined either in reagent grade carbon tetrachloride using 0.0388 molar solutions and 1.0 mm. matched sodium chloride cells or as a potassium bromide pellet. The recording instrument was a Perkin-Elmer Model 21 double beam recording spectrophotometer and was employed over a range of 625 to 4000 cm^{-1}.

Ultraviolet absorption maxima and extinction coefficients were determined in either 95% ethanol, reagent grade methanol or spectrograde iso-octane, employing 1.00×10^{-4} molar solutions and 1.000 cm. matched fused silica cells. The recording instrument was a Cary Model 11-MS recording spectrophotometer and was employed over a range of 210 to 400 mμ.

Proton magnetic resonance spectra were obtained in reagent grade carbon tetrachloride or deuterochloroform using tetramethylsilane (τ10.00) as internal reference employing standard Varian sample cells. The recording instrument was a Varian Model A-60 high-resolution spectrophotometer and was employed over a range of τ1.67 to τ10.00. τ-Values have the units of p.p.m.

The spectro-recording instruments were operated either by Mrs. Margaret M. Wheeler, Spectroscopist, or by the author.

Elementary analyses were performed by Micro-Tech Laboratories, Skokie, Illinois.

A. Synthesis and Reactions of trans- α-Methylchalcone

1. trans- α-Methylchalcone (I).[38] --- A 67.1 g. (0.500 mole) sample of propiophenone and 53.0 g. (0.500 mole) of benzaldehyde were introduced into a 1000 ml. flask. Dry hydrogen bromide gas was passed slowly into the flask until the reaction mixture solidified. The reaction mixture was kept near 0°C. and was stirred magnetically. The solidified reaction mixture was allowed to stand for 24 hours. The water formed by the condensation and excess hydrogen bromide were then removed in vacuo. To the reaction mixture was added 500 ml. of ethanol, 49.0 g. (0.500 mole) of potassium acetate and 69.1 g. (0.500 mole) of potassium carbonate. The alcoholic mixture was refluxed for 8 hours. The ethanol was removed in vacuo with heating. The residue was taken up in water and ethyl ether. The aqueous layer was discarded and the ethereal layer was washed with distilled water until the washings gave no test with 5% aqueous silver nitrate and was then dried over Drierite. Evaporation of the ether in vacuo and distillation of the resulting oil produced 99.6 g. (89.6% of the theoretical yield) of halogen-free (Beilstein Test) trans- α-methylchalcone, b.p. 155-160°C./1mm.; λmax 256, 290 mμ (ϵ, 12,400, 16,300, 95% ethanol); $\gamma_{C=O}$ 1654 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum of the pure oil showed peaks corresponding to one benzal and ten aromatic protons in the range τ2.1 to τ3.0 and a sharp peak corresponding to three α-methyl protons at τ7.77.

2. 2,3-Dibromo-2-methyl-3-phenyl-propiophenone (II).[38] --- To a stirred solution of 44.4 g. (0.200 mole) of α-methylchalcone in 60 ml. of glacial acetic acid, a solution of 33.6 g. (0.210 mole) of bromine in 60 ml. of glacial acetic acid was added dropwise as rapidly as it was decolorized. The mixture was allowed to react for five hours after addition was completed. The mixture was poured into a liter of water

and extracted with chloroform. The chloroform extract was washed and dried. Evaporation of the chloroform in vacuo produced an oil which crystallized on long standing. Recrystallization from Skelly Solve B (petroleum ether, b.p. 60-70°C.) yielded 59.8 g. (78% of theoretical yield) of white crystals, m.p. 53-55°C.; $\nu_{C=O}$ 1694 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in carbon tetrachloride showed peaks corresponding to ten aromatic protons in the range τ1.8 to τ2.8, a sharp peak corresponding to one benzyl proton at τ4.08 and a sharp peak corresponding to three α-methyl protons at τ7.88.

Anal. Calcd. for $C_{16}H_{14}Br_2O$: C, 50.29; H, 3.69; Br, 41.83.
Found: C, 50.41; H, 3.79; Br, 41.65.

3. Attempted reaction of α-methylchalcone with cyclohexylamine --- A 11.1 g. (0.050 mole) sample of α-methylchalcone and 4.96 g. (0.050 mole) of cyclohexylamine were dissolved in 25 ml. of ethyl ether and kept near 0°C. for 120 hours. The ethereal solution was washed and dried. Evaporation of the ether in vacuo recovered 10.8 g. of α-methylchalcone, identified by its infrared spectrum.

A 11.1 g. (0.050 mole) sample of α-methylchalcone and 9.92 g. (0.100 mole) of cyclohexylamine were dissolved in 50 ml. of benzene and refluxed for 26 hours. After washing and drying, evaporation of the benzene in vacuo with heating recovered 10.5 g. of α-methylchalcone, identified by its infrared spectrum.

B. Synthesis and Reactions of trans-α-(Bromomethyl)-chalcone

1. trans-α-(Bromomethyl)-chalcone (III). --- To a solution of 88.9 g. (0.400 mole) of α-methylchalcone in 300 ml. of carbon tetrachloride, 71.2 g. (0.400 mole) of N-bromosuccinimide was added with stirring. The mixture was heated to gentle reflux and a solution of 0.97 g. (0.004 mole) of benzoyl peroxide in 100 ml. of carbon tetrachloride

was added over a period of an hour. After refluxing for 2.5 hours, the reaction mixture was cooled and the succinimide was filtered off. The carbon tetrachloride was removed *in vacuo* with heating (40°C.). The resulting oil crystallized on addition of ethyl ether. Recrystallization from ethyl ether-hexane gave 111.1 g. (92.3% of theoretical yield) of light yellow crystals, m.p. 78.5-79.5°C.; λ max 257, 290mμ (ϵ, 13,700, 13,800, 95% ethanol); $\nu_{C=O}$ 1663 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in carbon tetrachloride showed peaks corresponding to ten aromatic protons in the range τ 2.1 to τ 2.7, a sharp peak corresponding to one benzal proton at τ 2.91 and a sharp peak corresponding to two α-bromomethyl protons at τ 5.50.

Anal. Calcd. for $C_{16}H_{13}BrO$: C, 63.80; H, 4.36; Br, 26.53.
Found: C, 63.83, H, 4.64; Br, 26.26.

2. 2-(Bromomethyl)-3-bromo-3-phenylpropiophenone (IV). — A 15.1 g. (0.050 mole) sample of α-(bromomethyl)-chalcone in 300 ml. of ethyl ether was cooled to near 0°C. and saturated with hydrogen bromide for one hour. Evaporation of the ether and recrystallization from Skelly Solve B gave 13.4 g. (70.2% of the theoretical yield) of white crystals, m.p. 123.5-124°C.; $\nu_{C=O}$ 1683 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in deuteriochloroform showed peaks corresponding to ten aromatic protons in the range τ 2.0 to τ 3.0, two peaks corresponding to one benzyl proton (split by 11 c.p.s.) at τ 4.73, eight peaks corresponding to one α-proton in the range τ 5.13 to τ 5.53 and five peaks corresponding to two α-(bromo-methyl) protons in the range τ 5.75 to τ 6.05.

Anal. Calcd. for $C_{16}H_{14}Br_2O$: C, 50.29; H, 3.69; Br, 41.83.
Found: C, 50.14; H, 3.88; Br, 41.48.

3. trans-1-Phenyl-2-benzoylcyclopropane (V). --- A 3.82 g. (0.010 mole) sample of 2-(bromomethyl)-3-bromo-3-phenylpropiophenone was added to 400 ml. of 80% ethanol. To this was added, with rapid stirring, 1.06 g. (0.010 mole) of sodium carbonate, 1.35 g. (0.020 mole) of zinc dust and 0.30 g. (0.002 mole) of sodium iodide.[39] The mixture was refluxed for 48 hours, filtered, cooled and filtered again. The mixture was evaporated to dryness, taken up in ether, washed and dried over Drierite. Evaporation of the ether in vacuo gave 1.44 g. (65% of theoretical yield) of pale yellow oil; λmax 247 mμ (ϵ, 14,200, 95% ethanol); $\nu_{C=O}$ 1675 cm.$^{-1}$(CCl_4). The infrared spectrum was identical with that of an authentic sample of trans-1-phenyl-2-benzoylcyclopropane.[40]

4. α-(Morpholinomethyl)-chalcone (VI). --- A 6.02 g. (0.020 mole) sample of α-(bromomethyl)-chalcone dissolved in 200 ml. of ethyl ether was added to a solution of 3.5 g. (0.040 mole) of morpholine in 100 ml. of ethyl ether. The mixture was stirred for 24 hours, filtered to remove 3.24 g. (96.4% of theoretical yield) of morpholine hydrobromide and was washed and dried. Evaporation of ether in vacuo, using no heat, produced 5.90 g. (95.9% of theoretical yield) of white crystals. Recrystallization from Skelly Solve B gave crystals, m.p. 61.5-63°C.; λmax 256, 285 mμ (ϵ, 14,300, 16,100, 95% ethanol); $\nu_{C=O}$ 1653 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in deuteriochloroform showed peaks corresponding to ten aromatic protons in the range τ2.0 to τ2.6, a peak corresponding to one benzal proton at τ2.68, three peaks corresponding to six protons (two α-N methylene and four α to morpholino oxygen) in the range τ6.2 to τ6.5, and four peaks corresponding to four protons (α to morpholino nitrogen) in the range τ7.4 to τ7.6.

Anal. Calcd. for $C_{20}H_{21}NO_2$: C, 78.14; H, 6.89; N, 4.56.
Found: C, 78.15; H, 6.90; N, 4.74.

The hydrochloride was prepared by dissolving 1.54 g. (0.0050 mole) of VI in 500 ml. of pentane, cooling to 0°C. and exposing the solution to a stream of hydrogen chloride for five minutes, with stirring. The precipitate was filtered and washed with ethyl ether. Several recrystallizations from methanol-ethyl ether gave 0.75 g. (44% of theoretical yield) of white crystals, m.p. 140-141°C.; λmax, 284 mμ (ϵ, 13,500, methanol); νc=o 1654 cm.$^{-1}$ (KBr).

Anal. Calcd. for $C_{20}H_{22}ClNO_2$: Cl, 10.31.

Found: Cl, 10.19.

5. α-(Piperidinomethyl)-chalcone (VII). --- A 6.02 g. (0.020 mole) sample of α-(bromomethyl)-chalcone dissolved in 200 ml. of ethyl ether was added to a solution of 3.52 g. (0.0414 mole) of piperidine in 100 ml. of ethyl ether. The mixture was stirred for 12 hours, filtered to remove 3.28 g. (98.8% of theoretical yield) of piperidine hydrobromide, and was washed and dried. Evaporation of the ether in vacuo and recrystallization from methanol gave 3.36 g. (54.4% of theoretical yield) of white crystals, m.p. 71-72°C.; λmax 250, 285 mμ (ϵ, 14,100, 13,900, 95% ethanol); νc=o 1652 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in carbon tetrachloride showed peaks corresponding to ten aromatic protons in the range τ2.0 to τ2.8, a sharp peak corresponding to one benzal proton at τ2.85, a sharp peak corresponding to two protons (α-N methylene) at τ6.56, two broad peaks corresponding to four protons (α to piperidino nitrogen) in the range τ7.4 to τ7.8, and a broad peak corresponding to six protons (β and γ to piperidino nitrogen) in the range τ8.4 to τ8.7.

Anal. Calcd. for $C_{21}H_{23}NO$: C, 82.59; H, 7.59; N, 4.59.
Found: C, 82.60; H, 7.61; N, 4.74.

The hydrochloride was prepared in the same manner as the hydrochloride of VI. From a 1.53 g. (0.0050 mole) sample of VII the yield of the hydrochloride from methanol-ethyl ether was 1.09 g. (63.8% of theoretical yield) of white crystals, m.p. 132-133°C.; λ max, 282 mμ (ϵ, 14,600, methanol); $\nu_{C=O}$ 1647 cm.$^{-1}$ (KBr).

Anal. Calcd. for $C_{21}H_{24}ClNO$: Cl, 10.37.
Found: Cl, 10.24.

6. α-(N-Methyl-cyclohexylaminomethyl)-chalcone (VIII). --- A 0.753 g. (0.0025 mole) sample of α-(bromomethyl)-chalcone dissolved in 10 ml. of ethyl ether was added to a solution of 0.566 g. (0.0050 mole) of N-methylcylohexylamine in 10 ml. of ether. The mixture was allowed to stand for 3 hours then filtered to remove 0.437 g. (90.2% of theoretical yield) of the N-methylcyclohexylamine hydrobromide. Evaporation yielded a yellow oil which slowly crystallized on standing. Several recrystallizations from pentane yielded 0.465 g. (55.8% of theoretical yield) of white crystals, m.p. 53-54°C.; λ max, 253, 279 mμ (ϵ, 13,800 13,700, 95% ethanol); $\nu_{C=O}$ 1654 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in deuteriochloroform showed peaks corresponding to ten aromatic protons in the range τ 2.0 to τ 2.8, a sharp peak corresponding to one benzal proton at τ 2.83, a sharp peak corresponding to two α-N methlyene protons at τ 6.33, a sharp peak corresponding to three N-methyl protons at τ 7.81, and several broad peaks corresponding to eleven cyclohexyl protons in the range τ 8.1 to τ 9.2.

Anal. Calcd. for $C_{23}H_{27}NO$: C, 82.84; H, 8.16; N, 4.20.
Found: C, 82.75; H, 8.04; N, 4.23.

7. α-(α-Cyclohexylaminobenzyl)-acrylophenone (IX). --- A 6.02 g. sample of α-(bromomethyl)-chalcone dissolved in 500 ml. of pentane

was added to a solution of 4.1 g. (0.040 mole) of cyclohexylamine in 25 ml. of pentane. The mixture was stirred and allowed to react for 15 hours, filtered to remove 3.51 g. (97.5% of theoretical yield) of cyclohexylamine hydrobromide, and was washed and dried. Evaporation of the pentane in vacuo and several recrystallizations from Skelly Solve B gave 4.43 g. (69.3% of theoretical yield) of white crystals, m.p. 96.5-97.5°C.; λmax, 250, 282mμ(ϵ , 13,200, 7,000, 95% ethanol); νc=o 1662 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in deuteriochloroform showed peaks corresponding to ten aromatic protons in the range τ2.2 to τ3.0, two peaks each corresponding to a terminal methylene (vinyl) proton at τ3.92 and τ4.30, a peak corresponding to one benzyl proton at τ4.86 and a broad peak corresponding to cyclohexylamino (C-H and N-H) protons in the range τ7.4 to τ9.2.

Anal. Calcd. for $C_{22}H_{25}NO$: C, 82.72; H, 7.89; N, 4.38.
Found: C, 82.91; H, 8.15; N, 4.45.

8. α-(α-t-Butylaminobenzyl)-acrylophenone (X). A 6.02 g. (0.020 mole) sample of α-(bromomethyl)-chalcone dissolved in 500 ml. of pentane was added to a solution of 3.00 g. (0.041 mole) of t-butylamine in 50 ml. of pentane. The mixture was stirred and allowed to stand for 48 hours, filtered to remove 2.92 g. (94.7% of theoretical yield) of t-butylamine hydrobromide and evaporated to dryness. Recrystallization from pentane gave 4.20 g. (71.5% of theoretical yield) of white crystals, m.p. 68.5-69°C.; λmax, 234 mμ (ϵ , 11,900, isooctane); νc=o 1660 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in deuteriochloroform showed peaks corresponding to ten aromatic protons in the range τ2.1 to τ2.8, two peaks each corresponding to a terminal methylene (vinyl) proton at τ3.68

and τ4.28, a peak corresponding to one benzyl proton at τ4.85, and a very sharp peak corresponding to ten t-butylamino (nine C-H and one N-H) protons at τ8.92.

Anal. Calcd. for $C_{20}H_{23}NO$: C, 81.87; H, 7.90; N, 4.77.
Found: C, 81.83; H, 7.85; N, 4.86.

The hydrochloride was prepared in the same manner as the hydrochloride of VI. From a 1.47 g. (0.0050 mole) sample of X the yield of the hydrochloride from methanol-ethyl ether was 0.98 g. (59% of theoretical yield) of white crystals, m.p. 183-184°C.; λmax, 255 mμ (ϵ, 10,000, methanol); νc=o 1658 cm.$^{-1}$ (KBr).

Anal. Calcd. for $C_{20}H_{24}ClNO$: Cl, 10.75.
Found: Cl, 10.84.

9. α-(t-Butylaminomethyl)-chalcone (XI).---- A 2.94 g. (0.010 mole) samples of α-(α-t-butylaminobenzyl)-acrylophenone was dissolved in 25 ml. of chloroform and refluxed for 48 hours. Evaporation of the chloroform and recrystallization from ethyl ether yielded 2.54 g. (86.5% of theoretical yield) of pale yellow crystals, m.p. 104.5-105°C.; λmax, 255, 283 mμ (ϵ,11,500, 16,100, isooctane); νc=o 1647 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in deuteriochloroform showed peaks corresponding to ten aromatic protons in the range τ2.1 to τ2.6, a peak corresponding to one benzyl proton atτ2.71, a peak corresponding to two α-N methylene protons at τ6.28, and a very sharp peak corresponding to ten t-butylamino (nine C-H and one N-H) protons at τ8.83.

Anal. Calcd. for $C_{20}H_{23}NO$: C, 81.87; H, 7.90; N, 4.77.
Found: C, 81.80; H, 7.71; N, 4.92.

The hydrochloride was prepared in the same manner as the hydrochloride of VI. From a 1.47 g. (0.0050 mole) sample of XI the yield of the hydrochloride from methanol-ethyl ether was 1.20 g. (72.7% of theoretical yield) of white crystals, m.p. 227-228°C.; λmax, 285 mμ

(ϵ, 15,700, methanol); $\nu_{C=O}$ 1647 cm.$^{-1}$ (KBr).

Anal. Calcd. for $C_{20}H_{24}ClNO$: Cl, 10.75.
Found: Cl, 10.60.

10. α-(α-Piperidinobenzyl)-acrylophenone hydrochloride (XII). --- A 3.01 g. (0.010 mole) sample of α-(bromomethyl)-chalcone dissolved in 500 ml. of pentane was added to 1.70 g. (0.020 mole) of piperidine in 100 ml. of pentane with stirring. After one hour, the mixture was cooled to 0°C. and stirring was continued for five hours. The mixture was filtered to remove piperidine hydrobromide and exposed to a stream of hydrogen chloride for five minutes while still cold. The precipitate was filtered and washed with ethyl ether. Several recrystallizations from methanol-ethyl ether gave 2.14 g. (62.8% of theoretical yield) of white crystals, m.p. 120-121°C.; λ_{max}, 257 mμ (ϵ, 8,600, methanol); $\nu_{C=O}$ 1660 cm.$^{-1}$ (KBr).

Anal. Calcd. for $C_{21}H_{24}ClNO$: C, 73.78; H, 7.07; Cl, 10.37; N, 4.10.
Found: C, 73.49; H, 7.16; Cl, 10.49; N, 4.17.

11. α-(α-Morpholinobenzyl)-acrylophenone hydrochloride (XIII).--- A 3.01 g. (0.010 mole) sample of α-(bromomethyl)-chalcone dissolved in 500 ml. of pentane was added to a solution of 1.75 g. (0.020 mole) of morpholine in 100 ml. of pentane with stirring. After one hour, the mixture was cooled to 0°C. and stirring was continued for five hours. The mixture was filtered to remove morpholine hydrobromide and exposed to a stream of hydrogen chloride for five minutes while still cold. The precipitate was filtered and washed with ethyl ether. Several recrystallizations from methanol-ethyl ether gave 1.64 g. (47.8% of theoretical yield) of white crystals, m.p. 139-140°C.; λ_{max}, 258 mμ (ϵ, 9,800, methanol); $\nu_{C=O}$ 1659 cm.$^{-1}$ (KBr).

Anal. Calcd. for $C_{20}H_{22}ClNO_2$: C, 69.86; H, 6.45; Cl, 10.31; N, 4.07.
Found : C, 68.95; H, 6.69; Cl, 10.17; N, 4.08.

In another experiment, the identical reagents, quantities, and conditions were used as in the preparation of XIII. After filtration of the morpholine hydrobromide, the pentane was evaporated in vacuo, using no heat, yielding a pale yellow oil.

The p.m.r. spectrum in carbon tetrachloride showed peaks corresponding to ten aromatic protons in the range τ2.1 to τ3.0, two peaks each corresponding to a terminal methylene (vinyl) proton at τ3.83 and τ4.33, a peak corresponding to one benzyl proton at τ5.50, three peaks corresponding to four protons (α to morpholino oxygen) in the range τ6.3 to τ6.6, and three peaks corresponding to four protons (α to morpholino nitrogen) in the range τ7.4 to τ7.8.

The sample cell and its contents were allowed to stand for 24 hours. The p.m.r. spectrum was almost identical to that of VI, indicating almost complete rearrangement of the original oil which was identified on this basis as the free base, α-(α-morpholinobenzyl)-acrylophenone.

12. α-(Iodomethyl)-chalcone (XIV). --- To a solution of 3.01 g. (0.010 mole) of α-(bromomethyl)-chalcone in 50 ml. of dry acetone was added a solution of 2.25 g. (0.015 mole) of sodium iodide in 100 ml. of dry acetone. After standing for 24 hours, the acetone was evaporated in vacuo and ethyl ether added to the residue. The mixture was filtered to remove the sodium halides and the ethereal solution was washed with water and dried. Evaporation of the ether in vacuo and several recrystallizations from Skelly Solve B gave 2.92 g. (83.8% of theoretical yield) of bright yellow crystals, m.p. 75-76°C.; λmax, 255, 290 mμ (ϵ, 15,000, 17,100, isooctane); νc=o 1660 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in carbon tetrachloride showed peaks corresponding to ten aromatic protons in the range τ2.1 to τ2.8, a sharp peak corresponding to one benzal proton at τ3.03, and a sharp peak corresponding to two α-iodomethyl protons at τ5.59.

Anal. Calcd. for $C_{16}H_{13}IO$: C, 55.19; H, 3.76; I, 36.45.
Found: C, 55.14; H, 3.84; I, 36.52.

13. α-(Chloromethyl)-chalcone (XV). --- A 1.50 g. (0.0050 mole) sample of α-(bromomethyl)-chalcone and 2.49 g. (0.015 mole) of tetraethylammonium chloride were added to 25 ml. of acetonitrile. After refluxing for 10 hours, the acetonitrile was evaporated in vacuo. A 100 ml. portion of ether was added to the residue and the tetraethylammonium halides were removed by filtration. The ether was evaporated in vacuo and 25 ml. of acetonitrile added. Another 2.49 g. sample of tetraethylammonium chloride was added and the solution was refluxed for six hours. Evaporation of the acetonitrile and addition of ether, followed by filtration and evaporation of the ether resulted in a colorless oil, which was crystallized from methanol. Recrystallization gave 0.75 g. (58% of theoretical yield) of white crystals, m.p. 62-63°C.; λmax, 261, 281 mμ (ϵ, 14,200, 17,000, isooctane); $\nu_{C=O}$ 1660 cm.$^{-1}$ (CCl_4).

The p.m.r. spectrum in deuteriochloroform showed peaks corresponding to ten aromatic protons in the range τ2.0 to τ2.7, a sharp peak corresponding to one benzal proton at τ2.75, and a sharp peak corresponding to two α-chloromethyl protons at τ5.37.

Anal. Calcd. for $C_{16}H_{13}ClO$: C, 74.85; H, 5.11; Cl, 13.81.
Found: C, 74.84; H, 5.21; Cl, 13.93.

C. Miscellaneous Reactions

1. Rearrangement of α-(α-cyclohexylaminobenzyl)-acrylophenone (IX) in solvent deuteriochloroform --- A 100 mg. sample of IX in deuteriochloroform was allowed to stand in the sunlight for six days in a p.m.r. sample cell.

The p.m.r. spectrum showed peaks corresponding to aromatic protons in the range τ2.0 to τ3.0, a sharp peak corresponding to a

benzal proton at τ2.68, a peak corresponding to α-cyclohexylamino-methyl protons at τ6.17, and broad peaks corresponding to cyclohexyl-amino protons in the range τ7.9 to τ9.1. This spectrum is consistent with the expected rearrangement product of IX, α-(cyclohexylaminomethyl)-chalcone.

Well purified samples of IX, exposed to the atmosphere, were found to decompose to a yellow oil over a period of a week, but were found to be stable in the dark at lower temperatures (0 to -20°C).

By p.m.r. analysis, IX was also found to slowly rearrange in carbon tetrachloride in the dark.

2. Relative rates of rearrangement of α-(α-t-butylamino-benzyl)-acrylophenone (X) in solvents benzene, carbon tetrachloride, and deuteriochloroform. --- The p.m.r. sample cells labeled (A), (B), and (C), each containing 100 mg. of X and 0.5 ml. of solvent, benzene, carbon tetrachloride, and deuteriochloroform respectively, were allowed to stand for six days. Periodic analysis by p.m.r. showed that the relative rates of rearrangement of the contents of cells (A), (B), and (C) to be, very roughtly, 1:2:10.

3. Reaction of α-(α-t-butylaminobenzyl)-acrylophenone (X) with excess t-butylamine in solvent pentane. --- A 100 mg. sample of X was placed in each of two p.m.r. sample cells, labeled (A) and (B). To cell (A) was added 0.5 ml. of pentane. To cell (B) was added 0.4 ml. of pentane and 0.10 ml. (0.00095 mole) of t-butylamine. The cells were allowed to stand 16 hours. By p.m.r. analysis, the contents of cell (A) showed no rearrangement. The contents of cell (B) had solidified. The solid was shown to be the rearrangement product XI, α-(t-butylamino-methyl)-chalcone, by mixed melting point.

4. Reaction of α-(α-t-butylaminobenzyl)-acrylophenone (X) with excess morpholine in solvent pentane. ---- A 2.93 g. (0.010 mole) sample of X was dissolved in 50 ml. of pentane to which was added 8.71 g. (0.10 mole) of morpholine. After standing for 48 hours, the pentane was evaporated in vacuo and the residue was taken up in ether. The ether solution was washed and dried. Evaporation of ether in vacuo gave 2.80 g. (91.2% of theoretical yield) of VI, α-(morpholinomethyl)-chalcone.

5. Attempted reaction of α-(t-butylaminomethyl)-chalcone (XI) with excess morpholine in solvent pentane. ---- A 2.93 g. (0.010 mole) sample of XI was dissolved in 100 ml. of pentane to which was added 8.71 g. (0.10 mole) of morpholine. After standing for 52 hours, the pentane was evaporated in vacuo and the residue taken up in ether. After washing and drying the ether solution, evaporation gave 2.64 g. (90.2% of theoretical recovery) of starting material, XI.

6. Rearrangements of α-(α-t-butylaminobenzyl)-acrylophenone (X) and α-(t-butylaminomethyl)-chalcone (XI) in solvent methanol. ---- A 2.94 g. (0.010 mole) sample of X and an equal amount of XI were each dissolved in 25 ml. of methanol and allowed to stand for 8 days. The methanol was evaporated in vacuo and the colorless oils were subjected to p.m.r. analysis.

The p.m.r. spectra in carbon tetrachloride were nearly identical, but were poorly resolved and were not integrated. Since no tetramethylsilane was immediately available the peak possibly corresponding to the α-methylene protons was arbitrarily assigned a value of τ5.65. The spectra both showed peaks corresponding to benzyl and aromatic protons in the range τ2.0 to τ3.3, the peak at τ5.65, two small peaks at τ6.1 and τ6.4, four larger peaks in the range τ6.6 to τ7.1, a small peak at τ7.5 and three larger peaks in the range τ8.8 to τ9.3.

7. Relative rates of rearrangement of α-(t-butylaminomethyl)-chalcone (XI) in solvents acetonitrile, 95% ethanol, and methanol. --- Acetonitrile, 95% ethanol, and methanol solutions, each 1 x 10^{-4} molar in XI, were allowed to stand in flasks labeled A, B, and C, respectively. Periodic analysis by ultraviolet showed rearrangement of XI in flasks B and C only, rearrangement being evidenced by a decrease in the intensity of the peak at 283 mu. Rearrangement of XI in flask A was subsequently observed only on keeping the flask at 41.5°C. for a period of time. Assigning the rate of rearrangement of XI observed for flask A a value of one, the relative values observed for flasks B and C were multiplied by a factor of five to correct for the observed temperature coefficient of reaction rate for a ca. 15°C. increase in temperature. The relative rates of rearrangement of the contents of flasks A, B, and C were then, given, very roughly, by the ratio 1:10:30.

8. Reaction of α-(t-butylaminomethyl)-chalcone (XI) with excess morpholine in solvent methanol. --- A 2.93 g. (0.010 mole) sample of XI was dissolved in 25 ml. of methanol to which was added 8.71 g. (0.10 mole) of morpholine. After standing three days, the solution was added to ethyl ether, washed until neutral, then evaporated in vacuo. The infrared spectrum of the resulting oil was identical to that of VI, α-(morpholinomethyl)-chalcone.

9. Attempted reaction of α-(morpholinomethyl)-chalcone (VI) with excess t-butylamine in solvent methanol. --- A 3.07 g. (0.010 mole) sample of VI was dissolved in 25 ml. of methanol to which was added 7.3 g. (0.10 mole) of t-butylamine. After standing for four days, the methanol and t-butylamine were evaporated in vacuo. The infrared spectrum of the resulting oil was identical to that of the starting material, VI.

10. Reaction of α-(bromomethyl)-chalcone (III) with t-butyl alcohol. --- A 3.01 g. (0.010 mole) sample of III was added to 25 ml. of t-butyl alcohol and refluxed for 46 hours. The cooled solution was added to ethyl ether, washed and dried, and evaporated in vacuo.

The p.m.r. spectrum in carbon tetrachloride of the resulting oil showed peaks corresponding to benzal and aromatic protons in the range τ2.1 to τ3.1, a peak corresponding to unreacted bromomethyl protons at τ5.52, a peak corresponding to (t-butoxy)-methyl protons at τ5.66, and two peaks corresponding to t-butoxy protons in the range τ8.7 to τ8.9

11. Reaction of α-(bromomethyl)-chalcone (III) with thiophenoxide ion in solvent methanol. --- A solution of 1.21 g. (0.011 mole) of thiophenol and 0.59 g. (0.011 mole) of sodium methoxide in 50 ml. of methanol was added dropwise to a solution of 3.01 g. (0.010 mole)of III in 50 ml. of methanol. After standing 26 hours, the solution was added to ethyl ether, was washed with dilute aqueous sodium carbonate, then with water and then dried. Evaporation in vacuo gave a colorless oil.

The p.m.r. spectrum in carbon tetrachloride showed peaks corresponding to 15 aromatic protons in the range τ2.2 to τ3.0, a peak corresponding to one benzal proton at τ3.08, and a peak corresponding to two (thiophenoxy)-methyl protons at τ5.80.

12. Reaction of α-(bromomethyl)-chalcone (III) with methoxide ion in solvent methanol. --- A solution of 0.54 g. (0.010 mole) of sodium methoxide in 50 ml. of methanol was added dropwise to a solution of 3.01 g. (0.010 mole) of (III) in 50 ml. of methanol. After standing 50 hours, the solution was added to ether, was washed and dried. Evaporation in vacuo gave a colorless oil.

The p.m.r. spectrum in carbon tetrachloride showed peaks

corresponding to benzal and aromatic protons in the range τ1.9 to τ3.0, two peaks corresponding to terminal methylene (vinyl) protons at τ4.10 and τ4.46, a peak corresponding to bromomethyl protons at τ 5.5 (unreacted starting material), a peak corresponding to methoxy methyl protons at τ5.63, and six unassigned peaks in the range τ6.1 to τ7.0.

13. Reaction of 2-(bromomethyl)-3-bromo-3-phenylpropiophenone (IV) with excess t-butylamine. --- A 3.82 g. (0.010 mole) sample of IV was added to 25 ml. of t-butylamine and refluxed for four hours. The amine was evaporated in vacuo and the residue was washed in a filter with three 25 ml. portions of ether. Evaporation of ether and recrystallization from ether gave 2.76 g. (94.2% of theoretical yield) of XI, α-(t-butylaminomethyl)-chalcone, identified by mixed melting point.

D. The Kinetics of the Rearrangement of α-(α-t-Butylaminobenzyl)-acrylophenone (X) in Solvent Deuteriochloroform. ---

Equipment and materials. --- The p.m.r. spectro-recording instrument and the preparation of X were described previously. The deuteriochloroform was obtained from Columbia Organic Chemicals.

Kinetic method and measurement --- The p.m.r. analyses of the deuteriochloroform solutions of X were carried out in sealed standard Varian sample cells, which were immersed in a constant temperature bath between analyses. Sunlight was excluded from the cells at all times.

The kinetics were followed by measuring the change in the relative amounts of the t-butylamino proton peak due to X to the peak due to XI. Determination of the relative amounts of the two isomers could not be made from the integration curve due to the proximity of the two peaks (τ8.83 and τ8.92). The relative heights of the two peaks above the baseline were used to measure the extent of rearrangement.

For each spectrum, the sum of the two peak heights H_X and H_{XI} divided by the peak height H_X was equated to C_o/C.

Rate law and data. --- If the rearrangement is first order with respect to X, then the following relationship should hold:

$$2.303\ t^{-1} \log (C_o/C) = k, \text{ and}$$

$$2.303\ t^{-1} \log (H_X = H_{XI}/H_X) = k$$

where t is the time in seconds and k is the specific rate constant in seconds^{-1}.

The individual k values were calculated by the long-interval method. The overall k values were calculated by the least squares method, using an IBM 7074 computer, by feeding in log C_o/C values vs. t and obtaining a regression line equal to k/2.303. The fit of the data to the obtained regression line was excellent.

The values reported for E_a, A, ΔH^*, and ΔS^* are taken from the Appendix, where the equations and calculations may be found.

1. Temperature: 36.5°C.; (X): 100 mg. in 0.25 ml. $CDCl_3$.

Time, hours	$H_X + H_{XI}/H_X$, cm./cm.	% Rearr'd	k x 10^6, sec.$^{-1}$
24	22.7/14.3	37	
34	23.0/10.9	53	8.06
46	24.0/8.3	65	7.62
54	22.6/6.2	73	7.73
70	23.8/4.0	83	7.99
80	20.5/2.5	88	8.18
96	16.7/1.2	93	8.38

The average overall k = 8.43 x 10^{-6} seconds $^{-1}$.

2. Temperature: 41.5°C.; (X): 100 mg. in 0.30 ml. $CDCl_3$.

Time, hours	$H_X + H_{XI}/H_X$, cm./cm.	% Rearr'd	k x 10^6, $sec.^{-1}$
20	21.2/12.0	43	
26	19.3/9.0	53	8.95
30	21.7/8.8	59	9.27
44	20.5/5.0	76	9.66
56.5	18.6/2.9	84	9.78
68	19.8/2.1	89	9.92
94	18.4/0.8	96	9.66

The average overall k = 9.72 x 10^{-6} seconds $^{-1}$.

The values for the thermodynamic parameters for this rearrangement are given: E_a, 5.5 kcal. $mole^{-1}$; A, 6.6 x 10^{-2} or $10^{-1.18}$ sec^{-1}.; ΔH^*, 4.9 kcal. $mole^{-1}$; ΔS^*, -66 cal. $deg.^{-1}$ $mole^{-1}$. The latter three parameters were calculated at 36.5°C.

E. The Kinetics of the Rearrangement of α-(t-butylaminomethyl)-chalcone (XI) in Solvent Methanol.---

Equipment and materials. --- The ultraviolet spectrophotometer and the preparation of XI were described previously. The methanol was reagent grade.

Kinetic method and measurement. --- Samples for analysis were withdrawn at the required intervals from the bulk of the solution, which was kept in a darkened constant-temperature bath. After analysis, the samples were discarded.

In alcohols, XI was found to rearrange to a species whose structure is not known with certainty. The rearrangement was evidenced by the change in the ultraviolet spectrum of XI in methanol. Compound XI absorbs at 283 mμ (ε , 15,000) while the rearrangement product absrobs at 248 mμ (ε , 10,500). The change in the optical density (O.D.) at 290 mμ was used to determine the extent of rearrangement of XI.

Rate law and data. --- The change in the O.D. can be shown to be proportional to the change in concentration for first order kinetics so that the relations should hold:

$$O.D._{t_o} - O.D._{\infty} / O.D._{t} - O.D._{\infty} = C_o/C$$

$$2.303\ t^{-1} \log (C_o/C) = k.$$

Zero time was taken to be 2-3 hours after mixing and infinite time was taken to be 8-10 half-lives of reaction.

The individual and average overall values for k were obtained as described in the previous section. The data gave excellent fit to the regression lines obtained. The values reported for the thermodynamic parameters are taken from the Appendix, where the equations and the calculations may be found.

1. Temperature: 35.0°C.; (XI): 1.5×10^{-4} M. in methanol.

Time, hours	log (C_o/C)	% Rearranged	k x 10^6, sec^{-1}.
0	0.000	0	
6	0.073	15	7.78
24	0.283	48	7.53

The average overall k = 7.52×10^{-6} seconds $^{-1}$.

2. Temperature: 40.0°C; (XI): 1.5×10^{-4} M. in methanol.

Time, hours	log (C_o/C)	% Rearranged	k x 10^6, sec^{-1}.
0	0.000	0	
5	0.098	20	12.5
21	0.398	60	12.1
27	0.509	69	12.0

The average overall k = 12.0×10^{-6} seconds^{-1}.

The values for the thermodynamic parameters for this rearrangement are given: E_a, 18.0 kcal. $mole^{-1}$; A, 4.5×10^7 or $10^{7.66}$ sec^{-1}; ΔH^*, 17.4 kcal. $mole^{-1}$; ΔS^*, -26 cal. $deg.^{-1}$ $mole^{-1}$. The latter three parameters were calculated at 30.0°C.

IV. DISCUSSION OF RESULTS

A. Synthesis

α-Methylchalcone (I), the most obvious precursor of α-(bromomethyl)-chalcone (III), was first prepared by Abell[38] by the condensation of propiophenone with benzaldehyde. The potassium hydroxide catalyzed condensation gave low (10%) yields of pure I. Condensation in the presence of excess gaseous hydrogen chloride, however, produced a chloro-compound which after elimination of hydrogen chloride gave a good yield of the unsaturated ketone I.

The unsaturated ketone I was assigned a trans configuration on the basis of its ultraviolet spectra[41].

The intermediate β-chloro-α-methyl-β-phenylpropiophenone as well as the corresponding β-bromo compound were later characterized by Abell[42] and both were found to exist in two diastereoisomeric forms.

The dibromo compound II was obtained by Abell[38] as an obviously impure oil of variable analysis.

The attempted reaction of I with cyclohexylamine, contrary to expectation, did not give a saturated β-aminoketone, the reason for which may be due to one of several factors discussed in a review article by Cromwell[43].

The synthesis of the previousl unreported α-(bromomethyl)-chalcone (III) was modeled after the reported synthesis of the isomeric β-(bromomethyl)-chalcone (γ-bromodypnone)[44].

The reaction of III with gaseous hydrogen bromide in ethyl ether at ambient temperatures gave only oil, while reaction near 0°C. gave crystals of IV. The oil was assumed to be a mixture of the several possible diasteriooisomeric monobromoketones.

The gross structure of IV (and therefore of III) was shown chemically by the cyclization to the known trans-1-phenyl-2-benzoyl-cyclopropane (V)[40]. The assigned structures of III and IV were also consistent with their p.m.r. spectra. The trans structure was assigned to III since only a small hypochromic shift was observed in the ultraviolet spectrum (as compared to the model compound I). A large hypochromic shift would be expected for a cis configuration[41].

B. Structures of the Unsaturated Aminoketones

The structures of the various unsaturated aminoketones were established primarily by analysis of the p.m.r., ultraviolet, and infrared spectra, after the molecular formula had been established by means of molecular weight determination and elemental analysis.

The p.m.r. spectra of compounds VI, VII, VIII, and XI all showed the one benzal proton and the $-CH_2-N<$ protons expected for α-(aminomethyl)-chalcones. The ultraviolet spectra of the four compounds were similar to the spectra of the parent compounds I and III, indicating retention of the cinnamoyl-acrylophenone conjugated systems. The infrared spectra also indicated a highly conjugated carbonyl system.

The p.m.r. spectra of compounds IX and X each showed a triad of peaks, each peak corresponding to one proton. This triad could best be accounted for by two vinyl and one benzyl proton, which would be present in an α-(α-aminobenzyl)-acrylophenone. The ultraviolet spectra, while definitely excluding the presence of the cinnamoyl system, was otherwise non-specific, the peak observed being typical of many phenones, both saturated and unsaturated. The infrared spectra indicated that the carbonyl group present was still highly conjugated.

An attempt was made to prepare a model compound, α-(bromomethyl)-acrylophenone, in order to obtain the p.m.r., ultraviolet, and

infrared spectra of it and of its amino derivatives for comparison. α-Methylacrylophenone was obtained *via* the Mannich reaction but attempts to obtain the allyl bromination product were unsuccessful. The p.m.r. spectrum of α-methylacrylophenone showed peaks corresponding to five aromatic protons in the range τ2.5 to τ3.5, two peaks each corresponding to a vinyl proton at τ4.80 and τ5.02, and a sharp peak corresponding to three methyl protons at τ8.58. The ultraviolet spectrum showed a peak at 243 mμ (ϵ , 9,200, 95% ethanol) and the infrared spectrum showed $\nu_{C=O}$, 1663 cm^{-1}.

The combined spectral evidence indicated quite clearly that compounds IX and X had the α-(α-aminobenzyl)-acrylophenone structure. The observation that both IX and X were thermodynamically unstable led to attempts to trap the corresponding morpolino and piperidino compounds, using pentane as a solvent rather than the more polar ethyl ether. While the crystalline free bases could not be isolated, the hydrochlorides XII and XIII were obtained. The ultraviolet and infrared spectra of XII and XIII, compared to the spectra of IX and X, identified them as also possessing the α-(α-aminobenzyl)-acrylophenone structure. In addition, an oil resulting from the reaction of morpholine with III in pentane at 0°C., assumed to be α-(α-morpholinobenzyl)-acrylophenone on the basis of its p.m.r. spectrum, showed almost complete rearrangement in carbon tetrachloride to VI over a 24-hour period.

All the compounds having the α-(aminomethyl)-chalcone structure were assigned the *trans* configuration on the basis of the intensity of absorption in the 279 mμ to 290 mμ region of their respective ultraviolet spectra, as compared to the model parent compound *trans*-α-methylchalcone (I)[41]. The small hypochromic and hypsochromic shifts observed for the α-(subst.-methyl)-chalcone compounds III, VI-VIII, XI

XIV, and XV may be due to steric hindrance to conjugation by the interaction of the subst.-methyl group with the benzoyl group, twisting the S-bond between the carbonyl-carbon and the α-carbon[45].

The reactions of III with iodide, chloride, thiophenoxide, and methoxide anions gave the corresponding α-(subst.-methyl)-chalcone compounds as evidenced by their p.m.r. and ultraviolet spectra. The p.m.r. spectra of the crude reaction product of the reaction of III with methoxide anion, however, indicated a small amount of α-(α-methoxybenzyl)-acrylophenone may be present as evidenced by a slight indication of a "vinyl-benzyl triad".

C. Proposed Mechanisms

1. Rearrangement of amino-acrylophenone X in solvents of low polarity. --- The thermodynamic parameters obtained from the kinetic study of the rearrangement of X in solvent deuteriochloroform suggests several possibilities concerning the topology, the geometry, and the polarity of the transition state. The extremely low value for E_a, 5.5 kcal., suggests that the rearrangement is not concerted, i.e., that bond-making is far ahead of bond-breaking, thereby significantly reducing the energy "debt"[46]. Secondly, the extremely low negative value for ΔS^*, -66 cal.deg.$^{-1}$ mole^{-1}, corresponding to a value for A of $10^{-1.18}$ sec.$^{-1}$, suggests a highly polar transition state[47]. This possibility is further enhanced by the extreme sensitivity of the rate of rearrangement to the polarity of the solvent. The increasing rates of rearrangement in the order pentane, benzene, carbon tetrachloride, and deuteriochloroform, corresponds roughly to the increasing polarity of the solvent, as measured by the respective dielectric constants[48], 1.8, 2.2, 2.2, and 4.8 (chloroform).

It is interesting to compare the above thermodynamic parameters

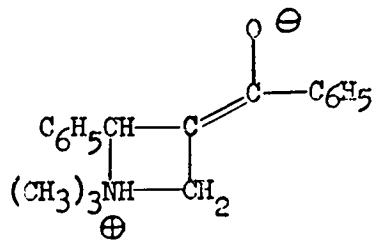
with values obtained in other ring closure reactions. Salomon[49] has studied the formation of cyclic imines in water at 25°C. from ω-haloalkylamines. In the formation of the 4-ring azetidine from 3-bromopropylamine, E_a and A were found to be ≈ 23 kcal. and 10^{11} sec.$^{-1}$, respectively. In the 3-ring aziridine series, cyclization of 2-bromoethylamine gave values of ≈ 25 kcal. and 10^{15} sec.$^{-1}$, while the cyclization of 2-bromo-2-phenylethylamine gave values for E_a and A of ≈ 15 kcal. and 10^{13} sec^{-1}. Cyclization of 5-chloro-pentylamine to give the 6-ring piperidine in water, wet carbon tetrachloride, and wet benzene, resulted in values for E_a of ≈ 21, 15 and 15 kcal. respectively, while the corresponding values for A were found to be ≈ 10^{11}, 10^6, and 10^5, respectively.

Bennett[50] et al. have studied the formation of cyclic sulfonium chlorides in 50% aqueous acetone at 70°C., the cyclization of phenyl 4-chlorobutyl sulfide yielding a 5-ring, and phenyl 5-chlorobutyl sulfide yielding a 6-ring. Salomon[49] later calculated the thermodynamic parameters of the cyclizations and found E_a and A for the formation of the 5-ring to be ≈ 23 kcal. and 10^{11} sec.$^{-1}$, and for the 6-ring, 24 kcal. and 10^{10} sec.$^{-1}$, respectively.

There are some obvious trends in the values of E_a and A for these ring closure reactions. As the ring size increases from 3 to 4 to 5, the E_a values are found to decrease, which can be ascribed to decrease in ring strain. As the polarity of the solvent decreases, the E_a value also decreases. The substitution of phenyl for hydrogen at the halogen-carbon lowers the E_a by a very large amount, which may be ascribed to the ability of the phenyl ring to act as an electron donor or acceptor as required, thus facilitating a process in which the bond-making is ahead of a breaking of the carbon-halogen bond. As the ring size increases from 3 to 4 to 5 to 6, the A values decrease as would be expected from

the standpoint of the decreased probability of the chain-ends meeting. As the polarity of the solvent decreases, the A values also decrease. When a phenyl group is substituted for hydrogen on the halogen-carbon, the A value decreases due to steric interaction.

It is now obvious that the rearrangement of amino-acrylophenone X in solvents of low polarity is facilitated by the electron delocalization provided by the carbonyl group. A cyclic, highly polar transition state as implied by the structure below best accounts for all the experimental evidence.

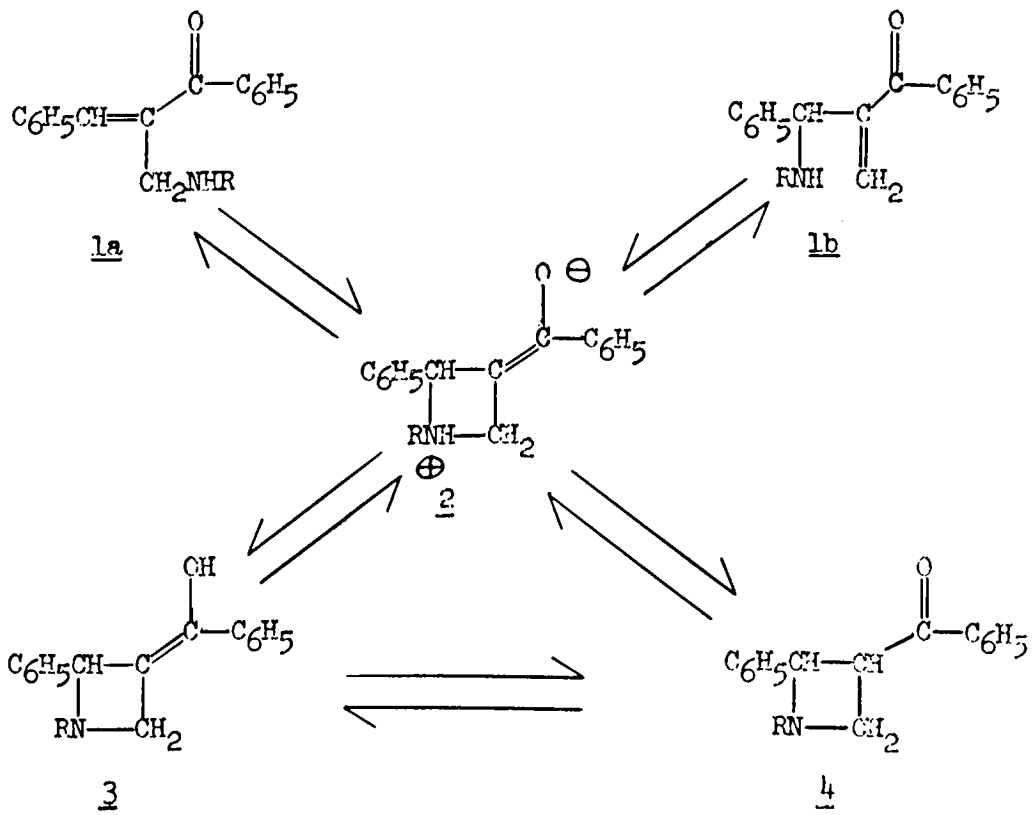


The relative steric requirements and nucleophilicities[51] of the amino groups attached to the substituted acrylophenone structure no doubt plays a major role in determining the relative rates of rearrangement in this reaction series.

2. Rearrangement of amino-acrylophenone X and amino-chalcone XI in solvents of high polarity. --- Amino-acrylophenone X and amino-chalcone XI, both stable with respect to rearrangement in solvent pentane, rearrange readily in solvent methanol to form an unidentified common product(s). X was found to be subject to amine exchange (with rearrangement) in either solvent, pentane or methanol, while XI exchanges amines (without rearrangement) only in methanol.

The kinetics of the rearrangement of XI in methanol were conveniently followed by ultraviolet absorbtion and were found to be first order with respect to XI. The relatively high activation energy, 18 kcal. $mole^{-1}$, was consistent with the disruption of the highly conjugated

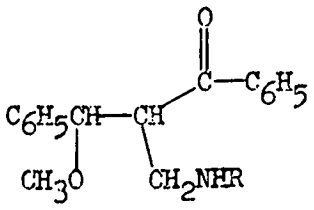
cinnamoyl system, as indicated by the disappearance of the peak at 283 mμ. The low negative entropy of activation, -26 cal. deg.$^{-1}$ mole^{-1}, corresponding to a value for A of $10^{7.66}$ sec.$^{-1}$ (calculated on a presumption of overall first-order kinetics), suggested that a highly polar transition state may be involved. The amine exchange reactions also suggested that a cyclic intermediate is formed at some stage. It was thought to be significant that the rate of rearrangement increased as the polarity of the solvent increased in going from 95% ethanol to methanol, whose dielectric constants are 27 and 34, respectively. However, in acetonitrile which has a dielectric constant of 39, the rate of rearrangement was very slow relative to the rates in the alcohols. This indicated that a proton transfer step may be important, or that a different mechanism may be operating in acetonitrile, or both.



Tranannular protopy is assumed to be possible, leading to 4 directly from 2.

Several mechanisms may be drawn for an amine exchange reaction involving attack by amine on 2 (or 3 or 4).

The p.m.r. spectra of the rearrangement products suggest that in methanol, a slow solvolysis process may be occuring. Reaction of methanol with 2 (or 3 or 4) might lead to compounds such as those shown below.



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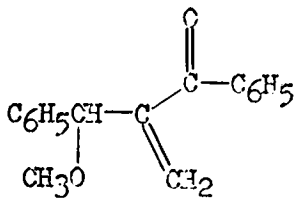

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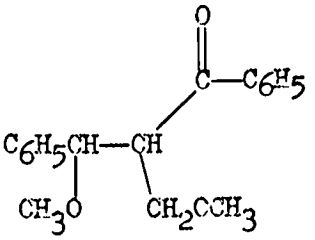

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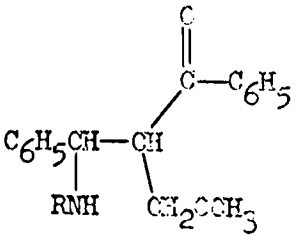

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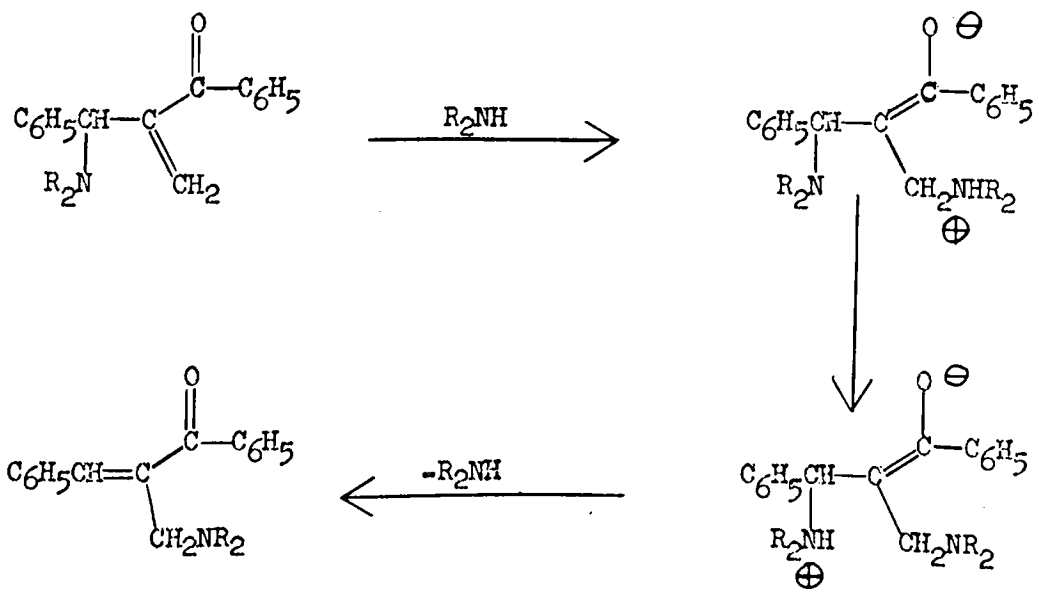
The possibility of the formation of the methoxy-chalcone isomer of 6 is eliminated by the absence of the chalcone band in the ultraviolet spectra of the reaction products.

It may be found convenient to study the rearrangement of X and XI by p.m.r. in solvent formamide in order to eliminate the possibility of solvolysis.

3. Reaction of amines with amino-acrylophenone X in solvent pentane. ---- The reaction of amines with amino-acrylophenone X in pentane cannot be simply a base-catalyzed SNi' rearrangement as proton transfer

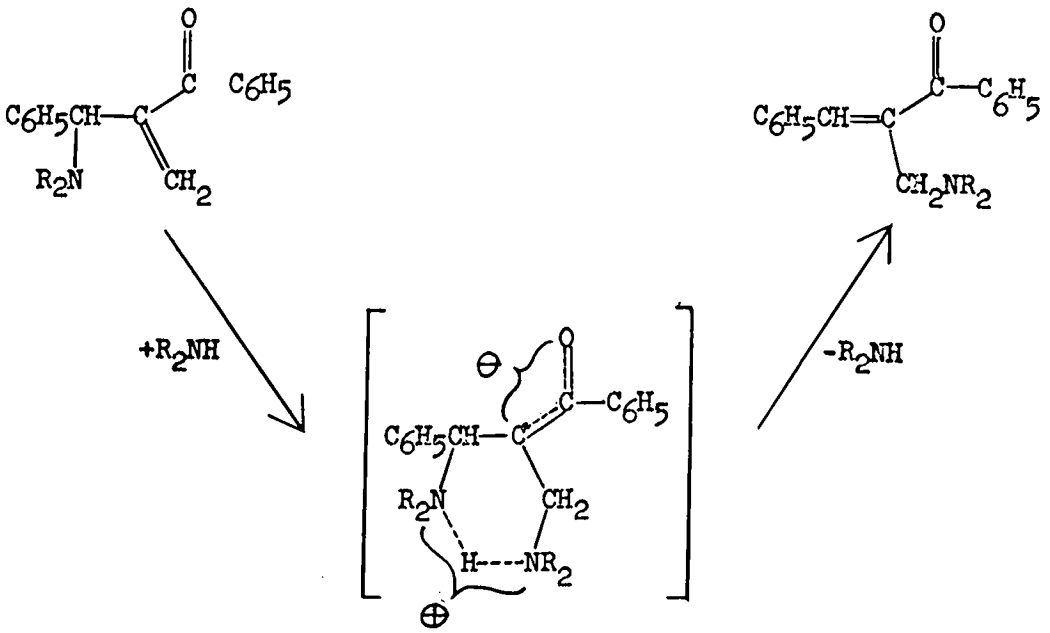
from the substrate to the amine during formation of the cyclic transition state would lead to stabilization of the azetidine ring, slowing the rate, while in fact the reaction is speeded greatly in pentane relative to the SNi' reaction rate (essentially zero). A simple base-catalyzed SNi' rearrangement is further ruled out by the fact that amine exchange may occur in the presence of other amines, leading to the exchanged amino-chalcone. It is significant in this connection that amino-chalcone XI in pentane is stable with respect to amine exchange.

Since the kinetics of the amine exchange reaction have not been examined, the mechanism is presumed to be bimolecular. Two extremes can be considered: The SN2' mechanism of concerted displacement-rearrangement involving only slight polarity in the transition state, and a non-concerted mechanism utilizing the carbonyl group to yield highly polar intermediates (and transition states).



R_2NH = I° or II° amine

However, features of a somewhat intermediate mechanism are more attractive than either of the above extremes.



Here, the hydrogen-bonded structure in brackets represents a highly polar transition state in a concerted bimolecular mechanism of amine exchange. The driving force is of course the establishment of the highly conjugated cinnamoyl system.

This mechanism might in part be evaluated by determining the thermodynamic parameters for amine exchange reactions in non-hydroxylic solvents of widely differing polarity, using, say, amino-acrylophenone X where the competing SNi' rearrangement would be relatively slow, and could be mathematically compensated for or even ignored where slow enough. Operation of a mechanism of the nature suggested would be expected to lead to a very low activation energy and a very low negative entropy of activation in the less polar solvents, the entropy becoming less negative as the polarity of the solvent is increased.

4. Reaction of bromoketone III with amines. --- Here, just as in the above example, utilization of the carbonyl group in the transition state is strongly indicated, as Bordwell[21] has pointed out that primary allylic halides are not generally subject to SN2' displacement by nucleo-

philes (p. 8,9). Again, several extreme mechanisms may be considered, similar to those mentioned just previously. A complete kinetic and product study of this reaction is indicated, with particular attention being given to the possible formation of intermediates, such as might be formed by a simple addition of amine to III.

5. Reaction of bromoketone III with other nucleophiles. --- Little can be said with certainty of the mechanism(s) of the reactions of III with the iodide, chloride, thiophenoxide, and methoxide anions and with t-butyl alcohol other than the products observed can be accounted for by a simple SN2 mechanism. However, in view of the diversity of the conditions used in these reactions and the findings in the detailed study of the reaction of III with amines, the possibility of similar mechanisms operating here cannot be ruled out.

D. Conclusions

1. The 2-benzal-1-indanone system.[35,36] --- In the light of the present work, it seems quite probable that C (p. 13) undergoes SN2' displacement by amine to give E directly. On the other hand, B probably undergoes SN2' displacement by amine to give D, which rearranges by either the SNi' or SN2' mechanism (or both) to give E.

2. The 2-benzal-1-tetralone system.[37] --- Here again, the operation of a SN2' displacement by amine on G (p.15), followed by either SNi' or SN2' rearrangement (or both) of the resulting amine H to give J, appears to be quite likely.

In the α-(bromomethyl)-chalcone system and in both of the above systems, two general rules may be postulated: (a) SN2' displacement by amines is much faster than SN2 displacement; (b) Either SNi' or SN2' rearrangement (or both) of the resulting allylic amine occurs if the rearrangement product to be obtained is the thermodynamically more stable isomer.

3. The β-(bromomethyl)-chalcone system. ---- The reaction of morpholine with β-(bromomethyl)-chalcone (γ-bromodypnone) has been reported, but the reaction was carried out under conditions expected to lead to thermodynamic control (excess amine, solvent ethyl ether, reaction at room temperature overnight). The possibility of rearrangement in this system is interesting in that here the phenyl group would be called upon to facilitate the mechanisms in the way that it was suggested the carbonyl group operates in the α-(bromomethyl)-chalcone system.

Since the phenyl group also has electron-accepting properties, it might be expected that under the proper conditions β-(bromomethyl)-chalcone would undergo a SN2' displacement by amine, followed by either a SNi' or SN2' rearrangement (or both) of the resulting α-amino-α-(β-styryl)-acetophenone to the thermodynamically more stable β-(aminomethyl)-chalcone.

4. The 3-halomethylbenzothiophene-1,1-dioxide system. ---- Bordwell[54] claimed to have demonstrated the concerted nature of the SN2' mechanism shown to be operating in this system. His claim has no basis in fact, however, since Ingold[55] has concluded, after a survey of the literature, that the ratio of the rate constants of halogen displacement from RCl, RBr, and RI, are roughly the same whether displacement occurs by first order kinetics or by second order kinetics. Thus Bordwell did not eliminate the addition-elimination mechanism, in which he quite arbitrarily assumed the addition to be the rate-controlling step, since all the kinetic facts can be accomodated by a situation[56] such that

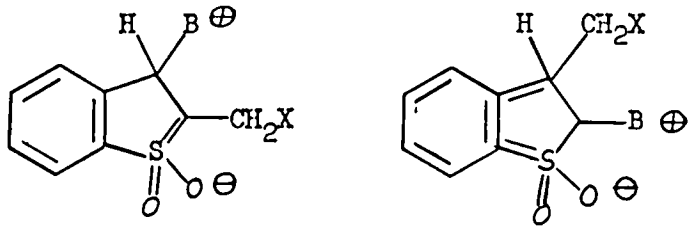
$$\text{Nucleophile} + \text{Allyl halide} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{Adduct}$$

$$\text{Adduct} \xrightarrow{k_3} \text{Rearranged product} + \text{HX,}$$

where regardless of relative velocities of steps 1, 2, and 3, second order kinetics are observed.

A rationale based on other mechanisms accounts just as well for the observed facts as the rationale that Bordwell proposed (p.8).

Assuming that either an addition--elimination mechanism or a concerted SN2' mechanism, involving the sulfonyl group in a polar transition state, is operating, the activation energy for the SN2' displacement of halogen would be expected to be much lower in the case of the 3-halomethyl compound than in the case of the 2-halomethyl compound. The reason for this is due to the energy lowering of the transition state relative to the ground state by electron delocalization operating through the benzene ring; said lowering being much greater in the case of the 3-halomethyl compound than in the case of the 2-halomethyl compound.



In the case of the 3-halo-1-p-toluenesulfonyl-1-propene, a similar rationale predicts a high activation energy for SN2' displacement.

5. The 3-chloro-2-benzoyl-1-propene system. --- Shortly after the conclusion of the experimental phase of this present work, Piskov[57] reported the synthesis of one of the model compounds that were desired (but not obtained) by this author, ∝-(morpholinomethyl)-acrylophenone. The compound was obtained by the action of one equivalent of morpholine and three equivalents of triethylamine on 2-chloro-1-chloromethyl-propiophenone. It was suggested that the reaction proceeded through an intermediate, 3-chloro-2-benzoyl-1-propene, with no suggestion being made as to the mechanism, be it SN2 or SN2', for the displacement of halogen from this intermediate.

A similar reaction was carried out by this author. Displacement by excess t-butylamine on 2-(bromomethyl)-3-bromo-3-phenylpropiophenone (IV) resulted in the formation of XI, with III (and X) assumed to be an intermediate. In the case of III, the chemical consequence of SN2' displacement of amine can be observed (under the proper conditions), while in the case of 3-chloro-2-benzoyl-1-propene it cannot, since the chemical consequence would be identical to that resulting from SN2 displacement.

It is suggested then, that the reaction reported by Piskov probably proceeds by SN2' displacement by amine on the proposed intermediate, 3-chloro-2-benzoyl-1-propene.

V. APPENDIX

Thermodynamic equations. --- The Arrhenius activation energy E_a was obtained from the equation

$$d(\ln k)/dT = E_a/RT^2$$

$$E_a = 2.303RT_2T_1(T_2-T_1)^{-1} \log(k_2/k_1)$$

where E_a is in cal. $mole^{-1}$, R is the gas constant in cal. deg^{-1}. $mole^{-1}$, and T is the temperature in °K.

The Arrhenius frequency factor A was obtained from the equation

$$k = Ae^{-Ea/RT}$$

$$\log A = \log k + E_a/2.303\ RT$$

where A is frequency of occurence in $seconds^{-1}$.

The enthalpy of activation ΔH^* is defined by

$$\Delta H^* = E_a - RT$$

where ΔH^* is in cal.$mole^{-1}$.

The entropy of activation ΔS^* was obtained from the equation

$$k = (RT/Nh)e^{\Delta S^*/R_e - \Delta H^*/RT}$$

$$\Delta S^* = 2.303R \log (kNh/RT) + H^*/RT$$

where ΔS^* is in cal. $deg.^{-1}$ $mole.^{-1}$, N is Avogadro's number in $mole^{-1}$, and h is Planck's constant in cal. sec. For all unimolecular reactions, ΔS^* is independent of the standard state.

Thermodynamic calculations for Section D. ---

$k_2 = 9.72 \times 10^{-6}$ sec.$^{-1}$ $\quad$ $R = 1.987$ cal. $deg.^{-1}$ $mole^{-1}$

$k_1 = 8.43 \times 10^{-6}$ sec.$^{-1}$ $\quad$ $h = 1.5835 \times 10^{-34}$ cal. sec.

$T_2 = 314.7$°K. $\quad$ $N = 6.024 \times 10^{23}$ $mole^{-1}$

$T_1 = 309.7$°K. (used in calculation of A, ΔH^*, and ΔS^*.)

$E_a = (2.303)\ (1.987)\ (314.7)\ (309.7)\ (5)^{-1} \log\ (9.72/8.43)$

$= (446{,}000/5)\ (0.06183)$

$= 5515$ cal. $mole^{-1} = 5.5$ kcal. $mole^{-1}$

$\log A = \log (8.43 \times 10^{-6} + 5515/(2.303)(1.987)(309.7)$

$= -6.0 + 0.9258 + 3.892$

$= -1.182$

$A = 6.6 \times 10^{-2}$ sec.$^{-1}$ $= 10^{-1.18}$ sec.$^{-1}$

$\Delta H^* = 5515 - (1.987)(309.7)$

$= 4900$ cal. mole^{-1} $= 4.9$ kcal. mole^{-1}

$\Delta S^* = (2.303)(1.987) \log \left[(8.43 \times 10^{-6})(6.023 \times 10^{23})(1.584 \times 10^{-34})/(1.987)(309.7)\right] + 4900/309.7$

$= -81.8 + 15.8$

$= -66$ cal. deg.$^{-1}$ mole^{-1}

Thermodynamic calculations for Section E. ---

$k_2 = 12.0 \times 10^{-6}$ sec.$^{-1}$ $\quad R = 1.987$ cal. deg.$^{-1}$ mole^{-1}

$k_1 = 7.52 \times 10^{-6}$ sec.$^{-1}$ $\quad h = 1.5835 \times 10^{-34}$ cal. sec.

$T_2 = 313.2°K$ $\quad N = 6.024 \times 10^{23}$ mole^{-1}

$T_1 = 308.2°K$. (used in calculation of A, ΔH^*, and ΔS^*).

$E_a = (2.303)(1.987)(313.2)(308.2)(5)^{-1} \log (12.0/7.52)$

$= (441,700/5)(0.204)$

$= 18,021$ cal mole^{-1} $= 18.0$ kcal. mole^{-1}

$\log A = \log (7.52 \times 10^{-6}) + 18,021/(2.303)(1.987)(308.2)$

$= -5.1238 + 12.7808$

$= 7.657$

$A = 4.5 \times 10^7$ sec.$^{-1}$ $= 10^{7.66}$ sec.$^{-1}$

$\Delta H^* = 18,021 - (1.987)(308.2)$

$= 17,409$ cal. mole^{-1} $= 17.4$ kcal. mole^{-1}

$\Delta S^* = (2.303)(1.987) \log \left[(7.52 \times 10^{-6})(6.023 \times 10^{23})(1.584 \times 10^{-34})/(1.987)(308.2)\right] + 17,409/308.2$

$= -82.0 + 56.5$

$= -26$ cal. deg.$^{-1}$ mole^{-1}

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