[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NEBRASKA]

Ethylene Imine Ketones. IX.[1] Stereochemistry and Mechanisms of Three-Ring Cleavage and Closure[2]

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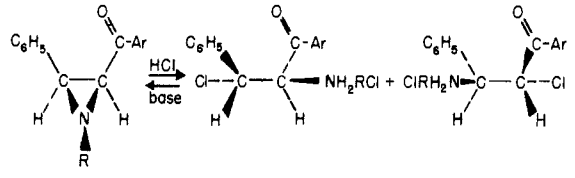
The stereochemical courses of the hydrogen chloride three-ring cleavage reactions at both the α- and the β-carbon atoms of the *cis*- and *trans*-arylaroylaziridines to produce aminochloro ketone hydrochlorides, and the ring closures of such products to reproduce the arylaroylaziridines have been established. Each ring opening and each ring closure involves a Walden inversion at the carbon undergoing valency changes. It has been found that these ring cleavages at the α- and β-carbon atoms are not simultaneous reactions proceeding wholly by the same mechanism. The evidence indicates, (1) the SN2 ring cleavage reaction with hydrogen chloride is relatively more important for the production of α-chloro-β-amino ketone hydrochlorides than is the SN1 mechanism for both the *cis*- and *trans*-ethylenimine ketones; (2) the SN1 mechanism for both the *cis* and *trans* isomers is relatively more important than the SN2 process in the attack at the β-carbon atom to produce the β-chloro-α-amino ketone hydrochlorides; (3) the three-ring carbonyl hyperconjugation effect in the *trans* structures acts in opposition to the inductive effect and causes the SN2 process to be somewhat more important at the β-carbon atom than it is with the *cis*-arylaroylaziridines. In the ionizing medium, methanol, the SN1 process is favored over the SN2 process and the major products are the β-chloro-α-amino ketone hydrochlorides.

Preliminary investigations of the reactions of the ethylenimine ketones (arylaroylaziridines) with hydrogen halides under various conditions have shown that the three-ring in these molecules cleaves in the two possible directions.[5,6,7] Unfortunately all of these earlier investigations were made before the geometrical configurations of the *cis* and *trans* isomeric arylaroylaziridines had been established.[8]

The investigations reported here were mainly concerned with, (1) establishing the stereochemical course of the hydrogen chloride ring cleavage reactions of *cis* and *trans* pairs of the arylaroylaziridines, (2) a study of the effect of chloride ion concentration and solvent variation on product composition, and finally, (3) the establishment of the stereochemistry of ring closures with the α-chloro-β-amino ketones and the α-amino-β-chloro ketones. It is the general purpose of these studies, and others being continued in this Laboratory, to interrelate the absorption spectra,[8,9] mechanisms[10] and stereochemistry of ring cleavage reactions, and carbonyl reactions[11] with the geometrical configurations of the arylaroylcyclopropanes, ethylene oxides and aziridines.

The *cis*-arylaroylaziridines (ethylenimines) have been found to give mainly a β-chloro-α-amino ketone hydrochloride when treated with excess amounts of dry hydrogen chloride in benzene–ether mixtures. Careful treatment of these hydrochlorides with one molar equivalent of a mildly basic amine in benzene or ether solution produces the free bases, β-chloro-α-amino ketones.[5] The hydrochlorides on warming with an absolute alcohol solution of morpholine reproduce the *cis*-arylaroylaziridine. These experiments may be taken as evidence that both ring cleavage and ring closure proceeded with a Walden inversion at the carbon atom undergoing bond change. Thus the *cis*-arylaroylaziridines under these conditions probably produce the *threo*-β-chloro-α-amino ketone hydrochlorides as the major products. These results and conclusions bear a direct relationship to the stereochemical observations and conclusions reported by Lucas and co-workers in two recent excellent papers.[12] Using optically active materials in several instances it was shown that one Walden inversion is associated with a number of ring openings and closings, *viz.*, opening of the imine ring of 2,3-dimethylethylenimine with ammonia and with water, and the closing of the same ring.[12a]



cis *threo*

Ar	R
C_6H_5	$C_6H_5CH_2$
p-$CH_3C_6H_4$	$C_6H_5CH_2$
p-$CH_3C_6H_4$	C_6H_{11}

The *trans* form of 1-benzyl-2-phenyl-3-*p*-toluylethylenimine[8b] under the same conditions described above produced a mixed hydrochloride whose percentage composition and extent of reaction with acidified potassium iodide solution at 66° in 15 minutes[13] indicated it to be made up of about 36% α-chloro-β-benzylaminobenzyl-p-methylacetophenone hydrochloride and 64% of the β-chloro-α-amino isomer. The fact that treatment of this mixed hy-

(1) For paper VIII, see N. H. Cromwell, *et al.*, THIS JOURNAL, **73**, 2803 (1951).

(2) Presented before a session of the Division of Organic Chemistry, 123d Meeting of the American Chemical Society, Los Angeles, Calif., March 18, 1953.

(3) du Pont Fellows, 1952–1953 and 1947–1948, respectively.

(4) Master of Science Thesis, University of Nebraska, May, 1950.

(5) N. H. Cromwell and R. A. Wankel, THIS JOURNAL, **71**, 711 (1949).

(6) N. H. Cromwell and H. Hoeksema, *ibid.*, **71**, 708 (1949).

(7) N. H. Cromwell and J. A. Caughlan, *ibid.*, **67**, 2235 (1945).

(8) For the use of spectral methods in assigning the configurations to the arylaroylaziridines, see (a) N. H. Cromwell and M. A. Graff, *J. Org. Chem.*, **17**, 414 (1952); and (b) N. H. Cromwell, *et al.*, THIS JOURNAL, **73**, 1044 (1951).

(9) N. H. Cromwell and G. V. Hudson, *ibid.*, **75**, 872 (1953).

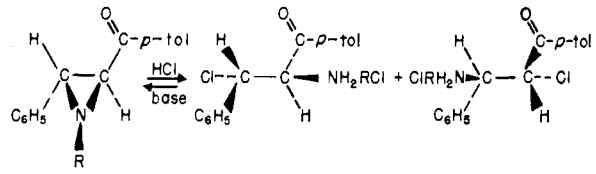
(10) For a study of the mechanism of cleavage of the epoxide ring in epoxy ketones by amines, see N. G. Barker and N. H. Cromwell, *ibid.*, **73**, 1051 (1951).

(11) (a) For reactions with phenylhydrazine see ref. 8b; (b) reactions with organometallic compounds are reported in ref. 1.

(12) (a) F. H. Dickey, W. Fickett and H. J. Lucas, THIS JOURNAL, **74**, 944 (1952); (b) G. K. Helmkamp and H. J. Lucas, *ibid.*, **74**, 951 (1952).

(13) This method of determining the relative amounts of α-halo and β-halo ketones in a mixture has been described and applied previously, see: (a) ref. 7; (b) N. H. Cromwell and R. A. Wankel, THIS JOURNAL, **70**, 1320 (1948); (c) ref. 5.

drochloride with base reproduced the *trans*-ethylenimine ketone indicates again that ring cleavage and ring closure at both the α- and β-carbon atoms proceeded by rearward attacks at the carbon atoms undergoing bond change. Moreover, it follows then that this *trans*-ethylenimine ketone produces *erythro*-chloroamino ketone hydrochlorides.



trans *erythro*

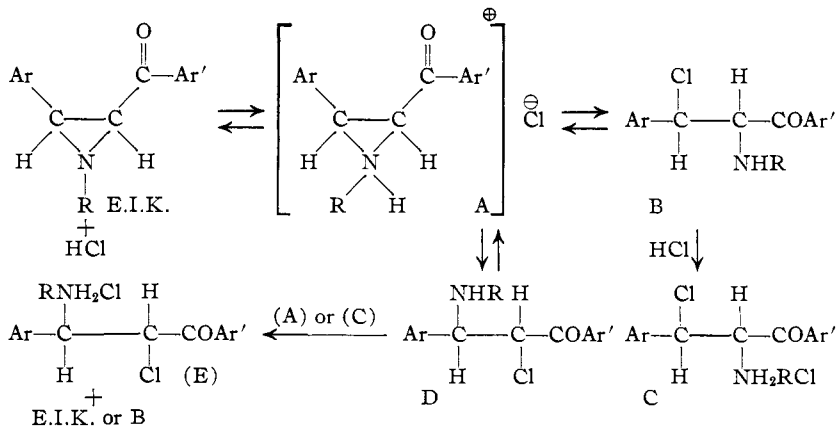
In sharp contrast with the results from using excess hydrogen chloride were those obtained with only two equiv. of hydrogen chloride in acetone medium. In a previous article[5] it was reported that with carefully controlled minimum amounts of hydrogen chloride in acetone–ether solutions the arylaroylaziridine higher melting geometrical isomers, since shown to have the *cis* structures,[8b] undergo ring cleavage to produce mixed chloroamino ketone hydrochlorides consisting mainly of the α-chloro-β-amino ketone hydrochloride. The free bases were readily obtained by treating the hydrochlorides with one mole of benzylamine in dry ether solution. Ring closure of the hydrochlorides with triethylamine in benzene solution produced the *cis*-ethylenimine ketones. Thus it was shown that ring cleavage and closure proceed essentially by means of rearward attacks at the carbon atoms undergoing valence bond change, and that the chloroamino ketones are of the *threo* form as produced under these conditions. To date *cis*-1-benzyl-2-phenyl-3-benzoylethylenimine, *cis*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine and *cis*-1-cyclohexyl-2-phenyl-3-*p*-toluylethylenimine have been studied in this manner.

When the lower melting *trans*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine was treated slowly with two equivalents of hydrogen chloride in acetone–ether solution at room temperature, or at $-13°$ in a benzene–ether solution, a mixed hydrochloride resulted which was shown to consist of approximately 56% α-chloro-β-benzylaminobenzyl-*p*-methylacetophenone hydrochloride and 44% of the α-benzylamino-β-chloro isomer. Ring closure of the mixed product produced the *trans*-ethylenimine ketone. Again it is indicated that ring cleavage and closure have involved Walden inversions at the carbon atoms undergoing valency changes, and that the chloroamino ketones are of the *erythro* form.

The ring closure reactions of the chloroamino ketones using amines and absolute alcohol proceed more rapidly than those carried out in benzene solution. However, in the former solvent medium the yields are considerably lower than in the latter, in the case of the reactions with the α-chloro-β-amino ketone hydrochlorides. The α-chloro-β-amino ketones are not as stable in ethanol as they are in benzene and tend to decompose to give the amine and the α-chloro-α,β-unsaturated ketone.[13b]

It was established that both the α-chloro-β-amino ketone hydrochlorides and the α-amino-β-chloro ketone hydrochlorides are reasonably stable on standing in benzene, ether, acetone or methanol media. However, in a series of equilibration experiments it was found that *threo*-α-benzylamino-β-chlorobenzyl-*p*-methylacetophenone hydrochloride in the presence of a molar equivalent of *cis*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine slowly rearranges (or interacts with the ethylenimine ketone) to produce the isomeric *threo*-α-chloro-β-benzylaminobenzyl-*p*-methylacetophenone hydrochloride. This change was most complete in acetone, less in ethanol and least in methanol; see Table I. It has been shown previously[5] that an α-chloro-β-amino ketone is a stronger base than the isomeric α-amino-β-chloro ketone, and that such compounds can be separated from each other by selective reaction with a limited amount of hydrogen chloride. The fact that auto ring closure of α-halo-β-amino ketones leads to equivalent amounts of the hydrohalide of the α-halo-β-amino ketones and the expected ethylenimine ketone, indicates that the α-halo-β-amino-ketones are stronger bases than their corresponding ethylenimine ketones.[14] Consequently, under conditions of thermodynamic control (*i.e.*, two equivalents of hydrogen chloride in acetone medium) in non-homogeneous reaction mixtures in which the hydrochlorides have some but not great solubility in the medium one might expect the α-chloro-β-amino ketone hydrochlorides to be favored in the final equilibrium product mixture. In the reaction chart given below it is implied that (D) competes successfully with (E.I.K.) and (B) for hydrogen chloride to give (E). Thus (B) and/or (C) can eventually be converted to (E) under conditions of thermodynamic control as indicated in the chart.

Reaction Course Under Conditions of Thermodynamic Control



Although the speeds of these reactions have been surmised to be too fast to lend themselves to prac-

(14) See the auto ring closure reported by N. H. Cromwell and R. D. Babson, THIS JOURNAL, **65**, 312 (1943), for α-bromo-β-benzylaminobenzylacetophenone.

tical kinetic studies a series of product study experiments designed to employ kinetic controls was devised. With two molar equivalents of hydrogen chloride to one molar equivalent of the *cis*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine in methanol it was found that the proportion of α-chloro-β-aminoketone hydrochloride in the product increased as the solutions studied were made more concentrated; see Table II. Also it was found that the proportion of α-chloro-β-amino ketone hydrochloride in the total ring cleavage product increased as the amount of excess chloride ion supplied by added tetraethylammonium chloride was increased in the reaction mixture using this same *cis*-ethylenimine ketone; see Table III. As a check on the course of the reactions under these conditions products from certain experiments were analyzed for percentage composition and ring-closed to reproduce the *cis*-ethylenimine ketone.

The same type of product composition variation was observed although the effect was less pronounced when *trans*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine was studied under these same conditions with excess chloride ion added. Again analyses indicated the correct percentage composition for the ring cleavage products. Ring closure of one of the mixed hydrochlorides from these latter experiments reproduced the *trans*-ethylenimine ketone; see Table IV.

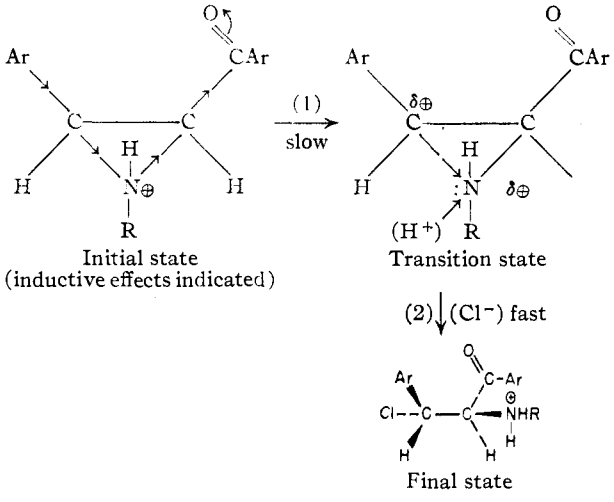
Discussion of the Ring-Cleavage Reaction Mechanisms

The results given in Tables II, III and IV seem to constitute adequate proof that the simultaneous cleavage reactions at the α- and β-carbon atoms are not proceeding wholly by the same mechanism. In methanol solution, at the higher chloride ion concentrations for both the *cis* and *trans* forms of these arylaroylaziridines, the SN2 ring cleavage reaction with hydrogen chloride must be relatively more important for the production of the α-chloro-β-amino ketone hydrochloride than is the SN1 (chloride ion concn. independent) reaction. It may also be inferred that the SN2 mechanism is relatively more important for the formation of the α-chloro compounds than it is for the formation of β-chloro compounds under these conditions.

Based upon the limited evidence at hand, and ignoring for the present the possibility of important salt effects, it is postulated that hydrogen chloride cleavage of the arylaroylaziridines takes place by way of SN2 and SN1 reaction types, both of which involve essentially rearward attack at either the α- or β-carbon atoms. In the homogeneous reaction mixtures (methanol solution) where kinetic control mainly determines the product composition, both the *cis*- and the *trans*-1-benzyl-2-phenyl-3-*p*-toluylethylenimines produce largely the α-amino-β-chloro ketone hydrochlorides.

In the case of the *cis* structure where three-ring carbonyl hyperconjugation[8,9] is not expected to aid in developing a partial positive charge at the β-position, the inductive effect (*i.e.*, aroyl is electron attracting, phenyl is electron releasing) apparently controls the relative electron densities at the two competitive carbon atoms of the imine ring in the *ground state*. Thus we might expect the SN2 reaction to predominate in the attack at the α-carbon atom while the SN1 process should be the major one involving the β-carbon atom. In all cases the ethylenimine ketone first forms the ethylenimonium chloride which then undergoes ring cleavage by the respective mechanisms.

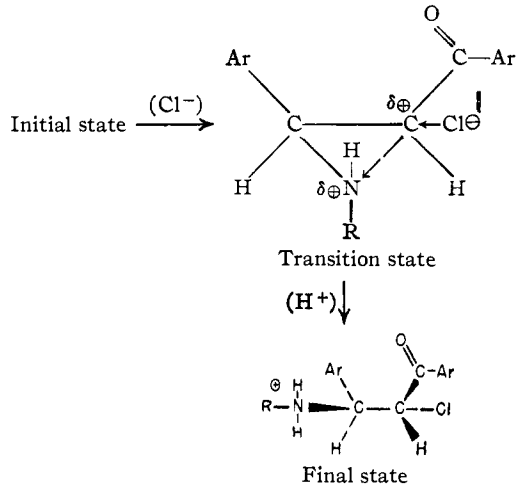
SN1 Process for β-Chloro-α-amino Ketone Production



In step 1 of the SN1 process the β-carbon to nitrogen bond stretches becoming more ionic while the α-carbon to nitrogen bond shortens becoming more covalent, and the formal positive charge on nitrogen is partially transferred to the β-carbon unassisted by chloride ion. This partial positive charge developed on the β-carbon atom in the *transition state* is supported by orbital overlap with the π-electron orbitals of the aryl ring. Undoubtedly the electron transfer to nitrogen is aided by the presence of protons in the reaction mixture. The chloride ion attaches itself to the β-carbon atom on the side opposite to the carbon to nitrogen bond in step 2 nearly simultaneously with the complete charge transfer to carbon. The major driving force for these β-ring cleavages is the stretching of the carbon-to-nitrogen linkage resulting from the proton assisted electron transfer to nitrogen. Unlike normal σ-bond electrons which are mainly localized symmetrically between two nuclei, the *bent* bond[8a] electrons between carbon and nitrogen may be somewhat more susceptible to electrophilic attack by protons.

SN2 Process for α-Chloro-β-amino Ketone Production

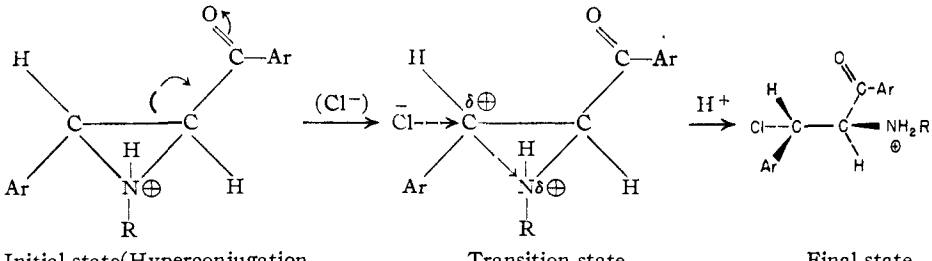
In the wholly concerted SN2 process the chloride ion preferentially attacks the electron deficient α-carbon atoms from the side opposite to the C–N bond. As the chloride ion draws closer to this α-carbon atom the electron transfer to nitrogen begins, assisted again by the presence of protons in the mixture. Here the major driving force for the α-ring cleavage is supplied by the nucleophilic attack of the chloride ions. This SN2 process is probably a slower one than the SN1 reaction with these *cis* isomers.



The interpretation of the course of the ring cleavage reactions of the *trans*-arylaroylaziridines is made more complicated by the thought that three-ring carbonyl hyperconjugation may play an important part in determining the relative electron densities at the α- and β-carbon atoms in both the ground and excited states.[8,9] The hyperconjugation effect would be expected to act in opposition to the inductive effect described above, tending to develop a partial positive charge or lowered electron density at the β-carbon atoms even in the initial ground state of the *trans*-arylaroylaziridines or their hydrochlorides; see Chart 2, p. 419, ref. 8a.

The hyperconjugation effect in the *trans* structures would be expected to make the SN2 process more important at the β-carbon atom than it was with the *cis* isomers. The fact that the amount of α-chloro-β-amino ketone hydrochloride is increased slightly in the total product produced from the *trans* isomer in methanol when excess chloride ion is added indicates that the SN2 process is still relatively more important at the α-carbon than it is at the β-carbon atom. However, the fact that only a very slight increase occurs bears out the thought that the SN2 process is now of relatively greater importance at the β-carbon atom in these *trans* structures because of the hyperconjugation effect than it is with the *cis* structures.

SN2 Process for β-Chloro-α-amino Ketone Production



Methanol, which is a good ionizing medium, might be expected to favor the SN1 process over the SN2 reaction since the latter involves a charge reduction in the formation of the transition state. It seems probable that the major reaction taking place in methanol with both the *cis* and *trans* isomers is the SN1 process.

Studies with *cis*- and *trans*-arylaroylaziridines having electron attracting and releasing groups in the *p*-position of the β-aryl groups as well as salt effect studies can be expected to aid in completing our understanding of these complex competitive reactions. Such studies are contemplated.

Acknowledgment.—A portion of the work described here was supported by research grant NSF-G57 from the National Science Foundation. The senior author greatly appreciates the several informative discussions of these reactions with Prof. E. D. Hughes of University College, London, while holding a John Simon Guggenheim Memorial Fellowship and a Fulbright Advanced Research Scholarship during the 1950–1951 academic year.

Experimental

Ring Cleavage of *cis*- and *trans*-Arylaroylaziridines with Excess Amounts of Hydrogen Chloride in Benzene–Ether Solution.—In general the ethylenimine ketones were dissolved in the ratio of 5.0 g. to 20 ml. of dry ether and 10 ml. of dry benzene. The temperature of these solutions was maintained between 23–25° while dry hydrogen chloride gas was passed into them for a period of about ten minutes. The solutions developed a heavy white precipitate and were allowed to stand at room temperature overnight. The products were removed by filtration and studied without further purification.

From ***cis*-1-benzyl-2-phenyl-3-benzoylethylenimine**, m.p. 108°,[5,8b] resulted a 91% yield of *threo*-α-benzylamino-β-chlorobenzylacetophenone hydrochloride, m.p. 165–166°[15]; iodine release value 0% in 15 minutes at 66°.[13b] The free base, *threo*-α-benzylamino-β-chlorobenzylacetophenone, m.p. 92–93°, has been reported previously.[5] Ring closure of this *threo*-hydrochloride (4 g.) by warming on the steam-bath with 15 ml. of abs. ethanol solution of 2.7 g. of morpholine reproduced 2.2 g. (68% yield) of *cis*-1-benzyl-2-phenyl-3-benzoylethylenimine, m.p. 104–107°.

From ***cis*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine**, m.p. 116–118°,[8b] a 92% yield of *threo* mixed product, m.p. 167–169°,[16] resulted consisting of 96% *threo*-α-benzylamino-β-chlorobenzyl-*p*-methylacetophenone hydrochloride and 4% *threo*-α-chloro-β-benzylaminobenzyl-*p*-methylacetophenone hydrochloride, based on iodine release values.[13b] Ring closure of this mixed *threo*-hydrochloride product with morpholine in abs. ethanol produced an 84% yield of *cis*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine, m.p. 115–116°.

From ***trans*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine**, m.p. 72–74°,[8b] was obtained a 95% yield of an *erythro* mixed product, m.p. 168–170°,[16] consisting of 36% α-chloro-β-benzylaminobenzyl-*p*-methylacetophenone hydrochloride and 64% α-benzylamino-β-chlorobenzyl-*p*-methylacetophenone hydrochloride based on iodine release values.

A 0.6-g. sample of the mixed hydrochloride was mixed with 0.3 g. of triethylamine in 10 ml. of benzene and the solution allowed to stand in the dark for four days. The triethylamine hydrochloride was removed by filtration. Concentration of the benzene solution gave 0.4 g. (80% yield) of *trans*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine, m.p. 71–74°.

(15) The analysis of this compound has been reported previously in ref. 14 as compound IX, erroneously assigned an α-chloro-β-benzylaminobenzylacetophenone hydrochloride structure at that time.

(16) N. H. Cromwell and H. Hoeksema in ref. 6 have reported previous ring cleavage experiments with these ethylenimine ketones in which they obtained mixed products of similar compositions and melting points which had the expected correct percentage composition.

From *cis*-1-**cyclohexyl-2-phenyl-3-*p*-toluylethylenimine**, m.p. 111–112°,[8b] a 77% yield of a mixed *threo* product, m.p. 161–163°, resulted.

Anal. Calcd. for $C_{22}H_{27}NOCl_2$: C, 67.34; H, 6.94, N, 3.57. Found: C, 67.36; H, 6.80; N, 3.44.

Iodine release values indicated this mixed product to consist of 10.2% α-chloro-β-cyclohexylaminobenzyl-*p*-methylacetophenone hydrochloride and 89.8% α-cyclohexylamino-β-chlorobenzyl-*p*-methylacetophenone hydrochloride. Ring closure of the mixed *threo* product with morpholine in abs. ethanol produced a 78% yield of the *cis*-ethylenimine ketone, m.p. 110–112°.

Ring Cleavage of *cis*- and *trans*-Arylaroylaziridines with Two Molecular Equivalents of Hydrogen Chloride in Acetone–Ether Solutions.—In general the ethylenimine ketones were dissolved in the ratio of 0.03 mole to 40 ml. of acetone and 20 ml. of dry ether. To the stirred solution 0.03 mole of dry hydrogen chloride in 18 ml. of ether was added all at once; after standing at room temperature for four hours an additional 0.015 mole was added; after four more hours an additional 0.0075 mole; and finally after two more hours standing 0.0060 mole of hydrogen chloride in dry ether was added slowly to the reaction mixture. The colorless precipitates were removed by filtration and studied without further purification.

From *cis*-1-benzyl-2-**phenyl-3-benzoylethylenimine**, m.p. 108°, was obtained a 97.5% yield of a mixed *threo*-hydrochloride, m.p. 148–149°,[17] which the iodine release value indicated consisted of 93% *threo*-α-chloro-β-benzylaminobenzylacetophenone hydrochloride and 7% of the *threo*-β-chloro isomer. Six grams of the mixed *threo*-hydrochloride was warmed on the steam-bath for five minutes with 1.66 g. of benzylamine (one molar equiv.) in 75 ml. of dry ether. Filtration of the precipitated benzylamine hydrochloride and concentration of the ether solution produced 3.8 g. (70% yield) of *threo*-α-chloro-β-benzylaminobenzylacetophenone, m.p. 82–83°, recrystallized from benzene and petroleum ether.

Anal. Calcd. for $C_{22}H_{20}NOCl$: C, 75.52; H, 5.76; N, 4.00. Found: C, 75.53; H, 5.94; N, 4.10.

Ring closure of the mixed *threo*-hydrochloride with triethylamine in benzene produced an 80% yield of *cis*-1-benzyl-2-phenyl-3-benzoylethylenimine, m.p. 107–108°.

From *cis*-1-**benzyl-2-phenyl-3-*p*-toluylethylenimine**, m.p. 116–118°, an 80% yield of mixed *threo* product, m.p. 167–169°, resulted which iodine release values indicated to consist of 89% *threo*-α-chloro-β-benzylaminobenzyl-*p*-methylacetophenone hydrochloride and 11% *threo*-α-benzylamino-β-chlorobenzyl-*p*-methylacetophenone hydrochloride. **The free base,** *threo*-α-chloro-β-benzylaminobenzyl-*p*-methylacetophenone was obtained in 72% yield by warming the mixed hydrochloride on the steam-bath for ten minutes with an ether solution containing one molecular equivalent of benzylamine, filtering off the benzylamine hydrochloride and evaporating the ether. The product was recrystallized rapidly from benzene and petroleum ether mixtures, m.p. 115°.

Anal. Calcd. for $C_{23}H_{22}NOCl$: C, 75.91; H, 6.09; N, 3.85. Found: C, 75.74; H, 5.91; N, 3.96.

Ring closure of the *threo* mixed hydrochloride was accomplished by mixing 2.0 g. (0.005 mole) with 1.01 g. (0.01 mole) of triethylamine in 18 ml. of benzene. The reaction mixture was allowed to stand in the dark at room temperature for 96 hours. About 25 ml. of dry ether was added to complete the precipitation of the triethylamine hydrochloride. Filtration and concentration of the solution produced 1.3 g. (76% yield) of *cis*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine, m.p. 115–116°. Repetition of this experiment using ethanol as a solvent gave only a 38% yield of the *cis*-ethylenimine ketone.

From *trans*-1-benzyl-2-**phenyl-3-*p*-toluylethylenimine**, m.p. 72–74°, and 80% yield of a mixed *erythro*-hydrochloride, m.p. 168–170°, which iodine release studies indicated consisted of 56% *erythro*-α-chloro-β-benzylaminobenzyl-*p*-methylacetophenone hydrochloride and 44% *erythro*-α-benzylamino-β-chlorobenzyl-*p*-methylacetophenone hydrochloride.

Anal. Calcd. for $C_{23}H_{23}NOCl_2$: C, 68.99; H, 5.79; N, 3.50; Cl, 17.72. Found: C, 68.81; H, 5.78; N, 3.49; Cl, 17.82.

Using a mixture of benzene and ether as a solvent and a temperature of −13° the results were approximately the same. Ring closure of the mixed *erythro*-hydrochloride with triethylamine in benzene solution produced a 79% yield of *trans*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine, m.p. 72–74°.

From *cis*-1-**cyclohexyl-2-phenyl-3-*p*-toluylethylenimine**, m.p. 111–112°, a 76% yield of a mixed *threo*-hydrochloride, m.p. 180–181°, resulted consisting of 79.6% *threo*-α-chloro-β-cyclohexylaminobenzyl-*p*-methylacetophenone hydrochloride and 20.4% of *threo*-α-cyclohexylamino-β-chlorobenzyl-*p*-methylacetophenone hydrochloride.

Anal. Calcd. for $C_{22}H_{27}NOCl_2$: C, 67.34; H, 6.94; N, 3.57. Found: C, 67.19; H, 7.07; N, 3.32.

Ring closure of this mixed *threo*-hydrochloride with triethylamine in benzene solution at room temperature produced a 72% yield of the *cis*-ethylenimine ketone, m.p. 111–112°.

Equilibration Experiments with *threo*-α-Chloro-β-benzylaminobenzyl-*p*-methylacetophenone Hydrochloride and *threo*-α-Benzylamino-β-chlorobenzyl-*p*-methylacetophenone Hydrochloride.—Solutions consisting of 20 ml. of solvent, 0.3 g. of the hydrochloride and 0.3 g. of *cis*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine were allowed to stand for three days at room temperature. The solvent was removed under reduced pressure at room temperature and the residues well washed with ether; wt. 0.23 to 0.25 g. The iodine release values of the resulting materials were determined for comparison with the values known for the starting hydrochlorides; see Table I. *cis*-Ethylenimine ketone was recovered from the ether washings of the hydrochlorides.

TABLE I

REARRANGEMENT OF AN α-AMINO-β-CHLORO KETONE TO AN α-CHLORO-β-AMINO KETONE

Solvent	I.R. value of initial chloroamino ketone HCl α-Chloro ketone, %	I.R. value of resulting chloroamino ketone HCl α-Chloro ketone, %
Methanol	73.6	71.0
	0.0	9.6
Ethanol	73.6	80.5
	0.0	16.2
Acetone	73.6	82.1
	0.0	60.5[a]

[a] Ring closure produced a 77% yield of *cis*-ethylenimine ketone.

Ring Cleavage of *cis*-1-Benzyl-2-phenyl-3-*p*-toluylethylenimine with Hydrogen Chloride in Methanol.—(1) A 0.3-g. sample of the *cis* isomer, m.p. 116–118°, was dissolved in 10 ml. of methanol and 20 molar equivalents of hydrogen chloride in 10 ml. of methanol added all at once. After standing for 12 hours at room temperature the solvent was evaporated under reduced pressure and the iodine release (I.R.) values of the products determined. Run 1 product, wt. 0.31 g., m.p. 167–168°, I.R. value 28.2%; run 2 product, wt. 0.33 g., m.p. 166–167°, I.R. value 26.5%.

(2) A 3.0-g. (0.00916 mole) sample of the *cis*-ethylenimine ketone was dissolved in 100 ml. of methanol and added in 30 minutes to a three-neck flask equipped with a stirrer, simultaneously with and at the same rate as 100 ml. of methanol containing 0.0183 mole of hydrogen chloride. After standing at room temperature for 24 hours the solvent was removed under reduced pressure and the resultant product well washed with dry ether, wt. 3.34 g. (91.0% yield), m.p. 167–168°, I.R. value 25.2%. Ring closure of this product with triethylamine in benzene solution produced a 76% yield of the *cis*-ethylenimine ketone, m.p. 116–117°. A duplicate set of experiments gave nearly identical results.

(3) Samples of the *cis*-ethylenimine ketone (0.3 g.) along with two molar equivalents of hydrogen chloride and various amounts of methanol were quickly mixed at 25° in a thermostat and allowed to stand for 24 hours before isolating the product; see Table II for results.

Ring Cleavage of *cis*- and *trans*-1-Benzyl-2-phenyl-3-*p*-toluylethylenimines with Hydrogen Chloride in the Pres-

(17) This same product has been obtained previously, m.p. 149°, in a somewhat lower yield, ref. (5), see *anal.* p. 715, top of first column.

TABLE II

EFFECT OF IMMONIUM CHLORIDE CONCENTRATION ON PRODUCT COMPOSITION

Total volume, ml.	Chloroamino ketone hydrochloride product Wt., g.	M.p., °C.	I.R. value α-chloro ketone, %
	Run I		
10	0.33	168–169	18.5
40	.32	168–169	15.6
80	.33	169–170	12.6
	Run II		
10	.34	167–168	20.2
40	.33	167–168	17.4
80	.34	168–169	10.8

TABLE III

EFFECT OF EXCESS Cl^- ADDED AS Et_4NCl UPON PRODUCT COMPOSITION FROM *cis*-ETHYLENIMINE KETONE

Expt. no.	Molar equiv. Et_4NCl (excess Cl^- ion)	*threo*-Hydrochloride products Wt., g.	M.p., °C.	I.R. value (α-chloro ketone, %)
1	0	0.34	170–171	13.8
2	0	.33[a]	170–171	13.2
3	1	.34	170–171	14.5
4	1	.30	169–170	15.0
5	8	.33[a]	170–171	32.9
6	8	.34	167–168	32.9
7	16	.34	169–170	40.7
8	16	.33[b]	169–170	39.0

[a] *Anal.* Calcd. for $C_{23}H_{23}NOCl_2$: C, 68.99; H, 5.79. Found for expt. 2 product: C, 68.76; H, 5.83. Found for expt. 5 product: C, 69.38; H, 5.90. [b] Ring closure of expt. 8 *threo*-hydrochloride with triethylamine in benzene gave a 79% yield of *cis*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine, m.p. 114–116°.

ence of Excess Chloride Ion.—(1) Methanol, pure tetraethylammonium chloride, two molar equivalents of hydrogen chloride and 0.3 g. (0.000916 mole) of the *cis*-ethylenimine ketone were quickly mixed to give 20 ml. of clear colorless solutions which were maintained in a thermostat at 25° for 24 hours. No precipitate appeared. All of the solvent was then evaporated from the solutions and the residues shaken with a mixture of 25 ml. of ether, 25 ml. of water and 0.098 g. (0.000916 mole) of benzylamine. The ether layers were washed with two 15-ml. portions of water and dried over Drierite for 20 minutes. The dry ether solutions were saturated with dry hydrogen chloride and the precipitated products removed immediately by filtration, washed with ether and dried in a vacuum desiccator. The I.R. values of the products were determined; see Table III for the results.

(2) Using conditions and techniques identical with those described in (1) above, samples of the *trans*-ethylenimine ketone (0.3 g., 0.000916 mole) were studied; see Table IV for results.

TABLE IV

EFFECT OF EXCESS Cl^- ADDED AS Et_4NCl UPON PRODUCT COMPOSITION FROM *trans*-ETHYLENIMINE KETONE

Expt. no.	Molar equiv. Et_4NCl (excess Cl^- ion)	*erythro*-Hydrochloride products Wt., g.	M.p., °C.	I.R. values (α-chloro-ketone, %)
1	0	0.33[a]	170–171	8.4
2	0	.32[a]	169–170	9.1
3	1	.34[b]	168–169	11.4
4	1	.33	168–169	12.0
5	8	.33	168–169	13.5
6	8	.32	167–168	13.8
7	16	.33[b]	169–170	14.9
8	16	.31	170–171	15.2

[a] Ring closure of the *erythro*-hydrochloride product from expt. 1 and 2 with triethylamine in benzene solution produced a 76% yield of *trans*-1-benzyl-2-phenyl-3-*p*-toluylethylenimine, m.p. 71–73°. [b] *Anal.* Calcd. for $C_{23}H_{23}NOCl_2$: C, 68.99; H, 5.79. Found for expt. 3 product: C, 68.78; H, 5.61. Found for expt. 7 product: C, 68.72; H, 5.70.

LINCOLN, NEBRASKA

[CONTRIBUTION FROM THE WALKER LABORATORY, DEPARTMENT OF CHEMISTRY, RENSSELAER POLYTECHNIC INSTITUTE]

The Reaction of Cyanogen and Related Nitriles with 1,3-Dienes. V. Acrylonitrile and Butadiene[1]

BY G. J. JANZ AND N. E. DUNCAN[2]

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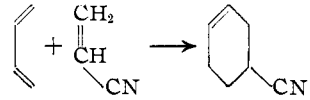
The reactions of acrylonitrile and butadiene in the temperature region of 400° and atmospheric pressure are reported. In the uncatalyzed reaction, cyanocyclohexene only is formed, but in the presence of a chromia–alumina catalyst, vinylpyridine and cyanocyclohexene are obtained. The experimental data are correlated with the thermodynamic free energies and relative rates calculated for these reactions. The results indicate a considerable preferential catalysis of the pyridinic cyclization since the reactivity of the (C≡N) group is much more nearly that of the (C=C) group in presence of the catalyst than in the uncatalyzed reaction.

The addition of acrylonitrile to butadiene to yield 3-cyanocyclohexene (I) has been studied in toluene solution[3,4] and in aqueous dispersion.[5] This is an example of a typical Diels–Alder reaction in which a stable six-membered cyclic product is formed by 1,4-addition of the (C=C) group to butadiene. Acrylonitrile has in fact been classified by Alder and Rickert[6] as belonging in the group of dienophiles having greatest reactivity in the Diels–



(1)

Alder reaction. At 400°, Janz and associates have found that the (C≡N) group of nitriles adds to butadiene yielding a 2-substituted pyridinic deriva-

(1) Abstracted in part from the thesis submitted by N. E. Duncan in partial fulfilment of the requirements for the degree of Master of Science in Chemistry at Rensselaer Polytechnic Institute, June, 1952.

(2) Cyanamid Research Fellow.

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(6) K. Alder and H. F. Rickert, *Ann.*, **543**, 1 (1939).