

the organic layer was separated. The water layer was washed once with pentane. The organic layers were combined and dried ( $\text{MgSO}_4$ ). A significant amount (20 g., dried) of black amorphous material remained, which was insoluble in both water and pentane. The composition of this amorphous material was not determined.

Concentration of the dried organic solution yielded a dark, solid residue which was sublimed under vacuum ( $150^\circ$ , 0.1 mm.). The sublimate (6.5 g.) was crystallized from benzene, affording 6.0 g. (10%) of trichloroacetamide, m.p.  $142\text{--}143^\circ$  (m.p., mixture m.p. and infrared spectra identical with an authentic sample).

Acidification (dil.  $\text{HNO}_3$ ) of the remaining aqueous layer and subsequent precipitation with silver nitrate solution yielded silver chloride. An infrared spectrum of the dried precipitate showed no absorption in the  $2000\text{--}2300\text{ cm.}^{-1}$  region (silver cyanide absorbs<sup>10</sup> strongly at  $2178\text{ cm.}^{-1}$ ), thus it was concluded that no cyanide ion was formed in the reaction.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

## Migration of Aryl Groups in the Deamination of Amines

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The evidence on aryl group migration in the nitrous acid deamination of amines has been examined insofar as it bears on the problem of the mechanism by which nitrogen is lost in the reaction. It has proved possible to reconcile the results of Curtin<sup>8,18</sup> on the migration aptitudes of aryl groups in the 1,1-diaryl-2-amino-1-propanols with the scheme proposed by Collins<sup>6</sup> to explain results using  $\text{C}^{14}$  labeling experiments in the same system. The relative rates of aryl migration and interconversion of rotational isomers of the open carbonium ion intermediates have been calculated.

The concept of the phenonium ion<sup>1</sup> has become quite firmly established in organic chemistry in recent years. The study of limiting solvolysis reactions of systems yielding carbonium ions which could be expected to gain energetically by the bridging of a neighboring phenyl<sup>2</sup> has yielded much good evidence for this bridged ion as an intermediate. Phenyl participation to give a phenonium ion has come to be expected in such cases, although modification of the molecule in a manner calculated to stabilize the open (nonbridged) carbonium ion may decrease the importance of such bridging.<sup>3</sup>

It is of interest, in this context, that recent studies<sup>4,5,6</sup> of the nitrous acid deaminations of amines with neighboring aryl groups has produced evidence that open carbonium ions are important intermediates in such reactions, even in systems which give only bridged ions in ordinary solvolysis reactions.

The deamination reaction is closely related to other solvolysis reactions with the principal difference being that the leaving group, a nitrogen molecule, is unusually stable, compared to the usual leaving groups in solvolysis reactions.

Because of the driving force for the deamination reaction, which originates in this great stability of

one of the products, the diazonium ion is a very unstable intermediate which may lose a nitrogen molecule as an integral part of the mechanism of any one of several exothermic reactions. The exothermic nature of these reactions would be expected to cause all of the reactions of the diazonium ion (rearrangement, solvolysis, elimination) to have activation energies not only smaller but more closely similar than those of related reactions of the alkyl halides or sulfonate esters.<sup>7</sup>

Such reasoning was used by Curtin and Crew<sup>8</sup> to explain the small size of the increase in migration aptitude of a neighboring phenyl when it is substituted by a *p*-methoxy group in the semipinacolic deaminations of the 2-amino-1,1-diarylethanol. If the loss of nitrogen is exothermic, the transition state resembles starting material<sup>7</sup> and the small substituent effect results from the limited amount of bonding in the transition state between the migrating aryl group and the developing carbonium ion center.

Streitwieser<sup>9a,b</sup> and Huisgen<sup>10</sup> have explained the products observed in a variety of deamination reactions on the basis of a similar argument, the high energy diazonium ion reacting rather indiscriminately in the various possible modes.

If, indeed, activation enthalpy terms are monotonously constant and small in reactions involv-

(1) D. J. Cram, *J. Am. Chem. Soc.*, **71**, 3863, 3875, 3883 (1949).

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(7) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

(8) D. Y. Curtin and M. C. Crew, *J. Am. Chem. Soc.*, **76**, 3718 (1954). See also D. Y. Curtin and M. von Wilhelm, *Helv. Chim. Acta*, **40**, 2129 (1957).

(9) (a) A. Streitwieser, Jr., and W. D. Schaeffer, *J. Am. Chem. Soc.*, **79**, 2888 (1957). (b) A. Streitwieser, Jr., *J. Org. Chem.*, **22**, 861 (1957).

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ing the loss of nitrogen molecules, the entropy of activation becomes correspondingly more important. It is not surprising to find that the reaction expected to have the most favorable entropy of activation, namely the loss of nitrogen to give an open carbonium ion without participation of solvent or of neighboring groups, is much more important than in dissociation reactions involving leaving groups other than nitrogen.

This view of the deamination reaction pictures the formation of a highly energetic carbonium ion, not necessarily stabilized by bridging to neighboring groups, by optimum solvation, or by any resonance interaction requiring a particular orientation in space. The postulated formation of such a "hot" carbonium ion has been used to explain many observations in various deamination reactions.<sup>4,11-13</sup>

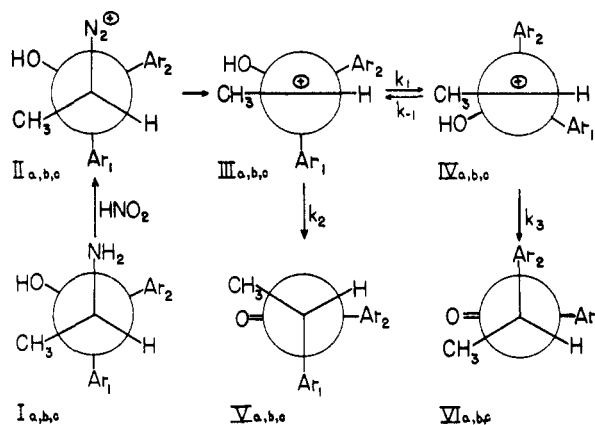
Ciereszko and Burr<sup>11</sup> have proposed such a high energy primary carbonium ion as an intermediate in the deamination of the 2-amino-1,1-diarylethanol. The small spread in migration aptitudes for *p*-anisyl and phenyl is explained to result from an indiscriminate attack on the neighboring aryl groups by the carbonium ion.

The first reported experimental demonstration of such open carbonium ions in systems which give bridged ions in ordinary solvolysis reaction was by Cram and McCarty.<sup>4</sup> They studied the stereochemical results of the deaminations of the optically pure diastereoisomeric 3-phenyl-2-butylamines and obtained results which they explained to result from "conformational control of the migrating group." In the scheme advanced here a particular rotational isomer of the open carbonium ion is produced depending on which rotational isomer of the diazotized amine loses nitrogen.<sup>14</sup> The fate of this open carbonium ion then depends upon its rotational isomerism and upon the solvent.<sup>15</sup> Any rearrangement occurs by a very rapid attack of this carbonium ion on the neighboring aryl group which is geometrically most favorably situated in that particular rotational isomer of the carbonium ion. Such attack is considered fast compared to the interconversion of rotational isomers.

Collins<sup>5,6</sup> has carried out isotopic labelling experiments on the semipinacolic deaminations of 1,1-diphenyl-2-amino-1-propanols (Ia). It had been established earlier<sup>16,17</sup> that phenyl migration in this

series proceeded principally with inversion at the migration terminus to give V from I. Collins<sup>5,6</sup> showed that open ions were important intermediates in this series since an appreciable portion of the phenyl rearrangement went to give retention of configuration at the terminus (VIa from Ia). In this case the results are explained without postulating any important contribution of phenonium ion intermediates in the reaction scheme.

It is of interest to determine the extent to which the reaction scheme deduced by Benjamin, Schaeffer, and Collins<sup>5,6</sup> to explain the results of their isotopic labeling experiments will accommodate the migration aptitudes observed earlier in such reactions by Curtin and Crew.<sup>8,18</sup> Fortunately both groups of workers have studied the semipinacolic deamination of 1,1-diaryl-2-amino-1-propanols. Collins<sup>5</sup> studied the aryl migration by following the movement of stereospecifically C<sup>14</sup>-labeled phenyl rings in optically active Ia. Curtin<sup>18</sup> determined the products when the aryl groups were variously substituted phenyl rings in racemic Ib and Ic.



Ia, IIa, IIIa, IVa, Va, and VIa. Ar<sub>1</sub> = C<sub>6</sub><sup>14</sup>H<sub>5</sub>, Ar<sub>2</sub> = C<sub>6</sub>H<sub>5</sub>  
 Ib, IIb, IIIb, IVb, Vb, and VIb. Ar<sub>1</sub> = C<sub>6</sub>H<sub>5</sub>, Ar<sub>2</sub> = *p*-anisyl  
 Ic, IIc, IIIc, IVc, Vc, and VIc. Ar<sub>1</sub> = *p*-anisyl, Ar<sub>2</sub> = C<sub>6</sub>H<sub>5</sub>

When optically active Ia was treated<sup>5</sup> with nitrous acid the product mixture of ketones consisted of 88% Va, in which the carbon to which the labeled phenyl moved showed an inversion of configuration, and 12% VIa, the product resulting from a migration of unlabeled phenyl with retention of configuration at the migration terminus. On the basis of these results the reaction scheme outlined above was postulated for Ia.

The assumption is made here that all of the reaction occurs through molecules in the thermodynamically most favored conformation, IIa. This yields the open carbonium ion, IIIa, which may either rearrange to Va, with migration of labeled phenyl, or in a step of comparable rate undergo rotation

(11) L. S. Ciereszko and J. G. Burr, *J. Am. Chem. Soc.*, **74**, 5431 (1952).

(12) D. Semenow, C. Shih, and W. G. Young, *J. Am. Chem. Soc.*, **80**, 5472 (1958).

(13) J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **76**, 4501 (1954).

(14) See P. I. Pollack and D. Y. Curtin, *J. Am. Chem. Soc.*, **72**, 961 (1950) for a closely related idea.

(15) See W. A. Bonner and D. D. Tanner, *J. Am. Chem. Soc.*, **80**, 1447 (1958).

(16) A. McKenzie, R. Roger, and G. O. Wills, *J. Chem. Soc.*, 779 (1926).

(17) H. I. Bernstein and F. C. Whitmore, *J. Am. Chem. Soc.*, **61**, 1324, (1939).

(18) D. Y. Curtin and M. C. Crew, *J. Am. Chem. Soc.*, **77**, 354 (1955).

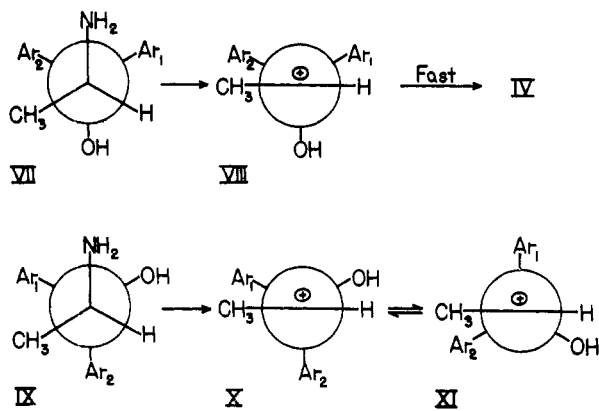


Figure 2.

about the C—C bond to yield carbonium ion IVa. Rearrangement of IVa to VIa, involving migration of configuration at the migration terminus, is considered to occur with a rate comparable to that of reversion to IIIa. The observation of a product mixture containing 88% of Va and 12% of VIa demands, within this framework of assumptions, that  $k_1 < k_3$ . The symmetry of the starting material demands in this case that  $k_2 = k_3$  (ignoring kinetic isotope effects) and  $k_1 = k_{-1}$ .

Applying the steady state approximation<sup>19</sup> to the intermediate present in lowest concentration, carbonium ion IVa, we may obtain relative values of  $k_1$ ,  $k_{-1}$ ,  $k_2$  and  $k_3$ .

$$\frac{d[\text{Va}]}{dt} = R_2[\text{IIIa}]; \quad \frac{d[\text{VIa}]}{dt} = k_3[\text{IVa}] \quad (1)$$

$$\frac{d[\text{IVa}]}{dt} = k_1[\text{IIIa}] - k_{-1}[\text{IVa}] - k_3[\text{IVa}] = 0 \quad (2)$$

Combining (1) and (2) and integrating we get

$$[\text{VIa}] = \frac{k_1 k_3}{k_2(k_{-1} + k_3)} [\text{Va}] \quad (3)$$

Since, in this case,  $k_3 = k_2$  and  $k_1 = k_{-1}$  and we know that  $[\text{VIa}]/[\text{Va}] = 12/88$  we can calculate from (3) that

$$k_2 = k_3 = 6.3k_1$$

Any important contribution of IX to the reaction scheme is ruled out by the failure to observe any appreciable amount (<2%) of product with inverted terminal configuration in which unlabelled phenyl (Ar<sub>2</sub>) had migrated. (Such a product would result from rearrangement of ion X derived from amine IX.)

The experimental facts of ref. (5) are equally well explained, however, by postulating an importance of amine conformation VII in the reaction scheme. Reaction of VII with nitrous acid would give carbonium ion VIII, which could not give aryl migration but would be expected to be quickly converted to IV, as such a conversion would involve eclipsing only of hydrogen with Ar<sub>1</sub>. Postulating 12% of the

reaction to take this path we could accommodate the observed product composition in a scheme in which aryl migration is much faster than the interconversion of rotational isomers IIIa and IVa.

It is possible to choose between these two explanations by considering the results of Curtin and Crew<sup>18</sup> on ratios for *p*-anisyl and phenyl migration in the diastereoisomeric forms of 1-*p*-anisyl 1-phenyl-2-aminopropanol (Ib and Ic). The *erythro* isomer (Ib) gave 88% phenyl migration (Vb) and 12% *p*-anisyl migration (VIb). If we make the reasonable assumption that *para* substitution affects neither conformational equilibria nor rates of interconversion of IIIb and IVb, we may use the same kinetic treatment in this case as we used for Ia.

We would expect the electronic effect of the *p*-methoxy group to increase the rate of *p*-anisyl migration over that for phenyl migration, so the ratio  $k_3/k_2$  in Equation 3 would not be expected to be unity. A reasonable value for this ratio may be derived from the migration ratios observed<sup>8</sup> in the pinacolic deamination of 2-amino-1-*p*-anisyl-1-phenylethanol (XII). In this compound the carbon from which nitrogen is lost is symmetrically substituted with two hydrogen atoms. One would, therefore, expect the migration ratio to express only the electronic effects of the remote *para* substituents in this case. The ratio of  $k_{p\text{-anisyl}}/k_{\text{phenyl}}$  was found<sup>20</sup> to be 1.56.

In the reaction of Ib the ratio  $k_3/k_2$  in Equation 3 may be set equal to 1.5 and we calculate:

$$k_2 = 7.0 k_1 \text{ and } k_3 = 10.5 k_1 \quad (5)$$

We may apply these calculated ratios of rate constant [equations (5)] to predict the product composition for the reaction of the diastereoisomeric amine (Ic). Recognizing that this compound is the same as Ib except that the phenyl and *p*-anisyl are exchanged, we may write for Ic:

$$k_2 = 10.5 k_1 \text{ and } k_3 = 7.0 k_1 \quad (6)$$

Then from Equation 3 we predict:

$$[\text{Vc}]/[\text{VIc}] = 0.084; \quad [\text{Vc}] = 7.7\%; \quad [\text{VIc}] = 92.3\%$$

The experimentally determined composition of the reaction product in this case was 6% of Vc and 94% of VIc. The close agreement between the calculated and actual percentage compositions may be considered as confirmation of the postulated reaction scheme.

It is of interest to note that from the data on C<sup>14</sup>-labeled phenyl migration in Ia the migration rate was 6.3 times as fast as interconversion of IIIa and IVa ( $k_2/k_1 = 6.3$ ). The rate of phenyl migration

(19) A. A. Frost and R. G. Pearson, *Kinetics and Mechanism*, J. Wiley and Sons, Inc., New York, 1953, p. 159.

(20) Curtin<sup>8</sup> has calculated this same ratio, 1.5, to represent the purely electronic component of the migration ratios observed in the deaminations of Ib and Ic. This compares with ratios of up to 500 in other reactions. [W. E. Bachmann and F. H. Moser, *J. Am. Chem. Soc.*, **54**, 1124 (1932).]

when the group left behind is *p*-anisyl (in Ib) is 7.0 times as fast as interconversion of IIIb and IVb ( $k_2/k_1 = 7.0$ ). Again assuming that the remote *para* substituent has no effect on rates of rotation (*i.e.*, the value of  $k_1$  is the same for each reactant), we conclude that phenyl migration, leaving behind a

carbonium ion stabilized by a hydroxyl group and a *p*-anisyl group, is faster by 10% than the migration of phenyl in a system in which the developing carbonium ion center is stabilized by the hydroxyl group and an unsubstituted phenyl group.

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[CONTRIBUTION FROM EASTERN RESEARCH LABORATORY, THE DOW CHEMICAL COMPANY]

## Addition of Hydrogen Cyanide to Aromatic Schiff Bases

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Details are presented on the synthesis of *N,N'*-alkylenebis[(2-substituted) glycinonitriles] by the addition of hydrogen cyanide to aromatic bis-Schiff bases. Where thermally stable, the nitriles may be hydrolyzed to the *N,N'*-alkylenebis-2-arylglycines.

In previous publications<sup>2</sup> we have reported on the properties of a novel chelating agent, *N,N'*-ethylenebis[2-(*o*-hydroxyphenyl)] glycine<sup>3</sup> and we wish now to report the synthesis of this and of related compounds. In essence, our method consists of the addition of 2 mol. of anhydrous hydrogen cyanide to a bis-Schiff base derived from an aromatic aldehyde and a diamine, and subsequent hydrolysis of the resulting glycinonitrile to an *N,N'*-alkylenebis-2-arylglycine. Though bis-glycinonitriles have been prepared from diamine dihydrochlorides, carbonyl compounds and potassium cyanide in aqueous solution,<sup>4,5</sup> little data is available on the addition of anhydrous hydrogen cyanide to Schiff bases, a reaction originally discovered by Plöchl.<sup>6</sup>

Inasmuch as the aromatic Schiff bases are readily prepared and purified, this method offers an alternate to the usual processes for the preparation of 2-substituted amino acids. However, the reaction sequence is limited severely by the lack of reactivity of certain of the aromatic Schiff bases with hydrogen cyanide and the thermal instability of the bis-glycinonitriles. Thus, of the twenty-seven Schiff bases reported in Table I, seven (19–27) did not react at all with hydrogen cyanide and a number of the others yielded intractable oils. Attempts to catalyze the cyanide addition were not successful and the use of solvents of varied polarity, other than liquid

hydrogen cyanide, offered little advantage in the case of the non-reactive Schiff bases, but was of some advantage in moderating the reaction for the more reactive compounds. The electronic nature of the substituent on the aromatic ring seems to have little or no effect on the formation of these adducts. Thus, while the *ortho*-hydroxyphenyl derivative affords product in almost quantitative yield, the corresponding 2,4-dihydroxyphenyl counterpart yields no glycinonitrile whatsoever, and is recovered unchanged.

A characteristic property of the glycinonitriles listed in Table II is their thermal instability. This undesirable feature greatly limited the number of compounds which were successfully hydrolyzed to the corresponding amino acids. Even those nitriles which could be successfully hydrolyzed had a limited stability; *N,N'*-ethylenebis[2-(*o*-hydroxyphenyl)]glycinonitrile though almost white when stored in the cold, slowly decomposed at room temperatures to give an orange brown solid which could not be characterized. A second mode of decomposition, which was typical of the heterocyclic derived Schiff bases, was their reversion to starting compounds with evolution of hydrogen cyanide. Thus, it is not surprising that only the most stable of the glycinonitriles were successfully hydrolyzed whereas the majority afforded only intractable highly colored tars. The *N,N'*-alkylenebis-2-substituted glycines are listed in Table III and some details of their preparation are given in the experimental section.

### EXPERIMENTAL

*Schiff bases.* These were synthesized in the usual manner by reaction of the appropriate aldehyde with the proper anhydrous diamine in alcohol in a 2:1 molar ratio. Purification was accomplished by recrystallization from alcohol. In the case of the 2-pyridinealdehyde- and 6-methyl-2-pyridinealdehyde-derived Schiff bases, reaction was conducted under a blanket of nitrogen using a few drops of glacial acetic acid to expedite reaction. Ligroin (66–75°)

(1) Present address: Chas. Pfizer and Co., Inc., Brooklyn, New York.

(2) H. H. Freedman, A. E. Frost, S. J. Westerback, and A. E. Martell, *Nature*, **179**, 1020 (1957); *J. Am. Chem. Soc.*, **80**, 530 (1958).

(3) Concurrent with our initial publication, a communication appeared by H. Kroll, M. Knell, J. Powers, and J. Simonian, *J. Am. Chem. Soc.*, **79**, 2024 (1957), which reported the synthesis of this compound by a method substantially identical to ours.

(4) N. Schlesinger, *Ber.*, **45**, 1486 (1912).

(5) H. Zahn and H. Wilhelm, *Ann.*, **579**, 1 (1953).

(6) J. Plöchl, *Ber.*, **13**, 2118 (1880).