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"FRAGMENTATION" AND A. N. NESMEYANOV'S CONCEPT OF σ-CONJUGATION

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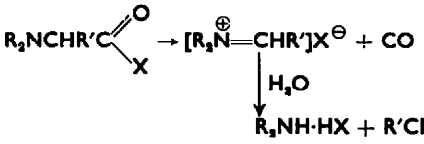
Abstract—This communication presents: (a) results of experimental work on decarbonylation of α-amino acid derivatives, (b) a discussion of the relationship between the concept of "fragmentation" and σ-conjugation as proposed by A. N. Nesmeyanov in 1950,[1] (c) support for the consideration that decarbonylation of α-amino acid derivatives and a number of other properties are due to conjugation of σ-bonds, and (d) a discussion on the role of the steric-orientation effect.

I

IN A number of experimental studies[2–5] it has been established that the α-amino acid derivatives with a tertiary nitrogen atom are capable of undergoing decomposition according to the equation:



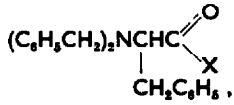
where R and R′ are hydrocarbon radicals and X is an electronegative substituent.

This reaction was first reported in 1959,[2] the N,N-dibenzylleucine and N,N-dibenzylglycyl chlorides being used as examples. In subsequent communications,[4,5] this reaction was shown to be characteristic of N,N-dialkyl- and N,N-diaralkyl-α-amino acids, the presence of a tertiary nitrogen being of crucial importance. According to the reported data, the α-amino acid chlorides with a primary nitrogen atom and the N-benzyl-α-amino acid chlorides, in the form of hydrochlorides, are used in syntheses.[6–9] In contrast, the α-amino acid chlorides with a tertiary nitrogen atom undergo decarbonylation at the moment of formation, e.g. when the amino acids are acted upon by PCl_5 or $SOCl_2$ in an inert solvent (benzene, chloroform, ether) either without heating or by raising the temperature to 30–40°. N,N-Dibenzylglycine is an exception since it yields an acid chloride stable at the ordinary temperature. An amine and aldehyde are obtained upon addition of water, the yield of amine sometimes being quantitative although this yield may be diminished owing to a side reaction. Thus the

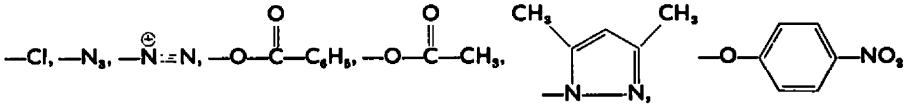
[1] A. N. Nesmeyanov, *Proc. Moscow University* **132**, 5 (1950).
[2] N. A. Poddubnaya and V. I. Maksimov, *ZhOKh; (Organic Sci. J.)* **29**, 3483 (1959).
[3] V. I. Maksimov, *Izvestia AN SSSR*, Chemical Science Dept. 112 (1962).
[4] V. I. Maksimov, *Dokl. AN SSSR* **145**, 567 (1962).
[5] V. I. Maksimov, *Izv. AN SSSR* (*Chem. Sci. Dept.*) 1074 (1963).
[6] A. F. Beecham, *J. Amer. Chem. Soc.* **79**, 3257 (1957).
[7] T. Curtius, *J. Prakt. Chem.* **94**, 273 (1916).
[8] V. Wollman, P. M. Gallop and A. Patchornik, *J. Amer. Chem. Soc.* **83**, 1263 (1963).
[9] E. Rothstein and M. A. Saboor, *J. Chem. Soc.* 425 (1943).

yield of di-*p*-nitrobenzyl-α-alanine may fall to 50% on account of the *p*-nitrobenzyl group being split off from the nitrogen, as in the formation of *p*-nitrobenzylchloride.[5]

The chlorine atom in the acid chloride may be replaced by another electrophilic substituent. The following N,N-dibenzylphenylalanine derivatives of the general formula:

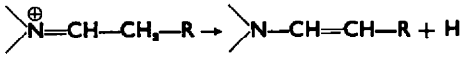


where X denotes



have been investigated.[3] The azide (X = $-N_3$) and the acid diazonium salt (X = $-\overset{\oplus}{N}\equiv N$) are both as unstable as the acid chlorides (X = —CL). The remaining compounds were obtained individually as their stability permits recrystallization from alcohol heated to boiling point. *p*-Nitrophenyl ester (X = $-O-C_6H_4-NO_2$) is stable to strong heating, which generally corresponds to X being the least electronegative. The azide (X = $-N_3$) on decomposition yields neither CO nor CO_2, which is due to the complex nature of the azide group. It is interesting that the decomposition of the azides of N-tosyl-α-amino acids, when acted upon by an alkali, as described by Beecham in 1957, also proceeds differently from that of the chlorides.[6] It is worth nothing that the decomposition of the dimethylalanine and dimethylaspartic acid azides to dimethylamine, aldehyde and other substances was described by Curtius in 1916, who regarded this reaction as a special case of the rearrangement named after him. However, the possibility of this reaction being akin to the one investigated is not excluded. The decomposition of the acyl diazonium salt (X = $-\overset{\ominus}{N}\equiv N$) obtained by the NBS treatment of the respective hydrazide (according to the method described[8]) was noted by us from the formation of dibenzylamine.

During the study of the kinetics of decarbonylation of the mixed anhydride of dibenzylphenylalanine and benzoic acid (X = $-O-CO-C_6H_5$), it was noted that this reaction* is strongly catalysed by acids and inhibited by bases; thus, the assumption of a proton catalysis was quite legitimate. The decomposition rate of this compound is represented by S-curve, i.e. an autocatalytic process takes place. It can be assumed that the autocatalysis is due to a side reaction:



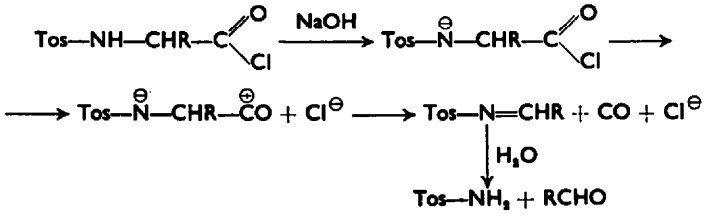
This reaction is highly probable theoretically; the formation of enamine can be observed when the dibenzylphenylalanine azide undergoes decomposition.[5]

The literature reports carboxylic acid chlorides (by the action of $AlCl_3$ in Friedel-Craft reactions) undergoing decarbonylation, the resulting carbonium ion either forming an olefine by splitting off a proton[9] or acting as an electrophilic reagent in

* The results of this work were reported at the 4th European Peptide Symposium which was held in Moscow in August 1961.

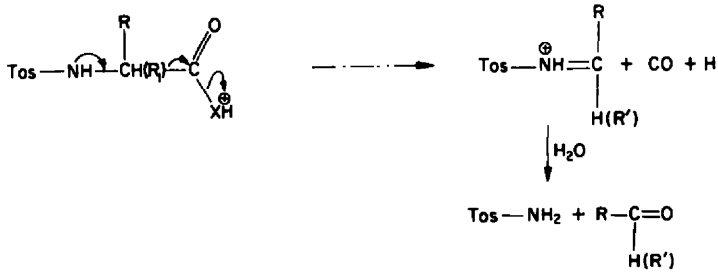
further transformations,[10] (also the Braun reaction[11,12]). The reaction described by Mannich and Kuphal is of particular interest,[13] in that the hydrochloride of the N-methyl-N-benzylglycyl chloride may be heated to 180° without undergoing decomposition, whereas in the presence of $AlCl_3$ decomposition take place without heating. The phthalylglycine acid chloride, according to Gabriel,[14] undergoes decomposition when acted upon by $ZnCl_2$.

There are cases when bases are the catalysts in the decarbonylation of acid chlorides.[6,15–18] The decarbonylation of the N-tosyl-α-amino acid chlorides is catalysed by alkali. The reaction mechanism, according to Beecham,[6] involves the splitting off of a proton from the nitrogen with the appearance of a negative charge, splitting off the chlor-anion and disintegration of the dipole:



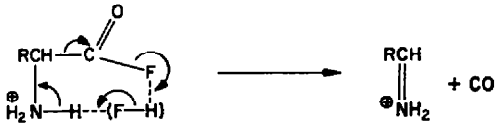
A similar reaction with pyridine as the catalyst was described in 1962.[18] It is assumed that the mechanism of acidic decarbonylation takes place in one-step:[3]

Beecham[19] reported the catalytic action in the decarbonylation of N-tozyl-α-amino acids and their esters and chlorides and assumed the mechanism to be as follows:



[10] E. Rothstein and R. W. Saville, *J. Chem. Soc.* 1946 (1949).
[11] J. Braun, G. Blessing and R. S. Cahn, *Ber. Dtsch. Chem. Ges.* **57**, 908 (1924).
[12] J. Braun and O. Bayer, *Ber. Dtsch. Chem. Ges.* **60**, 1257 (1927).
[13] C. Mannich and R. Kuphal, *Ber. Dtsch. Chem. Ges.* **45**, 314 (1912).
[14] S. Gabriel, *Ber. Dtsch. Chem. Ges.* **41**, 242 (1908).
[15] R. H. Wiley, H. L. Davis, D. E. Gensheimer and N. R. Smith, *J. Amer. Chem. Soc.* **74**, 936 (1952).
[16] R. H. Wiley and R. P. Davis, *J. Amer. Chem. Soc.* **76**, 3496 (1954).
[17] A. F. Beecham, *Chem & Ind.* 1120 (1955).
[18] J. C. Sheehan and J. W. Frankenfeld, *J. Org. Chem.* **27**, 628 (1962).
[19] A. F. Beecham, *Austr. J. Chem.* **16**, 889 (1963).

In 1962 it became known that leucyl fluoride in the presence of excess of hydrogen fluoride undergoes partial decarbonylation and the following mechanism was suggested:[20]



Both the reaction and its interpretation are almost in full agreement with the data presented. The main difference in the description of the mechanism is that the nitrogen is assumed here to be carrying a positive charge, which is very unlikely, because this must interfere with the transfer of the electron pair from the nitrogen to the α-carbon atom. This appears to be the first case of an α-amino acid derivative with a primary nitrogen atom being subjected to decarbonylation.

In general the following conclusions can be made concerning this reaction:

(1) Decarbonylation for carboxylic acid derivatives is general, i.e. they are potentially unstable.

(2) The more electronegative X is in the COX group, the easier the reaction takes place.

(3) The reaction is generally catalysed by acids and particularly by proton-donors. The mechanism of the acid catalysis may be assumed to be the same in different cases, i.e. an increase in the electronegativity of X is due to the electrophylic effect of the acid.

(4) The reaction is promoted by nucleophilic substituents in the α- and β-position.

(5) The reaction may be catalysed by bases due to the nucleophilic effect at the β-atom.

(6) The presence in the α-position of the R_2N-group has an unusually strong effect on this reaction. No such effect is produced either by the RNH- or the H_2N-groups.

In a general form the mechanism of these reactions can be represented as follows:

Here B and X are electron-donor and electron-acceptor substituents, respectively. The following variation is also possible:

The oxalic acid monochloride undergoes decomposition, apparently according to this scheme:[21]

[20] K. D. Kopple, L. A. Quartermann and J. J. Katz, *J. Org. Chem.* **27**, 1062 (1962).

[21] J. Ugi and F. Beck, *Chem. Ber.* **94**, 1839 (1961).

II

In recent years a new term "fragmentation" has been recognized in the literature, embracing a large group of known decomposition reactions based on an electron scheme common to all.[22–25] This term was introduced by Grob in order to systematise decomposition reactions. The theoretical aspect of this problem was first presented by Grob and Baumann in 1955[22] and was later repeatedly elucidated and supplemented.[23–25] Fragmentation is based on the conjunction of different bonds, owing to which the interaction of various groups of opposite character (electron-donor and electron-acceptor) and removed from each other becomes effective. Before 1950, p- and π-conjugation and hyperconjunction of the C—H bond with other conjugation systems were considered. The concept of σ-bonds as participating in conjugation generally was put forward by Nesmeyanov in 1950,[1] although in experimental investigations this concept was used even earlier.[26] The concept of fragmentation is not opposed to σ-conjugation, in fact, the former is a part of the latter.

Nesmeyanov developed his concept[1,26–30] from the analogy between the 1,4-addition to π,π-conjugated systems and the 1,4-attack at the σ,π- and σ,σ-conjugated systems. This analogy finding expression in the electromeric displacement of the bonding electrons in such attacks was illustrated by him for a number of reactions, such as follows:

Type of conjugation

I π,π $\overset{1}{CH_2}=\overset{2}{CH}-\overset{3}{CH}=\overset{4}{CH_2} + HX \rightarrow \overset{1}{CH_3}-\overset{2}{CH}=\overset{3}{CH}-\overset{4}{CH_2}X$ (1,4-addition to diene-1,3)

II σ,π $\overset{1}{CH_2}=\overset{2}{CH}-\overset{3}{CH_2}-\overset{4}{Y} + HX \rightarrow \overset{1}{X}-\overset{2}{CH_2}-\overset{3}{CH}=\overset{4}{CH_2} + YH$ (allyl rearrangement)

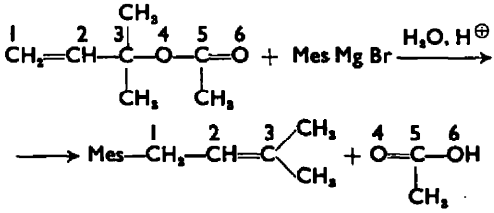
III σ,σ $\overset{1}{HO}-\overset{2}{CH_2}-\overset{3}{CH_2}-\overset{4}{HgCl} + HCl \rightarrow \overset{1}{H_2O} + \overset{2}{CH_2}=\overset{3}{CH_2} + \overset{4}{HgCl_2}$ (β-elimination)

IV σ,σ $\overset{1}{Cl}-\overset{2}{CH}=\overset{3}{CH}-\overset{4}{HgCl} + KI \rightarrow \overset{1}{KCl} + \overset{2}{HC}\equiv\overset{3}{CH} + \overset{4}{HgI_4^{2-}}$ (β-elimination)

According to Nesmeyanov "in every case the effect of the conjugated system amounts to an easily evokable coordinated electromeric shift of 2 electron pairs in the 1–2 and 3–4 bonds. Whether both the sidemost atoms (1 and 4) are found to be bound by the new covalent bonds, or only one of them, is just a detail of the picture." Such electromeric displacement results in the 2 and 3 chain atoms being held by a new

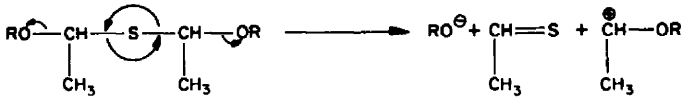
[22] C. A. Grob and W. Baumann, *Helv. Chim. Acta* **38**, 594 (1955).
[23] C. A. Grob, *Experimentia* **13**, 126 (1957).
[24] C. A. Grob, *Theoretical Organic Chemistry. Proceedings and Discussions of the Kekulé Symposium* London (1959).
[25] C. A. Grob, *Bull. Soc. Chim. Fr.* **7**, 1360 (1960).
[26] A. N. Nesmeyanov, R. K. Freidlina and N. K. Kochetkov, *Izv. AN SSSR (Chem. Sci. Dept.)* 623 (1949).
[27] A. N. Nesmeyanov, R. K. Freidlina and N. K. Kochetkov, *Izv. AN SSSR (Chem. Sci. Dept.)* 273 (1951).
[28] A. N. Nesmeyanov, M. I. Kabachnik, *ZhOKh (Organic Chem. J.)* **25**, 41 (1955).
[29] A. N. Nesmeyanov, *Selected Works in Organic Chemistry*. Pergamon Press (1963).
[30] A. N. Nesmeyanov, I. I. Kritskaya, *Dokl. AN SSSR* **121**, 477 (1958).

π-bond, whereas between the 1 and 2 as well as between the 3 and 4 atoms either the π-bond (in the case of π-conjugation) or the σ-bond (in the case of σ-conjugation) is ruptured. In the latter case the molecule with the σ,σ-conjugated bonds will break. Hence, β-elimination proves to be a particular case arising from the σ,σ-conjugation and at the same time the simplest case of fragmentation. In the case of longer conjugated systems comprising σ-bonds, more sophisticated (compared to β-elimination) fragmentation occurs. Thus Nesmeyanov *et al.*[27] gave a description of the action of mesitylmagnesium bromide on dimethylvinylcarbinol acetate, accompanied by fragmentation resulting from the 1,6-attack at the π,σ,π-conjugated system:

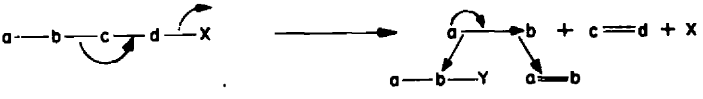


This type of β-elimination or fragmentation has been extensively studied by Nesmeyanov with collaborators using metallo organic quasicomplex compounds as examples,[29] and steric conditions of σ-conjugation formulated in a number of papers.[1,30] According to Nesmeyanov "for a full display of conjugation between two σ-bonds they should be arranged in parallel (or nearly parallel). However, this condition alone is not sufficient.... It is also necessary (at least in heterolytic conjugation phenomena) that of the two conjugated σ-bonds one has the donor and the other the acceptor character and that they be in *trans*-position with respect to one another. Farther, it is necessary that between the second and third atoms of the conjugated system the formation of a new multiple bond is possible". According to the above there are 4 requirements for σ-conjugation.

Shostakovsky *et al.*[31] observed in 1951 the conjugation of simple bonds in α-alkoxyethylmercaptans or in α,α'-dialkoxydialkylsulphide. In the presence of an acid the latter easily undergo decomposition. The authors have suggested the following reaction scheme:[31]



α-Alkoxyethylmercaptans undergo decomposition more readily. The general scheme of fragmentation may be present as follows:[25]



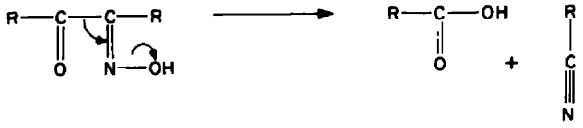
The fragmentation requirements are: (1) the stereoelectron factor, which, generally, corresponds to the requirements of parallelism in σ-conjugation; (2) the presence of an electron-donor ("a" in the scheme) and electron-acceptor ("X" in the scheme)

[31] M. F. Shostakovsky, E. N. Prilezhaeva and E. S. Shapiro, *Izv. AN SSSR (Chem. Sci. Dept.)* 284 (1951).

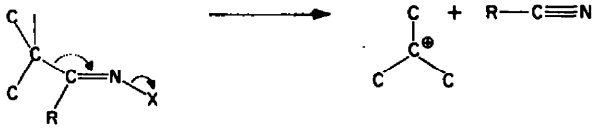
substituents, which correspond to the 2nd requirement of σ-conjugation; (3) the fragmentation of α-aminoketone oximes can be facilitated in the case of *trans*-configuration (the 3rd requirement of σ-conjugation); (4) the requirement of σ-conjugation ensues from the cited scheme of "fragmentation". The reaction itself is due to a synchronous displacement of electron densities in the respective bonds from "a" to "X".

If "a—b" is substituted by "B", the equation for the fragmentation reaction becomes:

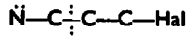
In this form, the conditions noted by Nesmeyanov for σ-conjugation in 1950 and by Grob for fragmentation in 1955–1960 are equivalent. Therefore, it is not accidental, that the examples cited by Nesmeyanov and Grob are similar. As early as 1950 Nesmeyanov considered the Beckman rearrangement of the type II as a reaction, accounted for by the σ-conjugation:[1]



Grob, in 1957, considered it as a fragmentation reaction[24] (e.g. for camphor oxime, 1960[25]):



Conjugation as a property of the bonds is encountered not only in decomposition reactions, and therefore the study of the laws underlying such conjugation is of great significance. Fragmentation of longer chains (in γ-amino halides) in accordance with such laws



can be split in two parts in compliance with the concept of "ethylogy":[23]

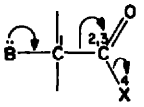
Each one has been considered individually in terms of the conjugation concept (p,σ-conjugation in the left part, σ,σ-conjugation in the right part[23]) the geometric factors of the reaction having been elucidated. The fragmentation stereochemistry of the entire chain has been studied more thoroughly by Grob. Since conjugation of the bonds is characterised by transfer of the respective electron pairs either before or at the moment of reaction (static or dynamic conjugation), certain stereochemical requirements for conjugation signify conditions under which the carbon chain is

endowed with electrical conductivity. The general requirements for every case of conjugation (p, π, σ) is apparently a geometric factor, and this means that the influence along the chain of carbon compounds is transmitted with a maximum force when the interacting bonds occupy either the parallel or transoid positions.

Nesmeyanov's concept of σ-conjugation amounts to a generalization of the extensive experimental material accumulated in organic chemistry and reflects a fundamental property of organic compounds observed in reactions of certain types, particularly, in decomposition reactions and from it follows the affinity of π- and σ-conjugation phenomena. The theory of the "fragmentation" problem is confined to a comparatively narrow sphere *viz.* the elucidation of the requirements for a synchronous displacement of electrons along the chain of atoms in decomposition reactions, which in fact amounts to the clarification of the force of interaction (conjugation) between removed atoms or groups. Therefore all examples of fragmentation reactions[21,32–36] may be considered as new examples of reactions involving σ-conjugation.

III

By supplementing the 4th requirement of σ-conjugation, the decarbonylation reaction of α-amino acid derivatives may also be considered within the framework of this concept. If the 4th requirement is stated as: "It is necessary that between the second and third atoms of the conjugated system the formation of a new multiple bond is possible; the second and third carbon atoms can be replaced by one capable of taking up an electron pair", then in the proposed electron mechanism of the reaction all conjugation requirements will be satisfied:



Here the carbonyl group may play the part of the "$\overset{2}{C}—\overset{3}{C}$" link in the ordinary σ-conjugation.

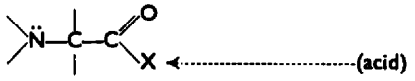
The special effect of the tertiary nitrogen ($B{=}R_2N—$) on this reaction apparently is accounted for by its effect on the conformation of the molecule. In such compounds the R_2N-group is deprived of free rotation in contrast to the H_2N-group. As demonstrated by the Stuart-Briegleb models, it may occupy one of two positions (e.g. in diethyl-α-alanine); in either position the free electron pair of the notrogen, the nitrogen atom, the α-C-atom and the carboxyl C-atom are all in the same plane, being distinguished by the orientation of the electron cloud of the free electron pair of the nitrogen (similarly to the *cis-trans*-configuration in a double bond). One of these conformations is less advantageous, because the dialkylamino group and the alkyl substituent in the amino acid α-C-atom come close to one another. In α-amino acids with primary nitrogen atoms, the H_2N-group rotates freely and therefore, although fragmentation is not completely excluded because of the possibility of a favourable

[21] R. H. Leittinger and D. E. Pollart, *J. Amer. Chem. Soc.* **78**, 6079 (1956).
[32] C. Wittig and W. Tochtermann, *Chem. Ber.* **94**, 1692 (1961).
[34] F. Weygand and H. Daniel, *Chem. Ber.* **94**, 1688, 3145 (1961).
[35] R. K. Hill, *J. Org. Chem.* **27**, 29 (1962).
[36] H. Stetter and P. Tacke, *Chem. Ber.* **96**, 694 (1963).

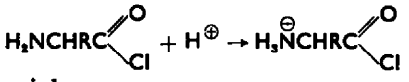
conformation, it is, however, not likely. The crucial importance of the geometric factor is also born out by the fact that the nucleophility of the substituent at the nitrogen plays a subsidiary role.

According to the terminology,[28] the decarbonylation of α-amino acids can be classed with reactions of p,σ,σ-conjugation.

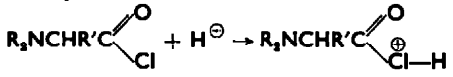
It has already been mentioned that the catalytic effect of an acid on decarbonylation can only be attained through an attack at the carboxyl end of the molecule:



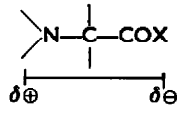
Normally it would appear that the proton should join the nitrogen. But then it would inhibit the reaction. Apparently this accounts for the difference between the α-amino acid chlorides with primary and tertiary nitrogen atom. In the first case the reaction is mainly as follows:



In the second case, it is mainly:

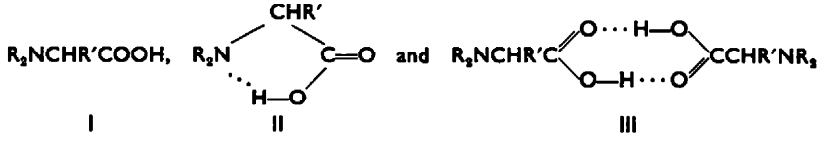


Decarbonylation is absent in the first case and present in the second i.e. here the reaction centre is transferred along the conjugated system. In the second case a favourable geometric factor accounts for strong p,σ,σ-conjugation, as a result of which the molecule can be represented as a dipole with its negative sign facing the COX-group:



Whether this dipole is induced by the acid, or whether it exists as a ready-made entity, in other words, whether dynamic or static conjugation is involved cannot be determined with certainty. In the case of conjugation with the primary amino-group static conjugation must be absent in a majority of cases, because the H_2N-group rotates freely.

However, in the case of amino acids with a tertiary nitrogen atom the possibility of static conjugation also exists. The validity of this conclusion is corroborated by the structure of these compounds. Iakovlev and the author[37] used the IR spectrum technique to show that in organic solvents (C_6H_6, CCl_4, $CHCl_3$ etc.) they display either exclusively or largely a nonpolar structure in the form of three possible states:



I II III

The quantitative relation between the structure varies with concentration; the higher concentration the greater the number of associated molecules. The quantitative relation between structures is considerably affected by the character of the substituent on

[37] I. P. Yakovlev and V. I. Maksimov, *Izv. AN SSSR (Chem. Sci. Dept.)* 877 (1963).

the nitrogen. A survey of published data[38] indicates that in such characteristics as m.p. and solubility these substances conspicuously stand out from the class of α-amino acids. In contrast to α-amino acids with primary nitrogen atoms those with tertiary nitrogen atoms are distinguished by low m.ps (usually below 100°) and good solubility in organic solvents. The m.p. of N-ethyl-N-isopropylvaline is 50–54°, it is soluble in petroleum ether. Such changes in the properties are not merely due to an increased hydrophobicity of the molecules, because the C-dialkyl derivatives of glycine, no matter, how long are the alkyl radicals and despite their raminification, are, however, distinguished by m.ps lying around 300° and occasionally going down to 230°; they are quite insoluble in organic solvents. For example, the m.p. of C_β,C_β-dibenzyl-α-alanine is 250–270°,[39] whereas that of N,N-dibenzyl-α-alanine is 96–98°.[40] Some data are presented in Table form, the isomers being placed in horizontal lines. A drop in m.p. can be observed in every case, being as a rule very pronounced in transition to N,N-derivatives.

As in the case of decarbonylation in considering the specific effect of the tertiary nitrogen, if it is assumed that owing to the p,σ,σ-conjugation the reaction centre is transferred, the reaction may proceed along two paths:

$$(1)\quad H_2NCHRCOO^{\ominus} + H^{\ominus} \rightarrow \overset{\oplus}{H_3}NCHRCOO^{\ominus}$$

$$(2)\quad R_2NCHR'COO^{\ominus} + H^{\oplus} \rightarrow R_2NCHR'COOH$$

i.e. in the case of the α-amino acids with tertiary nitrogen atoms the carboxyl must take up a proton more readily than α-amino acids with primary nitrogen atoms. Undoubtedly, there may be a tendency towards molecular ion formation as in water, for example, N,N-diethyl-α-alanine largely exists in the form of bipolar ions.[41] Also a tendency to form largely molecular rather than bipolar structures is common in aminobenzoic acids.[42]

IV

There is a close relationship between the decarbonylation reaction of α-amino acid derivatives, and the fragmentation reaction of α-aminoketoximes. Both reactions are accounted for by the p,σ,σ-conjugation. Obviously, when using correlation equations in such cases, it is necessary to take into account the effect arising from the conjugation of simple bonds. Fisher and Grob, in 1963,[53] point to the tremendous accelerating

[38] V. I. Maksimov, *Theses*, Moscow (1963).
[39] H. E. Carter, *J. Biol. Chem.* **108**, 619 (1935).
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[52] L. Velluz, G. Amiard and R. Heymes, *Bull. Soc. Chim. Fr.* (5)**21**, 1013 (1954).
[53] H. P. Fischer and C. A. Grob, *Helv. Chim. Acta* **46**, 936 (1963).

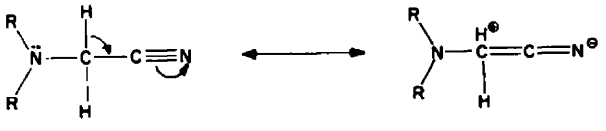
TABLE 1. MELTING TEMPERATURES OF DIALKYL-DERIVATIVES OF GLYCINE RACEMATES

Alkyl radicals	Atoms with alkyl radicals					
	C	Ref.	N, C	Ref.	N	Ref.
Dimethyl	280–281° (sublim)	43	315–317°	44	182–183°	45
Diethyl	309	46	282 (decomp)		131	47
Dipropyl	312	48			130	47
Dibutyl	303	48			134	47
Diisobutyl	279	48			94	47
Diisoamyl	290	48				
Isobutyl, isopropyl			269	47		
Isopropyl, isobutyl			260 (sublim)	49		
Diisopropyl	295	48	250 (sublim)	49		
Di-n-heptyl					131	47
Isopropyl, propyl			250 (sublim)	49		
Methyl, benzyl	294, 5–295	50	252–254	51	198–199	13
Benzyl, methyl			250	52		

effect of the α-amino group in ketoximes, noting that there is no proportionality between log K and pK_a^+. They introduce the notion of a special "frangomeric acceleration" which is assumed to be the result of the "electromeric effect". As can be seen, Grob used the conjugation terminology in the theory of electronic displacements.

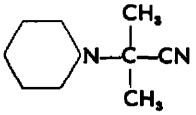
The conclusion about the special effect of the amino group is in agreement with our results obtained in the decarbonylation of amino acid derivatives. We reported in 1962[4] that this reaction is not affected by the basicity of the nitrogen, the presence of two substituents at the nitrogen being the necessary requirement. We attributed this to the steric-orientation effect of the alkyl substituents at the nitrogen. It would be interesting to study from this angle the type-II Beckmann rearrangement (fragmentation) of α-aminoketoximes. One of the examples in the experimental data obtained by Fisher *et al.*[54] indicates that the replacement in syn-oximes of the H_2N-group by a R_2N-group leads to a 1–1·5 order increase in fragmentation rate.

The effect of the tertiary nitrogen has, apparently, a greater significance, affecting not only the dynamic factor of conjugation (electromeric effect) but also the static factor. This is most convincingly proved, in our opinion, by the basicity of the nitrogen in dialkylacetonitriles being reduced about 6·5 pK units, as compared with the respective dialkylamines.[55] Marxer proposed a likely mechanism for this effect and is in favour of the electronic displacement of conjugation. It is true that the state of the substance is described by him as being represented by two boundary forms:

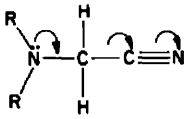


[54] H. P. Fischer, C. A. Grob and E. Renk, *Helv. Chim. Acta* **45**, 2539 (1962).
[55] A. Marxer, *Helv. Chim. Acta* **37**, 167 (1954).

In this explanation the central role is attributed to the hyperconjugation of the C—H bond with the CN-group. This view is assumed by the author as confirmation for the small value of ΔpK (equal to ~ 2) in piperidine–dimethylacetonitrile, where conjugation is absent:



In our opinion, the explanation is more tenable if this example is considered as analogous to the fragmentation of α-aminoketoximes. The pK reduction may be accounted for by the static p,σ,π-conjugation:



If both H atoms are replaced by R-groups, this must lead to supplementary steric effects resulting in the orientation of the respective electron densities being unfavourable for conjugation. A similar case occurs, for example, in *o*-substituted dialkylanilines, where conjugation is adversely affected by the steric-orientation effect.

CONCLUSION

The principal assumptions of the concept of σ-conjugation, which are again stated in the "fragmentation" concept, were first presented by Nesmeyanov in 1950, i.e. five years before the first exposition of the "fragmentation" concept. The concept of "fragmentation" lacks such notions, or their equivalent, as the transfer of the reaction centre, the dynamic and static conjugation, being, therefore, less comprehensive in its contents and potentialities for the explanation of facts.

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