Acid. This transformation (Table III) was performed by refluxing (−)-4-cyano-4-phenylacetamidobutyric acid, $[\alpha]^{20}_D$ −12.0° (c 2.0, methanol), recovered from the enzymatic hydrolysis of (±)-**32**, with 3 N hydrochloric acid.

Registry No.—(*R*)-**26**, 65414-95-1; (*R*)-**27**, 65414-96-2; **28** PA ester, 65414-97-3; (*R*)-**29**, 65414-98-4; **29** THP ether, 65414-99-5; (*S*)-**32**, 65414-60-0; (*R*)-**34**, 65414-61-1; (*R*)-**34** salt, 65414-62-2; (*S*)-**34** salt, 65414-64-4; (*R*)-**35**, 65414-65-5; (*S*)-**36**, 65414-66-6; (*R*)-**36**, 65414-67-7; (*R*)-**37**, 65414-68-8; norleucinonitrile, 65414-69-9; phenylacetyl chloride, 103-80-0; leucinonitrile, 65451-12-9; valinol, 16369-05-4; (*S*)-valinol, 22464-36-4; (2-tetrahydropyranyloxy)acetaldehyde, 65414-70-2; *O*-(2-tetrahydropyranyl)-2-iminoethanol, 65414-71-3; 2-amino-3-(2-tetrahydropyranyl)propionitrile, 65414-72-4; (±)-serinamide hydrochloride, 65414-73-5; (*S*)-serinamide hydrochloride, 65414-74-6; (±)-2-cyano-2-phenylacetamidoglutaric acid, 65414-75-7; (±)-2-cyano-2-phenylacetamidoglutaric acid dimethyl ester, 65414-76-8; diazomethane, 334-88-3; (±)-aspartic acid α-methyl ester, 65414-77-9; (*S*)-aspartic acid α-methyl ester, 17812-32-7; (*R*)-aspartic acid α-methyl ester, 65414-78-0; (±)-glutamic acid α-methyl ester, 65414-79-1; (*S*)-glutamic acid α-methyl ester, 6384-08-3; (*R*)-glutamic acid α-methyl ester, 26566-13-2; (*S*)-norleucine, 327-57-1; *N*-phenylacetyl-(*S*)-norleucine, 65414-80-4; benzylpenicillinacylase, 9014-06-6.

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Reactions of Protonated Diamino Acids in the Gas Phase

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The methane chemical ionization mass spectra of series of α,ω-diamino acids, ω-amino acids, cyclic and acyclic α-amino acids, and methyl esters have been obtained. Protonated α,ω-diamino acids react in the gas phase through the competitive cycloelimination of water or ammonia, decarboxylation, or collision stabilization of the intramolecularly hydrogen bonded protonated molecular ion. Structural factors which select between decarboxylation and lactam, lactone, and cyclic amino acid formation are determined by comparison of spectra of these related compounds. The prevalence of reactions correlates with the product ion stability and not with the site of protonation, the thermodynamically preferred site of protonation, or the stability of the intramolecularly hydrogen-bonded complex.

Reactions of protonated diamino acids in the gas phase may be studied under conditions of chemical ionization mass spectrometry. Under these conditions the diamino acid is protonated on a single site by way of an exothermic proton transfer reaction with reagent gas ions CH_5^+ or $CH_3CH_2^+$. The protonated molecular ions may undergo collision stabilization while in the ion source[1] or react through elimination of water, ammonia, or carbon monoxide.[2] In many ways these conditions are analogous to those in solution. The reactions of protonated molecules which occur in the gas phase but are not observed in solution demonstrate the influence of solvent effects on molecular reactivity.

Protonated molecules such as the diamino acids, 2,3-diaminopropionic to 2,6-diaminohexanoic acid (lysine), may react in the gas phase through simple S_E1 elimination analogous to reactions in strongly acid solution[3,4] or neighboring group displacement reactions involving three- to seven-membered cyclic transition states.[5-7] While gas phase reaction mechanisms may be analogous to solution chemistry, the charge on a protonated site is not distributed through solvation so that internal effects such as substituent polarizability,[6] hydrogen bonding,[8,9,10] and ion–dipole interactions[11,12,13] are relatively more important.

The reactions of protonated diamino acids are related to the interfunctional distance between the terminal amine and the α-amino acid moiety which indicates that neighboring group interactions may be involved. Lactam, lactone, and cyclic amino acid formation as well as decarboxylation reactions are believed to occur in the gas phase.

Our investigation of these reactions has centered on determining which intramolecular interactions (amine–amine or amine–carboxyl) are involved in diamino acid fragmentation and the structural features which regulate the probability of their occurrence. Although reaction product structures cannot be determined directly, supporting evidence may be obtained by comparing product ion reactivities to the reactivity of ions generated from other sources. For example, the subsequent fragmentation of the $MH-NH_3$ ion products, reactions 1–3, may be compared to protonated cyclic amino acid reactions.

The general features of 2,5-diaminopentanoic acid (ornithine) and 2,6-diaminohexanoic acid (lysine) methane chemical ionization mass spectra have been reported previously. Milne et al.[2] noted the selective initial elimination of ammonia from the 6 position of lysine, reaction 1. The cyclization mechanism postulated was supported by studies of diaminoalkanes,[5] $NH_2(CH_2)_nNH_2$, in which the probability of ammonia loss paralleled the rate of cyclization of $Br(CH_2)_nNH_2$ in solution.[14] An additional sequence leading to the cyclic iminium ion with loss of ammonia from the 2 position was also indicated.[2] Leclercq and Desiderio[15] noted the facile loss of water from ornithine and suggested that this

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Table I. Diamino Acid Chemical Ionization Mass Spectra (Methane, 200 °C)

	$NH_2(CH_2)_{n-2}CH(NH_2)COOH$,[c] n =			
	3	4	5	6
M + C_3H_7	0.6			0.7
$-NH_3$	1.7			0.7
$-H_2O$		2.4	1.3	
$-H_2O$, CO				0.3
M + C_2H_5				0.6
$-NH_3$	3.9		0.2	1.3
$-H_2O$		1.2	0.4	
MH	26.6	0.8	0.7	28.0
$-NH_3$	27.6	1.2	3.0	23.9
$-H_2O$[a]	0.8	49.0	40.3	3.4
$-H_2O$, NH_3	1.7	1.6	3.1	1.6
$-H_2O$, CO	25.9	17.6	3.0	2.2
$-NH_3$, H_2O, CO	1	7.8	30.7	29.0
M − H				.2
$-NH_3$	0.3	4.1	3.7	4.2
$-H_2O$	0.9	6.9	2.3	
Misc	6.6			
ΣI	93.6	91.4	88.6	96.0

[a] Isobaric with M 29–46. [b] *(m/e, % ΣI)* 76, 38; 58, 0.7; 30, 2.3. [c] Registry No.—$C_3H_8N_2O_2$, 515-94-6; $C_4H_{10}N_2O_2$, 305-62-4; $C_5H_{12}N_2O_2$, 70-26-8; $C_6H_{14}N_2O_2$, 56-87-1.

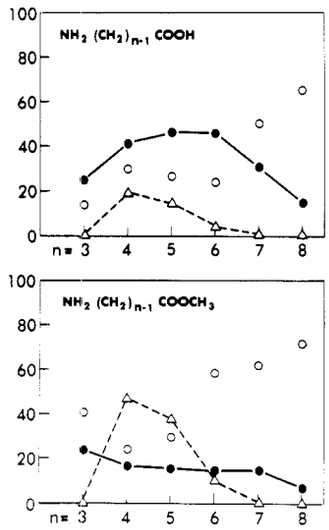


Figure 1. Chemical ionization mass spectra of ω-amino acids and methyl esters (methane, 200 °C) showing the variation in abundance of MH^+ (○), MH − HOR (●), R = H, CH_3, and MH − NH_3 (△) with interfunctional separation.

may involve lactam formation. Loss of water from simple amino acids is always accompanied by the subsequent loss of carbon monoxide.[16] In this study the properties of model compounds have been investigated in an effort to obtain experimental evidence in support of fragmentation reaction mechanisms.

Experimental Section

Amino acids were obtained from commercial sources. Mass spectra were obtained using an Associated Electrical Industries MS-902 double focusing mass spectrometer which had been modified to operate under chemical ionization conditions[17] and in the ion kinetic energy scan mode.[18] Samples were introduced using a direct insertion probe. Methane was used as the reagent gas at 0.7 Torr. All spectra were taken under similar conditions of sample partial pressure, source temperature, 200–210 °C, and instrumental parameters.

Table II. Diamino Acid Methyl Ester Chemical Ionization Mass Spectra (Methane, 200 °C)

	$NH_2(CH_2)_{n-2}CH(NH_2)COOCH_3$,[e] n =			
	3	4	5	6
M + C_3H_7	0.4	0.4		1.1
$-NH_3$	1.0	.3		0.5
$-HOCH_3$		.3	0.4	
$-HOCH_3$, CO	0.4	.4	0.1	0.1
M + C_2H_5				1.0
$-NH_3$	2.9	0.4		1.2
$-H_2O$		0.4	0.7	
$-HOCH_3$		0.7	0.7	0.6
MH	15.4	13.6	18.6	34.3
$-NH_3$	35.9	22.1	34.4	28.2
$-H_2O$[a]	3.3	16.6	3.1	1.6
$-HOCH_3$[b]	1.4	22.8	10.6	2.1
$-H_2O$, NH_3		0.6	0.1	0.1
$-HOCH_3$, NH_3		1.4	1.8	1.7
$-H_2O$, $HOCH_3$		1.8	1.3	1.2
$-HOCH_3$, CO	15.9	10.9	1.5	1.8
$-HOCH_3$, CO, NH_3	*c*	1.5	22.4	18.2
M − H	1.0			
$-NH_3$			1.6	2.7
$-H_2O$		0.4		
$-HOCH_3$			0.2	0.2
Misc	12.3[d]			
ΣI	94.7	94.3	98.3	96.2

[a] Isobaric with M + 29–46. [b] Isobaric with M + 29–60. [c] *m/e* 42 concealed by reagent gas ions, assumed to be zero. [d] *(m/e, %ΣI)* 30, 9.0; 58, 1.8; 88, 1.5. [e] Registry No.—$C_3H_{10}N_2O_2$, 20610-20-2; $C_4H_{12}N_2O_2$, 37529-96-7; $C_5H_{14}N_2O_2$, 6384-10-7; $C_6H_{16}N_2O_2$, 687-64-9.

Ion intensities are corrected for ^{13}C natural abundance. The formulas for ions in the 2,6-diaminohexanoic acid spectra were determined from accurate mass measurements and are consistent with the structures shown.

Results

The methane chemical ionization mass spectra of four diamino acids, 2,3-diaminopropionic to 2,6-diaminohexanoic acid, are shown in Table I. Each of these compounds fragment following protonation by the loss, or successive losses, of ammonia, water, and carbon monoxide. The relative abundance of these ions varies over a wide range even within this limited series. Ions formed by association of $C_2H_5^+$ or $C_3H_7^+$ are of low intensity at the source pressure used[19] (0.7 Torr) and their fragmentation parallels that of the protonated molecular ion. The ions derived from $(M - H)^+$ are also of low intensity in these spectra.

The spectra for the methyl ester of each of these diamino acids are shown in Table II. The differences in the acid and methyl ester spectra can be attributed to the fact that loss of methanol from an alkyl methyl ester (MH = 100, MH − $HOCH_3$ = 13) is less facile than loss of water from an acid (MH = 100, MH − H_2O = 65).[11] As a consequence all of the fragmentation reactions which involve loss of methanol are less abundant than the corresponding acid fragment ions and the percent abundance of the remaining ions is increased. The close parallel between the acid and methyl ester spectra tend to confirm that pyrolysis of the diamino acids has been avoided. Elimination of water from the diamino acid methyl esters implicates a reaction mechanism through which either water or methanol may be lost from the ester function.

Table III shows the spectra of ω-amino acids and methyl esters which were taken under the same conditions as the α,ω-diamino acids and esters of Tables I and II. These spectra are similar to the two previously reported ω-amino acid

Table III. Terminal Amino Acid and Methyl Ester Chemical Ionization Mass Spectra (Methane, 200 °C)

	$NH_2(CH_2)_{n-1}COOH$,[a,2] n =						$NH_2(CH_2)_{n-1}COOCH_3$,[b,h] n =					
	3	4	5	6	7	8	3	4	5	6	7	8
M + C_3H_7	1.0	1.0	1.1	1.8	0.2	2.4	0.5	0.8	2.0	1.3	1.8	1.7
-HOR		1.1	1.9									
M + C_2H_5	0.1	0.3	0.9	4.1	5.6	4.9		0.2	0.9	3.6	8.1	9.3
-HOR		1.4	2.8	1.3	1.3	0.8		1.3	0.4	0.7	0.5	0.4
M + H	14.0	29.6	26.9	24.3	49.9	64.5	41.1	24.0	29.6	57.5	61.9	71.6
$-NH_3$	0.9	18.9	14.5	4.3	0.4	0.1	0.5	47.2	38.3	10.4	1.1	0.4
$-H_2O$[c]	24.8	41.5	46.2	46.0	30.6	15.1		1.0	1.0	0.3	0.3	0.6
$-HOCH_3$[d]							24.5	17.4	16.3	14.9	16.1	7.8
$-NH_3$, HOR	1.6	1.4	0.5	7.1	2.2	1.0		1.3	1.4	3.2	2.3	1.4
-HOR, CO	0.9	0.2	0.2	2.1	0.2	0.9			1.7			
$-NH_3$, HOR, CO			1.0	4.3	2.2				1.5	2.5	2.1	0.9
M − H	0.9	1.0	0.6	1.6	1.8	2.8		0.7	0.8	0.9	1.9	3.0
$-NH_3$		0.5	1.1	0.3	0.7						0.3	
-HOR		0.7	0.9	1.0	0.9	0.6	0.9	0.4	0.3	0.4	0.3	
Misc	47.0[e]	1.0[f]					26.1[g]					
ΣI	91.2	97.6	98.6	98.2	96.0	93.1	93.6	94.3	92.2	95.7	96.7	97.1

[a] R = H. [b] R = CH_3. [c] An isobar of M + 29–46. [d] An isobar of M + 29–60. [e] (*m/e*, % ΣI) 30, 17.9; 58, 3.7; 102, 4.7. [f] (*m/e*, % ΣI) 44, 1.0. [g] 30, 33.6; 48, 6.0; 58, 7.4; 70, 0.9. [g] Registry No.—$C_3H_7NO_2$, 107-95-9; $C_4H_9NO_2$, 56-12-2; $C_5H_{11}NO_2$, 660-88-8; $C_6H_{13}NO_2$, 60-32-2; $C_7H_{15}NO_2$, 929-17-9; $C_8H_{17}NO_2$, 1002-57-9. [h] Registry No.—$C_4H_9NO_2$, 4138-35-6; $C_5H_{11}NO_2$, 3251-07-8; $C_6H_{13}NO_2$, 63984-02-1; $C_7H_{15}NO_2$, 2780-89-4; $C_8H_{17}NO_2$, 39979-08-3; $C_9H_{19}NO_2$, 59080-49-8.

Table IV. Cyclic and Acyclic α-Amino Acid Chemical Ionization Mass Spectra (Methane, 200 °C)

	$CH_3(CH_2)_{n-2}CH(NH_2)COOH$,[c] n =		$CH_2NHCH(CH_2)_{n-3}COOH$,[d] n =		
	2	3	4	5	6
M + C_3H_7	1.3	2.2	2.2	2.1	1.5
$-H_2$			0.4	0.1	0.4
$-H_2O$, CO	0.8	0.3	0.2	0.3	1.9
M + C_2H_5	1.2	2.4	1.2	2.0	2.1
$-H_2$			0.4	0.1	1.2
$-H_2O$, CO[a]	8.0	4.5	2.0	2.3	2.5
MH	20.4	6.4	63.2	59.6	35.3
$-H_2O$, CO	65.7	75.7	24.1	27.0	35.3
M − H	0.7	2.4	0.4	5.8	7.7
$-H_2O$, CO	0.8	2.8	0.2	0.2	3.1
gly[b]	0.4	2.6			
ΣI	99.2	99.3	94.3	99.2	91.0

[a] Isobaric with MH − H_2O. [b] gly = $(NH_2{=}CHCOOH)^+$. [c] Registry No.—$C_3H_7NO_2$, 56-41-7. [d] Registry No.—$C_4H_7NO_2$, 2517-04-6; $C_5H_9NO_2$, 147-85-3; $C_6H_{11}NO_2$, 3105-95-1.

Table V. Diamino Alkane, $NH_2(CH_2)_nNH_2$, Chemical Ionization Mass Spectra (Methane, 200 °C)

	Percent total ionization,[a] n =			
	3	4	5	6
M + C_3H_7				1.0
$-NH_3$	1.3	1.8	1.5	0.4
M + C_2H_5	0.06	0.07	0.1	3.5
$-NH_3$	4.1	5.1	3.5	4.1
MH	22.5	6.0	6.6	20.1
$-NH_3$	68.4	72.0	69.4	63.3
$-CH_2NH_2$	1.2	2.7	0.8	0.3
M − H	0.5	0.5	0.6	0.5
$-NH_3$	0.8	8.9	11.8	4.3
ΣI	98.8	97.0	95.2	97.5

[a] Registry No.—$C_3H_{10}N_2$, 109-76-2; $C_4H_{12}N_2$, 110-60-1; $C_5H_{14}N_2$, 462-94-2; $C_6H_{16}N_2$, 124-09-4.

spectra.[16] The ω-amino acids and esters are bifunctional molecules in which the terminal amino and carboxyl interactive reactions may occur without influence of the α-amino group. Decarboxylation is a minor process in these compounds due to the absence of the α-amino group. Elimination of water or methanol and ammonia are facilitated relative to monofunctional *n*-alkyl amines[10] and acids[11] which suggests the presence of bifunctional interactions. These elimination reactions are dependent on the number of methylene groups, *n*, separating the terminal functions $NH_2(CH_2)_nCOOR$, as shown in Figure 1. Structural dependence of the MH − H_2O and MH − $HOCH_3$ reactions is similar to that observed for the elimination of water and methanol from dicarboxylic acids and methyl esters.[11] Elimination of H_2O from the ω-amino acid methyl esters is also observed in these compounds.

Presence of the amino group increases the extent of decarboxylation in acyclic α-amino acids relative to ω-amino acids, Table IV. This is probably due to the stability of the product iminium ion.[16] Decarboxylation of cyclic α-amino acids is less facile than that observed in the acyclic α-amino acids. The extent of decarboxylation is inversely proportional to the ring size of the cyclic iminium product ion, Table IV.

Spectra of diamino alkanes have been discussed previously.[5] Table V shows the methane CI spectral data for those diamino alkanes which have amine–amine orientations related to the diamino acids of this study.

Discussion

Ion intensity data available from mass spectrometry reflect the steady state reaction products formed during the average ion residence time within the source (10^{-5} to 10^{-6} s).[1] The rate of each initial fragmentation reaction affects the intensity of the protonated molecular ions, MH^+, while fragment ion intensity is determined by the probability of competitive reactions of the parent ion and secondary reactions of the fragment ion. The transitions which occur in the diamino acids are apparent from the ion kinetic energy scan of lysine, Table VI. Losses of water and ammonia from the parent ion are observed but the minor decarboxylation transition (MH − H_2O, CO

Table VI. Ion Kinetic Energy and Metastable Chemical Ionization Scans of Lysine (Methane, 205 °C)[a]

Transition ion (m/e)	Calcd		Obsd	
	m_2/m_1	m_2^2/m_1	E_i/E	M*
MH(147) → MH − NH_3(130)	0.884	115.0	0.881	114.8
MH(147) → MH − H_2O(129)	0.878	113.2	0.881	113.8
MH − H_2O,CO(101) → MH − H_2O,CO,NH_3(84)	0.831	69.9	0.832	70.6
MH − NH_3(130) → MH − NH_3,H_2O,CO(84)	0.646	54.3	0.648	54.7

[a] Slow transitions $M_1 \rightarrow M_2$ with metastable ions M* are observed on the ion monitor at normal accelerating voltage, V, by lowering the normal electric sector voltage E to E_i when $E_1/E = M_2/M_1$. A magnet scan at V and E_i shows M* at mass M_2^2/M_1.

2.2% ΣI) was not detectable. Two secondary fragments, (MH − H_2O,CO) − NH_3 and (MH − NH_3) − H_2O,CO, were also observed. These transitions account for more than 80% of the diamino acid fragments.

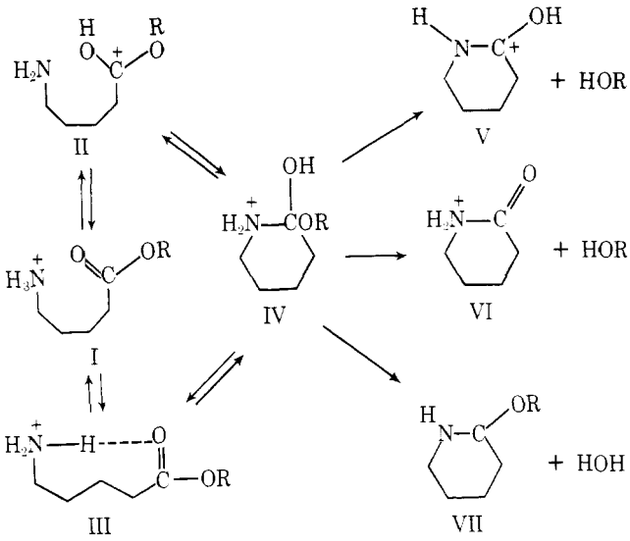
If proton transfer were directed toward the single most basic site of a polyfunctional molecule then this factor would increase the probability of fragmentation of that function. This, however, does not appear to occur in polyfunctional compounds. Although proton transfer efficiency to different functional groups is not well understood any exothermic proton transfer reaction should be facile.[20] Proton transfers from CH_5^+ and $C_2H_5^+$ (PA_{CH_4} = 128, $PA_{CH_2CH_2}$ = 158 kcal/mol) to amino and carboxyl groups ($PA_{RNH_2} \approx 217$, $PA_{RCOOH} \approx 192$ kcal/mol) of diamino acids are all exothermic so that collision probability rather than the amount of energy transfer would determine the extent of initial protonation of distal ω-amino and α-amino acid moieties.

An isolated protonated site within a polyfunctional molecule may undergo an S_Ni type elimination reaction;[3,4] however, the frequency of intramolecular interactions is competitive with unifunctional fragmentations even for very facile reactions.[5] For example: 1-decanol, MH = 0, MH − H_2O = 100%; 1,10-decanediol, MH = 59, MH − H_2O = 100%[10] and 1-acetoxydecane, MH = 68, MH − HOAc = 100%; 10-diacetoxydecane, MH = 100, MH − HOAc = 9%.[11] When amino acids are ionized with deuterated reagent gases (CD_4, D_2) extensive exchange with labile amino acid protons was observed prior to fragmentation.[16] These observations support the fact that intramolecular interactions including hydrogen bond formation and proton transfer between accessible functions may occur before fragmentation. The enthalpy of hydrogen bond formation increases the internal energy of the protonated molecular ion until collision stabilization[19] with a reagent gas molecule occurs (10^{-7} to 10^{-8} s at 1.0 Torr).[1] This internal energy may facilitate some fragmentation reactions as well as reversible proton transfer between functional groups within MH^+. Neighboring group reactions involving 3- to 7-membered transition states also occur prior to complete collision stabilization of MH^+ and localization of the proton on the thermodynamically preferred site.[5]

The thermodynamics and kinetics implicit in these observations do not support the fact that protons are localized at a single site within a molecular ion[21] before collision stabilization is complete. While this does not justify the assumption that the site of protonation is evenly distributed within the molecular ion our discussion is consistent with the fact that product ion stability rather than the site of protonation determines the extent of fragmentation of the protonated molecular ion.

Initial Reactions. Loss of water from MH^+ is a major process for 2,4- and 2,5-diamino acids (Table I). Elimination of water is not observed for simple α-amino acids[16] so the

Scheme I

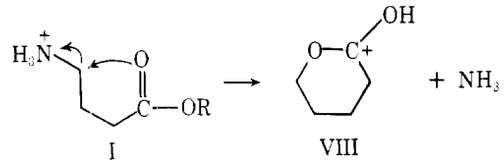


prevalence of MH − H_2O must involve participation of the ω-amino group. In order to focus on the amine–carboxyl interaction, a series of ω-amino acids and methyl esters were studied (Table III). All of these compounds show facile loss of water and/or methanol but the reaction is not critically dependent on interfunctional separation, Figure 1. When the influence of competitive reactions is considered it appears that there is a gradual decrease in MH − HOR from n = 3 to 8. This is analogous to the gradual decrease in MH − HOR observed in dicarboxylic acids and methyl esters[11] and contrasts to the highly specific elimination of ammonia from ω-amino acids and methyl esters (Table III). These contrasts may be explained if carboxyl compounds, such as 5-aminopentanoic acid, can react from the intramolecular hydrogen bonded structure[13] of Scheme I, (III → IV) as well as by direct association (II → IV) of the carbonyl protonated molecular ion. Direct association reactions are dependent on interfunctional separation and collision frequency[5] while hydrogen bond formation in the gas phase may precede fragmentation even for larger molecules in which the distal functions are separated by more than ten methylene units. For this reason elimination reactions which occur prior to collision stabilization of III, Scheme I, would not be highly dependent on the interfunctional distances between the amine and carboxyl function. If, however, no reaction pathway were accessible to the hydrogen-bonded complex, III, this exothermic bond (I → III ≈ −20 kcal/mol) would be stabilized through collision with reagent gas molecules and no further reactions would occur.

Evidence for the tetrahedral carbon intermediate[22] (IV) comes from the observation that water as well as methanol is lost from ω-amino and diamino acid methyl esters (Tables II and III). Loss of methanol from IV may occur following proton transfer from nitrogen (V) or oxygen (VI); water loss may occur only from NH proton transfer (VII). This may explain the preferential loss of methanol from the ω-amino esters. The presence of the α-amino group greatly facilitates elimination of water from the diamino acid methyl esters (Table II).

Loss of ammonia from the ω-amino acids and methyl esters is highly dependent on interfunctional separation and prominent only for n = 4 and 5, Figure 1. This structural dependence suggests a cyclization step, Scheme II, leading to formation of 5- and 6-membered lactones through direct displacement of the terminal amine. This reaction is in competition with lactam formation, Scheme I. The relative abundance of this reaction correlates with the rate of ring closure in cyclization reactions and not with differences in the site of protonation or with the stability of intramolecular

Scheme II

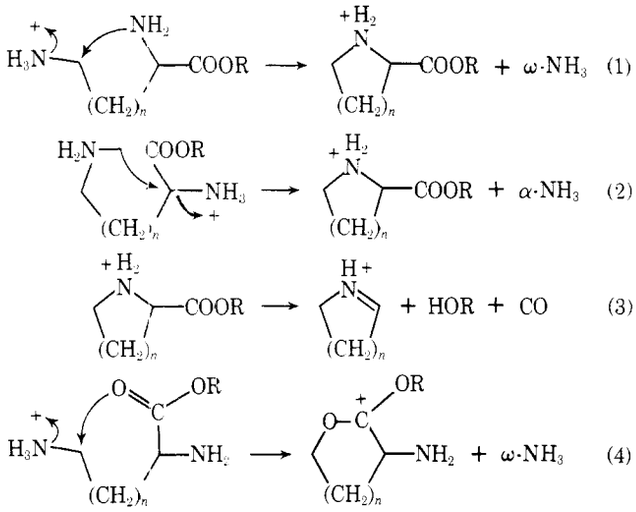


I VIII

hydrogen bonding which should be maximal in the gas phase for $n \geq 5$.[8,9]

Elimination of ammonia may also occur through an amine–amine interaction as in diamino alkanes (Table V). Loss of ammonia in compounds where $n = 3$ to 6 is faciliated relative to monofunctional amines and long-chain diamino alkanes.[5] There is apparently no favorable elimination mechanism for intramolecularly hydrogen bound diamines, diols, and dithiols[10] so that collision stabilization of these species results in stabilization of the protonated molecular ion. Facile loss of ammonia is observed in these diamino alkanes and ω-amino acids when the elimination rate is rapid relative to collision stabilization and/or competitive reactions.

Elimination of ammonia from diamino acids may proceed by the same reaction pathways that occur in the diaminoalkanes and ω-amino acids, reactions 1, 2, and 4. Displacement



(1)

(2)

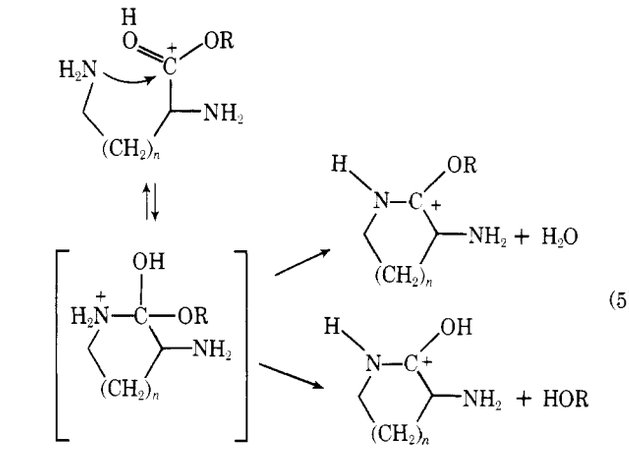
(3)

(4)

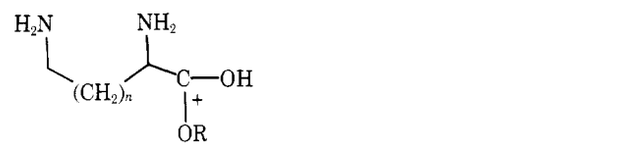
of the α-amino group, reaction 2, is reduced in the diamino acids by the influence of the carboxyl group adjacent to the α-amino function. The remaining initial diamino acid fragmentation reaction is decarboxylation, or rapid sequential loss of water and carbon monoxide, reaction 6. Alkyl carboxylic acids eliminate water (10–20% ΣI) with little subsequent loss of CO under methane CIMS conditions.[11] The presence of the α-amino function facilitates loss of CO from $(MH - H_2O)^+$ to give an iminium ion. Decarboxylation of simple amino acids, Table IV, is a facile process, $MH - H_2O,CO$ = 65–75% ΣI. The corresponding reaction of the diamino acids is less abundant, $MH - H_2O,CO$ < 25% ΣI, so that there is no reason to postulate participation of the ω-amino group in the decarboxylation reaction.[2] This reaction is a unifunctional process so that its occurrence should be independent of structural variation. Rapid competitive reactions of MH^+ would, however, decrease the relative abundance of the decarboxylation reaction.

The relative abundance of these initial reactions varies over a wide range in the 2,3- to 2,6-diamino acid series of Table I. These spectra do not directly reflect the prevalence of these reactions since some of the initial products may react further.

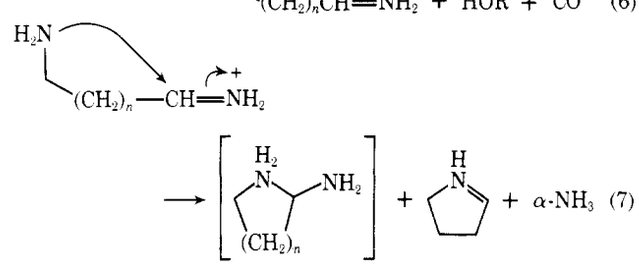
Secondary Reactions. Two of the initial diamino acid reaction products undergo subsequent fragmentation. The proposed reactions 1 and 2 lead to formation of a protonated cyclic amino acid. Protonated cyclic amino acids are found to



(5)



(6)



(7)

fragment through decarboxylation, reaction 3, where the extent of H_2O,CO loss is a function of ring size. Presumably strain and bond angle distortion of small rings destabilizes the cyclic iminium product ion of reaction 3, R = H.

Reaction 6 leads to the formation of an acylic iminium ion through an initial decarboxylation reaction. This same ion may be generated as $(M - H)^+$ from diamino alkanes, Table V. The homologous series of $NH_2(CH_2)_{n-1}CH{=}NH_2^+$ ions shows a pronounced loss of NH_3 for n = 4, 5, and 6. Higher homologues $n \geq 8$ and $n = 3$ show much less fragmentation.[5] These data, and the fact that there is no apparent driving force for elimination of ammonia from the acyclic iminium ion, suggest a cyclization step preceding loss of NH_3, as in reaction 7. Both reactions 3 and 7 yield the same cyclic iminium ion. The influence of ring size observed in the decarboxylation of protonated cyclic amino acids of reaction 3 would also operate to reduce elimination of ammonia through reaction 7 for the lower diamino acid homologues. The abundance of this $(MH - H_2O,CO,NH_3)^+$ ion is low (1 to 8% ΣI) for the 2,3- and 2,4-diamino acids, respectively.

Other initial diamino acid reactions, 4 and 5, yield either α-amino lactams, which do not fragment significantly under these conditions,[15] or α-amino lactones. By analogy to acyclic esters, these lactones should ring open on protonation, i.e., alcohol elimination, and then lose carbon monoxide. This product ion, $MH - NH_3,CO$, is not observed in any of the diamino acid spectra. Since $MH - NH_3$ is a minor ion for 2,5-diaminopentanoic acid, none of the lactone fragment ions are observed, and since this is the optimal steric arrangement for the competitive formation of the lactam, one must conclude that lactone formation is not an important process in the diamino acids. The absence of lactone formation in the diamino acids may also be due to competitive amine–amine interactions, which are possible in these compounds, reactions 1 and 2.

Table VII. Ion Abundance[a] for Initial Reaction Processes of Diamino Acids (Methane, 200 °C)

	$NH_2(CH_2)_{n-2}CH(NH_2)COOH$, n =			
	3	4	5	6
MH	30	1	1	32
$-H_2O$	1	63	50	4
$-NH_3$	31	5	38	57
$-H_2O,CO$	29	27	7	6

[a] Ion abundance calculated as percent of total MH related ions only.

The prevalence of initial reaction processes can be approximated by assigning secondary reaction products to their respective precursor ions. The significant secondary reactions follow initial loss of NH_3 and H_2O,CO from 2,5- and 2,6-diamino acids. Assignment of precursor ions for the latter compound may be made from the spectra of the α-^{15}N-labeled analogue. This spectra shows 13% of the initial NH_3 loss occurs from the α position, reaction 2, and 19% of the ammonia lost in formation of the $(MH - H_2O,CO,NH_3)^+$ ion is from the α position. This increase in the percent of α-NH_3 loss is due to the contribution of reaction 7 which involves elimination only from the α position. The maximum amount of initial decarboxylation from 2,6-diamino acid MH^+ is 9%, reaction 6. This should approximately be true for 2,5-diaminopentanoic acid if one assumes that reactions involving 5- and 6-membered cyclic products occur at a similar rate. Precursor ions may then be assigned as shown in Table VII.

Table VII shows MH^+ ion intensity to be 1% for $n = 4$ and 5 indicating very rapid initial reactions. This correlates with the high abundance of $MH - H_2O$, reaction 5, resulting in formation of 5- and 6-membered lactams. A high abundance of $MH - NH_3$ is observed for $n = 3$, 5, and 6 involving formation of 3-, 5-, and 6-membered cyclic amino acids by way of reaction 1. Decarboxylation is abundant only for $n = 3$ and 4 and is less prevalent than in simple α-amino acids. The factors which determine the abundance of $MH - H_2O,CO$ may be complex and relate to the rate of competitive processes and inductive effects in this case of 2,3-diaminopropionic acid.

Conclusion

Protonated diamino acids undergo a variety of reactions which may be correlated with bifunctional model compounds. Reactions are highly dependent on interfunctional separation and appear to involve neighboring group interactions. The diamino acids show a hierarchy of reactions with water loss more rapid than ammonia loss which is more rapid than decarboxylation. The prevalence of each cyclization reaction, as in solution, follows the order 5 > 6 > 3 > 7 for ring formation rates.

The gas phase reaction conditions give rise to a number of products, lactones and cyclic amino acids, which are not observed in solution. The most facile reaction, lactam formation, is common in solution for 2,5- and 2,6-diamino acids, however. Reaction products can be rationalized on the bases of product ion stability and neighboring group reaction rates and do not appear to correlate with preferred sites of protonation, proton affinity of functional groups, or the stability of intramolecular hydrogen bonds.

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