Pyrolysis of Phenylalanine, 3,6-Dibenzyl-2,5-piperazinedione, and Phenethylamine

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Phenylalanine and its low-temperature pyrolysis products, 3,6-dibenzyl-2,5-piperazinedione and phenethylamine, were found to undergo pyrodegradation and pyrosynthesis reactions at 650 and 850°. While the pyrolysates obtained from the three substances contained the same kinds of compounds, variations in quantities were observed. The chief constituent (650°) of the phenylalanine and dibenzylpiperazinedione pyrolysates was toluene, while that of the phenethylamine pyrolysate was styrene. Other substances found in moderate quantities were bibenzyl, biphenyl, stilbene, phenanthrene–anthracene, and benzene. Dibenzylpiperazinedione pyrolysate contained, in addition, moderate amounts of benzonitrile and phenylacetonitrile. Hydrogen cyanide was produced in all pyrolyses. At the higher pyrolysis temperatures yields of fluorene, pyrene, and phenanthrene–anthracene increased while yields of bibenzyl and stilbene diminished or fell to zero. These data suggest that both simultaneous and nonsimultaneous multiple bond cleavages are competitive in the thermally induced breakdown of phenylalanine and that at higher temperatures the simultaneous multiple processes become more prominent.

The thermolysis of complex plant materials, such as tobacco, gives rise to a wide variety of organic substances,[1] most of which are produced through the processes of pyrodegradation and pyrosynthesis. Experiments in which individual components of the plant, such as proteins[2] and amino acid,[2,3] have been pyrolyzed show that pyrolysis mixtures of similar composition are produced. The low-temperature pyrolysis of amino acids to give amines and nitriles[4-7] by decarboxylation and piperazinedione by cyclodehydration[4-8] suggests that these substances may be primary pyrolysis products at higher temperatures. The investigation described here was conducted to determine, by examination of pyrolysate composition, in what way the high-temperature pyrolysis of these intermediates contributes to the pyrolysate composition of phenylalanine.

Phenylalanine, phenethylamine, and 3,6-dibenzyl-2,5-piperazinedione (I) were pyrolyzed under the same conditions at 650 and 850° in a nitrogen atmosphere. The results are reported in Tables I, II, and III. Another possible breakdown pathway involves deamination of phenylalanine to cinnamic acid. Products arising from the thermolysis of cinnamic acid previously described by Jones and Schmeltz[9] are included for comparison.

Evidence that these probable primary pyrolysis products, or their precursors, are involved at least to some extent in the thermolytic decomposition of phenylalanine in the present experiments was provided by the isolation of the intermediates. Thus phenethylamine was isolated from 450 and 650° pyrolysis experiments in 6.9 and 0.5% yields, respectively, and 3,6-dibenzyl-2,5-piperazinedione (I) was isolated from a 850° pyrolysis experiment. Only trace quantities of cinnamic acid were found in 450 and 650° pyrolysis experiments. In spite of the relatively high stability of cinnamic acid (Jones and Schmeltz[9] recovered 42% cinnamic acid on pyrolysis at 700°) only very small amounts of total acid fraction (0.05–0.06%) were produced in the pyrolysis of phenylalanine at 450–850°. Because of these observations it appears that the deamination of phenylalanine probably represents a very minor decomposition pathway in the thermolysis of the amino acid.

The production of the gases HCN, NH_3, CO, and CO_2 during each of the pyrolyses is consistent with the formation of the possible intermediates, but this production, with the exception of HCN formation, does not allow distinction between the paths followed. The low ammonia yields observed do not provide a reliable indication of the fraction of reaction occurring by a deamination pathway (of phenylalanine or phenethylanime) since ammonia is known to dissociate almost completely to nitrogen and hydrogen at *ca.* 625°.[10]

Although CO_2 yields were expected to be relatively large in view of the ease with which amino acids decarboxylate at low temperatures, especially in the presence of radicals,[6] the low CO_2 yields do not rule out this path. Carbon dioxide is readily reduced to carbon monoxide by carbon at 1000°[11] or by hydrogen at 600–1000°.[12] In the experiments reported here, it is likely that the CO_2 is not significantly reduced by carbon, since no reduction of CO_2 was observed when the gas passed over carbonized amino acid in the pyrolysis apparatus at 850°. Some additional contribution to the CO_2 and CO yields could have arisen from the thermal decomposition of cinnamic acid, the deamination product of phenylalanine, since conjugated unsaturated acids have been reported to produce CO_2 and CO in ratio of *ca.* 1–2:1 at 500°.[13] In view of the CO_2:CO ratio observed in the present experiments and of the stability of cinnamic acid under pyrolytic conditions,[6] this path is probably a minor one. The quantities of carbon monoxide and carbon dioxide produced in the present experiments suggest that some of the carbon monoxide arises from interaction of water with carbon, carbon radicals, or alkanes.

The intermediacy of 3,6-dibenzyl-2,5-piperazinedione

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TABLE I

RELATIVE CONCENTRATIONS OF COMPONENTS[a] PRODUCED IN THE PYROLYSIS OF PHENYLALANINE AND ITS PRIMARY PYROLYSIS PRODUCTS, 3,5-DIBENZYL-2,5-PIPERAZINEDIONE, PHENETHYLAMINE, AND CINNAMIC ACID

	Phenylalanine		Dibenzylpiperazinedione[b]		Phenethylamine		Cinnamic acid[c]	
Component	650°	850°	650°	850°	650°	850°	700°	900°
Acenaphthylene						0.1		0.2
Aniline	<0.1	0.1	<0.1	0.1	<0.1	0.1		
Benzene	2.1	7.6	4.8	13.0	0.5	0.8	<0.1	0.8
Benzonitrile	0.2	1.9	1.9	5.0	0.2	3.1		
Bibenzyl	13.5		2.5		9.9			
Biphenyl	<0.1	1.6	0.4	1.7	0.1	2.4	<0.1	0.6
9,10-Dihydrophenanthrene	1.4		0.5					
Diphenylmethane	<0.1	0.7	0.4	0.2	7.5		<0.1	0.1
Ethylbenzene	3.4		1.6		4.1		0.2	0.6
Fluoranthene		0.5		2.7		0.7		<0.1
Fluorene	0.5	1.6	0.6	0.8	1.9	1.4	0.2	0.8
Indene and *m*-tolunitrile	0.2	0.9	0.6	1.1		1.2	0.7[d]	0.7[d]
Indole and cinnamonitrile	0.7	1.0	2.9	1.4	1.8	0.4		
Isoquinoline	0.9	0.6	1.7	1.6	0.4	0.1		
m-Methylbiphenyl		0.5	1.0	0.7		1.2		
p-Methylbiphenyl		1.4		0.6		0.4		
1-Methylindole	0.2				<0.1			
2- and 3-Methylindole	<0.1		0.1					
2-Methylquinoline		<0.1	<0.1	<0.1				
3-Methylquinoline		<0.1	<0.1					
α-Methylstyrene	0.3	0.1	0.1		0.3			
β-Methylstyrene					0.2			
m- and *p*-Methylstyrene				<0.1				
Naphthalene	0.2	1.2	0.9	1.9	0.1	2.5	0.3	2.5
1-Naphthonitrile				0.2				
2-Naphthonitrile						<0.1		
Phenanthrene and anthracene	5.1	9.3	7.1	9.1	5.6	6.0	0.9[e]	2.6[e]
Phenanthridine		0.1	<0.1	0.4		0.1		
Phenethylamine	0.6				13.8			
Phenylacetonitrile	0.3	0.3	3.7	0.8	0.4	0.3		
Phenylacetylene		0.5		<0.1				
1-Phenylnaphthalene			<0.1				0.8	1.5
2-Phenylnaphthalene	4.6	1.6	1.1	1.8	0.1	0.6		
Pyrene		0.5		0.1		0.1		<0.1
Quinoline	0.1	0.7	0.8	2.3	0.4	0.1		
trans-Stilbene	5.5	1.7	3.8	0.5	10.2		1.3	2.3
Styrene	8.2	7.5	6.1	1.3	19.5	0.1	21.3	26.8
Toluene	20.6	21.8	30.6	8.9	7.3	3.2	0.6	0.9
o-Toluidine				<0.1				
o-Tolunitrile		0.3	0.3	0.5		0.1		
p-Tolunitrile						0.4		
m-Xylene		0.1		<0.1				

[a] Reported in grams component produced per mole of substance pyrolyzed. [b] Values of grams/mole divided by 2. [c] Values calculated from ref 9. [d] Reported as indene only, ref 9. [e] Reported as phenanthrene only, ref 9.

TABLE II

YIELDS[a] OF GASES OBTAINED ON THE PYROLYSIS OF PHENYLALANINE, 3,6-DIBENZYL-2,5-PIPERAZINEDIONE, AND PHENETHYLAMINE

	Phenylalanine		3,6-Dibenzyl-2,5-piperazinedione		Phenethylamine	
Product	650°	850°	650°	850°	650°	850°
CO_2	3.6	5.8	8.1	12.9		
CO	*c*	98.7	39.7[b]	77.0[b]		
HCN	0.3	17.2	25.3[b]	29.5[b]	8.2	50.0
NH_3	2.7	0.3	*c*	*c*	1.2	0.5

[a] Moles of gas per mole of substance pyrolyzed × 100. [b] Moles of gas per mole of substance pyrolyzed × 50. [c] Found but not determined quantitatively.

TABLE III

WEIGHTS OF PYROLYSATES AND MAJOR FRACTIONS OF THE PYROLYSATE

Compd pyrolyzed	Temp, °C	Weight pyrolyzed, g	Weight of pyrolysate, g	Weight of neutrals, g	Weight of bases, g
Phenylalanine	650[a]	93.0	71.0	41.6	2.4
Phenylalanine	850[a]	94.0	68.0	36.9	1.3
Dibenzylpiperazinedione	650[a]	65.0	36.0	29.2	1.3
Dibenzylpiperazinedione	850[a]	41.0	24.5	13.9	1.6
Phenethylamine	650	51.7	44.6	24.2	7.4
Phenethylamine	850	36.3	27.7	11.2	0.2

[a] Trace amounts of phenols were also obtained.

provides an attractive explanation for the formation of both HCN and CO. The propensity of nitrogen heterocycles,[14-16] including piperazinedione, to form HCN is well known and in the present work considerable quantities of HCN and CO were obtained on the pyrolysis of dibenzylpiperazinedione. Possible decom-

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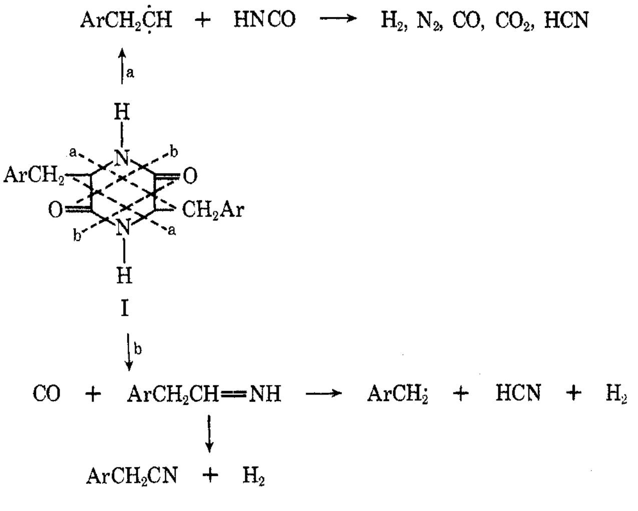
position modes of the piperazinedione I which produce HCN and CO are summarized in Scheme I.

Scheme I



Mode a produces benzylcarbene and isocyanic acid with the isocyanic acid further decomposing (500–700°) to H_2, N_2, CO_2, CO, and HCN,[17] while mode b produces carbon monoxide and phenylethylidenimine, which in turn produces phenylacetonitrile or HCN, H_2, and benzyl radical. Since the HCN yield from phenylalanine (pyrolyzed at 650°) is only 0.3% while under the same conditions the yield from piperazinedione is 25%, it is concluded that piperazinedione formation is minimal during the pyrolysis of phenylalanine. At 850° piperazinedione formation may be involved to a greater extent, but it seems more likely that at this temperature the HCN is formed from phenethylamine or its radical precursor II formed by decarboxylation. Under similar conditions (800°) trimethylamine

$$ArCH_2\dot{C}HNH_2$$

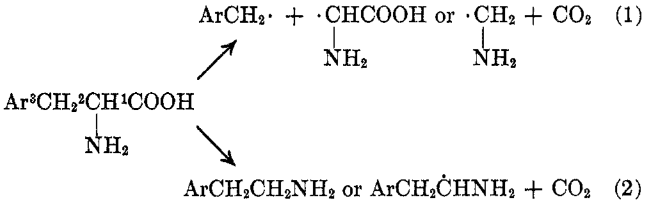
II

is converted into HCN in 98% yield.[18] The interaction of ammonia with carbon to form HCN and H_2 does not appear to be involved to any great extent in these pyrolyses, since the conversion to HCN at 800° was only 2%.[18]

The pyrolyses products observed can be explained in terms of an initial benzylic bond cleavage followed by additional competitive paths in which reactive intermediates (phenyl and benzyl radicals, carbenes) and thermally unstable molecules (styrene) are formed. The ways by which these reactive species produce pyrolysis products have been described previously.[9,19,20]

Although the pyrolysate compositions obtained from the compounds studied show qualitative similarities, the quantitative differences imply that there is a relationship between the structure of the substance pyrolyzed and the makeup of its pyrolysate. It is suggested that these quantitative differences arise from variations in reactive intermediate concentrations which in turn are related to the structure of the substance pyrolyzed.

The yields of HCN, toluene, and styrene, and the fact that amino acids undergo a facile radical-catalyzed decarboxylation,[6] suggest that phenylalanine decomposes by two competing paths: one involving a concerted or nearly concerted rupturing of bonds at positions 1 and 2 (eq 1) and the other involving decarboxylation followed by decomposition of the phenethylamine or its radical precursor (eq 2).



$$Ar^3CH_2{}^2CH(NH_2)^1COOH \longrightarrow ArCH_2\cdot + \cdot CH(NH_2)COOH \text{ or } \cdot CH_2NH_2 + CO_2 \qquad (1)$$

$$Ar^3CH_2{}^2CH(NH_2)^1COOH \longrightarrow ArCH_2CH_2NH_2 \text{ or } ArCH_2\dot{C}HNH_2 + CO_2 \qquad (2)$$

Benzyl C–C bond cleavage appears to be a major decomposition pathway in the decomposition of dibenzylpiperazinedione in view of the high yields of toluene produced. Thermal scission of the ring (Scheme I) by modes a and/or b probably also contributes to benzyl radical formation. The benzylcarbene formed in the mode a cleavage can dissociate into benzyl radical and methine or dimerize to form a dibenzylethylene and then decompose.[9] The higher yields of benzene (relative to those obtained from phenethylamine or phenylalanine) could also have arisen from the benzylcarbene by dissociation into phenyl and vinyl radicals (eq 3) or from its dimer by subsequent decomposition. This species (benzylcarbene) could also be one of the precursors of styrene (eq 4).

$$ArCH_2\dot{C}H\cdot \longrightarrow Ar\cdot + CH_2{=}CH\cdot \qquad (3)$$

$$ArCH_2\dot{C}H\cdot \xrightarrow{H\cdot} ArCH_2\dot{C}H_2 \xrightarrow{-H\cdot} ArCH{=}CH_2 \qquad (4)$$

In the pyrolysis of phenethylamine, the initial benzylic C–H and C–C cleavages result in the formation of phenethylamine radical and benzyl radical, respectively. The phenethylamine radical, in turn, eliminates amino radical, producing styrene or undergoes cleavage, producing phenylcarbene and methylamine radical.

At 850°, random bond cleavage occurs to a greater extent in the phenylalanine pyrolysis and participation of the decarboxylation intermediate becomes less important. Formation of a greater abundance of phenyl and benzyl radicals is reflected in the increases in yields of benzene, biphenyl, benzonitrile, toluene, and diphenylmethane. The pyrolyses of dibenzylpiperazinedione and phenethylamine at 850° likewise produce increased phenyl radical concentrations which are responsible for increases in yields of benzene, benzonitrile, and biphenyl. These increases in yields also may be due, in part at least, to the fact that substances formed from these radicals at 650° such as bibenzyl,[21] *trans*-stilbene,[9] and diphenylmethane[21] are not stable at 850°.

The absence of bibenzyl from the pyrolytic products of the three compounds at 850° may be attributed to the relative ease with which bibenzyl undergoes either cleavage at the carbon–carbon single bond or dehydro-

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[18] G. A. Voerkelius, *Chem.-Ztg.*, **23**, 1078, 1090 (1909); *Chem. Abstr.*, **4**, 1653 (1910).

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[21] J. W. Sweeting and J. R. Wilshire, *Aust. J. Chem.*, **15**, 89 (1962).

genation to *trans*-stilbene. The observation that the decrease in the yield of *trans*-stilbene at 850° in the phenylalanine, dibenzylpiperazinedione, and phenethylamine experiments is accompanied by an increase in the yield of phenanthrene is in accord with the observations of previous researchers that *trans*-stilbene may act as a precursor of phenanthrene at high temperatures.[9]

Consistent with the low yield of styrene from phenethylamine and dibenzylpiperazinedione at 850° is the production of fluoranthene and the higher yield of 2-phenylnaphthalene as compared with the yield at 650°. At 850°, styryl radicals may be more abundantly formed and formation of $C_6H_5CH{=}CH(C_6H_5)\dot{C}CH_2$ from two styryl radicals can explain the formation of 2-phenylnaphthalene, especially since the high yield of 2-phenylnaphthalene cannot be accounted for by the reaction of naphthyl radicals and phenyl radicals.[22] On the other hand, formation of a distyryl type intermediate, $C_6H_5\dot{C}HCH{=}CH\dot{C}HC_6H_5$, can give rise to 1-phenylnaphthalene, which has been shown to cyclodehydrogenate to fluoranthene.[22]

The formation of acenaphthylene, fluoranthene, and pyrene at 850° only and the higher yield of naphthalene at 850° as compared with the yield at 650° (in all three cases) are consistent with the decrease in the yield of styrene or of compounds that could give rise to styrene upon pyrolysis (such as bibenzyl[21] and *trans*-stilbene[9]), with the mechanisms of formation of these compounds from styrene moieties,[19] and with the evident increase in the production of gases made up of two carbon fragments at 850° as compared with 650°. The absence of acenaphthylene, fluoranthene, and pyrene from the products at 650° is in agreement with earlier observations that these compounds are not formed in the pyrolysis of styrene at 700°.[3]

Experimental Section

Ultraviolet spectra were measured in cyclohexane using a Perkin-Elmer Model 202 spectrophotometer, and infrared spectra were measured in chloroform or carbon tetrachloride using a Beckman IR-8 spectrophotometer equipped with a mirror beam condenser. Glpc retention times were measured and separation of the pyrolysate constituents was carried out on an F & M Model 810 gas chromatograph.

Materials.—Phenylalanine and phenethylamine were commercially available samples and were used as received. 3,6-Dibenzyl-2,5-piperazinedione was prepared from DL-phenylalanine by the method of Akimova[23] and recrystallized from dimethylformamide after washing with ethanol, mp 297–299° (uncorrected). The pure cis and trans isomers are reported[24] to melt at 311–312 and 289–291°, respectively. The product gave a satisfactory elemental analysis, a correct molecular weight (mass spectrum), and an infrared spectrum consistent with the piperazinedione structure.

Pyrolyses.—The pyrolyses were carried out in the apparatus previously described[15] using 20–30 ml of Berl saddles and a nitrogen flow of 100 ml/min for phenylalanine and dibenzylpiperazinedione pyrolyses and of 60 ml/min for phenethylamine pyrolyses.

The liquid products were collected in two traps, each of which was cooled in a Dry Ice–chloroform–carbon tetrachloride mixture. Gases which were not condensed by these traps were examined by infrared spectroscopy using a 100-mm gas cell. Identifications were based upon comparisons of the absorption bands observed with those reported in the literature[25] and with those obtained from authentic samples.

Quantitative gas analyses were carried out in separate experiments in which the compounds under investigation (10–20 g) were pyrolyzed under the conditions previously described. The gases were directed through a series of traps. Carbon dioxide and hydrogen cyanide were absorbed in 2 *M* KOH and ammonia in 3.5 *M* H_2SO_4. Carbonate was precipitated with barium nitrate solution and determined gravimetrically, and checked by titration with hydrochloric acid to a methyl red end point. Cyanide was determined on the filtrate from the carbonate determination using the Liebig–Deniges method.[26] The ammonia collected in the sulfuric acid trap was distilled into boric acid solution after basification and titrated potentiometrically with hydrochloric acid. The yield of carbon monoxide relative to carbon dioxide was determined by gas chromatography using a 4 ft × 0.25 in. silica gel (100–120 mesh) column at 25°. The moles of carbon monoxide produced was calculated from electronic integration data after correction for thermal conductivity differences and from the moles of carbon dioxide found by gravimetric analysis. The data are summarized in Table II.

The pyrolysate was heated in a water bath at 100° (the gases evolved were analyzed by infrared spectroscopy) and the distillate was collected. The residue was extracted with ether and the ether-soluble material was separated into acidic, neutral, and basic fractions by extraction with successive portions of 5% HCl and 5% NaOH, each saturated with NaCl. The neutral fraction was further separated into "volatile" and "nonvolatile" neutrals by distillation under reduced pressure (0.1 mm; maximum bath temperature, 150°). The compounds pyrolyzed along with the weights of the major fractions obtained are reported in Table III.

Separation and Identification of Components.—Components of the neutral and basic fractions were separated by glpc using a 30 ft × 0.375 in. 20% Apiezon L column (Anakrom 50/60 U) heated at 75° for 8 min and then programmed at 2°/min to 280°. The final temperature was maintained for an extended period to ensure elution of high-boiling components. In some experiments neutrals were also separated on a 20 ft × 0.375 in. 20% polyphenyl ether column and on a 30 ft × 0.375 in. 20% Apiezon W column. The bases were also separated on a 20 ft × 0.375 in. 20% SE-30 column.

Identifications of components are based on comparisons of glpc retention times, ultraviolet spectra, and infrared spectra with those obtained from authentic samples. Estimation of relative abundances of constituents are based on area per cent values obtained from glpc. The results are reported in Table I.

Registry No.—Phenylalanine, 63-91-2; 3,6-dibenzyl-2,5-piperazinedione, 2308-61-4; phenethylamine, 64-04-0; cinnamic acid, 621-82-9.

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