The chloroform extract was dried over magnesium sulfate and evaporated to yield a white solid. The solid was dissolved in a few milliliters of chloroform and 50 ml of ethanol was added. After a few seconds, crystallization occurred giving 0.95 g (69%) of dienes **11** and **12** (about 2:1 by nmr). Evaporation of the mother liquor gave an oily solid. This solid was dissolved in a few drops of chloroform and 10 ml of ether was added. After standing several hours, a white crystalline solid was obtained. Recrystallization from chloroform–ether gave 0.18 g of pure **14**: mp 131–132.5°; mass spectrometric mol wt 436; infrared ($CHCl_3$), hydroxyl absorbance at 2.88 μ; acetate (mass spectrometric mol wt 478).

Anal. Calcd for $C_{20}H_{24}N_2O_5S_2$: C, 55.02; H, 5.54; N, 6.41. Found: C, 54.90; H, 5.62; N, 6.70.

Reduction of 17 with Lithium Aluminum Hydride.—A solution of 416 mg of **3** in 25 ml of 1,2-dimethoxyethane was treated with an excess of lithium aluminum hydride and the mixture was heated at reflux overnight. The excess reagent was decomposed by the careful addition of a 10:1 mixture of tetrahydrofuran and water. The mixture was then diluted with 200 ml of water and extracted with chloroform. The chloroform extract was dried over magnesium sulfate. Removal of the solvent gave a colorless oily solid. This material was treated with a solution of 1 g of *p*-toluenesulfonyl chloride in 20 ml of pyridine and the mixture was heated at reflux for 10 min. The reaction mixture was diluted with 20 ml of water and 50 ml of concentrated hydrochloric acid was added. The resulting suspension was extracted with chloroform, the chloroform extract was dried over magnesium sulfate, and the filtrate was evaporated to dryness to leave a brown solid. Recrystallization of this solid from methanol–chloroform gave 236 mg of **19**: mp 227–228°; nmr ($CDCl_3$), eight aromatic protons H_A at τ 2.34 and H_B at 2.73 (J_{AB} = 8.5 cps), two-proton multiplet at 5.58, four-proton multiplet at 6.60, six-proton singlet at 7.58, six-proton doublet at 9.08 (J = 7 cps); mass spectrum [*m/e* (%)], 422 (P, 6.2), 407 (0.4), 267 (100), 252 (3.8), 212 (4), 155 (15), 91 (47), 84 (24), 70 (11.5), 56 (37).

Anal. Calcd for $C_{20}H_{26}N_2S_2O_4$: C, 56.84; H, 6.20; N, 6.63. Found: C, 56.61; H, 5.81; N, 6.68.

The nmr and infrared spectra of **19** were identical with those of an authentic sample which was prepared from *trans*-2,5-dimethylpiperazine.

Reduction of 18 with Lithium Aluminum Hydride.—A solution of 1.5 g of **18** in 50 ml of tetrahydrofuran was treated with an excess of lithium aluminum hydride and refluxed for 2 hr. Excess reagent was decomposed by addition of a 10:1 mixture of tetrahydrofuran and water. The mixture was acidified with concentrated hydrochloric acid and extracted with chloroform. The chloroform extract was dried over magnesium sulfate and filtered, and the filtrate was evaporated *in vacuo* to yield a white solid. A 400-mg portion of this material was chromatographed on 150 g of grade III neutral alumina. Elution with a mixture of benzene and ethyl acetate (20:1) yielded two compounds.

The first compound was recrystallized from chloroform–methanol to give 1,5-bis(*p*-toluenesulfonyl)-6-chloro-2-methyl-1,4-diazepine: mp 190–191.5°; nmr ($CDCl_3$), eight-proton multiplet at τ 2.25, eight-proton multiplet from 5.5 to 7.5, six-proton singlet at 7.61, three-proton doublet at 8.98 (J = 7 cps); mass spectrum [*m/e* (%)], 456 (P, 0.5), 420 (6), 301 (100), 265 (11), 198 (19), 155 (32), 91 (79).

Anal. Calcd for $C_{20}H_{25}N_2S_2O_4Cl$: C, 52.56; H, 5.51; N, 6.13. Found: C, 52.57; H, 5.47; N, 6.28.

The second compound was recrystallized from methanol–chloroform to give 84 mg of pure **20**: mp 150–151°; nmr ($CDCl_3$), eight-proton multiplet at τ 2.6, one-proton multiplet at 5.8, six-proton multiplet at 6.7, six-proton singlet at 7.6, two-proton multiplet at 8.2, three-proton doublet at 8.96 (J = 7 cps); mass spectrum [*m/e* (%)], 422 (P, 0.1), 267 (93), 252 (1), 212 (2), 155 (22), 91 (91), 84 (15), 70 (100), 56 (23.5).

Anal. Calcd for $C_{20}H_{26}N_2S_2O_4$: C, 56.84; H, 6.20; N, 6.63. Found: C, 56.30; H, 5.88; N, 6.66.

Registry No.—**1**, 6204-13-3; **2**, 5997-54-6; **5**, 13116-96-6; **6**, 13116-97-7; **8**, 13116-98-8; **9**, 13116-99-9; **11**, 13117-00-5; **12**, 13117-01-6; **14**, 13117-02-7; **15**, 13199-99-0; **16**, 13143-65-2; **17**, 13117-03-8; **18**, 13117-04-9; **19**, 13117-05-0; **20**, 13117-06-1; 3,7-bis(*p*-toluenesulfonyl)-3,7-diaza-1,5-dimethyl-1,9-oxabicyclo[3.3.1]nonane, 13117-07-2; 1,5-bis(*p*-toluenesulfonyl)-6-chloro-2-methyl-1,4-diazepine, 13117-08-3.

Acknowledgment.—This investigation was supported in part by a research grant (CA-07917-02) from the National Cancer Institute, U. S. Public Health Service.

The Conversion of Imidazo[1,5-*a*]pyridines into 3-(2-Pyridyl)-1,2,4-oxadiazoles

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Received March 20, 1967

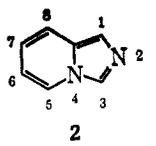
Imidazo[1,5-*a*]pyridine (**2**) and its 3-methyl and 3-phenyl derivatives rearrange, upon treatment with nitrous acid, to 3-(2-pyridyl)-1,2,4-oxadiazole (**4**) and its 5-methyl (**5**) and 5-phenyl (**6**) derivatives, respectively. Pyrolysis, alkaline hydrolysis, as well as mass, ultraviolet, and nuclear magnetic resonance spectral studies were used to establish the structures of the rearrangement products. Compounds **4** and **5** were prepared by unequivocal syntheses.

Electrophilic substitution reactions in polyazaindenes (**1**) have been the subject of several recent publications from different laboratories.[1-8]

These studies have shown that, generally, electrophilic substitution occurs in either the 3, or in the 1 position, or both depending upon the location of the nonbridge nitrogen atom or atoms.

1

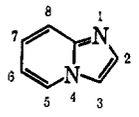
Imidazo[1,5-*a*]pyridine (**2**) has been acetylated,[5] for example, at position 1 and brominated to form a 1,3-



2

dibromo derivative exclusively.[6] Imidazo[1,2-*a*]pyridine (**3**), on the other hand, forms 3-bromo,[7] 3-nitro, as well as 3-nitroso[8] derivatives.

(1) Th. Pyl and W. Baufeld, *Ann.*, **699**, 112 (1966).
(2) W. W. Paudler and J. E. Kuder, *J. Org. Chem.*, **31**, 809 (1966).
(3) J. G. Lombardino, *ibid.*, **30**, 403 (1965).
(4) J. P. Paolini and R. K. Robbins, *ibid.*, **30**, 4085 (1965).
(5) J. D. Bower and G. R. Ramage, *J. Chem. Soc.*, 2834 (1955).
(6) W. W. Paudler and J. E. Kuder, unpublished results.
(7) W. W. Paudler and H. L. Blewitt, *J. Org. Chem.*, **30**, 4081 (1965).
(8) H. L. Blewitt, Ph.D. Thesis, Ohio University, 1965, Athens, Ohio.



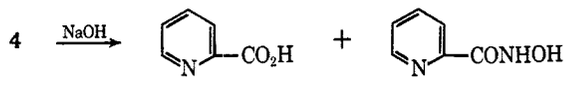
3

Nitrosation of imidazo[1,5-*a*]pyridine (**2**) yields a white crystalline solid, $C_7H_5N_3O$ (**4**). The molecular weight of this compound, both osmometrically (151), as well as mass spectrometrically (*m/e* 147), shows that the material is monomeric. The fact that this compound is colorless, and not green, as would be expected (3-nitrosoimidazo[1,2-*a*]pyridine is a dark green solid,[8] for example), implies that it is not a nitroso derivative of imidazo[1,5-*a*]pyridine. This is further substantiated by the absence of typical nitroso-group absorption bands[9] in the infrared spectrum of the compound.

Nitrosation of 3-methylimidazo[1,5-*a*]pyridine and of 3-phenylimidazo[1,5-*a*]pyridine afford similar "nitroso derivatives," $C_8H_7N_3O$ (**5**) and $C_{13}H_9N_3O$ (**6**), respectively, with properties closely analogous to those of compound **4** (*cf.* Experimental Section).

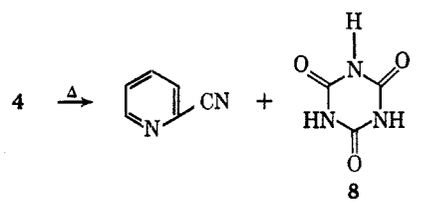
The mass spectrum of compound **4** shows the loss of HCN (P − 27) from the parent ion, a fact which suggests the presence of an aromatic nitrogen atom bonded to a sp^2 carbon atom bearing, probably, a hydrogen atom. Another large fragment ion is obtained from the loss of HCNO from the parent ion or from the loss of an oxygen atom from the P − HCN fragment to afford a *m/e* 104 species. From recent studies in our laboratories dealing with the mass spectral cleavage patterns of pyridine derivatives, it became clear that the mass spectrum of compound **4** below 105 mass units is typically that of a monosubstituted pyridine. The *m/e* 104 fragment might well be a cyanopyridine ion, formed by electron impact on the parent ion of compound **4**. The mass spectrum of 2-cyanopyridine (*cf.* Table I) is, in fact, essentially superimposable upon that of compound **4** in the mass range of 28 to 104. It thus appears that compound **4** contains a pyridine ring, or a structural moiety which affords such a ring upon electron impact.

The results of a base hydrolysis of compound **4** are of further aid in the establishment of its structure. The hydrolysis affords picolinic acid and picolinohydroxamic acid (**7**).



7

When compound **4** is heated above its melting point (111–112°), a strongly exothermic reaction takes place at 140°, with the evolution of 2-cyanopyridine and the formation of cyanuric acid.



8

(9) B. G. Gowenlock and W. Luettke, *Quart. Rev.*, **12**, 321 (1958).

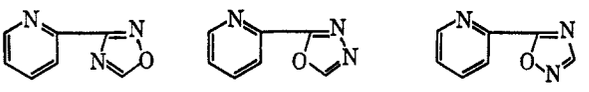
TABLE I

MASS SPECTRAL DATA

m/e[a]	4	5	2-(2-Pyridyl)-1,3,4-oxadiazole	2-Cyanopyridine
162	...	8.8	...	...
161	...	81 (P^+)	...	...
148	9.6	...	8.9	...
147	100 (P^+)	...	100 (P^+)	...
121	6	7	...	...
120	66	100	...	...
117	13	...	...	...
106	...	...	16	...
105	10	10	...	8.7
104	71	5	49	100 (P^+)
103	...	...	...	5
92	6	...	5	...
91	7	...	36	...
90	40	27	...	...
79	7	8	16	17
78	65	50	76	64
77	38	7	25	21
76	18	6	10	14
75	13	...	17	...
65	14	8	9	...
64	28	15	37	8
63	22	12	15	...
62	10	6	7	...
61	6	...	...	...
53	11	...	7	12
52	35	16	29	23
51	73	31	47	39
50	46	14	28	44
49	9	...	7	10
44	5	...	...	11
43	24	30	...	...
42	8	...	...	...
41	...	...	10	...
40	6	...	11	21
39	31	15	17	9
38	23	9	15	11
37	21	6	12	10
30	9	6	...	...
29	21	...	14	14
27	19	14	13	10
26	26	9	16	25

[a] Only peaks of 5% or larger relative intensity are listed.

It is well known that cyanuric acid is formed in an exothermic reaction from cyanic acid.[10] Thus, it seems reasonable that the cyanuric acid is formed from cyanic acid or one of its tautomers. These data are consistent with any one of the following three possible structures (R = H).[11]



9 10 11

Compounds **9** (R = CH_3) and **10** (R = H) are known substances, but the melting point of compound **8** does not appear to be reported.[12] The melting point of compound **10** is reported to be 115°.[13] This melting

(10) P. Klason, *J. Prakt. Chem.*, **33**, 129 (1886).

(11) C. Ainsworth [*J. Heterocyclic Chem.*, **3**, 470 (1966)] has recently described the thermal fragmentation of 3-phenyl-1,2,4-oxadiazole which yields cyanuric acid and benzonitrile.

(12) C. Cogrossi, *Chem. Ind.* (Milan), **48**, 481 (1966); *Chem. Abstr.*, **65**, 5333*e* (1966).

(13) C. Ainsworth, *J. Am. Chem. Soc.*, **77**, 1148 (1955).

point is quite close to that of compound **4**, but the mixture melting point was depressed. Thus, compound **4** is not the oxadiazole **10** (R = H). It is of interest that the mass spectra and the ultraviolet spectra of compounds **4** and **10** are essentially superimposable. The nuclear magnetic resonance (nmr) spectra of these two compounds are very similar, the only difference being in the chemical shift of a one-proton singlet (*cf.* Table II). These spectral similarities suggest very

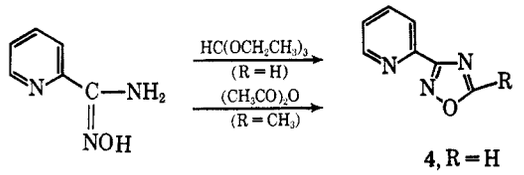
TABLE II

NMR SPECTRAL DATA OF SOME PYRIDYLOXADIAZOLES[a]

	4	5	10
H_5	0.97	...	1.25
$H_{3'}$	1.83	1.90	1.77
$H_{4'}$	2.13	2.17	2.12
$H_{5'}$	2.57	2.60	2.53
$H_{6'}$	1.03	1.22	1.27
5-CH_3	...	7.32	...
$J_{3'4'}$	7.8	7.8	7.8
$J_{3'5'}$	1.6	1.6	1.3
$J_{3'6'}$	1.0	1.0	1.0
$J_{4'5'}$	7.5	7.3	7.2
$J_{4'6'}$	1.8	1.8	1.8
$J_{5'6'}$	4.8	4.7	4.8

[a] Solutions are 2 *M* in deuteriochloroform. Chemical shifts are given in τ units, coupling constants in Hertz.

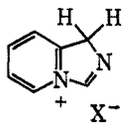
strongly that compounds **4**, **5**, and **6** are indeed substituted oxadiazoles such as **9** or **11**. Mechanistically, the oxadiazole **9** is preferred however. The structures of compounds **4** and **5**, and by analogy of compound **6**, were finally proven by their unequivocal syntheses as shown below.



4, R = H
5, R = CH_3

We can now write the reaction sequence shown in Scheme I to account for this transformation.

The involvement of compound **12** is tentatively suggested by the observation[14] that these polyazaindenes possess a great tendency to form indene-type structures such as **13**, in acid solution.

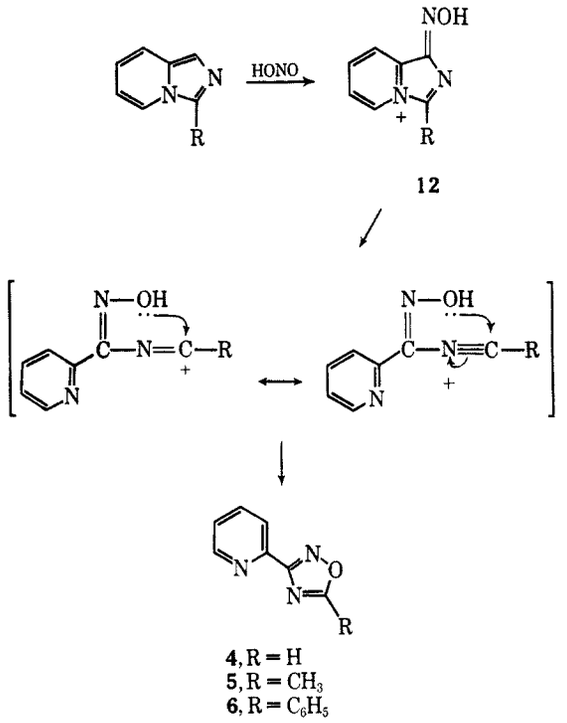


13

Experimental Section[15]

Nitrosation of Imidazo[1,5-*a*]pyridine.—To a stirred solution of 1.77 g (15.0 mmoles) of imidazo[1,5-*a*]pyridine[5] (**2**) in 45 ml of 4 *N* hydrochloric acid at 0–5° was added, over a 30-min period, a solution of 7.5 g of sodium nitrite in 22 ml of water. The reaction mixture was allowed to stand overnight in the refrigerator and the reaction mixture made slightly basic (pH 9) with sodium

SCHEME I



bicarbonate. The basic solution was extracted with six 100-ml portions of chloroform. The dried (anhydrous magnesium sulfate chloroform extracts were evaporated to dryness. The remaining pale yellow solid (mp 104–108°) weighed 1.87 g. The crude product was purified by sublimation and recrystallization from acetone–cyclohexane to yield 1.54 g (70% of theory) of white needles of compound **4**: mp 111–112°; λ_{max} 270 mμ (log ϵ 3.60), 226 mμ (log ϵ 3.87).

Anal. Calcd for $C_7H_5N_3O$: C, 57.14; H, 3.52; N, 28.56; mol wt, 147. Found: C, 56.96; H, 3.54; N, 28.45; mol wt (osmometry), 151; mol wt (mass spectrometry), 147.

Nitrosation of 3-Methylimidazo[1,5-*a*]pyridine.—3-Methylimidazo[1,5-*a*]pyridine[5] (1.04 g, 7.9 mmoles) was treated in the same manner as above to yield 1.04 g (6.5 mmoles, 82%) of white crystalline compound **5**: mp 88–89°; $\lambda_{max}^{CH_3OH}$ 270 mμ (log ϵ 3.68), 226 mμ (log ϵ 3.93).

Anal. Calcd for $C_8H_7N_3O$: C, 59.61; H, 4.37; N, 26.07; mol wt, 161. Found: C, 59.89; H, 4.61; N, 26.52; mol wt (osmometry), 164; mol wt (mass spectrometry), 161.

Nitrosation of 3-Phenylimidazo[1,5-*a*]pyridine.—3-Phenylimidazo[1,5-*a*]pyridine[5] (0.45 g, 2.3 mmoles) treated in the above manner yielded 0.39 g (1.7 mmoles, 75%) of white crystalline compound **6**, mp 128.5–129.5°.

Anal. Calcd for $C_{13}H_9N_3O$: C, 69.94; H, 4.06; N, 18.82. Found: C, 69.62; H, 3.89; N, 18.74.

Basic Hydrolysis of 4.—Compound **4** (0.211 g, 1.4 mmoles) was refluxed for 24 hr with 10 ml of 10% aqueous sodium hydroxide. The basic solution was extracted with four 100-ml portions of chloroform. The dried (anhydrous magnesium sulfate chloroform extract was evaporated to dryness to leave 0.011 g of a white solid, mp 117–118°. This compound is identical with the known picolinohydroxamic acid,[16] mp 120°. The major mass spectral fragments are found at *m/e* 138, 121, 104, and 78.

The basic solution was acidified with concentrated hydrochloric acid and extracted with chloroform. The chloroform solution was dried (anhydrous magnesium sulfate) and evaporated to dryness to leave 9 mg of a light brown solid (mp 133–134°). The infrared spectrum of this compound is identical with that of an authentic sample of picolinic acid.

Pyrolysis of 4.—Pyrolysis of 253 mg (1.72 mmoles) of nitrosation product **4** was accomplished by slowly heating the material to 140°. At this temperature a strongly exothermic reaction took place with the formation of a white solid and a pale yellow oil. The reaction product was washed several times with

(14) W. L. F. Armarego, *J. Chem. Soc., Sect. B*, 191 (1966).

(15) Melting points are corrected. Elemental analyses were by Mrs. S. De Boer of this department. Nmr spectra were obtained with a Varian A-60 instrument; infrared spectra were measured with a Perkin-Elmer 237; ultraviolet spectra were measured with a Cary 14; mass spectra were obtained with a Hitachi Perkin-Elmer RMU-6E.

(16) B. E. Hackley, R. Plapinger, M. Stolberg, and T. Wagner-Jauregg, *J. Am. Chem. Soc.*, **77**, 3651 (1955).

chloroform; then the washings were combined and evaporated to dryness leaving a pale yellow oil (86 mg, 0.83 mmole). The infrared spectrum of this material was completely superimposable upon that of an authentic sample of 2-cyanopyridine.

The solid residue (63 mg), which was neither soluble in hexane, chloroform, nor water, did not melt below 310°. The compound was identified as cyanuric acid (**8**) by a comparison of its infrared spectrum with than of an authentic sample.[17]

2-(2-Pyridyl)-1,3,4-oxadiazole.—This compound was prepared by the method of Ainsworth.[18] Recrystallized from ethyl acetate, it had mp 117.5–118.5° (lit.[18] mp 115°); $\lambda_{max}^{CH_3OH}$ 273 mμ (log ε 3.56), 237 mμ (log ε 3.75).

3-(2-Pyridyl)-1,2,4-oxadiazole.—2-Pyridineamidoxime, mp 117.5°[18] (0.60 g, 4.4 mmoles), was treated with 5 ml of ethyl orthoformate according to the general procedure of Ainsworth.[19] The product after vacuum distillation and recrystallization from acetone–cyclohexane was obtained as white needles, mp 109–110°, yield 0.25 g (1.7 mmoles, 39%). The infrared spectrum of the product was superimposable on that of compound **4**.

5-Methyl-3-(2-pyridyl)-1,2,4-oxadiazole.—2-Pyridineamidoxime[18] (1.42 g, 10.4 mmoles) was refluxed for 10 min with 7 ml of acetic anhydride. The reaction mixture was allowed to cool and the excess acetic anhydride decomposed with ice and ammonium hydroxide. The reaction mixture was then made basic (pH 11) with 10% aqueous sodium hydroxide. This basic solution was extracted with five 50-ml portions of chloroform. The dried (anhydrous magnesium sulfate) solution was evaporated to dryness to yield a brown solid. This solid was purified by chromatography on grade III neutral alumina, to afford 1.33 g (8.3 mmoles, 79%) of 5-methyl-3-(2-pyridyl)-1,2,4-oxadiazole, mp 87–88.5°. A mixture melting point of this product with compound **5** was not depressed (mp 88–89°). The infrared spectra of these two compounds were completely superimposable, as are their nmr and mass spectra.

Registry No.—**4**, 13389-59-8; **5**, 10350-68-2; **6**, 13389-61-2; **10**, 13428-22-3.

(17) Sadtler Infrared Spectra Catalog, Spectrum No. 12554.
(18) E. Bernasek, *J. Org. Chem.*, **22**, 1263 (1957).
(19) C. Ainsworth, W. E. Bunting, J. Davenport, M. E. Callender, and M. C. McCowen, *J. Med. Chem.*, **10**, 208 (1967).

Pyrolysis of Aromatic Azines[1]

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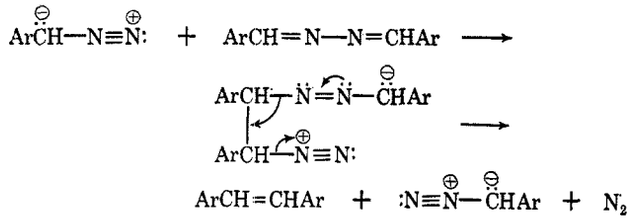
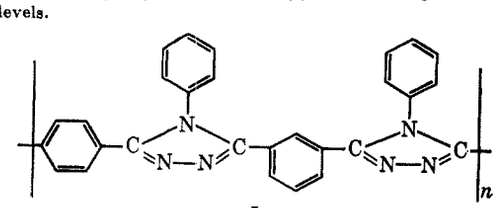
Received January 9, 1967

The pyrolysis of benzal azine to stilbene and nitrogen *via* an aryldiazomethane mechanism has been reported. The observation that benzophenone azine gave no tetraphenylethylene and only a trace of nitrogen prompted an investigation of the differences between aldazine and ketazine pyrolysis mechanisms. Benzophenone azine decomposes by a free-radical process at 375–500° to afford principally benzhydrylidenimine, benzonitrile, and 6-phenylphenanthridine accompanied by lesser quantities of benzene, biphenyl, diphenylmethane, and benzhydrylideneaniline. Details of the mechanism proposed will be discussed. Failure of the aryldiazomethane moiety to participate is attributed to steric effects. The large quantity of benzhydrylidenimine formed is noteworthy, as the only source of hydrogen present is aromatic. Because aldazines and the ketazine pyrolyze so differently, the "mixed" azine, benzhydrylidene–benzylidene azine, was investigated. Identification of the pyrolysis products revealed that both the molecular and free-radical mechanisms were participating. Analysis of the data showed that in this case the aryldiazomethane mechanism proceeds *via* diphenyldiazomethane rather than phenyldiazomethane.

Few references to the pyrolysis of azines have appeared in the literature. While an earlier study by Howard, *et al.*,[2] was incomplete, the more recent work by Zimmerman and Somasekhara[3] dealing with aldazine pyrolysis was definitive. The latter workers demonstrated that aldazines decompose thermally by the following mechanism which involves participation of an aryldiazomethane intermediate. Nitrogen is not merely "split out". It was expected, then,



(1) Presented at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966. This work was undertaken as part of a study to determine the reason for failure of fibers and films of poly-3,5-(*m*,*p*-phenylene)-4-phenyl-1,2,4-triazole (I) to meet expected thermostability levels.



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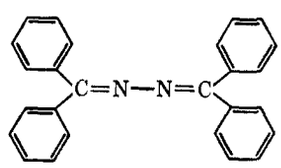
that tetraphenylethylene would be observed as a major product from the pyrolysis of benzophenone azine (II) in analogy to the formation of stilbene from



II

benzal azine. Examination of the gas chromatogram of the benzophenone azine pyrolysate from an experiment conducted at 476° (Figure 1) failed to show the presence of any significant quantity of tetraphenylethylene, while only a trace peak attributable to nitrogen was observed. Clearly, reaction was not occurring according to the scheme advocated for aldazine pyrolysis.

The major products of the flash pyrolysis of benzophenone azine over the temperature range 375–500° are benzhydrylidenimine (III), benzonitrile (IV), and 6-phenylphenanthridine (V), together with lesser quantities of benzene and benzhydrylideneaniline and traces of biphenyl, diphenylmethane, and nitrogen. Identification of these products was made by gas

(2) L. B. Howard, G. E. Hilbert, R. Wiebe, and V. L. Gaddy, *J. Am. Chem. Soc.*, **54**, 3628 (1932).
(3) H. E. Zimmerman and S. Somasekhara, *ibid.*, **82**, 5865 (1960).