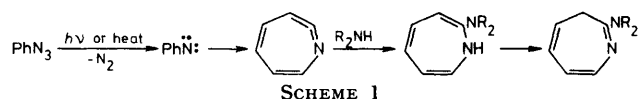


Photolysis and Thermolysis of Phenyl Azide in Acetic Acid. Trapping of 1-Azacyclohepta-1,2,4,6-tetraene and Nucleophilic Aromatic Substitution

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Photolysis and thermolysis of phenyl azide in acetic acid yielded 1*H*-azepin-2(3*H*)-one (4), 2-methylbenzoxazole (15), 2- and 4-acetamidophenyl acetates (16) and (12), 2- and 4-acetamidophenols (14) and (13), acetanilide, and azobenzene. Addition of ethanol to the system caused a linear decrease in the yield of (4) and a more remarkable decrease in total yield for the *para*-products than that for the *ortho*-products to give 2- and 4-acetamidophenyl ethyl ethers (9) and (8). Photolysis of the azide in ethanol in the presence of phenol afforded 2-phenoxy-3*H*-azepine (5) and aniline, but no 2- and 4-phenetidines. The yield of compounds (4) and (12)–(16) was independent of the presence of penta-1,3-diene (0.01 M), and somewhat decreased by an addition of bromobenzene. The rate of decomposition of azide in acetic acid was not accelerated as compared with that in 1,4-dioxan, and the activation parameters varied little in the two solvents. The results suggest that 1-azacyclohepta-1,2,4,6-tetraene (1) formed *via* singlet phenylnitrene or *via* singlet excited phenyl azide is trapped by acetic acid or phenol to give (4) or (5), and that a resonance-stabilized ion (3) neighbouring acetate anion is formed by an attack of the singlet nitrene on acetic acid to give aromatic nucleophilic substitution.

ARYL AZIDES undergo ring-expansion to azepines on decomposition in nucleophilic solvent, amine,^{1–4} or in the presence of methoxide ion.^{5,6} It has been reported that the reaction proceeds *via* nucleophilic attack of an intermediate benzazirine, a valence tautomer of initially formed singlet phenylnitrene. However, Chapman *et al.*^{7,8} have recently reported the spectroscopic observation that it is 1-azacyclohepta-1,2,4,6-tetraene (1) not the azirine which reacts with nucleophiles (Scheme 1).

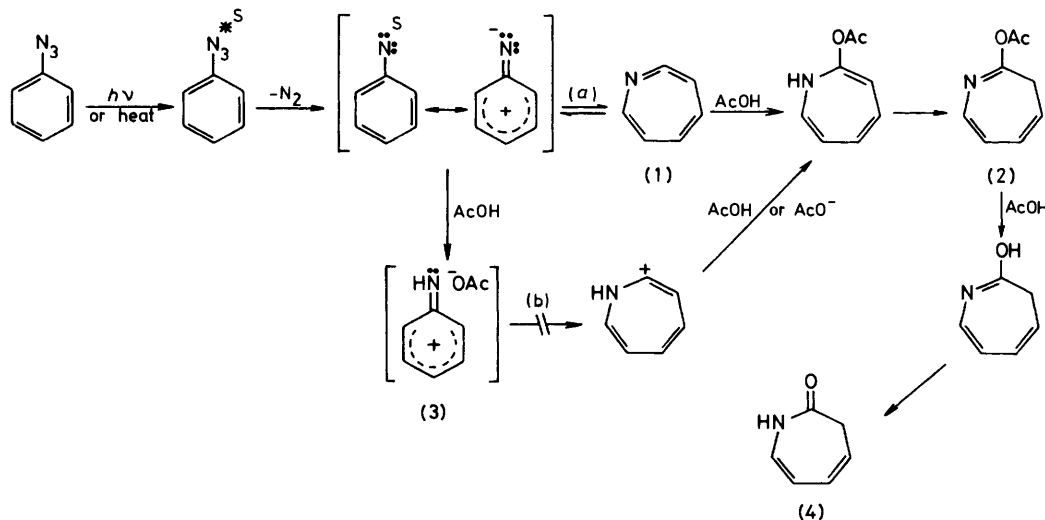


Sulphur and oxygen nucleophiles (hydrogen sulphide,² methanol,⁹ or diethyl ether²) give only modest yields of azepines except in the photolysis in methanol of aryl azides bearing an *o*-carbonyl substituent.^{10,11} Since structure (1) has an eight-electron π system together

with adjacent filled and vacant in-plane orbitals,⁷ we assume that it may react both with electrophiles and nucleophiles. This paper deals with the first example¹² of a phenyl azide undergoing ring-expansion to give 1*H*-azepin-2(3*H*)-one (4) in the presence of an electrophile, acetic acid (see Scheme 2).

RESULTS AND DISCUSSION

Photolysis and Thermolysis of Phenyl Azide in Acetic Acid.—A solution of phenyl azide (0.91M) in acetic acid was purged with dry nitrogen and irradiated at 25 °C with a high-pressure mercury lamp. The solution was also heated in a sealed tube at 138 °C for 6 h. These reactions gave 1*H*-azepin-2(3*H*)-one (4), 2-methylbenzoxazole (15), 2- and 4-acetamidophenyl acetates (16) and (12), 2- and 4-acetamidophenols (14) and (13), acetanilide, and azobenzene (Table 1). The procedure for the analysis and characterization of the products is described in the Experimental section.



Irradiation of phenyl azide in acetic acid has previously been reported to lead to compounds (16) and (12).^{2,13} Doering and Odum² have reported 'Although these products can be envisaged to arise by way of the elusive phenylnitrene, there are other plausible modes of formation.'

TABLE 1

Photolysis and thermolysis of phenyl azide in acetic acid and the effect of added ethanol

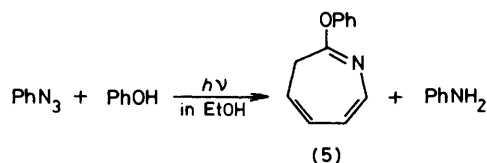
[EtOH] (M)	0 ^a	1.7 ^a	6.9 ^a	13.7 ^a	0 ^b	1.7 ^b
% of azide decomposed	41.2	36.9	58.9	26.6	54.8	52.9
(4)	39.2	34.8	21.0	2.2	6.5	5.1
(12)	12.2	6.4	0.99	0.14	8.8	2.0
(13)	2.3	3.9	0.95	ca. 0	13.5	19.2
(14)	7.9	10.7	13.1	2.7	2.7	19.6
(15)	4.2	3.8	0.97	ca. 0	41.7	22.8
(16)	5.6	2.5	0.87	0.09	Trace	Trace
Acetanilide	8.7	7.3	5.6	2.2	16.8	18.5
Azobenzene	0.31	0.54	0.09	0.87	0.34	0.38
(9)		0.71	0.93	0.21		ca. 0
(8)		2.1	2.2	0.47		0.90
<i>o/p</i> ratio (9)/(8)		0.34	0.42	0.45		
<i>o/p</i> ratio for (12)—(16)	1.3	1.7	7.7	19.9		

^a Photolysis. ^b Thermolysis.

Effect of Addition of Ethanol.—The formation of the azepinone (4) decreased linearly with an increase in the concentration of ethanol added to the system, whilst the total yield of the *para*-products (12) and (13) was lowered by the addition more markedly than that of the *ortho*-products (15), (16), and (14) to afford 2- and 4-acetamidophenyl ethyl ethers (9) and (8) (Table 1 and Figure).

Mechanism for Formation of the Azepinone (4).—There are two possible mechanisms for the formation of compound (4) as seen in Scheme 2: the reaction of acetic acid with 1-azacyclohepta-1,2,4,6-tetraene (1) formed by ring-expansion [pathway (a)], and a mechanism involving rearrangement of a resonance-stabilized ion (3) [pathway (b)].

Photolysis of phenyl azide in the presence of phenol yielded 2-phenoxy-3*H*-azepine (5) and aniline but none of the ring-disubstituted compounds 2- and 4-phenetidines (7) and (6) which are precursors of the ethyl ethers (9) and (8) (see Scheme 3). This suggests that

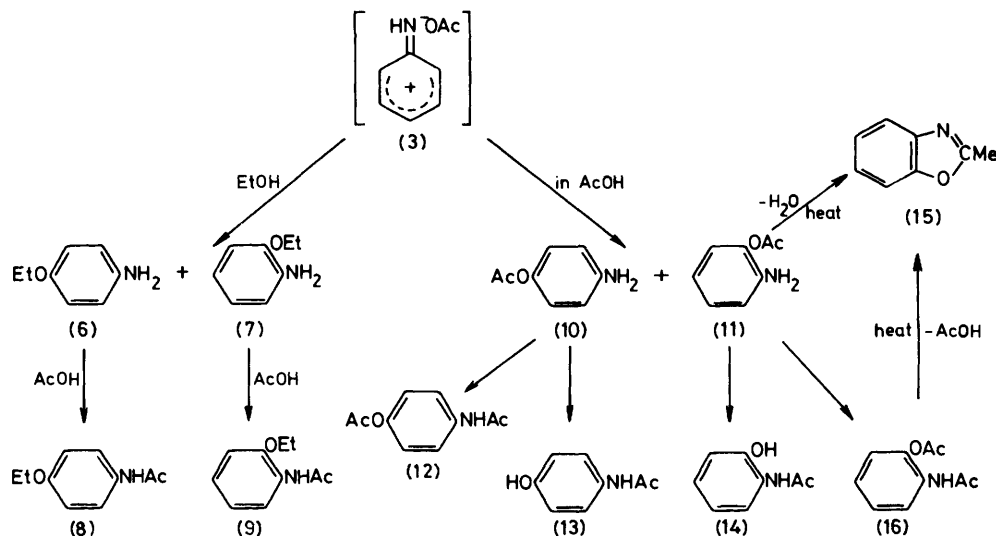


SCHEME 3

the ring-expansion to azepine and the formation of ring-disubstituted products occur *via* different intermediates. Since the ring-disubstituted products are formed *via* the intermediate (3) as described below, there is no longer any doubt as to the formation of the azepinone (4) by pathway (a), the final step of which is the acetylation of 2-acetoxy-3*H*-azepine (2). Both the linear decrease in the yield of (4) by the addition of ethanol and the absence of azepine formation in the photolysis of phenyl azide in ethanol support the idea that ethanol causes (1) to decay to phenylnitrene.

Mechanism for Formation of Ring-disubstituted Products.—The addition of ethanol to the system resulted in a decrease in the total yield of compounds (12)—(16), and the ethyl ethers (8) and (9) were obtained (Table 1). Photolysis of phenyl azide in ethanol, however, did not afford the phenetidines (6) and (7), which are precursors of (8) and (9) in the above reaction. Thermal and photochemical treatment of the mixture of compounds (4) and (12)—(16) in AcOH-EtOH did not give (8) and (9). Thus, the cation of (3) may react with acetic acid (or acetate anion) or ethanol at either the activated *ortho*- and *para*-positions to lead eventually to ring-disubstituted products (Scheme 4).

For the reasons detailed below, it is evident that the



SCHEME 4

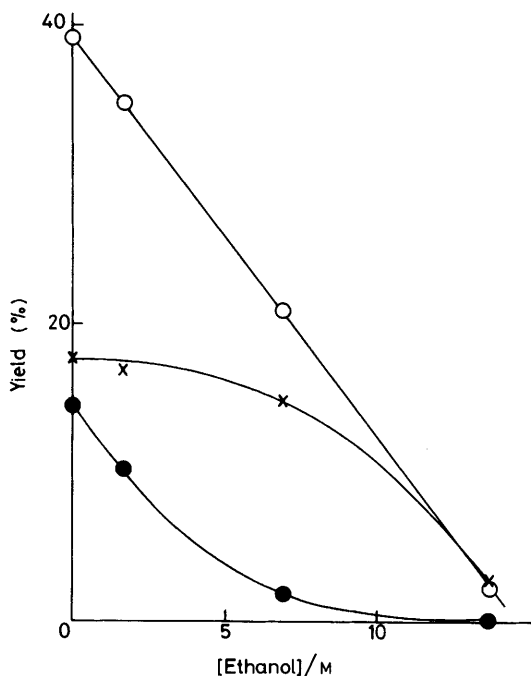


FIGURE 1 Effect of ethanol on the photochemical reaction of phenyl azide with acetic acid for the formation: ○, of aze-pinone (4); ×, of *o*-products (14), (15), and (16); ●, of *p*-products (12) and (13)

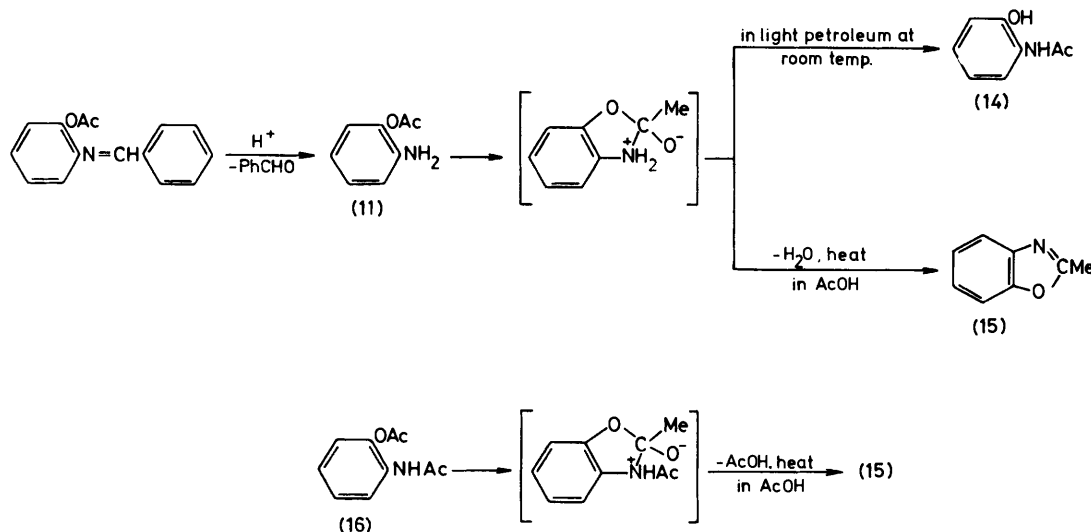
cation (3) has an acetate anion adjacent to the nitrogen or to the *ortho*- rather than the *para*-position. (i) The *o/p* ratio for compounds (12)–(16) was >1 , but the ratio (9)/(8) was <0.5 (Table 1). (ii) The yield of compounds (9) and (8) was small in spite of the greater nucleophilicity of ethanol over acetic acid, and the total yield of *para*-products (12) and (13) was decreased by the addition of ethanol more markedly than that of *ortho*-products (14), (15), and (16) (see Figure).

Compound (15) was formed under the thermal con-

ditions from (16) almost quantitatively or from 2-amidophenyl acetate (11) in 41% yield. Treatment of (11) in light petroleum at room temperature afforded compound (14) in 45% yield. Treatment of 4-amido-phenyl acetate (10) in acetic acid yielded (12) (43%) and (13) (19%) at room temperature, and (12) (41%) and (13) (35%) under the thermal conditions for 3 h. Since in acetic acid aniline was converted into acetanilide nearly quantitatively under the thermal and photochemical conditions, acetanilide derivatives (8), (9), (12), and (16) may be formed from the corresponding aniline derivatives, (6), (7), (10), and (11), respectively (see Scheme 4). The formation of (14) and (15) from (11) appears to be explained by an identical intermediate as indicated in Scheme 5. The product (15) would be also formed *via* a similar intermediate to that mentioned above from (16). Further, thermal reactions of (12) and (16) in AcOH-EtOH gave (13) (47%) and (15) (39%) together with (14) (45%), respectively. This shows that it is possible that (13) and (14) are formed by the reaction of (12) and (16), respectively, with acetic acid or water in the system.

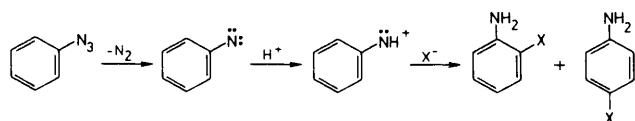
The photolysis of phenyl azide in methanol, in methanol containing 10% acetic acid, in ethanol, or in ethanol containing 10% acetic acid has been reported by Sundberg and Smith.⁹ They failed to detect alkoxyanilines, indicating that the path shown in Scheme 6 *via* a phenylnitrenium ion is inoperative. According to our data, the photolysis in ethanol containing acetic acid did not produce ethoxyanilines (phenetidines) but ring-disubstituted products, (8), (9), and (12)–(16). Phenylnitrenium ion can be shown as one contribution form to the structure of cation of (3), but its real contribution is ambiguous since we could not prove the formation of a product (such as acetanilide) *via* the phenylnitrenium ion.

Primary Formation of Phenylnitrene in Acetic Acid.—The rate of thermal decomposition of phenyl azide in acetic acid or in 1,4-dioxan was determined by measure-



SCHEME 5

ment of the concentration of the azide; it indicated that the decomposition is first order in azide. Rate constants were determined from the slope of linear plots of $\ln a_0/(a_0-x)$ versus time where a_0 and x mean the concentrations of azide at time zero and t , respectively. The enthalpies of activation, ΔH^\ddagger , and the entropies of



SCHEME 6

activation, ΔS^\ddagger , were calculated from the equation derived from transition-state theory. The results are summarized in Table 2. The rate in acetic acid was not accelerated as compared with that in 1,4-dioxan, and the activation parameters in the two solvents varied little. The result indicates that the decomposition in acetic acid does not proceed *via* a conjugate acid of azide since the decomposition *via* the conjugate acid, PhNH-N_2^+ , which has a reduced double-bond character of the N-N_2 bond rather than phenyl azide should have smaller activation enthalpy than that *via* phenyl azide in 1,4-dioxan. Thus, phenylnitrene may be primarily generated from the azide.

TABLE 2

Rate constants and activation parameters for the decomposition of phenyl azide

Solvent	Temp. (°C)	$10^6 k/s^{-1}$	$\Delta H^\ddagger/kcal\ mol^{-1}$	$\Delta S^\ddagger/cal\ mol^{-1}\ K^{-1}$
Acetic acid	130.0	1.8	32.5	-0.16
	137.5	4.3		
	151.5	16.1		
1,4-Dioxan	128.2	2.3	31.5	-2.1
	137.5	5.1		
	151.5	21.2		

The intermediates (1) and (3) would be formed *via* singlet phenylnitrene and/or *via* singlet excited phenyl azide according to the following observations. The yield of (4) and the total yield of (12)—(16) are almost independent of the presence of penta-1,3-diene (0.01M) as a triplet quencher in photolysis, and somewhat decreased by an addition to the system of a heavy atom solvent, bromobenzene (20% v/v), compared with an addition of the same amount of benzene.

The singlet nitrene generated appears to abstract a proton from acetic acid since a large contribution to the structure of phenylnitrene by the dipolar resonance form diminishes the electron deficiency at nitrogen.^{14,15} However, we consider that no clear experiments have been performed to distinguish between direct proton abstraction and an alternative mechanism *via* an O-N ylide intermediate which is formed by an attack of the nitrene on the oxygen atom of acetic acid. Details of the mechanism remain to be elucidated.

The difference between the product ratios on photolysis and thermolysis presumably depends upon both the ease of formation of (1) and (3) and the stability of some of the precursors.

EXPERIMENTAL

I.r. spectra were obtained on a Hitachi model EPI-G3 spectrometer. ¹H N.m.r. spectra were taken with a Varian EM-360 spectrometer with tetramethylsilane as internal standard. Mass spectra were recorded on a Hitachi RMU-6E spectrometer. G.l.c. for quantitative analyses was carried out with Shimadzu GC-6A unit using glass column (1 m × 3 mm) packed with polyethylene glycol 20M (10%) on 60—80 mesh Uniport KS (oven temperature, 90—240 °C at a rate 20 °C min⁻¹; nitrogen flow 40 ml min⁻¹). Temperatures of injection and detector for the analysis of azide were 120 °C, and those for the other materials were 220 °C. Each material showed only one peak under the analytical conditions, presumably because of the stability of the material. Photolyses were carried out externally in a quartz tube (25 cm × 1.8 cm) with a 300 W high-pressure mercury lamp (Halos PIH-300).

Acetic acid, ethanol, benzene, bromobenzene, and 1,4-dioxan were purified by standard methods before use. Phenyl azide,¹⁶ 2-methylbenzoxazole (15),¹⁷ 2-acetamidophenyl acetate (16),¹⁸ 4-acetamidophenyl acetate (12),¹⁷ 2-acetamidophenol (14),¹⁸ 4-acetamidophenol (13),¹⁹ 2-acetamidophenyl ethyl ether (9),²⁰ and 4-acetamidophenyl ethyl ether (8),²¹ were prepared by methods described in the literature. Acetanilide, azobenzene, 2- and 4-phenetidines (7) and (6), and phenol were commercial materials (Wako).

Photolysis of Phenyl Azide in Acetic Acid.—Phenyl azide (9.1 mmol) was dissolved in acetic acid to give a total volume of 10 ml. Dry nitrogen was bubbled through the solution for 1 h after which it was irradiated at 25 °C for 2—3 days. Unchanged azide and the products (4), (12)—(16), acetanilide, and azobenzene were analysed by g.l.c., the amounts being calculated from the peak areas in the usual manner. Yields for these products on two runs were obtained on the basis of the azide decomposed (Table 1). The analytical conditions were capable of detecting a 0.1% yield. Non-photolysed mixtures did not produce the above products and none of the g.l.c. peaks of the starting materials and products overlapped. After evaporation of solvent from the reaction mixture, azepinone (4) was easily isolated by preparative g.l.c. (Hitachi model 063-0012) on an aluminium column (2 m × 3 mm) packed with 10% polyethylene glycol on 60—80 mesh Uniport KS at 160 °C, ν_{\max} (Nujol) 3 400 and 3 200 (NH), 1 660 (C=O), 1 640 and 1 590 (C=C=C), and 1 335 cm⁻¹ (C-N); δ (CDCl₃) 2.95 (2 H, d, CH₂), 5.5—6.1 (2 H, m, 6- and 7-CH), 6.2—6.6 (2 H, m, 4- and 5-CH), and 8.9—9.4 (1 H, NH); λ_{\max} (EtOH) 260 nm (log ϵ 3.5); m/e 109 (M^+), 88, 66, and 53. The product had i.r. and n.m.r. spectra identical with those of specimens synthesized by the method of Vogel *et al.*²²

The experiment in the presence of penta-1,3-diene (0.01 M), bromobenzene (20%, v/v), benzene (20%, v/v) or various amounts of ethanol was carried out under conditions similar to those described above. The yield of products (8) and (9) along with (4), (12)—(16), acetanilide and azobenzene was determined by a procedure similar to that described above (Table 1). Again the analytical conditions were capable of detecting a 0.1% yield of (8) and (9).

Thermolysis of Phenyl Azide in Acetic Acid.—A solution (1.0 ml) consisting of the same components as those for the photolysis was placed in a sealed tube, and heated at 138 °C for 6 h. Thermolysis in acetic acid containing ethanol (1.7 M) was also performed under the above conditions. The

yield of products was determined by the same procedure as the photochemical one.

Photolysis of Phenyl Azide in Ethanol in the Presence and Absence of Phenol.—Phenyl azide (9.1 mmol) was dissolved in ethanol to give a total volume of 10 ml. After being purged with dry nitrogen for 1 h, the solution was irradiated at 25 °C for 4 days; this resulted in 13% of the azide being decomposed. Quantitative g.l.c. indicated that aniline (1.5%) was formed, but no 2- and 4-phenetidines (7) and (6) were detected. Irradiation for 1 day in the presence of phenol (0.94 M) was performed under conditions similar to those described above. The g.l.c. analysis showed that no (7) and (8) were detected, but aniline (2.5%) and 2-phenoxy-3H-azepine (5) (7.7%) were formed. The structure of (5) was confirmed as follows: ν_{max} (neat) 1 630 and 1 590 (C=C), 1 490 (C=N), 1 310, 1 250, and 1 210 (C-O), and 760 and 690 cm^{-1} (Ph); $\delta(\text{CCl}_4)$ 2.8–2.9 (2 H, d, CH_2), 5.2–6.8 (4 H, m, CH), and 6.8–7.7 (5 H, m, Ph); m/e 185 (M^+), 156, 92, and 65.

Photochemical and Thermal Reactions of a Mixture of Compounds (12)–(16) and Acetanilide in Acetic Acid–Ethanol.—A mixture of compounds (12)–(16) and acetanilide was dissolved in acetic acid–ethanol (8 : 1, v/v). The composition of the products was nearly identical with those for the photolysis and thermolysis of phenyl azide in acetic acid. The solution was irradiated for 12 h, or heated at 138 °C for 3 h. The g.l.c. analysis of the reaction mixture did not show the presence of (8) and (9) in significant quantities.

Thermal Reaction of (12) or (16) in Acetic Acid.—A solution (1.0 ml) containing 14 mg of (12) or (16) in acetic acid was heated at 138 °C for 6 h; 9.5 or 36% of starting material was consumed. Compounds (15) and (13) were formed from (16) and (12) in 94.5 and 9% yields, respectively. The yield is based on the starting material consumed.

Thermal Reaction of Mixture of Compounds (12) and (16) in Acetic Acid–Ethanol.—A solution (1.0 ml) containing (12) (7.5 mg) and (16) (7.5 mg) in acetic acid–ethanol (8 : 1, v/v) was heated at 138 °C for 6 h, resulting in 74 and 92% consumption of (12) and (16), respectively. On the basis of starting material consumed, (15) and (14) were produced in 39 and 45% yields, respectively, and (13) was formed in 47% yield. Compounds (12) and (16) were stable even on being allowed to stand in the above solution at room temperature for 2 days.

Reaction of 2- or 4-Aminophenyl Acetate (11) or (10).—By warming equimolar amounts of benzaldehyde and 2-aminophenol on a water-bath, 2-benzylideneaminophenol was prepared, m.p. 89 °C (recryst. from ethanol).²³ We tried to prepare (11) by a similar method [treatment with dilute H_2SO_4 of 2-benzylideneaminophenyl acetate formed from 2-benzylideneaminophenol] to that applied to the synthesis of (10).²⁴ But (11) was not isolated by recrystallization from light petroleum, converting to (15) (2.6%), (16) (1.7%), and

(14) (45%). Heating of the solution containing (11) in acetic acid at 138 °C for 3 h produced (15) (41%), (16) (0.5%), and (14) (3.6%).

Compound (10) (12 mg) synthesized by the method of Galatis²⁴ was dissolved in acetic acid (1.0 ml). Treatment of the solution at room temperature for 4 days gave (12) (43%) and (13) (19%) on the basis of (10) decomposed, 32%. Thermolysis of the solutions at 138 °C for 3 h also afforded (12) (41%) and (13) (36%) based on (10) consumed, 68%.

Kinetic Measurements.—Phenyl azide (9.1 mmol) was dissolved in acetic acid or in 1,4-dioxan to make a total volume of 10 ml. A number of identical solutions were made up, the individual mixtures taken one by one at fixed times during the course of the reaction at three definite temperatures; the rates of decomposition of azide were determined by measurement of the concentration of azide by g.l.c.

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