

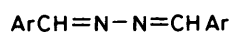
# The Reactions of Hydrazones and Related Compounds with Strong Bases. Part 4.<sup>1</sup> 4,5-Diaryl-1,2,3-triazoles from Aromatic Aldehyde Azines and from the Reaction of Arenecarbonitriles with Aryldiazomethanes

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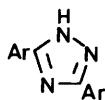
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Reaction of aromatic aldehyde azines in dimethyl sulphoxide at 20 °C with potassium t-butoxide gave 4,5-diaryl-1,2,3-triazoles (**4**) and stilbenes. Mechanisms were studied by addition of possible intermediates and by <sup>14</sup>C tracer methods. The synthesis of 4,5-diaryl-1,2,3-triazoles from arenecarbonitriles, aryldiazomethanes, and potassium t-butoxide in toluene is described and the mechanism is discussed.

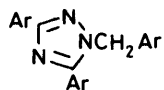
Our earlier investigations<sup>1</sup> showed that reaction of aromatic aldehyde azines (**1**) in boiling toluene with potassium t-butoxide gave 3,5-diaryl-1,2,4-triazoles (**2**) and trisubstituted 1,2,4-triazoles (**3**) as major products (26–54% yields); mechanisms involving addition of nitriles or dipolar species to an azine molecule were proposed on the basis of tracer experiments and studies of 'mixed' azines. Other products isolated included benzoic acids, benzonitriles, triaryl 1,2,4-triazine and 1,3,5-triazine derivatives, imidazoles, and pyrazoles. Reaction of



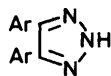
(1)



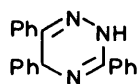
(2)



(3)



(4)



(5)

- a**; Ar = Ph  
**b**; Ar = 3-MeOC<sub>6</sub>H<sub>4</sub>  
**c**; Ar = 4-ClC<sub>6</sub>H<sub>4</sub>

benzaldehyde azine with sodamide in boiling xylene gave 3,5-diphenyl-1,2,4-triazole, an imidazole, and a pyrazole.<sup>2</sup> Since the wide variety of compounds obtained may be due to the elevated temperatures employed, we decided to use a strong base in an aprotic solvent at lower temperature and now describe the results.

## Results and Discussion

When benzaldehyde azine (**1a**) in dimethyl sulphoxide (DMSO) was treated with potassium t-butoxide (1 mol equiv.) at room temperature and in the absence of oxygen, the azine was consumed completely. The unexpected major product, which was isolated from the weakly acidic fraction, was 4,5-diphenyl-1,2,3-triazole† (**4a**) (37%) and the only products identical with those isolated previously from the reaction in toluene were *trans*-stilbene (32%), benzoic acid (1%), and the dihydrotriphenyl-

**Table 1.** Reaction of aldehyde azines (**1**) with potassium t-butoxide in DMSO at 20 °C for 24 h

Azine	Mol equiv. of base	Other reactant	Yields (%) <sup>a</sup> of products	
			1,2,3-Triazoles	Stilbenes
(1a)	1.0		37 <sup>b</sup>	32
(1a)	2.0		37	64
(1a)	0.2		6	
(1a)	1.0 <sup>c</sup>		35	68
(1a)	1.0 <sup>d</sup>		18	28
(1a)	1.0	PhCHN <sub>2</sub>	92 <sup>e</sup>	18
(1b)	1.0		31	28
(1c)	1.0		20 <sup>f</sup>	2
(1c)	1.0	4-ClC <sub>6</sub> H <sub>4</sub> CHN <sub>2</sub>	38 <sup>g</sup>	

<sup>a</sup> Calculated assuming that azine (2 mol) gives triazoles (1 mol) and that azine (4 mol) gave stilbenes (1 mol) (Scheme 1), except where stated otherwise. <sup>b</sup> The dihydro-1,2,4-triazine (**5**) (1%) and benzoic acid (1%) were also isolated. <sup>c</sup> Carried out at 110 °C for 40 h. <sup>d</sup> With sodium hydride instead of potassium t-butoxide. <sup>e</sup> Calculated from azine consumed (80%) and assuming that azine (1 mol) gives triazole (1 mol) (Scheme 1). <sup>f</sup> Calculated from azine consumed (23%). <sup>g</sup> Calculated from azine consumed (44%) and assuming that azine (1 mol) gives triazole (1 mol) (Scheme 1).

triazine (**5**) (1%). When the reaction was carried out with 0.2 mol equiv. of base, azine (90%) was recovered and the triazole (**4a**) was obtained in only 6% yield, but with more base and at higher temperature the yield of triazole was unaffected although that of *trans*-stilbene was doubled (Table 1). Sodium hydride in DMSO was less effective and gave the triazole in lower yield (Table 1).

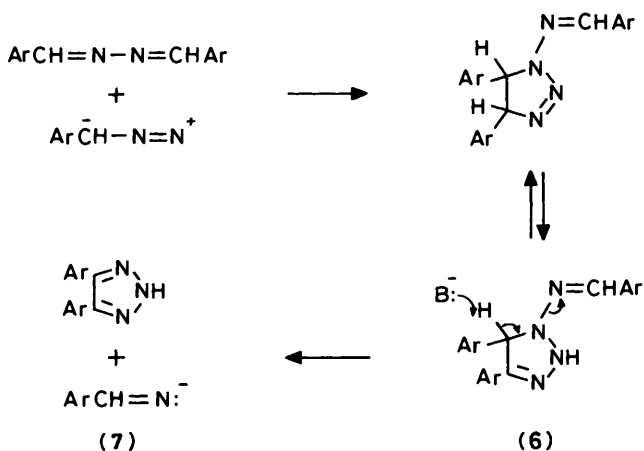
In order to explore the generality of the reaction, other symmetrical azines were studied (Table 1). Reaction of 3-methoxybenzaldehyde azine with potassium t-butoxide gave 4,5-bis(3-methoxyphenyl)-1,2,3-triazole (**4b**) (31%) as an oil; its structure was established by i.r. and <sup>1</sup>H n.m.r. spectroscopy (see Experimental section) and it was characterized as the benzoyl derivative. The only product isolated from the neutral fraction was *trans*-3,3'-dimethoxystilbene. 4-Methoxybenzaldehyde azine was too insoluble in DMSO for reaction with t-butoxide to occur. 4-Chlorobenzaldehyde azine was also insoluble in

† The triazoles (**4**) and (**10**) are written as the 2*H*-tautomers in this paper and their benzoyl derivatives arbitrarily formulated as 2-benzoyl-triazoles.

DMSO at 20 °C, but at 100 °C a homogeneous solution was formed and addition of base resulted in recovery of azine (67%) and isolation of the triazole (4c) (20%, based on azine consumed); the identity of the product was confirmed by independent synthesis (see below).

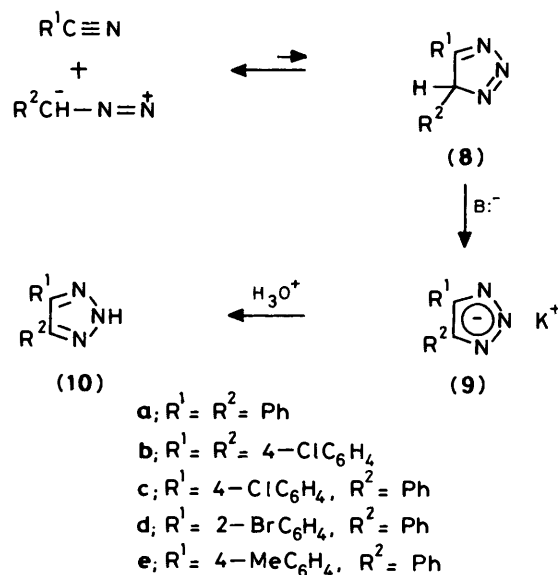
**Mechanisms.**—The most striking result of these experiments is that changing the solvent from toluene to DMSO and reducing the temperature of the reaction entirely changes the nature of the major products; it was therefore of interest to study the mechanisms of the reactions in the new solvent.

Five-membered heterocycles such as pyrazolones,<sup>3</sup> pyrazoles,<sup>4</sup> and 1,2,3-triazolines<sup>5</sup> are formed by 1,3-dipolar cycloaddition of diazomethane and its derivatives to activated double and triple bonds. On this basis, aryldiazomethanes are plausible intermediates in the formation of diaryl-1,2,3-triazoles in our experiments; this suggestion was supported by the substantial increase in yields of triazoles (4a) (37–92%) and (4c) (20–38%) that occurred in the presence of phenyldiazomethane or 4-chlorophenyldiazomethane, respectively (Table 1). Zimmerman and Somasekhara<sup>6</sup> showed that pyrolysis of arenecarbaldehyde azines to give stilbenes was catalysed by sodium hydroxide and appeared to involve the formation of aryldiazomethanes. Our azine–base reactions may occur similarly and then lead to diaryl-1,2,3-triazoles by 1,3-dipolar cycloaddition of aryldiazomethanes to azines (Scheme 1) or to arenecarbonitriles (Scheme 2).



The role of the latter compounds (which can be regarded as elimination products of azines<sup>1</sup>), was tested by adding <sup>14</sup>C-labelled benzonitrile to the reaction of benzaldehyde azine with potassium *t*-butoxide; since incorporation of radioactivity into triazole (4a) was negligible (Experimental section), mechanisms involving arenecarbonitriles, *cf.* (Scheme 2), can be discounted.

The aryldiazomethane–azine addition (Scheme 1) has the merit of providing a role for the base in the elimination reaction of the intermediate (6). Earlier work<sup>1</sup> and the present tracer experiment indicated that benzoic acid was not formed from benzonitrile; its isolation is indicative of the formation of imine (7), from which it is probably obtained by hydrolysis to benzaldehyde and subsequent oxidation, and thus supports the mechanism given in Scheme 1. We found, however, that reaction of phenyldiazomethane, benzonitrile, and potassium *t*-butoxide in DMSO gave 4,5-diphenyl-1,2,3-triazole (4a) (20%). Thus, if phenyldiazomethane is an intermediate in the azine–base reaction, it should have been trapped as radioactive triazole on addition of <sup>14</sup>C-labelled benzonitrile. The absence of significant



**Table 2.** Synthesis of 4,5-diaryl-1,2,3-triazoles (10) from reaction of aryldiazomethanes (1 mol equiv.), arenecarbonitriles (1 mol equiv.) and potassium *t*-butoxide (1 mol equiv.) in toluene

Reactants		Temp. (°C)	Yield (%)
R <sup>1</sup> CN	R <sup>2</sup> CHN <sub>2</sub>		
R <sup>1</sup> = Ph	R <sup>2</sup> = Ph	20, 24	69
R <sup>1</sup> = Ph	R <sup>2</sup> = Ph	110, 2	75
R <sup>1</sup> = 4-ClC <sub>6</sub> H <sub>4</sub>	R <sup>2</sup> = 4-ClC <sub>6</sub> H <sub>4</sub>	110, 2	70
R <sup>1</sup> = 4-ClC <sub>6</sub> H <sub>4</sub>	R <sup>2</sup> = Ph	110, 2	44
R <sup>1</sup> = 2-BrC <sub>6</sub> H <sub>4</sub>	R <sup>2</sup> = Ph	20, 24	66
R <sup>1</sup> = 4-MeC <sub>6</sub> H <sub>4</sub>	R <sup>2</sup> = Ph	110, 2	26

incorporation argues against aryldiazomethanes as discrete intermediates (Scheme 1) but does not exclude alternative concerted mechanisms; a full discussion must await further investigation.

**Synthesis of 4,5-Diaryl-1,2,3-triazoles.**—The reaction of aldehyde azines with base just described is not likely to be a useful synthesis of 1,2,3-triazoles. A potentially convenient route, particularly for the synthesis of 1,2,3-triazoles unsymmetrically substituted at C-4 and C-5, involves 1,3-dipolar cycloaddition of diazo derivatives to compounds containing a carbon–nitrogen triple bond, but this method appears to have been successful only with activated nitriles.<sup>7</sup> A recent example<sup>8</sup> is the reaction of an excess of diazomethane with methyl cyanofornate, which furnished a mixture of *N*-methyltriazoles *via* 4-methoxycarbonyl-2*H*-1,2,3-triazole. Our observation that phenyldiazomethane does not react with unactivated benzonitrile but that triazole (4a) was formed on addition of potassium *t*-butoxide (see before) showed that base can play a critical role in the reaction. We now find that a mixture of aryldiazomethanes, benzonitriles, and potassium *t*-butoxide (molar ratio 1 : 1 : 1) in toluene gives 4,5-diaryl-1,2,3-triazoles (10), mostly in good to satisfactory yields (Scheme 2) (Table 2). Thus, 4,5-diphenyl-1,2,3-triazole (10a) was obtained in 69% yield at 20 °C for 24 h and in 75% yield at 40 °C for 2 h. The method was applied to the preparation of 4,5-bis(4-chlorophenyl)-1,2,3-triazole (10b) (70%), 4-(4-chlorophenyl)-5-phenyl-1,2,3-triazole (10c) (44%), 4-(2-bromophenyl)-5-phenyl-1,2,3-triazole (10d) (66%), and 4-

(4-methylphenyl)-5-phenyl-1,2,3-triazole (**10e**) (26%); the latter compound failed to crystallize and was characterized as its benzoyl derivative. In several cases benzaldehyde azine or 4-chlorobenzaldehyde azine was also isolated and presumably arose by dimerization of aryldiazomethanes.

Although the mechanism of the reaction, and particularly the role of the base, is unknown, one possibility (Scheme 2) is that minor products of equilibrium mixtures are the 1,3-dipolar cycloaddition products (**8**), which are converted by butoxide into the stable anions (**9**); acidification then affords the 1,2,3-triazoles (**10**). An alternative mechanism, which was proposed previously for the reaction of diazomethane lithium with benzonitrile,<sup>9</sup> is nucleophilic addition of a diazoalkyl anion to the triple bond of a nitrile.

## Experimental

Instruments and general experimental conditions used are as specified previously.<sup>1</sup>

*Reaction of Arylaldehyde Azines (1) with Potassium t-Butoxide.*—The general procedure is illustrated by the following account of the reaction of benzaldehyde azine (**1a**).

A solution of benzaldehyde azine (5 g) and potassium t-butoxide (2.8 g) in dimethyl sulphoxide (DMSO) (250 ml) was kept in nitrogen for 24 h, and after evaporation below 40 °C, water (250 ml) was added and the mixture was extracted with dichloromethane. Acidification of the aqueous solution, extraction with dichloromethane, washing the organic layer with aqueous sodium carbonate and evaporation gave 4,5-diphenyl-1,2,3-triazole (**4a**) (0.97 g), m.p. 134–135 °C (lit.,<sup>10</sup> 125 °C) (from benzene), further characterized as its benzoyl derivative, m.p. 163–164 °C (lit.,<sup>10</sup> 164 °C) (from ethanol); both compounds were identical with authentic samples.

Acidification of the sodium carbonate solution gave benzoic acid (0.026 g).

The non-acidic fraction, obtained by evaporation of the original dichloromethane solution, was chromatographed on alumina. Elution with light petroleum (b.p. 40–60 °C) (3:1) gave 2,5-dihydro-3,5,6-triphenyl-1,2,4-triazine (**5**) (0.024 g), m.p. and mixed m.p. 239–240 °C (from ethanol) (lit.,<sup>11</sup> 239 °C).

The procedure was applied to 3-methoxybenzaldehyde azine (**1b**) (Table 1) to give the triazole (**4b**) as a red oil;  $\nu_{\max}$  (KBr) 2950 cm<sup>-1</sup> (NH);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 7.35–6.93 (8 H, m, ArH) and 5.80 (6 H, s, 2 × OMe), which was converted with benzoyl chloride in refluxing pyridine into 2-benzoyl-4,5-bis(3-methoxyphenyl)-1,2,3-triazole, m.p. 154 °C (needles from ethanol);  $\nu_{\max}$  1730 cm<sup>-1</sup> (NCO) (Found: C, 71.4; H, 5.1; N, 11.0. C<sub>23</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub> requires C, 71.7; H, 4.9; N, 11.0%), and also gave 3,3'-dimethoxystilbene, m.p. 97 °C (needles from ethanol) (lit.,<sup>12</sup> 97.5 °C) (Found: C, 79.8; H, 6.6. Calc. for C<sub>16</sub>H<sub>16</sub>O<sub>2</sub>: C, 80.0; H, 6.7%).

4-Chlorobenzaldehyde azine gave the triazole (**4c**), m.p. and mixed m.p. 187–188 °C (see below) and 4,4'-dichlorostilbene, m.p. 168–169 °C (needles from ethanol) (lit.,<sup>13</sup> 170 °C) (Table 1).

*Reaction of Benzaldehyde Azine with Potassium t-Butoxide in the Presence of Benzo[<sup>14</sup>C]nitrile.*—A solution of benzaldehyde

azine (5 g), potassium t-butoxide (2.8 g), benzo[<sup>14</sup>C]nitrile (100 mg, total activity 6.16 × 10<sup>7</sup> counts 100 s<sup>-1</sup>) in DMSO (250 ml) was kept for 24 h in nitrogen and worked up to give 4,5-diphenyl-1,2,3-triazole (activity 0.0012%, calc. on total activity × 100/total activity of Ph<sup>14</sup>CN) and benzoic acid (activity 0.024%).

*4,5-Diaryl-1,2,3-triazoles (10) from Aryldiazomethanes, Arene Nitriles and Potassium t-Butoxide.*—The general procedure is illustrated with benzonitrile as follows. A solution of phenyldiazomethane (1.12 g), benzonitrile (1.0 g), and potassium t-butoxide (1.12 g) in toluene (25 ml) was refluxed for 2 h and worked up as described for the reaction of benzaldehyde azine with potassium t-butoxide (see before) to give 4,5-diphenyl-1,2,3-triazole (**10a**) (1.035 g), m.p. and mixed m.p. 130–132 °C; chromatography of the non-acidic fraction on alumina and elution with ether–light petroleum (b.p. 40–60 °C) (1:3) gave benzaldehyde azine (**1a**) (0.11 g), m.p. and mixed m.p. 91–92 °C (from ethanol).

Yields of other triazoles (**10**) are given in Table 2. 4,5-Bis(4-chlorophenyl)-1,2,3-triazole (**10b**) was obtained as needles, m.p. 187–188 °C (from ethanol–benzene) (Found: C, 58.1; H, 3.0; N, 14.7. C<sub>14</sub>H<sub>8</sub>Cl<sub>2</sub>N<sub>3</sub> requires C, 58.1; H, 3.1; N, 14.5%).

Also prepared were 4-(4-chlorophenyl)-5-phenyl-1,2,3-triazole (**10c**), m.p. 57–58 °C (plates from ethanol) (Found: C, 65.3; H, 4.1. C<sub>14</sub>H<sub>10</sub>ClN<sub>3</sub> requires C, 65.7; H, 3.9%) and 4-(2-bromophenyl)-5-phenyl-1,2,3-triazole (**10d**), m.p. 48–49 °C (Found: C, 56.5; H, 3.4. C<sub>14</sub>H<sub>10</sub>BrN<sub>3</sub> requires C, 56.0; H, 3.3%).

5-(4-Methylphenyl)-4-phenyl-1,2,3-triazole (**10e**) was obtained as an oil; reaction with benzoyl chloride in refluxing pyridine gave 2-benzoyl-5-(4-methylphenyl)-4-phenyl-1,2,3-triazole, m.p. 154 °C (needles from ethanol);  $\nu_{\max}$  1730 cm<sup>-1</sup> (NCO) (Found: C, 77.6; H, 5.1; N, 12.6. C<sub>22</sub>H<sub>17</sub>N<sub>3</sub>O requires C, 77.9; H, 5.1; N, 12.4%).

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