1 : 2 : 4-*Triazoles. Part I. A Synthesis of* 3 : 5-*Disubstituted* 1 : 2 : 4-*Triazoles.*

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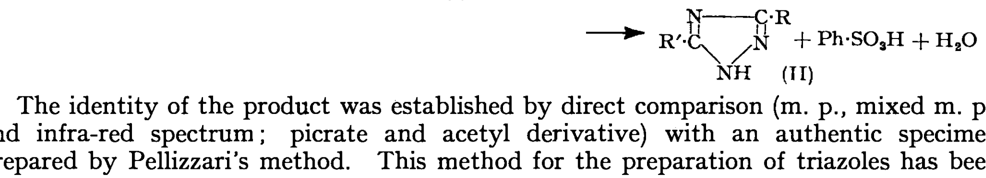
[Reprint Order No. 5363.]

The reaction of benzhydrazide benzenesulphonate or *p*-nitrobenzhydrazide benzenesulphonate with various aromatic cyanides results in the formation of 3 : 5-diaryl-1 : 2 : 4-triazoles.

Oxley and Short (*J.*, 1946, 147) established a new method for the preparation of amidines and their *N*-monosubstituted derivatives by heating the ammonium or alkyl- or aryl-ammonium salt of an aromatic or aliphatic sulphonic acid with a cyanide at high temperatures. The present paper describes an application of their method to the preparation of 3 : 5-diaryl-1 : 2 : 4-triazoles by heating an unsubstituted acylhydrazide benzene- or toluene-*p*-sulphonate with an aromatic cyanide at 200—250°. Cyanides have been used previously to obtain sodio-derivatives of amidines by reaction with an aromatic amine in the presence of sodium (von Walther, *J. prakt. Chem.*, 1894, **50**, 91; von Walther and Grossmann, *ibid.*, 1908, **78**, 478; Engelhardt, *ibid.*, 1896, **54**, 143) and, when two molecules of the cyanide and one molecule of phenylhydrazine reacted in the presence of sodium, a 1 : 2 : 4-triazole was formed. Atkinson and Polya (*J.*, 1952, 3418) were unable to effect condensation of a nitrile with a benzhydrazide under the conditions employed by Pellizzari (*Gazzetta*, 1911, **41**, II, 20) and they are of the opinion that the low yields obtained from such condensations are due to the formation of nitriles.

It is most likely that the reaction may be represented by the following stages:



The identity of the product was established by direct comparison (m. p., mixed m. p., and infra-red spectrum; picrate and acetyl derivative) with an authentic specimen prepared by Pellizzari's method. This method for the preparation of triazoles has been restricted to the use of aromatic cyanides, and the results are shown in the Table. Further applications of this method are being studied. The influence of reaction conditions has not been thoroughly investigated, so that the recorded yields (of crude material) are not necessarily the highest obtainable. The method has the advantage of being a one-stage process which can be operated without employing a solvent. In common with other similar systems containing an imino-group triazoles are weakly acidic and form salts with metals; use is made of this property in the isolation and purification.

The triazole (II; R = Ph, R′ = *p*-$C_6H_4{\cdot}NO_2$) obtained from the condensation of *p*-nitrophenyl cyanide and benzhydrazide benzenesulphonate was identical with that obtained from phenyl cyanide and the corresponding *p*-nitrobenzhydrazide benzenesulphonate. The fact that only one form was isolated supports the hypothesis that a true tautomeric system is present in the triazole nucleus for otherwise two isomers would be expected. The ultra-violet absorption spectra of several of these triazoles have been determined but they fail to exhibit any selective absorption other than that due to the phenyl nucleus. In the infra-red spectrum the presence of a highly associated imino-group is indicated, and 3 : 5-diphenyl-1 : 2 : 4-triazole and 3-phenyl-5-*p*-tolyl-1 : 2 : 4-triazole show this effect very strongly. Molecular-weight determinations, however, yield normal results. It is quite possible that the tautomeric nature of the triazoles might be due to such an interaction between two or more molecules and not involve the shift of hydrogen from one nitrogen to another. In the corresponding *N*-acetyl-1 : 2 : 4-triazoles no imino-band is present and the carbonyl band occurs at 5·7 μ which is somewhat lower than that which would be expected for an amide group. As is expected, little or no association occurs and this is supported by molecular-weight determinations (cf. Hunter and Marriott, *J.*, 1941, 777).

TABLE 1. 3-R^1-5-R^2-1 : 2 : 4-*triazoles*.

					Found, %			Reqd., %			
R^1	R^2	M. p.	Yield, %	Formula	C	H	N	C	H	N	
Ph	Ph	190°	92	$C_{14}H_{11}N_3$	76·1	5·0	18·9	76·0	5·0	19·0	[a]
Ph	*p*-C_6H_4Me	189	quant.	$C_{15}H_{13}N_3$	76·3	5·9	17·8	76·6	5·6	17·9	[b]
Ph	*o*-C_6H_4Me	—	—	—	—	—	—	—	—	—	[c]
Ph	α-$C_{10}H_7$	118	88	$C_{18}H_{13}N_3$	78·8	5·1	15·9	79·7	4·8	15·5	[d]
Ph	*p*-$C_6H_4{\cdot}NO_2$	239	quant.	$C_{14}H_{10}O_2N_4$	62·5	3·9	21·2	63·1	3·8	21·0	[e]
p-$C_6H_4{\cdot}NO_2$	Ph	240	86	$C_{14}H_{10}O_2N_4$	63·2	3·9	20·6	63·1	3·8	21·0	[e]
p-$C_6H_4{\cdot}NO_2$	*p*-C_6H_4Me	244	quant.	$C_{15}H_{12}O_2N_4$	64·6	4·6	20·4	64·3	4·3	20·0	[f]
p-$C_6H_4{\cdot}NO_2$	CH_2Ph	212	84	$C_{15}H_{12}O_2N_4$	64·6	4·5	20·3	64·3	4·3	20·0	[g]
p-$C_6H_4{\cdot}NO_2$	*p*-$C_6H_4{\cdot}NO_2$	250—251	58	$C_{14}H_{19}O_4N_5$	54·1	3·2	22·5	54·0	2·9	22·5	[h]
p-$C_6H_4{\cdot}NO_2$	α-$C_{10}H_7$	192	80	$C_{18}H_{12}O_2N_4$	68·5	4·0	17·5	68·4	3·8	17·7	[j]
α-C_5H_4N	Ph	212	86	$C_{13}H_{10}N_4$	70·0	4·7	25·3	70·3	4·6	25·1	[i]
α-C_5H_4N	*p*-C_6H_4Me	202	77	$C_{14}H_{12}N_4$	71·2	5·3	23·8	71·1	5·1	23·7	[k]

[a] Needles from light petroleum. [b] Needles from light petroleum. *Picrate*, brilliant yellow needles, m. p. 156°, from benzene (Found : C, 60·0; H, 4·3; N, 16·1. $C_{21}H_{16}O_7N_6,C_6H_6$ requires C, 59·8; H, 4·1; N, 15·5%). N-*Acetyl* derivative, needles, m. p. 93°, from light petroleum (Found : C, 74·0; H, 5·6; N, 14·9. $C_{17}H_{15}ON_3$ requires C, 73·6; H, 5·5; N, 15·2%). [c] Isolated as the *picrate*, yellow needles, m. p. 176° , from aqueous alcohol (Found : C, 51·5; H, 3·9. $C_{21}H_{16}O_7N_6,1{\cdot}5H_2O$ requires C, 51·3; H, 3·9%). The water was not lost on drying, and the infra-red spectrum indicated the presence of a highly-bonded hydroxyl group. [d] Long needles from light petroleum. Analytical results obtained for carbon were always low. *Picrate*, irregular, yellow prisms, m. p. 206°, from methanol (Found : C, 57·5; H, 3·3. $C_{24}H_{16}O_7N_6$ requires C, 57·6; H, 3·2%). [e] Needles from light petroleum. These two compounds were identical in m. p., mixed m. p., and infra-red spectra. [f] Fluffy needles from light petroleum. [g] Plates from light petroleum. [h] Fawn needles from aqueous alcohol. [i] Glistening fawn needles from aqueous alcohol. [j] Needles from aqueous alcohol. *Picrate*, small, yellow needles, m. p. 201°, from benzene (Found : C, 50·7; H, 3·2; N, 21·5. $C_{19}H_{13}O_7N_7$ requires C, 50·6; H, 2·9; N, 21·7%). [k] Cubes from light petroleum. *Picrate*, yellow needles, m. p. 194°, from alcohol (Found : N, 20·9. $C_{20}H_{15}O_7N_7$ requires N, 21·1%).

A convenient method for the characterization of 1 : 2 : 4-triazoles was to prepare the picrate, either in benzene or in alcohol solution. The introduction of a nitro-group into the *para*-position of a phenyl nucleus reduced the basicity of the triazole nucleus to such an extent that the corresponding picrates could not be isolated in a pure condition. In the glyoxaline series the direct introduction of a nitro-group into the nucleus has a similar effect (Forsyth and Pyman, *J.*, 1925, **127**, 573).

The triazoles listed in the Table were prepared by the fusion technique of which examples are given in the Experimental section.

EXPERIMENTAL

Light petroleum refers to the fraction of b. p. 60—80°, unless otherwise stated. A steady temperature could be maintained during the fusions by the use of the appropriate solvent in a three-neck flask; the centre neck contained a large (8″ × 1″) test tube and a reflux condenser was fitted to another neck.

Benzhydrazide Benzenesulphonate.—Benzhydrazide [104 g.; Curtius and Struve, *J. prakt. Chem.*, 1894, (2), **50**, 295], dissolved in the minimum amount of boiling alcohol (*ca.* 150 c.c.), was treated, in small portions and with shaking, with benzenesulphonic acid (140 g.; commercial). After the solution had been refluxed for 1 hr., a small amount of dry ether was added, and on cooling the product (84 g.; 37%) crystallized. *Benzhydrazide benzenesulphonate* crystallized from alcohol–ether as white needles, m. p. 169° (Found: C, 52·9; H, 4·9; N, 9·6. $C_{13}H_{14}O_4N_2S$ requires C, 53·1; H, 4·8; N, 9·5%).

Benzhydrazide toluene-p-*sulphonate* was prepared similarly from benzhydrazide and toluene-*p*-sulphonic acid monohydrate. It crystallized from alcohol–ether as white needles, m. p. 205° (Found: C, 51·1; H, 5·5; N, 8·6. $C_{14}H_{16}O_4N_2S,1H_2O$ requires C, 51·5; H, 5·5; N, 8·6%). The molecule of water was not lost even after several hours at 117°/0·5 mm.

p-*Nitrobenzhydrazide Benzenesulphonate.*—Benzenesulphonic acid (150 g.) was added, slowly and with shaking, to *p*-nitrobenzhydrazide [182 g.; Curtius and Trachmann, *J. prakt. Chem.*, 1895, (2), **51**, 168] dissolved in hot alcohol (4000 c.c.). The mixture was heated under reflux for 30 min. and cooled in an ice-bath; p-*nitrobenzhydrazide benzenesulphonate* (256 g.; 76%) crystallized from water as shiny, white plates, m. p. 254° (with frothing) (Found: C, 46·4; H, 4·0; N, 12·2; S, 9·5. $C_{13}H_{13}O_6N_3S$ requires C, 46·0; H, 3·9; N, 12·4; S, 9·5%).

α-*Picolinhydrazide Benzenesulphonate.*—Prepared as in the previous experiment, from α-picolinhydrazide (22·0 g.; Meyer and Mally, *Monatsh.*, 1912, **33**, 393), and benzenesulphonic acid (28·4 g.) in the minimum amount of boiling alcohol (200 c.c.), the *benzenesulphonate* crystallized from alcohol–ether (charcoal) as stout, golden needles, m. p. 150° (Found: C, 48·6; H, 4·5; N, 14·5. $C_{12}H_{13}O_4N_3S$ requires C, 48·8; H, 4·4; N, 14·3%).

3 : 5-*Diphenyl*-1 : 2 : 4-*triazole.*—(a) *New method.* A mixture of phenyl cyanide (3·0 g.; 0·029 mole) and benzhydrazide benzenesulphonate (9·4 g.; 0·032 mole) was heated at 200° for 3 hr. The cooled melt was extracted with cold sodium hydroxide solution (10%; *ca.* 500 c.c.); on acidification of this extract with concentrated hydrochloric acid a white precipitate (6·0 g., 92%; m. p. 169—170°) was obtained. 3 : 5-Diphenyl-1 : 2 : 4-triazole, after several crystallizations from dilute alcohol and then from light petroleum, was obtained as white needles, m. p. 190°. (b) *Pellazzari's method.* The product was isolated by extraction with alkali and precipitation with acid. It crystallized from methanol as white, opaque plates, and, after being dried at 117°/0·5 mm. for 3 hr., had m. p. 188—189°. The m. p. of a mixture with a specimen prepared by method (a) was 189°.

The acetyl derivative was prepared by use of acetic anhydride under reflux for 4 hr. (Atkinson and Polya, *loc. cit.*). It was prepared from the triazole prepared by each of the above methods, and separated from ether–light petroleum as rosettes of white needles, m. p. 107—108° (Pellizzari, *Gazzetta*, 1911, **41**, II, 20, gives m. p. 107—108°).

The picrate was prepared by use of an excess of picric acid in benzene. After 10 min. on the water-bath and cooling, and crystallization from benzene the derivative formed brilliant yellow plates, m. p. 166°, containing a molecule of benzene of crystallization. It lost benzene at 145° and began to decompose at 100°/0·5 mm. (Atkinson and Polya, *loc. cit.*, report m. p. 171°) (Found: C, 58·9; H, 3·7; N, 16·5. Calc. for $C_{20}H_{14}O_7N_6,C_6H_6$: C, 59·1; H, 3·8; N, 15·9%).

3-p-*Nitrophenyl*-5-*phenyl*-1 : 2 : 4-*triazole.*—Phenyl cyanide (5·0 g.; 0·048 mole) and *p*-nitrobenzhydrazide benzenesulphonate (17·9 g.; 0·053 mole) were heated at 200° for 3 hr.; slight frothing occurred and a small amount of a pale yellow substance, m. p. 170°, sublimed. After cooling, the crystalline melt was extracted with cold sodium hydroxide solution (10%; *ca.* 300 c.c.) and the extract acidified with concentrated hydrochloric acid. The precipitated 3-p-*nitrophenyl*-5-*phenyl*-1 : 2 : 4-*triazole* (11·2 g., 86%) was crystallized from methanol or acetone and then from light petroleum, forming white needles, m. p. 240° (Found: C, 63·2; H, 3·9; N, 20·6. $C_{14}H_{10}O_2N_4$ requires C, 63·1; H, 3·8; N, 21·0%).

5-*Phenyl*-3-α-*pyridyl*-1 : 2 : 4-*triazole.*—A mixture of phenyl cyanide (2·0 g.; 0·019 mole) and α-picolinhydrazide benzenesulphonate (6·3 g.; 0·021 mole) was heated at 200° for 3 hr. The reaction commenced with vigorous effervescence. The dark melt was extracted with sodium hydroxide solution (10%) and, on neutralization of the extract with concentrated hydrochloric acid, a pale pink solid (3·7 g., 86%) was precipitated. 5-*Phenyl*-3-α-*pyridyl*-1 : 2 : 4-

triazole crystallized from dilute alcohol as feathery, white needles, m. p. 212° (Found: C, 70·0; H, 4·7; N, 25·3. $C_{13}H_{10}N_4$ requires C, 70·3; H, 4·6; N, 25·1%).

The author is indebted to Dr. F. Lions under whose direction the early part of this work was carried out, and to Professor Sir Robert Robinson, O.M., F.R.S., for his interest. The spectra were measured by Mr. F. Hastings and Dr. F. B. Strauss.

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[*Received, May 5th,* 1954.]