

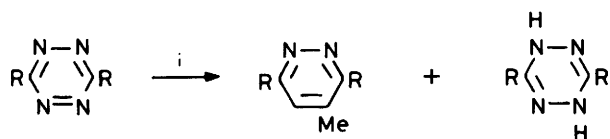
Thermal Rearrangement of 1-Alkyl-3,6-diaryl-1,4-dihydro-s-tetrazines to 1-Alkylamino-3,5-diaryl-1,2,4-triazoles

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s-Tetrazines having aryl substituents in either the 3- or 3,6-positions react readily with alkyl or aryl Grignard reagents to give 1-alkyl(or aryl)-1,4-dihydro-*s*-tetrazines. The 1-alkyl-1,4-dihydro-*s*-tetrazines rearrange in methanolic hydrogen chloride to 4-alkylamino-1,2,4-triazoles, but thermolyse readily to the less well known, isomeric 1-alkylamino-1,2,4-triazoles. Possible reaction pathways involving breakdown to nitrile and reactive intermediates such as 1,3-dipolar species are discussed.

We recently reported that 3,6-diaryl-*s*-tetrazines could be attacked by lithium amides, acting as reducing agents, to give 3,6-diaryl-1,4-dihydro-*s*-tetrazines and 3,6-diarylpyridazines¹ (Scheme 1). Grignard reagents can also act as bases² and/or as alkylating agents; hence a logical extension of this work



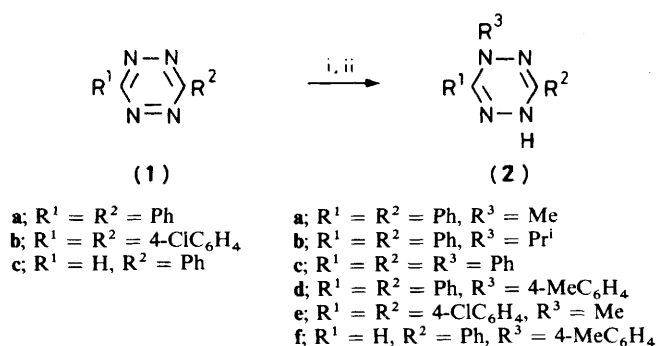
Scheme 1. Reagents: i, $\text{Pr}^i_2\text{N}^-\text{Li}^+$

appeared to be the study of the effect of Grignard reagents on *s*-tetrazines and this investigation is now reported.

Grignard reagents, both alkyl and aryl, were found to react readily with 3,6-diaryl-*s*-tetrazines (1) attacking at ring nitrogen, giving on work-up 1-alkyl(or aryl)-3,6-diaryl-1,4-dihydro-*s*-tetrazines (2) (Scheme 2). During the course of this study Neugebauer and co-workers³ published work on the action of methylmagnesium iodide on the tetrazine (1a) in which they confirmed the 1,4-substitution pattern of the product (2a) by *X*-ray analysis and spectral data. Their findings support our own, earlier crystal structure analysis⁴ [compound (2; $\text{R}^1 = \text{R}^2 = 4\text{-ClC}_6\text{H}_4\text{CH}_2$, $\text{R}^3 = \text{H}$)] which suggested that the 1,4-dihydro-*s*-tetrazine arrangement was preferred to the

Table.

	$\delta/\text{p.p.m.}$			
	H_a	H_b	H_c	H_d
<p>(1a)</p>	8.5 (4 H)	7.5 (6 H)		
<p>(2, $\text{R}^1 = \text{R}^2 = \text{Ph}$, $\text{R}^3 = \text{H}$)</p>	7.7 (4 H)	7.4 (6 H)		
<p>(2d)</p>	7.8 (2 H)	7.4 (3 H)	6.9 (4 H)	7.2 (5 H)
<p>(2f)</p>	7.8 (2 H)	7.4 (3 H)	7.2 (4 H)	



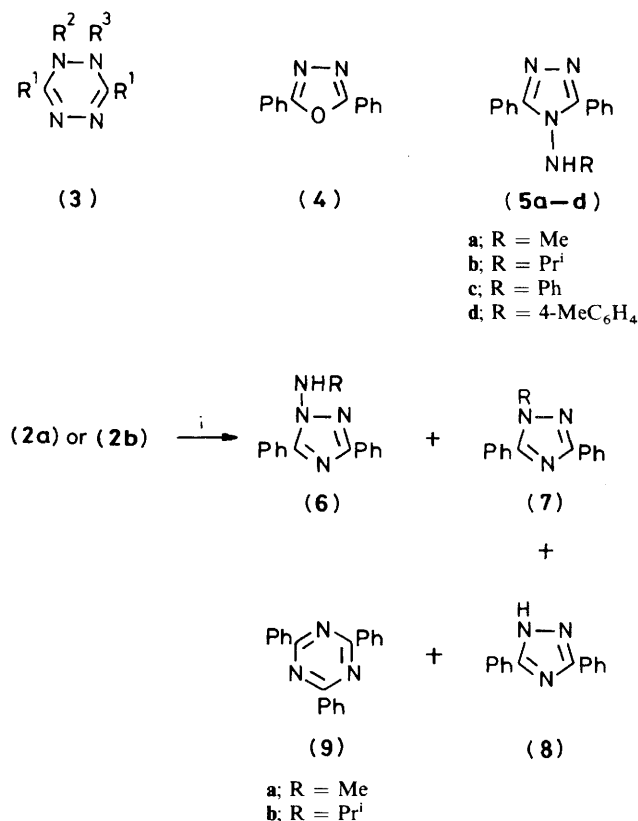
Scheme 2. Reagents: i, R^3MgBr ; ii, H_3O^+

previously often quoted 1,2-dihydro forms (3; $\text{R}^2 = \text{R}^3 = \text{H}$) which appear to exist³ only if R^2 and $\text{R}^3 \neq \text{H}$ [compound (3)].

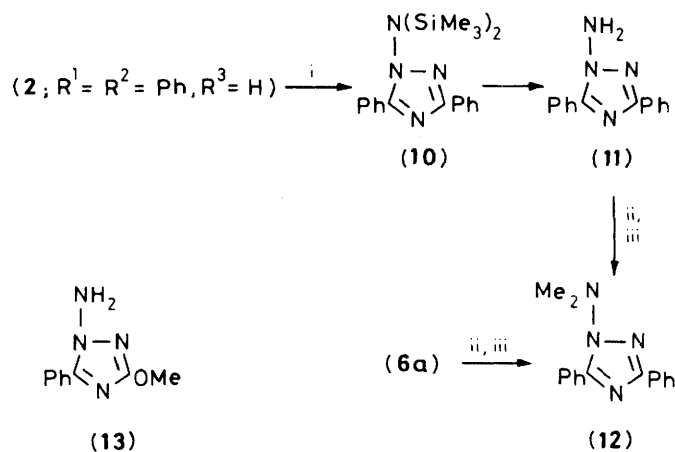
In the case of the tetrazine (1c) with an unsymmetrical 3,6-disubstitution pattern, the Grignard reagent was shown to have attacked a nitrogen adjacent to the CH rather than that adjacent to the CPh group, giving compound (2f). Although this might have been predicted on steric grounds, n.m.r. evidence points to the fact that the *ortho* protons of the 3,6-diaryl substituents of the tetrazines (1a) and (1c) are deshielded by up to 1 p.p.m. over the *meta* and *para* protons, but the introduction of a bulky aryl group on nitrogen forces the adjacent C-aryl group [e.g. of compound (2d)] out of the plane of the tetrazine ring with resultant loss of this deshielding effect. The n.m.r. spectrum of the dihydrotetrazine (2f) clearly shows that the *ortho* protons of the 3-phenyl substituent are deshielded relative to the *meta* and *para* protons, suggesting that there is no adjacent N-aryl substituent. Hence attack has clearly taken place at the less hindered nitrogen site to give the species (2f) (cf. Table).

Continuing our earlier studies on the rearrangement reactions of tetrazines and their derivatives,⁵ the dihydrotetrazine (2b) was treated with aqueous acid at room temperature and found to give 2,5-diphenyl-1,3,4-oxadiazole (4). This particular reaction appears to be sensitive to the substitution pattern of the dihydrotetrazine (2) as earlier reports quote 4-amino-1,2,4-triazoles,⁶ and diacylhydrazines⁵ as well as oxadiazoles⁷ as identified products. On the other hand, the 4-alkyl(or aryl)amino-1,2,4-triazoles (5a–d) were produced by the action of methanolic hydrogen chloride on the dihydrotetrazines in keeping with our earlier findings^{5,8} for compounds of the type (2; $\text{R}^3 = \text{H}$).

When the dihydrotetrazines (2a) and (2b) [i.e. (2; $\text{R}^3 = \text{alkyl}$)] were heated at 190 °C for 15 min, four products were isolated (Scheme 3). The principal products were the 1-alkylamino-1,2,4-triazoles (6a) and (6b) and the 1-alkyl-1,2,4-triazoles (7a) and (7b); smaller amounts of 3,5-diphenyl-1,2,4-triazole (8) and 2,4,6-triphenyl-*s*-triazine (9) were also obtained and the residues showed, by t.l.c., traces of 3,6-diphenyl-*s*-tetrazine (1a). The 1-alkyl-3,6-diaryl-1,4-dihydrotetrazines (2a) and (2b) undergo rearrangement much more readily than their non alkyl counterparts (2; $\text{R}^1 = \text{R}^2 = \text{aryl}, \text{R}^3 = \text{H}$) which according to Huisgen and co-workers,⁹ required heating at 190 °C for 15 h. Indeed we have confirmed that heating compound (2; $\text{R}^1 = \text{R}^2 = \text{Ph}, \text{R}^3 = \text{H}$) at 190 °C for 15 min results in almost total recovery of starting material along with some tetrazine (1a). Compounds of type (6) are relatively novel, groups associated with Birkofer¹⁰ and with Adembri¹¹ having prepared the only examples [(10), (11), and (13)] which we have been able to find in the literature (Scheme 4). The analyses and mass spectra of compounds (6a) and (6b) showed them to be isomeric with their precursors (2a) and (2b)

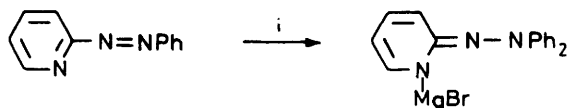


Scheme 3. Conditions: i, 190 °C, 15 min

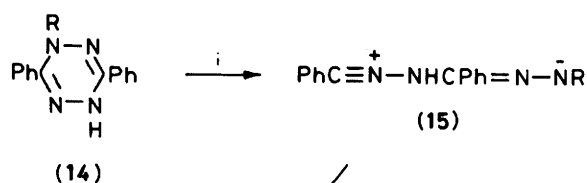


Scheme 4. Reagents: i, 130 °C, 24 h, $(\text{SiMe}_3)_2\text{NH}$; ii, BuLi; iii, MeI

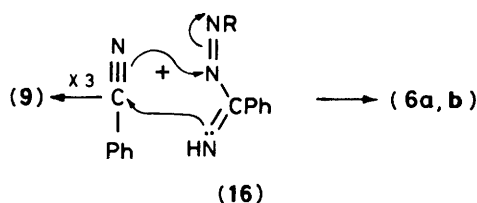
and with the 4-amino-1,2,4-triazoles (5a) and (5b). The ^1H n.m.r. spectra showed NH–CH coupling and the ^{13}C n.m.r. data showed the ring carbons to be sp^2 in compounds (6a) and (6b), ruling out the 3-alkylamino-1,2,4-triazole and 1,6-dihydro-*s*-tetrazine structures. Final proof of the 1-alkylamino-1,2,4-triazole structure was obtained by preparing compound (10) and desilylating it to the amino derivative (11) by Birkofer's procedure.¹⁰ The free amine (11) was then treated with butyllithium to give a coloured dianion which reacted with methyl iodide (2 equiv.) to yield the *N,N*-dimethylamine (12). The identical amine (12) was obtained by monomethylation of the amine (6a) under analogous conditions, finally establishing the structure of the species (6).



Scheme 5. Reagents: i, PhMgBr



a; R = Alkyl
b; R = H

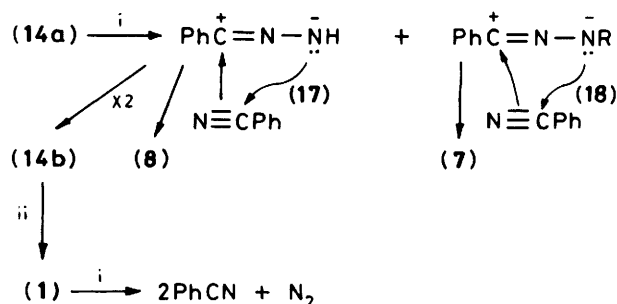


Scheme 6. Conditions: i, heat

Mechanistic Aspects.—Grignard reagents tend in most reactions to give C alkylation rather than N-alkylation but, analogously to their reaction with *s*-tetrazines, they react at nitrogen with some pyridine-azo compounds¹² (Scheme 5). The *s*-tetrazine system resembles these azo species in having an N=N moiety in both its Kekulé formulations, unlike most other nitrogen heterocyclic compounds. Indeed, the 1,2,3-benzotriazines appear to be the only other heterocyclic species which have been reported to undergo nucleophilic attack by Grignard reagents at a ring nitrogen (N-2); in this case the nature of the product depends markedly on the 4-substituent.¹³

The presence of small amounts of triphenyl-*s*-triazine in the thermolysis products (Scheme 3) suggests that benzonitrile was one product of the decomposition of the dihydrotetrazines (2a) and (2b) although the nitrile itself was never identified. The nitrile can arise from compound (14a) by cleavage of a C–N ring bond to give the betaine (15a) which eliminates benzonitrile and forms the dehydroamidrazone (16a). The 1-alkylaminotriazole (6) can then be formed by attack of the nitrile on the intermediate (16) as illustrated (Scheme 6). Support for such a mechanism comes from the work of the groups associated with Birkofer¹⁰ and Huisgen.⁹ Huisgen and co-workers postulate the betaine (15b) and the intermediate (16b) as breakdown products of the thermolysis of 1,4-dihydro-3,6-diphenyl-*s*-tetrazine (14b), benzonitrile also being a product of this reaction. In their case,⁹ the intermediate (16b) went on to react by loss of nitrogen but this route is blocked in our compound (16a) owing to the presence of the *N*-alkyl group, and we suggest that recombination of benzonitrile and the species (16a) to give the novel 1-alkylamino-1,2,4-triazoles (6a) and (6b) (Scheme 6) takes place.

In order to account for the presence of the two 1,2,4-triazoles (7) and (8), it is postulated that the dihydrotetrazine (14a) cleaves thermally giving rise to two, 1,3-dipolar intermediates (17) and (18). Such intermediates (17) and (18) are known to react with nitriles to give 1,2,4-triazoles.^{14,15} The higher yield of the *N*¹-alkyltriazoles (7) than that of the parent compound (8) could be accounted for by the inductive effect of the alkyl group (R) of the intermediate (18) rendering it more reactive than the species (17) towards the nitrile. As traces of 3,6-diphenyl-*s*-



Scheme 7. Conditions: i, heat; ii, [O]

tetrazine were found on work-up of the mixture, it is postulated that dimerisation of the dipolar species (17) occurs. Huisgen and co-workers¹⁵ report the related dimerisation of dipolar intermediates of the type (18), giving 1,3,4,6-tetrasubstituted 1,4-dihydrotetrazines. The dihydrotetrazine (14b) so formed in our reaction will readily undergo oxidation, e.g. by air, to give 3,6-diphenyl-*s*-tetrazine (1) which itself can be a source of benzonitrile (and nitrogen) on thermolysis; hence it can give rise to further nitrile for the formation of products (6)–(9) (Scheme 7).

Thermal decomposition of 1,3,6-triaryl-1,4-dihydro-*s*-tetrazines follows a different reaction pathway; this reaction is at present being investigated and will be reported later.

Experimental

M.p.s are uncorrected. ¹H N.m.r. spectra were run on a Varian EM 360 (60 MHz) instrument. ¹³C N.m.r. spectra were run on a Bruker WP 60 FT instrument resonating at 15.08 MHz.

Preparation of the *s*-Tetrazines.—The tetrazines (1a) and (1b)¹ and (1c)⁸ were prepared by the methods in the literature, and had the following m.p.s: compound (1a), 196–198 °C (lit.,¹⁶ 198 °C); compound (1b) sublimes above 300 °C (lit.,¹⁷ 315 °C); compound (1c), 123–125 °C (lit.,¹⁸ 125 °C).

Preparation of 1,4-Dihydro-3,6-diphenyl-*s*-tetrazine.—1,4-Dihydro-3,6-diphenyl-*s*-tetrazine was prepared as described in the literature,¹⁸ m.p. 192 °C (lit.,¹⁹ 192–193 °C).

Preparation of the 1-Substituted 1,4-Dihydro-3,6-diphenyl-*s*-tetrazines (2a–d).—Alkyl- and aryl-magnesium halides (Grignard reagents) were prepared in diethyl ether by the methods in the literature.²

The appropriate Grignard reagent was added dropwise to a suspension of 3,6-diphenyl-*s*-tetrazine (1a) (0.46 g) in dry diethyl ether (20 ml) under dry nitrogen at room temperature with stirring, until the red colour of the tetrazine had disappeared. The resulting yellow slurry was refluxed under nitrogen for 1 h and then poured into ice-cold dilute hydrochloric acid (0.1M; 50 ml), and extracted with ethyl acetate. The dried extract (MgSO₄) yielded, on evaporation of solvent, the 1-substituted 1,4-dihydro-3,6-diphenyl-*s*-tetrazines (2a–d) as below.

1,4-Dihydro-1-methyl-3,6-diphenyl-*s*-tetrazine (2a).—The Grignard reagent was prepared from methyl iodide. Compound (2a) (0.33 g) had m.p. 159 °C (lit.,⁷ 159 °C) (from ethanol); δ_{H} (CDCl₃) 3.0 (3 H, s, CH₃), 7.4–7.7 (10 H, m, aromatic), and 7.8 (1 H, s, NH); δ_{C} (CDCl₃) 40.7, 126.4, 127.5, 128.8, 129.0, 129.2, 129.9, 130.7, 131.3, 132.4, 150.0, and 152.6 p.p.m.; ν_{max} . (Nujol mull) 3 220 cm^{−1} (NH).

1,4-Dihydro-1-isopropyl-3,6-diphenyl-s-tetrazine (2b).—The Grignard reagent was prepared from 2-bromopropane. Compound (2b) (0.27 g) had m.p. 172–173 °C (from diethyl ether); $\delta_{\text{H}}(\text{CDCl}_3)$ 1.3 (6 H, d, 2 CH_3), 3.7 (1 H, septet, CHMe_2), 7.1 (1 H, s, NH), and 7.4–7.7 (10 H, m, aromatic); $\delta_{\text{C}}(\text{CDCl}_3)$ 20.8, 51.2, 122.8, 125.9, 126.5, 127.3, 128.6, 128.8, 129.6, 130.3, 130.7, 132.5, 149.7, and 152.2 p.p.m.; ν_{max} (Nujol mull) 3 290 cm^{-1} (NH) (Found: C, 73.7; H, 6.5; N, 20.2. $\text{C}_{17}\text{H}_{18}\text{N}_4$ requires C, 73.4; H, 6.5; N, 20.1%).

1,4-Dihydro-1,3,6-triphenyl-s-tetrazine (2c).—The Grignard reagent was prepared from bromobenzene. Compound (2c) (0.57 g) had m.p. 124–125 °C (lit.²⁰ 125–126 °C) [from diethyl ether–light petroleum (b.p. 40–60 °C)]; $\delta_{\text{H}}(\text{CDCl}_3)$ 7.1–7.7 (15 H, m, aromatic), and 7.8 (1 H, s, NH); ν_{max} (Nujol mull) 3 250 cm^{-1} (NH).

1,4-Dihydro-1-(4-methylphenyl)-3,6-diphenyl-s-tetrazine (2d).—The Grignard reagent was prepared from 4-bromotoluene. Compound (2d) (0.46 g) had m.p. 188 °C (from acetone); $\delta_{\text{H}}(\text{CDCl}_3)$ 2.2 (3 H, s, CH_3), 6.9–7.8 (14 H, m, aromatic), and 8.4 (1 H, s, NH); ν_{max} (Nujol mull) 3 320 cm^{-1} (NH) (Found: C, 78.0; H, 5.5; N, 17.3. $\text{C}_{21}\text{H}_{18}\text{N}_4$ requires C, 77.3; H, 5.5; N, 17.2%).

3,6-Bis(4-chlorophenyl)-1,4-dihydro-1-methyl-s-tetrazine (2e).—The method described above for the preparation of compounds (2a–d) was used to prepare compound (2e) from the tetrazine (1b) (0.46 g).

The Grignard reagent was prepared from methyl iodide. Compound (2e) (0.36 g) had m.p. 189–190 °C (from acetone); $\delta_{\text{H}}[\text{CDCl}_3-(\text{CD}_3)_2\text{SO}]$ 3.0 (3 H, s, CH_3), 7.4–7.9 (8 H, m, aromatic), and 9.1 (1 H, s, NH); ν_{max} (Nujol mull) 3 200 cm^{-1} (NH) (Found: M^+ 318.047 62. $\text{C}_{15}\text{H}_{12}\text{Cl}_2\text{N}_4$ requires M^+ 318.043 88).

Preparation of 1,4-Dihydro-1-(4-methylphenyl)-3-phenyl-s-tetrazine (2f).—4-Methylphenylmagnesium bromide in diethyl ether was added dropwise with stirring at room temperature to a mixture of the tetrazine (1c) (0.316 g) in dry diethyl ether (30 ml) until the red colour of the tetrazine disappeared. The mixture was refluxed for 1 h and then poured into ice-cold dilute hydrochloric acid (0.1M; 50 ml), and extracted with ethyl acetate. The dried extract (MgSO_4) yielded, on evaporation of solvent, the dihydrotetrazine (2f) (0.22 g) which was purified by chromatography [silica eluted with diethyl ether–light petroleum (b.p. 40–60 °C), 1:3] and had m.p. 140–141 °C (from diethyl ether); $\delta_{\text{H}}(\text{CDCl}_3)$ 2.3 (3 H, s, CH_3), 6.8 (1 H, s, =CH–), 7.1 (1 H, s, NH), and 7.2–7.8 (9 H, m, aromatic) (Found: C, 71.6; H, 5.6; N, 22.3. $\text{C}_{15}\text{H}_{14}\text{N}_4$ requires C, 72.0; H, 5.6; N, 22.4%).

Treatment of 1,4-Dihydro-1-isopropyl-3,6-diphenyl-s-tetrazine (2b) with Aqueous Acid.—The dihydrotetrazine (2b) (0.5 g) was dissolved in ethanol (50 ml), and dilute hydrochloric acid (6M; 15 ml) was added with stirring at room temperature under nitrogen. Stirring was continued for 8 h, and the mixture left under nitrogen for 4 days. Removal of ethanol under reduced pressure and extraction with diethyl ether gave 2,5-diphenyl-1,3,4-oxadiazole (4) (66 mg), m.p. 138–140 °C (lit.²¹ 138 °C) (from light petroleum, b.p. 40–60 °C), and had an i.r. spectrum identical with the known compound (4).²²

Treatment of the Dihydrotetrazines (2a–d) with Methanolic Hydrogen Chloride.—The dihydrotetrazine (2a–d) (0.5 g) was dissolved in dry methanol (100 ml), and dry hydrogen chloride was bubbled through the solution for $\frac{1}{2}$ h under a drying-tube (CaCl_2). The solution was left for 8 days at room temperature

(by which time the yellow colour of the dihydrotetrazine had discharged) and poured into aqueous ammonia (1M; 500 ml). Aqueous ammonia (d 0.880) was added dropwise until the solution was alkaline to litmus. Extraction with ether, drying (MgSO_4), and removal of the solvent gave the triazole (5a–d), as below.

4-Methylamino-3,5-diphenyl-1,2,4-triazole (5a). By the above method the dihydrotetrazine (2a) gave the triazole (5a) (0.301 g) which had m.p. 195–197 °C (from toluene); $\delta_{\text{H}}(\text{CDCl}_3)$ 2.47 (3 H, d, CH_3), 5.23 (1 H, d, NH), and 7.4–7.8 (10 H, m, aromatic); $\delta_{\text{C}}[(\text{CD}_3)_2\text{SO}]$ 37.7, 127.0, 127.8, 128.5, 129.7, and 153.3 p.p.m.; ν_{max} (Nujol mull) 3 300 cm^{-1} (NH) (Found: C, 72.0; H, 5.6; N, 22.6. $\text{C}_{15}\text{H}_{14}\text{N}_4$ requires C, 72.0; H, 5.6; N, 22.4%).

4-Isopropylamino-3,5-diphenyl-1,2,4-triazole (5b). By the above method the dihydrotetrazine (2b) gave the triazole (5b) (0.274 g) which had m.p. 225–227 °C (from toluene); $\delta_{\text{H}}(\text{CDCl}_3)$ 0.7 (6 H, d, 2 CH_3), 2.9 (1 H, m, CHMe_2), 5.2 (1 H, d, NH), and 7.5–8.0 (10 H, m, aromatic); ν_{max} (Nujol mull) 3 300 cm^{-1} (NH) (Found: C, 73.2; H, 6.5; N, 20.2. $\text{C}_{17}\text{H}_{18}\text{N}_4$ requires C, 73.4; H, 6.5; N, 20.1%).

4-Anilino-3,5-diphenyl-1,2,4-triazole (5c). By the above method the dihydrotetrazine (2c) gave the triazole (5c) (0.223 g) which had m.p. 264 °C (lit.²³ 263 °C) (from ethanol); $\delta_{\text{H}}[\text{CDCl}_3-(\text{CD}_3)_2\text{SO}]$ 6.4–7.9 (15 H, m, aromatic), 9.6 (1 H, s, NH); ν_{max} (Nujol mull) 3 300 cm^{-1} (NH) (lit.²³ 3 300 cm^{-1}).

4-(4-Methylphenyl)-3,5-diphenyl-1,2,4-triazole (5d). By the above method the dihydrotetrazine (2d) gave the triazole (5d) (0.303 g) which had m.p. 224–226 °C (from acetone); $\delta_{\text{H}}[\text{CDCl}_3-(\text{CD}_3)_2\text{SO}]$ 2.1 (3 H, s, CH_3), 6.8–7.8 (14 H, m, aromatic), and 9.2 (1 H, s, NH); ν_{max} (Nujol mull) 3 300 cm^{-1} (NH) (Found: C, 77.0; H, 5.5; N, 17.2. $\text{C}_{21}\text{H}_{18}\text{N}_4$ requires C, 77.3; H, 5.5; N, 17.2%).

Thermolysis of the Dihydrotetrazines (2a) and (2b).—The dihydrotetrazine (2a) or (2b) (0.5 g) was heated in an oil bath at 190–200 °C (bath temperature) for 15 min. On cooling, a glassy product formed which was dissolved in acetone and separated chromatographically [silica eluted with diethyl ether–light petroleum (b.p. 40–60 °C), 1:1]. The products obtained were as below.

From 1,4-dihydro-1-methyl-3,6-diphenyl-s-tetrazine (2a). (i) 1-Methylamino-3,5-diphenyl-1,2,4-triazole (6a) (0.154 g) had m.p. 107–109 °C (from light petroleum, b.p. 40–60 °C); $\delta_{\text{H}}(\text{CDCl}_3)$ 3.0 (3 H, d, CH_3), 5.2 (1 H, d, NH), and 7.5–8.2 (10 H, m, aromatic); $\delta_{\text{C}}(\text{CDCl}_3)$ 38.9, 126.2, 128.4, 129.1, 129.9, 131.2, 151.7, and 158.8 p.p.m.; ν_{max} (Nujol mull) 3 240 cm^{-1} (NH) (Found: C, 71.9; H, 5.7; N, 22.4. $\text{C}_{15}\text{H}_{14}\text{N}_4$ requires C, 72.0; H, 5.6; N, 22.4%).

(ii) 1-Methyl-3,5-diphenyl-1,2,4-triazole (7a) (0.098 g) had m.p. 82–83 °C (lit.²⁴ 80–82 °C) (from diethyl ether); $\delta_{\text{H}}(\text{CDCl}_3)$ 3.9 (3 H, s, CH_3), 7.4–8.1 (10 H, m, aromatic).

(iii) 3,5-Diphenyl-1,2,4-triazole (8) (0.050 g) had m.p. 187–189 °C (lit.²⁵ 189–190 °C) (from ethanol) and was identical with compound (8) prepared by an independent route.²⁵

(iv) 2,4,6-Triphenyl-s-triazole (9) which was identified by t.l.c. [diethyl ether–light petroleum (b.p. 40–60 °C), 1:3].

(v) 3,6-Diphenyl-s-tetrazine (1a) which was identified by t.l.c. [diethyl ether–light petroleum (b.p. 40–60 °C), 1:3].

From 1,4-dihydro-1-isopropyl-3,6-diphenyl-s-tetrazine (2b). (i) 1-Isopropylamino-3,5-diphenyl-1,2,4-triazole (6b) (0.13 g) had m.p. 112–113 °C (from light petroleum, b.p. 40–60 °C); $\delta_{\text{H}}(\text{CDCl}_3)$ 1.0 (6 H, d, CHMe_2), 3.8 (1 H, double septet, CHMe_2), 5.1 (1 H, d, NH), and 7.4–8.2 (10 H, m, aromatic); ν_{max} (Nujol mull) 3 250 cm^{-1} (NH) (Found: C, 73.0; H, 6.3; N, 20.0. $\text{C}_{17}\text{H}_{18}\text{N}_4$ requires C, 73.4; H, 6.5; N, 20.1%).

(ii) 1-Isopropyl-3,5-diphenyl-1,2,4-triazole (7b) (0.085 g) had m.p. 79 °C (from diethyl ether); $\delta_{\text{H}}(\text{CDCl}_3)$ 1.5 (6 H, d, CHMe_2), 4.5 (1 H, septet, CHMe_2), and 7.3–8.1 (10 H, m, aromatic)

(Found: C, 77.4; H, 6.7; N, 16.0. $C_{17}H_{17}N_3$ requires C, 77.6; H, 6.5; N, 16.0%).

(iii) 3,5-Diphenyl-1,2,4-triazole (**8**) (0.048 g), as above.

(iv) 2,4,6-Triphenyl-*s*-triazine (**9**) (0.030 g) which had m.p. 225–227 °C (lit.,²⁶ 232 °C), and an i.r. spectrum identical with that of authentic triazine (**9**) prepared by literature methods.²⁶

(v) 3,6-Diphenyl-*s*-tetrazine (**1a**) which was identified by t.l.c. [diethyl ether–light petroleum (b.p. 40–60 °C), 1:3].

Preparation of 1-Dimethylamino-3,5-diphenyl-1,2,4-triazole (12).—1-Amino-3,5-diphenyl-1,2,4-triazole (**11**) was prepared according to the literature method¹⁰ and had m.p. 194–195 °C (lit.,¹⁰ 195 °C) (from ethanol).

The triazole (**11**) (1.18 g) was dissolved in dry tetrahydrofuran (40 ml) under dry nitrogen and cooled to –10 °C. *n*-Butyl-lithium (1.6M; 6.2 ml) was added dropwise with stirring, the dark red solution was stirred at –10 °C for 10 min, and the temperature was then lowered to –70 °C. A solution of methyl iodide (0.7 ml) in dry tetrahydrofuran (10 ml) was then added dropwise with stirring, and the solution allowed to reach room temperature during 1 h before being poured into a solution of ammonium chloride (2 g) in water (400 ml). Extraction with ethyl acetate gave, after drying ($MgSO_4$) and evaporation of solvent, the triazole (**12**) (1.3 g) which had m.p. 98–99 °C (from diethyl ether); $\delta_H(CDCl_3)$ 2.9 (6 H, s, 2 CH_3), 7.3–8.1 (10 H, m, aromatic) (Found: C, 72.6; H, 6.2; N, 21.2. $C_{16}H_{16}N_4$ requires C, 72.7; H, 6.1; N, 21.2%).

Methylation of 1-Methylamino-3,5-diphenyl-1,2,4-triazole (6a).—The triazole (**6a**) (0.036 g), obtained by thermolysis of the dihydrotetrazine (**2a**), was dissolved in dry tetrahydrofuran (2 ml) under dry nitrogen, and cooled to –10 °C. *n*-Butyl-lithium (1.6M; 0.09 ml) was added dropwise with stirring, the pale straw-coloured solution was stirred at –10 °C for 10 min, and the temperature was then lowered to –70 °C. A solution of methyl iodide (0.009 ml) in dry tetrahydrofuran (2 ml) was added dropwise with stirring, and the solution allowed to reach room temperature during 1 h before being poured into a solution of ammonium chloride (0.4 g) in water (50 ml). Extraction with ethyl acetate gave, after drying ($MgSO_4$) and evaporation of solvent, the triazole (**12**) (0.042g), identical by t.l.c., mixed m.p., and i.r. spectra with that obtained above.

References

- 1 D. Hunter and D. G. Neilson, *J. Chem. Soc., Perkin Trans. I*, 1983, 1601.
- 2 J. B. Conant and A. H. Blatt, *J. Am. Chem. Soc.*, 1929, **51**, 1227.
- 3 A. Neugebauer, C. Krieger, H. Fischer, and R. Siegel, *Chem. Ber.*, 1983, **116**, 2261.
- 4 D. Hunter, D. G. Neilson, and T. J. R. Weakley, *J. Chem. Soc., Perkin Trans. I*, 1982, 1165.
- 5 D. G. Neilson, S. Mahmood, and K. M. Watson, *J. Chem. Soc., Perkin Trans. I*, 1973, 335.
- 6 A. Pinner, *Liebigs Ann. Chem.*, 1897, **297**, 221.
- 7 O. P. Shvaika and V. I. Fomenko, *Dokl. Akad. Nauk. SSSR*, 1971, **200**, 134.
- 8 R. A. Bowie, M. D. Gardner, D. G. Neilson, K. M. Watson, S. Mahmood, and V. Ridd, *J. Chem. Soc., Perkin Trans. I*, 1972, 2395.
- 9 R. Huisgen, J. Sauer, and M. Seidel, *Chem. Ber.*, 1962, **654**, 146.
- 10 L. Birkofer, A. Ritter, and P. Richter, *Chem. Ber.*, 1963, **96**, 2750.
- 11 G. Adembri, A. Camparini, F. Ponticelli, and P. Tedeschi, *J. Chem. Soc., Perkin Trans. I*, 1981, 1703.
- 12 P. F. Holt and B. P. Hughes, *J. Chem. Soc.*, 1954, 764.
- 13 J. J. A. Campbell, S. J. Noyce, and R. C. Storr, *J. Chem. Soc., Chem. Commun.*, 1983, 1345.
- 14 R. Huisgen, R. Grashey, M. Seidel, G. Wallbillich, H. Knupfer, and R. Schmidt, *Liebigs Ann. Chem.*, 1962, **653**, 105.
- 15 W. Fliege, R. Grashey, and R. Huisgen, *Chem. Ber.*, 1984, **117**, 1194.
- 16 E. Steininger, *Monatsh. Chem.*, 1966, **97**, 1195.
- 17 F. L. Scott, J. K. O'Halloran, J. O'Driscoll, and A. F. Hegarty, *J. Chem. Soc., Perkin Trans. I*, 1972, 2224.
- 18 V. A. Grakauskas, A. J. Tomaszewski, and J. P. Horwitz, *J. Am. Chem. Soc.*, 1958, **80**, 3155.
- 19 M. O. Abdel-Rahman, M. A. Kira, and M. N. Tolba, *Tetrahedron Lett.*, 1968, **35**, 3871.
- 20 O. P. Shvaika and V. I. Fomenko, *Zh. Org. Khim.*, 1974, 377.
- 21 R. Stollé, *J. Prakt. Chem.*, 1902, **69**, 157.
- 22 C. J. Pouchert, 'The Aldrich Library of Infrared Spectra,' 3rd edn, Aldrich Chemical Co. Inc., Milwaukee, 1981.
- 23 R. Stollé and K. Thoma, *J. Prakt. Chem.*, 1906, **73**, 288.
- 24 B. Buzykin, *Zh. Org. Khim.*, 1974, 2200.
- 25 I. Ya. Postovskii and N. N. Vereshchagina, *Zh. Obshch. Khim.*, 1959, **29**, 2139.
- 26 A. H. Cook and D. G. Jones, *J. Chem. Soc.*, 1941, 278.

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