Studies on Some Symmetrically and Unsymmetrically 3,6-Disubstituted 1,2-Dihydro-1,2,4,5-tetrazines including their Conversion into the Corresponding Tetrazines and 3,5-Disubstituted 4-Amino-1,2,4-triazoles

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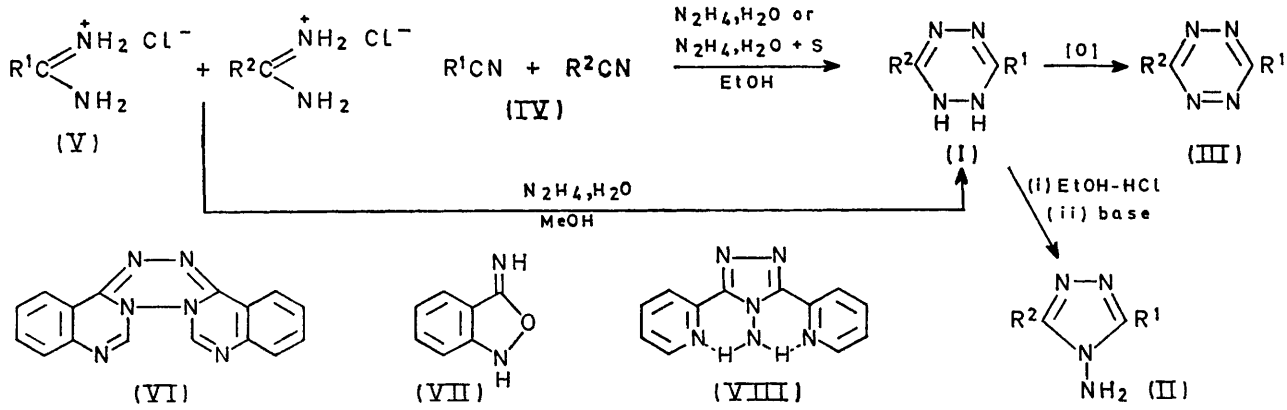
A number of symmetrically 3,6-disubstituted 1,2-dihydro-1,2,4,5-tetrazines have been prepared by the action of hydrazine hydrate on (*a*) nitriles in the presence of sulphur or (*b*) amidinium chlorides. The dihydrotetrazines yield the corresponding 1,2,4,5-tetrazines by oxidation or 4-amino-1,2,4-triazoles by rearrangement. A reliable method for distinguishing between 1,2-dihydro-1,2,4,5-tetrazines and 4-amino-1,2,4-triazoles has been obtained from n.m.r. studies.

SYMMETRICAL 3,5-disubstituted 4-amino-1,2,4-triazoles[1-3] (II) or 3,6-disubstituted 1,2,4,5-tetrazines[2,4] (III) can be prepared by the nucleophilic attack of hydrazine or its hydrate on nitriles,[5-7] imidates,[8,9] amidines,[10] or thioamides.[3] The initial product[1,2,4] tetrazines[2,4,11-13] and 4-amino-1,2,4-triazoles[1,14] are considerably more difficult to synthesise and only a few of these compounds are reported in the literature. We now report further examples of these types of compounds (I)—(III) prepared by the direct action of



Compounds (I)—(V)

	R^1	R^2		R^1	R^2
a;	Ph	Ph	h;	Ph	*p*-MeC_6H_4·CMe(OH)·
b;	*o*-NH_2·C_6H_4	*o*-NH_2·C_6H_4	i;	Ph	Me
c;	Ph	$PhCH_2$	j;	Me	*p*-MeC_6H_4·CMe(OH)·
d;	Me	Me	k;	*p*-MeC_6H_4·CMe(OH)·	*p*-MeC_6H_4·CMe(OH)·
e;	$PhCH_2$	$PhCH_2$	l;	2-pyridyl	2-pyridyl
f;	Me	Et	m;	3-pyridyl	3-pyridyl
g;	Ph	H	n;	4-pyridyl	4-pyridyl

in each case is the 1,2-dihydro-1,2,4,5-tetrazine (I) which is readily oxidised to the corresponding 1,2,4,5-tetrazine (III) or rearranges at elevated temperatures or on treatment with acid to the corresponding 4-amino-1,2,4-triazole (II). Unsymmetrically substituted 1,2,4,5-tetrazines are obtained by the action of hydrazine hydrate on either (*a*) nitriles in the presence of sulphur or (*b*) amidinium salts.

(*a*) *Nitriles and Hydrazine Hydrate in the Presence of Sulphur.*—This reaction has previously been described as a reasonable method for the preparation of dihydrotetrazines.[7] However, we found that generally the

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products tended to be the isomeric 4-amino-1,2,4-triazoles and only in the reactions involving benzonitrile [7] (IVa) and anthranilonitrile (IVb) did we isolate the corresponding 1,2-dihydro-1,2,4,5-tetrazines (Ia and b). 3,6-Diphenyl-1,2-dihydro-1,2,4,5-tetrazine (Ia) was converted under acid conditions[15] into 4-amino-3,5-diphenyl-1,2,4-triazole (IIa) and comparison of the n.m.r. spectra showed that the nitrogen protons of the dihydrotetrazine (Ia) appeared at much lower field (τ 0·9) than those of the 4-aminotriazole (IIa; τ 3·78 (see Tables 1 and 2). Similarly the 1,2-dihydrotetrazine (Ib) prepared from anthranilonitrile had the nitrogen protons at τ 1·12 in the n.m.r. spectrum. However, this compound (Ib) did not isomerise with ethanolic hydrogen chloride but yielded the hydrochloride (Ib as the hydrochloride). The dihydrotetrazine (Ib) with triethyl orthoformate gave the novel tetrazinodiquinazoline (VI).

With *o*-nitrobenzonitrile under the same conditions, a very exothermic reaction ensued, resulting in the formation of *o*-aminobenzamide. In the absence of sulphur the same product was again obtained. *p*-Nitrobenzonitrile and hydrazine hydrate–sulphur gave only unchanged *p*-nitrobenzonitrile. The formation of *o*-aminobenzamide from *o*-nitrobenzonitrile has been reported [16] under different conditions [(*a*) platinum or palladium in methanol and (*b*) hydrazine hydrate and Raney nickel [6]] and it has also been shown that the oxygen atom of the amide function comes from the nitro-group.[16] Evidence has been presented [17,18] for the formation of the intermediate (VII) which is then reduced to *o*-aminobenzamide.

Reaction of equimolar quantities of benzonitrile and benzyl cyanide with hydrazine hydrate–sulphur is very sensitive to the conditions employed. In one instance, 4-amino-3-benzyl-5-phenyl-1,2,4-triazole (IIc) [τ 3·93 (NH_2)] was obtained together with 3,5-diphenylthiadiazole and the tetrazine (IIIa). In another experiment, oxidative work-up yielded the diphenyltetrazine (IIIa), 4-amino-3,5-dibenzyl-1,2,4-triazole (IIe), and also the unsymmetrical 3-benzyl-6-phenyltetrazine (IIIc). Compounds (IIIc) and (IIc) appear to be the first known examples of aryl-aralkyl-substituted tetrazines and 4-amino-triazoles.

Treatment of acetonitrile with hydrazine hydrate–sulphur gave the dimethyltriazole [19] (IId) and not 3,6-dimethyl-1,2-dihydro-1,2,4,5-tetrazine as earlier reported.[7] The n.m.r. spectrum of compound (IId) was in agreement with the 4-amino-1,2,4-triazole structure (NH_2 at τ 4·26, see Table 2). Similarly with benzyl cyanide the product was 4-amino-3,5-dibenzyl-1,2,4-triazole (IIe) (NH_2 at τ 4·15) and not the corresponding 3,6-dibenzyl-1,2-dihydro-1,2,4,5-tetrazine.[7]

Treatment of equimolar amounts of acetonitrile and propionitrile with hydrazine hydrate–sulphur yielded the 3-ethyl-5-methyl compound (IIf) (NH_2 at τ 4·22), which is the first reported example of a mixed 3,5-dialkyl-4-amino-1,2,4-triazole.

(*b*) *Amidinium Salts in the Presence of Hydrazine Hydrate.*—Symmetrically 3,6-disubstituted 1,2,4,5-tetrazines are readily available from the action of hydrazine hydrate on amidinium salts.[10] We have now extended this synthesis to give unsymmetrically 3,6-disubstituted 1,2,4,5-tetrazines by the action of hydrazine hydrate on a mixture of two amidines. The products, albeit in some cases in small yields, were separated by chromatography. Apart from 3-phenyl-1,2,4,5-tetrazine [11] (IIg) the four other unsymmetrical products represent new substitution patterns (IIIc, h, i, and j). Neither 1,2,4,5-tetrazine (III; $R^1 = R^2 =$ H) nor its 2,6-dimethyl derivative (IIId) were recovered in our work-up procedure. This was to be expected, since the parent tetrazine (III; $R^1 = R^2 =$ H) is known to be unstable in air [4,20] and the 3,6-dialkyltetrazine (III) is also difficult to handle.[4,21,22] The synthesis of compounds (IIIh and j) also afforded as by-products the new diastereoisomeric 1-hydroxy-1-*p*-tolylethyltetrazines (IIIk). Compound (IIIk) exists as a mixture of *meso*- and (±)-isomers which can be separated by crystallisation. The higher-melting isomer has been allocated the *meso*-structure on the basis of previous work on centrosymmetric tetrazines.[10,23,24] The related triazoles (IIh and j) were prepared by the treatment of the corresponding dihydrotetrazines (Ih and j) with ethanolic hydrogen chloride.

If tetrazines (or their dihydro-derivatives) are the desired products, the amidines provide a better synthetic route; nitriles tend to give rise to aminotriazoles despite earlier suggestions to the contrary.[7]

N.m.r. Studies.—1,2-Dihydro-1,2,4,5-tetrazines (I) are usually differentiated from 4-amino-1,2,4-triazoles (II) by oxidation of the former to the highly coloured tetrazines.[2,4] However, a further reliable basis of differentiation is their n.m.r. spectra. The nitrogen protons of dihydrotetrazines (I) appear at much lower field (τ 0·9—1·12) than do those of 4-amino-1,2,4-triazoles [τ 3·78—4·26 (lit.,[14] 3·9—6·6)] (see Tables 1 and 2). For comparison purposes and completeness, the n.m.r. spectra of a number of known [25] dipyridyldihydrotetrazines * (Il—n) and dipyridyltriazoles * (IIl—n) were recorded (see Tables 1 and 2) and the signals for the nitrogen protons were found to lie approximately within the above ranges except for the di-(2-pyridyl)

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triazole (III). The nitrogen protons for compound (III) resonated at much lower field (τ 2·2) than expected and we believe this to be due to hydrogen bonding between the amino-group and the pyridyl nitrogen atoms [see (VIII)]. The i.r. spectra of compounds (IIm and n) showed two sharp, medium strong bands at 3320 and 3200 cm^{-1}. Compound (III) showed a different spectrum in the N–H region with a sharp, medium strong band at 3310 cm^{-1} and a broad, weak band centred at 3200 cm^{-1}; both bands were independent of concentration in chloroform suggesting intramolecular hydrogen bonding. Compounds (IIm and n) did not dissolve in chloroform or any other non-hydrogen-bonding solvent and had much higher m.p.s than the dipyridyltriazole (III), all factors strongly indicative of strong intramolecular hydrogen bonding for compound (III).

Nicholson [26] has calculated that for 1,2,4,5-tetrazine (III; $R^1 = R^2 = H$) the 3- and 6-protons should appear at τ −0·48 in the n.m.r. spectrum, and in carbon tetrachloride, the spectrum of 3-phenyl-1,2,4,5-tetrazine (IIIg) showed a singlet due to the lone C–H proton at τ −0·15.

TABLE 1

N.m.r. data [τ values, $(CD_3)_2SO$, J/Hz] for 3,6-disubstituted 1,2-dihydro-1,2,4,5-tetrazines

Compounds	Aromatic signals *	–NH–NH–	NH_2
(Ia)	1·95—2·3 (4H, m, *ortho*-H) 2·3—2·55 (6H, m)	0·9 (2H, s)	
(Ib)	2·45 (2H, dd, *ortho*-H, J_{ortho} 8·0, J_{meta} 1·5) 2·70—3·64 (6H, m)	1·12 (2H, s)	3·48 (4H, s)
(Il)	1·28 (2H, m, 6-H) 1·8—2·1 (4H, m, 3- and 4-H) 2·4 (2H, m, 5-H)	0·98 (2H, s)	
(Im)	1·0 (2H, d, $J_{2,4}$ 2·0, 2-H) 1·34 (2H, dd, $J_{5,6}$ 5·0, $J_{4,6}$ 2·0, 6-H) 1·84 (2H, m, 4-H) 2·53 (2H, dd, $J_{4,5}$ 8·0, 5-H)	0·68 (2H, s)	
(In)	1·25 (4H, AA′ of AA′BB′, 2- and 6-H) 2·17 (4H, BB′ of AA′BB′, 3- and 5-H)	0·53 (2H, s)	

* *Ortho*-H refers to the protons *ortho* to dihydrotetrazine ring.

TABLE 2

N.m.r. data [τ values, $(CD_3)_2SO$, J/Hz[for 3,5-disubstituted 4-amino-1,2,4-triazoles

Compounds	Aromatic signals *	CH_2Ar	CH_2Me	Me	NH_2
(IIa)	1·9—2·1 (4H, m, *ortho*-H) 2·4—2·6 (6H, m)				3·78 (2H, s)
(III)	1·28 (2H, m, 6-H) 1·80 (2H, m, 3-H) 2·01 (2H, m, 4-H) 2·50 (2H, m, 5-H)				2·2 (2H, s)
(IIm)	0·71 (2H, m, 2-H) 1·21 (2H, dd, $J_{5,6}$ 5·0, $J_{4,6}$ 2·0, 6-H) 1·50 (2H, m, 4-H) 2·33 (2H, m, 5-H)				3·5 (2H, s)
(IIn)	1·18 (4H, AA′, of AA′BB′, 2- and 6-H) 1·90 (4H, BB′ or AA′BB′, 3- and 5-H)				3·47 (2H, s)
(IIc)	1·85—2·1 (2H, m, *ortho*-H) 2·35—2·75 (8H, m)	5·83 (2H, s)			3·93 (2H, s)
(IId)				7·8 (6H, s)	4·26 (2H, s)
(IIe)	2·65 (10H, s)		5·86 (4H, s)		4·15 (2H, s)
(IIf)			7·33 (2H, q, J 7·5)	8·8 (3H, *t*, J 7·5) 7·74 (3H, s)	4·22 (2H, s)

* *Ortho*-H refers to the protons *ortho* to the triazole ring.

EXPERIMENTAL

N.m.r. spectra were determined on a Varian A60 or a Varian HA 100 instrument with tetramethylsilane as internal reference. I.r. spectra are for Nujol mulls unless otherwise stated and were recorded on a Perkin-Elmer model 157 spectrophotometer. Mass spectra were measured using a Hitachi model RMU-6E or an A.E.I. model MS-9 spectrometer.

3,6-*Diphenyl*-1,2-*dihydro*-1,2,4,5-*tetrazine* (Ia).—This was prepared as described in the literature,[7] m.p. 192° (lit.,[7,27] 192—193°).

4-*Amino*-3,5-*diphenyl*-1,2,4-*triazole* (IIa).—This was prepared by the acid rearrangement [15] of the dihydrotetrazine (Ia), m.p. 268—269° (lit.,[27] 267—269°).

3,6-*Bis*-(o-*aminophenyl*)-1,2-*dihydro*-1,2,4,5-*tetrazine* (Ib).—A mixture of anthranilonitrile (5 g), ethanol (15 ml) and hydrazine hydrate (10 ml) was cooled to 0° before the addition of flowers of sulphur (0·85 g). The mixture was left to warm to room temperature before heating under reflux in an atmosphere of nitrogen for 3 h. On

[26] I. Nicholson, *Chem. Comm.*, 1968, 1028.
[27] E. Steininger, *Monatsh.*, 1966, **97**, 1195

cooling, the *solid* (Ib) (2·4 g) was filtered off, m.p. 206—207° (from methanol) (Found: C, 62·9; H, 5·5; N, 31·8%; M^+ 266. $C_{14}H_{14}N_6$ requires C, 63·15; H, 5·3; N, 31·55%; *M*, 266), $\nu_{max.}$ 3450 and 3300 (NH_2) cm^{-1}.

1,2,4,5-*Tetrazino*[1,6-c:3,2-c']- *or* -[1,6-c:4,3-c']-*diquinazoline* (VI).—3,6-Bis-(*o*-aminophenyl)-1,2-dihydro-1,2,4,5-tetrazine (0·3 g) was heated under reflux with triethyl orthoformate (20 ml) for 16 h. On cooling, *compound* (VI) (0·2 g) was filtered off, washed with ethanol, and dried, m.p. 300° (Found: C, 66·9; H, 3·6; N, 29·7%; M^+, 286. $C_{16}H_{10}N_6$ requires C, 67·1; H, 3·5; N, 29·35%; *M*, 266), τ(CF_3·CO_2H) 1·35 (2H, s) and 1·72—2·5 (8H, m, ArH).

Reaction of o- *and* p-*Nitrobenzonitrile with Hydrazine Hydrate–Sulphur.*—The reaction was carried out as for dihydrotetrazine (Ib), except with *o*-nitrobenzonitrile (5·0 g) instead of anthranilonitrile. The solid was crystallised from chloroform to give *o*-aminobenzamide (3·0 g), m.p. 109—111° (lit.,[28] 109—111·5°). The same product was obtained in the absence of sulphur. With *p*-nitrobenzonitrile under the same conditions, no reaction took place.

4-*Amino*-3-*benzyl*-5-*phenyl*-1,2,4-*triazole* (IIc).—To a solution of benzonitrile (5·15 g), benzyl cyanide (5·85 g), ethanol (40 ml), and hydrazine hydrate (20 ml) at 0° were added flowers of sulphur (2 g). When the effervescence had subsided, the mixture was heated under reflux in an atmosphere of nitrogen for 1·5 h. On cooling, the solid was filtered off to yield the required *product* (IIc) (3·8 g), m.p. 190—192° (from chloroform) (Found: C, 71·8; H, 5·6; N, 22·7%; M^+, 250. $C_{15}H_{14}N_4$ requires C, 71·95; H, 5·65; N, 22·4%; *M*, 250), $\nu_{max.}$ 3300 and 3100 (NH_2) cm^{-1}.

The filtrate was evaporated to dryness and the residue was chromatographed on a column of silica gel (40 g). Elution (chloroform) gave red 3,6-diphenyl-1,2,4,5-tetrazine (2·9 g), m.p. 199—200° (lit.,[27] 198°). Further elution with chloroform–methanol (9 : 1) and finally methanol gave 2,5-diphenyl-1,3,4-thiadiazole (0·68 g), m.p. 141—143° (lit.,[29] m.p. 142—143°) [see also preparation of (IIIc)].

4-*Amino*-3,5-*dimethyl*-1,2,4-*triazole* (IId).—To a solution of acetonitrile (4·1 g), ethanol (75 ml), and hydrazine hydrate (50 ml) at 0° were added flowers of sulphur (3 g). When the effervescence had subsided the mixture was heated under reflux in an atmosphere of nitrogen for 3 h. After evaporation to dryness the residue was crystallised from chloroform to yield the required product (0·8 g), m.p. 195° (lit.,[19] 196·5—197·5°), $\nu_{max.}$ 3220 and 3120 (NH_2) cm^{-1}.

4-*Amino*-3,5-*dibenzyl*-1,2,4-*triazole* (IIe).—This was prepared as was the triazole (IId) except that benzyl cyanide (5·85 g) was used instead of acetonitrile. After evaporation, the residue was chromatographed [column; silica gel (40 g)]. Elution [chloroform–methanol (9 : 1)] eventually gave the required product (IIe) (2·0 g), m.p. 163—164° (from aqueous methanol) (lit.,[30] 160—162°) (Found: C, 72·5; H, 6·1; N, 21·1%; M^+, 264. $C_{16}H_{16}N_4$ requires C, 72·7; H, 6·1; N, 21·2%; *M*, 264), $\nu_{max.}$ 3250 and 3150 (NH_2) cm^{-1}.

4-*Amino*-3-*ethyl*-5-*methyl*-1,2,4-*triazole* (IIf).—The preparation was as before except that a mixture of acetonitrile (4·1 g) and propionitrile (5·5 g) was used. After evaporation, the residue was passed down a silica gel (40 g) column. Elution [chloroform–methanol (9 : 1)] removed impurities and final elution with methanol gave the required *product* (IIf) (1·0 g), m.p. 122—124° [from methanol–light petroleum (b.p. 40—60°)] (Found: C, 47·3; H, 7·9; N, 44·6%; M^+, 126. $C_5H_{10}N_4$ requires C, 47·6; H, 8·0; N, 44·4%; *M*, 126), $\nu_{max.}$ 3200 and 3100 (NH_2) cm^{-1}.

3-*Phenyl*-1,2,4,5-*tetrazine* (IIIg).—Formamidine acetate (4·2 g) and benzamidine hydrochloride (6·2 g) were heated under reflux with hydrazine hydrate (99%; 12 ml) in methanol (80 ml) under nitrogen for 3 h. After addition to water, a small amount (0·3 g) of dihydrotetrazine was filtered off and the solution was extracted with ether to give further impure dihydrotetrazine (3·6 g), which was oxidised by exposure to air (*ca.* 60 h). A sample of the tetrazine mixture (1 g) was chromatographed [silica, cyclohexane–ether (19 : 1)] yielding 3,6-diphenyl-1,2,4,5-tetrazine (IIIa) (0·35 g), m.p. 195—198° (identical with authentic material; lit.,[27] 198°), followed, on elution with ether, by 3-phenyl-1,2,4,5-tetrazine (IIIg) (0·15 g), m.p. 123—125° (lit.,[11] 125°). A yellow band remained on the column but was not further investigated. Tetrazine (IIIg) showed n.m.r. signals at τ (CCl_4) −0·15 (1H, s), 1·1—1·5 (2H, m), and 2·2—2·8 (3H, m), the multiplets representing the phenyl group.

(±)-3-(1-*Hydroxy*-1-p-*tolylethyl*)-6-*phenyl*-1,2,4,5-*tetrazine* (IIIh).—Similarly, benzamidine hydrochloride (1·2 g), (±)-2-hydroxy-2-*p*-tolylpropionamidinium chloride[31] (1·2 g) and hydrazine hydrate (99%) (15 ml) in methanol (50 ml) yielded a dihydrotetrazine mixture which was oxidised in the usual way[10] with sodium nitrite and sulphuric acid. Addition of ice–water yielded tetrazine (1·3 g) which slowly precipitated. The tetrazine mixture (1 g) was chromatographed [cyclohexane–ethyl acetate (99 : 1), silica] to yield 3,6-diphenyl-1,2,4,5-tetrazine (0·3 g) (IIIa) as above. Cyclohexane–acetone (98 : 2) eluted the *tetrazine* (IIIh) (0·25 g), m.p. 122—124° (from aqueous methanol) (Found: C, 69·8; H, 5·6; N, 19·1. $C_{17}H_{16}N_4O$ requires C, 69·9; H, 5·5; N, 19·2%). Finally there was eluted from the column with chloroform a mixture of meso- and (±)-3,6-*bis*-(1-*hydroxy*-1-p-*tolylethyl*)-1,2,4,5-*tetrazines* (IIIk) (0·3 g), m.p. 140—144°. Fractional crystallisation of the diastereoisomers from aqueous methanol (100 ml; 1 : 2) yielded the meso-*tetrazine*[10,23,24] (IIIk), m.p. 166—167° (Found: C, 68·8; H, 6·3; N, 16·0. $C_{20}H_{22}N_4O_2$ requires C, 68·6; H, 6·3; N, 16·0%) and the (±)-*tetrazine* (IIIk), m.p. 139—144° (Found: C, 68·6; H, 6·3; N, 16·0%).

3-*Methyl*-6-*phenyl*-1,2,4,5-*tetrazine* (IIIi) *and its Dihydro-derivative* (Ii).—Acetamidine hydrochloride (9·4 g), benzamidine hydrochloride (14·4 g), and hydrazine hydrate (99%; 15 ml) were treated as before. Addition of water (500 ml) yielded 3,6-diphenyl-1,2-dihydro-1,2,4,5-tetrazine (0·45 g), m.p. 192° (lit.,[7,27] 192—193°). Extraction with ether yielded a solid (3 g), which was oxidised in the usual way[10] and separated on a ' dry column ' [silica gel (500 g) deactivated with 15% water on a 5 ft nylon column;[32] cyclohexane–ethyl acetate (4 : 1)]. Two tetrazine bands were cut from the column and extracted with ether, the first yielded 3,6-diphenyl-1,2,4,5-tetrazine (IIIa) (0·2 g) and the second 3-*methyl*-6-*phenyl*-1,2,4,5-*tetrazine* (IIIi) (1·3 g), m.p. 75—77° (Found: C, 62·7; H, 4·8; N, 32·6. $C_9H_8N_4$ requires C, 62·8; H, 4·7; N, 32·6%). A methanolic

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extract of the residue from the column gave 4-amino-3,5-diphenyl-1,2,4-triazole (0·8 g), m.p. 261—264° (lit.,[27] 267—269°). The original mother liquors, on oxidation with nitrous acid and ether extraction, gave a solid (2·9 g), which yielded tetrazine (IIIi) (0·7 g) in addition to the above. The tetrazine (IIIi) (1 g) was reduced with sodium dithionite,[10,33] added to water (200 ml) and extracted with ether. The light yellow *3-methyl-5-phenyl-1,2-dihydro-1,2,4,5-tetrazine* (0·8 g) had m.p. 140—142° (Found: C, 62·1; H, 5·8; N, 32·3. $C_9H_{10}N_4$ requires C, 62·1; H, 5·8; N, 32·2%).

(±)-3-(1-*Hydroxy*-1-p-*tolylethyl*)-6-*methyl*-1,2,4,5-*tetrazine* (IIIj).—2-Hydroxy-2-*p*-tolylpropionamidinium chloride [31] (10·7 g), acetamidinium chloride (4·7 g), hydrazine hydrate (99%; 7·5 ml), and methanol (75 ml) yielded dihydrotetrazine mixture (3·8 g), which was oxidised [10] to tetrazine (3·1 g) and separated on a dry column [32] as before. The separated tetrazine bands were extracted from the cut column with acetone giving the desired *tetrazine* (IIIj) (0·6 g), m.p. 83—86° (from aqueous methanol) (Found: C, 62·6; H, 6·1; N, 24·1. $C_{12}H_{14}N_4O$ requires C, 62·4; H, 6·1; N, 24·5%) and the diastereoisomeric tetrazines (IIIk) (2·1 g) described before.

3-*Benzyl*-6-*phenyl*-1,2,4,5-*tetrazine* (IIIc).—(*a*) Benzamidine hydrochloride (4·1 g) and phenylacetamidine hydrochloride (5·1 g) were stirred at 30—40° in methanol (50 ml) under nitrogen with hydrazine hydrate (99%; 7·5 ml) for 3 h. The resultant precipitate (0·9 g) on oxidation [10] gave 3,6-diphenyl-1,2,4,5-tetrazine (IIIa) (0·8 g) The mother liquors were diluted with water (150 ml) and extracted with ether to give 4-amino-3-benzyl-5-phenyl-1,2,4-triazole (0·2 g), m.p. 191—194° [as before; (IIc)] and, on evaporation, further solid (1·3 g), which was oxidised with nitrous acid in the cold. A dried (K_2CO_3) ethereal extract of this acidic solution yielded solid (1·3 g) which was eluted from a silica column with benzene giving four fractions; (i) 3,6-diphenyl-1,2,4,5-tetrazine (IIIa) (0·9 g), (ii) 3,6-dibenzyl-1,2,4,5-tetrazine (IIIe) (0·1 g), m.p. 74° (lit.,[34] 74°), (iii) 2,5-dibenzyl-1,3,4-oxadiazole (0·14 g), m.p. 97—98° (lit.,[35] 98°), and (iv) 3-*benzyl*-6-*phenyl* 1,2,4,5-*tetrazine* (IIIc) (0·1 g), m.p. 110—111° (from aqueous ethanol) (Found; C, 72·7; H, 4·9; N, 22·7. $C_{15}H_{12}N_4$ requires C, 72·5; H, 4·8; N, 22·6%). The n.m.r. spectrum of (IIIc) showed signals at τ 5·45 (2H, s), 1·25—1·55 (2H, m), and 2·45—2·80 (8H, m).

(*b*) To a mixture of benzyl cyanide (5·8 g), benzonitrile (5·1 g), and hydrazine hydrate (99%; 20 ml) in ethanol (30 ml) was cautiously added sulphur (2 g). The mixture was heated under reflux for 3 h, cooled, and filtered. The solution was heated with more sulphur (1 g) for 3 h, cooled then filtered. The combined residues, on oxidation,[10] yielded a red solid which was extracted with hot hydrochloric acid (5M). The acidic fraction, on being made basic, yielded 4-amino-3,5-dibenzyl-1,2,4-triazole (IIe) (2·2 g), m.p. 160—161° (from aqueous ethanol) (lit.,[30] 160—162°). The residual red solid was recrystallised from cyclohexane to yield 3,6-diphenyl-1,2,4,5-tetrazine (IIIa) (1·7 g). The evaporated liquors, on chromatographic separation [silica, cyclohexane–ether (1 : 1)], yielded 3-benzyl-6-phenyl-1,2,4,5-tetrazine (0·43 g) (IIIc).

4-*Amino*-3-(1-*hydroxy*-1-p-*tolylethyl*)-5-*phenyl*-1,2,4-*triazole* (IIh).—Tetrazine (IIIh) (0·17 g) was dissolved in ethanol–water (10 ml; 1 : 1) and sodium dithionite added slowly to the stirred solution until the red colour was discharged. Water (100 ml) was then added and the resultant crude dihydrotetrazine (Ih) (0·17 g), m.p. 170—174°, was filtered and dried. This solid was dissolved in dry methanol and treated with hydrogen chloride at 0° for 10 min. The solution, after standing for 12 h was evaporated and the residue was dissolved in the minimum of ethanol. Ammonia (*d* 0·88) was then added, yielding the desired 4-*amino*-1,2,4-*triazole* (IIh) (0·05 g), m.p. 170—171° (from aqueous ethanol) (Found: C, 69·6; H, 6·0; N, 19·2. $C_{17}H_{18}N_4O$ requires C, 69·4; H, 6·1; N, 19·1%).

4-Amino-3-(1-*hydroxy*-1-p-*tolylethyl*)-5-*methyl*-1,2,4-*triazole* (IIj).—Tetrazine (IIIj) (0·3 g) was treated as for compound (IIIh). Evaporation of the methanolic hydrogen chloride yielded the *4-aminotriazole hydrochloride hemihydrate* (0·2 g) (IIj as the hydrochloride), m.p. 159—162° (from methanol–ether) (Found: C, 52·3; H, 6·6; N, 19·9. $C_{12}H_{17}ClN_4O,0{\cdot}5H_2O$ requires C, 51·9; H, 6·5; N, 20·1%).

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