Lead Tetraacetate Oxidation of 1- and 2-Amino-5-phenyl[1,2,3]triazolo[4,5-*d*]-[1,2,3]triazoles; Synthesis of a Fused 1,2,3,4-Tetrazine

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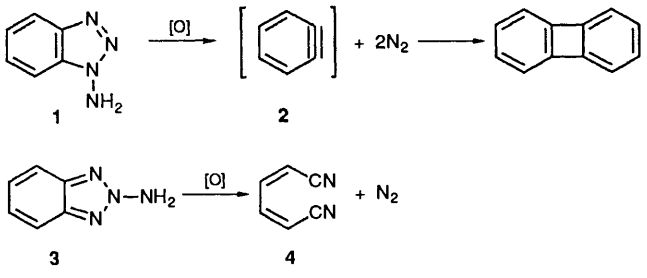
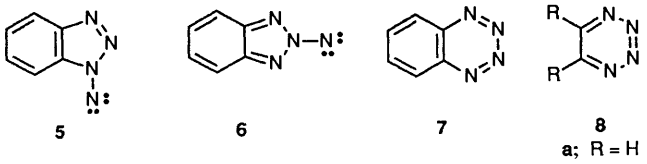
N-Amination of 5-phenyl-1,5-dihydro[1,2,3]triazolo[4,5-*d*][1,2,3]triazole with *O*-(mesitylsulphonyl)-hydroxylamine afforded 1-amino and 2-amino derivatives. The oxidation of the 1-amino derivative with lead tetraacetate gave 2-phenyl[1,2,3]triazolo[4,5-*e*][1,2,3,4]tetrazine, whereas that of the 2-amino derivative resulted in the formation of 1,3-dicyano-2-phenyltriazenimide. The tetrazine was decomposed in solvent to form 2-phenyl-5-cyano-2*H*-1,2,3,4-tetrazole and 2-phenyl-2*H*-1,2,3-triazole. The degradation mechanism is also reported.

It has been reported that the oxidation of *N*-amino-1,2,3-triazoles gives rise to two types of reaction products, depending upon the site of the amino substituent.[1] For example, the oxidation of 1-amino-1*H*-benzotriazole **1** with lead tetraacetate (LTA) afforded biphenylene which was supposed to be formed *via* the dimerization of benzyne **2**, produced from the elimination of two molecules of nitrogen from substrate **1**. On the other hand, 2-amino-2*H*-benzotriazole **3** gave muconononitrile **4** *via* the elimination of one mole of nitrogen under the same oxidation conditions (Scheme 1).[2] These products were



Scheme 1

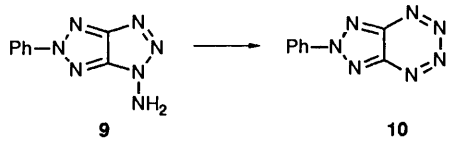
supposed to be obtained from the direct denitrogenation of *N*-nitrenes **5** and **6**[1-3] which were derived from the oxidation of compounds **3** and **4**, respectively, whereas, there is a possibility that 1,2,3,4-benzotetrazine **7** might exist as an intermediate formed *via* ring expansion of the nitrene **5** or **6**.[2,3] However, the isolation or the characterization of 1,2,3,4-tetrazines **8**,



including the bicycle **7** has never been reported in spite of their fundamental structure.[4] In a previous paper,[5] we have shown that the LTA oxidation of 1-amino-5-phenyl-1,5-dihydro[1,2,3]triazolo[4,5-*d*][1,2,3]triazole **9** afforded 2-phenyl-2*H*-[1,2,3]triazolo[4,5-*e*][1,2,3,4]tetrazine **10** (Scheme 2). This paper describes our detailed results, including the oxidation of 2-amino-5-phenyl-2,5-dihydro[1,2,3]triazolo[4,5-*d*][1,2,3]triazole **11** with LTA.

Results and Discussion

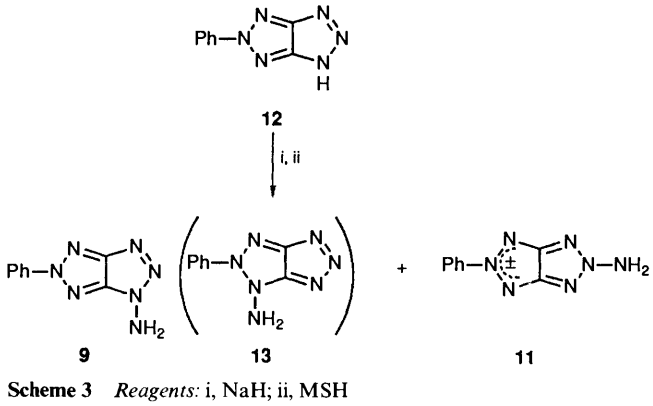
At the preliminary planning of a tetrazine synthesis, we assumed that 1,2,3,4-tetrazines were involved as intermediates of the oxidation of *N*-aminotriazoles; this was based on our previous



Scheme 2 *Reagents:* LTA

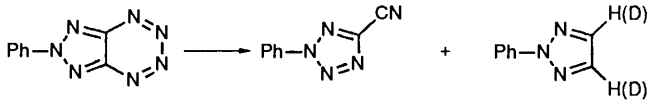
studies on the oxidation of *N*-aminopyrazoles to afford 1,2,3-triazines.[6] The denitrogenation was supposed to occur because of the instability of intermediary tetrazines to give the decomposition products. Therefore, in order to stabilize the tetrazine which would be formed by the oxidation of the *N*-amino derivative, ring-fused aminotriazoles were selected as the substrate. We thought that the fusion with a five-membered ring would be suitable because the fusing bond was represented as a single bond in the most probable canonical structure. It was supposed that such a ring system could hardly form the energetically unfavoured five-membered heteroaryne which was obtained by nitrogen elimination from the tetrazine. We selected 5-phenyl-1,5-dihydro[1,2,3]triazolo[4,5-*d*][1,2,3]triazole **12**,[7] which is consistent with the above conditions.

The *N*-amination of compound **12**[7] with *O*-(mesitylsulphonyl)hydroxylamine[8] (MSH) afforded two *N*-aminated compounds. The major one (46%) was determined to be the 2-amino derivative **11** because its ^{13}C NMR spectrum showed one carbon signal other than those of a phenyl group. The ^{13}C NMR spectrum of the minor product (22%) showed two carbon signals not arising from a phenyl group, hence the compound must be the 1-amino-2-phenyl or 1-amino-5-phenyl derivative (**13** or **9**). It is difficult to distinguish between these two compounds, but the NMR spectrum of the 1-acetyl-5-phenyl derivative (which is a synthetic precursor of compound **12**) was closely similar to that of the amine **9** (or **13**), therefore the structure of the minor product was proposed as being **9** (Scheme 3).



Scheme 3 *Reagents:* i, NaH; ii, MSH

The LTA oxidation of compound **9** provided the reddish solid **10** (81%) *which exploded on impact or on the application of heat.* Its NMR spectra at −20 °C showed only phenyl protons and one quaternary carbon signal other than those of a phenyl group. A methylene dichloride solution of the tetrazine **10** was kept at room temperature whereupon degradation occurred to afford 5-cyano-2-phenyl-2*H*-1,2,3,4-tetrazole[9] **14** and 2-phenyl-2*H*-1,2,3-triazole[10] **15** accompanied by evolution of nitrogen (Scheme 4). When the degradation

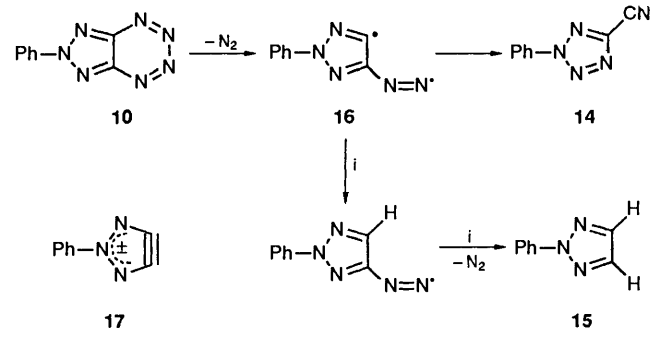


10 **14** **15**

Scheme 4 *Reaction conditions:* room temperature

Solvent	Yield (%)	
	14	**15**
$CHCl_3$	50	50
$CDCl_3$	78	8

was performed in $CDCl_3$, the introduction of deuterium at the 4- and 5-position of compound **15** was confirmed by GC-MS. The yield of product **15** was lower, but that of product **14** was higher in $CDCl_3$ than in $CHCl_3$. This fact suggested that the change in product distribution was due to a first-order isotope effect which originated from the hydrogen-abstraction step of the azo diradical (see structure **16**, Scheme 5) to form the



10 **16** **14** **17** **15**

Scheme 5 *Reagent:* i, R–H

triazole. The spectral data and the degradation process of the compound **10** suggested that it had the triazolotetrazine structure indicated. The structure of compound **10** was finally concluded by an X-ray crystallographic analysis.

The X-ray crystallographic analysis of compound **10**, which was presented in our previous communication,[5] was not sufficiently accurate (*R* 0.168) because of the instability of the crystal of compound **10** at room temperature. X-Ray crystallography at −120 °C afforded satisfactory data (*R* 0.069).[11] Fig. 1 exhibits an ORTEP drawing of compound **10**, together with bond lengths and angles. The triazolotetrazine ring is almost planar, and C(9) shows the biggest deviation (0.017 Å) from the least-squares plane. The bond length N(5)–N(6) (1.388 Å) is longer than the other N(4)–N(5) (1.328 Å) or N(6)–N(7) (1.323 Å) N–N bonds, hence the N(5)–N(6) bond might have more single-bond character than the other two bonds. This elongated bond might give rise to the stability of compound **10**. The planarity and the symmetrical character of compound **10**, which were shown by X-ray analysis and the ^{13}C NMR spectrum, suggested its aromatic nature.

With respect to the degradation pathway of compound **10**, semiempirical AM1[12] calculations were performed concerning the decomposition of the parent 1,2,3,4-tetrazine **8a**, and the results suggested that the degradation to $C_2H_2 + 2N_2$ rather

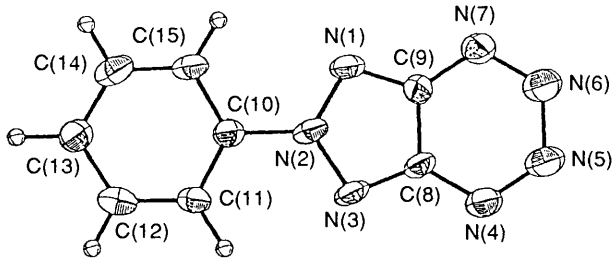


Fig. 1 ORTEP drawing of compound **10**. Bond lengths and angles are as follows: N(1)–N(2) 1.335, N(2)–N(3) 1.348, N(1)–C(9) 1.344, N(2)–C(10) 1.444, N(3)–C(8) 1.334, N(4)–N(5) 1.328, N(5)–N(6) 1.388, N(6)–N(7) 1.323, N(4)–C(8) 1.354, N(7)–C(9) 1.332, C(8)–C(9) 1.383 Å; N(1)–N(2)–N(3) 118.3, N(1)–C(9)–C(8) 108.9, N(2)–N(3)–C(8) 100.1, N(2)–N(1)–C(9) 101.3, N(3)–C(8)–C(9) 111.2, N(4)–N(5)–N(6) 122.6, N(4)–C(8)–C(9) 121.3, N(7)–C(9)–C(8) 122.8, N(1)–N(2)–C(10) 120.6, N(3)–N(2)–C(10) 121.9°.

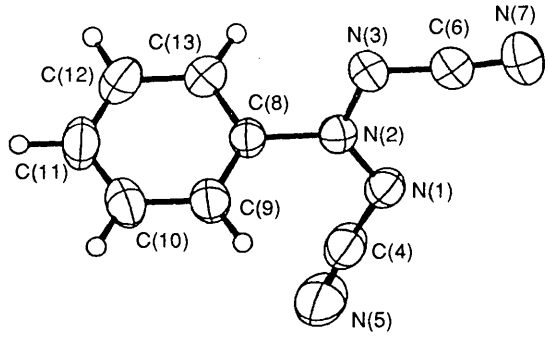
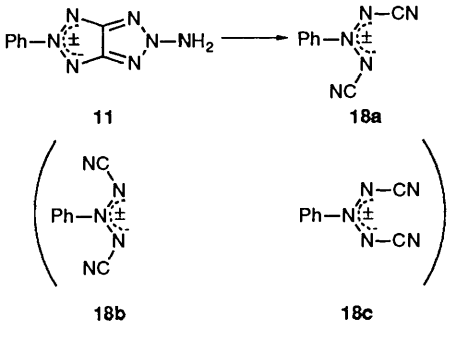


Fig. 2 ORTEP drawing of compound **18a**. Bond lengths and angles are as follows: N(1)–N(2) 1.296, N(2)–N(3) 1.299, N(1)–C(4) 1.344, C(4)–N(5) 1.145, N(3)–C(6) 1.346, C(6)–N(7) 1.148, N(2)–C(8) 1.462 Å; N(1)–N(2)–N(3) 121.2, N(2)–N(3)–C(6) 113.4, N(3)–C(6)–N(7) 173.6, N(2)–N(1)–C(4) 115.2 (N(1)–C(4)–N(5) 171.4, N(1)–N(2)–C(8) 124.1, N(3)–N(2)–C(8) 114.5°.

than $2HCN + N_2$ was favoured and that the pathway was non-concerted; the N(2)–N(3) bond breaks first, followed by stepwise N_2 eliminations.[13]

The degradation mechanism for compound **10** was considered by reference to the above calculation results. First, compound **10** breaks at the N(5)–N(6) bond, followed by denitrogenation to afford the biradical intermediate **16**. The biradical **16** was transformed into a cyanotetrazole **14**, or else it abstracted hydrogen (from solvent) to form a triazole **15**. The observed isotope effect was due to the step in which biradical **16** abstracted hydrogen from the solvent. Triazoloheteroaryne **17** would be a minor intermediate, if formed at all, because of its energetically unfavoured structure. Therefore the biradical **16** was transferred into compound **14** or compound **15** without going through the intermediate **17** (Scheme 5).

The LTA oxidation of compound **11** afforded (*E*,*Z*)-1,3-dicyano-2-phenyltriazeniumide **18a** (Scheme 6). The structure of compound **18a** was determined by its spectral data, elemental



11 **18a** **18b** **18c**

Scheme 6 *Reagent:* LTA

analysis and X-ray crystallographic analysis.[14] Fig. 2 exhibits the result of the X-ray crystallographic analysis of the mesoionic compound **18a**. The *E,Z* configuration of compound **18a** was determined from its non-equivalent cyano carbon signals (δ_C 109.6 and 109.8), and was confirmed by X-ray crystallographic analysis. The equivalent bond lengths for N(1)–N(2) and N(2)–N(3) indicated the delocalization of 4π electrons on N(1), N(2) and N(3). Among three possible geometrical isomers [*E,Z*; *E,E* (**18b**); and *Z,Z* (**18c**)], only the *E,Z* form was obtained (Scheme 6). It was reported[15] that *ab initio* MO calculation predicted the relative stabilities of the parent azimines (triazeniumides) as *Z,Z* > *E,Z* ≫ *E,E*, and that the energy difference between the *Z,Z* and *E,Z* forms was small (7 kJ mol^{-1}). When the ^{13}C NMR spectrum of compound **18a** was measured on the GX-400 machine in deuteriated toluene at 100 °C, two cyano carbon signals became broadened. Cooling of the sample caused the broad signals to revert again to the sharp signals which originated from the *E,Z* form. The substituent effects might have resulted in the reversal of the stabilities of *Z,Z* and *E,Z* forms in our case. It was reported that open-chain azimines were synthesized by the reaction of an azo compound and nitrenes[16] and by the ring-opening reaction of tetrazolium salts.[17] Oxidation of compound **11** was therefore a new synthetic route to the azimines.

Conclusions.—The synthesis of the triazolotetrazine **10**, which is the first example of an aromatic 1,2,3,4-tetrazine ring system, was performed by the oxidation of the 1-amino-1,5-dihydrotriazolotriazole **9**, and the oxidation of 2-amino-triazolotriazole **11** resulted in the formation of 1,3-dicyano-2-phenyltriazeniumide **18a** which was a ring-opening product of the *N*-nitrene. It was shown that the degradation of compound **10** proceeded *via* stepwise elimination of nitrogen, and this result was supported by the AM1 calculations. Accordingly, the stability of the 1,2,3,4-tetrazine ring is suggested to depend on the facility of the requisite bond [**8a**; N(2)–N(3); **10**; N(5)–N(6)]-breaking process. Hence the reason for the isolation of compound **10** might not be the instability of the corresponding heteroaryne. The rationale behind the stability of various 1,2,3,4-tetrazines is the subject of continuing studies.

Experimental

All m.p.s were taken on a Yanaco micro melting point apparatus and are uncorrected. NMR spectra were measured with a JEOL JNM-FX100 or a GX-400 spectrometer, using tetramethylsilane as internal standard. IR spectra were recorded on a JASCO A102 spectrometer. Mass spectra were taken on a JEOL D-300 instrument. Gas chromatography was performed with a Shimadzu GC-9A instrument with 2% SE-30 on Chromosorb as column-packing material. For the X-ray crystallographic analysis, see the cited references.

1-Amino-5-phenyl-1,5-dihydro[1,2,3]triazolo[4,5-d][1,2,3]-triazole **9** *and 2-Amino-5-phenyl-2,5-dihydro[1,2,3]triazolo[4,5-d][1,2,3]triazole* **11**.—A suspension of sodium hydride (60%; 129 mg, 3.23 mmol) in tetrahydrofuran (THF) (2 cm^3) was cooled at 0 °C under N_2, and a THF solution (5 cm^3) of 5-phenyl-1,5-dihydro[1,2,3]triazolo[4,5-*d*][1,2,3]triazole[6] **12** (0.5 g, 2.69 mmol) was added. After the mixture had been stirred for 15 min, a dry benzene solution (20 cm^3) of MSH* [35%; (stored with frozen water, and the content was determined by iodometry) 1.68 g, 2.13 mmol] was added dropwise to the vigorously stirred mixture at 0 °C. The reaction was allowed to continue for 15 min, and then the mixture was filtered through Celite. The filtrate was washed successively with 20% aq. $KHCO_3$ and 25% aq. Na_2SO_3, dried over $MgSO_4$, and evaporated at low temperature. The residue was recrystallized from THF–hexane to afford compound **9** (105 mg). The mother liquor was evaporated to leave a residue, which was chromatographed on silica gel (hexane–AcOEt, 2:1) to give more compound **9** (13 mg) and compound **11** (249 mg, 46%). Total yield of compound **9** was 22%.

1-Amino-5-phenyl-1,5-dihydro[1,2,3]triazolo[4,5-d][1,2,3]-triazole **9** was obtained as needles from Et_2O; m.p. 110–112 °C (decomp.) (Found: C, 47.5; H, 3.45; N, 48.65. $C_8H_7N_7$ requires C, 47.8; H, 3.5; N, 48.7%); δ_H[100 MHz; $(CD_3)_2SO$] 7.19 (2 H, s), 7.40–7.65 (3 H, m) and 8.04–8.20 (2 H, m); δ_C[400 MHz; $(CD_3)_2SO$] 119.7, 129.2, 129.6, 139.6, 144.9 and 159.4; *m/z* 173 ($M^+ - N_2$) and 145 ($M^+ - NCNNH_2$).

2-Amino-5-phenyl-2,5-dihydro[1,2,3]triazolo[4,5-d][1,2,3]triazole **11** was obtained as pale brown needles from aq. EtOH, m.p. 151–153 °C (decomp.) (Found: C, 47.9; H, 3.4; N, 48.75. $C_8H_7N_7$ requires C, 47.8; H, 3.5; N, 48.7%); δ_H[100 MHz; $(CD_3)_2SO$] 7.40–7.70 (3 H, m), 8.10–8.22 (2 H, m) and 9.25 (2 H, s); δ_C[400 MHz; $(CD_3)_2SO$] 119.7, 128.8, 129.7, 144.1 and 155.3; *m/z* 201 (M^+).

Oxidation of 1-Amino-5-phenyl-1,5-dihydro[1,2,3]triazolo-[4,5-d][1,2,3]triazole **9**.—To a stirred solution of compound **9** (50 mg, 0.25 mmol) in CH_2Cl_2 at 0 °C was added LTA (90%; 125 mg, 0.25 mmol) by portions. After reaction for 15 min at 0 °C, the mixture was washed with 20% aq. $KHCO_3$, dried over $MgSO_4$ and evaporated at low temperature. The residue was chromatographed on silica gel (CH_2Cl_2) cooled to −30 to −40 °C, to afford 2-phenyl-2*H*-[1,2,3]triazolo[4,5-*e*][1,2,3,4]-tetrazine **10** (40 mg, 81%) as reddish flakes from CH_2Cl_2, m.p. 76–77 °C (decomp.); δ_H(400 MHz; CD_2Cl_2; −20 °C) 7.68–7.85 (3 H, m) and 8.63–8.80 (2 H, m); δ_C(400 MHz; CD_2Cl_2; −20 °C) 122.9 (d), 130.8 (d), 134.2 (d), 139.0 (s) and 145.7 (s); ν_{max}(KBr)/cm^{-1} 3075, 1578, 1552, 1482 and 1458. Attempted elemental analysis was unsuccessful because of the instability of compound **10**.

Degradation of Compound **10**.—To a solution of compound **9** (30 mg, 0.15 mmol) in CH_2Cl_2 (5 cm^3) at 0 °C was added LTA (90%; 74 mg, 0.15 mmol) by portions. The reactions was allowed to continue for 15 min, then the mixture was washed with 20% aq. $KHCO_3$, dried over $MgSO_4$ and altered. The filtrate was kept at room temperature for 2 h. Consumption of the tetrazine **10** was confirmed by TLC, and the solvent was evaporated off. The residue was applied to silica gel preparative TLC plates (hexane–CH_2Cl_2, 1:1) to give 5-cyano-2-phenyl-2*H*-tetrazole **14** (7 mg) and 2-phenyl-2*H*-1,2,3-triazole **15** (2 mg). The degradation in various solvents and under various conditions was monitored by GLC.

5-Cyano-2-phenyltetrazole **14** was obtained as needles from hexane–Et_2O; m.p. 52–53 °C (lit.,[9] 53–54 °C); δ_H(100 MHz; $CDCl_3$) 7.51–7.61 (3 H, m) and 8.03–8.13 (2 H, m); δ_C(400 MHz; $CDCl_3$) 108.9, 120.3, 130.1, 131.3, 136.0 and 142.6; *m/z* 171 (M^+) (Found: M^+, 171.055. Calc. for $C_8H_5N_5$: M, 171.055).

2-Phenyl-1,2,3-triazole **15** was obtained as an oil; δ_H(100 MHz; $CDCl_3$) 7.32–7.58 (3 H, m), 7.80 (2 H, s) and 8.03–8.14 (2 H, m); *m/z* 145 (M^+). The spectral data were identical with those of an authentic sample.[10]

Oxidation of 2-Amino-5-phenyl-2,5-dihydro[1,2,3]triazolo-[4,5-d][1,2,3]triazole **11**.—To a stirred solution of compound **11** (50 mg, 0.25 mmol) of CH_2Cl_2 (8 cm^3) at room temperature was added LTA (90%; 107 mg, 0.22 mmol) by portions. After the mixture had been stirred for 15 min it was washed with 20% aq.

* MSH is known to be unstable unless it is frozen with water.[8] When used, MSH was suspended in an organic solvent, and the organic layer was separated and dried over $MgSO_4$.

$KHCO_3$, dried over $MgSO_4$ and evaporated. The residue was chromatographed on preparative silica gel TLC (CH_2Cl_2) plates to afford the starting material (3 mg recovery) and (E,Z)-1,3-*dicyano*-2-*phenyltriazeniumide* **18a** (35 mg, 82%) as pale yellow needles from hexane–Et_2O; m.p. 91–91.5 °C (Found: C, 55.9; H, 3.0; N, 40.85. $C_8H_5N_5$ requires C, 56.1; H, 2.9; N, 40.9%); δ_H(100 MHz; $CDCl_3$) 7.68–7.83 (5 H, m); δ_C(400 MHz; $CDCl_3$) 109.6, 109.8, 123.1, 130.0, 134.7 and 143.3; *m/z* 171 (M^+) and 131 ($M^+ - CN_2$); ν_{max}(KBr)/cm^{-1} 2190.

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