Reactions of 3-Aryl-1-(tetrazol-5'-yl)triazenes with some Electrophiles: Mercury Derivatives and Fragmentations: A New Route to Aryl Diazocyanides

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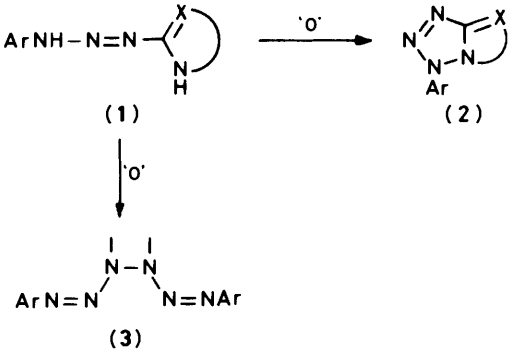
Treatment of 3-aryl-1-(tetrazol-5'-yl)triazenes (**4**) with lead tetra-acetate resulted in a fragmentation to aryl diazocyanides. The triazenes (**4**) and their monomethyl derivatives when treated with mercuric acetate and phenylmercury hydroxide gave stable mercuri compounds with mercury bonded at N-3 and the tetrazole N-2'. The reaction of the triazenes with acetic anhydride resulted in acetylation of the triazene unit with fragmentation to aryl diazonium ions and 5-acetamidotetrazoles. These reactions are discussed and the ^{13}C n.m.r. spectra of the products are analysed.

The pharmacological properties of substituted triazenes and, in particular, their carcinogenic and anti-tumor properties,[1-3] have prompted considerable interest in these systems in recent years.[4] In reactions with strong oxidising agents such as Pb^{IV} the triazene unit of 1,3-diaryltriazenes fragmented homolytically and gave complex product mixtures derived mainly from substituted nitrogen and aryl radicals.[5] Oxidations of some heterocyclic triazenes of type (**1**) resulted in cyclizations to fused bicyclic systems (**2**),[6] while in other cases high yield dimerizations to substituted hexa-aza-1,5,dienes of type (**3**) have been observed[7] (Scheme 1). Recently we have reported[8] the

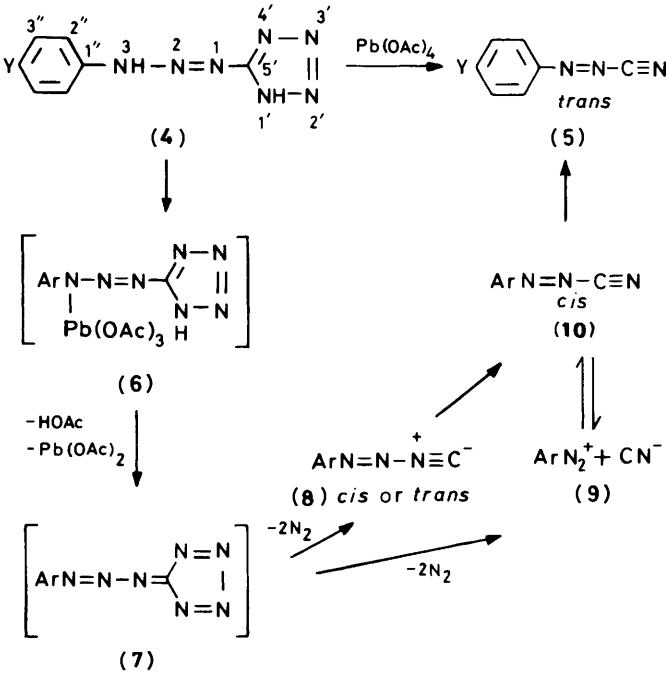


Scheme 1.

synthesis and structure of the new tetrazol-5-yltriazenes (**4**) and herein we report[9] interesting reactions of these systems with some electrophiles and oxidizing agents. Oxidation of the triazenes (**4**) could, in theory, give rise to all of the product types encountered previously. For example a reaction of the type (**1**) ⟶ (**2**) should give 2-aryl-5-azidotetrazoles assuming the expected[10] cleavage of the fused tetrazolotetrazole system.

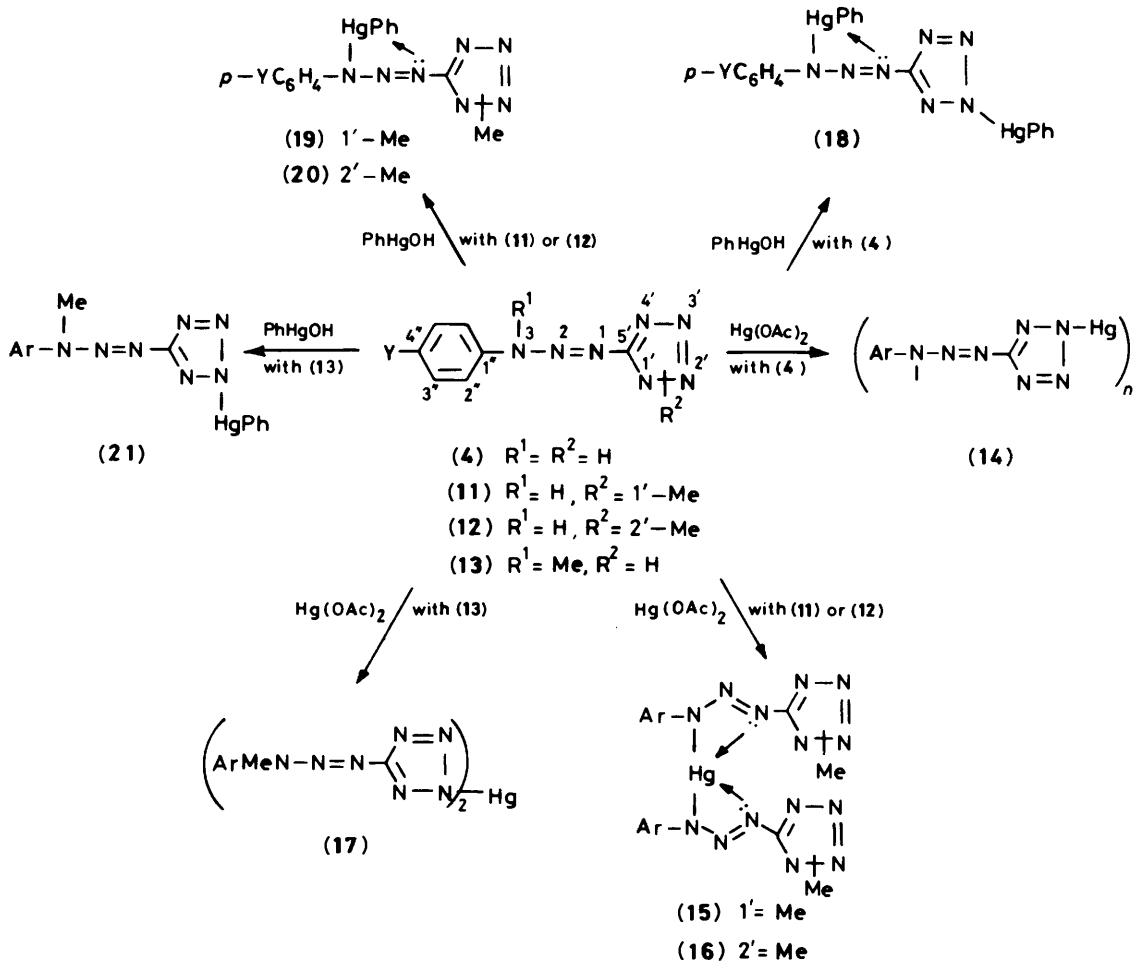
Results and Discussion

Reactions with $Pb(OAc)_4$.—Oxidation of the compounds (**4**) with lead tetra-acetate (LTA) at 20 °C in solvents such as dichloromethane, chloroform, and pyridine gave rise to triazene fragmentation and high yields of the *trans*-diazo cyanides (**5**). The reaction was unaffected by triethylamine added to remove the acetic acid generated. When the reaction was carried out in deuteriochloroform at 0 °C and the products immediately analysed by ^{13}C n.m.r. at 0 °C, the *cis*-diazocyanides (**10**) were the initial products detected (Scheme 2); these rapidly isomerized to the *trans* compounds (**5**) on warming to room temperature. Further low-temperature work failed to show other intermediates. The products (Table 1) were identified from i.r. and ^1H and ^{13}C n.m.r. spectroscopic evidence and were identical with samples prepared by direct coupling of arenediazonium salts with cyanide ion.[11,12]



Scheme 2. a, Y = Cl; b, Y = Br; c, Y = NO_2

The reaction probably involved the sequence shown in Scheme 2. Oxidative dehydrogenation of the compounds (**4**) may occur through an unstable *N*-metallo species,[13] possibly of type (**6**). The preferred bonding sites for Hg^{II}, which often parallels that of the isoelectronic Pb^{IV}, were at N-3 and N-2' (Scheme 3). An internal redox in the *N*-metallo intermediate would lead to an unstable tetra-azafulvene intermediate (**7**), such intermediates having been postulated in previous oxidations of the 5-aminotetrazole moiety; they appear to fragment to isocyanides.[14,15] Thus it has recently been reported[14] that 5-aminotetrazoles, $RNHCN_4H$, on oxidation with LTA gave stable isocyanides $R-\overset{+}{N}\equiv C^-$. The corresponding isocyanides in the present reaction would be the species (**8**) but



Scheme 3. **a**, Y = Cl; **b**, Y = Br; **c**, Y = NO_2; **d**, Y = H

attempts to trap such intermediates with a range of additives were unsuccessful. Since the *trans* forms of compounds (**8a**) and (**8b**), generated in pyridine from *N*-formyltriazenes,[16] were recently reported as stable low-melting solids, our reactions were carried out in pyridine where compounds (**8**) if present should be stable; they were not, however, encountered. We were unable to obtain compounds (**8**) as reported,[16] numerous attempts to obtain the stable *N*-formyltriazene precursors of the diazoisocyanides (**8**) having failed. These attempts included both the simple expedient of generating diazonium ion (which readily coupled to give dyes) in organic solvents using the *cis* diazocyanides (**10**) in the presence of formamide as well as the reported[16] procedures. We conclude that the reported *N*-formyltriazenes must be highly sensitive and note that others[17] have also reported their failure to make these compounds. While diazoisocyanides (**8**) could be transient precursors to the diazocyanides, in the present case a direct fragmentation of the species (**7**) to a diazonium ion and cyanide ion may be an alternative route to the diazocyanides. The presence of aryldiazonium ion in the system was confirmed by introduction of 2-naphthol to the reaction mixture shortly after the oxidizing agent was added when an azo dye was obtained in high yield, although this could also arise from the diazocyanide products and does not preclude a diazoisocyanide intermediate. The initial formation of the diazocyanides in the *cis*-configuration (**10**) is, however, consistent with their generation by an intermolecular reaction between diazonium ion and cyanide.

Mercuric Acetate and Phenylmercury Hydroxide.—Since mercuric acetate (Hg2A) is isoelectronic with LTA but a milder oxidizing agent its behaviour may sometimes assist in understanding LTA oxidations. Treatment of the triazenes (**4**) with mercuric acetate in methanol did not result in an oxidation but gave highly insoluble powders which appeared to be polymeric in nature. Their i.r. spectra showed the absence of N–H bonds and their empirical formulae indicated one mercury atom per triazene moiety; this was not precisely stoicheiometric, however, in some cases. The insolubility of the compounds precluded any n.m.r. or solution data. The products are probably polymers with mercury bonding at N-3 and N-2′ as in structure (**14**). The suggested bonding sites at N-3 and N-2′ emerged with the substrates (**11**)—(**13**) (Scheme 3) where the tetrazole N–H and the triazene N–H moieties were separately replaced by methyl groups. With the substrates (**11**) and (**12**) mercury-bonding occurred at the triazene N-3 and gave the bis(triazenyl)mercury derivatives (**15**) and (**16**) when treated with Hg2A, while the compounds (**13**) gave the products (**17**) with mercury bonded to the tetrazole N-2′. These bonding sites for mercury were further confirmed with phenylmercury hydroxide as reagent. In this case the parent triazenes (**4**) gave the products (**18**) and when one of the NH moieties was methylated the products (**19**), (**20**), and (**21**) were obtained from the substrates (**11**), (**12**), and (**13**) respectively, (Scheme 3).

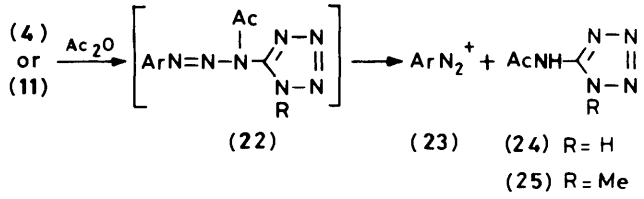
These mercuri derivatives (Scheme 3) (Table 2) were obtained as powders in good yields and with the exception of a few were

soluble and amenable to structural study. Some examples of bis(aryltriazenyl)mercury compounds have been reported previously[18–20] and the structures have been represented variously with the mercury bridging the triazene N-1 and N-3 atoms as in (A) or with the mercury covalently bonded to one nitrogen atom and coordinated to the other as in (B). In

(A) (B)

phenylmercuri derivatives of aryltriazenes the mercury is considered to be in rapid exchange between the N-1 and N-3 sites in solution.[21] Carbon-13 n.m.r. spectra have not been reported for such compounds previously. With all the compounds (Scheme 3) in which the mercury was bonded to the triazene unit the ^{13}C n.m.r. spectra (Table 2) suggested strong bonding at N-3 and relatively little or weak bonding at N-1. Thus the influence of the adjacent Hg^{II} atom caused a large deshielding of the 3-*N*-phenyl C-1″ (6—7 p.p.m.) and a significant deshielding also of the phenyl C-2″ (3—4 p.p.m.) while in each case the shift of the tetrazole C-5′, adjacent to N-1 was hardly affected, being changed by ±0.2 p.p.m. (Table 2). When the mercury was bonded to the tetrazole ring, as expected it had virtually no influence on the shifts of the distant N-3 aryl ring [Table 2, compounds (**17d**), (**21d**)]. Similar effects were observed in the ^1H n.m.r. spectra of compounds (**15**) and (**16**) where the *ortho* protons in the N-3 aryl ring were deshielded by 0.3—0.4 p.p.m. with the mercury bonded at nearby N-3. Hence we conclude that the mercury is strongly bonded at N-3 with possible weak co-ordination from nearby nitrogen atoms such as triazene N-1 or tetrazole N-4′. This co-ordination may be somewhat stronger in the compounds (**19**) and (**20**) containing only one N–Hg bond with a PhHg group bonded to the triazene chain, since in these cases the deshielding of the tetrazole C-5′ was somewhat larger (0.7—1.5 p.p.m.) [Table 2, compound (**19a**), (**19b**), (**20b**)] although still much smaller than that of the aryl C-1″. When the mercury was bonded to the tetrazole ring the tetrazole C-5′ shift in each case indicated a 2,5-disubstituted tetrazole structure. It is well established[10,22–24] that the C-5′ shift of 5-substituted tetrazoles is *ca.* 10 p.p.m. downfield (at δ 166—170 p.p.m.) in 2,5-disubstituted tetrazoles relative to 1,5-disubstituted tetrazoles (δ 156—160 p.p.m.). This applied also in the parent tetrazol-5-yltriazenes,[8] and from these carbon shifts we conclude that N-2′ is the preferred bonding site of Hg^{II} in the tetrazole ring of these systems.

Acetic Anhydride.—*N*-Acyltriazenes have proved of interest because of acyl migrations and homolytic fragmentations encountered in their chemistry.[20,25,26] Acylation of 5-substituted tetrazoles occurs mainly at the 2-N-position to give unstable products which lose nitrogen to form an acylnitrilimine; this rapidly cyclises to an oxadiazole ring.[27–29] With 5-aminotetrazoles however, acylation was found to occur initially on the amino group by early termination of the reaction.[30] Hence the reaction of the substrates (**4**) with acetic anhydride was interesting because of the variety of possible pathways. In the event, treatment of the compounds (**4**) and (**11**) with acetic anhydride (1—10 mol) in acetic acid at 25 °C or in dichloromethane at 0 °C resulted in fragmentation to an aryldiazonium ion (**23**) and the 5-acetamidotetrazoles (**24**) and (**25**) (Scheme 4). The intermediate *N*-acyltriazene was not detected, even at 0 °C, and it appears to undergo a rapid heterolytic fragmentation.



(22) (23) (24) R = H (25) R = Me

Scheme 4.

The arenediazonium ions were detected by coupling with 2-naphthol and *N*,*N*-dimethylaniline to give azo dyes in yields of up to 65%, suggesting at least 65% formation of diazonium ion in the fragmentation. The 5-acetamidotetrazoles were isolated from the work-up in yields of up to 35% along with resins. The site of the initial acyl attack is not necessarily indicated as N-1 by these results and attack at N-3 followed by acyl migration cannot be ruled out. No evidence was encountered for acyl attack at the tetrazole ring and the observed reaction was identical when the tetrazole NH was removed by methylation as for the substrates (**11**).

Experimental

M.p.s. were measured with an Electrothermal apparatus. I.r. spectra were measured for Nujol mulls with Perkin-Elmer 377 and 983G spectrophotometers. ^1H and ^{13}C N.m.r. spectra were measured for solutions in $(CD_3)_2SO$ with Me_4Si as internal reference on JEOL JNM-100 and CFT-20 spectrometers. The substrates (**4**), (**11**), (**12**), and (**13**) were prepared as previously described.[8] All of the compounds gave satisfactory microanalyses [See Supplementary Publication no. 56511 (3pp.)] *

Lead Tetra-acetate Reactions: General Method.—A solution of compound (**4**) (2 mmol) and LTA (2 mmol) in dichloromethane (20 ml) was stirred at ambient temperatures for 18 h, or at 0 °C for 250 h, after which time insoluble salts were removed and the solution was washed with water and evaporated to give the products (**5**) (Table 1), which were recrystallised from pentane. Similar results were obtained using the solvents, pyridine, deuteriochloroform and dichloromethane containing the separate additives, triethylamine, cyclohexene, ethyl acrylate. For the reaction of compound (**4b**) in $CDCl_3$ at 0 °C, a direct ^{13}C n.m.r. spectrum of the reaction solution measured at 0 °C, showed the initial product to be compound (**10b**), identical with a sample prepared by coupling *p*-bromobenzenediazonium chloride with cyanide ion.[11] On warming to 25 °C in the n.m.r. tube the spectrum rapidly changed to that of compound (**5b**).

Mercuric Acetate and Phenylmercury Hydroxide Reactions: General Methods.—(*a*) A solution of mercuric acetate (1 mmol) in methanol (10 ml) was added dropwise with stirring to a solution of the appropriate triazene (**4**) or (**11**)—(**13**) (1 mmol) in methanol (10 ml) and the mixture stirred at ambient temperatures for 12 h. The mercuri products (**14**)—(**17**) (Table 2) which separated were collected and washed with ether and water. Evaporation of the methanol filtrate led to recovery of small quantities of starting material.

(*b*) A solution of phenylmercury hydroxide (1 mmol) in isopropyl alcohol (15 ml) was added dropwise with stirring to a solution of the triazene (1 mmol) in isopropyl alcohol (15 ml) and the mixture was stirred first at 65 °C for 1 h and then at ambient temperatures for 12 h. The insoluble mercuri products

* For details of the Supplementary Publications Scheme, see Instructions for Authors (1986), *J. Chem. Soc., Perkin Trans. 1*, 1986, Issue 1.

Table 1. Aryl diazocyanides

Product	Yield (%)	M.p. (°C)	$\nu_{max.}$(C≡N)/cm^{-1}	Carbon shift (δ) CN	C-1′,	C-2′,	C-3′,	C-4′
(**5a**)	70	102—103	2 187	115.4	151.5	125.9	130.6	143.6
(**5b**)	73	130—131	2 184	115.4	151.6	125.8	133.5	124.5
(**5c**)	76	84—85	2 186	114.8	154.9	125.3	125.3	150.7
(**10b**)	73	40—42	2 146	110.7	154.6	123.6	133.05	130.2

Table 2. Mercuric derivatives

Compd.	m.p.[a] (°C)	Yield (%)[b]	Carbon shifts[c] C-1″(△)[d]	C-2″(△)[d]	C-3″(△)[d]	C-4″(△)[d]	C-5′(△)[d]
(**14a**)	252	100	—	Insoluble			—
(**14b**)	250	100	—	"			—
(**14c**)	270	100	—	"			—
(**18a**)	236	65	147.1(6.2)	122.1(3.5)	128.8(−0.6)	129.8(0.4)	166.5[e]
(**18b**)	249	65	147.5(6.4)	122.5(3.3)	132.6(0.3)	118.1(0.3)	166.5[e]
(**18c**)	254	61	153.3(7.2)	119.5(3.7)	124.6(−0.9)	143.3(−0.1)	166.2[e]
(**15a**)	194	77	145.3(5.9)	121.5(3.8)	129.3(−0.2)	129.9(0.6)	157.6(−0.1)
(**15b**)	191	83	145.8(6.0)	121.9(3.6)	132.3(−0.1)	118.3(1.0)	157.9(0.15)
(**15c**)	250	84	152.2(6.6)	119.9(4.1)	125.3(−0.5)	143.85(0.1)	157.6(−0.1)
(**16b**)	215	90	146.5(5.1)	121.6(3.6)	132.15(−0.15)	117.8(1.0)	168.7(0.2)
(**19a**)	184	65	146.3(6.9)	121.2(3.5)	129.1(−0.65)	129.6(−0.1)	158.5(0.7)
(**19b**)	182	70	146.7(6.9)	121.6(3.7)	132.1(−0.3)	117.8(0.5)	158.5(0.7)
(**19c**)	234	71	153.2(7.7)	119.3(3.5)	125.1(−0.6)	143.6(−0.1)	158.1(0.3)
(**20b**)	188	80	147.9(6.5)	121.7(3.7)	131.9(−0.4)	117.6(0.8)	170(1.5)
(**17d**)	205	85	143.2(−0.1)	119.4(0.6)	128.7(−0.6)	126.2(0.15)	164.3[e]
(**21d**)	222	72	143.5(0.2)	119.5(0)	129.1(−0.2)	125.7(−0.25)	167.0[e]

[a] The compounds decomposed, sometimes explosively, at these temperatures. [b] For yields < 100% the remainder was starting material recovered. [c] Solvent, $(CD_3)_2SO$. [d] △ Is the shift difference relative to the parent unmercuriated compound (*cf.* ref. 8), positive is downfield (deshielding) and negative is upfield (shielding). [e] Since the parent compound is tautomeric and mainly the 1-NH form (ref. 8), △ is not given. The shifts indicate a 2,5-disubstituted tetrazole ring.

(**18**)—(**21**) (Table 2) were collected and washed with water. Evaporation of the isopropyl alcohol filtrate led to recovery of small quantities of starting triazene.

Acetic Anhydride Reactions.—Solutions of the triazenes (**4**) and (**11**) (1 mmol) in glacial acetic acid (6 ml) were treated with acetic anhydride (1—10 mmol) and stirred at ambient temperatures for 4 h. Addition of 2-naphthol or *N,N*-dimethylaniline to the stirred solution caused immediate precipitation of the *p*-substituted phenylazo dye (58—65%) (identical mixture m.p.s and i.r. spectra with authentic samples). The acetic acid filtrate was treated with water (40 ml.) and extracted with ether (3 × 30 ml). Evaporation of the combined ethereal extract gave some intractable products and evaporation of the aqueous layer gave 5-acetamidotetrazole (**24**) (32%), m.p. 277 °C (lit.,[30] m.p. 277—278 °C) from the substrates (**4**) and 5-acetamido-1-methyltetrazole (**25**) (35%), m.p. 165—166 °C (lit.,[30] 166.5—167.5 °C) from the substrates (**11**). These products (**24**) and (**25**) were identical (mixture m.p.s and i.r. spectra) with authentic samples.

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