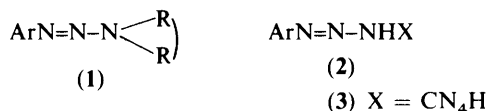


### 3-Aryl-1-tetrazol-5-yltriazenes, Bench-stable Arenediazonium Ion Synthons: Synthesis of Biaryls and Aryl Halides

Richard N. Butler,\* Paul D. O'Shea, and (in part) Declan P. Shelly  
Chemistry Department, University College, Galway, Ireland

3-Aryl-1-tetrazol-5-yltriazenes have been used as a bench-stable source of diazonium ions for the synthesis of substituted biaryls, aryl halides (iodides, bromides, and chlorides) and azo dyes. The dediazonation process when induced by trihalogenoacetic acid or acetic acid did not involve free radicals.

The synthetic usefulness of arenediazonium ions is often limited by side reactions and the generation of nitrogen oxides in the diazotisation process. These oxides may act as reducing agents for the aryl nitrogen bond and give rise to unwanted side-products. Earlier attempts<sup>1-3</sup> to circumvent such problems by using triazenes as a source of diazonium ions did not supersede the classical methods. However in recent years there has been much renewed interest in the use of triazenes of the *N,N*-dialkyl type (1) as diazonium ion synthons, particularly for the synthesis of halogenobenzenes.<sup>4-11</sup> Triazenes of type (2) where the  $\text{NH}_2\text{X}$  moiety is a good leaving group should be equally effective, particularly if this amine is stable, cheap, and widely available commercially. Amines of the higher azoles which should be good leaving groups have not been tried in this context and 5-aminotetrazole in particular fulfils all of the required criteria. Hence our recent studies<sup>12,13</sup> of the new triazenes (3) led us to explore their potential use as a ready, long-lived bench-stable source of arenediazonium ions. Herein we report their successful use in the synthesis of biaryls, azo dyes, and aryl halides.

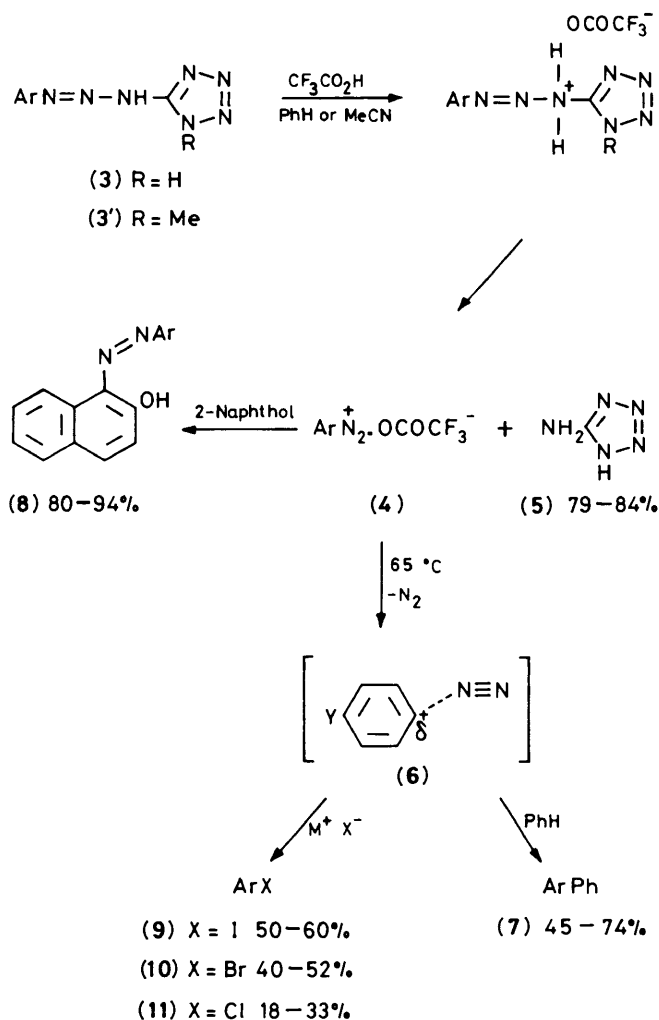


The most effective of the triazenes (3) proved to be those containing electron-withdrawing substituents in the aryl ring. This is significant because in the generation of arenediazonium ions from other triazenes difficulties have been encountered with electron-withdrawing substituents.<sup>5,7</sup>

#### Results and Discussion

**Biaryls and Azo Dyes.**—A series of the triazenes (3) when treated with trifluoroacetic acid, trichloroacetic acid, or acetic acid at 65 °C in benzene or benzene-acetonitrile gave good yields of the biaryls (7) (Table 1) (Scheme). The reaction involved an arenediazonium ion (4) (Scheme) which, when trapped by addition of 2-naphthol gave high yields of the azo dyes (8) (Table 1, Entries 21–25). The other fragmentation product was 5-aminotetrazole (5) which was present in the aqueous extract from the work-up and was quantified by its conversion into an azo dye with *N,N*-dimethylaniline.

The mechanism of dediazonation, which can occur by free radical, cationic  $\text{S}_{\text{N}}1$  type, or bimolecular pathways,<sup>14</sup> has been controversial.<sup>15,16</sup> It has recently been suggested<sup>1</sup> that the free radical pathway is dominant in the synthesis of biaryls from *N,N*-dialkyltriazenes with trifluoroacetic acid. We rule out a free-radical path for the biaryl synthesis with the triazenes (3) for the following reasons. (i) The reactions using trifluoro- and trichloro-acetic acids were relatively insensitive and the yields



Scheme. Ar = *p*-YC<sub>6</sub>H<sub>4</sub>; Y = a, H; b, Br; c, Cl; d, NO<sub>2</sub>; e, Me

showed little change in the presence of radical inhibitors in quantities in the range 0.02–1.0 molar equiv. (Table 1, Entries 2, 6–8, 10, 13, 18). In a control reaction biphenyl (7a) was obtained in 57% yield by prolonged heating of benzoyl peroxide in benzene. In the presence of hydroquinone this reaction was strongly inhibited and the yield was reduced to 6%, confirming the expected radical nature of the reaction and the effectiveness of the inhibitor tests being used (Table 1, Entries 19, 20). Similar results were obtained using benzoyl peroxide in the absence and in the presence of hydroquinone in toluene and nitrobenzene. Compound (7c) was also obtained in 35% yield when sodium

Table 1. Reactions in benzene at 65 °C

Entry	Substrate		Reagent	Additive (mol%)	Product <sup>d</sup>		
	Compd.	Y			Compd.	M.p. (°C)	Yield (%)
1	(3a)	H	TFA <sup>a</sup>	—	(7a)	68–69	43
2	(3a)	H	TFA <sup>a</sup>	Hydroquinone (6)	(7a)	68–69	40
3	(3c)	Cl	TFA <sup>a</sup>	—	(7c)	76–77	58
4	(3c)	Cl	TFA <sup>a</sup>	MeCN <sup>c</sup>	(7c)	76–77	66
5	(3c)	Cl	TFA <sup>a</sup>	I <sub>2</sub> (2.5)	(7c)	76–77	54
6	(3c)	Cl	TFA <sup>a</sup>	Hydroquinone (6)	(7c)	76–77	60
7	(3c)	Cl	TFA <sup>a</sup>	Hydroquinone (100)	(7c)	76–77	48
8	(3c)	Cl	TFA <sup>a</sup>	Quinone (2)	(7c)	76–77	56
9	(3c)	Cl	TCA <sup>b</sup>	—	(7c)	76–77	66
10	(3c)	Cl	TCA <sup>b</sup>	Hydroquinone (50)	(7c)	76–77	62
11	(3c)	Cl	HOAc	—	(7c)	76–77	74
12	(3c)	Cl	NaOAc	—	(7c)	76–77	35
13	(3c)	Cl	NaOAc	Hydroquinone (50)	(7c)	76–77	5
14	(3c)	Cl	TFA <sup>a</sup>	—	(7c)	76–77	69
15	(3b)	Br	TFA <sup>a</sup>	—	(7b)	89–90	45
16	(3d)	NO <sub>2</sub>	TFA <sup>a</sup>	—	(7d)	112–113	58
17	(3e)	Me	TFA <sup>a</sup>	—	(7e)	46–47	35
18	(3e)	Me	TFA <sup>a</sup>	Hydroquinone (50)	(7e)	46–47	35
19	Benzoyl peroxide		—	—	(7a)	68–69	57
20	Benzoyl peroxide		—	Hydroquinone (50)	(7a)	68–69	6
21	(3a)	H	TFA	2-Naphthol (100)	(8a)	131–133	84
22	(3b)	Br	TFA	2-Naphthol (100)	(8b)	169–171	81
23	(3c)	Cl	TFA	2-Naphthol (100)	(8c)	157–159	80
24	(3d)	NO <sub>2</sub>	TFA	2-Naphthol (100)	(8d)	254–256	94
25	(3e)	Me	TFA	2-Naphthol (100)	(8e)	130–132	82

<sup>a</sup> Trifluoroacetic acid. <sup>b</sup> Trichloroacetic acid. <sup>c</sup> Solvent: benzene–acetonitrile (4:1, v/v). <sup>d</sup> Products were identical with authentic samples.

acetate was used in place of trifluoroacetic acid with the triazene (3c). This low-yield reaction, under basic conditions, was free radical in nature. It was strongly inhibited by the presence of 0.5 mol equiv. of hydroquinone, which reduced the yield of compound (7c) to 5% (Table 1, Entries 12, 13). (ii) When nitrobenzene was used as solvent in place of benzene in the biaryl synthesis the character of the reaction changed. It proved sluggish and difficult and only low yields (3–5%) of a mixture of biaryls was formed. It was not possible to obtain an accurate *o*-, *m*-, *p*-substitution ratio because of the difficulties with the reaction but the result was consistent with a retarded cationic attack on nitrobenzene and inconsistent with a radical attack which is enhanced relative to benzene<sup>17</sup> as we confirmed using benzoyl peroxide in nitrobenzene. (iii) The ready formation of halogenobenzenes in the presence of halide ions (below) is consistent with a cationic mechanism or a bimolecular mechanism but not with a radical mechanism. (iv) In the presence of iodine the reaction of compound (3c) was not inhibited and no trace of 4-chloriodobenzene was formed (Table 1, Entry 5). Iodine is known<sup>18</sup> to act as a more effective radical trap than benzene by a factor of  $2 \times 10^3$ .

**Halogenobenzenes.** The non-radical nature of the biaryl reaction suggested the possibility of using halide ions in the dediazonation process thereby providing a route to substituted aryl halides. This was readily achieved with iodide, bromide, and chloride anions using acetonitrile as solvent (Scheme). Significantly, aryl radicals did not react with iodide ion under the conditions used and when benzoyl peroxide was heated in acetonitrile containing potassium iodide no trace of iodobenzene was detected.

Good yields of the aryl iodides (9) were obtained when the triazenes (3) were treated with trifluoroacetic acid in acetonitrile in the presence of potassium iodide or tetramethylammonium iodide and the results were similar for both cations (Table 2). The yields of the aryl iodides related to those of the biaryls for the same substituents Y in the triazene substrates. The

Table 2. Synthesis of aryl halides

Entry	Substrate		Product <sup>a</sup>			
	Compd.	Y	Compd.	M.p. (°C)	Yield (%) <sup>c</sup> from KI	Yield (%) <sup>c</sup> from [Me <sub>4</sub> N]I
(a) Aryl iodides						
1.	(3a)	H	(9a)	— <sup>b</sup>	47	49
2.	(3b)	Br	(9b)	90–92	57	61
3.	(3c)	Cl	(9c)	55–57	51	52
4.	(3d)	NO <sub>2</sub>	(9d)	172–174	58	56
5.	(3e)	Me	(9e)	36–37	42	51
(b) Aryl bromides						
6.	(3b)	Br	(10b)	86–87	10	40
7.	(3c)	Cl	(10c)	66–68	7	40
8.	(3d)	NO <sub>2</sub>	(10d)	125–127	39	52
(c) Aryl chlorides						
9.	(3b)	Br	(11b)	66–68	0 <sup>c</sup>	21
10.	(3c)	Cl	(11c)	51–53	0	18
11.	(3d)	NO <sub>2</sub>	(11d)	82–83	0	33

<sup>a</sup> Products were identical with authentic samples. <sup>b</sup> Liquid, b.p. 187 °C.

<sup>c</sup> The remaining products were intractable resins and no starting materials were recovered.

decreasing nucleophilicity of the anion gave progressively lower yields of aryl bromides and chlorides and a much increased sensitivity to the nature of the cation (Table 2). The use of tetrabutylammonium bromide gave medium yields of aryl bromides (10) and these were significantly reduced when the cation was potassium (Table 2). The aryl chlorides (11) were obtained only with tetrabutylammonium chloride and they were not formed when potassium chloride was used. The yields of the chlorides were low but in the context of the Sandmeyer reaction<sup>19</sup> where yields may be of the order of 20% they are still acceptable. Indeed the versatility and convenience of the overall

process with the substrates (3) was such that the various pure products could be obtained quickly and large numbers of reactions could be run off on an efficient batch-basis which compensated for the low yields.

### Experimental

M.p.s were measured on an Electrothermal apparatus. The triazenes (3) were prepared as previously described.<sup>12</sup> The products (7)–(11) were identified by comparisons of mixture melting points and i.r., <sup>1</sup>H and <sup>13</sup>C n.m.r. spectra with authentic samples. All the compounds gave satisfactory microanalyses. Benzene was dried over calcium chloride, distilled twice, and stored over sodium wire. Nitrobenzene was extracted three times with concentrated aqueous sodium hydroxide and once with water, steam distilled, dried (CaCl<sub>2</sub>), and finally distilled under reduced pressure. H.p.l.c. grade acetonitrile (Rothburn Ltd.) was used directly without further purification.

**Biaryls (7): General Procedure.**—A mixture of the triazene (3) (5.0 mmol) in dry benzene (50 ml) was stirred at 65 °C and treated dropwise with the trihalogenoacetic acid (10 mmol) (or other reagent, Table 1) over 15 min. The heterogeneous mixture darkened and became homogeneous. Heating was continued for 3 h after which the solution was cooled and washed with 5% aqueous sodium carbonate (50 ml). The sodium carbonate washing was extracted with ether (3 × 50 ml) and the combined ethereal extract and main benzene solution was evaporated under reduced pressure. The residue was chromatographed on a column of alumina (Merck 1097) with hexane–dichloromethane (3:1, v/v) as eluant. The biaryls (7) were eluted in the first fractions.

The reactions with inhibitor additives present were carried out in identical fashion. Benzoyl peroxide (May and Baker) was purified by a literature procedure.<sup>20</sup> The control reactions of phenyl radicals in benzene, toluene, and nitrobenzene were carried by heating benzoyl peroxide at 90 °C (reflux for benzene) for 24 h and worked up as for the biaryls above.

**Azo Dyes (8): General Procedure.**—A mixture of the triazene (5.0 mmol), 2-naphthol (0.72 g; 5.0 mmol) in benzene (50 ml) was warmed to 65 °C and trifluoroacetic acid (10 mmol) was added dropwise with stirring over 15 min. The heterogeneous mixture turned to a deep red solution and heating was continued for 3 h after which the solution was cooled and washed with 5% aqueous sodium carbonate. The sodium carbonate washing was extracted with ether (3 × 50 ml) and the combined ethereal extract and main benzene solution was evaporated to give the red solids (8) which were recrystallised from ethanol.

**Aryl Halides (9)–(11): General Procedure.**—A mixture of the triazene (3) (2.5 mmol), the appropriate halide (2.5 mmol), and acetonitrile (35 ml) was heated to 70–80 °C and treated directly with trifluoroacetic acid (5.0 mmol). The reaction could be visibly monitored by nitrogen evolution and by t.l.c. on silica gel plates using the same solvent mixtures as for the columns (below). On completion of nitrogen evolution the mixture was

cooled, treated with diethyl ether (35 ml), and then washed with 5% aqueous sodium carbonate (50 ml). The ethereal extract and acetonitrile–ether mother-liquor was dried (MgSO<sub>4</sub>) and evaporated under reduced pressure to give a black oily residue (which may solidify). The residue dissolved in dichloromethane (2 ml) was placed on a column of alumina (Merck 1097) and eluted with dichloromethane–hexane (1:2 v/v) for aryl iodides and (1:1, v/v) for aryl bromides and chlorides.

**Detection of the 5-Aminotetrazole Fragment.**—In the synthesis of biaryls (see above) the benzene solution was extracted with water (5 × 30 ml) instead of aqueous sodium carbonate. The combined aqueous extract was treated with concentrated hydrochloric acid (1.45 ml) cooled to 0 °C, treated dropwise with aqueous sodium nitrite (0.34 g, 5.0 mmol in 5 ml water), stirred for 10 min and the whole then slowly added to a cooled aqueous solution of *N,N*-dimethylaniline [0.636 ml, 5.0 mmol in water (40 ml) containing conc. hydrochloric acid (1.42 ml) and crushed ice (*ca.* 10 g)]. Purple crystals of 5-(4'-*N,N*-dimethylphenylazo)tetrazole separated in yields of 79–84%; m.p. 141–142 °C (from ethanol). This compound was identical with a sample prepared by coupling diazotised 5-aminotetrazole hydrate with *N,N*-dimethylaniline.

### References

- 1 J. Elks and D. H. Hey, *J. Chem. Soc.*, 1943, 441.
- 2 A. Johnson, *J. Chem. Soc.*, 1946, 895.
- 3 C. S. Rondstedt, Jr., and O. Vogl, *J. Am. Chem. Soc.*, 1955, **77**, 3067.
- 4 T. B. Patrick, R. P. Willaredt, and D. DeGonia, *J. Org. Chem.*, 1985, **50**, 2232.
- 5 M. N. Rosenfeld and D. A. Widdowson, *J. Chem. Soc., Chem. Commun.*, 1979, 914.
- 6 T. J. Tewson and M. J. Welch, *J. Chem. Soc., Chem. Commun.*, 1979, 1149.
- 7 N. I. Foster, *Synthesis*, 1980, 572.
- 8 I. Ng, J. Katzenellenbogen, and M. R. Kilbourn, *J. Org. Chem.*, 1981, **46**, 2520.
- 9 M. M. Goodman and F. F. Knapp, Jr., *J. Org. Chem.*, 1982, **47**, 3004.
- 10 H. Ku and J. R. Barrio, *J. Org. Chem.*, 1981, **46**, 5239.
- 11 J. R. Barrio, N. Satyamurthy, H. Ku, and M. E. Phelps, *J. Chem. Soc., Chem. Commun.*, 1983, 443.
- 12 R. N. Butler, D. P. Shelly, and V. C. Garvin, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1589.
- 13 R. N. Butler and D. P. Shelly, *Tetrahedron Lett.*, 1985, **26**, 3401; *J. Chem. Soc., Perkin Trans. 1*, 1986, 1101.
- 14 A. F. Hegarty, 'The Chemistry Diazonium and Diazo Groups,' Wiley-Interscience, New York, 1978, part II, pp. 511–591.
- 15 H. Zollinger, *Angew. Chem.*, 1978, **90**, 151.
- 16 J. E. Packer, C. J. Heighway, H. M. Miller, and B. C. Dobson, *Aust. J. Chem.*, 1980, **33**, 965.
- 17 D. H. Hey, A. Nechvatal, and T. S. Robinson, *J. Chem. Soc.*, 1951, 2892.
- 18 L. Frideman and J. F. Chlebowski, *J. Org. Chem.*, 1968, **33**, 1636.
- 19 J. I. G. Cadogan, D. A. Roy, and D. M. Smith, *J. Chem. Soc. C*, 1966, 1250.
- 20 D. R. Augood, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 1952, 2094.

Received 7th July 1986; Paper 6/1363