

Approaches to 1,2,3,5-Tetrazines. Synthesis of 1,2,3,5-Tetrazinones and the Formation of Zwitterionic 1,2,4-Triazolin-3-ones and 1-Arylimino-1,2,4-triazolium Salts¹

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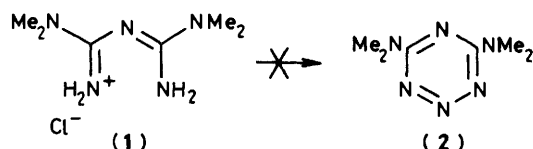
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The reaction of phosgene with 1,1-dialkyl-2-arylazoguanidines (**3**) yields 4-dialkylamino-1-aryl-1,2,3,5-tetrazin-6-ones (**5**), together with traces of zwitterionic 5-dialkylamino-1-arylimino-1,2,4-triazolin-3-ones (**7**); both decompose when heated to give nitrogen, dialkylcyanamides, and aryl isocyanates. 1,1-Dimethyl-2-aryazo-3-chloro(dimethylamino)methyleneguanidines (**10**) cyclise spontaneously to give 1-arylimino-3,5-bis(dimethylamino)-1,2,4-triazolium salts (**12**).

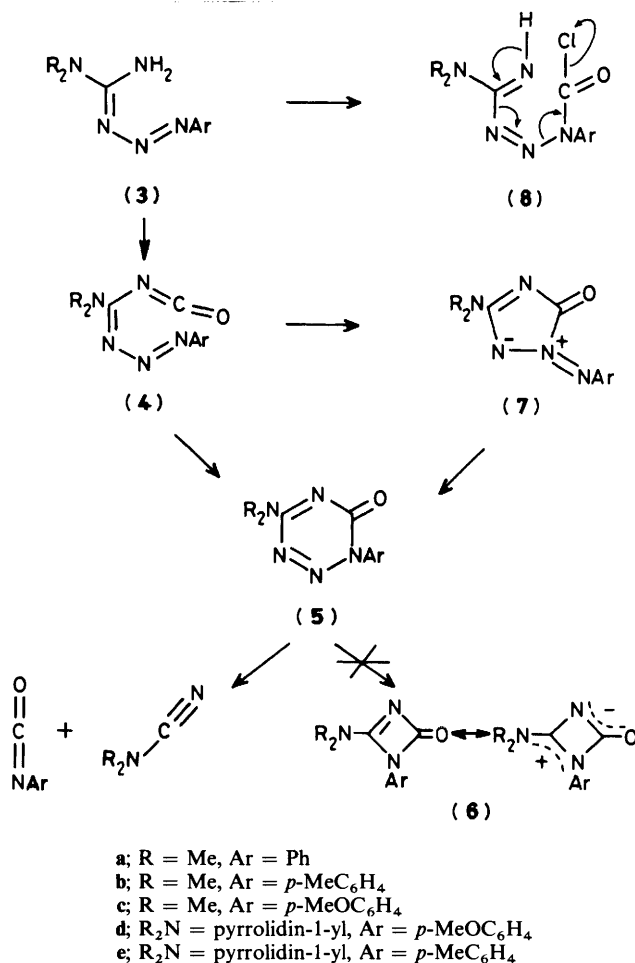
Of the three possible tetrazines, 1,2,4,5-tetrazines are well-studied compounds,² 1,2,3,4-tetrazines are unknown, and the only 1,2,3,5-tetrazines are complex cyanoamino-derivatives, which are reported³ to be produced by the electrochemical oxidation of cyanamide. We were interested in 1,2,3,5-tetrazines as possible precursors of 1,3-diazetes, but, like our predecessors,⁴ we failed to obtain simple members of this class. Attempts to prepare the 4,6-bis(dimethylamino) derivative (**2**) by diazotisation of the salt (**1**)⁵ in various ways were unsuccessful. We then



turned our attention to the tetrazinone system, in particular 4-dialkylamino-1-aryl-1,2,3,5-tetrazin-6-ones (**5**), which might yield stabilised 1,3-diazetones (**6**) on pyrolysis. The tetrazinones should result from electrocyclisation of isocyanates (see Scheme 1) and we investigated methods for generating the latter.

Pinner⁶ had shown that benzamidine couples with arenediazonium salts to yield the expected triazenes. Accordingly, we treated *NN*-dimethylguanidinium sulphate with several arenediazonium fluoroborates and obtained the triazenes (**3a—c**) as orange crystalline solids. The success of the reaction depends on the nature of the diazonium salt; it failed with *p*-nitro-, 2,4-dinitro-, and 2,6-dimethyl-benzenediazonium fluoroborate. 1-Amidinopyrrolidinium nitrate⁷ yielded the triazenes (**3d** and **e**). The i.r. spectra of the five triazenes, determined for Nujol mulls as well as for chloroform solutions, indicated that they were primary amines (**3**) rather than tautomeric imines, in which a hydrogen atom is attached to one of the nitrogen atoms of the triazene chain.

The conversion of the triazenes into the tetrazinones (**5**) via the isocyanates (**4**) was difficult and erratic. The best results (maximum yield 43%) were obtained by treating them with phosgene in toluene in the presence of a large excess of pyridine at -70°C . There was copious evolution of nitrogen and the products were contaminated with the corresponding aryl isocyanates, dimethylcyanamide (or *N*-cyanopyrrolidine), and much tar. *N*-Phenylazobenzamidine⁶ did not give 1,4-diphenyl-1,2,3,5-tetrazin-6-one and an attempt to prepare a tetrazine-thione by the action of thiophosgene on the triazene (**3b**) failed;



Scheme 1.

only dimethylcyanamide and *p*-tolyl isothiocyanate were isolated.

The tetrazinones are stable pale-yellow solids, which absorb in the range $1700\text{--}1712\text{ cm}^{-1}$. Their structures were confirmed by *X*-ray analysis of the phenyl derivative (**5a**).† The

† Details of the *X*-ray analysis will be published elsewhere.

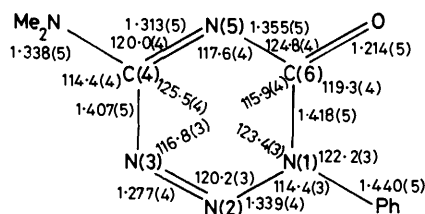


Figure 1. Intramolecular bond lengths (Å) and angles (°) for the tetrazine ring in (5a).

bond lengths in the tetrazine ring (see Figure 1) show a pronounced alternation. The ring is slightly puckered into a boat conformation with a mirror plane bisecting N(1) and C(4). N(1) and C(4) are displaced by $-0.060(8)$ and $-0.070(6)$ Å, respectively, out of the plane defined by the remaining ring atoms; the oxygen atom lies $0.059(12)$ Å from this plane. The crystals of compound (5a) were unstable to X-rays at room temperature; all the tetrazines decomposed at ca. 120°C to give nitrogen, aryl isocyanates, and dimethylcyanamide (or *N*-cyanopyrrolidine). The same fragmentation was observed in their mass spectra, the parent ion being that of the isocyanate. The tetrazinones decomposed in the same way during one week in cold dichloromethane solution and on attempted protonation with trifluoroacetic acid, alkylation with methyl fluorosulphonate, and attempted cycloaddition reactions with *N*-phenylmaleimide, 4-phenyl-1,2,4-triazoline-3,5-dione, diphenylcyclopropanone, and 1-diethylaminopyrene.

The i.r. spectra of the crude products of the reactions of the triazenes with phosgene contained bands near 1800 cm^{-1} and two compounds showing these absorptions were isolated in very low yields by column chromatography: a deep-yellow compound, m.p. 183°C , isomeric with the *p*-tolyltetrazinone (5b), and an orange *p*-methoxyphenyl analogue, m.p. 190°C (decomp.). The ^1H n.m.r. spectra of the two by-products were similar to those of the corresponding tetrazinones and the mass spectra of the members of each isomeric pair were essentially identical. The decomposition to nitrogen, dimethylcyanamide, and aryl isocyanate also occurred when the compounds were heated in boiling *o*-dichlorobenzene. The structure of the *p*-tolyl derivative was solved by X-ray analysis,* which showed it to be the betaine (7b), a member of the rare class of 1,3-dipolar azimines.⁸ Figure 2 shows the pertinent bond lengths and

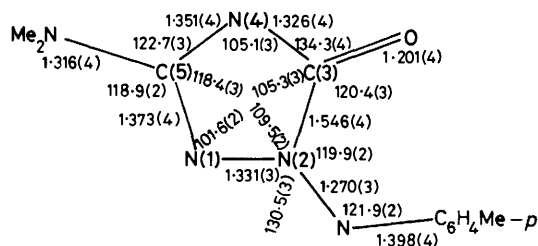


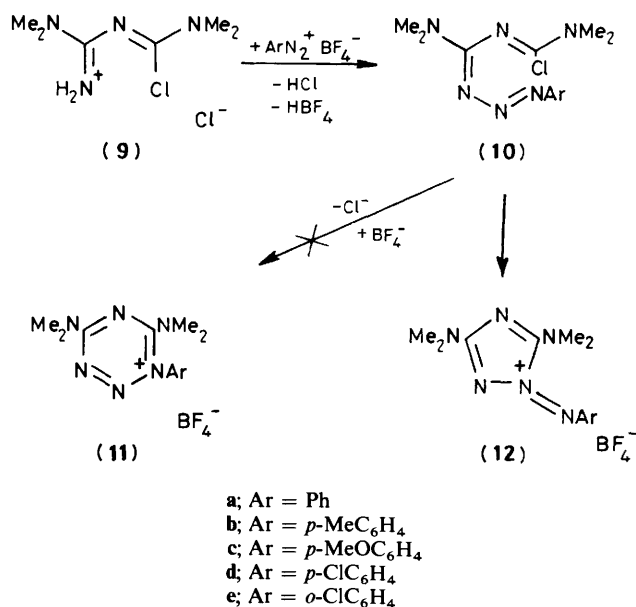
Figure 2. Intramolecular bond lengths (Å) and angles (°) for the betaine moiety in (7b).

angles. The heterocyclic ring is planar and the exocyclic oxygen and nitrogen atoms also lie in this plane. The exocyclic N-N distance, $1.270(3)$ Å, indicates considerable double-bond character, whilst the N(2)-C(3) distance is greater than normal. The oxygen atom is hydrogen-bonded to a water molecule of crystallisation at a distance of $2.929(5)$ Å.

* See footnote on previous page.

We suggest that the triazolinones (7) are formed by ring-closure of the isocyanates (4) onto the central atom of the triazene chain, which is activated by the two-fold α -effect of the flanking nitrogen atoms, and that the thermal decomposition of the triazolinones proceeds by preliminary rearrangement to the tetrazinones. The formation of nitrogen, cyanamides, and aryl isocyanates in the reaction of the triazenes (3) with phosgene at low temperatures may be initiated by attack of phosgene at the terminal nitrogen atom of the triazene moiety, followed by fragmentation [see (8)].

In conclusion, we describe an electrocyclic reaction which was thought to lead to 1-aryl-1,2,3,5-tetrazinium salts. Arenediazonium fluoroborates were found to couple with the guanidine derivative (9)⁹ in the presence of sodium hydroxide to yield bright-red fluoroborates, the analyses, i.r., and ^1H n.m.r. spectra of which appeared to indicate that they were the desired tetrazinium salts (11), resulting from spontaneous ring-closure of the intermediate tetra-azahexatrienes (10) (Scheme 2).



Scheme 2.

However, the colour of the salts was not consistent with the proposed structures and we again turned to X-ray crystallography. Several compounds of this kind had to be prepared until one was obtained which was suitable for the analysis,* namely the *o*-chlorophenyl derivative. It was shown to be the 1-arylimino-1,2,4-triazolium fluoroborate (12e); the other salts are formulated analogously (12a-d). In the structure (see Figure 3) the heterocyclic ring is planar and, as in the

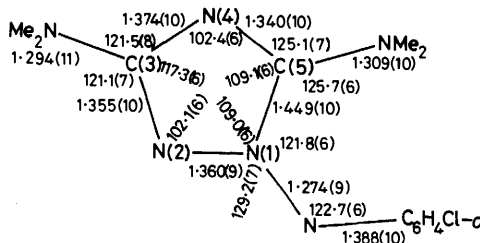


Figure 3. Intramolecular bond lengths (Å) and angles (°) for the heterocyclic ring in the cation of compound (12e).

zwitterionic triazolinone (**7b**), the exocyclic N–N bond, 1.274(9) Å, has considerable double-bond character. The formation of these unusual azo compounds is another instance of ring-closure by electrophilic attack at the central atom of triazenes.¹⁰

Experimental

I.r. spectra refer to Nujol mulls. ¹H N.m.r. spectra were determined for deuteriochloroform solutions and u.v. spectra for ethanolic solutions, unless stated otherwise.

1,1-Dialkyl-2-arylazoguanidines (3).—A stirred solution of *N,N*-dimethylguanidinium sulphate⁷ (3.7 g, 1.09 mol equiv.) and benzenediazonium fluoroborate (4.8 g) in water (130 ml) was treated with 2*M*-sodium hydroxide (25 ml), when 1,1-dimethyl-2-phenylazoguanidine (**3a**) (3.54 g, 74%) separated, yellow needles (from ethyl acetate), m.p. 212 °C (decomp.), ν_{\max} . 3 450, 3 275, 3 170, 1 620, and 1 580 cm⁻¹ (the spectrum of a chloroform solution was virtually the same), δ 8.1—6.5 (m, 5 H, Ph), 5.62 (br s, disappears on adding D₂O) (NH₂), and 3.11 (s, 2 × N-Me) (Found: C, 56.2; H, 7.1; N, 36.3. C₉H₁₃N₅ requires C, 56.5; H, 6.9; N, 36.6%). The following were obtained similarly: 1,1-dimethyl-2-*p*-tolylazoguanidine (**3b**) (78%), m.p. 193 °C (decomp.) (from ethyl acetate), ν_{\max} . 3 425, 3 280, 3 180, 1 610, and 1 570 cm⁻¹, δ 7.45 (d, 2 H) and 7.15 (d, 2 H) (AB_q, *J* 8.5 Hz, Ar), 5.58 (br s, exchangeable with D₂O, NH₂), 3.12 (s, 2 × N-Me), and 2.35 (s, C-Me) (Found: C, 58.3; H, 7.6; N, 34.1. C₁₀H₁₅N₅ requires C, 58.5; H, 7.4; N, 34.1%). 2-*p*-methoxyphenylazo-1,1-dimethylguanidine (**3c**) (42%), m.p. 190 °C (decomp.) (from ethyl acetate), ν_{\max} . 3 420, 3 280, 3 175, 1 622, 1 580, and 1 500 cm⁻¹, δ 7.52 (d, 2 H) and 6.88 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 5.74 (br s, exchangeable for D, NH₂), 3.8 (s, O-Me), 3.1 (s, N-Me), and 3.08 (s, N-Me) (Found: C, 54.3; H, 6.7; N, 31.8. C₁₀H₁₅N₅O requires C, 54.3; H, 6.85; N, 31.65%). *N*-(*N*-*p*-methoxyphenylazoamidino)pyrrolidine (**3d**) (89%), yellow plates (from ethyl acetate), m.p. 221 °C (decomp.), ν_{\max} . 3 450, 3 340, 1 620, and 1 570 cm⁻¹, δ 7.55 (d, 2 H) and 6.9 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 5.42 (br s, exchangeable for D, NH₂), 3.81 (s, O-Me), and 3.55 (m, 4 H), and 1.95 (m, 4 H) (pyrrolidino) (Found: C, 58.3; H, 6.9; N, 28.2. C₁₂H₁₇N₅O requires C, 58.3; H, 6.9; N, 28.3%), and *N*-(*N*-*p*-tolylazoamidino)pyrrolidine (**3e**) (90%), yellow, m.p. 219 °C (decomp.) (from ethanol–ethyl acetate), ν_{\max} . 3 490, 3 385, 1 630, and 1 550 cm⁻¹, δ [(CD₃)₂CO] 7.43 (d, 2 H) and 7.15 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 3.4—2.9 (m, 4 H), and 2.2—1.9 (m, 4 H) (pyrrolidino), 2.75 (br s, exchangeable for D, NH₂), and 2.3 (s, C-Me) (Found: C, 62.1; H, 7.5; N, 30.3. C₁₂H₁₇N₅ requires C, 62.3; H, 7.4; N, 30.3%).

Tetrazinones (5) and Zwitterionic Triazolinones (7).—(a) A stirred solution of 1,1-dimethylamino-2-phenylazoguanidine (**3a**) (3.82 g, 0.02 mol) in a mixture of pyridine (7 ml) and dichloromethane (40 ml) was cooled in a bath of solid carbon dioxide and acetone and a 20% solution of phosgene in toluene (21 ml, 2 mol. equiv.) was added during 30 min. There was continuous gas evolution. The mixture was allowed to reach room temperature and then washed six times with water. The organic phase was dried with sodium sulphate. Its i.r. spectrum showed that it contained as by-products dimethylcyanamide (ν_{\max} . 2 218 cm⁻¹), phenyl isocyanate (2 280 cm⁻¹), and a trace of another compound (1 800 cm⁻¹). The solution was evaporated and the residue was taken up in benzene; the solution deposited cream-coloured 4-dimethylamino-1-phenyl-1,2,3,5-tetrazin-6-one (**5a**) (1.0 g, 23%), m.p. 115 °C (decomp.), ν_{\max} . 1 700, 1 610, 1 590, and 1 580 cm⁻¹; λ_{\max} . 234 and 315 nm; δ 7.7—7.4 (m, Ph), 3.4 (s, N-Me), and 3.15 (s, N-Me); *m/z* 119 (100%) (PhNCO) and 70 (35%) (Me₂NCN) (Found: C, 55.3; H, 5.0; N, 31.9. C₁₀H₁₁N₅O requires C, 55.3; H, 5.1; N, 32.2%).

(b) A similar reaction with 1,1-dimethylamino-2-*p*-tolyl-

azoguanidine (**3b**) on the same scale gave pale-yellow 4-dimethylamino-1-*p*-tolyl-1,2,3,5-tetrazin-6-one (**5b**) (22%), m.p. 117 °C (decomp.) (from ethyl acetate), ν_{\max} . 1 705, 1 615, and 1 560 cm⁻¹; λ_{\max} . 240 and 325 nm; δ 7.48 (d, 2 H) and 7.3 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 3.47 (s, N-Me), 3.25 (s, N-Me), and 2.41 (s, C-Me); *m/z* 133 (100%) (*p*-MeC₆H₄NCO) and 70 (31%) (Found: C, 57.4; H, 5.8; N, 30.1. C₁₁H₁₃N₅O requires C, 57.1; H, 5.7; N, 30.3%). Column chromatography of the benzene mother liquor with ethyl acetate–light petroleum as eluant yielded 2,3-dihydro-3,5-dimethylamino-3-oxo-2-*p*-tolylimino-1*H*-1,2,4-triazol-2-ium-1-ide (**7b**), (5%) deep-yellow needles (from ethyl acetate), m.p. 183 °C (decomp.), ν_{\max} . 1 805, 1 640, 1 600, and 1 500 cm⁻¹; λ_{\max} . 225 and 402 nm; δ 8.42 (d, 2 H) and 7.35 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 3.4 (s, N-Me), 3.38 (s, N-Me), and 2.44 (s, C-Me); *m/z* 133 (100%) and 70 (25%) (Found: C, 57.2; H, 5.7; N, 30.4. C₁₁H₁₃N₅O requires C, 57.1; H, 5.7; N, 30.3%).

(c) A similar reaction on the same scale with the *p*-methoxy compound (**3c**) gave 1-*p*-methoxyphenyl-4-dimethylamino-1,2,3,5-tetrazin-6-one (**5c**) (42%), pale-yellow, m.p. 124 °C (decomp.) (from ethyl acetate), ν_{\max} . 1 712, 1 618, 1 598, and 1 520 cm⁻¹; λ_{\max} . 257 and 340 nm; δ 7.53 (d, 2 H) and 7.02 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 3.85 (s, O-Me), 3.5 (s, N-Me), and 3.26 (s, N-Me); *m/z* 149 (100%) (*p*-MeOC₆H₄NCO) and 70 (30%) (Found: C, 53.6; H, 5.4; N, 28.4. C₁₁H₁₃N₅O₂ requires C, 53.4; H, 5.3; N, 28.3%). and 5-dimethylamino-2,3-dihydro-2-*p*-methoxyphenylimino-3-oxo-1*H*-1,2,4-triazolin-2-ium-1-ide (**7c**) (9%), orange needles (from ethanol–ethyl acetate), m.p. 190 °C (decomp.), ν_{\max} . 1 790, 1 638, and 1 595 cm⁻¹; λ_{\max} . 260 and 425 nm; δ 8.45 (d, 2 H) and 7.04 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 3.9 (s, O-Me), 3.37 (s, N-Me), and 3.33 (s, N-Me); *m/z* 149 (100%) and 70 (22%) (Found: C, 53.3; H, 5.2; N, 28.0%).

(d) *N*-(*N*-*p*-Methoxyphenylazoamidino)pyrrolidine (**3d**) similarly gave 1-*p*-methoxyphenyl-4-pyrrolidino-1,2,3,5-tetrazin-6-one (**5d**) (43%), pale yellow, m.p. 124 °C (decomp.) (from ethyl acetate), ν_{\max} . 1 710, 1 610, 1 580, and 1 505 cm⁻¹; λ_{\max} . 260 and 348 nm; δ 7.5 (d, 2 H) and 7.0 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 4.0—3.5 (m, 4 H), and 2.2—1.8 (m, 4 H) (pyrrolidino), and 3.83 (s, O-Me), *m/z* 149 (100%) (*p*-MeOC₆H₄NCO) and 96 (21%) (*N*-cyanopyrrolidine) (Found: C, 57.4; H, 5.6; N, 25.2. C₁₃H₁₅N₅O₂ requires C, 57.1; H, 5.55; N, 25.6%).

1-Arylimino-3,5-bis(dimethylamino)-1,2,4-triazolium Fluoroborates (12).—A stirred solution of 2-chloro(dimethylamino)methylene-1,1-dimethylguanidinium chloride (**9**)⁹ (4.26 g, 0.02 mol) and the appropriate arenediazonium fluoroborate (1 mol equiv.) in water (80 ml) was slowly treated with 2*M*-aqueous sodium hydroxide (18 ml, 1.8 mol equiv.). The resulting orange-red precipitate was filtered off and recrystallised from acetonitrile–ethyl acetate. The following 3,5-bis(dimethylamino)-1,2,4-triazol-2-ium fluoroborates were obtained: 1-phenylimino- (**12a**) (51%), m.p. 214 °C (decomp.), ν_{\max} . 1 702, 1 650, 1 588, and 1 090 (BF₄⁻) cm⁻¹, λ_{\max} . (MeCN) 432 nm, δ [(CD₃)₂SO] 8.5—7.0 (Ph), 3.8 (s, N-Me), 3.64 (s, N-Me), and 3.51 (s, 2 × N-Me) (Found: C, 43.6; H, 5.15; N, 25.4. C₁₂H₁₇BF₄N₆ requires C, 43.4; H, 5.2; N, 25.3%); 1-*p*-tolylimino- (**12b**) (65%), hygroscopic, m.p. 191 °C (decomp.), ν_{\max} . 1 705, 1 650, 1 600, and 1 070 cm⁻¹, λ_{\max} . (MeCN) 450 nm, δ (CF₃CO₂D) 8.43 (d, 2 H) and 7.55 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 3.88 (s, N-Me), 3.7 (s, N-Me), 3.56 (s, N-Me), 3.53 (s, N-Me), and 2.56 (s, C-Me) (Found: C, 44.2; H, 5.4; N, 23.7. C₁₃H₁₉BF₄N₆·0.5H₂O requires C, 44.5; H, 5.5; N, 23.9%); 1-*p*-methoxyphenylimino- (**12c**) (29%), m.p. 181 °C (decomp.), ν_{\max} . 1 700, 1 650, 1 600, and 1 080 cm⁻¹, λ_{\max} . (MeCN) 493 nm, δ (CF₃CO₂D) 8.6 (d, 2 H) and 7.25 (d, 2 H) (AB_q, *J* 9 Hz, Ar), 4.05 (s, O-Me), 3.75 (br s, 2 × N-Me), and 3.5 (s, 2 × N-Me) (Found: C, 42.8; H, 5.2; N, 23.2. C₁₃H₁₉BF₄N₆O requires C, 43.1; H, 5.3; N, 23.1%); 1-*p*-chlorophenylimino- (**12d**) (54%), m.p. 225 °C (decomp.), ν_{\max} . 1 700, 1 650, 1 580, and 1 050 cm⁻¹, λ_{\max} . (MeCN) 440 nm, δ [(CD₃)₂SO] 8.5 (d, 2 H) and

7.82 (d, 2 H) (AB_q , J 9 Hz, Ar), 3.71 (s, N-Me), 3.58 (s, N-Me), 3.5 (s, N-Me), and 3.3 (s, N-Me) (Found: C, 39.0; H, 4.3; N, 22.5). $C_{12}H_{16}BClF_4N_6$ requires C, 39.3; H, 4.4; N, 22.9%; and 1-*o*-chlorophenylimino- (12e) (42%), m.p. 221 °C (decomp.), ν_{max} . 1 700, 1 655, 1 600, and 1 090 cm^{-1} , λ_{max} . (MeCN) 440 nm, $\delta(CF_3CO_2D)$ 9.1—8.9 (m, 1 H) and 7.95—7.8 (m, 3 H) (Ar), 3.73 (s, N-Me), 3.59 (s, N-Me), 3.46 (s, N-Me), and 3.4 (s, N-Me) (Found: C, 39.0; H, 4.45; N, 22.9%).

Acknowledgements

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