Triazines and Related Products. Part XII.[1] Reactions of 3,4-Dihydro-4-imino-1,2,3-benzotriazines and 1,2,3-Benzotriazin-4(3*H*)-ones in Secondary Amines

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3-Substituted 3,4-dihydro-4-imino-1,2,3-benzotriazines (1a—g) undergo ring opening in piperidine, morpholine, and pyrrolidine to afford the *o*-cyanophenyltriazenes (2a—g), respectively. Attack by the bases at the exocyclic imino-substituent is implicated in these isomerisations since the 3-benzyltriazine (1h) and the 3-substituted 4-arylimino-3,4-dihydro-1,2,3-benzotriazines (4a—e) are all unreactive. Similarly, reaction of the bases at the exocyclic imino-group of the *N*-hydroxy-tautomer of 4-aminobenzotriazine 3-oxide (6) leads to *o*-azidobenzonitrile (8).

The fused 1,2,3-benzotriazines (11) and (13) react with secondary amines to afford 3,3-dialkyl- or polymethylenetriazenes, but the reactivity of 3-substituted 1,2,3-benzotriazin-4(3*H*)-ones (19) towards piperidine and its analogues is dependent on the nature of the 3-substituent.

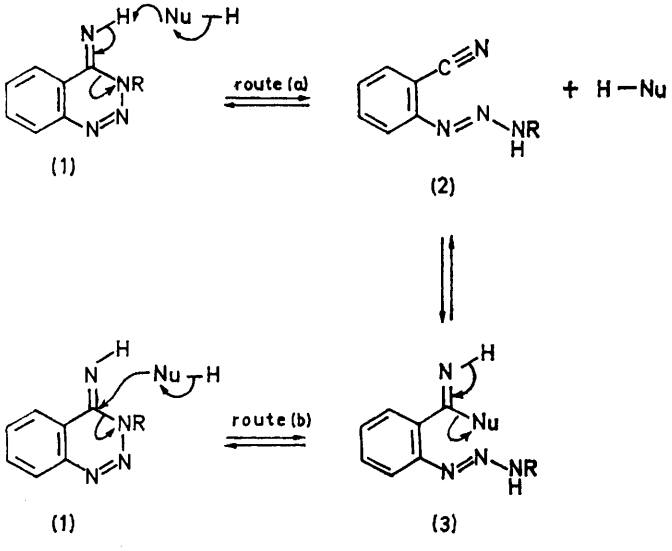
In the preceding paper, the behaviour of 3-substituted 3,4-dihydro-4-imino-1,2,3-benzotriazines towards acetic acid was described: these triazines undergo cleavage of the N(2)–N(3) bond and rearrange to substituted 4-amino-1,2,3-benzotriazines (Dimroth rearrangement).[2] Here we describe the reactivity of some 3,4-dihydro-4-iminobenzotriazines and related compounds towards secondary alkyl amines: in these cases initial attack of the reagent occurs either at the exocyclic substituent, or at N-2 or C-4 of the triazine ring.

When the triazines (1a—d) were boiled in piperidine for 15 min, deep red solutions were produced. If these solutions were diluted with 95% ethanol, and their u.v.–visible spectra recorded immediately, maxima in the range 360—370 nm characteristic of the acyclic triazenes (2a—d) were observed. If, however, recording of the spectra was delayed for 15 min, the absorbing species were mixtures of the cyclic and acyclic forms; after 24 h the cyclic imines (showing the diagnostic two pairs of absorption maxima in the range 260—270 and 305—320 nm) [3] predominated.

If the piperidine solutions were allowed to evaporate, the residues were the (apparently) unchanged iminotriazines (1a—d): if, however, the red solutions were quenched with an excess of ice-cold 0·5N-sulphuric acid, the acyclic triazenes (2a—d) could be isolated in 75—85% yields.

We interpret these phenomena in terms of a reversible reaction as follows: in an excess of boiling piperidine the iminotriazines (1a—d) undergo ring opening to the *o*-cyanophenyltriazenes (2a—d), which can be isolated in an acidic medium; at low concentration of the base, *i.e.* when the solutions are diluted with 95% ethanol or evaporated, the triazenes recyclise to the iminotriazines. This behaviour explains the difficulties which have occasionally arisen in large-scale preparations of the iminotriazines (1). These syntheses may be accomplished rapidly by boiling *o*-cyanophenyltriazenes (2) in 70% aqueous ethanol, or, more slowly, in 95% ethanol containing 2% piperidine.[3] In the latter cyclisation adding base in more than a catalytic amount in an attempt to accelerate the cyclisation merely leads to ring opening of any iminotriazine that might have formed.

The iminotriazines (1e—g) also undergo ring-opening



a; R = Ph
b; R = *o* -Me C_6H_4
c; R = *p* - Me C_6H_4
d; R = *p* - Et C_6H_4
e; R = *o* - Cl C_6H_4
f; R = *m* - CN·C_6H_4
g; R = *p* - [N:C(NH$_2$)·N:C(NH$_2$)·N:C-]C_6H_4
h; R = $PhCH_2$

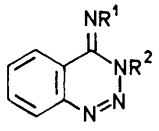
Scheme 1

in piperidine as shown by the u.v.–visible spectral changes during the reaction. Furthermore, morpholine and pyrrolidine are as effective as piperidine as base components.

We can envisage two mechanisms to account for the ring-opening step (Scheme 1): in route (a) the base

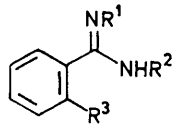
[1] M. S. S. Siddiqui and M. F. G. Stevens, preceding paper.
[2] D. J. Brown, 'Mechanisms of Molecular Migrations,' ed. Thyagarajan, vol. 1, Wiley, New York, 1968, p. 209.
[3] H. N. E. Stevens and M. F. G. Stevens, *J. Chem. Soc.* (*C*), 1970, 765.

(Nu–H) abstracts the acidic imino-proton; in route (b) initial attack by the nucleophile occurs at C-4. We prefer the former mechanism since it explains the stability of the 3-benzyltriazine (1h) and the 3,4-disubstituted benzotriazines (4a—e) towards boiling



(4)

	R^1	R^2
a;	Ph	Ph
b;	Ph	Me
c;	Ph	Pr^i
d;	Ph	$PhCH_2$
e;	o-ClC_6H_4	Me



(5)

	R^1	R^2	R^3
a;	H	Ph	H
b;	Ph	Ph	NO_2
c;	Ph	$PhCH_2$	NO_2
d;	Ph	$PhCH_2$	NH_2

piperidine. In the benzyltriazine, the $+I$ substituent would decrease the acidity of the imino-proton to render its removal by base more difficult; the disubstituted triazines (4) would also be stable since they possess no abstractable imino-proton.

If attack at C-4 were operative, intermediate amidines (3) would be involved. There is no evidence that such derivatives should be particularly unstable and be degraded to nitriles [4] (see also following paper). The amidines (5a—d), for example, are all stable in boiling piperidine. The fact that no amidines were detected from the benzyltriazine (1h) and the disubstituted triazines (4a—e) also argues against nucleophilic attack at C-4 in the triazines (1a—g).

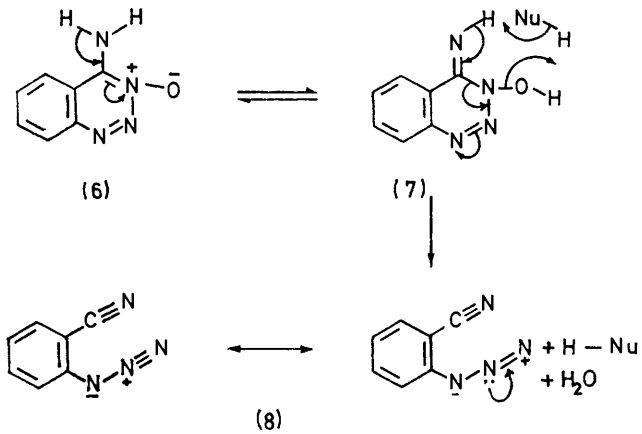
The isolation of *o*-cyanophenyltriazenes from reactions of substituted 3,4-dihydro-4-iminobenzotriazines in ethanolic sodium ethoxide [5] has obvious mechanistic affinities with the present work. Again, attack of ethoxide ion at the exocyclic substituent or at C-4 is possible (Scheme 1; Nu = OEt)—if the latter, an intermediate imidate (3; Nu = OEt) would be formed. Although the literature on imidates [6] contains many examples of their decomposition to nitriles (' retro-Pinner reactions '), the inertness of the diphenyltriazine (4a) towards sodium ethoxide supports the proton-abstraction process in these examples also.

4-Amino-1,2,3-benzotriazine 3-oxide (6), formed by diazotisation of *o*-aminobenzamide oxime [7] affords *o*-azidobenzonitrile (8) in high yield in both boiling piperidine and boiling pyrrolidine. Again, we believe that ring cleavage is initiated by proton abstraction (Scheme 2) from the 4-imino-group of the *N*-hydroxy-tautomer (7).

There are precedents for azide formation from 1,2,3-triazines; indeed, the *N*-oxide (6) has been reported to yield *o*-azidobenzonitrile (84%) when fused with ammonium acetate,[8] although no mechanism was advanced to explain the transformation. The ring opening of the intriguing 2-aminonaphthotriazine (9) in weak acid or alkali described by Rees and Storr [9] yields 1-amino-8-azidonaphthalene (10) in high yield. These authors contend that ring opening involves abstraction of the acidic amino-proton, and a mechanism can be written (Scheme 3) which is similar to that in Scheme 2.

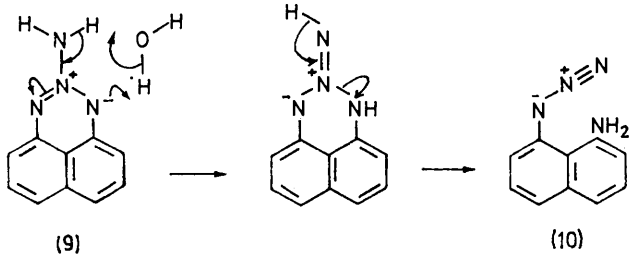
Azides have also been isolated from the decomposition of 1,2,3-benzotriazine 3-oxides [10,11] and 3-substituted 1,2,3-benzotriazin-4(3*H*)-ones [12,13] in acids and bases, but in these cases nucleophilic attack at an activated 4-position seems to be involved.

In those modified 3-substituted 3,4-dihydro-4-iminobenzotriazines where both N-3 and C-4 occupy bridgehead positions in polycyclic systems, reaction at N-2 is observed. For example, the *s*-triazino[1,2-*c*][1,2,3]-benzotriazine (11) [14] affords the triazenes (12a—e) in



(6) (7) (8)

SCHEME 2



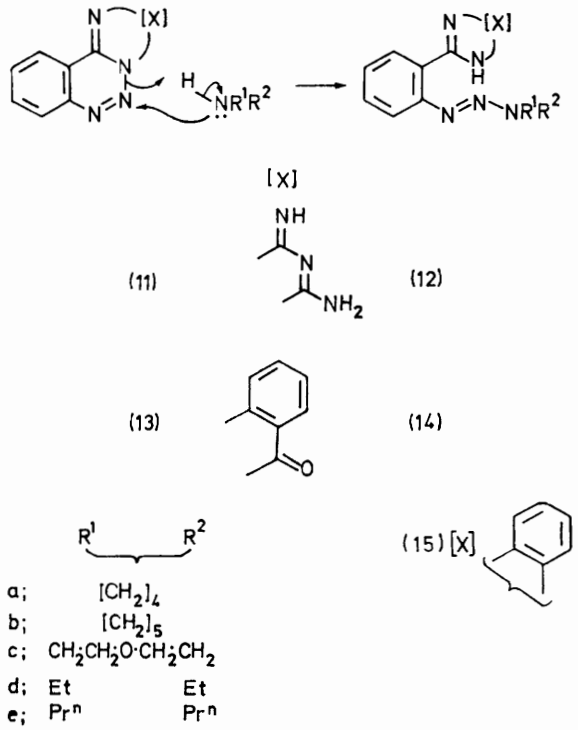
(9) (10)

SCHEME 3

boiling secondary alkylamines (Scheme 4). Similarly, the quinazolino[3,2-*c*][1,2,3]benzotriazine (13) reacts with pyrrolidine, piperidine, and morpholine to yield the triazenes (14a—c), respectively. The benzimidazo-

[4] R. L. Shriner and F. W. Neumann, *Chem. Rev.*, 1944, **35**, 351.
[5] H. N. E. Stevens and M. F. G. Stevens, *J. Chem. Soc.* (*C*), 1970, 2284.
[6] R. Roger and D. G. Neilson, *Chem. Rev.*, 1961, **61**, 179.
[7] J. Pinnow and C. Sämann, *Ber.*, 1896, **29**, 623.
[8] E. W. Parnell, *J. Chem. Soc.*, 1961, 4930.
[9] C. W. Rees and R. C. Storr, *J. Chem. Soc.* (*C*), 1969, 756.
[10] E. Bamberger and E. Demuth, *Ber.*, 1901, **34**, 1309.
[11] J. Meisenheimer, O. Senn, and P. Zimmermann, *Ber.*, 1927, **60**, 1736.
[12] D. Harrison and A. C. B. Smith, *J. Chem. Soc.*, 1960, 2157.
[13] M. S. Gibson and M. Green, *Tetrahedron*, 1965, **21**, 2191.
[14] S. M. Mackenzie and M. F. G. Stevens, *J. Chem. Soc.* (*C*), 1970, 2298.

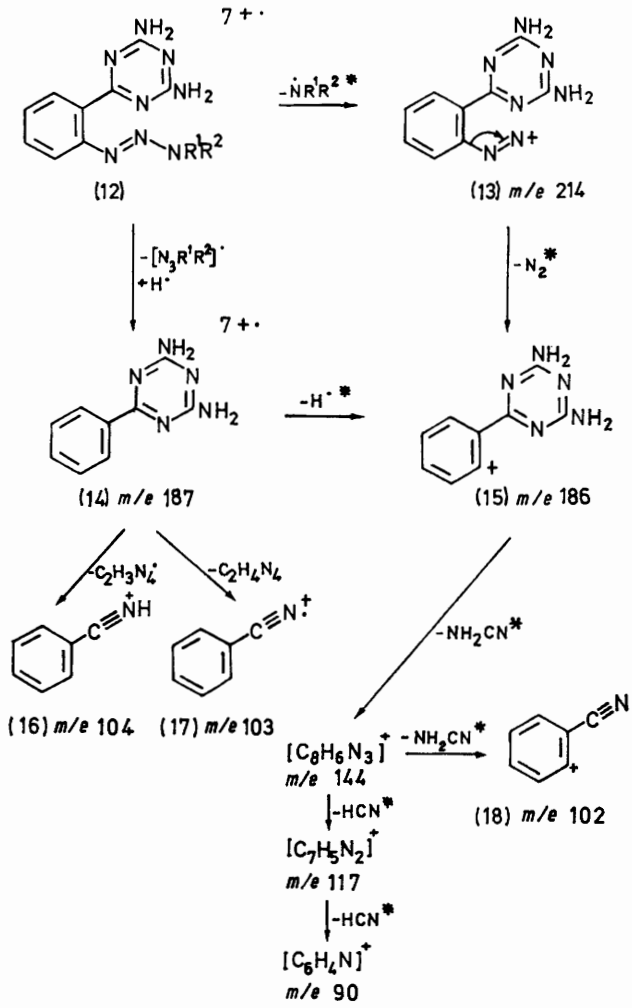
[1,2-*c*][1,2,3]benzotriazine (15), in contrast, is stable in boiling piperidine.



SCHEME 4

The most abundant ions in the mass spectra of the triazenes (12) occur at *m/e* 187, 186, and 144, and we interpret the fragmentation pathway as outlined in Scheme 5. Loss of the dialkylamino-radical to give the diazonium ion (13) at *m/e* 214, followed by loss of nitrogen to afford the aryl cation (15) at *m/e* 186 has precedents in the ion-impact-promoted decompositions of diaryltriazenes.[15] Alternatively, the ion at *m/e* 186 can be formed by loss of a hydrogen atom from the 2,4-diamino-6-phenyl-*s*-triazine radical ion (14), itself formed indirectly from the molecular ion. The rest of the spectrum is very similar to that of the diamino-phenyl-*s*-triazine (14) [16] and shows a cluster of peaks at *m/e* 104, 103, and 102 attributable to protonated benzonitrile (16), the benzonitrile radical ion (17), and the benzonitrile cation (18), respectively. High resolution mass measurements confirm the constitution of the fragment ions, and the fragmentations are supported by metastable ion peaks (denoted *).

The behaviour of the triazin-4(3*H*)-ones (19) towards boiling piperidine is markedly influenced by the nature of the 3-substituent (Scheme 6). With the unsubstituted triazinone (19; R = H) nucleophilic attack at C-4 affords the unstable triazene (20), which decomposes to the substituted anthranilamide (21) in the manner proposed for related decompositions in high-boiling amines.[17] We obtained similar anthranilamides with morpholine and pyrrolidine, but surprisingly not with diethylamine or di-n-propylamine. When the triazinone was substituted with a range of alkyl, aralkyl, and aryl substituents there was no reaction in piperidine with the exception of the 3-*p*-nitrophenyltriazinone. This nitro-triazinone afforded a yellow solid which gave a positive Bamberger–Goldberger test,[18] confirming the presence of the intact NNN-linkage. Two structures are possible for this triazene [(22) or (23)] depending on whether the piperidine reacts at C-4 or N-2, respectively, but the spectroscopic evidence is consistent only with structure (22). The electronic absorption spectrum shows a long-wavelength absorption at 367 nm (log ε 4·19); the mass



SCHEME 5

spectrum shows abundant ions at *m/e* 150 and 122 assigned to the *p*-nitrophenyldiazonium ion and its

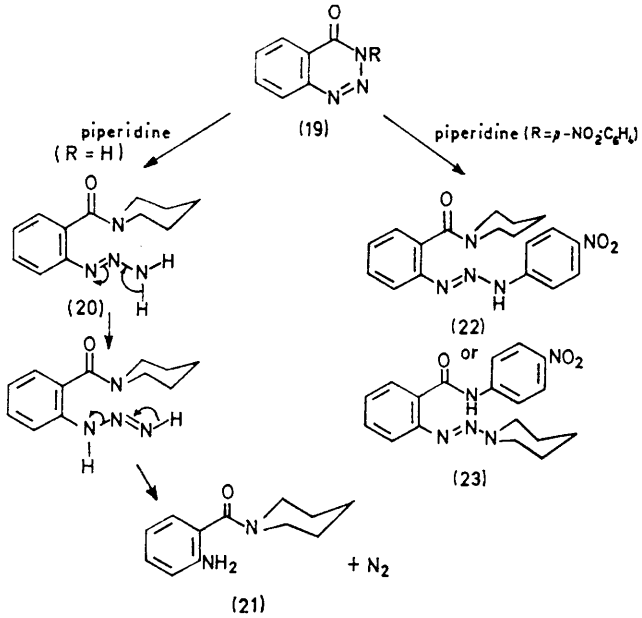
[15] R. A. W. Johnstone, D. W. Payling, P. N. Preston, H. N. E. Stevens, and M. F. G. Stevens, *J. Chem. Soc.* (*C*), 1970, 1238.

[16] P. N. Preston, W. Steedman, M. H. Palmer, S. M. Mackenzie, and M. F. G. Stevens, *Org. Mass Spectrometry*, 1970, **3**, 863.

[17] A. W. Murray and K. Vaughan, *J. Chem. Soc.* (*C*), 1970, 2070.

[18] 'The Chemistry of Heterocyclic Compounds,' ed. A. Weissberger, Interscience, New York, 1956, vol. 10, p. 1.

decomposition ion, the *p*-nitrophenyl cation, respectively. These characteristics are in accord with the u.v.–visible [3] and mass spectral [15] data of 1,3-diaryltriazenes, and exclude structure (23).



SCHEME 6

EXPERIMENTAL

Reactions of 3-Substituted 3,4-Dihydro-4-imino- and 4-arylimino-1,2,3-benzotriazines in Piperidine.—(i) 3,4-Dihydro-4-imino-3-phenyl-1,2,3-benzotriazine (2·0 g) [3] was boiled in piperidine (10 ml) for 15 min. The cooled red solution was poured into an excess of ice-cold 0·5N-sulphuric acid, and the precipitated product was extracted into ether. The crystalline solid (1·6 g, 80%) left when the ether was removed was identical (i.r. and m.p.) with an authentic sample of 1-*o*-cyanophenyl-3-phenyltriazene.[3]

The same phenyltriazene was isolated (78 and 85% yields, respectively) when the iminobenzotriazine was boiled (15 min) in morpholine or pyrrolidine and the solutions were poured into 0·5N-sulphuric acid.

(ii) When 3,4-dihydro-4-imino-3-phenyl-1,2,3-benzotriazine was boiled in piperidine (1 h) and the solution allowed slowly to evaporate, the crystalline product was identical (i.r.) with the starting material.

(iii) The 3-substituted benzotriazines (1b),[3] (1c),[1] and (1d),[1] were boiled in piperidine (15 min). The triazenes (2b) (78%),[3] (2c) (75%),[1] and (2d) (85%) [1] were isolated when the solutions were poured into ice-cold 0·5N-sulphuric acid.

(iv) Solutions of the triazines (1e and f) [3] and (1g) [1] in boiling piperidine rapidly turned yellow. The electronic absorption spectra of these solutions (in ethanol) showed long-wavelength absorptions at 361, 362, and 366 nm, identical with the values recorded for the pure triazenes (2e and f) [3] and (2g),[1] respectively.

(v) 3-Benzyl-3,4-dihydro-4-imino-1,2,3-benzotriazine crystallised unchanged from refluxing piperidine (1 h).

(vi) The 3-substituted 4-arylimino-3,4-dihydro-1,2,3-benzotriazines (4a—e) were quantitatively recovered after being boiled in piperidine or morpholine for 6 h.

o-Azidobenzonitrile.—4-Amino-1,2,3-benzotriazine 3-oxide (1·0 g) [7] was boiled in piperidine (10 ml) for 30 min. The solution was concentrated and diluted with ice–water, and the precipitated crude *o*-azidobenzonitrile crystallised from light petroleum (b.p. 40—60°) as buff prisms (0·7 g, 77%), identical {m.p. and i.r. spectrum [$\nu_{max.}$ (Nujol) 2220 (C≡N) and 2135 and 2105 cm^{-1} (N_3)]} with a sample prepared by treating diazotised *o*-aminobenzonitrile with sodium azide.

The same azidonitrile was formed (80%) from 4-amino-1,2,3-benzotriazine 3-oxide in boiling pyrrolidine.

2,4-*Diamino*-6-[2-(*pyrrolidin*-1-*ylazo*)*phenyl*]-s-*triazine* (12a).—A solution of 4-amino-2-imino-*s*-triazino[1,2-*c*]-[1,2,3]benzotriazine [14] (4·0 g) in pyrrolidine (30 ml) was boiled for 6 h, concentrated (to 5 ml), and diluted with water. The precipitated *pyrrolidinylazo*-s-*triazine* (4·8 g) crystallised from methanol as brown flakes, m.p. 220—222° (efferv.) (Found: C, 54·6; H, 5·7; N, 39·4%; M^+, 284. $C_{13}H_{16}N_8$ requires C, 54·9; H, 5·6; N, 39·4%; *M*, 284).

2,4-*Diamino*-6-[2-(*piperidin*-1-*ylazo*)*phenyl*]-s-*triazine* (12b).—This *piperidinoazo*-s-*triazine* (95%), similarly prepared from the *s*-triazino[1,2-*c*][1,2,3]benzotriazine (11) and piperidine, crystallised from methanol as flakes, m.p. 227—228° (efferv.) (Found: C, 56·1; H, 6·1; N, 37·9%; M^+, 298. $C_{14}H_{18}N_8$ requires C, 56·4; H, 6·0; N, 37·6%; *M*, 298).

2,4-*Diamino*-6-[2-(*morpholin*-4-*ylazo*)*phenyl*]-s-*triazine* (12c).—Formed (85%) from the benzotriazine (11) and boiling morpholine (6 h), this *triazine* crystallised from methanol as buff flakes, m.p. 208—210° (efferv.) (Found: C, 52·2; H, 5·4; N, 37·4%; M^+, 300. $C_{13}H_{16}N_8O$ requires C, 52·0; H, 5·3; N, 37·3%; *M*, 300).

2,4-*Diamino*-6-[2-(3,3-*diethyltriazen*-1-*yl*)*phenyl*]-s-*triazine* (12d).—When the benzotriazine (11) (4·3 g) was refluxed in diethylamine (100 ml) for 6 h, insoluble unchanged starting material (2·5 g) was recovered from the cooled solution. Dilution of the concentrated mother liquor with water afforded the *phenyl*-s-*triazine* (1·9 g), which crystallised from aqueous methanol as brown prisms, m.p. 215—217° (efferv.) (Found: C, 54·7; H, 6·5; N, 39·0%; M^+, 286. $C_{13}H_{18}N_8$ requires C, 54·5; H, 6·3; N, 39·2%; *M*, 286).

2,4-*Diamino*-6-[2-(3,3-*di-n-propyltriazen*-1-*yl*)*phenyl*]-s-*triazine* (12e).—Obtained from the *s*-triazinobenzotriazine (11) and boiling di-n-propylamine, this *triazenylphenyl*-s-*triazine* (75%) crystallised from aqueous ethanol as cream needles, m.p. 206—208° (efferv.) (Found: C, 57·5; H, 7·0; N, 35·8%; M^+, 314. $C_{15}H_{22}N_8$ requires C, 57·3; H, 7·0; N, 35·7%; *M*, 314).

2-[2-(*Pyrrolidin*-1-*ylazo*)*phenyl*]*quinazolin*-4(3H)-*one* (14a).—A solution of quinazolino[3,2-*c*][1,2,3]benzotriazine-8-one (1·0 g) [17] in pyrrolidine (5 ml) was boiled (4 h) and evaporated to dryness under reduced pressure. The residue crystallised from methanol to afford the *pyrrolidinylazoquinazolone* (1·1 g) as buff needles, m.p. 160—161° (efferv.) (Found: C, 67·4; H, 5·3; N, 22·0. $C_{18}H_{17}N_5O$ requires C, 67·7; H, 5·4; N, 21·9%).

2-[2-(*Piperidin*-1-*ylazo*)*phenyl*]*quinazolin*-4(3H)-*one* (14b).—Interaction of the quinazolinobenzotriazinone (13) and piperidine as before yielded the *piperidinylazoquinazolone* (80%), which crystallised from light petroleum as buff flakes, m.p. 133—134° (efferv.) (Found: C, 68·3; H, 5·9; N, 20·7. $C_{19}H_{19}N_5O$ requires C, 68·4; H, 5·7; N, 21·0%).

2-[2-(*Morpholin*-4-*ylazo*)*phenyl*]*quinazolin*-4(3H)-*one* (14c).—Formed from the quinazolinobenzotriazinone (13) and refluxing morpholine, this *morpholinoazoquinazolone* (85%)

crystallised from methanol as white needles, m.p. 189—190° (efferv.) (Found: C, 64·3; H, 5·0; N, 21·1. $C_{18}H_{17}N_5O_2$ requires C, 64·4; H, 5·0; N, 20·8%).

1-(2-*Aminobenzoyl*)*piperidine* (21).—1,2,3-Benzotriazin-4(3*H*)-one (8·0 g) in piperidine (20 ml) was boiled (8 h) and the excess of solvent was removed by vacuum distillation. The residue crystallised from benzene–light petroleum to afford the aminobenzoylpiperidine (7·1 g) as needles, m.p. 75—76° (lit.,[19] 77—78°).

Similarly prepared from the triazinone and morpholine or pyrrolidine were 4-(2-aminobenzoyl)morpholine (70%) [19] and 1-(2-aminobenzoyl)pyrrolidine (75%), respectively. There is a large discrepancy between the m.p. (75—76°) of our sample of the aminobenzoylpyrrolidine and that recorded for a sample (m.p. 237—239°) prepared from isatoic anhydride and pyrrolidine.[20] When we repeated this latter synthesis we obtained a sample of the aminobenzoylpyrrolidine with spectroscopic properties identical with those of the triazinone–pyrrolidine product, and with m.p. 75—76°.

[19] N. J. Leonard, W. V. Ruyle, and L. C. Bannister, *J. Org. Chem.*, 1948, **13**, 617.

2-[3-(p-*Nitrophenyl*)*triazen*-1-*yl*]-NN-*pentamethylenebenzamide* (22).—A solution of 3-*p*-nitrophenyl-1,2,3-benzotriazin-4(3*H*)-one (5·0 g) [3] was boiled in piperidine (25 ml) for 48 h; the excess of solvent was then removed by vacuum distillation. The residue, crystallised from ethanol, afforded the *amide* (3·2 g) as orange needles, m.p. 197—199° (efferv.) (Found: C, 61·1; H, 5·3; N, 19·9%; M^+, 353. $C_{18}H_{19}N_5O_3$ requires C, 61·1; H, 5·3; N, 20·0%; *M*, 353); $\lambda_{max.}$ (EtOH) 249, 273, and 367 nm (log ε 3·90, 3·85, and 4·19).

The 1,2,3-benzotriazin-4(3*H*)-ones (19) with 3-methyl, ethyl, isopropyl, benzyl, phenethyl, phenyl, *o*-tolyl, *o*-chlorophenyl, and *o*-nitrophenyl substituents were all recovered unchanged from boiling piperidine (8 h).

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[3/1946 *Received*, 24*th September*, 1973]

[20] R. P. Staiger, C. L. Moyer, and G. R. Pitcher, *J. Chem. Eng. Data*, 1963, **8**, 454.