1,2,3-Benzotriazin-4-ones and Related Systems. Part 6.[1] Thermal and Photolytic Decomposition of 3-Arylideneamino-, 3-Imidoyl-, and 3-Heteroaryl-1,2,3-benzotriazin-4-ones

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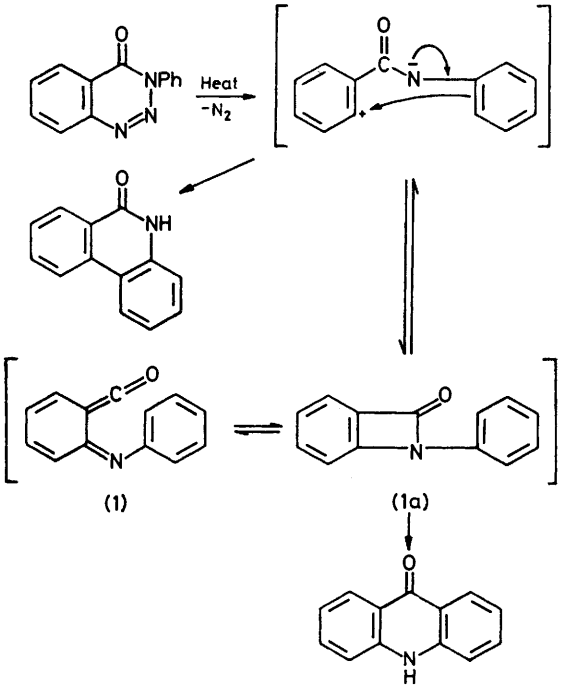
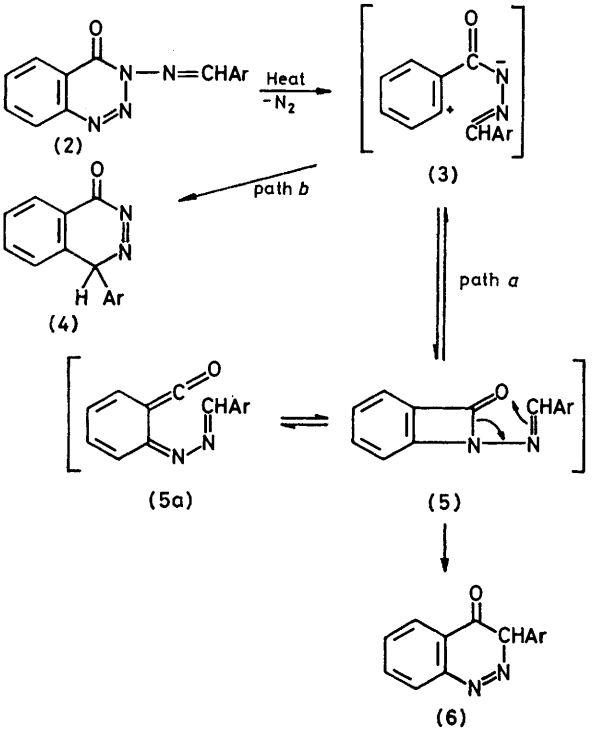
Thermal decomposition of 3-arylideneamino- and 3-imidoyl-1,2,3-benzotriazin-4-ones in solution gives 2-arylquinazolin-4-ones and 1,2-diaryl-1,4-dihydroquinazolin-4-ones, respectively. In the latter decompositions phenanthridones are also formed in minor but substantial (20%) yield. Possible mechanisms to account for these products are discussed. Photolysis of the 3-arylideneamino-derivatives in methanol provides a useful synthesis of aldehyde *o*-(methoxycarbonyl)phenylhydrazones. 3-(α-Pyridyl)- and 3-thiazol-2-yl-1,2,3-benzotriazin-4-one undergo thermal decomposition to pyrido[2,1-*b*]quinazolin-11-one and thiazolo[2,3-*b*]quinazolin-5-one, respectively.

PREVIOUS investigations have shown that 3-aryl-1,2,3-benzotriazin-4-ones on thermal decomposition yield mainly acridones [2,3] accompanied, in certain instances,[2] by phenanthridones. Formation of these products has been rationalised on the basis of either a radical process [2] or an iminoketen–benzazetinone intermediate [(1) ⇌ (1a) [3]] as outlined in Scheme 1. In a similar manner 3-alkenyl-1,2,3-benzotriazin-4-ones yield 3-substituted-4-quinolones.[1] By analogy it was expected that thermolysis of 3-arylideneamino- (2) and 3-imidoyl-1,2,3-benzotriazin-4-ones (7), in which the C=C moiety of the 3-



SCHEME 1

substituent has been replaced by N=C and C=N, respectively, would yield mainly 3-arylcinnolones (6) and 2,3-diarylquinazolinones (10) *via* the appropriately *N*-substituted iminoketen–benzazetinone systems as illustrated in Schemes 2 and 3 (path *a*). Alternatively, 'phenanthridone-type' products, *i.e.* the 1-arylphthalazinones (4) and the 1,2-diarylquinazolinones (9) are possible by direct cyclisation of the open-chain charged intermediates (3) and (8) (Schemes 2 and 3, path *b*). In



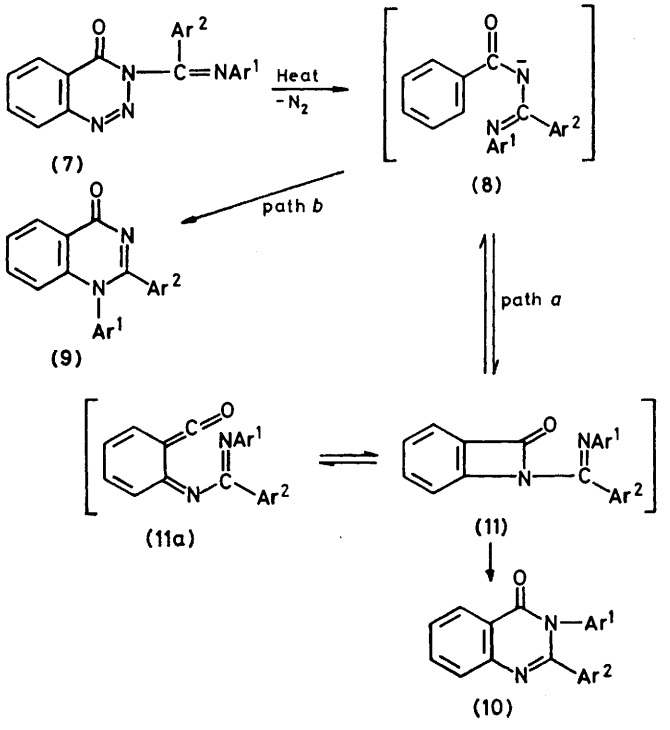
SCHEME 2

the event it was found that the 3-arylideneamino-derivatives (2) gave neither of the anticipated products but instead the isomeric 2-arylquinazolin-4-ones (14),[4a] whereas the imidoyl derivatives furnished not the expected 2,3-diarylquinazolin-4-ones (10) but a mixture of the hitherto little known 1,2-diaryl-1,4-dihydroquinazolin-4-ones (9) and, surprisingly, phenanthridones in minor but significant yields (*ca.* 20%).[4b]

RESULTS AND DISCUSSION

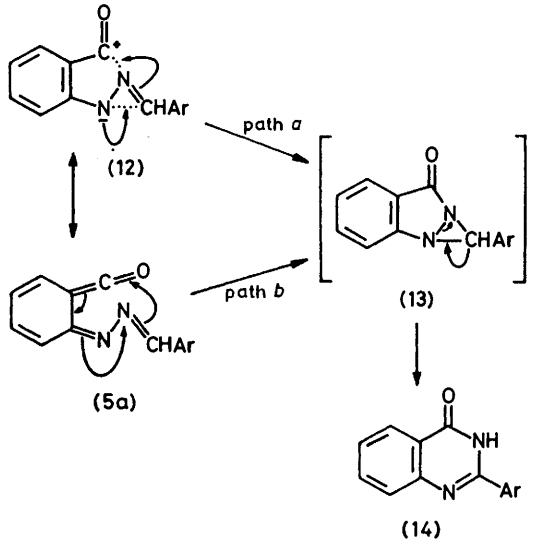
The arylideneamino-derivatives listed in Table 1 (and in reference 4*a*) were prepared in excellent yield by condensing 3-amino-1,2,3-benzotriazin-4-one [5] with the ap-

priate aldehyde in ethanol solution containing a catalytic amount of *p*-toluenesulphonic acid. Decomposition of the arylideneamino-derivatives in paraffin oil at 300 °C, with the exception of those listed in Table 1 which gave



SCHEME 3

only intractable tars, furnished 2-arylquinazolin-4-ones (14) in practicable yields (47—71%).[4a] The mode of quinazolinone formation is not immediately obvious. An earlier suggestion[4a] that the unsubstituted iminoketen, formed by loss of aryl cyanide from either intermediate (5) or from the benzotriazinone (2) by a McLafferty-type elimination, enters into a ($4\pi + 2\pi$) intermolecular cycloaddition with the extruded arylnitrile fragment is hardly likely, as decomposition of 1,2,3-benzotriazin-4-one, a well-known[3] precursor of the unsubstituted iminoketen intermediate, in benzonitrile gave only low yields (<2%) of the 2-arylquinazolinone, a result in keeping with the low dienophilicity of arylnitriles.[6] The major product from the reaction was 2-(*o*-aminophenyl)-3,1-benzoxazin-4-one, *i.e.* the ($4\pi + 2\pi$) dimer of the iminoketen (1).[3a] Certainly, the quinazolinones are not formed by thermal isomerisation of the cinnolones (6) or the phthalazinones (4) since their phenyl derivatives (Ar = Ph), prepared unambiguously by literature methods,[7,8] remained unchanged under the thermolysis conditions. A possible mechanism to explain quinazolinone formation is outlined in Scheme 4. Heterolytic ring-opening of the benzazetinone (5) yields the polar intermediate (12), cyclisation of which (path *a*) produces the tricyclic intermediate (13), and hence the 2-arylquinazolinone (14). Alternatively, the fused diaziridine (13) may be formed by a geometrically unfavourable but symmetry allowed ($_4\pi_a + _2\pi_a$) intramolecular cycloaddition as shown (Scheme 4, path *b*). Analogous



SCHEME 4

($_4\pi_a + _2\pi_a$) intramolecular cyclisations of *o*-quinonoid intermediates have been proposed recently by Padwa and his co-workers [9] to explain indene oxide formation in the photo-rearrangement of isochromenes, and by Rees and his co-workers [10] to account for the thermally-induced ring-contraction of 1,2,4-benzoxadiazines to benzoxazoles.

The absence of heterocycles (6) and (4) in the decomposition products may be due to polar effects. Cyclisation of the charged intermediate (3) to the iminoketen–benzazetinone system (5) is preferred over phthalazinone

TABLE 1

3-Arylideneamino-1,2,3-benzotriazin-4-ones (2)

Ar	M.p. (°C)	Yield (%)	Found (%) C	H	N	Molecular formula	Required (%) C	H	N
m-$O_2NC_6H_4$	260	93	56.7	3.2	23.8	$C_{14}H_9N_5O_3$	56.95	3.05	23.7
p-$O_2NC_6H_4$	230 *	89	56.6	3.4	23.9	$C_{14}H_9N_5O_3$	56.95	3.05	23.7
p-HOC_6H_4	250 (decomp.)	99	63.3	4.2	20.8	$C_{14}H_{10}N_4O_2$	63.15	3.8	21.0
p-$Me_2NC_6H_4$	152	70	65.8	5.2	24.1	$C_{16}H_{15}N_5O$	65.3	5.2	23.9
2-pyridyl	148	85	61.8	4.0	27.6	$C_{13}H_9N_5O$	62.1	3.6	27.9
2-furyl	175	100	60.3	3.5	23.6	$C_{12}H_8N_4O_2$	60.0	3.4	23.3
2-thienyl	202	98	56.0	2.9	21.8	$C_{12}H_8N_4OS$	56.2	3.1	21.9

* Decomposes at 230 °C without melting.

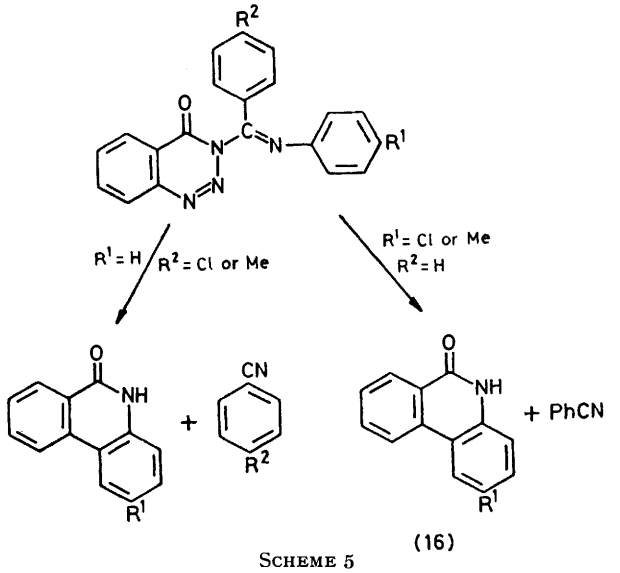
formation (4), as the latter would involve location of the negative charge on the less electronegative, and hence less favoured, carbon centre. This effect should also deter cinnolone formation from the polar intermediate (12).

In contrast to the photostability of 1,2,3-benzotriazin-4-ones bearing a saturated 3-substituent, other 3-substituted benzotriazinones undergo interesting photo-transformations.[11] However, photolysis of the 3-aryl-ideneamino-derivatives (2) in acetonitrile proved to be disappointing in that only intractable tars were formed.

TABLE 2

(*o*-Methoxycarbonyl)phenylhydrazones (15), $ArCH{=}NNHC_6H_4CO_2Me$-*o*

Ar	M.p. (°C)	Yield (%)	Found (%) C	H	N	Molecular formula	Required (%) C	H	N
p-MeC_6H_4	103	69	71.9	5.6	10.9	$C_{16}H_{16}N_2O_2$	71.6	6.0	10.45
p-$MeOC_6H_4$	105	59	67.9	5.8	9.9	$C_{16}H_{16}N_2O_3$	67.6	5.7	9.7
p-ClC_6H_4	132	44	62.5	4.7	9.4	$C_{15}H_{13}ClN_2O_2$	62.4	4.5	9.7
p-HOC_6H_4	157	49	66.7	4.9	10.6	$C_{15}H_{14}N_2O_3$	66.7	5.2	10.4
3-furyl	93	59	64.1	4.8	11.6	$C_{13}H_{12}N_2O_3$	63.9	4.9	11.5
2-thienyl	73	44	60.5	4.7	11.1	$C_{13}H_{12}N_2O_2S$	60.0	4.65	10.8
$C_6H_5CH{=}CH-$	99	44	73.1	6.0	10.0	$C_{17}H_{16}N_2O_2$	72.8	5.75	10.0

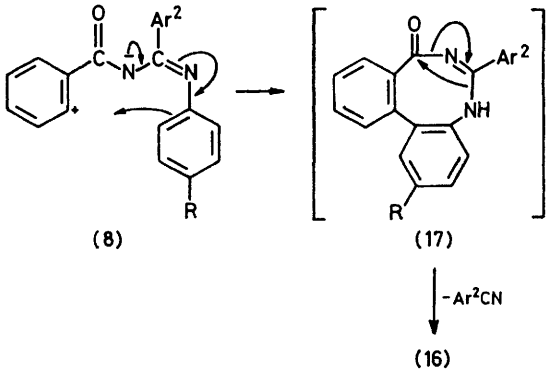


SCHEME 5

Of more interest were their photo-decompositions in methanol which produced the *o*-methoxycarbonylphenyl-hydrazones, (15), in good yield (see Table 2). Hydrazone formation is in keeping with the findings of Ege,[12] and can be explained on the basis of an initial formation and subsequent methanolysis of the imino-ketens (5a). The structure of the hydrazone (15; Ar = Ph) was confirmed by synthesis.[13]

Imidoylation of 1,2,3-benzotriazin-4-one in the presence of either sodium hydride in tetrahydrofuran or potassium t-butoxide in t-butyl alcohol gave the 3-imidoyl derivatives *e.g.* (7) in good yield.[4b] The structure of the diphenyl derivative (7; $Ar^1 = Ar^2 = Ph$) was confirmed by acid hydrolysis under mild conditions to the known[14] 3-benzoyl-1,2,3-benzotriazin-4-one. Surprisingly, and in contrast to the 3-aryl-, 3-alkenyl-, and 3-arylidene-amino-1,2,3-benzotriazinones, the 3-imidoyl derivatives on thermolysis in paraffin oil gave no products derived from the iminoketen–benzazetinone intermediate (Scheme 3, path *a*), but gave the 1,2-diaryl-1,4-dihydroquinazolinones (9), by loss of nitrogen and cyclisation of the mesomeric amidine anion (Scheme 3, path *b*).[4b] Also formed are phenanthridones (*ca.* 20%) the origins of which are of mechanistic interest. Thermal rearrangement of the 1,4-dihydroquinazolinones or of the 2,3-diarylquinazolinones (10)[15] as a source of the phenanthridones may be discounted as both these systems (Ar = Ph) are stable under the conditions used to thermolyse the imidoylbenzotriazinones.

Obviously, phenanthridone formation necessitates linking of two phenyl rings. Decomposition of substituted imidoyl derivatives showed that only substituents that reside on the *N*-phenyl group are retained in the final phenanthridone, *e.g.* see Scheme 5. Hence production of this heterocycle must involve loss of the *C*-phenyl ring of the imidoyl derivative. A plausible route to explain phenanthridone formation is outlined in Scheme 6, and involves cyclisation of the mesomeric anion (8) to the dibenzodiazocinone (17) which after loss (concerted or stepwise) of the *C*-phenyl group as aryl cyanide (detected and characterised by g.l.c.) yields the phenanthridone (16). This ring-contraction is similar to that

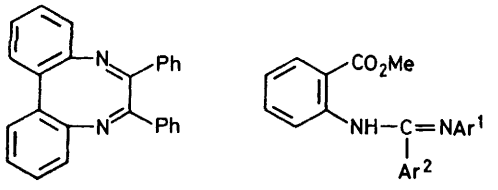


SCHEME 6

undergone by 2,3-diphenyldibenzo[*e*,*g*][1,4]diazocine (18) which on heating at >240 °C extrudes benzonitrile to form 9-phenylphenanthridine.[16]

The absence of iminoketen–benzazetinone intermediates in the thermolysis of the 3-imidoylbenzotriazinones is supported by photolysis studies. For example, photodecomposition of the diphenyl derivative (7; $Ar^1 = Ar^2 = Ph$) in methanol gave a complex

mixture from which only 1,2-diphenyl-1,4-dihydroquinazolin-4-one (9; $Ar^1 = Ar^2 = Ph$) (7%) and phenanthridone (20%) could be isolated and identified. The *N*-(*o*-methoxycarbonyl)phenylamidine (19), expected by addition of methanol to the iminoketen intermediate

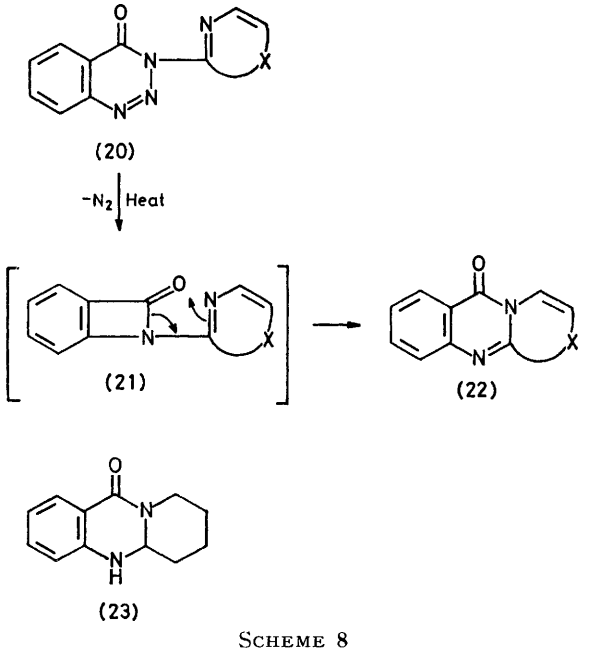


(18) (19)

SCHEME 7

(11a; Scheme 3), or its cyclisation product,[17] *i.e.* 2,3-diphenylquinazolin-4-one (10; $Ar^1 = Ar^2 = Ph$), were not detected.

In contrast, 3-(α-pyridyl)- (20; X = -CH=CH-) and 3-thiazol-2-yl-1,2,3-benzotriazin-4-one (20; X = S), structures in which the C=N function is now an integral part of a heterocyclic ring, on thermolysis gave not the angular but the linear pyrido- and thiazolo-quinazolinones (22; X = CH=CH-) and S) respectively. Obviously, these products must have arisen from their respective iminoketen–benzazetinone intermediates (21;



SCHEME 8

X = CH=CH or S) as outlined in Scheme 8. The structure of the pyrido[2,1-*b*]quinazolin-11-one (22; X = CH=CH) [18] was confirmed by synthesis from 2-chloropyridine and an excess of methyl anthranilate.[19] In addition catalytic reduction (Pd–C) of the pyridoquinazolinone gave the known [20] hexahydro-derivative (23). Similarly condensation of 2-bromothiazole with an excess of methyl anthanilate gave thiazolo[2,3-*b*]-quinazolin-5-one (22; X = S) which proved to be identical to the product from thermolysis of the thiazolylbenzotriazinone. Surprisingly the unsubstituted thiazolo[2,3-*b*]quinazolinone does not appear to have been described previously, although many derivatives have been prepared [21] by condensing 2-chlorothiazoles with anthranilic acids.

Photo-decomposition of the 3-heteroarylbenzotriazinones in tetrahydrofuran was very slow. In both cases irradiation for 72 h (Pyrex filter) furnished only small amounts of quinazolinone (<5%) along with unchanged benzotriazinone (95%).

EXPERIMENTAL

Mass spectra were obtained on an AEI MS12 spectrometer. I.r. spectra were recorded as Nujol mulls on either a Perkin-Elmer 297 or 257 grating infrared spectrophotometer and ^1H n.m.r. spectra on a Perkin-Elmer R32 spectrophotometer ($SiMe_4$ as internal standard).

The 3-arylideneamino-1,2,3-benzotriazinones listed in Table 1 were prepared as described previously [4a] from 3-amino-1,2,3-benzotriazin-4-one and the appropriate aldehyde. Decompositions were also as described before.[4a]

Decomposition of 1,2,3-*Benzotriazin-4-one in the Presence of Benzonitrile.*—A slurry of 1,2,3-benzotriazin-4-one (3 g) in liquid paraffin (20 ml) was added portionwise to a mixture of liquid paraffin (25 ml) and benzonitrile (2 g) at 300 °C. When nitrogen evolution ceased (*ca.* 15 min), the mixture was allowed to cool and then diluted with light petroleum (b.p. 60—80 °C) in order to precipitate the products. The yellow-brown tarry solid so obtained was chromatographed on silica, chloroform as eluant, to give as first fraction, 2-(*o*-aminophenyl)-3,1-benzoxazin-4-one (1 g, 40%), m.p. 171 °C (lit.,[3a] 172 °C). Further elution gave 2-phenylquinazolin-4-one (0.05 g, 1%), m.p. 237 °C (lit.,[22] 236 °C).

Attempted Thermolysis of 3-*Phenyl-4-cinnolone* [7] *and* 1-*Phenyl-4-phthalazinone.*[8]—A solution of the heterocycle (0.5 g) in liquid paraffin (5 ml) was heated at 300 °C for 10—15 min. The solution was cooled, and the products precipitated by the addition of light petroleum (b.p. 60—80 °C). In each case only starting material (0.48 g) was recovered.

Photolysis of 3-*Arylideneamino*-1,2,3-*benzotriazin*-4-*ones.*—(a) *In acetonitrile.* A solution of 3-benzylideneamino-1,2,3-benzotriazin-4-one (1 g) in acetonitrile (200 ml) was photolysed for 12 h using a medium-pressure lamp and Pyrex filter. A dark-brown photolysate was obtained which, on evaporation to dryness, gave a brown tar. T.l.c. (Al_2O_3, EtOAc) indicated a complex mixture. Column chromatography (Al_2O_3, EtOAc) failed to yield any solid, identifiable products. Similar results were obtained with 3-(4-hydroxybenzylideneamino)- and 3-furylideneamino-1,2,3-benzotriazin-4-one.

(b) *In methanol.* A solution of 3-benzylideneamino-1,2,3-benzotriazin-4-one (1.5 g) in methanol (200 ml) was photolysed as in the previous experiment for 16 h. The yellow photolysate was evaporated to dryness and the yellow residue chromatographed on alumina ($CHCl_3$ as eluant). The only solid product obtained proved to be *benzaldehyde* (*o-methoxycarbonyl*)*phenylhydrazone.* The hydrazone (0.8 g, 53%) crystallised from light petroleum (b.p. 60—80 °C) as pale yellow prisms, m.p. 76 °C (Found: C, 70.8; H, 5.2; N, 10.8. $C_{15}H_{14}N_2O_2$ requires C, 70.9; H, 5.5; N, 11.0%). This product was identical to the (*o*-methoxycarbonyl)-phenylhydrazone prepared by condensing methyl *o*-hydrazinobenzoate [13] with benzaldehyde in hot ethanol containing a catalytic amount of *p*-toluenesulphonic acid.

Details of other (*o*-methoxycarbonyl)phenyl hydrazones are given in Table 2.

3-Imidoyl-1,2,3-benzotriazin-4-ones.—The imidoylated benzotriazinones were prepared as described previously [4b] and also by adding dropwise a solution of *N*-phenylbenzimidoyl chloride [23] in ethyl acetate to a stirred suspension of the sodium salt of 1,2,3-benzotriazin-4-one in dry t-butyl alcohol. After 1 h at room temperature the orange mixture was heated at 50 °C for 15 min and then evaporated to dryness. Water was added and the mixture ether-extracted to give the 3-imidoylated-1,2,3-benzotriazinone. Decompositions were carried out as described previously.[4b]

3-Benzoyl-1,2,3-benzotriazin-4-one.—A suspension of 3-(*N*-phenylbenzimidoyl)-1,2,3-benzotriazin-4-one (1 g) in 2M hydrochloric acid was stirred at room temperature for 6 h. The mixture was filtered to give crude 3-benzoyl-1,2,3-benzotriazin-4-one (0.65 g, 85%) which crystallised from light petroleum (b.p. 100—120 °C) as white needles, m.p. 129 °C, mixed m.p. with an authentic sample [14] (m.p. 132 °C) was undepressed; i.r. spectra were superimposable.

Photolysis of 3-Imidoyl-1,2,3-benzotriazin-4-ones.—A solution of 3-(*N*-phenylbenzimidoyl)-1,2,3-benzotriazin-4-one (1.5 g) in methanol (250 ml) was photolysed, using a medium-pressure lamp and Pyrex filter, for one week. The solution was evaporated to dryness and the residue triturated with ethyl acetate to give phenanthridone as an insoluble residue (0.2 g), m.p. 292 °C. The ethyl acetate solution was allowed to evaporate slowly, whereupon 1,2-diphenyl-1,4-dihydroquinazolin-4-one (0.1 g) precipitated. T.l.c. (Al_2O_3,$CHCl_3$) investigation of the remaining ethyl acetate solution indicated a complex mixture of products. Column chromatography (Al_2O_3) failed to separate any identifiable compounds.

Photolysis of the imidoyl derivatives (3; $Ar^1 = p$-MeC_6H_4, Ar^2 = Ph; and $Ar^1 = Ar^2 = p$-MeC_6H_4) gave similar results.

3-Heteroaryl-1,2,3-benzotriazin-4-ones.— 3-(α-Pyridyl)-1,2,3-benzotriazin-4-one, m.p. 196 °C (lit.,[24] 190 °C), was prepared in 60% yield by diazotisation of *N*-(*o*-aminobenzoyl)-2-aminopyridine.[25]

3-Thiazol-2-yl-1,2,3-benzotriazin-4-one.—A suspension of *N*-(*o*-aminobenzoyl)-2-aminothiazole, m.p. 164 °C (lit.,[26] 164 °C) (1.88 g) in hydrochloric acid (5 ml) and water (15 ml) at 0 °C was diazotised using a solution of sodium nitrite (2 g) in water (10 ml). The solution was neutralised (Na_2CO_3) to give the product as a yellow solid (1.2 g, 52%). *3-Thiazol-2-yl-1,2,3-benzotriazin-4-one* crystallised from ethanol as a tan solid, m.p. 193 °C (decomp.) (Found: C, 52.2; H, 2.6; N, 24.1. $C_{10}H_6N_4OS$ requires C, 52.2; H, 2.6; N, 24.3%).

Thermolysis of 3-(α-Pyridyl)-1,2,3-benzotriazin-4-one.—A suspension of the benzotriazinone (1 g) in 1-methylnaphthalene (50 ml) was heated under reflux for 2 h. On cooling the reaction mixture a yellow precipitate of pyrido[2,1-*b*]-quinazolin-11-one was obtained, which crystallised from light petroleum, m.p. 209 °C (lit.,[18] 211 °C) (Found: C, 73.7; H, 3.8; N, 14.0. Calc. for $C_{12}H_8N_2O$: C, 73.45; H, 4.1; N, 14.3%); ν (C=O) 1 702 cm^{-1}; *m/e* 196 (M^+); δ ($CDCl_3$) 8.85 (1 H, d, H-9), 8.43 (1 H, d, H-6), 7.8 (2 H, m, H-1 and H-4), 7.45 (3 H, m, H-7, H-2, and H-3), and 6.8 (1 H, m, H-8); $J_{8,9}$ 7, $J_{6,7}$ 8 Hz.

The product proved to be identical to pyrido[2,1-*b*]-quinazolin-11-one (57.5% yield) prepared by heating 2-chloropyridine (1.13 g) and methyl anthranilate (3 g) under reflux for 75 min.

A lower yield (11%) of pyridoquinazolinone along with much tar was obtained on pyrolysing the pyridylbenzotriazinone in paraffin oil at 300 °C.

Reduction of Pyrido[2,1-b]quinazolin-11-one.—A solution of the pyridoquinazolinone (0.5 g) in ethanol (100 ml) was reduced at atmospheric pressure using H_2 and a 5% Pd–C catalyst for 4 d. Evaporation of the solvent and trituration of the residue with diethyl ether gave 5,5a,6,7,8,9-hexahydropyrido[2,1-*b*]quinazolin-11-one, which crystallised from ethyl acetate–light petroleum (b.p. 80—100 °C) as white needles, m.p. 134 °C (lit.,[20] 135 °C); ν(C=O) 1 675 cm^{-1}, ν(NH) 3 400 cm^{-1} (Found: C, 71.65; H, 7.1; N, 13.95. Calc. for $C_{12}H_{14}N_2O$: C, 71.35; H, 7.0; N, 13.9%); *m/e* 202 (M^+).

Thermolysis of 3-Thiazol-2-yl-1,2,3-benzotriazin-4-one.—The thiazolylbenzotriazinone (1 g) was thermolysed in 1-methylnaphthalene as described for the 3-(α-pyridyl) derivative. *Thiazolo[2,3-b]quinazolin-5-one* (0.2 g, 21%) crystallised from ethanol, m.p. 152 °C (Found: C, 59.1; H, 3.2; N, 13.7. $C_{10}H_6N_2OS$ requires C, 59.4; H, 3.0; N, 13.85%); ν(C=O) 1 700 cm^{-1}; δ ($CDCl_3$) 8.35 (1 H, dd, H-6), 7.9 (1 H, d, H-3), 7.3—7.8 (3 H, m, H-7, H-8, H-9), and 6.82 (1 H, d, H-2); $J_{2,3}$ 5, $J_{6,7}$ 7, and $J_{6,8}$ 1.5 Hz; *m/e* 202 (M^+).

This product was identical to a sample of thiazolo[2,3-*b*]-quinazolin-5-one prepared by heating 2-bromothiazole [27] (1.64 g) with methyl anthranilate (3.1 g) under reflux for 1 h. The thiazoloquinazolin-5-one was isolated as its hydrobromide (1.72 g), m.p. 319 °C (decomp.) (Found: C, 42.9; H, 2.46; N, 9.8. $C_{10}H_7BrN_2OS$ requires C, 42.6; H, 2.49; N, 9.9%). The free base (m.p. 152 °C) was obtained by dissolving the HBr salt in 1M NaOH and then extracting the solution with diethyl ether.

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