Triazines and Related Products. Part XIV.[1] Decomposition of 1,2,3-Benzotriazin-4(3*H*)-ones in the Presence of Reactive Methylene Systems

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In the presence of βγ-unsaturated esters, 1,2,3-benzotriazin-4(3*H*)-one (1) is thermally transformed into the quinazolino[3,2-*c*][1,2,3]benzotriazinone (13), which then undergoes cleavage of the N(2)—N(3) bond in the triazine ring to afford the quinazolinylphenylhydrazones (14). The initial step in the reaction probably involves a nucleophilic attack of one molecule of the triazinone (1) at the reactive 4-position of another molecule. 3-Alkyl- and 3-aralkyl-1,2,3-benzotriazin-4(3*H*)-ones are all stable in boiling ethyl cyanoacetate, but the 3-arylbenzotriazinones undergo thermal heterolysis of the N(2)—N(3) bond, followed by reaction with the ester, to yield phenylcarbamoylphenylhydrazones.

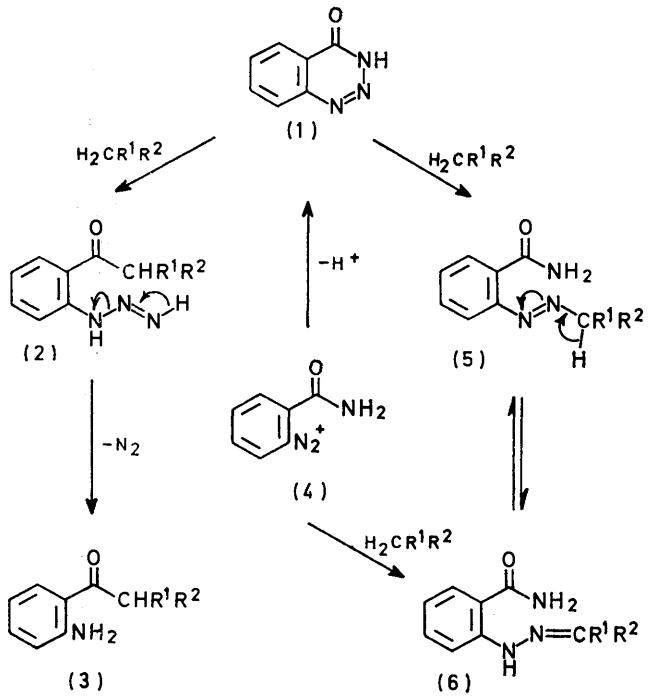
In Part XII [2] decompositions of 1,2,3-benzotriazin-4(3*H*)-ones in piperidine and its heteroalicyclic analogues were described.[2] The parent triazinone (1) suffered nucleophilic attack at C-4 and afforded anthranilamide derivatives, whereas the 3-alkyl or 3-aralkyl analogues were unreactive; 3-aryltriazinones in general were also unreactive.

As an extension of this and other studies [1,3] on the effect of nucleophiles on 1,2,3-benzotriazines, we have examined the behaviour of the same triazinones towards reactive methylene compounds: the triazinones display a diversity of reactivity depending on the nature of the 3-substituent.

We at first anticipated that interaction of 1,2,3-benzotriazin-4(3*H*)-one (1) and reactive methylene compounds would take either (or both) of two courses (Scheme 1). If reaction took place at C-4 in the manner of attack by piperidine,[2] the unstable 3-aryltriazenes (2) would be produced, which could subsequently decompose with loss of nitrogen to afford the *o*-aminophenyl ketones (3). Alternatively, reaction at N-2 could lead to the arylazo-

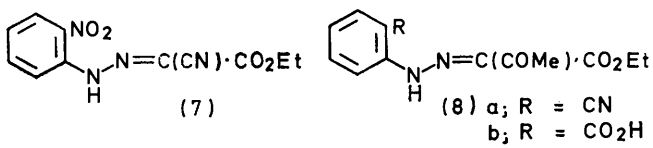
[1] Part XIII, M. F. G. Stevens, *J.C.S. Perkin I*, 1974, 616.
[2] M. S. S. Siddiqui and M. F. G. Stevens, *J.C.S. Perkin I*, 1974, 611.
[3] A. W. Murray and K. Vaughan, *J. Chem. Soc.* (*C*), 1970, 2070.

alkanes (5) or arylhydrazones (6). This latter process has a direct parallel in the reaction of the triazinone with 2-naphthol in acidic media.[4]



SCHEME 1

Accordingly, the series of hydrazones (6a—d) was prepared by coupling diazotised anthranilamide (4) with the appropriate activated methylenic nitriles or esters in sodium acetate buffer. A slight modification of the established procedure [5] was required to inhibit competitive intramolecular cyclisation of the diazonium salt to the triazinone (1). This was achieved by using 10N-hydrochloric acid as the diazotising medium, but even so minor contamination of the hydrazones was observed. The competing side-reaction interfered sufficiently to prevent isolation of the corresponding hydrazones from nitroethane and ethyl benzoylacetate. No such problems



were encountered in formation of the hydrazones (7) and (8a and b) from the appropriate diazotised aminoarenes and βγ-unsaturated esters.

The reference hydrazones (6a—d), (7), and (8a and b) are formulated as the arylhydrazono- rather than aryl-azo-tautomers because the positions of the long-wavelength maxima in their electronic absorption spectra (Table) are similar to those of hydrazones of unequivocal structure. Arylazoalkanes have qualitatively different spectra (Table).[6]

Spectroscopic characteristics of arylhydrazones and arylazoalkanes

Compound	$\lambda_{max.}$/nm [a] *	$\nu_{max.}$/cm^{-1} [b]
(6a) [c]	362	3495 and 3382 (NH_2), 2230 (C≡N), 1705 (CO_2Et), 1665 ($CONH_2$), 1612 (C=N)
(6b)	370	3460 and 3340 (NH_2), 2236 and 2210 (C≡N), 1669 ($CONH_2$), 1615 (C=N)
(6c)	358	3425 and 3350 (NH_2), 3180 (NH), 1700—1665br (CO_2Et, COMe, and $CONH_2$), 1625 (C=N)
(6d)	358	3440 and 3330 (NH_2), 3190 (NH), 1690br (CO_2Me and COMe), 1641 ($CONH_2$), 1613 (C=N)
(7) [d]	390	3240 (NH), 2216 (C≡N), 1722 (CO_2Et), 1613 (C=N), 1515 and 1340 (NO_2)
(8a)	355	2222 (C≡N), 1705br (CO_2Et and COMe), 1638 (C=N)
(8b)	365	3100—2500 (bonded OH), 1706—1660 (CO_2H, CO_2Et, and COMe), 1605br (C=N)
(14a)	375	3200—2900 (bonded NH), 2220 (C≡N), 1743 (CO_2Et), 1680 (C=O), 1608 (C=N)
(14b)	374	3200—2900 (bonded NH), 1690br (CO_2Et, COMe, and C=O), 1608 (C=N)
(14c)	372	3150—2900 (bonded NH), 1690br (CO_2Me, COMe, and C=O), 1608 (C=N)
(14d)	380	3200—2900 (bonded NH), 1690 and 1670 (CO_2Et, COPh, and C=O), 1608 (C=N)
(19g)	364	3340 (NH), 2230 (C≡N), 1685 (CO_2Et), 1640 (CONH), 1598 (C=N)
(19h)	366	3290 (NH), 2228 (C≡N), 1690 (CO_2Et), 1640 (CONH), 1605 (C=N)
(19j)	368	3310 (NH), 2228 (C≡N), 1688 (CO_2Et), 1643 (CONH), 1600 (C=N), 1528 and 1355 (NO_2)
(19k)	367	3340 (NH), 2228 (C≡N), 1687 (CO_2Et), 1645 (CONH), 1592 (C=N)

[a] In 95% ethanol. [b] As potassium bromide discs. [c] Low-melting form from aqueous pyridine. [d] Low-melting form from ether.

* For comparison, benzil mono-(*N*-methylphenylhydrazone) has $\lambda_{max.}$ 335 nm, pyruvanilide *N*-methylphenylhydrazone has $\lambda_{max.}$ 334 nm, ethyl 2-methyl-2-phenylazoacetoacetate has $\lambda_{max.}$ 272 nm, and 2-methyl-2-phenylazoacetoacetanilide has $\lambda_{max.}$ 280 nm.[6]

The hydrazone (6a) exists in two forms with distinctive i.r. spectra. It crystallises in a yellow form from aqueous pyridine (m.p. 188°) and a cream form from acetic acid (m.p. 203°) and the two forms are interconvertible depending on the solvent used for crystallisation. The related hydrazone (7) has been reported to crystallise in two distinct forms.[7] We have not closely examined these phenomena, but it seems that geometrical isomerism about the C=N bond could be an explanation.

Contrary to our predictions, when 1,2,3-benzotriazin-4(3*H*)-one (1) was boiled in ethyl cyanoacetate, ethyl

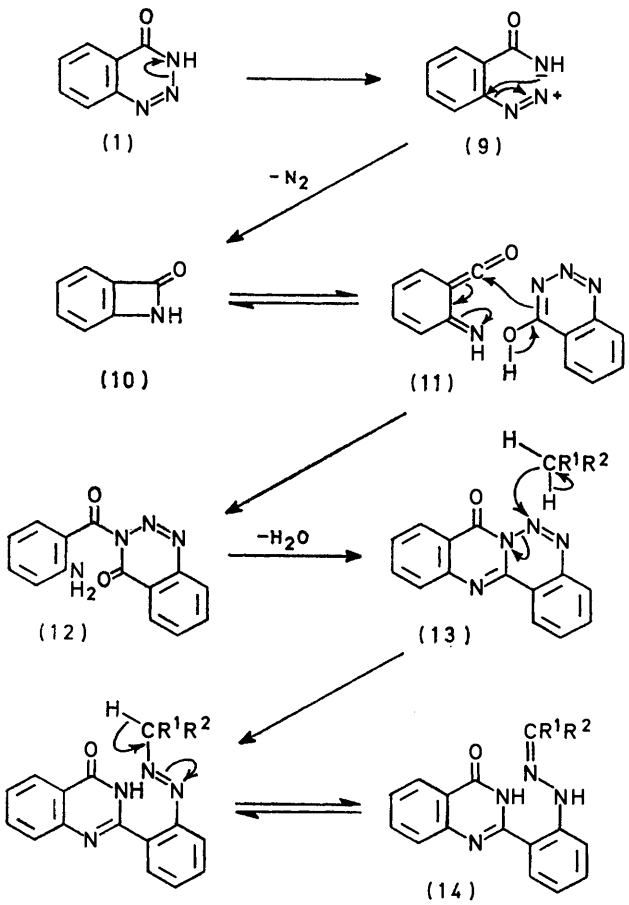
[4] J. G. Erickson, ' The 1,2,3-Triazines,' in ' The Chemistry of Heterocyclic Compounds,' ed. A. Weissberger, Interscience, New York, vol. 10, p. 1.

[5] S. M. Parmenter, ' Organic Reactions,' Wiley, New York, 1959, vol. 10, p. 1.

[6] H. C. Yao and P. Resnick, *J. Amer. Chem. Soc.*, 1962, **84**, 3514.

[7] P. W. Uhlmann, *J. prakt. Chem.*, 1895, **51**, 217.

acetoacetate, methyl acetoacetate, or ethyl benzoylacetate, the products were the quinazolinylphenylhydrazones (14a—d). We can envisage two possible



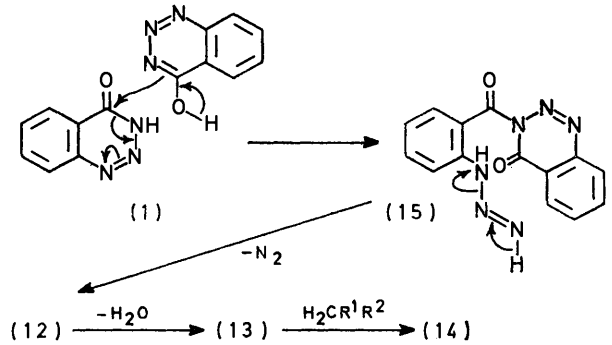
	R^1	R^2
a;	CN	CO_2Et
b;	COMe	CO_2Et
c;	COMe	CO_2Me
d;	COPh	CO_2Et

SCHEME 2

mechanisms for this transformation. In the first (Scheme 2) the triazinone undergoes initial pyrolytic heterolysis of the N(2)–N(3) bond to afford the betaine (9) and thence the benzazetinone (10). Support for this decomposition mode is available from other work on the pyrolytic,[8-11] photolytic,[11-14] and electron-impact-promoted [10,15,16] fragmentations of 1,2,3-benzotriazinones. Reaction of the imino-keten valence-tautomer (11) of the benzazetinone with a second molecule of triazine would lead to the anthraniloyltriazinone (12), which could then cyclise to the quinazolino[3,2-*c*][1,2,3]benzotriazinone (13). We have previously observed that when both N-3 and C-4 of the triazine ring in polycyclic 1,2,3-triazines occupy bridgehead positions, ring-opening with amine nucleophiles can only take place at N-2.[2] A similar ring fission of the tetracyclic triazinone (13) with the reactive methylene compounds would afford the quinazolinylphenylhydrazones (14a—d) *via* the arylazo-tautomers.

Murray and Vaughan [3] prepared the quinazolinobenzotriazinone (13) by thermolysis of the triazinone (1) in refluxing diethylene glycol dimethyl ether (b.p. **162—164°**). As this product was formed at a temperature considerably below the decomposition temperature of the triazinone (215°), these authors reasoned that an imino-keten is an unlikely intermediate, and argued in favour of a mechanism (Scheme 3) in which the triazinone suffers nucleophilic attack at the exposed and reactive C-4 position by a further molecule of triazinone. The unstable 3-aryltriazene (15) formed in this process would decompose to the anthraniloyltriazinone (12) by loss of nitrogen, and then cyclise to the tetracyclic triazine (13).

This latter mechanism is also more likely in the present examples, since decomposition of the triazinone (1) in ethyl cyanoacetate started at 120° and was followed rapidly by the precipitation of the quinazolinylphenylhydrazone (14a). The triazinone behaved similarly in ethyl acetoacetate, methyl acetoacetate, and ethyl benzoylacetate although in these solvents and in ethyl cyanoacetate the decomposition was more conveniently accomplished at reflux temperature (10 min). However, the modest temperatures involved, again well below the



	R^1	R^2
a;	CN	CO_2Et
b;	COMe	CO_2Et
c;	COMe	CO_2Me
d;	COPh	CO_2Et

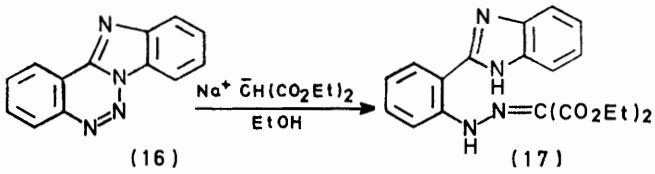
SCHEME 3

thermolysis temperature of the triazinone, appear to preclude the intervention of a benzazetinone in these reactions.

Whatever mechanism operates, however, it is clear that the reactive methylene compounds do not partici-

[8] D. H. Hey, C. W. Rees, and A. R. Todd, *J. Chem. Soc.* (*C*), 1968, 1028.
[9] H. E. Crabtree, R. K. Smalley, and H. Suschitzky, *J. Chem. Soc.* (*C*), 1968, 2730.
[10] J. G. Archer, A. J. Barker, and R. K. Smalley, *J.C.S. Perkin I*, 1973, 1169.
[11] N. Bashir and T. L. Gilchrist, *J.C.S. Perkin I*, 1973, 868.
[12] E. M. Burgess and G. Milne, *Tetrahedron Letters*, 1966, 93.
[13] G. Ege, *Chem. Ber.*, 1968, **101**, 3079.
[14] G. Ege and F. Pasedach, *Chem. Ber.*, 1968, **101**, 3089.
[15] G. Wünsche, G. Ege, E. Beisiegel, and F. Pasedach, *Tetrahedron*, 1969, **25**, 5869.
[16] 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.

pate as *reactants* until a late stage in the reaction. In corroboration, a sample of the quinazolinobenzotriazinone (13) prepared by diazotisation of 2-*o*-aminophenylquinazolin-4(3*H*)-one [3] decomposed quantitatively in



(16) (17)

reactive methylenic solvents to afford the same series of hydrazones (14a—d). The spectral characteristics of these hydrazones are fully consistent with their assigned structures (see Table).

In contrast to the smooth decompositions mentioned above, the reaction of the triazinone (1) in diethyl malonate or ethyl 2-methylacetoacetate gave inseparable mixtures: in the latter solvent a Japp–Klingemann reaction might have been expected.[17]

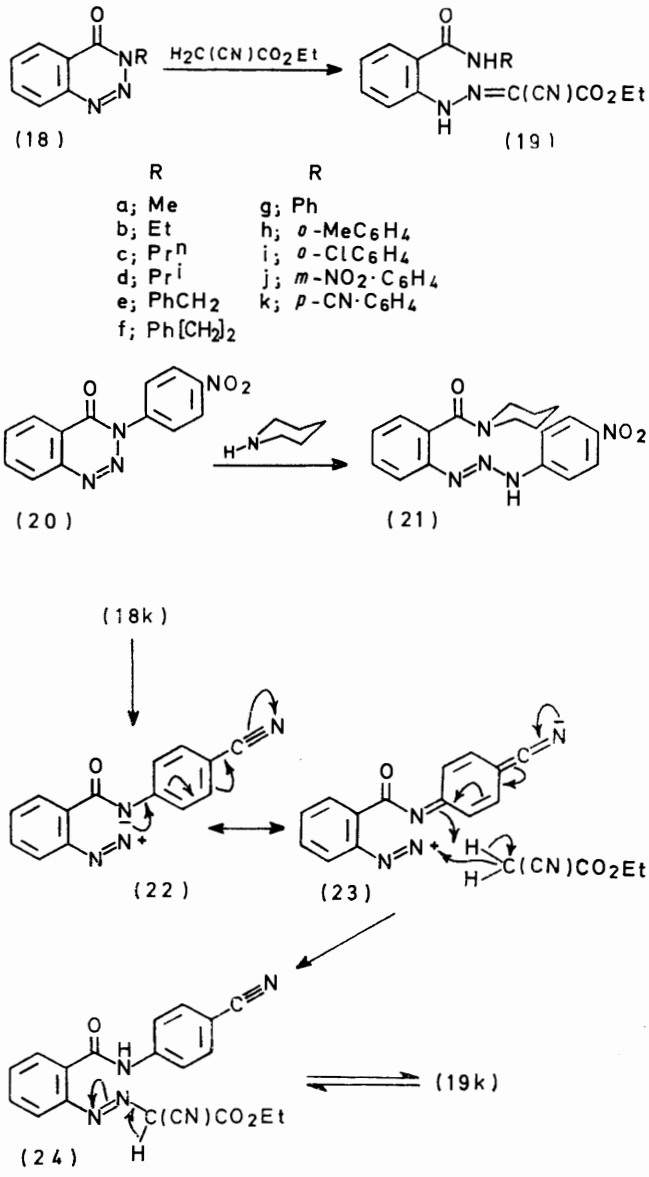
To our knowledge, there is only one previous report dealing with interactions of 1,2,3-benzotriazines and reactive methylene compounds: the benzimidazo[1,2-*c*]-[1,2,3]benzotriazine (16) reacts with diethyl sodiomalonate in ethanol to yield the hydrazone (17).[18] Our previous experience with this tetracyclic triazine showed it to be unusually resistant to amine nucleophiles.[2]

With regard to the behaviour of 3-substituted triazinones in boiling reactive methylenic solvents, it is apparent that electronic effects exert a controlling influence. The 3-alkyl- and 3-aralkyl-triazinones (18a—f) are inert to boiling ethyl cyanoacetate, but the 3-aryltriazinones (18g—k) decompose. The products in these latter decompositions are not 1,3-diaryltriazenes: they do not give a positive indication in a Bamberger–Goldberger test for an intact NNN linkage.[4] Their chemical and spectral properties (Table) are in accord with the hydrazone structures (19g—k).

However, there remains a discrepancy in the reactivities of the 3-aryltriazinones towards piperidine and ethyl cyanoacetate. The triazinones (18g—k) are all stable in boiling piperidine, and the only triazinone that does react [the *p*-nitrophenyltriazinone (20)] ring-opens at C-4 to give the diaryltriazene (21).[2] In ethyl cyanoacetate we suggest that the *p*-cyanophenyltriazinone (18k) undergoes thermal heterolysis of the N(2)–N(3) bond to give the zwitterion (22), which can be stabilised by the mesomeric effect of the cyanophenyl substituent [(22) ⟷ (23)]: similar stabilising influences would operate to a lesser extent in the other 3-aryltriazinones (18g—j). Coupling between the diazonium ion (23) and ethyl cyanoacetate would then lead to the hydrazone (19k) *via* the arylazo-tautomer (24) (Scheme 4). The lack of reactivity of the 3-aryltriazinones (18g—k) in boiling piperidine (b.p. 106°) and their reactivity in boiling ethyl cyanoacetate (b.p. 208°) presumably reflect the severity of the conditions in the latter decompositions which favour heterolysis of the N(2)–N(3) bond.

In the case of the 3-alkyl- and 3-aralkyl-triazinones (18a—f) the $+I$ effect of the substituents would destabilise the corresponding acyclic zwitterions and render these triazinones unreactive towards ethyl cyanoacetate.

A parallel situation has been reported in 3-substituted 1,2,3-benzotriazine-4(3*H*)-imines: the 3-*p*-cyano- and 3-*p*-nitrophenyl-triazines undergo a ready thermal Dimroth rearrangement to 4-*p*-cyano- and 4-*p*-nitro-anilino-1,2,3-benzotriazine, respectively, whereas the 3-benzyl



SCHEME 4

analogue is thermally stable. Mesomeric stabilisation of the acyclic zwitterionic intermediates in the former examples provides an explanation for these differences.[19]

[17] R. R. Phillips, ' Organic Reactions,' Wiley, New York, 1959, vol. 10, p. 143.

[18] R. H. Spector and M. M. Joullié, *J. Heterocyclic Chem.*, 1969, **6**, 605.

[19] M. S. S. Siddiqui and M. F. G. Stevens, *J.C.S. Perkin I*, 1974, 609.

EXPERIMENTAL

Synthesis of Model Hydrazones.—*Ethyl* 2-(2-*carbamoylphenylhydrazono*)*cyanoacetate* (6a).—A solution of anthranilamide (13·6 g) in 10N-hydrochloric acid (50 ml) was diazotised at 0° with sodium nitrite (1 mol. equiv.) in water (20 ml). The ice-cold diazonium solution was neutralised with an excess of sodium acetate trihydrate and vigorously stirred with ethyl cyanoacetate (1 mol. equiv.) for 2 h. The precipitated *hydrazonocyanoacetate* (85%) was collected, washed with water, and crystallised from aqueous pyridine to give yellow needles, m.p. 185° (Found: C, 55·2; H, 4·0; N, 21·8. $C_{12}H_{12}N_4O_3$ requires C, 55·4; H, 4·6; N, 21·5%).

Similarly prepared from the appropriate diazotised aminoarene and reactive methylene compound were the following: 2-(2-*carbamoylphenylhydrazono*)*malononitrile* (6b), from anthranilamide and malononitrile (80%), as yellow needles (from ethanol), m.p. 248—249° (Found: C, 56·1; H, 3·2; N, 32·6. $C_{10}H_7N_5O$ requires C, 56·3; H, 3·3; N, 32·9%); *ethyl* 2-(2-*carbamoylphenylhydrazono*)*acetoacetate* (6c), from anthranilamide and ethyl acetoacetate (85%), as long yellow needles (from ethanol), m.p. 163—165° (Found: C, 55·9; H, 5·2; N, 15·6. $C_{13}H_{15}N_3O_4$ requires C, 56·3; H, 5·4; N, 15·2%); *methyl* 2-(2-*carbamoylphenylhydrazono*)-*acetoacetate* (6d), from anthranilamide and methyl acetoacetate (90%), as yellow needles (from ethanol), m.p. 188—190° (Found: C, 54·5; H, 5·0; N, 16·1. $C_{12}H_{13}N_3O_4$ requires C, 54·8; H, 4·9; N, 16·0%); ethyl 2-(2-nitrophenylhydrazono)cyanoacetate (7), by diazotisation of *o*-nitroaniline in N-hydrochloric acid, followed by treatment with sodium acetate and ethyl cyanoacetate (1 mol. equiv.), as yellow prisms (75%), m.p. 130° (from ether) (lit.,[7] 116° for the low-melting form); *ethyl* 2-(2-*cyanophenylhydrazono*)-*acetoacetate* (8a), from diazotised anthranilonitrile and ethyl acetoacetate (94%), as yellow prisms, m.p. 139—140° (from methanol) (Found: C, 60·0; H, 4·7; N, 16·4. $C_{13}H_{13}N_3O_3$ requires C, 60·2; H, 5·1; N, 16·2%); and ethyl 2-(2-carboxyphenylhydrazono)acetoacetate (8b), from diazotised anthranilic acid and ethyl acetoacetate (75%), m.p. 162—163° (lit.,[20] 162—163°).

Decomposition of 1,2,3-*Benzotriazin*-4(3H)-*one in the Presence of* βγ-*Unsaturated Esters. Ethyl* 2-[2-(3,4-*dihydro*-4-*oxoquinazolin*-2-*yl*)*phenylhydrazono*]*cyanoacetate* (14a). Prepared from 1,2,3-benzotriazin-4(3*H*)-one (2 g) by boiling in ethyl cyanoacetate (10 ml) for 10 min, this *hydrazonocyanoacetate* (90%) was left as a brown residue when the excess of ethyl cyanoacetate was distilled off under reduced pressure. It crystallised as yellow micro-needles (from aqueous dimethylformamide), m.p. 299—300° (Found: C, 63·0; H, 4·1; N, 19·6. $C_{19}H_{15}N_5O_3$ requires C, 63·2; H, 4·2; N, 19·9%).

The same hydrazonocyanoacetate was formed (85%) from the quinazolinobenzotriazinone (13) [3] in boiling ethyl cyanoacetate (10 min).

Ethyl 2-[2-(3,4-*dihydro*-4-*oxoquinazolin*-2-*yl*)*phenylhydrazono*]*acetoacetate* (14b). This *hydrazonoacetoacetate* was prepared from ethyl acetoacetate and either the triazinone (1) or the quinazolinotriazinone (13) in 65 and 85% yields, respectively. It crystallised from ethanol as yellow microneedles, m.p. 212—214° (Found: C, 63·3; H, 4·5; N, 14·7. $C_{20}H_{18}N_4O_4$ requires C, 63·5; H, 4·8; N, 14·8%).

Methyl 2-[2-(3,4-*dihydro*-4-*oxoquinazolin*-2-*yl*)*phenylhydrazono*]*acetoacetate* (14c). From the triazinone (1) and boiling methyl acetoacetate (70%), this *hydrazonoacetoacetate* formed yellow microneedles (from ethanol), m.p. 264—266° (Found: C, 62·7; H, 4·1; N, 15·7. $C_{19}H_{16}N_4O_4$ requires C, 62·6; H, 4·4; N, 15·4%).

Ethyl 2-[2-(3,4-*dihydro*-4-*oxoquinazolin*-2-*yl*)*phenylhydrazono*]*benzoylacetate* (14d). Prepared by the decomposition of 1,2,3-benzotriazin-4(3*H*)-one in ethyl benzoylacetate (10 min), this *hydrazonobenzoylacetate* (87%) crystallised from ethanol as bright yellow needles, m.p. 205—207° (Found: C, 68·2; H, 4·5; N, 12·5. $C_{25}H_{20}N_4O_4$ requires C, 68·2; H, 4·5; N, 12·7%).

Decomposition of 3-*Substituted* 1,2,3-*Benzotriazin*-4(3H)-*ones in Ethyl Cyanoacetate.*—*Ethyl* 2-[2-(*phenylcarbamoyl*)-*phenylhydrazono*]*cyanoacetate* (19 g). A solution of 3-phenyl-1,2,3-benzotriazin-4(3*H*)-one (1·0 g) in ethyl cyanoacetate (5 ml) was boiled (4 h) and the excess of ethyl cyanoacetate was removed by vacuum distillation. The residue, crystallised from ethanol, afforded the *hydrazonocyanoacetate* (85%) as yellow needles, m.p. 236—238° (Found: C, 64·0; H, 4·8; N, 16·4. $C_{18}H_{16}N_4O_3$ requires C, 64·2; H, 4·7; N, 16·6%). Similarly prepared were the following: *ethyl* 2-[2-(o-*tolylcarbamoyl*)*phenylhydrazono*]*cyanoacetate* (19h), m.p. 147—149° (brown needles, from methanol) (Found: C, 65·3; H, 4·9; N, 16·4. $C_{19}H_{18}N_4O_3$ requires C, 65·1; H, 5·1; N, 16·0%); *ethyl* 2-[2-(o-*chlorophenylcarbamoyl*)*phenylhydrazono*]*cyanoacetate* (19i), m.p. 200—202° (85%) (yellow needles, from ethanol) (Found: C, 58·3; H, 4·0; N, 15·2. $C_{18}H_{15}ClN_4O_3$ requires C, 58·2; H, 4·0; N, 15·1%); *ethyl* 2-[2-(m-*nitrophenylcarbamoyl*)*phenylhydrazono*]*cyanoacetate* (19j), crystallised from ethanol as yellow needles (80%), m.p. 242—243° (Found: C, 56·8; H, 3·9; N, 18·1. $C_{18}H_{15}N_5O_5$ requires C, 56·6; H, 3·9; N, 18·3%); and *ethyl* 2-[2-(p-*cyanophenylcarbamoyl*)*phenylhydrazono*]*cyanoacetate* (19k) (80%) as yellow rosettes, m.p. 232—234° (from ethanol) (Found: C, 62·8; H, 4·1; N, 19·4. $C_{19}H_{15}N_5O_3$ requires C, 63·1; H, 4·1; N, 19·3%).

No reaction occurred and starting material was recovered when the 3-substituted 1,2,3-triazin-4(3*H*)-ones (18a—f) were boiled in ethyl cyanoacetate (4 h).

We thank the Directors of Allen and Hanbury's Ltd. for a research scholarship (to M. S. S. S.).

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[20] C. Bülow and F. Schaub, *Ber.*, 1908, **41**, 2355.