Triazines and Related Products. Part 28.[1] Conversion of 3-Aryl-1-(2-cyanophenyl)triazenes into 3-Arylquinazolin-4(3*H*)-ones with Formamide

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The thermolysis of 4-anilino-1,2,3-benzotriazines and their precursor 3-aryl-1-(2-cyanophenyl)-triazenes in hot formamide to give 3-arylquinazolin-4(3*H*)-ones in high yield is described. The reaction cannot be extended to the preparation of 2-alkyl-3-arylquinazolinones. In hot acetamide–diglyme 4-(4-nitroanilino)-1,2,3-benzotriazine (**5c**) gives a high yield of the 3-substituted 4-(4-nitrophenylimino)-3,4-dihydro-1,2,3-benzotriazine (**11c**).

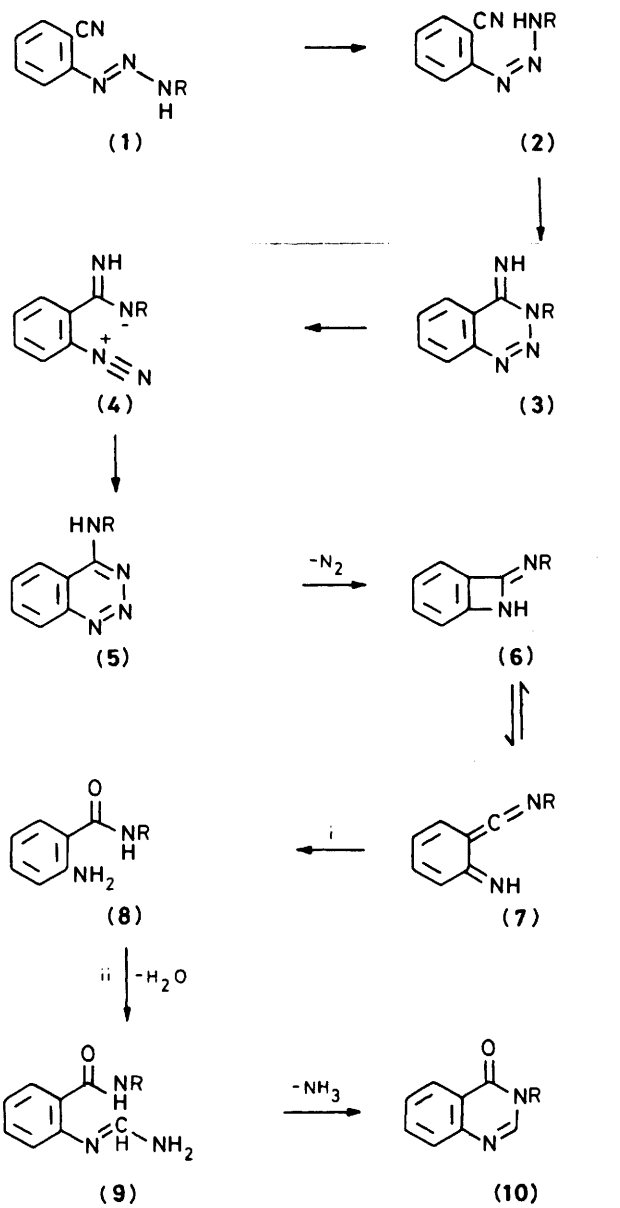
The cyclisation of 3-aryl-1-(2-cyanophenyl)triazenes (**1**) in basic media affords 1,2,3-benzotriazine derivatives which decompose further in the presence of reactive substrates: in some cases quinazoline derivatives are the end-products.[1–6]

4-Anilino-1,2,3-benzotriazine (**5a**) and its *p*-cyano (**5b**) and *p*-nitro analogues (**5c**) effervesced smoothly in refluxing formamide to afford high yields of the corresponding 3-arylquinazolin-4(3*H*)-ones (**10a**—**c**) respectively (Table). The quinazolinones were characterised by i.r., ^{1}H n.m.r., and mass spectrometry and two of them [(**10a**) and (**10b**)] proved to be identical with specimens prepared by treating the corresponding anthraniloylanilines (**8a**) and (**8b**) in warm formamide. Subsequently it was shown that, whereas 3-(2-cyanophenyl)-1-phenyltriazene (**1a**) decomposed to an intractable mixture of products in hot formamide, the cyano and nitro analogues (**1b**) and (**1c**) afforded the same quinazolinones (**10b**) and (**10c**) in very respectable yields. Moreover, the 3-aryl-4-iminobenzotriazines (**3b**) and (**3c**) also yielded the quinazolinones upon brief treatment in hot formamide.

We have encountered the transformation (**1**)→(**2**)→(**3**)→(**4**)→(**5**)→(**6**)→(**7**)→products in several other other thermolytic degradations of 2-cyanophenyltriazenes[1,4–6] and the same intermediates undoubtedly participate in the overall 'one-pot' reaction (**1**)→(**10**) which, remarkably, must involve *nine* discrete steps. We propose that the ketenimine intermediates (**7a**—**c**) react with traces of water in the formamide yielding the anthranilamides (**8a**—**c**) which subsequently react with formamide to generate the formamidines (**9a**—**c**); these finally cyclise to the quinazolinones (**10a**—**c**) with loss of ammonia. The water liberated in the conversion of compounds (**8**) into (**9**) can be recycled to react with the ketenimines (**7a**—**c**). Only a catalytic amount of water, therefore, is required to bring the reaction to completion (Scheme).

3-Aryl-1,2,3-benzotriazin-4(3*H*)-ones are definitely not intermediates in the pathway (**1**)→(**10**) as the 3-phenylbenzotriazinone (**12a**) decomposed slowly in boiling formamide to yield benzanilide in 80% yield, presumably by a radical mechanism.[7]

N-Methylformamide can be employed as the solvent/reactant in the conversion of the anilinobenzotriazines (**5b**) and (**5c**) into the quinazolinones (**10b**) and (**10c**), but efforts to extend the synthesis to simple 2-alkyl-3-arylquinazolines were not successful. Thus the 4-anilinobenzotriazines (**5b**) and (**5c**) in boiling *N*-methylacetamide instead gave the products (**11b**) and (**11c**), previously identified in thermolysis reactions of the same triazines:[1] in fact a combination of boiling diglyme and acetamide was the most effective medium for the optimum (95%) formation of compound (**11c**) from (**5c**).



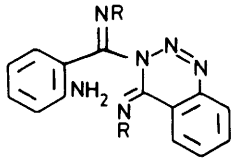
a, R = Ph; **b**, R = C_6H_4CN-*p*; **c**, R = $C_6H_4NO_2$-*p*

Scheme. *Reagents:* i, H_2O; ii, $HCONH_2$

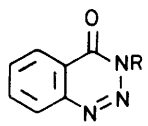
Table. Formation of 3-arylquinazolin-4(3*H*)-ones (**10**) and 4-arylimino-3,4-dihydro-1,2,3-benzotriazines (**11**)

Starting material	Solvent/reactant	Refluxing time (h)	Product	Yield (%)
(**1a**)[a]	Formamide	1	Mixture[b]	
(**1b**)[a]	Formamide	3	(**10b**)[c]	45
(**1c**)[a]	Formamide	0.5	(**10c**)[d]	55
(**3b**)[a]	Formamide	1	(**10b**)	78
(**3c**)[a]	Formamide	1	(**10c**)	80
(**5a**)[a]	Formamide	1.5	(**10a**)[e]	60
(**5b**)[a]	Formamide	0.5	(**10b**)	90
(**5b**)	*N*-Methylformamide	4	(**10b**)	80
(**5b**)	*N*-Methylacetamide	0.5	(**11b**)[f]	50
(**5b**)	*N*,*N*-Dimethylacetamide	0.5	(**11b**)	40
(**5b**)	*N*,*N*-Dimethylacetamide[g]	2	(**11b**)[h]	45
(**5c**)[a]	Formamide	0.5	(**10c**)[i]	90
(**5c**)	*N*-Methylformamide	0.25	(**10c**)	95
(**5c**)	*N*,*N*-Dimethylformamide	0.5	(**5c**)[j]	96
(**5c**)	*N*-Methylacetamide	2	(**11c**)[f]	43
(**5c**)	Diglyme	3	(**5c**)[c]	98
(**5c**)	Acetamide–diglyme[k]	5	(**11c**)	95
(**8a**)[l]	Formamide	1	(**10a**)	90
(**8b**)[m]	Formamide	0.5	(**10b**)	85
(**8b**)	*N*-Methylformamide	0.5	(**10b**)	80
(**12a**)	Formamide	10	Benzanilide	45

[a] Ref. 3 for synthesis. [b] Extensive decomposition. [c] M.p. 258—260 °C (from ethanol–dimethylformamide) (Found: C, 72.6; H, 3.7; N, 16.95%; M^+, 247. $C_{15}H_9N_3O$ requires C, 72.9; H, 3.6; N, 17.0%; *M*, 247); $\nu_{max.}$(KBr) 2 220 cm^{-1}; δ(trifluoroacetic acid) 9.5 (1 H, s, 2-H). [d] See Experimental section for physical data. [e] M.p. 138—140 °C (lit., m.p. 139 °C), see C. Paal and M. Busch, *Ber.*, 1889, **22**, 2683). [f] Product identical (i.r.) with an authentic sample (ref. 1). [g] 4-(4-Cyanoanilino)-1,2,3-benzotriazine (0.5 g) boiled in dimethylacetamide (5 ml) containing water (0.1 ml). [h] Starting material (36%) also recovered. [i] See Experimental section for details of reaction conditions. [j] Unchanged starting material. [k] 4-(4-Nitroanilino)-1,2,3-benzotriazine (1.5 g) boiled in diglyme (40 ml) containing acetamide (5 g). Mixture diluted with water (100 ml) at end of reaction and product collected. [l] For synthesis see H. N. E. Stevens and M. F. G. Stevens, *J. Chem. Soc. C*, 1970, 2308. [m] Prepared by hydrogenation of *N*-(4-cyanophenyl)-2-nitrobenzamide with a palladium–charcoal catalyst in ethanol. The product (80%) had m.p. 194—196 °C (Found: C, 70.7; H, 4.7; N, 17.6; $C_{14}H_{11}N_3O$ requires C, 70.9; H, 4.6; N, 17.7%).



(**11**)



(**12**)

a, R = Ph; **b**, R = C_6H_4CN-*p*; **c**, R = $C_6H_4NO_2$-*p*

Experimental

3-(4-*Nitrophenyl*)*quinazolin*-4(3H)-*one* (**10c**).—A mixture of 4-(4-nitroanilino)-1,2,3-benzotriazine (**5c**) (2.0 g)[3] and formamide (20 ml) was boiled (0.5 h). The brown solution was cooled, diluted with water, and the white crystalline mass collected (1.8 g). The *quinazolinone* (**10c**) had m.p. 265—267 °C (from aqueous dimethylformamide) (Found: C, 62.8; H, 3.2; N, 15.7%; M^+, 267. $C_{14}H_9N_3O_3$ requires C, 62.9; H, 3.4; N, 15.7%; *M*, 267); $\nu_{max.}$(KBr) 1 690 (C=O), 1 525 and 1 355 cm^{-1} (NO_2); δ(trifluoroacetic acid) 9.52 (1 H, s, 2-H).

Details of related syntheses are recorded in the Table.

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