

1,2,4-Triazines. XII. Syntheses of 5-Carboxamido-1,2,4-triazines *via* an Addition-Oxidation Reaction (1)

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Received September 10, 1973

5-Unsubstituted 1,2,4-triazines, when treated with potassium cyanide suspended in moist dioxane afford 5-carboxamido as well as 5,5'-bi-1,2,4-triazinyl derivatives. A probable reaction sequence is described.

We have recently described some potassium cyanide catalyzed dimerizations of various 5-unsubstituted 1,2,4-triazines (**1**), and proposed the intermediate formation of the addition compound **2**, which, in the presence of water, forms anion **3** (I). This anion then presumably attacks a 1,2,4-triazine molecule nucleophilically at C₅ to form, after air oxidation, 5,5'-bi-1,2,4-triazinyls (**4**) (see Scheme 1).

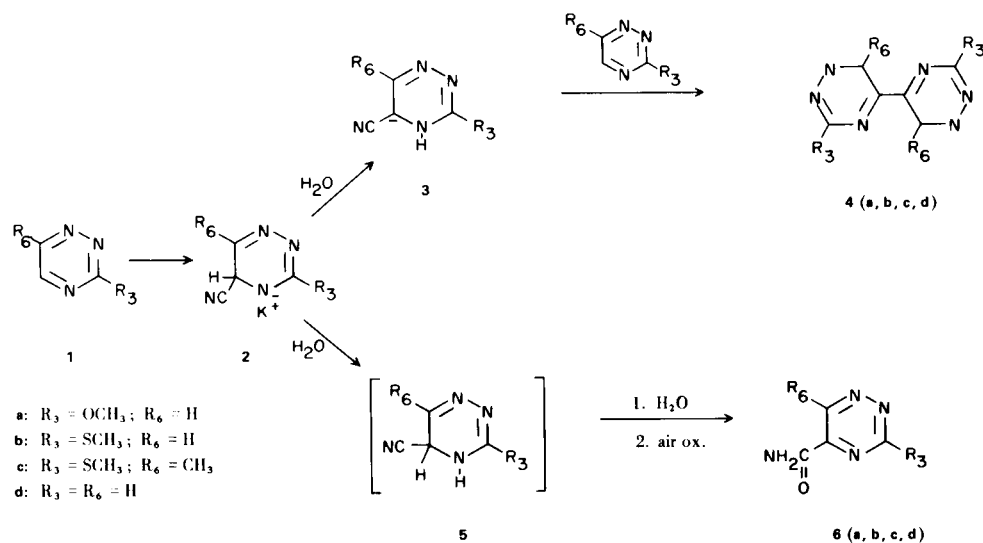
Thus, one might predict that, in the absence of water, the addition compound **2** would be the sole product formed, and, upon hydrolysis with water, would be converted to a 4,5-dihydro-5-cyano-1,2,4-triazine (**5**). This compound should be readily air oxidizable to the corresponding 5-cyano-1,2,4-triazine.

This note describes our initial results of a study directed towards examining the validity of these considerations.

When any one of the 1,2,4-triazines, **1a-d**, was added to a suspension of potassium cyanide in dioxane, and the mixture was heated under reflux for 5 hours, none of the organic starting material was left and two products (as determined by TLC) were obtained. These materials were readily separated by preparatory-scale tlc to afford the dimers, **4a-d**, along with compounds whose elemental analyses and mass spectrometric molecular weights identified them as carboxamido derivatives of the reactant 1,2,4-triazines (**1a-d**). Thus, the probable intermediate cyano-1,2,4-triazines were hydrolyzed to the carboxamido derivatives.

The question as to whether the carboxamido grouping is at C₅ or C₆ can be resolved by the observations that the 6-methyl derivative **1c** affords a carboxamido derivative, and that compound **6d** shows proton-proton coupling ($J_{3,6} = 1.8$ hz), typical for $J_{3,6}$ coupling in

SCHEME 1



Elemental Analyses

Compound No.	(Mol. formula)	Calcd.			Found		
		%C	%H	%N	%C	%H	%N
4a	(C ₈ H ₈ N ₆ O ₂)	43.63	3.66	38.13	43.34	3.57	37.91
6a	(C ₅ H ₆ N ₄ O ₂)	38.96	3.89	36.36	38.97	3.99	36.28
4b	(C ₈ H ₈ N ₆ S ₂)	38.10	3.18	33.33	38.23	3.65	33.15
6b	(C ₅ H ₆ N ₄ OS)	35.29	3.52	32.94	35.29	3.53	32.86
4c	(C ₁₀ H ₁₂ N ₆ S ₂)	42.85	4.28	30.00	42.97	4.41	30.18
6c	(C ₆ H ₈ N ₄ OS)	39.13	4.34	30.43	39.16	4.39	30.48
4d	(C ₆ H ₁₄ N ₆)	44.99	2.51	52.49	44.77	2.31	52.26
6d	(C ₄ H ₄ N ₄ O)	38.70	4.03	45.16	38.57	3.92	45.28

TABLE I

Preparative and Spectral Data of Some 5-Carboxamido-1,2,4-triazines and 5,5'-Bi-1,2,4-triazinyl Derivatives (a,b)

Starting Material (c) (Compound No.)	Compound No.	Products		
		% Yield	M.P.	Recrystallization solvents
1a	4a	58.7	175-176.5°	MeOH
	6a	19.7	173.5-175°	CHCl ₃
1b	4b	61.8	168.5-170°	MeOH
	6b	21.4	180-181.5°	CHCl ₃
1c	4c	52.4	116.5-118°	<i>n</i> -C ₆ H ₁₄
	6c	17.9	124-126°	<i>n</i> -C ₆ H ₁₄
1d	4d	65.6	210-212°	EtOH
	6d	18.3	133-135°	CHCl ₃

(a) All reaction products gave the correct elemental analyses and mass spectrometric molecular weights. (b) The chemical shifts of H₆ for compounds **6a**, **b** and **d** are τ , 0.31, 0.38, 0.02, respectively. The chemical shift of H₃ in compound **6d** is τ , 0.46 with J_{3,6} = 1.8 Hz. (c) The starting materials were prepared according to the procedures described in references 4-6.

1,2,4-triazines (2,3). Thus, as expected, these carbox-amido derivatives are 5 carboxamido-1,2,4-triazines (**6a-d**). These results not only confirm our earlier mechanistic proposals, but also offer a new and unique route to the otherwise almost inaccessible 5-functionally substituted 1,2,4-triazines.

Further studies of the general applicability of this addition-oxidation reaction to other heterocyclic systems (e.g. quinazolines, pteridines, substituted pyrimidines) are in progress.

EXPERIMENTAL (5)

General Procedure.

To a boiling suspension of finely ground potassium cyanide (1.0 g.) in 20 ml. of moist (3% water) dioxane was added (during a period of 1 hour) the appropriate 1,2,4-triazine (3 mmoles) dissolved in 15 ml. of dioxane. The mixture was then heated at reflux for 5 hours and the inorganic material was removed by filtration. The filtrate was concentrated to 5 ml. and applied to a preparative scale tlc plate (neutral, grade VI alumina) and the plate was developed with a 1:1 mixture of chloroform-benzene. The two yellow bands were removed and eluted from the alumina

with ethyl acetate. Evaporation of the eluates to dryness afforded the products (see Table I), after recrystallization from the solvents indicated in Table I.

REFERENCES

- (1) Previous paper in this series is: W. W. Paudler, J. Lee and T. K. Chen, *Tetrahedron*, **29**, 2495 (1973).
- (2) D. K. Krass, T. K. Chen and W. W. Paudler, *J. Heterocyclic Chem.*, **10**, 343 (1973). The similarity of these reactions to the Reissert compound formations is mentioned in this reference.
- (3) W. W. Paudler and J. M. Barton, *J. Org. Chem.*, **31**, 1720 (1966).
- (4) W. W. Paudler and Teh-Kuei Chen, *ibid.*, **36**, 787 (1971).
- (5) W. W. Paudler and T. K. Chen, *J. Heterocyclic Chem.*, **7**, 767 (1970).
- (6) T. K. Chen, Ph.D. Thesis, Ohio University, 1971, Athens, Ohio 45701.
- (7) T. K. Chen, J. Lee and W. W. Paudler, *Tetrahedron*, **29**, in press (1973).
- (8) The nmr spectra were obtained with a Varian HA-100 instrument as dilute solutions in deuteriochloroform. The mass spectrometric molecular weights of all compounds were obtained with a Hitachi-Perkin Elmer RMU-6E instrument.