Tetrahedron Letters No. 25, pp. 2315-2316, 1971. Pergamon Press. Printed in Great Britain.

A NOVEL SYNTHESIS OF 1,2,4-TRIAZINES[+]

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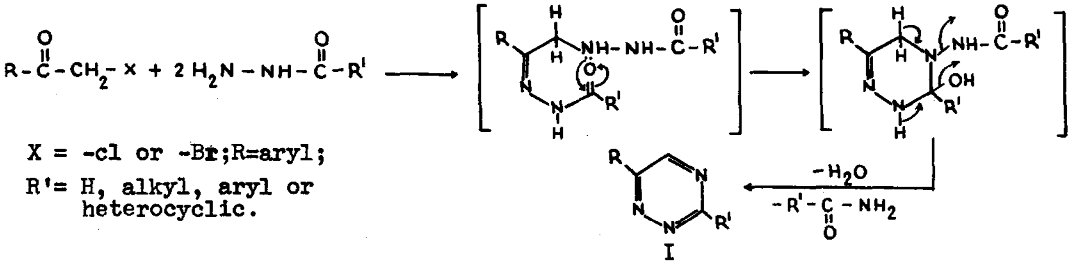
(Received in UK 3 May 1971; accepted in UK for publication 20 May 1971)

A number of 6-aryl- and 3-substituted-6-aryl-1,2,4-triazines (as-triazines) have been prepared by a very facile procedure in these laboratories. Heating a mixture of an acid hydrazide and an ω-haloacetophenone (2:1), in EtOH or AcOH on a boiling water-bath in the presence of molar quantities or a slight excess of NaOAc, KOAc or AgOAc for a few minutes, results in I in 60-93% yields (Scheme 1). Only two instances of 3,6-disubstituted-1,2,4-triazines I(R=C_6H_5, R'=CH_3, and R=R'=C_6H_5) have been hitherto reported[1,2]. A tentative mechanism by which these compounds are obtained is also given in Scheme 1. The elimination product, the amide, has been isolated in a few cases.

SCHEME 1



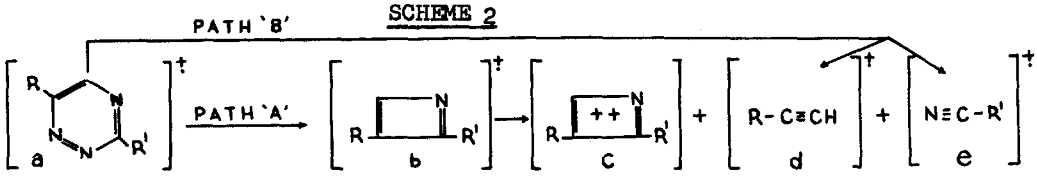
X = -cl or -Br;R=aryl;
R'= H, alkyl, aryl or heterocyclic.

Mass spectra of these compounds I(i-v)(Scheme 2) are in agreement with their respective molecular weights and indicate two general modes of fragmentation (paths A and B). The M^+ion a loses N_2[3,4] with formation of a 4-membered ring ion[*]b represented as an aromatic azacyclobutadiene. This further fragments to give rise to the acetylenic and nitrile fragments d and e. Interestingly, compound v follows path B, evidenced by the absence of peaks at m/e values corresponding to fragments b and c; d and e fragment further in the usual manner, full details of which will be published elsewhere.

[+] An account of a part of this work was presented at a National Seminar on "Recent Advances in Heterocyclic Chemistry", NCL, Poona, India, Sept.1970.

[*] This transition is supported by the occurrence of a metastable peak at 179-183 (theor. 180.3) and 192-196(theor. 194.1) in compounds i and ii respectively.

SCHEME 2



i.R=R'=phenyl-	m/e 233,84%	m/e 205,53%	m/e 102,5, @	m/e 102,98%	m/e 103,100%
ii.R=phenyl- R'=p-Me-phenyl-	" 247,31%	" 219,20%	" 109.5,9.5%	" 102,100%	" 117,20%
iii.R=p-Me-phenyl- R'=phenyl-	" 247,87%	" 219,20%	" 109.5,25%	" 116,100%	" 103,26%
iv.R=phenyl- R'=2-furyl	" 223,89%	" 195,9.5%	" 97.5,9.5%	" 102,100%	" 93,27%
v.R=phenyl R'= trimethyl gallyl"	323,55%	..	..	" 102,100%	" 193,97%

Some of the compounds were authenticated by an unambiguous synthesis[1,2]. The penultimate stage in the synthesis is the formation of dihydro triazines whose structures have not been established so far. A 1,2[1]-, 2,5-or 4,5[5]- dihydro structure has been proposed for these intermediates. However the 1,2-,2,3- or 5,6-dihydro structures were excluded by IR studies by Atkinson and Cossey[2]. Attempted methylation by these authors[2] to differentiate between the 2,5- or 4,5-dihydro structures failed. Our study of the NMR spectrum of 3,6-diphenyldihydro-1,2,4-triazine clearly indicates that this dihydro compound has a 2,5-dihydro structure and not the alternative 4,5-structure because of the clear methylene peak appearing as a singlet at 4.55δ. The 4,5-dihydro structure would show a doublet for the methylene due to coupling with the -NH-proton.

Acknowledgements: The authors are greatly indebted to Dr.A.J.Boulton, University of East Anglia, England, for the mass and NMR spectra. TVS is thankful to the UGC, New Delhi, for the award of a Fellowship.

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@ The 102.5 peak is under the peaks at m/e 102 and m/e 103.