

STUDIES ON AS-TRIAZINE DERIVATIVES. XVII¹CHLORINATION OF 5,6-DIMETHYL-3-PHENYL-as-TRIAZINE

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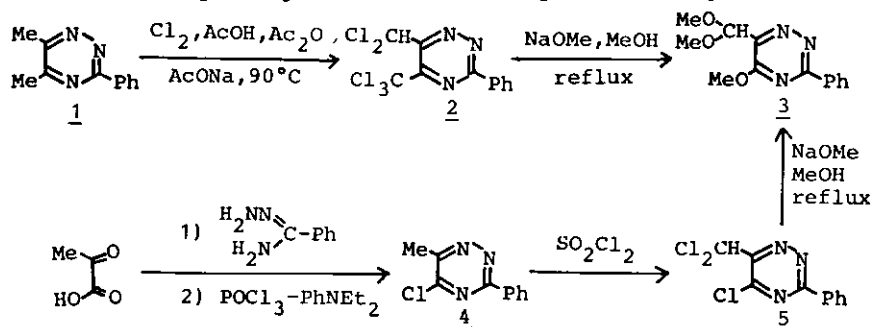
Abstract——Homolytic chlorination of 5,6-dimethyl-as-triazine(1) with Cl₂ gave 6-dichloromethyl-5-trichloromethyl-as-triazine(2) selectively. Structural determination of 2 by chemical method and synthesis of 5-amino-6-formyl-as-triazine derivatives are described.

It is well known that the methyl groups attached to the 3-, 5-, and 6-positions of 1,2,4-triazine(as-triazine) ring are highly active towards homolytic chlorination, and monomethyl-as-triazines are, in principle, converted into the corresponding trichloromethyl compounds.² In the present paper, we report an exhaustive chlorination of 5,6-dimethyl-3-phenyl-as-triazine(1), the structural determination of the resulting pentachloro compound(2), and the synthesis of 6-formyl-as-triazine derivatives from 2.

When chlorine gas was bubbled slowly into a solution of 1 in acetic acid and acetic anhydride in the presence of sodium acetate at 90°C, the pentachloride, mp 156-158°C, 77%, of 1 was obtained as a single product. The product(2) smoothly reacted with sodium methoxide(5 eq. mol) to give 5-methoxy-6-dimethoxymethyl-3-phenyl-as-triazine(3), mp 124-126°C, 43%, which was identical with an authentic specimen prepared by the following procedure.

5-Chloro-6-methyl-as-triazine(4) site-selectively synthesized by the condensation of pyruvic acid with benzamidrazone³ and subsequent dehydroxy-chlorination of the

resulted 5-triazinone with phosphoryl chloride was easily chlorinated with sulfonyl chloride to give 5-chloro-6-dichloromethyl-3-phenyl-as-triazine(5), mp 129-131°C, in 74% yield from 4. On heating with sodium methoxide(3 eq. mol) in methanol, 5 was readily changed to 3 in almost quantitative yield.



Scheme 1

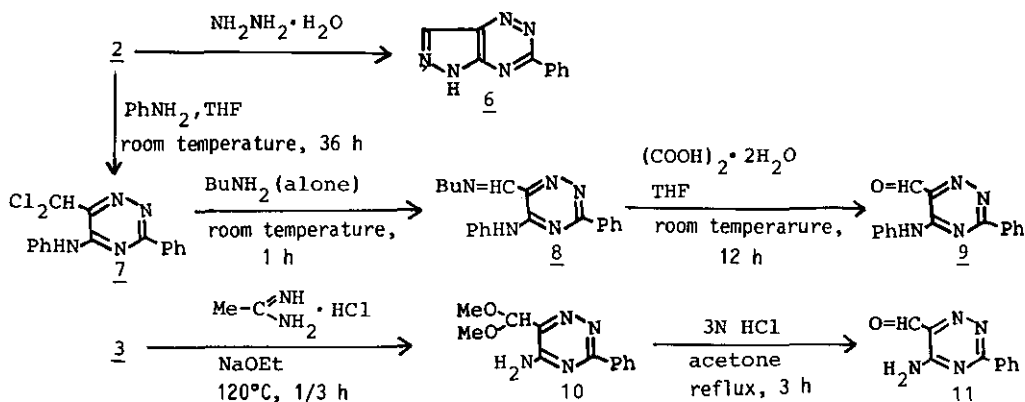
These findings clearly demonstrated the structure of the pentachloride to be 6-dichloromethyl-5-trichloromethyl-3-phenyl-as-triazine(2). In connection with the conversion of 2 into 3, it has been known that a trichloromethyl group on as-triazine rings acts as an efficient leaving group towards nucleophilic substitution.⁴ Furthermore, no formation of 5,6-bis(trichloromethyl)-3-phenyl-as-triazine was observed on the exhaustive chlorination of 1. Probably, the 5-trichloromethyl group predominantly formed retards the trichlorination of the less reactive 6-methyl group by its steric hindrance.⁵

When 2 was heated with hydrazine hydrate under reflux, the 6-dichloromethyl group and 5-trichloromethyl group acted as a masked formyl group and a leaving group respectively, and as a result, 3-phenyl-5H-pyrazolo[3,4-e]-1,2,4-triazine(6), mp 268-270°C, was isolated in 75% yield.

Based on the result described above, the synthesis of 6-formyl-as-triazine derivatives from the 6-dichloromethyl compounds was examined as follows. The reaction of 2 with aniline(2 eq. mol) in THF at room temperature gave 5-anilino-6-dichloromethyl-3-phenyl-as-triazine(7), mp 121-123°C, in 76% yield. Compound 7 reacted with butylamine alone to give the Schiff base(8), mp 109-111°C, which was easily hydrolyzed with oxalic acid dihydrate to the desired aldehyde(9), mp 147-148°C, in 80% overall yield from 7.

On the other hand, the reaction of 2 with ammonia in methanol failed to give 5-amino-6-formyl-3-phenyl-as-triazine(11). In this case, the reaction mixture turned to dark brown immediately, and no formation of 11 or the corresponding aldimine was detected in the reaction mixture. Thus, in place of 2, the acetal(3) was heated with acetamidine(free base) at 120°C to afford 5-amino-6-dimethoxy-

methyl-3-phenyl-as-triazine(**10**), on treatment of which with 3N hydrochloric acid in acetone, 5-amino-6-formyl-3-phenyl-as-triazine(**11**), mp 212-215 °C(decomp.) [¹H-nmr(DMSO-d₆): 7.4-7.8 (3H, m), 7.8-8.3 (1H, br), 8.3-9.0 (3H, m), 10.23 (1H, s)] was obtained in 44% yield from **3**.



Scheme 2

These reactions are the first synthesis of as-triazine derivatives with bifunctional character corresponding to o-aminobenzaldehyde, although further investigations on reaction procedure are still remain. The synthesis of compounds containing bicyclic as-triazine nucleus from **11** is now under investigation, which will be reported in the near future.

REFERENCES AND NOTES

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2. S. Konno, M. Sagi, E. Takaharu, S. Fujimura, K. Hayashi, and H. Yamanaka, *Chem. Pharm. Bull.*, 1988, **36**, 1721.
3. V. Uchytilova, P. Fiedler, M. Prystas, and J. Gut, *Coll. Czech. Chem. Commun.*, 1971, **36**, 1955.
4. S. Konno, M. Yokoyama, and H. Yamanaka, *Heterocycles*, 1982, **19**, 1865.
5. It is known that o-xylene is chlorinated with excess chlorine to give 1-dichloromethyl-2-trichloromethylbenzene in 70% yield since the size of the chlorine atoms prevents the introduction of six chlorine atoms into the side chains of o-xylene [J. Fernandez-Bolanos, W. G. Overend, A. Sykes, J. C. Tatlow, and E. H. Wiseman, *J. Chem. Soc.*, 1960, 4003].

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