REACTION OF 2,4-DIPHENYL-1,3,5-TRIAZINE DERIVATIVES WITH NUCLEOPHILES

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Abstract — The addition of hydrogen cyanide to 2,4-diphenyl-1,3,5-triazine (1) followed by spontaneous oxidation of the adduct gave 4,6-diphenyl-1,3,5-triazine-2-carbonitrile (4) in considerable yield. Similarly, 1 reacted with various active methylene compounds in the presence of sodium hydride to give the corresponding 2-substituted 4,6-diphenyl-1,3,5-triazines (8a-c). Additionally, the condensation of 2-chloro-4,6-diphenyl-1,3,5-triazine (2) with benzaldehyde in the presence of 1,3-dimethylbenzimidazolium iodide under basic conditions, gave the corresponding 2-benzoyl-1,3,5-triazine (9).

As reported previously, 1,2,4-triazine derivatives whose 5-position is free, are highly susceptible to the nucleophilic addition with weak nucleophilic reagents (hydrogen cyanide, sodium bisulfite, and hydrazine) to give adducts. Similar properties have been observed at the 4-position of quinazoline and at the 9-position of acridine, although the parent compounds of these ring systems are classified as aromatic compounds. A typical example is the reaction of sodium bisulfite with these compounds, which is shown in Scheme 1.

Based on these results, our next interests were focussed on the reaction of 2,4-diphenyl-1,3,5-triazine (s-triazine) (1) with various nucleophiles, of which results are described in the present paper.

when hydrogen cyanide was bubbled into a DMF solution of 1, 4,6-diphenyl-g-triazine-2-carbonitrile (4), mp 177-178°C (lit. 5 mp 181.5-183°C), colorless needles from hexane-AcOEt, $^{\rm C}_{16}{}^{\rm H}_{10}{}^{\rm N}_4$, was isolated in 62% yield as expected. In this case, spontaneous aromatization of the adduct (3) may be caused by air oxidation.

The reaction of 1 with hydrazine hydrate, like that of quinazoline, 2 afforded 2-hydrazino-4,6-diphenyl-s-triazine (6), mp 187-188°C, colorless needles from EtOH, $C_{15}H_{13}N_5$, in 33% yield. The hydrogen acceptor in this reaction is supposed to be hydrazine itself.

a : X=CN , Y=Ph ; b: X=CN , Y=CO2Et ; c: X=H , Y=COPh

Scheme 2

Treatment of 1 with active methylene compounds such as phenylacetonitrile, ethyl cyanoacetate, and acetophenone in the presence of sodium hydride, smoothly afforded the corresponding adducts (7a-c). The purification of these adducts failed, but the oxidation by passing of oxygen into a DMF solution of the crude adducts gave the aromatic s-triazine derivatives (8a-c), as described in the following paragraph.

General Procedure for the Reaction of 1 with Active Methylene Compounds: A dry THF (10 ml) solution of 1 (0.003 mol) was added to a dry THF suspension (20 ml) of an active methylene compound (0.010 mol) and sodium hydride (0.010 mol). The reaction mixture was refluxed for 60 h. The solvent was evaporated under reduced pressure, and dil. HCl (5 ml) and DMF (15 ml) were added to the residue. Oxygen was bubbled into this solution until the oxidation was completed (monitored by TLC). The resulting solution was extracted with benzene. The benzene layer was washed with H₂O and dried over Na₂SO₄. After removal of the solvent, the residue was purified by chromatography on a silica gel column and recrystallization from appropriate solvents.

According to the general procedure, the following compounds were obtained: α -Phenyl-4,6~diphenyl-s-triazine-2-acetonitrile (8a), mp 177-178°C, colorless prisms from AcOEt, 19%, $C_{23}H_{16}N_4$.

Ethyl 4,6-diphenyl-s-triazine-2-cyanoacetate (8b), mp 213-215°C, orange needles from AcOEt, 26%, $C_{20}H_{16}N_4O_2$.

2-Phenacyl-4,6-diphenyl-s-triazine (8c), mp 182-183°C, colorless needles from hexane-AcOEt, 32%, $C_{23}H_{17}N_3O$.

These products (8a-c) are identical with authentic samples obtained by the reaction of 2-chloro-4,6-diphenyl-s-triazine (2) with the corresponding active methylene compounds in THF in the presence of sodium hydride.

The compounds (4,6) were also identical with authentic specimens derived from 2 by nucleophilic substitutions under conventional conditions, as shown in Scheme 2. 6 Futhermore, the condensation of 2 with benzaldehyde in the presence of 1,3-dimethylbenzimidazolium iodide gave 2-benzoyl-4,6-diphenyl-s-triazine (9), mp 144-145°C, colorless needles from hexane-AcOEt, $C_{22}H_{15}N_3O$, IR $v_{C=O}$ 1690 cm⁻¹, in 68% yield. The same type reaction has been known on 4-chloroquinazoline, 7 9-chloro-acridine, 7 and 5-chloro-1,2,4-triazine derivatives. 1a

Scheme 3

In conclusion, our present results demonstrate that acridine (at the 9-position), quinazoline (at the 4-position), 1,2,4-triazine (at the 5-position), and 1,3,5-triazine are in a similar level of reactivity for nucleophilic additionelimination reactions.

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- 4. The compound 1 is conveniently prepared by catalytic reduction of the chloride (2) derived from 4,6-diphenyl-1,3,5-triazin-2(lH)-one. H. Schroeder and Ch. Grundmann transferred 2-chloro-4,6-dimethyl-1,3,5-triazine to 2,4-dimethyl-1,3,5-triazine by this method (J. Am. Chem. Soc., 1956, 78, 2447).
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- 6. For the preparation of the compounds 4,6,8a-c, this route is rather suitable in laboratory practice. Yields from 2: 4, 79%; 6, 89%; 8a, 71%; 8b, 62%; 8c, 55%.
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