SYNTHESIS OF 3-SUBSTITUTED 1,2,4-TRIAZINES

Masaaki Yokoyama, Etsuko Takaharu, Yuichi Aizawa, Shoetsu Konno,

and Hiroshi Yamanaka

Pharmaceutical Institute, Tohoku University

Aobayama, Sendai 980, Japan

The synthesis of 1,2,4-triazine(as-triazine) derivatives having a carbon functional group at the 3-position was achieved by the following routes.

1) The reaction of 3-methylsulfonyl-as-triazines with C-nucleophiles:

5,6-Diphenyl-3-methylthio-as-triazine was oxidized with potassium permanganate to give 5,6-diphenyl-3-methylsulfonyl-as-triazine(1). When 1 was treated with C-nucleophiles such as active methylene compounds, methyl ketones, methylene ketones, and cyanide ion under basic conditions the corresponding 3-substituted as-triazines (2,3,4) were obtained in good yields.
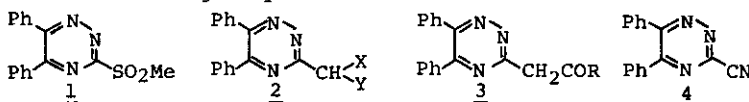
2) The synthesis of 3-alkenyl-as-triazines by means of Wittig reaction:

5,6-Diphenyl-3-methyl-as-triazine was chlorinated with chlorine gas in acetic acid to give trichloromethyl derivative(5). The reaction of 5 with triphenylphosphine in benzene gave the phosphorane(6) reductively in 86% yield. The condensation of 6 with various aldehydes afforded the corresponding 3-alkenyl-as-triazines(7).
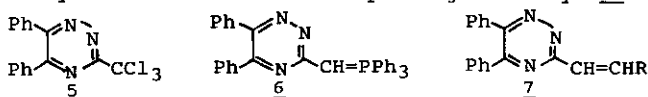
During the investigation described above, a unique ring-cleavage reaction was occasionally observed. Namely, when 5 was allowed to react with sodium ethoxide in ethanol, a ring-opened product(8) was obtained as a sole product. In contrast, the reaction of 5 with sodium hydroxide in aqueous methanol gave the as-triazinone(9), which demonstrated the trichloromethyl group to behave as a leaving group in nucleophilic substitution. Furthermore, the trichloride(5) was transformed into 5,6-diphenyl-3-ethoxy-as-triazine, when 5 was treated with sodium ethoxide in DMF. The mechanism and limitation of these reactions are also discussed.