A One-Pot Synthesis of Ring-fused 1,3,5-Triazine-2,4(3*H*)-diones: Reactions with Chlorocarbonyl Isocyanate

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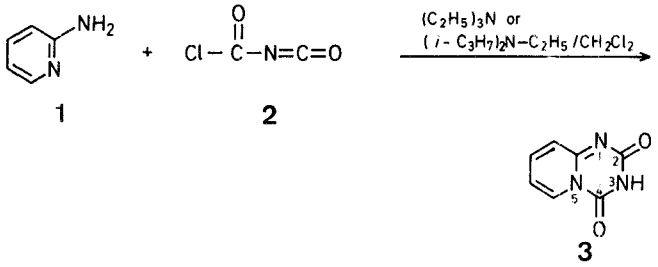
Ring-fused 2,4-dioxo-1,2,3,4-tetrahydro-1,3,5-triazines are prepared by cyclocondensation of α-amino-*N*-heteroarenes with chlorocarbonyl isocyanate in the presence of tertiary amines.

The title compounds **(3, 5, 7)** have been claimed to be useful intermediates in the synthesis of compounds exhibiting herbicidal[1,3] and antitumour activities[2]. The earlier method[3] for

the preparation of compound **3** involves the treatment of ethyl 4-(2-pyridyl)-allophanate (obtained from 2-aminopyridine and ethoxycarbonyl isocyanate in 85% yield) with alkali metal hydroxides to give 2*H*-pyrido[1,2-*a*]-1,3,5-triazine-2,4(3*H*)-dione (**3**) in 91% yield. More recently, another approach has been reported[4] which consists of the reaction of 2-aminopyridine with ethoxycarbonyl isocyanate or diethyl iminodicarboxylate affording ethyl 4-(2-pyridyl)-allophanate in 72% and 43% yields, respectively, which on cyclization gives **3** in 15% yield. Treatment of **3** with alkyl halides in the presence of a strong base such as sodium hydride leads to *N*-alkyl-substituted compounds of biological interest.

In the past few years, chlorocarbonyl isocyanate has found increased application in organic synthesis[5], particularly in the synthesis of heterocyclic compounds such as 1,3-oxazinediones, uracils, benzoxazinediones, quinazolinediones, and triazepinediones. During our studies on the reactions of chlorocarbonyl isocyanate[6] (**2**) we found that the addition of this reagent to 2-aminopyridine (**1**) followed by treatment with triethylamine/diisopropylethylamine leads to 2*H*-pyrido[1,2-*a*]-1,3,5-triazine-2,4(3*H*)-dione (**3**) in high yield (88%).



In order to investigate the scope of the method we subjected other α-amino-*N*-heteroarenes such as 2-aminopyrimidine (**4**) and 2-amino-4-phenylquinazolines (**6a, b**) to the reaction with chlorocarbonyl isocyanate (**2**) under the same conditions; we thus obtained 2*H*-pyrimido[1,2-*a*]-1,3,5-triazine-2,4(3*H*)-dione (**5**) and 1*H*-triazino[1,2-*a*]quinazoline-1,3(2*H*)-diones (**7a, b**), respectively, in high yields.

Compounds **3**, **5**, and **7** were characterized by analytical and spectral data.

The ease of the reaction as well as the commercial availability of the starting materials make this approach a useful one-pot synthesis of the title compounds.

2*H*-Pyrido[1,2-*a*]-1,3,5-triazine-2,4(3*H*)-dione (3); Typical Procedure:

A solution of chlorocarbonyl isocyanate (**2**; 2 ml, 0.025 mol) in dichloromethane (4 ml) is added, over a period of 10 min, to a stirred solution of 2-aminopyridine (**1**; 2.353 g, 0.025 mol) in dichloromethane (35 ml) at room temperature, and stirring is continued for 30 min. Then, triethylamine (2.53 g, 0.025 mol) is added and the mixture is stirred for a further 30 min. The dichloromethane is then removed in vacuo and the residual product is washed with water (40 ml) and recrystallized from methanol.

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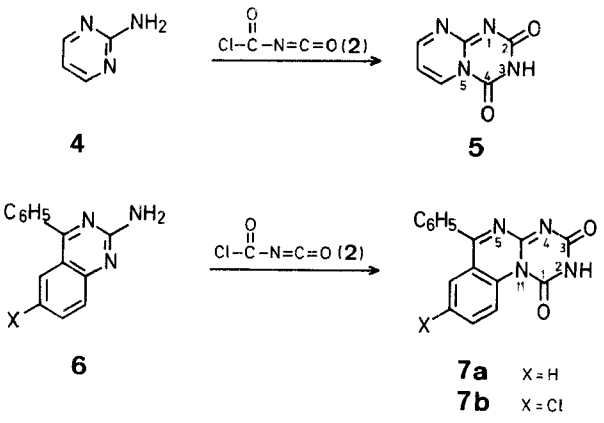
Table. Ring-fused 1,3,5-Triazine-2,4(3*H*)-diones (**3, 5, 7**)

Product	Yield [%]	m.p. [°C]	Molecular Formula[a]	M.S. *m/e* (M^+)	I.R. (KBr) ν[cm^{-1}]
3	88	203–206° (210–215°)[4]	$C_7H_5N_3O_2$ (163.1)	163	3030, 1735, 1660
5	83	173–175°	$C_6H_4N_4O_2$ (164.1)	164	3035, 1735, 1665
7a	86	194–198°	$C_{16}H_{10}N_4O_2$ (290.3)	290	3040, 1730, 1665
7b	91	220–225°	$C_{16}H_9ClN_4O_2$ (324.7)	324	3045, 1725, 1660

[a] The microanalyses were in satisfactory agreement with the calculated values: C ±0.20, H ±0.21, N ±0.17.



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