

An Improved Synthesis of 3,5,6-Trichloro-1,2,4-triazine

B. A. Loving, C. E. Snyder, Jr., G. L. Whittier (1), and K. R. Fountain (1)

Air Force Materials Laboratory, Wright-Patterson Air Force Base, Ohio 45433

Received April 12, 1971

Analogous to cyanuric chloride in the chemistry of 1,3,5-triazine; 3,5,6-trichloro-1,2,4-triazine provides a synthetic intermediate for preparation of alkoxy *as*-triazines, which hold some promise as fluid materials. Compounds with this ring system, including derivatives of 6-azauracil, have been shown to exhibit biological activity (2-4). The available procedure for making this compound (3,4) gave a 30% yield of an oil which was neither purified nor characterized but was employed directly as an intermediate. Subsequent syntheses by other workers provided an unreported quantity of purer material (5). This communication reports a procedure giving a greatly increased yield of high purity product obtained in substantially reduced reaction time. The method of Chang (3,4), heating 5-bromo-6-azauracil under reflux in phosphorus oxychloride for 48 hours, in our hands provided only 9 to 11% yields. It was found that the use of phosphorus pentachloride in phosphorus oxychloride substantially reduced the optimum temperature and heating time for reaction. Addition of *N,N*-diethylaniline with the phosphorus pentachloride increased yields further, the maximum being 78%. Larger scale reactions produced lower yields. However, when the product is removed by

continuous extraction using carbon tetrachloride in a liquid-liquid extractor, yields of 50-60% are obtained. Results of these methods are summarized in Table I.

The dramatic effect of base and phosphorus pentachloride on the reaction can be explained by the following mechanism analogous to the second stage of the Arbusov reaction. Further precedent is found in the mechanism of *gem*-dihalide production proposed by Newman and Wood (7), and amide reaction to form nitriles (8).

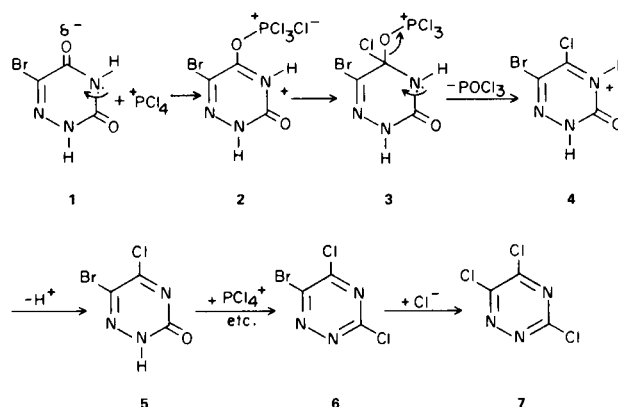


TABLE I

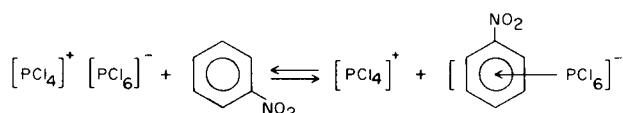
Effectiveness of Phosphorus Pentachloride and Solvent Modification On Yields of 3,5,6-Trichloro-*as*-triazine

Run No.	PCl ₅ /Substrate	Solvent (6)	Temp (°C)	Heating Time (hr)	Yield (%)
1 (3,5)	0.0	POCl ₃	90-100	48-60	11
2	2.0	POCl ₃	68	1	6
3	2.0	POCl ₃	60	2	38
4	2.0	POCl ₃	60	14	21
5	2.0	POCl ₃	108	7	15
6	2.0	POCl ₃	108	2	35
			Rm Temp	15	
7	2.0	POCl ₃ + <i>N,N</i> -diethylaniline	Reflux	2	56
8	2.0	POCl ₃ + <i>N,N</i> -diethylaniline	Reflux	2	78
			Rm Temp	24	

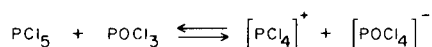
Replacement of bromine by chlorine in the 5 position (*i.e.* **6** to **7**) is easily rationalized when one recognizes the behavior of halo triazines as weak acid halides (9). The high chloride ion concentration will drive the reaction far to the right. Piskala showed halogen in the 5 position to be the most labile (5).

Formation of the strong P = O (128 K cal) (10) bond furnishes the driving force for the reaction. Action of added base presumably aids proton removal from intermediate **4**. Phosphorus oxychloride seems necessary as a solvent and no doubt promotes ionization since changing to other solvents (6) reduced yields to zero. The only product of those reactions was a polymeric amorphous powder containing nitrogen and bromine with molecular weight 431 (mass spectroscopy), which was present in all reactions as a by-product. Polymerization was extensive in the absence of base.

In the gas phase phosphorus pentachloride is covalent and has a bipyramidal structure as predicted by group theory. However in the solid state it exists largely in the ionic form $^+PCl_4^-PCl_6^-$ (8,11). If phosphorus oxychloride (dipole moment 2.41 D) acts only as a solvent, it would appear that use of nitrobenzene (dipole moment 3.92 D) would increase both rate and yield due to its greater dipole moment and non-acid character. Further, it should promote formation of the PCl_4^+ moiety by both solvation and complexation, *i.e.*



However, use of nitrobenzene both neat and with *N,N*-diethylaniline rather than phosphorus oxychloride yielded only polymer. This fact supports the concept that the following interaction is more effective, the negative charge



being more highly stabilized by the oxygenated species. This unique synergism has been observed in other systems (12).

The infrared spectra of 3,5,6-trichloro-1,2,4-triazine can be interpreted on the basis of its comparison with that of 2,4,6-trichloro-*s*-triazine and 5-alkyl-6-azauracils (2) and are of interest since no spectral data has been previously published on this aromatic ring system. Two strong bands appear at 1480 cm^{-1} and 1450 cm^{-1} (ring in-plane stretching), a very strong band at 1265 cm^{-1} (C=N-C), a strong band at 865 cm^{-1} (C-Cl in-plane stretching) and a sharp medium peak at 763 cm^{-1} (C-Cl out-of-

plane bending). Analogous bands can be found in the spectrum of 2,4,6-trichloro-*s*-triazine.

Chang (2) reported a 730-750 cm^{-1} band which was ascribed to the *as*-triazine ring. The spectrum of **7** showed a very weak band at 730 cm^{-1} in nujol and carbon tetrachloride but in potassium bromide none was observed. However, four sharp medium to strong peaks were observed at 1200, 1160, 1075 and 1045 cm^{-1} that are absent in the two reference compounds. Appearing in the aromatic double bond region, these most probably arise from the aromatic *as*-triazine ring.

EXPERIMENTAL

To 4.8 g. (0.025 mole) of 5-bromo-6-azauracil in 100 ml. of phosphorus oxychloride was added 10.4 g. (0.05 mole) of phosphorus pentachloride and 10 ml. (0.075 mole) of *N,N*-diethylaniline. The mixture was magnetically stirred and heated under reflux for 2 hours, allowed to stand at room temperature for 24 hours, the excess solvent removed under reduced pressure and the residue extracted with five 100-ml. portions of dry ether. Distillation (55-60°, 0.05 mm) of the residue remaining from the ether phase gave 3.54 g. (78%) of 3,5,6-trichloro-1,2,4-triazine, m.p. 58-60°, which is pure enough for most chemical purposes.

When scaled up to 24 g. of 5-bromo-6-azauracil the residue after solvent removal was subjected to continuous extraction with carbon tetrachloride to yield 50-60% of **7**. 3,5,6-Trichloro-1,2,4-triazine when stored in a dark bottle under nitrogen remained unchanged after a year but hydrolyzed slowly in air.

A sample vacuum-sublimed for analysis gave m.p. 60-62° (lit. 57-58°) (6); uv max (*n*-hexane) 290 $m\mu$ ($\epsilon = 4460$), sh. 301 $m\mu$ ($\epsilon = 2829$), 363 $m\mu$ ($\epsilon = 598$); ir (carbon tetrachloride, potassium bromide, nujol) 1480, 1450, 1265, 1200, 1160, 1075, 1045, 865 and 763 cm^{-1} .

Anal. Calcd. for $C_3N_3Cl_3$: C, 19.54; N, 22.79. Found: C, 19.54; N, 23.05; H, 0.0.

REFERENCES

- (1) Midwest Research Institute, Kansas City, Missouri.
- (2) P. K. Chang, *J. Org. Chem.*, **23**, 1951 (1958).
- (3) P. K. Chang, *ibid.*, **26**, 1118 (1961).
- (4) P. K. Chang and T. L. V. Ulbright, *J. Am. Chem. Soc.*, **80**, 976 (1957).
- (5) A. Piskala, J. Gut, and F. Sorm, *Chem. Ind. (London)*, 1752 (1964).
- (6) Other solvent combinations failed to produce the desired reaction product. These included neat THF, $POCl_3$ + pyridine, neat nitrobenzene, nitrobenzene + *N,N*-diethylaniline and neat *N,N*-diethylaniline at a variety of temperatures.
- (7) M. S. Newman and L. L. Wood, Jr., *J. Am. Chem. Soc.*, **81**, 4300 (1959).
- (8) L. Horner, H. Oediger, and H. Hoffmann, *Ann. Chem.*, **626**, 26 (1959).
- (9) C. W. L. Beven and R. F. Hudson, *J. Chem. Soc.*, 2187 (1953).
- (10) R. F. Hudson, "Structure and Mechanism in Organo-Phosphorus Chemistry," Academic Press, New York, 1965, p. 68.
- (11) R. F. Hudson, *ibid.*, p. 47.
- (12) R. F. Hudson, *ibid.*, p. 215.