mol) of ethyl malonate was allowed to react at 65° for 8.5 hr in 200 ml of DMSO. The conversions into 2-nitrooctane (11%), 2-octanol (38%), and 2-octanone (36%) were determined by vpc analysis on a 6 ft × 0.25 in. 5% Carbowax on 20M Chromosorb G column.

1,5-Dinitropentane and 5-Nitro-1-pentanol.—A mixture of 48.51 g (0.25 mol) of 1,5-pentamethylene dinitrate, 48.3 g (0.70 mol) of sodium nitrite, and 64.01 g (0.04 mol) of ethyl malonate in 400 ml of DMSO was allowed to react at 60° for 2 hr. The conversion into 1,5-pentamethylene glycol (34%) was determined by vpc analysis on the 5% SF-96 column. The conversions into 1,5-dinitropentane (11%) and 5-nitro-1-pentanol (44%) were determined by analysis on the 5% Carbowax 20M column. 5-Nitropentanol (44%) is a new compound and has the following physical constants: bp 262–266°; $n^{20}\text{D}$ 1.4546.

Anal. Calcd for $C_5H_{11}NO_3$: C, 45.11; H, 8.27; N, 10.52. Found: C, 44.58; H, 8.26; N, 10.50.

Registry No.—Dinitrogen pentoxide, 10102-03-1; 5-nitropentanol, 21823-27-8; dinitrogen tetroxide, 10544-72-6.

The Reaction of Nitriles with Phosgene. III.[1]
A New Synthesis of 2-Chloro-4,6-diaryl-s-triazines

SHOZO YANAGIDA, HIROSHI HAYAMA, MASAAKI YOKOE, AND SABURO KOMORI

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamadakami, Suita City, Osaka, Japan

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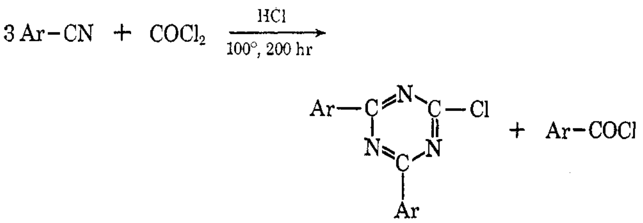
The reaction of benzonitrile with phosgene in the presence of hydrogen chloride at 100° in a sealed glass tube gives approximately equal yields of 2-chloro-4,6-diphenyl-*s*-triazine and benzoyl chloride. This has also been demonstrated with *p*-tolunitrile and *p*-methoxybenzonitrile. In the case of *p*-chloro- and *p*-nitrobenzonitrile, however, the reactions are unsuccessful. The mechanism of this reaction is discussed.

It is well known that nitriles having no α-hydrogens easily trimerize into *s*-triazines in the presence of strong acids, such as hydrogen chloride[2] and chlorosulfonic acid,[3] or under the influence of high pressure.[4] In the preceding papers of this series,[1,5] we reported that upon treatment of aliphatic nitriles with phosgene in the presence of hydrogen chloride at 60–70°, 6-chloro-2,5-dialkyl-4(3H)-pyrimidones were obtained in good yields, in addition to small amounts of 4,6-dichloro-2,5-dialkylpyrimidines.

It has now been found that when benzonitrile reacts with phosgene in the presence of hydrogen chloride at 100° for 200 hr and the well-cooled reaction mixture is filtered, 2-chloro-4,6-diphenyl-*s*-triazine is obtained in high yield. It was identified by direct comparison of its physical properties with those of an authentic sample prepared by the reaction of cyanuric chloride with phenylmagnesium bromide.[6] Glpc analysis of the filtrate showed the presence of benzoyl chloride, which was confirmed by converting it into benzamide. Both products were found in almost equal yields (Scheme I).

SCHEME I



This cyclization did not occur in the absence of hydrogen chloride. Employment of other chlorinating agents, such as phosphorus pentachloride, phosphorus trichloride, phosphorus oxychloride, sulfuryl chloride, and thionyl chloride instead of phosgene, gave only 2,4,6-triphenyl-*s*-triazine.[7]

We examined the yields of the reaction with varying molar ratios of the reactants. It was demonstrated (Table I) that excess hydrogen chloride favored this reaction, but that a large excess of phosgene lowered the yield.

TABLE I
EFFECT OF MOLAR RATIO OF REACTANTS

	Product yields, %[a]	
Molar ratio $C_6H_5CN:COCl_2:HCl$	2-Chloro-4,6-diphenyl-*s*-triazine	Benzoyl chloride[b]
3:0.5:1	10	15
3:1:1	16	19
3:1.5:1	25	26
3:2:1	6	10
3:1:1.5	62	
3:1:2	83	
2:0:1	20[c]	0

[a] Reaction time 200 hr, based on phosgene used. [b] Determined by glpc. [c] 2,4,6-Triphenyl-*s*-triazine.

On close examination of the reaction mixture obtained when excess phosgene was employed, a small amount of a high-boiling product was detected. It was isolated by distillation under reduced pressure and identified as N-(1-chlorobenzylidene)carbamoyl chloride (II, Ar = phenyl) on the basis of ir and mass spectra and elemental analysis.

The reaction of benzonitrile with phosgene and hydrogen chloride has been extended to *p*-tolunitrile, *p*-methoxybenzonitrile, *p*-chlorobenzonitrile, and *p*-nitrobenzonitrile. In the case of *p*-tolunitrile, the products were 2-chloro-4,6-bis(*p*-tolyl)-*s*-triazine and *p*-toluoyl chloride. Glpc analysis of the filtrate also showed the formation of a small amount of the corresponding carbamoyl chloride. The reaction of *p*-

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(1) Part II: S. Yanagida, M. Ohoka, M. Okahara, and S. Komori, *J. Org. Chem.*, **34**, 2972 (1969).

(2) C. Grundmann, G. Weisse, and S. Seide, *Ann. Chem.*, **577**, 77 (1952).

(3) A. H. Cook and D. G. Jones, *J. Chem. Soc.*, 278 (1941).

(4) T. L. Cairns, A. W. Larchar, and B. C. McKusick, *J. Amer. Chem. Soc.*, **74**, 5633 (1952).

(5) S. Yanagida, M. Ohoka, M. Okahara, and S. Komori, *Tetrahedron Lett.*, 2351 (1968).

(6) A. Ostrogovich, *Chem.-Ztg.*, **36**, 738 (1912).

(7) In our laboratory, it has been found that phosphorus pentachloride was able to catalyze the trimerization to 2,4,6-triphenyl-*s*-triazine. This reaction is now under investigation.

TABLE II

2-CHLORO-4,6-DIARYL-*s*-TRIAZINES FROM ARYL CYANIDE, PHOSGENE, AND HYDROGEN CHLORIDE

Triazines	Yield,[a] %	Mp, °C (crystn solvent)	Ir spectra (KBr), cm^{-1}	Mol wt[b]	Elemental analysis Calcd, %	Found, %
2-Chloro-4,6-diphenyl-*s*-triazine	83[c]	138–140[e]	1540, 1500	267	C, 67.30	C, 62.27
	(27)[d]	(acetone)	1380, 850		H, 3.77	H, 3.27
			750, 685		N, 15.70	N, 15.74
2-Chloro-4,6-bis(*p*-tolyl)-*s*-triazine	16[d]	207–210	1545, 1503[f]	295	C, 69.02	C, 68.98
		(acetone)	1380, 845		H, 4.77	H, 5.03
			800		N, 14.21	N, 14.51
2-Chloro-4,6-bis(*p*-methoxyphenyl)-*s*-triazine[g]	2.4[d]	195–197	1530, 1490	327	C, 62.30	C, 62.64
		(cyclohexane)	1375, 850		H, 4.30	H, 4.47
			803		N, 12.82	N, 12.90

[a] Based on phosgene used. [b] By analysis of mass spectra. [c] By the procedure of A. [d] By the procedure of B. [e] Lit.[6] 138.0–139.2°. [f] Nujol. [g] The filtrate was allowed to stand at room temperature overnight giving another precipitate. It was filtered, recrystallized from benzene, and identified as 2,4,6-tris(*p*-methoxyphenyl)-*s*-triazine: mp 222–224.5° (lit.[8] 217), ir spectrum (Nujol), 1590, 1510, 1375, 1172, 1020, and 820 cm^{-1}; mass spectrum (70 eV) m/e (rel intensity) 399 (65) (M$^+$), 133 (100), 103 (17), 90 (17).

methoxybenzonitrile with phosgene and hydrogen chloride in nitrobenzene, however, led to the isolation of 2-chloro-4,6-bis(*p*-methoxyphenyl)-*s*-triazine and a larger amount of 2,4,6-tris(*p*-methoxyphenyl)-*s*-triazine (Table II). In the case of *p*-chloro- and *p*-nitrobenzonitrile, the nitriles were recovered unchanged.

To gain some information about the mechanism of the ring closing, the isolated N-(1-chlorobenzylidene)carbamoyl chloride (II, Ar = phenyl) was allowed to react with benzonitrile in the presence of hydrogen chloride using a sealed glass tube. As expected, 2-chloro-4,6-diphenyl-*s*-triazine and benzoyl chloride were obtained in 70% yields, respectively. Accordingly, we assumed that the ring closure might proceed through the attack of the imidoyl chloride (I) on the carbamoyl chloride (II). Treatment of the carbamoyl chloride (II, Ar = phenyl) with *p*-tolunitrile under comparable conditions, however, led to the isolation of the mixture of 2-chloro-4-phenyl-6-*p*-tolyl-*s*-triazine, 2-chloro-4,6-bis(*p*-tolyl)-*s*-triazine, and a very small amount of 2-chloro-4,6-diphenyl-*s*-triazine, these being identified by mass spectra. Glpc analysis of the filtrate showed the formation of benzonitrile and *p*-toluoyl chloride, but not benzoyl chloride. It was ascertained that the carbamoyl chloride (II, Ar = phenyl)decomposes slowly to benzonitrile and phosgene. This fact may account for the formation of 2-chloro-4,6-bis(*p*-tolyl)-*s*-triazine and 2-chloro-4,6-diphenyl-*s*-triazine. Accordingly, the formation of 2-chloro-4-phenyl-6-*p*-tolyl-*s*-triazine and *p*-toluoyl chloride should be noted.

Furthermore, in order to determine whether the carbon atom of phosgene is included in the triazine or in benzoyl chloride, the reaction was carried out using phosgene labeled with ^{14}C. In this experiment, the labeled carbon was found only in the triazine. We assumed that the chlorine-bearing carbon in the triazine is labeled (Scheme II).

Meerwein, *et al.*,[9] have reported that aryl cyanide reacts with aroyl chloride in the presence of Lewis acid giving diazapyrylium salts. On the other hand, many 1,4-cycloaddition reactions of imidoyl chloride to conjugated diens have been reported.[10]

In view of these facts, we propose the reaction mechanism given in Scheme II.[11]

Experimental Section[13]

General Procedures. A. Without Solvent.—In a 100-ml glass tube were placed a solution of hydrogen chloride (2.0–4.0 g, 0.055–0.11 mol) in nitrile (10 g) and a solution of phosgene (3.0–9.0 g, 0.03–0.09 mol) in nitrile (10 g). The tube was stoppered, cooled in Dry Ice–acetone, sealed carefully, and heated to 95–100° in an oil bath. After the usual reaction period (200 hr), the reaction tube was chilled in Dry Ice–acetone and opened. The resulting precipitate was filtered, washed with a small portion of ether, and dried in a desiccator under reduced pressure. Further material precipitated on distillation of the filtrate. The precipitates were combined and purified by recrystallization and sublimation. The distillate from the filtrate was found to contain acid chloride by glpc and was treated with ammonia water. The resulting amide was filtered, washed with water, dried in a desiccator, and purified by sublimation. The isolated amides in appropriate experiments were benzamide, mp 126.0–128.0° (lit.[14] 127–127.5°), and *p*-toluamide, mp 157.0–159.0° (lit.[15] 155°).

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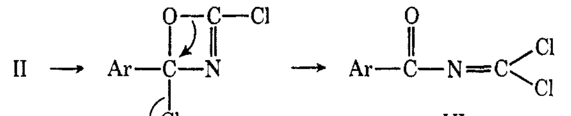
(8) F. Davis, *J. Chem. Soc.*, **85**, 1538 (1896).

(9) H. Meerwein, P. Laasch, R. Mersch, and J. Spille, *Chem. Ber.*, **89**, 209 (1956); see also R. R. Schmidt, *ibid.*, **98**, 334 (1965).

(10) M. Lora-tamayo and R. Madroñero, "1,4-Cycloaddition Reactions," Academic Press Inc., London, 1967, p 131.

(11) The decomposition of IV or V may produce cyanogen chloride. Thus, as an alternate reaction mechanism, Diels–Alder type reaction of cyanogen chloride with N-(1-chlorobenzylidene)benzamidine produced by dimerization of I was considered possible. However, the reaction of cyanogen chloride with benzonitrile in the presence of hydrogen chloride gave the mixture of cyanuric chloride and 2,4,6-triphenyl-*s*-triazine. Thus this reaction mechanism was excluded.

N-(Dichloromethylene)benzamide (VI, Ar = phenyl)[12] was considered to be another intermediate as shown below.



VI

However, treatment of VI with benzonitrile under comparable conditions did not lead to the formation of 2-chloro-4,6-diphenyl-*s*-triazine. Thus VI is excluded as an intermediate.

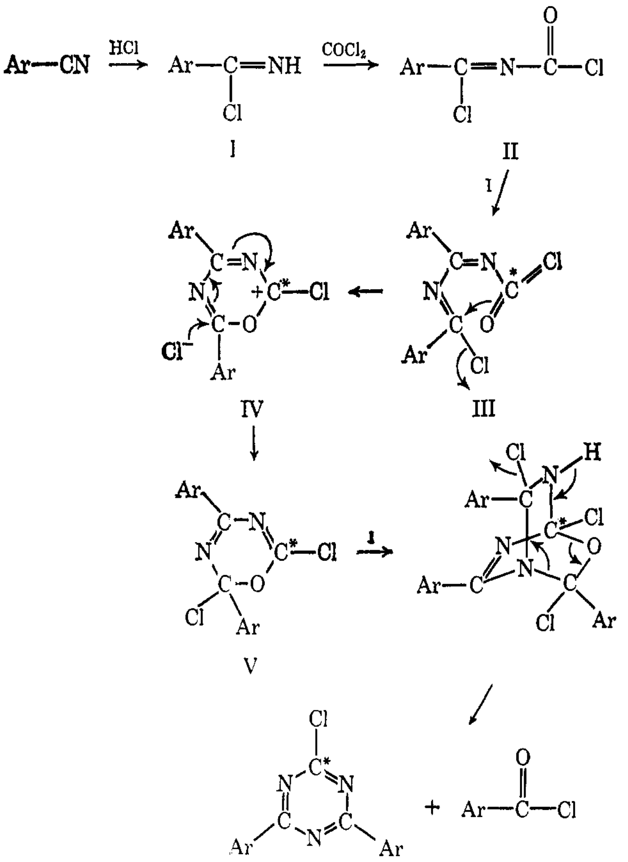
(12) This compound was prepared from benzoyl isothiocyanate by the method of Johnson [T. B. Johnson and L. H. Chernoff, *J. Amer. Chem. Soc.*, **34**, 164 (1912)].

(13) Melting points were determined on a Yanagimoto micro melting point apparatus and were corrected. The nmr spectra were obtained using a Model J. N. M-G-60 spectrometer (Japan Electronic Optics Laboratory Co.) with tetramethylsilane as an internal reference. The ir spectra were recorded with a Japan Electroscopic IR-E spectrophotometer. The mass spectra were recorded with a Hitachi mass spectrometer, Model RMU-6E. Glpc was performed with a column of Silicone DC 200, 10% on Diasolid L (60–80 mesh, 2-m column, 138° with hydrogen as the carrier gas.)

(14) H. A. Taylor and T. W. Davis, *J. Phys. Chem.*, **33**, 1470 (1928).

(15) L. McMaster and F. B. Langreck, *J. Amer. Chem. Soc.*, **39**, 106 (1917).

SCHEME II



(*) designates labeled atom

B. In Nitrobenzene.—To a mixture of nitrile (0.02–0.03 mol), nitrobenzene (3.3 g), and hydrogen chloride (0.01–0.02 mol) in a 50-ml glass tube was added a solution of phosgene (0.9–1.0 g, 0.009–0.01 mol) in nitrobenzene (3.0 g). The tube was sealed carefully and heated to 95–100° in an oil bath for 200 hr. The reaction mixture was treated as above (see Tables I and II).

Isolation of N-(1-Chlorobenzylidene)carbamoyl Chloride (II, Ar = Phenyl).—In accordance with procedure A, the reaction was carried out at a molar ratio of 4:2:1 ($C_6H_5CN:COCl_2:HCl$). After removal of the triazine by filtration, the filtrate was distilled under reduced pressure giving 10 g (15% based on phosgene used) of the carbamoyl chloride (II, Ar = phenyl): bp 85–90° (1 mm); ir(neat) 1740, 1640, 1040, 767, 740, and 677 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 201 (8) (M$^+$), 168 (34), 166 (98), 65 (33), 63 (100), 77 (34), 76 (49), 51 (33), 50 (34).

Anal. Calcd for $C_8H_5Cl_2NO$: C, 47.56; H, 2.50. Found: C, 47.55; H, 2.80.

Reaction of II (Ar = Phenyl) with Benzonitrile in the Presence of Hydrogen Chloride.—In a 20-ml glass tube were placed a solution of hydrogen chloride (0.95 g, 0.026 mol) in benzonitrile (4 g) and 2 g of II (Ar = phenyl). The glass tube was sealed and heated to 100–105° for 90 hr. The formation of 2-chloro-4,6-diphenyl-*s*-triazine (3.69 g, 70% yield) and benzoyl chloride was confirmed by ir spectrum and glpc.

Reaction of II (Ar = Phenyl) with *p*-Tolunitrile in the Presence of Hydrogen Chloride.—The mixture of II (Ar = phenyl) (2.77 g), *p*-tolunitrile (3.00 g), and hydrogen chloride (1.05 g) was heated to 100–105° for 130 hr. The precipitate (1.31 g) obtained was purified by sublimation and recrystallization from acetone giving a crystalline product which melted at 145–148°; mass spectrum (70 eV) *m/e* (rel intensity) 297 (15), 295 (42), 283 (20), 281 (52), 267 (0.3), 143 (23), 129 (15), 117 (100), 103 (41). The peaks at 297 and 295, 283 and 281, and 267 were in accord with the parent ions of 2-chloro-4,6-bis(*p*-tolyl)-*s*-triazine, 2-chloro-4-phenyl-6-*p*-tolyl-*s*-triazine, and 2-chloro-4,6-diphenyl-*s*-triazine, respectively.

Treatment of the filtrate with aqueous ammonia gave *p*-toluamide.

Registry No.—Phosgene, 75-44-5; 2-chloro-4,6-diphenyl-*s*-triazine, 3842-55-5; 2-chloro-4,6-bis(*p*-tolyl)-*s*-triazine, 21902-34-1; 2-chloro-4,6-bis-(*p*-methoxyphenyl)-*s*-triazine, 21902-35-2; II, Ar = phenyl, 4547-71-1.

The Reaction of Nitriles with Phosgene. IV.[1]
A Facile One-Step Synthesis of the Isoquinoline Nucleus

SHOZO YANAGIDA, MASATAKA OHOKA, AND SABURO KOMORI

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamadakami, Suita City, Osaka, Japan

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The treatment of arylacetonitrile or α-naphthylacetonitrile (I) with phosgene in the presence of hydrogen chloride leads to substituted 1,3-dichloroisoquinolines (II) with a trace of 6-chloro-2,5-disubstituted 4(3H)-pyrimidones (III) and 4,6-dichloro-2,5-disubstituted pyrimidines (IV). This method is general in nature and represents a new, facile, and one-step synthesis of 1,3-dichloroisoquinoline derivatives. The reaction of phenylacetamide with phosgene under the comparable conditions also gives 1,3-dichloroisoquinoline (IIa). The isocyanate derivatives (V) were confirmed as intermediates of the reaction. The mechanism of this reaction is discussed.

The frequent occurrence of the isoquinoline nucleus in alkaloids has led to interest in the synthesis of isoquinoline derivatives. Various methods have been developed, but most of them still require many steps.[2] In accompanying papers,[3,4] the reaction of aliphatic nitriles or amides with phosgene in the presence of hydrogen chloride was shown to give 6-chloro-2,5-dialkyl-4(3H)-pyrimidones in good yields, with a trace of 4,6-dichloro-2,5-dialkylpyrimidines. In an extension of the studies on this reaction, we have found a new, one-step synthesis of the isoquinoline nucleus.

In a sealed glass tube, phenylacetonitrile was allowed to react with phosgene in the presence of hydrogen chloride in chlorobenzene at 60–65° for 72 hr. 1,3-Dichloroisoquinoline (IIa) was obtained in 10.8% yield in addition to 6-chloro-2-benzyl-5-phenyl-4(3H)-pyrimidone (IIIa) and 4,6-dichloro-2-benzyl-5-phenylpyrimidine (IVa) (Table I). The isoquinoline IIa was identified by direct comparison of its physical properties with those of an authentic sample prepared from 1,3-

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[1] Part III: S. Yanagida, H. Hayama, M. Yokoe, and S. Komori, *J. Org. Chem.*, **34**, 4125 (1969).

[2] W. M. Whaley and T. R. Govindachari, *Org. Reactions*, **6**, 72 (1951).

[3] S. Yanagida, M. Ohoka, M. Okahara, and S. Komori, *J. Org. Chem.*, **34**, 2972 (1969).

[4] S. Yanagida, H. Hayama, and S. Komori, *J. Org. Chem.*, **34**, 4180 (1969).