Studies of N-(α-Chlorobenzylidene)carbamoyl Chloride. I. Preparation of N-(α-Chlorobenzylidene)carbamoyl Chloride and Its Reaction with Sodium Azide

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N-(α-Chlorobenzylidene)carbamoyl chloride, $C_6H_5C(Cl)=NCOCl$ (**1**), is obtained in good yield by chlorination of C_6H_5CSNCO. The reaction of **1** with NaN_3 in anhydrous glyme gave 5-phenyltetrazole, benzonitrile, 2,5-diphenyl-*s*-triazolo[3,4-*b*]-1,3,4-oxadiazole (**5a**) and a product tentatively considered to be 2,5-diphenyl-1,3,4-oxadiazolo[2,3-*e*]-1,2,3,4,6-pentazepine.

Two methods have been available for the preparation of *N*-(α-chlorobenzylidene)carbamoyl chloride (**1**) having two reactive chlorine atoms in the molecule: one is based on the reaction of benzoyl isocyanate with phosphorus(V) chloride[2] and the other, the reaction of benzonitrile with phosgene in the presence of hydrogen chloride.[3] However, the former must be carried out under drastic conditions (in refluxing chlorobenzene for 48 hr), and the latter gives a low yield of **1** because of a side reaction yielding a *s*-triazine derivative.

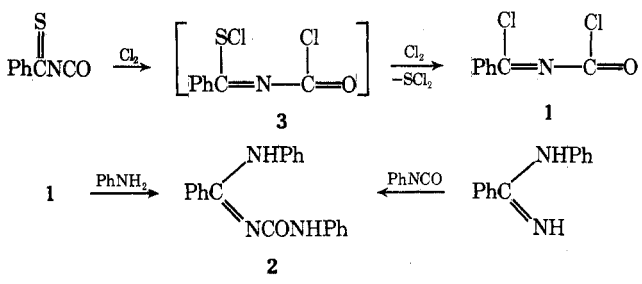
Carbamoyl chloride **1** can be expected to be useful as a precursor for the synthesis of heterocyclic compounds.[4] Recently, Yanagida, *et al.*,[5] have reported some cyclization reactions of **1** with nucleophiles, including sodium azide. These reports prompted us to describe our findings of a new, convenient preparative method for the preparation of **1** and of its reaction with sodium azide.

From our previous work on the cycloaddition reactions of benzoyl and thiobenzoyl isocyanates with a variety of compounds having a C=N bond,[6-9] the reactivity of thiobenzoyl isocyanate in 1,4 additions was found to be somewhat higher than that of benzoyl isocyanate. Thus, it might be expected that thiobenzoyl isocyanate could easily react with chlorine to form **1**.

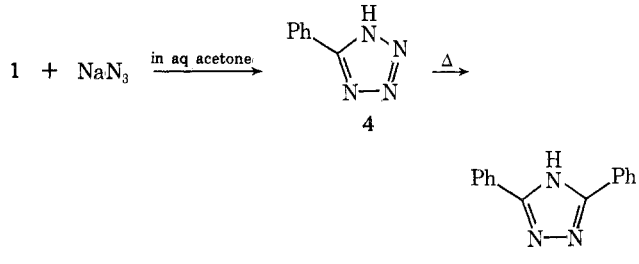
The chlorination of thiobenzoyl isocyanate with chlorine gas at room temperature afforded the expected carbamoyl chloride **1** in a good yield. The structure of **1** was confirmed by the spectral data, microanalysis, and chemical conversion. The reaction of **1** with aniline gave *N*-phenyl-*N'*-anilinoformylbenzamidine (**2**), which was identical with an authentic sample prepared from *N*-phenylbenzamidine and phenyl isocyanate.

Although the exact pathway for the formation of **1** is not clear, it might be viewed as proceeding *via* an initial formation of *N*-(α-chlorosulfinylbenzylidene)carbamoyl chloride (**3**), followed by further chlorination with the concurrent elimination of sulfinyl chloride as shown in Scheme I.

Scheme I



As reported by Yanagida, *et al.*,[5] the reaction of **1** with sodium azide in aqueous acetone gave 5-phenyltetrazole (**4**), which was thermally converted to 3,5-diphenyl-1,2,4-triazole.[10] It is evident that water is involved in the formation of **4**, because the evolution of carbon dioxide was observed during the reaction. Yanagida, *et al.*,[5] described that this reaction did not occur under anhydrous conditions. However, we found that in *anhydrous* 1,2-dimethoxyethane (glyme) **1** reacted with sodium azide to give different products from **4**.



The reaction of **1** with 2 mol of sodium azide in glyme at room temperature afforded novel products **5** and **6** in 52 and 13% yields, accompanied by small amounts of **4** and benzonitrile.

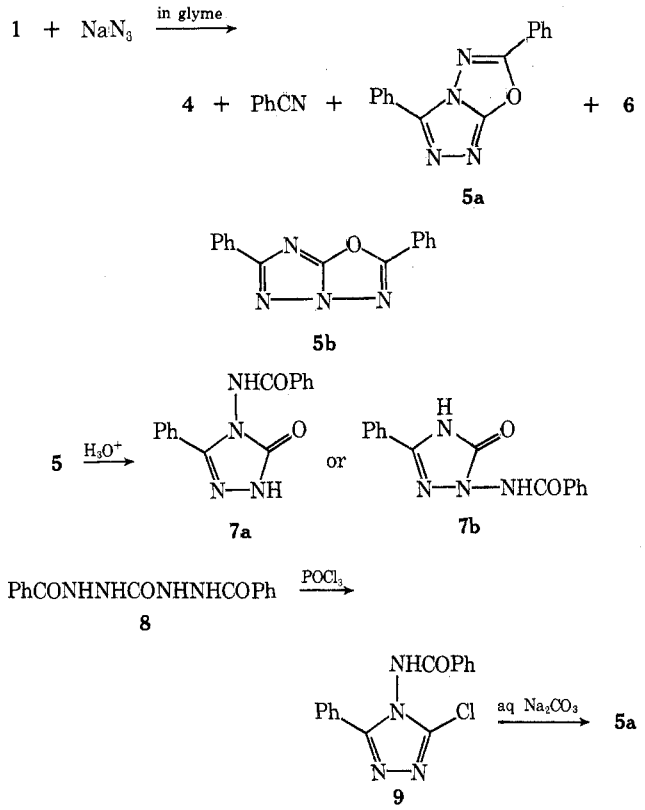
The molecular formula of **5** agreed with that of a compound arising from the diazide by the elimination of 2 mol of nitrogen, followed by the addition of benzonitrile. The ir spectrum of **5** did not show any bands ascribable to NH and C=O absorptions. Hydrolysis of **5** with dilute hydrochloric acid afforded a product **7**, whose structure was assumed to be either 4-benzoylamino-3-phenyl-Δ^2-1,2,4-triazolin-5-one (**7a**) or the 1-benzoylamino isomer (**7b**) from the spectral data. On the basis of these observations and the mode of formation of **5**, either of two isomers, 2,5-diphenyl-*s*-triazolo[3,4-*b*]-1,3,4-oxadiazole (**5a**) or 2,6-diphenyl-*s*-triazolo[3,2-*b*]-1,3,4-oxadiazole (**5b**), is thought possible for the structure of **5** (Scheme II).

Kanaoka[11] reported the preparation of the sulfur analog of **5a**, 2-alkyl- (or aryl-) 5-phenyl-*s*-triazolo[3,4-*b*]-1,3,4-thiadiazole, from methyl benzoyldithiocarbazinate. It was found by Yoshida and Asai[12] that the reaction of isonicotinylhydrazine with carbon disulfide gave small quantities of 4-isonicotinylamino-3-pyridyl-Δ^2-1,2,4-triazoline-5-thione *via* 1,5-diisonicotinylthiocarbazide. The 1,2,4-triazoline-5-thione corresponds to a sulfur analog of **7a**.

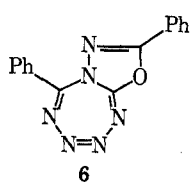
In order to elucidate the structure of **5**, **5a** was prepared by modification of the above methods. Treatment of 1,5-dibenzoylcarbohydrazide (**8**) with phosphorus oxychloride afforded 4-benzoylamino-5-chloro-3-phenyl-1,2,4-triazole (**9**), whose structure was confirmed by the result of microanalysis and spectral data. Cyclization of **9** with aqueous sodium carbonate gave **5a**, which was identical with **5**.

On the other hand, the molecular formula of a minor product **6** agreed with that of an adduct of the diazide and benzonitrile with the elimination of 1 mol of nitrogen. On the basis of its spectral data and mode of formation, **6** is

Scheme II



tentatively assigned as 2,5-diphenyl-1,3,4-oxadiazolo[2,3-*e*]-1,2,3,4,6-pentazepine. Although **6** was quite stable under the reaction conditions, thermal decomposition of **6** did not give **5a**, but afforded resinous materials.

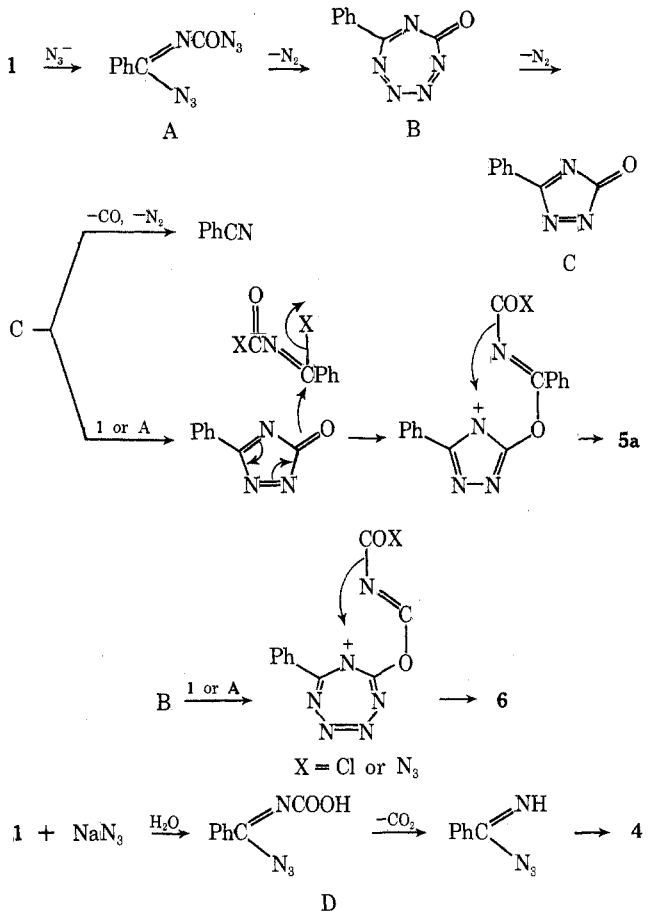


Although the exact pathway of the reaction of **1** with sodium azide under anhydrous conditions is not clear, it might be viewed as proceeding *via* initial formation of diazide A. This is followed by cyclization with the concurrent elimination of nitrogen to form 1,2,3,4,6-pentazepin-7-one B, because no insertion products derived from potential nitrene intermediates from A were formed. Then, B is converted to *s*-triazolone C with the elimination of nitrogen.[13] Recently, it has been reported that the oxidation of 5-substituted *s*-triazolin-3-ones with lead tetraacetate led to the formation of the intermediate *s*-triazolones which in the absence of 1,3-dienes decomposed to nitriles, carbon monoxide, and nitrogen.[14] The formation of benzonitrile in the reaction can be viewed as arising from *s*-triazolone C.

No crossover products were formed in the reaction in the presence of *p*-methoxybenzonitrile. Therefore, the pathways for the formation of **5** and **6** *via* the reactions of C and B with benzonitrile can be excluded. Thus, the reactions of C and B with **1** or diazide A give the novel products **5** and **6** as shown in Scheme III.

On the other hand, under the influence of water **1** reacts competitively with sodium azide and water. In general, the carbamoyl chlorine atom is more reactive than the imidoyl chlorine atom in **1**.[15] Thus, water would attack the former and sodium azide would react with the latter to form intermediate D, followed by cyclization with the

Scheme III



elimination of carbon dioxide to lead to the formation of **4**.

Experimental Section[16]

***N*-(α-Chlorobenzylidene)carbamoyl Chloride (1).** Into a reddish-violet solution of thiobenzoyl isocyanate[17] generated *in situ* from 10 g of 2-phenylthiazoline-4,5-dione[18] in 40 ml of dry chlorobenzene was introduced dry chlorine gas at room temperature for about 5.5 hr, during which time the solution turned to pale yellow. After removal of the solvent, the residue was distilled *in vacuo* to give 7.5 g (71% based on 2-phenylthiazoline-4,5-dione used) of carbamoyl chloride **1**: bp 99–100° (1 mm) [lit. bp 75–80° (0.02 mm),[2] 85–90° (1 mm)[3]]; ir (neat) 1770, 1750 (sh), 1640, 1045, 920, 780, 750, 690 cm^{-1}; mass spectrum *m/e* 205, 203, 201 (M^+), 168, 166 ($M^+ - Cl$), 140, 138 ($M^+ - Cl - CO$), 103 ($PhCN^+$).

Anal. Calcd for $C_8H_5NOCl_2$: C, 47.56; H, 2.50; N, 6.93. Found: C, 47.81; H, 2.46; N, 6.95.

The reaction of **1** with 2 equiv of aniline in diethyl ether at room temperature afforded a 72% yield of *N*-phenyl-*N'*-anilinoformylbenzamidine (**2**) as colorless needles (from MeOH), mp 175–175.5° (lit. mp 179–180°,[19] 159–172°[5]). This compound was identical with an authentic sample[19] prepared from *N*-phenylbenzamidine and phenyl isocyanate.

Reaction of 1 with Sodium Azide. A. In Aqueous Acetone. To a solution of 0.65 g (0.01 mol) of sodium azide in 10 ml of aqueous acetone (containing 2 ml of water) was added 1.0 g (4.95 mmol) of **1** under water cooling. The reaction mixture was stirred at room temperature for 1 hr and then concentrated *in vacuo* to leave a residue. The residue was washed with hot acetone and the washings were again concentrated *in vacuo* to leave crystals. Recrystallization from dioxane afforded 0.53 g (73%) of 5-phenyltetrazole (**4**) as colorless plates: mp 212.5–213° dec (lit.[20] mp 212° dec); ir (KBr) 3020–2800 (NH), 1610 cm^{-1} (C=N).

Heating of 0.1 g of **4** at 230–240° for 15 min afforded 35 mg (47%) of 3,5-diphenyl-1,2,4-triazole as colorless needles, mp 185–186° (lit.[10] mp 187–189°).

B. In Glyme. To a suspension of 0.65 g (0.01 mol) of sodium azide in 25 ml of dry glyme was added 1.0 g (4.95 mmol) of **1** under water cooling at 10°. The reaction mixture was stirred at room temperature for 9 hr. The precipitate was filtered and ex-

tracted with hot benzene. The benzene extract was evaporated *in vacuo* to leave crystals. Recrystallization from petroleum ether (bp 60–75°) gave 0.34 g (52%) of 2,5-diphenyl-*s*-triazolo[3,4-*b*]-1,3,4-oxadiazole (**5a**) as colorless prisms: mp 179–180° dec; ir (KBr) 1600, 1550, 1460, 1380, 1150, 1050, 960, 768, 730, 700, 680, cm^{-1}; mass spectrum *m/e* 262 (M^+), 245, 234 ($M^+ - N_2$), 206 ($234^+ - N_2$ or CO), 192 ($234^+ - NCO$), 145 ($234^+ - PhC$), 117 ($PhCN_2^+$), 105 ($PhCO^+$), 103 ($PhCN^+$), 77 (Ph^+).

Anal. Calcd for $C_{15}H_{10}N_4O$: C, 68.69; H, 3.84; N, 21.37. Found: C, 68.84; H, 3.56; N, 21.59.

The glyme filtrate was concentrated *in vacuo* below 50° to leave resinous materials, which were chromatographed on silica gel to give trace amounts of 4 and 95 mg (13%) of 2,5-diphenyl-1,3,4-oxadiazolo[2,3-*e*]-1,2,4,6-pentazepine (**6**). The formation of benzonitrile was confirmed by gas chromatography of the glyme filtrate.

6 had mp 124–125° dec [from petroleum ether (bp 60–70°)] and was obtained as colorless plates: ir (KBr) 1600, 1550, 1500, 1460, 1350, 1300, 1170, 1080, 980, 790, 755, 730, 700 cm^{-1}; mass spectrum *m/e* 262 ($M^+ - N_2$ or CO), 145, 117, 105, 103, 77.

Anal. Calcd for $C_{15}H_{10}N_6O$: C, 62.06; H, 3.47; N, 28.95. Found: C, 62.18; H, 3.26; N, 28.71.

Hydrolysis of 5a. A solution of 0.5 g of **5a** in 30 ml of ethanol was refluxed with 20 ml of 1 *N* hydrochloric acid for 9 hr, and then the mixture was neutralized with aqueous sodium carbonate. The precipitate was filtered and recrystallized from acetone to give 0.35 g (66%) of 4-benzoylamino-3-phenyl-Δ^2-1,2,4-triazolin-5-one (**7a**) as colorless prisms: mp 259.5–260° dec; ir (KBr) 3300–3000 (NH), 1745, 1670 cm^{-1} (C=O); nmr (DMSO-d_6) δ 7.4–8.05 (m, 10, aromatic protons), 11.64, 12.22 (each s, 1, NH); mass spectrum *m/e* 280 (M^+), 161 ($M^+ - PhNCO$), 119, 118 ($161^+ - HNCO$), 105 ($PhCO^+$, base peak); uv max (EtOH) 267 nm (log ϵ 4.0).[21]

Anal. Calcd for $C_{15}H_{12}N_4O_2$: C, 64.27; H, 4.32; N, 19.99. Found: C, 64.02; H, 4.14; N, 19.79.

Preparation of 5a. After a solution of 1.0 g of 1,5-dibenzoylcarbohydrazide (**8**)[22] in 10 ml of phosphorus oxychloride was heated at 80–90° for 2 hr, the reaction mixture was poured into ice–water. The precipitate was filtered and recrystallized from benzene to afford 0.29 g (29%) of 4-benzoylamino-5-chloro-3-phenyl-1,2,4-triazole (**9**) as colorless needles: mp 152.5–153° dec; ir (KBr) 3400 (broad, NH), 1640 cm^{-1} (C=O); mass spectrum *m/e* 300, 298 (M^+).

Anal. Calcd for $C_{15}H_{11}N_4OCl$: C, 60.31; H, 3.71; N, 18.75. Found: C, 60.54; H, 3.64; N, 18.63.

A solution of 0.17 g of **9** in 20 ml of acetone–water mixture (10:1 v/v) was stirred with 1.0 g of sodium carbonate at room temperature for 4 hr. The reaction mixture was neutralized with dilute hydrochloric acid to precipitate a solid, which on recrystallization from petroleum ether (bp 60–75°) gave 0.11 g (74%) of colorless prisms, mp 179–180° dec. This compound was identical with the product **5**.

Registry No.—**1**, 4547-71-1; **2**, 33655-23-1; **4**, 18039-42-4; **5a**, 32550-72-4; **6a**, 51003-52-2; **7**, 3658-32-0; **8**, 51003-53-3; thiobenzoyl isocyanate, 3553-61-5.

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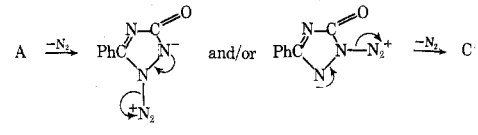
(13) The following possible route to C can be excluded because of the formation of **6**.



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(15) From the reaction of **1** with active methylene compounds, it has been found that the carbamoyl chlorine atom is more reactive than the imidoyl chlorine atom: O. Tsuge, M. Tashiro, and S. Hagio, *J. Org. Chem.*, **39**, 1228 (1974).
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Studies on *N*-(α-Chlorobenzylidene)carbamoyl Chloride. II.[1] Reaction of *N*-(α-Chlorobenzylidene)carbamoyl Chloride with Active Methylene Compounds

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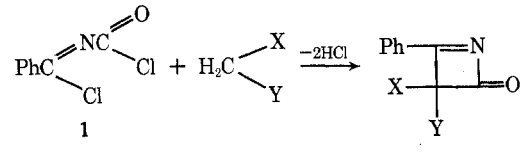
The reaction of *N*-(α-chlorobenzylidene)carbamoyl chloride (**1**) with active methylene compounds has been investigated. In general, the imidoyl chlorine atom in **1** reacts faster with active methylene compounds in the presence of NEt_3. An azetinone intermediate (**7**) is proposed as an initial product in the reaction with ethyl cyanoacetate (**2**) in the presence of 2 equiv of NEt_3. The reactions of **1** with acenaphthenone (**13**) and dimedone (**18**) give oxazin-2-one (**14a**) and oxazin-4-one derivatives (**19**), respectively. On the other hand, **1** reacts with **13** in the presence of metallic sodium to yield a pyridine derivative (**17**).

In the preceding paper,[1] we have reported a convenient synthesis of *N*-(α-chlorobenzylidene)carbamoyl chloride (**1**), which is useful as a precursor for the synthesis of heterocycles.[1-3] It could be expected that **1** might react with active methylene compounds to form azetinones, and fur-



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