6 H, 3-Me), 2.42 (6 H, 2-Me), 2.80 (6 H, 6-Me), 4.25 (2 H, bridge methylene), 5.52 (q, J = 7.5 Hz, 2 H, 3-methine), 8.16 (2 H, H-7), and 8.16 (2 H, H-8); cation **8** (68%), 1.93 (d, J = 7.5 Hz, 3 H, 3-Me), 2.30 (3 H, 2′-Me), 2.40 (3 H, 2-Me), 2.67 (3 H, 3′-Me), 2.80 (3 H, 6-Me), 2.85 (3 H, 6′-Me), 4.36 (t, J = 14 Hz, 2 H, $H_\alpha H_\beta$ bridge methylene), 5.44 (q, J = 7.5 Hz, 1-H, 3-methine), 6.82 (d, J = 8.5 Hz, 1 H, H-7′), 7.77 (d, J = 8.5 Hz, 1 H, H-7), 7.97 (d, J = 8.5 Hz, 1 H, H-8), and 8.32 (d, J = 8.5 Hz, H-8′). Cation **8** showed no signal arising from a proton bonded to nitrogen; the two hydrogens H_α and H_β of the bridging methylene though magnetically nonequivalent would appear to experience a similar magnetic environment since the anticipated AB quartet is observed rather as a broad singlet at δ 4.36 with small wings at δ 4.50 and 4.24, the latter wing being obscured by the bridging methylene signal of the cation **7**.

Anal. Calcd for $C_{21}H_{24}N_4$: C, 75.9; H, 7.3; N, 16.8. Found: C, 75.8; H, 7.2; N, 16.8.

Registry No.—**2e**, 34876-65-8; **2f**, 34876-66-9; **2g**, 34876-67-0; **2h**, 34876-68-1; **3c**, 34876-69-2; **3d**, 34876-70-5; **4c**, 34876-71-6; **4d**, 34876-72-7; **5a**, 34876-73-8; **5b**, 34876-74-9; **6**, 34876-75-0.

Acknowledgments.—The author wishes to thank Mr. N. Faulkes for operating the Varian HA-100B spectrometer and to record thanks to Drs. Buchan, Reid, Watson, Webster, and Youngson for helpful suggestions.

Synthesis of β-Cyano-α,β-Unsaturated Isocyanates and Their Reactions with Hydrogen Chloride

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When enaminonitriles with a primary nitrogen atom were allowed to react with phosgene in refluxing ethyl acetate, N-acylation occurred to give the corresponding β-cyano-α,β-unsaturated isocyanates in 37–79% yield. The reaction of thus obtained isocyanates with hydrogen chloride in dioxane at 100° for 24 hr gave 5,6-disubstituted uracils in good yields. Reaction of isocyanate **2c** with hydrogen chloride at 60° for 6 hr afforded 6-chloro-5-methyl-4-phenyl-2(3*H*)-pyrimidinone in 74% yield.

The reactions of enaminonitriles having a primary or a secondary nitrogen atom with acylating agents such as carboxylic acid chlorides and carboxylic acid anhydrides have been reported.[1–3] In these reactions C-acylation or N-acylation products were obtained, depending on the nature of enaminonitriles and acylating agents.

Recently, Samaraj, *et al.*,[4] have reported the synthesis of α,β-unsaturated isocyanates from ketimine and phosgene. However, the reaction of primary enamines (tautomers of ketimines) with phosgene has not been reported yet.

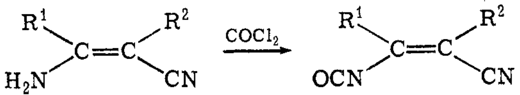
In addition, recently N-acylations of nitriles in the presence of hydrogen halide with acylating agents have been reported to yield various heterocycles. Simchen, *et al.*, have widely investigated the intramolecular cyclization reactions of various acid chlorides[5–9] or isocyanates[10] having a cyano group in the same molecule in the presence of hydrogen halide; for instance, they obtained quinazolones from *o*-cyanophenyl isocyanates.[10] In view of these studies intramolecular cyclization of β-cyano-α,β-unsaturated isocyanates is synthetically of interest.

We have now attempted the synthesis of β-cyano-α,β-unsaturated isocyanates by reacting phosgene with enaminonitriles, easily obtainable by condensation of nitriles in the presence of sodium.[11,12] In addition, the cyclization reaction of isocyanates thus obtained was carried out.

Results and Discussion

Synthesis of Unsaturated Isocyanates.—All the enaminonitriles used in this study were shown to exist predominantly as enamine tautomer in $CDCl_3$ by nmr analysis.

When enaminonitriles **1a–d** were allowed to react with phosgene in refluxing ethyl acetate, the expected N-acylation occurred to give the corresponding β-cyano-α,β-unsaturated isocyanates **2a–d** in 37–79% yield.



1 **2**

a, $R^1 = CH_3CH_2$; $R^2 = CH_3$
b, $R^1 = CH_3CH_2CH_2$; $R^2 = CH_3CH_2$
c, $R^1 = C_6H_5$; $R^2 = CH_3$
d, $R^1, R^2 = -(CH_2)_4-$

In the cases of **1a** and **1b**, considerable amounts of resinous substances were formed. They may be formed by polymerization of once-formed isocyanates or may be derived from C-phosgenated intermediates; this is not clear at present.

The structures of **2a–d** were established on the basis of ir and nmr spectra and elemental analysis. Yields and spectra are listed in Table I. Nmr spectra of **2a–c** showed that they are mixtures of the cis and trans isomer.

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TABLE I

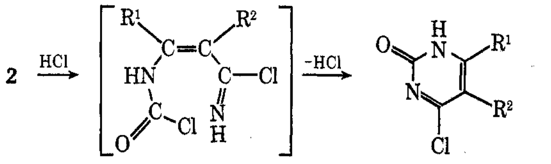
β-CYANO-α,β-UNSATURATED ISOCYANATES **2**[a,c]

Compd	Bp, °C (mm)	Yield, %	Ir,[b] cm^{-1} NCO	Ir,[b] cm^{-1} CN	Ir,[b] cm^{-1} C=C
2a	85–87 (17)	37	2262	2212	1627
2b	89–90.5 (10)	55	2260	2221	1623
2c	121–123 (1.5)	72	2257	2210	1613
2d	108 (2)	79	2255	2215	1642

[a] Nmr (CCl_4): **2a**, δ 1.24 (t, 3 H, J = 7.5 Hz), 1.89 (s) and 1.91 (s) (total 3 H), 2.62 (q, 2 H, J = 7.5 Hz); **2b**, 1.04 (t, 3 H, J = 7.5 Hz), 1.14 (t, 3 H, J = 7.5 Hz), 1.65 (m, 2 H), 2.41 (m, 4 H); **2c**, 1.85 (s) and 2.05 (s) (area ratio 1:2.6) (total 3 H), 7.40 (m, 5 H); **2d**, *ca.* 1.7 (br, 4 H), *ca.* 2.3 (br, 4 H). [b] Liquid film. [c] Satisfactory analytical values (±0.4% for C, H, and N) were reported for **2a–c**. The carbon value for **2d** was 0.9% low: Ed.

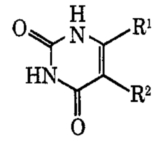
The reaction of 1-amino-2-cyanocyclopentene with phosgene also gave the corresponding isocyanate (22% yield), which was characterized only by ir spectroscopy since it was very unstable and became dark in a few days at room temperature.

Reactions of Isocyanates with Hydrogen Chloride.—In the reaction of isocyanate 2 with hydrogen chloride, the formation of 6-chloro-2(3*H*)-pyrimidinone **4** *via* intermediate **3** was expected.



3 **4**

The cyclization of **2** was carried out with a large excess of anhydrous hydrogen chloride in a glass tube. Dioxane was used as the solvent since hydrogen chloride is very soluble in it. The reaction at 100° for 24 hr did not give the expected 2-pyrimidinone **4**, but afforded 5,6-disubstituted uracil **5** in good yield (Table II).



5

In the cases of the reactions of **2b** and **2d** the yields of uracils were slightly low and much unidentified resinous substantces were formed; this is probably due to side reactions of the isocyanates such as degradation and polymerization. The structures of uracils were established by ir, nmr, and mass spectroscopy and elemental analysis. Yields and spectra are summarized in Table II.

The reaction of **2c** with hydrogen chloride in dioxane at 60° for 6 hr gave the expected 6-chloro-5-methyl-4-phenyl-2(3*H*)-pyrimidinone (**4c**) in 74% yield along with **5c** (10% yield).

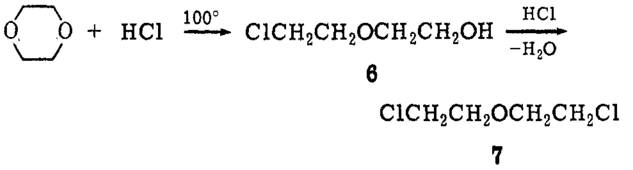
To clarify the reaction pathway to uracils, byproducts of the reaction at 100° were analyzed; a small amount of a mixture of 2-(2-chloroethoxy)-ethanol (**6**) (minor) and bis(2-chloroethyl) ether (**7**) (major) was obtained in every case. The cleavage of the ether linkage by hydrogen halide to an alcohol and a halide and halogenation of the alcohol by hydrogen halide are well known.[13] In fact, the reaction of dioxane with hydrogen chloride at 100° for 24 hr in a glass tube gave a small amount of a mixture of **6** and **7**. In this case **6** was the major product.

TABLE II

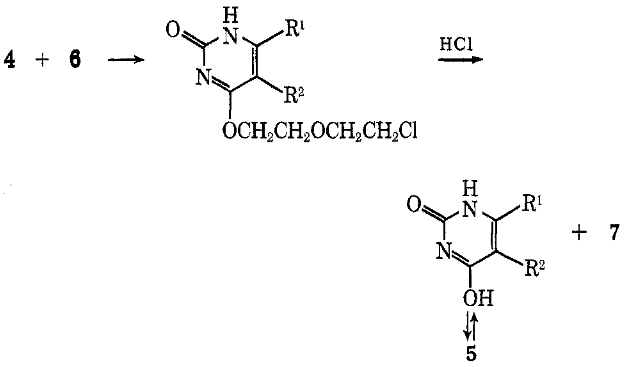
5,6-DISUBSTITUTED URACILS[a,f]

Compd	Mp, °C	Recrystn solvent	Yield, %	Ir,[b] cm^{-1}	Mass (M$^+$)
5a	258–260	EtOH–H_2O (1:3)	70	1710, 1645	154
5b	229–232[c]	EtOH	47	1735, 1670, 1643 (sh)	182
5c	241–243	Dioxane	95	1705, 1665,[e] 1640	202
5d	297–301[d]	MeOH	58	1705, 1640	166

[a] Nmr: **5a** (DMSO-d_6) δ 1.09 (t, 3 H, J = 7.5 Hz), 1.75 (s, 3 H), 2.37 (q, 2 H, J = 7.5 Hz), 10.57 (br s, 1 H), 10.90 (br s, 1 H); **5b**, (CF_3COOH) 1.20 (m, 6 H), 1.82 (m, 2 H), 2.65 (m, 4 H), 10.27 (br s, 1 H); **5c**, (DMSO-d_6), 1.68 (s, 3 H), 7.42 (s, 5 H), 10.79 (br s, 1 H), 11.04 (br s, 1 H); **5d** (CF_3COOH), 1.90 (br s, 4 H), 2.54 (br, 4 H), 10.14 (br s, 1 H). [b] Nujol. [c] Mp 228–229°: Z. Bukac and J. Sebenda, *Collect. Czech. Chem. Commun.*, **32**, 3537 (1967); *Chem. Abstr.*, **68**, 12940 (1968). [d] Mp 295–297°: Z. Budesinsky and F. Roubinec, *Collect. Czech. Chem. Commun.*, **29**, 2341 (1964); *Chem. Abstr.*, **62**, 555 (1965). [e] The crude product has different absorption bands in the C=O region, 1730, 1700 (sh), and 1675 cm^{-1}. When it was recrystallized from dioxane or heated around 240°, crystals which have absorption bands shown in the table were obtained. This phenomenon may be explained in terms of the difference of crystal structures. [f] Satisfactory analytical values (±0.3% for C, H, and N) were reported for all compounds in table: Ed.



Moreover, the reaction of **4c** with hydrogen chloride in dioxane at 100° for 20 hr afforded uracil **5c** in 88% yield. Pyrimidinone **4c** was easily hydrolyzed to **5c** upon refluxing in H_2O–MeOH for 30 min. On the basis of these facts, uracils were apparently formed *via* 2-pyrimidinone **4** according to the following reaction scheme.



Uracils might be formed in part by the reaction of **4** with water formed during chlorination of **6** to **7**.

Under such reaction conditions that the cleavage of dioxane by hydrogen chloride is suppressed, that is, at lower temperature and for shorter reaction time, it is possible to obtain 6-chloro-5-methyl-4-phenyl-2-(3*H*)-pyrimidinone (**4c**) exclusively.

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In the case of **2a–c**, mixtures of two geometrical isomers were used for cyclization. In view of the almost quantitative yield of **5c** from **2c** (ratio of two geometrical isomers, 3:1), it is clear that cis–trans equilibria between two isomers of isocyanates **2** are established in this reaction.

Experimental Section

Melting points were determined on a Yanagimoto micro melting point apparatus and are corrected. Boiling points are uncorrected. Nmr spectra were obtained using a JNM-G-60 spectrometer (Japan Electronic Optics Laboratory Co.) with tetramethylsilane as an internal reference. Ir spectra were recorded with a Japan Electronic IR-E spectrophotometer or with a Hitachi 225 spectrophotometer equipped with gratings. Mass spectra were recorded with a Hitachi RMU-6E mass spectrometer.

Materials.—Enaminonitriles **1** were prepared according to the known methods.[3,11,14]

Synthesis of Unsaturated Isocyanates 2.—A typical procedure is as follows. In a 100-ml round-bottomed four-necked flask, equipped with a stirrer, a condenser, a dropping funnel, and a gas inlet tube, was placed 30 ml of ethyl acetate and it was saturated with phosgene under reflux. To this solution was added 7.5 g (0.05 mol) of enaminonitrile **1c** in 30 ml of ethyl acetate in 25 min; then the reaction mixture was heated under reflux with stirring for an additional 30 min. The introduction of phosgene was continued throughout these procedures. After phosgene was purged with dry N_2, the solvent was removed under reduced pressure to yield a viscous reddish liquid, which was distilled under reduced pressure to give 6.7 g (72%) of **2c** (colorless liquid).

Reaction of Isocyanate 2 with HCl at 100°.—A typical procedure is as follows. In a 35-ml glass tube were placed 1.1 g (6 mmol) of **2c** and 5 ml of dioxane; then to the mixture 1.45 g (40 mmol) of anhydrous HCl was allowed to be absorbed under cooling. The glass tube was sealed and heated at 100° for 24 hr. After removal of HCl, the precipitates formed were filtered, washed with a small portion of dioxane, and dried *in vacuo* to yield 1.0 g of uracil **5c**. From the filtrate 0.15 g of **5c** was obtained. The total yield was 95%.

Reaction of 2c with HCl at 60°.—In a 35-ml glass tube, a mixture of 0.63 g (3.4 mmol) of **2c**, 1.3 g (36 mmol) of HCl, and 5 ml of dioxane was heated at 60° for 6 hr. After HCl was purged, the precipitates formed were filtered, washed with dioxane, and dried at 80° *in vacuo* to yield a white powder of 6-chloro-5-methyl-4-phenyl-2(3*H*)-pyrimidinone (**4c**) (0.56 g, 74%). The crude product was recrystallized from anhydrous CH_3CN to give colorless needles: mp 190–195°; ir (Nujol) 1665 cm^{-1} (C=O); nmr (CF_3COOH) δ 2.53 (s, 3 H) and 7.82 (s, 5 H); mass spectrum (70 eV) *m/e* (rel intensity) 220 (45, M^+) and 219 (100).

Anal. Calcd for $C_{11}H_9N_2OCl$: C, 59.87; H, 4.11; N, 12.70. Found: C, 59.70; H, 4.05; N, 12.80.

The dioxane was evaporated from the filtrate and the residue was washed with a small portion of dioxane and dried *in vacuo* to yield 0.076 g (10%) of **5c**.

Reaction of Pyrimidinone 4c with HCl in Dioxane.—In a 35-ml glass tube a mixture of 0.119 g of **4c**, 0.8 g of HCl, and 2 ml of dioxane was heated at 100° for 20 hr. The reaction mixture was evaporated to dryness and the resulting residue was washed with ether and dried *in vacuo* to give 0.096 g (88%) of **5c**.

Reaction of Dioxane with HCl at 100°.—In a 50-ml glass tube a mixture of 9.0 g of dioxane and 3.2 g of HCl was heated at 100° for 24 hr. The dioxane was removed under reduced pressure to yield 0.6 g of a mixture of **6** (major) and **7** (minor) (glpc analysis).

Registry No.—*cis*-**2a**, 35042-37-6; *trans*-**2a**, 35042-38-7; *cis*-**2b**, 35042-39-8; *trans*-**2b**, 35042-40-1; *cis*-**2c**, 35042-41-2; *trans*-**2c**, 35042-42-3; **2d**, 30542-43-4 **4c**, 35042-44-5; **5a**, 32796-82-0; **5b**, 16372-00-2; **5c**, 35042-47-8; **5d**, 35042-48-9.

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A *p*-Fluoro Labeling Study of Partial Scrambling before Fragmentation in Some Five-Membered Heterocycles Containing Nitrogen

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Illustrative examples of *p*-fluoro labeled triphenyloxazole, -imidazole, -thiazole, and isoxazole were studied in the mass spectrometer to determine scrambling patterns in major fragmentations. No trends were observed which would have been analogous to the photochemical analogy in the scrambling patterns of furans and thiophenes.

Previously the *p*-fluoro substituent has been used as a label[1] to study scrambling in the decomposition of several five-[2,3] and six-membered[4] heterocycles in the mass spectrometer. Partial to complete scrambling before fragmentation was observed in the cases of tetraphenylfuran and tetraphenylthiophene,[3] in analogy to the behavior of furan and thiophene themselves in the mass spectrometer[5] and to the photochemical behavior of substituted thiophenes[6] and furans.[7] In distinction to the mass spectral behavior of pyridine,[8] however, the completely phenylated derivatives of pyridine, pyrazine, and 1,2,4-triazine were found not to scramble appreciably before decomposition.[4] We therefore thought it of interest to examine the extent of scrambling before fragmentation for several fully phenylated five-membered heterocycles containing nitrogen. This report is concerned with the scrambling in various fragment ions of 4,5-diphenyl-2-*p*-fluorophenyloxazole (I), 4,5-diphenyl-2-*p*-fluorophenylimidazole (II), 2,5-bis(*p*-fluorophenyl)-4-phenylthiazole (III), and 3,5-diphenyl-4-*p*-fluorophenylisoxazole (IV). Fragmentation of other substituted triphenyl isox-

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