(R)-(+)-2-Methylthietane 1,1-dioxide (13) was prepared similarly from 12, 85% yield, $n^{26.5}$D 1.4689; $[\alpha]^{25}$D +21.0 ± 0.2° (c 9.740, C_2H_5OH).

Chemistry of Isocyanurates. I. Synthesis of Disubstituted Isocyanuric Acids from the Reaction of Alkali Metal Cyanates with Organic Isocyanates[1]

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Cyanate ion, unlike other anions, reacts with organic isocyanates to give salts of disubstituted isocyanurates (I^-) which are readily converted to the corresponding acid (I). Trimerization of the isocyanate to the trisubstituted isocyanurate (II) is a competing reaction which can seriously detract from the yield of I. The selectivity to I^- was found to be sensitive to the concentration of cyanate ion, temperature, solvent type, isocyanate structure, concentration of isocyanate, and ionic strength of medium. The mechanistic implication of these parameters on selectivity is discussed.

In the course of a recent investigation into the mechanism by which cyanate ion (NCO^-) reacts with organic halides, a new and convenient synthesis of disubstituted isocyanuric acids (I) evolved.[3] Thus, it was shown that alkali metal cyanates (MOCN) in dipolar aprotic media react with organic isocyanates (RNCO) to give the salt (I^-) of the corresponding disubstituted isocyanuric acid (eq 1). The singular

R—NCO + MOCN ⟶
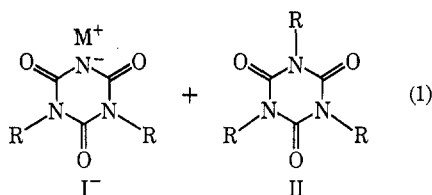
by-product is the trisubstituted isocyanurate (II), a product anticipated in view of the ease with which isocyanates undergo base-catalyzed trimerization.[4,5]

Salt I^- is readily separated from trimer II by extracting the solvent-free reaction mixture with water (II is insoluble); subsequent acidification of the aqueous salt solution with hydrochloric acid precipitates the acid I. The present paper deals with the scope of the reaction of eq 1 in terms of the parameters governing the selectivity to I^-.

Results

Although the preparation of disubstituted isocyanurates from RNCO and MOCN is quite general, the selec-

tivity to I^- is dependent on a number of reaction variables. The following parameters were shown to have a marked influence on the competition between trimerization and salt formation.

Isocyanate Structure.—As shown in Table I, a large number of structurally divergent isocyanates are applicable in this synthesis. It is clear that the nature of R has a profound influence on selectivity. The order in decreasing selectivity is aryl > benzyl, allyl ≫ alkyl. This is the same order of reactivity reported for the reaction of RNCO with amines to form ureas;[6] the most electrophilic isocyanate gives the highest selectivity.

Concentration of RNCO.—Selectivity varies inversely with the initial concentration of RNCO. As shown in Table II, a tenfold increase in the initial isocyanate concentration reduced the selectivity by nearly 50%.

Solvent.—A modest study was undertaken to determine the effect of solvent on selectivity. As shown in Table III, the dipolar solvents, such as dimethylformamide (DMF), afford the highest selectivities in addition to rate acceleration. These findings probably reflect changes in KNCO solubility (*vide infra*) rather than changes in dielectric constant or solvent polarity. DMF was employed throughout this study because of its availability and ease of purification.

Temperature.—At moderate temperatures, the selectivity gradually increases with temperature reaching a plateau at 75°. Unfortunately, the temperature effect is complicated by the fact that increasing the reaction temperature also increases the solubility of the metal cyanate (see Table IV).

Concentration of NCO^-.—Owing to the limited solubilities of NaOCN and KOCN (the only readily available alkali metal cyanates), the NCO^- concentra-

(1) Presented in part at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., March 1968.

(2) To whom inquiries should be directed.

(3) P. A. Argabright, B. L. Phillips, and C. H. DePuy, *Tetrahedron Lett.*, 5033 (1968).

(4) R. G. Arnold, J. A. Nelson, and J. J. Verbanc, *Chem. Rev.*, **57**, 59 (1957).

(5) J. H. Saunders and R. J. Slocombe, *ibid.*, **43**, 211 (1948).

(6) C. Naegeli, A. Tyabji, L. Conrad, and F. Litwan, *Helv. Chim. Acta*, **21**, 1100 (1938).

TABLE I
DISUBSTITUTED ISOCYANURIC ACIDS (I) FROM THE REACTION OF
NCOR WITH KOCN IN DMF (1 HR AT 75°)[a]

I
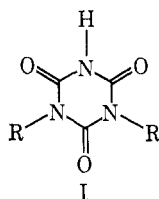
R	Registry no.	Selectivity, %[b]	Crude yield, %[c]	Mp, °C (solvent[d])
C$_6$H$_5$	20931-62-8	93	91	265–266[e] (E–W)
o-CH$_3$C$_6$H$_4$	24807-22-5	86	76	241–242 (E)
m-CH$_3$C$_6$H$_4$	24807-23-6	84	76	200–202 (B–H)
p-CH$_3$C$_6$H$_4$	24807-24-7	93	84	255–256 (E)
m-ClC$_6$H$_4$	24807-25-8	95	92	198–200 (E–B)
p-ClC$_6$H$_4$	24807-26-9	82	76	259–260 (T)
p-CH$_3$OC$_6$H$_4$[f]	24807-27-0	58	48	220–223 (E)
o-NO$_2$C$_6$H$_4$	24807-28-1	89	75	300–301 (E–W)
C$_2$H$_5$OCOCH$_2$	24807-29-2	59	56	149–151 (D–W)
CH$_2$=CHCH$_2$	6294-79-7	64	49	147–148[g] (B)
C$_6$H$_5$CH$_2$	21742-97-2	59	50	179–180 (E)
CH$_3$[h]	6726-48-3	42	26	222–223[i] (W)
n-C$_4$H$_9$[h]	24807-33-8	33	20	89–90[j] (H)

[a] Satisfactory analytical values (±0.30%) for C, H, and N were reported for all compounds. [b] Per cent of reacted RNCO converted to I. [c] Mole per cent RNCO converted to I. [d] Recrystallization solvent: B = benzene, D = dioxane, E = ethanol, H = hexane, T = toluene, W = water. [e] A. Hofmann, *Ber.*, **18**, 3217 (1885). [f] Difficult to remove water from crude product. [g] H. Priebe, B. Falk, and K. Deutsch, *Plaste Kaut.*, **13** (4), 223 (1966). [h] Carried out for 24 hr at 100°. [i] A. Hofmann, *Ber.*, **14**, 2728 (1881). [j] British Patent 928,637 (1963) to Olin Mathieson Chemical Corp.

TABLE II
EFFECT OF ISOCYANATE CONCENTRATION ON SELECTIVITY FOR
THE REACTION OF PHENYL ISOCYANATE WITH KOCN[a]

[PhNCO]$_0$, mol/l.	Selectivity to diphenyl isocyanurate, %	Conversion of PhNCO, %[b]
2.00	56	96
1.00	72	85
0.20	98	64

[a] Carried out in DMF at 75° for 1 hr. [b] Per cent of PhNCO reacted.

TABLE III
EFFECT OF SOLVENT ON SELECTIVITY FOR THE
REACTION OF PHENYL ISOCYANATE WITH KOCN[a]

Solvent	Selectivity to diphenyl isocyanurate, %	Conversion of PhNCO, %
Dimethylformamide	82	95
Dimethyl sulfoxide	84	89
Acetonitrile	19	82
Acetone	0	20

[a] Carried out at 35° for 1 hr.

TABLE IV
EFFECT OF TEMPERATURE ON SELECTIVITY FOR
THE REACTION OF PHENYL ISOCYANATE WITH NaOCN[a]

Temp, °C	Selectivity to diphenyl isocyanurate, %	Conversion of PhNCO, %	[NaOCN] × 10^3, mol/l.
6	52	85	
35	61	91	5.51
75	83	92	
100	81	89	7.26

[a] Carried out in DMF for 1 hr.

TABLE V
EFFECT OF CYANATE ION CONCENTRATION ON SELECTIVITY FOR
THE REACTION OF PHENYL ISOCYANATE WITH MOCN[a]

M	MOCN × 10^3, mol/l.[b]	Selectivity to diphenyl isocyanurate, %	Conversion of PhNCO, %
Na	5.51	61	91
K	21.2	82	95
Li	800	79	91

[a] Carried out in DMF at 35° for 1 hr. [b] Determined by the method of F. C. Trusell, P. A. Argabright, and W. F. McKenzie, *Anal. Chem.*, **39**, 1025 (1967).

TABLE VI
EFFECT OF ADDED ELECTROLYTES ON SELECTIVITY FOR
THE REACTION OF PHENYL ISOCYANATE WITH NaOCN[a]

Electrolyte	Concn, mol/l.	Selectivity to diphenyl isocyanurate, %	Conversion of PhNCO, %
None		61	91
LiClO$_4$	0.25	41	82
KI	0.25	39	89
LiClO$_4$	0.50	8	70

[a] Carried out in DMF at 35° for 1 hr.

by a factor of 4 leads to a 33% increase in selectivity. Surprisingly enough, when the concentration was increased by an additional factor of 40, the selectivity failed to increase. One other change was made in the system when the NCO⁻ concentration was dramatically increased in going from KOCN to LiOCN: the ionic strength of the medium was also raised.

Ionic Strength.—The possibility that an adverse ionic strength effect was responsible for the absence of a selectivity increase in passing from KOCN to the very soluble LiOCN was tested. Thus, phenyl isocyanate was allowed to react with NaOCN in the presence of LiClO$_4$ (an inert electrolyte) at different concentrations, and selectivities were compared with those in the absence of added electrolyte. As summarized in Table VI, the ionic strength of the medium has a marked effect on selectivity. For example, when the ionic strength of the medium is adjusted with LiClO$_4$ to coincide with that when LiOCN is employed, the selectivity drops from 61 to 8%. The fact that KI had essentially the same effect as LiClO$_4$ on selectivity discounts the possibility of a specific cation (Li⁺) effect.

In the absence of an adverse ionic strength effect, the LiOCN experiment of Table V would have resulted in a selectivity near 100%.

A general reaction of organic isocyanates is their base-catalyzed trimerization to 1,3,5-trisubstituted isocyanurates, II.[5] Basic salts (*e.g.*, sodium acetate) and tertiary amines are particularly effective catalysts.
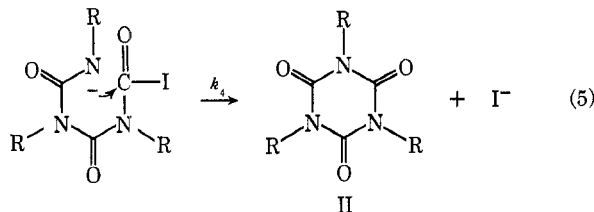
In the reaction of RNCO with MOCN, then, there

tion is essentially constant throughout the reaction. From a practical point, the low solubilities of NaOCN and KOCN in dipolar aprotic solvents necessitate an indirect method be used to vary the concentration of NCO⁻ to determine its effect on selectivity. In view of the solubility differences of the alkali metal cyanates, NaOCN, KOCN, and LiOCN, it appeared that a means was available for varying NCO⁻ concentration. As shown in Table V, an increase in NCO⁻
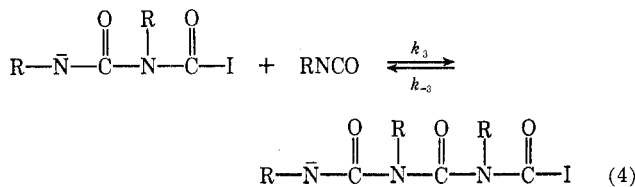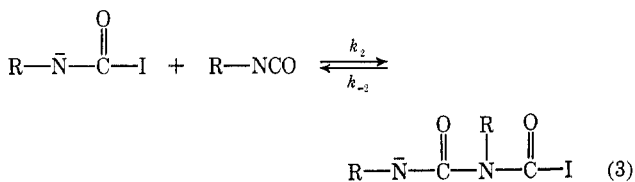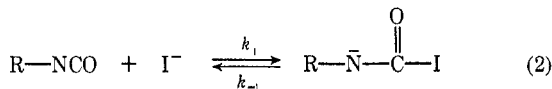
are several candidates for the active catalyst for the concomitant trimerization of RNCO to II. However, the most probable catalysts, from the standpoint of concentration, are NCO^- and the product, I^-. Of the two, the latter appears to be the more likely catalyst for the following reasons: (1) I^-, for example potassium diphenyl isocyanurate, is an effective trimerization catalyst at temperatures as low as 25°, and (2) the concentration of I^-, as derived from NaOCN or KOCN, exceeds by nearly an order of magnitude the concentration of NCO^- (after 1–4% reaction). Again, the low concentration of NCO^- is a consequence of the limited solubility of NaOCN (5 × 10^{-3} M) and KOCN (2.2 × 10^{-2} M) in DMF; on the other hand, the salts of disubstituted isocyanuric acids are extremely soluble in DMF.

From the immediate foregoing, it becomes apparent that the reaction of RNCO with NCO^- is quite unique in that the desired product, I^- induces the undesired trimerization of RNCO, thereby detracting from the selectivity to the product, I^-.

Discussion

Selectivity.—In accordance with the mechanism proposed by Shashoua et al.,[7] the I^- catalyzed trimerization of RNCO may be considered a series of isoenergetic addition reactions (eq 2–4) terminated by displacement of catalyst (eq 5).

$$R-NCO + I^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R-\overset{O}{\overset{\parallel}{\underset{}{N}}}-\overset{}{C}-I \tag{2}$$

$$R-\overset{O}{\overset{\parallel}{N}}-C-I + R-NCO \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}}$$

$$R-\overset{O}{\overset{\parallel}{N}}-\overset{R}{\overset{|}{C}}-\overset{O}{\overset{\parallel}{N}}-C-I \tag{3}$$

$$R-\overset{O}{\overset{\parallel}{N}}-\overset{R}{\overset{|}{C}}-\overset{O}{\overset{\parallel}{N}}-C-I + RNCO \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}}$$

$$R-\overset{O}{\overset{\parallel}{N}}-\overset{R}{\overset{|}{C}}-\overset{O}{\overset{\parallel}{N}}-\overset{R}{\overset{|}{C}}-\overset{O}{\overset{\parallel}{N}}-C-I \tag{4}$$
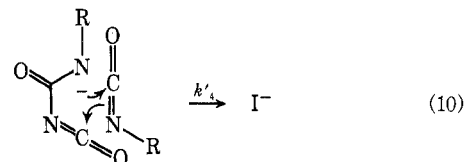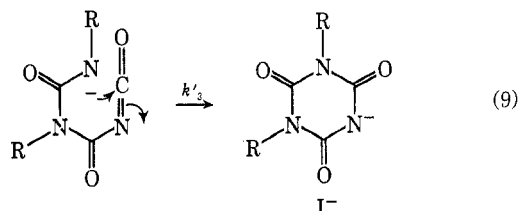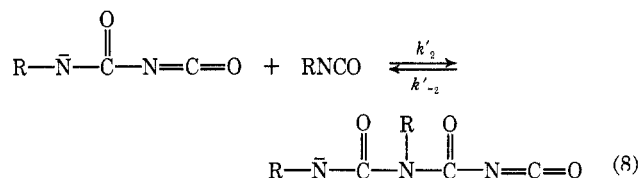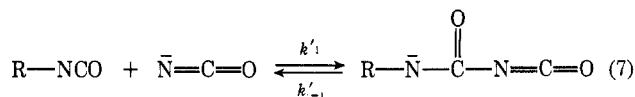

$$\tag{5}$$

II

If step 4 or 5 is rate controlling, the rate expression for the formation of II is

$$\frac{d[II]}{dt} = k_T[I^-][RNCO]^3 \tag{6}$$

if $k_{-1} \gg k_2$, $k_{-2} \gg k_3$, and $k_{-3} \gg k_4$, where k_T is the overall rate constant for trimerization.

When I^- is replaced by NCO^-, other paths are made available for one or more of the reaction intermediates. As illustrated in the following reaction sequence

(7) V. Shashoua, W. Sweeny, and R. Tietz, *J. Amer. Chem. Soc.*, **82**, 867 (1960).

quence (eq 7–10), either intramolecular ring closure (eq 9) or a quasi Diels–Alder reaction (eq 10) can

$$R-NCO + \overset{-}{N}=C=O \underset{k'_{-1}}{\overset{k'_1}{\rightleftharpoons}} R-\overset{O}{\overset{\parallel}{N}}-\overset{}{C}-N=C=O \tag{7}$$

$$R-\overset{O}{\overset{\parallel}{N}}-\overset{}{C}-N=C=O + RNCO \underset{k'_{-2}}{\overset{k'_2}{\rightleftharpoons}}$$

$$R-\overset{O}{\overset{\parallel}{N}}-\overset{R}{\overset{|}{C}}-\overset{O}{\overset{\parallel}{N}}-\overset{}{C}-N=C=O \tag{8}$$

$$\tag{9}$$

$$I^-$$

$$\overset{k'_4}{\rightarrow} I^- \tag{10}$$

account for the formation of I^-. At present, a choice cannot be made between the two steps.

If step 9 or 10 is rate controlling, the overall rate expression for the formation of I^- is

$$\frac{d[I^-]}{dt} = k_S[NCO^-][RNCO]^2 \tag{11}$$

if $k'_{-1} \gg k'_2$, and $k'_{-2} \gg k'_3$, or $k'_{-1} \gg k'_4$ where k_S is the overall rate constant for salt formation.

It follows from eq 6 and 11 that the fraction of RNCO converted to I^- (*i.e.*, the selectivity to I^-) may be defined by the general expression given in eq 13.

$$\frac{\frac{d[I^-]}{dt}}{\frac{d[I^-]}{dt} + \frac{d[II]}{dt}} = \frac{k_S[NCO^-][RNCO]^2}{k_S[NCO^-][RNCO]^2 + k_T[I^-][RNCO]^3} \tag{12}$$

or

$$\text{selectivity} = \frac{k_S[NCO^-]}{k_S[NCO^-] + k_T[I^-][RNCO]} \tag{13}$$

The kinetic expression (eq 13) for selectivity is consistent with the observation that the selectivity is an inverse function of the initial RNCO concentration (Table II). For synthetic purposes, the technique used to obtain maximum selectivities is dropwise addition of the RNCO to the MOCN–DMF slurry.

The observation that the selectivity increases with increasing NCO^- concentration (in spite of an adverse ionic strength effect) further supports eq 13.

The relative influence of ionic strength on the rates of formation of I^- and II (as reflected by the selectivity) can be rationalized in terms of the relative changes in charge dispersal between reactants and transition state for the primary steps (eq 2 and 7) for both processes. It has been demonstrated by Ingold and coworkers[8] that increasing the ionic strength of the

(8) For a good review of the subject, see C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p 361.

LARGE CHANGE IN CHARGE DISPERSAL
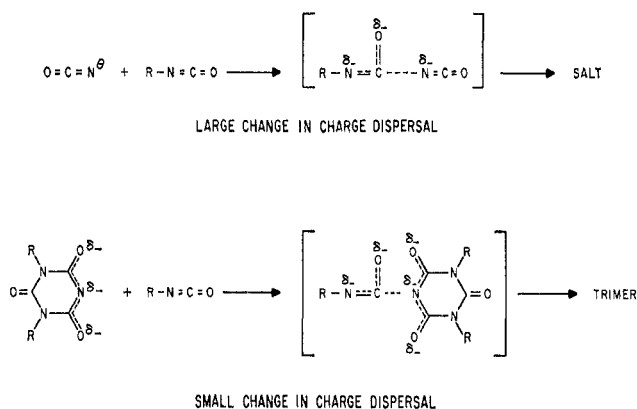

SMALL CHANGE IN CHARGE DISPERSAL

Figure 1.—Comparison of reactant with transition state for salt formation and trimerization.

medium for a reaction in which the charge is more diffuse in the transition state than in the reactants will result in rate retardation.

As shown in Figure 1, the initial steps for both the formation of I^- and II involve an increase in charge dispersal on passing from reactants to transition state. However, the increase in charge dispersal for I^- formation is greater than that for the formation of II owing to the greater charge delocalization in ground state I^- than NCO^-. Thus, increasing the ionic strength of the medium suppresses the overall rate of I^- formation more than the formation of II resulting in a decrease in the selectivity to I^-.

This concept is consistent with the effect of isocyanate structure on selectivity (Table I). That is, electron-withdrawing groups are associated with high selectivities. Referring again to the transition states in Figure 1, it is apparent that negative charge is more localized on the nitrogen in the transition state to I^- than in the case of II. Therefore, electron-withdrawing groups (*e.g.*, aryl and, to a lesser extent, benzyl and allyl) should play a bigger role in charge delocalization in the transition state to product, I^-, than in the transition state leading to trimer, II.

Trimerization.—The I^- induced trimerization of RNCO is a straightforward process, not involving ring opening of I^-. This was demonstrated by the following experiment. When 2 equiv of *p*-tolyl isocyanate (III) and 1 equiv of potassium diphenyl isocyanurate (IV) were contacted for 18 hr at 25° in DMF, the only product isolated was tri-*p*-tolyl isocyanurate (V), as shown in eq 14.

(14)
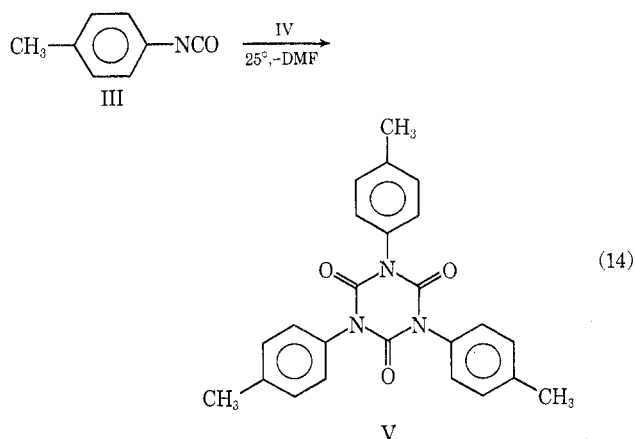
At least 90% of the starting salt, IV, was recovered.

If the catalyst, IV, underwent ring opening and retrogression, the reaction product would consist of a mixture of cotrimers and disubstituted isocyanurate salts in addition to IV and V.

Experimental Section

Materials.—DMF was purified by drying over CaH_2 followed by distillation at reduced pressure through a packed column. A center cut was used for all experiments. Reagent grade isocyanates were used as received from the manufacturer; technical grade isocyanates were purified by distillation. Benzyl isocyanate was prepared by reacting benzylamine hydrochloride with phosgene in refluxing xylene. After removal of the solvent, the product, bp 110–111° at 40 mm (lit.[9] bp 104–110° at 31–36 mm), was collected. Potassium cyanate (Matheson Coleman and Bell) and sodium cyanate (Fairmount Chemical Co.) were vacuum dried at 60° and stored in desiccators. Lithium cyanate was prepared according to the method of ter Horst.[10] Reagent grade lithium perchlorate (G. Frederick Smith Chemical Co.) and potassium iodide (Mallinckrodt) were used as received.

Infrared spectra were recorded on a Perkin-Elmer Model 521 spectrophotometer using KBr disks. Nuclear magnetic resonance spectra were run on a Varian A-60 spectrometer in hexadeuteriodimethyl sulfoxide solution using TMS as an internal standard. The ir and nmr spectra of the compounds in Table I were consistent with the assigned structures. The melting points reported are uncorrected. Elemental analyses were performed by Huffman Laboratories, Inc., Wheatridge, Colo.

Diphenyl Isocyanurate.—The procedure for preparing diphenyl isocyanurate is typical of that used for treating the aromatic isocyanates, benzyl isocyanate, and allyl isocyanate with metal cyanates.

A slurry of 13.0 g (0.16 mol) of KOCN and 200 ml of DMF was heated to 75° in a nitrogen atmosphere. A solution of 35.7 g (0.30 mol) of phenyl isocyanate in 100 ml of DMF was added dropwise over 1 hr. After stirring at 75° for an additional 30 min, the reaction mixture was allowed to cool, then transferred to a flash evaporator where the DMF was removed *in vacuo*. The residue obtained was stirred with 300 ml of distilled water and the insoluble material was collected by filtration and dried giving 3.70 g. The nmr spectrum of this fraction indicated its composition was 67% triphenyl isocyanurate, 27% 1,3-diphenylurea, and 6% DMF. The aqueous filtrate was acidified with concentrated HCl to precipitate 38.50 g of a white solid. This material was recrystallized from ethanol–water giving pure diphenyl isocyanurate, mp 265–266°.

It should be noted that in some instances the crude product precipitated on acidification was an infusible complex (nmr and infrared) of the desired acid and the potassium salt. The salt component could be removed by stirring the infusible solid with distilled water at room temperature for 24–72 hr. After filtration and drying, the product melted completely and was then purified by recrystallization.

Di-*n*-butyl Isocyanurate.—The preparation of di-*n*-butyl isocyanurate is typical of the reaction of aliphatic isocyanates with metal cyanates.

A mixture of 10.5 g (0.16 mol) of sodium cyanate, 29.7 g (0.30 mol) of butyl isocyanate, and 300 ml of DMF was stirred at 100° for 24 hr. The cooled reaction mixture was filtered, and the DMF was distilled at reduced pressure from the filtrate. The residue was stirred with distilled water causing an oil to separate. The oil was removed, dissolved in $CHCl_3$, and dried over $MgSO_4$. Removal of the solvent left 14.6 g of an oil which consisted of (nmr) 84% tri-*n*-butyl isocyanurate and 16% di-*n*-butylurea. The aqueous phase was acidified with concentrated HCl giving a precipitate of 7.1 g. This product was recrystallized from hexane to give di-*n*-butyl isocyanurate, mp 89–90°.

Effect of Isocyanate Concentration (Table II).—The KOCN (0.53 mol/mol of phenyl isocyanate) and DMF were equilibrated at 75° and the phenyl isocyanate added rapidly to the slurry. The initial exotherm was moderated as required with an

(9) J. N. Tilley and A. A. R. Sayigh, *J. Org. Chem.* **28**, 2076 (1963).

(10) W. P. ter Horst (to Mathieson Chemical Corp.), U. S. Patent 2,690,957 (1954).

ice bath to maintain 75°; later heating was commenced as necessary. The reaction was allowed to proceed for 1 hr and was then worked up as described above.

Effect of Solvent (Table III).—A solution of 0.30 mol of phenyl isocyanate in 100 ml of the appropriate solvent was added dropwise over 1 hr to a slurry of 0.16 mol of KOCN in 200 ml of solvent. The temperature (initially ambient) rose to 35–40° during the addition. The reaction was stirred for 0.5 hr after completing the addition and then worked up in the usual manner. In the reactions using acetone and acetonitrile, part of the reaction product precipitated from solution and was therefore isolated in admixture with KOCN. The organic materials were separated by stirring the mixture with DMF, filtering, and distilling off the DMF.

Effect of Temperature (Table IV).—A solution of 0.30 mol of phenyl isocyanate in 100 ml of DMF was added over 1 hr to a stirred slurry of 0.16 mol of sodium cyanate in 200 ml of DMF at the appropriate reaction temperature. After stirring at temperature for 1 hr additional, the reaction was worked up in the usual manner.

Effect of Cyanate Ion Concentration (Table V).—Phenyl isocyanate (0.3 mol) in 100 ml of DMF was added over 1 hr to a mixture of 0.16 mol of the appropriate metal cyanate and 200 ml of DMF. The temperature rose from ambient to 35–40° during the addition, and the reaction was stirred 1 hr thereafter. The products were isolated as usual.

Effect of Added Electrolytes (Table VI).—The LiClO₄ or KI (to give the indicated concentration in the total amount of DMF used) was dissolved in 200 ml of DMF and cooled to ambient. A charge of 0.16 mol of NaOCN was added to the solution, and 0.30 mol of phenyl isocyanate in 100 ml of DMF was added over 1 hr. The reaction was stirred at ambient for 1 hr afterward, and the products were then isolated as previously described.

Studies on Reactions of Isoprenoids. IX.[1] The Ritter Reaction of 5,5-Dimethyl-1-vinylbicyclo[2.1.1]hexane

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Treatment of the olefin (1) in the title with benzonitrile in H₂SO₄ afforded 2,3,3-trimethyl-1-benzamidobicyclo-[2.2.1]heptane (2), 2-phenyl-4,4-dimethyl-8-ethyl-3-azabicyclo[3.3.0]octa-2,7-diene (3), and 2-phenyl-4,4-di-methyl-8-ethyl-8-benzamido-3-azabicyclo[3.3.0]oct-2-ene (4), indicating that this Ritter reaction involved the competing reactions between the cyclobutane ring expansion (C-5 migration) to give a 2,3,3-trimethylbicyclo-[2.2.1]heptyl-1 cation and the cyclobutane ring opening at the C-1–C-5 linkage. In the reactions of 1 with a large excess of acetonitrile in H₂SO₄ and with a small excess of acetonitrile in AcOH–H₂SO₄, 2,3,3-trimethyl-1-hydroxybicyclo[2.2.1]heptane (7), 2,3,3-trimethyl-1-acetamidobicyclo[2.2.1]heptane (9), and, furthermore, 2,3,3-trimethyl-1-acetoxybicyclo[2.2.1]heptane (8) only in the latter reaction, together with a small amount of 8-(2,3,3-trimethylbicyclo[2.2.1]heptyl)-γ-sultone (6), were obtained, while treatment of 1 in AcOH–H₂SO₄ afforded 7 and 8. These results suggest that only the cyclobutane ring expansion of 1 occurred in diluted sulfuric acid. The C-2 stereochemistry of 2, 7, 8, and 9 disclosed that the cyclobutane ring enlargement is nonstereospecific. A plausible mechanism for the formation of 2–9 was proposed.

Heterocyclic syntheses with nitriles under the Ritter reaction conditions have attracted much attention from the preparative point of view.[2] Most of the examples, however, are limited to intramolecular cyclizations of appropriate 1,*n*-bifunctional systems *via* intermediate nitrilium cations.[3] In a previous paper,[4] we reported the ring-enlargement reaction of 5,5-dimethylbicyclo[2.1.1]hexane-1-epoxyethane to a bicyclo[2.2.1]heptane ring system by acidic hydrolysis, where no cyclobutane ring-fission products were isolated. This paper deals with the results of the Ritter reaction of 5,5-dimethyl-1-vinylbicyclo[2.1.1]hexane (1) with benzonitrile and acetonitrile under several reaction conditions.

We expected that the cyclobutane ring fission of 1 might be caused by initial protonation of the vinyl group in such strongly acidic media as H₂SO₄, and sub-

sequent reactions of the resulting carbonium ions with nitriles might afford azabicyclic compounds after rearrangement and cyclization.

Results and Discussion

Structural Elucidation of Products.—Products 2–9 were isolated in the Ritter reaction of 1 with benzonitrile and acetonitrile under several conditions as summarized in Table I. Their melting points and analyses are summarized in Table II. Products 2–5 were produced only in the presence of benzonitrile, and 9 was formed in the presence of acetonitrile, indicating that these might be derived from 1 and nitriles, but 6–8 were produced also in absence of nitriles, indicating that these were derived only from 1 and solvents.

The structural elucidation of 2–9 was carried out as follows. Product 2 (C₁₇H₂₃NO) contained a benzamido group (ir); the nmr spectrum had a doublet at τ 9.20 assignable to CHCH₃ as well as two singlets (τ 8.96 and 9.08) assignable to a *gem*-dimethyl protons, suggesting that 2 is not a normal Ritter reaction product of 1 involving the same ring system, but a cyclobutane ring-expansion product, 2,3,3-trimethyl-1-benzamido-bicyclo[2.2.1]heptane or 2,7,7-trimethyl-1-benzamido-

(1) Part VIII: T. Sasaki, S. Eguchi, and T. Ishii, *Bull. Chem. Soc. Jap.,* **43**, 543 (1970).

(2) (a) F. Johnson and R. Madronero, *Advan. Heterocycl. Chem.,* **6**, 95 (1966); (b) L. I. Krimen and D. J. Cota, *Org. React.,* **17**, 213 (1969); (c) A. Hassner, R. A. Arnold, R. Geult, and A. Terada, *Tetrahedron Lett.,* 1241 (1968).

(3) Recently an example of the double intermolecular Ritter reactions of 4-methyl-3-pentenenitrile has been reported: J. W. Ducker and M. J. Gunter, *Aust. J. Chem.,* **21**, 2809 (1968).

(4) Part VII of this series: T. Sasaki, S. Eguchi, and T. Ishii, *J. Org. Chem.,* **35**, 219 (1970).