

## Kinetics of the Tin-Catalyzed Reactions of Phenyl Isocyanate with Ureas\*

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### Synopsis

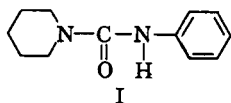
The initial rates have been determined for the second-order equilibrium reaction of phenyl isocyanate with a series of phenyl-substituted 1,1-pentamethylene-3-phenyl ureas in the presence of butyltin trichloride catalyst in chlorobenzene at 60°C. These results were compared with the rates of reaction of phenyl isocyanate with 1,1-di-*n*-butyl-3-phenylurea, 1,3-diphenyl-1-methylurea, *N*-phenylbenzamide, methyl-*N*-phenyl carbamate, and 1-butanol. The activation energy for the butyltin trichloride-catalyzed reaction of phenyl isocyanate and 1,1-pentamethylene-3-phenylurea was 12 kcal./mole. At 60°C. this reaction was approximately 11 times as fast as the reverse reaction. The rate of the reaction of phenyl isocyanate and 1,1-pentamethylene-3-phenylurea was directly proportional to the concentration of butyltin trichloride. The activity of this catalyst was 28 times as great as that of triethyltin chloride. Dibutyltin dilaurate, dibutyltin diacetate, dibutyltin dichloride, tributyltin chloride, tetramethyltin, trimethyltin bromide, triethyltin fluoride, and 1,2,4-trimethylpiperazine were not catalysts for these reactions. The ureas formed solid complexes with stannic chloride and with butyltin trichloride in which the tin compounds were coordinated through the carbonyl oxygen. A tentative reaction mechanism has been proposed, which involves nucleophilic attack of the urea on the isocyanate through an intermediate ternary complex. The stannic chloride-catalyzed reaction of ureas with isocyanates at room temperature has been shown to have wide application.

### INTRODUCTION

The effect of tin catalysts on the reaction of isocyanates with ureas is of interest because of the presence of urea groups in many formulations for the preparation of polyurethans.<sup>1</sup> There are few detailed studies of the kinetics of catalyzed reactions of isocyanates with ureas to give biurets. Bennet, Saunders, and Hardy<sup>2</sup> observed the rates of the reaction of mono-phenylurea and 1,3-diphenylurea at 140°C. with *N*-ethylmorpholine, a relatively inactive catalyst. Hostettler and Cox<sup>3</sup> studied the reaction of 1,3-diphenylurea with phenyl isocyanate in dioxane at 70°C. with various catalysts, but the low solubility of the urea caused difficulties. Case and Li<sup>4</sup> recently reported dibutyltin dilaurate to be a good catalyst for reactions of two 1-alkyl-3-arylureas with a disubstituted isocyanate in diglyme at 100°C.

\* From the Ph.D. dissertation, University of Delaware, 1964, of R. Bruce Pinkerton, Armstrong Cork Co. Research Fellow, 1962-1964.

The object of the present investigation was to make a thorough study of the factors affecting the tin-catalyzed reaction of phenyl isocyanate with ureas, under conditions which excluded side reactions, in the hopes of throwing light on the mechanism. The urea chosen as a standard was 1,1-pentamethylene-3-phenylurea (I), which has the advantages of only one active hydrogen, moderate solubility in chlorobenzene, and the possibility of substitution on the benzene ring.



Stannic chloride was shown by Baker and Holdsworth<sup>5</sup> to be a powerful catalyst for the formation of 1,3,5-triphenylbiuret from phenyl isocyanate and 1,3-diphenylurea at room temperature. A more convenient catalyst for the kinetic studies is butyltin trichloride, which has been used throughout the present work.

## RESULTS AND DISCUSSION

### Catalysts

The formation of biurets from the reaction of an isocyanate and an aromatic urea requires vigorous conditions in the absence of a catalyst.<sup>6</sup> Under these conditions, where the temperature may be in the range of 100–150°C., many side products often occur.<sup>7</sup> In order to avoid competing reactions, such as trimerization of the isocyanate or thermal decomposition of the urea or biuret, a catalyst was desired which would be active at low temperatures, 50–70°C.

The following organotin compounds and one tertiary amine were screened for catalytic activity in the reaction of 1,1-pentamethylene-3-phenylurea and phenyl isocyanate in chloroform or chlorobenzene at 60–61°C.: dibutyltin dilaurate, dibutyltin diacetate, dibutyltin dichloride, tributyltin chloride, butyltin trichloride, stannic chloride, triethyltin chloride, trimethyltin bromide, tetraethyltin, dibutyltin difluoride, triethyltin fluoride, and 1,2,4-trimethylpiperazine. The only active compounds for the present reaction were found to be stannic chloride, butyltin trichloride, and triethyltin chloride. However, many of the above compounds have been shown to be excellent catalysts for the isocyanate-hydroxyl reaction.<sup>3</sup>

The screening reactions were usually carried out in refluxing chloroform (61°C.) for 3–19 hr. with the use of approximately 1:1 or 1:2 mole ratios of the urea and phenyl isocyanate, respectively, with approximately 1–2 mole-% of the various catalysts based on the urea concentration. The reaction mixtures were then stripped of volatiles under vacuum. The resulting solids were separated into 3,5-diphenyl-1,1-pentamethylenebiuret, identified by comparison with an authentic sample, and starting material by taking advantage of their relative solubilities. In some cases, in

chlorobenzene, the solvent used in the kinetics, samples were withdrawn and analyzed for phenyl isocyanate by the di-*n*-butylamine titration method.<sup>8</sup> Compounds which showed no activity in the above product analyses also did not cause any uptake of phenyl isocyanate in these volumetric analyses. In every case there were no indications of the formation of any side products.

In the above standard reaction, butyltin trichloride produced an equilibrium mixture of approximately 68% biuret, the rest being starting material. At 80°C. in refluxing benzene, the equilibrium mixture contained 52% biuret. In the absence of this catalyst the reaction did not take place. Similar tests with 1,3-diphenyl-1-methylurea and *N*-phenylbenzamide using butyltin trichloride as a catalyst showed that these reactions were also uncomplicated by side reactions.

In the current work dibutyltin diacetate was shown to be inactive toward the urea-isocyanate reaction at 60°C. in chloroform or chlorobenzene. This is contrary to previous results<sup>8</sup> in dioxane. With this solvent, the rate of reaction of phenyl isocyanate with 1,3-diphenylurea, catalyzed by 10 mole-% of dibutyltin diacetate, was 6000 times as fast<sup>8</sup> as the uncatalyzed reaction at 70°C. Hence this work was repeated.

Three runs were carried out simultaneously in highly purified dioxane at 70°C.; one containing 0.05*M* phenyl isocyanate, 0.05*M* 1,3-diphenylurea and 0.005*M* dibutyltin diacetate followed titrimetrically<sup>8</sup> for loss of phenyl isocyanate; another containing these same components left unopened under

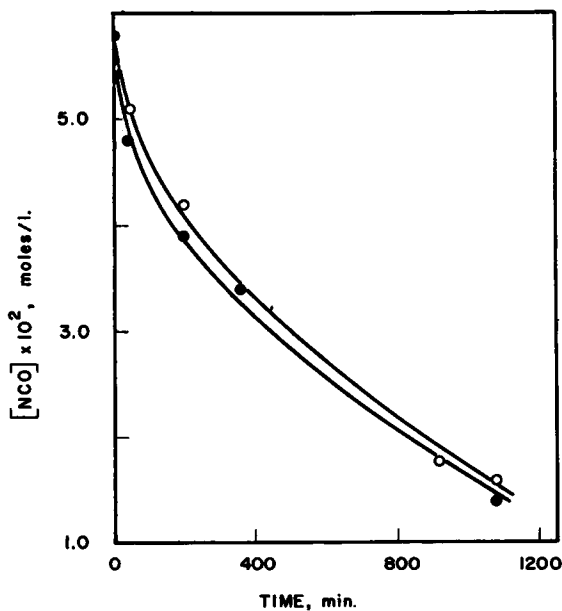


Fig. 1. Change in concentration of  $C_6H_5NCO$  in dioxane at 70°C. with 0.005*M* dibutyltin diacetate: (O) blank on 0.05*M*  $C_6H_5NCO$ ; (●) 0.05*M*  $C_6H_5NCO$  and 0.05*M* 1,3-diphenylurea.

nitrogen as a control; and a blank containing only 0.05*M* phenyl isocyanate and 0.005*M* catalyst, also titrated periodically for isocyanate. The results show (Fig. 1) that the rate of loss of phenyl isocyanate was the same for the reaction mixture as for the blank containing no urea. Although 76% of the phenyl isocyanate disappeared in 19 hr., it did not react with the urea; the control run gave a 98% recovery of the starting urea and no biuret was formed. Neither were homopolymers of the isocyanate present.

Qualitative evidence suggests that the isocyanate reacted with the dioxane. During the heating period the three colorless solutions containing phenyl isocyanate with dibutyltin diacetate in dioxane became yellow and then brownish orange. The dark material, isolated as an oil, gave tests for unsaturation, but has not been further characterized.

### Kinetics

The initial rates for the reactions of the ureas and phenyl isocyanate in the presence of butyltin trichloride were determined in chlorobenzene solution at 60°C., concentrations of the urea and isocyanate of 0.05*M* and 0.09*M*, respectively, being used. Butyltin trichloride concentrations ranged from 0.00015 to 0.0009*M*. The rates were followed by the di-*n*-butylamine titration procedure.<sup>8</sup>

Typical second-order graphs of the data are shown in Figure 2. For each reaction the rate constant,  $k_{\text{obs}}$ , was obtained from the slope of the

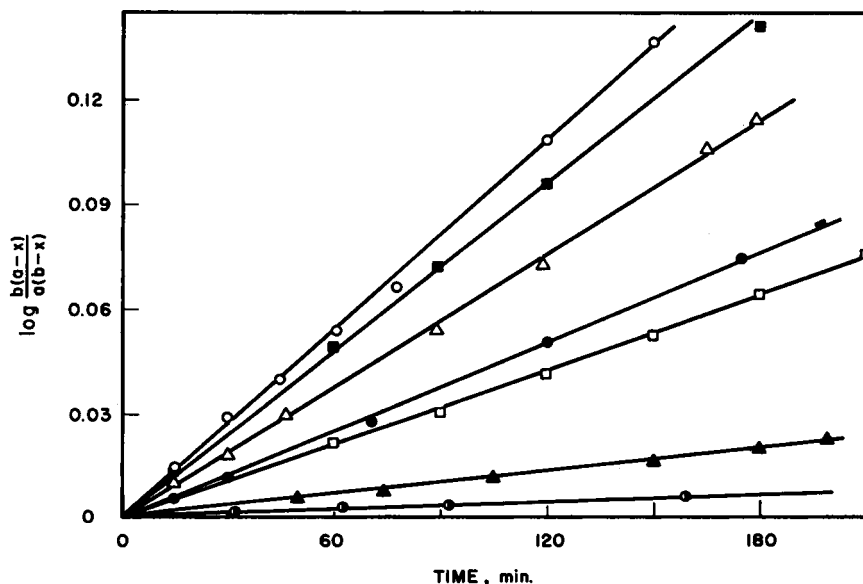


Fig. 2. Second-order plots of the reaction of  $\text{C}_6\text{H}_5\text{NCO}$  and  $\text{X-C}_6\text{H}_4\text{NHCONC}_6\text{H}_{10}$  to give a biuret in chlorobenzene at 60°C. where X is: (O) *p*-CH<sub>3</sub>; (■) *p*-H; (Δ) *p*-OCH<sub>3</sub>; (●) *p*-Cl; (□) *m*-Cl; (▲) *p*-NO<sub>2</sub>; (○) *p*-H with EtSnCl<sub>3</sub> as the catalyst.

line in the graph of  $\log [b(a - x/a(b - x))]$  versus time. The  $k_{\text{obs}}$  of runs done at approximately equal catalyst concentrations was then divided by the catalyst concentration to give the true rate constant,  $k'$ , according to eq. (1):

$$v_{\text{obs}} = k' [\text{urea}] [\text{NCO}] [\text{cat.}] \quad (1)$$

At constant concentration of catalyst,

$$v_{\text{obs}} = k_{\text{obs}} [\text{urea}] [\text{NCO}] \quad (2)$$

and thus

$$k' = k_{\text{obs}} / [\text{cat.}] \quad (3)$$

In accord with these equations is the fact that a graph of the  $k_{\text{obs}}$  values for reaction of 1,1-pentamethylene-3-phenylurea with phenyl isocyanate against catalyst concentration (data from Table I) is linear. The slope of the line,  $k'$ , is 0.858 l./mole-sec.

TABLE I  
Reaction Rates of Substituted 1,1-Pentamethylene-3-phenylureas with Phenyl Isocyanate at 60°C. in Chlorobenzene<sup>a</sup>  
 $\text{X}-\text{C}_6\text{H}_4\text{NHCONC}_5\text{H}_{10} + \text{C}_6\text{H}_5\text{NCO} \rightleftharpoons \text{C}_6\text{H}_5\text{NHCON}(\text{X}-\text{C}_6\text{H}_4)\text{CONC}_5\text{H}_{10}$

X	Catalyst	Cat. concn., $10^4 \times M$	$10^4 \times k_{\text{obs}}$ , l./mole-sec.	$10 \times k'$ , l./mole-sec.	$10 \times k'$ (ave.), l./mole-sec.	Relative rate	Reaction, %	
							Straight line <sup>b</sup>	Equilibrium
	BuSnCl <sub>3</sub>							
<i>p</i> -H		7.97	6.76	8.48 <sup>c</sup>	8.64	1.00	44	56
<i>p</i> -H		7.73	6.81	8.81 <sup>c</sup>			47	53
<i>p</i> -H		4.51	3.60	7.98 <sup>c</sup>			24	—
<i>p</i> -H		3.79	3.35	8.84 <sup>c</sup>			—	—
<i>p</i> -H		1.84	1.51	8.21 <sup>c</sup>			15	—
<i>p</i> -H		1.49	1.55	10.40 <sup>c</sup>			—	—
<i>p</i> -CH <sub>3</sub>		8.54	8.41	9.85	9.75	1.13	53	59
<i>p</i> -CH <sub>3</sub>		8.25	7.97	9.66			50	56
<i>p</i> -OCH <sub>3</sub>		8.47	5.83	6.77	7.01	0.84	48	63
<i>p</i> -OCH <sub>3</sub>		8.61	6.15	7.26			50	ca. 56
<i>p</i> -Cl		7.65	4.26	4.29	4.62	0.53	37	—
<i>p</i> -Cl		9.92	3.80	4.96			36	—
<i>m</i> -Cl		7.44	3.13	4.21	3.64	0.42	29	47
<i>m</i> -Cl		8.54	2.16	3.04			26	—
<i>p</i> -NO <sub>2</sub>		10.16	1.05	0.103	0.101	0.012	14	—
<i>p</i> -NO <sub>2</sub>		10.48	1.03	0.098			13	—
	Et <sub>3</sub> SnCl							
<i>p</i> -H		7.86	0.239	0.304	0.311	0.036	7	—
<i>p</i> -H		7.69	0.245	0.318				

<sup>a</sup> Concentration: 0.05M urea, 0.09M isocyanate.

<sup>b</sup> Minimum % of reaction following a straight line.

<sup>c</sup> Average of these  $k'$  is 0.878.

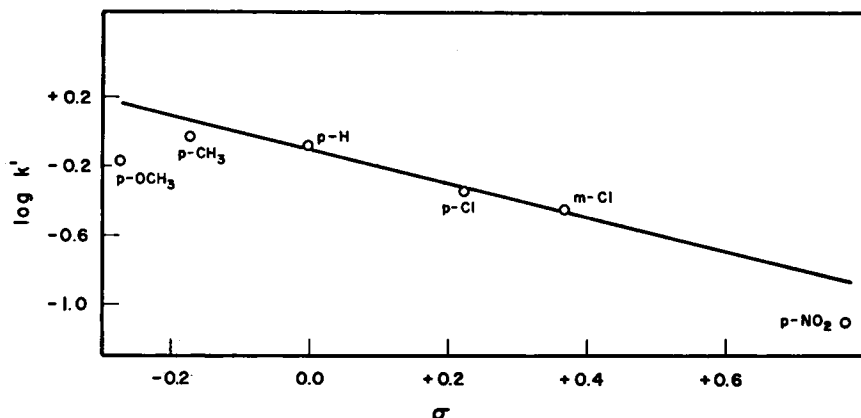


Fig. 3. Correlation of rate data with the Hammett equation,  $\rho = 0.965$ . Solvent, chlorobenzene, temperature,  $60.3 \pm 0.2^\circ\text{C}$ .

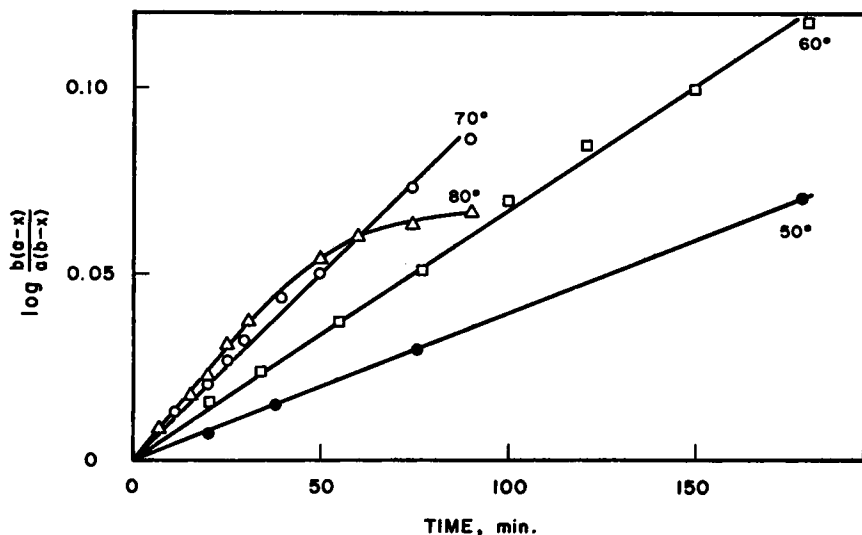


Fig. 4. Second-order rate plots for the reaction of phenyl isocyanate with 1,1-pentamethylene-3-phenylurea in chlorobenzene at 50, 60, 70, and  $80^\circ\text{C}$ .

The kinetic data from the reactions at  $60^\circ\text{C}$ . of phenyl isocyanate with six phenyl-substituted 1,1-penta-methylene-3-phenylureas in the presence of butyltin trichloride (Table I and Fig. 2) show that electron-withdrawing substituents decrease the rate slightly and electron-donating groups enhance the rate slightly. Figure 3 is a Hammett plot of these data, the Hammett substituent constant<sup>9</sup> being used. A straight line was obtained. The small negative  $\rho$  value of  $-0.965$  shows that the substituents do not affect the rate greatly. This probably indicates that the intermediate complex between one or more reactants and the catalyst is so reactive that it makes little difference what the substituent is.

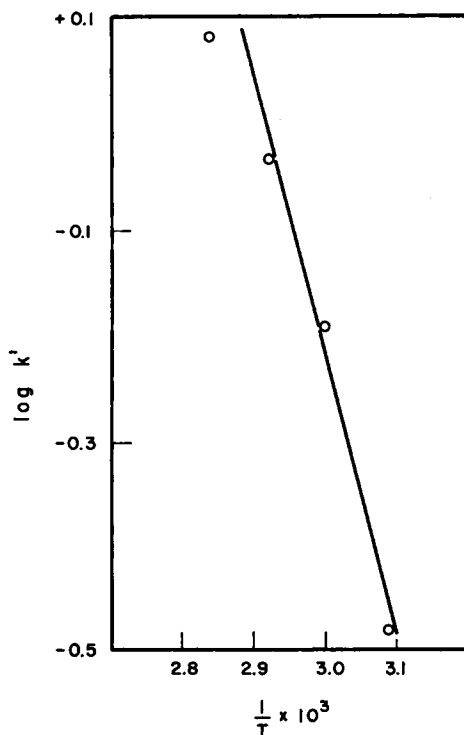


Fig. 5. Arrhenius plot for the reaction of phenyl isocyanate and 1,1-pentamethylene-3-phenylurea in chlorobenzene.

A comparison of butyltin trichloride and triethyltin chloride in the reaction of 1,1-pentamethylene-3-phenylurea with isocyanate (Table I) shows that the former catalyst is 28 times as active as the latter. Dibutyltin dichloride and tributyltin chloride had no catalytic activity in this reaction. The comparison of these alkyltin halides is clear evidence of steric inhibition for the formation of the active complex, since the electronic character of ethyl and butyl groups do not differ significantly. However, for materials with smaller alkyl groups, such as tetramethyltin, tetraethyltin, and trimethyltin bromide, which did not act as catalyst, one must consider electronic factors and their effect on the ability of these less electrophilic materials to coordinate with the reactants in order to form an active complex.

The effect of temperature on the rate of reaction of phenyl isocyanate and 1,1-pentamethylene-3-phenylurea was determined at 50, 60, 70, and 80°C., and the results are shown in Table II. The second-order plots are shown in Figure 4. Although the reaction at 60°C. followed a straight line graph up to 44% completion, at 80°C. the reaction followed second-order kinetics to only 10% completion. This is probably because at this temperature the competing decomposition of the biuret became appreciable. The Arrhenius graph of the  $k'$  values (Fig. 5) shows divergence from the straight

line at the highest temperature (80°C.). From the other three values, the approximate energy of activation for this reaction was calculated to be 12 kcal./mole.

TABLE II  
Effect of Temperature on Rate of the Reaction of 1,1-Pentamethylene-3-phenylurea and Phenyl Isocyanate in Chlorobenzene with Butyltin Trichloride<sup>a</sup>

Temp., °C.	$10^4 \times \text{BuSnCl}_3$ concn., <i>M</i>	$10^4 \times k_{\text{obs}}$ , l./mole-sec.	$10 \times k'$ , l./mole-sec.
49.9 ± 0.1	9.53	2.99	3.14
	9.43	3.30	3.49
60.3 ± 0.2	8.75	6.04	6.90
	9.04	5.38	5.95
69.9 ± 0.1	9.35	8.63 <sup>b</sup>	9.23
79.9 ± 0.1	8.68	10.00	11.5
	8.43	10.65	12.6

<sup>a</sup> Urea concentration, 0.05*M*; isocyanate, 0.09*M*.

<sup>b</sup> Single determination.

The butyltin trichloride-catalyzed decomposition of 3,5-diphenyl-1,1-pentamethylenebiuret (0.05*M* in chlorobenzene at 60°C.), to phenyl isocyanate and 1,1-pentamethylene-3-phenylurea, proceeded approximately 11 times more slowly than the rate of formation for approximately equal catalyst concentrations. In the absence of catalyst this decomposition was too slow to measure at 60°C. This reaction followed the first-order rate law:

$$k_{\text{obs}} = (1/t) [x/a(a - x)] \quad (4)$$

and

$$k_1 = k_{\text{obs}}/[\text{cat.}] \quad (5)$$

The rate and equilibrium constants for this decomposition were:  $k_{\text{obs}}$ ,  $8.92 \times 10^{-5}$  l./mole-sec.;  $k_1$ ,  $9.25 \times 10^{-2}$  l./mole-sec.; and  $K$  (72%), 0.095 (1/ $K$ , 10.6). The equilibrium constant obtained from the forward reaction was 10.4 at 44% reaction.

It is apparent that at 60°C. determinations can be made of both the rate of formation of the biuret and of its slower rate of decomposition. However, as the temperature is increased, the rate of decomposition becomes the major reaction. This is suggested by the data of Figure 4 at 80°C. At 130–150°C. Kogon<sup>10</sup> showed that the rate of decomposition of biurets was so rapid that the rate of formation could be neglected.

In Table III are data on the rates of the tin-catalyzed reaction of phenyl isocyanate with certain other trisubstituted ureas, a carbamate, an amide, and an alcohol. By replacing the pentamethylene group on a urea nitrogen by the more bulky di-*n*-butyl groups, the rate of reaction was reduced about 10 times. This shows that substituents on one nitrogen of the urea can influence, by a steric effect, the reactivity of the hydrogen atom on the other nitrogen.



TABLE III

Rates of Catalyzed Reactions of *N*-Substituted Ureas and Active Hydrogen Compounds at 60°C. in Chlorobenzene. Active Hydrogen Compound, 0.05*M*; Isocyanate, 0.09*M*

Compound	10 <sup>4</sup> × BuSnCl <sub>3</sub> , concn., <i>M</i>	10 <sup>6</sup> × <i>k</i> <sub>obs</sub> , l./mole- sec.	10 <sup>2</sup> × <i>k</i> ', l./mole- sec.	Relative rate	Straight line, % <sup>a</sup>
C <sub>6</sub> H <sub>5</sub> NHCONC <sub>6</sub> H <sub>10</sub>	7.97	67.6	84.8	1.00	44.0
	7.73	68.1	88.1		
C <sub>6</sub> H <sub>5</sub> NHCON(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub>	9.57	7.99	8.35	0.09	11.5
	9.11	7.86	8.63		
C <sub>6</sub> H <sub>5</sub> NHCON(CH <sub>3</sub> )C <sub>6</sub> H <sub>5</sub>	9.53	4.91	5.15	0.06	3.2
	9.99	4.95	4.95		
C <sub>6</sub> H <sub>5</sub> NHCOC <sub>6</sub> H <sub>5</sub> <sup>b</sup>	8.68	7.30	8.41	0.10	
C <sub>6</sub> H <sub>5</sub> NHCOOCH <sub>3</sub> <sup>b</sup>	9.88	3.37	3.41-	0.04	10.9
C <sub>6</sub> H <sub>5</sub> OH <sup>c</sup>	9.46	1670	1760		
C <sub>6</sub> H <sub>5</sub> NHCONC <sub>6</sub> H <sub>10</sub> <sup>d</sup>	—	—	17		

<sup>a</sup> Minimum per cent reaction following a straight line.

<sup>b</sup> Single determination.

<sup>c</sup> Run at 30°C.

<sup>d</sup> Data obtained by extrapolation from the graph of activation energy.

The rate of reaction of *N*-phenylbenzamide was of the same order of magnitude as the 1,1-di-*n*-butyl-3-phenylurea, and the methyl carbanilate showed a somewhat smaller rate. Because the reaction of 1-butanol and phenyl isocyanate at 60°C. in the presence of butyltin trichloride was too fast to measure, data were obtained at 30°C. The rate was approximately 100 times as great for the alcohol as for 1,1-pentamethylene-3-phenylurea. (The *k*' value for this urea at 30°C. was estimated by extrapolation of the graph of activation energy.) Hence the order of decreasing reactivity of these compounds with phenyl isocyanate when catalyzed by butyltin trichloride is: alcohol > urea > amide > carbamate. This is the same order as for the uncatalyzed reactions.<sup>11</sup>

### Complexes

All of the ureas and biurets encountered in this investigation formed complexes with anhydrous stannic chloride at room temperature. A 3:2 complex of 1,3-diphenylurea with stannic chloride, first described by Baker and Holdsworth,<sup>5</sup> was easily obtained in pure condition, although with a different melting point than previously reported. Complexes of 1,1-pentamethylene-3-phenylurea with stannic chloride were too unstable to be isolated in analytical purity. However, a stable 1:1 complex of this urea with butyltin trichloride was isolated and well characterized. No complex was formed with this urea and tetraethyltin.

The infrared absorption of the ureas and their complexes (Table IV) indicates that the tin compound is coordinated to the carbonyl oxygen, not to the nitrogen of the urea. In going from the urea to its tin complex there are small shifts in the CO absorption and much larger shifts, in the

direction of higher frequencies, in the NH absorption. The uncomplexed ureas are known<sup>12</sup> to have extensive hydrogen bonding in the solid state. The observed small changes in carbonyl absorption would represent the slight difference between polarization by bonding to hydrogen or to tin, whereas the large difference in NH absorption reflects the removal of the opportunity for hydrogen bonding with the carbonyl.

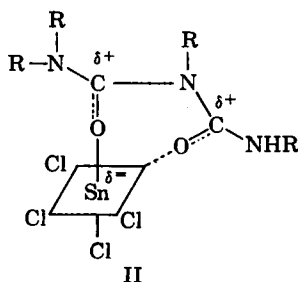
TABLE IV  
Comparison of Infrared Spectra of Some Ureas and Their Tin IV Halide Complexes

Urea	Tin halide complex	$\nu$ , $\text{cm.}^{-1}$		
		Urea	Complex	$\Delta\nu$
NH (C <sub>6</sub> H <sub>5</sub> NH) <sub>2</sub> CO	3(C <sub>6</sub> H <sub>5</sub> NH) <sub>2</sub> CO · 2SnCl <sub>4</sub>	3278(s) <sup>a</sup>	3355(s) <sup>a</sup>	77
C=O		1642(m)	1646(m)	4
Amide II		1551(s)	1551(s)	0
NH C <sub>6</sub> H <sub>10</sub> NHCONHC <sub>6</sub> H <sub>5</sub> <sup>b</sup>	C <sub>6</sub> H <sub>10</sub> NHCONHC <sub>6</sub> H <sub>5</sub> · C <sub>4</sub> H <sub>9</sub> SnCl <sub>3</sub> <sup>b</sup>	3350(m)	3430(s)	50
C=O		1640(s)	1660(s)	20
Amide II		1550(m)	1565(s)	15

<sup>a</sup> Intensity measured as (s), strong; (m) medium.

<sup>b</sup> Data from Infracord, other from Baird using KBr technique.

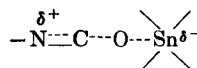
Complexes of stannic chloride and 1,3,5-trisubstituted biurets formed instantly on contact of the reagents at room temperature and these were much more stable and easily handled than the urea complexes. They were shown, by analysis, to have a 1:1 ratio of biuret to stannic chloride. The infrared spectra of these complexes also indicated coordination through the biuret carbonyls. A possible structure is II:



Evidence of complex formation between isocyanates and Lewis acids was reported by Pestemer and Lauerer<sup>13</sup> and by Smith<sup>14</sup> on the basis of shifts in absorption. Smith proposed a ternary complex of alcohol, isocyanate, and organotin or cobalt catalysts as the basis for carbamate formation.

Bloodworth and Davies<sup>15</sup> established the existence of an adduct between aryl isocyanates and alkyltin alkoxides when they isolated and characterized the *N*-stannyl carbamates of the structure ArN(SnBu<sub>3</sub>)-COOCH<sub>3</sub>.

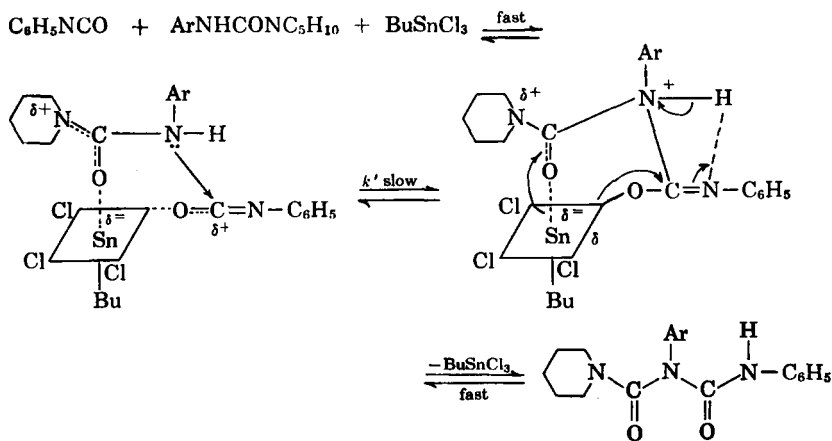
In the present investigation, fine precipitates were obtained when phenyl isocyanate was added to pentane or hexane solutions of stannic chloride, butyltin trichloride, and tributyltin chloride. The infrared spectra of these materials were different from those of either of the components; e.g., the typical isocyanate absorption disappeared and a weak band was observed at  $2600\text{ cm.}^{-1}$  which was common to all of these precipitates. It is thought that this may be due to the formation of a group such as:



Further work is being done on these substances.

### Proposed Mechanism

The mechanism proposed by Baker and Holdsworth<sup>5</sup> involving a complex between stannic chloride and a urea nitrogen is not in accord with the current findings indicating complex formation on the urea carbonyl. However, the prior formation of a tin complex on the urea followed by attack of the isocyanate is unlikely because such a complex would not be expected to have greater nucleophilicity than the uncomplexed urea. The remaining possibilities are the prior formation of an isocyanate-tin complex, or of a ternary complex of isocyanate, urea, and tin compound. The latter possibility, which is in accord with the data, is presented in eq. (6).



In this mechanism the urea and isocyanate are held, by the catalyst, in a favorable position for reaction to occur. It is thought that the positive charge developed on the urea-carbonyl carbon could be satisfied by the piperidine nitrogen, still allowing the attacking nitrogen enough electron density for interaction with the polarized isocyanate carbonyl. This mechanism explains the steric effects of bulky groups on a urea nitrogen,

the rate enhancement by electron-donating substituents on the aryl group, and the participation of the urea in the complex.

This proposal is similar to that suggested by Britain and Gemeinhardt<sup>16</sup> for the metal-catalyzed reactions of isocyanates and alcohols, except that the present mechanism shows a reasonable path from the ternary complex to the final product. Another similarity to the work of Britain and Gemeinhardt is the relative reactivity of the butyltin chlorides. They found the activity to be: butyltin trichloride > di-*n*-butyltin dichloride > tri-*n*-butyltin chloride > tetra-*n*-butyltin. In the present isocyanate-urea reactions, in which the intermediate complexes are much bulkier, the only one of the series that acts as a catalyst is butyltin trichloride.

The mechanism proposed by Bloodworth and Davies<sup>15</sup> for the tin alkoxide-catalyzed reaction of isocyanates and alcohols, involving the *N*-stannyl carbamates, cannot be applied to the present system, by assuming the possibility of the formation of the analogous *N*-stannyl carbamoyl chloride, followed by nucleophilic attack of the urea. Evidence against such a mechanism is the fact that trimethyltin bromide did not act as a catalyst in the standard screening reaction, whereas triethyltin chloride did. If the *N*-stannyl analog is the active intermediate, the more easily ionizable bromo compound should be more effective as a catalyst than the chloro compound. But if the active intermediate has the tin coordinated to carbonyl oxygens, as proposed above, the trimethyltin bromide should be less effective as a catalyst since it is less electrophilic. This is in accord with the present data. This work is being continued to secure further evidence as to the mechanism.

### Biurets

The use of anhydrous stannic chloride to catalyze the reaction of phenyl isocyanate with a urea to give a biuret, first mentioned by Baker and Holdsworth,<sup>5</sup> was used by Kogon<sup>17</sup> for two compounds, but no details were given. In the present work the method was developed for the low-temperature synthesis of 13 biurets (Table V). In addition, *N*-phenylbenzamide was converted to 1-benzoyl-3,5-diphenylurea by this procedure.

## EXPERIMENTAL

### Procedure for Kinetic Studies

All glassware that came into contact with phenyl isocyanate, catalyst, or solvents was thoroughly cleaned, oven- or flame-dried, and cooled in a desiccator. Preparation and transfer of solutions of isocyanates were done in a dry box.

The dry urea, 0.005 mole, was weighed into a 250 ml. round-bottomed flask equipped with a short condenser and an adapter for removal of samples by syringe through a neoprene rubber gasket. The butyltin trichloride 0.023-0.028 g. (ca. 0.00008 mole) was weighed in with the urea. The closed flask was placed in the dry box and 75 ml. of chlorobenzene was

added. In a 50-ml. Erlenmeyer flask was placed 25 ml. of 0.4*M* phenyl isocyanate in chlorobenzene. The two flasks were placed in a thermostat at  $60.3 \pm 0.2^\circ\text{C}$ . for about 35 min. before mixing. The reaction flask was connected from the short condenser to a large calcium chloride drying tower attached to a balloon of dry nitrogen. The two solutions were then quickly mixed, giving 100 ml. of reaction mixture now 0.05*M* in urea, 0.09*M* in isocyanate, and ca. 0.0008*M* in butyltin trichloride. The first 5-ml. aliquot, withdrawn within 1 min. of mixing, was used to find the concentration of isocyanate at zero time. The aliquots were quenched with 5 ml. of 0.17*M* di-*n*-butylamine in tetrahydrofuran and titrated with 0.05*M* hydrochloric acid solution. The reaction flask was shaken periodically by hand during the 3–5 hr. period of reaction.

The procedure for studying the rate of decomposition of 3,5-diphenyl-1,1-pentamethylenebiuret was analogous to the above, except that a chlorobenzene solution of the catalyst was not added to the biuret until the moment of starting the reaction.

### Reagents

Phenyl isocyanate, dried over phosphorus pentoxide, was distilled under reduced pressure and stored in small bottles inside a container with silica gel, all kept in the dry box. Other reagents and solvents were purified by standard procedures. Dioxane, after the usual treatment,<sup>18</sup> was distilled from sodium, then from lithium aluminum hydride. Vapor chromatography showed only one peak.

### Tin Compounds

Butyltin trichloride, obtained from M and T Chemicals as a pale straw-colored liquid, was purified to water white by distillation, b.p.  $97\text{--}98^\circ\text{C}/8$  mm. (lit.:<sup>19</sup>  $94^\circ\text{C}/10$  mm.) It was stored in a desiccator, as were the others. Dibutyltin dichloride (Matheson, Coleman and Bell) was distilled, b.p.  $107^\circ\text{C}/0.5$  mm. (lit.:<sup>19</sup>  $104\text{--}108^\circ\text{C}/0.7$  mm.) giving crystals, m.p.  $40.5^\circ\text{C}$ . Tributyltin chloride (Matheson, Coleman and Bell) was distilled, b.p.  $98\text{--}99.5^\circ\text{C}/0.5$  mm.

Dibutyltin dilaurate (T-12), obtained from M and T Chemicals as a straw-colored liquid, was used directly. Dibutyltin diacetate (Matheson, Coleman and Bell) was distilled prior to use and was of analytical purity, b.p.  $147^\circ\text{C}/8$  mm.,  $n_D^{20}$ , 1.4723 (lit.:<sup>20</sup> b.p.  $142\text{--}145^\circ\text{C}/10$  mm.,  $n_D^{20}$ , 1.5142). Fisher certified anhydrous stannic chloride was used directly.

Tetraethyltin, trimethyltin chloride, and trimethyltin bromide samples, obtained from the du Pont Jackson Laboratory, were used directly.

Triethyltin fluoride was prepared by the reaction of triethyltin bromide and potassium fluoride.<sup>21</sup>

### Ureas

The ureas were generally prepared by adding the isocyanate to a slight excess of the amine in dry benzene or ether. All were recrystallized to

analytical purity. One new urea was 3-*p*-methoxyphenyl-1,1-pentamethyleneurea, m.p. 125–126°C., from ethanol.

ANAL. Calcd. for  $C_{12}H_{13}N_2O_2$ : C, 66.64%; H, 7.71%. Found: C, 66.29%; H, 7.60%.

1-Benzoyl-3,5-diphenylurea<sup>22</sup> was prepared in 31% yield from *N*-phenylbenzamide and phenyl isocyanate with stannic chloride by the method used for the biurets.

### Biurets

The stannic chloride-catalyzed reaction of ureas with isocyanates was used to prepare biurets; one typical case is described. New compounds are listed in Table V. Known biurets prepared in analytical purity by this method include 1,3,5-triphenylbiuret (67%), m.p. 148–149°C. (lit.<sup>5</sup> 147–148°C.); 1-phenyl-3,5-di-*p*-tolylbiuret (74%), m.p. 145–146°C. (lit.<sup>6</sup> 140°C.); 1-methyl-1,3,5-triphenylbiuret (74%), m.p. 136–137°C. (lit.<sup>23</sup> 133°C.); and 1,3-diphenyl-5-*p*-tolylbiuret (54%), m.p. 128–129°C. (lit.<sup>6</sup> 214–216°C.). The difference from the literature in melting point of the last compound should be noted.

**3,5-Diphenyl-1,1-pentamethylenebiuret.** A solution of 10 g. (0.049 mole) of 1,1-pentamethylene-3-phenylurea, 100 ml. of anhydrous benzene, 5 ml. of anhydrous stannic chloride, and 6 g. (0.05 mole) of phenyl isocyanate was stirred at room temperature for about 12 hr. The heavy white precipitate, which was washed with hexane consisted of 35 g. of the 1:1 biuret-stannic chloride complex, m.p. 185–188°C. (dec.).

ANAL. Calcd. for  $C_{19}H_{21}N_3O_2 \cdot SnCl_4$ : C, 39.08%; H, 3.63%; N, 7.19%; Cl, 24.29%. Found: C, 39.61%; H, 3.85%; N, 7.13%; Cl, 23.80%.

The complex was converted to the free biuret by dissolving it in ethanol and pouring the solution into one liter of water in a Waring Blendor. The resulting precipitate was recrystallized from methanol until the filtrate gave a negative test for chloride ion. The yield of the biurets was lowered by the recrystallization needed to remove adhering stannic chloride.

### Complexes of Ureas with Stannic Compounds

**$3(C_6H_5NH)_2CO \cdot 2SnCl_4$ .** A mixture of 1.0 g. of 1,3-diphenylurea, 20 ml. of benzene, and 5.0 g. of anhydrous stannic chloride was stirred at room temperature (with exclusion of moisture) for 2 days. After removal of volatile materials by vacuum and washing the residue with dry petroleum ether, 1.7 g. (a 31% yield) of the solid complex was obtained, m.p. 155–157°C. (dec.).

ANAL. Calcd. for  $C_{39}H_{39}N_6O_3Sn_2Cl_8$ : C, 40.45%; H, 3.13%; N, 7.25%; Cl, 24.50%. Found: C, 39.88%; H, 3.30%; N, 6.94%; Cl, 24.47%.

Three preparations gave the same substance, which had a lower melting point than the 3:2 complex reported by Baker and Holdsworth<sup>5</sup> (m.p. 251–220°C., dec.). However, when the white product was isolated after

TABLE V  
 New Biurets

Biuret	Molecular formula	Yield, %	Calculated			Found			M.p. (obs.), °C.
			C, %	H, %	N, %	C, %	H, %	N, %	
3,5-Diphenyl-1,1-pentamethylene-5-phenyl-3- <i>p</i> -tolyl-1,1-pentamethylene-	$C_{19}H_{21}N_3O_2$	61	70.57	6.55	12.98	70.62	6.54	12.93	135-135 <sup>a</sup>
ene-	$C_{20}H_{22}N_3O_2$	69	71.19	6.87	12.45	70.89	6.97	12.48	118 <sup>a</sup>
3- <i>p</i> -Methoxyphenyl-5-phenyl-1,1-pentamethylene-	$C_{20}H_{22}N_3O_3$	54	67.97	6.56	11.89	67.75	6.65	12.07	110-111 <sup>b</sup>
3- <i>p</i> -Chlorophenyl-5-phenyl-1,1-pentamethylene-	$C_{19}H_{20}N_3O_2Cl$	68	63.78	5.63	11.74	63.95	5.85	11.80	135-136 <sup>c</sup>
3- <i>p</i> -Nitrophenyl-5-phenyl-1,1-pentamethylene-	$C_{19}H_{20}N_4O_4$	83	61.95	5.47	15.22	61.75	5.48	15.38	110-111 <sup>d</sup>
3-Phenyl-5- <i>p</i> -tolyl-1,1-pentamethylene-	$C_{20}H_{22}N_3O_2$	55	71.19	6.87	12.45	71.42	6.87	12.36	120-122 <sup>e</sup>
5- <i>p</i> -Nitrophenyl-3-phenyl-1,1-pentamethylene-	$C_{19}H_{20}N_4O_4$	31	61.95	5.47	15.22	61.04	5.64	15.72	130-131 <sup>a</sup>
3- <i>n</i> -Butyl-5-phenyl-1,1-pentamethylene-	$C_{17}H_{26}N_3O_2$	32	67.08	8.61	13.80	67.37	8.14	13.96	79-80 <sup>e</sup>
1,1-Di- <i>n</i> -butyl-3,5-diphenyl-	$C_{22}H_{28}N_3O_2$	78	71.91	7.95	11.43	72.21	8.08	11.50	Viscous liquid <sup>f</sup>

<sup>a</sup> Recrystallized from methanol.

<sup>b</sup> From methanol-petroleum ether (60-75°C.).

<sup>c</sup> From ethanol-petroleum ether.

<sup>d</sup> From acetone-pentane.

<sup>e</sup> From petroleum ether.

<sup>f</sup> Product was dissolved in ether, dried over magnesium sulfate, and the ether evaporated to give pure material,  $n_D^{25}$  1.5564.

only 2 hr. of stirring, the melting range was 60–65°C. and the composition indefinite.

This 3:2 diphenylurea-stannic chloride complex was converted quantitatively to the 1,3,5-triphenylbiuret-stannic chloride complex (1:1) by stirring with phenyl isocyanate in benzene.

$C_5H_{10}NCONHC_6H_5 \cdot C_4H_9SnCl_3$ . A mixture of 0.5 g. of 1,1-pentamethylene-3-phenylurea and excess butyltin trichloride was heated at 60°C. for a short time until a clear, viscous liquid was formed. The excess butyltin trichloride was removed by several triturations with hexane, and the clear viscous residue was vacuum-dried. It slowly crystallized to give 0.9 g. of material melting at 63–64°C. The complex dissociated completely at 80°C.

ANAL. Calcd. for  $C_{16}H_{22}N_2OSnCl_3$ : C, 39.51%; H, 5.18%; mol. wt. 486. Found: C, 39.41%; H, 5.18%; mol. wt. (ebullioscopic in benzene), 511.

### Isocyanate Complex with Butyltin Trichloride

Evidence for a complex between phenyl isocyanate and butyltin trichloride was obtained when the two components (1:1 molar ratio) gave a precipitate when placed in spectro grade *n*-hexane and cooled below room temperature with Dry Ice. Control tests on phenyl isocyanate in hexane and butyltin trichloride in hexane, each boiled for 1 hr. and then similarly cooled, produced no precipitate. This material melted at 86–90°C. The infrared spectrum was unlike either that of the components. No analysis was obtained.

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### Résumé

Les vitesses initiales ont été déterminées pour la réaction équilibrée du second ordre de l'isocyanate de phényle avec une série de dérivés aromatiques substitués de la 1,1-pentaméthylène-3-phényl urée en présence de trichlorure de butylétain comme catalyseur dans le chlorobenzène à 60°. Ces résultats sont comparés avec les vitesses de réaction de l'isocyanate de phényle avec la 1,1-di-*n*-butyl-3-phénylurée, la 1,3-diphényl-1-méthylurée, la *N*-phénylbenzamide, la méthyl-*N*-phénylcarbamate et le 1-butanol. L'énergie d'activation pour la réaction, catalysée par le trichlorure de butylétain, de l'isocyanate de phényle et 1,1-pentaméthylène-3-phényl-urée était de 12 Kcal/mole. A 60° cette réaction est à peu près 11 fois plus rapide que la réaction inverse. La vitesse de la réaction de l'isocyanate de phényle et de la 1,1-pentaméthylène-3-phénylurée est directement proportionnelle à la concentration en trichlorure de butylétain. L'activité de ce catalyseur est 28 fois plus grande que celle du chlorure de triéthylétain. Le dilaurate de dibutylétain, le diacétate de dibutylétain, le dichlorure de dibutylétain, le chlorure de tributylétain, le tétraméthylétain, le bromure de triméthylétain, le fluorure de triéthylétain et la 1,2,4-triméthylpipérazine, ne sont pas des catalyseurs pour ces réactions. Les urées forment des complexes solides avec le chlorure stannique et avec le trichlorure de butylétain dans lesquels les dérivés de l'étain sont coordonnés à l'oxygène du carbonyle. Un mécanisme de réaction a été avancé, mécanisme qui comprend une attaque nucléophile de l'urée sur l'isocyanate par l'intermédiaire d'un complexe ternaire. Les réactions des urées avec les isocyanates catalysés par le chlorure stannique, à température normale, connaissent un grand domaine d'application.

### Zusammenfassung

Die Anfangsgeschwindigkeit für die Gleichgewichtsreaktion zweiter Ordnung zwischen Phenylisocyanat und einer Reihe von phenyl-substituierten 1,1-Pentamethylen-3-Phenylharnstoff en in Gegenwart eines Butylzintrichloridkatalysators wurde in Chlorbenzol bei 60°C bestimmt. Die Ergebnisse wurden mit der Geschwindigkeit der Reaktion von Phenylisocyanat mit 1,1-Di-*n*-butyl-3-phenylharnstoff, 1,3-Diphenyl-1-methylharnstoff, *N*-Phenylbenzamid, Methyl-*N*-phenylcarbamat und 1-Butanol verglichen. Die Aktivierungsenergie für die butylzintrichlorid-katalysierte Reaktion zwischen Phenylisocyanat und 1,1-Pentamethylen-3-phenylharnstoff betrug 12 Kcal pro Mol. Bei 60° war diese Reaktion ungefähr elf Mal so rasch als die Reaktion in umgekehrter Richtung. Die Geschwindigkeit der Reaktion zwischen Phenylisocyanat und 1,1-Pentamethylen-3-phenylharnstoff war der Butylzinnkonzentration direkt proportional. Die Aktivität dieses Katalysators war 28 Mal so gross als diejenige von Triäthylzinchlorid. Dibutylzindilaurat, Dibutylzinndiacetat, Dibutylzinndichlorid, Tributylzinchlorid, Tetramethylzinn, Trimethylzinnboimid, Triäthylzinnfluorid und 1,2,4-Trimethylpiperazin bildeten keine Katalysatoren für diese Reaktion. Die Harnstoffe bildeten mit Zinnchlorid und mit Butylzintrichlorid feste Komplexe, in welchen die Zinnverbindungen an der Karbonylsauerstoff koordinativ gebunden waren. Es wird ein Reaktionsmechanismus vorgeschlagen, bei welchem ein nukleophiler Angriff des Harnstoffs auf das Isocyanat durch einen ternären Zwischenkomplex angeommen wird. Es wird gezeigt, dass die zinnchlorid-katalysierte Reaktion vom Harnstoffen mit Isocyanaten bei Raumtemperatur einen weiten Anwendungsbereich besitzt.

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