Fig. 9. Plasma residence time dependence of fluorine to carbon ratio (F/C) of fluorinated high-density polyethylene prepared by CF_3H glow discharge (vertical placement).

this still does not explain why only the CF_3H provides extraction resistant grafting in vertical position. Glow discharge chemistry of multiatomic molecules are still too complex to explain this unexpected behavior; nevertheless, it is an excellent method to obtain extraction resistant fluorocarbon surfaces.

CONCLUSIONS

It was found that extraction-resistant fluorocarbon surfaces can be obtained in an electric glow discharge using simple saturated fluorocarbons as starting materials. The presence of chlorine and bromine in the starting materials appears to be undesirable, since the grafting is not limited to fluorocarbon radicals, although more readily available fluorobromocarbons might be useful, since only a small amount of bromine is grafted to the surface. The starting materials do not necessarily have to be perhalogenated compounds, although high fluorine content is desirable. The success with CF_3H indicates that the presence of one hydrogen at the end of the fluorocarbon chain might be beneficial. It is further evident that care should be used to decide the location of the sample in the glow discharge and residence time in the glow is an important factor.

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Catalysis of the Reaction between Isocyanates and Protonic Substrates. II. Kinetic Study of the Polyurea Foaming Process Catalyzed by a Series of Amino Compounds
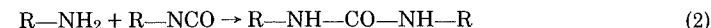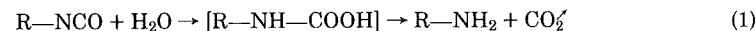
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Synopsis

The catalytic activity of secondary and tertiary amines were determined in the reaction of phenyl isocyanate with water and aniline, respectively, in dioxane at 25°C. The polyurea formation is largely controlled by a base-type catalysis. However, this general behavior can be perturbed by steric factors, and still more obvious deviations appear with protic catalysts reacting rapidly with the isocyanate. The resulting urea or urethane groups can display a significant activity in relation to the nature and the composition of the reaction medium. Very good quality foams can be obtained with these protic catalysts.

INTRODUCTION

Polymeric foams have been a major progress in the development of insulating materials. Polyurethanes and polyisocyanurates are suitable for that application, but, since a few years ago, increasing attention is paid to polyureas. Their synthesis only requires a polyfunctional isocyanate and water, and furthermore the carbon dioxide evolving during the reaction favors a spontaneous foaming. The mechanism and the catalysis of polyurea formation is unfortunately poorly understood. The scheme of the reaction is a two-step process consisting of a foaming reaction [eq. (1)] followed by polymerization [eq. (2)].

$$R\text{—}NCO + H_2O \rightarrow [R\text{—}NH\text{—}COOH] \rightarrow R\text{—}NH_2 + CO_2' \qquad (1)$$

$$R\text{—}NH_2 + R\text{—}NCO \rightarrow R\text{—}NH\text{—}CO\text{—}NH\text{—}R \qquad (2)$$

The balance of foaming and polymerization deeply affects the quality of the polyurea foams. The proper adjustment of the two reactions requires the study of their kinetics, and of their activation by secondary and tertiary amines, which are recognized as effective catalysts.[1] A previous investigation has demonstrated a synergistic effect between amines and metal salts; these new catalytic combinations offer a large versatility in defining suitable formulations.[2]

The overall objective of this study is to explore the kinetics of both phenyl isocyanate–water and phenyl isocyanate–aniline model reactions catalyzed by amines in dioxane at 25°C. These results will be extended to the industrial foaming conditions. The tested catalysts are gathered in Table I with their molecular structure.

EXPERIMENTAL

Products

Solvents, reagents, and catalysts were purified before use.

Tetramethylguanidine (TMG), N,N,N'',N''-tetramethyl-N'-phenylguanidine (TMPG) and tris(dimethylaminomethyl)phenol (DMP) were distilled under reduced pressure. Diazabicyclo[2,2,2]octane (DABCO) and 2-methylimidazole (2MI) were recrystallized from benzene. Aniline, pyridine (Py), diethylamine (DEA), 2 (β-methylaminoethyl)pyridine (MAEP), N,N-dimethylbenzylamine (DB), 2,2′-oxy-bis(N,N-dimethylethylamine) (DMEA), triethylamine (NEt$_3$) and N-ethylmorpholine (NEM) were refluxed over calcium hydride and distilled before use. Dioxane and phenyl isocyanate were refluxed over sodium and calcium hydride, respectively; they were recovered by distillation. Water was refluxed over potassium permanganate and distilled twice. Tris(2-chloroethyl)

TABLE I
The Amine Catalysts and Their Molecular Structure

DABCO	Diazabicyclo[2,2,2]octane	
DB	N,N-dimethylbenzylamine	$-CH_2-N(CH_3)_2$
DEA	Diethylamine	$H-N(CH_2-CH_3)_2$
DMEA	2,2′-Oxy-bis-(N,N dimethylethylamine)	$(CH_3)_2N\diagdown\diagup^O\diagdown\diagup N(CH_3)_2$
DMP	Tris(dimethylaminomethyl) phenol	
MAEP	2(β-methylaminoethyl) pyridine	
2MI	2-Methylimidazole	
NEM	N-Ethylmorpholine	
NEt$_3$	Triethylamine	$N(CH_2-CH_3)_3$
Py	Pyridine	
TMG	Tetramethylguanidine	$H-N=C\diagup^{N(CH_3)_2}_{\diagdown N(CH_3)_2}$

phosphate (TCEP) was added in pentane and refluxed in a Soxhlet apparatus, the thimble of which contained calcium hydride. The water–pentane azeotrope was continuously circulated over the dehydrating agent, allowing the ultimate drying of TCEP.

Crude diphenylmethane-4,4′-diisocyanate (MDI) containing about 31.5 wt % of isocyanate, TCEP, and the amine catalysts were kindly supplied by Recticel, Division of P.R.B., Wetteren, Belgium.

Kinetics of the Phenyl Isocyanate–Water Reaction

This model reaction was carried out at 25°C in a three-necked flask and equipped with a mechanical stirrer, a dropping funnel, and thermometer. 100 mL of 1 mol/L phenyl isocyanate solution in dioxane were introduced in the reaction flask. Only 50 mL were used when an excess of water reacted with phenyl isocyanate. The catalyst and water were dissolved together in dioxane, adjusting the total volume of solvent to 200 mL in the reaction medium. The solution containing catalyst and water was introduced in the dropping funnel maintained at 25°C and then quickly added into the isocyanate solution. The whole mixture was thoroughly mixed with a magnetic stirrer. Samples (10 mL) were regularly withdrawn from the reaction medium and added into a known amount of dibutylamine (DBA) dissolved in dioxane (0.3 mol/L). The excess of DBA was determined by potentiometry with a standard hydrochloric acid solution (0.1 mol/L). The catalyst concentration was adjusted so that a ca. 20% conversion was obtained after about 1 h. Kresta et al. have previously established the kinetic equation when phenyl isocyanate and water react in equimolar amounts[3]:

$$\frac{1}{a}\ln\frac{a-x}{a-2x} = k_{exp}\cdot t \tag{3}$$

a is the initial concentration of both reagents, whereas $2x$ is the concentration of phenyl isocyanate consumed at time t. k_{exp} is the experimental second-order rate constant obtained from the slope of the straight line $\{(1/a)\ln(a-x)/(a-2x)]$ $vs.\ t\}$ observed for all the catalysts herein tested, except for TMG. When a large excess of water is used, its effective concentration is practically constant, and eq. (3) becomes

$$\frac{1}{a}\ln\frac{a}{a-2x} = k'_{exp}\cdot t \tag{4}$$

where $k'_{exp}/[H_2O]_i = k_{exp}$ and $[H_2O]_i$ is the initial concentration of water. In the presence of TMG, $\{\ln[a/(a-2x)]$ vs. $t\}$ is a straight line which enables the calculation of k_{exp}.

When phenyl isocyanate and water react in nonequimolar amounts, the kinetic equation is

$$\frac{1}{a-2b}\ln\frac{b}{a}\frac{a-2x}{b-x} = k_{exp}\cdot t \tag{5}$$

a and b being the initial concentrations of phenyl isocyanate and water, respectively, while x is the concentration of diphenylurea formed at time t.

As the order in amine catalyst is known to be 1,[3] eq. (6) can be proposed

$$k_{exp} = k_0 + k_C[C] \tag{6}$$

where [C] is the catalyst concentration and k_C the catalytic rate constant, whereas k_0 is determined from the uncatalyzed reaction. This k_C value will be determined for the catalysts mentioned in Table I.

Kinetics of the Phenyl Isocyanate–Aniline Reaction

The kinetic study of this second model reaction was performed under the same conditions as before. 150 mL of the 0.1 mol/L phenyl isocyanate solution in dioxane were added into a 500-mL three-necked flask. The dropping funnel was filled with 15 mL of 1 mol/L aniline solution, and 30 mL of 0.1 mol/L catalyst solution, both in dioxane, and with 105 mL of pure dioxane, respectively. 20-mL samples were regularly withdrawn from the reaction medium, added into 20 mL of 0.08 mol/L DBA solution in dioxane. The excess of DBA was titrated with 0.05 mol/L hydrochloric acid solution, the previous addition of a small amount of water being recommended.

It is well known that the phenyl isocyanate–aniline reaction is self-activated by the diphenylurea formed and the unreacted aniline.[4-6] The kinetic behavior is described by

$$\frac{d[U]}{dt} = [k_s + k_A[A] + k_U[U] + k_C[C]][I][A] \qquad (7)$$

k_s is the spontaneous rate constant; k_A, k_U and k_C are the specific rate constants for aniline, urea, and catalyst. [I], [A], [U], and [C] are the concentrations of isocyanate, aniline, urea, and catalyst, respectively. The values of k_A (1.6 L^2 · mol^{-2} · min^{-1}) and k_U (5.5 L^2 · mol^{-2} · min^{-1}) were determined by Erdmann and Schwetlick[4] in the same conditions as ours. The catalytic effect of both aniline and diphenylurea is assumed to be constant up to 20% of conversion; eq. (7) is accordingly simplified to

$$\frac{d[U]}{dt} = [k_0 + k_C[C]][I][A] = k_{exp}[I][A] \qquad (8)$$

where k_0 is a pseudoconstant characteristic of the uncatalyzed reaction. By integrating eq. (8), there results:

$$\frac{1}{b-a} \ln \frac{b}{a} \frac{b-x}{a-x} = k_{exp} \cdot t \qquad (9)$$

a and b being the initial concentrations of isocyanate and aniline, respectively, and x the diphenylurea concentration at time t. When $a = b$, eq. (9) is transformed into

$$\frac{1}{a-x} - \frac{1}{a} = k_{exp} \cdot t \qquad (10)$$

k_{exp} is easily obtained from eq. (9) or (10), and k_C is finally calculated from eq. (6) or (8).

Kinetics of the Polyurea Formation

In order to study the kinetics of polyurea formation under the conditions of industrial production, CO_2 evolution was monitored by a device previously de-

scribed.[2] The standard formulations used were based on: crude MDI (100 parts), water (20–40 parts), TCEP (30–50 parts), and catalyst.

Foaming was tested on a reduced scale by pouring the reactive formulation into a cubic brown-paper box (15 cm side) lined with polyethylene foil.[2]

Basicity of the Amine Catalyts in Dioxane

This parameter was inferred from the titration curve with hydrochloric acid: pK_a = pH at half-neutralization. These curves were recorded with a Metrohm Herisau pH meter E 603, multidosimat E 415 and impulsomat E 473. As the conductivity in pure dioxane was too low, the measurements took place in a medium of 5 mL of 0.2 mol/L catalyst solution in dioxane, 45 mL of dioxane and 5 mL of water, respectively. A 0.1 mol/L hydrochloric acid solution in water was used as titrating agent. As far as pyridine is concerned, the corresponding hydrochloride was titrated with KOH according to the same procedure.

Partition Coefficient of the Catalysts between TCEP and Water

$K_p = [C]_{TCEP}/[C]_{H_2O}$. Equal volumes (50 mL) of TCEP and catalyst solution in water were vigorously stirred together at 25°C, for 15 min. After complete phase separation, 10 mL of each phase were withdrawn and titrated with HCl standard solutions in water. It was ascertained that these results were not affected by further stirring of the nonmiscible system.

RESULTS AND DISCUSSION

Kinetics of the Model Reactions of Phenyl Isocyanate with Water and Aniline Respectively, in Dioxane at 25°C

The catalytic rate constants (k_C) of the phenyl isocyanate water reaction was measured for a series of amine catalysts and reported in Table II in the order of decreasing values. A rather good correlation appears between the activity of the catalysts and their basicity measured in dioxane at 25°C: the higher the pK_a of the catalyst, the higher its activity. The reaction of isocyanate with water would accordingly be sensitive to a base-type catalysis. The few disagreements noted in the dependence of k_C on pK_a can furthermore be explained individually.

On the basis of its pK_a, DABCO displays a too high catalytic rate constant. This observation agrees with the high catalytic activity of DABCO reported in the literature, and explained in terms of its very low steric hindrance.[5-7]

TMG has a surprising low activity with respect to its basicity. The secondary imino group of TMG is responsible for an instantaneous reaction with phenyl isocyanate (in less than 15 s, as experimentally observed), and the urea formed is accordingly the efficient catalyst [eq. (11)]. When TMG is
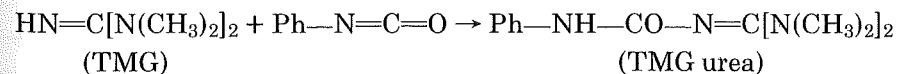
$$HN=C[N(CH_3)_2]_2 + Ph—N=C=O \rightarrow Ph—NH—CO—N=C[N(CH_3)_2]_2$$
$$\text{(TMG)} \qquad\qquad\qquad\qquad\qquad \text{(TMG urea)}$$

$$(11)$$

TABLE II
Catalytic Rate Constants of the Phenyl Isocyanate–Water Reaction in Dioxane at 25°C: $[PhNCO]/[H_2O] = 1/1^a$

Catalyst	$[catalyst] \times 10^3$ (mol/L)	k_C ($L^2 \cdot mol^{-2} \cdot min^{-1}$)	pk_a
DMEA	0.25	11.20	8.50
DABCO	2.50	3.95	7.05
TMG[b]	10.00	1.45	11.30
NEt₃	5.00	0.90	7.60
DMP	1.00	0.45	7.05
DB	25.00	0.20	6.00
NEM	5.00	0.09	5.50
2MI	35.00	0.07	5.80
Py	25.00	0.04	2.90
DEA urea/Py	25.00	0.04	
MAEP urea	25.00	0.02(5)	~2.50
DEA urea	25.00	0.005	~3.00

[a] $[Ph—NCO] = [H_2O] = 0.5$ mol/L; $k_0 = 8.5 \times 10^{-4}$ L·mol⁻¹·min⁻¹.

[b] k_c of TMG has been determined by using a 10-fold excess of water (see experimental part).

added into phenyl isocyanate 2-(N-phenylcarbamoyl)-1,1,3,3-tetramethylguanidine (or TMG urea) is indeed recovered and identified by IR spectroscopy (Table III). This compound is, however, unstable at a higher temperature, as evidenced by its transformation into 1,1,3,3-tetramethyl-2-phenylguanidine (TMPG) when analyzed by mass spectrometry through the temperature range from 70°C to 230°C:

$$Ph—NH—CO—N=C[N(CH_3)_2]_2 \xrightarrow{\Delta} Ph—N=C[N(CH_3)_2]_2 \quad (12)$$
$$(TMPG)$$
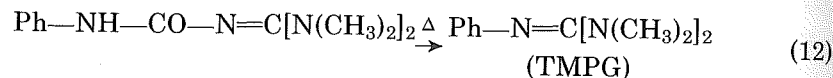
The main compound observed in the mass spectrum has actually a mass of 191, and it is identical to TMPG synthesized separately[8,9] and characterized by IR and mass spectrometry. Surprisingly, TMG urea and TMPG exhibit the same catalytic rate constant (1.45 $L^2 \cdot mol^{-2} \cdot min^{-1}$) whereas their pK_a are 8.85 and 9.9, respectively. Thus basicity is not the only parameter which controls the catalytic activity of 1,1,3,3-tetramethylguanidine derivatives. Steric factors could explain the similar but too low activity of the tertiary amines compared to their basicity. Furthermore, the urea group appears to be very poorly active, if not at all.

TABLE III
Main I—R Absorptions of Guanidine Derivatives

	H—N = C[N(CH₃)₂]₂ (TMG)	$\overset{O}{\overset{\|}{Ph—NH—C—N=C[N(CH_3)_2]_2}}$ (TMG urea)	Ph—N = C[N(CH₃)₂]₂ (TMPG)
—Nl=C<	1 600 cm⁻¹	1 680 cm⁻¹	1 570 cm⁻¹
O=C<		1 630 cm⁻¹	

The 2MI molecule contains also a tertiary and a secondary amine. The apparent inversion between NEM (pK_a 5.5) and 2MI (pK_a 5.8) could be explained by the "in situ" formation of the less-basic 2MI urea ($pK_a < 5.8$, although it is difficult to determine accurately).

Similarly, both MAEP (pK_a 8.5) and DEA (pK_a 8.6) have a secondary amino group in their structure, and the corresponding ureas are expected as the operative catalysts. Thanks to its additional tertiary amine, MAEP urea is more active than DEA urea. MAEP urea combines the molecular characteristics of DEA urea and pyridine (Table I), but it is less active than the stoichiometric combination of DEA urea and pyridine.

The catalytic rate constants of the phenyl isocyanate–aniline reaction are gathered in Table IV. The dependence of k_C on the basicity of the catalyst is less straightforward than in Table II. However, as aniline is more hindered than water, the reaction of phenyl isocyanate with aniline is expected to be more dependent on steric effects. Accordingly, DABCO, which exhibits a very low steric hindrance, displays now a still more surprisingly high activity according to its basicity. The increase of the relative catalytic activity of 2MI, i.e., of 2MI urea, can similarly be explained by the easier approach of the tertiary amine. In the same respect, it is noteworthy that the activity of hindered catalysts, such as NEt₃ and TMG urea, is significantly depressed. These observations are consistent with the results published by de Aguirre on the catalysis of the phenyl isocyanate–N-methylaniline reaction.[5,6]

DEA urea is inactive in this phenyl isocyanate–aniline reaction, whereas the catalytic activity of the MAEP urea and of a stoichiometric combination of DEA urea and pyridine is comparable but higher than that of pyridine. This DEA urea–pyridine combination is accordingly responsible for a synergic effect in the reaction of phenyl isocyanate with aniline (Table IV) but not with water (Table II).

From the catalytic rate constants of phenyl isocyanate reaction with water (Table II) and aniline (Table IV), respectively, it can be concluded that the first step of the catalyzed polyurea formation [eq. (1)] is rate-determining.

TABLE IV
Catalytic Rate Constants of the Phenyl Isocyanate–Aniline Reaction in Dioxane at 25°C[a]

Catalyst	k_C ($L^2 \cdot mol^{-2} \cdot min^{-1}$)	pk_a
DABCO	395.0	7.05
DMEA	276.0	8.50
TMG	57.0	11.30
DMP	55.2	7.05
2MI	42.5	5.80
NEt₃	33.3	7.60
DB	21.2	6.00
NEM	19.3	5.50
DEA urea/Py	6.1	—
MAEP urea	6.0	~2.50
Py	3.60	2.90
DEA urea	—	~3.00

[a] $[PhNCO] = [Ph—NH_2] = 0.05$ mol/L, $[C] = 10^{-2}$ mol/L, $k_0 = 5.5 \times 10^{-2}$ L·mol⁻¹·min⁻¹.

The Influence of Solvent and Excess Water on the Catalytic Rate Constants

Industrial production of polyurea foams requires the exclusion of organic solvents. However, the course of the reaction can be modified by additives, which improve the properties of the end product. As an example, trichloroethyl-phosphate (TCEP) can be used as an emulsifying agent, a plasticizer, and a fire-resistance improver. Furthermore, an excess of water is recommended to control the temperature rise during the polyurea formation; its vaporization is indeed a heat-consuming process. In order to gain meaningful information on the catalysis of the reaction proceeding in actual conditions, the influence of both the reaction stoichiometry and the nature of reaction medium on the rate-determining step are to be considered.

The catalytic rate constants are systematically higher in TCEP than in dioxane (Table V). The dielectric constant (ϵ) of dioxane at 25°C is rather low ($\epsilon = 2.2$), whereas that of TCEP is expected to be much higher [ϵ is indeed 7 at 40°C for tricresylphosphate ($C_{21}H_{21}O_4P$) and 30 at 25°C for hexamethylphosphotriamide [$(CH_3)_2$—N]$_3$ P(O)]. Furthermore, TCEP is recognized as a specific solvating agent for cations.[10] In that respect, the catalysis of the ioscyanate–water reaction by tertiary amines is currently described below, where the activation of the isocyanate by the amine would be the rate-determining step[11]:

$$Ph—N=C=O + \,|N\!\!<\; \longrightarrow \; Ph—N=C—\overline{O}|^{\ominus} \xrightarrow{+H_2O}$$

$$[I]$$

$$Ph—NH—COOH \; + \; |N\!\!< \quad (13)$$
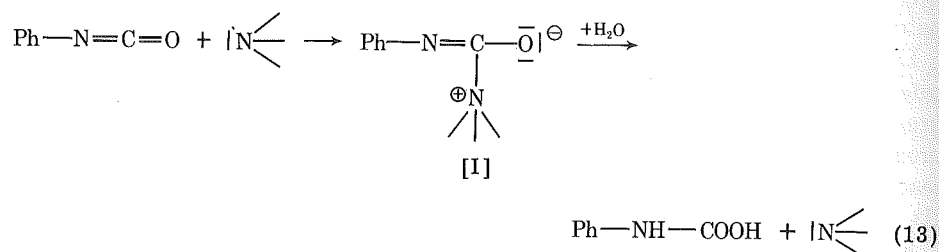
By solvating the cation of intermediate [I], TCEP could stabilize this species and favor its formation. Furthermore, the effect of TCEP (Table V) is significantly more pronounced for both DMP and 2MI.

Table VI summarizes the effect of a moderate excess of water on the phenyl isocyanate–water reaction in dioxane. Except for DMP and 2MI, the activity of the tested catalysts remains unchanged as the water–isocyanate stoichiometry

TABLE V
Catalytic Rate Constants of the Phenyl Isocyanate–Water Reaction in TCEP at 25°C: [PhNCO]/[H$_2$O] = 1/1[a]

| Catalyst	[C] × 10³ (mol/L)	k_C (TCEP) (L²·mol⁻²·min⁻¹)	$\dfrac{k_C \text{ (TCEP)}}{k_C \text{ (diox)}}$
DMEA	0.025	74	6.6
DABCO	0.25	16	4.0
N(Et)$_3$	0.33	6.7	7.4
DMP	0.20	6.5	14.8
DB	2.50	1.4	7.8
2MI	3.00	0.9	12.8

[a] [PhNCO] = [H$_2$O] = 0.25 mol/L, $k_0 = 3.2 \times 10^{-3}$ L·mol⁻¹·min⁻¹.

TABLE VI
Influence of Excess Water on the Catalytic Rate Constants of the Phenyl Isocyanate–Water Reaction in Dioxane at 25°C: [H$_2$O]/[PhNCO] = 2.3[a]

Catalyst	[C] × 10³ (mol/L)	k_C (2.3)	$\dfrac{k_C \text{ (2.3)}}{k_C \text{ (1)}}$
DMEA	1.25	12.20	1.10
DABCO	1.25	3.65	0.95
N(Et)$_3$	5.00	1.00	1.10
DMP	5.00	0.66	1.50
DB	10.00	0.20	1.10
2MI	25.00	0.10	1.40

[a] [PhNCO] = 0.25 mol/L, [H$_2$O] = 0.575 mol/L, $k_0 = 4 \times 10^{-4}$ L·mol⁻¹·min⁻¹.

increases from 1 to 2.3. The simplest way to explain the particular behavior of DMP and 2MI (Tables V and VI) relies upon their ability to react with the isocyanate (eq. 14)

$$Ph—N=C=O + \begin{cases} 2MI \\ DMP \end{cases} \longrightarrow Ph—NH—CO \quad [II]$$

$$(14)$$
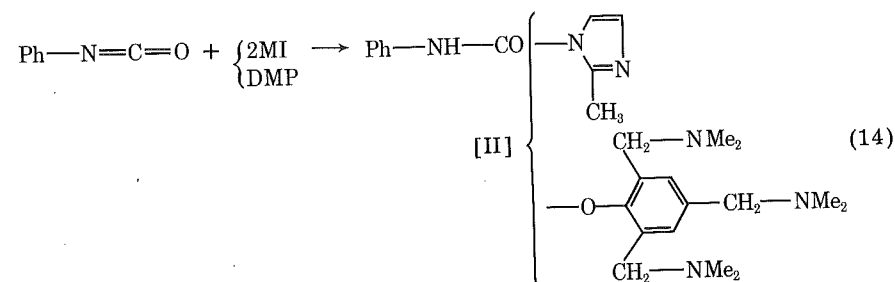
The common NH—CO group of the formed urea (2MI) or urethane (DMP) could display a catalytic activity accounting for the slightly more favorable effect of 2MI and DMP, when used in TCEP (Table V), or in dioxane but with an excess of water (Table VI). In this respect, a concerted mechanism known for its low sensitivity to solvent effects, could be proposed:

$$\longrightarrow Ph—NH—COOH + [II] \quad (15)$$
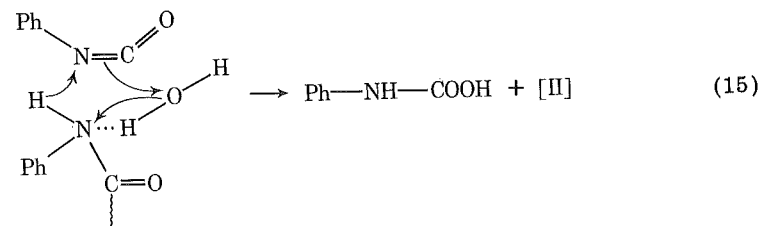
The NH group of the urea or urethane [II] is probably solvated by water, as suggested by the favorable effect of an excess of this compound (Table VI). The proposed reaction scheme would therefore be an operative two-partner mechanism

It is important to outline here the probably excessive value of k_C as reported for TMG in Table II. It has indeed been determined by using a 10-fold excess of water (see Experimental Section); the discrepancy previously discussed in the catalytic behavior of TMG in the phenyl isocyanate–water reaction has accordingly to be still more pronounced.
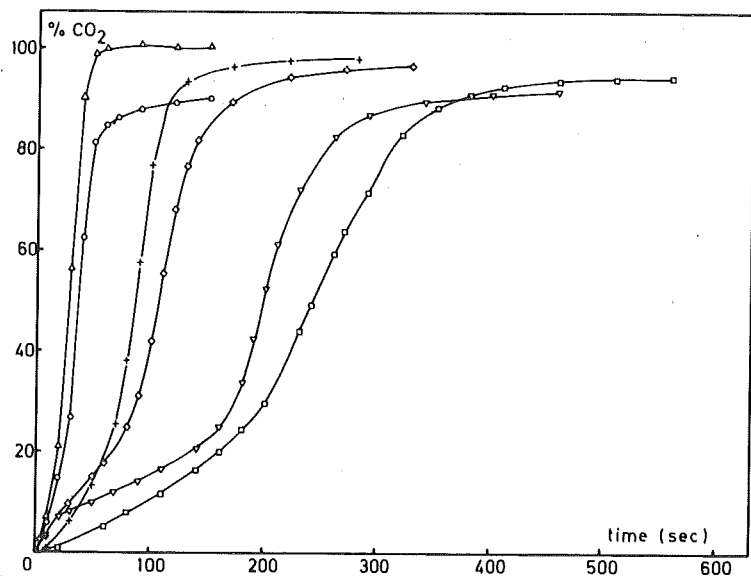
Fig. 1. CO_2 evolution curves: (+) DB; (□) 2MI; (○) TMG; (◇) NEt_3; (▽) DMEA; (△) DMP.

Modelling the Foaming Process

The industrial production of polyurea is based on formulations containing water, a polyfunctional isocyanate and additives like TCEP. The reaction medium is heterophase as water and the organic compounds are nonmiscible. The heat of reaction is hardly dissipated and responsible for a large temperature
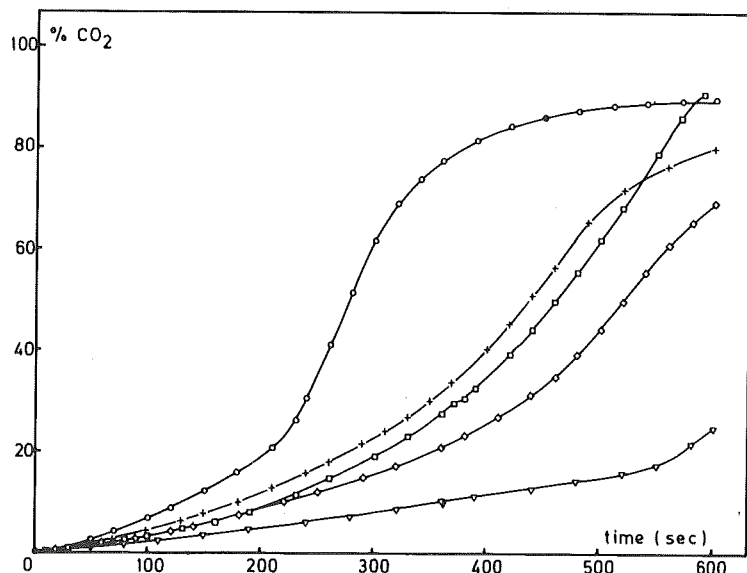

Fig. 2. CO_2 evolution curves: (+) DEA/Py; (□) MAEP; (○) NEM; (◇) Py; (▽) DABCO.

TABLE VII
Pseudocatalytic Rate Constant k_C' of the Polyurea Foaming Process[a]

Catalyst	k_C' (L·mol⁻¹·min⁻¹)	k_C (Table II) (L²·mol⁻²·min⁻¹)
DMEA	1.10	11.20
DABCO	0.06	3.95
TMG	1.55	1.45
NEt_3	0.85	0.90
DMP	1.90	0.45
DB	0.41	0.20
NEM	0.09	0.09
2MI	0.15	0.07
Py	0.05	0.04
DEA urea/Py	0.08	0.04
MAEP urea	0.08	0.02 (5)

[a] 30 mL of water were added to 113 mL of organic phase. The following concentrations are calculated in the organic phase: [C] = 0.11 mol/L, [NCO] = 5.5 mol/L, [TCEP] = 1.32 mol/L, $[H_2O]$ = 0.066 mol/L; 5 g of water are dissolved into 95 g of TCEP.

increase. These conditions are much different from the homogeneous and thermostated systems studied here above. It is therefore necessary to establish whether the conclusions drawn from model systems can be significantly extrapolated to technical conditions or not. For this purpose, the CO_2 produced by industrial-type formulations has been measured as explained in the Experimental Section.

The reaction proceeds in the organic phase[2] wherein the water concentration $[H_2O]_{org}$ remains constant, i.e., at the saturation level. The simplified kinetic equation [eq. (4)] is applicable, whereas the concentration of the phenyl isocyanate converted at any reaction time is easily calculated from the CO_2 evolution curve. k_{exp}' is deduced from the slope of the plot $\{\ln [a/(a - 2x)]$ vs. $t\}$. From eq. (6) and accounting for the very large catalytic effect ($k_0 \ll k_C[C]$, see Table II), it results that

TABLE VIII
Catalysts Partition Coefficient between TCEP and Water $[K_p = [C]_{TCEP}/[C]_{H_2O}]$ at 25°C, and Corrected Pseudocatalytic Rate Constants

Catalyst	K_p	Corrected k_C' (L·mol⁻¹·min⁻¹)	k_C (Table II) (L²·mol⁻²·min⁻¹)
DMEA	0.14	3.00	11.20
DABCO	0.01	1.05	3.95
TMG	∞[a]	1.55	1.45
NEt_3	4.40	0.90	0.90
DMP	∞[a]	1.90	0.45
DB	37.00	0.40	0.20
NEM	0.55	0.15	0.09
2MI	0.85[a]	0.15	0.07
Py	3.40	0.05	0.04
MAEP urea	0.40[a]	0.08	0.02 (5)

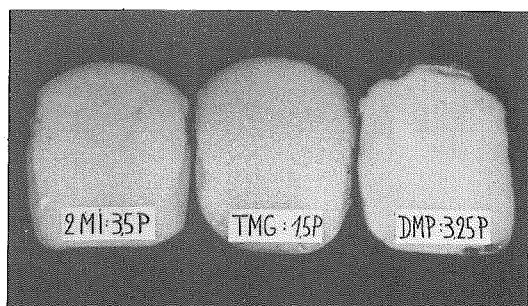[a] Catalyst reacting with the isocyanate and accordingly present in the organic phase.

Fig. 3. Polyurea foams prepared with 2MI, TMG, and DMP as catalysts (parts for 100 parts of MDI are mentioned).

$$k_{\mathrm{exp}} = \frac{k'_{\mathrm{exp}}}{[\mathrm{H_2O}]_{\mathrm{org}}} = k_C \cdot [\mathrm{C}]$$

or

$$k'_{\mathrm{exp}} = k_C \cdot [\mathrm{H_2O}]_{\mathrm{org}} \cdot [\mathrm{C}] = k'_C \cdot [\mathrm{C}] \tag{16}$$

As $[\mathrm{H_2O}]_{\mathrm{org}}$, i.e., the water concentration in the organic phase, is independent of the nature of the catalysts, the catalytic activity can be compared on the basis of the pseudorate constant k'_C which was calculated in the early stages of the reaction, i.e., up to about 20% conversion.

The CO_2 evolution curves are gathered in Figures 1 and 2, whereas the k'_C values are reported in Table VII. It appears that relative activity of the catalysts operating in industrial-type formulations is inconsistent, if not even contradic-
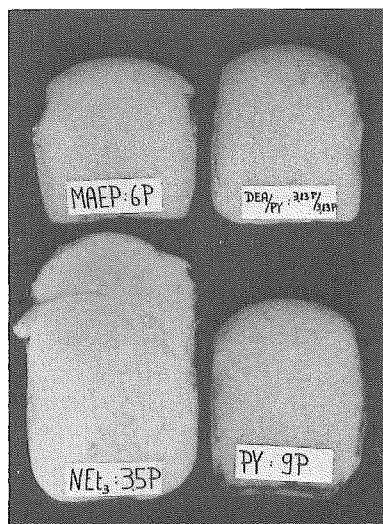

Fig. 4. Polyurea foams prepared with MAEP, DEA/Py, Py, and NEt₃ as catalysts (parts for 100 parts of MDI are mentioned).
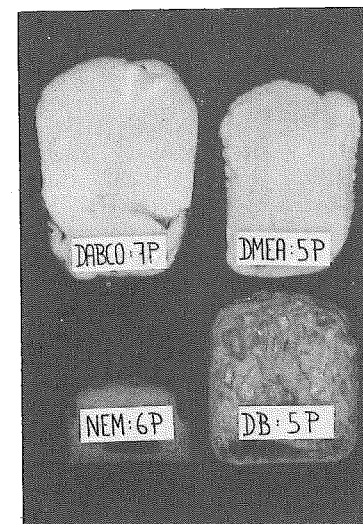
Fig. 5. Polyurea foams prepared with DABCO, DMEA, DB, and NEM as catalysts (parts for 100 parts of MDI are mentioned).

tory, with the data reported (dioxane at 25°C) for the rate-determining step (Table VII). It is, however, to be outlined that the concentration of the catalyst has been calculated assuming that it was completely solubilized in the organic phase. This approximation is suitable for the catalysts (TMG, DMP, 2MI, MAEP) which react spontaneously with the polyfunctional isocyanate (MDI). For the other ones, their effective concentration in the organic phase has been calculated again on the basis of their partition coefficient K_p between water and TCEP at 25°C. Table VIII summarizes the experimental values of K_p together with the corrected values of k'_C. This treatment results in a better fit in the relative catalytic activity established from k_C and corrected k'_C values, respectively. In reference to the decreasing k_C values, the corrected k'_C of the catalysts carrying a mobile hydrogen still appears to be excessive, especially for TMG and DMP. This observation is, of course, in good agreement with the earlier noted effect of solvent on the potential catalytic activity of the urea or urethane group of those catalysts. It can be concluded that the catalytic information obtained from model systems are meaningful even under more complex operating conditions.

Finally, polyurea foams have been prepared on a reduced scale by adjusting, by trial and error, the most favorable concentration of each catalyst. From Figures 3, 4, and 5, it appears that the best results, i.e., finely controlled cellular structure and regular foaming without collapse or shrinkage, are noted for the catalysts reacting with the isocyanate.

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Gradient-IPN-Modified Hydrogel Beads: Their Synthesis by Diffusion–Polycondensation and Function as Controlled Drug Delivery Agents

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Synopsis

Interpenetrating polymer network (IPN) membranes and gradient–IPN polymers were synthesized by immersing crosslinked, 2-hydroxyethylmethacrylate copolymer beads which were swollen in polyol in solutions of diisocyanates. Diffusion of reactants and polycondensation take place simultaneously, and the polymer beads are modified by a polyurethane–IPN layer whose thickness and compositional gradient are a function of reaction rate and diffusion rate. When the reaction is fast relative to diffusion, the reaction zone is narrow and the IPN boundary layer is sharp, whereas when diffusion dominates, the reaction zone and the IPN-modified region becomes broader and more diffuse. A water-soluble drug imbibed into such gradient–IPN-modified hydrogel beads is released over a prolonged time period due to the less permeable IPN barrier and because of a drug-distribution gradient in the polymer, which follows the polyurethane gradient. Diffusion polycondensation can be considered a special case of interfacial polycondensation, one in which the interface area is expanded into and stabilized by a preformed polymer matrix, which serves as reaction medium.

INTRODUCTION

This article describes the synthesis of polymer beads modified by interpenetrating polymer networks (IPN) and the effect of these IPN's on the release of a water-soluble drug from hydrogel beads into an aqueous environment.

Conventional oral dosage forms of water-soluble drugs consist of coated tablets which after dissolution of the coating disintegrate more or less rapidly in the stomach. As a result, drug concentrations in the blood quickly reach a sharp peak and then decrease at a rate determined by their metabolic half-life in the body. The desire to eliminate this initial peak in blood level and thereby toxic or other unwanted side effects, while at the same time maintaining drug concentrations in the blood within the therapeutic range for an extended time period without an increase in overall dose size, has led to the development of more sophisticated oral drug-delivery systems. Examples are injection molded drug containing hydrophilic polymer beads[1] or drug-containing, microporous polystyrene beads.[2] In this laboratory we have developed a family of hydrogels[3] which can, after purification, be imbibed with a drug whose release is diffusion-controlled and dependent on polymer composition and water solubility of the drug. For use as an oral dosage form, these hydrogels are manufactured in the form of round beads by suspension polymerization. As monolithic hydrogel beads uniform in composition, swelling behavior, and drug concentration, they release the drug by a concentration dependent first-order mechanism. This diffusion controlled-release rate is fast at the beginning followed by a gradual and reproducible drop whose slope is determined by the water solubility of the