a viscous liquid under evolution of ammonia after a short storage period at room temperature and atmospheric pressure. The diethylamine salt of nootkatin decomposed in a similar way within one hour at 1 mm. pressure. Some salts of cyclohexylamine showed an extremely strong tendency to sublime, and the melting points had to be taken in a sealed tube.

In view of these findings, it seemed that the best procedure would involve the strongly basic amines of high boiling points which, to minimize any decomposition during recrystallization, should also have the solubility characteristics similar to those of the tropolones in question.

Among amines used, dicyclohexylamine appeared to give the best results. It is easily soluble in all common organic solvents, including saturated hydrocarbons, but is insoluble in water. Its basicity compares with that of other aliphatic amines, and it has a high boiling point (254°–256° at atmospheric pressure). Because of its high molecular weight, it is capable of giving high weight yields of derivatives. Thus, 1 g. of β-thujaplicin could theoretically yield 2.1 g. of the derivative. In all cases, the derivatives had a high tendency to crystallize. The yields in all cases were near theoretical, as the only losses were those inherent in the process of crystallization. The derivatives could be purified by recrystallization from isooctane or similar solvents or from ethanol/water mixtures. The melting points fell within the desired temperature range, were characteristic and sharp, with mixed melting points showing depressions from 5–12°. The original tropolones can be easily liberated by treating the derivatives with 10% sulfuric acid.[11]

Table I lists the dicyclohexylamine derivatives prepared from a number of tropolones, together with their melting points and analyses.

TABLE I[12]

DICYCLOHEXYLAMINE DERIVATIVES OF TROPOLONES

Tropolone	Melting point, °C.	Calcd.		Found	
		% C	% H	% C	% H
β-thujaplicin	134–135	76.47	10.21	76.57	10.36
γ-thujaplicin	138–139	76.47	10.21	76.54	10.11
Nootkatin	114–115	78.40	10.48	78.42	10.56
Pygmaein[13]	86–87	73.56	9.93	73.70	9.74
3,5-Dibromo-α-thujaplicin	179–180	52.50	6.61	52.66	6.58
β-thujaplicinol	124–125	73.09	9.76	73.44	9.87

EXPERIMENTAL

Reagent. Monsanto's dicyclohexylamine was purified by fractional distillation, and the fraction that boiled within 120–121° at 8.3–8.5 mm. pressure was used in the experiments.

Preparation of a derivative. Pygmaein, 263 mg., m.p. 37.1–38.1°, was mixed with 500 mg. of dicyclohexylamine, and heated to 100° on a steam bath to effect solution. The resulting material was cooled to 0°, diluted with 5 ml. of cold isooctane, and allowed to stand for 1 hr. The separated crystals were filtered, the filtrate was reduced to 2 ml., cooled to 0°, and the second crop of crystals was recovered. The combined crystallization fractions were recrystallized from 10 ml. of isooctane to give 479 mg. of the derivative, m.p. 86–87° (94% yield).

Recovery of a tropolone from a derivative. A 246 mg. portion of nootkatin dicyclohexylamine salt, m.p. 113–114°, was stirred with 25 ml. of 10% sulfuric acid, and the precipitate was filtered, washed with 50 ml. of distilled water, air dried, and recrystallized from methanol-water to give 190 mg. of nootkatin, m.p. 93–94° (98% yield).

Acknowledgments. We are indebted to Monsanto Chemical Company for a sample of dicyclohexylamine and to Mr. G. M. Barton for β-thujaplicinol.

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[11] The hydrochloric acid salt of dicyclohexylamine is not very soluble in water.

[12] All melting points are corrected; microanalysis by Microchemical Laboratory, University of California, Berkeley, California.

[13] A methoxy thujaplicin isolated from *Cupressus pygmaea*, the structure of which will be the subject of a forthcoming publication.

Rates of Diisocyanate-Alcohol Reactions at Elevated Temperatures. Effect of Tri-*n*-butyl Amine Catalysis[1]

ROBERT E. CUNNINGHAM AND THOMAS G. MASTIN

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Considerable work has been done in the past decade on the rates and mechanism of the reaction of organic isocyanates with hydroxyl-containing compounds to form urethanes, starting with the pioneering work of Baker and his associates.[2–6] It is difficult to relate many of the fundamental kinetic studies directly with the industrial production of polyurethanes. Hence, it was of interest to obtain reaction rate data on systems which

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[1] Paper presented in part before the Division of Polymer Chemistry, 134th meeting, ACS, Chicago, Ill., September 1958.

[2] (a) J. W. Baker and J. B. Holdsworth, *J. Chem. Soc.*, 713 (1947); (b) J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 9 (1949); (c) J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 19, (1949); (d) J. W. Baker, M. M. Davies, and J. Gaunt, *J. Chem. Soc.*, 24 (1949); (e) J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 27 (1949).

[3] E. Dyer, H. A. Taylor, S. J. Mason, and J. Samson, *J. Am. Chem. Soc.*, **71**, 4106 (1949).

[4] C. E. McGinn and R. G. Spaunburgh, paper presented before the Division of Paint, Plastics, and Printing Ink Chemistry, 130th meeting, ACS, Atlantic City, N. J., September 1956.

[5] M. E. Bailey, V. Kirss, and R. G. Spaunburgh, *Ind. Eng. Chem.*, **8**, 794 (1956).

[6] J. Burkus and C. F. Eckert, *J. Am. Chem. Soc.*, **80**, 5948 (1958).

TABLE I

SECOND-ORDER REACTION RATE CONSTANTS FOR ARYL DIISOCYANATES *vs.* 1- OR 2-OCTANOL AT 115° IN CHLOROBENZENE SOLUTION

	With 1-octanol[b]			With 2-octanol[b]		
Diisocyanate	Cat.	Uncat.	$\frac{k \text{ cat.}}{k \text{ uncat.}}$	Cat.	Uncat.	$\frac{k \text{ cat.}}{k \text{ uncat}}$
m-Phenylene diisocyanate (k_1)[a]	75.0	14.0	5.4	20.8	8.25	2.5
m-Phenylene diisocyanate (k_2)	46.2	11.8	3.9	14.6	4.16	3.5
2,4-Tolylene diisocyanate (k_1)	30.3	5.41	5.6	10.1	3.29	3.1
2,4-Tolylene diisocyanate (k_2)	15.8	2.67	5.9	4.64	0.69	6.7
4,4′-Methylenebis(phenyl isocyanate)	29.3	4.02	7.3	8.42	3.11	2.7
3,3′-Dimethyl-4,4′-biphenylene diisocyanate	10.1	1.06	9.5	3.49	0.70	5.0

[a] For explanation of k_1 and k_2 values, see experimental section. [b] All k values are multiplied by 10^2. Units of k are liters equiv.$^{-1}$ min.$^{-1}$

more nearly simulate conditions under which polyurethanes are made commercially (*i.e.*, reactions of organic diisocyanates with primary and secondary alcohols, at elevated temperatures and in the presence of a basic catalyst, with the isocyanate and alcohol groups at equal initial concentrations). In this work, studies were confined to model alcohols; 1- and 2-octanol were used as representative primary and secondary alcohols. Four common aryl diisocyanates were used, which are listed in Table I. Because of the mechanical difficulty of handling a bulk reaction between these materials, these studies were also confined to reactions in dilute chlorobenzene solution.

The second order rate constants for the various reactants at 115° are listed in Table I. The diisocyanates are listed in their general decreasing order of reactivity, using the k_1 values for 2,4-tolylene diisocyanate and *m*-phenylene diisocyanate. The primary alcohol reacts faster with a given diisocyanate than does the secondary, either catalyzed or uncatalyzed. This agrees with data in the literature.[2,3]

Uncatalyzed reactions. For uncatalyzed reactions with 1-octanol, the four diisocyanates are listed in decreasing order of reactivity in Table I, on the basis of initial rates of reaction. Because of the smaller k_1 value for 2,4-tolylene diisocyanate, however, this diisocyanate may approach 100% reaction, with 1-octanol, in about the same length of time as 4,4′-methylenebis(phenyl isocyanate). Likewise in the uncatalyzed reactions with 2-octanol, 4,4′-methylenebis(phenyl isocyanate) is undoubtedly more reactive than 2,4-tolylene diisocyanate at high extents of reaction, because of the markedly smaller k_2 value of the latter diisocyanate.

Catalyzed reactions. In order to express the effect of basic catalysis on the rates of these various reactions, the ratio of the rate constant for the catalyzed reaction to that for the uncatalyzed reaction was used. These ratios have been included in Table I. From the data for the catalyzed reactions, the following observations can be made:

(1) Considering the rates of reaction of the primary and secondary alcohols with a given diisocyanate, it can be seen that a basic catalyst usually affects the reactivity of the primary more than the secondary. One exception can be noted, however. The k_2 values for 2,4-tolylene diisocyanate show that, in this case, the reactivity of 2-octanol is increased more by basic catalysis than that of 1-octanol.

(2) The slowest reacting diisocyanate, 3,3′-dimethyl-4,4′-biphenylene diisocyanate, is affected the most by basic catalysis. The absolute value of its rate constant for the catalyzed reaction with either alcohol is still less, however, than that of any of the other diisocyanates.

(3) For the reaction of *m*-phenylene diisocyanate with 1-octanol, basic catalysis affects the early stages more than the latter stages (k_2). With 2-octanol, the opposite is true; here k_2 is affected more than k_1.

(4) For 2,4-tolylene diisocyanate, k_2 is always increased more by basic catalysis than k_1, but the effect is much more marked with 2-octanol.

(5) As was the case with the uncatalyzed reactions, the order of decreasing reactivity of the diisocyanates, as listed in Table I, probably changes at high extents of reaction. For catalyzed reactions with either 1- or 2- octanol, 4,4′-methylenebis(phenyl isocyanate) should approach 100% reaction faster than 2,4-tolylene diisocyanate, because of the smaller k_2 values of the latter diisocyanate.

EXPERIMENTAL

Materials. All materials, except the diisocyanates, were distilled before use. Their boiling points corresponded to values in the literature. The diisocyanates were commercial samples, used as received. The 4,4′-methylenebis(phenyl isocyanate) analyzed as 97% pure; all the others were 99+% pure.

Procedure. Reactions were carried out in a double chambered vapor bath, using boiling *n*-butanol as the bath material. This gave an average working temperature of about 115°. Bath temperatures varied slightly from day to day (from a minimum of 113° to a maximum of 115.5°) due to the influence of varying barometric pressure on the boiling point of the *n*-butanol. Within a given run, however, the temperature was usually quite constant.

Stock solutions (0.10N) of the alcohols were prepared in chlorobenzene. For a kinetic run, 100 ml. of solution were placed in the inner chamber of the vapor bath and brought to temperature. Then weighed amounts of tri-*n*-butyl amine (when used) and diisocyanate were added in amounts sufficient to prepare 0.01*N* and 0.1*N* solutions respectively. The inner chamber of the bath was stoppered to prevent undue exposure of the reaction mixture to moisture.

Reaction rates were determined by following the disappearance of isocyanate by a modified Stagg method.[7] Samples were removed periodically, and warmed with excess dibutyl amine to react completely the remaining diisocyanate in the sample. Unreacted dibutyl amine was titrated potentiometrically with 0.025*N* HCl, using a Beckman Model K Automatic Titrator. In catalyzed runs, titrations were corrected for the amount of tri-*n*-butyl amine in the sample.

Data were calculated and plotted according to the usual second-order reaction rate equation for reactants at equal initial concentration. Representative rate plots are given in Fig. 1. Rate constants were determined from the slope of the best straight line drawn (by visual methods) through the points of the plot. Reproducibility of runs was quite good (*i.e.*, agreement of duplicate runs was ±1.5%), and all sets of data fitted the second-order rate equation with two exceptions. For both catalyzed and uncatalyzed reactions of 1-octanol with 4,4′-methylenebis (phenyl isocyanate), the rate plots drifted upward slightly at high extents of reaction. No satisfactory explanation could be found for this, so rate constants for these reactions were determined from the best straight lines drawn through the first few points of the plots (up to about 30% reaction). Blank runs, in which the diisocyanates were heated alone, with or without the amine catalyst, resulted in negligible or no disappearance of the diisocyanate. No evidence was found for any reaction taking place other than urethane formation except for the above-mentioned reactions of 4,4′-methylenebis(phenyl isocyanate) and 1-octanol. Even in these cases, deviation of the rate plots from linearity corresponded to only a few percent of the total diisocyanate that had reacted. Consideration of data in the literature,[8] as well as the experiments of this work, indicated that allophanate formation, or dimerization or trimerization of the diisocyanate, either would not occur at all under the experimental conditions of this work, or would take place only slowly in comparison to the rate of urethane formation.

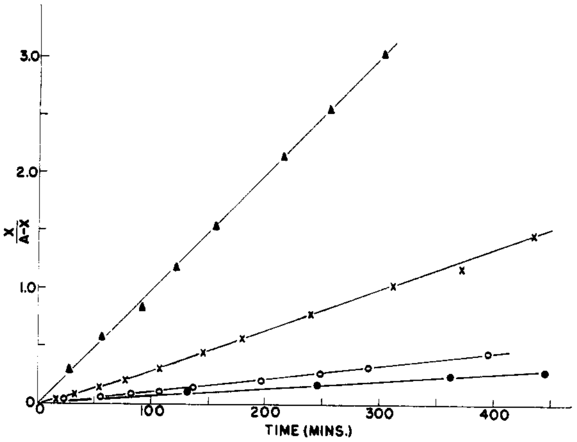

Fig. 1. Representative second-order rate plots for the reaction of 3,3′-dimethyl-4,4′-biphenylene diisocyanate with ▲ 1-octanol, catalyzed; × 2-octanol, catalyzed; ○ 1-octanol, uncatalyzed; ● 2-octanol, uncatalyzed. Additional points were obtained on the first and last curves which established the linearity of the plots at higher extents of reaction.

When two isocyanate groups are attached to the same benzene nucleus, as in *m*-phenylene diisocyanate and 2,4-tolylene diisocyanate, two separate rate constants are obtained for each diisocyanate.[4–6] With *m*-phenylene diisocyanate, the two isocyanate groups have equal initial reactivity. Beyond 50% reaction, however, when one isocyanate group has been converted to a urethane group, the second isocyanate group exhibits a slightly lower reactivity, due to the lesser activating effect of a *m*-urethane group in comparison to that of a *m*-isocyanate group.[4–6] With 2,4-tolylene diisocyanate, because of the presence of the methyl group on the benzene nucleus, the 4-isocyanate group has higher initial reactivity.[4–6] When rate data for such diisocyanates are plotted, curvatures are obtained in the plots near 50% reaction. The best straight line was drawn through the first few points of the plot, and from this k_1, the rate constant for the more reactive isocyanate group, was determined. Similarly, k_2, the rate constant for the less reactive group, was determined from the last few points on the curve beyond 50% reaction.

For all such reactions, the two rate constants so obtained were of the same order of magnitude. Hence, there was probably some overlapping and interfering reaction of both isocyanate groups throughout the entire course of each reaction. It was felt, however, that because of the reasonably good linearity obtained in the early and late stages of each such rate plot, there was sufficient justification for determining the two rate constants independently of each other by simple graphical means. All such rate constants in this work probably do contain some degree of approximation, however.

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[8] J. H. Saunders, *Rubber Chem. and Technol.*, **32**, 337 (1959), and references therein.

Some 2,2-Disubstituted-3,5-morpholinediones

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These compounds were synthesized for comparison with the previously reported 2,2-disubstituted-3,5-thiomorpholinediones.[3] In general, the 3,5-morpholinediones were prepared from the suitably substituted esters of glycolic acid by converting them to diesters of diglycolic acid, then to the diamides or ammonium salts which were pyrolyzed to the substituted 3,5-morpholinediones. Preliminary pharmacological screening tests indicate that compounds with like substituents possess similar activities as hypnotics and anticonvulsants.

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[1] Work done at University of Delaware, Newark, Del.

[2] Work done at Merck, Sharp and Dohme Laboratories, West Point, Pa.

[3] G. S. Skinner and J. B. Bicking, *J. Am. Chem. Soc.*, **76**, 2776 (1954).