[Contribution from the Department of Chemistry, University of Delaware]

The Kinetics of the Reactions of Phenyl Isocyanate with Certain Thiols[1]

By Elizabeth Dyer and John F. Glenn

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The reactions of phenyl isocyanate in the presence of triethylamine with 1-butanethiol and with 1-dodecanethiol, each in toluene solution at 25°, followed approximate second-order kinetics during the early stages and showed product catalysis as the reactions progressed. No product catalysis occurred in the absence of triethylamine. The amine-catalyzed reaction of phenyl isocyanate with 2-methylpropane-2-thiol in xylene solution at 25° showed second-order kinetics without product catalysis. The reactions of all three thiols with phenyl isocyanate were first order with respect to the concentration of the amine. The rate constants decreased in the order: 1-butanethiol, 1-dodecanethiol, 2-methylpropane-2-thiol. Two new thiolcarbanilates were obtained, *t*-butyl thiolcarbanilate and *n*-dodecyl thiolcarbanilate.

Extensive work has been done[2] on the rates of reaction of monofunctional isocyanates with alcohols, but there are no reported studies of the kinetics of the interaction of isocyanates and thiols. For the current investigation 1-butanethiol and 1-dodecanethiol were chosen as examples of primary mercaptans having different chain lengths and 2-methylpropane-2-thiol as an example of a tertiary mercaptan. Triethylamine was found to be a powerful catalyst for the reactions of phenyl isocyanate with each of these thiols. Previously thiols have been caused to react with the isocyanates at elevated temperatures to produce thiol carbamates.[3] In the present work the thiolcarbamates have been obtained in yields of 98–100% by use of amine catalyst.

$$C_6H_5NCO + RSH \xrightarrow[Et_3N]{} C_6H_5NHCOSR$$

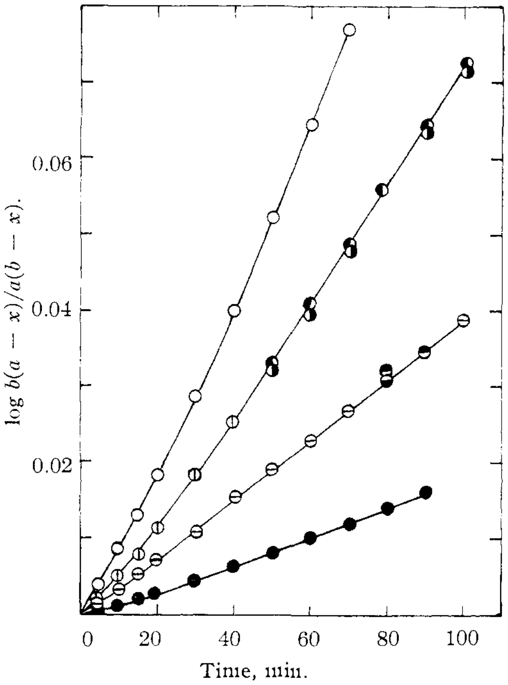

Fig. 1.—Second-order curves for the reaction of 1-butane thiol with phenyl isocyanate at various amine concentrations at 25°; ○, NCO 0.2406 M, SH 1.3399 M, Et_3N 0.000224 M; ◐, NCO 0.2492 M, SH 0.5252 M, Et_3N 0.000592 M; ◑, NCO 0.2415 M, SH 0.5315 M, Et_3N 0.000574 M; ○, coincident points above two runs; ●, NCO 0.2525 M, SH 0.5000 M, Et_3N 0.000207 M and NCO 0.2588 M, SH 0.4966 M, Et_3N 0.000205 M, all points coincident these two runs; ◓, NCO 0.2426 M, SH 0.5142 M, Et_3N 0.000205 M, product 0.2406 M; ◒, MCO 0.2428 M, SH 0.5165 M, Et_3N 0.000214 M, product 0.2598 M; ⊖, coincident points above two runs.

In the case of the primary thiols it was possible to follow the kinetics by a dilatometric method using toluene as a solvent. A chemical method was necessary with the tertiary thiol, because the product precipitated from the solvent, xylene.

Results and Discussion

The results obtained from the reactions of phenyl isocyanate with 1-butanethiol and 1-dodecanethiol are summarized in Table I and those from 2-methylpropane-2-thiol in Table II. A portion of these data is plotted in Figs. 1, 2 and 3. These plots show that the reactions followed second-order kinetics, at least during the early stages. In duplicate runs the precision was good, as evidenced by the number of coincident points in the plots.

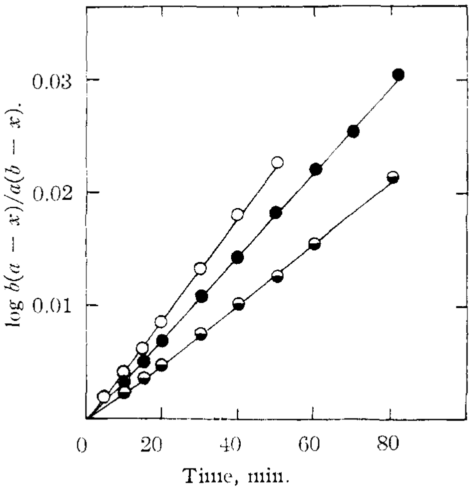

Fig. 2.—Second-order curves for the reaction of 1-dodecane thiol with phenyl isocyanate at various amine concentrations at 25°: ○, NCO 0.2229 M, SH 0.2376 M, Et_3N, 0.000972 M; ●, NCO 0.2222 M, SH 0.2380 M, Et_3N 0.000743 M; ◒, NCO 0.2215 M, SH 0.2359 M, Et_3N 0.000575 M.

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[1] From the M.S. thesis of John F. Glenn, University of Delaware, 1956.

[2] (a) J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 9, 27 (1949); (b) J. W. Baker and J. B. Holdsworth, *ibid.*, 713 (1947); (c) E. Dyer, H. Taylor, S. J. Mason and J. Samson, This Journal, **71**, 4106 (1949).

[3] H. Goldschmidt and A. Meissler, *Ber.*, **23**, 272 (1890); (b) H. L. Snape, *ibid.*, **18**, 2432 (1885), and *J. Chem. Soc.*, **69**, 100 (1896).

TABLE I

RATES OF REACTION OF PRIMARY THIOLS WITH PHENYL ISOCYANATE IN TOLUENE AT 25°

PnNCO: RSH	[Et_3N], $M \times 10^4$	[PhNCO], M	[RSH], M	$k_{\text{obsd.}}$[a] $\times 10^4$, l. mole^{-1} sec.$^{-1}$	P, %[b]	$t_{1/2}$, min.[d]
1-Butane thiol with phenyl isocyanate						
1:2	2.05	0.2588	0.4966	2.36	9	70
1:2	2.07	.2525	0.5007	2.33	9	90
1:5	2.24	.2406	1.3399	2.99	23	27
1:2	3.95	.2523	0.5214	5.36	16	45
1:2	5.74	.2415	0.5315	7.96	23	30
1:5	5.81	.2528	1.3286	9.15	50	11
1:2	5.92	.2492	.5252	8.13	22	30
1:1	6.10	.2412	.2582	8.36	12	70
1:1	6.21	.2416	.2805	7.67	12	70
1:2	7.98	.2417	.5297	10.8	28	22
1:1	8.04	.2507	.2535	11.9	17	70
1:2	8.19	.2233	.4929	11.0	29	25
1:5	10.07	.2427	1.3232	23.4[c]	100	7
1:1	10.11	.2514	0.2522	13.6	19	40
1:1	10.79	.2381	.2584	14.4	20	41
1:2	10.80	.2413	.4327	15.2	38	20
1:2	12.30	.2288	.4875	19.3	40	16
1:1	14.73	.2483	.2695	21.6	25	28
1:2	15.56	.2704	.4683	23.6	41	14
1:2	15.96	.2725	.4681	24.1	45	12
1:2	18.10	.2814	.4655	35.4	49	10
1:1	20.30	.2488	.2874	26.4	33	20
1:2	21.18	.2545	.4550	31.2	48	12
1-Dodecane thiol with phenyl isocyanate						
1:2	2.07	0.2441	0.5012	2.01	9	70
1:2	2.13	.2495	.4994	2.13	8	70
1:2	3.68	.2520	.5008	3.90	11	55
1:2	3.96	.2425	.4982	4.45	12	60
1:2	3.98	.2529	.5000	4.29	12	55
1:2	5.71	.2464	.5074	8.01	20	38
1:1	5.75	.2215	.2359	6.43	9	95
1:1	7.43	.2222	.2380	7.83	12	80
1:2	7.67	.2512	.5104	9.21	24	28
1:1	9.62	.2273	.2354	11.7	14	60
1:1	9.72	.2229	.2376	11.7	14	60

[a] Calculated by method of least squares from initial slope. [b] Percentage reacted during initial slope selected for calculation of k_{obsd}. [c] Calculated from slope of straight line of rate plot. [d] Approximate time for 50% reaction of NCO.

TABLE II

RATES OF REACTION OF 2-METHYL PROPANE-2-THIOL WITH PHENYL ISOCYANATE IN XYLENE AT 25°

PhNCO: RSH	[Et_3N], $M \times 10^2$	[PhNCO], M	[t-BuSH], M	$k_{\text{obsd.}}$[a] $\times 10^4$, l. mole^{-1} sec.$^{-1}$	P, %[b]
1:1	1.037	0.2354	0.2482	1.25	20
1:1	2.005	.2574	.2594	2.20	28
1:2	2.012	.2505	.4996	1.69	51
1:1	2.047	.2448	.2540	2.71	32
1:2	2.963	.2498	.4976	3.34	71
1:2	4.029	.2464	.4927	5.70	80

[a] $k_{\text{obsd.}}$ calculated by method of least squares. [b] Percentage reacted during period followed by the chemical method.

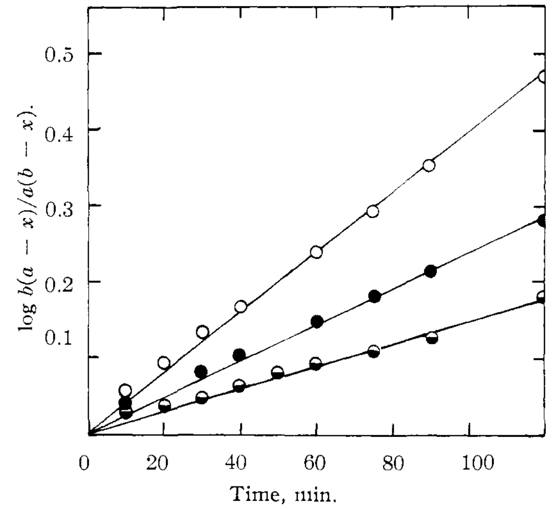

Fig. 3.—Second-order curves for the reaction of 2-methylpropane-2-thiol with phenyl isocyanate at various amine concentrations at 25°: ○, NCO 0.2498 M, SH 0.4976 M, Et_3N 0.02963 M; ●, NCO 0.2464 M, SH 0.4927 M. Et_3N 0.02464 M; ◒, NCO 0.2505 M, SH, 0.4996 M, Et_3N 0.02012 M.

The ratio of phenyl isocyanate to the thiol had an appreciable effect upon the second-order rate constant. For example, at a triethylamine concentration of 0.0006 mole per liter the k-values for reactions at 1:1, 2:1 or 5:1 thiol-isocyanate ratios were found to be, respectively, 6.5×10^{-4}, 7.6×10^{-4}, 9.1×10^{-4} liter mole^{-1} sec.$^{-1}$. At lower amine concentrations the reactant ratio effect was less pronounced.

The marked effect of the amine concentration on the rate constants is shown in the tables. Figure 4 demonstrates that there is a straight line relationship between the concentration of triethylamine and the second-order rate constant for the reactions of 1-butanethiol and 1-dodecanethiol with phenyl isocyanate. A similar relationship holds for the

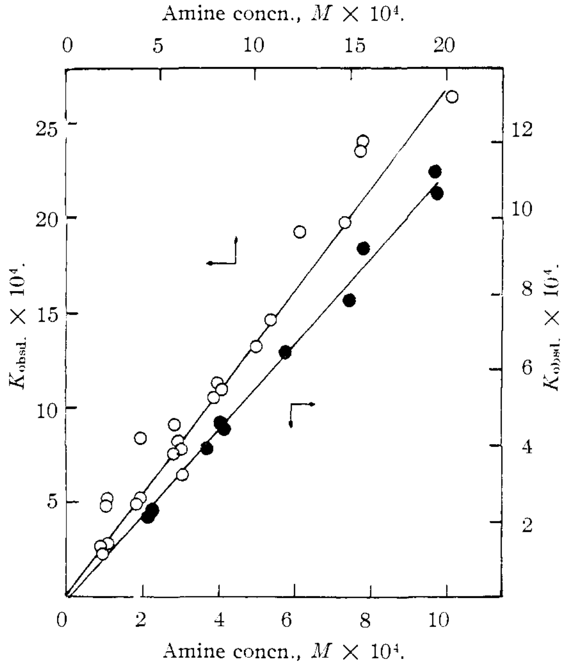

Fig. 4.—Second-order rate constants plotted against triethylamine concentration: ○, 1-butane thiol with phenyl isocyanate; ●, 1-dodecane thiol with phenyl isocyanate.

amine-catalyzed reaction of phenyl isocyanate with 2-methylpropane-2-thiol. These plots also indicate that it is not possible to measure the rate constants of the uncatalyzed reactions by extrapolation, as was done by Baker,[2b] since their values are extremely small. A single attempt to estimate the second-order rate constant of the very slow uncatalyzed reaction of phenyl isocyanate (0.5938 *M*) with 1-butanethiol (1.0614 *M*) gave a value of 5 × 10^{-7} l. mole^{-1} sec.^{-1}. This approximate figure was secured from dilatometric data for partial reaction and from data on the average shrinkage per mole of isocyanate in the catalyzed reactions.

To determine whether there was a reaction between the product, the thiolcarbanilate and phenyl isocyanate, an experiment was made in which the reactants were only phenyl isocyanate and *n*-butyl thiolcarbanilate. There was no evidence of reaction after observation in a dilatometer for 5100 minutes.

To test whether the product, the thiolcarbanilate, could react with the isocyanate in the presence of the triethylamine, a dilatometric experiment was done using 0.2400 *M* phenyl isocyanate, 0.2352 *M* *n*-butyl thiolcarbanilate and 0.001 *M* triethylamine. Since no appreciable reaction was observed after 5100 minutes, it is apparent that the product did not react with the isocyanate at the amine concentrations used in the kinetic studies. However, at a considerably higher amine concentration (0.03 *M*) a very slow reaction took place during 8900 minutes.

In order to test the catalytic activity of the product in the absence of the amine, the following experiment was performed. A solution of phenyl isocyanate, 1-butanethiol and *n*-butyl thiolcarbanilate was observed for shrinkage in a dilatometer (Table III, first line). After 1100 minutes, only a very small change in liquid level (2 mm.) was observed. This change corresponded very closely to that found in the uncatalyzed reaction between phenyl isocyanate and 1-butanethiol. It was concluded, therefore, that the product in this particular combination does not exhibit catalytic properties.

Several experiments were performed to measure the reaction rate of phenyl isocyanate and 1-butanethiol in the presence of both the triethylamine catalyst and the product, *n*-butyl thiolcarbanilate. In each case the product was present in the same quantity as would be expected to form in the reaction, 0.25 mole per liter. The data are summarized in Table III, and two of these runs are plotted in Fig. 1. This plot shows excellent fit to the second-order kinetic equation. The addition of a large amount of product to the reactants had a profound effect upon the second-order rate constant. This value was found to be almost double in the presence of 0.25 mole of product for comparable amine concentrations. For example, at a triethylamine concentration of 2.05 × 10^{-4} mole per liter, the rate constant was observed to be 2.36 × 10^{-4} liter mole^{-1} sec.^{-1}, while in the presence of 0.25 mole of product and the same amount of triethylamine, the rate constant was observed to be 4.96 × 10^{-4} liter mole^{-1} sec.^{-1}. It is therefore apparent that the acceleration in the rates shown in the amine-catalyzed reactions of phenyl isocyanate with the primary thiols is due to product catalysis.

TABLE III

RATES OF REACTION OF 1-BUTANE THIOL WITH PHENYL ISOCYANATE IN THE PRESENCE OF *n*-BUTYL THIOLCARBANILATE IN TOLUENE AT 25°

[Carbamate], *M*	[Et_3N] *M* × 10^4	[PhNCO], *M*	[*n*-BuSH], *M*	$k_{obsd.}$[a] × 10^4, l. mole^{-1} sec.^{-1}	P, %[b]
0.2526	None	0.2411	0.5052	Too slow to measure	
.2406	2.05	.2426	.5142	4.96	16
.2598	2.14	.2428	.5165	5.14	17
.2512	3.964	.2436	.5198	8.50	23

[a] $k_{obsd.}$ calculated by method of least squares from initial slope. [b] Percentage reacted during initial slope selected for calculation of k_{obsd}.

With the tertiary thiol, product catalysis did not occur. The reactions plotted in Fig. 3 showed close agreement to second-order kinetics up to 51–80% completion. A possible reason for the lack of product catalysis is the insolubility of this thiolcarbanilate in the reaction medium.

It is not possible at this time to propose a mechanism to account for the combined effects of the amine and the product as catalysts as well as the concentration ratio of the thiol. Further work in this direction is in progress with the primary thiols.

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Experimental

Dilatometric Procedure.—Dilatometers of approximately 40-ml. capacity were prepared with 0.5-mm. capillaries of uniform bore.[2c] To avoid having the isocyanate solution in contact with the moist air during the filling of the dilatometer, the filling was done from a closed erlenmeyer flask attached to one leg of the dilatometer by a butt joint held securely with a rubber sleeve. Filling was controlled by a stop-cock at the base of the flask. A thermostat containing water at 25 ± 0.03° was controlled by an Aminco thermoregulator in conjunction with an external infrared lamp. All small glassware was dried in a vacuum oven for 1 hr. at 120°. The dilatometers were dried by drawing dry air through the tubes for 1 hr. prior to making a run. Solutions of the reactants were prepared in a Lucite dry-box containing indicating silica gel which was changed every 24 hr. Luer syringes and stainless steel needles of large gage were used to facilitate the transfer of reagents in the preparation of solutions. Readings of the scale were made every minute for the first 20 minutes, at 5- or 10-minute intervals for about 2 hr. and then at suitable intervals up to completion. Temperature measurements made during the initial period showed that the temperature rise was negligible. The calculation procedure was that used previously.[2c]

The molar contraction of phenyl isocyanate was calculated for the triethylamine-catalyzed reaction of phenyl isocyanate with the two primary thiols. The average shrinkage found with 1-butanethiol was 27.6 ml. per mole of phenyl isocyanate and with 1-dodecanethiol, 27.3 ml. per mole of phenyl isocyanate.

Chemical Method.—The reaction vessels consisted of U-tubes of approximately 25-ml. capacity prepared from 8-mm. diameter glass tubing. In order to facilitate more rapid transfer and mixing of the reagents, a volume of only 10 ml. was used. Into 5 ml. of the mercaptan–triethylamine solution in the U-tube, there was pipetted an equal volume of the phenyl isocyanate solution. These solutions were mixed rapidly and the U-tubes stoppered with silicone impregnated corks. Disappearance of phenyl isocyanate was followed by a modification of the Stagg method[4] using di-*n*-butylamine

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(4) H. E. Stagg, *Analyst*, **71**, 557 (1946).

in place of piperidine and titrating with 0.3 *M* hydrochloric acid and brom phenol blue. Two blank determinations on the di-*n*-butylamine solution were made at the beginning of each run and one blank determination on the di-*n*-butylamine solution for each phenyl isocyanate titration if the interval was more than 2 hr. Two blank determinations were made on the phenyl isocyanate solution at the beginning of each run. A blank on the phenyl isocyanate solution was made during the run if a time was more than 2 hr. from a previous blank.

Materials.—Toluene and xylene were purified by distillation from sodium. Triethylamine and di-*n*-butylamine were fractionated from sodium hydroxide after standing for several days over solid sodium hydroxide. The three thiols were dried by storage for several days over calcium oxide and distilling from the calcium oxide. Eastman Kodak Co. phenyl isocyanate was fractionated, the fraction b.p. 164.5–165.5° being used. Acetone was dried and purified by storage over and distillation from Linde molecular sieve #4A. All reagents and solvents, except the acetone, were stored in dry glass-stoppered bottles in the dry-box until used.

Preparation of *n*-Butyl Thiolcarbanilate.[5]—To a solution of 3.2 g. (0.0355 mole) of 1-butanethiol and 0.0084 g. (0.0006 mole per liter) of triethylamine in 70 ml. of dry toluene was added a solution of 4.11 g. (0.0345 mole) of phenyl isocyanate in 70 ml. of dry toluene. This mixture was set aside at approximately 25° for 2 days. After removal of the solvent, the excess thiol and amine, the product crystallized as long needles, yield 7.1 g. (98.5%). On recrystallization from alcohol 6.8 g. (94%) was recovered, m.p. 69°, λ_{max} 249 mμ. *Anal.* Calcd. for $C_{11}H_{15}ONS$: N, 6.70; S, 15.30. Found: N, 6.82; S, 15.41.

Preparation of *t*-Butyl Thiolcarbanilate.—To a solution of 4.5 g. (0.05 mole) of 2-methylpropane-2-thiol and 0.2 g. (0.02 mole per liter) of triethylamine in 50 ml. of dry toluene was added a solution of 2.9 g. (0.0244 mole) of phenyl isocyanate in 50 ml. of dry toluene. The mixture was allowed to stand at approximately 25° for 7 days, during which period a crystalline precipitate formed. After removal of the solvent and the excess reactants, the product crystallized in long needle crystals; yield 5.1 g. (100%). When recrystallized from benzene, 4.5 g. (88%) was recovered, m.p. 147.5°. There is a marked tendency to sublime at approximately 110°; λ_{max} 254 mμ. *Anal.* Calcd. for $C_{11}H_{15}ONS$: N, 6.70; S, 15.30. Found: N, 6.66; S, 15.28.

Preparation of *n*-Dodecyl Thiolcarbanilate.—To a solution of 6.7 g. (0.0331 mole) of 1-dodecanethiol and 0.00795 g. (0.0006 mole per liter) of triethylamine in 70 ml. of dry toluene was added a solution of 3.9 g. (0.0328 mole) of phenyl isocyanate in 70 ml. of dry toluene. The mixture was allowed to stand at approximately 25° for 3 days. After removal of the solvent and excess reactants, the product crystallized as plates, yield 10.3 g. (98%). On recrystallizing from ethanol 9.1 g. (87%) was recovered, m.p. 72°, λ_{max} 2.51 mμ. *Anal.* Calcd. for $C_{19}H_{31}ONS$: N, 4.36; S, 9.96. Found: N, 4.14; S, 10.13.

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[5] This compound has been made by a different method by J. W. Batty, H. E. Jackson and F. G. Jeffers, British Patent 599,178, March 5, 1948; m. p. 68°.

[CONTRIBUTION NO. 743 FROM THE DEPARTMENT OF CHEMISTRY, INDIANA UNIVERSITY]

Solvent Effects on the Rates of Solvolysis of Some Alkylbenzhydryl Chlorides[1]

BY V. J. SHINER, JR., AND C. J. VERBANIC[2]

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The rates of solvolysis of a number of alkylbenzhydryl chlorides were determined conductimetrically in aqueous ethanol and aqueous acetone solutions. The substituent groups studied, in decreasing order of their effectiveness in promoting reactivity, were: *p*-methyl, *p*-ethyl, *p*-*n*-propyl, *p*-isopropyl, *p*-isobutyl, *p*-neopentyl, *p*-*t*-butyl, *m*-methyl and *m*-*t*-butyl. It has been found that the relative rate constants show a marked systematic dependence upon the composition of the aqueous solvent. The order of reactivity of the *m*-methyl and *m*-*t*-butyl compounds can be reversed by proper choice of solvent. The importance of the role of the solvent in kinetic studies of the Baker–Nathan effect is thus emphasized. The rates of solvolysis of the benzhydryl chlorides with the less highly branched substituents in general are more sensitive to solvent variations than their homologs with the more highly branched alkyl substituents. These results may be most readily rationalized in terms of solvation assistance to hyperconjugation and/or of steric hindrance to solvation.

The problem of the mode of electron release of saturated alkyl groups attached to unsaturated centers has been the subject of considerable investigation and discussion recently.[3–6] It is apparent that the concepts of the inductive and the hyperconjugative effects alone do not suffice to explain the pertinent data. Several additional effects have been proposed[7–11] and the importance of hyperconjugation has been questioned.[3] Nevertheless the data presently available do not seem to give a sufficient basis for judging conclusively the merits of the different proposals. The Baker–Nathan effect has probably been most clearly demonstrated by Hughes, Ingold and Taher in their studies on the solvolysis of *p*-alkylbenzhydryl chlorides.[12] In spite of, and indeed mainly because of, these extensive investigations it seemed that additional studies on this system would be pertinent to the present problem.

The approach has been to synthesize a series of α- and β-branched *p*-alkylbenzhydryl chlorides and to study their solvolysis rates as a function of solvent composition in "80%," "70%," "66.7%" aqueous acetone and "90%" aqueous alcohol at 0°. The rate measurements were made conductimetrically using a Jones–Joseph type conductance bridge. The mechanism of the solvolysis reactions of these compounds has been the object of considerable investigation by numerous workers.[12] The

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(1) (a) Abstracted from the thesis submitted by C. J. Verbanic to the Graduate School of Indiana University in partial fulfillment of the requirements for the Ph.D. degree. (b) Presented in part before the Division of Organic Chemistry at the 129th National Meeting of the American Chemical Society, Dallas, Texas, April 12, 1956. (c) Supported in part by the National Science Foundation.

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