

stirred at 20° and 37.3 g. (0.3 mole) of benzyl mercaptan in 300 ml. of ethanol was added during 10 min. The mixture became maroon, and then changed to garnet as the temperature rose to 31°. Solid began to separate after about 20 min. After stirring for 1.5 hr., the temperature had fallen to 25°. The red-orange solid was then collected and washed with about 75 ml. of cold ethanol (to remove hydroquinone) and dried, giving 34.0 g. of crude 2-benzylthiobenzoquinone, m.p. 119–121.5°. Evaporation of the filtrates under reduced pressures left a nearly black residue, which was boiled in about 300 ml. of ethanol and the solution chilled. The reddish crystals were collected, washed with about 50 ml. of cold ethanol and dried; 22.2 g. of product melting at 122–123° resulted. Crystallization of the two fractions (81.5% yield) from hexane gave 43.1 g. (62.4% yield, based on benzyl mercaptan) of pure compound as fan-shaped aggregates of orange-red needles, m.p. 124–124.5° (lit.,¹⁷ m.p. 119°).

Anal. Calcd. for $C_{13}H_{10}O_2S$: C, 67.80; H, 4.38; O, 13.90; S, 13.92. Found: C, 68.20; H, 4.36; O, 13.80; S, 14.18.

A ten-fold run gave a 60% yield of 2-benzylthiobenzoquinone (m.p. 123–124°, from carbon tetrachloride) and an alcohol-insoluble fraction (50 g.) which melted over 200°. The latter was crystallized twice from diethylene glycol methyl ether (Methylcarbitol) to give 37.0 grams of lustrous scarlet plates which melted at 230.5–231.5°. This proved to be the 3,6-bis(benzylthio) compound, for which Posner and Lipski¹⁸ recorded the m.p. 223–224°.

Anal. Calcd. for $C_{20}H_{16}O_2S_2$: C, 68.15; H, 4.58; S, 18.19. Found: C, 67.90; H, 4.70; S, 18.37.

C. Nenitzescu reactions. The limited accessibility of the original work of Nenitzescu⁸ renders desirable a recounting of the procedure. It is to be noted that, while the yields were generally very low, the ease of manipulation was considerable. All of the new 1-substituted 3-carbethoxy-5-hydroxy-2-methylindoles were made as described for the parent type.

Ethyl 5-hydroxy-2-methylindole-3-carboxylate. Ethyl β -aminocrotonate (1104 g., 8.55 moles) was dissolved in acetone (6 l.) and an atmosphere of nitrogen was maintained over the stirred solution and the addition of *p*-benzoquinone (970 g., 8.95 moles) made in 20 min. There was little exothermic effect until the red solution was warmed to about 40°, whereupon ensuing reaction caused sufficient liberation of heat to start vigorous boiling. Gentle cooling was applied for some 20 min., after which time, there was refluxing for 0.5 hr. without need for warming. It was further refluxed for 1 hr., and then nearly 5 l. of solvent were removed, with the still under nitrogen. After chilling, the sticky garnet magma was filtered, washed at the pump with 2 l. of cold 1:10 mixture of acetone and pentane, then it was slurried in a minimal amount of acetone and stored in the cold for

a day. The crude ester was collected, washed with some cold acetone, and dried. Six hundred forty-three grams (34.3% yield) of light tan solid resulted, m.p. 200–202°. The crude product could be crystallized well from methanol containing traces of sodium dithionite, or from aqueous acetone, however the large batch was more readily purified by a somewhat different method. It was dissolved in hot acetic acid to produce a solution of some 3 liters volume, then hot ethyl acetate was added, after charcoaling, to a total volume of 4 l. The purified ester was collected after chilling, then it was washed with cold ethyl acetate and dried. Ethyl 5-hydroxy-2-methylindole-3-carboxylate was obtained as fine white needles, m.p. 211–212° (lit.^{2,3} reports m.p. 205°); the yield was 483 g., or 25.8%. Other preparations of the "Nenitzescu product" gave purified yields of 22–28%, and only intractable gums were obtained from the liquors.

Ethyl 1,2-dimethyl-5-hydroxyindole-2-carboxylate was obtained in 32% yield in the form of cryptocrystals from Methylcellosolve; m.p. 211–212° (lit.² m.p. 207–208°).

Anal. Calcd. for $C_{13}H_{13}NO_3$: C, 66.93; H, 6.48; N, 6.00. Found: C, 66.91; H, 6.44; N, 6.19.

Ethyl 1-hexyl-5-hydroxy-2-methylindole-2-carboxylate: 22% yield of chalky, cryptocrystalline solid, m.p. 134.5–135° (from cyclohexane).

Anal. Calcd. for $C_{18}H_{23}NO_3$: C, 71.28; H, 8.30; N, 15.83. Found: C, 71.66; H, 8.19; N, 15.70.

Ethyl 1-(3-dimethylaminopropyl)-5-hydroxy-1-methylindole-2-carboxylate hydrochloride was a light tan cryptocrystalline solid, m.p. 267.5–269.5°. It was prepared directly from the crude Nenitzescu product and crystallized repeatedly from aqueous ethanol; the yield of pure product was only 10%.

Anal. Calcd. for $C_{18}H_{22}N_2O_3 \cdot HCl$: N, 8.22; Cl, 10.40. Found: N, 8.25; Cl, 10.43.

Ethyl 1-benzyl-5-hydroxy-1-methylindole-2-carboxylate was a pinkish cryptocrystalline solid as obtained from ethyl acetate, m.p. 196.5–197.5°. The yield was 22%.

Anal. Calcd. for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; O, 15.52. Found: C, 73.92; H, 6.17; O, 15.85.

Ethyl 6-benzylthio-1,2-dimethyl-5-hydroxyindole-2-carboxylate. 2-Benzylmercapto-1,4-benzoquinone (228 g., 0.99 mole) was caused to react with ethyl β -methylaminocrotonate (144 g., 1 mole) in acetone (1 l.) in the usual manner. The yield of crude product (162 g., m.p. 176–180°) was 46%. It was crystallized from glacial acetic acid to obtain a 38% yield of pure compound in the form of off-white needles, m.p. 182.5–184°.

Anal. Calcd. for $C_{20}H_{21}NO_2S$: C, 67.58; H, 5.96; S, 9.02. Found: C, 67.53; H, 5.68; S, 8.93.

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(17) W. Alcalay, *Helv. Chim. Acta*, **30**, 578 (1947).

(18) T. Posner and J. Lipski, *Ann.*, **336**, 150 (1904).

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Vinylation Rates of Primary, Secondary, and Tertiary Alcohols

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Because of the low acidity of tertiary alcohols and since alkoxide ion is the catalyst, it is necessary to use an alkali metal alkoxide rather than a hydroxide in the vinylation of tertiary alcohols. Relative vinylation rates of *n*-, *sec*- and *tert*-butyl alcohols are reported. It is suggested that F-strain in the transition state accounts for the order of vinylation rates.

The base-catalyzed vinylation of alcohols was reported in 1931 by W. Reppe.¹ At the time of the

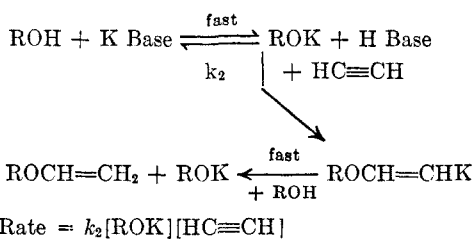
(1) W. Reppe, U. S. Patent 1,959,927 (1934); Ger. Patent 584,840 (1932); Brit. Patent 369,297 (1932); French Patent 724,955 (1931).

tertiary alcohol had appeared despite considerable present work no description of the vinylation of a interest in the vinylation reaction.^{2–8} Since the

(2) P. B. Reports 40,816; 1112; 13,366; 11,394; 67,694 and 18,842-s.

completion of this work such a description has been published.⁹ The present work gives relative rates of vinylation of *n*-, *sec*- and *tert*-butyl alcohols. The catalyst was the respective potassium alkoxide and the reaction was studied both without solvent and in a glycol ether.

Reppe^{1,2} considered the vinylation reaction to involve an equilibration of the basic catalyst with the alcohol to form alkoxide. This would be followed by addition of the alkoxide to acetylene forming the salt of the vinyl ether. Reaction of this salt with alcohol would form the vinyl ether and regenerate alkoxide. This is very similar to the mechanism proposed by Hanford and Fuller.⁴ Such a mechanism is consistent with the kinetics found by Miller and Shkapenko⁸ for the methoxide-catalyzed addition of methanol to phenylacetylene. They found the reaction to be first order in methoxide and in phenylacetylene but zero order in methanol.



The bases used by Reppe included the hydroxides and alkoxides of sodium and potassium. The potassium salts were generally superior to the sodium salts. In the vinylation of ethanol, the 95% azeotrope reacted as well as absolute alcohol. Potassium hydroxide was as good a catalyst as the ethoxide. These observations must have contributed to the attitude that potassium hydroxide was the best and most convenient catalyst.¹⁰ The general use of potassium hydroxide as catalyst must, in turn, account for previous difficulties in the vinylation of tertiary alcohols.

The reason for such difficulties is apparent from consideration of the equilibrium between hydroxide and alkoxide. For ethanol, a primary alcohol, Cal-

(3) J. W. Copenhaver and M. H. Bigelow, "Acetylene and Carbon Monoxide Chemistry," Reinhold Publishing Corp., New York, 1949, Chapter 2.

(4) W. E. Hanford and D. L. Fuller, *Ind. and Eng. Chem.*, **40**, 1171 (1948).

(5) C. E. Schildknecht, A. O. Zoss, and C. McKinley, *Ind. and Eng. Chem.*, **39**, 180 (1947).

(6) G. M. Kline, *Modern Plastics*, **23**, 152A (Oct. 1945); **23**, 169 (February 1946); **24**, 159 (January 1947).

(7) J. Furukawa, T. Ando, and M. Yokoyama, *Bull. Inst. for Chem. Res. of Kyoto Univ.*, **31**, #3, 220 (1953).

(8) S. I. Miller and G. Shkapenko, *J. Am. Chem. Soc.*, **77**, 5038 (1955).

(9) S. Otsuka, Y. Matsui and S. Murahashi, *Nippon Kagaku Zasshi*, **77**, 766 (1956); *Chem. Abstr.*, **52**, 8935 (1958).

(10) Hanford and Fuller,⁴ for instance, recommend the use of potassium hydroxide with anhydrous alcohols while stating that potassium hydroxide and alkoxide give better results than other bases tried.

din and Long¹¹ have found an equilibrium constant of 0.7. In 2% aqueous ethanol, which is about the composition of a reaction mixture made up by dissolving 5% of potassium hydroxide pellets in absolute alcohol, 94% of the base is present as ethoxide. Thus, in the vinylation of a primary alcohol, the use of potassium hydroxide is satisfactory, as nearly all the base is present as alkoxide.

Secondary alcohols are weaker acids than are primary and hence the equilibrium will be less favorable. Indeed, Nummy¹² found, in competitive vinylation of equal parts of 1-octanol and 2-octanol at 190° using 4 mole % potassium hydroxide, that the primary alcohol was initially vinylation about 7 times as fast as the secondary alcohol (see Fig. 1).

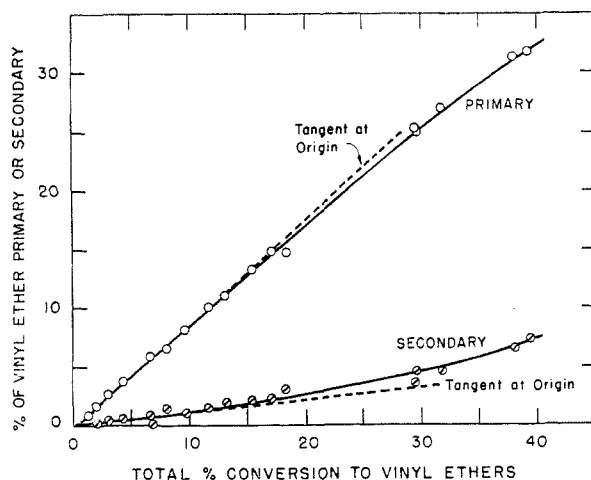


Fig. 1. Competitive vinylation of 1-octanol and 2-octanol

The reactivities found in the present work suggest that the major portion of this difference (about a factor of three) is due to the greater acidity of the primary alcohol. The acidity of tertiary alcohols must, then, be too low for a significant amount of alkoxide to be present in equilibrium with hydroxide.

With these considerations in mind, potassium *tert*-butoxide was used to catalyze the vinylation of *tert*-butyl alcohol. The vinylation proceeded to high conversion and, under the conditions initially chosen, nearly as fast as with *n*-butyl alcohol or *sec*-butyl alcohol (Figure 2). Suspecting from this that the rate at which acetylene dissolved in the reaction solution was determining the rate of vinylation, two series of experiments were run leaving acetylene pressure constant but lowering the rate of vinylation by changing the temperature or the butoxide concentration.

In one series, the temperature and the catalyst concentration were lowered and the alcohol was diluted with a better solvent for acetylene. The relative rates, corrected for catalyst concentration, were *n*-butyl alcohol 5.4, *sec*-butyl alcohol 2.4 and

(11) E. F. Caldin and G. Long, *Nature*, **172**, 583 (1953).

(12) W. R. Nummy, previously unpublished results in this laboratory.

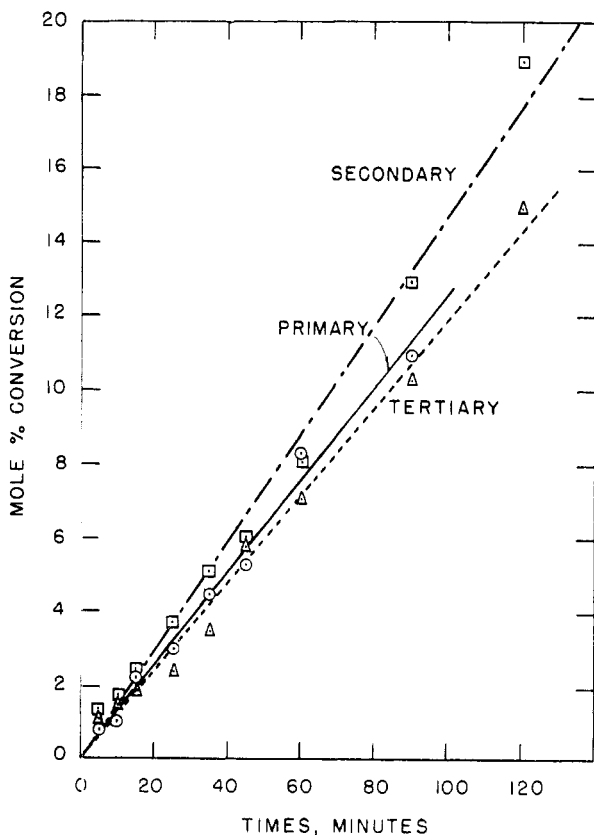


Fig. 2. Diffusion-controlled vinylation of butyl alcohols

tert-butyl alcohol 1.0 (see Figure 3 and Table I). In straight alcohol at low catalyst concentrations, the primary alcohol reacted 3.7 times as fast as the tertiary (see Figure 4).

The reaction rates given here cannot be compared directly with those given by Otsuka, Matsui and Murahashi.⁹ Moreover, the method they used to calculate the vinylation rates of primary alcohols by difference is open to objection. They vinyolated solutions of primary alcohols in *tert*-butyl alcohol containing potassium *tert*-butoxide. From the rate at which *tert*-butyl alcohol alone was vinyolated, they tried to correct the observed rate to obtain the rate for the primary alcohol. However, with no information regarding the distribution of the catalyst between primary alkoxide and *tert*-butoxide, it is not possible either to correct for the vinylation of *tert*-butyl alcohol in the mixture or to tell the primary alkoxide concentration responsible for the vinylation of the primary alcohol. However, the rate curves in their paper show that the rates were leveling off with increasing concentration of primary alcohol. One may, therefore, estimate that in the pure primary alcohols the rates relative to *tert*-butyl alcohol would be 2-ethoxyethanol 9, 1-octanol 5 and *iso*-butyl alcohol 4. The latter two values are in general agreement with the values reported here for *n*-butyl alcohol.

The observed order of reactivity of the butoxide ions toward acetylene is the reverse of their base

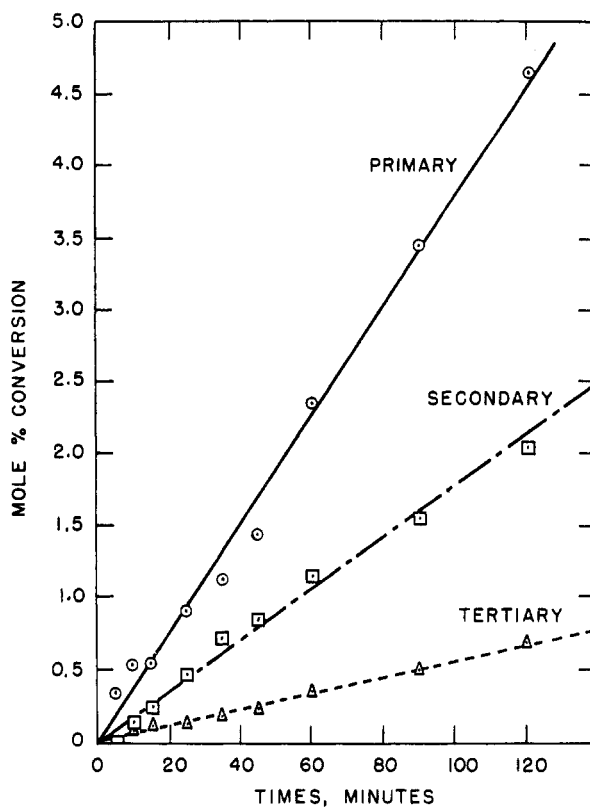


Fig. 3. Vinylation of butyl alcohols in dimethyl ether of diethylene glycol

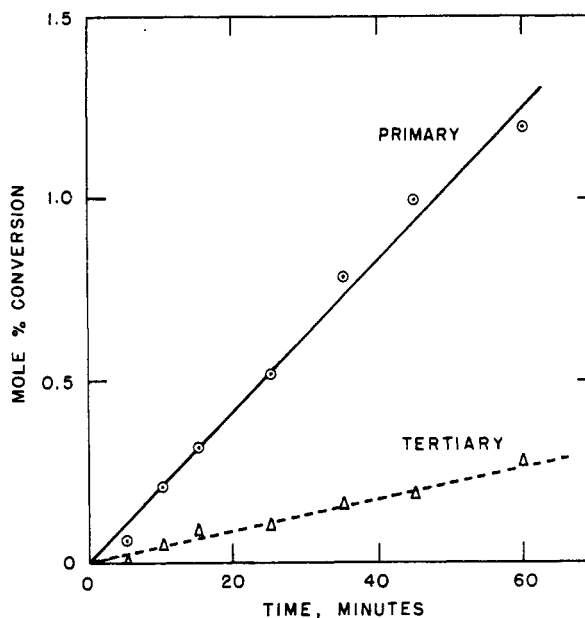


Fig. 4. Vinylation of butyl alcohols at low catalyst concentrations

strengths and the reverse of the expected electron densities on the oxygen atoms. An explanation for this observation is to be sought, then, not in the differences in activation energy but rather in increasing entropy of activation as the alkyl group is branched. Such an interpretation seems reasonable when one examines molecular models of alkoxide

TABLE I
 VINYLATION OF BUTYL ALCOHOLS

Medium Mole % cat. Temp.	<i>n</i> -BuOH	<i>sec</i> - BuOH	<i>tert</i> - BuOH	10%		10%		<i>n</i> -BuOH	<i>tert</i> - BuOH
				<i>n</i> -BuOH 90% E-141	<i>sec</i> -BuOH 90% E-141	<i>tert</i> -BuOH 90% E-141	<i>n</i> -BuOH 90% E-141		
	3.9	4.5	4.6	1.6	1.7	1.3	1.3	1.3	1.0
	147	147	147	122	122	122	147	147	
Time, Min.	Mole % vinyl ether								
5	0.52	0.61	0.27	0.11	0.09	(>0.05)	0.07	0.03	
10	0.76	0.97	0.61	0.30	0.27	0.06	0.22	0.08	
15	1.9	1.6	0.97	0.30	0.40	0.08	0.33	0.12	
25	2.7	2.9	1.5	0.66	0.62	0.10	0.53	0.14	
35	4.2	4.3	2.6	0.88	0.86	0.15	0.80	0.19	
45	5.0	5.2	4.9	1.2	1.0	0.20	1.0	0.22	
60	8.0	7.3	6.2	2.1	1.3	0.33	1.2	0.29	
90	11	12	9.4	3.2	1.7	0.46			
120		18	14	4.4	2.2	0.68			
m	0.127	0.148	0.120	0.0380	0.0178	0.0057	0.0210	0.0043	
b	-0.27	-0.79	-0.89	-0.25	0.14	-0.03	0.01	0.03	
r	0.0326	0.0329	0.0261	0.0237	0.0104	0.0044	0.0161	0.0043	
Rel. rate				5.4	2.4	1.0	3.7	1.0	

ions and acetylene. The presence of any carbon atoms attached to the alkoxide carbon atom restricts effective approach of the oxygen atom to acetylene. In effect, then, it is suggested that F-strain determines the reactivity of the butoxide ions toward acetylene.¹³

A similar effect has been noted by Brown and Moritani¹⁴ in the reaction of potassium alkoxides in the respective alcohols with *tert*-amyl bromide. The relative rates were ethoxide 4.46, isopropoxide 2.28 and *tert*-butoxide 1.00. The similarity of these results with those for the vinylation reaction is consistent with a like cause, steric strain in the transition state, despite the fact that one is an elimination reaction whereas the other is an addition reaction.

A parallel case to alkoxide reactivity is the base strength of corresponding primary amines toward various reference acids. Toward the proton, branching slightly decreases relative base strength¹⁵ in the series *n*-butyl 1.5, *sec*-butyl 1.3 and *tert*-butyl 1.0 and somewhat more so in the series ethyl 2.0, *iso*-propyl 1.5 and *tert*-butyl 1.0. Brown and Pearsall¹⁶

(13) Even if the transition state were termolecular involving concerted transfer of a proton from the alcohol to the β -carbon atom of the vinyl group, one would expect that formation of the oxygen-carbon bond would be the more important process in determining the rate of reaction. Moreover, the greater ease of breaking the hydrogen-oxygen bond of the primary alcohol should be reflected in the lesser reactivity of the alkoxide thus formed toward acetylene unless a further effect such as F-strain is also operative.

(14) H. C. Brown and I. Moritani, *J. Am. Chem. Soc.*, **76**, 455 (1954); cf. also H. C. Brown, I. Moritani, and Y. Okamoto, *J. Am. Chem. Soc.*, **78**, 2193 (1956) for a discussion of the effect of steric requirements of alkoxide bases on the direction of bimolecular elimination.

(15) "Handbook of Chemistry," N. A. Lange, Editor, Handbook Publishers, Inc., Sandusky, Ohio, 9th Edition (1956), pages 1202-1204.

(16) H. C. Brown and H. Pearsall, *J. Am. Chem. Soc.*, **67**, 1765 (1945).

showed a much greater effect of branching upon the relative base strength in the latter series of amines toward trimethyl boron, a larger reference acid: Ethyl 14.5, *isopropyl* 6.9 and *tert*-butyl 1.0. Here, too, the magnitude of the effect of branching the alkyl group depends upon the steric requirements of the reaction in question.

EXPERIMENTAL

The vinylation was done in an American Instrument Company 316 stainless steel bomb of 1.5 l. capacity. The bomb was packed in 0.5 in. lengths of 0.5 in. stainless steel pipe and fitted with a gas inlet line and a dip tube for sampling the liquid phase. It was heated electrically, to maintain the internal temperature within a range of 5°. The heater was clamped in a horizontal reciprocating shaker which has been found to give less efficient mixing than the more common rockers.

The alcohols used were dried by the method of Lund and Bjerrum¹⁷ using magnesium turnings to form hydroxide and alkoxide, then distilled with precautions to exclude water. The approximate amount of potassium desired was allowed to react with 500 g. of the alcohol. The concentration of potassium alkoxide was determined by titration with standard hydrochloric acid. The dimethylether of diethylene glycol used in the solvent runs was Ansul Chemical Company E-141 which had been dried by reaction with sodium wire and redistilled.

The bomb was charged but butoxide solution, sealed, purged with nitrogen, and heated to temperature. Acetylene was then admitted to maintain the total pressure constant at 50 (\pm 2) p.s.i.g. in excess of the vapor pressure observed. Samples of the reaction solution were withdrawn at intervals and analyzed by vapor phase chromatography at the Dow Spectroscopy Research Laboratory. The data are given in Table I. For each experiment a straight line described by the slope *m* and intercept *b* was obtained by the method of least squares. Taking the rate to be first order in butoxide concentration, a rate *r* was calculated by dividing the slope by this concentration. The data, shifted to pass through the origin, is presented in Figs. 2, 3 and 4.

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(17) H. Lund and J. Bjerrum, *Chem. Ber.*, **64**, 210 (1931).