Some Reactions of Benzyne and α-Naphthalyne[1]

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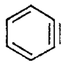
This report describes some reactions of bromobenzene with various nucleophilic reagents in the presence of sodium or potassium amide in liquid ammonia solution. These reactions assuredly occur *via* the benzyne mechanism.[3] Similar experiments were performed several years ago by Bergstrom and co-workers[4] and recently by Scardiglia and Roberts[5] and by Leake and Levine.[6]

Our experimental procedure was to add bromobenzene to a mixture of sodium or potassium amide and the relevant nucleophilic reagent in liquid ammonia. Bergstrom *et al.*[4] showed that many nucleophilic reagents are unreactive with halobenzenes in liquid ammonia unless an alkali metal amide is also present, and Roberts *et al.*[3] demonstrated that the function of the metal amide is to convert the halobenzene to benzyne (I)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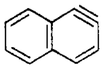
II

which then reacts with the nucleophilic reagent. Thus our experiments, most of which are summarized in Table I, are essentially an exploration of the reactivity of benzyne.

Experiments 1, 2, and 3 in Table I show that thiophenoxide ion is reactive with benzyne. The same discovery has been made in other current investigations.[5,6] It should be noted that the metal amide was in considerable excess in these experiments, yet the benzyne intermediate combined with thiophenoxide ion to a greater extent than with amide ion. Thiophenoxide ion is evidently more reactive than amide ion with benzyne.

The two experiments (Expts. 4 and 5) with piperidine reagent differ in the metal amide used and in the results obtained. With sodium amide, 29% of *N*-phenylpiperidine was produced in addition to phenylamines resulting from combination of amide ion with benzyne. But with potassium amide no *N*-phenylpiperidine was formed; only phenylamines were obtained. It was noted that a precipitate formed when piperidine was added to a solution of potassium amide in liquid ammonia. The precipitate is presumably potassium piperidide; if so, the non-formation of *N*-phenylpiperidine is easily understood in terms of the potassium piperidide being effectively removed from the reaction system. Sodium piperidide is presumed to be soluble in liquid ammonia, although admittedly the formation of a new precipitate on addition of piperidine to a suspension of sodium amide in liquid ammonia would be hard to detect. The formation of *N*-phenylpiperidine in the sodium amide reaction is then explicable in terms of the solubility of sodium piperidide and the relative insolubility of sodium amide.

Phenylation of isobutyronitrile *via* benzyne (Expt. 6) is analogous to phenylation of acetonitrile and propionitrile as performed by Bergstrom and Agostinho.[4c]

It is remarkable that sulfide ion (Expt. 7) did not react with benzyne, especially in view of the high reactivity of thiophenoxide ion. Cyanide ion is also unreactive (Expt. 8). The objective of the experiment with chloroform (Expt. 9) was to see whether some product from the interaction of benzyne and dichlorocarbene[7] might be obtained. No such product was isolated.

The reaction of 1-bromonaphthalene, sodium thiophenoxide, and sodium amide was investigated. A 27% yield of mixed 1- and 2-naphthyl phenyl sulfides was obtained. The mixture of sulfides was oxidized and from the resulting mixture of sulfones both 1- and 2-naphthyl phenyl sulfones were isolated by fractional crystallization in yields, based on 1-bromonaphthalene, of 8.2% and 15.7%, respectively (total: 23.9%). Thus of the sulfones isolated, 34% was 1-naphthyl and 66% was 2-naphthyl phenyl sulfone.

This experment is significant in two respects. First, the fact that 2-naphthyl phenyl sulfide, a rearranged product, was formed gives assurance that the reaction in which it was generated proceeded by the elimination-addition mechanism, in this case *via* α-naphthalyne (II). The benzyne mechanism for reactions 1, 2, and 3 of Table I is thus further supported. Second, because the efficiency of the transformation of mixed sulfides to isolated sulfones was high, the ratio in which the two sulfones were obtained, 34:66, may be taken as representative of the rates of attachment of the thiophenoxide ion to the 1- and 2-positions of II, respectively. Within experimental error, the ratio is identical to the corresponding ratios pertaining to

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(2) American Enka Fellow, 1954–55; R. J. Reynolds Fellow, 1955–56. This note is based on the Ph.D. thesis of T. K. Brotherton, October, 1956.

(3) J. D. Roberts, H. E. Simmons, Jr., L. A. Carlsmith, and C W. Vaughan, *J. Am. Chem. Soc.*, **75**, 3290 (1953); J. D. Roberts, D. A. Semenow, H. E. Simmons, and L. A Carlsmith, *J. Am. Chem. Soc.*, **78**, 601 (1956).

(4) (a) R. E. Wright and F. W. Bergstrom, *J. Org. Chem.*, **1**, 179 (1936); (b) R. A. Seibert and F. W. Bergstrom, *J. Org. Chem.*, **10**, 544 (1945); (c) F. W. Bergstrom and R. Agostinho, *J. Am. Chem. Soc.*, **67**, 2152 (1945).

(5) F. Scardiglia and J. D. Roberts, *Tetrahedron*, in press.

(6) W. W. Leake and R. Levine, *Chem. & Ind.* (*London*), 1160 (1955); Abstracts, ACS Meeting, New York, N.Y., Sept., 1957, p. 37P.

(7) J. Hine, *J. Am. Chem. Soc.*, **72**, 2438 (1950); W. von E. Doering and A. K. Hoffman, *J. Am. Chem. Soc.*, **76**, 6162 (1954); W. E. Parham and H. E. Reiff, *J. Am. Chem. Soc.*, **77**, 1177 (1955).

TABLE I

REACTIONS OF BENZYNE WITH VARIOUS REAGENTS IN LIQUID AMMONIA

Expt. No.	Amide Used[a] (moles per mole C_6H_5Br)	Other Reactant (moles per mole C_6H_5Br)	Yields (%) of Products Isolated[b]			
			$C_6H_5NH_2$	$(C_6H_5)_2NH$	$(C_6H_5)_3N$	Others
1	Na (4)	C_6H_5SH (2)	10	12		52% of $(C_6H_5)_2S$
2	K (3)	C_6H_5SH (1)	Not sought			62% of $(C_6H_5)_2S$
3	Na (4)	C_6H_5SH (2) NaCN (8)	33			48% of $(C_6H_5)_2S$
4	Na (4)	Piperidine (2)	28	24	6	29% of $C_6H_5NC_5H_{10}$
5	K (4)	Piperidine (2)	55	2	13	
6	Na (3)	$(CH_3)_2CHCN$ (1)	29			23% of $C_6H_5(CH_3)_2CCN$ + 38% of $(CH_3)_2CHCONH_2$
7	Na (4)	Na_2S (2)	33	48		
8	Na (2)	NaCN (2)	26	44	8	
9	Na (2)	$CHCl_3$ (1)	11	7	13	44% of C_6H_5Br

[a] Total amide used is listed, including that necessary to free the nucleophilic reagents from their conjugate acids. [b] See Experimental section for details.

the addition of other nucleophilic reagents to II.[8] All reagents attach to the 2-position of II about twice as fast as to the 1-position. It is remarkable that this ratio is virtually unaffected not only by steric effects in the reagent, as Huisgen and Zirngibl[8] have pointed out, but also by changes in the reagent as diverse as from phenyllithium to piperidide ion to thiophenoxide ion, by changes in reaction temperature as great as 140°, and by wide changes in the reaction medium.

Bromobenzene was heated with sodium amide at reflux in *tert*-butyl alcohol for 22 hours; 77% of bromobenzene was recovered and no products were isolated. Benzyne is evidently not formed in this system.

EXPERIMENTAL

Reactions summarized in Table I. In each experiment 15.7 g. (0.1 mole) of bromobenzene was used; the mole ratios of other reactants to bromobenzene are noted in Table I. In each experiment, the requisite amount of sodium or potassium metal was added to about 500 cc. of liquid ammonia in a three-necked round bottom flask equipped with a mechanical stirrer and an acetone-solid carbon dioxide condenser. A trace of ferric nitrate was added and the metal amide was allowed to form. The conjugate acid of the nucleophilic reagent under study was added in the amount noted in Table I. The bromobenzene was next added cautiously from a dropping funnel and the mixture was stirred for a period of from 30 minutes to several hours. An excess of ammonium chloride was then added and the ammonia was allowed to evaporate. The residue was separated into neutral, basic and acidic fractions by standard extraction techniques. Each fraction was submitted to distillation at reduced pressure or was examined by chromatography on alumina.

Aniline was isolated from the basic fraction and was recognized by its refractive index; the observed n_D^{25} ranged from 1.5786 to 1.5836 in various experiments. Diphenylamine was isolated from the neutral fraction and was recognized by its melting point, which ranged from 52–54° to 54–55° in various experiments, and by the observation of non-depression of mixed melting points with authentic samples. Triphenylamine was also isolated from the neutral fraction and was recognized by its melting point, which ranged from 123–125° to 129° in various experiments, and by the failure of mixed melting points with authentic samples to be depressed.

Diphenyl sulfide was isolated, in Expts. 1, 2 and 3, from the neutral fraction by distillation at reduced pressure; its identity was established by its boiling point (118–122°/4 mm., 120–130°/4–5 mm. and 101–103°/2 mm., respectively; lit.[9] 157–158°/16.5 mm.), by its refractive index (n_D^{18} 1.6326, n_D^{18} 1.6391 and n_D^{22} 1.6339, respectively; lit.[10] $n_D^{18.5}$ 1.635) and by oxidation (in the cases of Expts. 1 and 2) to diphenyl sulfone of m.p. 122–123°, not depressed on admixture with an authentic sample.

In Expt. 4, *N*-phenylpiperidine was isolated, as was aniline, by fractional distillation of the basic fraction. It had b.p. 92–96°/4–5 mm. and n_D^{24} 1.5619; authentic *N*-phenylpiperidine has b.p. 98°/5 mm. and n_D^{23} 1.5606.[11] Distillation of the basic fraction from Expt. 5 yielded only aniline; a trace of dark distillation residue had n_D^{25} 1.5799, quite different from the refractive index of *N*-phenylpiperidine.

α-Methyl-α-phenylpropionitrile was isolated by distillation of the neutral fraction from Expt. 6; it had b.p. 100–103°/12 mm. It was hydrolyzed by treatment with 90% sulfuric acid[12] to α-methyl-α-phenylpropionamide of m.p. 159.5–160° (lit.[12] 160–161°). Isobutyramide of m.p. 130–131°, not depressed on admixture with an authentic sample, was isolated from aqueous solutions in the separation of products from Expt. 6.

Reaction of 1-bromonaphthalene with sodium amide and sodium thiophenoxide in liquid ammonia. To 500 cc. of liquid ammonia in a three-necked flask equipped with a mechanical stirrer and an acetone-solid carbon dioxide condenser, 9.2 g. (0.4 mole) of sodium metal and a trace of ferric nitrate were added. When the formation of sodium amide was complete, 22 g. (0.2 mole) of thiophenol was introduced, and then 20.7 g. (0.1 mole) of 1-bromonaphthalene was added cautiously. The mixture was stirred for 3 hr., excess ammonium chloride was added, and the condenser was removed and the ammonia allowed to evaporate. The residue was separated into acidic, neutral, and basic fractions by standard extraction procedures. By distillation of the neutral

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(8) J. F. Bunnett and T. K. Brotherton, *J. Am. Chem. Soc.*, **78**, 155, 6265 (1956); R. Huisgen and L. Zirngibl, *Angew. Chem.*, **69**, 389 (1957).

(9) F. Kraft and W. Vorster, *Ber.*, **26**, 2816 (1893).

(10) A. Himmelbauer, *Zent. Min. Geol.* (*Wien*), 396 (1909); *Chem. Zent.*, **80**, II, 597 (1909).

(11) J. F. Bunnett and T. K. Brotherton, *J. Org. Chem.*, **22**, 832 (1957).

(12) G. Darzens and A. Levy, *Compt. rend.*, **189**, 1287 (1929).

fraction, 6.2 g. of a yellow oil, b.p. 106–132°/3–4 mm., was obtained. The oil was dissolved in 125 cc. of acetic acid and then treated with 3 l. of a 5% potassium permanganate solution. After 1 hr. standing at room temperature, the mixture was treated with sulfur dioxide until the excess permanganate had been destroyed and it was then filtered. The solid collected on the filter melted at 69–91°. The solid was fractionally crystallized from ethanol. The early fractions consisted of grey plates of m.p. 115 ± 1°, but later fractions had much lower melting points and were therefore treated again with potassium permanganate. The resulting solid was fractionally crystallized, first from ethanol and then from an ethanol-ether mixture. The first fractions from ethanol were grey plates of m.p. 115 ± 1°, and the later fractions from ethanol-ether were tan crystals of m.p. about 99°. On recrystallization from ethanol, the lower-melting crystals yielded 2.2 g. of tan crystalline 1-naphthyl phenyl sulfone, m.p. 100.5–101.5° (lit.[13] 99.5–100.5°), and the higher-melting material furnished 4.2 g. of grey 2-naphthyl phenyl sulfone, m.p. 116.5–117.5° (lit.[13] 115–116°). Each sulfone gave a positive qualitative test for sulfur and a negative test for nitrogen, and a mixture of equal parts of the two sulfones melted at 77–111°. The final product composition was 34% 1-naphthyl phenyl sulfone and 66% 2-naphthyl phenyl sulfone, and the combined yield was 27%.

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(13) A. Michael and A. Adair, *Ber.*, **10**, 585 (1877).

Carbamates. I. From Monohydric Alcohols and Toluene-2,4-diisocyanate[1]

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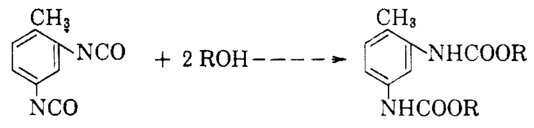
The reaction between an isocyanate and an alcohol to give the carbamate (urethan) is well known.[2] The early application of the reaction to the identification of alcohols was suggested by A. W. Hoffman[3,4] in 1885. The use of various isocyanates has appeared over the years, and a review was presented by Witten and Reid[5] in 1947. The formation of the dicarbamates from toluene-2,4-diisocyanate (or, 4-methyl-*m*-phenylene diisocyanate) has been reported for several of the monohydric alcohols.[6–9] This paper confirms compounds already presented and gives data for fifteen new ones.

Toluene-2,4-diisocyanate(I) reacts readily with monohydric alcohols to form the corresponding dialkyltoluene-2,4-dicarbamates(II).



I II

The reaction proceeds readily at room temperature for the lower, normal, primary alcohols with a definite evolution of heat. The higher, normal, primary alcohols (above eight carbon atoms) react less vigorously. Triethylamine in dry ether was employed as the catalyst for the higher alcohols, together with a heating process of 100° for a period of 4–6 hr. Tertiary butyl and tertiary amyl alcohols failed to give satisfactory derivatives.

The dialkyl toluene-2,4-dicarbamates are colorless, crystalline solids which are readily purified by crystallization from ethyl alcohol. The derivatives above ten carbon atoms show greater solubility in petroleum ether and can be crystallized from this medium.

The application of the dialkyl toluene-2,4 dicarbamates to the qualitative identification of monohydric alcohols offers a good spread of melting points when compared with the various series of carbamates.[5] The total data for the dicarbamates of the monohydric alcohols are presented in Table I.

EXPERIMENTAL

Materials. The toluene-2,4-diisocyanate was obtained from both Monsanto and Du Pont, and was fractionated *in vacuo*. A cut of not over 2° in range was used. Typical boiling ranges: 104–105° (5 mm.); 110–110.5°C. (9.5 mm.). The material was freshly distilled as used, and was stored and handled in a "dry box." The alcohols were obtained from Eastman, or Matheson, and were distilled after drying over Drierite; a cut of not over 0.5° was taken. The solid alcohols were recrystallized from petroleum ether or ethyl alcohol.

Preparation. Two and one-half milliliters (2.5 ml., 0.017 mole) of the diisocyanate were transferred to a test tube (dry box) which contained 0.035 mole of the given alcohol, and 2–3 drops of triethylamine in dry ether. The test tube carried a drying tube of calcium chloride for protection against moisture. The test tube and contents were heated in an oil bath from 4–6 hr. (higher alcohols were heated from 8–10 hr.) at 100°. (For purposes of qualitative identification, 2 ml. of the alcohol are heated on the boiling water bath for 1 hr. with 0.5 ml. of the diisocyanate.) The reaction mixture sets to a crystalline mass upon cooling. The lower members were recrystallized from ethyl alcohol (95%). The higher members were recrystallized from petroleum ether (35–60°). Usually, a highly crystalline product with a sharp melting point resulted after 4–5 recrystallizations. Each sample was dried under reduced pressure in a drying pistol prior to the analysis for nitrogen.

Physiological and herbicidal testing. Since a number of car-

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(1) This paper was presented before the Organic Chemistry Section at the fall meeting of the American Chemical Society at Chicago, Sept. 6–11, 1953.

(2) J. H. Saunders and R. J. Slocombe, *Chem. Revs.*, **43**, 209 (1948).

(3) A. W. Hoffman, *Ber.*, **18**, 518 (1885).

(4) H. L. Snape, *Ber.*, **18**, 2428 (1885); see also: Fr. Gumpert, *J. prakt. Chem.* (2), **31**, 119 (1885); E. Knoevenagel and A. Schurenberg, *Ann.*, **297**, 148 (1897).

(5) B. Witten and E. Emmett Reid, *J. Am. Chem. Soc.*, **69**, 2470 (1947).

(6) R. Lussy, *Ber.*, **7**, 1263 (1874).

(7) W. Siefken, *Ann.*, **562**, 75 (1949); *Chem. Abstr.*, **44**, 109 (1950).

(8) N. G. Gaylord and J. J. O'Brien, *Rec. trav. chim.*, **741**, 218 (1955).

(9) J. A. Parker, J. J. Thomas, and C. L. Zeise, *J. Org. Chem.*, **22**, 594 (1957).