produces a greater tautomeric effect than it does in the ortho position. The cleavage of *o,m'*-substituted diphenyl ether bears out this statement, since it occurs to a greater extent at the linkage between oxygen and the *o*-substituted phenyl group.

Although the above is an attempt to explain the experimental results on the basis of tautomeric and inductive effects, it is quite obvious that these effects do not deal entirely satisfactorily with ortho substituted compounds.

Summary

Several diphenyl ethers with substituents in the meta position of one of the phenyl groups have been prepared and cleaved quantitatively by sodium in liquid ammonia.

Exactly two gram atoms of sodium were required to cleave one gram molecule of the diphenyl ether except in the case of 3-carboxydiphenyl ether, in which case three gram atoms were required.

The positions arranged according to decreasing effectiveness of the inductive influence of the methyl group are: para, meta, ortho.

The cleavage products of the methoxy group in the meta and ortho position are not explained satisfactorily on the basis of inductive and tautomeric effects alone.

Groups that strengthen the linkage between oxygen and the substituted phenyl group against cleavage, arranged in the order of their increasing effectiveness, are: *o*-CH_3, *m*-CH_3, *m*-NH_2, *p*-CH_3, *p*-OCH_3, *o*-NH_2, and *p*-NH_2.

Groups that weaken the linkage between oxygen and the substituted phenyl group toward cleavage, arranged in the order of their increasing effectiveness, are: *m*-OCH_3, *o*-OCH_3, *m*-CO_2Na, *o*-CO_2Na, and *p*-CO_2Na.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Sulfonic and Sulfuric Esters as Alkylating Agents in Liquid Ammonia

BY ARTHUR L. KRANZFELDER AND FRANK J. SOWA

Introduction

Alkylation in liquid ammonia was accomplished by Picon,[1] who utilized the reaction of the alkyl iodides upon sodium acetylide to prepare the alkylacetylenes. Vaughn, Vogt and Nieuwland[2] showed that the alkyl bromides could be used with sodium phenoxide and the sodium alkoxides in liquid ammonia under pressures of from one to ten atmospheres to give fair yields of ethers.

Hurd and Meinert[3] substituted methyl and ethyl sulfates for the alkyl iodides in the preparation of methyl- and ethylacetylene, while Heisig[4] and Heisig and Davis[5] have reported that sodium methyl acetylide can be alkylated by either methyl iodide or methyl sulfate in liquid ammonia.

Although various esters other than the alkyl halides have been employed as alkylating agents, the only such reactions that have been carried out in a liquid ammonia medium have involved the use of methyl and ethyl sulfates. The purpose of this investigation, therefore, was to extend the reaction to other alkyl sulfates, and to test the generality of the reaction with *p*-toluenesulfonic, phosphoric and acetic esters.

Experimental Part

Preparation of Esters.—*n*-Propyl *p*-toluenesulfonate,[6] *n*-amyl sulfate,[7] and sodium phenyl sulfate[8] were prepared by methods described in the literature.

Preparation of *n*-Butyl *p*-Toluenesulfonate.—A modification of the above method[6] was used with the result that the yields were increased considerably. To 185 g. (2.5 moles) of *n*-butyl alcohol was added 11.5 g. (0.5 mole) of sodium, which was first granulated by heating in xylene to its melting point (97.5°) and shaking. The sodium was added in small portions and the alcohol heated to melt the metal. The temperature was allowed to drop to 50° and 97 g. (0.5 mole) of *p*-toluenesulfonyl chloride added in small portions with stirring. The mixture was filtered to remove the sodium chloride formed and washed with *n*-butyl alcohol. The excess alcohol was recovered by distillation at temperatures below 60° (12 mm.). The yield of ester amounted to 98 g. (98% of the theoretical), b. p. 170–172° (10 mm.).

Preparation of *n*-Propyl Sulfate.—Cyclopropane was bubbled into one mole of concd. sulfuric acid with vigorous

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(1) Picon and Lebeau, *Compt. rend.*, **156**, 1077 (1913).

(2) Vaughn, Vogt and Nieuwland, THIS JOURNAL, **57**, 510 (1935).

(3) Hurd and Meinert, *ibid.*, **52**, 4540 (1930); **53**, 289 (1931).

(4) Heisig, *ibid.*, **53**, 3245 (1931).

(5) Heisig and Davis, *ibid.*, **57**, 339 (1935).

(6) Gilman, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932.

(7) Barkenbus and Owen, THIS JOURNAL, **56**, 1204 (1934).

(8) Burkhardt, *J. Chem. Soc.*, 336 (1933).

stirring until exactly 2 moles had been absorbed, using the apparatus described by Wunderly, Sowa and Nieuwland.[9] The reaction mixture was kept at a temperature of −3° by immersion in an ice–salt bath. When the reaction was complete, the reaction mixture was poured over ice, and the oily layer washed five or six times with ice water to remove the excess sulfuric acid. The product was dried over anhydrous sodium sulfate and distilled under reduced pressure. The yield was practically quantitative; b. p. 120° (20 mm.).

Preparation of *i*-Propyl Sulfate.—Exactly the same procedure was employed as for the preparation of *n*-propyl sulfate, using propylene instead of cyclopropane. The best yields (50%) were obtained when 1.5–2.0 moles of sulfuric acid were used and the reaction allowed to proceed for twelve hours.

Preparation of Sodium Acetylide.—The calculated amount of sodium was dissolved in liquid ammonia, in concentrations of approximately one mole per liter. The solution was then added slowly and with stirring to a second volume of liquid ammonia, through which acetylene gas, washed by passing through concd. sulfuric acid, was being bubbled. The disappearance of the blue color, characteristic of free sodium in liquid ammonia, indicated the completion of the reaction.

Preparation of Sodium Phenoxide and Alkoxides.—The calculated quantity of the phenol or alcohol was dissolved in liquid ammonia. To this solution was added, with stirring, a solution of the theoretical amount of sodium in liquid ammonia. Again, the disappearance of the blue color indicated the complete reaction of the sodium.

General Procedure Used in Alkylation.—The liquid ammonia solution of the compound to be alkylated was placed in a three-necked flask fitted with a mercury-sealed stirrer, dropping funnel and an efficient condenser cooled with liquid ammonia. The alkylating agent was added slowly after which stirring was continued until the ammonia had evaporated. The residue was hydrolyzed by the addition of water and the organic oily layer was purified in the usual manner.

In the preparation of the more volatile compounds such as *n*-propyl- and *i*-propylacetylene, where the losses due to entrainment and volatilization are large, added precautions were necessary. Following this procedure, phenol, acetylene, butyl alcohol and amyl alcohol each was treated with methyl, propyl and butyl *p*-toluenesulfonate and with ethyl, *n*-propyl, *i*-propyl, and *n*-amyl sulfates. Phenol was also treated with sodium phenyl sulfate. The results are summarized under "Discussion of Results."

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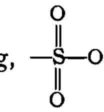
Discussion of Results

By treating phenol, acetylene, butyl alcohol and amyl alcohol each with methyl, *n*-propyl and *n*-butyl *p*-toluenesulfonate the yields were 37–47% if the ratio of reactants was either 1.0:1.4 or 1:2. By treating the same compounds each with ethyl, *n*-propyl, *i*-propyl and *n*-amyl sulfates the yields varied between 29–50% whereas sodium phenoxide gave higher yields (60–88%). Sodium phenyl sulfate with phenol gave a 25% yield of diphenyl oxide.

Of the esters used, only those containing the grouping,  $-\overset{\overset{\large O}{\|}}{\underset{\underset{\large O}{\|}}{S}}-OR$, were found to be of use as alkylating agents. Attempts were made to alkylate sodium acetylide and sodium phenoxide by means of *n*-amyl acetate, but in each case only *n*-amyl alcohol and some of the original ester were recovered. In the case of tributyl phosphate, some *n*-butyl alcohol was recovered from the highly decomposed reaction mixture, but none of the desired product was obtained, indicating in each case that the particular esters were insufficiently stable in the reaction medium to be of value.

In using the esters of *p*-toluenesulfonic acid, it was found that only the liquid esters produced a reaction. The crystalline esters, *n*-amyl and phenyl *p*-toluenesulfonates, were insoluble in liquid ammonia, and could not be made to react by merely adding them to the reaction mixture. The only crystalline ester of sulfuric acid employed was sodium phenyl sulfate, which proved to be soluble in the reaction medium and capable of being used as an alkylating agent, to form diphenyl oxide.

In general, as good yields were obtained with the higher members of each series as with those containing alkyl groups of lower carbon content. The percentage yields listed undoubtedly do not represent the maximum obtainable due to the fact that entrainment losses assume a considerable importance when small quantities of ester are employed. Only one alkyl group of the ester is useful in the alkylation, although the yields are increased considerably by increasing the molal ratio of the compound alkylated to the ester used. The best yields were obtained when this ratio was 2:1. It was also found advantageous to add the alkylating agent quite slowly, and to supply more liquid ammonia when addition was complete, thus ensuring complete reaction of the ester. The ammonia vapors caused some of the esters to become cloudy and viscous in the dropping funnel, but this was remedied by dissolving them in anhydrous ether.

The sodium salts of the compounds to be alkylated can be prepared with great facility in liquid

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(9) Wunderly, Sowa and Nieuwland, This Journal, 58, 1007 (1936).

ammonia, and in this respect the latter possesses a distinct advantage over either an aqueous or organic medium in carrying out the alkylation reactions studied in this investigation. By using the alkyl *p*-toluenesulfonates and alkyl sulfates as alkylating agents, this advantage is combined with the facts that the alkylations are capable of being carried out at atmospheric pressure, and that the final product as obtained directly from the reaction mixture is in a high state of purity. The latter presents a serious problem when alkylating with the alkyl halides, due to the difficulty in separating them from the desired product by fractionation. This is especially true in the case of the alkylacetylenes.

The preparation of *i*-propylacetylene by means of *i*-propyl sulfate represents, as far as is possible to ascertain, the first direct method for the synthesis of this compound. Investigations will be continued along this line in an attempt to synthesize various branched chain alkyl acetylenes by means of the appropriate alkyl sulfates.

Summary

The alkylation of acetylene, phenol and alcohols has been accomplished by means of the alkyl esters of *p*-toluenesulfonic acid and sulfuric acid in liquid ammonia.

It has been found that the yields are increased considerably by increasing the molal ratio of compound alkylated to ester used, the best yields resulting when this ratio was 2:1.

i-Propyl sulfate has been employed for the synthesis of the corresponding branched chain alkyl acetylene.

A modified method for the preparation of *n*-butyl *p*-toluenesulfonate has been described.

A convenient method has been given for the synthesis of *n*-propyl and *i*-propyl sulfates.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FORDHAM UNIVERSITY]

Equilibria in Protium Oxide–Deuterium Oxide Mixtures

BY WILLIAM H. HAMILL

Ionization of a Weak Acid in H_2O–D_2O.—The dissociation equilibrium expression for a weak acid in aqueous medium of normal isotopic composition is expressed satisfactorily in the conventional manner: $K = (H^+)(A^-)/(HA)$. For isotopic mixtures an apparent equilibrium constant ($K_{ap.}$) is defined in terms of all isotopically variable molecular species involved in the component equilibria. In general, for the isotopically distinct reactants A_i, B_i,... and products X_i, Y_i,... this is (1) and becomes (2) for a weak monobasic acid.

$$\frac{(\Sigma X_i)^x(\Sigma Y_i)^y\ldots}{(\Sigma A_i)^a(\Sigma B_i)^b\ldots} \equiv K_{ap.} \qquad (1)$$

$$\frac{(H_3O^+ + H_2DO^+ + HD_2O^+ + D_3O^+)(A-)}{(HA + DA)(H_2O + HDO + D_2O)} \equiv K_{ap.} \equiv K_2 \qquad (2)$$

In terms of equilibria (3) to (7) of Table I, where $R = HDO/H_2O$, equation (2) is simply resolved and becomes (8a). An exchange constant of the

$$\frac{(H_3O^+)(A^-)(1 + K_3R + K_3K_4R^2 + K_3K_4K_5R^3)}{(HA)(H_2O)(1 + K_6R)(1 + R + R^2/K_7)} = K_{ap.} = K_8 \qquad (8a)$$

type K_6 ordinarily can be determined by experiment or from spectroscopic data, or indirectly as appears below. The evaluation of K_3, K_4, K_5 depends upon a knowledge of $K_{ap.}$ for H_2O–D_2O mixtures. K_3 can be determined at small deuterium concentrations where R is very small and (8a) becomes approximately

$$\frac{K_{HA}(1 + K_3R)}{(1 + K_6R)(1 + R + R^2/K_7)} = K_8 \qquad (8b)$$

In the limit for deuterium oxide the product $K_3K_4K_5$ is obtained since (8a) becomes

$$K_3K_4K_5K_7/K_6 = K_{DA}/K_{HA} \qquad (8c)$$

TABLE I

$H_3O^+ + HDO = H_2DO^+ + H_2O$;	$(H_2DO^+) = K_3R(H_3O^+)$	(3)
$H_2DO^+ + HDO = HD_2O^+ + H_2O$;	$(HD_2O^+) = K_3K_4R^2(H_3O^+)$	(4)
$HD_2O^+ + HDO = D_3O^+ + H_2O$;	$(D_3O^+) = K_3K_4K_5R^3(H_3O^+)$	(5)
$HA + HDO = DA + H_2O$;	$(DA) = K_6R(HA)$	(6)
$H_2O + D_2O = 2HDO$;	$K_7 = 3.27$	(7)
$QH_2 + HDO = QHD + H_2O$;	K_9	(9)
$QHD + HDO = QD_2 + H_2O$;	K_{10}	(10)
$H_2DO^+ + D_2O = D_3O^+ + H_2O$;	$K = K_4K_5K_7$	(12a)
$H_3O^+ + D_2O = HD_2O^+ + H_2O$;	$K = K_3K_4K_7$	(12b)
etc.		

K_4 is obtained readily at intermediate H_2O–D_2O concentrations. It is clear that K_6 is the only variable at constant temperature which is required to fix the ratio K_{DA}/K_{HA}.