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A new method for the preparation of alkylnaphthyl ethers and sulfides

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A NEW METHOD FOR THE PREPARATION OF ALKYLNAPHTHYL ETHERS AND SULFIDES

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I. INTRODUCTION

Over the past three decades the chemistry of dehydrobenzene has been extensively studied. The chemistry of dehydronaphthalene has developed along with and as a natural consequence of the development of dehydrobenzene chemistry. Most of the early work, carried out in the 1950's, concerned the generation of 1,2- and 2,3-dehydronaphthalenes by reacting halonaphthalenes with strong bases such as carbanions and metal amides. Recently, methods of generating dehydrobenzene by metal alkoxides, made strongly basic in dipolar aprotic solvents, have been accomplished (9, 14, 29). We were very interested in these kinds of reactions and began a study to extend them to the formation of 1,2-dehydronaphthalene. Specifically, the 1,2-dehydronaphthalene has been generated by the reaction of monohalonaphthalene with potassium t-butoxide in a dimethyl sulfoxide (DMSO) and t-butyl alcohol mixture (4). Potassium n-butoxide and sodium methoxide in a solvent mixture of the corresponding alcohol and DMSO has also been studied to a limited extent. We have carried out this work with the following objectives in mind: (a) to find conditions under which the desired products, i.g. t-butylnaphthyl ether, would be formed in major yield and at the same time minimizing the yields of any other products; (b) to compare the ratio of 1-substituted products to 2-substituted products formed in our reaction when the metal alkoxide was changed from potassium t-butoxide to potassium n-butoxide to sodium methoxide; (c) to find the effect of basicity of metal alkoxide on our reactions.

Generally speaking, aromatic ethers are not difficult to prepare. The appropriate naphthol is reacted with an alkyl halide in alkaline solution (e.g. aqueous sodium hydroxide). However, t-butylaryl ethers can be prepared in this way only with considerable difficulty because the base-catalyzed elimination of the t-butyl halide competes seriously with substitution. R.A. Smith (49) reported the preparation of t-butylphenyl ether only in very poor yield on reacting sodium phenoxide with t-butyl chloride. Olsen and his coworkers (41) reacted phenol with t-butyl alcohol in the presence of a large amount of 80% sulfuric acid at 50°C for 1½ hours to obtain a 6.7% yield of t-butyl phenyl ether. Recently, pure t-butylnaphthyl ethers have been prepared by reacting the naphthylmagnesium halide with t-butyl perbenzoate in ethyl ether (32). Good yields of the t-butylnaphthyl ethers can also be obtained by reacting fluoronaphthalene with potassium t-butoxide in a t-butyl alcohol and DMSO mixture (22).

Although there is much reported in the literature concerning the reactions of aromatic halogen compounds with thiophenoxide, thiocyanate, phenylsulfinate (43, 44) and thiosulfate and thiourea (54), very little work has been done with the alkyl mercaptides. J. Miller has reported that methyl mercaptide is a much stronger nucleophile in aromatic nucleophilic substitution than thiophenoxide (37). Caubere and his coworkers have reacted methyl and ethyl mercaptide with phenyl halides in hexamethylphosphotriamide (HMPT) to prepare alkylphenyl sulfides (10, 11). The alkyl naphthyl sulfides are in general not as readily prepared and available as the corresponding ethers. One method is the reaction of an appropriate naphthol with a mercaptan in the presence of acid catalyst (e.g. p-toluenesulfonic acid) without a solvent

(19). The present method is an excellent way to prepare the alkyl naphthyl sulfides.

II. LITERATURE REVIEW

Dehydronaphthalene

Since the structure of dehydronaphthalene is very similar to that of dehydrobenzene, the chemical properties of these two reactive intermediates have much in common. They also have been shown to have similar structures as far as the dehydro bond is concerned. Since the bond distance of the dehydro bond would be expected to parallel that of the corresponding bonds in the parent hydrocarbon, i.e. 1.36 Å in the 1,2 position and 1.40 Å in the 2,3 position in naphthalene, a shorter hydro bond, therefore, should lead to greater overlap of the two orbitals and should consequently increase the stability and selectivity of the dehydroaromatic intermediate (23). This makes the 1,2-dehydronaphthalene more stable and more available than the 2,3-dehydronaphthalene.

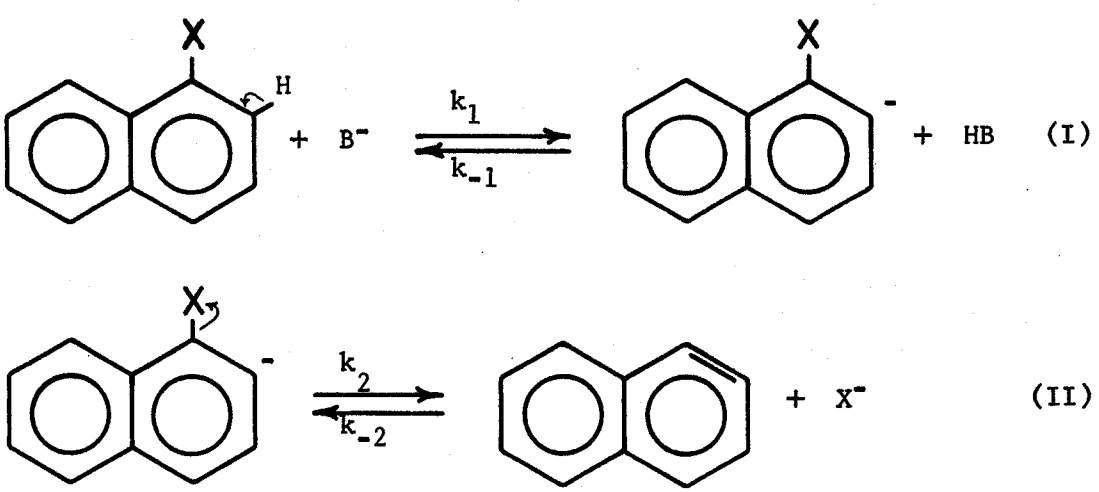
Generation of Dehydronaphthalene

Like dehydrobenzene, dehydronaphthalene has been generated most often by metalation reactions. The reagents used have been organometallic compounds and metal amides. Dehydronaphthalene has been formed by reacting phenyllithium with 1- and 2-fluoro (26) or 1- and 2-chloronaphthalene (24, 25, 26). The use of a leaving group other than halide has been reported in the formation of dehydronaphthalene by the reaction in ether of 2-methoxynaphthalene with n-butyllithium (53). Metal amides have found greater use in the formation of dehydronaphthalene. The reaction of sodium amide with 1- and 2-fluoro, chloro, bromo and iodonaphthalene in piperidine (7) are the examples. Gilman and his coworkers

have also reported the generation of dehydronaphthalene from the reaction of 1-fluoro, chloro and bromonaphthalene with lithium diethylamide in ether (20). Recently, Bradshaw and his coworkers were the first to report the generation of dehydronaphthalene by reacting potassium t-butoxide with 1-bromonaphthalene in a solvent mixture of t-butyl alcohol and dimethyl sulfoxide (5).

Mechanism of Dehydronaphthalene Formation

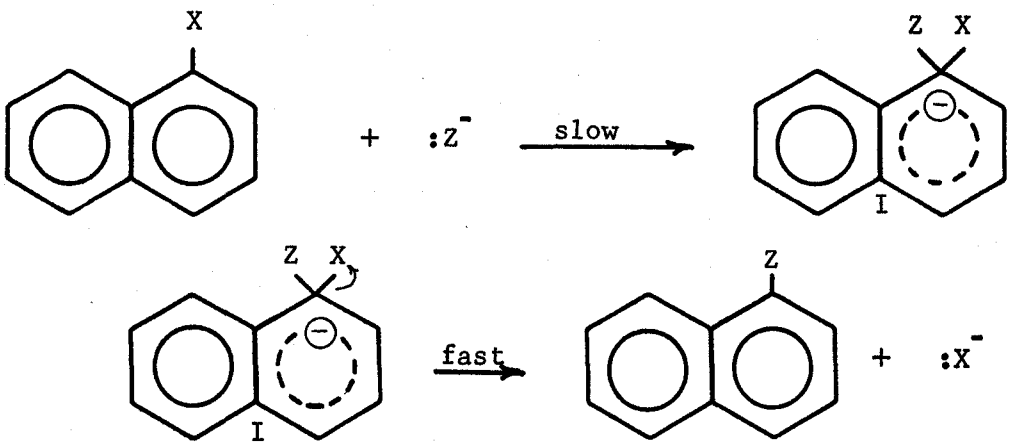
The basic mechanism for the formation of 1,2-dehydronaphthalene by the metalation of halonaphthalenes can be summarized in the following mechanistic scheme:



Because of the extreme instability of unsubstituted 2-halonaphthyl anions, k_1 in step I should be the rate determining step. The order of reactivity in k_1 should be F > Cl > Br > I, because the removal of the ortho hydrogen would be enhanced by the increased electronegative properties in going from iodine to fluorine. The order of reactivity for k_2, however, is known to be I > Br > Cl > F (22).

Aromatic Nucleophilic Substitution in Halonaphthalenes

It is well known that the aryl halides are characterized by very low reactivity toward the nucleophilic reagents such as OH^-, OR^-, NH_3 and CN^-. However, the presence of certain electron-withdrawing groups such as NO_2, COOH, CN ortho and/or para to the halogen greatly increases the reactivity. The bimolecular displacement mechanism for nucleophilic aromatic substitution in halonaphthalene can be summarized in the following mechanistic scheme:



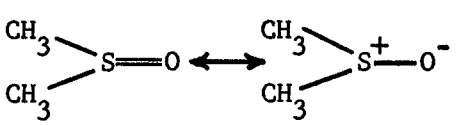
There are two essential steps: attack by a nucleophilic reagent upon the ring to form the carbanion intermediate I and the expulsion of halide ion from this carbanion intermediate to yield the product. Both steps are directly and markedly involved in the reactivity of the nucleophile. The carbanion intermediate containing a tetrahedral carbon and having the negative charge distributed about the ring is comparatively stable, especially in some instances.

Nature of DMSO as a Solvent

A number of excellent reviews concerning DMSO as a reaction solvent have been published in recent years (27, 35, 42, 45). The most important solvent characteristics of DMSO are its high polarity, its

essentially aprotic nature and its solvating ability. The high dipole moment of the sulfur-oxygen bond (4.3) and the high dielectric constant (approximately 48) for DMSO suggest the solvating properties and ability to disperse charged solutes. The hydrogen atoms of DMSO are quite inert except to very strong bases. DMSO is not a hydrogen donor in hydrogen bonding and poorly solvates anions (but strongly solvates cations) except by dipolar association to polarizable anions.

Among the dipolar aprotic solvents such as dimethylformamide (DMF), dimethylacetamide (DMAC), tetramethylurea, acetonitrile, dimethylsulfone, dimethyl sulfoxide (DMSO), tetrahydrothiophene dioxide (sulfolane), DMSO, first prepared in 1866 (48), has become increasingly important in recent years. The physical properties of DMSO have been studied and tabulated (15, 35) and its pharmacological harmlessness has been well established (2, 17, 33). DMSO is a colorless, odorless and a very hygroscopic liquid with a slightly bitter taste. Prolonged refluxing at atmospheric pressure will cause slow decomposition. If this occurs, it can be readily detected by the odor of a trace amount of methylmercaptan and bis-methylthiomethane. The rate of decomposition, however, is accelerated by addition of acids and retarded by ases (15). DMSO has a bipyramidal structure with sulfur, oxygen and carbon atoms at the corners (33, p. 3) and its structure is usually represented by the resonance hybrid of the canonical structure



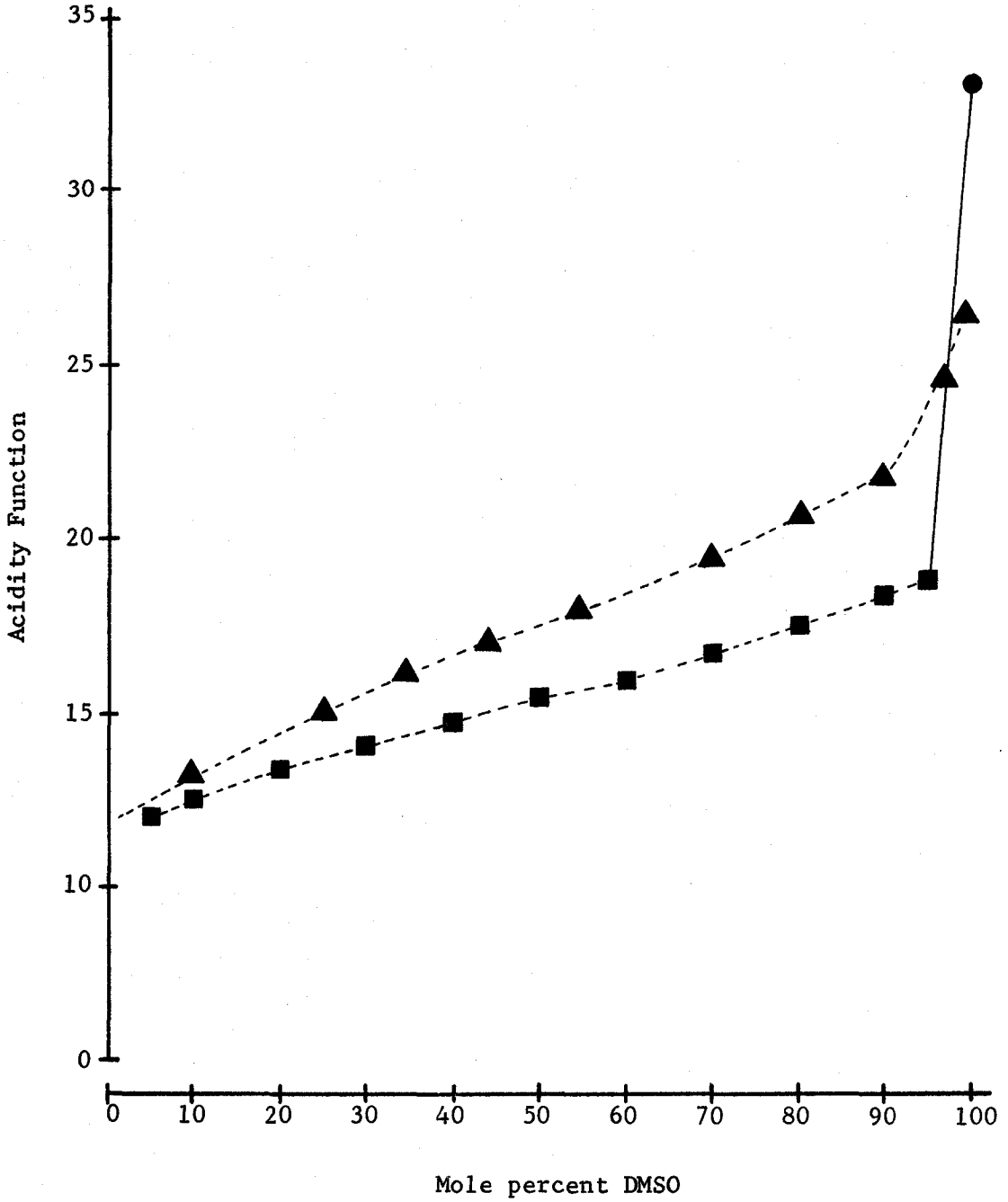
having a polarized S--O bond and that having a (p--d) sulfur and oxygen double bond (42).

Basicity in DMSO

The reactivity of nucleophiles in DMSO mixtures with water or alcohols consistently increases as the content of DMSO in the mixture increases. When the nucleophile is hydroxide ion in the aqueous system, or alkoxide ion in the alcoholic system, the reactivities of the bases can be presented in terms of acidity function, giving the picture shown in Fig. 1 (16). Since the acidity function is a logarithmic scale measuring the ability of the system to remove a proton from the reference indicator, the data show the basicity to be enhanced by some 14 powers of 10 upon changing the solvent from water or alcohol to 99% DMSO. Such a protic aprotic system thus offers a means of adjusting the basicity of a reaction medium over a wide range. The simple aliphatic alcohols are one thousand times as acidic as DMSO in substantially pure DMSO and have about the same acidity as triphenylmethane (46, 51).

Displacement Reactions in DMSO

The high activity of alkoxide ions in DMSO shows up both in their enhanced basicity (51) and the greater rate at which displacement and elimination reactions occur. The activity of the alkoxide ion in DMSO is influenced by the cation and is greatest with cesium and least with lithium (13). The rate of reaction of alkoxide ions with alkyl halides in alcohol and DMSO mixtures to form ethers increases with the content of DMSO. The same is true for displacement reaction of aromatic halides in the nitroaryl halides where the reaction rate with methoxide ion in methanol and DMSO mixture is increased one thousand fold by increasing the DMSO concentration to 80% (28). The common procedure of preparing ethers by reacting aliphatic sulfonate esters with alkoxides occurs readily in DMSO. It is not surprising that mercaptide ions



■ Methanol--DMSO containing 0.025 M Sodium Methoxide (52)

● Potassium t-butoxide in 99.89 mole percent DMSO (51)

▲ Water--DMSO containing 0.011 M Me_4NOH (18)

Fig.--1

should displace halide or sulfonate group at a good rate in DMSO whether the mercaptide is aliphatic, aryl or heterocyclic (28, 31, 39). DMSO enhances the rate at which halides are displaced by phenoxides almost as much as it does for alkoxides or mercaptides (28). With ions such as naphthoxide where a choice exists between carbon and oxygen alkylation, the reaction in DMSO gives almost exclusive oxygen alkylation (30) and DMSO has found considerable use as a solvent for preparing aromatic ethers and sulfides (36, 38).

III. RESULTS AND DISCUSSION

Aromatic ethers in general are not difficult to prepare. The appropriate phenol is reacted with an alkyl halide in the presence of sodium hydroxide (40). But t-butyl ethers cannot be prepared in this manner. The preparation of t-butyl 2-naphthyl ether using the procedure of Sahyun and Cram (47) was conducted by J. S. Bradshaw, N. B. Nielsen and D. P. Rees (5) by reacting 1-bromonaphthalene with potassium t-butoxide in a mixed solvent of t-butyl alcohol and dimethyl sulfoxide (DMSO). At that time, no t-butyl-1-naphthyl ether was found and a mixture of 1- and 2-naphthol was the major product. Based on these initial results, a detailed study of the reaction of monohalonaphthalenes with potassium t-butoxide in a t-butyl alcohol and DMSO solvent mixture was undertaken and reported (21).

Reaction of 2-Fluoronaphthalene with Potassium n-Butoxide in a n-Butyl Alcohol and DMSO Mixture

The reaction of 2-fluoronaphthalene with potassium n-butoxide at various conditions gave only one ether product in a very high yield (92-96%) (Table 1). There is only a minute amount of 2-naphthol formed in this reaction, because the n-butyl 2-naphthyl ether does not decompose in the basic solution. The formation of naphthalene in this reaction could not be detected by vapor phase chromatography (vpc) analysis or thin layer chromatography.

On reviewing the results in Table 1, it becomes apparent that

TABLE 1

MOLE PERCENT YIELDS OF PRODUCTS AND CONDITIONS EMPLOYED IN THE REACTION OF 2-FLUORONAPHTHALENE WITH POTASSIUM n-BUTOXIDE IN A n-BUTYL ALCOHOL AND DMSO MIXTURE

Temp. °C	Time hr.	I	II	III
100	7	94.3	trace	0.7
120	3	92.0	1.5	0.5
150	1	96.1	1.0	trace

I: n-butyl 2-naphthyl ether; II: 2-fluoronaphthalene; III: 2-naphthol

the same mechanism is leading to the major product in every experiment no matter what reaction conditions under which it was run. Since the 2-naphthyl ether was the only product, the reaction of fluoronaphthalene with potassium n-butoxide is proceeding by direct nucleophilic substitution. The fact that no 1-naphthyl ether was detected is evidence that the reaction was not through the 1,2-dehydronaphthalene intermediate. This is in contrast to the reaction of bromonaphthalene with potassium t-butoxide which has the 1,2-dehydronaphthalene intermediate (4). Similar results were also reported by Bradshaw and coworkers (6) for the reaction of fluoro and bromonaphthalene with sodium n-butyl mercaptide in DMSO. This latter reaction also gave only the corresponding alkyl naphthyl sulfides by way of direct nucleophilic substitution.

Reaction of Fluoronaphthalenes with Potassium t-Butoxide in a t-Butyl Alcohol and DMSO Mixture

Because of elimination, t-butyl naphthyl ethers are in general not easy to prepare. We reacted 1- and 2-fluoronaphthalene with potassium t-butoxide in a t-butyl alcohol and DMSO mixture. As shown in Table 2,

about 26-36% of the starting materials was recovered and about 21-29% ether products decomposed to the corresponding naphthol even under the optimal reaction conditions.

TABLE 2

MOLE PERCENT YIELDS OF PRODUCTS AND CONDITIONS EMPLOYED IN THE REACTION OF FLUORONAPHTHALENE WITH POTASSIUM t-BUTOXIDE IN A t-BUTYL ALCOHOL AND DMSO MIXTURE

Run	Temp. (°C)	Time	I	II	III	IV	V	VI
1*	140	5 min.	28.1		42.2		26.7	
2*	100	10 min.	29.5		38.4		30.1	
3*	80	15 min.	31.7		30.8		35.8	
4*	120	15 min.	29.0		40.1		28.6	
5*	60	12 hrs.	45.4		20.6		30.9	
6**	80	14 hrs.		39.6		28.7		30.2
7**	70	14 hrs.		48.2		22.0		28.3

*1-Fluoronaphthalene used as starting material.

**2-fluoronaphthalene used as starting material.

I: t-butyl 1-naphthyl ether; II: t-butyl 2-naphthyl ether; III: 1-naphthol; IV: 2-naphthol; V: 1-fluoronaphthalene; VI: 2-fluoronaphthalene.

Bromonaphthalene cannot be used to prepare the t-butyl naphthyl ethers because a mixture of t-butyl 1-naphthyl ether and t-butyl 2-naphthyl ether was obtained in this reaction (4). Fluoronaphthalene, on the other hand, reacted with potassium t-butoxide to yield only the one corresponding ether product and naphthol. The formation of naphthol in each case proved to be from the base catalyzed degradation of the corresponding ether (4). Table 2 shows that lower temperature and longer reaction times were the best reaction conditions for maximizing the yield

of the desired ether products and at the same time minimizing the formation of the naphthols.

Reaction of Bromonaphthalene with Sodium Methoxide in Methanol and DMSO Mixture

The reaction of bromonaphthalene with sodium methoxide in a mixture of methanol and DMSO gave only the one corresponding ether product in good yield (65-72%) and some naphthalene (5.6-7.1%) and methylnaphthalene (3-8%) (Table 3). The presence of naphthol in the acidic

TABLE 3

MOLE PERCENT YIELDS OF PRODUCTS AND CONDITIONS EMPLOYED IN THE REACTION OF BROMONAPHTHALENES WITH SODIUM METHOXIDE IN A METHANOL AND DMSO MIXTURE

Run	Temp. (°C)	Time (hrs)	I	II	III	IV	V
1a	155	16	72.1		7.0	7.9	
2a	155	68	71.8		7.1	8.1	
1b*	150	16	15.0	66.0	5.6		3.2
2b*	150	10	15.0	65.2	6.0		3.1

[a] 2-bromonaphthalene used. [b] 1-bromonaphthalene used.

* Starting 1-bromonaphthalene was contaminated with 2-bromonaphthalene (see experimental section).

I: 2-methylnaphthyl ether; II: 1-methylnaphthyl ether; III: naphthalene; IV: 2-methylnaphthalene; V: 1-methylnaphthalene.

fraction and the recovered starting material in the neutral fraction could not be detected by the vpc analysis and thin layer chromatography. The formation of about 6% naphthalene in every case was somewhat surprising. The same observation was also reported by Bradshaw and Hales (4, p. 320) in the reaction of bromonaphthalene with potassium n-butoxide in n-butyl alcohol and DMSO.

Since there was only one ether product obtained from the corresponding starting bromonaphthalene, direct nucleophilic substitution is the probable mechanism. The presence of 15% 2-methylnaphthyl ether in the 1-methylnaphthyl ether product (runs 1b, 2b) is due to the fact that 15% 2-bromonaphthalene contaminated the starting 1-bromonaphthalene. (See Analysis of Starting Materials, p. 20.)

The methylnaphthalenes are probably being formed from naphthalene and methylsulfinyl carbanion as reported by Schriesheim and his coworkers (1). They found a ratio of 96% 1-methylnaphthalene to 4% 2-methylnaphthalene when naphthalene was treated with DMSO and potassium t-butoxide in diglyme.

Reaction of 2-Bromonaphthalene with 1-Butanethiol in a Sodium Methoxide and DMSO Mixture

The alkyl naphthyl sulfides are not as readily available as the ethers. One preparative method is the acid catalyzed reaction of naphthol and a mercaptan (19). In our reaction, 2-bromonaphthalene was rapidly added to a mixture of DMSO, 1-butanethiol and sodium methoxide and 110°C. Since the thiol is a very much stronger acid than methanol, sodium methoxide was used as the base (34). Thus the solution would contain essentially methanol and sodium n-butyl mercaptide. The n-butyl 2-naphthyl sulfide was obtained in a 58% yield. This reaction has been carried out on 1-, and 2-bromonaphthalenes using both n-butyl and t-butyl mercaptans (6), and also on 1-chloronaphthalene using n-butyl mercaptan to give good yields of sulfide products (69-75%) (3). Since only the corresponding butyl naphthyl sulfide was obtained, these reactions probably are direct aromatic nucleophilic substitution reactions. Di-n-butyl disulfide was also isolated in every case. This is due to the

base-catalyzed oxidation of mercaptans to disulfides (55, 56).

In the previous work reported by Bradshaw and his coworkers (4, 21, 22), the reaction of 1- and 2-bromo-, chloro- and iodonaphthalenes with potassium t-butoxide in a t-butyl alcohol and DMSO mixture all gave the same mixture of t-butyl 1-naphthyl ether and t-butyl 2-naphthyl ether with a ratio of 0.35 ± 0.03. The fact that all these reactions gave the same product ratio indicates that 1,2-dehydronaphthalene is indeed an intermediate in the reaction of monohalonaphthalenes with potassium t-butoxide in a solvent mixture of t-butyl alcohol and DMSO when the halogen is either chlorine, bromine or iodine. On the other hand, the reaction of fluoronaphthalene with potassium t-butoxide gave only one product as well as with potassium n-butoxide and sodium n-butyl mercaptide. Direct nucleophilic substitution was observed in these fluoronaphthalene reactions presumably because fluoride ion is a particularly good leaving group in aromatic nucleophilic substitution. Apparently, the rate for step 2 in the mechanistic scheme shown on page 4 is very much slower than that for step -1 when X = F.

In the present work, only direct nucleophilic substitution was observed in the reactions of bromonaphthalene with sodium methoxide and sodium n-butyl mercaptide. The potassium n-butoxide reaction gave both direct nucleophilic substitution and the 1,2-dehydronaphthalene intermediate (21, p. 73). Alkoxides are all very powerful bases in DMSO. t-Butyl alcohol has a pk_a in DMSO of 29.2 (12). The use of a base which is weaker than t-butoxide can change the apparent reaction mechanism from the dehydronaphthalene to direct nucleophilic substitution. This is shown by the fact that the reaction of bromonaphthalene with t-butoxide whose pk_a in DMSO is 29.2 (12) gave the dehydronaphthalene intermediate

(4), whereas, with n-butoxide whose pk_a in DMSO is probably the same as that of n-propyl alcohol approximately 28.0 (12), both the dehydronaphthalene intermediate and direct nucleophilic substitution were observed (4), and with methoxide (pk_a = 27.0) (12), only direct nucleophilic substitution was found. It appears that a relatively small decrease in the pk_a of the alcohol can shift the reaction from that proceeding by way of a dehydronaphthalene mechanism to direct nucleophilic substitution in the bromonaphthalene system.

IV. EXPERIMENTAL

General Information

Melting points.--All melting points were determined on a Thomas-Hoover capillary melting point apparatus and were not corrected.

Refractive index.--All refractive indexes were determined on a Bausch and Lomb refractometer.

Infrared spectra.--All infrared (ir) spectra were recorded on a Perkin-Elmer 457 spectrophotometer. All liquids were run as capillary neat films between sodium chloride pellets. All solids were run by preparing a transparent window of the sample in a potassium bromide matrix.

Gas chromatography.--Reaction products and recovered starting materials were separated, isolated, analyzed and in part, identified by gas chromatography. Collections and quantitative determinations of products and recovered starting materials were made on a Varian Aerograph Model 90-P3 vapor phase chromatograph (vpc). A Honeywell Electronik recorder was used for every case. The column used was 6% carbowax 20M (polyethylene oxide) and 6% SE-30 (silicone rubber) on 60/80 mesh, chromosorb G acid washed, loaded in 1/8" x 5' column.

Thin layer chromatography.--Alumina (80-200 mesh, Fisher Scientific Co.) was used as the absorbent after it had first been neutralized and activated. Reagent grade benzene was used as eluant without further purification.

Materials.--The reagents, solvents and other chemicals used in

this study are listed in Table 4 along with their sources. The starting materials were used as obtained from their sources without further purification. The solvents, however, were especially treated. Reagent grade DMSO (dimethyl sulfoxide) was passed through silica gel (J. T. Baker Chemical Co.) and stored over type 4A, 1/16" pellet molecular sieves (Fisher Scientific Co.). Reagent grade t-butyl alcohol, n-butyl alcohol and methanol were also stored over type 4A molecular sieves. All bottles containing DMSO, n-butyl alcohol, t-butyl alcohol, methanol, iodomethane, potassium t-butoxide, sodium methoxide and n-butanethiol were sealed with paraffin wax to avoid absorbing moisture during storage.

TABLE 4

MATERIALS USED

Material	Source
1-Fluoronaphthalene	Eastman Kodak Co.
2-Fluoronaphthalene	PCR Inc.
1-Bromonaphthalene	J.T. Baker Chemical Co.
2-Bromonaphthalene	J.T. Baker Chemical Co.
Dimethyl sulfoxide (DMSO)	J.T. Baker Chemical Co.
Sodium methoxide	Olin Mathieson Chemical Co.
Potassium t-butoxide	MSA Research Co.
Iodomethane	Matheson, Coleman and Bell Co.
n-Butanethiol	Aldrich Chemical Co.
Potassium metal	Fisher Scientific Co.
n-Butyl alcohol	J. T. Baker Chemical Co.
t-Butyl alcohol	J. T. Baker Chemical Co.
Methanol	J. T. Baker Chemical Co.
Naphthalene	Aldrich Chemical Co.
1-Naphthol	Aldrich Chemical Co.
2-Naphthol	Aldrich Chemical Co.

Analysis of starting materials.--The fluoro- and bromonaphthalenes used as reactants in the every reaction were analyzed quantitively by gas chromatography. It was found that a small amount (about 0.9%) of naphthalene contamination was present in either the 1- or 2-bromonaphthalene and about 15% of 2-bromonaphthalene contaminated the 1-bromonaphthalene. The presence of naphthalene in either 1- or 2-fluoronaphthalene could not be determined by vpc analysis because conditions could not be found under which naphthalene and fluoronaphthalene could be separated. However, an ir spectrum and a thin layer chromatograph of either the starting materials or the recovered fluoronaphthalenes did not show any presence of naphthalene.

Preparation of Authentic Sample Methyl 1-Naphthyl Ether

An authentic sample of methyl 1-naphthyl ether was prepared by the method of Musser and Adkins (40). 1-Naphthol (14.4g, 0.1 mole) was mixed with 4.3 g sodium hydroxide dissolved in 20 ml water in a 50 ml three neck-round bottom flask equipped with a magnetic stirrer and a heating mantle. Slight heating was necessary to dissolve the 1-naphthol. After the 1-naphthol had all dissolved and the temperature had maintained at 70°C, 15.8 g (0.1 mole) iodomethane was added by means of the addition funnel. The reaction was run for 9 hours under reflux. The reaction mixture was distilled under vacuum. The product was collected at 105-110°C/1mm, $n_D^{22} = 1.6195$, (literature value (57): $n_D^{14} = 1.6232$). The product exhibited an ir spectrum identical to that assigned. The ir bands are as follows: 3000, 1760, 1600, 1584, 1473, 1450, 1400, 1360, 1270, 1228, 1208, 1180, 1124, 1040, 972, 960, 908, 888, 850, 828, 778, 750, 705 cm^{-1}.

Reaction of 1-Fluoronaphthalene with Potassium t-Butoxide

The procedure of R. H. Hales was followed for this reaction (21). A mixture of 16.055 g (0.2054 mole) DMSO (IV), 3.04 g (0.041 mole) t-butyl alcohol (II) and 3.07 g (0.0274 mole) potassium t-butoxide (III) was placed in a 50 ml three neck round bottom flask equipped with a thermometer, a reflux condenser and an addition funnel. The potassium t-butoxide dissolved when the stirred (magnetic stirring bar) reaction mixture was heated up to about 120°C. After the temperature of the reaction mixture had maintained at 140°C, 1-fluoronaphthalene (I) (2.0 g, 0.013687 mole) (the mole ratio of I to II to III to IV was 1/2/3/15) (21, p. 113) was quickly added by means of the addition funnel. The reaction mixture turned dark brown and the temperature went down to about 120°C. After 5 minutes the reaction mixture was quenched with 50 ml ice water saturated with sodium chloride, and extracted four times with 50 ml portions of ethyl ether. The combined ether extracts were washed with a 5% aqueous sodium hydroxide solution and filtered through anhydrous magnesium sulfate. The ether extract was evaporated, leaving 1.15 g of an orange liquid. This is called the neutral fraction.

The remaining aqueous DMSO reaction mixture was acidified with concentrated hydrochloric acid to a pH of 1, and extracted four times with 50 ml portions of ethyl ether. The combined ether extracts were washed with distilled water and dried by filtering through anhydrous magnesium sulfate, then evaporated leaving 0.82 g light yellow solid. This is called the acidic fraction.

Analysis of neutral fraction.--The neutral fraction was subjected to vpc analysis (column temperature was 200°C, detector 260°C, injector 250°C). Three peaks were observed. These three peaks were collected

for ir analysis. The ir spectra were compared to authentic samples and they were proved to be 1-fluoronaphthalene, t-butyl 1-naphthyl ether and 1-naphthol. The presence of 1-naphthol in the neutral fraction was a surprise. Nevertheless, the thin layer chromatograph did not show any 1-naphthol to be present in the neutral fraction. The same observation was reported by Bradshaw and co workers (5). Apparently the t-butyl 1-naphthyl ether was decomposing to 1-naphthol in the vpc column. The area of each vpc peak was used to determine the yield of that particular product. The mole percent yields are listed in Table 2.

Analysis of acidic fraction.--The solid acidic fraction was dissolved in a few mililiters of reagent grade acetone, and subjected to vpc analysis using the same column and conditions as reported for the neutral fraction. Only one peack was observed. The ir spectrum of this peak as well as that of the crude fraction was exactly the same as that of an authentic sample of 1-naphthol. Results are listed in Table 2.

Optimizing Conditions for Reaction of Fluoronaphthalenes with Potassium t-Butoxide

A series of reactions of 1-, and 2-fluoronaphthalenes with potassium t-butoxide and t-butyl alcohol in DMSO was carried out under various reaction conditions in order to determine the reaction conditions under which t-butyl naphthyl ethers would be produced in maximum yields while naphthols would be produced in minimum yields. The mole ratio of reactants and solvents was not changed. The analysis procedure was also carried out in the same manner as reported above. The results and the conditions employed are listed in Table 2.

Large Scale Reaction of 2-Fluoronaphthalene with Potassium t-Butoxide in t-Butyl Alcohol and DMSO Mixture

A large scale reaction was run using the same reaction conditions that were employed in run 7 in Table 2. 140.0 g DMSO and 30.5 g (0.41 mole) t-butyl alcohol were mixed in a 500 ml three neck-round bottom flask equipped with a thermometer, a condenser and an addition funnel. The mixture was heated to about 80°C. Potassium t-butoxide, 31.0 g (0.247 mole), was added to the mixture. The potassium t-butoxide dissolved slowly. The stirred reaction mixture was maintained at 70°C and 20.0 g (0.14 mole) of 2-fluoronaphthalene dissolved in 20.0 g DMSO (to make a total of 160.0 g, 2.054 mole DMSO) was added rapidly through the addition funnel. After stirring for 14 hours at 70°C, the reaction mixture was quenched with ice water and analyzed as described above for the 1-fluoronaphthalene reaction. The neutral fraction was distilled under vacuum. Unreacted 2-fluoronaphthalene (4.67 g, 23.0%) was obtained at 75-90°C/1mm. t-Butyl 2-naphthyl ether (8.2 g, 0.041 mole, 38.1%) was obtained at 95-105°C/1mm, n_D^{22} = 1.5740 (literature value: n_D^{20} = 1.5724) (5). Since the boiling points of 2-fluoronaphthalene and of t-butyl 2-naphthyl ether were very close, it was difficult making a clean separation. 2-Naphthol (4.25 g, 0.0295 mole, 21.0%) was also obtained from the acidic fraction.

Reaction of 2-Fluoronaphthalene with Potassium n-Butoxide

All glass aparatus was the same as previously described. n-Butyl alcohol (5.07 g, 0.0685 mole) was placed in a 50 ml three neck-round bottom flask. Freshly cut potassium metal (1.07 g, 0.0274 mole), weighed under hexane, was added in small pieces to the stirred n-butyl alcohol.

Even though the exothermic reaction allowed most of the potassium metal to dissolve, heating was necessary to dissolve all the metal. After all the potassium metal had reacted (about 1 hour) (the mole ratio of n-butyl alcohol to potassium n-butoxide was 3 to 2), 16.06 g (0.2054 mole) DMSO was added and the temperature was raised to and maintained at 150°C. Nitrogen gas was passed into the top of the dropping funnel and out through a mercury bubbler. 2-Fluoronaphthalene (2.0 g, 0.013687 mole) was rapidly added to the reaction mixture. The reaction was exothermic and the temperature immediately increased to about 170°C. After one hour the reaction mixture was poured into 100 ml ice water saturated with sodium chloride and worked up in a manner similar to the procedure described previously for the reaction of 1-fluoronaphthalene with potassium t-butoxide to give 2.77 g of neutral fraction (yellow solid) and 0.04 g acidic fraction (dark brown solid).

The neutral fraction was analyzed as described previously using the same vpc column and conditions. Only two peaks were observed (area ratio was 1 to 12). The ir spectra of these two peaks showed that they were the starting 2-fluoronaphthalene and the desired product, n-butyl 2-naphthyl ether (2.63 g, 0.01315 mole). The mole percent yield was 96.1%.

Repeat of Reaction of 2-Fluoronaphthalene with Potassium n-Butoxide

The above reaction of 2-fluoronaphthalene with potassium n-butoxide was repeated using the same procedure and analysis techniques except the reaction temperature was maintained at 100°C for 7 hours. 2.58 g of neutral fraction (dark yellow solid) and 0.10 g of acidic fraction were obtained. Only one peak was observed in the vpc analysis.

The ir spectrum of this peak matched exactly that of the crude neutral fraction. No starting 2-fluoronaphthalene was found in the neutral fraction. Mole percent yield was 94.3%.

Large Scale Reaction of 2-Fluoronaphthalene with Potassium n-Butoxide in a n-Butyl Alcohol and DMSO Mixture

Exactly the same reaction as reported above starting with 20.0 g (0.13687 mole) of 2-fluoronaphthalene was carried out at 150°C for one hour. 26.03 g (0.13015 mole) of the neutral fraction and 0.9 g of the acidic fraction were obtained. The mole percent yield of the ether product was 95.9%.

The crude ether product was recrystallized as a method of product purification. Several kinds of solvents were tried and it was found that 90% ethyl alcohol was the best for this purpose. 5.0 g of the crude product (dark yellow solid) was dissolved in an 100 ml 90% aqueous ethanol solution. Heating was necessary to dissolve all solid. The solution was cooled to about 3°C and filtered. 4.8 g light yellow crystals were obtained. These crystals were recrystallized once again by the same procedure to obtain 4.5 g white crystals, mp, 33.5-34.5°C (literature value: mp = 33-35°C) (58).

Large Scale Reaction of 2-Bromonaphthalene with Sodium n-Butyl Mercaptide in a Methanol and DMSO Mixture

All glass aparatus was the same as used in the fluoronaphthalene system reported above. The small scale reactions (2.0 g of starting material) and best reaction conditions for the maximum yield were reported by J. A. South (50). 70.0 g DMSO (IV) and 43.55 g (0.4828 mole) 1-butanethiol (III) were mixed in a three neck-round bottom flask equipped

ith a thermometer, a condenser and an addition funnel. The stirred (magnetic stirring bar) reaction mixture was heated to about 70°C and 15.7 g (0.2907 mole) sodium methoxide (II) was added and dissolved in a few seconds. After the temperature had maintained at 110°C, 20.0 g (0.09656 mole) of 2-bromonaphthalene (I) dissolved in 44.0 g DMSO (IV) (to make a total of 114.0 g, 1.46 mole) was added rapidly by means of the addition funnel. The mole ratio of I to II to III to IV was 1/3/5/15 instead of 1/2/3/15 in the fluoronaphthalene system. The reaction mixture became dark orange. After one hour the mixture was quenched with ice water and worked up as previously reported for the fluoronaphthalene reaction. The neutral fraction was distilled under vacuum (1mm). The desired product, n-butyl 2-naphthyl sulfide (12.12g, 58%) was collected at 147-152°C, n_D^{25} = 1.6205 (literature value: n_D^{29} = 1.6196) (6). The ir spectrum also confirmed the structure assigned.

Reaction of Bromonaphthalene with Sodium Methoxide in a Methanol and DMSO Mixture

14.3 g (0.181 mole) DMSO (IV) and 1.9 g (0.0604 mole) methanol (III) was mixed in a 100 ml glass bomb equipped with a rubbered seal and a magnetic stirrer. 1.3 g (0.02414 mole) of sodium methoxide (II) was then added to the mixture. The mixture was heated up to about 100°C; the sodium methoxide was still not completely dissolved. The reaction mixture was cooled to room temperature and 2.5 g (0.01207 mole) of 2-bromononaphthalene (I) was added. The mole ratio of I to II to III to IV was 1/2/5/15. After the resulting reaction mixture had been heated to about 100°C the rubbered seal was closed and the temperature was raised to and maintained at 155°C. After 16 hours the glass bomb was cooled to room temperature and the mixture was worked up as previously

reported for the fluoronaphthalene reaction, resulting in 1.56 g of a neutral fraction. Only two peaks were observed in the vpc analysis of this neutral fraction. The ratio of these two peaks was 5 to 13. These peaks were collected for ir analysis and proved to be naphthalene and methyl 2-naphthyl ether, respectively. The mole percent yield of the ether product was 58.3%. Methyl 1-naphthyl ether could not be separated from methyl 2-naphthyl ether by vpc analysis. Methyl 1-naphthyl ether, however, was not found in the reaction mixture since the two ethers could be separated by thin layer chromatography.

Exactly the same reaction was carried out once again except that 1-bromonaphthalene was used in place of 2-bromonaphthalene. The vpc analysis of the neutral fraction worked up as previously reported for the fluoronaphthalene reaction showed 2 major peaks at a ratio of 17 to 1. The smaller peak was proved by its ir spectrum to be naphthalene. The ir spectrum of the larger peak was slightly different from that of an authentic sample of pure methyl 1-naphthyl ether prepared as reported on p. 20. Since the methyl 1-naphthyl ether and methyl 2-naphthyl ether could not be separated by vpc, and since the thin layer chromatogram showed the presence of both ethers in the neutral fraction, the ir spectra of 5%, 10%, 15% and 20% mixtures of the 2-naphthyl ether in the 1-naphthyl ether were taken and compared with that of the sample collected from the larger vpc peak. It was found that there was about 15% of methyl 2-naphthyl ether present in the methyl 1-naphthyl ether.

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A NEW METHOD FOR THE PREPARATION OF ALKYLNAPHTHYL ETHERS AND SULFIDES

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ABSTRACT

The reaction of monohalonaphthalenes with metal alkoxides and mercaptides in a solvent mixture of the corresponding alcohol and dimethyl sulfoxide (DMSO) has been studied. These reactions are convenient methods for the preparation of alkylnaphthyl ethers and sulfides.

Only direct nucleophilic substitution was observed in the reactions of bromonaphthalenes with sodium methoxide and sodium n-butyl mercaptide. The reaction of fluoronaphthalene with potassium t-butoxide also proceeded by way of direct nucleophilic substitution rather than the 1,2-dehydronaphthalene intermediate as in the reactions of bromonaphthalene with potassium t-butoxide. The use of a base which is weaker than t-butoxide can change the apparent reaction mechanism from the dehydronaphthalene to direct nucleophilic substitution.