

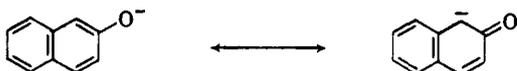
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Solvation as a Factor in the Alkylation of Ambident Anions: The Importance of the Dielectric Factor^{1,2}BY NATHAN KORNBLUM, RAYMOND SELTZER³ AND PAUL HABERFIELD

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Solutions of sodium β -naphthoxide in a variety of solvents have been alkylated with benzyl bromide, methyl iodide and *n*-propyl bromide. The results of these studies provide a clear demonstration of the ability of the solvent to decide the course of an ambident anion reaction. A discussion of solvent effects on the course of ambident anion processes is presented which distinguishes between protic and aprotic solvents and which emphasizes the utility of this distinction. As a consequence, it is now possible to correlate the dielectric constant of an aprotic solvent with its influence on the alkylation process. Finally, the interdependence of solvent and cation effects is explicitly recognized and employed so that insights concerning the ability of solvents to determine the course of ambident anion reactions are obtained.

The β -naphthoxide ion is an ambident anion⁴ capable of covalency formation at oxygen or at the α -carbon. With very few exceptions the literature reports only the

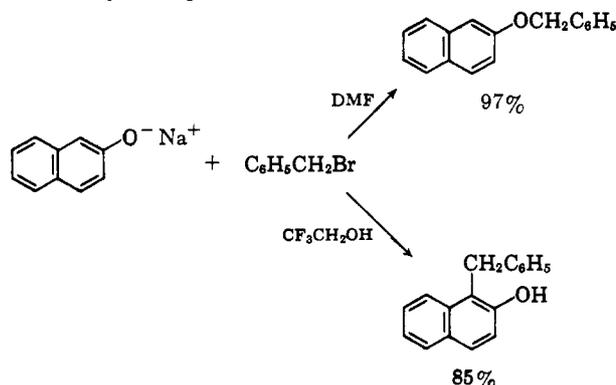


ether as the product when the salts of β -naphthol are alkylated in solution. Gomberg and Buchler⁵ were the first to observe carbon alkylation; they obtained a 50% yield of 1-benzyl-2-naphthol upon heating an aqueous solution of sodium β -naphthoxide with benzyl chloride. Details were not given and the result was described as "wholly unanticipated." More recently, Zagorevsky⁶ has investigated the alkylation of solutions of β -naphthoxide salts in acetone, dioxane, alcohol-benzene and acetone-benzene; when treated with various benzyl bromides 1-benzyl-2-naphthols were obtained in 0 to 29% yields.

The discovery⁷ that solvation is a factor in the alkylation of phenoxide ions, coupled with the knowledge that in the β -naphthoxide ion competition between oxygen and carbon for the alkylating agent is rather more evenly balanced than in phenoxide ions,⁸ suggested that a study of the influence of solvents on reactions involving sodium β -naphthoxide would be rewarding. This has proved to be the case.

The consequences of conducting the reaction of sodium β -naphthoxide with benzyl bromide in a variety of solvents are recorded in Table I. It is clear that the course which the reaction takes depends on the solvent employed. Reactions conducted in dimethylformamide (DMF) or in dimethyl sulfoxide (DMSO) solution stand at one extreme: in DMF a 97% yield of benzyl β -naphthyl ether results while in DMSO the yield of ether is 95%; in DMF and in DMSO carbon alkylation occurs to the extent of only 1% or less.⁹

In contrast, the reaction of an aqueous solution of sodium β -naphthoxide with benzyl bromide gives but a 10% yield of the ether and an 84% yield of the carbon alkylate, 1-benzyl-2-naphthol¹⁰; thus a simple change in solvent produces an overturn in reaction course. As in the study employing sodium phenoxide,⁷ 2,2,2-trifluoroethanol has the same effect as water; a solution of sodium β -naphthoxide in trifluoroethanol gives but a 7% yield of benzyl β -naphthyl ether and an 85% yield of 1-benzyl-2-naphthol.¹¹



The fact that benzylation of sodium β -naphthoxide in DMF and DMSO results, essentially quantitatively, in oxygen alkylation, while in the excellent¹² hydrogen bonding solvents trifluoroethanol and water carbon alkylation preponderates, is fully consonant with previous experience⁷ involving sodium phenoxide. Here, as with phenoxide, carbon alkylation is presumed to derive from the excellent hydrogen-bonding capabilities of trifluoroethanol and water.⁷

The experiments employing sodium β -naphthoxide are, however, especially valuable because of the differences they reveal within the aprotic group of solvents, DMF, DMSO, ethylene glycol dimethyl ether and tetrahydrofuran (THF). Whereas sodium phenoxide on being alkylated in any of these solvents gives the oxygen alkylate as the sole product, this is not the

measurable rate under the reaction conditions, the rate is negligible compared to the extremely rapid reaction with sodium β -naphthoxide.

(10) Here, and in a number of other instances, the carbon alkylate initially produced is, in part, further alkylated; *vide infra*.

(11) As in the preceding paper,⁷ the possibility that the large amount of carbon alkylation obtained in water and in trifluoroethanol derives from a carbonium ion process has been considered. This possibility is rejected because: (1) the reaction of benzyl bromide with sodium β -naphthoxide in water proceeds at a rate which is clearly dependent on the β -naphthoxide ion concentration, and this is not an ionic strength effect, and (2) product analysis shows that, in water, at least 78% of the benzyl groups end up imbedded in the β -naphthoxide ion, while in trifluoroethanol at least 84% of the benzyl groups are accounted for as alkylation products of the β -naphthoxide ion. If these reactions involved carbonium ions one would anticipate the formation of large amounts of solvolysis products, *e.g.*, benzyl alcohol.

(12) We refer to the ability of the solvent to function as the H donor in forming a hydrogen bond; *cf.* footnote 19 of ref. 7.

(1) This research was supported, in part, by a grant from the Explosives Department of E. I. du Pont de Nemours and Co. and, in part, by the United States Air Force under Contract No. AF49(638)-324 monitored by the A. F. Office of Scientific Research of the Air Research and Development Command.

(2) Paper VI in the series "The Chemistry of Ambident Anions"; presented at the American Chemical Society Natl. Meeting, Atlantic City, N. J., September 10, 1962.

(3) From the Doctoral Dissertation of Raymond Seltzer. XR Fellow of the Purdue Research Foundation 1958-1960.

(4) N. Kornblum, R. A. Smiley, R. K. Blackwood and D. C. Iffland, *J. Am. Chem. Soc.*, **77**, 6269 (1955).

(5) M. Gomberg and C. C. Buchler, *ibid.*, **42**, 2066 (1920).

(6) V. A. Zagorevsky, *J. Gen. Chem. U.S.S.R.*, **27**, 3055 (1957); **28**, 488 (1958).

(7) N. Kornblum, P. J. Berrigan and W. J. le Noble, *J. Am. Chem. Soc.*, **85**, 1141 (1963); **82**, 1257 (1960).

(8) N. Kornblum and A. P. Lurie, *ibid.*, **81**, 2707 (1959).

(9) Since it is known that alkyl halides react with DMF and DMSO [N. Kornblum and R. K. Blackwood, *ibid.*, **78**, 4037 (1956); N. Kornblum, W. J. Jones and G. J. Anderson, *ibid.*, **81**, 4113 (1959); S. Smith and S. Winstein, *Tetrahedron*, **3**, 317 (1958)] the possibility that benzyl bromide forms an adduct with these solvents which then reacts with sodium β -naphthoxide was considered. However, this possibility was rejected when it was found that although benzyl bromide reacts with DMSO and DMF at a

TABLE I
REACTIONS OF BENZYL BROMIDE WITH SODIUM β -NAPHTHOXIDE^o

| Solvent | Dielectric constant ^f | O-Alkylation, % ^b | C-Alkylation, % ^b |
|--|----------------------------------|------------------------------|------------------------------|
| Dimethylformamide ^c (DMF) | 37 | 97 | 0 |
| Dimethyl sulfoxide ^d (DMSO) | 45 | 95 | 0 |
| Ethylene glycol dimethyl ether | 7 | 70 | 22 |
| Tetrahydrofuran (THF) | 7 | 60 | 36 |
| Methanol | 33 | 57 | 34 |
| Ethanol | 24 | 52 | 28 |
| 2,2,2-Trifluoroethanol | 27 | 7 | 85 |
| Water | 80 | 10 | 84 |
| Water (for 5 minutes) ^e | | 8 | 81 |
| Benzene-water | | 7 | 83 |

^a All reactions conducted at room temperature except when otherwise noted. ^b This yield includes any dialkylated products arising from further alkylation of 1-benzyl-2-naphthol. ^c At 10 to 15°; a duplicate at 35° gave 93% O + 1% C. ^d A duplicate at 40° gave 95% C + 1% O. ^e During this time no solid phase appears. When the reaction is permitted to go beyond this point a solid phase consisting of the organic products is precipitated (*cf.* Experimental). ^f Temp. 20 to 25°.

case with sodium β -naphthoxide.¹³ As noted above, in DMF, or in DMSO, the reaction of benzyl bromide with sodium β -naphthoxide yields virtually quantitatively the ether; but in ethylene glycol dimethyl ether or THF, carbon alkylation occurs to a substantial extent (*cf.* Table I). The fact that in THF, for example, a 36% yield of the carbon alkylate is produced cannot be attributed to hydrogen bonding. Clearly a second factor must be reckoned with and this, we propose, is the ability of the solvent to decrease electrostatic interactions as a result of its dielectric effect, a measure of which is the dielectric constant of the solvent.¹⁴

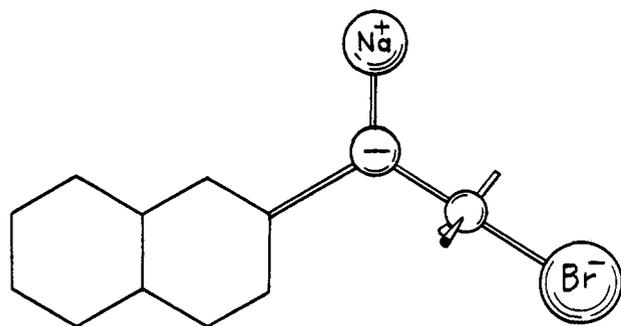


Figure 1.

Of the four aprotic solvents employed, the two which have relatively high dielectric constants, DMF and DMSO (*cf.* Table I), strongly favor oxygen alkylation, whereas THF and ethylene glycol dimethyl ether, which have relatively low dielectric constants (Table I), bring about an unmistakable shift in the direction of carbon alkylation.¹⁵ The fact that an aprotic solvent

(13) As pointed out earlier in this paper, the phenoxide ion has a much greater intrinsic predisposition toward oxygen alkylation than the β -naphthoxide ion; only under the influence of powerful countervailing factors does carbon alkylation of the phenoxide ion become discernible.⁸

(14) It is recognized that in the transition state some of the lines of force from the charges will proceed partly through the reactants. [Compare J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); F. H. Westheimer and M. W. Shookhoff, *J. Am. Chem. Soc.*, **61**, 555 (1939)]. But since reactions employing the *same* reactants are being compared, with only the solvent being changed, the error incurred by this oversimplification is in good part (if not completely) cancelled out. Furthermore, the use of the "macroscopic" (*i.e.*, bulk) dielectric constant as a measure of the solvent's ability to reduce electrostatic interactions between the component atoms of a transition state, *i.e.*, as a measure of the "microscopic" dielectric character of the solvent, is, presumably, something of an oversimplification.

(15) Analogous shifts are observed in the alkylation of the lithium salt of 2-nitropropane and in the alkylation of the sodium salt of 1-methyl-2-naphthol (unpublished work by R. C. Kerber and R. Derby in this Laboratory).

of high dielectric constant favors oxygen alkylation while one with a low dielectric constant favors carbon alkylation can be rendered intelligible on a rather simple basis.

In a medium of low dielectric constant such as THF, it is a reasonable assumption that, at concentrations of the order of 0.8 molar, sodium β -naphthoxide exists essentially completely as ion-pairs and higher aggregates. Consider now the transition state (Fig. 1) for the oxygen alkylation of an ion-pair. Oxygen alkylation involves the transfer of charge from oxygen to bromine and, since the bromine is relatively remote from the sodium, this must be accomplished against the attractive force exerted by the sodium ion. We have here a factor disfavoring oxygen alkylation and this factor is maximally important in a medium of low dielectric; for in a medium of low dielectric constant the attractive force exerted by the sodium ion on the departing bromide ion is greatest. In contrast to the linear oxygen-carbon-bromine disposition which characterizes oxygen alkylation (Fig. 1), carbon alkylation proceeds through a non-linear arrangement in which the developing bromide ion is relatively close to the sodium ion (Fig. 2). Here, as in the transition state for oxygen

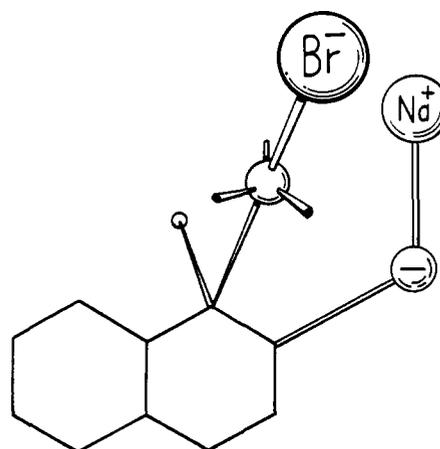


Figure 2.

alkylation, part of the charge on oxygen is transferred to bromine; but now the bromine is proximate to the sodium ion which, in essence, nestles between the oxygen and bromine.¹⁶ This transition state, because it involves relatively little removal of charge from the vicinity of the sodium ion, will be comparatively insensitive to the dielectric constant of the medium. The upshot is that a solvent of low dielectric constant favors carbon alkylation by disfavoring oxygen alkylation.

In an aprotic solvent of relatively high dielectric constant, *e.g.*, DMF, the reacting species may again be the ion pair, or, if the solution is sufficiently dilute in sodium β -naphthoxide, it may be the free β -naphthoxide

(16) While not essential to the argument, it is plausible to assume that oxygen alkylation (Fig. 1) proceeds *via* a transition state in which the departing halogen, and the carbon it leaves, lie in the plane of the naphthoxide ion. In this way the naphthoxide ion is able to furnish a bonding pair of electrons without losing the resonance stabilization derived from the interaction of the oxygen's electrons with the aromatic π -system. In contrast, in the transition state of Fig. 2 the carbon from which the halogen is departing is above (or below) the plane of the naphthoxide ion. Actually, the crux of the matter is that we deal here with S_N2 processes and, hence, the β -naphthoxide ion is attacking rearward to the departing bromine. As a consequence, carbon alkylation proceeds *via* a quasi-six-membered transition state with sodium close to bromine, *i.e.*, with the energetically desirable close proximity of opposite charges. In contrast, oxygen alkylation occurs *via* a transition state in which close proximity of the sodium and bromine is not possible, *i.e.*



ion.¹⁷ The reaction, if it involves an ion pair, will again proceed *via* the transition states of Fig. 1 and 2, but now the transition state leading to oxygen alkylation is of significantly lower energy than in THF because the DMF, having a high dielectric constant, shields the departing bromide ion relatively well from the attractive force exerted by the sodium ion. Consequently, the coulombic factor, which in a solvent of low dielectric operates as a deterrent to oxygen alkylation, loses importance when the reaction is conducted in a medium of high dielectric. In contrast, the transition state leading to carbon alkylation, as before, is relatively insensitive to the dielectric constant of the medium. Thus, a solvent with a high dielectric constant favors oxygen alkylation by minimizing a force which opposes oxygen alkylation.

In a solvent such as DMF or DMSO it is conceivable that the alkylation reaction involves the free β -naphthoxide ion.¹⁷ With the sodium ion absent a force which resists the transfer of charge from oxygen to bromine in the oxygen alkylation process (Fig. 1) is removed and the β -naphthoxide ion is able to exercise its intrinsic preference for nucleophilic displacements involving oxygen with little, if any, restriction.¹⁸

The study of β -naphthoxide alkylations, in addition to bringing out the significance of the dielectric factor, also provides some instructive examples of the importance of selective solvation.⁷

(a) Methanol and DMF give quite different proportions of carbon and oxygen alkylation when sodium β -naphthoxide is treated with benzyl bromide (Table I). Here, with virtually the same values for the dielectric constant, DMF, the solvent incapable of hydrogen bonding, gives little or no carbon alkylation while methanol, which can form hydrogen bonds,⁷ gives 34% carbon alkylation. Methanol may not be the equal of trifluoroethanol or water or phenol as a hydrogen bond, but sodium β -naphthoxide is so much more prone to carbon alkylation than sodium phenoxide⁸ that even a relatively weak hydrogen bond produces a substantial shift in the direction of carbon alkylation.¹⁹

(b) A comparison of the two protic solvents trifluoroethanol and ethanol serves to emphasize the importance of differences in hydrogen-bonding capacity. These two alcohols have quite similar dielectric constants (27 and 24, respectively) but trifluoroethanol has, unmistakably, the greater hydrogen-bonding capability.¹² As a consequence, whereas the reaction of benzyl bromide with sodium β -naphthoxide in trifluoroethanol gives an 85% yield of the carbon alkylation product, when conducted in ethanol it gives but a 28% yield of carbon alkylate (Table I).

The Nature of the Cation.²⁰—The influence of the cation on the reactions of an ambident anion cannot be

(17) Studies of the alkylation of ambident anions designed to distinguish the contributions of free ions, ion pairs and higher aggregates with the particular object of obtaining reliable information concerning the position of alkylation and the rates of reaction are being undertaken.

(18) It is presumed that in DMF and in DMSO solvation of the anion is minimal. Among other things, the extraordinarily high reactivity of anions in these solvents makes sense on this basis. See, for example, H. E. Zaugg, *J. Am. Chem. Soc.*, **83**, 837 (1961); D. J. Cram, B. Rickborn and G. R. Knox, *ibid.*, **82**, 6412 (1960); N. Kornblum, H. O. Larson, R. K. Blackwood, D. Mooberry, E. P. Oliveto and G. E. Graham, *ibid.*, **78**, 1498 (1956).

(19) A relevant, earlier, observation has been reported by H. D. Zook and T. J. Russo [*ibid.*, **82**, 1258 (1960)]. They found that the ethylation of sodiodiphenylacetophenone undergoes a significant shift from oxygen to carbon when the solvent is changed from the dimethyl ether of diethylene glycol to *i*-butyl alcohol (*cf.* ref. 7, footnote 20).

(20) It has long been recognized that silver salts and alkali metal salts of ambident anions react differently with alkyl halides⁴ and that even among the alkali metal salts significant differences in reaction course may appear. See, for example, (a) O. L. Brady and J. Jakobovits, *J. Chem. Soc.*, 767 (1950); (b) A. Brändström, *Arkiv Kemi*, **6**, 155 (1953); (c) A. N. Nesmeyanov and M. I. Kabachnik, *J. Gen. Chem. U.S.S.R.*, **25**, 37 (1955); (d) D. Y. Curtin, R. J. Crawford and M. Wilhelm, *J. Am. Chem. Soc.*, **80**,

discussed satisfactorily unless the role of the solvent is explicitly recognized. This is because ions in solution are to a greater or lesser extent associated with solvent molecules by hydrogen bonds or by other ion-dipole interactions; consequently, what the cation does to the anion depends on what the solvent has already done to the cation (and to the anion) in the process of dissolving the salt.

In aprotic solvents having a low dielectric constant, such as THF and diethyl ether, the anion is likely to be part of an ion aggregate when it reacts. With a small cation such as lithium the ion pairs will be relatively "tight" and the electrostatic restraint to ether formation (*cf.* Fig. 1) relatively large. As we pass from Li^+ to Na^+ to K^+ to R_4N^+ , the ion pairs become progressively looser and the positive charge is spread over a larger volume; consequently, the electrostatic constraint to ether formation progressively falls off. It is to be anticipated, therefore, that in aprotic solvents of low dielectric constant the influence of the cation is likely to be relatively large and that a progressive decrease in the yield of carbon alkylate as the series Li^+ , Na^+ , K^+ , NR_4^+ is traversed will be observed.²¹

In contrast, DMF and DMSO, while aprotic, are solvents of relatively high dielectric constant. Moreover, they are noteworthy for being especially effective at solvating the positive ion (*vide infra*) but relatively ineffective at solvating the β -naphthoxide anion.¹⁸ Thus, in DMF and in DMSO, the dissociated anion has not only got away from the cation but, furthermore, relative to its condition in protic solvents, it is very poorly solvated; a dissociated anion in DMF, or in DMSO, has something approaching the character of a "free" anion including, among other things, a very high degree of reactivity.¹⁸ It is, therefore, relatively easy in these two solvents to arrive at a situation in which a kinetically significant number of dissociated β -naphthoxide anions are present and, thus, of the common solvents, it is in DMF, and in DMSO, that one is most likely to observe the properties of the "free" ambident anion. Furthermore, as noted earlier in this paper, even if the β -naphthoxide ion reacts as an ion-pair, in a medium of high dielectric constant such as DMF or DMSO the electrostatic constraint to oxygen alkylation of the β -naphthoxide ion is minimized; which is to say, the influence of the cation on the course of the alkylation is minimized. There is still another reason why the influence of the cation on the course of ambident anion alkylations conducted in DMF, and in DMSO, will tend to be minimal. In these solvents cationic solvation is important (*vide infra*); since the solvent molecules tend to solvate the cations to an extent which is a function of ionic size, lithium ion will be the most powerfully solvated of the series Li^+ , Na^+ , K^+ , N^+R_4 , and the quaternary ammonium ion least well solvated. In essence, then, a "leveling effect" as regards the dispersal of charge through solvation results and this tends to even out the electrostatic influence of the various cations on the β -naphthoxide ion in an ion pair.²²

1394 (1958); (e) I. Forsblad, *Arkiv Kemi*, **15**, 403 (1960); (f) C. F. Hobbs, C. K. McMillin, E. P. Papadopoulos and C. A. VanderWerf, *J. Am. Chem. Soc.*, **84**, 43 (1962); (g) P. A. S. Smith and J. E. Robertson, *ibid.*, **84**, 1197 (1962).

(21) This generalization has to be qualified in two respects: (1) Cationic solvation (*vide infra*) if it is especially intense for a particular member of this set of cations, as it might be, for example, because of a peculiarly favorable size relationship between the cation and solvent molecules, will disrupt the progression. That is to say, as a consequence of such specific cationic solvation the dispersal of the charge of that particular cation would be uniquely increased. (2) With some ambident anions the ambident anion may have so strong a preference for one of the two possible modes of alkylation that the cation, even in aprotic solvents of low dielectric constant, may be unable to modify this preference.

In protic solvents, *e.g.*, alcohols, the nature of the cation will, in general, be relatively unimportant as a factor controlling the proportions of oxygen and carbon alkylation.²³ Protic solvents usually possess relatively high dielectric constants and this, coupled with the "leveling effect" derived from effective solvation of both the cation and anion, as discussed above, operates to reduce the cation's influence. But probably the most important cause of the relative unimportance of the cation in protic solvents is "selective solvation";⁷ selective solvation of the β -naphthoxide ion is a potent force favoring carbon alkylation and, especially in excellent hydrogen-bonding media,¹² it will minimize the role of the cation.²⁴

In general, such data as are available accord with this description of the solvent dependence of cation effects. For example, alkylations conducted in methanol or ethanol exhibit little variation in product ratio as the cation is varied.^{20e, 20g, 25} In contrast, for alkylations conducted in diethyl ether, THF, benzene and toluene, substantial decreases in the proportion of carbon alkylation are observed as the cation is varied from Li^+ to Na^+ to K^+ to R_4N^+ .^{20d, 20f, 25, 26}

Cationic Solvation.—Certain solvents are especially effective at solvating cations; these include the dimethyl ether of ethylene glycol, DMF and DMSO.^{27–30} When a cation is well solvated this spreads the charge over a larger volume and such dispersal of cationic charge will, for reasons discussed in the preceding section, minimize the coulombic restraint to ether formation. This factor should be most significant in aprotic solvents of low dielectric constant.

It is generally agreed that ethylene glycol dimethyl ether is superior to THF in solvating sodium ions. Furthermore, these two solvents possess nearly identical dielectric constants ($\epsilon = 7.3$ for THF and 6.8 for ethylene glycol dimethyl ether²⁷). Consequently, the fact that the reaction of benzyl bromide with sodium β -naphthoxide on being conducted in ethylene glycol dimethyl ether gives more of the oxygen alkylate than in THF (*cf.* Table I) is of interest. An even more striking result has been observed in the alkylation of the lithium salt of 2-nitropropane: alkylations conducted in the dimethyl ether of diethylene glycol (a good cation solvator²⁸) give much more oxygen alkylation than in dioxane (a relatively poor cation solvator²⁹).³¹ How general and important such cationic solvation effects are remains to be established and relevant studies are in progress.

(22) While the discussion deals with the alkylation of phenolic salts it is presumably applicable to the reactions of other types of ambident anions *e.g.*, nitroparaffin and pyrrole salts, in which differences analogous to those of Fig. 1 and 2 exist in the transition states corresponding to the two isomeric alkylation products.

(23) In water, to pick an extreme example, one would anticipate little, if any, variation in the proportions of oxygen and carbon alkylation as the cation is varied.

(24) One can anticipate selective solvation not only for the dissociated anion but also in ion pairs. For, as Cram has pointed out, one and the same solvent (alcohol) molecule can be visualized as solvating both the cation and the anion of an ion pair, the hydroxyl oxygen of the solvent being associated with the metal cation and the hydroxyl hydrogen of the solvent being hydrogen bonded to the anion of the ion-pair [D. J. Cram, J. L. Mateos, R. Hauck, A. Langeman, K. R. Kopecky, W. D. Nielsen and J. Allinger, *J. Am. Chem. Soc.*, **81**, 5778 (1959)].

(25) R. Derby, unpublished work.

(26) A. N. Nesmeyanov, V. A. Saznova and E. J. Vasilyeva, *Bull. Acad. Sci. U.S.S.R.*, **78** (1952).

(27) G. Wittig and E. Stahnecker, *Ann.*, **605**, 69 (1957).

(28) H. D. Zook and T. J. Russo, *J. Am. Chem. Soc.*, **82**, 1258 (1960); H. D. Zook and W. L. Gumby, *ibid.*, **82**, 1386 (1960).

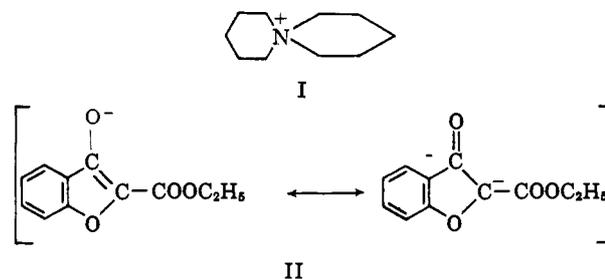
(29) H. E. Zaugg, B. W. Horrom and S. Borgwardt, *ibid.*, **82**, 2895 (1960); H. E. Zaugg, *ibid.*, **82**, 2903 (1960); H. E. Zaugg, *ibid.*, **83**, 837 (1961).

(30) J. F. Garst, C. Hewitt, D. Walmsley and W. Richards, *ibid.*, **83**, 5034 (1961).

(31) R. C. Kerber, unpublished work.

Dissociated Anions vs. Ion Pairs.—In 1926, Ingold³² proposed that carbon alkylation of phenolic salts derives from the reaction of the ion-pair with the alkyl halide and that oxygen alkylation results from the reaction of the dissociated phenoxide anion; in one form or another this view has appeared in many of the subsequent discussions of ambident anion alkylations. On the basis of this explanation it is necessary to assume that the alkylation of potassium *p*-*t*-octylphenoxide in toluene solution, which gives rise only to oxygen alkylation,⁸ proceeds *via* the dissociated anion. In the same way it becomes necessary to postulate that the dissociated pyrrolyl ion is the reactive species in the alkylation of toluene solutions of the lithium, sodium and potassium salts of pyrrole in order to account for the preponderant N-alkylation.^{20f} These are rather dubious assumptions.

Most important of all, there exists a direct experimental refutation of the oft-repeated proposition that free ions favor oxygen alkylation while ion-pairs favor carbon alkylation. In 1960, Forsblad^{20e} reported the results of a study of the reaction of the lithium, sodium, potassium and bispiperidinium (I) salts of the ethyl ester of β -hydroxycoumarilic acid (II) with methyl iodide in methanol solution. Although Forsblad's



paper does not list carbon to oxygen alkylation ratios for the various ion-pairs, and for the dissociated anion, these numbers are readily obtainable from the data in Table 2 (p. 405) of his paper and they are given in Table II. It will be seen that *the dissociated anion actually gives more carbon alkylation than any of the ion pairs.*

TABLE II

| | C/O for ion-pairs | C/O for dissociated anion II |
|-----------------|-------------------|------------------------------|
| Lithium | 5.0 | 6.2 |
| Sodium | 2.1 | 5.7 |
| Potassium | 2.6 | 6.0 |
| Bispiperidinium | 4.1 | 6.2 |

This startling discovery serves to emphasize the importance of solvation. In methanol the dissociated anion II is selectively solvated⁷ at oxygen and this shielding operates in favor of carbon alkylation.³³ In contrast to this strongly hydrogen-bonded "dissociated" anion in methanol, a "dissociated" anion in an aprotic solvent must be a very different thing. In DMF, for example, the "dissociated" anion II would be expected to give *less* carbon alkylation than the ion-pairs.

Alkylation Employing Methyl Iodide and *n*-Propyl Bromide.—The results of the reaction of sodium β -naphthoxide with methyl iodide and with *n*-propyl bromide are summarized in Tables III and IV. There again the influence of solvents is easily discerned. The

(32) C. K. Ingold, *Ann. Rept. Chem. Soc.*, 142 (1926).

(33) In this instance it appears that hydrogen bonding is more effective in favoring C-alkylation (by shielding the oxygen atom) than is ion-pairing, which favors C-alkylation by providing a transition state having minimal charge separation (*cf.* Fig. 2). Furthermore, when it is recognized that ion-pairing probably results in preferential shielding of oxygen by the cation this result becomes all the more striking.

question of the relationship between the structure of the alkyl halide and the proportions of oxygen and carbon alkylation in various solvents will be taken up in a subsequent paper.

TABLE III

| REACTIONS OF METHYL IODIDE WITH SODIUM β -NAPHTHOXIDE ^a | | |
|--|-----------------|-----------------|
| Solvent | O-Alkylation, % | C-Alkylation, % |
| Dimethylformamide (DMF) ^b | 91 | 3 |
| Dimethyl sulfoxide (DMSO) ^b | 90 | 4 |
| Ethylene glycol dimethyl ether | 86 | 10 |
| Tetrahydrofuran (THF) | 80 | 13 |
| Ethanol | 83 | 12 |
| 2,2,2-Trifluoroethanol | 57 | 34 |
| Water | 66 | 30 |

^a All reactions conducted at room temperature except when otherwise noted. ^b At 30°.

TABLE IV

| REACTIONS OF <i>n</i> -PROPYL BROMIDE WITH SODIUM β -NAPHTHOXIDE ^a | | |
|---|-----------------|-----------------|
| Solvent | O-Alkylation, % | C-Alkylation, % |
| Dimethylformamide (DMF) ^b | 98 | 0 |
| Dimethyl sulfoxide (DMSO) ^b | 95 | 0 |
| Ethylene glycol dimethyl ether | 96 | 0 |
| Tetrahydrofuran (THF) | 96 | 0 |
| Ethanol | 95 | Trace |
| 2,2,2-Trifluoroethanol | 81 | 10 |
| Water | 88 | 5 |

^a All reactions conducted at room temperature except when otherwise noted. ^b At 35°.

Experimental

Analyses are by Dr. C. S. Yeh and Mrs. K. V. Keblys, Purdue University. The infrared absorption spectra were determined by Mrs. W. Dilling on a Perkin-Elmer model 21 spectrophotometer (unless otherwise stated, in carbon tetrachloride solution). Ultraviolet absorption spectra were determined on a Cary model 14 spectrophotometer in absolute ethanol.

All solvents were distilled from calcium hydride or lithium aluminum hydride. Eastman Kodak Co. white label 2-naphthol was used without further recrystallization, m.p. 121–122°. The alkyl halides (commercial samples) were used directly provided the physical constants agreed with the literature values. If not, they were either recrystallized or distilled until the correct melting point or refractive index was realized.

Except as otherwise noted, reactions were followed to better than 90% completion by titrating the liberated halide ion with silver nitrate or by titrating unreacted sodium β -naphthoxide with standard hydrochloric acid to a methyl red end-point. Yields take into account losses incurred in following reaction rates (usually 2 to 4%) and, also, recovered 2-naphthol.

Sodium β -Naphthoxide.—To 75.0 g. (0.521 mole) of 2-naphthol dissolved in 260 ml. of methanol was added 20.0 g. (0.500 mole) of Baker analyzed reagent quality sodium hydroxide dissolved in 40 ml. of water. The methanol and water were removed under reduced pressure (water aspirator) at 100°; the last traces of solvent were removed by heating for 3 hours at 100° at 1 mm. On cooling, the crude salt was dissolved in 120 ml. of tetrahydrofuran and the solution was filtered. The filtrate was treated with 300 ml. of benzene and the precipitated sodium β -naphthoxide was isolated by filtration, washed thoroughly with ethyl ether, and dried at 100° at 1 mm. for 24 hours; yield 40–50 g. (48–60%).

Anal. Calcd. for C₁₀H₇ONa: neut. equiv., 166. Found: neut. equiv., 166–169.

Vapor Phase Chromatographic Analysis (V.P.C.).—Analyses were carried out with a Wilkens Aerograph using a 5-ft. silicone oil (GE SF96, 35–80 mesh) column on Chromosorb W. Before being analyzed, each reaction mixture was separated into a base-soluble and a neutral fraction. The sample to be analyzed was dissolved in benzene, or benzene-diethyl ether, and after removal of the very small amount needed for V.P.C. analysis, the remainder of the solution was used for the isolation of products either by column chromatography or recrystallization (see below). V.P.C. analyses were conducted at a column temp. of ca. 230° for the benzylated products, ca. 170° for the methylated products and ca. 185° for the *n*-propylated products.

In the *n*-propyl series a procedure was devised whereby 0.3% 1-*n*-propyl-2-naphthol could be detected in the base-soluble fraction. A standard of 2.9910 g. (99.7%) of 2-naphthol and 0.0090 g. (0.3%) of 1-*n*-propyl-2-naphthol was made up to a volume of 10 ml. with diethyl ether. At 184° and at a flow rate

of 75 cc./min., using a 20- λ aliquot, 1-*n*-propyl-2-naphthol could readily be detected. Under these conditions 2-naphthol and 1-*n*-propyl-2-naphthol have retention times of 8.6 and 14.7 minutes, respectively. In analyzing unknowns the base-soluble fraction was made up to the same concentration (by weight) as the standard, and a 20- λ aliquot was analyzed; absence of 1-*n*-propyl-2-naphthol meant that less than 0.3% C-alkylate was present in the base-soluble fraction. In all quantitative analyses retention times and relative thermal conductivities were determined using an authentic sample of each component.

Benzyl Bromide with Sodium β -Naphthoxide. In Dimethylformamide.—To a stirred solution of 8.00 g. (0.048 mole) of sodium β -naphthoxide in 35 ml. of dimethylformamide was added dropwise over a 2-hour period a solution of 8.23 g. (0.048 mole) of benzyl bromide (*n*_D²⁰ 1.5760) in 15 ml. of dimethylformamide. Upon adding a few drops of the benzyl bromide solution the temperature rose to 35° and was kept there by controlling the rate of addition. No precipitation was observed. After an additional half-hour the product was poured into water, acidified with 18% aq. hydrochloric acid, and extracted with benzene. The benzene extract was washed with Claisen potash,³⁴ with water, and dried over anhydrous sodium sulfate. Removal of solvent gave 9.95 g. of a yellow solid (I), m.p. 91–99°. The Claisen potash extract was acidified at 0° with 18% aq. hydrochloric acid, extracted with benzene and dried over anhydrous sodium sulfate; removal of the solvent gave 0.52 g. of a red solid (II).

By V.P.C. analysis, II was found to consist of 0.11 g. of 1-benzyl-2-naphthol (1% yield) and 0.41 g. of 2-naphthol. On chromatographing a benzene solution of II on silica gel (Davison 200 mesh), 0.10 g. of 1-benzyl-2-naphthol (m.p. 109–111°) followed by 0.40 g. of 2-naphthol (m.p. 120–122°) was obtained. Recrystallization of the 1-benzyl-2-naphthol from hexane gave 0.04 g., m.p. 112.5–113°, mixed m.p. with an analytically pure sample, 112–113°; lit.³⁴ m.p. for 1-benzyl-2-naphthol, 111–112°. V.P.C. analysis of I showed that 9.86 g. (93% yield) of benzyl-2-naphthyl ether was present. Recrystallization of I from methanol gave 8.72 g. of benzyl-2-naphthyl ether, m.p. 99–100°, mixed m.p. with an analytically pure sample, 99–100°; lit.³⁵ m.p. for benzyl-2-naphthyl ether, 99°.

In Dimethyl Sulfoxide. A duplicate of the experiment in DMF was carried out except that the reaction temperature was 40°.

(A) In Ethylene Glycol Dimethyl Ether.—To a solution of 8.00 g. (0.048 mole) of sodium β -naphthoxide in 50 ml. of ethylene glycol dimethyl ether was added 8.23 g. (0.048 mole) of benzyl bromide (*n*_D²⁰ 1.5760). Within a few minutes sodium bromide started to precipitate; after 1 day at room temperature the reaction mixture was worked up in the usual way. The 2.18 g. of base-soluble product on V.P.C. analysis was found to consist of 1.02 g. (11% yield) of 1-benzyl-2-naphthol and 1.16 g. of 2-naphthol. On chromatographing on silica gel (Davison, 200 mesh) with benzene there was obtained 1.06 g. of 1-benzyl-2-naphthol (m.p. 109–111°) and 1.11 g. of 2-naphthol, m.p. 120–121°. Recrystallization of the 1-benzyl-2-naphthol from hexane gave 0.52 g., m.p. 112.5–113°; mixed m.p. with an analytical sample undepressed.

The ethers which comprise the neutral fraction were cleaved by the action of sodium in liquid ammonia.³⁶ The neutral fraction (8.34 g.) was dissolved in 250 ml. of tetrahydrofuran and added to about 200 ml. of liquid ammonia. To the clear solution small pieces of sodium were added until a permanent blue color resulted; the reaction mixture was then stirred for 2 hours at reflux following which the ammonia was allowed to evaporate. The residue was carefully treated with water, then 18% aq. hydrochloric acid, and extracted with benzene. The benzene extract was washed with Claisen potash and dried. Removal of solvent gave 0.58 g. of a red oil which was not investigated. The Claisen potash phase was acidified at 0° with 18% aq. hydrochloric acid, extracted with benzene and dried over anhydrous sodium sulfate. Removal of the solvent gave 4.98 g. of product (A) which V.P.C. analysis showed to be 3.98 g. of 2-naphthol and 1.00 g. of 1-benzyl-2-naphthol. This is equivalent to 0.0276 mole of benzyl 2-naphthyl ether (70% yield) and 0.0043 mole of 1-benzyl-2-naphthyl benzyl ether (11% yield). Fraction A was made up to 100 ml. with benzene; when a 10-ml. aliquot was chromatographed on silica gel with benzene there was obtained 0.10 g. of 1-benzyl-2-naphthol (m.p. 109.5–111°) and 0.38 g. of 2-naphthol, m.p. 120–121°. Recrystallization of the 1-benzyl-2-naphthol from hexane gave 0.04 g., m.p. 111.5–113°, mixed m.p. with an analytical sample 112–113°.

(34) L. Claisen, *Ann.*, **443**, 243 (1925).

(35) W. Staedel, *ibid.*, **217**, 43 (1883).

(36) A. J. Birch, *J. Chem. Soc.*, 102 (1947); C. D. Hurd and G. L. Oliver, *J. Am. Chem. Soc.*, **81**, 2795 (1959). Using the procedure described herein, cleavage of a mixture of 2.0 g. of benzyl 2-naphthyl ether and 1.0 g. of 1-benzyl-2-naphthyl benzyl ether gave a 90% yield of 2-naphthol and a 96% yield of 1-benzyl-2-naphthol.

Reaction in tetrahydrofuran (THF) was performed as in A.

(B) In Ethanol.—To 8.00 g. (0.048 mole) of sodium β -naphthoxide dissolved in 50 ml. of ethanol was added 8.23 g. (0.048 mole) of benzyl bromide (n_D^{20} 1.5760). Within a few minutes sodium bromide started to form, and after 1 day at room temperature the reaction mixture was worked up in the usual way. The Claisen potash-soluble fraction gave 3.48 g. of product (I) which V.P.C. analysis showed to be 2.22 g. (24% yield) of 1-benzyl-2-naphthol and 1.26 g. of 2-naphthol. On chromatographing I in the usual way there was obtained 2.15 g. of 1-benzyl-2-naphthol (m.p. 109–111°) and 1.20 g. of 2-naphthol, m.p. 120–122°. Recrystallization of the 1-benzyl-2-naphthol from hexane gave 1.33 g., m.p. 112.5–113°, mixed m.p. with a pure sample, 112–113°. The neutral fraction (7.81 g.) was dissolved in benzene and chromatographed on Merck basic alumina. Elution with benzene gave: (A) 0.36 g., m.p. 67–94°; (B) 6.61 g. of a white solid, m.p. 90–96°. Finally, elution with ethyl ether gave (C) 0.72 g. of a pale yellow solid, m.p. 94–97°. Fraction B was recrystallized from methanol to yield 4.82 g. (52% yield) of benzyl 2-naphthyl ether, m.p. 99–100°, mixed m.p. with an analytically pure sample 99–100°. Fraction C was recrystallized from hexane to give 0.49 g. (4% yield) of 1,1-dibenzyl-2(1)-naphthalenone, m.p. 96–97.5°, mixed m.p. with an authentic sample, 96–97°. ³⁷

Reaction in methanol was performed as in B.

In 2,2,2-Trifluoroethanol.—To 8.00 g. (0.048 mole) of sodium β -naphthoxide dissolved in 50 ml. of 2,2,2-trifluoroethanol was added 8.23 g. (0.048 mole) of benzyl bromide (n_D^{20} 1.5760). Precipitation of sodium bromide took place and, after 1 day at room temperature, the reaction mixture was worked up in the usual way.

The Claisen potash-soluble fraction (I), 8.01 g., on V.P.C. analysis was found to be 6.89 g. (75% yield) of 1-benzyl-2-naphthol and 1.12 g. of 2-naphthol. Fraction I was made up to 100 ml. with benzene, and a 10-ml. aliquot was chromatographed in the usual way to give 0.64 g. of 1-benzyl-2-naphthol (m.p. 108–111°) and 0.14 g. of 2-naphthol, m.p. 119–120°. Recrystallization of the 1-benzyl-2-naphthol from hexane gave 0.35 g., m.p. 112–113°, mixed m.p. with an authentic sample, 112–113°.

The neutral fraction, 2.97 g., was dissolved in benzene, and chromatographed on Merck basic alumina. Elution with benzene gave 1.16 g. of a white solid, m.p. 80–94° (A). Further elution with ethyl ether gave 1.71 g. of a pale yellow solid, m.p. 93–96° (B). Recrystallization of A from methanol gave 0.61 g. (7% yield) of benzyl 2-naphthyl ether, m.p. 97.5–99°, mixed m.p. with an authentic sample, 97.5–99°. Recrystallization of B from hexane gave 1.20 g. (10% yield) of 1,1-dibenzyl-2(1)-naphthalenone, m.p. 96–97°, mixed m.p. with an authentic sample, 96–97°.

In Water. (a) To Completion.—To 1.93 g. (0.048 mole) of sodium hydroxide dissolved in 50 ml. of water was added 6.93 g. (0.048 mole) of 2-naphthol. When the stirred mixture became homogeneous, 8.23 g. (0.048 mole) of benzyl bromide (n_D^{20} 1.5760) was added. In about 10 minutes solid started to form. After stirring (two liquid phases are present initially) for 1 day at room temperature, the reaction mixture was worked up in the usual way. The Claisen potash-soluble fraction (I), 8.74 g., on V.P.C. analysis was shown to be 7.77 g. (83% yield) 1-benzyl-2-naphthol and 0.97 g. of recovered 2-naphthol. Fraction I was made up to 100 ml. with benzene; on chromatographing a 10-ml. aliquot in the usual way 0.69 g. of 1-benzyl-2-naphthol (m.p. 110–111°) and 0.09 g. of 2-naphthol, m.p. 119–121°, were isolated. Recrystallization of the 1-benzyl-2-naphthol from hexane gave 0.31 g., m.p. 112.5–113°, mixed m.p. with an authentic sample, 112–113°. The neutral fraction, 2.54 g., was dissolved in benzene and chromatographed on Merck basic alumina. Elution with benzene gave 1.37 g. of a white solid, m.p. 84–96° (A). Further elution with ethyl ether gave 0.61 g. of a pale yellow solid, m.p. 84–94° (B). Recrystallization of A from hexane gave 0.90 g. (10% yield) of analytically pure benzyl 2-naphthyl ether, m.p. 99–100°. Two recrystallizations of B from hexane gave 0.10 g. (1% yield) of 1,1-dibenzyl-2(1)-naphthalenone, m.p. 96–97°, mixed m.p. with an authentic sample, 95.5–96.5°.

(b) For Five Minutes.—This experiment shows that the formation of a solid phase consisting of organic material is not responsible for the large amount of carbon alkylation observed when reactions are conducted using an aqueous solution of sodium β -naphthoxide. It is a duplicate of (a) except that reaction was allowed to proceed for only 5 minutes after the benzyl bromide had been added and then the reaction was quenched by quickly filtering into 100 ml. of ice-cold 18% aq. hydrochloric acid. No

solid was seen during the reaction, and no residue remained on the funnel after filtration. The filtrate was worked up in the usual way except that the neutral fraction was not dried. Instead, the benzene was stripped from the neutral fraction and to the oily residue was added 100 ml. of acetone and 10 g. of thio-urea; after stirring for 1 day at room temperature, the acetone was removed, and the residue was taken up in a benzene–water mixture. The aqueous phase was washed with benzene, and the benzene extracts were combined and dried over anhydrous sodium sulfate (I).

The Claisen potash-soluble fraction (II), 7.50 g., on V.P.C. analysis was shown to consist of 2.40 g. (80% yield) of 1-benzyl-2-naphthol and 5.10 g. of recovered 2-naphthol. Fraction II was made up to 100 ml. with benzene and by chromatographing a 10-ml. aliquot in the usual way, 0.19 g. of 1-benzyl-2-naphthol (m.p. 110–111°) and 0.54 g. of 2-naphthol, m.p. 118–121°, were obtained. Recrystallization of the 1-benzyl-2-naphthol from hexane gave 0.09 g., m.p. 112.5–113°; mixed m.p. with an authentic sample, 112–113°.

Removal of the solvent from I gave 0.65 g. of product which was dissolved in benzene and chromatographed on Merck basic alumina. Elution with benzene gave 0.48 g. of a white solid, m.p. 79–94° (A), and 0.08 g., m.p. 75–87° (B). Further elution with ethyl ether gave 0.10 g. of a pale yellow solid, m.p. 92–97° (C). Fractions A and B when combined and recrystallized from hexane gave 0.25 g. (8% yield) of benzyl 2-naphthyl ether, m.p. 98–99.5°, mixed m.p. with an authentic sample, 98.5–99.5°. Fraction C when recrystallized from hexane yielded 0.03 g. (1% yield) of 1,1-dibenzyl-2(1)-naphthalenone, m.p. 96–97°, mixed m.p. with an authentic sample, 96–97°.

In a Benzene–Water Mixture.—With benzene present the reaction can be carried to completion without a solid phase forming. Once again it is demonstrated that the large amount of carbon alkylation noted when an aqueous solution of sodium β -naphthoxide is employed is not a consequence of the formation of a solid organic phase. To 1.93 g. (0.048 mole) of sodium hydroxide dissolved in 50 ml. of water was added 6.93 g. (0.048 mole) of 2-naphthol. When the stirred mixture became homogeneous a solution of 8.23 g. (0.048 mole) of benzyl bromide (n_D^{20} 1.5760) in 50 ml. of benzene was added; at no time during the reaction did a solid phase appear (two liquid phases). After stirring 5 days at room temperature the reaction mixture, on being worked up in the usual way, gave 8.08 g., an 82% yield, of 1-benzyl-2-naphthol; 0.61 g. of recovered 2-naphthol; a 7% yield (0.71 g.) of pure benzyl-2-naphthyl ether and 0.15 g. (1% yield) of pure 1,1-dibenzyl-2(1)-naphthalenone. In addition, from the neutral fraction 0.12 g. of a pale yellow solid (m.p. 157–159° after recrystallization from methanol) was isolated. Its infrared spectrum showed absorption at 5.94 μ while the ultraviolet spectrum exhibited a strong maximum at 233 $m\mu$ and minima at 270, 282, 292 and 319 $m\mu$. This material was not further examined.

Rate of Solvolysis of Benzyl Bromide in Water. (Demonstration of a Rate Dependence on Sodium β -Naphthoxide).—To 25 ml. of distilled water was added 4.12 g. (0.024 mole) of benzyl bromide (n_D^{20} 1.5760). The two-phase system was stirred, and periodically the amount of bromide ion in the aqueous phase was determined. After 3 hours only 0.7% of the theoretical amount of bromide ion had been liberated. At that time 3.34 g. (0.024 mole) of potassium perchlorate was added and solvolysis was allowed to continue for 2 more hours; at this point a total of 2% of the theoretical amount of bromide ion had been produced. Now, 4.00 g. (0.024 mole) of sodium β -naphthoxide was added; in 15 minutes the amount of bromide ion liberated jumped to 52%; and 1.25 hours after adding the naphthoxide the bromide ion liberated was 64%. Clearly the rate of bromide ion formation depends on the sodium β -naphthoxide concentration and this is not an ionic strength effect.

Rate of Solvolysis of Benzyl Bromide in DMF and in DMSO.—To 50 ml. of dimethylformamide was added 8.23 g. (0.048 mole) of benzyl bromide (n_D^{20} 1.5760). Periodically bromide ion liberated was determined; after 4 hours a total of only 2% of the theoretical amount of bromide ion had been produced. By way of contrast, the reaction of benzyl bromide with sodium β -naphthoxide is complete in less than 1.25 hours at room temperature.

A duplicate experiment employing DMSO in place of DMF revealed that after 1.5 hours 6% of the theoretical amount of bromide ion had been liberated. By way of contrast, the reaction of benzyl bromide with sodium β -naphthoxide in DMSO is complete in less than 1.25 hours at room temperature.

Methyl Iodide with Sodium β -Naphthoxide. In Dimethylformamide.—To a stirred solution of 8.00 g. (0.048 mole) of sodium β -naphthoxide in 50 ml. of DMF was added, dropwise over a 3-hour period, 25 ml. (0.398 mole) of methyl iodide (n_D^{20} 1.5320). Soon after addition began the temperature rose to 30°; it was kept at or below 30° by the rate of addition. After all the methyl iodide had been added, stirring was discontinued and the reaction mixture was allowed to stand for 15 minutes at room temperature. No precipitation occurred. The reaction mixture was worked up in the usual way except that the benzene solution of reaction products was extracted with 10% aq. sodium

(37) Obtained by treating the sodium salt of 1-benzyl-2-naphthol with benzyl bromide; m.p. 95–96°. The infrared spectrum (Nujol) was devoid of OH absorption and showed strong carbonyl absorption at 6.03 μ (1650 cm^{-1}) and a shoulder at 6.0 μ (1620 cm^{-1}). The ultraviolet spectrum showed maxima at 312 and 243 $m\mu$. *Anal.* Calcd. for $C_{20}H_{20}O$: C, 88.85; H, 6.21. Found: C, 88.76; H, 6.37. D. Y. Curtin, R. C. Tuites and D. H. Dybvig [*J. Org. Chem.*, **28**, 155 (1960)] report m.p. 96–97°.

hydroxide rather than Claisen potash. The base-soluble fraction (I), 0.22 g., was shown by V.P.C. analysis to consist of 0.04 g. (1% yield) of 1-methyl-2-naphthol and 0.18 g. of recovered 2-naphthol. Chromatographing I on silica gel (Davison, 200 mesh) with benzene gave 0.01 g. of 1-methyl-2-naphthol (m.p. 109.5–110.5°, mixed m.p. with an analytically pure sample, 109–110°),³⁸ then, after a 0.10-g. interfraction (m.p. 91–120°), pure 2-naphthol (0.10 g.) was obtained, m.p. 121–122°. The neutral fraction II, 6.92 g., was found by V.P.C. analysis to contain 6.78 g. (91% yield) of methyl 2-naphthyl ether and 0.14 g. (2% yield) of 1-methyl-2-naphthyl methyl ether; when a hexane solution of II was chromatographed on Merck basic alumina, 0.91 g. of material, m.p. 60–71° (mixture of ethers), was obtained. Further elution with hexane and then with benzene gave 5.90 g. of methyl 2-naphthyl ether (m.p. 71–73°), which on recrystallization from 95% ethanol yielded 5.47 g., m.p. 72–73°, mixed m.p. with an authentic sample, 72–73°; lit.³⁵ m.p. for methyl-2-naphthyl ether, 72°.

In Dimethyl Sulfoxide.—A duplicate of the experiment in DMF was carried out.

Reaction in ethylene glycol dimethyl ether was a duplicate of the experiment in DMF.

In Tetrahydrofuran.—A duplicate of the experiment in DMF was performed except that the neutral fraction (6.28 g.), which by V.P.C. analysis consisted of 5.53 g. (80% yield) of methyl-2-naphthyl ether and 0.75 g. (10% yield) of 1-methyl-2-naphthyl methyl ether, was cleaved by heating on a steam-bath for 9 hours with 150 ml. of glacial acetic acid and 25 g. of 48% hydriodic acid. From the resulting mixture of naphthols, 0.28 g. of pure 1-methyl-2-naphthol (equivalent to a 4% yield of 1-methyl-2-naphthyl methyl ether), m.p. and mixed m.p. 110–110.5°, was isolated by chromatography on silica gel. In addition, 4.36 g. (equivalent to a 70% yield of methyl 2-naphthyl ether) of pure 2-naphthol, m.p. and mixed m.p. 121–122°, was obtained.

Reaction in ethanol was a duplicate of the experiment in DMF.

In 2,2,2-Trifluoroethanol.—Reaction duplicated the experiment in DMF except that trifluoroethanol was employed. As the reaction proceeded precipitation of sodium iodide occurred. After stirring the reaction mixture (2,2,2-trifluoroethanol and methyl iodide are immiscible) for 9 days the reaction mixture was worked up in the usual way. At the end of this time only 67% reaction had occurred. By V.P.C. analysis the 3.97 g. of base-soluble product was shown to consist of 1.55 g. (31% yield) of 1-methyl-2-naphthol and 2.42 g. of 2-naphthol, a result which was verified by the isolation of 1.29 g. of pure 1-methyl-2-naphthol, m.p. and mixed m.p. 110–110.5°, and 1.90 g. of pure 2-naphthol, m.p. and mixed m.p. 121–122°. The 2.95 g. of neutral product was shown by V.P.C. to contain 2.80 g. (57% yield) of methyl 2-naphthyl ether and 0.15 g. (3% yield) of 1-methyl-2-naphthyl methyl ether. This was confirmed by the isolation of 1.85 g. of pure methyl 2-naphthyl ether, m.p. and mixed m.p. 72–73°.

In Water.—To 1.93 g. (0.048 mole) of sodium hydroxide dissolved in 50 ml. of water was added 6.93 g. (0.048 mole) of 2-naphthol. When homogeneity was achieved, 25 ml. (0.398 mole) of methyl iodide (*n*_D²⁰ 1.5320) was added. The two-phase system was stirred at room temperature; no precipitation occurred. After 1 week the reaction mixture was worked up in the usual way. The 2.24 g. of base-soluble product by V.P.C. analysis was found to consist of 1.54 g. (22% yield) of 1-methyl-2-naphthol and 0.70 g. of 2-naphthol. Chromatographing gave 1.38 g. of 1-methyl-2-naphthol, m.p. and mixed m.p. with an analytical sample, 110–110.5°. Also, there was isolated 0.28 g. of material, m.p. 90–118° (mixture of naphthols), and 0.49 g. of 2-naphthol, m.p. 120–122°. The neutral fraction, 5.07 g., on V.P.C. analysis was shown to contain 4.51 g. (66% yield) of methyl 2-naphthyl

ether and 0.56 g. (8% yield) of 1-methyl-2-naphthyl methyl ether; chromatography on basic alumina followed by recrystallization from 95% ethanol gave 3.78 g. of methyl-2-naphthyl ether, m.p. and mixed m.p. with an analytical sample 72–73°.

Preparation of 1-Methyl-2-Naphthyl Methyl Ether.—To 0.50 g. (0.0032 mole) of 1-methyl-2-naphthol dissolved in 10 ml. of ethylene glycol dimethyl ether was added 0.13 g. (0.0032 mole) of sodium hydroxide. When homogeneity was achieved, 5 ml. (0.080 mole) of methyl iodide was added; after 1 day at room temperature the product was worked up. A benzene solution of the neutral fraction (0.56 g.), when chromatographed on basic alumina, yielded 0.51 g. (93% yield) of 1-methyl-2-naphthyl methyl ether, m.p. 39–40°, lit.³⁸ m.p. 39°. The infrared spectrum was devoid of OH absorption and α,β -unsaturated ketone absorption, but exhibited ether absorption at 8.00 μ .

***n*-Propyl Bromide with Sodium β -Naphthoxide.** In Dimethylformamide.—To a stirred solution of 8.00 g. (0.048 mole) of sodium β -naphthoxide in 50 ml. of DMF was added, dropwise over a 30-minute period, 36 ml. (0.398 mole) of *n*-propyl bromide (*n*_D²⁰ 1.4344). During the addition the temperature rose to 35° and sodium bromide precipitated. After the addition of *n*-propyl bromide was complete, the reaction mixture was allowed to stand for an hour. It was then worked up in the usual way except that 10% aqueous sodium hydroxide was used to obtain the base-soluble fraction instead of Claisen potash; V.P.C. analysis of the 0.36 g. of base-soluble material showed only the presence of 2-naphthol. The crude neutral fraction (8.46 g.) had m.p. 35–37° and, when chromatographed on basic alumina, gave 8.29 g. (98% yield) of *n*-propyl 2-naphthyl ether, m.p. and mixed m.p. with an analytical sample, 39.5–40.5°; lit.³⁹ m.p. 40°.

Dimethyl sulfoxide duplicated the above run in DMF.

In Ethylene Glycol Dimethyl Ether.—To 8.00 g. (0.048 mole) of sodium β -naphthoxide dissolved in 50 ml. of ethylene glycol dimethyl ether was added 36 ml. (0.398 mole) of *n*-propyl bromide (*n*_D²⁰ 1.4344). As the reaction proceeded, sodium bromide precipitated, and after 6 days at room temperature, the reaction mixture was worked up in the usual way; V.P.C. analysis of the base-soluble fraction (0.30 g.) showed only the presence of 2-naphthol. The neutral fraction (8.24 g., m.p. 37–40°) gave, on chromatography, 8.19 g. (96% yield) of *n*-propyl 2-naphthyl ether, m.p. and mixed m.p. 39.5–40.5°.

In Tetrahydrofuran.—A duplicate of the run in glycol dimethyl ether was carried out.

Reaction in ethanol was a duplicate of the run in glycol dimethyl ether.

In 2,2,2-Trifluoroethanol.—A duplicate of the run in glycol dimethyl ether; reaction time 3 weeks; V.P.C. analysis of the base-soluble fraction (4.18 g.) showed it to be 0.41 g. (10% yield) of 1-*n*-propyl-2-naphthol and 3.77 g. of recovered 2-naphthol. Chromatography on silica gel (Davison) with benzene gave 0.39 g. of 1-*n*-propyl-2-naphthol (m.p. 50–57°) which, on recrystallization from pentane, gave 0.11 g., m.p. and mixed m.p. with an analytically pure sample, 58–59°; lit.⁴⁰ m.p. for 1-*n*-propyl-2-naphthol 56–58°. Further elution with benzene gave 0.31 g. melting 115–122° (mixture of naphthols), and 3.30 g. of 2-naphthol, m.p. 120–122°. The neutral fraction, 3.40 g. (m.p. 34–38°), on chromatography on basic alumina gave 3.31 g. (81% yield) of *n*-propyl 2-naphthyl ether, m.p. and mixed m.p. with an analytical sample, 39–40.5°.

In Water.—To 1.93 g. (0.048 mole) of sodium hydroxide in 50 ml. of water was added 6.93 g. (0.048 mole) of 2-naphthol. When homogeneity was achieved, 36 ml. (0.398 mole) of *n*-propyl bromide (*n*_D²⁰ 1.4344) was added. The two-liquid phase system was stirred at room temp. for 3 weeks and then worked up in the usual way.

(38) K. Fries and E. Hübner [*Ber.*, **39**, 442 (1906)] report a m.p. of 110° for 1-methyl-2-naphthol.

(39) K. H. Slotka and W. Franke, *Ber.*, **63**, 678 (1930).

(40) K. Takeda and H. Osaka, *J. Pharm. Soc. Japan*, **75**, 210 (1955).