excess dimethyl sulfate and dried. Alterations in reaction time of from 4 to 144 hours gave 20–52% complete quaternization. Requaternization according to procedure c below gave the increased values noted in the table.

(b) **With Dimethyl Sulfate, Sodium Bicarbonate and Water.**—A four-to-one mole ratio of dimethyl sulfate to amino groups was used. A mixture of 0.8717 g. of resin 8 (Table I), 2.52 g. of dimethyl sulfate, 1.88 g. of sodium bicarbonate and 2.58 ml. of distilled water was heated in a closed flask at 80° for 48 hours. The beads were washed with water and dried.

(c) **With Methyl Iodide.**—A twenty-to-one mole ratio of methyl iodide to amino groups was used. A mixture of 1.196 g. of resin 8 (Table I) and 19.9 g. of freshly distilled methyl iodide was allowed to stand at room temperature in a stoppered flask for 24 hours with frequent shaking. A small amount of white precipitate formed in the first few minutes. The beads were collected on a filter, washed with water and dried. A sample of the white precipitate was collected and its infrared spectrum found to be identical with that from *p*-dimethylaminostyrene methiodide prepared from the styrene and methyl iodide, m.p. 193–194°.

Anal. Calcd. for $C_{11}H_{16}NI$: C, 45.69; H, 5.58; I, 43.88. Found: C, 45.32; H, 5.68; I, 43.61, 43.68.

Total Capacity Measurements.—Results of the capacity determinations are given in Table II. Some of these measurements were made by the titration procedure previously described[7] and others were made by the following weight difference procedure.

The resin in the iodide form was washed thoroughly and dried to constant weight (one week) under vacuum in a rotary drier. This resin (1.9346 g. of resin 8) was placed in a column, washed with 2 liters of 1 *N* sodium sulfate, and then washed with water until the effluent no longer contained sulfate. The resin was then redried as before and weighed (1.4802 g.) in the sulfate form. The difference in weight for the beads in the iodide and in the sulfate forms (0.4544 g.) was divided by the difference (78.89) in molecular weight of iodine (126.92) and one-half sulfate (48.03) to give the meq. of replaceable ionic groups. The meq. of replaceable ions divided by the weight of resin in the iodide form gave the total capacity (3.0) in meq. per g. of dried resin in the iodide form.

---

[7] R. Kunin and R. J. Myers, "Ion Exchange Resins," John Wiley and Sons, Inc., New York, N. Y., 1950, p 153.

LOUISVILLE, KY.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, UNIVERSITY OF ILLINOIS]

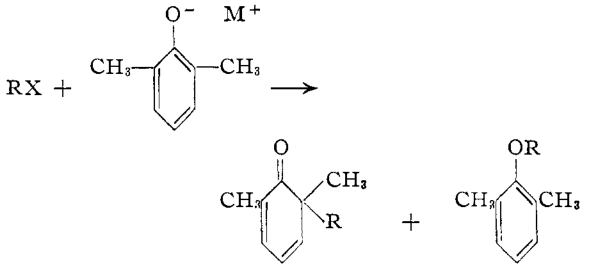
Factors Controlling Position of Alkylation of Alkali Metal Salts of Phenols, Benzyl and Allyl Halides[1,2]

BY DAVID Y. CURTIN, ROBERT J. CRAWFORD AND MAX WILHELM

RECEIVED OCTOBER 4, 1957

The alkylation of metal salts of 2,6-dimethylphenol and its 4-methyl and 4-bromo derivatives with benzyl and allyl halides has been examined. In general a mixture of allyl or benzyl aryl ether and 6-allyl (or benzyl) 2,4-cyclohexadienone is obtained and the objective of this study has been to determine some of the factors which influence the dienone/ether ratio. It has been found that dienone formation is favored by non-polar solvents, use of salts of less acidic phenols, higher salt concentrations, use of the lithium rather than sodium and sodium rather than potassium salt, and allyl or benzyl rather than saturated halides, and markedly decreased by the addition of tetrabutylammonium bromide. The ratio seems to be independent of the nature of the halide in a comparison of chloride, bromide and iodide. Only *ortho* alkylation is found. These results readily can be interpreted in terms of a postulation made in 1926 by Ingold that dissociated ions give a preponderance of allyl or benzyl ether and that ion aggregates give largely dienone.

In the course of a study of the *para* Claisen rearrangement, it was found[2,3] that sodium 2,6-dimethylphenoxide can be made to react with allyl halides, the attack occurring at an *o*-position with the formation of 6-allyl-2,6-dimethyl-2,4-cyclohexadienone (I). The conditions employed (suspension of the sodium salt in benzene) were patterned after those previously shown by Claisen and his associates[4,5] to cause *o*-alkylation of sodium phenoxide and salts of certain other phenols with unoccupied *o*-positions. It has been of interest to attempt to learn more about the factors controlling the relative amounts of carbon- and oxygen-alkylation of phenol salts. A study of the alkylation with benzyl and allyl halides of sodium 2,6-dimethylphenoxide is reported here.



I (R = allyl) II (R = allyl)
III (R = benzyl) IV (R = benzyl)

Certain examples of the formation of dienones by the direct carbon-alkylation of phenols have been reported which differ in important respects from the alkylations to be discussed but which should be mentioned briefly. The abnormal Reimer–Tiemann reaction[6] introduces a dichloromethyl unit into an *o*- or *p*-position of a methylated phenol. This reaction has two unique features. The product of oxygen attack is an α-halo ether which is probably immediately reconverted to the starting phenol in the reaction medium. Further, the reaction in which the position of substitution is deter-

---

[1] Supported in part by a grant from the Office of Ordance Research, U. S. Army (Contract No. DA-11-022-ORD-1985). Abstracted in part from the Ph.D. Thesis of Dr. Robert Crawford submitted to the University of Illinois, 1956, and available from Univ. Microfilms, Ann Arbor, Michigan.

[2] Most of this work was presented at the Fifteenth National Organic Symposium, Rochester, N. Y., June, 1957. A preliminary report was made by David Y. Curtin and Robert J. Crawford, *Chemistry & Industry*, 313 (1956).

[3] D. Y. Curtin and R. J. Crawford, THIS JOURNAL, **79**, 3156 (1957).

[4] L. Claisen, *Z. angew. Chem.*, **36**, 478 (1923).

[5] L. Claisen, F. Kremers, F. Roth and E. Tietze, *Ann.*, **442**, 210 (1925).

[6] K. Auwers and F. Winternitz, *Ber.*, **35**, 465 (1902).

mined probably does not involve chloroform but rather preformed dichlorocarbene.[7]

Certain polynuclear phenols have been reported to undergo alkylation at a nuclear position (as well as at oxygen). For example, the sodium salt of anthranol has been reported to react with methyl iodide in ethanol to yield 9,9-dimethylanthrone.[8] Polyhydric phenols, phloroglucinol[9] for example, have been found to undergo alkylation, the position of which depends on the order of mixing of the reagents.[10] Finally, the driving force of neighboring group participation has been used to produce carbon-alkylation leading to 4,4-dimethylene- and 4,4-tetramethylene-2,5-cyclohexadienone.[11]

The problem of predicting and controlling the position of reaction of an ion which can undergo attack at more than one position (an "ambident ion")[12] is a general one which many investigators have discussed. Three approaches to the problem might be mentioned. The first considers the state of aggregation of the reacting species as of primary importance in determining the position of reaction. Ingold as early as 1926 suggested[13] that Claisen's *o*-alkylation reaction of phenol salts with allyl and benzyl halides in non-polar solvents such as benzene involved the reaction of the alkyl halide with associated sodium phenoxide, whereas the oxygen-alkylation in more polar solvents such as ethanol was attributed to reaction of the dissociated phenoxide ion. Brady and his associates have advanced evidence that in the methylation of oximes,[14,15] ion aggregates and dissociated ions behave differently. Investigations have also been made of the effect of change of cation or medium on the Kolbe[16] and Reimer–Tiemann[17] reactions, on the position of alkylation of β-keto esters,[18] the position of protonation of sodium allylbenzene[19] and other reactions.[17]

A second approach to the problem has been to consider that only dissociated ions need react and that differences in position of reaction brought about by changes in the solvent are due to changes in structures of the transition states. Thus, in explaining the preferential attack on oxygen in the reaction of phenoxide ion with allyl or benzyl halides it has been argued[12] that relatively good solvolyzing solvents like ethanol lead to mechanisms which are near the SN1 or lim end of the mechanistic spectrum of nucleophilic replacement reactions.[20] In the limiting case the reactants would be allylcarbonium ion and phenoxide. In such a case the product-determining step is highly exothermic and the structures of the two possible transition states (for the reactions leading to carbon- or oxygen-alkylation) are approximated by the structures of the starting materials according to a postulate stated in its most general form by Hammond,[21] thus the preferred transition state would be that leading to oxygen-alkylation on electrostatic grounds. On the other hand, in the solvent benzene, the reactions should have mechanisms more nearly at the SN2 or **N** end of the mechanistic spectrum, that is, there should be considerable covalent bonding of the oxygen (or the *o*-carbon atom of phenoxide ion) with the central carbon atom of the halide and since such reactions are neither highly endothermic nor highly exothermic the two transition states leading to carbon- or oxygen-alkylation cannot be approximated by either the starting materials or the products of the reactions but differ in a number of ways which make their relative energies difficult to evaluate. However, it is not inconceivable that in this case dienone formation might be favored. The importance of the position of the replacement mechanism in the mechanistic spectrum in determining the nature of the product ratio has been independently conceived and convincingly demonstrated by Kornblum and his associates[12,22] for the alkylation of metal nitrites.

A third alternative which might be considered is that dissociated ions solvated by certain solvents prefer to react at oxygen while those solvated by others react preferentially at carbon.

It can be stated at the outset that although each of these considerations may play a part in determining the position of alkylation of phenol salts (and other ambident ions) an explanation which is essentially a modernized statement of that advance by Ingold[13] serves to explain quite satisfactorily the data to be presented in this paper without the necessity of calling upon the other factors mentioned.

It is well known that in dilute solution in most organic solvents, even strong electrolytes are associated.[23–25] At concentrations of the order of 10^{-5} or less, in a solvent such as benzene, salts are present almost entirely as ion pairs.[26] At the

---

(7) J. Hine, "Physical Organic Chemistry," McGraw–Hill Book Co., Inc., New York, N. Y., 1956, pp. 131 ff.

(8) K. H. Meyer and H. Schlosser, *Ann.*, **420**, 126 (1920).

(9) J. Herzig and F. Wenzel, *Monatsh.*, **27**, 781 (1906); A. Spitzer, *ibid.*, **11**, 104, 287 (1890).

(10) It is reasonable that the monoanion might undergo oxygen alkylation under conditions which lead to preferential carbon-alkylation of the di- or trianion of phloroglucinol as is suggested by these observations. One factor which may be involved is that the carbon-alkylation of the trianion leads to a dianion with the two remaining charges distributed over three oxygen atoms, whereas oxygen-alkylation leads to their distribution over only two oxygen atoms. Such a difference in product stabilities should also show up as a difference in transition state stabilities and so affect the relative rates of the two alkylations.

(11) S. Winstein and R. Baird, This Journal, **79**, 757, 4238 (1957); paper presented by S. Winstein, Fifteenth National Organic Symposium, Rochester, N. Y., June, 1957.

(12) N. Kornblum, R. A. Smiley, R. K. Blackwood and C. Iffland, This Journal, **77**, 6269 (1955).

(13) C. K. Ingold, *Ann. Repts.*, 142 (1926).

(14) O. L. Brady and R. F. Goldstein, *J. Chem. Soc.*, 2405 (1926).

(15) O. L. Brady and N. M. Chokshi, *ibid.*, 2271 (1929).

(16) J. R. Johnson, This Journal, **55**, 3029 (1933); K. Brunner, *Ann.*, **351**, 313 (1907); S. Widequist, *Arkiv. Kemi*, **7**, 229 (1954).

(17) O. L. Brady and J. Jakobovits, *J. Chem. Soc.*, 767 (1950).

(18) W. v. E. Doering and S. J. Rhoads, This Journal, **73**, 3082 (1951); S. J. Rhoads, R. D. Reynolds and R. Raulins, *ibid.*, **74**, 2889 (1952).

(19) R. Y. Mixer and W. G. Young, *ibid.*, **78**, 3379 (1956).

(20) E. Grunwald and S. Winstein, *ibid.*, **70**, 846 (1948); S. Winstein, A. Fainberg and E. Grunwald, *ibid.*, **79**, 4146 (1957); C. G. Swain and W. P. Langsdorf, *ibid.*, **73**, 2813 (1951).

(21) G. S. Hammond, *ibid.*, **77**, 334 (1955).

(22) N. Kornblum, R. K. Blackwood and J. W. Powers, *ibid.*, **79**, 2507 (1957).

(23) For an excellent summary see C. A. Kraus, *J. Phys. Chem.*, **60**, 129 (1956).

(24) R. A. Robinson and R. H. Stokes, "Electrolytic Solutions," Butterworth, Ltd., London, Eng., 1950.

(25) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, N. Y., 1950.

(26) Reference 23, p. 132.

TABLE I

REACTIONS OF 0.40 *M* SODIUM 2,6-DIMETHYLPHENOXIDE WITH ALLYL AND BENZYL HALIDES

17–20°, 44–48 hours unless otherwise specified

Solvent	Halide	Phenol recovd., %	Ketone, %	Ether, %	Ketone/ether
Diethyl ether[a,b] (purified) (D 4.3)	Allyl bromide	62	7.5[c]	26	0.29[d,e]
		66	8.5[c]	27	.31[d,e]
	Benzyl chloride	100	1	2.5	.36[d]
	Benzyl bromide[f]	62	8	29	.36[d]
Diethyl ether[a,g] (unpurified) "anal. reag."	Allyl bromide	..	28[c,h]	28[h]	1.0, 1.0, 1.1[e,i,j]
		..	...	...	0.54[d]
Diethyl ether[a,b] + 0.044 *M* water	Allyl bromide	..	15[c]	29	0.51[d,e]
	Benzyl chloride	90	4	4	1[d,c]
	Benzyl bromide[f]	..	21	37	0.57[d,e]
Diethyl ether[k] satd. $Bu_4N^+Br^-$	Allyl bromide	18	9.2[c]	78	.12[d,e]
		..	3[c]	53	.05[i]
Dioxane (*D* 2.2)[l]	Benzyl chloride[m]	73	1	30	.03[d]
Toluene (*D* 2.4)[n]	Benzyl chloride[m]	..	25	6	4.2[d]
	Benzyl chloride[o]	..	71	16	4.4[d]
Toluene + 0.49 *M* tetrahydrofuran[p]	Benzyl chloride[m]	..	3	1	3[d]
	Benzyl chloride[o]	50	49	18	2.7[d]
Benzene (*D* 2.3)[n]	Allyl bromide	24	40[c]	3	12
Diisopropyl ether (d. 3.8)[n]	Benzyl chloride[m]	60	27	15	1.8[d]
Tetrahydrofuran[l] (d. 7.4)	Benzyl chloride	56	0.5	48	0.01[d]
	Benzyl iodide[q]	..	0	43	0[d]
Tetrahydrofuran + 0.05 *M* NaI	Benzyl iodide[q]	..	0	51	0[d]
Ethanol (*D* 24)[l]	Allyl bromide	57	1.7[c]	10.3	0.16[i]
	Benzyl iodide[r]	..	7	80	.09[d]
Ethanol satd. with NaI	Benzyl iodide[r]	..	10	57	.18[d]

[a] Reaction mixture initially appeared homogeneous but the sodium halide formed during the reaction precipitated. [b] Purified by distillation directly into the reaction flask from lithium aluminum hydride or sodium. [c] The dienone concentration in the product was calculated using a value for ϵ of 4400.[8] It seems likely, judging from the value for the benzyl dienone of 5100 that this may be low by as much as 20%. This does not change the relative values of the ketone/ether ratios when the results with the allyl halides are compared among themselves and, in fact, is probably negligible compared to other sources of error. [d] Determined by infrared and ultraviolet analysis of undistilled neutral fraction (procedure B). [e] Infrared showed less than 2.5% of the dimer present. [f] 21 hr. at 20°. [g] According to the label contained 0.01% ethanol, 0.01% water and a small amount of sodium diethyldithiocarbamate as a preservative. [h] Estimated from the weight of neutral fraction before distillation. [i] Product distilled before infrared and ultraviolet analysis (procedure A). [j] Each of these values obtained from a different reaction. [k] Excess solid tetrabutylammonium bromide suspended in reaction mixture. Reaction was visibly faster—in one run ether solvent began to boil but was cooled to 17° for duration of the reaction. [l] Homogeneous. [m] 40° for 21 hr. [n] Heterogeneous throughout. [o] 65° for 21 hr. [p] The sodium phenoxide was soluble in this mixture (note that mole ratio of tetrahydrofuran to sodium salt nearly 1:1). [q] Concentration of the sodium phenoxide was 0.005 *M*. The reaction time was 9 hr. at 22°. Excess benzyl iodide was removed by crystallization from petroleum ether at −60°. [r] Eight hr. at 20°.

higher concentrations employed in this work there are also larger aggregates. In general, ion pairs are sufficiently inert chemically so that even though their concentration is high relative to the concentration of dissociated ions, the reaction of the latter is the stoichiometrically important one.[27] It might be anticipated, then, that reactions of ion aggregates not involving preliminary dissociation should seldom be observed except in the poorest dissociating solvents such as benzene.

The effect of the nature of the medium on the alkylation with benzyl or allyl halides of the sodium salt of 2,6-dimethylphenol may be seen in Table I. It will be noted that of the solvents studied benzene and toluene give the largest proportion of dienone. However, even in ethanol, a solvent which was reported by Claisen, Kremers, Roth and Tietze[5] to result in the formation only of phenyl allyl ether in the reaction with sodium phenoxide, the dimethylphenoxide yields appreciable amounts (of the order of 10%) of dienone.

Tetrahydrofuran gave least dienone (amount not spectroscopically detectable) of the solvents examined. Certain of the reaction mixtures (*i.e.*, benzene, diisopropyl ether) were heterogeneous throughout. In ethanol and tetrahydrofuran the reaction was homogeneous and in diethyl ether, although the sodium salt of 2,6-dimethylphenol is soluble initially, the sodium halide which is formed precipitates during reaction. It seems likely that the presence or absence of a solid phase has no effect on the ratio of dienone except insofar as it affects the concentration of ions in solution as will be mentioned later. It is apparent that although there is a general correlation of increasing dienone formation with increasing "non-polarity" the correlation of the ketone ether ratio with dielectric constant (given in parentheses after each solvent in Table I) is poor. Such a correlation could hardly be expected, however, in view of the general failure of the correlation of ion pair dissociation with dielectric constant over a wide range of solvents.[23] Unfortunately no reliable conductivity data are available for solutions of salts in most of the solvents in Table I.

---

[27] C. C. Evans and S. Sugden, *J. Chem. Soc.*, 270 (1949); L. J. LeRoux and E. R. Swart, *ibid.*, 1475 (1955); J. R. Bevan and C. B. Monk, *ibid.*, 1396 (1956).

Certain difficulties which arise in making and interpreting these measurements should be discussed. The dienone I is rather unstable and care was taken to prevent it from rearranging[3] either by not distilling the reaction mixture or distilling it at temperatures not much above 30°. The dienone I and 6-benzyl-2,6-dimethyl-2,4-cyclohexadienone (III) undergo a Diels-Alder dimerization rather rapidly.[3] When they are allowed to stand either neat or in relatively concentrated solution, dimerization occurs to an appreciable extent in a few hours. For this reason care was taken to use concentrated solutions promptly or else to store in the freezing compartment of a refrigerator. The amount of dimer is estimated readily from its characteristic carbonyl absorption in the infrared spectrum. The dienone/ether ratio was affected to some extent by small amounts of water in the ether solvent. Thus, as the data in Table I show, the fraction of dienone was increased by a factor of nearly 2 when 0.044 M water was added to the originally anhydrous ether. The use of unpurified "analytical reagent" grade ether also seemed to increase somewhat the dienone fraction. The method of estimating the product ratio also affected the results. When the total neutral fraction was distilled before the product ratio was determined spectrophotometrically (procedure A) the fraction of dienone was somewhat higher than when the neutral product was analyzed directly although each method appeared to be self-consistent and reproducible. Since most of the more refined arguments to be presented here will depend only on changes brought about by a single variable under standard conditions, we believe the comparisons to be made are significant.

Orientation.—In their studies of the alkylation of sodium phenoxide and other phenol salts Claisen, Kremers, Roth and Tietze[5] had concluded that carbon-alkylation occurred only at an *o*-position. An examination of the products of alkylation by allyl and benzyl halides of the sodium salts in benzene of *o*- and *p*-cresol,[28] 2,6-dimethylphenol and mesitol has failed to show any evidence of *p*-alkylation. The benzylation of the salts of *p*-cresol and mesitol[29] are particularly significant since the interconversion of *o*- and *p*-dienones by a Claisen-type rearrangement possible with the allyl compounds is avoided with the benzyl substituent and since even small amounts of the 2,5-dienone should be detectable because of its characteristic[11] ultraviolet and infrared spectrum. However, when more bulky halides such as benzhydryl chloride are employed in the alkylation of sodium 2,6-dimethylphenoxide there is formed in addition to a small amount of dienone, considerable of the *p*-alkylation product.[29] This reaction may proceed by a substantially different mechanism, however.

The report by Tarbell and Kincaid[30] (confirmed in our work) that the alkylation of 2,6-dimethylphenol as the sodium salt in boiling ethanol yields 4-allyl-2,6-dimethylphenol might be interpreted as suggestive of a direct *p*-alkylation. In view of the results of the alkylations with benzyl halides, however, it seems more likely that the 4-allyl product was formed by rearrangement of the dienone I during the alkylation reaction. The dienone is known to rearrange under these conditions.[3,31]

Effect of Varying the Metal Ion.—If dienone formation is due primarily to the reaction of ion aggregates, and allyl ether formation to reaction of dissociated ions it would be anticipated that even a minor change in the nature of the metal ion might change the ratio of products. Such effects have been observed with other reactions.[14,16,17] It was found that under conditions (in diethyl ether) which lead to about 55% reaction of the sodium salt with a dienone/ether ratio of 1, the lithium salt of 2,6-dimethylphenol failed to react appreciably with allyl bromide. The potassium salt, although not very soluble in ether, reacted to the extent of at least 63% under the same conditions to give a significantly larger fraction of the allyl ether (dienone/ether ratio 0.5). It is tempting to interpret the increase in ether formation as due primarily to increased dissociation of the potassium salt[32] with the dissociated ion reacting to give largely allyl ether. If this explanation is correct the increase in dissociation must more than compensate for any increased reactivity of potassium ion aggregates relative to sodium, the ion aggregates reacting to give principally dienone. Caution must be observed in using this kind of argument, however, since potassium salts are less dissociated than sodium salts in some solvents.[33] It may be noted that in boiling ethanol as solvent the lithium salt reacted only slightly more slowly than the sodium salt of 2,6-dimethylphenol but gave no detectable carbon-alkylation products in contrast to the behavior of the sodium salt. This result is readily explained if the difference in reactivities of the lithium and sodium ion aggregates more than compensates for the increased dissociation of the sodium salt. The unreactivity of the lithium salt in ether apparently is due to a combination of its low degree of dissociation and the unreactivity of the ion aggregates. The few data which are available[23] support the implication of these results that the dissociation constants of sodium and lithium salts may be much more nearly equal in polar solvents such as ethanol than in relatively non-polar solvents such as ether. The relative unreactivity of associated lithium salts has been noted in other reactions.[17,34]

In view of the work of Kornblum and his associates[12,22] mentioned earlier, the behavior of the silver salt of 2,6-dimethylphenol in alkylation reactions was of interest. However, preliminary attempts to obtain this salt in a reasonably pure form have been unsuccessful. The magnesium salt was prepared and found to be insoluble in ether. It failed to react under conditions satisfactory for the sodium salt.

---

(28) D. Y. Curtin and M. Wilhelm, *J. Org. Chem.*, **23**, 9 (1958).

(29) R. Tuites, unpublished results.

(30) D. S. Tarbell and J. F. Kincaid, THIS JOURNAL, **62**, 728 (1940).

(31) We are indebted to Professor Tarbell for independently observing this possibility and calling it to our attention.

(32) See ref. 23, p. 135 for data on alkali metal picrate dissociation (Table XII) in nitrobenzene and acetone, for example.

(33) See, for example E. L. Purlee and E. Grunwald, THIS JOURNAL, **79**, 1366, 1372 (1957).

(34) See, for example, W. Doering, G. Cortes and L. Knox, *ibid.*, **69**, 1705 (1947); D. Y. Curtin and S. Leskowitz, *ibid.*, **73**, 2630 (1951).

Since the cesium and tetramethylammonium salts might be expected[23] to be more highly dissociated than the potassium salt, their synthesis was attempted also, but in exploratory experiments it was found difficult to obtain them in satisfactorily anhydrous form.

It will be noted in Table I that, although tetrabutylammonium bromide (as shown by preliminary tests) is only soluble to the extent of about 0.4 g./l. in ether, it had a rather dramatic effect on the reaction of sodium 2,6-dimethylphenoxide with allyl bromide. It both accelerated the reaction rate markedly and increased the proportion of allyl ether. It is of interest that the qualitative experiments carried out indicate that there was little effect of the quaternary salt on the rate of dienone formation. These results are readily explained if the principal reactant is the quaternary ammonium phenoxide, formed by ion exchange (probably with precipitation of part of the sodium bromide formed).

In other experiments, lithium or sodium phenoxide or tetramethylammonium bromide were found to have a negligible effect on the ratio of products formed and the rate. The inactivity of the tetramethylammonium salt probably is due to its low solubility in ether.

The problem of the structures of the lithium and sodium salts is of some interest in view of the difference in their reactivity. Considerable covalency has been often attributed to the lithium–oxygen bond.[17] In the hope that a significant difference in the degree of covalency might be evident in the ultraviolet spectra of the sodium and lithium salts, the spectra were measured in ether solution but were found to be essentially identical. It appears unnecessary to attribute the difference in reactivity to a fundamental difference in the structure of the salts since it may equally well be due to a difference in the transition states.

Concentration Effects.—Consideration of possible kinetic schemes in which dissociated ions react to form chiefly allyl or benzyl ethers and ion aggregates give predominantly dienones shows that the instantaneous dienone/ether ratio is a function of the degree of dissociation of the ion aggregates which is in turn a function both of the concentration of metal phenoxide present and of any added common ion. The situation is complicated since during a run the sodium phenoxide is replaced by sodium halide which, in diethyl ether, is precipitated in part during the reaction. The effect on the product composition of the precipitation should be small, however, in a reaction carried to only about 50% completion as were the experiments reported here; this expectation is verified by an experimental demonstration that the dienone/ether ratio was essentially constant when a reaction of allyl bromide with sodium 2,6-dimethylphenoxide was intercepted after times covering the range of 3600–414,000 sec. (or 5–80% reaction). It might be anticipated that, as Brady and Chokshi[15] suggested in their study of the alkylation of oximes, an increase in the degree of dissociation with an accompanying increase in the relative amount of oxygen attack should be observed on going to lower initial concentrations of phenol sodium salt. Such an effect is observed qualitatively. In the alkylation with allyl bromide in ether of sodium 2,6-dimethylphenoxide the dienone/ether ratio drops from 1.0 with an initial concentration of 0.40 *M* sodium salt to 0.45 at an initial concentration of 0.025 *M*. While such an effect is readily accommodated by the argument in terms of ion pair dissociation here employed, caution must be observed since at concentrations as high as 0.4 *M* the degree of dissociation may actually decrease with decreasing concentration.[35]

Effect of Halide Structure.—It had been concluded by Claisen[4,5] that only those halides which were unusually reactive could take part in the *o*-alkylation of sodium phenoxide. This led to the presumption that a change of the halogen from chloride to iodide in the series, allyl chloride, allyl bromide, allyl iodide or in the corresponding benzyl series might change the dienone/ether ratio. That such is not the case, however, is suggested by the data in Table I. Furthermore, the use of the three allyl halides under standard conditions gave an increase in % reaction (6, 60, 66, respectively) in going from the chloride to the iodide but no change in the ratio of dienone to ether. Although preliminary experiments in the solvent ether led us to accept Claisen's conclusion that only "reactive" halides such as benzyl and allyl halides could be made to give alkylation on carbon,[2] a further investigation has shown that this is not the case. Propyl iodide and methyl iodide react with sodium 2,6-dimethylphenoxide to yield considerable amounts of dienone although the dienone/ether ratio is smaller than that with benzyl or allyl halides under the same conditions.[36] Since dimethylcarbamyl chloride has been shown[37] to react by way of an intermediate, presumably the cation $(CH_3)_2$-$N^+{=}C{=}O$, it was chosen as the most promising acid chloride in an effort to obtain a dienone from the sodium salt of 2,6-dimethylphenol; but a spectral analysis of the neutral product mixture showed no evidence of dienone formation.[29]

Effect of Phenol Structure.—A comparison of the ratio of dienone to ether formed in the reaction of allyl bromide in diethyl ether has been made with the sodium salts of 2,4,6-trimethylphenol (mesitol) and 4-bromo-2,6-dimethylphenol. The dienone/ether ratios so obtained were for the *p*-methyl compound 2.7, for the unsubstituted 1.0 and for the *p*-bromo, 0.3.[38]

It is evident that the more strongly acidic (*p*-bromo) phenol gives more ether and the less acidic more dienone. Claisen's data[5] for the alkylation of sodium phenoxide and sodium *p*-methylphenoxide show a similar trend. A comparable effect was observed by Brady and Chokshi[15] in their study of the relative amount of oxygen- and nitrogen-alkylation of oximes, the more strongly acidic oximes undergoing a larger fraction of oxygen alkyla-

---

(35) See ref. 23, p. 141.

(36) D. Y. Curtin and R. Fraser, *Chemistry & Industry*, 1358 (1957).

(37) H. K. Hall, Jr., THIS JOURNAL, **77**, 5993 (1955).

(38) The alkylation of the sodium salt of 2,4,6-trimethylphenol has been reported by F. Kalberer and H. Schmid [*Helv. Chim. Acta*, **40**, 779 (1957)] to lead to a mixture of ether and dienone, but no product ratio was reported.

tion. It is of interest that a plot of the logarithm of the dienone ether ratio *vs.* σ gives a straight line with a slope of -2.6. Brady and Chokshi's nitrogen/oxygen ratios also give a straight line with a slope of -0.295. Since our plot has only three points, any conclusions must be tentative; but a linear plot of this type is accommodated readily by the picture in which ion aggregates give rise to dienone and dissociated ions to ether.[39]

Although it is premature to postulate a detailed mechanism before a thorough kinetic study provides information as to just what species are present in the transition state, it might be pointed out that a modification of the picture presented by Ingold[12] in 1926 suggests at least one factor which could contribute to the preferential *o*-alkylation in non-polar solvents. The transition state resulting from attack at oxygen has the two atoms bearing most of the negative charge (oxygen and halogen) disposed in a linear fashion while the transition state resulting from carbon attack has a more favorable non-linear arrangement in which the metal ion can bridge the negatively charged oxygen and halogen. It seems likely, however, that the situation is much more complex and that other factors are involved. For example, the picture here presented accounts less satisfactorily for the *p*-alkylation, which although less favorable than the *ortho*, has been observed as was mentioned earlier.

It is important to note that the division of ions into ion pairs and dissociated ions on the basis of conductivity measurements probably assigns many species to the ion pair category which, in fact, have their component ions so far apart that their behavior in the alkylation is almost certainly the same as that of dissociate phenoxide ions insofar as the product-ratio is concerned.[41] Winstein[42] has used a kinetic criterion to classify ion pairs occurring as reaction intermediates in certain solvolysis reactions as "intimate" and "solvent separated" and it is likely that those which show distinctive behavior in the phenoxide alkylation correspond most closely to the "intimate" ion pairs of the latter study. It is most desirable that further studies of ambident ion behavior should be undertaken with the aim of deciding what effect changes in conditions may have on reactions involving only dissociated ions and in sorting out further the three expected influences determining the position of reaction of an ambident ion.

As a further word of caution, it might be noted that in certain studies, in particular on the *para*-Claisen rearrangement,[43] results obtained may be significantly affected by the presence of previously unsuspected dienone as a product of alkylation of a 2- or 6-substituted phenol salt even in a solvent as polar as ethanol.

Experimental[44]

Allyl 2,6-Dimethylphenyl Ether (II).—Alkylation of sodium 2,6-dimethylphenoxide prepared in 300 ml. of absolute ethanol from 10.8 g. (0.20 mole) of sodium methoxide and 24.4 g. (0.20 mole) of 2,6-dimethylphenol with allyl bromide (28 g., 0.23 mole) in 80 ml. of ethanol was carried out for 3 hr. under reflux after 40 min. required for the dropwise addition of the bromide, in a procedure which is essentially that of Tarbell and Kincaid.[30] After the extraction of the neutral fraction with Claisen alkali[5] it was distilled at 45–46° (0.2 mm.) to yield 17.2 g. (53%) of ether II, $n^{23}\text{D}$ 1.5051. Examination of the ultraviolet spectrum of this fraction indicated that it contained about 0.2% of dienone as shown by an absorbancy of 0.08 at 303 mμ of a 0.001 *M* solution in cyclohexane where ϵ for the pure ether II is less than 5. However, most of the dienone I should have rearranged[5] under the reaction conditions. A second fraction (2.0 g.), b.p. 72–73° (0.2 mm.), $n^{23}\text{D}$ 1.5134, was apparently diallyl product formed by a second allylation of the 4-allyl-2,6-dimethylphenol from the rearrangement of the dienone I.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.1; H, 9.0. Found: C, 83.1; H, 9.0.

The phenolic fraction (2.3 g.) separated with Claisen alkali as described above was shown by infrared examination to contain approximately 55% of 4-allyl-2,6-dimethylphenol, very probably formed by rearrangement of the dienone I, and 45% of unreacted 2,6-dimethylphenol.

When the lithium rather than the sodium salt of 2,6-dimethylphenol was employed under the conditions described above, the % conversion was lower (30% of ether II was obtained), but no dienone nor products resulting from its rearrangement were detected.

Alkylation of Sodium 2,6-Dimethylphenoxide in Benzene. 6-Benzyl-2,6-dimethyl-2,4-cyclohexadienone (III) and Dimer V.—The sodium salt (0.025 mole) was prepared in 60 ml. of benzene by the reaction of 3.05 g. of the phenol I with 580 mg. of sodium. After the addition of benzyl bromide (9 ml., 0.075 mole) the mixture was heated for 6 hr. under reflux. Separation of the phenolic products from the neutral fraction was achieved by extraction with Claisen alkali (350 g. of potassium hydroxide in 250 ml. of water/l. of solution in methanol) after the addition of 60 ml. of petroleum ether. Comparison of the infrared and ultraviolet spectra of the neutral fraction in cyclohexane with those of purified samples below indicated that it contained 900 mg. (17%) of benzyl 2,6-dimethylphenyl ether (IV) (as shown by absorption at 1096 and 1204 cm.$^{-1}$) and 1.8 g. (34%) of the dienone III (as shown by the absorption at 306 mμ in the ultraviolet).

The neutral fraction partially crystallized after several hours. Separation of the crystals and recrystallization from ethanol yielded *dimer V*, m.p. 172°, of dienone III. The infrared spectrum of the dimer (10% solution in chloroform in 0.1-mm. cell) showed strong absorption bands of nearly equal intensity at 1678 and 1716 cm.$^{-1}$. The ultraviolet spectrum in ethanol showed a maximum at 235 mμ, ϵ 7.5 × 10^3.

Anal. Calcd. for $C_{30}H_{32}O_2$: C, 84.9; H, 7.6. Found: C, 84.83; H, 7.59.

2,6-Dimethyl-6-benzyl-2,4-cyclohexadienone (III) was best prepared free from the benzyl ether IV by decomposition of the dimer V by heating it to its m.p. and then dis-

---

(39) To illustrate it can be considered that only ion pairs and dissociated ions are involved so that the rate of formation of dienone, dD/dt, and ether, dE/dt, are $dD/dt = k_D(\text{ArO}^-\text{Na}^+)(\text{RX})$ and $dE/dt = k_E(\text{ArO}^-)(\text{RX})$; $(\text{ArO}^-)(\text{Na}^+)/(\text{ArO}^-\text{Na}^+) = K$. It follows then that $dD/dE = k_D(\text{Na}^+)/k_EK$. If, as has been discussed previously, (Na^+) is approximately constant during a reaction, this expression may be integrated to give $(D)/(E) = k_D(\text{Na}^+)/k_EK$ = dienone/ether ratio measured. If each of the rate and equilibrium constants in this expression obeys the Hammett equation,[40] $\log k = \log k_0 + \sigma\rho$, the logarithm of the dienone/ether ratio, $\log R$ is given by $\log R = \sigma(\rho_D - \rho_E - \rho) - \log(\text{Na}^+)$. Since $\log(\text{Na}^+)$ is independent of the substituent to a first approximation (all starting concentrations were identical) the linear relationship follows.

(40) L. P. Hammett, "Physical Organic Chemistry," McGraw Hill Book Co., Inc., New York, N. Y., 1940, p. 184.

(41) See ref. 24, pp. 381ff.

(42) S. Winstein, *et al.*, THIS JOURNAL, (a) **73**, 1458 (1951); (b) **74**, 2165 (1952); (c) **74**, 2171 (1952).

(43) See, for example, E. R. Alexander and R. W. Kluiber, *ibid.*, **73**, 4304 (1951).

(44) All melting points are corrected. Microanalyses were carried out by Mr. J. Nemeth, Mrs. K. Pih, Mrs. L. Chang, Mrs. E. Fett, Mr. R. N. Benassi, Miss C. Higham and Mrs. M. Stingl. Some of the ultraviolet spectra were determined by Miss Gerardine Meerman with a Cary model 11 spectrophotometer, the remainder were determined with a Cary model 14 M spectrophotometer using 1-cm. cells. The infrared spectra were determined with a Perkin-Elmer model 21 spectrophotometer by Mr. James Brader, Mrs. Louise Griffing and Mr. Brian Cloonan.

tilling at 102° (0.2 mm.). The ultraviolet spectrum[45] of the best sample in cyclohexane had $\lambda_{\max}$ 306 mμ, ϵ 5.2×10^3.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.9; H, 7.6. Found: C, 84.8; H, 7.9.

Benzyl 2,6-Dimethylphenyl Ether (IV). Alkylation of Sodium 2,6-Dimethylphenoxide in Tetrahydrofuran.—The alkylation was carried out at 18° for 44 hr. with sodium salt prepared from 580 mg. (0.025 mole) of sodium and 3.05 g. (0.025 mole) of 2,6-dimethylphenol in 60 ml. of tetrahydrofuran and 9 ml. (0.075 mole) of benzyl chloride. The neutral fraction (9.83 g.) isolated as previously described was a light yellow oil. The intensity of the ultraviolet absorption in cyclohexane at 306 mμ indicated the presence of a concentration of 0.3% of dienone III. The yield of dienone was thus 30 mg. (0.5%). The infrared spectrum (intensity of 1206 cm.$^{-1}$ band) indicated the presence of 26% of the benzyl ether IV in the neutral fraction or a yield of 2.53 g. (48%). The recovered 2,6-dimethylphenol amounted to only 1.7 g.

Distillation of the neutral fraction in a Holzman column gave unreacted benzyl chloride, b.p. 85–95° (22 mm.), together with 1.7 g. of **benzyl 2,6-dimethylphenyl ether** (IV), b.p. 115–116° (0.3 mm.). The infrared spectrum in chloroform showed moderate to strong bands in the fingerprint region at 1268, 1203, 1097, 1025, 1003, 796, 753, 701 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.9; H, 7.6. Found: C, 84.7; H, 7.7.

6-Allyl-2,4,6-trimethyl-2,4-cyclohexadienone (VI).—2,4,6-Trimethylphenol (6.8 g., 0.050 mole) was converted to the dienone by conversion to the sodium salt and treatment with allyl bromide (10 ml., 0.19 mole) in benzene following the procedure used for the allyldienone I. The dienone VI was obtained as a yellow oil, n^{25}D 1.5050, $\lambda_{\max}$ 312 mμ, ϵ 4700 (reported[38] $\lambda_{\max}$ (ethanol) 318 mμ, ϵ 3800).

The infrared spectrum of a 10% solution in cyclohexane showed strong carbonyl and olefin absorption at 1668(sh) and 1652 cm.$^{-1}$. The infrared spectrum of the dienone even before distillation showed small absorption at 856, 1152 and 1220 cm.$^{-1}$, frequencies which are characteristic of the allyl ether. From the 855-cm.$^{-1}$ band it is estimated that a maximum of 20% of the allyl ether could be present. This, together with a comparison of the value (4700) of the ϵ of the ultraviolet absorption maximum with that (5100) of the purest sample of the benzyl dienone, indicated that there was contamination of the dienone by an appreciable amount (at least 8–10%) of the allyl ether. Upon distillation under reduced pressure the ultraviolet spectrum indicated that some rearrangement had occurred ($\lambda_{\max}$ 312, ϵ 3600). There was also evidence in the ultraviolet spectrum (shoulder at 244 mμ) of the distillate of the presence of 4-allyl-2,4,6-trimethyl-2,5-cyclohexadienone. (There was a minimum at 244 mμ in the spectrum of the undistilled material.)

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.8; H, 9.2. Found: C, 81.4; H, 8.8.

Allyl 2,4,6-trimethylphenyl ether was obtained by the alkylation of lithium 2,4,6-trimethylphenoxide in ethanol with allyl bromide. An infrared spectrum in cyclohexane (10% solution) showed strong bands at 1220, 1152, 927 and 856 cm.$^{-1}$. The absorption at 1650 cm.$^{-1}$ when compared with the spectrum of the dienone VI indicated the presence of a small amount (<4%) of dienone.

Allyl 4-bromo-2,6-dimethylphenyl ether (VII) was prepared from the reaction of the lithium salt of 4-bromo-2,6-dimethylphenol, m.p. 78.5–80° (lit.[46] 79°), prepared in 100 ml. of ethanol from 0.21 g. of lithium wire and 6.0 g. (0.03 mole) of the phenol with 10 ml. of allyl bromide. Extraction with Claisen alkali and distillation gave 3.2 g. (40%) of ether VII, b.p. 83° (0.50 mm.), n^{25}D 1.5408. The infrared spectrum (10% solution in cyclohexane) showed strong absorption at 1208, 1005(sh), 993, 930(sh) and 927 cm.$^{-1}$. The small absorption at 1650 cm.$^{-1}$ indicated that less than 5% of dienone was present.

Attempted Preparation of 6-Allyl-4-bromo-2,6-dimethyl-2,4-cyclohexadienone (VIII).—When the sodium salt of 4-bromo-2,6-dimethylphenol (8.8 g.) was stirred for 44 hours at room temperature with 10 ml. (0.19 mole) of allyl bromide and the neutral isolated by extraction of the phenolic fraction with Claisen alkali, a liquid was obtained which decomposed upon attempted distillation to a solid, m.p. 170–172° after recrystallization from hexane. This solid showed no carbonyl frequency in the infrared spectrum. When the experiment was repeated with the addition of 3.0 g. of allyl 4-bromo-2,6-dimethylphenyl ether as a carrier, distillation gave 3.5 g. of a mixture, b. p. 65° (0.10 mm.), n^{25}D 1.5399. The infrared spectrum in chloroform showed absorption at 1660 cm.$^{-1}$ attributable to the presence of dienone.

Determination of Dienone/Ether Ratios in Various Solvents. Procedure A.—Sodium metal (2.3 g., 0.10 g.-atom) was placed in 200 ml. of Merck or Mallinckrodt "anhydrous" diethyl ether in a nitrogen atmosphere. 2,6-Dimethylphenol (12.2 g.) or its 4-substituted derivative (0.10 mole) in 50 ml. of ether was added slowly with continuous stirring and the mixture heated for 1 hr. upon completion of the addition. The solution was then cooled to 15° and 20 ml. of allyl bromide added after which it was stirred for 44 hr. at 17°. The reaction mixture was then poured into an equal volume of 1 *N* hydrochloric acid and 100 ml. of petroleum ether was added. Extraction with two 150-ml. portions of Claisen alkali, a wash with water, drying over sodium sulfate and distillation under reduced pressure through a Holzman column gave the neutral fraction [b.p. 34–36° (0.02 mm.)] which was then submitted to infrared and ultraviolet examination. In general the amount of ether was estimated from the intensity of the absorption at 1098 cm.$^{-1}$ characteristic of the ether but absent in the dienone spectrum (corresponding maxima were employed with 2,4,6-trimethylphenol products). The amount of dienone was estimated from the ultraviolet spectrum in cyclohexane using the dienone maximum in the 300 mμ region where the absorption of the corresponding ether is negligible.

Reactions in which the effect of dilution was studied were carried out in the same way except for the amount of ether used as solvent.

The reaction with 4-bromo-2,6-dimethylphenol yielded 6.5 g. of yellow oil, b.p. 65° (0.10 mm.), n^{25}D 1.5395.

Anal. Calcd. for $C_{11}H_{13}BrO$: C, 54.8; H, 5.4. Found: C, 55.4; H, 5.4.

The infrared spectrum of a 10% solution of this mixture in cyclohexane was compared with a corresponding solution of the ether VII. Using the intensities of the maxima at 1120 and 1274 cm.$^{-1}$ it was estimated that the product contained 77% of the allyl ether VII. Although the dienone could not be isolated, it was noted that the absorption intensity of the maximum at 1675 cm.$^{-1}$ of the product in a 10% solution was comparable to that of a 2% solution of the other dienones obtained in this work and the dienone/ether ratio has thus been estimated as 20/80.

Procedure B differed in that the product, after removal of the acidic fraction with Claisen alkali and of the solvent under vacuum at room temperature, was not distilled but was submitted directly to infrared and ultraviolet spectral examination.

Spectra of Lithium and Sodium 2,6-Dimethylphenoxide.—The salts were prepared in ether directly from the alkali metal and the phenol. The spectrum of the phenol in ether showed $\lambda_{\max}$ at 272.5, 278 (doublet) with ϵ 1610. The sodium salt had $\lambda_{\max}$ 298, ϵ 1000.

URBANA, ILLINOIS

---

(45) H. Conroy and R. A. Firestone [THIS JOURNAL, **78**, 2290 (1956)] have reported a maximum (solvent 95% ethanol) at 312 mμ, log ϵ 3.48 (ϵ 3020), for the analogous 6-propyl-2,6-dimethyl-2,4-cyclohexadienone. The corresponding allyldienone I has $\lambda_{\max}$ at 309 mμ in ethanol, but at 303 mμ in cyclohexane.

(46) G. Lockemann and T. Kunzmann, *Z. angew. Chem.*, **46**, 296 (1933).