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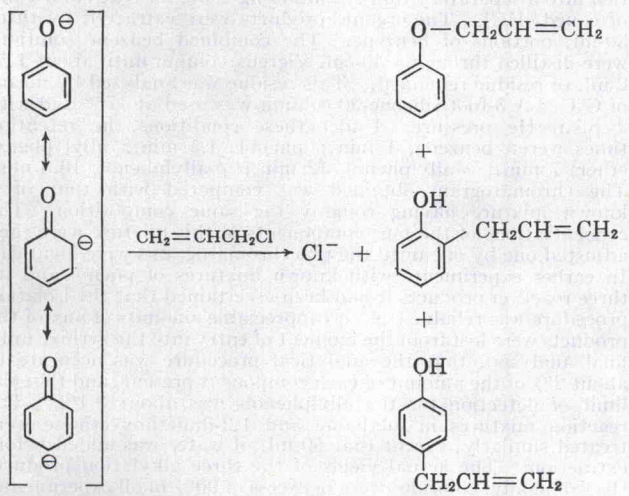
The Effect of Pressure on the Homogeneous Alkylation of Phenoxide Ion

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The homogeneous reaction of phenoxide ion with allyl chloride in the solvents water, methanol and 1,2-dimethoxyethane has been studied in the pressure range 1–7000 atm. In water, the yield of *p*-allylphenol increases at the expense of allyl phenyl ether as the pressure is increased. In methanol, C-alkylation is observed at high pressure but not at 1 atm. In 1,2-dimethoxyethane, only O-alkylation is observed in the entire range of pressures studied. These results are consistent with Kornblum's hypothesis regarding the solvent effect in this reaction, and furthermore suggest that the *o*- to *p*-ratio is similarly affected. The differences in molar volume between the three transition states were calculated.

The homogeneous reaction of allyl chloride with sodium phenoxide in most organic solvents gives excellent yields of allyl phenyl ether; in fact, usually no other alkylation products can be found.[1] Recently, however, it has been reported[2] that in certain solvents considerable amounts of *o*- and *p*-allylphenols are also obtained.



O-Alkylation alone was found to take place in ethers, unsubstituted aliphatic alcohols and N,N-dimethylformamide; C-alkylation occurs to the extent of 40–75% in water, phenol and fluorinated alcohols. On the basis of this solvent effect and of kinetic studies Kornblum concluded that O-alkylation of the phenoxide ion takes place exclusively unless the reaction occurs in a solvent highly effective as a proton donor in hydrogen bonding. It appears that the oxygen atom, where the charge is largely concentrated, is intensely solvated in such solvents, and that this solvation sphere hinders the approach of the alkylating agent to that position, but not to the *o*- and *p*-carbon atoms. An alternative way to state this explanation is to say that of the three transition states the one leading to O-alkylation is favored in a non-polar solvent since the oxygen atom carries most of the charge, but those leading to ring alkylation are favored in an effectively solvating medium because they require the least interference with solvation.

One question invited by this interpretation is concerned with the fact that no C-alkylation is observed at all when unsubstituted aliphatic alcohols are used, since these solvents are also capable of H-bonding. Apparently these hydrogen bonds are much less effective. There appears to be some evidence for this. If the acid strengths may be regarded as a rough measure of H-bonding ability, the following correlation is found to exist: phenol, pK_a 9.9, 75% C-alkylation; 2,2,3,3-tetrafluoropropanol, pK_a[3] 11.3, 50% C-alkylation; methanol, pK_a[3] 15.9, 0% C-alkylation. On this basis, however, it is surprising that water (pK_a 15.7) is so effective in promoting C-alkylation (45%). Perhaps water, with its ability to form two H-bonds, allows the formation of an extensive (rather than a tightly bound) solvation sphere, thus interfering with the approach to the oxygen atom of phenoxide ion. A second question concerns the ratio of *o*- to *p*-alkylation; the greater proximity of the *o*-carbon atom to the solvated oxygen might be expected to affect that ratio also.

One of the methods available for approaching problems of this type is a study of the effect of hydrostatic pressure. It is known that immersion of an ion in a dielectric causes a decrease in the total volume (electrostriction).[4] The solvent near the ion becomes oriented and compressed into a smaller volume. Conversely, the application of pressure always enhances solvation. If therefore the interpretation quoted above for the solvent effect is correct, it should be expected that C-alkylation will be increased in effective H-bonding solvents if pressure is applied. Similarly, some C-alkylation might be observed in an ineffectively H-bonding solvent such as methanol under pressure, but not in a non-protonic solvent such as 1,2-dimethoxyethane. Finally, if the solvation sphere is large enough, the *o*- to *p*-ratio will be observed to diminish as the pressure is increased. To test these predictions the product distribution in this reaction was measured in several solvents as a function of the external pressure.

(1) D. S. Tarbell, Vol. II of R. Adams, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 22.

(2) N. Kornblum, P. J. Berrigan and W. J. le Noble, *J. Am. Chem. Soc.*, **82**, 1257 (1960). Similar results have been obtained by R. Barner and H. Schmid, *Helv. Chim. Acta*, **43**, 1393 (1960).

(3) P. B. Allinger and F. A. Long, *J. Am. Chem. Soc.*, **82**, 795 (1960).

(4) S. D. Hamann, "Physico-chemical Effects of Pressure," Academic Press, Inc., New York, N. Y., 1957, Chap. IX.

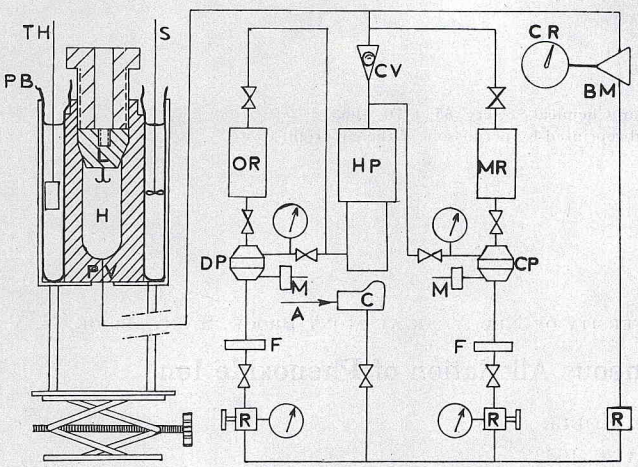


Fig. 1.—Schematic drawing of high pressure equipment: A, air inlet; BM, bulk modulus cell; C, air compressor; CP, charge pump; CR, recorder; CV, check valve; DP, drive pump; F, air filter; H, high pressure cavity; HP, hydraulic press; L, closure; M, muffler; MR, methanol reservoir; OR, oil reservoir; PB, polyethylene lining; PV, pressure vessel; R, air pressure regulator; S, stirrer; TH, thermoregulator and heater.

Experimental

Materials.—Allyl chloride, methanol and 1,2-dimethoxyethane were purified by fractional distillation, the latter from lithium aluminum hydride. The preparation of sodium phenoxide has been described.[5] Allyl phenyl ether, *o*-allylphenol and *p*-allylphenol were prepared by the reaction of allyl chloride on sodium phenoxide in water, run on a one-mole scale. After several days at room temperature, the mixture was neutralized with dilute HCl and extracted several times with benzene. The combined benzene solutions were evaporated to a small volume and subsequently fractionated under vacuum. The three products so obtained were shown to be pure by G.C. analysis; allyl phenyl ether, $n^{25}D$ 1.5194; *o*-allylphenol, $n^{25}D$ 1.5428; *p*-allylphenol, $n^{25}D$ 1.5422.

Apparatus.—The pressure vessel, constructed by the Harwood Engineering Co., has a cylindrical working space of 8 in. height and 1 in. diameter. The closure is of the Bridgman type; a rubber O-ring serves as packing. The pressure in cavity H (see Fig. 1) is built up in two stages. The charge pump, a pneumatically operated Sprague pump, brings the pressure up to about 1000 atm. and simultaneously pushes the floating piston in the hydraulic press down to its lowest position. The drive pump forces the piston (area ratio is 16:1) up in the next step to bring about a further pressure increase up to 14000 atm. The operation of the bulk modulus cell has been described by Newhall and Abbot[6]; this method of pressure measurement has a precision of 1%. The transmission fluid is methanol with 3% Immunol 517 rust inhibitor. The pressure vessel is thermostated at 30.0°. It was found that the heat of compression (which brings about a temperature rise of about 15° at the highest pressures used) was completely dissipated in 10 minutes; in these experiments no correction was necessary on this account.

Since liquids under the pressures used are compressed to a considerable degree (the density of methanol for instance increases by more than 20% between 1 and 7000 atm.[7]), it is necessary to use containers of variable capacity. Hypodermic syringes with sealed needles and plungers open to transmission fluid (see Fig. 2, type A) were used; Teflon tubing and stoppers (B), stainless steel bellows (C), an all-glass vessel using mercury to separate the reaction mixture from the transmission fluid (D) and a glass and rubber tube using mercury to avoid contact between the reaction mixture and the rubber tubing (E) all have been found to be useful. In all cases the container is wrapped in a rubber sack to protect the high pressure vessel from the reaction mixture and mercury in case of leaks or breakage; the whole assembly is suspended from the closure.

Alkylation and Analysis.—A sample of 0.56 g. (6 mmoles) of phenol was dissolved in 1.00 ml. of 3.00 *F* NaOH.[8] To this solution was added 30 ml. of water saturated at 0° with allyl chloride. The mixture was introduced into a hypodermic syringe, after which the needle was replaced by a solid seal. The piston of the syringe was filled with pressure transmission fluid. The syringe was attached to the closure, which was then put in place in the vessel. During compression the temperature rose as much as 10°; however, heat exchange with the pre-cooled reaction mixture was found to be rapid, and within 10 minutes the temperature reached equilibrium. The reaction was then allowed 48 hours to go to completion. When methanol or 1,2-dimethoxyethane were used as solvent, the mixture consisted of 0.5 g. of allyl chloride, 0.84 g. of phenol and 1.1 g. of sodium phenoxide.

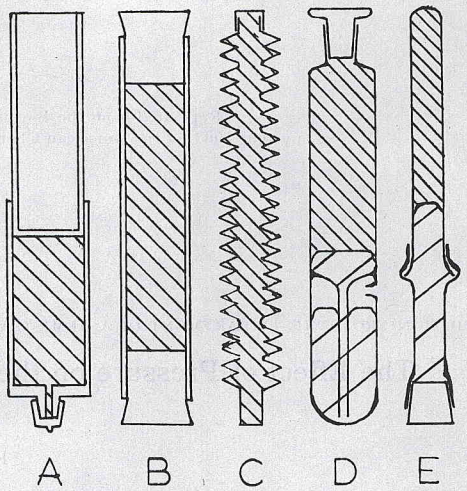


Fig. 2.—Reaction vessels of variable capacity. The lightly shaded areas show mercury.

After decompression and disassembly, the syringe was emptied into a separatory funnel containing 1–3 g. of NaCl and 1 ml. of concd. HCl. The organic products were extracted by three 30-ml. portions of benzene. The combined benzene solutions were distilled through a 30-cm. Vigreux column until about 1.5–2 ml. of residue remained. This residue was analyzed by means of G.C. A 3-foot silicone-90 column was used at 175° and with 2 p.s.i. He pressure. Under these conditions the retention times were: benzene, 1 min.; phenol, 4.5 min.; allyl phenyl ether, 7 min.; *o*-allylphenol, 12 min.; *p*-allylphenol, 16.5 min. The chromatogram obtained was compared with that of a known mixture having roughly the same composition. The concentrations of the four components of this mixture were then adjusted one by one until the two chromatograms were identical. In earlier experiments with known mixtures of phenol and its three reaction products it had been ascertained that the isolation procedure was reliable (*i.e.*, no appreciable amounts of any of the products were lost from the moment of entry into the syringe until final analysis), that the analytical procedure was accurate to about 2% of the amount of each component present, and that the limit of detection for the allylphenols was about 0.1%. The reaction mixtures in methanol and 1,2-dimethoxyethane were treated similarly, except that 50 ml. of water was added before extraction. The actual yields of the three alkylation products (based on allyl chloride) were in excess of 90% in all experiments. The yields were roughly estimated from the solubility of allyl chloride in water at 0° (4.2 g./l.) and from a comparison of the volumes of the solution to be analyzed and of a known mixture having the identical chromatogram. In some experiments very minor amounts (~1%) of two dialkylation products were observed.

Results and Discussion

It is clear from the results of these experiments, shown in Table I, that the application of pressure results in increased C-alkylation in water. Whereas at atmospheric pressure the ratio of O- to C-alkylated products is about 1.5, at 7000 atm. it is roughly 0.7. This result is clearly in accord with the suggestion that solvation of the oxygen atom is responsible for attack at the *o*- and *p*-positions.[9] This is further borne out by the

(5) N. Kornblum and A. P. Lurie, *J. Am. Chem. Soc.*, **81**, 2705 (1959).

(6) D. H. Newhall and L. H. Abbot, *Chem. Eng. Progr.*, **56**, 112 (1960).

(7) P. W. Bridgman, "The Physics of High Pressures," 2nd Ed., G. Bell and Sons, London, 1948, Chap. V.

(8) An excess of phenol was used to suppress equilibrium formation of allyl phenoxides and thus secondary alkylation of the product allylphenols. It was ascertained that phenol itself was not alkylated under any of the conditions used.

(9) In a recent paper (S. W. Benson and J. A. Berson, *J. Am. Chem. Soc.*, **84**, 152 (1962)) it has been pointed out that the $\Delta V^{\ddagger}$ term may include significant contributions from changes in activity coefficients with pressure and from changes in the dielectric constant of the solvent. The former term has been neglected here since it does not seem likely that the activity coefficients of the three transition states are very different; the latter has not been considered since it predicts a *decrease* in C-alkylation at increasing pressure (N. Kornblum, R. Seltzer and P. Haberfield, *ibid.*, **85**, 1148 (1963)).

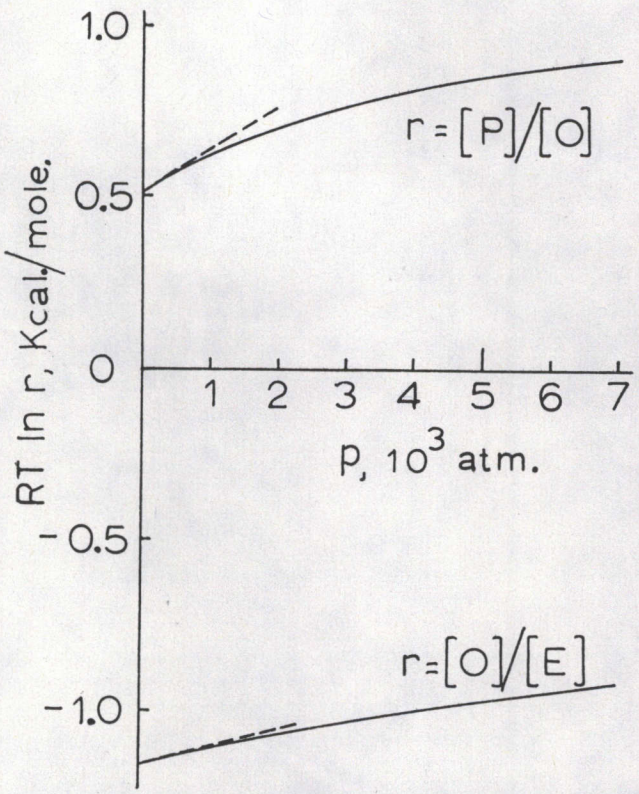


Fig. 3.—Effect of pressure on the product ratio in the reaction of allyl chloride with sodium phenoxide in water at 30.0°. The curves are based on smoothed data shown in Table I.

fact that pressure causes moderate C-alkylation in methanol, but not in 1,2-dimethoxyethane.

The data furthermore suggest that the *o*-positions are also affected by the solvation sphere; the decrease of reaction at the site of the O-atom increases only the amount of *p*-allylphenol formed. It should be noted also that *o*-allylphenol is the main ring-substituted product at 5500 atm. in methanol, conditions under which the combination of solvent and pressure effects is just beginning to lead to C-alkylation.

The data obtained for the reaction in water permit a rough calculation of the differences in molar volume between the three transition states in this solvent. The effect of pressure on a rate constant is governed by the approximate expression $(\partial \ln k/\partial p)_T = -\Delta V^{\ddagger}/RT$. The term $\Delta V^{\ddagger}$, known as the activation volume, is the difference in molar volume between the transition state and the reactant or reactants. The individual

TABLE I

ALKYLATION OF SODIUM PHENOXIDE WITH ALLYL CHLORIDE; PRODUCT DISTRIBUTION AS A FUNCTION OF PRESSURE AT 30.0°

Solvent	p in atm.	Allyl phenyl ether, %	*o*-Allylphenol, %	*p*-Allylphenol, %
Water	1	62	17.5	20.5
Water	1	63	16	21
Water	800	55	20.5	24.5
Water	1000	57	19	24
Water	2700	52	18.5	29.5
Water	2700	49	20.5	30.5
Water	4000	50	16.5	33.5
Water	4500	46	17.5	36.5
Water	5600	42.5	18	39.5
Water	6100	41.5	18.5	40.5
Water	7000	41	17.5	41.5
Water	7000	42	17.5	40.5
1,2-Dimethoxy-	1	100	0	0
ethane	5500	100	0	0
Methanol	1	100	0.4	<0.1
Methanol	5500	92	5.1	2.9

rate constants for the three reactions were not determined. However, since the reactants are the same in each case, and if the reasonable assumption[2] is made that the three reactions obey rate laws differing only in the magnitude of the rate constants, it can readily be shown for instance that $\partial \ln (^1/_2[O]/[E])/\partial p = (V_O^{\ddagger} - V_E^{\ddagger})/RT$, where O denotes *o*-allylphenol and E denotes allyl phenyl ether.[10] In a plot of $RT \ln (^1/_2[O]/[E])$ *vs.* p the slope should thus be equal to $V_O^{\ddagger} - V_E^{\ddagger}$ (see Fig. 3). The curvature evident in the graphs is usually observed in such plots; the reason for this is that the transition states may and usually do have different compressibilities. The curves show that at zero pressure $V_E^{\ddagger} - V_O^{\ddagger} \approx +2.2$ ml. and $V_O^{\ddagger} - V_P^{\ddagger} \approx +5.4$ ml., so that $V_E^{\ddagger} - V_P^{\ddagger} \approx 7.6$ ml. These differences do not reside in the phenoxide–allyl chloride complexes themselves, but rather in the solvent around them. Thus, formation of a transition state leading to the allyl phenyl ether requires moderately greater reorganization and expansion of the solvent than does the activated complex preceding the formation of an *o*-allylphenol molecule, and much greater expansion of solvent than the formation of *p*-allylphenol.

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(10) The factor $^1/_2$ appearing in this expression is a correction for the fact that there are two *o*-positions.