

CHEMISTRY OF "NAKED" ANIONS II. REACTIONS OF THE
18-CROWN-6 COMPLEX OF POTASSIUM ACETATE WITH ORGANIC SUBSTRATES IN APROTIC ORGANIC SOLVENTS.^{1,2}

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The poor nucleophilicity of acetate ion toward various substrates in condensed systems has been attributed to a combination of polarizability, basicity and solvation factors.^{3,4} We wish to report that acetate solubilized as the potassium salt in acetonitrile or benzene containing 1,4,7,10, 13, 16-hexaoxacyclooctadecane (18-crown-6)^{5,6} becomes sufficiently nucleophilic to react smoothly and quantitatively, even at room temperature, with a wide variety of organic substrates. Displacement reactions at 1°, 2°, 3° and benzylic positions along with competing elimination processes are demonstrated with this reagent which we have termed "naked" acetate. The data summarized in Table I deal specifically with the solvent acetonitrile. Benzene solvent behaves similarly only reactions are slower. In the absence of crown, little or no reaction takes place under identical conditions covering the same periods of time. For instance, in the case of benzyl bromide, the most reactive substrate reported in this communication, less than 5% benzyl acetate is formed after several days with potassium acetate in the absence of crown whereas the conversion is complete within two hours in the presence of crown.

The acetate reagent is prepared by dissolving 18-crown-6 in dry acetonitrile or dry benzene and then simply adding dry potassium acetate. After the heterogeneous system is stirred for 30 minutes, the organic substrate is added and the resulting mixture stirred until reaction is complete. In all cases, the crown is present in catalytic concentrations indicating that the reactions shown in Table I are examples of phase transfer catalysis between solids and liquid phases.⁷

The products of reaction are primarily acetates. Small amounts of alkene products are sometimes observed. Highly activated bromides, such as benzyl bromide, react rapidly with "naked" acetate at room temperature to produce benzyl acetate. Primary alkyl halides require several days at ambient temperatures to reach completion. The rate, however, is substantially increased at reflux temperatures (ca. 83°C). Interestingly, virtually no alkene product can be detected by g.l.c. or nmr techniques in these reactions. In order to determine the approximate relative rates of re-

action for primary bromides, tosylates and chlorides, 1-substituted hexanes were reacted with "naked" acetate in acetonitrile at 25°C. The rates of reaction were in the order Br>OTs>Cl (ca.4:2:1) suggesting that alkyl bromides are the best substrates for synthetic purposes. 2-Bromooctane produces the corresponding acetate in approximately 20 hours at reflux temperatures with formation of ca. 10-15% alkene products. Reaction of "naked" acetate with ethylene bromide may be conducted to yield either ethylene diacetate or predominantly 2-bromoethyl acetate depending upon which reagent is present in excess. Reaction of 2-chloro-2-methylcyclohexanone with "naked" acetate in acetonitrile at reflux yields a mixture of acetates with only 10% 2-methylcyclohexanone. The results reported here are in direct contrast to those obtained in the reaction of "naked" fluoride with 1°, 2°, and 3° halides in that the fluoride reagent produced much larger quantities of alkene products.^{1,2} This suggests that "naked" fluoride is a stronger base than "naked" acetate.

The concentration of "naked" acetate in solutions at 25° has been determined from nmr analysis as a function of crown concentration. The protons of the 18-crown-6 and the acetate appear as singlets which may be easily integrated. The results in benzene and acetonitrile-d₃ are shown in Table II.⁸ It is clear that high concentrations of acetate may be achieved in these solvents and that at least 80% of the crown is complexed with potassium acetate. The nature of the species in solution is presently being explored by means of conductance experiments.

In conclusion, it has been shown (1) that high concentration of potassium acetate may be achieved in benzene and acetonitrile containing 18-crown-6, (2) that solubilized acetate ("naked acetate") is a powerful nucleophile but a rather weak base and (3) that "naked" acetate is an excellent reagent for preparing organic acetates in high yield.

Table I

Substrate	Products	Concentrations (M)		Temp °C	Time (hrs)
		crowne	substrate		
Benzyl bromide	Benzyl acetate (100%)	0.16	3.4	25°	2
$n\text{-C}_6\text{H}_{13}\text{Br}$	$n\text{-C}_6\text{H}_{13}\text{OAC}$ (100%)	0.10	1.4	25°	150
$n\text{-C}_8\text{H}_{17}\text{Br}$	$n\text{-C}_8\text{H}_{17}\text{OAC}$ (96%)	0.10	1.4	83°	3
1,2-Dibromoethane	Ethylene diacetate (90%)	0.09	1.3	83°	3
1,2-Dibromoethane	Ethylene diacetate (23%) 2-Bromoethyl acetate (77%)	0.06	1.9	83°	3
2-Bromooctane	2-Acetoxyoctane (ca. 90%) Octenes (ca. 10%)	0.10	1.4	83°	20
2-Chloro-2-methyl-cyclohexanone ^c	2-methylcyclohexanone (ca. 10%) cis-2-acetoxy-6-methyl-cyclohexanone (ca. 54%) trans-2-acetoxy-6-methyl-cyclohexanone (ca. 10%) 2-acetoxy-2-methyl-cyclohexanone (ca. 25%)	0.15	2.9	83°	1

^aAll reactions were run using at least a two-fold excess of potassium acetate.

^bAll products show ir, nmr and mass spectra consistent with the proposed structure.

^cEquimolar quantities of 1,2-dibromoethane and potassium acetate were used in this experiment.

^dThe product acetates were assigned structures based upon evidence from a known mixture prepared by the method of H. O. House and F. A. Richey, *J. Org. Chem.*, **34**, (5), 1430 (1969).

Table II

Solubility of Potassium Acetate in Acetonitrile and Benzene Solutions Containing 18-Crown-6

<u>Benzene</u>	
Crown (M)	Potassium Acetate (M)
0.55	0.4
1.0	0.8
<u>Acetonitrile-d₃</u>	
0.14	0.1

References

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- (2) Part I: C. L. Liotta and H. P. Harris, J. Amer. Chem. Soc., 95, (1974).
- (3) C. G. Swain and C. B. Scott, ibid., 75, 141 (1953).
- (4) J. O. Edwards and R. G. Pearson, ibid., 84, 16 (1962).
- (5) For excellent reviews concerning crown ethers see: (a) C. J. Pedersen, J. Amer. Chem., 89, 7017 (1967); 92, 391 (1970); Fed. Proc. Fed. Amer. Soc. Exp. Biol., 27, 1305 (1968); C. J. Pedersen and H. K. Frensdorff, Angew. Chem., Int. Ed. Engl., 84, 16 (1972); J. J. Christensen, J. O. Hill and R. M. Izatt, Science, 174, 459 (1971); D. J. Sam and H. E. Simmons, J. Amer. Chem. Soc., 94, 4024 (1972).
- (6) 18-Crown-6 can be prepared according to the procedure of R. N. Greene, Tetrahedron Letters, 1793 (1972) or by the procedure of G. W. Gokel and D. J. Cram, Department of Chemistry, University of California at Los Angeles, private communication.
- (7) J. Dockx, Synthesis, #8, 441 (1973).
- (8) The solubility of potassium acetate in pure acetonitrile has been found to be 5×10^{-4} moles/liter at 25° as determined from flame photometry. The solubility of potassium acetate in pure benzene is undetectable.