canula over 5 min, and the resulting cuprate reagent was stirred at -70 °C for 30 min. A solution of *dl*-4-(*tert*-butyldimethylsiloxy)-2-cyclopentenone (**1**)[18] (1.08 g, 5 mmol) in 3 mL of THF was added over 30 min. After an additional 30 min at -70 °C, HMPA (9.5 mL) in 3 mL of THF was added followed by a solution of triphenyltin chloride (1.94 g, 5 mmol) in 4 mL of THF. Following another 10-min period of stirring at -70 °C, a solution of bromide **14** (5.47 g, 25 mmol) in 2 mL of THF was added. The reaction mixture was then placed in a -22 °C bath for 18 h, after which it was poured in aqueous NH_4Cl. Extraction with ether followed by washing the organic layer with brine, drying over $MgSO_4$, and evaporation gave a product mixture. Chromatography of this mixture on silica gel, eluting with 5-12% ether/hexane mixtures, gave the desired produce **3** (0.796 g, 28%) as a mixture of diastereomers: IR (film) 2930, 2860, 1965, 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.65-5.3 (m, 2 H), 5.2-5.0 (m, 2 H), 4.15-4.0 (m, 2 H), 3.69 and 3.67 (2 s, total 3 H), 2.70-2.55 (m, 2 H), 2.5-2.05 (m, 8 H), 1.5-1.4 (m, 2 H), 1.4-1.2 (m, 6 H), 0.9 (s, 21 H), 0.05 (m, 12 H); HRMS *m/z* calcd for $C_{33}H_{60}O_5Si_2$ (M^+) 592.3979, found 592.3984.

***dl*-4,5-Didehydro and *dl*-15-Epi-4,5-didehydro Prostaglandins E_2 Methyl Esters (4a and 4b).** A solution of bis-silyl ethers **3a** and **3b** (85 mg, 0.143 mmol) in 3 mL of CH_3CN at 0 °C was treated with 0.10 mL of 48% HF. The reaction mixture was stirred 1 h at room temperature and then quenched in aqueous $NaHCO_3$. Extraction with ethyl acetate, drying with $MgSO_4$ and evaporation gave a mixture of **4a** and **4b** which was separated by rotary chromatography on silica gel, eluting with ethyl acetate-/hexane/methanol, 3:7:0.5. Isomer **4b** (11 mg, 21%) eluted first: IR (CCl_4) 2930, 2860, 1960, 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.72-5.62 (m, 1 H), 5.60-5.50 (m, 1 H), 5.18-5.10 (m, 1 H), 5.10-5.00 (m, 1 H), 4.15-4.05 (m, 2 H), 3.677 and 3.672 (2 s, total 3 H), 2.78 (d, J = 6.5 Hz, 1 H), 2.72 (d, J = 7.5 Hz, 1 H), 2.6-2.1 (m, 8 H), 1.65-1.45 (m, 2 H), 1.4-1.25 (m, 6 H), 0.89 (t, J = 6.6 Hz, 3 H); HRMS *m/z* calcd for $C_{21}H_{32}O_5$ (M^+) 364.2249, found 364.2254. Isomer **4a**[6a] (30 mg, 58%) eluted second: IR (CCl_4) 2930, 2860, 1960, 1735 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ 5.8-5.7 (m, 1 H), 5.65-5.55 (m, 1 H), 5.18-5.10 (m, 1 H), 5.10-5.0 (m, 1 H), 4.2-4.1 (m, 2 H), 3.68-3.67 (2 s, total 3 H), 2.83-2.72 (m, 1 H), 2.65-2.50 (m, 1 H), 2.45-2.15 (m, 8 H), 1.60-1.50 (m, 2 H), 1.4-1.25 (m, 6 H), 0.90 (s, J = 6.6 Hz, 3 H); HRMS *m/z* calcd for $C_{21}H_{32}O_5$ (M^+) 364.2249, found 364.2257.

Supplementary Material Available: ^1H and ^{13}C NMR spectra for **3a** + **3b**, **4a,b**, **11**, **13**, and **14** (12 pages). Ordering information is given on any current masthead page.

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(18) Dave, R.; Untch, K. G. *J. Org. Chem.* **1979**, *44*, 3755.

Crown Ethers as a Mechanistic Probe. 2.[1] On the Mechanism of Acetyl Transfer between Phenolates

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Crown ethers exert various effects on organic reactions through complex formation with cations.[2] Upon complexation with a cation, a crown ether increases the effective radius of the cation, reducing the charge density. This would result in the decrease in the electrostatic interaction between the cation and its counteranion. When the cation is present as the countercation for an anionic reactant, complexation of the cation with a crown ether would affect the degree of electrostatic stabilization of the anionic centers of both the transition state and the ground state. Whether the overall rate is enhanced or retarded by the addition of a crown ether, therefore, may provide information on the distribution of negative charge in the transition state relative to the ground state. In the previous study, the inhibitory effects of crown ethers on the reactivity of anionic nucleophiles toward diphenyl *p*-nitrophenyl phosphate were taken to indicate the greater negative charge density in the transition state compared with the ground state.[1]

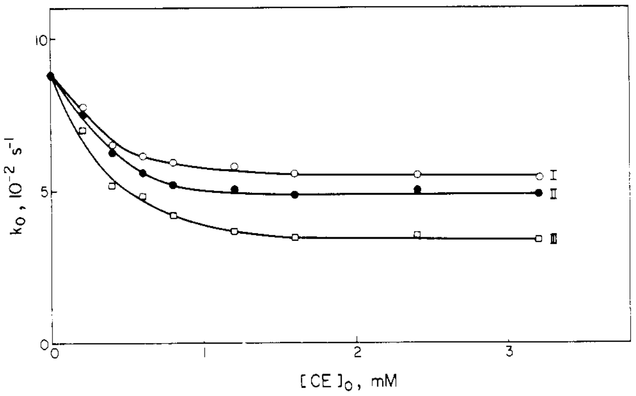
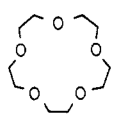
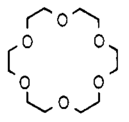


Figure 1. Dependence of k_0 on $[CE]_0$ for the release of *p*-nitrophenol by the reaction of A (1×10^{-5} M) with the sodium salt of B (8×10^{-4} M) in the presence of crown ethers I, II, and III in acetonitrile at 25 °C.

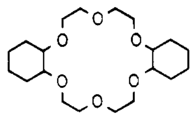
The nucleophilic displacement of carboxyl esters has been dominated by the idea of the addition-elimination mechanism involving tetrahedral intermediates.[3] Recently, however, Williams and co-workers proposed an S_N2-type concerted mechanism for the nucleophilic attack by phenolates on *p*-nitrophenyl acetate.[4] Knowledge of the distribution of negative charge in the transition state of the acetyl transfer reaction relative to that in the ground state might provide clues for the structure of the transition state. Therefore, we examined the effects of 15-crown-5 (I), 18-crown-6 (II), and dicyclohexano-18-crown-6 (III) on the rate of release of *p*-nitrophenol from the reaction of *p*-nitrophenyl acetate (A) with the sodium salt of *m*-methoxyphenolate (B) anion.



I



II



III

Results and Discussion

Pseudo-first-order rate constants (k_0) for the release of *p*-nitrophenol by the reaction of A (initial concentration, 1×10^{-5} M) with the sodium salt of B (initial concentration, 8×10^{-4} M)[5] were measured in the presence or absence of

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(1) Preceding paper in this series: Suh, J.; Mun, B. S. *J. Org. Chem.* **1989**, *54*, 2009.

(2) (a) De Jong, F.; Reinhoudt, D. M. *Adv. Phys. Org. Chem.* **1980**, *17*, 279. (b) Smid, J.; Varma, A. J.; Shar, S. C. *J. Am. Chem. Soc.* **1978**, *100*, 1426. (c) Cook, F. L.; Bowers, C. N.; Liotta, C. L. *J. Org. Chem.* **1974**, *39*, 3416. (d) Suh, J.; Yoon, Y. *Bull. Korean Chem. Soc.* **1985**, *6*, 249. (e) Cram, D. J.; Katz, H. E. *J. Am. Chem. Soc.* **1983**, *105*, 135. (f) Cram, D. J. *Application of Biochemical Systems in Organic Chemistry*; Jones, J. B., Sih, C. J., Perlamn, D., Eds.; Wiley: New York, 1976; Part II, Chapter V.

(3) (a) Capon, B.; Ghosh, A. K.; Grieve, D. M. A. *Acc. Chem. Res.* **1981**, *14*, 306. (b) McClelland, R. A.; Santry, L. J. *Acc. Chem. Res.* **1983**, *16*, 394.

(4) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 6362.

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I-III in acetonitrile at 25 °C. The dependence of k_0 on the initially added concentration ($[CE]_0$) of crown ethers I-III is illustrated in Figure 1. From the curves for the dependence of k_0 on $[CE]_0$, the pseudo-first-order rate constant (k_0^{sp}) observed in the absence of the added crown ethers and the limiting value of the pseudo-first-order rate constant (k_0^{CE}) observed in the presence of a sufficient amount of a crown ether can be estimated.

The data illustrated in Figure 1 indicate that k_0^{CE} is attained when $[CE]_0$ is similar to the concentration of the added sodium salt of B. The data of Figure 1 indicate k_0^{sp} of 8.7×10^{-2} s^{-1} and k_0^{CE} of 5.5×10^{-2} s^{-1} (for I), 4.8×10^{-2} s^{-1} (for II), and 3.3×10^{-2} s^{-1} (for III). Thus, k_0^{CE}/k_0^{sp} is 0.63 for I, 0.55 for II, and 0.38 for III. Crown ethers I-III considerably retard the rate of the reaction of A with B. Furthermore, the inhibitory effect increases in the order of I < II < III. In this sequence, the size of the countercation increases and the corresponding charge density decreases.[1]

If the inhibitory effects of the crown ethers originates mainly from the electrostatic effects, the kinetic data may be taken to suggest that the density of negative charge in the transition state is greater than that in anion B.

Whether the negative charge is more dispersed in the ground state or in the transition state would be correlated with the mechanism of the reaction. Either in the addition–elimination mechanism or in the S_N2-type concerted mechanism, three oxygen atoms are attached to the carbonyl carbon atom of A and bear negative charges in the transition state. In an extreme mechanism, the transition state would resemble the tetrahedral intermediate very closely. In the other extreme case, the transition state might have a "exploded" structure with small bond order between the carbonyl carbon atom and the two phenolate oxygen atoms of both the leaving group and the nucleophile. The exact structure of the rate-determining transition state would depend on the reaction path, which in turn would be governed by several factors including the structures of the ester and the nucleophile. The inhibitory effects of the crown ethers observed in the present study is compatible with the less dispersed negative charge in the transition state compared with the ground state.

In acetonitrile, both anion B and the anionic transition state would be present as aggregates with the countercations. Upon complexation with crown ethers, the countercation becomes bulkier, affecting the relative stability of the ground state and the transition state. The anionic centers in the transition states for both the stepwise and the concerted mechanisms are more crowded than that in B. Thus, an increase in the size of the countercation can retard the reaction regardless of the mechanism, if only the steric effects are considered.

In this regard, however, it is noteworthy that the aliphatic S_N2 reaction between cyanide anion and alkyl halides in acetonitrile is remarkably accelerated by the addition of crown ethers.[2c] In this reaction, the negative charge density is more dispersed in the transition state compared with the ground state,[6] and crown ethers are expected to accelerate the reaction if only electrostatic effects are considered. On the other hand, the anionic center becomes more crowded in the transition state, and crown ethers can retard the reaction on the basis of the steric effects. The electrostatic effects, therefore, predominate over the steric effects in the action of crown ethers on the S_N2 reaction of cyanide ion.

Experimental Section

Compound A was prepared according to the literature,[7] mp 166–167 °C (lit.[7] mp 166–167 °C). Purification of other materials and kinetic measurements were carried out as reported previously.[1]

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Registry No. I, 33100-27-5; II, 17455-13-9; III, 16069-36-6; *p*-nitrophenyl acetate, 830-03-5; sodium of *m*-methoxyphenolate, 51113-99-6.

Supplementary Material Available: Table including the kinetic data (1 page). Ordering information is given on any current masthead page.

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[5] Anionic nucleophile B (8×10^{-4} M) was generated by mixing 1×10^{-3} M *m*-methoxyphenol with 8×10^{-4} M sodium ethoxide.[1]

[6] Jones, R. A. Y. In *Physical and Mechanistic Organic Chemistry*, 2nd ed.; Cambridge University Press: Cambridge, 1984; Chapter 7.

[7] Galatis, L. C. *J. Am. Chem. Soc.* **1947**, *69*, 2062.

Wittig Rearrangement of Aromatic Acetals and Ketals Induced by Reductive Electron Transfer

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The [1,2]-Wittig rearrangement, i.e., the migration of groups from oxygen to carbon in benzyl and related ethers promoted by alkyl- or aryllithium derivatives to afford alkoxides, is well known. Much effort has been devoted to the study of both its mechanistic aspects[1] and synthetic usefulness.[2] It is generally accepted[1-7] that the reaction proceeds through the formation of an intermediate benzylic carbanion, which subsequently rearranges via a nonconcerted radical cleavage–recombination mechanism (Scheme I). This view is supported by the migratory aptitude of substituents R (allyl ≅ benzyl > methyl > ethyl > phenyl), which parallels the order of free radical stabilities,[8,9] and by the fact that optically active precursors usually lead to partial racemization.[1,10] Far less studied is the related rearrangement of aromatic acetals or ketals promoted by electron transfer from alkali metals. To the best of our knowledge, nothing further has appeared in the literature since the early report of Schlenk and Bergmann[11] on the

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[1] Schollkopf, U. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 763.

[2] Nakai, T.; Mikami, K. *Chem. Rev.* **1986**, *86*, 885.

[3] Eichinger, P. C. H.; Bowie, J. H. *J. Chem. Soc., Perkin Trans. 2* **1988**, 497.

[4] Eichinger, P. C. H.; Bowie, J. H.; Blumenthal, T. *J. Org. Chem.* **1986**, *51*, 5078.

[5] D'Orchymont, H.; Goeldner, M. P.; Biellmann, J. F. *Tetrahedron Lett.* **1982**, *23*, 1727.

[6] Davies, S.G.; Holman, N. J.; Laughton, C. A.; Mobbs, B. E. *J. Chem. Soc., Chem. Commun.* **1983**, 1316.

[7] Landsbury, P. T.; Pattison, V. A.; Sidler, J. D.; Bieber, J. B. *J. Am. Chem. Soc.* **1966**, *88*, 78.

[8] Hauser, C. R.; Kantor, S. W. *J. Am. Chem. Soc.* **1951**, *73*, 1437.

[9] Cast, J.; Stevens, T. S.; Holmes, J. *J. Chem. Soc.* **1960**, 3521.

[10] Schollkopf, U.; Fabian, W. *Justus Liebigs Ann. Chem.* **1961**, *642*, 1.

[11] Schlenk, W.; Bergmann, E. *Justus Liebigs Ann. Chem.* **1928**, *464*, 1.