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Communications

A Mechanistic Study on the Reaction of Aryl Substituted Benzoates with Aryloxides

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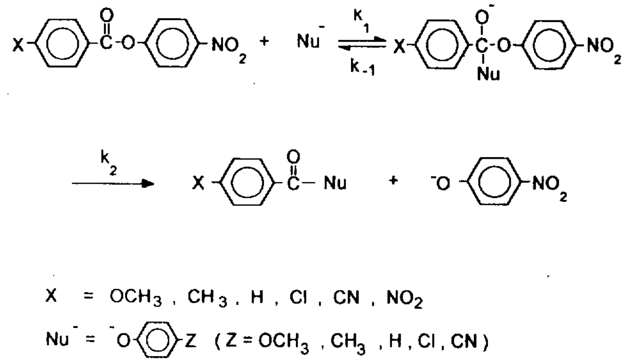
Due to the great importance of acyl-transfer reactions in chemistry and biochemistry, numerous studies have been performed in order to investigate the reaction mechanism.[1~6] However, the mechanism of acyl-transfer reactions has not been completely understood but remains under a subject of controversy.[7] It has been concluded in many studies that acyl-transfer reactions proceed *via* a concerted mechanism,[4~6] but this conclusion has not been universally accepted.[1~3,7]

Williams has concluded that the acyl-transfer reaction proceeds *via* a concerted pathway based on a linear Brönsted-type plot for the acyl-transfer reaction of aryl acetates, possessing good leaving groups.[4] Recently, a similar conclusion has been drawn by Hengge, *i.e.* acyl-transfer reaction of 4-nitrophenyl acetate with various oxyanion nucleophiles proceeds *via* a concerted mechanism based on the results of ^{18}O isotope effect studies.[5] On the contrary, Buncel and Um have suggested that acyl-transfer reactions proceed *via* a stepwise mechanism, based on the Hammett correlations obtained for the similar reactions.[2,3] The controversy concerning the reaction mechanism has been attributed to lack of systematic study.[2,3]

We have performed a systematic study on the acyl-transfer reaction of 4-nitrophenyl substituted benzoates with a series of aryloxides (Scheme 1), and found that the Brönsted-type plots for these reactions are not linear. The nonlinear Brönsted-type plots obtained in this study are considered to be the first time for the reaction of aryl benzoates with aryloxides in aqueous media. Therefore, we wish to communicate our results rapidly.

The reactions were followed by monitoring the appearance of 4-nitrophenoxide at 400nm using a Hitachi U-2000 UV-vis spectrophotometer or an Applied Photophysics SX. 17 MV stopped-flow spectrofluorimeter depending on the reaction rate. All the reactions were performed under pseudo-first-order conditions at 25.0± 0.1℃ in water containing 20 mole % dimethyl sulfoxide in order to eliminate a solubility problem. The observed rate constants (k_{obs}) were calculated from the equation, $\ln(A_\infty - A_t) = -k_{obs}t + C$. The apparent second-order rate constants (k_{app}) were obtained from the slope of the plot of k_{obs} versus nucleophile concentrations. The kinetic results are graphically summarized in Figures 1 and 2.



Scheme 1.

In Figure 1 are demonstrated Brönsted-type plots for the reaction of 4-nitrophenyl X substituted benzoates with a series of aryloxides. The reactivity of an aryloxide toward a given substrate increases with increasing its basicity, and results in excellent Brönsted-type correlations. The Brönsted coefficients (β_{nuc}) are calculated to be 0.98, 1.04 and 1.18 for X=4-OCH_3, H and 4-NO_2, respectively. The magnitude of these values appears to be much larger than that of the corresponding reaction with 4-nitrophenyl acetate (e.g. β_{nuc}= 0.7-0.8).[1~3]

The presence of an electron withdrawing substituent (EWS) on the acyl moiety of the substrate would enhance the electrophilicity of the carbonyl carbon, which would increase the reactivity of the substrate toward a given aryloxide. On the contrary, an electron donating substituent (EDS) on the acyl moiety would reduce the reactivity of the substrate by decreasing the electrophilicity of the carbonyl carbon. Therefore, one might expect that the bond formation

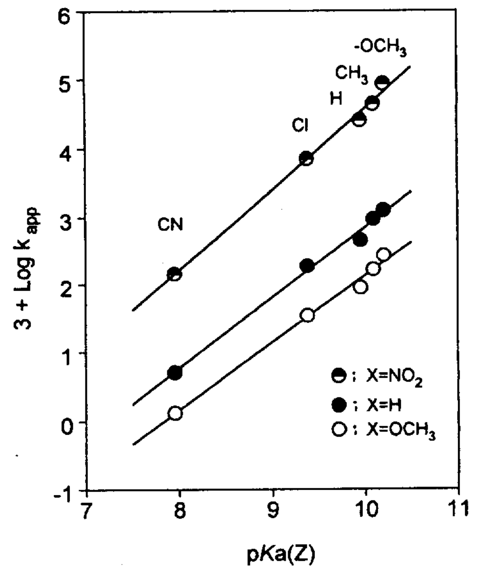


Figure 1. Brönsted type plots for the reaction of 4-X-$C_6H_4CO_2C_6H_4$-4-NO_2 with aryloxides (4-Z-$C_6H_4O^-$) in H_2O containing 20 mole % dimethyl sulfoxide at 25.0±0.1 ℃.

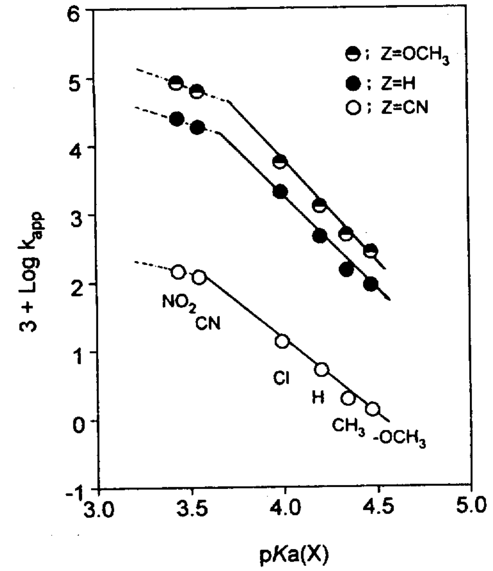


Figure 2. Brönsted type plots for the reaction of 4-X-$C_6H_4CO_2C_6H_4$-4-NO_2 with aryloxides (4-Z-$C_6H_4O^-$) in H_2O containing 20 mole % dimethyl sulfoxide at 25.0±0.1 ℃.

would be more tightly advanced for the more reactive substrate with an aryloxide at the transition state. The increasing β_{nuc} value trend in the present system is nicely consistent with this expectation, since the magnitude of β_{nuc} value can represent a relative degree of bond formation at the transition state of the rate-determining step (RDS).[8]

It has generally been admitted that a linear Brönsted-type plot represents a common reaction mechanism for a series of reactants.[8] Similarly, a break in a Brönsted-type plot has been interpreted as a change in the reaction mechanism.[8] Since both the attacking and leaving groups in the present system are in a family of aryloxides, the present acyl-transfer reaction is symmetrical.[1c] In a symmetrical reaction, a break in a Brönsted-type plot should occur at a point where the basicity of the attacking phenoxide and the leaving 4-nitrophenoxide is the same (e.g. $pKa=7.14$), if there is a change in RDS.[1c] However, the nucleophiles used in the present reactions are only limited to the aryloxides having higher basicity than the leaving 4-nitrophenoxide. Therefore, the linearity shown in Figure 1 could not give any significant information regarding the reaction mechanism.

It is necessary to study the reactions with low basic aryloxides ($pKa \leq 7.14$). However, these reactions have not been performed due to extremely slow reaction rate and possible errors due to the backward reaction.[1c] Instead, we have introduced various substituents in the acyl moiety of the substrate. In Figure 2 are demonstrated Brönsted-type plots for the acyl-transfer reactions of 4-nitrophenyl X substituted benzoates with three aryloxides. Generally, the reactivity of the substrates appears to increase with increasing electron withdrawing ability of the acyl substituent. However, the Brönsted-type plots are not linear, *i.e.* the points for the substrates containing a strong EWS (X=4-NO_2 and 4-CN) exhibit negative deviations from the linearity. The slopes (β_{acyl}) for the solid lines are significantly large, *i.e.* −2.80, −2.61 and −2.17 for Z=4-OCH_3, H and 4-CN, respectively, but the ones for the dotted lines appear to be much smaller.

It is evident that nucleophilic attack would be accelerated by an EWS on the acyl moiety but retarded by an EDS. Consequently, a large negative β_{acyl} value would be expected for the nucleophilic attacking process (k_1 step in Scheme 1). On the contrary, leaving group departure would be inhibited by an EWS but promoted by an EDS on the acyl moiety. In this case, one would expect a large positive β_{acyl} value for the leaving group departing process (k_2 step in Scheme 1). Therefore, the large β_{acyl} values (the solid lines in Figure 2) suggest that the acyl-transfer reaction of these benzoate esters proceeds *via* a rate-determining attack of the nucleophile to form a tetrahedral intermediate. This is consistent with the fact that the attacking aryloxides are more basic and less nucleofugitive than the leaving 4-nitrophenoxide.

However, as the electron withdrawing ability of the acyl substituent increases, the nucleophilic attack would become faster but the leaving group departure would be more difficult. In this case, nucleophilic attack would be no longer the slow step. When the leaving group departure is the slow step, the apparent second-order rate constant (k_{app}) is a composite of the equilibrium constant for the formation of a tetrahedral intermediate (k_1/k_{-1}) and the rate constant for the leaving group departure (k_2). Therefore, the overall substituent effect would be small (small β_{acyl} value) because of the opposite substituent effects as mentioned above. The breaks in the present Brönsted-type plots and the small β_{acyl} values (dotted lines) are nicely consistent with the proposal that there is a change in the RDS.

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References

1. (a) Stefanidis, D.; Cho, S.; Dhe-Paganon, S.; Jencks, W. P. *J. Am. Chem. Soc.* **1993**, *115*, 1650. (b) Hupe, D. J.;

Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451. (c) Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1968**, *90*, 2622.

2. (a) Buncel, E.; Um, I. H.; Hoz, S. *J. Am. Chem. Soc.* **1989**, *111*, 971. (b) Buncel, E.; Shaik, S. S.; Um, I. H.; Wolfe, S. *J. Am. Chem. Soc.* **1988**, *110*, 1275.
3. (a) Kwon, D. S.; Lee, G. J.; Um, I. H. *Bull. Korean Chem. Soc.* **1990**, *11*, 262. (b) Um I. H.; Jeon, J. S.; Kwon, D. S. *Bull. Korean Chem. Soc.* **1991**, *12*, 406. (c) Um I. H.; Lee, S. J.; Kim, J. J.; Kwon, D. S. *Bull. Korean Chem. Soc.* **1994**, *15*, 473.
4. (a) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1989**, *111*, 2647. (b) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 6362. (c) Bourne, N.; Chrystiuk, E.; Davis, A. M.; Williams, A. *J. Am. Chem. Soc.* **1988**, *110*, 1890.
5. (a) Hengge, A. C.; Hess, R. A. *J. Am. Chem. Soc.* **1994**, *116*, 11256. (b) Hengge, A. C.; Edens, W. A.; Elsing, H. *J. Am. Chem. Soc.* **1994**, *116*, 5045. (c) Hengge, A. C. *J. Am. Chem. Soc.* **1992**, *114*, 6575.
6. (a) Guthrie, P. J. *J. Am. Chem. Soc.* **1991**, *113*, 3941. (b) Yamabe, S.; Minato, T. *J. Org. Chem.* **1983**, *48*, 2972. (c) Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1978**, *100*, 3861. (d) Bentley, J. W.; Koo, I. S. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1385.
7. Tarkka, R. M.; Buncel, E. *J. Am. Chem. Soc.* **1995**, *117*, 1503.
8. Chapman, N. B.; Shorter, J. Eds.; *Advances in Linear Free Energy Relationship*; Plenum: London, 1972.

Syntheses of Tripodand and Cage-Type Hosts, and Their Binding Properties with Alkali Metal and Ammonium Ions

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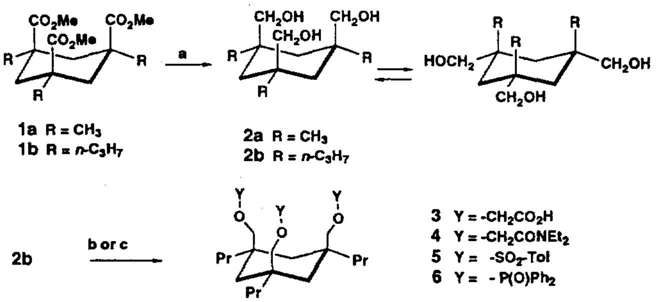
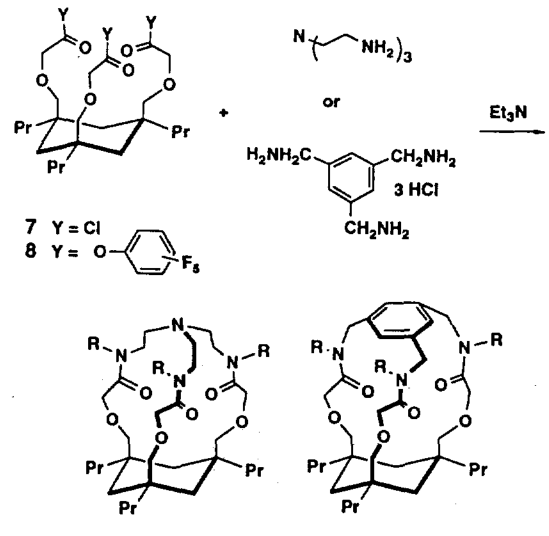
The construction of a well defined host is the most difficult but important work in molecular recognition chemistry. Design of metal ion host is relatively simple due to the spherical shape of metal ion with the positive charge. Studies for the selective recognition of a metal ion have been focused on the two or three-dimensional cyclic arrangement of electron donor atoms such as oxygen and nitrogen.[1] It has been little studied for the contribution of the donor atom basicity to the stability of complex. We report here syntheses and complexation properties of three tripodands having oxygen atoms with different basicities, that is, amide, sulfonate, and phosphinate groups. In addition, we also describe the syntheses of the cage-type hosts based on a new molecular building block derived from tripropyl Kemp triacid.[2] Several C_3-symmetric molecules have been employed for the syntheses of cage-type artificial hosts. The representative examples are tren, 1,3,5-substituted benzene,[3] and cyclotriveratrylene,[4] etc.



a) $LiAlH_4$ / THF b) i) t-BuO^-K^+ / t-BuOH, $ClCH_2CO_2H$ ii) $(COCl)_2$ / bezene iii) excess $HNEt_2$ c) i) n-BuLi / p-TosCl, or $Ph_2P(O)Cl$ / THF

Scheme 1.



9 R = H
10 R = CH_3
11 R = H
12 R = CH_3

Scheme 2.

Syntheses of molecular building blocks **2a**, **2b** and tripodands **4-6** are summarized in Scheme 1. The building blocks **2a**, **2b** were derived from the reduction (85-90% yield) of triesters **1a**, **1b** which were prepared by following a literature procedure[2] from the commercially available 1,3,5-trimethyl *cis,cis*-cyclohexanetricarboxylate. Reaction of tripropyl triol **2b** with chloroacetic acid in presence of t-BuO^-K^+ gave triacid **3** in 61% yield.[5] Amide tripodand **4** was obtained in 81% yield from activation of **3** with oxalyl chloride followed by treatment with excess diethylamine. Additionally, reaction of tripropyl triol **2b** with n-butyllithium /p-toluenesulfonyl chloride or diphenylphosphinic chloride afforded the corresponding tripodand **5** (58% yield) or **6** (82% yield), respectively.

Instead of trimethyl triol **2a**, tripropyl triol **2b** has been used for the preparations of hosts in this study by the following reasons. First, tripropyl triol **2b** is highly soluble in organic solvents ($CHCl_3$, CH_2Cl_2, and EtOAc etc.) but trimethyl triol **2a** is sparingly. Secondly, bulkier propyl group may increase the population of the conformation in which methanolic groups are located in the axial positions.

Syntheses of cage-type hosts **9-12** are outlined in Scheme