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Doubly Activated Supramolecular Reaction: Transesterification of Acyclic Oligoether Esters with Metal Alkoxides

Kazumitsu Kawakami,[†] Yoshihisa Sei,[‡] Kentaro Yamaguchi,[‡] and Akihiko Tsuda*[,†]

[†]*Department of Chemistry, Graduate School of Science, Kobe University, 1-1 Rokkodai-cho, Nada-ku, Kobe 657-8501, Japan, and* [‡]*Kagawa School of Pharmaceutical Sciences, Faculty of Pharmaceutical Sciences at Kagawa Campus, Tokushima Bunri University, 1314-1 Shido, Sanuki 769-2193, Japan*

tsuda@harbor.kobe-u.ac.jp

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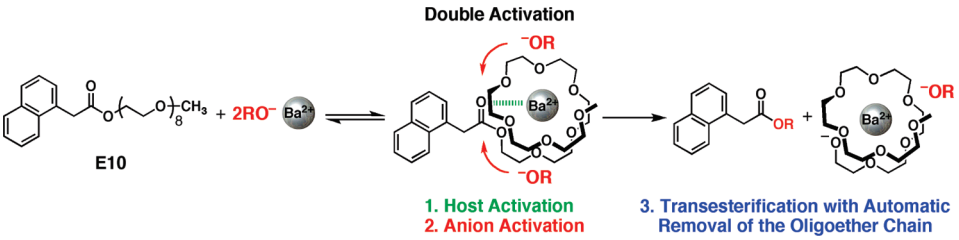

Transesterification reactions of acyclic oligoether esters **E3**−**E10** with metal alkoxides were accelerated upon noncovalent complexation of the esters with metal ions. In the reaction of monovalent alkaline metal alkoxides, CH_3ONa and CH_3OK, plots of the observed rate constants k_{obs} with respect to the chain length of **E3**−**E10** showed selective acceleration of the transesterification. Compared with the shortest **E3**, which can hardly bind metal ion, 4.3- and 6.6-fold accelerations in the maxima were achieved in the combinations of **E5**/CH_3ONa and **E6**/CH_3OK, respectively. Supramolecular intermediate complex could be spectrometrically visualized by ESI-FT-ICR-MS in the course of reaction. Kinetic experiments, together with structural analyses by means of NMR, mass spectrometry, and DFT calculations of the intermediate complexes, indicate that a size-fit complex of host substitute with alkali metal ion allows strong electron withdrawing due to the close contact of the carbonyl oxygen to the metal ion, resulting in the selective rate enhancement of the reaction, while in the reaction of **E3**−**E10** with a divalent alkaline earth metal alkoxide, $(CH_3CH_2O)_2Ba$, the k_{obs} values increased stepwise with elongation of the side arm to attain an dramatic large acceleration. In comparison with the k_{obs} of **E3**, 4610-fold acceleration was achieved in the reaction of **E10**. The double activation of the host substrate and guest counter nucleophile at once brings about this extraordinary rate acceleration. The strong wrapping complexation of long oligoether ester with barium ethoxide allows for the effective electron withdrawal from the ester carbonyl group (host activation) as well as separation of the accompanying guest alkoxide anions (guest activation).

Introduction

Weak interactions play important roles in a variety of chemical and biomolecular reactions.[1−5] In the field of supramolecular chemistry, as a mimic of biomolecular systems, dynamic metal complexes of crown ethers, which selectively bind metal cations in a cavity, have been actively studied.[6] Then, chemical reactions of the supramolecules, which can bring about specific reactions with high efficiency and selectivity, have attracted much attention.[7−15] One of the widely recognized characteristic functions of the supramolecular complexes is their ability to activate a counteranion that surrounds the metal cation through donation of the

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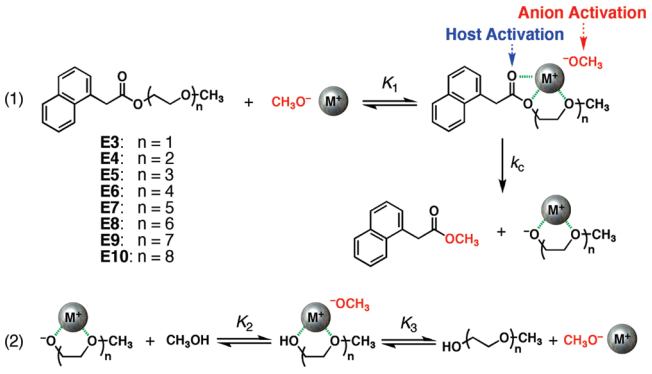
unpaired electrons of the oxygen atoms in the crown ether.[16−18] On the other hand, it is also well-known that metal ions, which work as Lewis acids, can catalyze a variety of organic reactions upon interaction with the reaction substrate. However, a few examples have been reported regarding the exploitation of efficient activation systems by construction of the supramolecular activated metal complex in the course of chemical reactions.[19−25] Mandolini and co-workers reported that the metal complexations of certain host substrates bearing an ester group, accelerate their acetyl and aryl transfer reactions, due to stabilization of the transition states.[24] We also reported self-activated supramolecular reactions, where metal complexes of *p*-benzoquinone bearing a cyclic or acyclic oligoether chain dramatically accelerated Diels−Alder reaction of *p*-benzoquinone with cyclopentadiene.[25] Induced electron withdrawal from the *p*-benzoquinone moiety toward the incorporated metal ion, which acts as a Lewis acid,

SCHEME 1. Schematic Illustration of a Possible Complexation and Transesterification Reaction of E3−E10 with an Alkaline Metal Methoxide[a]



[a] *K* and *k* represent binding and rate constants, respectively.

allows for such accelerated reactions. Although supramolecular reactions due to the former guest-activation and the later host-activation seem to be separately developed, some catalytic reactions, developed previously, most probably include both the guest and host activation effects (double activation). For example, transesterification reactions of esters with metal alkoxides proceed via an intermediate activated metal complexation in the transition state, where the counter alkoxide anion should also increase its nucleophilicity in a certain extent. Upon attachment of a metal-hosting side arm to the ester substrate, in the present study, we found that transesterification reactions of **E3−E10** show selective rate accelerations with alkaline metal alkoxides and a dramatic acceleration with a divalent metal alkoxide upon enhancement the possible anion-activation effect. A double activation of the host substrate and guest counter nucleophile at once upon complexation is, thus, achieved in the systematic study of the transesterification reaction of acyclic oligoether esters of **E3−E10** with metal alkoxides of CH_3OLi, CH_3ONa CH_3OK, and $Ba(OCH_2CH_3)_2$ (Scheme 1). Additionally, their supramolecular reactions have an important advantage, particularly for application in synthetic chemistry sequences, of undergoing automatic removal of the oligoethylene side chain. The supramolecular reaction, presented herein, suggests a general important concept to control a wide variety of chemical reactions.

Results and Discussion

Monovalent Reactions. Transesterification of esters with metal alkoxides has been known to proceed via an intermediate activated complex. We initially demonstrated the transesterification of a series of oligoether esters **E3−E10** with monovalent alkaline metal methoxides (Scheme 1). The oligoether esters were newly synthesized by stepwise elongation

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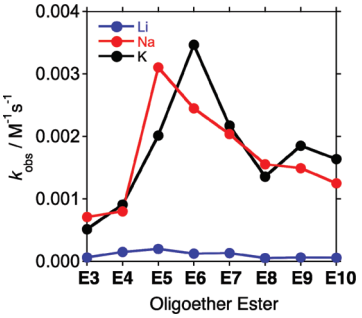

FIGURE 1. Plots of rate constants k_{obs} for transesterification of **E3**−**E10** with 0.5 equiv of CH_3OLi (blue curve), CH_3ONa (red curve), and CH_3OK (black curve) in a 50:1 mixture of CH_3CN and CH_3OH at 10 °C. The values of k_{obs} are listed in Table 1.

TABLE 1. Observed Rate Constants (k_{obs}) for the Transesterification of E3−E10 with 0.5 equiv of CH_3OLi, CH_3ONa, and CH_3OK in a CH_3CN/CH_3OH (50:1) Solution at 10 °C

	$k_{obs}/10^{-2}$ M^{-1} s^{-1}		
oligoether ester	CH_3OLi	CH_3ONa	CH_3OK
E3	0.0063	0.0710	0.0515
E4	0.0148	0.0810	0.0906
E5	0.0200	0.3103	0.2013
E6	0.0123	0.2446	0.3465
E7	0.0131	0.2035	0.2171
E8	0.0051	0.1551	0.1355
E9	0.0063	0.1491	0.1850
E10	0.0058	0.1248	0.1636

TABLE 2. Binding Constants (K_{ref}) of E3−E10 with the Trifluoromethanesulfonate Salts of Li, Na, and K in CD_3CN at 20 °C[a]

	K_{ref}/M^{-1}		
oligoether ester	LiOTf	NaOTf	KOTf
E3			
E4			
E5	30	21	21
E6	52	67	40
E7	71	157	106
E8	93	210	258
E9	127	200	402
E10	211	182	439

[a]The binding constants were determined by ^{1}H NMR spectroscopy, except for in the case of **E3** and **E4**, which did not give peak shifts.

of oligoethyleneglycol monomethylethers followed by subsequent attachment of the ethers to 1-naphthaleneacetic acid.[26] When **E3**−**E10** were mixed with 0.5 equiv of monovalent alkali metal methoxides in a solution containing a 50:1 mixture of CH_3CN and CH_3OH at 10 °C ([**E3**−**E10**] = 2.0 mM, [CH_3OM] = 1.0 mM), transesterification occurred quantitatively to give the corresponding methyl esters. The reactions were monitored by HPLC analysis via a naphthyl probe attached to the oligoether ester chain, and the observed ratio of reactant to product indicated a kinetic profile with a pseudo first order rate constant.[26] Hence, the transesterification reaction most likely occurs via a metal-complexed substrate as a key intermediate and can be represented by the

(26) See the Supporting Information.
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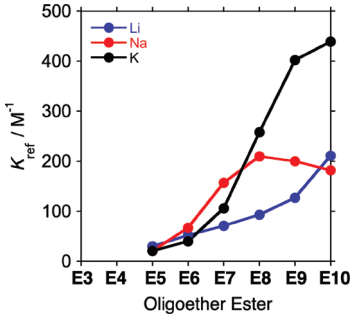

FIGURE 2. Plots of the binding constants K_{ref} of **E3**−**E10** with LiOTf (blue curve), NaOTf (red curve), and KOTf (black curve) in CD_3CN at 20 °C. The binding constants were determined by ^{1}H NMR spectroscopy, where the sample solutions contain 3.6×10^{-3} to 6.0×10^{-3} M of oligoether ester **E5**−**E10** with varying concentrations of the metal salt. The values of K_{ref} are listed in Table 2.

rate coefficient k_c, which is dependent on the binding constant K_1 (Scheme 1). Since the observed first-order rate constants were not affected during the reactions (an excellent correlation coefficient of $r > 0.999$ was attained),[26] the eliminated side arm, whose anionic charge should be neutralized by anion exchange with the excess CH_3OH to reproduce CH_3OM, may have a negligibly small difference on the binding constants between K_1 in eq 1 and K_3 in eq 2 (Scheme 1).

Interestingly, plots of the k_{obs} values with respect to the chain length of **E3**−**E10** showed selective acceleration of the transesterification for CH_3ONa and CH_3OK (Figure 1, red and black curve, respectively). In comparison with the k_{obs} of **E3**, which hardly binds the metal ions, a 4.3- and 6.6-fold acceleration in the maxima were achieved in the combinations of **E5**/CH_3ONa and **E6**/CH_3OK, respectively (Table 1).[26] In contrast, minor accelerations with no notable selectivity were observed in combinations of **E3**−**E10** with CH_3OLi (Figure 1, blue curve). The corresponding plots of reference binding constants K_{ref} of **E5**−**E10** with the trifluoromethanesulfonate salts of Li^+, Na^+, and K^+, which were determined by ^{1}H NMR spectroscopy (Table 2 and Figure 2),[27] do not agree with these kinetic profiles. Hence, the observed selectivity in acceleration indicates that the ester carbonyl group most likely participates in an interaction with the metal ion to form a size-fitted complex, which does not exclusively provide the largest binding constant, like those observed with metal complexes of crown ethers. Since 15-crown-5 and 18-crown-6 form a size-fit complex with Na^+ and K^+, respectively, the observed k_{obs} maxima of oligoether esters **E5** and **E6**, which correspond to these crown ether, is quite reasonably explained with the size-fit concept.[6] The decreased accelerations of **E7**−**E10**, having longer oligoether side arms, also suggest importance of direct interaction between ester carbonyl group and metal ion, which may weaken electrically as well as sterically upon increase of oxygen atom in the arm. Thus, no notable selective acceleration was observed in the reactions with CH_3OLi, where Li^+ hardly interacts with the unpaired electrons of the ester carbonyl group.

In a variety of metal-catalyzed organic reactions, it is well-known that weak interactions of the metal ions with the reaction substrates play a very important role in the catalytic step. Here, attachment of the long oligoether chain to the substrate allowed detection of the intermediate metal

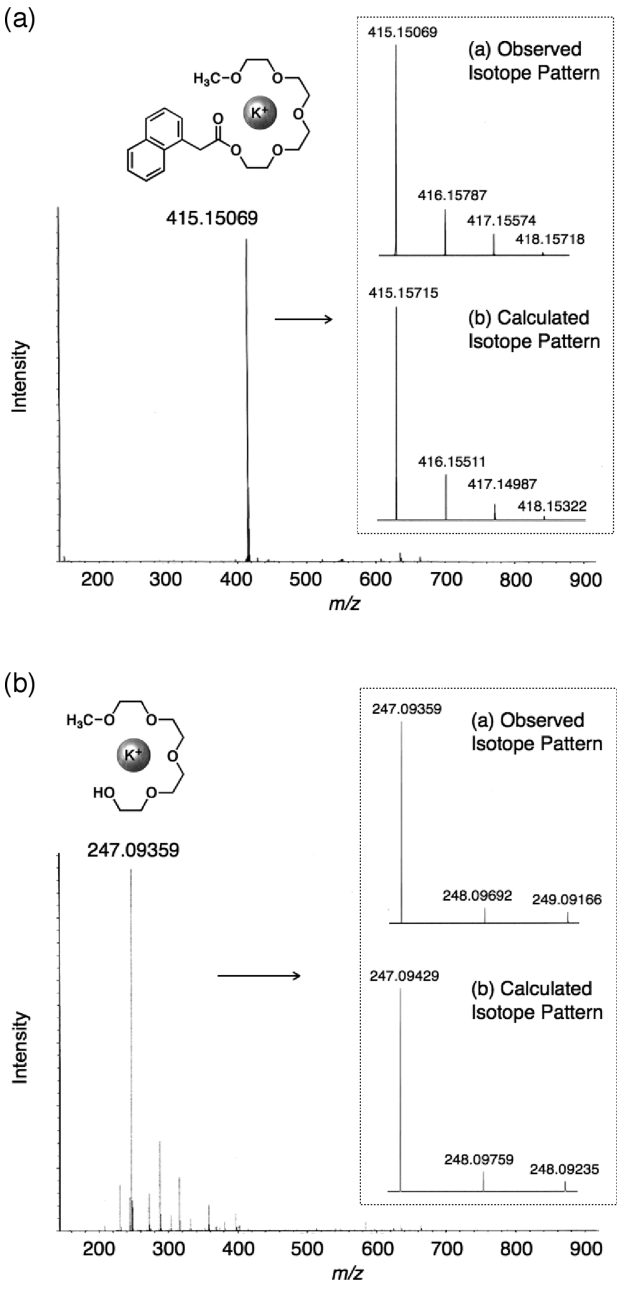

FIGURE 3. ESI-FT-ICR MS of (a) a CH_3CN/CH_3OH (50:1) solution of **E6** and CH_3OK ([**E6**] = [CH_3OK] = 20 μM) and (b) the solution after the reaction. Inset shows the magnified observed and calculated isotope patterns of the parent peak.

complex during the course of the transesterification reaction using Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS) combined with an electrospray ionization (ESI) technique. When a diluted CH_3CN solution of **E6**/CH_3OK ([**E6**] = 20 μM) was subjected to mass spectrometry, only a strong signal with m/z = 415.151 appeared. The observed value and its isotope pattern are in good agreement with the calculated values (parent signal at m/z = 415.157; Figure 3a) of the 1:1 intermediate complex of **E6** and K^+ formed in the reaction. Then, a strong signal with m/z = 247.094, whose value is corresponding to the calculated value of a 1:1 complex of tetraethyleneglycol monomethylether with potassium ions (parent signal at m/z = 247.094),

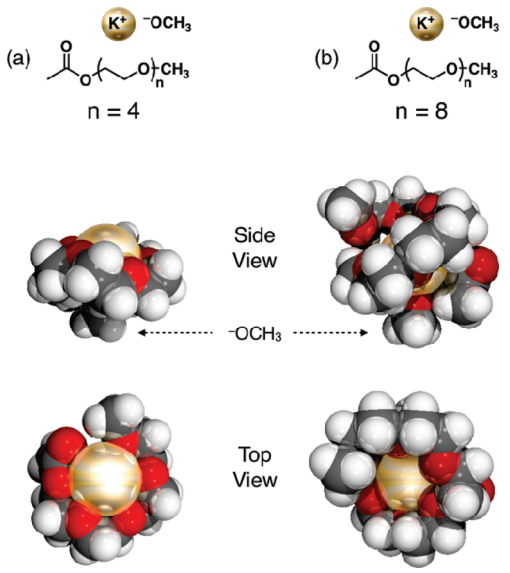

FIGURE 4. Calculated structures (B3LYP/6-31+G(d,p)) for the noncovalent metal complexes of CH_3OK and the oligoether ester moiety of (a) **E6** and (b) **E10** without the naphthyl group. Space-filling model: gold, K; red, O; gray, C; white, H).

TABLE 3. Observed Rate Constants (k_{obs}) for the Transesterification of E3 with 0.5 equiv of CH_3OK in the Absence or Presence of 1.0 equiv of a Host Molecule in a CH_3CN/CH_3OH (50:1) Solution at 10 °C

compd	$k_{obs}/10^{-2}$ M^{-1} s^{-1}
E3	0.0515
E3 + pentaglyme	0.0415
E3 + 18-crown-6	0.0306

appeared after completion of the reaction (Figure 3b). Hence, these observed profiles successfully visualize spectrometrically the reaction progress of the transesterification reaction.

DFT calculations for the complexes of the oligoether ester side arms of **E6** and **E10** with CH_3OK indicate a size-fit complexation for **E6** and a helically wrapped structure for **E10** with C═O---M^+ distances of 3.2 and 4.3 Å, respectively (Figure 4).[28] These calculated structures may explain the observed selective rate acceleration of **E6**/CH_3OK with the maximum k_{obs}, in which the size-fit complex allows strong electron withdrawing due to the close contact of the carbonyl oxygen to the metal ion.

To evaluate the possible anion activation effect, transesterification of the reference **E3** oligoether ester with CH_3OK was demonstrated in the presence of 18-crown-6 or pentaglyme (1.0 equiv for [**E3**]) with a cyclic or acyclic structure, respectively (Table 3). The transesterification reactions of **E3** initially appeared to be sensitive to the nucleophilicity and/or structure of the alkoxide anion since CH_3CH_2OK, whose alkoxide may have a larger nucleophilicity than the methoxide, provided a larger k_{obs} value (6.8×10^{-4} M^{-1} s^{-1}) than CH_3OK (5.1×10^{-4} M^{-1} s^{-1}). Unexpectedly, however, 0.6- and 0.8-fold decelerations occurred in the presence of the crown ether and pentaglyme. These results are probably due to the steric hindrance and/or weakness of electron withdrawal

(28) DFT calculations were carried out using Gaussian 09. Geometry optimizations were performed for a single molecule in the gas phase using the B3LYP/6-31+G(d,p) level of theory.

TABLE 4. Observed Rate Constants (k_{obs}) for the Transesterification of E3−E10 with 1.0 equiv of $Ba(OCH_2CH_3)_2$ and Reaction of E3 in the Presence of 1.0 equiv of 18-Crown-6, in CH_3CN/CH_3CH_2OH (50:1) at 30 °C, plus Binding Constants (K_{ref}) of E5−E9 with Barium Trifluoromethanesulfonate in CD_3CN at 20 °C

oligoether ester	$k_{obs}/10^{-2}$ M^{-1} s^{-1}	k_{ref}/M^{-1}
E3	0.0005	*a*
E4	0.0055	*a*
E5	0.0075	250
E6	0.0278	4500
E7	0.0515	15000
E8	0.2148	40000
E9	0.6435	300000
E10	2.3063	*a*
E3 + 18-crown-6	0.0030	

[a]The binding constants could not be determined for **E3** and **E4** because of a lack of notable peak shifts and for **E10** due to broadening of the signals.

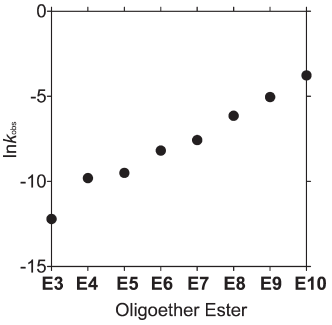

FIGURE 5. Plots of rate constants $\ln k_{obs}$ for transesterification of **E3−E10** with 1.0 equiv of $Ba(OCH_2CH_3)_2$ in a 50:1 mixture of CH_3CN and CH_3CH_2OH at 30 °C. The values of k_{obs} are listed in Table 4.

in the interaction of the metal ion with the ester carbonyl group upon complexation. This effect should also be expected to occur for longer oligoether esters and would provide the gradual decrease of k_{obs} with elongation of the side arm, resulting in selective rate acceleration (Figure 1). These results suggest that the host activation upon interaction of the metal ion and ester carbonyl is a main factor for accelerating the monovalent reactions.

Reactions with Barium Ethoxide. Next, we carried out the transesterification of **E3−E10** with the divalent metal alkoxide $Ba(OCH_2CH_3)_2$ (Table 4, and Figure 5). Since the solubility problem of divalent metal alkoxides into CH_3CN, the transesterification with divalent alkoxides such as $Ca(OCH_3)_2$ and $Mg(OCH_2CH_3)_2$ could not be carried out, and $Ba(OCH_2CH_3)_2$ having relatively larger solubility was adopted in the experiment. When **E3** was mixed with $Ba(OCH_2CH_3)_2$ in a CH_3CN/CH_3CH_2OH (50:1) solution, the k_{obs} (5.0×10^{-7} M^{-1} s^{-1}) was dramatically decreased compared with the corresponding monovalent reaction (6.8×10^{-4} M^{-1} s^{-1} for CH_3CH_2OK). Since divalent Ba^{2+} binds counter alkoxide anions more strongly than monovalent cations, the nucleophilicity of its ethoxide anion may decrease and thus provide smaller k_{obs} values. For the experimental convenience of the study, the reactions of **E3−E10** were thus investigated with 1.0 equiv of $Ba(OCH_2CH_3)_2$ in a CH_3CN/CH_3CH_2OH solution (50:1) at 30 °C. The reaction of **E3**/$Ba(OCH_2CH_3)_2$ was accelerated with a k_{obs} = 5.0×10^{-6} M^{-1} s^{-1} under these conditions. Quite interestingly, for kinetic experiments with **E3−E10**, it was found that

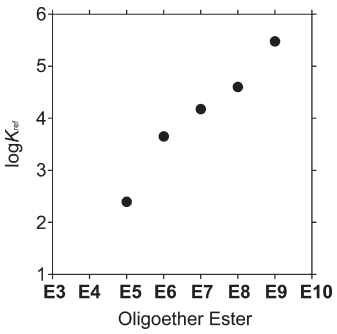

FIGURE 6. Plots of binding constants log K_{ref} of **E3−E10** with $Ba(OTf)_2$ in CD_3CN at 20 °C. The binding constants were determined by ^1H NMR spectroscopy, except **E3** and **E4** due to a lack of notable peak shifts, and **E10** due to broadening of the signals. The values of K_{ref} are listed in Table 4.

the k_{obs} values increased stepwise with elongation of the side arm to attain an extremely large acceleration, with the maximum rate constant $k_{obs} = 2.3 \times 10^{-2}$ M^{-1} s^{-1} for **E10**. In comparison with the k_{obs} of **E3**, 4610-folds acceleration was achieved. Binding constants of the oligoether esters with Ba^{2+} were notably larger than those for the monovalent cations, and the values increased stepwise with elongation of the side arm (Table 4 and Figure 6) as similar to the kinetic profile (Figure 5). Since the ion radius of Ba^{2+} (1.35 Å) is approximately the same as that for K^+ (1.33 Å), here the observed trend of k_{obs} cannot be explained according to the size-fit concept as observed with the monovalent reactions.

Considering the possible anion activation effect of $Ba(OCH_2CH_3)_2$ upon complexation, the transesterification of **E3** with $Ba(OCH_2CH_3)_2$ was carried out in the presence of 18-crown-6 (1.0 equiv for [**E3**] and [$Ba(OCH_2CH_3)_2$]).[29] In contrast to the case of the monovalent alkoxide, 6-fold accelerations were observed in the reaction. Although the crown ether also should prevent interaction of bound metal ion and ester carbonyl group by analogy with the monovalent reaction, it can be expected that the anion activation, whose contribution may larger than that of monovalent alkoxide due to separation of two counteranions, effectively works in this system. As expected from the DFT calculation for **E10**/CH_3OK, the long oligoether side arm helically traps a metal ion along with the separation of the counter alkoxide anions, resulting in both strong association and rate acceleration, respectively (Figure 4). Actually, the ^{13}C NMR spectrum of **E10** with Ba^{2+}, in which the signals of the oligoether moieties shows peak shifts in the range of −0.9 to +0.4 ppm and the signal of the ester carbonyl group is downfield shifted by 1.7 ppm, suggests such a structure, while in sharp contrast, no notable shifts (∼0.1 ppm) were observed in the naphthyl moiety.[26]

Activation parameters for the transesterification of **E3** and **E10** with $Ba(OCH_2CH_3)_2$ were evaluated from their temperature dependent k_{obs}.[26,30] **E3** and **E10** provided $\Delta G^{\ddagger}$ = 111 and 88 kJ mol^{-1}, $\Delta H^{\ddagger}$ = 55 and 65 kJ mol^{-1}, and $\Delta S^{\ddagger}$ = −183 and −80 J K^{-1} mol^{-1}, respectively, at 30 °C. The smaller $\Delta H^{\ddagger}$ in the reaction of **E3** suggests a larger contribution of the ester carbonyl group in the temporary formation

(29) Cacciapaglia, R.; Mandolini, L.; Castelli, V. V. A. *J. Org. Chem.* **1997**, *62*, 3089–3092.
(30) Os'kina, I. A.; Vlasov, V. M. *Russ. J. Org. Chem.* **2009**, *45*, 523–527.

of an intermediate activated complex. A positive increase in the value of $\Delta S^{\ddagger}$ for the reaction of **E10** may result from activation of alkoxide anions that are being liberated from the metal ion upon complexation. These experimental results therefore strongly suggest that the observed dramatic rate accelerations of the long oligoether esters with $Ba(OCH_2CH_3)_2$ most likely result from the double activation of the metal complex and its counteranion.

Conclusion

Systematic elongations of the side arm of oligoether esters **E3**−**E10**, which can capture metal ions, in the transesterification reactions allowed interesting finding of a novel doubly activated supramolecular reaction. In comparison with the shortest **E3**, which hardly binds the metal ions, oligoether esters with monovalent metal alkoxides showed selective rate accelerations due mainly to an effect of host activation, while dramatic rate enhancement could be achieved in combinations of longer oligoether esters with a divalent metal alkoxide as a result of double activation of the host substrate and guest counter nucleophile at once. Additionally, these activation effects are accompanied by automatic removal of the oligoethylene side chain, which provides a notable advantage, particularly for application in complex synthetic chemistry sequences. We believe that the supramolecular reaction presented herein is a general important concept to control a wide variety of reactions and will ultimately represent a significant milestone in synthetic chemistry.

Experimental Section

General Procedure for the Synthesis of Oligoether Esters E3−E10. To a benzene solution (5 mL) of 1-naphthalene acetic acid **1** (1.8 mmol) was added thionyl chloride (5 mL) and the reaction mixture refluxed for 2 h and then evaporated to dryness. The residue was mixed with oligoethyleneglycol monomethylether (1.2 mmol) and *N*,*N*′-dimethyl-4-aminopyridine (2.4 mmol) in CH_2Cl_2 (10 mL) and the solution stirred under Ar for 24 h at room temperature and then evaporated to dryness. The residue was then dissolved into ethyl acetate and washed with aqueous solutions of 1 N HCl, saturated $NaHCO_3$ and saturated NaCl. The organic layer was then extracted, dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was subjected to column chromatography on alumina with CH_2Cl_2 (for **E3**−**E4**) or a mixture of CH_2Cl_2 and MeOH (∼10%) (for **E5**−**E10**) as eluent, where the second fraction was collected and evaporated. The products obtained were unambiguously characterized by means of ^{1}H NMR, ^{13}C NMR, IR spectroscopy, elemental analysis, and fast atom bombardment (FAB) mass spectrometry.

2-Methoxyethyl 1-Naphthaleneacetate (E3). Compound **E3** was isolated as a yellow oil in 49% yield from the reaction of 1-naphthalene acetic acid and ethyleneglycol monomethylether: FAB-MS *m*/*z* calcd for M^+ ($C_{15}H_{16}O_3$) 244, found 245 ($M + H^+$); ^{1}H NMR (400 MHz, $CDCl_3$, 20 °C) δ 8.01−7.99 (d, 1H, J = 8.8 Hz), 7.87−7.85 (d, 1H, J = 7.5 Hz), 7.80−7.78 (q, 1H, J = 3.5 Hz), 7.55−7.47 (m, 2H), 7.45−7.42 (m, 2H), 4.27−4.25 (t, 2H, J = 4.8 Hz), 4.12 (s, 2H), 3.57−3.55 (t, 2H, J = 4.8 Hz), 3.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C) δ 171.5, 133.7, 132.0, 130.4, 128.5, 127.9, 126.2, 125.7, 125.4, 124.0, 70.3, 65.9, 58.8, 38.9; IR (KBr) 2890, 1735, 1171, 1128, 781 cm^{-1}; UV−vis (MeOH, 20 °C) λ_{max} 290, 280, 271 nm. Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.6. Found: C, 73.49; H, 6.85.

2-(2′-Methoxyethoxy)ethyl 1-Naphthaleneacetate (E4). Compound **E4** was isolated as a yellow oil in 41% yield from the reaction of 1-naphthalene acetic acid and diethyleneglycol monomethylether: FAB-MS *m*/*z* calcd for M^+ ($C_{17}H_{20}O_4$) 288, found 289 ($M + H^+$); ^{1}H NMR (400 MHz, $CDCl_3$, 20 °C) δ 8.01−7.99 (d, 1H, J = 8.8 Hz), 7.87−7.85 (d, 1H, J = 7.5 Hz), 7.80−7.78 (q, 1H, J = 3.5 Hz), 7.55−7.47 (m, 2H), 7.45−7.42 (m, 2H), 4.28−4.26 (t, 2H, J = 4.8 Hz), 4.11 (s, 2H), 3.66−3.64 (t, 2H, J = 4.8 Hz), 3.50−3.48 (m, 2H), 3.45−3.43 (m, 2H), 3.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C) δ 171.4, 133.7, 132.0, 130.4, 128.6, 127.9, 126.2, 125.6, 125.4, 123.7, 71.7, 70.3, 68.9, 64.0, 58.9, 38.9; IR (KBr) 2879, 1735, 1137, 1109, 782, cm^{-1}; UV−vis (MeOH, 20 °C) λ_{max} 290, 280, 271 nm. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.73; H, 6.98.

2-(2′(2″-Methoxyethoxy)ethoxy)ethyl 1-Naphthaleneacetate (E5). Compound **E5** was isolated as a yellow oil in 22% yield from the reaction of 1-naphthalene acetic acid and triethyleneglycol monomethylether: FAB-MS *m*/*z* calcd for M^+ ($C_{19}H_{24}O_5$) 332, found 333 ($M + H^+$); ^{1}H NMR (400 MHz, $CDCl_3$, 20 °C) δ 8.01−7.99 (d, 1H, J = 8.8 Hz), 7.87−7.85 (d, 1H, J = 7.5 Hz), 7.80−7.78 (q, 1H, J = 3.5 Hz), 7.55−7.47 (m, 2H), 7.45−7.42 (m, 2H), 4.27−4.25 (t, 2H, J = 4.8 Hz), 4.11 (s, 2H), 3.66−3.64 (t, 2H, J = 4.8 Hz), 3.60−3.58 (m, 2H), 3.54−3.52 (m, 6H), 3.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C) δ 171.4, 133.7, 132.0, 130.4, 128.6, 127.9, 126.2, 125.6, 125.3, 123.7, 71.8, 70.4, 68.9, 64.0, 58.9, 38.9; IR (KBr) 2879, 1734, 1132, 1108, 784, cm^{-1}; UV−vis (MeOH, 20 °C) λ_{max} 290, 280, 271 nm. Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.40; H, 7.35.

2-(2′-(2″-(2‴-Methoxyethoxy)ethoxy)ethoxy)ethyl 1-Naphthaleneacetate (E6). Compound **E6** was isolated as a yellow oil in 30% yield from the reaction of 1-naphthaleneacetic acid and tetraethyleneglycol monomethylether: FAB-MS *m*/*z* calcd for M^+ ($C_{21}H_{28}O_6$) 376, found 377 ($M + H^+$); ^{1}H NMR (400 MHz, $CDCl_3$, 20 °C):δ 8.01−7.99 (d, 1H, J = 8.8 Hz), 7.87−7.85 (d, 1H, J = 7.5 Hz), 7.80−7.78 (q, 1H, J = 3.5 Hz), 7.55−7.47 (m, 2H), 7.45−7.42 (m, 2H), 4.27−4.25 (t, 2H, J = 4.8 Hz), 4.10 (s, 2H), 3.66−3.62 (m, 8H), 3.56−3.54 (m, 6H), 3.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C) δ 171.4, 133.7, 132.0, 130.4, 128.6, 127.9, 126.2, 125.6, 125.3, 123.7, 71.8, 70.4, 68.9, 64.0, 58.9, 38.9; IR (KBr) 2873, 1734, 1135, 1107, 783, cm^{-1}; UV−vis (MeOH, 20 °C) λ_{max} 290, 280, 271 nm. Anal. Calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 66.83; H, 7.79.

2-(2′-(2″-(2‴-(2⁗-Methoxyethoxy)ethoxy)ethoxy)ethoxy)-ethyl 1-Naphthaleneacetate (E7). Compound **E7** was isolated as a yellow oil in 27% yield from the reaction of 1-naphthaleneacetic acid and pentaethyleneglycol monomethylether: FAB-MS *m*/*z* calcd for M^+ ($C_{23}H_{32}O_7$) 420, found 421 ($M + H^+$); ^{1}H NMR (400 MHz, $CDCl_3$, 20 °C) δ 8.01−7.99 (d, 1H, J = 8.8 Hz), 7.87−7.85 (d, 1H, J = 7.5 Hz), 7.80−7.78 (q, 1H, J = 3.5 Hz), 7.55−7.47 (m, 2H), 7.45−7.42 (m, 2H), 4.27−4.25 (t, 2H, J = 4.8 Hz), 4.10 (s, 2H), 3.66−3.62 (m, 12H), 3.56−3.54 (m, 6H), 3.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C) δ 171.4, 133.7, 132.0, 130.4, 128.6, 127.9, 126.2, 125.7, 125.4, 123.7, 71.8, 70.4, 68.9, 64.1, 58.9, 38.9; IR (KBr) 2873, 1735, 1136, 1109, 784, cm^{-1}; UV−vis (MeOH, 20 °C) λ_{max} 290, 280, 271 nm. Anal. Calcd for $C_{23}H_{32}O_7$: C, 65.70; H, 7.67. Found: C, 67.28; H, 7.83.

2-(2′-(2″-(2‴-(2⁗-(2⁗′-Methoxyethoxy)ethoxy)ethoxy)-ethoxy)ethoxy)ethyl 1-Naphthaleneacetate (E8). Compound **E8** was isolated as a yellow oil in 52% yield from the reaction of 1-naphthalene acetic acid and hexaethyleneglycol monomethylether: FAB-MS *m*/*z* calcd for M^+ ($C_{25}H_{36}O_8$) 464, found 465 ($M + H^+$); ^{1}H NMR (400 MHz, $CDCl_3$, 20 °C) δ 8.01−7.99 (d, 1H, J = 8.8 Hz), 7.87−7.85 (d, 1H, J = 7.5 Hz), 7.80−7.78 (q, 1H, J = 3.5 Hz), 7.55−7.47 (m, 2H), 7.45−7.42 (m, 2H), 4.27−4.25 (t, 2H, J = 4.8 Hz), 4.11 (s, 2H), 3.66−3.62 (m, 16H), 3.55−3.49 (m, 6H), 3.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C) δ 171.4, 133.7, 132.0, 130.4, 128.6, 127.9, 126.2, 125.7, 125.4, 123.7, 71.8, 70.4, 68.9, 64.1, 58.9, 38.9; IR (KBr) 2873, 1735, 1136, 1109, 784, cm^{-1}; UV−vis (MeOH, 20 °C) λ_{max} 290, 280, 271 nm. Anal. Calcd for $C_{25}H_{36}O_8$: C, 64.64; H, 7.81. Found: C, 64.03; H, 7.76.

2-(2′-(2″-(2‴-(2⁗-(2⁗′-(2⁗′′-Methoxyethoxy)ethoxy)ethoxy)-ethoxy)ethoxy)ethoxy)ethyl 1-Naphthaleneacetate (E9). Compound **E9** was isolated as a yellow oil in 48% yield from the reaction of 1-naphthalene acetic acid and heptaethyleneglycol monomethylether. FAB-MS *m*/*z* calcd for M^+ ($C_{27}H_{40}O_9$) 508, found 509 ($M + H^+$); ^{1}H NMR (400 MHz, $CDCl_3$, 20 °C) δ 8.01−7.99 (d, 1H, J = 8.8 Hz), 7.87−7.85 (d, 1H, J = 7.5 Hz), 7.80−7.78 (q, 1H, J = 3.5 Hz), 7.55−7.47 (m, 2H), 7.45−7.42 (m, 2H), 4.27−4.25 (t, 2H, J = 4.8 Hz), 4.11 (s, 2H), 3.66−3.62 (m, 20H), 3.55−3.52 (m, 6H), 3.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C) δ 171.4, 133.7, 132.0, 130.4, 128.6, 128.0, 126.2, 125.7, 125.4, 123.7, 71.8, 70.5, 70.4, 68.9, 64.1, 58.9, 38.9; IR (KBr) 2872, 1735, 1136, 1106, 784, cm^{-1}; UV−vis (MeOH, 20 °C) λ_{max} 290, 280, 271 nm. Anal. Calcd for $C_{27}H_{40}O_9$: C, 63.76; H, 7.93. Found: C, 64.11; H, 7.82.

2-(2′-(2″-(2‴-(2⁗-(2⁗′(2⁗′′-(2⁗′′′-Methoxyethoxy)ethoxy)-ethoxy)ethoxy)ethoxy)ethoxy)ethoxy)ethyl 1-Naphthaleneacetate (E10). Compound **E10** was isolated as a yellow oil in 48% yield from the reaction of 1-naphthalene acetic acid and octaethyleneglycol monomethylether: FAB-MS *m*/*z* calcd for M^+ ($C_{29}H_{44}O_{10}$) 552, found 553 ($M + H^+$); ^{1}H NMR (400 MHz, $CDCl_3$, 20 °C) δ 8.01−7.99 (d, 1H, J = 8.8 Hz), 7.87−7.85 (d, 1H, J = 7.5 Hz), 7.80−7.78 (q, 1H, J = 3.5 Hz), 7.55−7.47 (m, 2H), 7.45−7.42 (m, 2H), 4.27−4.25 (t, 2H, J = 4.8 Hz), 4.11 (s, 2H), 3.66−3.60 (m, 24H), 3.55−3.52 (m, 6H), 3.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C) δ 171.4, 133.7, 132.0, 130.4, 128.6, 128.0, 126.2, 125.7, 125.4, 123.7, 71.8, 70.5, 70.4, 68.9, 64.1, 58.9, 38.9; IR (KBr) 2878, 1735, 1136, 11063, 784, cm^{-1}; UV−vis (MeOH, 20 °C) λ_{max} 290, 280, 271 nm. Anal. Calcd for $C_{29}H_{44}O_{10}$: C, 63.36; H, 8.09. Found: C, 63.03; H, 8.02.

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Supporting Information Available: General synthetic scheme, ^{1}H and ^{13}C NMR spectra of compounds **E3**−**E10**, experimental details of kinetic and thermodynamic measurements, ^{1}H and ^{13}C NMR spectra of intermediate complexes prepared, and Cartesian coordinates of the DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.