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A New Reaction Pathway in the Ester Aminolysis Catalyzed by Glymes and Crown Ethers

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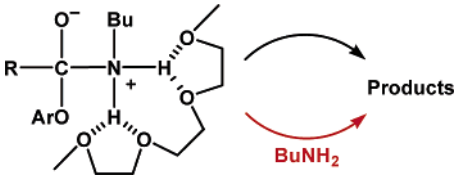

Butylaminolysis of *p*-nitrophenyl acetate in chlorobenzene in the presence of different kinds of phase-transfer catalysts (crown ethers and glymes) supports the existence of a reaction pathway exhibiting a first-order dependence on the concentration of the phase transfer catalyst and a second-order dependence on the concentration of butylamine. This novel reaction pathway must be included in the mechanism traditionally accepted for the catalysis by phase-transfer agents of aminolysis reactions in aprotic solvents.

Introduction

Catalysis by phase-transfer agents (crown ethers or glymes) of aminolysis reactions of carboxylic esters is a well-studied process.[1−8] The generally accepted catalytic mechanism in aprotic solvents is shown in Scheme 1.

Nucleophilic attack of *n*-butylamine on the ester generates a tetrahedral intermediate, T ±.[9−12] This intermediate may either proceed with the catalytic assistance of a second *n*-butylamine molecule or form a complex with the phase-transfer agent C·T ±. Subsequently, this complex gives rise to the reaction products in the rate-determining step. From this mechanism, the following rate equation can be obtained

$$k_{obs} = k_B[BuNH_2]^2 + k_C[BuNH_2][catalyst] \qquad (1)$$

where the second-order term in butylamine corresponds to the base-catalyzed decomposition, $k_B = K^T k_2$. The rate constant term given in eq 1 which shows a first-order dependence on butylamine and catalyst concentration is for the reaction pathway catalyzed by the phase-transfer agent $k_C = K^T K^{CT} k^1_{cat}$. This reaction mechanism has been widely reported in the literature, and the presence or absence of phase transfer agent catalysis has been used as a test to identify the rate-determining step in ester aminolysis in solvents of different polarity[13] and in other mechanistic studies.[14]

In the present work, we report results obtained in our laboratory by studying the butylaminolysis of 4-nitrophenyl acetate (NPA) in chlorobenzene in the presence of glymes or crown ethers (Scheme 2). Glymes were chosen on the basis of Hogan and Gandour's studies,[15−17] which conclude that a glyme

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(1) Gandour, R. D.; Walker, D. A.; Nayak, A.; Newkome, G. R. *J. Am. Chem. Soc.* **1978**, *100*, 3608−3609.
(2) Komives, T.; Marton, A. F.; Dutka, F.; Low, M.; Kisfaludy, L. *React. Kinet. Catal. L.* **1980**, *13*, 357−359.
(3) Maude, A. B.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1995**, 691−696.
(4) Zipse, H.; Wang, L. H.; Houk, K. N. *Liebigs Ann.* **1996**, 1511−1522.
(5) Koh, H. J.; Han, K. L.; Lee, I. *J. Org. Chem.* **1999**, *64*, 4783−4789.
(6) Baldini, L.; Bracchini, C.; Cacciapaglia, R.; Casnati, A.; Mandolini, L.; Ungaro, R. *Chem.—Eur. J.* **2000**, *6*, 1322−1330.
(7) Vakhitova, L. N.; Burdina, Y. F.; Skrypka, A. V.; Popov, A. F.; Savelova, V. A. *Theor. Exp. Chem.* **2002**, *37*, 225−229.
(8) Vakhitova, L. N.; Savelova, V. A.; Burdina, Y. F.; Belousova, I. A.; Popov, A. F. *Russ. J. Org. Chem.* **2003**, *39*, 968−971.
(9) Satterthwait, A. C.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 7018−7031.
(10) Gresser, M. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6970−6980.
(11) Fishbein, J. C.; Baum, H.; Cox, M. M.; Jencks, W. P. *J. Am. Chem. Soc.* **1987**, *109*, 5790−5800.
(12) Marlier, J. F. *Acc. Chem. Res.* **2001**, *34*, 283−290.
(13) Maude, A. B.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1997**, 179−183.
(14) García-Río, L.; Leis, J. R.; Moreira, J. A.; Serantes, D. *Eur. J. Org. Chem.* **2004**, 614−622.

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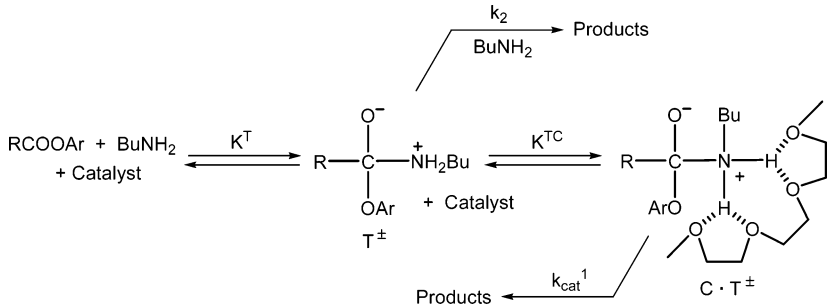
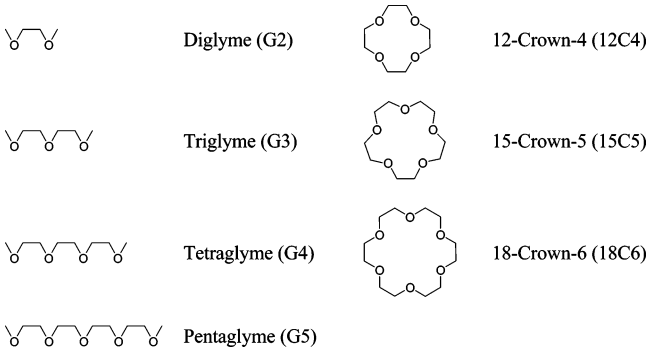
SCHEME 1



SCHEME 2



with four oxygen atoms in a $-(CH_2OCH_2)_4-$ type subunit provides optimal catalysis for this kind of processes. Crown ethers were chosen on the basis of Maude and Williams' studies.[3,13] Catalytic efficiency of these phase-transfer agents is due to a specific *host*−*guest* interaction between the catalysts and the tetrahedral intermediate of the reaction, suggesting the existence of a C·T $^{\pm}$ complex where the oxygens donate electron density in order to stabilize the hydrogens of the ammonium ion of T $^{\pm}$. Given the size of the $-^{+}NH_2-$ fragment, the maximum number of oxygen atoms that will be able to bond is four. The structure of the *guest* rearranges the *host*, leading to the recognition of the transition state by the *host*. The results obtained suggest that the reaction mechanism shown in Scheme 1 needs to be modified through the addition of a new reaction pathway.

Results

Figures 1 and 2 show the influence of butylamine concentration on k_{obs} for the butylaminolysis of *p*-nitrophenyl acetate (NPA) in chlorobenzene at 25 °C at different catalyst concentrations. In all cases, a second-order polynomial dependence of k_{obs} on [butylamine] is observed (eq 2). The existence of this dependence is consistent with an aminolysis mechanism proceeding through the formation of a tetrahedral intermediate in nonaqueous solvents.[18−24] Kinetic data were fitted to an equation of the type

$$k_{obs} = a[BuNH_2] + b[BuNH_2]^2 \qquad (2)$$

Equation 2 is formally analogous to eq 1, commonly used for the mechanism depicted in Scheme 1. Figures 3 and 4 illustrate the influence of phase-transfer agent concentration on the *a* and *b* terms of eq 2. As can be observed, the *a* term exhibits a linear dependence on [catalyst]. This result is consistent with the mechanism generally accepted for the catalysis by crown ethers and glymes of the aminolysis of carboxylic esters.

We have studied the influence of temperature (from −20.0 to +45.0 °C) on the butylaminolysis of NPA in chlorobenzene in the presence of glyme G4. In all cases, the butylaminolysis rate constant of NPA increases as temperature increases.

Discussion

(a) Evidence of a New Catalytic Pathway. The mechanism shown in Scheme 1 predicts that the *b* term of eq 2 should be

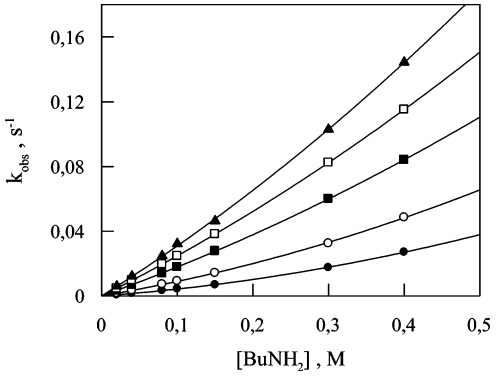


FIGURE 1. Influence of *n*-butylamine concentration on k_{obs} for the aminolysis of NPA, T = 25.0 °C, [NPA] = 5×10^{-5} M. (●) [G4] = 0.10 M; (○) [G4] = 0.25 M; (■) [G4] = 0.50 M; (□) [G4] = 0.75 M, and (▲) [G4] = 1.00 M.

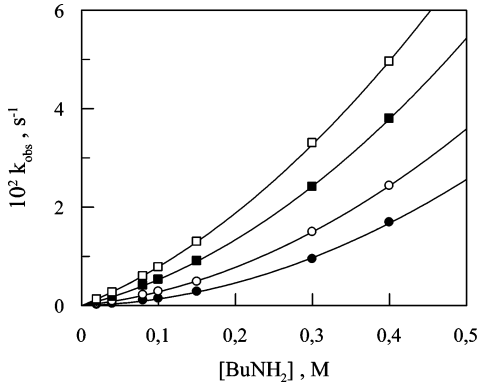
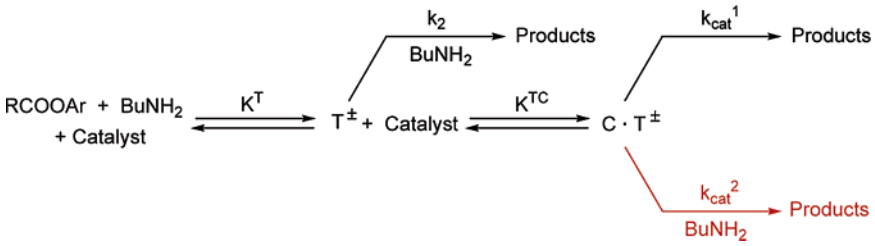


FIGURE 2. Influence of *n*-butylamine concentration on k_{obs} for the aminolysis of NPA, T = 25.0 °C, [NPA] = 5×10^{-5} M. (●) [15C5] = 0.10 M; (○) [15C5] = 0.26 M; (■) [15C5] = 0.51 M, and (□) [15C5] = 0.75 M.

(15) Hogan, J. C.; Gandour, R. D. *J. Am. Chem. Soc.* **1980**, *102*, 2865−2866.
(16) Hogan, J. C.; Gandour, R. D. *J. Org. Chem.* **1991**, *56*, 2821−2826.
(17) Hogan, J. C.; Gandour, R. D. *J. Org. Chem.* **1992**, *57*, 55−61.

SCHEME 3



independent of the glyme concentration. However, the results reported in Figures 3 and 4 for the butylaminolysis of NPA indicate that this term shows a linear dependence on catalyst concentration.

As we have shown previously,[25] the mechanism presented in Scheme 1 needs to be further developed in order to explain the observed kinetic data. The presence of a kinetic term showing a second-order dependence on butylamine concentration and a first-order dependence on glyme concentration may be accounted for by the possibility that the C·T $^{\pm}$ complex may decompose by a base-catalyzed pathway. The proposed mechanism is shown in Scheme 3 along with the new reaction pathway.

From this scheme, the following rate equation can be obtained:

$$k_{obs} = k_C[\text{catalyst}][\text{BuNH}_2] + (k_B + k_D[\text{catalyst}])[\text{BuNH}_2]^2 \quad (3)$$

Previous studies reported in the bibliography have investigated the influence of glymes or crown ethers on the butylaminolysis rate constant. These studies were carried out keeping the butylamine concentration constant, so that only a term that is first order in glyme or crown ether concentration can be detected. Rate constants, k_C, for the phase transfer agent-catalyzed butylaminolysis of *p*-nitrophenyl acetate, can be determined from the influence of catalyst concentration on the *a* term (Figures 3 and 4).

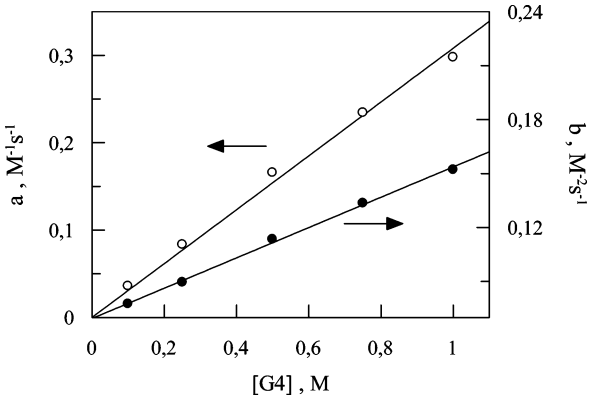


FIGURE 3. Influence of glyme G4 concentration on the a and b terms (eq 2) for the butylaminolysis of NPA. (○) a and (●) b. $T = 25.0$ °C.

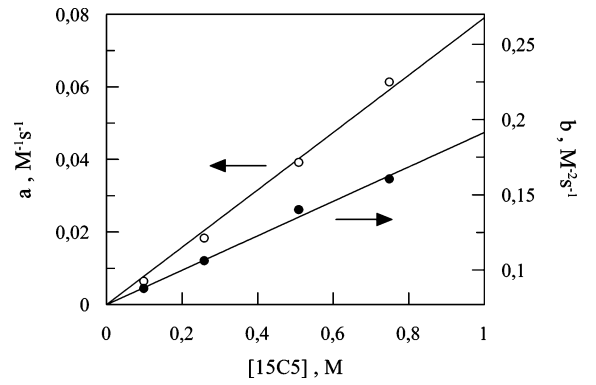


FIGURE 4. Influence of 15C5 concentration on the a and b terms (eq 2) for the butylaminolysis of NPA. (○) a and (●) b. $T = 25.0$ °C.

TABLE 1. Rate Constants for the Phase Transfer Agent-Catalyzed Butylaminolysis of NPA ($T = 25.0$ °C)

catalyst	k_C, M^{-2} s^{-1}	k_B, M^{-2} s^{-1}	k_D, M^{-3} s^{-1}
G2	0.017	0.075	0.041
G3	0.183	0.071	0.060
G4	0.308	0.069	0.084
G5	0.353	0.078	0.106
12C4	0.043	0.077	0.077
15C5	0.085	0.077	0.114
18C6	0.105	0.074	0.143

TABLE 2. Rate Constants for the G4-Catalyzed Butylaminolysis of NPA

T, °C	k_C, M^{-2} s^{-1}	k_B, M^{-2} s^{-1}	k_D, M^{-3} s^{-1}
−20	0.144	0.031	0.044
25	0.308	0.069	0.084
45	0.375	0.147	0.170
$\Delta H^{\ddagger}$, kJ mol^{-1}	7.67	12.6	10.5
$\Delta S^{\ddagger}$, J $mol^{-1}K^{-1}$	−229	−223	−228

Equation 3 accounts for the intercepts in the plots of the influence of [catalyst] on the *b* term (Figures 3 and 4), which correspond to the base-catalyzed decomposition of the intermediate, T $^{\pm}$. Application of eq 3 leads to the values of k_B for the butylaminolysis of *p*-nitrophenyl acetate. The rate constants can be determined for this new reaction pathway which shows base and glyme or crown ether catalysis simultaneously. The values of k_D for the butylaminolysis of *p*-nitrophenyl acetate can be obtained from eq 3 and Figures 3 and 4. Values of k_C, $k_{,B}$ and k_D are shown in Table 1.

From experiments at different temperatures and using eq 3, the values of k_C, k_B, and k_D were obtained (shown in Table 2). The existence of an Arrhenius behavior allows us to obtain the values for the activation energies for the different reaction pathways. The absence of anti-Arrhenius behavior is an argu-

(18) Menger, F. *J. Am. Chem. Soc.* **1966**, *88*, 3081−3084.
(19) Anderson, H.; Su, C.-W.; Watson, J. W. *J. Am. Chem. Soc.* **1969**, *91*, 482−484.
(20) Menger, F. M.; Smith, J. H. *J. Am. Chem. Soc.* **1972**, *94*, 3824−3829.
(21) Su, C.-W.; Watson, J. W. *J. Am. Chem. Soc.* **1974**, *96*, 1854−1857.
(22) Pfeiffer, M. J.; Hanna, S. B. *J. Org. Chem.* **1993**, *58*, 735−740.
(23) Cho, B. R.; Kim, Y. K.; Yoon, C.-O. M. *J. Am. Chem. Soc.* **1997**, *119*, 691−697.
(24) Melander, C.; Horne, D. A. *J. Org. Chem.* **1997**, *62*, 9295−9297.
(25) Basilio, N.; García-Río, L.; Leis, J. R.; Mejuto, J. C.; Pérez-Lorenzo, M. *Chem. Commun.* **2005**, 3817.

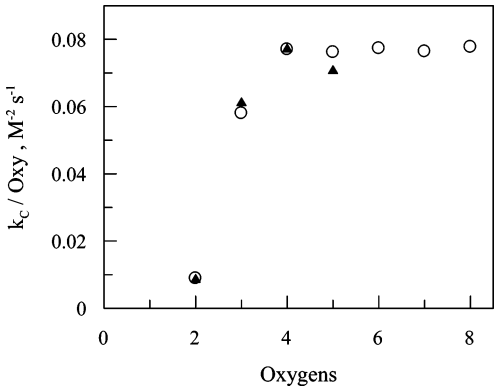


FIGURE 5. Plot of the per oxygen catalytic rate constant, k_C/Oxy, for butylaminolysis of NPA vs the number of oxygens in the glyme. (▲) this work, (○) ref 17.

ment against a complexation preequilibrium amine catalyst. Anti-Arrhenius behavior has previously been observed for the aminolysis of carboxylic esters[26] and for nucleophilic aromatic substitution involving amine nucleophiles in apolar media.[27] Although the precise mechanisms reponsible for this behavior are still disputed, various authors have suggested that exothermic preequilibria which contribute to the overall rate coefficient might be involved. If the amount of energy evolved in these preequilibria were sufficiently large, it could exceed the activation energy for the endothermic rate-controlling step and thus produce a negative overall activation energy. The preequilibrium step involved is thought to be the formation of charge-transfer complexes[26] or amine self-association.[28]

Activation parameters, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, for the butylaminolysis of NPA are shown in Table 2. The relatively low positive $\Delta H^{\ddagger}$ and negative $\Delta S^{\ddagger}$ are in line with the stepwise mechanism.[29]

(b) Catalytic efficiency of glymes on k_C. Figure 5 shows the catalytic efficiency of glymes in butylaminolysis of NPA obtained in this work as well as those previously obtained by Hogan and Gandour.[17] The first point to be noted in our results is that the values obtained for k_C in this work (eq 3) for the NPA aminolysis catalyzed by glymes are in good agreement with the previous results obtained by Hogan and Gandour[17] (eq 1). The explanation for this concordance is based on the butylamine concentration used by Hogan and Gandour,[17] $[BuNH_2] = 0.40$ M, and the values of the rate constants summarized in Table 1. It is straightforward to notice that in their experimental conditions the simplification $(k_C + k_D[BuNH_2]) \cong k_C$ is verified so that there is a quantitative agreement between the experimental results.

Figure 5 plots k_C/Oxy vs the number of oxygens in the corresponding glymes. As can be seen, our k_C/Oxy values agree quantitatively with those reported in the bibliography and show a plateau that represents the maximum catalysis per oxygen for glymes. Catalysis increases as the number of oxygen increases.

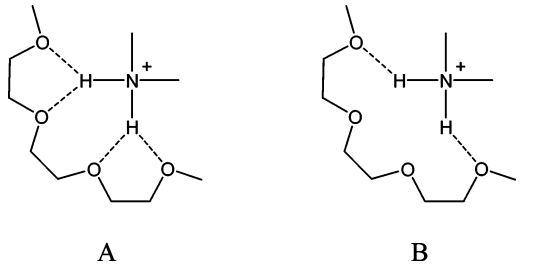
(26) (a) Nagy, J. B.; Nagy, O. B.; Bruylants, A. *Bull. Soc. Chim. Belg.* **1973**, 82, 539. (b) Mukana, D.; Nagy, J. B.; Nagy, O. B.; Bruylants, A. *Bull. Soc. Chim. Belg.* **1974**, 83, 201. (c) Nagy, O. B.; Muanda, M.; Nagy, J. B. *J. Phys. Chem.* **1979**, *83*, 1961.

(27) (a) Banjoki, O.; Ezeami, C. *J. Chem. Soc., Perkin Trans. 2* **1986**, 531. (b) Nudelman, N. S.; Palleros, D. R. *J. Org. Chem.* **1983**, *48*, 1607.

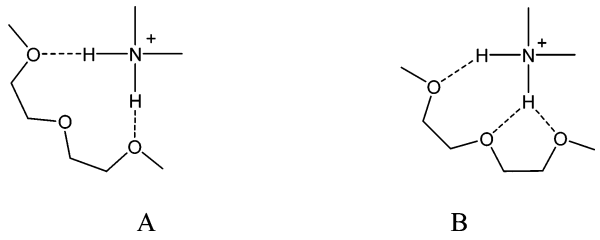
(28) Nudelman, N. S. *J. Phys. Org. Chem.* **1989**, 2, 1.

(29) (a) Castro, E. A.; Freudenberg, M. *J. Org. Chem.* **1980**, *45*, 906. (b) Koh, H. J.; Kim, T. H.; Lee, B. S.; Lee, I. *J. Chem. Res. Synop.* **1996**, 482. (c) Neuvonen, H. *J. Chem. Soc., Perkin Trans. 2* **1995**, 951. (d) Koh, H. J.; Shin, C. H.; Lee, H. W.; Lee, I. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1329.

SCHEME 4



SCHEME 5



The profile then levels off at four oxygens, and successive oxygens only contribute to the catalysis in a statistical manner. Figure 5 indicates that glymes with four or more oxygen atoms use only four oxygens to catalyze the butylaminolysis of *p*-nitophenylacetate.

The identification of $-(CH_2OCH_2)_4-$ as the optimal catalytic segment for stabilizing a two-proton ammonium ion suggests that two bifurcated hydrogen bonds are formed. Because glyme G4 exhibits more catalysis than just doubling the effect of glyme G2, the four oxygens of glyme G4 must cooperate in stabilizing the ion (Scheme 4A) and we can neglect the possibility that the central oxygens of $-(CH_2OCH_2)_4-$ are only spacers, and the first and fourth oxygens each bind one of the two ammonium protons (Scheme 4B).

The value of k_C/Oxy for glyme G3 is over six times that of glyme G2. This substantial increase suggests that glyme G3 catalyzes by binding both ammonium protons at the catalytic site (Scheme 5). Glyme G3 uses either two (Scheme 5A) or three oxygens (Scheme 5B) to bind the two protons. The two oxygen−two proton model (Scheme 5A) resembles the typical ammonium−polyether structure observed in crystals. The central oxygen might contribute electrostatically or conformationlly or both.

Glyme G4 shows a 30% larger k_C/Oxy than glyme G3 in butylaminolysis. Glyme G4 likely binds all four oxygens to the two ammonium protons at the catalytic site and bridges these protons more effectively than glyme G3. Apparently, glyme G4 catalyzes butylaminolysis by bringing together two pairs of bifurcated oxygens to form a doubly bifurcated hydrogen-bonded catalyst−substrate complex (Scheme 4A).

(c) Catalytic Efficiency of Glymes on k_D. Figure 6 profiles the catalytic efficiency of glymes **2**−**5** in butylaminolysis, k_D/Oxy, and in *N*-methylbutylaminolysis, k_C/Oxy, of NPA. The plateau represents the maximum catalysis per oxygen for glymes, showing a value of two oxygens for both the term k_D/Oxy in butylaminolysis of NPA and k_C/Oxy in *N*-methylbutylaminolysis of NPA.[17]

Glyme catalysis of *N*-methylbutylaminolysis occurs by formation of a bifurcated hydrogen bond to two contiguous polyether oxygens. No matter what the oligomer length, k_C/Oxy remains constant. Additional oxygens only contribute on a statistical basis. k_C for glyme G3 exceeds that for glyme G2,

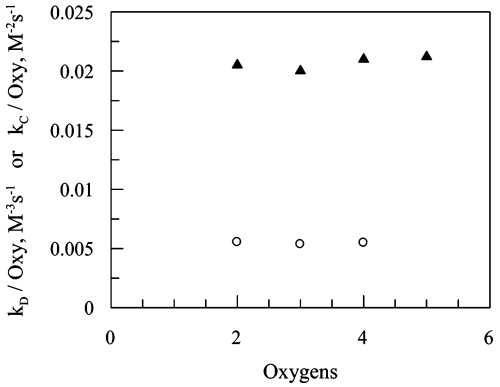
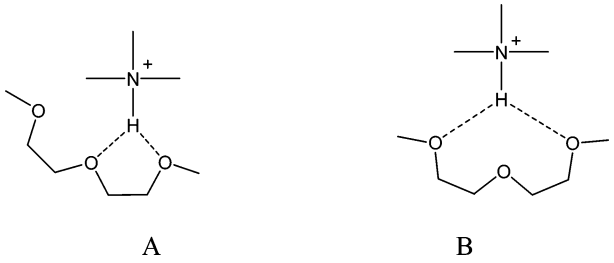
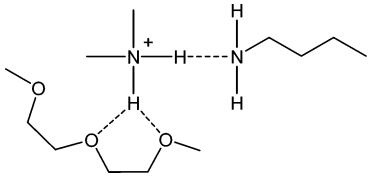


FIGURE 6. Plot of the per oxygen catalytic rate constant, k_D/Oxy, for butylaminolysis of NPA vs the number of oxygens in the glyme (▲) and k_C/Oxy for *N*-methylbutylaminolysis of NPA (○) ref 17.

SCHEME 6



SCHEME 7



but both have identical values of k_C/Oxy. Glyme G3 has two sites for a bifurcated hydrogen bond to two contiguous oxygens (Scheme 6A), but glyme G2 has only one. The two terminal oxygens in glyme G3 might form a bifurcated hydrogen bond (Scheme 6B), but this possibility has been ruled out.[17]

The behavior observed for the k_D term in the butylaminolysis of NPA is similar to that observed for the k_C term in the *N*-methylbutylaminolysis of NPA. As can be observed in Figure 6, the ratio k_D/Oxy reaches a leveling off for glyme G2. This behavior agrees with the existence of a single hydrogen atom in $T^{\pm}$ available to be bound to the glyme, since the other hydrogen atom is tranferred to a second butylamine molecule (Scheme 7).

(d) Catalysis by Crown Ethers. Figure 7 shows a plot of the per oxygen catalytic rate constants of crown ethers in the NPA butylaminolysis. Two features are worthy of note. First, it can be observed that the catalytic term corresponding to the decomposition of $T^{\pm}$ catalyzed by bases and crown ether, k_D/Oxy, is more important than that corresponding to the noncatalyzed decomposition of $T^{\pm}$, k_C/Oxy. This result is in contrast to that previously obtained for glymes (Table 1). As a result of the larger value of k_D compared to k_C, the approach ($k_C + k_D$-[$BuNH_2$]) ≅ k_C is not verified. Therefore, the values for k_C obtained in this work differ from the results obtained previously by Hogan and Gandour[15] as can be deduced from Figure 7.

The second point to be noted is that the per oxygen catalytic rate constants, k_C/Oxy and k_D/Oxy, increase with the number

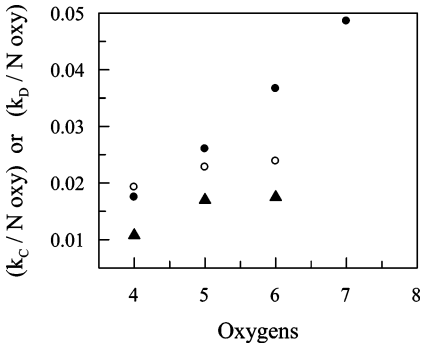
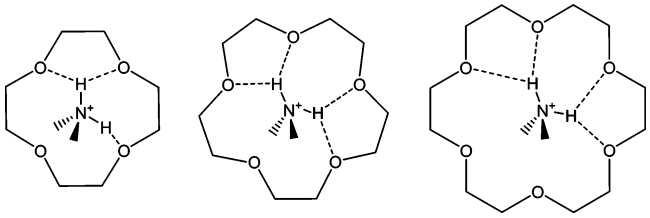


FIGURE 7. Plot of the per oxygen catalytic rate constants, k_C/Oxy (▲) and k_D/Oxy (○), for butylaminolysis of NPA vs the number of oxygens in the crown ether and k_C/Oxy for *N*-methylbutylaminolysis of NPA (●) ref 17.

SCHEME 8



of oxygen atoms in the crown reaching a plateau for five to six oxygen atoms. It is important to emphasize that we found no difference in the behavior of the per oxygen catalytic rate constants, k_C/Oxy and k_D/Oxy, to that in the catalysis by glymes.

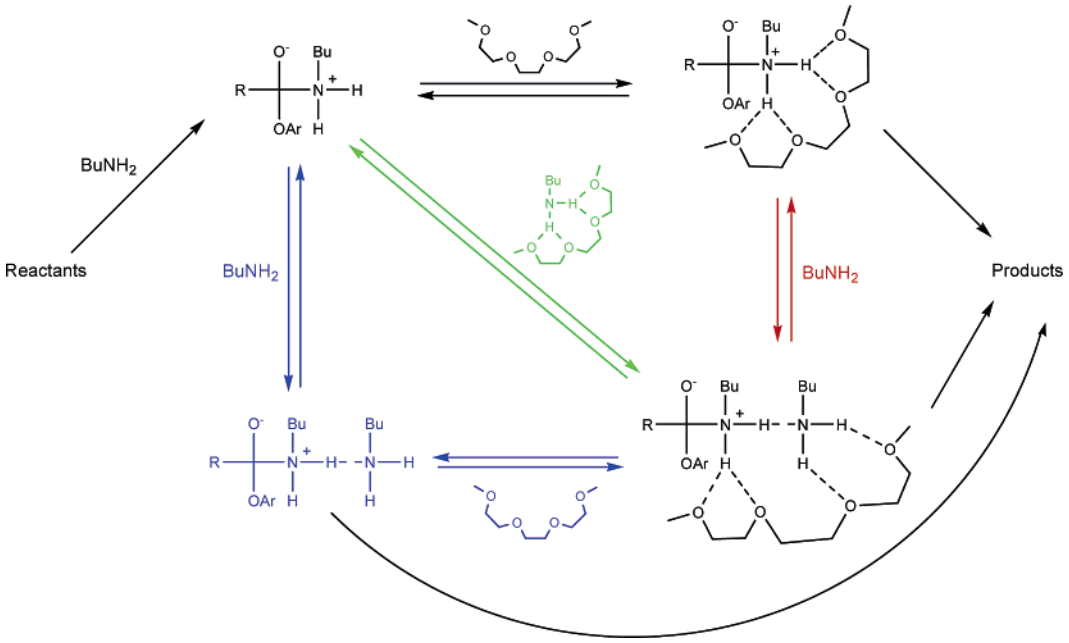
12C4 catalyzes the aminolysis by binding both ammonium protons at the catalytic site by using three oxygens to bind the two protons (Scheme 8). Both 15C5 and 18C6 can catalyze the butylaminolysis by formation of two bifurcated hydrogen bonds to four contiguous oxygens (Scheme 8). Apparently, 15C5 and 18C6 catalyze butylaminolysis by bringing together two pairs of bifurcated oxygens to form a doubly bifurcated hydrogen-bonded catalyst−substrate complex.

The proposed mechanism is conservative by only including one pathway departing from the ether−TI (ether−tetrahedral intermediate) complex with an amine molecule. A more encompassing scheme is showed in Scheme 9 where the previously proposed pathway is indicated by red arrows. Two additional pathways can produce the same kinetic result: (i, indicated by green arrows) butylamine attacks the ester to form the tetrahedral intermediate (TI), the amine is precomplexed to the ether catalyst and this complex binds the TI; (ii, indicated by blue arrows) butylamine attacks the ester to form the tetrahedral intermediate and a second butylamine hydrogen bonds to the TI. Glyme binds to both butylamine components.

(e) Mechanism of Catalysis. In a recent study of aminolysis of various esters in aprotic solvents, Su and Watson[30] reported that hydrogen bonding to the ammonium ion part of $T^{\pm}$ is more important than proton basicity for catalysis. Glymes and crown ethers catalyze the aminolysis of NPA in chlorobenzene by binding to the ammonium ion part of $T^{\pm}$. The binding interaction should have an electron-donating effect to $T^{\pm}$ and accelerates the breakdown of $T^{\pm}$. What remains unclear is whether butylamine preferentially preassociates with the glyme followed by attack of the resulting complex on the ester to form

(30) Su, C. W.; Watson, J. W. *J. Am. Chem. Soc.* **1974**, *96*, 1854.

SCHEME 9



T ± or, alternatively, butylamine attacks the ester to form uncomplexed T ± followed by binding to glyme. The rate-determining transition structure occurs after the formation of complexed T ±. How the product forms is also uncertain, but there are two likely possibilities. One is a stepwise process where complexed T ± decomposes to a tight ion pair (aryloxide and complexed N-protonated amide) followed by a proton transfer to give the phenol and the amide. The other, a concerted path, avoids the tight ion pair. In other words, glyme transfers a proton from the ammonium ion to the aryl oxide.

A tentative explanation on how a butylamine molecule can attack C·T ± to help the reaction is that one of the two nitrogen−hydrogen bonds breaks in all cases, but frequently it reverses and reforms the C·T ± complex (since the entities are still bonded together). In turn decomplexation can be assisted (enforced) by transfer of the proton (removed by the glyme from the nitrogen) to a butylamine molecule, then followed by decomplexation as the favored pathway and regeneration of the carbonyl group and loss of the aryloxide group, in preference to loss of the butyl amino group, giving the aminolysis product.

Experimental Section

All of the chemicals were of the highest available purity and were used as supplied. The aminolysis reactions were followed by monitoring the UV−vis absorbance of the products of the reaction at $\lambda = 320$ nm, using a spectrophotometer fitted with thermostated cell holders. At low temperatures the experiments were carried out in a four-necked flask placed over a magnetic stirrer in a cryostat and under exclusion of moisture. The photometric measurements were performed by use of a quartz immersion probe (1 cm light path) equipped with a ground joint and optical fiber cables with standard SMA connectors. The temperature of solutions during kinetic studies was monitored with a thermocouple probe that was inserted into the reaction mixture. In all experiments the ester concentration, typically 5.00×10^{-5} M, was much smaller than that of $BuNH_2$ and catalyst. The kinetic absorbance vs time data always fitted the first-order integrated rate equation satisfactorily ($r > 0.999$). In what follows, k_{obs} denotes the pseudo-first-order rate constant. We were able to reproduce the observed rate constants with an error margin of ±5%. A compilation of the kinetic data is supplied as Supporting Information.

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Supporting Information Available: Tables showing the influence of *n*-butylamine and glyme or crown ether concentration on the observed rate constant in NPA aminolysis in chlorobenzene. This material is available free of charge via the Internet at http://pubs.acs.org.

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