cis hydrogens in **4b**, which decreases θ_{4b}. Better N–C$_{1,3}$ overlap is thus achieved, and the pericyclic shift is facilitated. The same factor apparently operates in the *O*-oxides, and presumably in the *S*-oxides as well.[16]

In summary, we find no evidence in the bicyclo systems **3b–i** for the lone-pair participation implied by the pseudopericyclic concept. The idea that pericyclic transformations may experience secondary perturbations by nonbonding electrons, or conceivably may be strongly influenced by electron-deficient centers,[2,18] nevertheless appears to be a useful one. However, it needs to be appreciated that such effects, in general, can be expected to express themselves strongly only in special cases. In the systems considered here, the pseudopericyclic concept is redundant and possibly misleading.

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(12) Interestingly, the canonical (delocalized) MO eigenvalues indicated that the endo lone pairs are destabilized relative to exo lone pairs without any compensating drop in the π_s(allyl) orbital of the same symmetry. For example, the $(\pi + n)$ S and A combinations for **4b** and **4c** are split by 3.47 and 3.43 eV, respectively.

(13) For **4a–c,e,f,** The Boys localization actually yields somewhat asymmetric versions of the LMO's shown in Figures 1a,b. Analysis shows, however, that this asymmetry is a mathematical artifact of the Boys criterion and is of no chemical significance.

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(15) The orientation of the substituent principally affects the transition-state energy. Thus, the PRDDO and MINDO/3 energies for **3b,c** and **3e,**f differ by only 0.2–3.1 kcal/mol.

(16) To more fully examine the sulfur-containing systems, semiempirical MNDO[17]-optimized structures were determined for **3**a–**i** and **4a**–i. More facile rearrangements were indeed predicted for the *exo*- and *endo-S*-oxides [ΔE(**4–3**) = 18.4 and 17.0 kcal/mol] than for Dewar thiophene (ΔE = 32.9 kcal/mol), and rearrangement of exo-NH **3b** (ΔE = 44.7 kcal/mol) was favored over that of endo-NH **3c** (ΔE = 55.3 kcal/mol). Unfortunately, certain results pertaining to the analogous oxygen systems seem implausible. Thus, further computational study of the relationship between the S and O rearrangements will have to be deferred until more sophisticated methods can be employed.

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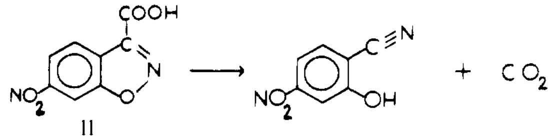
Decarboxylation Reactions: Reactivity of a Free Carboxylate Anion in Ethereal Solvents

Sir:

Because of their biological significance and synthetic prominence, decarboxylation reactions have been extensively studied in both protic and aprotic media. Studies by Verhoek et al.[1-3] showed that, in water mixtures with dioxane or alcohol, acids such as trinitrobenzoic acid or trichloroacetic acid decompose through the free carboxylate anion. More recent work by Kemp et al.[4,5] has demonstrated the unusually high solvent sensitivity of the decarboxylation of the tetramethylguanidinium (TMG) salt of benzisoxazole-3-carboxylic acids (I). This solvent sensitivity was also noticed by Hunter et al.[6] in crown ether induced decarboxylations of alkali salts of triphenylacetic acid and other carboxylic acids. In the latter system, ion pairing was found to be important since the reaction appears to proceed through the dissociated ions.

Dispersion interactions between solvent and the transition state have been advanced as the principal cause for the solvent sensitivity of the decarboxylation of benzisoxazole-3-carboxylates in aprotic media.[4] Similarities were noted in the solvent effects reported by Parker[7] for anionic reactants, although evidence was found that in the less polar solvents ion pairing of the TMG salt of I contributed to its reactivity in these solvents. In a recent study[8] on the decarboxylation of crown ether and cryptand complexes of the potassium salt of 6-nitrobenzisoxazole-3-carboxylic acid (II), we showed that the rate constant of the cryptated ion pair in benzene is nearly three orders of magnitude higher than the decarboxylation rate constant previously reported for the TMG$^+$ salt of II. It approaches the rate constant found for the latter salt in Me$_2$SO, suggesting that ion pairing plays a major role in determining the reactivity of these carboxylates in less polar solvents. We have now been able to determine the absolute rate constant of the free carboxylate anion of II in ethereal solvents. The results imply that the solvent effects in media such as benzene, tetrahydrofuran, and glymes are almost exclusively caused by ion pairing, the free ion rate constant of II in THF being even higher than in hexamethylphosphoramide.

In tetrahydrofuran, acid II itself slowly decomposes to form 2-cyano-5-nitrophenol, a product which can be monitored spectrophotometrically at 340 nm. However, while in benzene the decarboxylation kinetics for the crown complexed alkali carboxylates are perfectly first order,[8] a ln C_0/C vs. t plot for acid II in THF and other ethers curves upward. The reaction



II

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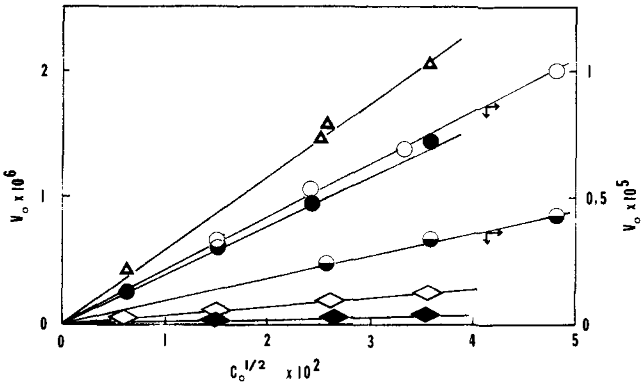

Figure 1. Concentration dependence of initial decarboxylation rate, v_0, of 6-nitrobenzisoxazole-3-carboxylic acid at 20 °C. Solvents: (△) 1,2-dimethoxyethane; (○) triglyme; (●) THF; (◒) diglyme; (◇) 2-methyltetrahydrofuran; (◆) tetrahydropyran.

is inhibited by small amounts of *p*-toluenesulfonic acid (PTSA) or salts like sodium tetraphenylboron. These observations suggest a decomposition mechanism via the free carboxylate anion (eq 1), similar to that previously suggested for carboxylic

$$\begin{array}{ccc} \mathrm{RCOOH} \rightleftharpoons \mathrm{RCOO^-,\ H^+\cdots S} \rightleftharpoons & \mathrm{RCOO^- + H^+\cdots S} & (1)\\ (K_1) & \downarrow k & \\ & \mathrm{RH(phenol) + CO_2} & \end{array}$$

acids in protic media[1,2] or for crown complexed alkali carboxylates[6] where S denotes a solvent molecule, e.g., THF.

The mechanism predicts the initial rate v_0 to be proportional to the square root of the initial acid concentration, C_0, as long as $[\mathrm{RCOO^-}] \ll [\mathrm{RCOOH}]$:

$$v_0 = kK_1^{1/2}C_0^{1/2} \tag{2}$$

The relationship is depicted in Figure 1 for several ether solvents in the concentration range $C_0 = 3.8 \times 10^{-5}$ to 1.3×10^{-3} M. The slopes of the straight lines chiefly reflect differences in the dissociation constants, K_1, of acid II in the respective ether solvents. These constants depend on the dielectric constants of these solvents as well as their basicity and specific structural features (e.g., interaction of H^+ with the two oxygen atoms of 1,2-dimethoxyethane).

Addition of the more dissociable PTSA provides a proton source which inhibits the decarboxylation of II by supressing its dissociation into free ions. Assuming a low degree of dissociation for both acid II and PTSA, the following relationship can be obtained

$$\frac{C_0}{v_0^2} = \frac{1}{k^2K_1} + \frac{K_2}{k^2K_1^2}\frac{[\mathrm{PTSA}]_0}{C_0} \tag{3}$$

where K_2 is the dissociation constant of PTSA and the other parameters and constants are the same as in eq 2. Note that the intercept of eq 3 is the same as the inverse of the square of the slope of eq 2. Equation 3 was tested at 2×10^{-4} M acid II by varying PTSA between 3×10^{-6} and 6×10^{-7} M. The results for several solvents are shown in Figure 2. In all cases the intercepts of the lines equal the inverse of the square of the slopes obtained from Figure 1. The agreement between these two independent measurements implies that the data are reliable in spite of the very low free carboxylate ion concentration present in these solutions. To obtain the rate constant, conductance measurements of PTSA in THF were carried out. A linear Fuoss plot was obtained for [PTSA] being $<4 \times 10^{-4}$ M. The slope of this plot, $1/K_2\Lambda_0^2$, yielded $K_2(20\ °\mathrm{C}) = 3.9 \times 10^{-12}$ M, where Λ_0 was computed by means of Walden's rule, using the measured value of $\Lambda_0 = 185\ \mathrm{cm^2\ \Omega^{-1}\ equiv^{-1}}$ in acetonitrile. The uncertainty in Λ_0 created by the necessity to use Walden's rule is probably not more than 25%. Combining the kinetic and conductance data gives a dissociation constant $K_1(20\ °\mathrm{C}) = 7.0 \times 10^{-15}$ M for acid II and a decarboxylation rate constant for the carboxylate anion in THF of $k(20\ °\mathrm{C}) = 450\ \mathrm{s^{-1}}$. Preliminary conductance data in other ether solvents give k values of the same order of magnitude.

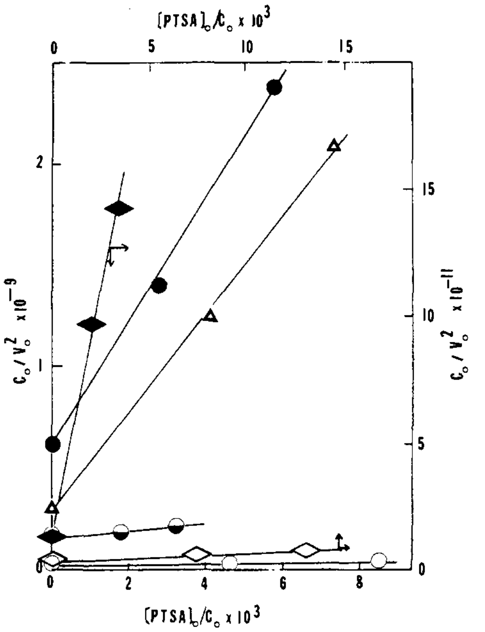

Figure 2. Plot of C_0/v_0^2 vs. $[\mathrm{PTSA}]_0/C_0$ at 20 °C. Solvents: (△) 1,2-dimethoxyethane; (○) triglyme; (●) THF; (◒) diglyme; (◇) 2-methyltetrahydrofuran; (◆) tetrahydropyran. The intercept data were calculated from the respective slopes of Figure 1; see text.

The decarboxylation rate constants for the TMG salt of II in THF, diglyme, Me_2SO, acetone, and HMPA at 20 °C were reported to be 1.0, 1.2, 2.5, 6.2, and 200 $\mathrm{s^{-1}}$, respectively (recalculated from rate constants given at 30 °C, $E_{\mathrm{act}} = 24$ kcal/mol; see ref 4). Our value $k = 450\ \mathrm{s^{-1}}$ found for the free carboxylate anion in THF implies that in ether-type solvents and probably in other solvents of low polarity, e.g., benzene, dichloromethane, ion pairing of the TMG salts of acids I is the dominating factor governing solvent effects on decarboxylation rate constants. The free ion rate constant in THF considerably exceeds the rate constant found for the TMG salt in Me_2SO and even that in HMPA, solvents in which this salt presumably is completely dissociated. This observation could explain the rate maxima found in mixtures of Me_2SO with benzene and diglyme.[4] Higher free ion rate constants in less polar solvents are consistent with the effect of ion–solvent dipole interactions in reactions involving charge delocalized transition states.

The use of acids in these studies rather than alkali carboxylates has distinct advantages since the salts are poorly soluble in less polar solvents and their crown ether induced decarboxylations appear to require water.[6] Both factors complicate interpretation of the kinetic data.

Crown ethers are known to promote the dissociation of acids in low polarity media,[9] and addition of benzo-15-crown-5 or benzo-18-crown-6 to acid II greatly accelerates its decomposition. Preliminary data again show a perfect square root dependence on acid concentration, and a rate enhancement which is solely due to an increase in the fraction of free carboxylate anions, even in dioxane.

Decarboxylations of other acids, combined with conductance measurements, are planned to explore the generality of the observed phenomena and to determine if present theoretical approaches to anion reactivity in aprotic media can adequately account for the solvent effects. The results should also be relevant to the reactivity behavior of carboxylate anions in bimolecular reactions.

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The Remarkable Catalytic Power of Glymes in Ester Aminolysis Carried Out in Nonpolar Media

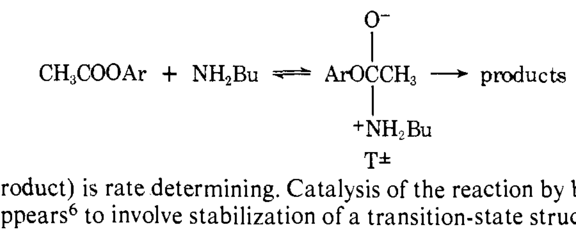
Sir:

Recently we reported[1] that crown ethers with pyridine rings incorporated into their macrocyclic arrays are very effective catalysts in the butylaminolysis of *p*-nitrophenyl acetate (*p*-NPA) in chlorobenzene. In an effort to elucidate the nature of the observed catalysis, we decided to systematically compare the catalytic efficacies of simple (unsubstituted) crown ethers (hereinafter referred to as crowns) with the catalytic efficacies of their open-chain analogues, oligo(ethylene glycol dimethyl ethers), viz., glymes.

Crowns are generally known[2] to be better complexing agents than glymes, and might therefore be expected to be better aminolysis catalysts as well. It is known,[3] for example, that in binding *tert*-butylammonium ion, 18-crown-6 is a better complexing agent than pentaglyme by a factor of $>10^4$. Thus the enforced convergence of binding sites (oxygens) provided by the crown results in an increase in stabilization in the complex of ~5.9 kcal/mol at 24 °C. It might be anticipated that a similar macrocyclic effect[2] should be observed for catalysis of reactions (such as aminolysis) involving ammonium-ion-like intermediates. Much to our surprise the glymes have turned out to better catalysts than the corresponding crowns! In addition, we have found that crowns with pyridine rings incorporated into their macrocyclic arrays were not as catalytically effective as unsubstituted crowns.

These results lead us to suggest that a flexible polyether species which can adapt is a better catalyst than a more rigid polyether which does not have the correct features for catalysis. The "guest" transition-state structure whose stabilization leads to catalysis prefers a "host" polyether with sufficient rotational freedom to adopt a conformation that results in catalysis. For macrocycles, this rotational freedom exists only in the larger rings.

Ester aminolysis carried out in a nonpolar solvent is believed[4,5] to involve the initial formation of a tetrahedral intermediate, T±, whose breakdown (in one or more steps to form



$$\mathrm{CH_3COOAr + NH_2Bu \rightleftharpoons ArO\overset{O^-}{\underset{^+NH_2Bu}{C}}CH_3 \longrightarrow products}$$

T±

product) is rate determining. Catalysis of the reaction by bases appears[6] to involve stabilization of a transition-state structure resembling T± by a catalyst, possibly via a hydrogen-bonded complex. Hydrogen bonding to or transfer of an ammonium proton in T± appears[6] to facilitate the expulsion of ArO$^-$. This type of catalytic role seems reasonable for crown and glyme catalysts in the light of the well-known[2] ability of crowns and glymes to complex with a wide variety of cations,[7-12] including ammonium ions.[2,3,8,11,12] However, secondary ammonium species such as T± are not complexed[12] well by 18-crown-6.

Table I. Catalytic Rate Constants for Butylaminolysis of *p*-NPA in Chlorobenzene at 25 °C

catalyst	$k' \times 10^3$ ($M^{-2}\,s^{-1}$)	k'_{rel}	$-RT \ln k'_{rel}$ (kcal/mol)[a]
1, $n = 2$	25 ± 6[b]	1.0	0.00
n = 3	123 ± 7	4.9	−0.94
n = 4	280 ± 20	11	−1.43
n = 5	340 ± 40	14	−1.55
n = 7	550 ± 10	22	−1.83
n = 8	590 ± 30	24	−1.87
n = 11	920 ± 30	37	−2.14
n = 22.3[c]	1,900 ± 100	76	−2.57
2, n = 2	16 ± 7	0.52	0.39
n = 4	70 ± 8	2.8	−0.61
n = 5	130 ± 10	5.2	−0.98
n = 6	220 ± 20	8.8	−1.29
n = 7	340 ± 20	14	−1.55
3, n = 5[d]	7 ± 2	0.29	0.74
n = 6[d]	27 ± 2	1.1	−0.046
n = 7[d]	62 ± 1	2.5	−0.54
4, n = 10[d]	210 ± 3	8.4	−1.26
n = 12[d]	290 ± 4	12	−1.45
n = 14[d]	430 ± 10	17	−1.69
dibenzo-18-crown-6[d]	34 ± 3	1.4	−0.18

[a] $\Delta\Delta G$ for pure catalytic pathway relative to monoglyme. [b] Standard error. [c] Based on the average molecular weight of Carbowax 1000. See ref 7 for preparation of dimethyl ether. [d] Taken from ref 1.

The kinetics of the butylaminolysis of *p*-NPA in PhCl followed the rate law[1,6]

$$k_{obsd} = k_0[\text{amine}]^2 + k'[\text{amine}][\text{catalyst}]$$

at 25 °C, where k_{obsd} was the pseudo-first-order rate constant for the decomposition of *p*-NPA. In practice the appearance of *p*-nitrophenol (a product of the aminolysis) was followed spectrophotometrically rather than the disappearance of *p*-NPA. Values of k' were obtained from plots of $k_{obsd}/[\text{amine}]$ vs. [catalyst]. Usually five determinations were made at each of five different concentrations of catalyst. Glymes (**1**, n = 2-5, 11, 22), crown ethers (**2**, n = 2, 4-6), and crown ethers with one or two pyridine rings incorporated into their macrocyclic arrays (**3**, n = 5-7, and **4**, n = 9, 10, 12, 14; respectively) were compared as catalysts for this reaction.

Our results are summarized in Table I and Figure 1. Table I lists the values of k' measured for the species **1**-**4**, and Figure 1 is a plot of these catalytic rate constants as a function of the number of oxygens, n, in the catalytic species. This plot is definitely linear through the glymes studied, and appears to curve gently upwards through the crowns. The significance of the curvature through the crowns and the linearity for the glymes is currently a topic for conjecture.[13] It is, however, interesting to speculate that the latter may arise from a linear relationship between the complexation constants of glymes complexed to some reactive intermediate (such as T±)[12b] and the number of oxygens per molecule in the glymes studied. In any case, the fact that the catalytic rate constants, on a per oxygen basis, decrease in going through the series **1** > **2** > **3** ≃ **4** seems to indicate to us that in order for a catalyst to be effective in this reaction it must have some conformational freedom. (The conformational freedom of the catalysts studied

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