

THE ROLE OF SOLVENT REORGANIZATION IN PROTON TRANSFER AND NUCLEOPHILIC ADDITION REACTIONS

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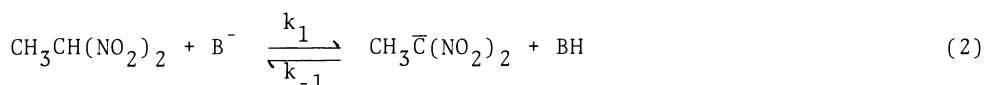
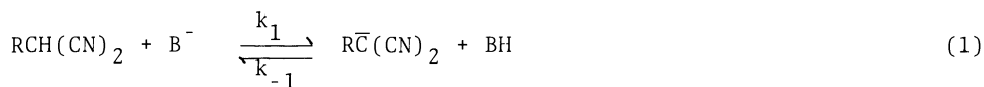
Abstract - The factors believed to be of primary importance in determining the intrinsic barrier and affecting transition state structure in proton transfers at carbon are critically reviewed. They include the absence of strong hydrogen bonding between carbon and solvent and the occurrence of extensive structural and solvent reorganization in going from reactants to products. Structural and solvent reorganization depend strongly on the activating substituent's capabilities in delocalizing or dispersing negative charge. Our recent work on nucleophilic additions to olefins and preliminary work on the addition of carbanions to aldehydes is then discussed. There exist both similarities and differences between nucleophilic additions and proton transfers. Similarities are expected since carbanions of similar structure are involved. Differences exist because in the olefin reactions the carbon bearing the activating groups remains essentially sp^2 -hybridized while in the proton transfers and the aldehyde reactions there is a change from sp^3 to sp^2 or vice versa. Our results indicate that solvent reorganization indeed plays a qualitatively similar role as in proton transfers. The influence of structural reorganization is also similar to that in proton transfers for the aldehyde reactions but in the olefin reactions it is affecting the kinetic barriers in the opposite direction.

INTRODUCTION

There seems to be an increasing awareness among chemists that meaningful discussions of structure-reactivity relationships should be based on both kinetic and equilibrium data rather than on kinetic data alone. This is because the rate of a chemical reaction is affected both by its thermodynamic driving force and by a purely kinetic parameter which is frequently called the "intrinsic barrier" (Refs. 1-4).

Let me illustrate this with an example. The rate constant for deprotonation of 1,1-dinitroethane by OH^- in water, $3.6 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ (Ref. 5), is virtually the same as that for deprotonation of *t*-butylmalononitrile by the same base, $4.3 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ (Ref. 6). Do these two compounds have the same intrinsic reactivity with respect to deprotonation by OH^- ? No, because the comparison is distorted by the fact that the reaction of 1,1-dinitroethane is thermodynamically more favored ($pK_a = 5.24$) than that of *t*-butylmalononitrile ($pK_a = 13.1$). The situation is best illustrated by the free energy profile of Fig. 1. For example, if a dicyano compound of the same pK_a as 1,1-dinitroethane could be studied it would be deprotonated much more rapidly than the latter (dashed line).

Hence, in order to obtain at least an approximate measure of relative intrinsic reactivities one should compare systems which have the same equilibrium constants. Better yet, one should try to eliminate the thermodynamic factor altogether and determine absolute intrinsic rate constants, k_0 , or intrinsic barriers, ΔG_0^\ddagger , by comparing systems for which the equilibrium constants are unity ($\Delta G_0^\circ = 0$). In practice, k_0 is obtained by interpolation or extrapolation of $\log k$ versus $\log K$ plots as shown schematically in Fig. 2 for reactions 1 and 2. Based on the data by Hibbert et al. (Ref. 6) and Bell et al. (Ref. 5) one obtains $k_0 \approx 10^7 \text{ M}^{-1} \text{ s}^{-1}$ ($\Delta G_0^\ddagger \approx 7.9 \text{ kcal/mole}$) for reaction 1, $k_0 \approx 10 \text{ M}^{-1} \text{ s}^{-1}$ ($\Delta G_0^\ddagger \approx 16.0 \text{ kcal/mole}$) for reaction 2. It should be noted that, in keeping with Marcus (Ref. 2), our definition of



ΔG_0^\ddagger does not distinguish between intrinsic barrier and work terms (Refs. 7, 8) but includes them both.

INTRINSIC BARRIERS IN PROTON TRANSFERS

There exists a substantial body of data on proton transfers at carbon which permits the determination of k_0 or ΔG_0^\ddagger values. We have calculated these parameters for a representative number of C-H acids and summarized them in Table 1. By way of comparison, $\log k_0 \approx 9.5-10.0$ ($\Delta G_0^\ddagger \approx 3.8-4.5$ kcal/mole) for typical "normal" acids (Ref. 15).

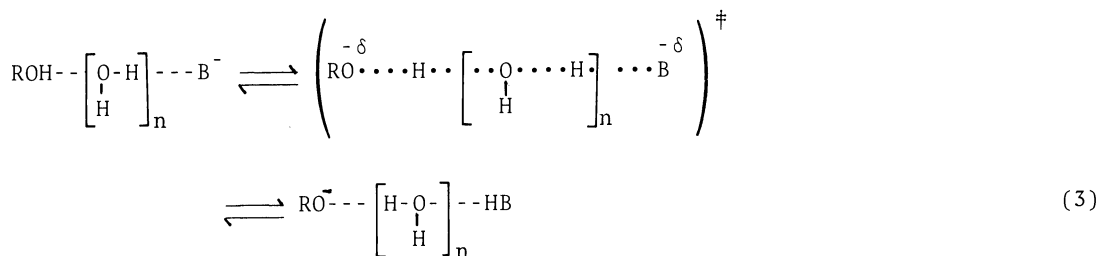
TABLE 1. $\log k_0$ and ΔG_0^\ddagger for proton transfers involving various classes of C-H acids in protic solvents.

C-H acid	Solvent	$\log k_0$	ΔG_0^\ddagger kcal/mole	Source
RCH(CN)_2	H_2O	7.0	7.9	Ref. 9
$4\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{CN}$	H_2O	$\approx 3.1^a$	≈ 13.1	Ref. 10
$2,4\text{-(NO}_2)_2\text{C}_6\text{H}_3\text{CH}_2\text{CN}$	50% Me_2SO -50% H_2O	3.0	13.3	Ref. 11
RCH(COR')COR''	H_2O	2.4	14.1	Ref. 12
9-X-Fluorene	MeOH	$\approx 2.0^b$	≈ 14.7	Ref. 13
$\text{CH}_3\text{CH(NO}_2)_2$	H_2O	1.0	16.0	Ref. 5
PhCH_2NO_2	H_2O	-1.5	19.4	Ref. 14

^aEstimated from detritiation rates assuming a tritium kinetic isotope effect of 14.

^bEstimated based on reaction of 9-COCH₃-fluorene with MeO^- and assuming $d \log k/d \log K = 0.5$.

In the early discussions (Refs. 15, 16) as to the possible reasons why the intrinsic barriers for C-H acids are so much higher than for "normal" acids (Ref. 15) two major factors were stressed. The first was that the poor hydrogen bond donor and acceptor properties of the carbon acids and bases prevent their entering into the hydrogen bond network of the solvent. Thus the proton-jump mechanism (Ref. 15) typical for normal acids shown in eq 3



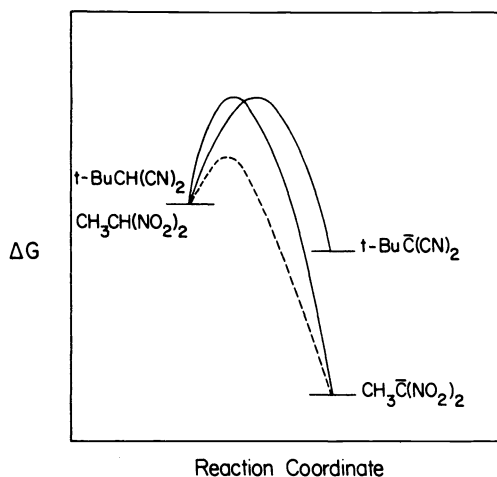


Fig. 1

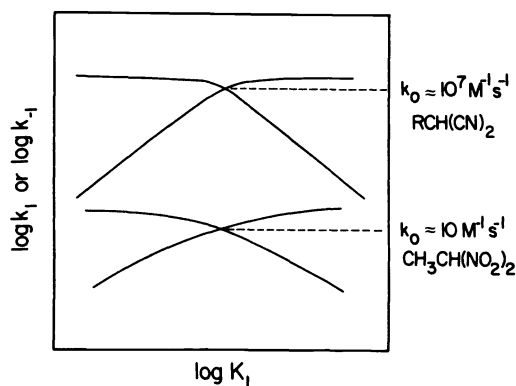


Fig. 2

Fig. 1. Schematic representation of free energy vs. reaction coordinates for the deprotonation of 1,1-dinitroethane and of t-butylmalononitrile. Dashed line: deprotonation of a hypothetical dicyano compound of the same pK_a as 1,1-dinitroethane.

Fig. 2. Determination of k_0 for reactions 1 and 2 from $\log k$ vs $\log K$ plots.

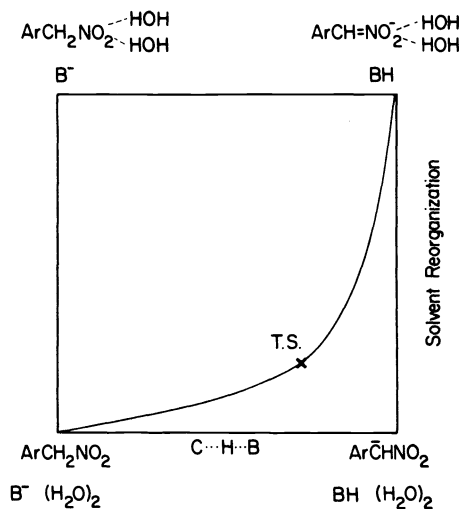


Fig. 3

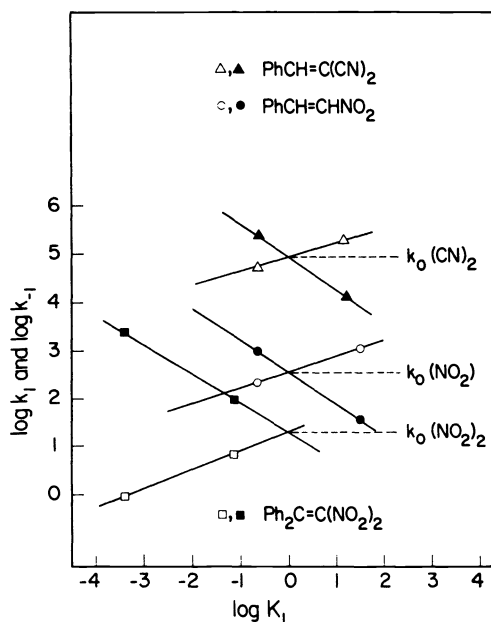


Fig. 4

Fig. 3. Structure-reactivity diagram for nitroalkanes with separate axes for C-H bond cleavage/formation and type II solvent reorganization (assumed to be synchronous with structural reorganization).

Fig. 4. Reactions of morpholine and piperidine with activated olefins. Open symbols refer to k_1 , filled symbols to k_{-1} .

i.e., type I reorganization) for a nitroalkane and is to be contrasted with eq 3. In cases where the negative charge in the carbanion is more dispersed, e.g., with the nitriles or fluorenes, dipole-dipole interactions probably become dominant.

It is this second type of solvent reorganization we shall be mainly concerned with. Since it involves the motion of solvent molecules along the reaction coordinate the question of timing becomes an interesting one, i.e., is the solvent reorganization synchronous or not with structural reorganization? Evidence presented below indicates that solvent reorganization can indeed lag behind structural reorganization in one direction and be ahead of it in the reverse direction. Our representation of the transition state in eq 4 in which no hydrogen bonding to the nitro oxygens is shown takes this feature into account.

SOLVENT EFFECTS ON PROTON TRANSFERS

Traditional notions about solvent effects on reactions are based on the implicit assumption that the transition state, just as a stable species, is at equilibrium with the solvent, or that solvent reorganization is synchronous with say electronic reorganization such as charge development. Type II solvent reorganization does not require this assumption and is therefore a concept which has not yet been generally accepted by chemists.

What is the experimental evidence for it? Since solvent reorganization has much to do with the breaking and reforming of hydrogen bonds one would anticipate that a change from a protic to an aprotic solvent should lead to a significant decrease in ΔG_0^\ddagger or an increase in k_0 . Such increases in k_0 have in fact been observed, notably in Me_2SO or Me_2SO -water mixtures. Representative examples where the solvent effect on k_0 could either be determined directly or where the data at least allowed us to estimate the ratio $k_{\text{aprotic}}/k_{\text{protic}}$ are summarized in Table 2. We note that the solvent effect increases in the order dicarbonyl < dinitro < nitro, with the 9-X-fluorenes probably somewhere between the dinitro and dicarbonyl compounds. This is precisely the order observed for ΔG_0^\ddagger in protic media (Table 1).

Do these results really prove that solvent reorganization and in particular type II reorganization is involved or is there possibly a different interpretation? Cox and Gibson (Refs. 24, 27) indeed offer a more traditional view according to which k_0 increases because the reactants (oxyanion base) and products (e.g., 2) are destabilized in the aprotic solvent (Ref. 28) while the transition state whose negative charge is more dispersed is less severely affected by the change in solvent.

A comparison between the solvent effects on k_0 (Table 2) with the effect of changing from water to Me_2SO on the pK_a of carbon acids (Table 3) is revealing in this context. The solvent effect on pK_a shows very nicely the trend from the most effective charge dispersion in the fluorenyl anions ($\Delta\text{pK} = -5.5$, strong stabilization in Me_2SO) to the most extreme charge concentration onto oxygen in the nitronate ion ($\Delta\text{pK} = 7.0$, strong stabilization in water), with the other compounds falling in between. If one focuses just on the nitroalkanes and the β -dicarbonyl compounds one notices that the $\Delta\text{pK} \approx 3-4$ for the latter is approximately half that for the nitroalkanes. The same relative order holds true for the solvent effects on k_0 for the respective carbon acids: e.g., $\Delta\log k_0 \approx 0.8-1.0$ for the dicarbonyl, $\Delta\log k_0 = 2.16$ for the nitro compound at a $\chi_{\text{Me}_2\text{SO}} = 0.39$. This correlation would seem consistent with the traditional view on solvent effects and we believe that this is likely to be part of the picture.

However it cannot be the whole story. For example, the solvent effect on k_0 for 1,1-dinitroethane is almost as large as that for the nitroalkane yet the solvent effect on pK_a is very small ($\Delta\text{pK} = 1.4$). Worse yet, for the 9-X-fluorenes the solvent effect on pK_a suggests that there would probably be more charge dispersion in the product anion than in the transition state which should lead to a decrease for k_0 in Me_2SO . Experimentally a 100-fold increase was observed. These observations indicate that solvent reorganization as visualized by Caldin and Ritchie must be important. For the 1,1-dinitroalkane it is probably mainly type II reorganization which causes the solvent effect on k_0 . For the fluorenes Ritchie (Ref. 13) has also argued in favor of type II reorganization. However, in light of more recent work (Refs. 35, 36) which shows a significant rate depressing effect caused by

TABLE 2. Effect of Me₂SO on k_o for proton transfers

Reaction ^a	X _{Me₂SO}	$\frac{\Delta \log k_o = \log(k_o^{\text{aprotic}}/k_o^{\text{protic}})}{\log(k_o)}$	Source
CH ₃ COCH(Me)COOEt + AcO ⁻	0.20	≈0.4-0.5 ^b	Ref. 24
	0.39	≈0.8-1.0 ^b	Ref. 24
9-X-Fluorenes + MeO ⁻ (MeOH)	1.0	≈2.0	Ref. 13
9-X-Fluorenes + ArCOO ⁻ (Me ₂ SO)			
CH ₃ CH(NO ₂) ₂ + RCOO ⁻ , ArO ⁻	0.20	1.0	Ref. 25
CH ₃ CH ₂ NO ₂ + ArO ⁻	0.20	1.14	Ref. 24
	0.39	≈2.16	Ref. 24
ArCH ₂ NO ₂ + PhCOO ⁻	1.0	≈5.0	Ref. 26

^aProtic solvent is water except for 9-X-Fluorenes.

^bEstimates required relatively large extrapolations.

TABLE 3. Solvent effects on pK_a

Compound	pK _a (H ₂ O)	pK _a (Me ₂ SO)	ΔpK ^a	Source
9-COOEt-Fluorene	15.8 ^b	10.3	-5.5	Refs. 13, 19
4-NO ₂ C ₆ H ₄ CH ₂ CN	13.4	12.3	-1.1	Refs. 29, 30
CH ₂ (CN) ₂	11.1	11.0	-0.1	Refs. 31, 32
CH ₃ CH(NO ₂) ₂	5.2	6.6	1.4	Refs. 5, 27
CH ₂ (COOEt) ₂	13.3	16.4	3.1	Refs. 33, 34
CH ₂ (COCH ₃) ₂	9.0	13.4	4.4	Refs. 33, 34
CH ₃ NO ₂	10.2	17.2	7.0	Refs. 33, 34
PhCOOH	4.2	11.0	6.8	Ref. 34

^aΔpK = pK_a(Me₂SO) - pK_a(H₂O)

^bIn MeOH.

the very strong solvation of highly basic oxyanions (MeO⁻) it appears that the increase in k_o seen in changing from the system MeO⁻ in methanol to ArCOO⁻ in Me₂SO may be due, at least in part, to type I solvent reorganization.

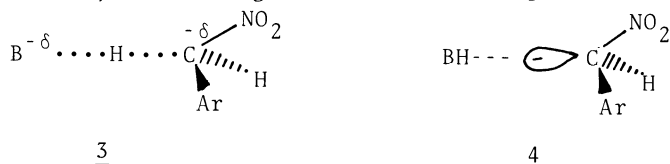
Another indication that solvent motion must be an integral part of the reaction coordinate comes from kinetic deuterium isotope effect studies. Caldin and Wilson (Ref. 37) showed that the isotope effect on the deprotonation of 4-nitrophenylnitromethane depends dramatically on the solvent. They argued that the effective mass of the proton is increased by a coupling between solvent motion and proton transfer, an effect which becomes increasingly important as solvent polarity increases.

TRANSITION STATE IMBALANCES IN PROTON TRANSFERS

Perhaps the strongest piece of evidence demonstrating type II solvent reorganization is the observation that substituent effects on the rate of proton transfer involving nitroalkanes are larger than the substituent effects on the equilibrium, a phenomenon known as the nitroalkane anomaly (Refs. 38-40). For example, in the deprotonation of arylnitromethanes by OH⁻

or by amines in aqueous solution the Bronsted α value is larger than unity ($\alpha = 1.54$ for OH^- , 1.29 for morpholine) and, as a consequence, the β -value in the reverse direction is negative.

Various interpretations have been offered (Refs. 38-42) but most of them boil down to a description of a transition state in which the negative charge is mostly localized on carbon whose geometry is essentially pyramidal as shown in 3. Thus, even though the amount of negative charge transferred from the



base to the nitroalkane is less than in the product anion, it is located much closer to the aryl substituent. This is further accentuated by the fact that in the product the negative charge is partially dispersed by the solvent (see eq 4). As a consequence, the aryl substituent "sees" more negative charge in the transition state than in the product and this leads to a $\alpha > 1$.

Bordwell (Ref. 39, 40) has gone one step further and suggested that there is actually an intermediate or "virtual intermediate," 4 whose formation, via 3, is rate limiting. Whether there is an intermediate or not, the interpretation of the nitroalkane anomaly remains essentially the same. The idea that a discrete intermediate may exist is supported by the observation of two forms of the anion generated by deprotonation of 4-nitrophenylacetonitrile in Me_2SO -water mixtures. According to Walters (Ref. 43) one form is specifically solvated by hydrogen bonding to the nitro group while the other is not, with the former being dominant in highly aqueous Me_2SO , the latter becoming dominant at higher Me_2SO .

Turning back to the nitroalkane anomaly one wonders why in the transition state the negative charge would rather be located on carbon where it cannot benefit from hydrogen bonding solvation, or why the reaction might even go through an unstable intermediate like 4. This behavior suggests that for the charge to be shifted from carbon to oxygen the solvent molecules must already be in correct alignment for the formation of the hydrogen bonds, or the hydrogen bonds must already be preformed. This process has apparently not occurred when the transition state is reached, i.e., type II solvent reorganization lags behind C-H bond breaking. For the reverse reaction this implies that the charge can only be shifted back to carbon as (or after) the hydrogen bonds are being broken. The situation may be described by a curved reaction coordinate on a structure-reactivity diagram (Ref. 35) which has separate axes for C-H bond cleavage/formation and for type II solvent reorganization as shown in Fig. 3. Note that this diagram implies that structural and solvational reorganization is essentially synchronous; if, on the other hand, C-H bond cleavage were synchronous with solvent reorganization the reaction coordinate would be diagonal.

Strong evidence that the nitroalkane anomaly is indeed mainly caused by a lag in type II solvent reorganization comes from the observation that in Me_2SO there is not only a large decrease in ΔG_0^\ddagger but that α is reduced to 0.92 for the reaction of ArCH_2NO_2 with benzoate ion (Ref. 26). Agmon (Ref. 44) has interpreted this solvent effect along similar lines by making use of the Marcus (Ref. 1-4) formalism which dissects ΔG_0^\ddagger into work terms (which refer essentially to solvent reorganization) and the intrinsic barrier (Refs. 7, 8) for the actual proton transfer. However, his treatment emphasizes type I solvent reorganization (desolvation of the base) more than we have.

It should be pointed out that similar, though less dramatic, manifestations of what presumably is a lag in solvent reorganization have been observed in the deprotonation of β -dicarbonyl compounds (Ref. 45). In these reactions the lag is diagnosed by a Bronsted α -value determined by varying the acidity of the C-H acid which is larger than the Bronsted β -value determined by varying the pK_a of the deprotonating base. This imbalance in the transition state indicates that the apparent charge "seen" by the substituent on the carbon acid is larger than that "seen" by the base. In this context the nitroalkane anomaly is just an extreme manifestation of a transition state imbalance where α is not only larger than 1 but where it falls outside the normal range. If $I = \alpha - \beta$ is accepted as a measure of the imbalance the

data summarized in Table 4 show clearly the expected trend $\text{NO}_2 > \text{CO} > \text{CN}$; in fact for the malononitrile derivatives no imbalance is observed.

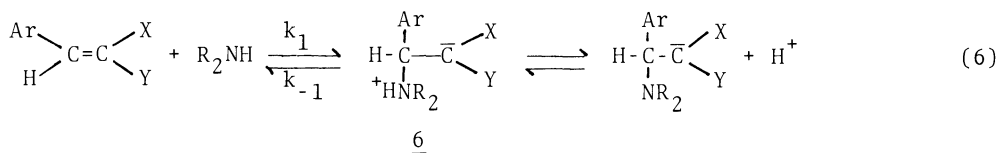
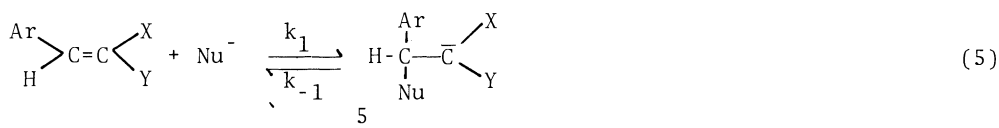
TABLE 4. Transition state imbalances in proton transfers.

Reaction	$\alpha(\text{pK}_a^{\text{CH}})$	$\beta(\text{pK}_a^{\text{BH}})$	$I=\alpha-\beta$	Source
$\text{ArCH}(\text{CN})_2 + \text{RCOO}^-$	0.98	≈ 1.0	≈ 0	Ref. 45
$\text{ArCH}_2\text{CH}(\text{COMe})\text{COOEt} + \text{RCOO}^-$	0.76	0.44	0.32	Ref. 45
$\text{ArCH}_2\text{NO}_2 + \text{R}_2\text{NH}$	1.29	0.55	0.74	Ref. 38
$\text{ArCH}_2\text{NO}_2 + \text{OH}^-$	1.54			Ref. 38
$\text{ArCH}_2\text{NO}_2 + \text{PhCOO}^- (\text{Me}_2\text{SO})$	0.92			Ref. 26

INTRINSIC BARRIERS IN NUCLEOPHILIC ADDITIONS TO OLEFINS

About five years ago we began to study nucleophilic additions to activated olefins. The reactions with anionic nucleophiles can be represented by eq 5, those with amines by eq 6. In the latter reactions the proton transfer step usually, but not always, equilibrates much more rapidly than the first step. In either case we were able to determine both k_1 and k_{-1} (and thus K_1) for a number of examples.

The processes shown in eq 5 and 6 constitute important elementary reactions in organic chemistry. Apart from being of interest in their own right (Refs. 46, 47) they also model crucial steps in nucleophilic vinyl substitutions (Refs. 48, 49) and in E1cB-elimination reactions (Ref. 50). Their scope is thus quite broad.



Inasmuch as the carbanions 5 and 6 are very similar to the carbanions formed in the deprotonation of the corresponding C-H acids one anticipates that our understanding of proton transfers may help in the interpretation of structure-reactivity effects in nucleophilic additions, and also, conversely, that a study of these olefin reactions can add to our understanding of proton transfers.

Figure 4 shows some representative data for the reactions of secondary amines with benzylidenemalononitrile, β -nitrostyrene and 1,1-dinitro-2,2-diphenyl-

ethylene in 50% Me₂SO-50% water. For any given olefin the variation in log k₁, log k₋₁ and log K₁ was achieved by varying the amine from morpholine to piperidine. Log k₀ values determined from these, and other similar, plots are summarized in Table 5 while similarly obtained values for the OH⁻/H₂O nucleophile pair are summarized in Table 6. We note the following patterns.

TABLE 5. Log k₀ for the addition of morpholine and piperidine to olefins.

	H ₂ O	Me ₂ SO-H ₂ O (x _{Me₂SO} =0.2) ^a	CH ₃ CN	Source
PhCH=C(CN) ₂	4.60 ^c	4.94		Ref. 51, 52
4-Me ₂ NC ₆ H ₄ CH=C(COO) ₂ C(CH ₃) ₂	(≈3.6) ^b		4.1	Ref. 53, 54
PhCH=CHNO ₂	2.05	2.55		Refs. 55, 56
PhCH=C(CN)C ₆ H ₃ -2,4-(NO ₂) ₂		1.98 ^c		Ref. 57
Ph ₂ C=C(NO ₂) ₂		1.25		Ref. 58

^aCorresponds to 50% Me₂SO-50% water (v/v)

^bUncertain due to large extrapolation involved.

^cPreliminary result.

TABLE 6. Log k₀ for the addition of water and hydroxide ion to olefins.

	H ₂ O	Me ₂ SO-H ₂ O (x _{Me₂SO} =0.2) ^a	Source
PhCH=C(CN) ₂	≈0.6 ^c		Ref. 59
PhCH=C(COO) ₂ C(CH ₃) ₂	0.2		Ref. 60
ArCH=CHNO ₂ ^b	-2.1		Ref. 61
Ph ₂ C=C(NO ₂) ₂		-2.6	Ref. 62

^aCorresponds to 50% Me₂SO-50% water (v/v)

^b3,4-methylenedioxy-β-nitrostyrene

^cPreliminary result.

(1) The order for k₀ is dicyano > dicarbonyl > nitro just as for the proton transfers but the quantitative differences are smaller than in proton transfers. For example, Δlog k₀ for dicyano versus nitro is 2.4 for amine addition, 2.7 for OH⁻/H₂O addition while for proton transfer it is ≈8.5.

(2) A change from water to 50% aqueous Me₂SO enhances log k₀ by 0.5 for the amine reactions with β-nitrostyrene while the much more drastic change from water to acetonitrile has about the same effect (Δlog k₀ ≈ 0.5) on the reaction of the Meldrum's acid derivative. This indicates an intrinsically larger solvent effect on k₀ for nitro as compared to dicarbonyl activation, which is qualitatively similar to the situation in proton transfer. Again though, quantitatively the effects seem significantly smaller: for x_{Me₂SO} = 0.2 Δlog k₀ = 0.5 for addition to β-nitrostyrene while Δlog k₀ = 1.14 for deprotonation of nitroethane by acetate ion.

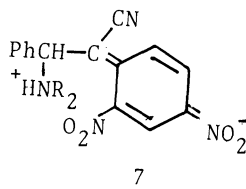
(3) The solvent effect on k₀ for the reactions of benzylidenemalonitrile with amines (Δlog k₀ = 0.34) is only slightly smaller than for β-nitrostyrene

($\Delta \log k_0 = 0.5$).

(4) In contrast to proton transfer k_0 for cyano-2,4-dinitrophenyl (Table 5) and 1,1-dinitro activation (Tables 5 and 6) is lower than for nitro activation.

In trying to understand these patterns we need to focus both on what the two types of reactions have in common and in what respects they might differ. Based on the similarity in structure of the carbanions formed one would anticipate type II solvent reorganization to play a qualitatively, though not necessarily quantitatively, similar role in both types of reactions. The smaller solvent effects on k_0 in the olefin reactions suggest in fact that the effect of type II solvent reorganization is attenuated.

Structural reorganization, on the other hand, is quite different in the two types of reactions. In the olefin reactions the carbon bearing the activating substituents is sp^2 -hybridized in the reactant state while for proton transfer it is sp^3 -hybridized. Thus for the olefin reactions there will be less structural reorganization around this carbon. What reorganization there is will in fact be most pronounced for the nitriles since the carbanion has some sp^3 -character and this will tend to counteract the effects of solvational reorganization. The fact that the order cyano > dicarbonyl > nitro for k_0 is maintained in the olefin reactions but that the differences in k_0 are rather small may then be taken to mean that the effect of solvent reorganization overrides the effects of structural reorganization. This conclusion does not apply to all activating groups, though. The lower k_0 for nucleophilic addition to α -cyano-2,4-dinitrostilbene compared to β -nitrostyrene which contrasts with the opposite sequence for the corresponding proton transfers seems to indicate that structural reorganization may be more important here. This can probably be understood in terms of resonance structure 7:



the delocalization of the negative charge requires a large number of bond length changes which add greatly to the amount of structural reorganization.

The situation with dinitro activation is more ambiguous. PLNM calculations for proton transfers indicate less structural reorganization for dinitroalkanes than for nitroalkanes (Ref. 3). Hence it is not clear why $\text{Ph}_2\text{C}=\text{C}(\text{NO}_2)_2$ should have a higher intrinsic barrier towards nucleophilic attack than β -nitrostyrene (Table 6). As molecular models indicate, the extra phenyl group in $\text{Ph}_2\text{C}=\text{C}(\text{NO}_2)_2$ probably hinders the establishment of complete coplanarity of the two nitro groups in the adduct. As a consequence part of the negative charge may reside on carbon which would have some sp^3 -character. This would require more structural (bond angles) reorganization in going from the olefin (sp^2) to the adduct just as for $\text{PhCH}=\text{C}(\text{CN})_2$. Enhanced proton transfer rates at the carbon of the OH-adduct of $\text{Ph}_2\text{C}=\text{C}(\text{NO}_2)_2$ support this view (Ref. 62). Incidentally, it has been suggested (Ref. 44) that even in ions derived from much less crowded 1,1-dinitroalkanes complete coplanarity of the two nitro groups may not be achieved. This could be part of the reason why the pK_a of 1,1-dinitroethane increases by only 1.4 units from water to Me_2SO (Table 3).

The fact that k_0 for amine addition to $\text{PhCH}=\text{C}(\text{CN})_2$ increases almost as much ($\Delta \log k_0 \approx 0.34$) as for $\text{PhCH}=\text{CHNO}_2$ ($\Delta \log k_0 = 0.5$) in going from water to 50% Me_2SO -50% water is noteworthy. This contrasts with the solvent effect on the equilibrium constant, K_1 , for the two olefins: K_1 for $\text{PhCH}=\text{CHNO}_2$ decreases nearly 20 fold while for $\text{PhCH}=\text{C}(\text{CN})_2$, it increases about 4-fold in the less aqueous solvent. The results for $\text{PhCN}=\text{C}(\text{CN})_2$ are reminiscent of the relatively large increase in k_0 for proton transfer in systems (fluorenes, 1,1-dinitroethane) where the solvent effect on pK_a would have suggested a decrease in k_0 according to classic solvent effect theory. Hence, just as for the proton transfer, our results can be interpreted as being a manifestation of solvent reorganization.

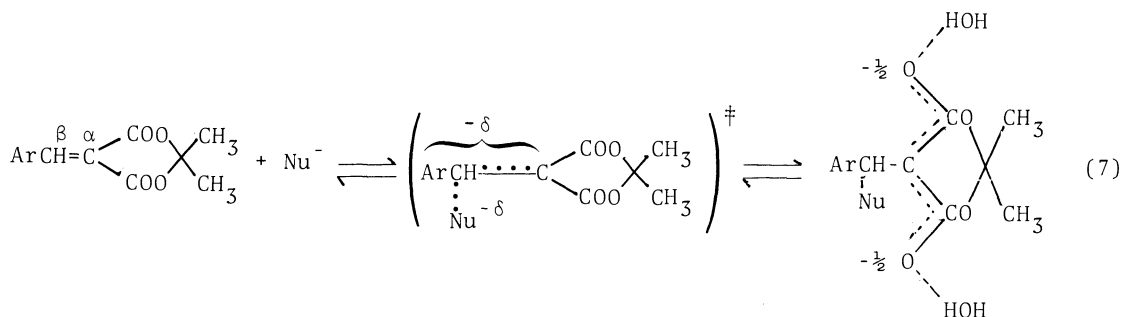
TRANSITION STATE IMBALANCES IN NUCLEOPHILIC ADDITIONS TO OLEFINS

One of the most compelling pieces of evidence demonstrating type II solvent reorganization in proton transfers was the observation of transition state imbalances in protic solvents. Table 7 summarizes structure-reactivity parameters which show that similar imbalances occur with olefins. ρ_n is a normalized Hammett ρ -value, obtained by varying the substituent in the Ar-group; it is defined as $\rho(k_1)/\rho(K_1)$ and is equivalent to α in the proton transfers, while β_{nuc}^n is a normalized β_{nuc} -value and corresponds to β in the proton transfers.

TABLE 7. Transition state imbalances in nucleophilic additions to olefins.

Reaction	ρ_n	β_{nuc}^n	$I = \rho_n - \beta_{nuc}^n$	Source
$ArCH=C(COO)_2C(CH_3)_2 + ArO^-(H_2O)$	0.59	0.39	0.20	Ref. 63
$ArCH=C(COO)_2C(CH_3)_2 + R_2NH(H_2O)$	0.42	0.08	0.34	Ref. 53
$ArCH=C(COO)_2C(CH_3)_2 + R_2NH(CH_3CN)$	0.53	0.43	0.10	Ref. 54

We note the following features: (1) There is a relatively large imbalance for the reactions of $ArCH=C(COO)_2C(CH_3)_2$ in water. This imbalance can be described in a similar way as that in proton transfers, i.e., some of the negative charge of the attacking nucleophile might tend to be localized on either the α - or β -carbon and/or be delocalized into the aryl group while in the adduct most of this charge is shifted onto the $(COO)_2C(CH_3)_2$ -moiety and/or dispersed by the solvent (eq 7). One would expect, though, that



since the α -carbon is not tetrahedral (sp^3) in the reactant it would not acquire much sp^3 -character in the transition state either and thus a build-up of negative charge away from the $(COO)_2C(CH_3)_2$ -moiety might be more difficult than in a comparable proton transfer reaction. Possibly the negative charge is located on the carbonyl oxygens even in the transition state but hydrogen bonding and with it charge dispersion by the solvent has not developed yet. The evidence on this point is inconclusive. The observation that the imbalance $I = 0.20$ for aryloxide ion attack is smaller than $I = 0.28$ for deprotonation of $ArCH_2CH(COMe)COOEt$ by $RCOO^-$ might be taken in support of this view but $I = 0.34$ for amine addition is larger than for proton transfer. Even though this latter value can probably be accounted for by an electrostatic effect of the positive charge on nitrogen (Ref. 63) there is another problem in comparing I -values for the two types of reactions. It is that ρ_n not only responds to the negative charge but also to the loss of conjugation between the aryl group and the activated $C=C$ double bond in the olefin (Refs. 53, 63). One should therefore not attach too much significance to the quantitative comparison of these I -values.

(2) When the solvent is changed from water to acetonitrile the imbalance in the $ArCH=C(COO)_2C(CH_3)_2$ reactions is greatly reduced. This is similar to the reduction of the imbalance in nitroalkane deprotonations and shows again the important role played by type II solvent reorganization.

CONCLUSIONS

Two major factors which affect the intrinsic barrier in proton transfers are structural and solvational reorganization which occurs during the reaction. This latter seems to be the dominant factor in protic solvents. Evidence based on solvent effects and on transition state imbalances indicates that this solvent reorganization occurs as a separate motion along the reaction coordinate which in some cases (nitroalkanes) is strongly decoupled from other processes such as bond formation and cleavage. This notion of a decoupling between solvent motion and other structural changes occurring during a reaction is an important one which has not been generally accepted by chemists.

Much less systematic work exists which would show how structural and solvent reorganization affect intrinsic barriers in nucleophilic additions to olefins and the addition of carbanions to carbonyl compounds. From the limited results which are available we have drawn the tentative conclusion that these two factors are also important in these reactions. In the carbonyl additions the two factors seem to operate in the same direction as in the proton transfers, producing large substituent effects on $\Delta G_{\text{O}}^{\ddagger}$ as in proton transfers. In the olefin reactions structural reorganization opposes solvent reorganization; this results in smaller substituent effects on $\Delta G_{\text{O}}^{\ddagger}$ and some reversals in the rank-ordering of substituents. It is clear that much more work is needed to put our tentative conclusions on firmer ground. Work to that end is in progress in my laboratory.

Viewed in a broader context it appears that the factors which determine reactivity and transition state structure in the reactions discussed in this talk, especially the role played by solvent reorganization, are also important in other reactions. For example, Ritchie (Ref. 65) has stated that "all patterns of reactivity and selectivity in $\text{S}_{\text{N}}2$ reactions arise primarily from solvent and not from some inherent property of the solute reactants." Arnett's (Ref. 66) recent work on the Menschutkin reaction demonstrates convincingly that solvent reorganization is indeed of paramount importance in this $\text{S}_{\text{N}}2$ reaction. Similarly, Ritchie (Ref. 67) believes that solvent reorganization is responsible for virtually the entire barrier in reactions of cations with anions in solution, a notion supported by theoretical calculations.

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