Imidate Anions: Stereochemistry, Equilibrium, Nitrogen Inversion, and Comparison with Proton Exchange

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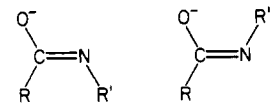
Soluble imidate anions, especially formimidate anions, $HC(O^-)=NR$, can be prepared by treating the amide with NaH or KH in THF or Me_2SO. *N*-Phenylformimidate anion can also be prepared in hydroxylic solvents by treating the amide with excess NaOH. The imidate anions have been characterized by proton NMR. The *E* stereoisomer is generally more stable than the *Z*, but the *E*/*Z* equilibrium constant is strongly solvent dependent. The results are compared with previous studies of base-catalyzed proton exchange. According to saturation-transfer measurements, the barrier to nitrogen inversion in these imidate anions is 19–23 kcal/mol. The imidate anions could be protonated by trifluoroethanol to regenerate the amide as a nonequilibrium *E*/*Z* mixture, which then returned to equilibrium at a measurable rate.

Introduction

Amides occupy a central position in the history of the study of stereochemistry by nuclear magnetic resonance.[1] The conjugate acids of amides continue to be a focus of research.[2] It is therefore surprising that scant attention has been paid to imidate anions **1E** and **1Z**, the conjugate

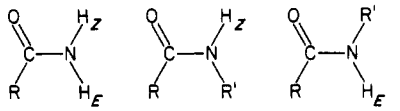


1E **1Z**

bases of amides. Far more effort has been devoted to *N*,*N*-dialkylamide[3] and amidine[4] conjugate bases that are obtained by deprotonation from carbon.[4] In some cases (*N*-alkyl amides[5]) an additional equivalent of base was needed in order to remove the more acidic NH proton, so that an imidate anion was formed incidentally. However, imidate anions themselves have not been studied or characterized, and they pose two fundamental stereochemical questions: (1) What is the position of the equilibrium between **1E** and **1Z**? (2) What is the rate at which that equilibrium is established? In enolates,[6] which are isoelectronic, and in thioimidate anions[7] and some anilides and related aromatics,[8] which are analogous, these questions have been answered, but not in imidate anions.

Imidate anions are of considerable and wide-ranging importance. Their formation complicates the kinetics of base-catalyzed amide hydrolysis,[9] although few pK_as of amides are known.[10] Imidate anions can be alkylated on nitrogen, even though the negative charge resides chiefly on oxygen.[11] Imidate anions are particularly significant for peptides and proteins, whose backbones complex only weakly to metal ions. In contrast, the imidate anions formed through deprotonation do complex strongly to a wide variety of metal ions.[12] Indeed, the color of the Cu(II) complex of imidate anions is the basis for the classic "biuret test" for peptides and proteins.

Imidate anions are the intermediates in base-catalyzed proton exchange of amides. This is a reaction that has long been used to probe protein structure and protein dynamics.[13] We have studied[14] the stereochemical aspects of this exchange, in both primary amides **2** and secondary amides



2 **3E** **3Z**

3E ⇌ **3Z**, where NMR techniques permit the determination of the relative reactivities of H_E and H_Z. In primary amides we have observed that exchange of H_E is generally faster than exchange of H_Z, although there are exceptions, and the reactivity order reverses in nonpolar solvents. In secondary amides it is H_Z that is generally faster than H_E. These relative reactivities have been interpreted in terms

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of the *supposed* relative stabilities of the stereoisomeric imidate anions (**1E**, **1Z**). On the basis of MO calculations[15] it was concluded that a *Z* imidate anion is inherently more stable. However, it was further surmised on the basis of the exchange kinetics[14] that the substituent on the nitrogen interferes with solvation such that the *E* imidate anion might become the more stable. Moreover, by equating the rates of forward and reverse reactions (eq 1), it is possible

$$\mathrm{RCONHR'} + \mathrm{OH^-} \underset{k_r}{\overset{k_E \text{ or } k_Z}{\rightleftharpoons}} \mathrm{RCONR'^-} + \mathrm{H_2O} \quad (1)$$

$$K_e^- = K_e k_E / k_Z \quad (2)$$

to derive a relationship (eq 2) between the exchange rate constants k_E and k_Z of H_E and H_Z, respectively, and the equilibrium constants $K_e^- = [\mathbf{1Z}]/[\mathbf{1E}]$ and $K_e = [\mathbf{3Z}]/[\mathbf{3E}]$ in imidate anion and amide, respectively. (For primary amides $K_e = 1$.) Implicit in this derivation is the assumption that k_r is independent of stereochemistry. This is reasonable, since most imidate anions are such strong bases that protonation by H_2O is expected to be exergonic and diffusion controlled.[16] Two aims of this paper are thus to show that eq 2 is satisfied and to verify the suppositions regarding relative stabilities of stereoisomeric imidate anions.

The fundamental purposes of this paper are to prepare imidate anions and to characterize them and their stereochemistry. It is true that imidate anions have long been known.[17] However, they have usually been obtained as insoluble powders, and very few have been characterized spectroscopically. Two exceptions are the report[18] of para ^{13}C shifts for four $RCONPh^-$ and the intriguing claim[19] that CsF in formamide produces ^1H NMR peaks at δ 5.8 and 1.2, attributed to $HCONCH_3^-$. On the basis of the previous studies, we judged that NaH or KH would be a suitable base, and that ethers and dimethyl sulfoxide (Me_2SO) would be solvents in which the imidate anion might be soluble. Also, an amide such as HCONHPh, with electron-withdrawing substituents that increase its acidity, might be deprotonated even in hydroxylic media containing excess base. We now report that these methods are successful, especially with secondary formamides, HCONHR. We have verified that the species seen by NMR are indeed imidate anions, and we have characterized their stereochemistry.

Experimental Section

Amides, Me_2SO-d_6, NaH (50% oil dispersion), KH (35% oil dispersion), and other substances were commercial samples from Aldrich, Eastman, Stohler, City Chemical, Alfa, or Mallinckrodt, used without further purification. Some N-methylamides had been prepared for a previous study.[20] Tetrahydrofuran (THF) was obtained from Mallinckrodt and was freshly distilled from benzophenone ketyl; cyclohexanol was redistilled from CaO.

Imidate anions were prepared by the following procedure: A slight excess of NaH or KH was placed in a flask equipped with a magnetic stirrer and with a rubber septum bearing syringe needles for gas inlet and outlet. The material was washed twice with reagent-grade cyclohexane and then dried by heating gently in a stream of N_2. A solution of the amide (ca. 1 M in THF or Me_2SO-d_6) was added, whereupon vigorous H_2 evolution ensued. The mixture was stirred for several minutes, to produce a clear solution with no residue. In some cases these solutions are supersaturated, and the imidate salt precipitated on standing. *N*-Phenylformimidate anion could also be prepared in hydroxylic media simply by adding formanilide to a twofold excess of NaOH.

Reprotonation was effected by adding excess precooled 2,2,2-trifluoroethanol (TFE) to the imidate anion in THF at −78 °C in an NMR tube, which was then shaken vigorously. The kinetics of reequilibration were then followed by immediately inserting the sample into the NMR probe and repeatedly acquiring spectra by frequent pulsing. The observed rate constant, $k_{EZ} + k_{ZE}$, was determined from the slope of a plot of ln $(I_\infty - I)$ vs. time, where I is the intensity of the formyl CH peak of the *Z* amide and I_∞ is the equilibrium value of I.

FT-NMR spectra were obtained with a Varian HR220 spectrometer adapted for FT use or with a Nicolet 1180E computer interfaced to an Oxford 360-MHz magnet. Unless otherwise stated, the probe temperature was 22 °C. Equilibrium constants were determined by integration of NMR peaks. Saturation-transfer studies of *N*-alkylformimidate anion inversion kinetics were performed by saturating the minor formyl CH resonance and measuring the intensity and spin–lattice relaxation time of the major formyl CH resonance. The rate constant was calculated according to eq 3, where $t_i(j)$ is the fractional decrease of peak

$$k_{ij} = M_i(j) t_i(j) / (1 - t_i(j)) \quad (3)$$

i on saturating peak j and $M_i(j)$ is the spin–lattice relaxation rate constant of peak i, under conditions of saturating peak j. Further details are available.[14,21]

Table I. NMR Chemical Shifts of *N*-Methyl Singlets of *N*-Methylimidate Anions, $RC(O^-)=NCH_3$

R	δ (in THF)	δ (in Me_2SO-d_6)
H	2.66	2.42,[a] 2.66
CH_3	2.59	2.47
CH_3CH_2	2.62	2.50
$(CH_3)_3C$	2.65	2.52
Ph	2.85	2.45
$PhCH_2$	2.60	2.50

[a] More abundant stereoisomer.

Results

NMR chemical shifts of the *N*-methyl peaks of some *N*-methylimidate anions (**1**, R′ = CH_3) are given in Table I. The *N*-methyl doublets of the amides have collapsed to sharp singlets. However, the chemical shifts are hardly different from those of the parent amide. Nor are there substantial changes in other peaks, except that alpha protons exchange slowly with Me_2SO-d_6. Consequently these results are inadequate to verify that we are observing the imidate anions rather than amides undergoing rapid base-catalyzed NH exchange.

NMR chemical shifts of the formyl CH peaks of some *N*-alkylformimidate anions (**1**, R = H) are given in Table II, along with the changes in chemical shift, relative to the parent amide **3**. (Substantial changes in chemical shifts of aromatic protons are also seen not only for *N*-phenylformimidate anion but also for *N*-benzylformimidate anion.) Also tabulated are the equilibrium constants, K_e^- =

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Table II. NMR Chemical Shifts of Formyl CH Singlets of Formimidate Anions, HC(O⁻)=NR, and $E \rightleftharpoons Z$ Equilibrium Constants at 22 °C

R	solvent	δ_Z	$\Delta\delta_Z$[a]	δ_E	$\Delta\delta_E$[a]	K_e^-	$K_e k_E/k_Z$[b]
CH_3	Me_2SO-d_6	7.54	−0.51	8.20	+0.25	4.09	5.0
t-Bu	Me_2SO-d_6	7.48	−0.37	8.44	0.25	0.19[c]	0.28[d]
CH_2Ph	THF	8.01	−0.11	8.44	0.32	<0.03	<0.07
CH_2Ph	THF[e]	8.06	−0.06	8.50	0.38	0.43	
CH_2Ph	Me_2SO-d_6	7.74[f]	−0.39	8.36	0.26	0.26[g]	
Ph	THF			8.67	0.01	<0.07	
Ph	cyclohexanol–dioxan (1:1)	7.97	−0.29	8.39	−0.30	0.17	0.23
Ph	cyclohexanol	8.11	−0.14	8.37	−0.25	0.42	0.31
Ph	Me_2SO-d_6			8.57[h]		~0.3[i]	
Ph	glycol	8.34	−0.02	8.59	−0.14	1.02[j]	0.91

[a] Shift relative to amide: $\Delta\delta \equiv \delta$(imidate) − δ(amide). [b] From ref 21b. [c] 0.54 at 57 °C. [d] In ethylene glycol. [e] With 18-Crown-6. [f] Triplet J = 1.5 Hz. [g] 0.45 at 83.5 °C. [h] Equilibrium mixture. [i] Estimated from average chemical shift of ortho protons. [j] 1.39 at 45.5 °C.

Table III. Kinetics of Restoration of E/Z Equilibrium in HCONHR

R	T, °C	k_{obsd}, s^{-1}	k_{ZE}, s^{-1}	k_{EZ}, s^{-1}	$\Delta G_{EZ}^{\ddagger}$, kcal/mol
CH_2Ph	21	$(5.7 \pm 0.5) \times 10^{-3}$	7.7×10^{-4}	4.9×10^{-3}	20.3 ± 0.1
Ph	~0	4×10^{-2}	1×10^{-2}	3×10^{-2}	18

Table IV. Saturation-Transfer Data for E–Z Interconversion of Imidate Anions, HC(O⁻)=NR

R	T, °C	$t_i(j)$[a]	$M_i(j)$, s^{-1}	k_{EZ}, s^{-1}	$\Delta G_{EZ}^{\ddagger}$, kcal/mol	$\Delta G_{ZE}^{\ddagger}$, kcal/mol
t-Bu[b]	57	0.478 ± 0.005	0.324 ± 0.005	0.29 ± 0.01	20.2 ± 0.1	19.8 ± 0.1
CH_2Ph[b]	83.5	0.13 ± 0.02	0.276 ± 0.006	0.04 ± 0.01	23.3 ± 0.2	22.7 ± 0.2
Ph[c]	45.5	0.40 ± 0.02	1.52 ± 0.03	1.00 ± 0.09[d]	18.5 ± 0.1	18.7 ± 0.1

[a] i, j = formyl CH of major and minor stereoisomers, respectively. [b] In Me_2SO-d_6. [c] In glycol. [d] k_{ZE}.

[1Z]/[1E]. The assignments as E and Z will be justified in the discussion. For now, we note that the appreciable changes in both chemical shifts and equilibrium constants, relative to parent amide, demonstrate that we are not merely observing amides whose doublet structure is collapsed by rapid base-catalyzed NH exchange. This holds even for *N*-phenylformimidate anion in hydroxylic solvents, and K_e^- does not vary by more than 10% on adding further excess NaOH. This is expected, since the pK_a of *N*-phenylformamide is 1–3 pK units lower than that of solvent.[22]

The chemical shifts of *N*-methyl and formyl CH resonances are consistently near δ 2.5 and 8, respectively. These are quite different from the δ 1.2 and 5.8 attributed[19] to $HCONCH_3^-$. We did not observe these latter in our system, and we conclude that whatever they are, they are not due to imidate anions.

Evidence that we really are observing imidate anions comes from reprotonation studies. Addition of an excess of TFE restores the peaks of the original amide, but with the convenient simplification that peaks are singlets. Indeed, TFE was selected as an acid strong enough (Δp$K_a \geq 2$) to given encounter-controlled[16] protonation of the imidate anion, but also weak enough that its conjugate base would give rapid base-catalyzed NH exchange in the resulting amide.

Reprotonation creates the amides **3E** and **3Z** in a nonequilibrium *E*:*Z* ratio characteristic of the imidate anion **1E** $\rightleftharpoons$ **1Z**. This is yet another way of creating a nonequilibrium mixture of amide stereoisomers.[23] The equilibrium is then restored at a rate that can be determined by repeated scanning of the NMR spectrum. Kinetic data are given in Table III. The values for *N*-phenylformamide are less certain, since reequilibration occurs during the warming period. In both cases extrapolation of kinetic data to zero time indicated that less than 7% of the *Z* amide was initially present. These limits are consistent with the equilibrium constants determined for the imidate anion. Moreover, the activation energies are similar to the 19.0,[24] 19.5,[23c] or 20.1[25] observed for *N*-methylformamide, except that, as expected,[26] the electron-withdrawing phenyl lowers the barrier.

Data for *E*–*Z* interconversion of three formimidate anions are given in Table IV. These data were obtained at the indicated temperatures, chosen so as to produce rates readily measurable by saturation transfer. This technique is applicable to reactions that are somewhat slower than those measurable by the more familiar line-shape methods, which would have necessitated higher temperatures and possible decomposition.

Discussion

Evidence for Imidate Anions. Since imidate anions have never been characterized, it is necessary to verify that the species observed by NMR are truly imidate anions. Indirect evidence comes by eliminating reasonable alternatives. The vigorous evolution of H_2 shows that an acid–base reaction has occurred. We have already rejected the possibility that we are merely observing the parent amides undergoing rapid base-catalyzed exchange. Addition of hydride or lyate to the carbonyl can be rejected because the chemical shifts are not appropriate and because C–N rotation would be so rapid that two forms would never be observed. Both hydrolysis to formate and oxidation to a hydroxamate (by Me_2SO[17e]) can be rejected because the parent amides could be regenerated simply by protonation.

The only direct evidence for an imidate anion is the 1.5-Hz four-bond coupling observed in one isomer of *N*-benzylformimidate anion. This is significantly greater than the 0.3 Hz that we have observed in the parent amide, and

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it is evidence that we are observing a species with a greater C–N double-bond character.

Assignment of Stereochemistry. Stereochemistries of formimidate anions were assigned on the basis of coupling constants, reprotonation studies, and correlations of chemical shifts. *N*-Benzylformimidate anion (1, R = H, R′ = CH_2Ph) in Me_2SO-d_6 shows two formyl CH resonances, the more abundant of which is a 1.5-Hz triplet. In amides and related compounds $^4J_{trans}$ is generally[27] greater than $^4J_{cis}$, so we may assign the more abundant isomer as *Z*. Similarly, *N*-methylformimidate anion (1, R = H, R′ = CH_3) in Me_2SO-d_6 shows two formyl CH resonances, the less abundant of which is broader. The extra broadening may be attributed to unresolved coupling to a trans methyl, so that this is the *Z* isomer.

In THF, *N*-benzylformimidate anion shows only one formyl CH resonance and only one CH_2 resonance, with any couplings unresolved. The chemical shifts are close to those assigned to the *E* isomer in Me_2SO-d_6. Assignment as the *E* isomer was confirmed by reprotonation, to produce almost exclusively the *E* isomer of *N*-benzylformamide, which reverted to the equilibrium mixture rich in the *Z* isomer. *N*-Phenylformimidate anion in THF exhibited the same behavior, so it too is predominantly the *E* isomer. This technique of "kinetic quenching" has been used previously to assign conformations of *N*-alkylpiperidines and -pyrrolidines.[28]

According to the above assignments and the chemical shift values in Table II, the formyl CH resonance of the *E* isomer of an *N*-alkylformamide is shifted downfield by ca. 0.3 ppm on deprotonation, whereas that of the *Z* isomer is shifted upfield by ca. 0.3 ppm. As a result, the *E* isomer of an imidate anion is substantially downfield of the *Z*. If this conclusion is general, we may use it to assign the other imidate anions in Table II.

***Z*/*E* Equilibrium Constants.** The K_e^- values in Table II show that with rare exceptions the *E* isomer of an imidate anion is more stable than the *Z*. Even those exceptions disappear if each imidate anion is compared with its parent amide, where the *Z* form is more stable, for obscure reasons.[29] This order of stability for imidate anions was predicted[14a] on the basis of the greater reactivities of H_Z toward base-catalyzed exchange, even though it is opposite to what is expected according to MO calculations.

The substantial variations of K_e^- with temperature and with solvent polarity suggest a resolution of this contradiction. The data in Table II show that K_e^- increases with temperature, and the dependence corresponds to a substantial (10–20 eu) positive $\Delta S°$ for isomerization of *E* imidate to *Z*. Such a $\Delta S°$ suggests that the two isomers are solvated differently, whereas the MO calculations do not take account of solvation. Furthermore, K_e^- decreases markedly in less polar solvents, and crown ether increases K_e^-. This behavior is opposite from what was seen in too limited a series,[14a] but it is credibly in line with solvent effects on imidate anions from primary amides. Such behavior suggests that a *Z* substituent exerts steric hindrance to solvation and to Coulombic stabilization by the counterion. Alternatively, the *E* imidate anions are favored since solvent or counterion can approach closer to the center of negative charge. In contrast, crown ether prevents close approach and shifts the equilibrium back toward the *Z* form. A similar counterion effect has been invoked to account for the relative stabilities of the stereoisomeric conjugate bases of *N*,*N*-dimethylformamide.[30]

Table II also includes values of $K_e k_E/k_Z$ from previous studies of base-catalyzed proton exchange. According to eq 2, these values should equal K_e^-. It can be seen that the agreement is reasonably good for those few cases where it was possible to determine all the quantities under comparable conditions. The discrepancies are beyond experimental error, but inasmuch as the solvent effect is large, they may be due to the inherent difference between the conditions of kinetics and the conditions where there is a high concentration of the imidate salt. Unfortunately the discrepancies are too large to permit a critical test of eq 2. The results show that the lifetimes of the *E* and *Z* imidate anions do not differ greatly, but any difference in the rates of reprotonation of two so similar species would have been expected to be quite small.

For *N*-phenylformamide the good agreement between K_e^- and $K_e k_E/k_Z$ is paradoxical. According to p*K* measurements[22] and our observation that excess base suffices to produce the imidate anion, this amide is a stronger acid than alcohol solvents. Therefore the assumption implicit in deriving eq 2 cannot be true. Instead of expecting k_r to be diffusion controlled and independent of stereochemistry, it is k_E and k_Z that ought to be diffusion controlled and thus equal. Nevertheless, k_E is significantly less than k_Z in all media.[21b] This selectivity would be understandable if the catalytic base were not OH^- or lyate but a weaker one whose reaction with the amide would not be diffusion controlled. However, the kinetic measurements were made in weakly buffered solutions, where the general-base contribution (by buffer or imidate) can be shown, both theoretically and experimentally, to be negligible. Therefore we must modify the mechanism of hydroxide-catalyzed exchange so that encounter of amide and hydroxide is not rate-limiting. The oversimplified eq 1 thereby becomes eq 4, which is known as the Swain–

$$\mathrm{RCONR'}H\cdots\mathrm{OH_2} + \mathrm{OH^-} \rightleftharpoons \mathrm{RCONR'}H\cdots\mathrm{OH^-} \quad (4)$$
$$\mathrm{RCONR'}\cdots\mathrm{HOH^-} \rightleftharpoons \mathrm{RCONR'}\cdots H\mathrm{OH^-}$$
(fast)

Grunwald mechanism.[31] Hydroxide does not remove the NH proton (italicized), which is hydrogen bonded to a solvent molecule. Even after encounter with OH^-, that proton remains in a hydrogen bond between imidate anion and a solvent molecule. Completion of the exchange reaction requires breaking that hydrogen bond, which may become the rate-limiting step. Such behavior is quite reasonable in this system, since the imidate anion is almost as strong a base as lyate, so that reversal of the first step can be faster than breaking the hydrogen bond. A similar interpretation was applied to selectivity in proton exchange of amidines,[32] which are also strong bases.

Nitrogen Inversion in Imidate Anions. The activation barriers for *E*/*Z* interconversion, listed in Table IV, are only 19–23 kcal/mol. These are too low to be due to rotation about the C–N bond. For comparison, the barriers

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to rotation in the parent amide are 18–20 kcal/mol (Table III). In imidate anions the greater double-bond character, as evidenced by the $^4J_{trans}$ of 1.5 Hz, ought to increase the barrier substantially. Therefore the mechanism for E/Z interconversion is not rotation, but nitrogen inversion. (Similar reasoning has been used previously to draw the same conclusion regarding imidate esters.[33])

Substituent and medium effects are as expected. The substituent effect at carbon has generally been considered to be small, on the basis of Hammett ρ values[34] and MO calculations.[35] Our results show that even the strong π donor, $-O^-$, does not change the inversion barrier substantially, relative to imines (e.g., $Me_2C{=}NPh$, $\Delta G^\ddagger$ = 20.3[36]) or imidate esters (e.g., MeC(O-*p*-tol)=NMe, $\Delta G^\ddagger$ = 20.2[33]). As for nitrogen substituents,[37] phenyl lowers the barrier to inversion because it can delocalize the 2p lone pair of the transition state. The bulky *tert*-butyl also lowers the barrier because interference with either formyl CH or $-O^-$ destabilizes the ground state.

With *N*-phenylformimidate anion it was also possible to demonstrate qualitatively a solvent effect on the inversion barrier. Although two stereoisomers were seen in protic solvents, only one set of NMR signals was seen in Me_2SO-d_6. This is not due to a predominance of a single stereoisomer (as in THF), since the kinetics of base-catalyzed exchange suggested that the two stereoisomers should be present in comparable amounts (Table II). Indeed, the chemical shifts observed in the aromatic region were consistent with a 3:1 mixture of *E* and *Z* forms, in rapid equilibrium. Apparently the barrier for *N*-phenylformimidate anion is so low in Me_2SO-d_6 that only an averaged spectrum is seen, but in protic solvents hydrogen bonding to the nitrogen lone pair retards the inversion so that the two forms can be seen.

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Conclusions

We have demonstrated that soluble imidate anions, especially formimidate anions, $HCONR^-$, can be readily prepared by treating the amides with suitable bases. *N*-phenylformamide is a special case, since it is so acidic that its imidate anion can be prepared in hydroxylic solvents. The NMR spectra show that the *E* stereoisomer is usually more stable than the *Z*. We have thus verified the prediction made on the basis of the kinetics of base-catalyzed proton exchange, even though this is opposite to the stability order predicted by MO calculations. Solvent effects on the equilibrium suggest that the stability of the *E* stereoisomer is due to more favorable solvation or coulombic stabilization by the counterion. Unfortunately the data are not good enough to test the further quantitative prediction that the rates of exergonic proton transfer are independent of stereochemistry. The behavior of *N*-phenylformamide is unusual, since lyate-catalyzed proton exchange shows stereoselectivity, which is attributed to the operation of the Swain–Grunwald mechanism. The imidate anions could be reprotonated to produce the parent amides but in a nonequilibrium E/Z ratio characteristic of the anion; the equilibrium was then reestablished at a measurable rate. Imidate anions undergo nitrogen inversion, with barriers ca. 20 kcal/mol; substituent and solvent effects are as expected.

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Registry No. 1 (R = R′ = Me), 77354-32-6; 1 (R = Et, R′ = Me), 95589-71-2; 1 (R = *t*-Bu, R′ = Me), 95589-72-3; 1 (R = Ph, R′ = Me), 87994-56-7; 1 (R = $PhCH_2$, R′ = Me), 95589-73-4; 1 (R = H, R′ = Me), 78715-78-3; 1 (R = H, R′ = *t*-Bu), 95589-74-5; 1 (R = H, R′ = $PhCH_2$), 95589-75-6; 1 (R = H, R′ = Ph), 55883-40-4.

Oxidation by Superoxide Ion of Catechols, Ascorbic Acid, Dihydrophenazine, and Reduced Flavins to Their Respective Anion Radicals. A Common Mechanism via a Sequential Proton–Hydrogen Atom Transfer

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In aprotic media superoxide ion ($O_2^{-}\cdot$) reacts with 3,5-di-*tert*-butylcatechol ($DTBCH_2$), ascorbic acid, dihydrophenazine, and dihydrolumiflavin to produce their respective anion radicals. With $DTBCH_2$ in the gas phase an analogous oxidation by $O_2^{-}\cdot$ occurs. On the basis of this, the rapid pseudo-first-order kinetics for the reactions in the solution phase, and the efficient production of single products (the respective anion radicals), the primary process for the $O_2^{-}\cdot$–substrate reactions is concluded to be a sequential transfer of a proton and a hydrogen atom to give the anion radical. The anion radicals of phenazine and lumiflavin are rapidly oxidized by molecular oxygen. Hence, superoxide ion acts as an initiator for the autoxidation of dihydrophenazine and dihydrolumiflavin.

A recent study[1] has demonstrated that superoxide ion ($O_2^{-}\cdot$) oxidizes 1,2-diphenylhydrazine to the anion radical of azobenzene. The process is rapid ($k_{bi} > 100\ M^{-1}\ s^{-1}$) and, on the basis of kinetic studies and gas-phase ion–molecule

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