thus ruling out any appreciable generation of I atoms by F atom attack on products of reactions 2 and 3, i.e., CH_2I and IF.

Reaction 3 is an extremely exothermic reaction. It is therefore reasonable to assume that some of the decline in the potential energy takes place already in the entrance channel; in other words the fluorine atom is attracted to the back side of the CH_3I molecule just as it is to the front. Supporting this assumption is the fact that when excess argon was added to the reaction mixture to thermalize the fluorine atoms, no effect was seen on the I atom yield. (The F atoms photodissociated from SF_6 move relatively slowly but an appreciable fraction have kinetic energies of 2–4 kcal/mol.[8]) However, when sufficiently bulky groups are present the fluorine atom cannot approach closely enough to the carbon atom to feel its attraction, and there is a barrier in the entrance channel.

How can one prove that the reaction producing iodine atoms is truly a Walden inversion, i.e., that the F atom approaches from the backside of the carbon atom? A classical proof would begin with an optically active iodide and show that the product fluoride had the opposite configuration. A direct proof would be to carry out the reaction with beams of F atoms and oriented CH_3I molecules[6,7] and to show that the reaction cross section increased when the CH_3 group was oriented toward the F atom beam. Here we rely on a less rigorous argument. The reaction does not take place with an alkyl iodide such as *tert*-butyl iodide that is strongly hindered on its backside. Neither does it take place with CF_3I. On the other hand the IF-producing reaction appears to take place with all alkyl iodides. Thus we conclude that reactive attack of the F atom on the I atom side of the molecule always produces IF and does not result in displacement of an I atom. Attack from the rear dislodges an I atom only when the steric hindrance is not too great.

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Registry No. CH_3I, 74-88-4; CH_3CH_2I, 75-03-6; $(CH_3)_2CHI$, 75-30-9; $(CH_3)_3CI$, 558-17-8; CF_3I, 2314-97-8; F, 14762-94-8.

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Oxidation of NADH by Ferrocenium Salts. Rate-Limiting One-Electron Transfer

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Because the coenzyme couples NADH/NAD$^+$ and NADPH/NADP$^+$ are ubiquitous and control so much of our oxidation, reduction nature, there has been a long standing interest in the mechanisms of the redox interconversions. Chemists have given considerable attention to oxidations of NADH and its analogues in enzyme-free systems[1] and the questions recently have become sharply focused on single-step hydride transfer vs. multistep processes involving initial electron transfer from NADH to the oxidant. Of particular interest have been studies that reported isotope effects[2] or correlations of thermodynamic and kinetic data.[3]

Scheme I

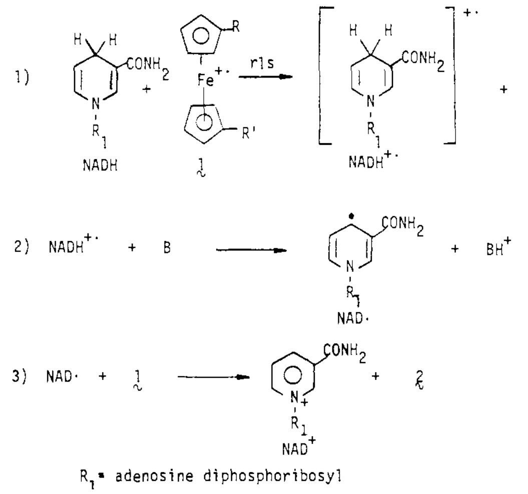

Table I. Oxidation of NADH by Ia[a]

[$NaClO_4$]	$k/(M^{-1}\ s^{-1})$ ± std deviation	no. of runs
0.1	5.41 ± 0.26	17
0.2	3.29 ± 0.13	15
0.3	2.40 ± 0.11	14
0.4	1.90 ± 0.05	8
0.5	1.55 ± 0.08	12

[a] Conditions cited in text.

Table II. Oxidation of NADH by Ferrocenium Ions I[a]

R, R' (in I)	$k_0/(M^{-1}\ s^{-1})$	K^b
H, H	13.7	15.6
HgCl, H	16.3	15.9
n-Bu, H	4.55	12.2
Et, H	2.99	9.2
CH_3, CH_3	0.629	7.6

[a] k_0 = extrapolated rate constant at zero [$NaClO_4$]. [b] K = apparent ion pair equilibrium constant obtained from slope of k_{-1} vs. [$NaClO_4$] plot.

In the present investigation we set out to study an NADH oxidation that could be demonstrated, as unequivocally as possible, to involve initial one-electron transfer from NADH to the oxidant. In this communication we document the experiments and report on some of the broader implications of the results. In particular, the data provide an estimate of the $E^{\circ\prime}$ for the *one-electron, no proton* NADH/NADH$^{+\cdot}$ couple. This value cannot be determined directly because of the instability of NADH$^{+\cdot}$,[4] and uncertainty remains in the literature about the energetics of NADH/NADH$^{+\cdot}$/NAD· interconversions.[5]

Kinetic experiments were performed using β-NADH and a series of substituted ferrocenium hexafluorophosphates.[6] Reaction products and the stoichiometry of the reaction of **1a** (R, R′ = H) and NADH in buffered aqueous propanol[7] were demonstrated by reacting a 2/1 molar ratio of **1a**/NADH. The two reactants were completely consumed and NAD$^+$ and ferrocene (**2a**) were isolated, each in >75% yield. Typical kinetic experiments involved

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[7] The solvent was 46/54 1-PrOH/H_2O (w/w) with the aqueous portion being 0.02 M in pH 7.0 phosphate buffer. Values cited for pH refer to the aqueous solutions before mixing. All reactions were conducted at 30.0 ± 0.2 °C under an atmosphere of argon. Various concentrations of $NaClO_4$ were added.

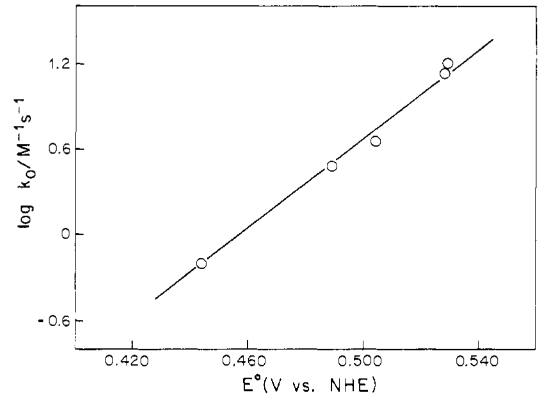

Figure 1. Correlations of NADH and **1** rate constants with **1/2** equilibrium constants.

reacting 4–8 mM NADH with 0.2–0.4 mM **1a**. NADH was always in at least 20-fold excess so that pseudo-first-order kinetics were observed. Rate constants were calculated from the measured decay of the absorption of **1a** at 618 nm. The reaction was found to be first order in NADH and first order in **1a**. The observed rate constants were independent of the pH in the range of pH 6–9. There was also no change in rate when [4-^{1}H,4-^{2}H]NADH[8] was reacted with **1a**. All of these results are consistent with rate-limiting electron transfer from NADH to **1a** according to Scheme I.

Rate constants were similarly determined for the other ferrocenium oxidants **1**. From data obtained at several concentrations, it was found in each case that the kinetics were strictly second order overall. As indicated by the data in Table I, the observed rate constants changed when the salt concentration was varied. Rate constants were, therefore, determined at several concentrations of $NaClO_4$ for each of the ferrocenium cations investigated. The rate constants were then extrapolated to zero salt concentration to give k_0, the rate constant in the absence of $NaClO_4$. The results are in Table II. All of the measured rate constants for each reactant **1** were reproducible to ±5% or better.

The electrochemical $E^{\circ\prime}$ values of the ferrocene/ferrocenium couples were determined by cyclic voltammetry in the same solvent as was used for the kinetic experiments.[9] A salt effect was again observed and the $E^{\circ\prime}$ values were extrapolated to zero $NaClO_4$ concentration. For the five ferrocenium cations investigated log k_0 was then plotted against $E^{\circ\prime}$ (Figure 1). A linear plot (r = 0.998) was observed with a slope of 16.0 V^{-1}. This is in good agreement with the value of 16.6 V^{-1} expected[10] at 30 °C for an endothermic rate-limiting electron transfer followed by rapid deprotonation of $NADH^{+\cdot}$ by a base.[11]

The $E^{\circ\prime}$ for the $NADH/NADH^{+\cdot}$ couple can be determined by extrapolating the log k_0 value up to the diffusion-controlled rate limit in the solvent system being used.[10c] Assuming $k_{\text{diff}} = 3 \times 10^9$ M^{-1} s^{-1}, this plot yields a value of 1.05 V vs. NHE. This is the first determination of this $E^{\circ\prime}$ value for NADH in an aqueous system. The value can be compared with the $E^{\circ\prime}$ = 1.00 V estimated for 1-benzyl-1,4-dihydronicotinamide in acetonitrile[12] where quenching of electronically excited dihydronicotinamide was used for the determination.

The rates reported here allow one to calculate certain rate constants for one-electron transfer from NADH. Such calculations can in principle lead to the critical evaluation of proposed mechanisms for chemical and electrochemical NADH oxidations, especially those in which electron transfer is the initial step.[2d,e4,13] In a future paper these evaluations will be performed. For the present we simply emphasize that we have been able to design an authentic example of an NADH oxidation with rate-controlling one-electron transfer. The data demonstrate that because the $E^{\circ\prime}$ for $NADH/NADH^{+\cdot}$ is so positive, rather powerful one-electron oxidants are required to enter this mechanistic manifold.

Acknowledgment. This work was supported by the National Science Foundation. Stimulating conversations with J. M Dumas-Bouchiat and P. Neta are also acknowledged.

Registry No. 1 (R = HgCl; R′ = H), 34742-71-7; **1** (R = Bu; R′ = H), 33306-90-0; **1** (R = Et; R′ = H), 12276-62-9; **1** (R = Me; R′ = Me), 12276-63-0; **1a**, 12125-80-3; NADH, 58-68-4.

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[8] The NADH was stereospecifically labeled with deuterium in the *pro-R* position. The lack of an observable isotope effect is surprising as a secondary isotope effect on the rate of electron transfer might be expected. The isotope effect on this and similar reactions will be investigated further.

[9] The values obtained are in satisfactory agreement with several that were previously reported. Pladziewicz, J. R.; Espenson, J. H. *J. Am. Chem. Soc.* **1973**, *95*, 56.

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Neutralization–Reionization Mass Spectrometry (NRMS)

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Reionization of neutral products of gaseous ion decompositions has been achieved by collisional activation;[1,2] the resulting mass spectra appear useful for characterizing these neutrals. Porter and co-workers[3] have generated unstable neutral species such as NH_4 and CH_5 by neutralization of the corresponding ions, measuring the energy released in dissociation to characterize the neutrals. We report here that combining neutralization and reionization[4] in tandem mass spectrometry[5] can provide valuable new information on the structures and chemistry of (a) such neutrals, (b) ions, and (c) normal molecules.

In NRMS the appropriate precursor ion of multikilovolt kinetic energy is generated and mass selected in the first mass spectrometer (MS-I).[6] From this ion the desired neutral is produced by charge exchange with an appropriate metal vapor[3] or by metastable or collisionally activated dissociation (CAD).[7] Residual ions are deflected electrostatically from the resulting beam of fast neutrals, which is then ionized[1] by collision with a neutral

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(6) The previous instrumentation[1] was used with an electrostatic sector as MS-II. A metal-vapor furnace was placed between the MS-I exit and the ion lens preceeding the beam collision region. The distance between neutralization and reionization is 18 cm, flight time ~10^{-6} s.

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