assignments are based on the point group C_{4v}. Also included are results from ab initio calculations.[8]

It is clear from this table that optimizing the X-ray crystal coordinates results in only minor changes in the allowed transitions. However, this change has a marked effect on the forbidden charge-transfer bands. The first of these bands now lies near the visible Q band and well below the intense Soret or B band.

Since charge separation plays an important role in photosynthesis, the geometry of the first charge-transfer state was optimized and the electronic spectrum calculated at this geometry. The results of these calculations are given in Table I. At this geometry, the lowest excited state is now the charge-transfer state.

Using the results listed in Table I along with the respective ground-state energies, we constructed a series of potential energy curves, and these are shown in Figure 1. (It should be noted that the energies plotted correspond to fully optimized geometries, while the reaction coordinate plotted is the nitrogen–magnesium distance. As expected, the Q, B, and ground-state curves parallel each other but not the charge-transfer curves. The most notable features of the figure is the crossing of the charge-transfer curves and the Q-state curve. This crossing makes the spectroscopically forbidden charge-transfer state accessible from the first excited state upon relaxation.

These results have prompted us to propose the following possibility: Upon absorption of light, the ground-state molecule is converted to its first excited state. Under the right geometric conditions this excited molecule can then undergo internal conversion to the $^1A_2$ charge-transfer state. The geometry relaxes, causing the magnesium to move from 0.79 to nearly 1.01 Å out of the plane of the ring. (The change in Mg charge is from 0.54 to −0.02.) Since this state is of A_2 symmetry, the excited state will not decay rapidly into the A_1 ground state. At this point, the magnesium could interact with a neighboring molecule or directly with an electron-acceptor molecule, initiating the charge separation necessary for photosynthesis.

We stress the following points that these calculations have suggested. Magnesium is formally Mg^{2+}, and porphine, Por^{2-}. Somewhere in the spectrum there *must* exist a charge-transfer excitation from Por^{2-} to Mg^{2+}. The magnesium ion Mg^+ is considerably larger than Mg^{2+}, the latter with a rare gas electronic configuration. Since Mg^{2+} is out of the plane, Mg^+ must be further out of the plane, suggesting a strong energy dependence of this state upon Mg atom out-of-plane motion. Mg^+, removed from the porphine plane, is a strong electron donor. These features are general and are independent of the calculation performed. The transition energies and the crossing of the curves in Figure 1 are *not* independent of the calculation. In addition, transition energies calculated are also found to depend on the molecules involved and their environments, and thus the crossings, if they are to occur, are extremely sensitive. Mg porphine is not photosynthetically active; chlorophylls in the right in vivo environments are. For this charge-transfer mechanism to play an important role we must speculate that the in vivo conditions are just those required to cause population of the charge-transfer state and curve crossings such as suggested in Figure 1. The reduced double bonds to form chlorins, the presence of ring V, and fifth and possibly sixth position ligands that set the Mg-to-porphine out-of-plane distance are probably all crucial. Furthermore, we do not insist upon the importance of this state in photosynthesis. This state does, however, assign a rather unique role to chlorophyll molecules and might explain the appearance of Mg in nearly all photosynthetic molecules.

Before concluding, we point out that Dupuis et al. have suggested that the $a_{1u}(\pi) \rightarrow 3s$ or $a_{1u}(\pi) \rightarrow 3s$ Rydberg transitions may play a role in photosynthesis.[10] These nearly degenerate states were estimated to lie at about 26 000 cm^{-1} from ionization information, or near the Soret band. Such transitions might be appealing, as they throw the electron into a diffuse orbital with an average radius of perhaps 6 Å, where the electron might be picked up by an acceptor. These transitions have the same symmetry as do the charge-transfer excitations suggested here. Their consideration into the configuration interaction calculation might be expected to further lower the energy of the predicted charge-transfer excitations, increasing further the potential of these states for being photochemically active.

This work is of course only preliminary. Additional calculations on magnesium chlorin as well as other Mg-containing systems are currently under way.

Acknowledgment. This work was supported in part through a grant from the Natural Sciences and Engineering Research Council of Canada.

Registry No. Magnesium porphine, 13007-95-9.

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Reinvestigation of NADH Analogue Redox Reactions in Acetonitrile: Consequences of Isotope Scrambling on Kinetic and Product Isotope Effects

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Of continuing interest and debate is the reaction mechanism for hydride-equivalent transfer from dihydronicotinamides.[1-6] The direct hydride transfer (H^-) mechanism was generally accepted until Chipman and Steffens reported, in what appeared to be evidence for a stepwise mechanism, a discrepancy between the kinetic (k_H/k_D) and product (Y_H/Y_D) isotope effects for reduction of trifluoroacetophenone by a dihydronicotinamide.[2] They later retracted their earlier conclusions,[7] when they realized hydration and reversible adduct formation could account for their observed difference in k_H/k_D and Y_H/Y_D values. Others, however, using dihydronicotinamide reductions in "dry" aprotic solvents[8-10] or employing the nonhydratable nicotinamide analogue *N*-benzyl-3-carbamoyl-1,4-dihydroquinoline,[9] have reported disparities between k_H/k_D and Y_H/Y_D that they considered to be consistent with a multistep mechanism for hydride-equivalent transfer. Of particular mention are the k_H/k_D and Y_H/Y_D values for the reaction (in acetonitrile) of *N*-methylacridinium ion (**1**) with *N*-benzyl-1,4-dihydronicotinamide[8] (**2**), *N*-benzyl-3-carbamoyl-1,4-dihydroquinoline[9] (**3**), and *N*-aryl-1,4-dihydronicotinamides.[10] We show herein that these reactions (although originally thought to provide good evidence for a multistep mechanism, in as much as hydration and adduct formation could not occur) can no longer be considered in support of a step-wise mechanism.

Reaction of **1** with hydride donors **2** and **3** was followed by observing the decrease in [**1**] at λ 415 nm by UV spectrophotometry (eq 1). The reactions were carried out in dry (<0.010% H_2O) acetonitrile solution ([**1**] = 3 × 10^{-5} M, [**2** or **3**] = 3.30

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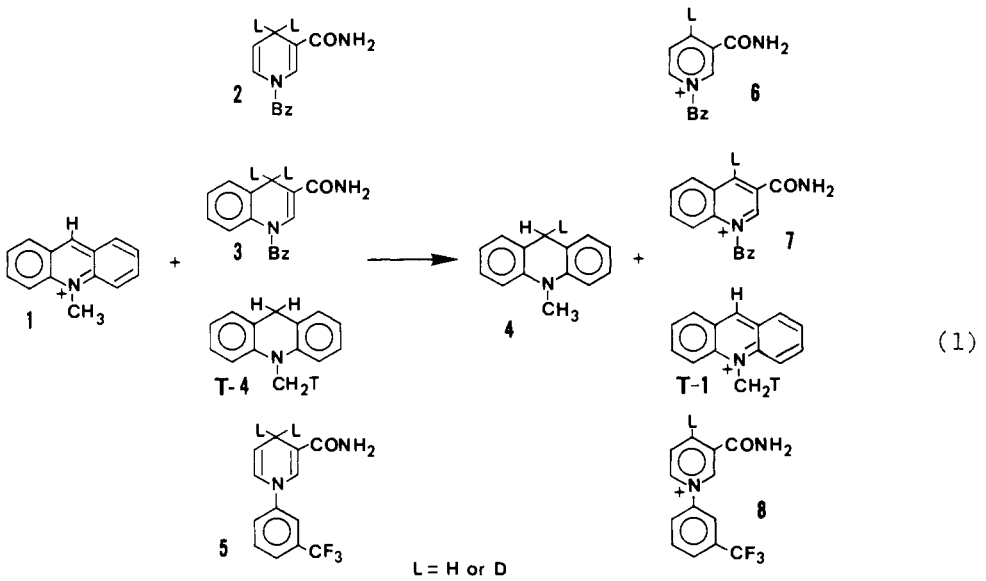

(1)

$\times 10^{-4}$ M) under anaerobic conditions at 30.0 ± 0.1 °C. Reaction of **1** with *N*-[3-(trifluoromethyl)phenyl]-1,4-dihydronicotinamide (**5**) was carried out under similar reaction conditions but at 50.0 ± 0.1 °C. Reaction of **1** with **4** was carried out by using radiochemical tracer techniques[11] in which the acridan (or in some cases, the acridinium ion) *N*-methyl group was labeled with tritium.[12,13] These reactions were carried out under identical reaction conditions as used for **2**, **3**, and **5**. A summary of the rate constants and isotope effects is given in Table I.

The measured rate constant for reaction of **1** with **2**-H,H agrees reasonably well with the value reported earlier;[8] however, the rate constants determined herein for the reaction of **1** and **3**-H,H are significantly less than those reported by Shinkai et al.[9] We attribute this discrepancy either to the presence of a stronger reductant in the kinetic solutions of ref 9, presumably residual dihydronicotinamide used in the preparation of the dihydroquinoline, (see footnote 14), or to isomers of **3** formed in the $NaBD_4$ reduction used in the synthesis of **3**-H,D (see footnote 14). A good correlation of the rates of reaction of **1** with **2**–**4**, reported here and those measured in Kreevoy's laboratory [1:4 water–isopropanol (v/v)] is noted.[15]

The deuterium kinetic isotope effect for reaction of **1** and **2** in dry acetonitrile at 30 °C is 4.11 ± 0.05, in close agreement with Y_H/Y_D reported earlier (4.0 ± 0.2[8]). Our value of k_H/k_D, however, is larger than that from the ratio of rates of **2**-H,H and **2**-H,D[8] reported earlier. This discrepancy may be attributed to the presence of water and/or oxygen in the kinetic solutions used in ref 8 or to the extreme sensitivity of k_H/k_D to the value of the secondary kinetic isotope effect when this method is used. It may be noted that the same reaction studied in acetonitrile with added Mg^{2+} gave nearly identical k_H/k_D and Y_H/Y_D values, consistent with the results obtained herein from the experiments carried out in dry acetonitrile (Mg^{2+} is thought to dry the solvent and thus remove the possiblity of hydration or adduct formation[7]).

The report that k_H/k_D for reaction of **1** and **3** is large (5.09 ± 0.15) but smaller than Y_H/Y_D (7.6 ± 0.3[9]) is due to "isotope scrambling" in the products. Thus, **4**-H,D formed in the reaction of **3**-H,D with **1**, can further react with the excess of **1** in solution to afford additional **4**-H,H. This, in turn, results in Y_H/Y_D being larger than its true value (eq 2). That step c of eq 2 is kinetically

$$\textbf{1}\text{-H} + \textbf{3}\text{-H,D} \overset{k_1}{\rightleftharpoons} \textbf{4}\text{-H,H} + \textbf{7}\text{-D} \quad (2a)$$

$$\textbf{1}\text{-H} + \textbf{3}\text{-H,D} \overset{k_2}{\rightleftharpoons} \textbf{4}\text{-H,D} + \textbf{7}\text{-H} \quad (2b)$$

$$\textbf{1}\text{-H} + \textbf{4}\text{-H,D} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \textbf{4}\text{-H,H} + \textbf{1}\text{-D} \quad (2c)$$

important was verified by the measurement of the rate constant [$k = 0.051 \pm 0.002$ M^{-1} s^{-1} (30.0 ± 0.1 °C)] for the reaction of **1**-H + T-**4**-H,H, which may be compared to the rate constant for reaction of **1**-H and **3**-H,H [$k = 0.762 \pm 0.013$ M^{-1} s^{-1} (30.0 ± 0.1 °C)]. Reaction scheme simulation by use of the appropriate rate constants of Table I and initial concentrations[9] gives a value of $Y_H/Y_D \simeq 7.9$ (at equilibrium), which is close to the observed value of Y_H/Y_D of 7.6 ± 0.3.[9]

The discrepancy between k_H/k_D and Y_H/Y_D for reaction of *N*-aryl-1,4-dihydronicotinamides[10] with **1** is also caused by isotope scrambling in the product studies. By reaction scheme simulation, we are able to show that the previously reported Y_H/Y_D are incorrect and that, when isotope scrambling is included, product isotope effects larger than the kinetic isotope effects are observed. The largest discrepancy between k_H/k_D and Y_H/Y_D values in ref 10 was observed in the reaction of *N*-[3-(trifluoromethyl)-phenyl]-1,4-dihydronicotinamide, **5**, and *N*-methylacridinium ion. Herein we obtained a kinetic isotope effect of 4.43 ± 0.08 from the ratio of rates of **1** with **5**-H,H and **5**-D,D. This is somewhat larger than that obtained from the ratio of rates of **1** with **5**-H,H and **5**-H,D reported elsewhere.[10] Reaction scheme simulation by use of the appropriate rate constants of Table I, initial concentrations,[10] and the reactions of eq 2 gave a value of Y_H/Y_D of 4.6, only slightly larger than the kinetic isotope effect. However, we have measured the equilibrium constant for the reaction of eq 3 and found that, on the time scale used in the product studies

$$\textbf{1}\text{-H} + \textbf{5}\text{-H,H} \underset{50\ °C}{\overset{K = 170}{\rightleftharpoons}} \textbf{4}\text{-H,H} + \textbf{8}\text{-H} \quad (3)$$

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(13) For example, labeled 4 was added to a solution containing a known concentration of **1** ([**1**] ≫ [4]) before aliquots of reaction solution were removed at known time intervals and quenched into 8 mL of toluene. The toluene layer was extracted three times with 50 mL of water before the organic layer was dried (anhydrous Na_2SO_4) and counted (5 mL) with 10 mL of PPO/POPOP/toluene–base "scintillation cocktail". The sample radioactivity decreased smoothly with time following the first-order rate law over 3–8 half-lives.

(14) We have found that **3** prepared by reduction of its oxidized form with **2** contains traces of **2** present even after repeated recrystallizations from ethanol/water mixtures. Support for contamination of **3** in ref 9 comes from the reported discrepancy between the rate constants and the length of time required to effect "100% reaction" in the product studies; with their rate constants, reaction should have been complete in 4–5 min rather than the 2 h, they observed.

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Table I. Rate Constants and Isotope Effects for Reaction of *N*-Methylacridinium Ion with Hydride Donors **2**, **3**, T-**4**, and **5** in Acetonitrile at 30 °C [Literature Values in Brackets]

hydride donor	k, M^{-1} s^{-1}	k_H/k_D	Y_H/Y_D
2-H,H	79.9 ± 0.9		
2-H,D		[2.76 ± 0.15[a]] [3.70 ± 0.18[a,b]]	[4.0 ± 0.2[a]]
2-D,D	19.5 ± 0.1	4.11 ± 0.05	
3-H,H	0.762 ± 0.013		
3-H,D	0.447 ± 0.007	4.95[c] [2.0 ± 0.2[d]]	[7.6 ± 0.3[d]]
3-D,D	0.149 ± 0.003	5.09 ± 0.15	
T-**4**-H,H	0.051 ± 0.002		
T-**4**-H,H	0.103 ± 0.005[e]		
5-H,H	2.90 ± 0.02[e]		
5-H,D		[3.30 ± 0.44[f]]	[6.2[f]]
5-D,D	0.655 ± 0.012[e]	4.43 ± 0.08	

[a] Reference 8. [b] $Mg(ClO_4)_2$ added (1.20×10^{-3} M). [c] This value is calculated from the rates of **3**-H,H, **3**-H,D, and **3**-D,D[g]; the secondary kinetic isotope effect is 1.03. Assumption of a secondary kinetic isotope effect of unity gives $k_H/k_D = 5.77$. [d] Reference 9. [e] Temperature 50.0 ± 0.1 °C. [f] Reference 10. [g] By mass spectral analysis, all dideuterated compounds were greater than 99% authentic.

of ref 10, the reaction of eq 3 is kinetically significant such that the measured ratio of **4**-H,H to **4**-H,D in ref 10 does not reflect the "true" value of Y_H/Y_D due to isotope scrambling caused by reaction in the reverse direction. A more detailed study including the effect of the reverse rates is currently in progress.

The present study has shown that mechanistic arguments based upon the supposed differences in k_H/k_D and Y_H/Y_D are invalid and should not be used to infer electron transfer in the hydride reductions of dihydronicotinamides.

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Registry No. 1, 13367-81-2; **2**-H,H, 952-92-1; **2**-D,D, 60172-94-3; **3**-H,H, 17260-79-6; **3**-H,D, 79798-57-5; **3**-D,D, 83077-37-6; **4**-H,D, 83077-38-7; T-**4**-H,H, 83077-39-8; **5**-H,H, 83077-40-1; **5**-D,D, 83077-41-2; D_2, 7782-39-0; NADH, 58-68-4.

Facile Stereospecific Synthesis of α-Fluoro-β-amino Acids

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Fluorinated analogues of bioactive compounds are finding increasing use as chemical probes for biomedical research, as radiographic tools, and as therapeutic agents of increasing lipid permeability and metabolic stability.[1]

Although β-amino acids occur fairly widely in nature,[2] only a few of them have been synthesized so far. α-Fluoro-β-alanine (a metabolite of the antitumor drug 5-fluorouracil) has been prepared in several steps from either fluoromalonic or from fluorooxaloacetic acid esters,[3,4] β-(fluoromethyl)-β-alanine (an inhibitor of γ-aminobutyric acid transaminase) has been synthesized by means of a series of reactions starting from fluoroacetonitrile,[5] and ω-perfluorinated β-amino acids have been obtained through the amination of ω-perfluorinated α-bromo acids,[6] probably via an elimination–addition mechanism.

In this communication we report a novel and stereospecific method for the preparation of α-fluoro-β-amino acids from β-hydroxy-α-amino acids. The method involves fluorination of *N*,*N*-dibenzyl derivatives of β-hydroxy-α-amino acid esters with (diethylamino)sulfur trifluoride (DAST) to the rearranged *N*,*N*-dibenzyl-α-fluoro-β-amino acid esters. Specifically, treatment of *N*,*N*-dibenzyl-L-serine benzyl ester (**1**)[7] with DAST[8] provided

Scheme I

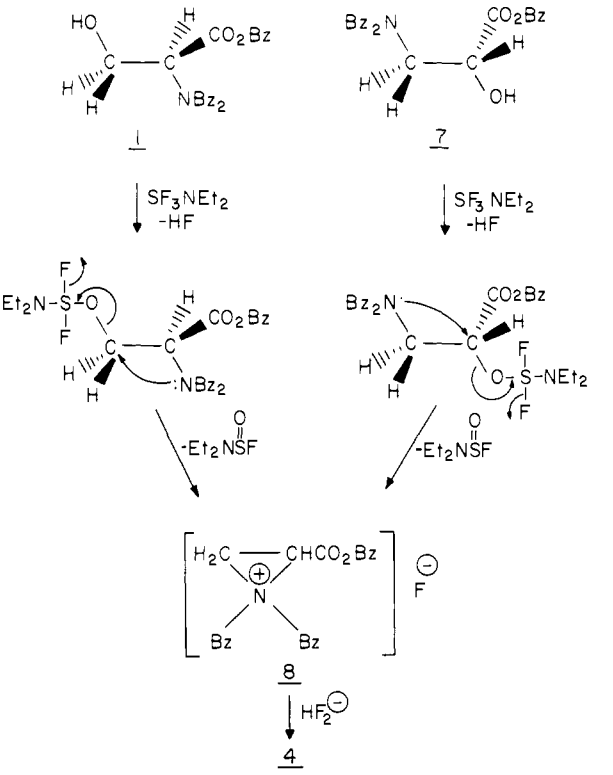

Table I. Preparation of α-Fluoro-β-amino Acids from *N*,*N*-Dibenzyl Derivatives of β-Hydroxy-α-amino Acids and DAST

product	yield,[a] %	mp, °C	^{1}H NMR, δ[b] CHF	CHN
4	90	80-81[c]	4.88 (dt, J = 49.0, 4.0)	2.93 (dd, J = 24.5, 4.0)
5A	60[d]	oil	4.86 (dd, J = 49.0, 3.8)	3.35 (m, J = 31.1, 7.0, 3.8)
5B	90	oil	5.21 (dd, J = 50.2, 3.8)	3.32 (m, J = 25.8, 6.9, 3.8)
6A	90	oil	5.18 (dd, J = 47.8, 2.6)	2.90 (dm, J = 33.2, 8.8, 2.6)
6B	90	83-84[c]	5.40 (d, J = 48.1)	2.88 (dd, J = 29.6, 10.0)

[a] The yields given are of isolated compounds. [b] The chemical shifts are in ppm from internal Me_4Si; the spectra were run at 270 MHz in $CDCl_3$ solutions; J values are in hertz. [c] Recrystallization solvent was ether–hexane. [d] Isomeric (2*R*,3*R*)-2-(dibenzylamino)-3-fluorobutyric acid benzyl ester was also isolated in 26% yield.

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