(5:2): mp 260–261 °C; ^{1}H NMR δ 0.87 (s, 3 H), 1.69 (s, 3 H), 5.09 (s, 1 H), 5.13 (s, 1 H), 6.81 (m, 2 H), 7.17 (m, 3 H), 7.80 (m, 6 H), 8.80 (m, 2 H); ^{13}C NMR δ 20.13 (CH_3), 20.72 (CH_3), 59.18 ($C(CH_3)_2$), 71.48 (CH), 71.93 (CH), 117.36, 123.01, 125.42, 126.78, 126.97, 127.01, 127.64, 128.19, 128.60, 128.86, 130.23, 130.47, 130.77, 132.10, 132.18, 135.50, 135.67 (aromatic C), 158.02 (C=O), 158.13 (C=O). Anal. Calcd for $C_{27}H_{21}N_3O_2$: C, 77.31; H, 5.05; N, 10.02. Found: C, 77.23; H, 5.07; N, 9.99.

A Typical Procedure for PBr_3/DMF Reaction with Primary or Secondary Alcohols. Conversion of 1-Octanol to 1-Bromooctane. A 170-mL sample of dry DMF was placed into a dry, 500-mL, round-bottomed flask. To this was added 53.9 g (0.2 mol) of PBr_3 dropwise with stirring and cooling. After allowing the mixture to come to room temperature, a solution of 13.0 g (0.10 mol) of 1-octanol in 40 mL of DMF was slowly added. The mixture was warmed at 50 °C for 24 h after which the mixture was poured into 750 mL of H_2O and extracted with ether (2 × 175 mL). After the ether extracts were washed with H_2O, and saturated $NaHCO_3$, the solution was dried over $MgSO_4$ and distilled to yield 18.3 g of 1-bromooctane (95% yield).

Acknowledgment. We acknowledge the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Registry No. 3, 81278-56-0; **4**, 81278-57-1; **10**, 81278-58-2; **11**, 81278-59-3; **12**, 81278-60-6; **13**, 20494-84-2; **15**, 81278-61-7; *cis*-**16**, 81278-62-8; *trans*-**16**, 81278-63-9; *cis*-**17**, 81278-64-0; *trans*-**17**, 81278-65-1; *cis*-**18**, 81278-66-2; *trans*-**18**, 81278-67-3; *cis*-**19**, 81278-68-4; *trans*-**19**, 81278-69-5; *cis*-**20**, 81278-70-8; *trans*-**20**, 81278-71-9; *cis*-**21**, 81278-72-0; *trans*-**21**, 81278-73-1; **23**, 81278-74-2; **24**, 81278-75-3; **25**, 81278-76-4; 2,2-dimethylmalonyl chloride, 5659-93-8; dimethylmalonic acid, 595-46-0; naphthalene, 91-20-3; 4-phenyl-1,2,4-triazoline-3,5-dione, 4233-33-4; phenanthrene, 85-01-8; 1-octanol, 111-87-5; 1-bromooctane, 111-83-1.

Kinetics of the Reduction of Isoquinolinium Cations by 1,4-Dihydronicotinamides

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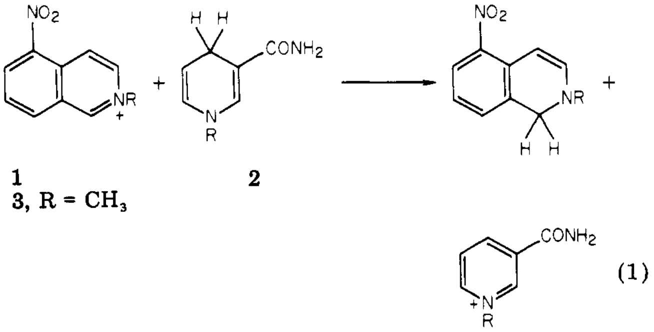
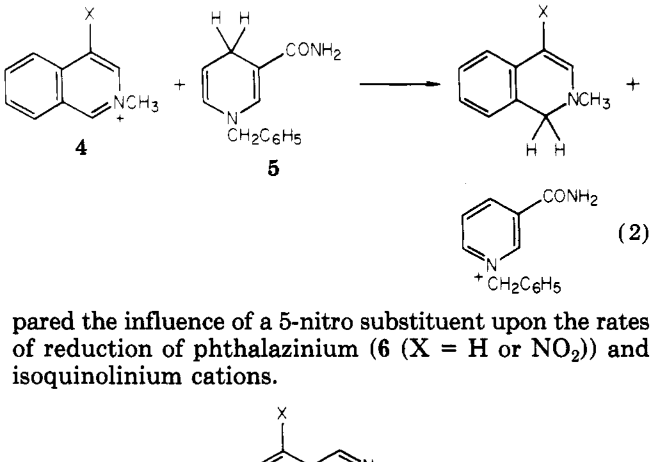
The kinetics of the reduction of a series of 2-methyl-4-X-isoquinolinium cations [**4** (X = H, Br, $CONH_2$, COC_6H_5, CN)] and 2-methyl-5-X-phthalazinium cations [**6** (X = H, NO_2)] by 1-benzyl-1,4-dihydronicotinamide (**5**) have been measured in 20% CH_3CN–80% H_2O (v/v) at pH 7, 25 °C, and an ionic strength of 1.0. Pseudo-first-order rate constants (k_{obsd}) show kinetic saturation at high concentrations of **4** (X = H and Br), and association constants of 2.1 and 1.5 M^{-1}, respectively, have been evaluated for 1:1 complex formation. Interpretation of these data and earlier data for the reduction of the 2-methyl-5-nitroisoquinolinium cation (**3**) in terms of nonproductive complex formation leads to a linear free-energy relationship between the second-order rate constant (k_2) for reduction and pK_{R^+} for pseudobase formation by these cations: $\log k_2 = -0.50pK_{R^+} + 4.9$. Substituent effects upon k_2 for the reduction of **3** and **4** (X = $CONH_2$, CN) by 1-benzyl-3-W-1,4-dihydropyridines (W = CN, $CONH_2$, $CONHCH_3$, $CON(CH_3)_2$) are similar to the substituent effects for cyanide ion dissociation from the corresponding 1-benzyl-4-cyano-3-W-1,4-dihydropyridines. The current study indicates that the relatively strong 1:1 complexes observed in the reduction of 5-nitroisoquinolinium cations by 1,4-dihydronicotinamides are nonproductive and also provides further evidence in support of a one-step hydride-transfer mechanism for these reactions.

We have recently reported[1] upon a detailed kinetic study of the reduction of 5-nitroisoquinolinium cations (**1**) by 1,4-dihydronicotinamides (eq 1). The interpretation of kinetic data for this reaction is complicated by kinetic saturation effects which are consistent with the formation of one or more 1:1 complexes between **1** and **2**. It was established that at least one nonproductive 1:1 complex is formed for **1** ($R = CH_2C_6H_4Z$); however, the description of the kinetically observed complex for **3** is made difficult by the kinetic equivalence of productive and nonproductive complexes in such systems. In an effort to gain further insight into the role of complexation in these reactions, we have now studied the rates of reduction of a variety of 4-substituted 2-methylisoquinolinium cations by 1-benzyl-1,4-dihydronicotinamide (eq 2) and have also compared the influence of a 5-nitro substituent upon the rates of reduction of phthalazinium (**6** (X = H or NO_2)) and isoquinolinium cations.



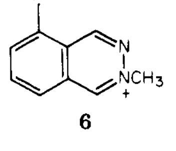
1
3, R = CH_3
2

(1)



4
5

(2)



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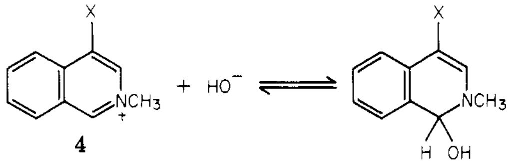
(1) Bunting, J. W.; Sindhuatmadja, S. *J. Org. Chem.* **1981**, *46*, 4211.

Table I. Kinetic Parameters[a] for the Reduction of Isoquinolinium Cations by 1,4-Dihydronicotinamides

reductant	isoquinolinium cation	pK_{R^+}	1/slope, $M^{-1}\ s^{-1}$	$1/Y_{int}$, s^{-1}	Y_{int}/slope, M^{-1}
5	**3**[b]	11.7[c]	0.12	2.1×10^{-3}	57
	4 (X = H)	16.29[d]	$(8.0 \pm 0.3) \times 10^{-4}$	$(3.9 \pm 0.2) \times 10^{-4}$	2.1 ± 0.2
	4 (X = Br)	13.81[d]	0.018 ± 0.001	0.012 ± 0.001	1.5 ± 0.2
	4 (X = $CONH_2$)	11.49[d]	0.046 ± 0.002	$>7 \times 10^{-4}$	<65
	4 (X = COC_6H_5)	9.34[d]	0.79 ± 0.06	*e*	*e*
	4 (X = CN)	7.80[d]	29 ± 1	>0.1	<290
	6 (X = H)	11.04[f]	0.040 ± 0.001	$>8 \times 10^{-3}$	<5
	6 (X = NO_2)	7.87[d]	3.29 ± 0.04	>0.09	<40
2 (R = $(CH_2)_2CH_3$)	**3**[b]	11.7[c]	0.55	0.051	10.8
	4 (X = H)	16.29[d]	$(2.3 \pm 0.1) \times 10^{-3}$	$(1.9 \pm 0.1) \times 10^{-3}$	1.2 ± 0.1

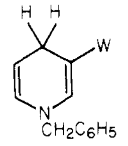
[a] Parameters for eq 5 in 20% CH_3CN–80% H_2O (v/v) and at 25 °C and an ionic strength of 1.0. [b] Data from ref. 1. [c] From: Bunting, J. W.; Meathrel, W. G. *Can. J. Chem.* **1974**, *52*, 962. [d] From ref. 2. [e] Studied under second-order kinetic conditions (see text). [f] From: Bunting, J. W.; Meathrel, W. G. *Can. J. Chem.* **1972**, *50*, 917.

Substituent effects in both **1** and **2** upon the rates of the reaction in eq 1 can only be readily rationalized[1] in terms of a reaction mechanism which involves a direct transfer of hydride ion from **2** to **1**. This suggests that rates of 1,4-dihydronicotinamide reductions of isoquinolinium cations should correlate with rates of other nucleophilic attacks at C-1 of these cations. The data obtained in this study allow a test of this hypothesis in terms of X substituent effects upon the rates of the reaction in eq 2 and the corresponding substituent effects upon the susceptibility of the cations **4** to hydroxide ion attack in pseudobase formation[2] (eq 3).



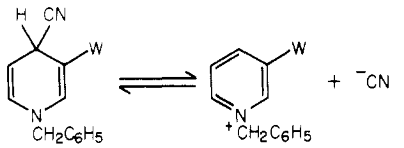
4 (3)

We have also investigated the influence of the C-3 substituent (W) in **7** upon the rates of reduction of three



7

isoquinolinium cations. We find that these substituent effects are closely correlated with W substituent effects upon cyanide ion dissociation from the corresponding 4-cyano-1,4-dihydropyridines (**8**, eq 4).



(4)

8 **9**

Results

Pseudo-first-order rate constants (k_{obsd}) for the reaction of 1-benzyl-1,4-dihydronicotinamide (**5**) with the 2-methylisoquinolinium cation (**4** (X = H)) and its 4-bromo derivative (**4** (X = Br)) as a function of isoquinolinium cation concentration display kinetic saturation effects. Double-reciprocal plots of these data are linear (Figure 1) and may be characterized by slope and ordinate intercept (Y_{int}) parameters which are listed as their reciprocals in Table I. Reduction of **4** (X = H) by 1-propyl-1,4-dihydronicotinamide (**2** (R = $CH_2CH_2CH_3$)) displays a similar kinetic saturation (Table I).

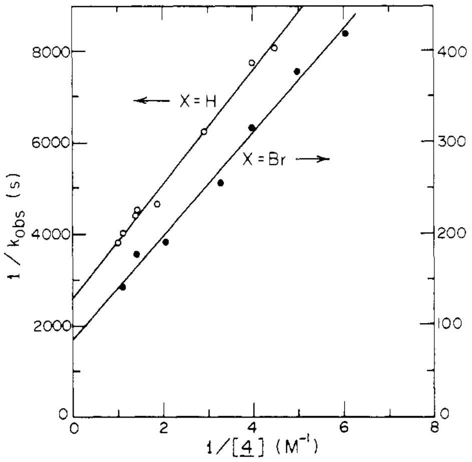


Figure 1. Reduction of **4** (X = H, Br) by **5**.

Pseudo-first-order rate constants for the reaction of **5** with **4** (X = $CONH_2$) and **4** (X = CN) were linear in [**4**] over the accessible concentration ranges which were limited by strong end absorption from these isoquinolinium cations at suitable analytical wavelengths and also by the speed of the reaction in the latter case. Plots of $1/k_{obsd}$ vs. 1/[**4**] are also linear, of course, but since kinetic saturation is not observable in these cases, only the 1/slope parameter can be evaluated (Table I), with the other parameter limits being set by the maximum concentrations of **4** that were experimentally accessible.

The extensive overlapping in the electronic absorption spectra of **4** (X = COC_6H_5) and **5** does not allow pseudo-first-order kinetic conditions to be used in the investigation of the rate of the reaction between these two species. This reaction proved to be strictly second order over 3 half-lives when [**4** (X = COC_6H_5)] = 0.4 mM and [**5**] was in the range 0.25–1.0 mM. For four runs under these conditions, the second-order rate constant was 0.79 ± 0.06 $M^{-1}\ s^{-1}$. This rate constant corresponds to the 1/slope parameter for the other cations in Table I.

The rates of reaction of **5** with the 2-methylphthalazinium cation (**6** (X = H)) and its 5-nitro derivative (**6** (X = NO_2)) were measurable under pseudo-first-order conditions, with **6** being in excess in the former case and **5** being in excess in the latter case. For each of these reactions, pseudo-first-order rate constants were strictly linear in the concentration of the excess species over the accessible concentration range. Parameters derived for these reactions are also included in Table I.

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(2) Bunting, J. W.; Chew, V. S. F.; Sindhuatmadja, S. *Can. J. Chem.* **1981**, *59*, 3195.

Table II. Kinetic Parameters[a] for the Reduction of Isoquinolinium Cations by 7

	3			1/slope, M^{-1} s^{-1}	
W	1/slope, M^{-1} s^{-1}	$1/Y_{int}$, s^{-1}	Y_{int}/slope, M^{-1}	4 (X = $CONH_2$)	4 (X = CN)
CN	b			b	0.52 ± 0.02
$CONH_2$	0.12[c]	2.1×10^{-3}	57	0.046 ± 0.002	29 ± 1
$CONHCH_3$	0.214 ± 0.009	0.011 ± 0.001	18 ± 5	0.108 ± 0.002	58 ± 3
$CON(CH_3)_2$	0.539 ± 0.009	$(3.11 \pm 0.03) \times 10^{-3}$	173 ± 5	0.22 ± 0.02	106 ± 3

[a] Parameters for eq 5 in 20% CH_3CN-80% H_2O (v/v) and at 25 °C and an ionic strength of 1.0. [b] Reaction too slow for accurate kinetic data. [c] From ref. 1.

Table III. Relative Substituent Effects upon Dissociation of 8 and Reactions[a] of 7

			k_2^{rel}		
W	K, M	K^{rel}	3	4 (X = $CONH_2$)	4 (X = CN)
CN	0.0007[b]	0.01			0.019
$CONH_2$	0.071[c]	1	1	1	1
$CONHCH_3$	0.139 ± 0.007	2.0	1.8	2.4	2.1
$CON(CH_3)_2$	0.40 ± 0.03	5.6	4.6	4.8	3.8

[a] From data of Table II. [b] Estimated from data in: Wallenfels, K.; Diekmann, H. *Justus Liebigs Ann. Chem.* **1959**, *621*, 166. [c] From ref 7.

The kinetics of reduction of **3**, **4** (X = $CONH_2$), and **4** (X = CN) by **7** (W = CN, $CONHCH_3$ and $CON(CH_3)_2$) were also investigated. For **7** (W = CN), these reactions were quite slow, and rate constants could only be confidently evaluated for **4** (X = CN) which is by far the most reactive of the above isoquinolinium cations. For **7** (W = $CONHCH_3$, $CON(CH_3)_2$), kinetic saturation effects were observed for k_{obsd} for the reduction of **3** (Figure 2) but not for that of **4** (X = $CONH_2$ or CN), under the accessible experimental conditions. These results parallel the observations above for the reduction of these cations by **5** (i.e., **7** (W = $CONH_2$)), and experimental data for the reactions of all **7** are summarized in Table II.

Equilibrium constants for the dissociation of eq 4 are summarized in Table III, and relative W substituent effects for this dissociation and for the above reductions are also compared in this table.

Discussion

The observation of kinetic saturation effects for the pseudo-first-order rate constants for the reduction of **4** (X = H or Br) by 1,4-dihydronicotinamides is consistent with the rapid formation of a 1:1 complex between these species. Such a complex may be productive (C in Scheme I) or nonproductive (C_{NP} in Scheme II). Schemes I and II are kinetically equivalent to one another and also kinetically equivalent to a number of more complex schemes containing several different productive and/or nonproductive 1:1 complexes.[1] All such schemes predict double-reciprocal plots of the form of eq 5. The present investigation was initiated in an attempt to differentiate between productive and nonproductive complexes, and the current results will first be considered in terms of the simple Schemes I and II.

Scheme I

$$\text{DHN} + \text{IQ}^+ \overset{K}{\rightleftharpoons} \text{C} \xrightarrow{k_c} \text{N}^+ + \text{DHIQ}$$

Scheme II

$$\text{DHN} + \text{IQ}^+ \overset{K_{NP}}{\rightleftharpoons} \text{C}_{NP}$$

$$\text{DHN} + \text{IQ}^+ \xrightarrow{k_2} \text{N}^+ + \text{DHIQ}$$

$$\frac{1}{k_{obsd}} = \frac{\text{slope}}{[\text{IQ}^+]} + Y_{int} \qquad (5)$$

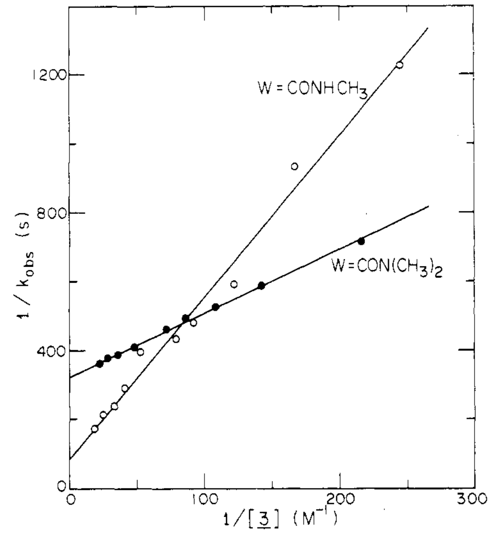

Figure 2. Reduction of **3** by **7** (W = $CONHCH_3$, $CON(CH_3)_2$).

For Scheme I the parameters in eq 5 are defined as 1/slope = k_cK, $1/Y_{int} = k_c$, and Y_{int}/slope = K. For Scheme II these parameters become 1/slope = k_2, $1/Y_{int} = k_2/K_{NP}$, and Y_{int}/slope = K_{NP}. If only productive complexes are formed, substituent effects upon the rates of the hydrogen-transfer step are directly reflected by $1/Y_{int}$; on the other hand, if only nonproductive complexes are formed, the substituent effects for the hydrogen-transfer step are most simply observed in 1/slope.

We have previously shown[1] that the mechanism of reduction of 5-nitroisoquinolinium cations by 1,4-dihydronicotinamides is consistent with a transition state in which the hydrogen atom being transferred is hydridic in character. Such a reaction is essentially a nucleophilic attack upon the isoquinolinium cation, and one would predict that the influence of substituents in the isoquinolinium cation upon the rates of these reductions would be similar to substituent effects in other nucleophilic additions at C-1 of isoquinolinium cations. Extensive data are now available[2,3] on substituent effects for equilibrium constants ($pK_R{}^+$) for hydroxide ion addition to isoquinolinium cations. For these cations a linear correlation has also been established[3] between log k_{OH} and pK_{R^+}, where k_{OH} is the second-order rate constant for hydroxide ion attack upon

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(3) Bunting, J. W.; Norris, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 1189.

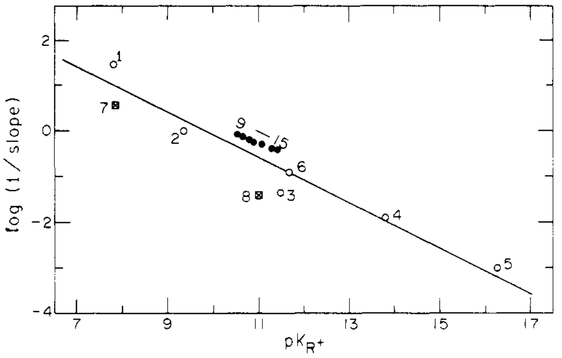

Figure 3. Plot of log (1/slope) vs. pK_{R^+} for reduction of isoquinolinium and phthalazinium cations by **5**. The cations are identified as follows: **4** (X = CN), 1; **4** (X = COC_6H_5), 2; **4** (X = $CONH_2$), 3; **4** (X = Br), 4; **4** (X = H), 5; **3**, 6; **6** (X = NO_2), 7; **6** (X = H), 8; **1** (R = substituted benzyl), 9–15. The correlation line is for cations no. 1–6 only.

the isoquinolinium cation to form the pseudobase. Since rate data are less extensive than pK_{R^+} values for these reactions, we shall initially consider substituent effects upon the kinetic parameters for reduction of the cations in Table I relative to the pK_{R^+} values for these cations.

Consideration of substituent effects upon $1/Y_{int}$ in Table I is difficult since in many cases experimental limitations only allow a lower limit to be placed upon this parameter. However, there is one feature of these data that is worthy of note; although the 2-methyl-5-nitroisoquinolinium cation (**3**; pK_{R^+} = 11.7) is considerably more susceptible to hydroxide ion attack than is the 4-bromo-2-methylisoquinolinium cation (**4** (X = Br); pK_{R^+} = 13.81), $1/Y_{int}$ for **3** is actually sixfold smaller than for **4** (X = Br). Thus, interpretation of $1/Y_{int}$ in terms of k_c for intramolecular hydride transfer within a productive complex (Scheme I) does not produce the relative reactivity expected on the basis of relative susceptibility to hydroxide ion addition. On the other hand, 1/slope for **3** (Table I) is almost sevenfold greater than for **4** (X = Br), and interpretation of 1/slope in terms of k_2 for the bimolecular reaction of Scheme II does give a relative reactivity for the reduction of these two cations that is consistent with their susceptibilities to hydroxide ion attack.

Consideration of the data in Table I suggests a direct correlation between 1/slope and pK_{R^+}. This relationship is shown in Figure 3, which clearly suggests a linear relationship between log (1/slope) and pK_{R^+} for the 2-methylisoquinolinium cations (**4** (X = H, Br, $CONH_2$, COC_6H_4, CN)) and also for **3**. Linear regression analysis of these data gives eq 6 (correlation coefficient = 0.975).

$$\log(1/\text{slope}) = -0.50\ \text{p}K_{R^+} + 4.9 \qquad (6)$$

$$\log k_2 = -0.50\ \text{p}K_{R^+} + 4.9 \qquad (7)$$

In terms of Scheme II, eq 6 becomes eq 7, and making use of the relationship in eq 8 previously established[3] for isoquinolinium cations, eq 7 may be expressed in the form of eq 9.

$$\log k_{OH} = -0.36\text{p}K_{R^+} + 8.84 \qquad (8)$$

$$\log k_2 = 1.4 \log k_{OH} - 7.4 \qquad (9)$$

Equation 9 shows that assumption of nonproductive complex formation as in Scheme II leads to a linear free-energy relationship between rates of hydrogen transfer from **4** to isoquinolinium cations and rates of hydroxide ion attack on these same cations. We therefore have (i) evidence for the importance of nonproductive complexes in the kinetic analysis of these systems and (ii) further support for the hydridic nature of the hydrogen atom in the transition state for these reductions.

The data points in Figure 3 for **6** (X = H and NO_2) were not included in the calculation of the correlation line of eq 6; however, it is clear that these two points do not show major deviations from the correlation line for isoquinolinium cations. Thus a similar relationship between k_2 and k_{OH} also appears to hold for phthalazinium cations. Also included in Figure 3 are data points for the reduction of a variety of 2-(Z-benzyl)-5-nitroisoquinolinium cations (**1** (R = $CH_2C_6H_4Z$)) by **5**. It has previously been shown[1] that nonproductive complexation of **5** with the substituted benzyl group of **1** (R = $CH_2C_6H_4Z$) complicates the reaction in this case. A similar type of nonproductive complex is not possible for **3** and **4**, and yet the data for **1** (R = $CH_2C_6H_4Z$) lie close to the correlation line described by these other cations. This observation further supports the use of Scheme II for the analysis of rate data in these reductions. The inclusion of all isoquinolinium cation data points in Figure 3 in a single correlation, gives eq 10 (correlation coefficient = 0.964) which differs little from eq 6 above.

$$\log(1/\text{slope}) = -0.51\text{p}K_{R^+} + 5.2 \qquad (10)$$

The data of Tables II and III for the influence of C-3 substituents in **7** upon the rates of reduction of isoquinolinium cations provides further support for the above interpretation based upon Scheme II. Whereas $1/Y_{int}$ and Y_{int}/slope of Table II follow no obvious trend for the reduction of **3** in the series **7** (W = $CONH_2$, $CONHCH_3$, $CON(CH_3)_2$), the 1/slope parameter does show a consistent trend, and furthermore, this trend is both qualitatively and quantitatively the same as that for each of **4** (X = $CONH_2$, CN) (Table III). This strongly suggests that the association constants represented by Y_{int}/slope in Table II refer to nonproductive complexes[4] and again points to the equivalence of 1/slope and k_2 of Scheme II.

We feel that it is particularly significant that the relative k_2 values as a function of W for each cation in Table III are quantitatively similar to the relative K value for cyanide ion dissociation from the 4-cyano-1,4-dihydropyridine derivatives **8**. These similar C-3 substituent effects upon equilibria for cyanide ion dissociation from **8** and rates of hydrogen transfer from **7** are most simply interpreted in terms of a nucleofugal hydrogen (i.e., hydride) transfer from **7** in analogy with the cyanide ion nucleofuge of eq 4. The fact that the range of substituent effects upon k_2 in Table III is only slightly smaller than for K is an expression of a transition state which is well advanced toward nicotinamide cation formation (i.e., quite product-like). This is consistent with the estimation[1] of +0.82 as the charge borne by the nicotinamide moiety in the transition state on the basis of substituent effects for the reduction of **1** by **2** (R = $CH_2C_6H_4X$).

In the foregoing discussion, it has been established that in the reduction of isoquinolinium cations by 1,4-dihydropyridines, the hydrogen atom that is transferred is nucleophilic toward the isoquinolinium cation and nucleofugal relative to the dihydropyridine. Thus, from the point of view of both the hydrogen donor and the hydrogen acceptor, the hydrogen atom is transferred as a hydridic species. The present investigation therefore confirms our earlier conclusion[1] that these reactions can be mechanistically represented as one-step hydride transfers.

In the light of the current study it is clear that the association constant of 57 M^{-1} for complexation between **3** and **5** must represent predominantly nonproductive

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[4] At least two different types of nonproductive complex seem to be present in view of the uneven variation of Y_{int}/slope in Table II.

complex formation. Such a complex presumably involves some form of π–π interaction between the dihydropyridine ring of **5** and the nitrobenzene unit of **3**, with hydrogen bonding and/or electrostatic interactions between the amide moiety and the nitro group also being probable in view of the variation of complex strength with W in **7** (Table II). The use of Scheme II also requires a nonproductive interpretation for the weaker complexes observed kinetically for **4** (X = H, Br). Intuitively, one might expect that the transfer of the small hydride unit between two relatively large organic molecules would occur intramolecularly within an association complex of some type. Such a species may be quite a weak complex, involving only minor hydrophobic interactions of various types. The data of Table I place an upper limit of ~1 M^{-1} upon the association constant for such a productive complex.

Experimental Section

Salts of isoquinolinium and phthalazinium cations were available from previous studies.[1,2] 1-Benzyl-1,4-dihydronicotinamide and 1-propyl-1,4-dihydronicotinamide were prepared as previously described.[1] Nicotinonitrile and *N*-methylnicotinamide were commercial products, and *N*,*N*-dimethylnicotinamide was synthesized by the method of Barczynski and Szafran.[5] The bromide salts of the 1-benzylpyridinium cations (**9**) were prepared by refluxing the appropriately substituted pyridine with excess benzyl bromide in acetone. The salts precipitated as white solids and were recrystallized several times from ethanol.

1-Benzyl-3-cyano-1,4-dihydropyridine (7 (W = CN)). 1-Benzyl-3-cyanopyridinium bromide (0.5 g) was added to an aqueous solution (25 mL) containing sodium carbonate (1.00 g) and sodium dithionite (1.70 g) with stirring. The clear yellow solution turned cloudy, but no observable precipitate formed. The solution was extracted with chloroform until the aqueous layer was colorless. After the chloroform solution was dried over sodium sulfate, the chloroform was removed, and the yellow oil was crystallized from ethanol–water (1:1) with cooling to room temperature followed by cooling in a freezer. Long yellow needlelike crystals were obtained. This compound was most stable when kept cold and in the dark; mp 57–59 °C (lit.[6] mp 56–58 °C).

1-Benzyl-3-[(methylamino)carbonyl]-1,4-dihydropyridine (7 (W = CONHCH$_3$)) was prepared as described above for **7** (W = CN) with recrystallization from ethanol–water (2:1): mp 43–44 °C; UV (CH_3CN) λ_{max} 264 nm (ϵ 20100), 354 (6060); ^1H NMR ($CDCl_3$) δ 2.83 (3 H, d), 3.12 (2 H, m), 4.25 (2 H, s), 4.67 (1 H, m), 5.30 (1 H, br NH), 5.72 (1 H, m), 7.07 (1 H, d), 7.25 (5 H, s).

1-Benzyl-3-[(dimethylamino)carbonyl]-1,4-dihydropyridine (7 (W = CON(CH$_3$)$_2$)) was prepared as described above for **7** (W = CN), but the oily product could not be induced to crystallize under any conditions tried: ^1H NMR ($CDCl_3$) δ 2.97 (6 H, s), 3.12 (2 H, m), 4.21 (2 H, s), 4.60 (1 H, m), 5.70 (1 H, m), 6.20 (1 H, s), 7.27 (5 H, s).

Kinetic Studies. Most rate data were obtained in 20% acetonitrile–80% water (v/v) at 25 °C, pH 7.0 (0.005 M phosphate buffer), and an ionic strength of 1.0 (KCl). Studies with **4** (X = CN) and **6** (X = NO_2) were done at pH 6.0 to avoid complications from pseudobase formation by these cations at pH 7.0. Absorbances of solutions were recorded as a function of time at a convenient wavelength on either a Unicam SP-1800 spectrophotometer equipped with a Unicam AR-25 linear recorder or, alternatively, on a Varian Cary 210 spectrophotometer. For most reactions the decrease in the absorbance due to the 1,4-dihydronicotinamide was followed at a convenient wavelength in the range 360–390 nm. Reactions of **3** were followed by the increase in absorbance of the 5-nitro-1,2-dihydroisoquinoline product at 440 nm, while reactions of **6** (X = NO_2) were followed at 450 nm. First-order kinetic plots for all reactions were linear for at least 3 half-times.

Dissociation constants for the reaction of eq 4 were measured as described previously.[7,8]

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Registry No. 2 (R = Pr), 17750-24-2; **4** (*R* = H), 33718-23-9; **4** (R = Br), 21979-34-0; **4** (R = $CONH_2$), 46271-22-1; **4** (R = COPh), 46965-37-1; **4** (R = CN), 46165-53-1; **5**, 952-92-1; **6** (X = H), 63858-86-6; **6** (X = NO_2), 80277-52-7; **7** (W = CN), 37589-77-8; **7** (W = $CONHCH_3$), 81246-16-4; **7** (W = $CONMe_2$), 59547-43-2; **3**, 46271-32-3.

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