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Redox Potentials and Acid–Base Equilibria of NADH/NAD$^+$ Analogues in Acetonitrile

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Redox potentials $E°_i$ of seven NADH/NAD$^+$ analogues (acridine, phenanthridine, quinoline, and pyridine derivatives) have been determined in acetonitrile. The pK_a's of the protonated forms of three reduced species A_iH have also been determined together with the formation constants pK_{B_x} and pK_{OH} of pseudobases resulting from the respective additions of amines and hydroxide to the seven oxidized forms A_i^+. Structural assignments and quantitative conclusions are based on ^{1}H NMR and UV–vis spectrometries. For derivatives of quinolinium or pyridinium ring systems, there exists a linear correlation between $E°_i$ and pK_{iOH} with a slope of −29.6 mV.

Presently, there is considerable interest in acquiring quantitative information about NADH/NAD$^+$ analogues. In particular, the choice of one compound as a reagent for a given nonenzymatic redox transformation,[2] e.g., the reduction of ketones,[2a,b,d,3] can be made rationally if the potentials of the redox couples are known. Since the neutral reduced forms AH are generally not water soluble in contrast to the cationic oxidized forms A$^+$, the reactions are usually carried out in dipolar organic solvents, most often acetonitrile.[3a–d,f–h] The potentials of the AH/A$^+$ redox couples are also pH dependent and reactions, such as the reductions of ketones by AH, are general-acid catalyzed.[3c–g,4] However, controls of the redox potentials of the AH/A$^+$ couples by means of pH adjustments are possible only in limited pH ranges since the A$^+$'s react with bases while the AH's react with acids, and both transformations annihilate the interesting redox abilities of the AH or A$^+$ species.[2c,d]

Fifteen independent equilibrium constants K_{ij} for redox reactions of the type shown in eq 1, where the oxidants

$$A_i^+ + A_jH \underset{k_{ji}}{\overset{k_{ij}}{\rightleftharpoons}} A_iH + A_j^+ \tag{1}$$

$A_{i(\text{or } j)}^+$ are a variety of substituted pyridinium, quinolinium, acridinium, and phenanthridinium cations, have been reported in the literature[5] for a 4:1 mixture of 2-propanol and water. As a result, reduction potentials have been estimated for the corresponding A_i^+ in aqueous solution by assuming that the K_{ij}'s would be the same and accepting −361 mV as the standard reduction potential of the 3-carbamoyl-1-benzylpyridinium cation against the standard hydrogen electrode, i.e., −503 mV vs SCE.[6] These reduction potentials span 430 mV. In the present report, we present six independent K_{ij}'s measured in pure acetonitrile and the standard potentials of seven AH_i/A_i^+ redox couples (see Figure 1), spanning 280 mV, deduced from the values of the six K_{ij}'s and the standard potential of the 10-methylacridan/10-methylacridinium (A_1H/A_1^+) redox couple previously determined in the same solvent.[7] We also present the pK_a's of the AH_2^+/AH acid–base couples when the reversibility of the protonation of AH has been ascertained and the equilibrium constants for pseudobase formation when the A_i^+'s react with various types of bases yielding A_iOH species or other kinds of adducts depending on the nucleophilicity of the base. For N-benzylquinolinium cations, the analyses of the ^{1}H NMR spectra of the two isomeric forms of the resulting adduct have been completed.

Results and Discussion

Redox Potentials. Values found for the standard potentials $E°_i$ of the redox couples A_iH/A_i^+ (eq 2) are gathered in Table I. These data were obtained according to

$$A_i^+ + \underbrace{2e + H^+}_{\text{or } H^-} \rightleftharpoons A_iH \tag{2}$$

procedures described in the Experimental Section. The dependence upon pH is also mentioned. Charge-transfer-type complex formation between A_i^+ and A_jH could cause some error in the reported second-order rate constants k_{ij} and k_{ji} if the equilibrium constant $K_{CT_{ij}}$ favoring complex formation is large, irrespective of whether or not the complex lies on the reaction coordinate.[8] In agreement with the reported small values of $K_{CT_{ij}}$ in neat solvents,[9] it appears that the complex formation is inefficient in the concentration range we used since halving the concentrations did not make significant changes in the k_{ij} and k_{ji}.

Qualitatively, it is worth noticing that the order of decrease in oxidizing power established previously in a mixed

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(2) Reviews: (a) Yasui, S.; Ohno, A. *Bioorg. Chem.* **1986**, *14*, 70. (b) Zehani, S.; Gelbard, G. *Nouv. J. Chim.* **1986**, *10*, 511. (c) Sliwa, W. *Heterocycles* **1986**, *24*, 181. (d) Sausins, A.; Duburs, G. *Heterocycles* **1988**, *27*, 291.

(3) (a) Ohno, A.; Nakai, J.; Nakamura, K.; Goto, T.; Oka, S. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3482. (b) Ohno, A.; Nakai, J.; Nakamura, K.; Goto, T.; Oka, S. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3486. (c) Tanner, D. D.; Stein, A. R. *J. Org. Chem.* **1988**, *53*, 1642. (d) Tanner, D. D.; Kharrat, A. *J. Org. Chem.* **1988**, *53*, 1646. (e) Shinkai, S.; Hamada, H.; Kusano, Y.; Manabe, O. *J. Chem. Soc., Perkin Trans. 2* **1979**, 699. (f) Fukuzumi, S.; Mochizuki, S.; Tanaka, T. *J. Am. Chem. Soc.* **1989**, *111*, 1497. (g) Mochizuki, S.; Fukuzumi, S.; Tanaka, T. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3049. (h) Fukuzumi, S.; Kitano, T.; Ishikawa, K.; Tanaka, T. *Chem. Lett.* **1989**, 1599.

(4) Zehani, S.; Lin, J.; Gelbard, G. *Tetrahedron* **1989**, *45*, 733.

(5) Ostovic, D.; Lee, I. S. H.; Roberts, R. M. G.; Kreevoy, M. M. *J. Org. Chem.* **1985**, *50*, 4206.

(6) SCE: aqueous KCl saturated calomel electrode to which all the potentials given in the present paper are referred.

(7) Hapiot, P.; Moiroux, J.; Saveant, J. M. *J. Am. Chem. Soc.* **1990**, *112*, 1337.

(8) (a) Rappoport, Z.; Horowitz, A. *J. Chem. Soc.* **1964**, 1348. (b) Powell, M. F.; Bruice, T. C. *J. Am. Chem. Soc.* **1983**, *105*, 7139.

(9) (a) Cilento, G.; Tedeshi, P. *J. Biol. Chem.* **1961**, *236*, 907. (b) Cilento, G.; Schreiber, S. *Arch. Biochem. Biophys.* **1964**, *107*, 102. (c) Shinkai, S.; Tamaki, K.; Kunitake, T. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1918. (d) Murakami, Y.; Aoyama, Y.; Kikuchi, J.; Nishida, K.; Nakano, A. *J. Am. Chem. Soc.* **1982**, *104*, 2937. (e) Martens, F. M.; Verhoeven, J. W. *J. Phys. Chem.* **1981**, *85*, 1773. (f) Itoh, Y.; Abe, K.; Senoh, S. *J. Polym. Sci. Polym. Chem.* **1987**, *25*, 2871. (g) Murakami, Y.; Kikuchi, J.; Tenna, H. *Chem. Lett.* **1985**, 103. (h) Kalyanasundaran, K.; Colassis, T.; Humphry-Baker, R.; Savarino, P.; Barni, E.; Pelizzetti, E.; Gratzel, M. *J. Am. Chem. Soc.* **1989**, *111*, 3300.

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Table I. Equilibrium Constants K_{ij} and Standard Potentials $E°_i$ of the A_iH/A_i^+ Redox Couples in Acetonitrile at 25 °C

oxidant	reductant	measured[a] $k_{ij}/M^{-1}\ min^{-1}$	measured[a] $k_{ji}/M^{-1}\ min^{-1}$	K_{ij} ( )[b]	$E°_i$[c]/mV vs SCE
A_4^+	A_1H	$(93 \pm 1) \times 10^{-2}$			$E°_4 = (257 - 29.6\ pH) \pm 26$
A_1^+	A_4H		$(52 \pm 2) \times 10^{-3}$	$K_{41} = 18 \pm 1\ (22)$	$E°_1 = (220 - 29.6\ pH) \pm 25$[d]
A_1^+	A_3H	34.1 ± 0.5			
A_3^+	A_1H		$(94 \pm 3) \times 10^{-4}$	$K_{13} = 3630 \pm 170\ (490)$	$E°_3 = (115 - 29.6\ pH) \pm 25$
A_3^+	A_7H	$(54 \pm 1) \times 10^{-2}$			
A_7^+	A_3H		$(30 \pm 1) \times 10^{-3}$	$K_{37} = 18 \pm 1\ (120)$	$E°_7 = (79 - 29.6\ pH) \pm 26$
A_7^+	A_2H	$(44 \pm 1) \times 10^{-3}$			
A_2^+	A_7H		$(40 \pm 1) \times 10^{-3}$	$K_{72} = 1.10 \pm 0.05\ (1.2)$	$E°_2 = (77 - 29.6\ pH) \pm 26$[e]
A_2^+	A_5H	2.4 ± 0.1			
A_5^+	A_2H		$(115 \pm 5) \times 10^{-4}$	$K_{25} = 210 \pm 20\ (110)$	$E°_5 = (8 - 29.6\ pH) \pm 28$
A_5^+	A_6H	1.10 ± 0.02			
A_6^+	A_5H		$(110 \pm 5) \times 10^{-3}$	$K_{56} = 10.0 \pm 0.5\ (540)$	$E°_6 = (-22 - 29.6\ pH) \pm 29$

[a] Mean and standard deviation (three separate experiments). [b] Values deduced from ref 4, which were determined in a mixture of 2-propanol and water in the ratio 4:1 by volume. [c] $E°_i = E°_j + 29.61 \log K_{ij}$. [d] From ref 7. [e] Deduced from the determination of $K_{32} = 19.5 \pm 1$.

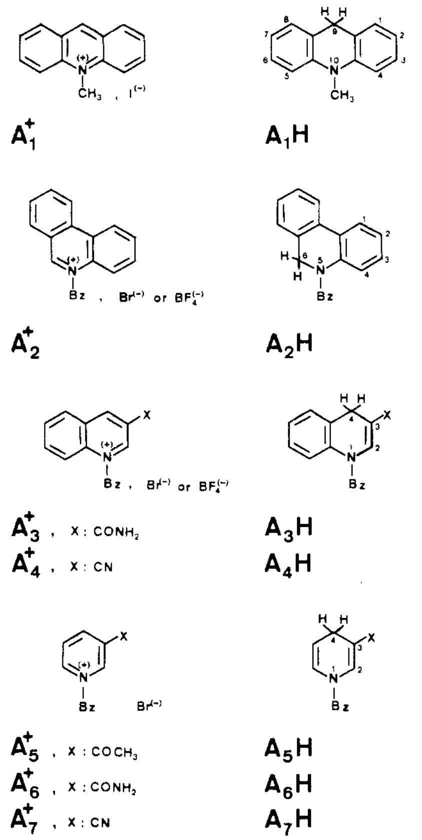

Figure 1. Skeletons of the A_iH/A_i^+ redox couples. Position numbers are mentioned on the rings of the reduced A_iH. Bz = $CH_2C_6H_5$ (benzyle).

solvent[5] is respected. Quantitatively, the few discrepancies can reasonably be ascribed to changes in the solvatation energies of A_i^+ and/or A_iH, the greatest amounting to 1 order of magnitude in the value of K_{37}, i.e., a ca. 30 mV difference on the potential scale. The potential span $E°_4/E°_6$ observed in acetonitrile is ca. 40 mV smaller than was estimated in water.[5]

The comparisons of the individual values of $E°_i$ given in Table I with those estimated in ref 5 cannot be meaningful for the following reasons: (i) All the equilibrium constants mentioned in the present paper, including the one leading to the evaluation of $E°_1$ (see ref 7), were determined directly in acetonitrile, whereas the estimations reported in ref 5 result from the combination of equilibrium constants determined directly in 2-propanol/water (4/1 by volume) with a reference potential estimated in water according to the cyanide affinity method.[10] (ii) The $E°_i$ listed in ref 5 are implicitely given at pH 7 in water and no straightforward relationship can be established with a corresponding pH value in acetonitrile.

Table II. pK_a's of the Conjugated Acids $A_iH_2^+$ of the Reduced Forms AH in Acetonitrile at 25 °C

	A_1H	A_2H	A_3H
pK_a	3.3 ± 0.1	8.6 ± 0.1	8.2 ± 0.1

Protonation of the Reduced Form AH. The thermodynamic pK_a's of three $A_iH_2^+$ species determined in the present work are given in Table II.

$$A_iH_2^+ \rightleftharpoons A_iH + H^+ \qquad (3)$$

$$K_a = (A_iH)(H^+)/(A_iH_2^+)$$

To our knowledge, only a tentative evaluation of the pK_a of $A_1H_2^+$ in acetonitrile has been reported in the literature.[11] However there was an important flaw in that case since the authors, starting with an unbuffered solution of A_1H, mistook the concentration of added $HClO_4$ (not in excess) for the proton concentration (H^+) at equilibrium. For these rather strong acids, the pK_a values are water concentration independent, up to 100 mM.

Reactions of A^+ with Amines and Hydroxide: Spectrophotometric and ^1H NMR Identifications of the Adducts at Equilibrium. For all the cations A^+, pH-dependent reversible UV-vis spectral changes are observable in basic acetonitrile, suggesting that pseudobase formation occurs (see Experimental Section). A closer investigation of the equilibrated solutions spectra over a wide pH range reveals that primary and secondary amine bases B_xH can successfully compete with hydroxide, as nucleophiles, to give amino-pseudobases according to equation 4.

$$A_i^+ + B_xH \rightleftharpoons A_iB_xH^+ \rightleftharpoons A_iB_x + H^+ \qquad (4)$$

UV-vis spectral characteristics of hydroxy and some amino adducts have been determined for cations A_i^+, when accessible, and are given in Table III. Corresponding isomeric structures were, in each case, assigned by reference to spectral data of closely related adducts resulting from nucleophilic additions at the same sites[12-14] and

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(10) (a) Wallenfels, K.; Diekmann, H. *Justus Liebigs Ann. Chem.* **1959**, *621*, 166. (b) Taylor, K. E.; Jones, J. B. *J. Am. Chem. Soc.* **1976**, *98*, 5689. (c) Kellogg, R. M.; Piepers, O. *J. Chem. Soc., Chem. Commun.* **1982**, 402.

(11) Fukuzumi, S.; Ishikawa, M.; Tanaka, T. *Tetrahedron* **1986**, *42*, 1021.

(12) Bunting, J. W.; Meathrel, W. G. *Can. J. Chem.* **1974**, *52*, 981.

Table III. Spectrophotometric Characteristics Used for the Determination of the K_{OH} and K_{B_x} Equilibrium Constants[a]

	AOH adducts		AB_x adducts	
	λ_w and (ϵ_w's)[b]	λ_{max} (ϵ_{max})[c]	λ_w (ϵ_w's)	λ_{max} (ϵ_{max})
A_1^+	356 nm (ϵ_A = 16 000) (ϵ_{AOH} ca. 0)[d]	280 nm (15 000)	356 nm (ϵ_A = 16 000) (ϵ_{AB_1} ca. 0)[d]	284 nm (ϵ_{AB_1} = 14 000)
A_2^+	370 nm (ϵ_A = 3600) (ϵ_{AOH} = 300)	stable 333 nm (7000)	320 nm (ϵ_A = 7400) (ϵ_{AB_2} = 2000)	350 nm (ϵ_{AB_2} = 6400)
A_3^+	379 nm[e] ($\epsilon_{A^{(4)}OH}$ ca. 0)[d]	stable 379 nm[f] ($\epsilon_{A^{(2)}OH}$ 6600)		
		stable 305 nm[g]	316 nm	stable 316 nm[g]
	isosbestic points[h,i] 285 nm 332 nm (1450) (9800) (ϵ_A = 7100) (ϵ_A = 1450)		(ϵ_A = 6600)	(ϵ_{AB_2} = 15 200)
A_4^+	370 nm[e] ($\epsilon_{A^{(4)}OH}$ ca. 0)[d]	stable 370 nm[f] ($\epsilon_{A^{(2)}OH}$ = 6600)		
		stable 302 nm[g]	309 nm	stable 309 nm[g]
	isobestic points[h,i] 288 nm 338 nm (7550) (2770) (ϵ_A = 2250) (ϵ_A = 4200)		(ϵ_A = 4000)	(ϵ_{AB_1} = 15 700)
A_5^+	324 nm (ϵ_A ca. 0)	324 nm[j] (10 000) sh[k] (376 nm)	332 nm (ϵ_A ca. 0)	332 nm[g] (ϵ_{AB_3} = 10 700)
A_6^+	320 nm (ϵ_A ca. 0)	320 nm[j] (7200) sh (375 nm)	325 nm (ϵ_A ca. 0)	325 nm[j] (ϵ_{AB_3} = 6900) sh (385 nm)
A_7^+	268 nm (ϵ_A = 3600) (ϵ_{AOH} = 1100)	310 nm[j] (6200) sh (360 nm)	268 nm (ϵ_A = 3600) (ϵ_{AB} = 1500)	316 nm[j] (ϵ_{AB_2} = 5350) sh (385 nm)

[a] For the experimental conditions and the nature of base B_xH, see Table V. [b] Wavelength that was chosen for the evaluation of the equilibrium constant (ϵ in M^{-1} cm^{-1}). [c] Adduct spectral characteristics. [d] Assumed to be equal to that of the A_iH species. [e] Chosen in order to evaluate the equilibrium constant $K_{OH^{(2)}}/K_{OH^{(4)}}$ between the isomeric adducts at the 2- and 4-positions. [f] Adduct at the 2-position. [g] Adduct at the 4-position. [h] Appearing during the transformation adduct at the 2-position → adduct at the 4-position till equilibrium. [i] Used for evaluating $K_{OH^{app}}$. [j] Mostly adduct at the 4-positions however the shoulder is probably due to the formation of additional adducts at the 2- and 6-positions.[13b,16] [k] Shoulder.

known spectra of the reduced species A_iH.

In the cases of the stable adducts derived from *N*-benzylphenanthridinium (A_2^+) and the two C-3 substituted quinolinium A_3^+ and A_4^+, structural assignments can be established by ^1H NMR analyses and are consistent with the UV–vis data. The site of nucleophilic addition in A_2^+ is unambiguously at the 6-position (i.e., at position α to the quaternarized nitrogen atom). Treatment of A_2^+ in acetonitrile with acetate or phenolate results in the formation of the same adduct spectrum, showing that the nucleophile must be HO^-. The ^1H NMR spectrum of the A_2OH adduct exhibits upfield signals (Table IV), with respect to the starting molecule, consistent with covalent addition at the 6-position and removal of the positive charge of the system.[15,16] In particular, the H-6 proton resonates as a singlet at higher field (δ 5.94 in A_2OH, δ 9.89 in A_2^+). Due to the presence of the chiral center at C-6, the *N*-methylene protons in A_2OH are nonequivalent (diastereotopic) and give rise to an AB pair of doublets at δ 4.78 and 4.90 (J = 15.5 Hz).

From the quinolinium cations A_3^+ and A_4^+, two isomeric pseudobases, involving nucleophilic attacks at the 2- and 4-positions, may possibly be formed. The equilibrium ^1H NMR spectra obtained for these cations in basic (acetate) CD_3CN clearly exhibit two distinct sets of signals characterized by a marked shift from the parent quinolinium A^+, showing that both C-2 and C-4 hydroxy adducts (noted $A^{(2)}OH$ and $A^{(4)}OH$, respectively) are formed in each case though in unequal amounts (Table IV). The assignment of the signals to the isomeric adducts they arise from can be made from chemical shifts arguments. The *N*-methylene signals, associated with the two isomeric adducts, are centered at chemical shift values that are nearly C-3 substituent independent (Table IV). The upfield signal is found at δ ca. 4.83 and corresponds very well with that observed for the *N*-methylene group of A_2OH. Therefore, the upfield signal can reasonably be assigned to the *N*-methylene group of the C-2 hydroxy adduct. Also consistent with this assignment is the downfield shift (ca. 0.20, see Table IV) of the *N*-methylene resonance in $A^{(4)}OH$ from that in $A^{(2)}OH$, since the nitrogen is linked to an sp^2 carbon in the former and to a substituted sp^3 carbon atom in the latter.[12,13a] For the same reason, the most shielded aromatic ring proton is likely to be H-8 (d, J = 8.4 Hz) and is located downfield in the $A^{(4)}OH$ adduct (by at least 0.24) from the corresponding proton in the $A^{(2)}OH$ adduct.

The *N*-methylene protons of the adducts $A_3{}^{(4)}OH$, $A_3{}^{(2)}OH$ and $A_4{}^{(4)}OH$ are diastereotopic. As expected, the largest separation between the main absorption lines of the AB multiplet (0.17) is observed for the geminal protons in $A_3{}^{(2)}OH$, which are closest to the asymmetric center. Interestingly, the corresponding protons in $A_4{}^{(2)}OH$ give rise to a singlet. This singlet is indicative of an exchange process that destroys the chirality of the C-2 carbon atom. Such a reaction is generally accepted to be the dissociation of the covalent adduct.[17] For $A_4{}^{(2)}OH$, the dissociation rate must be rapid enough, owing to the fact that this adduct is the kinetically favored product but is not the thermodynamically preferred species (see Table V). The relative amounts of the $A^{(4)}OH$ and $A^{(2)}OH$ adducts in the equilibrium mixture were determined from its ^1H NMR spectrum and further confirmed, with a better accuracy, but its UV–vis spectrum.

The quinolinium ions A_3^+ or A_4^+ can be completely converted, in the presence of a slight excess of the secondary amine pyrrolidine (B_4H) in unbuffered CD_3CN, to

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(13) (a) Roberts, R. M. G.; Ostovic, D.; Kreevoy, M. M. *J. Org. Chem.* **1983**, *48*, 2053. (b) Bunting, J. W.; Fitzgerald, N. P. *Can. J. Chem.* **1984**, *62*, 1301.

(14) (a) Lovesey, A. C.; Ross, W. C. J. *J. Chem. Soc. B* **1969**, 192. (b) Foster, R.; Fyfe, C. A. *Tetrahedron* **1969**, *25*, 1489. (c) Bunting, J. W. *Tetrahedron* **1987**, *43*, 4277.

(15) Zoltewicz, J. A.; Oestreich, T. M.; O'Halloran, J. K.; Helmick, S. *J. Org. Chem.* **1973**, *38*, 1949.

(16) (a) Damji, S. W. H.; Fyfe, C. A. *J. Org. Chem.* **1979**, *44*, 1757. (b) Damji, S. W. H.; Fyfe, C. A. *J. Org. Chem.* **1979**, *44*, 1761.

(17) Zoltewicz, J. A.; O'Halloran, J. K. *J. Am. Chem. Soc.* **1975**, *97*, 5531.

(18) (a) Kolthoff, I. M.; Chantooni, M. K.; Bhowmik, S. *J. Am. Chem. Soc.* **1968**, *90*, 23. (b) Coetzee, J. F. *Progress in Physical Organic Chemistry*; Cohen, S. G., Streitwieser, A., Taft, R. W., Eds.; Intersciences: New York, 1967; Vol. IV, p 77.

Table IV. ^{1}H NMR Spectral Data for Hydroxy and Amino Adducts in CD_3CN

compound	δ, ppm H-2	H-4	H-6	H-8	CH_2 (C_6H_5)	other	J_{CH_2}, Hz	ratio[a] $(A^{(4)}OH)/(A^{(2)}OH)$
A_2OH	6.90	6.80	5.92		4.78 4.90	other aromatic protons 7.1–8.0	15.5	
$A_3^{(2)}OH$[b]	6.20	7.56	6.69	6.63	4.75 4.92	H-5, H-7 and C_6H_5 7.2–7.5	16.9	
$A_3^{(4)}OH$[b]	7.50	5.87		6.90	5.03[c] 5.04[c]	H-5–H-7 and C_6H_5 7.2–7.4		0.8 ± 0.1
$A_4^{(2)}OH$[b]	5.70	7.53	6.80	6.73	4.82	H-5–H-7 and C_6H_5 7.2–7.5		
$A_4^{(4)}OH$[b]	7.48	5.53	7.12	6.97	5.01[c] 5.03[c]	H-5, H-7 and C_6H_5 7.2–7.4		3.5 ± 0.3
A_3B_4[b,d]	7.50	5.18	7.02	6.94	4.97	H-7, 7.17 H-5 and C_6H_5 7.2–7.4		
A_4B_4[b,d,e]	7.50	4.87	7.09	6.97	4.91 5.00	H-7, 7.19 H-5 and C_6H_5 7.2–7.4	16.1	

[a] Ratio at equilibrium from integrated areas of the singlets due to H-4 and H-2 in $A^{(4)}OH$ and $A^{(2)}OH$, respectively. [b] $J_{8,7}$ = 8.4 Hz. [c] Positions of the innermost peaks of the AB multiplet. [d] Adduct at the 4 position. B_4H = pyrrolidine ($HN(CH_2CH_2)_2$) (pK_a = 19.6).[18b] [e] $N(\mathit{CH_2}CH_2)_2$, δ 2.57 (m, 2 H), 2.34 (m, 2 H); $N(CH_2\mathit{CH_2})_2$, δ 1.64 (m, 4 H).

Table V. Equilibrium Constants for Pseudobase Formations. Hydroxy (pK_{OH}) and Amino (pK_{B_x}) Adducts in Acetonitrile at 25 °C

A_i^+	pK_{OH} = $-\log \frac{(AOH)(H^+)}{(A^+)(H_2O)}$	buffer (pK_a)[a,b]	pK_{B_x} = $-\log \frac{(AB_x)(H^+)}{(A^+)(B_xH)}$	buffer $B_xH_2^+/B_xH$ (pK_a)[a,b]
A_1^+	17.3 ± 0.1	tributylamine (18.1)	pK_{B_1} = 13.7 ± 0.1	B_1H = 1,4-diaminobutane monoprotonated form (15.35)
A_2^+	19.9 ± 0.05	acetate (22.3)	pK_{B_2} = 15.85 ± 0.05	B_2H = morpholine (16.6)
A_3^+	p$K_{OH^{(2)}}$[c] = 21.8 ± 0.1	acetate	pK_{B_2} = 15.35 ± 0.05	
	p$K_{OH^{(4)}}$[d] = 21.9 ± 0.1	acetate		
	p$K_{OH^{(2)}}$ − p$K_{OH^{(4)}}$ = −0.07 ± 0.04	phenolate (27.2)		
	p$K_{OH^{app}}$[e] = 21.5 ± 0.1			
A_4^+	p$K_{OH^{(2)}}$ = 17.4 ± 0.1	triethylamine (18.5)	pK_{B_1} = 13.00 ± 0.05	
	p$K_{OH^{(4)}}$ = 16.9 ± 0.1	triethylamine		
	p$K_{OH^{(2)}}$ − p$K_{OH^{(4)}}$ = 0.54 ± 0.02	acetate		
	p$K_{OH^{app}}$ = 16.8 ± 0.1			
A_5^+	p$K_{OH^{app}}$ = 22.5 ± 0.1	acetate	pK_{B_3} = 18.2 ± 0.1	B_3H = piperidine (18.9)
A_6^+	p$K_{OH^{app}}$ = 23.9 ± 0.2	phenolate	p$K_{B_3^{app}}$ = 19.7 ± 0.2	
A_7^+	p$K_{OH^{app}}$ = 20.2 ± 0.1	acetate	p$K_{B_2^{app}}$ = 15.65 ± 0.05	

[a] pK_a and accompanying homoconjugation constant values are from ref 18. [b] Buffer components were at least 10 times more concentrated than A^+. pK_{OH} and pK_{B_x} determinations were performed at pH < pK_a(buffer) and pH > pK_a(buffer), respectively. [c] Addition at the 2-position yielding the $A^{(2)}OH$ species. [d] Addition at the 4-position yielding the $A^{(4)}OH$ species. [e] $K_{OH^{app}} = ((A^{(2)}OH) + (A^{(4)}OH))(H^+)/(A+)(H_2O)$.

a single amino adduct A_3B_4 or A_4B_4. No spectral evidence was found for the presence of hydroxy adducts. The ^{1}H NMR spectral data for A_3B_4 and A_4B_4 are given in Table IV and are consistent, in each case, with an attack of the amine at the 4-position. In particular, the methylene protons of the *N*-benzyl group in the AB_4 adducts appear slightly upfield (by ca. 0.06, regardless of the C-3 substituent) from those in the $A^{(4)}OH$ adducts, while the H-4 singlet undergoes a large upfield displacement (ca. 0.67) as expected from the relative electronic effects of the OH and alkylamine substituents. In A_4B_4, diastereotopism is observed for the *N*-benzylmethylene protons, but also for the *N*-methylene groups of the bonded amine, these latter groups giving rise to separate signals (see Table IV); this indicates that the dissociation of the A_4B_4 adduct is slow. In contrast, rapid ligand exchange probably takes place for A_3B_4: a singlet signal is found for the *N*-benzylmethylene protons and a common set of averaged signals is obtained for free and bonded amine. Such a result falls in line with the fact that A_4^+ is a stronger acid than A_3^+ as can be deduced from the comparison of the corresponding p$K_{OH}{}^{app}$'s reported in Table V. Therefore the formation constant of A_3B_4 is surely much smaller than that of A_4B_4.

Reactivity of A$^+$ with Amines and Hydroxide: Pseudobase Formation Constants. The formation constants (K_{B_x}) of the amino-pseudobases (see definition in Table V) genuinely depend on the nature of the amine. Considering a given A^+ cation, quantitative predictions concerning its reactivity with various types of bases can be deduced from the values found for both K_{OH} (see definition in Table V) and K_{B_x} in full agreement with what can be experimentally observed, i.e., addition of a primary or a secondary amine occurs at a pH value lower than needed for the addition of HO^- and the addition of water does not provoke any appreciable shift of the equilibrium, thus confirming also the water concentration independences of both K_{B_x} and K_{OH} (up to 200 mM). Such results

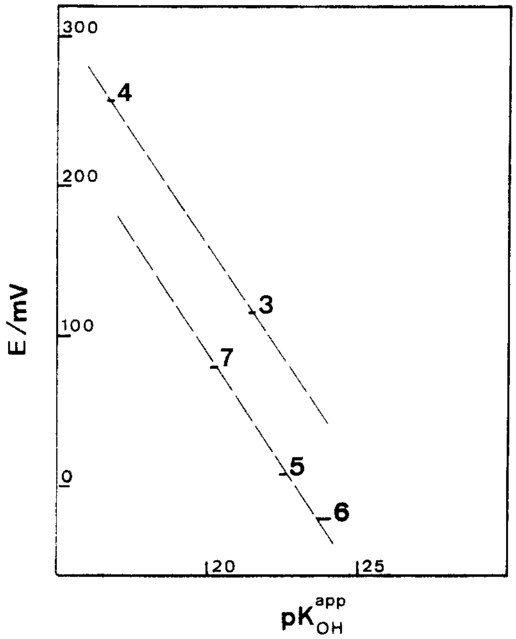

Figure 2. $E°$ vs $pK_{OH}{}^{app}$ plot. Numbers indicate the experimental data (mean and standard deviation) for the corresponding $A_i{}^+$'s. The slope of the discontinuous straight lines is −29.6 mV.

could not be established in water or aqueous mixtures, mostly aquoalcoholic, which were the solvents into which almost all the previous extensive investigations of constants similar to K_{OH} were carried out.[5,13b,14c,19] The pK_a of the AB_x adduct is certainly lower than that of B_xH since a diallylic carbon (adduct at the 4-position) or an allylic carbon also bonded to a nitrogen atom (adduct at the 2-position) substitutes for the N-H hydrogen atom of the B_xH reactant. Thus the determination of each pK_{B_x} was carried out at pH > $pK_{a(B_xH)}$ so that substantial interference of the adduct protonation could be avoided.

Attempts have been made formerly at modeling the K_{1j} values by the values of K'(eq 5)[5,20,21] and therefore at es-

$$A_1{}^+ + A_jOH \rightleftharpoons A_1OH + A_j{}^+ \qquad (5)$$

tablishing that there may exist a linear correlation of ln K_{1j} with ln K_{jOH} with a slope of −1. Accordingly, it was shown that such a model gives a good approximation of relative K_{1j} values in a series of meta- and para-substituted *N*-benzylquinolinium derivatives but that the model could only be used for comparing K_{1j} values generated by derivatives of the same ring system.[20] Our results confirm that a parallel linear correlation exists within experimental error in the case of the pyridinium cations variously substituted at position 3 as appears in the $E°$ vs $pK_{OH}{}^{app}$ plot reproduced in Figure 2 and once it is taken into account that a slope of −1 in the ln K_{1j} vs ln K_{jOH} plot becomes, at 25 °C, a slope of −29.6 mV in the potential-pK plot. Furthermore the observation of such a close correlation provides considerable confidence in the determined values of $E°$ and chiefly $pK_{OH}{}^{app}$. Incidentally, it is also worth underlining that the correlation established in ref 20 concerns *N*-benzylquinolinium derivatives in which the changes of substituents occur at positions meta and/or para of the phenyl ring while the present work deals with changes affecting the 3-positions of the pyridinium and quinolinium heterocycles.

The pK_R's (equivalents of the present pK_{OH}'s) determined previously[5,20] in aqueous 2-propanol are themselves complex constants that contain contributions from both the hydroxide and the alkoxide adducts in the mixture of pseudobase species. The $pK_{OH}{}^{app}$ constants whose values were used in Figure 2 are related only to hydroxide adducts but are still apparent since they contain contributions from adducts at the 2 and 4 positions (and also 6 for pyridinium derivatives) of the nitrogen heterocycles as is evident for the definition of $K_{OH}{}^{app}$ given in a footnote of Table V. The individual values of $pK_{OH^{(2)}}$ and $pK_{OH^{(4)}}$ corresponding to the productions of adducts at the 2 and 4 positions respectively, have been determined with confidence only for the quinolinium derivatives (see Experimental Section). Then the slope of the $E°_i$ vs $pK_{iOH^{(4)}}$ plot appears to be −28.5 ± 1.1 mV and is compatible with the −29.6 mV value, whereas the agreement is not as good in the case of $pK_{OH^{(2)}}$ since the slope is −32.3 ± 1.5 mV. A better parallelism between the $pK_{OH^{(2)}}$ and $pK_{OH^{(4)}}$ variations is observed when $pK_{OH^{(2)}}$ and $pK_{OH^{(4)}}$ are plotted against the Hammett σ_m and σ_{p^-} constants, respectively, as suggested in ref 13b, the slopes being then −11 ± 2 and −14 ± 2 with the σ_m and σ_{p^-} values given in ref 22. As already observed in water,[13b] the relative amount of adduct at the 4 position also increases in acetonitrile when the substituent $CONH_2$ at the 3 position of the quinolinium is replaced by CN (see Table V).

Experimental Section

Materials. Acridine, phenanthridine, 3-cyano- and 3-carbamoylquinolines, 3-cyano-, 3-acetyl-, and 3-carbamoylpyridines, benzyl bromide, methyl iodide, silver tetrafluoroborate, tetraethylammonium acetate tetrahydrate, and tetraethylammonium hydroxide (40 wt % solution in water) were Aldrich Chemical Co. commercial products. Acetonitrile (Spectrosol purity grade, 50 mM H_2O) and deuteriated solvents were obtained from SDS. Other chemicals were Merck products of the highest available purity grade. All the chemicals were used as received.

Preparations of the Quaternized $A_i{}^+$ Species. 10-Methylacridinium ($A_1{}^+$) iodide (mp 227 °C) and 5-benzylphenanthridinium ($A_2{}^+$) bromide (mp 249 °C) were prepared according to the procedures given in ref 5 except that the latter was thoroughly washed with dichloromethane before recrystallization from methanol. *N*-Benzyl-3-carbamoylquinolinium ($A_3{}^+$) bromide (mp 224 °C) was obtained by following the two-step procedure given in ref 3e. *N*-Benzyl-3-cyanoquinolinium ($A_4{}^+$) bromide was prepared by refluxing 3-cyanoquinoline with a 4-fold molar excess of benzyl bromide for ca. 14 h. After cooling of the reaction mixture, the precipitate was collected and washed several times with chloroform. The solid (mp 185 °C) was purified by recrystallization from an ethanol–methanol mixture. Both 3-substituted benzylpyridinium acetyl ($A_5{}^+$) and cyano ($A_7{}^+$) bromides were prepared by treating the corresponding 3-substituted pyridine derivatives with equimolar amounts of benzyl bromide in dioxane.[23] The reaction mixtures were stirred at room temperature for 2 to 4 days. The solids separated as fine powders and were collected by filtration. In the case of $A_7{}^+$, the precipitate was washed several times with acetone and purified by recrystallization from an acetone–benzene mixture (mp 148 °C). $A_5{}^+$ was recrystallized from an ethanol–methanol mixture (mp 195 °C). For 3-carbamoylbenzylpyridinium ($A_6{}^+$) bromide, methanol was added to dioxane in order to solubilize 3-carbamoylpyridine. A melting point of 218 °C was obtained after recrystallization from ethanol–methanol. When concentrations of $A_2{}^+$, $A_3{}^+$, and $A_4{}^+$ higher than 3 mM were required, i.e., for kinetic and ^1H NMR experiments, the tetrafluoroborate salts were used. They were obtained as follows: the bromide salt was treated in water with an equimolar quantity of $AgBF_4$. After centrifugation, the supernatant solution was filtered and the deposit was washed with

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(19) Reviews: (a) Bunting, J. W. *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, 1979; Vol. 25, pp 2–82. (b) Bunting, J. W. *Heterocycles* **1980**, *14*, 2015.

(20) Kreevoy, M. M.; Lee, I. S. H. *J. Org. Chem.* **1984**, *106*, 2550.

(21) Bunting, J. W.; Bolton, J. L. *Tetrahedron* **1986**, *42*, 1007.

(22) Jaffe, H. H. *Chem. Rev.* **1953**, *53*, 191.

(23) Brown, A.; Fisher, H. F. *J. Am. Chem. Soc.* **1976**, *98*, 5682.

Table VI. Kinetics of the $A_i^+ + A_jH$ and $A_j^+ + A_iH$ Reactions in Acetonitrile at 25 °C: Experimental Conditions

	A_1H 415[a] (0000)[b]	A_2H 327 (3100) 338 (4500) 350 (5200)	A_3H 338 (11800) 415 (00000)	A_4H 415 (0000)	A_5H 350 (8040) 361 (9030)	A_6H 361 (4820)	A_7H 327 (4850) 338 (5170)
A_1^+ 415 (4000)			3.7 mM A_1^+ + 1 mM A_3H 415 nm; 20 min	8.8 mM A_1^+ +4.6 mM A_4H 415 nm; 10 h			
A_2^+ 327 (6850) 338 (5000) 350 (3800)			1.3 mM A_2^+ +1.5 mM A_3H 338 nm; 10 h		1.5 mM A_2^+ +1.3 mM A_5H 350 nm; 2 h		1.6 mM A_2^+ +1.6 mM A_7H 327 nm; 40 h
A_3^+ 338 (3850) 415 (0000)	23.5 mM A_3^+ +22 mM A_1H 415 nm; 75 min	1.6 mM A_3^+ +1.6 mM A_2H 338 nm; 10 h					1.7 mM A_3^+ +1.7 mM A_7H 338 nm; 6 h
A_4^+ 415 (100)	0.47 mM A_4^+ +2.44 mM A_1H 415 mn; 25 h						
A_5^+ 350 (150) 361 (000)		3.4 mM A_5^+ +7.5 mM A_2H 350 nm; 2 h				3 mM A_5^+ +2.5 mM A_6H 361 nm; 90 min	
A_6^+ 361 (070)					3.4 mM A_6^+ +2.5 mM A_5H 361 nm; 2 h		
A_7^+ 327 (150) 338 (100)		3.5 mM A_7^+ +3 mM A_2H 327 nm; 40 h	1.6 mM A_7^+ +1.6 mM A_3H 338 nm; 6 h				

[a] Wavelength in nm. [b] Molar absorbances in M^{-1} cm^{-1}. In each entry are given in the following order the initial concentrations of the reactants; the wavelength at which the absorbance was monitored; and the duration of the experiment.

acetonitrile. The combined filtrates were evaporated in vacuo, affording a solid material that was purified by recrystallization from methanol; melting points of A_2^+, A_3^+, and A_4^+ BF_4^- salts were 248, 191, and 182 °C, respectively.

Preparations of the Reduced A_iH Species. A_1H (mp 90 °C) and A_2H (mp 107 °C) resulted from the reductions of A_1^+ and A_2^+ with borohydride.[5] A_3H (mp 158 °C) and A_4H (mp 145 °C) were prepared from A_3^+ and A_4^+ following a procedure that used *N*-propyl-1,4-dihydronicotinamide[21] as the reducing reagent. A_3H was recrystallized from ethanol. Reductions of A_5^+, A_6^+, and A_7^+ with sodium dithionite gave A_5H (mp 61–65 °C),[24] A_6H (mp 118 °C),[24] and A_7H (mp 56–58 °C).[25] The purity of all the products was confirmed by ^1H NMR and mass spectrometric analyses together with the comparison of their melting points with those reported in the literature.

^1H NMR. ^1H NMR spectra were taken at 250 MHz, on a Bruker spectrometer at 25 °C, using tetramethylsilane as an internal standard. Adduct solutions were prepared in NMR tubes by adding aliquots of stock solutions of tetraethylammonium acetate (2 to 3 equiv) or appropriate secondary amine (2 equiv) in CD_3CN to a solution of the heteroaromatic substrate (ca. 30 mM) in CD_3CN. The adduct solutions were stable for at least an hour. Quantitative regeneration of the starting material was obtained after adding a sufficient amount of concentrated $HClO_4$ as confirmed by ^1H NMR and UV–vis (using a 0.1-mm optical pathlength cell) analyses. No differences in the UV–vis spectral profiles were observed when varying the substrate concentration over a 100-fold range up to the value used for ^1H NMR spectrometry.

Spectrophotometric Determinations of the K_{ij}'s. UV–vis absorption spectra were recorded on a Varian Superscan 3 spectrophotometer. The K_{ij} constants were evaluated as k_{ij}/k_{ji} (see reaction 1), the forward and backward rate constants being determined as follows. All kinetic runs were initiated by mixing the temperature-equilibrated solutions of each reactant in acetonitrile. Reacting solutions were kept in a cell, shielded from light, with the temperature maintained at 25 °C by pumping water from a thermostat through the cell jacket, and aliquots were assayed spectrophotometrically at intervals. Absorbance vs time data at an appropriate wavelength were collected and fitted with either eq 6 in order to determine k_{ij} or eq 7 (see below) in order to determine both k_{ij} and K_{ij}, depending on whether the effect of the backward reaction had to be taken into account. The ratio $(A_t - A_0)/(A_\infty - A_0)$ (A_0, A_t, absorbances at times 0 and t; A_∞, absorbance that would have been observed upon total conversion of the initially less concentrated reactant is easily calculated from the spectra of pure samples) is thus a measure of the fraction x of the initially less concentrated reactant that has been converted at time t. When the effect of the backward reaction was negligible, the rate law

$$-dC^\circ(1 - x)/dt = -dC^\circ(r - x)/dt = C^\circ\, dx/dt = k_{ij}C^{\circ 2}(1 - x)(r - x)$$

was integrated by partial fractions to give[26]

$$\ln ((1 - x/r)/(1 - x)) = k_{ij}C^\circ(r - 1)t \qquad (6)$$

where C° is the initial concentration of the less concentrated reactant and r the ratio $C^{\circ\prime}/C^\circ$, $C^{\circ\prime}$ being the initial concentration of the other reactant with $r \gtrsim 1$. When the backward reaction occurred to an appreciable extent, the integration of the rate law

$$C^\circ\, dx/dt = k_{ij}C^{\circ 2}(1 - x)(r - x) - k_{ji}(C^\circ x)^2$$

by partial fractions gave[26]

$$\ln ((x - x_1)/(x - x_2)) - \ln (x_1/x_2) = (k_{ij}/K_{ij})(1 - K_{ij})(x_1 - x_2)C^\circ t \qquad (7)$$

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(24) Anderson, A. F.; Berkelhammer, G. *J. Am. Chem. Soc.* **1958**, *80*, 992.

(25) Mauzerall, D.; Westheimer, F. M. *J. Am. Chem. Soc.* **1955**, *77*, 2261.

(26) Moore, J. W.; Pearson, R. G. *Kinetics and Mechanism*, 3rd ed.; Wiley: New York, 1981; pp 305–306.

with x_1 and x_2 being the values of x for which

$$x^2 - K_{ij}x(r + 1)/(K_{ij} - 1) + K_{ij}r/(K_{ij} - 1) = 0$$

Then x_1, x_2, k_{ij}, and K_{ij} were obtained by iterative computation.

All the K_{ij} constants were determined according to the experimental conditions summarized in Table VI. In some cases, the duration of the experiment was limited by the occurrence of side reactions. Those were detected both by testing the spectral stabilities of separated solutions of each component A_i^+, A_j^+, A_iH, and A_jH within the same time scale and by monitoring the coherence of the evolution of the spectrum of the reaction mixture over the whole wavelength range. For example, the experiments allowing the determinations of K_{37} and K_{56} were ended before the formation of appreciable amounts of unidentified byproducts, which provoke abnormal changes in the absorbance at 350 and below 290 nm in the former case and in the 220 to 320 nm region (with a maximum effect at 295 nm) in the second case.

Spectrophotometric Determinations of the K_{OH}'s and K_{B_x}'s. The K_{OH} and K_{B_x} equilibrium constants were determined from spectra in a series of buffer solutions given in Table V. The spectra at pH or B_xH concentration high enough to ensure the total consumption of A^+ were taken as the spectra of the pseudobases unless otherwise specified. Regeneration of at least 95% of A^+ upon neutralization with $HClO_4$ ascertained the reversibility of the HO^- or B addition. Such a reversibility was always obtained when the time elapsed between the introduction of A^+ in the buffer and the neutralization with $HClO_4$ did not exceed 30 s. Within this time scale, the system was always at equilibrium except for the OH adducts of A^+_3 and A^+_4. However, in the cases of A^+_3 and/or A^+_4, reaching the equilibrium between the kinetically favored adduct at the 2 position and the thermodynamically favored adduct at the 4 position took less than 30 min and addition of $HClO_4$ after such a while still brought on regeneration of the original A_i^+. The word "stable" in Table III indicates that the total regeneration of A^+ could still be performed after an hour (at least). The spectrophotometric characteristics of the adducts, λ_{max} and ϵ_{max} (when the latter could be evaluated with confidence), are also gathered in Table III together with the wavelengths λ_w and molar absorbances ϵ_w, which were used in order to determine the concentrations at equilibrium and therefore calculate the equilibrium constants. The identification of the isosbestic points appearing during the transformation of the adduct at the 2 position to the adduct at the 4 position enabled us to determine the true apparent constants (pK_{OH}^{app}) of the cations A_3^+ and A_4^+. In the cases of the pyridinium cations A_5^+, A_6^+, and A_7^+, it is well known that the preferred products of kinetic and thermodynamic control are quite dependent on both the substituent on the ring and the nature of the attacking nucleophile.[13b,16,27] The pK_{OH}^{app} and $pK_{B_x}^{app}$ values given in Table V were obtained after making the following approximations: for A_5OH, A_6OH, A_7OH, AB_3, and AB_2, the molar absorbance of the adduct at the 4 position and its isomers, which were only minor products, were assumed identical at λ_w.

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(27) Ohno, A.; Ushida, S.; Oka, S. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 506.

Acid-Catalyzed Ring Expansion of 1-(1-Methoxy-1,2-propadienyl)-2-cyclobuten-1-ols. Synthesis of 5-Hydroxy-5-vinyl-2-cyclopenten-1-ones and Their Stereoselective Transformation to 5-(2-Acetoxyethylidene)-2-cyclopenten-1-ones

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The addition of 1-lithio-1-methoxy-1,2-propadiene to various cyclobutenones, cyclobutanones, and benzocyclobutenones produces sensitive 1,2-adducts that, in the presence of acid, rearrange to 5-hydroxy-5-vinyl-2-cyclopenten-1-ones in good to excellent yields. Acid-catalyzed ring expansion of the addition products of 1-lithio-1-methoxy-1,2-propadiene to cyclobutenones bearing a substituent at the 4-position occurs in a stereospecific fashion providing cyclopentenones with the 4-substituent and the 5-hydroxyl group in a cis relationship. After conversion of the 5-hydroxy-5-vinyl-2-cyclopenten-1-ones to the corresponding allylic acetates, palladium(II)-catalyzed [3,3]-sigmatropic rearrangement can be effected, furnishing 5-(2-acetoxyethylidene)-2-cyclopenten-1-ones with high kinetic selectivity favoring the isomer with the alkylidene substituent and the carbonyl group syn (*Z* stereochemistry in most cases). On exposure to a trace of acid, equilibration occurs to the more stable isomer with the alkylidene substituent and carbonyl group anti.

Introduction

Ring-enlargement reactions are commonly used to access cycloalkanoid derivatives; many of these methodologies utilizing ring strain in consort with the generation of positive charge on an atom adjacent to the ring as a driving force for the reaction.[2] During the course of studies on electrophilic transition-metal-catalyzed ring expansion–functionalization reactions of alkynyl-substituted cyclobutenol derivatives,[3] 1-(1-methoxy-1,2-propadienyl)-2-cyclobuten-1-ols (**2**), were prepared from the corresponding cyclobutenones **1** in anticipation of exploring similar metal-catalyzed transformations on allenyl-substituted cyclobutenols. However, the 1-(1-methoxy-1,2-propadienyl)-2-cyclobuten-1-ols were sensitive to exposure

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(1) Camille and Henry Dreyfus Foundation Teacher–Scholar, 1985–1990.

(2) Leading references: Cohen, T.; Brockunier, L. *Tetrahedron* **1989**, *45*, 2917. Salaün, J.; Karkour, B.; Ollivier, J. *Tetrahedron* **1989**, *45*, 3151. Salaün, J. R. Y. *Topics Curr. Chem.* **1988**, *144*, 1. Krief, A. *Topics Curr. Chem.* **1987**, *135*, 1. Trost, B. M. *Topics Curr. Chem.* **1986**, *133*, 1. Wong, H. N. C.; Lau, K.-L.; Tam, K.-F. *Topics Curr. Chem.* **1986**, *133*, 83. Trost, B. M. *Topics Curr. Chem.* **1986**, *133*, 3. Gutsche, C. D.; Redmore, D. *Carbocyclic Ring Expansion Reactions*; Academic: New York, 1968.

(3) Liebeskind, L. S.; Chidambaram, R.; Mitchell, D.; Foster, B. S. *Pure Appl. Chem.* **1988**, *60*, 2734. Liebeskind, L. S.; Mitchell, D.; Foster, B. S. *J. Am. Chem. Soc.* **1987**, *109*, 7908. Liebeskind, L. S. *Tetrahedron Symposium in Print* **1989**, *45*, 3053–3060. Liebeskind, L. S.; Lescosky, L. J.; McSwain, C. M., Jr. *J. Org. Chem.* **1989**, *54*, 1435. Mitchell, D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 291.

0022-3263/90/1955-4614$02.50/0