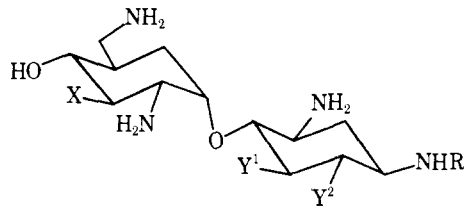
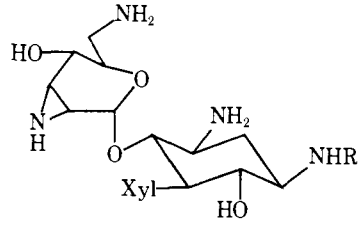
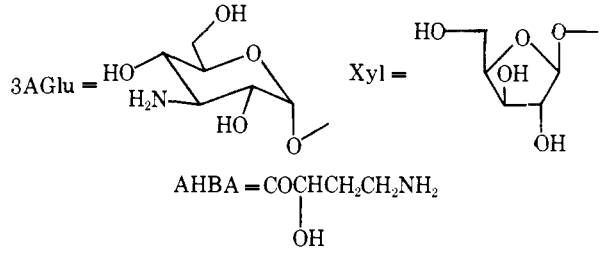


1, X = OH; Y^1 = OH; Y^2 = 3AGlu; R = H
2, X = OPO_3H_2; Y^1 = OH; Y^2 = 3AGlu; R = H
3, X = Cl; Y^1 = OH; Y^2 = 3AGlu; R = H
4, X = H; Y^1 = OH; Y^2 = 3AGlu; R = H
5, X = Cl; Y^1 = OH; Y^2 = OH; R = H
6, X = H; Y^1 = OH; Y^2 = OH; R = H
7, X = Cl; Y^1 = Xyl; Y^2 = OH; R = H
9, X = H; Y^1 = Xyl; Y^2 = OH; R = H
10, X = OH; Y^1 = Xyl; Y^2 = OH; R = AHBA
11, X = OPO_3H_2; Y^1 = Xyl; Y^2 = OH; R = AHBA
13, X = H; Y^1 = Xyl; Y^2 = OH; R = AHBA



8, R = H
12, R = AHBA



3′-phosphate (**11**)[11] proceeded in lower yield, presumably owing to an undesired side reaction on the acyl moiety. Kanamycin A 3′-phosphate[1] possessing a hydroxy group at the 2′-position was recovered unchanged in the chlorination reaction. The equatorial configuration of the chlorine atom at the 3′-position was established on the basis of the proton-proton coupling constants observed in **3** and 3′-chloro-3′-deoxyneamine (**5**) ($J_{2',3'}$ = 10 and 11 Hz, respectively).

Another dehydroxylation procedure is the one involving aziridine derivatives. Treatment of **11** with bistrimethylsilylacetamide (BSA)–TMCS (5:1 by volume) in pyridine in a sealed tube (105 °C, 30 h) afforded, after hydrolysis, 2′,3′-epimino-2′-deamino-3′-deoxybutirosin A (**12**), mp 212–214 °C (from CH_3OH), $[\alpha]_D$ +36° (c 0.5, H_2O), in 58% yield with 80% conversion of **11.** The assigned structure for **12** was confirmed by the comparison of ^{13}C NMR spectra of butirosin A (**10**)[12] and **12.** The signal of C-2′ and C-3′ forming the aziridine ring in **12** appeared at the higher field[13] (chemical shifts for C-2′ and C-3′: 33.7–34.9 ppm in **12;** 56.4 and 74.0 ppm in **10**).[14] Hydrogenation of **12** with Raney nickel in water at 70 °C, followed by separation by ligand exchange chromatography[15] (Amberlite CG-50, Cu–NH_3 form) gave 3′-deoxybutirosin A (**13**), mp 204–208 °C (from CH_3OH), $[\alpha]_D$ +22° (c 0.5, H_2O), in 57% yield in preference to the isomer (product ratio, 5:1). The structure of **13** was confirmed by hydrolysis leading to **6** and **9.** This method was successfully applied to 3′-phosphates of **1,** neamine,[1] xylostasin,[16] and butirosin B[17] to obtain **4, 6, 9,** and 3′-deoxybutirosin B,[18] respectively, via the corresponding 2′,3′-epiminoaminoglycosides.

3′-Chloro- and 2′,3′-epiminoaminoglycosides thus obtained are interconvertible. For example, 2′,3′-epimino-2′-deamino-3′-deoxyxylostasin (**8**) was converted into 3′-chloro-3′-deoxyxylostasin (**7**) in high yield under the chlorination condition, while treatment of **7** with BSA in pyridine in a sealed tube (120 °C, 25 h) gave **8** in moderate yield.[19]

These results, together with the aforementioned observation obtained in both the substitutions (**2** → **3, 11** → **12**), indicate that silylated epiminoglycosides are intermediates in the chlorination reaction.

Acknowledgment. The authors would like to thank Drs. E. Ohmura, H. Morimoto, T. Miki, M. Yoneda, and S. Igarasi for their advice and encouragement. Thanks are also due to Mr. H. Mabuchi and Mr. M. Yamamoto for their technical assistance.

Supplementary Material Available: Typical experimental procedures for the transformations (4 pages). Ordering information is given on any current masthead page.

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(14) The δ values are from spectra of D_2O solutions containing dioxane as an internal standard. They were recorded in parts per million downfield from Me_4Si (dioxane, 67.4 ppm). Four peaks due to C-2', C-3', C-2, and C-β (N^1-acyl part) appeared at 33.7, 34.0, 34.7, and 34.9 ppm, but the exact assignment has not yet been established.
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(19) Compound **7,** mp 180–185 °C dec (from C_2H_5OH–acetone), $[\alpha]_D$ +30° (c 0.6, H_2O); compound **8,** mp 146 °C (from CH_3OH), $[\alpha]_D$ +44° (c 1.1, H_2O).

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Intrinsic Basicity Determination Using Metastable Ions

Sir:

We report a new method for the determination of intrinsic relative proton affinities. The procedure is sensitive to small differences in base strength and is simple in concept and in practice. It appears to be capable of generalization to the determination of affinities toward other ions. Present mass

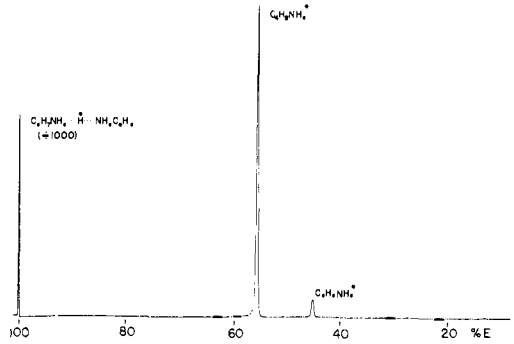

Figure 1. MIKE spectrum of the diaminated proton (*m/e* 133) formed from *n*-propylamine and *sec*-butylamine. The spectrum shows the preferential formation of the protonated butylamine as fragment ion.

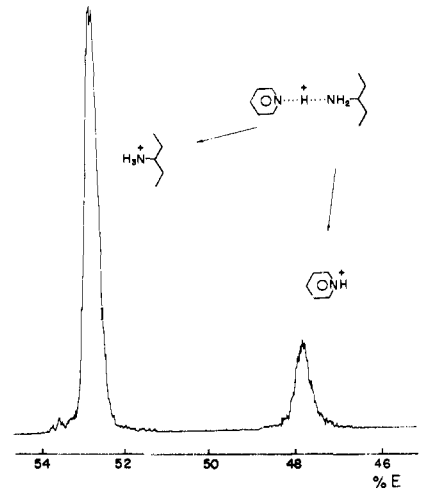

Figure 2. Part of the MIKE spectrum of the pyridine/3-aminopentane solvated proton showing the greater proton affinity of the aliphatic amine.

spectrometric methods (including ICR, CI, and flowing afterglow) determine gas phase proton affinities[1] from the position of equilibrium or the rate of proton transfer between two bases B_1 and B_2 (eq 1).

$$B_1H^+ + B_2 \rightleftharpoons B_1 + B_2H^+ \quad (1)$$

In our method we form a proton-bound adduct ($B_1HB_2^+$) and determine the relative abundances of the ions formed in the competitive reactions (eq 2).[2] The solvated proton ($B_1HB_2^+$)

$$B_1HB_2^+ \begin{cases} \nearrow B_1H^+ + B_2 \\ \searrow B_1 + B_2H^+ \end{cases} \quad (2)$$

is formed in the CI source, extracted, and separated from all other ions by mass analysis. Its spontaneous fragmentations (metastable ion reactions) are then characterized by ion kinetic energy analysis.[3] The relative abundance of the fragment ions B_1H^+ and B_2H^+ measures their relative proton affinity.

Consider two primary amines, *sec*-butylamine and *n*-propylamine. A mixture gave a CI mass spectrum showing ions at *m/e* 60 and 74 due to the protonated amines (BH^+), immonium ions at 114 and 128 formed by transamination of the $(M-H)^+$ ion and ions at 119, 133, 147 due to protons solvated with two molecules of amine. Our interest is in *m/e* 133, $PrNH_2\cdots H^+\cdots NH_2Bu$.[7] Figure 1 shows the MIKE spectrum of this ion. Two reactions occur[8] and they correspond to formation of the ions $C_4H_9NH_3^+$ (*m/e* 74) and $C_3H_7NH_3^+$ (*m/e* 60), respectively. From the ratio of these peaks we infer that *sec*-butylamine has a greater proton affinity than has *n*-propylamine. Literature data[9] confirm this point, the difference being 2.1 kcal mol^{-1}.

The basis of the method is a comparison of the rates of competitive metastable ion reactions.[10] This makes it independent of the exact form or magnitude of the internal energy distribution of the reactant ion and hence of ion source conditions. Since the competitive reactions must have virtually identical frequency factors, their rates are controlled by their relative activation energies.[11] In the absence of a reverse activation energy the difference in activation energies is *exactly* given by the difference in proton affinities of the bases. The presence of a reverse activation energy, which is expected to be small, should not spoil the correlation since similar potential surfaces are being traversed.

In an effort to determine whether the method is sensitive to even more subtle differences in proton affinities, 3-aminopentane and *sec*-butylamine, differing now in substitution at the β-carbon, were compared. Once again it was easy to identify the base with the higher proton affinity, the ion $C_5H_{11}NH_3^+$ having an abundance ten times that due to $C_4H_9NH_3^+$. (The estimated proton affinity difference[9] in this case is 1 kcal mol^{-1}.)

The relative proton affinities of aniline and *m*-toluidine are also expected to differ only slightly so these compounds were examined by this method. In doing so advantage was taken of the fact that the ions of interest can be selected after ionization of a complex mixture.[12] Thus, the two aromatic amines were introduced into the source simultaneously with *sec*-butylamine and 3-aminopentane and the mass spectrum showed ions corresponding to all possible combinations representing the diaminated proton $B_1HB_2^+$. The MIKE spectrum of the aniline/*m*-toluidine protonated dimer (*m/e* 201) showed protonated *m*-toluidine formation to be 20 times greater than protonated aniline. The aniline/*sec*-butylamine protonated dimer (*m/e* 167) gave a peak due to the protonated aromatic amine with only 1% of the intensity of that due to protonated *sec*-butylamine, which is clearly by far the stronger base. We also showed 3-aminopentane to have a considerably greater proton affinity than pyridine, the appropriate region of the MIKE spectrum being shown in Figure 2.

Two amines with very similar gas phase basicities[13] are *sec*-butylamine and pyridine, the latter having the greater basicity by 0.5 ± 0.2[14] kcal mol^{-1}. Correcting for entropy effects the difference in proton affinities is found[14] to be zero within experimental error (pyridine, 224.7 kcal mol^{-1}; *sec*-butylamine, 224.8 kcal mol^{-1}). We find the protonated pyridine ion to have an intensity 1.8 times[15] that of the protonated butylamine indicating that pyridine has the greater proton affinity.[16]

The sensitivity of the method to very small differences in basicity is a direct consequence of the fact that metastable ions have the minimal excitation energy to allow fragmentation.[11,17] Competitive reactions will not both give rise to abundant metastable ions unless they have similar activation energies.[18] For the $B_1HB_2^+$ ions, the difference required is particularly small (i) because of the similarity in frequency factors and hence in the internal energy (ϵ) dependence of the rate constants ($k(\epsilon)$) and (ii) because the reactions are expected to show steep $k(\epsilon)$ vs. ϵ curves. An analogous situation occurs[19] in competitive metastable H· and D· loss from a partially labeled ion: the isotope effect may be $\geq 10^3$. This is for a case in which the activation energy difference is of the order of 1 kcal mol^{-1}. (The difference in product enthalpies is $\Delta H_f(D\cdot) - \Delta H_f(H\cdot) = 0.9$ kcal mol^{-1}.) Recognizing that differences in metastable ion abundances of less than a factor of 2 could readily be measured, we estimate that our method should be sensitive to proton affinity differences of the order of 0.1 kcal mol^{-1}.

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Temperature Dependence of Proton Spin-Lattice Relaxation Times in Some Paramagnetic Transition Metal Acetylacetonate Complexes. The Possible Influence of the Jahn-Teller Effect on Electron Spin Relaxation

Sir:

Nuclear spin-lattice relaxation (T_1) in discrete paramagnetic transition metal complexes is dominated by electron-nuclear dipolar coupling time modulated by spin-lattice electron spin relaxation (τ_{e_1}) and molecular reorientation (τ_R); the overall correlation time (τ_c) is given by $\tau_c^{-1} = \tau_R^{-1} + \tau_{e_1}^{-1}$.[1] Electron spin relaxation is usually considered to arise by time modulation from rotational reorientation of either the anisotropic part of the g tensor (for $S = \frac{1}{2}$) and/or, for $S \geq 1$, the quadratic zero-field splitting. If the Redfield limit ($\tau_{e_1} > \tau_R$) holds for the electron spin relaxation, then, in general $\tau_{e_1}^{-1} = k\tau_R(1 + \omega_s^2\tau_R^2)^{-1}$, where k is a parameter and depends on the particular mechanism, and ω_s the electron resonance frequency. Usually $\omega_s\tau_R \gg 1$ and $\tau_{e_1}^{-1} = m\tau_R^{-1}$ and $\tau_c^{-1} = n\tau_R^{-1}$, where m and n are constants.[1] If the Redfield limit is not valid, τ_e is a simple fraction[2] of τ_R and the relationship $\tau_c^{-1} = n\tau_R^{-1}$ still holds. *Consequently, the temperature dependence of T_1 should always be that of τ_R.* τ_R varies with temperature as $\tau_R = \tau_0 \exp(E_R/RT)$ and because to good approximation,[3] $T_1^{-1} = K\tau_c$, we would expect a plot of ln (T_1^{-1}) vs. $1/T$ to be linear with slope E_R/R, where E_R is the activation energy for rotational reorientation. This behavior is only to be expected provided τ_R dominates τ_{e_1}.

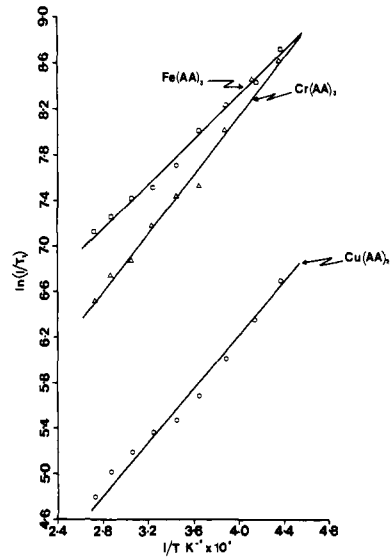

Figure 1. Plot of ln $(1/T_1)$ vs $1/T$ for the CH_3 proton T_1 of $Cu(AA)_2$, $Cr(AA)_3$, and $Fe(AA)_3$.

The solvent properties of dissolved transition metal acetylacetonate $M(AA)_l$ ($l = 2, 3$) complexes should be sufficiently similar for E_R to be approximately the same for each and so the temperature dependence of τ_R should be similar for all the Tris complexes of say the first or second transition series. Room-temperature ^1H relaxation studies of the CH_3 protons have demonstrated that for some of these complexes (M = Cr, Fe, Cu), τ_R dominates T_1 whereas for others (M = V, Mn, Ru), τ_e dominates.[2,4] Consequently, variable-temperature T_1 studies on a series of these complexes will yield information on the mechanism(s) of electron spin relaxation in solution. Specifically, for paramagnetic molecules in solution, is rotational reorientation the sole process affecting τ_e?

Plots of ln (T_1^{-1}) vs. $1/T$ for M = Cr, Fe, and Cu are shown in Figure 1.[5] A linear relationship is found with E_R (kJ mol^{-1}) 10.87 (Cr),[6] 9.20 (Cu), and 8.40 (Fe) demonstrating that the solution properties are approximately invariant to the metal ion.[7] Similar plots for M = V, Mn, and Ru are shown in Figure 2. The linearity of these plots is poor and for Mn and V there is a strong suggestion of curvature at the high-temperature end. If a linear least-squares fit[8] is performed E (kJ mol^{-1}) is estimated to be 2.16 (V), 1.34 (Mn), and 3.56 (Ru). We conclude that rotational reorientation is probably not the dominant time-dependent process for electron spin relaxation, the magnetic properties of the complex being modulated at a rate faster than τ_R. For Mn and V, in particular, the associated energy barrier is quite low.

There is no immediate connection between the ground states (in O_h symmetry) of those molecules Mn (^5E), V ($^3T_1$), Ru ($^2T_2$) which can account for the above behavior. All states, however, interact asymmetrically with the spatial environment and, in principle, are subject to Jahn-Teller forces.[9] It is known that Mn(III) complexes are strongly Jahn-Teller affected both in the solid and solution[10] and the ground state potential energy surfaces contain maxima and minima separated by low energy barriers. Estimates[10,11] of the barrier for $Mn(AA)_3$ from