Application of Lanthanide Shift Reagents to Alkyl Fluorides[1]

Sir:

The utility of certain lanthanide β-diketoenolate complexes in NMR studies of organic compounds, first demonstrated by Hinckley,[2] has been expanded on by others.[3] In practice, the use of these complexes has been restricted to systems containing relatively basic heteroatom centers, such as oxygen, nitrogen, and, to a lesser extent, phosphorus and sulfur. Here we wish to report the application of these reagents to the study of the ^{1}H NMR spectra of alkyl fluorides.

Figure 1 illustrates the influence of $Yb(fod)_3$ on the ^{1}H NMR spectrum of *n*-propyl fluoride.[4,5] Several features about these and related data are revealing. First, it is apparent that the induced chemical shift differences decrease as the average distance from the fluorine atom to the nucleus under observation increases. Second, resolution of shifted resonances is poorest for nuclei closest to the fluorine center and improves as the distance increases. Initial addition of $Yb(fod)_3$ eliminates the spin–spin coupling between adjacent methylene protons as well as remote proton–fluorine coupling. Further addition ultimately removes both the more remote proton–proton coupling and the large geminal proton–fluorine coupling. Third, successive observations carried out over a range of concentrations indicate that the observed chemical shift displacements increase monotonically with increasing lanthanide concentration. Fourth, under equivalent conditions, $Yb(fod)_3$ provides significantly greater chemical shift displacements (ca. an order of magnitude) than $Eu(fod)_3$. However, this advantage is partially offset by decreased spectral resolution (increased line widths), a characteristic of Yb(III) shift reagents that is presumably a reflection of the relatively longer spin–lattice relaxation time of the unpaired electrons on ytterbium compared to europium. Nonetheless, complimentary application of $Eu(fod)_3$ and $Yb(fod)_3$ provides a useful means of separating the resonances of alkyl fluorides: proximal protons can be shifted by $Eu(fod)_3$ without significant line width broadening while similar results can be achieved for more remote protons using $Yb(fod)_3$.[6] The dramatic effect which $Yb(fod)_3$ can have on the ^{1}H NMR spectrum of an alkyl fluoride is manifest in the spectrum of *n*-octyl fluoride (Figure 2) in which all eight nonequivalent protons are clearly visible. Equivalent results were obtained with *sec*-octyl fluoride. Induced shifts were not observed in the ^{1}H NMR spectrum of *n*-octyl chloride, bromide, or iodide under similar conditions.

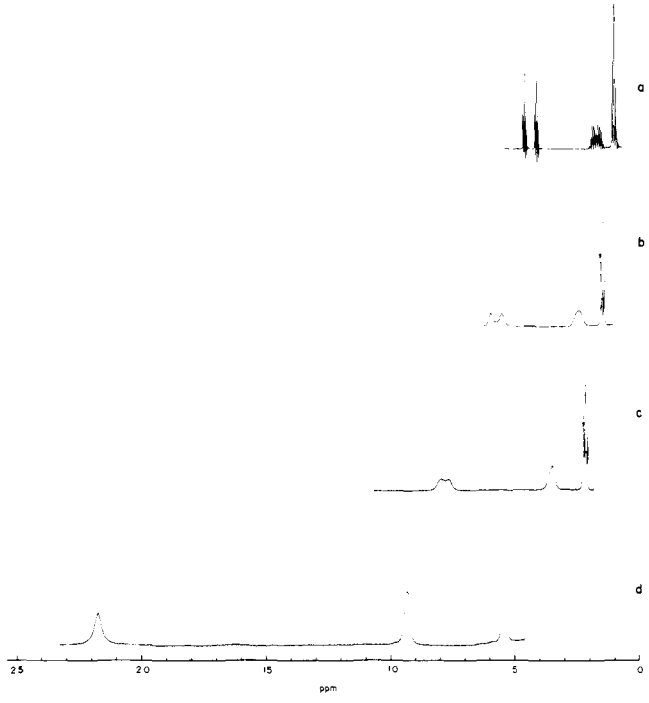

Figure 1. Spectra (100 MHz) of *n*-propyl fluoride (~0.3 *M*) in the presence of increasing concentrations of $Yb(fod)_3$ in CCl_4. The concentration of $Yb(fod)_3$ in these spectra is ca. (a) 0.0 *M*, (b) 0.1 *M*, (c) 0.2 *M*, and (d) 0.5 *M*.

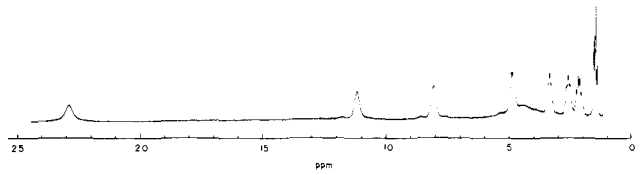

Figure 2. The influence of $Yb(fod)_3$ (ca. 0.5 *M*) on the ^{1}H NMR spectrum (100 MHz) of *n*-octyl fluoride (ca. 0.3 *M*) in CCl_4. The asterisk (*) denotes water impurity.

The nature of the interactions between an alkyl fluoride and a lanthanide shift reagent remains unclear. One possibility involves the formation of a fluorine-coordinated lanthanide–fluoroalkane complex accompanied by basically the same magnetic interactions responsible for the induced shifts witnessed in organic substrates containing much more basic heteroatom centers.[3] An alternative mechanism in which the lanthanide–substrate complex results from a purely electrostatic interaction between the highly polar C–F bond and the electropositive lanthanide center cannot at present be dismissed. A fuller discussion of these and related studies will be presented in other papers.

References and Notes

(1) Supported by the Research Corporation and the donors of the Petroleum Research Fund, administered by the American Chemical Society.
(2) C. C. Hinckley, *J. Am. Chem. Soc.*, **91**, 5160 (1969).
(3) R. E. Sievers, Ed., "Nuclear Magnetic Resonance Shift Reagents", Academic, New York, N.Y., 1973, and references therein.
(4) A detailed analysis of the ^{1}H NMR spectrum of *n*-propyl fluoride at room temperature has been carried out: D. L. Hooper, N. Sheppard, and C. M. Woodman, *J. Mol. Spectrosc.*, **24**, 277 (1967).
(5) Both $Yb(fod)_3$ and $Eu(fod)_3$ are commercially available from several sources.
(6) NOTE ADDED IN PROOF. Under comparable conditions, tris(1,1,1,5,5,6,6,7,7,7-decafluoro-2,4-heptanedionate)europium(III), $Eu(dfhd)_3$,[7] produces substantially greater chemical shift displacements (~4 ppm for the α-methylene protons in *n*-octyl fluoride) than does $Eu(fod)_3$.
(7) W. G. Scribner, B. H. Smith, R. W. Moshier, and R. E. Sievers, *J. Org. Chem.*, **35**, 1696 (1970); M. F. Richardson, W. F. Wagner, and D. E. Sands, *J. Inorg. Nucl. Chem.*, **30**, 1275 (1968); M. F. Richardson and R. E. Sievers, *Inorg. Chem.*, **10**, 498 (1971).

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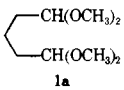
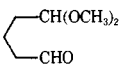
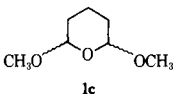
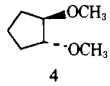
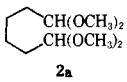
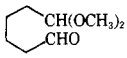
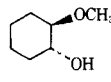
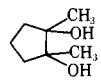
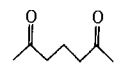
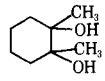
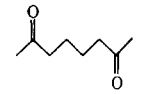
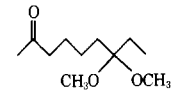
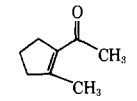
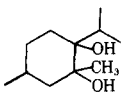
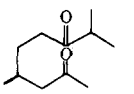
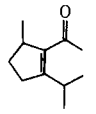
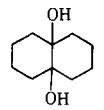
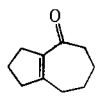
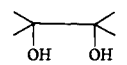
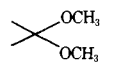
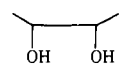
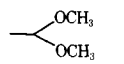
Electroorganic Chemistry. XXII. Novel Anodic Cleavage of Glycols to Carbonyl Compounds

Sir:

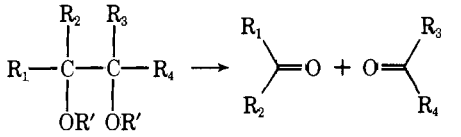
Although the cleavage of 1,2-diols by oxidizing agents such as chromic acid,[1] lead tetraacetate,[2,3] or periodic acid[2,3] has been well studied, these cleavages are not necessarily useful because of the troublesome work-up. However, in the present study, the anodic oxidation[4] of 1,2-glycols

Table I. Anodic Oxidation of 1,2-Diols and Related Compounds

Starting compound	Product	Anode potential (V vs. SCE)	Isolated yield (%)[a]
 1	 1a	2.18	56
	 1b		14 } 96
	 1c		26
 3	1a 1b 1c	2.13	56 20 } 94 18
 4	1a 1b 1c	1.75	65 2 } 67 0
 2	 2a	2.02	51 } 65
	 2b		14
 5	2a 2b	2.30	45 9 } 54
 6	2a 2b	–	43 9 } 52
 7		2.20	35
 8		2.20	36
			9 } 61
			16
 9		–	35 } 70
			35
 10		–	65
 11		2.02	11 } 89
			78
 12		2.22	47

[a] This yield corresponds to the current yield since it was determined at the stage when 2 F/mol of electricity was passed.

and related compounds was found to be a novel and remarkably clean method for the cleavage of the 1,2-diols to the corresponding carbonyl compounds (eq 1).



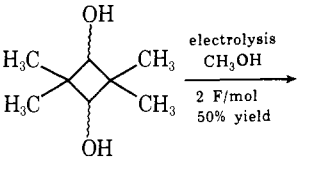
(1)

R′ = H or methyl

The anodic oxidation of compounds **1–12** in methanol containing tetraethylammonium *p*-toluenesulfonate as a supporting electrolyte was carried out using carbon rod electrodes. The results are shown in Table I. All of the products were identified by the elemental and spectroscopic analyses.

This anodic oxidation did not show any of the stereochemical limitations usually observed in the cleavage reaction by chemical oxidizing agents.[5] Furthermore, 1,2-dimethoxy (**4**) and 1-hydroxy-2-methoxy (**5**) compounds were also oxidizable in almost similar current efficiencies to those of 1,2-diols. Cyclohexene oxide was found to be oxidized by passing through the initial formation of the corresponding hydroxy ether.

On the basis of the lower ionization potentials of ethers or alcohols compared to those of saturated hydrocarbons,[6] the initiation step of this anodic oxidation may be the electron transfer from the lone pair electrons of oxygen to the anode. The similar electron transfer mechanism was suggested in the electrochemical fission of a vicinal diketal.[7] The electron transfer may be assisted by the neighboring hydroxy or ether group since 1,3-, or 1,4-dihydroxycyclohexane, 2-methylcyclohexanol, or 3,3-dimethylbutan-2-ol was anodically unoxidizable. Some strained compounds such as **13** and **14**, however, were found to be anodically oxidizable owing to the relief of the strain energy (eq 2 and 3).



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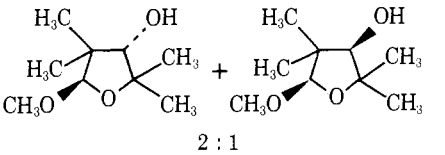
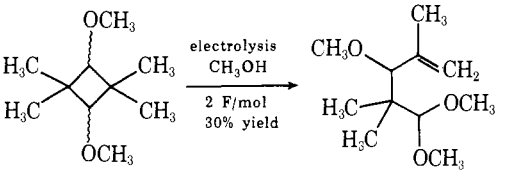


(2)

2 : 1



(3)

14

The simplicity, cleanness, and nonpolluting nature of this novel anodic cleavage reaction would possess a remarkable potentiality in organic syntheses.

References and Notes

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Kalinowski, *J. Am. Chem. Soc.*, **91**, 6863 (1969), and earlier work cited therein; (b) R. F. Michielli and P. J. Elving, *ibid.*, **91**, 6864 (1969).
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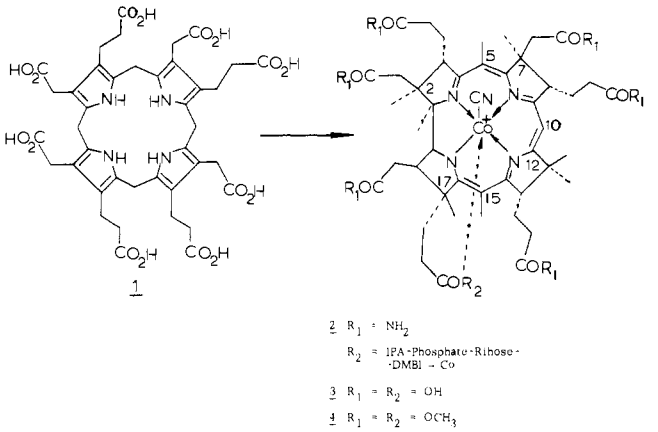
Concerning the Intermediacy of Uro'gen III and of a Heptacarboxylic Uro'gen in Corrinoid Biosynthesis

Sir:

Previous work from this laboratory has provided evidence that in whole-cell[1,2] and cell-free[3,4] systems, the enzymes of *Propionibacterium shermanii* utilize uro'gen III (**1**) for the production of cyanocobalamin[1,2] (**2**) via cobyrinic acid[3,4] (**3**). These experiments employed side-chain labeled samples of uro'gen III obtained both by chemical synthesis (in admixture with types I, II, and IV uro'gens) and enzymatic preparation (together with uro'gen I). It was clearly demonstrated in experiments with ^{13}C-enriched substrates that the label in the side-chain propionate groups was carried to the corresponding positions in the appropriate corrin. However,



the intrinsic symmetry of these labeling patterns together with the problems of employing an isomer mixture left open the logical (if unlikely) possibility that in vitro dissociation of the uro'gen into labeled fragments capable of assimilation by the enzyme system could give rise to the observed regiospecific enrichments *without mediation of the intact uro'gen III molecule.* In order to resolve this question of vital importance for the mechanism of corrin biosynthesis,[2,5] we have undertaken the regiospecific synthesis of a set of uro'gens whose patterns of enrichment with both stable and radioisotopes are designed to provide unambiguous probes for intact biotransformation and for the nature of the overall mechanism connecting the uro'gen and corrin structures.

The regiospecific syntheses of [α,γ-$^{14}C_2$]- and of ring B propionic acid [$^3H_2$]uro'gen III were carried out by the procedures of MacDonald[6] and Franck,[7] modified where appropriate for the introduction of radioisotope.[8] Incubation of the doubly labeled uro'gen ($^3H/^{14}C$, 4.10; Scheme I) in the cell-free system from *P. shermanii*[9] gave, after dilution with carrier, conversion to cobester (**4**), and crystallization to constant activity, a sample of cobester (**4**) with $^3H/^{14}C$

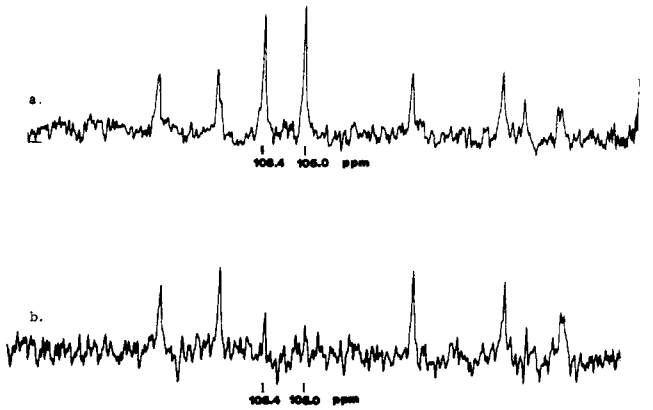
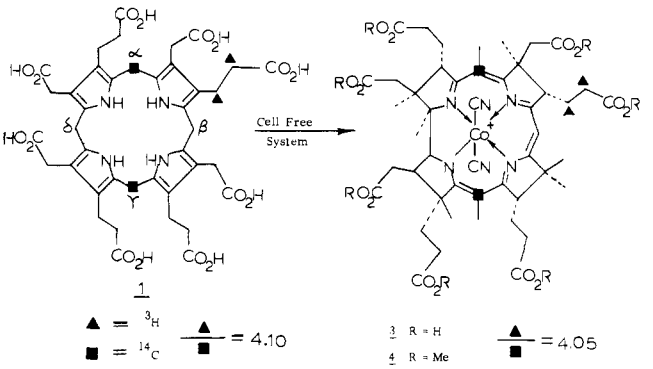


Figure 1. (a) Proton noise-decoupled ^{13}C-FT NMR spectrum of [^{13}C]uro'gen III enriched cyanocobalamin (D_2O; 4K points) and assigned labeling patterns. (b) Proton noise-decoupled ^{13}C-FT NMR spectrum of natural abundance cyanocobalamin (D_2O; 4K points).

Scheme I



4.05. Any randomization via fragmentation–recombination would have led, in the case of this unsymmetrically labeled substrate, to a profound change in the tritium–carbon ratio. To confirm this result and at the same time locate the site of label in the corrin, a specimen of [α,γ-$^{13}C_2$]uro'gen III was prepared via condensation of the dipyrromethane dialdehyde (**5**) and dipyrromethane (**6**), with introduction of ^{13}C from dimethylformamide (90% ^{13}C) by a procedure established above for the synthesis of the ^{14}C radiomer to give finally a sample of the α,γ-^{13}C-enriched uro'gen (90% ^{13}C). Administration of 365 mg of this "north-south" labeled substrate to resting whole cells of 340 g of *P. shermanii*[10] *gave (after the usual work-up)*[2,11] *pure cyanocobalamin (11 mg)* (**2**) whose FT ^{13}C NMR spectrum (Figure 1a) on comparison with the natural abundance spectrum taken under identical conditions (Figure 1b) revealed enhancement (4.5% specific incorporation) at only two resonances in the sp^2 region, viz., at 105.0 and 108.4 ppm downfield from Me_4Si. These signals had previously been assigned to C_{15} and C_5, respectively, both by the correlations of Allerhand[12] and by biosynthetic labeling.[1,2] This experiment