This view of the reaction led us to anticipate an especially high migrational aptitude for benzyl and benzhydryl β substituents, and this has been confirmed by experiments with III and IV. Thus, irradiation[9] of a 0.025 *M* solution of IV in ether for 3.5 hr gave roughly 50% conversion to a 1:4 mixture of XI and XII.[10] The sole rearrangement product obtained from a similar irradiation of III proved to be X (*ca.* 20%), but this was accompanied by significant quantities of fragmentation products (*e.g.*, IX, dibenzyl and α-benzylethyl ethyl ether). Since X was essentially unreactive under equivalent reaction conditions, the formation of the latter products suggests that intermediate C is in this case at least partly diverted to the radical pair D, and that the relatively stable benzyl radical escapes the solvent cage.

Other photochemical transformations recently established in our laboratory are: I to IX (*ca.* 40%) and XIII (*ca.* 4%); VI to XIV (*ca.* 40% by a technique involving continuous extraction of the product); and V to cyclopentane-1,3-dione and an unidentified base-soluble substance.

The rearrangements described in this communication together with previous findings[1-4] support the following rough order for the migrational aptitude of β substituents: benzhydryl and benzyl > hydrogen > methylene > methyl ≫ phenyl. The position of hydrogen in this listing argues against a general fragmentation mechanism for the rearrangement, since hydrogen atoms are not normally produced in preference to alkyl radicals. Also, the formation of a strained four-membered ring (XIV) in the photolysis of VI[11] leads us to prefer a single step or synchronous route for rearrangement from C. If a radical pair (*i.e.*, D) was an intermediate in this rearrangement, the formation of a six-membered heterocyclic system or possibly fragmentation with loss of ethylene would seem to provide attractive alternate reaction modes. Products of this type were not found.

Acknowledgment. This work was supported in part by Grant GP-02025 from the National Science Foundation. We thank Dr. Peter Wagner for helpful and stimulating discussions.

(9) These experiments employed a 450-w mercury lamp (Hanovia) equipped with a Corex filter.

(10) The compounds described in this paper were identified by a combination of carbon and hydrogen analysis, infrared, nmr, and mass spectroscopy, chemical degradation or derivative formation, and direct comparisons with authentic materials when possible.

(11) Wehrli, *et al.*,[4] have reported the first example of rearrangement to a cyclobutanone derivative.

Charles S. Markos, William Reusch
Department of Chemistry, Michigan State University
East Lansing, Michigan 48823
Received April 10, 1967

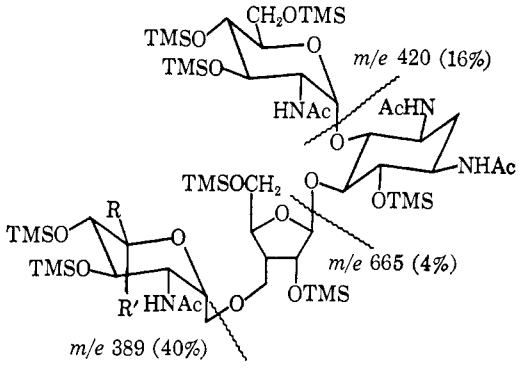
Mass Spectrometric Studies on Aminocyclitol Antibiotics

Sir:

We wish to report preliminary results of a mass spectrometric investigation of the antibiotics paromomycin[1] and paromomycin II[2] (**1a** and **1b**, respectively, TMS and Ac = H), members of the diaminocyclitol (deoxystreptamine) class of antibiotics.[2-4]

The above-mentioned antibiotics, together with the model compounds derived from them and from the neomycins by various degradative reactions,[2-4] were investigated in the form of their N-acetyl-O-trimethylsilyl derivatives. The use of the trimethylsilyl (TMS) blocking groups was found advantageous in the study of these molecules of low volatility. The N-acetyl and N-acetyl-3-*d* derivatives **1–6** (TMS = H) were prepared by selective N-acetylation of the respective free bases with acetic anhydride in methanol. The chromatographically homogeneous solids[5] (compounds **2**, **4–6**, TMS = H, were obtained crystalline) were then subjected to silylation with trimethylsilyl chloride and hexamethyldisilazane in dry pyridine.[6] The trimethylsilyl ethers **1–6** thus obtained were nonhygroscopic white solids which had the infrared and nmr spectral properties expected for N-acetyl-O-trimethylsilyl derivatives.

A minute molecular ion peak is present in the mass spectrum[7] of the N-acetyl-O-trimethylsilyl derivative of paromomycin II (**1b**). A peak of 2.5% intensity (relative to *m/e* 73, $(CH_3)_3Si^+$) at *m/e* 1386 is characteristic of the loss of a methyl radical from a trimethylsilyl group.[8] Relatively intense peaks are also present at *m/e* 665 (4.0%), 420 (16.0%), and 389 (40.0%) from cleavages of glycosidic bonds as indicated in structure **1**. Other fragments in the spectrum can be accounted for by further fragmentations of the molecular ion and of these fragment ions.



1a, R = H; R′ = CH_2NHAc
b, R = CH_2NHAc, R′ = H
(M − CH_3, *m/e* 1386 (2.5%)

(1) (a) T. H. Haskell, J. C. French, and Q. R. Bartz, *J. Am. Chem. Soc.*, **81**, 3480 (1959); (b) T. H. Haskell and S. Hanessian, *J. Org. Chem.*, **28**, 2598 (1963).

(2) K. L. Rinehart, Jr., "The Neomycins and Related Antibiotics," John Wiley and Sons, Inc., New York, N. Y., 1964; S. Tatsuoka and S. Horii, *Proc. Japan Acad.*, **39**, 314 (1963).

(3) J. D. Dutcher, *Advan. Carbohydrate Chem.*, **18**, 259 (1963).

(4) S. Hanessian and T. H. Haskell, "The Carbohydrates," Vol. 2, W. Pigman and D. Horton, Ed., Academic Press Inc., New York, N. Y., in press.

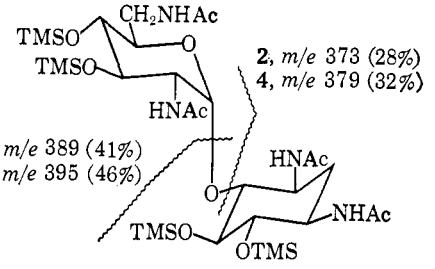
(5) Thin layer chromatography of the N-acetates was carried out on glass plates coated with Avirin (a product of American Viscose Corp., Marcus Hook, Pa.) and the compounds were detected by spraying lightly with a 1% solution of potassium permanganate in 1 *N* sulfuric acid or by exposure to iodine vapors.

(6) In a typical experiment, 0.1 g of N-acetyl derivative dissolved in 5 ml of dry pyridine was treated with 1 ml of trimethylsilyl chloride and 3 ml of hexamethyldisilazane at room temperature. After 1–2 hr the mixture was evaporated to dryness, the residue was suspended in benzene, and the soluble portion was evaporated to dryness and used as such.

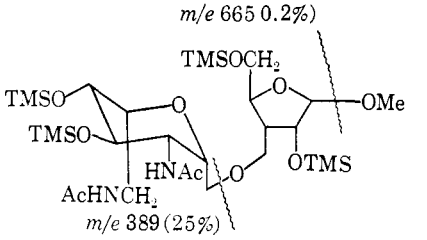
(7) The mass spectra of compounds **2–6** were obtained from an Atlas CH4 mass spectrometer, using a vacuum-lock direct-inlet system. The authors wish to thank Dr. W. J. McMurray, Yale University School of Medicine, for obtaining the spectrum of compound **1b** on an AEI MS9 mass spectrometer.

(8) A. G. Sharkey Jr. R. A. Friedel, and S. H. Langer, *Anal. Chem.*, **29**, 770 (1957).

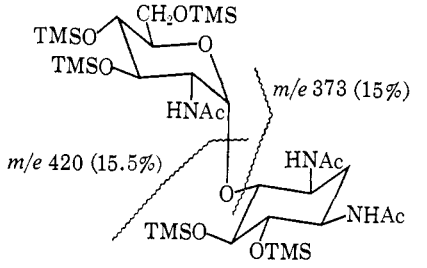
Prominent peaks at *m/e* 389 are also present in the mass spectra of model compounds **2** and **3** and shift to *m/e* 395 in the spectrum of the d_6 analog **4**. The mass spectra of compounds **5** and **6** have peaks at *m/e* 420, as does the spectrum of **1**. A few other important peaks are indicated in **2**–**6**. All peak intensities are relative to *m/e* 73, $(CH_3)_3Si^+$.



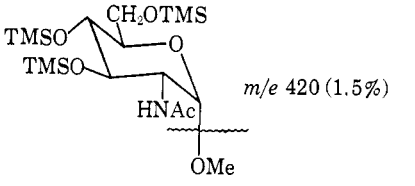
2, Ac = CH_3CO (M − CH_3, *m/e* 763, 8%)
4, Ac = CD_3CO (M − CH_3, *m/e* 775, 11%)



3 (M − CH_3, *m/e* 681, 4%)



5 (M − CH_3, *m/e* 794, 4%)



6 (M − CH_3, *m/e* 436, 13%)

From these data, it is possible to recognize the sequential arrangement and gross structures of the units of which the saccharides are comprised. Differences in stereochemistry and ring size most likely will not affect the indicated fragmentation paths. Compound **1** shows a preferential cleavage of glycosidic bonds, placing the charge on the carbon next to a ring oxygen where it can be stabilized by the nonbonding electrons on oxygen. Although all of the mass spectra in this study exhibited only minute molecular ion peaks (0.2–1% relative intensity), molecular weights can be readily determined from the more intense peaks 15 mass units lower.

Whereas the characterization of various amino and deoxy sugars derived from antibiotic substances has been successfully accomplished by mass spectrometric techniques,[4,9,10] the detailed analysis of intact antibiotics containing sugars is still relatively unexplored.[4] The few recorded examples belong to the class of macrolide (chalcomycin,[10] pimaricin,[11] and aldgamycin[12]) and nucleoside (cordycepin,[13] puromycin[14]) antibiotics. The present investigation represents the first reported example of the application of mass spectrometry to the study of the gross structure of *intact* aminocyclitol antibiotics. It demonstrates the potential usefulness of this technique in providing crucial information concerning the structure of related compounds, from submilligram quantities of the appropriate derivatives and from minutes of instrument time. Experiments on the electron-impact-induced fragmentation of related aminocyclitol antibiotics are in progress.

(9) D. C. DeJongh and S. Hanessian, *J. Am. Chem. Soc.*, **87**, 3744 (1965); **88**, 3114 (1966).
(10) K. L. Rinehart, Jr., R. F. Schimbor, and T. H. Kinstle, *Antimicrobial Agents Chemotherapy*, 119 (1965).
(11) O. Ceder, *Acta Chem. Scand.*, **18**, 126 (1964); B. T. Golding, R. W. Rickards, W. E. Meyer, J. B. Patrick, and M. Barber, *Tetrahedron Letters*, 3551 (1966).
(12) M. P. Kunstmann, L. A. Mitscher, and N. Bohonos, *ibid.*, 389 (1966).
(13) S. Hanessian, D. C. DeJongh, and J. A. McCloskey, *Biochim. Biophys. Acta*, **117**, 480 (1966).
(14) S. H. Eggers, S. I. Biedron, and A. O. Hawtrey, *Tetrahedron Letters*, 3271 (1966).
(15) The support of the Public Health Service of the Department of Health, Education, and Welfare, through Grant AI 07570, is gratefully acknowledged.

Don C. DeJongh,[15] Jeremy D. Hribar
Department of Chemistry, Wayne State University
Detroit, Michigan 48202

Stephen Hanessian, Peter W. K. Woo
Research Laboratories, Parke, Davis and Company
Ann Arbor and Detroit, Michigan
Received April 1, 1967

Metal–Ammonia Reduction of Nonconjugated Dienes and Enones[1]

Sir:

A consequence of a structurally imposed close proximity of two nonconjugated double bonds is that the energy of the lowest antibonding orbital of one is raised while that of the other is lowered. One of the several consequences of this which might be anticipated is the increased ability of the molecule to accept an electron in the relatively low energy antibonding orbital. It might be expected that the activation energy will be lowered and the equilibrium constant raised for the reversible process $M + e^- \rightleftarrows M\cdot^-$. An example of this structural feature is norbornadiene (I). It appears to have no resonance energy in the ground state, and thus can in no sense be considered aromatic, but it has a significant 2–6 bonding contribution in the excited state.[2] A spectroscopic manifestation of this is its relatively long wavelength untraviolet absorption (λ_{max} 211 mμ). We wish now to describe a chemical consequence of this perturbation, the reduction of such nonconjugated dienes and enones by metal–ammonia systems.

The reduction of I with sodium or lithium in carefully dried ammonia (−33°) afforded norbornene (II) in 98% yield.[3] No evidence for even traces of

(1) The authors are indebted to the National Science Foundation, Grant GP 6757, and to the University of Utah Research Fund for the support of this study.
(2) C. F. Wilcox, S. Winstein, and W. G. McMillan, *J. Am. Chem. Soc.*, **82**, 5450 (1960).