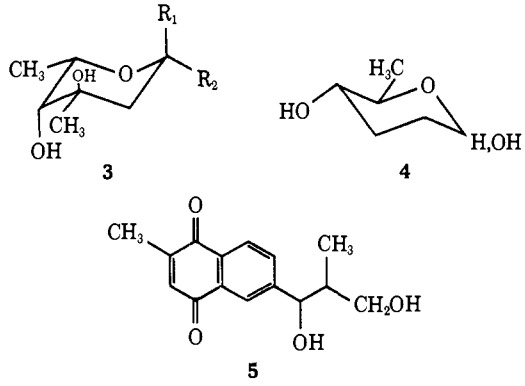
glycoside, R_1 = OMe, R_2 = H), $[\alpha]D$ −27.7°; **1b** (β-glycoside, R_1 = H, R_2 = OMe), $[\alpha]D$ +32°, $C_{29}H_{38}O_{10}$, mol wt 555[1] (calcd 546.7); **2** (3:1 mixture of α and β anomers), mp 114°, $[\alpha]D$ +107°; and anomeric axenose methyl glycosides **3a** (α anomer, R_1 = OMe, R_2 =



3 **4** **5**

H, mp 101–103°, $[\alpha]D$ −142°) and **3b** (β anomer, R_1 = H, R_2 = OMe, mp 122–123°, $[\alpha]D$ +38°). **1a** and **1b**, $\nu_{CO\ ester}$ 1735 cm^{-1}, gave monoacetate (pyridine and Ac_2O) containing one hydroxyl not acetylatable. They were converted by further methanolysis to **2**, **3a**, and **3b**, whereas **1b** yielded **6** on alkaline saponification.

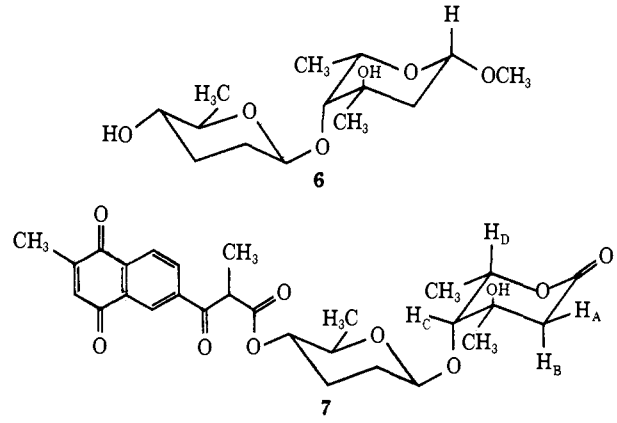
Compound **2**, *m/e* 402 (M), was saponified in methanolic 0.5 *N* NaOH to give, with concomitant decomposition of the chromophore, an anomeric mixture of methyl glycosides which were hydrolyzed with acid to the free sugar **4**, identified by direct comparison of the 2,4-dinitrophenylhydrazone (mp 156–157°, $[\alpha]D$ −10° (*c* 0.28), pyridine) with an authentic sample of D-amicetose 2,4-dinitrophenylhydrazone.[6] On the other hand, reductive hydrolysis of **2** with excess $NaBH_4$ in aqueous MeOH, followed by air reoxidation, gave, together with D-amicetose methyl glycosides, the chromophore fragment **5** (*m/e* 260 (M), diacetate *m/e* 344 (M)). The structure of **5** was determined from pmr data. The pmr spectrum ($CDCl_3$) of **3b** shows signals at δ 1.28 (C-5 Me, d, J = 6.5 Hz), 1.34 (C-3 Me, s), 1.50–1.85 (C-2 protons, m, AB part of an ABX system), 1.77 (C-3 OH, s), 2.27 (C-4 OH, d, J = 10 Hz), 2.98 (C-4 H, dd, $J_{H,OH}$ = 10 Hz, $J_{4,5}$ < 1 Hz), 3.51 (CH_3O, s), 4.13 (C-5 H, dq, $J_{4,5}$ < 1 Hz, J_{H,CH_3} = 6.5 Hz), and 4.63 (C-1 H, dd, $J_{1,2ax}$ + $J_{1,2eq}$ = 12.5 Hz). The methyl glycosides **3a** and **3b** are not oxidized by periodate, thus revealing the trans orientation of the C-3 OH and C-4 OH. Configuration at C-3 was established by ir (CCl_4, 0.005 *M*) absorption at 3590 (sharp, free OH) and at 3530 cm^{-1} (broad, H-bonded OH) of the α anomer **3a**, indicating 1,3-diaxial interaction of C-3 OH and OMe.[7] On acid treatment **3a** and **3b** afforded the new sugar axenose (2,6-dideoxy-3-*C*-methyl-L-xylohexose), *m/e* 145 (M − OH), mp 111–112°, $[\alpha]D$ at the equilibrium −28.5° (*c* 1, H_2O).[8]

(6) E. L. Albano and D. Horton, *J. Org. Chem.*, **34**, 3519 (1969).

(7) R. J. Ferrier, W. G. Overend, G. A. Rafferty, H. M. Wall, and N. R. Williams, *Proc. Chem. Soc.*, 133 (1963); B. Flaherty, W. G. Overend, and N. R. Williams, *J. Chem. Soc. C*, 398 (1966). The β anomer (**3b**) showed two sharp not associated hydroxyl absorptions at 3620 and 3580 cm^{-1}. As expected, the C-3 OH pmr signal of **3a** appeared at a lower field (δ 3.98) than in the spectrum of **3b**. The anomeric proton of **3a** absorbs at δ 4.82 (dd, $J_{1,2ax}$ + $J_{1,2eq}$ 5 Hz); the methoxy group is at δ 3.40.

(8) Racemic 2,6-dideoxy-3-*C*-methyl-DL-xylohexose (DL-4-epimycarose) was obtained by synthesis.[9] The 3-*O*-methyl derivative of axenose (L-arcanose) is a component of the antibiotic lankamycin.[10]

Compound **6** (mp 148–150°, *m/e* 290 (M), $[\alpha]D$



6 **7**

−120°) shows an axial glycosidic proton in the amicetose residue (pmr ($CDCl_3$) signal at δ 4.47, dd, $J_{1,2ax}$ + $J_{1,2eq}$ = 12 Hz), thus revealing the stereochemistry (β-glycoside) at this center. The pmr spectrum (DMSO-d_6)[11] shows two OH signals at δ 4.65 (amicetose C-4 OH, d, J = 5.0 Hz) and δ 4.53 (axenose C-3 OH, s). The above evidence fully agrees with structure **1**.

Additional support to this structure was provided by **7** (*m/e* 528 (M), ν_{OH} 3460, $\nu_{conj\ CO}$ 1700 cm^{-1}), obtained by mild chromic acid oxidation[2] of axenomycin B. The pmr spectrum ($CDCl_3$) of **7** shows, *inter alia*, signals at δ 1.51 (C-10 Me, d, J = 7.0 Hz), 2.43 and 2.64 (H_A, H_B, two d, $J_{A,B}$ = 17.5 Hz), and 4.92 (H_D, dq, $J_{D,Me}$ = 7 Hz, $J_{C,D}$ = 1.5 Hz).

Acknowledgments. We are indebted to Dr. G. Cassinelli for preparing reference deoxysugars, to C. Corti, B. Pellegatta, and E. Gandini for skillful technical assistance, and to A. Alemanni for the microanalyses.

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(10) W. Keller-Schierlein and G. Roncari, *Helv. Chim. Acta*, **45**, 138 (1962); **47**, 78 (1964).

(11) O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, **86**, 1256 (1964).

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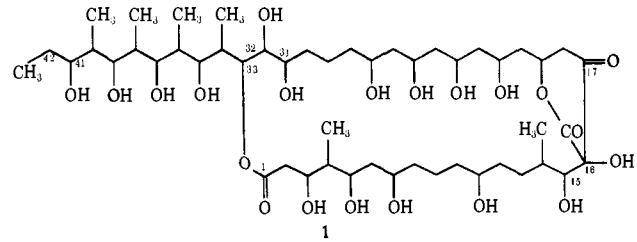
Axenomycins. II. The Structure of Axenolide

Sir:

Axenolide (**1**),[1] the aglycone of axenomycin B, is a



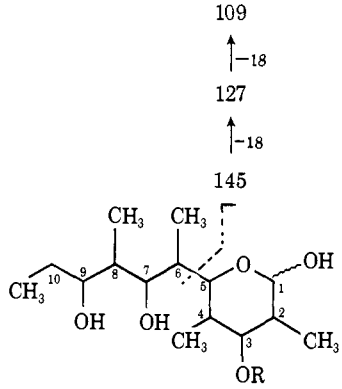
1

neutral, saturated, polyhydroxylated macrolide, C_{50}-

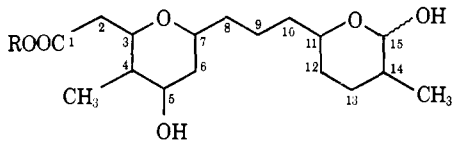
(1) F. Arcamone, W. Barbieri, G. Franceschi, S. Penco, and A. Vigevani, *J. Amer. Chem. Soc.*, **95**, 2008 (1973).

$H_{92}O_{21}$, mol wt 1033[2] (calcd 1028), containing two ester groups and consuming 3 mol of periodate.

Alkaline hydrolysis (0.025 *N* NaOH at 80°) followed by periodate cleavage gave the hemiacetal aldehydes **2** (*m/e* 273, M − OH), **3** (*m/e* 301, M − OH), and **4a**



2, R = H
3, R = CHO



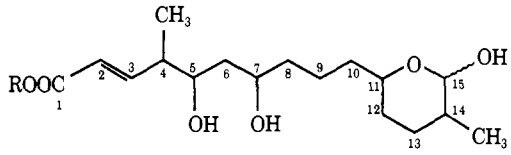
4a, R = H
b, R = CH_3

(methyl ester **4b**, *m/e* 326, M − H_2O) corresponding to the units C-33–C-43, C-32–C-43, and C-1–C-15, respectively.[3] The pmr spectrum of **2** (C_5D_5N) shows, *inter alia*, signals corresponding to the anomeric proton (δ 5.23), to three C*H*OH (C-9 H δ 4.09, C-7 H 3.84, and C-3 H 3.74), and to one ethereal proton (δ 3.41).

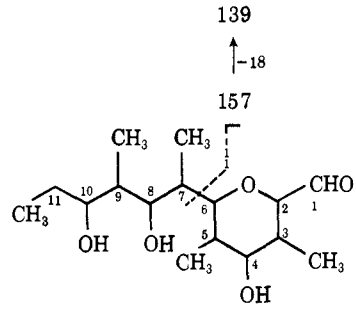
The pmr spectrum of **3** differs from that of **2** mainly because of the formate proton signal at δ 8.41. The isolation in a small amount of the formate **3** shows the presence in **1** of the vicinal triol at C-31–C-33. The pmr spectrum (C_6D_6) of the diacetate of **4b** shows the signals of the anomeric proton (δ 5.40), of the C-5 H (δ 4.88), and of the ethereal protons (C-3 H δ 4.39, C-7 H 3.66, and C-11 H 3.27). The formation of the tetrasubstituted ethereal ring of **4** is interpreted as due to a Michael-type addition of the C-7 OH to an intermediate with the double bond between C-2 and C-3.

By mild alkaline treatment alone (0.25 *N* NaOH at 20° for 72 hr), **1** undergoes a retro-aldol cleavage to give **4a**, indicating the presence of the carbonyl group in the 17 position. Moreover, the $NaBH_4$ treatment of **1** gives a product which no longer undergoes retro-aldol cleavage. On the other hand, the presence of the vicinal diol at C-15–C-16 is confirmed by the formation of **4a** by reaction with $NaBH_4$, NaOH, and $NaIO_4$, in that order.

The treatment of **1** with $NaIO_4$ in 0.5 *N* H_2SO_4 afforded a fragment (*m/e* 596, M − $3H_2O$) formed by oxidation of C-15 OH–C-16 OH and C-31 OH–C-32 OH; by alkaline treatment this compound gave **4a**, **5a**,[3] and **6**.[3] Methyl ester **5b** (*m/e* 326, M − H_2O) differs from **4b** because it has an uv absorption at 208



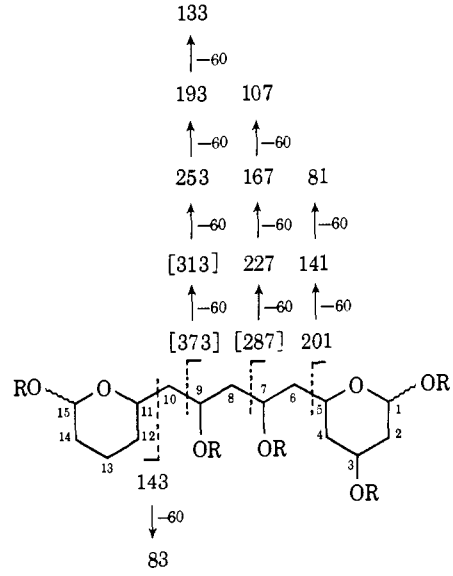
5a, R = H
b, R = CH_3



6

nm and the pmr spectrum (C_6D_6) of the triacetate shows two olefinic protons (C-3 H δ 7.02, and C-2 H 5.84) and only one ethereal proton (δ 3.26). Compound **6** (*m/e* 302, M) gave a triacetate whose pmr spectrum ($CDCl_3$) differs from that of **2** for the presence of one formyl proton (δ 9.24) and of two ethereal protons (C-2 H δ 3.82, and C-6 H 3.46). The isolation of **6** instead of **2** unequivocally shows that the carboxyl in position 1 of the axenolide is esterified with the C-33 OH. The same reaction also gave oxalic acid, originating from the periodate oxidation of the C-15 to C-17 CH(OH)C(OH)(COOH)CO sequence.

The remaining moiety C-17–C-31 was obtained by treating **1** with $NaBH_4$ and $NaIO_4$, in that order. Beside the products described, the hemiacetal aldehyde **7a** (*m/e* 284, M − $2H_2O$) was isolated and characterized



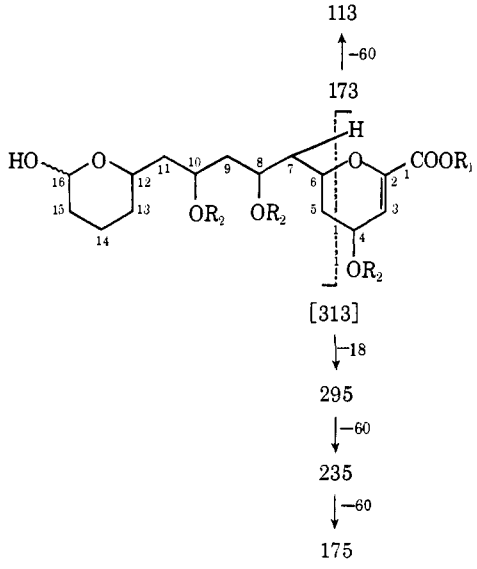
7a, R = H
b, R = Ac

as pentaacetate **7b** (*m/e* 471, M − 59). The pmr spectrum (CCl_4) of **7b** shows the signals of two anomeric protons (δ 6.10 and 5.54) and two ethereal protons (δ 4.1–3.2). The structure of **7b** was determined by

(2) See ref 1, footnote 1.
(3) The structures were determined from pmr data since double irradiation revealed the contiguity of all the protons. The mass spectra gave independent proofs of the structures.

means of the mass spectrum,[4] in which the most intense peaks correspond to pyrylium (*m/e* 81) and dihydropyrylium (*m/e* 83) ions.

Finally, treatment of **1** with $NaIO_4$ gave an acidic compound, **8a**, which, on treatment with CH_2N_2 and



8a, $R_1 = R_2 = H$
b, $R_1 = CH_3$; R_2 = Ac

Ac_2O, in that order, afforded **8b** (*m/e* 468, M − H_2O),[4] showing uv absorption at 224 nm and, in the pmr spectrum ($CDCl_3$), one olefinic proton (δ 6.03), three CHOAc groups, and a free anomeric proton absorbing in the range δ 5.3–4.7 derived from partial deacetylation during isolation.[5] Compound **8a** would originate from the cleavage of bonds C-15–C-16 and C-31–C-32, followed by decarboxylation of an α,β-diketo acid intermediate, oxidation at C-16, cyclization, and loss of an H_2O molecule from the resulting α-keto acid.

The above data require the axenolide be represented as **1**; the lactone ring formed by the carboxyl at C-16 (for which no data on the determination of the size are presently available) is supposed to be a six-membered ring.

(4) The masses of the principal fragment ions of the seco compounds were determined by high resolution mass spectrometry and agreed with the calculated values within acceptable limits. In the formulas the most significant ions are indicated.

(5) An acetylation experiment performed in the pmr tube (C_5D_5N) showed a shift to lower field of one proton.

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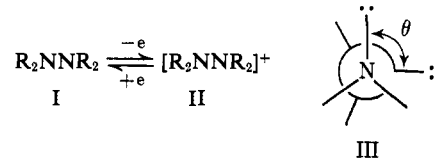
Photoelectron Spectra of Hydrazines. I. Dependence of the Lone Pair–Lone Pair Splitting on Dihedral Angle for Tetraalkylhydrazines

Sir:

We have been particularly interested in the molecular geometry of hydrazines in conjunction with studies of the tetraalkylhydrazine (I)–hydrazinium radical cation (II) redox couple,[1] which have shown a substantial sensitivity of $E_{1/2}$ to structure. *Ab initio* calculations on hydrazine[2] and methylhydrazine[2f] indicate that the lone pair–lone pair dihedral angle θ (see III) is about 90°



in agreement with far-infrared[3a] and microwave[3b–d] results. It has been widely accepted that this is largely a result of repulsion between the four lone pair electrons in two adjacent orbitals;[2] their overlap is minimized at $\theta = 90°$.[4]

In more complex molecules, steric effects can clearly alter θ, as nmr studies of cyclic tetraalkylhydrazines[5] and bis(hydrazines)[6] have shown.

We report here the photoelectron spectra[7] (pes) of several tetraalkylhydrazines, which demonstrate that pes show a substantial dependence upon θ. The pes for **1–9** had broad peaks which were usually well resolved from the continuum absorption caused by σ-bond ionization. Two such peaks were observed for all but **3**, **4**, and **7**, in which olefinic or oxygen lone pair ionizations result in low energy peaks (see Figure 1). From pes studies of amines[8] and other hydrazines,[9] ionization from the "lone pair" orbitals is expected to occur at lower energy than those from the σ bonds, and we have assigned the lowest energy ionizations, which occur below 10.5 eV, to the "lone pair" ionizations. Our data[10] are summarized in Table I.

Two "lone pair" ionizations are expected for a hydrazine group, corresponding to the symmetric (n_+) and antisymmetric (n_-) combinations of the "lone pair" orbitals. Substantial variation in the size of the difference of these ionization potentials (designated Δ in Table I) was observed with structure, and a dominant inductive effect is ruled out by the data. Included in Table I are estimates for θ, derived from nmr studies.[5,6]

1 exists in the anti conformation **1a**[6b] (θ about 180°), while **5** is in a syn conformation (**5a**), presumably twisted somewhat from $\theta = 0$ by both steric and electronic interactions. **2–4** are in approximately eclipsed ($\theta = 120°$) conformations like **2a**, which may well deform slightly to increase the methyl–methyl distance and lower θ, whereas **6** and **7** are more flexible, and should be able to more closely approach the electronically

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(4) Recently, Radom, Hehre, and Pople[2f] have suggested that "backbonding" between the N–H bonds and the lone pair orbitals, which is maximized at $\theta = 90°$, is responsible.

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(10) Determined on a Varian IEE-15 instrument.