calculations at the optimized geometry were done with a larger basis set of the form (13s9p1d/10s6p1d/5s1p)/[6s4p1d/5s3p1d/3s1p].[17] All of the calculations on **5** and **6** were done with basis set 1.

The calculated geometry for **3** has r(Si–C) = 1.872 Å, r(C–N) = 1.141 Å, r(Si–H) = 1.467 Å, and θ(HSiH) = 111.5° in good agreement with the experimental[18] values of r(Si–C) = 1.847 Å, r(C–N) = 1.158 Å, and r(Si–H) = 1.49 Å. For **4**, the geometry is not known, and we calculate r(Si–N) = 1.745 Å, r(N–C) = 1.165 Å, r(Si–H) = 1.466 Å, and θ(HSiH) = 111.0°. The cyano stretch in **3** is calculated to be at 2488 cm^{-1} (scaled, 2189 cm^{-1})[19] and in **4** at 2294 cm^{-1} (scaled, 2019 cm^{-1}). The calculated splitting is somewhat larger than what is found experimentally in **1** and **2** and for Me_3SiCN and Me_3SiNC.[1,3] The calculated intensity of the cyano stretch in **3** is 11 km/mol, almost 50 times less intense than the cyano stretch in **4**, 505 km/mol. At the SCF level, we predict that SiH_3CN is less stable than SiH_3NC by 1.5 kcal/mol.[20] However, this is reversed at the correlated level, and with MP-2 SiH_3CN is 7.8 kcal/mol more stable than SiH_3NC.[20] This is in agreement with the experiment since SiH_3NC is not observed.[18] The CNDO results significantly underestimate the stability of the isocyanide.

The calculated value for ΔE for the silyl cyanide/isocyanide isomerization can be compared to the values for the methyl cyanide/isocyanide and hydrogen cyanide/isocyanide isomerizations. The SCF value for ΔE for CH_3CN/NC is 19.2 kcal/mol, and the correlated value is 22.7 kcal/mol;[21] the latter value is in good agreement with the experimental value of 23.7 ± 0.1 kcal/mol.[22] For HCN/NC, the SCF value for ΔE is 9.5 kcal/mol, and the correlated value is 14.6 kcal/mol.[23] As R in RCN forms a more ionic R–C bond, the value for ΔE is decreasing. The CH_3 group (the most covalent character in the R–C bond) has the largest value for ΔE, 22.7 kcal/mol; the SiH_3 group (the most ionic character in the R–C bond) has the lowest value for ΔE, 7.8 kcal/mol. The correlation correction increases with decreasing covalent character in the R–C bond with ΔE_{corr} = 3.5 kcal/mol for R = CH_3, ΔE_{corr} = 5.1 kcal/mol for R = H, and ΔE_{corr} = 9.3 kcal/mol for R = SiH_3.

Substitution of three hydroxyl groups for hydrogen leads to only small changes in geometry with r(Si–C) = 1.883 Å and r(C–N) = 1.141 Å for **5** and r(Si–N) = 1.752 Å and r(C–N) = 1.165 Å for **6**. The vibrational positions show an increase of ~60 cm^{-1} for the CN stretch for both isomers and are at 2547 cm^{-1} (2241 cm^{-1}, scaled) for **5** and 2359 cm^{-1} (2076 cm^{-1}, scaled) for **6**. The intensities of the cyano stretch exhibit the same type of difference as seen previously and are calculated to be 12 km/mol for **5** and 440 km/mol for **6**. Substitution of OH for H makes the two structures closer in energy. Again the isocyanide is predicted to be more stable at the SCF level with **5** being 5.2 kcal/mol less stable than **6**.[24] However, correlation reverses the energy difference, and **5** is 3.7 kcal/mol more stable at the MP-2 level.[24] This is in very good agreement with the experimental value of 2.6 ± 1.1 kcal/mol considering the difference in the oxygen substituents, hydrogen and *tert*-butyl. Comparison of ΔE for **5** and **6** with that for **3** and **4** clearly shows a significant substituent effect.

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Polyether Biosynthesis. 3. Origin of the Carbon Skeleton and Oxygen Atoms of Lenoremycin

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Polyether antibiotics are naturally occurring ionophores produced by a variety of actinomycete species.[1] Extensive investigations in several laboratories have established that these branched chain, polyoxygenated fatty acids are formed from simple acetate, propionate, and butyrate precursors[2] and have led to the formulation of a general stereochemical model of polyether antibiotic structure and biogenesis.[3] According to this model, the characteristic oxygenation pattern of each polyether can be accounted for by a cascade of ring closures from a postulated polyepoxide intermediate. Indirect support for the polyepoxide theory has come from the determination of the origin of the oxygen atoms of monensin A (**1**),[4,5] as illustrated in Scheme I. Completely consistent results have also been reported for the polyether antibiotics lasalocid[6] and maduramycin.[7]

Lenoremycin (**2**)[8] and the closely related metabolites dianemycin,[9] leuseramycin,[10] and moyukamycin[11] are pentacyclic ethers containing a second tetrahydropyran–tetrahydrofuran spiroketal in place of the more commonly occurring pair of tetrahydrofuran rings typical of monensin. We have previously pointed out that the polyepoxide model can be extended to include the dianemycin class of polyethers by postulating the intermediacy of the appropriate diepoxy triketone **3** in place of the triepoxy diketone precursor **4** of monensin[3] (Scheme II). To test this model, we have now established the origins of the carbon skeleton and oxygen atoms of lenoremycin.

Previous work by Seto has established the acetate and propionate origins of dianemycin and led to a preliminary assignment of the ^{13}C NMR spectrum of lenoremycin.[9b] We have confirmed and extended these ^{13}C NMR assignments, including a number of small but important corrections, by a straightforward com-

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Table I. ^{13}C NMR Spectrum of Lenoremycin Sodium and Incorporation of ^{13}C-Labeled Precursors[a]

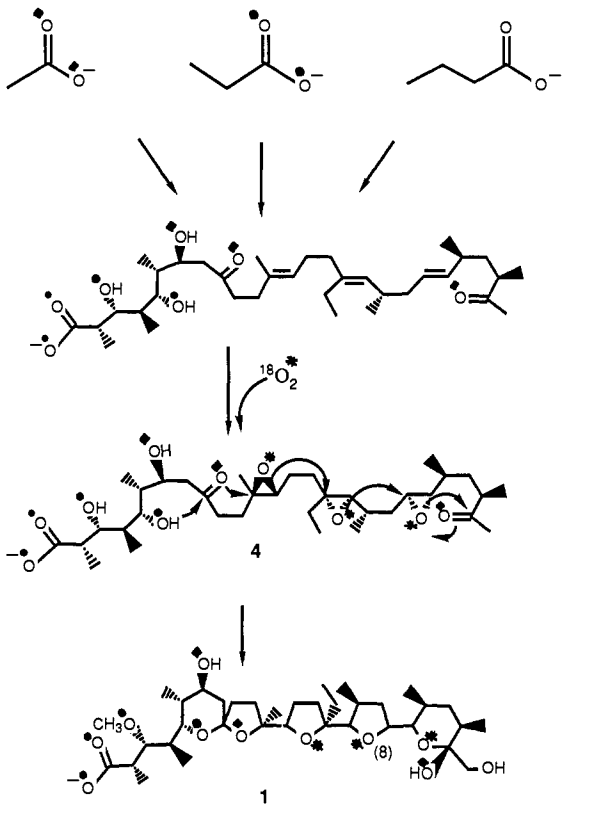
chemical shift δ (m)	C	precursor[b,c] [1-^{13}C]-acetate[d]	[1,2-$^{13}C_2$]-acetate J,[e] Hz	[1-^{13}C]-propionate[f]
207.4 (s)	5			●
181.3 (s)	1			●
146.2 (d)	7			●
134.0 (s)	6			
111.1 (s)	21			●
108.9 (s)	13	◆	42.7	
102.6 (d)	1′			
98.5 (s)	29	◆	45.6	
85.8 (s)	16			
80.9 (d)	17	◆	37.5	
79.5 (d)	4′			
79.4 (d)	24		34.2	
76.1 (d)	5′			
73.4 (d)	25			●
73.1 (d)	11			●
68.0 (d)	9	◆	36.8	
64.1 (t)	30		45.4	
56.7 (q)	7′			
41.2 (d)	8			
41.1 (t)	3			●
39.6 (d)	20			
39.5 (d)	2			
37.3 (d)	4			
36.4 (d)	12			
36.4 (t)	27			●
36.3 (t)	10		37.0	
35.6 (t)	14		42.8	
35.1 (d)	22			
33.0 (d)	26			
32.2 (t)	15			●
30.0 (d)	28			
29.8 (t)	23	◆	34.3	
28.1 (t)	2′			
27.5 (t)	19			●
27.0 (q)	35			
26.1 (t)	3′			
20.3 (q)	40			
18.3 (q)	6′			
17.8 (q)	32			
17.5 (t)	18		37.4	
17.1 (q)	39			
17.0 (q)	31			
15.3 (q)	33			
14.6 (q)	37			
13.9 (q)	34			
13.9 (q)	36			
11.2 (q)	38			

[a] $CDCl_3$, 100.63 MHz. [b] The indicated amounts of each precursor were administered in portions of 40%, 30%, and 30% to 100-mL cultures of *S. hygroscopicus* at 48, 72, and 96 h. After 7 days growth the culture was harvested, and the lenoremycin was isolated and purified. [c] Sites of enrichment indicated by ◆ ([1-^{13}C]acetate), ● ([1-^{13}C]-propionate), or J_{CC} coupling constants ([1,2-$^{13}C_2$]acetate). [d] Sodium [1-^{13}C]acetate, diluted to 75% ^{13}C; 430 mg (5.25 mmol); 300 mL of culture; 32.5 mg of lenoremycin, av atom % enrichment over natural abundance, 1.6% (indirect enrichment of C-1 propionate-derived sites, 4.4%). [e] Sodium [1,2-$^{13}C_2$]acetate, 90 atom % ^{13}C, diluted to 67%; 287 mg (3.50 mmol); 200 mL of culture; 34.9 mg of lenoremycin, av atom % enrichment over natural abundance, 1.5%. [f] Sodium [1-^{13}C]-propionate, diluted to 30% ^{13}C; 300 mg (3.12 mmol); 300 mL culture; 281 mg of lenoremycin, av atom % enrichment over natural abundance, 1.0%.

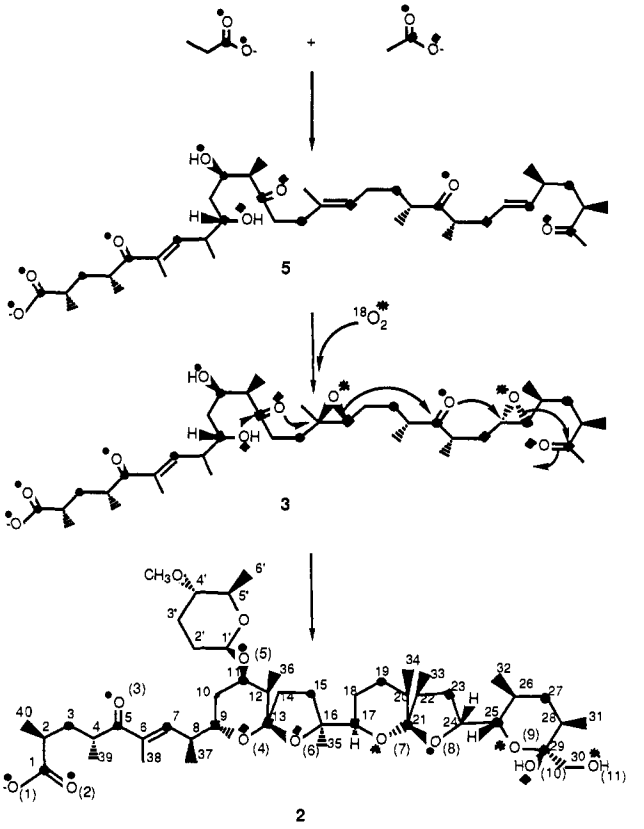
bination of INEPT, ^1H–^1H COSY, and ^1H–^{13}C HETEROCOSY experiments.[12] Feeding of sodium [1-^{13}C]propionate, [1-^{13}C]-acetate, and [1,2-$^{13}C_2$]acetate in separate incubations to actively fermenting cultures of *Streptomyces hygroscopicus* X-14540, followed by analysis of the resulting labeled samples of lenoremycin

(12) The ^1H NMR spectrum of lenoremycin has been assigned: Anteunis, M. J. O.; Rodios, N. A.; Verhegge, G. *Bull. Soc. Chim. Belg.* **1977**, *86*, 609. We have reassigned H-2 and H-4, in agreement with Seto, ref 9b.

Scheme I



Scheme II



by 100.63 MHz ^{13}C NMR, confirmed the expected origin of lenoremycin from five acetate and ten propionate building blocks (Scheme II). The coupling patterns resulting from incorporation of [1,2-$^{13}C_2$]acetate further substantiated several of the ^{13}C NMR signal assignments[13] (Table I).

Table II. Incorporation of ^{18}O-Labeled Precursors into Lenoremycin[a,b]

[1-^{13}C,1-$^{18}O_2$]acetate[c]				[1-^{13}C,1-$^{18}O_2$]propionate[d]				$^{18}O_2$[e]			
C	^{13}C shift, ppm	Δδ, ppm	^{18}O:^{16}O	C	^{13}C shift, ppm	Δδ, ppm	^{18}O:^{16}O	C	^{13}C shift, ppm	Δδ, ppm	^{18}O:^{16}O
9	68.012	0.024	55:45	1	181.296	0.04	20:80	17	80.939	0.028	20:80
13	108.888	0.032	75:25	5	207.480	0.048	20:80	21	111.091	0.024	15:85
29	98.559	0.024	50:50	11	73.015	0.029	20:80	25	73.113	0.024	20:80
				21	111.073	0.029	15:85	29	98.599	0.032	15:85
								30	64.161	0.024	30:70

[a] $CDCl_3$, 100.63 MHz. [b] Precursors were administered as described in Table I. [c] Sodium [1-^{13}C,1-$^{18}O_2$]acetate, Cambridge Isotope Laboratories, 99 atom % ^{13}C, 95 atom % ^{18}O, diluted to 75% ^{13}C; 143.5 mg (1.75 mmol); 100 mL of culture; 32.9 mg of lenoremycin, av ^{13}C atom % enrichment over natural abundance, 3.4%. [d] Sodium [1-^{13}C,1-$^{18}O_2$]propionate, 54.9% $^{18}O_2{}^{13}$C, 32.17% $^{18}O^{13}$C, 3.6% $^{16}O^{13}$C, diluted to 35% ^{13}C; 100 mg (1.04 mmol); 100 mL culture; 25.4 mg of lenoremycin, av ^{13}C atom % enrichment over natural abundance, 1.9%. [e] Cambridge Isotope Laboratories, 98 atom % $^{18}O_2$; 100 mL of culture; 6.4 mg of lenoremycin, diluted with 1.6 mg of natural abundance lenoremycin.

Having established appropriate conditions for incorporation experiments and identified the basic precursors of lenoremycin, we turned our attention to the origin of the oxygen atoms of the polyether. Thus incorporation of sodium [1-^{13}C,1-$^{18}O_2$]acetate resulted in characteristic ^{18}O-induced isotope shifts[15] of the ^{13}C NMR signals corresponding to C-9, C-13, and C-29 of lenoremycin, indicating that the attached O(4), O(6), and O(10) oxygen atoms are derived from the carboxylate oxygens of acetate. By contrast, no ^{18}O was present at C-17 (Scheme II, Table II). Similarly, incorporation of sodium [1-^{13}C,1-$^{18}O_2$]propionate[16] established that the O(1-2), O(3), O(5), and O(8) oxygen atoms of **2** originate from the carboxylate oxygens of the propionate precursor, based on the observed shifts of C-1, C-5, C-11, and C-21. No shift was observed for C-25. The origin of the remaining oxygen atoms was established by incubating *S. hygroscopicus* in the presence of a 1:4 mixture of $^{18}O_2$ and nitrogen gas.[17] The ^{13}C NMR spectrum of the resulting lenoremycin showed isotopically shifted signals corresponding to C-17 and C-21, C-25 and C-29, and C-30, demonstrating the derivation of O(7), O(9), and O(11) from molecular oxygen.

The above results are completely consistent with the postulated intermediacy of the diepoxy triketone **3**. Thus reductive polyketide chain elongation utilizing the appropriate combination of acetyl CoA (malonyl CoA) and propionyl CoA (methylmalonyl CoA) precursors could give rise to the *all*-(*E*)-triketodiene **5**, in which the individual oxygen atoms, including the C-21 keto oxygen, are all derived from the respective acetate and propionate precursors. Following its release from the polyketide synthetase, the diene **5** is postulated to undergo epoxidation by one or more oxygenases to give the 16*R*,17*R*,24*S*,25*S*-diepoxide **3**. Attack of the C-9 hydroxyl of **3** at the C-13 carbonyl carbon will initiate a cascade of ring closures to generate both spiroketals and the hemiketal ring of lenoremycin. Of particular importance is the derivation of the tetrahydrofuranyl oxygen atom O(8) from propionate, in contrast to the derivation of the analogously located O(8) oxygen atom of monensin from molecular oxygen. Subsequent oxidation at C-30 and glycosylation will complete the biosynthesis of the polyether. Further work on the details of the chain elongation mechanism is in progress.

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(13) Incorporation of [1-^{13}C]acetate led to efficient, indirect enrichment of the majority of the propionate carboxyl-derived carbon atoms of lenoremycin. The sites of labeling were unambiguously assigned by comparison with the results of incorporation of [1-^{13}C]propionate and confirmed by incorporation of [1,2-$^{13}C_2$]acetate. In the latter experiment, the ^{13}C–^{13}C satellites of indirectly enriched propionate-derived carbons, C-1, C-2, and C-3, amounted to ca. 10% of the intensity of the uncoupled but enriched natural abundance peak, in contrast to the ^{13}C–^{13}C satellites corresponding to acetate-derived carbons which constituted ca. 150% of the intensity of the natural abundance peak. The relatively small proportion of intramolecular coupling suggests that the bulk of the acetate-derived propionate units arise via succinyl CoA rather than from rearrangement of endogeneously generated butyrate.[14]

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(16) Synthesized as previously described.[3]

(17) Incubations in the presence of $^{18}O_2$ were carried out by a modification of the previously described apparatus[3] in which the proportion of oxygen to nitrogen was maintained at 1:4 by continual replenishment of oxygen as it was consumed. This technique also allowed the metabolic consumption of oxygen to be monitored continuously.

Anomalous Nitration of Fluoranthene with Nitrogen Dioxide in Carbon Tetrachloride

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In CH_2Cl_2, NO_2/N_2O_4 cleanly nitrates polycyclic aromatic hydrocarbons (PAH's) and is the method of choice for the synthesis of mononitrated derivatives.[1] The mechanism of the reaction of NO_2/N_2O_4 with PAH in aprotic solvents, however, remains controversial. Mechanisms involving free-radical attack,[2] electron-transfer,[3] and electrophilic substitution[4] have been proposed.

In order to obtain additional insights into the mechanism of reaction of NO_2/N_2O_4 with PAH, we have examined the nitration of fluoranthene, **1**, a nonalternant hydrocarbon. Frontier orbital calculations indicate that the positional reactivity in **1** will vary depending upon the nature of the attacking species;[5-7] for example, the order of reactivity for homolytic attack is predicted to be 3 > 1 > 7 > 8 > 2, while the order for electrophilic attack is expected to be 3 > 8 ≅ 7 > 1 > 2. Thus, **1** may provide a probe for distinguishing between radical and electrophilic substitution pathways.

Experimental data for electrophilic substitution[8] (Table I) affords an order of positional selectivity 3 > 8 > 7 > 1 > 2, in agreement with the theoretical prediction. The only previous data for radical substitution on **1** concerns its nitration by N_2O_5.[9] These data were interpreted in terms of the initial σ-complex

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