sertion reactions is under further study, as are alternative reaction pathways available to the lanthanide alkyl and hydride complexes exemplified by the intermediates shown in Scheme I.

Acknowledgment. The fine technical assistance of R. M. Swiatek is gratefully acknowledged. Discussions with Dr. F. N. Tebbe have been most helpful.

Registry No. 1, M = Lu, 80145-92-2; **1**, M = Yb, 80145-93-3; **2**, M = Lu, 80145-94-4; $Lu(\eta^5\text{-}C_5Me_5)_2CH_2CH(CH_3)CH_2CH(CH_3)_2$, 80160-33-4; $[Yb(\eta^5\text{-}C_5Me_5)_2(CH_3)_2]Li(THF)_3$, 80145-96-6; $[Lu(\eta^5\text{-}C_5Me_5)_2(CH_3)_2]Li(THF)_3$, 80145-98-8; $Yb(\eta^5\text{-}C_5Me_5)_2Al(CH_3)_4$, 80145-99-9; $Lu(\eta^5\text{-}C_5Me_5)_2Al(CH_3)_4$, 80146-00-5; propene, 115-07-1.

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Biosynthesis of Elaiomycin. 1. Incorporation of Labeled Forms of *n*-Octylamine

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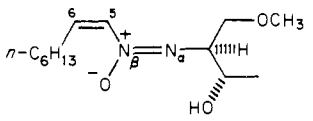
The antibiotic elaiomycin (**1**) is a naturally occurring azoxy compound isolated from the fermentation broth of *Streptomyces gelaticus*.[1] Elaiomycin exhibits novel biological activity since it only shows strong inhibition of certain virulent and avirulent mammalian strains of tubercle bacteria.[2] The antibiotic has also been found to induce tumors in rats.[3] As a naturally occurring azoxy compound, elaiomycin is a member of a small class of unusual natural products that includes (*p*-carboxyphenyl)azoxycyanide,[4] the cycad toxins macrozamin and cycasin,[5] and the antifungal agent LL-BH872α.[6] Up to the present time, no investigations of the biosynthesis of any of these naturally occurring azoxy compounds appear to have been carried out. We would now like to communicate the results of experiments that elucidate some aspects of the biosynthesis of elaiomycin.



1

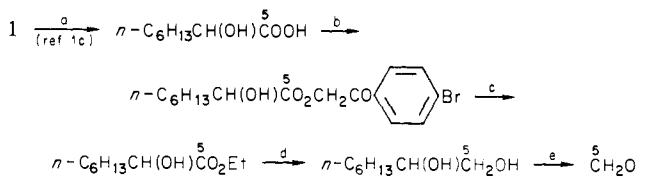
For the purpose of biosynthetic investigation, the elaiomycin molecule can be divided into two segments, a left-hand portion consisting of eight carbon atoms and a right-hand portion containing five carbon atoms. The left-hand portion has been the target of the experiments outlined here. The presence of an eight-carbon unit in the left-hand portion of elaiomycin led us to hypothesize that this part of the molecule would be derived from octanoic acid. Accordingly, sodium [1-^{14}C]octanoate was administered to cultures of *S. gelaticus* and radioactive elaiomycin was isolated (Table I, experiment 1). Intact incorporation of this precursor into elaiomycin was expected to label the antibiotic exclusively at C-5. However, degradation using the route outlined in Scheme I showed that the incorporation was largely nonspecific (Table I, experiment 1). *n*-Octylamine was therefore selected for evaluation as a precursor. [1-^{14}C]-*n*-Octylamine was synthesized by treatment of *n*-heptyl mesylate with potassium [^{14}C]cyanide followed by catalytic reduction of the resulting nitrile. Administration of the labeled *n*-octylamine to *S. gelaticus* yielded radioactive elaiomycin whose degradation proved that the incorporation was specific (Table I, experiment 2).

The specific incorporation of *n*-octylamine into elaiomycin having been established, an experiment was carried out to determine if the β-nitrogen atom of the antibiotic is derived from octylamine. [1-^{13}C,^{15}N]-*n*-Octylamine was synthesized from potassium [^{13}C,^{15}N]cyanide and *n*-heptyl mesylate, and the doubly labeled amine was administered to *S. gelaticus* cultures. The proton noise-decoupled ^{13}C NMR spectrum of the resulting elaiomycin exhibited a strong doublet ($^1J_{CN}$ = 16 Hz) at 135 ppm due to coupling between C-5 and N_β. The height of each of the

Table I. Incorporation of Radiolabeled Precursors into Elaiomycin

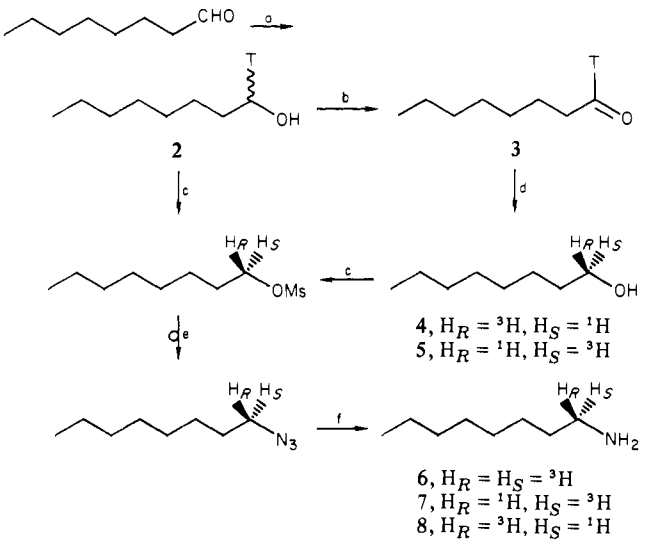
expt no.	precursor (^{3}H/^{14}C)	% incorpn (^{3}H/^{14}C)	labeling pattern (% ^{3}H retention)
1	sodium [1-^{14}C]octanoate	0.07	15% at C-5
2	[1-^{14}C]-*n*-octylamine	0.60	91% at C-5
3	[1(*R*,*S*)-^{3}H,1-^{14}C]-*n*-octylamine (6.16)	(3.06)	(49.7)
4	[1(*R*)-^{3}H,1-^{14}C]-*n*-octylamine (4.99)	(0.70)	(14.0)
5	[1(*S*)-^{3}H,1-^{14}C]-*n*-octylamine (4.09)	(4.07)	(99.5)
6	[2(*R*,*S*)-^{3}H,1-^{14}C]-*n*-octylamine (5.38)	(2.90)	(53.9)
7	[2(*R*)-^{3}H,1-^{14}C]-*n*-octylamine (3.88)	(0.34)	(8.8)
8	[2(*S*)-^{3}H,1-^{14}C]-*n*-octylamine (5.29)	(4.94)	(93.4)

Scheme I[a]



[a] (a) 6 N HCl. (b) *p*-BrPhCOCH$_2$Br, K_2CO_3, 18-crown-6. (c) NaOEt. (d) $LiAlH_4$. (e) $NaIO_4$, dimedone.

Scheme II[a]



[a] (a) [^{3}H]KBH_4. (b) PCC. (c) MsCl, Et_3N. (d) 9-BBN, (-)- or (+)-α-pinene. (e) LiN_3, DMF. (f) H_2, Pd/C.

†NSF Graduate Fellow.

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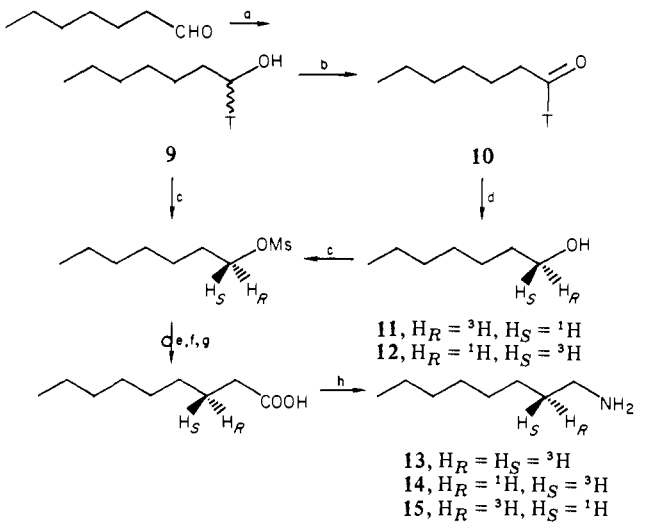
Scheme III[a]



[a] (a) $[^3H]KBH_4$. (b) PCC. (c) MsCl, Et_3N. (d) 9-BBN, (-)- or (+)-α-pinene. (e) *n*-BuONa, $CH_2(CO_2Et)_2$. (f) NaOH. (g) H^+, Δ. (h) HN_3.

lines of the doublet was about five times that of the singlet at the approximate center of the doublet corresponding to $[^{13}C,^{14}N]$-labeled molecules. One can therefore conclude that *n*-octylamine is incorporated into elaiomycin with retention of its nitrogen atom.[7]

The conversion of *n*-octylamine into elaiomycin leads to the formation of a cis double bond between C-1 and C-2 of the amine. The stereochemistry of hydrogen removal associated with the creation of this double bond has been elucidated by means of experiments with doubly labeled precursors. Samples of [1(*R*,*S*)-^{3}H]-, [1(*R*)-^{3}H]-, and [1(*S*)-^{3}H]-*n*-octylamine were synthesized by the route outlined in Scheme II. Reduction of *n*-octanal with tritiated borohydride yielded [1(*R*,*S*)-^{3}H]-*n*-octanol (**2**). The tritiated alcohol was converted to [1(*R*,*S*)-^{3}H]-*n*-octylamine (**6**) via formation of the mesylate, displacement with azide, and catalytic reduction. PCC oxidation[8] of **2** yielded [1-^{3}H]-*n*-octanal (**3**). Reduction of **3** with the adduct of 9-borabicyclononane and (-)- or (+)-α-pinene[9] was expected to give [1(*R*)-^{3}H]- and [1(*S*)-^{3}H]-*n*-octanol (**4**, **5**), respectively. The stereochemistry assigned to the alcohols **4** and **5** follows from literature precedents.[9,10] The chirally tritiated alcohols **4** and **5** were transformed into [1(*S*)-^{3}H]- and [1(*R*)-^{3}H]-*n*-octylamine (**7**, **8**) via mesylation, azide displacement, and reduction. On the basis of the assumption that the displacement step occurs with inversion of configuration, the chirally labeled alcohols **4** and **5** lead to [1(*S*)-^{3}H]- and [1(*R*)-^{3}H]-*n*-octylamine (**7**, **8**), respectively. Administration of the three forms of [1-^{3}H]-*n*-octylamine to *S. gelaticus* in conjunction with [1-^{14}C]-*n*-octylamine gave the results summarized in Table I (experiments 3-5). The data clearly reveals that *n*-octylamine is incorporated into elaiomycin with removal of the 1-*pro*-*R* hydrogen atom.

Scheme III portrays the methods that were utilized to synthesize three forms of [2-^{3}H]-*n*-octylamine. [1(*R*,*S*)-^{3}H]-*n*-Heptanol (**9**) was prepared in standard fashion and converted to the corresponding mesylate. Alkylation of diethyl malonate with the labeled mesylate was followed by ester hydrolysis, decarboxylation, and Schmidt degradation to yield [2(*R*,*S*)-^{3}H]-*n*-octylamine (**13**). A similar reaction sequence was then applied to [1(*R*)-^{3}H]- and [1(*S*)-^{3}H]-*n*-heptanol (**11**, **12**) obtained by 9-BBN-α-pinene reduction of [1-^{3}H]-*n*-heptanal (**10**). If it is assumed that the malonate alkylation step proceeds with inversion of configuration, then alcohols **11** and **12** will be converted to [2(*S*)-^{3}H]- and [2(*R*)-^{3}H]-*n*-octylamine (**14**, **15**). The results of precursor incorporation experiments employing **13**-**15** are shown in Table I (experiments 6-8). The tritium to carbon-14 ratios of the labeled samples of elaiomycin isolated in these experiments indicate that *n*-octylamine is incorporated into the antibiotic with loss of the 2-*pro*-*R* hydrogen atom. It therefore follows that the $\Delta^{5,6}$-double bond of elaiomycin is generated by the syn removal of two hydrogen atoms. A priori, this dehydrogenation process could proceed either by a direct removal of two hydrogen atoms or by oxidation to an imine followed by tautomerization. A decision between these two alternatives will require additional investigation.

Acknowledgment. We thank the National Institutes of Health (Grant CA-25142) and the Robert A. Welch Foundation (Grant C-729) for support of these investigations.

Registry No. 1, 23315-05-1; **6**, 80106-32-7; **7**, 80183-03-5; **8**, 80183-04-6; **13**, 80106-33-8; **14**, 80183-05-7; **15**, 80183-06-8; sodium [1-^{14}C]-octanoate, 13095-58-4; [1-^{14}C]-*n*-octylamine, 80106-34-9.

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Synthesis and Spectroscopic Properties of a Novel Cofacial Chlorophyll-Based Dimer

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We wish to report the synthesis and unique spectroscopic properties of a novel, doubly linked, cofacial chlorophyll (Chl) dimer. Considerable effort has been directed toward the synthesis and characterization of covalently connected porphyrins and Chls.[1,2] The work on porphyrins is motivated by an interest in the chemical consequences of positioning two multivalent metal ions in well-defined proximity without intervening ligands.[1e] The synthesis of covalently connected Chls is stimulated by the considerable body of evidence that a special pair of Chls and bacteriochlorophylls serve as the primary electron donors in green plant (photosystem I) and bacterial photosynthesis, respectively,[3] or by an interest in the synthesis of rigid models for photosynthetic electron transfer. The characteristic spectral properties of the in vivo electron donors are a red shift and split CD for the Q_y absorption bands. These observations provide evidence of interchromophore resonance (exciton) interactions,[4] and are further supported by ESR and ENDOR data on the cation radical of the electron donor in bacterial systems.[3a,b]

The properties of three synthetic Chl dimers are compared in this paper (see Figure 1): the novel cofacial dimer, Mg_2-I, the doubly linked "hinged" dimer, Mg_2-II, prepared by Wasielewski et al.,[2d] and the original singly linked dimer, Mg_2-III, prepared by Boxer and Closs,[2a] whose Q_y band exhibits a large red shift

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