

SYNTHETIC STUDY ON 1,3-POLYOLS. TOTAL SYNTHESIS OF (4S,6S,8S,10S,12R,14R,16R,18R,20R)-
 NONAMETHOXY-1-PENTACOSENE FROM BLUE-GREEN ALGAE

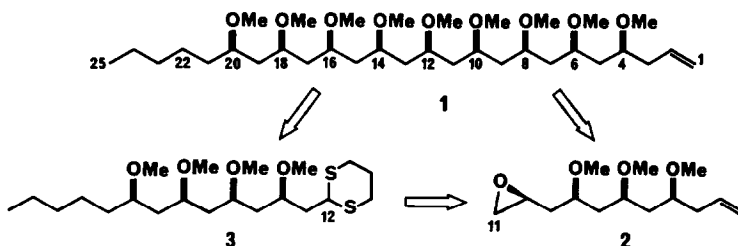
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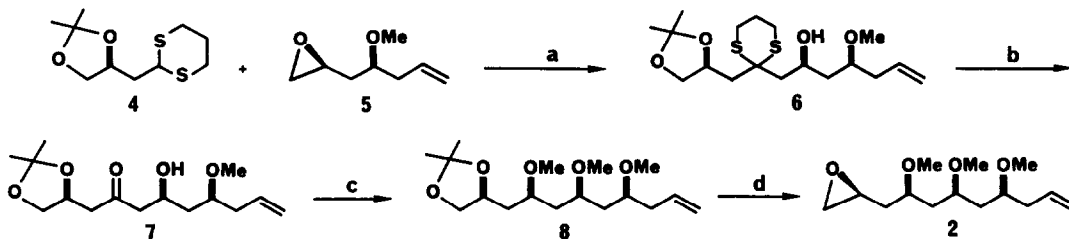
Summary: Isotactic nonamethoxy-1-pentacosene **1** isolated from certain blue-green algae has been synthesized and the absolute configuration was determined.

In connection with synthetic studies on 1,3-polyols, we have developed a general protocol for *syn* and *anti*-1,3-polyols¹⁾ which are often found on the backbone of biologically important polyene-macrolides. Recently, an isotactic 1,3-polymethoxyalkene **1** was isolated from a tolytoxin-producing blue-green alga *Tolypothrix conglutinata* var. *chlorata*²⁾ and a synthesis has been reported.³⁾ We report here the stereocontrolled synthesis and the absolute configuration of 4,6,8,10,12,14,16,18,20-nonamethoxy-1-pentacosene (**1**) using the method developed in our laboratory.⁴⁾

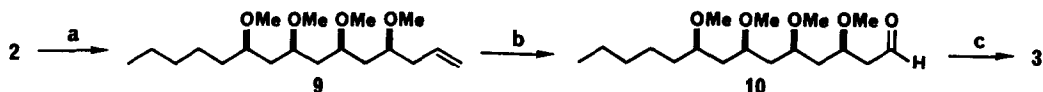
A logical retrosynthesis of **1** begins with the dissection of C(11)-C(12) to provide the segments **2** and **3**, the latter could be prepared from the right-half segment **2** by introduction of C₄ unit and conversion of the double bond to the dithioacetal group.



Coupling of lithiated 1,3-dithiane **4**, $[\alpha]_D^{23} -9.05^\circ$ (CHCl₃), with epoxide **5**, $[\alpha]_D^{25} +13.2^\circ$ (CHCl₃), prepared from (S)-(-)-butane-1,2,4-triol gave the adduct **6** which was treated with MeI-CaCO₃ to give hydroxy ketone **7** in 86% overall yield. A *syn*-stereoselective reduction of **7** with LiAlH₄-LiI⁵⁾ in ether at -100 °C (98%, *syn:anti*=96:4) followed by methylation gave **8** (95%). Routine synthetic operations converted the acetonide **8** to the right-half segment **2**, $[\alpha]_D^{25} +20.7^\circ$ (CHCl₃).



(a) *n*-BuLi, THF, -20°C. (b) MeI, CaCO₃, 80% aq. MeCN. (c) LiAlH₄, LiI, Et₂O, -100 °C; KH, MeI, THF, (d) 5% HCl-MeOH; TsCl, pyridine; *t*-BuOK, Et₂O-MeOH

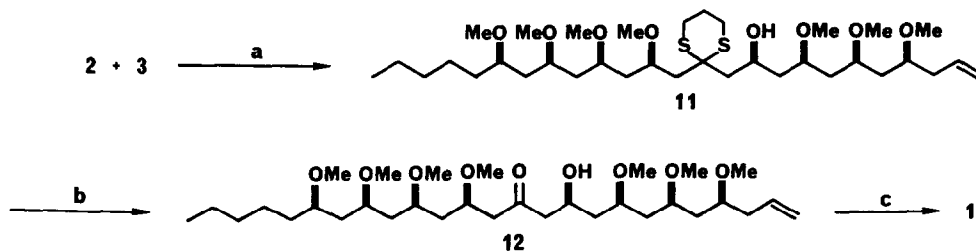


(a) $n\text{-Bu}_2\text{CuLi}$, Et_2O , -20°C ; KH , MeI , THF . (b) OsO_4 , NaIO_4 , aq. dioxane. (c) $\text{HS}(\text{CH}_2)_3\text{SH}$, BF_3OEt_2 , CH_2Cl_2

in 65% overall yield. The left-half segment 3, $[\alpha]_{\text{D}}^{25} -16.49^\circ$ (CHCl_3), was prepared from 2 as follows; 1) addition of butyl group with $n\text{-Bu}_2\text{CuLi}$, 2) methylation (9, 88% two steps), 3) Lemieux-Johnson oxidation (10, 87%), and 4) dithioacetalization (98%).

Second coupling reaction of the right-half segment 2 and the anion of the left-half segment 3 prepared by treatment with $n\text{-BuLi}$ gave the extended dialkylated dithiane 11 in 72% yield. Deprotection of the dithioacetal group yielded hydroxy ketone 12 (96%). Finally, stereocontrolled reduction of 12 with $\text{NaBH}_4\text{-Et}_2\text{BOMe}^{\text{d}}$ (99%, syn:anti=99:1) followed by methylation gave nonamethoxy-1-pentacosene 1 (93%), $[\alpha]_{\text{D}}^{25} +4.45^\circ$ (c 1.0, CHCl_3), which was identical with an authentic sample.³⁾

While natural 1 from *Tolypothrix conglutinata* contained two other homologs²⁾, a pure sample of 1, $[\alpha]_{\text{D}}^{25} +4.73^\circ$ (CHCl_3), was isolated quite recently from a blue-green alga *Scytonema mirabile*.⁷⁾ Direct comparison of the synthetic specimen with the natural one established the absolute structure of natural 1 to be (4S, 6S, 8S, 10S, 12R, 14R, 16R, 18R, 20R)-nonamethoxy-1-pentacosene.



(a) $n\text{-BuLi}$, THF , -20°C , (b) MeI , CaCO_3 , 80% aq. MeCN , (c) NaBH_4 , Et_2BOMe , THF-MeOH , -70°C ; KH , MeI , THF

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References

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