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(11) Spectral data for VII: NMR (CCl_4) 0.27 (6 H, s, Si–Me), 1.0–2.2 ppm (20 H, m, ring protons); IR (KBr) 1060–1080 (Si–O and C–O bands), 1260 cm^{-1} (Si–Me band); mass spectrum *m/e* 278. Anal. Calcd for $C_{18}H_{26}SiO_2$: C, 69.01, H= 9/4[/ Found: C, 68.9, H, 9.3. Spectral data for VIII: NMR (CCl_4) 0.17 (12 H, s, Si–Me), 1.0–2.1 ppm (20 H, m, ring protons); IR (KBr) 1080 (Si–O band), 1260 cm^{-1} (Si–Me band); mass spectrum *m/e* 336. Anal. Calcd for $C_{18}H_{38}Si_2O_2$; C, 64.23; H, 9.58. Found: C, 63.9, H, 9.3.
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Received December 23, 1977

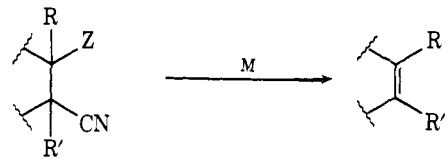
Stereochemistry of Vicinal Cyanohydrin Reduction–Elimination

Sir:

We recently described a method for converting vicinal cyanohydrins to olefins (Scheme I) through reduction–elimination of their methanesulfonate or methyl ether derivatives (Ia, Ib) with dissolving metals (M = Li or Ti).[1,2] We now wish to report findings with methylthiomethyl ether sulfones (Ic) and sodium naphthalenide which extend the synthetic potential of this reaction and shed light on its stereochemistry.

The starting cyanohydrins **1a** and **5a** for these studies were prepared in 91% yield as a 55:45 mixture by reduction of cyanocyclododecanone **4** with sodium borohydride (Chart I). The methylthiomethyl ether derivatives **2a** and **6a** (obtained in quantitative yield using dimethyl sulfoxide–acetic anhydride–acetic acid[4]) could be readily separated by chromatography. Oxidation with *m*-chloroperoxybenzoic acid yielded

Scheme I



Ia, R, R' = H or alkyl; Z = OMs
b, R, R' = H or alkyl; Z = OMe
c, R, R' = H or alkyl; Z = OCH_2SO_2Me

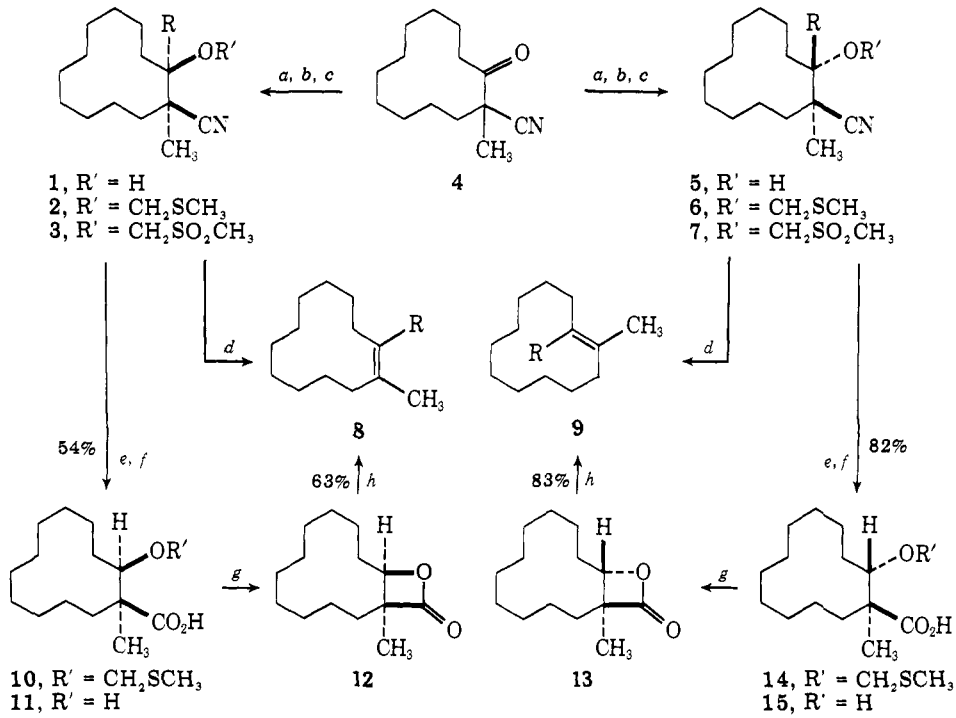
the crystalline sulfones **3a** (mp 94–95 °C, 84% yield) and **7a** (mp 96–97 °C, 67% yield). Reduction of the former with sodium naphthalenide in hexamethylphosphoramide (HMPA) gave *cis*-1-methylcyclododecene (**8a**, 85% yield) while the latter afforded the trans isomer **9a** (60% yield).

The stereochemistry of cyanohydrins **1a** and **5a** was ascertained as follows. Hydrolysis of the protected nitriles **2a** and **6a** followed by mercuric-catalyzed cleavage of the hemithioacetal acids **10** and **14** afforded the hydroxy acids **11** and **15.** Direct saponification of nitriles **1a** and **5a** could not be effected owing to their facile retroaldolization.

Hydroxy acids **11** and **15** were converted to the β-lactones **12** and **13** by treatment with benzenesulfonyl chloride.[5] Thermal decarboxylation of such lactones is known to proceed by syn elimination.[5] Consequently, the formation of *cis*-1-methylcyclododecene (**8a**)[6] from the former and *trans*-1-methylcyclododecene (**9a**) from the latter constitutes a proof of stereochemistry for both the hydroxy acids and their cyanohydrin precursors as well. These findings show that the conversion of cyano ethers **3a** and **7a** to olefins **8a** and **9a** must likewise proceed by a pathway involving syn elimination.

We have also examined the reduction decyanation of the 1,2-dimethylcyclododecyl cyanohydrin methylthiomethyl ether sulfones **3b** and **7b.** These isomers were secured via addition of methyllithium to cyano ketone **4** to give a 1:3 mixture of cyanohydrins **1b** and **5b** in 88% yield. Treatment, as before,

Chart I.



a series, R = H; b series, R = CH_3

[a] $NaBH_4$. [b] Me_2SO, Ac_2O, AcOH. [c] *m*-$ClC_6H_4CO_3H$. [d] $NaC_{10}H_8$, HMPA. [e] KOH, HCl. [f] $HgCl_2$, H_2O, $CdCO_3$. [g] $PhSO_2Cl$. [h] 150 °C.

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with dimethyl sulfoxide–acetic anhydride afforded the chromatographically separable methylthiomethyl ethers **2b** and **6b** in 98% yield. Conversion to the crystalline sulfones **3b** (mp 152–153 °C, 60% yield) and **7b** (mp 105–106 °C, 85% yield) was effected with *m*-chloroperoxybenzoic acid. Reduction of these sulfones with sodium naphthalenide in HMPA afforded pure *cis*-1,2-dimethylcyclododecene (**8b**, 74% yield) and *trans*-1,2-dimethylcyclododecene (**9b**, 83% yield). We were unable to rigorously establish the stereochemistry of cyanohydrins **1b** and **5b**, or derivatives thereof, owing to the extreme steric hindrance of the cyano grouping. Attempts at hydrolysis or conversion to the known vicinal glycol derivatives[6] were unsuccessful. However, the findings outlined in Chart I together with the high degree of stereoselectivity observed in the reduction–elimination leading to olefins **8b** and **9b** tend to support the stereochemistry assignments.

In an experiment performed after submission of our original manuscript, we found that the crystalline cyanohydrin methylthiomethyl ether **2b** (mp 51.5–52.5 °C) afforded *cis*-1,2-dimethylcyclododecene directly in 75% yield upon treatment with sodium naphthalenide in HMPA. Thus, conversion to the sulfone derivatives may be unnecessary for the synthesis of olefins by this route. We are exploring the use of methylthiomethyl ethers and their sulfone derivatives as leaving groups in other contexts.

Mechanistic interpretations for the stereochemical findings must await further studies in other cyclic as well as acyclic systems. It should be noted, however, that reduction–eliminations of cyclic phosphate derivatives under similar conditions likewise proceed by a preferred syn pathway.[7,8]

Acknowledgment. Support from the National Science Foundation through Research Grant CHE 75-0777 is gratefully acknowledged.

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Biosynthetic Studies with Carbon-13. Lankacidin Group of Antibiotics

Sir:

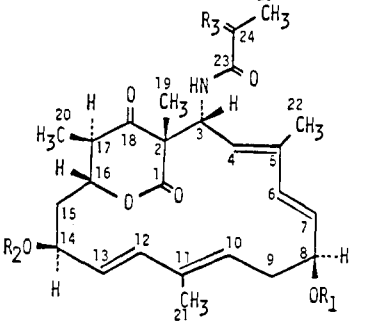
The lankacidins are a unique group of antibiotics that exhibit a broad spectrum of antibacterial activity.[1] Unlike other antibacterial substances, the lankacidins also possess antitumor activity.[2]

Their structures, which incorporate a δ lactone function imbedded into a unique 17-membered carbocyclic ring, have been firmly established by chemical and spectroscopic methods including x-ray crystallographic analyses. The lankacidins **1**, **2**, **3**, **4**, and **5** are interrelated by the presence or absence of an acetyl function at C-14 as well as by a variable oxidation level at C-24.

Table I. ^{13}C NMR Data for Lankacidin C Diacetate (**4**)

Carbon no.	δ_c[a]	Multiplicity[b]	Relative enrichments	J_{C-C}, Hz	
1[c]	169.8	s	6.4	52.2	1–2
2	56.7	s		52.2	
3	51.8	d			
4[d]	124.9	*e*	2.1		
5	139.1	s		53.3	5–6
6[c]	135.9	d	8.3	53.6	
7	126.7	*e*		50.4	7–8
8[c]	75.7	d	5.8	50.3	
9	33.7	t		44.8	9–10
10[c]	128.4	d	8.4	44.8	
11	136.9	s		53.6	11–12
12[c]	140.7	d	7.6	53.9	
13	124.9	*e*		49.2	13–14
14[c]	71.4	d	6.7	49.3	
15	34.2	t		39.7	15–16
16[c]	75.5	d	8.3	40.4	
17	46.4	d		37.8	17–18
18[c]	210.4	s	7.5	37.8	
19[f]	9.4	q	22.9		
20[f]	12.5	q	27.1		
21[f]	12.7	q	32.2		
22[f]	20.9	q	18.1		
23	159.8	s			
24	196.4	s			
25	24.4	q			
26	170.1	s			
27	21.2	q			
28	170.1	s			
29	21.2	q			

[a] Chemical shifts are given in parts per million downfield from internal Me_4Si in $CDCl_3$ and enrichments were measured by relative signal enhancements. [b] Multiplicities in the off-resonance decoupled spectrum: s, singlet; d, doublet; t, triplet; q, quartet. [c] These carbon atoms were enriched by sodium [1-^{13}C]acetate and enrichments are relative to C-25 as 1.0. [d] This carbon atom was enriched by [1-^{13}C]glycine and the enrichment is relative to C-25 as 1.0. [e] Multiplicities of these signals could not be recognized because of the overlapping with other peaks. [f] These carbon atoms were enriched by [$^{13}CH_3$]methionine and enrichments are relative to C-1 as 1.0.



No.	R_1	R_2	R_3	Compd
1	H	H	O	lankacidin C (bundlin A, T-2636 C)
2	$COCH_3$	$COCH_3$	O	lankacidin C diacetate
3	H	$COCH_3$	O	lankacidin A (bundlin B, T-2636 A)
4	H	H	H,OH	lankacidinol (T-2636 F)
5	H	$COCH_3$	H,OH	lankacidinol A (T-2636 D)

In this communication, we present our ^{13}C NMR results, which reveal a novel biosynthetic route to these biologically significant and structurally distinct macrolide substances. The ^{13}C-labeled antibiotics were prepared in feeding experiments

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