J. Org. Chem. 1984, 49, 709–712

Ethyl 3-methyl-2-(1-methylethyl)-4-pentynoate (20): bp 70–74 °C (7.0 mm); NMR ($CDCl_3$) δ 0.90 and 1.00 (dd, 6 H, isopropyl Me's), 1.10 and 1.28 (dd, 3 H, C_3-Me), 1.30 (t, $J = 6$ Hz, 3 H, ester Me), 1.97–2.53 (m, 3 H, isopropyl CH, C_3-CH, alkynyl CH), 2.53–3.20 (m, 1 H, C_2-CH), 4.20 (q, $J = 7$ Hz, 2 H, ester CH_2); IR (film) 3230, 2920, 1730, 1460, 1370, 1300, 1250, 1200, 1170, 1070 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.38; H, 9.83.

Registry No. 4, 13279-86-2; 5, 88302-98-1; 6, 88302-99-2; 8, 63547-55-7; 9, 88303-00-8; 10, 65946-52-3; 11, 83190-45-8; 12, 88303-01-9; 13, 88303-02-0; 14, 88303-03-1; 15, 88303-04-2; 16, 88303-05-3; 17, 88303-09-7; 18, 88303-10-0; 19, 88303-06-4; 20, 88303-11-1; $Cl_2C{=}CHCH(CH_3)_2$, 32363-91-0; $CH_3CH{=}C(OEt)Si(CH_3)_3$, 80675-53-2; $Cl_2C{=}CHCHClCH_2CH_3$, 88303-07-5; $HC{\equiv}CCHClCH_3$, 21020-24-6; $(CH_3)_2CHCH{=}C(OC(CH_3)_3)Si(CH_3)_3$, 88303-08-6; hexamethylphosphorous triamide, 1608-26-0; bromotrichloromethane, 75-62-7; isobutyraldehyde, 78-84-2; 1,1,1,3-tetrachloropentane, 19967-19-2.

Acid-Catalyzed Isomerization of Cycloartane Triterpene Alcohols. The Formation of Cucurbitane- and Lanostane-Type Isomers

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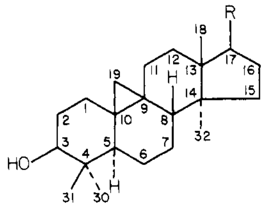
Cycloartane (9β,19-cyclolanostane) triterpene alcohols, for example, cycloartenol (9β,19-cyclo-5α-lanost-24-en-3β-ol, **1b**), contain a cyclopropane ring and are considered to be intermediates of sterol biosynthesis in photosynthetic eucaryotes.[1] The cyclopropane ring has olefinic properties and, upon treatment with acidic reagents, gives ring-opened products. The cyclopropane–alkene isomerization has been explained by invoking the formation of either of two types of protonated cyclopropanes, edge-protonated and corner-protonated, and subsequent C,C-bond fission with the elimination of a proton.[2] The acid-catalyzed isomerization of cycloartanol (9β,19-cyclo-5α-lanostan-3β-ol, **1a**) with gaseous hydrogen chloride in chloroform has been shown to afford three isomers of the lanostane-type, 5α-lanost-7-en-3β-ol (**2a**), 5α-lanost-8-en-3β-ol (**3a**), and, mainly, 5α-lanost-9(11)-en-3β-ol (**4a**).[3] However, Markovnikov cleavage might conceivably give rise to another type of isomerized triterpene, i.e., a cucurbitane [19(10→9β) abeolanostane]-type isomer, which would be generated by C_{10}–C_{19} bond cleavage, in addition to the lanostane-type isomers. We have, therefore, undertaken a detailed investigation of the isomerization of two cyclopropanes, **1a** and **1b**.

The isomerization was performed with three Brønsted acids: hydrochloric acid, sulfuric acid, and *p*-toluenesulfonic acid, while chloroform, isopropyl alcohol, and glacial acetic acid were used as the solvent. The results of the isomerization of **1a** are summarized in Table I. The treatment of **1a** with gaseous HCl in $CHCl_3$ at 0 °C for 1 h yielded only three lanostane-type isomers, **2a**, **3a**, and **4a**; this finding is consistent with the previous observations.[3] However, when **1a** was treated with hydrochloric acid in *i*-PrOH at 80 °C for 1 h, there were obtained very small amounts of two cucurbitane-type isomers, 10α-cucurbit-5-en-3β-ol (**5a**) and cucurbit-5(10)-en-3β-ol (**6a**), together with the three lanostane-type isomers, the dehydration products, and a substantial amount of the starting material. The formation of the two cucurbitane-type isomers was also observed in the isomerization with H_2SO_4 and *p*-$MePhSO_3H$ in *i*-PrOH. The exposure of **1a** to H_2SO_4 for 3 h resulted largely in the recovery of the starting material; after 12 h, the amount of the recovered starting material was considerably decreased, and increasing amounts of lanostane- and cucurbitane-type isomers and also of the dehydration products were obtained. After an extension of the reaction time to 24 h, although the starting material almost disappeared, the amounts of isomerized triterpene alcohols were found to be virtually unchanged or to have undergone a significant loss in the case of a cucurbitane-type isomer **6a**, with the amounts of the dehydration products increased appreciably. In AcOH as the solvent, the cyclopropane ring opening proceeded more smoothly than in *i*-PrOH, giving three lanostane-type isomers, **2a**, **3a**, and **4a**, and much larger amounts of the dehydration products, but we could identify no cucurbitane-type isomers, **5a** or **6a**, or only trace amounts of them.



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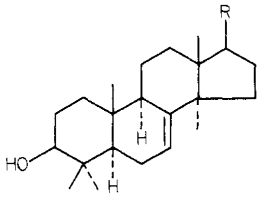

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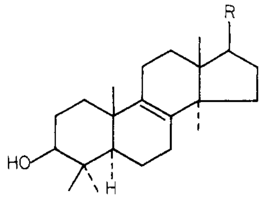

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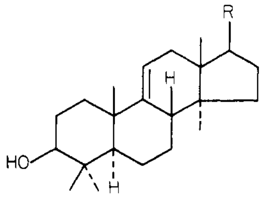

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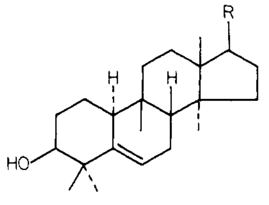

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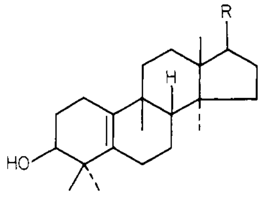

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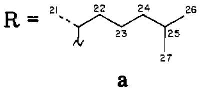

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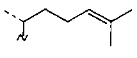

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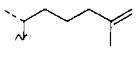

c

Isomerization of cycloartenol (**1b**), with a catalytic amount of H_2SO_4 in *i*-PrOH for 12 h, gave the following isomerized lanostane- and cucurbitane-type isomers: 5α-lanosta-7,24-dien-3β-ol (**2b**, 7%), lanosterol (5α-lanosta-8,24-dien-3β-ol, **3b**, 7%), parkeol [5α-lanosta-9(11),24-dien-3β-ol, **4b**, 30%], 5α-lanosta-7,25-dien-3β-ol (**2c**, 2%), 5α-lanosta-8,25-dien-3β-ol (**3c**, 2%), 5α-lanosta-9(11),25-dien-3β-ol (**4c**, 4%), anhydrolitsomentol (**5b**, 7%), cucurbita-5(10),24-dien-3β-ol (**6b**, 16%), 10α-cucurbita-5,25-

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[2] For reviews, see: (a) Charton, M. "The Chemistry of Alkenes"; Zabicky, J., Ed.; Interscience: London, 1970; Vol. 2, Chapter 10. (b) DePuy, C. H. *Top. Curr. Chem.* **1973**, *40*, 73. (c) Boyle, P. H. In "Rodd's Chemistry of Carbon Compounds"; Ansell, M. F., Ed.; Elsevier: Amsterdam, 1974; Vol. 2, Suppl., Chapter 2.

[3] (a) Cole, A. R. H. *Chem. Ind. (London)* **1953**, 946. (b) Cole, A. R. H. *J. Chem. Soc.* **1954**, 4810. (c) Bentley, H. R.; Henry, J. A.; Irvine, D. S.; Spring, F. S. *Ibid.* **1953**, 3673. (d) Barton, D. H. R.; Page, J. E.; Warnhoff, E. W. *Ibid.* **1954**, 2715.

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Table I. Percent Composition[a] from the Isomerization[b] of Cycloartanol (1a)

			components							
catalyst	solvent	rctn period, h	**1a**[c]	**2a**	**3a**	**4a**	**5a**	**6a**	dehydration products	others, uncharacterized
gaseous HCl	$CHCl_3$	1 (0 °C)		21	31	48			trace	
HCl	*i*-PrOH	1	63	trace	15	20	trace	1	1	
HCl	AcOH	1	trace	17	24	30		20	20	9
H_2SO_4	*i*-PrOH	3	76	trace	4	16	trace	4	trace	
H_2SO_4	*i*-PrOH	12	16	2	11	46	3	12	10	
H_2SO_4	*i*-PrOH	24	1	5	9	43	2	5	35	
H_2SO_4	AcOH	3		3	5	44	trace	trace	48	
p-$MePhSO_3H$	*i*-PrOH	6	25	8	22	29	2	2	12	
p-$MePhSO_3H$	AcOH	6	9	9	20	37	trace	trace	25	
H_2SO_4[d]	*i*-PrOH	6					13[c]	2	70	15
H_2SO_4[e]	*i*-PrOH	6					2	10[c]	85	3

[a] Determined by GLC after acetylation. [b] Reaction temperature was 80 °C if not otherwise stated; see Experimental Section for details of the reaction conditions. [c] Recovered starting material. [d] Using **5a** as the starting material. [e] Using **6a** as the starting material.

dien-3β-ol (**5c**, 1%), and cucurbita-5(10),25-dien-3β-ol (**6c**, 1%), aside from the recovered starting material **1b** (3%), uncharacterized and isomerized alcohols (4%), and the dehydration products (16%).

Table II. Melting Points and Chromatographic Data of the Acetate Derivatives of Triterpene Alcohols

acetate	mp,[a] °C	R_c in argentic TLC[b]	RRT in GLC[c]
1a	135-136	1.04	1.54
1b	125-126	0.84	1.86
2a	143-145	1.01	1.57
2b	166-168	0.84	1.89
2c	143-145	0.60	1.83
3a	119-121	1.05	1.30
3b	131-133	0.89	1.57
3c	104-106	0.63	1.51
4a	174-176	0.87	1.49
4b	166-168	0.58	1.79
4c	158-160	0.42	1.72
5a	119-121	0.83	1.19
5b	119-120	0.70	1.43
5c		0.52	1.38
6a	164-166	1.09	1.07
6b	164-166	1.05	1.28
6c	130-132	0.74	1.25

[a] Uncorrected values. [b] Mobility of cholesteryl acetate was taken as 1.00. [c] Determined on OV-17 glass capillary column. RRT was expressed relative to cholesteryl acetate.

Each product was characterized after having been isolated. For this purpose, the isomerization of **1a** and **1b** on a preparative scale with H_2SO_4 was undertaken in *i*-PrOH, and the reaction products were separated by chromatography on silica gel and by argentic TLC. The dehydration products were confirmed by the IR data, which showed no hydroxyl absorption. The identification of **2a**–**5a** and **3b**–**5b** was confirmed by a comparison of the chromatographic (argentic TLC and GLC) and spectral (MS and ^1H NMR) data with those of authentic compounds. One isomer had a double bond (acetate, M^+ *m/z* 470.4128). This was shown to be a tetrasubstituted olefin, since the ^1H NMR showed no olefinic signal and ^{13}C NMR showed two olefinic carbon signals, at δ 132.1 and 133.6, which were shown still to be singlet signals by the off-resonance decoupled spectrum. There was one tetrasubstituted olefin, the $\Delta^{5(10)}$-cucurbitene isomer, aside from the Δ^8-lanostene isomer (**3a**), which could be generated from the isomerization of cyclopropane **1a**. Therefore, it may be reasonable to assign the cucurbit-5(10)-en-3β-ol (**6a**) structure to the isomer. This was confirmed by the direct chemical correlation with **5a**. It has previously been reported that the Δ^5-triterpenes possessing a C_{19}-methyl group at the $C_{9\beta}$ position afford the $\Delta^{5(10)}$-isomer upon acid treatment.[4] Thus, the isomerization of **5a** with H_2SO_4 was performed in *i*-PrOH; a small amount of **6a** was obtained, together with a substantial amount of dehydration products (Table I). On the contrary, **6a** afforded **5a** upon the same acid treatment. Isomers **2c**–**6c** with Δ^{25}-unsaturated side chains (**c**) were structurally elucidated on the basis of their ^1H NMR data [side-chain proton signals at δ 1.71 (3 H, s, $C{=}CCH_3$, C_{27}) and 4.67 (2 H, m, $C{=}CH_2$, C_{26}), in addition to one methyl doublet at δ 0.86–0.90 due to the C_{21}-methyl group]. The skeleton structures of **2c**–**6c** and the whole structures of **2b** and **6b** were determined by means of a ^1H NMR comparison with the relevant compounds mentioned above. Table II summarizes the melting points, and the R_c values in argentic TLC and relative retention times (RRT) in the GLC of the acetate derivatives of the triterpene alcohols described here. Table III shows the ^1H NMR data of the acetate derivatives of new and uncommon triterpene alcohols of the lanostane and cucurbitane types. The location of the doublet signal due to the C_{21}-methyl group, which was ambiguous in the normal spectra at 100 MHz, and the signal assignments of $\Delta^{5(10)}$-cucurbitene triterpene were undertaken with the aid of lanthanide-induced-shift techniques.[5] Thus, it was shown that the two cyclopropanes **1a** and **1b** afforded cucurbitane-type isomers besides lanostane-type isomers in isomerization promoted by Brønsted-acid catalysts. This seems to be the first finding of generation of cucurbitane-type isomers from cycloartane triterpenes by means of acid isomerization. The isomerization of the cyclopropane proceeds more rapidly in polar AcOH than in less polar *i*-PrOH; this might be ascribed to the increasing possibility of the protonation of the cyclopropane ring in a more polar solvent. The protonation is most likely the rate-determining step in the cleavage of the three-membered ring.[6,7] The generation of olefins by electrophilic

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Table III. ^{1}H NMR Data (100 MHz, $CDCl_3$)[a] of the Acetate Derivatives of New and Uncommon Triterpene Alcohols

acetate	18-H_3[b]	19-H_3[b]	30-H_3[b]	31-H_3[b]	32-H_3[b]	21-H_3[c,d]	26-H_3[b]	27-H_3[b]	3β-OAc[b]	3α-H	others
2b	0.64	0.89	0.87	0.96	0.96	0.90 (J = 4.9)	1.60	1.68	2.05	4.52 (m)	5.20 (m, 7-H) 5.10 (t, J = 5.8, 24-H)
2c	0.64	0.89	0.87	0.96	0.96	0.88 (J = 4.9)		1.71	2.05	4.52 (m)	5.20 (m, 7-H) 4.67 (m, 26-H_2)
3c	0.69	1.00	0.88	0.88	0.88	0.90 (J = 4.9)		1.71	2.05	4.50 (m)	4.67 (m, 26-H_2)
4c	0.65	1.07	0.87	0.89	0.74	0.87 (J = 4.9)		1.71	2.05	4.45 (m)	5.20 (m, 11-H) 4.67 (m, 26-H_2)
5a	0.82	0.90	1.04	1.04	0.85	0.87 (J = 5.9)	0.86[c] (J = 6.8)		2.01	4.70 (t, J = 2.9)	5.50 (d, J = 5.5, 6-H)
5b	0.81	0.91	1.04	1.04	0.85	0.88 (J = 5.8)	1.60	1.69	2.02	4.70 (t, J = 2.9)	5.51 (d, J = 5.4, 6-H) 5.09 (t, J = 4.9, 24-H)
5c	0.81	0.91	1.04	1.04	0.85	0.86 (J = 4.9)		1.71	2.02	4.67 (t, J = 2.9)	5.52 (d, J = 5.4, 6-H) 4.67 (m, 26-H_2)
6a[d]	0.79	1.00	0.96[e]	0.93[e]	0.84	0.82 (J = 4.9)	0.86[c] (J = 6.4)		2.05	4.67 (dd, J = 3.9, 13.2)	
6b[d]	0.79	1.00	0.96[e]	0.92[e]	0.84	0.87 (J = 5.9)	1.59	1.67	2.05	4.66 (dd, J = 3.9, 13.2)	5.09 (t, J = 4.9, 24-H)
6c[d]	0.78	1.00	0.96[e]	0.92[e]	0.83	0.86 (J = 4.9)		1.71	2.05	4.66 (dd, J = 3.9, 13.2)	4.67 (m, 26-H_2)

[a] Given as δ values, J values in hertz. [b] Singlet unless otherwise specified. [c] Doublet. [d] Assigned with the aid of the lanthanide-induced-shift techniques.[5] [e] Assignment in each row may be reversed although those given here are preferred.

ring opening was found to be practically the sole reaction for cyclopropane **1**. This is probably because it is extremely difficult for the nucleophilic attack to compete against proton elimination on the initially generated protonated cyclopropane under the present conditions. This might be correlated with the regio- and stereochemical nature of the cyclopropane ring of **1**, since the three-membered rings located in the side chains of steroids undergo considerable nucleophilic attack under similar conditions.[7,8] The cucurbitane triterpenes were found to be highly susceptible to dehyration, as in the double-bond migration of **5a** and **6a** by the H_2SO_4 catalyst (Table I). This may also explain why cucurbitane-type isomers could not be detected or were detected in only trace amounts in the isomerization of **1a** in AcOH.

The anhydrolitsomentol (**5b**)[9] obtained here by the isomerization of **1b** with H_2SO_4 was recently isolated from the seeds of the gourd *Lagenaria leucantha* var. *Gourda* and some other cucurbitaceous plants[10] and constitutes the parent compound of a number of cucurbitacins, highly oxygenated tetracyclic triterpenoids found in Cucurbitaceae and some other flowering plants.[11]

Experimental Section

General Methods and Materials. The melting points were taken on a heated block and are uncorrected. The ^{1}H (100 MHz) and ^{13}C (25.05 MHz) NMR spectra were obtained on a JEOL JNM FX-100 instrument, with $CDCl_3$ as the solvent and with Me_4Si as the internal standard. The mass spectra were recorded on a Hitachi RMU-7M system at 70 eV, while the IR spectra were taken on a JASCO IRA-2 instrument. The GLC was performed on a Shimadzu GC-4CM chromatograph equipped with a 30 m × 0.3 mm i.d. SCOT glass capillary column coated with OV-17 at 260 °C.[12] Silica gel TLC (20 × 20 cm) coated with Wakogel B-10 (0.5 mm thick, Wako Pure Chemical Ind.) was developed three times with *n*-hexane–ethyl acetate (6:1, v/v). Argentic TLC (20 × 20 cm) on plates (0.5 mm thick) of Wakogel B-10 impregnated with 20% $AgNO_3$ (w/w) was developed four times with CCl_4–CH_2Cl_2 (5:1, v/v). The RRT in the GLC and R_c values in the argentic TLC of triterpene acetates were expressed relative to cholesteryl acetate (1.00). Acetylation was performed in acetic anhydride–pyridine (1:1, v/v) at room temperature overnight. The cyclopropane **1b** was kindly donated by the Riken Vitamin Co. (Tokyo), and **1a** was prepared from **1b** by hydrogenation over PtO_2 in ethyl alcohol under atmospheric pressure and temperature. Triterpene alcohols **2a–5a** and **3b–5b** were used as the reference specimens.[10,13] The percent composition (cf. Table I) of the isomerization mixture was determined by GLC after acetylation. Components with RRT values less than 0.5 in GLC were regarded as the dehydration products for the reason to be presented.

General Procedure for Isomerization of Triterpene Alcohols. (a) Isomerization by gaseous HCl: Triterpene alcohol (50 mg) was dissolved in dry, EtOH-free $CHCl_3$ (4 mL), and then dry HCl was bubbled into the solution at 0 °C. (b) Isomerization by hydrochloric acid: Triterpene alcohol (50 mg), dissolved in 40 mL of *i*-PrOH or AcOH containing 4 mL of concentrated hydrochloric acid, was stirred at 80 °C. (c) Isomerization by H_2SO_4: Triterpene alcohol (50 mg), dissolved in 40 mL of *i*-PrOH or AcOH containing 4 mL of concentrated H_2SO_4, was stirred at 80 °C. For preparative purposes, 700 mg of triterpene alcohol in *i*-PrOH was treated as above for 12 h. (d) Isomerization by

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p-MePhSO$_3$H: Triterpene alcohol (50 mg), dissolved in 40 mL of i-PrOH or AcOH containing 25 mg of p-toluenesulfonic acid monohydrate, was stirred at 80 °C. The isomerization product, extracted with diethyl ether, was neutralized by washing it with a sodium bicarbonate solution and then with water and dried over anhydrous sodium sulfate.

Separation of the Isomerization Products. The reaction product obtained by means of a preparative-scale isomerization of **1a** was separated into three bands, which were cochromatographed with authentic 5α-cholestane (R_c 5.6; the R_c value of cholesterol was taken as 1.0), **5a** (R_c 2.7), and **1a**/**3a** (R_c 2.1), respectively, on silica gel TLC. The oily material from the least polar band exhibited a number of peaks with short retention times (RRT <0.5) in GLC. This was regarded as a mixture of dehydrated triterpenes, since it had strong IR absorptions (capillary; ν_{max} 2950, 2850, 1460, 1380, 1370, 1363 cm^{-1}) correlated with steroidal hydrocarbons devoid of hydroxy groups and since the spectrum was quite similar to that of 5α-cholestane (KBr; ν_{max} 2950, 2850, 1460, 1380, 1370 cm^{-1}). The fraction from the medium-polar band was a mixture of two cucurbitane-type isomers (**5a** and **6a**). When subjected to argentic TLC after acetylation, this yielded the acetates of pure **5a** and **6a** separated. The fraction from the most polar band was a mixture of three lanostane-type isomers and the starting material. After acetylation, this was submitted to repetitive argentic TLC, which eventually led to the isolation of **2a**, **3a**, and **4a** as the acetate derivatives. The isolation of each reaction product from a preparative-scale isomerization of **1b** was performed in the same way as has been described above for the reaction product of **1a**.

Physical Data. For the melting points, the R_c values in argentic TLC, and the RRT in the GLC of the acetate derivatives of the triterpene alcohols described here, see Table II, and for the ^{1}H NMR data of the acetates of new and uncommon triterpene alcohols, see Table III. The mass spectral data (m/z > 200) for those triterpene acetates listed in Table III are given below. As for **6a** acetate, the ^{13}C NMR data also are described below.

5α-Lanosta-7,24-dien-3β-ol (2b) acetate: MS, m/z 468 (M$^+$, relative intensity, 39), 453 (92), 408 (6), 393 (100), 355 (31), 315 (13), 311 (11), 295 (13), 270 (24), 257 (18), 255 (31), 243 (15), 241 (13), 229 (18), 215 (11), 201 (11).

5α-Lanosta-7,25-dien-3β-ol (2c) acetate: MS, m/z 468 (M$^+$, relative intensity 33), 453 (86), 408 (5), 393 (100), 337 (16), 289 (10), 283 (24), 270 (23), 257 (16), 255 (33), 229 (19), 227 (12), 215 (12).

5α-Lanosta-8,25-dien-3β-ol (3c) acetate: MS, m/z 468 (M$^+$, relative intensity 37), 453 (80), 393 (100), 283 (16), 241 (12), 229 (13), 215 (13).

5α-Lanosta-9(11),25-dien-3β-ol (4c) acetate: MS, m/z 468 (M$^+$, relative intensity 24), 453 (67), 393 (100), 355 (71), 283 (12), 255 (12), 241 (12), 229 (14), 215 (12), 201 (12).

10α-Cucurbit-5-en-3β-ol (5a) acetate: MS, m/z 470 (M$^+$, relative intensity 5), 455 (14), 410 (18), 395 (22), 276 (100), 261 (77).

Anhydrolitsomentol (5b) acetate: MS, m/z 468 (M$^+$, relative intensity 4), 453 (4), 408 (28), 393 (14), 274 (100), 259 (69), 231 (16), 205 (16).

10α-Cucurbita-5,25-dien-3β-ol (5c) acetate: MS, m/z 468 (M$^+$, relative intensity 3), 453 (7), 408 (26), 393 (17), 274 (100), 259 (46), 218 (10), 205 (12).

Cucurbit-5(10)-en-3β-ol (6a) acetate: high-resolution MS, m/z 470.4128 (M$^+$, $C_{32}H_{54}O_2$, calcd 470.4121, relative intensity 5), 455,3843 ($C_{31}H_{51}O_2$, 28), 410.3932 ($C_{30}H_{50}$, 84), 395.3647 ($C_{29}H_{47}$, 100), 367.3346 ($C_{27}H_{33}$, 10), 297.2543 ($C_{22}H_{33}$, 10), 288.2772 ($C_{21}H_{36}$, 5), 273.2539 ($C_{20}H_{33}$, 7), 219.2085 ($C_{16}H_{27}$, 7), 207.2088 ($C_{15}H_{27}$, 26); ^{13}C NMR δ 15.2 (C_{31}), 19.2 (C_{32}), 21.3 ($\mathit{C}H_3OCO$), 22.5 (C_{26}), 22.8 (C_{27}), 24.1 (C_{23}), 28.0 (C_{25}), 36.2 (C_{20}), 36.5 (C_{22}), 39.5 (C_{24}), 78.3 (C_3), 132.1 and 133.6 (C_5 and C_{10}), 171.0 (MeO*C*O), 18.4, 18.6, 21.5, 22.1, 24.3, 27.9, 31.5, 32.0, 33.2, 34.1, 36.8, 42.7, 45.7, 50.0, 50.8. The partial assignment of the ^{13}C NMR given above was based on the comparison with the literature data.[14]

Cucurbita-5(10),24-dien-3β-ol (6b) acetate: MS, m/z 468 (M$^+$, relative intensity 9), 453 (18), 408 (100), 393 (98), 286 (9), 217 (24), 205 (65), 203 (24), 201 (15).

Cucurbita-5(10),25-dien-3β-ol (6c) acetate: MS, m/z 468 (M$^+$, relative intensity 10), 453 (30), 408 (100), 393 (95), 297 (13), 217 (11), 205 (33).

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Registry No. **1a**, 4657-58-3; **1a** acetate, 4575-74-0; **1b**, 469-38-5; **1b** acetate, 1259-10-5; **1c** acetate, 70587-99-4; **2a** acetate, 4488-99-7; **2b** acetate, 6562-09-0; **2c** acetate, 88392-47-6; **3a** acetate, 1724-19-2; **3b** acetate, 2671-68-3; **3c** acetate, 88392-48-7; **4a** acetate, 1180-88-7; **4b** acetate, 55570-91-7; **4c** acetate, 88392-49-8; **5a**, 35030-61-6; **5a** acetate, 33593-25-8; **5b**, 35012-08-9; **5b** acetate, 35030-57-0; **5c** acetate, 88392-50-1; **6a**, 88392-51-2; **6a** acetate, 88392-52-3; **6b** acetate, 88392-53-4; **6c** acetate, 88392-54-5.

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Regiospecific Synthesis of 9-Desoxoerythromycin A

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Recently, we described the synthesis of cyclic thionocarbonate 1[1] in conjunction with an investigation into erythromycin aglycon modifications. In the course of the investigation we recognized 1 as a potential entry into aglycon deoxygenated erythromycins. This note details the synthesis of 9-desoxoerythromycin A (3).

We anticipated that exposure of 1 to tri-n-butyltin hydride in the presence of a radical initiator[2] would lead to a mixture of C-9-desoxo (3) as well as C-11-desoxy (5) materials, and we fully expected the regioisomers to be amenable to separation via chromatography. Thus, we believed the sequence would permit rapid preparation of reasonable quantities of 3 and 5, although it would most certainly not be regiospecific. When the tin radical reaction was attempted, it did result in the preparation of 3 and 5, as well as a number of other products. Unfortunately, the yield of the desired materials was extremely low (<10%) and separation of these materials proved tedious. Thus, we sought an alternative synthetic route.

In our previous report on erythromycin aglycon modifications,[1] we described the regiospecific and stereospecific incorporation of nucleophiles at the C-9 position of erythromycin A via nucleophilic displacements on thionocarbonate 1. Since it is known[3] that thionocarbonates are susceptible to rearrangement to thiocarbonates, we considered the possibility of regiospecifically incorporating sulfur into the C-9 position of 1 via its conversion to thiocarbonate 2. In principle, this sequence would permit the preparation of only *one* desoxo material, after desulfurization with Raney Ni. Thus, exposure of 1 to KI in DMF solvent afforded thiocarbonate 2. The structural assignment of the thiocarbonate as a C-9-thia β-stereoisomer was established by ^{13}C NMR deuterium isotope experiments in analogy to those previously reported.[1,4] When 2 was treated with Raney Ni in ethanol solvent, the corresponding 9-desoxoerythromycin A (3) was smoothly produced. Alternatively, thiocarbonate 2 may first be

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