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Lycopodium Triterpenoids. (7).[1] The Structures and Partial Syntheses of 16-Oxoserratenediol, 16-Oxo-21-episerratenediol, 16-Oxodiepiserratenediol, 16-Oxoserratriol, 16-Oxo-21-episerratriol, and 16-Oxolycoclavanol, α,β-Unsaturated Ketones of Serratane Group[2]

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Five new triterpenoids occurring in various *Lycopodium* plants were shown to be 16-oxoserratenediol (**1a**), 16-oxo-21-episerratenediol (**2a**), 16-oxodiepiserratenediol (**3a**), 16-oxoserratriol (**6a**), and 16-oxolycoclavanol (**7a**) respectively, by spectral and chemical means, and the structures assigned were finally confirmed by partial syntheses from the corresponding deoxo-compounds. Potential utility of the solvent shift experiment in NMR and the resulting TH-effect for structural and stereochemical problems was indicated. A conjugated ketone isolated from *L. cernuum* by Inubushi, *et al.* was identical with the synthetic 16-oxo-21-episerratriol (**19c**).

Plants belong to the Genus *Lycopodium* are characteristic of containing triterpenoids of serratane group.[4] During separation of the triterpenoid constituents from various *Lycopodium* plants we have isolated several compounds which had a conjugated ketone chromophor.[5] They were tentatively designated as B_3, B_4, B_5, C_2, and SN-9[4] and proved to be 16-oxo-derivatives of 21-episerratenediol (**2c**), diepiserratenediol (**3c**), serratenediol (**1c**), lycoclavanol (**7c**), and serratriol (**6c**), respectively.[2] This report presents full document of experiments on their structural elucidations and partial syntheses from the corresponding deoxo-compounds.

The spectroscopic characteristics of their acetates given in Table I indicated that all compounds have the similar conjugated ketone of the partial structure (I) at the same position in the same skeletal structure (they show similar ORD curves with negative peaks at 350—380 nm) which probably is serratane since they have seven C-methyl groups or its equivalent as shown from their nuclear magnetic resonance (NMR) spectra (Table II).

16-Oxoserratenediol (1a), 16-Oxo-21-episerratenediol (2a), and 16-Oxodiepiserratenediol (3a)

The compounds, B_3, B_4, and B_5 are diols and formed diacetates whose NMR spectra (Table II) indicated that the original compounds are secondary alcohols. Chromium trioxide-pyridine complex oxidation of each diol gave the same triketone (**4**), indicating that they are epimeric diols. The chemical shifts and the shapes of the signal due to >C<u>H</u>–OAc revealed that the hydroxy groups are likely to be at C-3 and C-21, which are both equatorial for B_5, both axial for B_4, and equatorial-axial for B_3, since signals are almost identical in shapes and shifts with the corresponding signals of serratenediol diacetate (**1d**),[6] diepiserratenediol di-

1) This forms Part X of "Triterpenoid Chemistry." Part IX. Lycopodium Triterpenoids. (6): Y. Tsuda, K. Isobe, and T. Sano, *Chem. Pharm. Bull.* (Tokyo), **23**, 264 (1975).
2) Preliminary Communication: *a*) Y.Tsuda and T. Fujimoto, *Chem. Comm.*, **1969**, 1042; *b*) Y. Tsuda, T. Fujimoto, and K. Kimpara, *ibid.*, **1970**, 261.
3) Location: *Tsurumaki 5-1-8, Setagaya-ku, Tokyo, 154, Japan.*
4) Y. Tsuda, T. Fujimoto, K. Isobe, T. Sano, and M. Kobayashi, *Yakugaku Zasshi*, **94**, 970 (1974).
5) The following plants afforded these compounds: *L. clavatum* (B_3, B_4, B_5, and C_2), *L. serratum* (B_5 and SN-9), and *L. cernuum* (C_2). For detail of isolation see ref. 4).
6) Y. Inubushi, Y. Tsuda, T. Sano, T. Konita, S. Suzuki, H. Ageta, and Y. Otake, *Chem. Pharm. Bull.* (Tokyo), **15**, 1153 (1967).

Table I. Spectral Characterization of 16-Oxoserratenes (Acetates)

Compd.	IR (cm^{-1})[a]	UV (λ_{max} nm, ε)[b]	NMR (δ ppm)[c] >C=CH–	ORD[d] negative peaks (350—380 nm) maximum ([ϕ] *ca.* 372 nm)
1b (B_5)	1670 s., 1625m.	245(14000)	5.74	−273°
2b (B_3)	1671 s., 1625m.	245(13000)	5.75	−749°
3b (B_4)	1668 s., 1623m.	245(13000)	5.74	−1355°
6b (SN-9)	1668 s., 1622m.	245(15000)	5.75	−196°
7b (C_2)	1660 s., 1625m.	245(15000)	5.72	−1059°

a) KBr disc.
b) in 95% EtOH
c) $CDCl_3$ solution, 60 MHz., the signal appeared as broad singlet of 1H
d) dioxane solution, see Fig. 1

Table II. NMR Spectra of the Acetates (δ ppm, 60 MHz. in $CDCl_3$)

Compd.	–C(–)–Me[a]	–O–$COCH_3$[a]	>CH–OAc	–CH_2–OAc[b]	17-H[c]
1b (B_5)	0.83(1) 0.86(4) 1.19(2)	2.06(1) 2.08(1)	4.50 (2H, m., $W_{1/2}$=15 Hz)	—	2.18
2b (B_3)	0.82(1) 0.87(3) 0.91(1) 1.19(2)	2.05(1) 2.09(1)	*ca.* 4.5(1H, m.)[d] *ca.* 4.6(1H, broad s.)[d]	—	2.45
3b (B_4)	0.82(1) 0.87(2) 0.90(1) 0.92(1) 1.19(2)	2.06(1) 2.08(1)	4.61 (2H, broad s., $W_{1/2}$=7 Hz)	—	2.48
6b (SN-9)	0.83(1) 0.87(2) 1.02(1) 1.18(2)	2.05(1) 2.08(2)	4.53 (2H, m., $W_{1/2}$=15 Hz)	4.27 (J=11, $\Delta\delta$=18 Hz)	2.18
7b (C_2)	0.82(1) 0.88(1) 0.91(1) 0.96(1) 1.18(2)	2.05(1) 2.08(2)	4.57 (1H, broad s., $W_{1/2}$=5 Hz) 4.94 (1H, broad s., $W_{1/2}$=5 Hz)	4.08 (J=11, $\Delta\delta$=18 Hz)	2.48
19d[e]	0.83(1) 0.91(2) 1.02(1) 1.19(2)	2.05(1) 2.07(1) 2.10(1)	*ca.* 4.6(1H, m.)[d] *ca.* 4.65(1H, broad s.)[d]	4.26 (J=12, $\Delta\delta$=18 Hz)	2.46

a) numbers in parentheses denote number of Me groups
b) signals appeared as AB quartet of 2H
c) signals appeared as singlet of 1H
d) Signals were overlapped.
e) olefinic proton signal appeared as broad singlet of 1H at δ 5.75

>C=CH–CO– (I) >C=CH–CO–CH(–C–)(–C–) (II)

Chart 1

acetate (**3d**),[7] and 21-episerratenediol diacetate (**2d**),[8] respectively. In agreement with this assumption, the triketone (**4**) yielded exclucively diequatorial alcohol B_5 by sodium borohydride reduction in cold; the conjugated ketone system should be at a hindered position.

The singlet peaks appeared in their NMR spectra at δ 2.2—2.5 which were absent in **1d**, **2d**, and **3d** were assigned to the methine group attached to the carbonyl, the neighbouring carbon of which should be fully substituted. The partial structure (I) was then extended to the structure (II). If we assume that the compounds have the serratane skeleton, this system should be either 16-oxo-14-ene (partial structure III) or 11-oxo-12-ene (partial structure IV).

7) The NMR data are given in Experimental section.
8) Y. Inubushi, Y. Tsuda, T. Sano, and R. Nakagawa, *Chem. Pharm. Bull.* (Tokyo), **13**, 104 (1965).

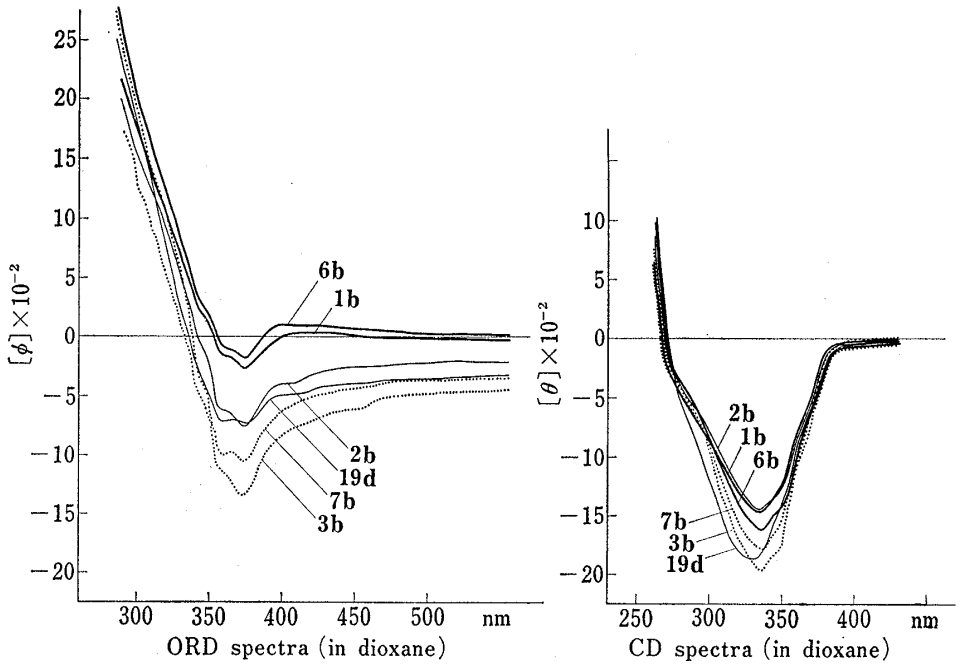
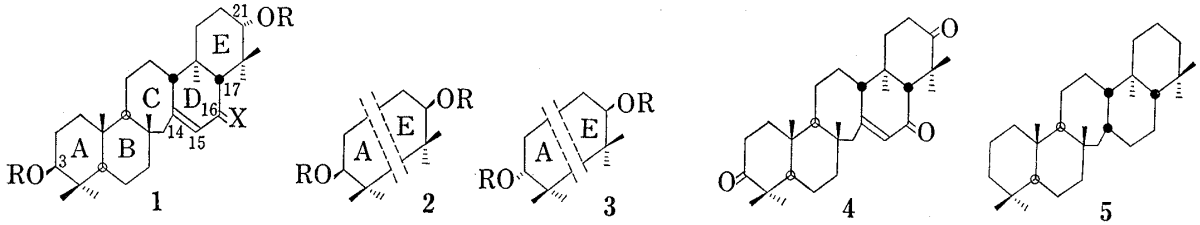


Fig. 1. ORD and CD Spectra of 16-Oxoserratenes(Acetates)

16-oxoserratenediol diacetate (**1b**), 16-oxoserratriol triacetate (**6b**);——
16-oxoepiserratenediol diacetate (**2b**), 16-oxoepiserratriol triacetate (**19d**);——
16-oxodiepiserratenediol diacetate (**3b**), 16-oxolycoclavanol triacetate (**7b**);·····



a : R=H, X=O
b : R=Ac, X=O
c : R=H, X=H_2
d : R=Ac, X=H_2

Chart 2

This problem was solved from the solvent shift experiment for NMR spectra. When the solvent for NMR measurement was changed from $CDCl_3$ to benzene, the two methyl-group signals of each compound showed marked down-field shifts, indicating that the compounds contain two methyl groups in front of the plane through the carbonyl-carbon at right angles to the carbonyl.[9,10] Thus they are 16-oxo-14-enes (III), for in 11-oxo-12-ene (IV) only one methyl (at C-10) should shift down-field. B_5 is therefore elucidated as 16-oxoserrat-14-en-3β,21α-diol (**1a**) and B_4 is 16-oxoserrat-14-en-3α,21β-diol (**3a**). B_3 is either 16-oxoserrat-14-en-3β,21β-diol (**2a**) or 16-oxoserrat-14-en-3α,21α-diol.

The stereochemistry of 21-OAc group of these compounds and thence the structure of B_3 were elucidated by the following evidence. The afore-mentioned methine (17-H) signal appeared at δ 2.2 when 21-OAc is equatorial and at δ 2.4—2.5 when it is axial (*cf.* **1b** and **3b**), apparently indicating the presence of field-direct interaction between 17-H and 21-OAc in

9) M. Hashimoto and Y. Tsuda, International Symposium on NMR Preliminary Report, M-2-13, Tokyo, 1965.
10) J.D. Connolly and R. McCrindle, *Chem. and Ind.*, **1965**, 379.

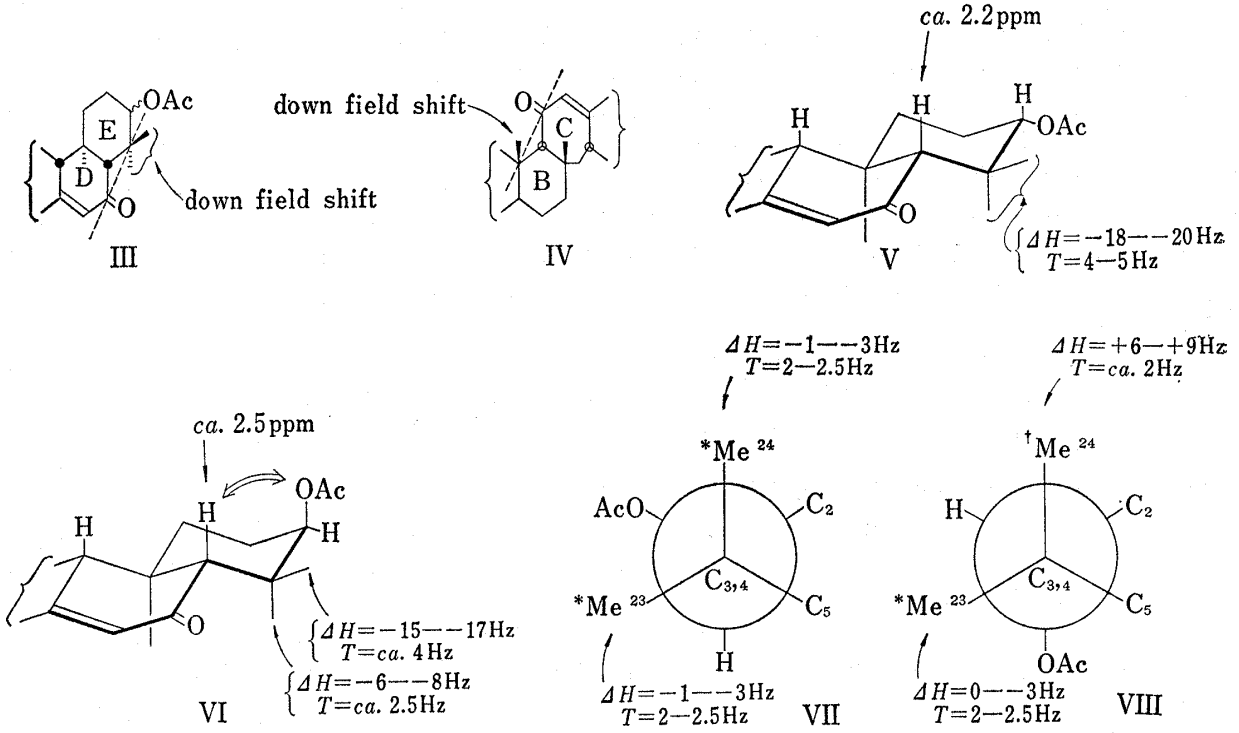


Chart 3

the latter case (*cf.* formulae V and VI). The 17-H signal of B_3-acetate appeared at δ 2.45; this indicates that the 21-OAc group of this compound is axial.

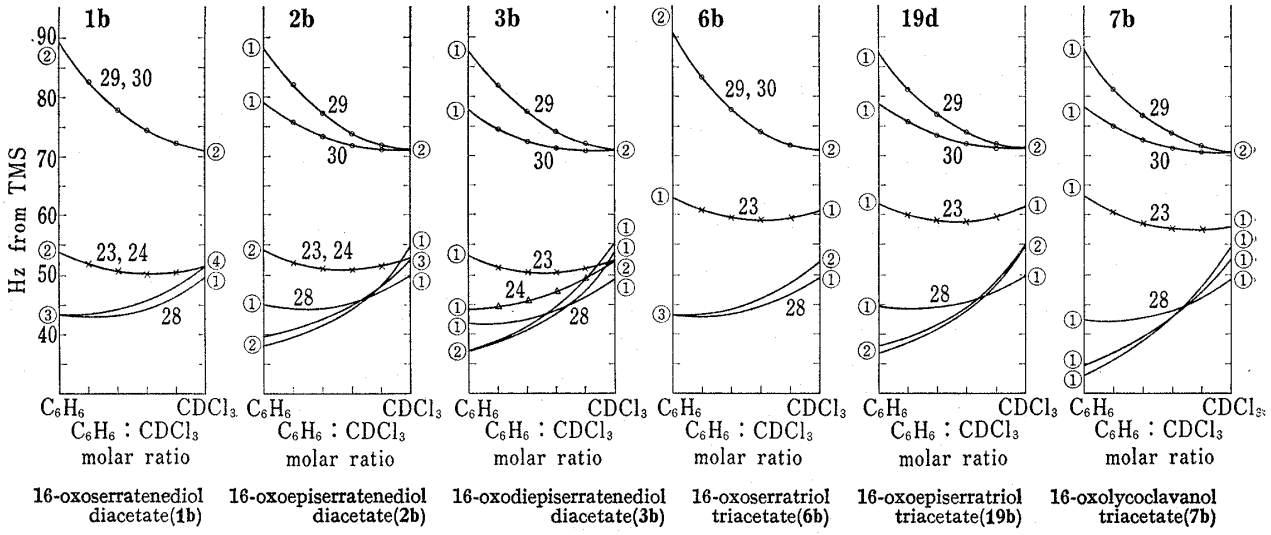


Fig. 2. TH-Effect of 16-Oxoserratenes (Acetates)

a) number in ○ indicates number of methyl groups, *b*) numbers on the curves indicate the position of hydrogens

The solvent shift experiment supported this conclusion. By continously changing the ratio of benzene to $CDCl_3$,[9] the methyl hydrogens at C-29 and C-30 (○ in Fig. 2) moved down-field without separation showing the same shift values and shapes (the same TH-effect) when 21-OAc is equatorial, but showed considerable difference in the case of 21-axial OAc (different TH-effect). A number of model compound revealed that the signal due to the protons of methyl group which is vicinal and in diaxial position with respect to OAc († in VIII) shift up-field (for example, △ in Fig. 2), while those of the methyl in diequatorial or equatorial-axial position to OAc (* in VII and VIII) shifted slightly down-field (for example, × in Fig. 2).

In the former the dihedral angle between OAc and Me is about 180° and in latters the angles are about 60°. The protons at C-29 and C-30 in **1b** and **3b** must experience the combined TH-effect of 16-oxo group (large down-field shift) and of 21-OAc. Since both 22-dimethyl group are in the almost same geometrical situation with respect to 16-carbonyl group, their difference in TH-effect is therefore the result of influence of 21-OAc; they shift to down-field without separation when 21-OAc is equatorial whereas the 21-axial OAc causes the separation of 29-H from 30-H to up-field. Two methyl groups (29-H_3 and 30-H_3) in B_3-acetate experienced the different TH-effects as those in **3b** and the protons of 4,4-dimethyl group shifted without separation, these establishing that 21-OAc is axial and 3-OAc is equatorial. The structure (**2a**) was therefore given to B_3.

Our assumption that these compounds have the serratane skeleton was proved by converting B_4 to 14β-serratane (**5**)[11] (see Experimental) and the structures (**1a**—**3a**) given above were firmly established by partial syntheses of each compound (see below).

16-Oxoserratriol (6a) and 16-Oxolycoclavanol (7a)

The compounds SN-9 and C_2 are triols and formed triacetates whose NMR spectra (Table II) indicated that each compound has an axial $-CH_2OAc$ and two secondary acetoxy-groups which in SN-9 (**6b**) are both equatorial and in C_2 (**7b**) both axial suggesting that the original triols are 16-oxo-derivatives of serratriol (**6c**)[12] and lycoclavanol (**7c**)[12] respectively.

They formed acetonides by application of the forced condition;[12b] SN-9 (**6a**) quantitatively gave **8**, while C_2 (**7a**) gave **9** with some difficulty. The type classification signals[13] (see Chart 4) of **8** and **9** indicated that the acetonide function in **8** is of type **A** and that in **9** is of type **B**. Jones' oxidation of these acetonides yielded, with simultaneous loss of isopropylidene functions as were in the cases of serratriol acetonide and lycoclavanol acetonide,[13] the same keto-aldehyde (**10**) from either compound, thus proving that SN-9 and C_2 are stereoisomeric at the secondary hydroxy groups. Sodium borohydride reduction of the keto-aldehyde (**10**) in cold regenerated SN-9 (**6a**) as expected.

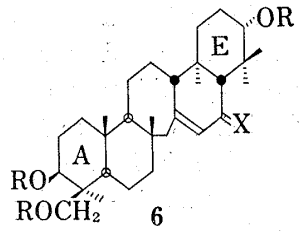
More detailed informations were available from the NMR solvent shift experiments for the acetates (see Fig. 2). By continuously changing the solvent from $CDCl_3$ to benzene, two methyl-group signals at the lowest field in each compound showed marked down-field shifts, the TH-effects being almost identical with those of C_{29}-H and C_{30}-H of **1b** and **3b** respectively; the methyls at δ 1.18 in SN-9 acetate moved without separation and the methyls at δ 1.18 in C_2-acetate shifted with appreciable separation. These facts indicated that neither C-29 and C-30 carries oxygenated function and that 21-OAc of SN-9 acetate is equatorial and that of C_2-acetate is axial. This conclusion was supported by difference in the chemical shift of 17-H signals; the peak for SN-9 acetate appeared at δ 2.18 and that for C_2-acetate appeared at δ 2.48 ppm. Hence, 1,3-glycol system which formed acetonide must be placed at ring A.

Thus SN-9 is 16-oxoserrat-14-en-3β,21α,24-triol (**6a**) and C_2 is 16-oxoserrat-14-en-3α,21β,24-triol (**7a**). This structural assignment was confirmed by converting SN-9 and serratriol (**6c**) to the same homoannular diene (**11**)[14] respectively, (see Experimental) and finally by partial syntheses of SN-9 and C_2 from serratriol and lycoclavanol.

Partial Syntheses of 16-Oxoserratenes

Introduction of oxygen function to C-16 of serratenediol (**1a**) and its congeners will finally establish the structures of these 16-oxo-compounds. There are some precedents of such

11) Y. Tsuda, T. Sano, and Y. Inubushi, *Tetrahedron*, **26**, 751 (1970).
12) *a*) Y. Tsuda, T. Sano, A. Morimoto, and Y. Inubushi, *Tetrahedron Letters*, **1966**, 5933; *b*) Y. Tsuda, T. Sano, A. Morimoto, M. Hatanaka, and Y. Inubushi, *Chem. Pharm. Bull.* (Tokyo), **22**, 2383 (1974).
13) Y. Tsuda, T. Sano, K. Isobe, and M. Miyauchi, *Chem. Pharm. Bull.* (Tokyo), **22**, 2396 (1974).
14) The structure of **11** in connection with acid isomerization behaviour of serratadienes will be fully discussed in a separate paper.



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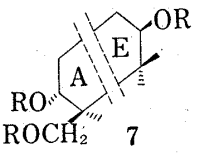

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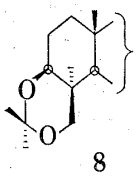
a : R=H, X=O
b : R=Ac, X=O
c : R=H, X=H$_2$
d : R=Ac, X=H$_2$



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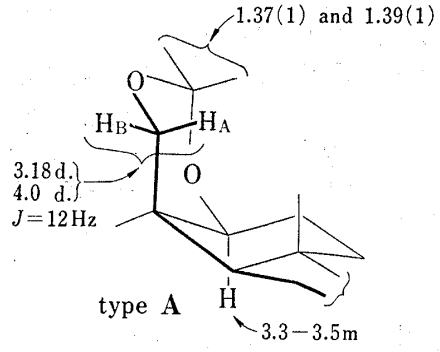

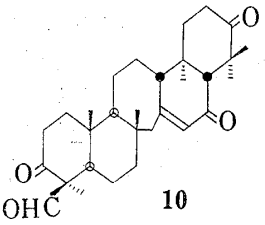

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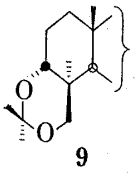

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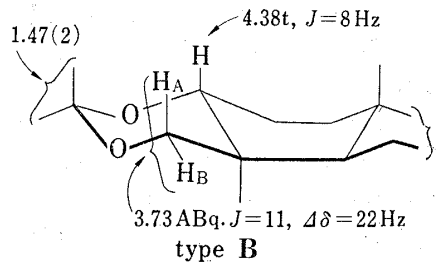

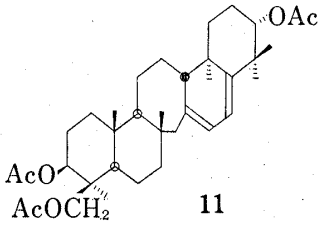

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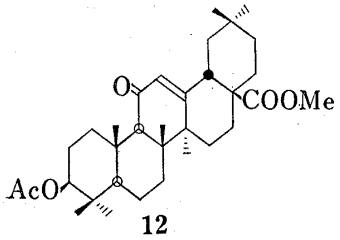
Chart 4



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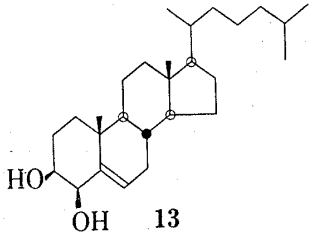

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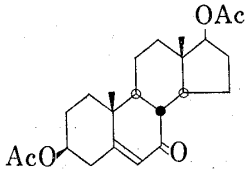

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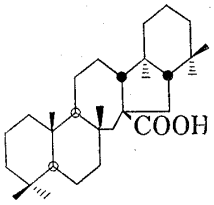

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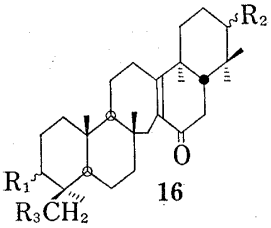

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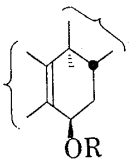

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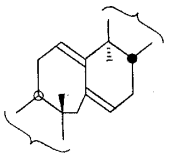

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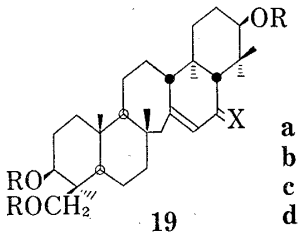
a : R$_1$=R$_2$=R$_3$=H
b : R$_1$=β-OAc, R$_2$=α-OAc, R$_3$=H
c : R$_1$=β-OAc, R$_2$=β-OAc, R$_3$=H
d : R$_1$=α-OAc, R$_2$=β-OAc, R$_3$=H
e : R$_1$=β-OAc, R$_2$=α-OAc, R$_3$=OAc
f : R$_1$=α-OAc, R$_2$=β-OAc, R$_3$=OAc



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a : R=H, X=H$_2$
b : R=Ac, X=H$_2$
c : R=H, X=O
d : R=Ac, X=O

Chart 5

allylic oxidation in steroid and triterpenoid field. Chromic acid in acetic acid oxidizes acetyl methyl oleanolate to the 11-oxo-derivative (**12**), the yield of which was increased when the reagent was replaced to sodium dichromate in acetic acid.[15] However, oxidation of serratenediol diacetate (**1d**) with sodium dichromate in acetic acid yielded the 15-oxo-13-ene (**16b**) as an only isolable product[6] and oxidation of serratene with chromic acid in acetic acid furnished the rearranged product, neoserratan-15-oic acid (**15**) as a major and a 15-oxo-13-ene (**16a**) as a minor product,[11] in neither case 16-oxo-14-ene being isolated.

Selenium dioxide often oxidizes an olefine to an allylic alcohol as was seen in oxidation of cholesterol to the 4β-hydroxy derivative (**13**).[16] This reagent was again useless for the present purpose since the product from **1b** was a derivative of 13-en-15β-ol (**17**) or a diene (**18**).[17]

Photosensitized oxidation of **1b** was therefore attempted. By irradiation of **1b** under bubbling oxygen for 18 hr in presence of catalytic amount of eosin, there was produced a minute amount of conjugated ketone which was a mixture of 15-oxo-13-ene (**16b**) (major) and a desired 16-oxo-14-ene (**1b**) (minor) as shown by spectral and thin-layer chromatography (TLC) data, more than 90% of the unchanged starting material being recovered. The method was still useless for preparative purpose.

t-Butyl chromate oxidized 3β,17β-diacetoxyandrost-5-ene to the 7-oxo compound (**14**).[18] Application of this reagent[19] to serratenes by using non-polar solvent gave satisfactory results.

The best yield (15—20%) was obtained when the compound was warmed in benzene with excess of the reagent at 50—60°, 15-oxo-13-ene (**16**) (15—20%) being produced simultaneously. When large excess of the reagent was used or prolonged reaction applied, there was produced a complex mixture from which only the 15-oxo-13-ene (**16**) was isolated but the 16-oxo-14-ene (**1b**) was absent. This indicates that 16-oxo-14-enes are vulnerable to the excess of oxidizing reagent while 15-oxo-13-enes are stable to the same reagent.

Thus, serratenediol diacetate (**1d**), 21-episerratenediol diacetate (**2d**), serratriol triacetate (**6d**), and lycoclavanol triacetate (**7d**) were converted the corresponding 16-oxo derivatives which were completely identical with the specimens obtained from the natural source, respectively. A comment must be required for oxidation of the triacetates (**6d** and **7d**), in which cases separation of 16-oxo-14-ene and 15-oxo-13-ene was difficult because of the same chromatographic behaviour of the two compounds. The mixture was therefore treated with $NaBH_4$ in cold; the procedure converted the 15-oxo-13-ene (**16**) to 15α-ol which could be further transformed to the 12,14-diene (**18**) by contact with acid while the hindered 16-oxo-14-ene remained intact, thus separation of the 16-oxo-14-ene being made easier.

Chromium trioxide-pyridine complex in methylene chloride[20] was also a suitable reagent to prepare 16-oxo-14-ene from a 14-ene. For example, oxidation of 21-episerratriol triacetate (**19b**)[12b,21] with this reagent gave in a comparable yield the corresponding 16-oxo compound (**19d**), mp 243—246°. Occurrence of **16-oxo-21-episerratriol** (**19c**) in *Lycopodium cernuum* was lately confirmed by Inubushi, *et al*,[22] whose triacetate was completely identical with the synthetic specimen (**19d**).

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15) E.J. Corey and J.J. Ursprung, *J. Am. Chem. Soc.*, **78**, 186 (1956).
16) O. Rosenheim and W.W. Starling, *J. Chem. Soc.*, **1937**, 377.
17) The datails of selenium dioxide oxidation on serratenediol derivative will be reported in a separate paper.
18) K. Hensler and A. Wettstein, *Helv. Chim. Acta*, **35**, 284 (1952).
19) The reagent was prepared according to the method by D.L. Roberts, R.A. Heckman, B.P. Hege, and S.A. Bellin, *J. Org. Chem.*, **33**, 3566 (1968).
20) W.G. Dauben, M. Lorber, and D.S. Fullerton, *J. Org. Chem.*, **34**, 3587 (1969).
21) Y. Tsuda and M. Hatanaka, *Chem. Comm.*, **1969**, 1040.
22) Y. Inubushi, T. Harayama, T. Hibino, and K. Akatsu, *Yakugaku Zasshi*, **91**, 980 (1971).

Experimental

Unless otherwise stated, the infrared (IR) spectra were taken as a KBr disc, the ultraviolet (UV) spectra measured in 95% EtOH. The optical rotatory dispersion (ORD) and circular dichroism (CD) spectra are for dioxane solutions at 23° by JASCO J-20 machine. The NMR spectra were measured in $CDCl_3$ solution by using a 60 MHz machine and the chemical shifts are given in δ ppm referred to the internal tetramethyl silane (TMS). For acetonides proton signals except those shown in Chart 4 (type classification signals) were given in this section. Melting points below 300° were determined on Yanagimoto mp apparatus and those above 300° were taken by an open capillary using Ishii block-heater apparatus, and uncorrected. All organic extracts had been washed with water and dried over K_2CO_3 or Na_2SO_4 before evaporation. Acid-washed alumina was used for column chromatography, and for TLC silica gel G as an absorbent and $CHCl_3$–MeOH as a developing solvent.

Acetylations were carried by heating the compound with excess acetic anhydride and pyridine for a few min and keeping the mixture overnight at room temp., then worked up as usual. Identities were confirmed by IR and TLC comparisons, and by mixed fusion with the authentic specimens when the melting points were below 300°.

16-Oxoserratenediol Diacetate (**1b**) formed colorless needles from CH_2Cl_2–MeOH, mp 308—309°. CD ($c=0.435\times10^{-3}$) [θ] (nm): −1470 (335) (negative maximum). On saponification it gave **16-oxoserratenediol** (**1a**), mp 294—297°, needles from $CHCl_3$.

16-Oxo-21-episerratenediol Diacetate (**2b**) formed colorless needles from *n*-hexane–ether, mp 242—244°. CD ($c=0.31\times10^{-3}$) [θ] (nm): −1460 (335) (negative maximum). On saponification it gave **16-oxo-21-episerratenediol** (**2a**), mp 300—304°, needles from $CHCl_3$.

16-Oxodiepiserratenediol Diacetate (**3b**) formed colorless needles from *n*-hexane–ether, mp 272—275°. CD ($c=0.36\times10^{-3}$) [θ] (nm): −2000 (335) (negative maximum). On saponification it gave **16-oxodiepiserratenediol** (**3a**), mp 318—323°, needles from $CHCl_3$.

Diepiserratenediol Diacetate (**3d**), mp 240—242°. NMR: $-\overset{|}{C}-CH_3$ 0.71 (3H), 0.85 (9H), 0.89 (6H), 0.95 (3H); $-OCOCH_3$ 2.08 (6H); >CH-OAc 4.67 (2H, broad s, $W_{1/2}=7$ Hz); >C=CH– 5.38 (1H, m).

3,16,21-Trioxoserrat-14-ene (**4**)——i) 16-Oxodiepiserratenediol (**3a**; 55 mg) and CrO_3 (100 mg)–pyridine (1 ml) complex in pyridine (6 ml) were kept overnight at room temp. The mixture was poured into water, extracted with CH_2Cl_2, and the extract was evaporated. The residue in benzene was passed through a short column of alumina to give **4**, mp 278—281°, needles from CH_2Cl_2–MeOH. IR cm^{-1}: 1715 (CO), 1665, 1625 (conj. CO). UV (λ_{max}) nm: 245 (ε 13000). NMR: $-\overset{|}{C}-CH_3$ 0.92 (6H), 1.05 (6H), 1.11 (3H), 1.37 (6H); >C=CH– 5.87 (1H, broad s). *Anal.* Calcd. for $C_{30}H_{44}O_3$: C, 79.60; H, 9.80. Found: C, 79.43; H, 9.61.

ii) 16-Oxo-21-episerratenediol (**2a**; 53 mg) in pyridine (6 ml) was oxidized as above with CrO_3 (100 mg)–pyridine (1 ml) complex. Crystallization of the product from CH_2Cl_2–MeOH gave needles, mp 271—273°, identical with **4** obtained above.

iii) 16-Oxoserratenediol (**1a**; 10 mg) in pyridine (3 ml) was oxidized as above to yield **4**, mp 275—278°.

$NaBH_4$ Reduction of the Trioxo-compound (**4**)——The trioxo-compound **4** (10 mg) and $NaBH_4$ (20 mg) in MeOH (3 ml) were stirred at 10° for 2 hr then the mixture was poured into water. The product isolated as usual way, was purified by preparative-TLC to give a compound whose *Rf* was identical with 16-oxoserratenediol. The crystalline alcohol obtained from the TLC plate was acetylated and the product crystallized from CH_2Cl_2–MeOH to give needles, mp 308—309°, which was identical with **1b**.

14β-Serratane (**5**) **from 16-Oxodiepiserratenediol** (**3a**)——The diacetate **3b** (36 mg) in AcOH (20 ml) containing 70% $HClO_4$ (4 drops) was hydrogenated over PtO_2 (56 mg) for 10 hr. Removal of the solvent and the catalyst left a residue which was hydrolysed in MeOH (5 ml)–dioxane (2 ml) with KOH (0.5 g) on heating under reflux for 2.5 hr. A solid product (25 mg) thus obtained was dissolved in pyridine (2 ml) and oxidized with CrO_3 (100 mg)–pyridine (1 ml) complex on standing overnight at room temp., then worked up as usual. The resulting gummy product (15 mg) was heated with anhy. hydrazine (0.6 ml) and diethyleneglycol (6 ml) under reflux for 1 hr. After removal of excess hydrazine, Na (0.5 g) dissolved in diethyleneglycol (3 n l) was added to the mixture which was heated under reflux for further 5 hr, and worked up as usual. The crude product isolated was dissolved in *n*-hexane and chromatographed over alumina to give a hydrocarbon mixture which was treated with Ac_2O–H_2SO_4 according to Anderson-Nabenhauer method[23] to remove contaminated unsaturated compound. The saturated hydrocarbon fraction thus obtained was sublimed at 200° to give a sublimate (5 mg) which showed on GC a major peak corresponding to that of 14β-serratane (**5**) together with small accompanying peaks.

16-Oxoserratriol Triacetate (**6b**) formed colorless needles from CH_2Cl_2–MeOH, mp 309—311°. CD ($c=0.415\times10^{-3}$) [θ] (nm): −1600 (335) (negative maximum). On saponification it gave **16-Oxoserratriol** (**6a**), mp 294—298°, needles from $CHCl_3$–MeOH.

23) R.J. Anderson and F.P. Nabenhauer, *J. Am. Chem. Soc.*, **46**, 1957 (1927).

16-Oxolycoclavanol Triacetate (7b) formed colorless needles from CH_2Cl_2–MeOH, mp 245—247°. CD ($c=0.345\times10^{-3}$) [θ] (nm): −1800 (335) (negative maximum). On saponification it gave **16-oxolycoclavanol (7a)**, mp 328—333°, needles from $CHCl_3$–MeOH.

16-Oxoserratriol Acetonide (8)——16-Oxoserratriol (**6a**; 112 mg) and *p*-TsOH (10 mg) in 2,2-dimethoxypropane (10 ml) and DMF (20 ml) were heated under gentle reflux for 6 hr. After cooling the mixture was poured into 5% K_2CO_3 (200 ml) and extracted with CH_2Cl_2. Crystallization of the product from acetone, then from *n*-hexane yielded **8** as colorless prisms, mp 291—293°. IR cm^{-1}: 3550 (OH), 1663, 1620 (conj. CO). NMR: $-\overset{|}{C}-CH_3$ 0.80 (3H), 0.89 (3H), 1.07 (6H), 1.15 (3H), 1.31 (3H); >CH–OH 3.30—3.50 (1H);[24] >C=CH– 5.76 (1H, broad s.). *Anal.* Calcd. for $C_{33}H_{52}O_4$: C, 77.29; H, 10.22. Found: C, 77.17; H, 10.04.

16-Oxolycoclavanol Acetonide (9)——16-Oxolycoclavanol (**7a**; 155 mg) and *p*-TsOH (10 mg) in 2,2-dimethoxypropane (7 ml) and DMF (14 ml) were heated as above. The product was chromatographed over Florisil which was eluted firstly with *n*-hexane then with benzene. The compound obtained from benzene eluate was crystallized from *n*-hexane–benzene to afford **9** (45 mg), mp 245—249°. NMR: $-\overset{|}{C}-CH_3$ 0.84 (3H), 0.89 (3H), 1.09 (3H), 1.19 (6H), 1.31 (3H); >CH–OH 3.41 (1H, broad s.); >C=CH– 5.76 (1H, broad s.). *Anal.* Calcd. for $C_{33}H_{52}O_4$: C, 77.29; H, 10.22. Found: C, 77.11; H, 10.13.

The Keto-aldehyde (10)——i) To a stirred solution of the acetonide **8** (20 mg) in acetone (20 ml), Jones' reagent (5 drops) was added dropwise during 5 min under ice-cooling. Water was then added and the mixture extracted with CH_2Cl_2 which was evaporated to give **10** (16 mg), mp 255—257°, needles from ether. IR cm^{-1}: 2730, 1725 (CHO), 1707 (CO), 1656, 1620 (conj. CO). NMR: $-\overset{|}{C}-CH_3$ 0.93 (3H), 0.97 (3H), 1.03 (3H), 1.27 (3H), 1.35 (6H); >C=CH– 5.84 (1H, broad s.); –CHO 9.73 (1H, s.). *Anal.* Calcd. for $C_{30}H_{42}O_4$: C, 77.21; H, 9.07. Found: C, 76.98; H, 8.89.

ii) The acetonide **9** (20 mg) was oxidized by Jones' reagent as above to yield **10** (11 mg), mp 254—257°.

$NaBH_4$ Reduction of the Keto-aldehyde (10)——The keto-aldehyde **10** (10 mg) and $NaBH_4$ (10 mg) in MeOH (5 ml) were stirred under ice-cooling for 30 min. Water was added to the mixture which was extracted with $CHCl_3$. Acetylation of the extract and crystallization of the product from CH_2Cl_2–MeOH gave needles, mp 309—311°, which was identical with 16-oxoserratriol triacetate (**6b**).

Homoannular Diene (11) from 16-Oxoserratriol (6a)——The triacetate **6b** (60 mg) and LAH (100 mg) in THF (30 ml) were heated under reflux for 5 hr. After decomposition of excess LAH by adding few drops of water, the mixture was filtered and the residue washed with CH_2Cl_2. Evaporation of the combined filtrates left a solid which showed no carbonyl absorption in IR and had only end absorption in UV spectra. This residue was dissolved in $CHCl_3$ (8 ml)–MeOH (9 ml) containing c.HCl (1.3 ml) and heated under reflux for 30 min. The solid obtained by evaporation of the solvent was acetylated and crystallized from CH_2Cl_2–MeOH to give **11** as colorless needles, mp 220—223°. IR cm^{-1}: 1735, 1245 (OAc), 800 (>C=CH–). UV (λ_{max}) nm: 275. NMR: $-\overset{|}{C}-CH_3$ 0.74 (3H), 0.79 (3H), 0.83 (3H), 1.01 (3H), 1.10 (6H); $-OCOCH_3$ 2.04 (3H), 2.06 (3H), 2.07 (3H); $-\overset{|}{C}-CH_2-OAc$ 4.26 (2H, ABq., $J=12$, $\delta_{AB}=19$ Hz); >CH–OAc 4.60 (2H, m); >C=CH– 5.71 (1H, m), 5.90 (1H, d., $J=5$ Hz). *Anal.* Calcd. for $C_{36}H_{54}O_6$: C, 74.19; H, 9.34. Found: C, 73.97; H, 9.27.

Homoannular Diene (11) from Serratriol (6c)——i) SeO_2 Oxidation of **6d**: Serratriol triacetate (**6d**; 500 mg) and $SeO_2\cdot2H_2O$ (500 mg) in AcOH (70 ml) were heated at 60—70° for 1 hr. The precipitated Se was filtered off and the filtrate was poured into water, extracted with ether, the extract was washed with 5% K_2CO_3 and evaporated. Chromatography of the residue gave the heteroannular diene **18e** (20 mg) (needles from MeOH) from *n*-hexane–benzene eluate, mp 188—191°. IR cm^{-1}: 1733, 1243 (OAc), 8.03 (>C=CH–). UV (λ_{max}) nm: 233, 240, 248. NMR: $-\overset{|}{C}-CH_3$ 0.84 (6H), 0.95 (6H), 1.02 (6H), $-OCOCH_3$ 2.05 (3H), 2.07 (6H); $-\overset{|}{C}-CH_2-OAc$ 4.26 (2H, ABq. $J=12$, $\delta_{AB}=18$ Hz); >CH–OAc 4.55 (2H, m); >C=CH– 5.45 (2H, m). *Anal.* Calcd. for $C_{36}H_{54}O_6$: C, 74.19; H, 9.34. Found: C, 74.03; H, 9.21. Following benzene eluate gave **17e** (R=Ac) as a gum which showed only end absorption in UV spectra.

ii) The Homoannular Diene (**11**) from **17e**: The compound **17** in EtOH (12 ml) containing c.HCl (1.5 ml) was heated under reflux for 2 hr. The solvent was evaporated and the residue acetylated. Chromatography and crystallization of the product afforded the diene **11**, mp 219—223°, which was identical with the diene **11** obtained from 16-oxoserratriol.

iii) The Homoannular Diene (**11**) from the Heteroannular Diene (**18e**): The diene **18e** (10 mg) in EtOH (5 ml) containing c.HCl (0.6 ml) was heated and worked up as above. The diene **11** (5 mg) was obtained.

Photochemical Oxidation of Serratenediol Diacetate (1d)——Serratenediol diacetate (172 mg) and eosin (1 mg) in benzene (50 ml)–EtOH (50 ml) were irradiated by 30 W mercury-lamp under bubbling oxygen for 18 hr at room temp. The solvent was evaporated and the residue chromatographed over alumina. Benzene eluate gave the unchanged starting material (150 mg). Following CH_2Cl_2 eluate was rechromatographed to give a crystalline solid (6 mg) which was shown to be a mixture of 15-oxo-isoserratenediol diacetate (**16b**) and 16-oxoserratenediol diacetate (**1b**) from its TLC and from the following spectral data. UV λ_{max}:

24) overlapped with type classification signals.

245 nm. IR cm^{-1}: 1725, 1245 (OAc), 1670, 1655, 1633, 1620 (conj. CO). Preparative-TLC of this mixture afforded pure 15-oxo-13-ene **16b** (1.2 mg), mp>300°, which was identified with the authentic specimen.

***t*-Butyl Chromate Reagent**——The reagent was prepared from CrO_3 (7.5 g), *t*-BuOH (20 ml), and Ac_2O (7 ml) according to the method by D.L. Roberts, *et al*,[19] which contains about 0.6 g of *t*-$BuOCrO_2(OH)$ per 1 ml of the solution.

***t*-Butyl Chromate Oxidation of 21-Episerratenediol Diacetate (2d)**——21-Episerratenediol diacetate (960 mg) and *t*-butyl chromate reagent (4 ml) in benzene (20 ml) were heated at 50—60° for 10 hr. Excess of the reagent was decomposed by oxalic acid, and the mixture diluted with water, then extracted with CH_2Cl_2. The extract, on evaporation, left a residue which was chromatographed in benzene over alumina. It was eluted with benzene (300 ml), with CH_2Cl_2–benzene (1 : 3) (150 ml), and finally with CH_2Cl_2 (180 ml). Benzene eluate gave a starting material **2d** (20 mg). CH_2Cl_2 eluate was rechromatographed in benzene and the eluate was collected in 30 ml fractions. Fraction 5 yielded the 16-oxo-14-ene (**2b**) which after crystallization from CH_2Cl_2–MeOH formed leaflets, mp 240—244°, and was identified with the authentic specimen. Fractions 4 and 6, and the above CH_2Cl_2–benzene eluate were combined and rechromatographed to give a further crop of **2b** (total yield, 83 mg). Fr. 9—20 gave 3β,21β-diacetoxyserrat-13-en-15-one (**16c**) (163 mg), mp 312—318°. IR cm^{-1}: 1731, 1248 (OAc), 1660, 1615 (conj. CO). NMR: –$\overset{|}{C}$–CH_3 0.68 (3H), 0.80 (3H), 0.85 (6H), 0.86 (3H), 0.98 (3H), 1.05 (3H); –OCOCH_3 2.01 (3H), 2.03 (3H); >CH–OAc 4.46 (1H, m), 4.73 (1H, broad s). *Anal.* Calcd. for $C_{34}H_{52}O_5$: C, 75.51; H, 9.69. Found: C, 75.32, H, 9.57.

***t*-Butyl Chromate Oxidation of Serratenediol Diacetate (1d)**——Serratenediol diacetate (1.004 g) in benzene (20 ml) was oxidized with *t*-butyl chromate reagent (4 ml) under gentle reflux for 10 hr and worked up as above. The starting material (30 mg), 16-oxo-compound (**1b**) (144 mg), and 15-oxoisoserratenediol diacetate (**16b**) (200 mg) were isolated.

***t*-Butyl Chromate Oxidation of Lycoclavanol Triacetate (7d)**——Lycoclavanol triacetate (200 mg) in benzene (10 ml) was treated with *t*-butyl chromate reagent (0.8 ml) at 50—60° for 45 min, then the mixture was kept at room temp overnight. Repeating chromatography of the product gave the starting material (65 mg), 16-oxo-14-ene **7b** (19 mg) being identical with the authentic specimen, and 15-oxo-13-ene **16f** (21 mg), mp 275—277°. IR cm^{-1}: 1740, 1251 (OAc), 1650, 1618 (conj. CO). NMR: –$\overset{|}{C}$–CH_3 0.70 (3H), 0.82 (3H), 0.90 (3H), 0.97 (3H), 1.00 (3H), 1.08 (3H); –OCOCH_3 2.07 (3H), 2.10 (6H); –$\overset{|}{C}$–CH_2–OAc 4.07 (2H, ABq. J=12, δ_{AB}=18 Hz); >CH–OAc 4.75 (1H, m), 4.93 (1H, m). *Anal.* Calcd. for $C_{36}H_{54}O_7$: C, 72.21; H, 9.09. Found: C, 72.07; H, 8.92.

***t*-Butyl Chromate Oxidation of Serratriol Triacetate (6d)**——Serratriol triacetate (1.004 g) in benzene (40 ml) was oxidized with *t*-butyl chromate reagent (2 ml) at 50—60° for 31 hr. Chromatography of the product gave the starting material (545 mg) and a mixture (211 mg) of 16-oxo-14-ene **6b** and 15-oxo-13-ene **16e**. The latter was reduced with $NaBH_4$ (31 mg) in MeOH (10 ml)–THF (10 ml) at 5—10° for 2 hr. The product was chromatographed in benzene and the eluate was collected in 50 ml fractions. Several crystallizations of fr. 6—15 from *n*-hexane–benzene gave pure **6b** (86 mg) as needles, mp 312—314°, which was identified with the authentic specimen.

Oxidation of 21-Episerratriol Triacetate (19b) with CrO_3–Pyridine Complex in Methylene Chloride——Chromium trioxide–pyridine complex was prepared from 1 g of CrO_3 and 1 ml of pyridine according to the method by Dauben, *et al*.[20] The precipitated complex was washed throughly with *n*-hexane and used immediately.

21-Episerratriol triacetate (210 mg) and CrO_3–pyridine complex in CH_2Cl_2 (80 ml) were stirred for 48 hr at room temp. The mixture was filtered and the residue washed well with CH_2Cl_2. The combined filtrate was evaporated to dryness, and the residue chromatographed to yield starting material **19b** (78 mg) and a mixture of conjugated ketones (60 mg). The latter in MeOH (25 ml)–THF (5 ml) was reduced with $NaBH_4$ (30 mg) for 90 min at 10°, then c.HCl (3 ml) was added and heated on water-bath for 3 min. The mixture was poured into water and extracted with CH_2Cl_2. Chromatography of the extract and crystallizations of the eluate from CH_2Cl_2–MeOH afforded 16-oxo-21-episerratriol triacetate (**19d**) (10 mg) as colorless needles, mp 243—246°. IR (Nujol) cm^{-1}: 1738, 1253 (OAc) 1670, 1625 (conj. CO). *Anal.* Calcd. for $C_{36}H_{54}O_7$: C, 72.21; H, 9.09. Found: C, 72.08; H, 8.96. CD ($c=0.345\times10^{-3}$) [θ] (nm): −1860 (330) (negative maximum).

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