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Triterpenoid Chemistry. IX.[1] Lycopodium Triterpenoid. (6). The Structures of Three New Tetra-ols, Lycocryptol, 21-Epilycocryptol, and Diepilycocryptol, and Two New Acids, Lycernuic Acid-A and -B[2]

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New triterpenoid-tetra-ols, lycocryptol, 21-epilycocryptol, and diepilycocryptol, isolated from various *Lycopodium* plants were shown to be serrat-14-en-3β,21α,24,30-tetraol (**1a**), serrat-14-en-3β,21β,24,30-tetraol (**2a**), and serrat-14-en-3α,21β,24,30-tetraol (**3a**) respectively, by spectral and chemical means. Two new acids, lycernuic acid-A and -B which were isolated from *L. cernuum* were settled to be 3β,21β-dihydroxyserrat-14-en-24-oic acid (**14a**) and 3β,21β,30-trihydroxyserrat-14-en-24-oic acid (**15a**) by correlating them to 21-episerratriol and 21-epilycocryptol respectively.

Recent extensive studies[4] on *Lycopodium* plants have revealed that the plants of this genus are characteristic of containing triterpenoid derivatives of serratane group which has the common structural feature of seven membered ring C,[5] or their precursor, α-onocerin. The same series of compounds have also been found in ferns,[6] and in the bark of species of pine[7] and spruce.[8] All of them were derivatives of mono-, di-, or tri-ols except tohogeninol[9] and lycoclavanin[10] which are only tetra-ols whose structures were so far established.[11]

As examples of further oxygenated series of this group, we report here three new tetra-ols, lycocryptol (**1a**), 21-epilycocryptol (**2a**), and diepilycocryptol (**3a**), and two acid derivatives, lycernuic acid-A (**14a**) and -B (**15a**), the latters being the first examples of carboxylic acid of this group.[11]

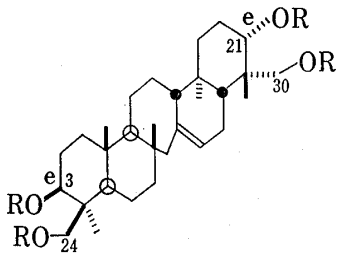
Lycocryptol, 21-Epilycocryptol, and Diepilycocryptol

Lycocryptol occurrs[4] in *L. cryptomerinum*, *L. sieboldii*, and *L. fargesii* and 21-epilycocryptol was isolated[4] from *L. complanatum* (collected at Fukushima pref. Japan), *L. sitchense*, and *L. annotinum* together with their diol and triol congeners. Diepilycocryptol is one of the

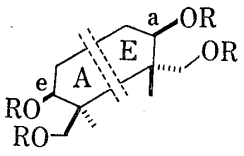
1) Part VIII: Y. Tsuda, K. Isobe, T. Sano, and A. Morimoto, *Chem. Pharm. Bull.* (Tokyo), **23**, 98 (1975).
2) This work was presented at the 14th Symposium on the Chemistry of Natural Products, Oct., 1970, Fukuoka, Japan (Abstract p. 327). In this preliminary report 21-epilycocryptol and diepilycocryptol were described as lycoplanatol and epilycoplanatol, respectively.
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), and references cited therein.
5) Y. Inubushi, Y. Tsuda, T. Sano, T. Konita, S. Suzuki, H. Ageta, and Y. Otake, *Chem. Pharm. Bull.* (Tokyo), **15**, 1153 (1967).
6) G. Berti, F. Bottari, A. Marsili, I. Morelli, and A. Mandelbaum, *Chem. Comm.*, **1967**, 50.
7) J.W. Rowe, *Tetrahedron Letters*, **1964**, 2347; J.W. Rowe and C.L. Bower, *ibid.*, **1965**, 2745.
8) J.P. Kutney and I.H. Rogers, *Tetrahedron Letters*, **1968**, 761; I.H. Rogers and L.R. Rozon, *Canad. J. Chem.*, **48**, 1021 (1970).
9) T. Sano, Y. Tsuda, and Y. Inubushi, *Tetrahedron*, **26**, 2981 (1970).
10) Y. Tsuda and T. Fujimoto, *Chem. Comm.*, **1970**, 260.
11) After our preliminary report, isolations of phlegmanol (3β,14β,21α,30-tetrahydroxy-14β-serratane) and phlegmaric acid (3α,21β-dihydroxyserrat-14-en-24-oic acid) from *L. phlegmaria* were reported [Y. Inubushi, T. Hibino, T. Hasegawa, and R. Somanathan, *Chem. Pharm. Bull.* (Tokyo), **19**, 2640 (1971); Y. Inubushi, T. Hibino, T. Harayama, T. Hasegawa, and R. Somanathan, *J. Chem. Soc.* (C), **1971**, 3109].

seventeen triterpenoid constituents of *L. clavatum*.[4] The non-basic fraction of the methanol extract of the respective plant material was saponified and acetylated and the resulting mixture of acetates separated essentially by chromatographic techniques.[4] They were well characterized as their tetra-acetates, $C_{38}H_{58}O_8$: **1b**, mp 242—247°; **2b**, mp 242—243°; and **3b**, mp 241—243°.

The nuclear magnetic resonance (NMR) spectra of the acetates (Table I) indicated that each compound has a trisubstituted double bond, five (tertiary) C-methyls, and two primary and two secondary acetoxy-groups; the latters are both equatorial for **1b**, equatorial-axial for **2b**, and both axial for **3b** as evidenced from their >CH–OAc signals. We can therefore assume that they are derivatives of serratenediol, episerratenediol, and diepiserratenediol, respectively.



1a : R=H
1b : R=Ac



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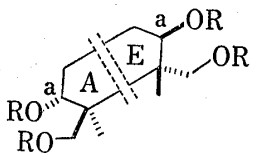

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Chart 1

TABLE I. NMR Spectra of Acetates (60 MHz)

Compound	C–Me[a]	–OCOCH$_3$[a]	–C$_4$–CH$_2$–OAc[b]	–C$_{22}$–CH$_2$–OAc	C$_3$H–OAc	C$_{21}$H–OAc	–C=CH–[c]	–COOMe[a]
1b	0.70(1), 0.85(2) 1.00(2)	2.05(4)	4.27 J=13 δ=19 Hz	4.35[b] J=13 δ=20 Hz	4.56[d] (1H, m)	4.56[d] (1H, m)	5.35	—
2b	0.70(1), 0.87(2) 0.94(1), 0.98(1)	2.03(1) 2.07(2) 2.10(1)	4.28 J=12 δ=19 Hz	4.22 (2H, b s)	4.53 (1H, m)	5.07 (1H, b s)	5.37	—
3b	0.71(1), 0.88(2) 0.96(2)	2.07(2) 2.11(2)	4.12 J=12 δ=18 Hz	4.21 (2H, b s)	5.04[d] (1H, b s)	5.04[d] (1H, b s)	5.39	—
14c	0.72(2), 0.86(2) 0.95(1), 1.23(1)	2.08(2)	—	—	4.53 (1H, m)	4.70 (1H, b s)	5.38	3.70(1)
15c	0.71(2), 0.87(1) 0.95(1), 1.24(1)	2.08(2) 2.11(1)	—	4.22 (2H, b s)	4.58 (1H, m)	5.08 (1H, b s)	5.38	3.72(1)

a) Numbers in parentheses denote number of methyl groups.
b) Signal appears as AB quartet of 2H.
c) Signal appears as multiplet of 1H.
d) Signal was overlapped.

Since 21-epilycocryptol was obtained most abundantly among the three, most of structural studies were carried out using this compound. When a forced condition[12] [heating with 2,2-dimethoxypropane and *p*-TsOH in dimethylformamide (DMF)] of acetonide formation was applied to 21-epilycocryptol for a short time, it gave a mixture of the diacetonide (**5**) and a monoacetonide-a (**4a**); the latter formed diacetate (**4b**), mp 249—251°. Further reaction converted **4a** to the diacetonide (**5**). On the other hand, the diacetonide (**5**) was hydrolysed to a different monoacetonide-b (**6a**) under mild condition (2% acetic acid–chloroform–methanol

12) Y. Tsuda, T. Sano, A. Morimoto, M. Hatanaka, and Y. Inubushi, *Chem. Pharm. Bull.* (Tokyo), **22**, 2383 (1974).

for 20 min) accompanying with minor amount of the monoacetonide-a (**4a**). The monoacetonide-b afforded a diacetate (**6b**) of mp 254—257°.

Tsuda, *et al.*[13] reported that the acetonides derived from triterpenoid 1,3-glycol sysetm were classified into four types (**A**—**D**) which were easily distinguished from each other by the NMR signals of the isopropylidene methyls and those of protons on the *m*-dioxan ring (type classification signals). Inspections of those of the acetonides (**4b**), (**5**), and (**6b**) disclosed following characteristic features (Table II). In the monoacetonide-a (**4b**) two isopropylidene methyls appeared as two separated peaks ($\Delta\delta$—3 Hz) and $-C\underline{H}_2-O-$ protons exhibited two doublets with significant separation ($\Delta\delta$—0.8 ppm). These evidence indicated the stereochemistry of type **A** (*cis*-fused configuration formed from eq-OH and ax-CH_2OH) to the acetonide **4b**. On the contrary, in the monoacetonide-b (**6b**) isopropylidene methyls showed no separation and $-C\underline{H}_2-O-$ appeared as ABq. of $\delta_{AB}=27$, $J=12$ Hz, but $>C\underline{H}-O-$ appeared at markedly down field (δ 4.33) as difused triplet (J—8.5 Hz), which is characteristic of type **B** acetonide (*trans*-fused one with a boat configuration formed from ax-OH and ax-CH_2OH). In agreement, two acetonide rings in the diacetonide (**5**) were attributable to type **A** and type **B** as evidenced from the data in Table II. Hence two primary hydroxy-groups in 21-epilycocryptol are at C_{24} and C_{30}.

Table II. Type Classification Signals of Acetonides (60 MHz)

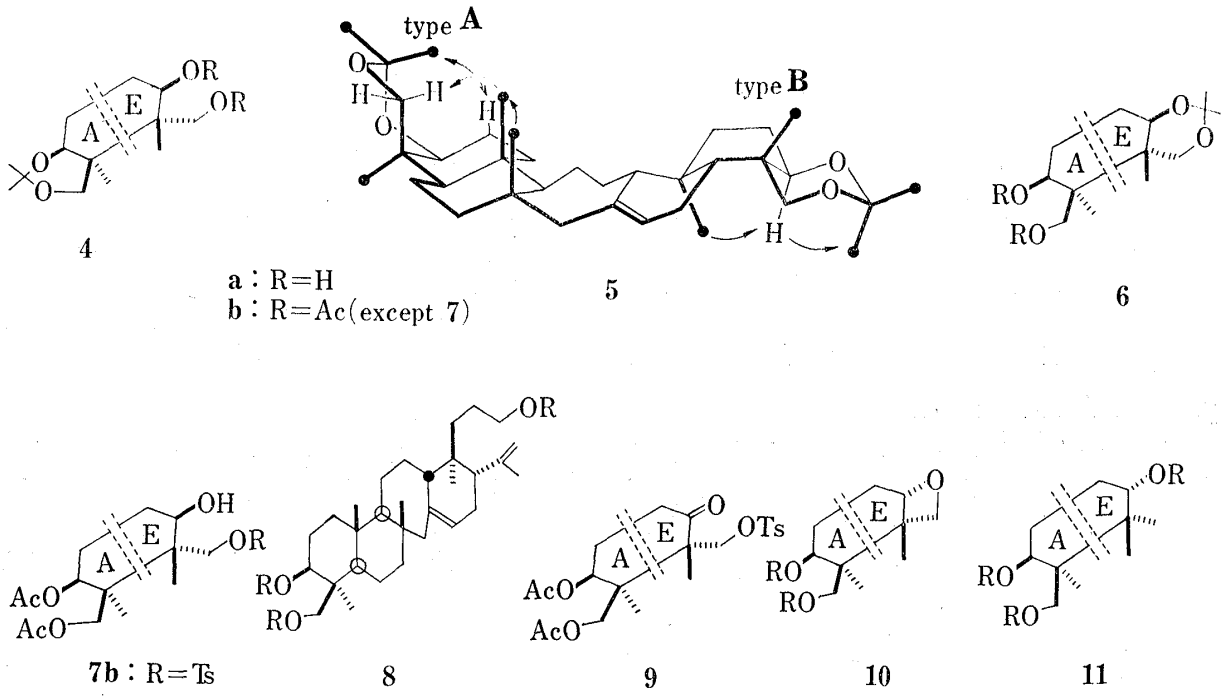
Compound	O\ /Me C O/ \Me	$-C\underline{H}_2-O-$	$>C\underline{H}-O-$	type
4b	1.36(1) 1.41(1)	3.20 d 4.00 d $J=12$ Hz	3.50m	**A**
5	1.37(1) 1.40(1)	3.19 d 4.01 d $J=12$ Hz	3.4—3.6[a]	**A**
	1.40(2)	3.67 ABq. $J=11$ $\delta_{AB}=27$ Hz	4.33[b]	**B**
6b	1.46(2)	3.70 ABq. $J=11$ $\delta_{AB}=26$ Hz	4.3—4.7[a]	**B**
12	1.41(2)	3.72 ABq. $J=11$ $\delta_{AB}=24$ Hz	4.35[b]	**B**
	1.41(2)	3.70 ABq. $J=11$ $\delta_{AB}=26$ Hz	4.35[b]	**B**
13a	1.43(2)	3.70 ABq. $J=11$ $\delta_{AB}=26$ Hz	4.33[b]	**B**

a) The signal was overlapped.
b) The signal appeared as difused triplet (J—8 Hz).

Generally type **B** acetonide in ring A is more labile to acid hydrolysis than that of type **A**, the reason of which was attributed to transmission of a steric compression caused by C_8–Me.[13] However, acid hydrolysis of the diacetonide (**5**) (see above) indicated that the acetonide of type **A** in this compound was more labile than that of type **B**. This fact suggests that the type **B** acetonide portion in **5** is lacking such 1,3-diaxial interaction. This situation is satisfied only when the type **A** acetonide is placed at ring A and the type **B** acetonide at ring E. The structure (**2a**) was therefore suggested for 21-epilycocryptol. This conclusion was confirmed by stereospecific cleavage[1] of the monotosylate (**7b**) which was prepared by hydrolysis of **6b**

13) Y. Tsuda, T. Sano, K. Isobe, and M. Miyauchi, *Chem. Pharm. Bull.* (Tokyo), **22**, 2396 (1974).

followed by tosylation of the resulting diol-diacetate (**7a**). Treatment of the mono-tosylate (**7b**) with potassium *t*-butoxide in *t*-butanol followed by sodium borohydride reduction furnished a seco-triol (**8a**) characterized as its acetate (**8b**). Its NMR signals at δ 1.78 (3H, s) and 4.83 (2H, broad s) and infrared (IR) absorption at 890 cm^{-1} confirmed the formation of an isopropenyl group, thus the trans arrangement of 21-OH and 22-CH_2OTs in (**7b**) being established.



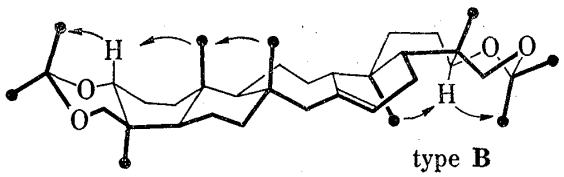
4 a : R=H b : R=Ac(except 7) 5 6

7b : R=Ts 8 9 10 11

Chart 2

If we reductively remove C_{30}–OTs from (**7b**) to known triol derivative, the whole structure of 21-epilycocryptol will be firmly established. However, since tosyloxy group of this type of 1,3-glycol monotosylate could not be reduced to deoxy-compound by LAH, the following modification[1] was employed for this purpose. Monotosylate (**7b**) was oxidized by Jones' reagent to a keto-tosylate (**9**) which was then reduced with LAH. By this modification the 21-keto group will be firstly reduced to the corresponding equatorial alcohol which will give detosyloxy compound *via* intramoleculer hydride transfer.[1] There were obtained three compounds. The most mobile one on chromatography was an oxetane derivative (**10a**) as shown by the NMR spectrum of its acetate (**10b**). The second compound was a tri-ol which was identical with serratriol[12] (**11a**) as confirmed by comparison of its acetate with the authentic specimen (**11b**). Therefore the structure of 21-epilycocryptol was rigidly established as serrat-14-en-3β,21β,24,30-tetraol (**2a**). The third product and its acetate gave the same spots with lycocryptol and its tetraacetate on thin-layer chromatography (TLC), respectively, which must be the S–O fission product.

Diepilycocryptol (**3a**) also formed a diacetonide (**12**), mp 277—280°, under a forced condition. The stereochemistry of both acetonide portions in **12** were of type **B** as evidenced from its type classification signals (Table II). Mild treatment with acetic acid converted it to a monoacetonide (**13**), mp 298—302°. Apparently more labile acetonide on ring A had been hydrolysed. Careful Jones' oxidation of **13** followed by sodium borohydride reduction gave an isomeric monoacetonide as a major product, which was identical with the monoacetonide-b (**6a**) obtained from 21-epilycocryptol, their identity being confirmed as the acetate (**6b**). Since 3β-OH in **6a** must be the one formed by hydride reduction of intermediate 3-ketone, diepilycocryptol is therefore serrat-14-en-3α,21β,24,30-tetraol (**3a**). The minor product of reduction was the starting monoacetonide (**13**).



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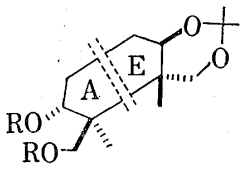


13a : R=H
13b : R=Ac

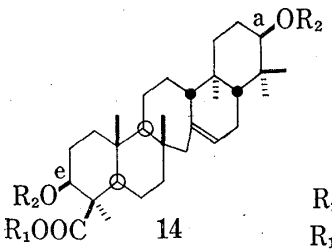
Chart 3

Serrat-14-en-3β,21α,24,30-tetraol (**1a**), the diequatorial isomer of the secondary hydroxy groups, was prepared as follows. 21-Epilycocryptol monoacetonide-b diacetate (**6b**) was oxidized with Jones' reagent after short treatment with acid and the resulting mixture of a keto-alcohol and a keto-aldehyde was reduced with sodium borohydride. Acetylation and purification of the product gave the expected tetra-ol acetate (**1b**) which was identical with lycocryptol tetraacetate obtained from natural source as confirmed by direct comparisons.

Lycernuic Acid-A and -B

Lycernuic acid-A and -B were isolated from *Lycopodium cernuum* (collected at Yakushima Island)[14] along with serratenediol, 21-episerratenediol, 21-episerratriol, and 16-oxolycoclavanol.[4] They were obtained as a mixture (mp 194—200°) of the acetates during chromatographic separation of the acetylated triterpenoid mixture prepared as before. This mixture was esterified with diazomethane and the resulting methyl ester-acetates were conveniently separated by chromatography into **14c** and **15c**. Saponification of **14c** and **15c** gave methyl lycernuate-A (**14b**), $C_{31}H_{50}O_4$, mp 240—244°, and methyl lycernuate-B (**15b**), $C_{31}H_{50}O_5$, mp 248—249°, respectively.

Methyl lycernuate-A (**14b**) formed diacetate (**14c**), mp 236—239°, whose NMR spectrum (Table I) indicated the presence of six C-methyls, and two secondary acetoxy-groups together with a methyl ester (δ 3.70). Reduction of this diacetate with lithium aluminum hydride afforded 21-episerratriol (**16a**)[12] which was characterized as its acetate (**16b**). Hence lycernuic acid-A is 3β,21β-dihydroxyserrat-14-en-24-oic acid (**14a**).



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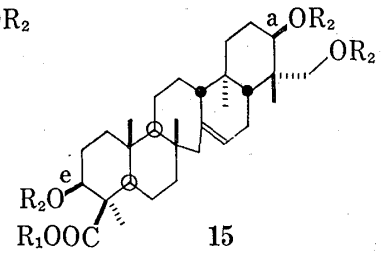

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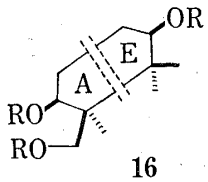

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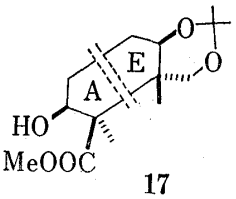
16a : R=H
16b : R=Ac



17

a : $R_1=R_2=H$
b : $R_1=Me$, $R_2=H$
c : $R_1=Me$, $R_2=Ac$

Chart 4

Methyl lycernuate-B (**15b**) formed triacetate (**15c**), mp 278—282°, whose NMR spectrum (Table I) indicated the presence of five C-methyls, two secondary and a primary acetoxy-groups, and a methyl ester (δ 3.72). Analogous hydride reduction of **15c** afforded 21-epilycocryptol (**2a**), whose identity was confirmed by direct comparison of its tetra-acetate (**2b**).

14) From the same plant collected at a different place, Inubushi, *et al.* [Y. Inubushi, T. Harayama, T. Hibino, and M. Akatsu, *Yakugaku Zasshi*, **91**, 980 (1971)] isolated serratenediol, α-onocerin, serratriol, 21-episerratriol, and 16-oxo-21-episerratriol as their acetates.

Methyl lycernuate-B (**15b**) was converted under a forced condition to an acetonide (**17**) which on lithium aluminum hydride reduction gave a diol-acetonide. The identity of this with the monoacetonide-b (**6a**) prepared from 21-epilycocryptol was confirmed by direct comparisons of its acetate (**6b**), thus the position of carboxyl group being established. Therefore lycernuic acid-B is 3β,21β,30-trihydroxyserrat-14-en-24-oic acid (**15a**).

Experimental

Unless otherwise stated, IR spectra were taken on Nujol mull, and NMR spectra were measured in $CDCl_3$ using a 60 MHz machine. For acetonides proton signals except those listed in Table II (type classification signals) were given in this section. Melting point below 300° were determined on Yanagimoto mp apparatus and those above 300° were taken by an open capillary. All organic extracts were washed with water and dried ($MgSO_4$ or K_2CO_3) before evaporation. Identities were confirmed by IR and TLC comparisons.

21-Epilycocryptol tetraacetate (2b) formed colorless needles from CH_2Cl_2–MeOH, mp 242—243°. On alkaline hydrolysis (5% KOH–MeOH) it gave **21-epilycocryptol** (**2a**) (fine prisms from DMF), mp >360°. **2a** regenerated **2b** on acetylation (Ac_2O–pyridine).

The Diacetonide (5) and the Monoacetonide-a (4) from 21-Epilycocryptol (**2a**)——i) 21-Epilycocryptol **2a** (180 mg), *p*-TsOH (20 mg), and 2,2-dimethoxypropane (1 ml) in dry acetone (9 ml) and DMF (10 ml) were heated on a water-bath for 10 min. The mixture was cooled and precipitate was collected by filtration, washed with cold *n*-hexane, and crystallized from *n*-hexane to yeild **5** (110 mg) as needles, mp 274—275°. NMR: δ 0.85(6H), 1.08(3H), 1.17(3H), 1.20(3H), 5.35(1H, m).

The filtrate, washings, and the mother liquor from **5** were combined and evaporated *in vacuo* to give a residue which was chromatographed in benzene over Florisil. Benzene eluate gave a further crop of **5** (20 mg) and CH_2Cl_2 eluate gave the monoacetonide-a **4a** (33 mg), which was acetylated with Ac_2O–pyridine. The product was taken up in ether which on evaporation yield the monoacetonide-a diacetate (**4b**) (needles from MeOH), mp 249—251°. IR: 1735 cm^{-1}. NMR: δ 0.70(3H), 0.88(3H), 0.95(3H), 1.10(3H), 1.17(3H), 2.07(3H), 2.10(3H), 4.21(2H, bs), 5.07(1H, m), 5.37(1H, m).

ii) 21-Epilycocryptol (250 mg), *p*-TsOH (50 mg), and 2,2-dimethoxypropane (10 ml) in DMF (10 ml) were heated on a water-bath for 2 hr. The product showed almost one spot corresponding to **5** on TLC. On working up the diacetonide **5** (180 mg) was isolated.

Acid Hydrolysis of the Diacetonide (**5**)——i) The diacetonide **5** (600 mg) and 50% AcOH (1 ml) in $CHCl_3$ (10 ml) and MeOH (15 ml) were heated under gentle reflux for 20 min. The mixture was poured into water and extracted with $CHCl_3$. A little precipitate when formed was removed by filtration (21-epilycocryptol). The organic extract was evaporated to dryness and the residue chromatographed over Florisil. Benzene eluate gave unchanged **5** (75 mg) and the following benzene and CH_2Cl_2 eluates gave a mixture of monoacetonides which were separated by repeating Florisil chromatography and preparative TLC. Stripping the upper zone gave the monoacetonide-b **6a** (334 mg), mp 280—300°, and the lower zone gave the monoacetonide-a **4a** (66 mg). Acetylation of **6a** with Ac_2O and pyridine yield the monoacetonide-b diacetate (**6b**) (needles from benzene), mp 254—257°. IR: 1722, 1739 cm^{-1}. NMR: δ 0.86(9H), 1.00(3H), 1.20(3H), 2.04(3H), 2.07(3H), 4.27(2H, ABq. J=12, δ_{AB}=20 Hz), 4.3—4.7[15] (1H), 5.38 (1H, m). Acetylation of **4a** gave **4b**, mp and mixed mp 249—251°.

ii) The diacetonide (100 mg) and 50% AcOH (4 ml) in $CHCl_3$ (10 ml) and MeOH (15 ml) were heated as above for 30 min. The product being isolated was **2a** as identified as its tetraacetate, mp and mixed mp 241—243°.

21-Epilycocryptol 3,24-Diacetate (**7a**)——The monoacetonide-b diacetate **6b** (200 mg) and 50% AcOH (2.6 ml) in $CHCl_3$ (10 ml) and MeOH (15 ml) were heated under reflux for 1 hr. Evaporation of the solvent *in vacuo* left a solid which was crystallized from acetone to afford **7a** (140 mg) as needles, mp 280—283°. IR: 3550, 3400, 1735, 1705 cm^{-1}.

The Tosylate (**7b**)——The compound **7a** (160 mg) and *p*-TsCl (20 mg) in pyridine (200 mg) were allowed to stand for 20 hr at room temp. The mixture was poured into ice-water and extracted with ether which was washed with 5% HCl, and evaporated to dryness. The residue in benzene–CH_2Cl_2 (1 : 1) was passed through a short column of alumina to yield **7b** (160 mg) (needles from *n*-hexane–benzene), mp 223—224°. NMR: δ 0.57(3H), 0.82(6H), 1.00(6H), 2.03(3H), 2.06(3H), 2.50(3H), 3.83(1H, m), 4.10(2H, ABq. J=10, δ_{AB}=20 Hz), 4.28(2H, ABq. J=12, δ_{AB}=19 Hz), 4.60(1H, m), 5.34(1H, m), 7.65(4H, ABq. J=9, δ_{AB}=26 Hz).

The Seco-compound (**8**)——The monotosylate **7b** (20 mg) and *t*-BuOK (50 mg) in *t*-BuOH were heated on a water-bath for 2 min, then $NaBH_4$ (50 mg) and MeOH (10 ml) were added to the mixture which was stirred for further 1 hr at room temp. After adding a drop of AcOH, the mixture was poured into water, extracted with CH_2Cl_2 and the extract evaporated to yield **8a** as a solid (IR: 887 cm^{-1}). Acetylation of

15) Overlapped with type classification signals.

this with Ac_2O (2 ml) and pyridine (4 ml) and purification of the product by passing through a short column of alumina yielded **8b** (20 mg) (needles from *n*-hexane), mp 182—186°. IR: 1739, 890 cm^{-1}. NMR: δ 0.74(3H), 0.88(6H), 1.01(3H), 1.78(3H, bs), 2.07(9H), 4.05(2H, t. J=5 Hz), 4.28(2H, ABq. J=12, δ_{AB}=19 Hz), 4.53(1H, m), 4.83(2H, bs), 5.37(1H, m).

The Keto-tosylate (9)——To a stirred solution of the tosylate **7b** (140 mg) in acetone was added Jone's reagent (1 ml) at 5° during 7 min and the mixture was kept for further 3 min at room temp., then poured into water and extracted with ether. The ethereal extract was evaporated to dryness and the residue in benzene–CH_2Cl_2 (5: 1) passed through alumina. Crystallization of the eluate from diisopropyl ether–CH_2Cl_2 gave **9** (74 mg) as colorless needles, mp 236—238°. IR: 1735, 1710, 1600 cm^{-1}. NMR: δ 0.80(3H), 0.84 (3H), 0.88(3H), 1.00(3H), 1.05(3H), 2.05(3H), 2.07(3H), 3.80(3H), 4.27(2H, ABq. J=12, δ_{AB}=19 Hz), 4.28 (2H, ABq. J=10, δ_{AB}=31 Hz), 4.60(1H, m), 5.30(1H, m), 7.60(4H, ABq. J=8, δ_{AB}=25 Hz).

The mother liquors from **9** and CH_2Cl_2 eluate were combined and treated again with Jone's reagent. Working up as above, further crop of **9** (50 mg) was obtained.

LAH Reduction of the Keto-tosylate (9)——The ketotosylate **9** (105 mg) and LAH (300 mg) in tetrahydrofurane (THF) (50 ml) were heated under reflux for 4 hr, then allowed to stand for 20 hr at room temp. After addition of a few drops of water, the mixture was filtered and the residue washed several times with $CHCl_3$–MeOH. The combined filtrate was dried over Na_2SO_4 and evaporated to give a solid (94 mg) which showed three spots on TLC and was separated by preparative TLC into 4 zones: the first zone gave a compound-A (**10a**; 21 mg), the second zone gave a mixture of A and B (30 mg) in ratio of *ca.* 2: 1, the third zone gave a compound-B (**11a**; 19 mg), and the fourth zone gave a compound-C (**1a**; 5 mg). Each compound was acetylated by Ac_2O and pyridine and purified by passing the product through a short column of alumina. The compound-A yielded the oxetane-acetate (**10b**) (needles from CH_2Cl_2–MeOH), mp 203—206°. IR: 1735 cm^{-1}. NMR: δ 0.85(6H), 0.97(3H), 1.00(3H), 1.37(3H), 2.04(3H), 2.07(3H), 4.06 (1H, d. J=6 Hz), 4.29(2H, ABq. J=12, δ_{AB}=19 Hz), 4.3—4.8(2H), 5.43(1H, m). The compound-B yielded an acetate of mp 232—239° (needles from MeOH), whose IR (in $CHCl_3$), and TLC were identical with serratriol triacetate (**11b**) (lit.[12] mp 245—247°). The compound-C and its acetate gave spots identical with those of lycocryptol (**1a**) and its tetraacetate (**1b**) respectively, on TLC.

Diepilycocryptol tetraacetate (**3b**) formed colorless needles from CH_2Cl_2–MeOH, mp 241—243°. On alkaline hydrolysis (5% KOH–MeOH) it afforded **diepilycocryptol** (**3a**). **3a** regenerated **3b** on acetylation (Ac_2O–pyridine).

Diepilycocryptol Diacetonide (12)——Diepilycocryptol (**3a**; 40 mg) and *p*-TsOH (20 mg) in 2,2-dimethoxypropane (20 ml) and DMF (20 ml) were heated under gentle reflux for 2 hr. A solid $NaHCO_3$ (20 mg) was added to the mixture and the solvent was evaporated to dryness. The residue was chromatographed in *n*-hexane–benzene over Florisil, and the column eluted first with *n*-hexane, then with benzene. The first *n*-hexane eluate was discarded. Following benzene eluate gave **12** (38 mg) (needles from MeOH), mp 277—280°. NMR: δ 0.82(3H), 0.83(3H), 1.01(3H), 1.13(3H), 1.18(3H), 5.36(1H, m).

Acid Hydrolysis of the Diacetonide (12)——i) The diacetonide **12** (28 mg) and 5% AcOH (0.75 ml) in $CHCl_3$ (5 ml) and MeOH (7.5 ml) were stirred for 2 hr at room temp., then poured into water. Extraction with $CHCl_3$ and evaporation of the solvent from the extract gave a solid which was chromatographed over Florisil. Elution with benzene gave unchanged **12**; further elutions with CH_2Cl_2–MeOH gave the monoacetonide (**13a**; 19 mg) (plates from CH_2Cl_2–MeOH), mp 298—302°. IR: 3400 cm^{-1}. NMR: δ 0.83(3H), 0.85(3H), 0.86(3H), 1.08(3H), 1.20(3H), 3.70(1H, m), 3.73(2H, ABq. J=11, δ_{AB}=12 Hz), 5.36(1H, m).

ii) On heating the diacetonide (**12**) with 5% AcOH–$CHCl_3$–MeOH for 1 hr, it regenerated diepilycocryptol (**3a**) as identified as its tetraacetate, mp and mixed mp 239—241°.

21-Epilycocryptol Monoacetonide-b Diacetate (**6b**) **from Diepilycocryptol Monoacetonide** (13)——The monoacetonide **13a** (33 mg) in acetone (50 ml) was oxidized with Jones' reagent (1 ml) at 5° for 7 min. The mixture was poured into water and extracted with ether. The extract was evaporated to give a residue which was a mixture of a keto-alcohol (major) and a keto-aldehyde (minor) as shown by IR (3500, 1705 cm^{-1}) and NMR spectra [δ 9.81 (very weak), 5.37, 3.67 (J=12, δ_{AB}=26 Hz), 1.40 (s)]. This residue was dissolved in MeOH (20 ml) and reduced with $NaBH_4$ (100 mg) at room temp. for 30 min. The product was taken up in CH_2Cl_2 which was evaporated and the residue (showed two spots on TLC) separated by preparative TLC. The major product (16 mg) obtained from upper zone was acetylated with Ac_2O and pyridine to yield the monoacetonide-b diacetate (**6b**), mp 252—255°, which was identical with the specimen obtained from 21-epilycocryptol. The minor product (5 mg) obtained from lower zone was identical, after acetylation, with the starting material (**13b**).

Lycocryptol tetraacetate (**1b**) crystallized in colorless needles from CH_2Cl_2–MeOH, mp 242—247°. On alkaline hydrolysis (5% KOH–MeOH) it gave **lycocryptol** (**1a**) (prisms from $CHCl_3$–MeOH), mp 338—344°. **1a** regenerated **1b** on acetylation (Ac_2O–pyridine).

Lycocryptol (**1**) **from 21-Epilycocryptol** (2)——The monoacetonide-b diacetate **6b** (20 mg) and conc. H_2SO_4 (1 drop) in acetone (20 ml) were stirred for 1 min at room temp. Jones' reagent (1 ml) was added to the mixture which was stirred for further 10 min and worked up as usual. The product was dissolved in MeOH (50 ml) and reduced with $NaBH_4$ (50 mg) for 1 hr at room temp., then the mixture poured into

water, and extracted with CH_2Cl_2. The solid obtained from CH_2Cl_2 extract was acetylated with Ac_2O (3 ml) and pyridine (6 ml). The crude acetate thus obtained was chromatographed over alumina and the fractions showing the same *Rf* with that of lycocryptol tetraacetate on TLC were collected, which was still contaminated with an acetonide as shown by NMR. Then, the crude acetate mixture was treated with 50% AcOH (1.2 ml) in $CHCl_3$ (5 ml) and MeOH (7.5 ml) on heating under gentle reflux for 1 hr and the product (showed two spots in ratio of 1: 1) obtained by evaporation of the solvent was chromatographed in benzene over Florisil. Crystallization of benzene eluate from MeOH afforded needles, mp 227—233°, which was identical with lycocryptol tetraacetate (**1b**).

Acetyl methyl lycernuate-A (**14c**) formed needles from *n*-hexane–acetone, mp 236—239°. IR: 1725 cm^{-1}. On alkaline hydrolysis with 5% KOH–MeOH for 2 hr, it gave **methyl lycernuate-A** (**14b**) (needles from methanol), mp 240—244°. IR: 3460, 1710 cm^{-1}. On acetylation **14b** regenerated **14c**.

LAH Reduction of Acetyl Methyl Lycernuate-A (**14c**)——Acetyl methyl lycernuate-A (**14c**; 18 mg) and LAH (25 mg) in THF (10 ml) were heated under reflux for 4 hr. Working up as usual, the product was acetylated with Ac_2O (1 ml) and pyridine (2 ml). The acetate formed was taken up in CH_2Cl_2 which was washed with 5% HCl, and evaporated to dryness. Chromatography of the residue afforded 21-episerratriol triacetate (**16**)[12] (prisms from CH_2Cl_2–MeOH), mp and mixed mp 234—237°.

Acetyl methyl lycernuate-B (**15c**) formed needles from $CHCl_3$–MeOH, mp 278—282°. IR: 1730 cm^{-1}. On alkaline hydrolysis with 5% KOH–MeOH for 2 hr, it gave **methyl lycernuate-B** (**15b**) (needles from acetone), mp 248—249°. IR: 3430, 1722, 1700 cm^{-1}; 3640, 3430, 1700 cm^{-1} in $CHCl_3$. On acetylation **15b** regenerated **15c**.

LAH Reduction of Acetyl Methyl Lycernuate-B (**15c**)——Acetyl methyl lycernuate-B (**15c**; 20 mg) and LAH (50 mg) in THF (15 ml) were heated under reflux for 3 hr. Working up as above, the product was acetylated with Ac_2O and pyridine. Crystallization of the acetate from MeOH yielded 21-epilycocryptol tetraacetate (**2b**), mp and mixed mp 234—236°.

21-Epilycocryptol Monoacetonide-b Diacetate (**6b**) **from Methyl Lycernuate-B** (**15b**)——Methyl lycernuate-B (**15b**; 40 mg) and *p*-TsOH (10 mg) in 2,2-dimethoxypropane (6 ml) and DMF (6 ml) were heated under gentle reflux for 2 hr, worked up as usual, and the product was chromatographed in benzene–CH_2Cl_2 over Florisil. Benzene–CH_2Cl_2 (1: 2) eluate gave an acetonide (**17**) which was reduced with LAH (100 mg) in THF (10 ml) for 5 hr under reflux. The crude product obtained on working up as usual was acetylated with Ac_2O and pyridine. The resulting acetate was purified by passing through a short column of Florisil and crystallized from benzene to yield needles, which was identical with the monoacetonide-b diacetate (**6b**) obtained from 21-epilycocryptol, mp and mixed mp 254—257°.