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Linear Steroid Analogues. I. Transformation of Steroid into Linear Steroid Analogues

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3β,20β-Diacetoxy-8,9-seco-5α-pregnane-8,9,11-trione (**4**) has been prepared from 3β,20β-diacetoxy-5α-pregnan-12-one (**1**) *via* keto-glycol (**3**).

Alumina catalyzed condensation of trione (**4**) furnished 3β,20β-diacetoxy-11β-hydroxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnane-8,9-dione (**5**), the structure of which was determined by chemical and physical means. The plausible stereochemistry of the compound has been proposed mainly on the basis of chemical behaviors.

In the part decade, many investigations on the modification of the steroid skeleton forming AB,[2] CD[3] seco-steroids, have been reported. Snatzke, using Ruthenium tetroxide as a facile reagent for oxidative cleavage of double bonds, published a few papers[4] on BC seco-steroids and their intramolecular condensation products taking triterpenoids and cholic acid as substrates.

For several years, we have been interested in the reactivities and physiological activities of the linear steroid analogues in the light of the category of steroids. We wish to present here the formations and the structural elucidation of some linear steroid analogues as well as their intermediate BC seco-steroid.

Formation of Cyclodecatrione (4)

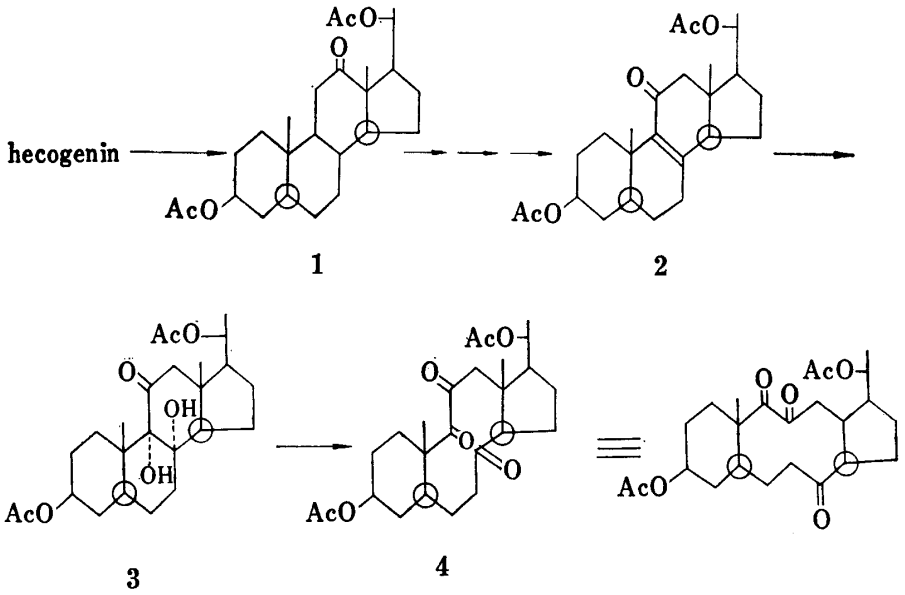

Chart 1

1) Location: *Fukushima-ku, Osaka.*
2) CIBA Ltd., Neth. Patent 6508559 (Jan. 4, 1966); M. Akhtar and S. Marsh, *J. Chem. Soc.* (*C*), **1966**, 937; M.Lj. Mihailović, Lj. Lorenc, M. Gašić, M. Rogić, A. Melera, and M. Stefanovič, *Tetrahedron*, **22**, 2345 (1966).
3) US Patent 3155729 (Nov. 3, 1964); M. Tanabe and D.F. Crowe, *J. Org. Chem.*, **30**, 2776 (1965); B. Krieger and E. Kaspar, *Chem. Ber.*, **100**, 1169 (1967).
4) G. Snatzke and H.W. Fehlhaber, *Ann. Chem.*, **663**, 123 (1963); G. Snatzke and A. Nisar, *ibid.*, **683**, 159 (1965); G. Snatzke and W. Nising, *ibid.*, **715**, 187 (1968).

3β,20β-Diacetoxy-5α-pregn-8(9)-en-11-one (**2**) was taken as a substrate, which was obtained from hecogenin *via* 3β,20β-diacetoxy-5α-pregnan-12-one (**1**).[5-7] Osmium tetroxide oxidation of this enone[8] (**2**) in ether in the presence of a trace of pyridine gave keto glycol (**3**). The hydroxy groups have probably α-configuration since the bulky osmium tetroxide reagent will attack the molecule from the less hindered α-side. Cleavage of the glycol portion of the compound (**3**) with lead tetraacetate in benzene gave cyclodecatrione (**4**) in 92% yield. This cyclodecatrione (**4**) exhibits the absorption maximum at 224 mμ (ε 1730), 287 mμ (ε 71) and 430 mμ (ε 40) reasonable for those of an α-diketone[9] in the ultraviolet (UV) spectrum and no absorption band due to a hydroxy group near the 3600—3500 cm^{-1} region in the infrared (IR) spectrum. Moreover its nuclear magnetic resonance (NMR) spectrum shows well resolved AB pattern signals corresponding to two protons of the 12-methylene moiety at τ 7.26 and τ 7.53 (J=17 cps). These facts substantiated the existence of the cyclodecatrione framework. As expected, the cyclodecatrione (**4**) is labile to acid and base.

Alumina Catalysed Condensation of Triketone (4)

The cyclodecatrione (**4**) on treatment with alumina in benzene for 2 hours gave, as a main product, a diketo-ol which was considered to be an intramolecular condensation product. Of the five theoretically possible condensation products (**5**), (**7**), (**8a**), (**8b**), (**8c**), the last three structures are extremely unlikely because of the high strain of the cylic system. Furthermore, the obtained diketo-ol could be easily dehydrated with thionyl chloride in pyridine to the conjugated ene-dione, and such reaction is not possible for **8a**, **8b**, and **8c**. For the diketo-ol (**7**), one would expect four protons in the region of active methine and methylene protons, but actually, two poorly resolved triplets integrated to two protons were found. This observation made the structure (**5**) more favorable than the structure (**7**) for the diketo-ol obtained.

The following chemical transformations confirmed the structure of the diketo-ol, the main condensation product, as **5**. Hydrogenation of **5** in acetic acid in the presence of platinum oxide gave triol (**9**) which on alkaline hydrolysis, yielded penta-ol (**10**). This penta-ol (**10**) was subjected to Criegee oxidation giving keto-aldehyde (**11**). The IR examination of **11** in diluted chloroform solution revealed only aldehyde (2710 and 1720 cm^{-1}) and six-membered ketone (1705 cm^{-1}) but no absorption near 1750—1740 cm^{-1} for a five-membered ketone. The NMR spectra shows the aldehyde proton at τ 1.77 as a singlet as expected for the tertiary aldehyde (**11**). Furthermore, acylation of **11** with trifloroacetic anhydride in pyridine gave a mixture of tri-trifloro-acetate (**12**) and di-trifloroacetate-enone (**13**). In the purification of the mixture, **12** was found to convert to **13** very easily on TLC plate and only **13** was obtained in pure state. The inclination of **12** to eliminate easily trifloroacetic acid may be regarded as a further support for the partial β-hydroxy on acyloxy-ketone structure.

In the alumina catalysed cyclisation reaction, a small amount of dehydrated products were obtained besides the diketo-ol (**5**). These by-products show three spots on TLC, the two of which were found to be identical with the products formed on treatment of the pure diketo-ol (**5**) with alumina in benzene for several hours.[10] These two products exhibit typical ene-dione absorptions in the UV spectra (*cf.* Table I) and were formulated as **6a** and **6b**. The compound (**6a**) was found to be identical with the ene-dione previously obtained on treatment of **5** with thionyl chloride in pyridine. The ene-dione (**6b**) was obtained also from **6a** on

5) Ch.R. Engel and S. Rakhit, *Can. J. Chem.*, **40**, 2153 (1962).
6) J. Fried and E. Sabo, *J. Am. Chem. Soc.*, **79**, 1130 (1957).
7) P.K. Callow and V.H.T. James, *J. Chem. Soc.*, **1956**, 4739.
8) For the sake of simplicity in this article only the names of the main functional group of the compounds under consideration were used and 3β-acetoxy, 20β-acetoxy groups were abbreviated usually which most of the compounds are conveying.
9) K. Alder, H.K. Schäfer, H. Esser, H. Krieger, and R. Reubke, *Ann. Chem.*, **593**, 23 (1955); N.J. Leonard and P.M. Mader, *J. Am. Chem. Soc.*, **72**, 5388 (1950).
10) Studies on the structure and properties of the third component will be reported elsewhere.

Table I. Physical Constants of Epimeric ene-dione (**6a**) and (**6b**)

	mp (°C)	$[\alpha]_D$	UV λ_{max}^{EtOH} mμ (ε)	IR $\nu_{C=O}^{CCl_4}$ cm^{-1}	NMR (τ) (18-CH_3)	NMR (τ) (19-CH_3)
(**6a**)	186—203[a]	− 61.4°	262 (9000)	1682	9.37	8.98
(**6b**)	174—184[a]	−119.0°	268 (9443)	1675	8.98	8.98

a) *Cf.* experimental; the footnote of the formation of the compound (**5**)

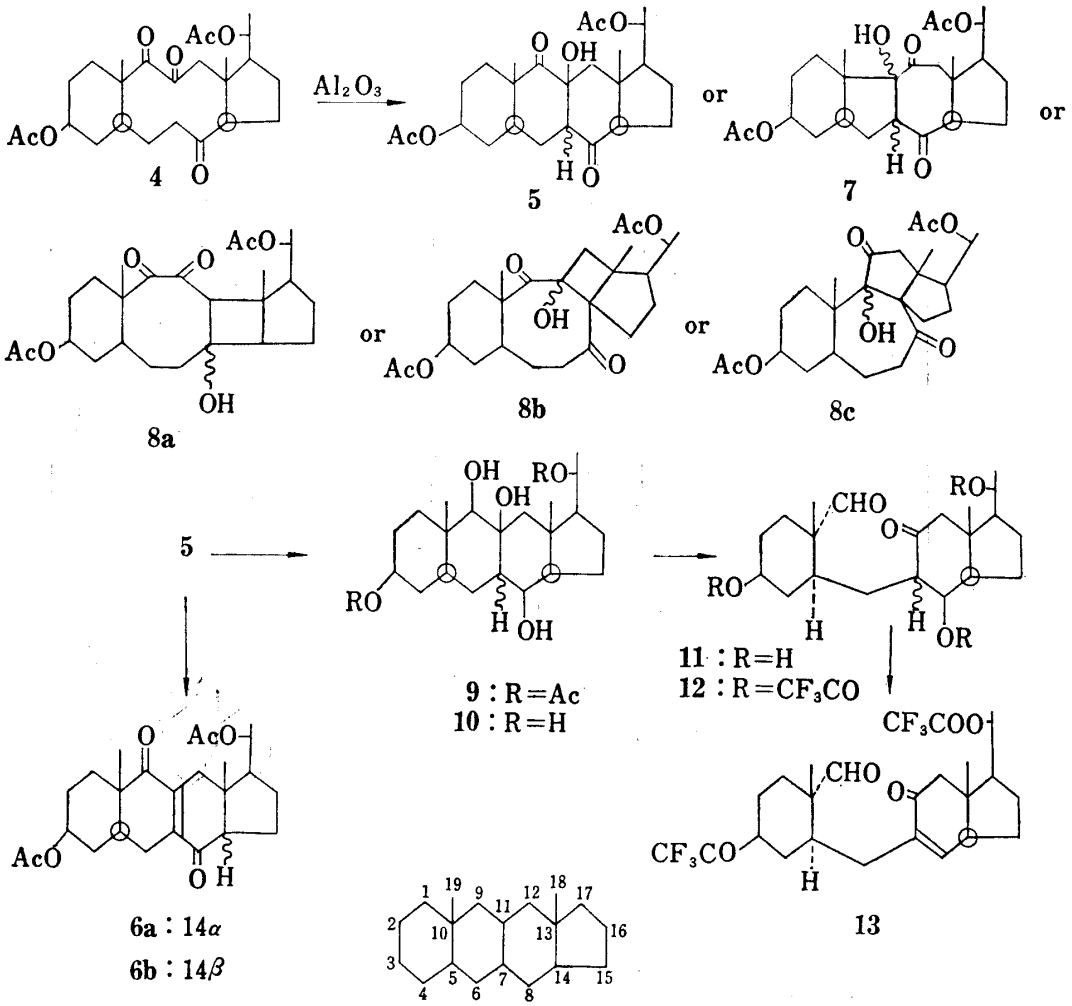

Chart 2

equilibration in alkaline medium (KOH–MeOH), and considered to be the 14β-epimer of **6a**. This is further supported by NMR spectra of these compounds (*cf.* Table I). Compared with **6a**, **6b** shows in the NMR a down field shift of 0.39 ppm for its 18 methyl protons. In the steroid series, Zürcher reported[11] a down field shift of 0.30 ppm for the 14β series as compared to the 14α. Even though no values are established for linear analogues of steroids, one would expect the same direction and similar extent of values for the shift.

Oxidation and Acylation of Triol (9)

Catalytic hydrogenation of the diketo-ol (**5**) gave as mentioned previously the triol (**9**) as a single product. This triol (**9**) on oxidation with chromium trioxide–pyridine complex

11) R.F. Zürcher, *Helv. Chim. Acta*, **46**, 2054 (1963).

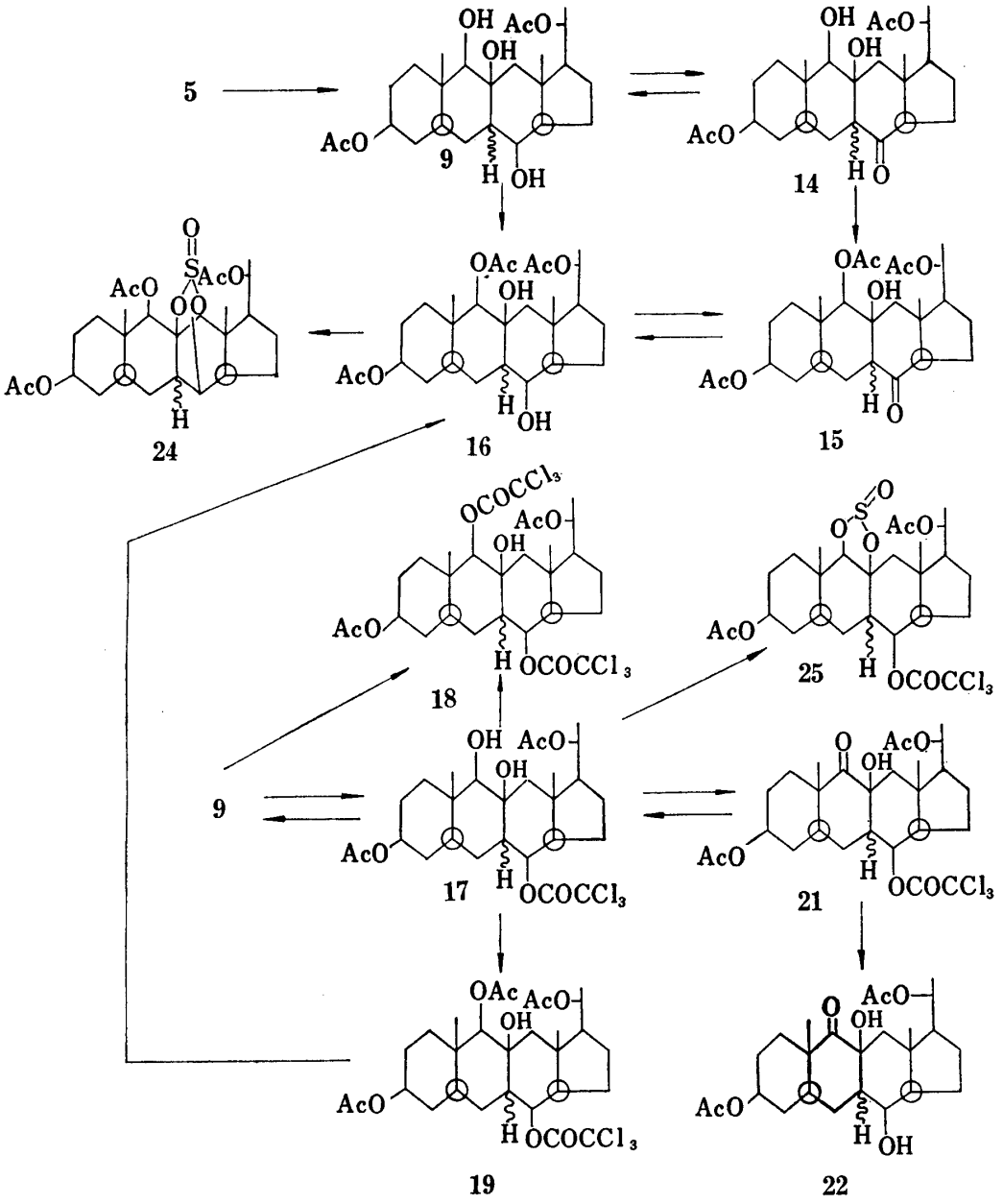

Chart 3

or with 1 equivalent mole of Jones reagent gave keto-diol (**14**). On the other hand, treatment of **9** with acetic anhydride–pyridine at room temperature yielded triol-monoacetate (**16**). And further, both acetylation of the keto-diol (**14**) with acetic anhydride-pyridine and oxidation of the triol-monoacetate (**16**) with Jones reagent afforded the same keto-diol-monoacetate (**15**). In the region characteristic of protons attached to an acetoxyl group bearing carbon, we found a singlet at τ 5.37 for **15** and τ 5.62 for **16**. One can expect a singlet only for the acetoxyl group in position 9. As a result, the hydroxyl group susceptible of selective oxidation was at position 8. This behavior of the hydroxyl groups toward oxidation and acetylation[12] suggests that the C-8 hydroxyl is axial and the C-9 hydroxyl equatorial. Treatment of the triol-monoacetate (**16**) with thionyl chloride in pyridine furnished triol-monoacetate 8,11-

12) It is generally accepted tendency among saturated secondary steroid alcohol that equatorial group is faster acetylated than axial one at the same position and reverse relation is held in case of oxidation and this is attributed to steric effects. *Cf.* L. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p. 216.

cyclic sulfite (**24**). This evidence led us to assume a 1,3-*cis*-diaxial relationship for the 8- and the 11-hydroxyl groups.

Meanwhile, the triol (**9**) on teratment with 1 equivalent mole of trichloroacetyl chloride in pyridine afforded triol-mono-trichloroacetate (**17**) in 91% yield, and with excess reagent gave triol-di-trichloroacetate (**18**). This compound (**18**) gave two signals for protons attached to the trichloroacetoxyl groups, one a sharp singlet at τ 5.53 the other one a broad signal centered at τ 4.60 ($W_{1/2}$=4.5 cps). For the triol-mono-trichloroacetate, we found a broad signal centered at τ 4.63 ($W_{1/2}$=5 cps) indicating that it corresponds to the structure (**17**). Acetylation of **17** with acetic anhyride in pyridine followed by selective hydrolysis with ammonia-methanol gave the triol-monoacetate (**16**). The given structure for these derivatives are in good accord with the physical data obtained. Oxidation of **17** with Jones reagent gave **21** and the subsequent selective hydrolysis with ammonia-methanol keto-diol (**22**) which is different from the keto-diol (**14**). The reaction of **17** with thionyl chloride-pyridine affected the formation of cyclic sulfite and gave **25**. These evidences show that the preferential attack of trichloroacetyl chloride is at the 8-hydroxyl group and that the 9- and 11-hyrodxyl groups will take a β-*cis* relationship.

It is not known why the trichloroacetylation is preferred at the more hindered axial hydroxyl group 8, but the same behavior was observed on benzoylation [13] of triol (**9**).

With these evidences and an assumption that the proton at 7 is α-oriented, for which we will give clear evidence in a following paper, one can establish the framework of the molecule, which is found to be almost plane quite similar to that of an usual steroid. Therefore, in the case of the catalytic hydrogenation of the diketo-ol (**5**) the attack of a hydrogenating agent should be expected from the less hindered α side and **5**, (in fact), gave 8β,9β,11β-triol (**9**) stereospecifically (*cf.* Chart 4).

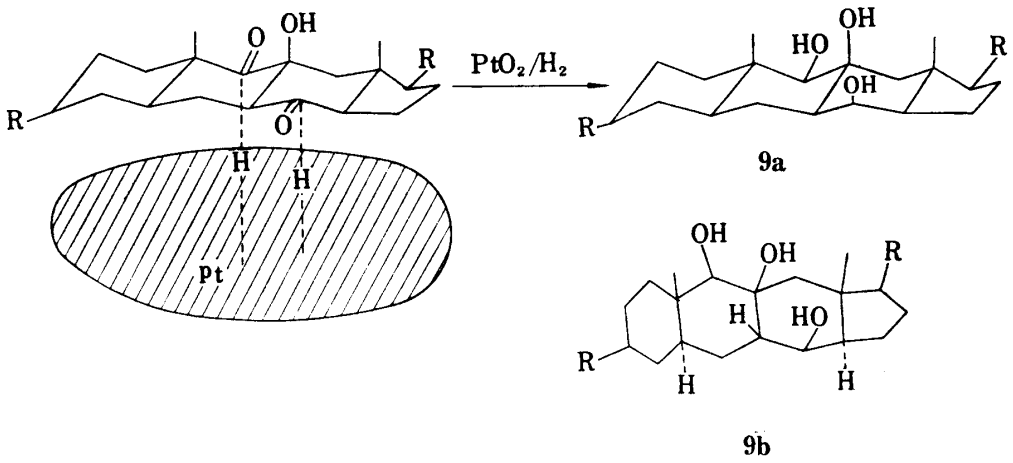

Chart 4

Although these results exclude the stereo structure (**9b**) not entirely but the structure (**9a**) seems to be much more likely and would be better explicable of the behavior of **9** toward acetylation and oxidation, and the sulfite formation. The effect of substituents on the chemical shift of the C-18 and the C-19 methyl protons in a series of similar compounds which will be presented in the following paper confirms that the triol (**9**) has the structure (**9a**).

13) Kakizawa (*Tetrahedron*, **21**, 3091 (1965)) reported the behavior of grayanotoxin toward acetic anhydride in pyridine, benzoyl chloride in pyridine respectively, and his findings are similar to ours in comparative case.

Experimental

Melting points were taken on a Yanagimoto Micromelting point Apparatus and are uncorrected. Optical rotations were measured in 1% EtOH–$CHCl_3$ with a Perkin Elmer Polarimeter type 141 (c=1.0—0.6, l=1 cm). Unless otherwise stated, UV spectra were recorded in 95% EtOH with a Hitachi EPE-2 spectrophotometer and IR spectra in CCl_4 by use of a Koken DS-201B spectrophotometer. NMR spectra were run in $CDCl_3$ solution with a Varian A-60 spectrometer, TMS serving as internal standard. Chemical shifts were reported in parts per million. Apparent coupling constants were obtained from the 1st order analysis. For preparative and analytical TLC, silicagel G (E. Merck Co.) was used as an adsorbent.

3β,20β-Diacetoxy-8α,9α-dihydroxy-5α-pregnan-11-one (3)——To a stirred solution of 680 mg of **2** in 20 ml of dry ether were added 570 mg of OsO_4 and 0.7 ml of pyridine. The solution was stored in the dark for 3 days and the dark brown crystals deposited were collected, washed with ether and dissolved in benzene. Into the benzene solution was bubbled H_2S gas for 30 min. Osmium sulfides appeared in the solution were filtered off and the filtrate was washed with 10% HCl, 10% Na_2CO_3 and water, dried and evaporated to dryness. The residue (620 mg) was crystallized from ether–pentane affording 560 mg of **3**, (yield: 81%), mp 194—195.5°. $[\alpha]_D^{23.5}$ −30.0°. IR ν_{max} cm^{-1}: 3450, 1733, 1244. NMR τ: 9.18 (3H, s, 18-CH_3), 8.98 (3H, s, 19-CH_3), 8.85 (3H, d, J=6 cps, 21-CH_3), 8.00 (3H, s, OAc), 7.97 (3H, s, OAc), 7.53, 7.25 (2H, AB-type d of d, J_{AB}=17 cps, 12 -CH_2–), 6.83 (1H, s, OH), 6.12 (1H, s, OH), 5.27 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_7$: C, 66.64; H, 8.50. Found: C, 66.73; H, 8.52.

3β,20β-Diacetoxy-8,9-seco-5α-pregnane-8,9,11-trione (4)——To a solution of 5.123 g of **3** in 30 ml of dry benzene was added under stirring 5.571 g (1.1 eq) of $Pb(OAc)_4$ in 30 ml of dry benzene and the mixture was stirred for 2 hr, then filtered. The filter cake was washed with benzene. The combined filtrates were washed with 5% HCl, 5% Na_2CO_3, water in order, and dried evaporated under reduced pressure. The semicrystalline yellow residue was recrystallized from ether–pentane to afford 4.84 g of (**4**) (yield: 94.5%), mp 165—172°. $[\alpha]_D^{27}$ +40.9°. IR ν_{max} cm^{-1}: 1737, 1707, 1682, 1243. UV λ_{max} mμ (ε): 244 (1730), 287 (71), 430 (40). NMR τ: 9.03 (3H, s, 18-CH_3), 8.78 (3H, s, 19-CH_3), 8.83 (3H, d, J=6 cps, 21-CH_3), 8.00 (6H, s, 3,20 AcO), 7.40, 6.67 (2H, AB-type d of d, J_{AB}=14 cps, 12-CH_2–), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{36}O_7$: C, 66.94; H, 8.09. Found: C, 67.23; H, 8.22.

3β,20β-Diacetoxy-11β-hydroxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnane-8,9-dione (5)——To a suspended solution of Al_2O_3 (25 g, Merck standardized) in 80 ml of benzene was added 3.18 g of **4** in 40 ml of benzene. The mixture was stirred at room temperature and yellow color of the solution was gradually faded then became colorless after 1.5 hr. After additional 1 hr's stirring Al_2O_3 was filtered off and washed with chloroform repeatedly. The combined filtrates were evaporated under reduced pressure. The residue was crystallized from acetone–hexane to give 2.6 g of **5**, mp 149—160°, 196—206° (dimorphous). $[\alpha]_D^{23.5}$ +9.0°. IR ν_{max}^{Nujol} cm^{-1}: 3473, 1730, 1711, 1250. UV λ_{max} mμ (ε): 298 (78). NMR τ: 9.17 (3H, s, 18-CH_3), 8.70 (3H, s, 19-CH_3), 8.85 (3H, d, J=6 cps, 21-CH_3), 7.98 (3H, s, OAc), 7.93 (3H, s, OAc), 6.78 (1H, s, C_{11}–OH), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{36}O_7$: C, 66.94; H, 8.09. Found: C, 66.74; H, 8.11. Mother liquor on TLC (ether–petroleum ether 2:1) shows 3 spots (dehydrated products) lying closely each others apart from the spot of **5**. A portion was separated by preparative TLC and two of them, the upper and the lower fractions could be isolated to give **6a** and **6b** in about a ratio of 1:2. Analytical samples were recrystallized from ether–pentane.

6a: mp[14] 186—203° (decomp.). $[\alpha]_D^{24}$ −61.4°. IR ν_{max} cm^{-1}: 1735, 1693, 1682, 1243. UV $\lambda_{max}^{Dioxane}$ mμ (ε): 262 (9000). NMR τ: 9.37 (3H, s, 18-CH_3), 8.98 (3H, s, 19-CH_3), 8.78 (3H, d, J=6 cps, 21-CH_3), 7.98 (3H, s, OAc), 7.92 (3H, s, OAc), 5.22 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.58; H, 7.91.

6b: mp[4] 174—184°. $[\alpha]_D^{23.5}$ −119.0°. IR ν_{max} cm^{-1}: 1740, 1675, 1243. UV $\lambda_{max}^{Dioxane}$ mμ (ε): 268 (9443). NMR τ: 8.98 (3H, s, 18-CH_3), 8.98 (3H, s, 19-CH_3), 8.87 (3H, d, J=7 cps, 21-CH_3), 7.97 (3H, s, OAc), 7.88 (3H, s, OAc), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.69; H, 7.93.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-$\Delta^{7(11)}$-5α,14α-pregnane-8,9-dione (6a)——Dehydration of **5** with Thionyl Chloride: To a solution of 500 mg of **5** in 5 ml of pyridine cooleed at −10° was added dropwise 0.5 ml of $SOCl_2$ and the mixture was stirred for 15 min at this temperature, then diluted with wet ether and washed with 10% HCl, 10% Na_2CO_3 and water in order, dried and evaporated. Recrystallization of the residue from ether–pentane gave **6a**, mp 184—202° the identity of which with the one formed by Al_2O_3 dehydration was made by analytical TLC and IR.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-$\Delta^{7(11)}$-5α,4β-pregnane-8,9-dione (6b)——By Equilibration with KOH–MeOH: A solution of 70 mg of **6a** and 100 mg of KOH in 4 ml of methanol was submitted to equilibration at reflux under N_2 atmosphere for 15 min. The reaction mixture was poured into ice water. After

14) Repeated recrystallization neither raised nor made sharper the melting point of these compounds but at least by following means, the homogenieties were guaranteed: elemental analysis, NMR, $[\alpha]_D$, analytical TLC.

extraction with chloroform, the organic layer was washed with water, dried and evaporated. The residue after acetylation (Ac_2O/pyridine) gave 68 mg of the mixture of **6a** and **6b**, which were separated by TLC using ether–petroleum ether (3:2) as a developing solvent to give 29 mg (40%) of **6a** and 44 mg (60%) of **6b**. Purified **6a** and **6b** obtained here were shown to be identical with the ones previously formed in Al_2O_3 dehydration by analytical TLC and IR. An equilibration using pure **6b** was done similarly as above and gave the same proportion of the mixture.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnane-8β,9β,11β-triol (9)——A solution of 2 g of **5** in 50 ml of acetic acid was hydrogenated in the presence of 1 g of prereduced platinum oxide under atmospheric pressure at room temperature for 2.5 hr After the catalyst was removed by decantation, the solution was neutralized by pouring into ice-cooled Na_2CO_3 solution. This neutralized solution was extracted with chloroform and the organic layer was washed dried and evaporated to dryness. The residue (2.05 g) was crystallized from acetone–hexane to afford 1.88 g of **9** (yield: 93%), mp 214—220°. Analytical sample was recrystallized 5 times from acetone–hexane, mp 219—221°. $[\alpha]_D^{23.5}$ +23.6°. IR $\nu_{max}^{Chloroform}$ cm^{-1}: 3528, 1720. NMR τ: 8.97 (6H, s, 18-CH_3, 19-CH_3), 8.87 (3H, d, J=7 cps, 21-CH_3), 7.98 (6H, s, 3,20-OAc), 7.62 (1H, broad s, C_8–OH), 6.89 (1H, d, J=7 cps, C_9–OH), 6.12 (1H, d, J=7 cps, C_9–H), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{40}O_7$: C, 66.34; H, 8.91. Found: C, 66.52; H, 8.91. Oxidation of the triol (**9**) with Jones reagent at −10° gave **5**.

9(8→7),8(9→11)-Diabeo-5α,7ξ,14α-pregnane-3β,8β,9β,11β,20β-pentaol (10)——A mixture of 750 mg of **9** and 750 mg of KOH in 8 ml of methanol was heated under reflux for 2 hr. After cooled the solution was carbonated by adding dry ice, then concentrated to syrup. The syrup was taken up in chloroform and the solution was washed with water dried and evaporated to give 600 mg of semicrystalline solid. This is crystallized from methanol-acetone-ether to afford 570 mg of **10**, mp 260—273°. Recrystallization from methanol–acetone gave analytical sample with mp 274—276°. $[\alpha]_D^{25}$ +7.6°. IR ν_{max}^{Nujol} cm^{-1}: 3250 (broad). *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 68.44; H, 9.85. Found: C, 68.15; H, 9.95.

1-(1-Hydroxyethyl)-4-hydroxy-5(2-formyl-2-methyl-5-hydroxycyclohexylmethyl)-7a-methylperhydroindan-6-one (11)——To a stirred solution of 80 mg of **10** in 4 ml of acetic acid was added 116 mg (1.1 eq) of $Pb(OAc)_4$ in 4 ml of the same solvent and the mixture was stirred for 3 hr at room temperature, then terminated with a small amount of aq $NaHSO_3$ solution. The reaction mixture was poured into water and extracted with chloroform. The organic layer was washed with water, dried and evaporated to dryness. The residue was crystallized from acetone giving 50 mg of **11**, mp 138—142°. IR ν_{max} cm^{-1}: (taken in 1/100 mole sol. in chloroform): 3620, 2710 (–CHO), 1720 (–CHO), 1705 (6-membered-ketone). NMR (pyridine) τ: 8.95 (3H, s, 19-CH_3), 8.67 (3H, s, 18-CH_3), 8.72 (3H, d, J=6 cps, 21-CH_3), 1.77 (1H, s, CHO). *Anal.* Calcd. for $C_{21}H_{34}O_5$: C, 68.82; H, 9.35. Found: C, 68.51; H, 9.40.

Treatment of 11 with Trifluoroacetic Anhydride-Pyridine——To a cooled solution of 60 mg of **11** in 1 ml of pyridine was added under stirring 0.5 ml of trifluoroacetic anhydride and the mixture was then poured into ice–water and extracted with methylene chloride. The organic layer was washed successively with 5% HCl, 5% Na_2CO_3 and water and dried, evaporated *in vacuo*. The residue (100 mg) on TLC (methylene chloride–ethyl acetate 20:1) shows two spots (Rf=0.66, 0.75) in comparable density, which was separated by TLC to each component. The lower fraction, showing one spot on TLC, was crystallized from chloroform–ether yielding crystals of **13**, mp 160—164°. IR $\nu_{max}^{chloroform}$ cm^{-1}: 2725 (CHO), 1773 (CF_3–CO), 1724 (CHO), 1670, 1150. UV λ_{max} mμ (ε): 243.5 (12100). *Anal.* Calcd. for $C_{25}H_{30}O_6F_6$: C, 55.55; H, 5.59; F, 21.09. Found: C, 55.46; H, 5.62; F, 22.20. The higher fraction exhibits again two spots which are corresponding to the ones before separation. And one more attempted separation gives the same result. This obviously shows the conversion of **12** to **13** on TLC plate.

3β,20β-Diacetoxy-9β,11β-dihydroxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnan-8-one (14)——a) With chromium trioxide–pyridine. To a solution of 35 mg of chromium trioxide in 2 ml of pyridine was added at 0° a solution of 40 mg of **9** in 0.5 ml of the same solvent. After the reaction had been stored for 16 hr at room temperature, it was diluted with water and extracted with chloroform. The organic layer was washed with 10% HCl, 10% Na_2CO_3 and water in order and dried evaporated. The residue was recrystallized from acetone–hexane to give **14**, mp 239—243°. $[\alpha]_D^{23.5}$ +5.8°. IR ν_{max}^{Nujol} cm^{-1}: 3484, 1729, 1709, 1258. NMR τ: 9.17 (3H, s, 18-CH_3), 9.00 (3H, s, 19-CH_3), 8.83 (3H, d, J=6 cps, 21-CH_3), 8.17 (1H, s, 11-OH), 7.98 (3H, s, OAc), 7.95 (3H, s, OAc), 7.85 (1H, d, J=6 cps, C_9–OH), 6.93 (1H, d, J=6 cps, C_9–H), 5.22 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_7$: C, 66.64; H, 8.50. Found: C, 66.85; H, 8.58.

b) With Jones reagent. To a solution of 140 mg of **9** in 4 ml of purified acetone (distilled from $KMnO_4$) was added at 0—5°, 0.08 ml (1.1 eq) of Jones reagent under stirring. The mixture was stirred for 5 min at room temperature. The usual work-up gave 106 mg (yield: 73%) of crystals with mp 237—243°. This substance was shown to be identical with the one obtained in the method a) by mixture melting point and the superimposability of the IR spectrum. The keto-diol (**14**), on reduction with $NaBH_4$ in MeOH or hydrogenation with Pt/H_2 gave the original triol (**9**).

3β,9β,20β-Triacetoxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnane-8β,11β-diol (16)——A mixture of 1.0 g of **9**, 5 ml of acetic anhydride and 7 ml of pyridine was stirred for 5 min and kept over night. Work-up gave 1.15 g of **16** (yield: 90%), mp 210—224°. Recrystallization from acetone–hexane led to the analytical

sample, mp 223.5—224.5°. $[\alpha]_D^{24.5}$ +41.6°. IR $\nu_{max}^{Chloroform}$ cm^{-1}: 3594, 3534, 1744, 1725. NMR τ: 8.97 (3H, s, 18-CH_3), 8.87 (3H, s, 19-CH_3), 8.90 (3H, d, J=6 cps, 21-CH_3), 8.03 (3H, s, OAc), 7.98 (3H, s, OAc), 7.87 (3H, s, OAc), 7.52 (1H, s, C_{11}–OH), 7.17 (1H, d, J=8 cps, C_8–OH), 6.10 (1H, d, J=8 cps, C_8–OH), 5.60 (1H, s, C_9–H), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{27}H_{42}O_8$: C, 65.56; H, 8.56. Found: C, 65.85; H, 8.64.

3β,9β,20β-Triacetoxy-11β-hydroxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnan-8-one (15)——a) From **14** by acetylation.

Keto-diol (**14**) (30 mg) was acetylated with Ac_2O–pyridine to give **15** (32 mg). Recrystallization from acetone–hexane gave analytical sample with mp 283—284° (decomp.). $[\alpha]_D^{24.5}$ +28.1°. IR ν_{max}^{Nujol} cm^{-1}: 3470, 1725, 1712, 1260. NMR τ: 9.17 (3H, s, 18-CH_3), 8.92 (3H, s, 19-CH_3), 8.85 (3H, d, J=6 cps, 21-CH_3), 8.27 (1H, s, C_{11}–OH), 8.02 (3H, s, OAc), 8.00 (3H, s, OAc), 7.87 (3H, s, OAc), 5.37 (1H, s, C_9–H), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{27}H_{40}O_8$: C, 65.83; H, 8.19. Found: C, 66.02; H, 8.16.

b) From **16** by oxidation. To a cooled solution of 1.006 g of **16** in 16 ml of acetone was added 0.8 ml (1.3 eq) of Jones reagent with stirring. The mixture was stirred for 15 min at room temperature. The usual work-up gave 990 mg of **15**, mp 279—282°., which was recrystallized from acetone–hexane to afford prisms with mp 281—283°. Identification was made by mixed melting point and IR. Hydrogenation (Pt/H_2, AcOH) of **15** led to **16**.

Trichloroacetylation of 9——3β,20β-Diacetoxy-8β-trichloroacetoxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnane-9β,11β-diol (**17**): To a stirred solution of 705 mg of **9** in 7 ml of pyridine under cooling with ice-water was added 298 mg (1.05 eq) of trichloroacetyl chloride in 1 ml of pyridine. The mixture was stirred for 1 hr at 0—8° and then poured into ice-water. This was extracted with ether and the organic layer was washed with cold 5% HCl, 5% Na_2CO_3 and water in order and dried. After evaporation of the solvent 900 mg of crude product was obtained. This was chromatographed on TLC (methylene chloride–acetone 9:1) to yield 687 mg of **17**, mp 160—195° along with the recovery of 135 mg of the starting material. The yield of **17** after deduction of the starting material was 91%. Analytical sample was recrystallized from ether–pentane to give needles, mp 161—164°, 195—197° (dimorphous). $[\alpha]_D^{25}$ +4.1°. IR ν_{max} cm^{-1}: 3635, 3565, 1770, 1735, 1243. NMR τ: 9.01 (3H, s, 18-CH_3), 8.93 (3H, s, 19-CH_3), 8,87 (3H, d, J=6 cps, 21-CH_3), 7.95 (3H, s, OAc), 7.89 (3H, s, OAc), 7.23 (1H, d, J=8 cps, C_9–H), 5.22 (2H, m, $C_{3,20}$–H), 4.63 (1H, broad, s, $W_{1/2}$=5 cps, C_8–H). *Anal.* Calcd. for $C_{27}H_{39}O_8Cl_3$: C, 54.23; H, 6.57; Cl, 17.79. Found: C, 53.94; H, 6.68; Cl, 17.79.

Regeneration of Triol (9)——To a solution of 20 mg of **17** in 2 ml of methanol was added 1 ml of NH_3-methanol (60 mg/ml) and the solution was heated at 50° for 1 hr then poured into water. After extraction of the solution with chloroform the solvent was evaporated. The residue on crystallization from ether gave **9**, mp 216—220°. The identification was made by mixed melting point and IR.

3β,20β-Diacetoxy-8β,9β-di(trichloroacetoxy)-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnan-11β-ol (18)——Treatment of **9** with excess amount of the reagent (CCl_3COCl–pyridine) gave **18** exclusively, which was recrystallized from acetone–hexane to give analytical sample with mp 249—251° (decomp.). $[\alpha]_D^{25.5}$ +14.2° IR $\nu_{max}^{chloroform}$ cm^{-1}: 3606, 1765, 1725. NMR τ: 8.92 (3H, s, 18-CH_3), 8.80 (3H, s, 19-CH_3), 8.87 (3H, d, J=6 cps, 21-CH_3), 8.02 (6H, s, $C_{3,20}$–OAc), 5.53 (1H, s, C_9–H), 5.25 (2H, m, $C_{3,20}$–H), 4.63 (1H, broad s, $W_{1/2}$=4.5 cps, C_8–H). *Anal.* Calcd. for $C_{29}H_{38}O_9Cl_3$: C, 46.86; H, 5.15; Cl, 28.62. Found: C, 46.85; H, 5.11; Cl, 28.72.

3β,9β,20β-Triacetoxy-8β-trichloroacetoxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnan-11β-ol (19)——A mixture of 110 mg of **17**, 0.6 ml of acetic anhydride and 1 ml of pyridine was kept for 1 hr at room temperature. The usual work-up gave 90 mg of **19**, mp 141—146°. Recrystallization from ether–pentane furnished needles with mp 142—146°. $[\alpha]_D^{28}$ +21.7°. IR ν_{max} cm^{-1}: 3596, 1765, 1750 (sh), 1738, 1244. *Anal.* Calcd. for $C_{29}H_{41}O_9Cl_3$: C, 54.42; H, 6.48; Cl, 16.63. Found: C, 54.52; H, 6.57; Cl, 16.64.

3β,9β,20β-Triacetoxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnane-8β,11β-diol (16)——A mixture of 70 mg of **19** in 1 ml of methanol and 1 ml of NH_3-methanol (60 mg/ml) was introduced into glass tube. The tube was sealed and heated at 55—60° for 3 hr in a water bath. Then, after cooled, the tube was opened and the reaction mixture was taken up in ether. The ether solution was washed with water and dried and evaporated. The residue was crystallized from ether–pentane yielding 50 mg of **16** with mp 216—219°, which was shown to be identical with the material obtained by monoacetylation of **9** by analytical TLC and the identity of IR.

3β,20β-Diacetoxy-8β-trichloroacetoxy-11β-hydroxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnan-9-one (21)——A solution of 428 mg of **17** in 5 ml of acetone was cooled at −3° under stirring. Into the solution was added 0.26 ml (1.5 eq) of Jones reagent. After 15 min stirring at 0—5° the reaction was terminated by adding 1 ml of methanol. Work-up gave 420 mg of **21** as foams which were crystallized from ether–pentane yielding 404 mg of crystal, mp 214—217°. $[\alpha]_D^{26}$ +15.3° (MeOH). IR ν_{max} cm^{-1}: 3618, 3448, 1768, 1735, 1714, 1244. NMR τ: 8.90 (3H, s, 18-CH_3), 8.67 (3H, s, 19-CH_3), 8.85 (3H, d, J=7 cps, 21-CH_3), 7.98 (3H, s, OAc), 7.92 (3H, s, OAc), 5.18 (2H, m, $C_{3,20}$–H), 4.57 (1H, broad t, $W_{1/2}$=5 cps, C_8–H). *Anal.* Calcd. for $C_{27}H_{37}O_8Cl_3$: C, 55.34; H, 6.36; Cl, 17.85. Found: C, 55.04; H, 6.33; Cl, 17.43. Hydrogenation of **21** with Pt/H_2 in acetic acid afforded **17**. The identity was checked by comparison of IR.

3β,20β-Diacetoxy-8β,11β-dihydroxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnan-9-one (22)——A solution of 300 mg of **21** in 3 ml of methanol was treated similarly as described in the formation of **16** from **19**. Work-up gave 179 mg (yield: 79%) of **22**, which was recrystallized from ether–pentane as prisms, mp 133—137°.

$[\alpha]_D^{26.5}$ +25.0°. IR ν_{max} cm^{-1}: 3410, 1733, 1710, 1245. NMR τ: 8.95 (3H, s, 18-CH_3), 8.68 (3H, s, 19-CH_3), 8.87 (3H, d, J=6 cps, 21-CH_3), 7.98 (3H, s, OAc), 7.93 (3H, s, OAc), 5.98 (1H, d, J=6 cps, C_8–H), 5.22 (2H m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_7$: C, 66.64; H, 8.50. Found: C, 66.63; H, 8.19.

Sulfite Formation——3β,20β-Diacetoxy-8-trichloroacetoxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnane-9β,11β-diol-9,11-cyclic Sulfite (**25**): To a cooled solution of 26 mg of **17** in 1 ml of pyridine was added with stirring 5 drops of thionyl chloride. The mixture was stirred for 15 min at 0°, then taken up in ether. The solution was washed with 10% HCl, 10% Na_2CO_3 and water in order and dried evaporated. The residue was crystallized from methanol to give **25** as prisms, mp 222—233° (decomp.). $[\alpha]_D^{28.5}$ +50.8°. IR ν_{max}^{Nujol} cm^{-1}: 1761, 1723, 1252, 1199, 780. *Anal.* Calcd. for $C_{27}H_{37}O_9SCl_3$: C, 50.35; H, 5.79; Cl, 4.98; S, 16.52. Found: C, 50.64; H, 6.00; Cl, 5.07; S, 16.51.

3β,9β,20β-Triacetoxy-9(8→7),8(9→11)-diabeo-5α,7ξ,14α-pregnane-8β,11β-diol-8,11-cyclic Sulfite (24)—— Triacetate **16** (50 mg) was treated with thionyl chloride–pyridine similarly as described above and work-up gave 55 mg of sulfite (**24**), which was recrystallized from methylene chloride–ether yielding 42 mg of crystals, mp 266—269° (decomp.). $[\alpha]_D^{28.3}$ +70.9°. IR $\nu_{max}^{chloroform}$ cm^{-1}: 1730, 1022, 938, 880. *Anal.* Calcd. for $C_{27}H_{40}O_9S$: C, 59.98; H, 7.46; S, 5.93. Found: C, 59.49; H, 7.38; S, 5.97.

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