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The Aromatisation Reaction of $\Delta^{7,9(11)}$-Triterpenoids[1]

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The "anthrasteroid"-type rearrangement of bauera-7,9(11)-dienyl acetate (**1**) was reexamined and the product was proved not to be **2** but to be expressed by **6**.

The aromatisation reaction was applied for 7,9(11)-dienes (**13**, **14**, **15**, **16**) of tirucallane, lanostane, fernane, and arborane series and the same type of hydrocarbons (**17**, **18**, **19**, **20**) were obtained in good yields.

Triterpenoids of fernane and arborane groups are now proved to be diastereomeric pairs, in which the absolute configurations of the ring A are same and those of the rings C, D, and E are antipodal.[3] The relation is analogous to that of tirucallane and lanostane groups in tetracyclic triterpenes.

A novel aromatisation reaction of ring B, similar to the anthrasteroid rearrangement, of bauera-7,9(11)-dienyl acetate (**1**) by acetic acid–sulfuric acid to form a hydrocarbon (**2**), was reported by Row and Rao.[4] If the reaction is applicable for the 7,9(11)-dienes of fernane and arborane systems, further introduction of unsaturation in the ring A will lead to a direct chemical correlation of the two series.[5]

However, contrary to the expectation, the structures of the hydrocarbons formed by the migration reactions were proved not to be the products of "anthrasteroid rearrangement" but those of retropinacolinic rearrangement followed by aromatization. The reexamination carried out on **1** clearly demonstrated the structures of the products. The evidences are presented in this paper.

Bauera-7,9(11)-dienyl acetate[6] (**1**), bauera-7,9(11)-dienol (**3**), 3β-methoxybauera-7,9(11)-diene (**4**) were prepared from bauerenol[7] (**5**). The treatment of **1**, **3**, and **4** with sulfuric acid in boiling acetic acid[4] gave the same hydrocarbon (**6**), mp 145°, $[\alpha]_D + 17.8°$, which was identified with the compound (**2**), so assigned as by Row and Rao,[4] by a direct comparison with the mixed mp, $[\alpha]_D$, infrared spectra (IR), and gas–liquid chromatography (GLC). The hydrocarbon showed the absorption due to the penta-substituted benzene ring at 1608, 810, 789 cm^{-1} and at 262, 270.5, 279.5 nm in IR and ultraviolet (UV) spectra, respectively. However the compound exhibited the base peak *m/e* 363.309 (Calcd. for $C_{27}H_{29}$, 363.305) ($M^+ - 43$) corresponding to the removal of the isopropyl group from the molecule in its mass spectrum (Fig. 1) and the nuclear magnetic resonance spectrum (NMR) showed the signals of one aromatic methyl (δ 2.24), five benzylic protons (δ 2.6, 4H, δ 3.15, 1H), one ring proton (δ 6.67), and seven methyl groups (δ 0.65—1.27). Irradiation at the benzylic proton signals showed that

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[1] A part of this work was presented at the 15th Symposium on the Chemistry of Natural Products, Nagoya, October 1971, Abstracts of Papers, p. 311; preliminary communication, M. Fukuoka and S. Natori, *Tetrahedron Letters*, **1970**, 4867.

[2] Location: *Kamiyoga-1-chome, Setagaya-ku, Tokyo.*

[3] K. Nishimoto, M. Ito, S. Natori, and T. Ohmoto, *Tetrahedron*, **24**, 735 (1968).

[4] L.R. Row and C.S. Rao, *Tetrahedron Letters*, **1967**, 4845.

[5] While our works were in progress Ageta and his coworkers reported the first successful results on the correlation (H. Ageta, K. Shiojima, and Y. Arai, the 13th Symposium on the Chemistry of Natural Products, Sapporo, September 1969, Abstracts of Papers, p. 161).

[6] P. Sengupta and H.N. Khastgir, *Tetrahedron*, **19**, 123 (1963).

[7] M. Fukuoka and S. Natori, *Chem. Pharm. Bull.* (Tokyo), **20**, 974 (1972).

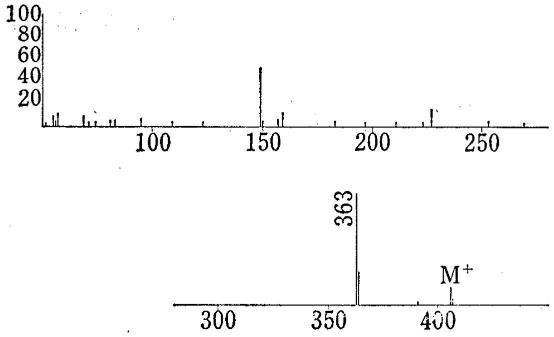

Fig. 1. The Mass Spectrum of the Hydrocarbon (6)

none of them is coupled with the secondary methyls. The nuclear Overhauser effects (NOE) between the aromatic methyl protons and the ring proton was observed (the irradiation of the former increased the area of the latter (13.2 %)), suggesting the presence of the two groups in vicinity. The structure **2** for the hydrocarbon was thus proved to be untenable.

The confirmation of the structure of the hydrocarbon was carried out as follows. Row and Rao[4] reported that the dehydration of bauera-7,9(11)-dien-3β-ol (**3**) with phosphorous pentachloride or phosphoryl chloride afforded a triene and the acid treatment of the triene gave the aromatic hydrocarbon (**2**). They proposed the structure (**7**) for the triene and assumed as the intermediate of the migration reaction (**1**→**2**). However, in the case of dihydroagnosterol (**8**), the formation of a normal retropinacolinic rearrangement product (**9**) and 2,7,9(11)-triene by the treatment with phosphorous pentachloride and phosphoryl chloride respectively was reported.[8] The treatment of **3** with phosphorous pentachloride gave a triene **10**, mp 130—132°, which had the absorption due to a transoid diene at 232.5, 239.5, 247.5 nm in its UV spectrum and was assumed to be identical with the triene[4] (**7**). However the NMR

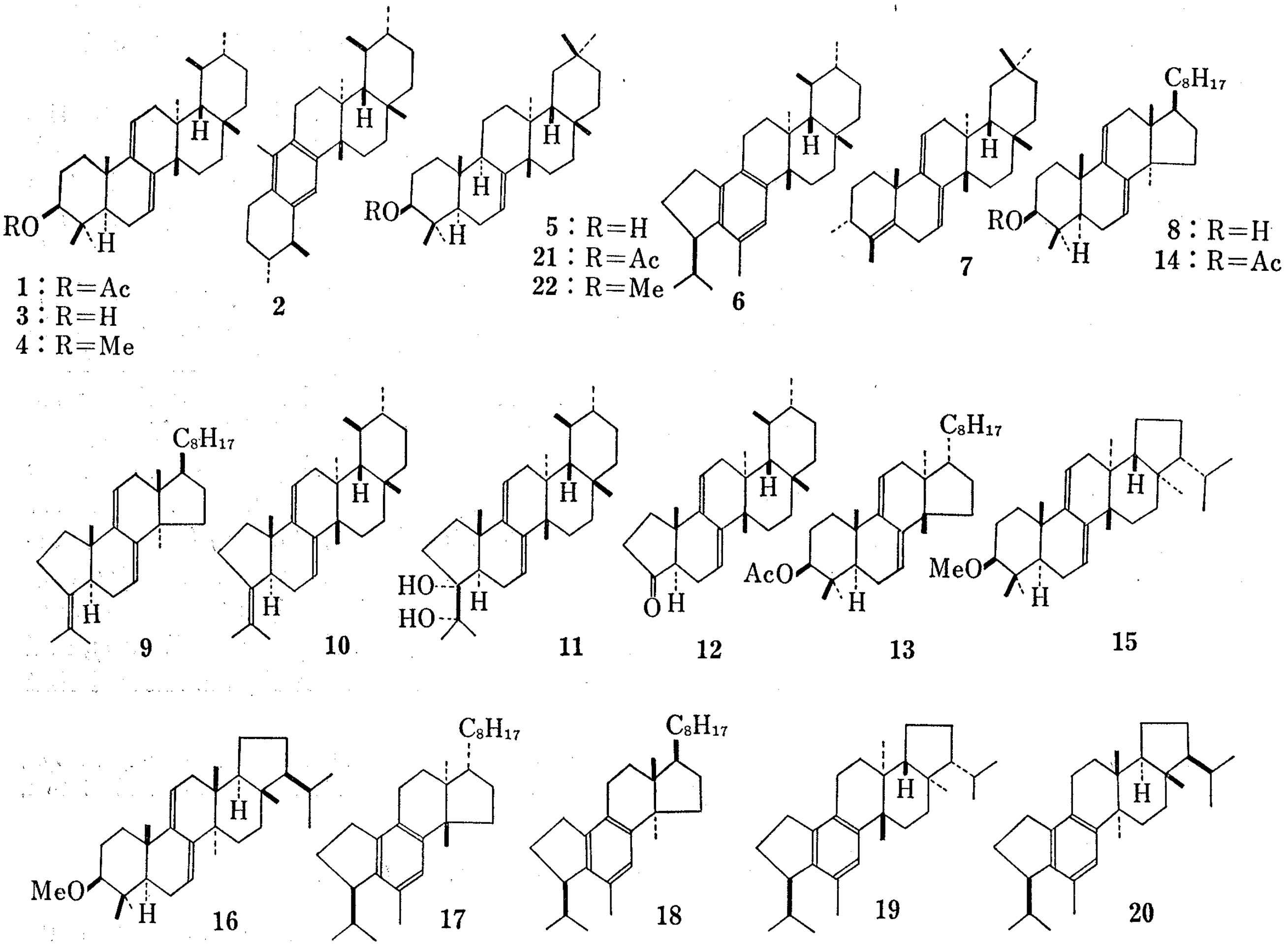

Chart 1

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[8] C. Doreé, J.F. McGhie, and F. Kurzer, *J. Chem. Soc.*, 1949, 167.

spectrum showed the signals of two allylic methyl groups at δ 1.70, 1.62 and of two vinylic protons[9] at δ 5.2, 5.4. Oxidation of **10** with osmium tetroxide gave a diol (**11**), mp 177—178°, which also showed the absorption of the diene in its UV and NMR spectra. The diol (**11**) was then treated with lead tetraacetate and a five-membered ketone (**12**) of mp 172—174°, $C_{27}H_{40}O_5$, $\nu_{max}^{CCl_4}$ 1741 cm^{-1}, and acetone (identified as the 2,4-dinitrophenylhydrazone) were obtained. These facts clearly disclosed the structures (**10**—**12**) for the products. Formation of the glycol **11** was assumed to take place at the α-side and the A/B *trans* juncture in **12** was suggested by the negative Cotton effects at 297 and 307 nm in CD curve. The acid-treatment of the triene **10** gave the aromatic hydrocarbon (**6**), which was identified with direct comparison. These facts along with the spectral properties shown above clearly verified the structure (**6**) for the hydrocarbon (the configuration of the isopropyl group will be discussed later) and the mechanisms of the reaction was assumed to be the retropinacolinic rearrangement followed by aromatisation accompanying the double methyl migration (Chart 2).

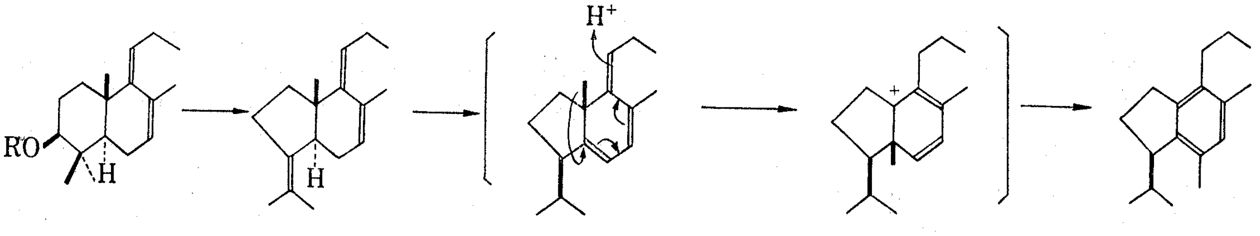

Chart 2

The same sort of aromatisation reaction accompanying methyl migration of enone system[10] and ene-diol system[11] have been known.

Now the aromatisation reaction was applied for 7,9(11)-dienes of tirucallane-lanostane series (**13**,[12] **14**[13]) and of fernane-arborane series (**15**,[3] **16**[3]) and two pairs of the diastereomeric aromatic hydrocarbons (**17**, **18** and **19**, **20**) were obtained. The physical properties supporting the structures were shown in Table I. The four compounds showed the same base peaks corresponding to M^+-43 (*m/e* 365 for **17** and **18**, 363 for **19** and **20**).[14]

Table I. Physical Properties of the Hydrocarbons

Compound	mp	$[\alpha]_{25}^{D}$ (in $CHCl_3$)	UV $\lambda_{max}^{cyclohexane}$ nm (ε)	NMR $\delta(CDCl_3)$		sec. CH_3
				arom. CH_3	arom. H	
17	141.5—142.5°	−20°	261.5, 270, 279.5 (270, 400, 300)	2.28[a]	6.72[a]	0.63, 0.90 0.90, 1.02
18	oil	+44.3°	262, 269.5, 279 (270, 390, 300)	2.29[a]	6.67[a]	0.57, 0.87 0.87, 1.02
19	157—159°	−16°	262, 270, 279.5 (272, 406, 298)	2.28[a]	6.83[a]	0.62, 0.85 0.95, 1.02
20	181.5—182.5°	+48.5°	262, 270, 279.5 (266, 380, 298)	2.29[a]	6.81[a]	0.57, 0.87 1.01, 1.06

a) w/2: 4 Hz

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[9] These signals were observed in **1**, **3**, and **4** as shown in "Experimental".

[10] Y. Sato, A. Mizuguchi, S. Tanaka, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **13**, 393 (1965); P. Bey, F. Lederer, and G. Ourisson, *ibid.*, **13**, 1138 (1965); R. Bixon, D. Amar, and Y. Mazur, *Chem. Comm.*, **1965**, 138.

[11] J. Meney, Y.-H. Kim, and R. Stevenson, *Chem. Comm.*, **1970**, 1706.

[12] J.B. Barbour, R.N.E. Bennett, and F.L. Warren, *J. Chem. Soc.*, **1951**, 2540.

[13] M.J. Birchenough and J.F. McGhie, *J. Chem. Soc.*, **1949**, 2038.

[14] NOE between the aromatic methyl and the aromatic proton and the isopropyl group in **18** were observed (the increase in the area,: CH_3→H, 18.5%, CH_3→isopropyl, 8%, 12.6%).

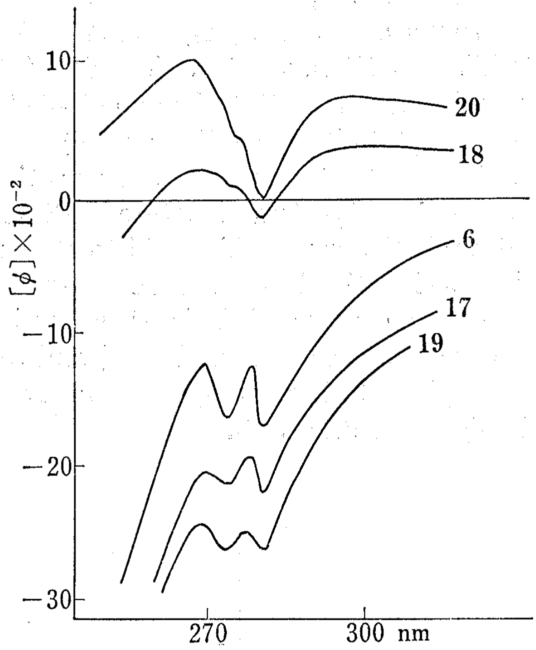

Fig. 2. The ORD Curves of the Hydrocarbons (**6**, **17**, **18**, **19**, and **20**)

The configuration of the isopropyl group in the hydrocarbons (**6, 17, 18, 19,** and **20**) was assumed to be the same, because they were formed from 3β-hydroxy-4,4-dimethyl compounds of the same configurations at the A and B rings. The ORD curves of the compounds **6, 17** and **19**, having the methyl groups at the 13α and 14β positions, showed negative Cotton effects around 260—290 nm superimposed on the negative plain curves in the back ground, while those of the compounds **18** and **20**, having the methyl groups at the 13β and 14α positions, showed the same negative Cotton effects superimposed on the positive back ground (Fig. 2). The ORD curves of the nonoxygenated benzene derivatives were shown to exhibit weak or negligible Cotton effects superimposed on a plane curves[15] and the ORD curves of 1-(*R*)-indane derivatives were reported to show the positive Cotton effects at *ca.* 270—280 nm.[16] The negative Cotton effects shown by the five hydrocarbons correspond to those of 1-(*S*)-indane derivatives and we propose β-orientation for the configuration of the isopropyl group in the aromatic hydrocarbons.[17]

Experimental[18]

Bauera-7,9(11)-dienol(3) and Bauera-7,9(11)-dienyl Acetate(1)——Bauerenyl acetate[7] (**21**) was oxidized with SeO_2 in AcOH to the diene[6] (**1**), mp 275°, $[\alpha]_D$ $-100°$ (c=0.81, $CHCl_3$), UV λ_{max} nm (ε): 233 (16000), 239.5(17700), 247.5(11800); IR ν_{max} cm^{-1}: 1740, 1250, 818, 799; NMR δ: 0.8—1.1 ($8\times CH_3$), 2.05 (acetate-CH_3), 4.5 (1H, m), 5.2 (1H, br.t[19]), 5.4 (1H, br.t); Mass Spectrum *m/e*: 466.380 (M^+) (Calcd. for $C_{32}H_{50}O_2$, 466.381).

The alcohol (**3**) was prepared from **1**, mp 205—206°, $[\alpha]_D$ $-139.7°$ ($CHCl_3$), UV λ_{max} nm (ε): 232.5(15000), 239.5(17400), 247(10300); NMR δ: 0.7—1.1 ($8\times CH_3$), 3.5(1H, m), 5.25(1H. br.t[19]), 5.5(1H, br.t[19]). *Anal.* Calcd. for $C_{30}H_{48}O$: C, 84.84; H, 11.39. Found: C, 84.66; H, 11.26.

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15) P. Crabé and W. Klyne, *Tetrahedron*, 23, 3449 (1967); A. Yogev and Y. Mazur, *Chem. Comm.*, **1965**, 388.

16) J.H. Brewster and J.G. Buta, *J. Am. Chem. Soc.*, **88**, 2233 (1966).

17) After our preliminary communication[1] we supplied the samples of the aromatic hydrocarbons (**6, 17, 19, 20**) to Dr. G. Snatzke, Bonn University, according to his request. He expected the contribution from the rings C, D, E should show one sign for **6, 17, 19,** and the opposite for **20** in ^1L_b-band of the CD (G. Snatzke and P.C. Ho, *Tetrahedron*, 27, 3645 (1971); G. Snatzke and M. Kajtár, *ibid.*, **28**, 281 (1972)). Contrary to the expectation the observed CD showed nearly the same negative effects for the four compounds. This indicates that the influence of "indane part" chromophore is much larger than that of "tetralin part" and the former retains a same conformation in the four compounds (Dr. G. Snatzke, private communication).

18) Melting points were measured in a Yanagimoto mp apparatus and are uncorrected. UV spectra were determined in cyclohexane solution and IR spectra in KBr discs unless otherwise specified. NMR spectra were measured in $CDCl_3$ with Me_4Si as an internal standard and chemical shifts are given in δ value (ppm). The mass spectra were determined on a JEOL 01SG-2 High Resolution Mass Spectrometer with direct inlet system. The optical rotatory dispersion (ORD) and circular dichroism (CD) curves were measured on a Nihon Bunko ORD-UV5. At each stage of the separation and purification, thin-layer chromatography (TLC) and GLC were adopted for monitorring the purity of the specimen. For thin-layer plates Kieselgel HF_{254} was used. Gas chromatography was carried out on 1.5% SE-30, or 1.5% OV-17 at 250° in a Hitachi F6D gas chromatograph.

19) broad triplet-like.

Bauera-7,9(11)-dienyl Methyl Ether (4)——To the refluxing solution of baueranol (2.0 g) (5) and K (3.0 g) in anhyd. benzene (100 ml), was added the solution of MeI (4.0 ml) in anhyd. benzene (50 ml) for a period of 1 hr and the mixture was refluxed for 3 hr. The excess K was decomposed with MeOH and the reaction mixture was washed with water. The residue from the benzene layer was dissolved in hexane and passed through a column of silica-gel (30 g). Recrystallization from CH_2Cl_2–MeOH afforded bauerenyl methyl ether (22), mp 216—217°, $[\alpha]_D$ ±0° ($CHCl_3$). NMR δ: 0.75—1.1 ($8\times CH_3$), 3.41 (3H, s), 2.73 (1H, q, J=11, 4.5 Hz), 4.45 (1H, m). *Anal.* Calcd. for $C_{31}H_{52}O$: C, 84.48; H, 11.89. Found: C, 84.65; H, 11.88.

Oxidation of 22 with SeO_2 in the boiling AcOH for 1.5 hr afforded the diene (4), mp 197°, $[\alpha]_D$ −116° ($CHCl_3$), UV λ_{max} nm (ε): 232.5(15900), 239.5(17500), 247.5(11500); NMR δ: 0.75—1.1 ($8\times CH_3$), 3.40 (3H, s), 5.25(1H, br.t[19]), 5.47(1H, br.t[19]). *Anal.* Calcd. for $C_{31}H_{50}O$: C, 84.86; H, 11.49. Found: C, 84.81; H, 11.23.

Aromatisation of Bauera-7,9(11)-diene Derivatives (**3**, **1**, **4**) **with Sulfuric Acid**——To a solution of **3** (96.9 mg) in AcOH (22 ml) was added conc. H_2SO_4 (1.75 ml) and the mixture was refluxed for 2 hr. The reaction mixture was diluted with water and extracted with benzene. The benzene layer was washed with 5% $NaHCO_3$ and water, dried and evaporated. The residue was applied on preparative layer chromatography (Kieselgel HF_{254}) using hexane as the developer. The main fraction (85 mg) was recrystallized from CH_2Cl_2–MeOH to give the hydrocarbon (**6**) (59 mg), mp 145°, $[\alpha]_D$ +17.8° (c=1.037, $CHCl_3$) (lit.[4] mp 144—146°, $[\alpha]_D^{30}$ +10°), UV λ_{max} nm (ε): 262 (310), 270.5 (400), 279.5 (330), IR ν_{max} cm^{-1}: 1608, 1589, 1470, 810, 789; NMR δ: 0.55—1.3 ($7\times CH_3$), 2.24 (3H, W/2 4 Hz), 2.60 (4H, m), 3.15 (1H, m), 6.76 (1H, W/2 4 Hz). Mass Spectrum m/e: 406.3610 (M^+) (Calcd. for $C_{30}H_{46}$, 406.3599). *Anal.* Calcd. for $C_{30}H_{46}$: C, 88.60; H, 11.40. Found: C, 88.57; H, 11.17. By the same procedure the same hydrocarbon (**6**) was obtained from **1** (21 mg of **6** from 30 mg of **1**) and **4** (278 mg of **6** from 415 mg of **4**).

Retropinacolinic Rearrangement of Baueradienol (3)——To a solution of **3** (90.3 mg) in petroleum ether (20 ml) was added PCl_5 (65.3 mg) and the mixture was stirred for 40 min at 0—3°. The reaction mixture was treated as usual.[8] Recrystallization from CH_2Cl_2–MeOH gave an unstable triene (**10**) (68.5 mg), mp 130—132°, $[\alpha]_D$ −167.5° (c=1.0, $CHCl_3$) (lit.[4] mp 138—140°, $[\alpha]_D^{30}$ −150°). UV λ_{max} nm (ε): 232.5 (13000), 239.5 (13700), 247.5 (8300); NMR δ: 0.75—1.05 ($6\times CH_3$), 1.62 (3H, s), 1.70 (3H, s), 5.0—5.4 (2H, m); Mass Spectrum m/e: 406.365 (M^+) (Calcd. for $C_{30}H_{46}$, 406.360).

OsO_4 Oxidation of the Triene (**10**)——To a solution of **10** (56 mg) in anhyd. ether (6 ml) was added OsO_4 (39 mg) and the mixture was allowed to stand at room temperature for 11 days. The reaction mixture was treated as usual[8] and the benzene extract was purified by the preparative TLC and recrystallization from MeOH to give a diol (42.5 mg) (**11**), mp 177—178°, $[\alpha]_D$ −143° (c=0.65, $CHCl_3$), UV λ_{max} nm (ε): 232.5 (15000), 239 (15200), 247 (9100); IR ν_{max} cm^{-1}: 3400; NMR δ: 0.75—1.25 ($8\times CH_3$), 5.1 (1H, br.t[19]), 5.35 (1H, br.t[19]). *Anal.* Calcd. for $C_{30}H_{48}O_2$: C, 81.76; H, 10.98. Found: C, 81.94; H, 11.09.

$Pb(OAc)_4$ Oxidation of the Diol (**11**)——To a solution of **11** (32.9 mg) in AcOH (2 ml) and benzene (3 ml) was added $Pb(OAc)_4$ (68 mg) and the mixture was allowed to stand at room temperature overnight. After destroying the excess reagent with 5% $Na_2S_2O_3$, and extracting with benzene, the benzene layer was washed with 5% $NaHCO_3$ and water, dried and evaporated. The residue was applied on preparative TLC (Kieselgel HF_{254}) using benzene as the developer. The main fraction (20 mg) was recrystallized from MeOH to give a ketone (**12**), mp 172—174°, $[\alpha]_D$ −236° (c=0.50, $CHCl_3$), UV λ_{max} nm (ε): 232 (13200), 239 (14000), 247.5 (8400); IR $\nu_{max}^{ccl_4}$ cm^{-1}: 1741. NMR δ: 0.75—1.1 ($6\times CH_3$), 5.4 (2H, m); CD nm ($\Delta\varepsilon$) (cyclohexane): 297 (−3.76), 307 (−3.75).[20] Mass Spectrum m/e: 380.308 (M^+) (Calcd. for $C_{27}H_{40}O$, 380.308).

The aqueous layer was distilled and the distillate was poured into a solution of 2,4-dinitrophenylhydrazine (15 mg) and H_2SO_4 (0.03 ml) in MeOH (3 ml) to give the hydrazone (1.15 mg) of acetone, mp 125°. The identity with the authentic sample was confirmed by a mixed mp, IR and TLC.

Aromatisation of the Triene (**10**) **with Sulfuric Acid**——To a solution of **10** (12.5 mg) in AcOH (2 ml) was added conc. H_2SO_4 (0.15 ml) and the mixture was treated as described above to give the hydrocarbon (**6**), which was identified by a mixed mp, IR, and mass spectra.

The Aromatisation Reaction of Tirucalla-7,9(11)-dienyl Acetate (**13**) **and Dihydroagnosteryl Acetate** (**14**) **with Sulfuric Acid**——The acetates (**13**[12], **14**[13]) prepared by the known method[3,12,13] were treated under the same condition as described above. The hydrocarbon (**17**), mp 141.5—142.5° from CH_2Cl_2–MeOH, ORD $[\alpha]_{270}$ −510.2°, $[\alpha]_{272}$ −540.8°, $[\alpha]_{279}$ −479.5°, $[\alpha]_{282}$ −540.8°. Mass Spectrum m/e: 408.3763 (M^+) (Calcd. for $C_{30}H_{48}$, 408.3756) (*cf.* Table I). Yield, **17** (63 mg) from **13** (101 mg). The hydrocarbon (**18**), crystalline powder, ORD $[\alpha]_{270}$ +61.9°, $[\alpha]_{282}$ −26.5°; Mass Spectrum m/e: 408.3747 (M^+) (Calcd. for $C_{30}H_{48}$, 408.3756) (*cf.* Table I). Yield, **18** (220 mg) from **14** (250 mg).

The Aromatisation of 3β-Methoxyferna-7,9(11)-diene (**15**) **and 3β-Methoxy-7,9(11)-arbora-7,9(11)-diene** (**16**) **with Sulfuric Acid**——The dienes (**15**, **16**) prepared by the known method[3] gave the hydrocarbons **19** and **20** under the same condition as described above. The compound (**19**), mp 157—159° from hexane. IR ν_{max} cm^{-1}: 1608, 1580, 1470. ORD $[\alpha]_{280}$ −614.0°. Mass Spectrum m/e: 406.3611 (M^+) (Calcd. for $C_{30}H_{46}$,

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[20] The negative Cotton effect changed into positive after standing in 5% MeOH–KOH, suggesting the equilibration to the A/B *cis* isomer.

406.3599) (*cf.* Table I). Yield, **19** (58.2 mg) from **15** (95.3 mg). The compound (**20**), mp 181.5—182.5° from CH_2Cl_2–MeOH. ORD: $[\alpha]_{266}$ +209.8°, $[\alpha]_{280}$ +28.0°; Mass Spectrum *m/e*: 406.3608 (M^+) (Calcd. for $C_{30}H_{46}$, 406.3599) (*cf.* Table I). Yield, **20** (57.0 mg) from **16** (92.5 mg).

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