January 1990 Chem. Pharm. Bull. 38(1) 79—85 (1990) 79

Ozone-Oxidation Products of Triterpenoid Hydrocarbons Belonging to the Hopane and Migrated Hopane Series

Kenji SHIOJIMA, Kazuo MASUDA and Hiroyuki AGETA*

Showa College of Pharmaceutical Sciences, 5-1-8 Tsurumaki, Setagaya-ku, Tokyo 154, Japan. *Received June 24, 1989*

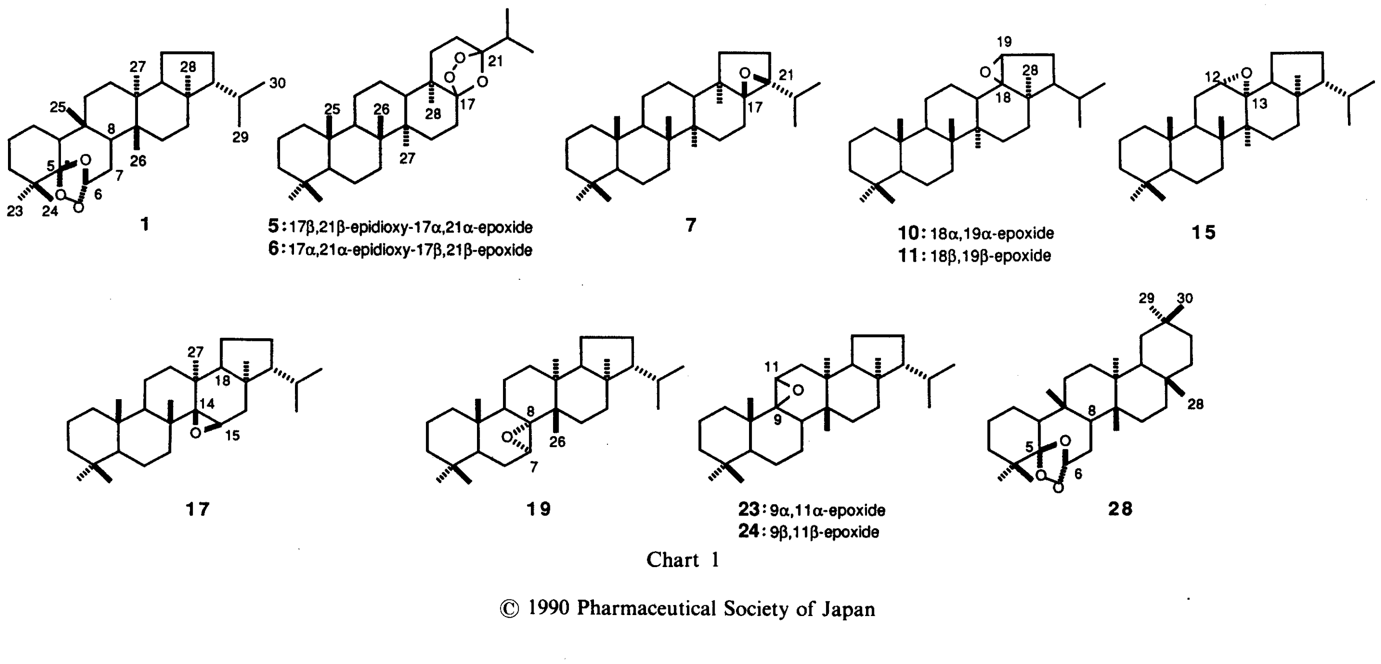
The ozone oxidation reaction of eleven triterpenoid monoenes belonging to the hopane and migrated hopane series was investigated. Under suitable reaction conditions, various reaction products including three ozonides, seven epoxides and one ketone were obtained from the eight starting materials. The reaction of glutin-5-ene was also examined for comparison.

Keywords ozone oxidation; triterpenoid hydrocarbon; hopane; migrated hopane; triterpenoid ozonide; triterpenoid epoxide; adianene ozonide; hop-17(21)-ene ozonide; glutinene ozonide

n-Hexane extraction of the fresh leaves of a fern, *Adiantum monochlamys* EATON collected in October, afforded a triterpenoid, mp 154—157 °C, as a main constituent (0.12%),[1] which was established to be adian-5-ene ozonide (1) by X-ray crystallography. Compound **1** was also isolated from the leaves of *Oleandra wallichii* (HOOK.) PRESL, and proved to be identical with the sole crystalline product of the ozone oxidation of adian-5-ene (**2**) in *n*-hexane solution.[1] Independently, another triterpenoid ozonide, gilvanol, was also isolated from *Quercus gilva* BLUME and its structure was established.[2] These findings are very interesting because fairly stable ozonides having the triterpenoid carbon skeleton are isolated as natural products and easily synthesized as crystalline products. To compare with the case of **2**, we subjected various triterpenoid monoenes belonging to the hopane and migrated hopane series and, in addition, a migrated oleanene, glutin-5-ene (**3**), to ozone oxidation under one or more reaction conditions to examine their reaction products.

Results

Oxidation of Hop-17(21)-ene (4) Although the reaction product of **4** under condition 2 (see Experimental) showed one spot on thin layer chromatography (TLC), it was found that the product is a mixture of two compounds having quite different solubilities. The less soluble compound from ether–methanol was hop-17(21)-ene ozonide A (**5**) and the more soluble one, hop-17(21)-ene ozonide B (**6**). Under condition 1 as well as 3, besides **5** and **6**, the third polar compound was obtained and identified as 17β,21β-epoxyhopane (**7**) by comparison with the authentic sample.[3] The mass spectra (MS) of **5** and **6** showed the molecular ions at m/z 458.3739 and 458.3744 (M^+, $C_{30}H_{50}O_3$), respectively, and a common fragment ion at m/z 191 (base peak) (Table I and Chart 2), the latter of which is a characteristic peak of hopanes without an oxygen function at rings A and B. The stereostructures of **5** and **6** were established by comparison of their proton magnetic resonance (^{1}H-NMR) spectra with that of **4**. The signals of three methyl groups (H-23, H-24 and H-25) among the six tertiary methyl groups of **5** and **6** were very similar to those of **4**, while the signals of H-26 (**5**, Δ +0.040) and H-28 (**5**, Δ +0.174; **6**, Δ +0.167) appeared at lower field and that of H-27 (**5**, Δ −0.066; **6**, Δ −0.049) at higher field than those of **4** (Table II). The solvent shift value [$\delta(C_6D_6)$-$\delta(CDCl_3)$] of the H-28 methyl signal of **5** was also smaller than that of **6**. These findings clearly indicated that **6** has an epidioxy group on the same side (α) as the C-28 methyl group. Thus, **5** was concluded to have a 17β,21β-epidioxy-17α,21α-epoxy structure and **6** a 17α,21α-epidioxy-17β,21β-epoxy structure. Furthermore the chemical shifts of the methyl protons (H-26, H-27 and H-28) of **5** were in good agreement with



1

5: 17β,21β-epidioxy-17α,21α-epoxide
6: 17α,21α-epidioxy-17β,21β-epoxide

7

10: 18α,19α-epoxide
11: 18β,19β-epoxide

15

17

19

23: 9α,11α-epoxide
24: 9β,11β-epoxide

28

Chart 1

TABLE I. Mass Spectral Data for Triterpenoid Ozonides and Oxides

	1	**5**	**6**	**7**	**10**	**11**	**15**	**17**	**19**	**23**	**24**	**28**
M^+	458 (3)	458 (23)	458 (14)	426 (87)	426 (14)	426 (15)	426 (36)	426 (85)	426 (100)	426 (100)	426 (100)	458 (3)
M^+-CH_3	443 (7)	443 (5)	443 (4)	411 (15)	411 (10)	411 (7)	411 (7)	411 (100)	411 (45)	411 (14)	411 (32)	443 (6)
M^+-H_2O	440 (6)	440 (6)	440 (5)	408 (7)	408 (14)	408 (9)	408 (12)	408 (23)	408 (17)	408 (7)	408 (55)	440 (5)
$M^+-C_3H_7$	415 (6)	415 (7)	415 (7)									
$M^+-CH_3-H_2O$				393 (7)	393 (5)	393 (5)	393 (6)	393 (21)	393 (42)	393 (4)	393 (4)	
$M^+-C_3H_7-H_2O$				365 (8)	365 (2)	365 (3)	365 (5)	365 (13)	365 (4)	365 (1)	365 (13)	
a+H				221[a)] (20)	221[a)] (10)	221[a)] (29)						
$a-H_2$		218 (18)	218 (14)									
b−H		205 (16)	205 (18)	205[b)] (40)	205[b)] (23)	205[b)] (28)	205 (15)					
$b-H_2$		204 (14)	204 (14)	204 (17)	204 (13)	204 (23)	204 (7)					
$b-H_3$		203 (11)	203 (10)	203 (23)	203 (22)	203 (20)	203 (13)					
c−H		191 (100)	191 (100)	191 (100)	191 (100)	191 (100)	191 (100)	191 (27)				
d	317 (46)											317 (25)
$d-H_2O$	299 (25)											299 (15)
e	274 (100)											274 (100)
e−H	273 (67)											273 (26)
$e-CH_3$	259 (65)											259 (64)
$e-CH_2-CH_3$	245 (18)											245 (13)
f	231 (27)											231 (8)
g−H	205 (55)								205 (20)	205 (23)	205 (71)	205 (99)
$g-H_2$									204 (32)	204 (43)	204 (84)	
$g-H_2-CH_3$									189 (14)	189 (22)	189 (71)	
h				234 (10)	234 (33)	234 (32)	234 (97)					
$h-H_2O$					216 (27)	216 (19)	216 (10)					
i+H				221[a)] (—)	221[a)] (—)	221[a)] (—)	221 (41)					
i−H							219 (21)					
j−H				205[b)] (—)	205[b)] (—)	205[b)] (—)						
k				152 (100)								
l−H								301 (53)				
m								288 (73)				
n+H								275 (17)				
o								259 (76)				
$o-CH_3$								244 (44)				
$p+H_3$								208 (14)				
$q-H_3$									271 (48)			

Table I. (continued)

	1	5	6	7	10	11	15	17	19	23	24	28
q−H−H_2O									255 (32)	255 (4)	255 (38)	
r−H_2									259 (20)			
s−H									191 (18)			
t−H										301 (41)	301 (87)	
u										288 (23)	288 (45)	

Relative intensities are shown in parentheses. *a, b*) Total intensities of two peaks.

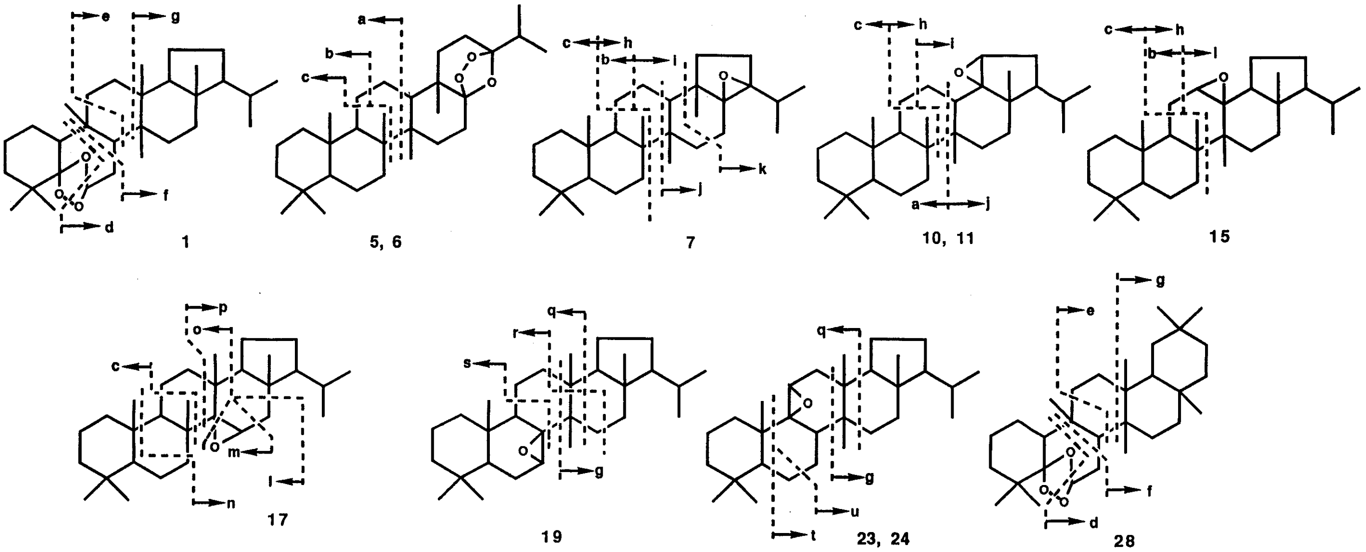


Chart 2

those of gilvanol (**8**),[2] whose stereostructure has been established by X-ray crystallography.

Oxidation of Neohop-18-ene (9) The product of oxidation of **9** under condition 3 gave more than ten spots on TLC and two epimeric epoxides, less polar **10** and more polar **11**, were isolated as crystals. Both compounds showed the molecular ions at *m/z* 426.3839 (**10**) and 426.3834 (**11**) ($C_{30}H_{50}O$), and the characteristic fragments of neohopane derivatives in their MS (Table I and Chart 2). No carbonyl or hydroxyl group absorption was observed in their infrared (IR) spectra. In the ^{1}H-NMR spectra of **10** and **11**, the chemical shifts of three methyl groups (H-23, H-24 and H-25) were very similar to those of **9**, while those of three other methyls (H-26, H-27 and H-28) were observed at remarkably lower fields (Table II). The configurations of the epoxide group in **10** and **11** were established by $CDCl_3$–C_6D_6 solvent shift and tris(6,6,7,7,8,8,8-heptafluoro-2-2-dimethyl-3,5-octanedionate)europium (Eu(fod)$_3$) shift experiments in their ^{1}H-NMR spectra.[4] The signals of H-27 (Δ −0.011) and H-28 (Δ −0.142) methyl groups of **10** in C_6D_6 were observed at a higher field, while that of the H-26 methyl group (Δ +0.277) was at a lower field than those in $CDCl_3$. On the contrary, the signal of the H-26 methyl group (Δ −0.070) of **11** was shifted to a higher field in C_6D_6 solution. The signals of three methyl groups (H-26, H-27 and H-28) of **11** in $CDCl_3$ solution with Eu(fod)$_3$ appeared at a remarkably lower field, while those of **10** in $CDCl_3$ solution with Eu(fod)$_3$ showed no shifts at all.[4] These findings clearly supported the conclusion that the structure of **10** is neohop-18α,19α-epoxide, and that of the major product, **11**, is neohop-18β,19β-epoxide.

Oxidation of Neohop-13(18)-ene (12) Compound **12** was oxidized under condition 2 to give an oily product, which showed many spots on TLC. Among them, a crystalline product having the absorption of a conjugated ketone in the IR spectrum, was obtained. The compound was identified as neohop-13(18)-en-19-one (**13**) by direct comparison with an authentic sample[5] obtained by the oxidation of **12** with $Na_2Cr_2O_7$.

Oxidation of Neohop-12-ene (14) Compound **14** gave an epoxide (**15**) almost quantitatively on oxidation under condition 1. Compound **15** showed neither carbonyl nor hydroxyl absorption in the IR spectrum, and gave a molecular ion at *m/z* 426.3854 (M^+, $C_{30}H_{50}O$) and a fragment ion at *m/z* 191 (base peak) in the MS (Table I and Chart 2). The signals of the two methyl groups (H-26 and H-28) among the six tertiary methyl groups appeared at lower field than those of **14** (Table II). The signal of H-12 was observed at δ 2.874 as a doublet (J=3.7 Hz), which indicated the bond angle between H-11α and H-12 to be 90°. Therefore, **15** was suggested to be 12α,13α-epoxyneohopane. In contrast, a 12β,13β-epoxy compound has been reported as a product of the ozone oxidation of a olean-12-en-11-one derivative.[6)]

Oxidation of Pteron-14-ene (16) Compound **16** afforded an epoxide (**17**) almost quantitatively on oxidation under condition 1. Compound **17** exhibited the molecular ion at *m/z* 426.3846 ($C_{30}H_{50}O$) and characteristic fragment peaks in the MS (Table I and Chart 2). The eight methyl signals were assigned as shown in Table II and the signal of H-18β was observed at a very low field (δ 2.314) in the ^{1}H-NMR spectrum. This implies that H-18β must be situated at a diaxial position with respect to the oxygen attached to C-14. Thus, **17** was concluded to be 14β,15β-epoxypteronane.

Oxidation of Fern-7-ene (18) Compound **18** was oxidized under condition 2 to give an epoxide (**19**) almost quantitatively. The molecular ion, *m/z* 426.3874 ($C_{30}H_{50}O$) and the characteristic fragments of fernane derivatives, were observed in the MS of **19** (Table I and Chart 2). The facts that only one methyl signal (H-27) appeared in the ^{1}H-NMR spectrum at lower field compared with the signals of **18** and that a proton signal (H-7) was observed as a double doublet (δ 3.086, $J=2.0$, 2.0 Hz) clearly suggested **19** to be 7α,8α-epoxyfernane (Table II). In addition, treatment of **19** with hot *n*-hexane–silica gel giving ferna-7,9(11)-diene (**20**) and pteron-14-en-7α-ol (**21**) also supported the 7α,8α-epoxide structure for **19**.

Oxidation of Fern-9(11)-ene (22) Although the oily product obtained by the ozone oxidation of **22** under condition 2 showed ten spots on TLC, only three compounds, 9α,11α-epoxyfernane (**23**), 9β,11β-epoxyfernane (**24**) and fern-9(11)-en-12-one (**25**) were obtained as crystals. The oxidation under conditions 1 and 3 gave products having almost the same TLC patterns as those under condition 2, with considerable amounts of the starting materials (23% and 12%, respectively). The MS of **23** and

Table II. ^{1}H-NMR Spectral Data for Triterpenoid Ozonides, Epoxides and Related Compounds

	Methyl proton signals							
	H-23	H-24	H-25	H-26	H-27	H-28	H-29, 30	Other protons
1	0.951	1.179	0.951	1.007	0.936	0.796	0.824 (d, 6.0) 0.937 (d, 6.0)	5.635 (dd, 2.5, 2.5) [H-6β] 2.885 (dd, 8.5, 5.9) [H-8α]
3	1.002	1.061	0.791	1.002	1.083	1.159	0.987 (H-29) 0.951 (H-30)	5.522 (m) [H-6]
4	0.845	0.794	0.835	0.938	1.044	0.845	0.917 (d, 6.5) 0.978 (d, 6.5)	
5	0.845	0.794	0.818	0.978	0.978	1.019	0.987 (d, 6.0) 1.014 (d, 6.0)	
6	0.850	0.801	0.821	0.928	0.995	1.012	0.976 (d, 6.0) 1.018 (d, 6.0)	
7	0.853	0.798	0.828	1.031	1.056	0.828	0.946 (d, 6.0) 1.060 (d, 6.0)	
9	0.848	0.781	0.840	0.921	1.105	1.083	0.880 (d, 6.1) 0.910 (d, 6.1)	5.216 (m) [H-19]
10	0.840	0.788	0.840	1.235	1.175	0.874	0.839 (d, 6.4) 0.852 (d, 6.4)	3.467 (s) [H-19β]
11	0.849	0.793	0.849	1.180	1.087	1.006	0.816 (d, 6.5) 0.838 (d, 6.5)	3.509 (d, 1.9) [H-19α]
13	0.861	0.795	0.826	0.925	1.187	0.891	0.903 (d, 6.4) 1.002 (d, 6.4)	
14	0.862	0.816	0.879	0.737	1.125	0.759	0.847 (d, 6.4) 0.936 (d, 6.4)	5.056 (ddd, 2.4, 2.4, 4.5) [H-12]
15	0.909	0.799	0.850	0.924	1.117	0.909	0.835 (d, 6.0) 0.939 (d, 6.0)	2.874 (d, 3.7) [H-12β]
16	0.877	0.811	0.843	1.022	1.112	0.774	0.835 (d, 6.0) 0.894 (d, 6.0)	5.283 (dd, 4.2, 3.4) [H-15]
17	0.888	0.836	0.858	1.055	1.017	0.803	0.816 (d, 6.6) 0.914 (d, 6.6)	2.999 (dd, 2.1, 2.0) [H-15α] 2.314 (dd, 15.0, 2.1) [H-18β]
18	0.843	0.877	0.742	0.995	0.906	0.742	0.829 (d, 6.6) 0.897 (d, 6.6)	5.354 (ddd, 3.7, 3.2, 3.2) [H-7]
19	0.877	0.828	0.850	0.995	1.046	0.737	0.818 (d, 6.0) 0.882 (d, 6.0)	3.086 (dd, 2.0, 2.0) [H-7β]
21	0.881	0.820	0.878	1.045	1.125	0.783	0.845 (d, 6.4) 0.903 (d, 6.4)	3.884 (dd, 2.9, 2.9) [H-7β] 5.462 (dd, 4.4, 3.2) [H-15]
22	0.857	0.892	1.052	0.735	0.823	0.759	0.830 (d, 6.4) 0.889 (d, 6.4)	5.286 (ddd, 4.4, 3.0, 3.0) [H-11]
23	0.907	0.865	0.744	0.935	0.976	0.734	0.817 (d, 6.6) 0.875 (d, 6.6)	2.981 (d, 5.9) [H-11β]
24	0.893	0.833	1.046	1.094	0.924	0.720	0.824 (d, 6.6) 0.873 (d, 6.6)	3.056 (dd, 1.9, 1.9) [H-11α]
26	1.002	0.872	0.921	0.936	0.936	0.786	0.818 (d, 6.4) 0.882 (d, 6.4)	5.247 (m) [H-1]
28	1.024	1.147	0.931	1.009	1.076	1.076	0.978 (H-29) 0.943 (H-30)	5.644 (dd, 2.2, 2.2) [H-6β] 2.858 (dd, 9.9, 3.9) [H-8α]
29	0.853	0.853	0.864	1.096	1.062	0.810	0.841 (d, 6.4) 0.911 (d, 6.4)	5.460 (dd, 4.8, 2.9) [H-15]

Multiplicity and coupling constants are shown in parentheses.

24 gave the molecular ions at *m/z* 426.3867 (**23**) and *m/z* 426.3838 (**24**) ($C_{30}H_{50}O$) and the common fragment ion at *m/z* 204 (base peak) (Table I and Chart 2). The IR spectra of both compounds showed neither hydroxyl nor carbonyl group absorption. Their ^{1}H-NMR spectra indicated the presence of eight methyl groups as shown in Table II and the proton at C-11 bearing oxygen at δ 2.891 (d, $J=5.9$ Hz) in **23** and at δ 3.056 (dd, $J=1.9$, 1.9 Hz) in **24**. Therefore, a 9α,11α-epoxide structure for **23** and a 9β,11β-epoxide for **24** were suggested. The ^{1}H-chemical shifts of methyl groups adjacent to the epoxide group also supported these structures. Compound **25** was identified by comparison with the authentic sample.[7]

Oxidation of Adian-5-ene (2) As reported earlier,[1] **2** afforded adianene ozonide (**1**) almost quantitatively on oxidation under condition 2. The MS of **1** exhibited the molecular ion at *m/z* 458.3803 ($C_{30}H_{50}O_3$) and the characteristic fragment ions of adianane derivatives (Table I and Chart 2). The stereochemistry of the ozonide can be assigned tentatively from the ^{1}H-NMR study of **1** (Table II) as follows. One signal at δ 5.635 was assigned to the proton at C-6 bearing two oxygen atoms, since it was observed as double doublets ($J=2.5$, 2.5 Hz), implying equal angles between H-6 and H-7α, and H-6 and H-7β. The other proton signal at δ 2.885 was assumed to be H-8α, which was remarkably shifted downfield by the anisotropic effect of the oxygen function at C-6 in a diaxial situation, and its splitting pattern (dd, $J=8.5$ and 5.9 Hz) suggested the stereochemical correlation between H-8α and H-7α, and H-8α and H-7β. The constants were $J(6,7\alpha)=J(6,7\beta)=2.5$ Hz, $J(8\alpha,7\alpha)=5.9$ Hz and $J(8\alpha,7\beta)=8.5$ Hz. These relationships can only be satisfied by the 5α,6α-epidioxy-5β,6β-epoxy structure (**1**).[1]

Oxidation of Adian-1(10)-ene (26) and Filic-3-ene (27) The oxidation of **26** and **27** under condition 3 gave oily products. The products revealed numerous spots on TLC, but no crystalline or stable compound was obtained.

Oxidation of Glutin-5-ene (3) Glutin-5-ene ozonide (**28**) was obtained almost quantitatively by the oxidation of **3** under condition 3. Compound **28** showed the molecular ion at *m/z* 458.3755 ($C_{30}H_{50}O_3$) and very similar fragment ions to those of **1** (Table I and Chart 2). The chemical shifts of three methyl groups (H-23, H-24 and H-25) of **28** were also very similar to those of **1** (Table II). The proton attached to C-6 bearing oxygens was observed at δ 5.644 (dd, $J=2.2$, 2.2 Hz) and another proton signal (H-8α) at δ 2.858 (dd, $J=9.9$, 3.9 Hz). Therefore, a 5α,6α-epidioxy-5β,6β-epoxy structure for **28** was suggested.

Discussion

Ozone-oxidation reaction of various kinds of triterpenoid monoenes described above can be classified into three groups according to their reaction products as follows.

A: Monoenes giving mainly epoxides: Neohop-18-ene (**9**), neohop-12-ene (**14**), pteron-14-ene (**16**), fern-7-ene (**18**).

B: Monoenes giving stable ozonide(s): Adian-5-ene (**2**), hop-17(21)-ene (**4**), glutin-5-ene (**3**).

C: Monoenes supposed to give epoxides and ozonides, but exhibiting many decomposition products on TLC because of the instability of the products: Neohop-13(18)-ene (**12**), fern-9(11)-ene (**22**), adian-1(10)-ene (**26**), filic-3-ene (**27**).

There have been many reports on the formation mechanism of ozonides, among which the mechanism proposed by Story *et al.*[8] could explain the present results very well. That is, initial addition of ozone to an olefinic bond gives a peroxyepoxide, which rapidly rearranges to the Staudinger molozonide. Opening of the molozonide may then lead to rearrangement, intramolecularly in a Bayer–Villiger fashion, to an ozonide.

In case A the transformation of the peroxyepoxide formed first is hindered sterically and the removal of the peroxy function gives an epoxide. In case B the transformation of the peroxyepoxide occurs smoothly to give an ozonide, which is unexpectedly stable. In the case of the ozone oxidation of **2**, only one ozonide (**1**) was formed by attack of ozone from the β-side of the Δ^5 double bond. This may be due to the stability of the Staudinger molozonide intermediate. If ozone attacks from the α-side of the Δ^5 double bond, the ring juncture of the AB rings of the molozonide must have the unstable *cis* configuration. On the other hand, the ozone oxidation of **4** gave the two ozonides (**5** and **6**). In this case, both the molozonides, which were formed by attack of ozone on the α and β sides of the $\Delta^{17(21)}$ double bond, are presumably stable because of their six-membered terminal structure.

It is very interesting that the ozone oxidation products of the triterpenoid monoenes belonging to the hopane and migrated hopane series vary so much according to the position of the double bond, and that the ozonides formed show quite different stability.

Experimental

Melting points were measured with a Yanagimoto microapparatus and were corrected. [α]$_D$s were observed in CHCl$_3$ solution ($c=0.34$—1.10) at 22—24 °C. ^{1}H-NMR spectra were taken at 100 MHz and/or 270 MHz by the FT method with tetramethylsilane as an internal standard. MS were recorded at 70 eV (direct inlet) and relative intensities of peaks referred to the most intense peak higher than *m/z* 100 are reported. Gas chromatography (GC) was performed on a 1 m glass column containing Chromosorb G AW DMCS with 1.4% SE-30 at 260 °C under N$_2$. Cholestane was used as an internal reference (its retention time was set at about 3.0 min), and the Rt_R values of compounds with respect to it are given.

The starting materials were obtained as described below. The MS data and the fragmentation patterns of the ozonides and oxides are given in Table I and Chart 2. The ^{1}H-NMR data of some of the starting materials and the reaction products are listed in Table II.

Hop-17(21)-ene (4) and Neohop-13(18)-ene (12) Hydroxyhopanone obtained from Dammar (Gum Dammar A) was reduced to hydroxyhopane, 1.0 g of which was treated with 4 N H$_2$SO$_4$ in AcOH–benzene at

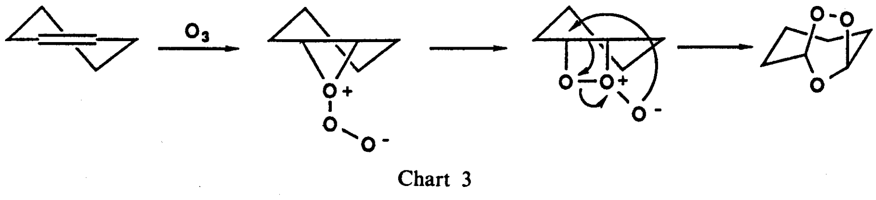


Chart 3

room temperature for 6 h. The products were separated into **12** (0.45 g) and **4** (0.31 g) by chromatography on 20% $AgNO_3$-impregnated silica gel followed by recrystallization.[7]

Neohop-18-ene (9) To a solution of **12** (1.6 g) in AcOH (60 ml) and benzene (50 ml) was added a solution of sodium dichromate (5.0 g) in AcOH (35 ml) at room temperature with shaking. The temperature was raised gradually during 40 min to 85 °C and the solution was kept at this temperature for a further 1 h. After addition of ethanol and water, the mixture was extracted with ether followed by evaporation to give a pale yellow crystalline product. The product was dissolved in *n*-hexane–benzene (7 : 3) and the solution was chromatographed on Al_2O_3 (100 g). The eluate with *n*-hexane–benzene (7 : 3) afforded white crystals (265 mg), which were recrystallized from ether–acetone to give neohop-13(18)-en-19-one (**13**),[5] mp 265—266 °C, $[\alpha]_D$ +56.1°, IR ν_{max}^{KBr} cm^{-1}: 1699, 1617. A mixture of **13** (250 mg) and sodium (1.0 g) in diethyleneglycol (50 ml) was heated at 70—80 °C and anhydrous hydrazine (1.0 ml) was added. The reaction mixture was heated at 220 °C for 4 h, then allowed to cool. Water was added to the reaction mixture, which was extracted with *n*-hexane. The *n*-hexane solution was washed with water, dried, and evaporated. The crystalline product was chromatographed successively on Al_2O_3 (20 g) with *n*-hexane and on $AgNO_3$-silica gel (10 g) with *n*-hexane to afford crystals (190 mg), which were recrystallized from ether –acetone to give **9**, mp 198.5—200 °C, $[\alpha]_D$ +18.5°. IR ν_{max}^{KBr} cm^{-1}: 815, 799. Rt_R 1.86.

Pteron-14-ene (16) A solution of **21** (90 mg, see later) in pyridine (5 ml) was added dropwise to a complex of CrO_3 (1.0 g) and pyridine (10 ml) at room temperature. The reaction mixture was kept at room temperature overnight, then treated in a usual manner and the product was chromatographed on silica gel (30 g). Elution with benzene afforded a crystalline solid (67 mg), which was recrystallized from ether–methanol to give pteron-14-en-7-one (**29**, mp 176—179 °C, $[\alpha]_D$ −104.1°. IR ν_{max}^{KBr} cm^{-1}: 1713. A mixture of **29** (75 mg) and sodium (300 mg) in diethyleneglycol (30 ml) was treated with anhydrous hydrazine (2 ml) at 70—80 °C and the reaction mixture was kept at 220 °C for 7 h, then allowed to cool. Water was added, and the whole was extracted with *n*-hexane. The *n*-hexane solution was washed with water, dried, and evaporated to give a crystalline product, which was chromatographed on Al_2O_3 (10 g). The eluate with *n*-hexane afforded a crystalline solid (55 mg), which was recrystallized from acetone to give **16**, mp 188—191 °C, $[\alpha]_D$ +2.3°. IR ν_{max}^{KBr} cm^{-1}: 826, 815. MS: M^+ 410.3923 ($C_{30}H_{50}$), Rt_R 1.99.

Neohop-12-ene (14), Fern-7-ene (18), Adian-5-ene (2) and Filic-3-ene (27) These materials were obtained from the dried leavers of *Adiantum monochlamys* EATON.[7,9]

Fern-9(11)-ene (22) **22** was obtained from the dried leaflets of *Dryopteris crassirhizoma* NAKAI.[7,10]

Adian-1(10)-ene (26) The dried rhizomes (1.24 kg) of *Arthromeris lehmanni* (METT.) CHING,[11] collected in August at Alishan in Taiwan, were extracted with *n*-hexane and the extract was chromatographed on silica gel and 20% $AgNO_3$-impregnated silica gel. The appropriate fraction was recrystallized to give **26** (550 mg), mp 204.5—205.5 °C, $[\alpha]_D$ +3.7°, Rt_R 2.42.

Glutin-5-ene (3) The *n*-hexane extract of dried fallen leaves (700 g) of *Quercus serrata* THUNB.[11] was chromatographed on silica gel. The eluate with benzene–ether (9 : 1) was recrystallized from acetone to give glutinol (923 mg), mp 210.5—211.5 °C. IR ν_{max}^{KBr} cm^{-1} 3440, 1032. Glutinol (100 mg) was oxidized with CrO_3/pyridine complex followed by Wolff-Kishner-Barton reduction to give **3**, mp 182—183 °C, $[\alpha]_D$ +57.7°, Rt_R 1.80.

General Procedure of Ozone Oxidation The starting material was dissolved in *n*-hexane and oxidized with 3% O_3/O_2 for 10 min at room temperature (condition 1), and for 1 or 3 h in ice-water bath (condition 2). The solution was also oxidized with 3% O_3/O_2 for 20 min under cooling in acetone/dry ice (condition 3).

Hop-17(21)-ene Ozonide A (5), B (6) and 17β,21β-Epoxyhopane (7) a) **4** (30 mg) was oxidized under condition 1. The *n*-hexane solution was evaporated to give a white crystalline product, which was chromatographed on silica gel (10 g). Elution with *n*-hexane–benzene (9 : 1) afforded a crystalline solid (18 mg), which was recrystallized from ether–methanol to give less soluble crystals, **5** (6 mg), mp 198—201 °C, $[\alpha]_D$ +15.5°. IR ν_{max}^{KBr} cm^{-1}: 1100, 1003, 987, and more soluble crystals, **6** (5 mg), mp 148—150 °C, $[\alpha]_D$ +75.1°. IR ν_{max}^{KBr} cm^{-1}: 1075, 1051. The subsequent fraction (4 mg) eluted with *n*-hexane–benzene (7 : 3) was recrystallized from ether–methanol to give **7**, mp 263—265 °C, $[\alpha]_D$ +48.0°. IR ν_{max}^{KBr} cm^{-1}: 1056, 1032, 1013, 998, 962, whose structure was confirmed by comparison (IR, mixed melting point) with an authentic sample.

b) **4** (200 mg) was oxidized under condition 2. The *n*-hexane solution was evaporated to give a white crystalline product, which was chromatographed on silica gel (20 g). The eluate with *n*-hexane–benzene (9 : 1) afforded crystals (180 mg), which were recrystallized from ether–methanol three times to give **5** (60 mg), mp 199—202 °C, and **6** (50 mg), mp 148—151 °C.

c) **4** (100 mg) was oxidized under condition 3. The *n*-hexane solution was treated as above to afford **5** (30 mg), mp 198—200 °C, **6** (22 mg), mp 147—150 °C, and **7** (6 mg), mp 263—265 °C.

18α,19α-Epoxyneohopane (10) and 18β,19β-Epoxyneohopane (11) **9** (50 mg) was treated under condition 3. The *n*-hexane solution was evaporated to give an oily material, which was chromatographed on silica gel (20 g). The eluate with *n*-hexane–benzene (9 : 1) afforded a crystalline solid (5 mg), which was recrystallized from ether–methanol to afford **10**, mp 218 °C, $[\alpha]_D$ −8.1°. IR ν_{max}^{KBr} cm^{-1}: 1035, 990, 970, 950. The second fraction (15 mg) eluted with the same solvent was recrystallized from ether–methanol to give **11**, mp 171—174 °C, $[\alpha]_D$ +3.0°. IR ν_{max}^{KBr} cm^{-1}: 1115, 1060, 1036, 1008.

Neohop-13(18)-en-19-one (13) **12** (50 mg) was treated under condition 3. The *n*-hexane solution was evaporated to give an oily material, which was chromatographed on silica gel (10 g). The eluate with *n*-hexane–benzene (7 : 3) afforded a crystalline material (7 mg), which was recrystallized from ether–acetone to give **13**, mp 265—266 °C, $[\alpha]_D$ +56.1°. IR ν_{max}^{KBr} cm^{-1}: 1699, 1617.

12α,13α-Epoxyneohopane (15) **14** (50 mg) was treated under condition 1. The *n*-hexane solution was evaporated to dryness, giving a crystalline product, which was purified by column chromatography on silica gel (10 g). The eluate with *n*-hexane–benzene (8.5 : 1.5) afforded crystals (43 mg), which were recrystallized from ether–methanol to give **15**, mp 218 °C, $[\alpha]_D$ +59.3°. IR ν_{max}^{KBr} cm^{-1}: 1043, 1008, 978, 934.

14β,15β-Epoxypteronane (17) **16** (20 mg) was treated under condition 1. The *n*-hexane solution was evaporated to give a white crystalline material, which was chromatographed on silica gel (20 g). The eluate with *n*-hexane–benzene (9 : 1) afforded crystals (14 mg), which were recrystallized from ether–methanol to give **17**, mp 239—242 °C, $[\alpha]_D$ +46.0°. IR ν_{max}^{KBr} cm^{-1}: 1020, 990. 968.

7α,8α-Epoxyfernane (19) **18** (100 mg) was treated under condition 1. The *n*-hexane solution was evaporated to give white crystals (93 mg), which were recrystallized from ether–ethanol to afford **19**, mp 208—211 °C, $[\alpha]_D$ −34.5°. IR ν_{max}^{KBr} cm^{-1}: 1012, 965, 945.

Ferna-7,9(11)-diene (20), 9α,11α-Epoxyfernane (23), 9β,11β-Epoxyfernane (24) and Fern-9(11)-en-12-one (25) a) **22** (200 mg) was oxidized under condition 1. The *n*-hexane solution was evaporated to give an oily material, which was chromatographed three times on silica gel (30 g). The eluate with *n*-hexane afforded the starting material (24 mg). The second fraction (3 mg) eluted with the same solvent was recrystallized from ether–acetone to give **20**, mp 201—202 °C, $[\alpha]_D$ −189.5°. IR ν_{max}^{KBr} cm^{-1}: 3030, 1633, 1614, 822, 817, 795. UV λ_{max}^{EtOH} nm (ε): 232 (12900), 239 (14900), 248 (9800). The third fraction (2 mg) eluted with *n*-hexane–benzene (9 : 1) was recrystallized from ether–methanol to give **24**, mp 256—258 °C, $[\alpha]_D$ −50.2°. IR ν_{max}^{KBr} cm^{-1}: 1097, 1040, 1010, 960. The fourth fraction (5 mg) eluted with the same solvent was recrystallized from ether–methanol to give **23**, mp 155—160°C, $[\alpha]_D$ +32.3°. IR ν_{max}^{KBr} cm^{-1}: 1010, 931. The fifth fraction (16 mg) eluted with *n*-hexane–benzene (1 : 1) was recrystallized from ether–methanol to give **25**, mp 221—223°C, $[\alpha]_D$ −31.0. IR ν_{max}^{KBr} cm^{-1}: 1672, 1611, 862.

b) **22** (200 mg) was treated under condition 2. The *n*-hexane solution was evaporated to give an oily material, which was chromatographed three times on silica gel (20 g each). The eluate with *n*-hexane–benzene (9.5 : 0.5) afforded a crystalline solid (5 mg), which was recrystallized from ether–methanol to give **24**, mp 256—258 °C. The subsequent fraction (10 mg) eluted with the same solvent was recrystallized from ether–methanol to afford **23**, mp 155—160 °C. The third fraction (10 mg) eluted with *n*-hexane–benzene (1 : 1) was recrystallized from ether–methanol to give **25**, mp 221—223 °C.

c) **22** (200 mg) was oxidized under condition 3. The *n*-hexane solution was evaporated to give an oily material, which was chromatographed four times on silica gel (30 g each). Elution with *n*-hexane afforded the starting material (46 mg). The second fraction (4 mg) eluted with *n*-hexane–benzene (9.5 : 0.5) was recrystallized from ether–methanol to give **24**, mp 256—258 °C. The third fraction (7 mg) eluted with the same solvent was recrystallized from ether–methanol to give **23**, mp 155—160 °C. The fourth fraction (20 mg) eluted with *n*-hexane–benzene (7 : 3) was recrystallized from ethermethanol to give **25**, mp 221—223 °C.

Adian-5-ene Ozonide (1) **2** (80 mg) was oxidized under condition 2. The *n*-hexane solution was evaporated to give a white crystalline material, which was chromatographed on silica gel (20 g). The eluate with *n*-hexane–benzene (9.5:0.5) afforded a crystalline solid (63 mg), which was recrystallized from ether–methanol to give **1**, mp 154—156 °C, $[\alpha]_D$ +20.1°. IR ν_{max}^{KBr} cm^{-1}: 1170, 1122, 1088, 1034, 1009.

Glutin-5-ene Ozonide (28) **3** (50 mg) was oxidized under condition 3. The *n*-hexane solution was evaporated to give a white crystalline product, which was chromatographed on silica gel (20 g). The eluate with *n*-hexane–benzene (8:2) afforded crystals (45 mg), which were recrystallized from ether–methanol to give **28**, mp 152—154 °C, $[\alpha]_D$ +11.8°. IR ν_{max}^{KBr} cm^{-1}: 1123, 1110, 1088, 1041, 1007.

Ferna-7,9(11)-diene (20) and Pteron-14-en-7α-ol (21) **19** (200 mg) dissolved in hot *n*-hexane was chromatographed on silica gel (30 g). The eluate with *n*-hexane afforded a crystalline solid (45 mg), which was recrystallized from ether–acetone to give **20**, mp 201—202 °C, whose structure was confirmed by comparison (IR, mixed melting point) with an authentic sample.7) The second fraction (115 mg) eluted with *n*-hexane–benzene (7:3) was recrystallized from ether–methanol to give **21**, mp 212—214 °C, $[\alpha]_D$ −16.5°. IR ν_{max}^{KBr} cm^{-1}: 3540, 1073, 1049, 1021.

Acknowledgement The authers are grateful to Mr. Y. Takase of this college for measurements of ^{1}H- and ^{13}C-NMR spectra and MS.

References and Notes

1) H. Ageta, K. Shiojima, R. Kamaya and K. Masuda, *Tetrahedron Lett.*, **1978**, 899.
2) H. Itokawa, Y. Tachi, Y. Yamano and Y. Iitaka, *Chem. Pharm. Bull.*, **26**, 331 (1978).
3) H. Ageta and Y. Arai, *Phytochemistry*, **22**, 1801 (1983).
4) H. Ageta, K. Shiojima and K. Masuda, *Chem. Pharm. Bull.*, **37**, 1665 (1989).
5) H. Fazakerley, T. G. Halsall and E. R. H. Jones, *J. Chem. Soc.*, **1959**, 1877.
6) R. K. Gayanov, K. O. Kim, M. P. Irismetov and M. I. Goryaev, *Zh. Org. Khim.*, **13**, 895 (1977).
7) H. Ageta, K. Shiojima and Y. Arai, *Chem. Pharm. Bull.*, **35**, 2705 (1987).
8) P. R. Story, J. A. Alford, W. C. Ray and J. R. Burgess, *J. Am. Chem. Soc.*, **93**, 3044 (1971).
9) H. Ageta, K. Iwata and S. Natori, *Tetrahedron Lett.*, **1964**, 3413; H. Ageta, K. Shiojima and Y. Arai, *Chem. Comm.*, **1968**, 1105.
10) H. Ageta, K. Iwata and S. Natori, *Tetrahedron Lett.*, **1963**, 1447.
11) Unpublished data from our laboratory.