Oxygenation of Olefinic Hydrocarbons Catalyzed by Iron(II) Acetonitrile Solvate

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Oxygenation reactions of olefins having an *endo*- or *exo*-cyclic double bond, namely, cyclohexene, norbornene, camphene, longifolene, and *ent*-kaurene, with a simple model reagent, $\text{Fe}(\text{MeCN})_6^{2+}-\text{H}_2\text{O}_2-\text{Ac}_2\text{O}$, for mono-oxygenase were investigated in connection with their biotransformations.

Keywords oxygenation; olefin; *endo*-cyclic double bond; *exo*-cyclic double bond; iron(II) acetonitrile solvate; hydrogen peroxide; model enzyme; mono-oxygenase

A large number of investigations on oxygenation reactions of olefinic hydrocarbons with metalloporphyrin-containing mono-oxygenases, in particular cytochrome P-450, and relevant synthetic model compounds¹⁾ have been made with the aim of elucidating the reaction mechanisms. This paper describes oxygenation reactions of olefins having an *endo*- or *exo*-cyclic double bond with a simple model reagent system for mono-oxygenase, $\text{Fe}(\text{AN})_6^{2+}-\text{H}_2\text{O}_2-\text{Ac}_2\text{O}$ ($\text{AN}=\text{CH}_3\text{CN}$).²⁾

Oxygenation reactions of olefins were performed by the addition of a solution of 30% H_2O_2 in AN to a solution of the olefins and the solvate $\text{Fe}(\text{AN})_6(\text{ClO}_4)_2$ ³⁾ in AN in the presence of Ac_2O at 25–30 °C.²⁾ Preliminary experiments using cyclohexene as a substrate showed that the optimum molar ratio of the olefin, H_2O_2 , and Fe^{2+} was 1 : 1 : 0.5, and 1,2-diacetoxycyclohexane (1), 1,2-dihydroxycyclohexane (2), and 3-acetoxycyclohexene (3) were obtained in the yields shown in Table I. Thus, subsequent experiments were

carried out at the ratio described above.

Oxygenation of norbornene was similarly explored as an additional example of olefins having an endocyclic double bond, to yield 2-*exo*-acetoxo-7-*anti*-acetoxynorbornane

TABLE I. Oxygenation of Cyclohexene Catalyzed by Iron(II) Acetonitrile Solvate

Run	Molar ratio of substrate : H_2O_2 : Fe^{2+}			Yield of product (mol%) ^{a)}			Recovered starting material (%)
				1 (<i>cis/trans</i>)	2	3	
1	1	1	0.1	3.4 (<i>trans</i> only)	—	—	93.3
2	1	1	0.2	12.2 (1/3.9)	4.4	1.2	77.9
3	1	1	0.5	69.8 (1/2.0)	11.9	1.2	11.8
4	1	1	1	50.6 (1/2.0)	13.9	4.9	20.2

a) Determined by GLC analysis (10% Chromosorb W, SE-30, 2 m, 80–250 °C (at 5 °C/min) and 10% Chromosorb W, DEGS, 3 m, at 150 °C).

Chart 1

(4),⁴⁾ 2-*exo*-acetoxy-7-*syn*-acetoxynorbornane (5),⁴⁾ norbornan-2-one (6), and 2-*exo*-acetamido-7-*anti*-acetoxynorbornane (7)⁵⁾ in yields of 10.8%, 15.1%, 1.0%, and 5.7%, respectively.

Oxygenations of *d,l*-camphene (8), longifolene (15), and *ent*-kaurene (20) were investigated as examples of olefins having an exocyclic double bond. Reaction of 8 (contaminated with a few percent of tricyclene) with the reagent system afforded 2-*endo*-10,10-diacetoxycamphane (9) and 2-*exo*-acetamidobornane (10) (an acid-catalyzed rearrangement product) in yields of 44.1% and 17.9%, respectively.

The structure of 9 was deduced by analysis of the proton nuclear magnetic resonance spectrum (¹H-NMR), in which the assignments were aided by off-resonance decoupling. The ¹H-NMR signal of C(2)-H in 9 has a ddd pattern centered at 1.83 ppm ($J_{C(2)-H, C(1)-H} = 3.7$ Hz, $J_{C(2)-H, C(6)-\beta H} = 1.2$ Hz, and $J_{C(1)-H, C(10)-H} = 10.0$ Hz). The coupling constants between C(2)-H and C(1)-H (3.7 Hz), and C(2)-H and C(6)- β H (1.2 Hz) suggest the structure of 9, because if C(2)-H of 9 possesses α conformation, the coupling constant between C(2)-H and C(1)-H should be smaller than 3.7 Hz and may be near zero. Compound 9 was transformed to the aldehyde 11 and the acid 12^{6,7)} by alkaline hydrolysis, and latter product 12 was also obtained from the oxidation of 11 with Jones' reagent. Analysis of the ¹H-NMR spectrum of the acid 12 [the C(2)-H signal at 1.99 ppm is a doublet ($J = 1.7$ Hz) split by coupling with the C(7) *anti*-H] showed that the C(2) carboxyl group possesses *exo* configuration. The ¹H-NMR spectrum of the epimeric acid 14, prepared by hydroboration⁸⁾ of *d,l*-camphene (8) to give the alcohol 13 followed by Jones' oxidation, showed a clear difference from that of 12, namely, the C(2)-H at 2.37 ppm has a dd signal with $J = 3.4$ Hz (coupling with C(1)-H) and 1.7 Hz (coupling with C(6) *exo*-H). These results showed that epimerization at C(2) took place in the transformation of 9 to 11 by alkaline hydrolysis.

Similar oxygenation reaction of longifolene (15) gave the diacetate 16, the imide 17, and the acetamide-acetate

18 in yields of 27.1, 3.6, and 21.2%, respectively. In the ¹H-NMR spectrum of 16, the signal of the C(7)-H was observed at 2.43 ppm, ddd, $J_{C(7)-H, C(8)-H} = 3.4$ Hz, $J_{C(7)-H, C(9)-\beta H} = 1.2$ Hz, and $J_{C(7)-H, C(13)-H} = 9.8$ Hz. The C(7)-H signal in the ¹H-NMR spectrum of 17 was found at 2.84 ppm, dd, $J_{C(7)-H, C(8)-H} = 3.7$ Hz and $J_{C(7)-H, C(9)-\beta H} = 1.7$ Hz. Thus, the structures of 16 and 17 were assigned in the same way as done in the case of 9. Though the structure of the acetamide-acetate 18 could not be elucidated by spectroscopic analysis, it may be suggested from mechanistic considerations that the acetamide group possesses *exo* configuration, because the carbonium ion lobe at the C(7) of 15 is larger at the *exo*-site than at the *endo*-site (Chart 4). Formation of the major product 16 in this reaction has implications regarding the metabolism of longifolene 19 in rabbits.⁹⁾

Oxygenation of *ent*-kaurene (20) afforded the diacetate 21, the imide 22, and the acetamide-acetate 23 in yields of 25.1%, 2.9%, and 29.2%, respectively. The structures of 21 and 22 were deduced by analyses of their ¹H-NMR spectra in the same way as described above, and the structure of 23 was based on mechanistic considerations as in the case of

18. The diacetate **21** was transformed to the aldehyde **24** by alkaline hydrolysis. Oxidation of the aldehyde **24** with Jones' reagent also afforded the acid **25**.¹⁰ Analysis of the ¹H-NMR spectra of **25** showed that the C(16)-H epimerized during the alkaline hydrolysis of **21**, as in the case of **9**.

Although we previously postulated involvement of either $\text{Fe}^{\text{IV}}(\text{OH})(\text{OAc})^{2+}$ ($=\text{Fe}^{\text{IV}}(=\text{O})(\text{OAc})^{1+}$) or $\text{Fe}^{\text{IV}}(\text{OAc})_2^{2+}$ in the reagent system $\text{Fe}(\text{AN})_6^{2+}-\text{H}_2\text{O}_2-\text{Ac}_2\text{O}$ depending on the organic substrate,²⁾ the following experiment was done to confirm the major active species. Reaction of menadione (vitamin K_3) (**26**) with the reagent system afforded the oxide **27**, exclusively. This result coincides with that of microsomal mono-oxygenation in liver,^{11,12)} and may suggest that the reactive species in this system is either $\text{Fe}^{\text{IV}}=\text{O}$ or $\text{Fe}^{\text{V}}=\text{O}$, and the complex $\text{Fe}^{\text{IV}}(\text{OAc})_2^{2+}$ can be excluded, or may be a minor species if present. Therefore, the reaction sequence with this reagent system should be as shown in Chart 2 instead of that suggested previously.²⁾

It is generally accepted that a higher valent iron-oxoporphyrin ($\text{Fe}^{\text{V}}=\text{O}$; oxene) is a reactive species in oxygenation reactions catalyzed by cytochromes P-450 or the model iron(III) porphyrins.¹⁾ Although several mechanisms have been proposed for the epoxidation of alkenes by cytochromes P-450 or relevant model compounds,¹³⁾ they can be summarized as shown in Chart 3. That is, the first step in the reaction of an oxene **28** with an alkene **29** has been postulated to be either direct attack to produce a metallocycle **30** which collapses to a radical **32** or carbocation **33** intermediate, or direct attack to produce one of these intermediates without formation of the metallocycle, or one-electron transfer to produce a caged pair **31** which collapses to one of these intermediates.

The present reactions may proceed in the ionic mode because stereospecificity is common in ionic reactions.

Chart 4

Thus, the following mechanism for these oxygenation reactions, particularly for exocyclic alkenes, is considered likely (Chart 4). Direct attack of a reactive species $\text{Fe}^{\text{IV}}=\text{O}$ (**35**) on the alkene **36** may produce a carbocation (**38**) through a radical (**37**), then intermediate **38** may be transformed to the aldehyde **40** through a carbocation (**39**) by hydride shift followed by acetylation with Ac_2O catalyzed by the iron(III) MeCN solvate to give the diacetate **41**. When participation of MeCN in the carbocation **39** takes place, the imide **43** may be produced by further oxidation of the addition product **42**.¹⁴⁾ On the other hand, direct reaction of intermediate **38** with MeCN followed by reaction with Ac_2O may afford the acetamide-acetate **44**.

Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded with a JASCO-A 100 spectrophotometer, ¹H- and ¹³C-NMR spectra with JEOL JNM-FX 100 and JEOL JNM-GX 270 spectrometer with tetramethylsilane as an internal standard (CDCl_3 solution), mass spectra (MS) with a JEOL JMS-D 300 spectrometer, and $[\alpha]_D$ with a JASCO DIP-140 digital polarimeter. Gas chromatographic analyses (GLC) were performed on a Hitachi 163 analyzer using flame ionization detectors. Thin-layer and column chromatographies were performed on Merck Kieselgel 60F-254 and Wakogel C-200 silica gel (100 mesh), respectively. Elementary analyses were done by Ms. A. Sakamoto and Ms. M. Takeda, Kissei Pharmaceutical Company, Matsumoto, Japan.

General Procedure for Oxygenation of Olefinic Hydrocarbons with $\text{Fe}(\text{AN})_6(\text{ClO}_4)_2-\text{H}_2\text{O}_2-\text{Ac}_2\text{O}$ A solution of 30% H_2O_2 (2.2 ml, 20 mmol) in acetonitrile (AN; 10 ml) was slowly added dropwise to a solution of $\text{Fe}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (1.81 g, 5 mmol), Ac_2O (18 ml), and an olefinic compound (10 mmol) in AN (80 ml) with stirring at ca. 30 °C for 5 min. The reaction mixture was poured into ice-water and extracted with dichloromethane (50 ml $\times$ 2). The combined organic layer was washed with brine, aqueous Na_2SO_3 , saturated aqueous NaHCO_3 , and H_2O , then dried on Na_2SO_4 and evaporated. The residue was subjected to silica gel column chromatography using dichloromethane-hexane (1:1) or dichloromethane as an eluent. An isomeric mixture which could not be isolated by column chromatography was identified by gas chromatography, by comparison of the retention times with those of authentic samples.

Oxygenation of Cyclohexene The reaction mixture was worked up according to the typical procedure and then the residue was subjected to GLC analysis (Table I).

Oxygenation of 2-Norbornene Silica gel column chromatography of the reaction residue of 2-norbornene afforded **4**, **5**, **6**, and **7** from the hexane-dichloromethane (1:1) eluates in yields of 10.8%, 15.1%, 1.0%, and 5.7%, respectively.

2-exo-Acetoxy-7-anti-acetoxynorbornane (4) Colorless oil (lit.⁴⁾ oil. IR (neat) cm^{-1} : 1740, 1230. ¹H-NMR (CDCl_3) δ : 1.18–1.26 (2H, m, C(5)-H), 1.60–1.73 (2H, m, C(6)-H), 1.75–1.86 (2H, m, C(3)-H), 2.02 (3H, s, $-\text{OCOMe}$), 2.04 (3H, s, $-\text{OCOMe}$), 2.30–2.32 (2H, br, fine coupling, C(1)-H and C(4)-H), 4.58 (1H, dd, $J=2.7, 8.1$ Hz, C(2)-endo-H), 4.97 (1H, br, fine coupling, half width 4.0 Hz, C(7)-syn-H). MS m/z : Calcd for $\text{C}_{11}\text{H}_{16}\text{O}_4$ (M^+): 212.1054. Found: 212.1059.

2-exo-Acetoxy-7-syn-acetoxynorbornane (5) Colorless oil (lit.⁴⁾ oil. IR (neat) cm^{-1} : 1738, 1240. ¹H-NMR (CDCl_3) δ : 1.09–1.29 (2H, m, C(5)-H), 1.54–1.83 (2H, m, C(6)-H), 1.92–1.97 (2H, m, C(3)-H), 1.99 (3H, s, $-\text{OCOMe}$), 2.04 (3H, s, $-\text{OCOMe}$), 2.30 (1H, br, fine coupling, C(4)-H), 2.50 (1H, br, fine coupling, C(1)-H), 4.63 (1H, m, $J=1.0$ Hz, C(7)-anti-H), 4.72 (1H, ddd, $J=1.0, 4.9, 5.9$ Hz, C(2)-endo-H). MS m/z : Calcd for $\text{C}_{11}\text{H}_{16}\text{O}_4$ (M^+): 212.1054. Found: 212.1088.

2-exo-Acetamido-7-anti-acetoxynorbornane (7) Colorless needles, mp 130–132 °C (ether). IR (KBr) cm^{-1} : 3280, 1735, 1640, 1540, 1240. ¹H-NMR (CDCl_3) δ : 1.20–1.45 (4H, m, C(5)-H and C(6)-H), 1.75–1.86 (2H, m, C(3)-H), 1.95 (3H, s, $-\text{NHCOMe}$), 2.05 (3H, s, $-\text{OCOMe}$), 2.22 (2H, br, fine coupling, C(1)-H and C(4)-H), 3.76 (1H, ddd, $J=4.4, 8.3, 11.0$ Hz, C(2)-endo-H), 4.82 (1H, m, half width 5 Hz, C(7)-syn-H), 5.66 (1H, br, $-\text{NHCO}-$). MS m/z : Calcd for $\text{C}_{11}\text{H}_{17}\text{NO}_3$ (M^+): 211.1208. Found: 211.1239.

Oxygenation of *d,l*-Camphene (8) The residue of the oxygenation reaction mixture was subjected to silica gel column chromatography to give **9** and **10**, mp 141–142 °C (lit.⁷⁾ mp 141–142 °C), from the hexane-dichloromethane (1:1) and dichloromethane eluates in yields of 44.1%

and 17.9%, respectively.

2-endo-10,10-Diacetoxycamphane (9) Colorless oil. IR (neat) cm^{-1} : 1760, 1230, 1200. $^1\text{H-NMR}$ (CDCl_3) δ : 0.88 (3H, s, C(3)-Me), 1.03 (3H, s, C(3)-Me), 1.05–1.89 (6H, m), 1.80 (1H, br, fine coupling, C(4)-H), 1.83 (1H, ddd, $J=1.2, 3.7, 10.0$ Hz, C(2)-*exo* H), 2.05 (3H, s, -OCOMe), 2.08 (3H, s, -OCOMe), 2.12 (1H, br, fine coupling, C(1)-H), 6.95 (1H, d, $J=10.0$ Hz, C(10)-H). MS m/z : Calcd for $\text{C}_{14}\text{H}_{22}\text{O}_4$ (M^+): 254.1518. Found: 254.1533.

Alkaline Hydrolysis of 9 The diacetate **9** (180 mg) was hydrolyzed with 0.1% NaOH MeOH solution (30 ml) under reflux for 30 min. The resulting solution was worked up and extracted with dichloromethane. The residue was purified by silica gel chromatography to give the aldehyde **11** (from the dichloromethane-hexane eluent) and the acid **12** (from the dichloromethane eluent). The aldehyde **11** (50 mg) was oxidized with Jones' reagent to give 2-*exo*-10-camphanoic acid (**12**).

2-*exo*-10-Camphanal (11) Colorless needles, mp 52–54°C. IR (Nujol) cm^{-1} : 2700, 1705. $^1\text{H-NMR}$ (CDCl_3) δ : 1.02 (3H, s, C(3)-Me), 1.17 (3H, s, C(3)-Me), 1.15–1.60 (6H, m), 1.62–1.80 (2H, m, fine coupling, C(2)-*endo* H and C(4)-H), 2.44 (1H, br, fine coupling, C(1)-H), 9.61 (1H, d, $J=3.5$ Hz, -CHO). MS m/z : Calcd for $\text{C}_{10}\text{H}_{16}\text{O}$ (M^+): 152.1202. Found: 152.1233.

2-*exo*-10-Camphanoic Acid (12) Colorless needles, mp 92–94°C (aqueous methanol) (literature melting points: 87–90, 96–105 and 118–119.5°C^{6,7}). IR (Nujol) cm^{-1} : 1705. $^1\text{H-NMR}$ (CDCl_3) δ : 1.01 (3H, s, C(3)-Me), 1.16 (3H, s, C(3)-Me), 1.22–1.7 (6H, m), 1.78 (1H, br, fine coupling, C(4)-H), 1.99 (1H, d, $J=1.7$ Hz, C(2)-*endo* H), 2.40 (1H, br, fine coupling, C(1)-H), 9.02 (1H, br, C(2)-CO₂H). $^{13}\text{C-NMR}$ (CDCl_3) ppm: 23.94, 25.40, 27.51, 28.40, 37.44, 40.82, 42.41, 47.95, 58.78, 180.09. MS m/z : Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_2$ (M^+): 168.1151. Found: 168.1167.

Synthesis of 2-*endo*-10-Camphanoic Acid (14) A solution of borane (30 mmol) in tetrahydrofuran (THF) was added slowly to a solution of *d,l*-camphene (20 mmol) in dry THF 80 ml under nitrogen atmosphere at 0–5°C and the mixture was stirred at room temperature for 2.5 h. Then, 3 N NaOH (5 ml) and 30% H_2O_2 (5 ml) were added, keeping the temperature below 10°C. The resulting solution was extracted with dichloromethane and worked up in the usual way. The residue was purified by silica gel chromatography using dichloromethane as an eluent to give 2-*endo*-10-camphanol (**13**).⁸ The alcohol **13** (400 mg) in acetone (20 ml) was oxidized with excess Jones' reagent (1 ml) for 1.5 h under ice cooling. The reaction mixture was diluted with water, and extracted with dichloromethane. The organic layer was washed with water, dried on Na_2SO_4 , and evaporated. The residue (390 mg) was chromatographed on silica gel using dichloromethane as an eluent to give 2-*endo*-10-camphanoic acid (**14**), colorless crystals, mp 80–82°C (aqueous methanol) (literature mp: 75–80, 78.5–80, and 90–91°C^{6,7}) and *exo*- and *endo*-mixture 64–65°C⁷). IR (Nujol) cm^{-1} : 1705. $^1\text{H-NMR}$ (CDCl_3) δ : 1.04 (3H, s, C(3)-Me), 1.13 (3H, s, C(3)-Me), 1.25–2.05 (6H, m), 1.86 (1H, br, fine coupling, C(4)-H), 2.37 (1H, dd, $J=1.7, 3.4$ Hz, C(2)-*exo* H), 2.43 (1H, br, fine coupling, C(1)-H). $^{13}\text{C-NMR}$ (CDCl_3) ppm: 21.30, 22.71, 24.42, 31.77, 37.48, 38.35, 40.69, 48.88, 55.85, 178.00. MS m/z : Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_2$ (M^+): 168.1150. Found: 168.1182.

Oxygenation of Longifolene (15) Oxygenation of **15**, $[\alpha]_D^{25} + 51.14^\circ$ ($c=0.114$, CHCl_3), was carried out according to the general procedure. Silica gel column chromatography of the reaction residue gave the diacetate **16** from the hexane-dichloromethane (1:1) eluate, and the imide **17** and the acetoxy-acetamide **18** from the dichloromethane eluates in yields of 27.1%, 3.6%, and 21.2%, respectively.

7-*endo*-13,13-Diacetoxylongifolane (16) Colorless oil. $[\alpha]_D^{25} - 18.35^\circ$ ($c=0.058$, CHCl_3). IR (neat) cm^{-1} : 1760, 1240, 1210. $^1\text{H-NMR}$ (CDCl_3) δ : 0.87 (3H, s, C(6)-Me), 0.97 (3H, s, C(2)-Me), 1.00 (3H, s, C(2)-Me), 1.20–2.00 (11H, m), 2.04 (2H, br, fine coupling, C(8)-H and C(11)-H), 2.06 (3H, s, -OCOMe), 2.08 (3H, s, -OCOMe), 2.43 (1H, ddd, $J=1.2, 3.4, 9.8$ Hz, C(7)-*exo* H), 7.01 (1H, d, $J=9.8$ Hz, C(13)-H). MS m/z : Calcd for $\text{C}_{19}\text{H}_{30}\text{O}_4$ (M^+): 322.2144. Found: 322.2159.

7-*endo*-N-Acetyl-13-longifolanamide (17) Colorless crystals, mp 169–170°C (hexane-dichloromethane). IR (Nujol) cm^{-1} : 3250, 3180, 1725, 1695. $^1\text{H-NMR}$ (CDCl_3) δ : 0.97 (3H, s, C(6)-Me), 1.03 (6H, s, $2 \times \text{C}(2)\text{-Me}$), 1.20–1.70 (11H, m), 2.06 (1H, br, fine coupling, C(11)-H), 2.39 (1H, br, fine coupling, C(8)-H), 2.45 (3H, s, OCOMe), 2.84 (1H, dd, $J=1.7, 3.7$ Hz, C(7)-*exo* H), 7.93 (1H, br, -CONHCO-). MS m/z : Calcd for $\text{C}_{17}\text{H}_{27}\text{NO}_2$ (M^+): 277.2041. Found: 277.2051.

13-Acetoxy-7-*exo*-acetamidolongifolane (18) Colorless oil. IR (Nujol) cm^{-1} : 3280, 3060, 1730, 1650, 1550, 1250. $^1\text{H-NMR}$ (CDCl_3) δ : 0.88 (3H, s, C(6)-Me), 0.94 (3H, s, C(2)-Me), 0.96 (3H, s, C(2)-Me), 1.10–2.00 (11H, m), 1.90 (3H, s, -NHCOMe), 2.08 (3H, s, -OCOMe), 4.09 (2H, d, $J=$

2.2 Hz, C(13)-H), 5.30 (1H, br, -NHCO-). MS m/z : Calcd for $\text{C}_{19}\text{H}_{31}\text{NO}_3$ (M^+): 321.2302. Found: 321.2290.

Oxygenation of *ent*-Kaurene (20) Oxygenation of **20** (2.72 g, 10 mmol), $[\alpha]_D^{25} - 53.33^\circ$ ($c=0.235$, CHCl_3), was carried out according to the general procedure. After removal of 1134 mg (29.2%) of **23** in the residue, the filtrate was subjected to silica gel column chromatography to give 980 mg (25.1%) of **21** from the hexane-dichloromethane (1:1) eluate and 100 mg (2.9%) of **22** from the dichloromethane eluate.

***ent*-16 β -17,17-Diacetoxykaurane (21)** Colorless crystals, mp 129–131°C (methanol-dichloromethane). $[\alpha]_D^{25} - 24.22^\circ$ ($c=0.112$, CHCl_3). IR (Nujol) cm^{-1} : 1755, 1240, 1210. $^1\text{H-NMR}$ (CDCl_3) δ : 0.79 (3H, s, C(4)-Me), 0.84 (3H, s, C(4)-Me), 0.99 (3H, s, C(10)-Me), 1.05–2.10 (19H, m), 2.05 (3H, s, -OCOMe), 2.03 (3H, s, -OCOMe), 2.15 (1H, br, fine coupling, C(13)-H), 2.36 (1H, dddd, $J=5.9, 6.9, 10.3, 11.7$ Hz, C(16)-H), 6.99 (1H, d, $J=10.26$ Hz, C(17)-H). $^{13}\text{C-NMR}$ (CDCl_3) ppm: 17.73, 18.61, 18.73, 20.49, 20.90, 21.55, 26.24, 33.28, 33.58, 37.34, 39.28, 40.28, 40.45, 41.27, 41.86, 42.04, 43.50, 44.27, 56.24, 57.06, 90.88, 168.96. MS m/z : Calcd for $\text{C}_{24}\text{H}_{38}\text{O}_4$ (M^+): 390.2770. Found: 390.2797. Anal. Calcd for $\text{C}_{24}\text{H}_{38}\text{O}_4$: C, 73.81; H, 9.81. Found: C, 73.58; H, 10.00.

***ent*-16 β -N-Acetyl-17-kauranamide (22)** Colorless crystals, mp 219–221°C (ether-dichloromethane). IR (Nujol) cm^{-1} : 3240, 3200, 1725, 1695, 1660, 1290. $^1\text{H-NMR}$ (CDCl_3) δ : 0.80 (3H, s, C(4)-Me), 0.85 (3H, s, C(4)-Me), 0.99 (3H, s, C(10)-Me), 1.13–2.16 (19H, m), 2.01 (1H, dd, $J=2.0, 5.9$ Hz, C(15)- β H), 2.53 (1H, br, fine coupling, C(13)-H), 2.90 (1H, ddd, $J=5.9, 6.1, 11.7$ Hz, C(16)-H), 8.07 (1H, br, -CONHCO-). MS m/z : Calcd for $\text{C}_{22}\text{H}_{35}\text{NO}_2$ (M^+): 345.2667. Found: 345.2667. Anal. Calcd for $\text{C}_{22}\text{H}_{35}\text{NO}_2$: C, 76.48; H, 10.21; N, 4.05. Found: C, 76.24; H, 10.49; N, 3.86.

***ent*-16 α -Acetamido-17-acetoxykaurane (23)** Colorless needles, mp 216–217°C (acetone-dichloromethane). $[\alpha]_D^{25} - 50.75^\circ$ ($c=0.105$, CHCl_3). IR (Nujol) cm^{-1} : 3350, 3290, 1740, 1639, 1530, 1240. $^1\text{H-NMR}$ (CDCl_3) δ : 0.79 (3H, s, C(4)-Me), 0.84 (3H, s, C(4)-Me), 0.99 (3H, s, C(10)-Me), 1.05–2.02 (20H, m), 1.93 (3H, s, -NHCOMe), 2.03 (3H, s, -OCOMe), 2.24 (1H, br, fine coupling, C(13)-H), 4.35 (1H, d, $J=15.0$ Hz, C(17)-H), 4.70 (1H, d, $J=15.0$ Hz, C(17)-H), 5.32 (1H, br, -NHCO-). $^{13}\text{C-NMR}$ (CDCl_3) ppm: 17.65, 18.41, 18.54, 20.46, 20.92, 21.55, 24.38, 26.13, 33.24, 33.54, 37.62, 39.37, 40.25, 42.00, 42.24, 44.14, 44.60, 51.51, 56.02, 56.67, 63.63, 64.07, 169.68, 170.87. MS m/z : Calcd for $\text{C}_{24}\text{H}_{39}\text{NO}_3$ (M^+): 389.2930. Found: 389.2961. Anal. Calcd for $\text{C}_{24}\text{H}_{39}\text{NO}_3 \cdot 1/2\text{H}_2\text{O}$: C, 72.32; H, 9.86; N, 3.51. Found: C, 72.28; H, 10.08; N, 3.32.

***ent*-16 α -17-Kauranal (24) and *ent*-16 α -17-Kauranoic Acid (25)** Compound **21** (180 mg) was hydrolyzed with 0.1% NaOH aqueous MeOH solution under reflux for 30 min, and worked up in the usual manner. The resulting residue was subjected to silica gel column chromatography using dichloromethane-hexane (1:1) as an eluent to give 130 mg (98.5%) of the aldehyde **24** as colorless crystals, mp 44–46°C. IR (Nujol) cm^{-1} : 2680, 1718. $^1\text{H-NMR}$ (CDCl_3) δ : 0.80 (3H, s, C(4)-Me), 0.85 (3H, s, C(4)-Me), 1.00 (3H, s, C(10)-Me), 1.05–1.95 (20H, m), 2.54 (1H, br, fine coupling, C(13)-H), 2.56 (1H, m, fine coupling, C(16)-H), 9.64 (1H, d, $J=1.9$ Hz, -CHO). MS m/z : Calcd for $\text{C}_{20}\text{H}_{32}\text{O}$ (M^+): 288.2451. Found: 288.2433.

Oxidation of the aldehyde **24** with CrO_3 in acetone (Jones' reagent) afforded the acid **25**¹⁰ as colorless needles (acetone), mp 208–209.5°C (lit.¹⁵ mp 217–218°C (*ent*-16 α -17-kauranoic acid); lit.¹⁰ mp 194–195°C (*ent*-16 β -17-kauranoic acid)). IR (Nujol) cm^{-1} : 1704. $^1\text{H-NMR}$ (CDCl_3) δ : 0.802 (3H, s, C(4)-Me), 0.85 (3H, s, C(4)-Me), 0.99 (3H, s, C(10)-Me), 1.10–1.92 (20H, m), 2.53 (1H, br, fine coupling, C(13)-H), 2.64 (1H, dd, $J=6.8, 8.9$ Hz, C(16)-H), 9.65 (1H, br, -COOH). $^{13}\text{C-NMR}$ (CDCl_3) δ : 17.48, 18.38, 18.68, 20.78, 21.63, 31.33, 33.27, 33.67, 38.18, 39.32, 40.47, 40.95, 41.46, 42.09, 44.78, 45.17, 45.40, 56.06, 56.22, 183.18. MS m/z : Calcd for $\text{C}_{20}\text{H}_{32}\text{O}_2$ (M^+): 304.2402. Found: 304.2412. Anal. Calcd for $\text{C}_{20}\text{H}_{32}\text{O}_2$: C, 78.89; H, 10.59. Found: C, 78.63; H, 10.61.

Oxygenation of 2-Methyl-1,4-naphthoquinone (Menadione) (26) Menadione (1.72 g) was oxidized according to the general procedure. The resulting residue was purified by silica gel column chromatography to give 1.38 g of the epoxide **27**, mp 83–85°C (hexane-dichloromethane) (lit.¹⁶ mp 49–50°C, mp 96–96.5°C).

References and Notes

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