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CONSTITUENTS OF GENUS *PETASITES*—IV[1]

BAKKENOLIDE-A, A SESQUITERPENE OF NOVEL CARBON SKELETON

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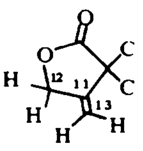
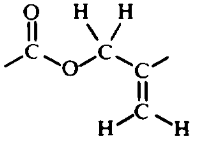
Abstract—A group of a new type of sesquiterpene, named bakkenolide-A, B, C, D, and E was isolated from the buds of *Petasites japonicus* (Sieb. et Zucc.) Maxim. subsp. *giganteus* (Fr. Schm.) Kitam. (Japanese name, Akita-buki). They have a novel spiro-γ-lactone grouping. The structure and stereochemistry including absolute configuration was established for bakkenolide-A (B–A) (1) on the basis of chemical degradations (Chart 1, 2) and physical measurements. The C_{11}-dicarboxylic acid (5), a main degradation product of B–A during potassium permanganate oxidation, was instrumental in determination of the full structure. The absolute configuration was based on the transformation of B–A to the known perhydroindanone derivative (12).

THE antitussive and peptic properties of buds of the genus Petasites have been known in Japan and groups[2] have reported the isolation of sesquiterpenes with the eremophilane skeleton from *Petasites japonicus*. Novotny *et al.*[3] also have reported many studies on the components of European Petasites. We were interested in the medicinal properties and the bitter principle of *Petasites japonicus* (Sieb. et Zucc.) Maxim. subsp. *giganteus* (Fr. Schm.) Kitam., the distribution of which is limited to the northern part of Japan. During the investigation of the components of the buds, we isolated new sesquiterpene lactones which were named bakkenolide-A, B, C, D, and E after the local name "Bakke" for the bud of this plant. The present paper discusses the complete structure including the stereochemistry of Bakkenolide-A.†

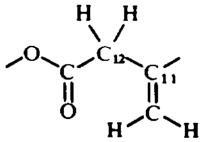
Bakkenolide-A (1), m.p. 80–81°, $C_{15}H_{22}O_2$ (M^+ 234, mol wt. 234·33), has IR absorption at 3070, 1767, 1666 and 899 cm^{-1} and has only weak end absorption in the UV spectrum. The spectral data indicated the presence of an unconjugated terminal methylene group and a γ-lactone grouping. This deduction was verified by an observation which led to the partial structure **1a**. B–A is insoluble in cold but soluble in hot aqueous alkali to form a sodium salt which regenerates B–A on acidification.



1a



1b



1c

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† A part of this work has been published in part I of this series as a short communication, see Ref. 1.

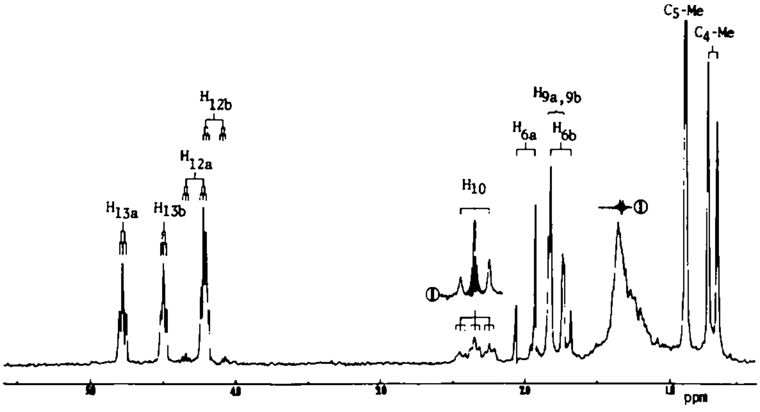
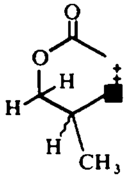


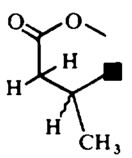
FIG. 1 100 Mc. NMR spectrum of bakkenolide-A(1) in deuteriobenzene

The NMR spectrum of B–A in deuteriobenzene (Fig. 1) shows the signals of four protons at 4·2–4·8 ppm [δH_{12a}[*][†] and δH_{12b} = 4·21, δH_{13a} and δH_{13b} = 4·78 and 4·50, J (12a–12b) = 13·0, J(12a–13a) = J(12a–13b) = J(12b–13a) = J(12b–13b)) = ca. 2], J(13a–13b) = ca. 0·5, which indicated the partial structure **1b** or **1c**.

B–A consumed one mole equivalent of hydrogen on catalytic reduction with Pd-C in ethanol to afford a mixture of stereoisomeric dihydro-derivatives (**2**) $C_{15}H_{24}O_2$. The IR spectrum of the mixture indicated a strong γ-lactone band at 1768 cm^{-1}. The NMR spectrum of the predominant isomer in deuteriochloroform (Fig. 2) shows two secondary Me groups at 1·05 ppm (doublet, J = 7·0) and 0·82 ppm (doublet, J = 6·0), (**2a** or **2b**) grouping [δH_{12a} and H_{12b} at 4·26 and 3·79 ppm, J(12a–12b) = 8·8, J(12a–11) = 6·1, J(12b–11) = 4·5], and a multiplet (H_{11}) at 2·29 ppm. The latter signal became a clear 1 : 3 : 3 : 1 quartet when both H_{12a} and H_{12b} were irradiated at the same time (Fig. 2 ①). This triple resonance experiment indicated absence of a proton on the carbon next to C_{11}. Strong irradiation of H_{11} at δ 2·29 resulted in decouplings of the new secondary Me doublet at 1·05 ppm to singlet (Fig. 2 ②) as well as both H_{12a} and H_{12b} to a pair of doublets. These observations indicated that the dihydro derivative has the partial structure **2a**, and not **2b**, particularly in view of the chemical shifts of H_{12a} and H_{12b}.



2a



2b

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[*] In the case of a signal due to two protons on the same carbon if the correct assignment could not be given, then the suffixes a and b were used. These suffixes, therefore, have not any structural meaning.

[†] The numbering was given after consideration of the biosynthesis of the carbon skeleton which may be derived from the eremophilane skeleton in the plant. See part III of this series.

[‡] The symbol ■ refers a carbon bearing no hydrogen.

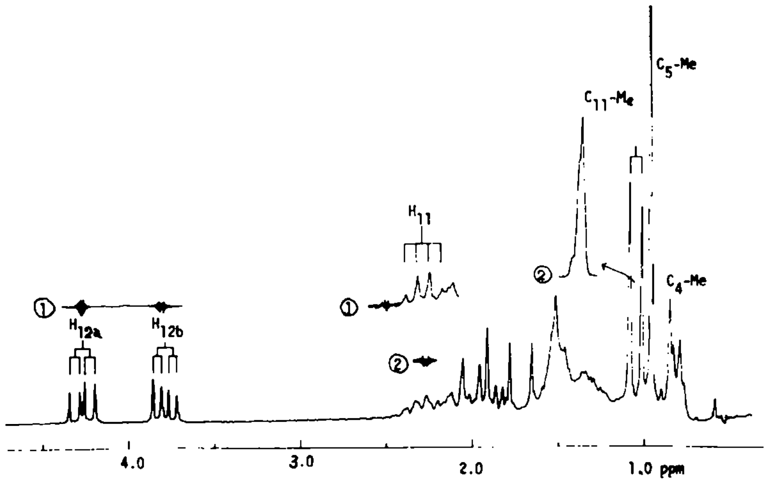

FIG. 2 100 Mc NMR spectrum of a mixture of dihydrobakkenolide-A (2) stereoisomers at C_{11} in deuteriochloroform

The nature of the lactone grouping was made evident by reduction of B–A with LAH. The product was a crystalline diol (3) $C_{15}H_{26}O_2$, m.p. 81–82° (IR band at 3280 cm^{-1}, formation of a diacetate 4). The NMR spectrum (Fig. 3) of 3 in deuteriochloroform exhibits a diffuse singlet at δ 3·00 (two OH), an AB-type quartet centered at δ 3·37. The new quartet could be assigned to the two hydrogens of the C_8 methylene. This splitting (J_{ab} = 10·5) was due to geminal coupling and hence showed that C_7 has no proton. The spectral data also confirmed the partial structure **2a** for **2** and **1a** for B–A.

Thus it was concluded that B–A is a spiro-γ-lactone* (C-ring)† having a terminal

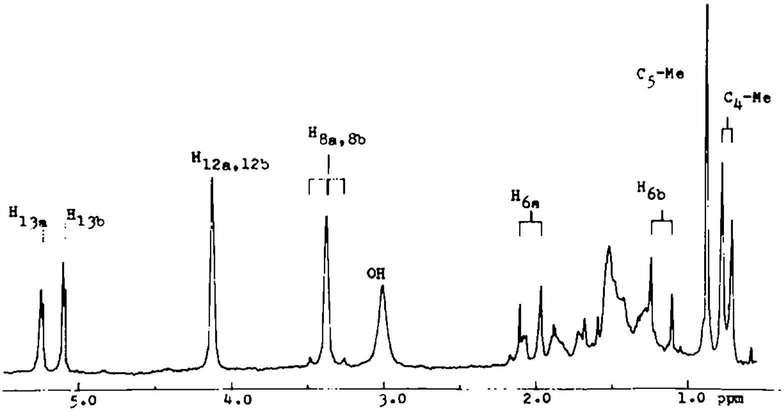

FIG. 3 100 Mc NMR spectrum of B–A diol (3) in deuteriochloroform

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* The spiro-γ-lactone such as B–A is not common in a sesquiterpene lactone. This is the first example as far as we know. K. Naya *et al.* have also reported that bakkenoldes-A, B and D were isolated from *Petasites japonicus* Maxim.[4]

† The 6- and 5-membered rings in turns are described as A- and B-ring. See structure 1.

methylene on the ring. In conjunction with the molecular formula, the presence of only one double bond and a lactone determines that B–A is tricyclic. The structure of the remainder (B, C-ring) of B–A was determined as follows.

Oxidation of B–A or the diol **3** with potassium permanganate in aqueous alkaline solution afforded a mixture of several degradation products, the main product of which was C_{11}-dicarboxylic acid (**5**) $C_{11}H_{18}O_4$. This dicarboxylic acid readily gave an acid anhydride (**6**) when heated in acetic anhydride, the IR spectrum of which showed bands at 1803 and 1760 cm^{-1} characteristic of an anhydride of a six or larger membered ring. The nature of the carboxyl groups was deduced from observation of the rate of ester exchange (conversion of $-CO_2CH_3$ to $-CO_2CD_3$) of the dimethyl ester (**7**) which was obtained by treatment of the dicarboxylic acid with diazomethane. The dimethyl ester was dissolved in methanol-d_4 containing sodium methoxide-d_3 (ca. 4·2% wt of sodium in methanol-d_4) and the rate in decrease of the Me signals was checked by NMR. Although the two ester Me signals have the same chemical shift, the signal area (6H, relative to tertiary Me, 3H) was reduced to half (3H) at room temperature but was not reduced to less than half after standing for 27 hr at room temperature and for another 17 hr at 53–55°.

This experiment demonstrated that only one of the two carbomethoxy groups in **7** is tertiary. Consideration of the presence of a tertiary Me group and its chemical shift (1·23 ppm) led to the partial structure **5a** to the dicarboxylic acid (another carboxyl group should not bond to C_{10} or C_4).

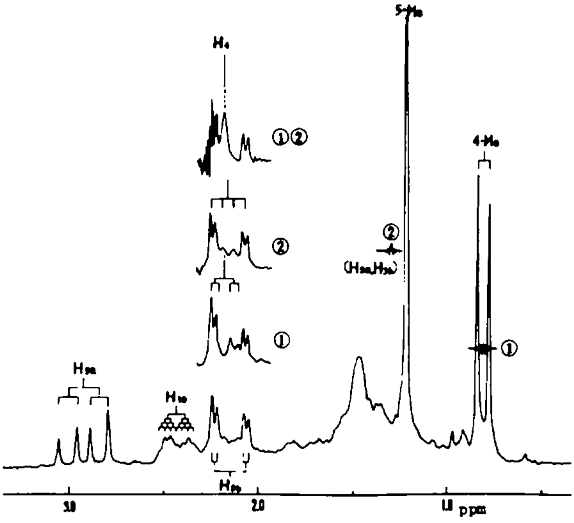
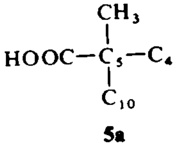


FIG. 4 100 Mc NMR spectrum of C_{11}-dicarboxylic acid in deuteriobenzene

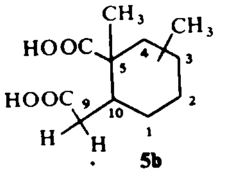
The NMR spectrum of **5** in deuteriobenzene (Fig. 4) shows, in addition to a tertiary Me group (singlet at δ 1·23) and a secondary Me group (doublet at δ 0·82, J = 6·5), a group of signals which is characteristic of an ABC-pattern where the C-proton (2·45 ppm) is further coupled to two additional protons [cf. Fig. 4, and structure **5b** H_{9a}(A) and H_{9b}(B) at 2·93 and 2·17 ppm, H_{10}(C) at 2·45 ppm; J(9a–9b) = 16·5,

$J(9a\text{–}10) = 9{\cdot}5$, $J(9b\text{–}10) = 2{\cdot}3$, $J(10\text{–}1a) = J(10\text{–}1b) =$ ca. 3]. These signals clearly indicated the presence of the sequence —CH—CH_2—COOH. The chemical shifts of H_9 and H_{10}, the magnitude of $J(9a\text{–}9b)$,[5] the presence of the partial structure **5a**,



$$\mathrm{HOOC{-}\overset{\displaystyle CH_3}{\underset{\displaystyle C_{10}}{C_5}}{-}C_4}$$

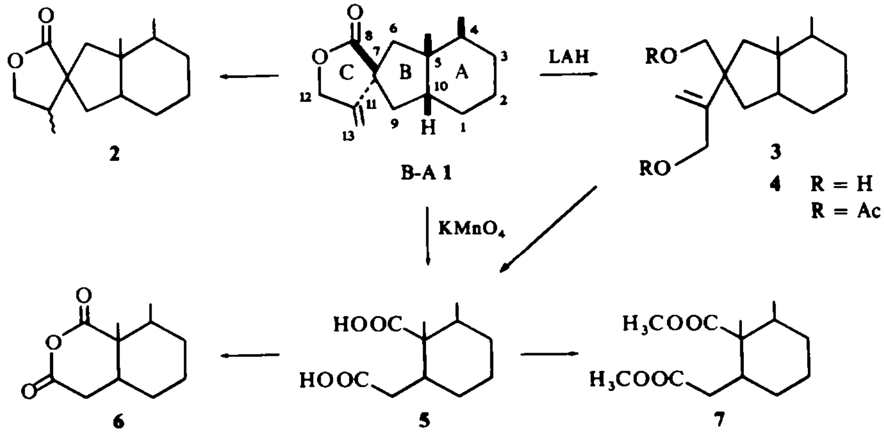
5a



5b

the facility with which the two carboxyl groups formed an anhydride and the anhydride ring larger than a 5-membered ring, as well as coupling of H_{10} to only two protons except H_{9a} and H_{9b}, all confirmed the presence of partial structure **5b**. Moreover, considering the presence of only one additional secondary Me group and the absence of any olefinic protons, the C_{11}-dicarboxylic acid (**5**) must be a saturated cyclohexane derivative. The position of the secondary Me group, and hence full structure of **5** was based on the following multiple resonance. (i) Irradiation of the secondary Me group at δ 0·82 caused the broad multiplet signal (H_4) underlying the H_{9b} signal to show as a doublet of doublet centered at 2·17 ppm, whereas (ii) irradiation near 1·30 ppm (H_{3a} and H_{3b}) changed this H_4 signal to a broad quartet again centered at near 2·2 ppm, and (iii) simultaneous irradiation at both 0·80 and 1·33 ppm converted the signal at δ 2·17 to a broad singlet.* These decoupling experiments,

CHART 1



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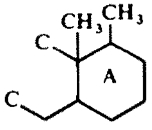
* The broadness of the quartet and singlet in the last two cases was attributed to incomplete decoupling of the apparently broad multiplets at near 1·30 ppm due to the C_3-protons.

particularly those of (i), are best explained in terms of a ■—CH(CH$_3$)—CH$_2$— grouping which immediately led to proposal of structure **5** for the carboxylic acid and of **6** for the anhydride, and hence A-ring of B–A was presented as **1d**.



1d

The NMR spectrum of B–A shows four sharp peaks at 1·68, 1·83, 1·92 and 2·07 ppm. The following spin tickling experiments indicated that these four peaks consist of an AB type quartet isolated from other spin systems. Weak irradiation of one of them at 1·68 ppm (Fig. 5 ①) made the peak at 1·92 ppm decrease in height and split to a doublet and made the peak at 2·07 ppm increase in height but not change the splitting. Similar irradiation of the peak at 1·83 ppm (Fig. 5 ②) made the former (δ 1·92) increase in height and split to a doublet and made the latter (δ 2·07) decrease in height and split to a doublet. Therefore, B–A has ■—CH$_2$—■ grouping in B-ring. All derivatives of B–A retaining B-ring also show the AB type quartet (Table 1). There is only one possible combination of part structures **1a**, **1d** and ■—CH$_2$—■ grouping and the full structure of B–A is therefore **1**. The stereochemistry was established as follows.

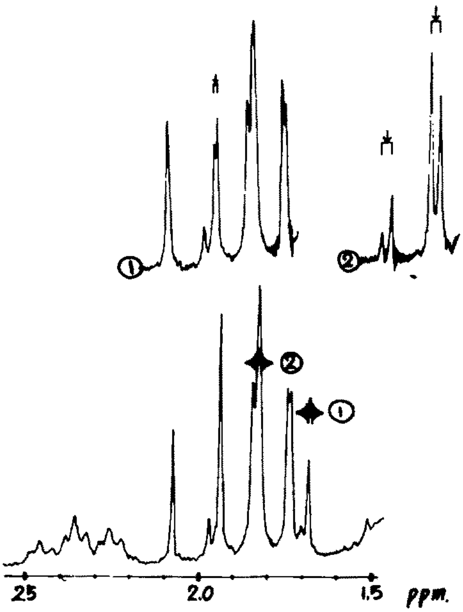


FIG. 5 Spin tickling of Bakkenolide-A

The NMR spectrum of B–A shows signals at 1·6–2·5 ppm due to three protons

TABLE 1. THE CHEMICAL SHIFTS OF AB-TYPE QUARTET OF C_6-METHYLENE PROTONS[a]

	B–A (1)	B–A diol (3)	B–A diacetate (4)	nor-ketone (8)	dimethylester (10)
H_{6a}	2·00 (13·8)	2·04 (14·0)	2·02 (14·0)	2·10 (13·7)	2·46 (14·5)
H_{6b}	1·75	1·17	1·10	1·76	1·76
solvents	C_6D_6	$CDCl_3$	C_6H_6	$CDCl_3$	CCl_4

[a] Chemical shifts are given in ppm from tetramethylsilane as an internal standard. Figures in parentheses are coupling constants in c/sec.

accompanying with C_6 methylene protons. These signals form the ABC pattern of an $ABCX_2\cdots$ system and should be assigned to H_{9a}, H_{9b}, and H_{10}. Although an exact first-order analysis of this system was impossible, A-proton ($\delta H_{10} = 2{\cdot}35$) appeared clearly as a triplet of triplet ($J = 10{\cdot}4$ and $3{\cdot}5$ c/s). Strong irradiation of the C_1-protons (near 1·32 ppm) converted the A-proton into a simple triplet with 10·4 c/s (Fig. 1). J(10–1a) and J(10–1b) were small (3·5 c/s). These small coupling constants indicated the C_{10}—H bond bisected roughly the angle between the C_1—H_{1a} bond and the C_1—H_{1b} bond. This can only be the case if the A/B junction is *cis*. The *cis* junction was also supported by the mass spectrum of B–A (Fig. 6). The mass spectrum of **1** gave fragment ions at *m/e* 124 and 111, the latter became *m/e* 113 in dihydro B–A. This fact indicated that the fragment peak *m/e* III comes from the spiro-γ-lactone part and the formation of these ions were explained by the fragmentation as follows.*

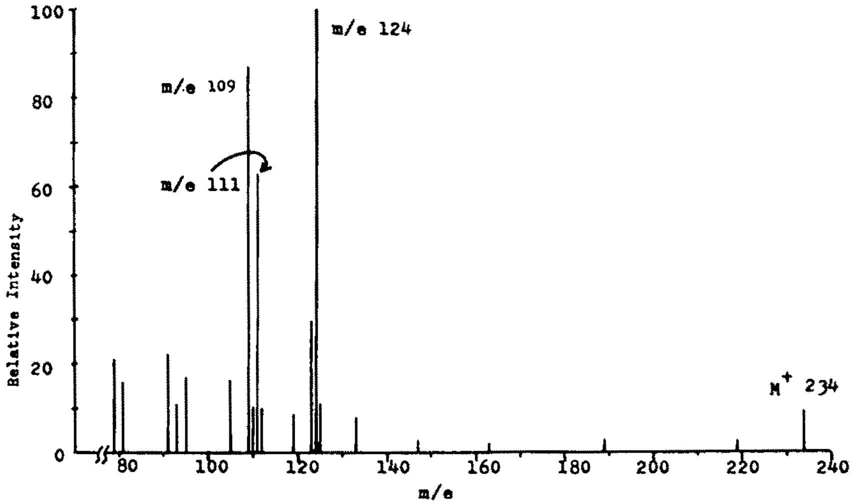


FIG. 6 Mass spectrum of bakkenolide-A

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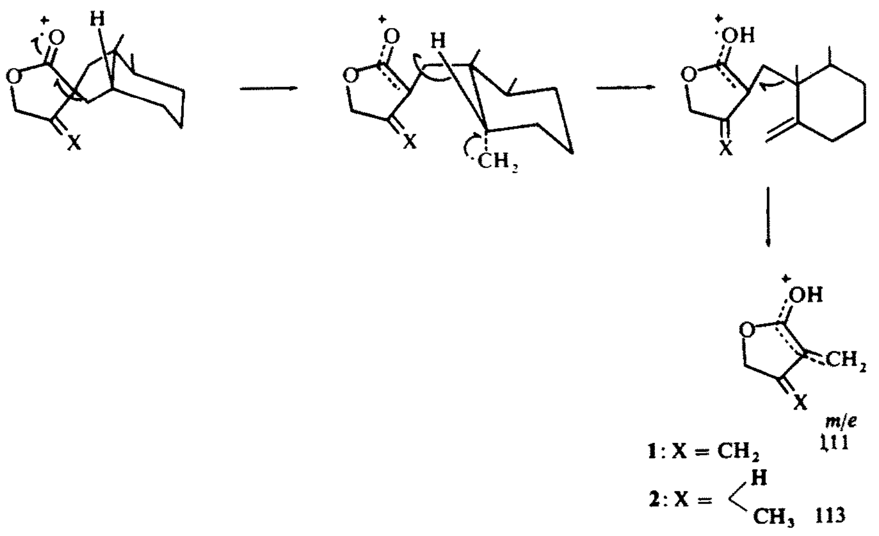
* Further consideration of mass spectra of Bakkenolides will be described elsewhere.

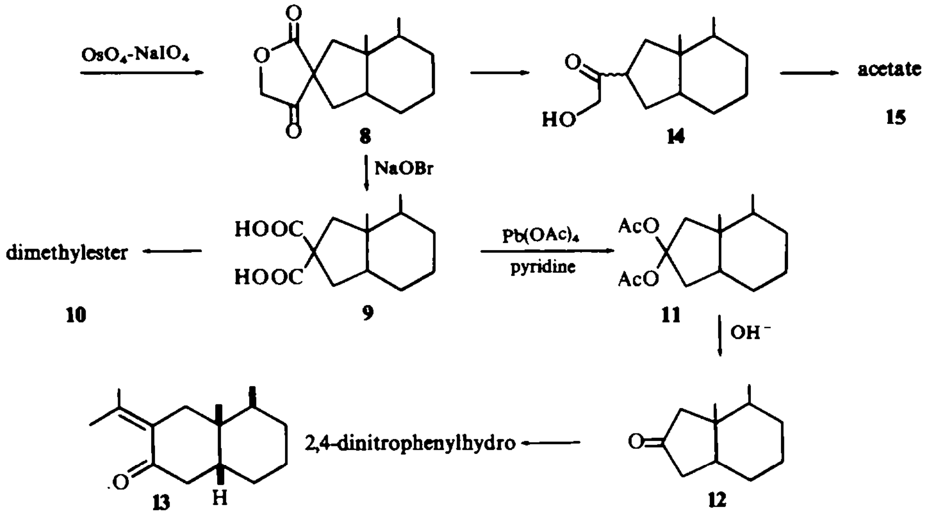


The relative configuration at C_7 was based on a consideration of anisotropy effects of lactone carbonyl and exocyclic methylene double bond to tertiary Me group (Table 2). The chemical shift of the Me group in deuteriochloroform solution was little affected when the double bond was saturated or oxidized to carbonyl. On the other hand the characteristic upfield displacement (0·1 ppm) was observed when the lactone carbonyl was removed by reduction to diol 3. These findings suggested that the CO group and the tertiary Me group are on the same side of the molecule in B–A. Absolute configuration and stereochemistry at all centers excepting C_7 were established by conversion of B–A to the perhydroindanone derivative (**12**) of known structure and stereochemistry. The treatment of B–A with osmium tetroxide and sodium periodate in dioxan afforded a degradation product, 13-nor-12-oxo-bakkenolide A (nor-ketone) (**8**), $C_{14}H_{20}O_3$, whose IR spectrum shows that the exocyclic methylene was converted to ketone (disappearance of IR bands at 3070, 1666 and 899 cm^{-1} originally present in B–A) and the NMR spectrum shows the C_{12} methylene protons at 4·60 ppm as a singlet. This nor-ketone was oxidized with sodium hypobromide to C_{13}-dicarboxylic acid (**9**), which was identified after it was converted to its dimethyl ester (**10**), $C_{15}H_{24}O_4$, which has strong absorption at 1737 cm^{-1}. Inspection of its NMR spectrum provided clear proof that the dimethyl ester retains the B-ring, i.e. a pair of doublets characteristic of C_6 methylene protons was shown at 2·46 and 1·76 ppm (J = 14·5 c/s) (Table 1). Treatment of **9** with lead tetra-acetate and pyridine[6] followed by hydrolysis of the resulting diacetate (**11**) with methanolic

TABLE 2. THE CHEMICAL SHIFTS OF C_5-ME IN $CDCl_3$

B–A (1)	Dihydro B–A (2)	Nor-ketone (8)	B–A diol (3)
0·98	0·96	0·99	0·87

CHART 2



potassium hydroxide gave a ketone (**12**) as a colorless liquid, whose IR spectrum shows a strong 5-membered CO band at 1743 cm^{-1}. The 2,4-dinitrophenylhydrazone of **12** was identical with that obtained from fukinone (**13**)[7] by comparison of their IR spectrum and m.ps. The full structure of B–A including absolute configuration was eventually established as **1**.

EXPERIMENTAL

M.ps were taken with a Thomas Hoover Capillary Melting Point Apparatus and are uncorrected. The IR spectra were measured with Hitachi-EPI-S2 model equipped with rock-salt prisms, while measurement of solution was carried out by a Hitachi-EPI-G2 grating spectrometer. The NMR spectra were measured with a Varian A-60 (60 Mc.) and a Varian HA-100 (100 Mc.) spectrometers equipped with spin decouplers. The chemical shifts are expressed in ppm using TMS as an internal reference. The mass spectra were recorded with a Hitachi Model RMU-6D spectrometer.

Isolation of bakkenolides. Fresh buds (25 Kg) of the plant were crushed and soaked in hot MeOH, and the soln (54 l.) containing large amount of water was concentrated and extracted with benzene. The benzene soln was concentrated *in vacuo* to afford a dark greenish viscous liquid (125 g), which was submitted to steam distillation. Bakkenolide-A (7·0 g) was obtained immediately from the distillate as leaflets. After B–A was filtered off, the filtrate was extracted with ether and the extracts were processed in the usual manner to afford a neutral liquid (15·2 g), which was distilled and the fraction (100–150°2 mmHg) was chromatographed over silica gel to give another crop of B–A (3 g).

The residue after steam distillation was taken up again with benzene, the benzene soluble part (62 g) was chromatographed over alumina with pet ether, benzene, benzene–ether, and MeOH as eluents. Bakkenolide-B (3·5 g), -D (0·2 g) and -C (0·8 g) were obtained in turn from the benzene, benzene–ether, and MeOH eluents respectively. After B–B and B–C were isolated by filtration, the combined residues were again chromatographed over silica gel. Elution with benzene–ether gave bakkenolide-E (0·8 g).

			m.p.
Bakkenolide-A	$C_{15}H_{22}O_2$	leaflets from n-pentane	80–81°
-B	$C_{22}H_{30}O_6$	needles from EtOH	101–102°
-C	$C_{20}H_{28}O_5$	needles from ether	166–167°
-D	$C_{21}H_{28}O_6S$	needles from MeOH	205–206°*
-E	$C_{22}H_{30}O_6$	needles from MeOH	168–169°

* In some cases different mps, i.e. 189–190° and 201–202°, were recorded, which could be due to polymorphism.

B–A (1) (Found: C, 76·79; H, 9·44. $C_{15}H_{22}O_2$ requires: C, 76·88; H, 9·46%), M^+ was measured at 234 ($C_{15}H_{22}O_2$ requires 234). ν_{max}(KBr) 3070, 2950, 2930, 1767, 1666, 1462, 1354, 1145, 1126, 1019 and 899 cm^{-1}. ν_{max} ($CHCl_3$)* 3080 (VW), 3020 (VW), 2940 (S), 1770 (VS), 1670 (M), 1464 (S), 1351 (S), 1147 (S), 1128(M), 1023(S), and 898 cm^{-1} (S). NMR data (deuteriobenzene; 100 Mc/sec): a doublet (J = 6·2) at 0·71 (3H, C_4-Me), a singlet at 0·89 (3H, C_5-Me), a pair of doublets (J = 13·8) at 2·00 and 1·75 (each 1H, H_{6a} and H_{6b}), a triplet (J = 10·4) of triplet (J = 3·4) at 2·35 (1H, H_{10}), a pair of doublets (J = 13·0) of triplets (J = 2·1) centered at 4·21 (2H, H_{12a} and H_{12b}), and a pair of triplets (J = 2·1) of doublets (J = 0·5) at 4·78 and 4·50 (each 1H, H_{13a} and H_{13b}). ($CDCl_3$; 100 Mc/s): a doublet (J = 6·4) at 0·84 (3H, C_4-Me), a singlet at 0·98 (3H, C_5-Me), multiplet at 4·76 (2H, H_{12a} and H_{12b}), and a pair of multiplets at 5·11 and 5·02 (each 1H, H_{13a} and H_{13b}).

Dihydrobakkenolide-A (2). A soln of 171 mg (1) in 10 ml EtOH was hydrogenated over 5% Pd-C. H_2 uptake ceased after one mole equiv of H_2 had been consumed. The crude product (170 mg colorless liquid) was separated in the usual manner. No by-products were revealed by VPC but the NMR spectrum of the product shows a mixture of two components (ca. 4:1), presumably a mixture of stereoisomers at C_{11}. (Found: C, 76·20; H, 10·33. $C_{15}H_{24}O_2$ requires: C, 76·22; H, 10·24%). M^+ was measured at m/e 236 ($C_{15}H_{24}O_2$ requires 236); ν_{max}(liquid) 2930, 1768 (γ-lactone), 1465, and 980 cm^{-1}. NMR data ($CDCl_3$; 100 Mc/s): a doublet (J = 6·0) at 0·82 (3H, C_4-Me), a singlet at 0·96 (3H, C_5-Me), a doublet (J = 7·0) at 1·05 (3H, C_{11}-Me), a multiplet at 2·29 (1H, H_{11}), a doublet of doublet (J = 8·8 and 4·5) at 3·79 (1H, H_{12b}), and a doublet of doublet (J = 8·8 and 6·1) at 4·26 (1H, H_{12a}) and also see Fig. 2.

Bakkenolide-A diol (3). To a dispersion of LAH (21 mg) in dry ether (5 ml) was added dropwise a soln of 1 (99 mg) in dry ether (7 ml) during 17 min under ice-cooling and stirring. After 50 min, cold water and dil HCl were added. The ethereal layer was separated and followed by washing with water and drying over $MgSO_4$. A colorless crystalline solid (100 mg) was obtained on evaporation of the solvent. Recrystallization from n-pentane gave needles of 3 m.p. 81–81·5°. (Found: 75·72; H, 10·96. $C_{15}H_{26}O_2$ requires: C, 75·58; H, 11·00%). The molecular ion was not detectable in the mass spectrometer but M-H_2O was at m/e 220 ($C_{15}H_{24}O$ requires 220); ν_{max}(KBr) 3280(OH), 1640 and 890 cm^{-1} ($C{=}CH_2$). NMR data ($CDCl_3$; 100 Mc/s): a doublet (J = 6·0) at 0·74 (C_4—Me), a singlet at 0·87 (C_5—Me), a pair of doublets (J = 14·0) at 2·04 and 1·17 (H_{6a} and H_{6b}), a broad singlet at 3·00 (2H, two OH), a pair of doublets (J = 10·5) centered at 3·37 (each 1H, H_{8a} and H_{8b}), a broad singlet at 4·12 (2H, H_{12a} and H_{12b}), and two multiplets at 5·24 and 5·09 (H_{13a} and H_{13b}). See Fig. 3.

Diacetate 4 *of bakkenolide*-A *diol* (3). Treatment of 3 (42 mg) with Ac_2O (2 ml) and pyridine (2 ml) gave the corresponding diacetate as a colorless liquid (52 mg) which was chromatographed on silica gel, Elution with benzene yielded pure 4. The molecular ion was too weak to measure in the mass spectrometer but M-CH_3COOH was at m/e 262 ($C_{17}H_{26}O_2$ requires 262); ν_{max}(liquid) 1745 (acetate), 1643 ($C{=}CH_2$), 1236 (acetate), and 905 cm^{-1} ($C{=}CH_2$). NMR data (benzene; 60 Mc/s): a doublet (J = 5·7) at 0·71 (C_4—Me), a singlet at 0·79 (C_5—Me), a pair of doublets (J = 14·0) at 2·02 (H_{6a}) and 1·10 (H_{6b}), two singlets at 1·72 and 1·75 (each 3H, two acetyl), a pair of doublets (J = 15·4) centered at 3·91 (2H, H_{8a} and H_{8b}), a multiplet at 4·65 (2H, H_{12a} and H_{12b}), and two multiplets at 5·17 (H_{13a}) and 5·05 (H_{13b}).

C_{11}-*Dicarboxylic acid* (5). To a dispersion of B–A (192 mg) in 2N KOH was added dropwise a soln of $KMnO_4$ (2·09 g) in 60 ml 2N KOH under ice-water cooling for 3·6 hr. After removal from the ice bath, stirring was continued for 16 hr at room temp. MeOH was added to the resulting dark greenish mixture under ice-cooling to destroy excess $KMnO_4$. The resulting ppt of MnO_2 was separated by filtration and washed with hot dil alkali twice. The combined aqueous layer was washed with ether twice and acidified with aqueous HCl and then extracted with $CHCl_3$ thrice. The $CHCl_3$ extracts were washed with water and evaporated to dryness to give a semi-solid (66 mg). Recrystallization from cyclohexane gave colorless fine needles. m.p. 138·5–139·0°. (Found: C, 61·66; H, 8·53. $C_{11}H_{18}O_4$ requires: C, 61·66; H, 8·47%); ν_{max} (KBr); 3500–2300 (COOH, broad), 1720 (COOH), 1689, 1289, 1110, and 980–830 cm^{-1} (broad). NMR data ($CDCl_3$ containing about 5% benzene; 100 Mc/s): a doublet (J = 6·5) at 0·80 (3H, C_4—Me), a singlet at 1·22 (3H, C_5—Me), a doublet (J = 16·6) of doublet (J = 2·3) at 2·16 (1H, H_{9b}), a diffuse doublet (J = 9·6) at 2·42 (1H, H_{10}), and a doublet (J = 16·6) of doublet (J = 9·6) (1H, H_{9a}).

From B–A diol (3). To a mixture of 3 (389 mg) in cyclohexane (50 ml) and 1N NaOH (40 ml) was added dropwise a soln of $KMnO_4$ (4·07 g) in water (130 ml) under ice-cooling. After removal from the ice bath, the stirring was continued for 61 hr. The excess $KMnO_4$ was destroyed with EtOH and the resulting ppt of MnO_2 was filtered off. The MnO_2 was washed thoroughly with 0·5N NaOH. After the cyclohexane

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* S, strong; M, medium; W, weak; V, very.

layer was separated, the combined aqueous layer was extracted with ether to remove neutral materials. The resulting aqueous layer was acidified to pH ca. 2 with 4N HCl and then extracted with ether 4 times (50 ml and 30 ml × 3). The extracts were washed with water, dried over $MgSO_4$ and evaporated to give a white solid (213 mg), which was divided into a n-pentane soluble part and insoluble part (93 mg). The former gave the C_{11}-dicarboxylic acid (156 mg), which was recrystallized from water to afford colorless needles, m.p. 140–141·5°. Trituration of a part of the latter with cyclohexane to obtain crystals resulted in decomposition and gaseous evolution. Treatment of another part of this with ethereal diazomethane gave a colorless liquid which was identified as C_{13}-dicarboxylic acid dimethylester (**10**) by VPC.

Acid anhydride (**6**). In a sealed tube a soln of **5** (23 mg) in Ac_2O (0·1 ml) was heated at 140–160° for 1·5 hr. After the solvent was evaporated, the resulting colorless liquid was kept *in vacuo* until the odour of Ac_2O disappeared. The crude acid anhydride (21 mg) contained ca. 14% of starting material (NMR evidence); ν_{max}(liquid) 2940, 1803 and 1760 (anhydride), 1034, 995 and 953 cm^{-1}. NMR data (CCl_4 containing ca. 5% benzene; 100 Mc/s): a d ($J = 7{\cdot}2$) at 0·92 (C_4—Me), a s at 1·22 (C_5—Me), a d of d ($J = 18{\cdot}4$ and 5·4) at 2·53 (1H, H_{9b}), a d of d ($J = 18{\cdot}4$ and 6·2) at 2·79 (1H, H_{9a}), and m at near 2·22* (C_4—H) and near 1·93† (C_{10}—H).

Dimethylester (**7**) *of* C_{11}*-dicarboxylic acid*. A soln of crude **5** (175 mg) in ether was treated with ethereal diazomethane under ice-cooling. The soln was washed successively with Na_2CO_3aq and water, and then dried. Evaporation of the solvent gave **7** as a colourless liquid (161 mg). A portion (141 mg) of this was chromatographed on 4 g silica gel in benzene–cyclohexane (3:2). Fractions containing the desired product were pooled and concentrated giving 117 mg of **7**, which was distilled at 1·5 mmHg and 91° (bath temp). (Found: C, 64·49; H, 9·19. $C_{13}H_{22}O_4$ requires: C, 64·44; H, 9·15%). M^+ was measured at *m/e* 242 ($C_{13}H_{22}O_2$ requires 242); ν_{max}(liquid); 2950, 1746 (ester), 1438, 1241, 1169 and 1101 cm^{-1}.

Ester exchange ($COOCH_3$ *to* $COOCD_3$). The dimethylester **7** (20 mg) was dissolved in MeOH-d_4 (0·32 ml) and the NMR spectrum was measured. To this soln in the NMR tube was added a soln of MeONa-d_3 in MeOH-d_4 [prepared by addition of Na (19 mg) to MeOH-d_4 (0·19 ml)] at room temp (22–26°). The first run of the NMR measurement started after 10 min. Inspection of the spectrum indicated when the exchange was complete. After standing for 27 hr at room temp and the solvent was distilled off under N_2 at 90° (bath temp), new MeOH-d_4 (about 0·1 ml) was added. After this operation was repeated thrice and followed by standing for 17 hr at 53–55°, the NMR was measured. The spectrum of this run revealed that no perceptible change in the ratio of $COOCH_3$ to $COOCD_3$ had occurred and any exchange of the active methylene protons to deuteriums at α-position of the carbomethoxy group was not observed (3H, 1·7–2·6 ppm) but the shape of the spectrum in this region was affected.

13-*Nor*-12-*oxo*-*bakkenolide*-A (**8**). To a soln of **1** (446 mg) in a mixture of dioxan (36 ml), water (8 ml) and AcOH (4 ml) was added 2 ml osmium tetroxide soln [prepared from osmium tetroxide (254 mg, 1 mmol), dioxan (10 ml) and water (3 ml)] and sodium periodide (1·60 g) during 15 min. After the mixture was stirred at room temp for 20 hr, it was diluted with water. The ethereal extract of the mixture was washed successively with Na_2CO_3aq and water and then dried and concentrated. The crude product (460 mg) was recrystallized twice from n-pentane to give a pure sample (368 mg, prisms), m.p. 106·5–107°. (Found: C, 71·09; H, 8·63. $C_{14}H_{20}O_3$ requires: C, 71·16; 8·53%). M^+ was measured at *m/e* 236 ($C_{14}H_{20}O_3$ requires 236); ν_{max}(KBr) 2930, 1794, and 1747 (γ-lactone and ketone), 1278, 1052 and 1135 cm^{-1}. NMR data ($CDCl_3$; 100 Mc/s): a d ($J = 6{\cdot}8$) at 0·80 (C_4—Me), a s at 0·99 (C_5—Me), a pair of d ($J = 13{\cdot}7$) at 1·76 (H_{6b}) and 2·10 (H_{6a}), and a s at 4·60 (2H, H_{12a} and H_{12b}). This compound sublimated at 91° (bath temp) under 1·8 mmHg.

During another run [241 mg of **1** was used], the crude product was purified by chromatography on neutral alumina to afford a colorless liquid (**14**; 59 mg) as well as **8** (119 mg). This liquid had IR absorption (liquid) at 3450(OH), 2960, 1716 (C=O), 1464, 1076 and 965 cm^{-1}. Acetylation of **14** (68 mg) in the usual way gave a mixture (64 mg) of two acetates (from NMR analysis) as colorless liquid. These acetates are presumably stereoisomers at C_7 of ketoacetate (**15**). After chromatography on silica gel, the IR, NMR, and mass spectra of the mixture of the two stereoisomers were measured. M^+ was not detectable but M—CH_3COOH was at *m/e* 192 ($C_{13}H_{20}O$ requires 192); ν_{max}(liquid) 2920, 1750 (acetate), 1728 (C=O), 1467, 1378, 1234 (acetate), 1041, and 840 cm^{-1}. NMR data (CCl_4; 60 Mc/s): C_4—Me (d, $J = 5{\cdot}5$ at 0·78

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* Irradiation at 2·22 caused collapse of the doublet of C_4-Me to singlet.

† Irradiation at 1·93 collapsed two pairs of doublets of doublet of H_{9a} and H_{9b} to a pair of doublets ($J = 18{\cdot}4$).

and 0·75), C_5—Me (s at 0·88 and 0·86), H_7 (m at near 2·92), H_{12a} and H_{12b} (s at 4·51), and CH_3COO— (s at 2·05).

C_{13}-*Dicarboxylic acid* (**9**). To a soln of **8** (100 mg) in dioxan (17 ml) was added dropwise a sodium hypobromide soln [prepared from NaOH (2·2 g), water (17 ml) and Br_2 (312 mg)] for 35 min under ice-cooling and stirring. After 15 min, the ice-cooling was removed and the stirring was continued for 14 hr at room temp. Small amount of $NaHSO_3$ was added to the reaction mixture, which was concentrated under reduced press on a water bath (90°). It was then acidified with dil HCl and again extracted four times with ether. The crude acid (94 mg) was obtained from the final ether extracts as a semi-solid, a portion of which was esterified with ethereal diazomethane. The resulting crude ester contained about 90% of a main product accompanies by five components (by VPC analysis). This dimethyl ester was chromatographed on silica gel to give a pure sample (**10**). (Found: C, 67·41; H, 9·01. $C_{15}H_{24}O_4$ requires: C, 67·13; H, 9·02%). M^+ 236 ($C_{15}H_{24}O_4$ requires 236); ν_{max}(liquid) 2950, 2920, 1737 (ester), 1437, 1252 (ester), and 1157 cm^{-1}. NMR data (CCl_4; 60 Mc/s): a d (J = 5·1) at 0·77 (C_4—Me), a s at 0·88 (C_5—Me), a pair of ds (J = 14·5) at 1·76 (H_{6b}) and 2·46 (H_{6a}), a m at 1·6–2·4 (3H), and a s at 3·65 (6H, two methyls of esters).

Diacetate (**11**). The crude **9** (126 mg) was dissolved in dry benzene (1 ml) and pyridine (114 mg). To the soln was added lead tetraacetate (337 mg). After the vigorous evolution of CO_2 ceased, the mixture was heated under reflux. When the mixture became paste, it was dissolved by addition of dry benzene (twice, each 1 ml). After 45 min additional lead tetraacetate (192 mg) was added and the refluxing was continued for another 3·5 hr. The mixture was then cooled and diluted with ether. After the inorganic ppt was filtered off, the filtrate was extracted thrice with ether. The combined extracts were washed successively with dil HCl, $NaHCO_3$ and water and then dried and concentrated to afford a colorless liquid (80 mg). This product was not purified and the IR spectrum was measured; ν_{max}(liquid) 2910, 1860, 1754 and 1738 (acetate), 1464, 1370, 1241 (acetate), 1190 and 1005 cm^{-1}.

cis-3a,4-*Dimethylhexahydroindanone*-2 (**12**). The crude diacetate obtained as described above was hydrolysed with 7% KOH aq in aqueous MeOH (5 ml) at room temp. Extraction with ether followed by the usual work up afforded a yellowish liquid (44 mg); $_{max}$(liquid) 2920, 2860, 1743 (C=O), 1464, 1408, 1380, 1203, 1121 cm^{-1}.

The optical rotatory dispersion in MeOH showed a strong negative cotton effect having two troughs at 325 mμ and 313 mμ but the correct magnitude of the rotation was not determined because the sample was not pure. This product yielded a 2,4-dinitrophenylhydrazone without purification.

2,4-*Dinitrophenylhydrazone of* **12** *and identification*. The perhydroindanone derivative (**12**) gave a 2,4-dinitrophenylhydrazone, which was purified by successive chromatography on alumina and silica gel. Elutions in both cases with benzene gave orange colored crystals as prisms. This 2,4-dinitrophenylhydrazone was identical with that derived from fukinone (**13**) by comparison of IR spectrum and mixed m.p. (142·5–144°), (m.p. of our sample was 142·3–144·2°), ν_{max}(KBr) 3300 and 3080 (NH), 2910, 1623 (phenyl), 1591, 1505, 1417, 1339, 1301, 1136, 1068, 912, 832, and 744 cm^{-1}.

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