assumptions of any kind being made.

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Registry No. 1, 28927-63-1; 1 Li, 82338-17-8; 1 K, 82338-18-9; 1 MgBr, 82351-39-1; 2-*3-d*, 82338-19-0; 4 Li, 82338-20-3; 5, 645-49-8; 17, 1564-64-3; 18, 90-11-9; 19, 108-86-1; 22-*3-d*, 73908-49-3; 23, 3806-60-8; chlorobenzene, 108-90-7; nitrobenzene, 98-95-3; naphthalene, 91-20-3; stilbene radical anion, 34467-73-7; anthracene, 120-12-7; anthracene radical anion, 34509-92-7; 1,3-cyclooctadiene, 1700-10-3; potassium *tert*-butoxide, 865-47-4; butyllithium, 109-72-8; potassium, 7440-09-7; 1,4-cyclooctadiene$(AgNO_3)_2$, 82338-21-4; magnesium bromide, 7789-48-2; cyclooctadienylnaphthalene, 82338-22-5.

Reaction and Interconversion of Norditerpenoid Dialactones, Biologically Active Principles Isolated from *Podocarpus* Plants[1]

Yuji Hayashi* and Takeshi Matsumoto

Faculty of Science, Osaka City University, Sumiyoshiku, Osaka 558, Japan

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The reactions of the B/C ring system and the ring A functional groups of the norditerpenoid dilactones isolated from *Podocarpus* plants are described. The interconversion of the three structural types of the natural dilactones is also presented, being focused on the transformation of type A (8(14),9(11)-dienolides) and type B (7α,8α-epoxy-9(11)-enolides) into type C (7(8),9(11)-dienolides) dilactones, minor constituents but biologically the most interesting type of the dilactone members.

Since 1968, there have been reported more than 40 norditerpenoid dilactones isolated from various species of *Podocarpus* plants.[2-11] Particularly, the constituents of the species *P. nagi* (Thunberg) Pilger[8] have been investigated most extensively in relation to their remarkable biological activity, including antitumor activity,[9,12] plant growth inhibitory activity,[13-15] termiticidal activity,[16] and insect toxicity.[17] The dilactones are classified into three major subgroups in accordance with the structure of the B/C ring part: A, α-pyrone [8(14),9(11)-dienolide] type; B, 7α,8α-epoxy-9(11)-enolide type; C, 7(8),9(11)-dienolide type.[15] It should be noted that the dilactone members in each of these structural types show fine differences in their biological activity. For example, type B, e.g., nagilactone E (**5**), and type C, e.g., nagilactone F (**6**), generally show stronger activity than type A for antitumor or plant growth inhibitory activity; especially for the latter effect, types B and C exhibit a simple inhibitory effect (≥0.005 ppm) proportional to the dilactone concentration, while type A dilactones, e.g., nagilactone B (**2**), show a dual activity, inhibitory (>0.5 ppm) or promotive (<0.05 ppm) depending on the concentration,[15] which may indicate their role as a growth regulator in the plant. The termiticidal activity has been found for only inumakilactone A (**11**, type B)[16] and nagilactone D (**4**, type A)[18] in spite of their natural coocurrence with other dilactones. Nagilactone D (**4**) is also sufficiently toxic (ED_{50} 0.7 ppm) for larvae of housefly and Lepidoptera,[17c] while the other 11 dilactones tested were $10-10^2$ times less active than **4**.

It is worthwhile to study the chemical reactivity and the interconversion of the three types of the dilactone members, since minor dilactones, particularly type C, were to be derived from other types of members for practical purposes, e.g., the synthetic study of nagilactone F (**6**)[19] and various biological investigations. Only a limited number of publications has dealt with the reactivities of the dilactones except for the preparation of simple functional derivatives for structure determination. This would be due to the poor content of the dilactone components in plant materials. Fortunately, we have collected a considerable quantity of seeds and root bark of *P. nagi*, which

(1) This article is dedicated to Emeritus Professor Takeo Sakan of Osaka City University for the 70th anniversary of his birth.
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(3) S. Ito, M. Kodama, M. Sunagawa, T. Takahashi, H. Imamura, and O. Honda, *Tetrahedron Lett.*, 2065 (1968).
(4) Reviews: K. S. Brown, Jr., and W. E. Sanchez L., *Biochem. Syst. Ecol.*, **2**, 11 (1974); S. Ito and M. Kodama, *Heterocycles*, **4**, 595 (1976).
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(14) Y. Hayashi, J. Yokoi, Y. Watanabe, T. Sakan, Y. Masuda, and R. Yamamoto, *Chem. Lett.*, 759 (1972).
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(16) I. Saeki, M. Sumimoto, and T. Kondo, *Holzforschung*, **24**, 83 (1970).
(17) (a) G. B. Russell, P. G. Fenemore, and P. Singh, *J. Chem. Soc., Chem. Commun.*, 166 (1973); (b) P. Singh, P. G. Fenemore, and G. B. Russell, *Aust. J. Biol. Sci.*, **26**, 911 (1973); (c) P. Singh, G. B. Russell, Y. Hayashi, R. T. Gallagher, and S. Fredericksen, *Entomol. Exp. Appl.*, **25**, 121 (1979).
(18) M. Sumimoto, private communication.
(19) Y. Hayashi, T. Matsumoto, T. Hyono, N. Nishikawa, M. Uemura, M. Nishizawa, M. Togami, and T. Sakan, *Tetrahedron Lett.*, 3311 (1979); *J. Org. Chem.*, following paper in this issue.

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contain much more dilactones than other more accessible parts of the plant, leaves, bark, and timber. The abundant dilactones in hand were nagilactones A and C (1 and 3, type A) from seeds and E (5, type B) from root bark. Accordingly, our studies on the reactivity have been focused on their transformation into the type C dilactone, much less available from natural sources.

Results and Discussions

Transformation of the B/C Ring Part. Hydrogenation of podolide (12),[9] prepared by dehydration of nagilactone E (5) as described below, with 10% Pd/C under uptake of 2 equiv of hydrogen gave a mixture of two compounds, a tetrahydro and a hexahydro derivative, 13 and 14, which were separable by column chromatography. Both of the compounds showed no olefinic proton signals, but 13 exhibited tetrasubstituted olefinic carbon signals at δ 127.4 and 138.9, which indicated the presence of the double bond at 8(9)-position.[20] 13 was smoothly converted with methanesulfonyl chloride in pyridine to a single dehydration product, completely identical with nagilactone F (6). This procedure supplied a quantity of nagilactone F sufficient for transformation to the important intermediates for its total synthesis.[19] An analogous dehydration of the hexahydro compound 14 gave 9,11-dihydronagilactone F (17), which was characterized by spectral analysis.

Direct hydrogenation of nagilactone E (5) proceeded similarly at the B/C ring part, giving a mixture of three components on absorption of 1 equiv of hydrogen.[21] However, nagilactone E acetate (5a) gave a much simpler result under the same conditions. On absorption of 1 equiv of hydrogen, only a cleavage of the 7,8-epoxy group took place, yielding 7α-hydroxy-9(11)-enolide 16a in a quantitative yield. The product 16a was dehydrated by phosphorus oxychloride in refluxing pyridine to form a 7-(8),9(11)-dienolide. This compound was identical with the acetate 8a of natural 3β-hydroxynagilactone F isolated from *P. nagi* (root bark).[8] The structure of the intermediate 16a was assigned on the basis of the ^{1}H NMR, in which H-11 and H-8 appeared as a doublet ($J_{8,11}$ = 2.5 Hz) at 6.01 ppm and a triple doublet ($J_{8,11}$ = 2.5, $J_{8,7}$ = 11.2, and $J_{8,14}$ = 11.2 Hz) at 3.01 ppm, respectively. The coupling constant $J_{8,14}$ shows a trans-diaxial orientation of both protons. This fact indicates hydrogen incorporation at C-8 from the less hindered α side.[22]

Hydrogenation of the type B dilactone with platinum catalyst gave rise to saturation of the 9,11 double bond prior to the epoxide opening; thus, 9,11-dihydronagilactone E was produced from 5 (see Chart I).

The reductive cleavage of the 7,8-epoxy group also took place with chromium(II) reagent. Nagilactone E was converted to diol 15 as a single product by the action of chromium(II) perchlorate in DMF in a moderate yield. The structure of 15 was established by mass spectral determination of the elemental composition and ^{1}H NMR correlation with the $\Delta^{8,9}$-7α-ol 13 derived from podolide (12). Dehydration of 15 proceeded quantitatively to form another type C dilactone, which was characterized as 2,3-dehydronagilactone F (18) by spectral analysis. In this compound, the B/C ring protons show an allylic ($J_{7,14}$ = ~2.0 Hz) and a homoallylic ($J_{6,14}$ = ~2.0 Hz) coupling, characteristic of type C dilactones.[14] The skeletal carbons show comparable δ values to those of podolide (12, for the ring A carbons) and nagilactone F (6, for the B/C ring carbons).[23] Hembree et al. recently reported milanjilactone B[10] as a component of *P. milanjianus* from Kenya and gave structure 20 for this compound. They have referenced its ^{1}H NMR data to those of podolactone D (21)[24] presented by the Australian workers. However, the latter authors have suggested revision of the structure of 21 to a 2:3 unsaturated formula in a later publication.[25] From the correlation of the ^{1}H NMR δ values,[26] compound 18 is, accordingly, identical with milanjilactone B.

The type B dilactones underwent another type of conversion at the B/C ring part. Refluxing of nagilactone E (5) with a large excess of alumina in benzene produced an acidic product, 22, in 73% yield after extraction from an acidified reaction mixture. The compound shows a UV absorption maximum at 260 nm, consistent with the 7-(8),9(11)-dienolide system. The spin–spin interactions for H-5/H-6, H-6/H-7, and H-7/H-11 were confirmed by decoupling experiments. The corresponding 3-acetate 22a was also formed from nagilactone E acetate (5a) under the same conditions. The acidic nature of 22 and 22a was shown by easy esterification with diazomethane. The UV absorption of the methyl ester 23 at 248 nm indicated the presence of a cross-conjugated system as shown in the formula. The appearance of the H-15 signal as a sharp quintet (J = 7.0 Hz) at 3.01 ppm (α hydrogen to the carbonyl group) and the carbonyl carbon signal (C-14) at 203.6 ppm supported this structure. 22 was reduced with sodium borohydride, and the product was fractionated over silica gel to give a type C dilactone identical with 3β-hydroxynagilactone F (8).[8]

A 7β-acetoxy derivative of the type A dilactones has been known to form a type C compound with sodium borohydride.[2,14,27] For example, nagilactone A diacetate (1a) and nagilactone C 7-monoacetate (3a) gave dienolides 24 and 25, respectively, in which the isopropyl group occupied a 14β orientation, epimeric to the natural type C dilactone at C-14 (25 corresponds to the 14-epimer of ponalactone A (26)[28]). A similar type of double bond migration from an 8:14- to 7:8-position also took place quantitatively under photolytic conditions with concomitant introduction of a hydroxyl (or a methoxyl) group at C-14.[29] When nagilactone A diacetate (1a) was irradiated with a high-pressure mercury lamp (Pyrex filter) in methanol, the starting material was rapidly replaced by a 1:1 mixture of an ep-

(20) Absence of any appreciable UV maximum supported this assignment.

(21) Separation of the mixture was not attempted, but the components were tentatively assigned as two dihydro compounds, 15 and 16, and a corresponding saturated analogue of 16 by mobility on a TLC plate and dehydration to a mixture of 18 and its 9,11-dihydro analogue 19. The structure of 19 was determined by the spectral correlation with 9,11-dihydronagilactone F (17).

(22) M. N. Galbraith, D. H. S. Horn, S. Ito, M. Kodama, and J. M. Sasse, *Agr. Biol. Chem. (Tokyo)*, **36**, 2393 (1972).

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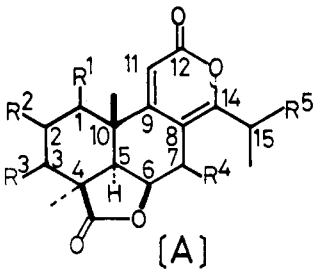
(26) The reported δ value (5.80–6.05, m) due to the ring A olefinic protons of milanjilactone B seems somewhat different from that of 18 (5.90, 2 H, br s). In 18, however, the olefinic protons exhibited narrow AB-type signals, which appear as a broad singlet centered at 5.90 ppm accompanied by weak satellite signals around 5.80 and 6.05 ppm, consistent with the reported range for milanjilactone B. If the ring A double bond is placed at the 1(2)-position, the δ value difference of the olefinic protons H-1 and H-2 should be much larger, as observed for the compounds 33 and 33a, because of the anisotropic influence of the ring C to H-1. Direct comparison of the both compounds was not achieved.

(27) This reaction does not proceed with the corresponding 7-hydroxy analogues.

(28) S. Ito, M. Kodama, M. Sunagawa, M. Koreeda, and K. Nakanishi, *J. Chem. Soc. D* 855 (1971).

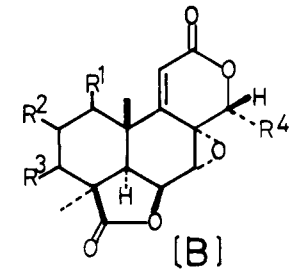
(29) A hydroxyl group was introduced at C-14 under other conditions, e.g., with hot mineral acid or with CrO_3 in pyridine (see ref 2).

Chart I



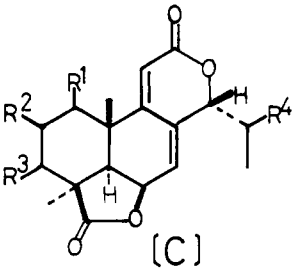
[A]

1, $R^1 = R^4 = \beta$-OH; $R^2 = R^3 = H$; $R^5 = CH_3$
1a, $R^1 = R^4 = \beta$-OAc; $R^2 = R^3 = H$; $R^5 = CH_3$
2, $R^1 = R^2 = R^4 = \beta$-OH; $R^3 = H$; $R^5 = CH_3$
3, $R^1,R^2 = \beta$-O<; $R^3 = R^4 = \beta$-OH; $R^5 = CH_3$
3a, $R^1,R^2 = \beta$-O<; $R^3 = \beta$-OH; $R^4 = \beta$-OAc; $R^5 = CH_3$
4, $R^1,R^2 = \beta$-O<; $R^3 = \beta$-OH; $R^4,R^5 = H$
4a, $R^1,R^2 = \beta$-O<; $R^3 = \beta$-OAc; $R^4 = R^5 = H$
29, $R^1 = \alpha$-Cl; $R^2 = R^3 = \beta$-OH; $R^4 = R^5 = H$
29a, $R^1 = \alpha$-Cl; $R^2 = R^3 = \beta$-OAc; $R^4 = R^5 = H$
30, $R^1 = R^3 = \beta$-OH; $R^2 = \alpha$-Cl; $R^4 = R^5 = H$
30a, $R^1 = \beta$-OH; $R^2 = \alpha$-Cl; $R^3 = \beta$-OAc; $R^4 = R^5 = H$
30b, $R^1 = R^3 = \beta$-OAc; $R^2 = \alpha$-Cl; $R^4 = R^5 = H$
34, $R^1 = R^2 = H$; $R^3 = R^4 = \beta$-OH; $R^5 = CH_3$
40, $R^1 = H$; $R^2,R^3 = \beta$-O<; $R^4 = \beta$-OH; $R^5 = CH_3$



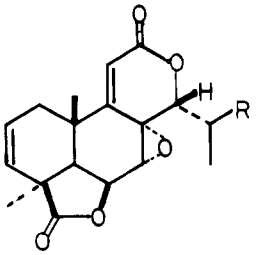
[B]

5, $R^1 = R^2 = H$; $R^3 = \beta$-OH; $R^4 = CH(CH_3)_2$
5a, $R^1 = R^2 = H$; $R^3 = \beta$-OAc; $R^4 = CH(CH_3)_2$
9, $R^1 = R^2 = H$; $R^4 = CH(CH_3)_2$; $R^3 = \beta$-$OPO(OH)_2$
10, $R^1 = R^2 = H$; $R^4 = CH(CH_3)_2$; $R^3 = \beta$-$OPO(OCH_3)_2$
11, $R^1,R^2 = \beta$-O<; $R^3 = \beta$-OH; $R^4 = CH(OH)CH_3$
31, $R^1 = H$; $R^2,R^3 = \beta$-O<; $R^4 = CH{=}CH_2$
32, $R^1 = H$; $R^2,R^3 = \beta$-O<; $R^4 = CH(CH_3)CH_2OH$
39, $R^1 = H$; $R^2,R^3 = \beta$-O<; $R^4 = CH(CH_3)_2$

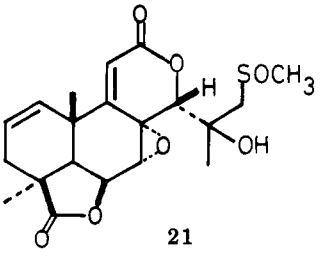


[C]

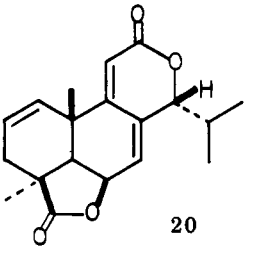
6, $R^1 = R^2 = R^3 = H$; $R^4 = CH_3$
7, $R^1 = \beta$-OH; $R^2 = R^3 = H$; $R^4 = CH_3$
7a, $R^1 = \beta$-OAc; $R^2 = R^3 = H$; $R^4 = CH_3$
8, $R^1 = R^2 = H$; $R^3 = \beta$-OH; $R^4 = CH_3$
8a, $R^1 = R^2 = H$; $R^3 = \beta$-OAc; $R^4 = CH_3$
26, $R^1,R^2 = \beta$-O<; $R^3 = \beta$-OH; $R^4 = CH_3$



12, R = CH_3
36, R = CH_2OH



21



20

imeric pair (at C-14) of 14-methoxydienolide **27**.[30] The irradiation of **1a** in aqueous THF produced the corresponding 14-hydroxy analogue **28** which shows chemical properties compatible with the 14-hydroxydienolides **22** and **22a**. Reduction of **28** with an excess of sodium borohydride in the presence of cerium chloride[31] gave two products, separable by preparative TLC. The higher R_f component was characterized as 14α-isopropyldienolide **7a**, the 1β-acetoxyl group of which was readily hydrolyzed with potassium carbonate in methanol. The 1β-hydroxy compound obtained was identical with nautral 1β-hydroxynagilactone F (**7**) isolated from *P. nagi* (root bark).[32] Thus, type C dilactone was successfully correlated with type A, nagilactone A (**1**), established by X-ray crystallography.[33] The lower R_f product from the borohydride reduction was identified with **24**, directly derived from **1a**.

Epoxidation of the 7(8)-double bond of type C dilactones to lead the type B gave no successful results after a variety of attempts.

Transformation of the Ring A Functional Groups. When nagilactone E (**5**, Scheme I) was treated with 1.2 equiv of tosyl chloride in refluxing pyridine, a dehydrated product was produced in an excellent yield. The product was identical with podolide (**12**), which has been isolated from an African *Podocapus*, *P. gracilior*,[9] as an antitumor component. With phosphorus oxychloride in pyridine, the same elimination of the 3-hydroxyl group took place at 70 °C, but the corresponding 3-dihydrogen phosphate **9** was

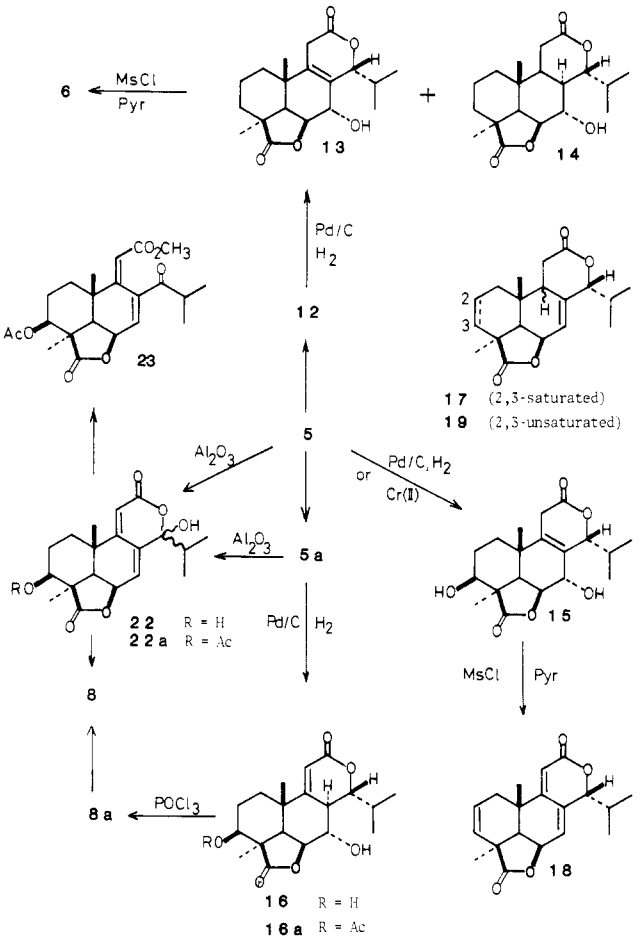
(30) Two epimeric components were separable by multidevelopment on TLC plate. Each component was characterized on a spectral basis (see Experimental Section). However, the assignment of their C-14 configuration remains undetermined. Conversion of **27** to **28** by acid treatment was not successful.

(31) J.-L. Luche, *J. Am. Chem. Soc.*, **100**, 2226 (1978). Reduction without $CeCl_3$ gave a lower yield of the desired product.

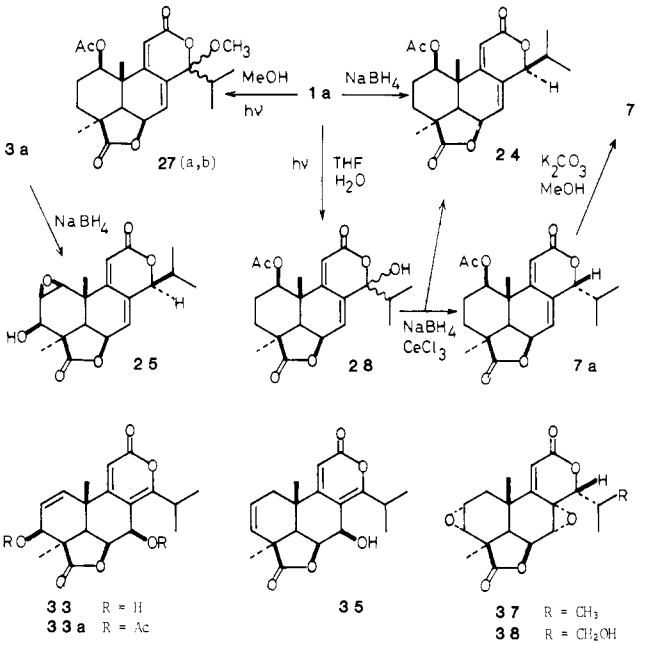
(32) Y. Hayashi, T. Matsumoto, and T. Nose, unpublished result.

(33) Y. Hayashi, T. Sakan, K. Hirotsu, and A. Shimada, *Chem. Lett.*, 349 (1972); K. Hirotsu, T. Higuchi, A. Shimada, Y. Hayashi, and T. Sakan, *Bull. Chem. Soc. Jpn.*, **48**, 1157 (1975).

Scheme I



Scheme II



isolable at 20 °C, which was characterized as the crystalline dimethyl ester **10**.

The β epoxide on ring A, which appears in many natural dilactones, underwent a cleavage under acidic conditions in contrast to the poor reactivity of $7\alpha,8\alpha$-epoxy group. The reactions of inumakilactone A (**11**)[34] and sellowins A (**32**) and B (**31**)[25,35] (type B) with aqueous mineral acids or trifluoroacetic acid have been recorded. The ring A epoxide of type A dilactones is similarly accessible to acid cleavage. Thus, nagilactone D acetate (**4a**) gave isomeric chlorohydrins **29** and **30** by refluxing with hydrochloric acid. The two chlorohydrins were discriminated by periodate titration. On acetylation, **29** gave a single diacetate, **29a**, easily, while **30** produced a mixture (ca. 3:5) of 3-mono- and diacetate, **30a** and **30b**, under the same conditions. The well-known high-field shift of the H-11 signal on acetylation of the 1β-hydroxyl group[2] established the assigned structures: that is, practically no high-field shift was observed in the conversions from **29** (6.04 ppm) to **29a** (6.06 ppm) and from **30** (6.69 ppm) to **30a** (6.66 ppm), but a large shift ($\Delta\delta$ ca. 1) was observed in the conversion from **30** to **30b** (5.70 ppm). The relative configurations of the ring A substituents of **29** and **30** were determined from the following bases: (i) possible steric course on the epoxide opening by chloride anion; (ii) the vicinal coupling constants ($J_{1,2}$ and $J_{2,3}$) in the ^{1}H NMR are 2–4.5 Hz (a–e and e–e interactions) in **29** and its acetate **29a**, and 9.5–10 Hz (a–a interaction) in **30** and its acetates, **30a** and **30b**, considering that the ring A adopted a chair conformation.[36] Chlorohydrin **29** was also formed from nagilactone D (**4**) by heating (150 °C) with rhodium chloride in a sealed tube. The mechanism of this epoxide cleavage remains unclear.

The epoxide group of nagilactone C (**3**) was not susceptible toward hydrogenolysis, but deoxygenation with a chromium(II) reagent produced allylic alcohol **33** (Scheme II) in an acceptable yield.[37] The newly formed double bond was placed unambiguously at the 1(2)-position for the following reasons: (i) the H-1 signal (6.89 ppm) appears at ca. 0.7 ppm lower field than that of H-2 (6.17 ppm) due to the anisotropic effect of the 9:11-enolide system; (ii) ca. 30% of NOE was observed between H-1 and H-11; (iii) two doublet signals due to olefinic carbons, C-1 and C-2, are placed at 136.9 and 129.6 ppm, which are differentiated from those of 2(3) double bond.[23] Brown and Sanchez[35] have reported the simultaneous saturation of the double bond on a similar deoxygenation of **3** with Cr(II) or Zn–Cu, by which sellowin C (**34**) was correlated to nagilactone C (**3**) in one step. However, the 1,2-saturated analogue was not detected under our condition [$Cr(ClO_4)_2$/ethylenediamine/DMF]. Allylic alcohol **33** was reduced to the 2,3-unsaturated compound **35** with the double bond migration. The signals due to H-2 and H-3 of **35** appeared at ca. 5.88 ppm as a broad three-proton singlet overlapped with the H-11 signal. This value is consistent with those of the $\Delta^{2,3}$ olefinic protons as reported for podolide (**12**)[9,38] (H-2 and H-3, 5.88 ppm; H-11, 6.00 ppm) and 16-hydroxypodolide (**36**)[7] (H-2 and H-3, 5.92 ppm; H-11, 6.04 ppm). The $\Delta^{2,3}$ structure may be energetically more favorable than the $\Delta^{1,2}$ isomer in this system.

(34) T. Hayashi, H. Kakisawa, S. Ito, Y. P. Chen, and H.-Y. Hsu, *Tetrahedron Lett.*, 3385 (1972). The stereochemistry of the substituents at C-1 and C-2, assigned for the 1,2-halohydrins in this reference, is to be corrected to 1α-halo-2β-hydroxy structure, since the configuration of the 1,2-epoxy group in **11** has been revised to $1\beta,2\beta$-epoxy by X-ray analysis: J. E. Godfrey and J. M. Waters, *Aust. J. Chem.*, **28**, 745 (1975).

(35) K. S. Brown, Jr., and W. E. Sanchez L., *Tetrahedron Lett.*, 675 (1974).

(36) The ring A in the dilactones can be considered to take a chair form unless a double bond or an epoxy group exists in the 1(2)- or 2(3)-position. This is supported by the X-ray crystallography of the 2,7-bis(*p*-bromobenzoate) of nagillactone B (**2**), in which a large 2β-acyloxyl group still takes an axial orientation in a chair form of the ring A: T. Higuchi, K. Takahashi, K. Hirotsu, and Y. Hayashi, *Z. Kristallogr.*, **150**, 335 (1979).

(37) J. K. Kochi, D. M. Singleton, and L. J. Andrews, *Tetrahedron*, **24**, 3503 (1968).

(38) Y. Hayashi, T. Matsumoto, T. Hyono, and T. Sakan, *Chem. Lett.*, 1461 (1977).

That most of the natural dilactones with the ring A double bond exist in the $\Delta^{2,3}$ type would support this consideration.

Podolide (**12**), 16-hydroxypodolide (**36**), and **35** would be correlated with the natural dilactones, **39**,[7] sellowin A (**32**),[35] and **40**,[8] if 2β,3β-epoxidation could be accessible. However, reaction with *m*-chloroperbenzoic acid under forcing conditions[39] took place from the α side of the molecule, yielding α-epoxides **37** and **38** respectively, from **12** and **36**. The assignment of the α epoxide was based on the NMR parameters of the ring A protons. Attempts to prepare the desired β epoxide via 2,3-halohydrins were not successful.

Distribution of the dilactones in the plant seems to be localized depending on the structural types insofar as our investigation on *P. nagi*. Thus, seeds include highly oxygenated dilactones of type A (nine components[2,5,6]) exclusively, while root bark contains mostly types B and C with a lower oxidation stage (13 components[7,8,14,32]). This fact may imply the initial formation of the dilactones in the root as type B and/or C, which would behave as an allelochemics, being excreted to the environmental soil. Later transportation from the root to other parts of the plant may be possible, and the type A dilactones stored in the seed would effect control of its germination as a plant growth regulator.

Experimental Section

All melting points are uncorrected and were determined on a Yanagimoto Model MPJ-2 apparatus. Necessary spectra were recorded by following spectrometers: IR, JASCO Model IRE or A-102; UV, Hitachi Model 323; NMR, JEOL Model PS-100 (CW, 100 MHz) or Model FX-100 (FT, 100 MHz); mass spectra, JEOL Model D-300; CD, JASCO Model J-20. Microanalysis was performed on a Perkin-Elmer Model 240 automatic elemental analyzer. All organic solvents were purified by a standard procedure before use.

Isolation of Nagilactones A (1), C (3), D (4), and E (5). (a) Dried and granulated endosperms of mature seeds of *P. nagi*, collected in April or May at Nara Park, Nara, Japan, were placed in a large Soxhlet apparatus (700 mm high, 120 mm diameter). After being washed with enough hot hexane for 2–3 days to remove a large quantity of oil, the material was extracted with boiling $CHCl_3$ for 1 week. Evaporation of $CHCl_3$ gave a white crystalline mass (0.3% yield), which was a complex mixture of norditerpenoid dilactone components. The crude mixture was first recrystallized roughly from acetone/$CHCl_3$ several times, and the partially purified crystalline product was further fractionated by a SiO_2 column and preparative TLC with $CHCl_3$/acetone (10:1 for column and 2:1 for TLC). The main components, nagilactones A (**1**), B (**2**), C (**3**), and D (**4**),[2] were separated by the column chromatography, and other minor components[5,6] were separated by multidevelopment of TLC. (b) Fresh root bark, collected in May at Nara Park, was immediately digested with MeOH for 17 days at 20 °C. After evaporation of MeOH, the residual aqueous mixture was partitioned successively with hexane, ether, $CHCl_3$, and EtOAc. The fractions from ether and $CHCl_3$ exhibited a strong inhibitory activity on germination of *Lepidium* seeds. The combined crude material from both of the fractions (ca. 0.3% of fresh root bark) was fractionated over SiO_2 column with $CHCl_3$/acetone system. The main component, nagilactone E (**5**, ca. 0.1% of the fresh root bark), was obtained as pure crystals by a single chromatographic separation followed by recrystallization from $CHCl_3$/ether. The minor components[7,8,32] were separated on further fractionation by a multidevelopment of TLC ($CHCl_3$/acetone) and droplet countercurrent chromatography ($CHCl_3$/MeOH/H_2O).

Hydrogenation of Podolide (12). Podolide (950 mg) was dissolved in EtOH (1000 mL), and the solution was stirred with 300 mg of 10% Pd/C under H_2 (1 atm) at 25 °C for 24 h. During this period, approximately 2 equiv of H_2 were absorbed. Filtration and concentration of the solution gave 970 mg of a colorless crystalline product. Chromatography on SiO_2 (300 g) gave an unsaturated alcohol, **13** (615 mg, 65%), and a saturated alcohol, **14** (265 mg, 28%). **13**: mp 203 °C; IR ($CHCl_3$) 3400, 1768, 1723 cm^{-1}; ^1H NMR(py-d_5) (py = pyridine) δ 0.95 (3 H, s, CH_3), 1.0–1.3 (9 H, $3CH_3$), 2.11 (3 H, d, J = 6.0 Hz, H-5), 3.32 (2 H, br s, H-11), 5.0–5.1 (2 H, m, H-6, H-7), 5.27 (1 H, br s, H-14); ^{13}C NMR ($CDCl_3$) δ 15.4 (q, C-16), 17.3 (t, C-2), 19.8 (q, C-17), 21.4 (q, C-20), 24.4 (q, C-18), 27.4 (t, C-1), 30.1 (t, C-3), 30.6 (t, C-11), 35.0 (d, C-15), 35.3 (s, C-10), 41.7 (s, C-4), 50.0 (d, C-5), 70.0 (d, C-6), 84.4 (d, C-7), 86.0 (d, C-14), 127.4 (s, C-8), 138.9 (s, C-9), 170.7 (s, C-12), 182.2 (s, C-19). **14**: mp 283 °C; ^1H NMR (py-d_5) δ 0.91 (3 H, s, CH_3), 1.14 (3 H, d, J = 7.0 Hz, CH_3), 1.21 (3 H, d, J = 7.0 Hz, CH_3), 1.24 (3 H, s, CH_3), 1.98 (1 H, d, J = 6.5 Hz, H-5), 4.60 (1 H, dd, J = 5.0, 6.5 Hz, H-7), 4.75 (1 H, dd, J = 5.0, 11.5 Hz, H-14), 5.09 (1 H, t, J = 6.5 Hz, H-6); mass spectrum (20 eV), $M^+ - H_2O$ 318.1835 (calcd for $C_{19}H_{26}O_4$, 318.1830).

Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.82; H, 8.26.

Nagilactone F (6) by Dehydration of 13. To a solution of **13** (500 mg) in anhydrous pyridine (15 mL) was added 1.5 mL of CH_3SO_2Cl at 25 °C. The mixture was refluxed under argon for 6 h. The cooled mixture was evaporated under vacuum to dryness, and the residue was chromatographed on 30 g of SiO_2 with $CHCl_3$. Pure nagilactone F (**6**, 460 mg, 97%) was obtained by recrystallization from $CHCl_3$/ether, mp 225 °C.

9,11-Dihydronagilactone F (17) by Dehydration of 14. A solution of **14** (170 mg) in 2 mL of pyridine was refluxed with $POCl_3$ (0.5 mL) for 5 h. After workup as usual, the product, **17**, was purified on SiO_2 with $CHCl_3$ (82 mg, 51%); mp 179–181 °C; ^1H NMR ($CDCl_3$) δ 0.86 (3 H, s, CH_3), 0.98 (3 H, d, J = 7.0 Hz, CH_3), 1.12 (3 H, d, J = 7.0 Hz, CH_3), 1.35 (3 H, s, CH_3), 1.88 (1 H, d, J = 5.0 Hz, H-5), 4.63 (1 H, m, H-14), 5.00 (1 H, m, H-6), 6.00 (1 H, m, H-7); ^{13}C NMR ($CDCl_3$) δ 15.3 (q, C-16), 17.0 (q, C-17), 17.4 (t, C-2), 19.4 (q, C-20), 23.9 (q, C-18), 27.6 (t, C-3), 28.8 (t, C-1), 29.9 (d, C-15), 32.1 (t, C-11), 33.1 (s, C-10), 42.2 (s, C-4), 44.7 (d, C-9), 50.5 (d, C-5), 72.3 (d, C-6), 84.7 (d, C-14), 118.8 (d, C-7), 140.3 (s, C-8), 172.3 (s, C-12), 181.2 (s, C-19).

Anal. Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.43; H, 8.25.

This dehydration did not proceed with CH_3SO_2Cl or TsCl in pyridine as described for **13**.

Hydrogenation (Pd/C) and Subsequent Dehydration of Nagilactone E (5). Nagilactone E (**5**, 200 mg) was hydrogenated in EtOH (200 mL) with 100 mg of 10% Pd/C under 1 atm. The reaction was stopped when 1 equiv of hydrogen was consumed (ca. 1 h). The mixture was filtered, and the solvent was evaporated to leave 200 mg of a crystalline solid, which was a mixture of three components, **15**, **16**, and a corresponding perhydro compound on TLC analysis. This mixture was treated with $POCl_3$ (0.6 mL, 10 equiv) in pyridine (2.4 mL, 50 equiv) at 75 °C for 14 h. After decomposition with ice and workup as usual, a crude product (167 mg), a mixture of two components, was fractionated over SiO_2 (30 g) with $CHCl_3$. The major product was identified with 2,3-dehydronagilactone F (**18**), described below. The other minor component was characterized as its 9:11-dihydro analogue **19** by the spectral correlation with 9:11-dihydronagilactone F (**17**).

Hydrogenation (Pd/C) of Nagilactone E Acetate (5a). Nagilactone E acetate (**5a**, 50 mg), prepared from **5** conventionally (Ac_2O/pyridine, 25 °C, quantitative yield), was hydrogenated in EtOH (10 mL) with 10% Pd/C (25 mg) under 1 atm at 25 °C. The reduction was completed in 20 min after 1 equiv of H_2 was absorbed. The mixture was filtered and evaporated to give 46 mg (92%) of 7α-hydroxyenolide **16a** as fine colorless needles: mp 272 °C (sublime); UV (EtOH) 216 nm (ε 8900); IR ($CHCl_3$) 3380, 1772, 1713, 1700 cm^{-1}; ^1H NMR(py-d_5) δ 1.20 (3 H, d, J = 6.8 Hz, CH_3), 1.24 (3 H, d, J = 6.8 Hz, CH_3), 1.30 (3 H, s, CH_3), 1.44 (3 H, s, CH_3), 2.16 (3 H, s, Ac), 2.26 (1 H, d, J = 5.4 Hz, H-5), 3.01 (1 H, td, J = 2.5, 11.2, 11.2 Hz, H-8), 4.42 (1 H, dd, J = 1.7, 11.2 Hz, H-14), 4.73 (1 H, dd, J = 4.5, 11.2 Hz, H-7), 5.19 (1 H, dd, J = 4.5, 5.4 Hz, H-6), 6.01 (1 H, d, J = 2.5 Hz, H-11).

Anal. Calcd for $C_{21}H_{28}O_7$: C, 64.27; H, 7.19. Found: C, 64.20 H, 7.22.

3β-Acetoxynagilactone F (8a). A solution of **16a** (20 mg) and $POCl_3$ (0.5 mL) in dry pyridine (2 mL) was heated at 70–80

(39) Unusually poor reactivity of the ring A double bond has been reported (see ref 35).

°C for 5 h under N_2. After workup as usual, the product was recrystallized from $CHCl_3$/ether to afford dienolide **8a** (16 mg, 84%): UV (EtOH) 263 nm; ^1H NMR ($CDCl_3$) δ 0.99 (3 H, d, J = 6.7 Hz, CH_3), 1.21 (3 H, d, J = 6.7 Hz, CH_3), 1.30 (3 H, s, CH_3), 1.42 (3 H, s, CH_3), 1.98 (1 H, d, J = 4.2 Hz, H-5), 2.19 (3 H, s, Ac), 4.88 (1 H, m, J = 1.7 Hz, H-14), 5.05 (2 H, m, H-3, H-6), 5.78 (1 H, d, J = 1.7 Hz, H-11), 6.17 (1 H, m, Hz, H-7). The spectrum of this product was in full agreement with those of the acetate of natural 3β-hydroxynagilactone F (**8**).

Hydrogenation (PtO_2) of Nagilactone E (5). Nagilactone E (**5**, 100 mg) was hydrogenated in EtOH (20 mL) with PtO_2 (20 mg) under 1 atm. After absorption of ca. 1 equiv of hydrogen, the mixture was worked up as usual. 9:11-Dihydronagilactone E was crystallized from MeOH, 89 mg (89%): mp ≥320 °C; IR (Nujol) 3500–3400, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (3 H, s, CH_3), 1.07 (6 H, d, J = 7.0 Hz, 2 CH_3), 1.50 (3 H, s, CH_3), 1.67 (1 H, d, J = 4.5 Hz, H-5), 2.49 (1 H, d, J = 2 Hz, H-11), 2.67 (1 H, d, J = 1 Hz, H-11), 3.6 (1 H, m, H-3), 3.96 (1 H, d, J = 1.5 Hz, H-7), 4.17 (1 H, d, J = 2.0 Hz, H-14), 4.88 (1 H, dd, J = 1.5, 4.5 Hz, H-6).

Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.12; H, 7.48. Found: C, 64.79, H, 7.37.

Chromium(II) Perchlorate Reduction of Nagilactone E (5). A solution of **5** (50 mg, 0.15 mmol) in purified DMF (5 mL) was treated at −30 °C with 0.08 mL (0.15 mmol) of $Cr(ClO_4)_2$ solution, prepared from 1 g of Cr metal and 10 mL of 20% $HClO_4$, under carefully deoxygenated nitrogen atmosphere. When the initial light blue turned to green, the mixture was poured into water (10 mL) and worked up as usual. By $CHCl_3$ extraction, a pure product, **15** (26 mg, 52%), was obtained: IR (Nujol) 3500–3300, 1770, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 (3 H, d, J = 7.0 Hz, CH_3), 1.08 (3 H, s, CH_3), 1.11 (3 H, d, J = 7.0 Hz, CH_3), 1.56 (3 H, s, CH_3), 1.85 (1 H, d, J = 4.5 Hz, H-5), 3.14 (2 H, br s, H-11), 3.78 (1 H, dd, J = 6.5, 8.5 Hz, H-3), 4.88 (1 H, d, J = 4.5 Hz, H-6), 4.88 (1 H, br s, H-7), 5.06 (1 H, br s, H-14); mass spectrum (10 eV), M^+ 350.1694 (calcd for $C_{19}H_{26}O_6$, 350.1659), M^+ − 18 336.1632 (calcd for $C_{19}H_{24}O_5$, 332.1624).

2,3-Dehydronagilactone F (18) by Dehydration of 15. **15** was dehydrated with CH_3SO_2Cl in pyridine as described for **13** in a quantitative yield to give **18**: mp 231 °C; IR (Nujol) 1775, 1705, 1650, 1615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (3H, d, J = 7.0 Hz, CH_3), 1.18 (3 H, s, CH_3), 1.24 (3 H, d, J = 7.0 Hz, CH_3), 1.41 (3 H, s, CH_3), 2.12 (1 H, d, J = 5.5 Hz, H-5), 2.2 (2 H, br d, H-1), 2.34 (1 H, m, J = 7.0, 2.0 Hz, H-15), 4.89 (1 H, q, J = 2.0 Hz, H-14), 5.06 (1 H, td, J = 5.5, 5.5, 2.0 Hz, H-6), 5.76 (1 H, d, J = 2.0 Hz, H-11), 5.90 (2 H, br s, H-2, H-3), 6.10 (1 H, dt, J = 5.5, 2.0, 2.0 Hz, H-7); ^{13}C NMR ($CDCl_3$) δ 15.3 (q, C-16), 19.7 (q, C-17), 22.5 (q, C-20), 23.3 (q, C-18), 29.5 (d, C-15), 33.2 (t, C-1), 34.8 (s, C-10), 44.7 (s, C-4), 47.1 (d, C-5), 71.2 (d, C-6), 83.0 (d, C-14), 112.1 (d, C-11), 121.6 (d, C-7), 126.6 (d, C-2), 128.1 (d, C-3), 134.3 (s, C-8), 157.9 (s, C-9), 164.1 (s, C-12), 178.3 (s, C-19).

Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.75, H, 7.00.

Isomerization of Nagilactone E (5) and Its Acetate 5a with Alumina. Nagilactone E (**5**, 100 mg) was stirred with 5 g of neutral Al_2O_3 (Merck HF_{254}) in boiling benzene (100 mL) for 15 h. The mixture was filtered, and Al_2O_3 was washed thoroughly with 100 mL of $CHCl_3$ and then 100 mL of 1 N HCl. The acid washing was extracted with $CHCl_3$. The combined organic layer was evaporated and the residue purified by preparative TLC. The acidic compound **22** (55 mg, 55%) was obtained along with recovered **5** (30 mg, 30%). The structure of this product was assigned by the spectral correlation with compound **28** described below.

This isomerization also took place with acetate **5a** to afford the corresponding 3-acetate **22a** in 64% yield under the same condition.

The acidic compound **22a** gave the methyl ester **23** of a dienone carboxylic acid by usual methylation with CH_2N_2 in ether. **23**: UV (EtOH) 248 nm; IR ($CHCl_3$) 1773, 1718, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (3 H, d, J = 7.0 Hz, CH_3), 1.15 (3 H, d, J = 7.0 Hz, CH_3), 1.24 (3 H, s, CH_3), 1.40 (3 H, s, CH_3), 1.98 (1 H, d, J = 5.0 Hz, H-5), 2.20 (3 H, s, Ac), 3.01 (1 H, m, J = 7.0 Hz, H-15), 3.65 (3 H, s, OCH_3), 5.10 (1 H, t, J = 5.0 Hz, H-6), 5.84 (1 H, d, J = 1.5 Hz, H-11), 6.75 (1 H, dd, J = 1.5, 5.0 Hz, H-7); ^{13}C NMR ($CDCl_3$) δ 18.8 (q, C-16), 19.7 (q, C-17), 21.0 (q, Ac), 21.4 (q, C-20), 22.4 (q, C-18), 25.2 (t, C-2), 31.5 (t, C-1), 36.9 (d, C-15), 38.3 (s, C-10), 45.6 (s, C-4), 52.0 (q, OCH_3), 52.4 (d, C-5), 71.5 (d, C-6), 73.6 (d, C-3), 115.4 (d, C-11), 130.3 (d, C-7), 143.0 (s, C-8), 154.3 (s, C-9), 166.4 (s, C-12), 170.9 (s, Ac), 174.5 (s, C-19), 203.6 (s, C-14); mass spectrum (20 eV), M^+ 404.1833 (calcd for $C_{22}H_{28}O_7$, 404.1835), $M^+ - CH_3$ 389.1591 (calcd for $C_{21}H_{25}O_7$, 389.1600), $M^+ - CH_3O$ 373.1638 (calcd for $C_{21}H_{25}O_6$, 373.1651), $M^+ - C_3H_7$ 361.1282 (calcd for $C_{19}H_{21}O_7$, 361.1287).

3β-Hydroxynagilactone F (8) from 22. **22** (100 mg) was reduced with $NaBH_4$ (92 mg, large excess) in EtOH (6 mL) at 25 °C under N_2. After dilution with acetone, the mixture was evaporated and extracted with $CHCl_3$ to give 103 mg of a solid, which was purified by preparative TLC. The product (18 mg, 18%) was identified with natural 3β-hydroxynagilactone F (**8**) by the spectral comparison. Mass spectrum (30 eV), M^+ 332.1610 (calcd for $C_{19}H_{24}O_5$, 332.1623).

Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.65; H, 7.28. Found, C, 68.29; H, 7.35.

$NaBH_4$ Reduction of Nagilactone A Diacetate (1a). Nagilactone A diacetate (**1a**, 20 mg, 0.046 mmol), prepared from nagilactone A (**1**) with Ac_2O in pyridine, was dissolved in 10 mL of MeOH and treated with an excess of $NaBH_4$ (40 mg, 0.26 mmol) at 0 °C overnight. After dilution with acetone, the mixture was worked up as usual to give 16 mg (92%) of dienolide **24**, which was crystallized from EtOH; mp 196–7 °C; UV (EtOH) 263.5 nm (ϵ 13 000); IR (Nujol) 1770, 1730, 1710, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (3 H, d, J = 7.0 Hz, CH_3), 1.09 (3 H, d, J = 7.0 Hz, CH_3), 1.31 (3 H, s, CH_3), 1.35 (3 H, s, CH_3), 2.01 (1 H, d, J = 5.0 Hz, H-5), 2.11 (3 H, s, Ac), 4.53 (1 H, d, J = 9.0 Hz, H-14), 5.12 (1 H, t, J = 5.0 Hz, H-6), 5.1 (1 H, br, H-1), 5.64 (1 H, d, J = 1.8 Hz, H-11), 6.18 (1 H, dd, J = 1.8, 5.0 Hz, H-7).

Anal. Calcd for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.29; H, 7.12.

$NaBH_4$ Reduction of Nagilactone C 7-Monoacetate (3a). Nagilactone C 7-monoacetate (**3a**) was prepared by the usual acetylation of nagilactone C (**3**, Ac_2O/pyridine, 25 °C), along with the 3,7-diacetate. The 7-monoacetate (150 mg, 0.37 mmol) was treated with an excess of $NaBH_4$ (300 mg, 7.9 mmol) at 0 °C as described above. After working up as usual, recrystallization of the product from EtOH gave 45 mg (35%) of dienolide **25**: mp 248–251 °C; UV (EtOH) 263 nm; IR (Nujol) 3500, 1777, 1720, 1610 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 0.95 (3 H, d, J = 6.0 Hz, CH_3), 1.06 (3 H, d, J = 6.0 Hz, CH_3), 1.20 (3 H, s, CH_3), 1.47 (3 H, s, CH_3), 2.00 (1 H, m, H-15), 2.27 (1 H, d, J = 5.0 Hz, H-5), 3.48 (1 H, dd, J = 4.5, 6.0 Hz, H-2), 3.64 (1 H, d, J = 4.5 Hz, H-1), 4.51 (1 H, d, J = 6.0 Hz, H-3), 4.78 (1 H, d, J = 8.0 Hz, H-14), 5.15 (1 H, t, J = 5.0 Hz, H-6), 6.26 (1 H, br s, H-11), 6.32 (1 H, br d, J = 5 Hz, H-7); ^{13}C NMR ($CDCl_3$) δ 18.4 (q, C-16), 18.6 (q, C-17), 19.2 (q, C-20), 25.4 (q, C-18), 33.4 (d, C-15), 36.3 (s, C-10), 48.3 (s, C-4), 49.4 (d, C-5), 50.2 (d, C-2), 55.4 (d, C-1), 68.4 (d, C-3), 71.2 (d, C-6), 86.1 (d, C-14), 113.2 (d, C-11), 122.4 (d, C-7), 134.9 (s, C-8), 154.0 (s, C-9), 162.7 (s, C-12), 178.2 (s, C-19).

Anal. Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40. Found: C, 65.84; H, 6.40.

Photochemical Transformation of Nagilactone A Diacetate (1a). A methanol (10 mL) solution of **1a** (20 mg) was irradiated by a high-pressure mercury lamp (Pyrex filter) externally at 0 °C for 4 h. Evaporation of MeOH gave a mixture (1:1) of dienolides, **27a** and **27b**, which was separated by preparative TLC (SiO_2, 5:1, $CHCl_3$/acetone, 5 developments). **27a**: 9 mg (48%); mp 196–8 °C; UV (EtOH) 267 nm; IR ($CHCl_3$) 1770, 1730, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.79 (3 H, d, J = 7.0 Hz, CH_3), 1.09 (3 H, d, J = 7.0 Hz, CH_3), 1.37 (6 H, s, CH_3), 1.90 (1 H, d, J = 5.0 Hz, H-5), 2.12 (3 H, s, Ac), 3.17 (3 H, s, OCH_3), 5.08 (1 H, t, J = 5.0 Hz, H-6), 5.1 (1 H, br t, H-1), 5.72 (1 H, d, J = 2.0 Hz, H-11), 6.41 (1 H, dd, J = 2.0, 5.0 Hz, H-7).

Anal. Calcd for $C_{22}H_{28}O_7$: C, 65.33; H, 6.98. Found: C, 65.21; H, 6.91.

27b was obtained as an amorphous solid (9 mg (48%)): UV (EtOH) 256 nm; IR ($CHCl_3$) 1770, 1730, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (3 H, d, J = 7.0 Hz, CH_3), 1.01 (3 H, d, J = 7.0 Hz, CH_3), 1.31 (3 H, s, CH_3), 1.36 (3 H, s, CH_3), 1.95 (1 H, d, J = 5.0 Hz, H-5), 3.25 (3 H, s, OCH_3), 5.05 (1 H, br t, H-1), 5.09 (1 H, t, J = 5.0 Hz, H-6), 5.62 (1 H, d, J = 2.0 Hz, H-11), 6.30 (1 H, dd, J = 2.0, 5.0 Hz, H-7). The R_f value of **27a** was slightly higher than that of **27b** on a SiO_2 plate (2:1 $CHCl_3$/acetone).

When the irradiation was carried out in aqueous THF, a corresponding 14-hydroxy analogue was produced. A solution of **1a** (30 mg) in 15 mL of 2:1 THF/H_2O was irradiated as described above. Evaporation of the solvent gave **28** quantitatively: UV (EtOH) 260 nm; ^1H NMR ($CDCl_3$) δ 0.95 (3 H, d, J = 7.0 Hz, CH_3), 1.09 (3 H, d, J = 7.0 Hz, CH_3), 1.30 (3 H, s, CH_3), 1.38 (3 H, s, CH_3), 2.01 (1 H, d, J = 5.0 Hz, H-5), 2.11 (3 H, s, Ac), 5.12 (1 H, t, J = 5.0 Hz, H-6), 5.59 (1 H, d, J = 2.0 Hz, H-11), 6.58 (1 H, dd, J = 2.0, 5.0 Hz, H-7).

28 was methylated with CH_2N_2 in ether to give a methyl ester, the 1β-acetoxy analogue of **23**; UV (EtOH) 248 nm; ^1H NMR ($CDCl_3$) δ 1.17 (6 H, d, J = 7.0 Hz, CH_3), 1.23 (3 H, s, CH_3), 1.34 (3 H, s, CH_3), 2.00 (1 H, d, J = 5.5 Hz, H-5), 2.14 (3 H, s, Ac), 3.07 (1 H, m, J = 7.0 Hz, H-15), 3.63 (3 H, s, OCH_3), 5.15 (1 H, dd, J = 3.5, 5.5 Hz, H-6), 5.67 (1 H, d, J = 1.5 Hz, H-11), 6.82 (1 H, dd, J = 1.5, 3.5 Hz, H-7).

1β-Hydroxynagilactone F (7) from 28. **28** (50 mg, 0.13 mmol) was dissolved in dry MeOH (0.5 mL) with 60 mg (0.16 mmol) of $CeCl_3 \cdot 7H_2O$. $NaBH_4$ was added in ca. 10-mg portions in every 30 min under constant stirring at 0 °C. The reaction was monitored by TLC on every addition of $NaBH_4$. After addition of total 40 mg of $NaBH_4$, the mixture was quenched by acidifying with cold 2 N HCl and extracted with EtOAc. The crude product was purified by preparative TLC to give two products. The lower R_f (SiO_2 plate) component (10 mg, 21%) was identified with 14β-isopropyl dienolide **24** by the spectral comparison. The higher R_f compound (10 mg, 21%) was hydrolyzed with 5% K_2CO_3 (100 μL) in MeOH (1 mL) at 25 °C for 24 h. After acidification with 1 N HCl, the mixture was extracted with EtOAc. Evaporation of the solvent gave a hydroxydienolide, which was identical with natural 1β-hydroxynagilactone F (**7**); mp 230 °C; UV (MeOH) 262 nm; IR (KBr) 3420, 1765, 1700, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (3 H, d, J = 6.5 Hz, CH_3), 1.19 (3 H, d, J = 6.5 Hz, CH_3), 1.19 (3 H, s, CH_3), 1.38 (3 H, s, CH_3), 2.11 (1 H, d, J = 5.0 Hz, H-5), 4.54 (1 H, dd, J = 4.5, 10.5 Hz, H-1), 4.85 (1 H, q, J = 2.0 Hz, H-14), 5.09 (1 H, td, J = 2.0, 5.0, 5.0 Hz, H-6), 5.78 (1 H, d, J = 2.0, H-11), 6.18 (1 H, dt, J = 2.0, 2.0, 5.0 Hz, H-7); ^{13}C NMR ($CDCl_3$) δ 15.3 (q, C-16), 16.3 (q, C-20), 19.7 (q, C-17), 26.2 (t, C-2), 27.4 (q, C-18), 29.1 (t, C-3), 30.0 (d, C-15), 34.6 (s, C-10), 47.7 (d, C-5), 48.4 (s, C-4), 66.1 (d, C-1), 72.7 (d, C-6), 83.1 (d, C-14), 112.5 (d, C-11), 121.6 (d, C-7), 134.0 (s, C-8), 158.9 (s, C-9), 164.1 (s, C-12), 179.3 (s, C-19); mass spectrum (30 eV), M^+ 332.1688 (calcd for $C_{19}H_{24}O_5$, 332.1624).

Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.65; H, 7.28. Found: C, 68.50; H, 7.59.

Podolide (12) from Nagilactone E (5). A solution of nagilactone E (1.000 g, 2.8 mmol) and TsCl (640 mg, 3.2 mmol) in dry pyridine (10 mL) was refluxed for 13 h under N_2. The mixture was poured into ice water and extracted with $CHCl_3$. The $CHCl_3$ solution was worked up as usual to give a solid product, which was recrystallized from $CHCl_3$/ether. Podolide (**12**) was obtained as colorless needles (950 mg (quantitative)): mp 236 °C; UV (EtOH) 219 nm (ϵ 10 900); IR (KBr) 1765, 1700 cm^{-1}; ^1H NMR (py-d_5) δ 1.05 (3 H, d, J = 7.0 Hz, CH_3), 1.16 (3 H, s, CH_3), 1.18 (3 H, d, J = 7.0 Hz, CH_3), 1.30 (3 H, s, CH_3), 2.05 (2 H, br d, H-1), 2.07 (1 H, d, J = 5.0 Hz, H-5), 4.24 (1 H, d, J = 1.5 Hz, H-7), 4.61 (1 H, d, J = 4.0 Hz, H-14), 5.16 (1 H, dd, J = 1.5, 5.0 Hz, H-6), 5.80 (1 H, dt, J = 3.0, 3.0, 10.0 Hz, H-2), 5.90 (1 H, d, J = 10.0 Hz, H-3), 6.17 (1 H, s, H-11); ^{13}C NMR ($CDCl_3$) δ 16.5 (q, C-16), 21.4 (q, C-17), 22.7 (q, C-20), 23.5 (q, C-18), 26.8 (d, C-15), 32.5 (t, C-1), 35.4 (s, C-10), 43.3 (d, C-5), 44.0 (s, C-4), 53.6 (d, C-7), 57.7 (s, C-8), 71.9 (d, C-6), 82.8 (d, C-14), 117.4 (d, C-11), 126.5 (d, C-2), 128.2 (d, C-3), 158.0 (s, C-9), 163.5 (s, C-12), 177.6 (s, C-19); mass spectrum (20 eV), M^+ 330, 287, 271, 259, 243, 229, 215, 199.

Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.04; H, 6.74.

This dehydration also proceeded by heating with $POCl_3$ in pyridine (**5**, 100 mg, pyridine 5 mL, 1 mL of $POCl_3$, 5 h, 70–80 °C; podolide 96 mg quantitative yield).

Formation of Phosphate Esters 9 and 10 of Nagilactone E (5). Treatment of **5** with $POCl_3$ in pyridine at 25 °C, as described above, gave a water-soluble dihydrogenphosphate **9**, which was isolated by complete evaporation of the aqueous solution after decomposing the reaction mixture with ice. Methylation of **9** with CH_2N_2 in ether gave dimethyl ester **10** in quantitative yield: mp 225 °C; IR (KBr) 1778, 1703, 1055, 1035 cm^{-1}; ^1H NMR (pyr-d_5) δ 1.04 (3 H, d, J = 7.0 Hz, CH_3), 1.18 (3 H, d, J = 7.0 Hz, CH_3), 1.27 (3 H, s, CH_3), 1.60 (3 H, s, CH_3), 2.06 (1 H, d, J = 4.0 Hz, H-5), 3.84 (3 H, d, J = 11.5 Hz, OCH_3), 3.90 (3 H, d, J = 11.5 Hz, OCH_3), 4.26 (1 H, d, J = 1.5 Hz, H-7), 4.62 (1 H, d, J = 4.0 Hz, H-14), 4.70 (1 H, br m, H-3), 5.18 (1 H, dd, J = 1.5, 4.0 Hz, H-6), 6.22 (1 H, s, H-11); mass spectrum (20 eV), M^+ 456, 441, 413, 330, 315, 287, 271, 259, 243, 229, 215.

Anal. Calcd for $C_{21}H_{29}O_9P$: C, 55.26; H, 6.40. Found: C, 54.95; H, 6.50.

Formation of Isomeric 1- and 2-Chlorohydrins 29 and 30 from Nagilactone D Acetate (4a). Nagilactone D acetate (515 mg, 1.38 mmol) was refluxed with 2 N HCl (40 mL) and EtOH (50 mL) for 15 h. After cooling, the mixture was concentrated under vacuum at 25 °C to one-third of the original volume. A colorless precipitate (280 mg, 55.2%) collected by filtration was almost homogeneous **29** and recrystallized from EtOH. 1α-Chloro-2β-hydroxy derivative **29**: mp 140 °C, UV (EtOH) 305 nm; IR (Nujol) 3500–3300, 1780, 1700, 1620, 1545 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (3 H, t, J = 6.5 Hz, H-16), 1.51 (3 H, s, CH_3), 1.64 (3 H, s, CH_3), 2.45 (1 H, d, J = 5.0 Hz, H-5), 2.58 (2 H, q, J = 6.5 Hz, H-15), 2.90 (1 H, dd, J = 5.0, 17.0 Hz, H-7β), 3.39 (1 H, dd, J = 10.0, 17.0 Hz, H-7α), 4.15 (1 H, d, J = 4.5 Hz, H-1), 4.44 (1 H, dd, J = 3.0, 4.5 Hz, H-2), 4.58 (1 H, d, J = 3.0 Hz, H-3), 5.16 (1 H, dt, J = 5.0, 5.0, 10.0 Hz, H-6), 6.03 (1 H, s, H-11). **29** consumed 1 equiv of $NaIO_4$ on titration.

Anal. Calcd for $C_{18}H_{21}O_6Cl$: C, 58.62; H, 5.74. Found: C, 58.53; H, 5.77.

The filtrate was neutralized with $NaHCO_3$ (excess) and extracted with $CHCl_3$. Evaporation of $CHCl_3$ gave a colorless solid (230 mg, 45%). This product was a mixture of **29** and its isomer **30**. **30** was separated by SiO_2 chromatography: mp 244–249 °C; UV (EtOH) 302 nm; IR (Nujol) 3400, 1770, 1680, 1630, 1560 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (3 H, t, J = 7.0 Hz, H-16), 1.29 (3 H, s, CH_3), 1.60 (3 H, s, CH_3), 1.81 (1 H, d, J = 4.5 Hz, H-5), 2.55 (2 H, q, J = 7.0 Hz, H-15), 2.90 (1 H, dd, J = 4.5, 17.0 Hz, H-7β), 3.33 (1 H, dd, J = 9.5, 17.0 Hz, H-7α), 3.73 (1 H, d, J = 9.5 Hz, H-1), 3.75 (1 H, d, J = 9.5 Hz, H-3), 4.03 (1 H, t, J = 9.5 Hz, H-2), 5.05 (1 H, dt, J = 4.5, 4.5, 9.5 Hz, H-6), 6.69 (1 H, s, H-11). **30** did not consume $NaIO_4$ on titration.

Anal. Calcd for $C_{18}H_{21}O_6Cl$: C, 58.62; H, 5.74. Found: C, 58.35; H, 5.84.

Chlorohydrin **29** gave a diacetate **29a** with Ac_2O in pyridine; mp 246–9 °C; UV (EtOH) 306 nm; IR (Nujol) 1780, 1755, 1715, 1640, 1545 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (3 H, t, J = 7.0 Hz, H-16), 1.47 (3 H, s, CH_3), 1.52 (3 H, s, CH_3), 2.12 (3 H, s, Ac), 2.15 (3 H, s, Ac), 2.52 (1 H, d, J = 5.0 Hz, H-5), 2.59 (2 H, q, J = 7.0 Hz, H-15), 2.86 (1 H, dd, J = 5.0, 17.0 Hz, H-7β), 3.42 (1 H, dd, J = 10.0, 17.0 Hz, H-7α), 4.47 (1 H, d, J = 1.8 Hz, H-1), 5.16 (1 H, dt, J = 5.0, 5.0, 10.0 Hz, H-6), 5.64 (2 H, br s, H-2, H-3), 6.06 (1 H, s, H-11).

Anal. Calcd for $C_{22}H_{25}O_8Cl$: C, 58.34; H, 5.56. Found: C, 58.51; H, 5.70.

Isomeric chlorohydrin **30** gave a mixture (3:5) of 3-monoacetate **30a** and 1,3-diacetate **30b** on treatment with excess Ac_2O in pyridine at 25 °C overnight. The two acetates were separable by preparative TLC and characterized by ^1H NMR spectra. **30a**: ^1H NMR ($CDCl_3$) δ 1.24 (3 H, t, J = 7.0 Hz, H-16), 1.42 (3 H, s, CH_3), 1.50 (3 H, s, CH_3), 1.94 (1 H, d, J = 4.5 Hz, H-5), 2.90 (1 H, dd, J = 4.5, 17.0 Hz, H-7β), 3.33 (1 H, dd, J = 9.5, 17.0 Hz, H-7α), 3.90 (1 H, d, J = 10.0 Hz, H-1), 4.20 (1 H, dd, J = 9.5, 10.0 Hz, H-2), 5.01 (1 H, dt, J = 4.5, 4.5, 9.5 Hz, H-6), 5.43 (1 H, d, J = 9.5 Hz, H-3), 6.66 (1 H, s, H-11). **30b**: ^1H NMR ($CDCl_3$) δ 1.24 (3 H, t, J = 7.0 Hz, H-16), 1.32 (3 H, s, CH_3), 1.40 (3 H, s, CH_3), 2.16 (1 H, d, J = 4.5 Hz, H-5), 2.55 (2 H, q, J = 7.0 Hz, H-15), 2.90 (1 H, dd, J = 4.5, 17.0 Hz, H-7β), 3.33 (1 H, dd, J = 9.5, 17.0 Hz, H-7α), 4.21 (1 H, t, J = 9.5 Hz, H-2), 4.99 (1 H, dt, J = 4.5, 4.5, 9.5 Hz, H-6), 5.27 (1 H, d, J = 9.5 Hz, H-1), 5.46 (1 H, d, J = 9.5 Hz, H-3), 5.70 (1 H, s, H-11).

Chlorohydrin **29** was also formed from nagilactone D (**4**) by reaction with $RhCl_3$. **4** (20 mg, 0.06 mmol) was treated with $RhCl_3 \cdot 3H_2O$ (5.5 mg, 0.02 mmol) in dry EtOH (100 μL) in a sealed tuve (N_2). After heating for 2 h at 150 °C, the mixture was filtered and evaported. Purification of the residue by TLC gave 10 mg (45%) of colorless crystals along with some recovered **4**. This product was identical with the chlorohydrin **29** by ^1H NMR and

IR comparison; mass spectrum (70 eV), M^+ 368, 370.

Deoxygenation of Nagilactone C (3) with Cr(II) Reagent. A solution of ethylenediamine (2 mL, 33.3 mmol) in purified DMF (170 mL) was carefully degassed and saturated with pure nitrogen. To this solution was added successively a $Cr(ClO_4)_2$ solution (10 mL, 14.2 mmol), prepared from 1.84 g of Cr metal and 25 mL of 20% $HClO_4$ at 70–80 °C under N_2, and then a DMF (10 mL) solution of nagilactone C (**3**, 1.00 g, 2.8 mmol) at 30 °C. After stirring for 4 h at 30 °C, the mixture was diluted with 300 mL of H_2O, acidified (pH ~2.0) with 6 N HCl, and extracted with $CHCl_3$. The $CHCl_3$ solution was worked up as usual to give 492 mg (52%) of the 1:2-deoxygenated product **33** as colorless crystals: mp 287–289 °C; UV (EtOH) 300 nm; IR (Nujol) 3500, 3300, 1750, 1695, 1630, 1550 cm^{-1}; ^1H NMR (py-d_5) δ 1.21 (3 H, d, J = 6.5 Hz, CH_3), 1.29 (3 H, d, J = 6.5 Hz, CH_3), 1.41 (3 H, s, CH_3), 1.98 (3 H, s, CH_3), 2.17 (1 H, d, J = 6.0 Hz, H-5), 3.48 (1 H, m, J = 6.5 Hz, H-15), 4.53 (1 H, d, J = 6.0 Hz, H-3), 5.02 (1 H, dd, J = 6.0, 8.5 Hz, H-6), 5.63 (1 H, d, J = 8.5 Hz, H-7), 6.17 (1 H, dd, J = 6.0, 9.5 Hz, H-2), 6.58 (1 H, s, H-11), 6.89 (1 H, d, J = 9.5 Hz, H-1); ^{13}C NMR (py-d_5) δ 20.2 (q, C-16), 20.8 (q, C-17), 25.9 (q, C-20), 27.0 (q, C-18), 29.7 (d, C-15), 38.2 (s, C-10), 48.4 (s, C-4), 54.8 (d, C-5), 60.5 (d, C-7), 69.3 (d, C-3), 74.0 (d, C-6), 105.5 (d, C-11), 111.7 (s, C-8), 129.6 (d, C-2), 136.9 (d, C-1), 162.2 (s, C-12), 163.1 (s, C-14), 170.7 (s, C-9), 178.8 (s, C-19).

Anal. Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40. Found: C, 65.77; H, 6.44.

Acetylation of **33** by the usual method (Ac_2O/pyridine) gave diacetate **33a**: mp 248 °C; IR (Nujol) 1780, 1740, 1720, 1630, 1545 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (3 H, d, J = 6.8 Hz, CH_3), 1.26 (3 H, d, J = 6.8 Hz, CH_3), 1.55 (6 H, s, 2 CH_3), 2.23 (1 H, d, J = 6.0 Hz, H-5), 3.00 (1 H, m, J = 6.8 Hz, H-15), 4.96 (1 H, dd, J = 6.0, 9.1 Hz, H-6), 5.88 (1 H, dd, J = 6.0, 9.8 Hz, H-2), 5.56 (1 H, d, J = 6.0 Hz, H-3), 6.22 (1 H, s, H-11), 6.36 (1 H, d, J = 9.1 Hz, H-7), 6.80 (1 H, d, J = 9.8 Hz, H-1).

Anal. Calcd for $C_{23}H_{26}O_8$: C, 64.17; H, 6.09. Found: C, 63.90; H, 5.97.

Hydrogenation of Allylic Alcohol 33. Catalytic hydrogenation of **33** was slow and gave a rather complicated mixture (3–4 spots on TLC). From the reduction of 130 mg of **33** (5% Pd/C 60 mg, EtOH 20 mL, 1 drop of 60% $HClO_4$, 25 °C, 1 atm of H_2, 2 h), 9 mg of a pure compound was obtained after repeated chromatography (ca. 55 mg of **33** was recovered). This product was assigned as the 2:3-unsaturated compound **35** from the following analytical data: mp 290 °C (sublime); IR (Nujol) 3440, 1760, 1695, 1635, 1550 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (3 H, d, J = 6.5 Hz, CH_3), 1.34 (3 H, d, J = 6.5 Hz, CH_3), 1.38 (6 H, s, 2 CH_3), 2.00 (1 H, d, J = 5.5 Hz, H-5), 2.14 (2 H, br d, H-1), 3.24 (1 H, m, J = 6.5 Hz, H-15), 4.95 (1 H, dd, J = 5.5, 9.0 Hz, H-6), 5.30 (1 H, d, J = 9.0 Hz, H-7), 5.88 (3 H, br s, H-2, H-3, H-11).

Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.08; H, 6.82.

Epoxidation of Podolide (12) and 16-Hydroxypodolide (36). A solution of podolide (30 mg, 0.09 mmol) in dry $CHCl_3$ (7 mL) containing a catalytic amount of 4,4′-thiobis[6-*tert*-butyl-3-methylphenol] as a radical inhibitor was refluxed with 60 mg (0.35 mmol) of m-$ClC_6H_4CO_3H$ for 48 h. Evaporation of the solvent and purification of the residue by preparative TLC (SiO_2, 4:1 $CHCl_3$/acetone) gave 23 mg (73%) of the 2α:3α-epoxide **37** as colorless needles: mp 275 °C 4.0 Hz, UV (EtOH) 218 nm (ϵ 9800); IR (KBr) 1770, 1705 cm^{-1}; ^1H NMR (py-d_5) δ 1.01 (3 H, d, J = 7.0 Hz, CH_3), 1.11 (3 H, s, CH_3), 1.13 (3 H, d, J = 7.0 Hz, CH_3), 1.45 (3 H, s, CH_3), 1.59 (1 H, dd, J = 1.5, 14.0 Hz, H-1α), 1.86 (1 H, d, J = 5.0 Hz, H-5), 2.14 (1 H, dd, J = 6.5, 14.0 Hz, H-1β), 3.37 (1 H, m, H-2), 3.52 (1 H, d, J = 4.0 Hz, H-3), 4.20 (1 H, d, J = 1.5 Hz, H-7), 4.53 (1 H, d, J = 4.0, H-14), 5.11 (1 H, dd, J = 1.5, 5.0 Hz, H-6), 6.07 (1 H, s, H-11); ^{13}C NMR ($CDCl_3$) δ 16.5 (q, C-16), 19.5 (q, C-20), 21.4 (q, C-17), 24.5 (q, C-18), 26.9 (d, C-15), 32.5 (t, C-1), 35.5 (s, C-10), 41.7 (d, C-5), 43.5 (s, C-4), 52.2 (d, C-2), 53.7 (d, C-7), 54.0 (d, C-3), 57.4 (s, C-8), 72.2 (d, C-6), 82.7 (d, C-14), 118.1 (d, C-11), 156.8 (s, C-9), 163.2 (s, C-12), 177.1 (s, C-19); mass spectrum (20 eV), M^+ 346, 318, 303, 275, 247, 229.

Anal. Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40. Found: C, 65.57; H, 6.39.

16-Hydroxypodolide (**36**), obtained from root bark of *Podocarpus nagi*, also gave a corresponding 2α,3α-epoxide **38** by the same procedure as described above; mp 272 °C dec; IR (KBr) 3540, 1777, 1700 cm^{-1}; ^1H NMR (py-d_5) δ 1.13 (3 H, s, CH_3), 1.30 (3 H, d, J = 7.0 Hz, CH_3), 1.46 (3 H, s, CH_3), 1.58 (1 H, dd, J = 1.5, 14.0 Hz, H-1α), 1.86 (1 H, d, J = 5.0 Hz, H-5), 2.12 (1 H, dd, J = 6.0, 14.0 Hz, H-1β), 3.38 (1 H, m, H-2), 3.52 (1 H, d, J = 3.5 Hz, H-3), 4.00 (1 H, dd, J = 7.0, 10.5 Hz, H-16), 4.11 (1 H, dd, J = 4.0, 10.5 Hz, H-16), 4.33 (1 H, d, J = 1.5 Hz, H-7), 4.82 (1 H, d, J = 5.0 Hz, H-14), 5.12 (1 H, dd, J = 1.5, 5.0 Hz, H-6), 6.16 (1 H, s, H-11); ^{13}C NMR (py-d_5) δ 16.1 (q, C-17), 19.5 (q, C-20), 23.7 (q, C-18), 32.3 (t, C-1), 34.7 (d, C-15), 35.8 (s, C-10), 41.7 (d, C-5), 43.7 (s, C-4), 52.5 (d, C-2), 54.4 (d, C-3), 54.9 (d, C-7), 57.8 (s, C-8), 62.5 (t, C-16), 72.7 (d, C-6), 82.2 (d, C-14), 118.1 (d, C-11), 157.3 (s, C-9), 163.6 (s, C-12), 177.8 (s, C-19); mass spectrum (20 eV), M^+ 362, 347, 332, 305.

Anal. Calcd for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12. Found: C, 62.96; H, 6.19.

Registry No. 1, 19891-50-0; **1a**, 19891-54-4; **2**, 19891-51-1; **3**, 24338-53-2; **4**, 19891-53-3; **3a**, 82335-10-2; **4a**, 19891-65-7; **5**, 36895-12-2; dihydro-**5**, 39024-02-7; **5a**, 39024-01-6; **6**, 36912-00-2; **7**, 81348-87-0; **8**, 70469-56-6; **8a**, 70469-58-8; **9**, 65688-70-2; **10**, 65688-71-3; **12**, 55786-36-2; **13**, 73616-59-8; **14**, 73616-58-7; **15**, 82280-79-3; **16**, 71431-95-3; **16a**, 70469-57-7; **17**, 82335-11-3; **18**, 81362-33-6; **19**, 82280-80-6; **22**, 82280-81-7; **22a**, 82280-82-8; **23**, 82280-83-9; 1β-AcO-**23**, 82280-84-0; **24**, 19891-61-3; **25**, 33722-80-4; **27a**, 82280-85-1; **27b**, 82335-12-4; **28**, 82280-86-2; **29**, 82280-87-3; **29a**, 82280-88-4; **30**, 82280-89-5; **30a**, 82293-65-0; **30b**, 82293-66-1; **33**, 65688-75-7; **35**, 65688-77-9; **36**, 65688-72-4; **37**, 65688-73-5; **38**, 65688-74-6.

Total Synthesis of Nagilactone F, a Biologically Active Norditerpenoid Dilactone Isolated from *Podocarpus nagi*

Yuji Hayashi,* Takeshi Matsumoto, Mugio Nishizawa, Masatoshi Togami, Toshiaki Hyono, Naomi Nishikawa, and Motokazu Uemura

Faculty of Science, Osaka City University, Sumiyoshiku, Osaka 558, Japan

Takeo Sakan

Suntory Institute of Bio-organic Research, Shimamotocho, Mishimagun, Osaka 618, Japan

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The details of the first total synthesis of nagilactone F (1), a member of the biologically active norditerpenoid dilactones isolated from *Podocarpus* plants, are described. The synthesis is accomplished by starting from a known resin acid, (4*S*)-(+)-podocarpic acid (4). Thus, the absolute configuration of the norditerpenoid is chemically established as represented by formula **1**.

Norditerpenoid dilactones isolated from various species of the *Podocarpus* genus[1] have attracted interest in natural product chemistry because of their wide variety of biological activity.[2] Even though more than 40 dilactone

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