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Synthetic Studies on Marasmane and iso-Marasmane Derivatives

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Cyclopropylcarbinyl alcohols with marasmane and isomarasmane carbon skeletons (compounds **21** and **26**) were synthesized from the azo compound **14** by a route involving an intramolecular carbene insertion reaction. The major product **21** was found to have an isomarasmane type stereostructure by X-ray crystallographic analysis of compound **23**.

Keywords——sesquiterpenes; marasmane derivatives; X-ray analysis; cyclopropylcarbinyl alcohol; carbene insertion

Recently, we reported the isolation and characterization of the protoilludane and marasmane derivatives **1**—**3**[2] from cultured mycellia of a wood-rotting fungus, *Fomitopsis insularis*, which produces the vellerane-type compounds **4** and **5**[3] as major metabolites.

Regarding the biosynthesis of these sesquiterpenes, we suggest that Δ^6-protoilludene **1** produced at the initial stage might be converted to an allylic system, such as **2**, which in turn, would be subject to carbonium ion rearrangement (Chart 1, A⇄B⇄C⇄D) followed by oxidative modifications leading to a variety of substances of this group.[2] Since we are interested in the solvolytic behavior of alcohols having the marasmane and protoilludane carbon skeletons in connection with biosynthetic studies, we have been engaged in synthetic studies of these compounds. This paper describes the synthesis of the alcohols **6** having a marasmane skeleton by a route involving an intramolecular carbene insertion reaction as a key step. Recently, marasmic acid **7**[4] was synthesized stereospecifically by Greenlee and Woodward,[5] while many other attempts to construct this skeleton have yielded isomeric derivatives with the isomarasmane skeleton.[6,7]

The bicyclic ketone **8**, prepared by the method of Matsumoto *et al.*,[8] was transformed to the tetramethylketone **9** by treatment with methyliodide and sodium hydride. The corresponding oxime **10**, mp 124—124.5°, underwent abnormal Beckmann rearrangement[9,10] on treatment with *p*-toluenesulfonyl chloride to afford a mixture of isomeric nitriles **11a** and **11b** in a ratio of 1:1, which could be separated by column chromatography on silica gel impregnated with silver nitrate. Compound **11a** showed NMR signals at 1.74 (3H, bs), 4.71

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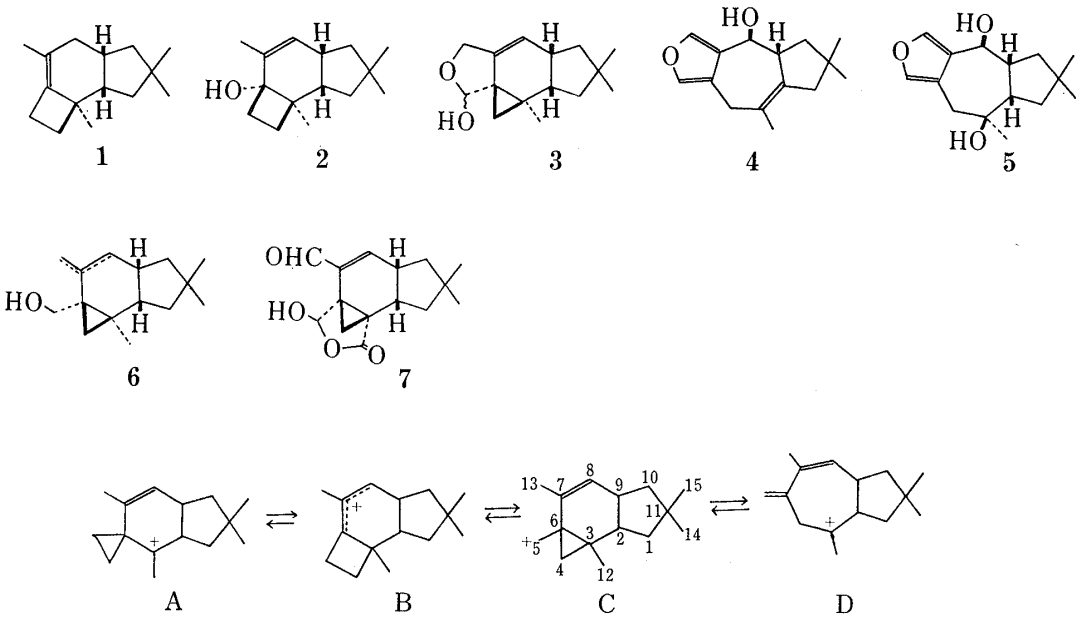

Chart 1

(1H, bs) and 4.87 (1H, bs) due to the ispropenyl group, while compound **11b** showed a signal at 1.64 (6H, bs) indicating the presence of an isopropylidene group. Attempts to increase the ratio of **11a** to **11b** by varying the reaction conditions were fruitless. Compound **11a** was converted to the methylketone **12** by treatment with methyllithium and then to the β-keto-ester **13** by treatment with diethylcarbonate in the presence of sodium hydride. The azo compound **14**[11] (IR, 2146 cm^{-1}) was prepared by the reaction of **13** with p-toluenesulfonyl azide in acetonitrile in the presence of triethylamine. Compound **14** was heated under reflux in toluene with trimethylphosphite cuprous iodide[12] to afford a mixture of three products **15**, **16** and **17** in a ratio of 5:1:1; these were separated by column chromatography and GLC to give the pure compounds. Each of the three products showed the same molecular ion peak at *m/e* 264. The major and the most polar compound **15** showed NMR signals at 0.97, 1.11, and 1.18 (each 3H, s) due to three methyl groups, with no olefinic proton signal, indicating that a new ring had been formed between the diazotized carbon and the double bond. Compound **15** did not show cyclopropane signals in the normal region, but when reduced with lithium aluminum hydride, it afforded an epimeric mixture of diols **18**, which showed clear cyclopropane methylene signals as two pairs of AB quartets (J=5 Hz) at 0.25 and 0.47 for the major alcohol, and 0.57 and 0.83 for the minor one. Similar reduction of **16** with lithium aluminum hydride gave the diol **19**; the presence of a cyclopropane ring was indicated by NMR signals at 0.23 (1H, d, J=5 Hz, B of AB type). Based on these findings, in conjunction with their similar mass and NMR spectra, compounds **15** and **16** were assumed to be stereoisomers in respect of the cyclopropane ring junction. Among the possible four stereoisomers, only two isomers with *cis* ring junction may correspond to **15** and **16** in view of the reported[13] behavior of the bicyclo[4,1,0]heptane system. The structure of **15** was determined by X-ray analysis of **23** derived from **15** as described below. The structure of the third product **17** remains unknown. Compound **15** was transformed by the usual Wittig condensation into the methylene-transferred product **20**, which was then reduced to the alcohol **21**

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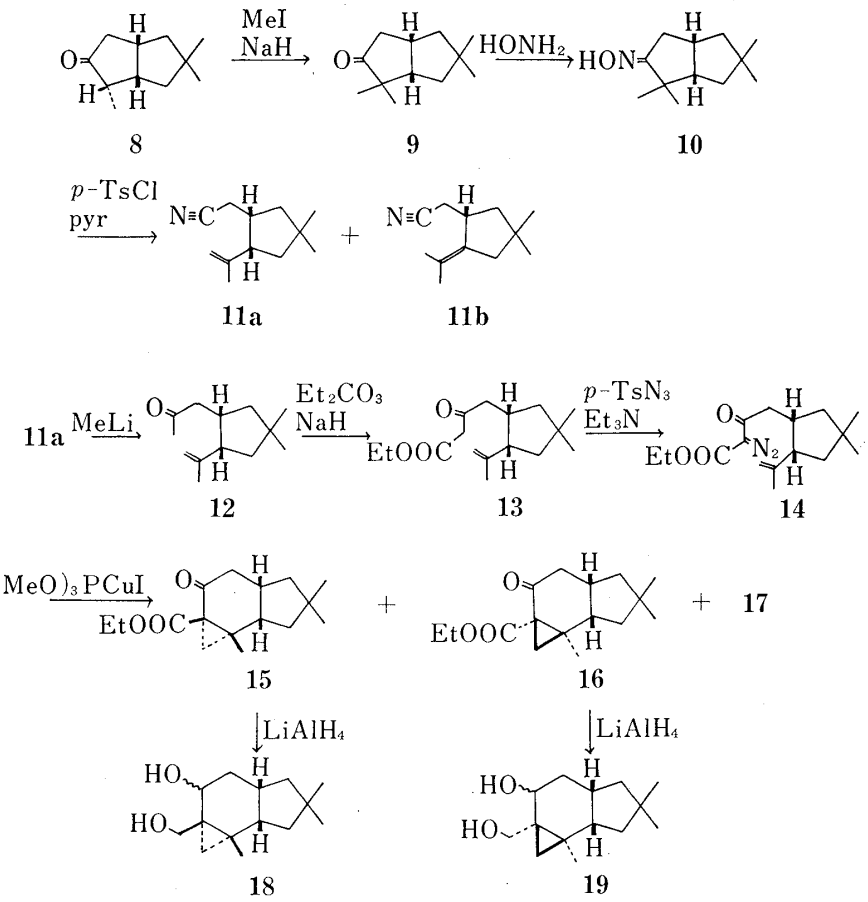

Chart 2

with lithium aluminum hydride. The acetate **22** was converted to the diol monoacetate **23** by osmium tetroxide oxidation under the usual conditions. The product **23** was obtained as a crystalline compound. The stereochemistry of **23** could not be determined physicochemically, so the structure was determined by X-ray crystallographic analysis.

The crystal of **23** belongs to the triclinic space group $P\bar{1}$ with two molecules in a unit cell having lattice parameters $a=14.833$, $b=10.614$, $c=5.871$ Å, $\alpha=106.19$, $\beta=80.83$, $\gamma=110.25$. The intensity data were collected on a Philips PW1100 automatic four-circle diffractometer using the θ-2θ scan method ($2\theta_{max}=140°$) with Cu$K\alpha$ radiation monochromated by means of a graphite plate. In all, 2303 independent, non-zero reflections were measured and were corrected for the Lorentz and polarization effects. The structure was solved by the direct method using MULTAN[14] and was refined by the block-diagonal least-squares procedure. Hydrogen atoms were located on a difference map. R was 0.057 after several cycles of least-squares calculation assuming anisotropic thermal parameters for the non-hydrogen atoms and isotropic ones for the hydrogen atoms. The weighting is unity for all reflections. The atomic scattering factors for C and O were those given in *International Tables for X-ray Crystallography* (1962)[15] as SX-6 and 8, respectively, and for H those given by Stewart *et al.*[16] were used.

The final positional and thermal parameters are given in Table I. The bond distances and angles are illustrated in Fig. 1. The average estimated standard deviations for C–C bonds

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TABLE I. (a) The Final Positional Parameters ($\times 10^4$) and Anisotropic Thermal Parameters ($\times 10^4$) for Non-hydrogen Atoms

The estimated standard deviations are given in parentheses as units in the last digit. The form of the anisotropic temperature factor is $T=\exp[-(h^2b_{11}+k^2b_{22}+l^2b_{33}+hkb_{12}+hlb_{13}+klb_{23})]$.

		x	y	z	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
1	C (1)	2695 (2)	5756 (3)	1206 (6)	45 (2)	74 (4)	269 (12)	30 (2)	6 (4)	18 (5)
2	C (2)	2482 (2)	7074 (3)	2757 (5)	34 (2)	65 (3)	174 (10)	18 (2)	−1 (3)	25 (4)
3	C (3)	2955 (2)	8334 (3)	1705 (5)	33 (2)	76 (3)	220 (11)	18 (2)	12 (3)	41 (5)
4	C (4)	2592 (2)	8362 (3)	−509 (5)	56 (2)	93 (4)	171 (11)	32 (2)	18 (4)	37 (5)
5	C (5)	2950 (3)	10832 (3)	1990 (6)	62 (2)	79 (4)	292 (13)	15 (2)	−26 (4)	59 (6)
6	C (6)	2406 (2)	9329 (3)	1852 (5)	42 (2)	66 (3)	178 (10)	21 (2)	−3 (3)	32 (4)
7	C (7)	1381 (2)	8997 (3)	3047 (5)	39 (2)	76 (3)	166 (10)	29 (2)	−8 (3)	20 (4)
8	C (8)	858 (2)	7453 (3)	2507 (6)	35 (2)	79 (4)	230 (11)	19 (2)	−5 (3)	13 (5)
9	C (9)	1366 (2)	6627 (3)	3259 (5)	33 (2)	70 (3)	208 (11)	14 (2)	11 (3)	30 (5)
10	C (10)	1008 (2)	5071 (3)	2026 (7)	43 (2)	68 (4)	384 (15)	11 (2)	3 (4)	29 (6)
11	C (11)	1863 (2)	4543 (3)	1843 (5)	57 (2)	67 (3)	189 (11)	25 (2)	−8 (4)	31 (5)
12	C (12)	4038 (2)	8900 (4)	1968 (7)	32 (2)	119 (5)	466 (17)	15 (2)	23 (4)	95 (7)
13	C (13)	1435 (2)	9653 (3)	5720 (5)	47 (2)	86 (4)	173 (11)	28 (2)	2 (3)	18 (5)
14	C (14)	1971 (4)	4312 (4)	4220 (7)	122 (4)	118 (5)	270 (15)	44 (4)	−48 (6)	59 (7)
15	C (15)	1747 (3)	3191 (3)	−64 (6)	85 (3)	69 (4)	287 (13)	30 (3)	−19 (5)	26 (6)
16	O (16)	845 (2)	9665 (2)	2178 (4)	62 (2)	126 (3)	191 (8)	61 (2)	−9 (3)	26 (4)
17	O (17)	575 (2)	9103 (2)	7112 (4)	53 (1)	118 (3)	200 (8)	47 (2)	22 (3)	54 (4)
18	O (18)	3353 (2)	11512 (2)	4291 (4)	57 (2)	80 (3)	320 (9)	1 (2)	−21 (3)	50 (4)
19	C (19)	4075 (3)	12686 (4)	4409 (8)	63 (3)	85 (4)	477 (18)	7 (3)	7 (5)	72 (7)
20	C (20)	4439 (4)	13331 (4)	6823 (8)	95 (4)	120 (6)	517 (21)	−18 (3)	−105 (7)	70 (8)
21	O (21)	4377 (3)	13149 (4)	2685 (7)	166 (4)	177 (5)	563 (17)	−74 (4)	−34 (6)	130 (8)

(b) The Final Positional Parameters ($\times 10^3$) and Isotropic Thermal Parameters ($\times 10$) for Hydrogen Atoms

		x	y	z	b
22	H(C 1)	262 (2)	573 (3)	−59 (6)	39 (7)
23	H′ (C 1)	340 (3)	574 (4)	135 (6)	58 (9)
24	H(C 2)	278 (2)	734 (3)	441 (5)	30 (6)
25	H(C 4)	309 (2)	883 (3)	−161 (6)	43 (8)
26	H′ (C 4)	203 (2)	754 (3)	−126 (6)	46 (8)
27	H(C 5)	256 (2)	1129 (3)	181 (6)	44 (8)
28	H′ (C 5)	352 (3)	1095 (4)	67 (6)	55 (9)
29	H(C 8)	73 (2)	713 (3)	78 (6)	41 (8)
30	H′ (C 8)	22 (2)	728 (3)	340 (6)	44 (8)
31	H(C 9)	126 (2)	677 (3)	515 (6)	43 (8)
32	H(C 10)	86 (2)	496 (3)	27 (6)	48 (8)
33	H′ (C 10)	38 (3)	454 (4)	274 (7)	64 (10)
34	H(C 12)	418 (3)	920 (4)	380 (7)	62 (10)
35	H′ (C 12)	437 (3)	817 (4)	118 (6)	52 (9)
36	H″ (C 12)	435 (3)	972 (4)	140 (7)	62 (10)
37	H(C 13)	159 (2)	1073 (3)	598 (6)	37 (7)
38	H′ (C 13)	203 (3)	945 (4)	643 (6)	52 (9)
39	H(C 14)	138 (3)	343 (5)	452 (8)	87 (13)
40	H′ (C 14)	203 (3)	522 (4)	557 (8)	78 (12)
41	H″ (C 14)	259 (3)	420 (4)	425 (7)	71 (11)
42	H(C 15)	126 (3)	240 (4)	34 (7)	62 (10)
43	H′ (C 15)	161 (3)	330 (4)	−177 (7)	61 (10)
44	H″ (C 15)	236 (3)	288 (4)	−24 (6)	56 (9)
45	H(O 16)	80 (2)	936 (3)	62 (6)	44 (8)
46	H(O 17)	18 (3)	948 (4)	695 (7)	66 (10)
47	H(C 20)	447 (3)	1439 (4)	735 (7)	89 (11)
48	H′ (C 20)	423 (3)	1275 (4)	772 (7)	81 (10)
49	H″ (C 20)	511 (3)	1400 (4)	660 (7)	92 (11)

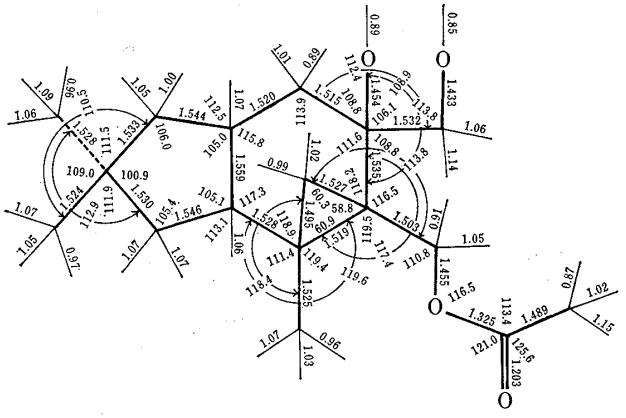


Fig. 1. Bond Distances and Angles

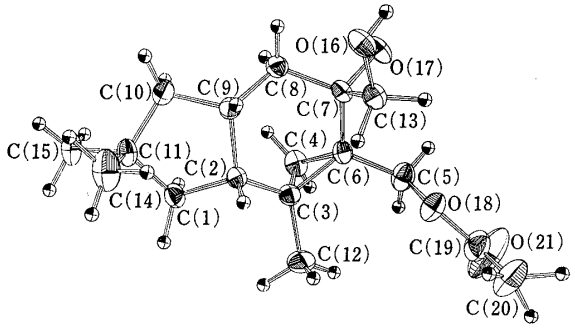


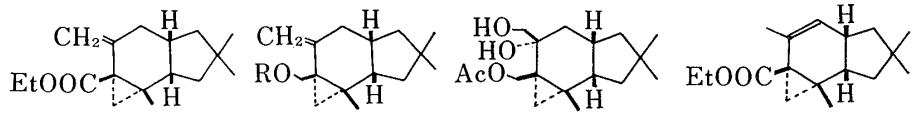
Fig. 2. An ORTEP Drawing[17] of the Molecule Showing Thermal Ellipsoids at the 40% Probability Level except for Hydrogen Atoms, which are artificially Small

and C–H (or O–H) bonds are 0.004 Å and 0.04 Å, respectively, and that for C–C–C angle is 0.3°.

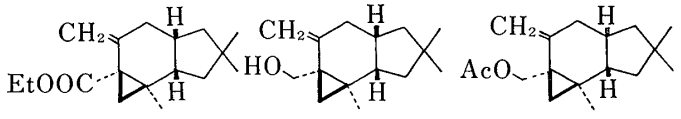
The molecular configuration is shown in Fig. 2, together with the atomic labeling. The ring junction between the five- and six-membered rings is *cis*. The methylenic carbon C(4) in the three-membered ring is oriented to the opposite side of the two hydrogens on C(2) and C(9).

The conformation of the molecule is also shown in Fig. 2. The five-membered ring takes an envelope form, while the conformation of the six-membered ring cannot be described in simple terms. However, it may be seen that two planar groups of atoms are involved in the six-membered ring; one consists of the atoms C(2), C(3), C(6) and C(7) and the other consists of C(3), C(2), C(9) and C(8). The former group is forced into a planar conformation by the cyclopropane ring and the latter by the *cis* junction of the five-membered ring.

The molecules are bound together in the crystal mainly through hydrogen bonds between the hydroxyl groups. These are O(16)–H···O(17) of the molecule translated to $-\boldsymbol{c}$ and O(17)–H···O(16) of the molecule translated to $-\boldsymbol{a}+\boldsymbol{b}$, and the distances between the oxygen atoms are 2.931 Å and 2.764 Å, respectively.



20 **21** : R=H, **22** : R=Ac **23** **24**



25 **26** **27**

Chart 3

As shown in Chart 3, compound **23** was found not to be the expected marasmane derivative but an iso-marasmane derivative. It can therefore be concluded that the norketone obtained as a major product in the carbene insertion reaction had the stereochemistry shown

17) C.K. Johnson, *ORTEP, Oak Ridge National Laboratory Report* ORNL-3794, (1965).

in **15** and that the minor norketone was a stereoisomer having the structure **16**. Compound **16**, which has the natural-type stereochemistry, was then transformed to the marasmane derivative **25** by Wittig reaction. The Wittig methylenation of **16** required more drastic conditions than that of **15**. The ester was then reduced with lithium aluminum hydride to the alcohol **26** and the alcohol was acetylated to give the acetate **27**.

The skeletal rearrangement of the alcohol **26** under solvolytic conditions is under investigation.

Experimental

NMR spectra were obtained using a JEOL 100 MHz instrument and chemical shifts are given in ppm downfield from internal TMS (δ) in $CDCl_3$. IR spectra were measured with a JASCO DS-301 instrument. UV spectra were obtained with a Shimadzu SV-50 spectrometer. Mass spectra (MS) were determined at 70 eV on a Shimadzu LKB 9000 instrument utilizing both a direct inlet system and a GC injection system. Melting points are uncorrected. Elementary analyses were performed by the Micro-analytical Laboratory, Institute of Applied Microbiology, the University of Tokyo. Gas chromatographic analyses (GC) were performed on a Shimadzu GC-4BPF unit. Gas chromatographic conditions were as follows: A) 1.5% OV-1 (1.5 m), 100°, N_2 flow rate, 50 ml/min. B) 1.5% OV-1 (1.5 m), 160°, N_2 flow rate, 50 ml/min. C) 1.5% OV-1 (1.5 m), 140°, N_2 flow rate, 50 ml/min. Column chromatography was carried out on silica gel (Wakogel C-200). Thin-layer chromatography (TLC) was performed on precoated Merck 5721 silica gel plates.

***cis*-4,4,7,7-Tetramethylbicyclo[3,3,0]octan-3-one (9)**——A well stirred suspension of NaH (0.79 g, 30 mmol) in dry dimethoxyethane (DME) (50 ml) was treated dropwise with a solution of the ketone **8** (4.98 g, 33 mmol) in DME (50 ml) for a period of 30 min under an atmosphere of N_2. The resulting suspension was refluxed for 2.5 hr and then cooled to 50°. A solution of methyl iodide (4.26 g, 29 mmol) in DME (50 ml) was then added with stirring for a period of 30 min and the mixture was heated under reflux for 30 min. After cooling, the solution was diluted with water. Extraction with Et_2O followed by washing the combined organic layer with a sat. solution of Na_2SO_4 and then with water afforded the tetramethyl ketone **9** (80% yield) as a colorless oil. NMR ($CDCl_3$) δ: 0.97 (6H, s), 1.05 (3H, s), 1.07 (3H, s), 1.15—1.75 (4H), 1.75—2.35 (2H), 2.35—2.9 (2H); MS, *m/e*: 180 (M^+); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 (C=O); GC, 4.3 min (conditions A).

***cis*-4,4,7,7-Tetramethylbicyclo[3,3,0]octan-3-one Oxime (10)**——A solution of the ketone **9** (6.05 g, 33.6 mmol) and hydroxylamine hydrochloride (4.67 g, 67.2 mmol) in a mixture of EtOH (30 ml) and pyridine (30 ml) was refluxed for 3 hr. Half of the solvent was removed *in vacuo* and the residue was diluted with water. The precipitated crystals were collected and dried to give the oxime **10** (6.26 g). mp 124—124.5° (MeOH); NMR ($CDCl_3$) δ: 0.95 (3H, s), 1.07 (3H, s), 1.13 (6H, s); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3650 (O–H), 1675 (C=N), 922 (N–O); GC, 10.4 min (conditions A); *Anal.* Calcd for $C_{12}H_{21}NO$: C, 73.85; H, 10.77; N, 7.18. Found: C, 73.42; H, 10.65; N, 6.78.

***cis*-1-Cyanomethyl-4,4-dimethyl-2-isopropenylcyclopentane (11a) and 1-Cyanomethyl-4,4-dimethyl-2-isopropylidenecyclopentane (11b)**——A mixture of 13.9 g of the oxime **10**, 42 g of *p*-TsCl and 168 ml of pyridine was heated at 80° for 1 hr. The mixture was cooled and diluted with 1.0 liter of 2% KOH, and then extracted with *n*-hexane. The extract was washed with water, dried over Na_2SO_4 and concentrated to give a mixture of **11a** and **11b** as an oily product (7 g). The mixture was chromatographed on silica gel impregnated with 10% $AgNO_3$, eluting with benzene–hexane (1: 1). The early fractions gave **11b** (2.72 g): NMR ($CDCl_3$) δ: 0.85 (3H, s), 1.11 (3H, s), 1.64 (6H, s); GC, 5.0 min (conditions A). From the later fractions eluted with the same solvent, the isomeric product **11a** was obtained. **11a** (2.34 g): NMR ($CDCl_3$) δ: 1.03 (3H, s), 1.14 (3H, s), 1.74 (3H, s), 4.71 (1H, br.s) and 4.87 (1H, br.s) ($C=CH_2$); MS, *m/e*: 177 (M^+); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2260 (C≡N), 900 (C=C); GC, 5.5 min (conditions A).

***cis*-1-Acetonyl-4,4-dimethyl-2-isopropenylcyclopentane (12)**——A solution of **11a** (2.26 g, 12.8 mmol) in Et_2O (25 ml) was mixed with 33 ml of MeLi–Et_2O solution (MeLi, 12.8 mmol) at −65°, and the whole was stirred for 1 hr under a stream of N_2. The temperature of the reaction mixture was gradually raised, and at −10°, 30 ml of saturated aqueous NH_4Cl solution was added. After stirring for 30 min, the solution was extracted with Et_2O. The extract was washed with water, dried over Na_2SO_4 and concentrated to give a methylketone **12** (2.5 g), which was used without further purification. NMR ($CDCl_3$) δ: 1.01 (3H, s), 1.10 (3H, s), 1.70 (3H, s), 2.10 (3H, s), 4.66 (1H, br.s) and 4.80 (1H, br.s); MS, *m/e* 194 (M^+), 179 (M-15), 161, 151 ($M-COCH_3$), 136, 121 (base peak); IR $\nu_{max}^{CS_2}$ cm^{-1}: 1721 (C=O), 886 (C=C); GC, 5.6 min (conditions A); TLC, Rf. 0.58 (benzene–acetone, 9: 1).

Ethyl *cis*-3-Oxo-4-(4,4-dimethyl-2-isopropenyl)butyrate (13)——A mixture of methylketone **12** (2.47 g, 13 mmol), Et_2CO_3 (13 ml) and DME (13 ml) was added to a suspension of NaH (0.91 g, 38 mmol, prewashed with petr. ether) in dry DME (13 ml). The reaction mixture was heated at 85° for 4 hr under an atmosphere of N_2. After cooling and addition of EtOH to decompose excess NaH, the mixture was poured into ice-water. The solution was then neutralized with acetic acid and extracted with Et_2O. After washing with water, the extract was dried over Na_2SO_4 and the Et_2O was evaporated off to give the ketoester **13** (3.6 g). NMR

($CDCl_3$) δ: 1.03 (3H, s), 1.11 (3H, s), 1.29 (3H, t, J=7 Hz), 1.70 (3H, s), 3.4 (2H, s, $COC\underline{H}_2COO$–), 4.19 (2H, q, J=7 Hz), 4.67 (1H, br.s) and 4.81 (1H, br.s) ($C=C\underline{H}_2$); MS, (direct inlet), *m/e* 266 (M^+), 178, 163, 137, 136, 121; IR $\nu_{max}^{CS_2}$ cm^{-1}: 1790 (COOEt), 1726 (C=O), 888 (C=C); TLC, Rf. 0.63 (benzene–acetone, 9: 1).

Ethyl *cis*-2-Diazo-3-oxo-4-(4,4-dimethyl-2-isopropenyl)butyrate (14)——A solution of the ketoester **13** (3.5 g, 13 mmol) in CH_3CN (13 ml) was treated with a solution of *p*-TsN_3[18] (2.8 g, 14 mmol) in CH_3CN (13 ml), and then Et_3N (1.97 g, 20 mmol) was added dropwise at 0°. The mixture was stirred overnight at room temperature and after dilution with water, was extracted with Et_2O. The extract was washed with 0.1 N HCl, and then with water. Drying over Na_2SO_4 followed by removal of the solvent gave an oily residue which was triturated with petr. ether. The resulting crystals of *p*-toluenesulfamide were filtered off, and the filtrate was concentrated. The oily residue was chromatographed on silica gel (10% benzene in hexane) to give the diazoketoester **14** (2.3 g, 60%). NMR ($CDCl_3$) δ: 1.02 (3H, s), 1.12 (3H, s), 1.33 (3H, t, J= 7 Hz), 1.76 (3H, s), 4.28 (2H, q, J=7 Hz), 4.70 (1H, br.s) and 4.80 (1H, br.s) ($C=C\underline{H}_2$); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2146 ($C=N_2$), 1715 (COOEt), 1653 (C=O).

Ethyl 13-Nor-7-oxo-isomarasman-5-oate (15) and Ethyl 13-Nor-7-oxo-marasman-5-oate (16)[19]——A solution of **14** (2.5 g, 8.5 mmol) in toluene (40 ml) and a solution of $(MeO)_3P$–CuI (360 mg, 1.1 mmol) prepared by Nishizawa's method[20] in toluene (45 ml) were mixed and the mixture was heated at 120° for 1.5 hr. During this reaction, N_2 gas evolution was seen. Toluene was removed *in vacuo*, and the residue was chromatographed on a silica gel column to give a mixture of **16** and **17**, 390 mg (benzene), and **15**, 1010 mg (5% Et_2O–benzene). Compounds **16** and **17** were separated by GC [10% OV-1 (1 m), 200°, He pressure 0.5 kg/cm^2; **16**, 8.6 min; **17**, 5.9 min]. **15**: NMR ($CDCl_3$) δ: 0.975 (3H, s), 1.11 (3H, s), 1.18 (3H, s), 1.29 (3H, t, J=7 Hz), 4.24 (2H, q, J=7 Hz); MS, *m/e* 264 (M^+), 249 (M−15), 236 (M−28), 218, 203, 190, 177, 175, 163, 162, 161, 147; IR $\nu_{max}^{CS_2}$ cm^{-1}: 1735 (COOEt), 1702 (C=O); UV $\lambda_{max}^{ethanol}$ nm (ε): 206 (4100); GC, 5.7 min (conditions B); *Anal.* Calcd for $C_{16}H_{24}O_3$: C, 72.73; H, 9.09. Found: C, 72.73; H, 9.13. **16**: NMR ($CDCl_3$) δ: 1.05 (3H, s), 1.14 (3H, s), 1.17 (3H, s), 1.28 (3H, t, J=7 Hz), 4.22 (2H, q, J=7 Hz); MS, *m/e* 264 (M^+), 249 (M−15), 236 (M−28) 218, 203, 190, 177, 175, 163, 162, 161, 147; IR $\nu_{max}^{CS_2}$ cm^{-1}: 1740 (COOEt), 1700 (C=O); UV $\lambda_{max}^{ethanol}$ nm (ε): 205 (2670); GC, 5.4 min (conditions B). **17**: NMR ($CDCl_3$) δ: 1.05 (3H, s), 1.13 (3H, s), 1.17 (3H, s), 1.22 (3H, s), 1.28 (3H, t, J=7 Hz), 4.21 (2H, q, J=7 Hz); MS, *m/e* 264 (M^+), 249 (M−15), 222, 218, 203, 177, 161, 148; IR $\nu_{max}^{CS_2}$ cm^{-1}: 1738 (C=O), 1730 (C=O); UV $\lambda_{max}^{ethanol}$ nm (ε): 207 (4990); GC, 3.6 min (conditions B).

13-Nor-7ξ-hydroxy-isomarasman-5-ol (18)——A solution of compound **15** (7 mg) in Et_2O (0.5 ml) was cooled to 0° and treated with an ice-cold solution of $LiAlH_4$ (7 mg) in Et_2O. After 30 min at room temperature, the excess $LiAlH_4$ was decomposed by adding moist Et_2O. The product was extracted with Et_2O and the solvent was removed *in vacuo* to give a mixture of diols. The major diol: NMR ($CDCl_3$) δ: 0.25 and 0.47 (2H, ABq, J=5 Hz, cyclopropyl methylene), 3.65 and 4.14 (2H, ABq, J=11 Hz, $C\underline{H}_2OH$). The minor diol: NMR ($CDCl_3$) δ: 0.57 and 0.83 (ABq, J=5 Hz, cyclopropyl methylene). MS (mixture), *m/e* 206 (M−18), 191 (M−18−15), 188 (M−18×2), 175 (M−18−31), 173, 163.

13-Nor-7ξ-hydroxy-marasman-5-ol (19)——Compound **16** (9 mg) was reduced with $LiAlH_4$ using the procedure employed for the preparation of **18** to give the diol **19** (8 mg). NMR ($CDCl_3$) δ: 0.23 (1H, d, J= 5 Hz, B of AB type, cyclopropyl methylene), 0.93 (3H, s), 1.06 (3H, s), 1.22 (3H, s), 3.6 and 4.07 (2H, ABq, J=12 Hz, $C\underline{H}_2OH$), 4.3 (1H, t, J=4 Hz, $C\underline{H}OH$).

Ethyl $\Delta^{7(13)}$-Isomarasmen-5-oate (20)——Dimethylsulfoxide (DMSO, 9 ml) and NaH (144 mg, 6 mmol, prewashed with petr. ether) were mixed and heated with stirring at 60—65° until a homogeneous solution was obtained (*ca.* 2 hr). A solution of $(C_6H_5)_3PCH_3Br$ (2.14 g, 6 mmol) in DMSO (9 ml) was added under ice-cooling, and the mixture was stirred at room temperature for 30 min. A solution of **15** (784 mg, 3 mmol) in DMSO (1.0 ml) was added to the Wittig reagent prepared as above, and the whole mixture was heated at 50—55° with stirring for 2 hr. After cooling to room temperature, the solution was poured into ice-water and then extracted with Et_2O. The extract was washed with water, dried over Na_2SO_4, and concentrated. The residue was chromatographed on a silica gel column, eluting with *n*-hexane–benzene (1: 1), to give 585 mg (75.3%) of the ester **20**. NMR ($CDCl_3$) δ: 0.95 (3H, s), 1.05 (3H, s), 1.07 (3H, s), 1.29 (3H, t, J=7 Hz), 4.14 (2H, q, J=7 Hz), 4.68 and 4.77 (2H, $C=C\underline{H}_2$); MS, *m/e* 262 (M^+), 247 (M−15), 233, 217 (M–OEt), 216, 201, 189 (M–COOEt), 173; IR $\nu_{max}^{CS_2}$ cm^{-1}: 1731 (COOEt), 874 (C=C); GC, 3.4 min (conditions B); *Anal.* Calcd for $C_{17}H_{26}O_2$: C, 77.86; H, 9.92. Found: C, 77.75; H, 9.81.

$\Delta^{7(13)}$-Isomarasmen-5-ol (21)——The ester **20** (96 mg) was reduced with $LiAlH_4$ by the procedure employed for the preparation of **18**, to give the alcohol **21** (80 mg). NMR ($CDCl_3$) δ: 0.43 (1H, d, J=5 Hz, B of AB type, cyclopropyl methylene), 0.94 (3H, s), 1.07 (3H, s), 1.28 (3H, s), 3.73 and 4.11 (2H, ABq, J=12 Hz, $C\underline{H}_2OH$), 4.91 (1H, br.s) and 4.95 (1H, br.s) ($C=C\underline{H}_2$); MS, *m/e* 220 (M^+), 205 (M−15), 202 (M−18), 187 (M−18−15); GC, 2.6 min (conditions B).

$\Delta^{7(13)}$-5-Acetoxy-isomarasmene (22)——Acetylation of **21** with Ac_2O–pyridine at room temperature furnished a monoacetate **22**. NMR ($CDCl_3$) δ: 0.48 (1H, d, J=5 Hz, B of AB type, cyclopropyl methylene),

18) W. von E. Doering and C.H. Depuy, *J. Am. Chem. Soc.*, **75**, 5955 (1953).
19) We termed the carbon skeleton of marasmic acid "marasman," using the carbon numbering shown in C in Chart 1. We used the term "isomarasman" for the stereoisomer of "marasman" at C-3 and C-6.
20) Y. Nishizawa, *Bull. Chem. Soc. Japan*, **34**, 1170 (1961).

0.93 (3H, s), 1.06 (3H, s), 1.19 (3H, s), 2.07 (3H, s), 4.15 and 4.55 (2H, ABq, $J=12$ Hz), 4.73 (1H, br.s) and 4.83 (1H, br.s) (C=C$\underline{H}_2$).

5-Acetoxy-isomarasman-7α,13-diol (**23**)——A solution of **22** (56 mg, 0.2 mmol) in pyridine (2 ml) was treated with a solution of OsO_4 (63 mg, 0.25 mmol) in pyridine (2 ml) at 0° then allowed to stand overnight at room temperature. A freshly prepared solution of $NaHSO_3$ in aqueous pyridine (0.5 ml of the solution prepared by dissolving 0.9 g of $NaHSO_3$ in 10 ml of pyridine and 15 ml of H_2O) was added to it, and the mixture was stirred for 2 hr. After dilution with water, the mixture was extracted with Et_2O and the Et_2O layer was washed with water. Drying over Na_2SO_4 followed by concentration gave 57 mg of **23** as a crystalline compound. mp 143—144° (acetone); NMR ($CDCl_3$) δ: 0.97 (3H, s), 1.05 (3H, s), 1.11 (3H, s), 2.07 (3H, s), 3.48—3.9 (2H, C$\underline{H}_2$OH), 4.16 and 4.54 (2H, ABq, $J=12$ Hz); MS (direct inlet), *m/e* 279 (M−17), 265 (M−31), 247 (M−31−18), 236 (M−60), 218 (M−60−18); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 3500 (OH), 1736 (CH_3COO); *Anal.* Calcd for $C_{17}H_{28}O_4$: C, 68.9; H, 9.46. Found: C, 69.11; H, 9.46.

Ethyl $\Delta^{7(8)}$-Isomarasmen-5-oate (**24**)——A solution of compound **20** (10 mg) and I_2 (2 mg) in xylene (3 ml) containing pyridine (0.3 ml) was heated under reflex for 4 hr. The products were collected by preparative GC (1.5% OV-1, 150°, He, 0.7 kg/cm^2), providing a pure sample of **24** (40% yield). NMR ($CDCl_3$) δ: 0.97 (3H, s), 1.04 (3H, s), 1.11 (3H, s), 1.28 (3H, t, $J=7$ Hz), 1.83 (3H, s), 4.18 (2H, q, $J=7$ Hz), 5.3 (1H, br.s, C=C$\underline{H}$–); MS, *m/e* 262 (M^+), 247 (M−15), 217 (M−OEt), 201, 189 (M–COOEt), 173; GC, 3.1 min (conditions B).

Ethyl $\Delta^{7(13)}$-Marasmen-5-oate (**25**)——A solution of dimethylsulfinyl carbanion prepared from NaH (27 mg, 1.12 mmol) and DMSO (4 ml, freshly distilled over CaH_2) was treated with neat $(C_6H_5)_3PCH_3Br$ (380 mg, 1.06 mmol, 10 eq.) (without solvent) under cooling, and the mixture was stirred for 1 hr at room temperature. A solution of the ketone **16** (26 mg, 0.098 mmol) in DMSO (0.5 ml) was added to the Wittig reagent and the mixture was heated at 50° for 24 hr. After pouring into ice-water, the mixture was extracted with Et_2O. The extract was washed with water, dried over Na_2SO_4 and concentrated *in vacuo* to give an oily residue. Subsequent column chromatography on silica gel (benzene–hexane 1: 1) afforded 17 mg (60% yield) of compound **25**. NMR ($CDCl_3$) δ: 0.88 and 1.35 (2H, ABq, $J=5$ Hz, cyclopropyl C$\underline{H}_2$), 1.00 (3H, s), 1.06 (3H, s), 1.11 (3H, s), 1.27 (3H, t, $J=7.5$ Hz), 4.19 (2H, q, $J=7$ Hz), 4.85 (1H, br.s) and 4.92 (1H, br.s) (C=C$\underline{H}_2$); MS, *m/e* 262 (M^+), 247 (M−15), 233 (M−29), 217, 216, 201, 189 (M–COOEt), 173; IR $\nu_{max}^{CS_2}$ cm^{-1}: 1732 (COOEt), 886 (C=C); GC, 4.2 min (conditions C).

$\Delta^{7(13)}$-Marasmen-5-ol (**26**)——Compound **25** (6 mg) was reduced with $LiAlH_4$ by the procedure employed for the preparation of **18** to give the alcohol **26**. NMR ($CDCl_3$) δ: 0.52 (1H, d, $J=6$ Hz, B of AB type, cyclopropyl C$\underline{H}_2$), 0.94 (3H, s), 1.04 (3H, s), 1.20 (3H, s), 3.67 and 4.08 (2H, ABq, $J=13$ Hz, C$\underline{H}_2$OH), 4.95 (1H, br.s) and 5.03 (1H, br.s) (C=C$\underline{H}_2$); MS, *m/e* 220 (M^+), 205 (M−15), 202 (M−18), 187, 173, 159; IR $\nu_{max}^{CS_2}$ cm^{-1}: 3640 (OH), 875 (C=C); GC, 3.3 min (condition C).

$\Delta^{7(13)}$-5-Acetoxymarasmene (**27**)——Acetylation of **26** with Ac_2O–pyridine at room temperature furnished a monoacetate **27**. NMR ($CDCl_3$) δ: 0.94 (3H, s), 1.05 (3H, s), 1.14 (3H, s), 2.07 (3H, s), 4.01 and 4.52 (2H, ABq, $J=11$ Hz, C$\underline{H}_2$OCOCH$_3$), 4.85 (2H, C=CH_2); MS, *m/e* 262 (M^+), 247 (M−15), 202 (M−60), 187, 173, 159, 146; IR $\nu_{max}^{CS_2}$ cm^{-1}: 1741 (CH_3COO), 904 (C=C), 731 (C=C); GC, 4.7 min (conditions C).