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# A Total Synthesis of (±)-Warburganal[1]

Tadashi Nakata,[2] Hiroyuki Akita,[2] Takanobu Naito,[2a]
and Takeshi Oishi[2]

*The Institute of Physical and Chemical Research (Riken)*[2]

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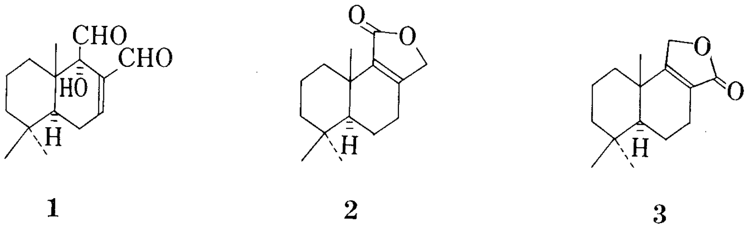
A total synthesis of (±)-warburganal has been completed starting from (±)-isodrimenin and other drimane-type compounds.

11,12-Diacetoxy-drim-8-ene (**9**), which can be readily obtained from the above starting compounds, was converted to the 7-oxo derivative (**7**). Treatment of **7** with 30% $H_2O_2$ followed by $NH_2NH_2 \cdot H_2O$ promoted reductive opening of the resulting keto epoxide group to afford the trialcohol (**11**). Selective silylation of the allylic primary alcohol in **11** with *tert*-butyldimethylsilyl chloride followed by protection of the $\alpha$-glycol with N,N′-carbonyldiimidazole afforded the carbonate (**14**). Desilylation of **14** and subsequent oxidation of the allyl alcohol moiety afforded **16**. Protection of the aldehyde followed by base-induced deprotection of the glycol afforded **18**, which was subjected to Moffatt oxidation to give **19**. Treatment of **19** with *p*-TsOH–acetone afforded (±)-warburganal.

**Keywords**——antifeedant; sesquiterpenes; oxidation of $\alpha$-glycol; protection of hydroxy group; epoxidation of $\alpha,\beta$-unsaturated ketone

Warburganal (**1**), isolated from the East African medicinal trees *Warburgia ugandensis* and *W. stuhlmannii* (Canellaceae),[3] exhibits effective antifeedant activity against the African army worms, *Spodoptera littoralis* and *S. exempta*, as well as molluscicidal activity against th schistosome-transmitting snail *Biomphalaria glabaratus*, cytotoxicity (KB test, 0.01 $\mu$g/ml), and a broad antimicrobial spectrum.

These remarkable bioactivity properties coupled with its unique structure, involving both $\beta$-hydroxy aldehyde and enal units in the same ring, have attracted the attention of many chemists, and total syntheses of **1** have already been achieved by us[1] and several other groups.[4a–c] The present paper describes in detail the results reported in our previous communication,[1] together with some significant improvements in the procedures and pathways developed since then.



**1** **2** **3**

Chart 1

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[1] A part of this work has been published as a short communication, T. Nakata, H. Akita, T. Naito, and T. Oishi, *J. Am. Chem. Soc.*, **101**, 4400 (1979).

[2] Location: *2-1 Hirosawa, Wako-shi, Saitama 351, Japan*; *a*) Present address: *Research Laboratory, Kaken Chemical Co., Ltd., 2-28-8 Honkomagome, Bunkyo-ku, Tokyo 113, Japan.*

[3] *a*) I. Kubo, Y.-W. Lee, M.J. Pettei, F. Pilkiewicz, and K. Nakanishi, *J. Chem. Soc. Chem. Commun.*, **1976**, 1013; *b*) I. Kubo, I. Miura, M.J. Pettei, Y.-W. Lee, F. Pilkiewicz, and K. Nakanishi, *Tetrahedron Lett.*, **1977**, 4553; *c*) K. Nakanishi and I. Kubo, *Isr. J. Chem.*, **16**, 28 (1977).

[4] *a*) S.P. Tanis and K. Nakanishi, *J. Am. Chem. Soc.*, **101**, 4398 (1979); *b*) A. Ohsuka and A. Matsukawa, *Chem. Lett.*, **1979**, 635; *c*) A. Kimura and S. Isoe, The 22nd Symposium on The Chemistry of Natural Products, Fukuoka, Japan, Abstracts of Papers, p. 198.

In the previous paper,[5] we described large scale preparations of (±)-isodrimenin (**2**) and (±)-confertifolin (**3**) from $\beta$-ionone. One of the features of the present synthesis is the use of readily obtainable racemic **2** or **3** as a starting material because, once the pathway leading to (±)-warburganal is established, the synthesis of optically active warburganal may become possible, since optically active isodrimenin (**2**) and confertifolin (**3**) are now obtainable from *l*-abietic acid.[6]

Oxidation of **2** with $CrO_3$ in acetic acid afforded 7-oxoisodrimenin (**4**),[7] which was converted to the ketal (**5**) in 94% yield. Reductive opening of the lactone ring of **5** with $LiAlH_4$ gave, after acidification with 10% HCl, the keto dialcohol (**6**), whose infrared spectrum (IR) exhibits a peak at 1665 $cm^{-1}$ in $CCl_4$ due to an unsaturated ketone. Acetylation of **6** gave the diacetate (**7**) in a yield of 67% from **5**. The pathway to **7** from **2** is rather long, so its direct preparation from the ene diacetate (**9**) was investigated. The compound (**9**) can be conveniently obtained from the diacetoxy acetal (**8**), an intermediate for the preparation of isodrimenin (**2**),[5] by $LiAlH_4$ reduction followed by acetylation in excellent yield. Oxidation of **9** with $CrO_3$ in acetic acid proceeded selectively to afford **7** in 63% yield,[8] although two other allylic methylenes were present in **9**. The overall yield of **7** from **8** was increased from 27% (yield *via* **2**) to 56% by adopting this new route.

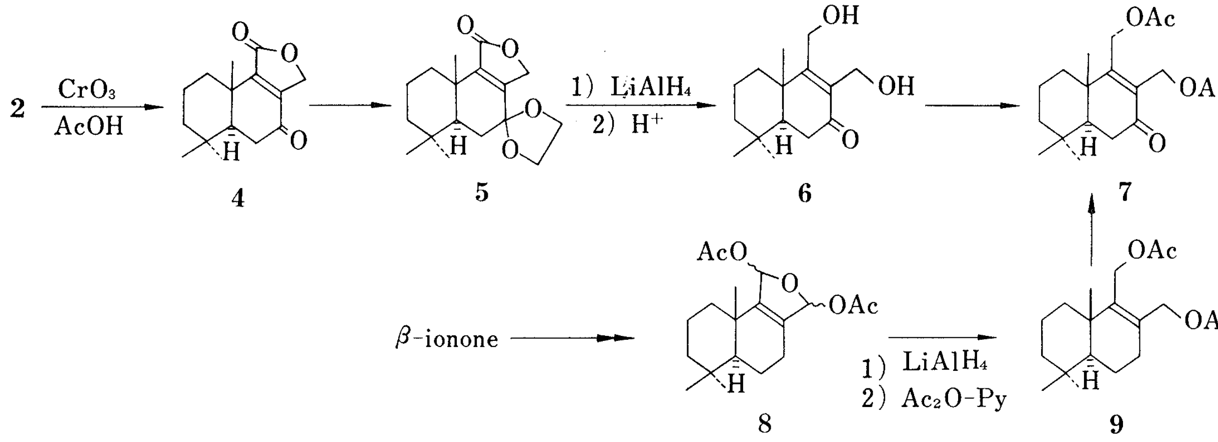

Chart 2

Epoxidation of the $\alpha,\beta$-unsaturated ketone (**7**) with 30% $H_2O_2$ in methanolic sodium hydroxide solution gave exclusively the single epoxide in 82% yield. As the $\beta$-side of the double bond of **7** is highly hindered, the reagent should attack from the $\alpha$-side, so the product was assigned as the $\alpha$-epoxide (**10**). When a mixture of **10** and an excess of 100% hydrazine hydrate was kept at 90—120° for a short time or stirred for three hours at room temperature, the allyl alcohol (**11**) was produced, as expected.[9] However, a nitrogen-containing compound, whose structure is presumed to be either **12a** or **12b**, was always obtained as a by-product.

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[5] H. Akita, T. Naito, and T. Oishi, *Chemistry Lett.*, **1979**, 1365. See also the preceding paper in this issue.

[6] H. Akita and T. Oishi, *Tetrahedron Lett.*, **1978**, 3733.

[7] *a*) E. Wenkert and D.P. Strike, *J. Am. Chem. Soc.*, **86**, 2044 (1964); *b*) H.H. Appel, J.D. Connolly, K.H. Overton, and R.P.M. Bond, *J. Chem. Soc.*, **1960**, 4685; *c*) T. Kato, T. Iida, T. Suzuki, and Y. Kitahara, *Tetrahedron Lett.*, **1972**, 4257. Confertifolin (**3**) is reported to be stable under these oxidation conditions.

[8] The compound (**9**) is also readily obtainable from racemic isodrimenin (**2**), confertifolin (**3**) and winterin.[5] Since the preparation of these optically active sesquiterpenes from *l*-abietic acid has already been achieved, the preparation of optically active **9** and **7** has been made much easier by this improvement.

[9] *a*) P.S. Wharton and D.H. Bohlen, *J. Org. Chem.*, **26**, 3615 (1961); P.S. Wharton, *ibid.*, **26**, 4781 (1961); *b*) C.D. Djerassi, D.H. Williams, and B. Berkoz, *ibid.*, **27**, 2205 (1962); *c*) P.D. Klimsta and R.E. Counsell, *J. Med. Chem.*, **8**, 48 (1965); *d*) H. Tada and Y.K. Sawa, *J. Org. Chem.*, **33**, 3347 (1968).

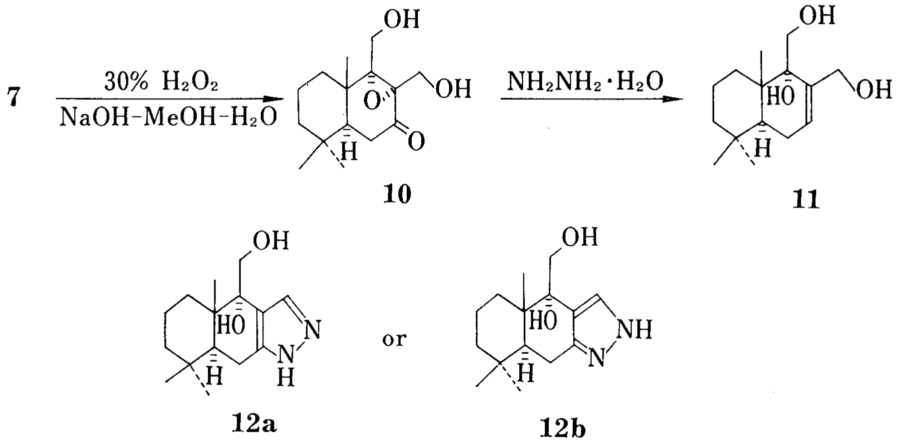

Chart 3

This difficulty was overcome, after many trials, by carrying out the reaction at room temperature in the presence of a small amount of acetic acid as a catalyst. The structure of **11** was confirmed by the appearance of the vinyl proton at $\delta$ 5.86 in the nuclear magnetic resonance spectrum (NMR).

The crucial point of the present synthesis is in the strategy for the selective and effective protection of the three different alcohol groups in **11**. In the hope of protecting the allylic primary alcohol selectively, **11** was, without purification, treated with *tert*-butyldimethylsilyl

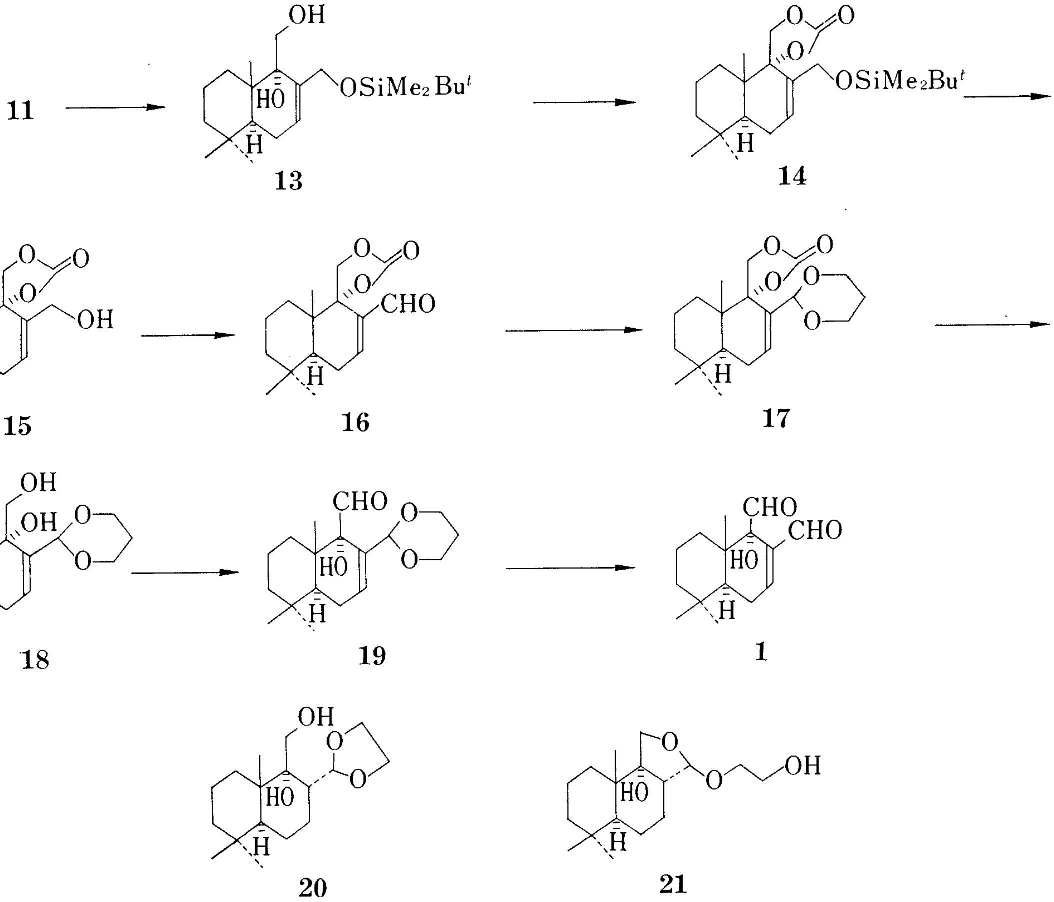

Chart 4

chloride[10] in dimethyl formamide (DMF) in the presence of imidazole to give the monosilyl ether (**13**) as a sole product in 84% overall yield from **10**. The next stage is the protection of vicinal alcohols in **13**. A protective group which is stable to acid but sensitive to base should be used, because an acid-catalyzed selective deprotection of the above introduced silyl group is required in the next steps. A carbonate protecting group[11] was chosen for this purpose. The glycol (**13**) was refluxed in benzene with N,N′-carbonyldiimidazole to produce the carbonate (**14**) in quiantitative yield, and this was desilylated with camphorsulfonic acid[12] in methanol to afford the allyl alcohol (**15**) in quantitative yield, the carbonate group being retained as expected. Jones oxidation[13] of **15** afforded the enal (**16**) in quantitative yield. The presence of two kinds of carbonyl group in **16** is evident from the peaks at 1790 and 1695 $cm^{-1}$ in the IR spectrum. After converting the aldehyde (**16**) to the acetal (**17**), the carbonate group was cleaved by base treatment at room temperature to give the glycol (**18**). Both steps proceeded almost quantitatively.

The compound (**18**) was presumed to be quite sensitive to acids, since its primary alcohol is located in a position which could assist in the acid-catalyzed cleavage of the cyclic acetal group. In fact, **18** gave several spots on thin layer chromatography (TLC) when exposed to *p*-TsOH in benzene. In a model study, the glycol acetal (**20**) gave the isomeric acetal (**21**) on brief contact with *p*-TsOH in benzene. Therefore, a neutral or rather basic state was required in the oxidation of the glycol. After several attempts,[14] the glycol (**18**) was successfuly converted to the $\alpha$-hydroxy aldehyde (**19**) by means of the Moffatt oxidation[15] in 73% yield. Treatment of **19** with *p*-TsOH in acetone at room temperature gave (±)-warburganal (**1**), mp 111—112°, in quantitative yield. The spectral data (IR, NMR, mass spectra) were all identical with those of the natural product.

## Experimental

Melting points were measured with a Kofler micro melting point apparatus and are uncorrected. IR spectra were measured on a JASCO A-3 spectrophotometer, NMR spectra on Varian HA-100 and JEOL MH-60 instruments, and MS spectra on a Hitachi RMU-6M mass spectrometer.

**7-Ethanedionylisodrimenin (5)**——A solution of 7-oxoisodrimenin (**4**) (254 mg), ethylene glycol (2 ml) and *p*-TsOH·$H_2O$ (30 mg) in benzene was refluxed overnight using a Dean-Stark apparatus. After the mixture had been cooled, the solvent was washed with 10% $Na_2CO_3$ solution and sat. NaCl solution, dried over $Na_2SO_4$, and concentrated. The residue was subjected to silica gel chromatography. Elution with hexane–ethyl acetate (3: 1) afforded 281 mg (94%) of the ketal (**5**), which was recrystallized from ether–hexane to give colorless prisms, mp 89—90°. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1760. NMR ($CDCl_3$) $\delta$: 3.8—4.2 (m, $OCH_2CH_2O$), 4.68 (2H, s, $C_{12}$–H). *Anal.* Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.82; H, 8.27.

**11,12-Dihydroxy-7-oxodrim-8-ene (6)**——A solution of the ketal (**5**) (3.3 g) in ether (100 ml) was treated with $LiAlH_4$ (2.0 g) at room temperature, and the mixture was stirred for 2.5 hr. After the addition of 10% HCl, the mixture was extracted with ether. The ether layer was washed with sat. NaCl solution, dried over $MgSO_4$ and concentrated to afford the enone diol (**6**) (2.96 g), which was used for the next reaction without purification. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3400, 1665. MS *m/e*: 234 ($M^+-H_2O$).

**11,12-Diacetoxy-7-oxodrim-8-ene (7)**——A mixture of the crude enone-diol (**6**) (2.96 g), pyridine (10 ml), and acetic anhydride (10 ml) was allowed to stand at room temperature for 4 hr. After the addition of water,

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10) E.J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, **94**, 6190 (1972); E.J. Corey and J. Mann, *ibid.*, **95**, 6832 (1973).

11) W. Hartmann, H.-G. Heine, H.-M. Fischler, and D. Wendisch, *Tetrahedron*, **29**, 2333 (1973); J.P. Kutney and A.H. Ratcliffe, *Synth. Commun.*, **5**, 47 (1975).

12) Hydrolysis of **14** with AcOH–THF–$H_2O$ (3: 1: 1) gave a much less satisfactory result (57% yield).

13) K.E. Harding, L.M. May, and K.F. Dick, *J. Org. Chem.*, **49**, 1664 (1975).

14) Corey's procedure for the oxidation of $\alpha$-glycol, used in the synthesis of gibberellin $A_3$ [$Me_2SO$, $(CCl_3CO)_2O$, followed by $Et_3N$ treatment] [E.J. Corey, R.L. Danheiser, S. Chandrasekaran, P. Siret, G.E. Keck, and J.-L. Gras, *J. Am. Chem. Soc.*, **100**, 8031 (1978); see also, K. Omura, A.K. Shama, and D. Swern, *J. Org. Chem.*, **41**, 957, 3329 (1976)], gave **19** in only 7% yield, although the model compound (**20**) afforded the corresponding aldehyde in much better yield (59%).

15) J.G. Moffatt, "Organic Syntheses," Vol. 47, ed. by W.D. Emmons, John Wiley and Sons, Inc., New York, 1967, p. 25.

the mixture was extracted with ether. The ether layer was washed successively with 10% HCl, 10% $Na_2CO_3$ solution, and sat. NaCl solution, then dried over $MgSO_4$ and concentrated. The residue was chromatographed on silica gel. Elution with hexane-ethyl acetate (1: 1) afforded 2.55 g (67% from **5**) of the enone-diacetate (**7**). Recrystallization from ether–hexane afforded colorless needles, mp 87—88°. IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm$^{-1}$: 1745, 1680. NMR ($CDCl_3$) $\delta$: 2.00 (3H, s, $OCOCH_3$), 2.05 (3H, s, $OCOCH_3$). *Anal.* Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.89; H, 8.36.

**11,12-Diacetoxy-drim-8-ene (9)**——A solution of the acetoxydihydrofuran (**8**)[16] (866 mg) in ether (50 ml) was treated with $LiAlH_4$ (490 mg) under ice-cooling and the mixture was stirred for 30 min at this temperature then for 1 hr at room temperature. After the addition of cold water and 10% HCl, the mixture was extracted with ether. The extract was washed with sat. $NaHCO_3$ solution and sat. NaCl solution, dried over $MgSO_4$, and concentrated to give 614 mg of diol, which was dissolved in a mixture of acetic anhydride (5 ml) and pyridine (5 ml) and allowed to stand overnight in a refrigerator. After the addition of water, the mixture was extracted with ether. The extract was washed successively with 5% HCl, 10% $Na_2CO_3$ solution and sat. NaCl solution, dried over $MgSO_4$, and concentrated to give 817 mg of an oil, which was chromatographed on silica gel. The fraction eluted from hexane–ethyl acetate (10: 1) afforded 769 mg (89% from **8**) of **9**. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm$^{-1}$: 1730. NMR ($CDCl_3$) $\delta$: 2.01 (3H, s, OAc), 2.03 (3H, s, OAc), 4.46 (1H, d, $J=$ 12 Hz), 4.63 (1H, d, $J=12$ Hz), 4.59 (2H, s). MS *m/e*: 322 ($M^+$).

**Preparation of 7 by $CrO_3$ Oxidation of 9**——$CrO_3$ (717 mg) was added to a solution of **9** (769 mg) in acetic acid (8 ml), and the mixture was stirred overnight. After the addition of water, the mixture was extracted with ether. After usual work-up and silica gel chromatography, 507 mg (63%) of the enone diacetate (**9**) was obtained. Recrystallization from ether–hexane afforded colorless needles, mp 87—88°; this material was identical with the sample prepared from **5**.

**8α,9α-Epoxy-7-oxodrimane-11,12-diol (10)**——To a solution of **7** (412 mg) in methanol (10 ml), 30% $H_2O_2$ (1.2 ml) was added, followed by 10% NaOH solution (0.6 ml), and the mixture was stirred for 1 hr at 0°. After the most of methanol had been evaporated off, ether was added to the residue and the ether layer was washed with sat. NaCl solution, dried over $MgSO_4$ and evaporated to dryness to give a solid, which was recrystallized from ether–hexane to give 218 mg of the epoxy ketone (**10**), mp 117—118°. The filtrate was chromatographed on silica gel. Elution with hexane–ethyl acetate (1: 1) afforded 51 mg of **10**, (total yield, 82%). IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm$^{-1}$: 3590, 3460, 1695. *Anal.* Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02. Found: C, 67.11; H, 9.08.

**Drim-7-ene-9α,11,12-triol (11)**——A mixture of the epoxy ketone (**10**) (114 mg) and 100% $NH_2NH_2$–$H_2O$ (2 ml) was stirred for 3 hr at room temperature under argon. After addition of water, the mixture was extracted with ether. The solvent was washed with sat. NaCl solution, dried over $MgSO_4$, and concentrated to give the crude triol (11) (87 mg), which was subjected to preparative thin-layer chromatography (PTLC) on silica gel using ethyl acetate as a developing solvent. The zone with *Rf* 0.5 gave 25 mg (23%) of the triol (**11**), mp 137—138° (recrystallized from ether). IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm$^{-1}$: 3470. NMR ($CDCl_3$) $\delta$: 5.86 (1H, m, $C_7$–H). MS *m/e*: 223 ($M^+-CH_2OH$). *Anal.* Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.14; H, 10.20. The zone with *Rf* 0.1 gave 23 mg of a nitrogen-containing compound (**12a** or **12b**), mp 137—139° (recrystallized from ether). NMR ($C_5D_5N$) $\delta$: 8.44 (1H, s, C=$\underline{\mathrm{H}}$–N=). *Anal.* Calcd for $C_{15}H_{24}O_2N_2$: C, 68.15; H, 9.15; N, 10.60. Found: C, 67.95; H, 9.23; N, 10.70.

**12-(*tert*-Butyl)dimethylsilyloxydrim-7-ene-9,11-diol (13)**——Imidazole (85 mg) and *tert*-butyldimethylsilyl chloride (63 mg) in DMF (1 ml) were added to a solution of the crude (11) (106 mg) in DMF (2 ml), and the mixture was stirred for 20 min under ice-cooling. After the addition of water, the mixture was washed with sat. NaCl solution, dried over $MgSO_4$ and concentrated to give an oil, which was chromatographed on silica gel. Elution with hexane–ether (1: 1) afforded 84 mg (50% from **10**) of **13**. NMR ($CDCl_3$) $\delta$: 5.81 (1H, m, $C_7$–H). MS *m/e*: 337 ($M^+-CH_2OH$).

**Improved Preparation of the Triol Monosilyl Ether (13)**——A solution of the epoxy ketone (**10**) (2.96 g) in acetic acid (19 ml) was added to 100% $NH_2NH_2\cdot H_2O$ (100 ml) under ice-cooling and the mixture was stirred for 1.5 hr at room temperature. Evolution of nitrogen gas was observed. The whole solution was poured into ice-water and extracted with ether. The ether layer was washed with sat. NaCl solution, dried over $MgSO_4$ and evaporated to dryness to give a solid, which was, without purification, dissolved in DMF (50 ml). Imidazole (2.244 g) and *tert*-butyldimethylsilyl chloride (1.66 g) were added to this solution under ice-cooling and the mixture was stirred for 2 hr. After usual work-up and chromatography on silica gel, 3.40 g (84% from **10**) of **13** was obtained.

**9α,11-Carbonyldioxy-12-(*tert*-butyl)dimethylsilyldrim-7-ene (14)**——N,N′-carbonyldiimidazole (342 mg) was added to a solution of **13** (194 mg) in benzene (15 ml), and the mixture was refluxed for 30 min. The solution was washed with sat. NaCl solution, dried over $MgSO_4$, and concentrated to afford 224 mg (100%) of **14**, mp 59—60° (recrystallized from hexane). IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm$^{-1}$: 1785. NMR ($CDCl_3$) $\delta$: 4.17 (2H, s, $C_{12}$–H), 4.32 (1H, d, $J=9$ Hz, $C_{11}$–$H_A$), 4.75 (1H, d, $J=9$ Hz, $C_{11}$–$H_B$), 6.05 (1H, m, $C_7$–H). *Anal.* Calcd for $C_{22}H_{37}O_4Si$: C, 66.96; H, 9.71. Found: C, 67.27, H, 9.73.

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[16] H. Akita, T. Naito, and T. Oishi, *Chem. Pharm. Bull.*, **28**, 2166 (1980).

**9α,11-Carbonyldioxydrim-7-en-12-ol (15)**——Camphorsulfonic acid (15 mg) was added to a solution of the carbonate (**14**) (63 mg) in methanol (6 ml), and the solution was stirred for 3 hr at room temperature. After the solvent had been evaporated off, the residue was extracted with a mixture of ether and $CH_2Cl_2$. The extract was washed with sat. $NaHCO_3$ solution and then with sat. NaCl solution, dried over $MgSO_4$, and concentrated to give a solid, which was triturated with ether–hexane to give 45 mg (100%) of the alcohol (**15**), mp 146—149° (recrystallized from benzene–hexane). IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3600, 3400, 1785. NMR ($CDCl_3$) $\delta$: 4.19 (2H, s, $C_{12}$–H), 4.36 (1H, d, $J=9$ Hz, $C_{11}$–$H_A$), 4.71 (1H, d, $J=9$ Hz, $C_{11}$–$H_B$), 6.15 (1H, dd, $J=5$ Hz, 2 Hz, $C_7$–H). *Anal.* Calcd for $C_{16}H_{24}O_4$: C, 68.45; H, 8.63. Found: C, 68.98; H, 8.80.

**9α,11-Carbonyldioxydrim-7-en-12-al (16)**——A solution of the alcohol (**15**) (69 mg) in acetone (6 ml) was treated with 6 drops of Jones reagent under ice-cooling and the solution was stirred for 5 min. After the addition of isopropanol, the solvent was evaporated off and water was added to the residue. The mixture was extracted with ether–$CH_2Cl_2$ and the solvent was washed with sat. $NaHCO_3$ solution and then with sat. NaCl solution, dried over $MgSO_4$ and concentrated to give 69 mg (100%) of the aldehyde (**16**), which was recrystallized from benzene–hexane to give colorless needles, mp 133—135°. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 1790, 1695. NMR ($CDCl_3$) $\delta$: 4.34 (1H, d, $J=9$ Hz, $C_{11}$–$H_A$), 4.62 (1H, d, $J=9$ Hz, $C_{11}$–$H_B$), 7.21 (1H, dd, $J=5$ Hz, 2 Hz, $C_7$–H), 9.40 (1H, s, CHO). *Anal.* Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.97; H, 8.13.

**9α,11-Carbonyldioxy-12-propanedionyldrim-7-ene (17)**——A mixture of the aldehyde (**16**) (308 mg), 1,3-propanediol (1.5 ml) and a catalytic amount of *p*-TsOH in benzene (40 ml) was refluxed for 15 min using a Dean-Stark apparatus. The mixture was then extracted with ether and the extract was washed with 10% $Na_2CO_3$ solution and then with sat. NaCl solution, dried over $MgSO_4$, and concentrated to give a solid, which was recrystallized from ether–hexane to give 360 mg (97%) of the acetal (**17**), mp 167—168°. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 1780. NMR ($CDCl_3$) $\delta$: 5.04 (1H, s, $C_{12}$–H). *Anal.* Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.92; H, 8.42.

**12-Propandionyldrim-7-ene-9α,11-diol (18)**——To a solution of the carbonate (**17**) (200 mg) in dioxane (10 ml), 10% NaOH solution (5 ml) and water (5 ml) were added. The mixture was stirred for 1.5 hr at room temperature and extracted with ether. The ether layer was washed with sat. NaCl solution, dried over $MgSO_4$ and concentrated to give a solid, which was chromatographed on silica gel. Elution with hexane–ether (1: 4) afforded 181 mg (98%) of the glycol (**18**), mp 99—100° (recrystallized from ether–hexane). IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3500. NMR ($CDCl_3$) $\delta$: 5.14 (1H, s, $C_{12}$–H), 6.23 (1H, m, $C_7$–H). *Anal.* Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.77; H, 9.75.

**9α-Hydroxy-12-propanedionyldrim-7-en-11-al (19)**——Dimethylsulfoxide (0.4 ml), pyridine (20 μl), trifluoroacetic acid (7 μl) and dicyclohexylcarbodiimide (109 mg) were added to a solution of **18** (55 mg) in benzene (3 ml). The mixture was stirred for 5 hr at room temperature and was, after removal of the undissolved material by filtration, extracted with ether. The ether layer was washed with sat. NaCl solution, dried over $MgSO_4$ and concentrated. The residue was subjected to PTLC on Silica gel using hexane–ether (1: 3) as a developing solvent to give 40 mg (73%) of the α-hydroxy aldehyde (**19**), mp 114—116° (recrystallized from ether–hexane). IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3480, 1710. NMR ($CDCl_3$) $\delta$: 4.84 (1H, s, $C_{12}$–H), 6.31 (1H, m, $C_7$–H), 9.77 (1H, d, $J=1$ Hz, CHO). *Anal.* Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 70.24; H, 9.15.

**(±)-Warburganal (1)**——*p*-TsOH (5 mg) was added to a solution of **19** (11 mg) in acetone (5 ml), and the mixture was stirred for 1 hr at room temperature. The solvent was evaporated off and the residue was dissolved in ether. The ether solution was washed with 10% $Na_2CO_3$ solution and then with sat. NaCl solution, dried over $MgSO_4$ and concentrated. The residue was subjected to PTLC on silica gel using ether–hexane (2:1) as a developing solvent to give 9 mg (100%) of (±)-warburganal (**1**), which was recrystallized from ether–hexane, colorless prisms, mp 111—112°. The spectral data (IR, NMR, MS) were identical with those of the natural product. *Anal.* Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.00; H, 8.89.

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