Isolation of Oxygenated Derivatives of Solanesol from Burley Tobacco

Norio YASUMATSU, Motoko EDA, Yasuko TSUJINO
and Masao NOGUCHI

*Central Research Institute, The Japan Tobacco and Salt Public Corporation,
6-2, Umegaoka, Midori-ku, Yokohama 227, Japan*

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Some monohydroxylated derivatives of solanesol were isolated from cured Burley tobacco and their structures were elucidated by chemical and spectrometric studies. One of them was shown to be 3,7,11,15,19,23,27,31,35-nonamethyl-2,6,10,14,18,22,26,30,33-hexatriacontanonaen-1,35-diol and another to be 3,7,11,15,19,23,27,31-octamethyl-35-methylen-2,6,10,14,18,22,26,30-hexatriacontaoctaen-1,34-diol. Evidence has also been presented to show the presence of other solanesol derivatives which have a hydroxylated internal isoprene residue.

Some characteristic terpenoids such as solanesol^{1,2)} and macrocyclic duvane diterpenoids^{3,4)} have been isolated from the nonvolatile resinous constituents of tobacco leaves. In the leaves, solanesol is the most abundant terpenoid and has been said to be accompanied with its analogues and oxidation products.⁵⁾ The presumption of the existence of solanesol analogues is based on the fact that some chromatographic fractions of the hexane extract of tobacco have IR absorption similar to that of solanesol. But any solanesol analogue has not yet been isolated.

In the course of our study on nonvolatile constituents of the dichloromethane extract of Burley tobacco (*Nicotiana tabacum*), three hydroxylated derivatives of solanesol were isolated. These derivatives were characterized as 3,7,11,15,19,23,27,31,35-nonamethyl-2,6,10,14,18,22,26,30,33-hexatriacontanonaen-1,35-diol (I), 3,7,11,15,19,23,27,31-octamethyl-35-methylen-2,6,10,14,18,22,26,30-hexatriacontaoctaen-1,34-diol (II) and a mixture of analogous solanesol derivatives having a hydroxylated internal isoprene residue. In this paper, we wish to report the isolation and structural elucidation of the derivatives.

The nonvolatile part of a dichloromethane extract of Burley tobacco was chromatographed on a silicic acid column. The fraction eluted by ether-hexane (1:1) was further

fractionated on Florisil and preparative high speed chromatography columns. These purification procedures gave two white crystals of mp 53.5~54.5°C (I) and mp 54.0~55.5°C (II) and an oil (III) which was chromatographically homogeneous.

The IR, PMR and MS data (Fig. 1) of the three isolates and solanesol were very similar to each other, suggesting that these three compounds were mutually related. The infrared spectra of the isolates all include hydroxyl bands (3620~3000 cm⁻¹), weak bands indicative of nonconjugated double bonds (1664 cm⁻¹) and bands due to allylic alcohols (995 cm⁻¹) and trisubstituted double bonds (840 cm⁻¹). The presence of allylic alcohols was also indicated by PMR signals of the protons bonded to allylic carbinol carbons at δ 4.03 (2H, d, $J=6$ Hz) which showed downfield shifts of about 0.5 ppm by acetylation. The lack of UV absorption above 220 nm suggested the absence of conjugated double bonds. Catalytic hydrogenation on palladium catalyst of the three isolates gave a hydrocarbon identical to the one obtained from the hydrogenation of solanesol. This result indicated that I, II and III have the same carbon skeleton as solanesol. From the data of elementary analysis and stronger IR absorptions at the hydroxyl region, I, II and III were assumed to be monohydroxylated derivatives

FIG. 1. Part of MS Spectra of I, II and III.

Intensities of peaks were related to 100 for each of the base peaks (m/e : I=43, II=81, III=59).

of solanesol.

The IR spectrum of I indicated the presence of geminal methyls ($1382, 1364\text{ cm}^{-1}$) and *trans* disubstituted double bonds (975 cm^{-1}). The PMR spectrum of I indicated the presence of geminal methyls bonded to an oxygen-bearing carbon, δ 1.20 (6H, s), seven allylic methyl groups assignable to those of the internal *trans* configured isoprene residue, δ 1.60 (21H, s), an allylic methyl group, δ 1.66 (3H, s) and fourteen allylic methylene groups, δ 2.00 (28H, broad). A signal at δ 2.62 (2H, broad) was assigned to the protons of a methylene group inserted between two ethylenic carbons. The spectrum showed a broad signal at δ 5.06 (7H) due to seven olefinic protons and a signal at δ 5.32 (1H, t, $J=6\text{ Hz}$) assignable to a proton of ethylenic carbon adjacent to a carbinol carbon of allylic alcohol. A slightly splitting signal of two olefinic protons at δ 5.50 was assumed to be due to a disubstituted ethylenic group. Although the presence of a *trans* disubstituted ethylenic group was suggested in the IR spectrum, the signal

of the two olefinic protons is not informative about the coupling constant to confirm the configuration. The addition of a shift reagent, $\text{Eu}(\text{fod})_3^{6)}$ induced a downfield shift of the olefinic protons signal resolved into a doublet ($J=16\text{ Hz}$) and a multiplet ($J=6\text{ Hz}$ and $J=16\text{ Hz}$), corresponding to the AB part of an ABX_2 system, thereby revealing the *trans* configuration of the double bond.

The MS spectrum of I showed two fragment ions corresponding to the loss of water at m/e 628 ($M-18$) and 610 ($M-36$). A prominent fragment of m/e 543 indicated that the ω -terminal isoprene residue of I was eliminated with 67 mass units from the fragment ion of m/e 610 whereas the ω -terminal isoprene residue of polyprenols has been known to be eliminated with 69 mass units.⁷⁾ This indicated that dehydration might have occurred in the ω -terminal isoprene residue.

Oxidative degradation of the ozonide of I followed by the methylation of the product gave methyl α -hydroxyisobutyrate, methyl glycolate and methyl levulinate with an ap-

proximate molar ratio of 1:1:7. This result showed the presence of a partial structure of IV, which, together with the other results described above, revealed the structure of I to be the formula I.

The absorption at $1648, 902\text{ cm}^{-1}$ in the IR spectrum of II indicated the presence of a terminal methylene grouping. The PMR spectrum of II showed the presence of nine allylic methyl groups, δ 1.62 (21H, s) 1.68 (3H, s) and 1.72 (3H, s) and fifteen allylic methylene groups, δ 2.01 (30H, broad). The signals at δ 3.92 (1H, t, $J=6\text{ Hz}$) and 4.03 (2H, d, $J=6\text{ Hz}$) were assigned to carbinol protons bonded to ethylenic carbons. The signals at δ 4.77 (1H, broad s) and 4.88 (1H, broad s) were assignable to two protons of a terminal methylene. Eight olefinic protons were shown by the signals at δ 5.08 (7H, broad) and 5.35 (1H, t, $J=6\text{ Hz}$).

The MS spectrum of II showed a molecular ion at m/e 646 and two fragment ions corresponding to the loss of water at m/e 628 (M-18) and 610 (M-36). Similarly as for I, a prominent ion peak at m/e 543 indicated that dehydration occurred in the ω -terminal isoprene residue cracking with 67 mass units.

The ozonization of the acetate of II and subsequent oxidative degradation and methylation with diazomethane gave three main products, methyl acetoxyacetate, methyl levulinate and a compound having the largest mass ion at m/e 144 in its MS spectrum. The compound was isolated by preparative gas liquid chromatography (glc). From the spectral data of IR, PMR and MS, this compound was suggested to be 3-acetoxy-2,6-heptanedione (XV). This assumption was confirmed by comparing the spectral data of the isolate with those of a synthetic specimen (see Experimental section).

Isolation of XV as a degradation product

indicates that a partial structure of V_a or V_b must be present in II. As described above, the MS spectrum of II indicated the presence of a hydroxylated ω -terminal isoprene residue. The presence of an appreciable difference in the PMR chemical shift between the two geminal protons of the terminal ethylenic group of II seems to support V_a as the partial structure of II. This assumption was confirmed by a triple irradiation experiment of II. By irradiating at δ 1.72 (terminal methyl protons) the broad singlets of terminal ethylenic protons at δ 4.77 and 4.88 were changed to slightly split ones and by simultaneous irradiation at δ 1.72 and 3.92 (carbinol proton) these signals were resolved into two doublets with *ca.* 2 Hz of geminal coupling constant. This result revealed a long-range coupling between the terminal ethylenic protons and the carbinol proton, indicating that the partial structure V_a can be adopted for II. The spectral data of II and the degradation experiment support II as represented by formula II.

The IR absorption of III indicated the presence of terminal methylene, 1648, 902 cm^{-1} . The PMR spectrum of III was similar to II and indicated the presence of nine allylic methyl groups, δ 1.60 (21H, s), 1.66 (6H, s), fifteen allylic methylene groups, δ 1.98 (30H, broad), three allylic carbinol protons, δ 3.90 (1H, t, $J=6$ Hz), 4.02 (2H, d, $J=6$ Hz) and ten olefinic protons, δ 4.78 (1H), 5.07 (7H, broad), 5.30 (1H, t) and 5.47 (1H). The MS spectrum of III showed a molecular ion at m/e 646 and two fragment ions corresponding to the loss of water at m/e 628 (M-18) and 610 (M-36). A prominent ion peak at m/e

541 indicated that the ω -terminal isoprene residue was eliminated with 69 mass units and, hence, the dehydration must have occurred in an internal isoprene residue.

An experiment of oxidative degradation was performed for the ozonide of the acetate of III. The methylation of the degradates with ethereal diazomethane gave three main products; methyl acetoxyacetate, methyl levulinate and an unidentified compound showing the largest ion at m/e 216. The compound was purified by preparative glc. The spectra of IR, PMR and MS of the compound were suggestive to be those of methyl 5-acetoxy-4,8-dioxo-nonanoate (XVII). This compound was synthesized from 1-acetoxy-2-(3-butenyl)-3-methyl-2-cyclopentene as a starting material. The spectral data of the synthetic specimen were identical with those of the isolate. On this base the partial structure VI is established for III.

For assignment of the position of the hydroxyl bearing internal isoprene residue, a series of experiments was undertaken as shown in Scheme I. III was acetylated with acetic anhydride and pyridine to give the monoacetate (VII) leaving the secondary hydroxyl group. Oxidation of VII with CrO_3 -pyridine complex gave the corresponding ketone (VIII). The ketone (VIII) was hydrogenated on palladium/charcoal to give a saturated ketone (IX). By Baeyer-Villiger oxidation with m -chloroperbenzoic acid, the saturated ketone (IX) was oxidized to the corresponding ester (X), which was hydrolyzed by methanolic potassium hydroxide to give an acid (XI) and an alcohol (XII). After the methylation of the hydrolysate with ethereal diazomethane, the methyl ester of XI was separated from the alcohol (XII) by high speed liquid chromatography (HLC). The glc of the methyl ester of XI and the TMS ester of XII revealed that each of them consisted of four peaks without any main ones. The individual largest fragment ions of the

four peaks were observed in GC-MS at m/e 284, 354, 424 and 494 for the methyl ester of XI and at m/e 257, 327, 397 and 467 for the TMS ester of XII, corresponding to the molecular ions of the esters of formula XI and XII where X is 1 to 4. These results indicated that III is not a pure compound but a mixture of analogous compounds represented by formula III where X is 1 to 4.

Attempts to separate the components from each other for III itself, or as the benzoate, 3,5-dinitrobenzoate and acidic phthalate derivatives by TLC and HLC were all unsuccessful.

EXPERIMENTAL

Melting points were uncorrected. UV spectra were

measured on a Hitachi 124 spectrometer. IR spectra were recorded on a Jasco IR-G spectrometer and PMR spectra on a JNM-PS-100 using carbon tetrachloride as a solvent, unless otherwise stated, and tetramethylsilane as an internal standard. HLC was carried out with a CSC 102 separation unit and a Pye LMC 2 detector using columns of LiChrosorb® SI 60 (Merk).

Isolation of the compounds

Shredded aged Burley tobacco, 370 kg, USA Government Grades B4F, X4T, T4R, was extracted with dichloromethane and the extract was concentrated to a residue of 18 kg (4.8%, based on tobacco). After the removal of the volatile components by steam distillation under reduced pressure (60 mmHg), the residue was extracted with ether and the ethereal extract was evaporated to give a viscous nonvolatile residue of 12.8 kg (3.2%, based on tobacco).

Using a silicic acid column (530×145 mm), 300 g portion of the residue was fractionated with a solvent system of ether-hexane. The results are shown in Table I. The residue of fraction 4, 25 g, was applied

hexane and the solution was kept at -20°C . White precipitates thus obtained were recrystallized from hexane and ether-hexane at 5°C , giving 359 mg of pure II (0.0039%, based on tobacco), white needles, mp $54.0\sim 55.5^{\circ}\text{C}$. Anal. Found: C, 83.06; H, 11.88. Calcd.: the same as III. TLC (the same condition as III) R_f 0.35. IR $\nu_{\text{max}}^{\text{CCl}_4}$ cm^{-1} : 3620~3000, 1664, 1648 (w), 1447, 1382, 1328, 1150, 1097, 995, 902, 842.

Fraction 5 in the table, 14 g, was applied to a Florisil column (305×72 mm) and eluted with 2 liters of hexane, 2 liters of ether-hexane 5:95 and 2 liters of ether-hexane 1:4 successively. These treatment eluted 148 mg of material. Subsequent treatment of 4 liters of ether-hexane 1:1 eluted 5 g of material. The residue of this fraction was dissolved in hexane and stored in a refrigerator. After a week, white solid precipitates were collected, which were recrystallized from hexane and ether-hexane giving white crystals of I (414 mg, 0.0045%, based on tobacco), mp $53.5\sim 54.5^{\circ}\text{C}$. Anal. Found: C, 83.13; H, 11.98. Calcd.: the same as III. TLC (the same condition as III) R_f 0.28. IR $\nu_{\text{max}}^{\text{CCl}_4}$ cm^{-1} : 3620~3000, 1664, 1447, 1382, 1364, 1152, 1097, 995, 975, 842.

TABLE I.

Fraction	Solvent	Volume liter	Wt. of residue, g
1	Hexane	20	12
2	Ether-hexane 1:19	40	105
3	Ether-hexane 1:4	30	50
4	Ether-hexane 1:1	10	25
5	Ether-hexane 1:1	10	14

to a Florisil column (425×72 mm). The column was successively treated with 3 liters of hexane, 3 liters of ether-hexane (1:19) and 3 liters of ether-hexane (1:4). These treatment eluted only 0.62 g of material. Subsequent treatment with 3 liters of ether-hexane (1:1) eluted 12.5 g of material. TLC of this fraction on a silica gel G (Merk) plate with ethyl acetate-chloroform (1:9) gave two hot sulfuric acid positive spots (II and III) accompanied with tailing impurities. Separation of II and III was effectively performed by repeated HLC (a 500×7.5 mm column, ethyl acetate-benzene 1:9, ethanol-hexane 2:98). Repeated purification by HLC gave III, 3.11 g (0.034%, based on tobacco) as a colorless oil which appeared to be homogeneous by TLC. d_4^{25} : 0.9136. n_D^{20} : 1.5118. Anal. Found: C, 83.08; H, 11.60. Calcd. for $\text{C}_{46}\text{H}_{74}\text{O}_2$: C, 83.53; H, 11.53%. TLC (silica gel G, ethyl acetate-chloroform 1:9) R_f 0.44 (solanesol, R_f 0.61). IR $\nu_{\text{max}}^{\text{CCl}_4}$ cm^{-1} : 3620~3000, 1664, 1638, 1447, 1382, 1328, 1152, 1097, 995, 920, 842.

Fractions containing II, which eluted after III by HLC, were collected and the solvent was evaporated off. The residue was dissolved in a small amount of

Catalytic hydrogenation of I, II, III and solanesol

Each small sample (20 mg) of I, II, III and solanesol was hydrogenated in absolute ethyl alcohol with 5% Pd/charcoal. The products were purified by HLC using a 300×3 mm column with ethyl acetate-benzene 1:9 as a solvent. In each treatment, about 10 mg of a saturated hydrocarbon and about 6 mg of a saturated alcohol were obtained. The hydrocarbons from the four compounds showed an identical retention time on glc (3% OV 101 on GasChrom Q, 1500×3 mm, 280°C) and the identical spectra of IR, PMR and MS.

Ozonolysis of I

After ozonization of 0.2 g of I in 20 ml of ethyl acetate at -40°C , the ozonide was oxidized with 5 ml of 3% H_2O_2 for 3 hr at 60°C . The excess of H_2O_2 was decomposed with Pd/charcoal catalyst and the product was methylated with ethereal diazomethane and subjected to glc. On a column (1500×3 mm) of 25% PEG 20 M on Celite 545 at a column temperature of $80\sim 240^{\circ}\text{C}$ (programmed 5°C per min), three major peaks were observed. The IR and PMR spectra of the isolates by preparative glc revealed that these products were the methyl esters of glycolic, α -hydroxyisobutyric and levulinic acids. Calculation of the gas chromatogram indicated that the approximate molar ratio of glycolate, α -hydroxyisobutyrate and levulinate is 1:1:7

Diacetate of II

A mixture of 0.1 g of II, 1 ml of chloroform, 0.05 ml of pyridine and 0.1 ml of acetic anhydride was heated under reflux for 3.5 hr. The reaction mixture was diluted with ether and the ethereal solution was suc-

cessively washed with a sodium bicarbonate solution and water. By preparative HLC (a 300×3 mm column, ethyl acetate-hexane 1:9), 100 mg of the acetate of II was obtained. MS m/e 730 (M^+). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1740, 1240, 1020, 975, 900, 840.

Ozonolysis of the diacetate of II

The ozonide obtained from the ozonization of 0.1 g of the diacetate in 10 ml of ethyl acetate at -40°C was oxidized with 3 ml of 3% H_2O_2 for 3.5 hr at 60°C . After a similar procedure as in the preceding section, the methylated products were separated by preparative glc. Three major products were isolated by using a column of 5% PEG 20 M on Chromosorb W, 2000×3 mm. The IR and PMR spectra of the two isolates were identical with those of authentic samples of methyl acetoxyacetate and methyl levulinate. The remaining one was identified as 3-acetoxy-2,6-heptanedione by the comparing its MS, IR and PMR spectra with those of synthetic 3-acetoxy-2,6-heptanedione (see later section).

Monoacetate of III (VII)

A mixture of 4 g of III, 20 ml of pyridine and 8 ml of acetic anhydride was heated for 5 min on a boiling water-bath. The reaction mixture was poured into water and extracted with ether. The ethereal layer was successively washed with a sodium bicarbonate solution and water. After evaporation of the solvent, the residue was separated to the mono- and diacetate of III by preparative HLC (a 500×7.5 mm column, ethyl acetate-hexane 5:95). This procedure gave 2.55 g of the monoacetate of III (VII). MS m/e : 670 ($M-18$). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3500, 1745, 1667, 1235, 1022, 973, 837. PMR δ : 1.62 (2H, s), 1.67 (3H, s), 1.73 (3H, s), 1.99 (30H, broad), 2.07 (3H), 4.00 (1H, t, $J=6$ Hz), 4.50 (2H, d, $J=6$ Hz), 4.80 (1H), 5.08 (8H, broad), 5.33 (1H).

Oxidation of the monoacetate (VII) with CrO_3 -pyridine complex

The monoacetate (VII) (2.55 g, 3.7 mmole, in 10 ml of methylene chloride) was added to a mechanically stirred solution of CrO_3 -pyridine complex (molar ratio of 12:1 to the acetate) prepared according to the method of Ratcliffe and Rodehorst.⁸⁾ After stirring additional 1 hr at room temperature, the solution was filtered on a glass filter and the residue on the filter was washed with ether. The combined solution was condensed *in vacuo* and the residue were then taken up in ether. The ether extract was filtered, washed with a sodium bicarbonate solution and saturated brine and dried over sodium sulfate. After removal of the solvent, preparative HLC of the residue under the same condition as in the preceding section afforded 690 mg of a ketone (VIII). MS m/e : 680 (M^+). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1747, 1682, 1240, 1030, 845.

Catalytic hydrogenation of the ketone (VIII)

The ketone (VIII, 425 mg) was hydrogenated in 25 ml of absolute ethyl alcohol with 5% palladium on charcoal under atmospheric pressure. The products were subjected to HLC (500×7.5 mm, ethyl acetate-hexane 1:99) to give a saturated ketone (IX), (345 mg). MS m/e 646 (M^+). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 2950, 2900, 2850, 1713, 1460, 1377.

Baeyer-Villiger oxidation of the saturated ketone (IX)

The saturated ketone (IX), (188 mg), was oxidized with *m*-chloroperbenzoic acid (89 mg, in 2.5 ml of chloroform) at room temperature for 2 weeks. At the end of this period, ether was added to the mixture and the organic layer was washed with a sodium bicarbonate solution and dried over sodium sulfate. After removal of the solvent, the residue was subjected to preparative HLC (a 500×7.5 mm column, hexane) to afford the corresponding saturated ester (X), (121 mg). MS m/e : 646 (M^+). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 2960, 2930, 2860, 1740, 1465, 1380, 1265 (w), 1175 (w), 1125.

Hydrolysis of X

The ester (X), (40 mg), was hydrolyzed with 3 ml of methanolic 5% potassium hydroxide solution for 3 hr under reflux. The reaction mixture was acidified with dil. hydrochloric acid, extracted with ether and the extract was dried over sodium sulfate. After the methylation with ethereal diazomethane, the products were subjected to preparative HLC using a 300×3 mm column. Elution with hexane gave a fraction of the methyl esters of an acid (XI) and subsequent elution with ethyl alcohol gave an alcohol (XII). XII was trimethylsilylated with dimethyldichlorosilane and hexamethyldisilazane in dry pyridine. Performance of GC-MS of the methyl esters showed four peaks, having the largest ions at m/e 284, 354, 424 and 494 respectively. Similarly as for the methyl esters, the four major peaks of TMS esters of the alcohols were observed with their largest ions in the MS spectra at m/e 257, 327, 397 and 467 respectively.

Synthesis of 3-acetoxy-2,6-heptanedione (XV)

a) 2,3-Dimethyl-2-cyclopenten-1-ol (XIII). 2,3-Dimethyl-2-cyclopenten-1-one⁹⁾ (19.5 g, 0.18 mole, in 40 ml of anhydrous ether) was added over 30 min (ice-cooling) to a slurry of lithium aluminium hydride (3.4 g, 0.09 mole, in 120 ml of anhydrous ether). After stirring under reflux for additional 1 hr, the mixture was quenched by careful dropping of water and filtered. The ethereal layer was dried over sodium sulfate and the solvent was evaporated. Distillation of the residue gave 13.5 g of XIII, bp 91°C (45 mmHg). Unstable colorless oil, d_4^{27} : 0.9325. n_D^{20} : 1.4775. MS m/e : 112 (M^+), 97, 94, 93, 91, 79 (base peak), 77, 51, 43, 41. IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3325, 1445, 1380, 1330, 1180,

1063, 1040, 1028, 993. PMR(CDCI₃) δ : 1.67 (3H, s), 1.70 (3H, s), 1.95~2.45 (4H, m), 2.88 (1H, broad), 4.60 (1H, broad).

b) *1-Acetoxy-2,3-dimethyl-2-cyclopentene (XIV)*. Acetylchloride (12 g, 0.15 mole, in 30 ml of anhydrous ether) was added over 20 min under ice-cooling to a mixture of XIII (13.5 g, 0.12 mole), triethylamine (50 g, 0.5 mole) and 100 ml of anhydrous ether under stirring. Stirring was continued for 1 hr at room temperature. The mixture was poured into 200 ml of water and the separated ethereal layer was washed with a sodium bicarbonate solution and water. After drying, the solvent was evaporated. Distillation of the residue *in vacuo* gave 13 g of XIV, bp 87°C (28 mmHg). Unstable colorless oil. d_4^{20} : 0.9538. n_D^{20} : 1.4557. MS m/e : 96 (M-58), 95, 94, 93, 91, 79 (base peak), 77, 65, 53, 51. PMR δ : 1.63 (3H, s), 1.71 (3H, s), 2.08 (3H, s), 1.95~2.90 (4H), 5.52 (1H, broad).

c) *3-Acetoxy-2,6-heptanedione (XV)*. After ozonization of 5 g of XIV in 100 ml of chloroform at -30°C, the product was extracted with ether and the solvent was evaporated. Preparative glc (a PEG 20M column, 190°C) of the residue gave 0.67 g of XV. d_4^{20} : 1.0757. n_D^{20} : 1.4417. MS m/e : 144 (M-42), 143, 126, 108, 101, 99, 83, 82, 55, 43 (base peak). IR $\nu_{\max}^{f11m}$ cm⁻¹: 1747, 1725, 1425, 1377, 1360, 1245, 1167. PMR(CDCI₃) δ : 2.17 (3H, s), 2.07 (2H, m), 2.19 (3H, s), 2.22 (3H, s), 2.58 (2H, t, $J=7$ Hz), 5.02 (1H, t, $J=7$ Hz).

Synthesis of methyl 5-acetoxy-4,8-dioxo-nonanoate (XVII)

a) *1-Acetoxy-2-(3-butenyl)-3-methyl-2-cyclopentene (XVI)*. 2-(3-Butenyl)-3-methyl-2-cyclopenten-1-one⁽¹⁰⁾ (7.5 g, 0.05 mole, in 15 ml of anhydrous ether) was added over 20 min (ice-cooling) to a slurry of lithium aluminium hydride (1.27 g, 0.025 mole, in 50 ml of anhydrous ether). After 1 hr stirring at room temperature, the mixture was quenched with water. The ethereal solution was dried over sodium sulfate and used for the subsequent acetylation without further purification.

To 150 ml of the ethereal solution of the product, triethylamine (25 g, 0.25 mole) was added and then acetylchloride (7.85 g, 0.1 mole, in 20 ml of anhydrous ether) was added dropwise under external cooling with ice-water. After further stirring for 1 hr at room temperature, the mixture was poured into 200 ml of water. The ethereal layer was washed three times with a sodium bicarbonate solution and then water, dried over sodium sulfate and the solvent was evaporated.

Distillation of the residue gave 4 g of the acetate (XVI), bp 94°C (7 mmHg). The acetate is unstable and a considerable part of the compound is decomposed within a week at room temperature. MS m/e : 134 (M-60), 119, 106, 94, 93, 92, 91, 78, 77, 41. IR $\nu_{\max}^{f11m}$ cm⁻¹: 1735, 1640, 1245, 910, 878. PMR δ : 1.68 (3H, s), 1.96 (3H, s), 2.0~2.44 (4H), 4.87 (1H, d, $J=10$ Hz), 4.92 (1H, d, $J=17$ Hz), 5.60 (1H, m), 5.68 (1H, m).

b) *Methyl 5-acetoxy-4,8-dioxo-nonanoate (XVII)*. After ozonization of 0.8 g of XVI in 10 ml of chloroform at -40°C, the ozonide was oxidized with 20 ml of 3% H₂O₂ by a similar manner as in the preceding section. The product was purified by preparative glc using two columns of 5% PEG 20M, 2 m, and 5% SE 30, 2 m, and column temperature at 150~240°C (programed 10°C per min). MS m/e : 216 (M-42), 167, 148, 115 (base peak), 101, 99, 85, 83, 55, 43. IR $\nu_{\max}^{f11m}$ cm⁻¹: 1740, 1720 (shoulder), 1440, 1376, 1240, 1168, 1078, 1030. PMR δ : 2.09 (3H, s), 2.11 (3H, s), 1.88~2.13 (2H, m), 2.39~2.72 (6H), 3.65 (3H, s), 4.91 (1H, t, $J=6$ Hz).

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