Synthesis of the Monoterpene Lactone from *Chrysanthemum flosculosum* L.

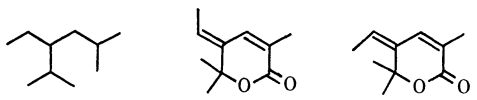
Shûichi YAMAGIWA, Hiroshi KOSUGI, and Hisashi UDA*

Chemical Research Institute of Non-Aqueous Solutions, Tohoku University, Katahira-2, Sendai 980

(Received March 2, 1978)

The synthesis of a lactonic constituent [(*Z*)-5-ethylidene-5,6-dihydro-3,6,6-trimethyl-2*H*-pyran-2-one] isolated from *Chrysanthemum flosculosum* L. is described. Dehydration of 5-ethyl-5,6-dihydro-5-hydroxy-3,6,6-trimethyl-2*H*-pyran-2-one derived from 5-ethyl-5,6-dihydro-6,6-dimethyl-3-phenylthio-2*H*-pyran-2-one *via* methylation, oxidation, [2,3]sigmatropic rearrangement, and saponification, gave the geoisomeric [(*E*)-5-ethylidene] lactone. Photochemical isomerization of the ethylidene side-chain furnished the natural lactone. The geometry of the ethylidene group in both isomers has been rigorously established.

The santolinyl group of monoterpenoids possesses the carbon skeleton **1**, which does not conform to the isoprene rule.[1] A representative member of this group of natural products is the crystalline lactone isolated as a minor polar constituent from *Chrysanthemum flosculosum* L.[2,3] Bohlmann and Grenz have assigned structure **2** to this lactone, but have not established the geometry of the ethylidene side-chain.[3,4]

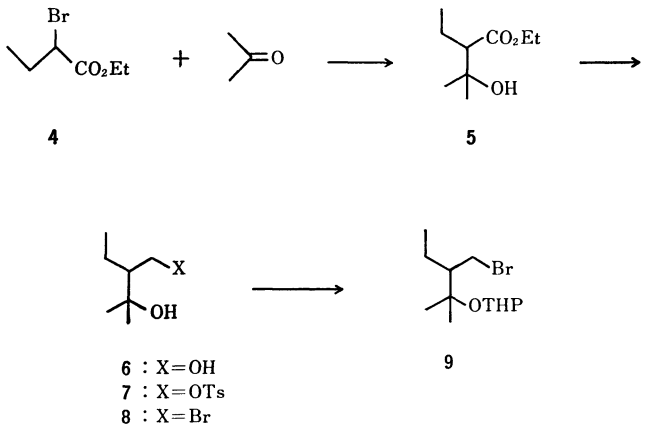


1 **2** **3**

The synthesis of both (*E*)- and (*Z*)-5-ethylidene isomers of this δ-lactone derivative, **2** and **3**, are reported which unambiguously establishes the structure of the natural lactone to be **3**. In view of the recent work on the reactions of (phenylthio)acetic acid and its ester,[5] and the rearrangement reactions of the α-phenylsulfinylacrylate derivatives,[6,7] the key intermediate chosen was the α-phenylthio-α,β-unsaturated δ-lactone **14**.

The Reformatsky reaction of ethyl α-bromobutyrate (**4**) with acetone in refluxing benzene gave the hydroxy ester **5** in 64% yield. Lithium aluminum hydride reduction of **5** afforded the glycol **6**, which was then transformed into the tetrahydropyranyloxy bromide **9** in 64% overall yield through the usual manner: monotosylation to **7**, substitution to the bromohydrin **8**, and finally tetrahydropyranylation (Scheme 1).

Methyl sodio(phenylthio)acetate (**10**), prepared from methyl (phenylthio)acetate by the action of sodium hydride in tetrahydrofuran and hexamethylphosphoric



4 **5**

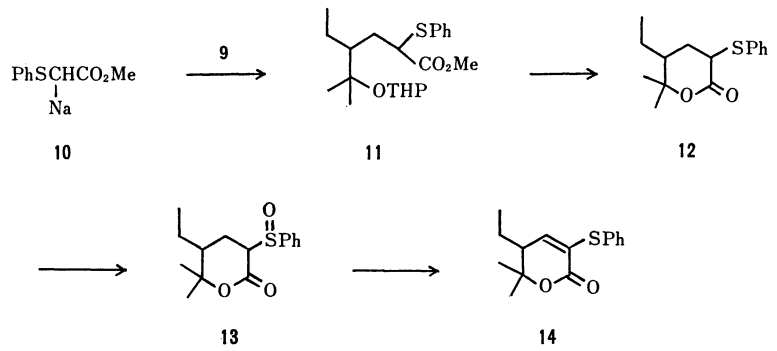
6 : X=OH
7 : X=OTs
8 : X=Br

9

Scheme 1.

triamide, reacted well with the bromide **9** to produce the substitution product **11**. Hydrolysis and lactonization by treating with *p*-toluenesulfonic acid, initially in boiling aqueous tetrahydrofuran and then in boiling benzene gave a 72% yield of a stereoisomeric mixture of the δ-lactone **12**. The lactone **12** was treated with sodium periodate in dilute methanol to give the sulfoxide **13**. Exposure of **13**, without purification, to trifluoroacetic anhydride in dichloromethane directly provided the desired intermediate **14**, mp 73—74 °C, in 80% yield from **12** through the spontaneous elimination of trifluoroacetic acid from the initially formed Pummerer rearrangement product, α-phenylthio-α-trifluoroacetoxy lactone (Scheme 2). The structure of **14** was verified by its analytical and spectroscopic properties.

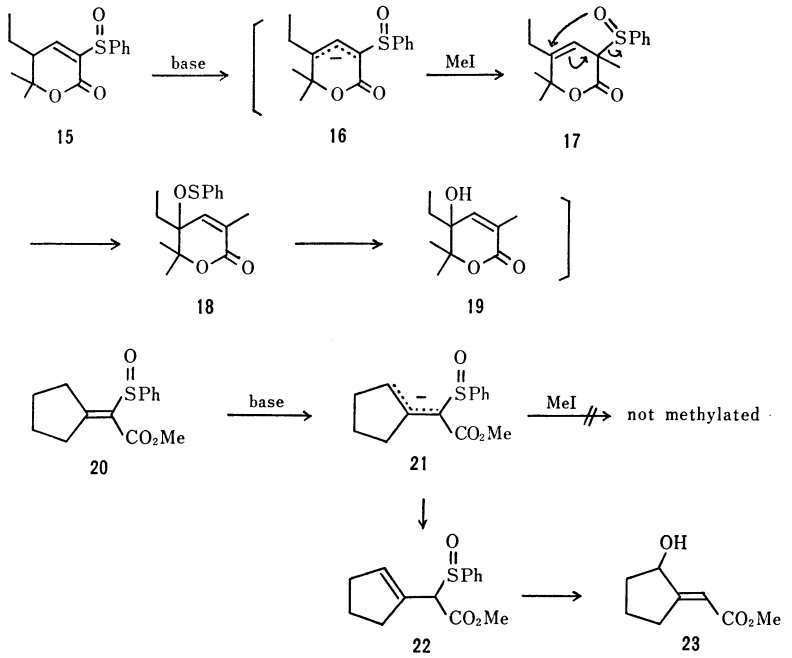
The planned synthesis of **2** or **3** involved the one-step introduction of a methyl group at the α-position and of



10 **11** **12**

13 **14**

Scheme 2.

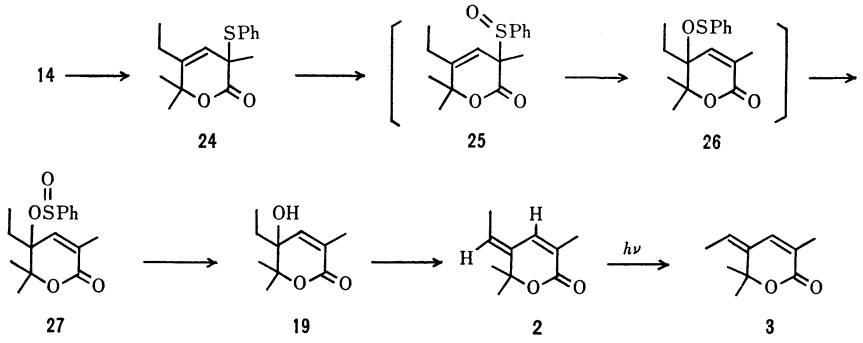


Scheme 3.

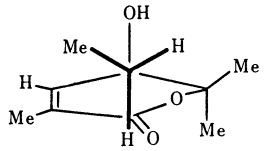
a hydroxyl group at the γ-position in the α-sulfinyl δ-lactone system **15** by applying the doubly double-bond migrating rearrangement reaction observed in the α-phenylsulfinylacrylate derivatives.[6,7] If the carbanion species **16** derived from **15** by an appropriate base reacts more rapidly with methyl iodide than the [2,3]-sigmatropic rearrangement of the sulfinyl group, the methylated sulfoxide **17** should be produced. Subsequent rearrangement and hydrolysis of the sulfenate **18** might give the precursor **19** of the natural product (Scheme 3). However, a number of preliminary experiments using methyl cyclopentylidene(phenylsulfinyl)acetate (**20**) as a model compound suggests that such a reaction process (alkylative rearrangement) is not applicable, since the migration of the double-bond of **20** and the [2,3]sigmatropic rearrangement of the resulting isomer **22** are extremely facile; methylation of the anion **21** did not take place, compound **23** being the only isolable product.[7]

The introduction of functional groups, methyl and hydroxyl, was then attempted in a stepwise manner (Scheme 4). Treatment of **14** with potassium *t*-butoxide in tetrahydrofuran and hexamethylphosphoric triamide and then with methyl iodide afforded the α-methylated product **24** in 72% yield. Oxidation of **24** with two equivalents of *m*-chloroperbenzoic acid in dichloromethane at 0 °C gave the rearranged sulfinyloxy lactone **27**. Compound **27** showed a very complicated pattern in the NMR spectrum, indicating that **27** was actually a mixture of diastereomers with respect to the γ-carbon and sulfur atoms. Compound **27** was treated with a catalytic amount of sodium methoxide in methanol to give a single crystalline hydroxy lactone **19**, mp 81—82 °C, in 65% yield from **24**; there was no indication of the presence of a translactonization product (γ-lactone). It should be noted that both the [2,3]sigmatropic rearrangement of the sulfoxide **25** and the oxidation of the resulting sulfenate **26** to the sulfinate **27** proceeded very rapidly. When one equivalent of *m*-chloroperbenzoic acid was employed in the oxidation of **24**, neither the sulfoxide **25** nor the sulfenate **26** was isolated; unchanged starting sulfide **24** and the sulfinate **27** were obtained in equal amounts.

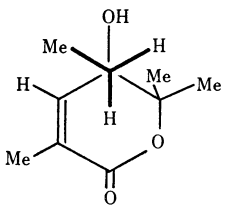
We now considered the conformation of the ethyl



Scheme 4.



19a



19b

group of **19** because this determined whether, at the next dehydration stage, the *E*- (**2**) or *Z*- (**3**) ethylidene group would be preferentially formed. Two conformations **19a** (quasi-equatorial ethyl) and **19b** (quasi-axial ethyl) are possible for the 2-pyrone ring of **19**. In both cases, if the conformation, in which the ring hydroxyl group and the one hydrogen atom of the ethyl-methylene are anti-periplanar, is the favorable one for dehydration, the methyl of the ethyl group would be apart from the gem-dimethyl group as a result of the severe steric interaction between these methyl groups. Furthermore, in the dehydration product the (*E*)-5-ethylidene isomer would be thermodynamically (or sterically) more stable than the (*Z*)-isomer due to the same steric interaction. Hence, dehydration of **19** would be expected to produce preferentially the isomer having the *E*-ethyliedne group.

Compound **19** was heated in boiling benzene containing a catalytic amount of *p*-toluenesulfonic acid and afforded a 63% yield of an unsaturated lactone **2** as the sole product. The lactone **2** was also obtained by treating **19** with thionyl chloride–pyridine at 0 °C. The spectral properties are fully in accord with the assigned structure **2** including the geometry of the ethylidene group. In the 100 MHz NMR spectroscopy, irradiation of the gem-dimethyl signal at δ 1.52 caused 11% of the NOE enhancement of the ethylidene olefinic proton signal at δ 5.72. Furthemore irradiation of the olefinic methyl signal centered at δ 1.92 resulted in 7% of the NOE enhancement of the ring olefinic proton signal at δ 7.00. Thus, the configuration of the ethylidene group of this lactone should be evidently *E*-geometry as expected.

It was found, however, that this compound **2** is oily and the spectral data (see Experimental section) is not entirely consistent with the reported values for the natural lactonic constituent. Consequently, the natural lactone must have the structure **3** possessing the *Z*-ethylidene side-chain, and the synthesis of **3** was achieved by photochemical isomerization. Irradiation of **2** in benzene with 100 W high-pressure mercury lamp through Pyrex provided the isomeric crystalline lactone **3**, mp 63.5—64.5 °C, in 73% yield. Although, the IR and UV absorption maxima [ν_{max} (CCl_4) 1710, 1640, and 1620 cm^{-1}; λ_{max} (EtOH) 276.5 nm (ε=17360)] are slightly different from the reported ones [ν_{max} (phase—not reported) 1725, 1650, and 1630 cm^{-1}; λ_{max} (solvent—not reported) 266.5 nm (ε=14900)], the melting point, the NMR spectrum [δ (CCl_4) 1.62 (s, 6H), 1.88 (s, 3H), 1.91 (d, J=7.0 Hz, 3H), 5.58 (q, J=7.0 Hz, 1H), and 6.42 (s, 1H)], and the mass spectrum [M^+ *m/e* 166 (35%), 151 (100%), and 123 (29%)] were consistent with the reported values for the natural lactone: mp 64.5 °C the NMR spectrum [δ (solvent—not reported) 1.60 (s, 6H), 1.87 (s, 3H), 1.89 (d, J=7.0 Hz, 3H), 5.57 (q, J=7.0 Hz, 1H), and 6.42 (s, 1H)], and mass spectrum [M^+ *m/e* 166 (25%), 151 (100%), and 123 (22%)].[8] From the present study, we conclude that the natural lactone has been assigned as (*Z*)-5-ethylidene-5,6-dihydro-3,6,6-trimethyl-2*H*-pyran-2-one.

Experimental

All the melting points were taken on a Yamato melting point apparatus and are uncorrected. Small amounts of liquid products were purified by evaporative short-path distillation; oil-bath temperatures are recorded. IR spectra were obtained with a Hitachi EPI-S2 or G2 spectrophotometer. A UV spectrum was taken on a Hitachi EPS-3T spectrometer. NMR spectra of solutions in carbon tetrachloride (unless otherwise indicated) were recorded with a JEOL PMX-60 (60 MHz) or PS-100 (100 MHz) instrument, with TMS as an internal standard; coupling constants are given in Hz. Mass spectra were taken with a Shimadzu LKB-9000 instrument. Microanalyses were carried out in the microanalytical laboratory of this Institute.

Tetrahydropyranyl Ether of 3-Bromomethyl-2-methyl-2-pentanol (8). To a slurry of zinc powder (11 g, 0.17 g atom) and iodine (a catalytic amount) in boiling anhydrous benzene (200 ml) was added dropwise over a period of 1 h a solution of ethyl α-bromobutyrate (26.5 g, 0.136 mol) and acetone (35 ml, 0.475 mol) in anhydrous benzene (40 ml), and the reaction mixture refluxed for 2 h. Dilute sulfuric acid (6 M, 150 ml) was added to the cooled reaction mixture, and the resulting solution vigorously stirred for 30 min at room temperature. The water layer was extracted twice with ether. The combined organic layers were washed twice with water and saturated brine, and dried. After removal of the solvent, the residual liquid was fractionated under reduced pressure, and the fraction of bp 62—63 °C/5 Torr (1 Torr≈133.322 Pa) collected to yield 15.22 g (64%) of ethyl 2-ethyl-3-hydroxy-3-methylbutyrate (**5**): IR (CCl_4) 3450, 1720 (sh), 1705, 1460, 1375, 1190, and 1160 cm^{-1}; NMR δ 0.89 (3H, t, J=7.0), 1.15 (6H, s), 1.27 (3H, t, J=7.0), 1.53 (2H, quint, J=7.0), 2.20 (1H, t, J=7.0), 2.81 (1H, s, OH), and 4.12 (2H, q, J=7.0).

To a slurry of lithium aluminum hydride (0.7 g, 18.5 mmol) in anhydrous ether (50 ml) was added dropwise a solution of **5** (1.74 g, 10 mmol) in anhydrous ether (20 ml) at room temperature under nitrogen, and the reaction mixture stirred for 30 min at room temperature. Ethyl acetate (10 ml) was added slowly to the mixture at 0 °C to decompose the excess hydride, and then a minimum amount of water was added until a jelly-like precipitate separated from the ether solution. The ether layer was decanted, and the precipitate thoroughly washed with ether. The combined ether solutions were evaporated under reduced pressure to give 1.32 g (100%) of 2-ethyl-3-methyl-1,3-butanediol (**6**): NMR δ 1.17 (3H, s), 1.28 (3H, s), 0.70—2.30 (6H, m), 3.74 (2H, m), and 4.70 (2H, m).

To a solution of **6** (660 mg, 5 mmol) in anhydrous pyridine (7 ml) was added portionwise *p*-toluenesulfonyl chloride (1.33 g, 7 mmol) at 0 °C, and the reaction mixture allowed to stand for 5 h at room temperature. Chopped ice was added to the mixture, and the resulting solution poured into a mixture of ether and water in a separatory funnel. The ether layer was washed with dilute HCl solution and twice with saturated brine. Evaporation of the ether left 1.22 g (86%) of 2-ethyl-3-hydroxy-3-methylbutyl *p*-toluenesulfonate (**7**): NMR δ 0.50—2.30 (6H, m), 1.13 (3H, s), 1.16 (3H, s),

1.97 (1H, br s), 2.46 (3H, s), 4.10 (2H, d, J=4.0), 7.24 (2H, d, J=8.0), and 7.74 (2H, d, J=8.0).

To a solution of sodium bromide (2.04 g, 20 mmol) in DMSO (15 ml) was added dropwise a solution of **7** (2.86 g, 10 mmol) in DMSO (7 ml) at 50 °C with stirring. After stirring at 60 °C for 30 min, more sodium bromide (2.5 g, 24 mmol) was added, and the reaction mixture was stirred for a further 2.5 h at 60 °C. The mixture was poured into water and extracted twice with ether. The combined ether extracts were washed twice with water and saturated brine. Evaporation of the ether gave 2.02 g (100%) of 3-bromomethyl-2-methyl-2-pentanol (**8**): bp 60—90 °C/47 Torr; IR (CCl_4) 3400, 1460, 1370, 1230, and 1115 cm^{-1}; NMR δ 0.50—2.30 (6H, m), 1.17 (3H, s), 1.21 (3H, s), 2.20 (1H, br s), and 3.27—3.83 (2H, m). Found: C, 42.96; H, 7.69; Br, 41.58%. Calcd for $C_7H_{15}OBr$: C, 43.09; H, 7.75; Br, 40.96%.

To a solution of **8** (2.5 g) and dihydropyrane (1.7 g) in CH_2Cl_2 (30 ml) was added a catalytic amount of anhydrous *p*-toluenesulfonic acid at 0 °C. After stirring for 30 min at room temperature, pyridine (2 drops) was added, and the mixture washed with saturated brine. The aqueous layer was further extracted with CH_2Cl_2. The combined organic layers were evaporated under reduced pressure and the residue chromatographed on silica gel (50 g) with petroleum ether to give 2.9 g (75%) of the tetrahydropyranyl ether **9**: NMR δ 0.60—2.50 (12H, m), 1.27 (6H, split s), 3.00—4.30 (4H, m), and 4.80 (1H, m).

5-Ethyl-6,6-dimethyl-3-phenylthiotetrahydropyran-2-one (12). To a slurry of sodium hydride (45% mineral oil dispersion, 2.2 g, washed three times with petroleum ether and once with anhydrous THF) in anhydrous THF (40 ml) was added dropwise a solution of methyl (phenylthio)acetate (5.5 g, 0.03 mol) in anhydrous THF (10 ml) at 0 °C under nitrogen, and the resulting mixture stirred for 1 h at 0 °C. A solution of **9** (14 g, 0.05 mol) in anhydrous THF (10 ml) and then HMPA (25 ml, 0.143 mol) were added dropwise to the above mixture. After stirring overnight at room temperature, the reaction mixture was poured into ice-water and extracted twice with ether. The combined extracts were washed twice with water and saturated brine. Evaporation of the ether left an oil (13.7 g), which was chromatographed on silica gel (150 g) with petroleum ether—petroleum ether–ether (gradient)—ether to give 9.2 g of methyl 4-[1-methyl-1-(tetrahydropyranyloxy)-ethyl]-2-phenylthiohexanoate (**11**): NMR δ 0.50—2.50 (20H, m), 3.00—4.20 (3H, m), 3.60 (3H, s), 4.80 (1H, m), and 7.00—7.70 (5H, m).

A solution of **11** (9.2 g) in dilute THF (80%, 50 ml) containing *p*-toluenesulfonic acid (0.1 g) was heated under reflux for 1 h. The reaction mixture was poured into ice-water and extracted twice with ether. The combined ether extracts were washed with brine and evaporated. The residue (8.53 g) was dissolved in anhydrous benzene (30 ml) containing anhydrous *p*-toluenesulfonic acid (a catalytic amount), and the solution heated under reflux for 40 min using a water separator. The reaction mixture was poured into ice-water, and the water layer extracted twice with ether. The combined organic layers were washed with saturated brine. After removal of the solvent, the residue (6.55 g) was chromatographed on silica gel (70 g) with petroleum ether—1: 2 petroleum ether–ether to give 5.7 g [72% based on methyl (phenylthio)-acetate] of **12**: bp 140 °C/1 Torr; IR (CCl_4) 1725, 1275, and 1125 cm^{-1}; NMR δ 1.03, 1.20, 1.34, and 1.40 (total 6H, each s), 0.50—2.80 (8H, m), 3.50—4.00 (1H, m), and 7.00—8.00 (5H, m). Found: C, 68.16; H, 7.63%. Calcd for $C_{15}H_{20}O_2S$: C, 68.49; H, 7.88%.

5-Ethyl-5,6-dihydro-6,6-dimethyl-3-phenylthio-2H-pyran-2-one (14). To a solution of **12** (1.27 g, 4.8 mmol) in methanol (30 ml) was added dropwise a solution of $NaIO_4$ (1.23 g, 5.75 mmol) in water (10 ml) at 0 °C, and the reaction mixture stirred for 18 h at room temperature. Inorganic material was removed by filtration, and the filtrate extracted twice with CH_2Cl_2. The combined extracts were washed with saturated brine. Evaporation of the solvent gave 1.34 g (99%) of 5-ethyl-6,6-dimethyl-3-phenylsulfinyltetrahydropyran-2-one (**13**): IR (CCl_4) 1720, 1275, 1135, 1085, and 1050 cm^{-1}; NMR δ 0.30—3.00 (14H, m), 3.40—4.50 (1H, m), and 7.00—8.30 (5H, m).

To a solution of **13** (1.14 g, 4.05 mmol) in CH_2Cl_2 (30 ml) was added dropwise a solution of trifluoroacetic anhydride (1 ml, 7.0 mmol) in CH_2Cl_2 (10 ml) at 0 °C. After stirring for 2 h at room temperature, the solvent was removed under reduced pressure. The residue (1.29 g) was chromatographed on silica gel (20 g) with 5: 1—1: 1 petroleum ether–ether to give 922 mg (86%) of **14**: mp 73—74 °C from petroleum ether–ether; IR ($CHCl_3$) 1710, 1600, 1140, and 1020 cm^{-1}; NMR ($CDCl_3$) δ 0.87 (3H, t, J=7.0), 1.00—1.80 (2H, m), 1.34 (3H, s), 1.45 (3H, s), 2.30 (1H, ddd, J=10.0, 4.0, and 4.0), 6.15 (1H, d, J=4.0), and 7.20—7.60 (5H, m). Found: C, 68.42; H, 6.99%. Calcd for $C_{15}H_{18}O_2S$: C, 68.68; H, 6.92%.

5-Ethyl-3,6-dihydro-3,6,6-trimethyl-3-phenylthio-2H-pyran-2-one (24). A solution of **14** (493 mg, 1.88 mmol) in anhydrous THF (4 ml) was added dropwise to a solution of potassium *t*-butoxide (260 mg, 2.3 mmol) in anhydrous THF (4 ml) at −60 °C under nitrogen, and the resulting solution was stirred for 1.5 h at −60——40 °C. Methyl iodide (0.5 ml, 8 mmol) and then HMPA (1 ml, 5.6 mmol) were added dropwise *via* syringes to the above solution at −60 °C. After stirring at −60——28 °C for 2 h, the reaction mixture was poured into ice-water, and the resulting aqueous solution extracted twice with ether. The combined extracts were washed with saturated brine and evaporatd. The residue (490 mg) was chromatographed on preparative TLC using silica gel with 1: 1 petroleum ether–ether to give 374 mg (72%) of **24**: bp 100 °C/1 Torr; IR (CCl_4) 1725. 1295, and 1150 cm^{-1}; NMR δ 1.10 (3H, t, J=7.0), 1.13 (3H, s), 1.36 (3H, s), 1.47 (3H, s), 2.01 (2H, q, J=7.0), 5.31 (1H, split s), and 7.17—7.60 (5H, m). Found: C, 69.70; H, 7.58%. Calcd for $C_{16}H_{20}O_2S$: C, 69.54; H, 7.30%.

5-Ethyl-5,6-dihydro-5-hydroxy-3,6,6-trimethyl-2H-pyran-2-one (19). To a solution of **24** (374 mg, 1.35 mmol) in CH_2Cl_2 (20 ml) was added portionwise *m*-chloroperbenzoic acid (80%, 640 mg, 3 mmol) at 0 °C. After stirring for 30 min at 0 °C, the reaction mixture was poured into a mixture of ice and dilute NaOH solution (3M), and the water layer extracted twice with CH_2Cl_2. The combined extracts were washed with water and saturated brine. Evaporation of the solvent gave 422 mg of 5-ethyl-5,6-dihydro-3,6,6-trimethyl-5-phenylsulfinyloxy-2*H*-pyran-2-one (**27**): IR (CCl_4) 1730 and 1150 cm^{-1}.

A solution of **27** in anhydrous methanol (2 ml) was added dropwise to a solution of sodium methoxide (a catalytic amount) in anhydrous methanol (3 ml) at 0 °C. After stirring at room temperature for 1 h, the mixture was poured into ice-water and extracted twice with ether. The combined extracts were washed with water and saturated brine, and evaporated. The residue (374 mg) was chromatographed on preparative TLC using silica gel with 1: 2 petroleum ether–ether to give 163 mg (66%) of **19**: mp 81—82 °C from petroleum ether–ether; IR ($CHCl_3$) 3570, 3400, 1700, 1120, and 1100 cm^{-1}; NMR ($CDCl_3$) δ 1.00 (3H, t, J=7.0), 1.38 (3H, s), 1.46 (3H, s), 1.60 (2H, q, J=7.0), 1.91 (3H, d, J=1.5), 3.27 (1H, br., OH), and 6.50 (1H, q, J=1.5). Found: C, 65.35; H, 8.42%. Calcd for $C_{10}H_{16}O_3$: C, 65.91; H, 8.75%.

(E)-5-Ethylidene-5,6-dihydro-3,6,6-trimethyl-2H-pyran-2-one (2). A solution of **19** (91 mg) in anhydrous benzene (7 ml) containing a trace of anhydrous *p*-toluenesulfonic acid was heated under reflux for 2 h using a water separator. The reaction mixture was diluted with ether, washed with water and brine, and evaporated. The residual liquid was chromatographed on preparative TLC using silica gel with 1:1 petroleum ether–ether to give 52 mg (63%) of **2**: bp 70 °C/1 Torr; IR (CCl_4) 1720 (sh), 1700, and 1115 cm^{-1}; NMR δ 1.52 (6H, s), 1.85 (3H, d, J=7.0), 1.98 (3H, s), 5.72 (1H, q, J=7.0), and 7.00 (1H, s); mass (70 eV) *m/e* 166 (M^+, 40%), 151 (100%), and 123 (25%). Found: C, 72.27; H, 8.73%. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49%.

(Z)-5-Ethylidene-5,6-dihydro-3,6,6-trimethyl-2H-pyran-2-one (3) =the Natural Lactone. A solution of **2** (67 mg) in anhydrous benzene (30 ml) in a Pyrex tube was externally irradiated for 3 h with a 100-W high-pressure mercury lamp under running water cooling and nitrogen. After removal of the solvent under reduced pressure, the residue was chromatographed on preparative TLC using silica gel with 1:1 petroleum ether–ether to give 18 mg (27%) of the recovered **2** and 51 mg (73%) of **3**: mp 63.5—64.5 °C from petroleum ether. Found: C, 72.60; H, 8.54%. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49%.

Acknowledgment is made to the Ministry of Education of Japan for financial support (a Grant-in-Aid for Scientific Research, No. 147028).

References

1) For a Review see S. Nozoe, "Natural Products Chemistry," ed by K. Nakanishi, T. Goto, S. Itô, S. Natori, and S. Nozoe, Kodansha, Tokyo, and Academic Press, New York (1974), Vol. 1, p. 42, and references cited therein.

2) F. Bohlmann and G. Florenz, *Chem. Ber.*, **99**, 990 (1966).

3) F. Bohlmann and M. Grenz, *Tetrahedron Lett.*, **1969**, 2413.

4) F. Bohlmann, private communication.

5) S. Yamagiwa, N. Hoshi, H. Sato, H. Kosugi, and H. Uda, *J. Chem. Soc., Perkin Trans. 1*, **1978**, 214.

6) H. Kosugi, H. Uda, and S. Yamagiwa, *J. Chem. Soc., Chem. Commun.*, **1975**, 192.

7) S. Yamagiwa, H. Sato, N. Hoshi, H. Kosugi, and H. Uda, *J. Chem. Soc., Perkin Trans. 1*, in press

8) We could not directly compare the physical properties of the synthetic sample with those of the natural one, because the physical data and a pure sample of the natural product were not available.[4)]