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Addition Reaction of 2-Pyrone-5-carboxylate with α-Terpinene. An Attempted Conversion of Monoterpene to Sesquiterpenoids

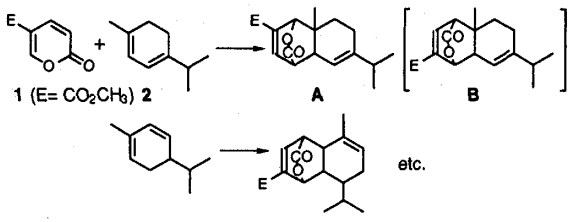
Toshihide HATSUI, Narukuni HIRATA* and Hitoshi TAKESHITA

Methyl 2-pyrone-5-carboxylate reacted with α-terpinene site- and regio-selectively to give tricyclic lactones at 110 °C. At a higher temperature, decarboxylation and subsequent intramolecular cycloaddition took place to afford a triene and a tetracyclic ester. A triene diester and hydroxy diesters were synthesized from the lactones. Attempted conversion of them to eudesmanoids are described.

1. Introduction.

2-Pyronecarboxylates are known to undergo cycloaddition reaction[1] in several ways; they react not only as dienophiles but also as diene components in the cycloaddition reactions to construct cyclohexene ring. In the latter case, they add to electron-rich alkenes, as well as to ordinary dienophiles, to give bicyclic lactones which decarboxylate to afford cyclohexadienes. This is known as 'reversely electron demanded cycloaddition reaction,' and dienes,[2-4] enamines[5] and vinyl ethers,[6,7] have been reported to react in such a way. This means the formation of six-membered ring by addition of C_5 unit to diene or vinyl ether *etc.* In addition, the option of the type of C_5 unit, straight chain or branched one (isoprene-unit), is possible by selecting the carboxylate, *e.g.*, 3-carboxylate for the former or 5-carboxylate for the latter. In fact several applications of this reaction to natural product synthesis have appeared.[2,3,7-9]

Considering the reactivity of 2-pyronecarboxylates this reaction might provide a good way for the conversion of monoterpenoids, *e.g.*, phellandrene and α-terpinene, readily obtainable conjugated terpene-dienes, to sesquiterpenoids, *e.g.*, cadinane and eudesmane derivatives.

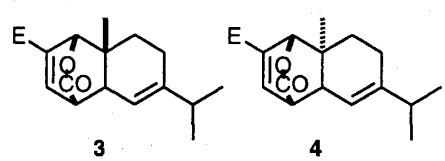


Herein we describe an attempt to construct an eudesmane skeleton by the reaction of methyl 2-pyrone-5-carboxylate (methyl coumalate) with α-terpinene.

2. Results

2.1. Cycloaddition reaction of methyl 2-pyrone-5-carboxylate with α-terpinene.

The reaction of methyl 2-pyrone-5-carboxylate (**1**) with α-terpinene (**2**) at 110 °C gave a pair of [4+2]-cycloadducts, **3** and **4** in good yields. At a higher reaction temperature, **5** and **6** were obtained as a 1:2 mixture. The structure of **5** was assigned to be triene carboxylate as shown below from its ^{13}C- and ^{1}H-NMR spectra disclosing six olefinic carbon signals and four olefinic protons, two of which, at δ 5.70 and 6.22, were cis-coupled each other with 9.5 Hz of *J* value, and they were also coupled with the methine proton at δ 2.65 with 4.8 and 1.7 Hz, respectively. Further, a singlet of angular methyl group was observed at δ 0.99. Thus the structure of **5** was determined.



3 **4**

The structures of **3** and **4** were deduced from the ^{1}H- and ^{13}C-NMR as follows: they showed an oxygenated methine proton at δ 5.20 and carbon at δ 82.4 (for **3**) or 5.16 and 81.5 (for **4**), and two olefinic proton at δ 5.16 and 7.19 (for **3**) or 5.30 and 7.42 (for **4**) which were not coupled each other. This suggested

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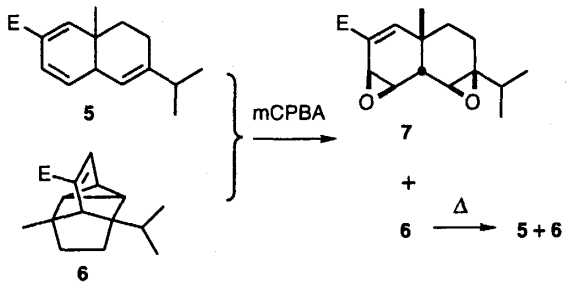
that the pyrone reacted as 4π component in the cycloaddition. The observation of quaternary methyl proton at δ 1.25 (for **3**) and 0.93 (for **4**), instead of vinyl methyl one, demonstrates the reaction site of α-terpinene as 1,2-position in both **3** and **4**. And the nuclear Oberhauser effects (NOEs) observed between these singlet methyl protons and the methine proton at δ 5.20 of **3** or 5.16 of **4** confirmed the structure of **3** and **4** as **A**. This is well correspondent with the structure of **5**, decarboxylated product of cycloadducts. The stereo-structures of **3** and **4** were assigned after the hydrolysis of lactone **4** (see next section).

The ^{13}C-NMR spectrum of **6** exhibited only two olefinic carbons and one carbonyl carbon along with thirteen sp^3 carbons. In the ^{1}H-NMR spectrum, the olefinic proton at d 7.45(dd) was coupled with the methine proton at δ 1.13 with 7.0 Hz of *J* and also with another methine proton at δ 2.55(d) with *J*= 1.5 Hz. The former was observed as quartet having *J*= 7.0 Hz. Comparing with the adduct of butadiene[2] or 2,3-dimethyl-1,3-cyclohexadiene,[4] **6** was assigned to be the tetracyclodecene derivative, formed by the intramolecular Diels-Alder reaction of **5**.

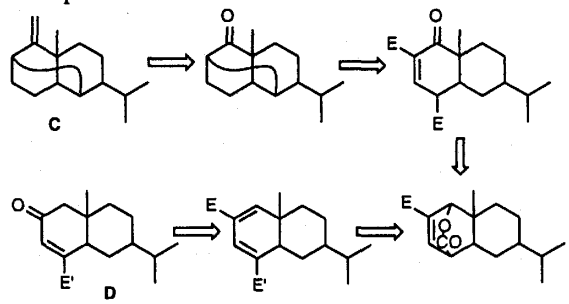
As the prolonged reaction did not affected the ratio of **5** to **6**, selective epoxidation of the mixture was examined, and an epoxide **7** and the unreacted **6** was obtained. When thus isolated **6** was heated under the same condition, the formation of **5** was confirmed. That is, the reaction of **5** to **6** is a reversal process, and the obtained mixture was equilibrated under the reaction conditions.



2.2. Attempt to convert the cycloadducts to the eudesmane derivative.

As several attempts for obtaining the pure triene(**5**) were failed, preparation of sesquiterpenoid skeleton from **3** or **4** was attempted. It is interesting to convert the above obtained **3** and **4** to sesquiterpenoids having eudesmane skeleton, because it would realize the monoterpene-to-sesquiterpenoid conversion by means of cycloaddition reaction of pyrone.

Two simplified ways were illustrated in Scheme 1. One is to eliminate the carboxyl group at 2-position selectively, *e.g.*, to convert to an enamine via Hofmann rearrangement, and another is the decarboxylation of the keto acid. Comparing these two, the direct product of the first way is **D**, which can be more easily prepared by the photo-reaction of methyl 2,4-dioxopentanoate with α-terpinene. On the other hand, effective decarboxylation of the keto ester might not only realize the conversion of **3** and **4** to eudesmanoid, but also give a possibility of making-up the sativane skeleton (**C**). So the second one was attempted.



Scheme 1. Derivation of sesquiterpenoid skeletons from 3 or 4.

First the alkaline hydrolysis in methanol of **3** and **4** was examined. Reaction of **3** with NaOH occurred rapidly, but gave diester(**8**) and monoester(**9**) of trienedicarboxylic acid. On the other hand, acidic hydrolysis of **3** gave the **10** and **11**. Contrary to these, the reaction with NaOH in *t*-butanol gave an expected hydroxy-acid, **12**, as a sole product, whereas the reaction of **3** with ammoniac methanol gave pure **8**.

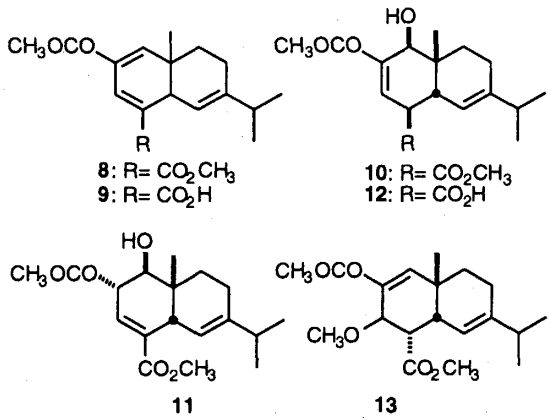
The isomer **4** gave methoxy acid **13** in alkaline hydrolysis, but rather stable in acidic condition.

Structure of **10** was assigned to be $\Delta^{2,3}$ unsaturated one, because the oxygenated methine proton at δ 4.16 was observed as singlet in the ^{1}H-NMR and the ring-contact methine proton at δ 2.64 was coupled with a methine proton at δ 3.64, neighboring to ester group, with 4.4 Hz of coupling constant, whereas **11** showed a methine proton at δ 4.05 having large coupling constant as large as 9.5 Hz.

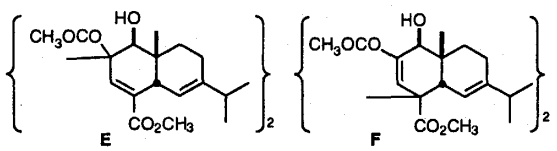
The ^{1}H-NMR of **13** revealed a different feature: the olefinic proton at δ 6.74 was observed as singlet, and the oxygenated methine proton at δ 4.65 was as doublet (*J*= 3.7 Hz). Further, another methine proton at δ 2.96, which must be alpha to ester group, was triplet (*J*= 3.7 Hz). Thus this methine group was determined to be located between the methoxy-substituted methine and the angular methine.

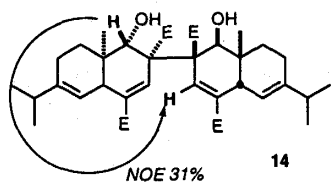
The stereochemistry of **13** was determined on the basis of the NOE, observed between methyl singlet at δ 1.06 and triplet methine proton at δ 2.96. From this, the stereostructure of **4** was concluded.

Attempted oxidation of **10** and **11** with pyridinium chlorochromate(PCC) or pyridinium dichromate (PDC) was unsuccessful. Oxidation of **10** with MnO_2 gave a dimeric product **14**, but no ketone. Similarly, **11** was oxidated with MnO_2 to give the same dimer **14**. This proved the position of hydroxyl group of **11** as the same as **10**.

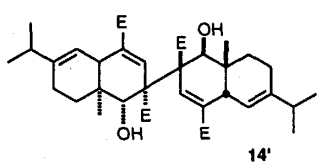


The mass spectrum clarified **14** as a dimeric product undoubtedly. Its ^{1}H- and ^{13}C-NMR spectra indicated its symmetrical structure. As its ^{1}H-NMR disclosed the existence of oxygenated methine proton at δ 4.26 having sole coupling (*J*= 10.5 Hz) with hydroxyl proton at δ 5.21, indicating the OH proton is fixed by intramolecular hydrogen bonding, and the conformation of these two protons should be anti. Therefore its structure must be **E** rather than **F**. The conclusive information was given from the NOE experiment. Upon irradiation of the hydroxylated methine proton at δ 4.26 caused 31% enhancement[10,11] of intensity of an olefinic proton at δ 6.52. This very large NOE, along with a large vicinal coupling constant between hydroxyl proton and methine proton, implied the structure of **14**. After the MM2 steric energy calculation, the structure was concluded not to be a meso but a racemic dimer(*R,R* and *S,S*). Although the meso dimer (**14'**), as well as the racemic one (**14**), might be possible to take a conformation satisfying above condition, *i. e.*, close contact of the methine and the olefinic protons and intramolecular hydrogen bonding, it is not the case in the most stable conformer. In the racemic dimer, these features are expected in the stable conformer.





14



14'

3. Experimental

All melting points are uncorrected. NMR spectra were measured with JEOL GSX-270H(270 MHz for ^{1}H and 67.5 MHz for ^{13}C) and FX-100(100 MHz for ^{1}H) spectrometer in $CDCl_3$ solution. IR-spectra were measured as KBr pellets for crystals or liquid film on NaCl plates for liquids using JASCO A-102 spectrophotometer.

Reaction of methyl 2-pyrone-5-carboxylate(1) with α-terpinene(2) at 110 °C: The toluene solution (7 cm^3) of **1**(1.08 g; 7.01 mmol) and **2**(1.84 g; 13.51 mmol) was heated under reflux for 23 h. The mixture was then chromatographed with silica-gel column, and were obtained **3**(pale yellow oil, 824 mg; 63%; ^{1}H-NMR: δ 0.94(3H, d, *J*= 7.0 Hz), 0.95(3H, d, *J*= 7.0 Hz), 1.25(3H, s), 1.50–1.91(4H, m), 2.11–2.21 (2H, m), 3.61(1H, dd, *J*= 6.4, 2.4 Hz), 3.79(3H, s), 5.16(1H, br. s), 5.20(1H, d, *J*= 2.2 Hz), and 7.19(1H, dd, *J*= 6.2, 2.4 Hz; ^{13}C-NMR: δ 20.5, 21.0, 22.9, 25.1, 31.4, 35.1, 40.4, 40.7, 48.9, 52.2, 82.3, 118.1, 137.0, 139.4, 148.3, 163.4 and 172.3; IR: ν(NaCl) 2950, 2860, 1762, 1720, 1440, 1260, 1150, 1082 and 999 cm^{-1}; MS: *m/z*(%) 290(2%), 137(11%), 136(100%) and 121 (4%); Exact mass: 290.1530(calcd for $C_{17}H_{22}O_4$: 290.1517)) and **4**(colorless prisms, mp 114–115 °C, 394 mg; 30%; ^{1}H-NMR: δ 0.93(3H, s), 0.99(3H, d, *J*= 7.0 Hz), 1.00(3H, d, *J*= 7.0 Hz), 1.52–2.10(5H, m), 2.25(1H, m), 3.47(1H, dd, *J*= 6.6, 2.2 H), 3.82(3H, s), 5.15(1H, d, *J*= 2.2 Hz), 5.29(1H, br. s), and 7.42(1H, dd, J= 6.6, 2.2 Hz); ^{13}C-NMR: δ 20.7, 21.2, 23.3, 25.5, 30.4, 35.2, 38.3, 40.9, 49.3, 52.2, 81.5, 117.6, 135.8, 140.7, 149.9, 163.4 and 171.0; IR: ν 2950, 2870, 1755, 1710, 1450, 1250, 1090 and 980 cm^{-1}; MS: *m/z*(%) 290(0.4%), 137(11%), 136(100%) and 121(5%); EA: Found C 70.30, H 7.01, Calcd for $C_{17}H_{22}O_4$ C 70.32, H 7.64), along with the unreacted **1**(390 mg).

Reaction of methyl 2-pyrone-5-carboxylate(1) with a-terpinene(2) at 144 °C: The *o*-xylene solution (7 cm^3) of **1**(207 mg; 1.34 mmol) and **2**(786 mg; 5.77 mmol) was heated under reflux for 17 h. The mixture was then chromatographed with silica-gel column, and were obtained a 1:2 mixture of **5** and **6** (161 mg, 56%; ^{1}H-NMR(**5**): δ 0.96(3H, d, *J*= 6.6 Hz), 0.97(3H, d, *J*= 6.6 Hz), 2.15(1H, sep, *J*= 6.6 Hz), 2.65(1H, m), 3.75(3H, s), 5.16(1H, m), 5.70(1H, dd, *J*= 9.7, 4.6 Hz), 6.22(1H, dt, *J*= 9.7, 1.5 Hz) and 6.52(1H, s) as a colorless oil and the unreacted **1**(27 mg). Attempted chromatographic isolation of **5** and **6** was failed.

Epoxidation of a mixture of 5 and 6: To a CH_2Cl_2 solution(6 cm^3) of the 1:2 mixture of **5** and **6**(174 mg), *m*-chloroperbenzoic acid(146 mg) was added and stirred for 1.5 h at room temperature. Addition of aqueous $NaHCO_3$ and extraction with $CHCl_3$ gave a diepoxide **7** (colorless oil, 22 mg, 33%; ^{1}H-NMR: δ

0.81(3H, d, *J*= 7.0 Hz), 0.90(1H, sep, *J*= 7.0 Hz), 0.92(3H. d, *J*= 7.0 Hz), 1.00(3H, s), 1.30-1.60(3H, m), 1.82(1H, m), 2.52(1H, m), 2.63(1H, s), 3.65(1H, dd, *J*= 4.0, 2.6 Hz), 3.82(3H, s), 3.96(1H, dd, *J*= 4.0, 2.0 Hz) and 6.72(1H, dd, *J*= 2.0, 1.0 Hz); ^{13}C-NMR: δ 17.5, 18.1, 21.2, 31.2, 32.0, 34.1, 34.2, 37.2, 45.3, 52.0, 57.9, 63.4, 127.5, 150.8 and 165.9) and unreacted **6** (98 mg, 84%; ^{1}H-NMR: δ 0.71(3H, s), 0.77(3H, d, = 7.0 Hz), 0.82(3H, d, *J*= 7.0 Hz), 1.14(1H, sep, *J*= 7.0 Hz), 1.22(1H, m), 1.32–1.47(2H, m), 1.53–1.62(3H, m), 1.72(1H, m), 2.55(1H, *d*, *J*= 1.5 Hz), 3.72(3H, s) and 7.45(1H, dd, *J*= 6.2, 1.5 Hz); ^{13}C-NMR: δ 15.9, 16.7, 18.2, 18.7, 26.0, 26.5, 27.5, 28.5, 34.7, 42.3, 48.3, 50.5, 51.3, 123.5, 139.9 and 166.3), which was used without further purification in the next experiment.

*Thermal reaction of **6** at 144 °C:* The above obtained **6** was heated in *o*-xylene under reflux for 5 h. The ^{1}H-NMR analysis of the mixture indicated the formation of **5** (**5**:**6**= 2:5).

*Alkaline hydrolysis of **3** in methanol:* In the methanol solution(6 cm^3) of **3** (140 mg), 3M-NaOH solution was added and stirred for 1 h at room temperature. After neutralization, the mixture was extracted with $CHCl_3$, dried over Na_2SO_4. Chromatographic separation gave **8** (pale yellow oil. 103 mg, 70%; ^{1}H-NMR: δ 0.92(6H, d, *J*= 7.0 Hz), 1.03(3H, s), 1.65(1H, m), 1.85-2.17(3H, m), 2.13(1H, sep, *J*= 7.0 Hz), 3.17(1H. br s), 3.89(3H, s), 3.82(3H, s), 5.01(1H, br s), 6.84(1H, s) and 7.38(1H, d, *J*= 1.5 Hz); ^{13}C-NMR: δ 21.0, 21.4, 24.0, 25.1, 34.5, 34.9, 36.1, 40.1, 51.9(2C), 117.9, 126.8, 128.2, 130.1, 143.5, 153.3, 165.4 and 167.4; IR: ν 2980, 2930, 2890, 1718, 1440, 1290, 1240, 1102, 1075, 1000 and 750 cm^{-1}; MS: *m/z*(%) 304(M+, 60), 245(47), 233(73), 189(47) and 96(100); Exact mass: 304.1671 (calcd for $C_{18}H_{24}O_4$: 304.1673)) and **9** (colorless oil. 14 mg, 10%; ^{1}H-NMR: δ 0.92(6H, d, *J*= 7.0 Hz), 1.05(3H, s), 1.75(td, *J*= 12.8, 5.5 Hz), 1.85–2.10(3H, m), 2.13(1H, sep, *J*= 7.0 Hz), 3.20(1H. m), 3.82(3H, s), 5.02(1H, br s), 6.97(1H, s) and 7.37(1H, d, *J*= 1.0 Hz); ^{13}C-NMR: δ 21.0, 21.4, 24.1, 24.9, 34.4, 34.9, 36.4, 40.1, 51.9, 117.8, 126.4, 127.6, 130.4, 143.6, 155.5, 167.3 and 169.9; IR: ν 2960, 2920, 1690, 1640, 1432, 1240, 1220, 1100, 1070 and 750 cm^{-1}; MS: *m/z*(%) 290(60), 275(25), 219(81), 171(40), 143(25), 131(29) and 96(100); Exact mass: 290.1513 (calcd for $C_{17}H_{22}O_4$: 290.1517)).

*Acidic hydrolysis of **3** in methanol:* In MeOH(2 cm^3) 108 mg of **3** and small amount of *p*-TsOH were dissolved and stirred overnight. After neutralized, the mixture was extracted with $CHCl_3$ and dried over Na_2SO_4. After column chromatography, **8** (6 mg, 6%), **10** (pale yellow oil. 36 mg(33%); ^{1}H-NMR: δ 0.99(6H, d, *J*= 7.0 Hz), 1.02(3H, s), 1.23(1H, m), 1.53(1H, m), 2.03–2.09(2H, m), 2.16(1H, sep, *J*= 7.0 Hz), 2.64(1H, m), 2.82(1H, br s), 3.02(1H, ddd, *J*= 6.5, 3.3, 1.0 Hz), 3.75(3H, s), 3.79(3H, s), 4.16(1H, br s), 5.46(1H, dm, *J*= 4.5 Hz) and 6.97(1H, d, *J*= 4.0 Hz); ^{13}C-NMR: δ 20.3, 21.5(2C), 22.9, 28.7, 34.7, 35.4, 36.9, 49.8, 52.0, 52.5, 68.8, 121.5, 132.4, 136.1, 143.2, 167.3 and 172.6; exact mass: 322.1776(calcd for $C_{18}H_{26}O_5$: 322.1779)), and **11** (pale yellow oil, 27 mg(25%); ^{1}H-NMR: δ 0.89(3H, s), 0.96(3H, d, *J*= 7.0 Hz), 0.97(3H, d, *J*= 7.0 Hz), 1.37(1H, m), 1.89–2.22(3H, m), 2.89(1H, m), 3.05(1H, br s), 3.21(1H, ddd, *J*= 9.5, 2.5 1.8 Hz), 3.79(6H, s), 4.02(1H, d, *J*= 9.5 Hz), 5.16(1H, br s) and 6.91(dd, *J*= 2.5, 0.7 Hz); ^{13}C-NMR: δ 19..8, 21.1, 21.5, 21.8, 31.6, 35.0(2C), 43.8, 48.2, 52.0, 52.6, 66.0, 118.2, 132.9, 133.8, 142.5, 166.9 and 174.4; IR: ν 3530, 2960, 1720, 1437, 1250, 1070, 1998 and 760 cm^{-1}; MS: *m/e*(%): 322(23), 304 (100), 272(68), 261(63) and 229(40); exact mass: 322.1778(calcd for $C_{18}H_{26}O_5$: 322.1779)) were obtained along with the recovered **3** (9 mg).

*Alkaline hydrolysis of **3** in t-butanol:* In the *t*-butanol solution(5 cm^3) of **3** (120 mg), was added 3M-NaOH(0.2 cm^3) and stirred for 1 h at room temperature. Adding 1M-HCl to neutralize, the mixture was extracted with chloroform and washed with brine. Evaporation gave a practically pure **12** (81 mg, 64%), which was treated with etherial CH_2N_2, and **10** was obtained quantitatively.

*Ammonia catalyzed methanolysis of **3**:* In the methanol solution(10 cm^3) of **3** (137 mg), 28%-aqueous NH_3(70 mm^3) was added and stirred for 27 h at room temperature. Neutralization with 1M-HCl and extract with chloroform gave 136 mg of **8** (94%).

*Alkaline hydrolysis of **4** in methanol:* In MeOH solution(6 cm^3) of **4** (54 mg), 0.1 cm^3 of 3M-NaOH solution was added and stirred for 5 min. Neutralization with 1M-HCl, extract with chloroform and column chromatographic separation gave **8** (21 mg, 38%) and **13** (colorless oil, 331 mg, 51%; ^{1}H-NMR: δ 0.92(3H, d, *J*= 7.0 Hz), 0.93(3H, d, *J*= 7.0 Hz), 1.07(3H, s), 1.58-1.90(4H, m), 2.11(1H, sep, *J*= 7.0 Hz), 2.72(1H, m), 2.96(1H, dd, *J*= 3.7 Hz), 3.42(3H, s), 3.78(3H, s), 4.65(1H, d, *J*= 3.7 Hz), 5.44(1H, br s) and 6.74(1H, s); ^{13}C-NMR: δ 20.9, 21.1, 23.7, 27.1, 34.8, 36.5, 36.7, 39.0, 45.6, 51.8, 59.1, 70.9, 119.2, 129.7, 140.7, 150.1, 167.3 and 177.5; IR: ν 2956, 2926, 2876, 2834, 1708, 1436, 1420, 1310, 1262, 1239 and 1073 cm^{-1}; MS: *m/z*(%) 322(36), 290(92), 258(62), 136(97), 134(100) and 119(53); exact mass: 322.1778 (calcd for $C_{18}H_{26}O_5$: 322.1779).

*Oxidation of **10** with MnO_2:* Activated MnO_2(Aldrich, 500 mg) and **10** (32 mg) were placed in chloroform(6 cm^3), and stirred for 4 h under N_2 atmosphere. Solid material was filtered off and organic layer was chromatographed to give **14** (colorless oil. 8 mg, 25%; ^{1}H-NMR: δ 0.71(6H, s), 1.06(6H, d, *J*= 7.0 Hz),

1.08(6H, d, *J*= 7.0 Hz), 1.26(2H, m), 1.88-2.20(6H, m), 2.30(2H, sep, *J*= 7.0 Hz), 3.05(2H, br s), 3.73(6H, s), 3.75(6H, s), 4.26(2H, d, *J*= 10.5 Hz), 5.14(2H, m), 5.21(2H, br d, *J*= 10.5 Hz), 6.52(2H, s); ^{13}C-NMR: δ 20.6, 20.9, 21.5, 21.7, 32.4, 35.6, 36.4, 43.2, 51.9, 52.0, 53.6, 67.3, 118.5, 132.8, 134.4, 143.2, 166.6 and 173.3; IR: ν 3430, 2950, 1712, 1432, 1235, 1090, 875, 755 and 728 cm^{-1}; MS: *m/z*(%) 642(6), 322(24), 321(90), 320(35) and 303(100); exact mass: 642.3402(calcd for $C_{36}H_{50}O_{10}$: 642.3401)).

References and Notes

1) Review article: K. Afarinkia, V. Vinader, T. Nelson, G. S. Posner, *Tetrahedron*, **48**, 9111(1992).

2) T. Imagawa, N. Sueda, M. Kawanishi, *Tetrahedron*, **30**, 2227(1974).

3) E. J. Corey, D. S. Watt, *J. Amer. Chem. Soc.*, **95**, 2303(1973).

4) T. Hatsui, T. Hashiguchi, H. Takeshita, *Chemistry Lett.*, **1994**, 1415.

5) H. L. Gingrich, D. M. Rousch, W. A. Van Saun, *J. Org. Chem.*, **48**, 4869(1983)

6) M. E. Jung, J. A. Hagenah, *J. Org. Chem.*, **52**, 1889(1987); K. Harano, T. Aoki, M. Eto, T. Hisano, *Chem. Pharm. Bull.*, **38**, 1182(1990).

7) G. A. Posner, N. Johnson, *J. Org. Chem.*, **59**, 7855(1994).

8) T. Hatsui, T. Hashiguchi, H. Takeshita, *Chemistry Express*, **8**, 581(1993).

9) T. Hatsui, N. Hirata, H. Takeshita, *Chemistry Express*, **8**, 581(1993).

10) Irradiation of the signal at δ 6.52 caused a smaller but enough large enhancement of intensity (19%) of the signal at δ 4.26.

11) A referee commented that this figure must be so large that we should add further discussion on the structure of **14**, because it is close to the theoretical maximum value of NOE (0.5) between two protons in the extreme narrowing limit.[12] An MM2 calculation, performed using Chem3D Plus program, v 3 (Cambridge Scientific Computing, Inc.) showed us the distance between the two protons under discussion in the preferred conformation of **14** (∠ECC'E'= 80.4°, where E and E' are ester group attached on quaternary carbon) was 2.15 and 2.18 Å, which are consistent with the observed NOE as large as 31%, whereas it was calculated as 2.63 and 2.84 Å in the stable conformer of **14'** (∠ECC'E'= 59.6°).

12) H. Iwamura, in '*Shin-jikken Kagaku Kouza*,' ed. by the Chemical Society of Japan, vol. 13(I), Maruzen, Tokyo(1977), p. 269-274.