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Synthetic Photochemistry. LIII.[1] Low-Temperature Irradiation of Methyl 2,4-Dioxopentanoate with α-Phellandrene, p-Mentha-1,5-diene. Product Distribution and Further Occurrence of "retro-Benzilic Acid Rearrangement"

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Low-temperature irradiation of methyl 2,4-dioxopentanoate with *p*-mentha-1,5-diene (α-phellandrene) gave *retro*-benzilic acid rearrangement products in low but reproducible yields, after a pyrolytic workup, together with isomeric [4 + 2] cycloadducts. This indicates an accumulation of the *proto*-photocycloadducts during the reaction. The product analysis indicated the [2+2] and [4+2] cycloadditions are mutually independent processes.

Introduction

For a long time, we have been interested in investigation of the photochemical cycloadditions of methyl 2,4-dioxopentanoate (**1**) with various olefins to synthesize natural products, e.g., terpenoids.[2] We recently noticed a formation of 5-substituted derivatives of 3-acetyl-2-hydroxy-2-cyclopentenone, in variable yields, which could be characterized after methylation with diazomethane.[3] Moreover, a polysubstituted conjugated diene, 2,5-dimethyl-2,4-hexadiene, disclosed an occurrence of several other types of photoproducts.[4] In this respect, α-phellandrene, *p*-mentha-1,5-diene (**2**), also seemed to be worthwhile to examine; this olefin is an unsymmtrically substituted, and, therefore, suitable to analyze a regioselectivity of the reaction. Herein, we will show results of photochemical reactions of **1** and **2**.

Results and Discussion

With a parallel manner to the previously reported,[3] an irradiation of **1** and **2** in an ethyl acetate solution by means of a 400-W high-pressure mercury lamp through a Pyrex glass filter at −60℃ was carried out to cause a smooth photoreaction. When the whole mixture was immediately heated in *p*-cymene after irradiation, and subsequently evaporated to remove the volatile material, the resultant residue afforded, via methylation with diazomethane and silica-gel column chromatography, a diastereomeric pair of *retro*-benzilic acid rearrangement products (**3** and **4**), bicyclo[2.2.2]octene derivatives (**5**, **6**, and **7**), and an ene-reaction product (**8**). When the reaction mixture was directly chromatographed on a silica-gel column, the products further characterized were the expected methyl dioxocarboxylates (**9** and **10**), in 4 and 0.2% yields, respectivery. The minor products (**5**, **6**, **7**, and

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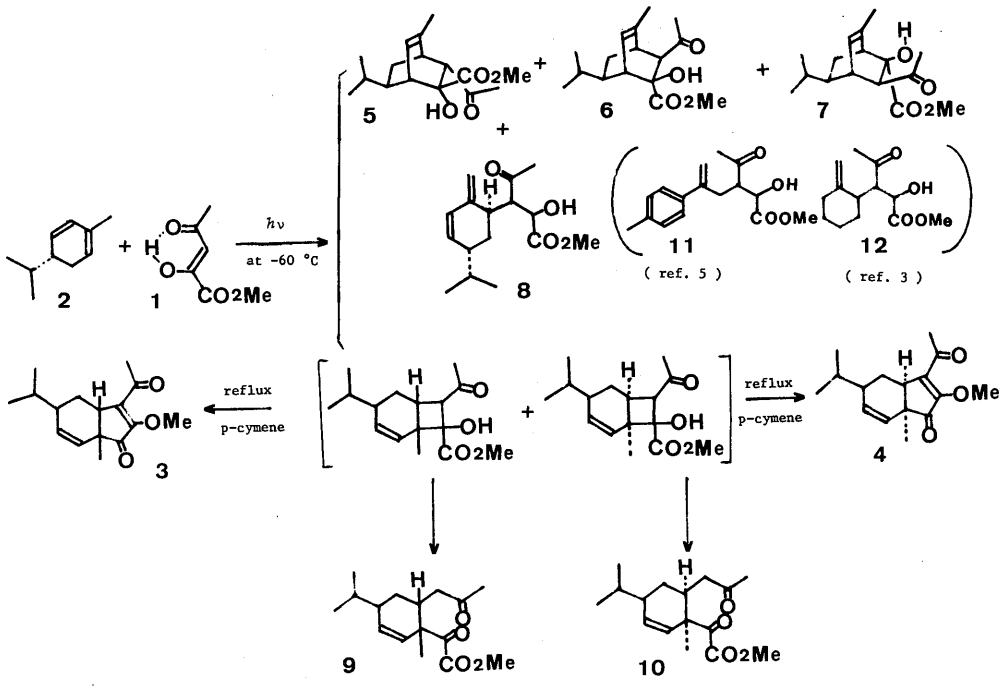


(Scheme 1)

8) were again isolated.

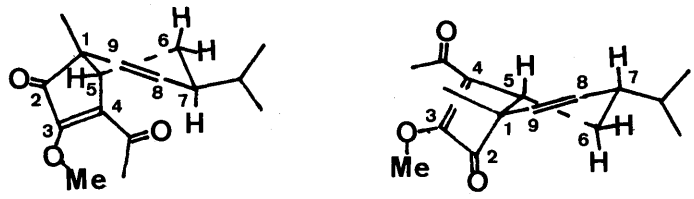
Structures of 3 and 4. The structures of **3** and **4** were elucidated by the IR and NMR spectral comparisons with the same type of products derived from various olefins.[3)4)] Their IR spectra showing two carbonyl stretching absorption bands at 1710 and 1670 (for **3**) and 1715 and 1660 cm^{-1} (for **4**), respectively, were similar to those derivatives characterized in the previous papers,[3)4)] and supported the formulation. Particularly diagnostic were considerably low-field-shifted acetyl methyl signals at $\delta = 2.48$ (in **3**) and 2.50 (in **4**) and enolic methoxy methyl signals at $\delta = 4.13$ (in **3**) and 4.16 (in **4**). Furthermore, mutual comparisons of the NMR spectra of **3** and **4** deduced the stereochemistry. One notable feature of the ^1H NMR spectra was chemical shift differences of the *cis-vic*-olefinic proton signals; those of **3** appeared at 5.29 and 5.78 with a mutual coupling constant, $J = 9.9$ Hz, while those of **4** appeared at 5.78 as an overlapped signal. Thus, in **3**, the two olefinic hydrogens are placed in a magnetically different circumstance. As a priority factor for determining the conformations of these compounds, the most bulky substituent, isopropyl group, should always be equatorial, as was consistent to the observed small chemical shift differences of two doublet methyls in the ^1H NMR spectra. In addition to this, the cyclopentenone moiety of **3** and **4** should be almost planer, and also four of the cyclohexene carbons must be in the other plane, thus, only the C-6 and C-7 of the whole molecules could have a freedom in changing the conformation. According to inspections with the Deiding's Stereomodel, there are two possible conformers for **3** and **4**; one is an extended (**A**), and the other, a folded (**B**). In the isomer having *anti*-configuration between the angular methyl

and isopropyl groups should have the extended **A** form, while the isomeric *syn*-isomer should have the folded **B** form. In the *anti*-isomer, the C-6 *quasi-axial* hydrogen, *cis* to the adjacent isopropyl group, is also *cis* to the sp^2-carbons of cyclopentenone moiety, and consequently, should suffer a large anisotropic effect to cause a high-field shift. In the folded conformer, **B**, the *quasi-axial* hydrogen at C-6 is *trans* to the cyclopentenone moiety. Therefore, **4**, the compound having a signal at 0.63, must be **A**, and the other, **3**, must be **B**. In parallel to the observation, the chemical shift difference of the methine protons on the C-7 between **3** and **4** was also consistent to the formulations; in the folded isomer, **3**, the methine proton should be confronted to the cyclopentenone moiety, and the chemical shift should be considerably higher than the isomer, **4**. Although C-7 methine signal in **3** was obscured by overlapping with isopropyl methine proton signal at around 1.5-1.7, it was clearly high-field-shifted than **4**, which showed a separated signal at 2.03 ($\Delta\delta=0.4$). This was also consistent to the prediction that the major product should have the *syn*-relationship between the angular methyl and isopropyl groups since the reactant should attack mainly from the opposite side to the bulky isopropyl group in **2**.

Structures of 5, 6, and 7. Since **2** is a cyclic conjugated diene, it is capable of forming [4+2]cycloadducts.[5] The products, **5, 6**, and **7** were indeed the type of compounds. Thus, their IR spectra showed strong absorption peaks at ca. 3,500 cm^{-1} region to indicate the presence of an aldol moiety. The ^{13}C NMR spectra revealed only two olefinic carbons other than those of carbonyl groups. Therefore, they are bicyclic. Unfortunately, their yields were low, and behaviors towards chromatography resembled each other, and were difficult to separate the compounds. Nevertheless, they were fully characterized and analyzed in respects of ^1H and ^{13}C NMR spectroscopies. Since the stereochemistry of the segment derived from the β-diketone, **1**, should be transfered from its ground state geometry, the stereochemical relationship of the α-methine proton and other polar substituents should be same for all the molecules in this category, and it should provide a good diagnostic information for structure analysis. The chemical shifts of the α-methine protons were 3.19 for **5** and 3.72 for **6** and **7**, and the difference should be ascribable to the different orientation to the double bond in the molecule. The molecular model inspections clearly show that *syn*-protons to the etheno bridge in the bicyclo[2.2.2]octene cause a high-field shift by an anisotropy from the double bond, and **5** should have such a stereochemistry. In addition, only the methine proton of **5** appeared as a triplet, $J=1.7$ Hz, being exhibited a *W*-lettered long-range coupling, should be assigned the position of the isopropyl group at the opposite side of the methine proton in the molecule. Thus, **5** is expressed as depicted, 6α-acetyl-5α-hydroxy-8*R**-isopropyl-5β-methoxycarbonyl-2-methylbicyclo[2.2.2]oct-2-ene.
The methine protons of **6** and **7** have anti-orientation to the etheno bridge. For selection of the correct stereostructures of these two, the chemical shifts of olefinic protons and methyl groups were compared; The chemical shifts of methyl groups were 2.00 for **6** and 1.85 for **7**, while those of methine protons were 5.60 for **6** and 6.17 for **7**. Taking considerations of anisotropic effect from the acetyl group into account, the methyl group of **6** and the methine proton of **7** must be confronted to the β-acetyl group. Consequently, the structures of **6** and **7** were elucidated unambiguously as shown in Scheme 1.

Structure of 8. The ^1H NMR spectral features of **8** were closely related to ene-

products (**11** and **12**) already isolated and characterized from the photoreactions of **1** to *p*-isopropenyltoluene[6] and 1-methylcyclohexene.[3] Particularly, a) both **8** and **12** showed a rather stable hydrogen-bonded hydroxyl signals, which exhibited spin-coupled spilittings with the methine protons, $J=8.4$ and 8.8 Hz, respectively, in chloroform-*d*, to indicate a formation of β-hydroxyketo function (thus, chelation must be six-membered), and b) the chemical shifts of mutually spin-coupled (with 2.9 and 2.6 Hz, respectively) methine protons caused a significant down-field shift due to a presence of other functional groups in this molecule, i.e., 3.14 *vs.* 2.94 and 4.37 *vs.* 4.28. The stereochemical relationship of the bulky substituents should be *cis* from the mechanistic point of view, but no other independent evidence is available. Therefore, **8** could be expressed as depicted.



Folded **B**-Conformation of **3** Extended **A**-Conformation of **4**

(Chart 1)

It is not surprising that for the [2+2] cycloadditions, the complete regio- and site-selectivities were observed as parallel to the previous examples, i.e., the reaction occurred at the double bond with larger electron density to give 3-alkenyl-2,6-dioxoheptanoates. However, in the [4+2]cycloadducts, the regioselectivity was rather poor; the ratio of head-to-head and head-to-tail products (**5** and **6** *vs.* **7**) was 5:1, and the ratio of *exo*- and *endo*-isomers (**5** *vs.* **6** and **7**) was 2:1. Therefore, the transition states leading to [2+2] and [4+2]cycloadducts were mutually independnet.

In conclusion, all the products characterized in this study were obtained in low yields. This does not mean, however, that the photochemical process was impractical; in order to identify the unstable compounds, the workup employed in the experiments was not optimized yet, and the material balance was sacrificed inevitably to some extent. Under the ordinary conditons, the 2,6-dioxoheptanoates derived from the [2+2] cycloadducts and the [4+2] cycloadducts could be obtained in reasonable yields.

Experimental

Elemental analyses were performed by Miss S. Hirashima, of Institute of Advanced Material Study, Kyushu University. NMR spectra were measured in $CDCl_3$ with a GSX 270H Model spectrometer, JEOL., and the chemical shifts were expressed in δ units. Mass spectra were measured with a 01SG-2 Model spectrometer, JEOL. IR spectra were obtained by a Jasco IR-A 102 Model spectrometer as KBr disks, liquid films, or in $CHCl_3$ solutions. The oxygen-free solvents for irradiations were obtained by careful distillation under an N_2 atmosphere.

Isolation of Photoproducts from 1 and p-Mentha-1,5-diene (2).[7] An EtOAc solution (40 cm^3) of **1** (372 mg) and **2** (853 mg) was irradiated by means of a 400-W high-pressure mercury lamp at −60℃ for 6 h. Then, the irradiation was stopped at the 88%-consumption of **1** (UV spectrometry). The mixture was divided to two parts, and one half of the mixture was diluted with *p*-cymene and heated at 180℃ for 1h; the mixture was then distilled in vacuo to remove the volatile material, and, after methylation with CH_2N_2, chromatographed on a silica-gel column to give **3** [a pale yellow oil, 34 mg; 7%. Found: *m/z*, 262.1573(M^+). Calcd for $C_{16}H_{22}O_3$: 262.1568. ^{1}H-NMR δ = 0.87(3H, d, J = 6.6 Hz), 0.88(3H, d, J=6.6 Hz), 1.23(3H, s), 1.41(1H, ddd, J=13.0, 10.5, 4.6 Hz), 1.54-1.66(2H, m), 2.00(1H, dtd, J=13.0, 4.4, 1.3 Hz), 2.48(3H, s), 3.02(1H, t, J=4.4 Hz), 4.13(3H, s), 5.29(1H, dd, J=9.9, 1.5 Hz), and 5.78(1H, ddd, J=9.9, 2.3, 1.3 Hz). ^{13}C NMR δ =19.5, 19.6, 22.0, 31.3, 31.5, 38.0, 41.3, 48.6, 58.6, 128.6, 133.7, 140.3, 157.2, 197.8, and 205.4. IR ν: 2960, 1715, 1670, 1610, 1450, 1380, 1220, 1160, 1130, 1055, and 755 cm^{-1}], **4** [a colorless oil, 1 mg; 0.2%. Found: *m/z*, 262.1598(M^+). Calcd for $C_{16}H_{22}O_3$: 262.1568. ^{1}H NMR δ =0.68(1H, ddd, J=12.1, 11.7, 1.2 Hz), 0.84(3H, d, J=6.6 Hz), 0.85(3H, d, J=7.0 Hz), 1.19(3H, s), 1.60(1H, sept of d, J=6.6, 5.0 Hz), 2.03(1H, ddd, J=11.2, 5.0, 3.4 Hz), 2.20(1H, ddd, J=12.1, 5.1, 3.4 Hz), 2.50(3H, s), 2.84(1H, dd, J=11.7, 5.1 Hz), 4.16(3H, s), and 5.78(2H, s). ^{13}C NMR δ =19.2, 19.3, 27.8, 31.4_8, 31.5_3, 33.6, 41.2, 43.1, 48.7, 58.5, 128.4, 133.1, 142.9, 154.2, 197.2, and 208.4. IR ν: 2950, 1710, 1660, 1605, 1450, 1380, 1220, 1030, and 960 cm^{-1}], **5** [a colorless oil, 27 mg; 4%. *m/z*, 280(M^+). 222(3), 147(19), 137(44), 93(base peak), 92(59), 77(20), 43(57), and 41(21). ^{1}H NMR δ = 0.80(3H, d, J=6.6 Hz), 0.85(3H, d, J=6.6 Hz), 1.09(1H, br m), 1.5-2.2(3H, m), 1.80(3H, d, J=1.5 Hz), 2.19(3H, s), 2.68(1H, m), 2.80(1H, dd, J=6.2, 2.0 Hz), 3.19(1H, t, J=1.7 Hz), 3.77(3H, s), 4.91(1H, s, OH), and 5.57(1H, dm, J=6.2 Hz). ^{13}C NMR δ =19.8, 20.5, 20.9, 26.4, 30.7, 32.6, 37.6, 38.8, 44.2, 51.9, 53.0, 78.3, 121.7, 144.4, 175.3, and 211.1. IR ν: 3500, 2950, 1720, 1440, 1360, 1235, 1180, 1160, 1100, 1050 cm^{-1}], **6** [a colorless oil, 5 mg; 1%. Found: *m/z*, 280.1674(M^+). Calcd for $C_{16}H_{24}O_4$: 280.1673. ^{1}H NMR δ =0.77(3H, d, J=6.2 Hz), 0.82(3H, d, J=6.2 Hz), 0.93(1H, br m), 1.4-1.8(3H, m), 2.00(3H, d, J=1.5 Hz), 2.11(3H, s), 2.47(1H, s, OH), 2.61(1H, m), 2.95(1H, dd, J=6.2, 1.5 Hz), 3.72(1H, br s), 3.88(3H, s), and 5.60(1H, dqm, J=6.2, 1.5 Hz). ^{13}C NMR δ = 20.4, 20.5, 21.0, 31.0, 32.5, 38.1, 40.6, 44.6, 53.1, 58.1, 80.9, 117.9, 148.0, 173.9, and 208.4. IR ν: 3500, 2960, 1720, 1440, 1360, 1220, 1160, 1065, and 1020 cm^{-1}], **7** [a colorless oil, 5 mg; 1%. Found: *m/z*, 280.1672(M^+). Calcd for $C_{16}H_{24}O_4$: 280.1673. ^{1}H NMR δ = 0.88(3H, d, J=6.6 Hz), 0.89(3H, d, J=6.6 Hz), 1.5-1.7(4H, m), 1.85(3H, d, J=1.5 Hz), 2.14(3H, s), 2.64(1H, m), 2.77(1H, dm, J=7.0 Hz), 3.57(1H, s, OH), 3.72(1H, br s), 3.87(3H, s), and 6.17(1H, dm, J=7.0 Hz). ^{13}C NMR δ =21.1, 22.1, 26.1, 30.9, 31.1, 34.4, 44.7, 46.9, 53.1, 51.5, 81.0, 128.2, 174.0, and 209.3. IR ν: 3450, 2950, 1705, 1440, 1360, 1220, 1100, and 1030 cm^{-1}], and **8** [a colorless oil, 10 mg; 2%. ^{1}H NMR δ =0.88(3H, d, J=6.2 Hz), 0.90(3H, d, J=6.2 Hz), 1.13(1H, br m), 1.5-2.2(3H, m), 2.24(3H, s), 3.04(1H, dd, J=12.2, 2.9 Hz), 3.12(1H, dtm, J=12.2, 3.0 Hz), 3.40(1H, d, J=8.4 Hz), 3.75(3H, s), 4.37(1H, dd, J=8.4, 2.9 Hz), 5.04(1H, br s), 5.09(1H, br s), 5.72(1H, dm, J=10.0 Hz), and 6.13(1H, dd, J=10.0, 3.0 Hz). ^{13}C NMR δ =19.1, 19.4, 28.1, 31.8, 32.4, 37.7, 38.4, 52.6, 54.2, 70.5, 114.8, 128.3, 132.8, 142.0, 174.5, and 212.9].

The other half of the mixture was directly chromatographed on a silica-gel column to give **9** [a colorless oil, 24 mg; 4%. Found: *m/z*, 280.1675(M^+). Calcd for $C_{16}H_{24}O_4$: 280.1673. ^1H NMR δ = 0.91(3H, d, J = 6.6 Hz), 0.92(3H, d, J = 7.0 Hz), 1.37(3H, s), 1.6-1.7(2H, m), 1.69(1H, qqm, J = 7.0, 6.6 Hz), 1.95(1H, qm, J = 6.4 Hz), 2.14(3H, s), 2.45-2.5(2H, m), 2.55(1H, m), 3.84(3H, s), 5.76(1H, dd, J = 10.3, 1.5 Hz), and 5.82(1H, dd, J = 10.3, 2.6 Hz). ^{13}C NMR δ = 20.6, 20.7, 25.2, 26.4, 31.2, 32.8, 36.2, 39.2, 51.0, 53.2, 129.0, 133.5, 164.7, 200.5, and 208.4. IR ν: 2960, 1730, 1440, 1370, 1280, 1240, 1160, and 1020 cm^{-1}] and **10** [a colorless oil, 1 mg; 0.2%. Found: *m/z*, 280.1679(M^+). Calcd for $C_{1}236H_{24}O_4$: 280.1673. ^1H NMR δ = 0.83(3H, d, J = 7.0 Hz), 0.85(3H, d, J = 7.0 Hz), 1.29(3H, s), 1.50(1H, br m), 1.63(1H, br m), 1.63(1H, sept, J = 7.0 Hz), 2.1-2.2(2H, m), 2.62(1H, dd, J = 18.4, 8.7 Hz), 2.66(1H, dd, J = 18.4, 3.3 Hz), 3.80(3H, s), 5.63(1H, dd, J = 10.3, 2.6 Hz), and 5.86(1H, dm, J = 10.3 Hz). IR ν: 2950, 1715, 1450, 1370, 1275, 1160, and 1025 cm^{-1}], together with **5**(12 mg; 2%), **6**(5 mg; 1%), **7**(5 mg; 1%), and **8**(5 mg; 1%).

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