DIELS-ALDER REACTION OF PHOTOENOL OF 2-METHYLBENZALDEHYDE WITH 5-ALKYLIDENE-1,3-DIOXANE-4,6-DIONE DERIVATIVES

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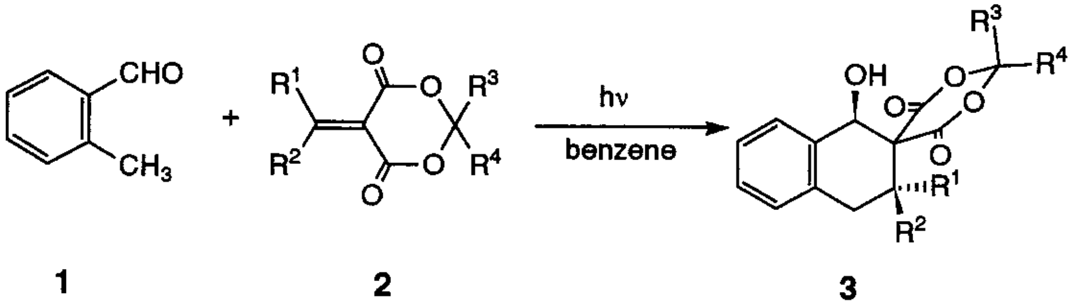
Abstract —— Spiro- and polyspirocyclic compounds containing the 1,2,3,4-tetrahydro-1-naphthol structure were obtained by the Diels-Alder reaction of the photoenol of 2-methylbenzaldehyde with 5-alkylidene-1,3-dioxane-4,6-dione derivatives. The cycloaddition proceeded regio- and stereoselectively. However, in the case using 5-benzylidene-2,2-dimethyl-1,3-dioxane-4,6-dione and diethyl isobutylidenemalonate, the cycloaddition failed.

Photoenolization[1] of *o*-alkyl-substituted aromatic carbonyl compounds such as 2-methylbenzaldehyde (**1**) is well-known and the photoenols allow the Diels-Alder reaction with dienophiles.[1-3] Similar reactions of the photoenols with other types of dienophile is expected in view of their regio- and stereoselectivities. However, there are very few reports on the cycloaddition of unsymmetrical dienophiles[3] to the photoenols of *o*-alkyl-substituted aromatic carbonyl compounds. Previously[4] we reported that 5-alkylidene-1,3-dioxane-4,6-dione derivatives (**2a-k**) were very reactive electrophiles which reacted with hydrogen peroxide in the absence of a catalyst to give spiro- and polyspirocyclic compounds containing an oxirane ring. These compounds (**2a-k**) are expected to act as effective unsymmetrical dienophiles activated by a cyclic acylal group in the Diels-Alder reaction.[5] Now we report the cycloaddition of the photoenol of **1** with **2a-k**.



Scheme 1

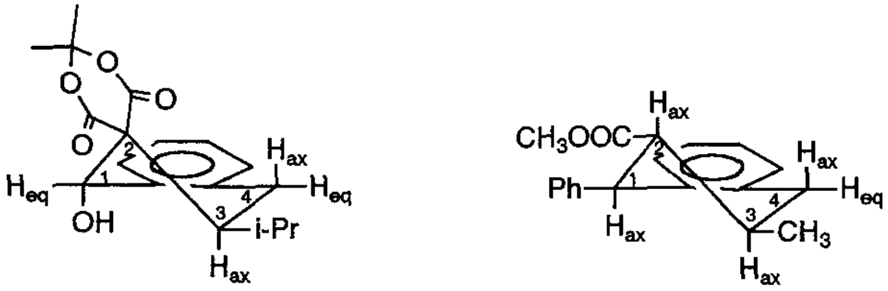
Table 1. Diels-Alder Reaction of Photoenol of 2-Methylbenzaldehyde with 5-Alkylidene-1,3-dioxane-4,6-dione Derivatives in Benzene[a)]

Entry	Dienophile	R^1	R^2	R^3	R^4	Product	Irradiation Time/h	Yield/%
1	**2a**	i-C_3H_7	H	CH_3	CH_3	**3a**	3	80
2	**2b**	-$(CH_2)_4$-		CH_3	CH_3	**3b**	2	37
3	**2c**	-$(CH_2)_5$-		CH_3	CH_3	**3c**	2	53
4	**2d**	CH_3	CH_3	CH_3	CH_3	**3d**	2	38
5	**2e**	c-C_6H_{11}	H	CH_3	CH_3	**3e**	3	62
6	**2f**	i-C_3H_7	H	-$(CH_2)_4$-		**3f**	2	54
7	**2g**	-$(CH_2)_4$-		-$(CH_2)_4$-		**3g**	2	38
8	**2h**	-$(CH_2)_5$-		-$(CH_2)_4$-		**3h**	2	69
9	**2i**	i-C_3H_7	H	-$(CH_2)_5$-		**3i**	3	49
10	**2j**	-$(CH_2)_4$-		-$(CH_2)_5$-		**3j**	2	29
11	**2k**	-$(CH_2)_5$-		-$(CH_2)_5$-		**3k**	3	65

a) All reactions were carried out using a 100-W high-pressure mercury lamp with a Pyrex jacket at room temperature under an argon atmosphere.

An equimolar benzene solution of **1** and **2a-k** was irradiated using a 100-W high-pressure mercury lamp with a Pyrex jacket under an argon atmosphere at room temperature to yield the corresponding cycloadducts (**3a-k**) (Scheme 1, Table 1).

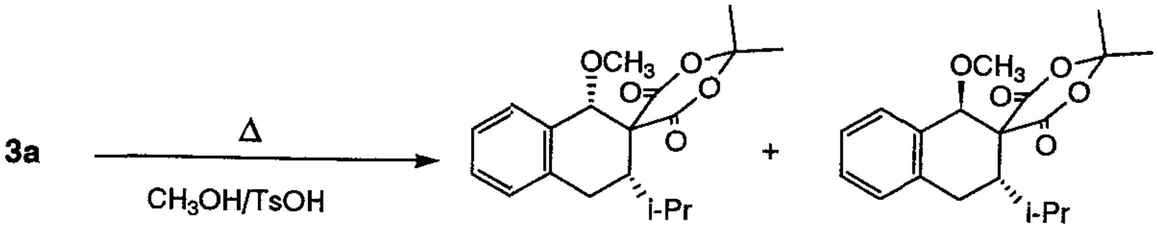
We confirmed the stereochemistry of the cycloadducts by the following spectral data. The ir spectra of the cycloadducts clearly showed the presence of hydroxyl (3700-3200 cm^{-1}) and two sorts of carbonyls on the 1,3-dioxane-4,6-dione ring (ca. 1765 and 1730 cm^{-1}).[6] Especially, the cycloadducts (**3a**-**e**) from **2a**-**e** showed the presence of a geminal dimethyl group of acylal (ca. 1395 and 1385 cm^{-1}).[5a] In addition, the coupling constants between pseudo-axial and pseudo-equatorial of 4-methylene protons in the ^1H nmr spectra appeared in the range of 16 to 18 Hz, the hydroxyl proton is exchangeable with D_2O, and the 1-methine proton signals showed significantly at low magnetic fields (δ 5.4-5.6) as a singlet or doublet (CHOH coupling, ca. J=7-9 Hz). Since no other stereoisomeric adducts could be found, these adducts (**3a**-**k**) are obviously regio- and stereoselective ones.



3a **4**

Scheme 2

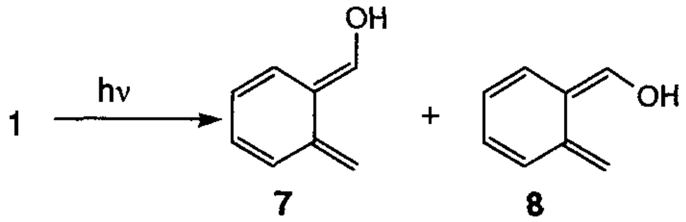
Moreover, the conformation of 1- and 3-methine protons for **3a**, **3e**, **3f**, and **3i** was determined as follows. On the 3-methine proton conformation, for example, signals of the 3-methine proton and 4-methylene protons of **3a** appeared at δ 2.55(1H, ddd, J=2.5, 4.5, and 12.9 Hz, 3-CH), 2.75(1H, dd, J=4.5 and 16.5 Hz, 4-CH_{eq}), and 3.09(1H, dd, J=12.9 and 16.5 Hz, 4-CH_{ax}), respectively. The ^1H nmr spectra of the other adducts were also satisfactorily assigned. Their spectral data were compared with those of similar cycloadduct (**4**) from α-phenyl-o-quinodimethane with methyl crotonate (Scheme 2) whose stereochemistry was reported by Durst et al.,[7] and the coupling constants of H_{3ax}-H_{4ax}, H_{3ax}-H_{4eq}, and H_{4ax}-H_{4eq} of **4** have 12.0, 5.0, and 16.0 Hz, respectively. The coupling constants of **3a** are in good agreement with those reported in the literature,[7] which suggests the pseudo-equatorial orientation of the 3-alkyl groups.



5 **6**

Scheme 3

On the other hand, since the stereochemistry of the 1-methine proton is difficult to determine from the spectral data alone, the adduct (**3a**) is converted to the methoxyl derivatives (**5** and **6**) (Scheme 3). When a methanol solution of **3a** in the presence of a catalytic amount of TsOH was refluxed for 30 min, the methoxyl compounds were obtained as a mixture of cis and trans epimers (5 and **6**) in a ratio of **5**:**6**=43:7 at a conversion of 50% of **3a** by the ^{1}H nmr analysis. The 3-methine and the 4-pseudo-axial methylenic proton signals of the major stereoisomer (**5**) in the ^{1}H nmr spectrum overlapped with the methine proton signal[8] in the isopropyl group and the 4-pseudo-equatorial methylenic proton signals, respectively, but could be separated after an incremental amount of paramagnetic chelates [Yb(fod)$_3$]. The coupling constants of H_{3ax}-H_{4ax} and H_{3ax}-H_{4eq} of **5** have J=11.8 Hz and J=3.5 Hz, respectively. If the 3-methine proton is the pseudo-equatorial orientation, the coupling constants of H_{3eq}-H_{4eq} and H_{3eq}-H_{4ax} should be observed ca. J=8-9 Hz and ca. J=2-3 Hz, respectively.[7,9] Therefore, the 3-isopropyl group of **5** is suggested to be the pseudo-equatorial orientation. The heating was further continued for 9 h to give mainly trans-epimer (**6**), hence the etherification of **3a** is confirmed to proceed with the Walden inversion. The isopropyl group of **6** was also observed to exist apparently in the pseudo-equatorial orientation by the coupling constants. Consequently, these results show that the epimers (**5** and **6**) are configurational isomers of the 1-methoxyl group. The 3-methine proton signal of **6** (δ 2.67) was observed at a lower magnetic field than that of **5**. Such a tendency indicates that a deshielding effect is exerted by the axial methoxyl group of **6**. In the ^{13}C nmr spectra, the 3-alkyl-1,2,3,4-tetrahydro-1-naphthols (**3a**, **3e**, **3f**, and **3i**), on which the chemical shifts of the carbon skeleton are in good agreement with those of **6**, have a configuration similar to that of **6**. The 3-carbon signals of **5** and **6** were observed at δ 55.1 and 48.2 ppm, respectively. According to the ^{13}C nmr study of cyclohexene stereochemistry,[10] the 5-carbon signal of 1-methoxy-2-cyclohexene (δ 18.8) has appeared at the upper magnetic field compared to the 4-carbon (δ 23.3) of cyclohexene because of the shielding effect owing to the 1,3-diaxial orientation between the 1-methoxyl group and the 5-methine proton. It has also been found that a similar tendency exists with regard to the 3-substituted 1,2,3,4,-tetrahydro-1-naphthols.[11] Concerning the conformation of the hydroxyl group in 3-substituted 1,2,3,4-tetrahydro-1-naphthols, it has been reported that the pseudo-axial orientation of the hydroxyl group is preferred for the pseudo-equatorial orientation owing to the existence of a large strain between the hydroxyl group and the aromatic 8-methine group.[11,12] Therefore, as shown in Scheme 2, the stable conformation of 3-alkyl-1-oxy-1,2,3,4-tetrahydro-1-naphthalenes (**3a**, **3e**, **3f**, **3i**, and **6**) is considered to be the pseudo-axial orientation of the hydroxyl or methoxyl group at the 1 position, whose configuration is 1,3-<u>trans</u> form.



Scheme 4

The first step in this reaction (Scheme 4) is probably an intramolecular hydrogen abstraction of **1** to yield (E)-enol (**7**) and/or (Z)-enol (**8**). According to Sammes et al.,[2c,2f] the stereochemistry of the cycloadduct of **1** with maleic anhydride can be explained by an endo-approach of **7**. However, the 3-alkyl group of **3a**, **3e**, **3f**, or **3i** is the pseudo-axial orientation through the reaction with **7**, as expected by an exo-approach of **7** with dienophiles (**2a**, **2e**, **2f**, and **2i**).

An attempt to react **1** with 5-benzylidene-2,2-dimethy-1,3-dioxane-4,6-dione (**2l**, R^1=Ph, R^2=H, R^3=R^4=CH_3) or diethyl isobutylidenemalonate failed. Since the reactivity of diethyl isobutylidenemalonate as the dienophile is less than those of **2a-e**, the case for the malonate is accountable.[5a,13] The compounds (**2a-e** and **2l**) were known as organic Lewis acids.[14] Kunz and Polansky discussed the relationship between the reactivities and Lewis acidities (pK_L) as dienophiles on the Diels-Alder reaction of **2a-e** or **2l** with 2,3-dimethyl-1,3-butadiene and concluded that the dienophiles with their pK_L values less than 8.2 react with the diene to afford the adducts.[5a] However, the thermal cycloaddition of **2c** (pK_L=8.7) and **2d** (pK_L=8.8) with 2,3-dimethyl-1,3-butadiene has been recently reported by Benzing et al.[15] Similarly **2b** (pK_L=8.6), **2c**, and **2d** underwent cycloaddition with the photoenol. On the other hand, from our MO calculation,[16] the LUMO levels of **2d**, **2l**, and diethyl isobutylidenemalonate were obtained as -1.156, -0.985, and -0.215 eV, respectively. This result suggests that their LUMO levels are rather too high for the latter two compounds to react.

In conclusion, 5-alkylidene-1,3-dioxane-4,6-dione derivatives were found to be efficient dienophiles for the Diels-Alder reaction with the photoenol of 2-methylbenzaldehyde to yield the regio- and stereoselective adducts.

EXPERIMENTAL

Melting points were taken using a Yamato melting point apparatus and are uncorrected. Ir spectra were taken with KBr disks using a BIO-RAD FTS-

60A spectrophotometer. Nmr spectra were measured in a $CDCl_3$ or DMSO-d_6 solution with a JEOL JNM-EX90 (90 MHz for ^1H and 22.5 MHz for ^{13}C) spectrometer or a JEOL JNM-MH-100 (100 MHz for ^1H) spectrometer using TMS as an internal standard. Microanalyses were performed with a Perkin-Elmer 240C elemental analyzer at the Analysis Center, Research Institute of Science and Technology, College of Science and Technology, Nihon University. Analytical tlc and preparative tlc were carried out on Merck (5714) silica gel $60F_{254}$ glass-backed plates and Merck (13792) silica gel $60F_{254}$ glass-backed plates, respectively.

Alkylidene Meldrum's acid (**2a-e**),[17,18] benzylidene Meldrum's acid (**2l**),[17] and diethyl isobutylidenemalonate[19] were obtained by the reaction of Meldrum's acid or diethyl malonate with the corresponding ketones or aldehydes according to a modified procedure of the reported methods.

General procedure of isobutylidenespirocyclic acylals (**2f** and **2i**). A benzene solution (150 ml) of isobutyraldehyde (4.0 g, 0.055 mol) and 6,10-dioxaspiro[4.5]decane-7,9-dione[20] or 1,5-dioxaspiro[5.5]undecane-2,4-dione[20] (0.05 mol) in the presence of piperidine (0.3 g) and acetic acid (0.2 g) was refluxed under an argon atmosphere for 1 h. The reaction mixture was washed with 1 mol l^{-1} aq. HCl solution (100 ml), dried over $MgSO_4$, and evaporated. The residue was recrystallized from ether-hexane to give the corresponding products.

8-Isobutylidene-6,10-dioxaspiro[4.5]decane-7,9-dione (**2f**). Yield 8.0 g (71%); colorless crystals; mp 79°C; ir (KBr) 1772, 1743, and 1637 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ 1.16(6H, d, J=6.7 Hz), 1.7-2.3(8H, m), 3.75(1H, d septet, J=10.5 and 6.7 Hz), and 7.66(1H, d, J=10.5 Hz); ^{13}C nmr ($CDCl_3$) δ 21.3(q, 2C), 23.2(t, 2C), 29.4(d), 38.4(t, 2C), 113.9(s), 117.2(s), 160.2(s), 162.6(s), and 172.8(d). Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found C, 64.12; H, 7.08.

3-Isobutylidene-1,5-dioxaspiro[5.5]undecane-2,4-dione (**2i**). Yield 9.3 g (78%); colorless crystals; mp 95°C; ir (KBr) 1767, 1740, and 1640 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ 1.09(6H, d, J=6.3 Hz), 1.3-2.0(10H, m), 3.70(1H, d septet, J=10.5 and 6.3 Hz), and 7.44(1H, d, J=10.5 Hz); ^{13}C nmr ($CDCl_3$) δ 21.3(q, 2C), 22.2(t, 2C), 24.1(t), 29.4(d), 36.5(t, 2C), 105.4(s), 116.9(s), 159.5(s), 161.9(s), and 172.6(d). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.54; H, 7.51.

General procedure for cyclohexylidene- and cyclopentylidenespirocyclic acylals (**2g**, **2h**, **2j**, and **2k**). A mixture of cyclopentanone or cyclohexanone (0.055 mol) and 6,10-dioxaspiro[4.5]decane-7,9-dione or 1,5-dioxaspiro-[5.5]undecane-2,4-dione (0.05 mol) in pyridine (2 ml) was stirred for 24 h under an argon atmosphere. The reaction mixture was poured into water (80 ml) to give crude crystals, from which the cyclopentylidene- and cyclohexylidenespirocyclic acylals were obtained by recrystallization.

8-Cyclopentylidene-6,10-dioxaspiro[4.5]decane-7,9-dione (**2g**). Yield 5.0 g (42%); colorless needles; mp 103-105°C (from methanol-water); ir (KBr) 1755, 1724, and 1609 cm^{-1}; ^{1}H nmr (100 MHz, $CDCl_3$) δ 1.7-2.2(12H, m) and 3.17(4H, m); ^{13}C nmr ($CDCl_3$) δ 23.2(t, 2C), 25.6(t, 2C), 38.3(t, 2C), 38.5(t, 2C), 111.5(s), 112.8(s), 161.8(s, 2C), and 193.8(s). Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.33; H, 6.78.

8-Cyclohexylidene-6,10-dioxaspiro[4.5]decane-7,9-dione (**2h**). Yield 3.4 g (27%); colorless needles; mp 114-116°C (from methanol-water); ir (KBr) 1754, 1729, and 1609 cm^{-1}; ^{1}H nmr (100 MHz, $CDCl_3$) δ 1.5-2.3(14H, m) and 2.8-3.0(4H, m); ^{13}C nmr ($CDCl_3$) δ 23.4(t, 2C), 25.8(t), 29.5(t, 2C), 34.2 (t, 2C), 38.2(t, 2C), 113.0(s), 115.0(s), 161.7(s, 2C), and 180.9(s). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.15; H, 7.22.

3-Cyclopentylidene-1,5-dioxaspiro[5.5]undecane-2,4-dione (**2j**). Yield 2.6 g (21%); colorless crystals; mp 120-122°C (from acetone-water); ir (KBr) 1750, 1722, and 1581 cm^{-1}; ^{1}H nmr (100 MHz, $CDCl_3$) δ 1.3-2.2(14H, m) and 3.15(4H, m); ^{13}C nmr ($CDCl_3$) δ 22.3(t, 2C), 24.3(t), 25.6(t, 2C), 36.4(t, 2C), 38.7(t, 2C), 104.2(s), 111.3(s), 161.0(s, 2C), and 193.5(s). *Anal. Calcd for* $C_{14}H_{18}O_4$*: C, 67.18; H, 7.25. Found: C, 67.09; H, 7.20.*

3-Cyclohexylidene-1,5-dioxaspiro[5.5]undecane-2,4-dione (**2k**). Yield 9.2 g (60%); colorless crystals; mp 129-132°C (from CH_2Cl_2-hexane); ir (KBr)

1757, 1726, and 1601 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ 1.5-2.2(16H, m) and 2.8-3.1(4H, m); ^{13}C nmr ($CDCl_3$) δ 22.3(t, 2C), 24.3(t), 25.8(t), 29.6(t, 2C), 34.6(t, 2C), 35.9(t, 2C), 104.3(s), 114.4(s), 161.0(s, 2C), and 181.5(s). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H,7.63. Found: C, 68.14; H, 7.54.

Diels-Alder reaction of photoenol of 2-methylbenzaldehyde with 5-alkylidene-1,3-dioxane-4,6-dione derivatives. A typical procedure is described for the reaction with **2a**. A solution of 2-methylbenzaldehyde (**1**; 0.96 g, 8.0 mmol) and **2a** (1.58 g, 8.0 mmol) in benzene (400 ml) was irradiated for 3 h using a 100-W high-pressure mercury lamp with a Pyrex jacket under an argon atmosphere at room temperature. The reaction was monitored by the disappearance of **1** on tlc. The reaction mixture was condenced *in vacuo* and the residue crystals were recrystallized from benzene to give *trans*-1',2',3',4'-tetrahydro-1'-hydroxy-3'-isopropyl-2,2-dimethylspiro[1,3-dioxane-5,2'-naphthalene]-4,6-dione (**3a**) in 2.03 g (80%) as colorless crystals: mp 131-134°C; ir (KBr) 3700-3200, 1773, 1725, 1384, and 1373 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ 0.89(3H, d, J=6.9 Hz), 0.99(3H, d, J=6.9 Hz), 1.64(3H, s), 1.65(3H, s), 1.81(1H, m), 2.55(1H, ddd, J=2.5, 4.5, and 12.9 Hz), 2.75(1H, dd, J=4.5 and 16.5 Hz), 3.06(1H, br s, exchangeable with D_2O), 3.09(1H, dd, J=12.9 and 16.5 Hz), 5.46(1H, s), and 7.0-7.6(4H, m); ^{13}C nmr ($CDCl_3$) δ 16.1(q), 23.0(q), 25.5(t, 4'-C), 28.5(q), 28.9(q), 30.2(d, $CHMe_2$), 48.3(d, 3'-C), 60.0(s, 2'-C), 74.9(d, 1'-C), 106.4(s), 125.6(d), 126.4(d), 127.3(d), 128.1(d), 135.6(s), 136.2 (s), 165.7(s), and 171.1(s). Anal. Calcd for $C_{18}H_{22}O_5$; C, 67.91; H, 6.97. Found. C, 67.54; H, 7.04.

The reaction with **2b-k** was carried out using the same procedure and the yields of adducts (**3b-k**) are summarized in Table 1. Physical and analytical data are as follows.

1',2',3',4'-Tetrahydro-1'-hydroxy-2",2"-dimethyldispiro[cyclopentane-1,3'-naphthalene-2',5"-[1,3]dioxane]-4",6"-dione (**3b**). Colorless powder; mp 158-162°C (from benzene); ir (KBr) 3700-3200, 1767, 1731, 1396, and 1387 cm^{-1}; ^{1}H nmr (100 MHz, $CDCl_3$) δ 1.5-1.8(8H, m), 1.65(6H, s), 2.66(1H, d, J=17.7 Hz), 2.93(1H, d, J=17.7 Hz), 2.98(1H, br s, exchangeable with D_2O), 5.59(1H, s), and 7.0-7.6(4H, m); ^{13}C nmr ($CDCl_3$) δ 23.7(t), 23.9(t), 27.5(q), 30.8(q), 32.2(t, 4'-C), 36.7(t), 39.5(t), 50.7(s, 3'-C), 64.5(s, 2'-C), 71.1(d, 1'-C), 105.6(s), 125.9(d), 126.6 (d), 127.2(d), 128.4(d), 134.5(s), 137.0(s), 166.9(s), and 168.6(s). Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.09; H, 6.56.

1',2',3',4'-Tetrahydro-1'-hydroxy-2",2"-dimethyldispiro[cyclohexane-1,3'-naphthalene-2',5"-[1,3]dioxane]-4",6"-dione (3c). Colorless powder; mp 183-186°C (from benzene); ir (KBr) 3700-3200, 1765, 1733, 1397, and 1385 cm^{-1}; ^{1}H nmr (100 MHz, $CDCl_3$) δ 1.3-2.0(10H, m), 1.66(6H, s), 2.74(1H, d, J=17.9 Hz), 2.85(1H, br s, exchangeable with D_2O), 3.26(1H, d, J=17.9 Hz), 5.57(1H, s), and 7.0-7.6(4H, m); ^{13}C nmr ($CDCl_3$) δ 21.5(t), 22.0(t), 24.6(t), 27.7(q), 28.9(q), 31.0(t, 4'-C), 33.7(t), 35.3(t), 43.7(s, 3'-C), 63.4(s, 2'-C), 70.5(d, 1'-C), 105.7(s), 126.0(d), 126.7(d), 127.6(d), 128.6(d), 136.4(s), 136.6(s), 166.6(s), and 168.5(s). Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.73; H, 7.00.

1',2',3',4'-Tetrahydro-1'-hydroxy-2,2,3',3'-tetramethylspiro[1,3-dioxane-5,2'-naphthalene]-4,6-dione (3d). Colorless powder; mp 182-186°C (from CH_2Cl_2-hexane); ir (KBr) 3700-3200, 1763, 1733, 1397, and 1386 cm^{-1}; ^{1}H nmr (100 MHz, $CDCl_3$) δ 1.11(3H, s), 1.12(3H, s), 1.69(6H, s), 2.52(1H, d, J=16.1 Hz), 3.12(1H, d, J=16.1 Hz), 3.21(1H, br s, exchangeable D_2O), 5.58(1H, s), and 6.9-7.6(4H, m); ^{13}C nmr ($CDCl_3$) δ 25.0(q), 27.6(q, 2C), 30.8(q), 39.7(s, 3'-C), 42.3(t, 4'-C), 65.3(s, 2'-C), 70.6(d, 1'-C), 105.6(s), 126.0(d), 126.6(d), 127.5(d), 128.2(d), 134.6(s), 136.1(s), 166.6(s), and 168.5(s). Anal. Calcd for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 67.17; H, 6.59.

trans-3'-Cyclohexyl-1',2',3',4'-tetrahydro-1'-hydroxy-2,2-dimethylspiro-[1,3-dioxane-5,2'-naphthalene]-4,6-dione (3e). Colorless powder; mp 159-160°C (from CH_2Cl_2-hexane); ir (KBr) 3700-3200, 1766, 1727, 1395, and 1381 cm^{-1}; ^{1}H nmr (90 MHz, $CDCl_3$) δ 0.9-2.0(11H, m), 1.75(3H, s), 1.84(3H, s), 2.50(1H, ddd, J=∿0, 4.4, and 13.3 Hz, 3'-CH$_{ax}$), 2.58(1H, d, J=9.3 Hz, exchangeable with D$_2$O), 2.75(1H, dd, J=4.4 and 16.7 Hz, 4'-CH$_{eq}$), 3.14(1H, dd, J=13.3 and 16.7 Hz, 4'-CH$_{ax}$), 5.52(1H, br d, J=9.3 Hz), and 7.0-7.6(4H, m); ^{13}C nmr (CDCl$_3$) δ 26.1(t), 26.4(t), 26.9(t), 27.0(t), 27.3(t), 28.6(q), 30.2(q), 33.1(t), 39.7(d), 48.5(d, 3'-C), 59.9(s, 2'-C), 74.8(d, 1'-C), 106.3(s), 125.6(d), 126.4(d), 127.4(d), 128.1(d), 135.8 (s), 136.2(s), 165.8(s), and 171.1(s). Anal. Calcd for C$_{21}$H$_{26}$O$_5$: C, 70.37; H, 7.31. Found: C, 70.22; H, 7.28.

trans-1",2",3",4"-Tetrahydro-1"-hydroxy-3"-isopropyldispiro[cyclopentane-1,2'-[1,3]dioxane-5',2"-naphthalene]-4',6'-dione (**3f**). Colorless powder; mp 129-131°C (from CH$_2$Cl$_2$-hexane); ir (KBr) 3700-3200, 1758, and 1723 cm^{-1}; ^{1}H nmr (100 MHz, CDCl$_3$) δ 0.90(3H, d, J=6.9 Hz), 1.02(3H, d, J=6.9 Hz), 1.7-2.4(9H, m), 2.56(1H, ddd, J=2.0, 4.5 and 16.5 Hz, 3"-CH$_{ax}$), 2.76 (1H, dd, J=4.5 and 16.5 Hz, 4"-CH$_{eq}$), 3.15(1H, dd, J=12.9 and 16.5 Hz, 4"-CH$_{ax}$), 3.51(1H, br s, exchangeable with D$_2$O), 5.42(1H, s), and 7.1-7.6(4H, m); ^{13}C nmr (CDCl$_3$) δ 16.3(q), 22.4(t), 22.8(q), 23.5(t), 25.7(t, 4"-C), 29.1(d, CHMe$_2$), 39.1(t), 40.7(t), 47.9(d, 3"-C), 60.3(s, 2"-C), 75.2(d, 1"-C), 115.3(s), 125.4(d), 126.4(d), 127.4(d), 128.1(d), 135.7(s), 136.0(s), 165.7(s), and 171.4(s). Anal. Calcd for C$_{20}$H$_{24}$O$_5$: C, 69.75; H, 7.02. Found: C, 69.64; H, 6.97.

1",2",3",4"-Tetrahydro-1"-hydroxytrispiro[cyclopentane-1,2'-[1,3]dioxane-5',2"-naphthalene-3",1"'-cyclopentane]-4',6'-dione (**3g**). Colorless powder; mp 165-169°C (from CH$_2$Cl$_2$-hexane); ir (KBr) 3700-3200, 1768, and 1731 cm^{-1}; ^{1}H nmr (100 MHz, CDCl$_3$) δ 1.2-2.4(16H, m), 2.63(1H, d, J=16.1 Hz), 2.97(1H, d, J=16.1 Hz), 2.97(1H, br s, exchangeable with D$_2$O), 5.54(1H, br d, J=7.0 Hz), and 6.9-7.6(4H, m); ^{13}C nmr (CDCl$_3$) δ 22.4(t), 23.4(t), 23.8(t), 24.0(t), 32.3(t, 4"-C), 36.8(t), 37.9(t), 39.5(t), 40.8(t), 50.7 (s, 3"-C), 64.8(s, 2"-C), 71.3(d, 1"-C), 114.6(s), 125.8(d), 126.6(d), 127.2(d), 128.4(d), 134.6(s), 137.0(s), 166.9(s), and 168.7(s). Anal. Calcd for C$_{21}$H$_{24}$O$_5$: C, 70.77; H,6.79. Found: C, 71.11; H, 6.70.

1',2',3',4'-Tetrahydro-1'-hydroxytrispiro[cyclohexane-1,3'-naphthalene-

2',5"-[1,3]dioxane-2",1"'-cyclopentane]-4",6"-dione (**3h**). Colorless powder; mp 163-165°C (from benzene-hexane); ir (KBr) 3700-3200, 1767, and 1734 cm^{-1}; ^{1}H nmr (100 MHz, $CDCl_3$) δ 0.9-2.2(18H, m), 2.82(1H, d, J=18.0 Hz), 3.02(1H, d, J=18.0 Hz), 3.32(1H, br s, exchangeable with D_2O), 5.61(1H, s), and 7.1-7.7(4H, m); ^{13}C nmr ($CDCl_3$) δ 21.3(t), 21.8(t), 22.4 (t), 23.4(t), 25.3(t), 28.7(t, 4'-C), 33.5(t), 35.1(t), 38.0(t), 40.8(t), 43.6(s, 3'-C), 67.5(s, 2'-C), 70.5(d, 1'-C), 114.4(s), 125.8(d), 126.5(d), 127.4(d), 128.3(d), 134.3(s), 136.4(s), 166.4(s), and 168.4(s). Anal. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.07. Found: C, 71.36; H, 7.03.

trans-1",2",3",4"-Tetrahydro-1"-hydroxy-3"-isopropyldispiro[cyclohexane-1,2'-[1,3]dioxane-5',2"-naphthalene]-4',6'-dione (**3i**). Colorless crystals; mp 123-124°C (from CH_2Cl_2-hexane); ir (KBr) 3700-3200, 1762, and 1725 cm^{-1}; ^{1}H nmr (100 MHz, $CDCl_3$) δ 0.89(3H, d, J=6.8 Hz), 1.02(3H, d, J=6.8 Hz), 1.2-2.2(11H, m), 2.54(1H, ddd, 2.0, 4.5 and 16.5 Hz, 3"-CH$_{ax}$), 2.75 (1H, dd, 4.5 and 16.5 Hz, 4"-CH$_{eq}$), 3.11(1H, dd, J=12.9 and 16.5 Hz, 4"-CH$_{ax}$), 3.54(1H, br s, exchangeable with D_2O), 5.45(1H, br d, J=7.0 Hz), and 7.0-7.6(4H, m); ^{13}C nmr ($CDCl_3$) δ 16.1(q), 21.9(t), 22.3(t), 22.9(q), 23.9(t), 25.5(t, 4"-C), 28.9(d, CHMe$_2$), 37.0(t), 39.2(t), 48.1(d, 3"-C), 60.3(s, 2"-C), 74.7(d, 1"-C), 106.9(s), 125.6(d), 126.2(d), 127.1(d), 127.9(d), 135.4(s), 136.2(s), 165.6(s), and 171.1(s). Anal. Calcd for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.40; H, 6.97.

1",2",3",4"-Tetrahydro-3"-hydroxytrispiro[cyclohexane-1,2'-[1,3]dioxane-5',2"-naphthalene-3",1"'-cyclopentane]-4',6'-dione (**3j**). Colorless powder; mp 174-175°C (from benzene-hexane); ir (KBr) 3700-3200, 1763, and 1732 cm^{-1}; ^{1}H nmr (90 MHz, $CDCl_3$) δ 1.1-2.4(18H, m), 2.50(1H, br d, J=9.3 Hz, exchangeable with D_2O), 2.65(1H, d, J=17.3 Hz), 2.92(1H, d, J=17.3 Hz), 5.56(1H, br d, J=9.3 Hz), and 6.9-7.6(4H, m); ^{13}C nmr ($CDCl_3$) δ 21.8(t), 22.5(t), 23.7(t), 23.9(t), 24.0(t), 32.2(t, 4"-C), 36.0(t), 36.7(t), 39.5 (t), 40.3(t), 50.7(s, 3"-C), 65.0(s, 2"-C), 71.0(d, 1"-C), 106.2(s), 125.9 (d), 126.6(d), 127.2(d), 128.3(d), 134.5(s), 137.1(s), 166.9(s), and 168.5 (s). Anal. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.07. Found: C, 71.21; H, 6.97.

1",2",3",4"-Tetrahydro-1"-hydroxytrispiro[cyclohexane-1,2'-[1,3]dioxane-5',2"-naphthalene-3",1"'-cyclohexane]-4',6'-dione (**3k**). Colorless powder; mp 185-189°C (from CH_2Cl_2-hexane); ir (KBr) 3700-3200, 1762, and 1729 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ 1.1-2.1(20H, m), 2.58(1H, br s, exchangeable with D_2O), 2.76(1H, d, J=16.1 Hz), 3.21(1H, d, J=16.1 Hz), 5.48(1H, br d, J=7.0 Hz), and 7.0-7.6(4H, m); ^{13}C nmr (DMSO-d_6) δ 20.7(t), 21.3(t), 21.6(t), 22.1(t), 23.4(t), 25.1(t), 28.8(t, 4"-C), 33.4(t), 34.9 (t), 35.7(t), 39.8(t), 42.3(s, 3"-C), 66.6(s, 2"-C), 68.4(d, 1"-C), 104.9 (s), 125.3(d), 125.7(d), 126.3(d), 127.8(d), 133.8(s), 137.7(s), 164.4(s), and 168.1(s). Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 72.05; H, 7.27.

Etherification of **3a** with methanol. A solution of **3a** (478 mg, 1.5 mmol) and p-toluenesulfonic acid (10 mg) in methanol (30 ml) was refluxed for 30 min and the reaction mixture was then evaporated under reduced pressure. The residue was observed to be a mixture of **3a**, cis-, and trans-1',2',3',4'-tetrahydro-3'-isopropyl-1'-methoxy-2,2-dimethylspiro[1,3-dioxane-5,2'-naphthalene]-4,6-diones (**5** and **6**) in a ratio of about **3a**:**5**:**6**=50:43:7 by the ^1H nmr analysis. The resulting mixture was subjected to preparative tlc using hexane-acetone (8:2, v/v) as a developing solvent to give the mixture of **5** and **6** (205 mg, 41%, **5**:**6**=83:17, mp 120-121°C) and **3a** (178 mg) was recovered. The analytical and physical data of the major stereoisomer (**5**) are as follows: ir (KBr) 1757, 1729, 1394, and 1380 cm^{-1}; ^1H nmr (90 MHz, $CDCl_3$) δ 0.94(3H, d, J=6.7 Hz), 1.01(3H, d, J=6.7 Hz), 1.77(3H, s), 1.88(3H, s), 1.8-2.2(2H, m, 3'-CH_{ax} and $CHMe_2$), 2.4-3.1(2H, m, 4'-CH_2), 3.60(3H, s), 4.93(1H, s), and 7.1-7.5(4H, m); ^{13}C nmr ($CDCl_3$) δ 20.6(q), 22.9(q), 28.6(d, $CHMe_2$), 29.0(q), 29.8(q), 30.2(t, 4'-C), 55.1(d, 3'-C), 58.8(s, 2'-C), 60.1(q, OCH_3), 84.7(d, 1'-C), 106.6(s), 123.0(d), 126.5(d), 126.6(d), 127.4(d), 134.3(s), 137.8(s), 167.7(s), and 169.9(s). Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.63; H, 7.27. The configuration of the 3-methine proton of

5 was determined by the ^{1}H nmr/Yb(fod)$_3$ study of the above mixture of **5** and **6**. In the ^{1}H nmr analysis of a $CDCl_3$ solution (0.3 ml) of stereoisomers (**5** and **6**, 20 mg) in the presence of Yb(fod)$_3$ (8 mg), the 3'-methine, 4'-pseudo-equatorial methylenic, and 4'-pseudo-axial methylenic protons of **5** appeared at δ 2.94(1H, ddd, J=1.7, 3.5, and 11.8 Hz), 3.13(1H, dd, J=3.5 and 14.0 Hz), and 3.41(1H, dd, J=11.8 and 14.0 Hz), respectivery. The above similar methanol solution of **3a** was refluxed for 9 h. The reaction mixture was evaporated under reduced pressure. The residue was observed to be a mixture of **5** and **6** (8:92) by the ^{1}H nmr analysis, then was dissolved with CH_2Cl_2 (20 ml), washed with 0.1 mol l^{-1} aq. NaOAc solution (20 ml), dried over $MgSO_4$, evaporated, and recrystallized from hexane to give **6** (136 mg, 27%, purity >99%) as a colorless powder. The analytical and physical data of **6** are as follows: mp 126-129°C; ir (KBr) 1774, 1733, 1394, and 1378 cm^{-1}; ^{1}H nmr (90 MHz, $CDCl_3$) δ 0.91(3H, d, J=6.7 Hz), 1.03(3H, d, J=6.7 Hz), 1.75(3H, s), 1.84(3H, s), 1.5-2.1(1H, m, $CHMe_2$), 2.67(1H, ddd, J=2.7, 5.2, and 12.6 Hz, 3'-CH_{ax}), 2.81(1H, dd, J=5.2 and 16.1 Hz, 4'-CH_{eq}), 3.04(1H, dd, J=12.6 and 16.1 Hz, 4'-CH_{ax}), 3.79(3H, s), 5.11(1H, s), and 7.0-7.4(4H, m); ^{13}C nmr ($CDCl_3$) δ 16.3(q), 22.9(q), 26.0(t, 4'-C), 28.8(q), 29.0 (d, $CHMe_2$), 30.1(q), 48.2(d, 3'-C), 58.0(s, 2'-C), 62.4(q, OCH_3), 85.9(d, 1'-C), 106.0(s), 124.4(d), 126.1(d), 127.2(d), 128.1(d), 135.1(s), 135.3(s), 164.0(s), and 170.8(s). Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.78; H, 7.23.

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