DIASTEREOSELECTIVE RING-EXPANSION REACTION OF METHANOCHROMANONE WITH ALDEHYDES: FORMATION OF TRANS-FUSED TETRAHYDROFURO[2,3-\textit{b}][1]BENZOPYRANONES AND THEIR ISOMERIZATION

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Abstract - In the presence of SnCl\textsubscript{4}, 2,3-dimethoxycarbonylmethanochromanone (4) was transformed into a zwitter-ion which easily reacted with aldehydes to give the trans-fused tetrahydrofuro[2,3-\textit{b}][1]benzopyranones in good yields with high diastereoselectivity. cis-Fused furanobenzopyranone derivatives were also obtained in good yields by isomerization of the trans isomers.

Cyclopropanes with donor and acceptor substituents at the vicinal positions on the cyclopropane ring are the equivalent of a ring-opened 1,3-zwitter-ion,\textsuperscript{1} which is expected to react with both nucleophiles\textsuperscript{2} and electrophiles.\textsuperscript{3} Under the Lewis acid-promoted conditions, methanochromanones (1) are equivalent for a cyclic zwitter-ion (2) because they have an alkoxy group as a donor and a carbonyl group as an acceptor on the benzopyran ring (Scheme 1).\textsuperscript{4} Also, methanochromanones having a strong electron-acceptor at the methano position are expected to be transformed into a zwitter-ion (3) different from the above ion by the action of a Lewis acid. We have recently reported that the reaction of methanochromanone (4) with symmetric ketones in the presence of a catalytic amount of SnCl\textsubscript{4} gave the tetrahydrofuro[2,3-\textit{b}][1]benzopyranone derivatives (5) in good yield (Scheme 2).\textsuperscript{5} In this reaction, interestingly, the trans-fused cycloaducts were predominantly obtained. We now report the control of the three stereo-centers by the Lewis acid-mediated ring-expansion reaction of methanochromanone (4) with various aldehydes and asymmetric ketones. For these reactions, four possible adducts are expected.
In the presence of SnCl$_4$ (10 mol%), methanochromanone (4)$^3$ smoothly reacted with benzaldehyde in CH$_2$Cl$_2$ at –78 °C to afford the tetrahydrofuro[2,3-b][1]benzopyran-4-one (6) in 89% yield.$^6$ In this reaction, the 2,3-t,9a-isomer was predominantly obtained while other isomers were not detected by the $^1$H-NMR analysis of the crude reaction mixture. Several examples of the ring expansion reaction were examined and these results are summarized in Table 1. In all cases, not only the aromatic but also aliphatic and unsaturated aldehydes, the trans-fused adducts (6a-10a) were obtained in good yields with excellent selectivity.

The stereochemical assignment of the adducts (6a-8a) was mainly established by the analysis of their NOE experiments and other products were assigned after a comparative analysis of the $^1$H-NMR spectra (Figure 1). In all products (6a-10a), the coupling constant between the vicinal protons was found to be over 10 Hz, thus supporting the trans-fused stereochemistry. Furthermore, the NOEs of the adducts (6a-8a) were observed between H-2 and H-9a and between H-3a and the substituent at the 2-position.

We next examined the reaction of 4 with asymmetric ketones. The treatment of 4 with acetophenone in the presence of SnCl$_4$ (10 mol%) smoothly promoted the cyclization, and the corresponding adduct was obtained in quantitative yield (Scheme 3). Even in this reaction, the trans isomer (11a) was predominantly obtained. Under the same reaction conditions, methyl vinyl ketone also reacted with 4 to

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**Table 1. Lewis Acid-Mediated Ring-expansion Reaction of 4 with Aldehydes**

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>2,3-t,9a / other isomers$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>-78</td>
<td>1.5</td>
<td>6</td>
<td>89 &gt;50 : 1</td>
</tr>
<tr>
<td>2</td>
<td>p-MeOC$_6$H$_4$</td>
<td>-10 rt</td>
<td>1</td>
<td>7</td>
<td>92 &gt;50 : 1</td>
</tr>
<tr>
<td>3</td>
<td>MeCH=CH</td>
<td>-78 0-15</td>
<td>3.5</td>
<td>8</td>
<td>99 &gt;20 : 1</td>
</tr>
<tr>
<td>4</td>
<td>PhCH=CH</td>
<td>-78 0</td>
<td>2.5</td>
<td>9</td>
<td>98 &gt;20 : 1</td>
</tr>
<tr>
<td>5</td>
<td>Me(CH$_2$)$_4$</td>
<td>0</td>
<td>4</td>
<td>10</td>
<td>40 &gt;20 : 1</td>
</tr>
</tbody>
</table>

$^a$The ratio of the isomers was determined by $^1$H-NMR.
give a mixture of the trans-fused adducts (12a, 12b) in 75% yield, but the diastereoselectivity at the 2-
position was not satisfactory. The stereochemistry of adducts was assigned by the NOE experiments (Figure 2).

We recently reported that the trans-fused adduct obtained from 4 and acetone was readily converted to the cis isomer by the treatment of Et₃N in CH₂Cl₂. Based on our previous report, we expected that the treatment of the 2,₉,3a,₉-3a,₉-9a-isomers under the same reaction conditions would promote the epimerization, and the corresponding 2,₉,3a,₉-3a,₉-9a-isomers would be obtained. However, the isomerization of 6a by the treatment with Et₃N in CH₂Cl₂, interestingly, predominantly gave the 2,₉,3a,₉-3a,₉-9a-isomer (6c) (Table 2, Entry 1). The coupling constant between the vicinal protons was analyzed to be 4.3 Hz. This coupling constant revealed that the vicinal protons were oriented in a cis relationship. Furthermore, the stereochemical assignment at the 2-position was established by analysis of its NOE experiments (Figure 3). In the case of the isomerization of 8a, a similar tendency was observed (Entry 2).

Table 2. Isomerization of 2,₉,3a,₉-9a-furobenzopyran

<table>
<thead>
<tr>
<th>Entry</th>
<th>Furobenzopyran Yield (%)</th>
<th>2,₉,3a,₉-9a / 2,₉,3a,₉-9a²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>98</td>
</tr>
</tbody>
</table>

²The ratio of the isomers was determined by ¹H-NMR.
It is noted that the reaction pathway for the isomerization of the trans-fused compound involves the initial ring-opening of the furobenzopyran ring via path a or b due to deprotonation at the 3a-position of the trans-fused compound followed by recyclization of the resulting intermediate (Scheme 4). These results indicate that the 2,1,3a,9a-isomer is more thermodynamically stable compared with other isomers.

As shown in Scheme 5, by the treatment of 11a with Et₃N, the corresponding dihydrofuran (13, via path a in Scheme 4) and the benzopyran derivative (14, via path c) were obtained in 10 and 22% yields, respectively, along with the two cis-fused isomers (66% yield, 11c:11d=3.1:1). Furthermore, the formation of the two cis-fused isomers (11c, 11d) was observed by TLC when the obtained dihydrofuran (13) was treated with Et₃N. This fact supports the above isomerization mechanism.
A plausible mechanism for the stereoselective SnCl₄-mediated reaction of 4 with aldehydes is as follows. By the action of SnCl₄, methanochromanone (4) would be initially transformed into a zwitter-ionic intermediate (15) which is expected to form the tin-enolate as depicted in Scheme 6.⁷ There have been some reports on the ring-opening reactions of the donor-acceptor cyclopropanes.¹⁻³ Among them, Saigo and co-workers reported the Lewis acid-promoted stereoselective ring-opening aldol type reaction of 2,2-dialkoxydicyclopropanecarboxylates with carbonyl compounds.³ In their reports, they describe that the high diastereoselectivity of these reactions is attributed to electronic and steric effects.³⁻⁵ Based on the reports by Saigo et al., two perpendicular models for the reaction of 4 with aldehydes were proposed. As shown in Figure 5, the cationic substituent favors the anti approach of the aldehyde due to the steric and the electronic repulsions between the cationic moiety and the polarized carbonyl carbon.

Furthermore, in the four possible six-membered transition states (A-D), A and C are favored over B and D because of the steric repulsion between the carbonyl group in the benzopyran ring and both of the methoxy group at the enolate moiety and the reacting aldehyde (Figure 6). Moreover, the diastereoselectivity at the 2,3a-position is attributed to the orientation of the aldehyde. Thus, in the transition states (A) and (C), the steric repulsions between R and the carbonyl group and between R and the ester group in C are expected to be seriously compared with that between R and OMe in A. Therefore, model (A) is the most favorable and the 2,3a-trans selectivity would be achieved. The diastereoselectivity at the 3a,9a-position in the final ring-closure reaction would be achieved in the same way as the reaction.
of 4 with symmetric ketones (Scheme 6). Consequently, the 2,\textit{t}-3a,\textit{t}-9a-adduct would be predominantly obtained.

![Image of chemical structures](image)

Figure 6

In summary, we have demonstrated that the SnCl\textsubscript{4}-catalyzed ring-opening addition reactions of methanochromanone (4) with aldehydes smoothly proceeded to afford the corresponding 2,\textit{t}-3a,\textit{t}-9a-tetrahydrofuro[2,3-\textit{b}]1benzopyranones in high yields with high diastereoselectivity. \textit{cis}-Fused furobenzopyranone derivatives were also obtained in good yields by the isomerization of the \textit{trans} isomers.

**EXPERIMENTAL**

All melting points were determined using a Yanagimoto micro-hot stage and are uncorrected. IR spectra were recorded using a JASCO FT/IR-5300 spectrophotometer and NMR spectra were measured using a JEOL JNM-A500 with tetramethylsilane as the internal standard. MS spectra were recorded using a JEOL JMS-700 spectrometer. Column chromatography was done on a BW-820 MH (Fuji silysia).

**General Procedure for the Ring-Expansion Reaction of Methanochromanone (4) with Aldehydes.**

To a stirred solution of 4 (138 mg, 0.5 mmol) and an aldehyde (1 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (4 mL) was added dropwise a solution of SnCl\textsubscript{4} (0.2 M solution in CH\textsubscript{2}Cl\textsubscript{2}, 0.25 mL, 0.05 mmol) at -78~0 °C under an argon atmosphere. After being stirred for 1~4 h at -78 °C~rt, the reaction was quenched by saturated aqueous NaHCO\textsubscript{3}. The mixture was vigorously stirred for 10 min and allowed to warm up to rt. The mixture was extracted with CH\textsubscript{2}Cl\textsubscript{2} (30 mL x 3) and the combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{4}. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (hexane / AcOEt = 5 : 1) to afford the cycloadduct (6-10). The yield is given in Table 1.
Dimethyl 2,6-tetrahydro-4-oxo-2-phenyl-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (6a): colorless prism (from AcOEt-hexane), mp 126-128 °C; IR (KBr) 1750, 1724, 1607, 1437 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.20 (3H, s, OMe), 3.90 (3H, s, OMe), 4.14 (1H, d, J = 10.7 Hz, H-3a), 5.80 (1H, s, H-2), 5.81 (1H, d, J = 10.7 Hz, H-9a), 7.14 (1H, ddd, J = 7.9, 7.3, 1.0 Hz, H-6), 7.21 (1H, dd, J = 8.5, 1.0 Hz, H-8), 7.30-7.40 (5H, m, Ph), 7.59 (1H, ddd, J = 8.5, 7.3, 1.5 Hz, H-7), 7.91 (1H, dd, J = 7.9, 1.5 Hz, H-5); ¹³C-NMR (CDCl₃) δ 52.48, 53.48, 56.39, 62.90, 86.23, 102.96, 118.45, 122.16, 122.57, 127.24, 127.42, 128.16, 129.01, 136.31, 136.73, 157.94, 166.79, 169.66, 187.94; MS m/z 381 (M⁺-1). Anal. Calcd for C₂₁H₁₈O₇: C, 65.97; H, 4.74. Found: C, 66.00; H, 4.80.

Dimethyl 2,6-tetrahydro-4-oxo-2-(4-methoxyphenyl)-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (7a): colorless needles (from AcOEt-hexane), mp 134-136 °C; IR (KBr) 1738, 1713, 1607, 1518, 1462 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.26 (3H, s, OMe), 3.80 (3H, s, OMe), 3.88 (3H, s, OMe), 4.12 (1H, d, J = 10.7 Hz, H-3a), 5.76 (1H, s, H-2), 5.79 (1H, d, J = 10.7 Hz, H-9a), 6.87 (2H, m, Ph), 7.14 (1H, ddd, J = 7.9, 7.3, 0.9 Hz, H-6), 7.20 (1H, dd, J = 8.2, 0.9 Hz, H-8), 7.30 (2H, m, Ph), 5.78 (1H, ddd, J = 8.2, 7.3, 1.5 Hz, H-7), 7.91 (1H, dd, J = 7.9, 1.5 Hz, H-5); ¹³C-NMR (CDCl₃) δ 52.59, 53.45, 55.25, 56.35, 62.86, 86.09, 102.93, 113.52, 118.46, 122.20, 122.55, 127.25, 127.84, 128.82, 136.30, 157.98, 160.03, 166.92, 169.75, 188.06; MS m/z 412 (M⁺). Anal. Calcd for C₂₂H₂₀O₄: C, 64.08; H, 4.89. Found: C, 63.95; H, 5.05.

Dimethyl 2,6-tetrahydro-4-oxo-2-(1-propenyl)-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (8a): colorless prism (from Et₂O-hexane), mp 111-113 °C; IR (KBr) 1736, 1715, 1607, 1458 cm⁻¹; ¹H-NMR (CDCl₃) δ 1.74 (3H, dd, J = 6.7, 1.5 Hz, Me), 3.77 (3H, s, OMe), 3.84 (3H, s, OMe), 3.88 (1H, d, J = 10.7 Hz, H-3a), 5.14 (1H, d, J = 7.3 Hz, H-2), 5.46 (1H, dq, J = 15.3, 7.3, 1.5 Hz, H-1'), 5.66 (1H, d, J = 10.7 Hz, H-9a), 5.99 (1H, dq, J = 15.3, 6.7, 1.0 Hz, H-2'), 7.11 (1H, ddd, J = 7.9, 7.3, 1.0 Hz, H-6), 7.14 (1H, dd, J = 8.5, 1.0 Hz, H-8), 7.55 (1H, ddd, J = 8.5, 7.3, 1.5 Hz, H-7), 7.89 (1H, dd, J = 7.9, 1.5 Hz, H-5); ¹³C-NMR (CDCl₃) δ 17.71, 52.93, 53.37, 55.80, 61.40, 84.69, 103.07, 118.40, 122.18, 122.39, 125.99, 127.15, 132.47, 136.17, 157.94, 166.97, 169.32, 187.91; MS m/z 345 (M⁺-1). Anal. Calcd for C₁₈H₁₅O₇: C, 62.42; H, 5.24. Found: C, 62.02; H, 5.32.

Dimethyl 2,6-tetrahydro-4-oxo-2-(2-phenyl-1-ethenyl)-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (9a): colorless prism (from Et₂O-hexane), mp 119-121 °C; IR (KBr) 1759, 1725, 1607, 1462 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.72 (3H, s, OMe), 3.88 (3H, s, OMe), 3.97 (1H, d, J = 10.4 Hz, H-3a), 5.38 (1H, dd, J = 7.0, 0.9 Hz, H-2), 5.75 (1H, d, J = 10.4 Hz, H-9a), 6.15 (1H, dd, J = 15.9, 7.0 Hz, CH=CH), 6.86 (1H, dd, J = 15.9, 0.9 Hz, CH=CH), 7.13 (1H, ddd, J = 7.9, 7.0, 1.0 Hz, H-6), 7.17 (1H, dd, J = 8.5, 1.0 Hz, H-8), 7.28 (1H, m, Ph), 7.32 (2H, m, Ph), 7.37 (2H, m, Ph), 7.57 (1H, ddd, J = 8.5, 7.0, 1.5 Hz, H-7), 7.91 (1H, dd, J = 7.9, 1.5 Hz, H-5); MS m/z 408 (M⁺). Anal. Calcd for C₂₁H₂₀O₅: C, 67.64; H, 4.94. Found: C, 67.45; H, 5.14.

Dimethyl 2,6-tetrahydro-4-oxo-2-pentyl-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (10a): colorless needles (from AcOEt-hexane), mp 92-94 °C; IR (KBr) 1750, 1728, 1711, 1607, 1462 cm⁻¹; ¹H-NMR (CDCl₃) δ 0.90 (3H, t, J = 7.0 Hz, Me), 1.28-1.36 (4H, m), 1.45-1.70 (4H, m), 3.83 (3H, s, OMe), 3.84 (3H, s, OMe), 3.88 (1H, d, J = 10.7 Hz, H-3a), 4.73 (1H, dd, J = 10.7, 3.1 Hz, H-2), 5.64 (1H, d, J = 10.7 Hz, H-9a), 7.10 (1H, ddd, J = 7.9, 7.0, 1.0 Hz, H-6), 7.13 (1H, dd, J = 8.5, 1.0 Hz, H-8), 7.54
(1H, ddd, J = 8.5, 7.0, 1.5 Hz, H-7), 7.89 (1H, dd, J = 7.9, 1.5 Hz, H-5); MS m/z 376 (M'). Anal. Calcd for C_{20}H_{24}O_{7}: C, 63.82; H, 6.43. Found: C, 63.38; H, 6.38.

**Reaction of methanochromanone (4) with acetophenone.** According to the general procedure for the reaction of 4 with aldehydes, 4 (138 mg, 0.5 mmol) and acetophenone (120 mg, 1 mmol) were treated with SnCl₄ (0.2 M solution in CH₂Cl₂, 0.25 mL, 0.05 mmol) to give 11 (196 mg, 99%).

Dimethyl 3a,9a-trans-tetrahydro-2-methyl-4-oxo-2-phenyl-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (11a): colorless prism (from AcOEt-hexane), mp 162-164 °C; IR (KBr) 1752, 1721, 1607, 1464, 1435 cm⁻¹; ¹H-NMR (CDCl₃) δ 2.19 (3H, s, Me), 3.39 (3H, s, OMe), 3.88 (3H, s, OMe), 4.19 (1H, dd, J = 10.4 Hz, H-3a), 6.25 (1H, d, J = 10.4 Hz, H-9a), 7.12 (1H, m, Ph), 7.25 (2H, m, Ph), 7.29 (1H, d, J = 8.5, 0.9 Hz, H-8), 7.35 (2H, m, Ph), 7.59 (1H, dd, J = 8.5, 7.3, 1.5 Hz, H-7), 7.64 (2H, m, Ph), 7.89 (1H, dd, J = 7.9, 1.5 Hz, H-5); ¹³C-NMR (CDCl₃) δ 24.61, 52.52, 53.21, 56.95, 65.73, 95.21, 104.68, 118.72, 122.30, 122.75, 127.17, 127.55, 127.83, 128.34, 136.08, 141.63, 158.29, 166.11, 167.83, 188.78; MS m/z 395 (M'-1). Anal. Calcd for C_{22}H_{20}O_{7}: C, 66.66; H, 5.09. Found: C, 66.42; H, 5.17.

**Reaction of methanochromanone (4) with methyl vinyl ketone.** According to the general procedure for the reaction of 4 with aldehydes, 4 (138 mg, 0.5 mmol) and methyl vinyl ketone (70 mg, 1 mmol) were treated with SnCl₄ (0.2 M solution in CH₂Cl₂, 0.25 mL, 0.05 mmol) to give 12 (130 mg, 75%).

Dimethyl 3a,9a-trans-tetrahydro-2-methyl-4-oxo-2-ethenyl-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (12a, 12b): The diastereomers (12a, 12b) were not separable by silica gel column chromatography. The mixture of the two isomers was submitted for elemental analysis. Anal. Calcd for C_{18}H_{18}O_{7}: C, 62.42; H, 5.24. Found: C, 62.38; H, 5.25. (12a): ¹H-NMR (CDCl₃) δ 1.61 (3H, s, Me), 3.80 (3H, s, OMe), 3.84 (3H, s, OMe), 3.92 (1H, d, J = 10.4 Hz, H-3a), 5.34 (1H, dd, J = 10.1, 1.8 Hz, CH=C₃H₂), 5.82 (1H, dd, J = 16.8, 1.8 Hz, CH=CH₂), 5.90 (1H, dd, J = 16.8, 10.1 Hz, CH=CH₂), 6.05 (1H, d, J = 10.4 Hz, H-9a), 7.10 (1H, ddd, J = 7.9, 7.3, 1.0 Hz, H-6), 7.14 (1H, dd, J = 8.5, 1.0 Hz, H-8), 7.54 (1H, ddd, J = 8.5, 7.3, 1.8 Hz, H-7), 7.87 (1H, dd, J = 7.9, 1.8 Hz, H-5); GC-MS m/z 346 (M'). (12b): ¹H-NMR (CDCl₃) δ 1.55 (3H, s, Me), 3.73 (3H, s, Me), 3.86 (3H, s, OMe), 3.97 (1H, d, J = 10.4 Hz, H-3a), 5.34 (1H, dd, J = 10.7, 1.2 Hz, CH=CH₂), 5.54 (1H, dd, J = 17.1, 1.2 Hz, CH=CH₂), 6.05 (1H, d, J = 10.4 Hz, H-9a), 6.07 (1H, dd, J = 17.1, 10.7 Hz, CH=CH₂), 7.10-7.14 (2H, m, H-6 and -8), 7.55 (1H, ddd, J = 8.5, 7.3, 1.8 Hz, H-7), 7.90 (1H, dd, J = 7.9, 1.8 Hz, H-5); GC-MS m/z 346 (M').

**General Procedure for Isomerization of 3a,9a-trans-Furobenzopyrans to 3a,9a-cis-Furobenzopyrans.** To a solution of the 3a,9a-trans-furobenzopyran (0.5 mmol) in CH₂Cl₂ (5 mL) was added Et₃N (202 mg, 2 mmol) at rt. After being stirred for 6-72 h, the reaction was quenched at 0 °C by adding 10% HCl (1 mL). The mixture was extracted with CH₂Cl₂ (20 mL x 3), the combined organic layers were dried over Na₂SO₄, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane / AcOEt = 10 : 1) to afford the 3a,9a-cis-furobenzopyran.

**Isomerization of the 3a,9a-trans-furobenzopyran (6a).** According to the general procedure for the isomerization of the 3a,9a-trans-furobenzopyrans, 6a (191 mg, 0.5 mmol) was treated with Et₃N (202 mg, 2 mmol) for 6 h to give the 3a,9a-cis-furobenzopyran (189 mg, 99%, 6c:6d > 20:1). The ratio of 6c and 6d was determined by ¹H-NMR.
Dimethyl 2,3a,9a-tetrahydro-4-oxo-2-phenyl-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (6c): colorless prism (from AcOEt-hexane), mp 184-186 °C; IR (KBr) 1744, 1696, 1609, 1470 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.16 (3H, s, OMe), 3.39 (3H, s, OMe), 4.21 (1H, d, J = 4.3 Hz, H-3a), 6.29 (1H, d, J = 4.3 Hz, H-9a), 6.37 (1H, s, H-2), 7.07 (1H, dd, J = 8.5, 1.5 Hz, H-8), 7.09 (1H, ddd, J = 7.9, 1.5 Hz, H-5); ¹³C-NMR (CDCl₃) δ 52.78, 52.83, 55.27, 67.63, 85.38, 103.10, 118.53, 120.02, 122.47, 126.51, 126.81, 128.07, 128.76, 136.11, 136.80, 157.96, 166.90, 167.55, 188.56; MS m/z 382 (M⁺). Anal. Calcd for C₂₁H₁₈O₇: C, 65.97; H, 4.74. Found: C, 65.76; H, 4.82.

Isomerization of the 3a,9a-trans-furobenzopyran (8a). According to the general procedure for the isomerization of the 3a,9a-trans-furobenzopyrans, 8a (173 mg, 0.5 mmol) was treated with Et₃N (202 mg, 2 mmol) for 6 h to give the 3a,9a-cis-furobenzopyran (169 mg, 98%, 8c : 8d > 20 : 1). The ratio of 8c and 8d was determined by ¹H-NMR.

Dimethyl 2,3a,9a-tetrahydro-4-oxo-2-(1-propenyl)-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (8c): colorless needles (from Et₂O-hexane), mp 122-123 °C; IR (KBr) 1746, 1698, 1609, 1464 cm⁻¹; ¹H-NMR (CDCl₃) δ 1.72 (3H, dd, J = 6.7, 1.5 Hz, Me), 3.32 (3H, s, OMe), 3.73 (3H, s, OMe), 4.02 (1H, d, J = 4.3 Hz, H-9a), 5.37 (1H, ddq, J = 15.3, 8.2, 1.5 Hz, H-1'), 5.67 (1H, d, J = 8.2 Hz, H-2), 5.93 (1H, ddd, J = 7.9, 1.5 Hz, H-2'), 6.00 (1H, d, J = 14.3 Hz, H-9a), 7.01 (1H, dd, J = 8.5, 1.0 Hz, H-8), 7.07 (1H, ddd, J = 7.9, 7.3, 1.0 Hz, H-6), 7.50 (1H, ddd, J = 8.5, 7.3, 1.5 Hz, H-7), 7.87 (1H, dd, J = 8.5, 1.5 Hz, H-5); ¹³C-NMR (CDCl₃) δ 17.70, 52.58, 53.23, 55.05, 65.87, 84.56, 102.68, 118.47, 120.33, 122.37, 125.36, 126.41, 132.38, 136.57, 157.74, 166.86, 167.29, 188.58; MS m/z 345 (M⁺ -1). Anal. Calcd for C₁₈H₁₈O₇: C, 62.42; H, 5.24. Found: C, 62.34; H, 5.28.

Isomerization of the 3a,9a-trans-furobenzopyran (11a). According to the general procedure for the isomerization of the 3a,9a-trans-furobenzopyrans, 11a (198 mg, 0.5 mmol) was treated with Et₃N (202 mg, 2 mmol) for 72 h to give the furobenzopyran (11c, 99 mg, 50%), the furobenzopyran (11d, 32 mg, 16%), the dihydrofuran (13, 20 mg, 10%), and the benzopyran (14, 30 mg, 22%).

Dimethyl 3a,9a-cis-tetrahydro-2-methyl-4-oxo-2-phenyl-4H-furo[2,3-b][1]benzopyran-3,3-dicarboxylate (11c): colorless prism (from Et₂O-hexane), mp 154-155 °C; IR (KBr) 1761, 1736, 1682, 1607, 1466 cm⁻¹; ¹H-NMR (CDCl₃) δ 1.88 (3H, s, Me), 3.09 (3H, s, OMe), 3.99 (1H, d, J = 5.5 Hz, H-3a), 6.68 (1H, d, J = 5.5 Hz, H-9a), 7.10 (1H, ddd, J = 7.9, 7.3, 1.2 Hz, H-6), 7.40 (1H, dd, J = 8.5, 1.2 Hz, H-8), 7.24 (1H, m, Ph), 7.31 (2H, m, Ph), 7.50 (2H, m, Ph), 7.58 (1H, ddd, J = 8.5, 7.3, 1.5 Hz, H-7), 7.91 (1H, dd, J = 7.9, 1.5 Hz, H-5); ¹³C-NMR (CDCl₃) δ 17.70, 27.24, 52.20, 52.50, 53.12, 70.29, 88.23, 101.00, 118.52, 119.88, 122.34, 125.57, 126.67, 127.65, 127.79, 139.00, 142.55, 157.40, 166.92, 168.38, 188.54; MS m/z 395 (M⁺ -1). Anal. Calcd for C₂₃H₁₈O₇: C, 66.66; H, 5.09. Found: C, 66.52; H, 5.12. (11d): colorless prism (from Et₂O-hexane), mp 162-165 °C; IR (KBr) 1769, 1742, 1688, 1607, 1464 cm⁻¹; ¹H-NMR (CDCl₃) δ 1.68 (3H, s, Me), 2.88 (3H, s, OMe), 3.99 (3H, s, OMe), 4.50 (1H, d, J = 6.4 Hz, H-3a), 6.21 (1H, d, J = 6.4 Hz, H-9a), 7.04 (1H, ddd, J = 7.9, 7.3, 1.2 Hz, H-6), 7.08 (1H, dd, J = 8.5, 1.2 Hz, H-8), 7.28 (1H, m, Ph), 7.34 (2H, m, Ph), 7.52 (1H, ddd, J = 8.5, 7.3, 1.5 Hz, H-7), 7.70 (2H, m, Ph), 7.81 (1H, dd, J = 7.9, 1.5 Hz, H-5); ¹³C-NMR (CDCl₃) δ 28.58, 51.73, 53.45, 55.44, 71.06, 90.70, 100.98, 118.42, 121.02, 122.02, 125.79, 126.53, 127.50, 127.56, 136.31, 141.76, 157.50,
166.06, 167.84, 188.98; MS m/z 395 (M+ - 1). *Anal.* Calcd for C$_22$H$_{20}$O$_7$: C, 66.66; H, 5.09. Found: C, 66.46; H, 5.19.

Dimethyl 2,3-dihydro-4-(2-hydroxybenzoyl)-2-methyl-2-phenylfuran-3,3-dicarboxylate (13): colorless oil; $^1$H-NMR (CDCl$_3$) $\delta$ 1.83 (3H, s, Me), 3.17 (3H, s, OMe), 3.88 (3H, s, OMe), 6.95 (1H, ddd, $J$ = 7.9, 7.3, 1.0 Hz, H-5’), 7.01 (1H, dd, $J$ = 8.5, 1.0 Hz, H-3’), 7.31 (1H, m, Ph), 7.37 (2H, m, Ph), 7.44 (1H, s, H-6), 7.50 (1H, ddd, $J$ = 8.5, 7.3, 1.8 Hz, H-4’), 7.63 (2H, m, Ph), 7.82 (1H, dd, $J$ = 7.9, 1.8 Hz, H-5’), High-resolution Ms m/z Calcd for C$_{22}$H$_{20}$O$_7$ (M+): 396.1209, Found: 396.1196.

Dimethyl (4-oxo-4H-1-benzopyran-3-yl)malonate (14): colorless powder (from Et$_2$O-hexane), mp 152-153 °C; IR (KBr) 1759, 1736, 1644, 1628, 1466, 1312 cm$^{-1}$; $^1$H-NMR (CDCl$_3$) $\delta$ 3.80 (6H, s, OMe), 5.20 (1H, s, CH), 7.43 (1H, ddd, $J$ = 7.9, 7.3, 0.9 Hz, H-6’), 7.49 (1H, dd, $J$ = 8.2, 0.9 Hz, H-8’), 7.70 (1H, ddd, $J$ = 8.2, 7.3, 1.8 Hz, H-7’), 8.23 (1H, dd, $J$ = 7.9, 1.8 Hz, H-5’), 8.23 (1H, s, H-2’); MS m/z 276 (M+). *Anal.* Calcd for C$_{14}$H$_{12}$O$_6$: C, 60.87; H, 4.38. Found: C, 60.46; H, 4.37.

**REFERENCE**