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DIASTEREOSELECTIVE RING-EXPANSION REACTION OF METHANOCHROMANONE WITH ALDEHYDES: FORMATION OF *TRANS*-FUSED TETRAHYDROFURO[2,3-*b*][1]BENZO-PYRANONES AND THEIR ISOMERIZATION

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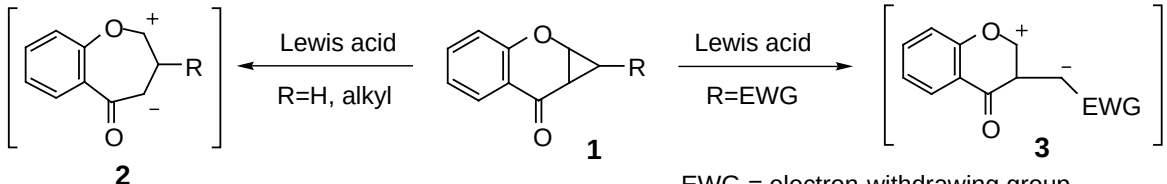
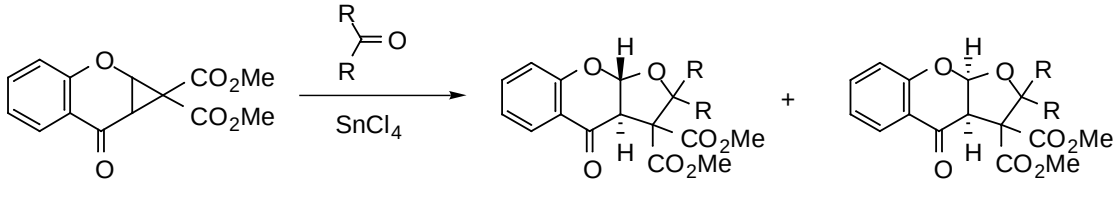
Abstract - In the presence of $SnCl_4$, 2,3-dimethoxycarbonylmethanochromanone (**4**) was transformed into a zwitter-ion which easily reacted with aldehydes to give the *trans*-fused tetrahydrofuro[2,3-*b*][1]benzopyranones in good yields with high diastereoselectivity. *cis*-Fused furobenzopyranone 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,[1] which is expected to react with both nucleophiles[2] and electrophiles.[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).[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 $SnCl_4$ gave the tetrahydrofuro[2,3-*b*][1]benzopyranone derivatives (**5**) in good yield (Scheme 2).[5] In this reaction, interestingly, the *trans*-fused cycloadducts 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.



Scheme 1

EWG = electron-withdrawing group



Scheme 2

In the presence of $SnCl_4$ (10 mol%), methanochromanone (**4**)[5] smoothly reacted with benzaldehyde in CH_2Cl_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,*t*-3a,*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.

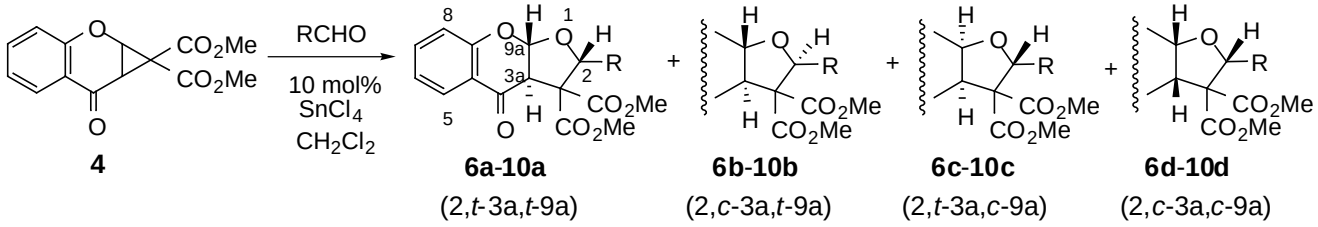


Table 1. Lewis Acid-Mediated Ring-expansion Reaction of **4** with Aldehydes

Entry	R	Temp (°C)	Time (h)	Product	Yield (%)	2,*t*-3a,*t*-9a / other isomers [a]
1	Ph	-78	1.5	**6**	89	>50 : 1
2	*p*-$MeOC_6H_4$	-10→rt	1	**7**	92	>50 : 1
3	MeCH=CH	-78→-15	3.5	**8**	99	>20 : 1
4	PhCH=CH	-78→0	2.5	**9**	98	>20 : 1
5	$Me(CH_2)_4$	0	4	**10**	40	>20 : 1

[a]The ratio of the isomers was determined by ^{1}H-NMR.

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.

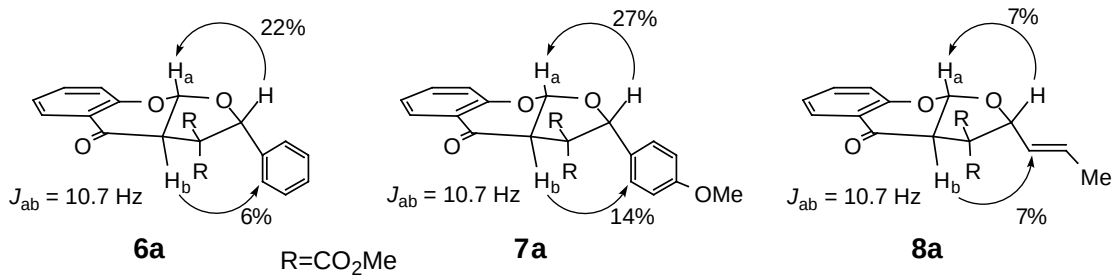
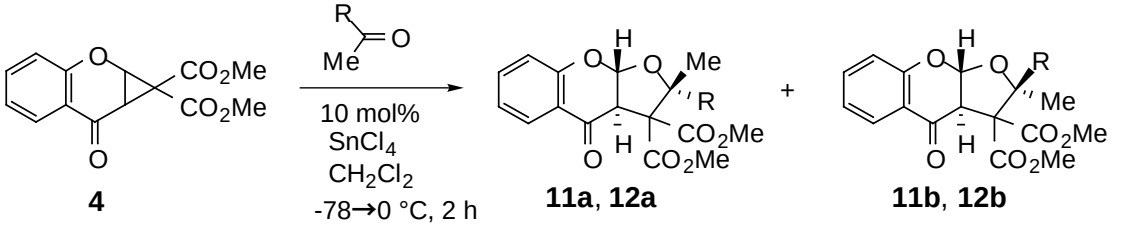


Figure 1. Selected NOE correlations for **6a**, **7a**, and **8a**

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

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).



Scheme 3

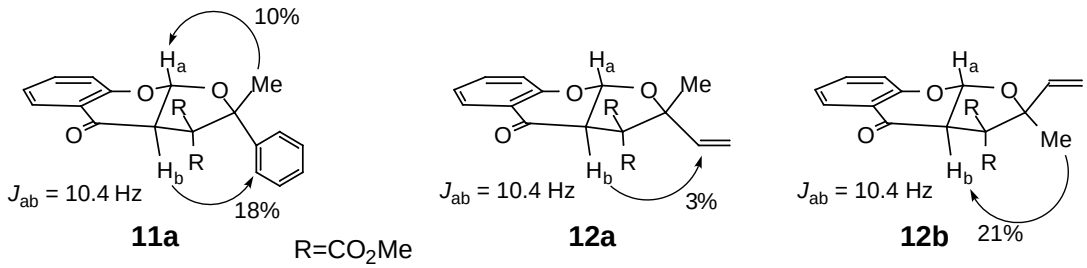


Figure 2. Selected NOE correlations for **11a**, **12a**, and **12b**

We recently reported that the *trans*-fused adduct obtained from **4** and acetone was readily converted to the *cis* isomer by the treatment of Et_3N in CH_2Cl_2.[5] Based on our previous report, we expected that the treatment of the 2,*t*-3a,*t*-9a-isomers under the same reaction conditions would promote the epimerization, and the corresponding 2,*c*-3a,*c*-9a-isomers would be obtained. However, the isomerization of **6a** by the treatment with Et_3N in CH_2Cl_2, interestingly, predominantly gave the 2,*t*-3a,*c*-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).

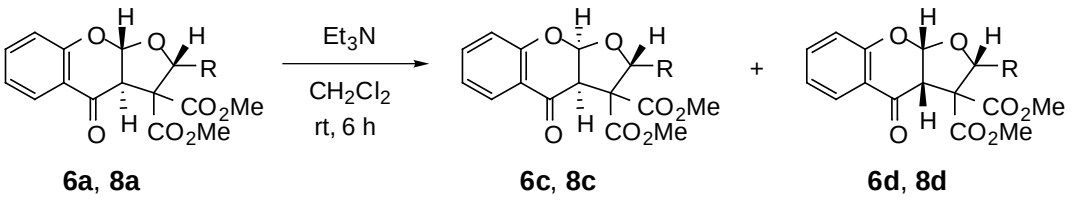


Table 2. Isomerization of 2,*t*-3a,*t*-9a-furobenzopyran

Entry	Furo-benzopyran	Yield (%)	2,*t*-3a,*c*-9a / 2,*c*-3a,*c*-9a [a]
1	**6**	99	>20 : 1
2	**8**	98	>20 : 1

[a]The ratio of the isomers was determined by ^{1}H-NMR.

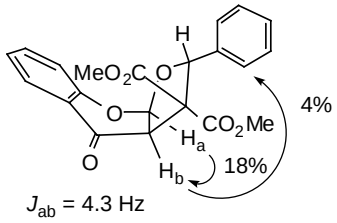
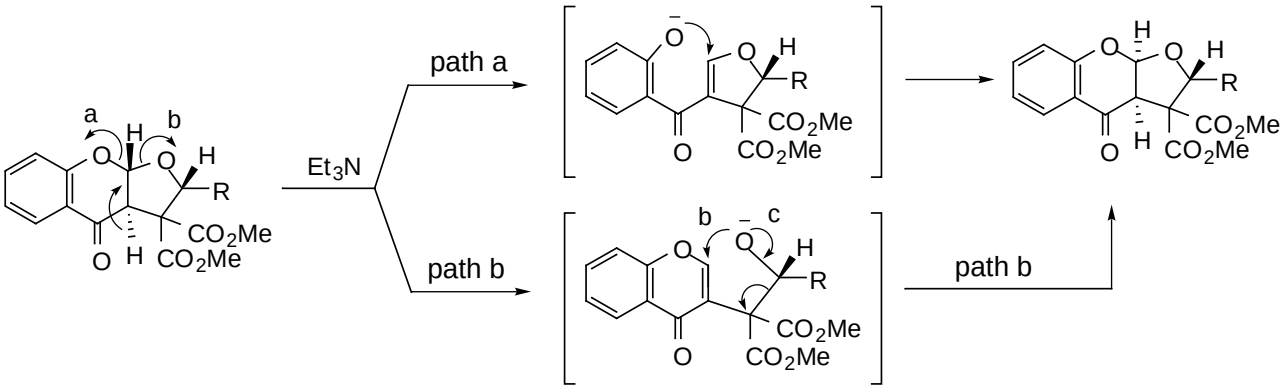


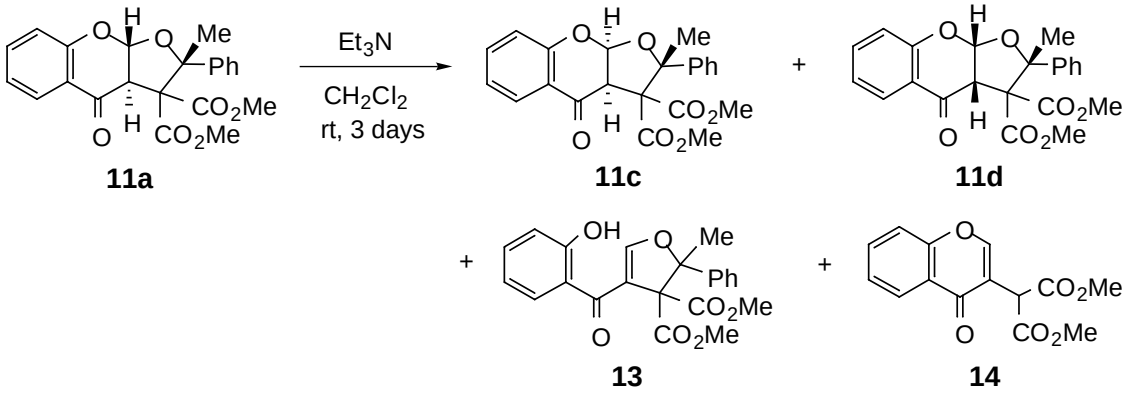
Figure 3. Selected NOE correlations for **6c**

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,*t*-3a,*c*-9a-isomer is more thermodynamically stable compared with other isomers.



Scheme 4

As shown in Scheme 5, by the treatment of **11a** with Et_3N, 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 Et_3N. This fact supports the above isomerization mechanism.



Scheme 5

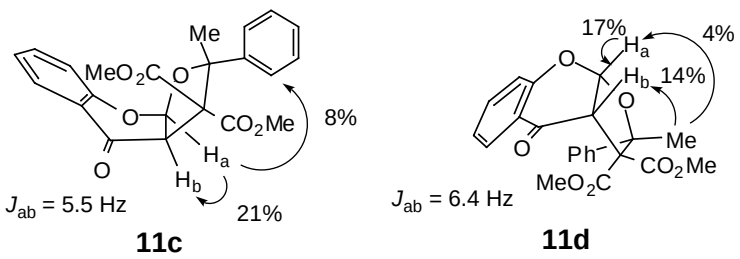
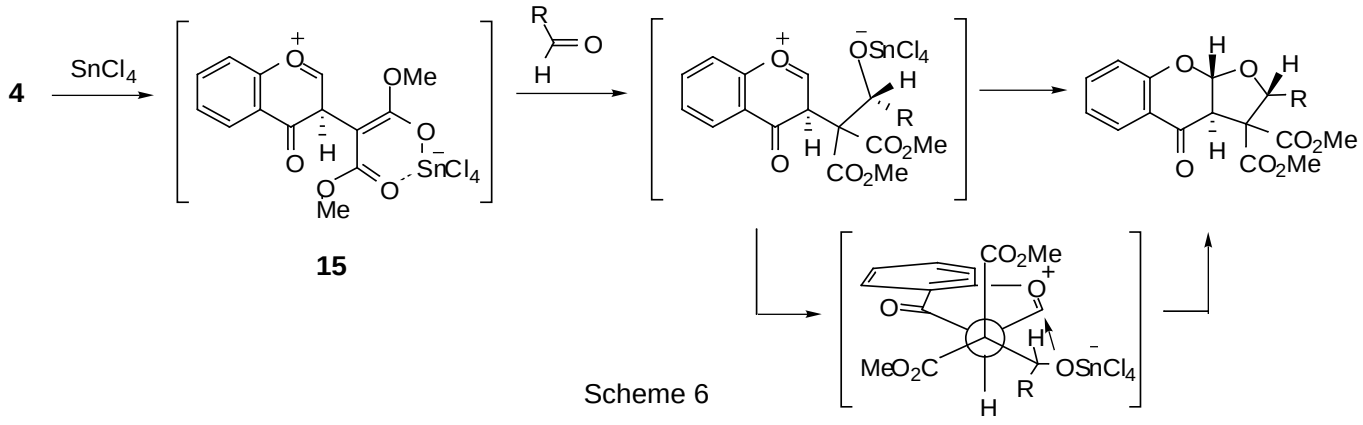


Figure 4. Selected NOE correlations for **11c** and **11d**

A plausible mechanism for the stereoselective $SnCl_4$-mediated reaction of **4** with aldehydes is as follows. By the action of $SnCl_4$, 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-dialkoxycyclopropanecarboxylates with carbonyl compounds.[3] In their reports, they describe that the high diastereoselectivity of these reactions is attributed to electronic and steric effects.[3d-3f] 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.



Scheme 6

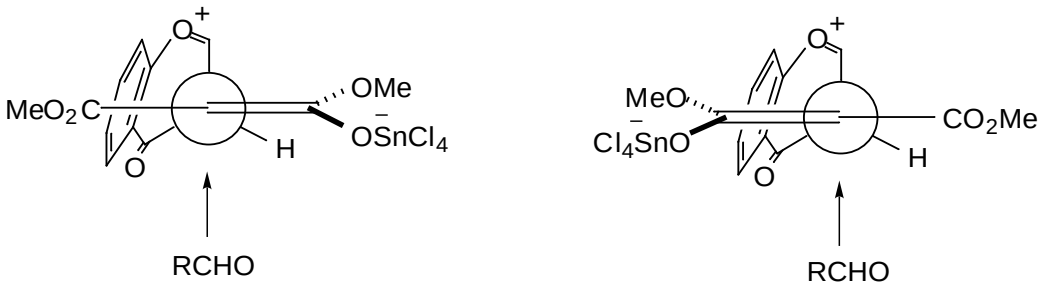


Figure 5

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).[5] Consequently, the 2,*t*-3a,*t*-9a-adduct would be predominantly obtained.

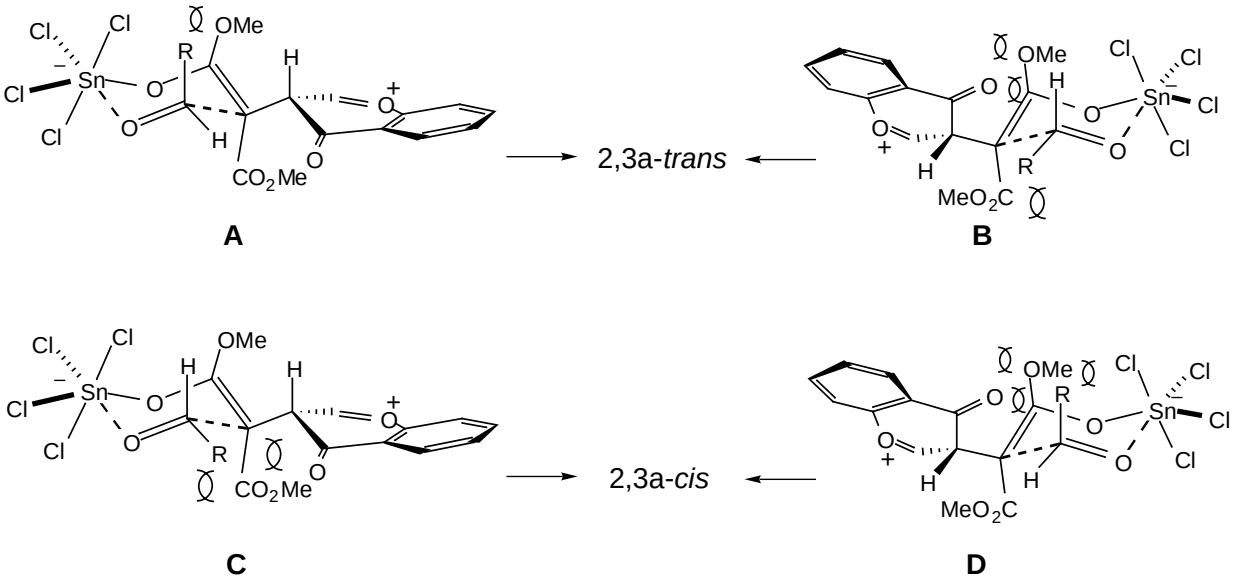


Figure 6

In summary, we have demonstrated that the $SnCl_4$-catalyzed ring-opening addition reactions of methanochromanone (**4**) with aldehydes smoothly proceeded to afford the corresponding 2,*t*-3a,*t*-9a-tetrahydrofuro[2,3-*b*][1]benzopyranones in high yields with high diastereoselectivity. *cis*-Fused furobenzopyranone derivatives were also obtained in good yields by the isomerization of the *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_2Cl_2 (4 mL) was added dropwise a solution of $SnCl_4$ (0.2 *M* solution in CH_2Cl_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 $NaHCO_3$. The mixture was vigorously stirred for 10 min and allowed to warm up to rt. The mixture was extracted with CH_2Cl_2 (30 mL x 3) and the combined organic layers were dried over Na_2SO_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,*t*-3a,*t*-9a-tetrahydro-4-oxo-2-phenyl-4*H*-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}; ^{1}H-NMR ($CDCl_3$) 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); ^{13}C-NMR ($CDCl_3$) 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 $C_{21}H_{18}O_7$: C, 65.97; H, 4.74. Found: C, 66.00; H, 4.80.

Dimethyl 2,*t*-3a,*t*-9a-tetrahydro-2-(4-methoxyphenyl)-4-oxo-4*H*-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}; ^{1}H-NMR ($CDCl_3$) 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), 7.58 (1H, ddd, *J* = 8.2, 7.3, 1.5 Hz, H-7), 7.91 (1H, dd, *J* = 7.9, 1.5 Hz, H-5); ^{13}C-NMR ($CDCl_3$) 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, 128.74, 128.82, 136.30, 157.98, 160.03, 166.92, 169.75, 188.06; MS *m/z* 412 (M^+). *Anal*. Calcd for $C_{22}H_{20}O_8$: C, 64.08; H, 4.89. Found: C, 63.95; H, 5.05.

Dimethyl 2,*t*-3a,*t*-9a-tetrahydro-4-oxo-2-(1-propenyl)-4*H*-furo[2,3-*b*][1]benzopyran-3,3-dicarboxylate (8a): colorless prism (from Et_2O-hexane), mp 111-113 °C; IR (KBr) 1736, 1715, 1607, 1458 cm^{-1}; ^{1}H-NMR ($CDCl_3$) 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, ddq, *J* = 15.3, 7.3, 1.5 Hz, H-1'), 5.66 (1H, d, *J* = 10.7 Hz, H-9a), 5.99 (1H, dqd, *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); ^{13}C-NMR ($CDCl_3$) δ17.71, 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 $C_{18}H_{18}O_7$: C, 62.42; H, 5.24. Found: C, 62.02; H, 5.32.

Dimethyl 2,*t*-3a,*t*-9a-tetrahydro-4-oxo-2-(2-phenyl-1-ethenyl)-4*H*-furo[2,3-*b*][1]benzopyran-3,3-dicarboxylate (9a): colorless prism (from Et_2O-hexane), mp 119-121 °C; IR (KBr) 1759, 1725, 1607, 1462 cm^{-1}; ^{1}H-NMR ($CDCl_3$) 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 $C_{23}H_{20}O_7$: C, 67.64; H, 4.94. Found: C, 67.45; H, 5.14.

Dimethyl 2,*t*-3a,*t*-9a-tetrahydro-4-oxo-2-pentyl-4*H*-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}; ^{1}H-NMR ($CDCl_3$) 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 $SnCl_4$ (0.2 *M* solution in CH_2Cl_2, 0.25 mL, 0.05 mmol) to give **11** (196 mg, 99%).

Dimethyl 3a,9a-*trans*-tetrahydro-2-methyl-4-oxo-2-phenyl-4*H*-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}; ^{1}H-NMR ($CDCl_3$) δ 2.19 (3H, s, Me), 3.39 (3H, s, OMe), 3.88 (3H, s, OMe), 4.19 (1H, d, *J* = 10.4 Hz, H-3a), 6.25 (1H, d, *J* = 10.4 Hz, H-9a), 7.12 (1H, ddd, *J* = 7.9, 7.3, 0.9 Hz, H-6), 7.25 (1H, dd, *J* = 8.5, 0.9 Hz, H-8), 7.29 (1H, m, Ph), 7.35 (2H, m, Ph), 7.59 (1H, ddd, *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); ^{13}C-NMR ($CDCl_3$) 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 $SnCl_4$ (0.2 *M* solution in CH_2Cl_2, 0.25 mL, 0.05 mmol) to give **12** (130 mg, 75%).

Dimethyl 3a,9a-*trans*-tetrahydro-2-methyl-4-oxo-2-ethenyl-4*H*-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**): ^{1}H-NMR ($CDCl_3$) 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=C*H*$_2$), 5.82 (1H, dd, *J* = 16.8, 1.8 Hz, CH=C*H*$_2$), 5.90 (1H, dd, *J* = 16.8, 10.1 Hz, C*H*=CH$_2$), 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**): ^{1}H-NMR ($CDCl_3$) δ 1.55 (3H, s, Me), 3.73 (3H, s, OMe), 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=C*H*$_2$), 5.54 (1H, dd, *J* = 17.1, 1.2 Hz, CH=C*H*$_2$), 6.05 (1H, d, *J* = 10.4 Hz, H-9a), 6.07 (1H, dd, *J* = 17.1, 10.7 Hz, C*H*=CH$_2$), 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 CH_2Cl_2 (5 mL) was added Et_3N (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 CH_2Cl_2 (20 mL x 3), the combined organic layers were dried over Na_2SO_4, 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 Et_3N (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 ^{1}H-NMR.

Dimethyl 2,*t*-3a,*c*-9a-tetrahydro-4-oxo-2-phenyl-4*H*-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}; ^{1}H-NMR ($CDCl_3$) 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, 0.9 Hz, H-8), 7.09 (1H, ddd, *J* = 7.9, 7.0, 0.9 Hz, H-6), 7.30-7.50 (5H, m, Ph), 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); ^{13}C-NMR ($CDCl_3$) 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 $C_{21}H_{18}O_7$: 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 Et_3N (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 ^{1}H-NMR.

Dimethyl 2,*t*-3a,*c*-9a-tetrahydro-4-oxo-2-(1-propenyl)-4*H*-furo[2,3-*b*][1]benzopyran-3,3-dicarboxylate (8c): colorless needles (from Et_2O-hexane), mp 122-123 °C; IR (KBr) 1746, 1698, 1609, 1464 cm^{-1}; ^{1}H-NMR ($CDCl_3$) 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-3a), 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, dqd, *J* = 15.3, 6.7, 1.0 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* = 7.9, 1.5 Hz, H-5); ^{13}C-NMR ($CDCl_3$) δ17.70, 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 $C_{18}H_{18}O_7$: 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 Et_3N (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-4*H*-furo[2,3-*b*][1]benzopyran-3,3-dicarboxylate (11c): colorless prism (from Et_2O-hexane), mp 154-155 °C; IR (KBr) 1761, 1736, 1682, 1607, 1466 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.88 (3H, s, Me), 3.09 (3H, s, OMe), 3.74 (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), 7.11 (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); ^{13}C-NMR ($CDCl_3$) δ27.24, 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, 137.00, 142.45, 157.40, 166.92, 168.38, 188.54; MS *m/z* 395 (M^+-1). *Anal*. Calcd for $C_{22}H_{20}O_7$: C, 66.66; H, 5.09. Found: C, 66.52; H, 5.12. **(11d)**: colorless prism (from Et_2O-hexane), mp 162-165 °C; IR (KBr) 1769, 1742, 1688, 1607, 1464 cm^{-1}; ^{1}H-NMR ($CDCl_3$) 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); ^{13}C-NMR ($CDCl_3$) δ28.58, 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 ($CDCl_3$) δ 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-4*H*-1-benzopyran-3-yl)malonate (14): colorless powder (from Et_2O-hexane), mp 152-153 °C; IR (KBr) 1759, 1736, 1644, 1628, 1466, 1312 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 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.

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