LEWIS ACID-MEDIATED RING EXPANSION REACTION OF 2,3-METHANOCHROMANONES WITH SILYL ENOL ETHERS

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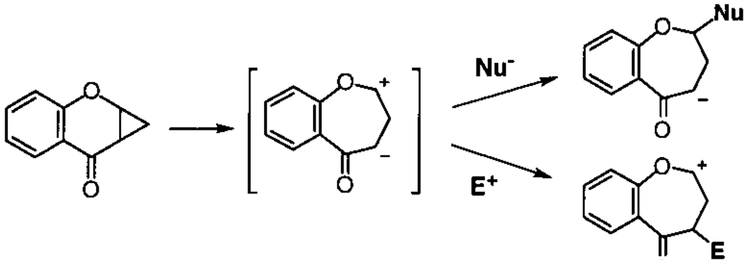
Abstract - In the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf), methanochromanones easily reacted with silyl enol ethers to give the [3+2] cycloadducts and the corresponding adducts in good yields.

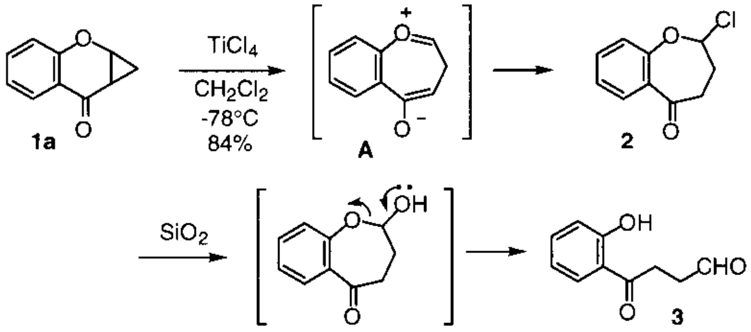
Cyclopropanes having an electron-withdrawing or -donating group are susceptible to ring-opening reactions.[1] Especially, cyclopropanes with donor and acceptor substituents at vicinal positions on the cyclopropane ring are the equivalent of a ring-opened 1,3-zwitterion, which is expected to react with both nucleophiles and electrophiles.[2] Saigo reported the syntheses of 5-membered carbo-[3] and heterocyclic compounds[4] by the reactions of 2,2-dialkoxycyclopropanecarboxylic acid esters having two electron-donating groups and one electron-withdrawing group with various substrates. Kuwajima also reported Lewis acid-mediated [3+2] cycloaddition reaction of vicinally donor-acceptor-substituted cyclopropane with silyl enol ethers.[5]

We were interested in the reactivity of 2,3-methanochromanones (**1**)[6] readily prepared from the corresponding chromone and dimethyloxosulfonium methylide.[7] Because methanochromanones have an alkoxy group as a donor and a carbonyl group as an acceptor in the benzopyran ring, formation of a 1,3-zwitterionic intermediate would be expected. We speculated that, upon treatment with various nucleophiles and/or electrophiles in the presence of a Lewis acid, the methanochromanones would undergo ring-opening and provide several 1-benzoxepins as the ring-expanded products[8] (Scheme 1). We report herein the Lewis acid-promoted reaction of methanochromanones with silyl enol ethers *via* a 1,3-zwitterionic intermediate.



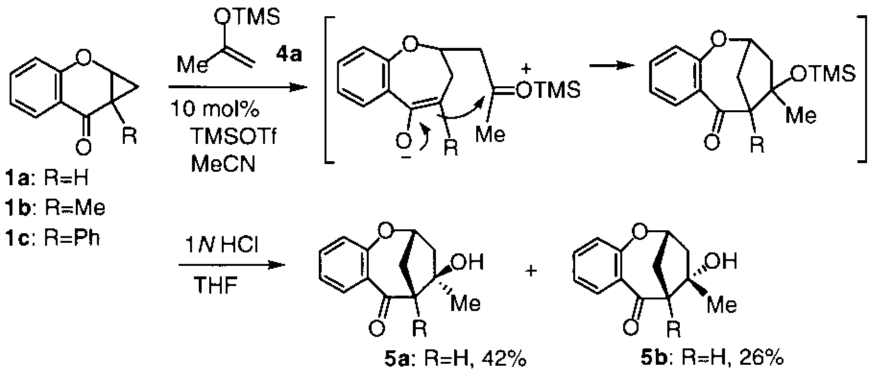
Scheme 1

At first, the reactivity of 2,3-methanochromanone (**1a**) by the action of a Lewis acid was examined. A solution of a stoichiometric amount of TiCl$_4$ in CH$_2$Cl$_2$ was added to a solution of **1a** in CH$_2$Cl$_2$ at -78 °C to give the 2-chloro-1-benzoxepinone (**2**)[9] in 84% yield along with a small amount of its ring-cleaved product (**3**).[6c] The obtained benzoxepin (**2**) is very unstable under acidic conditions and was converted into **3** even when **2** was treated with silica gel (Scheme 2). In this result, we considered that methanochromanone (**1a**) is the equivalent of a ring-opened zwitterion (**A**).



Scheme 2

We next examined the reaction of 2,3-methanochromanone (**1a**) with silyl enol ethers as the nucleophile. When the reaction was performed in the presence of TiCl$_4$ in CH$_2$Cl$_2$ at -78 °C, however, **3** was obtained as a major product and the desired adduct was obtained in low yield. In order to improve the yield of this reaction, we carried out the reaction of **1a** with **4a** under various conditions. Finally, it was found that the best yield of the adduct (**5**) was obtained using trimethylsilyl trifluoromethanesulfonate (TMSOTf) as a Lewis acid in MeCN.[10] Thus, the reaction of **1a** with **4a** in the presence of TMSOTf (10 mol%) in MeCN gave the cycloadducts (**5a** and **5b**)[11] in 42% and 26% yields, respectively (Scheme 3). The stereochemistry of the cycloadduct (**5a**) was assigned based on NOE experiments (Figure 1).



Scheme 3

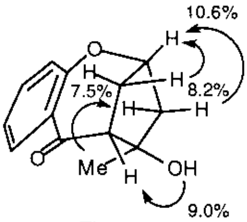
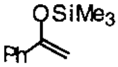
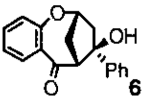
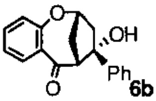
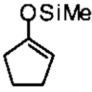
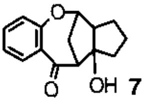
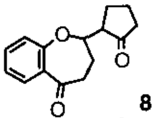
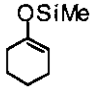
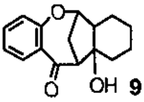
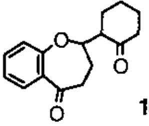
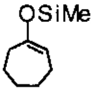
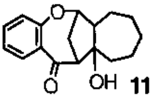
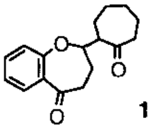
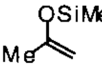
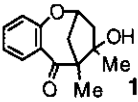
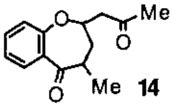
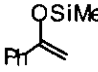
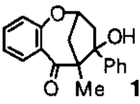
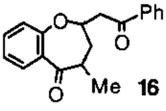
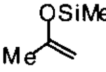
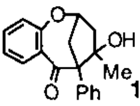
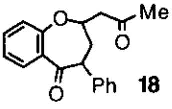
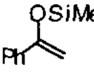
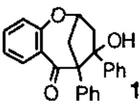
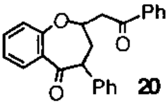


Figure 1

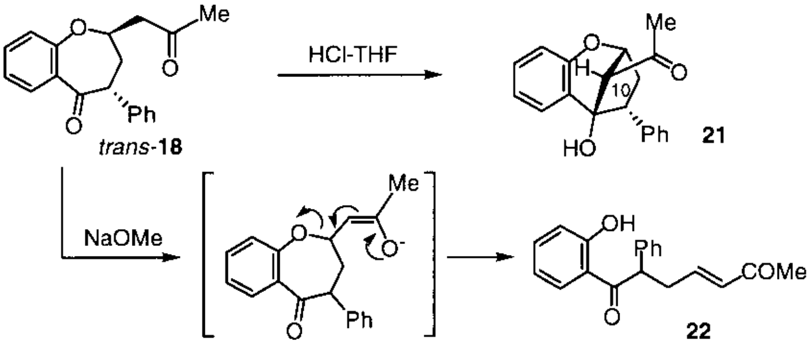
A similar reaction of **1a** with **4b** proceeded smoothly to give the corresponding cycloadducts (**6a** and **6b**) in high yield (Table 1, entry 1). The reaction of **1a** with cyclic silyl enol ethers under the same conditions also gave the cycloadducts in good yields (entries 2-4). 3-Methyl-2,3-methanochromanone (**1b**) was next treated with **4a** under the same conditions as described above to give the cycloadduct (**13**) and the 1-benzoxepin (**14**) in 35 and 50% yields, respectively (entry 5). It was found that introduction of a bulkier alkyl group at the 3-position of the pyrone ring increased the yield of the non-cyclized adduct. Thus, the adduct (**18**) was obtained in 68% yield along with a small amount of [3+2] cycloadduct when **1c** reacted with enol silyl ether (**4a**, entry 7). In addition, an enhancement of the *trans/cis* ratio of the non-cyclized adduct was observed when the methyl group at the 3-position of the pyrone ring was replaced with the phenyl group.

Table 1. Reaction of Methanochromanones (**1**) with Silyl Enol Ethers

entry	R	Silyl enol ether	temp. (°C)	products	yield (%)[a]	products	yield (%)[a]
1	H	 **4b**	-40	 **6a**	40	 **6b**	53
2	H	 **4c**	-40	 **7**	72[b] (2.5 : 1)[e]	 **8**	8[b]
3	H	 **4d**	-40	 **9**	76[b] (1.1 : 1)[e]	 **10**	0[d]
4	H	 **4e**	-40	 **11**	79[c] (25 : 9 : 1)[e]	 **12**	15[b]
5	Me	 **4a**	-40	 **13**	35 (>10 : 1)[e]	 **14**	50[b] (2.9 : 1)[f]
6	Me	 **4b**	-40	 **15**	38[b] (18 : 1)[e]	 **16**	26[b] (5 : 1)[f]
7	Ph	 **4a**	0	 **17**	2	 **18**	68[b] (10 : 1)[f]
8	Ph	 **4b**	0	 **19**	0[d]	 **20**	38[b] (10 : 1)[f]

[a] Isolated yields. [b] Two diastereomers were isolated. [c] Three diastereomers were isolated.
[d] Not detected. [e] Ratio of isomers. [f] Ratio of *trans*- : *cis*-isomers.

It was also found that when the adduct (*trans*-**18**) was treated with conc. HCl in THF, the newly formed cycloadduct (**21**) and its C-10 epimer were obtained in 76% and 20% yields, respectively. On the contrary, treatment of *trans*-**18** under basic conditions using NaOMe in ether gave **22** as the sole product in 80% yield (Scheme 4).



Scheme 4

In summary, we have demonstrated that the TMSOTf-catalyzed ring-opening addition reactions of **1** with silyl enol ethers proceeded smoothly to afford the corresponding adducts in high yields. We are now investigating the Lewis acid-mediated ring expansion reaction of methanochromanones with various substrates, and the results will be reported in due course.

REFERENCES AND NOTES

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6. Solvolytic ring-opening reactions of methanochromanones have been reported. See for example a) H. Yamaoka, I. Mishima, M. Miyamoto, and T. Hanafusa, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 469. b) F. M. Dean and R. S. Johnson, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2049. c) G. A. Caplin, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc. (C)*, 1968, 2302. d) C. K. Ghosh, S. Sahana, and C. Ghosh, *Indian J. Chem.*, 1996, **35**, 669.

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8. Synthesis of 2-phenylbenzoxepinones by means of the reductive cleavage of 2-phenyl-2,3-methanochromanones has been reported: T. Tastuoka, K. Imao, K. Suzuki, M. Shibata, and F. Satoh, *Heterocycles*, 1990, **30**, 749.
9. Compound (**2**): mp 66-68 ℃ (AcOEt-hexane). IR ($CDCl_3$) 1690 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (1H, dd, J = 7.6, 1.8 Hz, H-6), 7.59 (1H, ddd, J = 8.0, 7.6, 1.8 Hz, H-8), 7.35 (1H, td, J = 7.6, 1.0 Hz, H-7), 7.19 (1H, dd, J = 8.0, 1.0 Hz, H-9), 6.31 (1H, dd, J = 10.1, 5.2 Hz, H-2), 2.86-2.76 (2H, m, H-4), 2.60 (1H, m, H-3), 2.36 (1H, m, H-3). High-resolution MS m/z Calcd for $C_{10}H_9O_2{}^{35}Cl$ (M^+): 196.0291, Found: 196.0247.
10. A typical procedure is as follows: To a stirred solution of **1a** (80 mg, 0.5 mmol) and **4a** (130 mg, 1.0 mmol) in MeCN (4 mL) was added dropwise a solution of TMSOTf (11 mg, 0.05 mmol) in MeCN (0.5 mL) at -40 ℃ under argon atmosphere. After being stirred for 30 min, the reaction was quenched at the same temperature by adding saturated aqueous $NaHCO_3$ (2 mL). The mixture was stirred vigorously for 10 min and allowed to warm to room temperature. 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 dissolved in THF-1*N* HCl (2 : 1, 6 mL) and the solution was stirred for 1 h at 0 ℃. The mixture was extracted with ether (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 (eluent: hexane-AcOEt = 5 : 1) to give the cycloadducts (**5a** and **5b**) in 42% and 26% yields, respectively.
11. Compound (**5a**): mp 93-95 ℃ (ether-hexane). IR ($CDCl_3$) 3450, 1660 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (1H, dd, J = 8.2, 1.8 Hz, H-7), 7.42 (1H, ddd, J = 8.2, 7.0, 1.8 Hz, H-9), 6.99 (1H, ddd, J = 8.2, 7.0, 1.2 Hz, H-8), 6.90 (1H, dd, J = 8.2, 1.2 Hz, H-10), 5.26 (1H, ddt, J = 7.6, 6.1, 1.8 Hz, H-2), 3.05 (1H, br d, J = 6.1 Hz, H-5), 2.65 (1H, dt, J =14.7, 6.1 Hz, H-11), 2.36 (1H, ddd, J = 16.2, 7.6, 1.2 Hz, H-3), 2.30 (1H, dd, J = 14.7, 1.8 Hz, H-11), 2.06 (1H, dt, J = 16.2, 1.8 Hz, H-3), 1.64 (1H, br s, OH), 1.36 (3H, s, Me). ^{13}C NMR (500 MHz, $CDCl_3$) δ 199.01, 155.18, 135.20, 131.82, 123.37, 122.40, 121.01, 82.43, 80.95, 65.85, 46.52, 30.59, 25.38.

    Compound (**5b**): mp 82-83 ℃ (ether-hexane). IR ($CDCl_3$) 3400, 1660 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (1H, dd, J = 8.2, 1.8 Hz, H-7), 7.42 (1H, ddd, J = 8.2, 7.0, 1.8 Hz, H-9), 7.02 (1H, ddd, J = 8.2, 7.0, 1.2 Hz, H-8), 6.92 (1H, dd, J = 8.2, 1.2 Hz, H-10), 5.08 (1H, m, H-2), 3.04 (1H, dd, J = 6.7, 1.2 Hz, H-5), 2.45 (1H, dd, J =15.3, 2.2 Hz, H-11), 2.27 (1H, dt, J = 15.8, 2.2 Hz, H-3), 2.20 (1H, ddd, J = 15.3, 6.7, 5.2 Hz, H-11), 2.30-2.20 (1H, m, H-3), 2.12 (1H, br s, OH), 1.48 (3H, s, Me).

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