in the fluid phase. This chemical ion exchange reaction can be represented by the following Equation:

$$^{6}Li^{+}_{fluid} + {}^{7}Li^{+}_{resin} \rightleftarrows {}^{7}Li^{+}_{fluid} + {}^{6}Li^{+}_{resin} \quad (2)$$

The subscripted symbols, such as fluid and resin refer to the fluid phase and resin phase in this isotope exchange. Klinskii *et al.*[33] and Oi *et al.*[16] reported that the heavier isotopes were enriched in the resin phase of ion exchange chromatography. These phenomena are a contrast to the results of our experiments. On the other hand, Aaltonen,[34] Heumann and Lieser,[35] Russell and Papanastassiou,[36] Jepson and Shockey,[37] and Kobayashi *et al.*[38] stated that the heavier isotopes were preferentially concentrated into the solution phase of chromatography using strongly acidic cation exchangers. This discrepancy, still, cannot be explained at this time and further work must be done to resolve the phenomena.

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Introduction of Cyclopentene Annulation and Propargyl Group in Chromones

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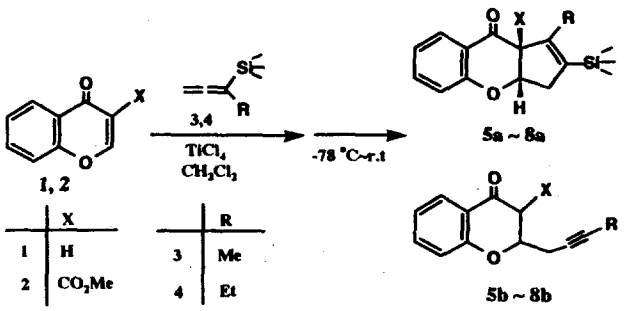
Although chromone can be regarded as an α,β-unsaturated ketone, there are few synthetic methods for the introduction of carbon nucleophiles at the C_2 position of the heterocyclic ring.[1] In this connection, Wallace *et al.*[2] showed that introduction of an alkyl group into the C_2 position of chromone derivatives by using a lithium dialkylcuprates is possible. More recently, Akiba and co-workers[3] reported a facile method for the regioselective introduction of an allyl group into chromone *via* siloxybenzopyrylium cations by means

Table 1. Reaction of **1** and **2** with 1-alkyl-1-(trimethylsilyl)allenes (3, 4) in the presence of $TiCl_4$



Entry	Reactants X	Reactants R	Products	Yield (%)[a]	Total yield
1	H	Me	**5a**	25 (11)[b]	30 (40)[b]
	H	Me	**5b**	5 (29)	
2	H	Et	**6a**	24 (9.5)	30.5 (33.5)
	H	Et	**6b**	6.5 (24)	
3	CO_2Me	Me	**7a**	18 (12.5)	25 (36)
	CO_2Me	Me	**7b**	7 (23.5)	
4	CO_2Me	Et	**8a**	19.5 (10)	27 (36)
	CO_2Me	Et	**8b**	7.5 (26)	

[a] Yields correspond to the isolated yield. [b] Yields in parentheses were obtained in the presence of *tert*-butyldimethylsilyl triflate.

of *tert*-butyldimethylsilyl triflate. Furthermore, they found that the reaction of chromones with 3-(trimethylsilyl)-1-butene in the presence of *tert*-butyldimetylsilyl triflate afforded five-membered ring adducts.

Recently, Danheiser reported that the TMS-cyclopentene annulation[4] was one of the most effective methods for the introduction of a five-membered ring into electron-deficient alkenes. As a part of our study on the introduction of five-membered rings into chromones, here we report the introduction of five-membered rings as well as propargyl groups at the C_2 position of chromones by using the TMS-cyclopentene annulation methodology.

Treatment of 1-methyl-1-(trimethylsilyl)allene (3)[5] with chromone (1) at −78 ℃ in the presence of one equiv of *tert*-butyldimethylsilyl triflate afforded the propargylation product **5b** in 29% yield along with the corresponding cyclopentene annulation product (**5a**) in 11% yield. However, under similar reaction conditions, when one equiv of titanium tetrachloride is used in place of the triflate reagent, the corresponding cyclopentene annulation product (**5a**) is obtained in 25% yield along with propargylation product (**5b**) as a mimor product (5%). Similar results were obtained by reaction of 3-(methoxycarbonyl)chromone **1b** and 1-alkyl-1-(trimethylsilyl)allene (3, 4). The results are summarized in Table 1.

Structural assignments of the resulting cyclopentene annulation products were established based on ^1H NMR spectral data.[6] For example, in the case of **5a**, the allylic protons ($H_{1'}$) appear at δ 2.75 as a broad singlet and the signals of the H_2 and H_3 are seen at δ 5.17 (m) and δ 3.50 (dd, J=1.6, 3.5 Hz) respectively. The small coupling constant (J= 3.5 Hz) between H_2 and H_3 indicates that the relative stereochemistry of the two methine protons is an equatorial-axial relationship. Since the other annulation product (**6a**) also shows a small coupling constant (J=3.6 Hz) between H_2 and H_3, the ring junction is considered to have the same *cis* geometry as that of **5a**. Although the relative stereochemistry of **7a** and **8a** could not be determined owing to the presence of the methoxycarbonyl group at C_3, the geometry of the ring junction could be the same *cis* relationship as those of **5a** and **6a** according to the known fact that "the TMS-cyclopentene annulation proceeds with a strong preference for *syn* addition of the allene to the two carbon allenophile.[4]"

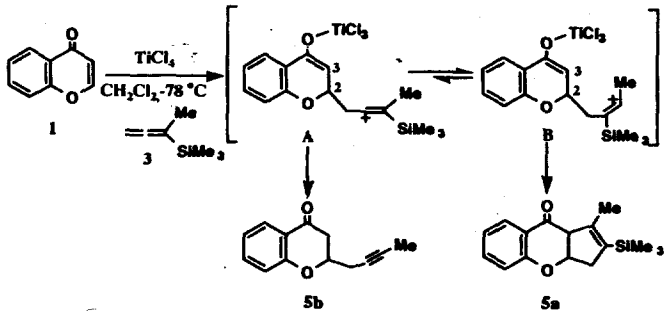
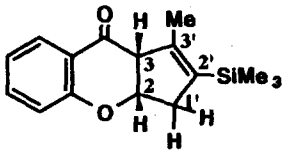


Figure 1. A possible mechanism for the formation of products **5a** and **5b**.



5a

A possible mechanism for the formation of products **5a** and **5b** is shown in Figure 1. In the presence of a Lewis acid such as titanium tetrachloride or *tert*-butyldimethylsilyl triflate, the allenyl silane reagent (3) attacks the chromone at the C_2 position, giving the intermediate vinyl cation A which is stabilized by interaction with the adjacent C-Si bond. A 1,2 shift[7] of the trimethylsilyl group then occurs to afford an isomeric vinyl cation B which stereoselectively cyclizes to produce the five-membered ring (**5a**).

As shown in Table 1, the ratio of cycloadducts and propargylation adducts varies depending upon the Lewis acid employed. When titanium tetrachloride is used, although the total yield appears somewhat lower as compared to the yield when *tert*-butyldimethylsilyl triflate is used, the ratio of the cycloadducts was distinctly superior. This result indicates that the intermediate titanium enolate is stabilized isomeric vinyl cation (B) more than vinyl cation (A). The intermediate silyl enolate readily desiylates relative to its titanium counterpart, and leads to the Michael type adducts.

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6. Spectral data of **5a**; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.15 (s, 9H), 1.84 (d, J=1.6 Hz, 3H), 2.75 (bs, 2H), 3.50 (dd, J=1.6, 3.5 Hz, 1H), 5.17 (m, 1H), 6.85-7.95 (m, 4H); Ms (m/z): M^+272 (92), M^++1 (65), M^++2 (22), 257 (96), 183 (78).
Spectral data of **5b**; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.81 (t, 3H), 2.65 (dd, 2H), 2.90 (dd, 2H), 4.55 (m, 1H), 7.01-7.84 (m, 4H); Ms (m/z): M^+200 (75), M^++1 (48), M^++2 (50), 185 (62), 72 (83).
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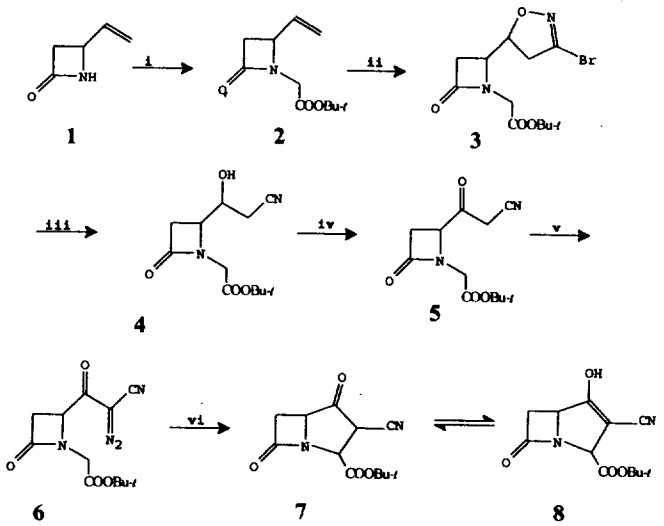

i) LiHMDS, THF, −78 ℃; $BrCH_2COOtBu$, rt; ii) Br_2C=NOH, $NaHCO_3$, EtOAc, rt; iii) EtSNa, MeOH, 0 ℃; iv) Jones reagent, acetone, 0 ℃; v) Et_3N, TsN_3, acetonitrile, rt; vi) $Rh_2(OAc)_4$, benzene, reflux.

Scheme 1.

Synthesis of 2-Cyano-1-oxocarbapenam-3-carboxylate

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Recently we found that when 3-bromo-2-isoxazolines were treated with sodium ethanethiolate, they could be converted effectively to β-hydroxy nitriles.[1] 3-Bromo-2-isoxazolines can be obtained easily from alkenes by treatment of bromonitrile oxide.[2] We adapted this reaction for the synthesis of an 1-oxocarbapenam derivative. Thus, we wish to report here the conversion of 4-vinyl-2-azetidinone to 1-oxocarbapenam.

4-Vinyl-2-azetidinone (**1**) was synthesized from 1,3-butadiene by reaction with chlorosulfonyl isocyanate.[3] 1-[(*t*-Butoxycarbonyl)methyl]-4-vinyl-2-azetidinone (**2**) was obtained from 4-vinyl-2-azetidinone (**1**) by reaction with *t*-butyl bromoacetate in the presence of LiHMDS in THF at −78 ℃ (yield : 83%). It was converted to 4-(3-bromo-2-isoxazolin-5-yl)-1-[(*t*-butoxycarbonyl)methyl]-2-azetidinone (**3**) in the yield of 86% by reaction with dibromoaldoxime in ethyl acetate in the presence of sodium bicarbonate (1.5 eq.) and a small amount of water. The intensities of two doublets at 3.23 and 4.03 ppm (J=18.0 Hz) and two doublets at 3.72 and 4.12 ppm (J=18.0 Hz) in the ^{1}H NMR spectrum of compound **3** implis that it is a mixture of two diastereomers (6 : 4). The two isomers could not be separated by column chromatography.

A β-hydroxy nitrile **4**, 1-[(*t*-butoxycarbony)methyl]-4-(2-cyano-1-hydroxyethyl)-2-azetidinone, was obtained in 68% yield from compound **3** by treatment of sodium ethanethiolate (1.1 eq.) in methanol. Compound **4** showed bands for a hydroxy group and a cyano group at 3450 and 2250 cm^{-1}, respectively. Compound **4** was oxidized to 1-[(*t*-butoxycarbony)methyl]-4-(2-cyano-1-oxoethyl)-2-azetidinone (**5**) with Jones reagent in acetone in 74% yield. The oxidized product showed no hydroxy band in its ir spectrum but two strong carbonyl (a β-lactam carbonyl and an ester carbonyl) bands around 1700-1750 cm^{-1} were observed. Diazotization of this compound by following the Regitz method[4] (TsN_3/Et_3N, acetonitrile, 25-35 ℃) gave 1-[(*t*-butoxycarbonyl)methyl]-4-(2-cyano-2-diazo-1-oxoethyl)-2-azetidinone (**6**) in 84% yield. The diazo compound **6** showed bands at 2250 and 2140 cm^{-1} for the cyano group and the diazo group, respectively. Refluxing of the benzene solutioon of compound **6** with rhodium acetate (cat. amount) for 12 hours gave 1-oxocarbapenam **7**, *t*-butyl 2-cyano-1-oxocarbapenam-3-carboxylate, in 52% yield. The 1-oxocarbapenam was unstable and decomposed slowly at room temperature.[5] It showed a band at 1775 cm^{-1} for a β-lactam carbonyl group and at 1720 cm^{-1} for an ester carbonyl group. In the ir spectrum, it showed a hydroxy group band at 3400 cm^{-1}, which might imply the existance of an enol tautomer (**8**).

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