Synthesis of Chromane Derivatives *via* Indium-mediated Intramolecular Allenylation and Allylation to Imines†

Han-Young Kang* and Yeon-Kwon Yu

Department of Chemistry and Institute for Basic Sciences, Chungbuk National University, Cheongju, Chungbuk 361-763, Korea
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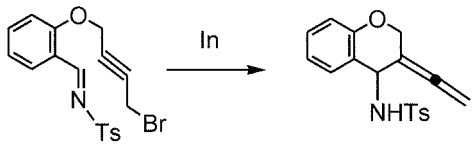
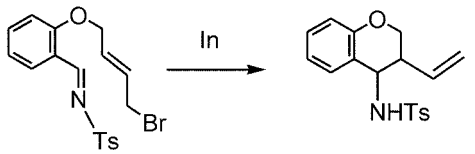
Indium-mediated intramolecular allylation and allenylation to carbonyl groups have been good methods to prepare chromane structures.[1,2] There are, however, still some limitations in these transformations. Especially, in the case of allylation mixtures of *cis* and *trans* isomers are always produced in about 2 : 1 ratio (*cis*/*trans*). The ratio was not improved under the various reaction conditions we attempted.

Since the indium-mediated addition to carbonyl groups has been successful,[3] it occurred to us that it would be worthwhile to test the addition to carbon-nitrogen double bonds, that is, imine groups. We wish to report here the results of the investigations on allylation and allenylation to C=N bond to provide the chromane structures. The whole transformations are shown below (Eq. 1 and 2).



1 **2** (1)



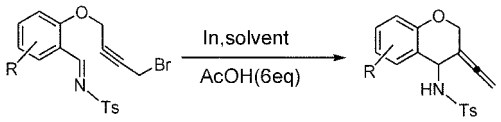
3 **4** (2)

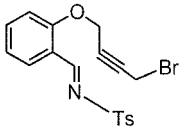
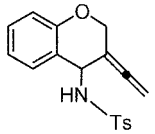
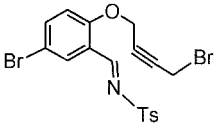
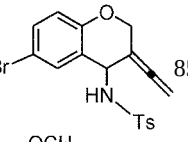
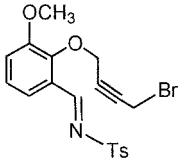
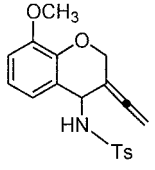
Intermolecular indium-mediated Barbier type allylation to C=N bonds could be performed in aqueous media.[4] The indium-mediated intramolecular allenylation proceeded with ease to produce the desired allenes in various solvents including aqueous media. Two equivalents of indium and acetic acid (6 eq) as an additive were used in the same manner as the allenylation and the allylation to C=O bonds.[2] In organic solvents such as THF, acetone, and DMF the cyclization proceeded efficiently to provide the desired product in good yields [75% (2 h), 81% (1 day), and 79% (2 h), respectively]. The reaction was completed in 1-2 h in aqueous solvent systems such as THF/water (1 : 3, *v*/*v*) and DMF/water (4 : 1, *v*/*v*) to afford the desired cyclized product in good yields (83 and 79%, respectively). The allenylation in aqueous media presents practical advantages compared to the organic media. The results of the preparation of chromane derivatives in DMF or THF/water (1 : 3, *v*/*v*) are summarized in Table 1. We conclude that the indium-mediated intramolecular allenylation to C=N bonds can be achieved in various solvents and is a good method to prepare chromanes.

Next, we turned our attention to the intramolecular allylation. Under the reaction conditions similar to those reported previously[2] cyclization of substrate **3** was performed. Reasonable yields were obtained in solvents such as THF, acetone, ethanol, and DMF [65% (5 h), 61% (1 day), 54% (6 h), and 53% (5 h), respectively], but acetonitrile or CH_2Cl_2 were found to be inappropriate. In aqueous THF the yield dropped to 21%, and however, only a single cyclized product was observed in all of the cases of cyclization.

The results of preparing chromans by intramolecular allylation are shown in Table 2. The results indicated that the indium-mediated allylation was not as efficient as the allenylation. About 10-20% decrease in yields was observed. As mentioned above, in each case only a single isomer was

Table 1. Preparation of chromane derivatives by allenylation[a]



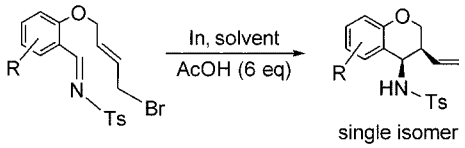
Entry	Compound	Product	DMF (Yield/ Time)	THF/H_2O[b] (Yield/ Time)
1			79%/2 h	83%/1 h
2			85%/3 h	80%/3 h
3			77%/5 h	73%/6 h

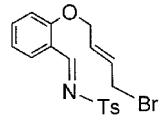
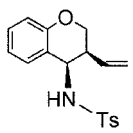
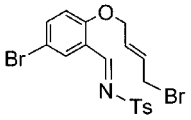
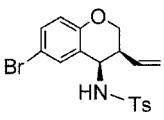
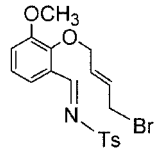
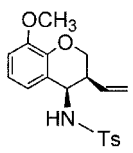
[a]Indium (2 eq) and acetic acid (6 eq) were used. [b]THF/H_2O = 1 : 3 (*v*/*v*)

†Dedicated to Professor Yong Hae Kim for his outstanding achievements in organic chemistry.

*Corresponding Author. Fax: +82-43-267-2279; e-mail: hykang@chungbuk.ac.kr

Table 2. Preparation of chromane derivatives by allylation[a]

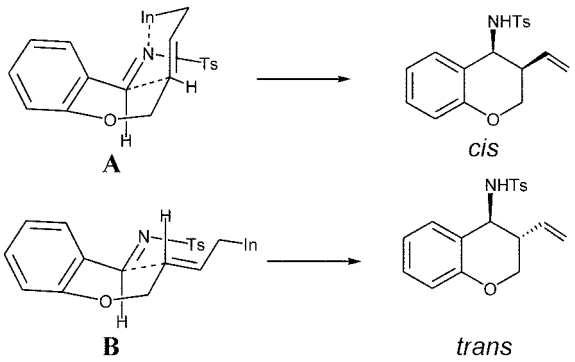


Entry	Compound	Product	DMF (Yield/Time)	THF (Yield/Time)
1			53%/5 h	65%/3 h
2			52%/6 h	38%/3 h
3			55%/10 h	61%/5 h

[a]Indium (2 eq) and acetic acid (6 eq) were used.

observed, and the stereochemistry of the product was determined as *cis* by analysis of ^{1}H NMR and NOE spectra.[5]

Formation of the *cis*-product can be explained by the possible chair-like transition state **A**. Considering the need of the bulky tosyl group to assume the axial geometry and possible chelation of the metal to the imino nitrogen, the chair-like transition state **A** is only possible to lead the observed *cis* product. Of course, the cyclization could proceed *via* the synclinal transition state **B**. Then, it would lead to the *trans*-isomer, which was not observed. It is unclear why the transition state **A** dominates over the transition state **B**. However, it might be appropriate to assume that in the solvent employed (DMF or THF), coordination of indium to the nitrogen atom becomes important and therefore, the chelated chair-like transition state **A** dominates.[4]



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References

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5. **Preparation of 3-vinylidene-4-(*p*-toluensulfonamino)chromane** (**2**) (Table 1, entry 1). To a solution of toluenesulfonimine **1** (59.0 mg, 0.145 mmol) in DMF (2 mL) was added indium powder (33.3 mg, 0.290 mmol) and acetic acid (52.2 mg, 0.870 mmol) under nitrogen atmosphere. The solution was stirred at room temperature for 2 h until the reaction was completed. The solution was extracted with ether (5 mL × 3). The organic layer was washed (saturated NaCl), dried ($MgSO_4$) and concentrated. Flash chromatography (hexane : ethyl acetate = 5 : 1) provided the desired product **2** as a white solid (37.4 mg, 79%). mp 137 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, 2H, J = 8.2 Hz, 2 × ArH in tosyl group), 7.33 (d, 2H, J = 8.0 Hz, 2 × ArH in tosyl group), 7.19 (dd, 2H, J = 7.8, 7.7 Hz, 2 × ArH), 6.91 (dd, 1H, J = 7.4, 7.4 Hz, ArH), 6.81 (d, 1H, J = 8.0 Hz, ArH), 5.0-5.1 (m, 1H, NH), 4.65-4.9 (m, 3H, OCH_2 + -NHC*H*), 4.53 (bs, 2H, C=C=CH_2), 2.45 (s, 3H, ArCH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 204.3, 154.4, 143.6, 137.9, 129.7, 129.6, 129.1, 128.0, 127.3, 121.3, 117.2, 94.8, 79.1, 65.4, 50.3, 21.6.

3-Vinyl-4-(*p*-toluenensulfonamino)chromane (**4**) (Table 2, entry 1). To a solution of toluenesulfonimine **3** (40.0 mg, 0.0980 mmol) in DMF (2 mL) was added indium powder (22.5 mg, 0.196 mmol) and acetic acid (35.3 mg, 0.588 mmol) under nitrogen atmosphere. The solution was stirred at room temperature for 5 h until the reaction was completed. The solution was extracted with ether (5 mL × 3). The organic layer was washed (saturated NaCl), dried ($MgSO_4$) and concentrated. Flash chromatography (hexane : ethyl acetate = 7 : 1) provided the desired product **4** as a white solid (17.2 mg, 53%). mp 162-164 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, 2H, J = 8.2 Hz, 2 × ArH in tosyl group), 7.35 (d, 2H, J = 8.0 Hz, 2 × ArH in tosyl group), 7.14 (dt, 1H, J = 7.8, 1.6 Hz, ArH), 7.07 (dd, 1H, J = 7.8, 1.4 Hz, ArH), 6.81 (dt, 1H, J = 7.1, 1.1 Hz, ArH), 6.76 (dd, 1H, J = 8.2, 1.0 Hz, ArH), 5.74 (ddd, 1H, J = 17.2, 10.3, 9.2 Hz, -C*H*=CH_2), 5.23 (dd, 1H, J = 10.4, 1.6 Hz, -CH=C*H*H), 5.09 (d, 1H, J = 17.3 Hz, -CH=CH*H*), 4.69 (m, 2H, N*H* + NHC*H*), 4.21 (dd, J = 11.2, 2.4 Hz, -OC*H*HC), 4.10 (dd, 1H, J = 11.2, 5.2 Hz, -OCH*H*C), 2.52 (br, 1H, C*H*CH=CH_2), 2.46 (s, 3H, ArCH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 154.1, 143.6, 138.1, 132.5, 129.8, 129.4, 129.0, 128.6, 126.8, 121.0, 120.8, 116.6, 67.9, 51.1, 41.4, 21.6.

The stereochemistry of **4** was established as *cis* by NOE analysis.