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A NOVEL "Ti(0)" INDUCED ALLYLATION OF IMINES IN A TiCl4 (cat.)/Al BIMETAL SYSTEM. CHIRALITY TRANSFER OF *l*-VALINE TO HOMOALLYLAMINE

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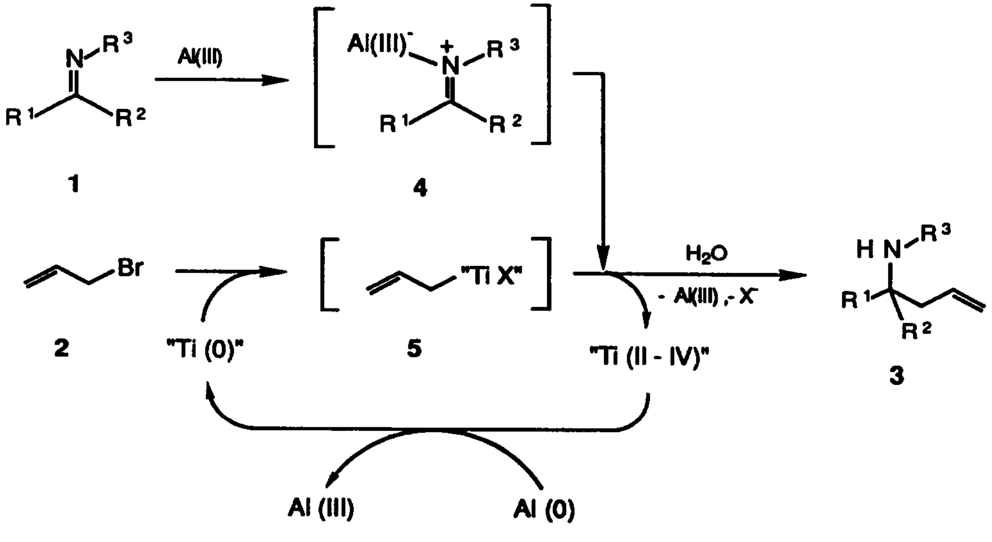
"Barbier Type" allylation of imines with allyl bromide has been performed successfully by the action of aluminum (1 equiv.) and titanium(IV) chloride (0.05 equiv.) in THF. The chirality transfer of α-amino acid esters to homoallyl amines is demonstrated by allylation of *N*-benzalvaline methyl ester followed by alkaline hydrolysis and electrolytic decarboxylation.

Low valent titanium, "Ti(0)", generated by the reduction of titanium(III or IV) salts with appropriate reductants, e.g., Mg,[1] Mg-Hg,[2] Zn,[3] and $LiAlH_4$,[4] has been widely utilized in modern organic synthesis. The low valent titanium "Ti(0)"[5] has always been prepared immediately before use. Therefore, the hitherto disclosed "Ti(0)"-promoted reactions are stoichiometric with respect to titanium and no successful attempt to recycle use of "Ti(0)" has been recorded,[6] presumably because of lack of proper reducing agents for regeneration of "Ti(0)" in the reaction media. Herein, we disclose the first example of a catalytic use of titanium which can effect "Barbier Type" allylation of imines **1** in combination with aluminum metal (reducing agent) (Scheme 1).



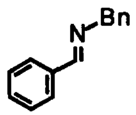
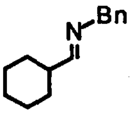
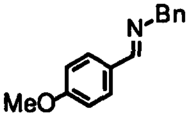
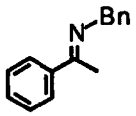
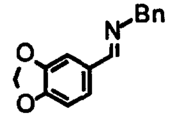
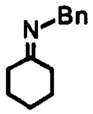
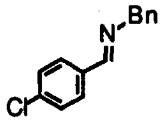
Scheme 1

A typical reaction procedure is as follows: Into a mixture of imine **1a** (R^1 = Ph, R^2 = H, R^3 = Bn; 196 mg, 1 mmol) and finely cut aluminum foil (27 mg, 1 mmol) in dry THF (4 ml) were successively added allyl bromide **2** (0.27 ml, 3 mmol)[7] and titanium(IV) chloride (0.05 mmol) at room temperature. After being stirred for 8 h, the mixture was poured into aqueous 5% sodium hydroxide and the usual workup afforded homoallylamine **3a** (R^1 = Ph, R^2 = H, R^3 = Bn; 83%).

The presence of a catalytic amount of titanium(IV) chloride is indispensable; otherwise, no detectable amount of product **3a** was obtained. Although the role of titanium(IV) chloride is still equivocal, it is likely that reduction of titanium(IV) with aluminum(0) provides low valent titanium "Ti(0)" [8] together with Al(III), former of which reacts with allyl bromide to give allyl metal reagent **5** (Scheme 1). The Al(III) salts accumulated in the media would work as a Lewis acid to form iminium ions **4** which would, in turn, undergo allylation with **5**, leading to **3**. The titanium salts "Ti(II-IV)", liberated in the final stage, would be again submitted to the reduction with aluminum(0).

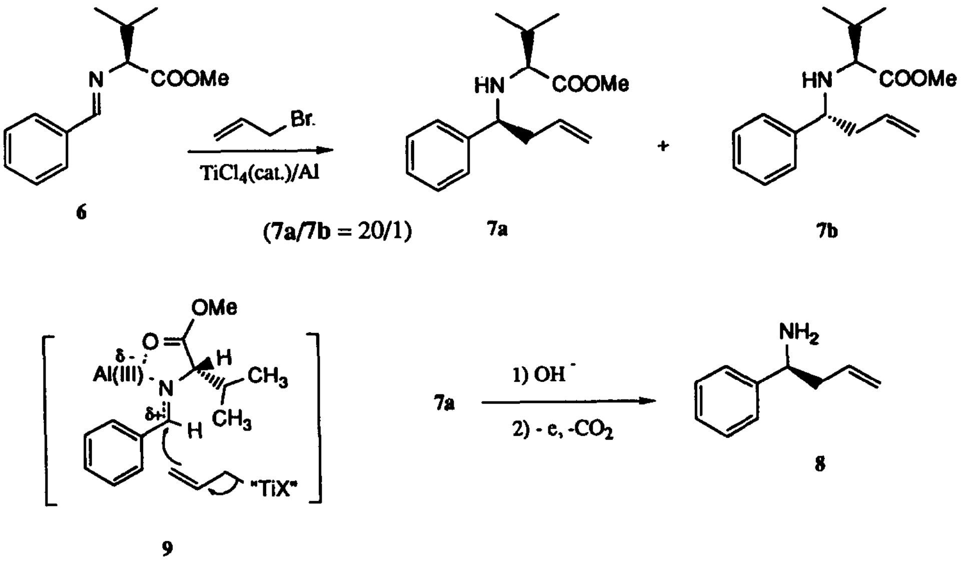
The reductive allylation in a $TiCl_4$(cat.)/Al system can be applied to various aldimines and ketimines **1**. Some of the results are indicated in Table 1.

Table 1. Allylation of Imines with Allyl Bromide in a $TiCl_4$(cat.)/Al/THF System[a]

Entry	Imine **1**	Yield /%[b]	Entry	Imine **1**	Yield /%[b]
1		83	5		75
2		85	6		55
3		91	7		67
4		84			

a) Carried out in the manner as described in the text. b) Isolated yields after column chromatography (SiO_2, hexane/benzene).

Chirality transfer of *l*-valine into homoallyl amine can be performed successfully by the $TiCl_4$(cat.)/Al-promoted allylation of *N*-benzal-*l*-valine methyl ester **6** followed by alkaline hydrolysis and electrolytic decarboxylation (Scheme 2). Thus, reaction of imine **6** with allyl bromide **2** (1.25 equiv.) in a $TiCl_4$(cat.)/Al/THF system at ambient temperature for 5 h afforded a 20:1 mixture of the adducts **7a** and **7b**[9] in 81% yield. The stereochemical outcome observed might be explained by assuming an acyclic transition model **9**. After column chromatography (SiO_2; hexane/AcOEt: 5/1), the major product **7a** (1 mmol) was submitted to alkaline hydrolysis [KOH (2 mmol)/ EtOH (3 ml), 12 h]. The alkaline solution was concentrated *in vacuo* and the residue was electrolyzed in a water (5 ml)/CH_2Cl_2 (5 ml) two phase solution with two platinum electrodes (3 cm^2 each). Regulated dc power (10 mA/cm^2) was supplied at ambient temperature for 3 h to afford homoallylamine **8** (81% from **7a**): $[\alpha]^{25}_D$ 44.6 (c 2.7, $CHCl_3$).



Scheme 2

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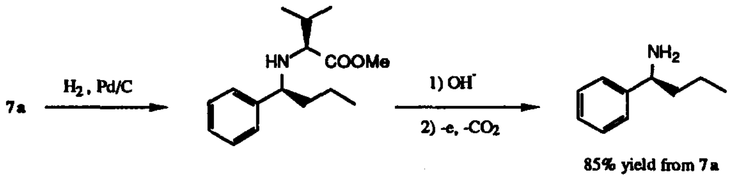
3) T. Mukaiyama, T. Sato, and J. Hanna, *Chem. Lett.*, **1973**, 1041.
4) J. E. McMurry and M. P. Fleming, *J. Am. Chem. Soc.*, **96**, 4708 (1974); J. E. McMurry, *Acc. Chem. Res.*, **16**, 405 (1983).
5) The valence of the low valent titanium "Ti(0)", generated by the reaction of titanium(IV or III) chlorides with various reducing agents, has not been specified (ref. 1-4).
6) For an exception to this statement, a Ti(III)/Ti(IV) redox mediatory system has been used as an electron transfer catalyst in electroreductive amination of dienes: T. Chiba and Y. Takata, *Bull. Chem. Soc. Jpn.*, **51**, 1418 (1978).
7) A similar reaction of **1a** with 1.25 equiv. bromide **2** afforded the adduct **3a** in 76% yield.
8) Reaction of $TiCl_4$ with 1/3 and 2/3 molar equiv. of Al in THF, formally corresponding to one and two electron reduction, provided suspensions of different color; green (Ti(III)?) and blue (Ti(II)?), each of which was treated with a mixture of imine **1a** and bromide **2** (1:1) to afford no appreciable adduct **3a**. On the other hand, the suspensions similarly obtained by the reaction of $TiCl_4$ with Al (1/1 and 4/3 molar equiv.) in THF, could effect the allylation but yields of the adduct **3a** (29% and 38%) were much less than that attained by the catalytic procedure (Table 1, entry 1). It can, therefore, be assumed that only low valent titanium, Ti(0) (or Ti(I) ?), freshly generated on the aluminum surface, may effectively promote the allylation (Scheme 1).
9) ^{1}H NMR (500 MHz, $CDCl_3$): **7a**, δ 0.85 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 1.78-1.85 (m, 1H), 1.99 (br. s, 1H), 2.27-2.42 (m, 2H), 2.78 (d, *J* = 6.2 Hz, 1H), 3.50 (dd, *J* = 4.2, 5.3 Hz, 1H), 3.70 (s, 3H), 5.09 (d, *J* = 10.2 Hz, 1H), 5.12 (d, *J* = 17.2 Hz, 1H), 5.69-5.77 (m, 1H), 7.21-7.35 (m, 5H); **7b**, δ 0.91 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 1.57 (br. s, 1H), 1.85-1.92 (m, 1H), 2.36-2.51 (m, 2H), 3.01 (d, *J* = 6.0 Hz, 1H), 3.47 (s, 3H), 3.58 (dd, *J* = 6.7, 6.8 Hz, 1H), 4.99 (d, *J* = 9.8 Hz, 1H), 5.05 (d, *J* = 17.1 Hz, 1H), 5.66-5.75 (m, 1H), 7.20-7.32 (m, 5H). The absolute configuration of **7a** was determined by transformation of **7a** into (1*S*)-1-phenylbutylamine, $[\alpha]_D$ -21.3° (*c* 1.3, $CHCl_3$) [lit.[10] $[\alpha]_D$ -22.2° (*c* 5.1, $CHCl_3$)], through hydrogenation, alkaline hydrolysis, and electrodecarboxylation:



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