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Indium-Mediated Allylation of Aldimines

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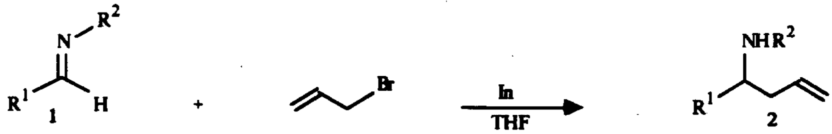
Abstract : *Aldimines are allylated under simple Barbier type conditions using allyl bromide and indium powder in THF.*

Addition of carbon nucleophiles to the imine function and its derivatives constitutes an important method for the preparation of secondary amines,[1] which has been well investigated both in terms of stereocontrol [2] and of asymmetric induction.[3] Mainly alkyl organolithiums and Grignard reagents have been used as carbon nucleophiles, although some attention has also been paid to allylic derivatives. While aldehydes and ketones have been allylated by many reagents,[4] aldimines are most commonly allylated by magnesium [5] and boron reagents [6] (allyl boronates and allyl-9-BBN). In some cases, allyl-zinc,[7] allylstannane,[8] an allyl-lead reagent,[9] as well as electrochemically generated intermediates,[10] allyl bromide-Al/$TiCl_4$,[11] and allylcuprates [12] have also been used.

Among the metallic elements which were successfully used for the allylation of carbonyl compounds to yield homoallylic alcohols, indium has enabled very mild and operationally simple reaction conditions.[4a] However, the use of this metal in organic chemistry has received only scant attention.[10] We report herein that aldimines are efficiently allylated by indium under simple Barbier type conditions.

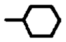
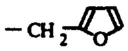
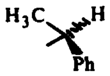
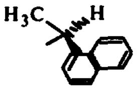
Allyl bromide (2.25 mmol) was added to a mixture of imine 1 (1 mmol) and indium powder [14] (1 mmol) in anhydrous THF (2 ml). After stirring at room temperature under nitrogen for the indicated time (see Table), 5 % aqueous sodium carbonate was added. Extractive isolation using ether, followed by purification by preparative TLC on silica gel, afforded the secondary homoallyl amines 2.



The aldimines were mainly prepared in this study from aromatic aldehydes. In cases where R¹ is an α,β-unsaturated group, the amine 2 resulting from a 1,2-addition was obtained and no 1,4-addition was observed. This contrasts with the reaction of organolithiums where both 1,2- and 1,4-addition occur.[7,15] Aldimines prepared from an aromatic amine such as aniline (entries 1-3) were found to give the highest yields with short reaction times. On the other hand, when R² has a sp^3 carbon linked to nitrogen, yields were substantially lower and longer reaction times were required. Furthermore, when this sp^3 carbon linked to nitrogen was di- or trisubstituted, corresponding aldimines proved generally to be the less reactive, leading to poor yields and uncomplete reactions (entries 6,7,9,10).

Furthermore, some stereocontrol (ca. 4 : 1) was obtained when a chiral imine derived from (S)-1-phenylethylamine was used (entry 9). However, the selectivity was not improved when the phenyl substituent of the chiral amine was replaced by the more bulky 1-naphthyl group (entry 10).

Table. Indium-mediated allylation of aldimines 1 by allyl bromide in THF.

Entry	R^1	R^2	Time (hrs)	Yield (%)
1	Ph	Ph	1	91
2		Ph	2	75
3		Ph	1.5	70
4	Ph	CH_2Ph	12	42
5	Ph	CH_3	24	49
6	Ph		24	30 a)
7	Ph	t-Bu	15	32 a)
8	Ph		2	58
9	Ph		15	25 a,b)
10	Ph		36	13 a,c)
11	- CH = CH -	- $CHPh_2$	1.5	52[16]

a) A partial reaction was observed. For these cases, starting imine and homoallyl amine have close polarities, so the amine was separated by an acid-base treatment before further purification.

b) A ca. 4 : 1 mixture of diastereomeric amines[d] was obtained.

c) A ca. 2 : 1 mixture of diastereomeric amines[d] was obtained.

d) The configuration of these amines was not determined.

In summary, metallic indium was found to mediate the allylation of a variety of aldimines under mild and simple operating conditions. Furthermore, in contrast to some other reagents, no additional Lewis acid was required.[8,9,11] Extension to substituted allylic reagents and determination of the stereochemistry of the resulting amines will be investigated.

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