



# Indium mediated allylation of C=N compounds in aqueous media

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Received 21 December 1999; revised 8 June 2000; accepted 27 September 2000

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## Abstract

Allylindium adds to a variety of tosyl and aryl hydrazones derived from aromatic aldehydes and ketones at ambient temperature in a DMF–H<sub>2</sub>O solvent system to afford homoallylic tosyl hydrazides and homoallylic hydrazines, respectively. Homoallylic hydroxylamines were isolated via addition of allylindium to aldonitrones. © 2000 Elsevier Science Ltd. All rights reserved.

*Keywords:* hydrazones; nitrones; allylindium.

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Organometallic reactions in aqueous media have recently found considerable application in organic synthesis as they offer significant advantages over conventional reactions using dry organic solvents. The metal mediated addition of an allylic moiety into a carbon framework is of particular interest and among various metals employed for this purpose,<sup>1</sup> indium attracts unique attention<sup>2</sup> due to the distinct advantages it offers in comparison with other metals such as Zn, Mg and Sn. C–N unsaturated compounds are good electrophiles<sup>3</sup> capable of reacting with organometallic compounds and allyl-indium reagents have been successfully added to various C–N unsaturated groups such as imines and nitriles, to generate a host of compounds bearing the homoallylic group. In continuation of our efforts for convenient metal mediated organic transformations,<sup>4</sup> we report here indium mediated allylation of C=N systems that have not been studied so far, such as tosyl and aryl hydrazones and aldonitrones in a DMF–water system.

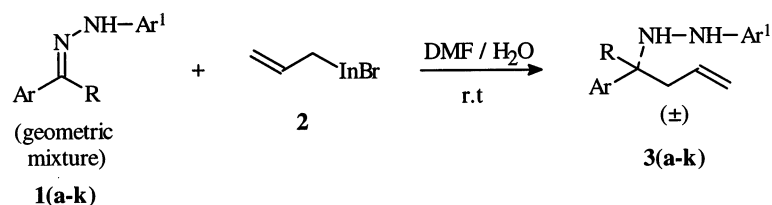
An allylindium reagent generated in situ readily undergoes addition to the ‘C=N’ bond of tosyl hydrazones in a DMF–H<sub>2</sub>O system at ambient temperature (Scheme 1).

Moderate to high yields of homoallylic tosyl hydrazides were isolated after 7–13 h of reaction. The product formation was ascertained by TLC monitoring and the product isolation was achieved by quenching the reaction with aqueous ammonium chloride solution followed by solvent extraction. The reactions are generally clean and no trace of *N*-allylated product could

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† IICT Communication No. 4289.



Scheme 1.

be detected in the  $^1\text{H}$  NMR spectra of the crude products. However, purification wherever necessary was performed by flash chromatography. On the basis of the good results obtained with sulfonyl hydrazones it seemed logical to investigate the possibility of extending this methodology to simple aryl substituted hydrazones, which gave unsymmetric homoallylic hydrazines in good yields. These results are summarised in Table 1, which clearly indicate that the present strategy becomes a general allylation protocol for a variety of tosyl and aryl hydrazones derived from different aldehydes and ketones.<sup>8a‡</sup>

Table 1  
Reaction of allylindium reagent with aryl and tosyl hydrazones<sup>a</sup>

Entry	Ar	R	Ar <sup>1</sup>	Reaction <sup>b</sup> time (h)	Yield <sup>c,d</sup> (%)
a	C <sub>6</sub> H <sub>5</sub>	H	SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	8	89
b	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	H	SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	10	83
c	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	H	SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	9	82
d	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H	SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	11	80
e	3,4-(OCH <sub>2</sub> O)C <sub>6</sub> H <sub>3</sub>	H	SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	10	80
f	4-ClC <sub>6</sub> H <sub>4</sub>	H	SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	12	75
g	3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	H	SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	13	77
h	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	7	77
i	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	8	90
j	C <sub>6</sub> H <sub>5</sub>	H	C <sub>6</sub> H <sub>5</sub>	8	85
k	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	H	C <sub>6</sub> H <sub>5</sub>	10	88

<sup>a</sup> Prepared by standard literature methods.<sup>4</sup>

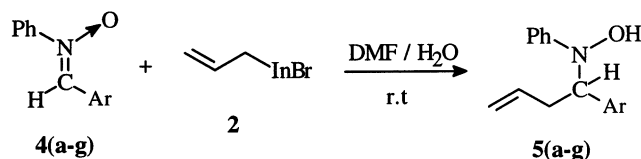
<sup>b</sup> Reactions carried out at room temperature (25°C).

<sup>c</sup> All products were characterised by  $^1\text{H}$  NMR and Mass spectrometry.

<sup>d</sup> Yields of the product after chromatography.

Homoallylic hydroxylamines are synthetically valuable intermediates<sup>5</sup> which can be generated through the allylation of aldonitrones which also act as good electrophiles for organometallic additions.<sup>6</sup> Even though this reaction has been reported using metals such as Zn, Mg and Sn in dry organic solvents, the same has not been investigated under aqueous conditions. We found that various aldonitrones derived from aromatic aldehydes undergo allylation when reacted with a stoichiometric quantity of the allylindium reagent (generated in situ) in a DMF–H<sub>2</sub>O system at ambient temperature (Scheme 2).<sup>8b</sup>

<sup>‡</sup> One limitation of the present methodology is that the reaction does not work with aliphatic hydrazones, as these do not work under these reaction conditions.



Scheme 2.

The results summarised in Table 2 reveal the generality of this methodology in terms of structural variations of the nitronone moiety and in each case homoallylic hydroxylamines were isolated in good yields (75–90%) within 3–4 h of reaction time.

Table 2  
Reaction of allylindium reagent with aldonitrones<sup>a</sup>

Entry	R	Reaction <sup>b</sup> time (h)	Yield <sup>c,d</sup> (%)
a	C <sub>6</sub> H <sub>5</sub>	3	90
b	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	3	86
c	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	3.5	85
d	4-ClC <sub>6</sub> H <sub>4</sub>	4	84
e	3-HOC <sub>6</sub> H <sub>4</sub>	4	75
f	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	3	76
g	3,4-(OCH <sub>2</sub> O)C <sub>6</sub> H <sub>3</sub>	3	88

<sup>a</sup> Prepared by standard literature methods.<sup>7</sup>

<sup>b</sup> Reactions carried out at room temperature (25°C).

<sup>c</sup> All products were characterised by <sup>1</sup>H NMR and Mass spectrometry studies.

<sup>d</sup> Yields of the product after chromatography.

In conclusion we present in this paper a high yielding allylation procedure for tosyl/aryl hydrazones and aldonitrones in a DMF–H<sub>2</sub>O system to generate structurally interesting homoallylic nitrogen compounds.

## Acknowledgements

S.A and E.J.R thank CSIR New Delhi for the award of fellowships.

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8. (a) In a typical procedure a suspension of indium powder (1.14 g, 10 mmol) and allyl bromide (1.2 g, 10 mmol) taken in 20 ml of DMF–H<sub>2</sub>O 15:5, was stirred until the metal dissolved completely to form a clear solution. To the allyl indium reagent generated as above, a solution of hydrazone (**1a**, 2.74 g, 10 mmol) in DMF (10 ml) was added. The resulting reaction mixture was stirred for 8 h at room temperature. The reaction was then quenched with aqueous ammonium chloride (10%, 20 ml) followed by extraction with ether (2×20 ml). The combined ether extract was washed with brine (2×10 ml), dried over anhydrous sodium sulfate and the residue obtained after evaporation of solvent was chromatographed on silica gel [Merck (finer than 200 mesh) EtOAc–*n*-hexane 1:4] to afford pure product (**3a**) as a colourless crystalline solid. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.15–2.30 (m, 2H), 2.40–2.50 (s, 3H), 4.00–4.10 (t, *J*=7.2 Hz, 1H), 5.00–5.20 (m, 2H), 5.65–5.90 (m, 1H), 7.20–7.40 (m, 5H), 7.50–7.60 (m, 2H), 7.80–7.90 (d, *J*=7.7 Hz, 2H), 8.60 (brs, NH). MS: *m/z* 316 (M<sup>+</sup>, 8%), 131 (100%), 116 (8%), 91 (80%), 77 (10%).  
(b) In a typical procedure, a suspension of indium powder (1.14 g, 10 mmol) and allyl bromide (1.2 g, 10 mmol) taken in 20 ml of DMF–H<sub>2</sub>O 15:5, was stirred until the metal dissolved completely to form a clear solution. To the allyl indium reagent, generated as above, a solution of aldonitrone (**4a**, 1.97 g, 10 mmol) in DMF (10 ml) was added. The resulting reaction mixture was stirred for 3 h at room temperature. The reaction was then quenched with aqueous ammonium chloride (10%, 20 ml) followed by extraction with ether (2×20 ml). The combined ether extract was washed with brine (2×10 ml), dried over anhydrous sodium sulfate and the residue obtained after evaporation of solvent was chromatographed on silica gel [Merck (finer than 200 mesh) EtOAc–*n*-hexane 1:4] to afford pure product (**5a**). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.50–2.70 (m, 2H), 4.30–4.40 (t, *J*=7.2, 1H), 5.05–5.25 (m, 2H), 5.60–5.80 (m, 1H), 6.45–6.60 (d, *J*=8.6 Hz, 2H), 6.65–6.70 (t, *J*=7.2 Hz, 1H), 7.00–7.10 (t, *J*=7.2 Hz, 2H), 7.20–7.40 (m, 6H). MS: *m/z* 238 (M<sup>+</sup>, 23%), 182 (100%), 131 (61%), 104 (31%), 91 (23%), 77 (49%), 41 (13%).