

Communications

Mild and Efficient Debromination of *vic*-Dibromides to Alkenes with NiCl₂·6H₂O/Indium System

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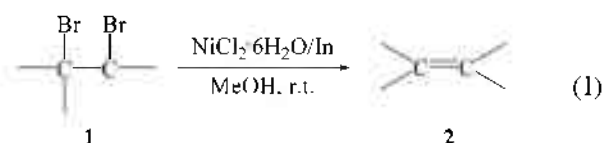
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The debromination of *vic*-dibromides to alkenes is important in organic synthesis as a double bond protection-deprotection strategy.¹ Although reductive debromination of *vic*-dibromides with various agents has been the subject of many reports, some of these methods are associated with limitations regarding low yields, prolonged reaction times, and harsh reaction conditions.² Consequently an efficient and mild procedure for debromination of *vic*-dibromides continues to be developed. The chemical reactivity of NiCl₂/M system (M = Zn, Al, Sm) has been the subject of considerable interest and the reducing ability of these systems has been extensively studied.³ Because of the close resemblance of indium to zinc in several respects, including first ionization, we considered that NiCl₂·6H₂O/In system could also be a useful addition to the conventional method. Recently, indium metal has drawn an increasing attention for its unique properties such as low toxicity and high stability in water and air compared with other metals.⁴



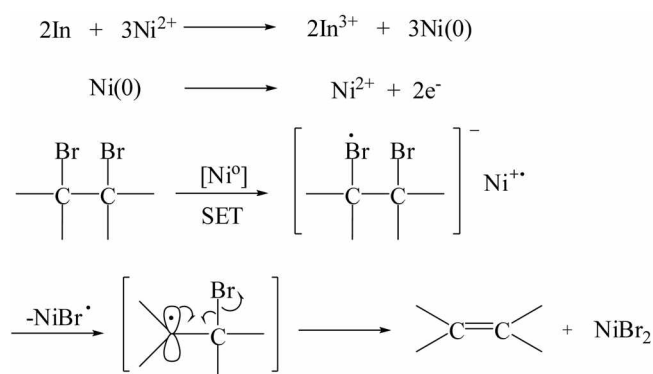
In continuation of our efforts towards the development of the low-valent metal reagents for organic transformations,⁵ we wish to report a mild and efficient procedure for debromination of *vic*-dibromides **1** to the corresponding alkenes **2** with NiCl₂·6H₂O/In system in methanol at room temperature. The reaction can be generalized as in eq. (1).⁶ The new reagent system was generated by the addition of indium powder to a stirred solution of nickel chloride hexahydrate in methanol under sonication.⁷ We have investigated the reactions of NiCl₂·6H₂O/In system with various *vic*-dibromides and observed that the debrominations generally proceeded with high yields and good selectivity over other labile substituents. Some control experiments revealed that *vic*-dibromides could not be debrominated by nickel chloride hexahydrate or indium alone under the reaction conditions. The high yields of the debromination products demonstrate the efficiency of this new method. A 2:1 ratio of

indium and NiCl₂·6H₂O was the best ratio in terms of yield and reaction time. And methanol has been found to be the most suitable solvent for the reaction. The result of this reduction is summarized in Table 1, where we examined a series of functionally and sterically diverse *vic*-dibromides.

Table 1. Reductive debromination of *vic*-dibromides with NiCl₂·6H₂O/In system

Entry	Substrate	Product	Reaction Time (hr)	Yield (%) ^a
1			0.5	95
2			0.5	92
3			2.0	91
4			1.0	85
5			1.5	86
6			0.5	90
7			1.0	88
8			2.0	87
9			1.5	86
10			1.0	85
11			0.5	82

^aIsolated yields.



Scheme 1

Clearly a broad range of functional groups (ester, acid, aldehyde, methoxy, chloro, and ketone) was tolerated under the reaction conditions and only *trans* olefins were obtained. There was no evidence for the formation of any over-reduction product. The formation of the reduced products can be conceived to proceed via alkenes by debromination of the dibromides and subsequent reduction as Khurana has suggested in his work.⁸ In comparison with other procedures, the present procedure reduces *vic*-dibromides in higher yields and showed a good chemoselectivity under mild conditions. The notable advantages of this methodology are mild reaction conditions, simple manipulation, high yields, and tolerance of various functional groups. All the compounds obtained showed IR, NMR and mass spectral data compatible with the structure. Some of the *vic*-dibromides in the table are commercially available, or could be prepared conveniently from the corresponding precursors through known olefin halogenation reactions.⁹ Although the reaction mechanism is still unclear, the reaction can be envisaged to proceed in two stages. In the first, nickel(II) chloride is probably reduced by indium to form low-valent nickel species, which in the subsequent step would debrominate *vic*-dibromides **1** to give the corresponding alkenes **2** through a SET (single electron transfer) process (Scheme 1). The reducing property exhibited by metal-metal salt combinations proceeds through transfer of one electron from the metal surface to the substrate. In such combinations elementary metal part needs to be more electropositive than the metal part of the salt.¹⁰ We have been able to demonstrate the utility of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ /indium system for effecting chemoselective debromination of *vic*-dibromides.

In conclusion, we have discovered that $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ /In system mediates an efficient and mild conversion of *vic*-dibromides to the corresponding alkenes with high yields.

Although the scope and limitations were not fully established, the present method could be a practical alternative to the conventional methods.

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- A typical procedure for the debromination of *vic*-dibromides is as follows: Indium powder (230 mg, 2.0 mmol), and nickel(II) chloride hexahydrate (238 mg, 1.0 mmol) were mixed in methanol (4 mL). The resulting mixture was stirred at room temperature for 0.5 hr under sonication to get a solution of the low-valent nickel-indium complex. 1,2-Dibromo-methylbenzene (264 mg, 1.0 mmol) was then added to this solution and the reaction mixture was stirred for 30 min. at room temperature. The solvent was removed under reduced pressure and the residue was extracted with ether, washed with brine, and dried over anhydrous Na_2SO_4 . The crude product was purified by silica gel column chromatography (hexane:ethyl acetate = 10:1) to afford styrene (99 mg, 95%). All of the products are commercially available compounds, and their identification was based on spectral comparison with authentic samples.
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