

Rapid and Efficient Debromination of *vic*-Dibromides with VCl_3 /Indium System

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ABSTRACT. The VCl_3/In system was found to be a new protocol for debromination of a variety of *vic*-dibromides to the corresponding alkenes in high yields with short reaction times under mild conditions. This new methodology is highly chemoselective, tolerating several functional groups such as chloro, bromo, fluoro, keto, ester, carboxyl, and methoxy groups.

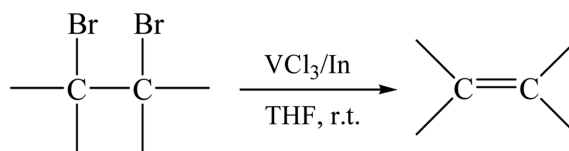
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INTRODUCTION

The protection and deprotection of double bonds *via* bromination-debromination strategy can conveniently be utilized in organic synthesis.¹ Although debromination reactions of *vic*-dibromides effected by various reagents have been reported previously, many of these methods suffer from one or more drawbacks such as low yields, long reaction times, poor chemoselectivity, and harsh reaction conditions.² As a consequence, there has been a search for the development of new improved methods for this conversion.

The chemical reactivity of VCl_3/Zn system has been the subject of considerable interest and the reducing ability of this system has been extensively studied.³ Low-valent vanadium reagents generated from vanadium(III) chloride and zinc serve as versatile one-electron reductant, but their synthetic utility in this respect has been limited. One-electron reduction has synthetic potential for the generation of radical intermediates. It has been reported that VCl_3/Zn system can be used as a reagent for the stereoselective debromination of *gem*-dibromocyclopropanes.⁴ We considered that VCl_3/In system could be a protocol for the debromination of *vic*-dibromides. To the best of our knowledge, there is no report in which VCl_3/In system is used as a reagent for reductive debromination of *vic*-dibromides to alkenes. The reaction can be generalized as shown by Scheme 1.

Over the past several decades, indium metal has attracted great interest in organic synthesis owing to its intriguing properties.⁵ As in the case of zinc, the reduction potential of indium is not too negative ($E^\circ(\text{In}^{3+}/\text{In}) = -0.345 \text{ V}$; $E^\circ(\text{Zn}^{2+}/\text{Zn}) = -0.763 \text{ V}$) and thus it is not only stable in the



Scheme 1. Conversion of *vic*-dibromides to alkenes.

air, but also practically inert in water. Moreover, indium metal apparently has no significant toxicity.⁶ As a part of our ongoing research program to explore highly efficient low valent metal for useful organic transformations,⁷ we report here a rapid and efficient procedure for debromination of *vic*-dibromides to the corresponding alkenes with VCl_3/In system.

EXPERIMENTAL

General

All commercial reagents were purchased from Aldrich and Fluka Chemical Company and used without any further purification. NMR spectra were recorded on a FT-Bruker AF-300 (300 MHz for ^1H NMR; 75 MHz for ^{13}C NMR) in CDCl_3 using TMS as an internal standard. Mass spectra were recorded on a Shimadzu GC MS-QP 1000 PX at 70 eV. TLC analysis was performed on silica gel plates (Merck, 60 F-254). All products were purified by flash column chromatography using silica gel 60 (79-230 mesh, Merck).

General Procedure for the Reaction

A 10-mL round-bottomed flask was charged with indium powder (230 mg, 2.0 mmol), vanadium trichloride (157 mg, 1.0 mmol) and THF (4 mL). The resulting mixture was

stirred for 30 min under sonication producing a solution of the low-valent vanadium-indium complex. 1,2-Dibromo-1,2-diphenylethane (170 mg, 0.5 mmol) was then added to this solution and the reaction mixture was stirred for 3 min at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure and the residue was then extracted with ethyl acetate (3×10 mL). The combined extract was washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The crude product was further purified by column chromatography on a silica gel (hexane:ethyl acetate = 10:1) to provide *trans*-stilbene (85 mg, 94%). All the products were identified by comparison of their spectroscopic data with authentic compounds.

Spectroscopic Data of Products

4-Chlorostyrene (Entry 1): ^1H NMR (300 MHz, CDCl_3): δ 7.24–7.34 (m, 4H), 6.64 (dd, 1H, $J = 17.6, 11.1$ Hz), 5.71 (d, 1H, $J = 17.8$ Hz), 5.25 (d, 1H, $J = 11.1$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ 136.0, 135.6, 133.4, 128.6, 127.4, 114.4. GC/MS (m/z): 138 (M^+), 140 ($\text{M}+2$).

4-Bromostyrene (Entry 2): ^1H NMR (300 MHz, CDCl_3): δ 7.45 (d, 2H, $J = 9.6$ Hz), 7.23 (d, 2H, $J = 9.6$ Hz), 6.63 (dd, 1H, $J = 17.6, 11.1$ Hz), 5.71 (d, 1H, $J = 17.6$ Hz), 5.25 (d, 1H, $J = 11.1$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ 136.4, 135.7, 131.6, 127.7, 121.5, 114.5. GC/MS (m/z): 183 (M^+), 185 ($\text{M}+2$).

4-Fluorostyrene (Entry 3): ^1H NMR (300 MHz, CDCl_3): δ 7.40–7.35 (m, 2H), 7.04–6.98 (m, 2H), 6.68 (dd, 1H, $J = 17.7, 11.1$ Hz), 5.66 (d, 1H, $J = 17.7$ Hz), 5.22 (d, 1H, $J = 10.8$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ 164.1, 135.7, 133.8, 127.8, 115.5, 113.4. GC/MS (m/z): 122 (M^+).

***trans*-Stilbene (Entry 4):** ^1H NMR (300 MHz, CDCl_3): δ 7.23–7.54 (m, 10H), 7.06 (s, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ 137.3, 128.6, 128.5, 127.5, 126.4. GC/MS (m/z): 180 (M^+).

4-Allylanisole (Entry 5): ^1H NMR (300 MHz, CDCl_3): δ 7.08 (d, 2H, $J = 8.4$ Hz), 6.82 (d, 2H, $J = 8.4$ Hz), 6.00–5.86 (m, 1H), 5.06–5.01 (m, 2H), 3.77 (s, 3H), 3.31 (d, 2H, $J = 6.9$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ 157.9, 137.8, 132.0, 129.4, 115.3, 113.8, 55.2, 39.2. GC/MS (m/z): 148 (M^+).

Indene (Entry 6): ^1H NMR (300 MHz, CDCl_3): δ 7.18–7.51 (m, 4H), 6.89–6.92 (m, 1H), 6.56–6.59 (m, 1H), 3.42 (s, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ 144.7, 143.5, 134.0, 131.9, 126.0, 124.4, 123.6, 120.8, 39.0. GC/MS (m/z): 116 (M^+).

4-Acetoxystyrene (Entry 7): ^1H NMR (300 MHz, CDCl_3): δ 7.42 (d, 2H, $J = 8.7$ Hz), 7.05 (d, 2H, $J = 8.7$ Hz), 6.71

(dd, 1H, $J = 17.4, 11.1$ Hz), 5.72 (d, 1H, $J = 17.4$ Hz), 5.25 (d, 1H, $J = 11.1$ Hz), 2.30 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 169.3, 150.1, 135.8, 135.2, 127.1, 121.6, 113.9, 21.1. GC/MS (m/z): 162 (M^+).

5-Dibenzosuberone (Entry 8): ^1H NMR (300 MHz, CDCl_3): δ 7.51–8.23 (m, 8H), 7.26 (s, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ 182.5, 138.1, 132.3, 130.8, 129.7, 128.0, 127.6, 127.0. GC/MS (m/z): 206 (M^+).

***trans*-Chalcone (Entry 9):** ^1H NMR (300 MHz, CDCl_3): δ 8.05 (d, 1H, $J = 8.7$ Hz), 7.41–7.83 (m, 11H). ^{13}C NMR (75 MHz, CDCl_3): δ 190.4, 144.7, 138.0, 134.8, 132.7, 130.4, 128.8, 128.5, 128.4, 128.3, 122.0. GC/MS (m/z): 208 (M^+).

Methyl *trans*-cinnamate (Entry 10): ^1H NMR (300 MHz, CD_3OD): δ 7.70 (d, 1H, $J = 15.1$ Hz), 7.36–7.54 (m, 5H), 6.42 (d, 1H, $J = 15.1$ Hz), 3.81 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 167.3, 144.7, 134.2, 130.2, 128.8, 127.9, 117.7, 51.7. GC/MS (m/z): 162 (M^+).

***trans*-4-Phenyl-3-buten-2-one (Entry 11):** ^1H NMR (300 MHz, CDCl_3): δ 7.38–7.56 (m, 6H), 6.72 (d, 1H, $J = 16.2$ Hz), 2.39 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 198.2, 143.3, 134.2, 130.4, 128.9, 128.1, 127.0, 27.5. GC/MS (m/z): 146 (M^+).

***trans*-Cinnamic acid (Entry 12):** ^1H NMR (300 MHz, CD_3OD): δ 11.18 (br, 1H), 7.82 (d, 1H, $J = 15.3$ Hz), 7.15–7.68 (m, 5H), 6.53 (d, 1H, $J = 15.3$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ 172.7, 147.0, 133.9, 130.7, 128.9, 128.3, 117.2. GC/MS (m/z): 148 (M^+).

RESULTS AND DISCUSSION

The new reducing system was readily generated by the addition of indium powder to a solution of vanadium (III) chloride in tetrahydrofuran (THF) under sonication.⁸ Treatment of *vic*-dibromides with VCl_3/In system at room temperature resulted in formation of the corresponding alkenes in high yields within a short period of time. To optimize the reaction condition, the amounts of VCl_3 and indium were varied and the optimum molar ratio of VCl_3 to indium (1:2) was found to be suitable in terms of yield and reaction time. With the optimized reaction conditions in hand, functionally and structurally diverse *vic*-dibromides as substrates for debromination were examined in an effort to elucidate the scope and limitations of this reaction. The representative results are summarized in Table 1.

The functional group tolerance of this method is evident from Table 1 which showed that chloro, bromo, fluoro, keto, ester, carboxyl, and methoxy groups are unaffected under the reaction conditions. It is worthwhile to note that the

Table 1. Reductive debromination of vic-dibromides with VCl₃/indium system

| Entry | Substrate | Product ^a | Time (min) | Yield(%) ^b |
|-------|-----------|----------------------|------------|-----------------------|
| 1 | | | 3 | 95 |
| 2 | | | 3 | 93 |
| 3 | | | 3 | 95 |
| 4 | | | 3 | 94 |
| 5 | | | 10 | 91 |
| 6 | | | 5 | 92 |
| 7 | | | 5 | 93 |
| 8 | | | 3 | 91 |
| 9 | | | 5 | 88 |
| 10 | | | 3 | 91 |
| 11 | | | 5 | 89 |
| 12 | | | 3 | 90 |

^aThe products were characterized by comparison of their spectral data with authentic samples. ^bIsolated yields.

sensitive carbonyl group remains intact without reduction of C=O bond (entries 7-12). Significantly, only *trans*-olefins are observed and there is no chance of overreduction of the C=C bond formed in this process.⁹ A control experiment revealed that the reaction was not initiated at all without VCl₃. Thus, a combination of indium and vanadium (III) chloride is essential to carry out the debromination. In comparison with other procedures, the VCl₃/indium system reduced vic-dibromides more rapidly (3-10 min) in higher yields (88-95%) with a good chemoselectivity.

Although the detailed mechanism of the reaction requires more investigation, a low-valent vanadium species generated in situ by treatment with indium is likely to be involved in a single electron transfer (SET) process. The reaction is believed to proceed *via* the formation of a relatively stable radical intermediate, which directly collapses to give the alkene. It may be proposed that the presence of an aryl substitution is beneficial to the preferential radical formation at the carbon adjacent to radical stabilizing group and therefore to the reaction rate as well.

The notable advantages offered by this method are mild reaction conditions, short reaction time, high yields, no overreduction of double bonds, and tolerance to various sensitive moieties.

CONCLUSION

In conclusion, we have developed an improved method for the debromination of vic-dibromides with VCl₃/indium system. The mildness and rapidity as well as high yields make the present method highly practical for debromination of various vic-dibromides. Further investigations for the more useful applications with the system are currently in progress.

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