4102 *J. Org. Chem.* **2001,** *66,* 4102−4103

Stereoselective Reduction of Aryl-Substituted *gem*-Dibromides to Vinyl Bromides by Indium Metal

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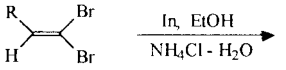
Received March 2, 2001

Vinyl bromides are very useful intermediates in organic synthesis, and thus, development of methods for their stereoselective synthesis is of much importance. One of the classical methods involves Wittig olefination of an aldehyde with bromomethylene triphenylphosphorane[1] leading primarily to *Z*-isomers. However, this method is not very convenient, as preparation of the ylide is rather complicated. Thus, reduction of *gem*-dibromides, readily available from a simple reaction of an aldehyde with carbon tetrabromide and triphenyl phosphine,[2] presents a practical alternative to the synthesis of vinyl bromides. Although a number of reagents have been reported to provide (*Z*)-[3] as well as (*E*)-vinyl bromides,[4] introduction of a simpler reagent in an environment-friendly reaction medium is still appreciated.

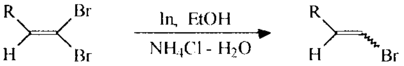
In recent times, indium has emerged as one of the metals of growing interest because of its great synthetic potential.[5] However, although indium has been used extensively in carbonyl addition reactions, its use in other domains has not been explored to any great extent.[5] Because of the close resemblance of indium to magnesium and zinc in several respects, including first ionization potential, indium could also be a potential reducing agent. Surprisingly, reduction by indium metal is virtually unexplored except for a number of recent examples.[6] This prompted us to initiate a systematic investigation into the reduction by indium metal,[6b,e] and as a part of this program we now disclose our results of reduction of *gem*-dibromides (Scheme 1).

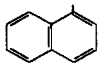
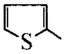
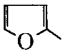
Scheme 1



(13 examples)

Table 1. Reduction of Aryl-Substituted *gem*-Dibromides to Vinyl Bromides by Indium Metal



entry	R	time (h)	yield[a] (%)	ratio of *E*/*Z*[b]	ref
1	Ph	16	95	95:5	7c
2		16	80	90:10	
3	*p*-Cl-Ph	15	92	82:18	7c
4	*p*-OMe-Ph	17	88	75:25	7c
5	*p*-Me-Ph	16	90	76:24	7c
6	*m*-Me-Ph	16	91	70:30	
7	*p*-OTBDMS-Ph	17	92	72:18	
8	*o*-O-allyl-Ph	16	85	80:20	
9	*m*,*p*-$(OMe)_2$-Ph	17	93	76:24	
10	*m*-OMe-*p*-OBz-Ph	16	90	75:25	
11	Ph-CH═CH	18	80	60:40	7d
12		15	70	50:50	
13		14	85	55:45	7f

[a] Yields refer to those of pure isolated products fully characterized by spectral data. [b] Ratio was determined by ^{1}H NMR integration of the corresponding peaks.

In a typical experimental procedure, a mixture of *gem*-dibromide (1 mmol) and indium metal (1 mmol, cut into small pieces) in ethanol and saturated ammonium chloride solution was heated under reflux for the period of time required to complete the reaction (TLC). The results are reported in Table 1.

A wide range of structurally varied aryl-substituted *gem*-dibromides underwent reductions by this procedure to provide the corresponding (*E*)-vinyl bromides predominantly in high yields. However, thiophene- and furan-substituted *gem*-dibromides (entries 12 and 13) did not show any stereoselectivity. Several sensitive functional groups such as OMe, OBz, Cl, OTBDMS, and *o*-allyl remained unaffected under the present reaction conditions. No over-reduction of the produced vinyl bromide was observed with any substrate. However, this procedure is not very effective in alkyl-substituted *gem*-dibromides. One very important aspect of this procedure is the use of aqueous medium, which is of much significance in the context of green synthesis. It may be assumed that these reductions are also going through a SET process like other metal-mediated reactions in aqueous media.

In conclusion, the present procedure provides a novel, efficient and general methodology for stereoselective reduction of aryl-substituted *gem*-dibromides to the corresponding (*E*)-vinyl bromides. To the best of our knowledge, this is the first report of indium-promoted reduction of *gem*-dibromides to vinyl bromides, and certainly it broadens the scope of indium-mediated reductions. The

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10.1021/jo0102314 CCC: $20.00

significant improvements offered by this method over existing procedures[1,3,4,7] are as follows: (a) no undesired side reaction including over-reduction, (b) mild conditions to tolerate several sensitive functional groups, (c) good stereoselectivity, (d) high yields, and (e) environment-friendly reaction conditions. Thus, this procedure is endowed with considerable synthetic potential and may provide a practical alternative to the existing methodologies.

Experimental Section

General Methods. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were run in $CDCl_3$ solutions. IR spectra were taken as thin films. Analyses were done on a Perkin-Elmer 2400 autoanalyzer. Indium metal (Ingot) was purchased from SRL, India, and was used without any treatment.

General Experimental Procedure. **Representative Procedure for the Reduction of 1,1-Dibromo-2-phenylethene.** A mixture of 1,1-dibromo-2-phenylethene (1 mmol, 262 mg) and indium metal (1 mmol, 115 mg, cut into small pieces) in ethanol (2 mL) and saturated aqueous ammonium chloride solution (2 mL) was heated under reflux for 16 h (monitored by TLC) in an oil bath (temperature 95−100 °C). The reaction mixture was then allowed to cool and extracted with ether. The ether extract was washed with brine, dried over Na_2SO_4, and evaporated to leave the crude product, which was purified by column chromatography over silica gel to furnish 1-bromo-2-phenylethene (174 mg, 95%) as an *E*/*Z* mixture (95.5 as determined by ^{1}H NMR analysis and GC). The ^{1}H and ^{13}C NMR spectra of this compound are identical with those reported.[7c]

This procedure has been followed for the conversion of all *gem*-dibromides listed in Table 1. However, for furan (entry 13) and thiophene (entry 12) derivatives purification was carried out through a column of basic alumina. All the products have been characterized by their IR and ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra.

Spectral [IR, ^{1}H (300 MHz) and ^{13}C (75 MHz)] and analytical data for new vinyl bromides, not reported in the literature, are presented below designated by their entries in Table 1.

2: IR 1600, 1587, 935 cm^{-1}; ^{1}H NMR δ 6.75 (d, J = 13.8 Hz, 1H), 7.38−7.55 (m, 5H), 7.79−7.87 (m, 3H); ^{13}C NMR δ 108.9, 124.1, 124.7, 125.9, 126.7, 126.9, 128.9, 129.2, 131.0, 133.0, 134.0, 135.5. Anal. Calcd for $C_{12}H_9Br$: C, 61.83; H, 3.80. Found: C, 62.37; H, 3.82.

6: IR 1600, 1614, 1581, 1197, 939 cm^{-1}; ^{1}H NMR δ 2.30 (s, 3H), 6.67 (d, J = 14.1 Hz, 1H), 6.95−7.24 (m, 5H); ^{13}C NMR δ 21.9, 106.8, 123.8, 127.3, 129.1, 129.5, 132.9, 135.3, 137.7. Anal. Calcd for C_9H_9Br: C, 54.85; H, 4.57. Found: C, 54.48; H, 4.54.

7: IR 1606, 1510, 1031, 948 cm^{-1}; ^{1}H NMR δ 0.00 (s, 6H), 0.78 (s, 9H), 6.38 (d, J = 13.95 Hz, 1H), 6.57−6.62 (m, 3H), 6.95 (d, J = 8.10 Hz, 2H); ^{13}C NMR δ −6.2 (2), 16.4, 23.8 (3), 102.3, 118.4 (2), 125.4 (2), 129.8, 134.7, 153.2. Anal. Calcd for $C_{14}H_{21}$-OSiBr: C, 53.67; H, 6.70. Found: C, 53.42; H, 6.77.

8: IR 1639, 1600, 1540, 1040, 965 cm^{-1}; ^{1}H NMR δ 4.50−4.53 (m, 2H), 5.25−5.41 (m, 2H), 5.99−6.02 (m, 1H), 6.80−6.98 (m, 3H), 7.17−7.35 (m, 3H); ^{13}C NMR δ 69.7, 108.3, 112.7, 118.3, 121.4, 128.4, 129.6, 130.0, 133.4, 134.3, 156.0. Anal. Calcd for $C_{11}H_{11}OBr$: C, 55.25; H, 4.60. Found: C, 54.78; H, 4.53.

9: IR 1600, 1514, 1139, 1026 cm^{-1}; ^{1}H NMR δ 3.80 (s, 3H), 3.82 (s, 3H), 6.55 (d, J = 14.1 Hz, 1H), 6.70−6.90 (m, 3H), 6.97 (d, J = 14.1 Hz, 1H); ^{13}C NMR δ 56.1, 56.2, 104.6, 109.0, 111.6, 122.3, 132.1, 137.1, 148.9, 149.7. Anal. Calcd for $C_{10}H_{11}O_2Br$: C, 49.39; H, 4.52. Found: C, 48.87; H, 4.29.

10: IR 1600, 1577, 1510, 1028, 939 cm^{-1}; ^{1}H NMR δ 3.80 (s, 3H), 5.07 (s, 2H), 6.56 (d, J = 14.1 Hz, 1H), 6.69−6.83 (m, 3H), 6.96 (d, J = 14.1 Hz, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR δ 56.4, 71.4, 104.9, 109.7, 114.2, 119.8, 127.7 (2), 128.4, 128.7, 129.0 (2), 132.3, 137.4, 148.9, 150.2. Anal. Calcd for $C_{16}H_{15}O_2Br$: C, 60.20; H, 4.70. Found: C, 60.67; H, 4.88.

Acknowledgment. We are pleased to acknowledge the financial support from CSIR, New Delhi, India, for this investigation. S.S. and S.K.G. are also thankful to CSIR for their fellowships.

JO0102314

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