ORGANIC LETTERS

2007
Vol. 9, No. 22
4427−4429

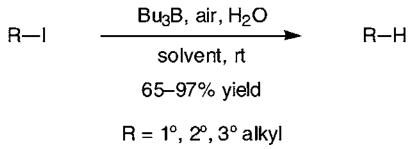
Expanding the Scope of Trialkylborane/Water-Mediated Radical Reactions

Matthew R. Medeiros, Laura N. Schacherer,[†] David A. Spiegel,[‡] and John L. Wood*

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523
john.l.wood@colostate.edu

Received July 13, 2007

ABSTRACT



$$R{-}I \xrightarrow[\text{solvent, rt}]{Bu_3B,\ air,\ H_2O} R{-}H$$

65–97% yield

R = 1°, 2°, 3° alkyl

The dehalogenation of alkyl iodides, as well as the chemoselective deoxygenation of a secondary alcohol in the presence of various alkyl and aryl halides, can be accomplished employing a trialkylborane/air/water system.

Functional group interconversions involving deamination, dehalogenation, deoxygenation, and other methods are ubiquitous in synthetic chemistry, and many useful procedures to accomplish these transformations have been developed.[1] Recently, we,[2] and others,[3] described the application of Lewis acid activated water as a hydrogen atom transfer reagent. Efforts to expand the scope of our previously disclosed radical deoxygenation reaction to dehalogenation and the fortuitous manifestation of a chemoselective deoxygenation are presented herein.

Triethylborane has been applied to halogen atom abstraction reactions to mediate intermolecular radical additions to alkenes and alkynes,[4] oxygenation of α-iodocarbonyl compounds,[5] carboazidation of olefins,[6] as well as intramolecular cyclization/atom transfer reactions.[7] This precedent, coupled with our desire to expand the application of organoboranes to radical reactions,[8] encouraged us to attempt the dehalogenation of alkyl halides.

Our initial deoxygenation studies using trialkylborane[9]/water mixtures to reduce simple alkyl bromide substrates were unsuccessful (Table 1, entries 2 and 3) but not unexpected. Typical reactions of triethylborane with alkyl bromides involve α-bromoesters,[4a] where a stabilized α-carbonyl radical is formed after halogen atom abstraction. However, given that examples of iodine atom abstraction from simple alkyl iodides are prevalent in the literature,[10] we next turned to the deiodination of alkyl iodides. In the event, attempts to dehalogenate alkyl iodides using tributylborane and water proved fruitful. The deiodination of

---

[†] Department of Chemistry, Columbia University, New York, NY, 10027.

[‡] Department of Chemistry, Yale University, New Haven, CT, 06520.

[1] Imamoto, T.; McCombie, S. W.; Fry, A. J. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991.

[2] Spiegel, D. A.; Schacherer, L. N.; Medeiros, M. R.; Wood, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 11056.

[3] (a) For evidence of a β-alkylcatecholborane/alcohol complex, see: Pozzi, D.; Scanlan, E. M.; Renaud, P *J. Am. Chem. Soc.* **2005**, *127*, 12067. (b) For evidence of the activation of water for hydrogen atom transfer by other Lewis acids, see: Cuerva, J. M.; Campaña, A. G.; Justicia, J.; Rosales, A.; Oller-López, J. L.; Robles, R.; Cárdenas, D. J.; Buñuel, E.; Oltra, J. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 5522−5526.

[4] (a) Usugi, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 2049−2052. (b) Usugi, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 2687−2690. (c) Baciocchi, E.; Muraglia, E. *Tetrahedron Lett.* **1993**, *34*, 5015−5018. (d) Baciocchi, E.; Muraglia, E. *Tetrahedron Lett.* **1994**, *35*, 2763−2766. (e) Miura, K.; Takeyama, Y.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1542−1553. (f) Nakamura, T.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Synlett* **1998**, 1351−1352. (g) Suzuki, A.; Nozawa, S.; Harada, M.; Itoh, M.; Brown, H. C.; Midland, M. M. *J. Am. Chem. Soc.* **1971**, *93*, 1508−1509.

[5] Kihara, N.; Ollivier, C.; Renaud, P. *Org. Lett.* **1999**, *1*, 1419−1422.

[6] Panchaud, P.; Renaud, P. *J. Org. Chem.* **2004**, *69*, 3205−3207.

[7] Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Synlett* **2002**, 674−686.

[8] For a comprehensive discussion of organoborane involvement in radical reactions, see: (a) Ollivier, C.; Renaud, P. *Chem. Rev.* **2001**, *101*, 3415−3434. (b) Renaud, P.; Beauseigneur, A.; Brecht-Forster, A.; Becattini, B.; Darmency, V.; Kandhasamy, S.; Montermini, F.; Ollivier, C.; Panchaud, P.; Pozzi, D.; Scanlan, E. M.; Schaffner, A.-P.; Weber, V. *Pure Appl. Chem.* **2007**, *79*, 223−233.

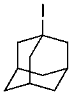
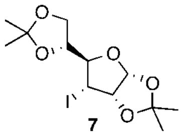
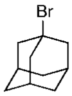
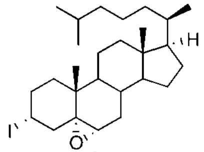
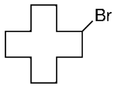
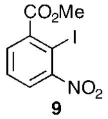
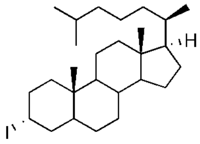
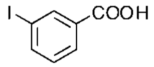
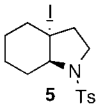
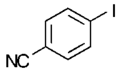
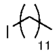
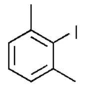
[9] Tributylborane was used in the experiments described herein due to its reduced pyrophoricity compared to triethylborane. Trimethylborane was employed due to our prior success using it for deoxygenation of alcohols (ref 2a).

[10] (a) Miyabe, H.; Yamaoka, Y.; Takemoto, Y. *J. Org. Chem.* **2005**, *70*, 3324−3327. (b) Liu, J.-Y.; Jang, Y.-J.; Lin, W.-W.; Liu, J.-T.; Yao, C.-F. *J. Org. Chem.* **2003**, *68*, 4030−4038.

10.1021/ol7016609 CCC: $37.00

Table 1. Dehalogenation Results Using Various Alkyl and Aryl Halides[a]

$$\text{R-X} \xrightarrow[\text{PhH, rt}]{\text{Bu}_3\text{B, air, H}_2\text{O}} \text{R-H}$$

entry	R-X	yield (%)[b]	entry	R-X	yield (%)[b]
1	 **1**	97	7	 **7**	76
2	 **2**	NR[c]	8	 **8**	85
3	 **3**	NR[c]	9	 **9**	32
4	 **4**	96	10	 **10**	NR[c]
5	 **5**	74	11	 **11**	NR[c]
6	 **6**	65[d]	12	 **12**	NR[c]

[a] See Supporting Information for experimental details. [b] Isolated yield unless otherwise specified. [c] No reaction. [d] Yield determined using gas chromatography.

primary, secondary, and tertiary alkyl iodides proceeded in good to excellent yields. Epoxides, acetals, and tosyl-protected amines appear to be stable to the reaction conditions. The lower yield in the case of primary iodide **6** (entry 6) likely results from the reversibility of iodine atom abstraction between the substrate and the alkyl radical.[11] Likewise, the energetically unfavorable abstraction of an aryl iodide by an alkyl radical was expected to render these substrates inert to tin-free conditions.[12] As predicted (entries 10−12), aryl iodides generally proved unreactive; however, as illustrated by iodide **9** (entry 9), deiodination could be realized. The latter result is consistent with the observation of Plesnicar and Dolenc who demonstrated that the combination of electron-withdrawing substituents and the release of steric strain due to ortho substituents makes iodine abstraction from aryl iodides by alkyl radicals more favorable.[13] It is noteworthy that the functional groups on the aryl iodides were unaffected during the reaction. To confirm the radical nature of this reaction, an inhibition study using galvinoxyl[14] was performed and resulted in the quantitative recovery of starting material (**4**). Additional control experiments performed either in the absence of trialkylborane or under anhydrous conditions resulted in quantitative recovery of **4** or reduced yields of deiodinated products, respectively. The latter is consistent with a recent report by Newcomb wherein the rate of background hydrogen atom transfer from triethylborane was determined to be appoximately 5 times slower

---

[11] Yorimitsu, H.; Oshima, K. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim. 2001; Vol. 1, p 19.

[12] Abstraction of iodine from aryl iodides by tin hydrides has been demonstrated to be a facile process. See: Curran, D. P.; Jasperse, C. P.; Totleben, M. J. *J. Org. Chem.* **1991**, *56*, 7169−7172.

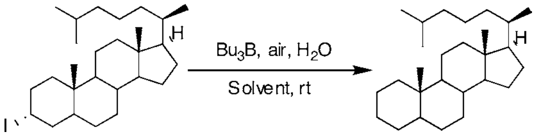
[13] (a) Dolenc, D.; Plesnicar, B. *J. Org. Chem.* **2006**, *71*, 8028−8036. (b) A similar phenomenon has been observed using Bu_3SnH and ortho-substituted aryl bromides: Crich, D.; Recupero, F. *Chem. Commun.* **1998**, 189−190.

[14] Midland, M. M.; Brown, H. C. *J. Am Chem. Soc.* **1971**, *93*, 1506−1508.

than hydrogen atom transfer from trialkylborane-complexed water.[15b]

A brief exploration of various solvents demonstrated the lack of any dramatic solvent effect on the reaction (Table 2). The mixed solvent systems (entries 5−7) were used due to the very low solubility of the substrate in alcohols and acetonitrile.

Table 2. Deiodination in Various Solvents



entry	solvent	yield (%)[a]
1	PhH	96
2	PhMe	80
3	THF	85
4	Et_2O	90
5	PhMe/MeOH (2:3)	94
6	PhMe/EtOH (2:3)	89
7	PhMe/CH_3CN (1:3)	75

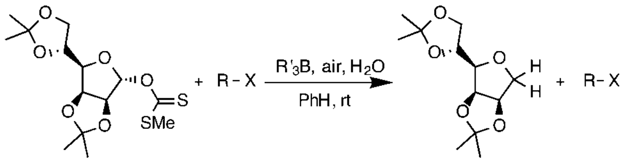
[a] Isolated yield.

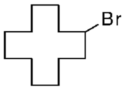
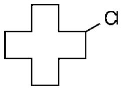
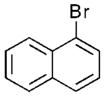
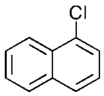
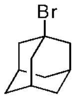
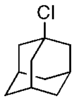
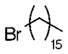
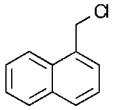
The observation that dehalogenation did not occur with alkyl bromides and presumably would not occur with alkyl chlorides[15c] prompted us to investigate the possibility of selective deoxygenation in the presence of alkyl halides. A literature search revealed only one method, developed by Barton and co-workers, that allows for radical-mediated deoxygenation in the presence of alkyl and aryl halides.[16] Barton's method utilizes phosphine-boranes to effect the deoxygenation of a secondary xanthate in the presence of various alkyl and aryl bromides and chlorides. To complement this chemoselective deoxygenation, we undertook a similar study using our trialkylborane/water system.

Table 3 shows the results of our attempts at deoxygenating the xanthate (**14**) derived from 2,3:5,6-D-*O*-isopropylidene-α-D-mannofuranose[17] in the presence of various alkyl and aryl chlorides and bromides. Good yields of deoxygenated product and excellent recovery of the respective halogenated substrates were obtained in most cases using either trimethyl- or tributylborane. GCMS analysis of the crude reaction mixture as well as the purified products did not reveal the presence of any dehalogenated materials.

In conclusion, we have demonstrated that a trialkylborane/air/water system is an effective method for the dehalogenation of alkyl iodides. The reaction proceeds with good to excellent yields and is tolerant of various functional groups. Additionally, these conditions were shown to allow for the chemoselective deoxygenation of a xanthate-derived secondary alcohol in the presence of various alkyl and aryl bromides and chlorides.

Table 3. Deoxygenation in the Presence of Alkyl and Aryl Halides[a]



entry	R−X	R'_3B	recovered R-X (%)[b]	yield 15 (%)[b]
1	 Br	Me_3B	99	81
2		Bu_3B	96	83
3	 Cl	Me_3B	95	81
4		Bu_3B	90	95
5	 Br	Me_3B	95	92
6		Bu_3B	88	81
7	 Cl	Me_3B	76	84
8		Bu_3B	79	84
9	 Br	Me_3B	96	97
10		Bu_3B	81	93
11	 Cl	Me_3B	99	80
12		Bu_3B	88	86
13	 Br 15	Me_3B	99	92
14		Bu_3B	98	84
15	 Cl	Me_3B	85	96
16		Bu_3B	94	81

[a] See Supporting Information for experimental details. [b] Isolated yield or recovery.

Acknowledgment. Funding from Amgen and the NIH (Grant No. 1 RO1 CA/GA 93591-O1A) is gratefully acknowledged. The authors would also like to thank Dr. Eric Paulson and Dr. Chris Incarvito (Yale) and Dr. Chris Rithner, Don Heyse, and Donald Dick (CSU) for assistance with instrumentation.

Supporting Information Available: Experimental details and spectra of unknown compounds can be found in the Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.

OL7016609

---

(15) (a)DH_{298}(*i*PrBr) = 73.9kcal/mol, DH_{298}(*i*PrCl) = 85.2kcal/mol. From: Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255−263. (b) Jin, J.; Newcomb, M. *J. Org. Chem.* **2007**, *72*, 5098−5103. (c) Selective deoxygenation is supported by Newcomb's kinetic study of hydrogen atom transfer from trialkylborane/water complexes.[15b]

(16) (a) Barton, D. H. R.; Jacob, M. *Tetrahedron Lett.* **1998**, *39*, 1331−1334. (b) For deoxygenation in the presence of fluorine, see: Takamatsu, S.; Katayama, S.; Hirose, N.; Naito, M.; Izawa, K. *Tetrahedron Lett.* **2001**, *42*, 7605−7608.

(17) Di Cesare, P.; Gross, B. *Synthesis* **1980**, 714−715.