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Dehalogenation of Vicinal Dihalo Compounds by 1,1'-Bis(trimethylsilyl)-1*H*,1'*H*-4,4'-bipyridinylidene for Giving Alkenes and Alkynes in a Salt-free Manner

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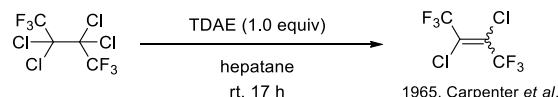
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We report transition metal-free dehalogenation of vicinal dihalo compounds by 1,1'-bis(trimethylsilyl)-1*H*,1'*H*-4,4'-bipyridinylidene (**1**) under mild conditions, in which trimethylsilyl halide and 4,4'-bipyridine were generated as byproducts. The synthetic protocol for this dehalogenation reaction was effective for a wide scope of dibromo compounds as substrates while keeping the various functional groups intact. Furthermore, reduction of vicinal dichloro alkanes and vicinal dibromo alkenes also proceeded in a salt-free manner to afford the corresponding alkenes and alkynes.

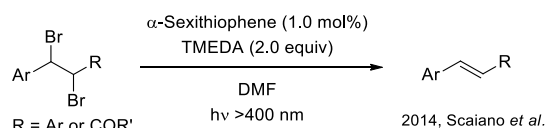
Protection/deprotection sequences comprise a key synthetic protocol in organic chemistry for preparing versatile organic compounds, such as natural and artificial bioactive compounds as well as functional organic materials.¹ In contrast to the availability of the protection-deprotection sequence to carbonyl, amine, and alcoholic groups,^{1,2} only halogenation/dehalogenation has been available for alkene functionalities, although alkenes are often been incorporated as important interfering intermediates suitable for oxidation, hydrogenation, olefin metathesis, etc.^{3,4} Halogenation of alkenes is easily achieved by adding typical reagents such as Br₂ to alkenes, whereas dehalogenation is much more complicated and requires the use of metal-based reductants, such as zinc, iron, copper powders, and metal hydrides, as well as photo-activated transition metal-mediated reductions.^{5–8} These reductants, however, result in narrow functional group compatibility due to their high tendency to further reduce interfering functionalities.⁵ Some organic reductants have been developed for the dehalogenation of vicinal dihalo compounds:^{9,10} Carpenter *et al.* used tetrakis(dimethylamino)ethylene (TDAE) for the

dehalogenation of 2,2,3,3-tetrachloro-1,1,1,4,4,4-hexafluorobutane to produce 2,3-dichloro-1,1,1,4,4,4-hexafluoro-2-butene (Scheme 1a);^{9a} Scaiano and coworkers demonstrated that 2,2':5',2'':5'',2''':5''',2''''-quinquethiophene (α -sexithiophene) worked as a photoredox catalyst for the dehalogenation of 1,2-dibromo-1,2-diarylethane as well as α -carbonyl dibromo compounds by tetramethylethylenediamine (TMEDA), giving the corresponding alkenes (Scheme 1b);^{10b} and Li *et al.* reported that the Hantzsch ester in the presence of Na₂CO₃ reduced vicinal dibromo compounds to give the corresponding alkenes (Scheme 1c).^{10c}

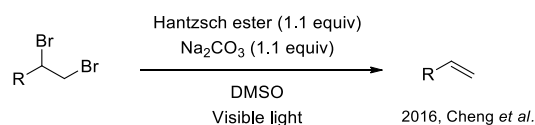
a) TDAE-promoted debromination



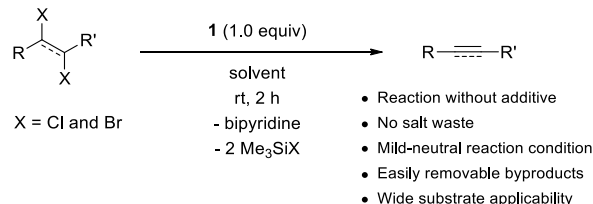
b) α -Sexithiophene-catalyzed debromination



c) Hantzsch ester-promoted debromination



d) This work



Scheme 1. Previous work for metal-free debromination reactions of vicinal dihalo compounds by (a) TDAE, (b) α -sexithiophene, or (c) Hantzsch ester. (d) This work: metal- and salt-free dehalogenation reaction of vicinal dihalo compounds by organosilicon reductant in mild condition.

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Aside from these pioneering works, the development of a dehalogenation reaction using organic reducing reagents without the formation of salt-wastes has remained a challenging task. We applied organosilicon reducing reagents, 1,1'-bis(trimethylsilyl)-1*H*,1'*H*-4,4'-bipyridinylidene (**1**), 1,4-bis(trimethylsilyl)-1,4-dihydropyrazine (**2a**), its methylated derivatives **2b**, **c**, and 1-methyl-3,6-bis(trimethylsilyl)-cyclohexa-2,5-diene (**3**) (Figure 1) to successfully reduce metal halides without the formation of salt-waste to afford the corresponding low-valent catalytically-active metal species.^{11,12} Herein, we report that organosilicon reductant **1** served as a stoichiometric reagent for the salt-free dehalogenation reaction of vicinal dibromo compounds under mild conditions while maintain high functional group tolerance to give the corresponding alkenes, as well as vicinal dichloro alkanes and vicinal dibromo alkenes to afford the corresponding alkenes and alkynes (Scheme 1d).

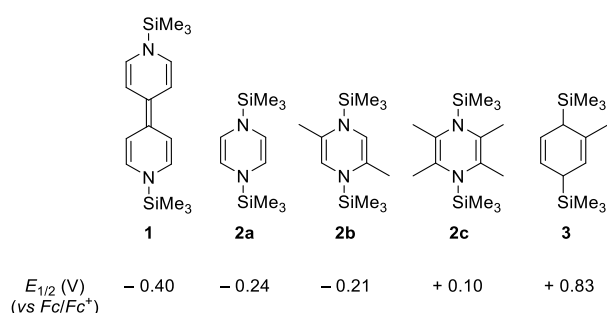


Figure 1. Salt-free organosilicon reductants **1**, **2a–c**, and **3**, and their redox potentials vs ferrocene (Fc).^{11b,12}

We began by searching for the best organosilicon reductant among **1**, **2a–c**, and **3** for the debromination reaction of 1,2-dibromoethylbenzene (**4a**) in CD₃CN at room temperature for 2 h to produce styrene (**5a**), and the results are summarized in Table 1. When the reaction was performed using **1**, the yield of **5a** reached 98% (entry 1). Notably, the by-products were trimethylsilyl bromide and 4,4'-bipyridine, both of which were readily removed during the work-up. We also observed solvent effects; the yield of **5a** decreased to some extent in toluene-*d*₈, C₆D₆, and THF-*d*₈ due to the lower solubility of **1** in those solvents at room temperature (entries 2–4). Compounds **2a** and **2b** gave **5a** in moderate yields (66% and 78%) (entries 5 and 6). The reaction using **2c** produced only a low yield of **5a** (21%), because of the low solubility of **2c** in CD₃CN (entry 7). In contrast, compound **3** showed no ability to reduce **4a** (entry 8). Accordingly, we selected **1** as the best reducing reagent, which was consistent with the most negative redox potential of **1** among the organosilicon reductant **1–3**.^{11b}

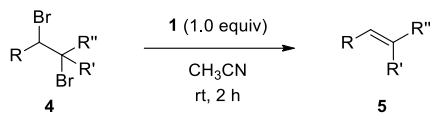
Table 1. Optimization of debromination reaction^a

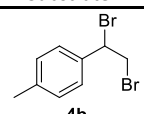
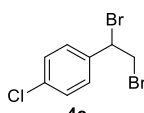
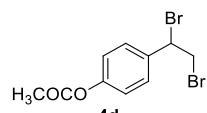
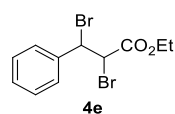
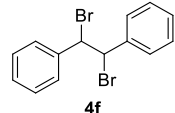
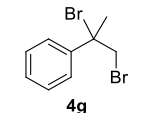
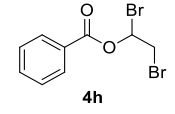
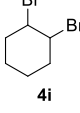
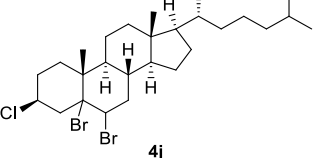
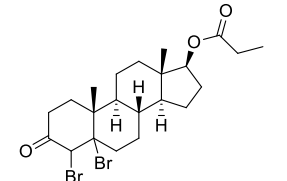
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Entry	Reductant	Solvent	Yield of 5a (%) ^b
1	1	CD ₃ CN	98 (94) ^c
2	1	toluene- <i>d</i> ₈	67
3	1	C ₆ D ₆	71
4	1	THF- <i>d</i> ₈	68
5	2a	CD ₃ CN	66
6	2b	CD ₃ CN	78
7	2c	CD ₃ CN	21
8	3	CD ₃ CN	0

^a Reaction conditions: **4a** (0.10 mmol) and reductant (1.0 equiv, 0.10 mmol) stirred in above mentioned solvent at room temperature for 2 h. ^b Yields were calculated by ¹H NMR spectroscopy in the presence of mesitylene as an internal standard. ^c Isolated yield is in parenthesis.

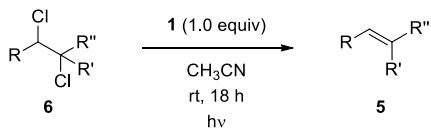
With the best reducing reagent **1** and optimized reaction conditions in hand, we examined the reduction of various vicinal dibromo compounds, and the results are shown in Table 2. Both electron-withdrawing and -donating substituents at the *para*-position of the phenyl group of **4a** afforded corresponding olefins **5b** and **5c** in 92% and 93% yields, respectively (entries 1 and 2). Compound **4d** bearing an acetoxy group at the *para*-position of the phenyl group gave the product **5d** in 91% yield, and the acetoxy group remained intact (entry 3). Similarly, the carboxylic group of *erythro*-ethyl 2,3-dibromo-3-phenylpropanoate (**4e**) remained intact during smooth reduction, giving (*E*)-ethyl cinnamate [(*E*)-**5e**] in 93% yield (entry 4). Compounds *meso*-**4f** and **4g** afforded (*E*)-stilbene [(*E*)-**5f**] in 95% yield and α -methylstyrene (**5g**) in 90% yield, respectively (entries 5 and 6). Interestingly, only (*E*)-stilbene obtained in 91% yield, even when a *dl*-1,2-dibromo-1,2-diphenylethane (*dl*-**4f**) was used as a substrate under the optimized condition.¹³ Our observation for the selective (*E*)-isomer formation from *meso*- and *dl*-isomers of **4f** suggested that this debromination might proceed in stepwise manner *via* formation of mono-debrominated radical or anionic species with generation of BrSiMe₃ to finally produce the thermodynamically stable (*E*)-alkene *via* sterically favorable common conformer of the mono-debrominated species, though we could not find any mono-debrominated adducts by *in situ* trapping experiments.^{5a,d,e,6b,c,7e} An advantage of this synthetic protocol using **1** was its applicability to the debromination of aliphatic substrates, in sharp contrast to the poor yield observed for debromination using metal-based reducing reagents.⁶ In fact, vinyl benzoate (**5h**) was obtained in 88% yield (entry 7), and cyclohexene (**5i**) was formed in 86% yield after a prolonged reaction time (8 h) by reducing 1,2-dibromocyclohexane (**4i**) (entry 8). Notably, we also demonstrated some functional group tolerance, as exemplified by the production of cholesteryl chloride (**5j**) (91% yield) and testosterone propionate (**5k**) (89% yield) (entries 9 and 10), with chloride and carbonyls, such as propionate and ketone moieties, remaining intact.

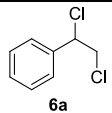
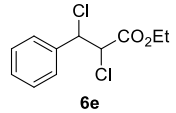
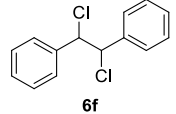
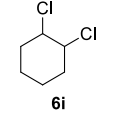
Table 2. Substrate scope for debromination reactions of vicinal dibromo compounds^a


Entry	Substrate 4	Yield of 5 (%) ^b
1		92 (5b)
2		93 (5c)
3		91 (5d)
4		93 (5e) ^c
5		95 (5f) ^c
6		90 (5g)
7		88 (5h)
8		86 (5i) ^{d,e}
9		91 (5j)
10		89 (5k)

^a Reaction conditions: **4** (1.0 equiv, 0.40 mmol) and **1** (1.0 equiv, 0.40 mmol) stirred in CH₃CN at room temperature for 2 h. ^b Isolated yields are reported. ^c *Erythro/meso*-dibromides were used as starting material and in products only (*E*)-isomers were formed as confirmed by ¹H NMR spectroscopy. ^d The reaction time was 8 h. ^e Yield was calculated by ¹H NMR spectroscopy in the presence of mesitylene as an internal standard.

We found that even under the optimized conditions, 1,2-dichloroethylbenzene (**6a**) was not reduced. However, UV irradiation enhanced the reduction of **6a** at room temperature for 18 h to give **5a** in 93% yield (Table 3, entry 1). In fact, the compound **1** was gradually decomposed under UV light with a release of Me₃Si groups in the absence of any substrates, which suggested that the UV light-induced degradation of **1** accelerated the dechlorination at room temperature. Under the same irradiation conditions, *erythro*-2,3-dichloro-3-phenylpropanoate (**6e**) and *meso*-1,2-dichloro-1,2-diphenylethane (**6f**) were converted to (*E*)-ethyl cinnamate (**5e**) (91% yield) and (*E*)-stilbene (**5f**) (87% yield), respectively (Table 3, entries 1–3). Remarkably, an aliphatic dichloride such as 1,2-dichlorocyclohexane (**6i**) was also reduced, producing **5i** in 51% yield (Table 3, entry 4).¹⁴

Table 3. Dechlorination of vicinal dichloro compounds^a


Entry	Substrate 6	Yield of 5 (%)
1		93 (5a) ^b
2		91 (5e) ^c
3		87 (5f) ^c
4		51 (5i) ^b

^a Reaction conditions: **6** (1.0 equiv, 0.40 mmol) and **1** (1.0 equiv, 0.40 mmol) stirred in CH₃CN at room temperature for 18 h under UV-irradiation. ^b Yields were calculated by ¹H NMR spectroscopy in the presence of mesitylene as an internal standard. ^c *Erythro/meso*-dibromides were used as starting material and in products only (*E*)-isomers were formed as confirmed by ¹H NMR spectroscopy.

Finally, we examined debromination of vicinal dibromo alkenes using reductant **1** at room temperature for 8 h to give the corresponding alkynes, and the results are shown in Table 4. Smooth reduction of (1,2-dibromovinyl)benzene (**7a**) proceeded to yield **8a** in 85% yield (entry 1). Dibromo alkene compounds **7b** and **7c** afforded ethyl phenyl propiolate (**8b**) (93% yield) and 1,2-diphenylacetylene (**8c**) (89% yield) (entries 2 and 3). Aliphatic dibromo alkene **7d** required UV irradiation for 8 h, to give 4-octyne (**8d**) in 85% yield (entry 4).

Table 4. Debromination of vicinal dibromo alkenes^a

Entry	Substrate 7	Yield of 8 (%) ^b
1		85 (8a)
2		93 (8b)
3		89 (8c)
4		85 (8d) ^{c,d}

^a Reaction conditions: **7** (1.0 equiv, 0.40 mmol) and **1** (1.0 equiv, 0.40 mmol) stirred in CH₃CN at room temperature for 8 h. ^b Isolated yields are reported. ^c Yield was calculated by ¹H NMR spectroscopy in the presence of mesitylene as an internal standard. ^d The reaction was done under UV irradiation.

We demonstrated that organosilicon compounds **1** and **2a–c** served as unique salt-free debromination reagents to reduce vicinal dibromo compounds under mild conditions to produce the corresponding alkenes. A notable advantage of organosilicon reductant **1** is the high compatibility of some functional groups, such as chloride and carbonyl groups. Moreover, vicinal dichloro substrates were also reduced under UV irradiation conditions to afford the corresponding alkenes in high yields. This salt-free protocol was applied to the debromination of vicinal dibromo alkenes, leading to the formation of the corresponding alkynes. Further application of these organosilicon compounds to reduce organic compounds is ongoing in our group.

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There are no conflicts to declare.

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- See Supporting Information.
- Note: The reaction between 1,2-difluoro-1,2-diphenylethane and **1** did not afford any stilbene as C–F bond was unreactive towards organosilicon reductant **1**.

TOC used only:

A transition metal free dehalogenation of vicinal dihalo compounds are reported by 1,1'-bis(trimethylsilyl)-1*H*,1'*H*-4,4'-bipyridinylidene in mild and convenient reaction condition. Wide variety of substrates including vicinal dibromo and vicinal dichloro substrates are applicable and giving corresponding alkenes in excellent yield. Moreover, the reduction of dibromo alkenes to form alkynes quantitatively is also achieved by this organosilicon reductant.

