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Silicon Powder: The First Nonmetal Elemental Catalyst for Aminobromination of Olefins with TsNH$_2$ and NBS

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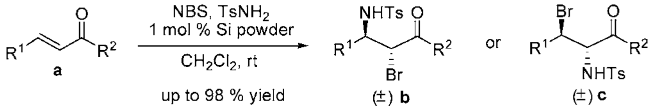
ABSTRACT



Silicon powder was found, for the first time, to be an efficient alternative to transition metal catalysts for aminobromination of α,*β*-unsaturated carbonyl compounds and simple olefins with *p*-toluenesulfonamide (4-TsNH$_2$) and NBS, affording the aminobrominated products in high yields and regio- and stereoselectivity. The high reactivity of electron-rich substrates reveals that the reaction has the electrophilic addition feature.

Aminohalogenations of olefinic double bonds have gained great interest recently, and they constitute a synthetic tool to prepare the vicinal haloamino functionality.[1−6] These reactions generally proceeded with transition metal salts or their complexes as catalysts, such as CuI, CuCl$_2$·2H$_2$O, CuCN, Cu(OAc)$_2$, CuOTf, V$_2$O$_5$, MnSO$_4$, Mn(III)-salen, FeCl$_3$−PPh$_3$, Co(OAc)$_2$·4H$_2$O, NiCl$_2$·6H$_2$O, ZnCl$_2$, LPdCl$_2$ (L = 1,10-phenanthroline), [(C$_3$F$_7$CO$_2$)$_2$Rh]$_2$, Pd/C, and so on.[7,8] Very recently, we have reported that copper powder promotes the aminobromination of α,*β*-unsaturated ketones with NBS and TsNH$_2$ as the nitrogen/bromine sources.[9] However, the use of transition metals or related ligands is generally limited for certain applications since the acceptable level of transition metal residuals is highly regulated in certain products, especially pharmaceutics and the removal of metal impurities is a challenging issue. Although a few noncatalyzed addition reactions have been reported[10] and several transition- or heavy-metal-free aminohalogenations

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were reported recently, significant shortcomings still remain including the need of a large quantity of ionic liquid,[11a] stoichiometric $PhI(OAc)_2$,[11b] a large quantity of sulfuric acid,[11c] or CO_2 at high pressure.[11d] Thus, less costly, metal-free, and operationally simple aminobromination methods for obtaining aminobromo products from olefins are desirable.

In our continuous efforts to seek more benign catalysts for difunctionalzations of carbon−carbon double bonds, we found recently that elemental silicon powder is an efficient yet still low-priced, comparatively nontoxic, metal- and ligand-free catalyst for aminobrominations. The reactions were carried out smoothly at room temperature in good to excellent yields of the desired products. We herein wish to report the use of elemental silicon powder as the catalyst for aminobromination of carbon−carbon double bonds including α,*β*-unsaturated ketones, cinnamic esters, and simple alkenes with a $TsNH_2$−NBS system. No report involving the use of elemental silicon as a catalyst in organic reactions was found in SCIfinder, though silicon is well-known as a semiconductor and wafer material.

Our initial experiments focused on examining the catalytic activity of silicon powder and other nonmetal elements in the aminobromination of α,*β*-unsaturated ketone by using chalcone (1,3-diphenyl-propen-1-one), chosen because of its simplicity and moderate reactivity to the reaction. The reaction was carried out by stirring at room temperature a mixture of catalyst, chalcone, NBS, and $TsNH_2$ in CH_2Cl_2 under the common conditions reported previously in literature,[7b] except for an inert atmosphere. The results are summarized in Table 1.

As shown in Table 1, silicon powder is an efficient catalyst for the aminobromination of chalcone at ambient conditions (entries 3−5). Even a 1 mol % loading (entry 5) is sufficient for a smooth reaction, affording the desired product in a slightly higher yield compared with the literature using Cu(I) salts as catalyst.[7b,c] Beyond these advantages it is particularly noteworthy that at the end of the reaction the catalyst can be removed by simple filtration. Furthermore, the silicon powder can be reused four times with no reduction in the yields of corresponding addition products. It is worthy to point out that because of low toxicity, low cost, recyclability, and simple separation of silicon from the reaction mixture, our method had green and economical advantages over other metallic catalysts.

Several other potential catalysts of nonmetals were tested, and the results indicated that boron powder was another effective catalyst (entry 2, 73% yield). However, selenium, phosphorus, and molecular iodine are less reactive (entries 7, 9, and 10); sulfur and bromine (entry 8 and 11) failed to give any aminobromo product.

Table 1. Catalytic Activity of Various Nonmetallic Elemental Substances in the Aminobromination of Chalcone[a]

entry	catalyst	amount (mol %)	yield (%)[b]
1	no catalyst	0	23
2	B	1	73
3	Si	10	75
4	Si	5	74
5	Si	1	74
6	Ge	1	19
7	P	1	10
8	S	1	NR
9	Se	1	45
10	I_2	1	30
11	Br_2	1	NR
12	$SiCl_4$	1	18

[a] Conditions: chalcone (5 mmol), $TsNH_2$ (5 mmol), NBS (6 mmol), silicon powder (amounts used in 1−10 mol %), CH_2Cl_2 (10 mL), 25 °C. [b] Isolated yield after chromatographic separation.

The scope and limitation of the silicon-powder-catalyzed aminobromination were investigated by various olefins such as α,*β*-unsaturated ketones and cinnamic esters (Table 2). The results show that the silicon-catalyzed aminobromination was influenced remarkably by the substituents and their positions at the phenyl rings, in particular, the phenyl ring linked to the carbon−carbon double bond, similar to the observations in our copper-powder-catalyzed reaction reported previously.[9] Entries **1a**−**4a** indicate that a strong electron-donating group (e.g., OCH_3) incorporated *para* to the double bond facilitated the reaction extraordinarily and gave the *trans* addition products as the sole products in nearly quantitative yields, regardless of the nature of the substituents on another phenyl linked to carbonyl group (entries **1a**−**4a**). In sharp contrast to the chalcones with an OCH_3 *para* to the double bond, the reaction was prohibited completely with the substrates having a strong electron-withdrawing group (NO_2) at the same position. In this case, the reaction failed even though there is a strong electron-donating group (OCH_3) present at 4′-position and reaction time was prolonged to 48 h (entries **5a** and **6a**).

Methoxy present at the 4′-position of benzene ring conjugated to the carbonyl group deactivates the reaction significantly in the absence of a 4-substituent (compare **8a** with **7a** and **9a**). However, 4′-OCH_3 is able to activate the chalcones that have a weak electron-withdrawing group such as flouro at the 4-position (compare **11a** with **10a** and **12a**). Notably, with 4-flouro-4′-chlorochalcone (**12a**) as starting olefin, silicon powder also worked, whereas it failed to afford the aminobrominated product when copper powder was used as catalyst.[9] Multisubstituted cholcones with 4-methoxy also afforded the desired addition products in good to excellent yields (**13b**−**14b**, 83−98%).

It is noteworthy that when OCH_3 was incorporated *meta* to the double bond, electrophilic aromatic substitution other than the addition reaction on the double bond occurred. 3-Methoxy and 3,5-dimethoxy chalcones afforded the corresponding 4-bromo chalcones as the sole products in high

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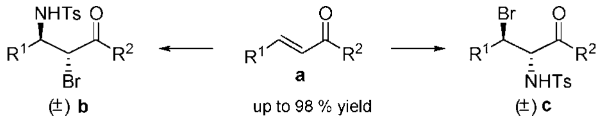
Table 2. Silicon-Powder-Catalyzed Aminobromiation of Various α,β-Unsaturated Carbonyl Compounds[a]



entry	R^1	R^2	product	yield (%)[b]	*anti*:*syn* (%)[c]	time (h)	mp (°C)
1a	4-$CH_3OC_6H_4$	C_6H_5	**1b**	91	>95	24	155−156
2a	4-$CH_3OC_6H_4$	4′-$CH_3OC_6H_4$	**2b**	98	>95	1	175
3a	4-$CH_3OC_6H_4$	4′-ClC_6H_4	**3b**	96	>95	2	162−163
4a	4-$CH_3OC_6H_4$	4′-$NO_2C_6H_4$	**4b**	98	>95	1	156−157
5a	4-$NO_2C_6H_4$	C_6H_5		NR[e]		48	
6a	4-$NO_2C_6H_4$	4′-$CH_3OC_6H_4$		NR		48	
7a	C_6H_5	C_6H_5	**7c**	75	>95	9	124−126
8a	C_6H_5	4′-$CH_3OC_6H_4$	**8c**	27	>95	24	159−159.5
9a	C_6H_5	4′-ClC_6H_4	**9c**	26	>95	26	139−140
10a	4-FC_6H_4	C_6H_5	**10c**	13	>95	48	150−151
11a	4-FC_6H_4	4′-$CH_3OC_6H_4$	**11c**	60	>95	24	164−165
12a	4-FC_6H_4	4′-ClC_6H_4	**12c**	32	>95	48	140−141
13a	3,4,5-$(CH_3O)_3C_6H_2$	C_6H_5	**13b**	83	>95	1	167−168
14a	2-Br-4,5-$(CH_3O)_2C_6H_2$	C_6H_5	**14b**	98	>95		152−153
15a	3-$CH_3OC_6H_4$	C_6H_5	**15d**[d]	90		24	59−60
16a	3-$CH_3OC_6H_4$	4′-$CH_3OC_6H_4$	**16c**	91	>95	24	182−184
17a	3,5-$(CH_3O)_2C_6H_3$	C_6H_5	**17d**[d]	98		2	174−175
18a	4-$CH_3OC_6H_4$	CH_3	**18b**	82	>95	2	93−95
19a	2-Br-4,5-$(CH_3O)_2C_6H_2$	CH_3	**19b**	77	>95	1	88−90
20a	3,4,5-$(MeO)_3C_6H_2$	CH_3	**20b**	65	>95	3	177−179
21a	C_6H_5	OC_2H_5	**21c**	25	>95	24	121−123
22a	4-$CH_3OC_6H_4$	OC_2H_5	**22b**	78	>95	24	118−119
23a	3,4,5-$(MeO)_3C_6H_2$	OC_2H_5	**23b**	65	>95	3	137−139
24a	H	OC_2H_5		NR			

[a] Conditions: α,β-unsaturated carbonyl compound (5.0 mmol), $TsNH_2$ (5.0 mmol), NBS (6.0 mmol), silicon powder (1 mol %), CH_2Cl_2 10 mL, 25 °C. [b] Isolated yield after chromatography separation. [c] The ratio of *anti*:*syn* products, >95%, means no *syn*-isomer in the product mixture was detected by ^1H NMR. [d] Aromatic substitution product. [e] NR: no reaction.

yields of 90% and 98% (**15d**, **17d**) under the same condition. However, 3,4′-dimethoxy chalcone gave the expected addition product in high yield (**16c**, 91%).

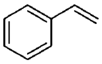
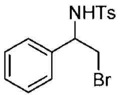
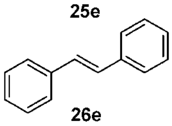
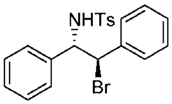
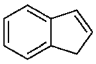
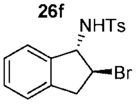
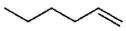
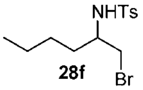
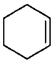
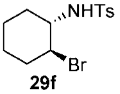
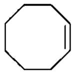
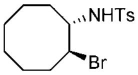
Aromatic enones underwent the silicon-powder-catalyzed aminobromination readily and gave the aminobromo products in good yields (**18b**−**20b**) under the same condition. The reaction also proceeded smoothly with α,β-unsaturated ester, i.e., ethyl cinnamate and its 4-methoxy analog (**22a**, **23a**) as starting olefins; the latter is clearly more reactive and gave the reversal in regioselective aminobromination. However, the reaction failed with ethyl acrylate, indicating that the aryl on the double bond plays a crucial role in the aminobrominations of α,β-unsaturated esters.

The synthetic application of this protocol is also suitable for the aminobromination of simple olefins (Table 3). The reaction was performed successfully for cyclic and acyclic alkenes. The corresponding chemical yields are from 85% to 95% in the investigated examples, except for cyclohexene.

Regio- and stereoselectivity of the addition products were determined by their melting points, ^1H NMR, ^{13}C NMR, and sometimes by MS or X-ray crystallography if possible. The results also show that all of the addition products have a *trans* relative relationship between bromo and amino groups. The α,β-unsaturated carbonyl compounds without a 4-methoxy substituent gave the *trans*-α-amino-β-bromo products alone (Table 2, **7c**−**12c**, **16c**, **21c**), which are spectrally consistent with that reported.[9] X-ray crystallographic analysis of **8c** (Figure 1) showed clearly that nitrogen atom was added to α-carbon and bromine atom to β-carbon in an *anti* manner. However, a feature of the reversal in regioselectivity was observed when the benzene ring linked to the double bond bears a 4-OCH_3 group (Table 2, **1b**−**4b**, **13b**−**14b**, **18b**−**20b**, and **23b**), as revealed by MS analysis that the prominent fragment ions, $[R^1CHNHTs]^+$ and $[R^2CO]^+$, present in the corresponding reversed products. Apart from the MS evidence, X-ray crystallographic analysis showed undoubtedly that **1b**, derived from 4-OCH_3 chalcone, has a completely reversed regioselectivity in which nitrogen and bromine were added to β- and α-carbon respectively in a *trans* relative stereochemistry (Figure 1).

Styrene-type olefins also gave only regioselective aminobromo products in which the amino is at the benzylic position and bromo is at the β-position (Table 3, entry 1 and 3). 1-Hexene gave the similar regioselective addition product in which bromine is at the terminal carbon and nitrogen is at the vicinal carbon, as evidenced by spectral analysis (^1H and ^{13}C NMR) and the mp was in good agreement with that of literature reported.[6] The product was further characterized

Table 3. Aminobromination of Simple Olefins[a]

entry	substrate	product	time (h)	yield (%)[b]
1	 **25e**	 **25f**	24	91
2	 **26e**	 **26f**	24	91
3	 **27e**	 **27f**	3	95
4	 **28e**	 **28f**	24	85
5	 **29e**	 **29f**	24	28
6	 **30e**	 **30f**	24	89

[a] Conditions: olefins (5 mmol), $TsNH_2$ (5 mmol), NBS (6 mmol), silicon powder (1 mol %), CH_2Cl_2 (10 mL), 25 °C. [b] Isolated yield after chromatographic separation.

by MS data in which $[CH_3(CH_2)_4CHNHTs]^+$ and $[TsNHCHCH_2Br]^+$ appeared as two main fragment ions.

This work reveals that the activity and the regioselectivity of the silicon-powder-catalyzed aminobromination depend significantly on the electron density of the double bond. The fact that electron-rich olefins are more reactive than electron-deficent ones suggests that the aminobromination is also an electrophilic addition reaction, as reported previously using metallic catalysts.[12−14] Although the exact mechanism of the reaction and the role of silicon played are not clear now, the observations of the high reactivity of electron-rich substrates, high *anti* stereochemistry, formation of dibromides in some cases, and the electrophilic aromatic substitution reaction suggest that a possible bridged bromonium mechanism is present. Additionally, the purely Lewis acid catalyzed mechanism could be excluded because $SiCl_4$ was ineffective toward the reaction. In this case, the yield reduced to 18%, even lower than that of the control experiment. However, the *trans*-α-amino-*β*-bromo products obtained indicate that aziridinium intermediate maybe present in this reaction.

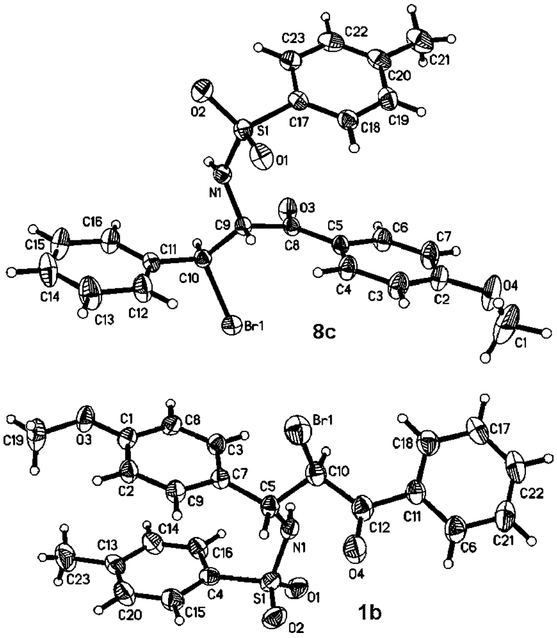


Figure 1. X-ray crystal structure of product **8c** and **1b**.

In conclusion, we have found that the elemental silicon can be used as an efficient catalyst for the aminobromination reaction. This protocol has the advantages of a large scope of olefins and high regio- and stereoselectivity with the NBS/$TsNH_2$ combination at ambient conditions. Additionally, silicon powder as catalyst has the advantage of avoiding any hazardous metals retained in products. The relative nontoxicity, low cost, recyclability, and simpleness of product isolation and silicon separation from reaction mixture make the methodology a useful tool for preparation of the vicinal aminobromo products, especially considering that the trace transition metal residues are highly regulated. More importantly, this may be the first example of using elemental silicon as catalyst in organic reactions.

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Supporting Information Available: Experimental procedure, analytical and spectral data of all componds, and X-ray crystal structure of products **8c** and **1b** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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