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A Free Radical Cascade Silylarylation of Activated Alkenes: Highly Selective Activation of the Si−H/C−H Bonds

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Supporting Information

ABSTRACT: The first example of silylarylation of activated alkenes with silanes is reported via selective activation of the Si−H/C−H bonds, which allows efficient access to silylated oxindoles through a free-radical cascade process.

Organosilicon compounds are widely used as powerful building blocks in synthetic organic chemistry.[1] The C−Si bond formation through direct C−H/Si−H bond activation represents one of the most atom-economical and waste-minimizing strategies for preparation of organosilicons.[2] Although considerable developments in C−Si bond construction via transition-metal-catalyzed Si−H/C−H bond functionalization have been made in the past decades,[3−6] more efficient and versatile methods are still highly desirable. Of particular interest are the C−H bond activations through free radical chemistry. We have developed a series of strategies for C−C bond formation by selective activation of the inert C−H bond in small molecules during the past years.[7] Very recently, several efficient radical cascade methods for synthesis of heterocycles via selective functionalization of sp^3C−H bonds have been achieved by us.[8] Inspired by these previous studies, we began to wonder whether the Si−H bond of silane could be selectively activated by free radical initiation. A silyl radical would be generated by Si−H bond cleavage, and then it would undergo a radical addition/cyclization cascade to give a silylated oxindole (Scheme 1).

Silicon-centered radicals[9] play an important role in material science, polymer science, and organic chemistry.[10] A variety of investigations focusing on generation, transformation, and application of silyl radicals have been widely studied in the past century. However, efficient free radical cascade systems involving silyl radicals through direct Si−H activation remain challenging in synthetic organic chemistry. Additionally, silane is used as a tin-free reductant alternative to organotin compounds in most of these radical systems.[11] Herein, we wish to report the first example of silylarylation of activated alkenes with silanes through a free-radical cascade process.

Scheme 1. Free-Radical-Initiated Si−H/C−H Bonds Activation in Radical Cascade Cyclization

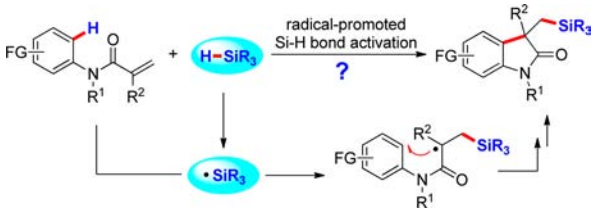
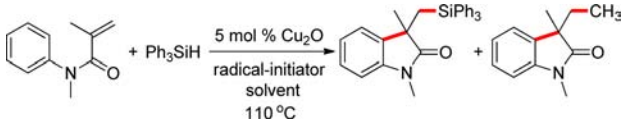


Table 1. Modification of the Typical Reaction Conditions[a]



entry	radical initiator (equiv)	solvent (mL)	silane (equiv)	yield (%)[b]
1	DCP (3)	Benzene (3)	3	56 (33)
2	DCP (3)	ClPh (3)	3	35
3	DCP (3)	DCE (3)	3	18
4	DCP (3)	DMSO (3)	3	28
5	DCP (3)	DMF (3)	3	10
6	DTBP (3)	Benzene (3)	3	30
7	TBHP[c] (3)	Benzene (3)	3	20
8	TBHP[d] (3)	Benzene (3)	3	18
9	DCP (3)	Benzene (1)	3	20 (34)
10	DCP (3)	Benzene (5)	3	36 (41)
11	DCP (3)	Benzene (3)	6	47 (25)
12	**DCP (3)**	**Benzene (3)**	**10**	**80 (17)**

[a]Reaction conditions: *N*-methyl-*N*-phenylmethacrylamide (1 equiv, 0.2 mmol), Cu_2O (5 mol %, 0.01 mmol), sealed tube, 110 °C, 22 h. [b]Isolated yields of the desired products and isolated yields of the methylated products in the parentheses. [c]TBHP (in water). [d]TBHP (in decane).

On the other hand, as an elegant radical acceptor, *N*-arylacrylamide and its derivatives are ready to proceed in radical cascade reactions resulting in substituted oxindoles.[12] Recently, we reported a free-radical addition/cyclization cascade reaction of alkanes with activated alkenes to produce a series of alkylated oxindoles.[8a] In order to prepare silylated oxindoles via radical promoted Si−H bond activation, triphenylsilane and *N*-methyl-

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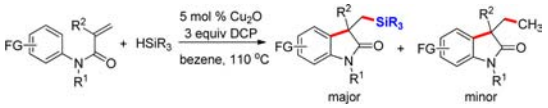
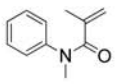
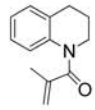
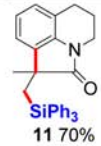
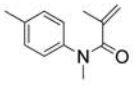
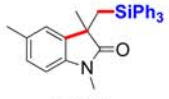
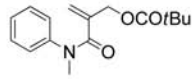
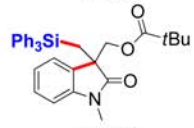
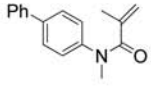
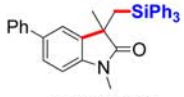
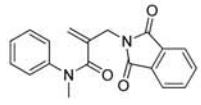
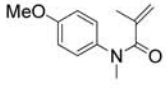
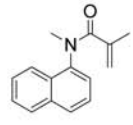
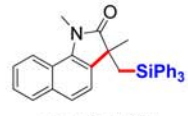
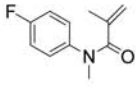
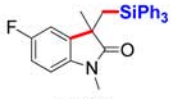
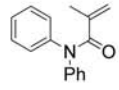
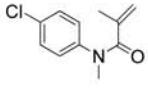
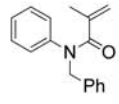
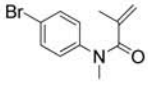
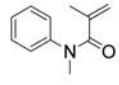
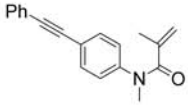
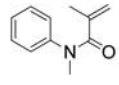
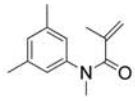
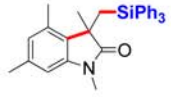
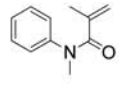
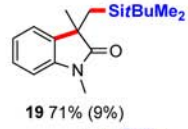
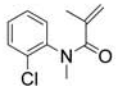
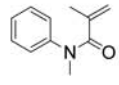
Table 2. Free-Radical Cascade Silylarylation of *N*-Arylacrylamide with Silanes[a]



entry	substrate	product, yield	entry	substrate	product, yield
1		 **1** 80%[b] (17%[c])	11		 **11** 70%
2		 **2** 85%	12		 **12** 72%
3		 **3** 76% (14%)	13		 **13** 40% (rsm 50%)
4		 **4** 78%	14		 **14** 71% (10%)
5		 **5** 42%	15		 **15** 43% (9%)
6		 **6** 79% (15%)	16		 **16** 56% (9%)
7		 **7** 77% (10%)	17		 **17** 82% (9%)
8		 **8** 28% (rsm[d] 60%)	18		 **18** 42% (7%)
9		 **9** 80% (16%)	19		 **19** 71% (9%)
10		 **10** 40% (rsm 50%)	20		**20** 42% (7%) (rsm 39%)

[a]Reaction conditions: *N*-arylacrylamide (1 equiv, 0.2 mmol), DCP (3 equiv, 0.6 mmol), Cu_2O (5 mol %, 0.01 mmol), silane (10 equiv, 2 mmol), benzene (3 mL) as solvent, sealed tube, 110 °C (measured temperature of the oil bath), 22 h. [b]Isolated yields of the desired products. [c]Isolated yields of the methylated products in the parentheses. [d]Recovery of starting materials (rsm).

N-phenylmethacrylamide were used as the model compounds to modify the reaction conditions (Table 1). The radical initiator, solvent, and the equivalent of silane, as shown in Table 1, critically affect the reaction efficiency. As the solvent, benzene is better than chlorobenzene, 1,2-dichloroethane (DCE), dimethyl sulfoxide (DMSO), dimethylformamide (DMF), etc. (entries 1−5). Dicumyl peroxide (DCP), used as the radical initiator, is more efficient than di-*tert*-butyl peroxide (DTBP), *tert*-butyl hydroperoxide (TBHP), etc. (entries 6−8). Variation of the solvent volume resulted in decreasing yield of the desired product but increasing yield of the methylated oxindoles (entries 9 and 10), which was

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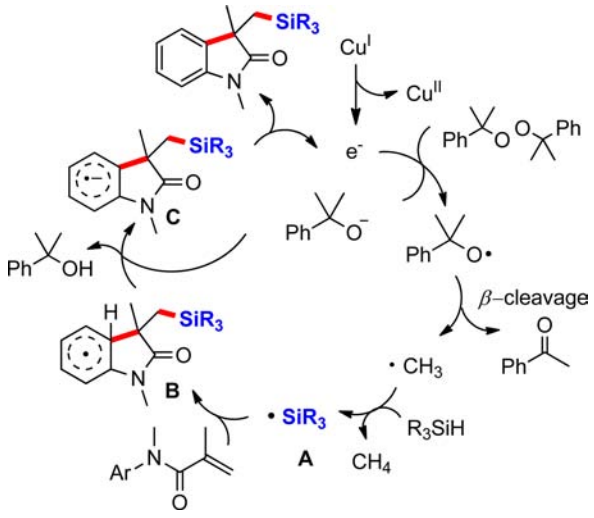
Scheme 2. Suggested Mechanism



reported by us very recently.[8d] Finally, the desired silylated oxindole and the methylation product were isolated in 80% and 17% yields by using 10 equiv of silane, respectively (entry 12).

As demonstrated in Table 2, a series of silylated oxindoles can be isolated in moderate to high yields under the typical reaction conditions. It was found that a wide range of substituted *N*-arylacrylamides and silanes are amenable to this method. The corresponding silylated oxindoles were obtained in good yields by reaction of triphenylsilane with various substituted *N*-arylacrylamides bearing alkyl, phenyl, and methoxyl groups as well as halogen atoms at the *para* position of the aromatic core (entries 1−7). Although only a 30% yield of the desired product was isolated, the alkynyl group can also be tolerated in this system (entry 8). In addition, the reaction occurred smoothly with polysubstituted and *ortho*-substituted *N*-arylacrylamides (entries 9−10). Interestingly, 1-(3,4-dihydroquinolin-1(2*H*)-yl)-2-methylprop-2-en-1-one gave a fused *N*-heterocycle in 70% yield (entry 11). Furthermore, substrates with other functional groups such as ester and amide can also be survived in this protocol (entries 12 and 13). *N*-Methyl-*N*-(naphthalen-1-yl)methacrylamide led to a high product yield (entry 14). Additional experiments showed that the *N*,*N*-diphenylmethacrylamide and *N*-benzyl-*N*-phenylmethacrylamide are effective substrates in this reaction (entries 15−16). Additionally, other silanes such as methyldiphenylsilane and dimethyl(phenyl)silane resulted in moderate to high yields of the corresponding silylated oxindoles (entries 17 and 18). Compared with triphenylsilane and methyldiphenylsilane, the dimethyl(phenyl)silane gave a relatively lower yield of the desired product, which might be due to the stability of the silyl radical intermediate. Finally, aliphatic silanes such as *tert*-butyldimethylsilane and triisopropylsilane were studied, which were also found to be effective substrates in this system (entries 19 and 20).

A series of experiments were carried out to investigate the details of the possible mechanism for this reaction. The reaction was inhibited, and no desired product was found while TEMPO was added into the system. GC-MS spectra show that it is not the 2,2,6,6-tetramethyl-1-((triphenylsilyl)oxy)piperidine but the 1-methoxy-2,2,6,6-tetramethylpiperidine which was formed (see Supporting Information (SI)). The possible reason may be that the reaction of the methyl radical with TEMPO occurs far more quickly than hydrogen abstration of silane by a methyl radical. Additionally, the intermolecular competing kinetic isotope effect (KIE) experiments through comparison of the parallel reactions of Ph_3SiH/Ph_3SiD and *N*-methyl-*N*-phenyl methacrylamide/*N*-methyl-*N*-(d_5-phenyl)methacrylamide with the same substrate were carried out (see SI). It was found that no silylated oxindole was observed in the reaction of *N*-methyl-*N*-phenylmethacrylamide with Ph_3SiD. However, reaction of *N*-methyl-*N*-(d_5-phenyl)methacrylamide with Ph_3SiH gave the desired product in 81% yield, which resulted in $k_H'/k_D' = 1.1$. These data indicate that it is not the C_{Ar}−H but the Si−H bond cleavage that should be involved in the rate-determining step of this reaction.

With the experimental data and precedent literature in hand, we postulated that an electron-catalyzed silyl free-radical addition/cyclization cascade process would be involved in this system (Scheme 2).[13] An electron is transferred from Cu(I) to DCP, which generates a Cu(II) species, cumyloxyl anion, and cumyloxyl radical. Subsequently, the silyl radical **A** would be formed through H atom abstraction by the cumyloxyl radical and/or methyl radical generated from *β*-cleavage of the cumyloxyl radical. Since acetophenone and 2-phenylpropan-2-ol were isolated as byproducts (please see SI), both of the pathways producing a silyl radical might be involved in this system. The methylated oxindoles could be formed via methyl radical addition/cyclization cascade processes. Addition of the silyl radical **A** to alkene followed by cyclization to the aromatic core would give radical intermediate **B**. Deprotonation of **B** by the cumyloxyl anion forms radical anion **C**, which could be confirmed by isolation of 1-*d*-2-phenylpropan-2-ol (see SI). **C** releases an electron to the next catalytic cycle and gives the silylated oxindole.

In conclusion, an efficient strategy for the synthesis of silylated oxindoles by a free-radical cascade reaction of *N*-arylacrylamides with silanes has been developed. It represents the first example of radical-initiated silylarylation of activated alkenes through selective activation of the Si−H/C−H bonds. Further investigation of C−Si bond formation through radical Si−H bond activation is underway in this laboratory.

■ ASSOCIATED CONTENT

Supporting Information

Full experimental details and characterization data for all products. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b01067.

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Notes

The authors declare no competing financial interest.

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