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One-pot Enyne Metathesis/Diels–Alder/Oxidation to Six-membered Silacycles with a Multi-ring Core: Discovery of Novel Fluorophores†

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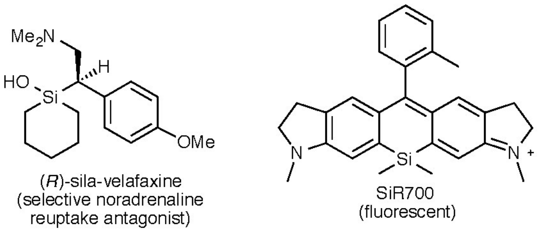
Polycyclic compounds containing a six-membered silacycle are important. However, we have limited knowledge of the nature of these six-membered silacycles because methodologies for their synthesis remain under-developed. Here, we have developed a one-pot enyne metathesis/Diels–Alder/oxidation methodology for the synthesis of six-membered molecules. Some of these compounds are novel fluorophores.

Silicon is different from carbon in several crucial aspects, for example, covalent radius and electronegativity. Thus, when a carbon atom is replaced with a silicon atom (the C/Si switch), the chemical and physicochemical properties of an organic compound are often dramatically changed.[1] The C/Si switch has been widely studied[2] since Barcza's pioneering work on silasteroids,[3] and the strategy is now applied intensively in the development of new pharmaceutical products,[4] and luminescent[5] and odorant[6] compounds. Furthermore, completely new silicon-containing compounds, for which the carbon analogues are difficult or even impossible to synthesize, are expected to have interesting properties. Thus, the development of synthetic methods for silacyclic compounds remains one of the most important frontiers in synthetic chemistry. The five-membered silacycles, or siloles, and six-membered silacycles[7] (Figure 1) are particularly important. Although a variety of methods have been developed for the preparation of siloles over the last 10 years,[8, 9] preparative methods for the six-membered silacycle ring system remain relatively unexplored. In the synthesis of six-membered silacycles, formation of the necessary C–Si bonds often relies on nucleophilic attack on a chlorosilane [Scheme 1, Eq. (1)],[10] although intramolecular cycloaddition of alkynylsilanes,[8, 11] and hydrosilylation of olefins[12] have also been successful. More recently, Pd-catalyzed cleavage of a C(sp^3)–Si bond in tetramethylsilane[13] [Scheme 1, Eq. (2)], and a Pd-catalyzed Heck reaction [Scheme 1, Eq. (3)] [14] have also been described.

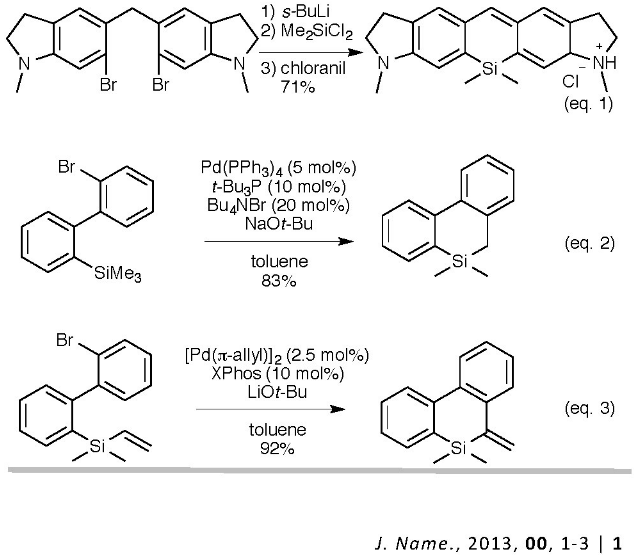
Here, we describe the first example of an enyne metathesis strategy, involving a one-pot enyne metathesis/Diels–Alder/oxidation, to give six-membered silacycle-containing multi-ring compounds. We also analyzed the optical properties of these silacyclic compounds and those of analogous nitrogen and carbon compounds, and found novel fluorophores.

Initially, we tested the ring-closing enyne metathesis of dimethylsilyl compound **1a**, which possesses alkynylbenzene and allyl moieties, using the Grubbs II catalyst (1 mol%) in several solvent at room temperature (Table 1). THF was not suitable for this reaction (entry 1), but **1a** was converted to **2a** in excellent yields with CH_2Cl_2, $(CHCl_2)_2$, or benzene solvents (entries 2–4). We did not observe a concentration effect in

Figure 1. Six-membered silacycle-containing functional molecules.



Scheme 1. Conventional preparative methods for six-membered silacycles.



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†Electronic Supplementary Information (ESI) available: Experimental procedure and NMR spectra of all new compounds. See DOI: 10.1039/x0xx00000x

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Scheme 2. Unprecedented preparative method for six-membered silacycles described in this work.

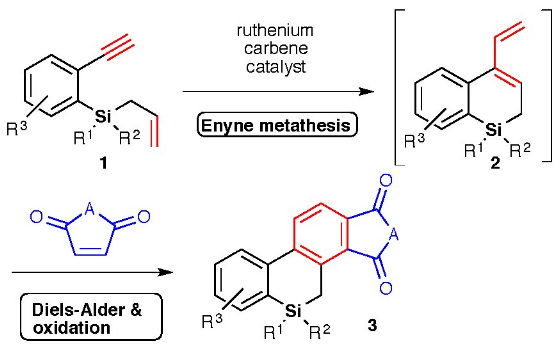
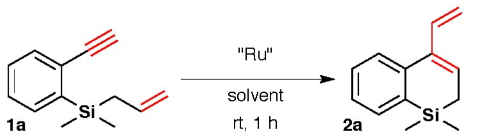


Table 1. Ring-closing enyne metathesis of **1a**.



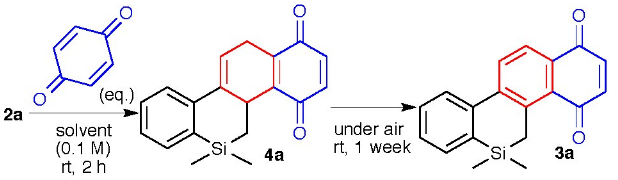
entry	"Ru" (mol%)	solvent (M)	yield of **2a** (%)
1	Grubbs II (1)	THF (0.005)	26
2	Grubbs II (1)	CH_2Cl_2 (0.005)	90
3	Grubbs II (1)	$(CHCl_2)_2$ (0.005)	85
4	Grubbs II (1)	benzene (0.005)	96
5	Grubbs II (1)	CH_2Cl_2 (0.2)	91
6	Grubbs I (1)	CH_2Cl_2 (0.005)	13
7	Hoveyda-Grubbs II (1)	CH_2Cl_2 (0.005)	89
8	Hoveyda-Grubbs I (1)	CH_2Cl_2 (0.005)	14
9	Grubbs II (0.5)	CH_2Cl_2 (0.005)	90

CH_2Cl_2 (entries 2 and 5). Both the Grubbs II and Hoveyda–Grubbs II catalysts, ruthenium carbene catalysts with nitrogen-containing heterocycles, worked well in this reaction (entries 2, 6, 7, and 8). Moreover, 0.5 mol% of the Grubbs II catalyst was sufficient for conversion of **1a** to **2a** in 90% yield (entries 2 and 9).

We next reacted diene **2a** with quinone in a Diels–Alder reaction with subsequent air oxidation at room temperature (Table 2). More than 1.5 equivalents of benzoquinone were necessary for these reactions (entries 1–3), and we obtained **4a** in quantitative yield in CH_2Cl_2, toluene or THF. Although **4a** was unstable and automatically oxidized to **3a**, this process took more than 1 week.

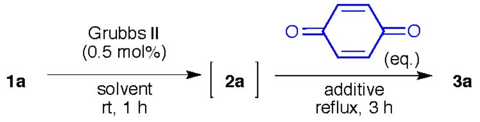
On the basis of these results, we examined the one-pot enyne metathesis/Diels–Alder/oxidation of **1a** to **3a** (Table 3). Our aim was to shorten the time required for air oxidation of **4a** to **3a** to 3 h. After treatment of **1a** with 0.5 mol% of the Grubbs II catalyst in CH_2Cl_2 (0.005 M) for 1.5 h, the resulting unpurified **2a** was refluxed with five equivalents of 1,4-benzoquinone for 3 h. However, expected product **3a** was not observed on TLC analysis (Table 3, entry 1). When the same reaction was performed using toluene or *p*-xylene solvents, **3a** was isolated in 0% and 29% yield, respectively.

Table 2. Diels–Alder reaction of **2a** and subsequent oxidation



entry	eq. of benzoquinone	solvent	yield of **4a** (%)
1	1	CH_2Cl_2	39
2	1.5	CH_2Cl_2	97
3	2	CH_2Cl_2	96
4	2	toluene	95
5	2	THF	92

Table 3. Optimization of the one-pot enyne metathesis/Diels–Alder/oxidation.



entry	solvent (M)	eq. of quinone	Yield (%)
1	CH_2Cl_2 (0.005)	5	0
2	toluene (0.005)	5	0
3	*p*-xylene (0.005)	5	29
4	*p*-xylene (0.2)	5	55
5[a]	toluene (0.2)	2	78

[a] Unpurified **2a** was treated with 1,4-benzoquinone (2 eq.) at room temperature (rt) for 1 h, then DDQ (3 eq.) was added and the mixture was stirred at 100 °C for 3 h.

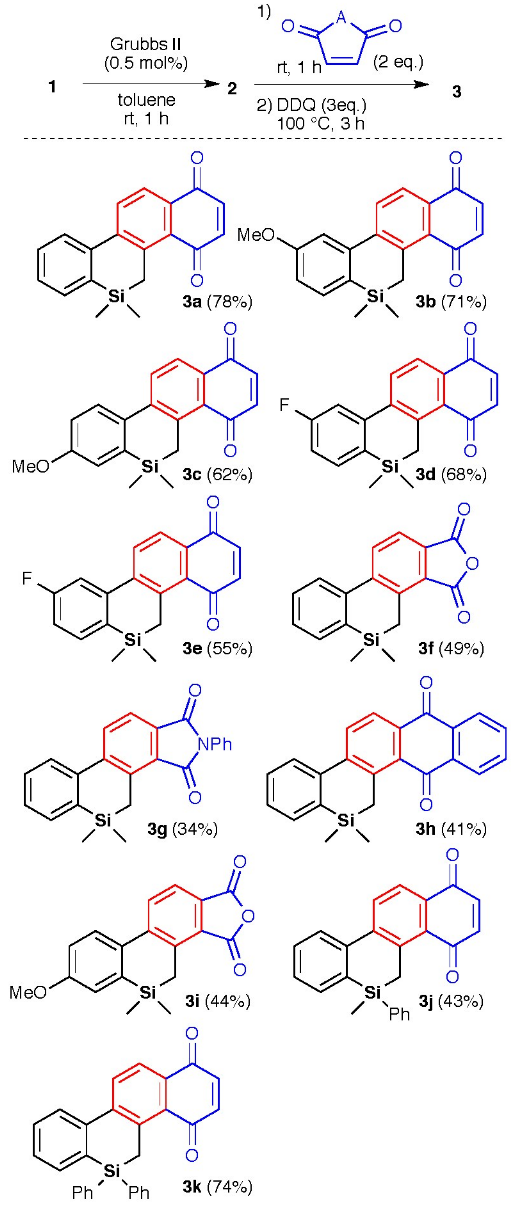
The yield of **3a** was increased to 55% on increasing the concentration from 0.005 to 0.2 M (entry 4). We thus concluded that 1,4-benzoquinone did not have sufficient oxidation ability. We therefore reduced the number of equivalents of 1,4-benzoquinone to 2, and added three equivalents of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) as the oxidizing agent. Unpurified **2a** was thus treated with 1,4-benzoquinone (2 eq.) at room temperature for 1 h, then DDQ (3 eq.) was added and the mixture was stirred at 100 °C for 3 h to give **3a** in 78% isolated yield (entry 5).

We next probed the substrate scope of the reaction (Scheme 3). Substrates with electron-withdrawing or -donating substituents were converted to corresponding cycloadducts **3** in good yields (**3b–e**).

Furthermore, in addition to 1,4-benzoquinone, maleic anhydride, *N*-phenylmaleimide, and 1,4-naphthoquinone also acted as dienophiles in the reaction (**3f–i**, and **n**). Substituents on the silicon atom were not limited to dimethyl groups, and substrates with methyl phenyl or diphenyl substituents afforded corresponding products **3j** and **3k** in 43% and 74% yields, respectively. Our one-pot methodology can also be used to synthesize the analogous polycyclic six-membered carbon and nitrogen compounds (Scheme 4).[15] We next investigated the absorption and emission profiles of **3a–n** (Figures 2, S1, S2 and S3). Compounds **3a–e**, prepared from the 1,4-benzoquinone dienophile, displayed clear absorption peaks with maxima at 404–433 nm (Figure S1). Compounds **3f–i**, prepared from the maleic anhydride or *N*-phenyl maleimide dienophiles, displayed clear absorption peaks with maxima at 346–387 nm (Figure S1).

Substituents on the silicon did not influence the absorption properties (**3a**, **3j**, and **3k**). In addition, carbon analogue **3l** and nitrogen analogue **3m** had similar absorption properties to **3a**. In most solvents, except for MeOH, the absorption spectra of **3a** were almost identical (Figure S2). Figure 2 shows the fluorescent properties of **3f**, **3i**, and **3n**; characteristic fluorescent absorption bands of **3f**, **3i**, and **3n** were observed at 420, 464, and 411 nm, respectively, in $CHCl_3$. The fluorescence intensity of quantum dots of silicon-containing **3f** was almost 300 times higher than that of carbon analogue **3n**.[16] In addition, the fluorescence intensity of **3f** was higher in MeOH and DMSO than in other solvents (Figure S3).

Scheme 3. Six-membered silacycles prepared by one-pot enyne metathesis/Diels–Alder/oxidation.



Scheme 4. Synthesis of six-membered carbon and nitrogen analogues

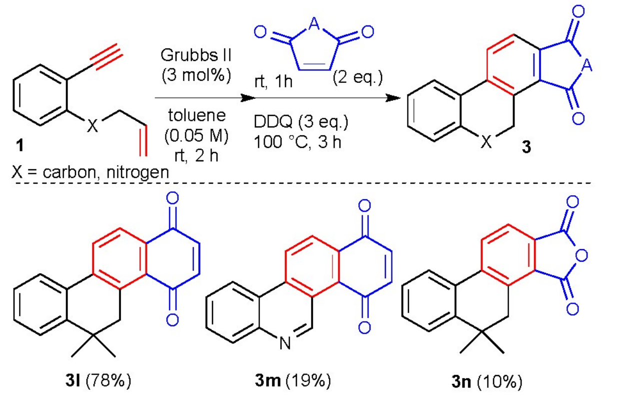
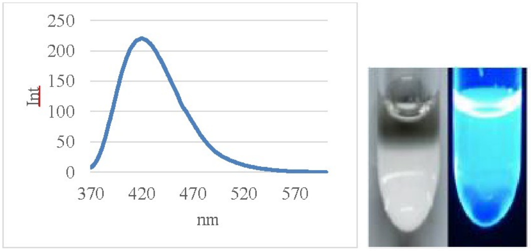
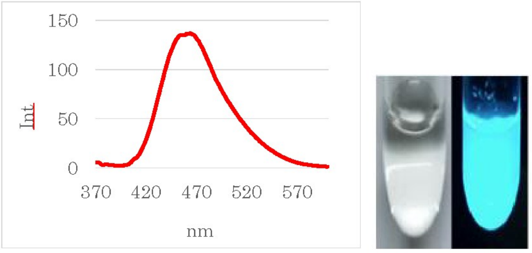


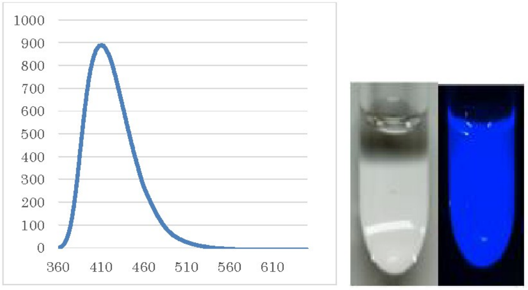
Figure 2. Fluorescence spectra of **3f**, **3i** and **3n**. Left photo: under visible light, right photo: UV irradiation (365 nm)



3f (10 nM in $CHCl_3$), $\varepsilon(346)=9930$, $\lambda_{ex}=346$ nm, $\lambda_{em}=420$ nm, $\Phi=0.888$.



3i (100 nM in $CHCl_3$), $\varepsilon(363)=11100$, $\lambda_{ex}=363$ nm, $\lambda_{em}=464$ nm, $\Phi=0.0727$.



3n (10 µM in $CHCl_3$), $\varepsilon(345)=8620$, λ_{ex} = 345 nm, λ_{em} = 411 nm, $\Phi=0.00311$.

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In conclusion, we have developed a one-pot enyne metathesis/Diels–Alder/oxidation methodology for the synthesis of six-membered silacycles that contain multiple rings. We have also revealed the optical properties of these polycyclic six-membered silacycles, which are widely used for the synthesis of functional molecules. These results are important because they introduce another structural moiety for fluorophores and will aid the development of practical six-membered silacyclic dyes. These results are of interest because these silacycles are widely used for the synthesis of functional molecules.

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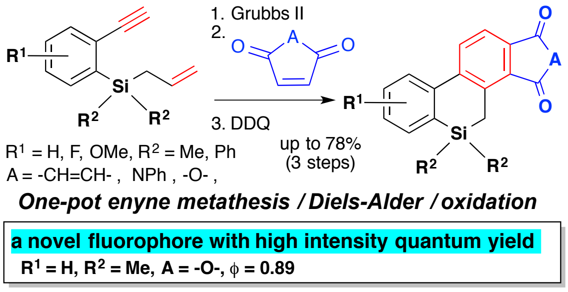

one-pot enyne metathesis/Diels–Alder/oxidation methodology was developed to give fluorescent six-membered silacycle with multi-ring core