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Preparation of siloxacyclopentene containing 1,3-dienes and their Diels–Alder reactions

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Abstract—A number of enynyloxy dimethyl and diisopropyl silanes have been prepared and converted into siloxacyclopentene containing 1,3-dienes via intramolecular hydrosilylation of the alkyne functional group. Diels–Alder reactions of these dienes are reported.

We have embarked on a synthetic program aimed at the synthesis of stable 2-boron and 2-silicon substituted 1,3-dienes and investigation of their reaction chemistry.[1,2] Earlier this year, we reported the simple preparation of 2-triethoxysilyl-1,3-butadiene and its conversion into 2-silatrane and 2-biscatecholsiloxy substituted 1,3-dienes. Those new siloxy substituted dienes proved to be remarkably reactive in Diels–Alder cycloadditon reactions, and the Diels–Alder cycloadducts could be used in Hiyama cross coupling reactions.[2] Reports of the preparation and use of 2-trialkoxysilyl-1,3-dienes are extremely rare. We found a report of 2-trimethoxysilyl- and 2-triethoxysilyl-1,3-butadiene in 1984,[3] and then a report of the polymerization of these materials in 1989.[4]

In 1988, Tamao, Ito, and co-workers reported the intramolecular hydrosilylation of the alkyne moiety of homopropargyl alcohols to make siloxacyclopentanes containing exocyclic alkenes.[5] Other routes to siloxacycle containing species, which have been used in cross coupling chemistry, have also been reported previously.[6–8] In 2004, Clark and Woerpel reported the reaction of a '^{t}Bu$_2$Si' source with a protected enynol to produce a siloxacyclopentene containing a silicon substituent at the 1 position of a 1,3-diene moiety.[9] This diene reacted with *N*-phenylmaleimide in a Diels–Alder reaction. Also in 2004, Lee and co-workers reported the synthesis of a number of siloxacyles that are part of a 1,3-diene unit via a condensation/metathesis strategy using alkenyl alcohols and alkynyl silanes.[10] No Diels–Alder or cross coupling reactions of these substrates were reported. Earlier this year Halvorsen and Roush reported using this procedure to make siloxacyclopentenes containing pendant dienophiles and demonstrated that they could be used in intramolecular Diels–Alder reactions, which were followed by protiodesilylation.[11] We had simultaneously been using a combination of the Tamao–Ito[5] and Lee protocols[12] to make siloxacyclopentenes, which could participate in intermolecular Diels–Alder reactions. Here, we report our preliminary results in this area.

We first prepared several enynyl silanes (Scheme 1) in excellent yields from pentenyne and tried to convert them into siloxacyclopentene containing 1,3-dienes (**4**) using Lee's alkynylation–hydrosilylation sequence.[12] Unfortunately, we recovered enynyl silanes (**1**–**3**) from these reactions. We then switched to the preparation of siloxy substituted enynes (**7a**, **7c**–**e**) (prepared from methylbutenyne (**5a**) and cyclohexenylethyne (**5b**) via condensation with carbonyl compounds followed by Denmark's protocol),[13] and converted them into siloxacyclopentenes (**8a**, **8e**, **10a**, **10e**) using Lee's KO^{t}Bu catalyzed trans-hydrosilylation protocol[12] (Scheme 2). Diisopropylsilyloxy substituted enynes (**7a**, **7c**–**e**) could be isolated and characterized prior to conversion to siloxacyclopentenes (**8a**, **8e**).

Dimethylsiloxy substituted enynes (**9a**, **9e**) were generated in situ by using the Tamo–Ito protocol[5] and then converted into siloxacyclopentenes (**10a**, **10e**), which

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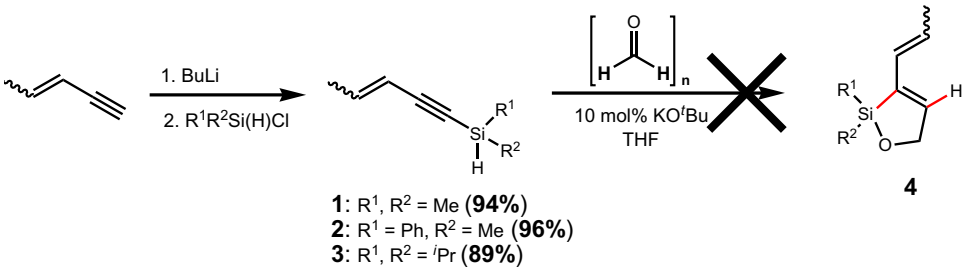
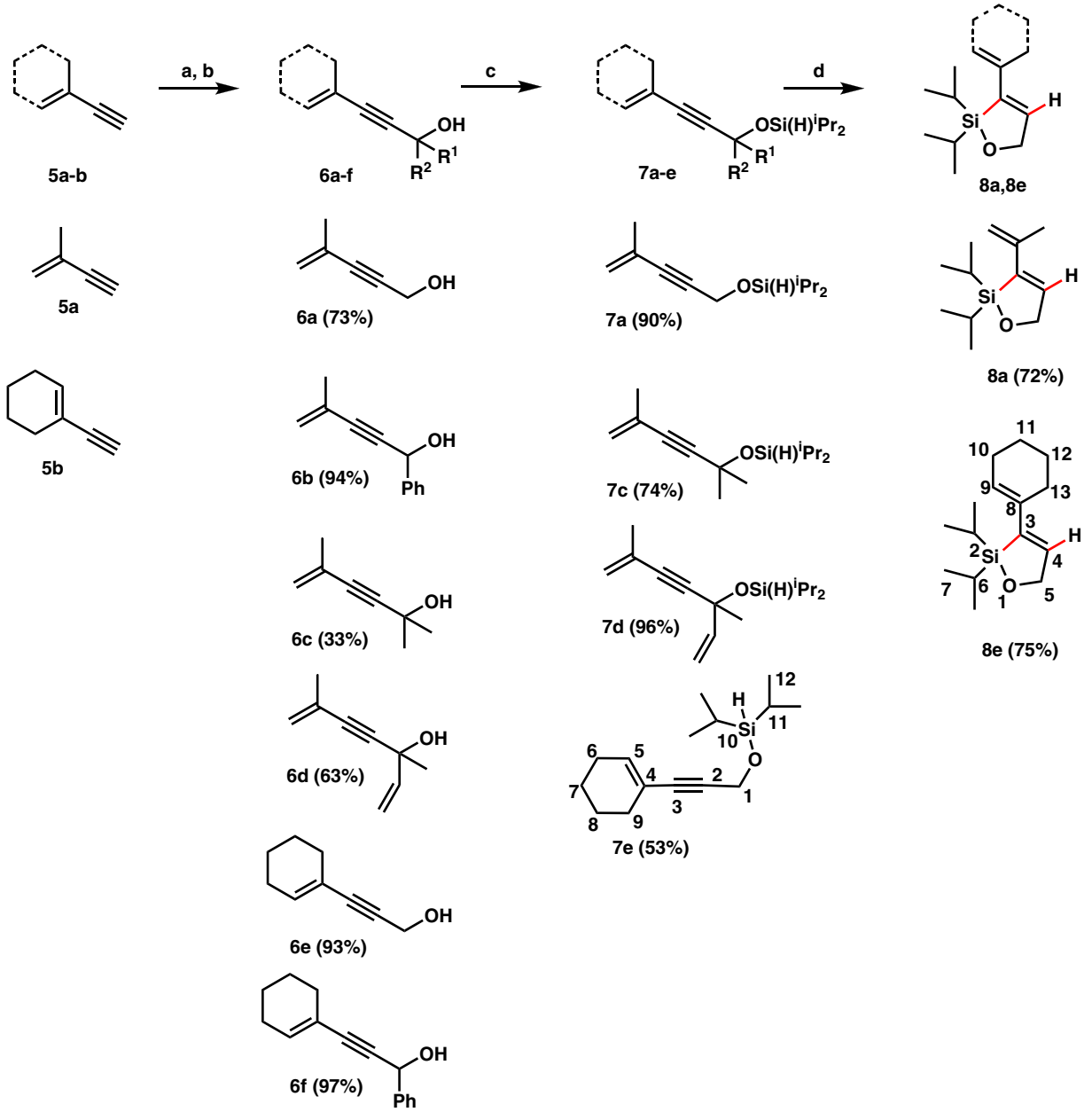
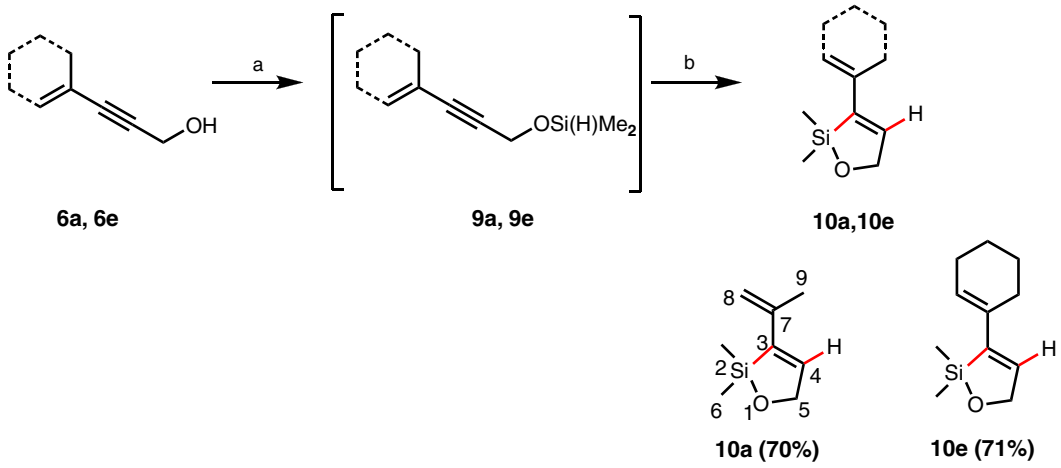


Scheme 1. Synthesis of enynylsilanes (**1**–**3**).

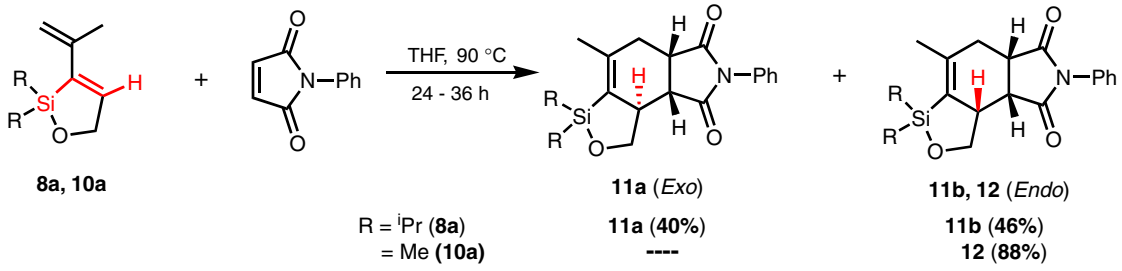


Scheme 2. Synthesis of diisopropylsilyloxy substituted enynes (**7a**–**e**) and siloxacyclopentene containing 1,3-dienes (**8a**, **8e**). Reagents and conditions: (a) (i) THF, −78 °C; (ii) ^{n}BuLi; (iii) −78 °C → 0 °C, 1 h; (b) (i) 0 °C → −78 °C; (ii) aldehyde/ketone; (iii) −78 °C → rt, overnight; (c) (i) hexanes, 0 °C; (ii) DMAP, NEt_3; (iii) $^{i}Pr_2Si(H)Cl$ in hex, 10 min; (iv) 0 °C rt, overnight; (d) (i) THF; (ii) water bath; (iii) KO^{t}Bu in THF; (iv) rt, 1 h.

were isolated and characterized (Scheme 3). All dienes are stable for weeks at 25 °C in the presence of air and can be purified by chromatography on silica gel. Representative experimental procedures for the preparation of



Scheme 3. Synthesis (Tandem) of dimethylsiloxacyclopentene containing 1,3-dienes (**10a**, **10e**). Reagents and conditions: (a) (i) water bath; (ii) $(Me_2SiH)_2NH$ (neat); (iii) rt, overnight; (b) (i) THF; (ii) water bath; (iii) KO^{t}Bu in THF; (iv) rt, 1 h.

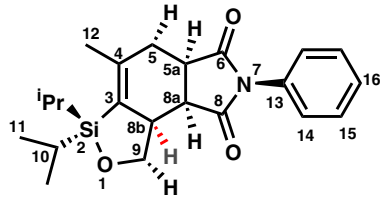


Scheme 4. Intermolecular Diels–Alder reactions of diene-**8a** and **10a** with *N*-phenylmaleimide.

all diene types reported are included in the reference section.[15–17]

With these dienes in hand, we have performed several Diels–Alder reactions. Methyl substituted dienes **8a** and **10a** both react completely with *N*-phenylmaleimide after 24–36 h at 90 °C (Scheme 4). The dimethylsiloxy substituted diene (**10a**) provides *endo* adduct (**12**), whereas the more bulky diisopropyl siloxy diene **8a** provides *exo* and *endo* cycloadducts (**11a** and **11b**, respectively) in almost equal proportions. This outcome can be rationalized by unfavorable steric interactions between the *N*-phenyl and the isopropyl groups in the electronically favored *endo* transition state. Cyclohexenyl substituted dienes **8e** and **10e** proved much less reactive in thermal Diels–Alder reactions and only started to show traces of Diels–Alder cycloadducts after 40–50 h of heating at 90 °C. Halvorsen and Roush found that siloxacyclopentene constrained nonatrienes participated in thermal Diels–Alder reactions with little stereoselectivity, whereas these substrates participated in Lewis acid catalyzed intramolecular Diels–Alder reactions through *endo* transition states to produce perhydroindene cycloadducts with high stereoselectivity.[11] They found that siloxacyclopentene constrained decatrienes participated in thermal or Lewis acid-catalyzed cycloadditions through *endo* transition states to produce octahydronaphthalenes with high stereoselectivity.

The stereochemistry of the Diels–Alder cycloadducts **11** and **12** were assigned using a combination of COSY, HMQC, and HMBC to make all the ^{1}H assignments followed by NOESY to assign stereochemistry. In the *cis* isomers that arise from the *endo* transition states (**11b**, **12**), one of the diastereotopic H5 protons exhibits NOE to both H8a and H8b, whereas the other H5 does not exhibit NOE to either of those protons (Scheme 5).



Scheme 5. Cycloadduct stereochemistry.

In summary, we have prepared a new diisopropylsiloxacyclopentene containing 1,3-dienes via a simple three-step procedure from enynes. We have prepared a new dimethylsililoxacyclopentene containing 1,3-dienes via a one pot, two-step sequence from enynols. These dienes participate in Diels–Alder reactions with a higher preference for the production of trans cycloadducts from the sterically more bulky diisopropylsiloxy substituted dienes.

Acknowledgements

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instrumentation used to characterize the compounds reported here. The Duke University Center for Mass Spectrometry and Mass Spectrometry Facility at UNC-CH performed high-resolution mass spectral analysis. We thank Dr. Marcus W. Wright for NMR assistance.

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15. *Typical procedure for the synthesis of siloxyenynes* (**7e**). Alkenynol (**6e**)[14] (1.236 g, 12.86 mmol), triethylamine (1.30 g, 12.85 mmol), dimethylaminopyridine (0.152 g, 1.267 mmol), and diisopropylchlorosilane (1.918 g, 12.73 mmol) were used to yield compound **7e** (1.680 g, 6.71 mmol, 53%) as a colorless, clear oily substance after purification by flash chromatography: R_f 0.85 (hexanes/Et_2O, 4:1); ^1H NMR (500 MHz, $CDCl_3$) δ 6.08 (h, $J = 1.8$ Hz, 1H, H-5), 4.48 (s, 2H, H-1), 4.20 (s, 1H, H-10), 1.98–2.17 (m, 4H, H6-9), 1.49–1.71 (m, 4H, H6-9), 0.96–1.12 (m, 14H, H-11, 12). ^{13}C NMR (300 MHz, $CDCl_3$) δ 134.8 (C-5), 120.3 (C-4), 87.1 (C-2/3), 84.4 (C-2/3), 54.3 (C-1), 29.0 (C6-9), 25.6 (C6-9), 22.2 (C6-9), 21.5 (C6-9), 17.3 (C-12), 17.2 (C-12), 12.3 (C-11); HRMS: $(M+Na)^+$ calcd for $C_{15}H_{26}NaOSi$, 273.1651; found, 273.1639.
16. *General procedure for diisopropylsiloxacyclodiene synthesis* (**8e**). (3-Cyclohexenylprop-2-ynyloxy)diisopropylsilane (**7e**) (0.715 g, 2.854 mmol) was taken into a 50 mL, round-bottomed flask kept in a water bath at ambient temperature. The flask was purged with N_2 for 2 min, then 10 mol % KO^{t}Bu (0.037 g, 0.330 mmol) was added in THF (3×5 mL) solution over a period of 10 min. After the addition, the water bath was removed and stirring continued for 1 h at room temperature. The reaction mixture was diluted with Et_2O (20 mL), followed by quenching with satd NH_4Cl (50 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3×20 mL). The combined organics were washed with satd NaCl solution (50 mL) and dried over $MgSO_4$. After the removal of volatiles, the crude product was purified by flash chromatography yielding **8e** as a colorless, clear liquid; R_f 0.45 (hexanes/Et_2O, 15:2). The isolated compound was found to have an impurity of about ~20% with a similar R_f value, hence the compound was further purified by using a chromatotron (2.0 mm silica gel) (0.537 g, 2.144 mmol, 75%). ^1H NMR (300 MHz, $CDCl_3$) δ 6.56 (s, 1H, H-4), 5.57 (s, 1H, H-9), 4.61 (s, 2H, H-5), 2.17–2.26 (m, 2H, H-13), 2.03–2.16 (m, 2H, H-10), 1.64–1.75 (m, 2H, H-12), 1.52–1.64 (m, 2H, H-11), 1.06–1.20 (m, 2H, H-6), 1.04 (d, $J = 6.6$ Hz, 6H, H-7), 0.98 (d, $J = 6.8$ Hz, 6H, H-7); ^{13}C NMR (300 MHz, $CDCl_3$) δ 140.3 (C-3), 138.0 (C-4), 135.7 (C-8), 128.9 (C-9), 72.8 (C-5), 26.2 (C-13), 26.0 (C-10), 22.8 (C-12), 22.4 (C-11), 17.4 (C-7), 17.1 (C-7), 13.4 (C-6); HRMS: $(M+H)^+$ calcd for $C_{15}H_{27}OSi$, 251.1831; found, 251.1828.
17. *Representative procedure for the synthesis (tandem) of dimethylsiloxacyclodiene* (**10a**): Alkenynol (**6a**) (1.792 g, 18.64 mmol) was taken into a 50 mL, round-bottomed flask kept in a water bath under N_2. After the slow addition of 1,1,3,3-tetramethyldisilazane (1.504 g, 11.28 mmol) over ~5 min using a syringe, the water bath (23 °C) was removed and stirring continued overnight at room temperature. Then the volatiles were removed by rotovap (30 °C, 20 mm) and the crude reaction mixture was dissolved in THF (10 mL), and the flask was cooled in a water bath at ambient temperature. The flask was purged with N_2 for 2 min, then KO^{t}Bu (0.217 g, 1.934 mmol) was added in THF (3×5 mL) solution over a period of 10 min. After the addition, the water bath was removed and stirring continued for 1 h at room temperature. The reaction mixture was diluted with Et_2O (20 mL), followed by quenching with satd NH_4Cl (50 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3×20 mL). The combined organics were washed with satd NaCl solution (50 mL), dried over $MgSO_4$ and the volatiles were removed by rotovap. A brown colored crude reaction mixture was produced, which upon purification by column chromatography yielded **10a** as a clear colorless oil (2.014 g, 13.05 mmol, 70%): R_f 0.68 (pentane/Et_2O, 3:1); ^1H NMR (500 MHz, $CDCl_3$) δ 6.60 (as, 1H, H-4), 4.99 (s, 1H, H-8′), 4.82 (s, 1H, H-8″), 4.66 (s, 2H, H-5), 1.93 (s, 3H, H-9), 0.33 (as, 6H, H-6); ^{13}C NMR (300 MHz, $CDCl_3$) δ 142.2 (C-3), 141.3 (C-7), 141.2 (C-4), 115.7 (C-8), 71.9 (C-5), 20.4 (C-9), 0.45 (C-6); HRMS: (M^+) calcd for $C_8H_{14}OSi$, 154.0814; found, 154.0813.