Diels–Alder Reactions of Silyl-Substituted Masked *o*-Benzoquinones: Expedient Access to Alkenylsilanes

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Abstract: A one-pot synthesis of several silyl bicyclic and oxatricyclic alkenes by inter- and intramolecular Diels–Alder reactions of 4-trimethylsilyl substituted masked *o*-benzoquinones derived from the corresponding 2-methoxyphenols is described.

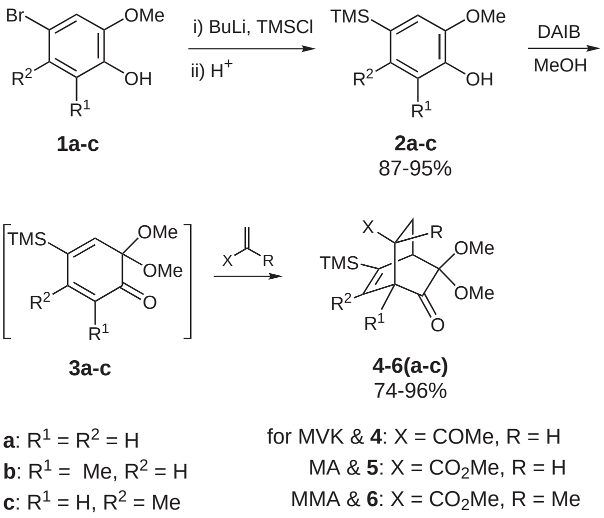
Key words: 2-methoxyphenols, 4-silyl masked *o*-benzoquinones, Diels–Alder reaction, silyl bicyclo[2.2.2]octenes, silyl oxatricyclo[4.3.1.0]decenes

Alkenylsilanes constitute important building blocks for olefin synthesis and serve as valuable synthons in organic synthesis.[1] Conventionally, vinylsilanes are prepared from alkynes, carbonyl compounds and vinyl halides. However, very few reports are available for the synthesis of silyl bicyclic and tricyclic alkenes.[2,3] In this Letter we report a novel and convenient one-pot synthesis for the preparation of various silyl bicyclo[2.2.2]octenes and oxatricyclo[4.3.1.0]decenes from 4-trimethylsilyl substituted 2-methoxyphenols via the Diels–Alder cycloadditions of transiently generated masked *o*-benzoquinones (MOBs).

MOBs are indeed highly reactive and versatile intermediates in organic synthesis.[4] We have demonstrated that these transients undergo the Diels–Alder reactions with an array of dienophiles under mild conditions in excellent selectivities enabling rapid access to highly functionalized bicyclic and tricyclic ring systems from readily available 2-methoxyphenols.[5] The intramolecular Diels–Alder reaction (IMDA) of MOBs provided an expeditious entry to polycyclic skeletons.[6] The MOB Diels–Alder protocol has been utilized as one of the key-steps in the total synthesis of several natural products.[7]

Owing to their highly reactive nature, MOBs undergo facile dimerization to provide Diels–Alder type dimers.[8] For instance, the MOBs generated by the oxidation of guaiacol and its 3- and 4-methyl derivatives are highly reactive and produce large amounts of the corresponding dimers even in the presence of large excess of external dineophile. The reactivity of a particular MOB is a function of substituent and substitution pattern. Recently, we have deduced a general trend for the stability and dimerization of these labile quinones.[5c,9] An electron-withdrawing group at position-4 of MOB enhances its reactivity (i.e. facilitates dimerization) and an electron-releasing group exerts an opposite effect. A large group at C_4 of MOB reduces the propensity of dimerization. It occurred to us that the introduction of a trimethylsilyl group at position-4 of the parent MOB not only stabilizes these latent quinones, but also provides an expedient route to the hitherto unknown alkenylsilanes.

The requisite 4-trimethylsilyl substituted 2-methoxyphenols **2a**–**c** were prepared in 87–95% yield from the corresponding 4-bromo-2-methoxyphenols **1a**–**c** via sequential metal-halide exchange with BuLi at –78 °C and treatment with TMSCl followed by quenching with 2 N HCl. We initiated our studies utilizing 2-methoxy-4-trimethyl-silylphenol (**2a**). When **2a** was subjected to oxidation with diacetoxyiodobenzene (DAIB) in methanol in the presence of methyl vinyl ketone (MVK), the in situ generated 4-trimethylsilyl MOB **3a** underwent the Diels–Alder reaction with MVK to provide the cycloadduct **4a** in high yield.[10,11] No trace of the dimer of MOB **3a** was observed from the ^{1}H NMR spectrum of the crude reaction mixture. Subsequently, the reactions of 2-methoxyphenol **2a** with methyl acrylate (MA) and methyl methacrylate (MMA) in the presence of DAIB in methanol were carried out to produce the corresponding cycloadducts **5a** and **6a** in good yields (Scheme 1, Table 1).



Scheme 1

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Table 1 Synthesis of Alkenylsilanes **4a**–**c** to **6a**–**c** via the Intermolecular Diels–Alder Reactions of 4-Silyl-Substituted Masked *o*-Benzoquinones **3a**–**c** with Electron-Deficient Dienophiles[a]

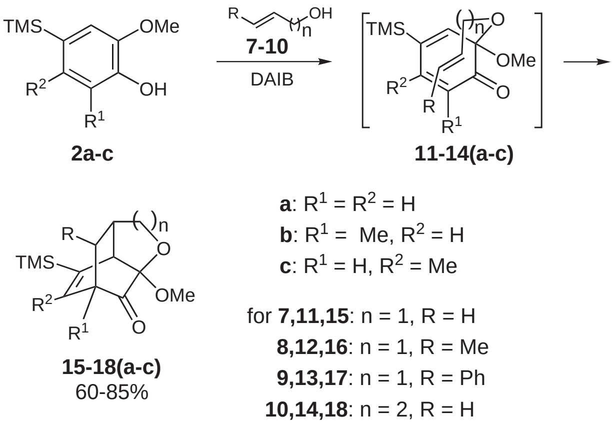
Entry	Phenol	MOB	Dienophile	Time	Adduct/ Yield (%)[b]
1	**2a**	**3a**	MVK	8 h	**4a**/88
2	**2a**	**3a**	MA	18 h	**5a**/94
3	**2a**	**3a**	MMA	36 h	**6a**/74
4	**2b**	**3b**	MVK	6 h	**4b**/92
5	**2b**	**3b**	MA	18 h	**5b**/96
6	**2b**	**3b**	MMA	18 h	**6b**/89
7	**2c**	**3c**	MVK	6 h	**4c**/91
8	**2c**	**3c**	MA	24 h	**5c**/94
9	**2c**	**3c**	MMA	72 h	**6c**/77

[a] All reactions were carried out at room temperature with 2 equiv of dienophile.

[b] Yields are of pure and isolated products.

The reaction was then extended to silyl-phenols **2b**,**c**. Thus, the Diels–Alder reactions of MOBs **3b**,**c** with MVK, MA and MMA proceeded smoothly to furnish the corresponding cycloadducts **4b**,**c**–**6b**,**c** in excellent yields. The results are presented in Table 1.

To broaden the scope of this methodology, we then tested the intramolecular Diels–Alder reactions of 4-silyl-substituted MOBs. As a preliminary case, the oxidation of **2c** by DAIB in the presence of allyl alcohol (**7**) and the subsequent cycloaddition were carried out under various conditions. After considerable experimentation, the crude MOB **11c** that was obtained from the oxidation-step underwent the internal Diels–Alder reaction to furnish **15c** in 78% yield.[12] Similarly, MOBs **12c**–**14c** derived from 2-methoxyphenol **2c** and alkenols **8**–**10** reacted intramolecularly to afford adducts **16c**–**18c**, respectively, in very good yields. Immediately, we extended this reaction to 4-silyl-2-methoxyphenols **2a** and **2b** (Scheme 2). Thus, the oxidation of **2a**,**b** with DAIB in the presence of alkenols **7**–**10** generated MOBs **11a**,**b**–**14a**,**b**, which underwent internal Diels–Alder reactions to provide silyl-substituted oxatricycles **15a**,**b**–**18a**,**b** in good yields. The results are summarized in Table 2.



Scheme 2

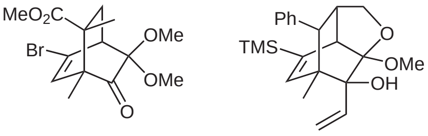
Table 2 Synthesis of Alkenylsilanes **15a**–**c** to **18a**–**c** via the Intramolecular Diels–Alder Reactions of 4-Silyl-Substituted Masked *o*-Benzoquinones **11a**–**c** to **14a**–**c**[a]

Entry	Phenol	MOB	Alkenol			Adduct/ Yield (%)[b]
				n	R	
1	**2a**	**11a**	**7**	1	H	**15a**/68
2	**2a**	**12a**	**8**	1	Me	**16a**/85
3	**2a**	**13a**	**9**	1	Ph	**17a**/60
4	**2a**	**14a**	**10**	2	H	**18a**/60
5	**2b**	**11b**	**7**	1	H	**15b**/73
6	**2b**	**12b**	**8**	1	Me	**16b**/77
7	**2b**	**13b**	**9**	1	Ph	**17b**/66
8	**2b**	**14b**	**10**	2	H	**18b**/68
9	**2c**	**11c**	**7**	1	H	**15c**/78
10	**2c**	**12c**	**8**	1	Me	**16c**/81
11	**2c**	**13c**	**9**	1	Ph	**17c**/74
12	**2c**	**14c**	**10**	2	H	**18c**/73

[a] All the Diels–Alder reactions of MOBs **11a**–**c** to **14a**–**c** were carried out at 80 °C for 10 h.

[b] Yields are of pure and isolated products.

The inter- and intramolecular Diels–Alder reactions of 4-silyl-substituted MOBs have proceeded in highly selective manner. The regio- and stereochemistry of these cycloadducts were in accordance with literature precedents[5c,6a,13] and were thoroughly determined from the ^{1}H-^{1}H decoupling NMR experiments. The stereochemical assignments of adducts **4a**,**b**, **5a**,**b** and **15a**,**b**–**18a**,**b** were further confirmed from the observed long-range *W*-coupling between the vinylic protons and the methine/methylene proton. The regio- and stereochemistries of the cycloadducts **6a**–**c** derived from methyl methacrylate were confirmed by comparing their ^{1}H NMR data with that of **19** (Figure 1), whose structure was known from single-crystal X-ray diffraction method.[8,14] Further, the structure of **17b** was confirmed by the single crystal X-ray structure of **20** (Figure 1),[15] which was derived from **17b**.



19 **20**

Figure 1

In summary, this Letter describes a general and efficient methodology for the synthesis of silyl bicyclic and oxatricyclic alkenes from easily accessible 2-methoxyphenols. Utilization of these alkenylsilanes in organic synthesis is under progress in our laboratory.

Acknowledgement

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(10) *General procedure for intermolecular Diels–Alder reaction:* To a stirred mixture of a 2-methoxyphenol (**2a**–**c**, 0.5 mmol) and dienophile (2 equiv) in MeOH (25 mL) at room temperature, was added DAIB (0.55 mmol, 1.1 equiv) at once and the reaction was continued at the same temperature. After a period of time (see Table 1), the reaction mixture was concentrated under reduced pressure and purified by silica gel column chromatography to get the pure adduct (**4a**–**c** to **6a**–**c**).

(11) All the new compounds were satisfactorily characterized by IR, ^{1}H NMR (400 MHz), and ^{13}C NMR (100 MHz), DEPT, and low and high resolution MS analyses.

(12) *General procedure for intramolecular Diels–Alder reaction:* To a stirred mixture of a 2-methoxyphenol (**2a**–**c**, 0.5 mmol) and an alkenol (**7**–**10**, 25 mmol, 50 equiv) at 0 °C, was added DAIB (0.55 mmol, 1.1 equiv) at once and the contents were stirred for 30 min at the same temperature [oxidations of 2-methoxyphenols in the presence of cinnamyl alcohol (**9**) were carried out at room temperature (entries 3, 7 and 11 in Table 2)]. The reaction was quenched with aq $NaHCO_3$, extracted with ether. The organic layer was washed with brine, dried over anhyd. $MgSO_4$, and concentrated. The crude residue that contains mainly MOB (**11a**–**c** to **14a-c**) and excess alkenol (**7**–**10**) was heated at 80 °C for 10 h. The reaction mixture was then cooled to room temperature, the excess alkenol was removed under reduced pressure and the residue was subjected to silica gel column chromatography to obtain the pure adduct (**15a**–**c** to **18a**–**c**).

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