Synthesis and Diels−Alder Reactions of 4-Substituted-1,3-diphenoxy-2-[(*tert*-butyldimethylsilyl)oxy]-1,3-butadienes: Application to the Synthesis of Triaryl Ethers

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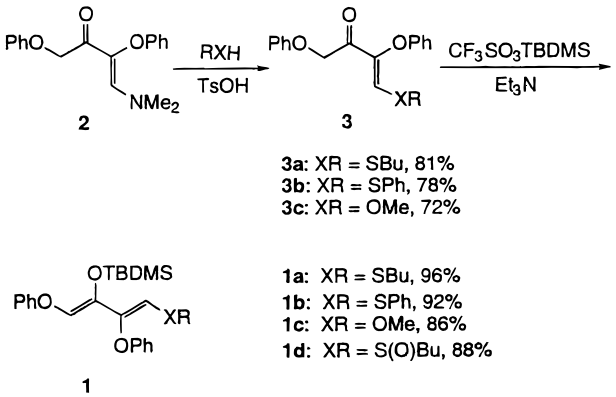
A novel class of tetrahetero-substituted 1,3-dienes **1a**−**d** having aryl ether substituents at the 1,3-positions were synthesized by enol silylation of 4-substituted 1,3-diphenoxy-3-buten-2-ones **3a**−**c**. The 1*Z*,3*Z* configuration of **1b** has been assigned by X-ray crystallography. The synthesis of triaryl ethers utilizing a Diels−Alder approach involved reaction of diene **1a** with methyl acrylate to furnish a 3:1 mixture of endo- and exo-adducts. Conversion of the adducts to cyclohexenone **8** and aromatization with DDQ gave triaryl ether **9**. Cycloaddition reactions of **1a**, **1b** with some conjugated alkenes exhibited excellent regiospecificity and endo stereoselectivity.

1,3-Dienes with hetero substituents have proven to be versatile reactants for the synthesis of highly functionalized ring systems via the Diels−Alder cycloaddition reaction. In addition, the heteroatoms in the substituent groups are known to impart enhanced reactivity, regioselectivity, and stereoselectivity to these dienes in the cycloaddition.[1] In preceding communications,[2−4] we reported the preparation of functionalized aryloxy 1,3-dienes and their use in a Diels−Alder approach to diaryl ethers related to isodityrosine. As a natural outgrowth of these studies, we were stimulated to effect the synthesis of a new class of diaryloxy 1,3-dienes that incorporate an additional oxygen substituent, which could lead to the triarylether components in glycopeptides of vancomycin.[5] Although the preparation and cycloaddition chemistry of dienes containing aryloxy and sulfur substituents have been examined in some detail,[1b,4,6] dienes containing four substituents have not, to the best of our knowledge, received significant study. In this paper, we describe a convenient synthesis of 4-substituted-1,3-diphenoxy-2-[(*tert*-butyldimethylsilyl)oxy]-1,3-butadiene (**1**), as also studies of their configuration and of the stereochemistry of their Diels−Alder cycloaddition products. A Diels−Alder approach using these dienes for the preparation of triaryl ethers is also described.

Enaminone **2** was readily converted into the corresponding enone or thioenone **3a**−**c** upon acid-catalyzed exchange.[4] The tetrahetero-substituted dienes **1a**−**c** were prepared by enol silylation of the enone or thioenone with *tert*-butyldimethylsilyl triflate in ether containing 2.5 equiv of triethylamine. Of significance, in comparison with the [(trimethylsilyl)oxy]-1,3-butadiene reported in our preliminary work,[4] these new dienes could be purified on silica gel in excellent yield and exhibited higher thermal stability during Diels−Alder cycloaddition. Sulfide diene **1a** could be oxidized with MCPBA to give the corresponding 4-(butylsulfinyl)-1,3-butadiene **1d**. These new tetrahetero-substituted dienes appear to be stable and could be kept for 2−3 months at −20 °C.

Scheme 1



Each diene was obtained as only one stereoisomer, as determined by their ^{1}H NMR spectra, in which the proton at C_4 is seen in each case as a singlet. The sulfide dienes **1a** and **1b** are crystalline solids, (mp **1a** 50 °C, **1b** 66 °C), which are well suited for X-ray crystallography. The X-ray analysis assigned diene **1b** to be the 1*Z*,3*Z* configuration and to exist in the s-trans conformation in the crystalline state.[7]

Prior studies[3,4] suggested that cycloaddition of tetrasubstituted dienes **1** with acetylenic dienophiles would generate triaryl ethers and serve as a model for the preparation of the triaryl ether unit present in vancomycin.[5] Reaction of diene **1a** with methyl propiolate in a sealed tube at 150 °C for 66 h gave, however, the diaryl ether **4** in 81% yield resulting from the elimination of butylmercaptan and one of the phenol groups, rather than the desired triaryl ether **5**.

Dienes **1c** and **1d**, having methoxy and sulfoxide substituents at the 4 position, gave similar results with no apparent triaryl ether product being formed. Variation in reaction conditions also did not result in triaryl ether formation. Thus, double elimination is a favored

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(1) For views, see: (a) Petrizilka, M.; Grayson, J. I. *Synthesis* **1981**, 753. (b) Trost, B. M., Fleming, I., Eds. *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, 1991; Vol. 5 (Paquette, L., Ed.), Chapter 4.1, pp 329−337.

(2) Olsen, R. K.; Feng, X. *Tetrahedron Lett.* **1991**, *32*, 5721.

(3) Feng, X.; Olsen, R. K. *J. Org. Chem.* **1992**, *57*, 5811.

(4) Olsen, R. K.; Feng, X.; Campbell, M.; Shao, R.-L.; Math, S. *J. Org. Chem.* **1995**, *60*, 6025.

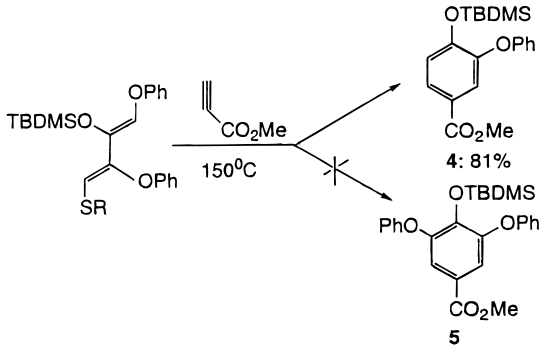
(5) Evans, D. A.; Ellman, J. A.; DeVries, K. M. *J. Am. Chem. Soc.* **1989**, *111*, 8912. Pearson, A. J.; Bignan, G. *Tetrahedron Lett.* **1996**, *37*, 735.

(6) Moreau, P.; Guillaumet, G.; Coudert, G. *Tetrahedron* **1994**, *50*, 3407.

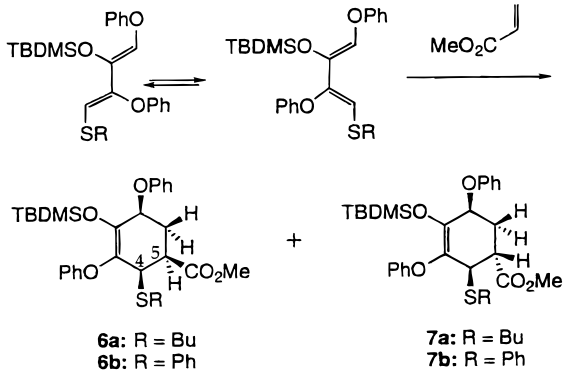
(7) The authors have deposited atomic coordinates, bond lengths, and angles for structure **1b** with the Cambridge Crystallographic Data Centre, the data for which can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

S0022-3263(96)00105-3 CCC: $12.00

Scheme 2



Scheme 3



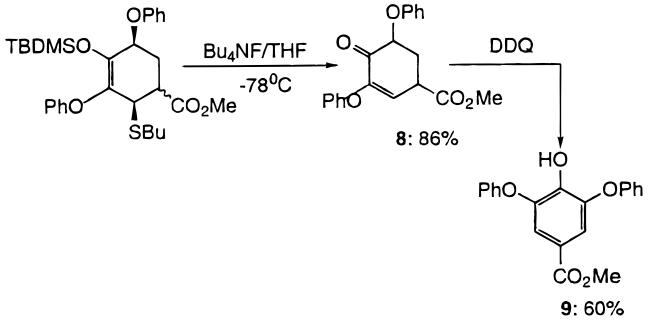
process that likely occurs during the aromatization of the cyclohexadiene Diels−Alder cycloadduct. The mechanism of this elimination process has not been studied, but is observed with various C-4 substituents as alkylthio, alkoxy, and sulfinyl, present in dienes **1a,c,d**. An attempt to effect cycloaddition under Lewis acid catalysis at low temperature (**1a**, methyl propiolate, $TiCl_4$ or *tert*-butyldimethylsilyl triflate, −78 °C) resulted in transformation of diene to thioenone **3** (66−70%) with no apparent cyclic product being formed.

Our attention now was focused on application of Diels−Alder reactions of diene **1** with dienophilic alkenes, which would lead to cyclohexene cycloadducts that should not directly undergo elimination to form a benzene ring, thereby allowing other procedures to be studied to effect formation of the aromatic ring. Our studies have been mainly concerned with **1a,b** that bear a butylthio or phenylthio group at position 4. This group conferred higher reactivity to the diene in its reactions with electrophilic dienophiles and functioned to control the regiochemistry of the cycloaddition step.

Cycloaddition of dienes **1a,b** with excess methyl acrylate was carried out at 150 °C for 72 h in a sealed tube. The products were isolated by column chromatography as a 3:1 mixture of *endo*-**6** and *exo*-**7** stereoisomers. Other regioisomers were not detected by TLC.

The cycloaddition was highly regiospecific and occurred with preferential endo-addition. The allylic hydrogen H_4 to the SR substituent was coupled to the acyl methine hydrogen H_5. This hydrogen was observed as a doublet both in the endo and exo isomers and collapsed to a singlet upon irradiation at the frequency of the methine hydrogen H_5. The complete regiocontrol exercised by the SR substituent demonstrates the excellent regiodirecting ability of these sulfur groups. As expected, the coupling constant between H_4 and H_5 showed a larger value for endo adducts, **6a** and **6b**, in each isomeric pair of

Scheme 4



adducts,[8] since H_4 tends toward eclipsing H_5 when these hydrogens are cis. The pseudoequatorial C_5 methine hydrogen of the endo stereoisomers **6** was observed as a doublet of doublet of doublets and occurred further downfield than in the corresponding exo-stereoisomer.[8] This downfield shift of the pseudoequatorial H_5 has been observed in other 4,5-disubstituted 2-cyclohexenes.[9,10]

Transformation of cycloadducts **6a**, **7a** to an aromatic ring was performed by a oxidation:dehydrogenation procedure using reagents such as peroxycarboxylic acids and dichlorodicyanoquinone (DDQ). However, the yields of products varied greatly, and the elimination of a phenoxy group was frequently a problem. For example, oxidation of a mixture of cycladducts **6a**, **7a** with MCPBA at −78 °C, followed by aromatization with DDQ gave diaryl ether **4** and triaryl ether **5** in yields of 62% and 13%, respectively.

The synthesis of the target triaryl ether **9** in acceptable yield finally was achieved with the transformation of the cyclohexene adducts to the α,β-unsaturated ketone **8** followed by dehydrogenation with DDQ. Deprotection of **6a**, **7a** with n-Bu_4NF effected removal of the silyl ether, ketolization, and elimination of the alkyl mercaptan to give **8** in 86% yield. Treatment of **8** with DDQ at reflux in dioxane afforded the triaryl ether **9** in 60% yield.

The thermal cycloaddition of diene **1a** or **1b** with maleic anhydride and *N*-phenylmaleimide also was studied. Maleic anhydride was caused to react with **1a** at 120 °C for 25 h to give the tetrahydrophthalic anhydride adduct **10a**.

The stereochemistry of the adduct was assigned on the basis of analysis of the ^1H NMR spectrum, with appropriate decoupling, and comparing those data with that of other related compounds.[9,11] The ^1H NMR data are consistent with the stereochemistry in **10a** having resulted from endo cycloaddition. Both of the coupling constants between the ring juncture hydrogens and the allylic methine hydrogens at C_1 and C_4 are typical gauche couplings. Thus, $J_{1,1a} = 5.50$ Hz and $J_{4,4a} = 8.20$ Hz; the latter value is indicative for a more eclipsed interaction between H_4 and H_{4a} as observed in related cases involving a somewhat deformed "extended" boat form.[11] However, analysis of the NMR data, coupled with the more highly substituted nature of compound **10a** compared to other

(8) **6a:** $\delta_{H5} = 3.15$ ppm, $\delta_{H4} = 3.87$ ppm, $J_{H4,H5} = 8.2$ Hz. **7a:** $\delta_{H5} = 3.08$ ppm, $\delta_{H4} = 3.76$ ppm, $J_{H4,H5} = 4.0$ Hz. **6b:** $\delta_{H5} = 3.12$ ppm, $\delta_{H4} = 4.27$ ppm, $J_{H4,H5} = 7.1$ Hz. **7b:** $\delta_{H5} = 3.05$ ppm, $\delta_{H4} = 4.19$ ppm, $J_{H4,H5} = 3.6$ Hz.

(9) Overman, L. E.; Taylor, G. F.; Houk, K. N.; Demelsmith, L. N. *J. Am. Chem. Soc.* **1978**, *100*, 3182 and references cited therein.

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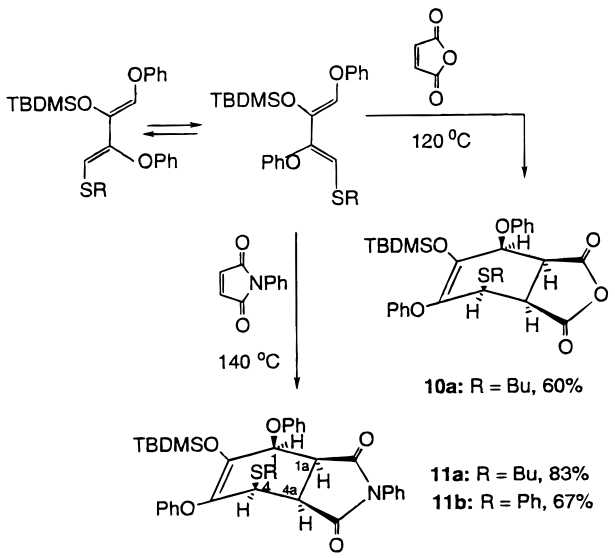
Scheme 5



described cyclohexenes, does not allow a definitive differentiation between possible "extended" and "folded" conformations. In contrast, if an exo product had been formed, **10a** would be expected to show either a large anti coupling for an extended boat or very small *J* value due to the coupling hydrogens being nearly perpendicular in a folded conformation.

Reaction of **1b** with *N*-phenylmaleimide was conducted in xylene under reflux for 48 h to afford the cyclohexene **11b**. The value of the coupling constants ($J_{1,1a} = 5.1$ Hz, $J_{4,4a} = 8.1$ Hz, $J_{1a,4a} = 10.6$ Hz) established an all cis configuration of the adducts, consistent with reaction via an endo-transition state. Furthermore, the large coupling constant between the bridgehead hydrogens (10.6 Hz) also suggested the "extended" boat conformation for the cyclohexene ring.[9,12]

In conclusion, 1,3-diaryloxy tetrahetero-substituted dienes reacted with several active dienophiles to provide access to a variety of aryloxy-functionalized cyclic systems. A most significant feature contributing to the synthetic applications of dienes **1a**, **1b** is the high regiospecificity and endo-selectivity observed in their thermal cycloaddition reactions. A method has been developed that effects the synthesis of triaryl ether products by Diels–Alder reaction of **1** with methyl acrylate, subsequent deprotection of the silyl ether with concurrent elimination of the sulfur substituent, and aromatization of the resulting enone with DDQ. This represents the first entry, utilizing a Diels–Alder approach, to the triaryl ether class of compounds; the method should have application to the synthesis of triaryl ether amino acid units as found in the glycopeptide vancomycin.

Experimental Section

General procedures and methods for characterization have been described previously.[4] X-ray crystal diffraction was performed on a Siemens P4 Autodiffractometer. Melting points were uncorrected. All solvents were purified when necessary according to standard procedures.

General Procedures for Preparation of 4-Substituted 1,3-Diphenoxy-3-buten-2-one (3). A stirred mixture of 4-(dimethylamino)-1,3-diphenoxy-3-buten-2-one (**2**) (12 mmol), *p*-toluenesulfonic acid monohydrate (10 mmol), and the required thio or alcohol (36 mmol) in benzene (60 mL) was heated at reflux under nitrogen for 5 h until the enaminone disappeared on TLC. The solvent was removed in vacuo, and the residue was purified by flash chromatography on silica gel with elution by 15% EtOAc in hexane to afford product.

4-(Butylthio)-1,3-diphenoxy-3-buten-2-one (3a). The product was obtained as a pale yellow solid in 81% yield: mp 56–58 °C (EtOAc/hexane); IR (CCl_4,cm^{-1}) 3068, 3042, 2959, 1703, 690; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, 3H, $J = 7.4$ Hz), 1.41 (m, 2H), 1.66 (m, 2H), 2.82 (t, 2H, $J = 7.4$ Hz), 4.81 (s, 2H), 6.79–7.33 (m, 10H), 7.63 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 21.3, 32.3, 34.1, 70.4, 114.7, 114.9, 121.4, 122.7, 129.4, 129.8, 134.8, 143.0, 155.6, 157.8, 188.3. Anal. Calcd for $C_{20}H_{22}O_3S$: C, 70.15; H, 6.48; S, 9.36. Found: C, 70.36; H, 6.35; S, 9.51.

1,3-Diphenoxy-4-(phenylthio)-3-buten-2-one (3b). The product was obtained as a pale-yellow solid in 78% yield: mp 79–80 °C; IR ($CHCl_3$, cm^{-1}) 3060, 2914, 1695, 1671, 690; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84 (s, 2H), 6.80–7.44 (m, 15H), 7.79 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.5, 114.7, 115.0, 121.6, 123.0, 128.5, 129.5, 129.6, 130.0, 130.8, 132.5, 133.9, 143.0, 155.7, 157.8, 188.6. Anal. Calcd for $C_{22}H_{18}O_3S$: C, 72.91; H, 5.01; S, 8.85. Found: C, 72.77; H, 5.23; S, 8.59.

1,3-Diphenoxy-4-methoxy-3-buten-2-one (3c). The product was obtained as a colorless viscous oil in 72.2% yield; IR (neat, cm^{-1}) 3402, 3042, 2944, 1704, 1685; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 4.81 (s, 2H), 6.81–7.31 (m, 10H), 7.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.6, 70.3, 114.5, 114.7, 121.5, 122.5, 129.4, 129.7, 131.6, 150.8, 156.8, 157.8, 191.8. Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.69; H, 5.69.

General Procedure for Preparation of 4-Substituted-2-[(*tert*-butyldimethylsilyl)oxy]-1,3-diphenoxy-1,3-butadiene (1). To a stirred solution of enone **3** (3 mmol) in dry ether (4 mL) under nitrogen at 0 °C was added triethylamine (7.5 mmol), and the resulting mixture was stirred at 0 °C for 30 min. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (4.5 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for 2 h. Hexane (30 mL) was added, the mixture swirled, and the top layer decanted. Two more 30 mL portion of hexane were added to the reaction mixture and swirled, and the top layer was decanted each time. The combined hexane layer was dried over $MgSO_4$ and purified by flash chromatography on silica gel using 10% EtOAc in hexane to give 1,3-butadiene.

2-[(*tert*-Butyldimethylsilyl)oxy]-4-(butylthio)-1,3-diphenoxy-1,3-butadiene (1a). The product was obtained as a white crystalline solid in 96% yield: mp 50 °C (CH_3OH); IR (CCl_4, cm^{-1}) 3077, 3042, 2958, 1655, 1592; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.20 (s, 4H), 0.93 (t, 3H, $J = 7.4$), 1.02 (s, 9H), 1.40 (m, 2H), 1.63 (m, 2H), 2.68 (t, 2H, $J = 7.4$), 6.26 (s, 1H), 6.38 (s, 1H), 6.80–7.31 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.2, 13.6, 18.6, 21.6, 26.0, 32.5, 33.7, 113.5, 115.2, 115.8, 122.0, 122.5, 126.7, 129.6, 129.7, 133.9, 143.5, 156.6, 157.1. Anal. Calcd for $C_{26}H_{36}O_3SSi$: C, 68.83; H, 7.95; S, 7.02. Found: C, 68.50; H, 7.95; S, 6.82.

2-[(*tert*-Butyldimethylsilyl)oxy]-1,3-diphenoxy-4-(phenylthio)-1,3-butadiene (1b). The product was obtained as a white crystal solid in 92% yield: mp 66–66.5 °C (CH_3OH); IR ($CHCl_3$, cm^{-1}) 3075, 3041, 2930, 1655, 1066; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.21 (s, 6H), 0.99 (s, 9H), 6.47 (s, 1H), 6.56 (s, 1H), 6.82–7.38 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.2, 18.5, 26.0, 111.4, 115.2, 115.9, 122.2, 122.7, 126.6, 127.8, 129.0, 129.1, 129.6, 129.7, 133.6, 135.5, 145.4, 156.8, 156.9. Anal. Calcd for $C_{28}H_{32}O_3SSi$: C, 70.55; H, 6.77; S, 6.73. Found: C, 70.61; H, 6.73; S, 6.66.

2-[(*tert*-Butyldimethylsilyl)oxy]-1,3-diphenoxy-4-methoxy-1,3-butadiene (1c). The product was obtained as a plae yellow oil in 68% yield: IR (neat, cm^{-1}) 3065, 2930, 2857, 1647, 1076; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.2 (s, 6H), 1.01 (s, 9H), 3.67 (s, 3H), 6.25 (s, 1H), 6.44 (s, 1H), 6.82–7.30 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.3, 18.6, 26.0, 60.9, 114.9, 115.7, 121.7, 122.3, 124.7, 129.4, 129.5, 130.6, 133.3, 137.6, 157.2, 157.4. Anal. Calcd for $C_{23}H_{30}O_4Si$: C, 69.31; H, 7.59. Found: C, 69.42; H, 7.45.

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2-[(*tert*-Butyldimethylsilyl)oxy]-4-butylsulfinyl-1,3-diphenoxy-1,3-butadiene (1d). To a solution of diene **1a** (550 mg, 1.2 mmol) in dichloromethane (12 mL) was added dropwise a solution of *m*-chloroperbenzoic acid (413 mg, of 50−60% mixture, 1.2 mmol) in dichloromethane (10 mL) at −78 °C. The reaction mixture was allowed to warm slowly to room temperature. TLC analysis (30% EtOAc in hexane) showed complete loss of starting material. The reaction mixture was partitioned between ether (40 mL) and 10% aqueous potassium carbonate solution (20 mL). The ether layer was washed twice with 10% aqueous potassium carbonate solution (2 mL), dried over $MgSO_4$, and purified by flash chromatography on silica gel with 30% EtOAc in hexane to yield 500 mg of sulfoxide (88%) as a pale yellow viscous oil: IR (neat, cm^{-1}) 3063, 2943, 1649, 1367, 1067; ^1H NMR (400 MHz, $CDCl_3$) δ 0.23 (d, 6H), 0.91 (t, 3H), 1.03 (s, 9H), 1.41 (m, 2H), 1.68 (m, 2H), 2.68 (m, 1H), 2.82 (m, 1H), 6.42 (s, 1H), 6.68 (s, 1H), 6.78 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.3, 13.5, 18.3, 21.7, 24.2, 25.7, 54.0, 115.5, 115.9, 119.5, 123.0, 123.3, 129.6, 129.8, 131.4, 132.6, 154.1, 156.3, 157.5. Anal. Calcd for $C_{26}H_{36}O_4SSi$: C, 66.06; H, 7.68; S, 6.78. Found: C, 65.97; H, 7.57; S, 7.00.

Reaction of 1a with Methyl Propiolate. A mixture of diene **1a** (456 mg, 1 mmol) and methyl propiolate (178 mg, 2 mmol) in xylene (1 mL) was heated in a sealed tube at 150 °C for 66 h. The solvent and excess methyl propiolate were removed in vacuo to give an oil which was purified by flash chromatography on silica gel with elution by 15% ethyl acetate in hexane to afford methyl 3-phenoxy-4-[(*tert*-butyldimethylsilyl)oxy]benzoate (**4**) (290 mg, 81%) as a clear liquid: IR (neat,cm^{-1}) 3041, 2954, 1724, 1608, 1024. ^1H NMR (400 MHz, $CDCl_3$) δ 0.16 (s, 6H), 0.87 (s, 9H), 3.85 (s, 3H), 6.87−7.77 (m, 8H); ^{13}CNMR (100 MHz, $CDCl_3$) δ −4.6, 18.2, 25.4, 51.9, 116.9, 121.1, 122.5, 122.9, 124.0, 126.7, 129.5, 146.5, 152.0, 157.4, 166.3. Anal. Calcd for $C_{20}H_{26}O_4Si$: C, 67.01; H, 7.31. Found: C, 67.00; H, 7.13.

Diels−Alder Reaction of 1a with Methyl Acrylate. Preparation of Cycloadducts 6a and 7a. A mixture of diene **1a** (456 mg, 1.0 mmol) and methyl acrylate (344 mg, 4.0 mmol) in xylene (1.5 mL) was heated in a sealed tube at 150 °C for 72 h. The solvent and excess methyl acrylate were removed in vacuo, and the adducts were isolated as a 3:1 mixture of diastereoisomers after flash chromatography on silica gel (ethyl acetate−hexane, 9:1, major isomer 320 mg and minor isomer 120 mg, yield 81%): ^1H NMR (400 MHz, $CDCl_3$) major isomer **6a**, δ 0.07 (d, 6H), 0.72 (s, 9H), 0.87 (t, J = 7.3 Hz, 3H), 1.35 (m, 2H), 1.49 (m, 2H), 2.16 (ddd, J = 4.1, 10.6, and 13.8 Hz, 1H), 2.31 (ddd, J = 4.1, 3.5, and 13.8 Hz, 1H), 2.55 (t, J = 7.3 Hz, 2H), 3.15 (ddd, J = 3.5, 8.2 and 10.6 Hz, 1H), 3.68 (s, 3H), 3.87 (d, J = 8.2 Hz, 1H), 4.96 (t, J = 4.1 Hz, 1H), 6.92−7.32 (m, 10H); minor isomer **7a**, δ 0.08 (s, 6H), 0.73 (s, 9H), 0.83 (t, J = 7.3 Hz, 3H), 1.30 (m, 2H), 1.44 (m, 2H), 2.10 (ddd, J = 9.2, 13.5 and 13.7, 1H), 2.52 (m, 2H), 2.63 (ddd, J = 2.6, 7.0, and 13.7 Hz, 1H), 3.08 (ddd, J = 2.6, 4.0, and 13.5 Hz, 1H), 3.66 (s, 3H), 3.76 (d, J = 4.0 Hz, 1H), 4.98 (dd, J = 7.0 and 9.2, Hz, 1H), 6.94−7.32 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) major isomer **6a**, δ −4.5, 13.5, 18.1, 21.9, 25.5, 29.3, 30.6, 31.6, 43.3, 43.7, 51.9, 72.7, 115.8, 116.2, 121.2, 121.8, 129.2, 129.5, 134.2, 139.7, 155.8, 157.4, 173.6; minor isomer **7a**, δ −4.2, −4.1, 13.6, 18.3, 21.8, 25.6, 26.9, 32.0, 33.0, 43.3, 44.0, 51.8, 72.8, 116.2, 116.3, 121.3, 122.0, 129.4, 129.5, 134.9, 139.5, 155.7, 157.4, 171.1. Anal. Calcd for $C_{30}H_{42}O_5SSi$ (major isomer **6a**): C, 66.38; H, 7.80; S, 5.91. Found: C, 66.41; H, 7.59; S, 6.17.

Diels−Alder Reaction of 1b with Methyl Acrylate. Preparation of Cycloadducts 6b and 7b. A mixture of diene **1b** (476 mg, 1.0 mmol) and methyl acrylate (344 mg, 4.0 mmol) in dioxane (1.5 mL) was heated in a sealed tube at 140−150 °C for 90 h. The solvent and excess methyl acrylate were removed in vacuo. The adducts were isolated as a 3:1 mixture of diastereoisomers after flash chromatography to yield cycloadduct (200 mg, 40%) and to recover 270 mg of diene **1b** (56%). ^1H NMR (400 MHz, $CDCl_3$) major isomer **6b**, δ 0.04 (s, 6H), 0.71 (s, 9H), 2.29 (m, J = 4.0, 8.6 and 4.8, 13.8 Hz, 2H), 3.12 (ddd, J = 4.0, 7.1 and 8.6 Hz, 1H), 3.64 (s, 3H), 4.27 (d, J = 7.1 Hz, 1H), 4.98 (t, J = 4.8 Hz, 1H), 6.92−7.27 (m, 15H); minor isomer **7b**, δ 0.09 (d, 6H), 0.75 (t, 9H), 2.23 (ddd, J = 9.4, 13.5 and 13.7 Hz, 1H), 2.60 (ddd, J = 2.6, 6.8 and 13.7 Hz, 1H), 3.05 (ddd, J = 2.6, 3.6 and 13.5 Hz, 1H), 3.20 (s, 3H), 4.19 (d, J = 3.6 Hz, 1H), 4.98 (dd, J = 6.8 and 9.4 Hz, 1H), 6.92−7.30 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) major isomer **6b**, δ −4.4, 18.2, 25.6, 28.6, 43.0, 47.6, 52.1, 72.3, 115.8, 116.5, 121.1, 122.0, 127.6, 128.8, 129.2, 129.5, 133.2, 133.4, 133.7, 140.4, 155.7, 157.4, 173.3; minor isomer **7b**, δ −4.2, −4.1, 18.4, 25.7, 26.7, 42.7, 49.8, 51.3, 72.9, 116.5, 116.6, 121.4, 122.2, 127.2, 128.6, 129.4, 129.5, 129.6, 132.8, 134.3, 140.5, 155.7, 157.5, 170.6. Anal. Calcd for $C_{32}H_{38}O_5SSi$ (major isomer **6b**): C, 68.29; H, 6.81; S, 5.69. Found: C, 68.46; H, 6.59; S, 5.44.

Aromatization of Diels−Alder Cycloadduct 6a with MCPBA and DDQ. To a solution of cyclic adduct **6a** (136 mg, 0.25 mmol) in dichloromethane (3 mL) was added dropwise a solution of MCPBA (86 mg 50−60%, 0.25 mmol) in CH_2Cl_2 (2 mL) at −78 °C. The reaction mixture was stirred for 30 min, allowed to warm to 0 °C, and partitioned between ether (20 mL) and 10% aqueous K_2CO_3 (5 mL). The ether layer was dried over $MgSO_4$ and concentrated in vacuo. The resulting sulfoxide was heated with DDQ (113 mg, 0.5 mmol) at 50 °C in benzene (3 mL) for 1 h. The reaction mixture was separated by flash chromatography on silica gel. The products were again subjected to TLC plate on silica gel using 15% EtOAc in hexane to provide 55 mg of **4** (61%) and 13 mg of methyl 3,5-diphenoxy-4-[(*tert*-butyldimethylsilyl)oxy]benzoate (**5**) as a white solid: mp 102−103 °C (MeOH); IR ($CHCl_3$, cm^{-1}) 3020, 2954, 1718, 1592, 1042; ^1H NMR (400 MHz, $CDCl_3$) δ 0.16 (s, 6H), 0.83 (s, 9H), 3.78 (s, 3H), 6.97−7.44 (m, 12H); ^{13}CNMR (100 MHz, $CDCl_3$) δ −4.4, 18.5, 25.4, 52.0, 116.9, 117.8, 123.0, 123.1, 129.8, 144.0, 148.5, 156.8, 166.0. Anal. Calcd for $C_{26}H_{30}O_5Si$: C, 69.30; H, 6.71. Found: C, 69.44; H, 6.79.

Preparation of Methyl 4-Oxo-3,5-diphenoxy-2-cyclohexene-1-carboxylate (8). Tetrabutylammonium fluoride (0.25 mL, 1.0 M in THF, 0.25 mmol) was added dropwise to a solution of mixture of **6a** and **7a** (109 mg, 0.2 mmol) in THF (2 mL) at −78 °C. The reaction mixture was stirred for 20 min at −78 °C and diluted with an equal mixture of ether and hexane (20 mL). The cooled reaction solution was washed with saturated aqueous NH_4Cl (5 mL containing 2 drops 1 N HCl) and extracted with ether. The ether layer was washed with saturated aqueous $NaHCO_3$ and dried over $MgSO_4$. The solvent was removed in vacuo to give the crude product which was washed with ether to afford **8** as a white solid, 58 mg (86%) mp 120−121 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.53 (ddd J = 10.1, 11.8, and 13.2 Hz, 1H), 2.77 (ddd J = 4.5, 4.8, and 13.2 Hz, 1H), 3.63 (ddd J = 3.1, 4.8, and 10.1 Hz, 1H), 3.74 (s, 1H), 4.84 (dd J = 4.5 and 11.8 Hz, 1H), 6.33 (d J = 3.1 Hz, 1H) 6.95−7.32 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.2, 39.0, 52.7, 77.8, 116.2, 118.8, 122.2, 124.0, 124.2, 129.5, 129.8, 149.5, 155.5, 157.8, 171.3, 189.8. Compound **8** appeared to be somewhat unstable, and an attempt to obtain elemental analysis did not give acceptable results.

Preparation of Methyl 3,5-Diphenoxy-4-hydroxybenzoate (9). The mixture of enone **8** (135 mg, 0.4 mmol) and DDQ (182 mg, 0.8 mmol) in 1,4-dioxane (8 mL) was heated at reflux under nitrogen for 18 h. The reaction mixture was diluted with EtOAc (20 mL) and washed with 10% K_2CO_3 and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$. The product was purified by flash chromatography on silica gel to yield triaryl ether **9** as a white solid: 80 mg (60%), mp 140−141 °C (EtOAc/hexane); IR ($CDCl_3$, cm^{-1}) 3308, 2949, 1698, 1587, 1218; ^1H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 6.05 (s, 1H), 7.05−7.43 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.1, 116.2, 118.2, 122.0, 123.9, 130.0, 143.7, 144.5, 156.5, 165.9. Anal. Calcd for $C_{20}H_{16}O_5$: C, 71.42; H, 4.80. Found: C, 71.56; H, 4.71.

Diels−Alder Reaction of Diene 1a with Maleic Anhydride. Preparation of Adduct (10a). A solution of diene **1a** (456 mg, 1 mmol) and maleic anhydride (108 mg, 1.1 mmol) in xylene (1 mL) was heated at 120 °C for 24 h. After cooling to room temperature, the solvent was removed in vacuo. The crude product was purified by chromatography on a column of silica gel using 25% EtOAc in hexane to yield cycloadduct **10a** (290 mg) as a colorless liquid (60.2%): IR (neat, cm^{-1}) 3065, 3041, 2931, 1785, 1023; ^1H NMR (400 MHz, $CDCl_3$) δ

0.03 (s, 6H), 0.72 (s, 9H), 0.77 (t, J = 7.3 Hz, 3H), 1.26 (m, 2H), 1.37 (m, 2H), 2.53 (m, 1H), 2.62 (m, 1H), 3.80 (d, J = 8.2 Hz, 1H), 3.84 (dd, J = 5.5 and 11.5 Hz, 1H), 4.08 (dd, J = 8.2 and 11.5 Hz, 1H), 5.09 (d, J = 5.5 Hz, 1H), 6.84−7.28 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.5, −4.3, 13.5, 17.9, 21.6, 25.3, 31.6, 35.9, 41.3, 46.7, 47.6, 75.2, 116.6, 117.8, 122.6, 122.8, 129.3, 129.5, 136.1, 137.7, 155.0, 157.4, 168.6, 169.0. Anal. Calcd for $C_{30}H_{38}O_6SSi$: C, 64.95; H, 6.90; S, 5.78. Found: C, 65.15; H, 6.70; S, 5.60.

Diels−Alder Reaction of Diene 1a with *N*-Phenylmaleimide. Preparation of Adduct (11a). To a solution of diene **1a** (456 mg, 1.0 mmol) in 2.0 mL of xylene was added *N*-phenylmaleimide (208 mg, 1.2 mmol). The mixture was heated in a sealed tube at 150 °C for 48 h. The solvent was evaporated in vacuo, and the resulting mixture was separated by flash chromatography on silica gel (ethyl acetate−hexane 1:4). Adduct **11a** was obtained as a white foam (520 mg, 83%): mp 52−54 °C; IR ($CHCl_3$, cm^{-1}) 3480, 3068, 2931, 1718, 1595; ^{1}H NMR (400 Hz, $CDCl_3$) δ 0.02 (d, 6H), 0.73 (s, 9H), 0.74 (t, J = 7.4, 3H), 1.21 (m, 2H), 1.35 (m, 2H), 2.49 (m, 1H), 2.64 (m, 1H), 3.67 (dd, J = 5.4 and 13.1 Hz, 1H), 3.88 (dd, J = 8.0 and 13.1 Hz, 1H), 3.89 (d, J = 8.0 Hz, 1H), 5.17 (d, J = 5.4 Hz, 1H), 6.87−7.48 (m, 15H); ^{13}C NMR (100 Hz, $CDCl_3$) δ −4.4, −4.3, 13.5, 17.9, 21.6, 25.3, 31.8, 35.8, 42.1, 45.4, 46.8, 75.7, 116.6, 117.8, 122.2, 122.5, 126.7, 128.6, 129.1, 129.4, 132.1, 136.7, 138.3, 155.2, 157.8, 173.8, 174.6. Anal. Calcd for $C_{36}H_{43}NO_5SSi$: C, 68.65; H, 6.88; N, 2.22. Found: C, 68.79; H, 6.95; N, 2.26.

Diels−Alder Reaction of Diene 1b with *N*-Phenylmaleimide. Preparation of Adduct (11b). Compound **11b** was obtained as a white solid in 67% yield; mp 198−200 °C; IR ($CHCl_3$, cm^{-1}) 3476, 3067, 2928, 1718, 1595; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (d, 6H), 0.75 (s, 9H), 3.69 (dd, J = 5.1 and 10.6 Hz, 1H), 3.91 (dd, J = 8.4 and 10.6 Hz, 1H), 4.25 (d, J = 8.4 Hz, 1H), 5.23 (d, J = 5.1 Hz, 1H), 6.85−7.50 (m, 20H); ^{13}C NMR (100 Hz, $CDCl_3$) δ −4.4, −4.2, 17.9, 25.3, 44.9, 47.0, 48.9, 75.8, 116.7, 117.6, 122.3, 122.6, 126.8, 127.4, 128.6, 128.8, 129.2, 129.3, 129.4, 132.1, 132.9, 137.1, 138.0, 138.4, 155.1, 157.6, 173.7, 174.1. Anal. Calcd for $C_{38}H_{39}NO_5SSi$: C, 70.23; H, 6.05; N, 2.16. Found: C, 70.38; H, 6.14; N, 1.96.

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