JOC Note

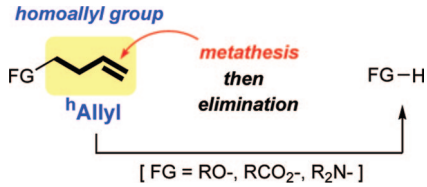
Deprotection of Homoallyl (^{h}Allyl) Derivatives of Phenols, Alcohols, Acids, and Amines

Bruce H. Lipshutz,* Subir Ghorai, and Wendy Wen Yi Leong

Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106

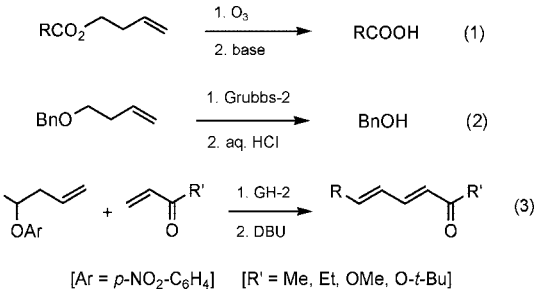
lipshutz@chem.ucsb.edu

Received January 7, 2009



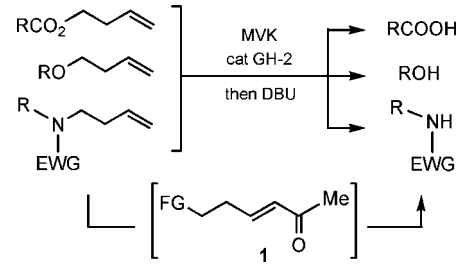
The homoallyl moiety, ^{h}Allyl, is presented as a general protecting group for several functionalities. It can be chemoselectively removed via a sequential, one-pot cross-metathesis/elimination sequence.

Chemoselective deprotection is among the most desirable features associated with a protecting group.[1] The extent of inertness and the conditions under which unmasking of a protecting group take place are of prime consideration. Availability and economics can also play important, albeit oftentimes secondary, roles. Surprisingly, the readily available hydrocarbon-based homoallyl residue is rarely seen in synthesis. Indeed, in the latest edition of *Greene's Protective Groups in Organic Synthesis* (2007),[2] the homoallyl moiety is not even listed among the myriad of hydroxyl protecting groups. The potential for this relatively unreactive 4-carbon unit to serve as a protecting group for alcohols,[3] amines,[4] and acids[5] has been recognized for decades, but existing conditions for removal may be responsible for its lack of utility to date. Thus, Barrett reported on the ozonolysis of homoallylic esters as a means of revealing a carboxylic acid following treatment with Et_3N (eq 1).[6] More recently, a single example from the Cossy group described a ruthenium-catalyzed isomerization of a homoallyl ether to an enol ether, which was subsequently hydrolyzed under aqueous acidic conditions to the free alcohol in modest overall yield (eq 2).[7]



In a recent report, we described the use of a one-pot tandem metathesis/elimination sequence for preparing polyenic arrays (eq 3).[8] In this report, a related strategy has been utilized, where the focus is on deprotection of the homoallyl moiety that can be used for a variety of functional group maskings: phenols, alcohols, amine derivatives, and acids (Scheme 1; EWG = electron-withdrawing group).

SCHEME 1. Deprotection of Homoallyl Derivatives



Conditions were developed using phenols derivatized as their homoallyl (^{h}Allyl) ethers.[9a] The coupling partner, methyl vinyl ketone (MVK), was selected given its availability, attractive economics, and loss on workup. Moreover, γ-proton abstraction en route to elimination was found to be far more facile from an intermediate enone **1** than is removal in the corresponding enoate **2** (Figure 1). Commercially available Grubbs−Hoveyda-2 catalyst[10] (GH-2; 2 mol %) in refluxing CH_2Cl_2 overnight led,

(1) Jarowicki, K.; Kocienski, P. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1589–1615; *J. Chem. Soc., Perkin Trans. 1* **2000**, 2495–2527.
(2) Wuts, P. G. M.; Green, T. W. *Greene's Protective Groups in Organic Synthesis*, 4th ed.; Wiley: Hoboken, NJ, 2007.
(3) (a) Kaleta, Z.; Makowski, B. T.; Soós, T.; Dembinski, R. *Org. Lett.* **2006**, *8*, 1625–1628. (b) Youn, S. W.; Pastine, S. J.; Sames, D. *Org. Lett.* **2004**, *6*, 581–584. (c) Zhu, X.-Z.; Chen, C.-F. *J. Am. Chem. Soc.* **2005**, *127*, 13158–13159. (d) Nicolaou, K. C.; Cho, S. Y.; Hughes, R.; Winssinger, N.; Smethurst, C.; Labischinski, H.; Endermann, R. *Chem.—Eur. J.* **2001**, *7*, 3798–3823.
(4) (a) Zhang, M.; Vedantham, P.; Flynn, D. L.; Hanson, P. R. *J. Org. Chem.* **2004**, *69*, 8340–8344. (b) Wipf, P.; Aslan, D. C. *J. Org. Chem.* **2001**, *66*, 337–343. (c) Kiyooka, S.-I.; Wada, Y.; Ueno, M.; Yokoyama, T.; Yokoyama, R. *Tetrahedron* **2007**, *63*, 12695–12701. (d) Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *Tetrahedron Lett.* **1995**, *36*, 3481–3484.
(5) (a) Grote, R. E.; Jarvo, E. R. *Org. Lett.* **2009**, *11*, 485–488. (b) Veenstra, S. J.; Schmid, P. *Tetrahedron Lett.* **1997**, *38*, 997–1000. (c) Vallee, E.; Loemba, F.; Etheve-Quelquejeu, M.; Valéry, J.-M. *Tetrahedron Lett.* **2006**, *47*, 2191–2195. (d) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293.
(6) Barrett, A. G. M.; Lebold, S. A.; Zhang, X. *Tetrahedron Lett.* **1989**, *30*, 7317–7320.
(7) Cadot, C.; Dalko, P. I.; Cossy, J. *Tetrahedron Lett.* **2002**, *43*, 1839–1841.
(8) (a) Lipshutz, B. H.; Ghorai, S.; Bošković, Z. V. *Tetrahedron* **2008**, *64*, 6949–6954. For related tandem reactions, see the following recent examples: (b) Bourcet, E.; Virolleaud, M.-A.; Fache, F.; Piva, O. *Tetrahedron Lett.* **2008**, *49*, 6816–6818. (c) Niethe, A.; Fischer, D.; Blechert, S. *J. Org. Chem.* **2008**, *73*, 3088–3093. (d) Hiebel, M.-A.; Pelotier, B.; Goekjian, P.; Piva, O. *Eur. J. Org. Chem.* **2008**, 713–720. (e) Jin, T.; Yamamoto, Y. *Org. Lett.* **2008**, *10*, 3137–3139. (f) Chen, J.-R.; Li, C.-F.; An, X.-L.; Zhang, J.-J.; Zhu, X.-Y.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 2489–2492. (g) Murelli, R. P.; Catalán, S.; Gannon, M. P.; Snapper, M. L. *Tetrahedron Lett.* **2008**, *49*, 5714–5717.
(9) (a) Homoallylic ethers (**3**) and amine derivatives (**5**) were prepared by O- or N-alkylation of the corresponding phenols or amines; see Experimental Section. (b) Homoallylic alcohol esters **6** were obtained using a Mitsunobu dehydration, as described in the Experimental Section.

10.1021/jo900012z CCC: $40.75 © 2009 American Chemical Society
Published on Web 03/11/2009

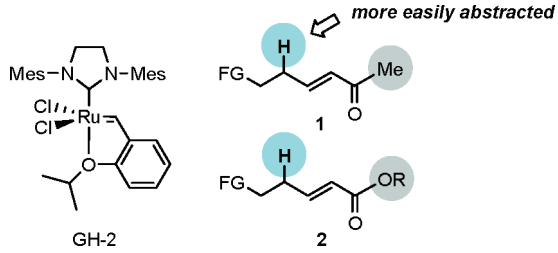
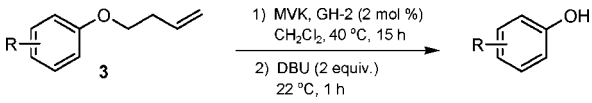


FIGURE 1. Grubbs−Hoveyda-2 (GH-2) catalyst; enone versus enoate intermediates.

TABLE 1. Deprotection of Homoallyl Ethers of Phenols



entry	3	R	yield (%)[a]
1	**3a**	H	98
2	**3b**	4-OMe	92
3	**3c**	4-NO_2	91
4	**3d**	4-I	92
5	**3e**	2-OMe, 4-Me	98
6	**3f**	3-OMe	93
7	**3g**	4-Bz	90
8	**3h**	4-CHO	86
9	**3i**	4-Ph	97
10	**3j**	4-^{t}Bu	90
11	**3k**	4-CN	82[b], 40[c]
12	**3l**	4-OTBS	92
13	**3m**	4-OAc	85
14	**3n**	4-OBn	94
15	**3o**	*d*	93
16	**3p**	*e*	88

[a] Isolated yield of chromatographically pure materials. [b] Based on recovered starting materials. [c] Isolated. [d] 2-Naphthyl homoallyl ether was used as educt. [e] Estrone homoallyl ether was the educt used.

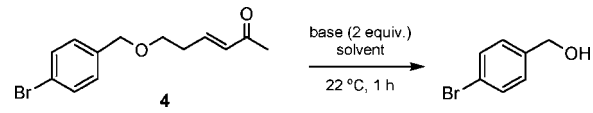
in general, to high levels of conversion to α,β-unsaturated ketones. After cooling to room temperature, addition of DBU quickly led to the free phenol upon acidic work up (Table 1). High levels of efficiency and functional group tolerance were observed. Thus, substituted aromatics, including nitro (entry 3), ester (entry 13), aldehyde (entry 8), and ketone (entries 7 and 16), all afforded high isolated yields of the desired phenols. Only the benzonitrile derivative **3k** was sluggish (entry 11), as expected from metathesis reactions involving this functionality.[11] Other common phenolic protecting groups such as methyl (entries 2, 5, and 6), TBS (entry 12), acetate (entry 13), and benzyl (entry 14) were found to be orthogonal to the relatively inert homoallylic residue and characteristically withstood these mild metathesis/elimination conditions.

Nonphenolic ^{h}Allyl-protected alcohols required a stronger base than DBU to effect elimination. Several bases were screened, as shown in Table 2. Of those identified as successful (KO^{t}Bu, NaOMe, or NaH in DMF), the final set of conditions was selected for enone **4**. Use of this procedure for deprotection of ^{h}Allyl benzyl alcohol compares very favorably with this single known literature example (Scheme 2).[7]

(10) Garber, S. B.; Kingsbury, J. S.; Grey, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.

(11) (a) Lipshutz, B. H.; Aguinaldo, G. T.; Ghorai, S.; Voigtritter, K. *Org. Lett.* **2008**, *10*, 1325–1328. (b) Ettari, R.; Micale, N. *J. Organomet. Chem.* **2007**, *692*, 3574–3576. (c) Rivard, M.; Blechert, S. *Eur. J. Org. Chem.* **2003**, 2225–2228. (d) Michrowska, A.; Bujok, R.; Harutyunyan, S.; Sashuk, V.; Dolgonos, G.; Grela, K. *J. Am. Chem. Soc.* **2004**, *126*, 9318–9325. (e) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 4035–4037.

TABLE 2. Bases Screened for Elimination of Alkanols



entry	base	solvent	yield (%)[a]
1	DBU	CH_2CI_2	NR
2	NaOAc	DMF	NR
3	KO^{t}Bu	CH_2Cl_2	57
4	KO^{t}Bu	toluene	60
5	KO^{t}Bu	THF	82
6	KO^{t}Bu	DMF	92
7	NaOMe	DMF	90
8	NaOMe	CH_2Cl_2	62
9	NaH	DMF	94

[a] Isolated yield of chromatographically pure materials.

SCHEME 2. Comparison with the Existing Literature Approach

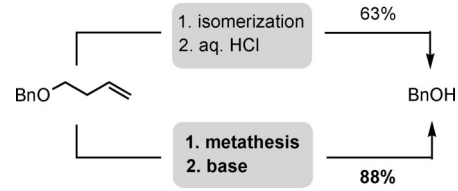
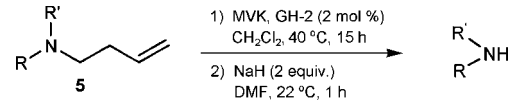


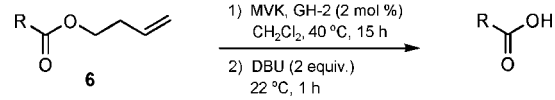
TABLE 3. Deprotection of Activated Amines



entry	5	R,R′	yield (%)[a]
1	**5a**	R = Bn, R′ = Ts	96
2	**5b**	*b*	95

[a] Isolated yield of chromatographically pure materials. [b] The ^{h}Allyl derivative of phthalimide is the substrate.

TABLE 4. Deprotection of Homoallyl Esters



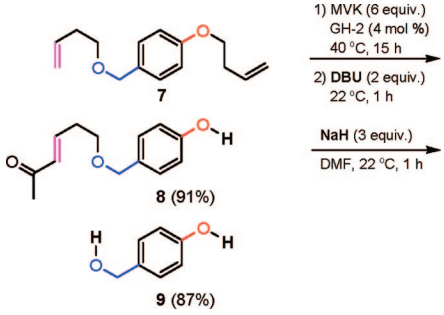
entry	6	R	yield (%)[a]
1	**6a**	Ph	95
2	**6b**	4-MeC_6H_4	94
3	**6c**	$PhCH_2CH_2$	91
4	**6d**	*n*-$C_{11}H_{23}$	92
5	**6e**	1-naphthyl	90
6	**6f**	(*Z*-NH)CH(Bn)	90

[a] Isolated yield of chromatographically pure materials.

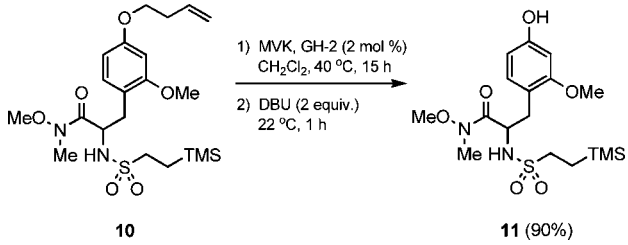
This combination of NaH in DMF was also found to be the most effective for the two cases of protected amines **5**,[9a] which were smoothly deprotected following metathesis with MVK (Table 3). Neither DBU nor NaH in CH_2Cl_2 afforded any elimination at room temperature.

Several homoallyl alcohol-derived esters **6**[9b] were deprotected in a one-pot fashion using the standard conditions of MVK, cat GH-2/DBU (Table 4). In the case of *Z*-protected (*S*)-phenylalanine derivative **6f**, epimerization during the elimination step

SCHEME 3. Selective Unmasking of Homoallylic Ethers



SCHEME 4. Deprotection of Compound 10



is not an issue, as DBU is known to have no effect on such educts.[6] High overall yields were obtained in all cases.

Selective unmasking of a phenolic homoallyl ether over a protected aliphatic derivative is readily accomplished. Thus, in the case of diether **7** (Scheme 3), metathesis at each olefinic site leads to an initial bisenone, which in the presence of DBU affords exclusively phenol **8**. Subsequent treatment with excess NaH in DMF ultimately affords diol **9**. The prognosis for use in more complex educts is apparent based on the case of homoallylic ether **10** (Scheme 4).

In summary, a simple, single vessel protocol has been developed for unmasking several functional groups protected as homoallylic derivatives. An initial olefin metathesis using methyl vinyl ketone is performed, after which the addition of base effects elimination to return the desired functionality in high overall yields.

Experimental Section

General Procedure for Homoallylation of Phenols and Amines. To a solution of aromatic alcohol or amine (2.00 mmol) and K_2CO_3 (5.00 mmol) in CH_3CN (8 mL) was added 4-bromobut-1-ene (0.40 mL, 4.00 mmol), and the mixture was refluxed for 12 h. The reaction mixture was then cooled to 22 °C, and the solvent was removed in vacuo. The residue was partitioned between CH_2Cl_2 and water, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL), dried over anhydrous Na_2SO_4, and removed in vacuo. The resulting residue was purified by silica gel flash chromatography to provide the title compounds. See Supporting Information for details on compounds **3a**−**p** and **5a**,**b**.

(*E*)-6-(4-Bromobenzyloxy)hex-3-en-2-one (4). But-3-ene-1-ol (0.15 mL, 1.67 mmol) was added dropwise to a stirred suspension of NaH (0.06 g, 2.50 mmol) in THF (7 mL) at 0 °C. After the addition, the mixture was stirred at 22 °C for 15 min. A solution of 4-bromobenzylbromide (0.62 g, 2.50 mmol) in THF (3 mL) was added dropwise to the mixture at 0 °C, and stirring continued for 30 min. The mixture was then heated under reflux for 6 h after which it was cooled to 0 °C and a few drops of water were added to quench excess NaH. After concentration of the mixture under vacuum, the residue was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were washed with water (2 × 20 mL), dried over anhydrous Na_2SO_4, and then concentrated in vacuo. The resulting residue was purified by flash column chromatography on silica gel (eluting with 6% EtOAc/hexane) to provide the 1-bromo-4-((but-3-enyloxy)methyl)benzene (precursor to compound **4**; 0.35 g, 87%) as a colorless liquid: IR (neat) 3078, 2979, 2858, 1641, 1594, 1488, 1431, 1393, 1358, 1096, 1070, 1011, 996, 914, 803, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 5.85 (ddt, J = 17.2, 10.4, 6.8 Hz, 1H), 5.12 (dq, J = 17.2, 1.2 Hz, 1H), 5.07 (dq, J = 10.2, 1.2 Hz, 1H), 4.48 (s, 2H), 3.53 (t, J = 6.8 Hz, 2H), 2.39 (qt, J = 6.8, 1.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 135.3, 131.6, 129.4, 121.6, 116.7, 72.3, 69.9, 34.4; MS (EI) m/z (%) 242 (M + 2, 2), 240 (M, 2), 171 (97), 169 (100), 161 (29), 90 (25), 89 (16); HREIMS calcd for $C_{11}H_{12}BrO$ $[M - H]^+$ = 239.0072, found 239.0066. To a solution of this ^{h}Allyl ether (0.22 g, 0.91 mmol) and methyl vinyl ketone (0.22 mL, 2.74 mmol) in CH_2Cl_2 (4.5 mL) was added GH-2 catalyst (11.5 mg, 0.018 mmol, 2.0 mol %), and the mixture was refluxed for 15 h. It was then reduced in volume under vacuum to 0.5 mL and purified directly on a silica gel flash column chromatography (eluting with 11% EtOAc/hexane) to provide the title compound **4** (0.25 g, 98%) as a colorless oil: IR (neat) 3032, 2862, 1697, 1673, 1628, 1592, 1488, 1424, 1395, 1360, 1254, 1202, 1176, 1096, 1070, 1011, 978, 804 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 6.80 (dt, J = 16.0, 6.8 Hz, 1H), 6.13 (dt, J = 16.0, 1.2 Hz, 1H), 4.46 (s, 2H), 3.58 (t, J = 6.8 Hz, 2H), 2.52 (qd, J = 6.8, 1.2 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 144.5, 137.3, 132.9, 131.7, 129.4, 121.7, 72.4, 68.6, 32.9, 27.0; MS (ESI) m/z 305 (M + Na); HRESIMS calcd for $C_{13}H_{15}BrO_2Na$ $[M + Na]^+$ = 305.0153, found 305.0158.

General Procedure for Homoallylation of Carboxylic Acids. A solution of DCAD[12] (2.75 mmol) in CH_2Cl_2 (10 mL) was slowly added at 22 °C via cannula to a solution of PPh_3 (2.75 mmol), but-3-ene-1-ol (2.75 mmol), and carboxylic acid (2.50 mmol) in CH_2Cl_2 (10 mL). The resulting cloudy mixture was stirred at this temperature for 12 h. Filtration gave reduced DCAD as a white powder. The filtrate was removed in vacuo to afford the crude product, which was subsequently purified by silica gel flash chromatography to provide the title compounds. See the Supporting Information for spectral details on compounds **6a**−**f**.

General Procedure for Deprotection of Homoallyl Derivatives. To a solution of a homoallyl derivative (0.50 mmol) and methyl vinyl ketone (122 μL, 1.50 mmol) in CH_2Cl_2 (2.5 mL) was added GH-2 catalyst (6.3 mg, 0.01 mmol, 2.0 mol %), and the mixture refluxed for 15 h. It was then cooled to 22 °C and DBU (149 μL, 1.00 mmol) was added dropwise and the mixture stirred for another 1 h at the same temperature. Then, 1.0 M HCl (3 mL) was added, and the mixture was extracted with CH_2Cl_2 (2 × 10 mL). The combined extracts were washed with water (2 × 10 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography to provide the deprotected compounds.

1-(But-3-enyloxy)-4-((but-3-enyloxy)methyl)benzene (7). But-3-ene-1-ol (0.05 mL, 0.58 mmol) was added dropwise to a stirred suspension of NaH (0.018 g, 0.76 mmol) in THF (1.0 mL) at 0 °C. After the addition, the mixture was stirred at 22 °C for 15 min. A solution of 1-(bromomethyl)-4-(but-3-enyloxy)benzene (see Supporting Information for procedure) (0.17 g, 0.69 mmol) in THF (1.0 mL) was added dropwise to the mixture at 0 °C, and stirring continued for 30 min. The mixture was then heated under reflux for 6 h after which it was cooled to 0 °C and a few drops of water were added to quench excess NaH. After concentration of the mixture under vacuum, the residue was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by flash chromatography

(12) Lipshutz, B. H.; Chung, D. W.; Rich, B.; Corral, R. *Org. Lett.* **2006**, *8*, 5069–5072.

on silica gel (eluting with 2% EtOAc/hexane) to provide the title compound **7** (0.13 g, 96%) as a colorless oil: IR (neat) 3077, 3002, 2979, 2928, 2858, 1642, 1613, 1585, 1512, 1472, 1431, 1387, 1361, 1301, 1245, 1173, 1097, 1038, 994, 916, 823 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 5.98−5.80 (m, 2H), 5.21−5.05 (m, 4H), 4.47 (s, 2H), 4.03 (t, J = 6.8 Hz, 2H), 3.51 (t, J = 6.8 Hz, 2H), 2.56 (q, J = 6.8 Hz, 2H), 2.38 (q, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 135.5, 134.6, 130.7, 129.4, 117.2, 116.5, 114.6, 72.7, 69.4, 67.4, 34.4, 33.8; MS (EI) *m/z* (%) 232 (M, 18), 161 (65), 107 (100), 55 (89); HREIMS calcd for $C_{15}H_{20}O_2$ $[M]^+$ = 232.1463, found 232.1472.

(*E*)-6-(4-Hydroxybenzyloxy)-hex-3-en-2-one (8). To a solution of **7** (0.10 g, 0.43 mmol) and methyl vinyl ketone (0.21 mL, 2.59 mmol) in CH_2Cl_2 (2.2 mL) was added GH-2 catalyst (0.011 g, 0.017 mmol, 4.0 mol %), and the mixture was refluxed for 15 h. It was then cooled to 22 °C, and DBU (128 μL, 0.86 mmol) was added dropwise and stirring continued for another 1 h at the same temperature. Then, 1.0 M HCl (2 mL) was added, and the mixture was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluting with 40% EtOAc/hexane) to provide the title compound **8** (0.086 g, 91%) as a colorless oil: IR (neat) 3374, 3024, 2862, 1668, 1614, 1597, 1517, 1445, 1361, 1266, 1170, 1092, 978, 912, 851, 830, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 8.4 Hz, 2H), 6.84 (dt, J = 16.0, 6.8 Hz, 1H), 6.83 (s, 1H), 6.79 (d, J = 8.4 Hz, 2H), 6.14 (dt, J = 8.0, 1.6 Hz, 1H), 4.44 (s, 2H), 3.58 (t, J = 6.4 Hz, 2H), 2.52 (qd, J = 6.4, 1.6 Hz, 2H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 156.1, 146.0, 132.7, 129.8, 129.5, 115.5, 73.0, 67.9, 33.0, 26.9; MS (ESI) *m/z* 243 (M + Na); HRESIMS calcd for $C_{13}H_{16}O_3Na$ $[M + Na]^+$ = 243.0997, found 243.0987.

4-(Hydroxymethyl)phenol (9). A solution of **8** (0.05 g, 0.227 mmol) in DMF (0.6 mL) was added dropwise to a stirred suspension of NaH (0.017 g, 0.68 mmol) in DMF (0.6 mL) at 0 °C. After the addition, the mixture was stirred at 22 °C for 1 h. Then, 1.0 M HCl (1 mL) was added, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (2 × 10 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluting with EtOAc) to provide the title compound **9** (0.024 g, 87%) as a white solid. The ^1H NMR obtained was in accord to the data previously reported for this compound.[13]

3-(4-(But-3-enyloxy)-2-methoxyphenyl)-*N*-methoxy-*N*-methyl-2-(2-(trimethylsilyl)ethylsulfonamido)propanamide (10). To a solution of **11** (0.05 g, 0.12 mmol) and K_2CO_3 (0.04 g, 0.30 mmol) in CH_3CN (0.8 mL) was added 4-bromobut-1-ene (0.024 mL, 0.24 mmol), and the mixture was refluxed for 12 h. The reaction mixture was then cooled to 22 °C, and the solvent was removed in vacuo. The residue was partitioned between EtOAc and water, and the aqueous layer was extracted with EtOAc (2 × 5 mL). The combined organic extracts were washed with water (2 × 5 mL), dried over anhydrous Na_2SO_4, and removed in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluting with 25% EtOAc/hexane) to provide the title compound **10** (0.055 g, 93%) as a colorless liquid: IR (neat) 3256, 3078, 2951, 1659, 1614, 1587, 1508, 1466, 1417, 1386, 1323, 1288, 1263, 1251, 1200, 1165, 1142, 1082, 1038, 990, 860, 839, 736, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, J = 8.4 Hz, 1H), 6.44 (d, J = 2.4 Hz, 1H), 6.41 (dd, J = 8.4, 2.4 Hz, 1H), 5.90 (ddt, J = 17.2, 10.4, 6.8 Hz, 1H), 5.20−5.10 (m, 3H), 4.70 (td, J = 9.6, 4.4 Hz, 1H), 3.97 (t, J = 6.8 Hz, 2H), 3.81 (s, 3H), 3.76 (s, 3H), 3.21 (s, 3H), 2.97 (dd, J = 13.2, 4.4 Hz, 1H), 2.75 (dd, J = 13.2, 9.6 Hz, 1H), 2.58−2.40 (m, 4H), 0.82−0.73 (m, 2H), −0.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 159.7, 158.8, 134.6, 132.2, 117.3, 104.7, 99.2, 67.3, 61.8, 55.6, 53.7, 49.9, 33.8, 32.4, 10.1, −2.0; MS (ESI) *m/z* 495 (M + Na); HRESIMS calcd for $C_{21}H_{36}N_2O_6SSiNa$ $[M + Na]^+$ = 495.1961, found 495.1955.

Acknowledgment. Financial support provided by Zymes, LLC is warmly acknowledged with thanks, as is the generous supply of phenol **11** by the Pettus group.

Supporting Information Available: Experimental procedures and spectral data for **3a**−**p**, **5a**,**b**, and **6a**−**f**, including copies of ^1H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO900012Z

(13) Zhou, Y.; Gao, G.; Li, H.; Qu, J. *Tetrahedron Lett.* **2008**, *49*, 3260–3263.