JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

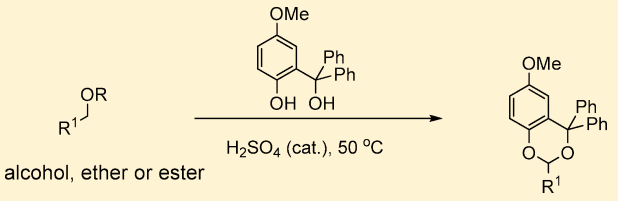
Oxidation with a Photolabile Carbonyl Protecting Group

Haishen Yang, Feng Mu, and Pengfei Wang*

Department of Chemistry, University of Alabama at Birmingham, 901 14th Street South, Birmingham, Alabama 35294, United States

Supporting Information

ABSTRACT: A novel oxidation approach utilizing a robust photolabile carbonyl protecting group reagent (**1**) as the oxidizing reagent has been developed. Different from existing methods, this approach oxidizes primary alcohols to the photosensitive acetals (e.g., **3**), providing another unique approach to the protected aldehydes. Thus, for the first time, oxidation and protection are achieved in one reaction. Secondary alcohols are oxidized to the corresponding ketones. Moreover, the photolabile protecting group (PPG) also oxidizes ethers and esters. The oxidation is presumably via hydride abstraction by the tritylium ion generated from **1** under acidic conditions. However, the mechanisms for primary alcohols and secondary alcohols are slightly different.

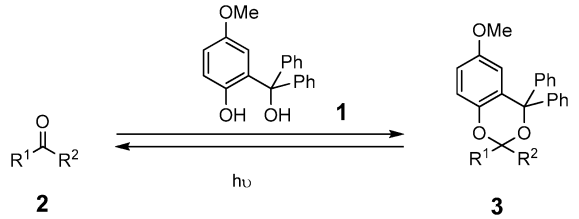


INTRODUCTION

It has long been known that the tritylium ion can oxidize ethers through hydride abstraction.[1−5] Triphenylcarbenium tetrafluoroborate ($TrBF_4$) is the source of the tritylium ion in these applications. However, oxidizing ethers of primary alcohols with $TrBF_4$ is not as successful as oxidizing ethers of secondary alcohols, due to the different stabilities of the involved carbenium ion intermediates.[4] Despite the success of oxidizing ethers with $TrBF_4$, a practical method of directly oxidizing alcohols with a tritylium ion is not known.[6] Herein we report a unique and effective oxidation method oxidizing both primary and secondary alcohols. This method utilizes α,α-diphenyl-5-methoxysalicyl alcohol (**1**), a robust photolabile carbonyl protecting group reagent,[7a] as the oxidizing reagent. Presumably, under acidic conditions, the salicyl alcohol is converted to a triarylcarbenium ion which is capable of hydride abstraction, similar in function to $TrBF_4$.

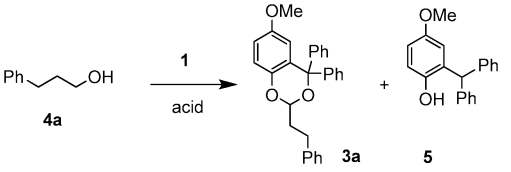
We have demonstrated that the reaction of the carbonyl compound **2** with the protecting group reagent **1** under mild acidic or neutral conditions generates the UV-sensitive acetal **3** (Scheme 1). Upon irradiation, the carbonyl compound will be released efficiently in high yields.[7a,f] The PPG in **3** and other salicyl alcohol based PPGs recently developed in our laboratory have some advantageous features.[7] For example, the PPG reagents are easily prepared from inexpensive, commercially available materials; they have high protection/deprotection efficiencies and remarkable dark stability. In particular, mindful of the unique structural features of these PPGs, we have developed a neutral protecting protocol and demonstrated for the first time that both protection and deprotection reactions can be conducted under neutral conditions without using any other chemical reagents.[7d−f] These PPGs have potential applications in controlled drug release[7e] and synthesis.[8] Interestingly, we found that salicyl alcohol **1** is also a unique oxidizing reagent.

Scheme 1. Photolabile Carbonyl Protecting Group



RESULTS AND DISCUSSION

The reaction of 3-phenyl-1-propanol (**4a**) with the PPG reagent **1** under acidic conditions led to the corresponding acetal **3a** along with the reduction product **5** (eq 1). The



(1)

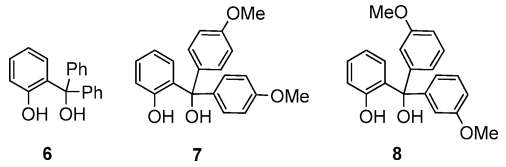
reaction provided better results at temperatures of 45 °C or above (up to 90 °C). Although the reactions did not require a solvent, a few drops of dichloromethane aided in mixing the reactants and the acid catalyst and improved the reaction outcome. The reaction slowed down with more solvent present. Toluene could also be used for this mixing purpose, but the reaction would be slower. A catalytic amount of concentrated H_2SO_4 is used. As expected, the amount of acid was positively correlated with the reaction rate. With a similar amount of catalyst, the reaction outcome with *p*-TsOH was similar to that with H_2SO_4. TfOH seemed to be more robust in catalyzing the

Received: August 10, 2011
Published: September 27, 2011

   dx.doi.org/10.1021/jo201671v | J. Org. Chem. 2011, 76, 8955–8961

reaction and much smaller amounts of TfOH were needed to produce similar results. TFA failed to promote a perceptible oxidation reaction under the same conditions.

With H_2SO_4 as the catalyst, we compared the oxidation capacities of salicyl alcohols **1** and **6**–**8** (Figure 1). Under the same conditions, the salicyl alcohols **1** and **6** demonstrated similar oxidation reactivity toward 3-phenyl-1-propanol (**4a**), resulting in a higher conversion of **4a** and cleaner reaction mixtures. Given the excellent PPG properties of the α,α-diphenyl-5-methoxysalicyl group,[7a] we focused on studying oxidation with **1**.

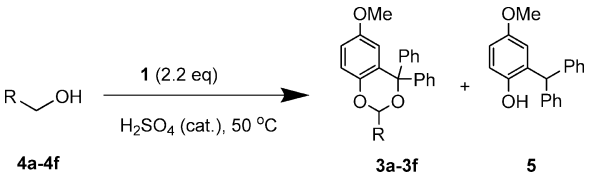


6 **7** **8**

Figure 1. Salicyl alcohols as oxidizing reagents.

In a typical run, the oxidation of **4a** with 2.2 equiv of **1** catalyzed by a 0.2 equiv of H_2SO_4 generated the acetal **3a** in 83% yield along with about an equal amount of the reduction product **5** (Table 1, entry 1). The reaction took about 15 h.

Table 1. Oxidation of Primary Alcohols with PPG 1



4a-4f **3a-3f** **5**

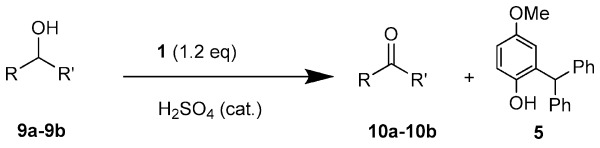
entry	alcohol	Yield of **3** (%)[a,b]	**3**/**5**	Reaction time (h)
1	Ph OH (**4a**)	83	1:1.07	15.5
		81[c]	1:1.01[c]	17.5[c]
2	Ph OH (**4b**)	81	1:1.08	16.5
3	Ph OH (**4c**)	90	1:1.03	4.7
4	OH (**4d**)	80	1:1.08	12
5	6 OH (**4e**)	91	1:1.02	13.7
6	3 OH Et (**4f**)	57[d]	1:1.7	103

[a]Reactions were carried out with 0.2 equiv of H_2SO_4 (conc) in a DCM slurry at 50 °C. [b]Isolated yields. [c]With 0.05 equiv of TfOH in a DCM slurry at 50 °C. [d]With 1 equiv of H_2SO_4 and 4.5 equiv of **1**.

With less than 2 equiv of the salicyl alcohol **1**, the unreacted alcohol was observed in the reaction mixture after **1** was completely consumed. Similar results were obtained when 0.05 equiv of TfOH was used as the catalyst. The acetal **3a** was isolated in 81% yield with a **3a**/**5** ratio of 1/1.01 after 17.5 h at 50 °C. Under the same conditions with H_2SO_4 as the catalyst, a series of primary alcohols (**4b**–**e**) were oxidized and produced the corresponding acetals (**3b**–**e**) in good yields (Table 1, entries 2–5). Surprisingly, the alcohol **4f** was difficult to oxidize, and the conversion to **3f** was slow. Increasing the reaction temperature to 70 °C did not improve the reaction outcome. Eventually, the desired **3f** was obtained in 56% yield after using 1 equiv of H_2SO_4 and excess of **1** for 4 days. The significantly different reactivity of **4f** in comparison to that of other primary alcohols was confirmed in a control experiment. A mixture of **4a** and **4f** (1/1) was treated with 2.2 equiv of **1** and 0.6 equiv of H_2SO_4. After 9 h at 50 °C, the acetals **3a** (78%) and **3f** (8%) were obtained along with the recovered **4a** (19%) and **4f** (80%).

The oxidation protocol is also applicable to simple secondary alcohols. Different from oxidizing primary alcohols, the oxidation reaction led to a ketone product instead of a ketal (Table 2). For instance, the reaction of **9a** with 1.2 equiv of **1** in the presence of 0.1 equiv of concentrated H_2SO_4 resulted in an 80% yield of the ketone **10a** in 30.5 h at 50 °C. A similar yield (e.g. 81%) was obtained from the reaction at 70 °C, and the reaction time became noticeably shorter (Table 2, entry 1). For another alcohol **9b**, the yield of the product ketone **10b** was 86% after 4.5 h of heating at 70 °C (Table 2, entry 2). A control experiment showed that, under the reaction conditions, it was not efficient to convert the ketone product to the corresponding ketal, even with an excess of more than 1 equiv of **1**. This oxidation process could compete with E1 elimination when the secondary alcohols are capable of forming stabilized secondary cationic intermediates under acidic conditions. For example, the oxidation of *sec*-phenethyl alcohol with **1** mainly produced the desired product, acetophenone; however, the reaction mixture was less clean and styrene was identified among the byproducts.

Table 2. Oxidation of Secondary Alcohols with PPG 1



9a-9b **10a-10b** **5**

entry	alcohol	Yield of **10** (%)[a,b]	**10**/**5**	Reaction time (h)
1	HO OMe (**9a**)	80[c]	1:1.01	30.5 (50°C)
		81[d]	1:1.06	10.3 (70°C)
2	OH 8 (**9b**)	86[d]	1:1.04	4.5 (70°C)

[a]Reactions were carried out with 0.1 equiv of H_2SO_4 in a DCM slurry. [b]Isolated yields. [c]Reaction at 50 °C. [d]Reaction at 70 °C.

To our surprise, the primary and secondary alcohols showed similar reactivity toward oxidation with **1** under the same reaction conditions. For example, after a mixture of **4a** and **9b** (1/1) was treated with 1.2 equiv of **1** and 0.6 equiv of H_2SO_4 for 9 h, the oxidation products **3a** and **10b** were obtained in

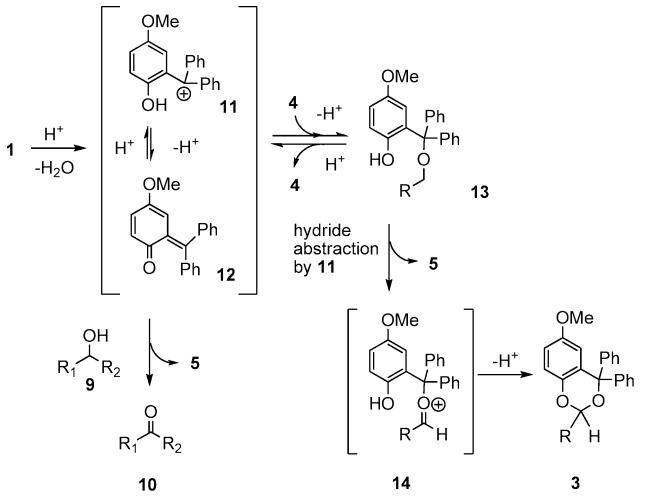
dx.doi.org/10.1021/jo201671v | J. Org. Chem. 2011, 76, 8955–8961

32% and 33% yields, respectively, along with recovered **4a** (50%), **9b** (66%), and an unknown derivative of **4a**.

This result was seemingly inconsistent with our initial mechanistic hypothesis. We assumed that the oxidation of an alcohol with PPG **1** was similar to the oxidation of ethers with $TrBF_4$ via hydride abstraction. With $TrBF_4$, the TMS, *t*-Bu, and Tr ethers of primary alcohols were oxidized more slowly than those of secondary alcohols, presumably due to the stability difference between the tertiary and secondary carbenium intermediates obtained from hydride abstraction by the tritylium ion.[4] The comparable rates of the oxidation of primary and secondary alcohols in our case suggest that different mechanisms are probably involved. In addition, aldehydes were not observed in oxidizing primary alcohols. Although aldehydes could be converted to the corresponding acetals **3** under the reaction conditions, control experiments achieved 90% conversion of 3-phenylpropanal to **3a** after 70 min.

To rationalize the experimental observations, we postulated that the tritylium ion **11** could be generated from the salicyl alcohol upon acid treatment (Scheme 2). It would be in

Scheme 2. Proposed Mechanism of Oxidation with PPG 1

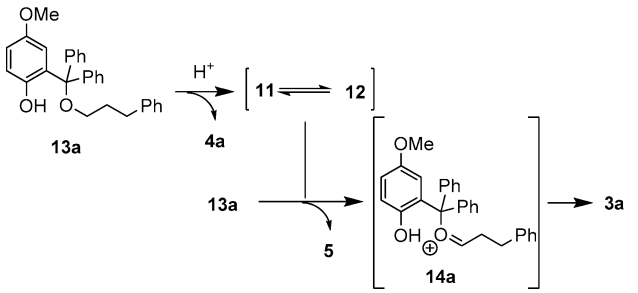


equilibrium with the *o*-quinone methide **12**. In the presence of the primary alcohol **4**, the ether **13** would probably form. Subsequent hydride abstraction from the ether **13**[3] rather than from the alcohol **4** by **11** resulted in the oxocarbenium ion **14**, which cyclized to produce the acetal **3**. The preference of hydride abstraction from the ether can be rationalized as a result of the different stabilities of the intermediates involved: i.e., hydride abstraction from **4** would lead to a simple primary carbenium ion while the primary carbenium ion generated from **13** could be stabilized by hyperconjugation with the PPG segment. This reaction pathway would not generate the aldehyde intermediate, which is consistent with our observations. This mechanistic postulation could also explain the lower reactivity of the primary alcohol **4f** in that hydride abstraction from the ether of **4f** (i.e. **13f**) by the bulky cation **11** should become difficult due to the increased steric hindrance introduced by the ethyl group in the ether.

For the secondary alcohol **9**, the equilibrium between the alcohol and its ether would also exist. However, hydride abstraction from the ether of the secondary alcohol by **11** should also encounter increased steric hindrance. Alternatively, direct hydride abstraction from the alcohol **9** is feasible, owing to the increased stability of the secondary carbenium intermediate, compared with a primary carbenium intermediate from a primary alcohol. This alternative pathway avoids formation of an oxocarbenium intermediate such as **14**, and, as a result, leads to the ketone **10** instead of a ketal product. The activation energies of generating a carbenium intermediate from **9** and generating **14** from **13** appear to be comparable.

We then synthesized the ether of 3-phenyl-1-propanol: i.e., **13a**.[7f] Treatment of **13a** with 0.2 equiv of H_2SO_4 at 50 °C for 30 min led to a clean conversion to a mixture of **3a**, **5**, and the alcohol **4a** in a 1/1/1 ratio (Scheme 3). Given that the

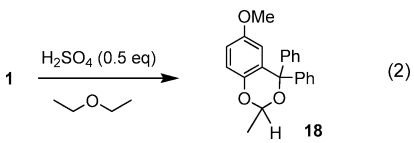
Scheme 3. Redox Reaction of the Ether 13a



oxidation of **4a** with **1** took more than 15 h (Table 1, entry 1), it seemed that the ether formation step in the pathway to **3** (Scheme 2) could be a rate-limiting step.[9] Under the same conditions, the reaction of **13f** became slow, and the reaction mixture was complex. For example, after 6 h, the reaction mixture contained **13f**, **1**, **3f**, **5**, and **4f** in a ratio of 14/33/14/24/72, along with other minor products on the basis of ^1H NMR analysis. We speculate that increasing steric hindrance slowed down the transformation from **13f** to **14f**. As a result, side reactions of the short-lived cationic intermediate **11** increased. Again, aldehydes were not observed in the reaction mixtures, consistent with the proposed mechanism in Scheme 2.

Owing to its unique structure, the carbonyl PPG **1** seemed to be particularly suitable for oxidizing primary alcohols to the stable acetals. The phenolic hydroxyl group not only helped to stabilize the benzylic cationic center of **11** through conjugation (i.e. **11** → **12** in Scheme 2) but also trapped the reactive carbenium intermediate intramolecularly (e.g. **14**) to afford the chemically stable oxidation product of a primary alcohol (i.e. the acetal **3**). For comparison, control experiments under the same conditions as for **13a** (Scheme 3) showed that the trityl ether (**15**), 4-methoxytrityl ether (**16**), and 2,5-dimethoxytrityl ether (**17**) of 3-phenyl-1-propanol all led to a complex reaction mixture containing various amounts of 3-phenyl-1-propanol, the corresponding reduced triarylmethane, and the oxidation product(s), including 3-phenylpropanal and its condensation product(s).

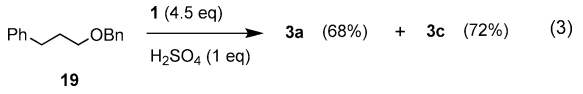
In addition to oxidizing alcohols, the PPG reagent **1** oxidizes ethers as well. For example, a diethyl ether solution of **1** was treated with 0.5 equiv of H_2SO_4 and heated at 50 °C in a sealed tube (eq 2). After 10.5 h, the acetal **18** was isolated in 40% yield (calculated on the basis of **1**) and the ratio of the obtained **18**/**5**



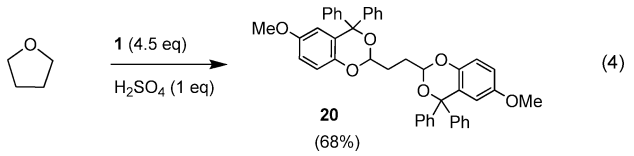
(2)

dx.doi.org/10.1021/jo201671v | J. Org. Chem. 2011, 76, 8955–8961

was 1/1.09. Another example is oxidation of benzyl-protected 3-phenyl-1-propanol (**19**) (eq 3). Reaction of **19** with 4.5 equiv

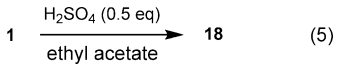


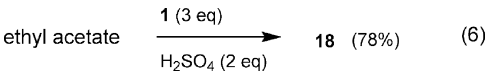
of **1** and 1 equiv of the acid at 50 °C for 15.5 h resulted in a mixture of **3a** (68%), **3c** (72%), **5**, and the unreacted **19** (18%) and **1** on the basis of ^{1}H NMR analysis. The ratio of the combined acetals **3a,c** to **5** was 1/1.15. In the case of oxidizing THF (eq 4) under the same conditions, the diacetal **20** was



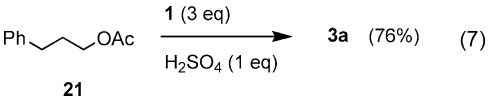
isolated in 68% yield and the ratio of the obtained **20** to **5** was 1/2.5. When the reaction was conducted in THF with **1** as the limiting reagent, multiple products were obtained. In these reactions, aldehydes were not observed during monitoring the reaction progress, suggesting aldehydes were not a reaction intermediate. Formation of the acetals was probably achieved through interaction of the salicyl alcohol **1** with the oxocarbenium intermediate generated from hydride abstraction.

Interestingly, the PPG **1** also oxidizes esters. Heating an ethyl acetate solution of **1** with 0.5 equiv of H_2SO_4 at 50 °C for 10.5 h led to the acetal **18** in 38% yield (calculated on the basis of **1**) with a **18**/**5** ratio of 1/1.13 (eq 5). When ethyl acetate was the

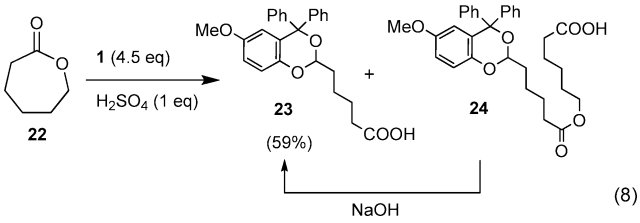




limiting reagent (eq 6), a similar yield (78%) was obtained after 13.9 h with an **18**/**5** ratio of 1/1.19. In the reaction of **21**, the



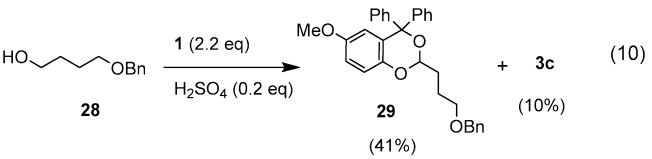
acetal **3a** was obtained in 76% yield after 18 h with a **3a**/**5** ratio of 1/1.12 (eq 7). Reaction of 6-hexanolactone led to the two



acetals **23** and **24** in a 4/1 ratio along with unreacted **22** (eq 8). The structure of **24** was supported by ^{1}H NMR and high-resolution mass spectrometry analysis. Saponification of **24** converted it to **23** cleanly, and the combined yield of **23** was 59%.

It seemed that the ester oxidation went through hydrolysis of the ester/lactone first. When 3-phenyl-1-propyl benzoate (**25**) was prepared and treated with H_2SO_4 and an excess of **1** at 50 °C (i.e., the same conditions as for **21**), no conversion of **25** was observed and the salicyl alcohol **1** gradually decomposed. In the control experiments, the acetate **21** and the benzoate **25** were treated separately with 1 equiv of H_2SO_4 at 50 °C for hydrolysis, and only the acetate **21** showed production of **4a**. The control experiments were repeated in the presence of 2 equiv of water. The hydrolysis product (**4a**) from **21** increased, but the benzoate **25** still did not show any sign of reaction. The different reactivities of hydrolysis under the reaction conditions might explain the different outcomes from the oxidation of **21** and **25**, which is also in agreement with the production of **24** in the reaction of **22**.

Since the PPG reagent **1** can oxidize alcohols as well as esters and ethers, the chemoselectivity of the approach was studied with the difunctional alcohols (eqs 9 and 10). In oxidizing the alcohol **26**, the acetal **27** was obtained in 78% yield, indicating that this approach is compatible with a benzoyl group. However, under the same reaction conditions, the acetyl group underwent intermolecular acetyl shifting and complicated the reaction outcome. In the reaction of **28**, oxidation of the primary hydroxyl group led to **29** in 41% yield along with **3c** in 10% yield, showing a rate of oxidizing the hydroxyl group 4 times faster than that of oxidizing a benzyl group.



In summary, a novel oxidation approach utilizing a robust photolabile carbonyl protecting group reagent (**1**) as the oxidizing reagent has been developed. Different from existing methods, this approach oxidizes primary alcohols to photosensitive acetals (e.g. **3**), providing another unique approach to the preparation of the protected aldehydes.[7a,d] Thus, for the first time, oxidation and protection are achieved in one reaction. Secondary alcohols are oxidized to the corresponding ketones. The primary and secondary alcohols showed unexpected similarities in reactivity, which was rationalized by the proposed slightly different mechanisms. Moreover, the PPG also oxidizes ethers and esters.

EXPERIMENTAL SECTION

General Considerations. Organic solutions were concentrated by rotary evaporation at ca. 12 Torr. Flash column chromatography was performed employing 230−400 mesh silica gel. Thin-layer chromatography was performed using glass plates precoated to a depth of 0.25 mm with 230−400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Infrared (IR) data are presented as frequency of absorption (cm^{-1}). Proton and carbon-13 nuclear magnetic resonance (^{1}H NMR or ^{13}C NMR) spectra were recorded on 300 and 400 MHz NMR spectrometers; chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ 7.26). Data are

dx.doi.org/10.1021/jo201671v | J. Org. Chem. 2011, 76, 8955–8961

presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances), coupling constant in Hertz (Hz), integration.

Materials. Tetrahydrofuran was distilled from appropriate drying reagents under a nitrogen atmosphere at 760 Torr. Other chemicals were obtained from commercial vendors and used without further purification.

*Oxidation to **3a** (Known Compound[7a]).* To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 110.2 mg, 0.36 mmol) and 3-phenyl-1-propanol (20.7 mg, 0.15 mmol) in dichloromethane (75 μL) was added H_2SO_4 (2 μL, 0.036 mmol). The mixture was heated at 50 °C for 15.5 h. The crude reaction mixture was directly purified with flash column chromatography (petroleum ether/ethyl acetate from 20/1 to 5/1) to provide **3a** (53.8 mg, 0.127 mmol, 83%) and **5** (39.5 mg, 0.136 mmol), both as white solids. Data for **5**: R_f = 0.33 (petroleum ether/ethyl acetate 5/1); mp 112.0−112.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28−7.11 (m, 7H), 7.11−7.03 (m, 3H), 6.68 (d, *J* = 8.7 Hz, 1H), 6.61 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.31 (d, *J* = 2.9 Hz, 1H), 5.62 (s, 1H), 4.22 (s, 1H), 3.58 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 147.4, 142.3, 131.8, 129.3, 128.6, 126.8, 116.8, 112.1, 55.6, 51.2; IR (neat; cm^{-1}) 3025, 1505, 1449, 1336, 1267, 1078, 700; MS (−ESI): *m*/*z* 212.3 (15%), 290.5 (15%); HRMS (ESI) *m*/*e* calcd for $C_{20}H_{18}O_2Na$ 313.1199, found 313.1198.

*Oxidation to **3b**.* To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**) (110.2 mg, 0.36 mmol) and 2-phenyl-1-ethanol (18.9 mg, 0.155 mmol) in dichloromethane (50 μL), H_2SO_4 (2 μL, 0.036 mmol) was added. The mixture was heated at 50 °C for 16.5 h. The crude product was directly loaded onto a flash column (petroleum ether/ethyl acetate from 15:1 to 5:1) to provide **3b** (51.6 mg, 0.126 mmol, 81%) and **5** (39.7 mg, 0.137 mmol), both as white solids. Data for **3b**: R_f = 0.53 (petroleum ether/ethyl acetate 15/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25−7.07 (m, 15H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.74 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.35 (d, *J* = 2.9 Hz, 1H), 5.10 (t, *J* = 5.3 Hz, 1H), 3.63 (s, 3H), 3.15 (d, *J* = 5.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.9, 146.4, 145.9, 143.8, 135.6, 130.0, 129.0, 128.07, 128.05, 127.85, 127.81, 127.78, 127.4, 126.4, 126.0, 117.6, 115.0, 114.0, 95.4, 84.3, 55.6, 41.2; IR (neat; cm^{-1}) 2988, 1662, 1643, 1624, 1458, 1207, 1171, 1089, 804, 684, 630; MS (+ESI): *m*/*z* 213.2 (25%), 289.4 (100%), 290.4 (25%), 291.4 (5%); HRMS (ESI) *m*/*e* calcd for $C_{28}H_{25}O_3$ 409.1798, found 409.1796.

*Oxidation to **3c** (Known Compound[7a]).* To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**) (112 mg 0.37 mmol) and benzyl alcohol (17.2 mg, 0.16 mmol) in dichloromethane (100 μL), H_2SO_4 (2 μL, 0.036 mmol) was added. The mixture was heated at 50 °C for 4.7 h. The crude product was directly loaded onto a flash column chromatography (petroleum ether/ethyl acetate from 12:1 to 5:1) to provide **3c** (56.8 mg, 0.144 mmol, 90%) and **5** (42.9 mg, 0.148 mmol) as white solids.

*Oxidation to **3d**.* To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**) (110.6 mg, 0.36 mmol) and 4-penten-1-ol (13.6 mg, 0.16 mmol) in dichloromethane (50 μL), H_2SO_4 (2 μL, 0.036 mmol) was added. The mixture was heated at 50 °C for 12 h. The crude product was directly loaded onto a flash column (petroleum ether/ethyl acetate from 16:1 to 6:1) to provide **3d** (47.1 mg, 0.126 mmol, 80%) and **5** (39.8 mg, 0.137 mmol), both as white solids. For **3d**, R_f0.47 (petroleum ether/ethyl acetate =16:1); mp 104.0−105.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.30 (m, 5H), 7.30−7.18 (m, 5H), 6.85 (d, *J* = 8.9 Hz, 1H), 6.74 (dd, *J* = 8.9, 2.9 Hz, 1H), 6.37 (d, *J* = 2.9 Hz, 1H), 5.75 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H), 5.00−4.82 (m, 3H), 3.62 (s, 3H), 2.32−2.06 (m, 2H), 2.00−1.82 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.9, 146.6, 146.1, 144.2, 137.7, 129.3, 128.1, 128.03, 127.99, 127.87, 127.5, 125.9, 117.6, 115.0, 114.8, 114.1, 94.6, 84.2, 55.6, 33.7, 27.6; IR (neat; cm^{-1}) 3128, 1493, 1446, 1273, 1230, 757, 701; MS (+ESI) *m*/*z* 289.5 (100%), 290.5 (25%); HRMS (ESI) *m*/*e* calcd for $C_{25}H_{25}O_3$ 373.1798, found 373.1790.

*Oxidation to **3e** (Known Compound[7a]).* To a suspension of octan-1-ol (22.0 mg, 0.17 mmol) and 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 112.1 mg, 0.37 mmol) in dichloromethane (50 μL) was added H_2SO_4 (2 μL, 0.036 mmol), and the resulting mixture was stirred at 50 °C for 13.7 h. Flash column chromatography (petroleum ether/ethyl acetate from 12/1 to 5/1) provided **3e** (64.5 mg, 0.155 mmol, 91%) as a colorless oil and **5** (45.8 mg, 0.158 mmol) as a white solid.

*Oxidation to **3f** (Known Compound[7d]).* To a suspension of 2-ethylhexanol (23.2 mg, 0.18 mmol) and 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 110 mg, 0.36 mmol) in dichloromethane (75 μL) was added H_2SO_4 (10 μL, 0.18 mmol), and the resulting mixture was stirred at 50 °C. More PPG **1** (55 mg) was added at 18 and 63 h. The reaction mixture was worked up after 4.3 days to provide **3f** in 57% yield with a **3f**/**5** ratio of 1/1.7 on the basis of NMR analysis with an internal standard (pyridinium *p*-toluenesulfonate as standard).

*Oxidation to **10a** (Known Compound[7a]). Method 1.* To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 66.6 mg, 0.22 mmol) and 4-(4-methoxyphenyl)-2-butanol (25.9 mg, 0.14 mmol) in dichloromethane (50 μL) was added H_2SO_4 (1 μL, 0.018 mmol). The mixture was heated to 50 °C for 30.5 h. The crude product was purified with flash column chromatography (petroleum ether/ethyl acetate from 9/1 to 5/1) to provide **10a** (20.7 mg, 0.116 mmol, 80%) as a colorless oil and **5** (34.0 mg, 0.117 mmol) as a white solid.

Method 2. To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 56.3 mg, 0.184 mmol) and 4-(4-methoxyphenyl)-2-butanol (27.8 mg, 0.154 mmol) in dichloromethane (25 μL) was added H_2SO_4 (1 μL, 0.018 mmol). The mixture was heated to 70 °C for 10.3 h. The same purification procedure provided **10a** (22.2 mg, 0.125 mmol, 81%) as a colorless oil and **5** (38.6 mg, 0.133 mmol) as a white solid.

*Oxidation to **10b** (Known Compound[7a]).* To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 56.1 mg, 0.183 mmol) and 2-undecanol (22.7 mg, 0.132 mmol) in dichloromethane (50 μL) was added H_2SO_4 (1 μL, 0.018 mmol). The mixture was heated to 70 °C for 4.5 h. Flash column chromatography (petroleum ether/ethyl acetate gradually from 6/1 to 3/1) provided **10b** (19.5 mg, 0.115 mmol, 86%) as a colorless oil and **5** (34.6 mg, 0.120 mmol) as a white solid.

*Preparation of **13a**.* To a stirred solution of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 380 mg, 1.25 mmol) in dichloromethane (2.5 mL) at 0 °C was added AcCl (89 μL, 98 mg), followed by Et_3N (190 μL, 1.38 mmol). The reaction solution was stirred at room temperature for 12.5 h before 3-phenyl-1-propanol (0.68 g, 5.0 mmol) was added. After 52 h, the solution was concentrated, and the residue was purified with flash chromatography (petroleum ether/ethyl acetate 6/1) to provide **13a** (432 mg, 81%) as a white solid: R_f = 0.3 (petroleum ether/ethyl acetate 5/1); mp 91.5−91.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.39−7.08 (m, 15H), 6.80 (dd, *J* = 0.4, 8.8 Hz, 1H), 6.74 (dd, *J* = 2.8, 8.8 Hz, 1H), 6.50 (dd, *J* = 0.4, 2.9 Hz, 1H), 3.63 (s, 3H), 3.30 (t, *J* = 6.4 Hz, 2H), 2.67 (d, *J* = 7.8 Hz, 2H), 2.01−1.92 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.9, 150.2, 141.2, 140.8, 129.0, 128.9, 128.2, 127.9, 127.7, 125.8, 117.8, 116.3, 113.8, 90.1, 63.8, 55.6, 32.2, 31.4; IR (neat; cm^{-1}) 2234, 2942, 1490, 1236, 1045, 739, 701; HRMS (ESI) *m*/*e* calcd for $C_{29}H_{28}O_3Na$ 447.1931, found 447.1930.

*Preparation of **13f**.* To a stirred solution of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 307 mg, 1.0 mmol) in dichloromethane (2 mL) at 0 °C was added AcCl (79 μL, 86 mg), followed by Et_3N (153 μL, 1.1 mmol). The obtained solution was stirred at room temperature for 4.5 h before 3-phenyl-1-propanol (290 mg, 2.2 mmol) was added. After 3.6 days, the solution was concentrated, and the residue was directly purified with a flash chromatography column to provide **13f** (343 mg, 82%) as a colorless oil: R_f = 0.5 (petroleum ether/ethyl acetate 7/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 (s, 1H), 7.42−7.30 (m, 10H), 6.79 (d, *J* = 8.8 Hz, 1H), 6.72 (dd, *J* = 2.9, 8.8 Hz, 1H), 6.48 (d, *J* = 2.9 Hz, 1H), 3.62 (s, 3H), 3.11−3.20 (m, 2H), 1.58−1.50 (m, 1H), 1.40−1.07 (m, 8H), 0.84 (t, *J* = 7.2 Hz, 3H), 0.77 (t, *J* = 7.4 H, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.9, 150.3, 140.8, 140.8, 129.3, 129.2, 127.8, 127.7, 117.8, 116.2, 113.7, 90.2, 66.6, 55.6, 39.9, 30.3, 28.8, 23.8, 22.8, 14.0, 10.8; MS (−-ESI): *m*/*z* 417.8 (5%); IR (neat) 2958, 2858, 1491, 1448, 1384, 1236, 1043; HRMS (ESI) *m*/*e* calcd for $C_{28}H_{34}O_3Na$ 441.2406, found 441.2403.

Competing Oxidation of 2-Undecanol (9b) and 3-Phenyl-1-propanol (4a). To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 66.7 mg, 0.2 mmol), **9b** (28.5 mg, 0.165 mmol), and **4a** (25.2 mg, 0.185 mmol) in dichloromethane (50 μL) was added

dx.doi.org/10.1021/jo201671v | J. Org. Chem. 2011, 76, 8955−8961

H_2SO_4 (6 μL, 0.108 mmol). The reaction mixture was stirred at 50 °C for 9 h. The ^1H NMR analysis with an internal reference indicated that the yields of **3a**, **10b**, **4a**, and **9b** were 32%, 33%, 50%, and 66%, respectively.

Competing Oxidation of 2-Ethylhexanol (4f) and 3-Phenyl-1-propanol (4a). To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 121 mg, 0.395 mmol), **4f** (23.1 mg, 0.178 mmol), and **4a** (25.1 mg, 0.184 mmol) in dichloromethane (50 μL) was added H_2SO_4 (6 μL, 0.108 mmol). The reaction mixture was stirred at 50 °C for 9 h. The ^1H NMR analysis with an internal reference indicated the yields of **3a,f** and **4a,f** were 78%, 8%, 19%, and 80%, respectively.

Oxidation of Diethyl Ether. To a solution of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 22.0 mg, 0.072 mmol) in diethyl ether (35 μL) was added H_2SO_4 (2 μL, 0.036 mmol). The resulting mixture was stirred at 50 °C for 10.5 h. The crude product was purified with flash column chromatography (petroleum ether/ethyl acetate gradually from 15/1 to 5/1) to provide **18** (9.7 mg, 0.029 mmol, 40%) and **5** (9.2 mg, 0.0317 mmol), both as white solids. Data for **18**: R_f = 0.53 (petroleum ether/ethyl acetate 15/1); mp 125.0−126.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−7.29 (m, 5H), 7.25 (d, J = 3.2 Hz, 5H), 6.85 (d, J = 8.9 Hz, 1H), 6.80−6.69 (m, 1H), 6.36 (d, J = 2.9 Hz, 1H), 5.11 (d, J = 5.1 Hz, 1H), 3.63 (s, 3H), 1.51 (d, J = 5.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.9, 146.6, 146.0, 144.3, 129.1, 128.13, 128.10, 128.0, 127.9, 127.5, 125.8, 117.5, 115.1, 114.1, 92.5, 84.3, 55.6, 20.8; IR (neat; cm^{-1}) 2994, 1493, 1446, 1400, 1274, 1231, 1098, 756, 701; HRMS (ESI) m/e calcd for $C_{22}H_{21}O_3$ 333.1485, found 333.1484.

Oxidation of 3-Phenylpropyl Benzyl Ether (19). To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 41.3 mg, 0.135 mmol) and 3-phenylpropyl benzyl ether (**19**; 12 mg, 0.053 mmol) in dichloromethane (25 μL) was added H_2SO_4 (3 μL, 0.054 mmol). The mixture was heated at 50 °C for 5.5 h before more PPG **1** (31.1 mg, 0.1 mmol) was added. The mixture was then heated at 50 °C for 10 h more. The crude product was filtrated through a silica gel plug (eluted with petroleum ether/ethyl acetate 1/1) to provide a yellow liquid, and its composition was determined by NMR analysis with an internal reference (i.e., DMAP). The yields of **3a,c** and the recovered **19** were 68%, 72%, and 18%, respectively. The ratio of the combined acetals **3a,c** to **5** was 1:1.15.

Oxidation of Tetrahydrofuran. To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 202.9 mg, 0.662 mmol) and THF (10.6 mg, 0.147 mmol) in dichloromethane (125 μL) was added H_2SO_4 (8 μL, 0.144 mmol). The mixture was heated to 50 °C for 6 h. The crude product was washed with acetonitrile (three times) to remove **5**. The combined acetonitrile solutions were concentrated and purified with flash column chromatography (benzene/ethyl acetate 100/1) to provide **5** (73.9 mg, 0.254 mmol). The white solid residue was washed with methanol and dichloromethane to provide compound **20** as a white solid (0.101 mmol, 68%). Data for **20**: R_f = 0.3 (petroleum ether/ethyl acetate 10/1); mp 263.0−264.0 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 7.40−7.34 (m, 5H), 7.28−7.22 (m, 5H), 6.82 (d, J = 8.9 Hz, 1H), 6.76 (dd, J = 9.0, 3.0 Hz, 1H), 5.02 (s, 1H), 3.66 (s, J = 5.1 Hz, 3H), 2.08 (dd, J = 9.9, 3.0 Hz, 1H), 1.97 (dd, J = 9.9, 3.0 Hz, 1H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 152.8, 146.4, 146.0, 144.1, 129.2, 128.1, 128.0, 127.9, 127.5, 125.8, 117.6, 115.0, 114.0, 94.7, 84.1, 55.6, 28.4; IR (neat; cm^{-1}) 2924, 2852, 1494, 1275, 1042, 729; HRMS (ESI) m/e calcd for $C_{44}H_{38}O_6Na$ 685.2563, found 685.2566.

Oxidation of Ethyl Acetate (with 1 as the Limiting Reagent). To a solution of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 22.1 mg, 0.072 mmol) in ethyl acetate (35 μL) was added H_2SO_4 (2 μL, 0.036 mmol), and the reaction mixture was stirred at 50 °C for 10.5 h. The crude product was purified with flash column chromatography (petroleum ether/ethyl acetate from 15/1 to 5/1) to provide **18** (9.2 mg, 0.0277 mmol, 38%) and **5** (9.1 mg, 0.0313 mmol) as white solids.

Oxidation of Ethyl Acetate. To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 91.9 mg, 0.3 mmol) and ethyl acetate (8.5 mg, 0.10 mmol) in dichloromethane (50 μL) was added H_2SO_4 (6 μL, 0.108 mmol). The mixture was heated to 50 °C for 13.9 h. The crude product was purified with flash column chromatography (petroleum ether/ethyl acetate from 12/1 to 5/1) to provide **18** (25.9 mg, 0.078 mmol, 78%) and **5** (27.0 mg, 0.093 mmol) as white solids.

Oxidation of 3-Phenylpropyl Acetate (21). To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 46.1 mg, 0.15 mmol) and **21** (8.9 mg, 0.05 mmol) in dichloromethane (25 μL) was added H_2SO_4 (6 μL, 0.108 mmol). The mixture was heated to 50 °C for 13.9 h. The crude product was purified with flash column chromatography (petroleum ether/ethyl acetate from 16/1 to 5/1) to provide **3a** (16.1 mg, 0.038 mmol, 76%) and **5** (12.3 mg, 0.042 mmol) as white solids.

Oxidation of ε-Caprolactone (22). To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 132.1 mg, 0.43 mmol) and ε-caprolactone (15.3 mg, 0.134 mmol) in dichloromethane (75 μL) was added H_2SO_4 (8 μL, 0.144 mmol). After 27 h, the reaction was quenched with Na_2CO_3 (20 mg, 0.19 mmol), and the solvent was removed. The obtained residue was treated with a solution of NaOH (9.6 mg, 0.24 mmol) in methanol (1.2 mL). After the mixture was stirred at room temperature for 24 h, it was quenched with HCl (6 N, 2 mL) and extracted with dichloromethane (1.3 mL × 5). The combined organic layers were concentrated, and the and the residue was purified first with a flash chromatography column (petroleum ether/ethyl acetate 5/1) to provide **5** (33.0 mg, 0.114 mmol) as a white solid. The column was then eluted with dichloromethane/ethyl acetate (4/1) to provide **23** (33.2 mg, 0.079 mmol, 59%) as a colorless oil. Data for **23**: R_f = 0.36 (dichloromethane/ethyl acetate 4/1); ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.33 (m, 5H), 7.26−7.22 (m, 5H), 6.84 (d, J = 8.9 Hz, 1H), 6.75 (dd, J = 8.9, 3.0 Hz, 1H), 6.36 (d, J = 2.9 Hz, 1H), 4.94 (t, J = 5.1 Hz, 1H), 3.63 (s, 3H), 2.33 (t, J = 7.3 Hz, 2H), 1.91−1.77 (m, 2H), 1.69−1.40 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 147.2, 143.64, 143.62, 132.7, 129.41, 129.37, 128.2, 126.1, 125.1, 115.8, 110.3, 82.2, 68.4, 55.6, 49.9, 33.0, 25.3; IR (neat; cm^{-1}) 2952, 1708, 1495, 1403, 1233, 1047, 909, 810, 758, 734, 704, 648; HRMS (ESI) m/e calcd for $C_{26}H_{26}O_5Na$ 441.1673, found 441.1672.

Oxidation of 26. To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 116.5 mg, 0.38 mmol) and the compound **26** (31.6 mg, 0.15 mmol) in dichloromethane (300 μL) was added H_2SO_4 (2 μL, 0.036 mmol). The mixture was heated to 50 °C for 23.3 h. The crude product was directly loaded onto a flash column and eluted with petroleum ether/ethyl acetate from 12/1 to 8/1 to provide **27** (59.1 mg, 0.119 mmol, 78%) as a yellow oil: R_f = 0.38 (petroleum ether/ethyl acetate 8/1); ^1H NMR (300 MHz, $CDCl_3$) δ 8.04−8.01 (m, 2H), 7.56−7.51 (m, 5H), 7.43−7.31 (m, 7H), 7.26−7.21 (m, 5H), 6.84 (d, J = 8.9 Hz, 1H), 6.74 (dd, J = 8.9, 2.9 Hz, 1H), 6.37 (d, J = 2.9 Hz, 1H), 4.97 (t, J = 5.0 Hz, 1H), 4.29 (t, J = 6.3 Hz, 2H), 3.62 (s, 3H), 1.95−1.87 (m, 2H), 1.79−1.55 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 152.8, 146.5, 146.0, 144.2, 132.8, 130.4, 129.5, 129.2, 128.3, 128.1, 128.0, 127.8, 127.5, 125.8, 117.5, 115.0, 114.1, 94.8, 84.2, 64.8, 55.5, 34.0, 28.4, 20.1; IR (neat; cm^{-1}) 3061, 3034, 2954, 1718, 1602, 1585, 1494, 1464, 1449, 1315, 1275, 1229, 1071, 1027, 758, 712, 703; HRMS (ESI) m/e calcd for $C_{32}H_{30}O_5Na$ 517.1991, found 517.1988.

Oxidation of 28. To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 121.2 mg, 0.40 mmol) and the compound **28** (32.0 mg, 0.18 mmol) in dichloromethane (300 μL) was added H_2SO_4 (2 μL, 0.036 mmol). The mixture was heated to 50 °C for 19 h. The crude product was directly loaded onto a flash column and eluted with petroleum ether/ethyl acetate from 15/1 to 10/1 to provide **3c** (7.0 mg, 0.018 mmol, 10%) and **29** (33.7 mg, 41%) as a yellow oil. Data for **29**: R_f = 0.38 (petroleum ether/ethyl acetate 8/1); ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.22 (m, 15H), 6.84 (d, J = 8.9 Hz, 1H), 6.74 (dd, J = 8.9, 2.9 Hz, 1H), 6.36 (d, J = 2.9 Hz, 1H), 4.96 (t, J = 5.0 Hz, 1H), 4.45 (s, 2H), 3.62 (s, 3H), 3.44 (dt, J = 6.4, 0.9 Hz, 2H), 1.97−1.68 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 146.5, 146.0, 144.2, 138.5, 129.2, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 127.49, 127.48, 125.8, 117.5, 115.0, 114.0, 94.8, 84.1, 72.8, 69.9, 55.5, 31.2, 23.8; IR (neat; cm^{-1}) 3059, 3031, 2933, 2856, 1494, 1447, 1274, 1231, 757, 700; HRMS (ESI) m/e calcd for $C_{31}H_{30}O_4Na$ 489.2042, found 489.2042.

dx.doi.org/10.1021/jo201671v | J. Org. Chem. 2011, 76, 8955−8961

Isotope Effect Studies. *Preparation of Deuterium-Labeled Octan-1-ol (i.e., $H(CH_2)_7CD_2OH$ (**4e(D)**)).* To a stirred solution of octanoyl choride (0.17 mL, 1.0 mmol) in DMF (1.0 mL) was added $NaBD_4$ (147.6 mg, 3.5 mmol) at −34 °C. The mixture was stirred at room temperature overnight. Workup followed by column chromatography (eluted with petroleum ether/ethyl acetate 8/1, R_f = 0.2) afforded **4e(*D*)** (76.3 mg, 57%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (t, J = 6.7 Hz, 2H), 1.39−1.28 (m, 10H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 62.4 (q, J_{CD} = 21.8 Hz), 32.6, 31.8, 29.3, 29.2, 25.6, 22.6, 14.0; IR (neat; cm^{-1}) 3337 (br), 2928, 1466, 968; MS (EI) m/e 56.1 (100%), 61.1, 70.1, 84.1.

*Reaction of **4e**.* To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**;102.0 mg, 0.33 mmol) and **4e** (19.6 mg, 0.15 mmol) in dichloromethane (300 μL) was added H_2SO_4 (2 μL, 0.036 mmol). The mixture was heated to 50 °C for 8.3 h, and **3e** was obtained in 75% yield (based on ^{1}H NMR).

*Reaction of **4e(D)**.* To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 102.7 mg, 0.33 mmol) and **4e(*D*)** (19.5 mg, 0.15 mmol) in dichloromethane (300 μL) was added H_2SO_4 (2 μL, 0.036 mmol). The mixture was heated to 50 °C for 8.3 h, and **3e(*D*)** was obtained in 42% yield (based on ^{1}H NMR). Data for **3e(*D*)**: R_f = 0.50 (petroleum ether/ethyl acetate 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.34 (m, 5H), δ 7.28−7.23 (m, 5H), 6.86 (d, J = 8.9 Hz, 1H), 6.76 (dd, J = 8.9, 3.0 Hz, 1H), 6.38 (d, J = 2.9 Hz, 1H), 3.65 (s, 3H), 1.91−1.75 (m, 2H), 1.51−1.37 (m, 2H), 1.31−1.25 (m, 8H), 0.88 (t, J = 6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 146.6, 146.1, 144.3, 129.2, 128.1, 128.0, 127.9, 127.8, 127.4, 125.9, 117.5, 115.0, 114.0, 94.8 (t, J_{CD} = 25.5), 84.1, 55.5, 34.3, 31.7, 29.2, 29.1, 23.4, 22.6, 14.0; IR (neat; cm^{-1}) 2953, 2928, 2856, 1493, 1447, 1255, 1177, 1255, 1137, 1042, 970, 756; HRMS (ESI) m/e calcd for $C_{28}H_{32}DO_3Na$ 440.2312, found 440.2316.

*Reaction of a **4e/4e(D)** Mixture (∼1:1).* To a suspension of 2-(hydroxydiphenylmethyl)-4-methoxyphenol (**1**; 102.0 mg, 0.33 mmol), **4e** (9.8 mg, 0.075 mmol), and **4e(*D*)** (9.5 mg, 0.072 mmol) in dichloromethane (300 μL) was added H_2SO_4 (2 μL, 0.036 mmol). The mixture was heated to 50 °C for 8.3 h, and the acetals **3e** and **3e(*D*)** were obtained in 54% yield (**3e**/**3e(*D*)** ≈ 2.0/1) (based on ^{1}H NMR).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving ^{1}H NMR and ^{13}C NMR spectra of **5**, **3b,d**, **3e(D)**, **4e(D)**, **13a,f**, **18**, **20**, **23**, **27**, and **29** and ^{1}H NMR spectra of the known compounds **3a,c,e,f** and **10a,b**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: wangp@uab.edu.

■ ACKNOWLEDGMENTS

We thank the NSF for its support (No. CHE-0848489).

■ REFERENCES

(1) Deno, N. C.; Potter, N. H. *J. Am. Chem. Soc.* **1967**, *89*, 3550.

(2) (a) Barton, D. H. R.; Magnus, P. D.; Smith, G.; Zurr, D. *Chem. Commun.* **1971**, 861. (b) Barton, D. H. R.; Magnus, P. D.; Streckert, G.; Zurr, D. *Chem. Commun.* **1971**, 1109. (c) Barton, D. H. R.; Magnus, P. D.; Smith, G.; Streckert, G.; Zurr, D. *J. Chem. Soc., Perkin Trans. 1* **1972**, 542.

(3) Doyle, M. P.; Siegfried, B. *J. Am. Chem. Soc.* **1976**, *98*, 163.

(4) (a) Jung, M. E. *J. Org. Chem.* **1976**, *41*, 1479. (b) Jung, M. E.; Speltz, L. M. *J. Am. Chem. Soc.* **1976**, *98*, 7882. (c) Jung, M. E.; Pan, Y.-G.; Rathke, M. W.; Sullivan, D. F.; Woodbury, R. P. *J. Org. Chem.* **1977**, *42*, 3961. (d) Jung, M. E.; Brown, R. W. *Tetrahedron Lett.* **1978**, 2771.

(5) Hoye, T. R.; Kurth, M. J. *J. Am. Chem. Soc.* **1979**, *101*, 5065.

(6) Reducing triphenylmethyl to triphenylmethane with alcohol under strongly acidic conditions has been reported: (a) Smith, H. A.; Smith, R. J. *J. Am. Chem. Soc.* **1948**, *70*, 2400. (b) Bartlett, P. D.; McCollum, J. D. *J. Am. Chem. Soc.* **1956**, *78*, 1441.

(7) (a) Wang, P.; Hu, H.; Wang, Y. *Org. Lett.* **2007**, *9*, 1533. (b) Wang, P.; Hu, H.; Wang, Y. *Org. Lett.* **2007**, *9*, 2831. (c) Wang, P.; Wang, Y.; Hu, H.; Spencer, C.; Liang, X.; Pan, L. *J. Org. Chem.* **2008**, *73*, 6152. (d) Wang, P.; Wang, Y.; Hu, H.; Liang, X. *Eur. J. Org. Chem.* **2009**, 208. (e) Wang, P.; Mondal, M.; Wang, Y. *Eur. J. Org. Chem.* **2009**, 2055. (f) Yang, H.; Zhang, X.; Zhou, L.; Wang, P. *J. Org. Chem.* **2011**, *76*, 2040.

(8) Kim, J.-H.; Huang, F.; Ly, M.; Linhardt, R. J. *J. Org. Chem.* **2008**, *73*, 9497.

(9) Isotope effects were studied with **4e** and its deuterium-substituted counterpart **4e(*D*)**: i.e., $H(CH_2)_7CD_2OH$. An inconclusive K_H/K_D ratio of 1.7 was obtained for the reactions involving C−H and C−D bond cleavage.