JOC*Note*

Silver(I) Oxide Mediated Selective Monoprotection of Diols in Pyranosides

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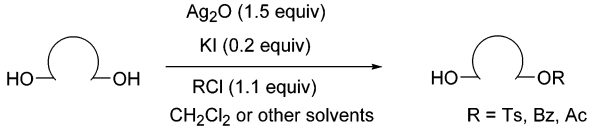
Received February 16, 2004

Abstract: The reaction of 4, 6-*O*-benzylidene-D-pyranosides with a stoichiometric amount of TsCl, AcCl, and BzCl in the presence of silver(I) oxide and a catalytic amount of potassium iodide led to monosubstituted derivatives in high regioselectivity and in good yields.

Oligosaccharides and glycoconjugates play a crucial role in a multitude of important biological processes.[1] The assembly of oligosaccharides and glycoconjugates is an intensive field of research.[2] Although enzymatic synthesis[3] of carbohydrates has shown advantages over chemical synthesis, its application is hampered by the fact useful enzymes are not yet widely available. The chemical synthesis of carbohydrates, which is traditionally a time-consuming process mainly due to the extensive need for protecting group manipulations, is still the method of choice in most cases. Therefore, regioselective protection of multihydroxyl groups in a monosaccharide building block is in great demand for the construction of an oligosaccharide. Herein, we wish to report a facile new method for the regioselective monoprotection of 2,3-diols in 4,6-*O*-benzylidene-protected pyranosides in the presence of silver(I) oxide (Ag_2O) and a catalytic amount of potassium iodide (KI) under neutral conditions using a stoichiometric amount of protecting reagents (Scheme 1).

Oligosaccharides with 1→2 and/or 1→3 linkages are abundant in nature.[4] Suitable protected galactopyranosides or glucopyranosides with one free hydroxyl group at the 2- or 3-position are very useful building blocks widely used in oligosaccharide synthesis. The regioselective protection of only one of the two similar secondary 2,3-dihydroxyl groups is frequently required. Usually, treatment of these diols with a stoichiometric equivalent of protecting reagents results in the formation of a mixture of the 2-protected, the 3-protected, and the 2,3-diprotected derivative; thus, the selectivity is difficult to control. Although some selective protection approaches such as the phase-transfer method,[5−7] the use of 1-(benzoyloxy)benzotriazole as the acylating reagent,[8,9] the dibutyltin oxide mediated selective monoprotection strategy,[10−18] the microwave irradiation technique,[19−21] the dimethyltin dichloride procedure,[22] and the Cu(II)-mediated acylation method[23] are available, "genuine" synthetic solutions of these compounds still await investigation. Recently, the silver(I) oxide mediated monoprotection of symmetrical diols was reported by Bouzide and Sauvé.[24,25] Inspired by their results, we were interested in exploring the selective monoprotection of 2,3-diols in 4,6-*O*-benzylidene galactopyranosides or glucopyranosides by virtue of this approach.

SCHEME 1. Regioselective Protection of Multihydroxyl Groups



First, a solution of *p*-methylphenyl 4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside (**3**)[26] in dichloromethane was treated with freshly prepared Ag_2O and TsCl in the presence of KI at room temperature yielding within 8 h the 3-monosulfonate ester **10** in 97% isolated yield (Table 1, entry 3). No 2-substituted or 2,3-disubstituted product was detected. After success of this example, we then tried to use other carbohydrate substrates to test the selectivity of tosylation. As illustrated in Table 1, *p*-methylphenyl-4,6-*O*-benzylidene-1-thio-*β*-D-galactopyranoside (**2**)[26] and methyl 4,6-*O*-benzylidene-*β*-D-galactopyranoside (**5**) also showed excellent selectivity and high yield for monotosylation at 3-position (entry 2 and entry 5). When methyl 4,6-*O*-benzylidene-α-D-galactopyranoside (**6**) was treated using the same conditions as mentioned above, a chromatographically inseparable mixture of the 3-to-

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(21) Morcuende, A.; Ors, M.; Valverde, S.; Herradón, B. *J. Org. Chem.* **1996**, *61*, 5264−5270.
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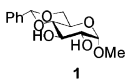
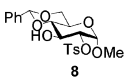
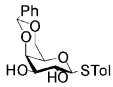
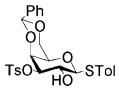
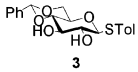
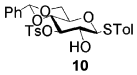
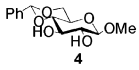
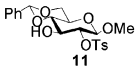
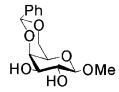
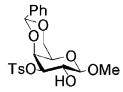
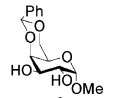
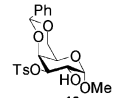
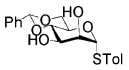
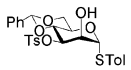
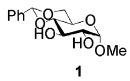
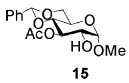
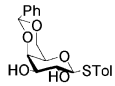
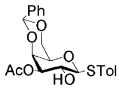
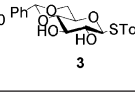
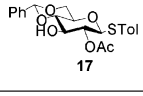
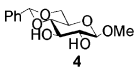
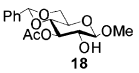
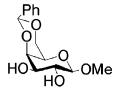
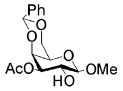
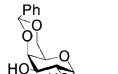
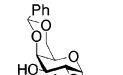
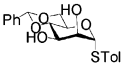
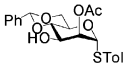
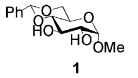
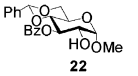
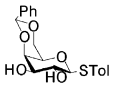
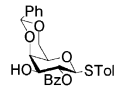
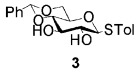
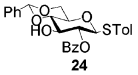
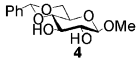
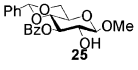
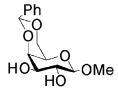
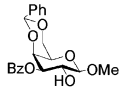
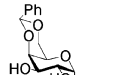
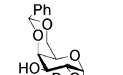
10.1021/jo0497252 CCC: $27.50
Published on Web 07/16/2004

TABLE 1. Selective Monoprotection of Pyranosides

Entry	Carb.	PG	Major product	Isolated yield	Note
1	 **1**	Ts	 **8**	83%	
2	 **2**	Ts	 **9**	87%	
3	 **3**	Ts	 **10**	97%	
4	 **4**	Ts	 **11**	88%	
5	 **5**	Ts	 **12**	98%	
6	 **6**	Ts	 **13**	72%	26% of 2-substituted product was also gained based on NMR
7	 **7**	Ts	 **14**	75%	
8	 **1**	Ac	 **15**	81%	15% of 2-substituted product was also gained
9	 **2**	Ac	 **16**	87%	12% of 2-substituted product was also gained
10	 **3**	Ac	 **17**	74%	20% of 3-substituted product was also gained

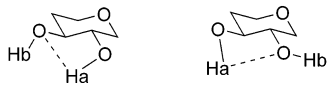
Entry	Carb.	PG	Major product	Isolated yield	Note
11	 **4**	Ac	 **18**	70%	26% of 2-substituted product was also gained
12	 **5**	Ac	 **19**	96%	
13	 **6**	Ac	 **20**	92%	
14	 **7**	Ac	 **21**	93%	
15	 **1**	Bz	 **22**	86%	12% of 2-substituted product was also gained
16	 **2**	Bz	 **23**	70%	12% of 2,3-disubstituted product was also gained
17	 **3**	Bz	 **24**	86%	13% of 3-substituted product was also gained
18	 **4**	Bz	 **25**	71%	19% of 2-substituted product was also gained
19	 **5**	Bz	 **26**	96%	
20	 **6**	Bz	 **27**	87%	

sylated product **13** and the 2-tosylated product was obtained in a total yield of 98% with the ratio of 2.8:1 based on ^{1}H and COSY NMR spectral analyses (entry 6). When the mannose derivative **7** was used as the substrate, the 3-tosylated product **14** was also gained in 75% isolated yield (entry 7). On the other hand, methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**1**)[27] and methyl 4,6-*O*-benzylidene-*β*-D-glucopyranoside (**4**) exhibited reverse regioselectivity to give the 2-tosylated product **8** in 83% and **11** in 88% isolated yield (entries 1 and 4). Acetylation was also performed utilizing these carbohydrate derivatives as reactants. They generally exhibited good selectivity and good yields (entries 8−14), leading to either 3-substituted or 2-substituted products. For the acetylation of saccharides **1**, **2**, **4**, and **5**, the 3-acetylated products were obtained (entries 8, 9, 11, and 12). On the contrary, for the acetylation of saccharides **3**, **6**, and **7**, reverse regioselectivity (acetylation at 2-position) was again observed (entries 10, 13, and 14). Finally, benzoylation was carried out to further investigate the regioselectivity. Treatment of glucoside **1** with benzoyl chloride, silver oxide, and potassium iodide produced the 3-benzoylated product **22** in 86% isolated yield and the 2-benzoylated product in 12% isolated yield (entry 15); likewise, monosaccharides **4** and **5** also gave the 3-benzoylated products **25** and **26** in good yields (entry 18 and 19). When the thiogalactoside **2**, thioglucoside **3**, and *O*-galactoside **6** were reacted with benzoyl chloride under the same conditions, the corresponding 2-substituted products were isolated as the major products in 70%, 86%, and 87% yield, respectively (entries 16, 17, and 20).[28] The reverse regioselectivity was once again detected. It seems that tosylation and acylation are dependent both on the reactivities among hydroxyl groups and on the tosylating and acylating reagents. The reac-

(27) Iacazio, G.; Rorberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1099−1101.

(28) The reaction of mannose derivative **7** with BzCl was also tried. The desired monobenzoylated product was too unstable to purify by column chromatography. The benzoyl group migrated from one hydroxyl to another hydroxyl position during standing and separation process, and we finally got the mixture of 2- and 3-benzoylated product in a ratio of ∼1:1.

SCHEME 2. Internal Hydrogen Bonding



tivities of different hydroxyl groups may be connected with the different acidities between 2- and 3-hydroxyl groups, which come from the mutual effects on the structural nature of saccharides and the substituents at 1-position. Based on our experimental results (Table 1), it appears that (1) acetylation and benzoylation almost display the same regioselectivity (compare entries 8 and 10−13 with entries 15 and 17−20) with the exception of thiogalactoside **2** (compare entry 9 with entry 16); (2) monotosylation at the 2- or 3-position depends on the anomeric substituents (compare entries 3 and 4) but not the anomeric configurations; this can be seen by that the anomers **1**/**4** and **5**/**6** over tosylation show the same regioselectivity (compare entries 1 and 4, 5 and 6); (3) for the glucose series, the regioselectivity does not depend on the anomeric configurations of saccharides (compare entries 1 and 4, 8 and 11, and 15 and 18); (4) for the glucose series, the change from *O*- to *S*-glycoside always modifies the regioselectivity (compare entries 1, 4 and 3, entries 8, 11 and 10, and entries 15, 18 and 17).

We may attribute this highly selective monoprotection of the pyranosides to an internal hydrogen bonding (IHB) interaction[25] (Scheme 2). The hydrogen atom Ha involved in the IHB becomes less acidic than Hb, so Hb will be first deprotonated by Ag_2O. When the hydroxyl group (Hb) with a lower PKa is deprotonated by Ag_2O, IHB will further decrease the acidity of the other hydroxyl group (Ha). It therefore amplifies the discrimination of the two hydroxyl groups, leading to a high level of regioselectivity. In some cases, the anomeric α-methoxyl group may probably participate in the formation of an internal hydrogen bonding with 2-hydroxyl group, resulting in outcomes of the 2-substituted product (see Table 1, entries 13 and 20). The steric factor may also influence the regioselectivity besides the internal hydrogen bonding; as observed, most galactose derivatives tend to undergo the substitutions at the 3-position (see Table 1, entries 2, 5, 6, 9, 12, and 19). Another issue that should be noted is that at least in some cases our results appear to show the reverse regioselectivity compared with the established organotin-mediated selective manipulation practice which usually produced 2-substituted products, for example, the benzoate ester at 2-position[10,22] for benzoylation of methyl 4,6-O-benzylidene-α-D-glucopyranoside (**1**). In our case, the 3-substituted benzoylated product was obtained. Another example is the tosylation of methyl 4,6-*O*-benzylidene-*β*-D-glucopyranoside (**4**), which gave the 3-substituted product under the conditions of TsCl−pyridine,[29] but by our approach the 2-substituted product was gained (Table 1, entry 4). The different regioselectivity can meet the requirements for the synthesis of different saccharide building blocks.

Other solvents such as ethyl acetate, toluene, and 1,2-dichloroethane also gave satisfactory results.[30] However, acetonitrile was an unsuitable solvent that gave decreased rates for the protection and led to hydrolysis of the protecting reagents. Tetrahydrofuran (THF) was also avoided since ring opening of THF was catalyzed by Ag_2O.[24,31]

In conclusion, we report a new method for the highly selective monoprotection of pyranosides. Due to its simplicity and its mild conditions, the reaction may find wide application in saccharide synthesis. And the mechanism of the regioselectivity will still await investigation.

Experimental Section

General Experimental Procedure. To a stirred solution of *p*-methylphenyl-4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside (**3**) (2.0 g, 5.35 mmol) in dichloromethane (50 mL) were added fresh Ag_2O[32] (1.91 g, 8.23 mmol), TsCl (1.28 g, 6.71 mmol), and KI (0.19 g, 1.14 mmol). The reaction mixture was stirred for 8 h at room temperature, filtered through a small pad of silica gel, and washed with dichloromethane. Evaporation of the solvent followed by column chromatography (petroleum ether/ethyl acetate 8:1) gave the monotosylated product **10** (2.74 g, 97%) as white crystals. For compound **10**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69 (td, 2H, J = 2.0, 8.5 Hz), 7.43 (td, 2H, J = 1.5, 8.0 Hz), 7.32−7.38 (m, 4H), 7.27 (m, 1H), 7.15 (d, 2H, J = 8.0 Hz), 6.98 (d, 2H, J = 8.0 Hz), 5.33 (s, 1H), 4.73 (dd, 1H, J = 9.5, 8.0 Hz), 4.59 (d, 1H, J = 9.5 Hz), 4.35 (dd, 1H, J = 4.5, 10.5 Hz), 3.70 (t, 1H, J = 10.0 Hz), 3.58 (dt, 1H, J = 2.0, 9.0 Hz), 3.53 (t, 1H, J = 9.5 Hz), 3.46 (dt, 1H, J = 5.0, 10.0 Hz), 3.11 (d, 1H, J = 2.0 Hz), 2.36 (s, 3H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.19, 21.64, 68.38, 70.49, 70.83, 77.71, 83.04, 88.58, 101.60, 126.23, 126.61, 128.09, 128.14, 129.12, 129.30, 129.91, 133.25, 134.18, 136.49, 139.12, 144.55; MS (FAB) *m*/*z* 528 [M$^+$]. Anal. Calcd for $C_{27}H_{28}O_7S_2$: C, 61.34; H, 5.34. Found: C, 61.70; H, 5.32.

Compound **8**. This compound was prepared from **1**, yielding **8** by column chromatography (petroleum ether/ethyl acetate 10:1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.83 (d, 2H, J = 8.4 Hz), 7.44−7.31(m, 7H), 5.47 (s, 1H), 4.82 (d, 1H, J = 3.6 Hz), 4.37 (dd, 1H, J = 9.0, 4.2 Hz), 4.25 (dd, 1H, J = 9.9, 4.2 Hz), 4.12 (t, 1H, J = 9.6 Hz), 3.84−3.76 (m, 1H), 3.69 (t, 1H, J = 10.0 Hz), 3.45 (t, 1H, J = 10.0 Hz), 3.34 (s, 3H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.69, 55.68, 61.89, 68.36, 68.73, 79.41, 80.97, 98.15, 101.98, 126.21, 128.07, 128.31, 129.28, 129.79, 133.19, 136.76, 145.17; MS (FAB) *m*/*z* 436 [M$^+$]. Anal. Calcd for $C_{21}H_{24}O_8S$: C, 57.79; H, 5.54. Found: C, 57.30; H, 5.46.

Compound **9**. This compound was prepared from **2**, yielding **9** by column chromatography (petroleum ether/ethyl acetate 8:1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.71 (d, 2H, J = 5.1 Hz), 6.95 (d, 2H, J = 7.8 Hz), 7.44 (d, 2H, J = 7.8 Hz), 7.27−7.29 (m, 7H), 5.26 (s, 1H), 4.50 (dd, 1H, J = 3.5 , 10.0 Hz), 4.38 (d, 1H, J = 9.0 Hz), 4.30 (m, 2H), 4.26 (d, 1H, J = 7.0, 13.0 Hz), 4.05 (d, 1H, J = 12.6 Hz), 3.76 (t, 1H, J = 9.6 Hz), 3.46 (s, 1H), 2.33 (s, 3H), 2.25 (s, 3H); MS (FAB) *m*/*z* 528 [M$^+$]. Anal. Calcd for $C_{27}H_{28}O_7S_2$: C, 61.34; H, 5.34. Found: C, 61.38; H, 5.69.

Compound **11**. This compound was prepared from **4**, yielding **11** by column chromatography (petroleum ether/ethyl acetate 8:1): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.44 (s, 3H), 2.87 (d, 1H, J = 3.0 Hz), 3.30 (s, 3H), 3.40 (dt, 1H, J = 5.0, 10.0 Hz), 3.56 (t, 1H, J = 9.5 Hz), 3.75 (t, 1H, J = 10.0 Hz), 3.95 (td, 1H, J = 3.0, 9.5 Hz), 4.40 (d, 1H, J = 7.5 Hz), 4.37 (t, 1H, J = 6.5 Hz), 4.34 (dd, 1H, J = 5.0, 10.0 Hz), 5.53 (s, 1H), 7.32−7.37 (m, 5H), 7.46−7.48 (m, 2H), 7.82−7.84 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.64, 57.30, 65.97, 68.42, 71.89, 80.24, 82.27, 101.75, 101.86, 126.22, 128.27, 128.32, 129.29, 129.43, 133.83, 136.70, 144.80;

(29) In contrast, we treated methyl 4,6-*O*-benzylidene-*β*-D-glucopyranoside (**4**) with TsCl and pyridine, the 3-tosylated product was isolated in 48% yield as the major product.

(30) Using ethyl acetate, toluene, or 1,2-dichloroethane as solvent, similar results (yields and product ratios) were also obtained. Because 1,2-dichloroethane is more toxic and the solubility of saccharides in ethyl acetate or toluene is not good, we eventually chose dichloromethane as the solvent to perform the reaction.

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(32) Tanabe, M.; Peters, R. H. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, pp 386-392.

MS (ESI) *m/z* 454 [M + NH_4^+]. Anal. Calcd for $C_{21}H_{24}O_8S$: C, 57.79; H, 5.54. Found: C, 57.77; H: 5.82.

Compound **12**. This compound was prepared from **5**, yielding **12** by column chromatography (petroleum ether/ethyl acetate 6:1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.75 (d, 2H, J = 8.1 Hz), 7.71−7.36 (m, 7H), 5.27 (s, 1H), 4.50 (dd, 1H, J = 3.6 Hz, J = 9.6 Hz), 4.20−4.25 (m, 2H), 4.14 (d, 1H, J = 7.8 Hz), 3.84−3.96 (m, 2H), 3.46 (s, 3H), 3.37 (s, 1H), 2.34 (d, 1H, J = 2.7 Hz), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.63, 57.24, 66.06, 68.36, 68.76, 74.09, 80.35, 100.84, 103.60, 126.14, 127.84, 128.00, 128.93, 129.63, 133.80, 137.20, 144.90; MS (ESI) *m/z* 454 [M + NH_4^+]. Anal. Calcd for $C_{21}H_{24}O_8S$: C, 57.79; H, 5.54. Found: C, 57.68; H, 5.68.

Compound **13**. This compound was prepared from **6**, yielding **13** by column chromatography (petroleum ether/ethyl acetate 5:1): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.41 (s, 3H), 3.44 (s, 3H), 3.67 (br s, 1H), 4.04 (d, 1H, J = 1.5 Hz), 4.15 (dd, 1H, J = 3.5, 9.5 Hz), 4.25−4.27 (m, 1H), 4.36 (d, 1H, J = 3.5 Hz), 4.82 (dd, 1H, J = 3.5, 9.5 Hz), 4.90 (d, 1H, J = 3.5 Hz), 5.39 (s, 1H), 7.28−7.46 (m, 7H), 7.84 (d, 2H J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.65, 55.73, 62.44, 66.32, 68.92, 74.76, 78.65, 100.17, 100.65, 126.05, 127.80, 128.07, 128.96, 129.67, 133.97, 137.23, 144.84; MS (ESI) *m/z* 454 [M + NH_4^+].

Compound **14**. This compound was prepared from **7**, yielding **14** by column chromatography (petroleum ether/ethyl acetate 8:1 containing 2% of Et_3N): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.36 (s, 3H), 2.37 (s, 3H), 2.78 (br s, 1H), 3.82 (t, 1H, J = 10.5 Hz), 4.16 (t, 1H, J = 9.5 Hz), 4.18 (dd, 1H, J = 5.0, 10.5 Hz), 4.32 (td, 1H, J = 5.0, 10.5 Hz), 4.59 (br s, 1H), 4.84 (dd, 1H, J = 3.5, 10.0 Hz), 5.44 (s, 1H), 5.52 (s, 1H), 7.11 (d, 2H, J = 8.0 Hz), 7.16 (d, 2H, J = 8.0 Hz), 7.27 (d, 2H, J = 8.0 Hz), 7.34−7.40 (m, 5H), 7.78 (d, 2H, J = 8.0 Hz); MS (ESI) *m/z* 546 [M + NH_4^+].

Compound **15**. This compound was prepared from **1**, yielding **15** by column chromatography (petroleum ether/ethyl acetate 8:1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47∼7.29 (m, 5H), 5.50 (s, 1H), 5.33 (t, 1H, J = 9.6 Hz), 4.81 (d, 1H, J = 4.2 Hz), 4.30 (dd, 1H, J = 4.5, 9.3 Hz), 3.63−3.91 (m, 3H), 3.59 (t, 1H, J = 9.6 Hz), 3.43 (s, 3H), 2.25 (s, 3H); MS (FAB) *m/z* 325 [M + H^+]. Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.09; H, 6.20.

Compound **16**. This compound was prepared from **2**, yielding **16** by column chromatography (petroleum ether/ethyl acetate 10:1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.57 (d, 2H, J = 7.8 Hz), 7.29−7.40 (m, 5H), 7.07 (d, 2H, J = 7.8 Hz), 5.46 (s, 1H), 4.90 (dd, 1H, J = 3.3, 12.0 Hz), 4.55 (d, 1H, J = 9.3 Hz), 4.37 (m, 2H), 4.02 (dd, 1H, J = 1.5, 12.0 Hz), 3.90 (t, 1H, J = 9.6 Hz), 3.60 (s, 1H), 2.60 (br, 1H), 2.34 (s, 3H), 2.13 (s, 3H); MS (FAB) *m/z* 455 [M + K^+]. Anal. Calcd for $C_{22}H_{24}O_6S$: C, 63.44; H, 5.81. Found: C, 63.69; H, 5.82.

Compound **17**. This compound was prepared from **3**, yielding **17** by column chromatography (petroleum ether/ethyl acetate 8:1): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.43−7.48 (m, 2H), 7.34−7.39 (m, 5H), 7.13 (d, 2H, J = 7.5 Hz), 5.53 (s, 1H), 4.91 (dd, 1H, J = 9.0, 10.0 Hz), 4.67 (d, 1H, J = 10.0 Hz), 4.38 (dd, 1H, J = 5.0, 10.5 Hz), 3.91 (dt, 1H, J = 3.5, 9.0 Hz), 3.78 (t, 1H, J = 10.0 Hz), 3.54 (t, 1H, J = 9.0 Hz), 3.46∼3.51 (m, 1H), 2.49 (d, 1H, J = 3.0 Hz), 2.35 (s, 3H), 2.19 (s, 3H); MS (FAB) *m/z* 416 [M^+]. Anal. Calcd for $C_{22}H_{24}O_6S$: C, 63.44; H, 5.81. Found: C, 63.07; H, 5.74.

Compound **18**. This compound was prepared from **4**, yielding **18** by column chromatography (petroleum ether/ethyl acetate 10:1): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.13 (s, 3H), 2.62 (br, 1H), 3.51−3.58 (m, 2H), 3.59 (s, 3H), 3.64 (t, 1H, J = 9.5 Hz), 3.79 (t, 1H, J = 10.0 Hz), 4.37 (dd, 1H, J = 5.0, 10.0 Hz), 4.38 (d, 1H, J = 7.5 Hz), 5.22 (t, 1H, J = 9.5 Hz), 5.50 (s, 1H), 7.35−7.38 (m, 3H), 7.44−7.46 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.97, 57.62, 66.46, 68.61, 73.44, 73.58, 78.46, 101.49, 104.52, 126.12, 128.23, 129.09, 136.88, 171.03; MS (ESI) *m/z* 342 [M + NH_4^+]. Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.37; H, 6.09.

Compound **19**. This compound was prepared from **5**, yielding **19** by column chromatography (petroleum ether/ethyl acetate 8:1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.14 (s, 3H), 2.43 (br., 1H), 3.51 (d, 1H, J = 1.5 Hz), 3.59 (s, 3H), 4.01 (dd, 1H, J = 7.5, 10.0 Hz), 4.07 (dd, 1H, J = 1.5, 7.5 Hz), 4.29 (d, 1H, J = 7.5 Hz), 4.34 (dd, 1H, J = 1.5, 12.5 Hz), 4.40 (dd, 1H, J = 1.0, 3.5 Hz), 4.86 (dd, 1H, J = 3.5, 10.0 Hz), 5.50 (s, 1H), 7.33−7.38 (m, 3H), 7.48−7.51 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 57.24, 66.44, 68.50, 68.99, 73.28, 73.79, 100.89, 103.99, 126.24, 128.10, 128.97, 137.54, 171.04; MS (ESI) *m/z* 342 [M + NH_4^+]. Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.03; H, 6.42.

Compound **20**. This compound was prepared from **6**, yielding **20** by column chromatography (petroleum ether/ethyl acetate 6:1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.15 (s, 3H), 2.40 (d, 1H, J = 10.5 Hz), 3.40 (s, 3H), 3.74 (br s, 1H), 4.07−4.12 (m, 2H), 4.28−4.32 (m, 2H), 4.98 (d, 1H, J = 3.6 Hz), 5.16 (dd, 1H, J = 3.6 Hz, J = 10.2 Hz), 5.57 (s, 1H), 7.37−7.40 (m, 3H), 7.50−7.52 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.05, 45.72, 55.53, 62.32, 67.15, 69.13, 71.19, 98.11, 101.35, 126.28, 128.26, 129.26, 137.30, 171.04; MS (ESI) *m/z* 342 [M + NH_4^+].

Compound **21**. This compound was prepared from **7**, yielding **21** by column chromatography (petroleum ether/ethyl acetate 6:1): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.16 (s, 3H), 2.33 (s, 3H), 2.42 (br s, 1H), 3.84 (t, 1H, J = 10.0 Hz), 3.98 (t, 1H, J = 10.0 Hz), 4.24 (d, 1H, J = 5.0 Hz), 4.25 (d, 1H, J = 5.0 Hz), 4.38 (dt, 1H, J = 5.0, 10.0 Hz), 5.40 (br s, 1H), 5.48 (dd, 1H, J = 1.0, 3.0 Hz), 5.62 (s, 1H), 7.13 (d, 2H, J = 8.0 Hz), 7.36 (d, 2H, J = 8.0 Hz), 7.38−7.39 (m, 3H), 7.51−7.53 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.97, 21.12, 64.5, 67.74, 68.40, 73.54, 79.14, 87.25, 102.24, 126.25, 128.37, 129.21, 129.32, 129.98, 132.71, 137.01, 138.38, 170.35; MS (ESI) *m/z* 434 [M + NH_4^+].

Acknowledgment. This work was financially supported by the National Natural Science Foundation of China. J.S. is on study leave from Guangdong Medical College, Zhanjiang, China.

Supporting Information Available: Experimental procedures and characterization data for compounds **22**−**27**. Selected ^{1}H NMR, ^{13}C NMR, and 2D NMR spectra for compounds **8**−**27**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0497252