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Development of a Photolabile Carbonyl-Protecting Group Toolbox†

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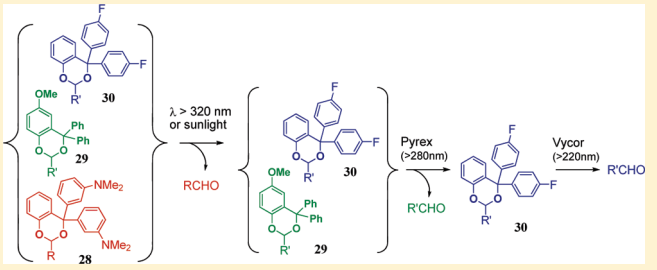
Supporting Information

ABSTRACT: New salicyl alcohol derived photolabile carbonyl protecting groups have been developed, and the effect of substituents on the photochemical properties of photolabile protecting groups (PPGs) has been studied. The 3-(dimethylamino)phenyl groups at the α position prove to be important to the efficiency of the deprotection reactions, as shown in the photo reactions of the acetal **9**. On the other hand, expansion of the salicyl alcohol's benzene skeleton to naphthalene does not improve the photochemical properties of PPGs. A neutral protecting protocol has been generalized to new PPGs with α,α-diaryl salicyl alcohol backbone. Thus, installation of PPGs onto aldehydes is readily achieved at 140 °C without using any other chemical reagents. These PPGs are stable under acidic conditions typical for hydrolyzing acetals and constitute orthogonal protecting groups with traditional 1,3-dioxane/1,3-dioxolane for carbonyl compounds. Highly efficient release of carbohydrate molecules is demonstrated, which can be potentially useful in site-specific release and immobilization of carbohydrates for preparation of high-density microarrays. With the enriched PPG toolbox, PPGs are divided into three subgroups based on their UV absorption profiles. PPGs from different subgroups can be sequentially removed by using different UV irradiation wavelengths. For PPGs absorbing UVA (λ >315 nm), photochemical deprotection can be carried out with sunlight in high yields.



Photolabile protecting groups (PPGs) are protecting groups that can be removed with photo irradiation under neutral and reagent-free conditions. In addition, photochemical deprotection reactions can be carried out with precise spatial and temporal control. These features are important to a broad spectrum of applications ranging from dynamic studies in biology to surface patterning and photolithographic preparation of high density biochips.[1,2] The past two decades have witnessed continuous emergence of new PPGs and their creative applications.[3]

Among various functional groups, we are particularly interested in developing PPGs for carbonyl groups. Carbonyl groups are important functional groups in organic chemistry and often need protection in the course of multistep syntheses.[1] Moreover, many biologically important molecules have a carbonyl moiety; deactivating these molecules through modifying carbonyl groups with PPGs and subsequent release in a desired environment upon irradiation is an appealing approach to controlled release of molecules.

Research in developing photolabile carbonyl protecting groups dates back several decades, and much progress has been made.[4] We recently reported a series of new PPGs for carbonyl groups featuring the salicyl alcohol skeleton (Scheme 1).[5] We hypothesize that irradiation of the acetal **I** results in cleavage of the benzylic C−O bond to produce the intermediate **II**. The depicted electron movement in **II** leads to release of the carbonyl compound **III** and formation of the intermediate **IV**. According to the excited state *meta* effect,[6] introducing an electron-donating group at the *meta* position(s) of the salicyl alcohol skeleton should facilitate the benzylic C−O bond cleavage. Therefore α,α-diphenyl-5-methoxysalicyl alcohol,[5a] α,α-diphenyl-3,5-dimethoxysalicyl alcohol, and α,α-diphenyl-5-(dimethylamino)-salicyl alcohol were examined as the PPG reagents.[5c] Indeed, *meta* electron-donating substitution improved the efficiency of deprotection reactions. However, the intermediate **IV** was not observed in the reaction mixture. Instead, in the presence of water, the PPG reagent **V** has been recovered to different extents depending on the structure of PPGs and reaction conditions.[5c,7]

These new PPGs have some advantageous features. For example, they are easily synthesized from commercially available inexpensive materials, they have high protection/deprotection efficiencies, and they possess 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.[8] These PPGs have found applications in controlled release of anticancer agents[9] and synthesis.[10] Herein we report our effort in further enriching the PPG tool box and applications of PPGs in releasing carbohydrates, selective deprotection, and deprotection with sunlight.

RESULTS AND DISCUSSION

In the search for more salicyl alcohol derived PPGs of different properties, we pursued structural modification of the salicyl

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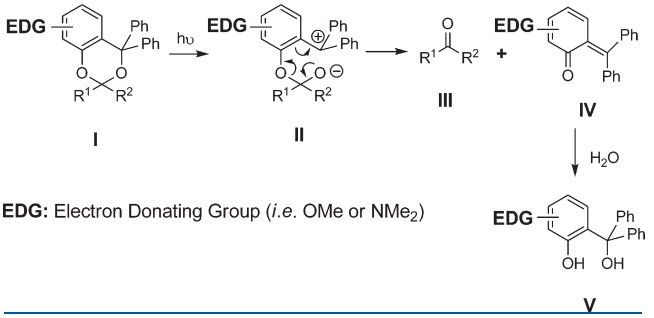
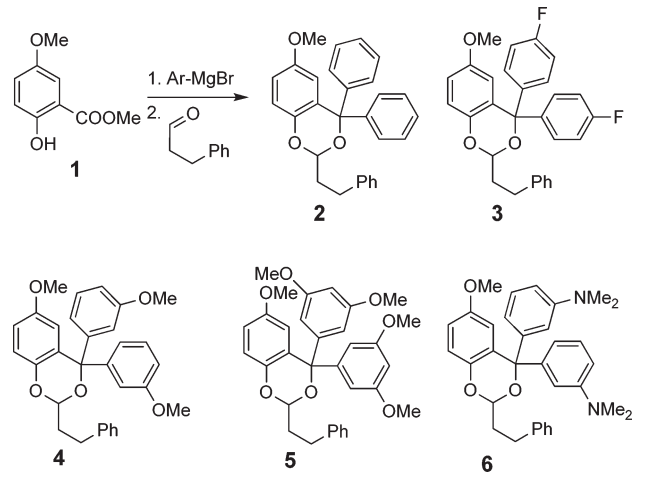
Scheme 1. Proposed Mechanism of Photochemical Deprotection



Scheme 2. Synthesis of Acetals 2−6



alcohol along two directions: (1) changing its α-substituents and (2) expanding the aromatic chromophore.

Changing α-Substituents. Because of ready access to the methyl salicylate **1** and known properties of the PPG in **2**,[5a] we designed various PPGs in the acetals **3**−**6** to study the α-substituent effect (Scheme 2). The acetals **2**−**6** were synthesized in two steps. First, the salicyl alcohols were prepared from reaction of the corresponding Grignard reagents with the ester **1**. Then the PPGs were installed onto 3-phenylpropanal. The known acetal **2** was used as a reference compound.

The UV spectrum of **2** resembles that of **3** (Figure 1), and both have an absorption peak centering at 297 nm with similar magnitude (i.e., $\varepsilon = 4.4 \times 10^3\ M^{-1}\ cm^{-1}$ for **2** and $\varepsilon = 3.6 \times 10^3\ M^{-1}\ cm^{-1}$ for **3**, respectively, Figure 1). We assume this absorption peak originates from the 5-methoxysalicyl chromophore. For the acetal **4**, in addition to the 297 nm absorption ($\varepsilon = 8.4 \times 10^3\ M^{-1}\ cm^{-1}$), there are two overlapping peaks at 277 nm ($\varepsilon = 10.4 \times 10^3\ M^{-1}\ cm^{-1}$) and 283 nm ($\varepsilon = 11.4 \times 10^3\ M^{-1}\ cm^{-1}$) that probably originate from the two α groups (i.e., 3-methoxyphenyl group). The high absorption of **4** at 297 nm relative to that of **2** and **3** can be attributed to its overlap with the long wavelength tail of the two 3-methoxyphenyl groups. For the acetal **5**, in addition to the shoulder peak at 297 nm, there is an absorption peak at 286 nm ($\varepsilon = 7.1 \times 10^3\ M^{-1}\ cm^{-1}$) that is probably from the two 3,5-dimethoxyphenyl groups at the α position. The acetal **6** has a slightly longer absorption maximum at around 302 nm ($\varepsilon = 8.5 \times 10^3\ M^{-1}\ cm^{-1}$) with the long

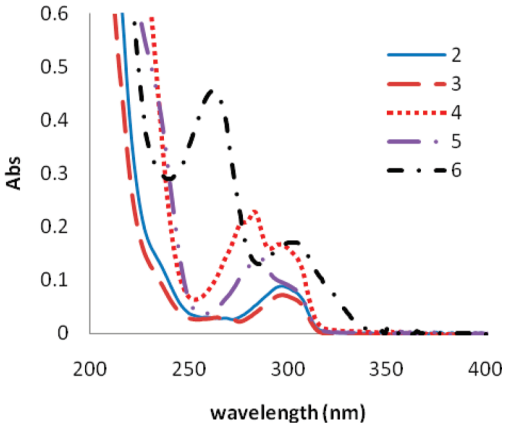


Figure 1. UV spectra of acetals **2**−**6**.

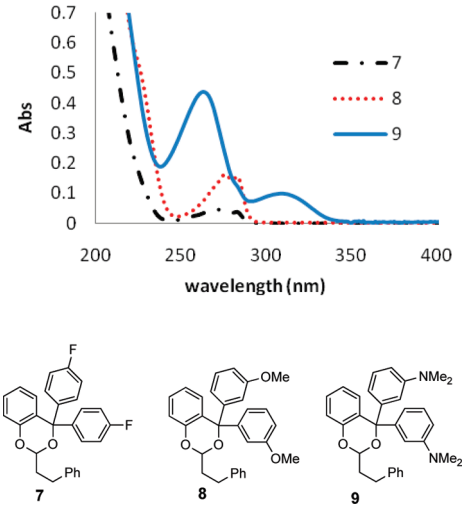


Figure 2. UV spectra of acetals **7**−**9**.

wavelength end extending to 350 nm. We attribute the red-shift to the two α groups (i.e., 3-(dimethylamino)phenyl group).

The acetals **7**−**9** (Figure 2) were also synthesized by using the same method depicted in Scheme 2. Comparison of the UV profiles between **3** and **7** ($\varepsilon_{283\,nm} = 1.9 \times 10^3\ M^{-1}\ cm^{-1}$, $\Phi = 0.1$)[11,12] revealed that the absorption peak at 297 nm should be of the 5-methoxysalicyl chromophore, which was also confirmed by the comparison between **4** and **8**. The UV spectrum of **8** also lacks the peak at 297 nm, but similar to **4**, it has the two overlapping peaks at 276 nm ($\varepsilon = 8.2 \times 10^3\ M^{-1}\ cm^{-1}$) and 283 nm ($\varepsilon = 7.8 \times 10^3\ M^{-1}\ cm^{-1}$), which were assigned to the two α 3-methoxyphenyl groups. The UV spectrum of **9** shows that the two 3-(dimethylamino)phenyl groups actually absorb at 309 nm ($\varepsilon = 4.9 \times 10^3\ M^{-1}\ cm^{-1}$); that should also be the case in **6** where absorption of the α groups and the salicyl skeleton are overlapping.

Photoreactions of **2**−**6** were carried out with a 450 W medium mercury lamp in a Hanovia photoreactor. The acetals **2**−**6** (5 mM in CD_3CN/D_2O 9:1) were irradiated with Pyrex-filtered light for 8 min. Although the acetals **2**−**5** have different UV profiles, they all showed similar photochemical efficiency in releasing the aldehyde, with the chemical yields ranging from 54% to 68% (Table 1, entries 1−4). The photochemical results combined with the common UV absorption at 297 nm suggest that UV absorption of the

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Table 1. Properties of Photocleavable Acetals

entry	acetal	ε (λ) of acetal (M^{-1} cm^{-1})/10^3	deprotection yield (%)[a,b,c]
1	**2**	4.4 (297 nm)	54[d]
2	**3**	3.6 (297 nm)	68[d]
3	**4**	8.4 (297 nm)	57[d]
		11.5 (283 nm)	
		10.4 (277 nm)	
4	**5**	7.1 (286 nm)	54[d]
5	**6**	8.5 (302 nm)	83[d]
			87[e]
6	**7**	1.9 (283 nm)	26[f]
7	**8**	7.8 (283 nm)	32[f]
		8.2 (276 nm)	
8	**9**	4.9 (309 nm)	87[d]
			94[e]
9	**10**	3.4 (327 nm)	92[d]
			92[e]
10	**11**	7.7 (314 nm)	84[d]
			80[e]

[a] Irradiated with a 450 W medium mercury lamp in a Hanovia photoreactor without excluding air. [b] The acetal (5 mM in CD_3CN/D_2O 9:1) was irradiated in a NMR tube unless indicated otherwise. [c] Yields determined by ^1H NMR analysis. [d] 8 min of irradiation with a Pyrex filter sleeve. [e] 5 min of irradiation without a filter. [f] The acetal (5 mM in CD_3CN/D_2O 9:1) was irradiated for 5 min in a quartz UV cell behind another UV cell containing a filter solution (centring at 283 nm in the useful UV region) prepared from $BiCl_3$ (0.264 mM) in conc HCl/H_2O (2:3).

5-methoxysalicyl chromophore at 297 nm should account for benzylic bond cleavage in the series of **2**−**5**.

However, the acetal **6** was apparently more efficient in releasing the aldehyde than **3**−**5**, with a yield of 83% (Table 1, entry 5). It seemed that the α substituents (i.e., two 3-(dimethylamino)phenyl groups) not only led to a bathochromic shift of the PPGs UV absorption but also notably facilitated the benzylic C−O bond breakage. To examine to what extent the α groups influence the photolysis, we compared the photochemical reactions of **6** and **9**. Under the same irradiation conditions with light from a Pyrex-filtered mercury lamp, the acetal **9** ($\varepsilon_{309\,nm}$ = 4.9×10^3 M^{-1} cm^{-1}, Φ = 0.23)[11,12] released the aldehyde in 87% yield. Given the fact that the unsubstituted salicyl chromophore does not absorb above 280 nm, the high yield of the benzylic C−O bond cleavage should be attributed to absorption by the two 3-(dimethylamino)phenyl groups. This chemical yield was also comparable to the yield of 92% obtained from the photoreaction of **10** (Figure 3, $\varepsilon_{327\,nm} = 3.4 \times 10^3$ M^{-1} cm^{-1}, Φ = 0.13)[5c] when **9** and **10** were irradiated side by side for 8 min (Table 1, entries 8 and 9). When both **9** and **10** were irradiated for 5 min with the medium-pressure lamp without a filter, they released the aldehyde in 94% and 92% yields, respectively. However, irradiation of **11** (Figure 3), with the PPG combining the effective absorptions of both **9** and **10**, resulted in 84% yield after 8 min irradiation with Pyrex-filtered light or 80% yield after 5 min irradiation without a filter (Table 1, entry 10). In both cases, the yields were inferior to that of either **9** or **10**.

Expanding Salicyl Chromophore. To examine the effects of an expanded salicyl chromophore, we studied PPGs with naphthalene backbones. Molecular orbital calculations[13] on the model compounds **12** and **13** (Figure 4) demonstrated that an

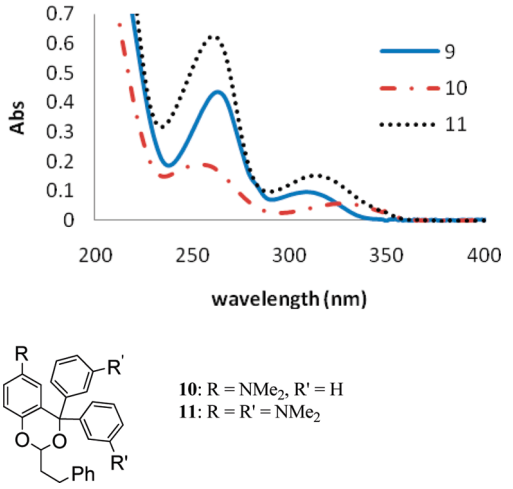

Figure 3. UV spectra of acetals **9**−**11**.

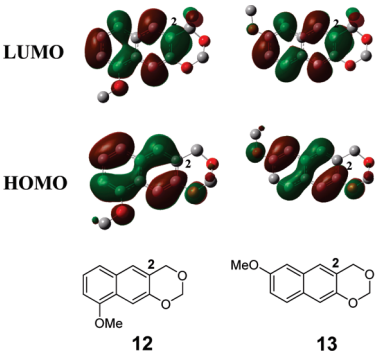

Figure 4. MO computations of **12** and **13**.

electron-donating substituent at C5 and/or C7 would increase electron density at C2 in the first excited state and was anticipated to facilitate heterolysis of the C−O bond.[5,6] Mindful of this favorable electronic effect, we synthesized the acetals **14**−**18** (Figure 5). Among them, the acetals **15** and **16** resembled the computation model compounds **12** and **13**, bearing a 5-OMe and 7-OMe, respectively.

As expected, spectral red-shifts of these acetals were observed with the expanded aromatic skeletons compared with methoxyl-substituted salicyl alcohol based PPGs (see Supporting Information). However, photochemical efficiencies were not improved. In fact, upon irradiation in CD_3CN/D_2O (9:1) (2.5 mM solution) with Pyrex-filtered light for 15 min, none of the acetals **14**−**18** had a higher conversion and released more 3-phenylpropanal than the reference acetal **2** did. The methoxyl group in **15** and **16** only slightly improved reaction yields. For example, NMR analysis showed that the aldehyde was released from **15** and **16** in 19% and 8% yields, respectively, whereas the yield from **14** was about 6%. Among the acetals **14**−**18**, the highest yield of releasing propanal was 44% from **18**, which was still lower than 93% from **2** under the same reaction conditions.

Selectively Removing Carbonyl Protecting Groups. Structural variation led to useful new PPGs. For instance, the acetal **9** released the aldehyde in similar yield as **10**, but the photoreaction was cleaner and more PPG reagent was recovered after deprotection. In addition, the particular PPG reagent was readily prepared in high yield from commercially available methyl salicylate in just one step.

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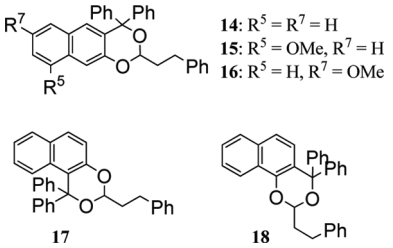
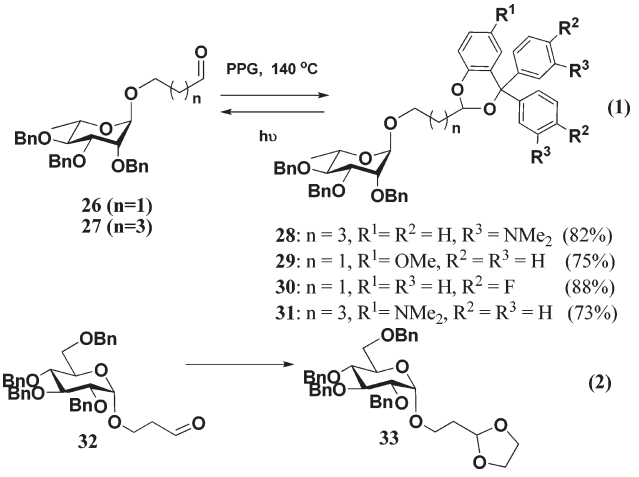


Figure 5. Acetals **14**−**18**.

The salicyl alcohol derived carbonyl PPGs can be divided into three subgroups A−C on the basis of their UV absorptions (Figure 6). Group A PPGs (e.g., PPGs in **19**[5c] and **20**) can be removed with long wavelength UV irradiation, e.g., by 350 nm lamps in a Rayonet reactor, by filtered light (λ > 320 nm) in a Honovia reactor setting,[14] or by sunlight. Group B PPGs (e.g., PPGs in **21** and **22**)[5a,c] have to be removed with UV of wavelength shorter than 320 nm. Removal of Group C PPGs (e.g., PPGs in **23**,[5c] **24**, and **25**) requires light wavelength shorter than 280 nm, i.e., they are inert to Pyrex-filtered light. The PPGs in **24** and **25** had good photochemical efficiency (*vide infra*). The low yields of the acetal **7** and **8** (possessing the same PPGs) in Table 1 were due to low conversion of **7** and **8** caused by low intensity of the filtered light. In general, these PPGs are more stable toward acid treatment than the traditional dioxane or dioxolane protection of carbonyls.

To demonstrate selective deprotection with carbonyl protecting groups, we synthesized acetals from the aldehydes **26** and **27** (eq 1). Notably, the acetals **28**−**31** were prepared by generalizing the neutral protection protocol we recently developed.[7] Thus, heating a neat mixture of an aldehyde and the corresponding PPG reagent at 140 °C led to **28**−**31** in 82%, 75%, 88%, and 73% yields, respectively. This protection procedure does not require any other chemical reagents, even solvent. We also converted the aldehyde **32** to the dioxolane **33** (eq 2). Under the typical conditions of releasing carbonyls from dioxolanes, e.g., treatment of the acetals **28**−**31** and **33** with HCl (2 N) in THF at 40 °C for over 24 h, the acetal **33** released the aldehyde **32** cleanly with only a trace amount of **33** left. In contrast, the acetals **28**−**31** showed no sign of reaction based on NMR and TLC analysis.



When the acetals **28**−**31** (in CD_3CN/D_2O 9:1) were irradiated individually in separate reaction vessels under the same conditions with UV (λ > 320 nm),[14] only the PPG in **28** and **31** was removed, whereas the acetal **29** and **30** remain intact based on NMR analysis. In a preparative run, the aldehyde **27** was released from **28** in 94% yield (Table 2, entry 1). The PPG reagent (i.e., α,α-di(dimethylamino)phenyl salicyl alcohol) was isolated in 82% yield, in agreement with the proposed mechanism in Scheme 1. Under the same conditions, the aldehyde **27** was obtained in 91% yield from **31**. However, the PPG portion in this case had a different fate and benzophenone instead of the corresponding PPG reagent (i.e., α,α-diphenyl-5-(dimethylamino)salicyl alcohol) was observed in more than 80% yield based on NMR analysis. It was presumably formed through a secondary photoreaction of the PPG reagent. Irradiation of **29** and **30** in two separate reaction vessels with Pyrex-filtered light (λ > 280 nm) removed the PPG from **29** only while the acetal **30** remained unchanged based on NMR analysis. The photoreaction of **29** was confirmed in a preparative run and the aldehyde **26** was isolated in 91% yield (Table 2, entry 2). Finally, a solution of **30** was irradiated with Vycor-filtered UV light (λ > 210 nm), and the reaction produced the aldehyde **26** in 75% yield (Table 2, entry 3). The lower yield of the isolated aldehyde was due to side reactions of the released aldehyde under low-wavelength UV irradiation, and the yield is aldehyde-structure-dependent. For example, with Vycor-filtered irradiation, the aldehyde **27** cleanly generated allyl rhamnoside via a Norrish type II pathway. On the other hand, 3-phenylpropanal was relatively more stable than the aldehyde **26**.[5c]

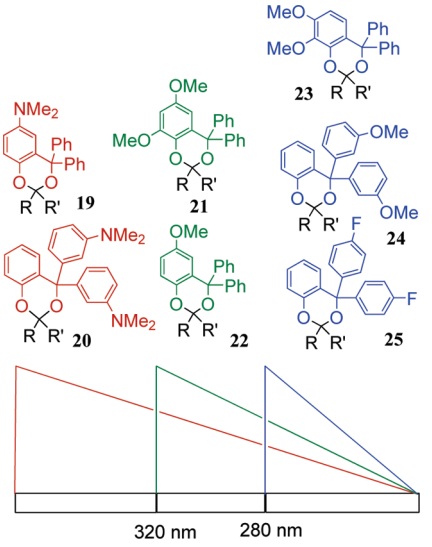


Figure 6. PPGs respond to different UV wavelength.

Table 2. Photoreactions of Acetals 28−31

entry	acetal[a]	irradiation λ (nm)[b]	reaction time (min)	deprotection yield (%)[f]
1	**28**	>320[c]	50	94
2	**31**	>320[c]	50	91
3	**29**	>280[d]	40	91
4	**30**	>210[e]	10	75

[a] [acetal] = 0.8 mM in 250 mL of $MeCN/H_2O$ (9:1). [b] Irradiated with a 450 W medium mercury lamp in a Hanovia photoreactor without excluding air. [c] Filtered with a Pyrex sleeve and 10% $NaNO_3$ solution. [d] Filtered with a Pyrex sleeve. [e] Filtered with a Vycor sleeve. [f] Isolated yield.

Deprotection with Sunlight. As with other PPGs shown in Figure 6, Group A protecting groups are stable under indoor lighting. As such, they do not require special precautions to

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prepare and handle the PPG-protected compounds. However, they can be conveniently removed with sunlight in high efficiency. For instance, a solution of **28** (5 mM in MeCN/H_2O 9:1) in a Pyrex test tube was kept in a water bath and placed outdoors under sunlight in clear weather. The reaction temperature varied between 20 to 30 °C during the reaction course. After 2 h, the reaction was complete, and the aldehyde was isolated in 81% yield. Prolonged irradiation did not significantly influence the yield of released aldehyde. For example, irradiation of **28** for 3 h led to 79% yield of **27**. Similarly, irradiation of **31** for 3 h led to 82% yield of **27**. However, the PPG reagents decomposed during extended irradiation in both cases. The reaction time could be affected by the shape of reaction vessels owing to their different efficiency in absorbing sunlight.

CONCLUSIONS

We studied the structure−property relationship of salicyl alcohol based photolabile carbonyl protecting groups. The 3-(dimethylamino)phenyl groups at the α position appear to be important to deprotection efficiency, while enlarging the aromatic backbone in salicyl alcohols from benzene to naphthalene does not improve photochemical efficiency. Furthermore, a group of new PPGs for carbonyl protection has been developed. These PPGs are divided into three subgroups based on their UV absorption profiles. PPGs from different subgroups can be removed sequentially with different UV irradiation, which is anticipated to be potentially useful in many applications. For PPGs absorbing long wavelength UV, photochemical deprotection can be carried out with sunlight in high yields. PPGs in the new toolbox share some important features, e.g., they all are structurally simple, chemically stable, and easy to prepare. They all can be installed and removed with high chemical efficiencies. Moreover, due to their common structural feature, the reagent-free green chemistry PPG-installation protocol can be readily generalized to new PPGs. For the first time, a group of PPGs that can be installed and removed under reagent-free conditions have been developed. In addition, our new PPGs constitute orthogonal protecting groups with traditional acid-labile 1,3-dioxane/1,3-dioxolane for carbonyl compounds. We have also demonstrated release of monosaccharides having an anomeric aldehyde moiety, which can be potentially useful in site-specific release and immobilization of carbohydrates to solid surfaces for preparation of high-density carbohydrate microchips.

EXPERIMENTAL SECTION

2-[Bis(4-fluoro-phenyl)-hydroxy-methyl]-phenol (PPG in 7). A solution of salicylic acid methyl ester (1.20 g, 7.89 mmol, 1 equiv) in THF was added to the solution of 4-fluorophenyl magnesium bromide (3.5 equiv), prepared from 4-bromofluorobenzene (4.83 g, 3.03 mL) and magnesium (0.80 g, 4.2 equiv) in 15 mL THF, and the resultant solution was stirred overnight. Workup as usual followed by flash chromatography (petroleum ether/ethyl acetate = 8/1, R_f 0.3) to afford the title compound (2.21 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1 H), 7.15−7.23 (m, 5 H), 7.01−7.06 (m, 4 H), 6.90 (dd, J = 1.1, 8.1 Hz, 1 H), 6.76 (dt, J = 1.2, 7.6 Hz, 1 H), 6.49 (dd, J = 1.6, 7.8 Hz, 1 H), 3.72 (s, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (d, J = 247.7 Hz), 155.4, 140.6 (d, J = 3.2 Hz), 130.0, 129.8, 129.7, 129.5 (d, J = 8.2 Hz), 119.4, 117.6, 115.1 (d, J = 21.5 Hz), 83.4; IR(neat) 3228, 1602, 1584, 1507, 1227, 1159, 838, 740; HRMS (ESI) m/e calcd for $C_{19}H_{14}F_2O_2Na$, 335.0860, found 335.0868.

2-[Bis(3-dimethylamino-phenyl)-hydroxy-methyl]-phenol (PPG of 9). To a solution of salicylic acid methyl ester (192 mg, 1.26 mmol, 1 equiv) in THF was added dropwise the solution of PhLi (2 M in n-Bu_2O, 0.63 mL, 1 equiv) at −78 °C under argon, and the mixture was stirred for a further 5 min. Then the resultant solution was transferred to the stirred solution of 3-dimethylaminophenyl magnesium bromide (2 equiv), prepared from (3-bromophenyl)-dimethylamine (0.50 g, 2.5 mmol, 0.36 mL) and magnesium (73 mg, 2.4 equiv) in 8 mL THF, and the resultant solution was stirred overnight. Workup as usual followed by flash chromatography (petroleum ether/ethyl acetate = 3/1, R_f 0.4) to afford the title compound (323 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1 H), 7.15−7.21 (m, 3 H), 6.89 (dd, J = 1.2, 8.1 Hz, 1 H), 6.61−6.74 (m, 6 H), 6.50 (dd, J = 0.7, 7.7 Hz, 2 H), 3.50 (s, 1 H), 2.86 (s, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.1, 150.3, 145.9, 130.5, 130.1, 129.1, 128.5, 118.7, 117.2, 116.7, 112.5, 112.0, 84.8, 40.6; IR(neat) 3228, 3073, 2885, 2803, 1600, 1495, 1351, 1236, 758; HRMS (ESI) m/e calcd for $C_{23}H_{27}N_2O_2$, 363.2073, found 363.2073.

General Procedure for Preparing Aetals 3−9 and 11 and Their Corresponding PPG. 4-Methoxysalicylic acid methyl ester (for PPGs in **2**−**6**), salicylic acid methyl ester (for PPGs in **7**−**9** and **11**), or 4-dimethylamino salicylic acid methyl ester (for PPG in **10**) and ArMgBr or ArLi were stirred at room temperature overnight. Workup as usual followed by recrystallization or flash chromatography afforded the corresponding PPGs. The PPG reagent and the aldehyde (PPG/aldehyde = 1: 2) were stirred at 140 °C under argon for 2 h. Upon completion, the reaction mixtures were purified by flash column chromatography to afford the desired acetals.

4,4-Bis(4-fluoro-phenyl)-6-methoxy-2-phenethyl-4*H*-benzo-[1,3]dioxine (3). Yield 73%; R_f 0.5 (petroleum ether/ethyl acetate = 7/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.36 (m, 2 H), 7.25−7.29 (m, 2 H), 7.18−7.22 (m, 2 H), 7.10−7.15 (m, 3 H), 7.01−7.08 (m, 3 H), 6.85 (dd, J = 0.4, 9.0 Hz, 1 H), 6.80 (dd, J = 2.9, 9.0 Hz, 1 H), 6.33 (dd, J = 0.3, 2.9 Hz, 1 H), 4.87 (dd, J = 4.2, 6.1 Hz, 1 H), 3.59 (s, 3 H), 2.77 (ddd, J = 6.0, 9.2, 14.6 Hz, 1 H), 2.62 (ddd, J = 7.2, 9.0, 14.0 Hz, 1 H), 2.04−2.18 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (d, J = 248.1 Hz), 162.0 (d, 1H, J = 246.9 Hz), 153.0, 146.3, 141.7 (d, J = 3.1 Hz), 141.2, 139.9 (d, J = 3.2 Hz), 131.1 (d, J = 8.1 Hz), 129.8 (d, J = 8.1 Hz), 128.28, 128.27, 125.8, 125.5, 117.8, 115.1, 114.9 (d, J = 3.4 Hz), 114.6 (d, J = 2.9 Hz), 114.2, 94.3, 83.3, 55.5, 35.9, 29.6; IR(neat) 3062, 3027, 2932, 2835, 1602, 1506, 1497, 1465, 1455, 1407, 1272, 1227, 1158, 1041, 831; HRMS (ESI) m/e calcd for $C_{29}H_{24}F_2O_3Na$, 481.1591, found 481.1593.

6-Methoxy-4,4-bis(3-methoxy-phenyl)-2-phenethyl-4*H*-benzo[1,3]dioxine (4). Yield 82%; R_f 0.3 (petroleum ether/ethyl acetate = 7/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, J = 8.0 Hz, 1 H), 7.18−7.24 (m, 3 H), 7.11−7.15 (m, 1 H), 7.07−7.09 (m, 2 H), 6.91−6.96 (m, 2 H), 6.78−6.86 (m, 6 H), 6.41 (d, J = 2.8 Hz, 1 H), 4.92 (dd, J = 4.1, 6.0 Hz, 1 H), 3.72 (s, 3 H), 3.70 (s, 3 H), 3.60 (s, 3 H), 2.80 (ddd, J = 5.8, 9.8, 14.1 Hz, 1 H), 2.64 (ddd, J = 7.2, 9.3, 14.0 Hz, 1 H), 2.04−2.21 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 159.1, 152.8, 147.3, 146.3, 145.7, 141.4, 128.9, 128.7, 128.27, 128.23, 125.7, 125.6, 121.8, 120.6, 117.5, 115.0, 114.8, 114.2, 114.0, 113.2, 112.4, 94.5, 84.0, 55.5, 55.1, 55.1, 36.1, 29.6; IR(neat) 3000, 2936, 2833, 1598, 1493, 1256, 1225, 1196, 1126, 814, 700; HRMS (ESI) m/e calcd for $C_{31}H_{30}O_5Na$, 505.1991, found 505.1999.

4,4-Bis(3,5-dimethoxy-phenyl)-6-methoxy-2-phenethyl-4*H*-benzo[1,3]dioxine (5). Yield 69%; R_f 0.1 (petroleum ether/ethyl acetate = 15/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.25 (m, 2 H), 7.15−7.28 (m, 1 H), 7.11−7.14 (m, 2 H), 6.82 (d, J = 8.9 Hz, 1 H), 6.74 (dd, J = 3.0, 8.9 Hz, 1 H), 6.54 (d, J = 2.3 Hz, 2 H), 6.47 (d, J = 2.3 Hz, 2 H), 6.44 (d, J = 2.9 Hz, 1 H), 6.42 (t, J = 2.3 Hz, 1 H), 6.34 (t, J = 2.3 Hz, 1 H), 5.03 (dd, J = 4.2, 5.8 Hz, 1 H), 3.73 (s, 6 H), 3.72 (s, 6 H), 3.65 (s, 3 H), 2.85 (ddd, J = 5.7, 10.3, 14.2 Hz, 1 H), 2.73 (ddd, J = 6.5, 10.1, 13.8 Hz, 1 H), 2.08−2.24 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3,

160.1, 152.8, 147.8, 146.3, 146.2, 141.4, 128.3, 125.8, 125.4, 117.4, 114.6, 114.1, 107.7, 106.7, 99.5, 98.9, 94.6, 84.2, 55.5, 55.3, 55.2, 36.2, 29.7; IR(neat) 3000, 2937, 2835, 1595, 1495, 1456, 1425, 1205, 1155, 1041; HRMS (ESI) *m/e* calcd for $C_{33}H_{35}O_7$, 543.2383, found 543.2374.

6-Methoxy-4,4-bis(3-dimethylamino)-2-phenethyl-4*H*-benzo[1,3]dioxine (6). Yield 71%; R_f 0.2 (petroleum ether/ethyl acetate = 12/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08−7.24 (m, 7 H), 6.81−6.84 (m, 3 H), 6.73 (dd, J = 2.9, 9.0 Hz, 3 H), 6.61 (dd, J = 2.7, 8.0 Hz, 1 H), 6.56 (d, J = 8.0 Hz, 1 H), 6.48 (d, J = 2.9 Hz, 1 H), 5.08 (dd, 1H, J = 4.0, 5.9 Hz), 3.63 (s, 3 H), 2.88 (s, 6 H), 2.86 (s, 6 H), 2.69−2.93 (m, 2 H), 2.06−2.24 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.6, 150.3, 150.1, 146.8, 146.4, 145.0, 141.7, 128.34, 128.29, 128.24, 128.19, 126.5, 125.7, 118.3, 117.2, 114.8, 113.9, 113.5, 112.6, 112.1, 111.7, 94.5, 84.8, 55.5, 40.63, 40.58, 36.3, 29. 7; IR(neat) 3026, 2928, 2803, 1600, 1494, 1434, 1352, 1272, 1229, 1041, 759, 700; HRMS (ESI) *m/e* calcd for $C_{33}H_{37}N_2O_3$, 509.2804, found 509.2805.

4,4-Bis(4-fluoro-phenyl)-2-phenethyl-4*H*-benzo[1,3]dioxine (7). Yield 71%; R_f 0.6 (petroleum ether/ethyl acetate = 15/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.32 (m, 2 H), 7.01−7.25 (m, 10 H), 6.90−6.96 (m, 3 H), 6.82 (dt, J = 1.1, 7.8 Hz, 1 H), 6.75 (dd, J = 1.5, 7.8 Hz, 1 H), 4.99 (dd, J = 4.4, 5.6 Hz, 1 H), 2.82 (ddd, J = 6.0, 9.6, 15.3 Hz, 1 H), 2.66−2.74 (m, 1 H), 2.10−2.24 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (d, J = 248.0 Hz), 162.0 (d, J = 246.9 Hz), 152.3, 141.8 (d, J = 3.0 Hz) 141.1, 139.9 (d, J = 3.2 Hz), 131.1 (d, J = 8.2 Hz), 129.8 (d, J = 8.1 Hz), 129.5, 128.6, 128.31, 128.28, 125.9, 125.0, 120.4, 117.2, 115.0 (d, J = 21.4 Hz), 114.7 (d, J = 21.4 Hz), 94.4, 83.3, 35.9, 29.5; IR(neat) 3063, 3028, 2929, 1603, 1584, 1506, 1485, 1457, 1407, 1228, 1158, 1038, 987, 836, 755, 700; HRMS (ESI) *m/e* calcd for $C_{28}H_{22}F_2O_2Na$, 451.1486, found 451.1499.

4,4-Bis(3-methoxy-phenyl)-2-phenethyl-4*H*-benzo[1,3]dioxine (8). Yield 71%; R_f 0.5 (petroleum ether/ethyl acetate = 15/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09−7.29 (m, 8 H), 6.77−6.95 (m, 9 H), 5.07 (dd, J = 4.1, 5.8 Hz, 1 H), 3.76 (s, 3 H), 3.74 (s, 3 H), 2.85 (ddd, J = 5.7, 9.9, 13.7 Hz, 1 H), 2.74 (ddd, J = 6.6, 10.1, 14.7 Hz, 1 H), 2.18 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 159.1, 152.2, 147.5, 145.8, 141.4, 129.6, 129.0, 128.7, 128.31, 128.27, 125.8, 125.1, 121.9, 120.7, 120.2, 117.0, 115.0, 114.3, 113.3, 112.4, 94.6, 84.0, 55.2, 55.1, 36.2, 29.6; IR(neat) 3061, 3028, 3002, 2957, 2936, 2834, 1598, 1583, 1485, 1455, 1433, 1403, 1290, 1257, 1124, 1040, 995, 780, 757, 737, 700; HRMS (ESI) *m/e* calcd for $C_{30}H_{28}O_4Na$, 475.1885, found 475.1890.

4,4-Bis(3-dimethylamino)-2-phenethyl-4*H*-benzo[1,3]dioxine (9). Yield 69%; R_f 0.3 (petroleum ether/ethyl acetate = 9/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19−7.24 (m, 3 H), 7.08−7.17 (m, 5 H), 6.86−6.93 (m, 2 H), 6.78−6.83 (m, 3 H), 6.69−6.73(m, 2 H), 6.56−6.63 (m, 2 H), 5.15 (dd, J = 4.1, 5.7 Hz, 1 H), 2.86 (s, 6 H), 2.84 (s, 6 H), 2.71−2.93 (m, 2 H), 2.07−2.27 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.3, 150.3, 150.1, 146.9, 145.1, 141.7, 129.8, 128.4, 128.3, 128.2, 128.0, 126.1, 125.7, 119.9, 118.3, 117.4, 116.7, 113.6, 112.8, 112.1, 111.7, 94.6, 84.8, 40.6, 40.6, 36.3, 29.6; IR(neat) 3062, 3027, 2927, 2803, 1681, 1600, 1581, 1496, 1485, 1455, 1434, 1352, 1236, 1126, 1038, 988, 930, 858, 756, 735, 700; HRMS (ESI) *m/e* calcd for $C_{32}H_{35}N_2O_2$, 479.2699, found 479.2697.

[4,4-Bis(3-dimethylamino-phenyl)-2-phenethyl-4*H*-benzo-[1,3]dioxin-6-yl]-dimethyl-amine (11). Yield 69%; R_f 0.2 (petroleum ether/ethyl acetate = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08−7.23 (m, 8 H), 6.85−6.88 (m, 2 H), 6.78−6.81 (m, 2 H), 6.72 (dd, J = 2.5, 8.2 Hz, 1 H), 6.66 (dd, J = 2.9, 8.9 Hz, 1 H), 6.60 (dd, J = 2.6, 8.2 Hz, 1 H), 6.57 (d, J = 7.7 Hz, 1 H), 6.36 (d, J = 2.9 Hz, 1 H), 5.07 (dd, J = 4.0, 5.9 Hz, 1 H), 2.69−2.93 (m, 20 H), 2.06−2.23 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.22, 150.18, 147.1, 145.4, 144.8, 144.6, 141.8, 128.4, 128.3, 128.2, 128.1, 126.1, 125.7, 118.4, 117.4, 116.8, 115.3, 114.4, 113.7, 112.8, 112.0, 111.7, 94.4, 84.9, 41.7, 40.7, 36.4, 29.7; IR(neat) 3026, 2927, 2883, 2800, 1600, 1498, 1434, 1239, 1134, 1060, 987, 934, 857, 756, 700; HRMS (ESI) *m/e* calcd for $C_{34}H_{40}N_3O_2$, 522.3121, found 522.3124.

Representative Procedure to Prepare the PPGs of 14, 15, 16, 17, and 18. *Method A: Synthesis of 3-(Hydroxydiphenylmethyl)naphthalen-2-ol (PPG of **14**).* To a solution of 3-hydroxy-2-naphthoic acid (0.94 g, 5 mmol) in methanol (6 mL) was added sulfuric acid (4 drops). The reaction mixture was refluxed at 80 °C for 8.5 h. The solvent was then removed, and the reaction mixture was neutralized with saturated sodium bicarbonate until pH = 7 and washed with brine. The product was extracted with dichloromethane, and the organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated to provide methyl 3-hydroxy-2-naphthoate (0.71 g, 70%) as a light yellow solid.

To a solution of methyl 3-hydroxy-2-naphthoate (0.71 g, 3.5 mmol) in freshly distilled tetrahydrofuran (35 mL) was slowly added phenyl lithium (14 mL, 7 mmol, 2.0 M solution in dibutylether) at −78 °C under argon protection. The reaction temperature was raised to room temperature over 6 h. The reaction was then quenched with saturated ammonium chloride until pH = 7. The aqueous layer was extracted with dichloromethane, and the organic layers were combined and concentrated. The residue was purified with flash column chromatography (petroleum ether/ethyl acetate = 4/1) to provide 3-(hydroxydiphenylmethyl) naphthalen-2-ol (0.85 g, 74%) as a pale yellow solid. R_f 0.4 (petroleum ether/ethyl acetate = 4/1).

*Method B: Synthesis of Methyl 2-Hydroxy-1-naphthoate (Ester Precursor of **17**).* To a solution of iodomethane (0.568 g, 14 mmol) in acetone (1 mL) were added 2-hydroxy-1-naphthoic acid (0.188 g, 1 mmol) and potassium carbonate (0.276 g, 2 mmol). The reaction mixture was stirred at 60 °C overnight. The crude product was washed with dichloromethane through Celite and concentrated. The residue was purified with flash column chromatography (petroleum ether/ethyl acetate = 9/1) to provide methyl 2-hydroxy-1-naphthoate (0.137 g, 68%). R_f 0.5 (petroleum ether/ethyl acetate = 9/1).

Representative Procedure of Installing the PPG: 2-Phenethyl-4,4-diphenyl-4*H*-naphtho[2,3-*d*][1,3]dioxine (14). To 3-(hydroxydiphenylmethyl) naphthalen-2-ol (32.6 mg, 0.10 mmol) and *p*-toluenesulfonic acid (1.9 mg, 0.01 mmol) in benzene (0.1 mL) was added 3-phenylpropionaldehyde (7 μL, 0.05 mmol). Upon completion, the reaction mixture was directly purified with flash column chromatography (petroleum ether/ethyl acetate = 7/1) to provide **14** (27 mg, 61%). R_f 0.6 (petroleum ether/ethyl acetate = 7/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J = 8.3 Hz, 1 H), 7.58 (d, J = 8.2 Hz, 1 H), 7.41−7.10 (m, 19 H), 5.16 (dd, J = 4.3, 5.6 Hz, 1 H), 2.82 (m, 2 H), 2.23 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.9, 146.3, 143.8, 141.5, 133.7, 129.6, 129.4, 128.3, 128.3, 128.2, 127.9, 127.6, 126.8, 126.5, 126.3, 125.8, 123.8, 111.8, 94.7, 84.7, 36.3, 29.6; IR (neat) 3058, 3027, 2958, 2928, 1637, 1603, 1501, 1462, 1256, 1170, 800, 748; HRMS (ESI) *m/z* calcd for $C_{32}H_{26}O_2Na$, 465.1830, found 465.1833.

9-Methoxy-2-phenethyl-4,4-diphenyl-4*H*-naphtho[2,3-*d*][1,3]dioxine (15). Yield 93%; R_f 0.5 (petroleum ether/ethyl acetate = 9/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (s, 1 H), 7.35−7.11 (d, 18 H), 6.72 (m, J = 4.3 Hz, 1 H), 5.15 (t, J = 4.9 Hz, 1 H), 3.97 (s, 1 H), 2.81 (ms, 2 H) 2.22 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.5, 150.6, 146.3, 143.9, 141.5, 129.4, 129.1, 128.3, 128.2, 127.9, 127.6, 127.1, 126.1, 125.8, 123.7, 120.2, 107.0, 103.9, 94.7, 84.7, 55.6, 36.4, 29.6; IR (neat) 3059, 3026, 2929, 1600, 1446, 1398, 1123, 807, 757, 700; HRMS (ESI) *m/z* calcd for $C_{33}H_{28}O_3Na$, 495.1936, found 495.1942.

7-Methoxy-2-phenethyl-4,4-diphenyl-4*H*-naphtho[2,3-*d*][1,3]dioxine (16). Yield 64%; R_f 0.6 (petroleum ether/ethyl acetate = 9/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, J = 9.1 Hz, 1 H), 7.39−7.05 (m, 20 H), 6.89 (d, J = 2.5 Hz, 1 H), 5.13 (dd, J = 4.3, 5.6 Hz, 1 H), 3.81 (s, 1 H), 2.81 (m, 2 H), 2.21 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2, 149.2, 146.4, 144.0, 141.5, 129.4, 129.1, 128.8, 128.4, 128.3, 128.1, 127.9, 127.5, 127.0, 125.8, 119.8, 112.0, 105.5, 94.6,

84.7, 55.2, 36.3, 29.6; IR (neat) 3060, 3026, 2932, 1612, 1507, 1251, 1214, 1033, 886, 700; HRMS (ESI) m/z calcd for $C_{33}H_{28}O_3Na$, 495.1936, found 495.1940.

3-Phenethyl-1,1-diphenyl-1*H*-naphtho[2,1-*d*][1,3]dioxine (17). Yield 90%; R_f 0.6 (petroleum ether/ethyl acetate = 7/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 8.9 Hz, 1 H), 7.68 (d, J = 8.1 Hz, 1 H), 7.54 (dd, J = 3.1, 6.4 Hz, 2 H), 7.40−7.3 (m, 5 H), 7.30 (d, J = 8.6 Hz, 1 H), 7.24−7.09 (m, 8 H), 7.04−6.99 (m, 3 H), 5.00 (dd, J = 4.2, 6.1 Hz, 1 H), 2.68 (m, 2 H), 2.14 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.9, 144.8, 141.8, 141.4, 131.8, 130.8, 130.3, 129.6, 128.4, 128.3, 128.2, 127.9, 127.7, 126.3, 125.8, 125.6, 123.0, 118.9, 94.3, 85.0, 35.9, 29.7; IR (neat) 3058, 3027, 2929, 1402, 1237, 817, 747, 701; HRMS (ESI) m/z calcd for $C_{32}H_{26}O_2Na$, 465.1830, found 465.1837.

2-Phenethyl-4,4-diphenyl-4*H*-naphtho[1,2-*d*][1,3]dioxine (18). Yield 92%; R_f 0.5 (petroleum ether/ethyl acetate = 7/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (m, 1 H), 7.73 (m, 1 H), 7.52−7.10 (m, 18 H), 6.93 (d, J = 8.6 Hz, 1 H), 5.21 (t, J = 5.0 Hz, 1 H), 2.87 (m, 2 H), 2.33 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.7, 145.8, 144.5, 141.5, 133.2, 129.6, 128.4, 128.1, 127.6, 127.5, 127.4, 126.6, 126.5, 125.8, 125.6, 124.8, 121.8, 119.5, 95.0, 84.3, 36.2, 29.8; IR (neat) 3060, 3026, 2928, 1604, 1575, 1463, 1266, 909, 734, 700; HRMS (ESI) m/z calcd for $C_{32}H_{26}O_2Na$, 465.1830, found 465.1842.

3-(3,4,5-Tris-benzyloxy-6-methyl-tetrahydro-pyran-2-yloxy)-propionaldehyde (26). The procedure for preparation of **26** was similar to the preparation of **27** from 2-allyloxy-3,4,5-tris-benzyloxy-6-methyl-tetrahydro-pyran. The yields of hydroboration-oxidation and Swern oxidation were 86% and 79%, respectively. R_f 0.6 (petroleum ether/ethyl acetate = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (t, J = 1.6 Hz, 1 H), 7.25−7.38 (m, 15 H), 4.93 (d, J = 10.8 Hz, 1 H), 4.68−4.77 (m, 3 H), 4.60−4.64 (m, 3 H), 3.95 (td, J = 5.9, 10.3 Hz, 1 H), 3.79 (dd, J = 3.1, 8.8 Hz, 1 H), 3.73 (dd, J = 2.0, 2.9 Hz, 1 H), 3.59−3.70 (m, 3 H), 2.60 (t, J = 6.0 Hz, 2 H), 1.34 (d, J = 5.8 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 138.4, 138.1, 128.3, 128.0, 127.8, 127.6, 127.58, 127.5, 127.46, 98.1, 80.2, 79.8, 75.3, 74.6, 72.8, 72.1, 68.2, 61.0, 43.3, 17.9; IR(neat) 3088, 3063, 3030, 2973, 2916, 1725, 1496, 1453, 1362, 1116, 1063, 1028, 737, 697; HRMS (ESI) m/e calcd for $C_{30}H_{34}O_6Na$, 513.2253, found 513.2257.

5-(3,4,5-Tris-benzyloxy-6-methyl-tetrahydro-pyran-2-yloxy)-pentanal (27). $BH_3 \cdot Me_2S$ (2 M, 0.3 mL) was added dropwise at 0 °C to a stirred solution of 3,4,5-tris-benzyloxy-2-methyl-6-pent-4-enyloxy-tetrahydro-pyran (0.608 g, 1.2 mmol). Following the addition of the hydride, the cooling bath was removed and the solution was stirred for 1.5 h at rt. Ethanol (0.4 mL) was then added followed by 0.18 mL of 3 *N* sodium hydroxide. After cooling to 0−5 °C in an ice−water bath, hydrogen peroxide (35%, 0.2 mL) was added dropwise, following the addition of the peroxide, the cooling bath was then removed and the reaction mixture was stirred overnight. After being heated at 80 °C for an hour, the cooled solution was extracted with ether (10 mL × 4). The combined extracts were washed with water and brine, dried (Na_2SO_4), concentrated. Flash column chromatography on silica gel, eluted with petroleum ether/ethyl acetate = 3/1, afforded 5-(3,4,5-tris-benzyloxy-6-methyl-tetrahydro-pyran-2-yloxy)-pentan-1-ol (0.557 g, 88%, R_f 0.3 (petroleum ether/ethyl acetate = 3/1)) as a colorless oil.

The above obtained alcohol (0.557 g, 1.07 mmol) was oxidized to aldehyde via Swern oxidation method. The general procedure and flash column chromatography on silica gel, eluted with petroleum ether/ethyl acetate = 4/1, afforded the title aldehyde **27** (0.39 g, 70%) as a colorless oil. R_f 0.6 (petroleum ether/ethyl acetate = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (t, J = 1.6 Hz, 1 H), 7.27−7.38 (m, 15 H), 4.95 (d, J = 10.8 Hz, 1 H), 4.70−4.79(m, 3 H), 4.63−4.65 (m, 3 H), 3.83 (dd, J = 3.1, 8.9 Hz, 1 H), 3.75 (dd, J = 1.9, 2.8 Hz, 1 H), 3.59−3.69 (m, 3 H), 3.32 (td, J = 6.2, 9.8 Hz, 1 H), 2.42 (dt, J = 1.4, 7.2 Hz, 2 H), 1.55−1.68 (m, 6 H), 1.33 (d, J = 5.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.2, 138.5, 138.33, 128.31, 128.28, 128.0, 127.8, 127.6, 127.5, 97.9, 80.5, 75.4, 75.0, 72.8, 72.1, 68.0, 66.8, 43.5, 28.8, 18.8, 18.0; IR(neat) 3088, 3063, 3031, 2919, 1725, 1603, 1497, 1454, 1363, 1115, 1064, 913, 737, 698; HRMS (ESI) m/e calcd for $C_{32}H_{38}O_6Na$, 541.2566, found 541.2567.

General Procedure for Preparation of Aetals 28−31. The PPG reagent and the aldehyde (PPG/aldehyde = 1.1:1) were stirred at 140 °C under argon for 2 h. Upon completion, the reaction mixtures were purified by flash column chromatography to afford the desired acetals.

4,4-Bis(3-dimethylamino-phenyl)-2-[4-(3,4,5-tris-benzyloxy-6-methyl-tetrahydro-pyran-2-yloxy)-butyl]-4*H*-benzo-[1,3]dioxine (28). Yield 82% (Mixture of two diastereomers), R_f 0.4 (petroleum ether/ethyl acetate = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.37 (m, 15 H), 7.17 (t, J = 7.9 Hz, 1 H), 7.10 (dd, J = 8.1, 19.0 Hz, 2 H), 6.87 (t, J = 7.5 Hz, 2 H), 6.79 (t, J = 7.8 Hz, 1 H), 6.73 (s, 1 H), 6.67 (t, J = 7.5 Hz, 2 H), 6.59 (d, J = 8.0 Hz, 1 H), 6.53 (d, J = 7.5 Hz, 1 H), 5.07 (t, J = 5.1 Hz, 1 H), 4.94 (d, J = 10.8 Hz, 1 H), 4.68−4.77 (m, 3 H), 4.61−4.65 (m, 3 H), 3.84 (dd, J = 3.1, 9.0 Hz, 1 H), 3.73−3.75 (m, 1 H), 3.58−3.69 (m, 3 H), 3.25−3.32 (m, 1 H), 2.83−2.84 (m, 12 H), 1.83−1.85 (m, 2 H), 1.48−1.53 (m, 4 H), 1.32 (d, J = 5.8 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.19, 150.20, 150.1, 146.9, 145.0, 138.6, 138.6, 138.3, 129.8, 128.4, 128.3, 128.2, 128.03, 128.01, 128.0, 127.9, 127.6, 127. 5, 126.1, 119.8, 118.08, 118.05, 117.3, 116.68, 116.67, 113.5, 112.8, 112.0, 111.7, 97.9, 97.8, 95.0, 84.7, 80.52, 80.50, 80.2, 80.1, 75.4, 75.4, 75.0, 74.9, 72.74, 72.70, 72.2, 72.1, 67.9, 67.20, 67.16, 40.6, 34.3, 29.3, 29.2, 20.2, 18.0; IR(neat) 3063, 3030, 2916, 2804, 1600, 1579, 1496, 1454, 1352, 1279, 1238, 1118, 1064, 736, 699; HRMS (ESI) m/e calcd for $C_{55}H_{63}N_2O_7$, 863.4635, found 863.4636.

6-Methoxy-4,4-diphenyl-2-[2-(3,4,5-tris-benzyloxy-6-methyl-tetrahydro-pyran-2-yloxy)-ethyl]-4*H*-benzo[1,3]dioxine (29). Yield 75% (mixture of two diastereomers), R_f 0.6 (petroleum ether/ethyl acetate = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17−7.38 (m, 25 H), 6.854 (d, J = 8.9 Hz, 0.5 H), 6.852 (d, J = 8.9 Hz, 0.5 H), 6.76 (dd, J = 3.0, 4.4 Hz, 0.5 H), 6.73 (dd, J = 3.1, 4.5 Hz, 0.5 H), 6.351 (d, J = 2.9 Hz, 0.5 H), 6.348 (d, J = 2.9 Hz, 0.5 H), 5.05 (t, J = 5.2 Hz, 0.5 H), 5.01 (t, J = 5.2 Hz, 0.5 H), 4.92 (d, J = 17.9 Hz, 1 H), 4.89 (d, J = 18.0 Hz, 1 H), 4.42−4.72 (m, 6 H), 3.72−3.84 (m, 1 H), 3.46−3.68 (m, 9 H), 2.04−2.08 (m, 2 H), 1.299 (d, J = 5.7 Hz, 1.5 H), 1.294 (d, J = 5.8 Hz, 1.5 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 152.77, 146.3, 146.1, 145.73, 145.69, 144.1, 143.8, 138.6, 138.54, 138.47, 138.42, 138.37, 138.2, 129.1, 128.9, 128.23, 128.19, 128.16, 128.03, 127.95, 127.83, 127.76, 127.73, 127.70, 127.45, 127.38, 125.7, 117.6, 117.5, 114.9, 114.8, 113.9, 97.8, 97.5, 92.9, 92.7, 84.2, 84.1, 80.3, 80.2, 80.0, 79.9, 75.2, 75.0, 74.7, 74.65, 72.6, 72.5, 72.0, 71.9, 67.89, 67.85, 62.4, 61.8, 55.38, 55.36, 34.6, 34.4, 17.9; IR(neat) 3062, 3030, 2908, 1494, 1453, 1225, 1115, 1066, 755, 737, 699; HRMS (ESI) m/e calcd for $C_{50}H_{50}O_8Na$, 801.3403, found 801.3394.

4,4-Bis(4-fluoro-phenyl)-2-[2-(3,4,5-tris-benzyloxy-6-methyl-tetrahydro-pyran-2-yloxy)-ethyl]-4*H*-benzo[1,3]-dioxine (30). Yield 88% (mixture of two diastereomers), R_f 0.6 (petroleum ether/ethyl acetate = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15−7.38 (m, 21 H), 7.01−7.05 (m, 1 H), 6.89−6.96 (m, 3 H), 6.83−6.87 (m, 1 H), 6.74 (d, J = 7.8 Hz, 0.5 H), 6.73 (d, J = 7.8 Hz, 0.5 H), 5.05 (t, J = 5.3 Hz, 0.5 H), 5.02 (t, J = 5.2 Hz, 0.5 H), 4.93 (d, J = 10.8 Hz, 0.5 H), 4.89 (d, J = 10.8 Hz, 0.5 H), 4.44−4.74 (m, 6 H), 3.83 (td, J = 5.9, 10.0 Hz, 0.5 H), 3.76 (td, J = 6.7, 10.3 Hz, 0.5 H), 3.68 (dd, J = 3.0, 9.1 Hz, 0.5 H), 3.45−3.62 (m, 4.5 H), 2.01−2.13 (m, 2 H), 1.300 (d, J = 5.7 Hz, 1 H), 1.296 (d, J = 5.7 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3 (d, J = 248.2 Hz), 162.2 (d, J = 248.1 Hz), 162.0 (d, J = 247.1 Hz), 152.1, 152.0, 141.6 (d, J = 3.1 Hz), 139.9 (d, J = 3.2 Hz), 139.62 (d, J = 3.2 Hz), 138.59, 138.57, 138.51, 138.43, 138.41, 138.3, 131.1 (d, J = 8.1 Hz), 130.9 (d, J = 8.2 Hz), 129.8 (d, J = 8.1 Hz), 129.43, 129.40, 128.6, 128.28, 128.3, 128.24, 128.23, 128.00 127.8, 127.7, 127.6, 127.53, 127.49, 127.41, 124.95, 124.94, 120.43, 120.38, 117.3, 117.2, 115.1 (d, J = 21.4 Hz), 114.9 (d, J = 21.3 Hz), 114.7 (d, J = 21.4 Hz), 98.0, 97.7,

92.9, 92.8, 83.4, 83.3, 80.4, 80.3, 80.1, 80.1, 75.4, 75.1, 74.8, 74.7, 72.7, 72.1, 72.0, 68.1, 67.99, 62.3, 61.8, 34.6, 34.5, 18.0, 17.98; IR(neat) 3064, 3032, 2971, 2915, 1734, 1603, 1584, 1486, 1455, 1281, 1227, 1159, 1117, 1067, 839, 737, 698; HRMS (ESI) *m/e* calcd for $C_{49}H_{46}F_2O_7Na$, 807.3109, found 807.3109.

{4,4-Diphenyl-2-[4-(3,4,5-tris-benzyloxy-6-methyl-tetrahydro-pyran-2-yloxy)-butyl]-4*H*-benzo[1,3]dioxin-6-yl}-dimethyl-amine (31). Yield 73% (mixture of two diastereomers), R_f 0.5 (petroleum ether/ethyl acetate = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16−7.41 (m, 25 H), 6.82 (d, J = 8.9 Hz, 1 H), 6.63 (dd, J = 2.9, 9.0 Hz, 1 H), 6.20 (d, J = 2.9 Hz), 1H, 4.91−4.96 (m, 2 H), 4.68−4.77 (m, 3 H), 4.56−4.65 (m, 3 H), 3.84 (td, J = 3.4, 9.0 Hz, 1 H), 3.74 (td, J = 1.6, 3.1 Hz, 1 H), 3.54−3.70 (m, 3 H), 3.25−3.29 (m, 1 H), 2.69 (s, 6 H), 1.76−1.86 (m, 2 H), 1.36−1.50 (m, 4 H), 1.32 (d, J = 5.9 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.27, 146.26, 144.64, 144.58, 144.4, 138.57, 138.52, 138.50, 138.3, 129.21, 129.19, 128.25, 128.23, 128.04, 127.98, 127.96, 127.87, 127.82, 127.80, 127.69, 127.56, 127.55, 127.51, 127.4, 127.2, 125.4, 117.2, 114.8, 114.4, 97.8, 97.7, 94.7, 84.2, 80.5, 80.1, 80.1, 75.34, 75.33, 74.92, 74.89, 72.7, 72.11, 72.06, 67.9, 67.14, 67.09, 41.5, 34.2, 29.1, 29.0, 20.1, 20.1, 18.0; IR(neat) 3087, 3062, 3031, 2920, 2796, 1601, 1505, 1453, 1447, 1400, 1362, 1241, 1117, 1066, 1028, 736, 699; HRMS (ESI) *m/e* calcd for $C_{53}H_{58}NO_7$, 820.4213, found 820.4216.

3-(3,4,5-Tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran-2-yloxy)-propionaldehyde (32). $BH_3\cdot Me_2S$ (0.35 mL, 1.7 mmol) was added dropwise at 0 °C under argon to a solution of 2-allyloxy-3,4,5-tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran (1.0 g, 1.7 mmol) in THF (8 mL), and the resultant solution was stirred at room temperature for 15 h. Then hydrogen peroxide (35%, 2.0 mL) and sodium hydroxide (3 N, 20 mL) were added at room temperature, and the reaction mixture was stirred for further 6 h. Workup as usual followed by flash column chromatography (petroleum ether/ethyl acetate = 3/1, R_f 0.3) afforded 5-(3,4,5-tris-benzyloxy-6-methyl-tetrahydro-pyran-2-yloxy)-pentan-1-ol (0.829 g, 80%) as a colorless oil.

The mixture of the above obtained alcohol (0.50 g, 0.835 mmol) and PCC (0.287 g, 1.25 mmol) in dichloromethane (10 mL) was stirred at room temperature for 13 h. Workup as usual followed by flash chromatography (petroleum ether/ethyl acetate = 3/1, R_f 0.5) afforded the title compound **32** (0.35 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (t, J = 1.3 Hz, 1 H), 7.21−7.35 (m, 18 H), 7.12 (dd, J = 1.9, 7.2 Hz, 1 H), 4.96 (d, J = 10.8 Hz, 1 H), 4.73−4.83 (m, 4 H), 4.62 (d, J = 9.1 Hz, 1 H), 4.59 (d, J = 9.3 Hz, 1 H), 4.46 (d, J = 10.7 Hz, 1 H), 4.45 (d, J = 12.1 Hz, 1 H), 3.91−4.00 (m, 2 H), 3.61−3.77 (m, 5 H), 3.56 (dd, J = 3.6, 9.7 Hz, 1 H), 2.61−2.77 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.2, 138.5, 137.9, 137.6, 128.24, 128.16, 128.14, 127.9, 127.70, 127.68, 127.5, 127.4, 97.1, 81.7, 79.7, 77.3, 75.5, 74.8, 73.2, 73.0, 70.1, 68.1, 61.4, 43.2; IR(neat) 3088, 3063, 3030, 2920, 2730, 1725, 1497, 1454, 1360, 1158, 1072, 738, 698; HRMS (ESI) *m/e* calcd for $C_{37}H_{40}O_7Na$, 619.2672, found 619.2669.

3,4,5-Tris-benzyloxy-2-benzyloxymethyl-6-(2-[1,3]dioxolan-2-yl-ethoxy)-tetrahydro-pyran (33). The mixture of aldehyde **32** (100 mg, 0.168 mmol), *p*-TsOH·H_2O (3 mg, 0.017 mmol), and DMF (0.5 mL) was placed into the 60 °C bath on rotary evaporator for 5 h under vacuum. Workup as usual followed by flash chromatography (petroleum ether/ethyl acetate = 3/1, R_f 0.4) afforded the title compound **33** (98 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.36 (m, 18 H), 7.11−7.14 (m, 2 H), 4.97−5.01 (m, 2 H), 4.75−4.84 (m, 4 H), 4.60−4.66 (m, 2 H), 4.46 (d, J = 11.7 Hz, 2 H), 3.89−3.40 (m, 3 H), 3.72−3.87 (m, 5 H), 3.62−3.67 (m, 2 H), 3.53−3.59 (m, 2 H), 1.95−2.06 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.3, 138.2, 137. 9, 128.39, 128.35, 128.34, 128.31, 127.94, 127.90, 127.8, 127.7, 127.6, 127.5, 102.1, 97.0, 82.0, 80.00, 77.6, 75.7, 75.1, 73.4, 73.0, 70.1, 68.4, 64.8, 63.7, 33.9; IR(neat) 3088, 3063, 3030, 2883, 1497, 1454, 1361, 1142, 1072, 1028, 737, 697; HRMS (ESI) *m/e* calcd for $C_{39}H_{44}O_8Na$, 663.2934, found 663.2935.

General Procedure of Photolysis. Acetals **28**−**31** (0.20 mmol) in 225 mL of acetonitrile and 25 mL of water were irradiated with a 450 W medium pressure mercury lamp with different filters without excluding air. The reaction mixture was then concentrated directly, and the residue was subjected to flash column chromatography. For **28** and **31**, acetonitrile was removed, and the residue was extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated, and then the residue was subjected to flash column chromatography.

For acetals **28** (172.9 mg, 0.200 mmol) and **31** (159.7 mg, 0.195 mmol), the solutions were irradiated for 50 min with a Pyrex sleeve and a 10% $NaNO_3$ solution (λ > 320 nm) to provide the aldehyde **27** (98 mg, 94% from **28** and 92 mg, 91% from **31**, respectively). R_f 0.6 (petroleum ether/ethyl acetate = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (t, J = 1.6 Hz, 1 H), 7.27−7.38 (m, 15 H), 4.95 (d, J = 10.8 Hz, 1 H), 4.70−4.79(m, 3 H), 4.63−4.65 (m, 3 H), 3.83 (dd, J = 3.1, 8.9 Hz, 1 H), 3.75 (dd, J = 1.9, 2.8 Hz, 1 H), 3.59−3.69 (m, 3 H), 3.32 (td, J = 6.2, 9.8 Hz, 1 H), 2.42 (dt, J = 1.4, 7.2 Hz, 2 H), 1.55−1.68 (m, 6 H), 1.33 (d, J = 5.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.2, 138.5, 138.33, 128.31, 128.28, 128.0, 127.8, 127.6, 127.5, 97.9, 80.5, 75.4, 75.0, 72.8, 72.1, 68.0, 66.8, 43.5, 28.8, 18.8, 18.0; IR(neat) 3088, 3063, 3031, 2919, 1725, 1603, 1497, 1454, 1363, 1115, 1064, 913, 737, 698; HRMS (ESI) *m/e* calcd for $C_{32}H_{38}O_6Na$, 541.2566, found 541.2567.

For acetal **29** (156.8 mg, 0.201 mmol) the wolution was irradiated for 40 min with a Pyrex sleeve as filter (λ > 280 nm) to provide the aldehyde **26** (90 mg, 91%). R_f 0.6 (petroleum ether/ethyl acetate = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (t, J = 1.6 Hz, 1 H), 7.25−7.38 (m, 15 H), 4.93 (d, J = 10.8 Hz, 1 H), 4.68−4.77 (m, 3 H), 4.60−4.64 (m, 3 H), 3.95 (td, J = 5.9, 10.3 Hz, 1 H), 3.79 (dd, J = 3.1, 8.8 Hz, 1 H), 3.73 (dd, J = 2.0, 2.9 Hz, 1 H), 3.59−3.70 (m, 3 H), 2.60 (t, J = 6.0 Hz, 2 H), 1.34 (d, J = 5.8 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 138.4, 138.1, 128.3, 128.0, 127.8, 127.6, 127.58, 127.52, 127.46, 98.1, 80.2, 79.8, 75.3, 74.6, 72.8, 72.1, 68.2, 61.0, 43.3, 17.9; IR(neat) 3088, 3063, 3030, 2973, 2916, 1725, 1496, 1453, 1362, 1116, 1063, 1028, 737, 697; HRMS (ESI) *m/e* calcd for $C_{30}H_{34}O_6Na$, 513.2253, found 513.2257.

For acetal **30** (157.6 mg, 0.200 mmol), the solution was irradiated for 10 min with a Vycor sleeve (λ > 210 nm) to provide the aldehyde **26** (73.5 mg, 75%).

Representative Procedure of Deprotection with Sunlight. A Pyrex test tube (16 mm × 150 mm) containing 15 mL solution of **28** (5 mM in MeCN/H_2O = 9/1) was kept in a water bath and placed outdoor under sunlight in clear weather. After 2 h, the mixture was concentrated directly, and the obtained residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 4/1) to provide the aldehyde **27** (31.4 mg, 81%).

Stability of Acetals 28−31 and 33 toward Acid Treatment. Acetals **33** and **28**−**31** (0.01 mmol) in THF (0.3 mL) and HCl (2 N, 0.1 mL) were stirred at 40 °C. After 18 h, ^{1}H NMR showed that there was almost no **33** left, whereas no aldehyde release from acetals **28**−**31** was detected.

■ ASSOCIATED CONTENT

Supporting Information. General procedure, UV spectra of **14**−**18**, and ^{1}H NMR and ^{13}C NMR spectra of **3**−**9**, **11**, **14**−**18**, and **26**−**33**. This material is available free of charge via the Internet at http://pubs.acs.org.

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DEDICATION

†Dedicated to Professor Howard E. Zimmerman.

REFERENCES

(1) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; Wiley: New York, 2006.

(2) For reviews and monographs, see: (a) Pillai, V. *Synthesis* **1980**, 1. (b) Binkley, R. W.; Flechtner, T. W. In *Synthetic Organic Photochemistry*; Horspool, W. M., Ed.; Plenum: New York, 1984; p 375. (c) Pillai, V. *Org. Photochem.* **1987**, *9*, 225. (d) Givens, R. S.; Kueper, L. W., III *Chem. Rev.* **1993**, *93*, 55. (e) Pirrung, M. C. *Chem. Rev.* **1997**, *97*, 473. (f) Guillier, F.; Orain, D.; Bradley, M. *Chem. Rev.* **2000**, *100*, 2091. (g) Bochet, C. G. *J. Chem. Soc., Perkin Trans. 1* **2002**, 125. (h) Pelliccioli, A. P.; Wirz *J. Photochem. Photobiol. Sci.* **2002**, *1*, 441.(i) *Dynamic studies in biology*; Goeldner, M.; Givens, R. S., Eds.; Wiley-VCH: Weinheim, Germany, 2005. (j) Mayer, G.; Heckel, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4900.

(3) (a) Goard, M.; Aakalu, G.; Fedoryak, O. D.; Quinonez, C.; St. Julien, J.; Poteet, S. J.; Schuman, E. M.; Dore, T. M. *Chem. Biol.* **2005**, *12*, 685. (b) Plunkett, K. N.; Mohraz, A.; Haasch, R. T.; Lewis, J. A.; Moore, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 14574. (c) Han, G.; You, C.-C.; Kim, B.-J.; Turingan, R. S.; Forbes, N. S.; Martin, C. T.; Rotello, V. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 3165. (d) Kostiainen, M. A.; Smith, D. K.; Ikkala, O. *Angew. Chem., Int. Ed.* **2007**, *46*, 7600. (e) Young, D. D.; Deiters, A. *Angew Chem., Int. Ed.* **2007**, *46*, 4290. (f) Park, C.; Lim, J.; Yun, M.; Kim, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 2959. (g) Ohmuro-Matsuyama, Y.; Tatsu, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 7527. (h) Muraoka, T.; Koh, C.-Y.; Cui, H.; Stupp, S. I. *Angew. Chem., Int. Ed.* **2009**, *48*, 5946. (i) Kotzur, N.; Briand, B.; Beyermann, M.; Hagen, V. *J. Am. Chem. Soc.* **2009**, *131*, 16927. (j) Cambridge, S.; Geissler, D.; Calegari, F.; Anastassiadis, K.; Hasan, M.; Stewart, A.; Huttner, W.; Hagen, V.; Bonhoeffer, T. *Nat. Methods* **2009**, *6*, 527. (k) Young, D.; Lively, M.; Deiters, A. *J. Am. Chem. Soc.* **2010**, *132*, 6183. (l) Mizukami, S.; Hosoda, M.; Satake, T.; Okada, S.; Hori, Y.; Furuta, T.; Kikuchi, K. *J. Am. Chem. Soc.* **2010**, *132*, 9524. (m) Fomina, N.; McFearin, C.; Sermsakdi, M.; Edigin, O.; Almutairi, A. *J. Am. Chem. Soc.* **2010**, *132*, 9540.

(4) (a) Hebert, J.; Gravel, D. *Can. J. Chem.* **1974**, *52*, 187. (b) Gravel, D.; Herbert, J.; Thoraval, D. *Can. J. Chem.* **1983**, *61*, 400. (c) Gravel, D.; Murray, S.; Ladouceur, G. *J. Chem. Soc., Chem. Commun.* **1985**, *24*, 1828. (d) Friedrich, E.; Lutz, W.; Eichenauer, H.; Enders, D. *Synthesis* **1977**, *12*, 893. (e) Hoshino, O.; Sawaki, S.; Umezawa, B. *Chem. Pharm. Bull.* **1979**, *27*, 538. (f) Aurell, M. J.; Boix, C.; Ceita, M. L.; Llopis, C.; Tortajada, A.; Mestres, R. *J. Chem. Res. Synop.* **1995**, *12*, 452. (g) Ceita, L.; Maiti, A. K.; Mestres, R.; Tortajada, A. *J. Chem. Res. Synop.* **2001**, *10*, 403. (h) McHale, W. A.; Kutateladze, A. G. *J. Org. Chem.* **1998**, *63*, 9924. (i) Lu, M.; Fedoryak, O. D.; Moister, B. R.; Dore, T. M. *Org. Lett.* **2003**, *5*, 2119. (j) Blanc, A.; Bochet, C. G. *J. Org. Chem.* **2003**, *68*, 1138. (k) Kantevari, S.; Narasimhaji, C. V.; Mereyala, H. B. *Tetrahedron* **2005**, *61*, 5849. (l) Kostikov, A. P.; Malashikhina, N.; Popik, V. V. *J. Org. Chem.* **2009**, *74*, 1802. (m) Hagen, V.; Kilic, F.; Schaal, J.; Dekowski, B.; Schmidt, R.; Kotzur, N. *J. Org. Chem.* **2010**, *75*, 2790.

(5) (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.

(6) (a) Zimmerman, H. E.; Sandel, V. R. *J. Am. Chem. Soc.* **1963**, *85*, 915. (b) Zimmerman, H. E.; Somasekhara, S. *J. Am. Chem. Soc.* **1963**, *85*, 922. (c) Zimmerman, H. E. *J. Am. Chem. Soc.* **1995**, *117*, 8988. (d) Zimmerman, H. E. *J. Phys. Chem. A* **1998**, *102*, 5616.

(7) The photoreactions became cleaner and more PPG reagent **V** could be obtained with more water as the cosolvent, albeit the yields of released carbonyl compounds were not affected. Taking into consideration of the poor solubility of the studied acetals in highly polar solvent systems, we conducted most of the photoreactions in acetonitrile/water (9:1). Photo deprotection reactions carried out in methanol did not provide cleaner reactions and better yields of released aldehydes than in acetonitrile/water (9:1). Instead some dimethyl acetal byproducts were detected in methanol. Reactions in other solvent systems were previously discussed.[5a,c]

(8) Wang, P.; Wang, Y.; Hu, H.; Liang, X. *Eur. J. Org. Chem.* **2009**, 208.

(9) Wang, P.; Mondal, M.; Wang, Y. *Eur. J. Org. Chem.* **2009**, 2055.

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

(11) (a) Quantum yields were determined by chemical actinometry. Defoin, A.; Defoin-Straatmann, R.; Hildenbrand, K.; Bittersmann, E.; Kreft, D.; Kuhn, H. J. *J. Photochem.* **1986**, *33*, 237.(b) Photoreaction of the acetal was carried out in CD_3CN/D_2O 9:1. (c) The monochromatic light centering at 285 nm was obtained by passing light from a 450 W medium pressure mercury lamp through three quartz cuvettes containing 2 M $NiSO_4$ in 5% H_2SO_4 (cell 1), 0.8 M $CoSO_4$ in 5% H_2SO_4 (cell 2), and 2.46×10^{-4} M $BiCl_3$ in conc HCl/H_2O (2:3) (cell 3). (d) The monochromatic light centering at 312 nm was obtained by passing light from a 450 W medium pressure mercury lamp through a 2 mM K_2CrO_4 solution in a quartz cuvette.

(12) (a) Zimmerman, H. E.; Nuss, J. M.; Tantillo, A. W. *J. Org. Chem.* **1988**, *53*, 3792. (b) Zimmerman, H. E. *Mol. Photochem.* **1971**, *3*, 281.

(13) The structures were optimized at the HF/6-311G (d, p) level by using Gaussian 03 software: Frisch, M. J. et al. *Gaussian 03*, Revision C. 02; Gaussian: Wallingford, CT, 2005

(14) A 450 W medium-pressure mercury lamp with 10% $NaNO_3$ filter solution and a Pyrex filter sleeve.