JOC The Journal of Organic Chemistry

FEATURED ARTICLE

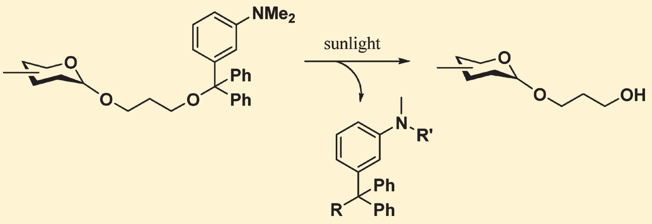
pubs.acs.org/joc

Development of Trityl-Based Photolabile Hydroxyl Protecting Groups

Lei Zhou, Haishen Yang, and Pengfei Wang*

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

Supporting Information



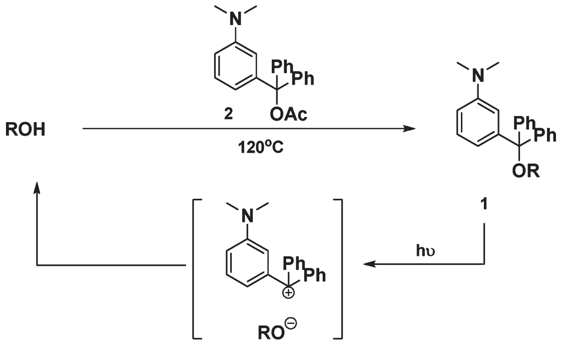
ABSTRACT: A series of trityl-based photolabile hydroxyl protecting groups have been examined. These PPGs evolve from the traditional acid-labile trityl protecting group with proper electron-donating substituents. Structure−reactivity relationships have been explored. A *m*-dimethylamino group is crucial to achieve high photochemical deprotection efficiency. The *o*-hydroxyl group in **8** greatly improves the yield of the photochemical deprotection reaction, compared with the corresponding *o*-methoxyl-substituted counterpart **7**. However, comparison between the photoreactions of **9** and **11** does not show similar structural relevance. The PPG in ether **1** (i.e., DMATr group) is structurally simple and easy to prepare and install. Its deprotection can be successfully carried out with irradiation of sunlight without requirement of photochemical devices.

INTRODUCTION

Photolabile protecting groups (PPGs) are unique and useful protecting groups not only in organic chemistry but also in biochemistry, photolithography, and material science.[1−3] Their advantages stem from using light as a traceless reagent in the removal process. Photochemical removal of protecting groups often occurs under mild conditions and does not require chemical reagents. In addition, light also provides precise temporal and spatial control over the course of a reaction. New PPGs and creative applications of PPGs have continued to emerge.[4,5] Development of more PPGs of different chemical and photochemical properties will provide more options for different applications and is highly desirable.

We have recently demonstrated that the traditional acid-sensitive hydroxyl protecting group, the trityl (Tr) group, can be converted to a robust photolabile hydroxyl protecting group relatively insensitive toward acid treatments by introducing a *m*-dimethylamino group to one of the three phenyl rings.[6] As shown in Scheme 1, an alcohol ROH can be protected as the triarylmethyl ether **1** by using a new protection protocol recently developed in our laboratory. Thus, heating the alcohol ROH with the protecting group reagent **2** at 120 °C will lead to the ether **1** in high yields without using any other chemical reagents. Upon irradiation of **1** with UV light, the alcohol ROH can be efficiently released in the presence of a hydrogen donor.[6] For the first time, both protection of an alcohol and removal of the protecting group to release the alcohol can be carried out without requiring any other chemical reagents. Moreover, owing to its increased stability toward acid treatment, the new PPG (i.e., DMATr in **1**) constitutes orthogonal protecting groups with the traditional acid-sensitive trityl type of protecting group. Herein we report our full account of developing new PPGs for hydroxyl protection.

Scheme 1. Protection of Alcohol with DMATr

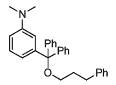
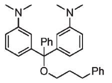
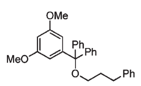
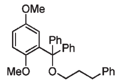
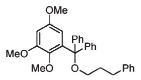
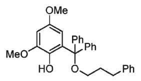
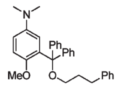
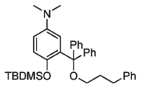
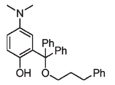
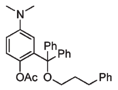


RESULTS AND DISCUSSION

Structural Effect. We have recently demonstrated that traditional acid-labile Tr and 4-methoxytrityl (MMTr) are also responsive to UV irradiation of wavelength shorter than 280 nm to release the protected alcohol.[6] However, DMATr has a much improved photochemical efficiency, which was attributed to the excited-state *meta* effect introduced by the *meta* electron-donating group, i.e., the dimethylamino group.[7] Interestingly, introducing additional *m*-dimethylamino group(s), whether to the same or to a different phenyl ring of the triarylmethyl group, does not necessarily further improve the photoreactivity of PPGs. On the contrary, photochemical efficiency actually decreased when a phenyl group in **1** was replaced with another 3-(dimethylamino)-phenyl group. For example, irradiation of **3** and **4** under the same reaction conditions in CD_3OD led to release of 3-phenylpropanol

Received: April 1, 2011
Published: May 25, 2011

Table 1. Photochemical Cleavage of Trityl-Based Hydroxyl Protecting Groups

entry	ether	$\varepsilon(\lambda)$ of ether[a] $(M^{-1}\,cm^{-1})/10^3$	Quantum yields (Φ)[b,c]	chemical yield (%)[g,h]
1	 **3**	2.7 (309 nm)	0.2[d] (0.12)[d]	84 (76)
2	 **4**		-	77 (48)
3	 **5**	1.8 (286 nm)	0.04[e] (0.02)[e]	- -
4	 **6**	4.6 (296 nm)	0.03[e]	20 (10 min) (23) (12 min)
5	 **7**	3.7 (291 nm)	0.04[e]	13 (10 min) (8) (12 min)
6	 **8**	-	-	82 (10 min) (94) (12 min)
7	 **9**	2.1 (322 nm)	0.19[f]	85 (85)
8	 **10**	3.2 (322 nm)	0.19[f]	89 (87)
9	 **11**	3.1 (325 nm)	0.2[f]	88 (90)
10	 **12**	3.0 (315 nm)	0.07[f]	51 (50)

[a] Measured in MeCN. [b] Measured in 5 mM CD_3OD solution. [c] Values in parentheses were measured in 5 mM CD_3CN/D_2O (9:1) solution irradiated in an NMR tube. [d] Monochromatic light centered at 312 nm by filtering through a 2 mM K_2CrO_4 in a 5% K_2CO_3 aqueous solution. [e] Monochromatic light centered at 286 nm by filtering through 2 M $NiSO_4$ in 5% H_2SO_4, 0.8 M $CoSO_4$ in 5% H_2SO_4 and 0.246 mM $BiCl_3$ in concd HCl/H_2O $(2:3)_3$. [f] Monochromatic light centered at 317 nm by filtering through a solution of 2.5 M $NiSO_4$ and 0.1 M $CoSO_4$. [g] Irradiated with Pyrex-filtered light for 7 min in CD_3OD and yields determined by ^1H NMR analysis. [h] Yields in parentheses were obtained from reactions in CD_3CN/D_2O (9:1) under the same irradiation conditions and determined by ^1H NMR analysis.

in 84% yield from **3**, but in 77% yield from **4** (Table 1, entries 1 and 2). Because of the solvent effects previously observed, we also examined the photoreactions in MeCN/water (9:1).[8] As expected, yields obtained in MeCN/D_2O (9:1) were inferior to those in methanol and cleavage of the benzylic C−O was achieved in 76% yield with the ether **3** while only in 48% yield with the ether **4** (Table 1, entries 1 and 2). In MeCN/water (9:1), photoreaction products contained a small fraction of 3-phenylpropanal, presumably resulting from oxidization that occurred during release of 3-phenylpropanol. Thus, the chemical yields of photochemically breaking the benzylic C−O bond in MeCN/water (9:1) in Table 1 were adjusted accordingly; i.e., the products included both the alcohol and the aldehyde. The amount of the aldehyde byproduct varied with different PPGs. In the case of **3**, the ratio of the aldehyde to the sum of the aldehyde and the alcohol was typically around 20%, similar to the value obtained from **4**. We speculate that formation of the aldehyde could originate from heterolysis of the benzylic C−O bond followed by hydride shift between the geminate ion pair (i.e., alkoxide and the tritylium ion in Scheme 1).[9,10] Inspection of the crude reaction mixture by NMR spectroscopy revealed that appearance of the aldehyde was accompanied by the reduced PPG moiety, i.e., 1-(dimethylamino)-phenyl-1,1-diphenylmethane. In control experiments, irradiation of pure 3-phenyl-1-propanol or a 1:1 mixture of the alcohol and the corresponding triarylmethyl alcohol in MeCN or in MeCN/water (9:1) did not produce any detectable aldehyde, seemingly in agreement with the speculated hydride transfer in the ion pair.

The nature of the electron-donating group(s) and the substitution pattern affects the photochemical efficiency. Compared with the dimethylamino group, a methoxyl group is less effective in causing a bathochromic shift of PPG's UV absorption and in improving its photochemical efficiency. For instance, the quantum yield of **3** was 0.2 in methanol, while the quantum yields of **5**−**7** were only 0.04, 0.03, and 0.04, respectively (Table 1, entries 1 and 3−5).[11,12] In MeCN/water (9:1), the quantum yield of **3** is also higher than that of **5**.[6] Chemical yields of the photoreactions of **6** and **7** were measured after irradiation for 10 min in methanol or 12 min in MeCN/water (9:1), and they were all considerably lower than that of **3** after 7 min of irradiation. Irradiation was carried out with a medium pressure mercury lamp equipped with a Pyrex filter sleeve. There was only a trace amount of 3-phenylpropanal observed in the reactions of **6** and **7** in MeCN/water (9:1).

However, compound **8** showed significantly improved photochemical yields compared with **6** and **7** in both methanol and MeCN/water (9:1) solutions (Table 1, entry 6). In methanol, irradiation of **8** for 10 min led to 82% yield of the C−O bond cleavage versus only 13% yield from **7**; in MeCN/water (9:1), irradiation of **8** for 12 min resulted in 94% yield of the bond cleavage versus only 8% yield from **7** under the same conditions. The compounds **7** and **8** have similar structures except that there is the *o*-hydroxyl group in **8** rather than a methoxyl group as in **7**. We attribute the increased reaction efficiency of **8** to the increased acidity of the phenolic hydrogen in its S_1 state. It can facilitate the cleavage of the benzylic C−O via intramolecular catalysis. It has been suggested that the high reactivity of generating quinone methides from *o*-hydroxybenzyl alcohols lies in the proximity of the phenolic hydroxyl with respect to the departing benzylic group.[13] This observed influence of the *o*-hydroxyl group on cleavage of the benzylic C−O (Table 1, entry 6) is in agreement with the literature results.[13,4k,14] In a control experiment, thermal decomposition of **8** was not detected when the solution of **8** was heated at 60 °C in the dark within the same time frame of irradiation.

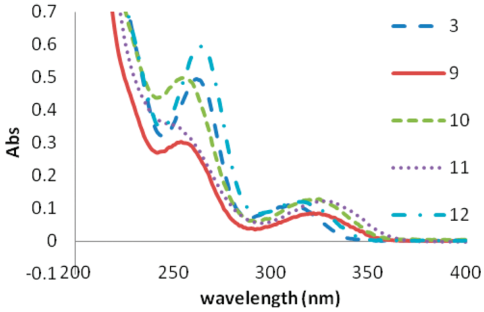


Figure 1. UV spectra of ethers **3** and **9**−**11**.

In MeCN/water (9:1), there was no oxidized 3-phenylpropanol observed in the photoreactions of **8**.

We were attracted to the PPG in **1** (i.e., DMATr) owing to its simple structure and associated advantageous properties in spite of the high photochemical efficiency of the PPG in **8**. We then attempted structural modifications of DMATr for property improvements. Thus, ethers **9**−**12** were synthesized (Table 1, entries 7−10). Structural modification of DMATr by introducing an additional electron-donating group to the (dimethylamino)phenyl ring of DMATr resulted in new trityl derivatives which are all photoreactive and can serve as PPGs for hydroxyl protection. Among them, the ethers **9**−**11** showed comparable photochemical yields of deprotection in both methanol and MeCN/water as the ether **3** equipped with DMATr. They all absorb UV of longer wavelengths (λ = 322−325 nm) than **3** (λ = 309 nm). For example, addition of a methoxyl group to DMATr at the position *para* to the dimethylamino group led to the new PPG in the ether **9**, with the UV absorption shifting to 322 nm from 309 nm of DMATr (Figure 1). The quantum yields of releasing the alcohol from **9** did not improve, i.e., 0.2 of **3** versus 0.19 of **9** in methanol (Table 1, entries 1 and 7). The chemical yields obtained upon irradiation with Pyrex-filtered mercury lamp were similar in methanol (i.e., 84% of **3** versus 85% of **9**) but slightly improved in MeCN/water (9:1) (i.e., 76% of **3** versus 85% of **9**). In the photoreaction of **9** in MeCN/water (9:1), the ratio of the generated aldehyde to the sum of the aldehyde and the alcohol dropped to ca. 10% (versus ca. 20% in the case of **3**).

There was no significant spectral shifting or change of ε values with other groups replacing the *o*-methoxyl group (Table 1, entries 8−10, and Figure 1). The photochemical efficiencies remained similar, except that the AcO-substituted PPG (as in **12**, Table 1, entry 10) showed declining reactivity. Under the same reaction conditions, the compound **12** released the alcohol in 51% yield, lower than the typical yields (84−89%) of other ethers bearing the *m*-dimethylamino group. In parallel, photoreactivity of **12** also declined in MeCN/water (9:1), i.e., 50% yield of benzylic C−O bond cleavage of **12** versus 76−90% yields of others.

While the comparison of photochemical reactivity between **7** and **8** revealed an obvious case of *ortho* phenolic hydrogen-facilitated benzylic C−O cleavage, the expected improved reactivity of the ether **11** (having an *o*-hydroxyl group) compared with that of **9** (having an *o*-methoxyl group) was not observed. Instead, the ethers **11** and **9** have similar photochemical efficiency. Under the same photoreaction conditions, the ether **9** released the alcohol in 85% yield, only slightly lower than the 88% yield obtained from **11**. Similar results were also obtained in MeCN/water (9:1) solutions where the photoreaction of **11** did not yield any detectable amount of 3-phenylpropanal.

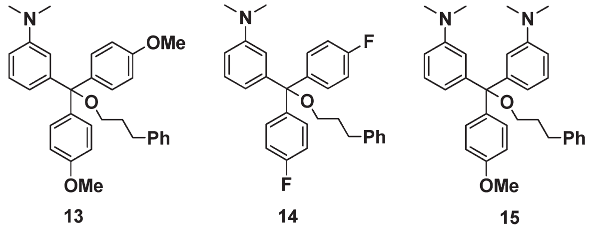


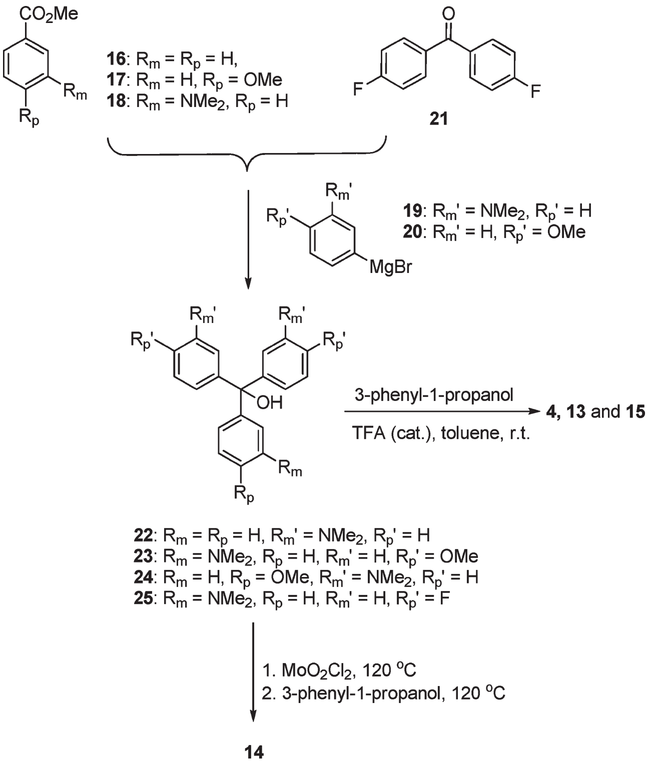
Figure 2. Photocleavable ethers **13**−**15**.

In addition to studying the effect of an additional electron-donating substitution at the (dimethylamino)phenyl ring of DMATr, we also screened photochemical efficiencies of the ethers **13**−**15** (Figure 2). In **13**, two 4-methoxyphenyl groups replaced the two phenyl groups in **3**. It is known that the 4-methoxyphenyl groups do not absorb Pyrex-filtered UV light.[6] However, we anticipated that they would stabilize the triarylmethyl cation better than two phenyl groups upon heterolysis of the benzylic C−O bond, which would facilitate the bond cleavage. However, irradiation of **13** (5 mM in CD_3CN/D_2O 9:1) for 7 min with a Pyrex-filtered mercury lamp led to cleavage of the benzylic C−O bond in 67% yield, slightly lower than the yield of **3** (i.e., 76%, Table 1, entry 1) under the same reaction conditions. The ether **14** has two 4-fluorophenyl groups, and its photochemical efficiency of breaking the benzylic C−O bond was 63%, only slightly lower than that of **13**. Similarly, comparison between **4** (48%) and **15** (50%) showed very similar efficiency, and both are lower than that of **3**, **13**, and **14** under the same irradiation conditions. These results revealed that additional substitution as shown in **13**−**15** would not yield new PPGs better than DMATr. Therefore, we focused on studying DMATr and expanding its scope.

Synthesis. The ethers **4** and **13**−**15** were readily prepared (Scheme 2). Thus, treatment of the substituted methyl benzoates **16**−**18** with the Grignard reagents **19** or **20** led to the triaryl alcohols **22**−**24**. Alternatively, the triarylmethanol can be prepared from the corresponding substituted benzophenone and Grignard reagent. For example, reaction of 4,4′-difluorobenzophenone **21** and the Grignard reagent **19** led to the triarylmethanol **25**. The ethers **4**, **13**, and **15** were obtained by reacting 3-phenylpropanol with the corresponding triaryl alcohols **22**, **23**, and **24**, respectively, in the presence of a catalytic amount of TFA. Alternatively, the triarylmethanol **25** was converted to its acetate which was used in the neutral protection protocol to afford the ether **14**.

The ethers **6**−**12** were prepared from the reactions of salicyl alcohols and 3-phenylpropanol. Thus, treating salicyl alcohols **26**, **27**, and **28** with acetyl chloride and triethylamine in methylene chloride for 2−3 h followed by addition of 3-phenylpropanol led to the ethers **29**, **8**, and **11**, respectively (Scheme 3). Presumably, treatment of the salicyl alcohols with acetyl chloride and triethylamine led to the intermediate **30** via acetylation of the phenolic hydroxyl group followed by intramolecular acetyl transfer. Direct acetylation of a triarylmethyl alcohol proved to be difficult.[15] Elimination of acetic acid from **30** would lead to the *o*-quinone methide intermediate **31**. Subsequent conjugate addition with the alcohol led to the ethers **29**, **8**, and **11**, respectively. Methylation of these intermediates provided the ethers **6**, **7**, and **9**. The ethers **10** and **12** were obtained by reacting **11** under

Scheme 2. Protection of Alcohol with New PPGs



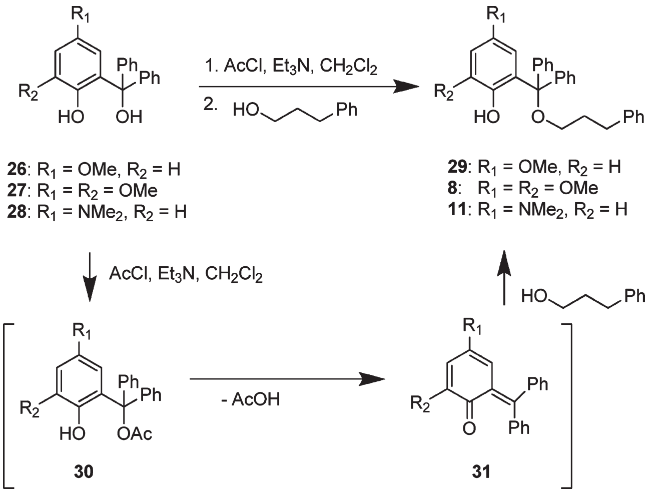
standard silylation and acetylation conditions with *tert*-butyldimethylsilyl chloride or acetyl chloride, respectively.

Deprotection with Sunlight. Among different PPGs, the appealing overall quality of DMATr as a PPG for hydroxyl protection warranted further investigation. We then examined its deprotection with sunlight to expand the scope in that efficient deprotection with sunlight is an economical green chemistry method which would not only avoid the use of any photochemical equipments but also be suitable for large-scale reactions and various applications.

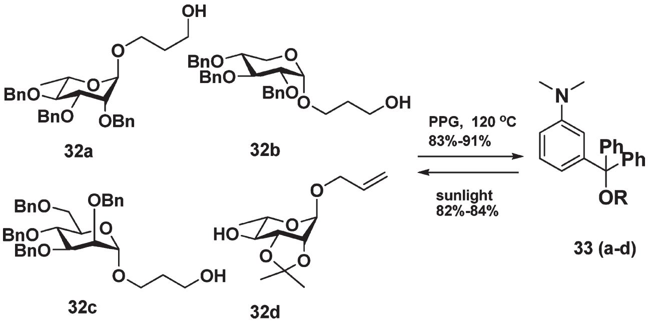
To demonstrate photochemical deprotection with sunlight, we synthesized monosaccharides **32a**−**d** and protected them with DMATr by using the simple protection protocol recently reported by us (Scheme 4).[6] The corresponding ethers **33a**−**d** were obtained in 89%, 91%, 91%, and 83% yields, respectively. These compounds were stable under indoor lighting and did not require special precautions to prepare and handle. A solution (MeOH/MeCN 14:1) of **33** in a Pyrex test tube was kept in a water bath and placed outdoors under sunlight in clear weather. Acetonitrile was used as the cosolvent because of the poor solubility of **33** in methanol. The reaction temperature varied between 20 and 30 °C during the reaction course. The photoreactions typically completed in 4.5 h. It appeared that the reaction time could be affected by the shape of the reaction vessel, and a larger exposure area of the reaction solution should accelerate the reaction. The monosaccharides **32a**−**d** were isolated in 84%, 84%, 82%, and 83% yields, respectively.

It appeared that the reactions preferred polar solvents.[6,8] In order to increase solubility of **33** in a solvent more polar than MeOH/MeCN (14:1), we chose to prepare compound **34** (Scheme 5). It can be obtained by removing the four benzyl groups in **33c** with a standard hydrogenolysis procedure using Pd/C. Alternatively, it could be readily prepared from the acetylated mannoside **35** via the intermediate **36** by using a routine procedure. The DMATr-protected mannoside **34** showed increased solubility in highly polar solvent systems.

Scheme 3. Protection of Alcohol with New PPGs

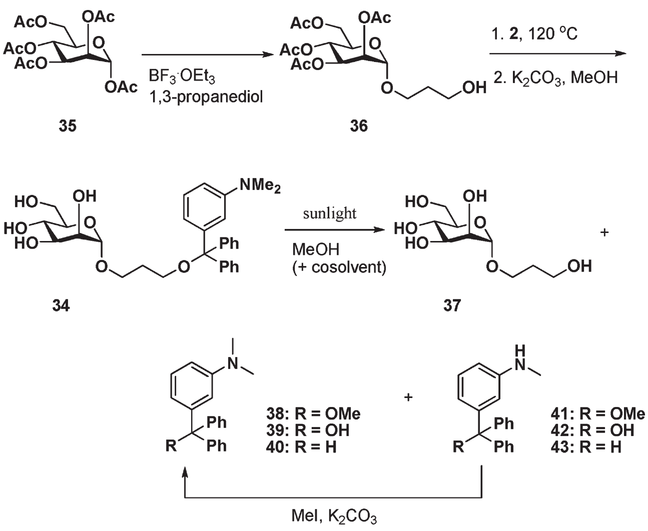


Scheme 4. Removal of DMATr with Sunlight

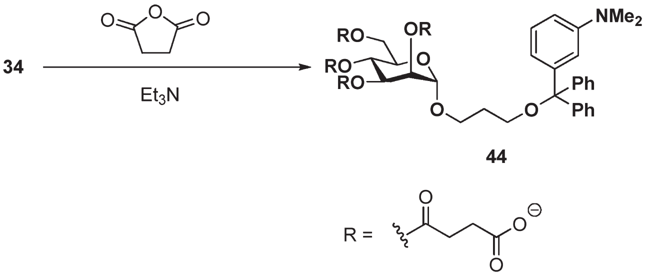


For comparison, the ether **34** was first irradiated under the same conditions as **33a**−**d** (i.e., 5 mM in MeOH/MeCN 14:1 irradiated with sunlight for ca. 4.5 h), and a similar product distribution was observed. The released mannoside **37** was obtained in 84% yield. Some other identified products included **38** (39%), **39** (5%), **40** (11%) and a trace amount of **41**−**43** and benzophenone (Scheme 5). The structures of **41**−**43** were elucidated on the basis of ^{1}H NMR analysis and confirmed by converting **41**−**43** to the corresponding dimethylamino counterparts **38**−**40** via methylation with methyl iodide. Formation of **40** could stem from either hydride abstraction of the trityl cationic intermediate in its ground-state singlet or hydrogen abstraction in its ground-state triplet.[9,10] However, the pathways leading to formation of **41**−**43** were unclear. Change of the solvent system from MeOH/MeCN (14:1) to pure MeOH only slightly affected the reaction outcome. The mannoside **37** was produced in 87% yield, while **38**−**40** were obtained in 43%, 5%, and 11%, respectively. However, the photoreaction of **34** in MeOH/H_2O (1:1) became cleaner and led to **37** in 97% yield after irradiation with sunlight under the same reaction conditions. The products **38** and **39** changed to 41% and 27% yields,

Scheme 5. Solvent Effect on Removal of DMATr with Sunlight



Scheme 6. Preparation of Water-Soluble Substrate



respectively, while **40** decreased to 4% and benzophenone did not appear. In both pure methanol and MeOH/water (1:1), there were similar amounts of compounds **41**–**43** as observed in the reaction conducted in MeOH/MeCN (14:1). These experimental results confirmed that the removal of DMATr could accomplish high yields and a cleaner reaction mixture would be obtained in more polar solvents in the presence of water.

To examine photoreactions in water, the mannoside **34** was converted to the more water-soluble derivative **44** by treatment with succinic anhydride and triethylamine (Scheme 6). Irradiation of **44** in water with sunlight was stopped after 4.5 h, and the R groups were then removed under basic conditions. The product ratio of **37**:**39**:**40**:**42**:**43** was about 52:27:12:7:7. The conversion of **44** (ca. 60%) was relatively lower than that of **34** in methanol-containing solvent systems. We attribute the low photoefficiency to low light absorption of **44** in the opaque reaction mixture caused by production of hydrophobic compounds (e.g., **39** and **40**) from the PPG part of **44**. Therefore, to fully study photochemical behavior of the new PPG in an aqueous environment, it is necessary to modify the PPG and convert it into a hydrophilic segment. Research along this direction is currently being undertaken in our laboratory.

In summary, we demonstrated that electron-donating group-substituted trityl groups can be photochemically active and be useful photolabile hydroxyl-protecting groups. Structure–reactivity studies showed that one *m*-dimethylamino group is crucial for high photochemical deprotection efficiency. The efficiency of DMATr was compared with a variety of differently substituted Tr, and it seemed to be more suitable for various applications not only because of its photochemical reactivity but also its simple structure, ease of preparation and installation, and its dark stability. The sunlight deprotection proved to be highly efficient, which could potentially expand its application, for example, in large-scale deprotection reactions without the requirement of special photochemical devices. We also observed the expected acceleration of benzylic C–O bond cleavage by an *o*-hydroxyl group in **8** when compared with the corresponding *o*-methoxyl-substituted counterpart **7**. Interestingly, the similar acceleration anticipated for **11** relative to its counterpart **9** was not observed.

EXPERIMENTAL SECTION

General Procedure for Preparation of PPG Reagents 22–25. To the Grignard reagents **19** (prepared from 3-bromo-*N*,*N*′-dimethylaniline) or **20** (prepared from 4-bromoanisole) was added methyl benzoate **16**, methyl 3-(dimethylamino)benzoate **18**, 4,4′-difluorobenzophenone **21**, or methyl 4-methoxybenzoate **17**. The reaction mixture was stirred at room temperature under argon overnight. Workup followed by flash chromatography afforded the corresponding PPG reagents **22**–**25**.

General Procedure for Preparation of 4, 13, and 15. A PPG reagent (i.e., **22**, **23**, or **25**), 3-phenyl-1-propanol, and *p*-TsOH were stirred in toluene at room temperature under argon overnight. Upon completion, the reaction mixture was purified by flash column chromatography to afford the corresponding ether.

3,3′-(Phenyl(3-phenylpropoxy)methylene)bis(*N*,*N*-dimethylaniline) (4). Prepared from **22** (145 mg, 0.42 mmol), 3-phenyl-1-propanol (85 μL, 0.63 mmol), and *p*-TsOH (40 mg, 0.21 mmol) in toluene (0.5 mL) by using the general procedure. The reaction mixture was directly purified with column chromatography (petroleum ether/ethyl acetate = 9/1) to provide **4** (45.9 mg, 24%): R_f 0.3 (petroleum ether/ethyl acetate = 9/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (m, 2 H), 7.31–7.10 (m, 10 H), 6.97 (s, 2 H), 6.81 (d, *J* = 7.9 Hz, 2 H), 6.62 (dd, *J* = 2.4, 8.1 Hz, 2 H), 3.17 (t, *J* = 6.3 Hz, 2 H), 2.88 (s, 12 H), 1.92 (m, 2 H), 2.74 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 145.2, 145.1, 142.4, 128.8, 128.4, 128.2, 128.1, 127.4, 126.6, 125.6, 118.1, 113.7, 111.2, 86.9, 62.9, 40.8, 32.8, 32.2; IR (neat) 2925, 1560, 1597, 1496, 1435, 1351, 1217, 978, 746, 704; HRMS (ESI) *m*/*e* calcd for $C_{32}H_{37}N_2O$ 465.2906, found 465.2911.

3-(Bis(4-methoxyphenyl)(3-phenylpropoxy)methyl)-*N*,*N*-dimethylaniline (13). Prepared from **23** (15 mg, 0.05 mmol), 3-phenyl-1-propanol (20 μL, 0.15 mmol), and *p*-TsOH (1.9 mg, 0.01 mmol) in toluene (0.05 mL) by using the general procedure. The reaction mixture was directly purified with column chromatography (petroleum ether/ethyl acetate = 5/1) to provide **13** (14.4 mg, 72%): R_f 0.5 (petroleum ether/ethyl acetate =5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 4 H), 7.28–7.09 (m, 6 H), 6.95 (s, 1 H), 6.79 (m, 5 H), 6.61 (d, *J* = 7.6 Hz, 1 H), 3.79 (s, 6 H), 3.12 (t, *J* = 6.3 Hz, 2 H), 2.89 (s, 6 H), 2.73 (m, 2 H), 1.91 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 150.1, 145.9, 142.3, 137.0, 130.1, 129.2, 128.4, 128.2, 125.6, 117.4, 113.0, 112.8, 110.9, 85.9, 62.7, 55.2, 40.7, 32.7, 32.0; IR (neat) 3023, 2935, 2842, 2793, 1597, 1495, 1446, 1335, 1247, 975, 800, 746; HRMS (ESI) *m*/*e* calcd for $C_{32}H_{36}NO_3$ 482.2695, found 482.2692.

3,3′-((4-Methoxyphenyl)(3-phenylpropoxy)methylene)-bis(*N*,*N*-dimethylaniline) (15). Prepared from **24** (38 mg, 0.10 mmol), 3-phenyl-1-propanol (40 μL, 0.30 mmol), and *p*-TsOH (1 mg, 0.005 mmol) in toluene (0.1 mL) by using the general procedure. The reaction mixture was directly purified with column chromatography (petroleum ether/ethyl acetate = 5/1) to provide **15** (23.7 mg, 48%): R_f 0.3 (petroleum ether/ethyl acetate = 5/1); ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.31 (m, 2 H), 7.21−7.00 (m, 7 H), 6.91 (s, 2 H), 6.73 (m, 4 H), 6.53 (dd, *J* = 2.3, 7.9 Hz, 2 H), 3.71 (s, 3 H), 3.08 (t, *J* = 6.3 Hz, 2 H), 2.81 (s, 12 H), 2.67 (m, 2 H), 1.84 (m, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 158.2, 150.1, 145.7, 142.5, 136.9, 130.4, 128.4, 128.2, 128.1, 125.6, 117.8, 113.4, 112.7, 111.0, 86.5, 62.8, 55.2, 40.8, 32.8, 32.2; IR (neat) 3431, 2930, 1602, 1495, 1458, 1438, 1352, 1250, 1185, 838, 732; HRMS (ESI) *m*/*e* calcd for $C_{33}H_{39}N_2O_2$ 495.3012, found 495.3016.

Preparation of 3-(Bis(4-fluorophenyl)(3-phenylpropoxy)methyl)-*N*,*N*-dimethylaniline (14). The PPG reagent **25** (34 mg, 0.10 mmol) was dissolved in distilled toluene (0.1 mL), followed by addition of molybdenum(VI) dichloride dioxide (0.2 mg, 0.001 mmol), acetic anhydride (14 μL, 0.15 mmol), and triethylamine (14 μL, 0.10 mmol). The reaction mixture was heated at 120 °C under argon for 2 h. Then the solvent was removed, and the residue was washed with petroleum ether. The combined petroleum ether solutions were concentrated to afford (3-(dimethylamino)phenyl)bis(4-fluorophenyl)methyl acetate (34 mg, 89%) as a light yellow oil. It was used without further purification.

(3-(Dimethylamino)phenyl)bis(4-fluorophenyl)methyl acetate (19 mg, 0.05 mmol) and 3-phenyl-1-propanol (10 μL, 0.075 mmol) in distilled toluene (0.05 mL) were heated at 120 °C under argon for 6 h. The reaction mixture was directly purified with column chromatography (petroleum ether/ethyl acetate = 25/1) to provide **14** (12 mg, 52%): R_f 0.3 (petroleum ether/ethyl acetate = 25/1); ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.40 (m, 4 H), 7.30−7.09 (m, 6 H), 6.96 (m, 4 H), 6.84 (s, 1 H), 6.70 (d, *J* = 7.6 Hz, 1 H), 6.62 (dd, *J* = 2.4, 8.1 Hz, 1 H), 3.11 (t, *J* = 6.3 Hz, 2 H), 2.89 (s, 6 H), 2.72 (m, 2 H), 1.92 (m, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 163.3, 160.0, 150.2, 144.5, 142.0, 140.4, 140.4, 130.4, 130.3, 128.4, 128.4, 128.3, 125.7, 117.3, 114.6, 114.3, 112.9, 111.3, 85.9, 62.8, 40.6, 32.6, 31.8, 29.7; IR (neat) 2925, 2862, 2259, 2244, 2195, 1597, 1510, 1228, 839; HRMS (ESI) *m*/*e* calcd for $C_{30}H_{30}NOF_2$ 458.2295, found 458.2298.

((3-Phenylpropoxy)(2,3,5-trimethoxyphenyl)methylene)dibenzene (7). To a stirred solution of 2-(hydroxydiphenylmethyl)-4,6-dimethoxyphenol[1] (135 mg, 0.40 mmol) in dichloromethane (0.4 mL) was added triethylamine (62 μL, 0.44 mmol). Then acetyl chloride (29 μL, 0.40 mmol) was slowly added dropwisely. The reaction mixture was stirred at room temperature under argon for 3 h. 3-Phenyl-1-propanol (214 μL, 1.60 mmol) was then added, and the reaction mixture was stirred at room temperature under argon overnight. The solvent was removed, and the reaction mixture was dissolved in THF (0.4 mL). Sodium hydride (19.2 mg, 0.48 mmol) was added at 0 °C, and the resulting mixture was stirred at room temperature for 3.5 h before iodomethane (252 μL, 4.00 mmol) was added. The reaction mixture was stirred for another 5 h. The solvent was removed, and the residue was purified with flash column chromatography (petroleum ether/ethyl acetate = 20/1) to provide **7** (153 mg, 82%) as a white solid: R_f 0.3 (petroleum ether/ethyl acetate = 20/1); ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.46 (m, 4 H), 7.24−6.97 (m, 12 H), 6.34 (d, *J* = 3.0 Hz, 1 H), 3.70 (s, 3 H), 3.62 (s, 3 H), 2.96 (s, 3 H), 2.92 (t, *J* = 6.4 Hz, 2 H), 2.59 (m, 2 H), 1.81 (m, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 154.9, 153.6, 142.6, 142.1, 140.2, 139.6, 128.7, 128.3, 128.2, 127.4, 126.6, 125.6, 103.4, 99.2, 84.7, 62.5, 59.1, 55.5, 55.4, 32.5, 31.8; IR (neat) 3023, 2940, 2878, 2250, 1594, 1469, 1423, 1325, 1275, 1238, 993, 981, 734; HRMS (ESI) *m*/*e* calcd for $C_{31}H_{32}O_4Na$ 491.2198, found 491.2196.

((2,5-Dimethoxyphenyl)(3-phenylpropoxy)methylene)dibenzene (6). Synthesis of **6**, starting with 2-(diphenyl(3-phenylpropoxy)methyl)-4-methoxyphenol (123 mg, 0.40 mmol), was similar to that of **7**. The crude product was purified with flash column chromatography (petroleum ether/ethyl acetate = 20/1) to provide **6** (120 mg, 68%) as a white solid: R_f 0.3 (petroleum ether/ethyl acetate = 20/1); ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.45 (d, *J* = 3.0 Hz, 1 H), 7.38 (m, 4 H), 7.19−6.96 (m, 11 H), 6.64 (dd, *J* = 3.0, 8.8 Hz, 1 H), 6.57 (d, *J* = 8.8 Hz, 1 H), 3.65 (s, 3 H), 3.19 (s, 3 H), 2.94 (t, *J* = 6.3 Hz, 2 H), 2.58 (m, 2 H), 1.80 (m, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 153.6, 150.6, 142.5, 142.1, 134.9, 128.7, 128.3, 128.13, 127.08, 126.5, 125.5, 114.2, 113.4, 112.4, 84.6, 62.5, 55.5, 55.4, 32.5, 31.8; IR (neat) 3030, 2941, 2249, 1465, 1418, 1275, 1224, 1181, 1021, 982, 881, 802, 731; HRMS (ESI) *m*/*e* calcd for $C_{30}H_{30}O_3Na$ 461.2093, found 461.2092.

2-(Hydroxydiphenylmethyl)-4,6-dimethoxyphenol (8). To a stirred solution of 2-(hydroxydiphenylmethyl)-4,6-dimethoxyphenol (168 mg, 0.50 mmol) in dichloromethane (0.5 mL) was added triethylamine (77 μL, 0.55 mmol). Then acetyl chloride (36 μL, 0.50 mmol) was slowly added dropwise. The reaction mixture was stirred at room temperature under argon for 3 h. Then 3-phenyl-1-propanol (267 μL, 2.00 mmol) was added, and the reaction mixture was stirred at room temperature under argon overnight. The solvent was removed, and the residue was purified with flash column chromatography (petroleum ether/ethyl acetate = 5/1) to provide **8** (138 mg, 61%) as a colorless oil: R_f 0.4 (petroleum ether/ethyl acetate = 5/1); ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.50 (s, 1 H), 7.49−7.00 (m, 15 H), 6.42 (d, *J* = 2.8 Hz, 1 H), 6.21 (d, *J* = 2.8 Hz, 1 H), 3.79 (s, 3 H), 3.57 (s, 3 H), 3.26 (t, *J* = 6.3 Hz, 2 H), 2.67 (m, 2 H), 1.94 (m, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 151.7, 148.7, 141.2, 140.8, 139.5, 128.9, 128.5, 128.2, 128.1, 127.6, 127.5, 125.6, 105.5, 98.8, 89.6, 63.5, 55.8, 55.4, 32.1, 31.3; IR (neat) 3517, 3331, 3059, 2940, 1602, 1485, 1468, 1208, 1166, 1153, 1054, 1035, 957, 835, 732, 699; HRMS (ESI) *m*/*e* calcd for $C_{30}H_{30}O_4Na$ 477.2042, found 477.2042.

4-(Dimethylamino)-2-(diphenyl(3-phenylpropoxy)methyl)phenol (11). To a solution of 5-amino-2-hydroxybenzoic acid (3.094 g, 20 mmol) in methanol (40 mL) was added sulfuric acid (4.5 mL). The reaction mixture was refluxed at 85 °C for 19 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 5-amino-2-hydroxybenzoate (3.276 g, 98%) as a pale yellow solid.

To a solution of methyl 5-amino-2-hydroxybenzoate (1.672 g, 10 mmol) in acetic acid (30 mL) were added paraformaldehyde (3.161 g, 100 mmol) and sodium cyanoborohydride (1.885 g, 30 mmol) at room temperature. The reaction mixture was stirred for 17 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 ethyl acetate, and the organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated to provide methyl 5-(dimethylamino)-2-hydroxybenzoate (1.952 g, 99%) as a yellow oil.

To a solution of methyl 5-(dimethylamino)-2-hydroxybenzoate (1.952 g, 10 mmol) in freshly distilled tetrahydrofuran (10 mL) was slowly added phenyllithium (20 mL, 40 mmol, 2.0 M solution in dibutylether) at −78 °C under argon protection. The reaction temperature was raised to room temperature over 8 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, washed with brine, and concentrated. The residue was purified by recrystallization to provide 4-(dimethylamino)-2-(hydroxydiphenylmethyl)phenol (2.565 g, 80%) as a pale white solid.

To a stirred solution of 4-(dimethylamino)-2-(hydroxydiphenylmethyl)phenol (160 mg, 0.50 mmol) in dichloromethane (0.5 mL) was added triethylamine (77 μL, 0.55 mmol). Then acetyl chloride (36 μL, 0.50 mmol) was slowly added dropwisely. The reaction mixture was stirred at room temperature under argon for 3 h. Then 3-phenyl-1-propanol (267 μL, 2.00 mmol) was added, and the reaction mixture was stirred at room temperature under argon overnight. The solvent was removed, and the residue was purified with flash column chromatography (petroleum ether/ethyl acetate = 4/1) to provide **11** (151 mg, 69%) as a colorless or light pink oil: R_f 0.5 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.35 (s, 1 H), 7.36−6.98 (m, 15 H), 6.71

(d, J = 8.8 Hz, 1 H), 6.62 (dd, J = 2.9, 8.8 Hz, 1 H), 6.33 (d, J = 2.9 Hz, 1 H), 3.24 (t, J = 6.4 Hz, 2 H), 2.62−2.57 (m, 8H), 1.84−1.94 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.7, 143.9, 141.3, 141.2, 129.0, 128.3, 128.2, 128.1, 127.8, 127.6, 125.8, 117.7, 116.7, 115.2, 90.2, 63.8, 41.9, 32.2, 31.5; IR (neat) 3348, 3032, 2936, 2875, 2798, 1673, 1497, 1449, 1236, 1210, 1121, 1022, 982, 883, 748, 701, 612; HRMS (ESI) m/e calcd for $C_{30}H_{32}NO_2$ 438.2433, found 438.2433.

3-(Diphenyl(3-phenylpropoxy)methyl)-4-methoxy-*N*,*N*-dimethylaniline (9). To a stirred solution of **11** (138 mg, 0.315 mmol) in THF (0.5 mL) was added sodium hydride (19 mg, 0.473 mmol). The reaction mixture was stirred at room temperature for 1 h. Then iodomethane (159 μL, 2.523 mmol) was added, and the reaction mixture was stirred for 5 h. The solvent was removed, and the reaction mixture was dissolved in DMF (1.0 mL). Sodium thiosulfate (157 mg, 0.631 mmol) was added, and the reaction mixture was stirred at 100 °C under argon. The crude product was washed with water and extracted with dichloromethane. The organic layer was combined, dried over anhydrous sodium sulfate, and concentrated. The residue was purified with flash column chromatography (petroleum ether/ethyl acetate = 7/1) to provide **9** (98 mg, 73%) as a pale yellow solid: R_f 0.4 (petroleum ether/ethyl acetate = 7/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (m, 5 H), 7.32−7.08 (m, 11 H), 6.74 (d, J = 8.7 Hz, 1 H), 6.68 (dd, J = 2.9, 8.7 Hz, 1 H), 3.32 (s, 3 H), 3.05 (t, J = 6.3 Hz, 2 H), 2.90 (s, 6 H), 2.70 (m, 2 H), 1.91 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 136.9, 130.4, 128.4, 128.2, 128.1, 125.6, 117.8, 113.4, 112.7, 111.0, 86.5, 62.8, 55.2, 40.8, 32.8, 32.2; IR(neat) 2941, 2845, 1605, 1502, 1452, 1249, 1181, 977, 802, 748, 732, 699; HRMS (ESI) m/e calcd for $C_{31}H_{34}NO_2$ 452.2590, found 452.2586.

4-((*tert*-Butyldimethylsilyl)oxy)-3-(diphenyl(3-phenylpropoxy)methyl)-*N*,*N*-dimethylaniline (10). To a stirred solution of **11** (44 mg, 0.10 mmol) in dichloromethane (0.1 mL) were added *tert*-butylchlorodimethylsilane (30 mg, 0.20 mmol) and imidazole (20 mg, 0.30 mmol). The reaction mixture was stirred at room temperature overnight. The solvent was removed, and the residue was purified with flash column chromatography (petroleum ether/ethyl acetate = 12/1) to provide **10** (51 mg, 93%) as a colorless oil: R_f 0.3 (petroleum ether/ethyl acetate = 12/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.50 (m, 4 H), 7.33 (d, J = 2.5 Hz, 1 H), 7.12−7.27 (m, 11 H), 6.66 (dd, J = 0.5, 8.6 Hz, 1 H), 6.62 (dd, J = 2.7, 8.8 Hz, 1 H), 3.07 (t, J = 6.5 Hz, 2 H), 2.86 (s, 6 H), 2.68−2.73 (m, 2 H), 1.88−1.98 (m, 2 H), 0.72 (s, 9 H), −0.13 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 144.8, 143.4, 142.3, 133.5, 128.5, 128.3, 128.2, 127.3, 126.3, 125.6, 119.1, 115.7, 113.3, 85.2, 62.8, 41.7, 32.7, 32.0, 26.1, 18.6, −4.5; IR (neat) 3030, 2937, 2864, 2797, 1605, 1496, 1473, 1450, 1254, 979, 836, 739; HRMS (ESI) m/e calcd for $C_{36}H_{46}NO_2Si$ 552.3298, found 552.3303.

4-(Dimethylamino)-2-(diphenyl(3-phenylpropoxy)methyl)-phenyl Acetate (12). To a stirred solution of **11** (44 mg, 0.10 mmol) in dichloromethane (0.1 mL) were added acetyl chloride (8 μL, 0.11 mmol) and pyridine (9 μL, 0.11 mmol). The reaction mixture was stirred at 40 °C for 6 h. The solvent was removed and the residue was purified with flash column chromatography (petroleum ether/ethyl acetate = 5/1) to provide **12** (39 mg, 81%) as a white solid: R_f 0.4 (petroleum ether/ethyl acetate = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (m, 4 H), 7.26−7.04 (m, 12 H), 6.85 (d, J = 8.8 Hz, 1 H), 6.60 (dd, J = 3.1, 8.8 Hz, 1 H), 3.04 (t, J = 6.3 Hz, 2 H), 2.84 (s, 6 H), 2.66 (m, 2 H), 1.86 (m, 2 H), 1.47 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 148.1, 143.6, 142.3, 138.8, 135.6, 128.4, 128.3, 127.8, 127.7, 126.7, 125.7, 124.6, 113.8, 112.2, 100.0, 84.9, 63.0, 41.0, 32.6, 20.5; IR (neat) 3353, 3039, 2785, 2771, 2105, 2083, 1758, 1606, 1499, 1454, 1366, 1209, 747; HRMS (ESI) m/e calcd for $C_{32}H_{34}NO_3$ 480.2539, found 480.2535.

3-(((2*R*,3*R*,4*R*,5*S*,6*S*)-3,4,5-Tris(benzyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)propan-1-ol (32a). $BH_3 \cdot Me_2S$ (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-enyloxytetrahydropyran (0.608 g, 1.2 mmol). Following the addition, the solution was stirred at room temperature for 1.5 h. Ethanol (0.4 mL) was then added followed by 0.18 mL of 3 N sodium hydroxide. After the mixture was cooled to 0−5 °C, hydrogen peroxide (35%, 0.2 mL) was added dropwise and the reaction mixture was stirred overnight. After being heated at 80 °C for 1 h, the cooled solution was extracted with ether (10 mL × 4). The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. Flash column chromatography on silica gel, eluted with petroleum ether/ethyl acetate = 3/1, afforded **32a** (0.557 g, 88%) as a colorless oil: R_f 0.3 (petroleum ether/ethyl acetate = 3/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.20 (m, 14 H), 4.93 (d, J = 10.8 Hz, 1 H), 4.69 (m, 6 H), 3.71 (m, 8 H), 3.43 (td, J = 6.0, 9.8 Hz, 1 H), 2.19 (s, 1 H), 1.74 (p, J = 6.0 Hz, 2 H), 1.33 (d, J = 5.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 138.3, 138.2, 128.2, 127.9, 127.7, 127.5, 127.4, 97.9, 80.3, 79.9, 75.2, 74.9, 72.7, 72.1, 67.9, 64.9, 60.2, 31.9, 17.9; IR (neat) 3426, 3036, 2920, 1724, 1456, 1383, 1281, 1145, 980, 843, 732; HRMS (ESI) m/e calcd for $C_{30}H_{36}O_6Na$ 515.2410, found 515.2414.

3-(((2*S*,3*R*,4*S*,5*R*)-3,4,5-Tris(benzyloxy)tetrahydro-2*H*-pyran-2-yl)oxy)propan-1-ol (32b). $BH_3 \cdot Me_2S$ (350 mg, 4.34 mmol) was added dropwise at 0 °C under argon to a solution of 2-allyloxy-3,4,5-tris(benzyloxy)tetrahydropyran (1.0 g, 2.17 mmol) in THF (8 mL), and the resultant solution was stirred at room temperature for 13 h. Then hydrogen peroxide (35%, 2.0 mL) and sodium hydroxide (3 N, 20 mL) were added subsequently at room temperature, and the reaction mixture was stirred for a further 6 h. Workup as usual followed by flash column chromatography afforded **32b** (0.845 g, 81%) as a colorless oil: R_f 0.3 (petroleum ether/ethyl acetate = 3/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.22 (m, 13 H), 4.87 (m, 2 H), 4.75 (dd, J = 11.9, 13.4 Hz, 2 H), 4.61 (m, 3 H), 3.81 (m, 5 H), 3.50 (m, 6 H), 1.83 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 138.1, 138.0, 128.32, 128.31, 128.2, 127.9, 127.8, 127.7, 127.6, 127.4, 97.2, 81.3, 79.3, 77.8, 75.6, 73.4, 73.3, 67.1, 61.3, 59.9, 31.5; IR (neat) 3464, 3034, 2929, 2884, 1723, 1455, 1366, 1274, 1207, 1156, 975, 726; HRMS (ESI) m/e calcd for $C_{29}H_{34}O_6Na$ 501.2253, found 501.2252.

3-(((2*S*,3*S*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-((benzyloxy)-methyl)tetrahydro-2*H*-pyran-2-yl)oxy)propan-1-ol (32c). $BH_3 \cdot Me_2S$ (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-tetrahydropyran (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 subsequently at room temperature, and the reaction mixture was stirred for further 6 h. Workup as usual followed by flash column chromatography afforded **32c** (0.829 g, 80%) as a colorless oil: R_f 0.3 (petroleum ether/ethyl acetate = 3/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.10 (m, 20 H), 4.93−4.49 (m, 9 H), 4.00−3.58 (m, 9 H), 3.48 (td, J = 5.7, 9.8 Hz, 1 H), 2.13 (s, 1H), 1.75 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 138.27, 138.26, 138.1, 128.28, 128.23, 127.9, 127.7, 127.58, 127.55, 127.5, 127.4, 97.9, 80.1, 75.0, 74.9, 74.8, 73.3, 72.6, 72.1, 71.9, 69.2, 64.9, 60.0, 32.0; IR (neat) 3466, 3037, 2915, 1722, 1455, 1362, 1270, 1020, 1010, 972, 847, 725; HRMS (ESI) m/e calcd for $C_{37}H_{42}O_7Na$ 621.2828, found 621.2829.

Preparation of 33a−c: Representative Procedure for Preparing 33a. In a reaction vessel, **32a** (98 mg, 0.2 mmol) and (3-(dimethylamino)phenyl)diphenylmethyl acetate (DMATr PPG) (104 mg, 0.3 mmol) in toluene (50 μL) were heated at 120 °C under argon protection for 3 h. The reaction mixture was directly purified with column chromatography (petroleum ether/ethyl acetate = 5/1) to provide **33a** (139 mg, 89%): R_f 0.4 (petroleum ether/ethyl acetate = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.07 (m, 26 H), 6.86 (s, 1 H), 6.75 (d, J = 7.8 Hz, 1 H), 6.59 (dd, J = 2.1, 8.1 Hz, 1 H), 4.93 (d, J = 10.8 Hz, 1 H), 4.71 (m, 3 H), 4.62 (d, J = 10.9 Hz, 1 H), 4.55 (s, 2 H), 3.64 (m, 6 H), 3.12 (m, 2 H), 2.85 (s, 6 H), 1.82 (m, J = 6.4 Hz, 2 H), 1.29 (d, J = 5.9 Hz, 3 H);); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 144.8, 144.6, 144.5, 138.7, 138.66, 138.4, 128.8, 128.7, 128.28, 128.26, 127.9, 127.8, 127.5, 127.4, 126.7, 117.6, 113.3, 111.1, 97.8, 86.6, 80.5, 80.3, 75.3, 75.0, 72.7, 72.1, 67.9, 64.5, 60.3, 40.7, 30.1, 18.0; IR (neat) 3034, 2925, 2808, 1600, 1491, 1452, 1354, 1267, 1211, 1142, 1020, 974, 745, 699; HRMS (ESI) *m/e* calcd for $C_{51}H_{56}NO_6$ 778.4108, found 778.4115.

33b. Prepared from **32b** (96 mg, 0.2 mmol) and (3-(dimethylamino)-phenyl)diphenylmethyl acetate (DMATr PPG) (104 mg, 0.3 mmol) in toluene (50 μL) by using the procedure of **33a**. The reaction mixture was directly purified with column chromatography (petroleum ether/ethyl acetate =5/1) to provide **33b** (140 mg, 91%): R_f 0.4 (petroleum ether/ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, J = 8.3 Hz, 4 H), 7.40−7.10 (m, 22 H), 6.89 (s, 1 H), 6.76 (d, J = 8.4 Hz, 1 H), 6.59 (dd, J = 2.1, 8.2 Hz, 1 H), 4.86 (q, J = 10.8 Hz, 2 H), 4.68 (m, 3 H), 4.57 (d, J = 12.3 Hz, 2 H), 3.83 (m, 2 H), 3.54 (m, 4 H), 3.40 (dd, J = 3.6, 9.6 Hz, 1 H), 3.20 (t, J = 6.1 Hz, 2 H), 2.86 (s, 6 H), 1.96 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 144.9, 144.6, 144.5, 139.0, 138.37, 138.35, 128.8, 128.7, 128.33, 128.32, 128.28, 128.25, 128.0, 127.9, 127.73, 127.68, 127.66, 127.54, 127.47, 126.70, 126.69, 117.6, 113.2, 111.1, 97.0, 86.7, 81.3, 79.7, 78.2, 75.7, 73.4, 73.1, 65.3, 60.6, 59.9, 40.6, 30.2; IR (neat) 3032, 2925, 2881, 1602, 1495, 1456, 1364, 746, 698; HRMS (ESI) *m/e* calcd for $C_{50}H_{54}NO_6$ 764.3951, found 764.3944.

33c. Prepared from **32c** (120 mg, 0.2 mmol) and (3-(dimethylamino)-phenyl)diphenylmethyl acetate (DMATr PPG) (104 mg, 0.3 mmol) in toluene (50 μL) by using the procedure of **33a**. The reaction mixture was directly purified with column chromatography (petroleum ether/ethyl acetate =9/1) to provide **33c** (162 mg, 91%): R_f 0.1(petroleum ether/ethyl acetate = 9/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, J = 7.2 Hz, 4 H), 7.39−7.00 (m, 27 H), 6.85 (s, 1 H), 6.76 (d, J = 8.1 Hz, 1 H), 6.56 (dd, J = 2.3, 8.1 Hz, 1 H), 4.87 (dd, J = 4.6, 6.2 Hz, 2 H), 4.67 (m, 3 H), 4.50 (m, 4 H), 4.01 (t, J = 9.5 Hz, 1 H), 3.77 (m, 6 H), 3.53 (m, 1 H), 3.13 (m, 2 H), 2.82 (s, 6 H), 1.84 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 144.7, 144.5, 144.4, 138.5, 138.4, 138.3, 128.7, 128.6, 128.20, 128.18, 128.14, 128.12, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 126.6, 117.5, 113.2, 111.0, 97.7, 86.6, 80.3, 74.9, 74.8, 73.3, 72.4, 72.0, 71.7, 69.1, 64.5, 60.2, 40.5, 30.0; IR (neat) 3036, 2925, 2874, 2806, 1600, 1495, 1453, 1359, 1267, 1211, 1141, 1013, 973, 729; HRMS (ESI) *m/e* calcd for $C_{58}H_{62}NO_7$ 884.4526, found 884.4542.

(2*R*,3*R*,4*S*,5*S*,6*S*)-2-(Acetoxymethyl)-6-(3-hydroxypropoxy)-tetrahydro-2*H*-pyran-3,4,5-triyl Triacetate (36). $BF_3 \cdot OEt_2$ (0.8 mL, 6.3 mmol) was added to the solution of **35** (0.8 g, 2.1 mmol) and 1,3-propanediol (0.346 g, 4.6 mmol) in DCM/CH_3CN (13 mL, 1:1, V/V) at 0 °C. The mixture was stirred at room temperature for 57 h. Workup as usual followed by flash chromatography (DCM/ethyl acetate =1/1, R_f 0.3) to afford the title compound **36** (0.157 g, 18%).

34. The mixture of **36** (0.134 g, 0.32 mmol) and DMATr PPG (0.157 g, 0.51 mmol) was heated at 120 °C for 3 h. The reaction mixture was purified by flash column chromatography (petroleum ether/ethyl acetate =5/2, R_f 0.3) to afford the desired PPG protected product (0.223 g, 99%). The above obtained product (0.200 g, 0.28 mmol, 1 equiv) was stirred with K_2CO_3 (0.120 g, 0.87 mmol) in methanol for 135 min. The solvent was removed, and the residue was extracted with ethyl acetate. The combined extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography to afford the title compound **34** (0.142 g, 96%): R_f 0.4 (DCM/ethyl acetate = 6/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J = 7.7 Hz, 4 H), 7.29−7.07 (m, 7 H), 6.83 (s, 1 H), 6.74 (d, J = 7.6 Hz, 1 H), 6.60 (dd, J = 2.1, 8.2 Hz, 1 H), 4.75 (s, 1 H), 3.65 (m, 9 H), 3.11 (m, 2 H), 2.82 (s, 6 H), 1.81 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 144.7, 144.5, 144.4, 128.6, 128.3, 127.6, 126.8, 118.0, 113.7, 111.5, 86.7, 72.0, 71.4, 70.9, 66.1, 65.0, 60.8, 60.7, 60.1, 40.8, 30.0; IR (neat) 3392, 2925, 1603, 1392, 1139, 675; HRMS (ESI) *m/e* calcd for $C_{30}H_{38}NO_7$ 524.2648, found 524.2649.

3-(Methoxydiphenylmethyl)-*N*,*N*-dimethylaniline (38): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (m, 4 H), 7.34−7.10 (m, 7 H), 6.88 (m, 1 H), 6.76 (d, J = 7.8 Hz, 1 H), 6.62 (dd, J = 2.6, 8.2 Hz, 1 H), 3.08 (s, 3 H), 2.88 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 144.4, 144.2, 128.7, 128.2, 127.5, 126.7, 117.7, 113.4, 111.1, 87.3, 52.1, 40.6; IR (neat) 3052, 2940, 2823, 1695, 1597, 1490, 1446, 1349, 1223, 1179, 858, 741; HRMS (ESI) *m/e* calcd for $C_{22}H_{24}NO$ 318.1858, found 318.1854.

(3-(Dimethylamino)phenyl)diphenylmethanol (39): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.20 (m, 10 H), 7.14 (t, J = 8.0 Hz, 1 H), 6.71 (m, 1 H), 6.64 (dd, J = 2.6, 8.2 Hz, 1 H), 6.51 (d, J = 7.7 Hz, 1 H), 2.84 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 147.7, 147.0, 128.4, 127.9, 127.7, 127.0, 116.7, 112.4, 111.4, 82.2, 40.5; IR (neat) 3455, 3066, 2886, 2804, 1719, 1602, 1490, 1446, 1349, 1150, 853, 746; HRMS (ESI) *m/e* calcd for $C_{21}H_{22}NO$ 304.1701, found 304.1696.

3-Benzhydryl-*N*,*N*-dimethylaniline (40): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.10 (m, 11 H), 6.60 (dd, J = 2.5, 7.8 Hz, 1 H), 6.52 (m, 1 H), 6.46 (d, J = 8.0 Hz, 1 H), 5.50 (s, 1 H), 2.87 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.5, 144.6, 144.1, 129.4, 128.8, 128.1, 126.1, 118.0, 114.0, 110.5, 57.2, 40.5; IR (neat) 2803, 1656, 1490, 1442, 1349, 1135, 828; HRMS (ESI) *m/e* calcd for $C_{21}H_{22}N$ 288.1752, found 288.1753.

General Procedure of Deprotection of 33a−d and 34 with Sunlight. The Pyrex test tubes (16 × 150 mm) containing the solution of **33a**−**d** or **34** (5 mM in MeOH/MeCN = 14/1, MeOH or MeOH/H_2O = 1/1) were kept in a water bath (20−30 °C) and placed outdoors under sunlight in clear weather. After 4.5 h, the reaction mixture was concentrated, and the residue was purified with column chromatography to provide **32a**−**d** or **37**.

Deprotection of 33a. Compound **33a** (58.3 mg, 0.075 mmol) was irradiated by using the general deprotection procedure to produce **32a** (29.8 mg, 84%) after column chromatography (petroleum ether/ethyl acetate = 1/1).

Deprotection of 33b. Compound **33b** (80 mg, 0.105 mmol) was irradiated by using the general deprotection procedure. The residue was purified with column chromatography (petroleum ether/ethyl acetate = 1/1) to provide **32b** (42.1 mg, 84%).

Deprotection of 33c. The compound **33c** (133 mg, 0.15 mmol) was irradiated by using the general deprotection procedure. The residue was purified with column chromatography (petroleum ether/ethyl acetate = 1/1) to provide **32c** (74.0 mg, 82%).

Deprotection of 33d. The compound **33d** (80 mg, 0.15 mmol) was irradiated by using the general deprotection procedure. The residue was purified with column chromatography (petroleum ether/ethyl acetate = 3/1) to provide **32d** (30.6 mg, 83%).

Deprotection of 34

1. Compound **34** (80 mg, 0.153 mmol) was irradiated by using the general deprotection procedure. The residue was purified with column chromatography to provide **38** (18.9 mg, 39%), **39** (2.1 mg, 5%), and **40** (4.8 mg, 11%) (eluted with petroleum ether/ethyl acetate = 9/1) and **37** (30.9 mg, 84%) (eluted with dichloromethane/methanol = 5/1).
2. A 26.7 mL solution of **34** (70 mg, 0.134 mmol) in MeOH in two Pyrex test tubes was irradiated by using the general deprotection procedure. The residue was purified with column chromatography to provide **38** (18.2 mg, 43%), **39** (2.0 mg, 5%) and **40** (4.3 mg, 11%) (eluted with petroleum ether/ethyl acetate = 9/1) and **37** (27.8 mg, 87%) (eluted with dichloromethane/methanol =5/1).
3. A 30 mL solution of **34** (80 mg, 0.153 mmol) in MeOH/H_2O = 1/1 in two Pyrex test tubes was irradiated by using the general deprotection procedure. The residue was purified with column chromatography to provide **38** (19.8 mg, 41%), **39** (12.4 mg, 27%) and **40** (1.8 mg, 4%) (eluted with petroleum ether/ethyl acetate = 9/1) and **37** (35.4 mg, 97%) (eluted with dichloromethane/methanol =5/1).

Photoreaction of Water-Soluble Compound 44. To the stirred solution of **34** (181.4 mg, 0.346 mmol) in 4.7 mL of dichloromethane was added succinic anhydride (175 mg, 1.732 mmol), followed by Et_3N (242 μL, 1.732 mmol). After 19 h, the reaction was complete. Formation of the derivative **44** was confirmed by the characteristic peaks in the ^{1}H NMR: δ 6.84 (s, 1H), 6.74 (d, J = 7.7 Hz, 1H), 6.61 (dd, J = 2.4, 8.2 Hz, 1H), 5.40 (dd, J = 10.1, 10.1 Hz, 1H), 5.25 (dd, J = 3.4, 10.1 Hz, 1H), 5.16 (m, 1H), 4.18 (dd, J = 3.0, 12.6 Hz, 1H), 4.75 (s, 1H), 4.02 (d, J = 5.5 Hz, 1H). The mixture was concentrated, and half of it was dissolved in water (34.6 mL) with Na_2CO_3 (1.3 mg, 0.1 equiv) in a test tube. The obtained clear solution was stirred under sunlight for 4.5 h and then was treated with NaOH (279 mg, 7 mmol). Water was removed, and the residue was subjected to flash column chromatography, eluted with PE/EA = 5:1 and DCM/MeOH = 5:1, to provide **34** (33.8 mg, 37%), **37** (21.8 mg, 52%), **39** (14.6 mg, 27%), **40** (6.2 mg, 12%), **42** (3.7 mg, 7%), and **43** (3.4 mg, 7%).

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** General procedure; ^{1}H NMR and ^{13}C NMR spectra of **4**, **6**−**15**, **32a**−**32c**, **33a**−**33c**, **36**, and **38**−**40**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: wangp@uab.edu.

■ ACKNOWLEDGMENT

We thank the NSF for its support (CHE-0848489).

■ REFERENCES

(1) (a) Pillai, V. *Synthesis* **1980**, 1. (b) Pillai, V. *Org. Photochem.* **1987**, *9*, 225. (c) Guillier, F.; Orain, D.; Bradley, M. *Chem. Rev.* **2000**, *100*, 2091. (d) Pellicioli, A.; Wirz, J. *Photochem. Photobiol. Sci.* **2002**, *1*, 441. (e) Bochet, C.; Blanc, A. In *Handbook of Synthetic Photochemistry*; Albini, A., Fagnoni, M., Eds.; Wiley-VCH: Weinheim, 2010.

(2) (a) Goeldner, M., Givens, R. S., Eds. *Dynamic Studies in Biology*; Wiley-VCH: Weinheim, 2005. (b) Mayer, G.; Heckel, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4900.

(3) (a) Pirrung, M. *Chem. Rev.* **1997**, *97*, 473. (b) Fodor, S.; Read, J.; Pirrung, M.; Stryer, L.; Lu, A.; Solas, D. *Synthesis* **1991**, *251*, 767. (c) Woll, D.; Walbert, S.; Stengele, K.; Green, R.; Albert, T.; Pfleiderer, W.; Steiner, U. *Nucleosides, Nucleotides Nucleic Acids* **2003**, *22*, 1395. (d) Bochet, C. *J. Chem. Soc., Perkin Trans. 1* **2002**, 125.

(4) For recent hydroxyl PPGs, see: (a) Pirrung, M.; Lee, Y.; Park, K.; Springer, J. *J. Org. Chem.* **1999**, *64*, 5042. (b) Furuta, T.; Hirayama, Y.; Iwamura, M. *Org. Lett.* **2001**, *3*, 1809. (c) Coleman, M.; Boyd, M. *J. Org. Chem.* **2002**, *67*, 7641. (d) Pika, J.; Konosonoks, A.; Robinson, R.; Singh, P.; Gudmundsdottir, A. *J. Org. Chem.* **2003**, *68*, 1964. (e) Suzuki, A.; Watanabe, T.; Kawamoto, M.; Nishiyama, K.; Yamashita, H.; Ishii, M.; Iwamura, M.; Furuta, T. *Org. Lett.* **2003**, *5*, 4867. (f) Lukeman, M.; Scaiano, J. *J. Am. Chem. Soc.* **2005**, *127*, 7698. (g) Woll, D.; Smirnova, J.; Pfleiderer, W.; Steiner, U. *Angew. Chem., Int. Ed.* **2006**, *45*, 2975. (h) Ma, C.; Chen, Y.; Steinmetz, M. *J. Org. Chem.* **2006**, *71*, 4206. (i) Momotake, A.; Lindegger, N.; Niggli, E.; Barsotti, R.; Ellis-Davies, G. *Nature Methods* **2006**, *3*, 35. (j) Zhu, Y.; Pavlos, C.; Toscano, J.; Dore, T. *J. Am. Chem. Soc.* **2006**, *128*, 4267. (k) Kostikov, A.; Popik, V. *J. Org. Chem.* **2007**, *72*, 9190. (l) Hagen, V.; Dekowski, B.; Kotzur, N.; Lechler, R.; Wiesner, B.; Briand, B.; Beyermann, M. *Chem.—Eur. J.* **2008**, *14*, 1621. (m) Hagen, V.; Kilic, F.; Schaal, J.; Dekowski, B.; Schmidt, R.; Kotzur, N. *J. Org. Chem.* **2010**, *75*, 2790. (n) Kammari, L.; Solomek, T.; Ngoy, B.; Heger, D.; Klan, P. *J. Am. Chem. Soc.* **2010**, *132*, 11431.

(5) A few examples of recent PPG applications: (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. *Nature Methods* **2009**, *6*, 527. (k) Casey, J.; Blidner, R.; Monroe, W. *Mol. Pharmaceutics* **2009**, *6*, 669. (l) Young, D.; Lively, M.; Deiters, A. *J. Am. Chem. Soc.* **2010**, *132*, 6183. (m) Mizukami, S.; Hosoda, M.; Satake, T.; Okada, S.; Hori, Y.; Furuta, T.; Kikuchi, K. *J. Am. Chem. Soc.* **2010**, *132*, 9524. (n) Fomina, N.; McFearin, C.; Sermsakdi, M.; Edigin, O.; Almutairi, A. *J. Am. Chem. Soc.* **2010**, *132*, 9540.

(6) Wang, P.; Zhou, L.; Zhang, X.; Liang, X. *Chem. Commun.* **2010**, *46*, 1514.

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

(8) Solvent effects were examined.[6] Among different solvents or solvent combinations, methanol leads to cleaner reactions and better yields of the released alcohols.

(9) A trityl cation has long been known as a good hydride acceptor: (a) Norris, J.; Young, R. *J. Am. Chem. Soc.* **1930**, *52*, 753. (b) Smith, H.; Smith, R. *J. Am. Chem. Soc.* **1948**, *70*, 2400. (c) Bartlett, P.; McCollum, J. *J. Am. Chem. Soc.* **1956**, *78*, 1441. (d) Barton, D.; Magnus, P.; Smith, G.; Zurr, D. *Chem. Commun.* **1971**, 861. (e) Doyle, M.; DeBruyn, D.; Scholten, D. *J. Org. Chem.* **1972**, *38*, 625. (f) June, M.; Speltz, L. *J. Am. Chem. Soc.* **1976**, *98*, 7882.

(10) (a) It is also likely that the oxidation occurred via hydrogen abstraction by the ground state triplet of α,α-diphenyl-3-(dimethylamino)-benzyl cation. (b) Perrotta, R.; Winter, A.; Falvey, D. *Org. Lett.* **2011**, *13*, 212. (c) Winter, A.; Falvey, D.; Cramer, C.; Gherman, B. *J. Am. Chem. Soc.* **2007**, *129*, 10113.

(11) Quantum yields were determined by chemical actinometry. Defoin, A.; Defoin-Straatmann, R.; Hildenbrand, K.; Bittersmann, E.; Kreft, D.; Kuhn, H. *J. Photochem.* **1986**, *33*, 237.

(12) The monochromatic lights were obtained by using various filter solutions: (a) Zimmerman, H.; Nuss, J.; Tantillo, A. *J. Org. Chem.* **1988**, *53*, 3792. (b) Zimmerman, H. *Mol. Photochem.* **1971**, *3*, 281.

(13) Wan, P.; Chak, B. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1751.

(14) (a) Kostikov, A.; Malashikhina, N.; Popik, V. *J. Org. Chem.* **2009**, *74*, 1802. (b) Kostikov, A.; Popik, V. *Org. Lett.* **2008**, *10*, 5277.

(15) Chen, C.; Kuo, J.; Pawar, V.; Munot, Y.; Weng, S.; Ku, C.; Liu, C. *J. Org. Chem.* **2005**, *70*, 1188.