Photochemically Removable Silyl Protecting Groups

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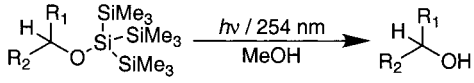
Abstract: Several *o*-phenol-containing alkoxyvinylsilanes were prepared and their photochemistry was investigated. These materials were prepared via hydrosilylation of the corresponding *o*-acetoxy arylacetylenes. Two major classes of photochemical processes were identified in these reactants: trans→cis isomerization, leading to an intramolecular nucleophilic substitution process at silicon, and 1,5-silyl shift, leading to an unsymmetrical dialkoxysilane. The major outcome of this work is a novel class of photochemically removable protecting groups. Two alkyl substitutions on silicon, the dimethyl and diisopropyl, were examined. The latter is more stable and is preferred for protecting groups that must tolerate multiple steps or reagents. Protection of alcohols is generally performed starting with the arylethynyl acetate, which can be subjected to hydrosilylation, alcohol substitution, and acetate deprotection without isolation of intermediates. Two groups were studied in detail, the phenol and 2-naphthol vinyl silane derivatives. A variety of primary and secondary alcohols were protected with these reagents. These groups can be deprotected cleanly and in high yield by irradiation from 250 to 350 nm.

Introduction

Photochemically removable protecting groups[1] are an essential part of several areas of science and technology. The ability to control the unmasking of particular N-, O-, and S-containing functionalities enables chemical reactivity to be "turned on" with the time resolution of the duration of a light pulse and the rate of deprotection. This ability has led to the widespread development of "caged" compounds for the kinetic study of biological processes.[2] It can also be applied to the three-dimensional mapping of biological processes, through spatially defined control of deprotection chemistry based on the optical direction of light. Spatial control of photochemistry is intrinsic to photolithography, which allows for the fabrication of microelectronic[3] and microfluidic[4] devices, and is essential to light-directed synthesis of polymer chains.[5]

One area of protecting group chemistry that has been heavily developed in recent years is that of silyl groups.[6] Important applications for silyl protecting groups have been found in the synthesis of nucleotides and nucleosides.[7] Extremely fine control over both the stability of groups to different reagents/reaction conditions and the ability to selectively remove them in the presence of other functionalities, including other silyl groups, has enabled many advances in organic synthesis. Given the general importance of photochemically removable protecting groups, it is somewhat surprising that photochemically removable silyl groups had not been developed. The first report of such a group appeared in 1993,[8] in a study that formed the basis for the work reported here. Subsequently, Brook reported that the tris(trimethylsilyl)silyl (sisyl) group is removed by short-wavelength UV irradiation (eq 1).[9] However, many of the



(1)

biological molecules that would be targets for use in photochemical protection would not be stable under these irradiation conditions. Our original work also used short-wavelength irradiation, though later studies showed that our initial groups were also sensitive at longer wavelengths. However, the continued development of this chemistry clearly called for a group that was reactive with longer wavelengths.

Results

Our strategy for removing a silyl group photochemically draws on the previous results of Porter, concerning the deprotection of serines at protease active sites that have been acylated with *o*-hydroxycinnamates.[10] It employs a photochemical trans→cis isomerization that brings the ester into the proximity of the phenol, which lactonizes, releasing the alcohol of the

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(1) Pillai, V. N. R. *Synthesis* **1980**, 1.
(2) *Methods Enzymol.* **1998**, *291*, 1−490.
(3) Wallraff, G. M.; Hinsberg, W. D. *Chem. Rev.* **1999**, *99*, 1801−1821. *Introduction to Microlithography*; Thompson, L. F., Willson, C. G., Bowden, M. J., Eds.; American Chemical Society: Washington, DC, 1994.
(4) Regnier, F. E.; He, B.; Lin, S.; Busse, J. *Trends Biotechnol.* **1999**, *17*, 101−106. Sundberg, S. A. *Curr. Opin. Biotechnol.* **2000**, *11*, 47−53.
(5) Lipshutz, R. J.; Fodor, S. P.; Gingeras, T. R.; Lockhart, D. J. *Nat. Genet.* **1999**, *21*, 20−24.
(6) Pouzar, V. *Chem. Listy* **1988**, *82*, 715.
(7) Ogilvie, K. K. In *Nucleosides, Nucleotides, Their Biol. Appl., Proc. Int. Round Table*, 5th ed.; Rideout, J. L., Henry, D. W., Beacham, L. M., III, Eds.; Academic: New York, 1983; pp 209−256. Ogilvie, K. K.; Beaucage, S. L.; Entwistle, D. W.; Thompson, E. A.; Quilliam, M. A.; Westmore, J. B. *J. Carbohydr., Nucleosides, Nucleotides* **1976**, *3*, 197−227.
(8) Pirrung, M. C.; Lee, Y. R. *J. Org. Chem.* **1993**, *58*, 6961−6962.
(9) Brook, M. A.; Balduzzi, S.; Mohamed, M.; Gottardo, C. *Tetrahedron* **1999**, *55*, 10027−10040. Brook, M. A.; Gottardo, C.; Balduzzi, S.; Mohamed, M. *Tetrahedron Lett.* **1997**, *38*, 6997−7000.

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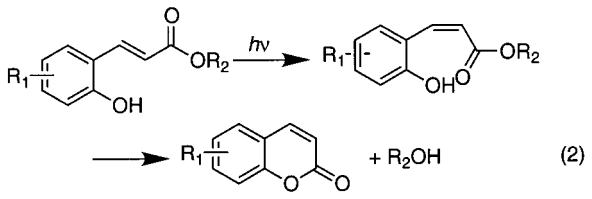
ester (eq 2). The stability of the ester, both to dark hydrolysis



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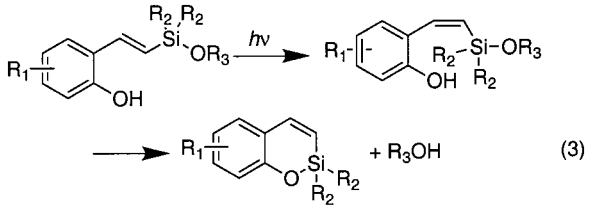
and to different wavelengths of light, can be tuned through substituent effects.

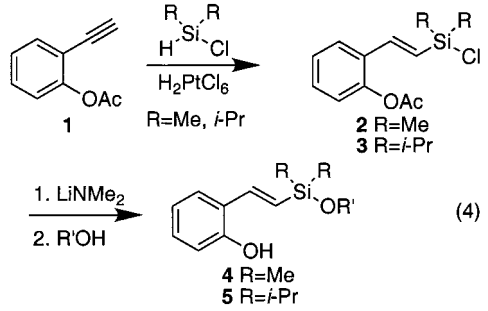
A similar principle could be applied to silyl deprotection (eq 3). Access to vinyl silanes suitable for formation of ethers of



(3)

this type was unknown, as was their stability and photochemistry.

The known *o*-ethynylphenol[11] was acetylated to form **1**, which was subjected to hydrosilation[12] with either dimethylchlorosilane or diisopropylchlorosilane catalyzed by chloroplatinic acid (eq 4). Product **2** was isolated and characterized, but both **2** and **3**



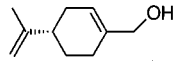
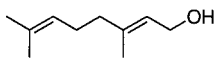
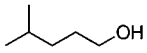
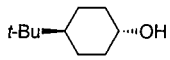
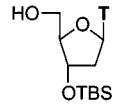
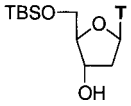
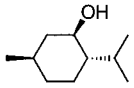
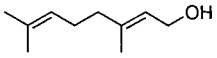
(4)

were generally taken forward without extensive purification. Simultaneous removal of the acetate and protection of the alcohol was accomplished in situ by treatment with lithium dimethylamide in THF (which also converts the chlorosilanes into the aminosilane derivatives), followed by addition of the alcohol to be protected (without any additional base).

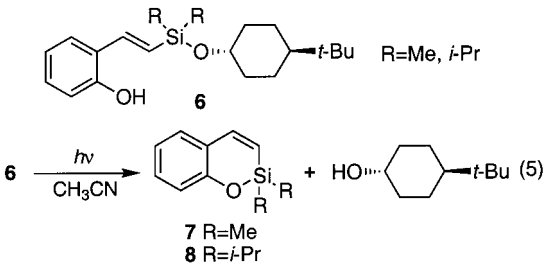
The protection of primary and secondary alcohols with **2** and **3** is readily accomplished, but tertiary alcohols are unreactive. The results are summarized in Table 1. The dimethylsilyl ethers form within 3 h, while the diisopropylsilyl ethers require overnight reaction, and in some cases warming. These compounds generally show a strong short-wavelength absorption band at 258 nm (log ϵ 4.28) and a somewhat weaker, but still significant, band at 309 nm (log ϵ 3.94).

The photochemistry of these compounds is solvent dependent. Irradiation of **6** (R = Me, Rayonet reactor, 254 nm, quartz reaction vessel) in acetonitrile produces **7** (84%) and the 4-*tert*-butylcyclohexanol within 30 min (eq 5). In benzene, **6** is

Table 1. Alcohols Protected with **2** and **3** and Their Deprotection Reactions

	Alcohol	Protection Yield[a]	Deprotection Yield[b]
a		80	83
b		92	91
c		95	89
d		86	84
e		76[c]	92
f		72[c]	91
g		91	87
h	H_3C-OH	82[d]	87
i		70[d]	75

[a] A THF solution of **2** or **3** (1.0 mmol) was treated with $LiNMe_2$ (1.0 mmol), and the alcohol (1.2 mmol), dissolved in 5 mL THF, was added. After stirring for 3 h at RT or 4 h at reflux (see below), thin-layer chromatography showed that the reaction was complete. [b] A 0.01 M acetonitrile solution of the ether was irradiated in a quartz cell at 254 nm in a Rayonet reactor for 30 min. Thin-layer chromatography showed that the reaction was complete, and the alcohol was isolated by chromatography in the indicated yield. [c] 4 h, reflux. [d] R = *i*−Pr.



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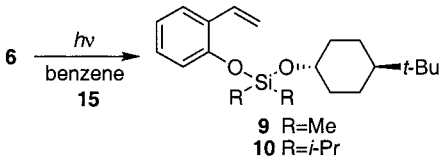
converted to the interesting dimethylsilylidene derivative **9** (91%) within 20 min (eq 6). Parallel results were observed with



(6)

(10) Turner, A. D.; Pizzo, S. V.; Rozakis, G. W.; Porter, N. A. *J. Am. Chem. Soc.* **1987**, *109*, 1274−1275. Turner, A. D.; Pizzo, S. V.; Rozakis, G. W.; Porter, N. A. *J. Am. Chem. Soc.* **1988**, *110*, 244−250. Porter, N. A.; Bruhnke, J. D. *J. Am. Chem. Soc.* **1989**, *111*, 7616−7618.

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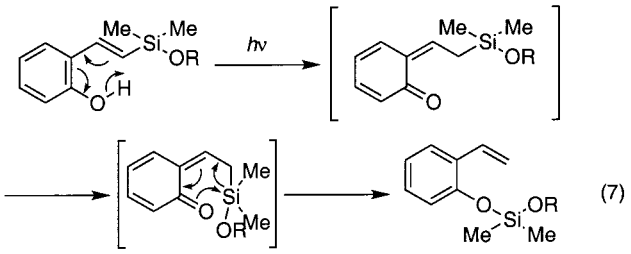
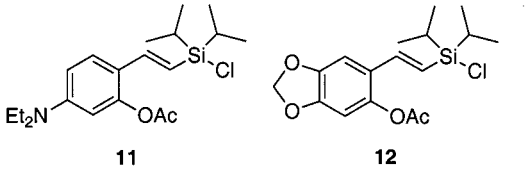
(12) Brook, M. A.; Neuy, A. *J. Org. Chem.* **1990**, *55*, 3909−3916.

the diisopropylsilyl derivatives. The observation of the silylidene products **9** and **10** at this point presaged significant difficulties later in the investigation. More detailed study of the mechanism of this process,[13] which can also be triggered thermally, showed that it likely involves a 1,5-hydrogen shift followed by a 1,5-silicon shift (eq 7).





Preparative photochemical deprotection reactions of derivatives **4** and **5** were conducted in acetonitrile at 10 mM with 254 nm irradiation over 30 min. The crude reaction mixtures reflected essentially quantitative conversion to the free alcohols and either **7** or **8**. The isolated yields of alcohols after silica gel chromatography are good to excellent, as reflected in Table 1.

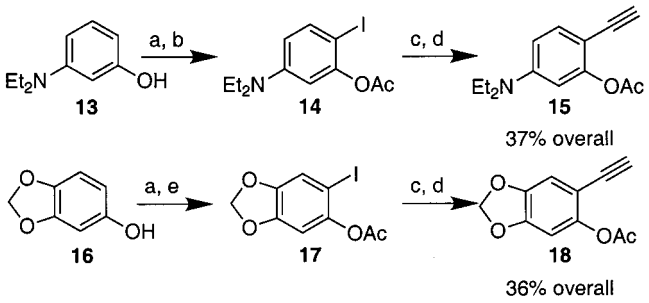
The chemical stability of the protected alcohols was examined. Derivatives of **4** are comparable in stability to trimethylsilyl ethers. They are deprotected on treatment with TBAF (5 equiv, 10 min, THF), 1 N NaOH (5 equiv, 30 min, THF), and 1 N HCl (5 equiv, 10 min, THF). Derivatives of **5** are more stable, as expected, and are comparable to triisopropylsilyl (TIPS) ethers. They can withstand the following reaction conditions: 5 equiv tetrazole/THF; excess EtMgBr, 0 °C; excess $NaBH_4$/MeOH, and excess PDC/CH_2Cl_2. Consequently, further efforts have focused on the more stable (hydroxystyryl)diisopropylsilyl (HSDIS) protecting groups.

With this successful demonstration of photochemically removable silyl protecting groups, we wished to improve their long-wavelength absorption properties to enable them to be removed in the near UV region. Lower energy radiation should minimize concurrent absorption by biopolymers, such as peptides and nucleic acids, when these silyl groups are used in their synthesis. In principle, this would involve the addition of red-shifting electron-donating groups to the chromophore. Two such modified silyl derivatizing reagents, incorporating diethylamino (**11**) and methylenedioxy (**12**) substituents, were initially targeted.

The synthetic approach to these compounds followed our precedent via the hydrosilylation of the respective aryl acetylenes, which were prepared as shown Scheme 1. Iodination of *m*-diethylaminophenyl acetate required use of a selective iodination procedure reported by Cambie.[14] The required acetylenes, **15** and **18**, were prepared in 36−37% overall yield from *m*-diethylaminophenol and methylenedioxyphenol, respectively.

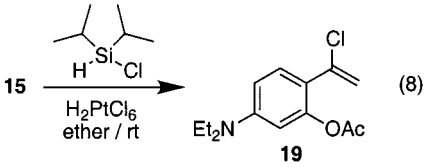
The hydrosilylation of **15** was investigated under a variety of conditions.[15] With diisopropylchlorosilane, the vinyl chloride

Scheme 1[a]



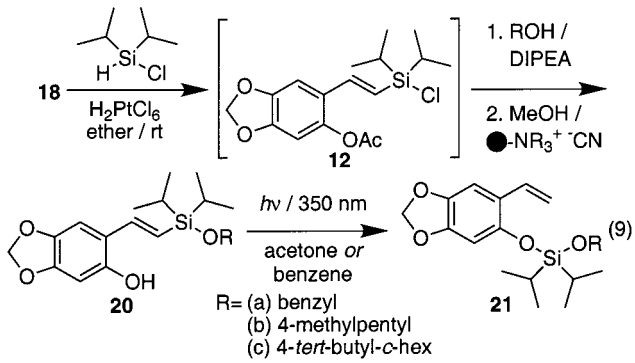
[a] Conditions: (a) Ac_2O/NaOH; (b) I_2/TlOAc; (c) $(Ph_3P)_4Pd$/CuI/Et_3N/TMSCCH; (d) $Et_3N{\cdot}3HF$/THF; and (e) ICl/AgOAc.

19, formally the product of HCl addition, was invariably produced (eq 8). Because hydrochloric acid was postulated to



be responsible for this reaction, a wide variety of precautions were implemented (freshly distilled silane, inert atmosphere box, and the addition of $NaHCO_3$) without significant effect. Since the source of HCl might also be the chloroplatinic acid, a variety of rhodium hydrosilylation catalysts were investigated, also without beneficial effect. Substitution of triethylsilane for the chlorosilane led to a complex mixture of hydrosilylation and reduction products. Encouraged that partial hydrosilylation resulted with a silane other than the chlorosilane, an alternative, two-step protecting strategy was considered on the basis on the formation of a diisopropylsilyl ether followed by hydrosilylation. A representative alcohol, 3′-acetylthymidine, was converted to its diisopropylsilyl ether and examined in hydrosilylation of **15**, but both internal and terminal silyl addition were observed. The aromatic nucleus **11** was therefore abandoned. Our unsuccessful efforts to hydrosilylate **15** and investigation of relevant hydrosilylation literature revealed a significant gap in current technology; very few acetylenes bearing functional groups have been studied in this reaction.

Acetylene **18** was subjected to the following three-step process without isolation of intermediates: hydrosilylation to give silyl chloride **12**, reaction with an alcohol (benzyl, 4-methylpentyl, and *trans*-4-*tert*-butylcyclohexyl), and removal of the acetate group with a cyanide resin in methanol, giving protected alcohol **20** (eq 9). However, long-wavelength irradia-

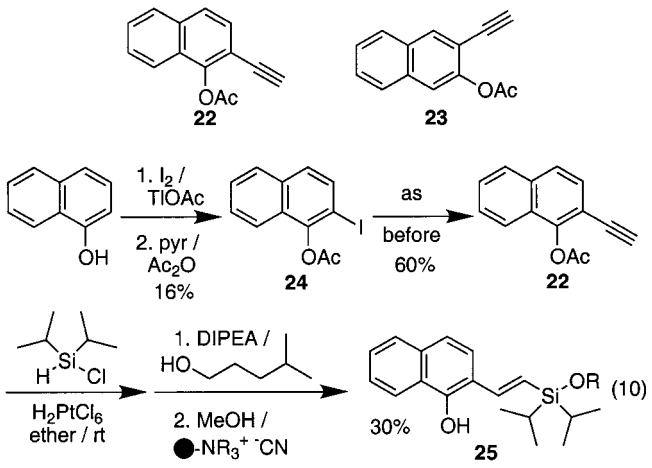


tion of these compounds afforded only the silylidene products **21**, and unlike the case of **6**, the outcome is solvent independent.

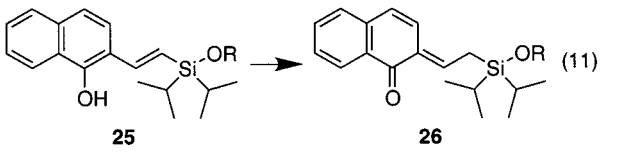
(13) Pirrung, M. C.; Lee, Y. R. *Tetrahedron Lett.* **1993**, *34*, 8217.
(14) Cambie, R. C.; Rutledge, P. S.; Smith−Palmer, T.; Woodgate, P. D. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1161−1164.
(15) Brook, M. A.; Neuy, A. *J. Org. Chem.* **1990**, *55*, 3609−3616.

We hypothesized that the difficulties with these two reactants lay in their polar substituents, which in one case disrupted hydrosilylation and in the other favored the polar reaction pathway previously invoked[8] to explain silylidene formation. An alternative strategy was therefore pursued for red-shifting the absorption maximum by extending the conjugation length using a naphthyl system. Two target molecules, the 1-naphthyl and 2-naphthyl systems **22** and **23**, were considered. The former was pursued initially because of the availability of starting materials.

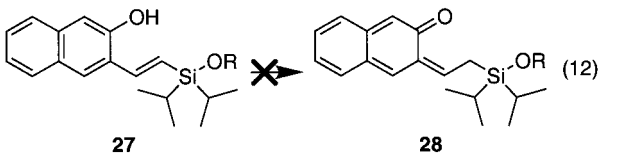
The preparation of **22** followed previous routes (eq 10).



Hydrosilylation was successful and delivered the protected alcohol **25**. However, this compound converted to the silylidene derivative even upon brief storage. The instability of this material is rationalized by the double migration pathway in which the putative quinone methide intermediate **26** is stabilized by benzo substitution (eq 11). If this is the case, it should be



possible to eliminate silylidene formation by using the 2-naphthyl derivative, where the initial 1,5-H shift would be energetically disfavored because it disrupts the aromaticity of the full naphthalene ring system (eq 12). This was the rationale behind



the targeting of **27**.

A new synthetic route was required to prepare the 2-naphthyl vinylsilane derivatives because of limited availability of starting materials. Selective protection of naphthalene-2,3-diol with TBDMSCl, which can be accomplished in 96% yield (eq 13), differentiates the alcohols. The remaining alcohol, after conversion to the triflate, is used to introduce the alkyne through Sonogashira coupling. This step is amenable to scale-up and has been used to prepare >10 g quantities of the trimethylsilyl acetylene. This material was usually converted to **23** in smaller batches. Hydrosilylation of **23** gives the intermediate chlorosilane **31**, which is directly treated with alcohols in the presence

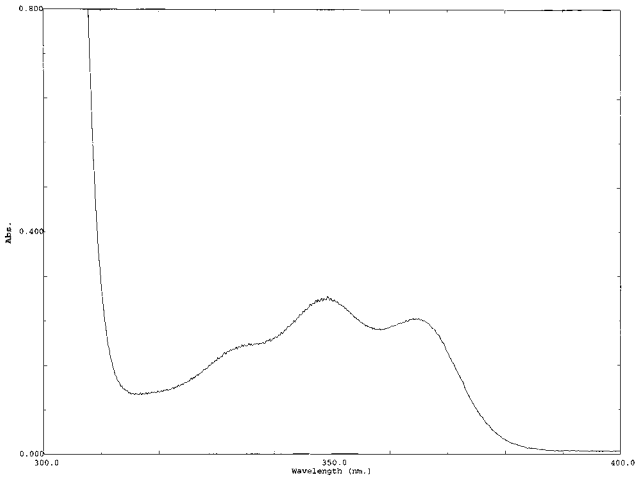
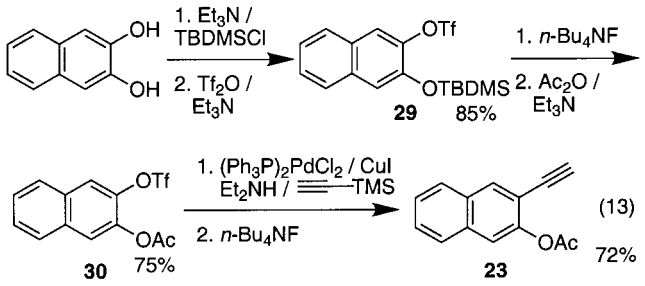
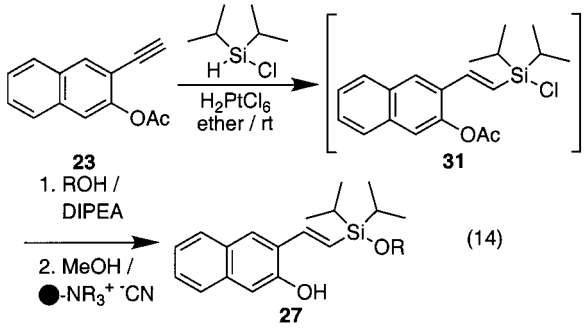


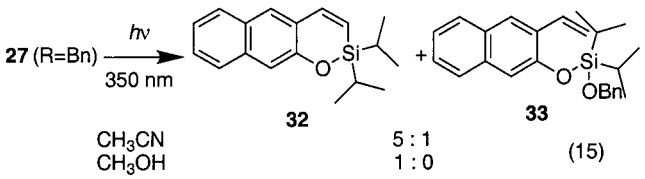
Figure 1. UV/vis spectrum of compound **27f** at 2.527×10^{-4} M in CH_3CN; A_{346} 0.697.



of a tertiary amine base to provide the silyl ethers. Removal of the acetate, as shown before, gives the protected ether **27**.

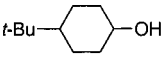
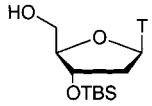
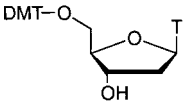
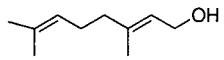


The absorption spectrum of the geranyl ether of **27** is shown in Figure 1. The absorption maximum at 346 nm has an extinction coefficient of nearly 3 000. Initial investigation of the photolysis of the benzyl ether of **27** in acetonitrile was somewhat disappointing. While the cyclic siloxane **32** was the major product, the silylidene derivative **33** was concurrently formed. Investigation of solvent effects on this process showed that the use of methanol completely suppressed the formation of **33** (eq 15). The UV spectrum of **32** has its major absorption



maximum at $\lambda < 310$ nm and, therefore, does not interfere with longer-wavelength irradiation/deprotection.

Table 2. Alcohols Protected with **31** and Their Deprotection Reactions

	Alcohol	Protection Yield	Deprotection Yield
a	*i*-PrOH	82	94[a]
b		80	89
c		77	90
d		79	92
e	CH_3OH	81	86[a]
f		85	90

[a] The yield of the cyclization product **32** is reported due to the volatility of the alcohol.

With this protecting group design verified, the protection of several alcohols with **31** and the photodeprotection of the resulting ((2-hydroxy-3-naphthyl)vinyl)diisopropylsilyl (HNVDS) groups **27** was investigated, as summarized in Table 2. The high isolated, purified yields on the relatively small scale and very clean crude reaction mixtures (^{1}H NMR) strongly suggest that deprotection is quantitative. This outcome strongly recommends this group for a variety of applications in photochemical deprotection.[16]

Summary

A new class of photochemically removable silyl protecting groups has been developed. The (hydroxystyryl)diisopropylsilyl (HSDIS) group can be formed by hydrosilylation of *o*-ethynylphenyl acetate with chlorodiisopropylsilane followed by conversion to the dimethylsilylamine and direct reaction with an alcohol to be protected. The ((2-hydroxy-3-naphthyl)vinyl)-diisopropylsilyl (HNVDS) group can be formed by a one-pot hydrosilylation of 3-ethynyl-2-naphthyl acetate, alcohol protection in the presence of a tertiary amine base, and acetate removal with cyanide in methanol. The HSDIS group is removed with 254 nm irradiation, while the HNVDS group is removed with 350 nm irradiation.

Experimental Section

Compounds described in Table 1 were previously reported in the Supporting Material for ref 8.

2,2-Dimethyl-2*H*-benzo[*e*][1,2]oxasiline (7). ^{1}H NMR ($CDCl_3$): δ 0.33 (s, 6H), 5.89 (d, J = 14.4, 1H), 6.87−7.13 (m, 4H), 7.23 (d, J = 14.4, 1H). IR (neat, cm^{-1}): 3061, 2995, 2974, 1599, 1552, 1480, 1449, 1273, 1263, 1101, 1030, 923, 795, 752. MS (m/z, CI): 177 (M^++ 1). HRMS (CI): calcd for $C_{10}H_{13}OSi$, 177.0736; found, 177.0726.

2,2-Diisopropyl-2*H*-benzo[*e*][1,2]oxasiline (8). ^{1}H NMR ($CDCl_3$): δ 1.02 (d, J = 4.2, 6H), 1.04 (d, J = 3.3, 6H), 1.06 (m, 2H), 5.84 (d, J = 14.4, 1H), 6.85−7.11 (m, 4H), 7.35 (d, J = 14.4, 1H). IR (neat, cm^{-1}): 2943, 2865, 1598, 1480, 1272, 1262, 1100, 920, 777, 751. MS (m/z, CI): 233 (M^++ 1). HRMS (EI): calcd for $C_{14}H_{20}OSi$, 232.1283; found, 232.1290.

(4-*tert*-Butyl-cyclohexyloxy)-dimethyl-(2-vinyl-phenoxy)-silane (9). ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.24 (s, 6H), 0.81 (s, 9H), 0.93−1.93 (m, 9H), 3.72 (m, 1H), 5.21 (dd, J = 11.4 and 1.2 Hz, 1H), 5.69 (dd, J = 17.4 and 1.2 Hz, 1H), 6.92 (m, 2H), 6.99 (dd, J = 17.4 and 11.4 Hz, 1H), 7.11 (ddd, J = 8.1, 7.5, and 1.8 Hz, 1H), 7.46 (dd, J = 7.5 and 1.8 Hz, 1H). IR (neat, cm^{-1}): 2946, 2867, 1598, 1552, 1484, 1452, 1255, 1088, 927, 801, 754. MS (m/z, CI): 333 (M^++ 1). HRMS (EI): calcd for $C_{20}H_{32}O_2Si$, 332.2171; found, 332.2168.

2-*O*-(*tert*-Butyldimethyl)silyl-3-hydroxynaphthalene. To a solution of 2,3-dihydroxynaphthalene (5.00 g, 31.2 mmol) in 50 mL of acetonitrile was added triethylamine (6.50 mL, 46.7 mmol). At −20 °C, *tert*-butyldimethylsilyl chloride (4.70 g, 31.2 mmol) in 50 mL acetonitrile was added dropwise to the solution over 3 h. The reaction mixture was poured into 200 mL ethyl acetate and washed with brine. The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane (6:1) as eluent. A colorless oil (8.21 g, 96%) was obtained. ^{1}H NMR ($CDCl_3$): δ 7.69 (2H, m), 7.36 (2H, m), 7.35 (1H, s), 7.22 (1H, s), 5.91 (1H, s), 1.11 (9H, s), 0.40 (6H, s). ^{13}C NMR ($CDCl_3$): δ 146.97, 143.09, 130.00, 128.66, 126.21, 126.08, 124.22, 123.47, 112.91, 109.31, 25.74, 18.28, −4.30. IR (CH_2Cl_2, cm^{-1}): 3529, 2928, 1474. Anal. Calcd for $C_{16}H_{22}O_2Si$: C, 70.03; H, 8.08. Found: C, 69.98; H, 8.00.

2-*O*-(*tert*-Butyldimethyl)silyl-3-*O*-(trifluoromethanesulfonyloxy)-naphthalene (29). 2-*O*-(*tert*-butyldimethyl)silyl-3-hydroxynaphthalene (0.95 g, 3.46 mmol) was taken up in 80 mL of triethylamine, and the solution was cooled to 0 °C. Triflic anhydride (0.79 mL, 4.67 mmol) was added to the solution, and the mixture was allowed to stir for 2 h. The mixture was poured into 100 mL ethyl acetate and washed with brine. The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane (9:1) as eluent. A light yellow oil (1.24 g, 89%) was obtained. ^{1}H NMR ($CDCl_3$): δ 7.79 (2H, m), 7.73 (1H, s), 7.48 (2H, m), 7.35 (1H, s), 1.11 (9H, s), 0.39 (6H, s). ^{13}C NMR ($CDCl_3$): δ 145.69, 141.03, 133.05, 127.95, 127.47, 127.09, 126.35, 124.97, 120.76, 120.32, 116.51, 116.15, 25.63, 18.40, −4.33. IR (CH_2Cl_2, cm^{-1}): 2962, 2939, 1600, 1468. Anal. Calcd for $C_{17}H_{21}F_3O_4SSi$: C, 50.23; H, 5.21. Found: C, 50.34; H, 5.20.

2-*O*-(Trifluoromethanesulfonyloxy)-3-hydroxynaphthalene. To a solution of compound **29** (10.0 g, 24.6 mmol) in 150 mL of dichloromethane at 0 °C was added 1.0 M tetrabutylammonium fluoride (32 mL, 32.0 mmol). The mixture was allowed to stir for 1 h, was poured into 100 mL ethyl acetate, and was washed with brine. The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane (5:1) as eluent. A light yellow oil (6.10 g, 83%) was obtained. ^{1}H NMR ($CDCl_3$): δ 7.74 (1H, d, J = 8.2 Hz), 7.72 (1H, s), 7.64 (1H, d, J = 8.2 Hz), 7.44 (2H, m), 7.30 (1H, s). ^{13}C NMR ($CDCl_3$): δ 145.44, 138.31, 133.50, 128.39, 128.02, 127.85, 126.57, 125.44, 121.14, 120.98, 116.90, 113.34. IR (CH_2Cl_2, cm^{-1}): 3529, 1634, 1594, 1531, 1417. LRMS 292.0 (M^+). HRMS: calcd for $C_{11}H_7F_3O_4S$, 292.0017; found, 292.0013 (M^+).

2-*O*-(Trifluoromethanesulfonyloxy)-3-acetoxynaphthalene (30). To a solution of 2-*O*-(trifluoromethanesulfonyloxy)-3-hydroxynaphthalene (6.50 g, 22.6 mmol) in 50 mL of dichloromethane was added acetic anhydride (2.80 mL, 29.7 mmol) followed by the addition of triethylamine (4.35 mL, 31.3 mmol) at room temperature. The mixture was allowed to stir for 4 h. The mixture was poured into 100 mL ethyl acetate and washed with brine. The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane (9:1) as eluent. A white solid (6.78 g, 91%) identified as compound **30** was obtained. Mp 126 °C. ^{1}H NMR ($CDCl_3$): δ 7.84 (2H, m), 7.80 (1H, s), 7.77 (1H, s), 7.57 (2H, m), 2.43 (3H, s). ^{13}C NMR ($CDCl_3$): δ 168.51, 140.13, 139.84, 132.65, 131.20, 128.09, 128.00, 127.89,

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127.46, 122.37, 121.08, 116.79, 21.07. IR (CH_2Cl_2, cm^{-1}): 1772, 1468, 1428. Anal. Calcd for $C_{13}H_9F_3O_5S$: C, 46.71; H, 2.71. Found: C, 46.75; H, 2.73.

2-(Trimethylsilylethynyl)-3-acetoxynaphthalene. To a solution of compound **30** (4.70 g, 14.0 mmol) in 100 mL DMF was added dichlorobis(triphenylphosphine)palladium(II) (196 mg, 0.28 mmol) followed by triethylamine (3.90 mL, 28.0 mmol). After stirring for 5 min, trimethylsilylacetylene (2.97 mL, 21.0 mmol) was added to the mixture. The mixture was stirred for 30 min, and the temperature was brought to 90 °C. After stirring for 10 h, the solvent was removed in vacuo. The residue was redissolved in diethyl ether and washed with 30 mL 1 N HCl and brine. The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane (9:1) as eluent. A white solid (3.32 g, 84%) was obtained. Mp 123 °C. ^{1}H NMR ($CDCl_3$): δ 8.05 (1H, s), 7.78 (2H, m), 7.53 (1H, s), 7.48 (2H, m), 2.39 (3H, s), 0.29 (9H, s). ^{13}C NMR ($CDCl_3$): δ 160.80, 148.07, 133.57, 133.13, 130.85, 127.42, 127.25, 127.20, 126.11, 119.19, 116.14, 99.87, 99.21, 20.84, −0.06. IR (CH_2Cl_2, cm^{-1}): 2962, 2355, 2161, 1766. Anal. Calcd for $C_{17}H_{18}O_2Si$: C, 72.30; H, 6.42. Found: C, 72.21; H, 6.47.

2-Ethynyl-3-acetoxynaphthalene (23). To a solution of 2-(trimethylsilylethynyl)-3-acetoxynaphthalene (300 mg, 1.06 mmol) in 50 mL of dichloromethane was added tetrabutylammonium fluoride (1.25 mmol fluoride/g on silica gel) (4.42 g, 5.30 mmol). The mixture was allowed to stir at room temperature for 2 h and was poured into 50 mL of saturated aqueous ammonium chloride. The mixture was extracted with ethyl acetate. The organic phase was dried over $MgSO_4$, and the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane (9:1) as eluent. A white solid (192 mg, 86%) identified as compound **23** was obtained. Mp 115 °C. ^{1}H NMR ($CDCl_3$): δ 8.08 (1H, s), 7.79 (2H, m), 7.55 (1H, s), 7.48 (2H, m), 3.29 (1H, s), 2.40 (3H, s). ^{13}C NMR ($CDCl_3$): δ 169.00, 148.00, 134.12, 133.29, 130.77, 127.39, 127.27, 126.21, 119.36, 115.10, 81.45, 78.87, 20.87. IR (CH_2Cl_2, cm^{-1}): 3248, 2355, 1760, 1537. Anal. Calcd for $C_{14}H_{10}O_2$: C, 79.98; H, 4.79. Found: C, 79.80; H, 4.91.

Hydrosilylation of 23. 2-Acetoxy-3-[*trans*-diisopropyl(benzyloxy)-silyl)vinyl] Naphthalene. The alkyne **23** (0.35 g, 1.66 mmol) was azeotroped from acetonitrile and taken up in 6.0 mL of diethyl ether. An aliquot (50 μL) of a prepared solution (0.10 M in 2-propanol) of hydrogen hexachloroplatinate(IV) hydrate was added to 1.0 mL of diethyl ether, and to this solution was added chlorodiisopropylsilane (0.65 mL, 3.81 mmol). This solution was stirred for 5 min followed by the addition of the alkyne solution. The reaction was stirred for 3 h at room temperature, and the solvent was removed in vacuo. The flask was refilled with argon, the resulting oil was taken up in 5 mL of tetrahydrofuran, and the solution was cooled in an ice bath. Diisopropylethylamine (1.66 mL, 9.50 mmol) and benzyl alcohol (1.97 mL, 19.04 mmol) were added to the reaction mixture that was allowed to stir overnight. The solution was poured into EtOAc, washed with water, and dried over $NaSO_4$. The desired compound was obtained following flash chromatography on silica gel eluting with 5:95 EtOAc:hexane to give 0.04 g of a clear oil that was slightly impure. The oil was further purified on silica gel eluting with a gradient of 0:100 to 2:98 diethyl ether:pentane to give 0.40 g (58%) of a clear oil. ^{1}H NMR ($CDCl_3$): δ 1.22−1.27 (14H, m), 2.32 (3H, s), 5.01 (2H, s), 6.65 (1H, d, J = 19.5 Hz), 7.32−7.62 (9H, m), 7.87 (1H, m), 7.95 (1H, m), 8.15 (1H, s). ^{13}C NMR ($CDCl_3$): δ 12.59 (CH), 17.52 (CH_3), 17.46 (CH_3), 20.64 (CH_3), 65.23 (CH_2), 119.58 (CH), 125.77 (CH), 125.92 (CH), 125.99 (CH), 126.12 (CH), 126.59 (CH), 126.92 (CH), 127.27 (CH), 127.99 (CH), 128.25 (CH), 130.48 (C), 131.66 (C), 133.40 (C), 140.65 (CH), 141.27 (C), 146.27 (C), 169.37 (C). HRMS (FAB, MH+): calcd for $C_{27}H_{33}O_3Si$, 433.2200; found, 433.2204.

2-Hydroxy-3-[*trans*-diisopropyl (benzyloxy)silyl)vinyl]naphthalene (27g). 2-Acetoxy-3-[*trans*-diisopropyl (benzyloxy)silyl)vinyl]-naphthalene (0.04 g, 0.10 mmol) was dissolved in 4 mL of methanol and treated with an excess of cyanide on Amberlyst (3 mmol/g). The solvent was poured off the beads and removed in vacuo. The resulting oil was purified using flash chromatography on silica gel eluting with 5:95 EtOAc:hexane to give 37 mg (78%) of the desired compound as a clear oil. ^{1}H NMR ($CDCl_3$): δ 1.12 (12H, m), 1.20 (2H, m), 4.89 (2H, s), 5.07 (1H, s), 6.51 (1H, d, J = 20 Hz), 7.23−7.39 (8H, m), 7.44 (1H, d, J = 20 Hz), 7.59 (1H, d, J = 8.4 Hz), 7.23 (1H, d, J = 8.4 Hz), 7.85 (1H, s). ^{13}C NMR ($CDCl_3$): δ 12.63 (CH), 17.64 (CH_3), 65.39 (CH_2), 110.05 (CH), 123.89 (CH), 125.28 (CH), 125.86 (CH), 126.11 (CH), 126.57 (CH), 126.97 (CH), 127.77 (C), 127.99 (CH), 128.28 (CH), 128.98 (C), 134.27 (C), 141.36 (C), 141.53 (CH), 151.35 (C). HRMS (FAB, MH+) calcd for $C_{25}H_{31}O_2Si$, 391.2093; found, 391.2090.

Photolysis of 27g. 2,2-Diisopropyl-2*H*-1-oxa-2-sila-anthracene (32). Compound **27g** (0.07 g, 0.19 mmol) was dissolved in 14 mL (0.013 M) of methanol and irradiated for 45 min in a Rayonet photochemical reactor (350 nm phosphor lamps). The solvent was removed in vacuo, and the photoproduct was isolated using flash chromatography on silica gel eluting with 2:98 EtOAc:hexanes to give 35.0 mg (66%) of a clear oil. ^{1}H NMR ($CDCl_3$): δ 1.01 (14H, m), 1.12 (2H, m), 6.00 (1H, d, J = 14.4 Hz), 7.23 (1H, s), 7.25 (1H, m), 7.34 (1H, m), 7.52 (1H, s), 7.55 (1H, d, J = 14.4 Hz), 7.61 (1H, d, J = 8.0 Hz), 7.68 (1H, d, J = 8.0 Hz). ^{13}C NMR ($CDCl_3$): δ 13.42 (CH), 16.65 (CH_3), 113.78 (CH), 121.26 (CH), 123.66 (CH), 126.20 (CH), 126.50 (CH), 127.76 (CH), 128.81 (C), 130.29 (CH), 134.61 (C), 147.44 (CH), 152.48 (C). HRMS (FAB, MH+): calcd for $C_{18}H_{23}$-OSi, 283.1518; found, 283.1510.

General Procedure for the Protection of Alcohols. The alkyne **23** (108 mg, 0.51 mmol) was azeotroped from toluene and taken up in 5.0 mL diethyl ether. An aliquot (30 μL) of a prepared solution (0.10 M in 2-propanol) of hydrogen hexachloroplatinate(IV) hydrate was added to 1.0 mL of diethyl ether, and to this solution was added chlorodiisopropylsilane (0.20 mL, 1.17 mmol). This solution was stirred for 5 min followed by the addition of the alkyne solution. The reaction was stirred for 10 h at room temperature, and the solvent was removed in vacuo. The flask was refilled with nitrogen. The resulting oil was taken up in 5 mL of tetrahydrofuran, and the solution was cooled to 0 °C. Diisopropylethylamine (0.18 mL, 1.03 mmol) and alcohol (0.46 mmol) were added to the reaction mixture. The mixture was allowed to stir overnight. The solution was poured into ethyl acetate, washed with brine, and dried over $MgSO_4$. The solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane (9:1) as eluent. This intermediate acetate (0.35 mmol) was dissolved in 4 mL of methanol and treated with an excess of cyanide (1.40 mmol) on Amberlyst (3 mmol cyanide/g). The solvent was poured off the beads and removed in vacuo. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane (7:1) as eluent. Evaporation of solvent afforded compounds **27**.

General Procedure for the Deprotection of Silyl Ethers 27. The protected alcohol (0.20 mmol) **27** was dissolved in 10 mL of methanol and irradiated for 45 min in a Rayonet photochemical reactor (350 nm phosphor lamps). The solvent was removed in vacuo, and the residue was purified by flash chromatography on silica gel using ethyl acetate and hexane (15:1) as eluent.

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Supporting Information Available: Experimental descriptions and/or spectral data for **14**, **15**, **17**−**19**, **20a**−**c**, **21**, **22**, **24**, **25**, **27a**−**f**; UV/vis spectrum of **32**; ^{1}H and ^{13}C NMR spectra of compound **27b**−**f** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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