An Efficient Photo-SET-Induced Cleavage of Dithiane−Carbonyl Adducts and Its Relevance to the Development of Photoremovable Protecting Groups for Ketones and Aldehydes

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Irradiation of dithiane−aldehyde/ketone adducts in the presence of benzophenone leads to C−C bond cleavage regenerating the carbonyl compounds. It is established that the mechanism of this reaction involves photochemically induced single electron transfer from the dithiane moiety to the excited molecule of ET-photosensitizer, accompanied by mesolytic C−C cleavage in the generated cation-radical, which is assisted by the anion-radical of benzophenone. This mechanism is confirmed by a Hammett plot study of the cleavage in the dithiane adducts of substituted aromatic aldehydes and a deuterium kinetic isotope effect study. Ab initio computations at UHF/6-31G* and MP2/6-31G* levels of theory in conjunction with self-consistent reaction field (self-consistent isodensity-polarized continuum model), to account for the solvent effect, also support the experimental findings. The reaction is most efficient for protection of aromatic aldehydes and ketones and aliphatic ketones, and is a novel method for protecting carbonyl functionalities with a photoremovable group.

Introduction

Recent developments in the chemistry of photoremovable protecting groups show the immense potential of *light* as a *reagent*. Most commonly it is nucleophilic functional groups, e.g., alcohol, thiol, or amino groups, which are protected with 2-nitrobenzyl, phenacyl, 2-benzoylbenzoic acid, 3,5-dimethoxybenzoin, substituted benzyloxycarbonyl, α-keto carbamates, etc.[1] We note, however, that a *true* photoremovable carbonyl protection is lacking from the representative list of functionalities for which photolabile protecting groups are found. A thorough search of the literature revealed several attempts to develop photoremovable protecting groups for aldehydes and ketones based on an acetal formation with *o*-nitrobenzyl alcohol or *o*-nitrophenylethylene glycol.[2] One significant problem with this method is that carbonyls are often protected to avoid an undesired reaction with organometallic compounds or hydrides, and the presence of the nitro group is, in our view, a limiting factor in such synthetic sequences.

Another example of a true photochemical deprotection of carbonyls is the photoreverse of the Schönberg−Mustafa reaction, although it can only be used for photodeprotection of masked *o*-quinones.[3]

To some extent the thioacetal protection of carbonyls, which is normally removed by Hg^{2+}-assisted hydrolysis, can also qualify as a photochemically removable protection. It appears from analysis of the literature, however, that thioacetal-based methods for *photochemical* deprotection of carbonyls would fall under the category *photooxidative hydrolysis of thioacetals in the presence of oxygen*.[4] Recent efforts in our laboratories have been focused on developing a somewhat orthogonal technique that utilizes not a 1,3-propanedithiol but rather a 1,3-dithiane ring "as a whole".

It was shown by Corey and Seebach[5] that 2-lithio-1,3-dithiane adds to carbonyl compounds to furnish 2-(1-hydroxyalkyl)-substituted dithianes in excellent yields (the reported yields were nearly quantitative for many of the cases studied), Scheme 1. Over the years this

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(2) (a) Aurell, M. J.; Boix, C.; Ceita, M. L.; Llopis, C.; Tortajada, A.; Mestres, R. *J. Chem. Res., Synop.* **1995**, 452−453. (b) Gravel, D.; Murray, S.; Ladouceur, G. *J. Chem. Soc., Chem. Commun.* **1985**, 1828−1829. (c) Gravel, D.; Hebert, J.; Thoraval, D. *Can. J. Chem.* **1983**, *61*, 400−410.

(3) Wilson, R. M.; Venkitachalam, S.; Layton, M.; Heckmann, J.; Barra, M.; Scaiano, J. C. In *10th Winter Conference of Inter-American Photochemical Society*; IAPS: Clearwater Beach, FL, 1998; p C7.

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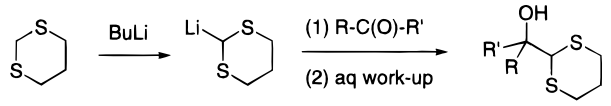
Scheme 1



reaction has been developed into a potent synthetic methodology used in many celebrated synthetic sequences.[6]

It is easy to see that the [−C(OH)C(SR)−] fragment bears a striking resemblance to vicinal diols and amino alcohols which are capable of cleaving under oxidative conditions (formation of cation-radicals). It is known that the removal of an electron from a ground state organic molecule frequently leads to molecular fragmentation due to the weakening of specific C−C bonds. The mechanistic aspects of such cleavage in cation-radicals has been studied extensively by several research groups, leading to the development of many novel organic reactions.[7] In contrast, organosulfur systems of this type were not studied in depth. In fact, we found only two publications in the literature where the C−C cleavage in β-phenylthioalkanols was utilized as a synthetic method of indirect cleavage of olefins[8] and also in carbohydrate synthesis.[9] This lack of experimental data may be attributed to the propensity of organosulfur systems to cleave the C−S bond rather than the C−C bond.

We now report a novel approach to photoreversibly protecting carbonyls based on SET-initiated C−C fragmentation in α-substituted hydroxymethyldithianes.

Results and Discussion

We found that irradiation of Corey−Seebach dithiane−aldehyde/ketone adducts in the presence of benzophenone in acetonitrile leads to efficient C−C bond cleavage, regenerating the carbonyl compounds nearly quantitatively.

Scheme 2

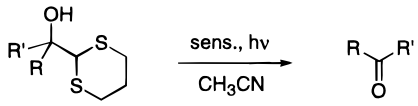
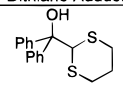
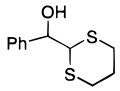
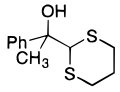
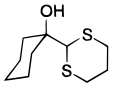
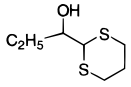
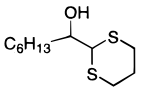
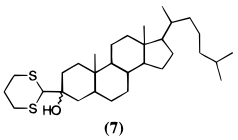


Table 1. Photochemical Deprotection Yields[a]

Dithiane Adduct	Irrad. Time	Carbonyl Compound	Yield[b]
 (1)	1.5-2 hrs	Benzophenone	97%
 (2)	1.5-2 hrs	Benzaldehyde	97%
 (3)	1.5-2 hrs	Acetophenone	96%
 (4)	3 hrs	Cyclohexanone	92%
 (5)	3 hrs	Propanal	38%
 (6)	3 hrs	Heptanal	35%
 (7)	3 hrs	5α-Cholestan-3-one	84%

[a] Pyrex-filtered irradiation of a medium-pressure Hanovia lamp was utilized as a UV source. [b] Yields are reported as determined by calibrated GC; benzophenone is used as a SET sensitizer.

The reaction is most efficient for aromatic/aliphatic ketones and aromatic aldehydes (Scheme 2). The yields and irradiation times of the studied adducts are presented in Table 1.

Mechanism. Our rationale of the reaction mechanism includes photochemically induced single electron transfer from the dithiane moiety to the excited molecule of ET-photosensitizer accompanied by mesolytic C−C cleavage in the generated cation-radical. Excited benzophenone is certainly capable of oxidizing 1,3-dithianes: the one-electron reduction potential of triplet benzophenone is −1.68 V (vs SCE in acetonitrile),[10] whereas various 2-substituted dithianes oxidize in the range of +0.73 to +1.18 V in the same solvent.[11]

To predict the "polarity" of the mesolytic fragmentation in the generated cation radical, we conducted ab initio computations for the benzaldehyde adduct **(2)** (see Table 2). The mp2/6-31g* energy difference obtained with fully optimized geometries (the same level of theory) showed a 14.5 kcal/mol preference for the 1,3-dithian-2-yl radical and protonated benzaldehyde (entries 1 and 2) over the {1,3-dithian-2-yl cation}−{phenyl-hydroxymethyl radi-

(7) (a) Bockman, T. M.; Hubig, S. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1998**, *120*, 6542−6547. (b) Sankararaman, S.; Perrier, S.; Kochi, J. K. *J. Am. Chem. Soc.* **1989**, *111*, 6448. (c) Han, D. S.; Shine, H. J. *J. Org. Chem.* **1996**, *61*, 3977. (d) Penn, J. H.; Duncan, J. H. *J. Org. Chem.* **1993**, *58*, 2003−2008. (e) Penn, J. H.; Lin, Z. *J. Org. Chem.* **1990**, *55*, 1554−1559. (f) Penn, J. H.; Deng, D. L.; Aleshire, S. K. *J. Org. Chem.* **1988**, *53*, 3572−3582. (g) Popielarz, R.; Arnold, D. R. *J. Am. Chem. Soc.* **1990**, *112*, 3068−3082. (h) Arnold, D. R.; Lamont, L. J. *Can. J. Chem.* **1989**, *67*, 2119−2127. (i) Okamoto, A.; Snow, M. S.; Arnold, D. R. *Tetrahedron* **1986**, *42*, 6175−6187. (j) Gaillard, E. R.; Whitten, D. G. *Acc. Chem. Res.* **1996**, *29*, 292−297. (k) Gan, H.; Leinhos, U.; Gould, I. R.; Whitten, D. G. *J. Phys. Chem.* **1995**, *99*, 3566−3573. (l) Kellett, M. A.; Whitten, D. G. *Res. Chem. Intermed.* **1995**, *21*, 587−611. (m) Leon, J. W.; Whitten, D. G. *J. Am. Chem. Soc.* **1995**, *117*, 2226−2235. (n) Whitten, D. G.; Kellett, M. A.; Leon, J.; Gan, H.; Tian, Z. W. *Photochem. Photoelectrochem. Convers. Storage Sol. Energy, Proc. Int. Conf., 9th* **1993**, 257−275. (o) Kellett, M. A.; Whitten, D. G. *Mol. Cryst. Liq. Cryst.* **1991**, *194*, 275−280. (p) Ci, X.; Whitten, D. G. *J. Am. Chem. Soc.* **1989**, *111*, 3459−3461. (q) Cl, X.; Whitten, D. G.; Fox, M. A.; Chanon, M. *Photoinduced Electron Transfer* **1988**, Part C, 553−578. (r) Lee, L. Y. C.; Ci, X.; Giannotti, C.; Whitten, D. G. *J. Am. Chem. Soc.* **1986**, *108*, 175−177. (s) Maslak, P.; Chapman, W. H., Jr. *J. Org. Chem.* **1996**, *61*, 2647. (t) Maslak, P.; Chapman, W. H., Jr.; Vallombroso, T. M.; Watson, B. A. *J. Am. Chem. Soc.* **1995**, *117*, 12380−12389. (u) Maslak, P. *Top. Curr. Chem.* **1993**, *168*, 1. (v) Wang, Y.; Lucia, L. A.; Schanze, K. S. *J. Phys. Chem.* **1995**, *99*, 1961−1968. (w) Burton, R. D.; Bartberger, M. D.; Zhang, Y.; Eyler, J. R.; Schanze, K. S. *J. Am. Chem. Soc.* **1996**, *118*, 5655−5664.

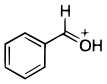
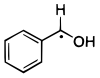
(8) Gravel, D.; Farmer, L.; Ayotte, C. *Tetrahedron Lett* **1990**, *31*, 63−66.

(9) Gravel, D.; Farmer, L.; Denis, R. C.; Schultz, E. *Tetrahedron Lett.* **1994**, *35*, 8981−8984.

(10) Roth, H. D.; Lamola, A. A. *J. Am. Chem. Soc.* **1974**, *96*, 6270−6275.

(11) Glass, R. S.; Petsom, A.; Wilson, G. S. *J. Org. Chem.* **1986**, *51*, 4337−4342.

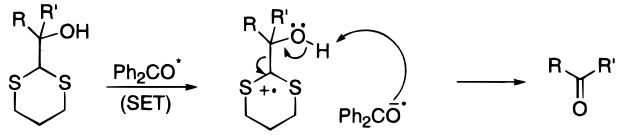
Table 2. Ab Initio Results

Entry	Fragment	MP2/6-31G* (full geometry opt.)	MP2/6-31G* SCRF-SCIPCM//MP2/6-31G*
1		-951.2759827	-951.2801778
2		-344.8066377	-344.8960968
3		-951.0769494	-951.1623967
4		-344.9825751	-344.9899398

cal} pair (entries 3 and 4). We estimated a possible impact of the solvent (acetonitrile, $\epsilon = 36.64$) at mp2/6-31g* level employing the self-consistent isodensity polarized continuum model. This produced additional stabilization for the corresponding cations, but the total energy difference stayed approximately the same, about 15 kcal/mol favoring 1,3-dithiane-2-yl radical and protonated benzaldehyde.

At the same time UHF/6-31g* computations showed that the energy of the predissociated cation-radical, −1294.312 280 92 hartree, is below the sum of the energies of the dithiane radical (−950.530 933 7 hartree) and protonated benzaldehyde (−343.766 345 3 hartree), a total of −1294.297 278 964 hartree, by about 10 kcal/mol. This would argue that an unassisted C−C cleavage in the cation-radical is an uphill process. Thus the actual mechanism for this fragmentation would likely involve a benzophenone anion-radical accelerating the cleavage via deprotonation of the hydroxy group (Scheme 3).

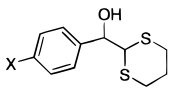
Scheme 3



Whitten[12] showed in a mechanistic study that a similar C−C cleavage in amino alcohol cation-radicals is indeed assisted by a benzophenone anion-radical. To prove that such assistance is in fact present in our case, we have conducted the following mechanistic study.

We first synthesized dithiane adducts of *para*-substituted benzaldehydes and studied the kinetic isotope effect of their cleavage in 3% $H_2O(D_2O)$ acetonitrile. Our findings are summarized in Table 3.

Table 3

	ϕ^H/ϕ^D
X=H **(2)**	1.13
X=CN **(8)**	1.14
X=MeO **(9)**	1.09

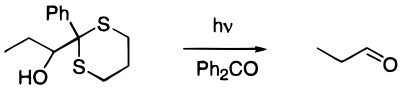
The relatively small values of the observed isotope effects may be attributed to fast hydrogen exchange in aqueous acetonitrile. It should also be noted that the trend, {MeO/1.09} − {H/1.13} − {CN/1.14}, is in keeping with the expected change in electronic demand for the cleavage. Unfortunately we cannot compare our values with that of Whitten's KIE experiments in *acetonitrile*, which in their case were inconclusive due to low quantum efficiency of amino alcohol cleavage.[12] (In *benzene* their reported KIE values were much higher—from 1.26 to 4.01).

Plotting the logarithms of relative quantum efficiencies of the dithiane adduct cleavage versus Hammett's substituent constants σ gave us the second experimental evidence for the benzophenone-assisted mechanism. The small value of ρ ($\rho = -0.2$, $r^2 = 0.994$), although indicative of some positive charge accumulation in the transition state, is in our view not nearly enough to explain the development of a full positive charge as in protonated benzaldehyde. For one thing, basicities of *para*-substituted benzaldehydes[13] do not correlate with σ, they correlate with σ^+, with ρ^+ being about −1.9 (we obtained this value by plotting pK_{BH^+} values from ref 13 against the latest σ^+ values found in ref 14). Depending on whether the transition state of the unassisted cleavage is *late* or *early*, the actual ρ value for such cleavage may vary. Our ab initio (UHF) results seem to point to the *late* transition state (an uphill process) in unassisted fragmentation. Although one can expect the absolute value of ρ to be less than 1.9, it is unlikely that it could be as insignificant as 0.2.

To summarize the mechanistic part, we believe that there is substantial evidence pointing to the involvement of a benzophenone anion-radical in the hydrogen abstraction during the cleavage of dithiane adducts. Admittedly, in acetonitrile this effect is not overly noticeable. Also, the mere fact that vicinal bis(dialkylamines) do cleave under similar conditions should indicate that slow unassisted cleavage is also a possibility, especially in polar solvents.[7j]

Protection of Aliphatic Aldehydes. The yields for deprotection of aliphatic aldehydes were modest. We attempted to improve the yield by utilizing lithiated 2-phenyl-1,3-dithiane as a protecting reagent in place of the unsubstituted dithiane. Scheme 4 shows a deprotection reaction that gave 65% of deprotected propanal. This 2-fold improvement over the result listed in Table 1 demonstrates that the lack of aryl/alkyl stabilization at one end of the to-be-cleaved bond can be partially compensated with enhanced aryl stabilization at the other end.

Scheme 4



10

Generally, 2-lithio-2-phenyl-1,3-dithiane addition to carbonyls cannot be utilized to protect ketones. The yields for the protection step may not be practical for more hindered carbonyls. Note, however, that we suggest using phenyldithiane as a remedy to boost deprotection yields for *aliphatic aldehydes*. It is known that aldehydes do

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(13) Yates, K.; Stewart, R. *Can. J. Chem.* **1959**, *37*, 664−671.
(14) Extner, O. In *Correlation Analysis in Chemistry*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978; Chapter 10.

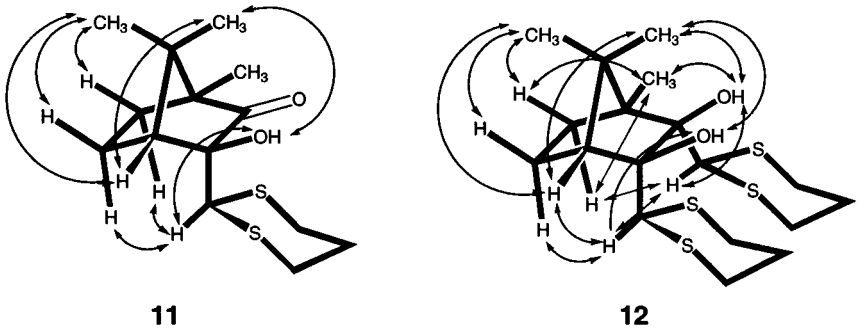


Figure 1. Schematic representation of major NOE interactions in the mono- and bis-dithiane adducts of camphorquinone.

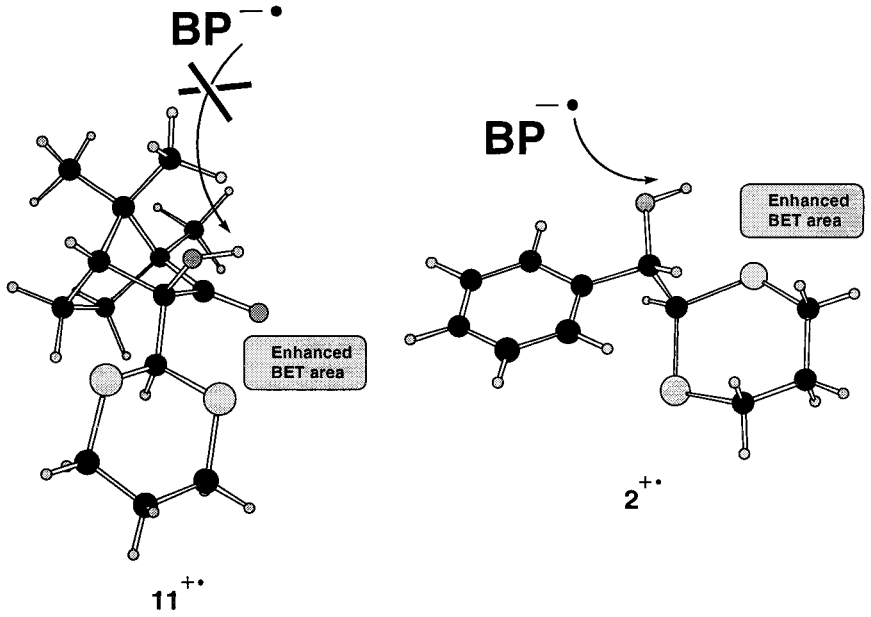


Figure 2. AM1 optimized geometry of camphorquinone−dithiane monoadduct cation-radical (**11**$^{+\bullet}$, left) and UHF/6-31g* optimized geometry of benzaldehyde-dithiane adduct cation-radical (**2**$^{+\bullet}$, right). The desired (anti- to the dithiane moiety) approach of benzophenone anion-radical allowing to minimize the back electron transfer is severely hindered in the case of camphorquinone adduct.

react with the phenyldithiane lithio derivative almost quantitatively.[15]

Scope. Camphorquinone reacted with lithiodithiane to give either the mono- or bisadduct depending on the molar ratio of the reagents. Both compounds were fully characterized by NMR, including an exhaustive NOE study to determine the stereo- and regiochemistry (Figure 1). As expected, the nucleophilic attack was *endo* leading to *exo* alcohols **11** and **12**.

To our disappointment, the yield of photodeprotected camphorquinone was essentially zero in both cases. Even after extended irradiation of **11** or **12** in acetonitrile in the presence of benzophenone we did not detect any significant amount of camphorquinone. In our view this fact may further illustrate the necessity of benzophenone anion-radical assistance. We optimized the geometry of the cation-radical **11**$^{+\bullet}$ at the AM1 level of theory and contend that in order for the benzophenone anion-radical to abstract the proton from the hindered OH group of **11**$^{+\bullet}$ it should approach/pass in the immediate vicinity of sulfur atoms bearing the positive charge. As shown in Figure 2, the *syn*-methyl group in position 7 of the norbornane ring prevents the kind of unhindered approach available for benzophenone anion-radical in the case of benzaldehyde adduct **2**. This should increase the probability of back electron transfer (BET) and effectively kill the fragmentation channel.

Admittedly, the presence of the carbonyl electron-withdrawing group in the monoadduct of camphorquinone makes the steric hindrance argument weaker. If,

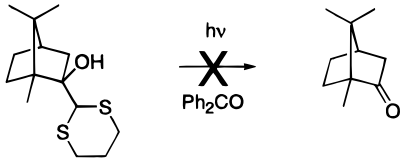
(15) Stowell, M. H. B.; Rock, R. S.; Rees, D. C.; Chan, S. I. *Tetrahedron Lett.* **1996**, *37*, 307−310.

(16) Kessar, S. V.; Singh, T.; Vohra, R. *Tetrahedron Lett.* **1987**, *28*, 5323−5326. Kessar, S. V.; Singh, T.; Vohra, R. *Indian J. Chem.* **1991**, *30B*, 999−1005.

(17) As we tried to optimize the reaction yield, we found the following. Upon extended irradiation (over 4 h) GC-MS analysis of the reaction mixture showed a growing peak of a secondary photoproduct with a molecular ion of 272 and a fragmentation pattern consistent with the 4-formyltriphenylmethane structure. It is conceivable that under reaction conditions trityl alcohol **18** photochemically ionizes to produce the corresponding trityl cation, which is subsequently reduced to the triphenylmethane. We also cannot rule out a radical mechanism for such reduction.

(18) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94, Revision E.2*; Gaussian, Inc.: Pittsburgh, PA, 1995.

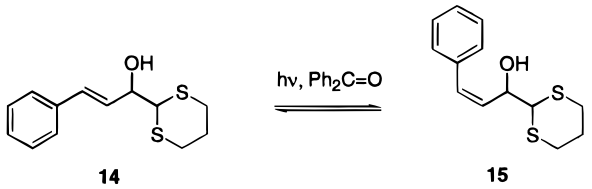
Scheme 5



13

however, the *BET vs fragmentation partition* is indeed controlled by the facility of anion-radical approach, one also should expect the *dithiane−camphor adduct* to be reluctant to cleave under the reaction conditions. In fact we found this to be exactly the case. Upon extended irradiation of the adduct **13** in the presence of benzophenone, it did not produce any detectable amount of camphor (Scheme 5). Except for the hindered approach, we can think of no other reason for this failure to cleave.

Scheme 6

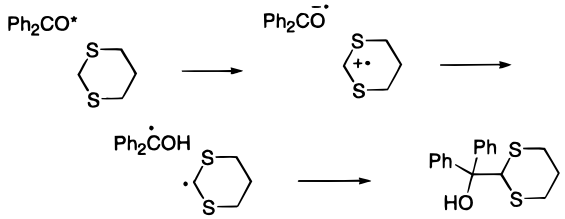


14 **15**

We also have encountered a case when triplet energy transfer from excited benzophenone was faster than the desired single electron transfer. Upon extended irradiation, *trans*-cinnamaldehyde−dithiane adduct undergoes *trans−cis* isomerization with little or no cleavage observed (Scheme 6).

Reverse Reaction: **C−C Bond Formation.** Another issue that needs to be addressed here is the reverse reaction (C−C bond formation). It is well-known that α-hydrogen abstraction in alkyl sulfides by excited carbonyls proceeds most commonly via an electron-transfer mechanism. However, in all the cases we studied, we did not observe any reverse reaction of the following type (Scheme 7).

Scheme 7



Although some rare (intramolecular) cases of the "backward" reaction, namely, a photochemically induced *coupling* of carbonyl compounds with 1,3-dithianes are found in the literature,[16] the photostationary intermolecular equilibrium between the carbonyl compounds we studied and 1,3-dithiane favors dissociated products. For example, the GC-MS analysis of the reaction between 1,3-dithiane and benzophenone after 30 min and 1 h shows no traces of 2-(diphenylhydroxymethyl)-1,3-dithiane. At the same time, irradiation of 2-(diphenylhydroxymethyl)-1,3-dithiane in the presence of an ET-sensitizer gives 97% of benzophenone back.

Synthetic Applications—Compatibility with Grignard Reagents. One of the most important features of any carbonyl protecting group should, in our view, be its compatibility with organometallic reagents and hydrides. Our dithianyl protection is perfectly compatible with, for example, Grignard reagents. We synthesized the following monoformyl-substituted trityl alcohol from ethyl 4-formylbenzoate with an overall yield of 87% (excluding the final deprotection step, it is a one-pot reaction), Scheme 8.[17]

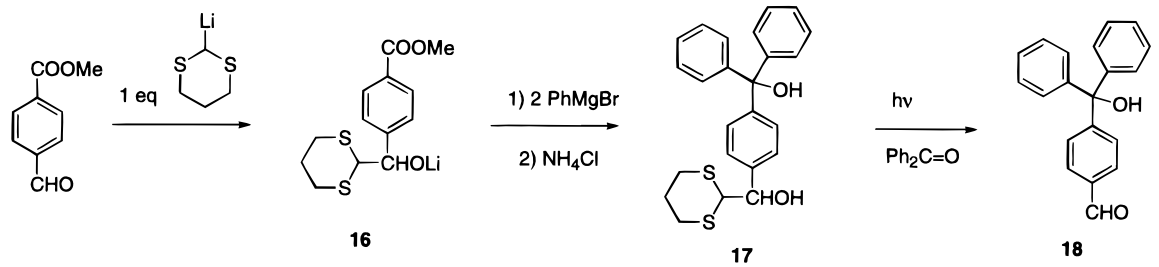
Conclusion

An efficient photoremovable protecting group based on utilization of a dithiane ring "as a whole" has been developed. Although some limitations for this protection reaction resulting from either the sterically hindered approach or due to fast triplet energy transfer were documented in the course of this research, the overall reaction is a general way to photoreversibly protect various aldehydes and ketones. The protection is compatible with organometallic reagents, which makes it a valuable addition to the arsenal of carbonyl protecting groups. It also makes it the only practical *photoremovable* protecting group for aldehydes and ketones.

Experimental Section

Melting points are uncorrected. Common solvents were purchased from Aldrich and used as is, except for THF, which was refluxed over and distilled from potassium benzophenone ketyl prior to use. *n*-BuLi (as a 2.0 M solution in *n*-pentane, *n*-hexane, or hexanes), 1,3-dithiane, 2-phenyl-1,3-dithiane, acetophenone, benzaldehyde and derivatives (*p*-MeO, CN), benzophenone, propanal, heptanal, *trans*-cinnamaldehyde, cyclohexanone, camphor, camphorquinone, 5α-cholestan-3-one, and ethyl 4-formylbenzoate were all purchased from Aldrich and used without additional purification. ^{1}H and ^{13}C NMR spectra were recorded at 25 °C on a Varian Mercury 400 MHz instrument in $CDCl_3$ with TMS as an internal standard (unless otherwise noted). Column chromatography was performed on silica gel, 70−230 mesh ASTM, using ethyl acetate−hexane mixtures as eluent. HP 6890 gas chromatograph (flame ionization detector) was used to determine the yields of the deprotected ketones and aldehydes with dodecane as an internal standard. Another HP 6890 with MSD detector was used to monitor the progress of photoreactions and to identify components of complex reaction mixtures. A Pyrex-filtered

Scheme 8



16 **17** **18**

output of a medium-pressure Hanovia lamp was utilized as the UV source.

Ab initio computations were performed on a dual mips R10000 processor SGI Octane workstation equipped with 1 G of memory using the Gaussian 94 Revision E.2 computational package.[18] The input geometries were created and preoptimized using a force field geometry optimization as implemented in Chem3D (Cambridgesoft). Full geometry optimizations were then performed at UHF/6-31G* and/or MP2/6-31G* levels of theory. Self-consistent reaction field (SCRF) computations were performed to account for solvent polarity effects utilizing the self-consistent isodensity polarized continuum model (SCIPCM). These were run as single-point calculations without further geometry optimization (MP2-SCIPCM/6-31G*//MP2/6-31G*).

General Method of the Adduct Preparation. A generic method by Corey and Seebach was used to prepare the desired dithiane−carbonyl adducts.[19] A total of 5 mmol of dithiane was dissolved in 40 mL of freshly distilled THF, and the solution was cooled to −20 °C under nitrogen. Then 5.6 mmol (2.8 mL) of *n*-butyllithium (a 2 M solution in hexanes) was added dropwise upon stirring. The resulting mixture was stirred for 2−2.5 h. The temperature was then lowered to −78 °C, and 5 mmol of an appropriate carbonyl compound dissolved in 10 mL of THF was added to the vigorously stirred solution of the dithianyl anion. The reaction mixture was stirred for 2−4 h at this temperature and then stored in a freezer at −25 °C overnight.[20] The subsequent aqueous workup included quenching the reaction mixture with a 1 M solution of ammonium chloride, extracting twice with ether, and drying the combined organic extracts over sodium sulfate. The solvent was then removed with a rotary evaporator, and the residue was purified using either column chromatography (silica gel, ethyl acetate−hexane) or recrystallization.

2-(Diphenylhydroxymethyl)-1,3-dithiane (1):[19] ^{1}H NMR ($CDCl_3$) δ 7.58−7.30 (m, 10H), 5.16 (s, 1H), 3.29 (s, 1H), 2.80−2.90 (m, 4H), 2.04−1.87 (m, 2H); MS (EI) *m*/*z* 302 (M^+), 119 (100%), 105, 77; mp 135 °C (lit.[19] mp 136.0−136.5 °C).

2-(Hydroxy-phenylmethyl)-1,3-dithiane (2):[21] ^{1}H NMR ($CDCl_3$) δ 7.44−7.30 (m, 5H), 4.91 (dd, 1H, J = 7.5, 2.2 Hz,), 4.08 (d, 1H, J = 7.5 Hz), 2.97 (d, 1H, J = 2.2 Hz), 2.99−2.89 (m, 2H), 2.76−2.68 (m, 2H), 2.11−1.92 (m, 2H); MS (EI) *m*/*z* 226 (M^+), 119 (100%); mp 74−75 °C (lit.[21] mp 73−74 °C).

2-(1-Hydroxy-1-phenylethyl)-1,3-dithiane (3):[22] ^{1}H NMR ($CDCl_3$) δ 7.55−7.26 (m, 5H), 4.44 (s, 1H), 2.88−2.70 (m, 5H), 2.4−2.0 (m, 1H), 1.82−1.76 (m, 1H), 1.74 (s, 3H); MS (EI) *m*/*z* 240 (M^+), 119, 43 (100%).

2-(1-Hydroxycyclohexyl)-1,3-dithiane (4):[19] ^{1}H NMR ($CDCl_3$) δ 4.19 (s, 1H), 3.0−2.80 (m, 5H), 2.10−1.89 (m, 2H), 1.85−1.10 (m, 10H); MS (EI) *m*/*z* 218 (M^+), 120 (100%).

2-(1-Hydroxypropyl)-1,3-dithiane (5):[23,24] ^{1}H NMR ($CDCl_3$) δ 3.90−3.78 (m, 2H), 2.81−2.75 (m, 4H), 2.30 (m, 1H), 2.15−1.85 (m, 4H), 0.89 (t, 3H, J = 7.6 Hz).

2-(1-Hydroxyheptyl)-1,3-dithiane (6):[24] ^{1}H NMR ($CDCl_3$) δ 3.93−3.85 (m, 2H), 2.98−2.90 (m, 2H), 2.84−2.70 (m, 2H), 2.37 (d, 1H), 2.14−2.04 (m, 1H), 2.04−1.92 (m, 1H), 1.85−1.38 (m, 10H), 0.96 (t, 3H); MS (EI) *m*/*z* 234 (M^+), 119 (100%).

3-(1,3-Dithian-2-yl)-5α-cholestan-3-ol (7). A 5:4 mixture of α-dithianyl to β-dithianyl compounds was obtained. The photodeprotection reaction was carried out with this original mixture of isomers. A small quantity of the α-isomer was also isolated using column chromatography (silica gel, ethyl acetate−hexane 1:3). **3α-(1,3-Dithian-2-yl)-5α-cholestan-3-ol:** ^{1}H NMR ($CDCl_3$) δ 4.12 (s, 1H), 2.97−2.83 (m, 4H), 2.15−2.05 (m, 1H), 2.03 (s, 1H), 2.0−0.6 (m, H), 0.89 (d, 3H, J = 6.5 Hz), 0.86 (d, 3H, J = 6.5 Hz), 0.85 (d, 3H, J = 6.5 Hz), 0.76 (s, 3H), 0.64 (s, 3H); ^{13}C NMR with C-type assignments based on DEPT experiment ($CDCl_3$) δ 74.053 (4°), 61.282 (3°), 56.445 (3°), 56.194 (3°), 53.911 (3°), 42.555 (4°), 40.791 (3°), 39.999 (2°), 39.486 (2°), 37.674 (2°), 36.139 (2°), 35.768 (3°), 35.686 (4°), 35.473 (3°), 33.775 (2°), 31.924 (2°), 30.952 (2°), 30.707 (2 carbons, 2°), 28.403 (2°), 28.217 (2°), 27.988 (3°), 25.957 (2°), 24.171 (2°), 23.811 (2°), 22.801 (1°), 22.544 (1°), 20.999 (1°), 18.662 (1°), 12.072 (1°), 11.204 (1°). Anal. Calcd for $C_{31}H_{54}OS_2$: C, 73.45; H, 10.74. Found: C, 73.73; H, 10.59.

2-(1-Hydroxy-1-(*p*-cyanophenyl)methyl)-1,3-dithiane (8): ^{1}H NMR ($CDCl_3$) δ 7.57 (d, 2H, J = 9.4 Hz), 7.48 (d, 2H, J = 9.4 Hz), 5.0 (dd, 1H, J = 8.2, 1.5 Hz), 3.98 (d, 1H, J = 8.2 Hz), 3.1 (d, 1H, J = 1.6 Hz), 3.0−2.85 (m, 2H), 2.8−2.65 (m, 2H), 2.15−1.95 (m, 2H); MS (EI) *m*/*z* 251 (M^+), 119 (100%). Anal. Calcd for $C_{12}H_{13}NOS_2$: C, 57.33; H, 5.21. Found: C, 57.22; H, 5.40.

2-(1-Hydroxy-1-(*p*-methoxyphenyl)methyl)-1,3-dithiane (9): ^{1}H NMR ($CDCl_3$) δ 7.33 (d, 2H, J = 9.5 Hz), 6.89 (d, 2H, J = 9.5 Hz), 4.83 (dd, 1H, J = 7.6, 1.9 Hz), 4.06 (d, 1H, J = 7.8 Hz), 3.80 (s, 3H), 2.85 (d, 1H, J = 2.0 Hz), 2.95−2.80 (m, 2H), 2.73−2.62 (m, 2H), 2.10−1.90 (m, 2H); MS (EI) *m*/*z* 256 (M^+), 137 (100%), 119. Anal. Calcd for $C_{12}H_{16}O_2S_2$: C, 56.22; H, 6.29. Found: C, 56.20; H, 6.46.

2-(1-Hydroxypropyl)-2-phenyl-1,3-dithiane (10): ^{1}H NMR ($CDCl_3$) δ 7.96 (d, 2H, J = 7.5 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.29 (t, 1H, J = 7.5 Hz), 3.73 (d, 1H, J = 10.4 Hz), 2.78−2.63 (m, 4H), 2.17 (s, 1H), 1.97−1.89 (m, 2H), 1.69−1.57 (m, 1H), 1.26−1.13 (m, 1H), 0.90 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 138.400, 129.725, 128.301, 127.120, 79.960, 65.936, 27.067, 26.898, 24.940, 24.388, 10.991; MS (EI) *m*/*z* 254 (M^+), 195 (100%). Anal. Calcd for $C_{13}H_{18}OS_2$: C, 61.37; H, 7.13. Found: C, 61.54; H, 7.29.

***endo*-3-(1,3-Dithian-2-yl)-*exo*-3-hydroxy-1,7,7-trimethyl-2-bicyclo[2.2.1]heptanone (11)**: ^{1}H NMR ($CDCl_3$) δ 4.37 (s, 1H), 3.11 (s, 1H), 2.95−2.83 (m, 4H), 2.19 (d, 1H, J = 4.3 Hz), 2.10−2.02 (m, 1H), 2.00−1.85 (m, 1H), 1.85−1.76 (m, 1H), 1.75−1.66 (m, 1H), 1.62−1.53 (m, 1H), 1.05 (s, 3H), 1.01 (s, 3H), 0.92 (s, 3H); ^{13}C NMR with C-type assignments based on DEPT experiment ($CDCl_3$) δ 215.18 (C=O); 79.401 (4°), 58.743 (4°), 54.117 (3°), 52.373 (3°), 45.456 (4°), 29.880 (2°), 29.698 (2°), 29.181 (2°), 25.163 (2°), 22.432 (2°), 22.220 (1°), 20.491 (1°), 9,753 (1°); MS (EI) *m*/*z* 286 (M^+), 119 (100%). Anal. Calcd for $C_{14}H_{22}O_2S_2$: C, 58.70; H, 7.74. Found: C, 58.41; H, 7.92.

***endo,endo*-2,3-Bis(1,3-dithian-2-yl)-1,7,7-trimethyl-*exo,exo*-2,3-bicyclo[2.2.1]heptanediol (12)**: mp 153−154 °C; ^{1}H NMR ($CDCl_3$) δ 5.83 (s, 1H), 5.52 (s, 1H), 4.23 (s, 1H), 4.07 (s, 1H), 3.10−2.90 (m, 8H), 2.25−2.05 (m, 3H), 2.04 (d, 1H, J = 4.8 Hz), 2.01−1.90 (m, 2H), 1.76−1.64 (m, 1H), 1.58−1.48 (m, 1H), 1.46−1.37 (m, 1H), 1.21 (s, 3H), 1.06 (s, 3H), 0.81 (s, 3H); ^{13}C NMR with C-type assignments based on DEPT experiment ($CDCl_3$) δ 86.399 (4°), 85.928 (4°), 61.267 (3°), 58,628 (3°), 55.299 (4°), 53.615 (3°), 48.974 (4°), 35.149 (2°), 34.535 (2°), 31.532 (2°), 30.971 (2°), 29.143 (2°), 26.504 (2°), 26.118 (2°), 22.849 (1°), 22.584 (1°), 21.803 (2°), 12.649 (1°). Anal. Calcd for $C_{18}H_{30}O_2S_4$: C, 53.16; H, 7.44. Found: C, 52.88; H, 7.58.

***endo*-2-(1,3-Dithian-2-yl)-1,7,7-trimethyl-*exo*-2-bicyclo-[2.2.1]heptanol (13)**:[25] mp 128−129 °C (lit.[25] mp 130−131 °C); ^{1}H NMR ($CDCl_3$) δ 4.26 (s, 1H), 3.02−2.80 (m, 4H), 2.31 (s, 1H), 2.12−2.03 (m, 2H), 1.90−1.62 (m, 5H), 1.52−1.43 (m, 1H), 1.15−1.09 (m, 1H), 1.08 (s, 3H), 1.05 (s, 3H), 0.83 (s, 3H); MS (EI) *m*/*z* 272 (M^+), 119 (100%).

***trans*-1-(1,3-Dithian-2-yl)-3-phenyl-2-propenol (14)**:[26] ^{1}H NMR ($CDCl_3$) δ 7.41 (d, 2H, J = 7.45 Hz), 7.32 (t, 2H, J = 7.45 Hz), 7.24 (t, 1H, J = 7.5 Hz), 6.74 (d, 1H, J = 16.1 Hz), 6.35 (dd, 1H, J = 16.1, 6.4 Hz), 4.59−4.52 (m, 1H), 4.02 (d, 1H, J = 6.8 Hz), 3.00−2.91 (m, 2H), 2.82−2.72 (m, 2H), 2.68 (d, 1H, J = 3.4 Hz), 2.14−2.04 (m, 1H), 2.04−1.93 (m, 1H).

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General Procedure for Photolysis of the Adducts in the Presence of Benzophenone. A 10^{-2} M solution of a dithiane−carbonyl adduct was irradiated in acetonitrile containing benzophenone as a sensitizer (the same 10^{-2} M concentration) for the period of time listed in Table 1. A medium-pressure Hg Hanovia lamp with a Pyrex sleeve was used as the UV source. After irradiation, an appropriate amount of dodecane was injected into the reaction mixture as an internal standard and the yield of the liberated carbonyls was determined by gas chromatography using a calibration curve set up for corresponding aldehydes and ketones. The calibration procedure utilized the same internal standard—dodecane. Several freeze−thaw degassing cycles were found to accelerate the reaction, without affecting the preparative yield of deprotection. The times listed in Table 1, however, are of nondegassed solutions to demonstrate that even in the presence of oxygen the reaction is completed within 2−3 h. Quantum yield determinations (see below) were carried out with thoroughly degassed solutions.

Photolysis of Cinnamaldehyde Adduct 14: ***Trans*−*Cis* Isomerization.** A degassed (four freeze−thaw cycles) 0.01 M acetonitrile-d_3 solution of *trans*-1-(1,3-dithian-2-yl)-3-phenyl-2-propenol **(14)** was irradiated in a Pyrex NMR tube with 0.01 M benzophenone present. The reaction progress was monitored by NMR. Before irradiation: ^{1}H NMR (CD_3CN) δ 7.8−7.2 (m, ∼15H), 6.66 (d, 1H, J = 15.9 Hz), 6.32 (dd, 1H, J = 15.9, 6.6 Hz), 4.45−4.39 (m, 1H), 4.16 (d, 1H, J = 6.1 Hz), 3.43 (d, 1H, J = 4.7 Hz), 2.93−2.77 (m, 4H), 2.09−2.00 (m, 1H), 1.86−1.74 (m, 1H). After 25 min of irradiation a 35:65 mixture of the *trans*−*cis* isomers was obtained: ^{1}H NMR (CD_3CN) δ 7.8−7.2 (m, ∼15H), 6.67 (d, 0.65H, J = 11.6 Hz), 6.66 (d, 0.35H, J = 15.9 Hz), 6.32 (dd, 0.35H, J = 15.9, 6.6 Hz), 5.77 (dd, 0.65H J = 11.6, 9.5 Hz), 4.63−4.56 (m, 0.65H), 4.45−4.39 (m, 0.35H), 4.16 (d, 0.35H, J = 6.1 Hz), 4.14 (d, 0.65H, J = 6.6 Hz), 3.43 (d, 0.35H, J = 4.7 Hz) 3.39 (d, 0.65H, J = 5.1 Hz), 2.94−2.71 (m, 4H), 2.09−1.97 (m, 1H), 1.86−1.70 (m, 1H). We also observed trace amounts of *cis*- and *trans*-cinnamaldehydes (<3% by NMR integration): 9.94 (d, J = 8.2 Hz) and 9.68 (d, J = 7.6 Hz) in a ratio of 2:7, respectively. After extended irradiation for 1.5 h, the ratio of *cis* and *trans* adducts did not change. The amount of free aldehydes also did not increase.

Relative Quantum Yield Study. Adducts 2, 8, and 9. All samples were irradiated in Pyrex test tubes. Since the absolute yields of deprotection of substituted benzaldehydes were found to approach 100%, the quantum yield study was based on monitoring the disappearance of the starting material, measured by GC as an adduct:sensitizer ratio. First, 56.6 mg of the unsubstituted adduct **2** was weighed into a 25 mL volumetric flask and diluted to volume with the sensitizer stock solution (0.02 M benzophenone). Next, 62.8 mg of the *p*-CN-substituted adduct **8** was weighed into another 25 mL volumetric flask and diluted to volume with the sensitizer stock solution. These amounts give 0.01 M solutions of each adduct. Each sample was injected into the GC to determine the prephotolysis ratio of adduct:sensitizer. After degassing by four freeze−pump−thaw cycles, each adduct was irradiated in duplicate (total of four samples) for 5 min. To ensure even distribution of light, a carousel Rayonet photoreactor was used in these experiments. After the irradiation, each sample was injected into the GC again to obtain the new ratios. The same procedure was used for comparison of the *p*-methoxy adduct **9**: 64.1 mg of the *p*-methoxybenzaldehyde adduct **9** was weighed into a 25 mL volumetric flask and diluted to volume with the sensitizer solution. Degassed solutions of **2** and **9** were irradiated in the carousel Rayonet photoreactor. Tables 4−6 contain the actual measured ratios and calculated percent conversion.

Kinetic Isotope Effect Study. Using the same stock solutions prepared for the relative quantum yield study for each of the three benzaldehyde adducts **2**, **8**, and **9**, we removed four 4 mL portions and placed them all in separate Pyrex tubes. Taking two tubes of each adduct solution, we added 100 μL of H_2O. To the remaining six tubes we added 100 μL of D_2O. These tubes were allowed to stand overnight for isotopic exchange to take place. The samples were 2.5% aqueous solutions. The sensitizer (benzophenone) was used again as an internal standard. The actual measured ratios, % conversions, and KIE are presented in Table 7.

Table 4

Adduct	Adduct to Benzophenone Ratio (before irradiation)*	Adduct to Benzophenone Ratio (after irradiation)*
First pair:		
2	0.281	0.137
8	0.096	0.06
Second pair:		
2	0.113	0.058
9	0.188	0.088

* Average of two measurements.

Table 5

Adduct	Ratio	% Conversion
First Pair:		
2	0.488	51.2
8	0.625	37.5
Second Pair:		
2	0.513	48.7
9	0.468	53.2

Table 6

Adduct	% Conversion	% Conversion	Relative QY
p-MeO **(9)**		53.2	1.09
H **(2)**	51.2	48.7	(1.00)
p-CN **(8)**	37.5		0.73

Table 7

Adduct	Adduct:Benzophenone Ratio (before irradiation)		Adduct to Benzophenone Ratio (after irradiation)		% Conversion		KIE
	H_2O	D_2O	H_2O	D_2O	H_2O	D_2O	
2	0.2760	0.2643	0.0899	0.1068	67.4	59.6	1.13
8	0.0885	0.0813	0.0271	0.0319	69.4	60.8	1.14
9	0.2139	0.2168	0.0407	0.0573	80.9	73.6	1.09

4-(Hydroxy-(1,3-dithian-2-yl)methyl)trityl alcohol (17). A total of 0.6 g (5 mmol) of dithiane was dissolved in 40 mL of freshly distilled THF, and the solution was cooled to −20 °C under nitrogen. Then 2.8 mL of *n*-butyllithium (a 2 M solution in hexanes) was added dropwise upon stirring. The resulting mixture was stirred for 2.5 h. After that the temperature was lowered to −78 °C and 0.82 g (5 mmol) of ethyl 4-formylbenzoate dissolved in 2 mL of THF was added upon stirring. The reaction mixture was stirred for 1 h at this temperature and then was allowed to warm to 0 °C and stirred for 1 h. At this point a small portion (0.2 mL) of the reaction mixture was quenched with aqueous ammonium chloride, extracted with 1 mL of ether, dried over anhydrous Na_2SO_4, and analyzed with GC-MS. The GC-MS analysis showed only one major product present with an M^+ of 284, which corresponds to adduct **16**: MS (EI) *m*/*z* 284 (M^+), 266, 253, 165, 147, 134, 119 (100%), 106, 105, 91, 85, 77, 59, 45. The reaction sequence was then continued without isolation of **16**. To the reaction mixture containing mainly **16** at 0 °C and under N_2 was added 12 mL of 1 M PhMgBr (12 mmol) in THF slowly. The reaction was allowed to warm to room temperature and stirred for another 2 h. It was then quenched with a 1 M aqueous solution of NH_4-Cl, extracted twice with ether, and dried over Na_2SO_4. The solvent was then removed with a rotary evaporator, and the residue was purified using column chromatography (silica gel, ethyl acetate−hexane, 1:3) furnishing 1.861 g (91%) of a white crystalline solid. Upon minimal heating, the compound turn brown and melted with decomposition, becoming a dark red-brown liquid: ^{1}H NMR ($CDCl_3$) δ 7.44−7.03 (m, 14H), 4.93 (d, 1H, J = 7.6 Hz), 4.06 (d, 1H, J = 7.6 Hz), 3.07 (s, 1H), 3.02−2.93 (m, 2H), 2.91 (s, 1H), 2.78−2.67 (m, 2H), 2.14−1.95 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 146.736, 146.538, 139.029, 127.754 (several Cs), 127.087, 126.377, 81.780, 74.114, 52.211, 27.837, 27.170, 25.240; MS (EI) *m*/*z* 390 ($M^+ - H_2O$), 119 (100%). Due to thermal instability of **17,** we were unable to completely remove traces of ethyl acetate from the solid and obtained the following analytical data (low in carbon); HRMS calcd for $C_{24}H_{24}O_2S_2$ 408.1218, found 408.1053 ± 0.005. Anal. Calcd for $C_{24}H_{24}O_2S_2$: C, 70.55; H, 5.92. Found: C, 66.85; H, 5.60.

Photolysis of 17 in the Presence of Benzophenone. A total of 204 mg (0.5 mmol) of **17** was dissolved in 50 mL of

acetonitrile containing 91 mg (0.5 mmol) of benzophenone, and the solution was irradiated with a Pyrex sleeve filter for 2.5 h. The solvent was evaporated, and the residual reaction mixture was column-chromatographed (silica gel, ethyl acetate−hexane, 1:3) to give 139 mg (96%) **18** as a faintly yellow solid: ^{1}H NMR ($CDCl_3$) δ 9.99 (s, 1H), 7.83 (d, 2H, J = 8.4 Hz), 7.52 (d, 2H, J = 8.4 Hz), 7.38−7.15 (m, 10H), 2.58 (s, 1H); MS (EI) m/z 288 (M^+), 241 (100%). Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 82.96; H, 5.83.

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Supporting Information Available: ^{1}H NMR, ^{13}C NMR, 1D NOE differences, and MS spectra for compounds **11**, **12**, **16** (MS only), **17**, **18,** and **7a** (26 pages). See any current masthead page for ordering or Internet access information.

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