(C11), 119.3 (C10), 118.0 (C9), 110.7 (C12), 108.3 (C7), 62.1 (C21), 60.3 (C3), 53.4 (C5), 37.0 (C20), 34.8 (C15), 32.8 (C14), 29.7 (C16), 26.7 (C18), 26.3 (C19), 21.8 (C6), 20.8 (C17); MS m/z EI 281, 280 (M^+, 100), 279, 265, 251, 237, 223, 209, 197, 184, 169, 156.

Acknowledgment. We gratefully acknowledge financial support from the National Cancer Institute (CA 51794). We are indebted to Dr. Sadahiko Iguchi, Ono Pharmaceutical Co., Osaka, Japan, for obtaining the mass spectra and to Professor H. Heimgartner, Universitat Zurich, Germany, for a sample of (-)-yohimban. We also thank Professor A. I. Meyers, Colorado State University, for providing references regarding 1 and NMR spectra of (-)-*allo*-yohimban and Professor J. Aube, University of Kansas, for NMR spectra of (-)-*allo*-yohimban.

Registry No. (-)-1, 10252-12-7; (-)-2, 483-26-1; (+)-3, 483-25-0; (-)-4, 523-06-8; (+)-5, 123642-79-5; 6, 1519-39-7; 8S, 1517-82-4; 9, 123642-81-9; 10, 123642-82-0; 11, 123749-02-0; 12, 89772-92-9; 14, 623-43-8; 15, 137119-54-1; 16, 137119-55-2; 17, 623-70-1; 18, 6284-46-4; 19, 137008-15-2; 20, 4358-59-2; 21, 10267-94-4; 22, 123642-83-1; 23, 123749-03-1; 24, 18448-47-0; 25, 137008-16-3; 26, 137119-56-3; 30, 137008-17-4; 31, 137008-18-5; 32, 137119-57-4; (+)-33, 137008-19-6; (-)-33, 137119-58-5; (+)-34, 137008-20-9; (-)-34, 137008-21-0; 35, 137008-22-1; 36, 137119-59-6; 37, 137119-60-9; (+)-38, 123642-80-8; (-)38, 137008-23-2; 39, 525-41-7; 46, 123642-84-2; 41, 137119-61-0; 42, 123642-85-3; (+)-43, 137119-62-1; (-)-43, 103321-76-2; 44, 137119-63-2; 45, 137119-64-3; *+)-46, 137119-65-4; (-)-46, 137119-66-5; 47, 137119-67-6; 48, 137119-68-7; 49, 137120-71-9; 50, 137119-69-8; CH_2=$CHCO_2Me$, 96-33-3; $BrCCH_2)_3CN$, 5332-06-9; $BrCCH_2)_2CO_2Et$, 539-74-2.

Supplementary Material Available: Two-dimensional COSY ^1H NMR spectra for 41, 44, and 50 (5 pages). Ordering information is given on any current masthead page.

Singlet Oxygen Oxidation of Substituted Furans to 5-Hydroxy-2(5*H*)-furanone[1]

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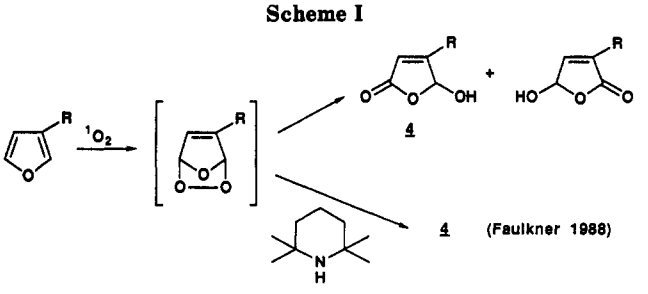
Received September 25, 1990 (Revised Manuscript Received August 2, 1991)

The conditions for the regiospecific singlet oxygen oxidation of various 2,4-disubstituted furans **9** to 4-substituted-2(5*H*)-furanones **3** are developed. The presence of a C-2 substituent (e.g., trimethylsilyl, *tert*-butyldimethylsilyl, or tributylstannyl) in **9** is an absolute requirement for the formation of the 4-substituted-5-hydroxy-2(5*H*)-furanone regioisomer **3**. When the C-2 substituent is triethylsilyl (TES) or TBDMS, however, apart from **3**, the corresponding 5-trialkylsiloxy derivative **11** is also isolated in a significant amount. These silyl acetals are unexpectedly stable but can be hydrolyzed back to **3** on stirring with dilute acid. The formation of silyl acetals, to our knowledge, has never been reported in the singlet oxygen oxidation of (trialkylsilyl)furan. A plausible mechanism for their formation is proposed. The presence of a catalytic amount of water in the oxidation of 2-(trialkylsilyl)-4-substituted-furans not only eliminates the formation of the silyl acetals but also speeds up the rate of the oxidation process. Moreover, the oxidation can then be carried out at 0 °C instead of at -78 °C. Oxidation of 2-(1-hydroxyalkyl)-4-substituted-furans in the absence of a reducing agent gives little or no sign of 2,5-disubstituted-6-hydroxy-3(2*H*)-pyranone **23** but instead **26** selectively. Thus, the (1-hydroxy)alkyl group can be utilized as the trialkylsilyl or trialkylstannyl group in dictating the regioselectivity in the singlet oxygen oxidation of substituted furans.

Introduction

The antiinflammatory properties of manoalide (**1**)[2] and luffarielloide (**2**)[3] in vivo have stimulated interest in developing a general and versatile method for constructing the 5-hydroxy-2(5*H*)-furanone nucleus. As part of our ongoing manoalide program, we desired to develop an efficient synthesis of a series of 4-substituted-5-hydroxy-2(5*H*)-furanones that contained an α-acetoxy group on the 4-alkyl chain (**3**). Herein we report the details of our general synthesis of this group based upon a thorough study of singlet oxygen oxidation of furans.

Scheme I



Results and Discussion

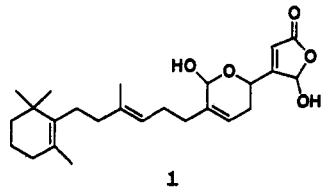
A number of methods have been developed for the synthesis of 5-hydroxy-2(5*H*)-furanones;[4] however, the one

(1) Part of this work was presented at the 198th National Meeting of the American Chemical Society, Division of Medicinal Chemistry, Miami Beach, FL, September 10-15, 1989, abstract no. 48. "Synthesis and Biological Evaluation of 2(5H)-Furanone Ring Analogs of Manoalide", Lee, G.; Amdahl, L.; Harcourt, D.; Holmes, J.; Syage, E.; Wenzel, M.; Whalin, G.; DeVries, G.; Wheeler, L.; and Garst, M. E.

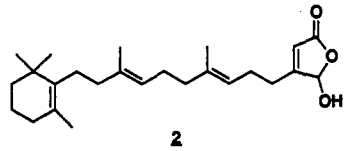
(2) (a) Lombardo, D.; Dennis, E. A. *J. Biol. Chem.* **1985**, *260*, 7234. (b) Glaser, K. B.; Jacobs, R. S. *Biochem. Pharmacol.* **1986**, *35*, 449. (c) Glaser, K. B.; Jacobs, R. S. *Biochem. Pharmacol.* **1987**, *36*, 2079.

(3) Albizati, K. F.; Holman, T.; Faulkner, D. J.; Glaser, K. B.; Jacobs, R. S. *Experientia* **1987**, *43*, 949.

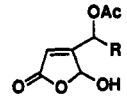
0022-3263/91/1956-7007$02.50/0



1



2



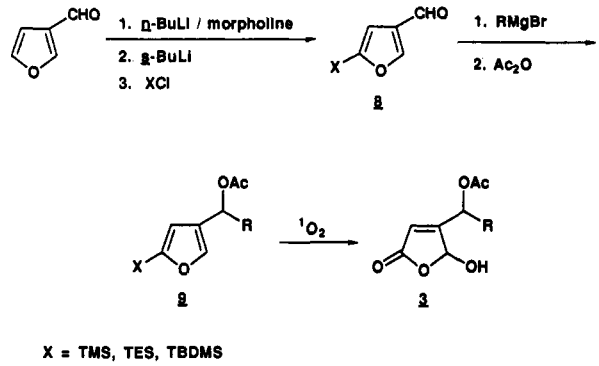
3

involving singlet oxygen oxidation of furan appears to be the most efficient and widely investigated.[5] The use of a furan as a 5-hydroxy-2(5*H*)-furanone synthon offers several potential advantages. The furan should be stable to nucleophilic reactions, mild oxidative conditions, and solvolysis. Alternatively, the furanone would require protection for side-chain manipulation by these reactions. Furthermore, singlet oxygen appeared to be a mild, potentially selective reagent, unmasking the hydroxyfuranone at the last stage of synthesis. The potential liabilities of this approach are related to the apparent lack of regiospecificity found from the oxidation of 3-substituted furans, an observation which we verified in our early work (Scheme I).[6,7] The most common solution to this problem makes use of a 4-alkylfuran substituted at the 2-position by a trimethylsilyl (TMS), formyl, or carboxylic acid group.[5a,6] At the onset of our work, this furan substitution pattern was not readily accessible, necessitating the development of a new synthesis of 2-silyl-4-furaldehyde.[8]

During the course of our work, Faulkner et al.[9] have shown that singlet oxygen oxidation of 3-alkylfuran gives the C-4 isomer (4) selectively, if a hindered base such as 2,2,6,6-tetramethylpiperidine is present during oxidation (Scheme I). On large scales, this reaction was very slow, often not going to completion. Frequently the base led to undesired product with our more complicated side chains. Hence this attractive modification was unsuitable for our purposes.

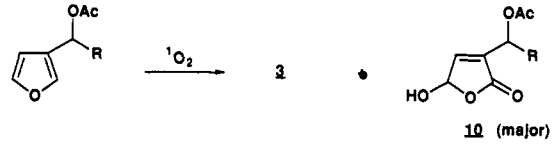
The aforementioned considerations led us to develop a synthesis via the corresponding precursor 2-(trialkylsilyl)-4-alkylfuran **9**. Our synthetic strategy to 4-(1-acetoxyalkyl)-5-hydroxy-2(5*H*)-furanone (**3**) is summarized in Scheme II. 2-(Trimethylsilyl)-4-(1-acetoxyalkyl)furan (**9**) should result from first adding the appropriate Grignard or alkyllithium reagent to 2-(alkylsilyl)-4-furaldehyde[7,10] **8** and then quenching with acetic anhydride. Subsequent singlet oxygen oxidation of **9** should lead to the desired regioisomer 5-hydroxy-2(5*H*)-furanone (**3**), as dictated by the TMS substituent at the C-2 position.

Scheme II



X = TMS, TES, TBDMS

Scheme III



10 (major)

Synthesis of Furans

Synthesis of 2-(Trimethylsilyl)-4-(1-acetoxyalkyl)furan (9). Most of the (trialkylsilyl)furans **9** were obtained by reacting the appropriate Grignard or alkyllithium reagent with 2-(trialkylsilyl)-4-furaldehyde **8** followed by acetic anhydride (Scheme II).

There are five points worth mentioning (Table I). (1) Most of the reactions in Table I were carried out in a one-pot fashion unless the resultant acetate **9** had a very similar R_f value to that of the starting halide. Under those circumstances, the acetylation step was carried out on the purified alcohol. (2) As expected for the allylic halide **6h**, the Grignard reagent not only was difficult to form but it also gave rearranged addition products.[19] (3) In many cases the electron-rich aryl halides **6w–6dd** and **6ii–6ll** only formed the Grignard reagents sluggishly, giving very poor yields of the adducts accompanied by many byproducts. Biphenyl bromide (**6w**) formed the corresponding Grignard reagent easily; however, it afforded a 25% yield of reduced 2-TBDMS-4-furaldehyde. Metal–halogen exchange of **6z** and **6aa** with *tert*-butyllithium, followed by quenching with the trialkylsilyl aldehyde also gave a very poor yield of the adduct accompanied by aldehyde reduction. (4) The Grignard/alkyllithium reagents from halides with internally acidic protons gave mixtures of addition products resulting from new carbanion sites generated by self-quenching (e.g., **6z**). (5) For analogues having organometallic sensitive functionalities on the alkyl (R) side chain (i.e. **9pp–9vv**), these functionalities were introduced by side-chain modification after the Grignard addition (**9**). The halides were prepared by standard methods detailed in the Experimental Section.

Singlet Oxidation of Furans

Most of the 4-(acetoxyalkyl)-5-hydroxy-2(5*H*)-furanones **3** reported here were synthesized by singlet oxygen oxi-

(4) See, for example: (a) Scheffold, R.; Dubs, P. *Helv. Chim. Acta* **1967**, *50*, 799. (b) Inoffen, H. H.; Krieser, W.; Nazir, M. *Liebigs. Ann. Chem.* **1972**, *755*, 1. (c) Kreiser, W.; Nazir, M. *Liebigs Ann. Chem.* **1972**, *755*, 12. (d) Sum, F. W.; Weiler, L. *J. Org. Chem.* **1979**, *44*, 1012. (e) Bourguignon, J. J.; Wermuth, C. G. *J. Org. Chem.* **1981**, *46*, 4889. (f) Laugrand, S.; Guingant, A.; d'Angele, J. *J. Org. Chem.* **1987**, *52*, 4788. (g) Ohta, T.; Tsuchiyama, H.; Nazoe, S. *Heterocycles* **1986**, *24*, 1137. (h) Cooper, G. K.; Dolby, L. J. *J. Org. Chem.* **1979**, *44*, 3414. (e) Larcheveque, M.; Lequent, Ch.; Debal, A.; Lallemand, J. Y. *Tetrahedron Lett.* **1981**, *22*, 1595.

(5) For recent reviews, see: (a) Feringa, B. L. *Recl. Trav. Chim. Pays-Bas* **1987**, *106*, 469. (b) Wasserman, H. R.; Ives, J. L. *Tetrahedron* **1981**, *37*, 1825. (c) Matsumoto, M. In *Singlet Oxygen*, Vol. II; Frimer A. A., Ed.; CRC Press Inc.: Boca Raton, FL, 1985.

(6) (a) Kuwajima, I.; Urabe, H. *Tetrahedron Lett.* **1981**, *22*, 5191. (b) Katsumura, S.; Hori, K.; Fujimara, S.; Isoe, S. *Tetrahedron Lett.* **1985**, *26*, 4625.

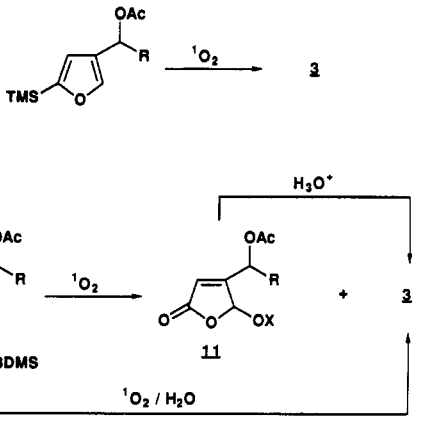
(7) Garst, M. E.; Tallman, E. A.; Bonfiglio, J. N.; Harcourt, D.; Ljungwe, E. B.; Tran, A. *Tetrahedron Lett.* **1986**, *27*, 4533.

(8) (a) Lee, G. C. M.; Holmes, J. M.; Harcourt, D. A.; Garst, M. E. *J. Org. Chem.* Submitted. (b) Lee, G. C. M. U.S. Patent 4,935,530, June 19, 1990.

(9) Kernan, M. R.; Faulkner, D. J. *J. Org. Chem.* **1988**, *53*, 2773.

(10) Katsumura, S.; Fujiwara, S.; Isoe, S. *Tetrahedron Lett.* **1985**, *26*, 5827.

Scheme IV

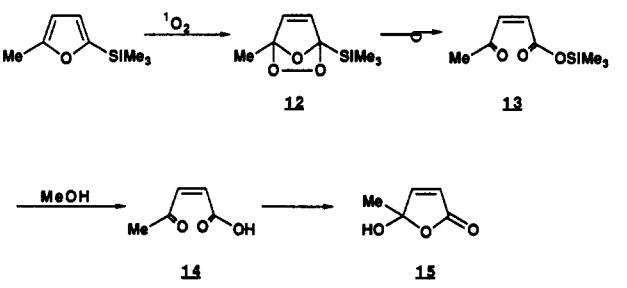


dation of the corresponding 2-TMS-4-(1-acetoxyalkyl)furan **9**. The reaction tolerates esters, acids, alcohols, isolated acetylenes or olefins, aromatics, and heteroaromatics in the side chain (Table II). The reaction was executed at −78 °C in THF, acetone, or methanol and in the presence of a catalytic amount of Rose Bengal. The use of polystyrene-bound Rose Bengal[11] is especially beneficial when the silylfuran **9** contains polar substituents. In these instances, most of the dye can be removed from the furanone by simple filtration. Typical reaction time was 1–2 h with the average yield of 5-hydroxy-2(5*H*)-furanone (**3**) of about 50–60% (Table II). The presence of a trialkylsilyl group at C-2 in **9** is an absolute requirement for formation of the 5-hydroxy-2(5*H*)-furanone regioisomer **3**. When the trialkylsilyl group as absent, singlet oxygen oxidation gave a mixture of isomers **3** and **10**, with **10** being the major product (Scheme III). We did not detect hydroperoxide intermediates despite the absence of any reducing agent. Furthermore, we saw no epoxybutenolides which often accompany furan oxidations.[5] The major disadvantage in the synthetic route (Scheme II) to 4-(1-acetoxyalkyl)-5-hydroxy-2(5*H*)-furanone (**3**) was the requirement of the relatively inaccessible 2-TMS-4-furaldehyde.[7,10]

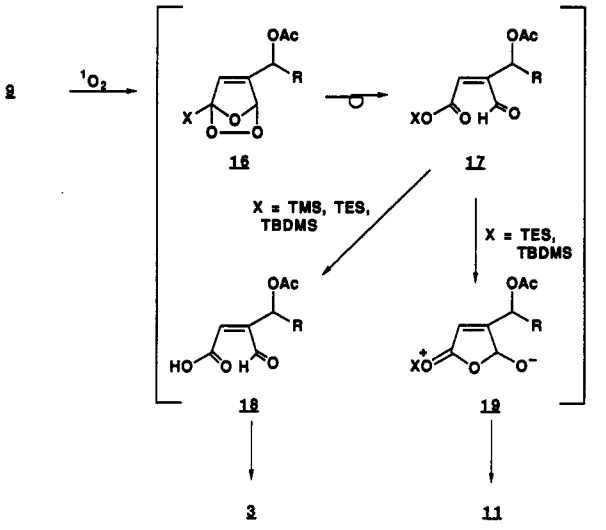
Concurrent with this work, we developed a novel one-pot synthesis of 2-substituted-4-furaldehyde from 3-furaldehyde, which more readily provides 2-(triethylsilyl)-4-furaldehyde (2-TES-4 furaldehyde) than the corresponding TMS analogue **8**.[8] As a result, using 2-(TES)-4-furaldehyde as the starting material (in Scheme II) to synthesize 4-(1-acetoxyalkyl)-5-hydroxy-2(5*H*)-furanone (**3**) is more attractive. Singlet oxygen oxidation of TMS, formyl, or carboxyfuran to hydroxyfuranone has been known for a number of years;[5,6b] however, oxidation of other (trialkylsilyl)furans had not been reported. We decided to investigate these oxidations in more detail and the results are summarized in Tables III and IV and Scheme IV. Most of the oxidations were carried out in THF at −78 °C. As seen from Table III, the size of the trialkylsilyl group does not seem to have a significant effect on the rate or yield of the reaction. With TES- or TBDMS-furan, however, apart from the expected 5-hydroxy-2(5*H*)-furanone **3**, the corresponding trialkylsiloxy derivative **11** was also isolated in a significant amount (entries 2, 4–6, Table III; Scheme IV). The silyl acetals **11b**, **11e**, and **11u** were unexpectedly stable, could be purified by flash chromatography, and hydrolyzed to the hydroxyfuranone **3** on stirring with dilute acid at room temperature (Scheme IV). The formation of these alkylsilyl acetals, to our knowledge, has never been reported

(11) Polystyrene-bound Rose Bengal is commercially available from Dyetel Inc.

Scheme V



Scheme VI



in the oxidation of (trialkylsilyl)furans. The mechanism of singlet oxygen oxidation of a 2-TMS-furan has been postulated[12] to involve an intramolecular trimethylsilyl migration in the endoperoxide intermediate **12** to the silyl ester **13**. Subsequent solvolysis of **13** gives carboxylic acid **14**, which on ring closure gives 5-hydroxy-2(5*H*)-furanone **15** (Scheme V). Thus, singlet oxygen oxidation of 2-(trialkylsilyl)-4-(1-acetoxyalkyl)furan **9** should give endoperoxide **16**, which on rearrangement gives silyl ester **17**. If the trialkylsilyl ester **17** (X = TES, TBDMS) undergoes solvolysis more slowly, intramolecular ring closure of **17** to **19** and hence to silyl ketal **11** becomes an important pathway (Scheme VI). Therefore, enhancing the rate of hydrolysis of **17** (X = TES, TBDMS) to **18** should eliminate the formation of **11**. To our delight, addition of water (ca. 20 equiv) to the photolysis mixture not only completely eliminated the formation of silyl ketal **11** (entries 3–5, 8, and 10; Table IV) but also increased the rate of the oxidation process. Moreover, the oxidation could then be carried out at 0 °C without any appreciable decrease in yield (Table IV).

We have also investigated the singlet oxygen oxidation of other substituted furans, including 2-bromo-, and 2-(tributylstannyl)-4-alkylfurans and 2-(1-hydroxyalkyl)-furans to determine the potential regiochemical directing effects of these substituents in the singlet oxygen oxidation reaction. Under the oxidation conditions (−78 °C/2 h) used for the corresponding 2-(trialkylsilyl)furans, 2-bromo-4-alkylfuran gave a very complicated mixture with no sign of hydroxyfuranone (data not shown). Quenching of the dye, presumably by the bromine radical liberated, was observed. 2-(Tributylstannyl)-4-(1-tridecenyl)furan (**20**), however, gave the expected hydroxyfuranone **21**, albeit in low yield (28%). In comparison, under identical

(12) Adam, W.; Rodriguez, A. *Tetrahedron Lett.* **1981**, *22*, 3505.

Table I

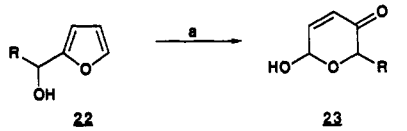
entry	halide/reagent	R	% yield[a]
1	n-C_4H_9Li (**7a**)	n-C_4H_9 (**9a**)	79
2	n-$C_8H_{17}Br$ (**6b**)	n-C_8H_{17} (**9b**)	84 (100,[a,c] 86[a,b])
3	n-$C_{10}H_{21}Br$ (**6c**)	n-$C_{10}H_{21}$ (**9c**)	40
4	n-$C_{11}H_{23}Br$ (**6d**)	n-$C_{11}H_{23}$ (**9d**)	68[b]
5	n-$C_{12}H_{25}Br$ (**6e**)	n-$C_{12}H_{25}$ (**9e**)	95 (80[a,b])
6	n-$C_{18}H_{37}Br$ (**6f**)	n-$C_{18}H_{37}$ (**9f**)	75
7	$Me_2C{=}CH(CH_2)_2Br$ (**6g**)	$Me_2C{=}CH(CH_2)_2$ (**9g**)	93
8	$Me[MeC{=}CH(CH_2)_2]_2MeC{=}CHCH_2Cl$ (**6h**)	$Me[MeC{=}CH(CH_2)_2]_2CMeCH{=}CH_2$ (**9h**)	95
9	$C_4H_9C{\equiv}C(CH_2)_2C{\equiv}CLi$ (**6i**)	$C_4H_9C{\equiv}C(CH_2)_2C{\equiv}C$ (**9i**)	52
10	 (**6j**)	 (**9j**)	82
11	t-$BuMe_2SiO(CH_2)_8Br$ (**6k**)	t-$BuMe_2SiO(CH_2)_8$ (**9k**)	100
12	t-$BuMe_2SiO(CH_2)_{11}Br$ (**6l**)	t-$BuMe_2SiO(CH_2)_{11}$ (**9l**)	55[d]
13	c-$C_6H_{11}MgCl$ (**7m**)	c-C_6H_{11} (**9m**)	95
14	PhLi (**7n**)	Ph (**9n**)	68
15	1-Br,2-(n-$C_{11}H_{23}C{\equiv}C$)C_6H_4 (**6p**)	2-(n-$C_{11}H_{23}C{\equiv}C$)C_6H_4 (**9p**)	27[a]
16	1-Br,4-(n-$C_3H_7C{\equiv}C$)C_6H_4 (**6q**)	4-(n-$C_3H_7C{\equiv}C$)C_6H_4 (**9q**)	65[a]
17	2-Li-benzo[b]thiophene (**7r**)	2-Benzo[b]thiophene (**9r**)	
18	$Ph(CH_2)_3Br$ (**6s**)	$Ph(CH_2)_3$ (**9s**)	79
19	c-$C_6H_{11}(CH_2)_5Br$ (**6t**)	c-$C_6H_{11}(CH_2)_5$ (**9t**)	100
20	$Ph(CH_2)_5Br$ (**6u**)	$Ph(CH_2)_5$ (**9u**)	91[a,b] (82[a,c])
21	$Ph(CH_2)_3C{\equiv}CLi$ (**7v**)	$Ph(CH_2)_3C{\equiv}C$ (**9v**)	60[a]
22	4-Ph-$C_6H_4(CH_2)_5Br$ (**6w**)	4-Ph-$C_6H_4(CH_2)_5$ (**9w**)	61[a,c]
23	2,4,5-$F_3C_6H_2(CH_2)_5Br$ (**6x**)	2,4,5-$F_3C_6H_2(CH_2)_5$ (**9x**)	57[a,c]
24	1-Napth$(CH_2)_5Br$ (**6y**)	1-Napth$(CH_2)_5$ (**9y**)	10
25	1-Napth$C{\equiv}C(CH_2)_3Br$ (**6z**)	1-Napth$C{\equiv}C(CH_2)_3$ (**9z**)	16
26	2-Napth$(CH_2)_5Br$ (**6aa**)	2-Napth$(CH_2)_5$ (**9aa**)	35
27	2-Py$(CH_2)_5Br$ (**6bb**)	2-Py$(CH_2)_5$ (**9bb**)	16[a]
28	2-Thienyl$(CH_2)_8Br$ (**6cc**)	2-Thienyl$(CH_2)_8$ (**9cc**)	80
29	2-Benzo[b]thienyl$(CH_2)_6Br$ (**6dd**)	2-Benzo[b]thienyl$(CH_2)_6$ (**9dd**)	88
30	$Ph(CH_2)_9Br$ (**6ee**)	$Ph(CH_2)_9$ (**9ee**)	84
31	(E)-$Ph(CH_2)_2CH{=}CH(CH_2)_5Br$ (**6ff**)	(E)-$Ph(CH_2)_2CH{=}CH(CH_2)_5$ (**9ff**)	88
32	$Ph(CH_2)_{10}Br$ (**6gg**)	$Ph(CH_2)_{10}$ (**9gg**)	68[a,c]
33	4-$HO_2CC_6H_4C{\equiv}C(CH_2)_3Br$ (**6hh**)		
34	4-$MeOC_6H_4(CH_2)_5Br$ (**6ii**)		
35	2,4-$(MeO)_2C_6H_3(CH_2)_5Br$ (**6jj**)		
36	2-Py$C{\equiv}C(CH_2)_3Br$ (**6kk**)		
37	2-Napth$C{\equiv}C(CH_2)_3Br$ (**6ll**)		
38	2-Quin$(CH_2)_5Br$ (**6mm**)		
39	2-Quin$C{\equiv}C(CH_2)_2CH{=}CBr_2$ (**6nn**)		
40		$HO(CH_2)_8$ (**9pp**)	87[d]
41		$AcO(CH_2)_8$ (**9qq**)	91[d]
42		$HO_2C(CH_2)_7$ (**9rr**)	81[d]
43		$EtO_2C(CH_2)_7$ (**9ss**)	47[d]
44		$HO(CH_2)_{11}$ (**9tt**)	87[d]
45		$AcO(CH_2)_{11}$ (**9uu**)	55[d]
46		$HO_2C(CH_2)_{10}$ (**9vv**)	29[d]
47		4-(n-C_5H_{11})C_6H_4 (**9ww**)	100[d]

[a] Yield was based on halide **6**. [b] Reaction was done on 2-(triethylsilyl)-4-furaldehyde. [c] Reaction was done on 2-(*tert*-butyldimethylsilyl)-4-furaldehyde. [d] Yield was based on its immediate precursor.

conditions, the corresponding 2-trimethylsilyl derivative of **20** gave **21** in 51% yield.

The singlet oxygen oxidation of 2-(1-hydroxyalkyl)furans **22**, however, gave more promising results. It is well documented that oxidation of 2-(1-hydroxyalkyl)furans **22** using singlet oxygen followed by a reducing agent/oxygen scavenger,[13] bromine/methanol,[14] pyridinium chlorochromate,[15] or *tert*-butyl hydroperoxide[16] gives 6-hydroxy-3(2*H*)-pyranones **23** (Scheme VII). When the singlet oxygen oxidation of 2-(1-hydroxyalkyl)furans **24a–d** were carried out *in the absence of a reducing agent*, a completely different course of reaction was observed.

Scheme VII[a]



22 **23**

[a] (a) $^1O_2$ or Br_2/MeOH/or PCC or ^{t}BuOOH/$VO(acac)_2$.

Exposure of 2-(1-hydroxybenzyl)furan (**24a**) to singlet oxygen under the usual conditions gave 5-hydroxy-2-(5*H*)-furanone (**26**, R_2 = H) and benzaldehyde. No sign of 2-phenyl-6-hydroxy-3(2*H*)-pyranone (**23**, R_1 = Ph) was detected (entry 1, Table V). Related fragmentations of α-substituted furans have been reported by several groups.[5a] When the reaction was carried out at −78 °C, the pyranone **23** was formed in about 1% or less (entries 3 and 4, Table V). Neither the solvents (entries 8 and 9, Table V) nor the presence of water in the solvent (entries 1 and 2, Table V) had any obvious effects. When the α-hydroxy group is protected as an acetate (entry 6, Table

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Table II

$$9 \xrightarrow{^1O_2} 3$$

entry	R	time (h)	% yield of 3[c]
1	n-C_4H_9 (**9a**)	2	79
2	n-C_8H_{17} (**9b**)	6	41
3	n-$C_{10}H_{21}$ (**9c**)	3.5	39
4	n-$C_{11}H_{23}$ (**9d**)	1.5	50[a]
5	n-$C_{12}H_{25}$ (**9e**)	2	60
6	n-$C_{18}H_{37}$ (**9f**)	2	98
7	$Me_2C{=}CH(CH_2)_2$ (**9g**)	2	89
8	$Me[MeC{=}CH(CH_2)_2]_2CMeCH{=}CH_2$ (**9h**)	2	13
9	$C_4H_9C{\equiv}C(CH_2)_2C{=}C$ (**9i**)	2	48
10	 $(CH_2)_2CMe{=}CH(CH_2)_2Br$ (**9j**)	2	48
11	t-$BuMe_2SiO(CH_2)_8$ (**9k**)	1	75
12	t-$BuMe_2SiO(CH_2)_{11}$ (**9l**)	1	56
13	c-C_6H_{11} (**9m**)	2	100
14	Ph (**9n**)	2	93
15	2-(n-$C_{11}H_{23}C{\equiv}C$)C_6H_4 (**9p**)	2.5	55
16	4-(n-$C_3H_7C{\equiv}C$)C_6H_4 (**9q**)	2	52
17	2-Benzo[*b*]thiophene (**9r**)	2	96
18	$Ph(CH_2)_3$ (**9s**)	4	78
19	c-$C_6H_{11}(CH_2)_5$ (**9t**)	1	87
20	$Ph(CH_2)_5$ (**9u**)	1	40
21	$Ph(CH_2)_3C{\equiv}C$ (**9v**)	2.5	80
22	4-Ph-$C_6H_4(CH_2)_5$ (**9w**)	2	24[b]
23	2,4,5-$F_3C_6H_2(CH_2)_5$ (**9x**)	2	39
24	1-Napth$(CH_2)_5$ (**9y**)	1.5	96
25	1-NapthC$\equiv$C$(CH_2)_3$ (**9z**)	2	53
26	2-Napth$(CH_2)_5$ (**9aa**)	1.5	76
27	2-Py$(CH_2)_5$ (**9bb**)	2	50
28	2-Thienyl$(CH_2)_8$ (**9cc**)	2	92
29	2-Benzo[*b*]thienyl$(CH_2)_6$ (**9dd**)	2	88
30	$Ph(CH_2)_9$ (**9ee**)	2	71
31	(*E*)-$Ph(CH_2)_2CH{=}CH(CH_2)_5$ (**9ff**)	2	92
32	$Ph(CH_2)_{10}$ (**9gg**)	2	51
33	$HO(CH_2)_8$ (**9pp**)	2	88
34	$AcO(CH_2)_8$ (**9qq**)	1	67
35	$HO_2C(CH_2)_7$ (**9rr**)	2	88
36	$EtO_2C(CH_2)_7$ (**9ss**)	2	88
37	$HO(CH_2)_{11}$ (**9tt**)	1	58
38	$AcO(CH_2)_{11}$ (**9uu**)	1	90
39	$HO_2C(CH_2)_{11}$ (**9vv**)	1	66
40	4-(n-C_5H_{11})C_6H_4 (**9ww**)	2	54

[a] Reaction was done on the triethylsilyl derivative. [b] Reaction was done on the *tert*-butyldimethylsilyl derivative. [c] All the yields refer to isolated material.

Table III

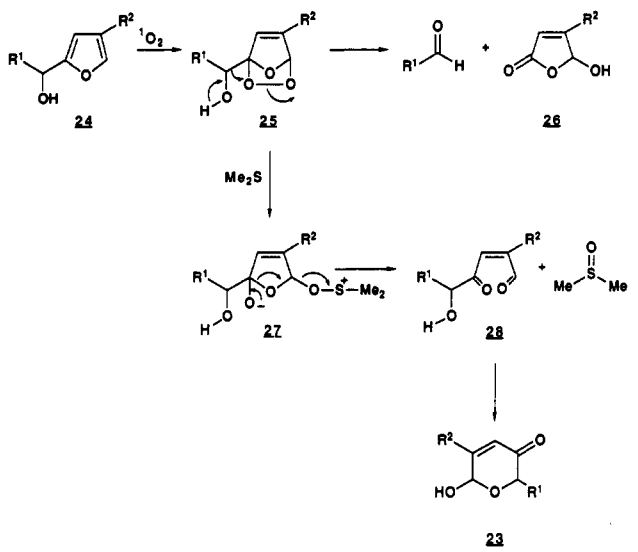
$$9 \xrightarrow[-78\ ^\circ C]{^1O_2} 3 + 11$$

entry	R	X	time (h)	% yield of 3[a]	% yield of 11
1	$CH_3(CH_2)_7$	TMS	5.5	43 (**3b**)	
2	$CH_3(CH_2)_7$	TES	1	43	37 (**11b**)
3	$CH_3(CH_2)_{11}$	TMS	2	60 (**3e**)	
4	$CH_3(CH_2)_{11}$	TES	2	46	33 (**11e**)
5[b]	$CH_3(CH_2)_{11}$	TBDMS	1	43	21 (**11e**)
6	$(CH_2)_5Ph$	TES	4	65 (**3u**)	20 (**11u**)

[a] All the yields refer to isolated material. [b] Executed at 0 °C.

V), under identical oxidation conditions, a complicated mixture of unidentified products with no sign of **26** or **23** was obtained. However, when the oxidation was carried out at −78 °C, followed by quenching with excess dimethyl sulfide at −60 °C,[14] the expected 2-substituted-6-hydroxy-3(2*H*)-pyranone **23** was obtained (entry 5, Table V). The successful formation of **23** depends on the quenching of the endoperoxide at low temperature (<−60 °C). At higher temperature, the endoperoxide fragments

Scheme VIII



readily to 5-hydroxy-2(5*H*)-furanone **26**. A plausible mechanism for the formation of **23** and **26** is outlined in Scheme VIII. Addition of singlet oxygen to **24** gives the endoperoxide **25**, which, on fragmentation as shown, yields the 5-hydroxy-2(5*H*)-furanone **26**. In the presence of dimethyl sulfide, the endoperoxide **25** is converted to **27**, which, on elimination of dimethyl sulfoxide, gives the keto aldehyde **28**. On ring closure, **28** is converted to 6-hydroxy-3(2*H*)-pyranone **23**. The results indicate that a (1-hydroxyalkyl) group can be used, like a trialkylsilyl group, to dictate the regioselectivity in the singlet oxygen oxidation of these substituted furans. The oxidation of some 2-bromo- and 2-(trialkylsilyl)-3-alkylfurans with other oxidants like pyridinium chlorochromate,[17] perbenzoic acid, or peracetic acid[18] were also examined. These oxidants had been reported to oxidize furans to the corresponding hydroxyfuranones. All of the 4-(1-acetoxyalkyl)-2-(trialkylsilyl)- or 2-bromofurans tried gave complex mixtures with any of the above oxidants.

Together with our previous report on the synthesis of 2-(triethylsilyl)-4-furaldehyde,[8] we have developed an extremely efficient synthesis of 4-(1-acetoxyalkyl)-5-hydroxy-2(5*H*)-furanones from commercially available 3-furaldehyde. The success of this whole process depends in part on the modifications developed for the singlet oxygen oxidation of the 2-(triethylsilyl)-4-alkylfuran **9**. All the 4-(1-acetoxyalkyl)-5-hydroxy-2(5*H*)-furanones **3** described here have significant biological activities which will be reported separately in due course.

Experimental Section

^1H NMR (299.943 MHz) and ^{13}C NMR spectra (75.429 MHz) were obtained in $CDCl_3$ and chemical shifts are reported in δ units (parts per million) downfield of tetramethylsilane. Analytical thin layer chromatography (TLC) was performed on precoated 0.25-mm silica gel 60PF-254 and the spots were visualized with UV or by spraying with a solution of 5% phosphomolybdic acid in ethanol and heated at ca. 200 °C for a few minutes. All reactions

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(19) (a) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1. (b) Benkeser, R. A. *Synthesis* 1971, 347.
(20) Schmidt, S. P.; Brooks, D. W. *Tetrahedron Lett.* **1987**, *28*, 767.
(21) Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 7408.
(22) Takacs, J. M.; Helle, M. A.; Seely, F. L. *Tetrahedron Lett.* **1986**, *27*, 1257.
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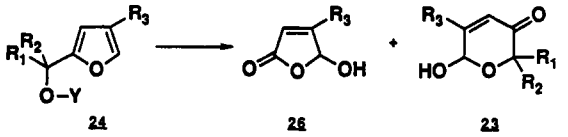
Table IV

$$9 \xrightarrow{^1O_2} 3 + 11$$

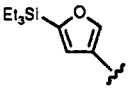
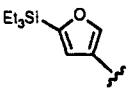
entry	R	solvent	water (equiv)	temp (°C)/time	% yield of 3[a]	% yield of 11
			X = TES			
1	$CH_3(CH_2)_7$	acetone		−78/4 h	55 (**3b**)	23 (**11b**)
2	$CH_3(CH_2)_7$	THF		−78/1 h	43	37
3	$CH_3(CH_2)_7$	THF	20	−78/35 min	76	
4	$CH_3(CH_2)_7$	THF	20	−78/20 min	45	
5	$CH_3(CH_2)_7$	THF	20	0/45 min	94	
6	$CH_3(CH_2)_{11}$	acetone		−78/2 h	45 (**3e**)	42 (**11e**)
7	$CH_3(CH_2)_{11}$	THF		−78/2 h	46	33
8	$CH_3(CH_2)_{11}$	THF	20	0/45 min	86	
			X = TBDMS			
9	$CH_3(CH_2)_{11}$	THF		0/1 h	42 (**3e**)	21 (**11e**)
10	$CH_3(CH_2)_{11}$	THF	20	0/1 h	68	

[a] All the yields refer to isolated material.

Table V



24 **26** **23**

entry	R_1	R_2	R_3	Y	oxidation conditions	% yield **26**	% yield **23**
1	Ph (**24a**)	H	H	H	0 °C, THF, 6 h	70	
2	Ph	H	H	H	0 °C, $3H_2O$, THF, 3 h	78	
3	Ph	H	H	H	−78 °C, THF, 5 h	81	1
4	*n*-Bu (**24b**)	H	H	H	0 °C, $3H_2O$, THF, 3 h	85	traces
5	*n*-Bu	H	H	H	−78 °C, THF, 7 h, excess Me_2S at −60 °C		65
6	*n*-Bu	H	H	Ac	0 °C, $3H_2O$, THF, 5 h		
7	 (**24c**)		H	H	0 °C, 5 H_2O, acetone, 7h	60	
8		H	$CH_3(CH_2)_{12}$	H	0 °C, $5H_2O$, THF, 1 h	44	
9		H	$CH_3(CH_2)_{12}$	H	−78 °C, $5H_2O$, acetone, 7 h	50	

involving moisture-sensitive reagents were carried out in oven- or flame-dried apparatus under Ar. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl under Ar before use. Unless otherwise stated, all commercial reagents were used as received.

General Procedure for the Synthesis of 4-(1-Acetoxyalkyl)-2-(trialkylsilyl)furan 9 from an Alkylmagnesium Halide or Alkyllithium with 2-(Trialkylsilyl)-4-furaldehyde. A solution of 2-(trialkylsilyl)-4-furaldehyde (1 equiv) in THF was added to an alkylmagnesium halide (prepared from magnesium turnings and the corresponding alkyl halide in THF) or alkyllithium (ca. 1.2 equiv) at 0 °C under Ar. When the reaction was completed, as shown by TLC, excess acetic anhydride (Ac_2O, 3 equiv) was added and stirring was continued at rt overnight (for convenience). The mixture was quenched with saturated NH_4Cl and was extracted with an appropriate solvent (usually ethyl ether). Evaporation of the dried ($MgSO_4$) extracts gave the crude product, which was chromatographed to give the desired acetate.

In some cases, the alcohol was isolated and purified before the acetylation (Ac_2O/pyridine) was carried out.

General Procedure for Singlet Oxygen Oxidation of 4-Alkyl-2-(trialkylsilyl)furan to 4-Alkyl-5-hydroxy-2(5*H*)-furanone 3. A mixture of 4-alkyl-2-(trialkylsilyl)furan and Rose Bengal (catalytic ca. 3 mg) in THF, acetone, or MeOH (ca. 0.05 M) was exposed to singlet oxygen (generated from oxygen with a 150-W flood lamp) at −78 °C (or 0 °C) until all the silylfuran was consumed. For 4-alkyl-2-(triethylsilyl)furan, the oxidation was done in the presence of about 5–20 equiv of water in THF or acetone at 0 °C. The residue, after solvent removal, was purified by chromatography or recrystallization to give the desired 5-hydroxy-2(5*H*)-furanone **3**.

The synthesis of a typical exmaple of **3** (e.g. **3d**) is illustrated below. Full experimental details for the synthesis of alcohols **5**, halides **6**, silylfurans **9**, and 5-hydroxy-2(5*H*)-furanones **10** disucssed in this paper are available as supplementary material.

4-(1-Acetoxydodecyl)-2-(triethylsilyl)furan (9d). A solution of 2-(triethylsilyl)-4-furaldehyde[8] (2.0 g, 9.52 mmol) in THF (5 mL) was added to a solution of undecylmagnesium bromide (19.0 mmol; prepared from 460 mg of Mg turnings and 4.50 g of 1-bromoundecane) in THF at 0 °C. After all the aldehyde has reacted, as followed by TLC (10% EtOAc/hexane), Ac_2O (2.7 mL, 28.6 mmol) was added. Stirring continued overnight and the mixture was poured into water. Extraction (ether) and evaporation of the dried ($MgSO_4$) extracts gave an oil, which was purified by flash chromatography (SiO_2, 2.5% ether/hexane) to give 3.26 g (84%) of **9d** as a pale yellow oil: ^1H NMR 0.76 (q, 6 H, J = 7.3 Hz), 0.88 (t, 3 H, J = 6.5 Hz), 0.97 (t, 9 H, J = 7.3 Hz), 1.25 (br s, 18 H), 1.80 (m, 2 H), 2.05 (s, 3 H), 5.78 (t, 1 H, J = 7.6 Hz), 6.59 (s, 1 H), and 7.60 (s, 1 H); ^{13}C NMR 2.8, 6.9, 13.8, 21.0, 22.4, 25.3, 29.0, 29.1, 29.2, 29.3, 29.4, 31.7, 34.6, 66.5, 119.8, 124.9, 144.7, 159.5, and 170.8; HRMS exact mass calcd for $C_{24}H_{44}O_3Si$ (M^+) 408.3060, found 408.3046.

4-(1-Acetoxydodecyl)-5-hydroxy-2(5*H*)-furanone (3d). A mixture of 4-(1-acetoxydodecyl)-2-(triethylsilyl)furan (377.2 mg, 0.92 mmol), water (a few drops), and Rose Bengal (3 mg) in acetone (100 mL) was exposed to singlet oxygen at 0 °C. The residue, after sovlent removal, was purified by flash chromatography (SiO_2, 60% ether/hexane) to give 150.3 mg (50%) of **3d**

as a colorless solid: mp 78–80 °C (recrystallized from ether/hexane); R_f (60% ether/hexane) 0.35; ^{1}H NMR 0.88 (t, 3 H, J = 6.5 Hz), 1.26 (m, 18 H), 1.79 (m, 2 H), 2.11 (s, 3 H), 2.14 (s, 3 H), 4.28 (br s, 1 H), 4.95 (br s, 1 H), 5.37 (t, 1 H, J = 6.3 Hz), 5.48 (t, 1 H, J = 6.3 Hz), 5.98 (s, 1 H), 6.00 (s, 1 H), and 6.20 (br s, 1 H); ^{13}C NMR 14.1, 20.8, 22.6, 24.9, 29.1, 29.2, 29.3, 29.4, 29.5, 31.9, 33.0, 69.2, 69.8, 98.0, 118.3, 119.1, 166.6, 167.2, 169.9, 170.3, 170.7, 170.8, and 171.2; HRMS exact mass calcd for $C_{13}H_{34}O_5N$ $(M + NH_4)^+$ 344.2437, found 344.2420.

(*E,Z*)-2-(1-Tridecenyl)-4-(tributylstannyl)furan (20). *n*-Butyllithium (a 2.5 M solution in hexane; 1.08 mL, 1.78 mmol) was added to a suspension of dodecyltriphenylphosphonium bromide (886 mg, 1.73 mmol) at 0 °C under Ar. After 20 min, a solution of 5-(tributylstannyl)-3-furaldehyde[8] (555 mg, 1.44 mmol) in THF (2 mL) was added. Stirring was continued (15 h), while the cooling bath attainted rt. The crude product was purified by chromatography on silica gel, eluting with 5% ether/hexane (R_f = 0.52) to give 390.4 mg (51%) of (*E,Z*)-3-(1-tridecyl)-5-(tributylstannyl)furan (**20**): ^{1}H NMR 0.90–1.70 (m, 48 H), 2.30 (m, 2 H), 5.60 (2t, 1 H), 5.95 (2t, 1 H), 6.15 (d, 1 H, J = 11.5 Hz), 6.25 (d, 1 H), 6.49 (s, 1 H), 6.53 (s, 1 H), 7.42 (s, 1 H), 7.43 (s, 1 H), and 7.47 (s, 1 H); LRMS m/e (rel abundance) 538 (M^+, 2), 509 (2), 481 (100), 425 (21), and 367 (2).

(*E,Z*)-4-(1-Tridecenyl)-5-hydroxy-2(5*H*)-furanone (21) was obtained from 4-(1-tridecenyl)-2-(tributylstannyl)furan (**20**, 154 mg, 0.29 mmol) and singlet oxygen (2 h/−78 °C). The crude product was purified on silica gel, eluting with 60% ether/hexane to give 22.8 mg (28%) of **21** as a colorless solid. The two isomers were separated by HPLC (SiO_2, 10% ethyl acetate/hexane): ^{1}H NMR *E* isomer 0.88 (t, 3 H, J = 7.0 Hz), 1.26 (br s, 16 H), 1.45 (m, 2 H), 2.25 (m, 2 H), 4.55 (br, 1 H), 5.84 (s, 1 H), 6.23 (s, 1 H), 6.29 (d, 1 H, J = 16.0 Hz), 6.55 (dt, 1 H, J = 16.0, 6.9 Hz); ^{13}C NMR *E* isomer 14.1, 22.7, 28.3, 29.2, 29.3, 29.4, 29.5, 29.6, 31.9, 33.6, 97.8, 115.0, 120.3, 145.7, 161.7, and 171.7; HRMS exact mass calcd for $C_{17}H_{29}O_3$ $(M + H)^+$ 281.2117, found 281.2127; ^{1}H NMR *Z* isomer 0.88 (t, 3 H, J = 6.4 Hz), 1.26 (br s, 16 H), 1.48 (m, 2 H), 2.30 (m, 2 H), 4.85 (br, 1 H), 6.00 (s, 1 H), 6.04 (d, 1 H, J = 11.8 Hz), 6.14 (s, 1 H), and 6.20 (dt, 1 H, J = 11.8, 7.2 Hz); ^{13}C NMR *Z* isomer 14.1, 22.7, 29.0, 29.1, 29.3, 29.5, 29.6, 30.4, 31.9, 99.2, 117.2, 117.7, 146.5, 160.5, and 172.0; HRMS exact mass calcd for $C_{17}H_{29}O_3$ $(M + H)^+$ 281.2117, found 281.2101.

2-(1-Hydroxybenzyl)furan (24a). 2-Furaldehyde (1.60 g, 16.7 mmol; freshly distilled) was added to a solution of phenylmagnesium chloride (a 2.0 M solution in THF; 8.32 mL, 16.7 mmol) at 0 °C under Ar. After 30 min, the mixture was quenched with saturated NH_4Cl. Extraction (ether) and evaporation of the dried ($MgSO_4$) extracts gave an oil, which was purified by flash chromatography on silica, using 20% EtOAc/hexane to give 2.41 g (83%) of **24a** as a pale yellow oil: ^{1}H NMR 2.50 (d, 1 H, J = 4.6 Hz), 5.78 (d, 1 H, J = 4.6 Hz), 6.12 (d, 1 H, J = 3.0 Hz), 6.30 (m, 1 H), and 7.35 (m, 6 H).

2-(1-Hydroxypentyl)furan (24b). *n*-BuLi (a 1.6 M solution in hexane; 15.1 mL, 24.1 mmol) was added dropwise to a solution of 2-furaldehyde (2.32 g, 24.1 mmol) in THF (10 mL) at −78 °C under Ar. After 1 h of stirring at rt, the mixture was processed and purified as above to give 2.12 g (57%) of **24b**: ^{1}H NMR 0.86 (t, 3 H, J = 6.3 Hz), 1.30 (m, 4 H), 1.80 (m, 2 H), 2.27 (br, 1 H), 4.60 (br t, 1 H), 6.17 (d, 1 H, J = 2.5 Hz), 6.27 (m, 1 H), and 7.32 (br s, 1 H); ^{13}C NMR 13.7, 22.2, 27.4, 35.0, 67.7, 105.7, 110.1, 141.9 and 157.2; HRMS exact mass calcd for $C_9H_{14}O_2$ 154.0994, found 154.0996.

2-(1-Acetoxypentyl)furan. A mixture of 2-(1-hydroxypentyl)furan (329 mg, 2.14 mmol), pyridine (0.26 mL, 3.2 mmol), and Ac_2O (1 mL) was stirred at room temperature for 12 h. After most of the solvent was removed, the residue was dissolved in water. Extraction (ether) and evaporation of the dried ($MgSO_4$) extracts gave an oil, which was purified by flash chromatography on silica with 5% EtOAc/hexane to give 109 mg (26%) of the desired acetate: ^{1}H NMR 0.86 (t, 3 H, J = 7.2 Hz), 1.30 (m, 4 H), 1.89 (m, 2 H), 2.02 (s, 3 H), 5.80 (t, 1 H, J = 7.8 Hz), 6.30 (m, 2 H), and 7.56 (br s, 1 H); ^{13}C NMR 13.6, 20.9, 22.1, 27.3, 32.0, 68.7, 108.4, 110.2, 142.6, 153.1, and 170.6; LRMS (m/e, rel abundance) 196 (M^+, 18), 154 (33), 137 (100), 107 (30), 97 (46), 94 (25), and 81 (31).

1-(2-Furyl)cyclohexan-1-ol (24c). *sec*-BuLi (a 1.3 M solution in cyclohexane; 14.9 mL, 19.4 mmol) was added to a solution of furan (1.41 mL, 19.4 mmol) in THF (5 mL) at −78 °C under Ar. After 2 h at −78 °C, cyclohexanone (2.11 mL, 20.4 mmol) was added. Stirring was continued for another 5 h before the mixture was quenched with water. Extraction (ether) and evaporation of the extract gave an oil, which was purified by flash chromatography on silica using 20% ether/hexane to give 916 mg (28%) of **24c**: ^{1}H NMR 1.51 (m, 4 H), 1.71 (m, 2 H), 1.84 (m, 3 H), 1.96 (m, 2 H), 6.20 (d, 1 H, J = 3.5 Hz), 6.32 (dd, 1 H, J = 3.5, 2.2 Hz), and 7.3 (d, 1 H, J = 2.2 Hz); ^{13}C NMR 21.8, 25.1, 36.3, 69.8, 104.3, 109.9, 141.3, and 160.3; LRMS (m/e, rel abundance) 166 (M^+, 37), 150 (3), 149 (31), 138 (11), 124 (9), 123 (100), 110 (27), and 95 (20).

2-[[2-(Triethylsilyl)-4-furyl]hydroxymethyl]-4-furaldehyde. *n*-BuLi (a 2.5 M solution in hexane; 5 mL, 12 mmol) was added to a solution of *N*-methylpiperazine (freshly distilled over BaO; 1.39 mL, 12 mmol) in THF (15 mL) at −78 °C under Ar. After 15 min, 3-furaldehyde (1.08 mL, 12 mmol) was added. After another 20 min, *sec*-BuLi (a 1.3 M solution in hexane; 9.62 mL, 12 mmol) was added. Stirring was continued at −78 °C for 2 h before a solution of 2-(triethylsilyl)-4-furaldehyde[8] (2.5 g, 11.9 mmol) was added. When all the silyl aldehyde was consumed (ca. 30 min), the mixture was quenched with ice-cold dilute HCl. The ether extracts were combined, washed (5% $NaHCO_3$), and dried ($MgSO_4$). Evaporation of extracts gave an oil, which was purified on silica using 30% ether/hexane to give 1.72 g (49%) of the titled compound: R_f (30% ethyl ether/hexane) 0.08; ^{1}H NMR 0.76 (q, 6 H, J = 7.8 Hz), 0.97 (t, 9 H, J = 7.8 Hz), 2.35 (br, 1 H), 5.82 (s, 1 H), 6.64 (s, 1 H), 6.68 (s, 1 H), 7.67 (s, 1 H), 8.06 (s, 1 H), and 9.91 (s, 1 H); ^{13}C NMR 2.9, 7.1, 62.5, 103.5, 119.5, 124.8, 128.9, 144.3, 151.3, 158.6, 159.8, and 184.7; HRMS exact mass calcd for $C_{16}H_{22}O_3Si$ 306.1287, found 306.1294.

(*E,Z*)-4-[Hydroxy[4-(tridec-1-enyl)-2-furyl]methyl]-2-(triethylsilyl)furan. Potassium bis(trimethylsilyl)amide (a 0.5 M solution in toluene; 4.14 mL, 2 mmol) was added to a solution of dodecylphosphonium bromide (1.06 g, 2 mmol) in THF (8 mL) at 0 °C under Ar. After 25 min a solution of 2-[[2-(triethylsilyl)-4-furyl]hydroxymethyl]-4-furaldehyde (300 mg, 1 mmol) in THF (3 mL) was added. Stirring was continued at 0 °C for 30 min and 25 min at rt. The mixture was poured into MeOH/water (1:1, 50 mL) and was extracted thoroughly with ether/hexane (1:1). Evaporation of the dried ($MgSO_4$) extracts gave the crude product, which was purified by flash chromatography on silica using 10% ether hexane to give 374.1 mg (82%) of the titled furan: R_f (10% ethyl ether (hexane) 0.16; ^{1}H NMR 0.78 (q, 6 H, J = 7.9 Hz), 0.89 (t, 3 H, J = 6.8 Hz), 0.99 (t, 9 H, J = 7.9 Hz), 1.27 (br s, 16 H), 1.40 (m, 2 H), 2.23 (m, 2 H), 5.57 (dt, 1 H, J = 7.1, 11.4 Hz), 5.77 (d, 1 H, J = 5.3 Hz), 6.21 (d, 1 H, J = 11.4 Hz), 6.31 (s, 1 H), 6.72 (s, 1 H), 7.41 (s, 1 H), and 7.66 (s, 1 H); ^{13}C NMR 3.1, 7.2, 14.0, 22.6, 29.2, 29.3, 29.4, 29.5, 29.6, 31.9, 63.0, 108.2, 118.4, 119.9, 123.3, 125.5, 132.2, 140.4, 144.3, 155.6, and 159.4; LRMS (m/e, rel abundance) 459 (M^+ + 1, 10), 458 (M^+, 24), 302 (26), 301 (85), 259 (29), 258 (100), 236 (35), 216 (13), 188 (27), 181 (17), 153 (15), 145 (28), 144 (23), 129 (25), 116 (19), 103 (14), 95 (15), 91 (21), and 69 (39).

4-[Hydroxy(4-tridecyl-2-furyl)methyl]-2-(triethylsilyl)-furan (24d). A solution of (*E,Z*)-4-[hydroxy[4-(tridec-1-enyl)-2-furylmethyl]methyl]-2-(triethylsilyl)furan (502 mg, 1.09 mmol) in ether (5 mL) was hydrogenated over Lindlar catalyst (5 mg) for 7 h at rt. The mixture was filtered through Celite and the filtrate concentrated to give an oil, which was purified by flash chromatography on silica using 10% ether/hexane to give 396 mg (79%) of **24d**: R_f (10% ethyl ether/hexane) 0.34; ^{1}H NMR 0.76 (q, 6 H, J = 7.8 Hz), 0.89 (t, 3 H, J = 6.4 Hz), 1.00 (t, 9 H, J = 7.8 Hz), 1.27 (br s, 20 H), 1.55 (m, 2 H), 2.25 (d, 1 H, J = 7.7 Hz), 2.37 (t, 2 H, J = 7.7 Hz), 5.75 (d, 1 H, J = 4.7 Hz), 6.12 (s, 1 H), 6.72 (s, 1 H), 7.20 (s, 1 H), and 7.66 (s, 1 H); ^{13}C NMR 3.1, 7.2, 14.1, 22.7, 24.8, 29.3, 29.4, 29.6, 29.7, 29.9, 31.9, 63.2, 108.5, 120.1, 125.7, 126.0, 138.4, 144.3, 147.2, 155.4, and 159.4; LRMS (m/e, rel abundance) 460 (M^+, 24), 459 (100), 445 (28), 369 (17), 284 (73), 267 (31), 228 (16), 211 (31), 198 (15), 132 (56), and 115 (15).

General Procedure for the Singlet Oxygen Oxidation of 24a–d. The procedure used was similar to that for 2-(trialkylsilyl)furans **9**. The spectroscopic data of **26a**, **26d**, and **23a** are summarized below.

5-Hydroxy-2(5*H*)-furanone (26a) (entries 1–4 and 7, Table V): ^{1}H NMR 5.90 (br, 1 H), 6.12 (d, 1 H, J = 6.0 Hz), 6.17 (br

s, 1 H), and 7.26 (d, 1 H, J = 6.0 Hz); ^{13}C NMR 99.2, 124.2, 153.0 and 172.6; HRMS exact mass calcd for $C_4H_4O_3$ 100.0160, found 100.0161.

2-Phenyl-6-hydroxy-3(2*H*)-pyranone (23a) (entry 3, Table V): ^{1}H NMR (mixture of diasteriomers) 5.14 (s, 1 H), 5.62 (s, 1 H), 5.78 (br d, 1 H), 5.85 (br d, 1 H), 6.25 (d, 1 H, J = 9.8 Hz), 6.30 (d, 1 H, J = 9.8 Hz), 76.0 (dd, 1 H, J = 9.8, 1.3 Hz), 7.05 (dd, 1 H, J = 9.8, 1.3 Hz), and 7.40 (m, 5 H); LRMS (m/e, rel abundance) 208 [(M + NH4)$^+$, 3], 190 (M$^+$, 10), 174 (14), 173 (100), 145 (14), 107 (22), 105 (51), and 84 (45).

2-Butyl-6-hydroxy-3(2*H*)-pyranone (23b) (entry 5, Table V): ^{1}H NMR (mixture of diasteriomers) 0.91 (t, 3 H, J = 7. Hz), 1.35 (m, 4 H), 1.70 (m + s, 3 H), 1.95 (m, 1 H), 3.19 (br 1 H), 3.45 (br, 1 H), 4.08 (dd, 1 H, J = 8.1, 3.6 Hz), 4.56 (dd, 1 H, J = 8.1, 3.9 Hz), 5.65 (m, 1 H), 6.10 (d, 1 H, J = 10.3 Hz), 6.14 (d, 1 H, J = 8.8 Hz), 6.89 (dd, 1 H, J = 10.3, 3.3 Hz), and 6.96 (d, 1 H, J = 8.8 Hz); ^{13}C NMR 13.9, 22.4, 22.5, 27.1, 7.2, 29.3, 30.3, 74.2, 78.9, 87.6, 90.8, 127.6, 128.7, 144.4, 147.2, 147.8, 163.1, 196.5, and 196.9.

5-Hydroxy-4-tridecyl-2(5*H*)-furanone (26d) (entries 8 and 9, Table IV): R_f (50% EtOAc/hexane) 0.08; ^{1}H NMR 0.89 (t, 3 H, J = 7.0 Hz), 1.27 (br s, 20 H), 1.60 (m, 2 H), 2.40 (m, 2 H), 4.15 (br, 1 H), 5.86 (s, 1 H), and 6.00 (s, 1 H); HRMS exact mass calcd for $C_{17}H_{30}O_3$ 282.2195, found 282.2201.

Registry No. **3a** (isomer 1), 120755-25-1; **3a** (isomer 2), 120771-27-9; **3aa** (isomer 1), 136617-51-1; **3aa** (isomer 2), 136617-52-2; **3b**, 120755-27-3; **3bb** (isomer 1), 136617-53-3; **3bb** (isomer 2), 136617-54-4; **3c**, 120755-30-8; **3cc** (isomer 1), 120755-60-4; **3cc** (isomer 2), 120756-81-2; **3d**, 136617-55-5; **3dd**, 120755-14-8; **3e**, 120755-15-9; **3ee** (isomer 1), 120755-52-4; **3ee** (isomer 2), 120756-78-7; **3f** (isomer 1), 120755-99-9; **3f** (isomer 2), 120756-72-1; **3ff** (isomer 1), 136617-56-6; **3ff** (isomer 2), 136617-57-7; **3g** (isomer 1), 120755-21-7; **3g** (isomer 2), 120756-65-2; **3gg**, 120755-58-0; **3h**, 120756-04-9; **3i**, 136617-58-8; **3j** (isomer 1), 120756-66-3; **3j** (isomer 2), 120756-67-4; **3k**, 136617-59-9; -3l, 136617-60-2; **3l** (isomer 2), 120756-85-6; **3m** (isomer 1), 120755-23-9; **3m** (isomer 2), 120756-62-9; **3n** (isomer 1), 120755-24-0; **3n** (isomer 2), 120756-63-0; **3p** (isomer 1), 136617-61-3; **3p** (isomer 2), 136617-62-4; **3pp** (isomer 1), 120755-63-7; **3pp** (isomer 2), 120756-84-5; **3q** (isomer 1), 120755-54-6; **3q** (isomer 2), 120756-79-8; **3qq** (isomer 1), 120755-61-5; **3qq** (isomer 2), 120756-82-3; **3r** (isomer 1), 120756-61-8; **3r** (isomer 2), 120755-26-2; **3rr** (isomer 1), 136617-63-5; **3rr** (isomer 2), 136617-64-6; **3s** (isomer 1), 120755-33-1; **3s** (isomer 2), 120756-69-6; **3ss**, 136617-65-7; **3t** (isomer 1), 136617-66-8; **3t** (isomer 2), 136617-67-9; **3tt** (isomer 1), 136617-68-0; **3tt** (isomer 2), 120756-86-7; **3u**, 120755-16-0; **3uu**, 120755-69-3; **3v**, 120755-68-2; **3vv**, 136617-69-1; **3w**, 120755-59-1; **3ww** (isomer 1), 120772-87-4; **3ww** (isomer 2), 120772-95-4; **3x**, 136617-70-4; **3y**, 120755-67-1; **3z**, 120755-66-0; **6aa**, 120756-31-2; **6b**, 111-83-1; **6bb**, 71590-03-9; **6c**, 112-29-8; **6cc**, 120756-37-8; **6d**, 693-67-4; **6dd**, 120772-89-6; **6e**, 143-15-7; **6ee**, 103602-67-1; **6f**, 112-89-0; **6ff**, 120756-24-3; **6g**, 2270-59-9; **6gg**, 85562-26-1; **6h**, 67023-84-1; **6hh**, 136617-71-5; **6i**, 90515-28-9; **6ii**, 14469-84-2; **6j**, 120756-54-9; **6jj**, 136617-72-6; **6k**, 96045-13-5; **6kk**, 136617-73-7; **6l**, 98008-53-8; **6ll**, 136617-74-8; **6mm**, 136617-75-9; **6nn**, 136617-76-0; **6p**, 120756-34-5; **6q**, 109027-84-1; **6s**, 637-59-2; **6t**, 54089-03-1; **6u**, 14469-83-1; **6w**, 136617-77-1; **6x**, 136617-78-2; **6y**, 123498-53-3; **6z**, 120756-47-0;)7a, 109-72-8; **7m**, 931-51-1; **7n**, 591-51-5; **7r**, 50779-55-0; **7v**, 105486-30-4; **9a**, 136617-79-3; **9aa**, 136617-80-6; **9b**, 130163-05-2; **9bb**, 136617-81-7; **9c**, 136617-82-8; **9cc**, 136617-83-9; **9d**, 136617-84-0; **9dd**, 136617-85-1; **9e**, 136617-86-2; **9ee**, 136617-87-3; **9f**, 136617-88-4; **9ff**, 136617-89-5; **9g**, 136617-90-8; **9gg**, 136617-91-9; **9h** (isomer 1), 136617-92-0; **9h** (isomer 2), 136617-93-1; **9i**, 136617-94-2; **9j**, 136617-95-3; **9k**, 136617-96-4; **9l**, 136617-97-5; **9m**, 136617-98-6; **9n**, 136617-99-7; **9p**, 136618-00-3; **9pp**, 136618-01-4; **9q**, 136618-02-5; **9qq**, 136618-03-6; **9r**, 136618-04-7; **9rr**, 136618-05-8; **9s**, 136618-06-9; **9ss**, 136618-07-0; **9t**, 136618-08-1; **9tt**, 136618-09-2; **9u**, 136618-10-5; **9uu**, 136618-11-6; **9v**, 136618-12-7; **9vv**, 136618-13-8; **9w**, 136618-14-9; **9ww**, 136618-15-0; **9x**, 136618-16-1; **9y**, 136618-17-2; **9z**, 136618-18-3; **11b**, 136618-19-4; **11e** (X = TES), 136618-20-7; **11e** (X = TBDMS), 136618-21-8; **11u**, 136618-22-9; (*E*)-**20**, 136618-23-0; (*Z*)-**20**, 136618-24-1; (*E*)-**21**, 136618-25-2; (*Z*)-**21**, 136618-26-3; **23a** (isomer 1), 132789-10-7; **23a** (isomer 2), 132789-11-8; **23b** (isomer 1), 136618-27-4; **23b** (isomer 2), 136618-28-5; **24a**, 4484-57-5; **24b**, 30478-77-4; **24c**, 36169-67-2; **24d**, 136618-29-6; **26a**, 14032-66-7; **26d**, 136618-30-9; **29aa**, 120756-30-1; **29bb**, 119981-54-3; **29ii**, 130248-77-0; **29jj**, 136618-31-0; **29mm**, 136618-32-1; **29w**, 136618-33-2; **29x**, 136618-34-3; **29z**, 120756-46-9; 4-(1-acetoxynonyl)-5-(*tert*-butyldimethylsilyl)furan, 136618-35-4; 4-(1-acetoxynonyl)-5-(triethylsilyl)furan, 136618-36-5; 4-(1-acetoxytridecyl)-2-(triethylsilyl)furan, 136618-37-6; 4-bromoiodobenzene, 589-87-7; 1-tridecyne, 26186-02-7; 1-pentyne, 627-19-0; 1-bromo-2-iodobenzene, 583-55-1; dodecyltriphenylphosphinium bromide, 15510-55-1; 5-(tributylstannyl)-3-furaldehyde, 130493-24-2; 2-furaldehyde, 98-01-1; phenylmagnesium chloride, 100-59-4; 2-(1-acetoxypentyl)furan, 92827-18-4; furan, 110-00-9; cyclohexanone, 108-94-1; 3-furaldehyde, 498-60-2; 2-(triethylsilyl)-4-furaldehyde, 130493-22-0; 2-[[2-(triethylsilyl)-4-furyl]hydroxymethyl]-4-furaldehyde, 136618-38-7; dodecyltriphenylphosphonium bromide, 15510-55-1; (*E*)-4-[hydroxy[4-(tridec-1-enyl)-2-furyl]methyl]-2-(triethylsilyl)furan, 136618-39-8; (*Z*)-4-[hydroxy[4-(tridec-1-enyl)-2-furyl]methyl]-2-(triethylsilyl)furan, 136618-40-1; singlet oxygen, 16833-27-5; 2-(*tert*-butyldimethylsilyl)-4-furaldehyde, 130493-23-1; 2-(trimethylsilyl)-4-furaldehyde, 105426-88-8; 1-bromo-4-phenylbenzene, 92-66-0; 1-bromo-2,4,5-trifluorobenzene, 327-52-6; 1-iodonaphthalene, 90-14-2; 2-bromonaphthalene, 580-13-2; 2-bromopyridine, 109-04-6; 4-pentyn-1-ol, 5390-04-5; (*E*)-4-methoxy-β-iodostyrene, 119950-15-1; (*Z*)-4-methoxy-β-iodostyrene, 136618-41-2; 4-methoxybenzaldehyde, 123-11-5; propargyl alcohol, 107-19-7; 2,4-dimethoxyiodobenzene, 20469-63-0; 2,4-dimethoxy-1-bromobenzene, 17715-69-4; 2-chloroquinoline, 612-62-4; benzyl 4-iodobenzoate, 136618-42-3; 4-iodobenzoic acid, 619-58-9; 5-[(4-carbobenzyloxy)phenyl]-4-pentyn-1-ol, 136618-43-4; 8-bromo-1-undecanol, 136618-44-5; 5-cyclohexylpentanol, 1129-66-4; 5-phenylpentanol, 10521-91-2; 5•(4-fluorophenyl)phenylpentan-1-ol, 120756-57-2; 5-(2,4,5-trifluorophenyl)pentan-1-ol, 136618-45-6; 5-(1-naphthyl)-pentan-1-ol, 120756-49-2; 5-(1-naphthyl)-4-pentyne-1-ol, 120756-46-9; 5-(2-naphthyl)pentan-1-ol, 2017-70-1; 5-(2-pyridyl)-1-pentanol, 84199-96-2; 1-bromo-8-(*tert*-butyldimethylsiloxy)octane, 96045-13-5; 8-bromooctan-1-ol, 50816-19-8; 2-bromothiophene, 1003-09-4; 8-(thiophen-2-yl)octan-1-ol, 120756-36-7; 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone, 7226-23-5; benzo[*b*]thiophene, 95-15-8; 1,6-dibromohexane, 629-03-8; ethyl 9-phenylnonanoate, 120756-17-4; 9-phenylnonan-1-ol, 3208-26-2; 5-phenylpent-1-en-3-ol, 37904-38-4; triethyl orthoacetate, 78-39-7; (*E*)-ethyl 7-phenyl-4-heptenoate, 120756-20-9; ethyl (diethylphosphono)acetate, 867-13-0; (*E,E*)-ethyl 9-phenyl-2,6-nonadienoate, 120756-56-1; (*E,Z*)-ethyl 9-phenyl-2,6-nonadienoate, 120756-21-0; (*E*)-ethyl 9-phenylnon-6-enoate, 120756-22-1; (*E*)-9-phenylnon-6-en-ol, 120756-23-2; 10-phenyl-1-decanol, 62607-69-6; 1-[4-(dibromomethyl)phenyl]-5-bromo-1-pentyne, 136618-46-7; 4-(5-hydroxy-1-pentynyl)benzaldehyde, 136618-47-8; 1,2-bis(diphenylphosphino)ethane, 1663-45-2; 4-(5-bromo-1-pentynyl)benzaldehyde, 136618-48-9; 5-(4-methoxyphenyl)-1-pentanol, 52244-55-0; (*E*)-5-(4-methoxyphenyl)-2-pentyn-4-en-ol, 130248-77-0; 5-(2,4-dimethoxyphenyl)-1-bromapentane, 136617-72-6; 5-(2,4-dimethoxyphenyl)-4-pentyn-1-ol, 136618-31-0; 5-(2-naphthyl)-4-pentyn-1-ol, 120756-30-1; 5-(2-quinolyl)pentan-1-ol, 136618-49-0; 5-(2-quinolyl)-4-pentyn-1-ol, 136618-32-1; 5-(2-quinolyl)-4-pentyn-1-al, 136618-50-3; Rose Bengal, 11121-48-5.

Supplementary Material Available: Full experimental details for the synthesis of **5**, **6**, **9**, and **10** (74 pages). Ordering information is given on any current masthead page.