JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

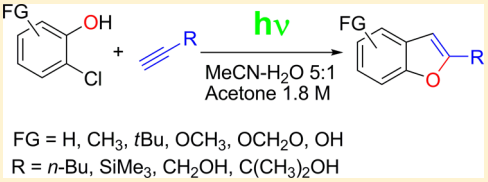
A Photochemical Route to 2-Substituted Benzo[*b*]furans

Stefano Protti,* Maurizio Fagnoni, and Angelo Albini

PhotoGreen Lab, Department of Chemistry, University of Pavia, Via Taramelli 12, 27100 Pavia, Italy

Supporting Information

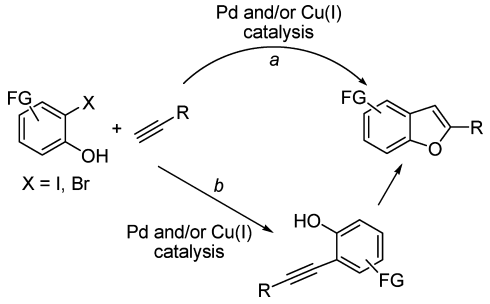
ABSTRACT: 2-Substituted benzo[*b*]furans were synthesized by a one-step metal-free photochemical reaction between 2-chlorophenol derivatives and terminal alkynes by tandem formation of an aryl-C and a C−O bond via an aryl cation intermediate. The mild conditions and the application to chlorophenols rather of the more expensive bromo or iodo analogues makes this procedure environmentally convenient.



INTRODUCTION

The benzo[*b*]furan moiety is largely diffuse in nature, in pharmaceutically active compounds,[1] both natural and man made, including antifungal, antimicrobial,[1] antitumor agents, as well as in drugs for the treatment of vascular diseases, such as arrhythmia and hypertension.[1c,d] Furthermore, some benzofuran derivatives have found applications as light collectors in photovoltaic cells.[2] An important access to these heterocycles is offered by metal-mediated heteroannulation of 2-halophenols with alkynes, as first demonstrated by Castro and co-workers in 1966.[3] This path has been strongly improved by the introduction of the Sonogashira procedure. The interest for this method is evidenced by the large number of reports in recent years, generally starting from 2-iodophenols[4−8] (Scheme 1 path *a*) in a one-pot procedure or with the separation of crude 2-alkynylphenol[9,1b] (Scheme 1 path *b*).

Scheme 1. Metal-Catalyzed Synthesis of 2-Substituted Benzo[*b*]furans from 2-Halophenols (FG = Functional Group)



This valuable reaction occurs at a moderate temperature (60−80 °C) and appears to be equally effective in water as in an organic solvent,[10] although the use of an expensive Pd complex and, most often, of a Cu(I) salt as cocatalyst has a negative environmental impact and increases the cost of the reaction. Actually, both copper[5,11] and palladium-free procedures[6] have been reported, but, particularly in the latter case, these required a higher temperature or at any rate more drastic conditions. Likewise, the use of less toxic and inexpensive iron salt catalysts (e.g., $FeCl_3$) has given poor results and then only with aromatic alkynes after heating at 135 °C for 72 h.[12]

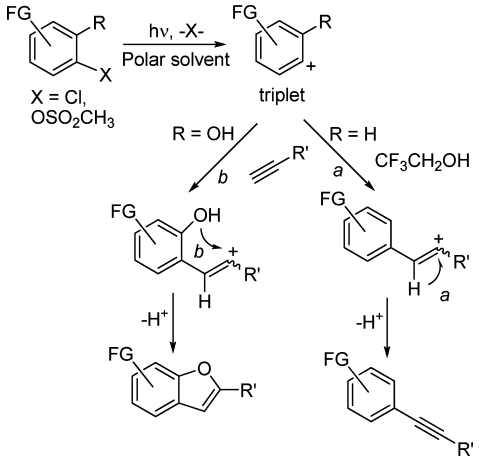
In polyhalophenols the reaction occurred selective at the iodo atom with no competition by other halides.[13] Bromophenols have been likewise used in the synthesis of benzofurans,[14,15] but the experimental procedure is less straightforward than with the corresponding iodides, and in some cases a preliminary protection of the hydroxy group as acetate had to be adopted. As a matter of fact, iodophenols gave benzofurans twice as efficiently[14] and as fast[16] as bromophenols, while requiring a smaller amount of catalyst. Finally, we are aware of two examples of the use of 2-chlorophenol for the synthesis of benzofurans. In the first case the desired product is obtained in a poor yield (under palladium/magnesium/lanthanum mixed oxide catalysis),[17] while in the second case, various benzo[*b*]furans have been prepared having recourse to a hydroxyterphenylphoshine−palladium catalyst, albeit the high temperatures (110−120 °C) employed limited the procedure exclusively to high-boiling alkynes such as dodecyne or phenylacetylenes.[18] On the other hand, we have developed a variety of arylation reactions based on the photogeneration of phenyl cations under mild conditions.[19] These involve the heterolytic cleavage in a polar solvent of an Ar−Cl or Ar−O bond upon irradiation of electron-rich aryl chlorides[20,21] or esters[22] and the addition of the thus formed triplet phenyl cation to π bond nucleophiles. In particular, alkynylation has been successful with the addition of a number of 4-substituted phenyl cations onto terminal alkynes[23] (Scheme 2, path *a*), one of the rare examples of a metal-free Sonogashira reaction.[19b]

We reasoned that introducing an *ortho* phenolic group in the starting aromatic may lead to a new synthesis of benzo[*b*]furans if the vinyl cation intermediate would be trapped intramolecularly (Scheme 2, path *b*), thus offering a metal-free annulation that would be environmentally advantageous, particularly if a convenient solvent could be used. *ortho*-Chloroanisole[21a] and *ortho*-chlorophenol[21a,b] have been used in related arylations, although these are less photoreactive in comparison to the corresponding *para*-derivatives. In fact, the

Received: May 17, 2012

   dx.doi.org/10.1021/jo3010183 | *J. Org. Chem.* XXXX, XXX, XXX−XXX

Scheme 2. Mechanism of Phenyl Cation Addition onto a Triple Bond



reaction quantum yield of *ortho*-chlorophenol (**1a**) in protic solvents such as MeOH and MeCN–H_2O mixture 5/1 is 0.040 and 0.045, respectively, almost five times lower than that of 4-chlorophenol in the same media (0.29 in MeOH and 0.26 in MeCN/H_2O). The fact that the reactivity was significant and the prospective advantage of a metal-free benzofuran synthesis made an exploratory study worthwhile.

RESULTS

The first part of the study aimed to individuate the conditions for a successful synthesis by using the reaction of phenol **1a** in the presence of 1-hexyne (**7a**) under different conditions.

As shown in Table 1, formation of the desired 2-butyl-benzo[*b*]furan (**8**) was accompanied by some reduction to phenol **1H**. Compound **1a** absorbs poorly at the wavelength used (310 nm), and it was found expedient to carry out the reaction under triplet sensitization (acetone, 0.9 M) and in the presence of an equimolar amount of a base (Cs_2CO_3) to buffer the acidity liberated.[24] As for the solvent, our previous alkynylation was carried out in CF_3CH_2OH (TFE), a rather toxic and expensive solvent, that was unsuitable in the present case since **1a** was completely consumed after 24 h irradiation, but only a negligible amount (<5%) of **8** was formed. Increasing the amount of acetone had a positive effect, with the yield of **8** reaching 20% (entry 2) in a 1 to 1 v/v mixture and 30% in neat acetone (no base added), although there the photoreduction became predominant. The presence of solid K_2CO_3 or of a protic solvent such as water led to a roughly equimolar mixture of **8** and **1H** (entries 4 and 5).

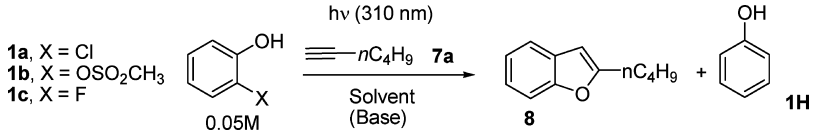
In recent years,[21,22,25] the use of aqueous acetonitrile has emerged as a greener alternative to TFE for the photocleavage of chlorophenols, as shown in the synthesis of γ-benzyl lactones,[21a] substituted benzonitriles,[25a] γ-benzyl tetrahydrofurans[25b] and allylphenols.[25] We were delighted to find that a MeCN/water 5/1 mixture was superior to all the other media tested. In fact, photoreaction of **1a** in this solvent (entries 6–8) strongly reduced the reduction to phenol, although the amount of benzofuran formed remained modest, and best results obtained (**1H**, 16%; benzofuran **8**, 49%) were those with 1.8 M acetone (20% v/v) and of a large excess of the trap (**7a**, 1 M) .

Then, the effect of changing the leaving group in the starting compound was explored. Irradiation of the catechol mesylate **1b** gave **8** in only 31% yield, but competitive reduction was almost suppressed. Under the same conditions, 2-fluorophenol (**1c**) exhibited a low photoreactivity (only 38% consumption after 24 h irradiation) and gave benzofuran in a reasonable yield (38% yield based on the consumption of **1c** accompanied by some **1H**).

The above data give some indication about the conditions under which a benzofuran may be obtained. In particular, *o*-chlorophenols appeared to be the best reagents. Thus the exploration was extended to further substituted derivatives (**2**–**6**) under the best conditions found (those of entry 8 in Table 1).

As shown in Table 2, the irradiation of **1a** in the presence of either 1-hexyne (**7a**) and trimethylsilylacetylene (**7b**) gave respectively the 2-butyl- (**8**, 49% yield, a compound recently investigated as antimicrobial[1a]) and the 2-trimethylsilyl derivative (**9**, 37% yield), along with some phenol but no significant amounts of the open-chain aryl alkynes. 5-Methyl-2-chlorophenol (**2**) gave likewise the corresponding benzofurans **10**, **11** in the presence of alkynes **7a** and **7b**, respectively. The benzofuran yield bordered here 60%, but reduction remained

Table 1. Irradiation of *o*-Halophenols (1a, 1c) or Mesylate 1b in the Presence of 1-Hexyne (7a)

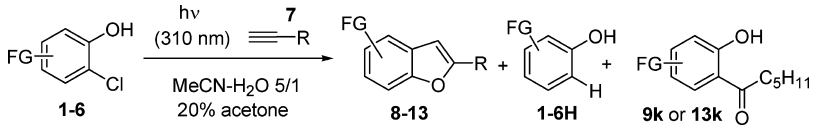


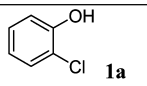
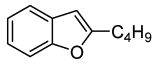
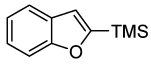
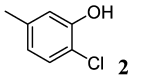
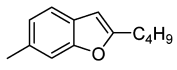
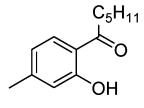
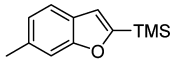
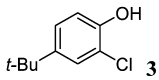
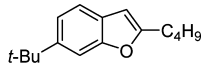
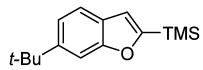
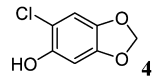
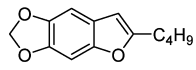
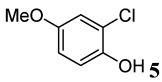
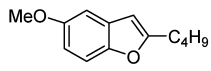
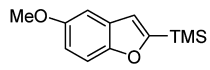
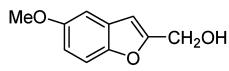
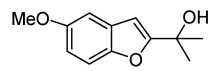
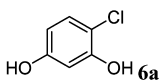
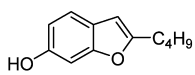
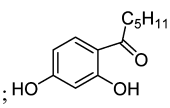
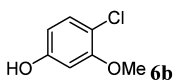
entry	conditions	t_{irr} (h)	consumption (%)	products (yield %)[a] 8	1H
1	**1a**, **7a** 0.5 M, acetone 0.9 M, Cs_2CO_3 0.025 M, Solvent: CF_3CH_2OH	24	100	<5	10
2	**1a**, **7a** 0.5 M, Cs_2CO_3 0.025 M, Solvent: CF_3CH_2OH/acetone 1/1	24	100	20	10
3	**1a**, **7a** 0.5 M, Solvent: acetone[b]	24	80	28	37
4	**1a**, **7a** 0.5 M, K_2CO_3 (s), Solvent: acetone	24	100	45	31
5	**1a**, **7a** 0.5 M, Solvent: acetone/H_2O 9/1[b]	24	90	30	45
6	**1a**, **7a** 0.5 M, acetone 0.9 M, Solvent: MeCN/H_2O 5/1[b]	35	85	42	17
7	**1a**, **7a** 0.5 M, acetone 1.8 M, Solvent: MeCN/H_2O 5/1[b]	24	100	42	18
8	**1a**, **7a** 1.0 M, acetone 1.8 M, Solvent: MeCN/H_2O 5/1[b]	24	100	49	16
9	**1b**, **7a** 1.0 M, acetone 1.8 M, Solvent: MeCN/H_2O 5/1[b]	24	100	31	5
10	**1c**, **7a** 1.0 M, acetone 1.8 M, Solvent: MeCN/H_2O 5/1[b]	24	38	38	14

[a]Yields were based on consumed phenol and determined by HPLC analysis. [b]No base added.

dx.doi.org/10.1021/jo3010183 | J. Org. Chem. XXXX, XXX, XXX–XXX

Table 2. Photolysis of Chlorophenols 1−6 in the Presence of Alkynes 7a−d



Ar-Cl (0.05M)	Alkyne (1M)	Products, (yield %)[a]
 **1a**	**7a**, R = *n*Bu	 **8**, 49; **1H**, 16
1a	**7b**, R = TMS	 **9**, 37; **1H**, 13
 **2**	**7a**	 **10**, 59;  **10k**, 7; **2H**, 20
2	**7b**	 **11**, 55 **2H**, 20
 **3**	**7a**	 **12**, 59; **3H**, 10
3	**7b**	 **13**, 65; **3H**, 11
 **4**	**7a**	 **14**, 54; **4H**, 4
 **5**	**7a**	 **15**, 85
5	**7b**	 **16**, 62
5	**7c**, R = CH_2OH	 **17**, 39, **5H**, 12
5	**7d**, R = CMe_2OH	 **18**, 44, **5H**, 8
 **6a**	**7a**	 **19**, 21;  **19k**, 12
 **6b**	**7a**	**19**, 41

[a]Isolated yields in the case of benzofurans and compounds **9k** and **13k**, HPLC yields in the case of compounds **1−6H**.

conspicuous (20%). Furthermore, in the reaction of **2** with **7a**, we obtained also a small amount (7%) of the aromatic ketone **10k**.

The yield of benzofurans (**12**, **13**) further increased when starting from 4-*tert*-butyl-2-chlorophenol (**3**) with both of the alkynes considered. Furthermore, good yields (up to 85%) of benzofurans, with no change in the paths followed, were obtained when oxygen based substituents, such as a methoxy or hydroxy group, were introduced. Thus, compound **14** was smoothly accessed through the photochemical reaction between chlorosesamol **4** and 1-hexyne (**7a**), while 4-methoxy-2-chlorophenol (**5**) reacted efficiently with both alkynes **7a** and **7b**, affording the corresponding benzofurans (**15**, **16**) in high yields. In this case, propargyl alcohols **7c,d** were added to the alkynes considered and gave indeed the corresponding benzofurans (**17**, **18**), though in less satisfactory yields. The reaction was less satisfactory with 4-chlororesorcinol (**6a**), where benzofuran **19** is obtained in only 21% yield, along with a significant amount of ketone **19k**.

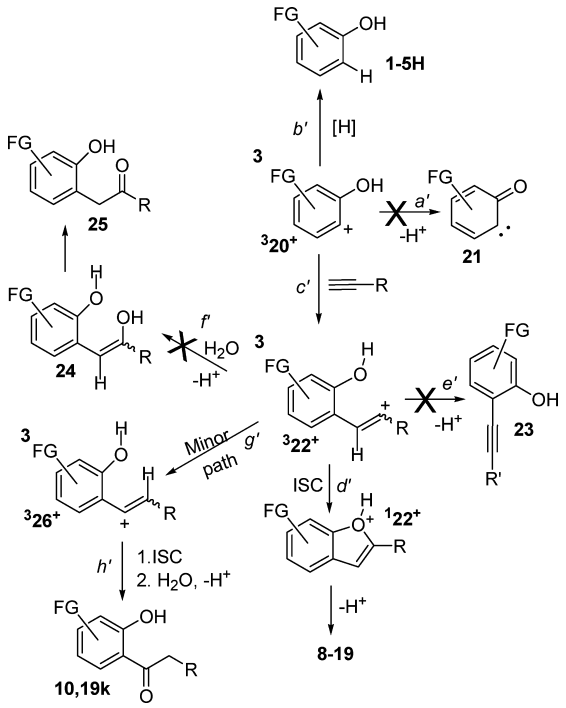
Finally, it was tested whether the presence of a free OH group in the *ortho* position was an absolute requirement for the occurring of the reaction. Accordingly, the irradiation of 4-chloro-3-methoxyphenol **6b** in the presence of **7a** (1 M) gave compound **19**, although in a moderate yield and at a slower rate (80% consumption after 40 h). Obtaining a benzofuran directly from *ortho*-haloanisoles has little precedent. Thus, the synthesis of benzofurans from iodoanisoles under metal catalysis has been found either to require two steps or to lead to mixtures.[26] A further explorative study showed that no benzofurans were formed when nonterminal alkynes such as 1-trimethylsilyl propyne were used.

Computational Studies. Experimental results were supplemented by computational data. The geometry and energy of both triplet and singlet 2-hydroxyphenyl cations

dx.doi.org/10.1021/jo3010183 | J. Org. Chem. XXXX, XXX, XXX−XXX

(^{1,3}**20**$^+$, FG = H, see Scheme 3), as well as of β-(2-hydroxyphenyl)-vinyl cations ^{1,3}**22**$^+$ (FG = H) modeling the

Scheme 3



putative intermediates in the described arylations, were optimized by DFT calculations at UB3LYP/6-31G(d) level (Supporting Information). Analogously to what was observed for 2-methoxyphenyl cation,[27] triplet ^{3}**20**$^+$ resulted more stable (3.6 kcal mol^{-1}) than the corresponding singlet cation. Since trapping by triple C−C bond took place only when the triplet phenyl cation (^{3}**20**$^+$) was involved, the cationic adducts were first formed in the same spin state. Considering all the possible orientations of both C(vinyl)−H and O−H bonds, four isomeric structures were found for ^{3}**22**$^+$, namely, ^{3}**22**$^+_{\text{in-in}}$

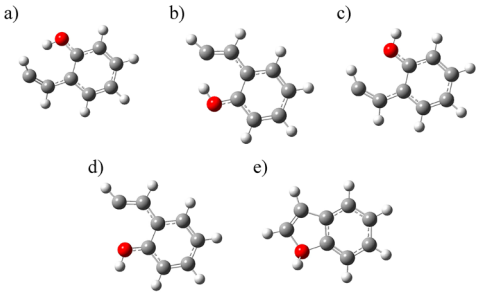


Figure 1. Calculated geometries of reaction intermediates: (a) ^{3}**22**$^+_{\text{in-in}}$; (b) ^{3}**22**$^+_{\text{out-in}}$; (c) ^{3}**22**$^+_{\text{in-out}}$; (d) ^{3}**22**$^+_{\text{out-out}}$; (e) ^{1}**22**$^+$ (see Scheme 3).

(Figure 1a), ^{3}**22**$^+_{\text{out-in}}$ (Figure 1b), ^{3}**22**$^+_{\text{in-out}}$ (Figure 1c) and ^{3}**22**$^+_{\text{out-out}}$ (Figure 1d). Significant energy differences were observed for the examined isomers and seemed to be due to steric effects, rather than electrostatic interactions. Thus, in structure ^{3}**22**$^+_{\text{in-in}}$ the planar geometry was distorted by the steric hindrance of both H atoms, which lowered the stability of this intermediate. The other three intermediates (^{3}**22**$^+_{\text{in-out}}$, ^{3}**22**$^+_{\text{out-in}}$ and ^{3}**22**$^+_{\text{out-out}}$) exhibited a comparable stability, the last one being the most stable (ca. 7.5 kcal mol^{-1} below ^{3}**22**$^+_{\text{in-in}}$). Interestingly, optimization of a similar singlet adduct led selectively to a protonated benzofuran structure (^{1}**22**$^+$, Figure 1e).

DISCUSSION

The fact that benzofurans **8**−**19** are obtained as the only arylated products from phenols **1**−**6** is remarkable and shows the selective reactivity of the 2-hydroxy substituted phenyl cation. This cation (^{3}**20**$^+$, see Scheme 3) is formed in the triplet state by irradiation of (substituted) 2-chlorophenol, as previously proposed.[21] The MeCN−H_2O 5:1 mixture is sufficiently polar and protic to favor the cleavage to ^{3}**20**$^+$ and was proved here again a useful substitute for 2,2,2-trifluoroethanol (TFE). The deprotonation of ^{3}**20**$^+$ in water to yield the corresponding neutral carbene, 2-oxocyclohexa-3,5-dienylidene carbene (**21**) is known to be facile (path *a*′).[28] However, the presence of a sufficiently high concentration of a π nucleophile prevents this alternative path and further limits photoreduction (path *b*′), fueling trapping of the cation (path *c*′), analogously to what observed with other phenyl cations[29] and analogously leading to a triplet β-aryl vinyl cation (as pointed out by computational data, addition of ^{3}**20**$^+$ leads to ^{3}**22**$^+_{\text{out-out}}$ as the preferred isomer),[30] which finally intersystem crosses (ISC) to the singlet cation ^{1}**22**$^+$ (path *d*′). Notable in the reaction are the C−O bonding step leading to ring closed ^{1}**22**$^+$ and precluding the intermediacy of a vinylidene phenonium ion,[31] as general for phenyl cations not bearing the OH group,[23,30] and the lack of competitive paths from the last intermediate. Thus, neither vinylic deprotonation (**23**, path *e*′) nor water addition (path *f*′) appear to have any role, despite the high water concentration (ca. 9 M in the solvent mixture). None of the hydroxyketones **25** expected from enol ether **24** were detected in the reaction mixture even at low irradiation times, and these may be intermediates in the way to benzofurans, since such process is known to occur, as in general "Paal-type" reactions, under acidic conditions.[32] The only exception was a minor product (hydroxyketones of formulas **10k**, **19k**), formed in a low yields via hydride shift from ^{3}**22**$^+$ to form the more stable α-phenyl vinyl cation (^{3}**26**$^+$, path *g*′) followed by intersystem crossing and water addition (path *h*′).[33]

These results further strengthen the knowledge about the reactivity of phenyl cations. Addition to a π bond nucleophile is always the preferred path for the selective triplet cation, whereas any addition from the singlet is barrierless. Thus, one takes full advantage from the selective trapping of the triplet even with weak π bond nucleophiles such as alkynes, but then at singlet multiplicity every nucleophile competes, with the obvious preference for intramolecular processes (and thus path *d*′ exclusively in the present case).

Finally, the formation of a benzofuran occurred in the case of compound **6b**, when a β-(2-methoxyphenyl)-vinyl cation is involved. The occurrence of a similar intermediate has been previously reported.[34,35] Preparatively, a benzofuran is formed directly from a 2-haloanisole, not requiring the intermediate isolation of a 2-alkynyl-anisole, a rare instance.[36]

The present synthesis of 2-substituted benzo[*b*]furans from 2-chlorophenol derivatives and terminal alkynes is a further addition to the synthetic versatility of phenyl cations, and give the one-step synthesis of benzo heterocycles through the

dx.doi.org/10.1021/jo3010183 | J. Org. Chem. XXXX, XXX, XXX−XXX

tandem formation of aryl−C and C−O bonds. This is a further example of the ability of photochemical reactions via phenyl cations to reproduce metal-catalyzed arylations, as well as of the peculiar experimental simplicity of this method (compare the often delicate requirement of the catalyzed method),[36] as well as the complementary nature (e.g., chlorides rather than iodides as the starting compounds). Yields are variable, but the process is quite general. In some cases, aromatic ketones (**10k**, **19k**) are formed and have to be separated by chromatography. In general, however, benzofurans are the only aromatic products formed, apart a variable amount of the low boiling phenol, and thus essentially a silica gel filtration is sufficient for the isolation, which adds synthetic interest to this protocol. Avoiding the use (and the recovery) of metals, employing water as cosolvent and using mild conditions are further appealing characteristics.

EXPERIMENTAL SECTION

NMR spectra were recorded on a 300 MHz spectrometer. The attributions were made on the basis of ^{1}H and ^{13}C NMR, as well as DEPT-135 experiments; chemical shifts are reported in ppm downfield from TMS. The photochemical reactions were performed by using nitrogen-purged solutions in quartz tubes and a multilamp reactor fitted with 12 15 W phosphor coated lamps (maximum of emission 310 nm) for the irradiation. Quantum yields were measured at 254 nm (4 Hg lamps, 15 W). The reaction course was followed by TLC (cyclohexane−ethyl acetate), GC and HPLC analyses. Workup of the photolytes involved concentration in vacuo and chromatographic separation by using silica gel. Chlorophenols **1a**,**c**, **2**, **5**, and **6a** and alkynes **7** are commercially available and freshly purified (by distillation or crystallization) before use. Phenols **1b**[37] (Anal. Calcd for $C_7H_8O_4S$: C, 44.67; H, 4.28. Found: C, 44.7; H, 4.3), **3**[38] (Anal. Calcd for $C_{10}H_{13}ClO$: C, 65.04; H, 7.10. Found: C, 65.0; H, 7.1) and **4**[39] (Anal. Calcd for $C_7H_5ClO_3$: C, 48.72; H, 2.92. Found: C, 48.7; H, 2.9) have been synthesized by known procedures, and their spectroscopic data are in accordance with the literature.[41] Solvents of HPLC purity grade have been employed in the photochemical reactions.

Synthesis of 4-Chloro-3-methoxyphenol (6b). A mixture of 4-chlororesorcine (**6a**, 4 g, 27.7 mmol), iodomethane (1.9 mL, 29.5 mmol) and K_2CO_3 (7.4 g, 53.5 mmol) in acetone (100 mL) was refluxed overnight. The solvent was then evaporated, and the residue was dissolved in water, acidified with concentrated HCl and extracted with Et_2O (3 × 30 mL). The organic phases were collected, dried over anhydrous Na_2SO_4 and Et_2O eliminated in vacuo. The resulting residue was purified by column chromatography (eluant: from neat cyclohexane to cyclohexane/ethyl acetate 9:1) to afford 1.9 g of **6b** (white solid, 43% yield, mp 76−77 °C (lit. 78 °C)[40] along with 1.5 g (31% yield) of 1-chloro-2,4-dimethoxy-benzene. **6b:** ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3H), 5.35 (bs, 1H), 6.35−6.40 (dd, 1 H, J = 7 and 2 Hz), 6.45−6.50 (d, 1H J = 2 Hz), 7.20−7.25 (d, 1H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 56.0 (CH_3), 100.5 (CH), 107.8 (CH), 113.9, 130.2 (CH), 155.2, 155.6; IR (neat) ν/cm^{-1} 3450, 2930, 1591, 1490, 1299, 1199, 1067, 1025, 951. Anal. Calcd for $C_7H_7ClO_2$: C, 53.02; H, 4.45. Found: C, 53.0; H, 4.5. Spectroscopic data of **6b** are in accordance with the literature.[41]

General Procedure for the Photochemical Synthesis of Benzo[*b*]furans. A solution of the chlorophenol (**1**−**6**, 1.5 mmol, 0.05M), the alkyne (**7a**−**d**, 30 mmol) and acetone (54 mmol, 1.8M) in MeCN−water 5:1 (30 mL) was argon purged in quartz tubes and irradiated by means of 12 15-W phosphor-coated lamps (emission centered at 310 nm) until complete consumption of the aromatic substrate. The photolyzed solution was saturated with sodium chloride and extracted with diethyl ether (3 × 20 mL). The organic phase was then removed in vacuo, and the resulting residue was purified by column chromatography (silica gel; cyclohexane/ethyl acetate as eluant). The yield of photoreduced products **1**−**5H** has been quantified by means of GC analyses.

Synthesis of 2-Butyl Benzo[*b*]furan (8). From 156 μL (1.5 mmol) of 2-chlorophenol (**1a**), 3.40 mL (30 mmol) of 1-hexyne (**7a**), and 6.0 mL of acetone (54 mmol) in 30 mL of MeCN−H_2O 5:1, irradiated for 24 h. Purification by column chromatography (eluant: neat cyclohexane) afforded 110 mg of 2-butyl benzo[*b*]furan (**8**, oil, 42%). Compound **8** was likewise obtained in 31% yield (GC yield) under the same conditions by irradiation of a solution of **1b** and **7**. Similarly, **8** was also obtained by irradiation of a solution of **1c** and **7** (38% GC yield based on the consumption of **1c**). Spectroscopic data of **8** are in accordance with the literature.[42] Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.7; H, 8.1.

Synthesis of 2-Trimethylsilyl Benzo[*b*]furan (9). 156 μL (1.5 mmol) of **1a**, 4.0 mL (30 mmol) of ethynyl-trimethylsilane (**7b**), and 3.0 mL of acetone (27 mmol) in 30 mL of MeCN−H_2O 5:1 were irradiated for 34 h. Purification by column chromatography (eluant: neat cyclohexane) afforded 106 mg of 2-trimethylsilyl benzo[*b*]furan (**9**, oil, 30% yield). Spectroscopic data of **9** are in accordance with the literature.[43] Anal. Calcd for $C_{11}H_{14}OSi$: C, 69.42; H, 7.41. Found: C, 69.4; H, 7.4.

Synthesis of 2-Butyl-6-methyl-benzo[*b*]furan (10). From 214 mg (1.5 mmol) of 5-methyl-2-chlorophenol (**2**), 3.40 mL (30 mmol) of **7a**, and 3.0 mL of acetone (27 mmol) in 30 mL of MeCN−H_2O 5:1, irradiated for 30 h. Purification by column chromatography (eluant: neat cyclohexane) gave 167 mg of 2-butyl-6-methylbenzo[*b*]-furan (**10**, oil, 59% yield) and 22 mg of 1-(2-hydroxy-4-methylphenyl)-hexan-1-one (**10k**, oil, 7% yield). **10:** ^{1}H NMR ($CDCl_3$) δ 0.95−1.00 (t, 3H, J = 7 Hz), 1.40−1.50 (sext, 2H, J = 7 Hz), 1.70−1.80 (qui, 2H, J = 7 Hz), 2.50 (s, 3H), 2.75−2.80 (t, 2H, J = 7 Hz), 6.30−6.55 (d, 1 H, J = 1 Hz), 7.00−7.10 (dd, 1H, J = 8 and 1 Hz), 7.55 (s, 1H), 7.30−7.40 (d, 1H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 15.1 (CH_3), 22.8 (CH_3), 23.5 (CH_2), 29.4 (CH_2), 31.1 (CH_2), 102.8 (CH), 112.3 (CH), 120.8 (CH), 124.9 (CH), 127.7, 134.5, 156.3, 160.4; IR (neat) ν/cm^{-1} 2928, 1490, 1266, 1118, 955, 812. Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.0; H, 8.6. IR (neat) ν/cm^{-1} 3392, 2958, 1627, 1489, 1145, 963. Spectroscopic data of **10k** are in accordance with the literature.[44] Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.8; H, 8.7.

Synthesis of 2-Trimethylsilyl-6-methyl-benzo[*b*]furan (11). From 214 mg (1.5 mmol) of **2**, 4.0 mL (30 mmol) of **7b**, and 3.0 mL of acetone (27 mmol) in 30 mL of MeCN−H_2O 5:1 irradiated for 26 h (90% consumption of **2**). Purification by column chromatography (eluant: cyclohexane/ethyl acetate 99:1) afforded 155 mg of 2-trimethylsilyl-6-methyl-benzo[*b*]furan (**11**, oil, 56% yield based on the consumption of **2**). **11:** ^{1}H NMR ($CDCl_3$) δ 0.35 (s, 9H), 2.50 (s, 3H), 6.90−6.95 (d, 1H, J = 1 Hz), 7.00−7.10 (d, 1H, J = 8 and 1 Hz), 7.30 (s, 1H), 7.40−7.50 (d, 1H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ −1.9 (CH_3), 21.5 CH_3), 111.4 (CH), 115.8 (CH), 120.2 (CH), 123.6 (CH), 125.4, 134.2, 158.5, 162.7; IR (neat) ν/cm^{-1} 2927, 1475, 1253, 1131, 954. Anal. Calcd for $C_{12}H_{16}OSi$: C, 70.53; H, 7.89. Found: C, 70.6; H, 7.9.

Synthesis of 2-Butyl-5-*tert*-butyl-benzo[*b*]furan (12). From 277 mg of 4-*tert*-butyl-2-chlorophenol (**3**, 1.5 mmol), 3.40 mL of **7a** (30 mmol) and 6.0 mL (54 mmol) of acetone in MeCN−H_2O 5:1, irradiated for 32 h. Purification by column chromatography afforded 204 mg of 2-butyl-5-*tert*-butyl-benzo[*b*]furan (**12**, oil, 59% yield). **12:** ^{1}H NMR ($CDCl_3$) δ 0.95−1.00 (t, 3H, J = 8 Hz), 1.40 (s, 9H), 1.40−1.50 (m, 2H), 1.70−1.80 (qui, 2H, J = 8 Hz), 2.75−2.80 (t, 2H, J = 3 Hz), 6.35 (s, 1H), 7.35−7.45 (m, 2H), 7.05 (d, 1H, J = 2 Hz); ^{13}C NMR ($CDCl_3$) δ 15.1 (CH_3), 23.5 (CH_2), 29.5 (CH_2), 31.0 (CH_2), 33.2 (CH_3), 35.9, 103.2 (CH), 111.2 (CH), 117.7 (CH), 122.1 (CH), 129.5, 146.6, 154.1, 161.1. IR (neat) ν/cm^{-1} 2958, 1600, 1478, 1271, 1124, 807. Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.4; H, 9.6.

Synthesis of 2-Trimethylsilyl-5-*tert*-butyl-benzo[*b*]furan (13). From 277 mg of **3** (1.5 mmol), 4.00 mL of **7b** (30 mmol) and 6.0 mL (54 mmol) of acetone in MeCN−H_2O 5:1, irradiated for 32 h. Purification by column chromatography afforded 240 mg of 2-trimethylsilylbenzo[*b*]furan (**13**, oil, 65% yield). **13:** ^{1}H NMR ($CDCl_3$) δ 0.35 (s, 9H), 1.40 (s, 9H), 6.95 (d, 1H, J = 1 Hz), 7.30−7.35 (dd, 1H, J = 8 and 2 Hz), 7.45−7.50 (d, 1H, J = 8 Hz),

dx.doi.org/10.1021/jo3010183 | J. Org. Chem. XXXX, XXX, XXX−XXX

7.55−7.60 (d, 1H, J = 2 Hz); ^{13}C NMR ($CDCl_3$) δ −1.9 (CH_3), 31.8 (CH_3), 34.5, 110.4 (CH), 116.1 (CH), 116.9 (CH), 122.2 (CH), 127.6, 145.3, 156.2, 163.6; IR (neat) ν/cm^{-1} 2961, 1259, 1249, 1130, 1063, 843. Anal. Calcd for $C_{15}H_{22}OSi$: C, 73.11; H, 9.00. Found: C, 73.1; H, 9.0.

Synthesis of 2-Butyl-5,6-methylendioxy-benzo[*b*]furan (14). From 259 mg (1.5 mmol) of 2-chloro-benzo-4,5-diox-1-ol (**4**), 3.40 mL of **7a** (30 mmol) and 6.00 mL of acetone (54 mmol) in 30 mL of MeCN−H_2O 5:1 irradiated for 20 h. Purification by column chromatography (eluant: neat cyclohexane) afforded 177 mg of 2-butyl-5,6-methylendioxy-benzo[*b*]furan (**14**, oil, 54% yield). **14:** ^{1}H NMR (CD_3COCD_3) δ 0.95−1.00 (t, 3H, J = 7 Hz), 1.20−1.45 (sext, 2H, J = 7 Hz), 1.65−1.80 (qui, 2H, J = 8 Hz), 2.70−2.85 (t, 2H, J = 8 Hz), 5.95 (s, 2H), 6.30 (s, 1H), 6.90 (s, 1H), 7.00 (s, 1H); ^{13}C NMR (CD_3COCD_3) δ 14.4 (CH_3), 23.2 (CH_2), 29.0 (CH_2), 31.0 (CH_2), 94.1 (CH), 100.1 (CH), 102.4 (CH_2), 103.5 (CH), 123.4, 143.2, 145.5, 146.6, 160.2; IR (neat) ν/cm^{-1} 2931, 1461, 1318, 1158, 945. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.5; H, 6.4.

Synthesis of 2-Butyl-5-methoxy-benzo[*b*]furan (15). From 238 mg (1.5 mmol) of 2-chloro-4-methoxyphenol (**5**), 3.40 mL of **7a** (30 mmol) and 6.00 mL of acetone (54 mmol) in 30 mL of MeCN−H_2O 5:1 irradiated for 16 h. Purification by column chromatography (eluant: cyclohexane/ethyl acetate 99:1) gave 260 mg of 2-butyl-5-methoxy-benzo[*b*]furan (**15**, oil, 85% yield). **15**: ^{1}H NMR ($CDCl_3$) δ 0.95−1.05 (t, 3H, J = 7 Hz), 1.40−1.50 (sext, 2H, J = 7 Hz), 1.70−1.85 (qui, 2H, J = 7 Hz), 2.75−2.80 (t, 2H, J = 8 Hz), 3.85 (s, 3H), 6.55 (d, 1H, J = 1 Hz), 6.80−6.85 (dd, 1H, J = 9 and 3 Hz), 6.95−7.00 (d, 1H, J = 3 Hz), 7.25−7.30 (d, 1H, J = 9 Hz); ^{13}C NMR ($CDCl_3$) δ 13.7 (CH_3), 22.2 (CH_2), 28.1 (CH_2), 29.7 (CH_2), 55.8 (CH_3), 101.8 (CH), 103.0 (CH), 110.9 (CH), 111.2 (CH), 129.4, 149.5, 155.6, 160.6; IR (neat) ν/cm^{-1} 2939, 1465, 1248, 1145, 961. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.4; H, 7.9.

Synthesis of 5-Methoxy-2-trimethylsilyl-benzo[*b*]furan (16). From 238 mg (1.5 mmol) of **5**, 4.00 mL of **7b** (30 mmol) and 6.0 mL of acetone (54 mmol) in 30 mL of MeCN−H_2O 5:1 irradiated for 16 h. Purification by column chromatography (eluant: cyclohexane/ethyl acetate 99:1) afforded 205 mg of 5-methoxy-2-trimethylsilyl-benzo-[*b*]furan (**16**, oil, 62% yield). **16:** ^{1}H NMR ($CDCl_3$) δ 0.40 (s, 9H), 3.85 (s, 3H), 6.85−6.95 (dd, 1H, J = 2 and 7 Hz), 6.90 (d, 1H, J = 1 Hz), 7.05−7.10 (d, 1H, J = 2 Hz), 7.40−7.45 (d, 1H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ −0.5 (CH_3), 57.2 (CH_3), 104.3 (CH), 112.9 (CH), 114.6 (CH), 117.4 (CH), 129.8, 154.5, 157.0, 165.9; IR (neat) ν/cm^{-1} 2930, 1491, 1228, 1143, 955. Anal. Calcd for $C_{12}H_{16}O_2Si$: C, 65.41; H, 7.32. Found: C, 65.4; H, 7.3.

Synthesis of 2-(Hydroxymethyl)-5-methoxy-benzo[*b*]furan (17). From 238 mg (1.5 mmol) of **5**, 1.75 mL (30 mmol) of propargyl alcohol (**7c**), and 6.0 mL of acetone (54 mmol) in 30 mL of MeCN−H_2O 5:1 irradiated for 24 h. Purification by column chromatography (eluant: cyclohexane/ethyl acetate 9:1) afforded 104 mg of 2-(hydroxymethyl)-5-methoxy-benzo[*b*]furan (**17**, white solid, 39% yield, mp = 64.5−65.0 °C). The spectroscopic data of compound **17** were in accordance with literature.[45] Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66. Found: C, 67.4; H, 5.7.

Synthesis of 2-(1-Methyl-1-hydroxyethyl)-5-methoxybenzo-[*b*]furan (18). From 238 mg (1.5 mmol) of 2-chloro-4-methoxyphenol (**5**), 2.90 mL (30 mmol) of 3-methyl-1-butyn-3-ol (**7d**), and 6.0 mL of acetone (54 mmol) in 30 mL of MeCN−H_2O 5:1 irradiated for 24 h. Purification by column chromatography (eluant: cyclohexane/ethyl acetate 9:1) afforded 136 mg of 2-(1-methyl-1-hydroxyethyl)-5-methoxybenzo[*b*]furan[46] (**18**, oil, 44% yield). **18:** ^{1}H NMR ($CDCl_3$) δ 1.70 (s, 6H), 2.35 (bs, 1H), 3.80 (s, 3H), 6.55 (s, 1H), 6.85−6.90 (dd, 1H, J = 8 and 2 Hz), 7.00−7.05 (d, 1H, J = 2 Hz), 7.25−7.35 (d, 1H, J = 8 Hz). ^{13}C NMR ($CDCl_3$) δ 28.6 (CH_3), 55.8 (CH_3), 69.2, 100.4 (CH), 103.5 (CH), 111.5 (CH), 112.4 (CH), 128.7, 149.5, 155.8, 163.8; IR (neat) ν/cm^{-1} 3450, 2967, 1490, 1287, 1167, 816. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.9; H, 6.8.

Synthesis of 2-Butyl-benzo[*b*]furan-6-ol (19). From 216 mg (1.5 mmol) of 4-chloro-resorcin (**6a**), 1.70 mL (30 mmol) of **7a**, and 6.00 mL of acetone (54 mmol) in 30 mL of MeCN−H_2O 5:1 irradiated for 60 h. Purification by column chromatography (eluant: cyclohexane/ethyl acetate 8:2) afforded 56 mg of 2-butyl-benzo[*b*]-furan-6-ol (**19**, oil, 21% yield) along with a mixture of **19** (4 mg) and of 1-(2,4-dihydroxyphenyl)hexan-1-one (**19k**, 37 mg, 12% yield). The same reaction, when performed by using 4-chloro-3-methoxyphenol (**6b**) in place of **6a**, gave **19** in 41% yield. Spectroscopic data of **19** are in accordance with the literature.[47] Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.8; H 7.3. **19k:** ^{1}H NMR ($CDCl_3$, from the mixture) δ 0.95−1.00 (t, 3H, J = 7 Hz), 1.20−1.30 (m, 4H), 1.80−1.90 (q, 2H, J = 7 Hz), 2.90−3.00 (t, 2H, J = 7 Hz), 5.80−5.90 (bs, 1H), 6.30−6.40 (m, 2H), 7.60−7.70 (d, 1H, J = 6.5 Hz), 12.40 (bs, 1H); ^{13}C NMR ($CDCl_3$, from the mixture) δ 13.4 (CH_3), 22.0 (CH_2), 24.1 (CH_2), 31.0 (CH_2), 37.5 (CH_2), 100.9 (CH), 107.2 (CH), 113.4, 131.9 (CH), 162.0. 164.8, 204.9. IR (of the mixture) ν/cm^{-1} 3307, 2957, 2872, 1633, 1455, 1245, 1145, 908.

Calculations. Geometries of all intermediates and adducts were optimized in vacuo at the UB3LYP/6-31G(d) level, by using the Gaussian03 package.[48] Frequency calculations were performed at the same level of theory, to check energy minima. Solvent effect was calculated by CPCM-UB3LYP/6-31G(d) method (acetonitrile bulk)[49] on the optimized geometries obtained in vacuo. Reported energies were evaluated by adding ZPE energies obtained in vacuo, to CPCM energies. Optimized geometries, listed in Cartesian format, and minimum energies (in Hartree) are available as Supporting Information.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C for compounds **1b**, **3**, **4**, **6b**, and **8**−**19** and computational data for the involved intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel: (+39)0382-987316. Fax: (+39)0382-987323. E-mail: prottistefano@gmail.com.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Dr. Valentina Dichiarante for her precious help. S.P. acknowledges MIUR, Rome (FIRB-Futuro in Ricerca 2008 Project RBFR08J78Q) for financial support. We acknowledge Dr. Daniele Dondi and Davide Ravelli (University of Pavia) for fruitful discussion. This work was funded by the CINECA Supercomputer Center, with computer time granted by ISCRA COMPDHT (HP10CZEHG6) project.

■ REFERENCES

(1) (a) Khan, M. W.; Alam, M. J.; Rashid, M. A.; Chowdhury, R. *Bioorg. Med. Chem.* **2005**, *13*, 4796−4805. (b) Jiang, X.; Liu, W.; Zhang, W.; Jiang, F.; Gao, Z.; Zhuang, H.; Fu, L. *Eur. J. Med. Chem.* **2011**, *46*, 3526−3530. (c) Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev.* **2003**, *103*, 893−930 and references cited therein. (d) Nattel, S.; Talajic, M.; Fermini, B.; Roy, D. *J. Cardiovasc. Electrophysiol.* **1992**, *3*, 266−280.

(2) Jung, I.; Lee, J. K.; Song, K. H.; Song, K.; Kang, S. O.; Ko, J. *J. Org. Chem.* **2007**, *72*, 3652−3658. Bogdal, D.; Matras, K.; Sanetra, J.; Pokladko, M. *Macromol. Symp.* **2008**, *268*, 48−52.

(3) Castro, C. E.; Gaughan, E. J.; Owsley, D. C. *J. Org. Chem.* **1966**, *31*, 4071−4078.

(4) Bernini, R.; Cacchi, S.; De Salve, I.; Fabrizi, G. *Synthesis* **2007**, 873−882.

(5) Rollet, P.; Kleist, W.; Dufaud, V.; Djakovitch, L. *J. Mol. Catal. A: Chem.* **2005**, *241*, 39−51.

(6) Li, J- H.; Li, J.-L.; Wang, D.-P.; Pi, S.-F.; Xie, Y.-X.; Zhang, M.-B.; Hu, X.-C. *J. Org. Chem.* **2007**, *72*, 2053−2057.
(7) Bates, C. G.; Saejueng, P.; Murphy, J. M.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 4727−4729.
(8) Wang, L.; Li, P.; Zhang, Y. *Chem. Commun.* **2004**, 514−515.
(9) Fürstner, A.; Davies, P. W. *J. Am. Chem. Soc.* **2005**, *127*, 15024−15025. Liao, Y.; Smith, J.; Fathi, R.; Yang, Z. *Org. Lett.* **2005**, *7*, 2707−2709.
(10) Pal, M.; Subramanian, V.; Yeleswarapu, K. R. *Tetrahedron Lett.* **2003**, *44*, 8221−8225. Genin, E.; Amengual, R.; Michelet, V.; Savignac, M.; Jutand, A.; Neuville, L.; Genêt, J.-P. *Adv. Synth. Catal.* **2004**, *346*, 1733−1741.
(11) Gill, G. S.; Grobelny, D. W.; Chaplin, J. H.; Flynn, B. L. *J. Org. Chem.* **2008**, *73*, 1131−1134.
(12) Carril, M.; Correa, A.; Bolm, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 4862−4865.
(13) Sanz, R.; Castroviejo, M. P.; Fernández, Y.; Fañanás, F. J. *J. Org. Chem.* **2005**, *70*, 6548−6551.
(14) Primault, G.; Legros, J.-Y.; Fiaud, J.-C. *J. Organomet. Chem.* **2003**, *687*, 353−364.
(15) Csékei, M.; Novák, Z.; Timári, G.; Kotschy, A. *ARKIVOC* **2004**, *vii*, 285−291. Harayama, T.; Nishita, Y. *Chem. Pharm. Bull.* **1996**, *44*, 1986−1988.
(16) Dawood, K. M.; Solodenko, W.; Kirschning, A. *ARKIVOC* **2007**, *v*, 104−124.
(17) Cwik, A.; Hell, Z.; Figueras, F. *Tetrahedron Lett.* **2006**, *47*, 3023−3026.
(18) Wang, J. R.; Manabe, K. *J. Org. Chem.* **2010**, *75*, 5340−5342.
(19) (a) Fagnoni, M.; Albini, A. *Acc. Chem. Res.* **2005**, *38*, 713−721. (b) Dichiarante, V.; Fagnoni, M. *Synlett* **2008**, 787−800.
(20) Protti, S.; Fagnoni, M.; Mella, M.; Albini, A. *J. Org. Chem.* **2004**, *69*, 3465−3473.
(21) (a) Protti, S.; Fagnoni, M.; Albini, A. *J. Am. Chem. Soc.* **2006**, *128*, 10670−10671. (b) Protti, S.; Dondi, D.; Fagnoni, M.; Albini, A. In *Experiments in Green and Sustainable Chemistry*; Roesky, H. W., Kennepohl, D. K., Eds.; Wiley-VCH: Weinheim, 2009; pp 260−265.
(22) De Carolis, M.; Protti, S.; Fagnoni, M; Albini, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 1232−1236.
(23) Protti, S.; Fagnoni, M.; Albini, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 5675−5678.
(24) Terpolilli, M.; Merli, D.; Protti, S.; Dichiarante, V.; Fagnoni, M.; Albini, A. *Photochem. Photobiol. Sci.* **2011**, *10*, 123−127.
(25) (a) Dichiarante, V.; Fagnoni, M.; Albini, A. *Chem. Commun.* **2006**, 3001−3003. (b) Protti, S.; Dondi, D.; Fagnoni, M.; Albini, A. *Eur. J. Org. Chem.* **2008**, 2240−2247. Protti, S.; Fagnoni, M.; Albini, A. *Org. Biomol. Chem.* **2005**, *3*, 2868−2871.
(26) See, for instance ,Dyker, G. *J. Org. Chem.* **1993**, *58*, 6426−6428. Colobert, F.; Castanet, A. S.; Abillard, O. *Eur. J. Org. Chem.* **2005**, 3334−3341. Oppenheimer, J.; Johnson, W. L.; Tracey, M. R.; Hsung, R. P.; Yao, P.-Y.; Liu, R.; Zhao, K. *Org. Lett.* **2007**, *12*, 2361−2364.
(27) Dichiarante, V.; Dondi, D.; Protti, S.; Fagnoni, M.; Albini, A. *J. Am. Chem. Soc.* **2007**, *129*, 5605−5611; Correction: **2007**, *129*, 11662.
(28) Shi, Z.; Sigman, M. E.; Ghosh, M. M.; Dabestani, R. *Environ. Sci. Technol.* **1997**, *31*, 3581−3587. Bonnichon, F.; Richard, C.; Grabner, G. *Chem. Commun.* **2001**, 73−74.
(29) Manet, I.; Monti, S.; Bortolus, P.; Fagnoni, M.; Albini, A. *Chem.—Eur. J.* **2005**, *11*, 4274−4282. Manet, I.; Monti, S; Fagnoni, M.; Protti, S.; Albini, A. *Chem.—Eur. J.* **2005**, *11*, 140−151.
(30) A related adduct cation has been previously observed by laser flash photolysis experiments in the addition of the 4-methoxyphenyl cation onto 1-hexyne; see: Manet, I.; Monti, S.; Grabner, G.; Protti, S.; Dondi, D.; Dichiarante, V.; Fagnoni, M.; Albini, A. *Chem.—Eur. J.* **2008**, *14*, 1029−1039.
(31) Stang, P. J.; Dueber, T. E. *J. Am. Chem. Soc.* **1973**, *95*, 2683−2686. Stang, P. J.; Dueber, T. E. *J. Am. Chem. Soc.* **1973**, *95*, 2686−2687.
(32) Macleod, C.; McKiernan, C. J.; Guthrie, E. J.; Farrugia, L. J.; Hamprecht, D. W.; Macritchie, J.; Hartley, R. C. *J. Org. Chem.* **2003**, *68*, 387−401. The chemical behaviour of differently substituted vinyl cations (generated via solvolysis of iodonium salts) has been recently resumed; see: Okuyama, T. *Acc. Chem. Res.* **2002**, *35*, 12−18.
(33) [1,2] H shift occurring in β-aryl vinyl cations to give the more stable α-aryl vinyl cations has been reported in the literature; see, for instance, Lee, C. C.; Ko, E. C. F. *J. Org. Chem.* **1975**, *40*, 2132−2133. Gronheid, R.; Lodder, G.; Okuyama, T. *J. Org. Chem.* **2002**, *67*, 693−702. Apeloig, Y.; Franke, W.; Rappoport, Z.; Schwarz, H.; Stahl, D. *J. Am. Chem. Soc.* **1981**, *103*, 2770−2780.
(34) Suzuki, T.; Kitamura, T.; Sonoda, T.-a.; Kobayashi, S.; Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 5324−5328. Xu, M.; Zhang, X.-H.; Zhong, P. *Tetrahedron Lett.* **2011**, *52*, 6800−6804.
(35) See, for instance, Maud Jacubert, M.; Hamze, A.; Provot, A.; Peyrat, J.-F.; Brion, J.-D.; Alami, M. *Tetrahedron Lett.* **2009**, *50*, 3588−3592. Kitamura, T.; Kobayashi, S.; Taniguchi, H. *Chem. Lett.* **1984**, 547−548. Kitamura, T.; Kobayashi, S.; Taniguchi, H.; Hori, K. *J. Am. Chem. Soc.* **1991**, *113*, 6240−6245.
(36) Doucet, H.; Hierso, J.-C. *Angew. Chem., Int. Ed.* **2007**, *46*, 834−871 and references cited therein.
(37) Lin, K.-S.; Ding, Y.-S. *Chirality* **2004**, *16*, 475−481.
(38) Masilamani, D.; Rogic, M. M. *J. Org. Chem.* **1981**, *46*, 4486−4489.
(39) Dichiarante, V.; Fagnoni, M.; Albini, A. *Green Chem.* **2009**, *11*, 942−946.
(40) Dodgson, W. *Biochem. J.* **1949**, *45*, 381−383.
(41) Bauta, W. E.; Lovett, D. P.; Cantrell, W. R., Jr.; Burke, B. D. *J. Org. Chem.* **2003**, *68*, 5967−5973.
(42) Ackermann, L.; Kaspar, L. T. *J. Org. Chem.* **2007**, *72*, 6149−6153.
(43) Crich, D.; Grant, D. *J. Org. Chem.* **2005**, *70*, 2384−2386.
(44) Sharghi, H.; Hosseini-Sarvari, M.; Eskandari, R. *Synthesis* **2006**, 2047−2052.
(45) Gabriele, B.; Mancuso, R.; Salerno, G. *J. Org. Chem.* **2008**, *73*, 7336−7341.
(46) De Bernardi, M; Vidari, G.; Vita Finzi, P; Fronza, G. *Tetrahedron* **1992**, *48*, 7331−7344.
(47) Misawa, N.; Shindo, K.; Takahashi, H.; Suenaga, H.; Iguchi, K.; Okazaki, H.; Harayama, S.; Furukawa, K. *Tetrahedron* **2002**, *58*, 9605−9612.
(48) *Gaussian 03*, Revision D.01; M. J. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P. J.; Dannenberg, J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. Gaussian, Inc.: Wallingford, CT, 2004.
(49) Barone, V.; Cossi, M. *J. Phys. Chem. A* **1998**, *102*, 1995−2001. Cossi, M.; Rega, N.; Scalmani, G.; Barone, V. *J. Comput. Chem.* **2003**, *24*, 669−681.