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Photochemical Arylation of Alkenols: Role of Intermediates and Synthetic Significance

Stefano Protti,*[a] Daniele Dondi,[b] Maurizio Fagnoni,[a] and Angelo Albini[a]

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A one-pot, tandem synthesis of cyclic ethers is obtained by addition of photogenerated phenyl cations to hydroxyalkenes. Thus, 2- (or 3-) phenyl-substituted tetrahydrofurans were prepared by irradiation of 4-chloro-*N*,*N*-dimethylaniline, -anisole, and -phenol with β-hydroxyalkenes and 2-benzyltetrahydrofurans with γ-hydroxyalkenes. With nonterminal alkenes [diastereomeric (*E*)- and (*Z*)-3-hexen-1-ols] *trans*-2-ethyl-3-aryltetrahydrofuran derivatives were stereoselectively formed from both isomers. The output of the photoreaction is structure and solvent dependent and is rationalized through the intermediacy of a phenonium ion from the addition of the primarily formed triplet phenyl cation to the alkenol double bond. Intramolecular addition of the OH group to form benzyl (aryl) tetrahydrofurans is favored in polar protic solvents, where hydride shifts to form aryltetrahydropyrans also occur, whereas in ethyl acetate, intermolecular addition of the chloride anion to the phenonium ion takes place. The mechanism of the above reactions is also discussed on the basis of computational data.

Introduction

The steric course of the solvolysis of 2-phenylethyl-1-tosylates and the rearrangements involved were rationalized more than half a century ago by Cram[1] through the intermediacy of a σ-bridged ethylenebenzenium cation (phenonium ion). The formation of this intermediate was later supported by NMR spectroscopic characterization in superacidic media.[2] Further studies[3] on the acetolysis of some β-arylethyltosylates demonstrated that both stereoselectivity and rate of the reaction were affected by ring substituents.[4] In particular, electron-donating groups such as the methoxy group induced complete stereoselectivity, which supports the role of the phenonium ion.

Interest in this intermediate, from both a mechanistic and a preparative point of view, has continued. Computational evidence for the role of the bridged cation and the effect of substituents has been recently reported by Sordo et al.[5] As for the synthetic applications of this carbocation, recent examples are the ring-contraction reactions of 2-phenyltetrahydropyrans to give 2-benzyltetrahydrofurans[6] and the lactonization that occurs either upon solvolysis of 4-aryl-5-tosyloxypentanoates[7] or by treatment of 4-aryl-4-pentenoic acid with hypervalent iodine reagents.[8] Recently, a synthetic strategy based on 1,2-aryl migration via phenonium ion was applied to the total synthesis of some phenolic sesquiterpenes.[9]

An alternative access to this intermediate is possible either by protonation of benzocyclobutene in superacidic media[10] or by addition of a triplet phenyl cation to an alkene.[11] The latter approach has been recently developed by our group[11] and involves the photoheterolysis of either a carbon–halogen bond in electron-rich aryl chlorides such as 4-chlorophenol[12] and 4-chloroaniline[11] or of a carbon–oxygen bond (in the corresponding aryl sulfonates and phosphates).[13] Thus, irradiation of such precursors gave the bridged cation II (in the singlet state, Scheme 1) by addition of triplet phenyl cation (I) to a double bond and intersystem crossing (ISC).[11,14] The intermediacy of phenonium II was confirmed by flash photolysis experiments, which revealed the addition of photogenerated 4-hydroxyphenyl cation (EDG = OH, Scheme 1) to 2-propenol.[12]

The structure of the end products depended on the competing paths occurring at the phenonium ion level, such as the addition of a nucleophile (the halide counterion[14–16] or the solvent;[14,15,17] Scheme 1, paths *a*, *b*), the elimination of a good electrofugal group[14,18,19] (H^+ or Me_3Si^+; Scheme 1, path *c*), and the possible occurrence of a Wagner–Meerwein rearrangement[1,15,20,21] (Scheme 1, path *d*).

The method is appealing because the phenonium ion is generated under mild neutral conditions and thus can be more easily directed towards the desired preparative target. However, in order to exploit the synthetic potential of the reactions via phenonium ions, the rationalization and thus

[a] Department of Organic Chemistry, University of Pavia, Via Taramelli 10, 27100 Pavia, Italy
Fax: +39-0382-987323
E-mail: prottistefano@gmail.com
[b] Department of General Chemistry, University of Pavia, Via Taramelli 12, 27100 Pavia, Italy
Fax: +39-0382-528544

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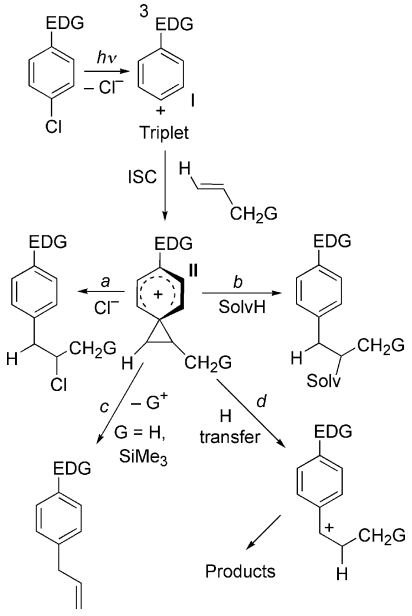


Scheme 1. Photochemical generation and fate of a phenonium ion.

the control of the competition between the above paths is required. A way to tackle this problem was by using a bifunctional trap containing two different nucleophilic sites. Previous work showed that triplet phenyl cations react with π and not with *n* nucleophilic functionalities. Thus, by using an alkene containing a nucleophile, for example, an alcohol functionality, the reaction should afford a phenonium ion that would then undergo intramolecular attack by the hydroxy group. We first explored this strategy by irradiating phenyl cation precursors in the presence of alkenoic acids, and indeed we obtained phenyl (benzyl) lactones in a tandem reaction in a number of cases.[22] This result had some synthetic appeal and understanding the scope of this approach seemed convenient. As a contribution towards this target, we report here a study of the reaction of photogenerated phenyl cations with selected alkenols under various conditions. It was hoped that the cations would add again to the C=C bond and intramolecular trap by the OH group would then occur in competition with intermolecular reactions. Accordingly, the chemistry observed and the medium effect on it would give information about the behavior of the phenonium ion.

Results

We chose, as phenyl cation precursors, some phenyl chlorides, viz. 4-chlorophenol (**1**-OH), 4-chloroanisole (**1**-OMe), and 4-chloro-*N*,*N*-dimethylaniline (**1**-NMe_2) and as traps two ω-alkenols, namely, 3-buten-1-ol (**2**) and 4-penten-1-ol (**3**), and two 1,2-disubstituted derivatives, viz. stereoisomeric (*E*)- and (*Z*)-3-hexen-1-ol [(*E*)-**4** and (*Z*)-**4**, respectively] in order to have information on the regio- and stereochemical course of the reaction. In view of the ionic nature of the intermediates, it appeared important to explore these reactions in solvents of different polarity [ethyl acetate, MeCN/H_2O (5:1), and 2,2,2-trifluoroethanol (TFE)].

Solutions (0.05 M) of **1** in the presence of the chosen alkenol (0.5 M) were externally irradiated up to complete consumption of the starting aromatic (except where indicated) and the reaction course was monitored by GC analysis. Cyclic or open-chain arylated products obtained from alkenes **2** and **3** are reported in Tables 1 and 2 and Schemes 2 and 3. Not included are the photoreactions of 4-chlorophenol (**1**-OH) in ethyl acetate (too slow) and that with **2** in TFE (a complex mixture is formed). Thus, phenol **1**-OH gave 2-(4-hydroxyphenyl)tetrahydrofuran **5**-OH as the only isolated product in 67% yield in the reaction with **2** in MeCN/H_2O (5:1) and gave again a single product, 2-(4-hydroxybenzyl)tetrahydrofuran **6**-OH, in the reaction with **3** both in TFE and MeCN/H_2O (5:1). The preparative viability of the method was checked by synthesizing compound **6**-OH on a larger scale (4.5 mmol) by using an immersion-well apparatus, and it was easily isolated in 84% yield by bulb-to-bulb distillation (see Experimental Section).

Table 1. Photolysis of aryl chlorides **1** in the presence of alkenol **2**.

Aryl chloride	Alcohol	CH_3COOEt	MeCN/H_2O (5:1)	CF_3CH_2OH
		Product, Yield [%]		
Cl–OH **1**-OH	OH **2**	[a]	**5**-OH, 67	[b]
Cl–OMe **1**-OMe	**2**	**7**-OMe, 59	**5**-OMe, 46	**5**-OMe, 61 **7**-OMe, 13
Cl–NMe_2 **1**-NMe_2	**2**	**5**-NMe_2, 8 **7**-NMe_2, 39	**5**-NMe_2, 21 **7**-NMe_2, 27	**5**-NMe_2, 43 **7**-NMe_2, tr

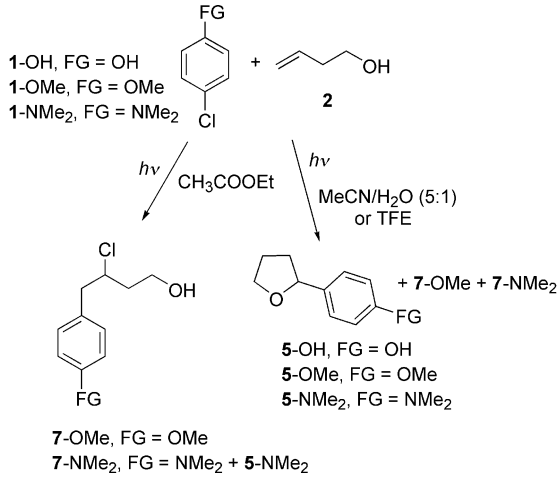
[a] No significant reaction of **1**-OH. [b] Complex mixture.

Table 2. Photolysis of aryl chlorides **1** in the presence of alkenol **3**.

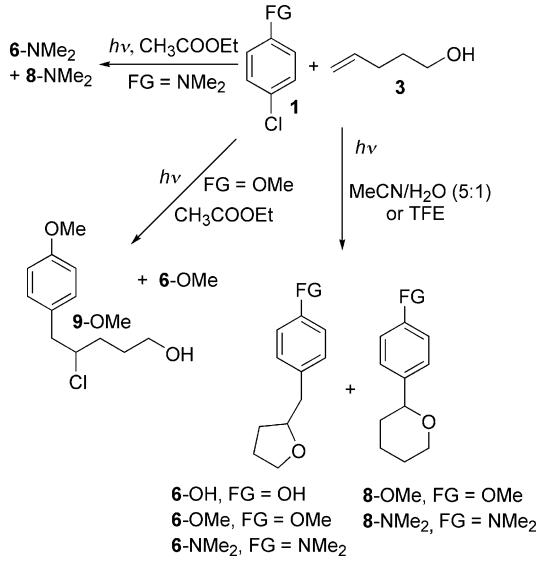
Aryl chloride	Alcohol	CH_3COOEt	MeCN/H_2O (5:1)	CF_3CH_2OH
		Product, Yield [%]		
Cl–OH **1**-OH	OH **3**	[a]	**6**-OH, 79 (84)[b]	**6**-OH, 54
Cl–OMe **1**-OMe	**3**	**6**-OMe, 43 **9**-OMe, 29	**6**-OMe, 33 **8**-OMe, 20	**6**-OMe, 43 **8**-OMe, 50
Cl–NMe_2 **1**-NMe_2	**3**	**6**-NMe_2, 62 **8**-NMe_2, 3	**6**-NMe_2, 50 **8**-NMe_2, 5	**6**-NMe_2, 76 **8**-NMe_2, 4

[a] No significant reaction of **1**-OH. [b] Reaction carried out in an immersion-well reactor.

4-Chloroanisole (**1**-OMe) and 4-chloro-*N*,*N*-dimethylaniline (**1**-NMe_2) were found to react efficiently in all of the solvents tested, but the products formed were dependent on the medium. Thus, irradiation of compound **1**-OMe in the presence of **2** gave 3-chloro-4-(4-methoxyphenyl)butan-1-ol (**7**-OMe) in ethyl acetate, 2-(4-methoxyphenyl)tetrahydrofuran (**5**-OMe) in MeCN/H_2O (5:1), and a mixture of **7**-OMe and **5**-OMe (the latter being the main product) in



Scheme 2. Irradiation of aryl chlorides **1** in the presence of 3-buten-1-ol (**2**).



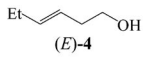
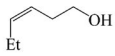
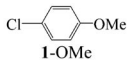
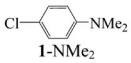
Scheme 3. Irradiation of **1** in the presence of 4-penten-ol (**3**).

TFE. The reaction between **1**-OMe and **3** gave 2-(4-methoxybenzyl)tetrahydrofuran (**6**-OMe) and 2-(4-methoxyphenyl)tetrahydropyran (**8**-OMe) in MeCN/H_2O and TFE, as well as **6**-OMe (43%) along with open-chain derivative **9**-OMe (29%) in ethyl acetate.

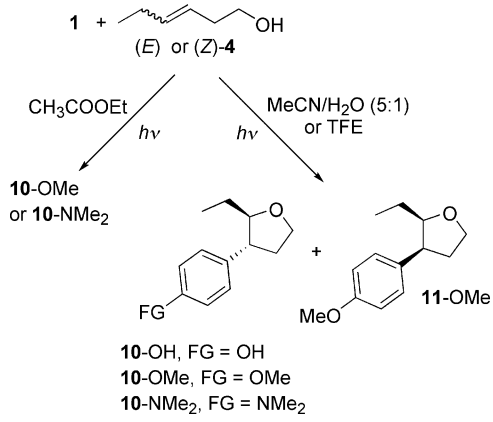
With alkenol **2**, 2-(4-*N*,*N*-dimethylaminophenyl)tetrahydrofuran (**5**-NMe_2) and 3-chloro-4-phenylbutanol (**7**-NMe_2) were formed in each case; the latter was predominant in ethyl acetate and the former was the almost-exclusive product in TFE. With **3**, 2-(4-*N*,*N*-dimethylaminobenzyl)tetrahydrofuran (**6**-NMe_2) and 2-(4-*N*,*N*-dimethylaminophenyl)tetrahydropyran (**8**-NMe_2) were found, and the former was consistently the predominating species.

The explorative study was pursued by irradiating aryl chlorides **1** in the presence of two diastereomeric alkenols, viz. (*E*)- and (*Z*)-3-hexen-1-ols (**4**) as shown in Table 3 and Scheme 4. Thus, with **1**-OH and **1**-NMe_2, the arylation occurred efficiently and afforded a single diastereoisomer (the *trans*-tetrahydrofurans **10**-OH and **10**-NMe_2, respectively) in the presence of both (*E*) and (*Z*)-**4** in all of the solvents tested. In the case of chloroanisole **1**-OMe, however, *trans* (**10**-OMe) and *cis* (**11**-OMe) tetrahydrofurans were obtained as a equal-ratio mixture of (*E*) and (*Z*)-**4** in TFE and MeCN/H_2O, whereas only the *trans* isomer **10**-OMe was obtained in ethyl acetate.

Table 3. Photolysis of aryl chlorides **1** in the presence of (*Z*)- or (*E*)-3-hexen-1-ol (**4**).

Aryl chloride	Alcohol	CH_3COOEt	MeCN/H_2O (5:1)	CF_3CH_2OH
		Product, Yield [%]		
 **1**-OH	 (*E*)-**4**	[a]	**10**-OH, 56	**10**-OH, 88
1-OH	 (*Z*)-**4**	[a]	**10**-OH, 53	**10**-OH, 48
 **1**-OMe	(*E*)-**4**	**10**-OMe, 33	**10**-OMe, 52 **11**-OMe, 18	**10**-OMe, 46 **11**-OMe, 29
1-OMe	(*Z*)-**4**	**10**-OMe, 39	**10**-OMe, 52 **11**-OMe, 14	**10**-OMe, 48 **11**-OMe, 31
 **1**-NMe_2	(*E*)-**4**	**10**-NMe_2, 18	**10**-NMe_2, 27	**10**-NMe_2, 58
1-NMe_2	(*Z*)-**4**	**10**-NMe_2, 10	**10**-NMe_2, 19	**10**-NMe_2, 51

[a] No significant reaction of **1**-OH.



Scheme 4. Irradiation of aryl chlorides **1** in the presence of alkenols (*E*)-**4** and (*Z*)-**4**.

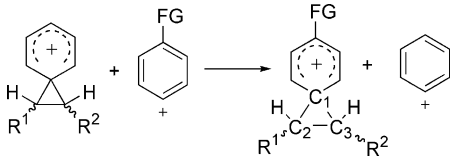
The experiments were supplemented by computational work. The geometry and energy of some phenonium ions modeling the putative intermediates in the above arylation of alkenes by the addition of substituted phenyl cations were calculated by the DFT method at the B3LYP 6-31G(d) level (see Supporting Information). The key geometric parameters for the adducts formed by the 4-methoxyphenyl cation with ethylene and propene are reported in Table 4, as well as those from phenyl and 4-aminophenyl cation with propene and from phenyl, 4-methoxy-, and 4-aminophenyl cation with 2-butene [in this case the bond length did not differ when starting from either the (*E*) or the (*Z*) isomer]. The substituent effect was evaluated by calculating the free energy associated with the isodesmic reaction shown in

Table 4. C–C Distances for the phenonium ions formed by the addition of phenyl cations to olefins.

Entry	FG	R^1	R^2	$d(C^1–C^2)$ [Å]	$d(C^1–C^3)$ [Å]	Relative free energies[a] [kcal/mol]
1	H	H	H	1.63	1.63	0
2	OCH_3	H	H	1.59	1.59	–11.5
3	NH_2	H	H	1.58	1.58	–14.2
4	H	H	CH_3	1.58	1.76	0
5	OCH_3	H	CH_3	1.58	1.65	–10.1
6	NH_2	H	CH_3	1.58	1.62	–12.3
7[b]	H	CH_3	CH_3	1.67	1.67	0
8[c]	H	CH_3	CH_3	1.67	1.67	–0.5
9[b]	OCH_3	CH_3	CH_3	1.63	1.63	–9.61
10[c]	OCH_3	CH_3	CH_3	1.63	1.63	–10.3
11[b]	NH_2	CH_3	CH_3	1.61	1.61	–11.4
12[c]	NH_2	CH_3	CH_3	1.61	1.61	–12.3

[a] Evaluated in MeCN. [b] From (*Z*)-2-butene. [c] From (*E*)-2-butene.

Scheme 5 and is likewise reported in Table 4. The data show that the phenonium ion was stabilized by ca. 10 kcal/mol by a 4-OMe group and by a further 2–3 kcal/mol by a 4-NH_2 group both when the phenyl cation added to ethylene and when it added to 2-butene,[23] as evidenced also by the considerable shortening of the $C^1–C^2$ and $C^1–C^3$ bond lengths in the adduct with butene when passing from FG = H to FG = NH_2.



Scheme 5.

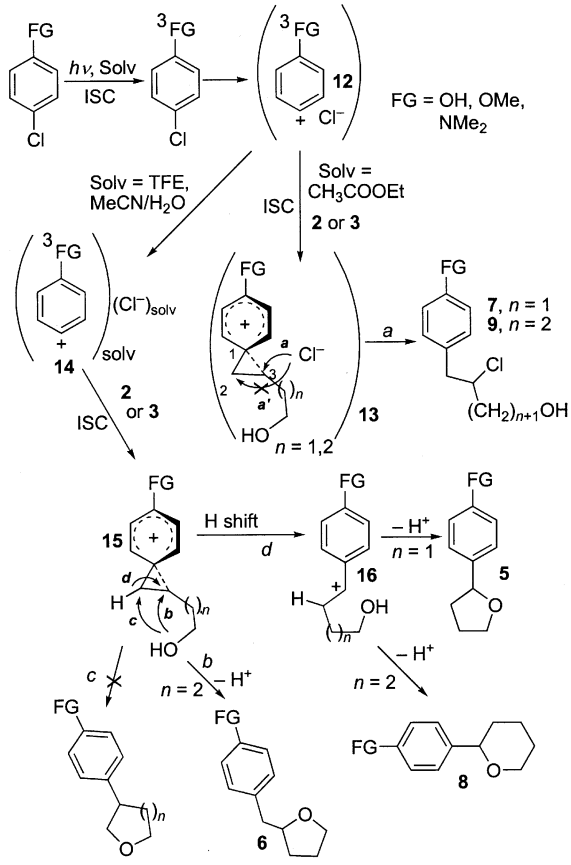
The attack of the parent phenyl cation to propene gave a highly asymmetric adduct, with a very weak $C^1–C^3$ bond. However, an electron-donating group considerably shortened that bond and stabilized the phenonium structure (Table 4).

Discussion

The photochemical generation of phenyl cations has been discussed previously. With a chlorinated phenol, anisole, or aniline, intersystem crossing to give the triplet is known to be efficient ($\Phi_{ISC} > 0.8$),[24] and heterolysis of the aryl chloride bond in polar media[11] occurs from that state forming the triplet cation (Scheme 6). With all of the present derivatives, the phenyl cation was conveniently generated, except for the case of 4-chlorophenol, which underwent photofragmentation in polar protic media[12,25a] but was quite photostable in ethyl acetate.

Addition to the alkenols occurs selectively at the C=C bond in a stepwise fashion, as expected because the triplet phenyl cation is the attacking species. From the single-bonded intermediate, intersystem crossing and formation of a second C–C bond may then lead to a phenonium ion as a further intermediate,[25b] unless cyclization on the OH group occurs first.

Considering first the reaction with terminal alkenols, it was noticed that the nucleophile that added was dependent on the medium. In a moderately polar solvent such as ethyl



Scheme 6. Mechanism of addition of phenyl cation to ω-alkenols **2** and **3**.

acetate, fragmentation gives an intimate phenyl cation–chloride ion pair (**12**), and adduct **13** is formed when still closely coupled with the chloride anion to give the corresponding chloroalcohol as the end product (Scheme 6, path *a*). In contrast, when the phenyl cation is generated in an ion-stabilizing medium such as MeCN/H_2O (5:1) or TFE, a solvent penetrated pair or free solvated ions (**14**) are formed, and the reaction of the phenyl cation with alkenols is followed by intramolecular attack by the OH group. This involves exclusive attack at the methine group (Scheme 6, path *b*) and not at the methylene group (Scheme 6, path *c*);

this is in competition with hydride shift to give the more stable benzyl cation (**16**) before nucleophilic attack (Scheme 6, path *d*).

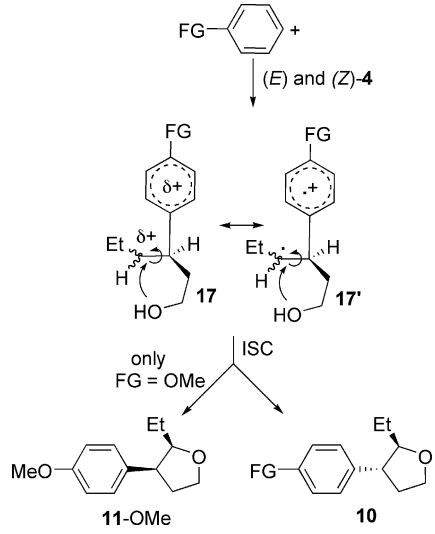
The result is both medium and structure dependent. Thus, in the photoreaction between 4-chloroanisole and pentenol (n = 2 in Scheme 6) the products observed arise from paths *a* and *b* in a ratio 40:60 in AcOEt, *b*/*d* (62:38) in MeCN/H_2O, and *b*/*d* (44:56) in TFE, whereas the same reaction with aniline **1**-NMe_2 yields only products from paths *b* and *d* (95:5, 91:9, and 95:5 in ethyl acetate, MeCN/H_2O, and TFE, respectively). The role of path *a* from the caged pair is expected to diminish on going to more polar solvents, whereas the other differences are informative about the role of the adduct ion. Two factors play a role in the determination: donation from the substituent on the aromatic ring and weakening of the C^1–C^3 cyclopropane bond by alkyl substituents (see above). Table 4 shows that the cyclopropane ring in these phenonium ions is highly asymmetric (structure **15**), which is in accord with exclusive cyclization at C^3.

Furthermore, the more localized the charge at C^3, the more likely a hydride shift will occur (Scheme 6, path *d*). This is minimal for the reactions of chloroaniline in an ion-stabilizing solvent, in which the large donation by the aminophenyl group strengthens the C^1–C^3 bond, and under these conditions, path *b* (Scheme 6) is almost the only process. However, when either the substituent is a less-donating group, such as the methoxy group, or the medium is less stabilizing, charge localization and thus the role of path *d* (Scheme 6) increases. The polarity/nucleophilicity of the solvent then determines whether it is path *a* or *b* that competes with *d* (Scheme 6).

In contrast, the seemingly appealing formation of β-aryltetrahydrofurans from butenol by attack at the methylene group (Scheme 6, path *c*) does not take place, even though path *b* is precluded, as it would lead to an unstable four-membered ring. In this case, rearrangement to **16** is the only process competing with the in-cage-occurring coupling (with Cl^-), which demonstrates once again that electrophilic reactivity resides at C^3. As above, the proportion between paths *b*/*d* vs. *a* (Scheme 6) is tuned by the solvent: the first process dominates in TFE and MeCN/H_2O[26] and the latter is by far the main path in ethyl acetate.

As for 1,2-disubstituted alkenes, calculations show that bonds to the phenyl cation are weaker and the C^1–C^2 and C^1–C^3 distances are considerably lengthened with respect to the unsubstituted ethylene [1.59 vs. 1.63 Å in the case of the methoxyphenyl derivative; compare Entry 2 with 9(10) in Table 4].[5] Again, a good electron-donating substituent stabilizes the phenonium and shortens the bonds (1.67 Å for FG = H, 1.61 Å for FG = NH_2 for 2-butene). With alkenes (*Z*)- and (*E*)-**4**, the geometrically favored attack at C^2 is the only process occurring and leads to 3-aryltetrahydrofurans. In addition to the reaction being chemoselective, it is also fully stereoselective when phenol **1**-OH and chloroaniline **1**-NMe_2 are used, and only the *trans* isomers **10**-OH and **10**-NMe_2 are formed by starting from both (*E*)- and (*Z*)-hexenols.[27]

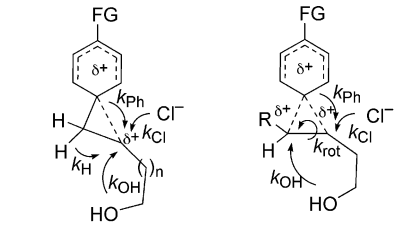
Thus, in the key step the C^2–C^3 bond can freely rotate (Scheme 7), in accord with the idea that the first intermediate from the triplet cation is single-bonded (formulae **17**/**17′**) and ISC and intramolecular cyclization on the OH group follow. Should a doubly bonded (phenonium) cation be the first intermediate, a stereospecific arylation would take place,[1,4] as equilibration of stereoisomeric phenonium ions over an open-chain isomer is too slow.[28] The exclusive formation of the *trans* isomers is determined by the steric hindering by the ethyl group. However, with **1**-OMe, *cis* tetrahydrofuran **11**-OMe is also formed, at least in polar solvents (**10**-OMe/**11**-OMe, 100:0 in ethyl acetate, 61:39 in TFE), but the *trans*–*cis* ratio is the same starting from either alkene. Thus, the single-bonded adduct is again the first intermediate, but the less-donating methoxy group does not sufficiently stabilize the cation to make attack by the OH group occur at the less-hindered side (Scheme 7).



Scheme 7. Proposed mechanism for the addition of phenyl cations onto alkenols **4**.

Conclusions

The phenylation of alkenes by triplet phenyl cations was studied with regard to the possible role of a phenonium ion, which is the intermediate previously invoked in the substitution of phenethyl derivatives. Evidence about this point was obtained through the competition of different reactions that act as "chemical clocks", as indicated in formulae **18** (arising from the attack of the phenyl cation on terminal olefins) and **19** (from 1,2-disubstituted alkenes). In the first case, intramolecular nucleophile trapping, k_{OH} (or, in less polar solvents, addition of paired chloride, k_{Cl}) is faster than hydride shift, k_H,[29] when the tether has the appropriate length (n = 2). The reverse is true when the tether is too short (n = 1, $k_H > k_{OH}$) in protic solvents, whereas intermolecular chloride attack (k_{Cl}) remains predominant in aprotic solvent. A stabilized phenonium (k_{Ph}, see formula **19**) is not the first intermediate and is preceded by a singly bonded triplet adduct cation where the C^2–C^3 bond can freely rotate ($k_{rot} > k_{Ph}$), as shown by the stereoselective addition to **4**.



$n = 2$: k_{OH}, $k_{Cl} > k_H > k_{Ph}$
$n = 1$: k_H, $k_{Cl} > k_{OH}$, k_{Ph}

18

$k_{rot} > k_{OH} > k_H$, k_{Ph}

19

This addition of a triplet phenyl cation to alkenes differs from the thermal generation of the phenonium ion by heterolytic cleavage of phenethyl derivatives.

Apart from the mechanistic indications, the above reaction of phenyl cations with alkenols is synthetically useful as an alternate method for preparing 2- (or 3) phenyl-substituted tetrahydrofurans (from β-hydroxyalkenes) and 2-benzyltetrahydrofurans (from γ-hydroxy alkenes). These targets are obtained by means of a one-step, tandem Ar–C, C–O bond reaction that has no close precedent and gives access to a class of tetrahydrofuran derivatives having potential biological interest.[30] As it appears from a recent review,[31] benzyltetrahydrofurans have been obtained by reaction of aryl bromides (and not of chlorides, as here) with substituted γ-hydroxy alkenes only in the presence of a palladium-based catalyst and a phosphane derivative as cocatalyst[32] or by a nickel-catalyzed reaction of aryl boronic acids with 2-bromomethyltetrahydrofuran.[33] As for aryl tetrahydrofurans, these were synthesized by metal-catalyzed arylation of *cis*-2-butene-1,4-diol by an aryl halide[34] or directly from tetrahydrofuran[35a] or its 2-benzenesulfonyl[35b] or 2-(1-benzotriazol-1-yl)[35c] derivatives in the reaction with aryl Grignard reagents.

In contrast to the drastic conditions of the thermal reactions, the present synthesis is carried out at room temperature and makes no use of expensive and labile metal catalysts; it also does not require strictly anhydrous conditions, and water actually favors the initial heterolytic step. Indeed, aqueous acetonitrile can be used as the reaction solvent in the place of the more expensive TFE and, noteworthy, with no competitive addition of nucleophilic water to the phenonium ion intermediates.[36] The selectivity is also an important issue, as with terminal alkenols the overall process of carboetherification is regio- and chemoselective (the latter can be tuned through the choice of the solvent). With nonterminal alkenols, the process is chemo- and stereoselective and affords a phenyl tetrahydropyran as a single diastereoisomer.

Experimental Section

General: NMR spectra were recorded with a 300 MHz spectrometer. The attributions were made on the basis of ^{1}H and ^{13}C NMR, as well as DEPT-135 and NOESY experiments; chemical shifts are reported downfield from TMS. The photochemical reactions were performed by using nitrogen-purged solutions in quartz tubes and a multilamp reactor fitted with six 15-W phosphor coated lamps (maximum emission of 310 nm) for the irradiation. Alcohols **2**–**4** and halides **1**-OH and **1**-OMe are commercially available and were freshly distilled before use. Aryl chloride **1**-NMe_2 was obtained from 4-chloroaniline as described previously.[37]

General Procedure for the Photochemical Arylation of Alkenols 2–4: A solution of halides **1** (0.05 M, 1.5 mmol) and alkenol **2**–**4** (0.5 M, 15 mmol) in the solvent chosen (30 mL) was poured into two quartz tubes and purged for 10 min with nitrogen, serum capped, and irradiated with six 15-W phosphor-coated lamps (emission centered at 310 nm). The solvent was eliminated in vacuo, and the residue was purified by column chromatography (cyclohexane/ethyl acetate).

Irradiation of 4-Chlorophenol (1-OH) in MeCN/H_2O (5:1) in the Presence of 3-Buten-1-ol (2): A solution of 4-chlorophenol (**1**-OH; 193 mg, 1.5 mmol) and 3-buten-1-ol (**2**; 1.3 mL 15 mmol) in MeCN/H_2O (5:1, 30 mL) was irradiated for 14 h. Purification by column chromatography (cyclohexane/ethyl acetate, 9:1) afforded 2-(4-hydroxyphenyl)tetrahydrofuran (**5**-OH;[38] 165 mg, 67%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.75–7.15 (AA′BB′, 4 H), 5.00 (br. s, 1 H), 4.80–4.85 (t, J = 7.0 Hz, 1 H), 4.05–4.15 (q, J = 7.0 Hz, 1 H), 3.90–4.00 (q, J = 7.0 Hz, 1 H), 2.35–2.45 (m, 1 H), 1.90–2.10 (m, 2 H), 1.75–1.85 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.7, 135.1, 127.1 (CH), 115.0 (CH), 80.4 (CH), 68.4 (CH_2), 34.3 (CH_2), 25.9 (CH_2) ppm. IR (neat): $\tilde{\nu}$ = 3401, 2960, 1617, 1234, 1041, 814 cm^{-1}. $C_{10}H_{12}O_2$ (164.08): calcd. C 73.15, H 7.37; found C 73.3, H 7.5.

Irradiation of 1-OH in MeCN/H_2O (5:1) in the Presence of 4-Penten-1-ol (3): A solution of **1**-OH (193 mg, 1.5 mmol) and 4-penten-1-ol (**3**; 1.53 mL, 15 mmol) in MeCN/H_2O (5:1, 30 mL) was irradiated for 14 h. Purification by column chromatography afforded 4-(4-hydroxybenzyl)tetrahydrofuran (**6**-OH;[38] 210 mg, 79%) as an oil. Product **6**-OH was synthesized on a larger scale starting from a solution of **1**-OH (580 mg, 4.5 mmol) and **3** (0.3 M, 2.76 mL, 27 mmol) in MeCN/H_2O (5:1, 90 mL) by irradiation for 6 h in an immersion-well apparatus. The photolyzed solution was evaporated, and the residue was purified by bulb-to-bulb distillation to give **6**-OH (666 mg, 84%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.70–7.15 (AA′BB′, 4 H), 6.50 (br. s, 1 H), 4.05–4.15 (quint., J = 7 Hz, 1 H), 3.90–4.00 (m, 1 H), 3.75–3.80 (m, 1 H), 2.75–2.90 (dd, J = 7 and 13 Hz, 1 H), 2.65–2.70 (dd, J = 7 and 13 Hz, 1 H), 1.80–2.00 (m, 3 H), 1.50–1.70 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.4, 130.2, 130.1 (CH), 115.2 (CH), 80.4 (CH), 67.7 (CH_2), 40.8 (CH_2), 30.8 (CH_2), 25.4 (CH_2) ppm. IR (neat): $\tilde{\nu}$ = 3338, 2956, 1517, 1240, 822 cm^{-1}. $C_{11}H_{14}O_2$ (178.1): calcd. C 74.13, H 7.92; found C 74.3, H 7.8.

Irradiation of 4-Chloroanisole (1-OMe) in Ethyl Acetate in the Presence of 3-Buten-1-ol (2): A solution of 4-chloroanisole (**1**-OMe; 200 μL, 1.5 mmol) and 3-buten-1-ol (**2**; 1.28 mL, 15 mmol) in ethyl acetate (30 mL) was irradiated for 36 h. Purification by column chromatography (cyclohexane/ethyl acetate, 99:1) afforded 3-chloro-4-(4-methoxyphenyl)-butan-1-ol (**7**-OMe;[39] 222 mg, 59%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.75–7.15 (AA′BB, 4 H), 4.20–4.30 (m, 1 H), 3.80–3.95 (t, J = 8 Hz, 2 H), 3.80 (s, 3 H), 2.95–3.00 (dd, J = 8 and 2 Hz, 2 H), 2.05–2.15 (m, 1 H), 1.80–1.95 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.3, 129.9 (CH), 128.8, 113.1 (CH), 59.9 (CH), 59.0 (CH_2), 54.4 (CH_3), 43.5 (CH_2), 39.0 (CH_2) ppm. IR (neat): $\tilde{\nu}$ = 3369, 2924, 1614, 1223, 1058, 821 cm^{-1}. $C_{11}H_{15}ClO_2$ (214.08): calcd. C 61.54, H 7.04; found C 61.4, H 7.2.

Irradiation of 4-Chloroanisole (1-OMe) in MeCN/H_2O (5:1) in the Presence of 2: A solution of 4-chloroanisole (**1**-OMe; 200 μL, 1.5 mmol) and 3-buten-1-ol (**2**; 1.28 mL, 15 mmol) in MeCN/H_2O (5:1, 30 mL) was irradiated for 24 h. Purification by column

chromatography (cyclohexane/ethyl acetate, 99:1) afforded 2-(4-methoxyphenyl)tetrahydrofuran (**5**-OMe; 122 mg, 46%) as an oil. ^{1}H NMR[40] (300 MHz, $CDCl_3$): δ = 6.80–7.30 (AA′BB′, 4 H), 4.80–4.90 (t, J = 7 Hz, 1 H), 4.05–4.15 (q, J = 7 Hz, 1 H), 3.85–3.95 (m, 1 H), 3.80 (s, 3 H), 2.10–2.20 (m, 1 H), 2.00–2.05 (m, 2 H), 1.90–1.95 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.7, 135.2, 126.8 (CH), 113.6 (CH), 80.3 (CH), 68.3 (CH_2), 55.1 (CH_3), 34.3 (CH_2), 25.9 (CH_2) ppm. IR (neat): $\tilde{\nu}$ = 2933, 1488, 1246, 1039, 843 cm^{-1}. $C_{11}H_{14}O_2$ (178.1): calcd. C 74.13, H 7.92; found C 74.2, H 7.8.

Irradiation of 1-OMe in Ethyl Acetate in the Presence of 4-Penten-1-ol (3): A solution of 4-chloroanisole (**1**-OMe; 200 μL, 1.5 mmol) and 4-penten-1-ol (**3**; 1.53 mL, 15 mmol) in ethyl acetate (30 mL) was irradiated for 36 h. Purification by column chromatography (cyclohexane/ethyl acetate, 99:1) afforded 4-(4-methoxybenzyl)-tetrahydrofuran (**6**-OMe;[41] 124 mg, 43%) and 4-chloro-5-(4-methoxyphenyl)pentan-1-ol (**9**-OMe; 99 mg, 29%) as an oil. Data for **6**-OMe: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.80–7.20 (AA′BB′, 4 H), 3.85–4.15 (m, 2 H), 3.80 (s, 3 H), 3.70–3.75 (m, 1 H), 2.85–2.90 (dd, J = 6 and 13 Hz, 1 H), 2.70–2.75 (dd, J = 6 and 13 Hz, 1 H), 2.05–2.10 (m, 1 H), 1.65–1.95 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9, 131.0, 130.0 (CH), 113.6 (CH), 80.1 (CH), 67.8 (CH_2), 55.1 (CH_3), 40.9 (CH_2), 30.8 (CH_2), 25.5 (CH_2) ppm. IR (neat): $\tilde{\nu}$ = 2933, 1513, 1242, 1037, 826 cm^{-1}. $C_{12}H_{16}O_2$ (192.12): calcd. C 74.97, H 8.39; found C 74.8, H 8.3. Data for **9**-OMe: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.85–7.10 (AA′BB′, 4 H), 4.00–4.20 (t, J = 6 Hz, 2 H), 3.80 (s, 3 H), 3.00–3.10 (m, 1 H), 1.60–2.00 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4, 130.2 (CH), 129.6, 113.7 (CH), 64.0 (CH), 63.4 (CH_2), 55.1 (CH_3), 44.0 (CH_2), 33.7 (CH), 25.6 (CH_2) ppm. IR (neat): $\tilde{\nu}$ = 3340, 2927, 1250 1026, 817 cm^{-1}. $C_{12}H_{17}ClO_2$ (228.09): calcd. C 63.02, H 7.49; found C 63.1, H 7.3.

Irradiation of 1-OMe in MeCN/H_2O (5:1) in the Presence of 3: A solution of 4-chloroanisole (**1**-OMe; 200 μL, 1.5 mmol) and 4-penten-1-ol (**3**; 1.53 mL, 15 mmol) in MeCN/H_2O (5:1; 30 mL) was irradiated for 24 h. Purification by column chromatography (cyclohexane/ethyl acetate, 99:1) afforded a mixture of **6**-OMe (152 mg, 33%) and 2-(4-methoxyphenyl)tetrahydropyran (**8**-OMe, 20%, oil). Data for **8**-OMe: ^{1}H NMR[42] (300 MHz, $CDCl_3$, from the mixture): δ = 6.80–7.10 (AA′BB′, 4 H), 4.15–4.30 (m, 2 H), 3.80 (s, 3 H), 3.70–3.75 (m, 2 H), 2.05–2.10 (m, 1 H), 1.60–1.90 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, from the mixture): δ = 158.7, 135.5, 127.0 (CH), 113.5 (CH), 79.9 (CH), 68.9 (CH_2), 55.1 (CH_3), 33.7 (CH_2), 25.5 (CH_2), 23.8 (CH_2) ppm. IR (neat, from the mixture): $\tilde{\nu}$ = 2933, 1513, 1242, 1037, 826 cm^{-1}.

Irradiation of 4-Chloro-*N*,*N*-dimethylaniline (1-NMe_2) in Ethyl Acetate in the Presence of 3-Buten-1ol (2): A solution of **1**-NMe_2 (233 mg, 1.5 mmol) and **2** (1.28 mL, 15 mmol) in ethyl acetate (30 mL) was irradiated for 14 h. Purification by column chromatography (cyclohexane/ethyl acetate, 9:1) afforded 3-chloro-4-(4-*N*,*N*-dimethylamino)butan-1-ol (**7**-NMe_2; 133 mg, 39%) and 2-(*N*,*N*-dimethylamino)tetrahydropyran (**5**-NMe_2; 23 mg, 8%) both as oils. Data for **7**-NMe_2: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.75–7.10 (AA′BB, 4 H), 4.15–4.25 (m, 1 H), 3.80–3.90 (t, J = 7 Hz, 1 H), 2.95–3.05 (m, 2 H), 2.95 (s, 6 H), 2.00–2.15 (m, 1 H), 1.80–1.90 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.3, 130.0 (CH), 128.3, 112.7 (CH), 61.3 (CH), 59.8 (CH_2), 44.2 (CH_3), 40.5 (CH_2), 39.7 (CH_2) ppm. IR (neat): $\tilde{\nu}$ = 3369, 2924, 1342, 1058, 821 cm^{-1}. $C_{12}H_{18}ClNO$ (227.11): calcd. C 63.29, H 7.97; found C 63.1, H 8.0.

Irradiation of 1-NMe_2 in TFE in the Presence of 2: A solution of 4-chloro-*N*,*N*-dimethylaniline (**1**-NMe_2; 233 mg, 1.5 mmol) and 3-buten-1-ol (**2**; 1.28 mL, 15 mmol) in TFE (30 mL) was irradiated for 10 h. Purification by column chromatography (cyclohexane/ethyl acetate, 9:1) afforded **5**-NMe_2 (123 mg, 43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.80–7.20 (AA′BB′, 4 H), 4.80–4.90 (t, J = 7 Hz, 1 H), 4.00–4.10 (m, 1 H), 3.90–3.95 (m, 1 H), 2.95 (s, 6 H), 2.20–2.25 (m, 1 H), 2.00–2.15 (m, 2 H), 1.80–1.90 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.0, 130.8, 126.7 (CH), 112.5 (CH), 80.6 (CH), 68.2 (CH_2), 40.7 (CH_3), 34.1 (CH_2), 26.0 (CH_2) ppm. IR (neat): $\tilde{\nu}$ = 3300, 2930, 1772, 1167, 819 cm^{-1}. $C_{12}H_{17}NO$ (191.13): calcd. C 75.35, H 8.96; found C 75.2, H 8.8.

Irradiation of 1-NMe_2 in MeCN/H_2O (5:1) in the Presence of 3: A solution of 4-chloro-*N*,*N*-dimethylaniline (**1**-NMe_2; 233 mg, 1.5 mmol) and 4-penten-1-ol (**3**; 1.53 mL, 15 mmol) in MeCN/H_2O (5:1, 30 mL) was irradiated for 6 h. Purification by column chromatography (cyclohexane/ethyl acetate, 9:1) afforded a mixture of 2-(4-*N*,*N*-dimethylaminobenzyl)tetrahydrofuran (**6**-NMe_2, 169 mg, 50%) and 2-(4-*N*,*N*-dimethylaminophenyl)tetrahydropyran (**8**-NMe_2, 5%). Spectroscopic data of compounds **6**-NMe_2 and **8**-NMe_2 are in accordance with the literature data.[43]

Irradiation of 1-OH in MeCN/H_2O (5:1) in the Presence of (*E*)-3-Hexen-1-ol (4): A solution of 4-chlorophenol (**1**-OH; 0.05 M, 193 mg, 1.5 mmol) and (*E*)-3-hexen-1-ol (**4**; 0.5 M, 1.78 mL, 15 mmol) in MeCN/H_2O (5:1, 30 mL) was irradiated for 14 h to give *trans*-2-ethyl-3-(4-hidroxyphenyl)tetrahydrofuran (**10**-OH, 161 mg, 0.84 mmol, 56%) as a colorless solid. M.p. 81–82 °C. The same reaction carried out in the presence of (*Z*)-3-hexen-1-ol (**4**; 0.5 M) gave again compound **10**-OH (53%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.80–7.10 (AA′BB′, 4 H), 5.50 (br. s, 1 H), 4.00–4.10 (m, 2 H), 3.70–3.75 (m, 1 H), 2.95–3.00 (q, J = 8 Hz, 1 H), 2.35–2.40 (m, 1 H), 2.05–2.10 (m, 1 H), 1.50–1.60 (m, 2 H), 0.95–1.00 (t, J = 8 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.3, 133.8, 128.6 (CH), 115.3 (CH), 87.4 (CH), 67.3 (CH_2), 49.9 (CH), 35.6 (CH_2), 26.7 (CH_2), 10.5 (CH_3) ppm. IR (neat): $\tilde{\nu}$ = 3272, 2967, 1517, 1230, 1018, 830 cm^{-1}. $C_{12}H_{16}O_2$ (192.12): calcd. C 74.97, H 8.39; found C 75.1, H 8.3

Irradiation of 1-OMe in MeCN/H_2O (5:1) in the Presence of (*Z*)-3-Hexen-1-ol (4): A solution of 4-chloroanisole (**1**-OMe; 200 μL, 1.5 mmol) and (*Z*)-3-hexen-1-ol (**4**; 1.78 mL, 15 mmol) in MeCN/H_2O (5:1, 30 mL) was irradiated for 30 h. Purification by column chromatography (cyclohexane/ethyl acetate, 99:1) afforded *trans*-2-ethyl-3-(4-methoxyphenyl)tetrahydrofuran (**10**-OMe; 111 mg) as an oil and a mixture containing **10**-OMe (93 mg, overall yield 52%) and *cis*-2-ethyl-3-(4-methoxyphenyl)tetrahydrofuran (**11**-OMe; 43 mg, 14%). Data for **10**-OMe: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.80–7.15 (AA′BB, 4 H), 4.20–4.30 (m, 1 H), 3.95–4.05 (m, 2 H), 3.80 (s, 3 H), 3.55–3.65 (dt, J = 8 and 4 Hz, 1 H), 2.80–2.95 (q, J = 8 Hz, 1 H), 2.15–2.35 (m, 1 H), 2.00–2.10 (m, 1 H), 1.50–1.60 (m, 2 H), 0.90–1.00 (t, J = 7 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.5, 134.0, 128.4 (CH), 113.9 (CH), 87.3 (CH), 67.3 (CH_2), 55.1 (CH_3), 49.9 (CH), 35.7 (CH_2), 26.7 (CH_2), 10.5 (CH_3) ppm. IR (neat): $\tilde{\nu}$ = 3401, 2930, 1510, 1247, 1034, 807 cm^{-1}. $C_{13}H_{18}O_2$ (206.13): calcd. C 75.69, H 8.80; found C 75.7, H 9.0. Data for **11**-OMe: ^{1}H NMR (300 MHz, $CDCl_3$, from the mixture): δ = 6.80–7.00 (AA′BB′, 4 H), 4.30–4.35 (d, J = 8 Hz, 1 H), 4.00–4.20 (m, 2 H), 3.85–3.90 (m, 1 H), 3.80 (s, 3 H), 2.10–2.20 (m, 1 H), 1.90–2.00 (m, 1 H), 1.30–1.45 (m, 2 H), 0.90–1.00 (t, J = 7 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, from the mixture): δ = 158.0, 134.1, 127.4 (CH), 113.6 (CH), 86.1 (CH), 66.7 (CH_2), 55.1 (CH_3), 49.6 (CH), 32.3 (CH_2), 24.7 (CH_2), 12.6 (CH_3) ppm. IR (neat, from the mixture): $\tilde{\nu}$ = 3401, 2930, 1510, 1247, 1034, 807 cm^{-1}.

Irradiation of 1-NMe_2 in TFE in the Presence of (*E*)-4: A solution of 4-chloro-*N*,*N*-dimethylaniline (**1**-NMe_2; 233 mg, 1.5 mmol) and

(*E*)-3-hexen-1-ol (**4**; 1.78 mL, 15 mmol) in TFE (30 mL) was irradiated for 8 h. Purification by column chromatography (cyclohexane/ethyl acetate, 9:1) afforded **10**-NMe_2 (191 mg, 58%) as a pale-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.75–7.20 (AA′BB′, 4 H), 3.95–4.10 (m, 2 H), 3.60–3.75 (dt, J = 4 and 8 Hz, 1 H), 2.95 (s, 6 H), 2.75–2.85 (q, J = 9 Hz, 1 H), 2.35–2.45 (m, 1 H), 2.00–2.15 (m, 1 H), 1.50–1.60 (m, 2 H), 0.90–1.00 (t, J = 8 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.3, 129.7, 128.1 (CH), 112.8 (CH), 87.3 (CH), 63.2 (CH_2), 49.8 (CH), 40.6 (CH_3), 35.6 (CH_2), 26.8 (CH_2), 10.5 (CH_3) ppm. IR (neat): $\tilde{\nu}$ = 3310, 2937, 1780, 1172, 808 cm^{-1}. $C_{14}H_{21}NO$ (219.16): calcd. C 76.67, H 9.65; found C 76.5, H 9.5.

Computational Study: Structure and energy were optimized at the UB3LYP/6-31G(d) level by using the Gaussian 03W package (see Supporting Information).

Supporting Information (see footnote on the first page of this article): Cartesian coordinates and energies for the adducts cited in the text.

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[27] The same selectivity was previously found in the reaction of 4-hydroxyphenyl cation with (*E* or *Z*)-3-hexenoic acid that gave exclusively a *trans*-aryl ethyl lactone (See ref.[22]).
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