Selective alkylation by photogenerated aryl and vinyl cation

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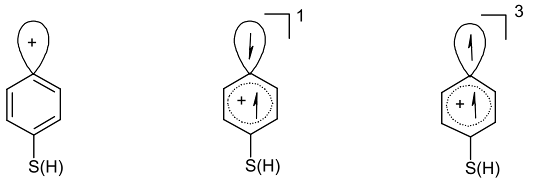
Chapter 4 | Fingerprints of singlet and triplet phenyl cations

Introduction

The possibility to steer reactions along singlet or triplet pathways by electronic excitation has led to the development of valuable chemo-, regio-, and stereoselective reactions [1,2,3,4]. The selectivity is achieved because differences in localisation of the electrons in the singlet and the triplet state affect the reactivity of the molecule as a whole. For example, specifically substituted (triplet) phenyl cations, generated by photolysis, show other chemoselectivity toward nucleophiles[5] than the photogenerated (singlet) parent phenyl cation[6]. Whereas singlet phenyl cations are fairly unselective, triplet phenyl cations display a selectivity for unsaturated compounds (π nucleophiles) over compounds with lone pairs (n nucleophiles) [7,8]. Practical implementations of these results are found in the photolysis of fluoroquinolones, a major class of antibiotics that react through a triplet aryl cation with cellular tissue[9], or in the photochemistry of the organophosphorous pesticide Fenthion, that degenerates via a singlet phenyl cation intermediate under the influence of sunlight[10].

The singlet or triplet nature of phenyl cations, which are among the most reactive intermediates known[11], has since long been subject of debate[12,13]. It was not until the parent phenyl cation was isolated in an Argon matrix, that its singlet closed shell ground state (**I**$_1$, Figure 1) was ascertained[14]. Isomers of this cation are possible. One electron of the aromatic sextet may be transferred, with spin retention, in the empty sp^2 orbital, yielding a species with a $\pi^5\sigma^1$ electronic configuration: the open-shell singlet phenyl cation **I**$_2$. If this process is followed by spin inversion the triplet phenyl cation **I**$_3$ is formed, which is an open-shell species by nature. Because in open-shell cations the unpaired electrons are in different orbitals, these species are also referred to as singlet and triplet diradical cations.

Figure 1: Singlet and triplet phenyl cations.



Closed shell singlet phenyl cation — **I**$_1$: $\pi^6\sigma^0$

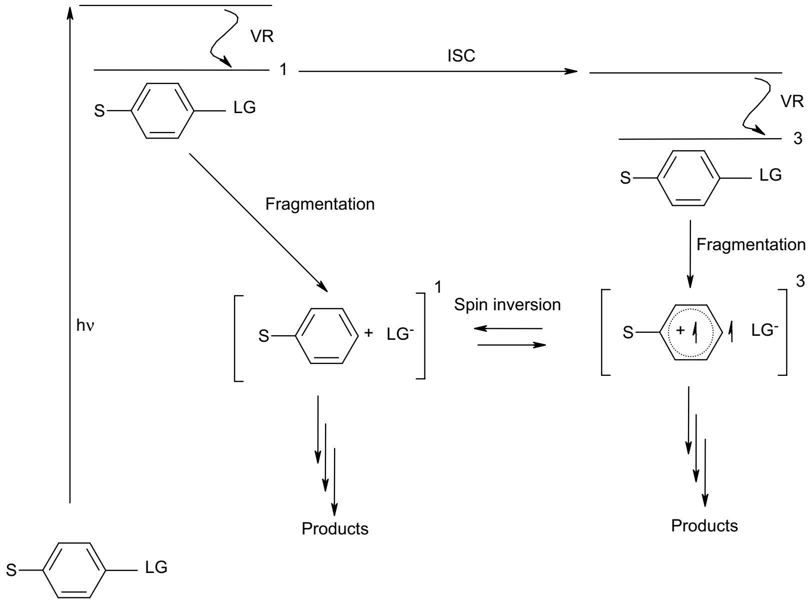
Open shell singlet phenyl cation — **I**$_2$: $\pi^5\sigma^1$

(Open shell) triplet phenyl cation — **I**$_3$: $\pi^5\sigma^1$

The textbook methods to thermally generate aryl cations are β-decay of tritiated precursors [15] and solvolysis of aryldiazonium salts [6]. In all cases studied but one, the *o*-nitrophenyl cation, the tritium decay method yields singlet aryl cations [16]. Whether or not phenyl cations are actually generated through solvolysis of their diazonium salt precursors in an S$_N$1 reaction is in doubt[17]. This is not so if light is used to trigger the loss of the N_2 leaving group[5,6,18]. In the photolysis of (substituted) phenyldiazonium salts both singlet and triplet phenyl cations are generated[5,6,7a,b]. Another photochemical entry to phenyl cations is the photolysis of 4-chloro (or fluoro) anilines [7c,d,8] or 4-chlorophenols [7e] in polar solvents with poor electron-donating capacity. These precursors yield triplet phenyl cations.

The singlet or triplet nature of photogenerated phenyl cations depends on two factors (a) the singlet or triplet nature of the reactive electronically excited state[19], (b) the relative stability of the singlet and triplet cations [20]. As depicted in Scheme 1, electronic excitation converts the ground state of the photolabile compound into a vibrationally excited singlet excited state. After vibrational relaxation (VR) to the vibrationally relaxed first singlet excited state, expulsion of the leaving group yields a singlet phenyl cation that can be trapped. If the rate of intersystem crossing (ISC) is larger than the rate of bond fission, the singlet excited state is converted into an iso-energetic triplet excited state. After vibrational relaxation to the first triplet excited state, the leaving group is cleaved off, forming a triplet phenyl cation. This ion is either trapped or undergoes spin inversion followed by intramolecular electron-transfer to yield a singlet cation, if that is energetically more stable. In principle, also spin inversion of the singlet to the triplet phenyl cation is possible.

Scheme 1: General scheme for photochemical singlet or triplet phenyl cation formation.



A time-honoured method to characterise cationic reactive intermediates is the determination of the *ortho*, *meta*, *para* ratios of aromatic substitution product mixtures. Apart for educational purposes, it is seldom used these days. This method however, turns out to be useful for the type of spin-chemistry discussed above. In this chapter a method is offered to fingerprint the nature of photogenerated phenyl cations of different background and manifold based on their different chemo- and regioselectivity toward the nucleophile methoxybenzene (= anisole).

Results

Compounds **1**-**7**, all proposed or expected precursors to phenyl cations, were photolyzed in acetonitrile/ anisole 1/1 v/v (Scheme 2). An excess of anisole was used to allow alkylation to take place in high yield. Acetonitrile was used as solvent, because it is a poor electron donor compared to e.g. methanol. This property precludes the formation of products derived from photoinduced electron-transfer from the solvent to the electron-accepting substrate (See Chapter 2). The reactions were carried out at 2°C; at that temperature, during the time of irradiation, there is no significant thermolytic product formation (< 5%). The results of the photolyses are summarised in Table 1. Table 2 contains the*ortho*, *meta*, *para* ratios of the methoxybiphenyls.

Scheme 2: Photolysis of compounds **1**-**7**.

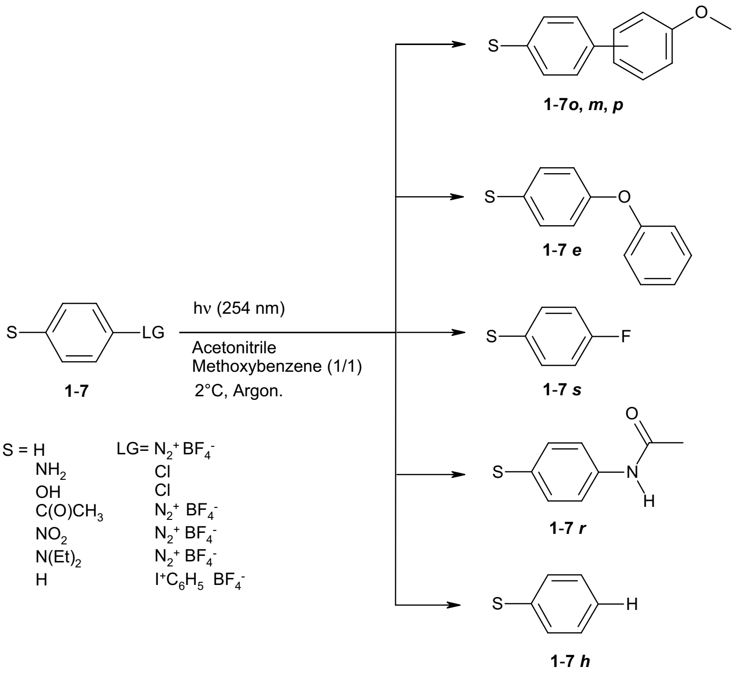
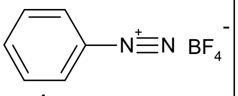
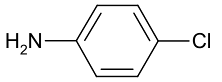
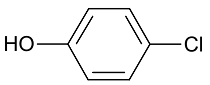
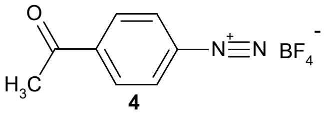
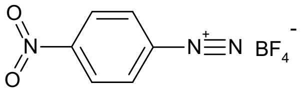
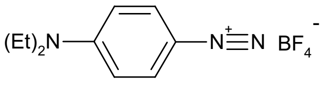
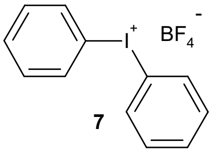


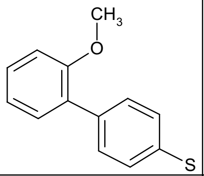
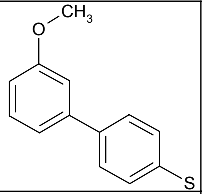
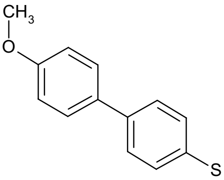
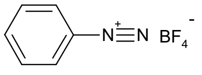
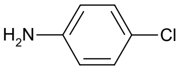
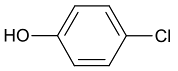
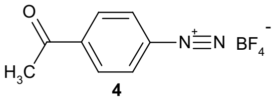
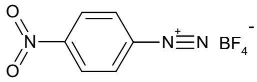
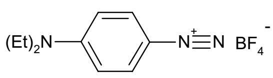
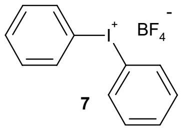
Table 1: Products of the photolysis of compounds **1**-**7** in acetonitrile/anisole[a].

Compounds	1-7 *o, m, p*	1-7 e	1-7 s	1-7 r	1-7 h
 **1**	72	2	2	4	12
 **2**	99	-	-	-	-
 **3**	4[b]	-	-	-	-
	60[b,c]	-	-	-	-
 **4**	88	-	-	-	11
 **5**	90	-	-	-	4
 **6**	83	13	2	-	<1
 **7**	64[b,d]	<1	-	<1	14

[a] Yields are calculated as % of total product formation upon complete conversion after 90 minutes of photolysis. [b] The precursor is not completely converted after 90 minutes of photolysis. [c] Reaction carried out in trifluoroethanol/anisole. [d] The lower yield of methoxybiphenyls is also caused by the in cage trapping of the leaving group iodobenzene yielding iodo-biphenyls, and by secondary product formation.

In all cases the major, or even exclusive, photoproducts are the 2-methoxy-, 3-methoxy- and 4-methoxybiphenyls **1**-**7*o***, ***m***, ***p*** (Table 1). The *ortho*-isomers of these Friedel-Crafts products are produced more abundantly than the*para*-isomers, and low to very low yields of the *meta*-methoxy isomers are obtained (Table 2). However, the *o*: *m*: *p* ratios vary with the precursor. Next to the C-alkylation products **1**-**7*o***, ***m***, ***p*** in three cases (entries 1, 6 and 7) O-alkylation products, the diphenylethers **1e**, **6e**, and **7e** are formed. In the photolysis of **1** and **6** also F-alkylation (Schiemann) products **1s** and **6s** are produced. The Ritter reaction, an alkylation on

Table 2: *Ortho*, *meta*, *para* ratios of the methoxybiphenyl photoproducts[a].

Photoproducts / Photolabile compounds			
 **1**	**1*o***: 68%	**1*m***: 13%	**1*p***: 19%
 **2**	**2*o***: 81%	**2*m***: 2%	**2*p***: 17%
 **3**	**3*o***: 81%[b]	**3*m***: 0%[b]	**3*p***: 19%[b]
	3*o*: 81%[c]	**3*m***: 0%[c]	**3*p***: 19%[c]
 **4**	**4*o***: 75%	**4*m***: 13%	**4*p***: 12%
 **5**	**5*o***: 75%	**5*m***: 12%	**5*p***: 13%
 **6**	**6*o***: 64%	**6*m***: 3%	**6*p***: 33%
 **7**	**7*o***: 69%	**7*m***: 12%	**7*p***: 19%

[a] Percentages are averages of the yields in three separate experiments, the maximum experimental error is ± 2%. [b] Photolysis in acetonitrile/ anisole 1/1. [c] Photolysis in trifluoroethanol/ anisole.

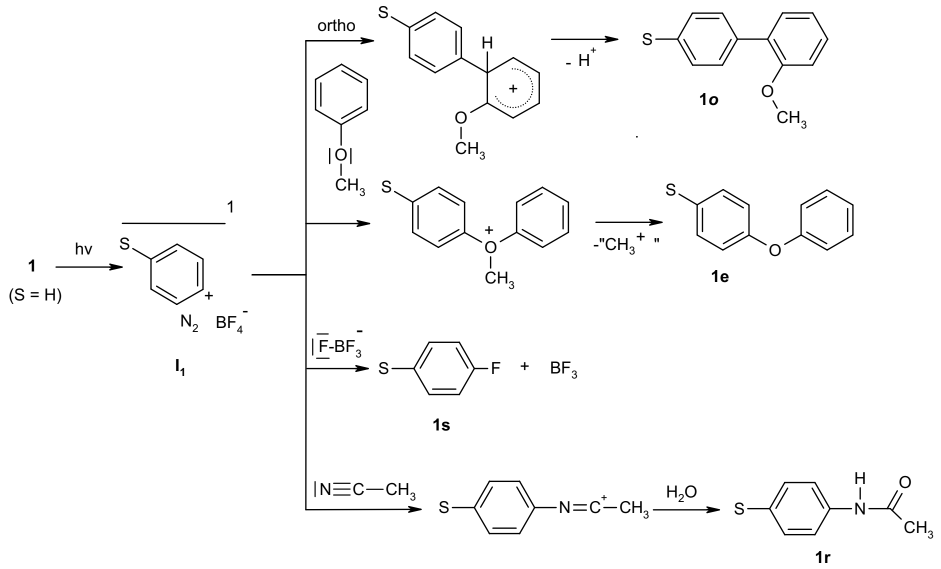
the nitrogen atom of acetonitrile, yields acetanilide **1r** (= **7r**) (entries 1 and 7). Finally, small amounts **1**-**7h**, where the leaving group is replaced by hydrogen, are found in most reaction mixtures.

Discussion

*Phenyldiazonium tetrafluoroborate (***1***)*

The methoxybiphenyls **1*o***, ***m***, ***p*** produced in the photolysis of **1** in acetonitrile/anisole result from the attack of the photogenerated phenyl cation on the π-electrons of anisole, as depicted for the *ortho* product in Scheme 3. The formation of diphenylether **1e** occurs via attack on the n-electrons of the oxygen atom of anisole [21]. The abstraction of F^- from the counter-ion BF_4^- (yielding the Schiemann product **1s**) is also a cation-mediated reaction[5,22]. Attack of the phenyl cation on the lone pair of the nitrogen atom of the solvent acetonitrile is responsible for the formation of acetanilide **1r** (Ritter product)[23].

Scheme 3: Mechanism of formation of photoproduct from **1**.



The *ortho*, *meta*, *para* ratio of 68:13:19 observed for **1*o***, ***m***, ***p*** produced in the photolysis of **1** is very similar to the ratio observed in the radiolytical phenylation of anisole, but dissimilar to the ratios in the thermolyses of various phenyldiazonium salts (Table 3). The similarity in *o*: *m*: *p* ratios in the photochemical and radiochemical phenylation of anisole shows that the Friedel-Crafts products in both reactions are produced via the same product-forming reactive intermediate, i.e. a (closed shell) singlet phenyl cation (I_1)[24]. Clearly, β-decay of tritium, producing helium as leaving group, best resembles the interaction of a photon with a molecule and subsequent extrusion of nitrogen. The different *o*: *m*: *p* ratios in the thermal solvolysis of phenyldiazonium salts compared to the photochemical and radiochemical results support the view expressed in an intriguing, recently published paper on the thermal solvolysis of phenyldiazonium cations in water, which argues against a discrete S_N1 mechanism[17]. According to the authors, no clear distinction between S_N1 and S_N2 mechanisms can be made.

Table 3: Reported *o: m: p* ratios in reactions of phenyl cation precursors from various precursors with anisole.

Reported ratio	Precursor	Reference
68:13:19	Phenyldiazonium-BF_4^- (hν)[a]	This work
65: 13: 22	1,4-Ditritiobenzene, (β-decay)	Ref[24]
56.0: 12.5: 31.5 59:10:31	Phenyldiazonium-BF_4^- (Δ)[b] Phenyldiazonium-BF_4^- (Δ)[c]	Ref[21]
55.2: 13.4: 31.6	Phenyldiazonium-BF_4^- (Δ)[d]	Ref[25]
64.0: 8.5: 27.5	Phenyldiazonium-BF_4^- (Δ)[e]	Ref[26]
57.6: 10.9: 31.5	Phenylazotriphenylmethane/ TFA (Δ)	Ref[27]
61.8: 9.7: 28.7	Phenyldiazonium triflate (Δ)	Ref[28]

[a] Molar ratio diazonium salt to anisole 1:460. [b] Molar ratio diazonium salt to anisole 1:80. [c] In pure Anisole. [d] Molar ratio diazonium salt to anisole 1:14. [e] Molar ratio diazonium salt to anisole 1:50.

In principle the phenylation products **1*o***, ***m***, ***p*** may also have been formed via attack on anisole by a photogenerated phenyl radical. This radical would also be the source of benzene (**1h**) produced by hydrogen atom abstraction from the solvent. A possible route for the production of the phenyl radical is photoinduced electron transfer from anisole to the diazonium salt, which yields PhN_2• and next Ph• [29,30]. This process is expected to be most efficient upon irradiation in the charge transfer bands of the anisole-diazonium salt complex. To probe the importance of a radical-mediated route toward product formation, a) the reactivity of an independently prepared phenyl radical was studied and b) the wavelength dependence of the photolysis reaction of **1** was investigated. (a) Photolysis of iodobenzene, which gives homolytic cleavage of the C-I bond[31], in acetonitrile/anisole under the same reactions conditions used for **1**-**7** yields **1*o***, ***m***, ***p*** (in a ratio of 75:13:12) and **1h** in a product ratio 2.1:1, quite different from the ratio 5.3:1 observed in the photolysis of **1**. (b) Irradiation of **1** at λ_{exc} = 300 nm and λ_{exc} = 350 nm yields the biphenyls **1*o***, ***m***, ***p*** in exactly the same *o*: *m*: *p* ratio as upon irradiation at λ_{exc} = 254 nm. The relative amount of benzene increases only slightly with the wavelength of excitation (the ratio **1*o***, ***m***, ***p***: **1h** is 5.1:1 at λ_{exc} = 300 and 350nm). Thus, reactions involving the phenyl radical are not a major product-forming route in the photolysis of **1**.

*4-Chloroaniline (**2**)*

The photolysis of **2** in acetonitrile/anisole exclusively yields the methoxybiphenyls **2*o***, ***m***, ***p*** in a ratio of 81:2:17[32]. Compared to the *o*: *m*: *p* ratio observed for **1** (Table 2, entries 1 and 2) the yield in *meta* product is remarkably low. The very limited production of the *meta*-biphenyl product is reminiscent of the product ratios obtained in the reactions of 2,6-dichloro-oxocyclohexadienyl carbene (73:0:27)[33] and tosylnitrene (71:2:27)[34] with anisole. The carbene-type regioselectivity is in agreement with the proposal that the photolysis of **2** produces a phenyl cation of triplet nature[7c,d]. The electron-donating amino substituent positioned *para* to the electron-withdrawing chlorine substituent causes a large dipole moment in the excited state[35]. In such an intramolecular charge transfer state there is considerable negative charge development on chlorine which facilitates, enhanced by a polar solvent, heterolysis. The high intersystem crossing rate of aniline[36] efficiently produces a triplet excited state which fragments (Scheme 1).

Triplet phenyl cations possess an open-shell diradical structure, much like a triplet carbene. Triplet carbenes add to unsaturated bonds in two radical-mediated steps to form cyclopropyl rings. Here the first step of the biphenyl formation is the addition of an electrophilic radical to anisole (Scheme 4). This step produces a triplet (Wigner's rules[37]) distonic diradical cation. The second step, after spin-inversion, is closure toward a phenonium ion that can take place in two directions. Formation of σ-complexes and loss of a proton lead to the formation of the biphenyls. Their isomer pattern thus is determined in no less than three steps. The first step takes place with the same regioselectivity as the attack of a phenyl radical on anisole (*vide supra*). Closure to a phenonium ion[38], and subsequent opening will preferentially lead to the more stable, *ortho* or *para* methoxy-substituted cyclohexadienyl cation. Thus, attack at the *meta* position of anisole seldom yields the *meta* biphenyl product.

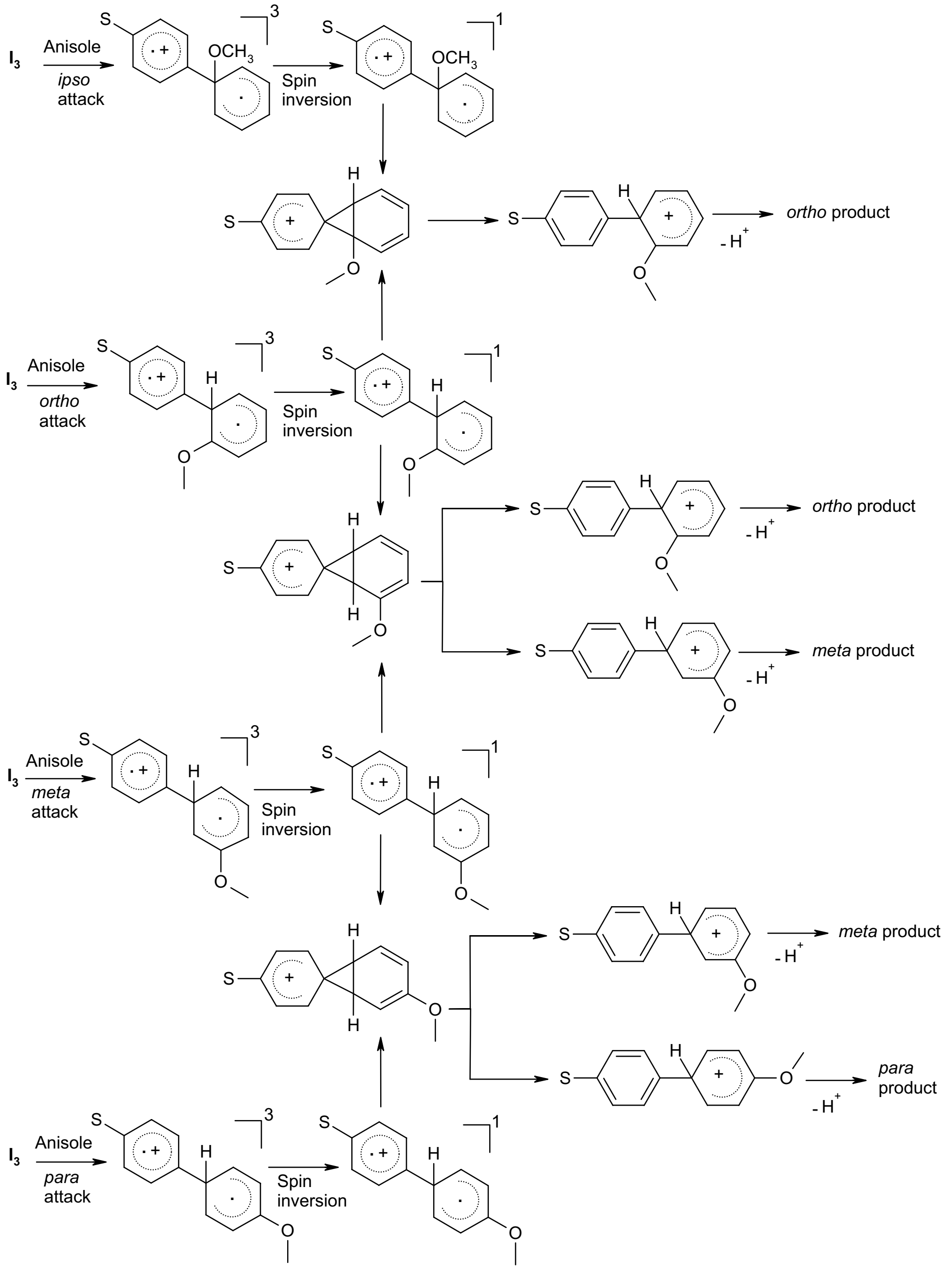
*4-Chlorophenol (**3**)*

The photolytic behaviour of **3** is solvent dependent[39,40]; the reaction occurs much more readily in trifluoroethanol than in acetonitrile. Therefore **3** was not only irradiated in acetonitrile/anisole but also in trifluoroethanol/anisole. In both solvent systems the only products are **3*o***, ***m***, ***p*** in a ratio 81:0:19. These ratios agree with the chemo- and regioselectivity of product formation observed in the photolysis of **2** and are due to the triplet phenyl cation mechanism of Scheme 4. The product-forming intermediate is either the triplet phenyl cation or the deprotonated form thereof, the triplet 4-oxocyclohexa-3,5-dienylidene. Independent generation of the latter species by photolysis of 4-diazoquinone (See Chapter 3) under the same reaction conditions as used for **3** yields **3*o***, ***m***, ***p*** in a ratio 72:0:28. Therefore 4-oxocyclohexadienylidene is unlikely to be the product-forming intermediate. Presumably, unlike in water[39,40], the rate of the reaction of the triplet cation with the nucleophile exceeds its rate of deprotonation.

*4-Acetylphenyldiazonium- (**4**) and 4-nitrophenyldiazonium tetrafluoroborate (**5**)*

The photolyses of **4** and **5** in acetonitrile/ anisole yield the methoxybiphenyls **4*o***, ***m***, ***p*** and **5*o***, ***m***, ***p*** in ratios of 75:12:13 and 75:13:12, respectively (Table 2, entries 4 and 5). As in the case of

Scheme 4: Mechanism of product formation upon attack of an EDG-substituted triplet phenyl cation (**I$_3$**) on anisole (S = NH$_2$, OH).



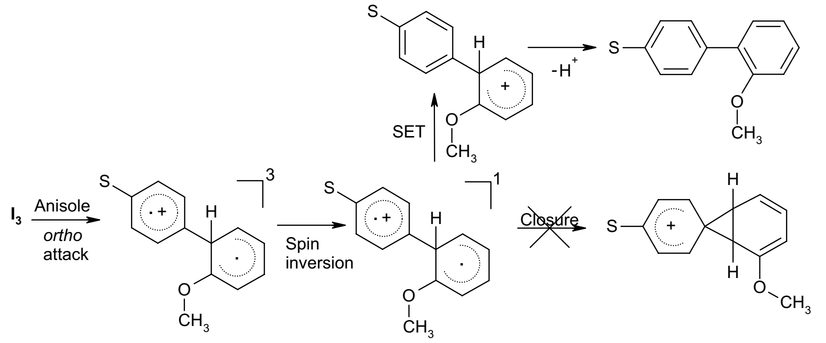
2 and **3**, no ether or Ritter products are formed. Also no Schiemann product is formed. The *o*, *m*, *p* ratio observed in the case of **5** differs from the ratio reported for its thermal solvolysis in a mixture of acetonitrile, benzene and anisole which yields **5*o*, *m*, *p*** in a ratio of 77.7:9.9:12.4[41]. This may be due to the occurrence of a pure S_N1 mechanism in the photolysis and an S_N1/ S_N2 borderline mechanism in the thermolysis. No thermal solvolysis data of **4** are known.

The observed *o*, *m*, *p* ratios of the biphenyl photoproducts of **4** and **5** are similar to the *o*, *m*, *p* ratio of the products of the 4-nitrophenyl radical with anisole which is known from two separate sources to be 68:16:16 and 69:15:16, respectively [42,43]. This suggests that the attack on anisole is governed by the radical qualities of an intermediate. However, this species is not the 4-acetylphenyl or the 4-nitrophenyl radical, formed via photoinduced electron transfer between the diazonium salts **4** and **5** and anisole. This was shown by performing the photoreactions at λ_{exc} = 300 and 350 nm, wavelengths which are closer to the charge transfer absorption bands than λ_{exc} = 254 nm[30]. No variations in *o*, *m*, *p* ratios and only slight increases of the amount of the radical derived arenes **4h** and **5h** were found (**4h:4*o*, *m*, *p*** = 1:7.8 at λ_{exc} = 254 nm, 1:7.6 at λ_{exc} = 300 nm and 1:7.6 at λ_{exc} = 350 nm) (**5h:5*o*, *m*, *p*** = 1:24 at λ_{exc} = 254 nm, 1:22 at λ_{exc} = 300 nm and 1:19 at λ_{exc} = 350 nm).

The difference between the *o*, *m*, *p* ratios observed in the photolysis of **4** and **5** and that in the photolysis of **1**, as well as the differences in product profiles, reflect the difference in the nature of the reactive intermediate responsible for product formation, in agreement with the proposal that irradiation of **4** and **5** produces triplet phenyl cations [7a,b] and that of **1** a singlet phenyl cation[6]. Both the nitro and the acetyl substituent are known to enhance intersystem crossing when coupled to an aromatic moiety. Upon excitation of the salts to a singlet excited state, ISC to a triplet excited state take place (Scheme 1). The subsequent fragmentation will yield a triplet phenyl cation. This phenyl cation is trapped before it can spin invert to a singlet state of lower energy.

Remarkably, the *o*, *m*, *p* ratios observed with **4** and **5** are different from the *o*, *m*, *p* ratios for **2** and **3**, even though both series involve triplet phenyl cations. Scheme 5 explains why the triplet phenyl cations derived from **4** and **5** produce biphenyls with a different regioselectivity than the triplet phenyl cations derived from **2** and **3**. Other than in the mechanism proposed for the photolysis of **2** and **3** in Scheme 4, the closure of the diradical cation toward the phenonium ion here does not take place (Scheme 5). The *para* EWG substituents are less able to harbour the positive charge and thereby reduce the carbenoid character of the reactive species involved. The methoxy biphenyls **4*o*, *m*, *p*** and **5*o*, *m*, *p*** are formed after electron transfer and loss of a proton. This means that the *o*, *m*, *p* ratio of the photoproducts is solely governed by the electrophilic radical addition step to anisole.

Scheme 5: *Ortho* attack of an EWG-substituted triplet phenyl cation (**I**$_3$) on anisole (S = NO_2, $C(=O)CH_3$).

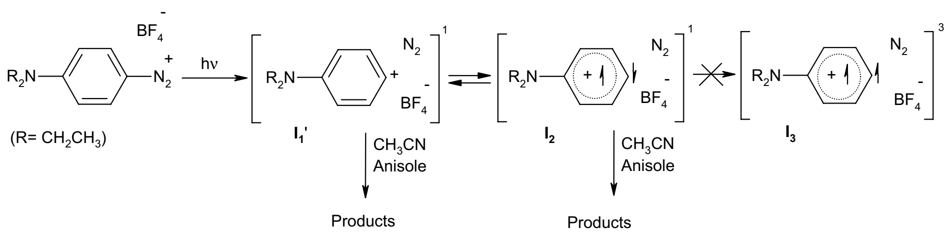


The EDG- and EWG-substituted triplet phenyl cations, derived from **2**, **3**, **4**, and **5** display a remarkable chemoselectivity. The n-electrons of anisole, acetonitrile and BF_4^- have no appeal for the electron deficient intermediate. Only reaction with π-electrons occurs. A rationale for this behaviour is that the dispersed charge- and electron density of the triplet phenyl cations makes them soft electrophiles (Lewis acids) which only react with soft nucleophiles (Lewis bases) according to the HSAB principle.

*4-Diethylaminophenyldiazonium tetrafluoroborate (**6**)*

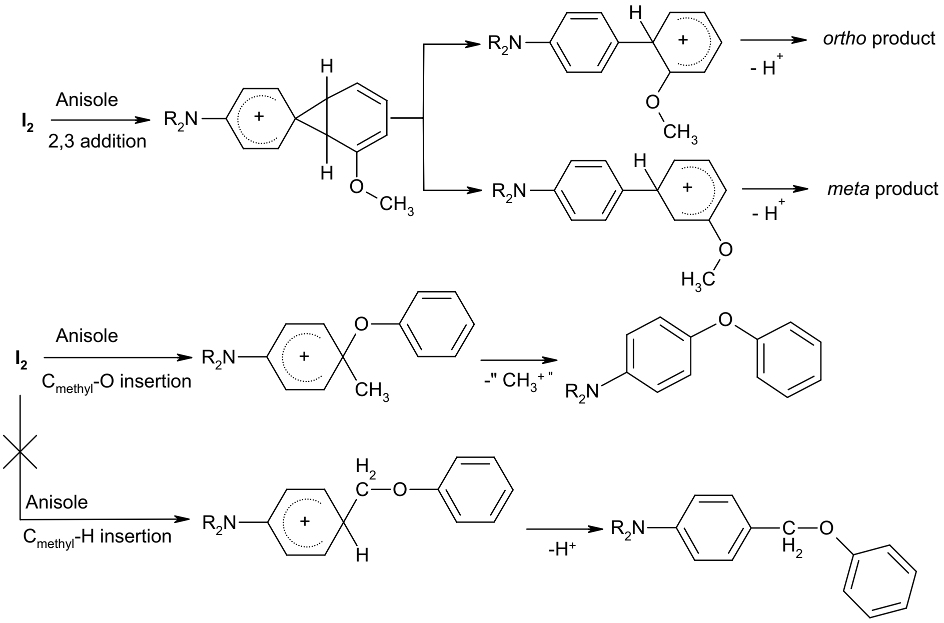
The photolysis of **6** yields the methoxybiphenyls **6*o***, ***m***, ***p*** in a ratio of 64:3:33 (Table 2 entry 6). Also an O- (**6e**) and a F- (**6s**) alkylation product are formed (Table 1). Neither the *o*, *m*, *p* ratio nor the product profile match that of the parent diazonium salt **1**, nor do they match the ratios and the profiles observed in the photolysis of **2**, **3**, **4** and **5**. Especially, the twofold higher *para* yield and the considerable yield of diphenylether **6e**, the O-alkylation product, stand out. Thus, the product-forming intermediate is neither a closed-shell singlet phenyl cation nor a triplet phenyl cation.

Scheme 6: Mechanism of the photolysis of 4-diethylaminophenyldiazonium salt **6**.



Presumably, diazonium salt **6** fragments in the singlet excited state and gives a non-planar closed-shell singlet phenyl cation **I**$_1$' which is 0.4 kcal/mol more stable than the singlet open-shell phenyl cation **I**$_2$ (Scheme 6) (Chapter 3, Table 3). The polarity of the solvent system is expected to govern the equilibrium between these two states. In a relatively apolar solvent system, the open-shell species, because the positive charge is more disperged, may gain importance over the closed shell species. The singlet open-shell species **I**$_2$ reacts with anisole before it can spin convert to its more stable triplet manifold **I**$_3$ (Scheme 6). That reaction yields phenonium ions in one step (Scheme 7). After opening to the more stable σ-complex and loss of a proton the methoxybiphenyls **6*o***, ***m***, ***p*** are produced. Thus, unlike the biphenyl formation from **2** and **3**, and unlike the biphenyls from **4** and **5**, the regioselectivity of biphenyl formation from **6** is determined in two steps: a) the selectivity of the initial singlet carbene like addition to anisole and b) the formation of the more stable σ-complex.

Scheme 7: Reactions of an open-shell singlet phenyl cation (**I**$_2$) with anisole.



The excess of diphenylether **6e** produced in the photoreaction of **6** can be rationalised by assuming a singlet carbene type insertion by the open-shell phenyl cation in the C$_{\text{methyl}}$-O bond of anisole (Scheme 6). No C$_{\text{methyl}}$-H insertion product is found.

The conversion of the closed-shell singlet- into the open-shell triplet phenyl cation is generally thought to consist of one single step. The trapping of an open-shell singlet 4-diethylaminophenyl cation disturbs this picture. The cationic molecule suffers considerable structural changes on going from the closed-shell singlet to an open-shell triplet (cf Chapter 2). Therefore, the displacement of the nuclei and the spin inversion process may be separate reaction steps.

*Diphenyliodonium tetrafluoroborate (**7**)*

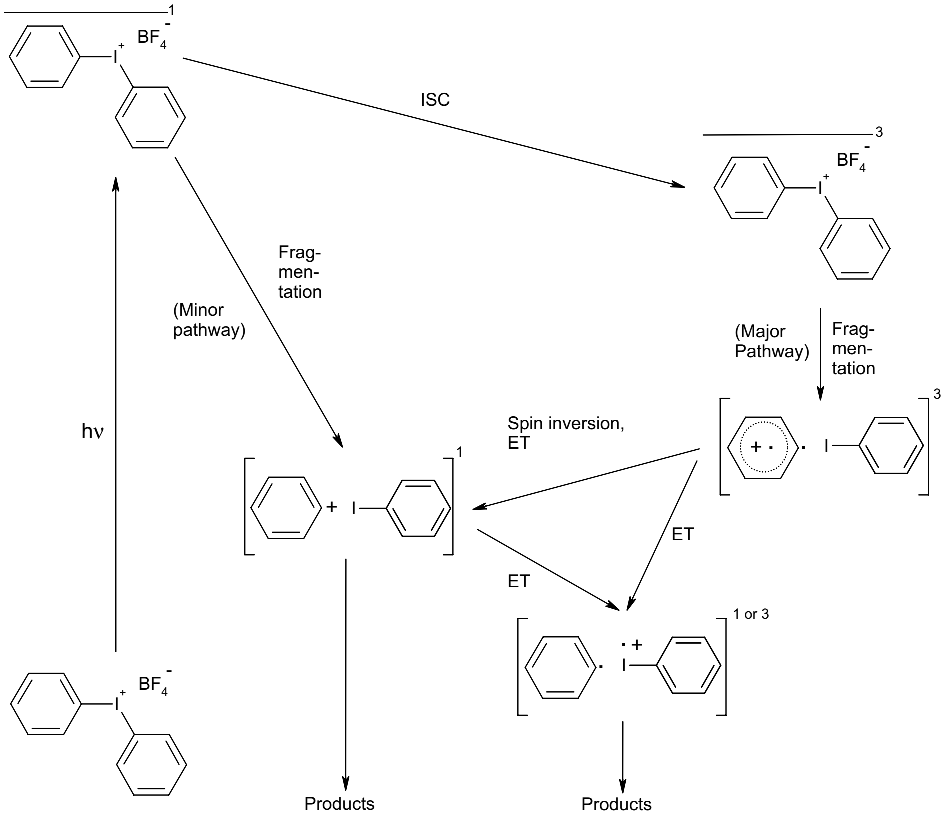
Diphenyliodonium salts are often applied in photolithography and in the photographic industry[44]. When subjected to UV light, they are reported to react through phenyl cations, stemming from the cleavage of a C-I bond in the singlet excited state, or through phenyl radicals, thought to originate from a C-I bond fission in the triplet excited state [45]. The photolysis of **7** in acetonitrile/anisole yields the methoxybiphenyls **7*o*, *m*, *p*** (= **1*o*, *m*, *p***) in a 68:12:19 ratio. Within experimental error this ratio is the same as the ratio in the photolysis of phenyldiazonium tetrafluoroborate (**1**). Also the O- and N-alkylation products diphenylether (**7e** = **1e**) and acetanilide (**7r** = **1r**) are formed as in the irradiation of **1**.

Study of the photoreaction of **7** in the presence of anisole as function of the wavelength of excitation shows that at λ_{exc} = 300 nm **7*o*, *m*, *p*** are formed in the same *o*, *m*, *p* ratio, within experimental error, as at λ_{exc} 254 nm[46]. Further, the relative amount of phenyl radical derived benzene (**7h** = (**1h**)) is the same at both wavelengths (**7h**:**7*o*, *m*, *p*** = 1:4.1) and much less than the amount of benzene produced upon independent generation of the phenyl radical by photolysis of iodobenzene under the exact same reaction conditions (**7h**:**7*o*, *m*, *p*** = 1:2.1). This indicates that a phenyl radical is not a major product-forming intermediate in the photolysis of **7**.

Both the methoxybiphenyl isomer ratio and the product profile in the photolysis of **7**, indicate that product formation largely takes place through a closed-shell singlet phenyl cation. This is quite surprising because the iodine atom is expected to enhance the rate of ISC and produce a triplet excited state and next a triplet cation after C-I bond fission.

Several transient absorption studies on the nano- and picosecond timescale of the photolysis of **7** reveal the radical cation of iodobenzene as intermediate[47,48]. Its presence has been used as support for the long-standing homolytic mechanism for triplet state dissociation yielding the iodobenzene radical cation and a (not detected) phenyl radical[45,49]. The iodobenzene radical cation however may be a secondary intermediate instead of a primary one. A triplet phenyl cation-iodobenzene pair produced on a femtosecond time scale may, by electron transfer, yield the iodobenzene radical cation observed on the nano- and picosecond timescale. The triplet phenyl cation also spin inverts to the lower energy singlet closed shell phenyl cation, the product-forming intermediate in the photolysis of **7** (Scheme 7). It is proposed that C-I bond cleavage mainly takes place in the triplet excited state.

Scheme 8: Proposed mechanism of the photolysis of diphenyliodonium tetrafluoroborate (**7**).



The mechanism of Scheme 8 is supported by results for diphenyliodonium, diphenyl bromonium and diphenyl chloronium hexafluorophosphate photochemistry reported in the literature[45b]. The *o*, *m*, *p* ratio of the halobiphenyls produced by the in-cage phenylation of halobenzene is a fingerprint for the nature of the reactive intermediate. The photolysis of the diphenyl chloronium salt in acetonitrile yields chlorobiphenyls in an *o*, *m*, *p* ratio of 48:31:21. Practically the same ratio is found for the diphenyl bromonium salt: 51:30:19. These ratios indicate a closed-shell singlet phenyl cation as reactive intermediate[50]. However, for the diphenyliodonium salt the *o*, *m*, *p* ratio is 73:13:15. Diphenyliodonium salt photolysis carried out in the high-energy triplet-sensitizing solvent acetone produces an even more different *o*, *m*, *p* ratio 70:5:24[45a,b]. The low yield of *meta* product for the latter photolyses is reminiscent of the photolysis of **2** and **3** which involve triplet phenyl cations. Already without the aid of a sensitiser, diphenyliodonium salts produce triplet excited states with considerable efficiency. Cleavage of a C-I bond in a triplet state produces a triplet phenyl cation that is either trapped by in cage iodobenzene or spin inverts to its singlet ground state.

Conclusion

The photolysis of seven photolabile compounds, known to produce phenyl cations, in acetonitrile in the presence of anisole yields methoxybiphenyls in four distinct *o*, *m*, *p* ratios. The differences in regioselectivity are due to the different nature, resulting in different mechanisms of reaction, of the product-forming intermediates: a singlet closed shell, a singlet open-shell, an EDG-substituted triplet cation, and an EWG-substituted triplet phenyl cation. This spin-selective chemistry provides a tool to fingerprint the singlet/triplet nature of any phenyl cation.

The fingerprint of the phenyl cation produced in the photolysis of diphenyliodonium tetrafluoroborate shows that the product-forming intermediate is a singlet species, despite the presence of the heavy atom iodine. An alternative for the widely accepted mechanism of phenyliodonium salt photolysis (often applied in photolithography) is proposed.

Experimental Section

Materials

Starting materials **2**, **3** and **6** are commercially available. Phenyl chlorides **2** and **3** were used as received. Diazonium salt **6** was dissolved in acetonitrile and crystallised with pentane prior to use. Compounds **1**[51], **4**[52], **5**[52] and **7**[53] were synthesised according to literature procedures. Anisole was distilled under Argon to obtain GC purity. Acetonitrile and anisole were Argon purged prior to their use in the photolysis experiments.

Photochemistry

The photochemical reactions were carried out under argon in quartz tubes equipped with a rubber seal. The starting materials were dissolved at 0.05M in 10 mL 1/1 acetonitrile/anisole. *n*-Decane was used as internal standard. The tubes were placed in a Rayonet Reactor (RPR200) fitted with 7 254 nm, 300 nm or 350 nm lamps and equipped with a magnetic stirrer. The photolyses of the salts **1**, **4**, **5**, **6**, and **7** were followed as a function of time by taking aliquots (0.050 mL sample) and adding them to 0.5 mL water + 0.050 mL diethyl ether. The organic layers were analyzed by GC and GC-MS and the assignment of the structures was confirmed by coinjection of commercially available or independently prepared products. After completion of the irradiations, the reaction mixtures were poured in 10 mL water and extracted two times with 5 mL diethyl ether. The combined ether fractions were GC and GC-MS analyzed. The photolyses of **2** and **3** were followed, and the products analyzed by direct injection of aliquots on GC and GC-MS.

Photoproducts

The products **1h** (= **7h**), **4h**, **5h**, **6h**, **1s** (= **7s**), **1r** (= **7r**), **1e** (= **7e**) **1*o*** and **1*p*** were identified by means of GC, GC-MS and coinjection with the aid of the commercially obtained reference samples. Of all *o*, *m*, *p* biphenyl mixtures **2**-**6*o***, ***m***, ***p*** the *para* and *ortho* isomers were independently synthesised, from commercially available starting materials, employing parallel Suzuki cross-coupling[54]. In 50 ml THF, under Argon, 1 mmol of *p*-iodoaniline, *p*-iodophenol, *p*-iodoacetophenone, *p*-iodonitrobenzene and 4-iodo-N,N-diethylamino-benzene were dissolved. As catalyst $5*10^{-2}$ mmol $Pd(PPh_3)_4$ was added (1 mole% on total amount of iodocompounds). Cesium carbonate was used as base in equimolair amount with respect to the total amount of iodocompounds (5 mmol). After addition of 6 mmol of 4-methoxyphenylboronic acid the temperature of the solution was raised to reflux and kept refluxing overnight. The reaction mixture was filtered over Celite and dried with Calcium chloride. After evaporation of the THF, the slurry was dissolved in 20 mL dry diethyl ether, filtered if necessary and analyzed on GC and GC-MS to confirm the identity of the products. The product were formed in yields varying from 20%-90%. The parallel Suzuki cross-coupling reaction was repeated using 2-methoxyphenylboronic acid which gave the desired *ortho* isomers in 20% to 90% yields. Schiemann product **6s** was prepared from **6** according to literature[55]. Diphenylether **6e** was prepared (among other products) by heating a mixture of 0.02 mol diazotised 4-N,N-diethylamino-aniline and 0.02 mol phenol in 2 mL acetonitrile to 50°C for 1 hour. Of the iodobiphenyls produced in trace amounts in the irradiation of **7**, the *ortho* and *para* product were synthesised separately by diazotiating 2- and 4-aminobiphenyl in 50% water/concentrated HCl at melting ice temperature, treating with KI followed by extraction with diethylether, washing the organic layer with a 5% $Na_2S_2O_3$ solution and brine, and evaporation of the solvent.

Equipment

UV spectra were recorded at room temperature on a double beam Varian DMS 200 Spectrophotometer, if applicable with pure solvent in the reference cell. ^{1}H-NMR spectra were recorded on a JEOL 200, using $CDCl_3$ as solvent. As analytical GC a Hewlett-Packard 6890 model was used, equipped with a automatic injector, fitted with a CP-Sil5-CB column (25 m, ø = 0.25 mm, 1.2 µm) using hydrogen as carrier gas. The Flame-Ionisation Detector (FID) was calibrated using commercially available reference chemicals. HP Chemstation was used for the analysis of the analytical data. Mass spectra were measured on a GC-MS set-up consisting of a Hewlett-Packard 5890 series 2 model GC, equipped with a automatic injector, fitted with a AT-5MS column (30 m, ø = 0.25 mm, 0.25 µm) using helium as carrier gas. The GC was coupled to a Finnigan Mat SSQ 710 mass spectrometer, employing electron-impact as the ionisation method. The GC-MS data was analyzed with Xcaliber.

References and Notes

[1] Griesbeck, A. G.; Abe, M.; Bondock, S. *Acc. Chem. Res.* **2004**, *37*, 919-928.

[2] a) Jones Jr., M.; Moss, R. A. In *Reactive Intermediate Chemistry*; Moss, R. A.; Platz, M. S. Jones Jr., M., Eds.; John Wiley & Sons Inc.: Hoboken, **2004**; pp 273-328. b) Tomioka, H. In *Reactive Intermediate Chemistry*; Moss, R. A.; Platz, M. S. Jones Jr., M., Eds.; John Wiley & Sons Inc.: Hoboken, **2004**; pp 375-461. c) Wright, B. B.; Platz, M. S. *J. Am. Chem. Soc.* **1984**, *106*, 4175-4180. d) Grasse, P. B.; Brauer, B-E.; Zupancic, J. J.; Kaufmann, K. J.; Schuster, G. B. *J. Am. Chem. Soc.* **1983**, *105*, 6833-6845.

[3] a) Platz, M. S. In *Reactive Intermediate Chemistry*; Moss, R. A.; Platz, M. S. Jones Jr., M., Eds.; John Wiley & Sons Inc.: Hoboken, **2004**; pp 501-560. b) Albini, A.; Bettinetti, G.; Minoli, G. *J. Am. Chem. Soc.* **1997**, *119*, 7308-7315.

[4] Falvey, D. E. In *Reactive Intermediate Chemistry*; Moss, R. A.; Platz, M. S. Jones Jr., M., Eds.; John Wiley & Sons Inc.: Hoboken, **2004**; pp 593-650.

[5] Gasper, S. M.; Devadoss, C.; Schuster, G. B. *J. Am. Chem. Soc.* **1995**, *117*, 5206-5211.

[6] a) Ando, W. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley, Chichester: **1978**; Part 1, pp 341-487. b) Zollinger, H. In *The Chemistry of the Triple-bonded Functional Groups*; Patai, S., Rappaport, Z., Eds.; Wiley & Sons: Chichester, **1983**; Part 1, pp 603-669.

[7] a) Milanesi, F.; Fagnoni, M.; Albini, A. *Chem. Commun.* **2003**, 216-217. b) Milanesi, S.; Fagnoni, M.; Albini, A. *J. Org. Chem*. **2005**, *70*, 603-610. c) Fagnoni, M.; Mella, M.; Albini, A. *Org. Lett*., **1999**, *1*, 1299-1301. d) Guizzardi, B.; Mella, M.; Fagnoni, M.; Freccero, M.; Albini, A. *J. Org. Chem.* **2001**, *66*, 6353-6363. e) Protti, S.; Fagnoni, M.; Mella, M.; Albini, A. *J. Org. Chem.* **2004**, *69*, 3465-3473.

[8] a) Boule, P.; Othmen, K.; Richard, C.; Szczepanik, B.; Grabner, G. *Int. J. Photoenergy* **1999**, *1*, 49. b) Othmen, K.; Boule, P.; Szczepanik, B.; Rotkiewicz, K.; Grabner, G. *J. Phys. Chem. A* **2000**, *104*, 9525-9534.

[9] a) Fasani, E.; Mella, M.; Cassia, D.; Tassi, S.; Fagnoni, M.; Albini, A. *Chem. Commun*. **1997**, 1329-1330. b) Fasani, E.; Profumo, A.; Albini, A. *Photochem. Photobiol.* **1998**, *68*, 666-674.

[10] Torrisi, S.; Sortino, S. *J. Agric. Food Chem.* **2004**, *52*, 5943-5949.

[11] *Dicoordinated Carbocations*; Rappoport, Z.; Stang, P., Eds.; John Wiley & Sons Ltd.: Chichester, UK, **1997**, Chapter 2, pp. 10-97.

[12] a) Gleiter, R.; Hoffmann, R.; Stohrer, W. D. *Chem. Ber.* **1972**, *105*, 8-24. b) Jaffe, H. H.; Koser, K. G. *J. Org. Chem.* **1975**, *40*, 3082-3084. c) Dill, J. D.; Schleyer, P. von R.; Binkley, J.S.; Seeger, R.; Pople, J.A.; Haselbach, E. *J. Am. Chem. Soc.* **1976**, *98*, 5428-5431.

[13] a) Kraus, M.; Roszak, S. *J. Mol. Struct. (THEOCHEM)* **1994**, *310*, 155-160. b) Hrusak, J.; Schroder, D.; Iwata, S. *J. Chem. Phys.* **1997**, *106*, 7541-7549. c) Nicolaides, A.; Smith, D. M.; Jensen, F.; Radom, L. *J. Am. Chem. Soc.* **1997**, *119*, 8083-8088. d) Harvey, J. N.; Aschi, M.; Schwarz, H.; Koch, W. *Theor. Chem. Acc.* **1998**, *99*, 95-99.

[14] Winkler, M.; Sander, W. *Angew. Chem., Int. Ed* **2000**, *39*, 2014-2016.

[15] Speranza, M. *Chem. Rev.* **1993**, *93*, 2933-2980.

[16] Filippi, A.; Lilla, G.; Occhiucci, G.; Sparapani, C.; Ursini, O.; Speranza, M. *J. Org. Chem.* **1995**, *60*, 1250-1264.

[17] In thermal solvolysis a pure S_N1 mechanism is cast in doubt: Ussing, B.; Singleton, D. *J. Am. Chem. Soc.* **2005**, *127*, 2888-2899.

[18] a) Canning, P. S. J.; Maskill, H.; McCruddem, K.; Sexton, B. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 789-800. b) Smith, D. M.; Maksic, Z. B.; Maskill, H. *J. Chem. Soc. Perkin Trans. 2* **2002**, 906-913.

[19] Klessinger, M.; Michl, J.; *Excited States and Photochemistry of Organic Molecules*; John Wiley & Sons, Inc.: Chichester, UK, **1995**.

[20] a) Dill, J. D.; Schleyer, P. von R.; Pople, J.A. *J. Am. Chem. Soc.* **1977**, *99*, 1-8. b) Laali, K.K.; Rasul, G.; Prakash, G. K. S.; Olah, G. A. *J. Org. Chem.* **2002**, *67*, 2913-2918.

[21] Eustathopoulos, H.; Court, J.; Bonnier, J. M. *J. Chem. Soc. Perkin Trans. 2* **1983**, 803-807.

[22] Suschitzky, H. *Adv. Fluorine. Chem.* **1965**, *4*, 1-30.

[23] Ritter, J. J.; Minieri, P. P. *J. Am. Chem. Soc.* **1948**, *70*, 4045-4048.

[24] Angelini, G.; Keheyan, Y.; Speranza, M. *Helv. Chim. Act* **1988**, *71*, 107-119.

[25] Abramovitch, R. A.; Gadallah, F. F. *J. Chem. Soc.(B) Phys. Org.* **1968**, 497-500.

[26] Kobayashi, M.; Minato, H.; Yamada, E.; Kobori, N. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 215-219.

[27] Kamigata, N.; Kobayashi, M.; Minato, H. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1231-1235.

[28] Kamigata, N.; Hisida, R.; Minato, H.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1016-1018.

[29] Kosynkin, D; Bockman, T. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1997**, *119*, 4846-4855.

[30] Bockman, T. M.; Kosynkin, D.; Kochi, J. K.; *J. Org. Chem.* **1997**, *62*, 5811-5820.

[31] a) Augood, D. R.; Cadogan, J. I. G.; Hey. D. H.; Williams, G. H. *J. Chem. Soc.* **1953**, 3412-3417. b) Dannley, R. L.; Gregg, E. C.; Phelps, R. E.; Coleman, C. B. *J. Am. Chem. Soc.* **1954**, *76*, 445-448.

[32] The photolysis of 4-bromo-N,N-dimethylaniline in a identical reaction set-up produces biaryls in a 79:6:15 *o*: *m*: *p* ratio.

[33] Dewar, M. J. S.; Narayanaswami, K. *J. Am. Chem. Soc.* **1964**, *86*, 2422-2427.

[34] Abramovitch, R. A.; Roy, J.; Uma, V. *Can. J. Chem.* **1965**, *43*, 3407-3418.

[35] Hara, M.; Sunagawa, T.; Oseki, Y.; Majima, T. *J. Photochem. Photobiol A: Chem* **2004**, *163*, 153-158.

[36] a) *Handbook of Photochemistry, 2nd edition*; Murov, S.L.; Carmichael, I.; Hug, G. L., Eds.; Marcel Dekker Inc.: New York, **1993**; pp 6. b) Koutek, B.; Lubomir, M.; Velek, J.; Souček, M. *Coll. Czech. Chem. Comm.*, **1985**, 50, 1753-1763.

[37] Wigner, E. *Z. Phys* **1927**, *40*, 492-500. Wigner, E. *Z. Phys* **1927**, *40*, 883-892. Wigner, E. *Z. Phys* **1927**, *43*, 624-652.

[38] Semi-empirical PM3 calculations show that the 1,2 complex is more stable than the 2,3 and 3,4 ones which are degenerate in energy.

[39] a) Grabner, G.; Richard, C.; Köhler, G. *J. Am. Chem. Soc.* **1994**, *116*, 11470-11480. b) Durand, A. P.; Brown, R. G.; Worall, D.; Wilkinson, F. *J. Chem. Soc. Perkin Trans. 2* **1998**, 365-370.

[40] a) Manet, I.; Monti, S.; Fagnoni, M.; Protti, S.; Albini, A. *Chem. Eur. J.* **2005**, *11*, 140-151. b) Protti, S.; Fagnoni, M.; Mella, M.; Albini, A. *J. Org. Chem.* **2004**, *69*, 3454-3473.

[41] Kamigata, N.; Kobayashi, M.; Minato, H. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2047-2050.

[42] Abramovitch, R. A.; Koleoso, O. A. *J. Chem. Soc.(B).* **1969**, 779-785

[43] Arai, N.; Koichi, N. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1707-1714.

[44] Crivello, J.V. In *Radiation Curing In Polymer Science and Technology*; Fouassier, J. P., Rabek, J. F., Chapman & Hall: Londen, **1993**; Vol. 2, pp 435-471.

[45] a) Dektar, J. L.; Hacker, N. P. *J. Org. Chem.* **1990**, *55*, 639-647. b) Dektar, J. L.; Hacker, N. P. *J. Org. Chem.* **1991**, *56*, 1838-1844. c) Hacker, N. P.; Leff, D. V.; Dektar, J. L. *J. Org. Chem.* **1991**, *56*, 2280-2282.

[46] The photoreaction of **7** at 350 nm, in our set-up, did not yield reproducible product formation, probably because it is very inefficient at this wavelength of excitation.

[47] Devoe, R. J.; Sahyun, M. R. V.; Serpone, N.; Sharma, D. K. *Can. J. Chem.* **1987**, *65*, 2342-2349.

[48] a) Klemm, E.; Riesenberg, E.; Graness, A. *Z. Chem.* **1983**, *23*, 222. b) Pappas, S. P.; Jilek, J. H. *Photogr. Sci. Eng.* **1979**, *23*, 140. c) Pappas, S. P.; Pappas, B. C.; Gatechair, L. R.; Schnabel, W. *J. Polym. Sci., Polym. Chem. Ed.* **1984**, *22*, 69-76. d) Pappas, S. P.; Gatechair, L. R.; Jilek, J. H. *J. Polym. Sci., Polym. Chem. Ed.* **1984**, *22*, 77-84. e) Pappas, S. P.; Pappas, B. C.; Gatechair, L. R.; Jilek, J. H.; Schnabel, W. *Polym. Photochem.* **1984**, *5*, 1-22.

[49] Knapczyk, J. W.; Lubinkowski, J. J.; McEwen, W. E. *Tetrahedron Lett* **1972**, *35*, 3739-3742.

[50] Angelini, G.; Keheyan, Y.; Speranza, M.; *Helv. Chim. Act*, **1988**, *71*, 107-119.

[51] Hanson, P.; Jones, J. R.; Taylor, A. B.; Walton, P. H.; Timms, A. W. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1135-1150.

[52] Canning, P. S. J.; McCrudden, K.; Maskill, H.; Sexton, B. *J. Chem. Soc., Perkin Trans. 2* **1999**, 2735-2740.

[53] Ochiai, M.; Toyonari, M.; Nagoaka, T.; Chen, D-W. Kida, M. *Tetrahedron Lett.* **1997**, *38*, 6709-6712.

[54] Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457-2483.

[55] Schiemann, G.; Winkelmüller, W. *Chem. Ber.* **1933**, *66*, 727-730.