Selective alkylation by photogenerated aryl and vinyl cation

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Selective Alkylation by Photogenerated Aryl and Vinyl Cations

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Selective Alkylation by Photogenerated Aryl and Vinyl Cations

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Prof. dr. G. A. van der Marel

"It matters where you are"

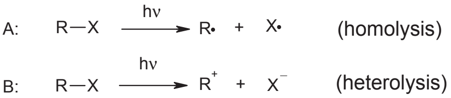
Slowdive

Contents

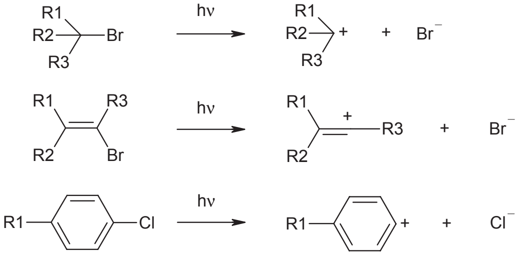
Chapter 1 | **Introduction**

Photochemistry, the breaking and making of bonds between atoms in molecules under the influence of light, is a very powerful method to execute chemical transformations. Using photons, reactions sometimes can be performed that cannot be achieved by heating and stirring. Ultraviolet (UV) light with a wavelength of 254 nm represents an energy of 112.6 kcal/mol photons, while light of 350 nm delivers 81.7 kcal/mol photons[1]. The energy of UV light is enough to cause fission of a single and sometimes even a double bond present in a molecule. In photochemistry textbooks the majority of bond-breaking reactions discussed are of the homolytic kind, yielding a pair of radicals[2] (Scheme 1A). Fission of the heterolytic kind, yielding a cation and an anion (Scheme 1B), is barely paid attention to, even though it is well-documented that the photolysis of alkyl, vinyl and some phenyl halides in solution gives ion-derived products[3,4] (Scheme 2).

Scheme 1: Homolysis and heterolysis upon irradiation.



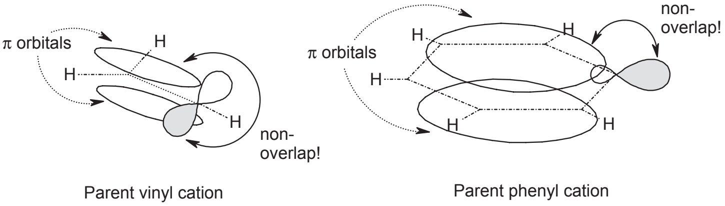
Scheme 2: The heterolytic photolysis of alkyl, vinyl, and phenyl halides.



Alkyl cations are quite common species, whereas vinyl and phenyl cations are not. These dicoordinated carbocations are among the most unstable intermediates known to organic chemists. Apart from the apparent electron-deficiency and the hybridisation, the instability originates from the inability of the π orbitals of these species to overlap with the vacant orbital of the C^+ atom[5] (Scheme 3). Further, the aryl and cyclic vinyl cations cannot adopt the preferred linear orientation around the C^+ atom.

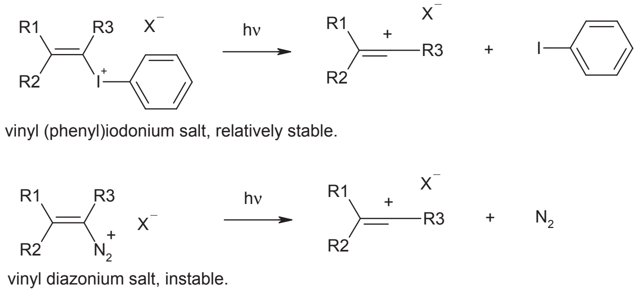
Photochemistry is especially suitable to effect the demanding reactions of Scheme 2. Employing photolysis of alkyl halides a broad range of alkyl cations has been generated under mild reaction conditions[3a,4]. The same is true for vinyl halides, which yield a score of vinyl cations[3b,4]. The photolysis of phenyl halides, however, only in exceptional cases proceeds through a heterolytic bond-cleavage mechanism[4]. In most cases photo-induced electron transfer (PET) from a donor to the phenyl halide yields a radical anion, which cleaves into a phenyl radical and a halide anion[6].

Scheme 3: Lack of overlap between electron rich and electron poor orbitals.



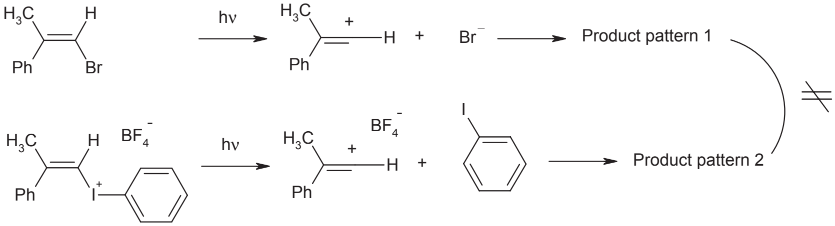
A new impulse to photo-induced heterolysis was the observation that vinyl pseudo-halides can be used as precursors to (highly unstable) vinyl cations[7] (Scheme 4). Iodobenzene is a far better leaving group than any halide anion[8]. The same is true for N_2 as leaving group, but unfortunately vinyldiazonium salts are considerably less stable than vinyl iodonium salts as precursors.

Scheme 4: Photoheterolysis of vinyl(phenyl)iodonium and vinyldiazonium salts.



The heterolytic bond cleavage reactions of the vinyl precursors in Schemes 2 and 4 yield ion pairs or free ions. In Scheme 2 the vinyl cations are generated next to a bromide leaving group, whereas for the precursors of Scheme 4 a non-nucleophilic counter-ion ($X^- = BF_4^-$) is chosen and photoheterolysis yields the vinyl cations amidst iodobenzene or N_2 leaving groups and the non-nucleophilic counter-ion. The leaving groups are neutral and less basic than halide anions and therefore interfere less with the reaction pathway of the cationic intermediates. This factor severely affects the outcome of the photochemical solvolysis reactions. For example, the primary vinyl cation in Scheme 5, prepared as an ion pair from its vinyl halide precursor, displays a distinctly different product pattern than the very efficiently prepared free cation accompanied by its neutral leaving group and non-nucleophilic counter-ion, generated from its pseudo-halide precursor[7b,9].

Scheme 5: Reactivity of an ion pair and an ion-molecule pair vinyl cation.

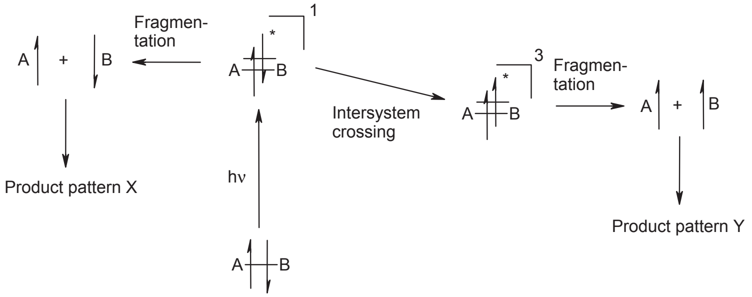


Phenyldiazonium salts are more stable than vinyldiazonium salts, therefore phenyl cations can conveniently be prepared by photoheterolysis[10], whereas this reaction is practically impossible to achieve with vinyldiazonium compounds. A range of substituted phenyl cations has been produced by this method. Also pseudo-halide leaving groups have been employed in the preparation of phenyl cations. The photolysis of diphenyliodonium salts, compounds that are known for over a century now, produces phenyl cations next to phenyl radicals[11]. The reaction has been extensively used by computer-chip manufacturers as a method to generate "photo-acid" using short wavelength UV irradiation, in their search for more refined, wavelength-dependent, patterning of the circuits[12].

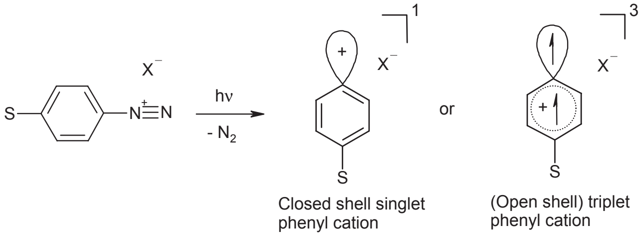
Using photons instead of heating not only allows to achieve high energy-demanding reactions, it also gives spin-selective (singlet or triplet) chemistry[13]. Normally, every chemical bond contains two electrons with anti-parallel spins, one spin-up and the other spin down. Electronic excitation produces a molecule in its singlet excited state. Thus, even though the light promotes one electron from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO), the spins of the electrons remain anti-parallel. If bond cleavage occurs faster than other possible processes, the two fragments formed, together, are of singlet nature: the principle of conservation of spin or Wigner's rule[14] (Scheme 6). If bond cleavage does not take place efficiently in the singlet excited state, the molecule may undergo intersystem crossing to its triplet excited state. In this process one of the electrons undergoes a spin inversion and the spins of the electrons are now both spin-up (or spin-down) and thus parallel. Bond cleavage from such a triplet state will yield the two fragments together as a triplet. Singlet and triplet fragments usually display different chemistry, hence the term spin-selectivity.

The picture of Scheme 6 should also be valid for the photogeneration of dicoordinated carbocations from halide and diazonium precursors. This was recently shown to be correct for a series of *para*-substituted phenyl cations generated from the corresponding benzene diazonium salts[15]. Depending on the substituents, the C-N bond cleavage occurs either from the singlet excited state, yielding a singlet phenyl cation and a molecule of nitrogen, or from the triplet state, yielding a triplet phenyl cation and nitrogen (Scheme 7).

Scheme 6: Spin-selective photochemistry: an adapted Jablonski-diagram.



Scheme 7: Singlet and triplet phenyl cations.



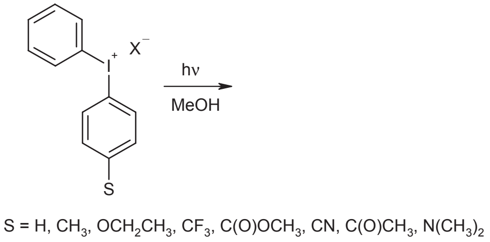
Variation of the leaving group should also enable spin-selective chemistry. Intersystem crossing, the conversion of an excited singlet state to its triplet state, is enhanced by the presence of so-called heavy atoms as bromine and iodine[16]. The utilisation of pseudo-halide iodonium salts in the photolysis of vinyl cation and phenyl cation precursors may direct the intermediate-forming pathway.

In this thesis various photochemical reactions are studied that produce phenyl, aryl and some vinyl cations through heterolytic cleavage of the bond between carbon and a leaving group. The primary goal is to understand and control the reactivity of these extremely reactive fragments. Further a sketch is offered on how the unique properties of these intermediates may be employed to the benefit of bioorganic and biological chemistry.

In all approaches reported in this thesis, product studies are the main tool to identify the (nature of the) product-forming intermediates. It is generally accepted that generation of the same intermediates through different chemical routes under similar reaction conditions leads to the same product profiles[17,18]. In many cases the product studies are complemented with quantum chemical studies.

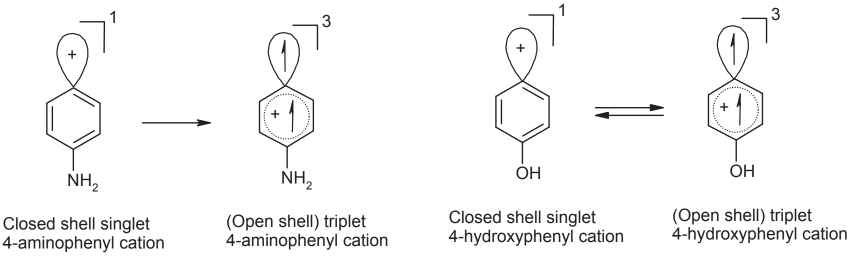
In **Chapter 2** of this thesis the nature of the intermediates formed in the photolysis of phenyliodonium salts is probed. In a classical physical organic chemistry approach, the effects of variation of substituents at the photolabile compound on the formation of intermediates and ensuing products were studied (Scheme 8). An important goal was to clarify some unsatisfactory aspects of the mechanism of photolysis of these compounds proposed fifteen years ago[11a].

Scheme 8: Photochemical reactions studied in Chapter 2.



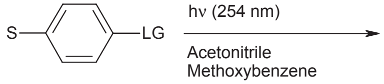
Chapter 3 of this thesis is devoted to the photogeneration of the singlet and the triplet 4-aminophenyl and 4-hydroxyphenyl cations (Scheme 9) from their iodonium salt precursors. For the 4-aminophenyl cation the singlet-triplet order of stability is calculated to be the reverse of the situation for the parent phenyl cation: its ground state is a triplet state[19]. For the 4-hydroxyphenyl cation a quite small singlet/triplet gap is calculated and reaction conditions may well determine whether the singlet or the triplet species is the ground state. The reactivity of the various intermediates was investigated and the circumstances were established under which either the singlet or the triplet state is the most stable.

Scheme 9: The 4-amino- and 4-hydroxy phenyl cations.



In **Chapter 4** a means is sought to profile the reactive intermediates produced in the photolysis of a series of phenyl cation precursors equipped with various substituents and leaving groups (Scheme 10). A method to fingerprint the singlet/ triplet cations is offered based on their chemoselectivity (Scheme 11) and regioselectivity toward the nucleophile methoxybenzene (Scheme 12).

Scheme 10: Photochemical reactions studied in Chapter 4.

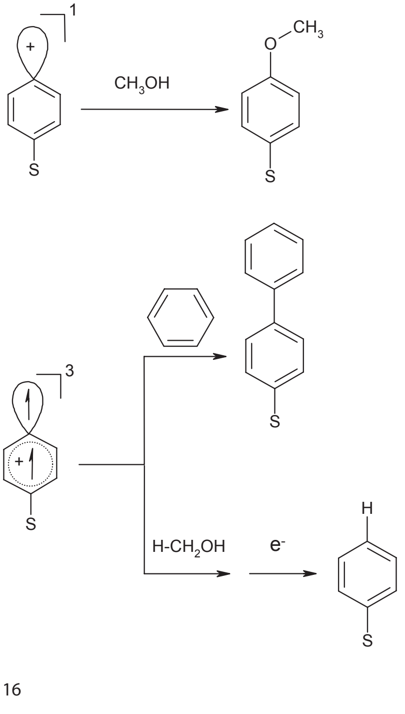


S =	LG =
H	$N_2^+ BF_4^-$
NH_2	Cl
OH	Cl
$C(O)CH_3$	$N_2^+ BF_4^-$
NO_2	$N_2^+ BF_4^-$
$N(Et)_2$	$N_2^+ BF_4^-$
H	$I^+C_6H_5\ BF_4^-$

The two spin states (singlet and triplet), and consequently the electronic configurations of phenyl cations, (see Schemes 7 and 9) each are identifiable by their reactivity[20,3c]. The parent phenyl cation, which possesses a singlet ground state, and a highly localised positive charge, is a hard Lewis acid that preferably reacts with hard nucleophiles (following the Hard Soft Acid Base Principle[21]). To a lesser extent, it also reacts with soft Lewis bases such as aromatic rings. Phenyl cations with a triplet ground state, such as the 4-aminophenyl cation, possess a more dispersed positive charge, and behave as soft Lewis acids that react with soft nucleophiles more efficiently than with hard nucleophiles (Scheme 11).

Triplet phenyl cations are also triplet carbene-like species, and are able to abstract a hydrogen atom. The electrophilicity of these cations, however, makes them better alkylating agents than hydrogen abstracting species[3c].

Scheme 11: Chemoselectivity.



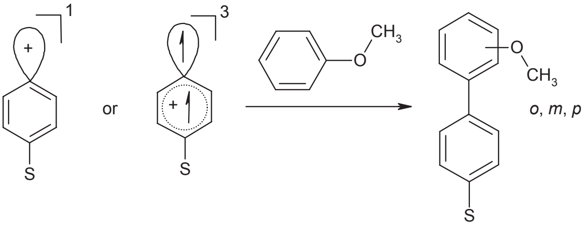
Localised positive charge of the phenyl cation reacts with the localized n-electrons of methanol

Delocalised positive charge of the phenyl cation reacts with the delocalized π-electrons of benzene

The unpaired electron abstracts a hydrogen atom from methanol

The different spin states of the phenyl cations were shown to lead to distinguishable *ortho*, *meta*, *para* ratios of the biaryls produced (Scheme 12).

Scheme 12: Regioselectivity.



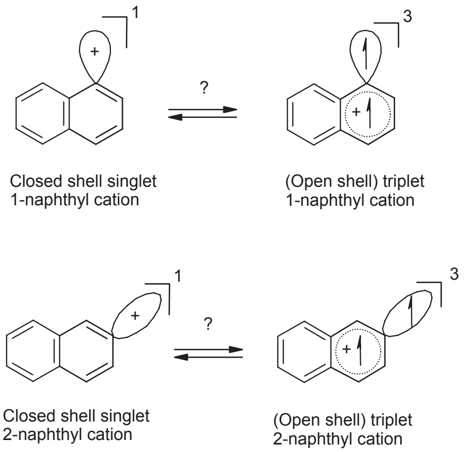
In **Chapter 5** the photogeneration of a 5-membered cyclic vinyl cation from its vinyl (phenyl) iodonium salt precursor is reported. Vinyl cations incorporated in a cycloalkenyl system cannot adopt the preferred linear orientation around the C^+ atom, and are highly strained. Over time, many attempts have been made to generate small cyclic vinyl cations[22]. The report shows that the power of a photon in combination with the use of the exceptionally good leaving group iodobenzene[8] is needed to achieve this goal.

Beyond vinyl and phenyl cations lies the uncharted territory of polynuclear aromatic (aryl) cations, such as the naphthyl, anthryl, phenanthryl and pyrenyl cations. At best, the singlet or triplet nature and the S/T energy gap of some of these species have been studied by quantum chemical calculations[19e,23]. Experimental studies of the reactivity of these intermediates in solution have not yet been reported.

Aryl cations are expected to have a small S/T gap, or even an inverted S/T gap, for two reasons: the annelating rings act as electron-donating substituents and the rigidity of the systems hampers the cations to adopt the preferred linear structures of singlet cations.

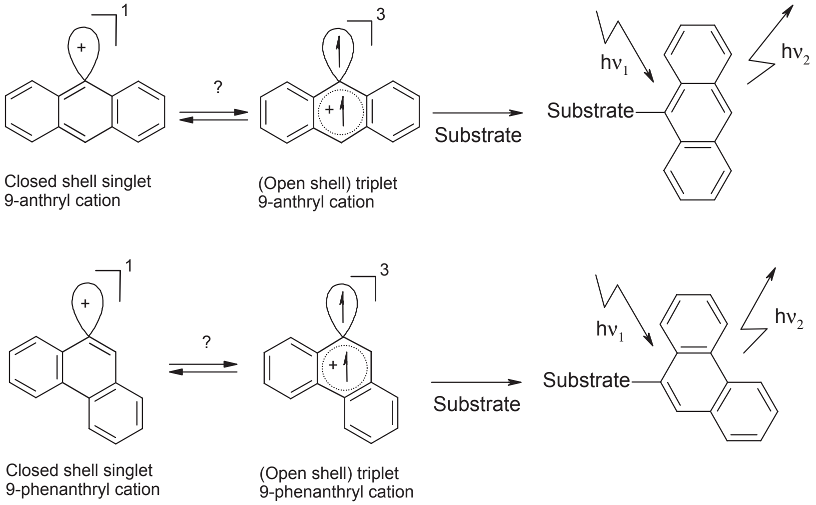
In **Chapter 6** the 1- and 2-naphthyl cations (Scheme 13) are prepared by photolysis of corresponding iodonium and diazonium salt precursors and their reactivity was studied. An assessment as to whether the singlet or triplet species is actually the lowest in energy was made through fingerprinting experiments and quantum chemical calculations in vacuum and in solution.

Scheme 13: The 1- and 2-naphthyl cations.



Chapter 7 reports the research performed to generate and employ the 9-anthryl and the 9-phenanthryl cation (Scheme 14). These cations are of particular interest because, if, after alkylation the substrate is to be retrieved by means of fluorescence recognition, both the anthryl and the phenanthryl group are avid fluorescers in the alkylated products but not in their precursors (i.e. the iodonium salts).

Scheme 14: The 9-anthryl and 9-phenanthryl cations.



Finally, the **Perspectives** of the research reported in Chapters 2-7, are discussed. Several new avenues are proposed to employ the very high reactivity, sometimes accompanied by high selectivity, of aryl and vinyl cations and to assess their initial (upon generation) and final (in product formation) multiplicity. Also the applicability of the photogenerated intermediates to alkylate nucleic acids and proteins is sketched and preliminary experimental results are presented.

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Chapter 2 | Photochemistry of para-substituted diphenyliodonium salts

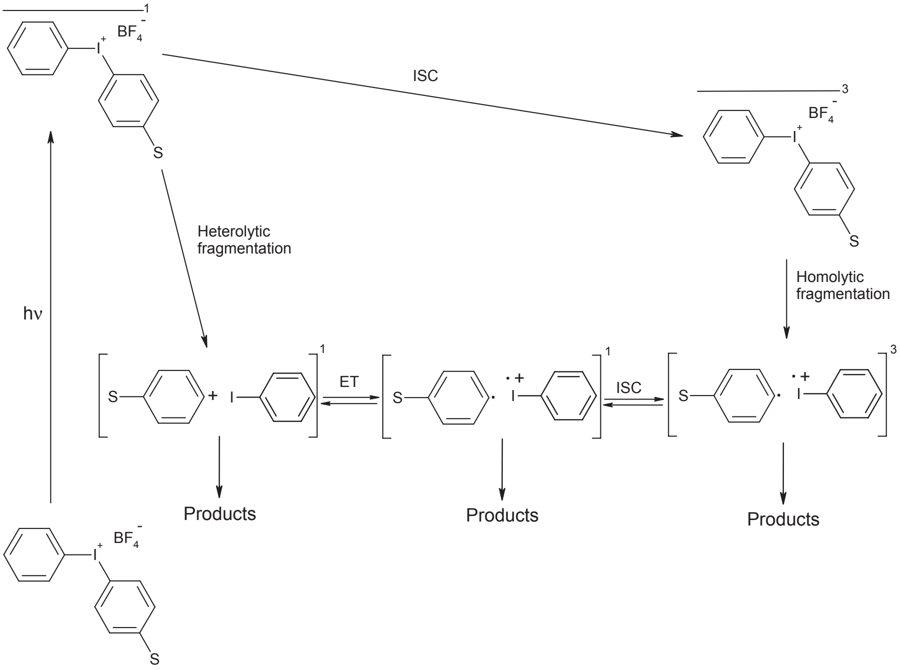
Introduction

The first publication concerning diphenyliodonium salts appeared in 1894 and reported their preparation[1]. This paper elaborated on even earlier work on the preparation of λ_3-iodane (hypervalent iodonium) compounds[2]. The methods of synthesis of these compounds and their applications in other syntheses have since continuously developed[3]. The photolability of iodonium salts was first noted in the late 1950's[4,5] which eventually led to extensive use of these salts in both negative and positive photoresists, in industries applying photolithography, such as computer-chip manufacturers[6].

Over 130 patents and over 50 scientific publications have appeared mainly dealing with alterations of the diphenyliodonium salts' basic structure, mostly to serve specific industrial applications. Lately, the industrial application of diphenyliodonium salts receives competition from the triphenylsulfonium salts[7]. The photochemistry of sulfonium salts, however, takes place along the same lines as the photochemistry of diphenyliodonium salts[8,9].

The industrial applications spurred research on the mechanism of photolysis of diphenyliodonium salts. The first flash photolysis experiments recognised the presence of the radical cation of iodobenzene[10], and since the publication of that finding homolysis of the C-I$^+$ bond has been considered a major, if not the major mechanistic pathway[11,12,13,14]. In 1990 a mechanism was

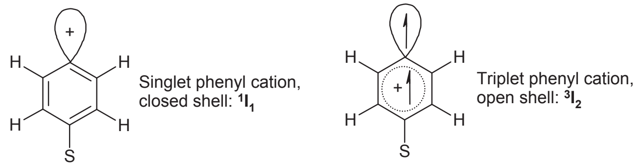
Scheme 1: The mechanism of photolysis of diphenyliodonium salts[16].



proposed that today still is regarded to be the golden standard for these reactions (Scheme 1)[15,16]. According to that mechanism the photolysis proceeds through heterolysis of the C-I$^+$ bond in the singlet excited state, which produces a phenyl cation-iodobenzene pair, and homolysis of the C-I$^+$ bond in the triplet excited state, which forms a phenyl radical-iodobenzene radical cation pair[16]. Both C-I bonds are prone to heterolysis and homolysis. The available information allows no conclusion about the feasibility of interconversion of the two pairs, nevertheless this process is thought to occur[17].

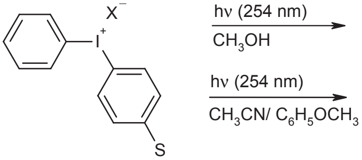
The intermediacy of phenyl cations[18] in the photolysis of diphenyliodonium salts renews the interest in (the mechanism of) the photolysis of these salts. The photochemical generation of singlet phenyl cations, and even more so of triplet phenyl cations (Figure 1), is a fast-moving area of research these days[19,20].

Figure 1: Singlet and triplet phenyl cations.



The reported chemoselectivity of triplet (open-shell) phenyl cations compared to fairly unselective singlet (closed shell) phenyl cations may offer a compromise between a hyper-reactive species and a desired selectivity of action. In this chapter investigations are reported about the photogeneration of phenyl cations from the series of *para*-substituted diphenyliodonium salts **1**-**8** (Chart 1). The compounds were photolyzed in methanol and in acetonitrile in the presence of anisole to probe the reactivity of the product-forming intermediates as a function of the substituent.

Chart 1: Compounds studied.



1) S = H, X = BF_4^-
2) S = CH_3, X = BF_4^-
3) S = OCH_2CH_3, X = BF_4^-
4) S = CF_3, X = BF_4^-
5) S = $C(O)OCH_3$, X = BF_4^-
6) S = CN, X = BF_4^-
7) S = $C(O)CH_3$, X = BF_4^-
8) S = $N(CH_3)_2$, X = Br^-

Results and discussion

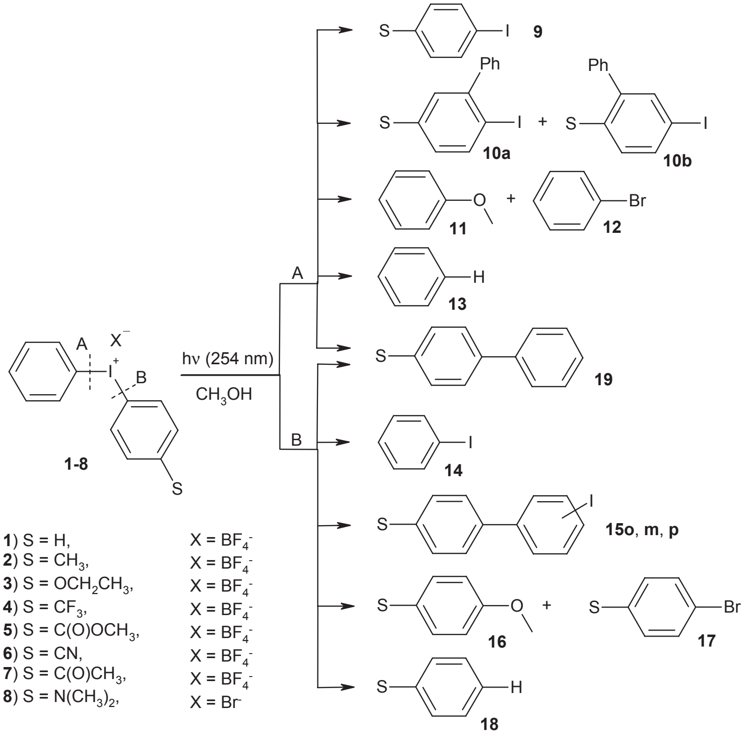
Syntheses

Six of the *para*-substituted phenyl(phenyl)iodonium tetrafluoroborates studied (**1**-**4**, **6** and **7**) are synthesised by treating the corresponding aryl boronic acids with an equimolar amount of (diacetoxy)iodobenzene in the presence of two mole equivalents of hydrogen tetrafluoroborate (in diethyl ether) at -30° C in dichloromethane, following a modified literature procedure[21,22]. Iodonium salt **5** is prepared from 4-(diacetoxy)iodobenzoic acid methyl ester and phenylboronic acid following the same procedure as for **1**-**4**, **6** and **7**. Compound **8** as tetrafluoroborate salt is not stable and therefore the bromide salt was prepared from 4-N,N-dimethylaminobenzene boronic acid and Koser's reagent, hydroxy(tosyloxy)iodobenzene, (1/1 mole/mole), in tetrahydrofuran at melting ice temperature, followed by tosylate/ bromide anion exchange.

*Photolyses of **1**-**8** in methanol*

Both the phenyl-iodonium bond A and the phenyl-iodonium bond B of the *para*-substituted diphenyliodonium salts **2**-**8** are photolabile (Scheme 2). Heterolytic or homolytic fission of

Scheme 2: Product formation upon irradiation of **1**-**8** in methanol.



either bond results in the formation of four types of products. Upon A bond cleavage, apart from the leaving group **9**, the Friedel-Crafts type products **10a** and **10b**, the nucleophilic substitution products with the solvent **11** and the counter-ion **12**, and the reductive dehalogenation products **13** are produced. Upon cleavage of bond B, also a leaving group **14** forms, next to the Friedel-Crafts products **15*o***, ***m***, ***p***, the nucleophilic substitution products, with the solvent (**16**), and the counter-ion (**17**), and the reduction products **18**. One product, the *ipso*-substitution Friedel-Crafts product **19**, can be produced through either A or B bond cleavage.

The composition of the product mixtures observed in the photolyses of **1**-**8** in methanol, at low conversion, is recorded in Table 1. Various effects of the substituents are immediately clear. The Friedel-Crafts type products **10a** and **10b** are formed only in the photolyses of **2** (S = CH_3) and **3** (S = OCH_2CH_3) and products **15** only in the irradiation of **1** (S = H); with **2**-**8** at best traces of products **15** are observed (*vide infra*). The formation of ethers **11** and **16** also shows a remarkable substituent effect. Whereas A bond cleavage produces ether **11** in all cases, B bond cleavage only yields ethers **16** in the case of the photolyses of **1**, **2**, **3** and **4** (S = CF_3). Nucleophilic substitution products with the counter-ion, **12** and **17**, are only found in the photolysis of **8**. The reduction products **13** and **18** occur in all experiments. The *ipso*-substitution Friedel-Crafts type products **19** are also generally encountered, but in the photolysis of **1**-**4** about twice as much of these products is formed as in the photolyses of **5**-**8**.

Table 1: Results of the photolyses of **1**-**8** in methanol^{a,e}.

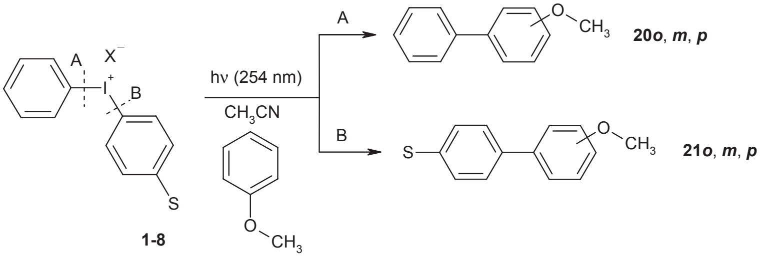
	S	9	10a,b	11	12	13	14	15	16	17	18	19
1	H	5.8		1.9		1.6	5.8	3.4	1.9		1.6	1.2
2	CH_3	5.1	3.9^{b}	1.3		1.3	4.3	^{d}	1.6		1.2	1.0
3	OCH_2CH_3	5.6	2.1^{c}	0.8		1.4	4.8	^{d}	0.3		2.3	1.4
4	CF_3	9.1		2.5		2.0	8.3	^{d}	0.4		5.6	1.1
5	$C(O)OCH_3$	3.8		1.9		1.3	5.6	^{d}			3.8	0.5
6	CN	3.3		2.7		1.6	6.7	^{d}			5.0	0.5
7	$C(O)CH_3$	2.7		1.7		1.5	5.9	^{d}			2.6	0.6
8	$N(CH_3)_2$	6.7		0.3	0.4	2.9	11.6	^{d}		3.6	1.6	0.7

[a] Percentages of product, relative to internal standard (GC), after 90 minutes of irradiation. [b] Ratio of **10a**: **10b** is 11:1. [c] Ratio of **10a**: **10b** is 2.1:1. [d] Formed in trace amounts, observed after evaporation of the solvent (*o*, *m*, *p* ratios in Table 4). [e] Under the reaction conditions used for the photolysis experiments, except for the light **1**-**8** are inert.

*Photolyses of **1**-**8** in acetonitrile/ anisole 1/1*

Under these conditions the same types of products can be formed as in methanol (cf. Scheme 2). The presence of the extra nucleophile anisole, however, does open an additional product-forming pathway: substitution with this substrate yielding methoxybiphenyls **20** upon A bond cleavage and 4'-substituted-methoxybiphenyls **21** upon B bond fission (Scheme 3).

Scheme 3: Additional products in the photolyses of **1**-**8** in acetonitrile/ anisole (compared to in methanol).



The composition of the product mixtures upon photolysis of **1**-**8** in acetonitrile/ anisole is recorded in Table 2. The Friedel-Crafts arylation of anisole yielding **20** and **21** is the major product-forming pathway upon both A and B bond fission; the Friedel-Crafts products **10**, **15** and **19** are formed in negligible amounts compared to **20** and **21**. No products of the nucleophilic substitution reaction with acetonitrile (acetanilides, formed through a Ritter reaction) are found. Nucleophilic substitution products with the counter-ion (**12** and **17**) are produced only in the irradiation of **8**. The reduction products **13** and **18** are formed in every experiment in this series.

Table 2: Results of the photolyses of **1**-**8** in acetonitrile/ anisole[a,b].

	S	9	12	13	20	14	17	18	21	20*o*: *m*: *p*	21*o*: *m*: *p*
1	H	20.8		6.9	27.1	20.8		6.9	27.1	69:11:20	69:11:20
2	CH_3	27.1		7.2	25.1	18.5		11.0	20.7	71:11:18	73:11:16
3	OCH_2CH_3	20.7		5.5	22.3	17.9		7.8	17.9	66:11:23	74:11:15
4	CF_3	19.8		5.7	19.1	24.3		5.6	45.2	70:09:21	71:11:18
5	$C(O)OCH_3$	16.3		5.4	22.1	23.6		4.3	26.8	67:09:24	74:10:16
6	CN	10.9		5.3	22.2	24.7		3.6	36.7	65:10:25	78:08:14
7	$C(O)CH_3$	13.1		5.1	22.4	22.8		4.8	31.2	67:10:23	76:10:14
8	$N(CH_3)_2$	14.2	4.1	5.2	9.6	18.1	12.0	1.1	1.6	77:12:11	100:0:0

[a] Percentages of total product formation (GC) after 90 minutes of irradiation. [b] Under the reaction conditions used for the photolysis experiments, except for the light **1**-**8** are inert.

The *ortho*: *meta*: *para* ratios in which the Friedel-Crafts products **20** and **21** are formed are also presented in Table 2. In general, the percentage of *ortho* isomer is more pronounced upon B bond cleavage, leading to **21**, than upon A bond cleavage, leading to **20**. For the *para* isomer the reverse is true. For both cleavages higher *ortho* yields are connected to lower *para* yields and vice versa.

Except for **8**, the *o*: *m*: *p* ratios in **20** observed upon A bond cleavage are similar: the results of the irradiations of **1**, **2** and **4** are alike, as are the ratios obtained in the photolysis of **3**, **5**, **6** and **7**. The results of the irradiation of **8** also stand out for the B bond fission. No systematic variation in the *o*: *m*: *p* ratios in **21** found upon B bond photocleavage of **2**-**7** is obvious.

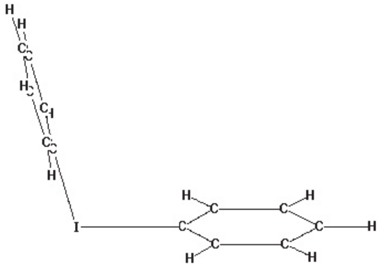
Theoretical evaluation of C-I$^+$ bond cleavage pathways

The photochemical bond cleavage pathways of iodonium species have not yet been theoretically evaluated even though this has been done for sulfonium compounds[9], and for onium compounds in general[23].

The diphenyliodonium compound [A-I$^+$-B] is considered as a system consisting of three separate parts, A, I$^+$ and B, connected by two C-I bonds. As with the triphenylsulfonium compounds[9] the thermal dissociation process is expected to result in either [A$^+$ /IB] or [AI /B$^+$] of which the cation-molecule pair of lower energy will be preferred.

To describe the photochemical processes the following orbitals were taken into account: the π and π^* orbitals of A (π_A and π_A^*) and B (π_B and π_B^*), the σ bonding and anti-bonding orbitals of A (σ_A and σ_A^*) and B (σ_A and σ_A^*) and a lone pair on iodine (n). The model was refined by taking interaction of the π and σ orbitals into consideration. The relative stabilities of the structures that occur upon elongation of the A-I$^+$ bond from the equilibrium geometry structure (Figure 2) were HF/CEP-121G calculated[24].

Figure 2: Equilibrium geometry of the diphenyliodonium compound.



The evaluation reported here indicates eight different intermediate-forming pathways. Electronic excitation of [A-I$^+$-B] may lead to a $\pi_A\pi_A^*$ or a $\pi_B\pi_B^*$ state. A relative preference of π_A^* over π_B^* or *vice versa* will depend on the electron richness of the aromatic rings. These configurations are non-dissociative. However, following the potential energy curve (along the C-I$^+$ bond elongation) they connect with the dissociative $\sigma\sigma^*$ states in the nearest and in the opposite C-I bond. The $\sigma_A\sigma_A^*$ state correlates with an A•/BI•+ pair and the $\sigma_B\sigma_B^*$ state with a B•/ AI•+ pair. So, in the case of e.g. a $\pi_A \rightarrow \pi_A^*$ excitation an A•/ BI•+ pair may be produced next to a B•/ AI•+ pair.

Also, direct dissociative $\pi\rightarrow\sigma^*$ excitations are possible: $\pi_A\rightarrow\sigma_A^*$, $\pi_A\rightarrow\sigma_B^*$, $\pi_B\rightarrow\sigma_A^*$, and $\pi_B\rightarrow\sigma_B^*$. The $\pi_A\sigma_A^*$ state leads to an $(A^+)^*$/BI ion pair, in which $(A^+)^*$ is the excited state of the phenyl cation (which is an open-shell species). The $\pi_A\sigma_B^*$ and the $\pi_B\sigma_A^*$ states lead to a B•/ AI•+ pair and an A•/BI•+ pair, respectively. The $\pi_B\sigma_B^*$ state leads to a $(B^+)^*$/AI ion pair. Like $(A^+)^*$, $(B^+)^*$ is the excited state of the phenyl cation. If $(A^+)^*$ and $(B^+)^*$ are not sufficiently stabilised by their substituents, or not efficiently trapped, they may convert to their ground state configuration.

Further, excitations to the dissociative $n\sigma^*$ state, of a lone pair on iodine to an anti-bonding σ^* orbital, are possible. They lead to an A•/ BI•+ pair from $n\sigma_A^*$ and a B•/AI•+ pair from $n\sigma_B^*$.

Product-formation may be possible through all 8 channels because energy differences are small. Many of the states are close in energy and may be connected. In particular the $\pi\sigma^*\rightarrow\sigma\sigma^*$ conversion is likely, if both states have a σ^* orbital in common. These processes ($\pi_A\sigma_A^*$ into $\sigma_A\sigma_A^*$, $\pi_A\sigma_B^*$ into $\sigma_B\sigma_B^*$, $\pi_B\sigma_A^*$ into $\sigma_A\sigma_A^*$, and $\pi_B\sigma_B^*$ into $\sigma_B\sigma_B^*$) result in interconversion of the radical pairs or conversion of a ion pair into a radical pair. The conversions are less likely if the fragments are well-separated or stabilised. Solvation upon elongation of the $C\text{-}I^+$ bond and/or stabilisation by means of appropriate substituents may be of decisive influence on the relative stabilities of the possible intermediates.

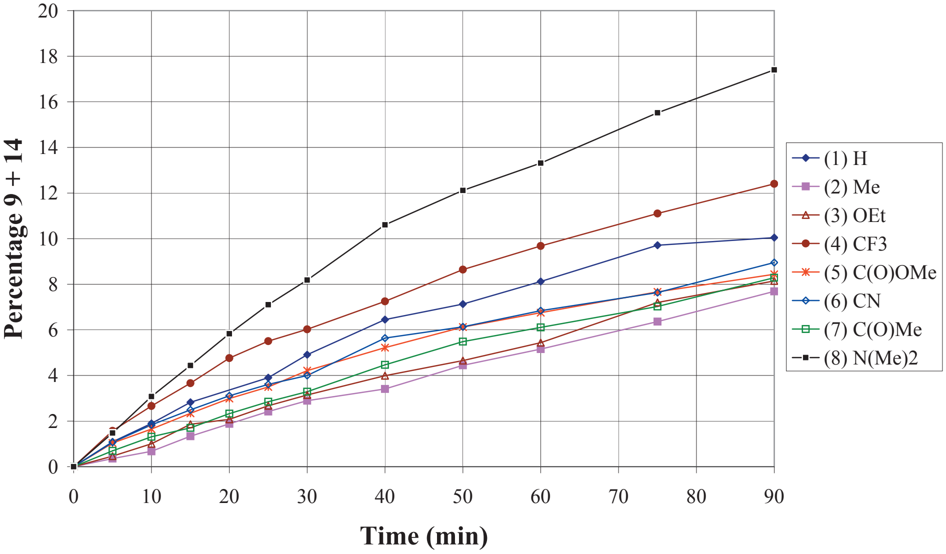
The presence of an iodine atom induces efficient intersystem crossing which converts a molecule from its singlet excited state into its triplet excited state. For that reason, the photochemistry of diphenyliodonium salts is thought to take place through the triplet excited state. That in these compounds, the iodine is dicoordinated should be of no concern, because the spin-orbit coupling, that causes the intersystem crossing, is only proportional to the atomic number[25].

Substituents on diphenyliodonium salts not only affect the relative stabilities of the fragments of the photoinitiated bond cleavage reactions. They also have more fundamental effects: a) On the energy and the nature of the orbital from which excitation takes place, the highest occupied molecular orbital (HOMO). b) On the efficiency of intersystem crossing (ISC). E.g. the acetyl substituent, that possesses an easily accessible triplet $n\pi^*$ state of its own, at the *para*-position of phenyldiazonium salts, gives efficient ISC and thereby a triplet pathway in product-formation[26,27]. The same effect may be exerted by other carbon-heteroatom double-bond containing substituents.

*Photoreactivity of **1**-**8** in methanol*

The sum of the amounts of leaving groups **9** and **14** as a function of the time of irradiation[28] forms an indication for the progress of the photoreactions (Figure 3). These graphs show that the photoreactivities of **1**-**8** are subject to an unexpected order of substituent effects, not similar to the effects in thermal reactions. In the thermolysis of iodonium compounds the difference in electron densities in the two C-I bonds, that are modified by substituents on the ring, determines the overall stability[29]. The stability is enhanced by *ortho* and *para* electron-donating substituents. This rationale does not hold for the stability upon irradiation.

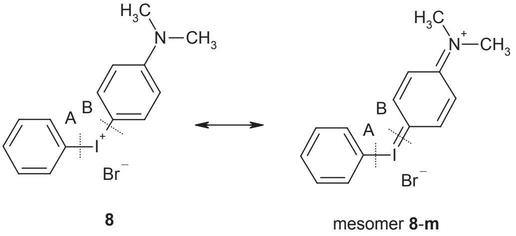
Figure 3: The formation of **9** + **14** from **1**-**8** as a function of time of irradiation.



The photoreactivities of both the EDG-substituted **2** and **3** and the EWG-substituted **5**-**7** are similar but all reactions proceed slower than the photolysis of **1**. On the other hand, the EWG-substituted **4** and the EDG-substituted **8** are more photoreactive than **1**. The decreased photoreactivity of **2** and **3** is probably due to the inductive or mesomeric stabilisation of the positive charge on the iodine centre. Likewise, the high photoreactivity of **4** is caused by destabilisation of the iodonium cation by the strongly electron-withdrawing CF_3 group. The EWG-substituents (S = $C(O)OCH_3$, CN, $C(O)CH_3$) in **5**, **6** and **7** also will destabilise the positive charge, but these substituents are known to induce an alternative pathway of deactivation of the excited state leading to non- or less-productive (photon wasting) $n\pi^*$ excited states.

The UV-Vis spectrum of **8**, the most reactive compound, in methanol and acetonitrile (Table S1 in the Experimental Section) shows an absorption maximum at much longer wavelength than the other salts, in solution. This red-shift is probably caused by strong mesomeric delocalisation of the positive charge by the electron-donating $N(Me)_2$ group (Scheme 4). Mesomeric[30] structure **8**-**m** is proposed to contribute to the instability toward light by opening alternative, more efficient, C=I/C-I bond cleavage channels.

Scheme 4: Mesomeric structure of **8**.



*Photoselectivity in **1**-**8***

The ratios in which the leaving groups **9** and **14** are produced, are indicative of the relative occurrence of A bond cleavage and B bond cleavage in **1**-**8**. These ratios are substituent dependent (Table 3). The EDG-substituted salts **2** and **3** favour A bond cleavage over B bond cleavage, probably because of the increased electron density in the B bond. The EWG-substituted **4** and **5**-**7** act the other way round. The ratio found in the photolysis of **8** does not fit the picture. The expected increase in the bond order of bond B[31] does not bring about a **9** to **14** ratio > 1 as with iodonium salts **2** and **3**. Fission of bond B in **8** presumably is more efficient than in **1** or **2** (See above)

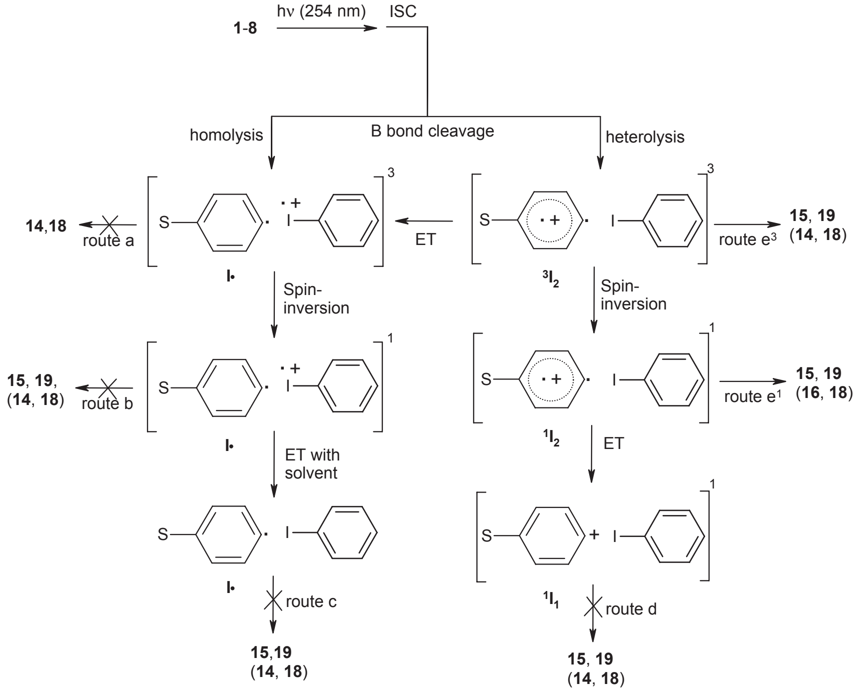
Table 3: The ratio of **9** to **14**.

Salt	S	Ratio
1	H	1.0
2	CH_3	1.5
3	OCH_2CH_3	1.2
4	CF_3	0.8
5	$C(O)OCH_3$	0.7
6	CN	0.4
7	$C(O)CH_3$	0.6
8	$N(CH_3)_2$	0.8

Regioselectivity of product formation

According to the theoretical evaluation, products **15** and **19** are formed via a Friedel-Crafts type recombination of the fragments produced upon either a homolytic or a heterolytic cleavage of the aryl-iodonium bond (B) of the triplet excited state (Scheme 5).

Scheme 5: Possible reactive intermediates, leading to recombination products **15** and **19**.



Homolysis gives a phenyl radical-iodobenzene radical cation pair in its triplet state, which also may be formed through heterolysis to the open-shell phenyl cation ($^3\mathbf{I}_2$)-iodobenzene pair followed by electron transfer. This triplet radical pair is less likely to produce recombination products and will preferentially form the leaving group **14** and the reduction product **18** (route a). Radical recombination yielding **15** and **19** (route b) is only possible in the singlet radical pair, which may have formed after spin-inversion. Oxidation of methanol by the iodobenzene radical cation, which produces the phenyl radical (**I•**)-iodobenzene pair, may also lead to recombination products (route c)[15]. The open-shell phenyl cation $^3\mathbf{I}_2$, formed upon heterolysis, may convert to its ground state singlet (closed shell) manifold $^1\mathbf{I}_1$ via spin-inversion to the singlet open-shell cation $^1\mathbf{I}_2$ followed by intramolecular electron transfer. The phenyl cation ($^1\mathbf{I}_1$)-iodobenzene pair may give rise to the recombination products **15** and **19** (route d), just like its predecessors, the phenyl cation ($^1\mathbf{I}_2$ and $^3\mathbf{I}_2$) iodobenzene pairs (routes e^1 and e^3). The *o*, *m*, *p* pattern of products **15**, (Table 4), albeit formed in minute amounts with **2**-**8**, sheds light on the actual product-forming intermediate (routes b-e).

Recombination of the singlet phenyl radical-iodobenzene radical cation pair (route b) is expected to take place at the position(s) with highest spin density. According to the PM3-calculated spin-densities in the radical cation of iodobenzene (Scheme 6), the *ipso* and the *para*

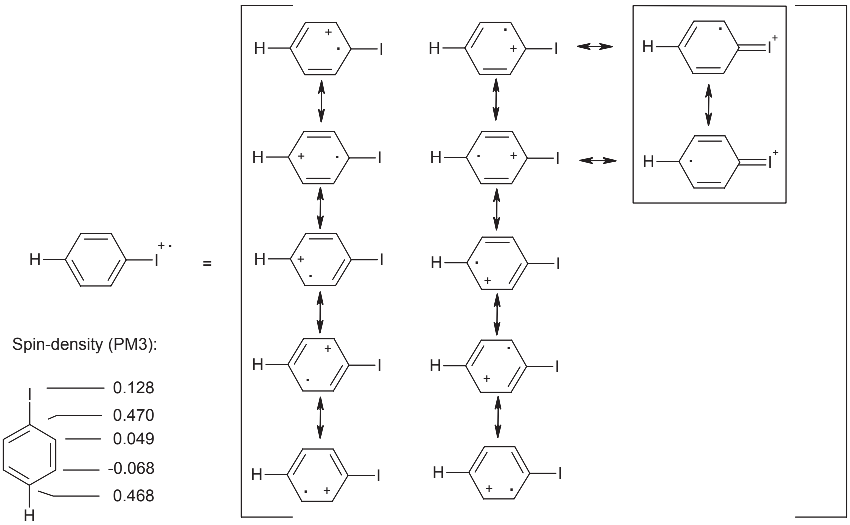
Table 4: *O*: *m*: *p* ratios of products **15** obtained after concentration of the reaction mixtures.

	S	**15*o*: *m*: *p* ratio**
1	H	85:6:9
2	CH_3	79:10:11
3	OCH_2CH_3	87:6:8
4	CF_3	66:6:27
5	$C(O)OCH_3$	72:5:23
6	CN	71:4:35
7	$C(O)CH_3$	66:5:29
8	$N(CH_3)_2$	82:3:15

position would be the preferred sites of attack leading to *ipso*- and *para*- substituted products. Mesomeric structures of the distonic iodobenzene radical cation also indicate that the *ortho* and *para* position possess most of the radical functionality. The thermolysis of diphenyliodonium salts in anisole, which predominantly produces the singlet phenyl radical-iodobenzene radical cation pair, yields products **15** in an *o*, *m*, *p* ratio of 35:11:54 and in 2.6 fold excess over the *ipso* substitution product **19**[32]. The different regio- and chemoselectivity in the thermolysis and the photolysis make route b unlikely for the formation of **15** and **19**.

A phenyl radical-iodobenzene pair[12] can also not be held accountable for the Friedel-Crafts type product pattern (route c). Photolysis of iodobenzene in acetonitrile (4/1) produces a phenyl radical that reacts with iodobenzene itself and yields **15** in an *o*, *m*, *p* ratio of 64:28:8, in 11 fold excess over biphenyl **19**. These data are in agreement with literature data for the radical phenylation of iodobenzene (*o*: *m*: *p* = 55:28:17)[33] but not with the data in Tables 1 and 4.

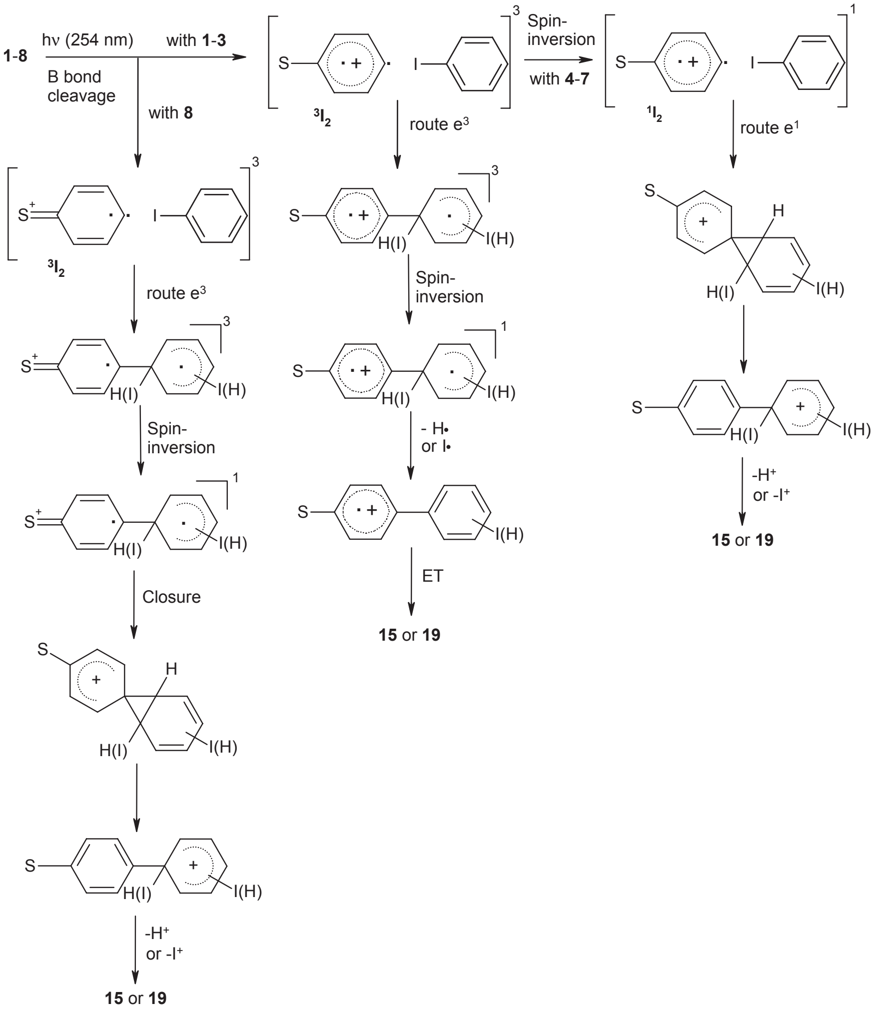
Scheme 6: PM3-calculated spin densities in and resonance structures of the radical cation of iodobenzene.



Recombination of the closed shell phenyl cation $^1\mathbf{I}_1$ and iodobenzene (route d) is also not the source of the iodobiphenyl products. The generation of the parent singlet phenyl cation by β-decay of ditritiobenzene in the presence of chlorobenzene yields chlorobiphenyls in an *o*, *m*, *p* ratio of 50:29:21[34]. A similar ratio is expected for the reaction between that cation and iodobenzene. The different *o*, *m*, *p* ratios in which the iodobiphenyls **15** are produced in the photolyses of **1**-**8** (Table 4) and in the β-decay, rule out $^1\mathbf{I}_1$ as product-forming intermediate.

The open-shell cation $^3\mathbf{I}_2$ is a soft Lewis acid and is expected to attack iodobenzene (route e³) with the regioselectivity of an electrophilic radicaloid species (*o* > *m* > *p*, as with **I•**, or with $^1\mathbf{I}_1$) but, contrary to these intermediates, also with a preference for polarisable (soft Lewis

Scheme 7: Mechanism of formation of **15** and **19**.



base) positions (*i* > *o* >> *m*, *p*). The cations formed upon irradiation of **1**-**3** (S = H, CH_3 and OCH_2CH_3) react with iodobenzene to produce mainly *ipso* and *ortho* diradical cation addition complexes (Scheme 7). After spin-inversion and loss of a hydrogen atom or an iodine atom **15** and **19** are produced. The *o*, *m*, *p* ratios of **15** produced upon photolysis of **1**-**3** (Table 4) indicate the cations to be of triplet nature ($^3\mathbf{I}_2$).

The higher percentage of the *para* isomer in product **15** in the irradiation of **8** is caused by the strong mesomeric electron-donating effect of the $N(CH_3)_2$ group. Upon formation of the initial addition complex and spin-inversion, the delocalisation of the positive charge onto the nitrogen substituent, grants a cationic spiro-compound to form (Scheme 7). In turn, the spiro-compound opens to the more stable Wheland-intermediate (*o*, *p* > *m*). Upon cleaving off I^+ or H^+, **19** and **15** are produced. This pathway allows conversion of the initial *meta* distonic diradical cation into either the *ortho* or the *para* Wheland-intermediate, which causes an increase in *para* and a depletion in *meta* product **15**.

The electron withdrawing substituents in **4**-**7** (S = CF_3, $C(O)OCH_3$, CN and $C(O)CH_3$) destabilise $^3\mathbf{I}_2$. Therefore a swift isomerisation to $^1\mathbf{I}_2$ (and further to $^1\mathbf{I}_1$) is expected. The open-shell cation $^1\mathbf{I}_2$ is expected to attack iodobenzene with the regioselectivity of a singlet carbene (route e^1) which directly yields the cationic spiro-compounds with a preference *i*, *o* > *o*, *m* and *m*, *p* (Scheme 7). Opening of the spiro-compounds to the more stable Wheland intermediate (*o*, *p* > *m*) and subsequent expulsion of I^+ or H^+ produces **19** and **15**. The *o*: *m*: *p* ratios of **15** produced upon photolysis of **4**-**7** (Table 4) substantiate the intermediacy of $^1\mathbf{I}_2$.

The formation of **10**, which occurs through A bond cleavage, only takes place in the photolyses of **2** and **3**. The isomeric distribution between **10a** and **10b** is caused by the balance of radical stabilizing effects of the two substituents at the substrate that govern the position of attack of the radicaloid electrophilic triplet phenyl cation. The non-formation of products **10** in the photolyses of **4**-**7** is caused by the double electron-withdrawing substituted aromatic fragment being less activated for electrophilic attack than the CH_3- and OCH_2CH_3-substituted fragments. The lack of formation of **10** in the photolysis of **8** is attributed to trapping of the product-forming intermediate by the counter-ion Br^- instead of by the iodoaromatic fragment. These arguments also explain why less **19** is formed in the photolyses of **5**-**8** than in the photolyses of **1**-**3**. The unexpectedly large percentage of **19** in the photolysis of **4** is due to the relatively high conversion in this photoreaction.

Chemoselectivity

Nucleophilic substitution with the solvent, yielding the methyl ethers **11** and **16**, is the result of the attack of the phenyl cation intermediate $^1\mathbf{I}_1$, a hard Lewis acid, at the n-electrons of methanol[15], a hard Lewis base. Subsequent loss of a proton gives the methyl ether products (as to the counter-ion, no Schiemann product of the parent phenyl cation with BF_4^- is observed under the reaction conditions). The reaction is a major product-forming route upon A bond cleavage of the iodonium salts under study (Table 5, column 3). Only in the case of the OCH_2CH_3- and $N(CH_3)_2$ substituted salts **3** and **8**, its role is diminished. Upon B bond fission, only in the photolysis of **1** and **2**, and much less so in **3** and **4**, reactions occur of the phenyl cation $^1\mathbf{I}_1$ with the solvent, leading to **16**.

Table 5: Formation of ethers **11** and **16** and reduction products **13** and **18** (relative to the formation of the leaving group in the cleavage leading to that product).

	S	11	16	13	18
1	H	0.33	0.33	0.28	0.28
2	CH_3	0.25	0.37	0.25	0.28
3	OCH_2CH_3	0.14	0.06	0.25	0.48
4	CF_3	0.27	0.06	0.22	0.67
5	$C(O)OCH_3$	0.5		0.34	0.67
6	CN	0.81		0.48	0.75
7	$C(O)CH_3$	0.63		0.56	0.44
8	$N(CH_3)_2$	0.04		0.43	0.14

Reduction, yielding **13** and **18**, is the result of hydrogen atom abstraction from the solvent by a phenyl radical intermediate **I•**, formed after homolysis from the triplet excited state. Unlike the nucleophilic substitution products, the reduction products **13** and **18** are found in all experiments (Table 5). An alternative route for the formation of the reduction products **13** and **18** is through the triplet (open-shell) phenyl cations. These ions may abstract a hydrogen atom from the solvent and produce radical cations, which upon electron transfer give **13** or **18**.

The bromides **12** and **17** in the photolysis of **8** (Table 1) are produced by trapping of the phenyl cations by the bromide anion. Cation $^3\mathbf{I}_2$, a soft Lewis acid, is expected to be trapped more efficiently by the bromide anion, a soft Lewis base, than the closed shell cation $^1\mathbf{I}_1$ (HSAB principle). The formation of **12** and **17** therefore is attributed to the intermediacy of the triplet phenyl cations $^3\mathbf{I}_2$ generated upon A and B bond cleavage.

*Regio- and chemoselectivity of **1**-**8** in acetonitrile/anisole*

Comparison of the product patterns in Table 2 with those of the phenyl cation and the phenyl radical under similar reaction conditions reveal the nature of the product-forming intermediate. The β-decay of 1,4-ditritiobenzene, which forms the singlet phenyl cation $^1\mathbf{I}_1$, in anisole, produces **20** in an *o*, *m*, *p* ratio of 65:13:22[34]. The amount of reduction product could not be determined because monotritiobenzene can not be distinguished from ditritiobenzene.

The photolysis of iodobenzene, which produces the phenyl radical, in acetonitrile/anisole yields products **20** in an *o*, *m*, *p* ratio of 75:13:12 and in a 2.1 fold excess over the reduction product **13**.

The *o*, *m*, *p* ratios of **20** collected in column 11 of Table 2, except for **8**, all are similar to the ratio observed in the literature for the singlet phenyl cation, which indicates $^1\mathbf{I}_1$ as product-forming intermediate in Scheme 3. The slightly higher percentages of **20**-*ortho* and lower percentages of **20**-*para* in the photolysis of **1**, **2** and **4** may be due to a contribution of a phenyl radical route to the formation of **20**.

The *o*, *m*, *p* ratios observed for biaryls **21** in the photolysis of **1**-**7** (Table 2, column 12) show similarity with the ratio typical for the singlet phenyl cation (65:13:22) and with the ratio typical for the phenyl radical (75:12:13). However, the excess of arylation over reduction with **1**-**7**, indicates that the radical pathway is not a major product-forming route. It does contribute to some extent in the photoreactions of **2** and **3**.

The *o*, *m*, *p* ratios found for products **21** are attributed to the combined reactivity of the closed shell phenyl cations ($^1\mathbf{I}_1$) and the triplet phenyl cations ($^3\mathbf{I}_2$). Triplet phenyl cations substituted with an EWG, prepared photochemically from the corresponding diazonium compounds, are also found to give products with *o*, *m*, *p* ratio characteristic of a phenyl radical, and to preferentially arylate an aromatic substrate over abstracting a hydrogen atom from the solvent (See Chapter 4).

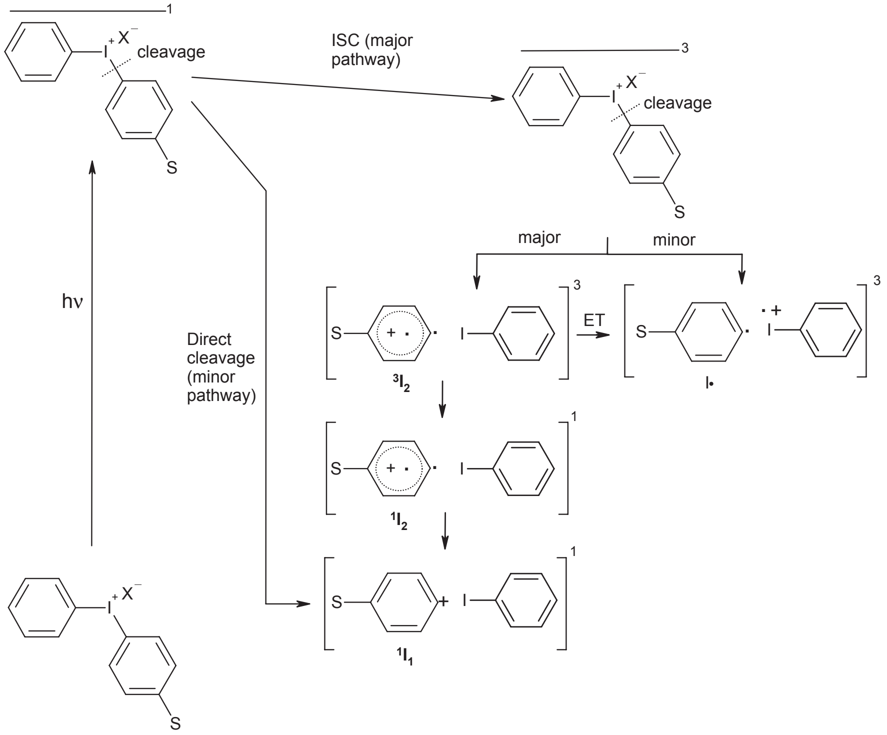
In the photolysis of **8** only a small (A: 1.8, B: 1.5 fold) excess of arylation over reduction is observed. The production of **20*o***, ***m***, ***p*** in a ratio typical for a phenyl radical intermediate and the selective formation of **21*o***, which is also observed in the photolysis of iodobenzene in anisole at very low conversion, indicate that the formation of **13**, **18**, **20** and **21** from **8** largely takes place through a phenyl radical intermediate.

This certainly does not mean that no phenyl cation is produced upon irradiation of **8**. If formed, the open-shell phenyl cation is trapped more efficiently by the counter-ion bromide than by anisole. The contribution of the photohomolysis now becomes visible through its distinct product pattern of aromatic substitution and hydrogen atom abstraction.

Conclusions

The regio- and chemoselectivities observed in the photoreactions of the iodonium salts **1**-**8** lead to the proposal for the mechanism of the photolysis of diphenyliodonium salts depicted in Scheme 8. The C-I$^+$ bond cleavages proceed from the triplet excited state. The bond fission occurs mainly heterolytically, yielding the open-shell aryl cations $^3\mathbf{I}_2$. Intermediates **I•** generated through homolysis, or through electron transfer from $^{3}\mathbf{I}_2$, play a minor role. This proposal is supported by the results of the theoretical evaluation of the bond cleavage reactions.

Scheme 8: Proposed mechanism of photolysis of diphenyliodonium salts.



If $^{3}\mathbf{I}_2$ is destabilised by an EWG, the triplet to singlet cation conversion is faster than trapping by the internal nucleophiles iodobenzene or bromide anion. In that case the $^{1}\mathbf{I}_2$ state is trapped by the internal π nucleophile iodobenzene. Further isomerisation leads to $^{1}\mathbf{I}_1$ which may be trapped by external nucleophiles such as methanol.

In the presence of the external n- and π-nucleophile anisole an almost uniform product pattern is found in all irradiations. The time necessary for the $^{3}\mathbf{I}_2$ intermediates formed in the irradiation of **1**-**7**, to react with anisole, is enough to almost completely isomerise to their $^{1}\mathbf{I}_1$ ground state and react as such. The cation $^{3}\mathbf{I}_2$ formed in the photolysis of **8** is the ground state.

Experimental Section

Materials

All solvents are distilled prior to their use in synthesis. The iodonium salts **1**-**4** and **6**,**7** are synthesised from the corresponding, commercially available, 4-substituted phenyl boronic acids, according to an altered literature procedure[21,22]. 1.61 g of (diacetoxyiodo)benzene (5 mmol) is suspended in 40 mL dichloromethane. The white suspension is cooled to -30°C in a dry ice/ acetone bath and 1.63 mL of 54% w/w HBF_4 in diethyl ether (10 mmol) is added drop by drop. A yellow solution is formed. After stirring for 30 minutes the reaction mixture is cooled to -30°C and the *para*-substituted phenyl boronic acid (5 mmol) is added. The mixture is stirred until all boronic acid has dissolved. If after two hours of stirring still some phenyl boronic acid is left, the mixture is filtered. The reaction mixture is dried with $MgSO_4$. Most of the dichloromethane is evaporated until about 5 mL solution is left. Diethyl ether is added dropwise which causes the raw product to precipitate. The white crystals are filtered and washed with diethyl ether. The products are crystallised three times from dichloromethane/ ether. Yields ± 80%. NMR (^1H, $CDCl_3$, 300 MHz): **1**: 7.50-7.56 (t, 4H); 7.66-7.72 (t, 2H); 8.15-8.19 (d, 4H). IR (neat, cm^{-1}): 447, 458 ($C\text{-}I^+$)[35], 521, 647-682-746 (peaks characteristic of diphenyliodonium salts), 1020 (broad, peak BF_4^-), 3090. **2**: NMR (^1H, $CDCl_3$, 300 MHz) 2.40 (s, 3H); 7.32-7.36 (d, 2H); 7.48-7.54 (t, 2H); 7.64-7.70 (t, 1H); 8.01-8.05 (d, 2H); 8.11-8.15 (d, 2H). IR (neat, cm^{-1}): 448, 479, 522, 650-676-744, 1020, 3090. **3**: NMR (^1H, CD_3OH 300 MHz) 1.35-1.41 (t, 3H); 3.96-4.04 (q, 2H); 6.88-6.92 (d, 2H); 7.37-7.43 (t, 2H); 7.51-7.57 (t, 1H); 7.93-7.98 (d, 4H). IR (neat, cm^{-1}): 454, 508, 520, 654-678-739, 1020, 1256 (C-O), 2983, 3099. **4**: NMR (^1H, CD_3OH, 300 MHz) 7.53 (t, 2H); 7.69-7.75 (t, 1H); 7.79-7.83 (d, 2H); 8.21-8.24 (d, 2H); 8.34-8.38 (d, 2H). IR (neat, cm^{-1}): 452, 493, 524, 654-678-746, 1020, 1322 (C-F), 1400, 3099. **6**: NMR (^1H, CD_3OH, 300 MHz) 7.53-7.59 (t, 2H); 7.70-7.76 (t, 1H); 7.84-7.88 (d, 2H); 8.19-8.23 (d, 2H); 8.30-8.34 (d, 2H). IR (neat, cm^{-1}): 457, 521, 543, 654-680-750, 1020, 2248 ($C\equiv N$), 3093. **7**: NMR (^1H, CD_3OH, 300 MHz) 2.61 (s, 3H); 7.52-7.58 (t, 2H); 7.68-7.74 (t, 1H); 8.04-8.08 (d, 2H); 8.19-8.22 (d, 2H); 8.27-8.30(d, 2H). IR (neat, cm^{-1}): 459, 522, 654-683-714, 1020, 1670 (C=O), 3090.

In order to synthesise **5,** 4-iodobenzoic acid is esterified to 4-iodobenzoic acid methyl ester according to a literature procedure[36]. This ester is oxidised to 4-iodobenzoic acid methyl ester diacetate[37]. From this compound **5** is synthesised by reacting it with phenyl boronic acid using the procedure described above. Yield = 75%. NMR (^1H, CD_3OH, 300 MHz): **5** 4.02 (s, 3H); 7.61-7.68 (t, 2H); 7.78-7.84 (t, 1H); 8.17-8.21 (d, 2H); 8.26-8.30 (d, 2H); 8.33-8.37 (d, 2H). IR (neat, cm^{-1}): 448, 471, 519, 652-679-748, 1020, 1303 (C-O), 1704 (C=O), 2950, 3090.

Iodonium salt **8** is synthesised from 4-N,N-dimethylaminobenzeneboronic acid (5 mmol) en hydroxy(tosyloxy) iodobenzene (Koser's reagent) (5 mmol) in THF. The reaction mixture is stirred for 90 min at 0°C. Evaporation of THF leaves a green product: the tosylate salt of **8**. This product is dissolved in dichloromethane and the solution is washed three times with a saturated KBr solution in water. The organic layer is dried with $MgSO_4$ and evaporated. Crystallisation from dichloromethane/pentane for three times yields green powderish bromide salt **8** in 28%. NMR (^1H, CD_3OH, 300 MHz): 3.03 (s, 6H); 6.72-6.79 (d, 2H) 7.45-7.52 (t, 2H); 7.60-7.66 (t, 1H); 7.86-7.92 (d, 2H); 8.00-8.04 (d, 2H). IR (neat, cm^{-1}): 456, 502, 652- 682-746, 1063 cm^{-1} (C-N), 1599 cm^{-1} (C=C), 2850 cm^{-1}, (C-H); 3090 cm^{-1}.

Table S1: UV-Vis spectra of **1**-**8** in methanol and acetonitrile (λ in nm, ε in $M^{-1}cm^{-1}$).

	S	$\lambda_{max, MeOH}$	ε_{max}#	ε_{254}#	$\lambda_{max, ACN}$	ε_{max}#	ε_{254}#
1	H	225.9	$2.56*10^4$	$4.21*10^3$	229.1	$2.02*10^4$	$9.10*10^3$
2	CH_3	244.9	$2.61*10^4$	$2.12*10^4$	250.0	$1.74*10^4$	$1.68*10^4$
3	OCH_2CH_3	247.0	$1.82*10^4$	$1.56*10^4$	251.1	$1.55*10^4$	$1.52*10^4$
4	CF_3	226.0	$1.75*10^4$	$1.76*10^3$	226.0	$2.14*10^4$	$8.52*10^3$
5	$C(O)OCH_3$	236.0	$1.83*10^4$	$6.68*10^3$	238.0	$2.60*10^4$	$6.68*10^3$
6	CN	236.9	$3.17*10^4$	$9.61*10^3$	239.0	$2.93*10^4$	$1.54*10^4$
7	$C(O)CH_3$	244.0	$3.36*10^4$	$2.35*10^4$	244.0	$0.27*10^4$	$2.09*10^4$
8	$N(Me)_2$	304.0	$2.03*10^4$	$1.37*10^4$	311.1	$1.70*10^3$	$1.95*10^4$

ε_{max} is absorption coefficient at maximum absorption, ε_{254} is absorption coefficient at λ = 254 nm.

Photochemistry

The photochemical reactions in methanol were carried out in quartz tubes equipped with a rubber seal, that are placed in a merry-go-round apparatus. A Hanau TNN-15/32 low pressure mercury lamp placed in a water cooled quartz tube is used to supply light with a main emission at λ = 254 nm. For the irradiations 0.02 M solutions of the iodonium salts **1**-**8** in 10 mL methanol are prepared. 25 µL n-decane is added as internal standard. Samples (200 µl) are taken at t = 0, 5, 10, 15, 20, 25, 30, 40, 50, 60, 70 and 90 minutes of irradiation. Up till that time the conversions are still low and all products are primary products. The samples are added to 500 µL water and 300 µL ethylacetate. The organic layers are analysed by GC and GC-MS. The 90 minutes irradiation mixtures are poured in 50 mL water and extracted with 10 mL ethylacetate. The organic layer is separated and dried with $MgSO_4$. The solvent is evaporated and the residues were redissolved in 0.5 mL dichloromethane for GC and GC-MS analysis.

The photochemical reactions in acetonitrile/anisole were carried out in quartz tubes equipped with a rubber seal. The starting materials were dissolved at 0.02 M in 10 mL 1/1 acetonitrile/anisole. 25 µL *n*-Decane was used as internal standard. The tubes were placed in a Rayonet Reactor (RPR200) fitted with seven 254 nm lamps and stirred. The photolyses of the salts **1**-**8** were followed as a function of time by taking aliquots (0.2 mL sample) and adding them to 0.5 mL water + 0.3 mL ethylacetate. The organic layers were analyzed by GC and GC-MS.

Photoproducts

The assignment of the structures by GC and GC-MS was confirmed by coinjection of commercially available or independently prepared products. Products **9**, **11**, **12**, **13**, **14**, **16**, **17**, **18** and **20*o*, *m*, *p*** are commercially available. Products **10a**-CH_3/**10b**-CH_3 and **10a**-OCH_2CH_3/**10b**- OCH_2CH_3 are prepared by reacting benzenediazonium tetrafluoroborate with **9**-CH_3 and **9**-OCH_2CH_3 in acetonitrile. The reaction mixtures were diluted with ethylacetate and used as such for coinjection. The Friedel-Crafts products **15**-H are prepared by reacting benzenediazonium tetrafluoroborate with iodobenzene in acetonitrile (1/1). The ethylacetate-diluted product mixture is used for coinjection. The structures of all other products **15** (Table 4) are assigned tentatively. The *ipso*-substitution products **19** were prepared photochemically from either **9** or **17** and benzene, dissolved in acetonitrile (1/1) at λ_{exc} = 254 nm in a RPR200 Rayonet reactor. The irradiation mixtures were poured in water and extracted with ethylacetate. Products **21** are prepared photochemically by reacting **9** with anisole dissolved in acetonitrile under the same reaction conditions as used for **19**.

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. ^1H-NMR spectra were recorded on a DMX 300, using DMSO D_6 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.

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[30] I am not sure whether **8**-**m** is a mesomer or an isomer of **8**. Crystal structures of phenyliodonium salts indicate an actual bond between iodine and the counter-ion, a structure often referred to as λ^3 iodane [Ochiai, M. in *Top. Curr. Chem. 224*, Wirth, T. Ed. Springer-Verlag: Heidelberg-Berlin: **2003**, p. 7]. The UV-Vis spectrum of **8** suggests a large delocalisation of the positive charge. If (near) complete transfer of the positive charge to nitrogen is achieved and the shift is accompanied by a reorientation of the counter-ion to near the nitrogen atom, the resulting structure is formally an isomer of **8**. Such a structure is reminiscent of that of iodonium ylides which are calculated to possess significant double bond character [a) Moriarty, R. M.; Bailey, B. R.; Prakash, O.; Prakash, I. *J. Am. Chem. Soc.* **1985**, *107*, 1375-1378 b) Camacho, M. B.; Clark, A. E.; Liebrecht, T. A.; DeLuca, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 5210-5211 c) Krimse, W. *Eur. J. Org. Chem*. **2005**, 237-260]. Since no accurate structural data on (molecules like) **8** are available and complete reorientation of the counter-ion is not proven, the term mesomer is maintained.

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Chapter 3 | Photogeneration and reactivity of 4-aminophenyl and 4-hydroxyphenyl cations; the influence of the leaving groups

Introduction

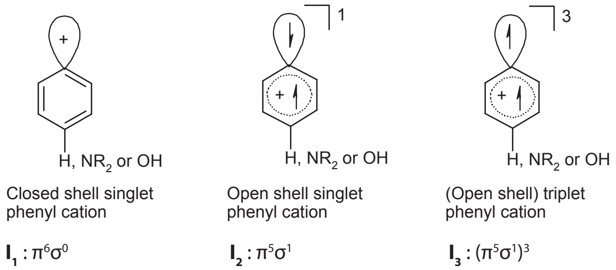
For quite some time now phenyl cations have been proposed as reactive intermediates, mainly in the thermal solvolysis of phenyldiazonium salts[1,2]. Even today the actual mechanism of this thermal dediazoniation reaction is still a matter of debate[3]. Unequivocal means to generate phenyl cations are the radiolytic extrusion of helium from tritiated aromatic compounds[4], and photolytic dediazoniation of photolabile benzenediazonium salts that proceed through an unimolecular mechanism[2,5]. These methods allowed studies of the reactivity of phenyl cations[6], but until recently only singlet species were synthesised[7].

Photochemistry allows preferential generation of triplet excited states over singlet excited states[8]. Appropriate substituents enhance intersystem crossing (ISC) which leads to efficient conversion of the singlet excited state formed after absorption of a photon into a triplet excited state. Alternatively, by adding a suitable sensitiser and by using selective excitation, the photolabile compound will be formed directly in a triplet excited state, by triplet energy transfer. Dissociation of a bond in a triplet excited state yields the reactive intermediate in its triplet manifold and a leaving group. This has been e.g. demonstrated in the photolysis of 4-nitro- and 4-acetyl substituted phenyldiazonium salts[9]. Both substituents enhance ISC which yields triplet phenyl cations as product-forming intermediates, even though the singlet state of these phenyl cations is of lower energy. The reactivity of the phenyl cation thus is a function of the type of substituent (and its position) at the precursor and not necessarily of the stability of the cation itself. A curiosity-driven study was started whether or not it is possible to generate a singlet phenyl cation as product-forming intermediate that possesses a triplet ground state.

Of the parent phenyl cation[10] the singlet closed shell ($\pi^6\sigma^0$) ground state ($^1A_1$) is calculated at the CAS-MP2 level to be 24.6 kcal/mol more stable than the triplet ($\pi^5\sigma^1$) phenyl cation ($^3B_1$)[11]. The open-shell ($\pi^5\sigma^1$) singlet phenyl cation ($^1B_1$) is computed to be 14 kcal/mol higher in energy than the $^3B_1$ cation. At other levels of theory larger or smaller differences are calculated but the trend in stabilities of the isomers stays the same[3e,12,13].

Amino- or hydroxy substituents positioned at the *para* position of a phenyl cation change the order of stability of the isomers[14]. The open-shell triplet phenyl cation $\mathbf{I_3}$ is calculated to be 9 kcal/mol more stable than (amino group), or about equal in energy with (hydroxy group), the closed-shell singlet phenyl cations $\mathbf{I_1}$[15]. Singlet open-shell structures $\mathbf{I_2}$ were not included in these calculations.

Figure 1: The phenyl cations.

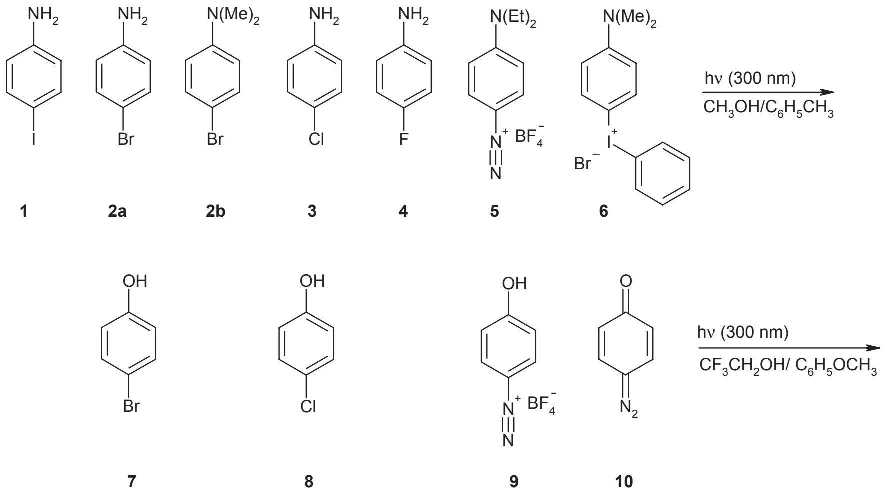


Reports in the literature suggest that the photolysis of 4-chloroaniline is a good entry to the 4-aminophenyl cation in its triplet ground state[16]. In the first part of this work, 4-chloroaniline is therefore subjected to competition experiments with various nucleophiles, which chart the chemoselectivity and the regioselectivity of the alleged phenyl cation intermediate.

With this information in hand, the photochemical behaviour of 4-iodoaniline (**1**), 4-bromoaniline (**2a**), 4-bromo-N,N-dimethylaniline (**2b**), 4-chloroaniline (**3**), 4-fluoroaniline (**4**), N,N-diethylaminobenzenediazonium tetrafluoroborate (**5**) and 4-N,N-dimethylaminophenyl-(phenyl)iodonium bromide (**6**) in methanol in the presence of toluene is compared (Chart 1). The product patterns obtained as a function of the leaving group reflect the reactivity and thus the nature of various 4-aminophenyl cations.

Next, the photochemistry of the 4-hydroxy substituted phenyl cation precursors 4-bromophenol (**7**), 4-chlorophenol (**8**), and 4-hydroxybenzenediazonium tetrafluoroborate (**9**) is studied

Chart 1: Compounds studied.



in trifluoroethanol in the presence of anisole. For purpose of reference and to probe the importance of deprotonation of the 4-hydroxyphenyl cation[17], 4-diazoquinone (**10**) is irradiated under the same reaction conditions.

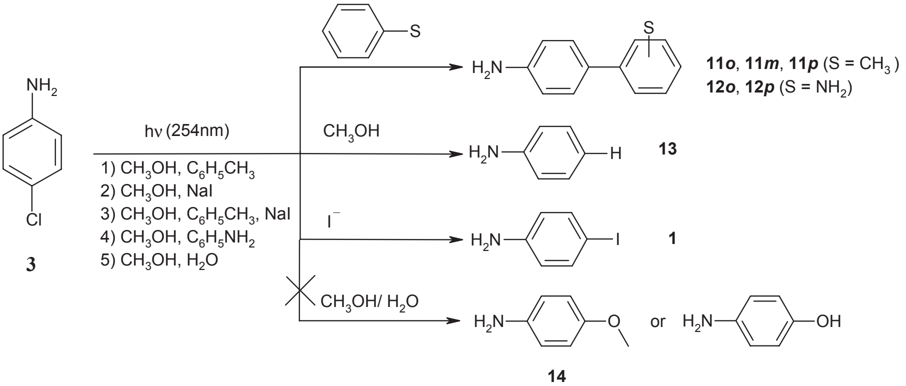
Finally, the structures and stabilities of the singlet and triplet isomers of the 4-aminophenyl and the 4-hydroxyphenyl cations **I**$_1$, **I**$_2$ and **I**$_3$ were studied by quantum chemical methods.

Results

*Photolysis of 4-chloroaniline (**3**), competition experiments*

The photoreaction of **3** at λ_{exc} = 254 nm was carried out at 0.05 M in methanol in the presence of the nucleophiles toluene (1/1 v/v), iodide (NaI, 0.05 M), a combination of the latter two, and aniline (1/1 v/v). Also the effect of the presence of water (2% and 1 v/v) was evaluated. The primary photoproducts under the various reaction conditions are depicted in Scheme 1.

Scheme 1: The photolysis of **3**, competition experiments.



(1) The photolysis of **3** in methanol in the presence of toluene yields the Friedel-Crafts products 2'-, 3'- and 4'-methyl-4-aminobiphenyl (**11*o***, **11*m*** and **11*p***) in a 78:4:18 ratio, next to the reductive dehalogenation product aniline (**13**). Also 2,4'-aminophenyl-4-chloroaniline is formed in trace amount. (2) With 0.05 M NaI in methanol, the main product is 4-iodoaniline (**1**). Reduction product **13** is produced as well. (3) With toluene as extra nucleophile, **11*o***, ***m***, ***p*** and **1** are the major products accompanied by some aniline (**13**). (4) The photolysis of **3** in methanol in the presence of aniline produces 2'- and 4'-amino-4-aminobiphenyl (**12*o***, **12*p***) in a 88:12 ratio. As side product diazobenzene is formed. (5) The presence of water in methanol does not change the product pattern: In methanol with 2% water and in methanol/water 1/1

v/v, the only photoproduct is aniline (**13**). In all five reactions no 4-aminoanisole (**14**) or 4-aminophenol is produced.

Photogeneration of 4-amino substituted phenyl cations

The irradiations of the 4-haloanilines **1**, **2a, 2b** and **4** (λ_{exc} = 300 nm) at 0.05 M in methanol/toluene (1/1 v/v) all yield the same types of products as the photolysis of **3** (Scheme 1). Differences occur in the conversions and the product profiles (Table 1, entries 1-5). The conversion of starting material is less efficient in the photoreaction of **1**, **2a** and **2b** than with **3** and **4**. The yield of the Friedel-Crafts arylation products **11*o***, **11*m***, **11*p*** is lowest in the photolysis of **1**, **2a** and **2b** and highest in the photoreaction of **3** and **4**. Photoreduction, producing **13**, is not a major product-forming route in the photolysis of **3** and **4** but becomes more important in the photolysis of **2a** and **2b**, and is the major product-forming route in the irradiation of **1**.

A typical feature of these photoreactions is the *o*: *m*: *p* ratio of the Friedel-Crafts products **11**. A low yield of *meta* isomer is obtained with **2a**, **2b**, **3** and **4** whereas in the photolysis of **1** the *meta* and *para* isomer yields are practically the same.

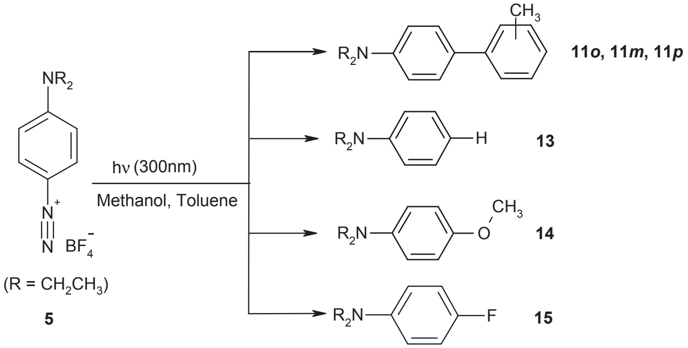
Table 1: Results of the photolyses of **1**-**6** (0.05 M) in methanol/toluene (1/1) at λ_{exc}= 300 nm[a].

Compound	LG	s.m. left	11	11*o*: *m*: *p*	13	14
1	I^-	70	6	79:10:11	20	-
2a	Br^-	87	8	83:6:11	5	-
2b	Br^-	86	7	79:6:15	6	-
3	Cl^-	32	58	78:4:18	6	-
4	F^-	37	53	78:3:19	8	-
5[b]	N_2	nd.	42	65:5:29	6	32[d]
6[b]	PhI	nd.	22[c]	73:8:19	5	6

[a] Percentages of total product formation (GC) after 2 hrs. of irradiation, nd = not determined. [b] Percentages after 1 hour of irradiation. [c] Also arylation of the leaving group occurs yielding **17a** and **17*o***, **17*m***, **17*p*** (*o*, *m*, *p* ratio 73:3:35) in 7%. [d] Also another nucleophilic substitution product, **15**, is formed in 6%.

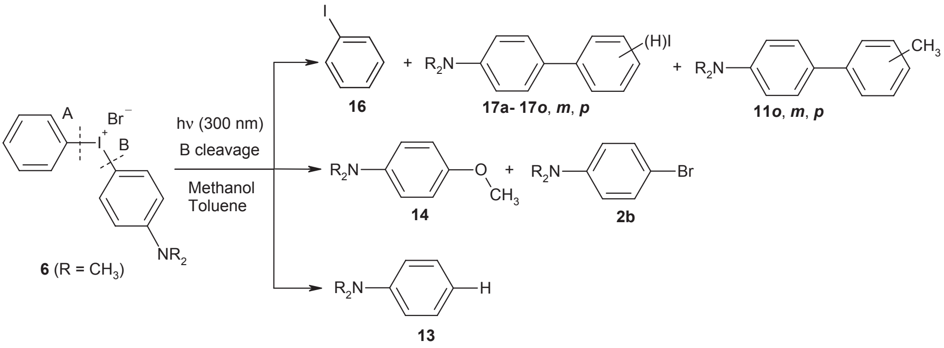
In the photolysis of 4-N,N-diethylaminophenyldiazonium tetrafluoroborate (**5**) in methanol/toluene the main products are 2', 3' and 4'-methyl-4-N,N-diethylaminobiphenyls **11*o***, **11*m***, **11*p*** (R = CH_2CH_3), the Friedel-Crafts products with toluene (Scheme 2). An unusually high percentage of **11*p*** is found (Table 1, entry 6). Here, the nucleophilic substitution product with methanol, 4-N,N-diethylaminoanisole (**14**, R = CH_2CH_3) is also a major product. Minor products are the Schiemann product 4-fluoro-N,N-diethylaminobenzene (**15**) and the reduction product N,N-diethylaniline (**13**, R = CH_2CH_3).

Scheme 2: The photolysis of **5**.



In the photolysis of 4-N,N-dimethylaminophenyl(phenyl)iodonium bromide (**6**) products of cleavage of both C-I bonds are formed but only the products resulting from the cleavage of bond B will be discussed (Scheme 3). Next to the leaving group iodobenzene (**16**), the Friedel-Crafts type products 4-N,N-dimethylaminobiphenyl (**17a**), 2'-, 3'- and 4'-iodo-4-N,N-dimethylamino-biphenyl (**17*o***, **17*m***, **17*p***) and 2'-, 3'- and 4'-methyl-4-N,N-dimethylaminobiphenyl (**11*o***, **11*m***, **11*p***, R = CH_3) are produced, as well as the nucleophilic substitution products 4-methoxy-N,N-dimethylaniline (**14**, R = CH_3) and 4-bromo-N,N-dimethylaniline (**2b**). Also the reduction product N,N-dimethylaniline (**13**, R = CH_3) is formed (Scheme 3, Table 1, entry 7).

Scheme 3: The photolysis of **6**: B bond cleavage products.



Photogeneration of 4-hydroxy substituted phenyl cations

The photolyses of 4-bromo- and 4-chlorophenol (**7**, **8**) in trifluoroethanol in the presence of anisole produce the Friedel-Crafts products 2'-, 3'-, 4'-methoxy-4-hydroxybiphenyls (**18*o***, ***m***, ***p***) and the reduction product phenol (**19**). Little or no nucleophilic substitution product 4-trifluoroethoxyphenol (**20**) is formed (Scheme 4, Table 2). The photolysis of *para*-hydroxy-benzenediazonium tetrafluoroborate (**9**) yields a larger amount of ether **20** next to the biaryls

18*o*, ***m***, ***p***, and phenol (**19**). The photoreaction of 4-diazoquinone (**10**) under the same reaction conditions produces the same products (**18*o***, ***m***, ***p***, **19** and **20**) albeit in a different ratio. The photoconversion of **8** is about twice as efficient as that of **7**, under the same reaction conditions. The photolyses of **7** and **9** on one hand and **8** and **10** on the other hand produce **18** in quite different *o*, *m*, *p* ratios.

Scheme 4: The photolyses of **7**-**10**.

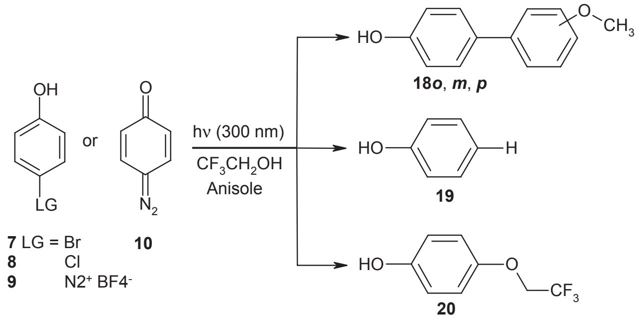


Table 2: Results of the photolyses of **7**-**10** (0.05 M) in trifluoroethanol/ anisole 1/1 v/v, at λ_{exc} = 300 nm[a].

Compound	**LG**	**s.m. left**	**18**	**18*o*:*m*:*p***	**19**	**20**
7[b]	Br^-	32	16	66:14:20	28	0.5
8	Cl^-	18	55	80:1:19	3.5	-
9[c]	N_2	nd.	40	66:9:25	9.2	3.1
10	N_2	nd.	74	72:0:28	1.1	2.7

[a] Percentages of total yield (GC) after 2 hrs of irradiation. [b] In this irradiation also some 4-bromoanisole is formed. This side product may stem from photoinduced electron transfer followed by cleavage of the C-Br bond of the radical anion and subsequent recombination of the bromide anion with the radical anion of anisole. [c] Percentages after 1 hour of irradiation.

Quantum chemical studies

To get insight in the mechanisms of reaction of the 4-aminophenyl cation and the 4-hydroxyphenyl cation, it is useful to inspect the electronic states of these ions. The relative energies of the 4-aminophenyl- and 4-hydroxyphenyl cation isomers $\mathbf{I}_1$-$\mathbf{I}_3$ are calculated[18] at the CASSCF(8,8)/6-31G(d)//CASSCF(8,8)/6-31G(d) level and the CASSCF(4,5)/6-31G(d)//CASSCF(4,5)/6-31G(d) level, respectively, and compared with literature data on these cations[14,15] and the parent phenyl cation[11,13d] (Table 3). CASSCF(8,8) level of theory calculations on the 4-hydroxyphenyl cation have not yet been successful. For the first time the open-shell singlet phenyl cations $\mathbf{I}_2$-NH_2 and $\mathbf{I}_2$-OH are considered as actual reactive intermediates.

Table 3: Relative stabilities of the 4-amino and 4-hydroxyphenyl cations **I_1**-**I_3** (kcal/mol).

	Parent[11]	**I**-NH_2	**I**-NH_2[15]	**I**-OH	**I**-OH[15]
Closed-shell singlet (**I_1**)	0	0[a]	0	0[b]	0
Non-planar singlet (**I_1'**)	-	-17.5[a]	-	-4.2[b]	-
Open-shell Singlet (**I_2**)	+38.6	-17.1[a]	-	+3.1[b]	-
Open-shell Triplet (**I_3**)	+24.6	-33.6[a]	-9.0	-11.5[b]	0.2

[a] CASSCF(8,8)/6-31G(d)//CASSCF(8,8)/6-31G(d). [b] CASSCF(4,5)/6-31G(d)//CASSCF(4,5)/6-31G(d).

The parent phenyl cation can be considered as a benzene molecule minus a hydride ion[14]; in that case six π electrons (occupying 3 molecular orbitals) and one vacant σ orbital are present. There are two planes of symmetry, i.e. the plane in which the nuclei lie and a plane orthogonal thereupon: the cation has C_{2v} symmetry[11-14]. The closed-shell singlet state (**I_1**) is represented as structure **I_1** ($\pi^6\sigma^0$) (Figure 1). It is also possible that the vacant orbital is occupied by one of the π electrons; the open-shell structure ($\pi^5\sigma^1$) is either a singlet (**I_2**) or a triplet state (**I_3**). (structures **I_2** and **I_3** in Figure 1). Published ab initio molecular orbital calculations indicate that the ground state of the parent phenyl cation is a singlet closed shell species ($\pi^6\sigma^0$)(**I_1**)[11]. At the CAS-MP2 level of calculation this state is 24.6 kcal/mol more stable than the triplet ($\pi^5\sigma^1$) state (**I_3**). The open-shell ($\pi^5\sigma^1$) singlet phenyl cation (**I_2**) is computed to be 14 kcal/mol higher in energy than the **I_3** cation at the optimum geometry of the phenyl radical. At the B3LYP/6-31G* level of calculation smaller energy gaps between **I_1**, **I_3** and **I_2** were predicted: 0.0, 18.9 and 23.9 kcal/mol, respectively[13d]. It was noticed that optimisation of the **I_2** state leads to a structure that is a second order saddle point[11].

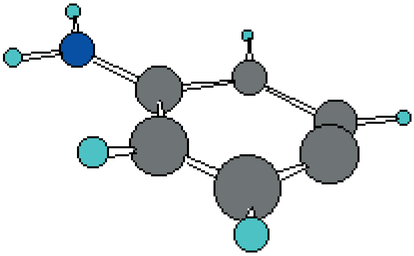
Already at calculations at the STO-3G level it was found that the geometries of the phenyl cation in the singlet **I_1** and triplet **I_3** state are quite different. In the singlet state the angle at the cationic center, α =147.3°, is widened with respect to the normal angle in benzene but not yet 180°. Thus the s character of the vacant orbital is reduced and the s character of the two other σ orbitals at the same atom is increased leading to a shortening of the C1-C2 and C1-C6 bond lengths. The triplet geometry is close to that of benzene (α =127.6°)[14].

The calculational results for the 4-aminophenyl cation (Table 3) differ from those for the parent phenyl cation. First, the order of stability for the lowest singlet and triplet state is inverted. The triplet 4-aminophenyl cation is calculated to be about 16 kcal/mol more stable than the lowest singlet 4-aminophenyl cation. Second, there are different changes in the geometry for the singlet state. Whereas in the triplet state the C_{2v} symmetry is preserved, the lowest singlet state has C_s symmetry; there is only one plane of symmetry, i.e. the plane in which the atoms lie. The width of the angle (α = 134.2°) is reduced with respect to the parent phenyl cation (α = 147.3°) and the 4-aminophenyl cation is no longer a planar molecule.

The CASSCF wave function for the singlet closed shell (**I_1**) state was poorly described by one single configuration as was published before[16b]. Assuming the 4-aminophenyl cation to be planar and symmetrical, like the parent phenyl cation, a construct of the closed shell and an open-shell structure can be made. In C_{2v} symmetry the electron configurations $\mathbf{I}_1$ and $\mathbf{I}_2$ have a different symmetry and will not interact. If planarity of the cation is not imposed, an interaction between the open-shell and the closed shell configurations occurs, leading to a lower singlet state $\mathbf{I}_1$' with α = 134.2° (Figure 2). The energy gap between the lowest singlet state and the planar state is small, only 0.4 kcal/mol. There are two mirror states $\mathbf{I}_1$', because the dihedral angle C1C2-C3C4 can be positive or negative. The planar state ($\mathbf{I}_2$) is probably a saddle point and acts as a barrier between the mirror states. These results indicate that the 4-aminophenyl cation in its lowest singlet state vibrates between two non-planar mirror geometries separated by a barrier very close in energy.

The ground state of the 4-hydroxyphenyl cation is CASSCF(4,5)/6-31G(d)// CASSCF(4,5)/6-31G(d) calculated to be a triplet ($\mathbf{I}_3$). The lowest singlet cation, just like the 4-aminophenyl cation, has C_S symmetry ($\mathbf{I}_1$') and is about 6 kcal/mol less stable than the triplet cation. The main difference with the aminophenyl cation is the energy gap between $\mathbf{I}_1$' and $\mathbf{I}_2$ which is larger with the 4-hydroxyphenyl cation. These results contradict published calculations on the 4-hydroxyphenyl cation that indicate that the singlet and triplet state are isoenergetic[15]. Calculations for the 4-hydroxyphenyl cations at the CASSCF(8,8)/6-31G(d) level of theory could not be completed before the publication of this thesis.

Figure 2: Structure of $\mathbf{I}_1$'-NH_2.



Discussion

Competition studies

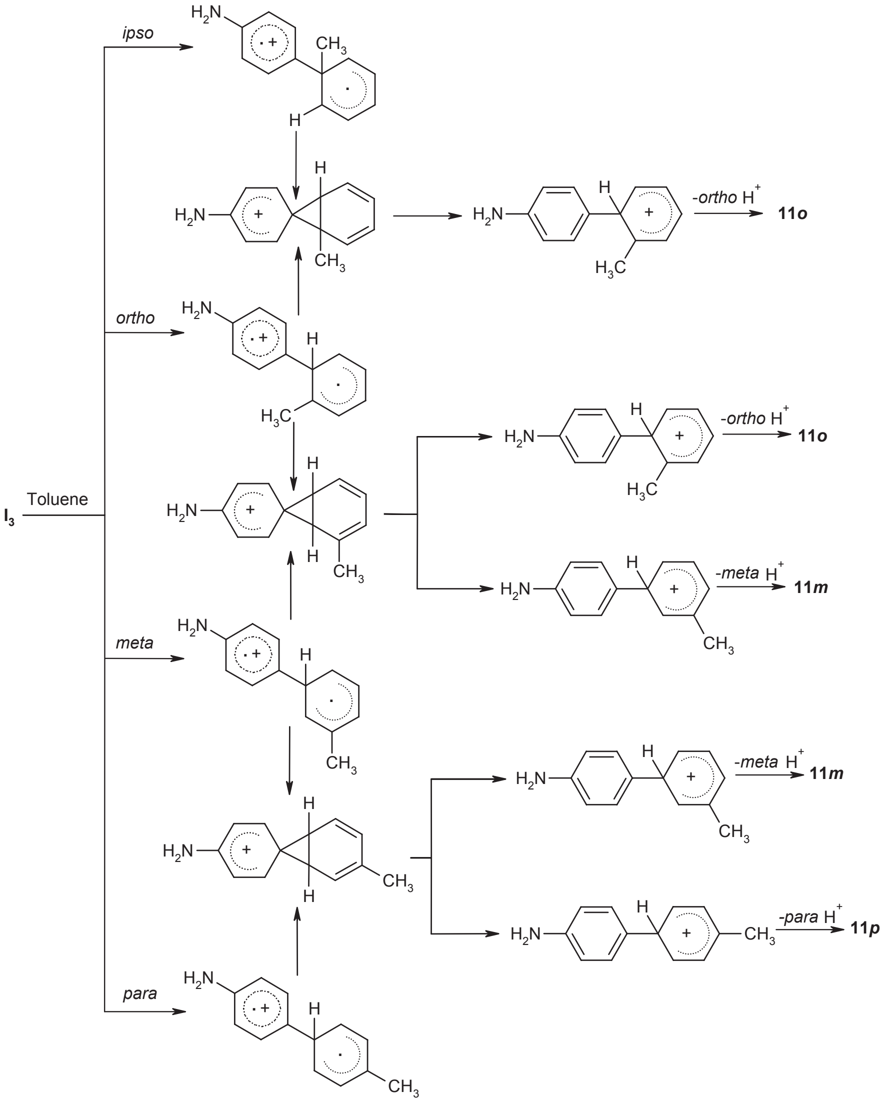
The product-forming intermediate in the photolysis of **3** is efficiently trapped by iodide, toluene, and aniline but not by methanol or water. In its reaction with toluene and aniline it shows a remarkable regioselectivity, *o*: *m*: *p* 73:4:23 and 88:0:12, respectively. As to the nature of the reactive species, four possibilities can be envisioned 1) It is a phenyl radical. 2) It is a non-planar singlet closed shell phenyl cation ($\mathbf{I}_1$'-NR$_2$. 3) It is a carbene like cation $\mathbf{I}_2$-NR$_2$. 4) It is a triplet phenyl cation $\mathbf{I}_3$-NR$_2$.

(1) The photolysis of iodobenzene, which is known to produce Ph•[19], under the same reaction condition as used for **3** yields **11** in an *o*: *m*: *p* ratio of 68:20:11. A similar ratio was found in the photolysis of dibenzoylperoxide, producing phenyl radicals, in toluene (*o*: *m*: *p* = 68:18:14[20]). These ratios, and especially the high yield of *meta* product, do not agree with the **11*o*: *m*: *p*** ratio produced in the photolysis of **3** in the presence of toluene. Further, the ratio between **11** and **13** in the phenyl radical reaction (1.1:1) is different from that in the photolysis of **3** (9.1:1). Finally, photohomolytic cleavage of the C-Cl bond of **3** is unlikely because C-Cl bond homolysis from the triplet excited state is endothermic[21]. Thus, a phenyl radical is not a (major) product-forming intermediate in the photolysis of **3**. (2) The non-planar singlet 4-aminophenyl cation ($\mathbf{I}_1$') is expected to display the same reactivity as the parent closed shell phenyl cation ($\mathbf{I}_1$). The radiolysis of ditritiobenzene, which produces the parent closed-shell singlet phenyl cation, in toluene yields **11** in an *o*: *m*: *p* ratio of 44:30:26[22]. The much lower *meta* methylbiaryl yield in the photolysis of **3** argues against the intermediacy of a singlet closed shell phenyl cation. (3) $\mathbf{I}_2$-NR$_2$ is expected to react like a singlet carbene or nitrene. Carbene and nitrene intermediates typically yield a low amount of *meta* product in their reaction with toluene (47:0:52 and 61:1:38 respectively)[23] as is the case in the photolysis of **3**. If $\mathbf{I}_2$-NR$_2$ is an intermediate in the photolysis of **3**, a ratio of **11*o***, ***m*** and ***p*** as with the carbene and nitrene intermediates may be expected. Such a ratio is not found. (4) Cation $\mathbf{I}_3$-NR$_2$ can be considered to be a triplet carbenoid species. The addition of $\mathbf{I}_3$ to toluene proceeds with the regioselectivity of the addition of a phenyl radical to toluene, producing a distonic triplet diradical cationic species (Scheme 5). After spin-inversion, this intermediate closes intra-molecularly to yield one or two cationic spiro-complexes. The spiro-intermediates preferentially open to their more stable cyclohexadienyl cation prior to the loss of a proton, leading to the methylbiaryl products **11**.

With aniline instead of toluene as substrate the preference for *ortho* biaryl formation is magnified while the percentage of *para* product is lower and the percentage of *meta* product is zero. This is completely in line with the mechanism proposed in Scheme 5. Attack of $\mathbf{I}_3$-NR$_2$ on aniline forms distonic diradical cation complexes just as in the reaction with toluene. The spin-inversion and closure to phenonium ions will also be similar. However, the preference for opening toward the more stable amino-substituted cyclohexadienyl complex will reflect the larger stability of the *ortho* and *para* amino isomers, compared to the *meta* isomer. Therefore formation of **12*o*, *p*** is heavily favored over formation of **12*m***.

The triplet cation $\mathbf{I}_3$-NR$_2$ as product-forming intermediate in the photolysis of **3** explains not only the regioselectivity toward arenes but also the distinct chemoselectivity toward n-nucleophiles and π-nucleophiles. Cation $\mathbf{I}_3$-NR$_2$ is a soft Lewis Acid and is not affected by a hard

Scheme 5: Mechanism of product formation upon attack of the triplet 4-aminophenyl cation $\mathbf{I_3}$-NR_2 on toluene.



Lewis base such as methanol or water. It is efficiently trapped, however, by toluene and aniline and even more so by the iodide anion, which are soft Lewis bases.

Presumably, the carbenoid cation $\mathbf{I_3}$-NR_2 also abstracts a hydrogen atom from the solvent (although less efficiently than it attacks π-nucleophiles) which produces the radical cation of aniline. This species forms aniline (**13**) by acquiring an electron. Formation of **13** via photo-homolytic cleavage of the C-Cl bond of **3** followed by hydrogen atom abstraction by the phenyl radical from the solvent is unlikely because C-Cl bond homolysis from the triplet excited state is endothermic[21] and because the product ratios found in the photolysis of **3** do not agree with a radical as intermediate (*vide supra*).

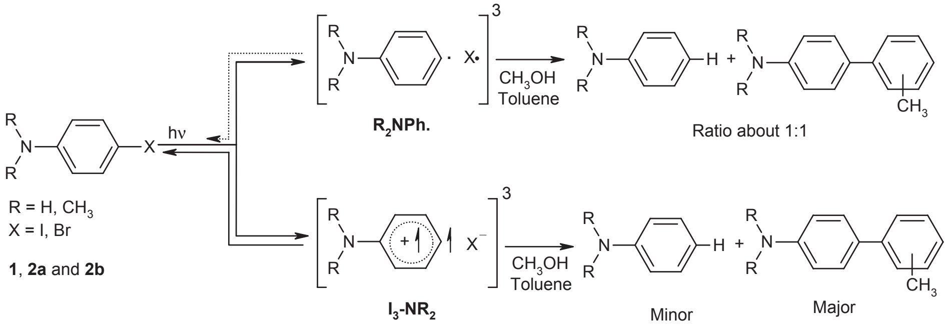
Triplet cation $\mathbf{I_3}$-NR_2 may have been formed via two routes. (1) Heterolytic cleavage of the C-Cl bond of singlet excited **3** produces singlet cation $\mathbf{I_1}$'-NR_2 ($\mathbf{I_2}$-NR_2) which spin-inverts to $\mathbf{I_3}$-NR_2. According to the MO calculations in Table 3, this spin-inversion is quite exothermic, which allows it to compete with reactions of $\mathbf{I_1}$'-NR_2 ($\mathbf{I_2}$-NR_2) with nucleophiles. (2) Singlet excited **3** intersystem crosses to triplet excited **3**, which cleaves to triplet $\mathbf{I_3}$-NR_2. All available experimental observations point to route (2). The involvement of triplet excited **3** is substantiated by triplet-triplet absorption studies using **3** and **4**[21]. Also, the S→T conversion quantum yield efficiencies of 4-halogen substituted anilines are high, the triplet excited states thus are efficiently formed[24]. Support for heterolysis from the triplet state is found in a recent microwave dielectric absorption measurement study of **3** which shows that the triplet excited state of **3** possesses ion pair character[25]. The fact that **3** photosolvolyzes readily in polar solvents[16], but refrains from doing so in apolar solvents is also supportive: a polar solvent makes the C-Cl bond heterolysis in the triplet state an exothermic process. Polar solvents stabilise both the charge transfer state and the development of charge in the elongating C-Cl bond.

The 4-Amino substituted phenyl cations

The photolysis of 4-iodoaniline (**1**) produces the biaryls **11*o***, ***m***, ***p*** in a ratio of 79:10:11 and **11** and reduction product **13** in a ratio of 1:3.3 (Table 1, entry 1). These results differ from the data of the photolysis of iodobenzene, which produces a phenyl radical[19], under the same reaction conditions (ratio **11*o***: ***m***: ***p*** is 68:20:11, ratio **11**: **13** is 1.1:1). Thus, the pattern of photoreactivity of **1** is unlike that of the aminophenyl radical, even though that species has been proposed as intermediate in the photolysis of **1**[21]. The results also differ from the data of the photolysis of **3**, which produces $\mathbf{I_3}$-NR_2 (ratio **11*o***, ***m***, ***p*** is 78:4:18, ratio **11**: **13** = 9.6:1): the product pattern is also not that of $\mathbf{I_3}$-NR_2. We propose that the pattern is due to the presence of two reactive intermediates, the 4-aminophenyl radical $R_2NPh•$ and the triplet cation $\mathbf{I_3}$-NR_2, side by side (Scheme 6).

The low overall yield, disproportionate to the low bond dissociation energy (BDE) of the C-I bond in the triplet excited state compared to that of the C-Cl or C-F bond[21], hints at a "hidden" reaction. One or both of the intermediates formed is efficiently trapped by the leaving group, remaking the starting material. The triplet radical pair $R_2NPh•$/ I• generated upon photolysis of **1**, will not recombine before singlet radical pair formation takes place. Radical $R_2NPh•$ is therefore expected to significantly react through hydrogen atom abstraction. On the other hand, cation $\mathbf{I_3}$-NR_2 is efficiently trapped by the iodide leaving group, as shown in the photolysis of **3** in NaI/ methanol (Scheme 1). This trapping reforms starting material and causes the

Scheme 6: The mechanisms of the photolyses of **1**, **2a** and **2b**; hidden reaction.



low productive yield. A fraction of **I_3**-NR_2 reacts out of cage, along with $R_2NPh\bullet$, with toluene which leads to the observed **11*o*, *m*, *p*** ratio.

The photolyses of bromoanilines **2a** and **2b** produce the biaryls **11*o*, *m*, *p*** in ratios of 83:6:11 (R=H) and 79:6:15 (R=CH_3) and **11** and **13** in ratios of 1.6:1 and 1.2:1. These data reflect the position of **2** in between **3** and **1**. As with **1**, homolysis and heterolysis probably occur side by side (Scheme 6). Here, also an "hidden" reaction takes place because the low overall yield is not in line with the BDE of the C-Br bond in the triplet excited state, compared to that of the C-Cl or the C-F bond[21]. The heterolytic cleavage of the C-Br bond is reversible but less so (and the heterolyses of the C-Cl or the C-F bond even less so) than the heterolytic C-I bond cleavage in the case of **1**, because bromide is a harder nucleophile than iodide. This leaves a larger fraction of **I_3**-NR_2 to react with toluene.

The photolysis of fluoroaniline **4** produces the same product-forming intermediate as **3** does: the triplet 4-aminophenyl open-shell cation **I_3**. This conclusion is based on the low yield of the *meta* product (the photoreactions of **3** and **4** produce **11*o*, *m*, *p*** in a ratio of 78:4:18 (with **3**) and 78:3:19 (with **4**)). Another indication for the intermediacy of **I_3**-NR_2 is the essentially equal preference for the formation of biaryls **11** over **13** (9.7: 1 with **3** and 6.6:1 with **4**). Further, no 4-aminoanisole (**14**), signalling the occurrence of the closed-shell singlet phenyl cation **I_1**-NR_2, is produced.

The photolysis of diazonium salt **5** produces the Friedel-Crafts products **11** (in an *o*, *m*, *p* ratio of 65:5:29) as well as the substitution products 4-methoxy-N,N-diethylaniline (**14**, R= CH_2CH_3) and 4-fluoro-N,N-diethylaniline (**15**) (Scheme 2). Both the *o*: *m*: *p* ratio, in particular the high percentage of *para* isomer, and the product profile however, are unlike any other ratio or profile observed thus far in this series of experiments (Table 1). The *o*: *m*: *p* ratio does not resemble the ratios observed with singlet phenyl cations, but does remind of the ratio obtained for triplet cation **I_3**-NR_2. On the other hand, the formation of O- and F-alkylation products **14** (R= CH_2CH_3)and **15** are typical for the closed-shell singlet cation **I_1**-NR_2. Is is proposed that the combination of singlet-type chemoselectivity and triplet-type regioselectivity is due to the closed-shell singlet phenyl cation **I**$_1$'-NR$_2$ in combination with the open-shell singlet phenyl cation **I**$_2$-NR$_2$ as the reactive intermediates responsible for product formation. After electronic excitation of **5**, extrusion of nitrogen takes place from the singlet excited state. This generates cation **I**$_1$'-NR$_2$ which is trapped, in part, by the solvent methanol, forming **14** and, in part, by the counter-ion BF$_4^-$, producing **15**. According to quantum chemical studies in vacuum (Table 3), **I**$_2$-NR$_2$ is slightly higher in energy than **I**$_1$**'**-NR$_2$. Formation of cation **I**$_2$-NR$_2$ from **I**$_1$'-NR$_2$ in solvent by intramolecular electron transfer may well be feasible. The species may exist next to each other.

I$_2$-NR$_2$ adds to toluene in a singlet carbene fashion and produces the spiro-complexes directly (Scheme 5). Opening to the more stable cyclohexadienyl cations and proton loss produce **11**. **I**$_2$-NR$_2$ may be responsible for a larger share of the product formation. In that case, methyl ether **14** is produced by trapping of **I**$_2$-NR$_2$ by methanol through singlet carbene type O-H bond insertion, instead of by trapping of **I**$_1$'-NR$_2$.

The photolysis of iodonium salt **6** through route B yields the Friedel-Crafts products **11*o***, ***m***, ***p*** and **17*o***, ***m***, ***p*** in ratios of 73:8:19 and 72:3:25, respectively. The relatively low percentages of *meta* product is reminiscent of results of the photolysis of **3** and **4** and thus are typical for **I**$_3$-NR$_2$ chemistry. The (acetone) sensitised irradiation of diphenyliodonium hexafluorophosphate, which presumably generates the parent **I**$_3$ yields Friedel-Crafts alkylation products in a similar ratio: 71:5:24[26]. The ratio of **11*o*, *m*, *p***, **17a** and **17*o*, *m*, *p*** to reduction product **13** (5.8:1) is alike the chemoselectivity of **I**$_3$-NR$_2$ in the irradiation of **3** (9.6:1) and **4** (6.6:1). The formation of **17a**, the *ipso* substitution product, is also conveniently explained with cation **I**$_3$-NR$_2$ as intermediate. Upon *ipso* addition to idobenzene a distonic diradical cation is formed, which after electron transfer and loss of an iodinium cation produces biphenyl **17a**.(For a more detailed discussion, see Chapter 2).

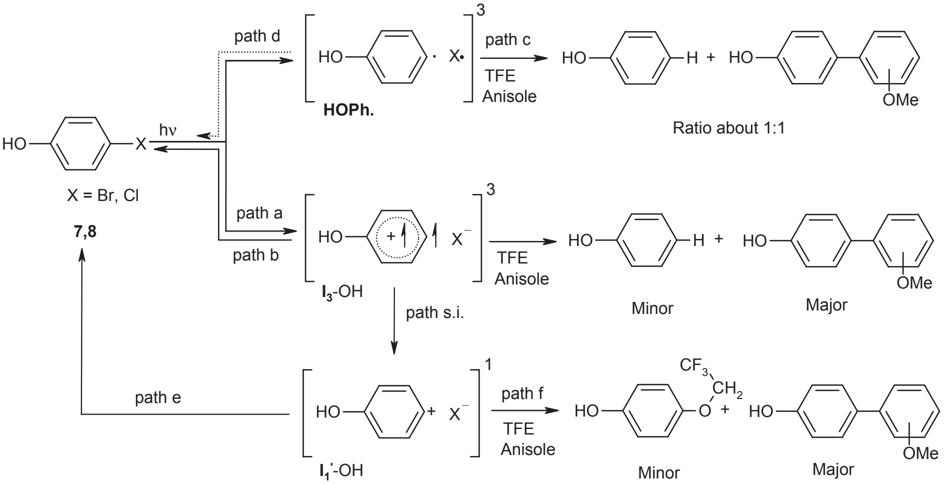
The nucleophilic substitution product 4-bromoaniline (**2b**) may also have been formed by trapping of **I**$_3$-NR$_2$, now by the counter-ion Br$^-$. As discussed earlier, HSAB considerations rationalise this: triplet cation **I**$_3$ is a soft Lewis acid while bromide is a relatively soft Lewis base.

The formation of ether **14** in the photolysis of **6** is not in agreement with triplet phenyl cation chemistry. The ether is either the trapping product of **I**$_1$'-NR$_2$ with methanol or the carbene type O-H bond insertion product of **I**$_2$-NR$_2$ with methanol, as proposed in the case of **5**. Thus, singlet excited **6** partially might cleave to **I**$_1$'-NR$_2$ (which next forms **I**$_2$-NR$_2$) and partially gives intersystem crossing to triplet excited **6** which cleaves to **I**$_3$-NR$_2$. This sequence of events is not the same as in the literature mechanism for diphenyliodonium photochemistry[27] (See also discussion in Chapter 2 and Scheme 7 in Chapter 4).

The 4-hydroxy substituted phenyl cations

The photoreaction of 4-bromophenol (**7**) produces the biaryls **18*o*, *m*, *p*** in a ratio of 66:14:20 (Table 2, entry 1). This ratio is quite similar to the one observed in the radiolysis of 1,4-ditritiobenzene in anisole (65:13:22)[22] and is therefore ascribed to the reactivity of the closed-shell singlet cation **I$_1$'**-OH (Scheme 7, path f). This conclusion does not contradict the expectation that the triplet excited state of **7** gives the C-Br bond fission and produces triplet cation **I$_3$**-OH (path a). The singlet 4-hydroxyphenyl cation minimum (**I$_1$'**-OH) is a non-planar closed shell species which is calculated to be less stable than the triplet state (**I$_3$**-OH) (Table 3). With the aid of a polar solvent, which reduces the energy gap between these species, it may be possible for the triplet cation **I$_3$**-OH, generated from the triplet excited state, to spin-invert to its singlet manifold **I$_1$'**-OH (Path s.i.). The quote of **I$_3$**-OH is efficiently trapped by the bromide anion (path b), while the fraction **I$_1$'**-OH is trapped less efficiently by bromide than by anisole. Some trapping of **I$_1$'**-OH also takes place by the poor nucleophile trifluoroethanol, yielding a small amount of ether **20** (path f) The excess of reduction product **19** formed relative to alkylation product **18** does not contradict a **I$_3$**-OH based machanism. As **I$_3$**-NR$_2$ in the photolysis of **1**, **2a** and **2b**, cation **I$_3$**-OH is effeciently trapped by the bromide leaving group, regenerating **7** (path b). The radical intermediate HOPh• is not trapped by the bromide atom (path d) and proceeds via a hydrogen atom abstraction to reduction product **19** (path c).

Scheme 7: The mechanisms of the photolyses of **7** and **8**.



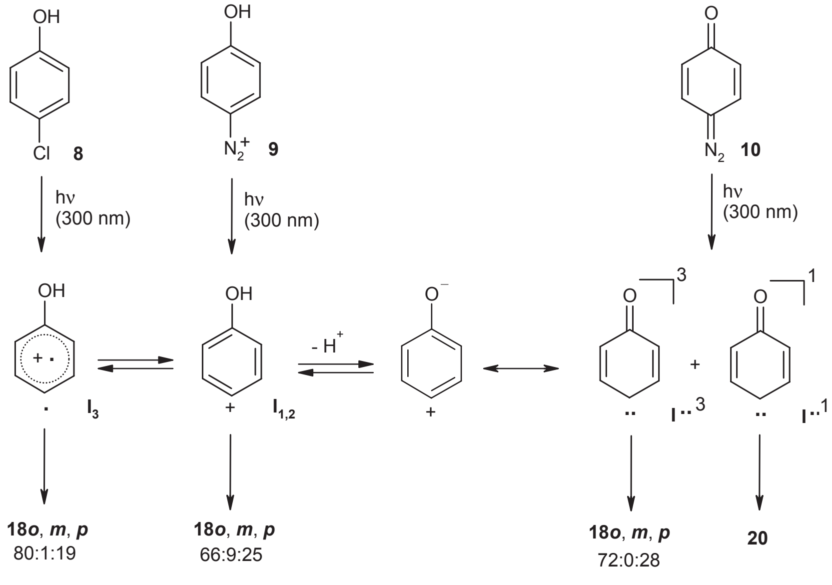
The photolysis of 4-chlorophenol (**8**) produces the biaryls **18*o*, *m*, *p*** in a ratio of 80:1:19 and **18** and the reduction product **19** in a ratio of 16:1. Such data pertain to triplet cation regioselectivity and chemoselectivity. Triplet cation **I$_3$**-OH is probably generated through cleavage of the C-Cl bond of the triplet excited state of **8**, just like in the photolysis of **3**[28] (path a). Contrary to the irradiation of **7**, the triplet cation **I$_3$**-OH is not trapped by the leaving group; path b does not apply to **8**. Also contrary to the irradiation of **7**, no ether **20** (path f) is found in the irradiation of **8**. Cation **I$_1$'**-OH produced from **I$_3$**-OH, is now trapped by the chloride anion (path e).

Photohomolysis and product-formation through hydrogen atom abstraction (path c) is not efficient with **8**.

The photolysis of diazonium salt **9** produces **18*o*, *m*, *p*** in a ratio of 66:9:25. That ratio has no obvious match with ratios typical for a closed-shell singlet phenyl cation (*o*: *m*: *p* = 65:13:22)[22], typical for a phenyl radical (*o*: *m*: *p* = 76:12:12)[19] or typical for the triplet cation $\mathbf{I_3}$-OH generated in the photolysis of **8** (80:1:19). It is proposed that, as in the case of **5**, more than one cationic reactive intermediate is responsible for product formation, most likely the closed-shell singlet cation $\mathbf{I_1}'$-OH and the open-shell singlet $\mathbf{I_2}$-OH. $\mathbf{I_2}$-OH adds to anisole in a singlet carbene fashion and forms spiro-complexes directly (see Scheme 5). These complexes open to the more stable cyclohexadienyl cations, which lose a proton and form **18**. The relatively high percentage of **18*p*** is due to that singlet carbenoid behaviour. The ether **20** is either the product of trapping of $\mathbf{I_1}'$-OH by trifluoroethanol or the product of trapping of $\mathbf{I_2}$-OH via carbene insertion in the O-H bond of TFE.

The photolysis of 4-diazo-2,5-cyclohexadien-1-one (**10**) yields the Friedel-Crafts products **18*o*, *m*, *p*** in a ratio of 72:0:28. The lack of *meta*-biaryl formation and the *o*/*p* ratio of about 2.5/1 are practically the same as the isomer ratios obtained in the reactions of 2,6-dichloro-oxocyclohexadienyl carbene[29] and tosylnitrene[30] with anisole. The photochemistry of **10** produces the 4-oxocyclohexadienyl carbene I••, probably of triplet nature[31,32] (Scheme 8). A stepwise addition to anisole gives spiro intermediates that rearrange to **18*o*, *m*, *p***. Ether **20** is presumably formed by carbene insertion into the O-H bond of TFE and subsequent rearrangement. Insertion is a typical singlet carbene type reaction[33].

Scheme 8: Product-forming intermediates in the photolyses of **8**, **9** and **10**.



4-Chlorophenol (**8**), the 4-hydroxybenzenediazonium salt **9** and 4-diazo-2,5-cyclohexadien-1-one (**10**) give **18*o, m, p*** in different ratios (Scheme 8). This shows that they have no common intermediate and answers the question whether or not the hydroxy cations $\mathbf{I_1}$ - $\mathbf{I_3}$ deprotonate to I••[17] prior to their reaction with nucleophiles, here with anisole. They do not.

Conclusion

The distinctive regioselectivities and chemoselectivities observed in the photolysis of the 4-aminophenyl cation precursors **1**-**6** demonstrate that these cations can be generated in different manifolds through different excited states. Whether a singlet or triplet cation is produced depends on the leaving group. With **1**-**4** (leaving groups: iodide, bromide, chloride and fluoride) cleavage of the carbon-halogen bond occurs in the triplet excited state yielding triplet cation $\mathbf{I_3}$-NR$_2$, which reacts much like a triplet carbene. With **5** (leaving group: nitrogen) cleavage occurs in the singlet excited state, which yields the non-planar closed-shell singlet cation $\mathbf{I_1}$'-NR$_2$ and the open-shell singlet cation $\mathbf{I_2}$-NR$_2$. Photolysis of **6** (leaving group: iodobenzene) gives both $\mathbf{I_3}$-NR$_2$ and $\mathbf{I_2}$-NR$_2$ (through $\mathbf{I_1}$'-NR$_2$). Similar observations have been made for the 4-hydroxyphenyl cation precursors **7**-**9**. With (bromide or) chloride as leaving group the triplet cation species $\mathbf{I_3}$-OH is produced, with nitrogen as leaving group the singlet cation(s) $\mathbf{I_2}$-OH (through $\mathbf{I_1}$'-OH). These intermediates do not deprotonate prior to their reaction with nucleophiles, as shown by the generation of that deprotonated species by photolysis of diazoquinone **10**. The assignments of the nature of the various phenyl cations are supported by the results of the CASSCF calculations.

Experimental Section

Materials

Starting materials **1**, **2a**, **2b**, **3**, **4**, **5**, **7** and **8** are commercially available. Aryl halides **1**, **2a**, **2b**, **3**, **4**, **7** and **8** were used as received. Diazonium salt **5** was dissolved in acetonitrile and crystallised with pentane prior to use. Compounds **9**[34] and **10**[35] were synthesised according to literature procedures. Iodonium salt **6** was prepared from 4-N,N-dimethylaminobenzene boronic acid and hydroxy(tosyloxy)iodobenzene (1/1 mol/mol) in 40 mL tetrahydrofuran at melting ice temperature. After stirring for 90 minutest he organic layer was evaporated. The residue was redissolved in dichloromethane and extracted 3 times with a saturated NaBr solution. The organic layer is dried with $MgSO_4$ and evaporated. The bromide salt obtained was purified by three crystallisations from dichloromethane and pentane. The yield of pure **6** was 28%. ^{1}H NMR (300MHz, MeOH d$_3$, δ): 2.9-3.1 (s, 6H), 6.7-6.8 (d, 2H), 7.4-7.5 (t, 2H), 7.6-7.7

(t, 1H), 7.8-7.9 (d, 2H), 8.0-8.1 (d, 2H). IR (neat): 457 cm^{-1}, medium ($C-I^+$)[36]; 652, 682, 745 cm^{-1}, strong, peaks characteristic of diphenyliodonium salts; 1063 cm^{-1}, medium (C-N); 1599 cm^{-1}, strong (C=C aromatic); 2850 cm^{-1}, weak (C-H methyl); 3050 cm^{-1}, weak (C-H aromatic). UV: in MeOH, λ_{max} = 304.0 nm, ε_{max} = 2.03 * 10^4 and in ACN, λ_{max} = 311.1 nm, ε_{max} = 1.70 * 10^3. Toluene and anisole were distilled under Argon to obtain GC purity. Diethyl ether, tetrahydrofuran and dichloromethane were distilled prior to use. Methanol, trifluoroethanol, toluene and anisole were Argon purged before 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 of the designated solvents mixtures. *n*-Decane was used as internal standard. For experiments followed in time, the solutions are placed in a merry-go-round apparatus. A Hanau low pressure Hg TNN-15/32 lamp placed in a water cooled quartz tube is used to supply light with a main emission at λ = 254 nm. The product studies were carried out in a Rayonet Reactor (RPR200) fitted with 7 254 nm or 300 nm lamps equipped with a magnetic stirrer. The photolyses were followed as a function of time by taking aliquots (0.050 mL sample). The samples of the photolyses of **1**, **2a**, **2b**, **3**, **4**, **7** and **8** were analyzed by direct injection of aliquots on GC and GC-MS. The aliquots of the irradiations of **5**, **6**, **9** and **10** were added 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.

Photoproducts

The products **1**, **2b**, **13**, **14** (R=H), **16**, **19** and **20** were identified by means of GC, GC-MS and coinjection with the commercially obtained reference samples. Of all *o*, *m*, *p* biaryl mixtures **11*o***, ***m***, ***p*** (R=H, CH_3, CH_2CH_3) the *ortho* and *para* isomers were independently synthesised, from commercially available starting materials, employing a literature Suzuki cross-coupling procedure[37]. Products **12*m*** and ***p*** were synthesised in two steps from 4-acetanilidobenzeneboronic acid and 3-bromo- and 4-bromoacetanilide. After Suzuki cross-coupling[38], the biaryls were deacetylated in ethanol/ hydrochloric acid[39]. Basic work-up gave the products, ready for coinjection. Biaryl **17a** was synthesised following a literature procedure[40]. Iodobiaryls **17*o***, ***m***, ***p*** were prepared (among other products) by heating a mixture of 0.02 mol diazotised 4-N,N-dimethylaminoaniline and 0.02 mol iodobenzene to 50°C for 12 hours. The assignment of the *o*, *m*, *p* isomers is based on the assumption that these products elude from the GC column in the usual order 1 = *ortho*, 2 = *meta*, 3 = *para*. Biaryls **18*o*** and **18*p*** were prepared through a literature Suzuki cross-coupling procedure[41]. Alkylaminoanisoles **14** (R=CH_3, CH_2CH_3) were prepared by refluxing 5% solutions of diazotised 4-N,N-dimethylaminoaniline or **5**, in methanol for 8 hrs, after evaporation of the solvent the product were ready for coinjection. Schiemann product **15** was prepared from **5**, according to literature[42]. Finally, commercially obtained 4-aminophenol was coinjected and observed to be no product in the photolysis of **3** in the presence of water.

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 Avance DPX 300 MHz, using CD_3OH 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.

Quantum Chemical Calculations

The relative stabilities of the 4-amino- and 4-hydroxyphenyl catios were evaluated with CASSCF instead of with (U)B3LYP methods because the latter may not be suitable for open-shell singlet species[43]. First, the relative stabilities of the 4-aminophenyl cations were CASSCF(2,2)/6-31G(d) calculated with C_{2v} symmetry. The singlet open-shell cation is lower in energy than the closed shell species. Both cations are found to be saddle points on the potential energy surface. With larger CASSCF and with the planarity of the cations let loose (CASSCF(8,8)/6-31G(d) level of theory) the non-planar closed shell species is a minimum and the open-shell species has become a saddle point. The minimum consists of two species with a positive and negative dihedral angle and with Cs symmetry.

For the 4-hydroxyphenyl cation the same approach was chosen. By the time of publication of this thesis only calculations at (4,5)CASSCF/6-31G(d) level of theory had been successful.

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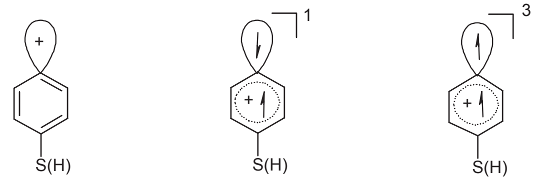
Chapter 4 | Fingerprints of singlet and triplet phenyl cations

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$_2$: $\pi^5\sigma^1$

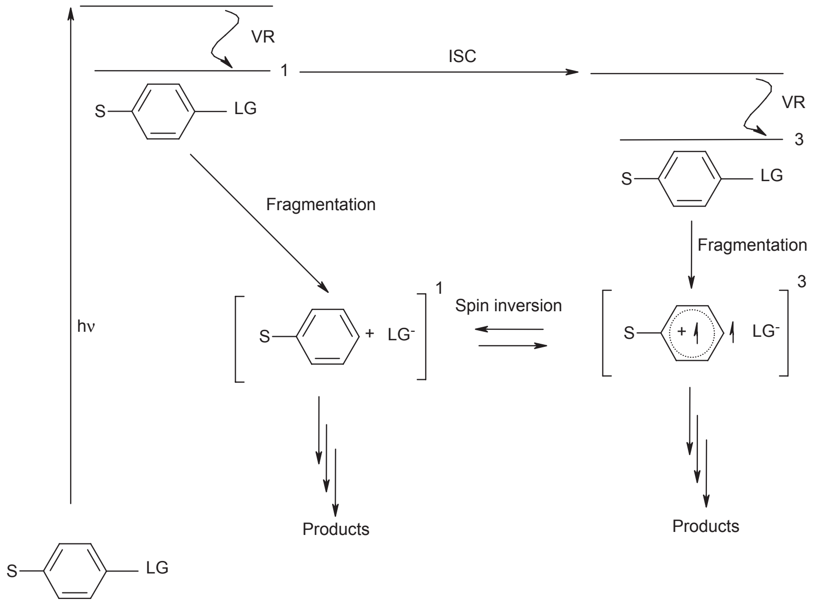
(Open shell) triplet phenyl cation

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**.

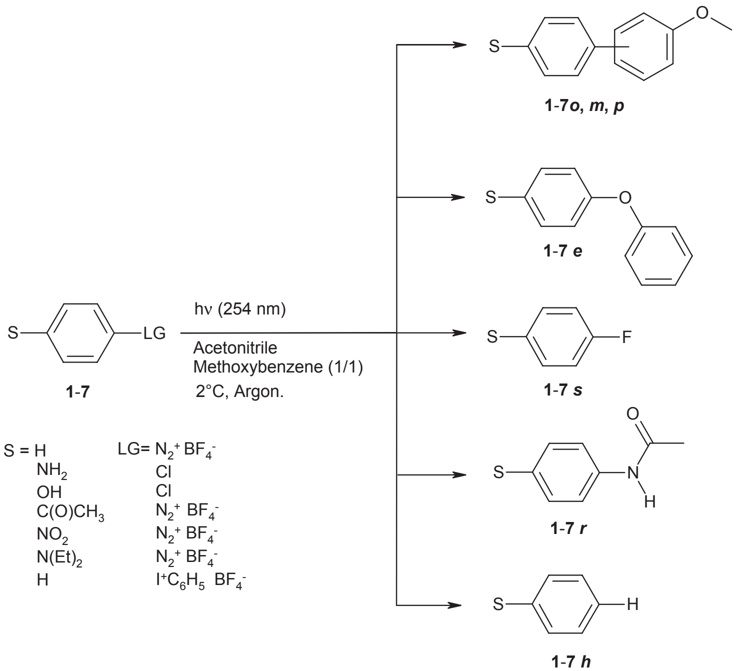
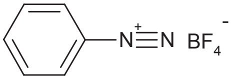
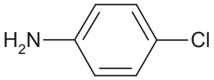
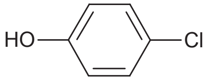
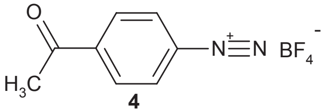
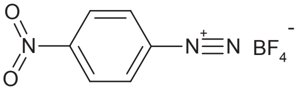
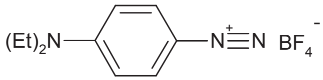
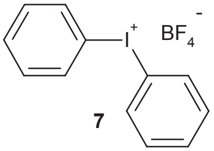


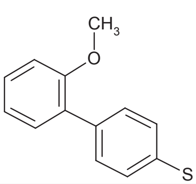
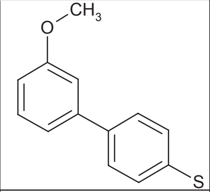
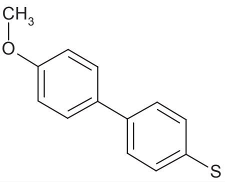
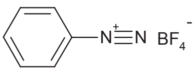
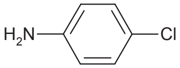
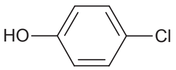
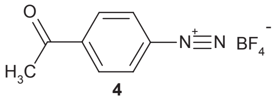
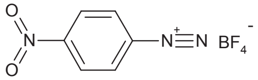
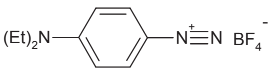
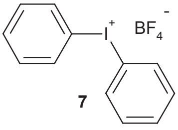
Table 1: Products of the photolysis of compounds **1**-**7** in acetonitrile/anisole[a].

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.

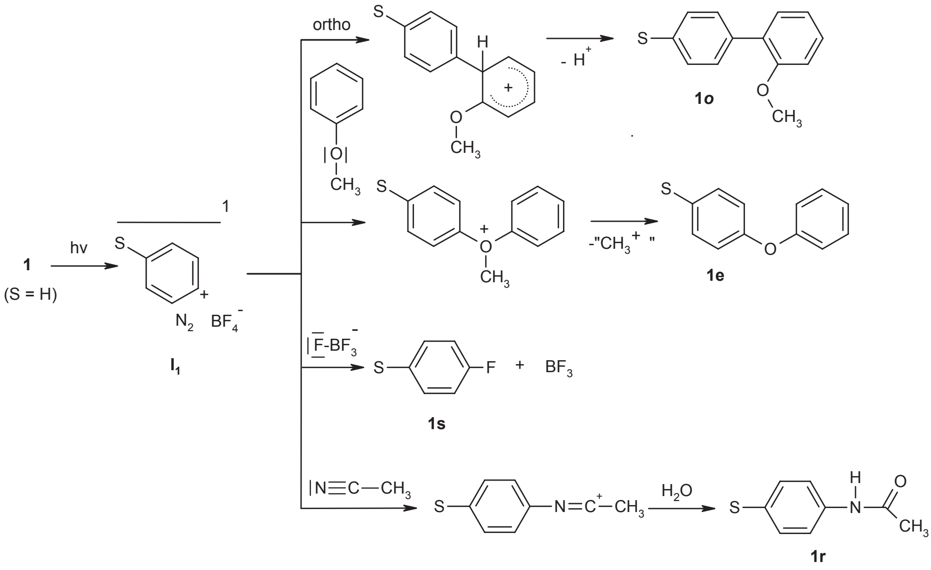
the nitrogen atom of acetonitrile, yields acetanilide **1r** (= **7r**) (entries 1 and 7). Finally, small amounts **1**-**7h**, where the leaving group is replaced by hydrogen, are found in most reaction mixtures.

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 ($\mathbf{I}_1$)[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^- (hv)[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.

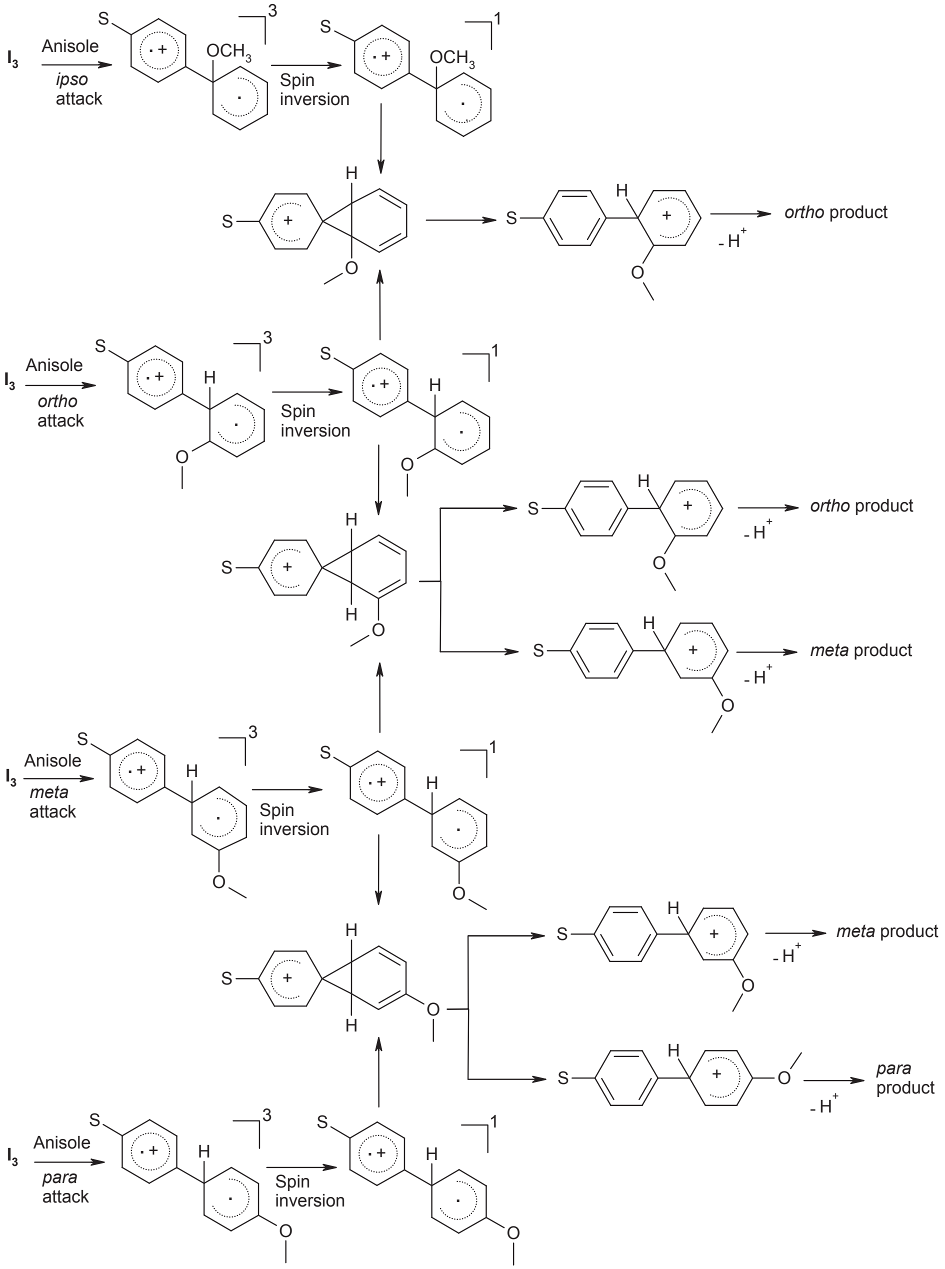
*4-Chlorophenol (**3**)*

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).



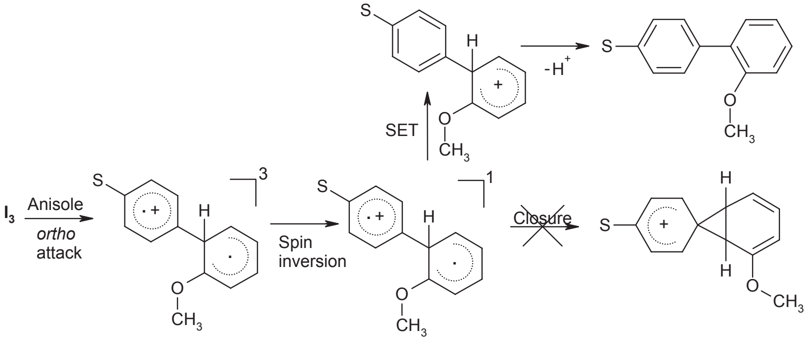
2 and **3**, no ether or Ritter products are formed. Also no Schiemann product is formed. The *o*, *m*, *p* ratio observed in the case of **5** differs from the ratio reported for its thermal solvolysis in a mixture of acetonitrile, benzene and anisole which yields **5*o*, *m*, *p*** in a ratio of 77.7:9.9:12.4[41]. 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).

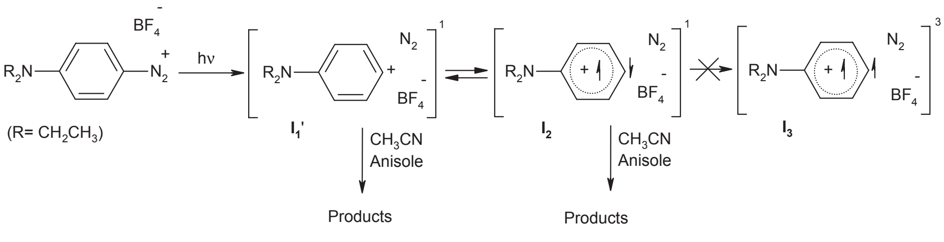


The EDG- and EWG-substituted triplet phenyl cations, derived from **2**, **3**, **4**, and **5** display a remarkable chemoselectivity. The n-electrons of anisole, acetonitrile and BF_4^- have no appeal for the electron deficient intermediate. Only reaction with π-electrons occurs. A rationale for this 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**)*

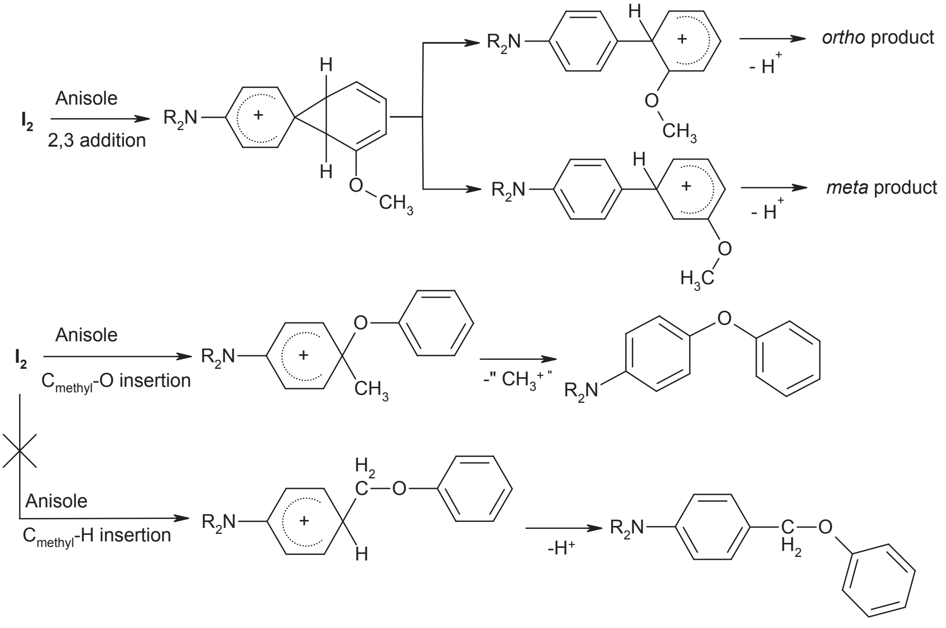
The photolysis of **6** yields the methoxybiphenyls **6*o***, ***m***, ***p*** in a ratio of 64:3:33 (Table 2 entry 6). Also an O- (**6e**) and a F- (**6s**) alkylation product are formed (Table 1). Neither the *o*, *m*, *p* ratio nor the product profile match that of the parent diazonium salt **1**, 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 $\mathbf{I}_1$' which is 0.4 kcal/mol more stable than the singlet open-shell phenyl cation $\mathbf{I}_2$ (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 $\mathbf{I}_2$ reacts with anisole before it can spin convert to its more stable triplet manifold $\mathbf{I}_3$ (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 (**I₂**) 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_{methyl}-O bond of anisole (Scheme 6). No C_{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**)*

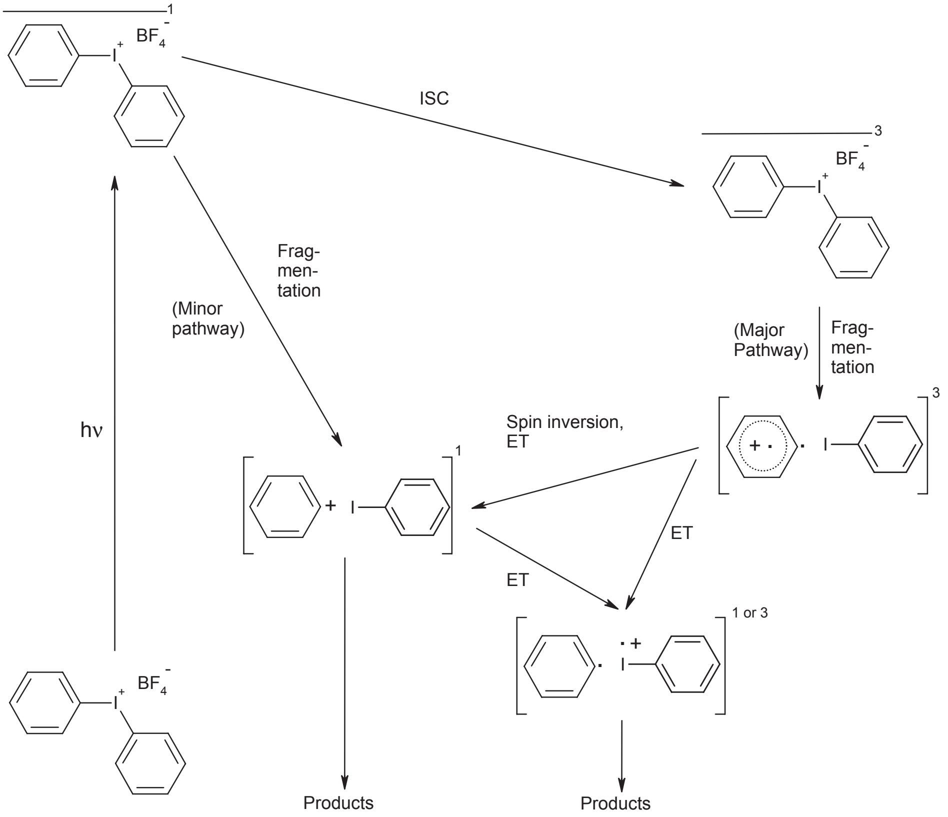
Diphenyliodonium salts are often applied in photolithography and in the photographic industry[44]. When subjected to UV light, they are reported to react through phenyl cations, stemming from the cleavage of a C-I bond in the singlet excited state, or through phenyl radicals, thought to originate from 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** (Scheme7). 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.

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Chapter 5 | Photochemical generation of six- and five-membered cyclic vinyl cations

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Introduction

The reactivity of vinyl cations, one of the most unstable types of intermediates known to organic chemists[1], has been the subject of extensive scrutiny in the past decades[1,2]. This research has culminated in the determination of the crystal structure of a tamed, i.e., highly stabilised, vinyl cation[3]. At the other end of the reactivity spectrum, destabilised vinyl cations are found. Destabilisation may be caused by electronic effects of electron-withdrawing groups at the α- or β- position[4], or by geometric effects if the vinyl cation is part of a cyclic system.

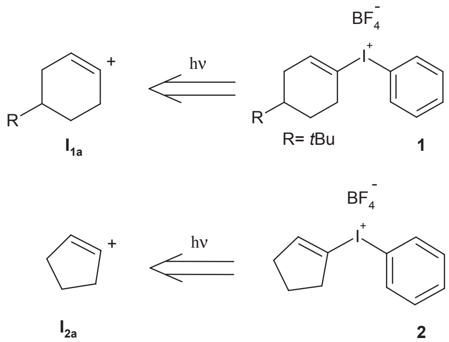
Vinyl cations are sp-hybridised, and possess a linear orientation at the positive carbon atom. A theoretical comparison of the prop-1-enyl cation with the cyclohex-1-enyl cation and the cylopent-1-enyl cation shows that decreases in the angle from 179° via 156° to 141° are accompanied by decreases in the relative stabilities of 17.0 and 27.3 kcal/mol, respectively[5]. The cyclopent-1-enyl cation may well be the ultimate in geometrical destabilisation of simple cyclic vinyl cations: calculations indicate that while this cation exists as a classical vinyl cation, the cyclobut-1-enyl cation is a bridged nonclassical ion[6]. The solvolysis products of cyclobut-1-enyl nonaflate can indeed be interpreted as stemming from such a nonclassical intermediate[7].

Several research groups have sought to generate and trap cyclic vinyl cations in thermal solvolysis reactions. But, whereas 1-methylprop-1-enyl triflate readily solvolyzes via an S_N1 mechanism in trifluoroethanol, cyclohex-1-enyl triflate does so very slowly, and cyclopent-1-enyl triflate does not exhibit unimolecular dissociation[8]. Due to the extremely good leaving group ability of neutral iodobenzene, 4-*tert*-butylcyclohex-1-enyl(phenyl)iodonium tetrafluoroborate solvolyzes much faster than cyclohex-1-enyl triflate, but cyclopent-1-enyl(phenyl)iodonium tetrafluoroborate still displays no reactivity[9,10].

Employing photolysis, it has been possible to generate a score of vinyl cations from their vinyl halide precursors[11]. Recent photochemical studies have shown that pseudo halides, such as vinyl(phenyl)iodonium salts, are an even better source of vinyl cations[12]. We surmised that the latter method is powerful enough to generate geometrically destabilised vinyl cations.

Here we report the results of the photolysis of 4-*tert*-butylcyclohex-1-enyl(phenyl)iodonium tetrafluoroborate (**1**) and cyclopent-1-enyl(phenyl)iodonium tetrafluoroborate (**2**) in methanol. Our findings unambiguously demonstrate that not only the 4-*tert*-butylcyclohex-1-enyl cation ($\mathbf{I_{1a}}$) but also the cyclopent-1-enyl cation ($\mathbf{I_{2a}}$) is accessible through photochemistry (Chart 1).

Chart 1: Cyclic vinyl cations produced from their corresponding iodonium salts.



Results and Discussion

Formation of photoproducts

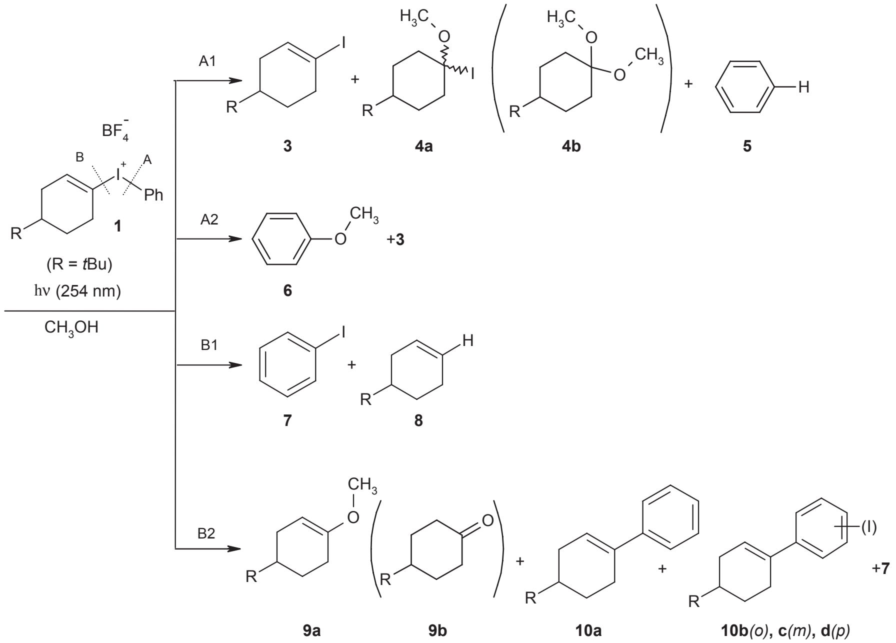
Irradiation of **1** in methanol, at λ_{exc} = 254 nm, yields the product mixture depicted in Scheme 1, in the composition recorded in Table 1. Next to the two leaving groups **3** and **7**, two reductive dehalogenation products, **5** and **8**, are produced by replacement of the phenyliodonium group by a hydrogen atom. Along with the nucleophilic vinylic substitution product, vinyl ether **9a**, four different products of Friedel-Crafts aromatic vinylation are formed, **10a** and **10b**-**d**. Anisole (**6**) results from a nucleophilic aromatic substitution reaction. Product **4a** is the formal Markovnikov addition product of methanol to the vinylic double bond of 4-*tert*-butyl-1-iodocyclohexene (**3**). The products are grouped along the proposed mechanisms for their formation (Scheme 2). In molecule **1** two bonds are prone to photolysis, the phenyl-iodonium (A) bond and the vinyl-iodonium (B) bond. Both bonds are subject to homolytic (A1, B1) and heterolytic (A2, B2) cleavage.

Table 1: Product composition[a] after 90 minutes of irradiation of **1** at λ_{exc} = 254 nm (ca. 10% conversion[b]).

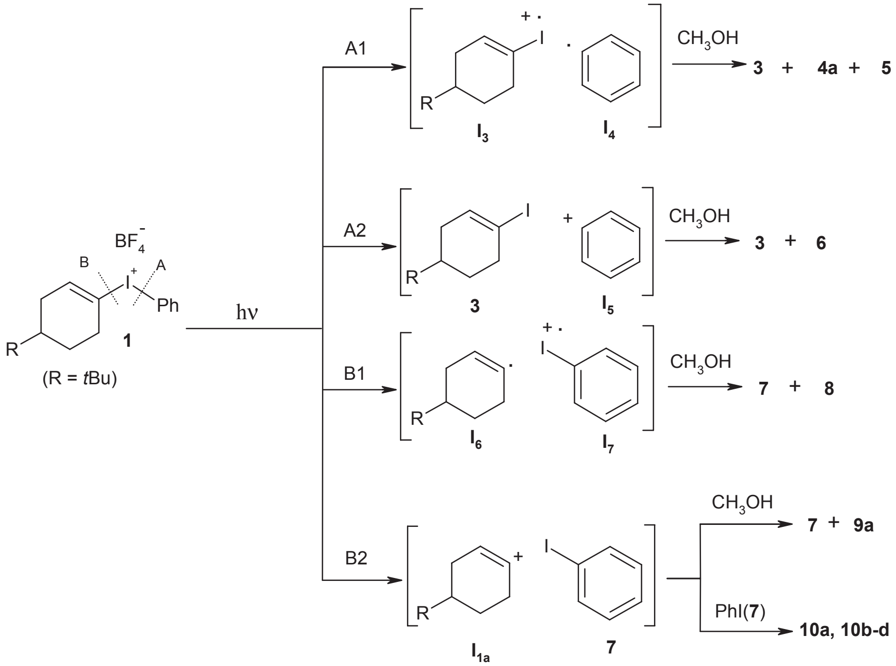
3	**4a**	**4b**	**5**	**6**	**7**	**8**	**9a**	**9b**	**10a**	**10b-d**
20	3.9	11.7[c]	16.8	5.2	80	1.3	2.9	1.5[d]	3.0	1.5/0.8/1.2

[a] As percentages of converted starting material. [b] 1.7% **3** and 8.2% **7** (GC yields relative to internal standard). [c] Secondary photoproduct (see text). [d] Secondary thermal product (see text).

Scheme 1: Product formation upon photolysis of **1** in methanol.



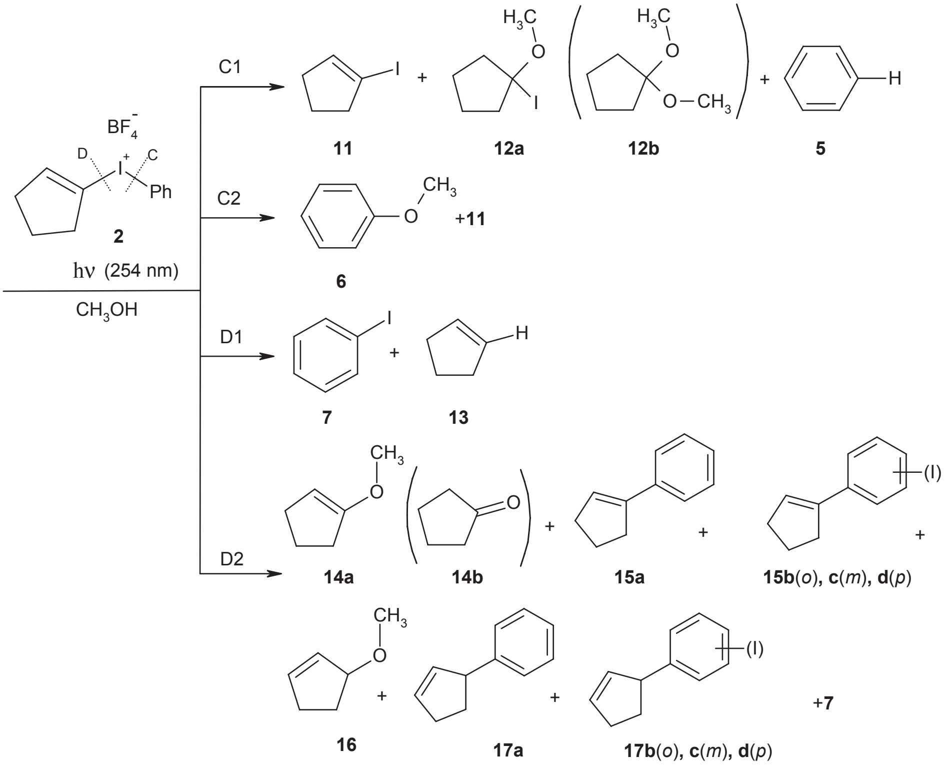
Scheme 2: Mechanism of formation of photoproducts from **1** in methanol.



Homolytic cleavage of the A bond (Route A1) yields the 4-*tert*-butyl-1-iodocyclohexene radical cation **I**$_3$ and the phenyl radical **I**$_4$. The radical cation **I**$_3$ can acquire an electron from its environment to form 4-*tert*-butyl-1-iodocyclohexene (**3**) or undergo addition of methanol with Markovnikov orientation, followed by abstraction of a hydrogen atom (*vide infra*, Scheme 5), to form 4-*tert*-butyl-1-iodo-1-methoxycyclohexane (**4a**). Benzene (**5**) is formed after hydrogen atom abstraction from the solvent by **I**$_4$. Upon heterolytic cleavage of bond A (Route A2), **3** is formed, alongside phenyl cation **I**$_5$. In methanol this elusive reactive intermediate will be trapped immediately, forming anisole (**6**).

Photohomolysis of bond B (Route B1) will yield the 4-*tert*-butylcyclohex-1-enyl radical **I**$_6$ and the iodobenzene radical cation **I**$_7$. Radical **I**$_6$ will abstract a hydrogen atom from the solvent and form 4-*tert*-butyl-cyclohex-1-ene (**8**). Radical cation **I**$_7$ forms iodobenzene (**7**) by acquiring an electron. Upon heterolysis of the B bond (Route B2), leaving group **7** and vinyl cation **I**$_{1a}$ are formed. The vinyl ether 4-*tert*-butyl-1-methoxycyclohexene (**9a**) is the trapping product of **I**$_{1a}$ with methanol. Vinyl ether **9a** is found to hydrolyze under the experimental conditions or upon work-up, in part, to 4-*tert*-butyl-cyclohexanone (**9b**). The 4-*tert*-butylcyclohex-1-enyliodobenzenes **10b** (*ortho*), **10c** (*meta*), and **10d** (*para*) are products of the Friedel-

Scheme 3: Product formation upon photolysis of **2** in methanol.



Crafts reaction of cation **I**$_{1a}$ with **7**. Electrophilic aromatic substitution on the *ipso* position of **7** results in the formation of 4-*tert*-butylcyclohex-1-enylbenzene (**10a**). In principle, product **10a** may also have been formed by attack of the phenyl cation **I**$_5$ on the leaving group **3** (Route A2) or by recombination of the radical pairs **I**$_3$ and **I**$_4$ (Route A1) or **I**$_6$ and **I**$_7$ (Route B1). Alternative routes toward the formation of the radical pairs may be photoheterolysis to **3** and **I**$_5$ (route A2) and to **I**$_{1a}$ and **7** (Route B2) followed by electron transfer within the ion-molecule pairs[13]. These alternatives would make routes A1 and B1 superfluous, which is unlikely in view of the observation of radical cation **I**$_7$ as transient in the picosecond flash photolysis of diphenyliodonium salts[14].

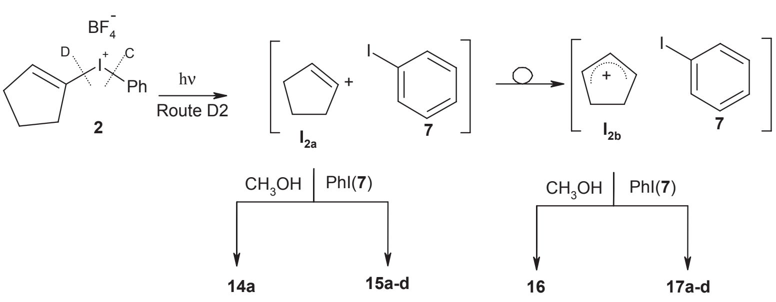
The results obtained in the photolysis of **1**, encouraged us to photolyse the cyclopent-1-enyl compound **2** in methanol at λ_{exc} = 254 nm (Scheme 3, Table 2). Most rewarding is the formation of two nucleophilic substitution products, the vinylic ether 1-methoxycyclopent-1-ene (**14a**) (and its hydrolysis product cyclopentanone (**14b**)), and the allylic ether 3-methoxycyclopent-1-ene (**16**). Also four Friedel-Crafts vinylation products, cyclopent-1-enylbenzene **15a** and cyclopent-1-enyliodobenzenes **15b-d**, and four allylation products, cyclopent-2-enylbenzene **17a** and cyclopent-2-enyliodobenzenes **17b-d,** are produced.

Table 2: Product composition[a] after 90 min. of irradiation of **2** at λ_{exc} = 254 nm (ca. 15% conversion[b]).

11	12a	12b	5	6	7	13	14a	14b	15a	15b-d	16	17a	17b-d
38	6.7	11[c]	61[d]	19	62	8.9	[e]	0.8[f]	3.8	8.8/4.7[g]/2.3	2.5	5.6	[e]

[a] As percentages of converted starting material. [b] 5.8% **11** and 9.3% **7** (GC yields relative to internal standard). [c] Secondary photoproduct (see text). [d] In part secondary photoproduct of **7**. [e] These products could only be identified on GC-MS. [f] Secondary thermal product (see text). [g] The GC-peak of **15c** somewhat overlaps with that of the internal standard).

Scheme 4: Mechanism of formation of photoproducts **14** –**17** from **2** in methanol.



Again, both carbon-iodine bonds (C and D) are photolabile and proposed to be subject to homolytic and heterolytic cleavage. Homolysis of the C bond (Route C1) will form the radical cation of 1-iodocyclopentene and the phenyl radical **I**$_4$. The products of these intermediates are 1-iodocyclopentene (**11**), 1-iodo-1-methoxycyclopentane (**12a**) (*vide infra*) and **5**. The heterolytic cleavage of the C bond (Route C2) yields the leaving group **11** and the phenyl cation $\mathbf{I}_5$, which is trapped by methanol to yield anisole (**6**). Homolytic cleavage of the D bond (Route D1) yields the radical cation of iodobenzene $\mathbf{I}_7$ and the cyclopent-1-enyl radical. These intermediates will produce **7**, after electron transfer, and cyclopentene (**13**), after hydrogen atom abstraction, respectively.

Crucial in this report is the photoheterolysis of bond D (Route D2) as depicted in Scheme 4. This cleavage generates **7** and vinyl cation $\mathbf{I}_{2a}$. In the product mixture the trapping product of $\mathbf{I}_{2a}$ and methanol, the vinyl ether **14a** (+**14b**), is accompanied by the allylic ether **16**, which is the trapping product of the allylic cation $\mathbf{I}_{2b}$. Further, next to the products of the electrophilic aromatic substitution reaction of **7** and $\mathbf{I}_{2a}$ (**15a** *(ipso)*, **b***(ortho)*, **c***(meta)*, **d***(para)*), also products reasoned to stem from the trapping of $\mathbf{I}_{2b}$ by **7**, the cyclopent-2-enyliodobenzenes **17a**, **b-d**, are observed.

All reactions were checked to be photochemical of origin. A "dark" thermal reaction of **1** in methanol, at 25 °C for 3 hours, yielded no appreciable amount of product. Thermal solvolysis of **2** in methanol shielded from light at 25 °C yielded no products at all after 3 h. Study of the composition of the photoproduct mixtures of **1** and **2** as a function of the time of irradiation shows that 4-tert-butyl-1,1-dimethoxycyclohexane (**4b**) and 1,1-dimethoxycyclopentane (**12b**) (presented in parentheses in Schemes 1 and 3) are secondary products, apparently produced from their 1-iodo-1-methoxycycloalkane precursors **4a** (See Scheme 5) and **12a**, respectively.

Quantum Chemical Studies

To assess the nature and plausibility of the possible cationic intermediates in the photolysis of **1** and **2**, CBS-Q calculations[15] were carried out on the structures and stabilities of the parent six- and five-membered cyclic vinyl and allyl cations $\mathbf{I}_{1a}$ and $\mathbf{I}_{1b}$ (R=H) and $\mathbf{I}_{2a}$ and $\mathbf{I}_{2b}$ (see Table 3, Figure 1). Such calculations have been shown to reproduce the relative stabilities of cations within experimental errors for a wide range of cationic species[16]. Also, some related species (cf. Scheme 6) were studied. The cyclohex-1-enyl cation $\mathbf{I}_{1a}$ is found to be less stable than the cyclohex-2-enyl cation $\mathbf{I}_{1b}$ by 27.8 kcal/mol. In the cyclopentenyl cations the vinyl cation is 47.8 kcal/mol less stable than the allyl cation.

Table 3: Relative stabilities of the cyclic vinylic cations and isomers.

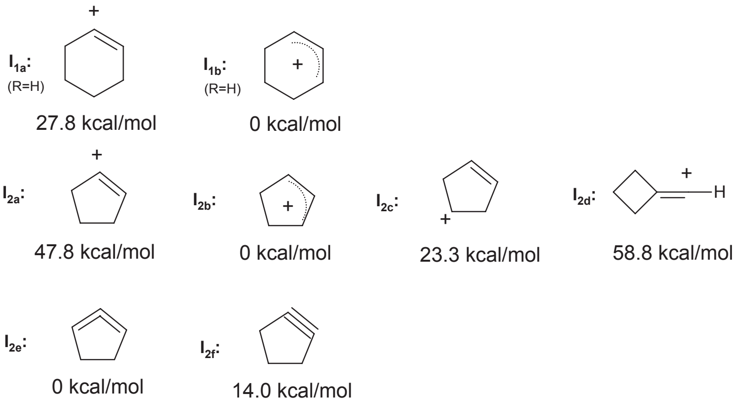
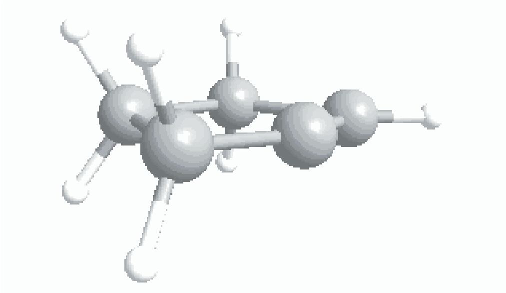
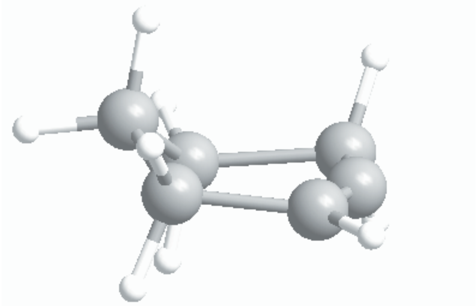


Figure 1: The B3LYP/6-311G(2d,2p)-calculated structures of the vinyl cations $\mathbf{I}_{2a}$ and $\mathbf{I}_{1a}$ (R=H).



Vinyl cation $\mathbf{I}_{2a}$



Vinyl cation $\mathbf{I}_{1a}$

Vinyl cation $\mathbf{I}_{2a}$ is a planar species (Cs symmetry) that corresponds to a real minimum at the potential energy surface at both the B3LYP/6-311G(2d,2p) and MP2/6-311G(2d,2p) levels of theory. While the positive charge, obtained with NBO analysis, is highest at the formally positively charged vinylic C^+ atom (+0.431), the remainder is delocalised significantly over the rest of the molecule. Of specific interest is that the charges of the CH and CH_2 moieties next to this vinylic C^+ atom are less positive (+0.093 in both cases) than at the remaining CH_2 moieties (+0.209 for the CH_2 next to the first CH_2 and +0.175 for the CH_2 next to the CH moiety). The strain in this molecule is significant. This is shown in two ways: first, the CH-C^+-CH_2 angle is 149.9°, which is significantly different from the 180° observed for an unstrained vinyl cation; second, the lengths of specifically the CH_2-CH_2 bonds are larger than in unstrained species: 1.611 Å for the C-C bond farthest away from the C^+ atom, and 1.642 Å for the other CH_2-CH_2 bond with a concomitantly low bond order of 0.822.

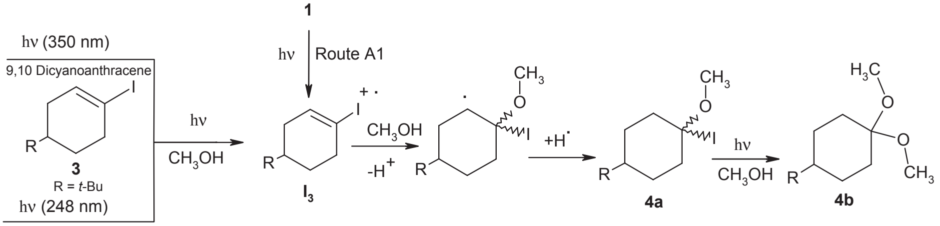
For the six-membered 1-cyclohexenyl cation (**I_{1a}**, R=H), similar observations are made. In this species the CH-C^+-CH_2 angle is 156.3°, which indicates a more relaxed structure. The vinylic C^+ atom bears a charge of +0.450 while the remainder of the charge is delocalised over the rest of the ring.

The C_6-ring vinyl cation

The parent cyclohex-1-enyl cation (**I_{1a}**, R=H) has already been postulated as an intermediate in thermal solvolyzes several times. The major indication for its generation is the formation of a vinyl ether accompanied by or completely converted to its hydrolysis product. Whereas cyclohex-1-enyl tosylate and brosylate are unreactive in 50% methanol at 130 °C for 17 days[17], the unimolecular solvolysis of cyclohex-1-enyl triflate in deuterated acetic acid (130 °C, for 4 weeks), does yield a mixture of cyclohex-1-enyl acetate and its hydrolysis product cyclohexanone[8]. In ethanol/ water, cyclohexanone is the sole product. This is also the case for the corresponding cyclohex-1-enyl nonaflate, which solvolyzes a factor of 2 faster than the triflate (ethanol/water 150 °C, 2 days)[18]. In the thermal solvolysis of **1** in methanol (25 °C, for 9 days), which occurs about 10^6 times faster than that of the triflate/ nonaflate, the formation of **10b**-**d**, next to **9a** and **9b**, provides additional evidence for the generation of the cyclic vinyl cation, these compounds being the trapping products of **I_{1a}** by iodobenzene **7**[9]. The photosolvolysis of **1** in methanol takes only hours at 20 °C, using a standard light source. The difference in reaction conditions needed to prepare the C_6-ring vinyl cation attests to the tremendous effect of photoexcitation upon leaving group abilities[11,12].

The cylohex-1-enyl cation (**I_{1a}**, R = H) has also been proposed as the product-forming intermediate in the photolysis of 1-iodocyclohexene (**3**, R = H) in methanol[19]. In this photoreaction, at almost complete conversion, the only product, next to cyclohexene (**8**, R = H), is 1,1-dimethoxycyclohexane (**4b**, R = H), which according to the authors was apparently a secondary product arising from acid-catalyzed addition of methanol to the nucleophilic trapping product 1-methoxycyclohexene (**9a**, R = H)[19]. In the photolysis of **1**, reported here, 4-*tert*-butyl-1,1-dimethoxycyclohexane (**4b**) is proposed to be a secondary photoproduct, formed at the expense of 1-iodo-1-methoxycyclohexane **4a**. The contradictory results prompted us to study the origin of **4a** and **4b** in more detail.

Scheme 5: Mechanism of formation of photoproducts **4a** and **4b**.



Irradiation of a solution of vinyl iodide **3** (R = *tert*-butyl) in methanol in the presence of 9,10-dicyanoanthracene at λ_{exc}= 350 nm (well outside the UV absorption band of **3**) produced **4a** (Scheme 5). Under these electron-transfer photosensitisation conditions alkenes are known to give radical cations. Here the radical cation $\mathbf{I_3}$ is generated, which adds to methanol and yields **4a** after a hydrogen atom transfer[20]. Compound **3** even yields **4a**, next to **8**, in the absence of the sensitiser and upon irradiation in methanol at λ_{exc}= 248 nm (Scheme 5). This means that radical cation $\mathbf{I_3}$ is also produced by a direct photoinduced ejection of an electron from the substrate into the solvent[21]. No vinyl ether **9a** (or its hydrolysis product **9b**) is formed. Only after prolonged irradiation of **3** are the reaction products cyclohexene **8** and 1,1-dimethoxy-cyclohexane **4b** indicating that **4b** is a secondary photoproduct of **4a**. 1-Iodo-1-methoxycycloalkanes are known to be photolabile and give the corresponding 1,1-dimethoxyalkanes as photoproduct[22].

In the photolysis of **1**, the formation of enol ether **9a** as primary photoproduct signals the generation of $\mathbf{I_{1a}}$ and its subsequent trapping by methanol. Vinyl cation $\mathbf{I_{1a}}$ also reacts with iodobenzene (**7**) yielding **10b**-**d**. These products are found in an *o*: *m*: *p* ratio of 43: 22: 34. This ratio is different from the ratio found in the thermal solvolysis of **1** (*o*: *m*: *p* = 87: 6: 9)[9]. Another difference between the thermal and photochemical reaction of **1** is that only the light-induced reaction yields *ipso* alkylation product **10a**, in a 1:1.2 ratio relative to the Friedel-Crafts products **10b**-**d**. Such *ipso* substitution is frequently observed in iodonium salt photolysis[12b,23]. Also, the relative importance of the two product-forming pathways from $\mathbf{I_{1a}}$, reaction with the solvent and with the leaving group, is significantly different in the thermal[9] and photochemical methanolysis of **1**. Upon thermolysis the ratio of products **9** and **10b**-**d** is 6:1, and upon photolysis the ratio of products **9** and **10** is 1:1.5. Clearly, the photogenerated C_6-ring vinyl cation differs from the thermally generated species in its regioselectivity toward iodobenzene and in its chemoselectivity toward the nucleophiles methanol and iodobenzene. The differences may be due to the formation of an aliphatic vinyl cation of high energy (a "hot" vinyl cation) in the photochemical reaction[19,24]. We speculate that the species generated in the photolysis is the triplet state of $\mathbf{I_{1a}}$, produced upon heterolytic cleavage of the C-I^+ bond of the triplet excited state of **1**. This triplet cation reacts (in part) faster with nucleophiles than it deactivates, by spin-inversion, to its singlet ground state[25]. As in the case of triplet phenyl cations[26], triplet vinyl cations are expected to prefer reaction with π-nucleophiles, such as iodobenzene, over reaction with n-nucleophiles, such as methanol.

In theory, as observed in the photochemistry of **2**, the C_6-ring vinylic cation $\mathbf{I_{1a}}$ can convert, by a hydride shift, to the allylic cation $\mathbf{I_{1b}}$. However, neither in the thermal solvolysis of cyclohex-1-enyl triflate, -nonaflate, and iodonium salts nor upon irradiation of **1**, are allylic products observed. The CBS-Q calculated stabilities (see Table 3) of $\mathbf{I_{1a}}$ and $\mathbf{I_{1b}}$ show that the production of allyl cation $\mathbf{I_{1b}}$ from $\mathbf{I_{1a}}$ is exothermic by 27.8 kcal/mol, but considerably less so than for the five–membered ring where 47.8 kcal/mol is gained in converting the vinyl cation $\mathbf{I_{2a}}$ into the allyl cation $\mathbf{I_{2b}}$. A 1,2-hydride shift does occur in a benzannellated form of $\mathbf{I_{1a}}$, the 1,2-dihydronaphthyl vinyl cation[27], where the driving force is 57 kcal/mol[28]. Apparently, for $\mathbf{I_{1a}}$ the driving force for a hydride shift is not large enough for that shift to compete with reaction of the vinyl cation with the solvent or the leaving group.

The C_5-ring vinyl cation

In the irradiation of **2** in methanol the heterolytic cleavage of bond **D** yields cation $\mathbf{I_{2a}}$. This conclusion is based on the formation of vinyl ether **14a**, next to its hydrolysis product **14b**, as well as on the formation of **15a**, and of three isomers of cyclopent-1-enyliodobenzene (**15b-d**), the trapping products of $\mathbf{I_{2a}}$ with iodobenzene. The conclusion is strongly supported by the formation of allylic ether **16** and the allylic, aromatic trapping products of $\mathbf{I_{2b}}$ (**17a**, **17b-d**). These products imply that upon generation of $\mathbf{I_{2a}}$, it is converted through a hydride shift to the allylic cation $\mathbf{I_{2b}}$, which is trapped by methanol or iodobenzene. Hydride shifts are typical of carbocation behavior and therefore products from $\mathbf{I_{2b}}$ provide direct evidence that a cation, i.e., $\mathbf{I_{2a}}$ is generated photochemically in methanol. The driving force for the 5-ring vinyl cation $\mathbf{I_{2a}}$ to undergo a hydride shift is much larger (See Table 3) than that for the 6-ring vinyl cation $\mathbf{I_{1a}}$, allowing the conversion of $\mathbf{I_{2a}}$ to allyl cation $\mathbf{I_{2b}}$ to compete with the trapping by the solvent or the leaving group. The ratio between vinyl and allyl cation-derived products is about 2.5:1.

The trapping of the C_5-ring vinyl cation $\mathbf{I_{2a}}$ by the leaving group **7** yields **15b**-**d** in an *o: m: p* ratio of about 56:30:14. The C_5-ring vinyl cation reacts less abundantly at the *ipso* position than at the combined *o*: *m*: *p* positions compared to the C_6-ring ion: a ratio of 1:4 between these two pathways is found. For the C_5-ring vinyl cation, the ratio between solvent trapped products versus leaving group trapped products is 1:25, compared to the 1:1.5 ratio for the C_6-ring vinyl cation. This difference in preference for the reaction with iodobenzene (**7**) over methanol probably reflects the higher reactivity of the C_5-ring species. As discussed for the C_6-ring vinyl cation, this species may be (in part) the triplet state of $\mathbf{I_{2a}}$[25].

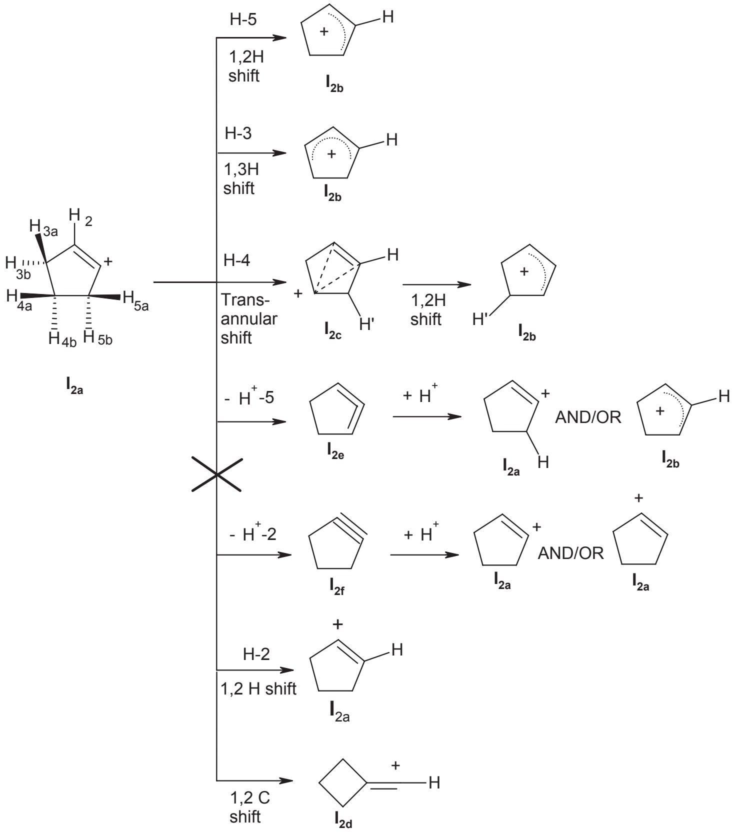
The formation of C_5-ring vinyl cation $\mathbf{I_{2a}}$-derived products also occurs in the irradiation of a derivative of **2** with a 4-tolyl instead of a phenyl ligand, cyclopent-1-enyl(4-methylphenyl)-iodonium tetrafluoroborate, in methanol (λ_{exc}= 254 nm). The photolysis of the tolyl salt proceeds 1.6 times more efficiently than the photoreaction of the phenyl salt. The product formation resembles that of the photolysis of **2**. The formation of vinyl ether **14a** through the presence of **14b** is confirmed in this experiment and also allyl ether **16** was found. The ratio between vinyl- and allyl cation-derived products is about 1.6:1. Vinyl cation $\mathbf{I_{2a}}$ reacts with the leaving group 4-iodotoluene to yield the *ipso* product 4-cyclopent-1-enyltoluene, and the Friedel-Crafts products 3-(cyclopent-1-enyl)-4-iodotoluene and 2-(cyclopent-1-enyl)-4-iodotoluene. The latter two are produced in a 3:1 ratio, which resembles the ratio obtained in the thermal solvolysis of the 4-tolyl derivative of **1** (76:24)[9]. The Friedel-Crafts products are formed in a 3.3-fold excess over the *ipso* products. The C_5-ring vinyl cation again shows a large preference for reaction with 4-iodotoluene over methanol. An exact ratio could not be determined because the GC peak of **14b** is obscured by that of toluene.

For the mechanism of conversion of the C_5-ring vinylic cation $\mathbf{I_{2a}}$ into the allylic cation $\mathbf{I_{2b}}$, four possibilities come to mind (Scheme 6). First, a 1,2-H shift across the single bond toward the carbon-carbon double bond. As already discussed, the resulting allylic cation is far more stable than the vinylic cation (data in Table 3), which thermodynamically allows this reaction. However, the activation energy for such a 1,2-H shift has both experimentally and computationally been shown to be considerable (18-20 kcal/mol) in linear systems[29,30,31]. Allylic stabilisation as in the product cannot be achieved in the bent transition state because of the lack of overlap between the newly created empty orbital and the double bond. In the rigid cyclopentenyl ring, the difficulty in creating the initial overlap may significantly add to an already high activation energy.

Second, a 1,3-H shift across the double bond, also yielding allylic cation $\mathbf{I_{2b}}$. The activation energy for such a 1,3-H shift is calculated to be 11.4 kcal/mol in the linear prop-1-enyl cation, considerably less than the activation energy for the corresponding 1,2- H shift[31]. This kinetic preference for a 1,3- over a 1,2-H shift for linear vinyl cations is probably even more pronounced for the ring vinyl cation, because of the higher conformational freedom of C-3 compared to C-5[32].

Third, a trans-annular hydride shift[33] from C-4 to C-1 producing the homo allylic cation $\mathbf{I_{2c}}$, which in turn may undergo a 1,2 H shift to yield allylic cation $\mathbf{I_{2b}}$. Several reports on the generation and reactivity of the cyclopent-3-enyl cation $\mathbf{I_{2c}}$ have appeared[34]. When generated in a non nucleophilic environment, the homoallylic cation $\mathbf{I_{2c}}$ yields allylic products, in a more nucleophilic reaction medium a mixture of homoallylic and allylic products is formed. Thus $\mathbf{I_{2c}}$ is easily converted, through a 1,2 H shift, in an allyl cation in competition with trapping by the solvent. In our experimental setup, however, employing the nucleophilic solvent methanol, the trapping product of cation $\mathbf{I_{2c}}$ should have been present, if this mechanism is operative. This is

Scheme 6: Possible mechanisms of conversion of $\mathbf{I_{2a}}$ into $\mathbf{I_{2b}}$.



not the case, no 4-methoxycyclopentene is produced. Therefore this sequence of reaction steps is unlikely.

Fourth, proton loss from C-5 of $\mathbf{I_{2a}}$ forming the highly strained cyclic allene $\mathbf{I_{2e}}$[35,36], which upon reprotonation may yield the allyl cation $\mathbf{I_{2b}}$ or the vinyl cation $\mathbf{I_{2a}}$, depending on the site of protonation. Alternatively, a proton may be lost from C-2 of $\mathbf{I_{2a}}$, yielding cyclopentyne ($\mathbf{I_{2f}}$). The latter proton-loss pathway is less likely because CBS-Q calculations show (data Table 3) that cyclopentyne $\mathbf{I_{2f}}$ is 14 kcal/mol less stable than cyclopenta-1,2-diene $\mathbf{I_{2e}}$. It is doubtful whether the deprotonation of $\mathbf{I_{2a}}$ to $\mathbf{I_{2e}}$ is thermodynamically feasible, the more so because only methanol or iodobenzene is available as base in the solvent cage[12b]. However, if a vinyl cation of higher energy is involved or if is the triplet state of $\mathbf{I_{2a}}$ that is involved, the propensity for proton loss may be enhanced[24,37]. Anyhow, the preferred reaction for structurally unbiased linear allenes is reprotonation at the terminal allene carbons atoms[38], here yielding $\mathbf{I_{2a}}$ and not $\mathbf{I_{2b}}$. This reaction sequence is not productive toward allylic ether formation and is therefore disregarded.

Other possible shifts, a 1,2-H shift across the double bond, or a 1,2-alkyl shift, do not contribute to $\mathbf{I}_{2b}$ formation. This particular 1,2-H shift would yield an intermediate indistinguishable from $\mathbf{I}_{2a}$. Formation of the primary vinyl cation $\mathbf{I}_{2d}$ from $\mathbf{I}_{2a}$ via a 1,2-alkyl shift is endothermic by 11 kcal/mol (see Table 3) and therefore thermodynamically not feasible. Also no products stemming from $\mathbf{I}_{2d}$ are observed.

Summarizing, we propose that $\mathbf{I}_{2b}$ is produced from $\mathbf{I}_{2a}$ by a 1,3-H shift. As far as we know, this mode of rearrangement is unprecedented in vinyl cation chemistry[39].

The data presented here constitute the first unambiguous case for the direct formation of C_5-ring vinyl cation $\mathbf{I}_{2a}$[40]. Attempts to thermally generate $\mathbf{I}_{2a}$ from cyclopent-1-enyl triflate or nonaflate did yield cyclopentanone, but in both cases the reaction occurred through S-O bond fission rather than vinyl-O bond fission[8b,41]. $\mathbf{I}_{2a}$ has been proposed as an intermediate in the photolysis of 1-iodocyclopentene in methanol at –25 °C which yielded 1,1-dimethoxycyclopentane (**12b**) next to cyclopentene (**13**)[19]. It may, however, well be that **12b**, in analogy with **4b**, is a radical cation-derived rather than a vinyl cation-derived product. The non formation of vinyl ether **14a** (and hence no cyclopentanone **14b**), or allyl ether **16**, is in line with this idea.

Relative photoefficiencies

Comparison of the rates of formation of the leaving groups from **1** and **2** (at low conversion) showed that photolysis of **2** is 1.4 times more efficient than that of **1**. Thus **2** is more photolabile than **1**, while **2** is far less thermolabile than **1**. Presumably, the cyclopentenyl ligand contributes less electron density to the carbon-iodine bond, in the reactive excited state than the cyclohexenyl moiety, which lowers the photostability.

In the irradiation of **1**, almost 5 times more iodobenzene (**7**) is cleaved off (B-bond fission) than vinyl iodide **3** (A-bond fission); in the photoreaction of **2** only 1.8 times more **7** than vinyl iodide **11** is produced. These efficiencies reflect the instability of the intermediates that are generated in these light-induced reactions, the phenyl cation, the cyclohex-1-enyl cation and the cyclopent-1-enyl cation. This is in agreement with a report about thienyl(phenyl)iodonium salts that the cationic iodine center allows π electron communication between the two ligands via its d-orbitals[42]. There is a substantial effect of one ligand at the iodonium center on the bond to the other ligand.

In summary, we have demonstrated that not only the C_6-ring vinyl cation, but also the C_5-ring vinyl cation can be generated photochemically, under mild reaction conditions. Compelling evidence for the formation of the C_5-ring vinyl cation $\mathbf{I}_{2a}$ is the production, next to the direct trapping products **14a** (and **14b**), of the allylic ether **16**, which is the trapping product of the hydride-shifted intermediate $\mathbf{I}_{2b}$. The formation of **17a** next to **15a**, and their iodine substituted counterparts, further substantiates this conclusion.

Experimental Section

Materials

The iodonium salts 4-*tert*-butylcyclohex-1-enyl(phenyl)iodonium tetrafluoroborate (**1**), cyclopent-1-enyl(phenyl)iodonium tetrafluoroborate (**2**), and cyclopent-1-enyl-(4-methylphenyl)iodonium tetrafluoroborate were synthesised as described in references[9,43]. Methanol (HPLC grade) was checked to be UV transparent and purged with Argon prior to use. *n*-Hexane and *n*-hexadecane were used as received as were all available reference compounds (**5**, **6**, **7**, **9b**, **13**, **14b**, and **16**). Non available reference compounds were synthesised following literature procedures with use of commercially available starting materials.

Photochemistry

All reaction mixtures were purged with Argon prior to irradiation. The solutions are irradiated in a quartz reaction tube that was sealed with a rubber septum (to allow sampling), and placed in a merry-go-round apparatus. A Hanau TNN-15/32 low pressure mercury lamp placed in a water cooled quartz tube is used to supply light with a main emission at $\lambda = 254$ nm.

In a typical experiment 10 mL of a 5 mM solution of the iodonium salt, containing 10 µL *n*-hexadecane as internal standard, was irradiated. At appropriate time intervals 50 µL samples were taken, using a syringe piercing through the septum. In kinetic runs, samples are taken every 5 min. The samples were injected in a test tube containing ~1 mL demineralised water and 100 µL of *n*-hexane or diethyl ether. Extraction was ensured by shaking the stoppered test tube. After settling of the layers, the organic layer was removed with a rinsed syringe and analyzed on GC and GC-MS. At the end of the irradiation, the remainder of the reaction mixture was reduced in volume by purging with nitrogen, and, if necessary, redissolved in 1 mL of diethyl ether. This sample is also analyzed on GC and GC-MS. Experiments were carried out in triplicate.

The $\lambda_{exc} = 248$ nm irradiations of **3** (R = *tert*-butyl) are carried out in a different set up. A high-pressure Hg/Xe arc, from which the IR output was removed by a water filter, was used as the irradiation source. The light beam was guided through a 77250 model Oriel monochromator to select the desired wavelength, and aimed at a 3 mL quartz cell, equipped with a glass stopper with Teflon septum. Per experiment 3 mL of 5 mM solutions of **3** and 1 mM *n*-hexadecane were used. The $\lambda_{exc} = 350$ nm 9, 10-dicyanoanthracene-sensitised irradiation of **3** is carried out in a Rayonet Photochemical Reactor, RPR 200 equipped with 350 nm lamps, which was placed in a cool room (4 °C). Reaction mixtures of 6 mM sensitiser and 50 mM starting material and 1 mM *n*-hexadecane (in methanol, 10 mL) in Pyrex were used.

Products

All reaction products were characterised by comparison of their retention times on analytical GC and of their mass spectra (by GC-MS) with those of authentic samples, using equipment described in ref[12b]. In many cases the product mixture was co-injected with the alleged product. Benzene (**5**), anisole (**6**), iodobenzene (**7**), 4-*tert*-butylcyclohexanone (**9b**), cyclopentene (**13**), cyclopentanone (**14b**), and 3-methoxycyclopentene (**16**) are commercially available. Most other products were synthesised according to literature procedures: 4-*tert*-butyl-1-iodocyclohexene (**3**)[19b], 4-*tert*-butyl-1,1-dimethoxycyclohexane (**4b**)[44], 4-*tert*-butylcyclohexene (**8**)[45], 4-*tert*-butyl-cyclohex-1-enylbenzene (**10a**)[46,47], 1-iodocyclopentene (**11**)[19b,48], 1,1-dimethoxycyclopentane (**12b**)[44], 1-methoxycyclopentene (**14a**)[49], cyclopent-1-enylbenzene (**15a**)[50], and 3-phenylcyclopentene (**17a**)[50]. Four products, 4-*tert*-butyl-1-methoxycyclohexene (**9a**) and the isomeric 4-*tert*-butyl-cyclohex-1-enyliodobenzenes **10b-d**, are assigned by comparison of the thermal solvolysis[9] products of **1** with the products of the photolysis. The isomeric cyclopent-1-enyliodobenzenes (**15b-d**), are tentatively assigned just as the cyclopent-2-enyliodobenzene isomers (**17b-d**) are. The MS patterns of the allylic products **17b-d** differ from those of the vinylic compounds **15b-d**, which do resemble the patterns obtained for the vinylic products **10b-d**. In the irradiation of **1** two products with a molecular mass of the diastereoisomers **4a** are formed. The occurrence of these products has been certified by comparing their retention times and mass spectra with the products of the (9,10-dicyanoanthracene sensitised) photoreaction of 4-tert-butyl-1-iodocyclohexene in methanol yielding **4a**. The formation of just one product **12a**, identified by its mass spectrum, in the photolysis of **2** is in line with these findings. Finally, two reference compounds were synthesised that turned out to be no products in the photolysis experiments. The homoallylic products 4-methoxycyclopentene[51], and 4-phenylcyclopentene[50], synthesised alongside **15a** and **17a,** are not present in the photoproduct mixture of **2**. Also 1-methoxymethylenecyclobutane[52] and cyclobutane carbaldehyde[53], the vinyl ether and its hydrolysis product that could have been formed if $\mathbf{I_{2d}}$ would have been an intermediate in the photolysis of **2**, are not present.

Quantum Chemical Calculations

The computations were performed with the Gaussian 03 program, version B3[54]. All optimisations on singlet and triplet states of $\mathbf{I_{a}}$ and $\mathbf{I_{2a}}$ were performed with B3LYP/6-311G(2d,2p) computations to properly account for ring strain effects. Relative thermodynamics on the compounds under study (Table 3) were obtained by using the CBS-Q model chemistry method[15].

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 DMX 300, using DMSO D_6 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.

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Chapter 6 | **Photochemical generation and reactivity of naphthyl cations; *cine* substitution**

Introduction

The research on aryl cation intermediates in organic (photo)chemistry has focussed mainly on phenyl cations[1]. Theoretical and experimental studies have shown that substituents have a decisive effect on the nature (singlet or triplet), and thus on the reactivity, of aryl ions[2]. Recently, density functional theory (DFT) calculations on the singlet-triplet gap in the 1-, and 2-naphthyl cation and in the 9-anthryl cation probed the influence of a larger electronic framework on spin-multiplicity[3].

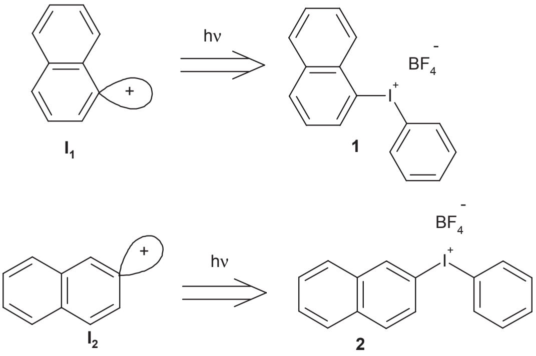
The unsubstituted phenyl cation possesses a singlet, closed shell $\pi^6\sigma^0$ structure. Phenyl cations substituted with electron-donating substituents in the *para* position prefer an open-shell $\pi^5\sigma^1$ structure, with triplet multiplicity[3].

The 1-naphthyl- and 2-naphthyl cations can be considered as phenyl cations bearing an electron-donating substituent. Due to their rigidity they are hampered to adopt the distorted structures normally encountered for singlet, closed shell species. Both effects lower the singlet-triplet gap. In fact, MO calculations[3] indicate that the singlet and triplet form of the naphthyl cations have about the same energy.

Naphthyl cations, and other cationic polyaromatic hydrocarbons, are not only of fundamental chemical interest. They play a relevant role in combustion processes and are present in the interstellar medium[4]. The chemistry of aryl cations and derivatives in the presence of H_2O, CO, NH_3, and especially H_2 and D_2 is subject of a continuous stream of reports[5].

Upon irradiation, vinyl iodonium salts efficiently yield vinyl cations[6]. Likewise, diphenyliodonium salts, commonly used as photo-acid generators in lithography, release phenyl cations upon photolysis[7]. It was therefore anticipated that photolysis of iodonium salts of polynuclear aromatic systems would provide the corresponding cations. The photochemical generation of the 1-naphthyl cation (**I$_1$**) and the 2-naphthyl cation (**I$_2$**), from 1-naphthyl(phenyl)iodonium tetrafluoroborate (**1**) and 2-naphthyl(phenyl)iodonium tetrafluoroborate (**2**) respectively

Chart 1: Naphthyl cations produced from their corresponding iodonium salts.



(Chart 1), and a study of their reactivity are presented. For reasons of comparison, also 1- and 2-naphthyldiazonium tetrafluoroborate and 1-iodonaphthalene were photolyzed.

Results and Discussion

Synthesis

Compounds **1** and **2** were synthesised by reaction of 1- and 2-(4, 4, 5, 5-tetramethyl-1, 3, 2-dioxoborolanyl)naphthalenes with an equimolar amount of (diacetoxy)iodobenzene in the presence of two mole equivalents of hydrogen tetrafluoroborate (in diethyl ether) at -30 °C in dichloromethane. After stirring the reaction mixture for 90 min., *n*-hexane is added which causes the products to crystallise. Repetitive crystallisation at 0 °C from tetrahydrofuran and *n*-hexane gives the pure salts **1** and **2** in 21% and 28% yield, respectively.

Photoproducts

Irradiation of 1-naphthyl(phenyl)iodonium tetrafluoroborate (**1**) in methanol at λ_{exc} = 254 nm yields the product mixture depicted in Scheme 1[8], in the composition recorded in Table 1. The products are grouped along the various C-I bond cleavage modes. Next to the two leaving groups 1-iodonaphthalene (**3**) and iodobenzene (**6**), and the reductive dehalogenation products benzene (**4**) and naphthalene (**7**), two nucleophilic aromatic substitution products, anisole (**5**) and 1-methoxynaphthalene (**8**), are produced. Further, the Friedel-Crafts type products 1-phenylnaphthalene (**9a**) and 1-(2-, 3-, and 4-iodophenyl)naphthalene (**9b**-**d**) are formed. Intriguingly, 2-phenylnaphthalene (**10a**) and 2- (2-, 3-, and 4-iodophenyl)naphthalene (**10b**-**d**) are produced as well. To the best of our knowledge this pattern of reactivity, commonly referred to as *cine* substitution, has not yet been observed in the aryl(phenyl)iodonium salt chemistry of unsubstituted precursors.

All products are proposed to have been formed via photolytic cleavage of either the phenyl-iodonium (A) or the 1-naphthyl-iodonium (B) bond of **1** (Scheme 2). Both cleavages can occur through homolysis (A1 and B1) or heterolysis (A2 and B2). Homolytic fission of the A bond produces the 1-iodonaphthyl radical cation $\mathbf{I_3}$ and the phenyl radical $\mathbf{I_4}$. Radical cation $\mathbf{I_3}$ can acquire an electron from the solvent and to form **3**. Phenyl radical $\mathbf{I_4}$ will produce **4** by hydrogen atom abstraction. The parent phenyl cation $\mathbf{I_5}$, formed after heterolytic fission of bond A, will be trapped by methanol and form **5**. Alongside $\mathbf{I_5}$, **3** is formed.

Scheme 1: Products of the photolysis of **1** in methanol.

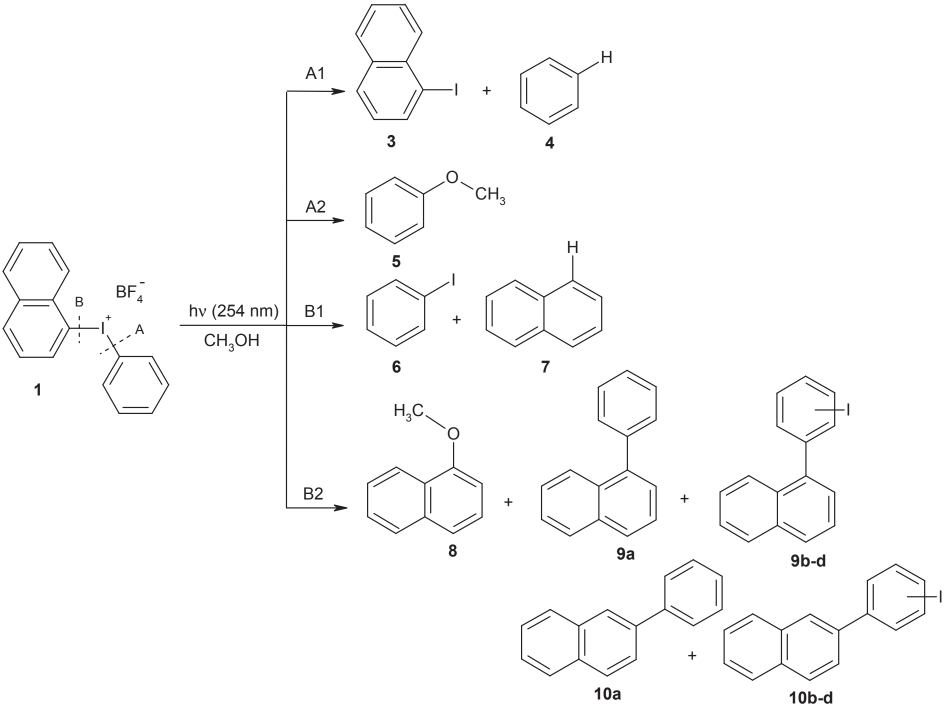


Table 1: Product composition upon photolysis of **1** in methanol at λ_{exc}= 254 nm[a,b] (ca. 4% conversion[c]).

3	4	5	6	7	8	9a	9b-d	10a	10b-d
8[d]	5	3	19	20	19	12	4	2	Traces

a) Percentages of total yield (GC). b) Product composition after 45 minutes of irradiation. c) 1.2% **3** and 2.4% **6** (GC yields relative to internal standard). d) Estimated yield, 1-iodonaphthalene overlaps with the internal standard.

Homolytic cleavage of the B bond gives two intermediates, iodobenzene radical cation $\mathbf{I}_6$ and naphthyl radical $\mathbf{I}_7$. These, in turn, produce **6** and **7** by abstraction of an electron and a hydrogen atom from the solvent, methanol, respectively. Upon heterolytic cleavage of bond B, the 1-naphthyl cation $\mathbf{I}_1$ will be produced next to the leaving group **6**. $\mathbf{I}_1$ is trapped by methanol to form **8** or by the leaving group iodobenzene to form **9a**, **9b-d**. The mode of formation of the *cine*-substitution products **10a** and **10b-d** will be discussed later.

Prompted by the formation of both **9** and **10** from the 1-naphthyl(phenyl)iodonium salt **1**, the 2-naphthyl(phenyl)iodonium salt **2** was subjected to photolysis under the same reaction con-

Scheme 2: Mechanism of product formation upon photolysis of **1** in methanol.

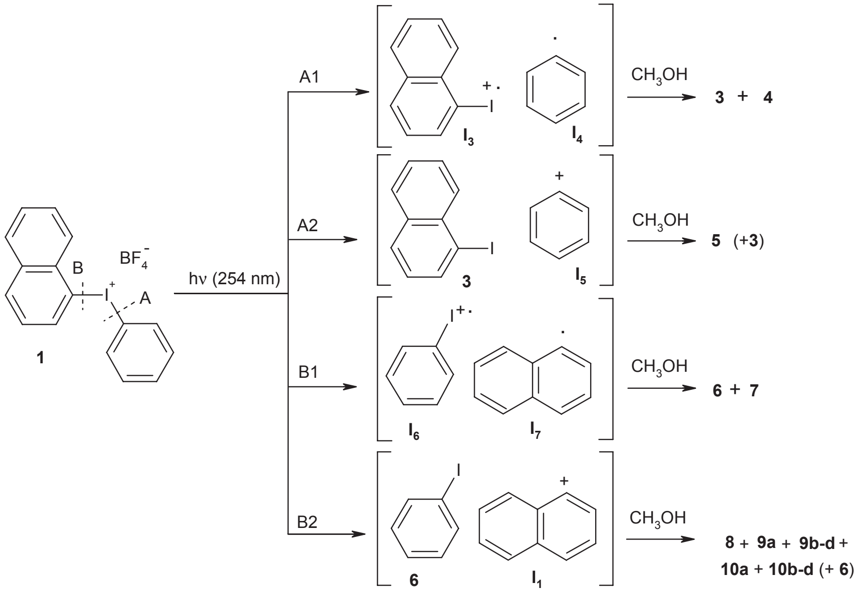


Table 2: Product composition upon photolysis of **2** in methanol at λ_{exc}= 254 nm[a,b] (ca. 10% conversion[c]).

11	4	5	6	7	12	10a	10b-d	9a	9b-d
8[d]	5	2	19	17	16	3	<2	7	Traces

a) Percentages of total yield (GC). b) Product composition after 45 minutes of irradiation. c) 3.0% **11** and 6.8% **6** (GC yields relative to internal standard). d) Estimated yield, 2-iodonaphthalene overlaps with the internal standard.

ditions (methanol, λ_{exc} = 254 nm) (Scheme 3, Table 2). In analogy with the results obtained in the photolysis of **1**, the product mixture consists of the two leaving groups 2-iodonaphthalene (**11**) and iodobenzene (**6**), the reductive dehalogenation products benzene (**4**) and naphthalene (**7**), anisole (**5**), 2-methoxynaphtalene (**12**), the 2-arylnaphthalenes **10a**-**d**, and the *cine*-substitution products **9a**-**d**.

The presence of both **9** and **10** in the photoproduct mixtures of **1** or **2** was confirmed when the the effect of the solvent was studied and the irradiations were carried out in acetonitrile and trifluoroethanol. The leaving groups **3**, **6** and **11** and the reductive dehalogenation product **4** and **7** are formed as before, as are the products resulting from trapping of the phenyl cation **I**$_5$ by the solvent. As shown in Scheme 4, in acetonitrile, the naphthyl cation intermediates **I**$_1$, and **I**$_2$ are trapped by that solvent and fortuitous water (Ritter reaction) yielding the acetanilido products **8**-NHAc and **12**-NHAc. The nucleophilic addition of trifluoroethanol to **I**$_1$, and **I**$_2$

Scheme 3: Products of the photolysis of **2** in methanol.

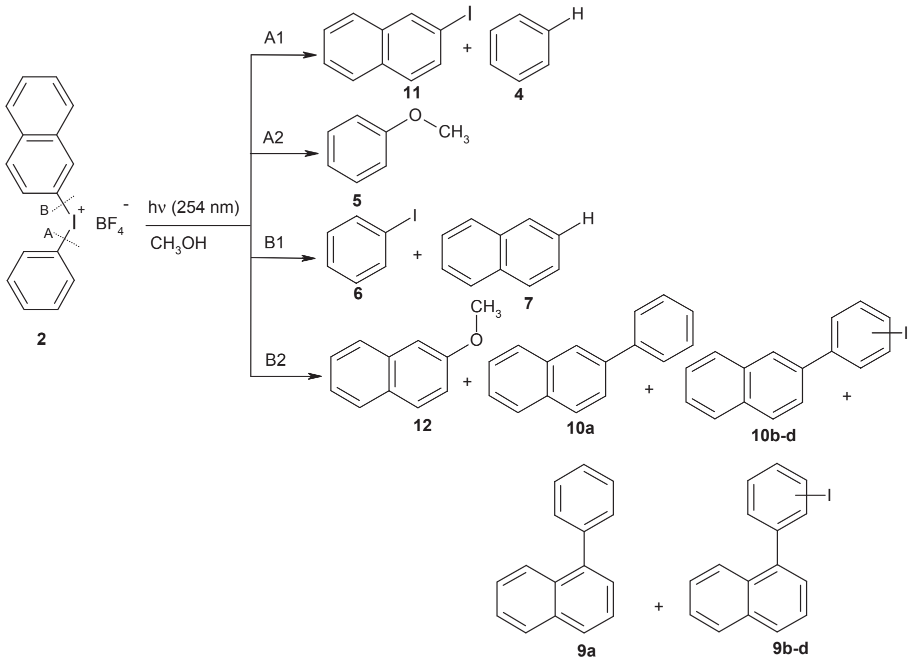


Table 3: Ratios of **8**: **9a**-**d and 12**: **10a-d** produced upon irradiation of **1** or **2** in various solvents.

Solvent	Ratio **8**: **9a-d** (precursor **1**)	Ratio **12**: **10a-d** (precursor **2**)
Methanol	1:1	1.5:1
Acetonitrile	1:3.3	1:1.1
Trifluoroethanol	1:4.3	1:2.3

yields the trifluoroethoxyethers **8**-OCH_2CF_3 and **12**-OCH_2CF_3, respectively. The Friedel-Crafts type products **9** and **10** are found in all irradiation mixtures.

The ratios in which the nucleophilic substitution products and the Friedel-Crafts products are formed depend on the solvent (Table 3). No *cine* substitution is found for **8** and **12**. Remarkably, the ratio of formation of **9** to **10**, starting from **1** or **2**, also varies with the solvent (Table 4).

Scheme 4: Products of the photolysis of **1** and **2** in acetonitrile and trifluoroethanol (only the products of route B2 are depicted).

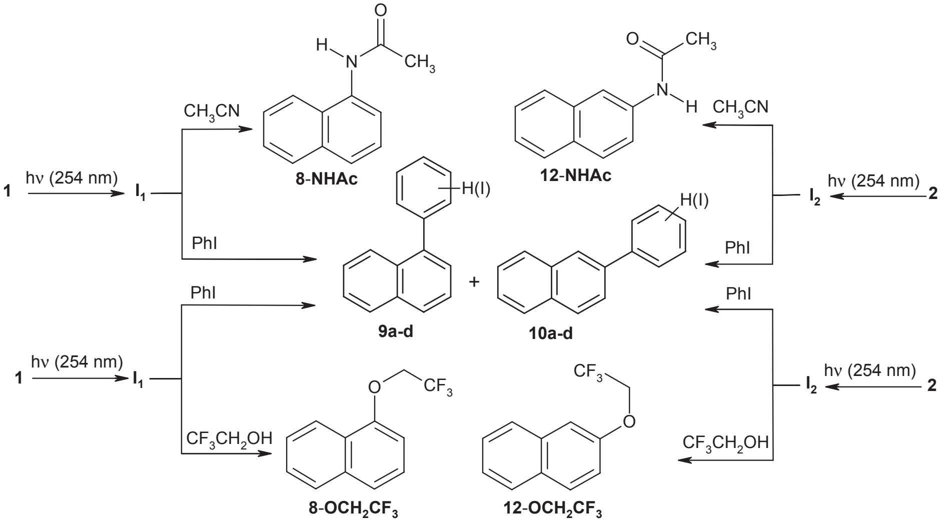


Table 4: Ratios of **9**: **10** produced upon irradiation of **1** or **2** in various solvents.

Solvent	Ratio **9**: **10** (precursor **1**)	Ratio **9**: **10** (precursor **2**)
Methanol	8:1	1.3:1
Acetonitrile	5:1	1:2
Trifluoroethanol	28:1	1:11

The *o*, *m*, *p* ratios of the iodobiaryls **9b**-**d** produced in the photolysis of **1** and **10b**-**d** produced in the photolysis of **2** also vary with the solvent (Table 5)[9]. These ratios could not be determined for the products **10b**-**d** in the irradiation of **1** and **9b**-**d** in the irradiation of **2**. They appear in minute amounts and can only be detected on GC-MS.

Table 5: Ratios of **9b**-**d** and **10b**-**d** produced upon irradiation of **1** or **2** in various solvents.

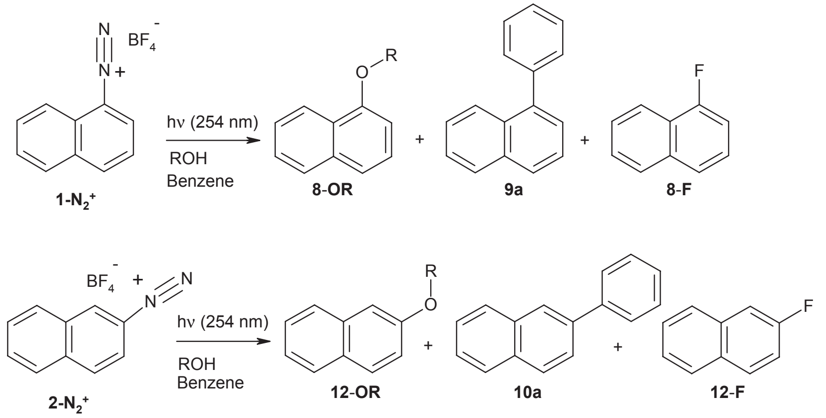
Solvent	Ratio **9b**: **9c**: **9d** (precursor **1**)	Ratio **10b**: **10c**: **10d** (precursor **2**)
Methanol	56:21:23	59:17:24
Acetonitrile	35:22:44	43:25:30
Trifluoroethanol	52:19:30	54:21:25

Only in trifluoroethanol the photolysis of **1** yields a phenylated iodonaphthalene as one of the products. The irradiation of **2** produces another phenylated iodonaphthalene. The identity of these products could not be established rigorously, but it is speculated that they are 1-iodo-2-or

4-phenyl-naphthalene in the photoproduct mixture of **1** and 1-phenyl-2-iodonaphthalene in that of **2**. They are the products of the trapping of the phenyl cation **I**$_5$ by the leaving group **3** or **11** (Scheme 2, route A2) which is only competitive with trapping by the solvent in the non-nucleophilic trifluoroethanol.

To study the effect of the nature of the leaving group on the substitution pattern of the photoproducts, the 1- and 2-naphthyldiazonium tetrafluoroborates **1**-N_2^+ and **2**-N_2^+ were photolyzed in methanol or trifluoroethanol, in the presence of benzene (Scheme 5)[8]. In methanol the photolysis of **1**-N_2^+ yields **8**-OR and **9a** in a 1.6:1 ratio, in trifluoroethanol the ratio of **8**-OR to **9a** is 1:1.7. Similar ratios are obtained in the photolysis of **2**-N_2^+; in methanol **12**-OR: **10a** = 1.5:1 and in trifluoroethanol **12**-OR : **10a** = 1:1.6. Solely 1- or 2-naphthyl products are formed. No *cine* substitution was observed.

Scheme 5: Products of the photolysis of **1**-N_2^+ and **2**-N_2^+ in methanol or trifluoroethanol and benzene.



(R = $-CH_3$, $-CH_2CF_3$)

Quantum Chemical Calculations

The singlet and triplet naphthyl cations **I**$_1$ and **I**$_2$ and the corresponding 1,2 naphthynes **I**$_8$ (vide infra, Scheme 8) were studied by density functional theory methods in vacuum, and single points in medium, and in methanol, respectively (Table 6, Figure 1)[10]. All optimisations were performed using B3LYP/6-311G(d,p). Next, single point characterisations were carried out using B3LYP/6-311++G(2d,2p). The data in columns 1 and 2 of Table 6 pertain to optimisation in vacuum (column 1) and optimisation after subsequent placement in solvent (column 2). The data in column 3 result from complete optimisation in methanol followed by single point characterisations. For the first time optimisation in a solvent worked at this level of calculation.

Table 6: B3LYP/6-311++G(2d,2p)-calculated energies[a,b] of the singlet and triplet 1,2-naphthyl cations **$\mathbf{I}_1$** and **$\mathbf{I}_2$** and 1,2-naphthyne **$\mathbf{I}_8$**, optimised in vacuum and in methanol.

	Vacuum	Rel.	Vacuum→MeOH	Rel.	MeOH	Rel.
$^1\mathbf{I}_1$	-385.02153	0	-385.10433	0	-385.10417	0
$^3\mathbf{I}_1$	-385.02330	-1.1	-385.10255	1.1	-385.10257	1.0
$^1\mathbf{I}_2$	-385.01968	1.2	-385.10290	0.9	-385.10335	0.5
$^3\mathbf{I}_2$	-385.02103	0.3	-385.10140	1.8	-385.10144	1.7
$^1\mathbf{I}_8$	-384.66696	0	-384.67488	0	-384.67483	0
$^3\mathbf{I}_8$	-384.61188	35	-384.60333	45	-384.61931	35

[a] Values absolute (Hartrees) and relative to $^1\mathbf{I}_1$ (kcal/mol) for the cations. [b] Values absolute (Hartrees) and relative to $^1\mathbf{I}_8$ (kcal/mol) for the naphthynes (1 Hartree = 627.51 kcal/mol).

Comparison of the data in column 1 with those in columns 2 and 3 shows a significant effect of stabilisation of the solvent on the cations. Vacuum-optimised structures that are placed in methanol have energies largely comparable to those of the solvent-optimised structures (columns 2 versus 3). According to the calculations in vacuum, the triplet cations $^3\mathbf{I}_1$ and $^3\mathbf{I}_2$ are slightly lower in energy than the singlet cations. This situation is reversed when the cations are placed in methanol. The differences are small; the energies of the singlet and triplet species are all within a few kcal/mol of each other. Most earlier reports on the calculated stabilities of $\mathbf{I}_1$ and $\mathbf{I}_2$ in vacuum grant the triplet manifolds the honour of being the lowest in energy, whereas one report finds the singlet cations more stable, albeit also with small differences[3,4b,11]. The near-equal energies ascertain that spin-inversion of the singlet to the triplet cations, or vice versa, is energetically feasible.

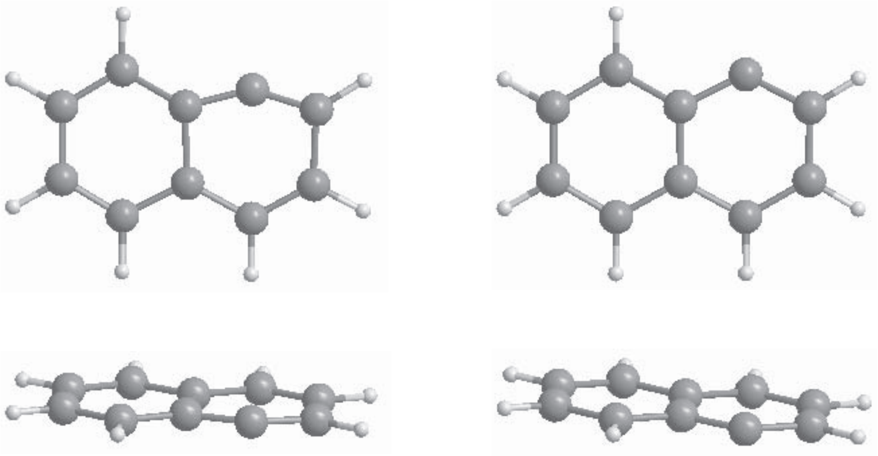
The triplet naphthyne $^3\mathbf{I}_8$ is calculated to be significantly less stable than the singlet naphthyne $^1\mathbf{I}_8$ in vacuum, in agreement with earlier calculations[12]. This is also the case in methanol.

All structures $\mathbf{I}_1$, $\mathbf{I}_2$ and $\mathbf{I}_8$ but one are calculated to be minima with a C_s symmetry (Figure 1). The exception is the singlet 2-naphthyl cation $^1\mathbf{I}_2$. Within the constraints of a C_s symmetry, the structure has one large imaginary frequency, and this structure thus is not a minimum. The real minimum is a distinctly nonplanar structure with C_1 symmetry.

Singlet/ triplet nature of the product-forming intermediates

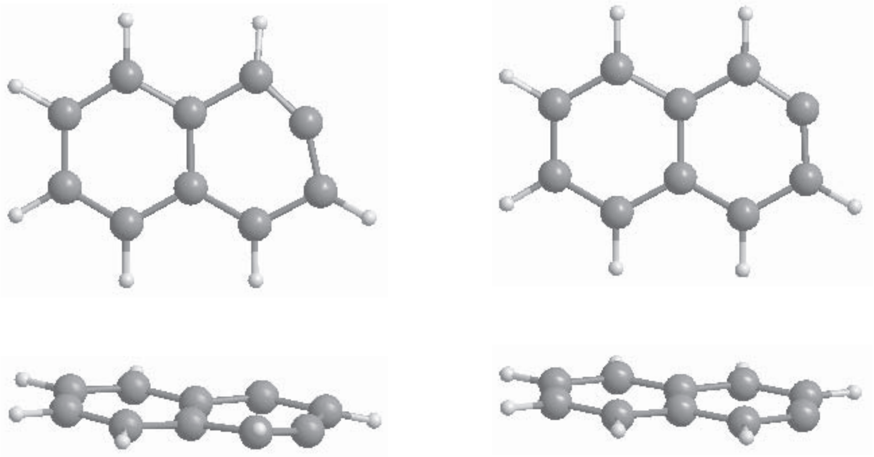
The formation of the nucleophilic substitution products **8** and **12**, and the Friedel-Crafts type products **9** and **10** upon irradiation of **1** and **2** indicate the intermediacy of the naphthyl cations $\mathbf{I}_1$ and $\mathbf{I}_2$, that are trapped by the solvent or by the leaving group iodobenzene (Scheme 2, route B2). It is of interest to know whether these intermediates are of singlet or triplet nature. As discussed in more detail in chapters 2, 3 and 4 of this thesis, diphenyliodonium salt photochemistry may directly form triplet phenyl cations from the triplet excited state, next to singlet phenyl cations from the singlet excited state. For example, singlet excited **1** can give cleavage

Figure 1: Calculated structures (top and side view) of **I_1** and **I_2**.



Cation ^{1}**I_1**:

Cation ^{3}**I_1**:



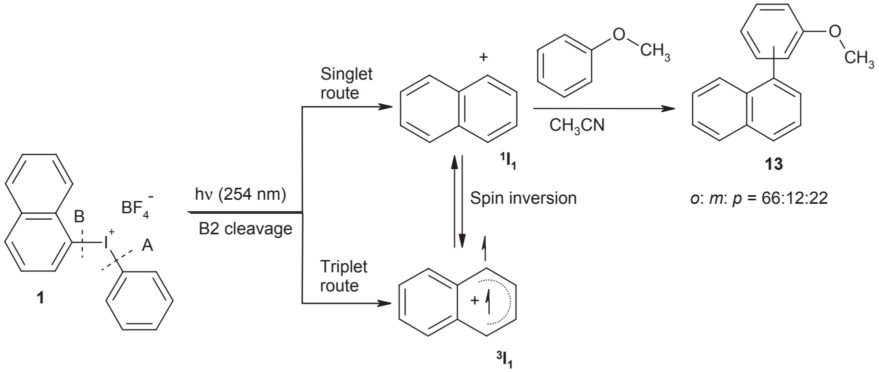
Cation ^{1}**I_2**:

Cation ^{3}**I_2**:

of the naphthyl-I bond and yield singlet ^{1}**I_1** (Scheme 6, singlet route). Alternatively, due to the heavy atom effect of iodine, it can undergo efficient intersystem crossing to triplet excited **1**, which upon cleavage of the naphthyl-I bond yields triplet ^{3}**I_1** (Scheme 6, triplet route). ^{1}**I_1** and ^{3}**I_1** may interconvert, provided their spin inversion is fast enough to compete with their reactions with nucleophiles.

A fingerprint of the singlet/ triplet nature of the product-forming naphthyl cation **I_1** was made by irradiating **1** in acetonitrile/ anisole 1/1 at λ_{exc} = 254 nm (Scheme 6). 1-(2-, 3- and 4-Methoxy-

Scheme 6: Formation of singlet or triplet $\mathbf{I_1}$ and their fingerprint by photolysis of **1** in acetonitrile/ anisole.



phenyl)naphthalene (**13**) are formed in an *o*, *m*, *p* ratio of 66:12:22. This ratio is quite similar to the ratio (71:11:17) observed for 2-, 3- and 4-methoxybiphenyl, produced through trapping of the phenyl cation by anisole, formed after heterolytic phenyl-I bond cleavage of **1** (Route A2 in Scheme 2). Moreover, the *o*, *m*, *p* ratio in **13** is practically the same as the ratio obtained with benzenediazonium tetrafluoroborate (68:13:19) and diphenyliodonium tetrafluoroborate (68:12:19) under the same photolysis conditions[13] and with the radiolysis of 1,4-ditritiobenzene in anisole (65:13:22)[14]. The product-forming intermediate in the latter three reactions is a phenyl cation of singlet nature. The results of the photolyses of 1-naphthyldiazonium tetrafluoroborate (**1**-N_2^+) and 1-iodonaphthalene (**3**) in acetonitrile/ anisole 1/1 at λ_{exc} = 254 nm further clarify the picture. The first reaction, which occurs through the singlet naphthyl cation intermediate $\mathbf{^1I_1}$, yields **13** in an *o*, *m*, *p* ratio of 61:15:25, and the second reaction, which occurs through the naphthyl radical intermediate $\mathbf{I_1}$•, produces **13** in an *o*, *m*, *p* ratio of 67:17:16. The ratio obtained with **1**-N_2^+ is similar to that obtained with **1** and to that of the singlet phenyl cation reference reactions[13,14]. The ratio obtained with **3** is unlike that of **1** and **1**-N_2^+, and is reminiscent of the ratio obtained upon irradiation of iodobenzene, which generates a phenyl radical intermediate, in acetonitrile/ anisole 1/1 (75:13:12)[13]. The regioselectivities in the reaction of **1** thus show that both the naphthyl and the phenyl cation intermediate in their singlet state are the product-forming intermediates in the formation of **13** and of 2-, 3- and 4-methoxybiphenyl, respectively.

That the singlet naphthyl cation $\mathbf{^1I_1}$ is the (major) product-forming intermediate, does not necessarily mean that a singlet cation is generated upon photolysis of **1**. The triplet naphthyl cation $\mathbf{^3I_1}$, if formed, may convert to $\mathbf{^1I_1}$ before being trapped by the solvent, provided trapping is slower than spin inversion (see Scheme 6), and provided $\mathbf{^1I_1}$ is of lower energy than $\mathbf{^3I_1}$. The calculated stabilities of the naphthyl cations in methanol assembled in Table 6 indicate that this process is thermodynamically feasible.

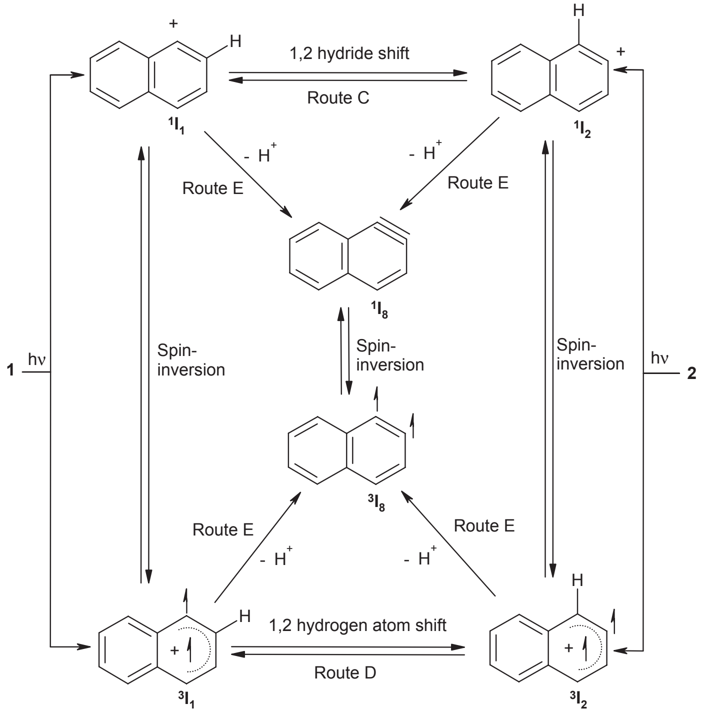
The *o*, *m*, *p* ratios of the iodobiaryls **9b**-**d** and **10b**-**d** formed in the irradiation of **1** and **2** (Table 4) are also fingerprints of the naphthyl cations $\mathbf{I_1}$ and $\mathbf{I_2}$, reacting with the leaving group iodobenzene in the solvent cage. Photolysis of diphenyliodonium hexafluorophosphate in acetonitrile produces iodobiaryls in a 73:13:15 ratio, whereas the bromonium and the chloronium salts under these reaction conditions produce halobiaryls in a 53:30:19 and a 48:31:21 ratio, respectively[7b]. In chapter 4 of this thesis, the latter two ratios are attributed to the in-cage attack of a singlet phenyl cation on bromobenzene or chlorobenzene and the ratio for the iodonium salt is reasoned to be the result of the combined reactivity of a singlet and a triplet phenyl cation. The *o*, *m*, *p* ratios of the biaryls **9b**-**d** and **10b**-**d** obtained in the photolyses of **1** and **2** (Table 5) differ from these data. The ratios in methanol and trifluoroethanol are more like the regioselectivity of the diphenylbromonium and -chloronium salt than of the -iodonium salt. They are therefore attributed to the reaction of singlet $\mathbf{^1I_1}$ and $\mathbf{^1I_2}$ with iodobenzene. It is not clear why in acetonitrile little or no regioselectivity is found.

The nucleophilic trapping of $\mathbf{I_1}$ and $\mathbf{I_2}$ by the solvent (methanol, acetonitrile or trifluoroethanol), producing **8** and **12**, relative to trapping by the leaving group iodobenzene, producing **9** and **10** (Scheme 4, Table 3), shows that the order of the efficiency of the solvents to trap the intermediates is: methanol, acetonitrile, trifluoroethanol. In trifluoroethanol the alkylation of the leaving group outperforms the alkylation of the solvent. The order parallels the nucleophilicities of the solvents[15].

Cine substitution

A number of pathways can be envisioned that may explain the observed *cine* substitution. The singlet 1-naphthyl cation $\mathbf{^1I_1}$, formed either directly or via the triplet cation, may undergo isomerisation to the singlet 2-naphthyl cation $\mathbf{^1I_2}$, and vice versa via a 1,2 hydride shift (Scheme 7, route C). Such a shift has been reported for $\mathbf{^1I_1}$, generated by β-decay of 1,4 ditritionaphthalene: with benzene both in solution and in the gas phase a mixture of 1- and 2-phenylnaphthalene is produced[16,17]. This shift is feasible because the intrinsic energy of the vibrationally excited naphthyl cation, left after expulsion of helium, is sufficient to allow isomerisation. Photolysis of **1** and **2** is not expected to yield vibrationally excited naphthyl cations. Anyhow, if interconversion of $\mathbf{^1I_1}$ and $\mathbf{^1I_2}$ takes place, not only 1- and 2-phenylnaphthalene but also 1- and 2-alkoxynaphthalene and the corresponding Ritter products should have been formed. This is not the case, therefore singlet cation isomerisation is not the operative mechanism.

Scheme 7: Interconversion of singlet and triplet naphthyl cations and corresponding naphthynes.



Isomerisation of the triplet naphthyl cations $^3\mathbf{I}_1$ and $^3\mathbf{I}_2$, formed directly or via the singlet cations, via a 1,2 hydrogen atom shift opens another route for isomerisation (Scheme 7, Route D). These triplet cations react selectively with the π-nucleophile iodobenzene and not with the n-nucleophiles R-OH and acetonitrile. This would explain why only scrambling of the phenylnaphthalenes is observed and no scrambling of the alkoxynaphthalenes. It also explains why no scrambling occurs with **1**-N_2^+ and **2**-N_2^+: photolysis of unsubstituted diazonium salts only yields singlet cations. It is not clear whether or not a 1,2 hydrogen atom shift in $^3\mathbf{I}_1$ and $^3\mathbf{I}_2$ is feasible, in other words what its energy of activation is. A 1,2 hydrogen shift has recently been observed in high temperature gas phase chemistry of naphthyl radicals[18]. In the phenyl radical the shift occurs with an activation energy of 58 kcal/mol[17]. The barrier is probably lower in naphthyl radicals, and even lower in $^3\mathbf{I}_1$ and $^3\mathbf{I}_2$ (for which naphthyl radicals may not be a good model) but may be still too high to overcome.

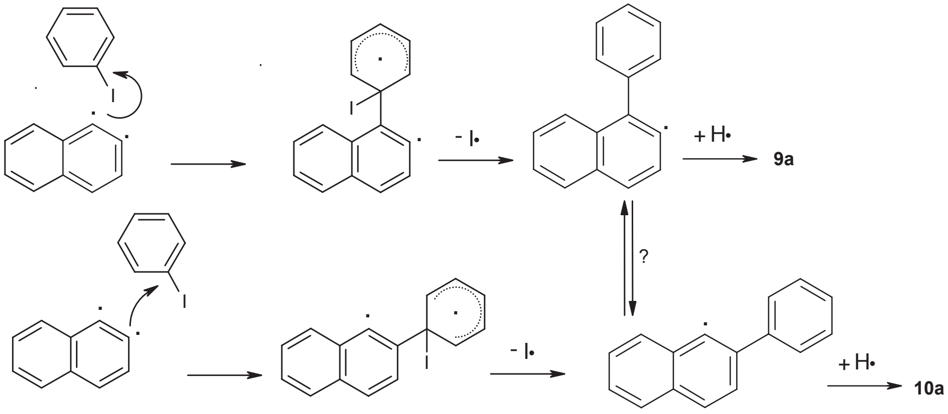
Cine substitution is typically found in alkyne[19] or aryne[20] chemistry. If a 1,2-naphthyne intermediate is accountable for *cine*-product formation in the photolysis of **1** and **2**, the singlet or triplet naphthyl cations $\mathbf{I}_1$ and $\mathbf{I}_2$ must be prone to lose a β-proton to their environment yielding singlet or triplet naphthyne $^1\mathbf{I}_8$ and $^3\mathbf{I}_8$ respectively (Scheme 8, Route E). Aryne formation through an aryl cation intermediate has been reported before in the thermolysis of 2,5-di-*tert*-butyl benzene diazonium acetate in dichloromethane[21]. The acetate counter-ion not only traps the aryl cation intermediate forming the acetate product, but also abstracts a proton forming 2,5-di-*tert*-butylbenzyne. 1,2-Naphthyne has been prepared as an intermediate by 1,2 HX elimination from halonaphthalenes by a strong base[22] and in matrix photodecarboxylation reactions[23]. All naphthynes found in matrix trapping experiments possess a singlet multiplicity. The singlet structure $^1\mathbf{I}_8$ is calculated to be far lower in energy than its triplet spin isomer $^3\mathbf{I}_8$, not only in the gas phase (in agreement with earlier calculations[12]) but also in methanol (Table 6). Still, singlet naphthyne $^1\mathbf{I}_8$ cannot be the *cine* product-forming intermediate. This species is expected to react with methanol to yield predominantly 2-methoxynaphthalene[24], a product not found in the photolysis of **1**. Also no *cine* substitution occurs with diazonium salts **1**-N_2^+ and **2**-N_2^+ which fragment in the singlet excited state producing $^1\mathbf{I}_1$ or $^1\mathbf{I}_2$, which upon proton loss would yield singlet naphthyne $^1\mathbf{I}_8$. On the other hand, the iodonium salts **1** and **2**, which do give *cine* substitution, fragment not only in the singlet but also in the triplet excited state, which yields triplet cation $^3\mathbf{I}_1$ or $^3\mathbf{I}_2$ and after proton loss triplet naphthyne $^3\mathbf{I}_8$. Proton abstraction from the triplet cations $^3\mathbf{I}_1$ and $^3\mathbf{I}_2$, yielding 1,2-naphthyne $^3\mathbf{I}_8$, is thought to be feasible because these species are also formal radical cations, which are known to easily lose a proton, specially from the benzylic position[25,26,27].

An argument in favour of naphthyne as *cine* product-forming intermediate is the variation in the ratio **9**:**10** as function of the solvent (Table 4). Under the photolysis reaction conditions the proton abstraction can only be effected by the solvent. Acetonitrile (779.2 kJ/mol), methanol (754.3 kJ/mol) and trifluoroethanol (700 kJ/mol) differ markedly in their proton-affinity[28]. It is reasonable to expect more aryne- derived product in the better proton-abstracting solvent. Indeed, in the photolyses of **1** in the three solvents, the relative abundance of the *cine* substitution products increases with the proton-affinity of the solvent. In the photolysis of **2**, scrambling is more outspoken than for **1** (Table 4). The triplet 2-naphthyl cation $^3\mathbf{I}_2$, which is a benzylic type radical cation, must be a stronger acid than the 1-naphthyl cation; already in the less basic solvent trifluoroethanol significant scrambling occurs. The photolysis of **2** in methanol yields more scrambled product than expected on the basis of the relative proton affinities. Currently we can offer no explanation for this observation.

An effort to trap naphthyne $\mathbf{I}_8$ in a [4+2] or [2+2] cycloaddition reaction with benzene was in vain. The products of those reactions would be 1,2-naphthobarrelene or dihydrobenzo[a]naphthalene[29], each with molecular mass 204. The photoreaction of **1** in methanol in the presence of benzene (**1**: benzene = 1:20) again produced, next to 1-methoxynaphthalene (**8**), 1- and 2-phenylnaphthalene (**9a**, **10a**) by in-cage reaction of $\mathbf{I}_1$ with iodobenzene and by reaction with benzene. No products with molecular mass 204 other than **9a** and **10a** were detected on GC-MS. An "ene" reaction may also produce **9a** and **10a** from $\mathbf{I}_8$ and benzene[30]. However, there is no reason why $^1\mathbf{I}_8$ should favor the "ene" reaction totally over [4+2] cycloaddition.

Triplet naphthyne $^3\mathbf{I}_8$ supposedly reacts with iodobenzene to form -in the case of ipso attack- an 1-[1'-iodocyclohexadienyl]-2-naphthyl diradical and a 2-[1'-iodocyclohexadienyl]-1-naphthyl diradical (Scheme 8). These distonic diradical intermediates will lose an iodine atom and acquire a hydrogen atom to yield **9a** and **10a**, respectively. The ratio of **9a**:**10a** will be determined by the regioselectivity of the attack of iodobenzene on the 1 or 2 position of $^3\mathbf{I}_8$. In theory, further scrambling may occur through a 1,2 phenyl shift (neophyl type rearrangement) of the 1- and 2-phenyl substituted 2- and 1-naphthyl radicals[31]. The activation energy of this shift is probably too high for efficient competition with the hydrogen atom abstraction, where a strong Csp^2-H bond is formed from a weak Csp^3-H bond of the solvent.

Scheme 8: Ipso-addition of iodobenzene to triplet naphthyne $^3\mathbf{I}_8$, forming **9a** and **10a**.



Conclusion

The 1- and 2-naphthyl cations $\mathbf{I}_1$ and $\mathbf{I}_2$ were generated by photolysis of their iodonium and diazonium salt precursors and their reactivity was studied. The naphthyl cations react (predominantly) through their singlet, closed-shell isomer. With the iodonium salt precursors, which fragment also from the triplet excited state, a contribution of the triplet naphthyl cations to the pattern of reactivity is found. Presumably, under the circumstances investigated, the singlet closed shell naphthyl cations are lower in energy than their triplet isomers.

It appears that, using the naphthyliodonium precursors, the triplet naphthyl cations formed isomerise via a 1,2 hydrogen atom shift or lose a proton to the solvent producing triplet 1,2-naphthyne. These processes lead to the *cine*-substitution patterns found in the photoproduct mixtures. No *cine* substitution occurs upon irradiation of 1- and 2-napthyldiazonium tetrafluoroborate, which generates only the singlet 1-, and 2-napthyl cation.

Experimental Section

Materials

Iodonium salts **1** and **2** were synthesised following a modified literature procedure[32,33]. To a mixture of 0.5 g (diacetoxy)iodobenzene in 25 mL dry dichloromethane at -30 °C, 0.50 mL HBF_4 in diethyl ether 54% wt. is added. The temperature is allowed to rise to 0 °C after which the clear yellow solution is cooled back to –30 °C. Stepwise, over a few min. 0.39 g of commercially available 1- or 2-(4, 4, 5, 5-tetramethyl-1, 3, 2-dioxoborolanyl)naphthalene is added. The reaction mixtures turn dark. After stirring the reaction mixtures for 90 min. at –30 °C the temperature is allowed to rise to 0 °C. *n*-Hexane (40 mL) is added which causes crystallisation. Filtration of the crude products and repetitive crystallisations from dichloromethane and *n*-hexane yield off-white, powdery crystals in 21% and 28% yield, respectively. (**1**: ^1H NMR[34] (200MHz, DMSO d_6, δ): 7.3-7.7 (m, 3H), 7.7-8.1 (m, 6H), 8.1-8.4 (d, 2H), 8.9 (s, 1H) and IR[35] (neat): 1000-1100 cm^{-1}, strong (BF_4^-)). (**2**: ^1H NMR (200MHz, DMSO d_6) 7.4-7.8 (m, 6H), 7.9-8.1 (d, 2H), 8.1-8.4 (t, 3H); 8.9 (s, 1H) and IR (neat): 1000-1100 cm^{-1}, strong (BF_4^-)). Diazonium salts **1**-N_2^+ and **2**-N_2^+ were prepared from commercially available starting materials according to a literature procedure[36]. 1-Iodonaphthalene (**3**) is commercially available. Anisole was distilled under argon to obtain GC purity. Methanol, acetonitrile, trifluoroethanol, 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 0.02M in 10 mL solvent. *n*-Decane was used as internal standard. For the experiments where product formation was followed as a function of time of irradiation, the tubes are placed in a merry-go-round apparatus. A Hanau TNN-15/32 low pressure mercury lamp placed in a water cooled quartz tube is used to supply light with a main emission at λ = 254 nm. For product studies, the tubes were placed in a Rayonet Reactor (RPR200) fitted with 7 254 nm or 300 nm lamps. The photolyses of the salts **1**, **2**, **1**-N_2^+ and **2**-N_2^+ in methanol and acetonitrile 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. Aliquots from the irradiation mixtures in trifluoroethanol were added to 0.5 mL water + 0.050 mL dichloromethane. 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 analyzed by GC and GC-MS.

Photoproducts

The products **3**, **4**, **5**, **6**, **7**, **8**, **8**-OCH_2CF_3, **8**-NHAc, **8**-F, **9a**, **10a**, **12**, **12**-NHAc and **12**-F were identified by means of GC, GC-MS and coinjection with the aid of commercially obtained reference samples. Products **11**[37] and **12**-OCH_2CF_3[38] were synthesised according to literature procedures. The *o*, *m*, *p* biaryl mixtures **9b**-**d**, **10b**-**d** and **13** were prepared by allowing the diazonium salts **1**-N_2^+ or **2**-N_2^+ to react with neat iodobenzene or anisole at 80°C for 6 hrs[9].

Quantum Chemical Calculations

The computations were performed with the Gaussian 03 program, version B3[10]. DFT calculations of the compounds under study were performed with the B3LYP functional[39] as implemented in G03. The total energies were corrected with zero-point energies, obtained at the level of optimisation.

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.

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[8] Under the same reaction conditions as used for the photolysis experiments, upon exclusion of light, **1**, **2**, **1**-N_2^+ and **2**-N_2^+ are inert.

[9] The assignments of the *o*, *m*, *p* isomers are based on the assumption that the products elude from the GC column in the usual order 1 = *ortho*, 2 = *meta*, 3 = *para*.

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Chapter 7 | Photochemical alkylation with a fluorescent label; photochemistry of 9-anthryl- and 9-phenanthryl(phenyl)iodonium tetrafluoroborate

Introduction

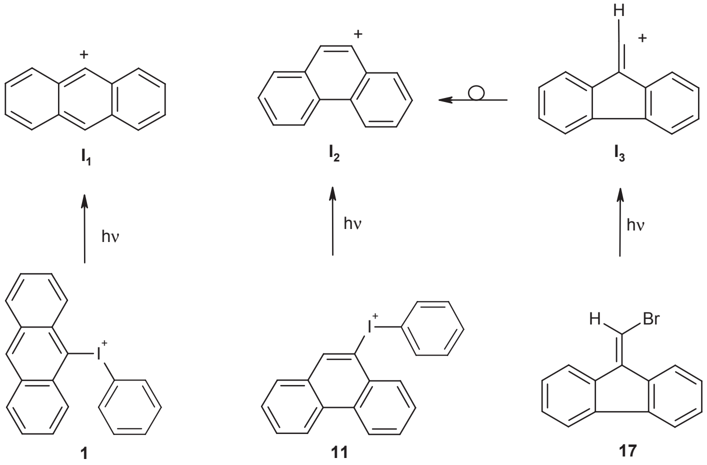
Photolysis of vinyl and phenyliodonium salts has proven to be a powerful entry to vinyl[1] and phenyl cations[2]. Both types of intermediates owe their high reactivity, apart from their electron-deficiency and the hybridisation, to the orthogonal orientation of the vacant orbital of the C^+ atom and the π-orbitals of the neighbouring double bond(s), which precludes stabilisation by overlap of these orbitals[3].

Highly reactive intermediates are usually unselective in their reactions with substrates. This is not the case if the product-forming cation is a triplet and not a singlet closed shell species. Introduction of substituents at the 4-position of phenyl cations alter the singlet-triplet gap and leads to chemo- and regioselectivity in the reaction of these cations with π nucleophiles (unsaturated substrates) vs. their reaction with σ nucleophiles[4]. Benzannelation of the phenyl cation also influences the singlet-triplet gap and thus the reactivity of the aryl cation[5]. The electron-donating effect of the annelating ring and the limited ability of the 1- and the 2-naphthyl cation to adopt the distorted structure normal for closed-shell singlet aryl cations makes the singlet and triplet forms of these cations degenerate in energy, with ensuing chemistry (Chapter 6 of this thesis).

In this chapter the generation of the 9-anthryl cation ($\mathbf{I}_1$) and the 9-phenanthryl cation ($\mathbf{I}_2$) and a study of their reactivity is reported. Cation $\mathbf{I}_1$ was prepared directly by photochemical removal of iodobenzene from iodonium salt **1**. Cation $\mathbf{I}_2$ was prepared directly from iodonium salt **11** and indirectly from **17**, by photogeneration of the primary vinyl cation $\mathbf{I}_3$ which converts to $\mathbf{I}_2$ via a 1,2 phenyl shift (Chart 1).

The ability to make unstable polynuclear aromatic cations such as $\mathbf{I}_1$ and $\mathbf{I}_2$ is not only of fundamental interest. The species can also be employed in arylation reactions with substrates of biological origin to provide them with reporter groups. The cations stem from non-fluorescent precursors, while the tagged molecules after arylation are fluorescent. The extended chromophoric groups (compared to e.g. diphenyliodonium salts) allow excitation with light of $\lambda_{exc} \geq$ 320 nm where the biological compounds are transparent and thus not subject to their own photochemistry.

Chart 1: Formation of the 9-anthryl and 9-phenanthryl cations.



Results and Discussion

*Part 1: Photochemical generation of the 9-anthryl cation (**I**$_1$).*

Synthesis

The precursor compounds 9-anthryl(phenyl)iodonium tetrafluoroborate (**1**BF_4) and 9-anthryl(phenyl)iodonium bromide (**1**Br) are synthesised from 9-(4, 4, 5, 5-tetramethyl-1, 3, 2-dioxoborolanyl)anthracene and Koser's reagent (hydroxy(tosyloxy))iodobenzene in dichloromethane at −60°C. After one hour of stirring at −60°C, the reaction mixture is warmed to 0°C and extracted three times with a 5% $NaBF_4$ solution or a 5% NaBr solution in demiwater. The organic layer is separated, dried on $MgSO_4$, and the solvent is evaporated. The residue is washed with ethylacetate and pentane and evaporated to dryness. After repeated crystallisation pure **1**BF_4 is obtained in 9% and **1**Br in 15% yield. Both salts are somewhat thermolabile and prior to their use they are washed with diethyl ether and pentane.

*Photolysis of **1**BF_4 and **1**Br in methanol and trifluoroethanol*

The iodonium salts **1**BF_4 and **1**Br are photolyzed in argon-purged methanol at λ_{exc} =254 nm and 350 nm and in argon-purged trifluoroethanol (TFE) at λ_{exc} =254 nm, all at 3°C under an argon atmosphere (Scheme 1, Table 1). As with other iodonium salts, both carbon-iodine bonds of **1** are photolabile and prone to homolysis and heterolysis. Upon A bond cleavage, next to the leaving group 9-iodoanthracene (**2**), the nucleophilic substitution products with the solvent

3-OR and the reduction product benzene (**4**) are produced. Fission of bond B yields the leaving group iodobenzene (**5**) next to the nucleophilic substitution products with the solvent **6**-OR and the reduction product anthracene (**7**). The *ipso*-substitution product 9-phenylanthracene (**8**) may be formed through both cleavages. Nucleophilic substitution with the counter-ion bromide in the photolyses of **1**Br produces **6**-Br but no **3**-Br.

Scheme 1: Product formation upon photolysis of **1**BF_4 and **1**Br in methanol or trifluoroethanol.

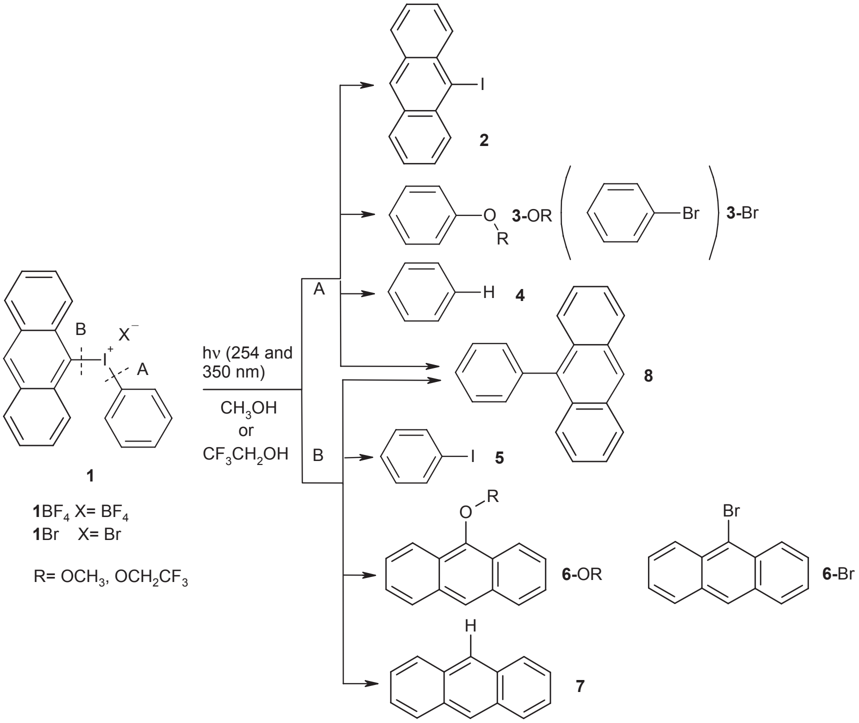


Table 1: Products of the photolyses of **1**BF_4 and **1**Br in methanol at λ_{exc}= 254 nm and 350 nm and of the photolysis of **1**BF_4 in trifluoroethanol at λ_{exc}= 254 nm[a,b].

	2	3-OR	3-Br	4	5	6-OR	6-Br	7	8
1BF_4 (254nm), MeOH	1.2	1.0	-	2.2	26.9	2.7	-	16.7	2.0
1BF_4 (350nm), MeOH	6.3	0.5	-	1.6	20.8	1.3	-	17.5	2.9
1BF_4 (254 nm),TFE	1.9	none	-	2.0	18.7	7.5	-	4.2	4.7
1Br (254nm), MeOH	trace	trace	none	1.0	9.8	0.9	0.7	6.5	0.5
1Br (350nm), MeOH	1.0	trace	none	1.5	9.6	0.7	1.7	8.9	0.5

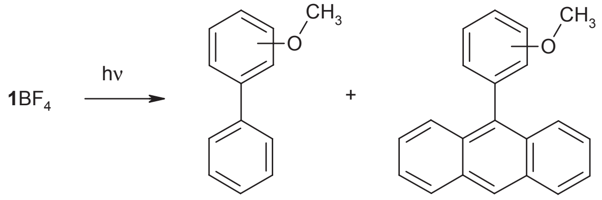
a) The data have been corrected for the small amounts of thermal products formed under the reaction conditions[6]. b) Product compositions after 45 minutes of irradiation (still low conversion).

Two side-products are commonly observed in the reactions: anthrone and anthraquinone. Anthrone is the hydrolysis product of 9-alkoxyanthracene (**6**-OR). Its low yield (ca. 0.2% after 45 minutes of irradiation) has been added to that of **6**-OR. Anthraquinone is formed in varying amounts and results from the photooxidation of **7** and derivatives with residual oxygen[7].

*Photolysis of **1**BF$_4$ in acetonitrile/anisole and trifluoroethanol/anisole*

To probe the nature of the reactive intermediates involved in the formation of its photoproducts, iodonium salt **1**BF$_4$ was also photolyzed, at three wavelengths of excitation, in acetonitrile (ACN), and in trifluoroethanol in the presence of anisole[8]. Next to the leaving groups **2** and **5** and the reduction products **4** and **7**, the Friedel-Crafts products 2-, 3-, and 4-methoxybiphenyl (**9*o***, ***m***, ***p***) and 9-(2-, 3-, and 4-methoxyphenyl)anthracene (**10*o***, ***m***, ***p***) are formed (Scheme 2, Table 2). No products of nucleophilic substitution with the solvents acetonitrile and trifluoroethanol (the Ritter products **3**-NHAc and **6**-NHAc, and **3**-OCH$_2$CF$_3$ and **6**-OCH$_2$CF$_3$) are found.

Scheme 2: Additional products upon photolysis of **1**BF$_4$ in ACN/Anisole or TFE/Anisole.



9*o*, *m*, *p*

10*o*, *m*, *p*

Table 2: Products of the photolysis of **1**BF$_4$ at λ_{exc}= 254 nm, 300 nm and 350 nm in acetonitrile/ anisole (ACN) and trifluoroethanol/ anisole (TFE)[a,b].

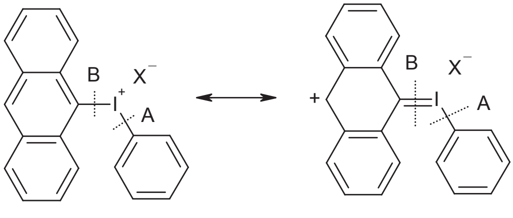
Exp	**2**	**4**	**9**	**9*o*:*m*:*p***	**5**	**7**	**10**	**10*o*:*m*:*p***
ACN(254)	9.5	0.6	4.4	62:11:17	17.7	9.4	8.7	68:4:28
ACN(300)	3.8	2.1	6.2	71:12:17	19.3	4.6	7.1	60:11:29
ACN(350)	1.8	0.9	3.2	74:13:14	13.9	3.2	5.5	60:11:29
TFE(254)	13.6	0.6	3.3	65:8:27	17.3	3.0	7.5	69:3:28
TFE(300)	5.4	1.6	2.3	67:11:22	18.7	2.6	7.0	77:6:17
TFE(350)	0.8	1.2	2.4	72:12:14	11.0	1.0	3.2	62:9:29

[a] Product mixture compositions after 45 minutes of irradiation. [b] Thermolysis of **1**BF$_4$ under the same reaction conditions does not produce the methoxybiaryls **9** and **10**.

*Photoproducts of **1**BF$_4$ and **1**Br in methanol and in trifluoroethanol*

In all experiments the formation of iodobenzene (**5**), product of the photocleavage of the anthryl C-I$^+$ (B) bond, significantly exceeds the formation of 9-iodoanthracene (**2**), product of fission of the phenyl C-I$^+$ (A) bond. This preponderance is reminiscent of the production of the leaving groups in the photolysis of *para*-dimethylamino-phenyl(phenyl)iodonium bromide (see Chapters 2 and 3) in which the B bond is also cleaved preferentially, probably because of the contribution to the photoinstability by a mesomeric form of the iodonium salt **1** (Scheme 3, **1**-**m**).

Scheme 3: Mesomeric form of **1**: **1**-**m**.



1

1-m

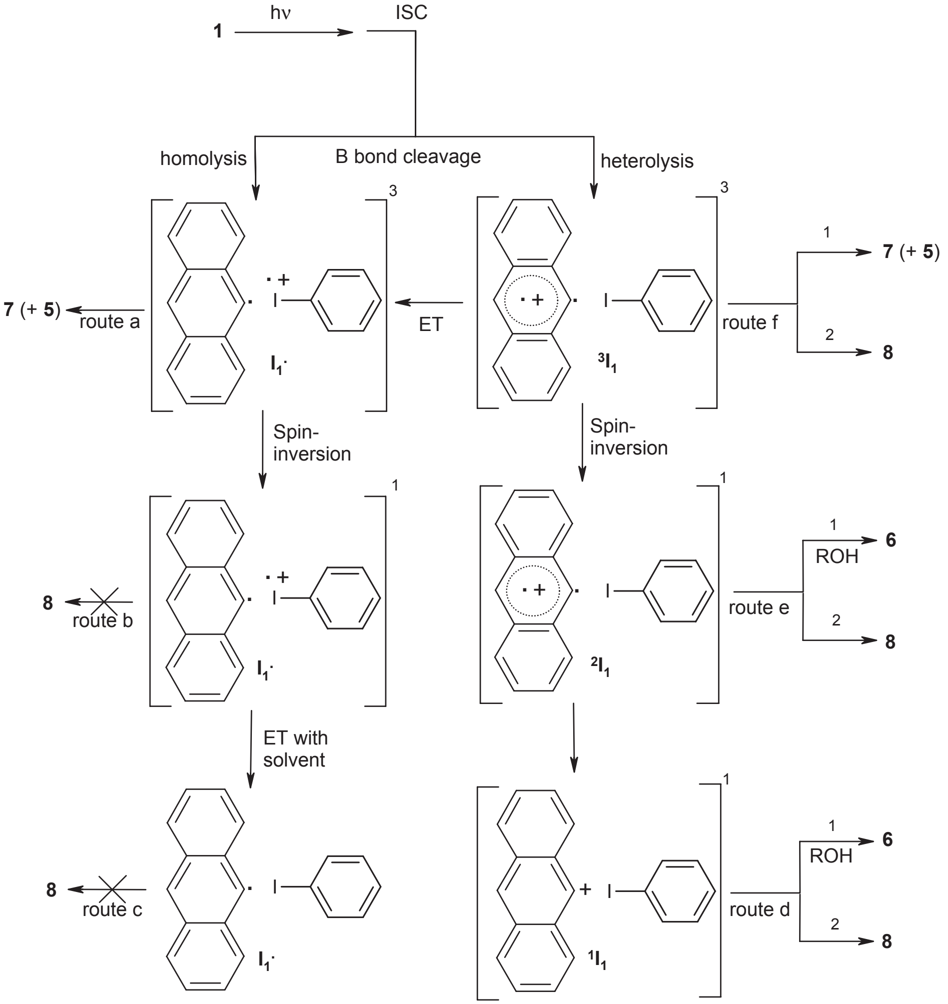
X = BF$_4$, Br

The production of anisole (**3**) upon A bond photocleavage of **1** in methanol, like the formation of that product in the photolysis of benzenediazonium tetrafluoroborate[8], and in the β-decay of [1,4]-ditritiobenzene in methanol[9], shows that a singlet phenyl cation (Ph$^+$) is generated. The product of nucleophilic addition of trifluoroethanol to Ph$^+$ (**3**-OCH_2CF_3) is not found, in line with the lower nucleophilicity of that solvent. Also, no nucleophilic substitution products with either of the counter-ions, tetrafluoroborate or bromide (**3**-F or **3**-Br) are observed. The reduction product benzene (**4**) may have been formed via hydrogen atom abstraction from the solvent by the phenyl radical (Ph•), generated upon homolysis of bond A. Alternatively, as argued in the preceding chapters, the formation of **4** may have occurred via hydrogen atom abstraction by the triplet phenyl cation, generated upon heterolysis of bond A, followed by electron transfer.

The production of 9-methoxyanthracene (**6**-OMe) in methanol is an indication of the photogeneration of the 9-anthryl cation in its closed-shell singlet manifold ($^1\mathbf{I}_1$) (Scheme 4, route d$_1$), in analogy with the formation of anisole by trapping of the closed shell phenyl cation by methanol. Alternatively, **6**-OMe may be produced from the singlet open-shell aryl cation ($^2\mathbf{I}_1$) (route e$_1$). Such a singlet carbenoid cation produces ethers, when trapped by methanol, as demonstrated for 4-N,N-diethylaminobenzenediazonium tetrafluoroborate in Chapters 3 and 4. Next, the electron-donating capacity of the annelating rings in an 9-anthryl cation, like that of the NR_2 group in the singlet 4-amino phenyl cation, is expected to enable the production of the open-shell singlet cation $^{2}\mathbf{I}_1$ out of a initially formed non-planar singlet closed shell cation $^{1}\mathbf{I}_1$' (Scheme 5) because of the large delocalisation of the positive charge in these systems.

The relatively high yield of **6**-OCH_2CF_3 in the photolysis of **1** in the less nucleophilic solvent trifluoroethanol is supportive of a carbene type insertion reaction rather than a nucleophilic addition reaction. The formation of **6** is therefore ascribed to the trapping of the open-shell singlet anthryl cation $^{2}\mathbf{I}_1$ (Scheme 4, route e_1).

Scheme 4: Possible reactive intermediates in the photolysis of **1** (B bond cleavage).



The production of **6**-Br in the photolysis of **1**Br in methanol also signals the intermediacy of an open-shell rather than a closed shell anthryl cation $^{1}\mathbf{I}_1'$. The bromide anion, a soft Lewis acid, for HSAB reasons is a good trap for the soft Lewis base open-shell cations $^{3}\mathbf{I}_1$ and $^{2}\mathbf{I}_1$ and less so for the hard Lewis base closed shell species $^{1}\mathbf{I}_1'$ [10].

Photoreduction yielding **7** is a major process in the photoreaction of **1**BF_4 and **1**Br. Its formation may occur via hydrogen atom abstraction from the solvent by the 9-anthryl radical ($\mathbf{I}_1\bullet$), produced via homolysis of the anthryl C-I bond in triplet excited **1** (Scheme 4, route a). $\mathbf{I}_1\bullet$ may also be produced via electron-transfer within the heterolytically formed triplet [$^{3}\mathbf{I}_1$ / **PhI**] pair (Scheme 4, route ET). This triplet cation may also produce **7** directly by abstraction of a hydrogen atom from the solvent, followed by electron transfer (route f_1).

The excess of reduction product **7** over alkylation product **8** in methanol hints at $\mathbf{I}_1\bullet$ rather than $^{3}\mathbf{I}_1$ as product-forming intermediate because triplet aryl cations usually display a preference for alkylation over hydrogen atom abstraction[8]. In the better cation-stabilising solvent trifluoroethanol the yields of hydrogen atom abstraction product **7** and alkylation product **8** are about the same, indicating that in this solvent relatively more $^{3}\mathbf{I}_1$ than $\mathbf{I}_1\bullet$ is generated compared to in methanol.

Other than in the photolyses of diphenyliodonium and naphthyl(phenyl)iodonium salts reported in Chapters 2 and 6 in this thesis, Friedel-Crafts type product formation upon B (and A) bond cleavage, is limited to one product, the *ipso* compound **8**. Clearly, *ipso* recombination of the fragments is far more efficient than regio-isomeric reaction steps. Since the photolysis of **1** gives mainly cleavage of bond B, the *ipso* selectivity is attributed to the reactivity of a reactive anthryl intermediate with iodobenzene rather than the reactivity of a phenyl intermediate with 9-iodoanthracene.

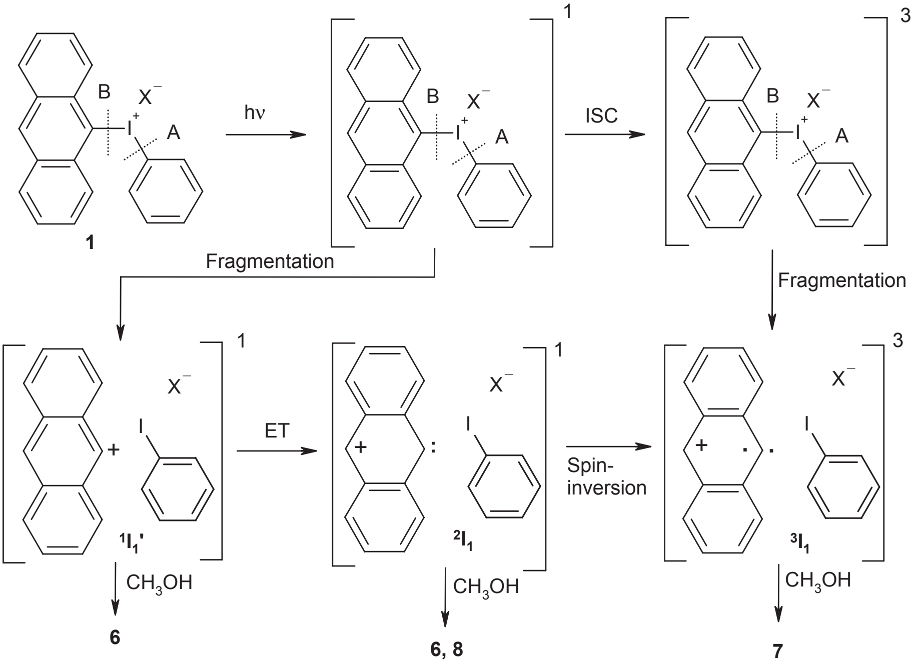
Recombination of the singlet [$\mathbf{I}_1\bullet$ / $\mathbf{PhI}^{\bullet+}$] pair (route b), formed by spin-inversion from the corresponding triplet pair, is ruled out as the source of **8** because the thermolysis of diphenyliodonium hexafluorophosphate, which produces the [$\mathbf{Ph}\bullet$ / $\mathbf{PhI}^{\bullet+}$] pair, forms *o*-, *m*- and *p*-iodobiphenyl next to biphenyl. A similar pattern is expected for the [$\mathbf{I}_1\bullet$ / $\mathbf{PhI}^{\bullet+}$] pair. Attack of $\mathbf{I}_1\bullet$ on iodobenzene (route c), formed by ET with the solvent, is expected to produce a similar product pattern as the attack of a phenyl radical on iodobenzene (with *o*, *m*, *p* iodobiphenyls in a ratio of 55:28:17[11]). This product pattern is not found. Consequently, formation of **8** does not involve the intermediacy of $\mathbf{I}_1\bullet$.

A singlet closed shell anthryl cation ($^{1}\mathbf{I}_1$ or $^{1}\mathbf{I}_1'$) is expected to display regioselectivity in its reaction with iodobenzene (route d_2) which is similar to the Friedel-Crafts product formation in the detritiation of [1,4]-ditritiobenzene in the presence of chlorobenzene (with *o*, *m*, *p* chlorobiphenyls in a ratio of 50:29:21)[12]. The triplet anthryl cation ($^{3}\mathbf{I}_1$) is expected to display the same regioselectivity toward iodobenzene (route f_2) as found in the photolysis of 4-dimethylaminophenyl(phenyl)iodonium tetrafluoroborate (with *o*-, *m*- and *p*-iodobiphenyl in a ratio of 82:3:15)[13], which is argued to produce a triplet phenyl cation-iodobenzene pair. Thus, formation of solely the *ipso*-substitution product **8** does not occur via $^1\mathbf{I}_1$ (thus also not via $^1\mathbf{I}_1$') or $^3\mathbf{I}_1$ as product-forming intermediate.

The selective formation of *ipso* product **8** is ascribed to the intermediacy of the open-shell singlet anthryl cation ($^2\mathbf{I}_1$) (route e_2). This species may react through two pathways with iodobenzene: formal insertion into the C-I bond, or addition to one of the double bonds of the aromatic ring. Since here only *ipso* product **8** is formed, unlike the typical products of carbenes[14] or nitrenes[15] with aromatic substrates, the electron-deficient carbenoid species $^2\mathbf{I}_1$ is thought to insert into the C-I bond, followed by loss of I^+.

The formation and trapping of the singlet open-shell anthryl cation $^2\mathbf{I}_1$ poses an interesting question regarding its generation. According to literature[5] and B3LYP/6-31G* calculations[16] the 9-anthryl cation $\mathbf{I}_1$ has a triplet (open-shell) ground state (S-T gap is -13.4 kcal/mol and -15.4 kcal/mol, respectively). Generation of the triplet cation $^3\mathbf{I}_1$ along the lines in Scheme 4 precludes the formation of the open-shell singlet species $^2\mathbf{I}_1$ because that would be a strongly endothermic process. So an alternative route of formation must exist for $^2\mathbf{I}_1$ (Scheme 5). This route is proposed to be similar to that of the formation of singlet aminophenyl cations, in which a singlet non planar closed shell $\mathbf{I}_1$'-NR_2 is initially formed that converts into an open-shell species $^2\mathbf{I}_1$-NR_2 (Chapters 3 and 4). The formation of intermediates from iodonium salt **1**, according to Scheme 5, is unlike the schemes employed in the literature[2] to account for the results of the photolysis of iodonium salts (Chapter 2, Scheme 1). The relative photoinstability of iodonium salt **1** (Scheme 3), compared to e.g. the parent diphenyliodonium salt, is thought to cause more efficient fission of C-I bonds in the singlet excited state rather than cleavage in the triplet excited state, even though a heavy atom is present in the molecule. The initially produced non-planar singlet anthryl cation $\mathbf{I}_1$' produced initially converts to the singlet open-shell cation $^2\mathbf{I}_1$. This species is the product-forming intermediate in most of the trapping reactions.

Scheme 5: Formation of intermediates upon electronic excitation of **1** (B bond cleavage).



Wavelength dependence of product formation

The ratio of A bond cleavage to B bond cleavage products is wavelength-dependent: A/B = 1/23 at λ_{exc} = 254 nm and 1/3 at λ_{exc} = 350 nm. At λ_{exc} = 254 nm in acetonitril (Experimental Section, Table S1) the anthryl ligand is a more efficient antenna for UV light than the phenyl ligand of the parent compound ($\varepsilon_{254} = 9.1*10^3$). A preference for B bond cleavage may be expected. Further, the energy content of the light is enough to cause fission of the anthryl C-I bond that possesses partial double bond character (Scheme 3). At λ_{exc} = 350 nm the energy of the photons is probably not enough to cause fission of bond B even though most of the light will be harvested by the anthryl ligand. According to the theoretical evaluation in Chapter 2, the fission of the bond opposite to the excited ligand is a feature of iodonium salt photolysis.

*Photoproducts of **1**BF$_4$ in acetonitrile/ anisole and trifluoroethanol/ anisole*

The *o*, *m*, *p* ratios observed in the phenylation products ***9o*, *m*, *p*** at λ_{exc} = 254 nm in acetonitrile and in trifluoroethanol (Table 2) are similar to the ratio observed in the β-decay of ditritiobenzene in anisole (65:13:22)[12]. This indicates the intermediacy of the closed-shell singlet phenyl cation as arylating agent. Changing the excitation wavelength from 254 nm via 300 nm to 350 nm leads to a shift from *para* to *ortho* product formation. The *o*, *m*, *p* ratio of ***9o*, *m*, *p*** at λ_{exc} = 350 nm resembles that of the photolysis of iodobenzene in anisole (75:13:12), and is probably the result of a phenyl radical as arylating agent. Thus, the ratios of **9*o***, ***m***, ***p*** in acetonitrile and trifluoroethanol reflect a shift from the phenyl cation (at λ_{exc} = 254 nm) to the phenyl radical (at λ_{exc} = 350 nm) as product-forming intermediate. Attempts to generate the 9-anthryl radical from **6**-Br were not successful; no product formation was found.

The *o*, *m*, *p* ratios of the arylation products **10*o***, ***m***, ***p*** are also wavelength-dependent (Table 2, column 9). At λ_{exc}= 254 nm in acetonitrile/anisole the ratio resembles ratios found upon generation of an open-shell singlet aryl cation intermediate (64:3:33)[8]. Excitation at 300 or 350 nm gives **10*o***, ***m***, ***p*** ratios which show that a mix of closed-shell singlet and open-shell singlet anthryl cations reacts with anisole. The same is true for the irradiation of **1**BF_4 in trifluoroethanol/anisole at λ_{exc}= 254 nm and 350 nm. However, for reasons yet unknown, at λ_{exc}= 300 nm an *o*, *m*, *p* ratio is observed which indicates a triplet anthryl cation as intermediate.

*Part 2: Photochemical generation of the 9-phenanthryl cation (**I_2**).*

Syntheses

9-Phenanthryl(phenyl)iodonium tetrafluoroborate (**11**) is synthesised from equimolar amounts of 9-phenanthrene boronic acid, iodobenzene diacetate and two equivalents of hydrogen tetrafluoroborate (dissolved in ether) in dichloromethane at –20°C. Extraction of the reaction mixture with a 5% $NaBF_4$ solution in demiwater, separation of the organic layer, drying on $MgSO_4$, followed by evaporation of the solvent yields **11** in 30%. 9-Bromomethylene-9*H*-fluorene (**17**) is prepared from methylene-9*H*-fluorene (**19**), which in turn was prepared by dehydration of 9-fluorenemethanol, by bromination and dehydrobromination according to a literature procedure[17].

*Photolysis of **11** in methanol*

Photolysis of iodonium salt **11** in argon-purged methanol at λ_{exc} = 254 nm at 4 °C under an argon atmosphere gives the primary photoproducts depicted in Scheme 6 and Table 3. Cleavage of bond A produces the nucleophilic substitution product anisole (**3**-OMe) and the reduction product benzene (**4**), next to the leaving group 9-iodophenanthrene (**12**)[18]. Fission of bond B yields the leaving group iodobenzene (**5**) as well as the nucleophilic substitution product 9-methoxyphenanthene (**14**-OMe) and the reduction product phenanthrene (**15**). All four possible Friedel-Crafts products, 9-(2-, 3-, and 4- iodophenyl)phenanthrene (**13*o***, ***m***, and ***p***) and the *ipso*-substitution product 9-phenylphenanthrene (**13*i***) are formed, but the former only in trace amounts.

Scheme 6: Product formation upon photolysis of **11** in methanol.

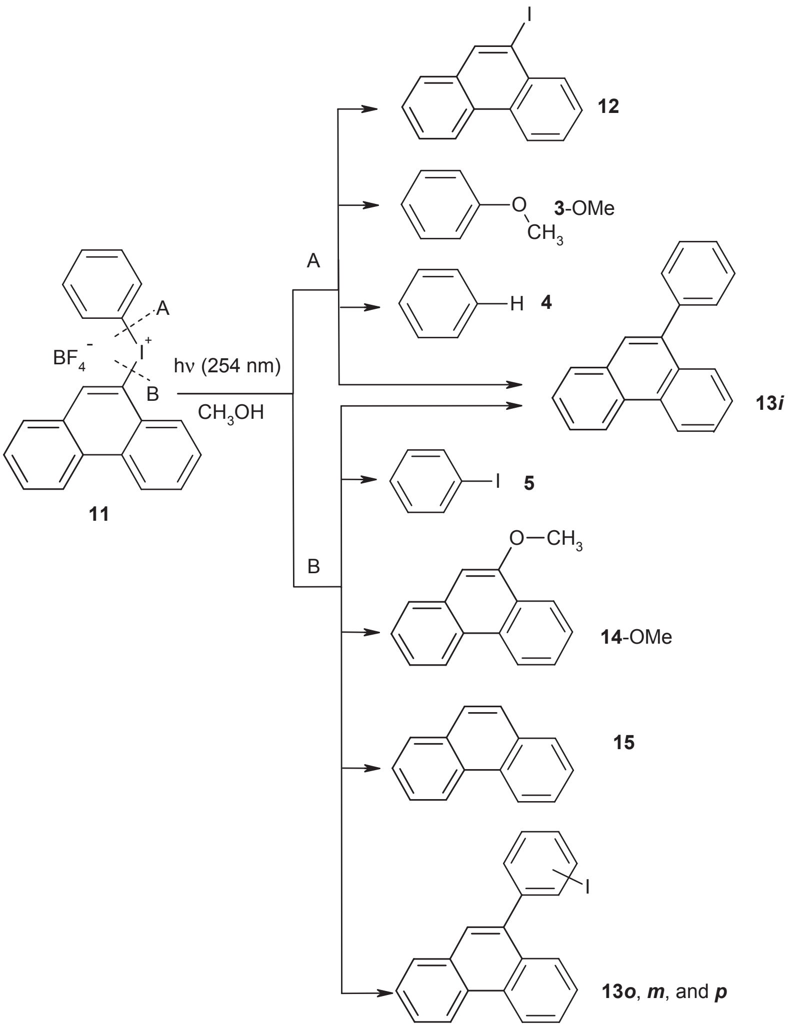


Table 3: Products of the photolysis of **11** in methanol at λ_{exc} = 254 nm at 4 °C[a,b,c].

Products:	**12**	**3**-OCH_3	**4**	**5**	**14**-OCH_3	**15**	**13**	**13o**: **m**: **p**	**13*i***
%	5	2	n.d.[c]	30	12	47	trace	76:6:19	1

[a] Under the reaction circumstances of the photolysis, thermolysis does not take place. [b] The composition of the product mixture after 90 minutes of irradiation. [c] The GC peak of benzene is obscured by those of the solvents, therefore the amount of **4** could not be determined (= n.d).

*Photolysis of **11** in trifluoroethanol/anisole*

To fingerprint the reactive intermediates formed in the irradiation of **11**, the salt is photolyzed in trifluoroethanol/anisole[8]. Next to the leaving groups **12** and **5** and the reduction products **4** and **15**, as new products 2-, 3-, and 4-methoxybiphenyl (**9*o***, ***m***, ***p***) and 9-(2-, 3-, and 4-methoxyphenyl)phenanthrene (**16*o***, ***m***, ***p***) are formed (Table 4). Of the products of nucleophilic substitution with the solvent trifluoroethanol (**3**-OCH_2CF_3 and **14**-OCH_2CF_3), only the latter is produced.

Because no literature data on the reactivity of phenanthryl radicals and cations toward anisole are available, the irradiation of 9-bromophenanthrene (**11**-Br) and 9-phenanthrenediazonium tetrafluoroborate (**11**-N_2) is performed under the same reaction conditions (Table 4). The photolysis of 9-bromophenanthrene (**11**-Br) yields mainly the reduction product phenanthrene (**15**) accompanied by the Friedel-Crafts products **16*o***, ***m***, ***p***. The photolysis of **11**-N_2 produces the reduction product phenanthrene (**15**), the nucleophilic substitution products 9-fluorophenanthrene (**14**-F) and 9-trifluoroethoxy phenanthrene (**14**-OCH_2CF_3), and the Friedel-Crafts products **16*o***, ***m***, ***p***.

Table 4: Products of the photolysis of compounds **11** in trifluoroethanol/anisole at λ_{exc}= 254 nm at 4 °C[a,b,c,d].

	s.m.	**12**	**3**-OCH_2CF_3	**4**	**9**	**9*o*:*m*:*p***	**5**	**14**-OCH_2CF_3	**15**	**16**	**16*o*:*m*:*p***
11	n.d.	15	none	n.d.[c]	11	66:11:23	19	2	0.4	10	65:11:25
11-Br	29	-	-	-	-	-	-	-	59	13	62:23:15
11-N_2	n.d.	-	-	-	-	-	-	10[b]	28	3	68:15:17

[a] The composition of the product mixture after 50 minutes of irradiation. [b] Also 5% of **14**-F is formed.
[c] The GC peak of benzene is obscured by those of the solvents, therefore the amount of **4** could not be determined (= n.d). [d] Under the reaction circumstances of the photolysis, thermolysis does not take place.

*Photoproducts of **11** in methanol*

The photolysis of **11** produces the leaving groups iodobenzene (**5**) and 9-iodophenanthrene (**12**) in a ratio of 6:1. This preference for B bond cleavage is less outspoken than in the case of **1**, where the ratio is 22:1. Like other π-donating substituents[19], the phenanthryl moiety is capable of delocalising the positive charge of the iodonium cation, but less so than the anthryl moiety.

Fission of bond B of **11** produces 9-methoxyphenanthrene (**14**-OMe) which is a strong indication for the occurrence of the 9-phenanthryl cation (**I_2**) formed through heterolytic cleavage of that bond. Just as anisole is the trapping product of the singlet closed shell phenyl cation, produced in the photolysis of benzenediazonium tetrafluoroborate or in the β-decay of ditritiobenzene, **14**-OMe is the trapping product of the singlet closed shell cation **$^1I_2$** by methanol. As discussed for the anthryl cation $\mathbf{I}_1$, trapping of the open-shell singlet cation $^2\mathbf{I}_2$ with methanol via a singlet carbene-type insertion into the O-H bond is also a possible pathway.

The major product of the irradiation of **11** is phenanthrene (**15**). This reduction product is either formed through homolysis of the C-I bond in triplet excited **11** followed by hydrogen atom abstraction from the solvent by the phenanthryl radical $\mathbf{I}_2\bullet$ or through hydrogen atom abstraction by the triplet cation $^3\mathbf{I}_2$ formed by heterolysis of the C-I bond in triplet excited **11**, followed by electron transfer.

The *ortho*, *meta* and *para* Friedel-Crafts products **13*o*, *m*, *p*** can be formed through all intermediates possible upon photohomolysis and photoheterolysis of bond B (cf. Scheme 4), the *ipso*-substitution product **13*i*** can even be formed through both A and B bond cleavage. The products **13*o*, *m*, *p*** are found in a ratio (75:6:19) very similar to the ratio in which the fragments of diphenyliodonium hexafluorophosphate recombine upon photolysis in the triplet sensitiser acetone at λ_{exc}= 300 nm (76:6:18)[2]. The latter ratio is due to the trapping of the triplet phenyl cation by the iodobenzene leaving group. Therefore **13*o*, *m*** and ***p***, and also **13*i***, are attributed to the trapping of the triplet phenanthryl cation $^3\mathbf{I}_2$ by iodobenzene.

*Photoproducts of **11** in trifluoroethanol/anisole*

The *o*, *m*, *p* ratio of biaryls **9*o*, *m*, *p*** and **16*o*, *m*, *p*** (Table 4) are similar to the ratios observed upon photolysis of benzenediazonium tetrafluoroborate (68:13:19) and diphenyliodonium tetrafluoroborate (69:12:19) under the same reaction conditions[8], and also similar to the ratio reported for the β-decay of ditritiobenzene in anisole (65:13:22)[12]. As the latter three reactions all produce the singlet closed shell phenyl cation, products **9** and **16** are ascribed to the trapping of the closed shell phenanthryl cation $^1\mathbf{I}_2$ by anisole. The formation of the nucleophilic substitution product with the solvent **14**-OCH_2CF_3 supports this proposal. Formation of this ether is evidence for the intermediacy of the singlet closed shell phenanthryl cation $^1\mathbf{I}_2$. Its production from $^2\mathbf{I}_2$ is less likely because the amount of ether product is relatively small. As observed with the open-shell singlet anthryl cation $^2\mathbf{I}_1$, trapping of open-shell singlet species with trifluoroethanol is an relatively efficient reaction.

Further, arylation of anisole by the phenanthryl intermediate, producing **16**, is 25 times more abundant than formation of reduction product **15**. This finding clearly signals that the product-forming intermediate is not the phenanthryl radical ($\mathbf{I}_2\bullet$), because with that intermediate the hydrogen atom abstraction reaction is expected to dominate. This was demonstrated to be the case by photolyzing 9-bromophenanthrene (**11**-Br) under the same reaction conditions. This gives 4.5 times more reduction product **15** than arylation products **16** (Table 4).

The control experiment in which 9-phenanthrenediazonium tetrafluoroborate (**11**-N_2) is photolyzed in trifluoroethanol/anisole, in the expectation that the closed shell cation $^1\mathbf{I}_2$ would be generated, indeed yields the nucleophilic substitution products **14**-F and **14**-OCH_2CF_3 derived from that ion. Surprisingly, a large amount of reduction product **15** is formed. Presumably, the diazonium salt is, in part, subject to photoinduced reduction by anisole. This produces phenanthryl-N_2• and next nitrogen and the phenanthryl radical $\mathbf{I_2}$• which abstracts a hydrogen atom from the solvent to yield phenanthrene (**15**). The *o*: *m*: *p* ratio in the arylation products **16** indicates that they are formed through both $\mathbf{^1I_2}$ and $\mathbf{I_2}$•.

The singlet closed shell phenanthryl cation $\mathbf{^1I_2}$, which reacts with anisole and solvent, is probably produced along the routes described for $\mathbf{^1I_1}$ in Scheme 4: hυ→ isc→ $\mathbf{^3I_2}$→ $\mathbf{^2I_2}$ → $\mathbf{^1I_2}$. This triplet to singlet conversion may be energetically feasible in solution, even though $\mathbf{^1I_2}$ is B3LYP/6-31G*-calculated to be 4.8 kcal/mol less stable than $\mathbf{^3I_2}$ in vacuum (Experimental Section, Table S2)[16]. This singlet-triplet gap is much smaller, and thus less prohibitive, than in the case of the anthryl cation $\mathbf{I_1}$ (15.4 kcal/mol). In view of the method of calculation and the effect of solvent on singlet-triplet gaps observed with the naphthyl cations (See Chapter 5, Table 3) it is safe to assume that $\mathbf{^1I_2}$ and $\mathbf{^3I_2}$ are more or less isoenergetic.

*Photolysis of 9-bromomethylene-9H-fluorene (**17**) in methanol*

The photolysis of vinylic halide **17** in argon-purged methanol under argon atmosphere yields in part the same products as the photolysis of **11** (Scheme 7, Table 5).

Next to the vinylic nucleophilic substitution product 9-methoxymethylene-9*H*-fluorene (**18a**), (its hydrolysis product 9-formylfluorene (**18b**), and the vinylic reduction product methylene-9*H*-fluorene (**19**), the aromatic substitution product 9-methoxyphenanthrene (**14**-OCH_3) and the aromatic reduction product phenanthrene (**15**) are formed. Also a hitherto unidentified product with molecular mass 288, 290 (formally the addition product of methanol to **17**) is produced.

*Photoproducts of **17** in methanol*

The formation of 9-methoxy-9H-methylenefluorene (**18a**) (and its acid hydrolysis product **18b**) signals that the photolysis of **17** occurs (in part) through heterolysis of the C-Br bond. The primary vinyl cation $\mathbf{I_3}$ formed is trapped by methanol which produces vinyl ether **18a** (Scheme 8). Also heterolysis of the C-Br bond followed by electron-transfer with the leaving group[20,1d], of the C-Br bond also takes place. This generates the vinyl radical $\mathbf{I_3}$• which by hydrogen atom abstraction produces methylene-9*H*-fluorene (**19**). The formation of the trapping product of the phenanthryl cation $\mathbf{I_2}$ with methanol (i.e. **14**-OCH_3) marks the ability of vinyl cation $\mathbf{I_3}$ to undergo a 1,2 phenyl shift across the C=C bond[21] (Scheme 8). Such a shift has also been found in the thermolysis of methylene-9*H*-fluorene-9-diazonium salt[22]. The driving force for the rearrangement must be the instability of the primary vinyl cation $\mathbf{I_3}$ compared to the

Scheme 7: Product formation upon photolysis of **17** in methanol.

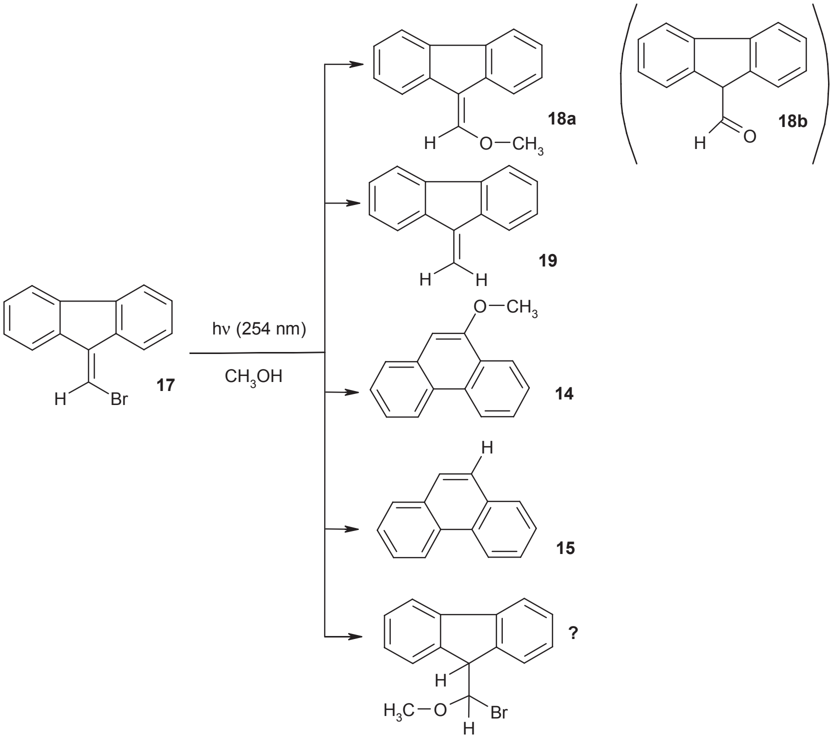


Table 5: Products of the photolysis of **17** in methanol at λ_{exc}= 254 nm at 4°C[a,b].

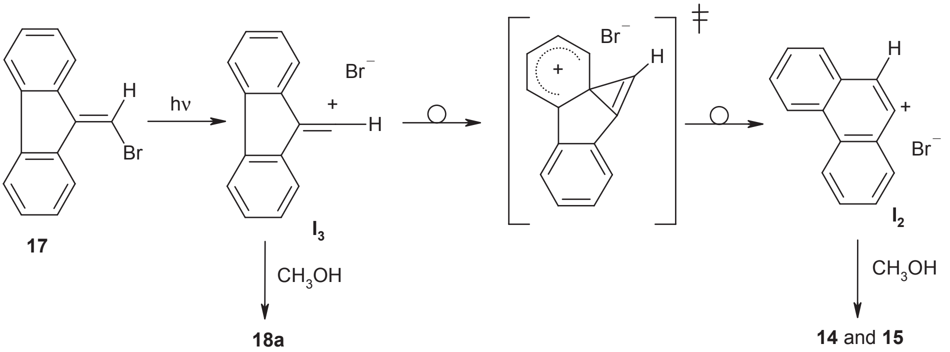
Products	**17**	**18a**+**b**	**19**	**14**-OMe	**15**	**?**
%	9	2	14	36	trace	39

[a] Under the reaction circumstances of the photolysis, thermolysis does not take place. [b] The composition of the product mixture after 120 minutes of irradiation.

aryl cation $\mathbf{I}_2$ (9.4 kcal/mol according to B3LYP/6-31G* calculations). With a phenyl group instead of a hydrogen atom at the α-position, which leads to a benzylic type stabilised vinyl cation, the shift is not observed[23]. The driving force for $\mathbf{I}_3$ to $\mathbf{I}_2$ allows rearrangement of $\mathbf{I}_3$ to effectively compete with addition of methanol to $\mathbf{I}_3$ (ratio **14**-OMe: **18** = 18:1).

A most remarkable photoproduct of **17** is the rearranged reduction product phenanthrene (**15**). It is well-established that vinyl cations undergo 1,2 phenyl shifts across the C=C bond[21]. Vinyl radicals, however, do not[24]. Possibly, upon irradiation, **17** produces the triplet vinyl cation $^3\mathbf{I}_3$ which upon rearrangement yields the triplet phenanthryl cation $^3\mathbf{I}_2$ which may be trapped by the bromide anion yielding **11**-Br (a product not observed) or abstract a hydrogen atom from the solvent and subsequently undergo electron-transfer to yield **15**. Alternatively, **15** is the

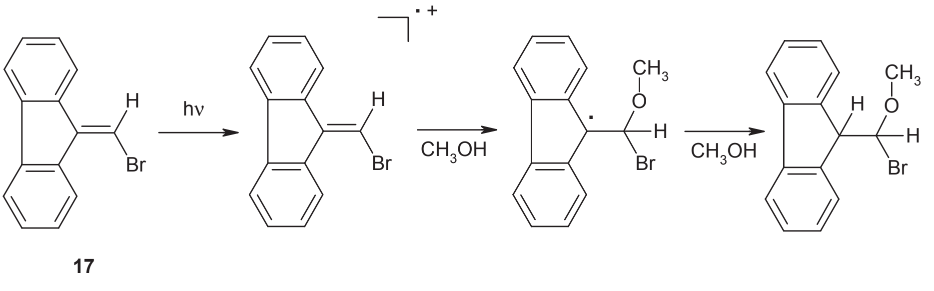
Scheme 8: Formation of the phenanthryl cation $\mathbf{I_2}$ from the vinylic cation $\mathbf{I_3}$.



result of electron-transfer between the aryl cation $\mathbf{I_2}$ and the bromide leaving group[25], producing the $\mathbf{I_2}$•/Br• radical pair. The aryl radical can abstract a hydrogen atom to yield **15**.

The product with mass 288, 290 is tentatively assigned to be the product of addition of methanol to **17**. This type of reactivity is encountered before in this thesis (Chapter 5, Scheme 5) and is thought to be photo-induced formation of the radical cation of **17** (via electron-transfer with the solvent) which next reacts with methanol (Scheme 9).

Scheme 9: Mechanism of formation of the m = 288, 290 product.



Conclusions

For the first time the 9-anthryl cation $\mathbf{I_1}$ and the 9-phenanthryl cation $\mathbf{I_2}$ have been generated and their reactivity has been studied. Trapping studies indicate that the product-forming intermediate, formed by photolysis of iodonium salt **1**, is the open-shell singlet state $\mathbf{^2I_1}$ of cation $\mathbf{I_1}$. The photolysis of **1** is wavelength-dependent: at λ_{exc} = 254 nm the anthryl C-I bond of the iodonium salt is preferentially cleaved while at λ_{exc} = 300 and 350 nm that preference is less outspoken.

Trapping studies of $\mathbf{I_2}$ show that it reacts in its closed-shell singlet state $^1\mathbf{I_2}$ in both routes through which the cation was produced: directly, by photolysis of the corresponding phenanthryl iodonium salt, or indirectly, by photolysis of the vinylic bromide 9-bromomethylene-*9H*-fluorene. The latter compound yields a primary vinyl cation $\mathbf{I_3}$ which undergoes rearrangement to $\mathbf{I_2}$. In the direct route, the singlet cation is preceded by the triplet cation $^3\mathbf{I_2}$, which forms by heterolysis of the C-I bond in the triplet excited state of the salt. The triplet cation is partly trapped by the leaving group iodobenzene, and partly isomerises to the (probably) more stable singlet closed shell species. In the indirect route it is not clear at which stage triplet/singlet conversion takes place.

The above results open a new perspective for the tagging of substrates with a fluorescent moiety. The precursors **1**, **11** and **17** do not fluorescence, because of the presence of a heavy atom in the molecule, but the tag after the alkylation event does. This offers the possibility to track the tagged substrate without interference of the pre-fluorescent photolabile group.

Experimental Section

Materials

The compounds 9-anthryl(phenyl)iodonium tetrafluoroborate (**1**BF_4) and 9-anthryl(phenyl)-iodonium bromide (**1**Br) are synthesised from 9-(4, 4, 5, 5-tetramethyl-1, 3, 2-dioxoborolanyl) anthracene and Koser's reagent (hydroxy(tosyloxy)iodobenzene) in dichloromethane at –60°C. After 1 hour of stirring at –60°C, the reaction mixture is warmed to 0°C and extracted three times with a 5% $NaBF_4$ solution or one with a 5% NaBr solution in demiwater. The organic layer is separated, dried on $MgSO_4$, and the solvent is evaporated. The residue is washed with ethylacetate and pentane and evaporated to dryness. Product **1**-BF_4 is obtained, after 5 crystallisations from THF/pentane, in 9% yield. NMR (^{1}H, DMSO d6, δ): 7.20-7.35 (t, 3H); 7.35-7.50 (d, 2H); 7.60-7.75 (t, 2H); 7.75-7.90 (t, 2H); 7.90-8.00 (d, 2H); 8.10-8.30 (d, 2H); 8.55-8.70 (d, 2H); 8.95-9.05 (s, 1H). IR (neat, cm^{-1}): 386, 454, 518, 679-696-734, 1018 (BF_4^-), 1676, 3000.

Table S1: UV-VIS data for compound **1**BF_4 at 1.0×10^{-5} M.

Solvent	$\lambda_{max,1}$ (nm)	$\varepsilon_{max,1}$ ($M^{-1}cm^{-1}$)	$\lambda_{max,2}$ (nm)	$\varepsilon_{max,2}$ ($M^{-1}cm^{-1}$)
Acetonitrile	386.0	$8.1*10^3$	254.0	$1.3*10^5$
Acetic Acid	385.5	$8.3*10^3$	254.0	$1.3*10^5$
Trifluoroethanol	385.0	$7.9*10^3$	251.0	$1.5*10^5$
Methanol	385.0	$8.8*10^3$	254.0	$1.5*10^5$

Product **1**Br is obtained in 15% yield. NMR (^{1}H, DMSO d6, δ): 7.15-7.35 (m, 5H); 7.55-7.70 (t, 2H); 7.70-7.85 (t, 2H); 7.85-7.95 (d, 2H); 8.10-8.20 (d, 2H); 8.50-8.60 (d, 2H); 8.90-8.95 (s, 1H).

Both salts are somewhat thermolabile, and they are washed with diethyl ether and pentane prior to their use. 9-Bromoanthracene (**6**-Br) is commercially available.

9-Phenanthryl(phenyl)iodonium tetrafluoroborate (**11**BF_4) is synthesised from equimolar amounts of 9-phenanthrene boronic acid, iodobenzene diacetate and two equivalents of hydrogen tetrafluoroborate (dissolved in ether) in dichloromethane at –20°C. Extraction of the reaction mixture with a 5% $NaBF_4$ solution in demiwater, separation of the organic layer and drying on $MgSO_4$, followed by evaporation of the solvent yields **11**BF_4 in 30% yield. NMR (^1H, $CDCl_3$, δ): 6.7-6.8 (d, 2H); 7.1-7.3 (q, 1H); 7.3-7.5 (t, 2H); 7.6-7.8 (m, 4H); 7.8-7.95 (d, 2H); 8.5-8.6 (d, 2H); 8.7 (s, 1H). NMR (^{13}C, Solid): 114.1 (C-I^+ phenanthryl), 119.6 (C-I^+ phenyl), 121.9, 126.6, 128.8, 131.6, 132.9, 133.8, 135.1, 136.3, 139.3. IR (neat, cm^{-1}): 406, 430, 449, 504, 519, 648-678-719-748, 1018 (BF_4^-), 3064. 9-Phenanthryldiazonium tetrafluoroborate **11**-N_2 is prepared from the corresponding amine by diazotation in 15% aqueous hydrotetrafluoroboric acid with 1.1 equivalent sodium nitrite at melting ice temperature. 9-Bromophenanthrene (**11**-Br) is commercially available.

9-Bromomethylene-9*H*-fluorene (**17**) is prepared from methylene-9*H*-fluorene (**19**), which in turn was prepared by dehydratation of 9-fluorenylmethanol, by bromination in CCl_4 followed by dehydrobromination with a saturated $NaHCO_3$ solution in demiwater[17]. After extraction with CCl_4, the combined organic layers are dried on $MgSO_4$ and the solvent is evaporated. The yield of **17** is 80% (based on **19**) NMR (^1H, $CDCl_3$, δ): 7.26 (s, 1H), 7.40 (m, 4H), 7.60 (d, 2H), 7.66 (d, 2H).

Photochemistry

The photochemical reactions in methanol or trifluoroethanol were carried out in quartz tubes equipped with a rubber seal, that are placed in a merry-go-round apparatus. A Hanau TNN-15/32 low pressure mercury lamp placed in a water cooled quartz tube is used to supply light with a main emission at $\lambda = 254$ nm. For the irradiations 0.02 M solutions of the photolabile compounds **1**BF_4, **1**Br, **6**-Br, **11**BF_4, **11**-Br, **11**-N_2 or **17** in 10 mL methanol are prepared. 25 µL n-decane is added as internal standard. Samples (200 µl) are taken at t = 0, 5, 10, 15, 20, 25, 30, 40, 50, 60, 70, 90 and 120 minutes of irradiation. Up till 50 minutes for compounds **1**, 90 minutes for compounds **11**, and 120 minutes for compound **6** and **17** the conversions are still low and all products are primary photoproducts. The samples are added to 500 µL water and 300 µL ethylacetate. The organic layers are analyzed by GC and GC-MS. The 90 minutes irradiation mixtures are poured into 50 mL water and extracted with 10 mL ethylacetate. The organic layer is separated and dried on $MgSO_4$. The solvent is evaporated and the residues were redissolved in 0.5 mL dichloromethane for GC and GC-MS analysis.

The products studies at λ_{exc}= 254, 300 and 350 nm are carried out in a Rayonet Reactor (RPR200) fitted with seven 254, 300 or 350 nm lamps. Samples and analysis as above.

The photochemical reactions in acetonitrile/anisole and trifluoroethanol/anisole were carried out in quartz tubes equipped with a rubber seal. The starting materials were dissolved at 0.02 M in 10 mL 1/1 (v/v) acetonitrile/anisole or 1/1 (v/v) trifluoroethanol/anisole. 25 μL *n*-Decane was used as internal standard. The tubes were placed in a Rayonet Reactor (RPR200) fitted with seven 2539 Å lamps. The photolyses of the photolabile compounds were followed as a function of time by taking aliquots (0.2 mL sample) and adding them to 0.5 mL water + 0.3 mL ethylacetate. The organic layers were analyzed by GC and GC-MS.

Photoproducts

The assignment of the structures of the photoproducts by GC and GC-MS was confirmed by coinjection of commercially available or independently prepared products. Compounds **3**-OCH$_3$, **3**-NHAc (not observed in the product mixtures), **3**-Br, **4**, **5**, **6**-Br, **7**, **8**, **9*o***, ***m***, ***p***, **11**-Br, and **15** are commercially available. Products **2**[26], **3**-OCH$_2$CF$_3$[4d], **6**-OCH$_3$[27], **6**-OCH$_2$CF$_3$[28], **6**-NHAc (not observed in the product mixtures)[29], **10*o***, ***m***, ***p***[30], **12**[26], **13*i***[31], **14**-OMe[32], **14**-F[33], **18a**[34] and **18b**[34], and **19**[35] are prepared according to literature procedures. The structures of **13*o***, ***m***, ***p***, **16*o***, ***m***, ***p*** and **14**-OCH$_2$CF$_3$ are assigned tentatively.

Quantum Chemical Calculations

Little or no information is available about the ground state multiplicity and the singlet-triplet gaps of anthryl, phenanthryl and larger aromatic cations. A short preliminary quantum chemical study is performed mapping the ground state of various aryl cations, their singlet-triplet gaps and aspects of their structures (Table S2). The results of the B3LYP/6-31G* are compared with the most recent theoretical data calculations on the properties of aryl cations[5,36,37].

Table S2: Results of the quantum chemical studies.

Method	Property	Phenyl	1-Naphthyl	9-Anthryl	9-Phenanthryl	1-Pyrenyl
AM1	S-T gap	+7.1	-14.4	-1.0	-13.9	-27.8
AM1	$^{1}\mathrm{C}^{+}\angle$	141°	143°	143°	144°	142°
AM1	$^{3}\mathrm{C}^{+}\angle$	131°	129°	131°	130°	130°
(U)HF 6-31G*	S-T gap	-11.0	-28.2	-42.2	-34.0	-47.2
(U)HF 6-31G*	$^{1}\mathrm{C}^{+}\angle$	146°	148°	113°	149°	148°
(U)HF 6-31G*	$^{3}\mathrm{C}^{+}\angle$	125°	125°	127°	127°	125°
B3LYP 6-31G*	S-T gap	+22.6	-2.6	-15.4	-4.8	-14.8
B3LYP 6-31G*	$^{1}\mathrm{C}^{+}\angle$	147°	149°	143°	142°	137°
B3LYP 6-31G*	$^{3}\mathrm{C}^{+}\angle$	124°	127°	128°	127°	126°
Literature[5]	S-T gap	+19.6	-0.6	-13.4	-	-15.3[37]
Literature[5]	$^{1}\mathrm{C}^{+}\angle$	147.3°	148.6°	-	-	-
Literature[5]	$^{3}\mathrm{C}^{+}\angle$	127.7°	-	-	-	-

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 DMX 300, using DMSO D_6 as solvent. As analytical GC a Hewlett-Packard 6890 model was used, equipped with an 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 an 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.

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[6] Stirring **1** for 40 minutes at room temperature produces 1.7% of iodobenzene. In 40 minutes of irradiation at λ_{exc} = 254 nm and 4°C, 21% iodobenzene is produced.

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Chapter 8 | **Perspectives**

"As many of the reactions are described poorly, if at all understood, this is not as unsatisfactorily as it may seem. Indeed, many photogenerated reagents have proved extremely useful in the absence of any detailed knowledge of the way in which they react!"

Hagan Bayley in: Photogenerated reagents in biochemistry and molecular biology; Work, T. S.; Burdon, R. H. Burdon, Eds., Elsevier, Amsterdam, 1983.

Photogeneration of aryl and vinyl cations

In Chapter 2 of this thesis it is proposed that photolysis of 4-substituted phenyliodonium salts gives a singlet phenyl cation-iodobenzene pair by heterolytic C-I bond cleavage in the singlet excited state, and a triplet phenyl cation-iodobenzene pair by heterolytic cleavage in the triplet excited state. This proposal is different from the mechanism embraced in the literature where homolytic cleavage in the triplet excited state, resulting in a phenyl radical and a iodobenzene radical cation, is an important intermediate-forming route next to heterolysis in the singlet excited state. The strongest evidence for the occurrence of homolytic cleavage is the observation of the iodobenzene radical cation (not the phenyl radical) by flash-photolysis on the picosecond time scale.

It is expected that flash-photolysis experiments on an even shorter time scale (<500 fs) will reveal the formation of extremely short-lived triplet aryl cation-iodobenzene pairs, which upon electron transfer form the radical/radical cation pair. Both the direct and the indirect formation of the phenyl radical account for the radical-derived productformation, but selectivity in the trapping of the leaving group by the reactive intermediate formed upon photolysis is best understood by assuming heterolytic cleavage from the triplet excited state.

Vinyl cations, like phenyl cations, probably can be formed in their singlet or triplet manifold. Triplet reactivity, however, is seldom or never considered in the discussion of the vinyl cations produced upon photolysis of vinyl(pseudo)halides. It is of interest to subject vinyl halides and vinyl(phenyl)iodonium salts to femtosecond range flash photolysis experiments, to establish a foothold for the interpretation of product patterns in terms of singlet or triplet product-forming reactive intermediates.

Hitherto, little or no attention has been paid to the issue that phenyl cations are generated either from the singlet or the triplet excited state, that both routes may yield cations, and that these cations may display different chemistry. The resulting chemo- and regioselectivity depend on the intersystem crossing ability of the electronically excited precursors and on the multiplicity of the cations. Photolysis of a variety of phenyl cation precursors in acetonitrile/anisole gives product patterns that are indicative of the spin-multiplicity of the reacting cationic intermediate ("fingerprinting") (Chapters 2 and 4). Also the cations can be distinguished from the corresponding phenyl radicals ("profiling"). That same method also gives indicative product patterns for the 1-naphthyl, 9-anthryl and 9-phenanthryl cation (Chapters 6 and 7). It is expected that this indicative reaction can be applied to all types of phenyl and aryl cations.

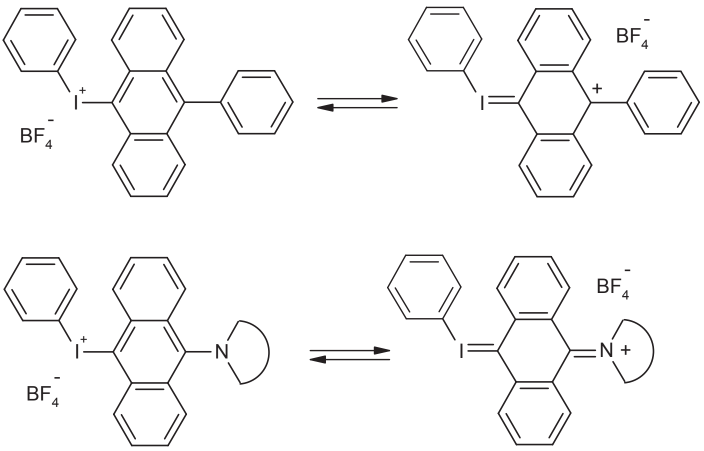
B3LYP/6-31G* calculations on the electronic ground state of a series of polynuclear aryl cations give singlet/triplet gaps which agree with the results of higher level calculations. In the case of small singlet/triplet gaps as for the 1- and 2-naphthyl and the 9-phenanthryl cation, the order of the states may invert by the presence of a polar solvent as observed for the naphthyl cations. For the 1-pyrenyl cation a quite large singlet/triplet gap is calculated, which is not inverted by the presence of any solvent. This ion is predicted to show typical triplet cation behavior. Because the synthesis of the precursors is time-consuming it may pay off to base the design of any such ions on the results of quantum mechanical calculations.

The photolysis of 1-naphthyl(phenyl)iodonium tetrafluoroborate and 2-naphthyl(phenyl)iodonium tetrafluoroborate yields 2- and 1-naphthyl substituted products, respectively (Chapter 5). This *cine*-substitution product pattern is attributed to the ability of the triplet naphthyl cations to undergo a 1,2-H-shift or lose a β-proton and form a triplet naphthyne. *Cine* substitution is also expected to occur the photolysis of 1-pyrenyl(phenyl)iodonium tetrafluoroborate because the 1-pyrenyl cation has a triplet ground state which will be generated from the triplet state of the iodonium salt.

Photolysis of appropriately (e.g. N,N-dimethylamino) substituted diphenyliodonium and benzenediazonium salts, produces mainly singlet, open-shell cations as product-forming intermediates with particular chemistry (Chapters 2 and 3). In *para* amino substituted phenyl cations this is probably due to the phenomenon that the initially formed singlet closed-shell phenyl cation resembles the singlet open-shell cation in energy. In the photolysis of 9-anthryl(phenyl)-iodonium tetrafluoroborate (Chapter 7), an open-shell aryl cation is also proposed as product-forming intermediate. For the 9-anthryl cation intermediate the same relation between the singlet closed shell and the singlet open cation is proposed as for the 4-amino phenyl cation.

It is predicted that the importance of the singlet open-shell cation as product-forming intermediate will be even more outspoken in the photolysis of 9-(10-phenylanthryl)(phenyl)-iodonium salt, (9-[1-anthracen-10-ylpyrrolidinyl])(phenyl)iodonium salt and (9-[1-anthracen-10-ylpiperidine])(phenyl) iodonium salt (Scheme 1). The first compound has already been prepared in our laboratory and is a mint green salt of which only solid state NMR and IR measurements could be made because of the insolubility of the material. Is is proposed that the isolated salt is the chinoid isomer of the iodonium salt that upon photolysis will mainly produce a singlet carbenoid cation next to some triplet carbenoid cation.

Scheme 1: Isomers of iodonium salts with an extended electron-rich ligand.



Photoalkylation of nucleic acids

In the photoalkylation of nucleic acids four types of precursors are commonly used: 1) azides, producing nitrenes, 2) photolabile compounds yielding carbocations, 3) photolabile compounds yielding quinone methides and, 4) psoralens, which form [2+2] photocycloaddition constructs. Precursors yielding radical intermediates are barely even used for alkylation purposes because radicals preferentially abstract a hydrogen atom from the (deoxy)ribose moiety, thereby inducing strand cleavage.

The use of photogenerated nitrenes, carbocations and quinone methides suffers from side reactions that are non-productive for photoalkylation. Singlet nitrenes produced in the photolysis of azides, isomerise in part to a less reactive intermediate prior to reaction with substrate. Triplet nitrenes react predominantly through hydrogen atom abstraction (from the sugar moiety). Carbocations alkylate the phosphate group rather than the nucleobases and also react readily, non-productively, with hydroxylic solvents such as water. Quinone methides react faster with hydroxylic solvents than with the nucleobases (at the exo-amino functions of guanine and adenine).

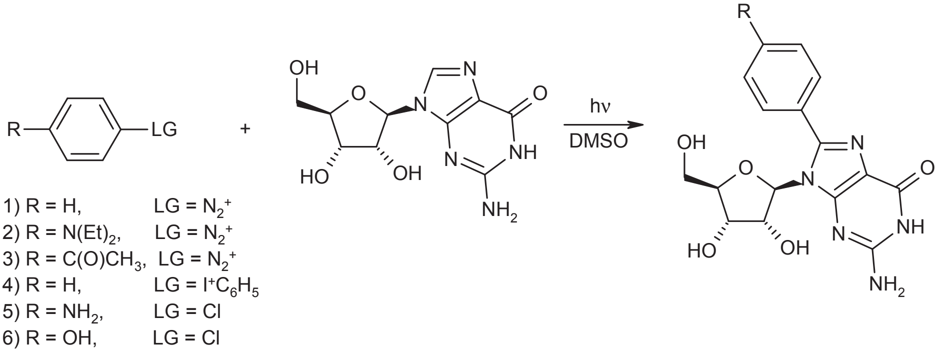
Aryl cations, in particular the triplet species, are expected to be more efficient in their reaction with the nucleobases of nucleic acids than the conventional intermediates and also to be more selective:

1. Aryl cations, trapped by a nucleophilic substrate, yield alkylation products in large excess over hydrogen abstraction products (Chapter 4).
2. The possibility to prepare singlet and triplet isomers of aryl cations (Chapter 6) provides chemoselectivity, leading to a preference for π over n nucleophiles (i.e. nucleo-

bases over phosphate groups and hydroxylic solvents). This feature is usually not compatible with high reactivity.

To illustrate this prospect a selection of typical aryl cation precursors (Chapter 4) was irradiated at 0.01 M in DMSO in the presence of an equimolar amount of guanosine at λ_{exc} = 300 or 350 nm (Scheme 2, Table 1). In experiment 1 and 4 the formation of 8-phenylguanosine (R = H), in experiment 3 the formation of 8-acetylphenylguanosine (R = C(O)CH_3, and in experiment 6 the formation 9-hydroxyphenylguanosine (R=OH) was confirmed by coinjection with independently prepared samples. Alkylation at position 8 of guanosine is in agreement with literature data that cationic intermediates (eventually) as well as radical intermediates alkylate C-8. (NB: the regioselectivity of triplet aryl cations is that of a phenyl radical (Chapter 4)). The preliminary results of Table 1 indicate that triplet phenyl cations, specially the ones destabilised by the electron-withdrawing carbonyl group, are significantly more reactive toward guanosine than singlet phenyl cations (entries 5, 6 and especially 3 versus 1 and 4).

Scheme 2: Indicative photoreactions of a selection of aryl cation precursors with guanosine.



1) R = H, LG = N_2^+
2) R = N(Et)$_2$, LG = N_2^+
3) R = C(O)CH_3, LG = N_2^+
4) R = H, LG = $I^+C_6H_5$
5) R = NH_2, LG = Cl
6) R = OH, LG = Cl

Table 1: Indicative photoreactions of a selection of aryl cation precursors with guanosine.

Exp.	Photolabile compound	λ_{exc} (nm)	Product[a]
1	benzenediazonium BF_4^-	300	4
2	N,N-diethylaminophenyldiazonium BF_4^-	350	0
3	4-acetyl benzenediazonium BF_4^-	300	36
4	diphenyliodonium BF_4^-	300	3
5	4-chloroaniline	300	20
6	4-chlorophenol	300	10

[a] Arylation product as percentage of total amount of LC-MS observed product after 3 hrs of irradiation.

Photoalkylated residues of nucleic acids are usually analyzed by mass spectrometry, by using radioactive tracers (mainly iodine) and by fluorescence. Fluorescence nowadays is the method of choice. It couples high sensitivity with the appealing possibility of fluorescence microscopy. Photolysis of iodonium salts substituted with a large aromatic ligand (e.g. anthryl, phenanthryl, pyrenyl) releases the corresponding anthryl and phenanthryl cations and probably also the pyrenyl cation. Reaction of these cations with nucleic acids, is predicted to produce fluorescent DNA or RNA residues that can be visualised or separated from the bulk. The best results are expected for tagging with the pyrenyl moiety which is an effective fluorescer and less sensitive to (photo)oxidation than e.g. the anthryl moiety.

A major disadvantage of all precursors discussed thus far is the unselectivity of their photoreactions with respect to the base sequence of the nucleic acids. This disadvantage has been addressed by coupling photolabile precursors to a strand-recognizing peptide nucleic acid (PNA) molecule. Provided that the photolabile compound can be excited at a wavelength beyond the absorption of nucleic acids and the PNA, such constructs, upon irradiation, give alkylations in a desired region of nucleobases. Coupling of photolabile triplet aryl cation precursors, which can be excited above $\lambda = 320$ nm, to molecules with base sequence-recognizing ability (e.g. PNA) is expected to result, upon photolysis, in a specifically tagged nucleic acid molecule that is traceable by means of fluorescence detection.

The method of synthesis of iodonium compounds described in this thesis may be used in a post-synthetic strategy to prepare constructs of a target identifying molecule and a photoactivatable aryl cation releasing agent. After synthesis and purification of the identifying strand in which one position is used to carry a (masked) phenyl boronic acid functionality the molecule is treated with (hydroxy(tosyloxy))iodoarene.

A covalent coupling leading to fluorescence between a recognizing molecule and a target molecule can also be achieved by employing a vinyl halide as 9-bromomethylene-*9H*-fluorene (Chapter 7) attached to a recognition unit. In this case a recognizing molecule has to be prepared in which one of the positions is still available for coupling the vinyl halide through a handle on one of the aromatic rings.

Photoalkylation of proteins

Photoalkylation of proteins is used extensively in photoaffinity labeling, a technique employed to study ligand-receptor interactions and membrane or protein topographies. The photolyses of azides (producing nitrenes), diazo-compounds (yielding carbenes), diazonium salts (producing carbocations or radicals) and diazirines (yielding carbenes) have found wide application. Disadvantages of these types of intermediates are: important side reactions such as hydrogen atom abstraction and formal insertion reaction with hydroxylic solvents, as has been outlined above. Because (triplet) aryl cations do not suffer these disadvantages (also see above), a high yielding photoreaction of aryliodonium salts with amino acids is expected. Pre-complexation will be an extra beneficial factor. The positively charged iodonium salts are able to coordinate with a hydroxyl or a carboxyl group in amino acids such as phenylalanine, tyrosine or tryptophane. Photolysis of the iodonium salt then liberates a highly reactive triplet aryl cation in close proximity to an amino acid bearing an aromatic substructure.

To illustrate this prospect a selection of aryl cation precursors (Chapter 4) was irradiated at 0.01 M in acetonitrile in the presence of an equimolar amount of acetylated phenylalanine at λ_{exc} = 254 or 300 nm (Scheme 3, Table 2). These preliminary results indicate that the triplet phenyl cations generated in experiments 2, 4 and 5 have similar reactivity as the carbenes generated in experiment 6. Purely judged on overall reactivity they are no match for the parent phenyl cation generated in experiment 1. But the chemoselectivity (C- and O- alkylation in experiments 1 and 3 versus only C-alkylation in experiments 2 and 4 to 6) makes the triplet phenyl cations more useful because they do not react with the carboxylic acid group.

Scheme 3: Indicative photoreactions of a selection of aryl cation precursors with N-acetylated phenylalanine.

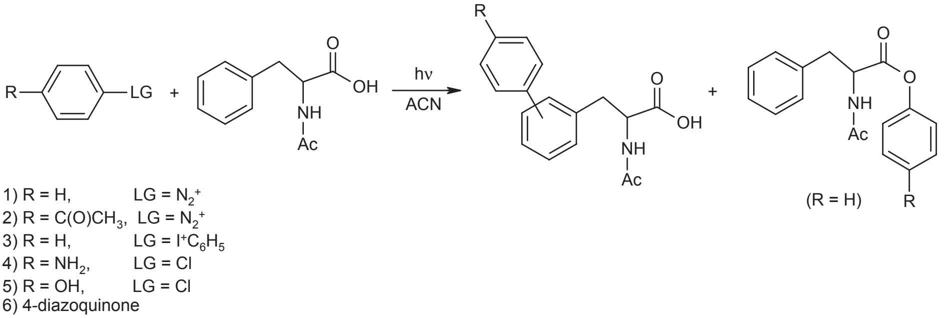


Table 2: Indicative photoreactions of a selection of aryl cation precursors with N-acetylated phenylalanine.

Exp.	Photolabile compound	λ_{exc} (nm)	Product[a]
1	benzenediazonium BF_4^-	254	22[b]
2	4-acetyl benzenediazonium BF_4^-	254	8
3	diphenyliodonium BF_4^-	254	7[b]
4	4-chlorophenol	254	5
5	4-chloroaniline	300	6
6	4-diazoquinone	254	11

[a] Alkylated product as percentage of total amount of LC-MS observed product after 3 hrs of irradiation.

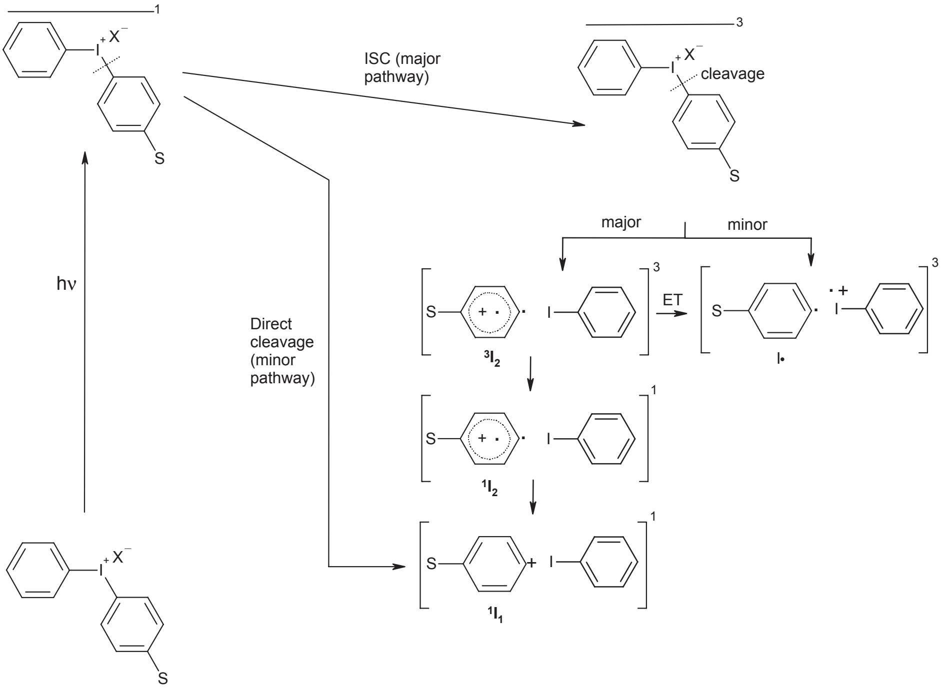
[b] Combined yield of the products of arylation at the phenyl ring and the carboxyl group.

Selective C-alkylation of amino acids is also predicted to occur upon photolysis of iodonium salts substituted with a large aromatic ligand (e.g. anthryl, phenanthryl, pyrenyl). These salts release the anthryl, phenanthryl and probably the pyrenyl cation, which will react at the soft nucleophilic spots on a protein molecule and produce fluorescent polypeptides that can be visualised or separated from the bulk.

Summary

This thesis describes the results of a project to develop novel strategies for the alkylation of nucleobases and amino acids. The foundations of the project were the knowledge about and experience with highly reactive vinyl and aryl cations of the organic photochemistry group, and the knowledge about and the experience with nucleotide and peptide chemistry of the bio-organic synthesis group. The primary aim of the research was to obtain selectivity of reaction of aryl and vinyl cations via photolysis of especially developed precursors. Applications of new (and existing) methods of photoalkylation are to be found in the diagnostic toolbox of biochemists and biological chemists, and possibly in the treatment of DNA-based malfunction of specific cell groups (photodynamic therapy).

Scheme 1: Proposed mechanism of photolysis of diphenyliodonium salts.

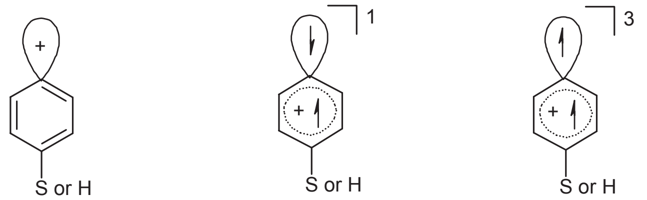


While charting the possibilities to apply diphenyliodonium salts, which are well-known as photo-acid generators (and anti-biotic agents), as photoalkylation agents, regio- and chemoselectivities were observed which led to the proposal for the mechanism of the photolysis of these compounds depicted in Scheme 1 (Chapter 2). The C-I$^+$ bond cleavage proceeds mainly from the triplet excited state. The ramifications of this proposal are that, compared to the widely embraced mechanism of the photolysis of diphenyliodonium salts, singlet excited state bond cleavage is less important and the triplet excited state predominantly produces a triplet phenyl cation (**$^3I_2$**) instead of a phenyl radical (**I•**). However, it should be noted that neither direct homolysis (producing **I•**) nor direct heterolysis of the singlet excited state (yielding $^{1}\mathbf{I}_1$) can be excluded completely.

Singlet and triplet phenyl cations were expected to differ in their reaction selectivity. This was tested by generating singlet and triplet phenyl cations through different routes in the presence of various substrates. Since published quantum chemical calculations indicated that the only phenyl cation with a triplet ground state is the 4-aminophenyl cation, precursors supposedly leading to this cation were photolyzed.

The distinct regioselectivities and chemoselectivities observed demonstrate that the 4-amino phenyl cation is generated in different manifolds depending on the excited state from which the bond cleavage occurs (Chapter 3). The nature of the leaving group determines whether a singlet or a triplet phenyl cation is produced. With halogen as leaving group, cleavage occurs in the triplet excited state yielding triplet cation $^{3}\mathbf{I}_2$. With N_2 as leaving group, cleavage occurs in the singlet excited state yielding the closed-shell singlet cation $^{1}\mathbf{I}_1$ and the open-shell singlet cation $^{1}\mathbf{I}_2$ (Scheme 2). Photolysis of the corresponding iodonium salt yields both the triplet and the singlet phenyl cation.

Scheme 2: Isomers of phenyl cations.



Closed shell singlet phenyl cation $S = NR_2$ or OH — $\mathbf{I}_1 : \pi^6\sigma^0$

Open shell singlet phenyl cation $S = NR_2$ or OH — $\mathbf{I}_2 : \pi^5\sigma^1$

(Open shell) triplet phenyl cation $S = NR_2$ or OH — $\mathbf{I}_3 : (\pi^5\sigma^1)^3$

According to quantum chemical calculations, the singlet and triplet species of the 4-hydroxyphenyl cation are of about the same stability. Observations of the reactivity of this cation as a function of its precursors were similar to those for the 4-aminophenyl cation. With (bromide or) chloride as leaving group the triplet cation $^{3}\mathbf{I}_2$ is produced, with nitrogen as leaving group the singlet cation(s) $^{1}\mathbf{I}_2$ and $^{1}\mathbf{I}_1$ are formed.

The study established a firm relation between the multiplicity of phenyl cations and the leaving group of their precursors. Additionally, it was shown that the 4-hydroxyphenyl cation does not deprotonate prior to its reaction with nucleophiles, as demonstrated by the generation and reactivity of that deprotonated species by photolysis of diazoquinone.

The photolysis of seven photolabile compounds, known to produce phenyl cations, in acetonitrile in the presence of anisole yields methoxybiaryls in four distinct *o*, *m*, *p* ratios (Chapter 4). The differences in regioselectivity are due to the different nature of the product-forming intermediates: a singlet closed shell cation, a singlet open-shell cation, an EDG-substituted triplet cation, and an EWG-substituted triplet phenyl cation, respectively. The differences in spin state of the cations, and consequently the differences in electronic configurations, result in different mechanisms of reaction. This spin-selective chemistry provides a tool to fingerprint the singlet/triplet nature of any aryl cation.

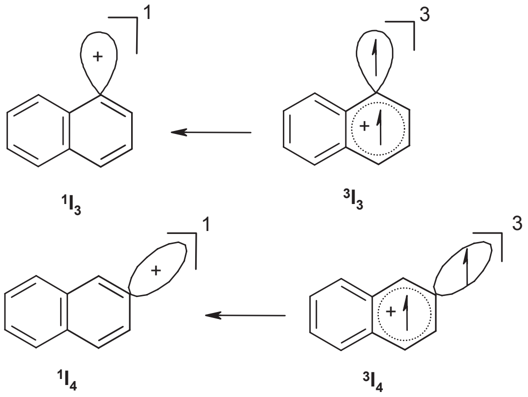
The fingerprint of the phenyl cation produced in the photolysis of diphenyliodonium tetrafluoroborate shows that the product-forming intermediate is a singlet species, despite the presence of the heavy atom iodine, which is expected to promote a triplet pathway. This finding complements the proposed mechanism depicted in Scheme 1, in which external nucleophiles only react with the cations after the complex has dissociated. This leaves time for the photogenerated phenyl cation to isomerise to its ground state.

The second pillar of the research in this thesis is the generation of vinyl cations. The project reported in Chapter 5 partook in an age-old quest for a "holy grail" of vinyl cation chemistry: the most unstable vinyl cation possible. For cyclic vinyl cations the most unstable species witnessed thus far was the 6-membered ring vinyl cation. Numerous attempts to thermally generate the 5-membered ring vinyl cation were unsuccessful. It is demonstrated that not only the C_6-ring vinyl cation, but also the C_5-ring vinyl cation is generated photochemically, under mild reaction conditions, from their iodonium salt precursors.

Next to trapping products of the C_5-ring vinyl cation also trapping products of the C_5-ring allyl cation were found. The hydride shift of a vinyl cation forming an allyl cation is a typical carbocationic process. The data presented constitute the first unambiguous case for the direct formation of a C_5-ring vinyl cation.

In pursuing the possibilities offered by the differences in chemo- and regioselectivity of singlet and triplet aryl cation species, the photogeneration of polyaromatic cations was attempted. The 1- and 2-naphthyl cations $\mathbf{I}_3$ and $\mathbf{I}_4$ were generated by photolysis of their iodonium and diazonium salt precursors and their reactivity was studied (Chapter 6). The naphthyl cations react (predominantly) through their singlet, closed shell isomer ($^1\mathbf{I}_{3,4}$) (Scheme 3). With the iodonium salt precursors, which fragment from the triplet excited state, a small contribution to the pattern of reactivity of their triplet naphthyl cations ($^3\mathbf{I}_{3,4}$) is found. Is is proposed that, under the experimental circumstances, the singlet closed shell naphthyl cations are lower in energy than their triplet isomers, even though high level quantum chemical calculations indicate that the singlet and triplet species are practically isoenergetic.

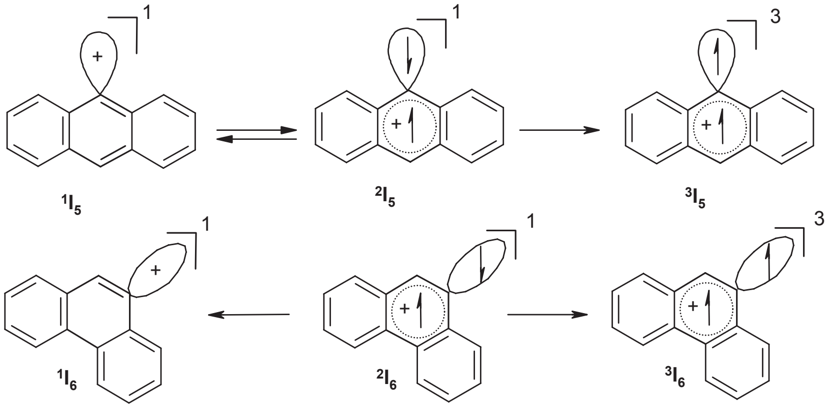
Scheme 3: The 1- and 2-naphthyl cations.



It appears that, using the naphthyliodonium salt precursors, the triplet naphthyl cations formed isomerise via a 1,2 hydrogen atom shift or lose a proton to the solvent producing triplet 1,2-naphthyne. These processes lead to the *cine*-substitution patterns observed in the photoproduct mixtures. No *cine* substitution occurs upon irradiation of 1- and 2-napthyldiazonium tetrafluoroborate, which generates only the singlet 1- and 2-napthyl cations.

Venturing further on uncharted territory, for the first time the 9-anthryl cation $\mathbf{I}_5$ and the 9-phenanthryl cation $\mathbf{I}_6$ have been generated in solution and their reactivity has been studied (Chapter 7) (Scheme 4). Trapping studies indicate that the 9-anthryl cation, formed by means of photolysis of the corresponding iodonium salt, is produced in its open-shell singlet state ($^2\mathbf{I}_5$). Trapping studies of $\mathbf{I}_6$ show that it reacts in its closed-shell singlet state ($^1\mathbf{I}_6$) via both

Scheme 4: The 9-anthryl and the 9-phenanthryl cation.



methods by which the cation was produced: directly, by photolysis of the corresponding phenanthryl iodonium salt, or indirectly, by photolysis of the vinylic bromide 9-bromomethylene-*9H*-fluorene. The latter reaction first produces a primary vinyl cation that in turn forms $\mathbf{I}_6$ through a 1,2 phenyl shift.

The above results open perspectives for tagging of substrates with a fluorescent moiety. The iodonium precursors do not fluoresce, owing to the presence of a heavy atom in the molecule, but the tag after the alkylation event does. This offers the possibility to track the tagged substrate without interference of the pre-fluorescent photolabile group.

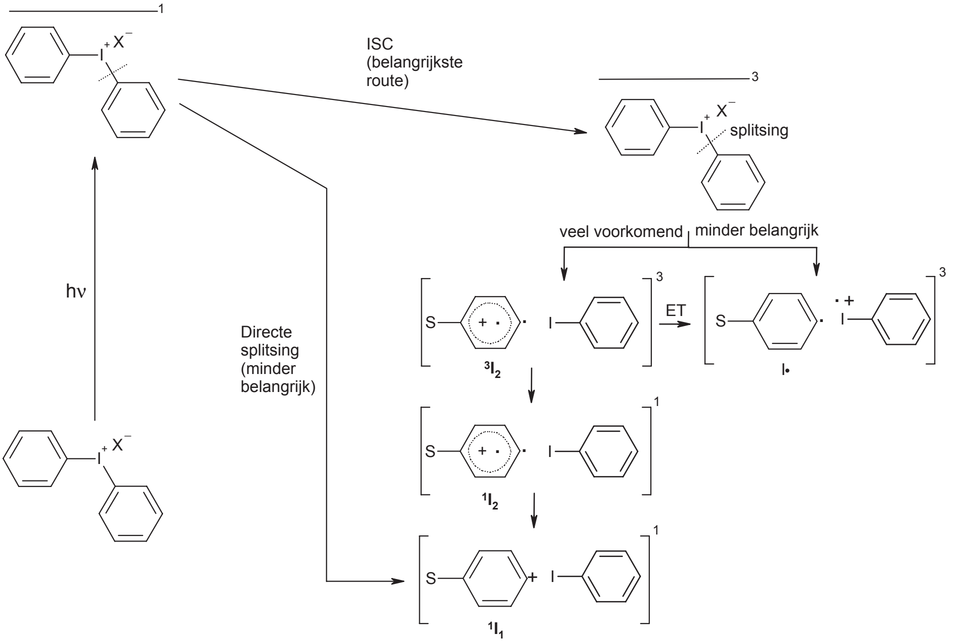
As an illustration of the perspectives of the research reported in this thesis, in Chapter 8 preliminary results are presented on the photoalkylation of guanosine and of phenylalanine in solution, using a variety of phenyl cation precursors. In general significant photoalkylation occurs.

Samenvatting

Dit proefschrift beschrijft een onderzoek naar nieuwe methodes om, met behulp van een fotochemische reactie, substraten (zoals eiwitten of nucleïnezuren) te koppelen aan een ander molecuul (= te alkyleren). Het onderzoek is gebouwd op de kennis over het maken van zeer reactieve intermediairen, vinyl- en arylkationen, in de werkgroep organische fotochemie, binnen de onderzoeksgroep bio-organische synthese. Het belangrijkste doel van het onderzoek was om de hoge reactiviteit van de genoemde intermediairen hand in hand te laten gaan met een gewenste selectiviteit. Toepassingen voor dit onderzoek liggen in die situaties waar fotoalkylering reeds wordt toegepast (als diagnostische methode in de biochemie en de biologische chemie) en mogelijk zelfs in de behandeling van celgroepen die een bedreigende activiteit vertonen in een menselijk lichaam (fotodynamische therapie).

De ervaring in de werkgroep met het maken van kationen ligt onder andere in de fotolyse van jodoniumzouten die naast vinylkationen ook fenylkationen oplevert. Een studie van de fotochemie van dit type verbindingen (Hoofdstuk 2), waarbij steeds kleine veranderingen aan het skelet van de uitgangsstof werden aangebracht, heeft geleid tot een voorstel om het breed geaccepteerde reactiemechanisme van de fotochemie van fenyljodoniumzouten aan te passen (Schema 1). De wijzigingen houden in dat de singulet aangeslagen toestand van het zout een minder prominente rol speelt en dat de triplet aangeslagen toestand triplet fenylkationen ($^3\mathbf{I}_2$) vormt. Het voorkomen van een singulet route, die een singulet fenylkation ($^1\mathbf{I}_1$) aan-

Schema 1: Het voorgestelde mechanisme van de fotolyse van difenyljodoniumzouten.



maakt, en een triplet route, die een fenyl radicaal (**I•**) maakt, kan echter niet volledig worden uitgesloten.

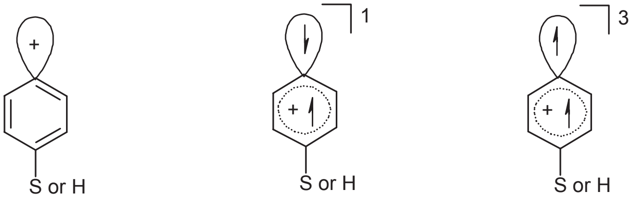
Triplet fenylkationen ($^3\mathbf{I}_2$) hebben, als gevolg van hun gewijzigde spintoestand, een andere elektronische huishouding dan hun singulet isomeren ($^1\mathbf{I}_1$) en vertonen daardoor verschil in selectiviteit bij hun reacties met substraten. Bij voorkeur worden onverzadigde verbindingen gealkyleerd (= chemoselectiviteit). Deze vaststelling opent de mogelijkheid om onverzadigde onderdelen van bijvoorbeeld een eiwit of een DNA molecuul te alkyleren in een waterige omgeving (in een diagnostische test of in een lichaam).

De vaststelling dat uit jodoniumzouten triplet kationen kunnen worden gemaakt, geeft ruim baan aan ideeën om deze zouten als productieve fotoalkyleringsmiddelen te gebruiken. Immers, deze klasse van verbindingen heeft zijn praktische nut reeds bewezen en wordt op grote schaal toegepast in de fotolithografie in de computerchip producerende industrie. In Hoofdstuk 3 is de vorming van triplet kationen door fotolyse uit andere types uitgangsverbindingen dan jodoniumzouten bestudeerd en zijn de resultaten onderling vergeleken. Het blijkt dat juist de groep die door het aanstralen met licht uit het molecuul wordt verwijderd (= vertrekkende groep) en daarmee het intermediair geeft, van cruciale invloed is op de uiteindelijke singulet of triplet reactiviteit van de kationen.

Vervolgens is een universele methode ontworpen om intermediaire singulet of triplet fenylkationen te identificeren (Hoofdstuk 4). Singulet en triplet fenylkationen blijken behalve in chemoselectiviteit ook in regioselectiviteit van elkaar te verschillen. Triplet fenylkationen reageren niet alleen bij voorkeur met een onverzadigde verbinding maar ook nog eens bij voorkeur op specifieke posities van dat molecuul. Tevens blijkt het mogelijk een onderscheid aan te brengen tussen twee types singulet fenylkationen: het "klassieke" singulet fenylkation ($^1\mathbf{I}_1$) en het singulet fenylkation ($^1\mathbf{I}_2$) waarin net als in het triplet fenylkation het aromatische sextet is opgebroken (Schema 2). Op basis van de waargenomen regioselectiviteiten kunnen de verschillende types singulet of triplet fenylkationen als intermediair in fotochemische reacties duidelijk worden onderscheiden. Dit type fotoreacties vormt, naast de zeer bekende experimenten met singulet en triplet carbenen, een nieuw voorbeeld van spinselectiviteit in chemische reacties.

De regioselectiviteit die gevonden wordt in de bestraling van difenyljodoniumzout is die van een singulet fenylkationen ($^1\mathbf{I}_1$). Dit resultaat is in overeenstemming met het voorgestelde mechanisme in Schema 1. Externe substraten reageren pas na verloop van tijd, na het opbreken van het complex, met het fenylkation. Het fenylkation dat direct na vorming in een triplet toestand verkeert heeft tijd om een isomerisatie naar de singulet grondtoestand te ondergaan en als zodanig te reageren.

Schema 2: Isomeren van de fenyl kationen.



Gesloten sextet
singulet fenyl kation
S = NR_2 or OH

$\mathbf{I}_1 : \pi^6\sigma^0$

Opgebroken sextet
singulet fenyl kation
S = NR_2 or OH

$\mathbf{I}_2 : \pi^5\sigma^1$

(Opgebroken sextet)
triplet fenyl cation
S = NR_2 or OH

$\mathbf{I}_3 : (\pi^5\sigma^1)^3$

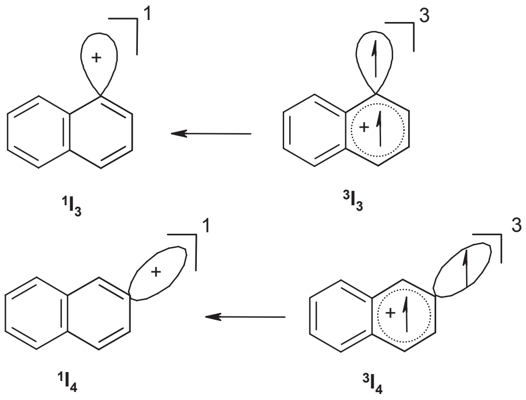
In een tweede onderzoeksrichting in dit proefschrift, is de vorming van vinylkationen onder invloed van licht onder de loep genomen. Dit project is onderdeel van de immer voortwoedende strijd om het meest instabiele vinylkation te maken. Voor cyclische vinylkationen is het meest instabiele deeltje dat tot dusver is gemaakt het 6-ring vinylkation. Pogingen om het 5-ring vinylkation te maken zijn tot nu toe op niets uitgelopen. Nu is met behulp van een fotochemische reactie, onder milde omstandigheden, uitgaande van jodoniumzout voorlopers, niet alleen het 6-ring vinylkation maar ook het 5-ring vinylkation gemaakt. De resultaten in Hoofdstuk 5 vormen het eerste harde bewijs van het voorkomen van dit illustere intermediair.

Verdere mogelijkheden achter de horizon van de verschillen in chemo- en regioselectiviteit tussen singulet en triplet kationen werden nagejaagd door grotere arylkationen zoals de naftylkationen te maken (Hoofdstuk 6). Na het synthetiseren van de naftyljodonium en naftyldiazonium uitgangsverbindingen, kon, na fotolyse, de reactiviteit van het 1- en het 2-naftylkation (respectievelijk $\mathbf{I}_3$ en $\mathbf{I}_4$ in Schema 3) worden bestudeerd. Beide kationen reageren voornamelijk in de singulet toestand met substraten.

Bij de bestraling van de jodoniumzouten zijn echter aanwijzingen gevonden voor het voorkomen van andere dan de singulet toestanden $^1\mathbf{I}_{3,4}$. Het 1-naftyl zout produceert 2-naftyl producten en omgekeerd (= *cine* substitutie). Dit effect is het gevolg van een deprotonering van of een 1,2-hydride verhuizing binnen het triplet naftylkationen $^3\mathbf{I}_{3,4}$, bereid in de fotolyse van de jodoniumzouten. Deze verschijnselen treden niet op bij het maken van singulet naftylkationen, bijvoorbeeld in de fotoreactie van 1- and 2-naftyldiazoniumzouten.

Op basis van de bestralingsexperimenten wordt aangenomen dat de singulet naftylkationen lager in energie zijn dan de triplet naftylkationen. Dit idee wordt weersproken door de resultaten van geavanceerde quantumchemische berekeningen die vrijwel gelijke energieën voor beide toestanden voorspellen.

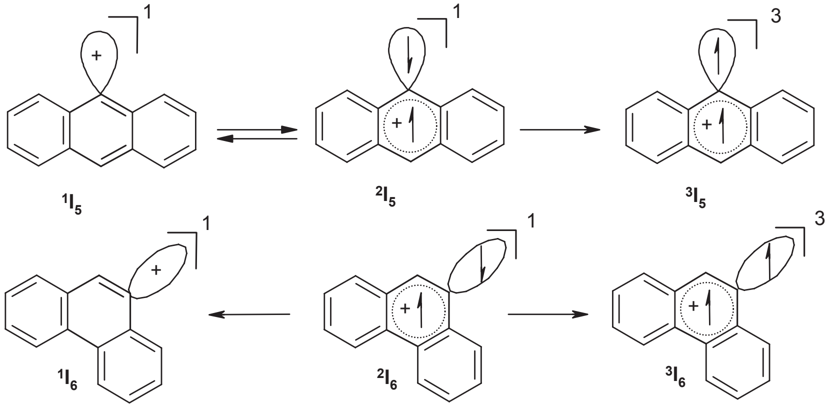
Schema 3: Het 1- en 2-naftyl kation.



In het verlengde van het maken van naftylkationen zijn, voor het eerst, het 9-antrylkation $\mathbf{I}_5$ en het 9-fenantrylkation $\mathbf{I}_6$ (Schema 4) gemaakt uit hun jodoniumzout voorlopers (Hoofdstuk 7). Het productpatroon van de bestraling van het antryl(fenyl) jodoniumzout levert onmiskenbare aanwijzingen voor het voorkomen van het 9-antrylkation. Het kation reageert waarschijnlijk in een singulet toestand met opgebroken aromatisch systeem ($^2\mathbf{I}_5$).

Het afvangen van $\mathbf{I}_6$, na bestraling van het corresponderende jodoniumzout en van het vinylische bromide 9-broommethyleen-*9H*-fluoreen, suggereert dat dit deeltje als een klassiek arylkation reageert ($^1\mathbf{I}_6$).

Schema 4: Het 9-antryl kation en het 9-fenantryl kation.



De resultaten van de fotoalkylering van guanosine en fenylalanine met verscheidene aryl kationen in oplossing, laten veelal een profijtelijke productvorming zien (Hoofdstuk 8). Het blijkt dat de zeer reactive aryl kationen dus ook selectief kunnen zijn in hun reacties. De bereikte resultaten van de experimenten bieden nieuwe perspectieven om, bijvoorbeeld, eiwitten te koppelen met een reactief intermediair dat pas na de reactie fluorescentie vertoont. De voorlopers van de reactieve groepen vertonen geen fluorescentie. De producten zijn dus eenvoudig te traceren.

Curriculum Vitae

Micha Slegt was born in Spijkenisse, The Netherlands, on the 10th of May 1973. In the process of completing his secondary education he looked out of the window and dreamt about a career in chemistry.

In June 1996 he graduated, as a Bachelor as it called nowadays, in Organic Chemistry from the H.L.O. in Delft after conducting polymer chemical research at DSM Research with dr. K. J. G. Janssen. He started his professional career in the same field of research and at the same company in the group of dr. ir. H. Dikland.

In february 1998 he started to work for AKZO NOBEL-Diosynth, conducting research in organic chemical production processes at their R&D department under the guidance of P. Kirchholtes. Later he joined Dr. M. van Loo to conduct automated organic chemical experiments and to implement automated "Design of Experiment" type of research in the R&D of the aforementioned company. A course in DoE was taken at Umetrics in Umeå, Sweden in 2000.

In the beginning of 2001 he joined the BIOSYN group (Leiden University); first under supervision of the late prof. dr. J. H. van Boom and next under supervision of prof. dr. H. S. Overkleeft and prof. dr. G. A. van der Marel, to start his PhD studies in the field of organic photochemistry under the guidance of dr. G. Lodder. Participation in the EPA New Perspectives in Photochemistry Summer School at Egmond aan Zee in 2003 yielded lots of ideas, tons of motivation and good contacts with young photochemists all over the world. Parts of Chapter 5 of this thesis have been presented in an oral presentation at the 20th IUPAC symposium on Photochemistry in Granada, Spain in 2004. Further, in 2004, he took part in the inter-university course Photophysics, Photochemistry and Photobiology at the Free University in Amsterdam, The Netherlands.

Since november 2005 he is employed by the Dutch Customs Laboratory in Amsterdam where he is concerned with polymer chemical and forensic chemical issues.

Nawoord

Met het werk beschreven in dit proefschrift hoop ik het estafettestokje, aangegeven door Kaj van Alem, Jane Sum en Roel Gronheid, een stapje verder te hebben gebracht. The high quality cooperation with professor Masahito Ochiai and professor Tadashi Okuyama has been of invaluable importance to this research. Overal in dit proefschrift zijn argumenten en redeneringen terug te vinden die zijn ontstaan tijdens werkbesprekingen met professor Jan Cornelisse en Johanna van der Hart. Floor Minne, Mahmut Yildirim, Natasja Wissenburg, Emile Mes, Dennis van der Vlugt, Sven Pappers, Arjaan Ringeling, Rob Hoogervorst, Annemiek Knijnenburg en Marcel Plugge hebben hun bijdrage geleverd tijdens hun stage periodes. Veel van de analyses vroegen om een deskundige ondersteuning waarin ruim werd voorzien door Jos van Brussel, Fons Lafeber, Hans van der Elst, Bertil Hofte en Bea Reeuwijk.

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Mijn vrienden Dirk-Jan, Dorien, Gijs, Krista, Martijn, Xandra, Rene en Hedwig, hebben me voor gek verklaard, m'n gezever aangehoord, mij een spiegel voorgehouden maar bovenal, door etentjes, discussie's en wandelingen, voor de onontbeerlijke ontspanning gezorgd. Huisgenoten van de Mathenesserlaan zorgden een voor een bank, wat bier en andere basale zaken. Mijn familie heeft me geleerd dat er altijd mensen zullen zijn die van je houden. Voor die wetenschap buig ik diep. Sinds drie jaar mag ik me koesteren in de warme omhelzing van Marjo, zij geeft mij het gevoel dat het altijd zo zou moeten zijn.