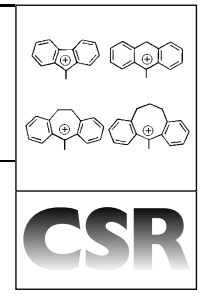
Cyclic diaryliodonium ions: old mysteries solved and new applications envisaged†



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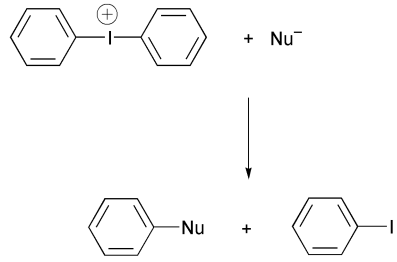
For a long time the unusually poor reactivity of cyclic diaryliodonium ions toward nucleophiles remained a mystery. Only very recently has a solution to this puzzle been found, shedding light on the mechanism of aromatic nucleophilic substitution reactions of iodonium salts. This article provides an overview of the most important current advances in the field, both theoretical and practical.

1 Introduction

Since the discovery of the first iodonium salt more than 100 years ago, diaryliodonium compounds have become a powerful tool in organic and inorganic synthesis.[1–6] Being capable of smoothly arylating nucleophiles under mild conditions (eqn. (1)), diaryliodonium ions $[Ar_2I]^+$ belong to the tiny yet very important family of synthetic equivalents of aryl cations. In terms of selectivity and yields, arylation reactions with $[Ar_2I]^+$ are often superior to those utilizing more traditional arenediazonium reagents. In addition, unlike most arenediazonium salts, diaryliodonium compounds are non-explosive, non-toxic and stable. Due to their long shelf lives various diaryliodonium salts are now commercially available.

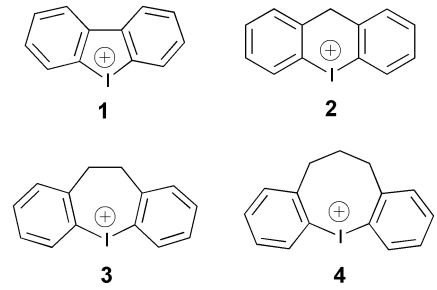


(1)

† Dedicated to the memory of Dr Aleksandr Nikolaevich Vanchikov (1952–1998), a brilliant experimentalist, a co-author of the most exciting recent pieces of work discussed in this review, and a great friend and teacher to me during the years of my graduate studies.
‡ Contribution No. 7981.

Vladimir Grushin, a native of Moscow, Russia, received his PhD degree in chemistry under the direction of Professor T. P. Tolstaya (Moscow State University) in 1984. After that he spent several years as a research chemist first at the Institute of Organo-Element Compounds of the USSR Academy of Sciences and then at the University of Ottawa. He was on faculty at Wilfrid Laurier University (Canada) before he moved to the United States to join CR&D of the DuPont Company in 1997. His research interests are in the areas of organometallic chemistry and homogeneous catalysis.

While the chemistry of the linear diaryliodonium compounds is well-developed and widely used, much less is known about their cyclic analogues, in which the two aryls on the iodine atom are bridged, so that the iodonium center is included in a heterocycle fused with two aromatic rings (*e.g.*, **1**–**4**).



Since no aromaticity is possessed by these iodine heterocycles, one might expect the cyclic diaryliodonium ions to exhibit reactivity patterns similar to those of their linear counterparts, $[Ar_2I]^+$. This, however, appears to be the case only in a limited number of instances. Normally, most diaryliodonium heterocycles are poorly reactive even in the presence of strong nucleophiles. This lack of reactivity has been emphasized in a number of papers and review articles, but until very recently[5] was viewed as puzzling and inexplicable.

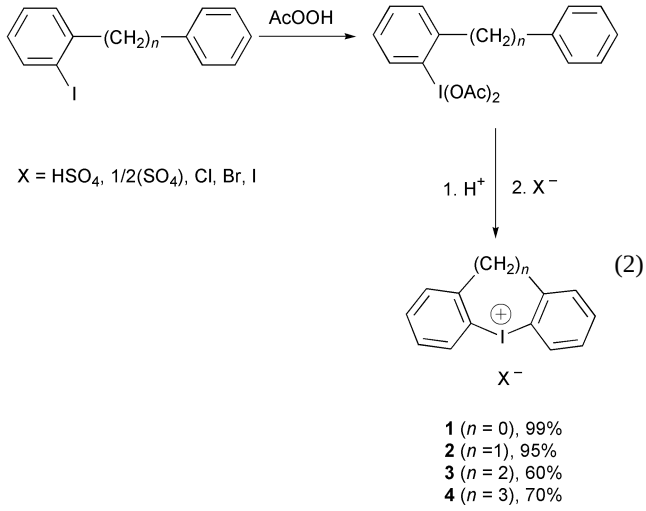
The chemistry of diaryliodonium heterocycles has never been the subject of a separate review article. Although a section on cyclic iodonium ions can be found in the comprehensive monograph by Varvoglis,[4] the most exciting findings in this area have been reported very recently, since the book was published. The goal of the present review is not to provide the reader with an exhaustive coverage of the literature in the field, but rather (i) summarize synthetic routes to diaryliodonium heterocycles, (ii) analyze, in considerable detail, the trends in the 'unusual' reactivity of the cyclic iodonium ions toward nucleophiles, (iii) rationalize the diminished electrophilicity of many of the iodonium heterocycles, and (iv) discuss the great synthetic potential of cyclic diaryliodonium salts. Beyond the scope of this review are macrocyclic compounds with more than one iodonium center involved in the ring and the biological activity of cyclic iodonium salts.[6] Of the extensive Chinese literature reporting the synthesis and biological studies of numerous cyclic diaryliodonium salts, only selected chemical aspects will be covered.

2 Synthesis

2.1 Ring closure

As early as 1956, Sandin and co-workers[7] reported that the condensation of iodosyl compounds with arenes to give linear

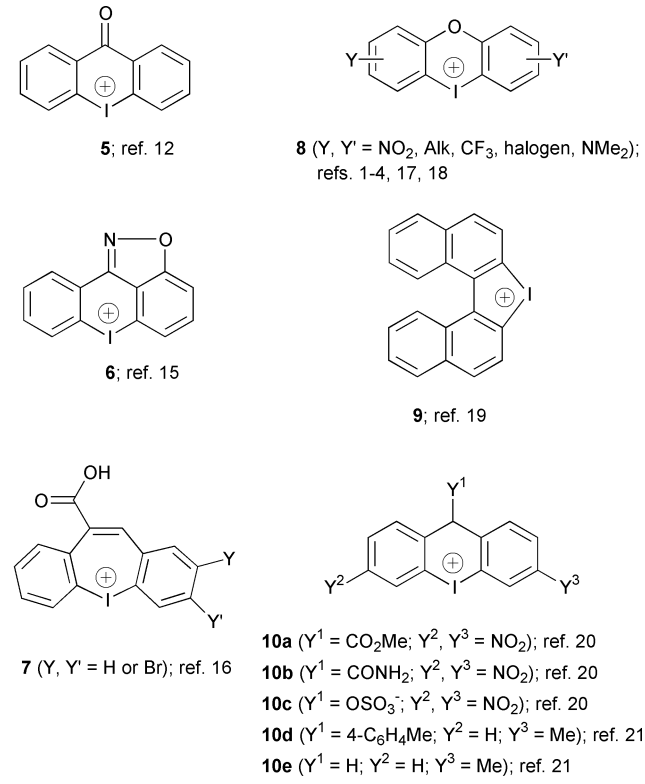
iodonium cations, can furnish cyclic iodonium salts if conducted intramolecularly (eqn. (2)). The reaction involves the oxidation of the starting iodoarene to the corresponding iodosyl derivative, followed by the acid-catalyzed S_E-type cyclization.[1–4]

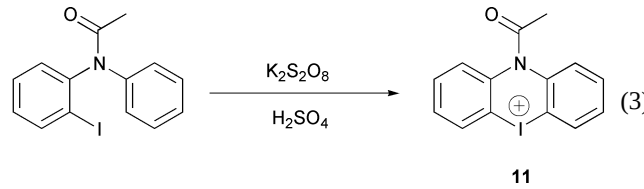


(2)

1 (*n* = 0), 99%
2 (*n* =1), 95%
3 (*n* = 2), 60%
4 (*n* = 3), 70%

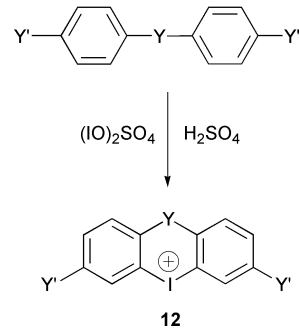
This strategy has since been successfully used for the synthesis of **1**,[8–11] **2**,[8,12,13] **3**,[14] and **4**[9] with various counterions and a wide variety of other iodonium heterocycles, *e.g.*, **5**–**10**.[12,15–21] The synthesis is conveniently carried out as a one-pot, two-step process. In the first step, the iodoarene is oxidized with peracetic acid to the corresponding iodoso derivative. In the second step, a strong acid, usually H_2SO_4, is added to the previously generated iodosyl reagent to catalyze the formation of the iodonium cation *via* ring closure. The yields are good to excellent and in some cases can be quantitative. The ring closure reaction can also be performed in one step by treating the starting iodoaromatic compound with potassium, sodium, or ammonium persulfate in the presence of H_2SO_4. This method has proven efficiency even when the two-step technique (eqn. (2)) does not produce satisfactory results.[1–4] For example, **11** can be obtained in 50% yield using $K_2S_2O_8$ (eqn. (3)) but is not formed at all when peracetic acid ($AcOH–H_2O_2$) is employed.[1]





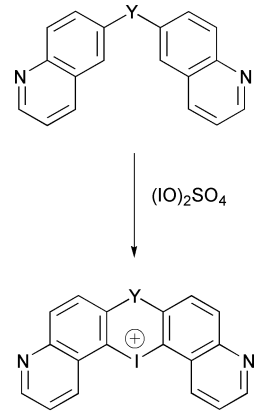
(3)

A very simple and efficient method to prepare cyclic diaryliodonium salts involves the reaction between a diaryl substrate with iodosyl sulfate, $(IO)_2SO_4$, which is easily prepared by reacting iodine with I_2O_5 or KIO_3 in sulfuric acid.[1–4] The yellow suspensions of $(IO)_2SO_4$ obtained readily react with 4,4′-disubstituted diphenyl substrates to give the desired iodonium cation (eqn. (4)). A similar iodosylating reagent, $I(OCOCF_3)_3$, is conveniently synthesized from I_2, CF_3COOH and HNO_3 in acetic anhydride.[1–4]



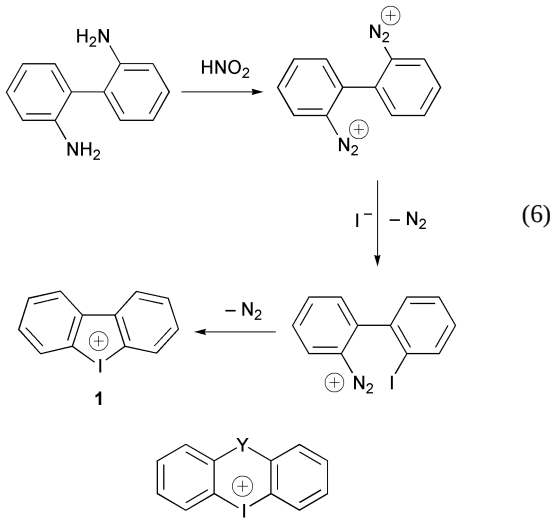
(4)

This method (eqn. (4)) originally developed by Huang in the 1950s[1] has been widely used by the Lanzhou University group for the preparation of cyclic iodonium salts of the type **12** (*e.g.*, Y = CH_2, CHAr, NH, O; Y′ = NO_2, NMe_2, CN)[22,23] and **13** (eqn. (5)).[24] Clearly, reaction 4 is limited to substrates which can undergo electrophilic iodosylation only at the carbon atoms *ortho* to the bridging group Y, otherwise electrophilic attack on a *para*-carbon would take place, eventually resulting in the formation of linear iodonium compounds, both monomeric and oligomeric. In particular, reaction 4 cannot be used for the synthesis of the simplest non-substituted heterocycles **1**–**4** and similar compounds, such as **5**–**9**, **10d**,**e** and **11**.



(5)

The above synthetic techniques employ strongly oxidizing conditions in acidic media and hence cannot be applied to easily oxidizable substrates, *e.g.*, diaryl sulfides. The Mascarelli reaction used for the first synthesis of **1** (eqn. (6))[25] may provide a solution to this problem. Thus, sulfur-containing iodonium heterocycles **14** have been prepared from the corresponding diamines *via* this route, albeit in low yield.[4,17]



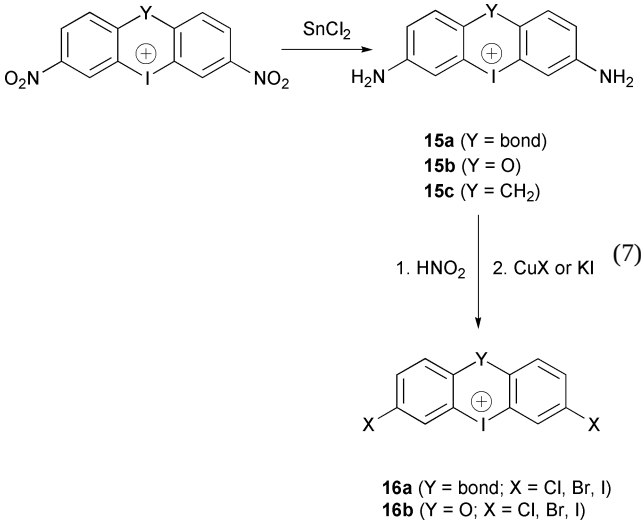
(6)

14a (Y = S); refs. 4,17
14b (Y = SO); ref. 4
14c (Y = SO_2); ref. 4

Excellent yields of **1** and its bromonium and chloronium analogues have been obtained by gently heating solid 2-halobiphenyl-2′-diazonium tetrafluoroborates or hexafluorophosphates in dry benzene.[26]

2.2 Chemical modification of the backbone

A number of methods have been developed for various functionalization reactions of diaryliodonium heterocycles without ring opening. For instance, **2** is nitrated to **12** (Y = CH_2; Y′ = NO_2)[1] and oxidized with CrO_3 or $NOHSO_4$ to **5**.[12] It has been demonstrated[27] that nitro groups on the benzene rings of some iodonium heterocycles can be reduced with $SnCl_2$–HCl to furnish the amino-substituted iodonium cations **15** in moderate yield. Diazotization of **15**, followed by treatment with CuCl, CuBr or KI affords the corresponding halo-derivatives **16** (eqn. (7)).

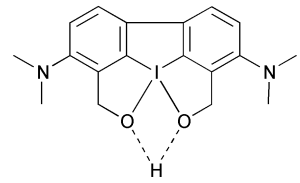


(7)

An interesting compound formulated as **17** has been reported to form upon methylation of **15c** under the Eschweiler–Clarke (CH_2O–HCOOH) conditions.[28]

2.3 Anion metathesis

All cyclic diaryliodonium cations whose synthesis is described above have been isolated in the form of salts of various anions,



17

such as I^-, Br^-, Cl^-, HSO_4^-, SO_4^{2-}, HCO_2^-, AcO^-, BF_4^-, PF_6^- and so forth. Different anion metathesis techniques have been developed for the preparation of iodonium salts containing a desired anion.[1–6] Over the past 15 years, Chen and co-workers have synthesized and characterized numerous cyclic iodonium salts of complex anions containing a wide variety of metals, such as Fe, W, Th, Y and the lanthanides. A considerable number of publications describing these compounds and their biological activity have appeared in the Chinese literature. Owing to limitations we cite here only one[29] of the recent papers which should help the reader track down other reports in the series.

Iodonium salts of weakly nucleophilic anions (*e.g.*, BF_4^-) are of special interest because such anions do not interfere when the cation is used to arylate a nucleophile. In addition to the well-known methods for preparing iodonium tertrafluoroborates, such as extraction, precipitation, and the reactions of a corresponding halide with $[Et_3O]^+$ BF_4^- or $AgBF_4$,[1–4] an elegant new technique has been recently developed.[9] This technique is exemplified by the preparation of [**4**]BF_4 from the reaction solution containing cation **4** (eqn. (2)). Adding $K_2Cr_2O_7$ to the reaction mixture leads to quantitative precipitation of water-insoluble [**4**]$_2Cr_2O_7$ which is separated by filtration and, without further purification, treated with aqueous HBF_4 and propan-2-ol to reduce the dichromate anion (eqn. (8)).[9] The readily soluble chromium complex is effortlessly removed from the iodonium tetrafluoroborate by washing with cold water.

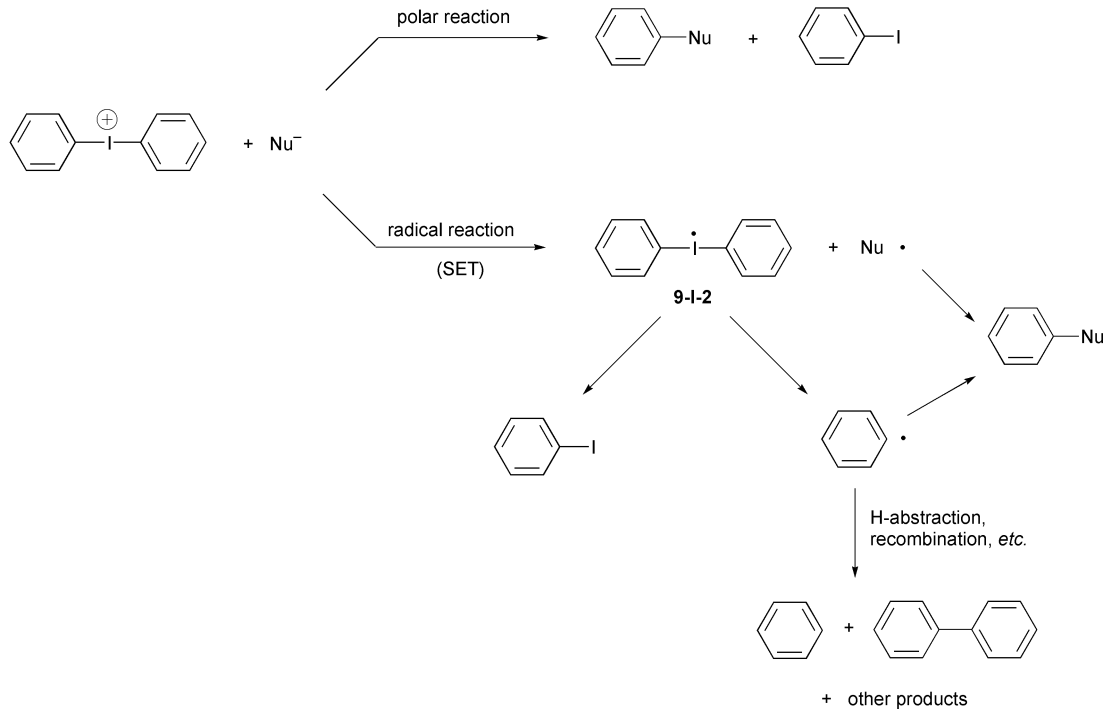
$$[\mathbf{4}]_2Cr_2O_7 + 3Me_2CHOH + 8HBF_4 + 5H_2O \longrightarrow 2[\mathbf{4}]BF_4 + 2[Cr(H_2O)_6](BF_4)_3 + 3Me_2CO \quad (8)$$

3 Reactions with nucleophiles

Most reactions of diaryliodonium ions with nucleophiles proceed *via* two paths, polar and radical (Scheme 1).[1–6] Arynes are sometimes generated from diaryliodonium salts[3,4] but these cases are rare and not closely related enough to the chemistry of the iodonium heterocycles to be considered in this review.

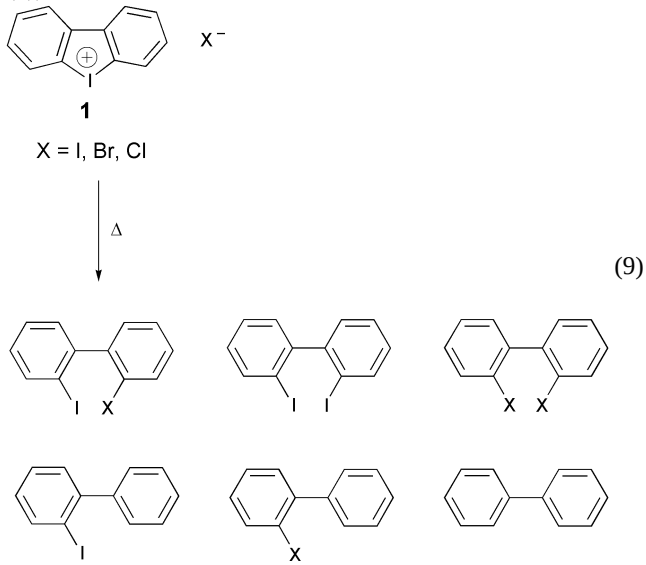
The polar reactions of $[Ph_2I]^+$ result in the clean formation of iodobenzene and the phenylated product (Scheme 1). If single electron transfer (SET) occurs from a nucleophile to the iodonium cation, the latter is reduced to diphenyliodine (9-I-2 intermediate; see below)[4,5] which readily decomposes to produce iodobenzene and a highly reactive Ph• radical. Depending on various factors, the phenyl radical may abstract a hydrogen atom from the solvent, dimerize, or react with the nucleophile and/or its oxidized form, Nu• (Scheme 1). In some cases, both the polar arylation and radical reactions occur simultaneously, competing with one another. A detailed mechanistic analysis has been reported[5] for polar and radical reactions of diaryliodonium compounds with nucleophiles.

Until very recently, little information was available on reactions of cyclic diaryliodonium compounds with nucleophiles. Most of the early studies were conducted with the simplest 5- and 6-membered heterocycles **1** and **2**, the results



Scheme 1

obtained by different groups being not without controversy.[26] In the late 60's and early 70's, Sato and co-workers[8] reported their meticulous studies of the thermal decomposition of dibenz[*b*,*d*]iodolium (**1**) and 10*H*-dibenz[*b*,*e*]iodinium (**2**) iodides, bromides, and chlorides. The decomposition was conducted in the molten state at 190–295 °C and in different solvents, such as triethylene glycol, quinoline, DMSO, *o*-dichlorobenzene, nitromethane, and hexachloroethane at 145–245 °C. Thorough GC analysis of the reaction mixtures revealed the formation of Ph_2 and various halogenated biphenyls upon decomposition of [**1**]X, where X = I, Br, or Cl (eqn. (9)).



(9)

Depending on the nature of X^- and reaction conditions employed, the total yield of biphenyls (18–100%) and the product ratio varied over a broad range. For instance, the decomposition of solid [**1**]I was quite selective, giving rise to 2,2′-diiodobiphenyl and 2-iodobiphenyl in a 98 : 2 ratio. This ratio changed, however, to 64 : 35 when the decomposition was performed in triethylene glycol. The thermal decomposition of [**2**]X (X = Cl, I) occurred more cleanly to afford 2-chloro-2′-iododiphenylmethane and 2,2′-diiododiphenylmethane, respectively, as the main products. Nonetheless, small amounts of diphenylmethane and other side-products were always detected. The complexity of products formed in both cases (**1** and **2**) pointed to the fact that a radical mechanism either governed or at least contributed substantially to the thermal decomposition processes.[8] In contrast, the arylation reactions of Cl^-, Br^-, and I^- with various linear iodonium cations are usually selective,[1–4] likely occurring *via* the polar mechanism.

In the 1980's, two groups pointed to the low reactivity of **1** and **2** toward dialkyldithiocarbamate[30] and nitrite ions,[31] respectively. Under reinforcing conditions, the arylation of both nucleophiles did occur but the yields of the desired products were low and a number of side-products of certainly radical origin were found in the reaction mixtures. Again, the reactivity of **1** and **2** was very different from that of $[Ph_2I]^+$ which can smoothly phenylate both $R_2NCS_2^-$ and NO_2^- under mild conditions. Although the chemical behavior of **1** and **2** was certainly puzzling, there were no reports in the literature describing a detailed study aimed at gaining insight into the reasons for the vastly different reactivity of the cyclic and linear aryliodonium ions. Because the data on the reactions of **1** and **2** originated from different research groups, different conditions and solvents were used for running the reactions, *e.g.*, the thermolysis of the solid halides,[8] polar aqueous[31] and non-polar (*p*-xylene)[30] media, and a water–1,2-dichloroethane biphasic system.[31] This additionally impeded analysis of the deficient data.

Very recently, Tolstaya, Vanchikov and co-workers[9,14] have reported the first systematic study of reactions of various diaryliodonium heterocycles with nucleophiles (N_3^-, NO_2^- and Br^-) in aqueous DMSO. It was found that the ability of the cyclic iodonium tetrafluoroborates to undergo non-radical nucleophilic substitution reactions is remarkably dependent on the ring size, increasing in the order **1** < **2** < **3** ≈ **4**. This trend is compellingly illustrated by the reaction of $NaNO_2$ with **1**,[9] **2**,[31] **3**[14] and **4**[9] in aqueous DMSO under similar conditions (eqn. (10)).

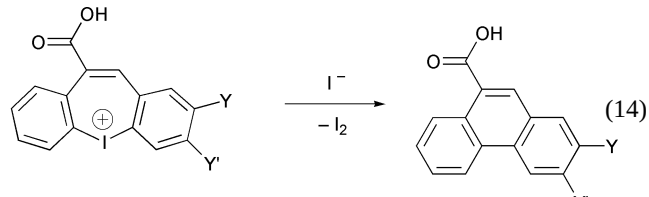
Likewise, the larger heterocycles **3**[14] and **4**[9] cleanly arylated the azide anion to produce the corresponding azidoarenes quantitatively, whereas **1**[9] having iodine in the smallest possible 5-membered ring, exhibited significantly lower reactivity toward NaN_3, the desired product being formed in only 55% yield at 100% conversion (eqn. (11)). The side products ob-

served (2,2′-diiodobiphenyl and 2-iodobiphenyl) originated from radical processes due to the formation and decomposition of the 9-I-2 radical intermediate.

Furthermore, no reaction took place when **1** was heated with NaBr in aqueous DMSO at 120–140 °C for 30 h.[9] At the same time, **4** readily reacted with NaBr under these conditions to give $IC_6H_4(CH_2)_3C_6H_4Br$ as the sole product in 87% yield after 11.5 h (eqn. (12)).[9]

Interestingly, the reaction of **3** with Br^- furnished 9,10-dihydrophenanthrene and phenanthrene as the main product, whereas the expected 2-bromo-2′-iododiphenylethane formed in only 10–20% yield (eqn. (13)).

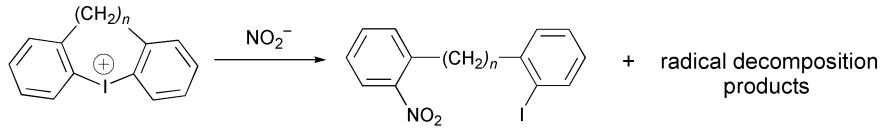
The formation of dihydrophenanthrene and phenanthrene in this reaction is closely related to the previously reported thermolysis of 10-carboxydibenz[*b*,*f*]iodepinium iodides to furnish the corresponding phenanthrenes in good yield (eqn. (14)).[16]



(14)

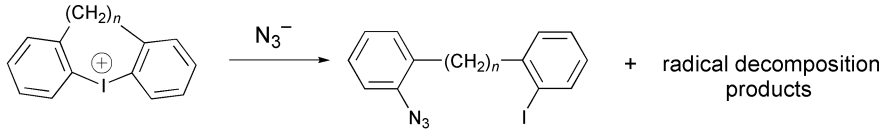
7a (Y = H; Y' = H)
7b (Y = Br; Y' = H)
7c (Y = H; Y' = Br)

Remarkably, no sign of a radical reaction was observed in any of the above experiments involving the 7- (**3**, **7**) and 8-membered (**4**) heterocycles, whereas their 5- (**1**) and 6-membered (**2**) counterparts all underwent SET, followed by homolytic decomposition in the presence of the *same* nucleophiles under *similar* conditions (eqns. (10)–(14)). While this



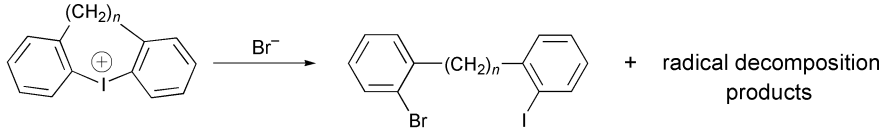
1 (*n* = 0)	26%	74%
2 (*n* = 1)	45%	ca. 50%
3 (*n* = 2)	93%	not found
4 (*n* = 3)	88%	not found

(10)



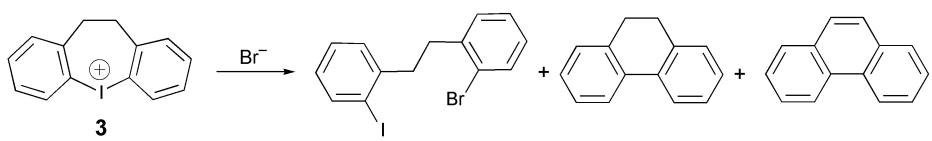
1 (*n* = 0)	55%	23%
3 (*n* = 2)	100%	not found
4 (*n* = 3)	100%	not found

(11)



1 (*n* = 0)	no reaction	
4 (*n* = 3)	87%	not found

(12)



3

$DMSO/H_2O$	20%	0%	68%
DMSO	10%	0%	80%
H_2O	0%	75%	5%

(13)

appears puzzling upon initial consideration, the markedly strong dependence of the reactivity on the ring size can be easily rationalized in terms of the mechanism presented in Scheme 2.[5]

Nucleophilic attack on the iodine atom of $[Ar_2I]^+$ results in the formation of the hypervalent 10-I-3 intermediate, $[Ar_2INu]$, which may undergo reductive elimination of Ar–Nu or, on a rare occurrence, Ar–Ar. The reductive elimination is a synchronous process that is symmetry forbidden for the lower energy T-shape conformation of the tricoordinate iodine(III) intermediate, but allowed for its higher energy Y-shape conformer which mediates the permutations (*e.g.*, *via* pseudorotation) around the tricoordinate iodine atom.[5]

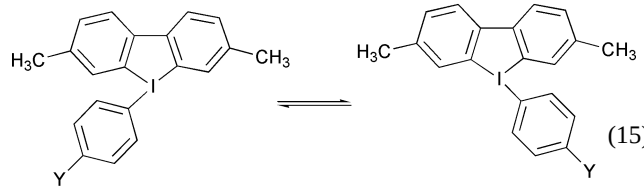
Due to the rigid geometry of **1** the tricoordinate iodine complexes formed with this cation experience difficulties adopting the Y-conformation required for the reductive elimination to occur. This accounts for the anomalously low reactivity of **1**. Even at elevated temperatures, the hypervalent derivatives of **1** may prefer to decompose homolytically to give complex mixtures of products. Clearly, the less rigid the geometry around the iodine center, the more prone the iodonium compound will be to react with nucleophiles *via* the reductive elimination mechanism shown in Scheme 2. In fact, **2** (6-membered ring) with a more flexible skeleton is a noticeably better arylating agent than **1** (5-membered ring). The reaction path (polar *vs*. radical) for **2** will be determined by the difference in the activation energy barriers to the 'T⇌Y' isomerization and to the homolytic decomposition of the tricoordinate iodine complex. These two barriers are apparently comparable, which accounts for (i) the borderline position of **2** in the series of **1**–**4** and (ii) the unusually high sensitivity of reactions of **2** to the reaction medium.[31] The three-coordinate 10-I-3 complexes deriving from the flexible cations **3** and **4** undergo the T⇌Y isomerization easily. As a result, both **3** and **4** exhibit reactivity patterns that are similar to those of the acyclic diphenyliodonium ion.

Additional experimental evidence for the above mechanism can be found in the literature.

I. Some 10-I-3 complexes such as **18**–**21** have been prepared from **1** and the corresponding nucleophile.[3,4] These compounds are stable enough for reliable characterization by various methods, single crystal X-ray diffraction included (*e.g.*, for **20** and **21**).[4,32]

Importantly, similar iodanes derived from acyclic diaryliodonium cations are much more unstable, seldom isolable compounds which rapidly decompose at ambient temperature.

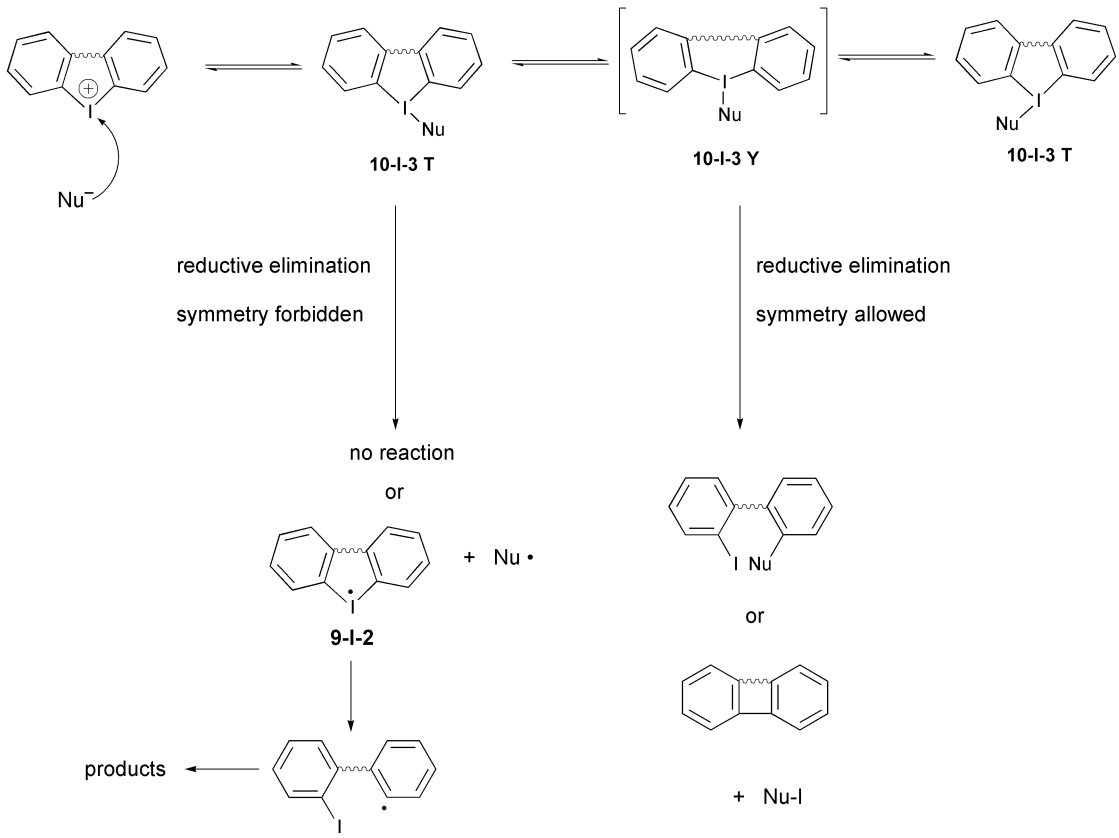
II. It has been demonstrated by VT NMR studies[33] that aryl-5*H*-dibenz[*b*,*d*]iodoles **22a,b**, analogues of **18**, are chemically and configurationally stable below 15 °C, with the barrier to isomerization being > 15 kcal mol^{-1}. Above room temperature the exchange (eqn. (15)) becomes fast on the NMR time scale (the two methyl resonances coalesce) and the 10-I-3 complexes decompose rapidly.



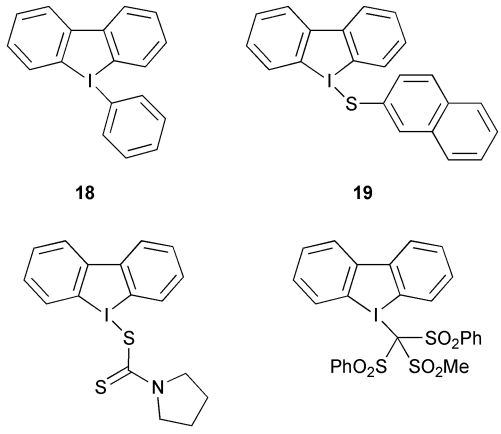
(15)

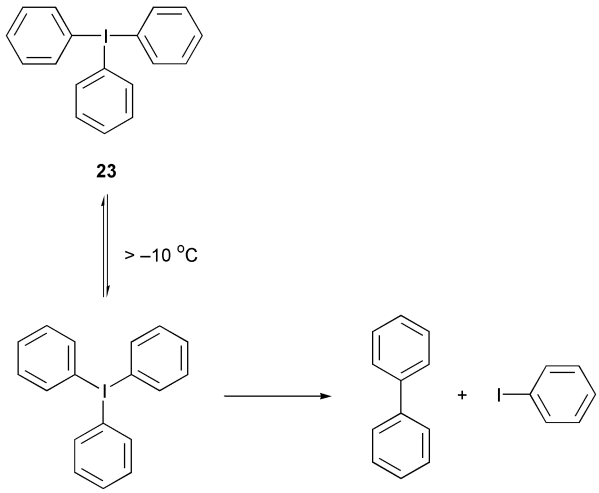
22a (Y = H)
22b (Y = CF_3)

III. Triphenyliodane **23** is unstable, rapidly decomposing to iodobenzene and biphenyl above −10 °C.[3,4] The selective formation of Ph_2 and PhI points to the synchronous reductive elimination occurring from the Y-conformation (Scheme 2) rather than a radical mechanism originally proposed for this reaction (eqn. (16)).



Scheme 2





(16)

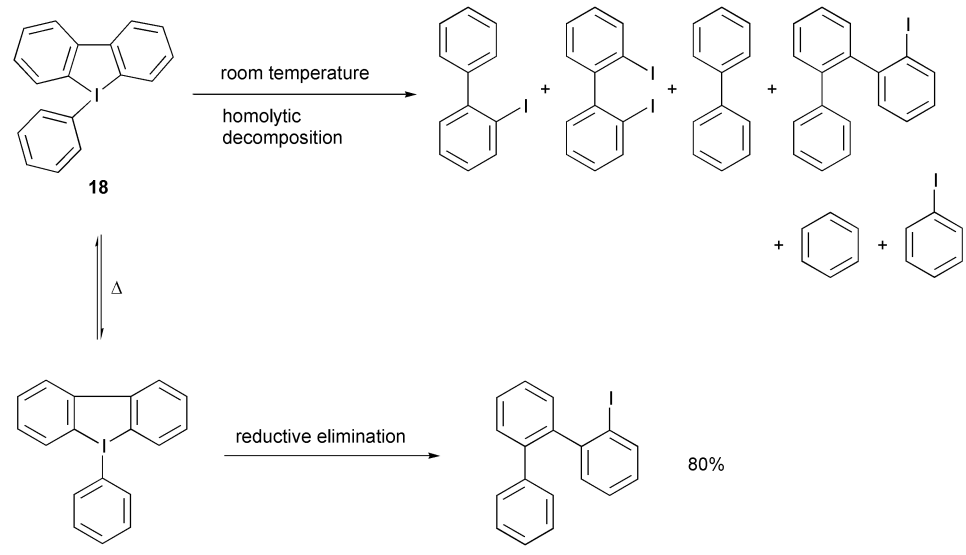
As mentioned above, the cyclic counterpart of **23**, 5-phenyl-5*H*-dibenz[*b*,*d*]iodole **18** is more stable. At room temperature, **18** undergoes slow homolytic decomposition in hexane to give a mixture of products (all in 10–15% yield).[3,4] When **18** is decomposed at *elevated* temperatures an abrupt *improvement* in the selectivity is observed, the yield of 2-iodo-*o*-terphenyl becoming as high as 80% (eqn. (17)).[3,4,34] This dramatic change in the selectivity suggests that at the higher temperature the decomposition of **18** is governed by a totally different, non-radical mechanism, *i.e.* C–C reductive elimination that becomes possible once the barrier to the T⇌Y isomerization is overcome.

Free-radical processes dominate[3,4,30] when **19** and **20** are thermally decomposed, probably due to the weakness of the I–S bond which is more prone to homolysis than the C–I bonds of **18**.

IV. Both **2** and **6** contain an iodonium center included in the 6-membered ring fused with two benzene rings. The presence of the isoxazole moiety in **6** constitutes the only difference between the two cations. This, however, leads to a dramatic difference in the rigidity of the two C_5I cycles (X-ray).[4,15] In **2**, the central ring is in the boat conformation, possessing some degree of conformational freedom, whereas in **6** the C_5I cyclic unit is almost ideally planar.[15] As a result, the more flexible **2** is capable of reacting with nucleophiles *via* the polar mechanism[8,9] (*e.g.*, eqn. (10)), whereas radical decomposition reactions of rigid **6** occur almost exclusively under similar conditions.[9]

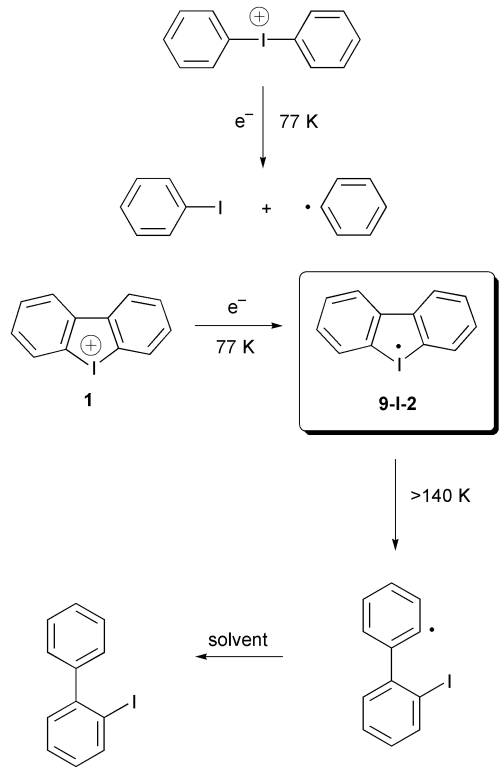
As may be seen from the above discussion, all reactivity patterns observed for the cyclic diaryliodonium salts are perfectly consistent with the two mechanisms shown in Scheme 2. The reductive elimination pathway is the only rationale for the reactivity of both acyclic (see the peculiar *ortho*-effect phenomenon)[5] and cyclic diaryliodonium compounds. Given the information accrued to date, there seems to be no reason to believe that polar reactions of diaryliodonium ions involve nucleophilic attack on one of the *ipso*-carbons, unless the aryl ligands on the iodine are activated by electron-withdrawing groups which would facilitate the classical Meisenheimer S_NAr reaction path.

Mechanistic studies of cyclic diaryliodonium compounds have also made a critical contribution to the radical chemistry of halonium ions. It has long been believed that radical reactions of iodonium ions are initiated by the formation of a 9-I-2 intermediate, either *via* direct SET or homolytic cleavage of one of the three bonds to the tricoordinate iodine in the iodane intermediate (Scheme 1). Although several pieces of indirect evidence for 9-I-2 diaryliodine radicals can be found in the literature, the first direct observation of such a species was reported only very recently.[11] The one-electron reduction of $[Ph_2I]^+$ and **1** *via* γ-irradiation from a ^{60}Co source was performed in aqueous LiCl or ethylene glycol glasses at 77 K.[11] When the diphenyliodonium cation was reduced, only the EPR signal from a phenyl radical was observed (eqn. (18)). The reduction of **1** and its 3-amino-derivative resulted, under similar conditions, in 9-I-2 iodine-centered radicals, as evidenced by EPR spectra with the characteristic ^{127}I (I = 5/2) anisotropic hyperfine structure (eqn. (19)). When trapped in aqueous ethylene glycol glass, these radicals are remarkably stable, showing no sign of decomposition below 140 K. The decay



(17)

above this temperature involved hydrogen abstraction from the matrix, in accord with the previously observed formation of 2-iodobiphenyl in various radical reactions of **1** (see above).



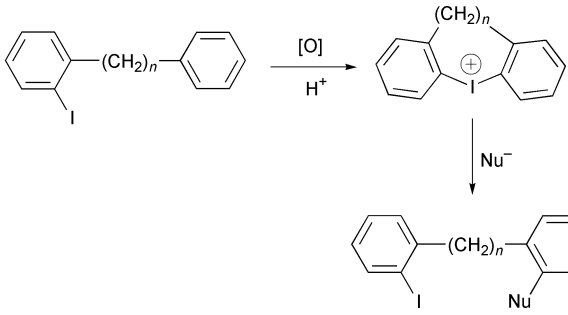
(18)

(19)

A similar 9-Br-2 species was generated upon reduction of the bromonium analogue of **1**, with the spin density on the bromine (0.13) being lower than on the iodine of the 2,2′-diphenyleneiodine radical (0.30). Theoretical calculations (PM3 and DFT) were performed on the cyclic 9-I-2 and 9-Br-2 radicals.[11]

4 Cyclic diaryliodonium salts in synthesis

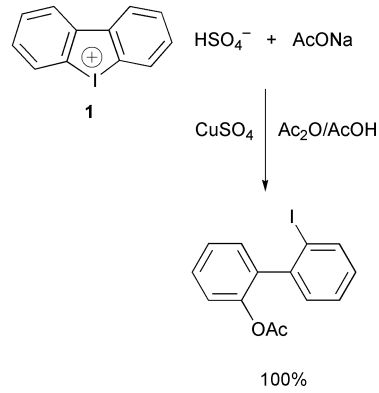
Nucleophilic substitution reactions of cyclic diaryliodonium salts would provide an easy entry to 2,2′-disubstituted α,ω-diarylalkanes and similar molecules *via* the two-step remote regiospecific *ortho*-functionalization (eqn. (20)).



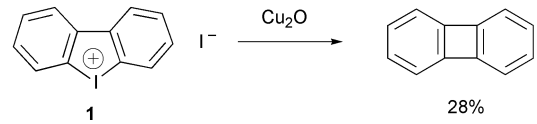
(20)

In the first step, the iodo compound is smoothly cyclized (*e.g.*, eqn. (2)) into the corresponding iodonium ion. The second step, nucleophilic displacement (eqn. (20)), would afford various bifunctional products that certainly have a great potential to serve as valuable building blocks in synthesis, *e.g.*, for the preparation of monomers, macrocycles, bidentate ligands, homo- and heterobimetallic complexes, and so forth. One can easily envision numerous exciting applications for the 2-functionalized 2′-iodo-α,ω-diarylalkane substrates in the Heck, Kumada, Sonogashira, Stille, Suzuki and Ullmann reactions, various lithiations, metal-catalyzed amination and carbonylation reactions, molecular self-assembly techniques, homo- and heterocoupling polymerization processes, and a wide variety of other transformations. The synthetic strategy with cyclic diaryliodonium salts can be exemplified by the synthesis of numerous cyclic aryl derivatives of P, As, Sb and Bi,[35] metalacycles[36] and the recently reported preparation of a novel interesting and useful diphosphine ligand (*e.g.*, Scheme 3)[13]

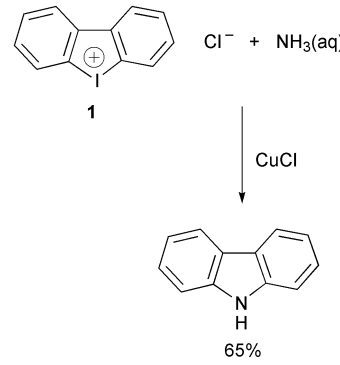
One skilled in the art of synthesis may easily imagine a similar synthetic approach employed for the preparation of other organometallics and ligands, such as P,P-, P,N-, P,S-, P,O- and so forth. The key to success with the cyclic diaryliodonium reagents is obviously the nucleophilic displacement step which can be very smooth and clean for the larger, non-rigid iodonium heterocycles, such as **3** and **4**, but is unlikely to be selective for the less flexible, smaller ring substrates, such as **2** and especially **1** (see above). Is there a way to improve on the selectivity of arylation reactions of the 5- and 6-membered iodonium heterocycles, and if there is what is the way? Catalysis with transition metals is apparently the answer to this question. It has long been known that copper compounds can efficiently catalyze some Ullmann-type reactions of **1** (eqns. (21)–(23)).[4]



(21)



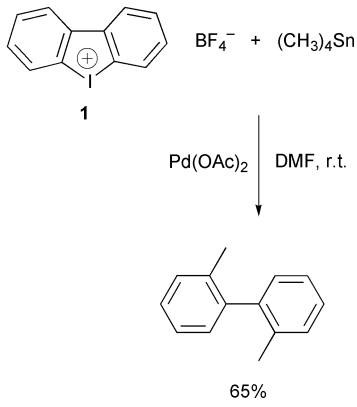
(22)



(23)

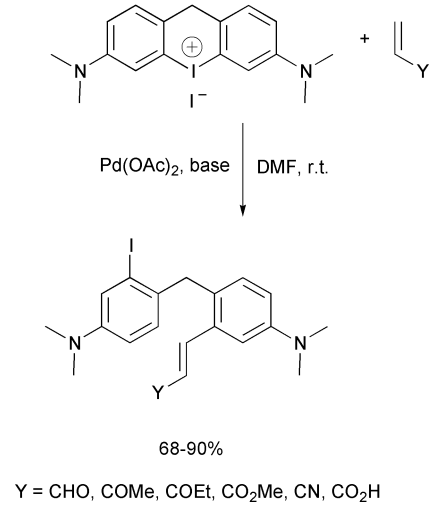
The ability of electron-rich, coordinatively-unsaturated complexes of Pd(0), Ni(0), Rh(I), *etc*. to oxidatively add and subsequently functionalize most unreactive Ar–X bonds (X = I, Br, or Cl) has been widely used in synthesis over the last three decades. In recent years, first reports have appeared describing Pd-catalyzed reactions of cyclic diaryliodonium salts. For

instance, the most unreactive dibenziodolium cation **1** readily undergoes the Stille-type double methylation with Me_4Sn to produce 2,2′-bitolyl in 65% yield (eqn. (24)).[37]



(24)

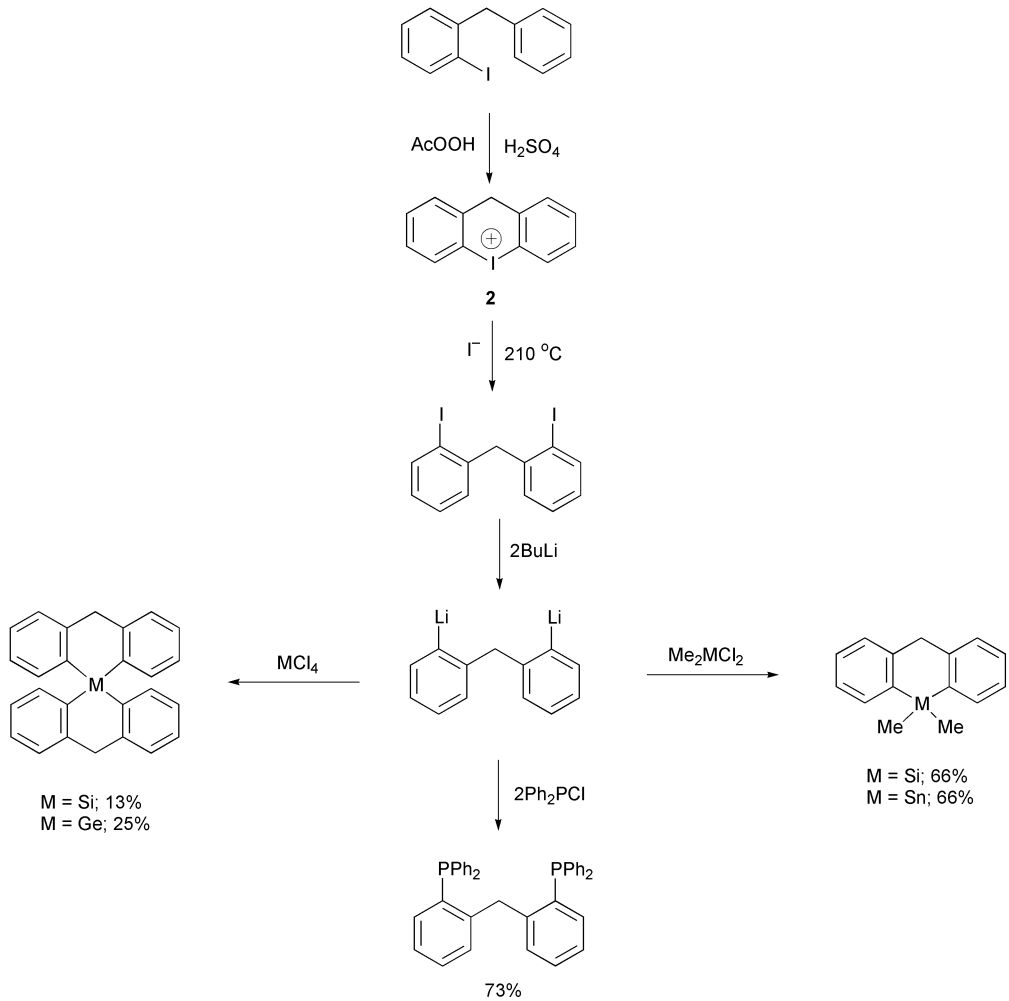
A Heck-type arylation of various acrylic compounds with the bis(dimethylamino) derivative of **2** has been reported to afford polyfunctional styrenes (all *trans*) in 68–90% isolated yield (eqn. (25)).[38] The catalyst of choice was $Pd(OAc)_2$, whereas $PdCl_2$, $[(Ph_3P)_2PdCl_2]$ and Pd metal all exhibited lower catalytic activity. Complex reaction mixtures were obtained when more electron-rich $[(Ph_3P)_4Pd]$ was used as a catalyst,[38] possibly due to further C–I activation of the iododiarylmethane product formed in the ring-opening step.



(25)

5 Conclusions

In recent years, a remarkable breakthrough has been made in the chemistry of cyclic diaryliodonium salts. Conformational non-rigidity has been recognized as the key factor determining the reactivity of the iodonium heterocycles toward nucleophiles, *i.e.*, the more flexible the heterocycle, the more readily and selectively it undergoes non-radical nucleophilic displacement. Thus, the polar reactions of the 7- and 8-membered iodonium heterocycles afford valuable bifunctional products in high yield. At the same time, radical processes are more characteristic of



Scheme 3

the more rigid 6- and especially 5-membered rings. These radical reactions are poorly selective, occurring *via* the formation and subsequent homolytic decomposition of the 9-I-2 intermediate which was for the first time directly observed (EPR) very recently. Importantly, the smaller rigid iodonium heterocycles may also be successfully used in synthesis if reacted with nucleophiles in the presence of transition metal catalysts.

6 Acknowledgement

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