Hypervalent Compounds

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Discovery of Stabilized Bisiodonium Salts as Intermediates in the Carbon–Carbon Bond Formation of Alkynes**

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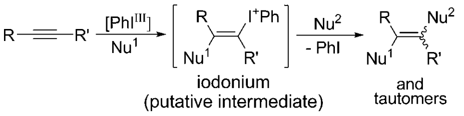
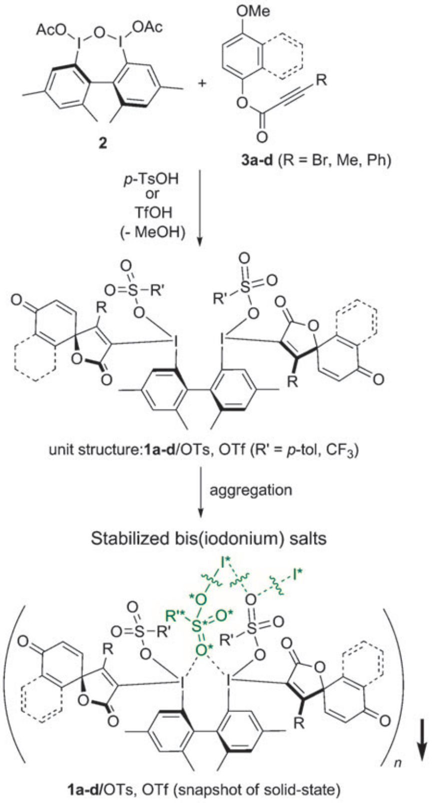
The oxidation of carbon–carbon triple bonds with hypervalent iodine reagents is an expedient strategy for the synthesis of 1,2-difunctionalized alkenes or their tautomers from alkynes through successive carbon–heteroatom bond-forming events [Eq. (1), Nu = heteroatom].[1,2] The postulated iodonium species, which have two carbon groups bound to an iodine atom, are putative reaction intermediates, but would sometimes be isolable as the salt forms, depending on the reaction conditions.[3] However, the possibility that similar iodonium-intermediate formation could accompany the installation of a new carbon–carbon bond has never been thoroughly confirmed. Such a transformation, to the best of our knowledge, has not appeared as a general method for alkyne functionalization in the long history of the chemistry of hypervalent iodine compounds.



(1)

Herein, we describe the discovery of a carbon–carbon bond-forming spirocyclization of alkynes with a hypervalent iodine reagent. We focus on the stabilization of unique and synthetically useful bisiodonium salts **1** through a hypervalent secondary bonding interaction: the $I^{III}\cdots O\cdots I^{III}$ pseudobridge linkage (Scheme 1). The results indicate a new concept and strategy for stabilizing iodonium intermediates during the course of alkyne transformations.



Scheme 1. Generation of stabilized bisiodonium salts **1a–d**. Tf = trifluoromethanesulfonyl, Ts = toluenesulfonyl.

Iodonium salts **1** were isolated as precipitates following the carbon–carbon bond-forming reaction of methoxy-substituted aryl alkynes **3** (**3a**: R = Br, **3b**: R = Me, **3c**: R = Ph, **3d**: aryl moiety: naphthalene, R = Br) with the hypervalent iodine compound **2**[4] in the presence of sulfonic acids in good yields (**1a**/OTs: 85 %, **1b**/OTs: 87 %, **1c**/OTs: quant., **1c**/OTf: 85 %, **1d**/OTs: 85 %). The reactions were carried out in wet polar solvents, acetonitrile, or 2,2,2-trifluoroethanol. The quantitative formation of the salts **1** was very surprising, since we had difficulty in detecting the iodonium salt when we treated ordinary hypervalent iodine compounds with alkynes **3**. Indeed, $PhI(OAc)_2$ did not react at all with the alkyne **3**, and neither $PhI(OCOCF_3)_2$ nor PhI(OH)OTs afforded the corresponding iodonium compound upon treatment with **3**, as expected.[2] Even the dimeric reagents PhI(OAc)O(AcO)IPh and $PhI(OCOCF_3)O(CF_3COO)IPh$, parent μ-oxo compounds of **2** without the biaryl linkage, gave a complex mixture. Apparently, only the use of compound **2** could enable the formation and isolation of iodonium salts such as **1**;

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other hypervalent iodine reagents would lead to undesirable oxidation reactions.

The unit structure of the salts **1** should consist of cationic bisiodonium parts and two anionic sulfonate ligands. All salts **1** obtained were solids stable enough to be stored under ambient conditions. Crystals suitable for X-ray crystallographic analysis were grown from solutions in acetonitrile/ether. Thus, **1c**/OTf, with triflate as a ligand, was subjected to structural refinement by X-ray crystallographic analysis (Figure 1).[5] The unique feature of **1c**/OTf is its unexpected pseudocyclic structure with I1···O8*···I2 secondary bonding interactions; the pseudobridging O8* atom is from a OTf group of another molecule in the salt (Figure 2). Thus, the pseudobridging O*Tf group is crystallographically identical to the other two OTf groups in Figure 1. Essentially, the μ-oxo bridging interaction seems to render the direct preparation of salts **1** and their isolation possible.

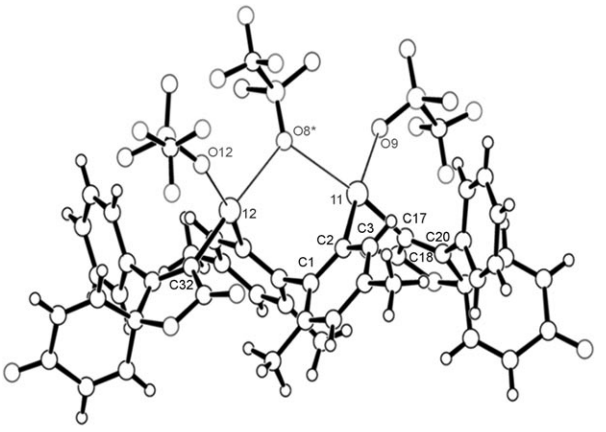


Figure 1. Snapshot of the stabilized bisiodonium salt oligomer **1c**/OTf. (The O8 atom with an asterisk belongs to another molecule of **1c**/OTf.) Selected bond lengths [Å] and angles [°]: I1–C2 2.127(6), I1–C17 2.091(6), I2–C32 2.072(7), I1···O8* 2.810(2), I2···O8* 2.782(3), I1···O9 2.844(2); C2-I1-C17 94.9(2), I1-C2-C1 120.3(4), I1-C2-C3 115.8(5), I1-C17-C18 117.8(4), I1-C17-C20 130.1(4), I1···O8*···I2 107.69(9), O8*···I1-C2 86.5(2), O8*···I1···O9 97.75(8), O8*···I1-C17 170.8(2), O9···I1-C2 175.2(2), O9···I1-C17 80.5(2).

In the salt **1c**/OTf, both the I1 and I2 atoms contact the O8* oxygen atom of the triflate ion. The interatomic distances are equal at around 2.8 Å and rather shorter than the sum of the van der Waals radii of iodine and oxygen atoms (ca. 3.5 Å). Accordingly, the O8* atom is located *trans* to the alkenyl moiety, and the I1···O8*···I2 bond angle is reasonably large at 107.69°. The dicoordinated oxygen atom was first found in the sulfonate ligand of an iodonium salt of this study.[6] Each iodine atom is cationic and surrounded by four atoms in an almost square-planar arrangement. The bisiodonium salt **1c**/OTf has slightly distorted bond angles, probably as a result of the unique configuration derived from the pseudocyclic structure. This new concept for stabilization observed in **1c**/OTf could provide a blueprint for the use of the postulated iodonium species in many alkyne transformations with hypervalent iodine reagents.[7]

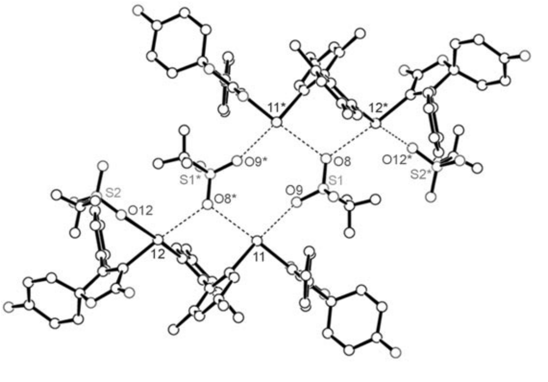
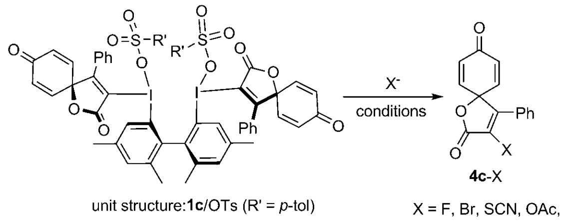


Figure 2. Solid-state packing of **1c**/OTf (dimeric structure).

It should be possible to exploit the chemical behavior of the series of isolable bisiodonium salts **1** and use them as a new synthetic module for the synthesis of spirocyclic compounds.[8] A preliminary investigation of the reactivity of salts **1** toward weak anionic nucleophiles could determine their usefulness for the synthesis of a wide array of functionalized spirocycles. Upon the treatment of **1c**/OTs with inorganic and organic salts, that is, CsF,[9a] KX (X = OAc, SCN),[9b,c] NaX (X = N_3, NO_2),[9c,d] and Bu_4NBr,[9d] the smooth replacement of the aryliodonio group in **1c**/OTs led to the generation of various functionalized spirocycles **4c**-X (X = F, Br, OAc, SCN, N_3, NO_2, etc.) under mild conditions (Table 1).[10] The introduction of nucleophiles in known spirocyclization procedures has rarely been reported.[11] Thus, the range of products **4** obtained by our method was quite different from that described by others,[12] and various spirocycles that are difficult to obtain, such as spiro products containing fluoro, oxygen, and nitrogen functionalities, could be prepared. This flexibility is the distinct advantage of the method with the stabilized salts **1**.

Table 1: Derivation of the bisiodonium salt **1c**/OTs to form functionalized spirocycles **4c**-X by the introduction of nucleophiles, X^-.[a]



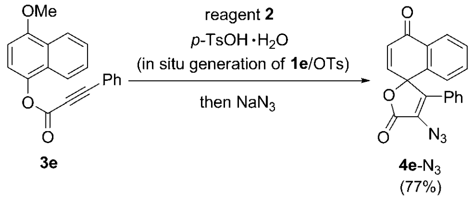
unit structure:**1c**/OTs (R' = *p*-tol)

4c-X

X = F, Br, SCN, OAc, N_3, NO_2

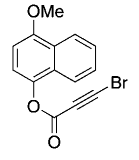
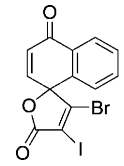
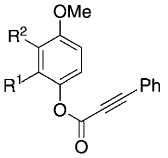
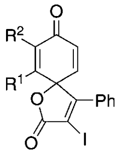
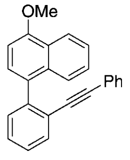
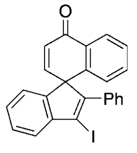
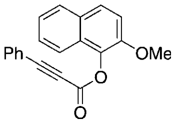
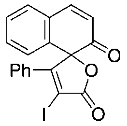
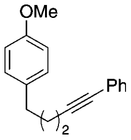
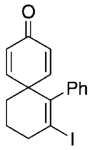
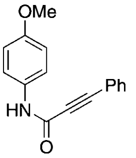
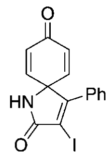
Entry	Conditions	X	Yield [%][b]
1	A	F	64
2	A	Br	99
3	A	OAc	85
4	B	SCN	94
5	B	N_3	76
6	B	NO_2	70

[a] Conditions A: CsF, Bu_4NBr, or KOAc, CH_3CN, 60 °C. Conditions B: KSCN or NaX (for X = N_3, NO_2), $CHCl_3/H_2O$ (3:1), room temperature. [b] Yield of the isolated pure product **4c**-X as calculated on the basis of the amount of **1c**/OTs used.



Scheme 2. One-pot approach to functionalized spirocycles from aryl alkynes **3** with bisiodonium salts **1** as intermediates.

Table 2: Scope of the one-pot spirocyclization–functionalization strategy with respect to the substrate **3**.[a]

Entry	Aryl alkyne **3**	Product **4**-I (Yield [%][b])
1	 **3d**	 **4d**-I (85)
		
2	**3f**: R^1 = Cl, R^2 = H	**4f**-I (83)
3	**3g**: R^1 = Ac, R^2 = H	**4g**-I (86)
4	**3h**: R^1 = *t*Bu, R^2 = H	**4h**-I (78)
5	**3i**: R^1 = H, R^2 = OMe	**4i**-I (94)
6	 **3j**	 **4j**-I (87)
7	 **3k**	 **4k**-I (99)
8	 **3l**	 **4l**-I (55)
9	 **3m**	 **4m**-I (99)

[a] Reactions were performed by a similar procedure to that outlined in Scheme 2 with Bu_4NI instead of NaN_3. [b] Yield of the isolated product after purification.

On the basis of these results, we developed a one-pot synthesis of spirocycles **4** by the spirocyclization of aryl alkynes **3**, followed by facile substitution at the iodonio position of intermediates **1** by added nucleophiles (Scheme 2). An extensive series of stabilized bisiodonium salts **1** were prepared as intermediates from aryl alkynes **3** in this one-pot procedure and converted into a variety of functionalized spirocycles **4**-I (Table 2).[13] Detailed investigations should enable the establishment of bisiodonium salts **1** as more useful synthetic tools owing to their potentially rich chemistry.[14,15]

In summary, we have reported the first carbon–carbon bond-forming reaction of alkynes with hypervalent iodine reagents, and the preparation and unique structure of these newly discovered stabilized iodonium salts **1**. The series of salts **1** obtained was found to serve as an excellent synthetic module for the preparation of various functionalized spirocyclic compounds **4**. The chiral structure of the μ-oxo-bridged hypervalent iodine compounds promises further extension of the utility of salts **1** to asymmetric synthesis.[16]

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Keywords: alkynes · bridging ligands · cyclization · iodine · spiro compounds

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