

Cyclic Homo- and Heterohalogen Di- λ^3 -diaryliodonium Structures

Wei W. Chen, Margalida Artigues, Mercè Font-Bardia, Ana B. Cuenca,* and Alexandr Shafir*



Cite This: *J. Am. Chem. Soc.* 2023, 145, 13796–13804



Read Online

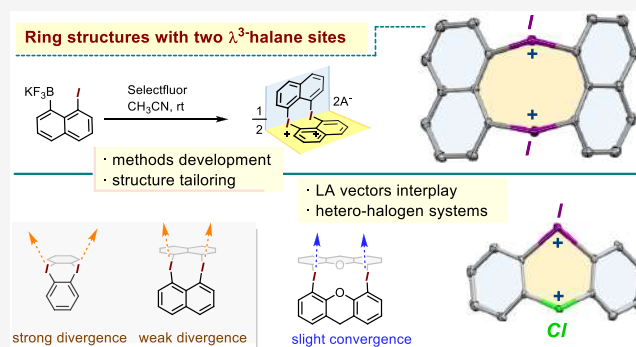
ACCESS |

Metrics & More

Article Recommendations

Supporting Information

ABSTRACT: In the context of the ever-growing interest in the cyclic diaryliodonium salts, this work presents synthetic design principles for a new family of structures with two hypervalent halogens in the ring. The smallest bis-phenylene derivative, $[(C_6H_4)_2I_2]^{2+}$, was prepared through oxidative dimerization of a precursor bearing the *ortho*-disposed iodine and trifluoroborate groups. We also report, for the first time, the formation of cycles containing two different halogen atoms. These present two phenylenes linked by hetero-(I/Br) or -(I/Cl) halogen pairs. This approach was also extended to the cyclic bis-naphthylene derivative $[(C_{10}H_6)_2I_2]^{2+}$. The structures of these bis-halogen(III) rings were further assessed through X-ray analysis. The simplest cyclic phenylene bis-iodine(III) derivative features the interplanar angle of $\sim 120^\circ$, while a smaller angle of $\sim 103^\circ$ was found for the analogous naphthylene-based salt. All dications form dimeric pairs through a combination of π - π and C-H/ π interactions. As the largest member of the family, a bis-I(III)-macrocycle was also assembled using the quasi-planar xanthene backbone. Its geometry enables the two iodine(III) centers to be bridged intramolecularly by two bidentate triflate anions. In a preliminary manner, the interaction of the phenylene- and naphthalene-based bis-iodine(III) dications with a new family of rigid bidentate bis-pyridine ligands was studied in solution and the solid state, with an X-ray structure showing the chelating donor bonding to just one of the two iodine centers.



INTRODUCTION

The term “diaryliodonium salt” refers to iodine(III) compounds in which the trivalent iodine center is bound to two aromatic rings and a third typically weakly coordinating anion (Figure 1). This structure class requires little introduction, given that the prototypical diaryliodonium motif (Figure 1, A)^{1,2} has been known for over 120 years,³ growing into an important class of aryl transfer agents. Diaryliodonium salts have been employed in a plethora of polar and radical processes, including metal-catalyzed and light-induced arylation reactions.⁴ In this context, the cyclic diaryliodonium derivatives containing mutually connected aryl groups have been of particular interest, with the iodine-containing ring structure imparting a series of new chemical and physical properties. For example, while the archetypal five-membered structure type B (Figure 1) is particularly stable toward conventional nucleophilic attack,⁵ this and the larger iodacycles (e.g., type C) undergo all sorts of ring-opening and ring-enlargement reactions under metal-catalyzed^{6,7} or single electron transfer (SET) conditions.⁸ Beyond this synthetic potential, cyclic diaryliodonium cations are also known to interfere with a variety of biological electron-transport systems. In fact, the parent diphenylene-iodonium (“DPI”) cation (archetype B) is widely used as a broad-spectrum go-to inhibitor of NADPH oxidases and other flavoenzymes,⁹ either as reporter/modulators of cellular activity^{9b} or as therapeutic

candidates.^{9c} Recently, the ability of the Lewis acidic iodine(III) center to engage in highly directional intermolecular interactions, sometimes referred to as “halogen bonding”,¹⁰ has come under a spotlight in the fields of crystal engineering, molecular recognition, and Lewis acid organocatalysts.^{11,12} Another center of focus has been the revival (after decades of relatively little interest) of the hypervalent derivatives of the lighter two halogens: Br and Cl.^{13,14} Fresh examples include the bromonium-based cycloaddition reactions from the Wencel–Delord laboratory (Figure 1, D),^{14a–c} as well as chiral Br- and Cl-centered onium salts as enantioselective halogen-bonding catalysts by Yoshida et al. (structure E).^{14d}

In this context, our attention was drawn to the scarcely explored cyclic onium salts containing more than one iodine atom in a ring. A notable example of such compounds is the square-shaped macrocycle developed by Zhdankin and Stang, in which the near- 90° C–I–C angles are used as corner pieces.¹⁵ Another example is the planar 3-fold symmetric

Received: March 6, 2023

Published: June 13, 2023



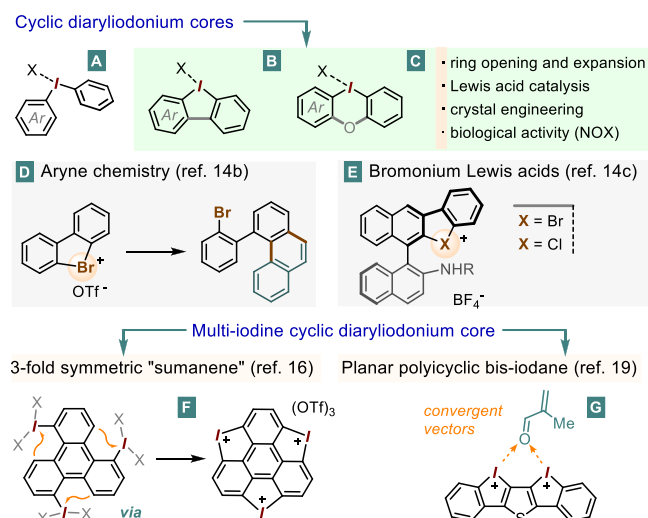


Figure 1. A sampling of cyclic diaryl-halogen(III) structures with some applications. **A:** canonical diaryliodonium motif; **B, C:** most common cyclic diaryliodonium structure types; **D, E:** recent application of bromonium and chloronium salts; **F, G:** examples of molecules presenting multiple diaryliodonium groups.

iodine-doped sumanene derivative (Figure 1, F)¹⁶ obtained via an oxidation/ E_A S cyclization sequence. We note that routes such as this one are commonly used to prepare a variety of cyclic bis-diaryliodonium species,^{17,18} including the planar bis-diaryliodonium dication **G** (Figure 1). Interestingly, the latter exhibits exceptional Lewis acidity due to spatial convergence of the two iodonium C–I σ^* vectors.¹⁹

With these precedents, and prompted by our own recent work on heteroatom-containing iodonium salts,²⁰ we wondered about the properties of a hitherto unknown cyclic structure related to the archetype **C** (Figures 1 and 2), but

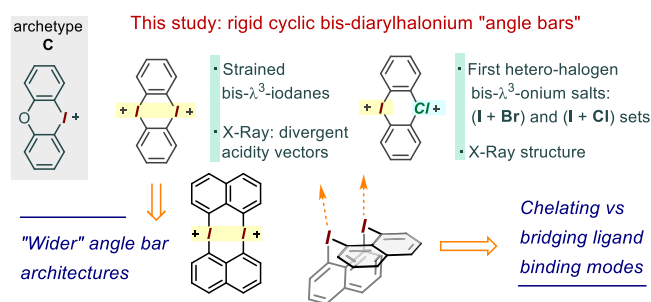


Figure 2. Principle bis- λ^3 -halonium angle bars developed in this study.

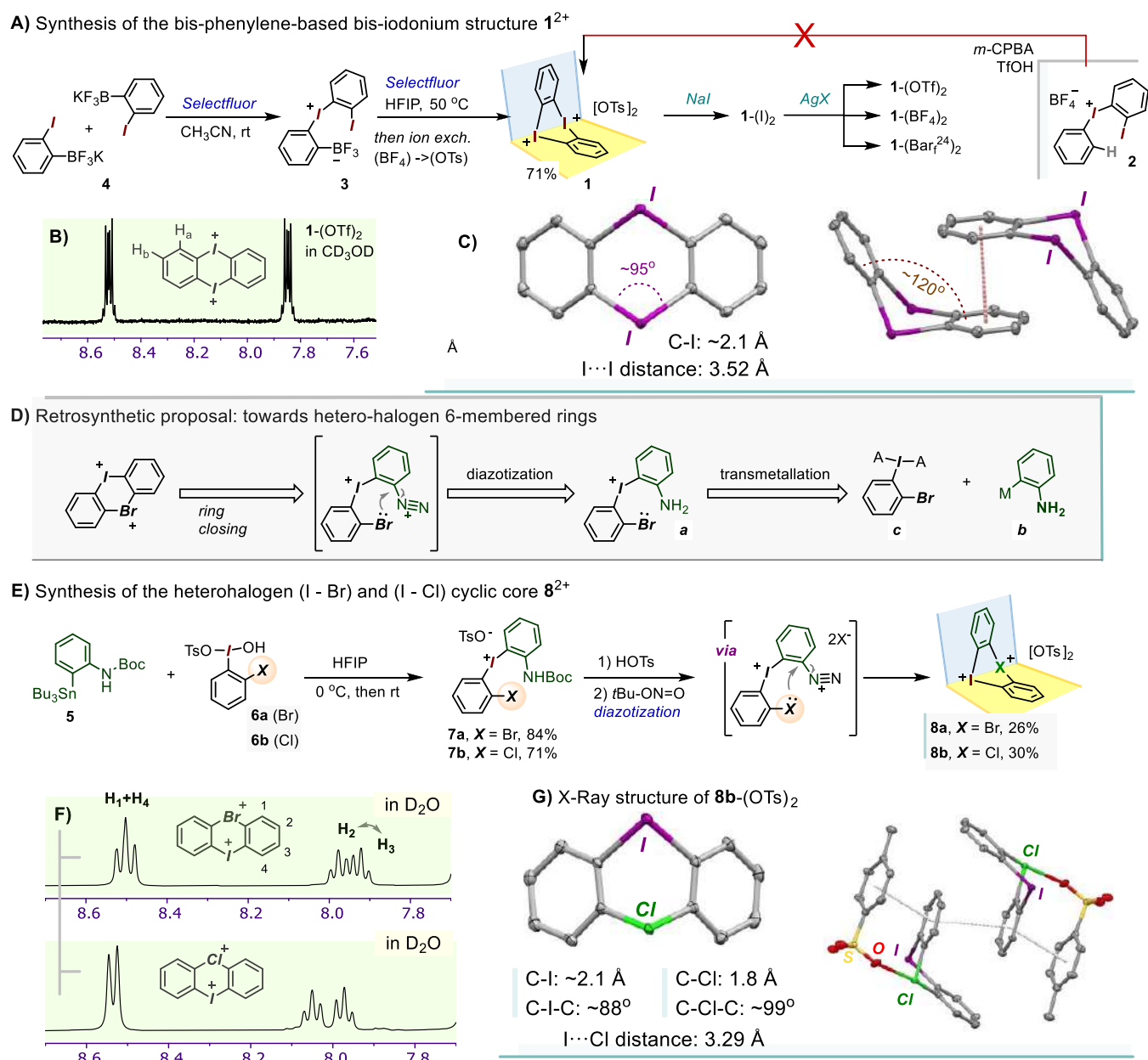
having not one, but two iodine(III) bridges. Beyond the sheer synthetic challenge of making this cycle, this structure class appears to be an interesting platform for new “angle bar” molecular geometries (provided a near-90° C–I–C angle), and for exploring other classes of interhalogen synergistic effects. As part of this new program in our lab, we now report the synthesis and X-ray structures of not only this bis- λ^3 -iodane architecture (I–I), but also the analogous heterohalogen six-membered cycle with the I–Br and I–Cl bridges. The latter two represent, to the best of our knowledge, the first examples of a bona fide hetero- λ^3 -organo-halogen derivative. We also report the synthesis and structure of larger (macro)cyclic bis- λ^3 -iodane angle bars, as well as their interaction modes—

including chelating and bridging—with bidentate donor structures.

RESULTS AND DISCUSSION

Bis-Halogen-Linked Bis-Phenylene Cores. Our initial approach to the cyclic bis-iodonium 1^{2+} was an electrophilic ring closing of the *ortho*-iodo-diphenyliodonium precursor **2**.²¹ However, attempts to cyclize **2** under oxidative conditions commonly used in the formation of cyclic iodonium salts were unsuccessful, likely due to the strongly electron-withdrawing effect exerted by the already-present iodine(III) group.²² Seeking to overcome this reluctance to C–H cyclization, we took notice of a recent report from the Legault laboratory on the oxidative dimerization of the *ortho*-iodo-phenyltrifluoroborate **4** to the interesting zwitterion **3**.²³ Since the latter contains both an iodine and an *ortho* trifluoroborate group, we hoped that **4** might be directly dimerized to 1^{2+} via two consecutive oxidation/transmetalation events. Our initial attempts to accomplish this transformation using Selectfluor as oxidant in CH_3CN inevitably stopped at the intermediate **3**, mirroring the original report.²³ In addition, attempts to use this solvent at higher temperatures led to significant amounts of the *ortho*-diiodobenzene side-product, ostensibly through the breakdown of **3** or of the putative cyclic target. Nevertheless, a breakthrough came thanks to the use of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) as solvent. Hence, exposing **3** to excess Selectfluor at 40–50 °C in HFIP suppressed the formation of *ortho*-diiodobenzene, leading instead to a gradual appearance of a new species with only two 1H NMR resonances, found at 8.5 and 7.9 ppm (see Scheme 1, A and B), in a pattern consistent with the C_{2v} -symmetric bis-diaryliodonium 1^{2+} . Further corroboration came from HR-MS(ESI+), which revealed a peak at $m/z = 202.9358$ for the target dication $[(C_6H_4)_2I_2]^{2+}$ (calcd 202.9352 for $z = 2$). The product was initially formed as the tetrafluoroborate salt, i.e., **1**-(BF_4)₂. Nevertheless, given the crucial influence often exerted by the counterions in the chemistry and applications of a diaryliodonium fragment, the family was expanded with additional counterions. Hence, the BF_4 salt could be converted to the virtually insoluble derivatives, either ditosylate **1**-(OTs)₂ (71% based on **3**) or the di-iodide **1**-(I₂)₂. The –OTf, – BF_4 , and even the BAR_f ²⁴ derivatives [$BAR_f^{24} = B(3,5$ -bis-trifluoromethyl- $C_6H_3)_4$] were also synthesized through anion exchange with the corresponding silver salt. X-ray-quality crystals of **1**-(OTf)₂ were grown through vapor diffusion of Et_2O into the CH_3CN solution. The salt crystallized in space group $P\bar{1}$ and the solid state structure featured the tricyclic dication 1^{2+} having a local C_{2v} -symmetry. The two phenyl-containing planes intersect (at the I··I line) at a 120° angle (Scheme 1, C); while the C–I–C angles were measured at ~95°. The I··I distance of 3.52 Å is somewhat shorter than the sum of the iodine van der Waals radii (~3.8–4.0 Å), suggesting a degree of steric crowding between the two halogens. The bis-iodonium fragments are arranged in pairs (see Scheme 1, C, right), which are held together through π -stacking on their inner (concave) sides. Not shown are the additional principal I··O interactions with neighboring triflate anions (see SI) completing the roughly square planar environment around each iodine(III) center.

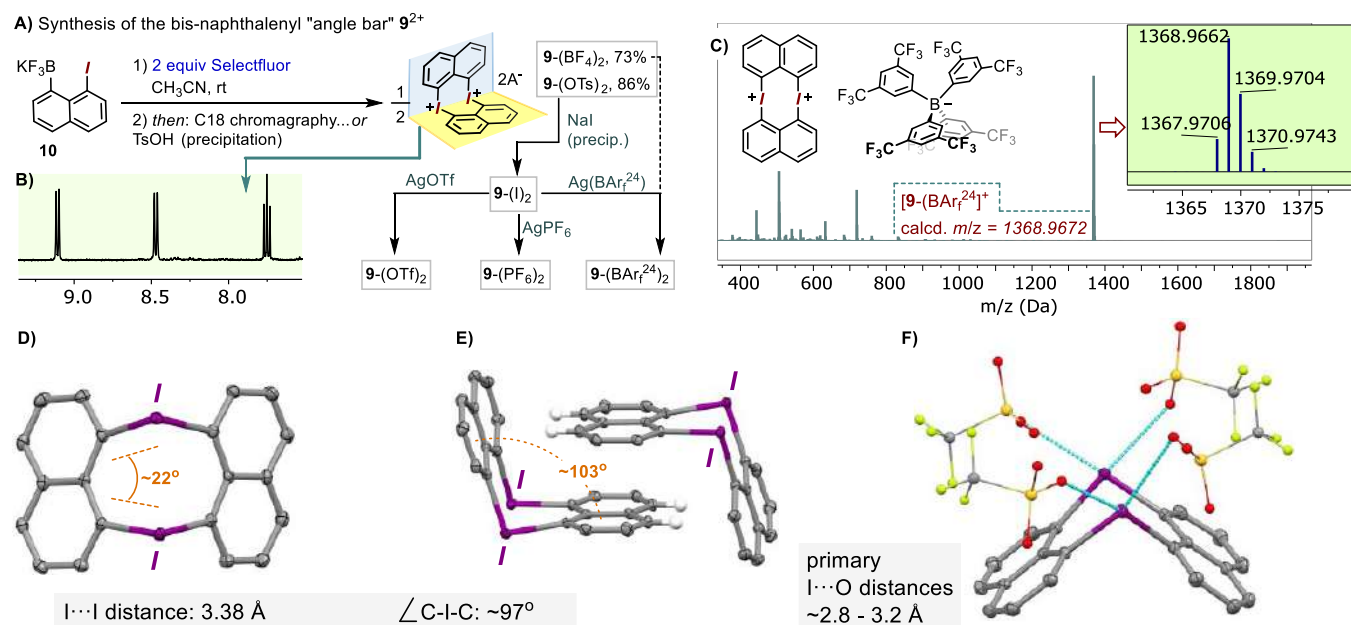
Having succeeded in the formation of the six-membered bis-iodane 1^{2+} , we sought to expand our study to rings incorporating two different halogen atoms. Indeed, despite a renewed spotlight on the organo-chloro(III) and -bromo(III)

Scheme 1. Synthesis and Characterization of the Cyclic Bis-diaryliodonium 1^{2+} and the Hetero-Bis-diaryl-Halonium $8a^{2+}$ and $8b^{2+}$


^aA and B: Synthesis of 1^{2+} , along with a portion of its ^1H NMR spectrum. C: Solid state structure of 1^{2+} along the molecular C_2 axis (left) and a view of the mutually fitting dication pairs (right) (thermal ellipsoids shown with a 50% probability, H and OTf omitted for clarity). D: retrosynthetic approach to 8^{2+} . E: synthesis of $8a^{2+}$ and $8b^{2+}$. F: Aromatic ^1H NMR regions of **8a** (top) and **8b** (bottom). G: Solid state structure of $8b^{2+}$; thermal ellipsoids shown with a 50% probability, H and OTf (fully or partially) omitted for clarity.

derivatives,^{14,24} we could find no precedent of molecules having two distinct high-valent halogen atoms, let alone an example of a heterohalogen ring structure.²⁵ Given that the synthetic route designed for 1^{2+} was deemed unsuitable for hard-to-oxidize lighter halogens, an alternative retrosynthetic sequence was envisioned to access the six-membered bromine(III)–iodine(III) cycle. The route would rely on the *ortho*- NH_2 diaryliodonium precursors **a** (Scheme 1, D), with ring closing achieved via diazotization followed by cyclizative N_2 displacement. The precursor **a**, in turn, could arise via transmetalation using a suitably *ortho*-metalated aniline **b**. This route, however, presents a series of challenges. One is the

question of whether the diazotization event is even possible on a diaryliodonium core. Another is the actual synthesis of the *ortho*-amino derivative **a**, a species with scarce precedent in the literature, having been described as difficult to prepare and highly unstable.²⁶ Fortunately, albeit after considerable effort, a route was identified in which a reaction between the *ortho*-stannyl *N*-Boc aniline **5** and the Koser-type *ortho*-bromo λ^3 -iodane **6a** took place in HFIP to give the diaryliodonium intermediate **7a** in 84% yield (Scheme 1-E). A one-pot *N*-deprotection of **7a** with HOTS, followed by the addition of the diazotizing reagent *t*Bu-ON=O^{14a} led to the precipitation of an off-white powder. To our delight, the ^1H NMR spectrum of

Scheme 2. Synthesis and Characterization of the Naphthalenyl-Based Bis- λ^3 -diaryliodonium Dication of 9^{2+} ^a

^aA and B: Synthetic route along with a portion of its ^1H NMR spectrum. C: HR-MS(ESI+) analysis of $9-(\text{BARf}^{24})_2$. D, E, and F: partial X-ray ORTEP diagrams of $9-(\text{OTf})_2$ at 50% thermal ellipsoids; most H omitted for clarity.

this product displayed an aromatic ABCD pattern (clustered into two groups of resonances), in line with the C_s -symmetric mixed iodine(III)–bromine(III) cyclic bis-halonium target **8a**-(OTs)₂ (Scheme 1, F, top). The structure was further corroborated via HR-MS(ESI+) analysis, which revealed the (**8a**-OTs)⁺ peak at $m/z = 528.8974$ (vs *calcd* 528.8964), including the expected Br isotope pattern (see SI).

Seeking to extend this approach to the analogous mixed iodine(III)–chlorine(III) derivative, the *o*-Cl Koser derivative **6b** was transformed into the diaryliodonium salt **7b** in 71% yield. As had been the case for **7a**, this salt underwent diazotizative cyclization to give, in this case, the mixed I(III)–Cl(III) cyclic salt **8b**-(OTs)₂.²⁷ The ^1H NMR analysis confirmed, once again, a C_s -symmetric dicationic portion, albeit with only minimal chemical shift separation between the two *ortho*-halo positions H₁ and H₄ (Scheme 1, F, bottom). The HR-MS(ESI+) peak for (**8b**-OTs)⁺ was recorded at $m/z = 484.9462$, in line with the calculated value of 484.9470.

Although **8a** and **8b** were only sparingly soluble in water, their ^1H NMR spectra in D₂O showed them to be surprisingly stable in aqueous solutions, remaining unchanged for several weeks at room temperature (see SI, Figures S3 and S5, respectively). Paradoxically, after just a few hours in dms-*d*₆, both compounds were observed to undergo clean hydrolytic ring opening to the phenolic derivatives **S4** and **S6**, as observed by NMR and confirmed by HR-MS (see SI).

This made it somewhat challenging to grow single crystals of **8a** and **8b**, with earlier attempts invariably leading to hydrolysis. Nevertheless, X-ray-quality crystals of both species were obtained by taking advantage of the low product solubility in the reaction mixture upon their synthesis. Hence, a solution containing precursor **7a** (or **7b**), HOTs, and *t*Bu-ON=O in MeNO₂ was briefly heated to 60 °C and then left undisturbed at room temperature. After several days, small colorless plate-like crystals of both **8a**-(OTs)₂ and **8b**-(OTs)₂ were observed. Their X-ray analysis revealed the expected cyclic heterohalogen structures which, as in the case

of **1**, form the π -stacked pairs of dications (Scheme 1, G, for **8b**-(OTs)₂; for **8a**-(OTs)₂ see SI and the CIF file); these pairs, in turn, are boxed in between two tosylate anions via additional π -stacking interaction with the counterion's tolyl group. For both **8a**²⁺ and **8b**²⁺ structures, the C–X–C angles for the lighter halogen bridges (93.5° for Br and 98.6° for Cl) are larger than those for the corresponding C–I–C fragments (90.0° and 87.9°, respectively). This trend is in line with the predominant halogen p-orbital contribution for iodine(III) bonding and a larger s-orbital component associated with lighter halogens, as discussed recently by Stuart and co-workers.²⁸

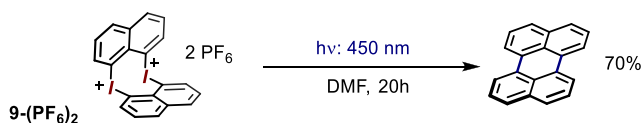
Toward the Bis-diaryliodonium Angle Bar Structure.

As part of our broader interest in the cyclic bis-halonium cyclic structures, we wondered whether the use of the 1,8-disubstituted naphthalene backbone, or even a wider-spaced anthracene scaffold, could afford rigid structures that approach a 90° "angle bar" geometry. We envisage that in addition to serving as a blueprint to other rigid halogen-based molecular architectures, such structures could allow for the study of new types of interplay between halogen(III) Lewis acidity (or halogen bonding) vectors. Hence, aiming to apply an oxidative head-to-tail dimerization process, as seen with **1**, we began by synthesizing the *peri*-iodo-trifluoroborate precursor **10** from 1,8-diiodonaphthalene via a selective mono-magnesium-borylation process (see SI). Gratifyingly, while the cyclization step in the synthesis of **1** required a stepwise approach and forcing conditions, simply treating **10** with excess Selectfluor in CH₃CN at room temperature led, after 17 h, directly to the clean formation of the C_{2v} -symmetric dication 9^{2+} (Scheme 2, A).²⁹ The resulting BF₄ salt could be obtained in pure form in a 73% yield via reversed phase chromatography on C18 silica gel. Alternatively, treating the crude mixture with TsOH resulted in the precipitation of **9**-(OTs)₂ as a clean pale-yellow solid in an 86% yield. The OTf, PF₆, and BARf₂₄ derivatives were also obtained through a double anion exchange route via the insoluble **9**-(I)₂ form, followed by treatment with the silver

salt of the corresponding counterion. Alternatively, $9\cdot(\text{BAr}_f^{24})_2$ could also be obtained directly from the initially formed tetrafluoroborate via salt metathesis with NaBAr_f^{24} . The C_{2v} -symmetric dication 9^{2+} presents three strongly deshielded ^1H NMR resonances at ~ 9.2 , 8.5 , and 7.9 ppm (see Scheme 2, B). The HR-MS(ESI+) analysis of the triflate salt (eluent spiked with formic acid) revealed a peak at $m/z = 550.8991$, in line with the value 550.8999 expected for $[9]\cdot(\text{O}_2\text{CH})^+$. Furthermore, the analysis of the BAr_f^{24} derivative led to $m/z = 1368.9662$, matching well the theoretical value of 1368.9672 for $[9]\cdot(\text{BAr}_f^{24})^+$ (Scheme 2, panel C). Crystals of $9\cdot(\text{OTf})_2$ suitable for X-ray structure determination grew in space group $P\bar{1}$ through vapor diffusion of Et_2O into a CH_3CN solution. As expected, the *peri* C–I vectors in each naphthalene unit diverged at an angle of $\sim 22^\circ$ due to the steric repulsion between iodine atoms, a situation further confirmed by the relatively short I··I contact distance of 3.38 \AA . The structure showed a 103° angle between the two naphthalene planes, a value closer to an idealized 90° angle than the $\sim 120^\circ$ angle observed in **1** (see panels D and E in Scheme 2). Once again, the bis-cationic fragments are arranged in tightly fitting mutually complementing pairs, which appear to be held together by a combination of π -stacking and CH– π interactions (panel E). Each iodine atom also presents two main I··O interactions with the neighboring triflate anions to form an approximate square plane geometry (see panel F), along with a number of secondary I··O interactions.

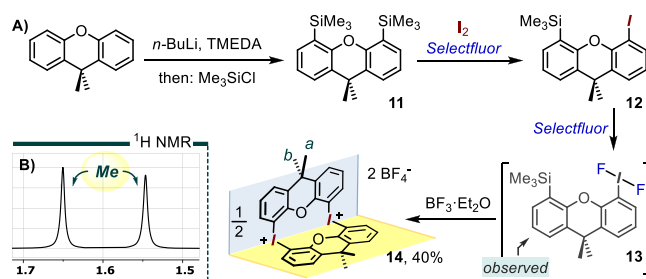
The newly obtained $9\cdot(\text{A})_2$ salts were found to degrade over time if not protected from light. Interestingly, perylene was identified as the main decomposition product. In fact, irradiation of $9\cdot(\text{PF}_6)_2$ in a DMF solution at 450 nm led to a rather clean formation of perylene in $\sim 70\%$ yield, likely through a sequence of homolytic C–I cleavage and C–C coupling steps (Scheme 3).

Scheme 3. Photolytic Evolution of $9\cdot(\text{PF}_6)_2$ to Perylene



To our initial disappointment, attempts to produce a wider-spaced anthracene analogue of **9** were unsuccessful, likely due to the poor solubility of the anthracene precursor and the facile oxidative degradation of the anthracene core. Instead, we turned our attention to the geometrically similar 9,9-dimethylxanthene backbone. Hence, as shown in Scheme 4, A, the bifunctional precursor **12** was prepared from the 4,5-disilyl-9,9-dimethylxanthene **11** by a selective exchange of one of the $-\text{SiMe}_3$ groups for I using the $\text{I}_2/\text{Selectfluor}$ combination. Next, exposing **12** to Selectfluor led to an initial formation of a new compound, **13**, tentatively identified by ^1H and ^{19}F NMR as bearing the hypervalent $\lambda^3\text{-IF}_2$ group.³⁰ Heating this intermediate in the presence of $\text{BF}_3\cdot\text{Et}_2\text{O}$ helped induce the aryl transfer from silicon to iodine(III), leading to a gradual conversion of **13** to the more symmetric 12-membered macrocycle 14^{2+} . This result was supported by the observation of a simple three-resonance ^1H NMR aromatic set for the new product (see SI). Furthermore, when measured in methanol- d_4 , the locked “angle bar” geometry leads to the splitting of the 9,9-di-Me signal into two Me singlets: one for the inner (*a*) and another for the outer (*b*) positions (Scheme 4, B). The

Scheme 4. Cyclic Bis-iodonium Structure **14** Based on 9,9-Dimethylxanthene: (A) Synthesis Starting with 9,9-Dimethylxanthene; (B) Upfield Portion of the ^1H NMR Spectrum



$14\cdot(\text{BF}_4)_2$ salt was isolated in 40% yield via reversed-phase chromatography, while the corresponding triflate salt was obtained through double anion metathesis via the sparingly insoluble $14\cdot(\text{I})_2$ derivative. The HR-MS(ESI+) analysis produced a peak at $m/z = 714.9847$, consistent with 714.9837 calculated for $[14]\cdot(\text{O}_2\text{CH})^+$.

The structure of $14\cdot(\text{OTf})_2$ was further assessed through single-crystal X-ray analysis (Figure 3). As expected, the

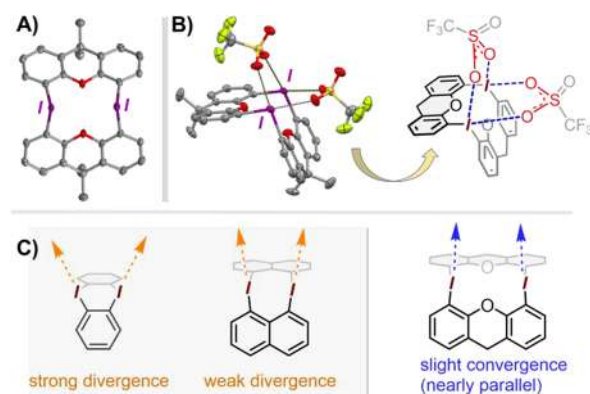


Figure 3. ORTEP-type diagram of the X-ray (single crystal) structure of $14\cdot(\text{OTf})_2$. Only one of the two independent molecules shown, with protons omitted for clarity. (A) Top view of 14^{2+} showing the 12-membered macrocycle. (B) Side view of the full molecule illustrating the bridging (I–O–S–O–I) η^2 -triflate ligands and the overall “paddle-wheel” geometry. (C) Comparison of divergence in the hypothetical C–I σ^* vectors in cyclic bis-iodonium dications.

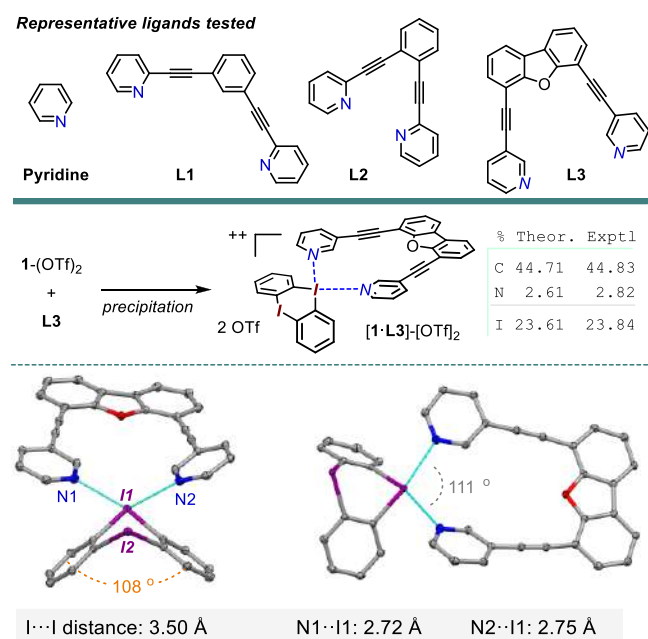
xanthene backbone imparts a relatively large I··I spacing of $\sim 4.2 \text{ \AA}$, a value similar to that expected in a hypothetical anthracene-based structure. At the same time, the xanthene moiety was found to display certain conformational flexibility around the central pyran ring.³¹ Interestingly, while the solid state structures of 1^{2+} and 9^{2+} show pairs of divergent Lewis acidity vectors stemming from the neighboring iodine(III) centers, the corresponding vector pairs in the xanthene-based 14^{2+} show a small degree of convergence (see Figure 3, C). Thanks to this, the two triflate ligands in the structure of 14^{2+} are each capable of connecting adjacent iodine centers via crystallographically symmetric I–S–O–S–I bridges, leading to a geometry broadly reminiscent of the “paddle-wheel” bimetallic complexes (see Figure 3, B).³²

Interaction with Rigid Bis-pyridine Ligands. Picking up on this last point, each halogen(III) center contributes with a pair of mutually perpendicular acidity directions. Therefore, all the bis-diarylhalonium dications shown thus far present four

principal Lewis acidity vectors. In this scenario, a bidentate donor ligand could bind to such a dication in a number of modes. One possibility includes a ligand bridging between two adjacent iodine centers, as observed for the OTf ligands in 14^{2+} (refer to Figure 3, B). Another is the chelating mode, i.e., two donor atoms binding to the same halogen site via its mutually perpendicular “vacant” sites.³³ For the simple cyclic structure type B (see Figure 1), such scarcely preceded chelating mode was recently explored by the Huber laboratory employing bis-R(OR')C=O: donor ligands based on a rigid bis-alkynyl-benzene backbone.³⁴

Combining this idea with the recent advances in pyridine-stabilized I^{3+} , I^{5+} , and, especially, I^{1+} structures,^{35,36} a small family of rigid bis-pyridine donors was synthesized varying the N–N distances and chelation angles (Scheme 5, top panel).

Scheme 5. Selected Rigid Bis-pyridine Ligand Set, along with the Formation of a 1:1 Adduct between I^{2+} and $L3^a$



^aLast panel (bottom) shows an X-ray ORTEP diagram (50% probability plots) of $[1 \cdot L3] \cdot (OTf)_2$; H and OTf omitted for clarity.

These were then used, along with pyridine itself, in binding studies with the bis-diaryliodonium Lewis acceptors. In fact, pyridine was previously used as model donor to measure and benchmark the Lewis acidities of various diaryliodonium cations,³⁷ as well as of their bromine(III) and chlorine(III) analogues.²⁸ Hence, in a very preliminary assay, a portionwise addition of pyridine to a CD_2Cl_2 solution of $1 \cdot (BARf^2)^+$ caused a gradual upfield shift of the I^{2+} resonances, which were then used to extract the binding constant. Assuming a 1:1 binding model, a value of $K_a \sim 609 M^{-1}$ was obtained, which would be 27 times higher than for the noncyclic salt A (Figure 1) and ~ 4.7 times higher than the value of $130 M^{-1}$ that had been previously measured for the simple cyclic diaryliodonium prototype B.²⁸ Even for the naphthalene-based $9 \cdot (BARf^2)^+$, this titration led to a $K_a \sim 308 M^{-1}$, which although not as high as in 1^{2+} is still ~ 2.4 times higher than for B. We are cognizant, however, that the assumption of the 1:1 binding stoichiometry in this model may break down, especially at higher pyridine concentration, where the potential rise of the 1:2 adduct (one

pyridine per each iodine center) may affect the accuracy of these preliminary binding constants. Next, the NMR titration of the model dications 1^{2+} and 9^{2+} with this ligand set revealed good levels of binding, achieving binding constants as high as $K \sim 10^4 M^{-1}$ (see SI). We note, however, that in this preliminary module the exact binding modes could not be established unequivocally. Nevertheless, a combination of $1 \cdot (OTf)_2$ with ligand L3 did produce X-ray-quality single crystals with a one-to-one $[1 \cdot L3] \cdot (OTf)_2$ stoichiometry and the bis-pyridine chelating one of the two iodine atoms (Scheme 5). The adduct composition was further confirmed through elemental analysis of CHN, S, and I. Interestingly, the pyridine rings of the ligand appear to “push down” upon the phenylene groups, leading to an interplane angle of 108°, down from the 120° angle observed in the original $1 \cdot (OTf)_2$.

CONCLUSIONS AND OUTLOOK

In conclusion, this work amplifies the structure space of diaryliodonium salts to a new family of cyclic diaryliodonium structures containing two halogens in a ring. Noteworthy, despite over half a century of the history of six-membered cyclic iodonium salts, this is the first report describing the synthesis and X-ray structure of even the simplest ring structure 1^{2+} having two iodine atoms bridging between two phenylene rings. This delay reflects the need to solve a synthetically difficult ring-closing step, now possible through a formal head-to-tail dimerization approach. Thanks to this methodology, cyclic bis-iodonium salts based on wider-spaced naphthalene and xanthene scaffolds were also synthesized, showing geometric features resembling a right-angle “angle bar” structure. Using a complementary stepwise approach, the structure class was further expanded to heterohalogen iodine(III)–bromine(III) and iodine(III)–chlorine(III) analogues 8^{2+} , which showed remarkable stability in water. The new bis-iodonium structures allow for the study of new types of interplay between chelating ligands and pairs of iodine(III) Lewis acid vectors, which includes both chelating and bridging binding modes. We envisage that this chemistry and the structure archetypes presented herein will serve as a blueprint for the development of a wider range of cyclic multihalogen structures that would be of interest in the realms such as synthetic methodology, molecular recognition, materials, organocatalysis, and self-assembly, to name a few.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jacs.3c02406>.

Details on the synthetic procedures and product characterization, including NMR and MS data, and details on single-crystal X-ray structural characterization (PDF)

Accession Codes

CCDC 2247127–2247132 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

AUTHOR INFORMATION

Corresponding Authors

Alexandr Shafir – BISI-Bonds Group, Institut de Química Avançada de Catalunya, IQAC-CSIC, and Centro de Innovación en Química Avanzada (ORFEO-CINQA), 08034 Barcelona, Spain; orcid.org/0000-0002-8127-2299; Email: alexandr.shafir@iqac.csic.es

Ana B. Cuenca – BISI-Bonds/CRISOL Group, Department of Organic and Pharmaceutical Chemistry, Universitat Ramon Llull and Centro de Innovación en Química Avanzada (ORFEO-CINQA), 08017 Barcelona, Spain; orcid.org/0000-0002-6842-1261; Email: anabelen.cuenca@iqs.url.edu

Authors

Wei W. Chen – BISI-Bonds Group, Institut de Química Avançada de Catalunya, IQAC-CSIC, 08034 Barcelona, Spain; orcid.org/0000-0003-1815-035X

Margalida Artigues – Department of Analytical and Applied Chemistry, Institut Químic de Sarrià, Universitat Ramon Llull, 08017 Barcelona, Spain; orcid.org/0000-0001-8599-980X

Mercè Font-Bardia – Unitat de Difracció de RX. Centres Científics i Tecnològics de la Universitat de Barcelona (CCiTUB), Universitat de Barcelona, 08028 Barcelona, Spain

Complete contact information is available at:
<https://pubs.acs.org/10.1021/jacs.3c02406>

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported through an MICINN grant (PID2020-113661GB-I00) and AGAUR (2021 SGR 00520, 2017 SGR 01051). IQS-URL is also acknowledged for the doctoral scholarship to W.W.C.

REFERENCES

- (1) (a) Yoshimura, A.; Zhdankin, V. V. Advances in Synthetic Applications of Hypervalent Iodine Compounds. *Chem. Rev.* **2016**, *116*, 3328–3435. (b) Villo, P.; Olofsson, B., Arylations promoted by hypervalent iodine reagents. In *PATAI'S Chemistry of Functional Groups*; Olofsson, B.; Marek, I.; Rappoport, Z., Eds.; Wiley, 2018; pp 1–42.
- (2) (a) Hartmann, C.; Meyer, V. Ueber eine neue Klasse jodhaltiger, stickstoffreicher organischer Basen. *Ber. Dtsch. Chem. Ges.* **1894**, *27*, 426. (b) Merritt, E. A.; Olofsson, B. Diaryliodonium Salts: A Journey from Obscurity to Fame. *Angew. Chem., Int. Ed.* **2009**, *48*, 9052–9070. (c) Olofsson, B. Arylation with Diaryliodonium Salts. In *Hypervalent Iodine Chemistry, Topics in Current Chemistry*; Wirth, T., Ed.; Springer International Publishing, 2016; Vol. 373, pp 135–166.
- (3) Grushin, V. V. Cyclic diaryliodonium ions: old mysteries solved and new applications envisaged. *Chem. Soc. Rev.* **2000**, *29*, 315–324.
- (4) For a recent review, see: Chatterjee, N.; Goswami, A. Synthesis and Application of Cyclic Diaryliodonium Salts: A Platform for

Bifunctionalization in a Single Step. *Eur. J. Org. Chem.* **2017**, *2017*, 3023–3032.

(7) For selected examples on metal-promoted ring opening, see (with Cu, atroposelective): (a) Zhao, K.; Duan, L.; Xu, S.; Jiang, J.; Fu, Y.; Gu, Z. Enhanced Reactivity by Torsional Strain of Cyclic Diaryliodonium in Cu-Catalyzed Enantioselective Ring-Opening Reaction. *Chem.* **2018**, *4*, 599–612. With Pd, enantioselective: (b) Han, J.; Xiao, B.; Sun, T.-Y.; Wang, M.; Jin, L.; Yu, W.; Wang, Y.; Fang, D.-M.; Zhou, Y.; Wu, X.-F.; Wu, Y.-D.; Liao, J. Enantioselective Double Carbonylation Enabled by High-Valent Palladium Catalysis. *J. Am. Chem. Soc.* **2022**, *144*, 21800–21807. With Pd, ring expansion: (c) Mathew, B. P.; Yang, H. J.; Kim, J.; Lee, J. B.; Kim, Y.-T.; Lee, S.; Lee, C. Y.; Choe, W.; Myung, K.; Park, J.-U.; Hong, S. Y. An Annulative Synthetic Strategy for Building Triphenylene Frameworks by Multiple C–H Bond Activations. *Angew. Chem., Int. Ed.* **2017**, *56*, S007–S011.

(8) For an interesting recent example on TM-free radical-based ring expansions, see: Lee, J. B.; Kim, G. H.; Jeon, J. H.; Jeong, S. Y.; Lee, S.; Park, J.; Lee, D.; Kwon, Y.; Seo, J. K.; Chun, J.-H.; Kang, S. J.; Choe, W.; Rohde, J.-U.; Hong, S. Y. Rapid access to polycyclic N-heteroarenes from unactivated, simple azines via a base-promoted Minisci-type annulation. *Nat. Commun.* **2022**, *13*, 2421–2429.

(9) (a) O'Donnell, V. B.; Tew, D. G.; Jones, O. T. G.; England, P. J. Studies on the inhibitory mechanism of iodonium compounds with special reference to neutrophil NADPH oxidase. *Biochem. J.* **1993**, *290*, 41–49. (b) Diaza, J. M.; Plummer, S.; Hansel, C. M.; Andeer, P. F.; Saito, M. A.; McIlvin, M. R. NADPH-dependent extracellular superoxide production is vital to photophysiology in the marine diatom *Thalassiosira oceanica*. *Proc. Natl. Acad. Sci. U.S.A.* **2019**, *116*, 16448–16453. For cyclic iodonium agents with low nanomolar activity against “problematic” bacteria, see: (c) Nguyen, N.; Wilson, D. W.; Nagalingam, G.; Triccas, J. A.; Schneider, E. K.; Li, J.; Velkov, T.; Baell, J. Broad activity of diphenyleneiodonium analogues against *Mycobacterium tuberculosis*, malaria parasites and bacterial pathogens. *Eur. J. Med. Chem.* **2018**, *148*, 507–518.

(10) Mayer, R. J.; Ofial, A. R.; Mayr, H.; Legault, C. Y. Lewis Acidity Scale of Diaryliodonium Ions toward Oxygen, Nitrogen, and Halogen Lewis Bases. *J. Am. Chem. Soc.* **2020**, *142*, 5221–5233.

(11) For selected recent examples, see: (a) Aliyarova, I. S.; Ivanov, D. M.; Soldatova, N. S.; Novikov, A. S.; Postnikov, P. S.; Yusubov, M. S.; Kukushkin, V. Y. Bifurcated Halogen Bonding Involving Diaryliodonium Cations as Iodine(III)-Based Double- σ -Hole Donors. *Cryst. Growth Des.* **2021**, *21*, 1136–1147. Wolf, J.; Huber, F.; Erochok, N.; Heinen, F.; Guérin, V.; Legault, C. Y.; Kirsch, S. F.; Huber, S. M. Activation of a Metal-Halogen Bond by Halogen Bonding. *Angew. Chem., Int. Ed.* **2020**, *59*, 16496–16500.

(12) Peng, X.; Rahim, A.; Peng, W.; Jiang, F.; Gu, Z.; Wen, S. Recent Progress in Cyclic Aryliodonium Chemistry: Syntheses and Applications. *Chem. Rev.* **2023**, DOI: [10.1021/acs.chemrev.2c00591](https://doi.org/10.1021/acs.chemrev.2c00591).

(13) (a) For the earliest report on cyclic bromonium and chloronium salts, see: Sandin, R. B.; Hay, A. S. Stable Bromonium and Chloronium Salts. *J. Am. Chem. Soc.* **1952**, *74*, 274–275. (b) Also, see: Egorova, L. D.; Lisichkina, I. N.; Tolstaya, T. P.; Kostitsyna, N. N. Synthesis of 10H-dibenzo[b,e]chlorinium tetrafluoroborate and deuterium exchange reaction in the methylene group of 10H-dibenzo[b,e]halogeninium cations. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1985**, 1347.

(14) (a) Lanzi, M.; Dherbassy, Q.; Wencel-Delord, J. Cyclic Diaryl λ^3 -Bromanes as Original Aryne Precursors. *Angew. Chem., Int. Ed.* **2021**, *60*, 14852–14857. (b) Lanzi, M.; Ali Abdine, R. A.; De Abreu, M.; Wencel-Delord, J. Cyclic Diaryl λ^3 -Bromanes: A Rapid Access to Molecular Complexity via Cycloaddition Reactions. *Org. Lett.* **2021**, *23*, 9047–9052. (c) Lanzi, M.; Rogge, T.; Truong, T. S.; Houk, K. N.; Wencel-Delord, J. Cyclic Diaryl λ^3 -Chloranes: Reagents and Their C–C and C–O Couplings with Phenols via Aryne Intermediates. *J. Am. Chem. Soc.* **2023**, *145*, 345–358. (d) Yoshida, Y.; Mino, T.; Sakamoto, M. Chiral Hypervalent Bromine(III) (Bromonium Salt): Hydrogen- and Halogen-Bonding Bifunctional Asymmetric Catalysis by Diaryl- λ^3 -bromanes. *ACS Catal.* **2021**, *11*, 13028–13033.

- (15) (a) Stang, P. J.; Zhdankin, V. V. Preparation and Characterization of a Macrocyclic Tetraaryltetraiodonium Compound, cyclo-(Ar₄I₄)⁴⁺·4X⁻. A Unique, Charged, Cationic Molecular Box. *J. Am. Chem. Soc.* **1993**, *115*, 9808–9809. (b) Radhakrishnan, U.; Stang, P. J. Synthesis and Characterization of Cationic Iodonium Macrocycles. *J. Org. Chem.* **2003**, *68*, 9209–9213.
- (16) Tan, Q.; Zhou, D.; Zhang, T.; Liu, B.; Xu, B. Iodine-doped sumanene and its application for the synthesis of chalcogenasumanenes and silasumanenes. *Chem. Commun.* **2017**, *53*, 10279–10282.
- (17) (a) Collette, J.; McGreer, D.; Crawford, R.; Chubb, F.; Sandin, R. B. *J. Am. Chem. Soc.* **1956**, *78*, 3819–3820. (b) Bielawski, M.; Olofsson, B. High-yielding one-pot synthesis of diaryliodonium triflates from arenes and iodine or aryl iodides. *Chem. Commun.* **2007**, 2521–2523. (c) Riedmüller, S.; Nachtsheim, B. J. Palladium-catalyzed synthesis of N-arylated carbazoles using anilines and cyclic diaryliodonium salts. *Beilstein J. Org. Chem.* **2013**, *9*, 1202–1209.
- (18) (a) For a systematic study, see: Postnikov, P. S.; Guselnikova, O. A.; Yusubov, M. S.; Yoshimura, A.; Nemykin, V. N.; Zhdankin, V. V. Preparation and X-ray Structural Study of Dibenziodolium Derivatives. *J. Org. Chem.* **2015**, *80*, 5783–5788. (b) For synthesis and conformational analysis of six-membered iodonium salts, see: Caspers, L. D.; Spils, J.; Damrath, M.; Lork, E.; Nachtsheim, B. J. One-Pot Synthesis and Conformational Analysis of Six-Membered Cyclic Iodonium Salts. *J. Org. Chem.* **2020**, *85*, 9161–9178.
- (19) (a) Wu, B.; Yoshikai, N. Conversion of 2-Iodobiarlys into 2,2'-Diodobiarlys via Oxidation-Iodination Sequences: A Versatile Route to Ladder-Type Heterofluorenes. *Angew. Chem., Int. Ed.* **2015**, *54*, 8736–8739. (b) Heinen, F.; Reinhard, D. L.; Engelage, E.; Huber, S. M. A Bidentate Iodine(III)-Based Halogen-Bond Donor as a Powerful Organocatalyst. *Angew. Chem., Int. Ed.* **2021**, *60*, 5069–5073. (c) Portela, S.; Cabrera-Trujillo, J. J.; Fernández, I. Catalysis by Bidentate Iodine(III)-Based Halogen Donors: Surpassing the Activity of Strong Lewis Acids. *J. Org. Chem.* **2021**, *86*, 5317–5326.
- (20) (a) Wu, Y.; Izquierdo, S.; Vidossich, P.; Lledós, A.; Shafir, A. NH-Heterocyclic Aryliodonium Salts and their Selective Conversion into N1-Aryl-5-iodoimidazoles. *Angew. Chem., Int. Ed.* **2016**, *55*, 7152–7156. (b) Antonkin, N. S.; Vlasenko, Y. A.; Yoshimura, A.; Smirnov, V. I.; Borodina, T. N.; Zhdankin, V. V.; Yusubov, M. S.; Shafir, A.; Postnikov, P. S. Preparation and Synthetic Applicability of Imidazole-Containing Cyclic Iodonium Salts. *J. Org. Chem.* **2021**, *86*, 7163–7178.
- (21) Kervefors, G.; Becker, A.; Dey, C.; Olofsson, B. Metal-free formal synthesis of phenoxazine. *Beilstein J. Org. Chem.* **2018**, *14*, 1491–1497.
- (22) NMR analysis seems to indicate the formation of I-oxidized noncyclized intermediates; see Figure S1 (SI). Similar reluctance to cyclize was recently documented during an attempted synthesis of an *ortho*-sulfone-bridged cyclic diaryliodonium salt: Reinhard, D. L.; Heinen, F.; Stoesser, J.; Engelage, E.; Huber, S. M. Tuning the Halogen Bonding Strength of Cyclic Diaryliodonium Salts. *Helv. Chim. Acta* **2021**, *104*, No. e2000221. We don't discard, however, that the cyclization of **2** to **1** may be possible under yet-to-be developed oxidative conditions.
- (23) (a) Robidas, R.; Guérin, V.; Provençal, L.; Echeverría, M.; Legault, C. L. Investigation of iodonium trifluoroborate zwitterions as bifunctional arene reagents. *Org. Lett.* **2017**, *19*, 6420–6423. (b) For a related report on the *ortho*-borylated diaryliodonium salts, see: Yoshimura, A.; Fuchs, J. M.; Middleton, K. R.; Maskavev, A. V.; Rohde, G. T.; Saito, A.; Postnikov, P. S.; Yusubov, M. S.; Nemykin, V. N.; Zhdankin, V. V. Pseudocyclic Arylbenziodoxaboroles: Efficient Benzene Precursors Triggered by Water at Room Temperature. *Chem.—Eur. J.* **2017**, *23*, 16738–16742.
- (24) (a) Nakajima, M.; Miyamoto, K.; Hirano, K.; Uchiyama, M. Diaryl-λ³-chloranes: versatile synthesis and unique reactivity as aryl cation equivalent. *J. Am. Chem. Soc.* **2019**, *141*, 6499–6503. (b) For a recent perspective on hypervalent bromine reagents, see: Winterson, B.; Patra, T.; Wirth, T. Hypervalent Bromine(III) Compounds: Synthesis, Applications, Prospects. *Synthesis* **2022**, *54*, 1261–1271.
- (25) We note, however, a mention by Olah and co-workers of in situ NMR observation of a species arising from 1-bromo-4-iodo-benzene upon accepting two Me⁺ cations: Olah, G. A.; Mo, Y. K.; Melby, E. G.; Lin, H. C. Onium ions. V. Di- and trihalonium ions. *J. Org. Chem.* **1973**, *38*, 367–372.
- (26) (a) Beringer, F. M.; Lillien, I. Diaryliodonium Salts. XIII. Salts in which the Cations Bear Carboxyl, Hydroxyl, Alkoxy or Amino Groups. *J. Am. Chem. Soc.* **1960**, *82*, 725–731. (b) Linstad, E. J.; Våvere, A. L.; Hu, B.; Kempinger, J. J.; Snyder, S. E.; DiMagno, S. G. Thermolysis and radiofluorination of diaryliodonium salts derived from anilines. *Org. Biomol. Chem.* **2017**, *15*, 2246–2252.
- (27) The modest yields obtained for **8a**²⁺ and **8b**²⁺ reflect the challenge of the diazotative cyclization in this case. Reaction byproducts (as per HPLC-MS) are mainly noncyclic iodonium species consistent with the entry of nucleophiles, e.g., OTs and CH₃CN (Ritter-type), either to the diazonium intermediate or (via ring-opening) to the final cycle.
- (28) Karandikar, S. S.; Bhattacharjee, A.; Metzke, B. E.; Javaly, N.; Valente, E. J.; McCormick, T. M.; Stuart, D. R. Orbital analysis of bonding in diarylhalonium salts and relevance to periodic trends in structure and reactivity. *Chem. Sci.* **2022**, *13*, 6532–6540.
- (29) At shorter reactions times (~1 h), or with less Selectfluor, we do observe a certain amount of the noncyclized species consistent with the zwitterionic intermediate (see Figure S7 in SI), i.e., an analogue of **3**.
- (30) Ye, C.; Twamley, B.; Shreeve, J. M. Straightforward Syntheses of Hypervalent Iodine(III) Reagents Mediated by Selectfluor. *Org. Lett.* **2005**, *18*, 3961–3964.
- (31) In fact, the asymmetric unit contained two crystallographically independent 14²⁺ structures differing somewhat in their degree and sense of puckering around the central pyran ring.
- (32) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 5th ed.; Wiley: New York, 1988.
- (33) Of course, a third possibility is that of a bidentate ligand bridging between two discreet iodonium species, which is what we see for most X-ray structures measured in this work.
- (34) (a) Heinen, F.; Engelage, E.; Cramer, C. J.; Huber, S. M. Hypervalent Iodine(III) Compounds as Biaxial Halogen Bond Donors. *J. Am. Chem. Soc.* **2020**, *142*, 8633–8640. (b) For an interesting recent approach to iodine(III) “noncovalent” chelation with metal-centered species acting as bis-O bidentate ligands, also see: Semenov, A. V.; Baykov, S. V.; Soldatova, N. S.; Geyl, K. K.; Ivanov, D. M.; Frontera, A.; Boyarskiy, V. P.; Postnikov, P. S.; Kukushkin, V. Yu. Noncovalent Chelation by Halogen Bonding in the Design of Metal-Containing Arrays: Assembly of Double σ-Hole Donating Halolium with CuI-Containing O,O-Donors. *Inorg. Chem.* **2023**, *62*, 6128–6137.
- (35) (a) For selected examples of iodine(III) and (V) chemistry with pyridine donors, see: Zhdankin, V. V.; Kuposov, A. Y.; Yashin, N. V. Complexes of hypervalent iodine compounds with nitrogen ligands. *Tetrahedron Lett.* **2002**, *43*, 5735–5737. (b) Tierno, A. F.; Walters, J. C.; Vazquez-Lopez, A.; Xiao, X.; Wengryniuk, S. E. Heterocyclic group transfer reactions with I(III) N-HVI reagents: access to N-alkyl(heteroaryl)onium salts via olefin aminolactonization. *Chem. Sci.* **2021**, *12*, 6385–6392. (c) Xiao, X.; Roth, J. M.; Greenwood, N. S.; Velopolcek, M. K.; Aguirre, J.; Jalali, M.; Ariafard, A.; Wengryniuk, S. E. Bidentate Nitrogen-Ligated I(V) Reagents, Bi(N)-HVIs: Preparation, Stability, Structure, and Reactivity. *J. Org. Chem.* **2021**, *86*, 6566–6576.
- (36) (a) For a wide-angle bis-pyridine donor adduct of monovalent iodine, see: Carlsson, A.-C. C.; Gräfenstein, J.; Budnjo, A.; Laurila, J. L.; Bergquist, J.; Karim, A.; Kleinmaier, R.; Brath, U.; Erdélyi, M. Symmetric Halogen Bonding Is Preferred in Solution. *J. Am. Chem. Soc.* **2012**, *134*, 5706–5715. (b) Vanderkooy, A.; Gupta, A. K.; Földes, T.; Lindblad, S.; Orthaber, A.; Pápai, I.; Erdélyi, M. Halogen Bonding Helicates Encompassing Iodonium Cations. *Angew. Chem. Int. Ed.* **2019**, *58*, 9012–9016. (c) Yu, S.; Kalenius, E.; Frontera, A.; Rissanen, K. Macrocyclic complexes based on [N···I···N]⁺ halogen bonds. *Chem. Commun.* **2021**, *57*, 12464–12467.

(37) (a) Ochiai, M.; Suefuji, T.; Shiro, M.; Yamaguchi, K. Complexation of Diphenyl(Tetrafluoroborato)- λ 3-Iodane with Pyridines. *Heterocycles* **2006**, *67*, 391. (b) Mayer, R. J.; Ofial, A. R.; Mayr, H.; Legault, C. Y. Lewis Acidity Scale of Diaryliodonium Ions toward Oxygen, Nitrogen, and Halogen Lewis Bases. *J. Am. Chem. Soc.* **2020**, *142*, 5221–5233.