JOC The Journal of Organic Chemistry

Article

Cite This: J. Org. Chem. 2018, 83, 12056−12070

pubs.acs.org/joc

Synthesis of Five-Membered Iodine−Nitrogen Heterocycles from Benzimidazole-Based Iodonium Salts

Yulia A. Vlasenko,[†] Pavel S. Postnikov,[#,†] Marina E. Trusova,[†] Alexandr Shafir,[‡,$] Viktor V. Zhdankin,[*,§] Akira Yoshimura,[†,§] and Mekhman S. Yusubov[*,†]

[†]The Tomsk Polytechnic University, 634050 Tomsk, Russia

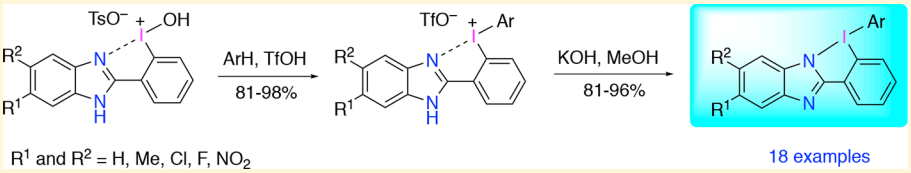
[#]University of Chemistry and Technology, 16628 Prague, Czech Republic

[‡]Institute of Chemical Research of Catalonia (ICIQ), Barcelona Institute of Science and Technology, Tarragona, Spain

[$]Institute of Advanced Chemistry of Catalonia (IQAC−CSIC), Jordi Girona 18-26, 08034 Barcelona, Spain

[§]Department of Chemistry and Biochemistry, University of Minnesota Duluth, Duluth, Minnesota 55812, United States

Supporting Information



ABSTRACT: Pseudocyclic 2-benzimidazolyl-substituted diaryliodonium salts were obtained by the reaction of the corresponding [hydroxy(tosyloxy)iodo]arenes with arenes in the presence of trifluoromethanesulfonic acid. X-ray structural analysis of these iodonium salts confirmed their pseudocyclic structure with a short (2.57−2.58 Å) noncovalent I···N interaction. Treatment of 2-benzimidazolyl-substituted diaryliodonium triflates with a base afforded novel five-membered iodine−nitrogen heterocycles.

INTRODUCTION

Since the beginning of the 21st century, the interest in hypervalent iodine heterocycles has experienced an unprecedented growth.[1] The five-membered iodine−oxygen heterocycles (benziodoxoles) represent one of the most important classes of hypervalent iodine(III) reagents.[1−6] Substituted benziodoxolones **1** (Scheme 1) are widely used as electrophilic or radical atom-transfer reagents for azidation,[2] amination,[3] cyanation,[4] alkynylation,[5] or chlorination.[6] Other important classes of five-membered hypervalent iodine(III) heterocycles include dibenziodolium derivatives **2** and **3** and benziodazolones **4**. Five-membered cyclic iodonium salts **2**, derivatives of the iodolium heterocyclic system, are particularly interesting because of the high thermal stability and applications in biological studies.[7−9] For example, dibenziodolium chloride (also known as diphenyleneiodonium chloride or DPI) has found numerous applications in biological studies.[8,9] In biochemical and pharmacological research, DPI is commonly used as an NADPH oxidase inhibitor.[9] The neutral dibenziodolium derivatives, 5-aryl-5*H*-5λ^3-dibenzo[*b*,*d*]iodoles **3**, have also been prepared as thermally unstable and air-sensitive compounds.[10]

The preparation of several five-membered iodine−nitrogen heterocycles, benziodazolones **4**, has been reported by Wolf and Steinberg,[11] Gougoutas,[12] Balthazor,[13] and our group.[14] Benziodazolone derivatives can be used as reagents for oxidative functionalization of organic substrates.[14a,15,16] For example, azidobenziodazolone was used as an azidation reagent with reactivity similar to that of azidobenziodoxoles.[14a] Very recently, we reported the preparation of a novel bicyclic benziodazolone, which is an efficient reagent for oxidatively assisted coupling of carboxylic acids with alcohols or amines.[16] To the best of our knowledge, all known five-membered iodine−nitrogen heterocycles have the benziodazolone structure **4**, which is characterized by the presence of the amido nitrogen in the ring. In this paper, we report the first synthesis of a stable polycyclic benziodazole system **5**, which represents a nitrogen analogue of the neutral diphenyleneiodonium system **4** (Scheme 1).

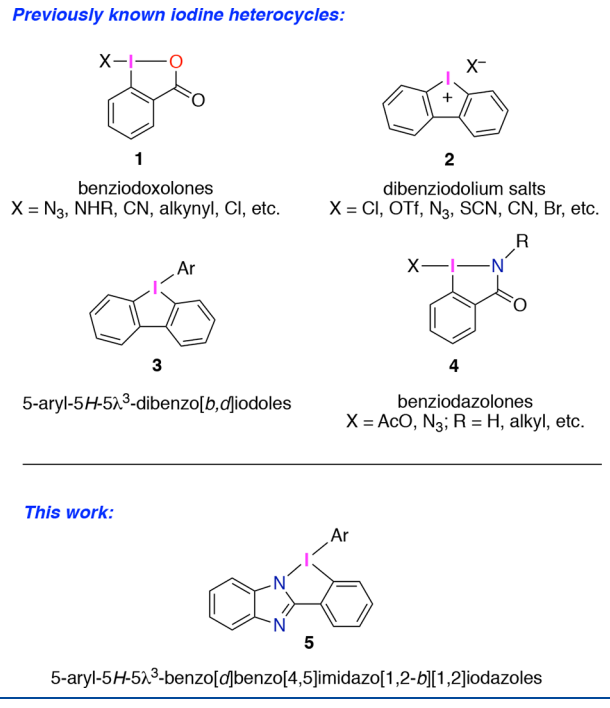
RESULTS AND DISCUSSION

We have developed an efficient three-step approach to the synthesis of benziodazole system **5** starting from readily available 2-(2-iodophenyl)-1*H*-benzo[*d*]imidazoles **6**. Iodides **6** were initially oxidized to [hydroxy(tosyloxy)iodo]arenes **7** by treatment with *m*-chloroperoxybenzoic acid in the presence of *p*-toluenesulfonic acid (Scheme 2) according to the modified procedure of Yamamoto and Togo.[17] Products with the general structure type **7** were isolated in high yields in the form of stable microcrystalline solids and were characterized by NMR and mass spectrometry. According to NMR, the nonsymmetrically substituted derivatives of **7** ($R^1 \neq R^2$) in solution exist in the form of two tautomers differing in the position of the protonated N-site in the benziodazole fragment.

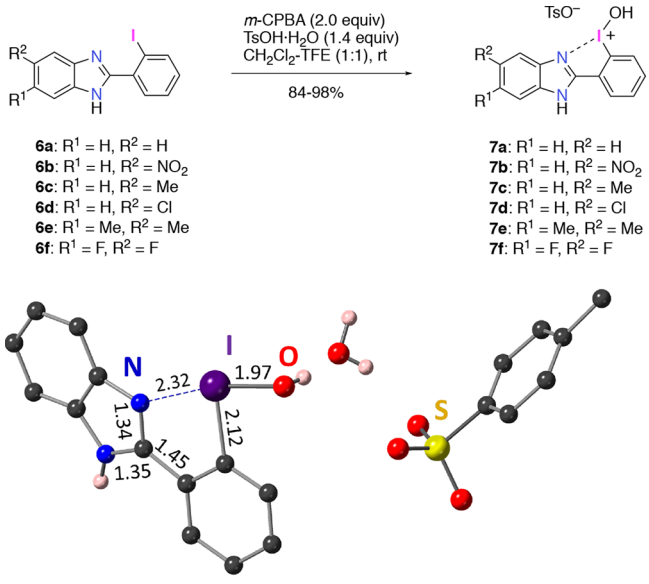
Received: August 2, 2018
Published: September 11, 2018

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

Scheme 1. Hypervalent Iodine Heterocycles: Benziodoxoles, Dibenziodolium Derivatives, and Benziodazoles



Scheme 2. Oxidation of 2-(2-Iodophenyl)-1*H*-benzo[*d*]imidazoles 6 to [Hydroxy(tosyloxy)iodo]arenes 7. X-ray Structure Diagram of 7a



Next we sought to convert the newly prepared [hydroxy(tosyloxy)iodo]arenes **7** into diaryliodonium species by a direct reaction with arenes. Initially, the model tosylate **7a** demonstrated extremely low reactivity toward arenes, and even the treatment with the electron-rich mesitylene did not lead to the formation of desired iodonium salt **8a** after 32 h of stirring in trifluoroethanol according to Kita's procedure.[18] Nevertheless, the addition of 1.5 equiv of TfOH led to a dramatic change in reactivity and allowed for the isolation of the iodonium salt **8a** in quantitative yield. Using this protocol, a series of N-coordinated diaryliodonium salts **8a–r** could be prepared in the presence of triflic acid, as shown in Scheme 3. These salts were isolated in excellent yields in their N–H triflate forms and were characterized by NMR and mass spectrometry. The presence of a proton on one of the benzimidazole nitrogens should in principle lead to all four benzimidazole C–H sites in **8a** to be chemically distinct. Experimentally, the ^{1}H NMR spectrum of **8a** showed a fluxional behavior for the benzimidazole moiety, evidenced by two broad resonances each integrating for 2H, suggesting a rather rapid equilibration of the two sides of the molecule. Similar behavior was observed for the rest for the derivatives within this family. The solid-state structures of two such salts, the nitro derivative **8e** and the chloro derivative **8m**, were subsequently determined to be borderline pseudocyclic on the basis of the presence of a long nitrogen-to-iodine donor bond (Figure 1). It should be noted that the presence of a substituent on the benzimidazole fragment leads to the possibility of two tautomeric structures, both of which were found to coexist in the solid state (via disorder) and in solution.

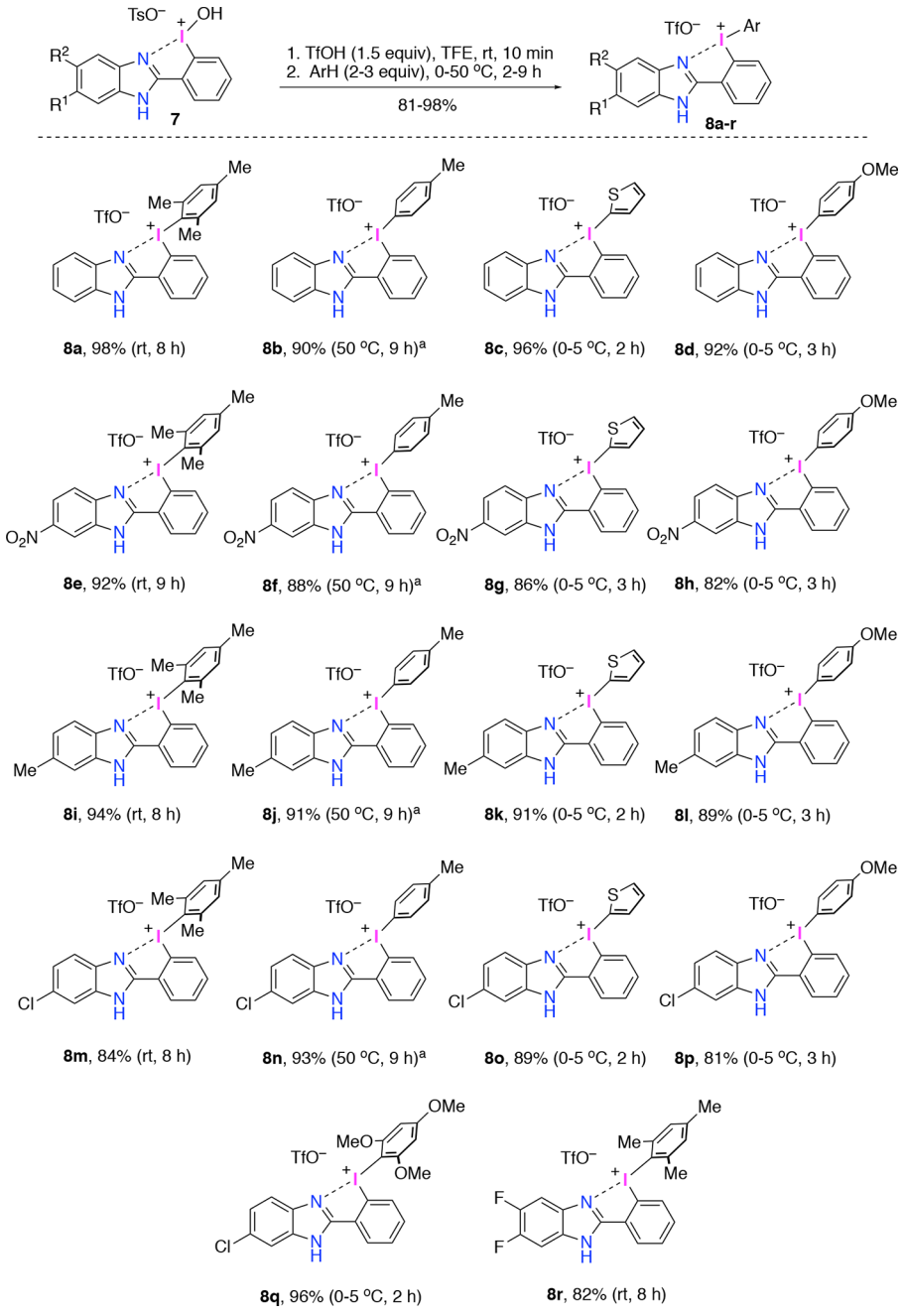
At this point, we wondered whether the pseudocyclic species **8** could readily form the corresponding cyclic derivative upon deprotonation. This possibility was tested by examining the ^{1}H NMR spectrum of the thienyl pseudocycle **8c** in DMSO-d_6 before and after the addition of 1.0 equiv of KOH (Figure 2a,b). Consistent with our hypothesis, the addition of the base led to a significant change in the spectrum, with benzimidazole resonances shifted upfield by up to 0.2 ppm (Figure 2b). The original chemical shifts of **8c** could be largely restored by treating the resulting solution of **9c** with 1.0 equiv of TfOH (Figure 2c), attesting to the reversibility of the cyclic-pseudocyclic interconversion. As a synthetic procedure, treating the methanolic solution of **8c** with potassium hydroxide led to the precipitation of the cyclic **9c** in nearly quantitative yield. Similarly, a series of cyclic hypervalent iodine heterocycles **9** (Scheme 4) were isolated as thermally stable solids in excellent yields and were characterized by NMR and mass spectrometry. Unfortunately, we were not able to grow single crystals of **9** suitable for X-ray analysis.

Interestingly, unlike the pseudocyclic triflates, the NMR spectra of **9** were at odds with what was expected for a stronger N–I bond. Hence, while the ^{19}F NMR spectrum of the pseudocyclic difluoro derivative **8r** showed two aromatic fluorine resonances (doublets in the proton-decoupled mode), the corresponding cyclic derivative **9r** showed a unique well-defined ^{19}F singlet, indicating either a low rotation barrier around the C–C bond (Figure 3) or a preference for a C_s-symmetric noncyclic conformation with the ArI ring perpendicular to the benzimidazole plane.

Due to the same phenomenon, the asymmetrically substituted derivatives, such as **9o**, displayed an NMR spectrum consistent with a relatively facile rotamer interconversion. To shed light on this phenomenon, the conformational analysis of the chloro-substituted **9o** was carried out using DFT calculations. It was found that the two cyclic forms do indeed represent the energetic minima, and the noncyclic perpendicular form a transition state in rotamer interconversion (Figure 4). The "proximal" isomer proved to be somewhat more stable (about ~2 kcal/mol) than the "remote" one, with an interconversion barrier of ~16 kcal/mol consistent with a medium velocity rotamer interconversion on the NMR time scale. For comparison, the barrier for a degenerate exchange (via C–N) bond rotation in *N*,*N*-dimethylformamide is close to $\Delta G^{\ddagger} \sim 19$ kcal/mol.[19] Interestingly, in the case of the pseudocyclic derivatives such as **8o**, the apparently higher barrier for tautomerization may seem contrary to what would

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056–12070

Scheme 3. Formation and Examples of the Pseudocyclic Diaryliodonium Species 8



[a]Hexafluoro-2-propanol (HFIP) was used as a solvent instead of trifluoroethanol (TFE).

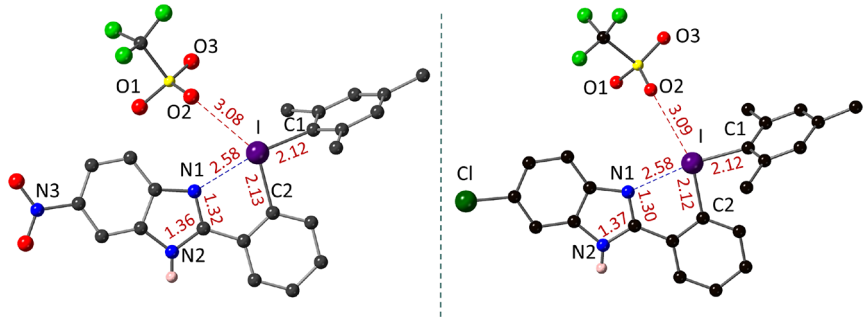


Figure 1. X-ray crystal structure diagrams for **8e** (left) and **8m** (right). All except N-bound protons have been omitted for clarity.

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

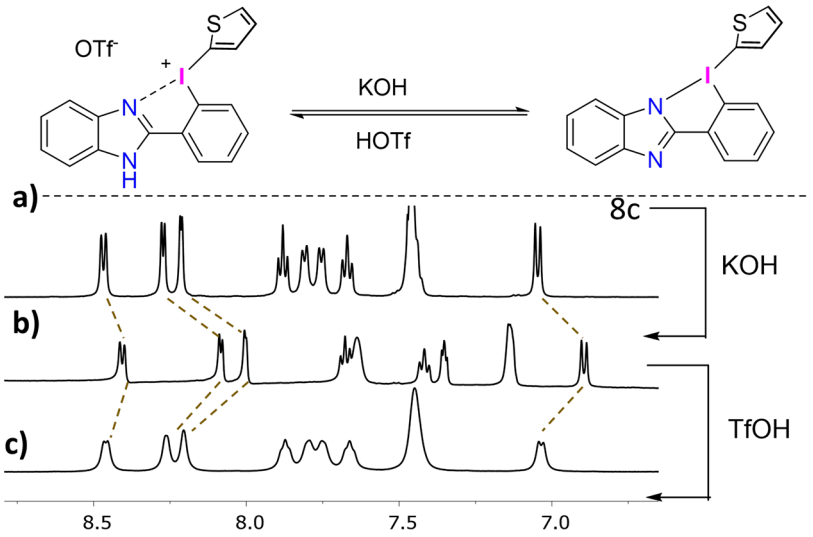


Figure 2. Changes observed in the ^{1}H NMR spectrum of **8c** upon addition of KOH (a and b). Bottom spectrum (c) was recorded upon addition of TfOH (1.0 equiv) to the sample b.

be expected for a weaker I−N bond. It should be noted, however, that while the tautomerization in **9o** may be achieved by a simple rotation (as shown in Figure 4), such a process in **8o** is precluded due to the protonation at the "remote" nitrogen atom. Hence, tautomerization in this case likely proceeds in a multistep sequence involving both a proton transfer and a rotation. In consequence, such a process would be more difficult to model and may show a strong medium dependence.

CONCLUSIONS

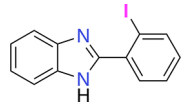
In summary, we have reported the synthesis of a novel, stable hypervalent iodine polyheterocyclic system derived from benziodazole. The hypervalent iodine heterocycles **9** were prepared starting from readily available 2-(2-iodophenyl)-1*H*-benzo[*d*]imidazoles **6** via benzimidazole-based diaryliodonium salts **8**. The prepared iodazoles exhibit a fast interconversion between tautomers according to NMR experiment and theoretical calculations.

EXPERIMENTAL SECTION

General Comments. All reagents and solvents were from commercial sources and used without further purification from freshly opened containers. ^{1}H NMR spectra were recorded at 300, 400 and 500 MHz, ^{13}C NMR spectra were recorded at 75, 100 and 125 MHz, and ^{19}F NMR spectra were recorded at 376 MHz. Chemical shifts are reported in parts per million (ppm). ^{1}H and ^{13}C chemical shifts are referenced relative to tetramethylsilane. High resolution mass spectra were recorded on Thermo Fisher Scientific LC-MS LTQ-Orbitrap Velos and MicroTof-Q from Bruker Daltronics Instruments with electrospray ionization (EI) in positive ionization mode.

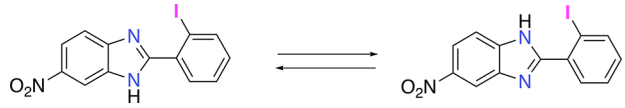
Synthesis of Benzimidazoles 6: General Procedure. Benzimidazoles **6a**−**f** were prepared according to a slightly modified published procedure.[20] The mixture of appropriate *o*-phenylenediamine (20 mmol) and 2-iodobenzoic acids (20 mmol, 5.6 g) in polyphosphoric acid (200 mmol, 30.2 g) was heated to 100 °C. $POCl_3$ (65 mmol, 9.87 g, 6 mL) was added portionwise (1 mL every 15 min) to a stirred reaction mixture at 100 °C. The heating was continued until full conversion of starting material (monitored by TLC, eluent hexane:EtOAc = 2:7). The reaction mixture was cooled to room temperature with the formation of solid material. The solid was suspended in water (70 mL) and was basified by the addition of solid $NaHCO_3$ until pH = 7−8. The precipitate was filtered off and washed on the filter with water 30 mL and recrystallized from a water−ethanol mixture. In the case of 5,6-difluoro-2-(2-iodophenyl)-1*H*-benzimidazole, the precipitate was filtered off, resuspended in 600 mL of EtOAc, and filtered through a short pad of Celite. The solvent was removed under reduced pressure at room temperature.

*2-(2-Iodophenyl)-1H-benzo[d]imidazole (**6a**).* Reaction of *o*-phenylenediamine (2.16 g, 20 mmol) according to the general



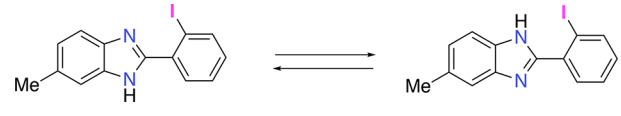
procedure afforded 5.12 g (80%) of product **6a**, isolated as a beige solid: mp 246−247 °C (lit.,[21] mp 230−232 °C); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 12.70 (s, 1H), 8.06 (dd, J = 8.0, 1,0 Hz, 1H), 7.62 (d, J = 7.5 Hz, 1H), 7.62 (dd, J = 7.5, 1.5 Hz, 1H), 7.57−7.53 (m, 2H), 7.29−7.20 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 152.6, 143.2, 139.6, 136.6, 134.3, 131.3, 131.1, 128.1, 122.5, 121.4, 119.1, 111.5, 97.3.

*2-(2-Iodophenyl)-6-nitro-1H-benzo[d]imidazole (**6b**).* Reaction of 4-nitrobenzene-1,2-diamine (3.06 g, 20 mmol) according to the



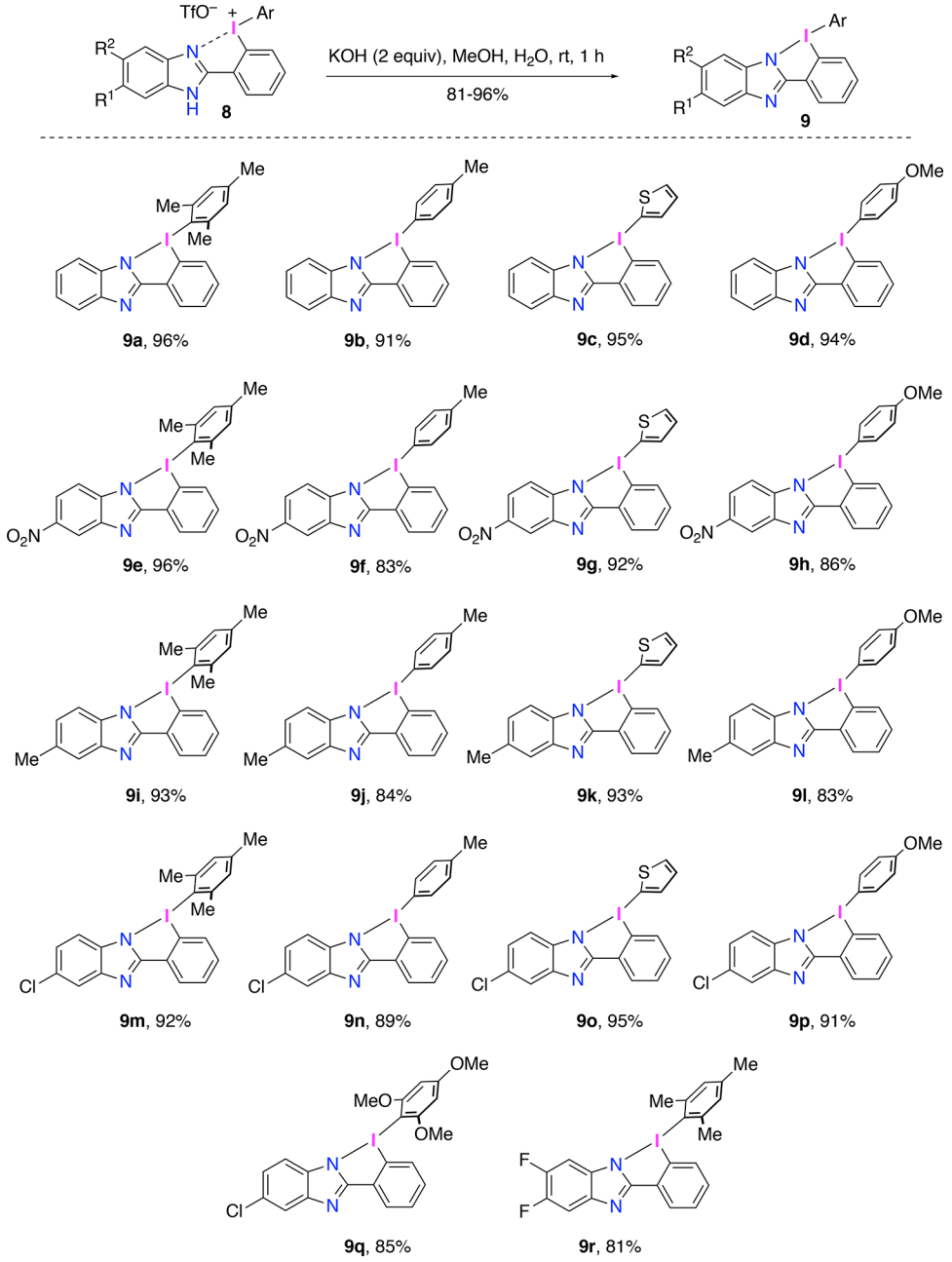
general procedure afforded 5.69 g (78%) of product **6b** (mixture of tautomers), isolated as a dark-orange solid: mp 207−208 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.20 (d, J = 5.6 Hz, 1H), 8.74 (s, 1H), 8.54 (s, 1H), 8.18 (d, J = 8.8 Hz, 1H), 8.09 (d, J = 7.6 Hz, 1H), 7.95 (d, J = 7.2 Hz, 1H), 7.81 (d, J = 8.8 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.25 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.1, 143.5, 142.8, 142.0, 141.9, 139.8, 139.2, 139.1, 136.1, 135.5, 131.9, 131.6, 131.4, 128.4, 128.3, 124.5, 120.7, 120.0, 118.1, 114.9, 112.7, 97.2; HRMS (ESI-TOF-positive ionization): calcd for $C_{13}H_9IN_3O_2$ ([M + H]$^+$): 365.9734, found: 365.9738. The crystal suitable for X-ray was prepared by slow evaporation of MeCN/H_2O solution (the structure is provided in SI).

*2-(2-Iodophenyl)-6-methyl-1H-benzo[d]imidazole (**6c**).* Reaction of 4-methylbenzene-1,2-diamine (2.44 g, 20 mmol) according to the general procedure afforded 5.41 g (81%) of product **6c** (mixture



DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

Scheme 4. Formation and Examples of the Cyclic Diaryliodonium Species 9



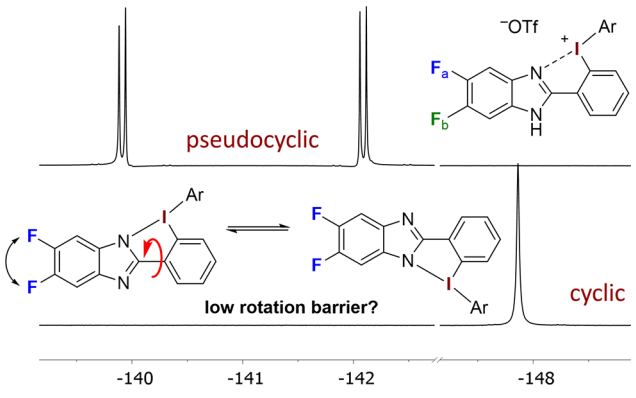
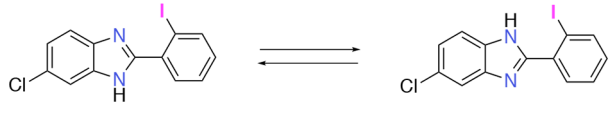


Figure 3. Aromatic region of the ^{19}F {^{1}H} NMR spectra of the difluoro derivatives **8r** (top) and **9r** (bottom).

of tautomers), isolated as a beige solid: mp 85−86 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.59 (s, 1H), 8.05 (d, J = 7.6 Hz, 1H), 7.60 (dd, J = 7.6, 1.6 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.49 (d, J = 8.4 Hz, 1H), 7.38 (s, 1H), 7.26 (td, J = 7.6, 1.6 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.5, 152.1, 143.6, 141.4, 139.7, 136.7, 134.7, 132.4, 131.9, 131.3, 131.1, 130.5, 128.1, 124.0, 123.1, 118.9, 118.7, 111.2, 111.0, 97.4, 21.4, 21.3; HRMS (ESI-TOF-positive ionization): calcd for $C_{14}H_{12}IN_2$ ([M + H]$^+$): 335.0040, found: 335.0041.

*6-Chloro-2-(2-iodophenyl)-1H-benzo[d]imidazole (**6d**).* Reaction of 4-chlorobenzene-1,2-diamine (2.85 g, 20 mmol) according to the



general procedure afforded 6.03 g (85%) of product **6d** (mixture of tautomers), isolated as a creamy-white solid: mp 189−190 °C;

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

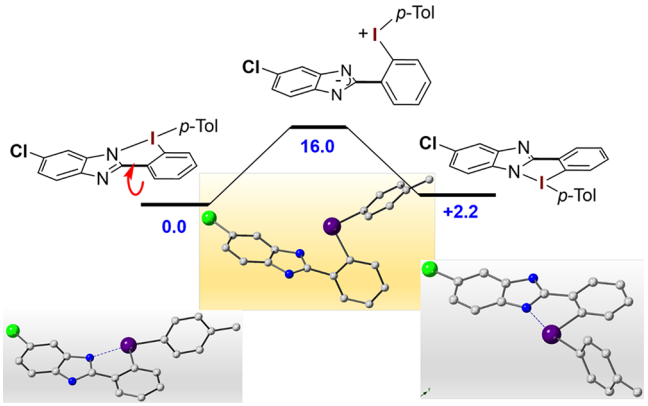
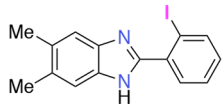


Figure 4. Energy profile for the rotamer interconversion of a cyclic benzimidazole-containing system. Values are given in kcal/mol: DFT: B3LYP, 6-31+G(d,p)/ LANL2DZ(d,p) for I.

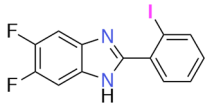
^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.91 (d, J = 11.6 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.76 (s, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.58–7.54 (m, 2H); 7.31–7.23 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 154.1, 153.7, 144.0, 141.9, 139.7, 136.1, 135.0, 133.1, 131.4, 131,3, 128.1, 126.9, 126.0, 122.7, 121.9, 120.4, 118.5, 112.8, 111.2, 97.2; HRMS (ESI-TOF-positive ionization): calcd for $C_{13}H_9ClIN_2$ ([M + H]$^+$): 354.9493, found: 354.9494.

*2-(2-Iodophenyl)-5,6-dimethyl-1H-benzo[d]imidazole (**6e**).* Reaction of 4,5-dimethylbenzene-1,2-diamine (2.72 g, 20 mmol) according



to the general procedure afforded 5.50 g (79%) of product **6e**, isolated as a beige solid: mp 203–204 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.41 (s, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.59 (dd, J = 7.6, 1.6 Hz, 1H), 7.53 (td, J = 7.6, 0.8 Hz, 1H), 7.44 (s, 1H), 7.28–7.23 (m, 2H), 2.33 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.1, 142.4, 140.1, 137.2, 133.4, 131.7, 131.6, 131.4, 130.2, 128.5, 119.6, 111.9, 97.8, 20.5; HRMS (ESI-TOF-positive ionization): calcd for $C_{15}H_{14}IN_2$ ([M + H]$^+$): 349.0196, found: 349.0198.

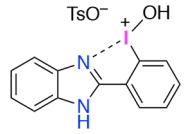
*5,6-Difluoro-2-(2-iodophenyl)-1H-benzo[d]imidazole (**6f**).* Reaction of 4,5-difluorobenzene-1,2-diamine (2.88 g, 20 mmol) according



to the general procedure afforded 4.98 g (70%) of product **6f**, isolated as a deep violet solid: mp 186–187 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.06 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 9.2 Hz, 2H), 7.62 (dd, J = 7.6, 1.6 Hz, 1H), 7.56 (t, J = 7.2 Hz, 2H), 7.30 (td, J = 7.6, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 154.49, 154.48, 154.46, 148.2 (d, J_{C-F} = 16.4 Hz), 145.8 (d, J_{C-F} = 16.4 Hz), 139.7, 135.7, 131.6, 131.4, 128.2, 103.1 (br. s), 97.4; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −143.7; HRMS (ESI-TOF-positive ionization): calcd for $C_{13}H_8F_2IN_2$ ([M + H]$^+$): 356.9695, found: 356.9700.

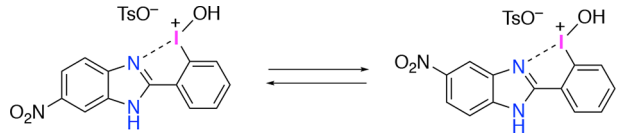
*Synthesis of [Hydroxy(tosyloxy)iodo]arenes **7**: General Procedure.* To a stirred solution of 2-(2-iodophenyl)-1*H*-benzo[*d*]imidazoles **6a–f** (1.0 equiv) in a mixture of DCM–TFE (1:1) were added mCPBA (77%, 2.0 equiv) and *p*-TsOH·H_2O (1.4 equiv). The stirring was continued at room temperature until full conversion of starting material (monitored by TLC, eluent hexane:EtOAc = 2:7), and solvents were evaporated at reduced pressure. The products were precipitated by the addition of Et_2O. The solids were filtered off, washed with Et_2O three times, and dried in a vacuum.

*(2-(1H-Benzo[d]imidazol-2-yl)phenyl)(hydroxy)iodonium Tosylate (**7a**).* Reaction of 2-(2-iodophenyl)-1*H*-benzo[*d*]imidazole **6a**



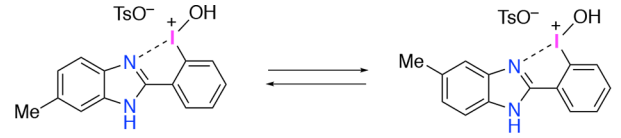
(1.60 g, 5 mmol) with mCPBA (77%, 3.46 g, 10 mmol) and *p*-TsOH·H_2O (1.33 g, 7 mmol) in 25 mL of DCM–TFE mixture (1:1) according to the general procedure afforded 2.49 g (98%) of product **7a**, isolated as a beige solid: mp 190–192 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.44 (d, J = 7.5 Hz, 1H), 8.08 (d, J = 8.1 Hz, 1H), 7.99–7.87 (m, 3H), 7.78–7.75 (m, 1H), 7.51–7.46 (m, 4H), 7.11 (d, J = 8.1 Hz, 2H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 151.3, 145.2, 138.4, 136.7, 134.2, 131.5, 128.5, 128.2, 128.0, 125.8, 125.7, 125.3, 124.8, 121.1, 117.1, 113.7, 21.0; HRMS (ESI-TOF-positive ionization): calcd for $C_{13}H_{10}IN_2O$ ([M − OTs]$^+$): 336.9838, found: 336.9832. The crystal suitable for X-ray was prepared by slow cooling of saturated MeCN/H_2O solution followed by evaporation.

*Hydroxy(2-(6-nitro-1H-benzo[d]imidazol-2-yl)phenyl)iodonium Tosylate (**7b**).* Reaction of 2-(2-iodophenyl)-1*H*-benzo[*d*]imidazole



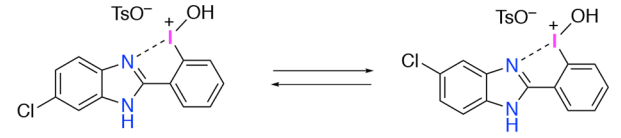
6b (1.83 g, 5 mmol) with mCPBA (77%, 3.46 g, 10 mmol) and *p*-TsOH·H_2O (1.33 g, 7 mmol) in 25 mL of DCM–TFE mixture (1:1) according to the general procedure afforded 2.49 g (90%) of product **7b** (mixture of tautomers), isolated as a yellow solid: mp 220–221 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.00 (d, J = 1.6 Hz, 1H), 8.61 (s, 1H), 8.55–8.51 (m, 2H), 8.32–8.30 (m, 2H), 8.12–8.09 (m, 2H), 8.05–7.93 (m, 4H), 7.49 (d, J = 7.6 Hz, 3H), 7.11 (d, J = 8.0 Hz, 3H), 2.28 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 145.4, 144.1, 143.0, 141.3, 140.0, 139.2, 138.2, 136.5, 134.9, 133.6, 132.2, 131.6, 130.9, 129.0, 128.8, 128.4, 127.9, 127.7, 125.7, 125.1, 121.4, 121.3, 120.6, 119.9, 118.4, 117.5, 114.6, 113.7, 110.6, 21.0; HRMS (ESI-TOF-positive ionization): calcd for $C_{13}H_9IN_3O_3$ ([M − OTs]$^+$): 381.9689, found: 381.9685.

*Hydroxy(2-(6-methyl-1H-benzo[d]imidazol-2-yl)phenyl)-iodonium Tosylate (**7c**).* Reaction of 2-(2-iodophenyl)-1*H*-benzo-[*d*]imidazole **6c** (1.67 g, 5 mmol) with mCPBA (77%, 3.46 g,



10 mmol) and *p*-TsOH·H_2O (1.33 g, 7 mmol) in 25 mL of DCM–TFE mixture (1:1) according to the general procedure afforded 2.19 g (84%) of product **7c** (mixture of tautomers), isolated as a creamy-white mp 175–176 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.52 (br. s, 1H), 14.46 (br. s, 1H), 8.44–8.41 (m, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.93 (t, J = 7.2 Hz, 1H), 7.87 (t, J = 7.6 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.71 (s, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.53–7.48 (m, 3H), 7.24 (t, J = 8.0 Hz, 1H), 7.11 (d, J = 8.0 Hz, 2H), 2.44 (d, J = 6.4 Hz, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 150.8, 150.6, 145.3, 138.0, 136.7, 135.4, 134.6, 134.2, 134.1, 133.7, 133.6, 132.0, 131.2, 128.2, 127.9, 127.7, 126.9, 126.0, 125.6, 125.2, 120.9, 120.8, 116.4, 116.3, 113.1, 112.9, 21.4, 21.3, 20.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{14}H_{12}IN_2O$ ([M − OTs]$^+$): 350.9994, found: 350.9994.

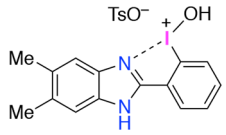
*(2-(6-Chloro-1H-benzo[d]imidazol-2-yl)phenyl)(hydroxy)-iodonium Tosylate (**7d**).* Reaction of 2-(2-iodophenyl)-1*H*-benzo-[*d*]imidazole **6d** (1.77 g, 5 mmol) with mCPBA (77%, 3.46 g,



DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056–12070

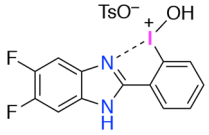
10 mmol) and *p*-TsOH·H_2O (1.33 g, 7 mmol) in 25 mL of DCM−TFE mixture (1:1) according to the general procedure afforded 2.61 g (96%) of product **7d** (mixture of tautomers), isolated as a beige solid: mp 188−190 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.22 (br. s, 1H), 8.44 (t, J = 6.8 Hz, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.98−7.86 (m, 3H), 7.80 (s, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.52 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.8 Hz, 1H), 7.12 (d, J = 7.6 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.3, 145.1, 138.1, 137.4, 135.6, 134.8, 134.2, 134.1, 133.0, 131.3, 129.8, 128.7, 128.3, 127.7, 127.6, 125.6, 125.0, 124.9, 121.0, 120.9, 118.3, 116.6, 115.0, 113.3, 20.9; HRMS (ESI-TOF-positive ionization): calcd for $C_{13}H_8ClIN_2$ ([M − OH − OTs]$^+$): 353.9415, found: 353.9415.

*(2-(5,6-Dimethyl-1H-benzo[d]imidazol-2-yl)phenyl)(hydroxy)-iodonium Tosylate (**7e**).* Reaction of 2-(2-iodophenyl)-1*H*-benzo[*d*]imidazole **6e** (0.70 g, 2 mmol) with mCPBA (77%, 1.38 g,



4 mmol) and *p*-TsOH·H_2O (0.53 g, 2.8 mmol) in 10 mL of DCM−TFE mixture (1:1) according to the general procedure afforded 0.97 g (91%) of product **7e**, isolated as a beige solid: mp 185−186 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.40 (s, 1H), 8.44 (dd, J = 7.6, 1.6 Hz, 1H), 8.08 (d, J = 7.6 Hz, 1H), 7.95 (td, J = 7.6, 1.6 Hz, 1H), 7.90 (td, J = 7.6, 1.2 Hz, 1H), 7.71 (s, 1H), 7.54 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 2.39 (s, 3H), 2.37 (s, 3H) 2.28 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 150.1, 145.6, 137.7, 135.0, 134.9, 134.0, 133.5, 132.4, 131.2, 128.1, 127.7, 125.5, 125.3, 120.7, 116.5, 113.1, 20.8, 20.1, 20.0; HRMS (ESI-TOF-positive ionization): calcd for $C_{15}H_{13}IN_2$ ([M − OH − OTs]$^+$): 348.0118, found: 348.0120.

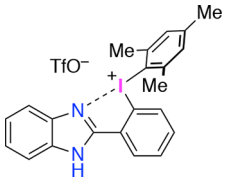
*(2-(5,6-Difluoro-1H-benzo[d]imidazol-2-yl)phenyl)(hydroxy)-iodonium Tosylate (**7f**).* Reaction of 2-(2-iodophenyl)-1*H*-benzo[*d*]-imidazole **6f** (0.71 g, 2 mmol) with mCPBA (77%, 1.38 g, 4 mmol)



and *p*-TsOH·H_2O (0.53 g, 2.8 mmol) in 10 mL of DCM−TFE mixture (1:1) according to the general procedure afforded 0.95 g (87%) of product **7f**, isolated as a light brown solid: mp 167−168 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.48 (dd, J = 7.6, 1.2 Hz, 1H), 8.08−8.03 (m, 2H), 8.00−7.96 (m, 2H), 7.91 (td, J = 7.5, 0.8 Hz, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.11(d, J = 7.6 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.0, 145.5, 139.7, 137.9, 134.1, 132.5 (d, J_{C-F} = 11.7 Hz), 131.5, 131.3, 129.9 (d, J_{C-F} = 12.0 Hz), 128.2, 127.6, 125.5, 125.0, 120.8, 104.9 (d, J_{C-F} = 21.8 Hz), 102.1 (d, J_{C-F} = 23.1 Hz), 20.8; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −138.6 (d, J = 23.2 Hz), −139.9 (d, J = 23.2 Hz); HRMS (ESI-TOF-positive ionization): calcd for $C_{13}H_7F_2IN_2$ ([M − OH − OTs]$^+$): 355.9616, found: 355.9621.

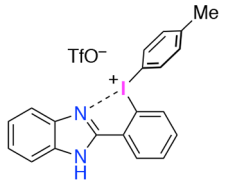
*Synthesis of (2-(1H-Benzo[d]imidazol-2-yl)phenyl)(aryl)-iodonium Triflates **8**: General Procedure.* To a stirred solution of [hydroxy(tosyloxy)iodo]arenes **7a−f** (0.2 mmol, 1 equiv) in 1.5 mL of TFE or HFIP was added trifluoromethanesulfonic acid (0.026 mL, 0.3 mmol, 1.5 equiv), and reaction mixture was stirred during 10 min. Then arene was added, and stirring was continued until full conversion of starting material according to NMR (temperature and reaction times are provided in the text). The solvent was evaporated at room temperature. The products were precipitated by the addition of Et_2O. The solids were filtered off, washed with Et_2O three times, and dried in a vacuum.

*(2-(1H-Benzo[d]imidazol-2-yl)phenyl)(mesityl)iodonium Triflate (**8a**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7a** (0.102 g, 0.2 mmol) with mesitylene (0.056 mL, 0.048 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at room



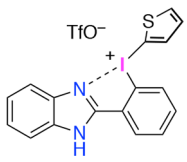
temperature during 8 h afforded 0.115 g (98%) of product **8a**, isolated as a beige solid: mp 195−196 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 13.90 (s, 1H), 8.47 (dd, J = 7.6, 1.6 Hz, 1H), 7.86 (t, J = 7.2 Hz, 1H), 7.78−7.76 (m, 2H), 7.60−7.56 (m, 1H), 7.44−7.40 (m, 2H), 7.37 (s, 2H), 6.92 (d, J = 8.0 Hz, 1H), 2.53 (s, 6H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 149.3, 144.0, 143.0, 133.8, 131.4, 130.0, 129.4, 128.9, 127.8, 124,2, 124.1, 121.0, 120.71 (q, J_{CF} = 320 Hz, $CF_3SO_3^-$), 111.6, 26.0, 20.8; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.7; HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{20}IN_2$ ([M − OTf]$^+$): 439.0671, found: 439.0666.

*(2-(1H-Benzo[d]imidazol-2-yl)phenyl)(p-tolyl)iodonium Triflate (**8b**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7a** (0.102 g,



0.2 mmol) with toluene (0.064 mL, 0.055 g, 0.6 mmol) in 1.5 mL of TFE (HFIP) according to the general procedure at 50 °C during 48 h (9 h with HFIP) afforded 0.092 g (82%) [or 0.101 g (90%) with HFIP] of product **8b** (contains 20% of ortho-isomer), isolated as a beige solid: mp 234−235 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 13.93 (s, 1H), 8.45 (dd, J = 8.0, 1.2 Hz, 1H), 8.36 (d, J = 7.6 Hz, 1H), 8.21 (d, J = 8.0 Hz, 2H), 7.84 (t, J = 7.2 Hz, 1H), 7.80 (d, J = 7.2 Hz, 1H), 7.74 (dd, J = 7.6, 1.6 Hz, 1H), 7.63−7.57 (m, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.49−7.46 (m, 1H), 7.42 (td, J = 7.2, 1.2 Hz, 2H), 7.11 (d,, J = 8.0 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 2.57 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 149.3, 145.7, 143.7, 142.3, 140.1, 138.8, 137.7, 137.4, 134.6, 133.9, 133.7, 133.4, 132.9, 131.8, 131.4, 131.2, 130.5, 129.9, 129.6, 129.2, 129.0, 128.1, 127.4, 127.1, 124.8, 123.6, 120.70 (q, J_{CF} = 320 Hz, $CF_3SO_3^-$), 118.4, 114.3, 113.0, 112.7, 111.9, 24.7, 21.3; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{16}IN_2$ ([M − OTf]$^+$): 411.0353, found: 411.0360.

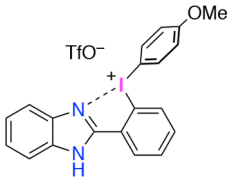
*(2-(1H-Benzo[d]imidazol-2-yl)phenyl)(thiophen-2-yl)iodonium Triflate (**8c**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7a** (0.102 g,



0.2 mmol) with thiophene (0.032 mL, 0.034 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at 0−5 °C during 2 h afforded 0.106 g (96%) of product **8c**, isolated as a beige solid: mp 221−222 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 14.03 (s, 1H), 8.43 (d, J = 7.2 Hz, 1H), 8.26 (d, J = 4.4 Hz, 1H), 8.19 (s, 1H), 7.85 (t, J = 7.2 Hz, 1H), 7.79 (d, J = 6.4 Hz, 1H), 7.73 (d, J = 6.4 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.44 (br s, 3H), 7.01 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 149.5, 143.5, 139.5, 139.2, 134.4, 133.7, 131.7, 130.6, 129.5, 128.6, 126.6, 124.9, 123.8, 120.67 (q, J_{CF} = 320 Hz, $CF_3SO_3^-$), 118.0, 116.9, 112.8, 102.2; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{17}H_{12}IN_2S$ ([M − OTf]$^+$): 402.9760, found: 402.9754.

*(2-(1H-Benzo[d]imidazol-2-yl)phenyl)(4-methoxyphenyl)-iodonium Triflate (**8d**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7a** (0.102 g, 0.2 mmol) with 4-anisole (0.040 mL, 0.043 g, 0.4 mmol) in

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

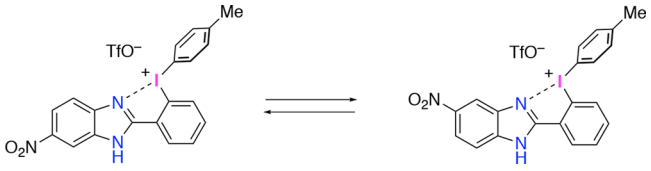


1.5 mL of TFE according to the general procedure at 0−5 °C during 3 h afforded 0.099 g (92%) of product **8d** (contains 15% of ortho-isomer), isolated as a beige solid: mp 151−152 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.44 (dd, J = 8.0, 1.5 Hz, 1H), 8.29 (dd, J = 7.5, 1.5 Hz, 1H), 8.26−8.21 (m, 2H), 8.19 (dd, J = 7.5, 1.0 Hz, 1H), 7.94−7.92 (m, 2H), 7.89−7.86 (m, 2H), 7.84 (td, J = 7.5, 1.0 Hz, 1H), 7.76 (br. s, 2H), 7.73 (dd, J = 7.5, 1.0 Hz, 1H), 7.68−7.66 (m, 2H), 7.60 (ddd, J = 8.7, 7.4, 1.5 Hz, 1H), 7.54−7.51 (m, 2H), 7.43−7.41 (m, 2H), 7.30−7.24 (m, 2H), 7.05 (dd, J = 8.5, 1.0 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.8, 149.3, 140.1, 139.4, 134.1, 133.4, 132.3, 131.1, 131.0, 130.3, 130.2, 128.9, 128.6, 127.0, 126.5, 120.68 (q, J_{CF} = 320 Hz, $CF_3SO_3^-$), 118.0, 114.7, 114.4, 104.3, 55.8, 55.2; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{16}IN_2O$ ([M − OTf]$^+$): 427.0302, found: 427.0301.

*Mesityl(2-(6-nitro-1H-benzo[d]imidazol-2-yl)phenyl)iodonium Triflate (**8e**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7b** (0.111 g,

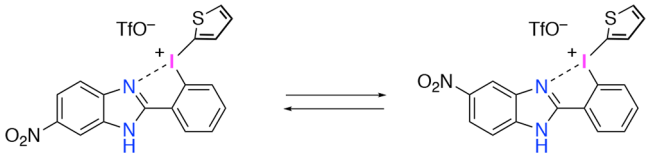
0.2 mmol) with mesitylene (0.056 mL, 0.048 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at room temperature during 9 h afforded 0.106 g (92%) of product **8e** (mixture of tautomers), isolated as a beige solid: mp 241−242 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 14.47 (s, 1H), 8.62 (s, 1H), 8.51−8.44 (m, 1H), 8.26 (t, J = 8.4 Hz, 1H), 7.96−7.88 (m, 2H), 7.65 (t, J = 8.0 Hz, 1H), 7.40 (s, 2H), 6.96 (d, J = 8.4 Hz, 1H), 2.55 (s, 6H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 154.0, 153.4, 144.5, 144.3, 144.0, 143.6, 143.1, 139.5, 139.1, 137.1, 134.8, 134.7, 134.0, 131.5, 130.3, 130.1, 129.2, 127.1, 126.8, 120.71 (q, J_{CF} = 321 Hz, $CF_3SO_3^-$), 120.6, 119.9, 119.0, 114.6, 113.2, 112.0, 109.0, 26.1, 20.9; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{19}IN_3O_2$ ([M − OTf]$^+$): 484.0516, found: 484.0534. The crystal suitable for X-ray was prepared by diffusion of ether to the saturated solution of **8e** in MeOH.

*(2-(6-Nitro-1H-benzo[d]imidazol-2-yl)phenyl)(p-tolyl)iodonium Triflate (**8f**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7b** (0.111 g,



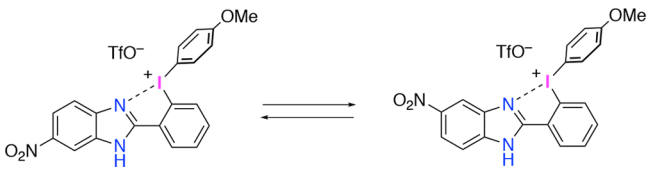
0.2 mmol) with toluene (0.064 mL, 0.055 g, 0.6 mmol) in 1.5 mL of TFE (HFIP) according to the general procedure at 50 °C during 48 h (9 h with HFIP) afforded 0.096 g (79%) [or 0.106 g (88%) with HFIP] of product **8f** (mixture of tautomers, contains 20% of ortho-isomer), isolated as a beige solid: mp 228−229 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.61 (s, 1H), 8.48 (d, J = 7.6 Hz, 1H), 8.37 (d, J = 7.6 Hz, 1H), 8.28 (dd, J = 8.8, 2.0 Hz, 1H), 8.23 (d, J = 8.0 Hz, 2H), 7.93 (d, J = 8.8 Hz, 1H), 7.87 (t, J = 7.2 Hz, 1H), 7.82−7.78 (m, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.51−7.47 (m, 1H), 7.08 (d, J = 8.4 Hz, 1H), 6.99 (d, J = 8.4 Hz, 1H), 2.57 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 154.6, 143.8, 143.4, 142.3, 138.8, 137.3, 134.0, 132.9, 131.8, 131.2, 130.7, 129.9, 129.7, 127.3, 122.3, 120.91 (q, J_{CF} = 322 Hz, $CF_3SO_3^-$), 119.1, 115.9, 115.6, 114.8, 113.5, 111.7, 24.7, 21.2; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{15}IN_3O_2$ ([M − OTf]$^+$): 456.0203, found: 456.0205.

*(2-(6-Nitro-1H-benzo[d]imidazol-2-yl)phenyl)(thiophen-2-yl)-iodonium Triflate (**8g**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7b**



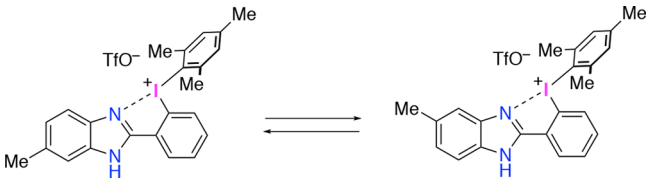
(0.111 g, 0.2 mmol) with thiophene (0.032 mL, 0.034 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at 0−5 °C during 3 h afforded 0.103 g (86%) of product **8g** (mixture of tautomers), isolated as a beige solid: mp 229−230 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.63 (br. s, 1H), 8.48 (d, J = 7.2 Hz, 1H), 8.29 (d, J = 6.4 Hz, 2H), 8.24 (d, J = 3.2 Hz, 1H), 7.95−7.89 (m, 2H), 7.72 (t, J = 7.2 Hz, 1H), 7.48−7.46 (m, 1H), 7.08 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 154.0, 153.4, 144.1, 143.9, 143.7, 140.1, 138.9, 138.7, 134.6, 133.9, 131.5, 130.7, 129.7, 129.5, 129.3, 125.9, 120.67 (q, J_{CF} = 321 Hz, $CF_3SO_3^-$), 120.1, 119.2, 118.6, 117.2, 114.2, 113.4, 109.2, 100.9, 100.7; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{17}H_{11}IN_3O_2S$ ([M − OTf]$^+$): 447.9611, found: 447.9622.

*(2-(6-Nitro-1H-benzo[d]imidazol-2-yl)phenyl)(4-methoxyphenyl)-iodonium Triflate (**8h**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7b**



(0.111 g, 0.2 mmol) with 4-anisole (0.040 mL, 0.043 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at 0−5 °C during 3 h afforded 0.102 g (82%) of product **8h** (mixture of tautomers, contains 15% of ortho-isomer), isolated as a beige solid: mp 191−192 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 14.08 (d, J = 9.2 Hz, 1H), 8.43 (d, J = 7.6 Hz, 1H), 8.30 (dd, J = 8.0, 1.6 Hz, 1H), 8.24 (d, J = 8.8 Hz, 2H), 7.91−7.89 (m, 1H), 7.87−7.80 (m, 3H), 7.64−7.60 (m, 1H), 7.53−7.48 (m, 2H), 7.45−7.44 (m, 1H), 7.27 (d, J = 9.2 Hz, 2H), 7.11 (d, J = 8.0 Hz, 1H), 7.06 (d, J = 8.0, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9, 139.5, 133.7, 131.2, 130.5, 129.1, 128.1, 126.8, 123.9, 123.87 (q, J_{CF} = 322 Hz, $CF_3SO_3^-$), 118.0, 114.7, 104.0, 55.8; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{15}IN_3O_3$ ([M − OTf]$^+$): 472.0158, found: 472.0149.

*Mesityl(2-(6-methyl-1H-benzo[d]imidazol-2-yl)phenyl)iodonium Triflate (**8i**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7c** (0.104 g,

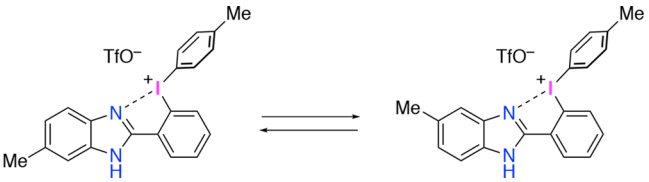


0.2 mmol) with mesitylene (0.056 mL, 0.048 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at room temperature during 8 h afforded 0.113 g (94%) of product **8i** (mixture of tautomers), isolated as a beige solid: mp 221−222 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 13.78 and 13.73 (2s, 1H), 8.44 (d, J = 7.6 Hz, 1H), 7.85 (t, J = 7.2 Hz, 1H), 7.67−7.51 (m, 3H), 7.31 (s, 2H), 7.26 and 7.22 (2d, J = 8.4 Hz, 1H), 6.91 (dd, J = 8.4, 2.4 Hz, 1H), 2.52 (s, 6H), 2.49 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 149.1, 148.8, 144.0, 143.0, 140.4, 138.3, 134.9, 134.5, 133.6, 133.5, 132.8, 132.7, 131.4, 130.0, 129.2, 128.8, 127.8, 126.3, 125.1, 121.1, 121.0, 120.70 (q, J_{CF} = 321 Hz, $CF_3SO_3^-$), 118.0, 112.1,

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

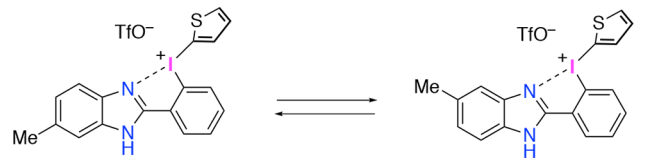
111.4, 111.4, 26.0, 21.4, 21.3, 20.9; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{23}H_{22}IN_2$ ([M − OTf]$^+$): 453.0822, found: 453.0824.

*(2-(6-Methyl-1H-benzo[d]imidazol-2-yl)phenyl)(p-tolyl)-iodonium Triflate (**8j**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7c**



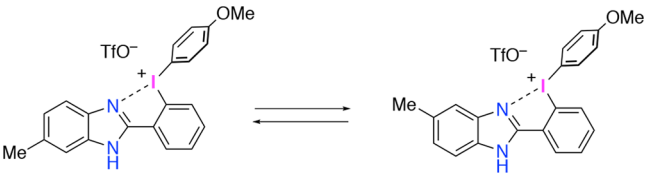
(0.104 g, 0.2 mmol) with toluene (0.064 mL, 0.055 g, 0.6 mmol) in 1.5 mL of TFE (HFIP) according to the general procedure at 50 °C during 48 h (9 h with HFIP) afforded 0.094 g (82%) [or 0.104 g (91%) with HFIP] of product **8j** (mixture of tautomers, contains 5% of ortho-isomer), isolated as a beige solid: mp 223−224 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.71 (s, 1H), 8.41 (dd, J = 7.5, 1.0 Hz, 1H), 8.19 (d, J = 8.0 Hz, 2H), 7.82 (t, J = 7.5 Hz, 1H), 7.64−7.49 (m, 5H), 7.24 (s, 1H), 6.99 (d, J = 8.5 Hz, 1H), 2.49 (s, 6H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 148.8, 143.7, 138.2, 137.3, 134.8, 134.5, 133.1, 132.8, 131.1, 130.4, 128.7, 128.1, 127.1, 126.2, 125.5, 125.1, 120.68 (q, J_{CF} = 321 Hz, $CF_3SO_3^-$), 117.8, 114.1, 112.1, 111.9, 24.7, 21.3, 21.2; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.7; HRMS (ESI-TOF-positive ionization): calcd for $C_{21}H_{18}IN_2$ ([M − OTf]$^+$): 425.0509, found: 425.0504.

*(2-(6-Methyl-1H-benzo[d]imidazol-2-yl)phenyl)(thiophen-2-yl)-iodonium Triflate (**8k**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7c**



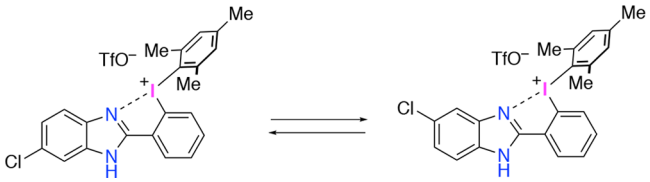
(0.104 g, 0.2 mmol) with thiophene (0.032 mL, 0.034 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at 0−5 °C during 2 h afforded 0.103 g (91%) of product **8k** (mixture of tautomers), isolated as a beige solid: mp 220−221 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 13.91 (s, 1H), 8.43 (d, J = 7.6 Hz, 1H), 8.26 (d, J = 5.2 Hz, 1H), 8.20 (t, J = 3.2 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H), 7.69−7.60 (m, 2H), 7.56 (s, 1H), 7.51 (s, 1H), 7.45 (t, J = 3.6 Hz, 1H), 7.29−7.22 (m, 1H), 7.01 (d, J = 8.0 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 149.3, 149.1, 143.5, 139.5, 137.4, 134.8, 134.7, 133.6, 133.5, 133.2, 132.5, 131.4, 130.6, 129.5, 128.5, 126.7, 126.5, 125.4, 120.70 (q, J_{CF} = 320 Hz, $CF_3SO_3^-$), 117.6, 117.5, 116.8, 112.4, 112.3, 102.5, 102.4, 21.4, 21.3; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{18}H_{14}IN_2S$ ([M − OTf]$^+$): 416.9917, found: 416.9918.

*(4-Methoxyphenyl)(2-(6-methyl-1H-benzo[d]imidazol-2-yl)-phenyl)iodonium Triflate (**8l**).* Reaction of [hydroxy(tosyloxy)iodo]-arene **7c** (0.104 g, 0.2 mmol) with 4-anisole (0.040 mL, 0.043 g,



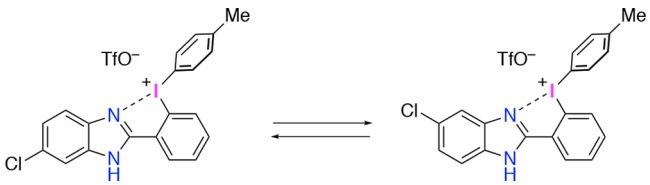
0.4 mmol) in 1.5 mL of TFE according to the general procedure at 0−5 °C during 3 h afforded 0.105 g (89%) of product **8l** (mixture of tautomers, contains 35% of ortho-isomer), isolated as a beige solid: mp 189−190 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 13.80 (s, 1H), 13.75 (s, 1H), 8.42 (d, J = 7.2 Hz, 1H), 8.24 (d, J = 7.2 Hz, 2H), 8.15 (d, J = 8.0 Hz, 1H), 7.85−7.82 (m, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.68−7.46 (m, 4H), 7.46−7.39 (m, 2H), 7.28−7.22 (m, 3H), 7.03 (d, J = 8.0 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.8, 148.9, 139.6, 139.5, 138.3, 134.9, 134.5, 133.3, 133.2, 132.1, 131.1, 130.3, 128.7, 128.5, 125.2, 124.66 (q, J_{CF} = 329 Hz, $CF_3SO_3^-$), 118.0, 114.5, 112.1, 104.4, 55.8, 21.4, 21.2; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{21}H_{18}IN_2O$ ([M − OTf]$^+$): 441.0458, found: 441.0468.

*(2-(6-Chloro-1H-benzo[d]imidazol-2-yl)phenyl)(mesityl)-iodonium Triflate (**8m**).* Reaction of [hydroxy(tosyloxy)iodo]arene



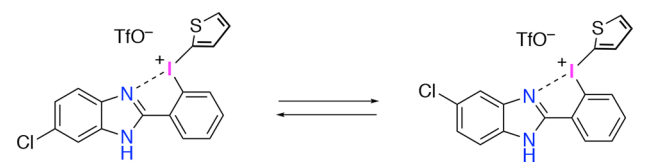
7d (0.109 g, 0.2 mmol) with mesitylene (0.056 mL, 0.048 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at room temperature during 8 h afforded 0.105 g (84%) of product **8m** (mixture of tautomers), isolated as a beige solid: mp 222−223 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 14.05 (d, J = 12.0 Hz, 1H), 8.46 (d, J = 7.6 Hz, 1H), 7.87 (td, J = 7.6, 0.4 Hz, 1H), 7.80 (br. s, 2H), 7.59 (ddd, J = 8.6, 7.5, 1.4 Hz, 1H), 7.44 (br. s, 1H), 7.38 (s, 2H), 6.93 (d, J = 8.0 Hz, 1H), 2.53 (s, 6H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 150.8, 150.6, 144.1, 143.0, 141.0, 139.0, 135.4, 134.1, 133.5, 131.5, 130.0, 129.7, 129.0, 128.2, 127.5, 124.8, 123.9, 120.9, 120.72 (q, J_{CF} = 321 Hz, $CF_3SO_3^-$), 119.9, 117.9, 114.1, 112.3, 111.7, 26.0, 20.9; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{19}ClIN_2$ ([M − OTf]$^+$): 473.0276, found: 473.0274. The crystal suitable for X-ray was prepared by diffusion of ether to the saturated solution of **8m** in MeOH.

*(2-(6-Chloro-1H-benzo[d]imidazol-2-yl)phenyl)(p-tolyl)iodonium Triflate (**8n**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7d** (0.109 g,



0.2 mmol) with toluene (0.064 mL, 0.055 g, 0.6 mmol) in 1.5 mL of TFE (HFIP) according to the general procedure at 50 °C during 48 h (9 h with HFIP) afforded 0.096 g (81%) or 0.111 g (93%) with HFIP of product **8n** (mixture of tautomers, contains 20% of ortho-isomer), isolated as a beige solid: mp 158−159 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 14.09 (s, 1H), 8.47 (s, 1H), 8.43 (dd, J = 8.0, 1.2 Hz, 1H), 8.35 (d, J = 7.2 Hz, 1H), 8.21 (d, J = 8.0 Hz, 2H), 7.88−7.76 (m, 4H), 7.63−7.59 (m, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.50−7.48 (m, 1H), 7.44 (dd, J = 8.4, 1.2 Hz, 1H), 7.04 (d, J = 7.6 Hz, 1H), 6.95 (d, J = 7.6 Hz, 1H), 2.57 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 150,7, 148.8, 143.8, 142.3, 138.8, 137.3, 133.9, 133.6, 132.9, 131.8, 131.3, 131.2, 130.0, 129.6, 129.4, 129.2, 127.2, 126.9, 120.67 (q, J_{CF} = 321 Hz, $CF_3SO_3^-$), 119.9, 114.4, 113.0, 111.6, 111.1, 24.7, 21.2; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{15}ClIN_2$ ([M − OTf]$^+$): 444.9963, found: 444.9956.

*(2-(6-Chloro-1H-benzo[d]imidazol-2-yl)phenyl)(thiophen-2-yl)-iodonium Triflate (**8o**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7d**

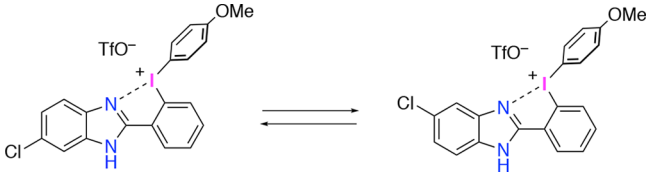


(0.109 g, 0.2 mmol) with thiophene (0.032 mL, 0.034 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at 0−5 °C during

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

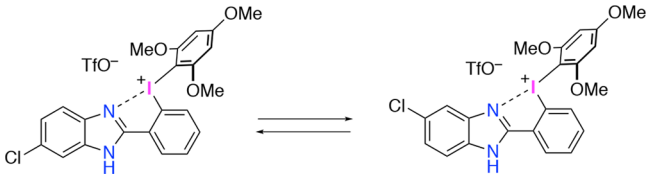
2 h afforded 0.104 g (89%) of product **8o** (mixture of tautomers), isolated as a beige solid: mp 238–239 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.43 (t, J = 6.4 Hz, 1H), 8.27 (d, J = 5.2 Hz, 1H), 8.21 (s, 1H), 7.87 (t, J = 7.6 Hz, 1H), 7.82–7.74 (m, 2H), 7.67 (t, J = 7.6 Hz, 1H), 7.47–7.43 (m, 2H), 7.03 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 151.0, 150.8, 143.8, 140.2, 139.8, 138.2, 135.3, 134.1, 134.0, 133.5, 131.5, 130.7, 129.6, 129.2, 128.9, 128.0, 126.5, 126.4, 125.1, 124.3, 120.72 (q, J_{CF} = 320 Hz, $CF_3SO_3^-$), 119.4, 117.5, 117.0, 114.3, 112.6, 101.7; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{17}H_{11}ClIN_2S$ ([M − OTf]$^+$): 436.9371, found: 436.9373.

*(2-(6-Chloro-1H-benzo[d]imidazol-2-yl)phenyl)(4-methoxyphenyl)-iodonium Triflate (**8p**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7d**



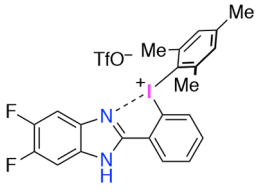
(0.109 g, 0.2 mmol) with 4-anisole (0.040 mL, 0.043 g, 0.4 mmol) in 1.5 mL of TFE according to the general procedure at 0–5 °C during 3 h afforded 0.099 g (81%) of product **8p** (mixture of tautomers, contains 13% of ortho-isomer), isolated as a beige solid: mp 191–192 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 14.06 (d, J = 9.2 Hz, 1H), 8.43 (d, J = 7.6 Hz, 1H), 8.29 (dd, J = 8.0, 1.6 Hz, 1H), 8.24 (d, J = 8.8 Hz, 2H), 7.90 (d, J = 7.6 Hz, 1H), 7.87–7.80 (m, 3H), 7.64–7.59 (m, 1H), 7.53–7.48 (m, 2H), 7.45 (m, 1H), 7.27 (d, J = 9.2 Hz, 2H), 7.11 (d, J = 8.0 Hz, 1H), 7.06 (d, J = 8.0 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9, 150.6, 139.5, 138.4, 133.7, 132.2, 131.2, 130.5, 129.1, 128.1, 126.8, 124.9, 123.9, 120.67 (q, J_{CF} = 320 Hz, $CF_3SO_3^-$), 119.7, 114.7, 114.1, 112.3, 104.0, 55.8; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{15}ClIN_2O$ ([M − OTf]$^+$): 460.9912, found: 460.9914.

*(2-(6-Chloro-1H-benzo[d]imidazol-2-yl)phenyl)(2,4,6-trimethoxyphenyl)iodonium Triflate (**8q**).* Reaction of [hydroxy-(tosyloxy)iodo]arene **7d** (0.109 g, 0.2 mmol) with 1,3,5-trimethoxybenzene (0.067 g, 0.4 mmol) in 1.5 mL of TFE according to the



general procedure at 0–5 °C during 2 h afforded 0.129 g (96%) of product **8q** (mixture of tautomers), isolated as a beige solid: mp 236–237 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 14.10 (s, 1H), 8.44 (t, J = 6.4 Hz, 1H), 7.87–7.73 (m, 3H), 7.61 (t, J = 7.6 Hz, 1H), 7.46–7.40 (m, 1H), 7.10 (d, J = 8.0 Hz, 1H), 6.63 (s, 2H), 3.98 (s, 4H), 3.89 (s, 7H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 167.3, 161.0, 150.8, 150.6, 140.7, 138.7, 135.3, 134.0, 133.9, 133.4, 131.3, 129.4, 129.0, 128.2, 127.7, 127.0, 124.9, 124.0, 122.3, 120.71 (q, J_{CF} = 320 Hz, $CF_3SO_3^-$), 119.7, 117.7, 114.1, 112.6, 112.4, 92.4, 85.7, 57.4, 56.4; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{19}ClIN_2O_3$ ([M − OTf]$^+$): 521.0123, found: 521.0117.

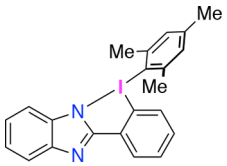
*(2-(5,6-Difluoro-1H-benzo[d]imidazol-2-yl)phenyl)(mesityl)-iodonium Triflate (**8r**).* Reaction of [hydroxy(tosyloxy)iodo]arene **7f**



(0.109 g, 0.2 mmol) with mesitylene (0.056 mL, 0.048 g, 0.4 mmol) in 1.5 mL HFIP according to the general procedure at room temperature during 8 h afforded 0.102 g (82%) of product **8r**, isolated as a beige solid: mp 166–167 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 14.14 (s, 1H), 8.45 (dd, J = 7.6, 1.2 Hz, 1H), 7.88–7.83 (m, 3H), 7.61–7.56 (m, 1H), 7.38 (s, 2H), 6.92 (d, J = 8.0 Hz, 1H), 2.52 (s, 6H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 151.3, 144.1, 142.9, 135.8 (d, J_{CF} = 10.3 Hz), 134.0, 131.5, 130.3 (d, J_{CF} = 10.3 Hz), 130.0, 129.6, 129.0, 128.3, 128.2, 127.5, 120.9, 120.63 (q, J_{CF} = 320 Hz, $CF_3SO_3^-$), 111.5, 106.0 (d, J_{CF} = 21.3 Hz), 100.8 (d, J_{CF} = 23.0 Hz), 26.0, 20.8; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −77.8, −139.9 (d, J = 5.8 Hz), −142.1 (d, J = 5.8 Hz); HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{18}F_2IN_2$ ([M − OTf]$^+$): 475.0477, found: 475.0480.

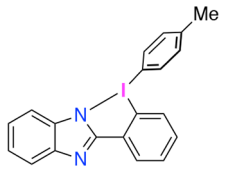
*Synthesis of 5-aryl-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b]-[1,2]iodazoles **9**: General Procedure.* A pseudocyclic iodonium salt **8a–8f** (0.2 mmol) was dissolved in methanol until the formation of a clear solution (2.5–10.0 mL of MeOH). An aqueous solution of potassium hydroxide (0.1 mL of solution containing 0.4 mmol, 2 equiv of KOH) was added to the solution under vigorous stirring. An immediate precipitation of cyclic iodonium products **9** was observed. The stirring was continued for 1 h. The methanol was removed using rotary evaporation and water (3 mL) was added. The stirring was continued for 15 min. The solid was filtered off, washed by water (2 × 1.5 mL), and dried under vacuum.

*5-Mesityl-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b][1,2]iodazole (**9a**).* Reaction of **8a** (0.118 g, 0.2 mmol) according to the general



procedure afforded 0.084 g (96%) of product **9a**, isolated as a creamy-white solid: mp 235–236 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.51 (d, J = 7.6 Hz, 1H), 7.80 (t, J = 7.2 Hz, 1H), 7.73 (br. s, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.37–7.34 (m, 4H), 6.87 (d, J = 8.4 Hz, 1H), 2.52 (s, 6H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 150.2, 143.5, 142.7, 133.2, 131.1, 129.8, 129.3, 128.8, 128.6, 124.0, 123.7, 123.5, 123.4, 122.1, 118.9, 113.5, 26.0, 20.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{20}IN_2$ ([M + H]$^+$): 439.0666, found: 439.0668.

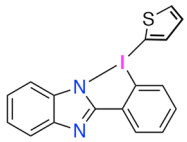
*5-(p-Tolyl)-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b][1,2]-iodazole (**9b**).* Reaction of **8b** (0.112 g, 0.2 mmol) according to the



general procedure afforded 0.075 g (91%) of product **9b** (contains 10% of ortho-isomer), isolated as a beige solid: mp 228–229 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.46 (d, J = 8.0 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 8.0 Hz, 2H), 8.06 (d, J = 8.0 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.65–7.63 (m, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.45 (t, J = 8.5 Hz, 1H), 7.20–7.18 (m, 2H), 7.11 (d, J = 7.5 Hz, 2H), 6.93 (d, J = 8.5 Hz, 1H), 6.85 (d, J = 8.5 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 143.0, 141.3, 137.1, 132.5, 131.6, 130.7, 129.5, 128.4, 128.0, 125.5, 121.7, 116.0, 114.2, 21.2; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{16}IN_2$ ([M + H]$^+$): 411.0353, found: 411.0356.

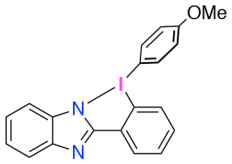
*5-(Thiophen-2-yl)-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b]-[1,2]iodazole (**9c**).* Reaction of **8c** (0.110 g, 0.2 mmol) according to the general procedure afforded 0.076 g (95%) of product **9c**, isolated as a linen solid: mp 210–211 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.44 (d, J = 6.8 Hz, 1H), 8.17 (dd, J = 5.2, 1.2 Hz, 1H), 8.11 (dd, J = 3.6, 1.2 Hz, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.66–7.63

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056–12070



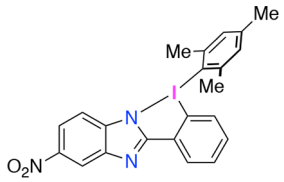
(m, 2H), 7.52−7.47 (m, 1H), 7.39 (dd, J = 5.2, 3.6 Hz, 1H), 7.19−7.17 (m, 2H), 6.95 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.4, 142.2, 138.1, 131.7, 130.9, 130.7, 130.3, 128.6, 127.9, 121.57, 121.55, 121.54, 116.8, 116.0, 107.4; HRMS (ESI-TOF-positive ionization): calcd for $C_{17}H_{12}IN_2S$ ([M + H]$^+$): 402.9760, found: 402.9762.

*5-(4-Methoxyphenyl)-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b][1,2]iodazole (**9d**).* Reaction of **8d** (0.115 g, 0.2 mmol) according to



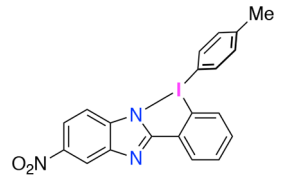
the general procedure afforded 0.080 g (94%) of product **9d** (contains 15% of ortho-isomer), isolated as a beige solid: mp 229−230 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.45 (d, J = 7.5 Hz, 1H), 8.28 (d, J = 8.5 Hz, 1H), 8.23 (d, J = 8.5 Hz, 2H), 8.05 (d, J = 8.0 Hz, 1H), 7.87 (m, 1H), 7.83 (t, J = 7.5 Hz, 1H), 7.75 (br. s, 2H), 7.62 (s, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.57−7.56 (m, 2H), 7.52 (d, J = 8.5 Hz, 1H), 7.40−7.38 (m, 2H), 7.26 (d, J = 8.5 Hz, 2H), 7.04 (d, J = 8.0 Hz, 1H), 7.01 (d, J = 8.0 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.2, 150.2, 140.1, 139.9, 133.6, 131.8, 131.7, 131.6, 130.7, 129.3, 128.6, 127.9, 124.3, 118.4, 115.1, 105.1, 56.3; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{16}IN_2O$ ([M + H]$^+$): 427.0302, found: 427.0304.

*5-Mesityl-9-nitro-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b][1,2]iodazole (**9e**).* Reaction of **8e** (0.127 g, 0.2 mmol) according to the



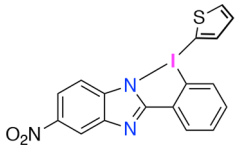
general procedure afforded 0.093 g (96%) of product **9e**, isolated as a light yellow solid: mp 237−238 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.55−8.52 (m, 2H), 8.12 (dd, J = 9.2, 2.4 Hz, 1H), 7.81−7.78 (m, 2H), 7.53 (t, J = 8.0 Hz, 1H), 7.36 (s, 2H), 6.89 (d, J = 8.4 Hz, 1H), 2.53 (s, 6H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 157.7, 157.6, 145.8, 143.7, 142.9, 142.0, 140.7, 134.0, 133.3, 132.7, 132.6, 131.8, 131.2, 130.48, 130.46, 130.3, 129.8, 129.2, 128.3, 127.6, 121.6, 111.9, 25.9, 20.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{19}IN_3O_2$ ([M + H]$^+$): 484.0516, found: 484.0526.

*5-(p-Tolyl)-9-nitro-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b][1,2]iodazole (**9f**).* Reaction of **8f** (0.121 g, 0.2 mmol) according to



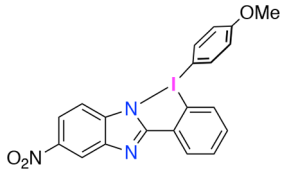
the general procedure afforded 0.076 g (83%) of product **9f** (contains 30% of ortho-isomer), isolated as a yellow solid: mp 208−209 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.57(d, J = 1.6 Hz, 1H), 8.54 (dd, J = 7.6, 1.6 Hz, 1H), 8.47 (d, J = 2.0 Hz, 1H), 8.32(d, J = 7.2 Hz, 1H), 8.17 (d, J = 8.4 Hz, 2H), 8.01 (dd, J = 8.8, 2.4 Hz, 1H), 7.74−7.67 (m, 3H), 7.51 (d, J = 8.0 Hz, 2H), 7.49−7.44 (m, 2H), 6.92 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H), 2.56 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.3, 143.1, 142.7, 142.1, 141.0, 139.0, 137.1, 133.4, 132.5, 132.3, 132.0, 131.7, 131.4, 130.8, 130.7, 129.4, 129.3, 129.2, 128.8, 121.7, 116.2, 116.0, 114.3, 113.9, 113.0, 112.7, 24.6, 21.2; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{15}IN_3O_2$ ([M + H]$^+$): 456.0203, found: 456.0208.

*5-(Thiophen-2-yl)-9-nitro-5H-5λ^3-benzo[d]benzo[4,5]imidazo-[1,2-b][1,2]iodazole (**9g**).* Reaction of **8g** (0.119 g, 0.2 mmol)



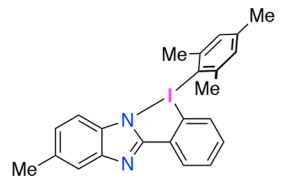
according to the general procedure afforded 0.082 g (92%) of product **9g**, isolated as a light yellow solid: mp 231−232 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.51 (dd, J = 6.0, 1.2 Hz, 2H), 8.29 (d, J = 6.4 Hz, 2H), 8.19 (dd, J = 5.2, 0.8 Hz, 1H), 8.13 (dd, J = 3.6, 0.8 Hz, 1H), 8.00 (dd, J = 8.8, 2.0 Hz, 1H), 7.74−7.68 (m, 2H), 7.54−7.50 (m, 1H), 7.41 (dd, J = 5.2, 3.6 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.6, 142.4, 141.0, 138.3, 132.1, 131.7, 130.9, 130.4, 128.6, 128.4, 117.0, 116.1, 112.75, 112.71, 112.0, 106.7; HRMS (ESI-TOF-positive ionization): calcd for $C_{17}H_{11}IN_3O_2S$ ([M + H]$^+$): 447.9611, found: 447.9617.

*5-(4-Methoxyphenyl)-9-nitro-5H-5λ^3-benzo[d]benzo[4,5]imidazo-[1,2-b][1,2]iodazole (**9h**).* Reaction of **8h** (0.124 g, 0.2 mmol)



according to the general procedure afforded 0.081 g (86%) of product **9h**, isolated as a yellow solid: mp 227−228 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.54 (d, J = 7.0 Hz, 1H), 8.46 (s, 1H), 8.20 (d, J = 8.0 Hz, 2H), 7.98 (d, J = 8.0 Hz, 1H), 7.70−7.65 (m, 2H), 7.46 (t, J = 7.5 Hz, 1H), 7.23 (d, J = 8.5 Hz, 2H), 6.92 (d, J = 8.5 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.4, 160.8, 149.6, 143.2, 140.7, 139.1, 132.1, 131.8, 130.5, 129.0, 128.0, 125.4, 117.6, 116.0, 115.8, 114.6, 112.7, 106.8, 55.7; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{15}IN_3O_3$ ([M + H]$^+$): 472.0158, found: 472.0154.

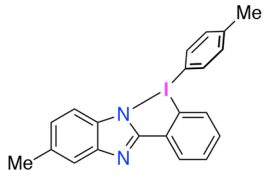
*5-Mesityl-9-methyl-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b][1,2]iodazole (**9i**).* Reaction of **8i** (0.120 g, 0.2 mmol) according to



the general procedure afforded 0.084 g (93%) of product **9i**, isolated as a creamy-white solid: mp 198−199 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.45 (d, J = 7.5 Hz, 1H), 7.77 (t, J = 7.5 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.48−7.46 (m, 2H), 7.34 (s, 2H), 7.11−7.09 (m, 1H), 6.86 (d, J = 8.6 Hz, 1H), 2.52 (s, 6H), 2.47 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 143.5, 142.8, 132.4, 131.1, 129.7, 128.9, 128.2, 128.04, 128.99, 127.6, 125.5, 124.1, 122.1, 111.4, 25.8, 21.4, 20.8; HRMS (ESI-TOF-positive ionization): calcd for $C_{23}H_{22}IN_2$ ([M + H]$^+$): 453.0822, found: 453.0826.

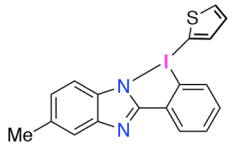
*5-(p-Tolyl)-9-methyl-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b][1,2]iodazole (**9j**).* Reaction of **8j** (0.115 g, 0.2 mmol) according to the general procedure afforded 0.071 g (84%) of product **9j**, isolated as a beige solid: mp 204−205 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.42 (d, J = 7.6 Hz, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 7.2 Hz, 1H), 7.57−7.48 (m, 3H), 7.40 (t, J = 7.6 Hz, 2H), 6.99 (d, J = 8.0 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 2.48 (s, 3H), 2.44 (s, 3H);

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070



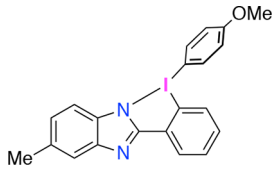
^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.9, 142.8, 141.9, 140.1, 137.1, 137.0, 136.9, 132.4, 131.4, 131.2, 131.1, 130.6, 129.4, 128.2, 123.0, 115.8, 115.6, 115.5, 114.7, 114.1, 21.5, 21.2.; HRMS (ESI-TOF-positive ionization): calcd for $C_{21}H_{18}IN_2$ ([M + H]$^+$): 425.0509, found: 425.0512.

*5-(Thiophen-2-yl)-9-methyl-5H-5λ^3-benzo[d]benzo[4,5]imidazo-[1,2-b][1,2]iodazole (**9k**).* Reaction of **8k** (0.113 g, 0.2 mmol)



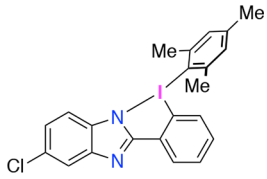
according to the general procedure afforded 0.077 g (93%) of product **9k**, isolated as a beige solid: mp 222−223 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.42 (d, J = 6.8 Hz, 1H), 8.21 (d, J = 4.8 Hz, 1H), 8.14 (d, J = 3.6 Hz, 1H), 7.79 (t, J = 7.6 Hz, 1H), 7.58−7.54 (m, 2H), 7.48 (s, 1H), 7.42 (dd, J = 5.2, 3.6 Hz, 1H), 7.14 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 142.9, 138.91, 138.89, 136.8, 132.70, 132.66, 132.3, 131.1, 130.4, 129.4, 129.1, 128.9, 128.2, 126.3, 116.7, 21.4; HRMS (ESI-TOF-positive ionization): calcd for $C_{18}H_{14}IN_2S$ ([M + H]$^+$): 416.9917, found: 416.9922.

*5-(4-Methoxyphenyl)-9-methyl-5H-5λ^3-benzo[d]benzo[4,5]-imidazo[1,2-b][1,2]iodazole (**9l**).* Reaction of **8l** (0.118 g, 0.2 mmol)



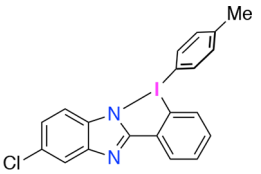
according to the general procedure afforded 0.073 g (83%) of product **9l** (contains 20% of ortho-isomer), isolated as a creamy-white solid: mp 235−236 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 13.81 (s, 1H), 13.76 (s, 1H), 8.43 (d, J = 7.6 Hz, 1H), 8.23 (dd, J = 9.2, 3.2 Hz, 2H), 8.07 (d, J = 8.0 Hz, 1H), 7.83 (t, J = 7.2 Hz, 1H), 7.67−7.51 (m, 3H), 7.44 (s, 1H), 8.32 (d, J = 8.0 Hz, 1H), 7.28−7.22 (m, 3H), 7.13 (d, J = 7.6 Hz, 1H), 7. Thirty (d, J = 8.4 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.8, 149.1, 148.9, 140.4, 139.7, 139.4, 138.3, 134.9, 134.5, 133.2, 132.9, 132.7, 131.1, 130.3, 128.7, 127.1, 125.2, 122.3, 121.5, 119.1, 118.0, 117.9, 114.7, 114.6, 114.4, 112.2, 112.1, 104.5, 104.4, 55.8, 21.4, 21.3; HRMS (ESI-TOF-positive ionization): calcd for $C_{21}H_{18}IN_2O$ ([M + H]$^+$): 441.0458, found: 441.0463.

*9-Chloro-5-mesityl-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b]-[1,2]iodazole (**9m**).* Reaction of **8m** (0.125 g, 0.2 mmol) according to



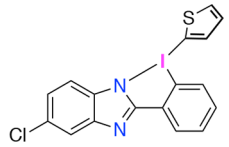
the general procedure afforded 0.087 g (92%) of product **9m**, isolated as a beige solid: mp 223−224 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.48 (dd, J = 7.6, 1.6 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.65−7.61 (m, 2H), 7.47−7.42 (m, 1H), 7.33 (s, 2H), 7.17 (dd, J = 8.8, 2.4 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 2.52 (s, 6H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 155.2, 143.8, 143.2, 141.1, 132.7, 131.9, 131.4, 130.2, 129.6, 128.4, 126.1, 122.8, 121.9, 117.7, 115.9, 115.8, 112.0, 26.3, 21.3; HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{19}ClIN_2$ ([M + H]$^+$): 473.0276, found: 473.0279.

*9-Chloro-5-(p-tolyl)-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b]-[1,2]iodazole (**9n**).* Reaction of **8n** (0.119 g, 0.2 mmol) according to



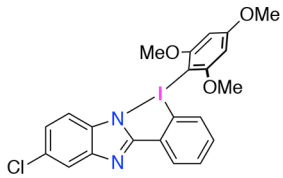
the general procedure afforded 0.079 g (89%) of product **9n** (contains 20% of ortho-isomer), isolated as a beige solid: mp 175−176 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.49 (s, 1H), 8.46 (dd, J = 7.5, 1.5 Hz, 1H), 8.28 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 8.0 Hz, 2H), 7.73−7.70 (m, 2H), 7.65 (t, J = 8.0 Hz, 1H), 7.57−7.54 (m, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.42−7.41 (m, 1H), 7.40−7.36 (m, 2H), 7.05 (dd, J = 8.5, 2.0 Hz, 1H), 6.86 (d, J = 8.0 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 2.54 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 156.7, 142.7, 142.0, 138.4, 137.0, 132.5, 132.3, 130.96, 130.64, 130.5, 129.0, 128.4, 124.3, 122.7, 120.1, 117.3, 115.6, 115.0, 114.1, 112.7, 24.5, 21.2; HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{15}ClIN_2$ ([M + H]$^+$): 444.9963, found: 444.9959.

*9-Chloro-5-(thiophen-2-yl)-5H-5λ^3-benzo[d]benzo[4,5]imidazo-[1,2-b][1,2]iodazole (**9o**).* Reaction of **8o** (0.117 g, 0.2 mmol)



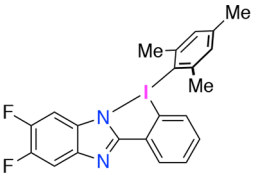
according to the general procedure afforded 0.083 g (95%) of product **9o**, isolated as a beige solid: mp 227−228 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.43 (d, J = 6.8 Hz, 1H), 8.20 (d, J = 4.8 Hz, 1H), 8.13 (d, J = 2.8 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.69−7.64 (m, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.41 (dd, J = 4.8, 4.0 Hz, 1H), 7.23 (dd, J = 8.4, 1.6 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 154.2, 142.7, 141.5, 139.5, 138.6, 132.4, 131.0, 130.4, 128.8, 128.3, 122.27, 122.16, 122.14, 116.8, 105.5; HRMS (ESI-TOF-positive ionization): calcd for $C_{17}H_{11}ClIN_2S$ ([M + H]$^+$): 436.9371, found: 436.9376.

*9-Chloro-5-(4-methoxyphenyl)-5H-5λ^3-benzo[d]benzo[4,5]-imidazo[1,2-b][1,2]iodazole (**9p**).* Reaction of **8p** (0.122 g, 0.2 mmol)



according to the general procedure afforded 0.084 g (91%) of product **9p**, isolated as a beige solid: mp 196−197 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.45 (d, J = 7.2 Hz, 1H), 8.15 (d, J = 8.4 Hz, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.54 (d, J = 9.2 Hz, 2H), 7.38 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 8.4 Hz, 2H), 7.04 (dd, J = 8.0, 0.8 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.2, 156.8, 144.91, 144.88, 142.68, 142.65, 139.0, 132.6, 130.9, 130.4, 128.9, 128.3, 124.2, 120.1, 117.4, 117.3, 115.6, 114.4, 107.8, 55.6. HRMS (ESI-TOF-positive ionization): calcd for $C_{20}H_{15}ClIN_2O$ ([M + H]$^+$): 460.9912, found: 460.9919.

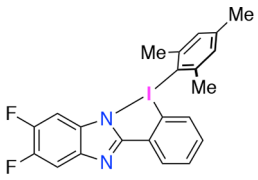
*9-Chloro-5-(2,4,6-trimethoxyphenyl)-5H-5λ^3-benzo[d]benzo-[4,5]imidazo[1,2-b][1,2]iodazole (**9q**).* Reaction of **8q** (0.115 g,



DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

0.2 mmol) according to the general procedure afforded 0.089 g (85%) of product **9q**, isolated as a beige solid: mp 178−179 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.44 (d, J = 5.6 Hz, 1H), 7.68 (t, J = 5.6 Hz, 1H), 7.61−7.58 (m, 2H), 7.43 (t, J = 6.0 Hz, 1H), 7.11 (d, J = 6.4 Hz, 1H), 6.99 (d, J = 6.4 Hz, 1H), 6.57 (s, 2H), 3.96 (s, 3H), 3.87 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.6, 161.1, 155.6, 131.8, 131.5, 130.6, 128.6, 127.8, 125.0, 120.9, 117.2, 115.5, 112.8, 92.0, 88.7, 57.0, 56.1; HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{19}ClIN_2O_3$ ([M + H]$^+$): 521.0123, found: 521.0121.

*8,9-Difluoro-5-mesityl-5H-5λ^3-benzo[d]benzo[4,5]imidazo[1,2-b][1,2]iodazole (**9r**).* Reaction of **8r** (0.125 g, 0.2 mmol) according to



the general procedure afforded 0.077 g (81%) of product **9r**, isolated as a light brown solid: mp 178−179 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.44 (d, J = 7.2 Hz, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 8.4 Hz, 2H), 7.31−7.27 (m, 3H), 6.72 (d, J = 8.0 Hz, 1H), 2.47 (s, 6H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.4, 146.8 (d, J_{C-F} = 17.5 Hz), 144.4 (d, J_{C-F} = 17.5 Hz), 142.9, 142.6, 134.2, 130.8, 130.7, 129.5, 128.6, 127.2, 123.2, 111.2, 102.8, 25.8, 20.8; ^{19}F NMR (376 MHz, DMSO-d_6): δ = −147.9; HRMS (ESI-TOF-positive ionization): calcd for $C_{22}H_{18}F_2IN_2$ ([M + H]$^+$): 475.0477, found: 475.0483.

COMPUTATIONAL DETAILS

All calculations were performed using Gaussian 09[22] by adapting a method described by Vasdev, Liang, and co-workers for a series of iodine(III)-containing species.[23]

Geometry Optimizations. All calculations were performed at the DFT level using the B3LYP functional with an ultrafine integration grid. The 6-31+G(d,p) basis set was used for C, H, O, and S, while using for iodine the augmented LANL2DZ(dp) set described by Gilbert, Sunderlin, and co-workers.[24] Empirical dispersion was applied using the D3 version of Grimme dispersion with Becke−Johnson damping (gd3BJ keyword).[25] All structures were fully optimized in DMSO using the SMD continuum model. Transition states were identified by having one imaginary frequency in the Hessian matrix. It was confirmed that transition states connect with the corresponding intermediates by means of application of the eigenvector corresponding to the imaginary frequency and subsequent optimization of the resulting structures. All energies collected in the text are Gibbs energies in solvent at 298 K.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b01995.

Copies of ^{1}H and ^{13}C NMR, details of computational studies, and ORTEP-style ellipsoid diagrams (PDF)
Crystallographic file for **6b** (CIF)
Crystallographic file for **7a** (CIF)
Crystallographic file for **8e** (CIF)
Crystallographic file for **8m** (CIF)

AUTHOR INFORMATION

Corresponding Authors

*E-mail: yusubov@mail.ru.
*E-mail: vzhdanki@d.umn.edu.

ORCID

Alexandr Shafir: 0000-0002-8127-2299
Viktor V. Zhdankin: 0000-0002-0315-8861

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by research grants from the Russian Science Foundation (RSF-17-73-20066) and the National Science Foundation (CHE-1759798). A.S. also acknowledges financial support from ICIQ and from Spain's MINECO (CTQ2017-86936-P).

REFERENCES

(1) For selected books and recent reviews, see: (a) Zhdankin, V. V. Iodine Heterocycles. *Adv. Heterocycl. Chem.* **2015**, *115*, 1−91. (b) Hypervalent Iodine Chemistry. In *Topics in Current Chemistry*; Wirth, T., Ed.; Springer: Switzerland, 2015; Vol. *373*. (c) Morimoto, K.; Dohi, T.; Kita, Y. Metal-free Oxidative Cross-Coupling Reaction of Aromatic Compounds Containing Heteroatoms. *Synlett* **2017**, *28*, 1680−1694. (d) Le Vaillant, F.; Waser, J. Decarboxylative Alkynylation and Cyanation of Carboxylic Acids using Photoredox Catalysis and Hypervalent Iodine Reagents. *Chimia* **2017**, *71*, 226−230. (e) Wang, X.; Studer, A. Iodine(III) Reagents in Radical Chemistry. *Acc. Chem. Res.* **2017**, *50*, 1712−1724. (f) Yoshimura, A.; Yusubov, M. S.; Zhdankin, V. V. Synthetic applications of pseudocyclic hypervalent iodine compounds. *Org. Biomol. Chem.* **2016**, *14*, 4771−4781. (g) Charpentier, J.; Früh, N.; Togni, A. Electrophilic Trifluoromethylation by Use of Hypervalent Iodine Reagents. *Chem. Rev.* **2015**, *115*, 650−682.

(2) For selected examples, see: (a) Sharma, A.; Hartwig, J. F. Metal-catalyzed azidation of tertiary C-H bonds suitable for late-stage functionalization. *Nature* **2015**, *517*, 600−604. (b) Krasutsky, A. P.; Kuehl, C. J.; Zhdankin, V. V. Direct azidation of adamantane and norbornane by stable azidoiodinanes. *Synlett* **1995**, *1995*, 1081−1082. (c) Alazet, S.; Le Vaillant, F.; Nicolai, S.; Courant, T.; Waser, J. Divergent Access to (1,1) and (1,2)-Azidolactones from Alkenes using Hypervalent Iodine Reagents. *Chem. - Eur. J.* **2017**, *23*, 9501−9504. (d) Rabet, P. T. G.; Fumagalli, G.; Boyd, S.; Greaney, M. F. Benzylic C−H Azidation Using the Zhdankin Reagent and a Copper Photoredox Catalyst. *Org. Lett.* **2016**, *18*, 1646−1649.

(3) For selected examples, see: (a) Hu, X.-H.; Yang, X.-F.; Loh, T.-P. Chelation-Assisted Rhodium-Catalyzed Direct Amidation with Amidobenziodoxolones: C(sp2)-H, C(sp3)-H, and Late-Stage Functionalizations. *ACS Catal.* **2016**, *6*, 5930−5934. (b) Zhdankin, V. V.; McSherry, M.; Mismash, B.; Bolz, J. T.; Woodward, J. K.; Arbit, R. M.; Erickson, S. 1-Amido-3-(1H)-1,2-benziodoxoles: stable amidoiodanes and reagents for direct amidation of organic substrates. *Tetrahedron Lett.* **1997**, *38*, 21−24.

(4) For selected examples, see: (a) Ma, B.; Lin, X.; Lin, L.; Feng, X.; Liu, X. Chiral N,N′-dioxide organocatalyzed asymmetric electrophilic α-cyanation of β-keto esters and β-keto amides. *J. Org. Chem.* **2017**, *82*, 701−708. (b) Le Vaillant, F.; Wodrich, M. D.; Waser, J. Room temperature decarboxylative cyanation of carboxylic acids using photoredox catalysis and cyanobenziodoxolones: a divergent mechanism compared to alkynylation. *Chem. Sci.* **2017**, *8*, 1790−1800. (c) Wang, Y.-F.; Qiu, J.; Kong, D.; Gao, Y.; Lu, F.; Karmaker, P. G.; Chen, F.-X. The direct electrophilic cyanation of β-keto esters and amides with cyano benziodoxole. *Org. Biomol. Chem.* **2015**, *13*, 365−368.

(5) For selected examples, see: (a) Hari, D. P.; Waser, J. Enantioselective Copper-Catalyzed Oxy-Alkynylation of Diazo Compounds. *J. Am. Chem. Soc.* **2017**, *139*, 8420−8423. (b) Shen, K.; Wang, Q. Copper-catalyzed aminoalkynylation of alkenes with hypervalent iodine reagents. *Chem. Sci.* **2017**, *8*, 8265−8270. (c) Wodrich, M. D.; Caramenti, P.; Waser, J. Alkynylation of Thiols

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

with Ethynylbenziodoxolone (EBX) Reagents: α- or β-π-Addition? *Org. Lett.* **2016**, *18*, 60−63.
(6) For selected examples, see: (a) Wang, M.; Zhang, Y.; Wang, T.; Wang, C.; Xue, D.; Xiao, J. Story of an Age-Old Reagent: An Electrophilic Chlorination of Arenes and Heterocycles by 1-Chloro-1,2-benziodoxol-3-one. *Org. Lett.* **2016**, *18*, 1976−1979. (b) Egami, H.; Yoneda, T.; Uku, M.; Ide, T.; Kawato, Y.; Hamashima, Y. Difunctionalization of Alkenes Using 1-Chloro-1,2-benziodoxol-3-(1*H*)-one. *J. Org. Chem.* **2016**, *81*, 4020−4030.
(7) 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.
(8) (a) Holland, P. C.; Clark, M. C.; Bloxham, D. P.; Lardy, H. A. Mechanism of action of the hypoglycemic agent diphenyleneiodonium. *J. Biol. Chem.* **1973**, *248*, 6050−6056. (b) Gatley, S. J.; Al-Bassam, S. S.; Taylor, J. R.; Sherratt, H. S. A. Inhibition of diphenyleneiodonium and by its substituted derivatives of gluconeogenesis in isolated rat hepatocytes. *Biochem. Soc. Trans.* **1975**, *3*, 333−335. (c) Holland, P. C.; Sherratt, H. S. A. Biochemical effects of the hypoglycemic compound diphenyleneiodonium. Catalysis of anion-hydroxyl ion exchange across the inner membrane of rat liver mitochondria and effects on oxygen uptake. *Biochem. J.* **1972**, *129*, 39−54. (d) Brosnan, M. J.; Hayes, D. J.; Challiss, R. A. J.; Radda, G. K. Diphenyleneiodonium-induced cardiomyopathy. *Biochem. Soc. Trans.* **1986**, *14*, 1209−1210. (e) Cooper, J. M.; Petty, R. K. H.; Hayes, D. J.; Challiss, R. A. J.; Brosnan, M. J.; Shoubridge, E. A.; Radda, G. K.; Morgan-Hughes, J. A.; Clark, J. B. An animal model of mitochondrial myopathy: a biochemical and physiological investigation of rats treated in vivo with the NADH-CoQ reductase inhibitor, diphenyleneiodonium. *J. Neurol. Sci.* **1988**, *83*, 335−347. (f) Cooper, J. M.; Petty, R. K. H.; Hayes, D. J.; Morgan-Hughes, J. A.; Clark, J. B. Chronic administration of the oral hypoglycemic agent diphenyleneiodonium to rats. An animal model of impaired oxidative phosphorylation (mitochondrial myopathy). *Biochem. Pharmacol.* **1988**, *37*, 687−694. (g) Doussiere, J.; Vignais, P. V. Inhibition of superoxide radical anion generating oxidase of neutrophils by iodonium biphenyl in a cell free system: effect of the redox state of the oxidase complex. *Biochem. Biophys. Res. Commun.* **1991**, *175*, 143−151. (h) Lee, H.-R.; Do, H.; Lee, S.-R.; Sohn, E.-S.; Pyo, S.; Son, E. Effects of fucoidan on neuronal cell proliferation: association with NO production through the iNOS pathway. *Prev. Nutr. Food Sci.* **2007**, *12*, 74−78.
(9) For representative examples, see: (a) Lien, G.-S.; Wu, M.-S.; Bien, M.-Y.; Chen, C.-H.; Lin, C.-H.; Chen, B.-C. Epidermal growth factor stimulates nuclear factor-κB activation and heme oxygenase-1 expression via c-Src, NADPH oxidase, PI3K and Akt in human colon cancer cells. *PLoS One* **2014**, *9*, e104891−e104815. (b) Song, S.-Y.; Jung, E. C.; Bae, C. H.; Choi, Y. S.; Kim, Y.-D. Visfatin induces MUC8 and MUC5B expression via p38 MAPK/ROS/NF-κB in human airway epithelial cells. *J. Biomed. Sci.* **2014**, *21*, 49. (c) Hino, S.; Kito, A.; Yokoshima, R.; Sugino, R.; Oshima, K.; Morita, T.; Okajima, T.; Nadano, D.; Uchida, K.; Matsuda, T. Discharge of solubilized and Dectin-1-reactive β-glucan from macrophage cells phagocytizing insoluble β-glucan particles: Involvement of reactive oxygen species (ROS)-driven degradation. *Biochem. Biophys. Res. Commun.* **2012**, *421*, 329−334. (d) Tsai, K.-H.; Wang, W.-J.; Lin, C.-W.; Pai, P.; Lai, T.-Y.; Tsai, C.-Y.; Kuo, W.-W. NADPH oxidase-derived superoxide Anion-induced apoptosis is mediated via the JNK-dependent activation of NF-κB in cardiomyocytes exposed to high glucose. *J. Cell. Physiol.* **2012**, *227*, 1347−1357. (e) Van De Veerdonk, F. L.; Smeekens, S. P.; Joosten, L. A. B.; Kullberg, B. J.; Dinarello, C. A.; Van Der Meer, J. W. M.; Netea, M. G. Reactive oxygen species-independent activation of the IL-1β inflammasome in cells from patients with chronic granulomatous disease. *Proc. Natl. Acad. Sci. U. S. A.* **2010**, *107*, 3030−3033.
(10) (a) Reich, H. J.; Cooperman, C. S. Structure and stereolability of triaryliodine (III) compounds. Degenerate isomerization of 5-phenyl-5H-dibenziodole. *J. Am. Chem. Soc.* **1973**, *95*, 5077−5078. (b) Beringer, F. M.; Chang, L. L. Electrophilic and homolytic cleavage of 5-aryl-5H-dibenziodoles. *J. Org. Chem.* **1971**, *36*, 4055−4060. (c) Beringer, F. M.; Chang, L. L. Exchange of aryl ligands to polyvalent iodine. *J. Org. Chem.* **1972**, *37*, 1516−1519.
(11) Wolf, W.; Steinberg, L. Benziodazole: a new heterocyclic ring system. *Chem. Commun.* **1965**, 449.
(12) Naae, D. G.; Gougoutas, J. Z. Novel heterocycle. Crystal structure and formation of N-chloro-3-aza-3H,2,1-benzoxiodol-1-yl chloride from the dichloride of o-iodobenzamide. *J. Org. Chem.* **1975**, *40*, 2129−2131.
(13) Balthazor, T. M.; Godar, D. E.; Stults, B. R. Synthesis and structure of benziodazoles. *J. Org. Chem.* **1979**, *44*, 1447−1449.
(14) (a) Zhdankin, V. V.; Arbit, R. M.; McSherry, M.; Mismash, B.; Young, V. G. Structure and chemistry of acetoxybenziodazole. Acid-catalyzed rearrangement of benziodazoles to 3-iminobenziodoxoles. *J. Am. Chem. Soc.* **1997**, *119*, 7408−7409. (b) Zhdankin, V. V.; Koposov, A. E.; Smart, J. T.; Tykwinski, R. R.; McDonald, R.; Morales-Izquierdo, A. Secondary Bonding-Directed Self-Assembly of Amino Acid Derived Benziodazoles: Synthesis and Structure of Novel Hypervalent Iodine Macrocycles. *J. Am. Chem. Soc.* **2001**, *123*, 4095−4096. (c) Zhdankin, V. V.; Koposov, A. Y.; Su, L.; Boyarskikh, V. V.; Netzel, B. C.; Young, V. G. Synthesis and structure of amino acid-derived benziodazoles: New hypervalent iodine heterocycles. *Org. Lett.* **2003**, *5*, 1583−1586.
(15) Gu, H.; Wang, C. Rhenium-catalyzed dehydrogenative olefination of C(sp3)-H bonds with hypervalent iodine(III) reagents. *Org. Biomol. Chem.* **2015**, *13*, 5880−5884.
(16) Yoshimura, A.; Shea, M. T.; Makitalo, C. L.; Jarvi, M. E.; Rohde, G. T.; Saito, A.; Yusubov, M. S.; Zhdankin, V. V. Preparation, structure, and reactivity of bicyclic benziodazole: a new hypervalent iodine heterocycle. *Beilstein J. Org. Chem.* **2018**, *14*, 1016−1020.
(17) Yamamoto, Y.; Togo, H. Facile one-pot preparation of [hydroxy(sulfonyloxy)iodo]arenes from iodoarenes with MCPBA in the presence of sulfonic acids. *Synlett* **2005**, 2486−2488.
(18) Dohi, T.; Yamaoka, N.; Kita, Y. Fluoroalcohols: versatile solvents in hypervalent iodine chemistry and syntheses of diaryliodonium(III) salts. *Tetrahedron* **2010**, *66*, 5775−5785.
(19) Wiberg, K. B.; Rablen, P. R.; Rush, D. J.; Keith, T. A. Amides. 3. Experimental and Theoretical Studies of the Effect of the Medium on the Rotational Barriers for N,N-Dimethylformamide and N,N-Dimethylacetamide. *J. Am. Chem. Soc.* **1995**, *117*, 4261−4270.
(20) Lim, C. J.; Kim, N.; Lee, E. K.; Lee, B. H.; Oh, K.-S.; Yoo, S.-e.; Yi, K. Y. Synthesis and SAR investigations of novel 2-arylbenzimidazole derivatives as melanin-concentrating hormone receptor 1 (MCH-R1) antagonists. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2309−2312.
(21) Hikawa, H.; Imani, M.; Suzuki, H.; Yokoyama, Y.; Azumaya, I. Benzoyl methyl phosphates as efficient reagents in the one-pot tandem approach for the synthesis of 2-phenylbenzimidazoles in water. *RSC Adv.* **2014**, *4*, 3768−3773.
(22) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision D.01*; Gaussian, Inc.: Wallingford, CT, 2009.
(23) Rotstein, B. H.; Wang, L.; Liu, R. Y.; Patteson, J.; Kwan, E. E.; Vasdev, N.; Liang, S. H. Mechanistic studies and radiofluorination of structurally diverse pharmaceuticals with spirocyclic iodonium(III) ylides. *Chem. Sci.* **2016**, *7*, 4407−4417.

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070

(24) Check, C. E.; Faust, T. O.; Bailey, J. M.; Wright, B. J.; Gilbert, T. M.; Sunderlin, L. S. Addition of Polarization and Diffuse Functions to the LANL2DZ Basis Set for P-Block Elements. *J. Phys. Chem. A* **2001**, *105*, 8111−8116.
(25) Grimme, S.; Ehrlich, S.; Goerigk, L. Effect of the damping function in dispersion corrected density functional theory. *J. Comput. Chem.* **2011**, *32*, 1456−1465.

DOI: 10.1021/acs.joc.8b01995
J. Org. Chem. 2018, 83, 12056−12070