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One-Pot Synthesis of Unsymmetric Diaryliodonium Salts from Iodine and Arenes

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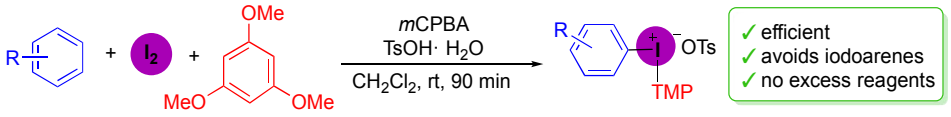
ABSTRACT

The first synthesis of unsymmetric diaryliodonium salts directly from iodine and arenes is presented. The methodology provides diaryliodonium salts with the trimethoxyphenyl (TMP) moiety as dummy group. The protocol avoids the customary use of iodoarenes, which can be both expensive and toxic. Excess reagents are not required, and the reactions are performed under mild conditions. *O*-Arylations with these TMP salts were demonstrated to be highly chemoselective.

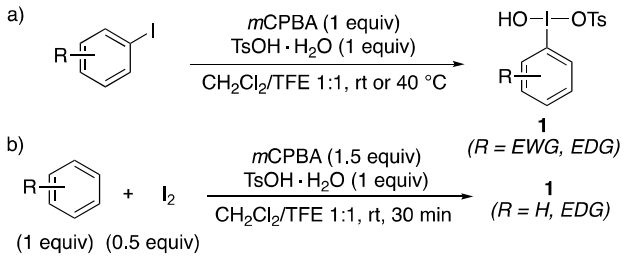


Diaryliodonium salts (diaryl-λ^3-iodanes) have become exceedingly popular electrophilic arylating reagents for a wide range of nucleophiles under both metal-free and metal-catalyzed conditions in the last decade.[1] The interest in applications with these hypervalent iodine reagents was accelerated by the development of novel synthetic routes to diaryliodonium salts, making these easily available at low cost. Our first contribution to this field was the development of a general one-pot route to diaryliodonium salts from iodoarenes using the reagent system *m*CPBA/triflic acid (TfOH) in dichloromethane, which delivered diaryliodonium triflates in high yields within short reaction times.[2] The reaction was extended to the direct synthesis of symmetric diaryliodonium salts from arenes and iodine, a cascade reaction involving iodination, oxidation and electrophilic aromatic substitution between the arene and the formed iodine(III) intermediate.[2]

The triflic acid system proved to be too reactive for the synthesis of iodonium salts with both aryl moieties substituted with electron-donating groups. Such diaryliodonium salts have previously been synthesized from [hydroxy(tosyloxy)iodo]benzene (HTIB, Koser's reagent) derivatives.[3] HTIB can be synthesized from the corresponding iodoarene using *m*CPBA/tosic acid,[4] and we recently improved the synthesis of HTIB derivatives **1** by two interconnected routes. They can either be obtained by *m*CPBA-oxidation of iodoarenes (Scheme 1a) or from iodine and arenes by initial oxidative iodination, followed by oxidation to yield **1** (Scheme 1b).[5] The iodination was found to

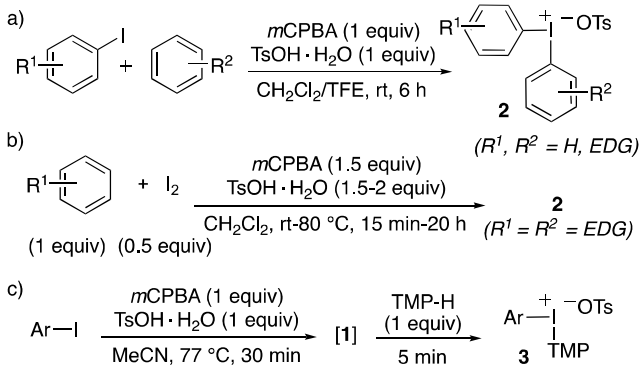
be the most difficult step in this sequence, limiting the substrate scope to arenes with electron-donating (EDG) substituents, and trifluoroethanol (TFE)[6] was employed as co-solvent to increase the reaction rates.

Scheme 1. Synthesis of [hydroxy(tosyloxy)iodo]arenes 1.[5]



To overcome the scope limitations in our *m*CPBA/triflic acid system, we developed a one-pot synthesis of electron-rich diaryliodonium salts **2** from iodoarenes, which likely proceeds via *in situ* formation of iodine(III) compounds **1** (Scheme 2a). That transformation could also be extended to the use of iodine and arenes as starting materials (Scheme 2b).[7] The latter route tolerated only arenes with EDG substituents, and the synthesis of unsymmetric diaryliodonium salts ($R^1 \neq R^2$) was unsuccessful due to product mixtures, further limiting the scope.[8]

Scheme 2. One-Pot Syntheses of Diaryliodonium Salts with *m*CPBA/TsOH [7, 9]



Stuart and coworkers later modified our *m*CPBA/TsOH conditions into a sequential one-pot reaction with iodoarenes and trimethoxybenzene (TMP-H) to obtain unsymmetric aryl(trimethoxyphenyl)iodonium salts **3** with a large scope (Scheme 2c).[9] Other oxidant systems have also been reported for one-pot syntheses, including $K_2S_2O_8$/TFA, Selectfluor™/TMSOTf and Oxone/TfOH.[10]

Arylations with symmetric diaryliodonium salts are straightforward, as only one aryl group can be transferred to the nucleophile.[1] Symmetric salts can, however, be difficult to prepare and sometimes require expensive boronic acids.

Furthermore, a potentially valuable iodoarene is wasted in the arylations. To avoid these drawbacks, we have thoroughly investigated the chemoselectivities in metal-free arylations with unsymmetric diaryliodonium salts.[11] While the anisyl dummy group was found to be sufficient in many applications,[1, 11-12] the use of the trimethoxyphenyl (TMP) dummy can sometimes increase the chemoselectivity further.[9, 11-12, 13]

DiMagno and Stuart have recently described one-pot protocols focused at the synthesis of unsymmetric diaryliodonium salts with anisyl and TMP dummies, respectively,[9, 10b, 14] but the synthesis of unsymmetric diaryliodonium salts from iodine and arenes has not been reported to date. We hence set out to develop such a one-pot synthesis of aryl(TMP)-iodonium salts, to circumvent the need for sometimes expensive and harmful iodoarenes.

To prevent the previous problems of product mixtures when using two different arenes,[2a, 7] our strategy involved careful control the stoichiometry of the reaction according to Scheme 1b, with sequential addition of the second arene. Furthermore, we wanted to avoid the co-solvent TFE to retard the final step in the sequence, when the arene reacts with iodine(III) intermediate **1**, although this would also slow down the formation of intermediate **1**. In this fashion, the reactive trimethoxybenzene (TMP-H) was expected to outperform the other arene (or iodoarene) as nucleophile in the last step.

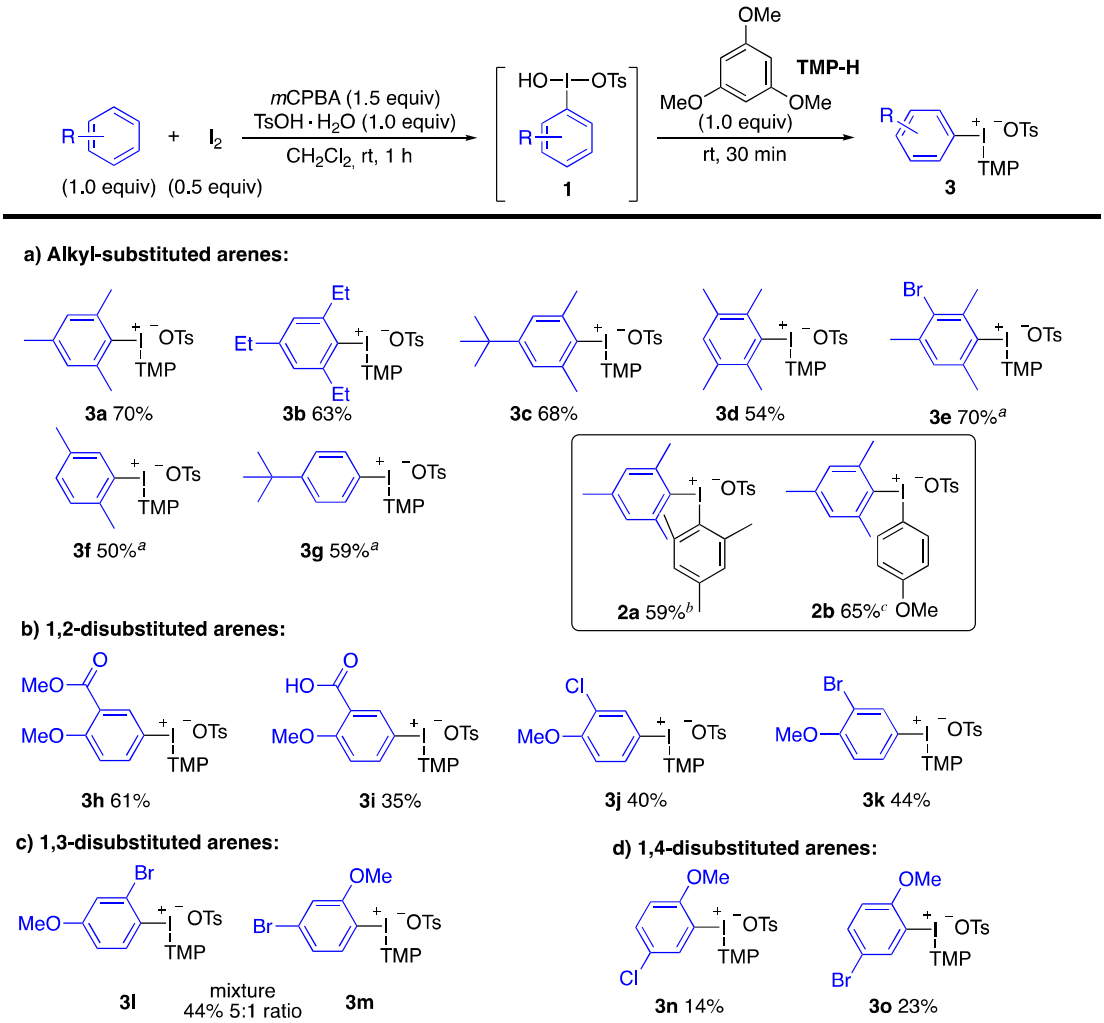
The reaction was investigated with mesitylene, and the formation of MesI(OH)OTs **1a** with *m*CPBA and tosic acid was performed using our previously reported conditions but without TFE.[5] The iodination and oxidation to **1a** was allowed to proceed for one hour, after which TMP-H was added. Under those conditions, mesityl(TMP)iodonium tosylate (**3a**) was isolated in 70% yield within 90 min at room temperature (Scheme 3). This should be compared to the symmetric dimesityliodonium tosylate (**2a**), which was obtained in 59% yield after 20 h reaction time using our previously reported method in Scheme 2b.[7] The difference in reaction times in the synthesis of **3a** and **2a** was reassuring and strengthened our hypothesis that product mixtures could be avoided in this fashion.

The substrate scope of the one-pot synthesis was subsequently investigated. The methodology proved compatible with a range of alkyl-substituted arenes, providing iodonium salts **3b**-**3g** in yields ranging from 50% to 70% (Scheme 3a). The reactions were all performed on a 2 mmol scale to demonstrate the ease of synthesis. The products were easily isolated by concentration and precipitation with diethyl ether.

Salts **3a**-**3e** have all four *ortho* positions substituted, which makes them of special interest in reactions where aryne formation poses a problem.[13b] Gratifyingly, the use of alkyl-substituted arenes that could be iodinated in different positions furnished products **3c** and **3g** with complete regioselectivity, both with the bulky *tert*-butyl group in the *para*

position. The synthesis of **3e-3g** benefitted from using TFE as co-solvent, as the purple iodine color remained in its absence. Despite our previous concerns, product mixtures were not obtained in TFE, illustrating the fine balance between the rates of the three reaction steps in this sequence.

Scheme 3. Scope of diaryliodonium salts from arenes and iodine



[a] CH_2Cl_2:TFE 1:1 was used. [b] 20 h reaction time using the conditions in Scheme 2b.[7] [c] Anisole (2.0 equiv) and additional TsOH (0.5 equiv) were added in the second step instead of TMP-H.

A series of disubstituted arenes was investigated next, to understand the regioselectivity of the reaction. The arenes were all decorated with one methoxy group to facilitate iodination, and a range of other substituents. Reactions with 1,2-disubstituted arenes proved completely regioselective, and provided *p*-methoxy iodonium salts **3h-3k** in moderate

yields (Scheme 3b). Ester, carboxylic acid and halide substituents were all tolerated, providing suitable handles for further transformation after arylations with these salts.

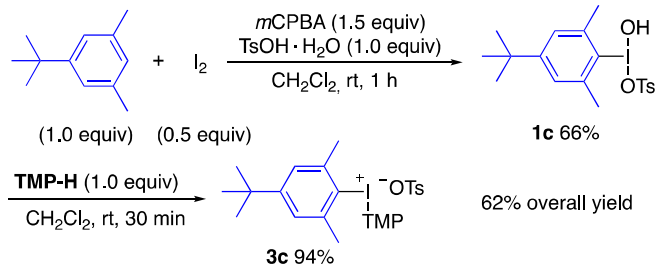
1,3-Disubstituted arenes proved more difficult, as exemplified with 3-bromoanisole (Scheme 3c). This reaction resulted in a mixture of salts **3l** and **3m** in a 5:1 ratio favoring the *para*-methoxy isomer. The third possible isomer, with both substituents *ortho*, was not observed. Finally, the corresponding 1,4-disubstituted arenes were investigated (Scheme 3d). As expected, these substrates reacted with complete regioselectivity, albeit salts **3n** and **3o** were formed in modest yields. The synthesis of **3o** was thus examined in acetonitrile at 77 °C (*cf* Scheme 2c),[9] but **3o** was not formed.

Some arenes were incompatible with the reaction, including benzene, fluorobenzene, acetanilide and 1,2-dimethoxybenzene. While no attempts were made to individually optimize the conditions for each arene, the methodology seems most suitable for arenes with moderately EDG substituents.[15] This can be explained by iodination of the arene being the most difficult step in this cascade reaction, resulting in retarded iodination of less reactive arenes. This conclusion is supported by the solution remaining purple, the negative result in acetonitrile, as well as the success in formation of Ph_2IOTs from iodobenzene but not from benzene in our previous report.[7] Reactions with highly reactive arenes, on the other hand, resulted in black reaction mixtures from which no iodonium salt could be precipitated.

As stated previously, iodonium salts with the anisyl dummy group give high chemoselectivity in many arylations. As the electron-rich TMP moiety is not tolerated in all arylations, we briefly investigated the use of anisole in the second step of the reaction with mesitylene and iodine. As expected, the lower nucleophilicity of anisole compared to TMP-H resulted in decreased reaction rate, which could be compensated by adding 2 equiv. anisole and more tosic acid to yield mesityl salt **2b** in 65% (Scheme 3, box).

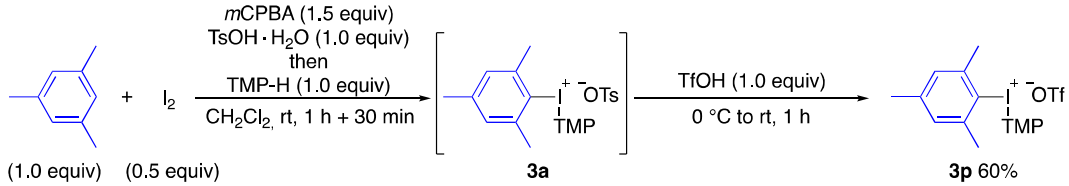
The efficiency of the one-pot synthesis of salt **3c** was compared with the step-wise synthesis with isolated **1c** (Scheme 4). The product was obtained in 62% overall yield, compared to 68% obtained with the one-pot reaction, further illustrating that the iodination is the most difficult step in the sequence, and that the TMP-H reaction is facile. With individual fine-tuning of the first part of the reaction, the yields can probably be considerably increased for some of salts **3**. Such optimization would include temperature, stoichiometry and using TFE as co-solvent. The use of TFE in the synthesis of **3b**, **3n** or **3o**, however, resulted in black reaction mixtures upon addition of TMP-H. The one-pot reaction is superior to the step-wise reaction both by avoiding problems associated with isolation of reagents **1**, such as instability and lack of crystallinity, and by giving higher yields of salts **3**.

Scheme 4. Step-wise synthesis of 3c.



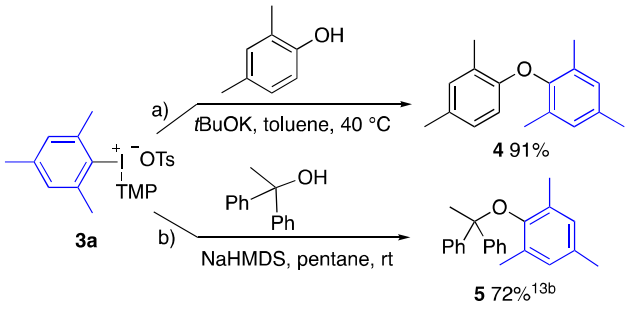
The nature of the counterion has shown to play an important role in many reactions employing diaryliodonium salts.[1] We therefore investigated the possibility of a one-pot anion exchange to the triflate counterion using our previously developed methodology (Scheme 5).[7] To our delight, addition of one equivalent of TfOH to the reaction mixture allowed the facile isolation of **3p** in 60% yield.

Scheme 5. *In situ* anion exchange from tosylate to triflate.



As described above, iodonium salts with a TMP dummy have resulted in highly chemoselective arylations with several nucleophiles, including enolates, phenols, hydroxyamides, alcohols, anilines, amines and azide.[9, 11-12, 13] The majority of the salts employed in those studies have had electron-withdrawing substituents, making the differences in electronic properties between the aryl groups wide. To the contrary, the aryl(TMP)iodonium salts synthesized with the present methodology have aryl groups with electron-donating substituents. To investigate the utility of these salts, a phenol was arylated with salt **3a** (Scheme 5a). The reaction indeed proved to be completely chemoselective, with diaryl ether **4** as the only observed product. Furthermore, we have recently demonstrated that salt **3a** gives excellent chemoselectivity in arylations of aliphatic alcohols,[13b] as exemplified by the synthesis of aryl ether **5** (Scheme 5b).

Scheme 5. Chemoselective arylations



To conclude, we have developed an efficient one-pot synthesis of unsymmetric diaryliodonium salts carrying the trimethoxyphenyl dummy group. The methodology employs iodine and arenes, hence avoiding the need for expensive and toxic iodoarenes. The conditions are mild, and the scope includes a variety of arenes with at least one electron-donating substituent, to ensure efficient iodination and oxidation to iodine(III) under the presented conditions. The efficacy in arylations with electron rich aryl(TMP) salts **3** has been demonstrated by chemoselective *O*-arylations of a phenol and an aliphatic alcohol.

EXPERIMENTAL SECTION

General Methods

Commercial CH_2Cl_2 (stabilized with ethanol), 2,2,2-trifluoroethanol and diethyl ether were used as received. Toluene was dried using a VAC purification system and stored over 4Å MS. Iodine, 2,4-dimethylphenol, *t*BuOK, *p*-toluenesulfonic acid monohydrate and all arenes were commercially available and used as received. *m*CPBA was purchased from commercial suppliers, then dried under vacuum at rt for 2-6 h and subsequently the percentage of active oxidizing reagent was determined by iodometric titration.[16] The aryl ether products were purified by flash column chromatography using automated flash system Teledyne ISCO CombiFlash Rf 200 with RediSep Rf columns. Melting points were measured using a STUART SMP3 and are reported uncorrected. All NMR spectra were recorded using a 400 MHz Bruker AVANCE II with a BBO probe at 298 K using $CDCl_3$, CD_3OD or DMSO-d_6 as solvents. Chemical shifts are given in ppm relative to the residual solvent peak (^{1}H NMR: $CDCl_3$ δ 7.26; CD_3OD 3.31; DMSO-d_6 2.50; ^{13}C NMR: $CDCl_3$ δ 77.16; CD_3OD 49.00 DMSO-d_6 39.52) with multiplicity (br = broad, s = singlet, d = doublet, dd = doublet of doublets, q = quartet, m = multiplet), coupling constants (in Hz) and integration. High-resolution mass analyses were obtained using a Bruker microTOF ESI.

General experimental procedure for synthesis of unsymmetric diaryliodonium salts 3. Iodine (0.5 equiv) was weighed into a round-bottomed flask or suitable vial to which CH_2Cl_2 (0.05 M) was added. *m*CPBA (1.5 equiv), arene

(1.0 equiv) and tosic acid (TsOH·H_2O 1.0 equiv) were added sequentially and the reaction mixture was stirred at ambient temperature for 1 h. The mixture gradually changed color from purple to yellow/clear solution or white precipitate, indicating formation of intermediate **1**. 1,3,5-Trimethoxybenzene (TMP-H, 1.0 equiv) was added in one portion and the resulting reaction mixture was stirred for additionally 30 min, after which the solvent was concentrated until signs of precipitation were seen. Diethyl ether (0.025 M) was added, the mixture was stirred at rt for 15 min and then kept in the freezer for 30 min. The resulting solid was filtered off, washed three times with diethyl ether, dried under water suction and further dried under high vacuum to afford the desired diaryliodonium tosylate.

Mesityl(4-methoxyphenyl)iodonium tosylate (2b). Synthesized according to general procedure using I_2 (587 mg, 2.3 mmol), mesitylene (0.64 mL, 4.6 mmol) and tosic acid (880 mg, 4.6 mmol) in CH_2Cl_2 (46 mL). Anisole (1.00 mL, 9.25 mmol) was added as the second arene, and after 15 min additional tosic acid ((440 mg, 2.3 mmol) was added. After the reaction the solvent was concentrated, still maintaining a homogenous solution, to which ether was added causing a precipitation of the desired compound. *Note:* The solution needs to be homogenous before addition of ether to ensure that the tosic acid remains in solution. **2b** was isolated as a white powder in 65% yield (1.57 g, 2.99 mmol). Spectral data matches literature.[17]

Mesityl(2,4,6-trimethoxyphenyl)iodonium tosylate (3a). Synthesized according to general procedure using using I_2 (511 mg, 2.0 mmol), mesitylene (0.56 mL, 4.0 mmol), tosic acid (766 mg, 4.0 mmol) and TMP-H (677 mg, 4.0 mmol) in CH_2Cl_2 (40 mL). The crude residue was precipitated from CH_2Cl_2 after initial trituration with ether. **3a** was isolated as a white powder in 70% yield (1.64 g, 2.81 mmol). Spectral data matches literature.[18]

(2,4,6-triethylphenyl)(2,4,6-trimethoxyphenyl)iodonium tosylate (3b). Synthesized according to general procedure using I_2 (761 mg, 3.0 mmol), 1,3,5-triethylbenzene (1.13 mL, 6.0 mmol), tosic acid (1.14 g, 6.0 mmol) and TMP-H (1.01 g, 6.0 mmol) in CH_2Cl_2 (60 mL). The crude residue was filtered through a basic alumina pad using 10% MeOH in acetone as eluent. **3b** was isolated as a white powder in 63% yield (2.36 g, 3.77 mmol). mp: 120-122 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.56 (d, J = 8.1 Hz, 2H), 7.00 (d, J = 7.9 Hz, 2H), 6.92 (s, 2H), 6.11 (s, 2H), 3.79 (s, 3H), 3.78 (s, 6H), 2.94 (q, J = 7.5 Hz, 4H), 2.58 (q, J = 7.6 Hz, 2H), 2.27 (s, 3H), 1.24-1.07 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 166.5, 160.3, 149.0, 147.5, 143.6, 138.8, 128.3, 127.0, 126.0, 122.5, 91.8, 82.3, 56.8, 56.1, 33.1, 28.5, 21.3, 15.2, 14.9; HRMS (ESI): calcd for $C_{21}H_{28}IO_3$ [M OTs]$^+$: 455.1078; found 455.1081.

(4-(*tert*-butyl)-2,6-dimethylphenyl)(2,4,6-trimethoxyphenyl)iodonium tosylate (3c). Synthesized according to general procedure using I_2 (508 mg, 2.0 mmol), 1-(*tert*-butyl)-3,5-dimethylbenzene (0.75 mL, 4.0 mmol), tosic acid

(761 mg, 4.0 mmol) and TMP-H (673 mg, 4.0 mmol) in CH_2Cl_2 (40 mL). **3c** was isolated as yellow powder in 68% yield (1.71 g, 2.72 mmol). mp: 175-177 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.09 (s, 2H), 7.05 (d, *J* = 8.2 Hz, 2H), 6.13 (s, 2H), 3.83 (s, 9H) (*Overlapping peaks*), 2.64 (s, 6H), 2.25 (s, 3H), 1.25 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 166.4, 160.6, 155.5, 143.2, 142.3, 139.2, 128.5, 126.2, 126.2, 122.3, 91.8, 82.6, 56.7, 56.0, 34.8, 31.2, 27.1, 21.4; HRMS (ESI): calcd for $C_{21}H_{28}IO_3$ [M OTs]$^+$: 455.1078; found 455.1080.

(2,3,5,6-tetramethylphenyl)(2,4,6-trimethoxyphenyl)iodonium tosylate (3d). Synthesized according to general procedure using using I_2 (270 mg, 1.1 mmol), 1,2,4,5-tetramethylbenzene (286 mg, 2.1 mmol), tosic acid (405 mg, 2.1 mmol) and TMP-H (358 mg, 2.1 mmol) in CH_2Cl_2 (20 mL). **3d** was isolated as slightly purple powder in 54% yield (686 mg, 1.15 mmol). mp: 156 °C (decomp); ^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 7.46 (d, *J* = 7.8 Hz, 2H), 7.18 (s, 1H), 7.10 (d, *J* = 7.8 Hz, 2H), 6.43 (s, 2H), 3.89 (s, 6H), 3.84 (s, 3H), 2.54 (s, 6H), 2.28 (s, 3H), 2.29 (s, 6H); ^{13}C{^{1}H} NMR (DMSO-*d*$_6$, 100 MHz) δ 165.8, 159.6, 145.8, 137.5, 137.4, 135..7, 134.8, 128.9, 128.0, 125.5, 92.2, 84.6, 57.0, 56.1, 23.9, 21.0, 20.8; HRMS (ESI): calcd for $C_{19}H_{24}IO_3$ [M OTs]$^+$: 427.0765; found 427.0758.

(3-bromo-2,4,6-trimethylphenyl)(2,4,6-trimethoxyphenyl)iodonium tosylate (3e). Synthesized according to general procedure using I_2 (520 mg, 2.0 mmol), 2-bromomesitylene (0.63 mL, 4.1 mmol), tosic acid (779 mg, 4.1 mmol) and TMP-H (689 mg, 4.1 mmol) in CH_2Cl_2 (20 mL) and TFE (20 mL). The crude residue was precipitated with ether after dissolved in CH_2Cl_2/MeOH after initial trituration with ether. **3e** was isolated as a white powder in 70% yield (1.9 g, 2.86 mmol). Spectral data matches literature.[13b]

(2,5-dimethylphenyl)(2,4,6-trimethoxyphenyl)iodonium tosylate (3f). Synthesized according to general procedure I_2 (508 mg, 2.0 mmol), 1,3-dimethylbenzene (0.49 mL, 4.0 mmol), tosic acid (761 mg, 4.0 mmol) and TMP-H (673 mg, 4.0 mmol) in CH_2Cl_2 (20 mL) and TFE (20 mL).. The crude residue was precipitated with ether after dissolved in CH_2Cl_2/MeOH after initial trituration with ether. **3f** was isolated as a grey powder in 50% yield (1.15 g, 2.02 mmol). mp: 146-148 °C; ^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 7.87 (s, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 2H), 6.44 (s, 2H), 3.95 (s, 6H), 3.85 (s, 3H), 2.54 (s, 3H), 2.28 (s, 6H); ^{13}C{^{1}H} NMR (DMSO-*d*$_6$, 100 MHz) δ 165.9, 159.4, 145.8, 138.5, 137.5, 137.3, 137.1, 132.9, 130.7, 128.0, 125.5, 121.1, 92.1, 86.5, 57.1, 56.1, 24.2, 20.8, 20.0; HRMS (ESI): calcd for $C_{17}H_{20}IO_3$ [M OTs]$^+$: 399.0452; found 399.0440.

(4-(*tert*-butyl)phenyl)(2,4,6-trimethoxyphenyl)iodonium tosylate (3g). Synthesized according to general procedure using I_2 (566 mg, 2.2 mmol), *tert*-butylbenzene (0.69 mL, 4.5 mmol), tosic acid (848 mg, 4.5 mmol) and TMP-H (750

mg, 4.5 mmol) in CH_2Cl_2 (20 mL) and TFE (20 mL).. The crude residue was precipitated with ether after dissolved in CH_2Cl_2/MeOH after initial trituration with ether. **3g** was isolated as a grey powder in 59% yield (1.57 g, 2.62 mmol). Spectral data matches literature.[9]

4-methoxy-3-methoxycarbonylphenyl(2,4,6-trimethoxyphenyl)iodonium tosylate (3h). Synthesized according to general procedure using I_2 (139 mg, 0.55 mmol), methyl 2-methoxybenzoate (0.15 mL, 1.1 mmol), tosic acid (208 mg, 1.1 mmol) and TMP-H (184 mg, 1.1 mmol) in CH_2Cl_2 (11 mL). **3h** was isolated as a white powder in 61% yield (418 mg, 0.66 mmol). mp: 186-189 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.20 (d, *J* = 2.3 Hz, 1H), 8.10 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 2H), 7.06 (d, *J* = 7.8 Hz, 2H), 6.90 (d, *J* = 9.1 Hz, 1H), 6.13 (s, 2H), 3.87 (s, 6H), 3.86 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H) *Overlapping peaks!*, 2.30 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 167.0, 164.6, 161.5, 160.5, 143.2, 140.4, 139.3, 138.0, 128.5, 126.1, 122.6, 115.0, 104.0, 91.7, 84.8, 57.0, 56.5, 56.1, 52.6, 21.4; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.17 (d, *J* = 2.4 Hz, 1H), 8.03 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 9.0 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 2H), 6.46 (s, 2H), 3.95 (s, 6H), 3.86 (s, 3H), 3.85 (s, 3H), 3.81 (s, 3H), 2.28 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ 166.1, 164.3, 160.2, 159.2, 145.8, 139.7, 137.5, 136.9, 128.0, 125.5, 122.3, 115.8, 104.5, 92.1, 87.6, 57.3, 56.4, 56.2, 52.5, 20.8; HRMS (ESI): calcd for $C_{18}H_{20}IO_6$ [M OTs]$^+$: 459.0299; found 459.0288.

3-carboxy-4-methoxyphenyl(2,4,6-trimethoxyphenyl)iodonium tosylate (3i). Synthesized according to general procedure using I_2 (139 mg, 0.55 mmol), 2-methoxybenzoic acid (167 mg, 1.1 mmol), tosic acid (208 mg, 1.1 mmol) and TMP-H (184 mg, 1.1 mmol) in CH_2Cl_2 (11 mL). The crude residue was precipitated with ether after dissolved in CH_2Cl_2/MeOH after initial trituration with ether. **3i** was isolated as a pale yellow powder in 35% yield (236 mg, 0.38 mmol). mp: 181-182 °C (decomp); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 13.17 (br s, 1H), 8.12 (d, *J* = 2.4 Hz, 1H), 8.00 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 9.0 Hz, 1H), 7.1 (d, *J* = 8.0 Hz, 2H), 6.46 (s, 2H), 3.95 (s, 6H), 3.86 (s, 3H), 3.84 (s, 3H), 2.28 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ 166.1, 165.4, 160.2, 159.2, 145.8, 139.3, 137.5, 136.7, 128.0, 125.5, 123.8, 115.7, 104.4, 92.1, 87.6, 57.3, 56.3, 56.2, 20.8; HRMS (ESI): calcd for $C_{17}H_{18}IO_6$ [M OTs]$^+$: 445.0143; found 445.0134.

3-chloro-4-methoxyphenyl(2,4,6-trimethoxyphenyl)iodonium tosylate (3j). Synthesized according to general procedure using I_2 (136 mg, 0.54 mmol), 2-chloroanisole (0.14 mL, 1.1 mmol), tosic acid (203 mg, 1.1 mmol) and TMP-H (180 mg, 1.1 mmol) in CH_2Cl_2 (11 mL). The crude residue was precipitated with ether after dissolved in CH_2Cl_2/MeOH after initial trituration with ether. **3j** was isolated as a white powder in 40% yield (259 mg, 0.43 mmol). mp: 196-197 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) d, *J* = 2.2 Hz, 1H), 7.84 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.46

(d, *J* = 8.0, 2H), 7.21 (d, *J* = 8.9 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.46 (s, 2H), 3.95 (s, 6H), 3.88 (s, 3H), 3.86 (s, 3H), 2.28 (s, 3H); $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 100 MHz) δ 166.6, 159.7, 157.6, 146.3, 138.0, 135.7, 135.6, 128.5, 126.0, 123.3, 116.0, 105.1, 92.5, 88.1, 57.8, 57.1, 56.6, 21.2; HRMS (ESI): calcd for $C_{16}H_{17}ClIO_4$ [M − OTs]$^+$: 434.9855; found 434.9850.

3-bromo-4-methoxyphenyl(2,4,6-trimethoxyphenyl)iodonium tosylate (3k). Synthesized according to general procedure using. I_2 (136 mg, 0.54 mmol), 2-bromoanisole (0.14 mL, 1.1 mmol), tosic acid (204 mg, 1.1 mmol) and TMP-H (180 mg, 1.1 mmol) in CH_2Cl_2 (11 mL). **3k** was isolated as a white powder in 44% yield (308 mg, 0.47 mmol). mp: 188-191 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.12 (d, *J* = 2.2 Hz, 1H), 7.87 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 8.9 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.46 (s, 2H), 3.95 (s, 6H), 3.85 (s, 3H), 3.85 (s, 3H), 2.28 (s, 3H); $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 100 MHz) δ 166.1, 159.2, 158.0, 145.8, 138.0, 137.5, 135.7, 128.0, 125.5, 115.4, 112.3, 105.1, 92.1, 87.7, 57.3, 56.8, 56.2, 20.8; HRMS (ESI): calcd for $C_{16}H_{17}BrIO_4$ [M − OTs]$^+$: 478.9349; found 478.9340.

2-bromo-4-methoxyphenyl(2,4,6-trimethoxyphenyl)iodonium tosylate (3l) and **4-bromo-2-methoxyphenyl(2,4,6-trimethoxyphenyl)iodonium tosylate (3m)**. Synthesized according to general procedure using I_2 (140 mg, 0.55 mmol), 3-bromoanisole (0.14 mL, 1.1 mmol), tosic acid (212 mg, 1.1 mmol) and TMP-H (186 mg, 1.1 mmol) in CH_2Cl_2 (10 mL). **3l** and **3m** were isolated as a 5:1 mixture as a yellow powder in 40% yield (288 mg, 0.44 mmol). *NMR Data for major isomer:* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.05 (d, *J* = 8.9 Hz, 1H), 7.49-7.42 (m, 3H), 7.10 (d, *J* = 7.8 Hz, 2H), 6.98 (dd, *J* = 8.0, 2.8 Hz, 1H), 6.43 (s, 2H), 3.93 (s, 6H), 3.85 (s, 3H), 3.80 (s, 3H), 2.28 (s, 3H); $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 100 MHz) δ 166.1, 162.5, 159.4, 145.9, 140.1, 137.5, 128.0, 127.9, 125.5, 118.7, 116.3, 111.3, 91.9, 57.1, 56.1, 56.1, 20.8.

(5-chloro-2-methoxyphenyl)(2,4,6-trimethoxyphenyl)iodonium tosylate (3n). Synthesized according to general procedure using I_2 (126 mg, 0.50 mmol), 4-chloroanisole (0.12 mL, 1.0 mmol), tosic acid (189 mg, 1.0 mmol) and TMP-H (167 mg, 1.0 mmol) in CH_2Cl_2 (10 mL). **3n** was isolated as a grey powder in 14% yield (86 mg, 0.14 mmol). mp: 158-159 °C; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.81 (d, *J* = 2.5 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.57 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.24-7.18 (m, 3H), 6.41 (s, 2H), 3.97 (s, 6H), 3.94 (s, 3H), 3.89 (s, 3H), 2.36 (s, 3H); $^{13}C\{^{1}H\}$ NMR (MeOH-d_4, 100 MHz) δ 168.8, 161.6, 157.4, 143.6, 141.6, 136.2, 135.1, 129.8, 128.0, 126.9, 114.6, 105.6, 92.9, 84.9, 57.9, 57.7, 56.7, 21.3; HRMS (ESI): calcd for $C_{16}H_{17}ClIO_4$ [M − OTs]$^+$: 434.9855; found 434.9839.

(5-bromo-2-methoxyphenyl)(2,4,6-trimethoxyphenyl)iodonium tosylate (3o). Synthesized according to general procedure using I_2 (138 mg, 0.54 mmol), 4-bromoanisole (0.14 mL, 1.1 mmol), tosic acid (207 mg, 1.1 mmol) and TMP-H (183 mg, 1.1 mmol) in CH_2Cl_2 (10 mL). **3o** was isolated as a yellow powder in 23% yield (165 mg, 0.25 mmol). mp: 172 °C (decomp); ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.94 (d, J = 2.4 Hz, 1 H), 7.72-7.66 (m, 3H), 7.21 (d, J = 7.9 Hz, 2H), 7.15 (d, J = 8.9 Hz, 1H), 6.41 (s, 2H), 3.96 (s, 6H), 3.93 (s, 3H), 3.89 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (MeOH-d_4, 100 MHz) δ 168.8, 161.6, 157.8, 143.6, 141.6, 139.0, 138.1, 129.8, 126.9, 115.4, 114.6, 106.5, 92.9, 84.9, 57.9, 57.7, 57.7, 21.3; HRMS (ESI): calcd for $C_{16}H_{17}BrIO_4$ [M OTs]$^+$: 478.9349; found 478.9341.

4-(*tert*-butyl)-2,6-dimethyl(hydroxy)(tosyloxy)iodobenzene (1c). Synthesized according to the general procedure except no second arene was added and the reaction time was limited to 1 h at RT, .starting from I_2 (635 mg, 2.5 mmol), *tert*-butylbenzene (0.94 mL, 5.0 mmol), and tosic acid (951 mg, 5.0 mmol) in CH_2Cl_2 (40 mL). The product was precipitated using a mixture of ether and pentane and was isolated as a white powder in 66% yield (1.56 g, 3.27 mmol). mp: 133 °C (decomp); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, J = 8.1 Hz, 2H), 7.18 (s, 2H), 7.05 (d, J = 8.1 Hz, 2H), 4.90 (br s, 1H), 2.68 (br s, 6H), 2.34 (s, 3H), 1.33 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 157.5, 141.9, 141.3, 139.3, 129.0, 126.0, 125.7, 35.1, 31.2, 26.9, 21.5 Note: *The C-I carbon could not be observed.* HRMS (ESI): calcd for $C_{12}H_{18}IO$ [M OTs]$^+$: 305.0397; found 305.0392.

Mesityl(2,4,6-trimethoxyphenyl)iodonium triflate (3p). Synthesized according to general procedure using using I_2 (251 mg, 1.0 mmol), mesitylene (0.28 mL, 2.0 mmol), tosic acid (376 mg, 2.0 mmol) and TMP-H (333 mg, 2.0 mmol) in CH_2Cl_2 (20 mL). The crude mixture was cooled to 0 °C and triflic acid (0.18 mL, 2.0 mmol) was added drop-wise followed by stirring at RT for 1 h. The crude residue was precipitated from CH_2Cl_2 after initial trituration with ether. **3a** was isolated as a white powder in 60% yield (0.66 g, 1.2 mmol). mp: 140-141 °C (decomp); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.13 (s, 2H), 6.44 (s, 2H), 3.90 (s, 6H), 3.85 (s, 3H), 2.56 (s, 6H), 2.26 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ 165.8, 159.6, 142.2, 141.7, 129.3 121.7, 120.7 (q, J = 321 Hz), 92.2, 84.3, 57.0, 56.1, 25.7, 20.4; ^{19}F NMR (DMSO-d_6, 337 MHz) -77.8. HRMS (ESI): calcd for $C_{18}H_{22}IO_3$ [M OTf]$^+$: 413.0608; found 413.0612.

2,4-Dimethylphenyl(2,4,6-trimethylphenyl) ether (4). Synthesized according to literature procedure.[19] Isolated as a transparent oil in 91% yield (109 mg, 0.45 mmol). Spectral data matches literature.[20]

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Notes
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ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/joc.xxxxxx: Copies of the ^{1}H and ^{13}C NMR spectra of all products (PDF).

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