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# One-Pot Synthesis of Diaryliodonium Salts using Toluenesulphonic Acid: A Fast Entry to Electron-Rich Diaryliodonium Tosylates and Triflates

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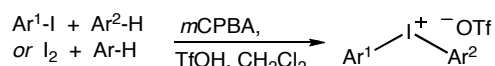
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**Abstract:** A direct synthesis of symmetric and unsymmetric electron-rich diaryliodonium salts is described. The use of *m*CPBA and toluenesulphonic acid delivers diaryliodonium tosylates in high yields. An *in situ* anion exchange has also been developed, giving access to the corresponding triflate salts.

**Key words:** Hypervalent iodine, Diaryliodonium salts, Oxidations, Arenes, Electrophilic aromatic substitutions.

Hypervalent iodine compounds have recently received considerable attention as mild, non-toxic and selective reagents.<sup>1, 2</sup> Iodine(III) reagents with two carbon ligands have similar properties to certain transition metal complexes, and can be used in C-C bond forming reactions.<sup>2</sup> Diaryl- $\lambda^3$ -iodanes, also called diaryliodonium salts, are the most well-known compounds in this class. Due to their highly electron-deficient nature and hyperleaving group ability, they are versatile arylating agents with a variety of nucleophiles, *e. g.* in  $\alpha$ -arylation of carbonyl compounds.<sup>3</sup> They can be employed in copper- and palladium-catalyzed cross-coupling reactions, allowing milder reaction conditions than in couplings with aryl halides.<sup>4</sup> Furthermore, diaryliodonium salts are used to generate benzyne<sup>5</sup> and serve as photo initiators in polymerizations.<sup>6</sup>

Synthetic routes to diaryliodonium salts generally require several reaction steps that often are time-consuming and moderate yielding.<sup>7, 8</sup> In order to make these efficient arylating agents more easily available, we have recently developed a high-yielding one-pot synthesis of diaryliodonium triflates from arenes and aryl iodides or molecular iodine (Equation 1).<sup>9</sup> This procedure is quite general, but fails in the synthesis of symmetric, electron-rich salts. We thus set out to find suitable conditions for a one-pot synthesis of electron-rich salts, and herein present our preliminary results.



**Equation 1** Synthesis of diaryliodonium triflates.

Acids with higher  $\text{pK}_a$  than TfOH were expected to promote the reaction with less byproduct formation. A screening with molecular iodine, anisole, *m*CPBA<sup>10</sup> and various acids revealed that this indeed was the case (Table 1, entries 1-5). Although perchloric acid had shown promising results with other substrates,<sup>11</sup> it was too reactive to allow formation of the di(4-methoxyphenyl)iodonium salt. Useful yields were obtained with

toluenesulphonic acid (tosic acid, TsOH) and trifluoroacetic acid (TFA), and the reaction was subsequently optimized with TsOH (entries 6-9).<sup>12</sup> The use of elevated temperature delivered di(4-methoxy-phenyl)iodonium tosylate (**2a**) in 73% yield within 10 minutes (entry 3). Although the reaction was considerably slower at room temperature, the yield was improved to 89% yield (entry 6). The amount of tosic acid was subsequently investigated, and 3 equiv was found sufficient to obtain **2a** in high yield (entries 7-9). Interestingly, the product seems to decompose slowly upon prolonged heating (*cf* entries 7, 8).

**Table 1** Screening of acids and optimization.<sup>a</sup>

Entry	Acid (equiv.)	Conditions	Anion (X)	Yield (%) <sup>b</sup>
1	TfOH (4)	0 °C, 10 min	OTf	0 <sup>c</sup>
2	HClO <sub>4</sub> (4)	rt, 30 min	ClO <sub>4</sub>	0 <sup>c</sup>
3	TsOH (4)	80 °C, 10 min	OTs	73
4	TFA (6)	60 °C, 30 min	O <sub>2</sub> CCF <sub>3</sub>	64
5	AcOH (6)	60 °C, 1 h	OAc	0
6	TsOH (4)	rt, 14 h	OTs	89
7	TsOH (2)	rt, 14 h	OTs	75
8	TsOH (2)	80 °C, 14 h	OTs	61
9	TsOH (3)	rt, 14 h	OTs	87

<sup>a</sup> 1 equiv I<sub>2</sub>, 4 equiv anisole and 3 equiv. *m*CPBA in CH<sub>2</sub>Cl<sub>2</sub> were used in all reactions.

<sup>b</sup> Isolated yield.

<sup>c</sup> Black tar was formed, no product could be isolated.

The optimized conditions were subsequently applied to various arenes, as depicted in Table 2. Thiophene gave salt **2b** in good yield both at rt and 40 °C (entries 2, 3). As expected, the reactivity of alkyl-substituted arenes was lower, and elevated temperature was needed to obtain salts **2d-2f** (entries 5-8). Toluene gave a regioisomeric mixture of symmetric salt **2f** and (2-methylphenyl)(4-methylphenyl)iodonium salt **2g** in a 2:1 ratio, resulting from iodination *para* and *ortho* to the methyl substituent, respectively (entry 8). All other products were obtained completely regioselectively.

The use of 2,2,2-trifluoroethanol (TFE) has recently been reported to enhance the reaction rate of iodine(III) compounds with arenes.<sup>13</sup> Although pure TFE proved inefficient in our system, the use of a 1:1 mixture of TFE and CH<sub>2</sub>Cl<sub>2</sub> resulted in higher yields than pure CH<sub>2</sub>Cl<sub>2</sub> for some salts (see entry 7 and Table 3). Our standard

purification of diaryliodonium triflates<sup>9</sup> could not be employed on salts **2**, since the excess tosic acid precipitated with the iodonium salt upon treatment with diethyl ether. The products were thus purified by column chromatography instead.

Table 2 Application to various arenes.<sup>a</sup>

Entry	Arene (1)	Conditions	Product 2	Yield (%) <sup>b</sup>
1	PhOMe (1a)	rt, 14 h		89
2	thiophene (1b)	rt, 14 h		66
3	thiophene (1b)	40 °C, 15 min		68
4	mesitylene (1c)	rt, 20 h		59
5	p-xylene (1d)	80 °C, 1 h		66
6	Ph'Bu (1e)	rt, 18 h		10
7 <sup>c</sup>	Ph'Bu (1e)	80 °C, 30 min		76
8	PhMe (1f)	80 °C, 10 min		49 <sup>d</sup>
9	PhH (1g)	80 °C, 1 h		0 <sup>e</sup>

<sup>a</sup> 1 equiv I<sub>2</sub>, 4 equiv arene, 3 equiv. mCPBA and 3-4 equiv TsOH were used in all reactions.

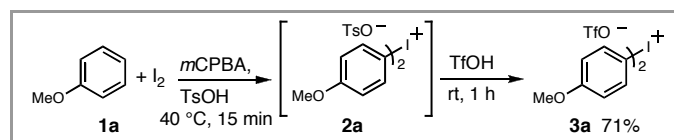
<sup>b</sup> Isolated yield of **2**.

<sup>c</sup> TFE was used as co-solvent.

<sup>d</sup> Regioisomeric mixture 2:1, see text.

<sup>e</sup> No reaction took place.

Diaryliodonium triflates are more easily applicable than tosylate salts, due to the non-nucleophilic properties of the triflate anion.<sup>4</sup> Thus, we subsequently investigated an *in situ* anion exchange of salt **2a** to the corresponding triflate salt **3a** (Equation 2). Fortunately, addition of 2.5 equiv triflic acid to the reaction mixture after complete conversion to the tosylate salt followed by 1 h stirring at room temperature resulted in **3a** in 71% yield. This *in situ* anion exchange should be generally applicable to synthesis of electron-rich diaryliodonium triflates that are unobtainable by the direct triflic acid-mediated reaction (Equation 1).



Equation 2 *In situ* anion exchange.

Finally, the synthesis of unsymmetrical diaryliodonium salts was investigated with tosic acid. As expected, the reaction of iodobenzene with electron-rich arenes delivered the corresponding diaryliodonium tosylates in good yields (Table 3). Biphenyl- and naphthyl salts cannot be synthesized in the TfOH-mediated reaction.<sup>9</sup> Gratefully, biphenyl could be successfully employed with tosic acid to give salt **2k** (entry 3). High yields could be obtained also with less electron-rich arenes (entries 4-8). Notably, diphenyliodonium tosylate (**2h**) could be formed in this reaction, whereas the direct reaction of iodine and benzene failed (*cf* Table 2, entry 9 and Table 3, entry 8).

Table 3 Synthesis of unsymmetrical salts from aryl iodides.

Entry	Ar <sup>1</sup> -I (4)	Ar <sup>2</sup> -H (1)	Product 2 (3)	Yield (%) <sup>a</sup>
1 <sup>b</sup>	PhI (4a)	PhOMe (1a)		100 (100) <sup>c</sup>
2 <sup>b,d</sup>	PhI (4a)	thiophene (1b)		98
3 <sup>b,d</sup>	PhI (4a)	biphenyl (1h)		50 (48) <sup>c</sup>
4 <sup>b</sup>	PhI (4a)	mesitylene (1c)		97
5 <sup>b,d</sup>	PhI (4a)	p-xylene (1d)		79
6	PhI (4a)	Ph'Bu (1e)		72
7	PhI (4a)	PhMe (1f)		79 <sup>e</sup>
8	PhI (4a)	PhH (1g)		85 <sup>e</sup>
9 <sup>d</sup>	1-Iodo-naphthalene (4b)	mesitylene (1c)		34

<sup>a</sup> Isolated yield of **2**.

<sup>b</sup> The arene was added after 1 h.

<sup>c</sup> Isolated yield of **3** after *in-situ* anion exchange.

<sup>d</sup> TFE was used as co-solvent.

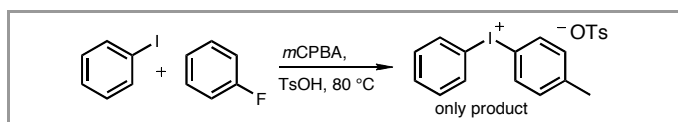
<sup>e</sup> NMR yield, **2** could not be separated from TsOH.

Electron-rich aryl iodides could also be used, as exemplified by 1-iodo-naphthalene (**4b**). This aryl iodide

delivered the unsymmetric, electron-rich salt **2p**, albeit in modest yield (entry 9). The reactions were initially run stepwise, with formation of  $\text{PhI}(\text{OH})\text{OTs}$  (Koser's salt)<sup>14</sup> before addition of the arene in order to avoid side reactions between the oxidant and the arene. Surprisingly, the true one-pot procedure proved as efficient, and in reactions with **4b** no product could be obtained in the stepwise reaction. All products were obtained completely regioselectively. 1 equiv of  $\text{TsOH}$  was found sufficient to mediate the reaction, which simplified the purification substantially as precipitation in diethyl ether could be employed.

The *in situ* anion exchange to the corresponding triflate salts could be employed also on this reaction, as exemplified by the synthesis of (4-methylphenyl)phenyliodonium triflate (**3i**) and (biphenyl)phenyliodonium triflate (**3k**). In both cases the anion exchange took place in near quantitative yields (entries 1, 3).

The limitations in this reaction are seen with electron-deficient arenes, which give byproducts by incorporation of the aryl moiety of  $\text{TsOH}$  rather than reaction with the added arene (Equation 3).<sup>15</sup>



Equation 3 Byproduct formation by reaction with  $\text{TsOH}$ .

To summarize, the use of tosic acid in combination with *mCPBA* enabled the one-pot synthesis of previously unobtainable, electron-rich diaryliodonium salts. Also less electron-rich salts can be synthesized in good yields. Furthermore, the described *in situ* anion exchange gives access also to the corresponding triflate salts, which are more useful in certain applications.

## Representative synthetic procedures<sup>16</sup>

**Synthesis of di(4-methoxyphenyl)iodonium tosylate (2a) from iodine and anisole:**  $\text{I}_2$  (23.7 mg, 0.093 mmol), *mCPBA*<sup>10</sup> (81%, 50 mg, 0.236 mmol) and anisole (35  $\mu\text{L}$ , 0.325 mmol) were dissolved in  $\text{CH}_2\text{Cl}_2$  (2 mL).  $\text{TsOH}\cdot\text{H}_2\text{O}$  (60 mg, 0.316 mmol) was added to the solution and the mixture was stirred at rt for 14 h. The solution was concentrated *in vacuo* and the residue was submitted to flash chromatography ( $\text{CH}_2\text{Cl}_2:\text{Et}_2\text{O}:\text{MeOH} = 100:50:2 \rightarrow \text{DCM}:\text{MeOH} = 20:1$ ) to give the desired salt as pale yellow crystals (72 mg, 89%). mp: 138–139 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.85 (d,  $J = 9.1$  Hz, 4 H), 7.52 (d,  $J = 8.1$  Hz, 2 H), 7.01 (d,  $J = 8.1$  Hz, 2 H), 6.79 (d,  $J = 9.1$  Hz, 4 H), 3.76 (s, 6 H), 2.29 (s, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  162.1, 142.9, 139.1, 136.8, 128.4, 126.0, 117.3, 140.4, 55.5, 21.2; IR (film): 2920.4, 2841.7, 1572.1, 1488.0, 1255.0, 118.5, 1012.0  $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{14}\text{H}_{14}\text{IO}_2$  ( $[\text{M} - \text{TsO}]^+$ ): 341.0033; found 341.0031.

**Synthesis of (4-methoxyphenyl)(phenyl)iodonium tosylate (2i) from iodobenzene and anisole:** *mCPBA*<sup>10</sup> (81%, 53 mg, 0.25 mmol), iodobenzene (25  $\mu\text{L}$ , 0.25 mmol) and anisole (35  $\mu\text{L}$ , 0.25 mmol) were dissolved in  $\text{CH}_2\text{Cl}_2$  (0.5 mL) and 2,2,2-trifluoroethanol (0.5 mL).  $\text{TsOH}\cdot\text{H}_2\text{O}$  (47 mg, 0.25 mmol) was added to the solution and the mixture was stirred at rt for 6 h and the solution was concentrated *in vacuo*.  $\text{Et}_2\text{O}$  (1 mL) was added and the mixture was stirred at rt for 10 min to precipitate out an off-white solid. The precipitate was filtered off, washed with  $\text{Et}_2\text{O}$  and dried under vacuum to give salt **2i** (113 mg, 100%).

**Analytical data for dithienyliodonium tosylate (2b):** mp: 134 °C (decomposed);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.76 (dd,  $J = 3.8, 1.1$  Hz, 2 H), 7.50 (dd,  $J = 5.4, 1.1$  Hz, 2 H), 7.46 (d-like,  $J = 8.0$  Hz, 2 H), 7.06 (d-like,  $J = 8.0$  Hz, 2 H), 6.95 (dd,  $J = 5.4, 3.8$  Hz, 2 H), 2.32 (s, 6 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  141.10, 140.3, 139.6, 135.3, 129.1, 128.7, 126.0, 102.2, 21.3; IR (film): 2975.2, 1659.7, 1381.6, 1214.8, 1187.1, 1048.1  $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_8\text{H}_6\text{IS}_2$  ( $[\text{M} - \text{TsO}]^+$ ): 292.8950; found 292.8955.

**Synthesis of di(4-methoxyphenyl)iodonium triflate (3a) by *in situ* anion exchange:**  $\text{I}_2$  (26.1 mg, 0.103 mmol), anisole (45  $\mu\text{L}$ , 0.412 mmol) and *mCPBA*<sup>10</sup> (81%, 66 mg, 0.309 mmol) were dissolved in 1 mL of DCM.  $\text{TsOH}\cdot\text{H}_2\text{O}$  (78 mg, 0.412 mmol) was added to the mixture and the solution was stirred at 40 °C for 15 min. At 0 °C  $\text{TfOH}$  (23  $\mu\text{L}$ , 0.258 mmol) was added dropwise and the mixture was stirred at rt for 1 h. After the solvents were evaporated *in vacuo*, the residue was submitted to a flash chromatography ( $\text{DCM} : \text{Et}_2\text{O} = 2 : 1 \rightarrow \text{DCM} : \text{MeOH} = 25 : 1$ ) to give **3a** as pale green crystals (72 mg, 71%).

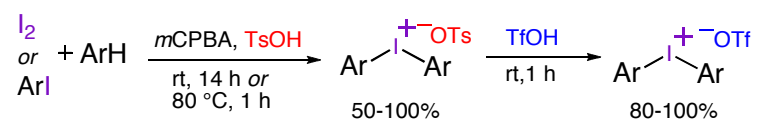
## Acknowledgment

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## References

- Wirth, T. *Angew. Chem. Int. Ed.* **2005**, *44*, 3656.
- Stang, P. J. *J. Org. Chem.* **2003**, *68*, 2997.
- (a) Aggarwal, V. K.; Olofsson, B. *Angew. Chem. Int. Ed.* **2005**, *44*, 5516. (b) Gao, P.; Portoghese, P. S. *J. Org. Chem.* **1995**, *60*, 2276. (c) Ryan, J. H.; Stang, P. J. *Tetrahedron Lett.* **1997**, *38*, 5061. (d) Beringer, F. M.; Daniel, W. J.; Galton, S. A.; Rubin, G. *J. Org. Chem.* **1966**, *31*, 4315.
- (a) Kang, S.-K.; Yamaguchi, T.; Kim, T.-H.; Ho, P.-S. *J. Org. Chem.* **1996**, *61*, 9082. (b) Deprez, N. R.; Sanford, M. S. *Inorg. Chem.* **2007**, *46*, 1924. (c) Kalyani, D.; Deprez, N. R.; Desai, L. V.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 7330.
- Kitamura, T.; Yamane, M.; Inoue, K.; Todaka, M.; Fukatsu, N.; Meng, Z.; Fujiwara, Y. *J. Am. Chem. Soc.* **1999**, *121*, 11674.
- Toba, Y. *J. Photopolym. Sci. Technol.* **2003**, *16*, 115.
- Stepwise reactions: (a) Ochiai, M.; Toyonari, M.; Nagaoka, T.; Chen, D.-W.; Kida, M. *Tetrahedron Lett.* **1997**, *38*, 6709. (b) Pike, V. W.; Butt, F.; Shah, A.; Widdowson, D. A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 245. (c) Kitamura, T.; Matsuyuki, J.; Taniguchi, H. *Synthesis* **1994**, 147. (d) Kitamura, T.; Kotani, M.; Fujiwara, Y. *Tetrahedron Lett.* **1996**, *37*, 3721. (e) Zhdankin, V. V.; Scheuller, M. C.; Stang, P. J. *Tetrahedron Lett.* **1993**, *34*, 6853. (f) Koser, G. F.; Wettach, R. H.; Smith, C. S. *J. Org. Chem.* **1980**, *45*,

1543. (f) Kitamura, T.; Matsuyuki, J.; Nagata, K.; Furuki, R.; Taniguchi, H. *Synthesis* **1992**, 945. (g) Shah, A.; Pike, V. W.; Widdowson, D. A. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2463. (h) Carroll, M. A.; Pike, V. W.; Widdowson, D. A. *Tetrahedron Lett.* **2000**, *41*, 5393.
- (8) Shorter reaction routes: (a) Stang, P. J.; Zhdankin, V. V.; Tykwinski, R. *Tetrahedron Lett.* **1992**, *33*, 1419. (b) Stang, P. J.; Zhdankin, V. V.; Tykwinski, R.; Zefirov, N. S. *Tetrahedron Lett.* **1991**, *32*, 7497. (c) Zefirov, N. S.; Kasumov, T. M.; Koz'min, A. S.; Sorokin, V. D.; Stang, P. J.; Zhdankin, V. V. *Synthesis* **1993**, 1209. (d) Beringer, F. M.; Falk, R. A.; Karniol, M.; Lillien, I.; Masulio, G.; Mausner, M.; Sommer, E. *J. Am. Chem. Soc.* **1959**, *81*, 342. (e) Iwama, T.; Birman, V. B.; Kozmin, S. A.; Rawal, V. H. *Org. Lett.* **1999**, *1*, 673. (f) Hossain, M. D.; Kitamura, T. *Tetrahedron* **2006**, *62*, 6955. (g) Hossain, M. D.; Kitamura, T. *J. Org. Chem.* **2006**, *71*, 9903. (h) Kryska, A.; Skulski, L. *Molecules* **2001**, *6*, 875. (i) Kazmierczak, P.; Skulski, L. *Synthesis* **1995**, 1027.
- (9) (a) Bielawski, M.; Olofsson, B. *Chem. Commun.* **2007**, 2521. (b) Bielawski, M.; Zhu, M.; Olofsson, B. *Adv. Synth. Catal.* **2007**, 2610.
- (10) New, commercially available cans of *m*CPBA were found to contain large and variable amounts of H<sub>2</sub>O. The *m*CPBA needs to be dried under vacuum at rt for 1 h to obtain reproducible results.
- (11) Unpublished results from our laboratory.
- (12) For syntheses of diaryliodonium tosylates see references 7b,f and (a) Margida, A. J.; Koser, G. F. *J. Org. Chem.* **1984**, *49*, 3643. (b) Zhdankin, V. V.; Maydanovych, O.; Herschbach, J.; Bruno, J.; Matveeva, E. D.; Zefirov, N. S. *Tetrahedron Lett.* **2002**, *43*, 2359. (c) Carroll, M. A.; Pike, V. W.; Widdowson, D. A. *Tetrahedron Lett.* **2000**, *41*, 5393. (d) Martin-Santamaria, S.; Carroll, M. A.; Carroll, C. M.; Carter, C. D.; Rzepa, H. S.; Widdowson, D. A.; Pike, V. W. *Chem. Commun.* **2000**, 649. Prof. Tsugio Kitamura presented some unpublished results on synthesis of these compounds at the SIS Conference at Chiba University in November 2007.
- (13) Dohi, T.; Ito, M.; Morimoto, K.; Minamitsuji, Y.; Takenaga, N.; Kita, Y. *Chem. Commun.* **2007**, 4152.
- (14) Togo, H.; Yamamoto, Y. *Synlett* **2005**, 2486.
- (15) The sulfonic acid moiety of TsOH is expected to form sulfuric acid upon formation of this byproduct. In order to confirm that, the reaction mixture described in equation 3 was diluted with methanol and a few drops of aq. BaCl<sub>2</sub> solution was added. White precipitates were formed, indicating the presence of SO<sub>4</sub><sup>2-</sup>. In a parallel reaction, toluene was used instead of fluorobenzene, which resulted in no precipitates in the test with BaCl<sub>2</sub>. See Jackson, D. D. *J. Am. Chem. Soc.* **1901**, *23*, 799.
- (16) General experimental conditions: The reactions were carried out in sealed tubes to allow for reaction temperatures above the boiling point of CH<sub>2</sub>Cl<sub>2</sub>, and were run without precaution to avoid moisture or air, *i.e.* without inert gas or dried solvent. TfOH (≥99%) was stored under argon atmosphere. The percentage of active oxidizing agent in *m*CPBA was determined by iodometric titration, see Vogel, A. I.; Furniss, B. S.; Hannaford, A. J.; Rogers, V.; Smith, P. W. G.; Tatchell, A. R.; *Vogel's Textbook of Practical Organic Chemistry*. 1978; p 1280.

**Graphical abstract:****Short title:**

Synthesis of electron-rich diaryliodonium tosylates and triflates