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of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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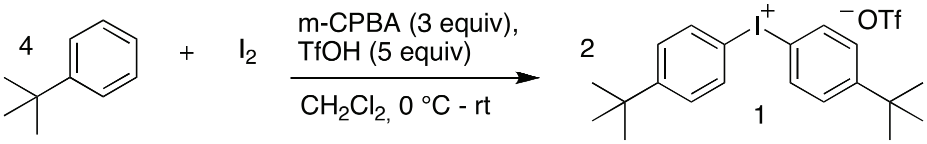
EFFICIENT ONE-POT SYNTHESIS OF BIS(4-*TERT*-BUTYLPHENYL)IODONIUM TRIFLATE



Submitted by Marcin Bielawski and Berit Olofsson.[1]
Checked by Katja Krämer and Mark Lautens.

1. Procedure

Caution! Reactions and subsequent operations involving peracids and peroxy compounds should be run behind a safety shield. For relatively fast reactions, the rate of addition of the peroxy compound should be slow enough so that it reacts rapidly and no significant unreacted excess is allowed to build up. The reaction mixture should be stirred efficiently while the peroxy compound is being added, and cooling should generally be provided since many reactions of peroxy compounds are exothermic. New or unfamiliar reactions, particularly those run at elevated temperatures, should be run first on a small scale. Reaction products should never be recovered from the final reaction mixture by distillation until all residual active oxygen compounds (including unreacted peroxy compounds) have been destroyed. Decomposition of active oxygen compounds may be accomplished by the procedure described in Korach, M.; Nielsen, D. R.; Rideout, W. H. Org. Synth. ***1962****, 42, 50 (Org. Synth.* ***1973****, Coll. Vol. 5, 414). [Note added January 2011].*

A single-necked, 250-mL round-bottomed flask equipped with a magnetic stirring bar is charged with iodine (2.30 g, 9.05 mmol) (Note 1). Dichloromethane (100 mL) (Note 2) is added, and the mixture is stirred at room temperature until the iodine is dissolved (approximately 10 min) with a plastic stopper loosely attached to the flask. *m*-Chloroperbenzoic acid (*m*-CPBA, 73%, 6.62 g, 28.0 mmol, 3.1 equiv) (Note 3) is added and the purple solution is stirred an additional 10 min. *t*-Butylbenzene (5.70 mL, 36.8 mmol, 4.1 equiv) (Note 4) is added and the flask is then cooled to 0 °C in an ice bath. Trifluoromethanesulfonic acid (TfOH, 4.00 mL, 45.2 mmol, 5 equiv) (Note 5) is then slowly added via a gas-tight Hamilton syringe over 5 min at 0 °C, resulting in a color change to darker purple/black (Note 6). The mixture is then stirred at room temperature for 20 min with a color change to grey and formation of a precipitate (Note 7).

The reaction mixture is subsequently transferred to a 250-mL separatory funnel containing distilled water (30 mL). The reaction flask is

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rinsed with dichloromethane (2 x 5 mL), and the rinses are added to the separatory funnel. After thorough mixing, the aqueous layer is separated and the organic phase is washed with additional distilled water (30 mL) (Note 8). The combined organic extracts are poured into a 250 mL round bottomed flask and evaporated under reduced pressure (45 °C, ~200 mmHg) using a rotary evaporator to leave 16.7 g of an orange residue (Note 9).

A stirring bar is added to the flask and diethyl ether (30 mL) is added, causing precipitation of the product as a white solid. After 20 min stirring at 0 °C, the solid is collected by suction filtration using a sintered glass filter funnel and washed with cold (0 °C) diethyl ether (2 x 30 mL) (Note 10).

The solid is transferred to a pre-weighed 50-mL round-bottomed flask and dried on a vacuum line (22 °C, <1 mmHg) for 14 h to afford bis(4-*tert*-butylphenyl)iodonium triflate (**1**) as a white solid (7.68 g, 78%) (Notes 11, 12, 13).

2. Notes

1. Iodine (≥ 99%) was purchased from Sigma-Aldrich and used as received.
2. The checkers used dichloromethane (A.C.S. reagent) purchased from ACP, which was used as received. The submitters purchased dichloromethane (puriss) from VWR and used as received. The reaction is run without precaution to avoid moisture or air, *i.e.* without inert gas or dried solvent. The submitters found that dry conditions did not improve the yield.
3. *m*-CPBA (≤ 77%) was purchased from Sigma-Aldrich. It is dried in a round-bottomed flask at room temperature under reduced pressure until the flask is no longer cold. The time required depends on the amount of *m*-CPBA and the pressure; 5 g takes about 1.5 h at 10 mmHg. The percentage of active oxidizing agent is determined by iodometric titration and amounts to 73% in the checker´s case. The submitters found the percentage of oxidizing agent to range from 76 to 82 % in different batches. The dried *m*-CPBA can be stored for prolonged time in the refrigerator.[2]
4. *t*-Butylbenzene (99%) was purchased from Sigma-Aldrich and was used as received.
5. Trifluoromethanesulfonic acid (TfOH, ≥98%) was purchased from Fluka. TfOH is highly corrosive, and a glass syringe must be used in the addition. Plastic syringes are rapidly destroyed by TfOH, leading to safety

hazards if used for this procedure. The use of 4.1 equiv TfOH results in slightly decreased yield, whereas <4 equiv TfOH gives long reaction times and poor yield.

6. Complete addition of TfOH in a single step results in an exothermic reaction causing the solvent to boil, thus mandating the described slow addition.

7. The precipitate is *m*-chlorobenzoic acid (*m*-CBA); the product is soluble in dichloromethane.

8. The workup removes TfOH and facilitates easier precipitation of the product. *m*-CBA dissolves during the workup, if a large volume of CH_2Cl_2 is used. The grey slurry may change color to a transparent orange. The use of drying agents, such as Na_2SO_4, should be avoided as partial anion exchange takes place, causing a melting point increase to 163–165 °C.

9. The submitters evaporated under reduced pressure (30 °C, ~150 mmHg) to obtain about 15.5 g of an orange residue.

10. The product is somewhat soluble in diethyl ether, therefore a minimum amount should be used for washing.

11. Running the reaction on half the reported scale afforded a comparable yield of bis(4-*tert*-butylphenyl)iodonium triflate (**1**) as a white solid (3.91 g, 79%).

12. A second crop of precipitate can be obtained by concentration of the filtrate under reduced pressure and addition of chloroform. This precipitates *m*-CBA, which is filtered off. After concentration of the filtrate, diethyl ether is added to precipitate a second crop of product **1** in the same manner as described above. This procedure usually contributes little to the overall yield, but can be employed if the first precipitation is low yielding.

13. Product **1** is stable to air and can be stored at room temperature. Analytical data: mp: 161–162 °C; A lower melting point, attributed to a faulty melting point apparatus, has been reported previously.[3] ^1H NMR (400 MHz, $CDCl_3$) δ: 1.29 (s, 18 H), 7.45 (app dt, J = 8.8 Hz, 4 H), 7.92 (app dt, J = 8.8 Hz, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.0, 35.2, 109.5, 120.3 (q, J = 318 Hz, $CF_3SO_3^-$), 129.5, 134.9, 156.4; IR (film): 2962, 2906, 2871, 1582, 1482, 1464, 1396, 1365, 1277, 1237, 1222, 1196, 1160, 1125, 1107, 1060, 1026, 993, 836, 820, 758, 714 cm^{-1}; HRMS (ESI): calcd for $C_{20}H_{26}I$ ([M – $TfO^-]^+$): 393.1074; found 393.1073: Anal. Calcd. for $C_{21}H_{26}F_3IO_3S$: C, 46.50; H, 4.83. Found: C, 46.52; H, 4.89.

Safety & Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

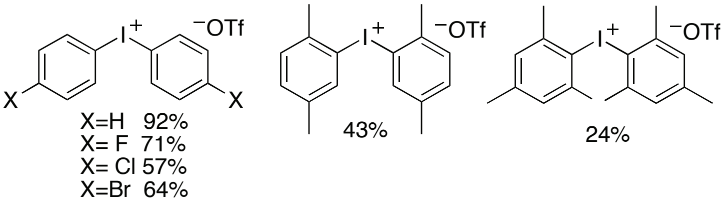
Diaryl-λ^3-iodanes, also called diaryliodonium salts, constitute the most well known compounds among the iodine(III) reagents with two carbon ligands.[4] Due to their highly electron-deficient nature and hyperleaving group ability, they serve as versatile arylating agents in α-arylation of carbonyl compounds[5] and copper- or palladium-catalyzed cross-coupling reactions.[6] Diaryliodonium salts are also used as photo initiators in polymerizations[7] and to generate benzynes.[8]

Synthetic routes to diaryliodonium salts typically involve 2-3 steps.[4,9] Preformed inorganic iodine(III) reagents can be employed to make symmetric salts.[10] Reported one-pot reactions from arenes and iodine or iodoarenes suffer from narrow substrate scope, need excess reagents and long reaction times.[11]

The one-pot synthesis of diaryliodonium triflates from arenes and iodine reported herein is fast, high yielding and operationally simple.[3] Alternatively, aryl iodides and arenes can be employed as starting materials, which gives access also to unsymmetric salts.[3] We have also developed a route to electron rich diaryliodonium salts[12] and a general, regiospecific route employing arylboronic acids.[13]

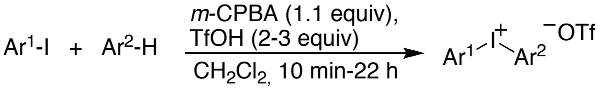
The scope of the reaction employing iodine and arenes is shown in Figure 1. The reaction time and temperature is varied depending on the reactivity of the arene.[3] Limitations include the use of very electron-poor arenes, which have low reactivity and very electron-rich arenes, which give byproduct formation. Substituted arenes can give a mixture of *ortho*- and *para*-iodination, *e.g.* toluene, which gives a 3:1 mixture of regioisomeric salts.

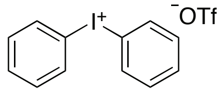
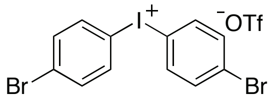
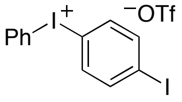
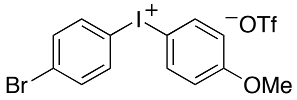
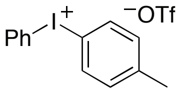
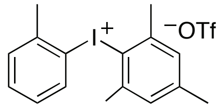
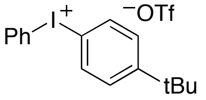
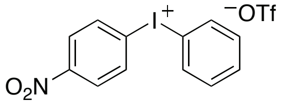
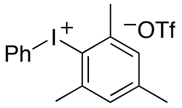
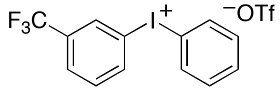
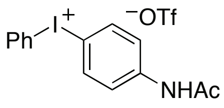
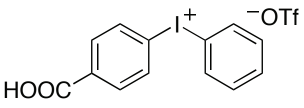
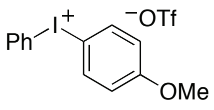
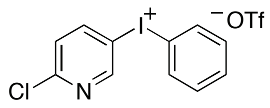
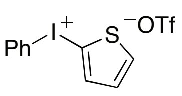
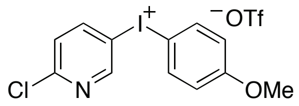
Figure 1. Scope of the one-pot synthesis from iodine and arenes.



The scope of the reaction is considerably widened when aryl iodides are employed instead of iodine (Table 1). Both symmetric and unsymmetric salts are efficiently obtained in short reaction times. Salts containing both electron poor and electron rich aryl moieties can be synthesized. The reaction time and temperature needed varies with the reactivity of the substrates.[3] When high temperature is used, the reaction can generally be performed with less trifluoromethanesulfonic acid. The limitations include the synthesis of symmetric electron rich salts and symmetric electron poor salts.

Table 1. Scope of the one-pot synthesis from aryl iodides and arenes.[a]



Entry	Salt	Yield (%)[b]	Entry	Salt	Yield (%)[b]
1		92	9		91
2		85	10		58
3		85	11		84
4		86	12		85
5		78	13		63
6		83	14		73
7		87	15		60
8		82	16		53

[a] Reactions performed on a 0.2-0.3 mmol scale. [b] Isolated yield.

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Appendix
Chemical Abstracts Nomenclature; (Collective Index Number); (Registry Number)

Bis(4-*tert*-butylphenyl)iodonium triflate; (84563-54-2)

Iodine; (8, 9); (7553-56-2)
tert-Butylbenzene; (98-06-6)
m-Chloroperbenzoic acid; Peroxybenzoic acid, *m*-chloro- (8);
  Benzocarboperoxoic acid, 3-chloro- (9); (937-14-4)
Trifluoromethanesulfonic acid; HIGHLY CORROSIVE, Methanesulfonic
  acid, trifluoro- (8, 9); (1493-13-6)

Berit Olofsson was born in 1972 in Sundsvall, Sweden. She got her M Sc in 1998 from Lund University, and finished her PhD in asymmetric synthesis at KTH, Stockholm (with P. Somfai) in 2002. She then moved to Bristol University, UK for a post doc in the field of methodology and natural product synthesis (with V. K. Aggarwal). Returning to Sweden, she became assistant supervisor at Stockholm University in the group of J.-E. Bäckvall. In 2006 she was appointed to Assistant Professor, and was promoted to Associate Professor in 2008. Her research interests include the synthesis and application of hypervalent iodine compounds in asymmetric synthesis.

Marcin Bielawski was born in 1981 in Augustów, Poland and moved to Sweden at the age of three. He obtained his M. Sc. in Chemistry at Lund University, and subsequently moved to Stockholm. He started his Ph. D studies at Stockholm University in 2006, under the supervision of Berit Olofsson. He has developed several synthetic routes to diaryliodonium salts, and is currently working with their application in organic synthesis.

Katja Krämer was born in 1979 in Saarbrücken, Germany. She studied Chemistry at the Saarland University, where she received her Ph. D. in 2008 under the supervision of Prof. Uli Kazmaier. After working on the synthesis of non-natural amino acids via palladium-catalyzed allylic alkylation, she is now pursuing post-doctoral research in Prof. Mark Lautens' group at the University of Toronto. Her research focuses on desymmetrization of strained alkenes.