Versatile direct dehydrative approach for diaryliodonium(III) salts in fluoroalcohol media†

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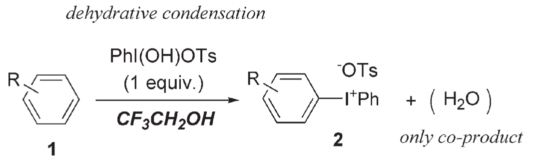
We have found that the use of fluoroalcohol media greatly enhanced the efficiency and scope of the direct dehydrative condensation of arenes 1 and hypervalent iodine(III) compounds; the present clean method has a broad range of applicability as well as unique selectivity in the aromatic substrates, and is highly efficient even in polymer functionalization.

The diaryliodonium(III) salts, $\mathrm{ArI^{+}Ar'X^{-}}$, represent one of the useful and important classes of hypervalent iodine compounds, which show a wide range of applicability as arylating agents and benzyne precursors in organic synthesis, active bactericides, photoacid generator (PAG) cationic polymerization processes, *etc.*[1] These beneficial chemical and physical properties highly depend on both the structure of the iodonium(III) and anionic counter part, $\mathrm{X^{-}}$, and hence the development of general synthetic methods for diaryliodonium(III) salts with a large structural diversity are strongly desired. The dehydrative condensation of iodine(III) compounds and arenes is considered to be the most simple, clean and facile approach for the synthesis of these diaryliodonium(III) salts.[2] Typically, such direct methods *via* electrophilic substitution were achieved for a limited number of aromatic compounds and counterions using activated iodine(III) compounds with the strong acids or [hydroxy(tosyloxy)iodo]arenes, in moderate yields and with poor regioselectivities. Therefore, the stepwise methods using a variety of organometallic nucleophiles, *i.e.*, lithio-, silyl-, stannyl- and boryl-arenes, instead of arenes themselves, have been developed for the purpose of surpassing the limitation of the original methodology.[3] More recently, synthesis of diaryliodonium(III) *triflates* by the most straightforward approach starting from iodoarenes or aromatic compounds has been explored with the use of stoichiometric co-oxidants.[4] Herein, we would report a direct waste-free method for preparation of diaryliodonium(III) salts from a variety of arenes using hypervalent iodine(III) reagents in the presence of 1 equiv. of Brønsted acids (eqn (1)). In the reaction, remarkable effects of the media were clearly observed.

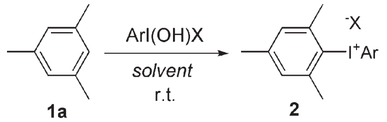


(1)

Recently, the high synthetic potential of fluoroalcohol media, as an attractive unique alternative to ordinary solvent systems, has been growing in interest in organic synthesis.[5] In this study, we have successfully introduced 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) and 2,2,2-trifluoroethanol (TFE) for the first time to hypervalent iodine-mediated[6] and -catalyzed[7] oxidative transformations as stabilizing solvents of reactive cationic intermediates, taking advantage of their unique acid-like behaviors.[8] Therefore, we examined dehydrative iodonium(III) salt formation using a weakly nucleophilic alkylbenzene **1a** in TFE, since usual solvents were not productive to the iodine(III) compound **2a** (Table 1, entries 1–3).[2b] The dehydrative condensation of **1a** and PhI(OH)OTs (Koser's reagent) in TFE proceeded at room temperature in accordance with our proposal, *but unexpectedly*, in a high yield of pure **2a** after precipitation (entry 4). Although TFE apparently plays a critical role for the initiation of the reaction, the use of a mixed solvent system with $\mathrm{CH_2Cl_2}$ was acceptable (entry 5). A large number of stable Koser's types of iodine(III) derivatives are now readily available,[9] and variation of the compounds in the reaction would expand the structural motif of the obtained iodonium(III) products. Selected examples utilizing these types of iodine(III) compounds are shown in entries 6–9.

Under the optimized reaction conditions, the new protocol provided a facile access to a wide range of products **2**, including aromatic and heteroaromatic rings, from **1** (Table 2).‡ Thus, all of

Table 1 Reaction of mesitylene **1a** with ArI(OH)X[a]



Entry	Ar	X	Product	Solvent	Yield[b] (%)
1	Ph	OTs	**2a**	$\mathrm{CH_2Cl_2}$	15[c]
2	Ph	OTs	**2a**	—[d]	n.r.[e]
3	Ph	OTs	**2a**	MeOH	n.d.[f]
4	Ph	OTs	**2a**	TFE	97
5	Ph	OTs	**2a**	TFE–$\mathrm{CH_2Cl_2}$ (1 : 1)	92
6	Ph	OMs[g]	**2a-OMs**	TFE	87
7	Ph	(+)-10-OCs[h]	**2a-OCs**	TFE	98
8	Mesityl	OTs	**2aa**	TFE	62
9	$\mathrm{C_6F_5}$	OTs	**2ab**	TFE	81

[a] All reactions were performed using an equimolar amount of **1a** and ArI(OH)X for 24 h. [b] Isolated yield. [c] Product was obtained as a mixture including a large amount of inseparable impurities. [d] Mesitylene was used as a solvent. [e] No reaction was observed with the recovery of PhI(OH)OTs. [f] n.d. = Not detected [g] OMs = methanesulfonyloxy [h] OCs = camphorsulfonyloxy

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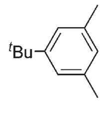
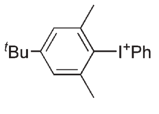
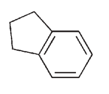
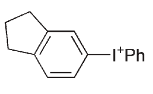
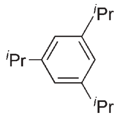
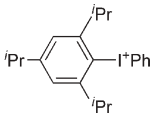
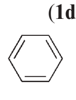
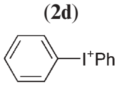
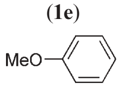
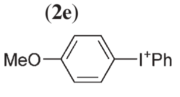
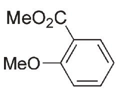
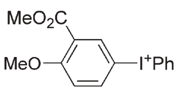
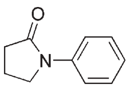
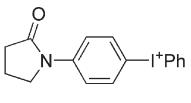
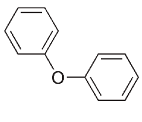
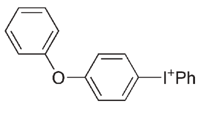
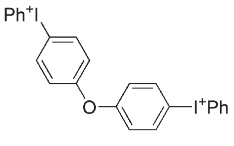
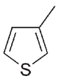
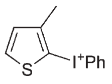
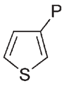
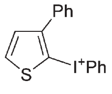
† Electronic supplementary information (ESI) available: Experimental section. See DOI: 10.1039/b708802g

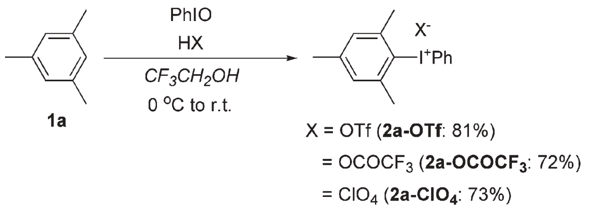
Table 2 Scope of the substrates[a]

Entry	Substrate (**1**)	Iodonium tosylate (**2**)	Time/h	Yield[b] (%)
1	 **(1b)**	 **(2b)**	2	99
2	 **(1c)**	 **(2c)**	24	81
3	 **(1d)**	 **(2d)**	18	62
4[c]	 **(1e)**	 **(2e)**	24	89
5	 **(1f)**	 **(2f)**	1	87
6	 **(1g)**	 **(2g)**	17	94
7	 **(1h)**	 **(2h)**	18	72
8	 **(1i)**	 **(2i)**	17	92
9[d]	//	 **(2i)-bis**	24	94
10	 **(1j)**	 **(2j)**	3	98
11	 **(1k)**	 **(2k)**	3	88

[a] Reactions were performed using an equimolar amount of **1** and PhI(OH)OTs in the TFE (0.2 M) at room temperature unless otherwise noted. [b] Isolated yield of pure product after precipitation. [c] HFIP was used as a solvent. [d] 2 equiv. of PhI(OH)OTs was used.

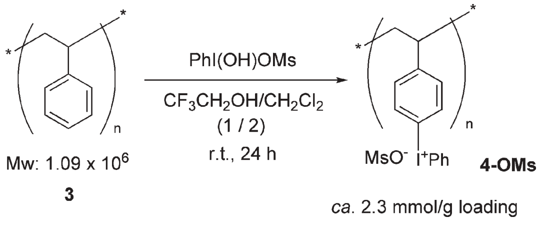
the products **2** were precipitated as solids after simple replacement of TFE with Et_2O, and did not contain other iodine(III) impurities and regioisomeric products. Although the reactions might be susceptible to the steric environments of the aromatic compounds resulting from using **1b** and **1c** (entries 1 and 2), sterically congested product **2d** could be obtained in good yield (entry 3). The electron-deficient benzene derivatives did not afford the corresponding iodonium(III) products as expected, but benzene was applicable for the reaction (entry 4). Similar results were obtained in electron-rich aromatic and heteroaromatic compounds with some functional groups (entries 5–11).[10] The reactions occurred selectively at the *p*-position of the oxygen or nitrogen atoms and the 2-position of the thiophene rings, respectively. In diphenyl ether **1i**, controlling the product distribution of **2i** and **2i-bis** was possible by a simple modulation of the amount of the reagent added (entries 8 and 9).[11]

Modification of the counter ions, X^-, was easily attainable by the utilization of iodosobenzene, PhIO (Scheme 1). Thus, a variety of the Brønsted acids were conveniently introduced to the products as the counterions, X^-, in good yields under similar reaction conditions; so avoiding circuitous anion metatheses work-up.[3,4]



Scheme 1 Incorporation of other counterions, X^-.

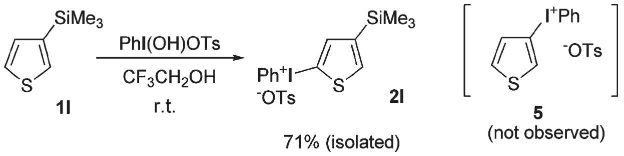
As described above, a new condensation method utilizing fluoroalcohol media is quite simple and versatile. The high efficiency of the method finally made us examine it for the polymer functionalization by the incorporation of the iodonium(III) cation. The transformation of poly(styrene)s to their iodonium(III) forms was reported more than thirty years ago, to control the physical and chemical properties of the polymers.[12] For this purpose, multistep transformations (*e.g.*, iodination, oxidation followed by conversion to the iodonium(III) forms) starting from poly(styrene)s were typically employed, and the loading of the function sites was generally unsatisfactory (~1.5 mmol loading of I(III) per gram). It became clear that our straightforward procedure was applicable to the low-reactive polymers, and accordingly, after dissolving the linear poly(styrene) **3** (100 mg) and PhI(OH)OMs (317 mg, 1 mmol) in a mixed solvent of TFE and CH_2Cl_2, and stirring for 24 h at an ambient temperature, 369 mg of iodine(III)-containing polymer **4-OMs** (*ca.* 85% incorporation of the iodine(III) reagent) was obtained by simple precipitation of the crude mixture in Et_2O (Scheme 2). Elemental analysis of the reformed polymer **4-OMs** disclosed that it contains *ca.* 2.3 mmol g^{-1} of the functionalized iodine(III) site. The high loading of the



Scheme 2 Application of the method for a poly(styrene) reforming.

iodonium(III) site in **4-OMs** allowed the umpolung of the polarity leading to high solubility of the polymer in MeOH compatible to the monomeric diphenyliodonium mesylate, $Ph_2I^+MsO^-$.[13]

On the mechanism, the reaction would involve the usual electrophilic attack of iodine(III) centers toward the arenes **1**, forming the corresponding Wheland type of σ-complexes as the first step.[3] However, based on our previous studies utilizing fluoroalcohol solvents for cation radical generation from electron-rich aromatic compounds by the iodine(III)-induced SET oxidation[6] as well as the recent participation of PhI(OH)OTs in that chemistry,[14] the involvement of the aromatic cation radicals as an alternative possible reaction intermediate was not excluded.[15] One interesting feature of the present reaction is that the organosilane **1l** did not give an *ipso*-substituted product **5** as a result of the usual electrophilic substitution using the organosilicon reagents,[3b] but instead gave a condensation product **2l** (Scheme 3).[16] Anyway, the TFE solvent can work for the generation and stabilization of the both σ-complexes and cation radicals,[5] which seems to be one of the key roles of the TFE solvent for an effective reaction progress.



Scheme 3 A unique selectivity in organosilane **1l**.

In conclusion, we have established a new direct condensation route for diaryliodonium(III) salts, utilizing the unique character of fluoroalcohol media. The present dehydrative method is very clean only producing water as a co-product, and versatile being capable of affording a variety of iodonium(III) salts. The high efficiency of the present method allowed even polymer functionalization, so called, a 'poly(styrene) reforming'. Furthermore, a remarkable solvent effect was observed through the reactions, and the reaction showed unique selectivity in the organosilicon compound to afford the iodonium(III) product, in which the C–Si bond is maintained.

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Notes and references

‡ *Representative experimental procedure*: To a stirred solution of arene **1b** (162 mg, 1 mmol) in 2,2,2-trifluoroethanol (5 mL), [hydroxyl(tosyloxy)iodo]benzene (392 mg, 1 mmol) was added in one portion at room temperature under air, and it was stirred for 2 h. MeOH was then added to the reaction mixture when the solvents were removed under vacuum. The resulting oily crude product **2b** was precipitated by the addition of Et_2O with stirring. The precipitate was filtered off and dried *in vacuo* to give **2b** (531 mg, 99%) as a white powder.

2b: mp 157 °C; ^1H NMR (300 MHz, CD_3OD): δ 1.30 (s, 9H), 2.34 (s, 3H), 2.68 (s, 6H), 7.18 (d, J = 8.4 Hz, 2H), 7.42–7.50 (m, 4H), 7.57–7.66 (m, 3H), 7.90 (d, J = 8.4 Hz, 2H) ppm; ^{13}C NMR (67.8 MHz, CD_3OD): δ 21.3, 27.3, 31.3, 35.8, 114.1, 122.5, 126.9, 127.9, 129.8, 133.2, 133.3, 135.3, 141.5, 143.2, 143.6, 158.3 ppm; IR (KBr): 3018, 2968, 1568, 1472, 1219, 1132, 1045, 928, 772, 665, 627 cm^{-1}; HRMS (FAB): calc. for $C_{18}H_{22}I$ $[M - OTs]^+$: 365.0761, found 365.0777.

1 (*a*) P. J. Stang, *J. Org. Chem.*, 2003, **68**, 2997; (*b*) V. V. Zhdankin and P. J. Stang, *Chem. Rev.*, 2002, **102**, 2523; (*c*) G. F. Koser, in *The Chemistry of Functional Groups, Supplement D*, ed. S. Patai and Z. Rappoport, Wiley, New York, 1983, ch. 25; (*d*) U. Múller, *Trends Photochem. Photobiol.*, 1999, **5**, 117; (*e*) J. M. C. Frechet, *Pure Appl. Chem.*, 1992, **64**, 1239.

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3 (*a*) F. M. Beringer, J. W. Dehn, Jr. and M. Winicov, *J. Am. Chem. Soc.*, 1960, **82**, 2948; (*b*) G. F. Koser, R. H. Wettach and C. S. Smith, *J. Org. Chem.*, 1980, **45**, 1543; (*c*) V. W. Pike, F. Butt, A. Shah and D. A. Widdowson, *J. Chem. Soc., Perkin Trans. 1*, 1999, 245; (*d*) M. A. Carroll, V. W. Pike and D. A. Widdowson, *Tetrahedron Lett.*, 2000, **41**, 5393.

4 (*a*) M. Bielawski and B. Olofsson, *Chem. Commun.*, 2007, 2521; (*b*) M. D. Hossain and T. Kitamura, *Tetrahedron*, 2006, **62**, 6955, and references therein.

5 (*a*) Y. Kita, T. Takada and H. Tohma, *Pure Appl. Chem.*, 1996, **68**, 627; (*b*) L. Eberson, M. P. Hartshorn, O. Persson and F. Radner, *Chem. Commun.*, 1996, 2105; (*c*) J.-P. Bégué, D. Bonnet-Delpon and B. Crousse, *Synlett*, 2004, 18.

6 (*a*) Y. Kita, H. Tohma, M. Inagaki, K. Hatanaka and T. Yakura, *Tetrahedron Lett.*, 1991, **32**, 4321; (*b*) Y. Kita, H. Tohma, K. Hatanaka, T. Takada, S. Fujita, S. Mitoh, H. Sakurai and S. Oka, *J. Am. Chem. Soc.*, 1994, **116**, 3684; (*c*) H. Tohma, M. Iwata, T. Maegawa and Y. Kita, *Tetrahedron Lett.*, 2002, **43**, 9241; (*d*) T. Dohi, K. Morimoto, Y. Kiyono, A. Maruyama, H. Tohma and Y. Kita, *Chem. Commun.*, 2005, 2930.

7 T. Dohi, A. Maruyama, Y. Minamitsuji, N. Takenaga and Y. Kita, *Chem. Commun.*, 2007, 1224.

8 TFE is a unique non-nucleophilic alcohol showing a nearly neutral pH, a high ionizing and strong hydrogen bond donor power. The pK_a value of TFE has been estimated around 12.5. See, ref. 5.

9 Typical [hydroxyl(sulfonyloxy)iodo]arene compounds are stable, non water-sensitive solids which are storable in a refrigerator for several months with light protection. For preparative methods of these compounds, see: (*a*) G. F. Koser and R. H. Wettach, *J. Org. Chem.*, 1980, **45**, 1542; (*b*) M. S. Yusubov and T. Wirth, *Org. Lett.*, 2005, **7**, 519; (*c*) Y. Yamamoto and H. Togo, *Synlett*, 2005, 2486.

10 We have confirmed that the reaction was also applicable to other nitrogen-containing heteroaromatic compounds having suitable N-protecting groups.

11 In contrast, substrate **1i** could react with PhI(OH)OTs or the other iodine(III) reagents in CH_2Cl_2 under the conditions of ref. 2, but afforded a mixture of **2i** and **2i-bis** in low product yields and chemoselectivities.

12 (*a*) Y. Yamada and M. Okawara, *Macromol. Chem.*, 1972, **152**, 153; (*b*) J. V. Crivello and J. L. Lee, *Polym. Bull.*, 1986, **16**, 243; (*c*) X. Huang, Q. Zhu and Y. Xu, *Synth. Commun.*, 2001, **31**, 2823.

13 In our measurement, the solubility of the polymer **4-OMs** in MeOH at 25 °C was at least >30 mg mL^{-1}.

14 (*a*) G. F. Koser, S. Telu and K. K. Laali, *Tetrahedron Lett.*, 2006, **47**, 7011; (*b*) S. Telu, S. Durmus and G. F. Koser, *Tetrahedron Lett.*, 2007, **48**, 1863.

15 We strongly propose the formation of the aromatic cation radical intermediates especially in electron-rich compounds, *i.e.*, phenyl ethers and alkylthiophenes. Further studies on the reaction mechanism will be described in due course.

16 2-Trimethylsilyl thiophene also gave condensation products as a mixture of regioisomers.