Solvolysis of methoxy-substituted diaryliodonium tetrafluoroborates: attempted generation of a stabilized aryl cation

Morifumi Fujita,* Eri Mishima and Tadashi Okuyama*

Graduate School of Material Science, Himeji Institute of Technology, University of Hyogo, Kohto, Kamigori, Hyogo 678-1297, Japan

ABSTRACT: Solvolyses of monomethoxy- and dimethoxyphenyl(phenyl)iodonium (ArI$^+$Ph) tetrafluoroborates were carried out in methanol and 2,2,2-trifluoroethanol (TFE) at 130 °C. The solvolysis products include alkoxide substitution products (ArOR and PhOR) as well as iodoarenes (PhI and ArI). The ratios of ArOR/PhOR range from 8/2 to 4/6. The results are argued against formation of aryl cation. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: diaryliodonium salt; phenyl cation; ligand coupling; nucleophilic aromatic substitution

INTRODUCTION

Phenyl cation is one of the most unstable carbocationic intermediates of mechanistic interest.[1] Considerable attempts have been undertaken for solvolytic generation of phenyl and substituted phenyl (aryl) cations, but the only definitive method for generation of these cations was dediazoniation of arenediazonium salts.[2,3] Hyperconjugatively stabilized aryl cations were successfully generated by another method, solvolysis of 2,6-bis(trimethylsilyl)phenyl triflate (Scheme 1).[4]

Although the parent phenyl cation is quite unstable, an *ortho*-silyl group can stabilize it hyperconjugatively.[1,4] Electron pair-donating *meta* substituents are also pointed out to stabilize the phenyl cation by conjugation taking a non-planar partially allenic structure (Fig. 1).[1,5,6] This type of conjugation was suggested to lower the barrier for the S_N1 solvolysis of 3,5-diaminophenyl triflate.[6]

Iodonium salts are much better progenitors for generation of unstable carbocationic species due to the high nucleofugality of the iodonio group.[7] Vinyl iodonium salts have been used to generate vinyl cations.[8] Diaryliodonium salts should similarly become good precursors for stabilized aryl cations.

Hydrolysis of diaryliodonium salts was investigated long time ago, in the hope of generating an aryl cation by S_N1-type solvolysis in a similar manner to that of diazonium salts. However, the reaction including 3- and 4-methoxy derivatives was suggested to occur by some

complicated mechanism without intermediary formation of aryl cation.[9] A more stabilized 3,5-dimethoxyphenyl cation may have more chance to be formed from the corresponding diaryliodonium salt. In the present investigation, 3,5-dimethoxyphenyl(phenyl)iodonium tetrafluoroborate as well as 3- and 4-methoxyphenyl iodonium salts has been prepared and subjected to alcoholysis.

RESULTS AND DISCUSSION

Solvolysis of diaryliodonium salts

Tetrafluoroborate salts of 3,5-dimethoxyphenyl(phenyl)iodonium (**1a**) and 3-methoxyphenyl derivative (**1b**) were prepared from phenylboronic acid and the corresponding methoxy-substituted (diacetoxyiodo)benzenes. The 4-methoxyphenyl iodonium salt (**1c**) was prepared according to the literature procedure.[10]

Solutions of diaryliodonium tetrafluoroborates **1a–c** in methanol and 2,2,2-trifluoroethanol (TFE) were heated in a sealed Pyrex tube at 130 °C for 1–7 days. The products were analyzed by gas chromatography (GC) with FID and MS detectors in comparison with authentic samples. The products include alkoxide substitution products **2–5** and iodoarenes, PhI and ArI. Yields of the products were determined by an FID detector of GC with tetra(ethylene glycol) dimethyl ether as an internal standard, and the results are summarized in Tables 1 and 2. On injection of the iodonium substrate **1** as an alcoholic solution into the GC column, **1** decomposes to give a mixture of

Correspondence to: M. Fujita and T. Okuyama, Graduate School of Material Science, Himeji Institute of Technology, University of Hyogo, Kohto, Kamigori, Hyogo 678-1297, Japan.
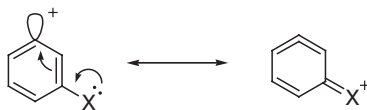E-mails: fuji@sci.u-hyogo.ac.jp and okuyama@sci.u-hyogo.ac.jp
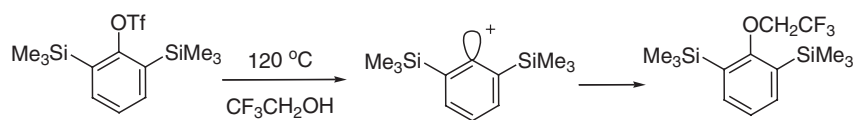
Scheme 1

**Figure 1.** Conjugation with meta substituents.

iodoarenes, PhI and ArI, but no detectable alkoxide substitution products **2–5**. Thermolysis of **1a** and **1b** gave a 55:45 mixture of PhI and ArI, and that of **1c** gave a 34:66 mixture. Thus, the yields of PhI and ArI in Tables 1 and 2 are partially derived from the unreacted iodonium substrate if it remains.

During the solvolysis of **1** in TFE, yields of substitution products **2** and **3** slightly increased with reaction time, but the ratio of **2** and **3** did not much change with time. Iodoarenes, PhI and ArI, must form as counterpart products of **2** and **3**, respectively. Although yields of the iodoarenes are affected by thermal decomposition of the remaining iodonium substrate during the GC analysis, the ratio of PhI/ArI is consistent with that of **2/3**. Solvolysis of **1a** gave more **2a** than **3** (**2/3** = 8/2); that is, the carbon—iodine bond cleavage occurs more readily on the side of the dimethoxyphenyl group than at the phenyl group of **1a**. The ratio of **2/3** (=7/3) from **1b** is only slightly smaller than that from **1a**, while the reaction of **1c** gave the ratio **2c/3** less than unity (4/6). Relative ease of

the aryl—iodine bond cleavage for methoxy-substituted diphenyliodonium salts **1** can be summarized as Ar = 3,5-dimethoxyphenyl > 3-methoxyphenyl > pheny- > phenyl > 4-methoxyphenyl.

A similar tendency of product distribution of **4/5** was observed for the solvolysis in methanol, but the radical reaction pathways are also apparent in this solvent as described below. An appreciable amount of 1,3-dimethoxybenzene (**6**), ArH, was obtained during the methanolysis of **1a**. The corresponding radical product ArH is anisole (**5**) for the reaction of **1b** and **1c**, and it has the same structure as the methoxide substitution product at the unsubstituted phenyl–iodine of the substrate. Thus, the ratios of **4/5** observed in the methanolysis are disturbed by the homolytic reactions. Nonetheless, the value of **4a/5** observed for **1a** must reflect the heterolytic reaction: the **4a/5** value of 8/2 in methanol is quite similar to the **2a/3** value obtained for the solvolysis of **1a** in TFE.

A homolytic pathway may occur via one-electron reduction of the iodonium substrate **1** as illustrated in Scheme 2. Homolysis of the molecular radical formed leads to aryl radical (Ar·) and iodobenzene (PhI) or phenyl radical (Ph·) and iodoarene (ArI). The radical intermediates must abstract hydrogen from the solvent to give ArH (**6** or **5**) or benzene. To distinguish the heterolysis product from the radical product, methanolyses of **1b** and **1c** were carried out in methanol-d_4. The GC-MS analyses show that the anisole obtained from **1b** or **1c** has molecular peaks both at $m/z = 109$ (anisole-d_1) and 111 (anisole-d_3), and their relative intensities are 12 and 100% (from **1b**) or

Table 1. Solvolysis of **1** in 2,2,2-trifluoroethanol at 130 °C[a]
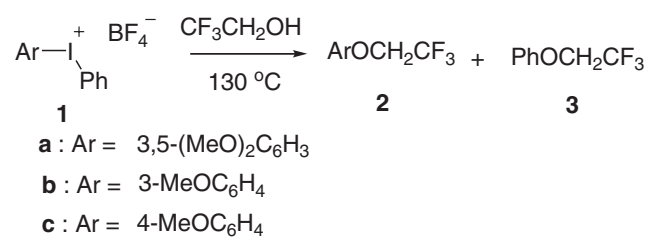
		Yield (%)				
1	Time (h)	**2**	**3**	PhI	ArI	**2/3**
1a	20	13	3	40	28	8/2
1a	45	22	5	42	24	8/2
1a	90	23	4	42	24	8/2
1b	22	13	5	31	22	7/3
1b	70	21	10	38	25	7/3
1b	166	37	16	42	24	7/3
1c	93	13	24	22	40	4/6
1c	340	21	27	42	57	4/6

[a] Yields were determined by GC.

Table 2. Solvolysis of **1** in methanol at 130 °C[a]
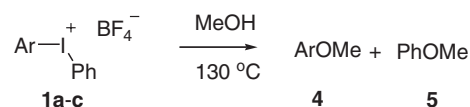
		Yield (%)				
1	Time (h)	**4**	**5**	PhI	ArI	**4/5**
1a	20[b]	6	1	56	44	8/2
1a	45[c]	6	1	56	44	8/2
1b	22	16	26	37	27	4/6
1b	70	15	25	37	26	4/6
1c	21	13	22	24	42	4/6
1c	164	15	23	24	39	4/6

[a] Yields were determined by GC.
[b] 1,3-Dimethoxybenzene (**6**) was obtained in 25% yield.
[c] Dimethoxybenzene **6** was obtained in 26% yield.
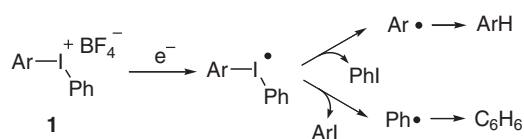
**Scheme 2.** A homolytic pathway in the reaction of **1**

13 and 100% (from **1b**). The anisole-d_1 and anisole-d_3 must arise from the homolytic and heterolytic pathways, respectively, and the former pathway occurs to the extent of about 10% in the reactions of **1b** and **1c**.

In contrast to the reaction in methanol, no methoxybenzenes (ArH) were observed in the reaction in TFE. Thus, the radical pathway can be excluded in the reaction in TFE. This may be due to the poor electron-donating ability of TFE in comparison with methanol. Direct homolysis of **1** could be an alternative pathway for generation of aryl radicals, but this process may not be much dependent on the solvent.
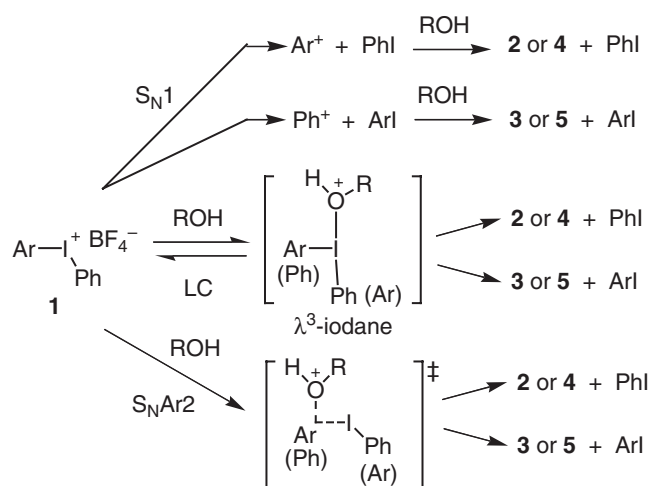
In order to compare the selectivity of bond cleavage, reaction of **1** with a bromide nucleophile was examined. The reaction with tetrabutylammonium bromide was carried out in chloroform at 55 °C to give both bromomethoxybenzene **7** and bromobenzene (**8**) as well as iodo products. The ratios of **7/8** are given in Scheme 3. This reaction is considered to proceed via ligand coupling of the intermediate λ^3-bromoiodane, and it was found that the phenyl ring carrying more electron-withdrawing group(s) tends to combine with the bromide ligand.[11] The present results are within this general tendency.

Possible mechanisms for the solvolysis

Three possible pathways are conceivable for the heterolytic reaction of the solvolysis of diaryliodonium salts **1** as illustrated in Scheme 4. The S_N1-type reaction via aryl cation was first considered. The relative stabilities of the aryl cations were evaluated by MO calculations at the level of MP2/6-31G*//RHF/6-31G*, and the stabilization energies by 3,5-dimethoxy, 3-methoxy, and 4-methoxy substitution of phenyl cation are 14.99, 4.62, and 0.09 kcal mol^{-1}, respectively.[6b] If the transition state for the S_N1 solvolysis has a character of the aryl cation, the ratio of the substitution products **2/3** should depend on the stabilization energy: Relative ease of aryl cation formation is expected to be 3,5-dimethoxyphenyl
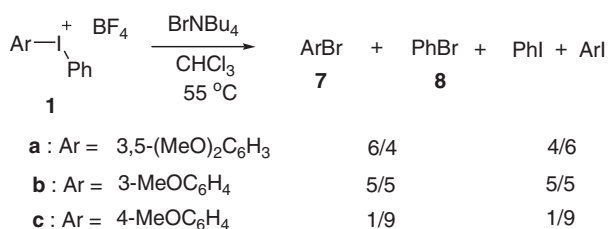
Scheme 4. Possible pathways of solvolysis of **1**

$\gg$ 3-methoxyphenyl > 4-methoxyphenyl $\approx$ phenyl from the calculated stabilization energies. The results given in Table 1 show rather small difference between aryl- and phenyl—iodine bond cleavages, and are not consistent with the S_N1 mechanism. The optimized geometry of the aryl cation stabilized by the *meta*-electron-donating group has a non-planar structure.[1,5,6] That is, large deformation accompanies with formation of the stabilized aryl cation. At the transition state of the S_N1 solvolysis, this deformation may not much develop, and the conjugative stabilization may not be attained to promote the solvolysis. In contrast, hyperconjugative stabilization of the phenyl cation by the *ortho*-silyl group does not require such deformation. This is why 2,6-disilylphenyl triflate undergoes S_N1 solvolysis.[1] 3,5-Dipyrrolidinylphenyl cation was evaluated to show large stabilization (51.83 kcal mol^{-1} at MP2/6-31G*//RHF/6-31G*)[6b] compared with 2,5-disilylphenyl cation (39 kcal mol^{-1} at RHF/6-31G*),[5b] but the relative solvolysis rates for the corresponding triflates are opposite to those expected from the cation stability.[6]

The other two pathways via ligand coupling and S_NAr2 involve a solvent molecule(s) as a nucleophile in the transition state, and they are admittedly not facile processes in TFE. However, under the enforced conditions employed, one of these processes may occur, and the relative ease of the bond cleavages observed is not inconsistent with expectation. The S_NAr2 mechanism should be concerted, if it occurs, due to the combination of a poor nucleophile and an excellent leaving group.[12]

Scheme 3. Reaction of **1** with tetrabutylammonium bromide (0.1 M) in chloroform at 55 °C

EXPERIMENTAL

General

Proton NMR spectra were measured on a JEOL ECA-600 spectrometer in CDCl$_3$ solution and recorded using residual CHCl$_3$ as an internal reference (7.24 ppm). Mass

spectrometers JEOL JMS-T100LC and JEOL Automass System II were used for MS and GC-MS, respectively. GC was conducted on a gas chromatograph Shimadzu 17A with TC-1 (i.d. 0.25 mm × 30 m). Methanol and 2,2,2-trifluoroethanol were simply distilled just before use for reaction.

Preparation of iodonium salts, 1a–c

3,5-Dimethoxyphenyl(phenyl)iodonium tetrafluoroborate (**1a**). A solution of 3-(diacetoxyiodo)-1,5-dimethoxybenzene (0.1 g, 0.38 mmol) in dichloromethane (11 mL) was added dropwise to a solution containing phenylboronic acid (0.085 g, 0.26 mmol) and BF$_3$·OEt$_2$ (0.06 mL, 0.5 mmol) in dichloromethane (16 mL) at rt. The solution was stirred for 7 min, and then quenched by NaBF$_4$ aq. The mixture was extracted with dichloromethane, and the organic layer was concentrated *in vacuo*. Crystallization of the crude mixture in dichloromethane-ether-hexane gave **1a** (0.030 g, 27% yield). ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.95 (d, J = 7.6 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.03 (s, 2H), 6.58 (s, 1H), 3.78 (s, 6H); MS (ESI+) *m/z* (relative intensity, %) 341 (M—BF$_4$, 100); HRMS (ESI+) calcd for C$_{14}$H$_{14}$O$_2$I (M—BF$_4$) 341.0039, found 340.9995.

3-Methoxyphenyl(phenyl)iodonium tetrafluoroborate (**1b**). A solution of 3-(diacetoxyiodo)anisole (0.55 g, 1.6 mmol) in dichloromethane (13.5 mL) was added dropwise to a solution containing phenylboronic acid (0.50 g, 1.6 mmol) and BF$_3$·OEt$_2$ (0.24 mL, 1.9 mmol) in dichloromethane (7 mL) at rt. The solution was stirred for 10 min, and then quenched by NaBF$_4$ aq. The mixture was extracted with dichloromethane, and the organic layer was concentrated *in vacuo*. Crystallization of the crude mixture in dichloromethane-ether-hexane gave **1b** (0.12 g, 19% yield). ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.95 (d, J = 7.6 Hz, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.54 (s, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.40 (d, J = 7.6 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.12 (d, J = 7.6 Hz, 1H), 3.82 (s, 3H); MS (ESI+) *m/z* (relative intensity, %) 311 (M—BF$_4$, 100); HRMS (ESI+) calcd for C$_{13}$H$_{12}$OI (M—BF$_4$) 310.9933, found 310.9965.

4-Methoxyphenyl(phenyl)iodonium tetrafluoroborate (**1c**) was prepared according to the literature method.[10]

Alcoholysis of 1

A sample of **1** (4 μmol) was dissolved in 1 mL of methanol or TFE containing tetra(ethylene glycol) dimethyl ether (10 μmol) in a Pyrex tube. The sealed tube was left standing in an oven at 130 ± 5 °C for 20–200 h. Yields of the products were determined by GC with tetra(ethylene glycol) dimethyl ether as an internal standard. The mixture was analyzed by GC: the column temperature was maintained at 100 °C during the initial 10 min and then raised at the rate of 10 °C min^{-1}. The retention times of PhI, 3-iodoanisole, 4-iodoanisole, and 1,5-dimethoxy-3-iodobenzene were 4.8, 12.8, 13.2, and 18.2 min, respectively. The retention times of **2a**, **2b**, **2c**, **3**, **4a**, **4b**, **4c**, **5**, **7a**, **7b**, **7c**, and **8** were 14.9, 7.2, 7.3, 3.15, 15.8, 8.0, 7.9, 3.23, 16.3, 8.8, 9.2, and 3.4 min, respectively.

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