Facile Preparation of Unsymmetrical Diaryl Ethers from Unsymmetrical Diaryliodonium Tosylates and Phenols with High Regioselectivity

Yohji Kakinuma, Katsuhiko Moriyama, Hideo Togo*

Graduate School of Science, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263-8522, Japan
Fax +81(43)2902792; E-mail: togo@faculty.chiba-u.jp

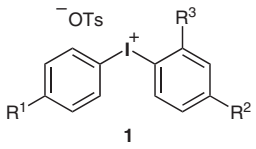
Received: 10.10.2012; Accepted after revision: 13.11.2012

Abstract: Unsymmetrical diaryl ethers were efficiently obtained in good yields by the reactions of aryl(4-methoxyphenyl)iodonium tosylates with phenols, and aryl(2,4-dimethoxyphenyl)iodonium tosylates with phenols, in the presence of potassium carbonate in acetonitrile, respectively. The latter iodonium tosylates provided the corresponding unsymmetrical diaryl ethers in good yields with high regioselectivities, together with the quantitative formation of 1-iodo-2,4-dimethoxybenzene.

Key words: unsymmetrical diaryliodonium tosylate, unsymmetrical diaryl ether, aryl(4-methoxyphenyl)iodonium tosylate, aryl(2,4-dimethoxyphenyl)iodonium tosylate

Diaryl ethers are one of the most important intermediates for organic synthesis[1f–h] in the fields of medicine, agrochemistry, and polymer science.[1] There are many naturally occurring biologically active compounds bearing a diaryl ether group.[1b] For example, L-thyroxin and L-thyronine (important thyroid hormones for human), gerfelin (inhibitor of human geranylgeranyl diphosphate GGPP-synthetase), aristogins A–F, rodgersinol (iNOS and COX-2 inhibitor), aspercyclides A–C (high-affinity IgE receptor inhibitor), and dictyomedin A are known as biologically active diaryl ethers.[1]

Conventionally, diaryl ethers are prepared by the reaction of aryl halides with phenols in the presence of copper at high temperature (Ullmann O-arylation)[1i,2,3] and S_NAr reaction of activated aryl halides with phenolates.[1b–d,i,k,3] In addition, thallium-mediated,[1d,i,3] copper-catalyzed,[1i,3,4] and palladium- or rhodium-catalyzed O-arylation[4,5] of phenols at high temperature are well known. Recently, the reaction of aryl bromides and phenols with potassium *tert*-butoxide at 120 °C in dimethyl sulfoxide was reported.[6] However, in view of the establishment of environmentally benign, less toxic, and less expensive methods for organic synthesis, the preparation of diaryl ethers from phenols without the use of transition metals under mild conditions, i.e., low reaction temperature, is required. Today, it is well-known that diaryliodonium salts[7] are efficient transition-metal-free O-arylation reagents for phenols in the presence of inorganic bases, and the reactions are carried out in methanol, water, dioxane, or *N*,*N*-dimethylformamide at temperatures ranging from 80 °C to 100 °C.[8] Recently, Olofsson reported the preparation of symmetrical and unsymmetrical diaryl ethers by the reaction of symmetrical diaryliodonium salts with phenols in the presence of potassium *tert*-butoxide in tetrahydrofuran at temperatures ranging from 40 °C to room temperature.[9a] This is a valuable method for the preparation of various diaryl ethers because the reaction can be carried out under mild conditions without having to use toxic metals or reagents. We are very much interested in Olofsson's report and here, would like to report our study on the reactivity and regioselectivity of unsymmetrical diaryliodonium salts, such as aryl(4-methoxyphenyl)iodonium tosylates and aryl(2,4-dimethoxyphenyl)iodonium tosylates, with various phenols, such as 4-methoxyphenol, 4-methylphenol, phenol, 4-chlorophenol, and 4-nitrophenol, respectively, to provide unsymmetrical diaryl ethers with high regioselectivities. Very recently during the course of our study, Olofsson et al.[9b] reported the O-arylation of oxygen nucleophiles, such as phenols and carboxylic acids, with diaryliodonium salts with potassium *tert*-butoxide in tetrahydrofuran at 40 °C, and mentioned that the reaction of phenols with aryl(4-methoxyphenyl)iodonium salts, which are unsymmetrical diaryliodonium salts, is effective for the preparation of unsymmetrical diaryl ethers. However, the reaction of various phenols, such as 4-methoxyphenol, 4-methylphenol, phenol, 4-chlorophenol, and 4-nitrophenol, with unsymmetrical diaryliodonium salts was not carried out.



1

1a $R^1 = R^2 = OMe$, $R^3 = H$

1b $R^1 = R^2 = t\text{-Bu}$, $R^3 = H$

1c $R^1 = R^2 = R^3 = H$

1d $R^1 = R^2 = Cl$, $R^3 = H$

1e $R^1 = Cl$, $R^2 = OMe$, $R^3 = H$

1f $R^1 = Me$, $R^2 = OMe$, $R^3 = H$

1g $R^1 = Cl$, $R^2 = R^3 = OMe$

1h $R^1 = Me$, $R^2 = R^3 = OMe$

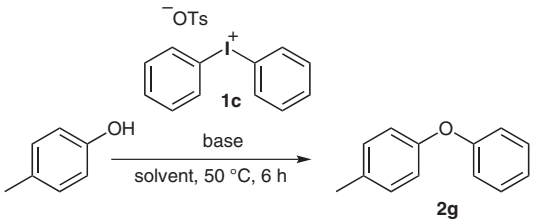
Figure 1 Diaryliodonium salts prepared

SYNTHESIS 2013, 45, 0183–0188
Advanced online publication: 30.11.2012
DOI: 10.1055/s-0032-1316824; Art ID: SS-2012-F0786-OP

Symmetrical diaryliodonium tosylates **1a–d** (Figure 1) bearing 4-methoxyphenyl, 4-*tert*-butylphenyl, phenyl, and 4-chlorophenyl groups, respectively, were prepared from arenes with iodine and potassium persulfate in the presence of 4-toluenesulfonic acid according to the literature method,[10] and unsymmetrical diaryliodonium tosylates **1e–h** (Figure 1) bearing 4-methoxyphenyl and 2,4-dimethoxyphenyl groups were prepared from the reaction of [(hydroxy)(tosyloxy)iodo]arenes with anisole and 1,3-dimethoxybenzene, respectively, in 2,2,2-trifluoroethanol according to the literature method.[11]

A preliminary study revealed that treatment of 4-methylphenol with diphenyliodonium tosylate (**1c**) in the presence of potassium carbonate at 50 °C for six hours in acetonitrile provided 4-methylphenyl phenyl ether (**2g**) in the best yield (96%) (Table 1, entry 3). Based on this result, 4-methoxyphenol, 4-methylphenol, phenol, 4-chlorophenol, and 4-nitrophenol were treated with symmetrical diaryliodonium tosylates, such as bis(4-methoxyphenyl)iodonium tosylate (**1a**), bis(4-*tert*-butylphenyl)iodonium tosylate (**1b**), diphenyliodonium tosylate (**1c**), and bis(4-chlorophenyl)iodonium tosylate (**1d**), in the presence of potassium carbonate in actonitrile at 50 °C to give the corresponding diaryl ethers **2** in good yields (Table 2). 4-Methoxyphenol, which is less acidic than phenol, and 4-nitrophenol, which has lower nucleophilicity than phenol, showed lower reactivity than phenol; their reactions required long reaction times to give the corresponding diaryl ethers **2a–d** (entries 1–4), **2c**,**i–k** (entries 9–12) and **2n–q** (entries 17–20) in good to moderate yields. In addition, the reactivity of bis(4-methoxyphenyl)iodonium tosylate (**1a**) was lower than those of diaryliodonium tosylates **1b–d**, due to the presence of an electron-donating methoxy group on each of the aromatic rings. Thus, the results indicate that the reaction proceeds through nucleophilic *ipso* attack onto the diaryliodonium tosylate by a phenolate anion to provide diaryl ethers **2** and iodoarenes. In this case, when unsymmetrical diaryliodonium tosylates were used, the phenolate anion would attack the *ipso* position of the diaryliodonium tosylate that has no electron-donating group on the aromatic ring. Based on this assumption, unsymmetrical diaryliodonium tosylates $Ar^1Ar^2I^+ {}^-OTs$ **1e–h** with an electron-rich aromatic ring as the Ar^2 group, such as a 4-methoxyphenyl or a 2,4-dimethoxyphenyl group, were treated with phenols, such as 4-methoxyphenol, 4-methylphenol, phenol, 4-chlorophenol, and 4-nitrophenol, in the presence of potassium carbonate in acetonitrile to provide the corresponding diaryl ethers **2** with high regioselectivity (Table 3). It should be noted that when 4-chlorophenyl(2,4-dimethoxyphenyl)iodonium tosylate (**1g**) and 2,4-dimethoxyphenyl(4-methylphenyl)iodonium tosylate (**1h**) were used, the corresponding aryl 4-chlorophenyl ethers **2d**,**h**,**k**,**m**,**q** and aryl 4-methylphenyl ethers **2e**,**r**,**g**,**h**,**s** were obtained predominantly (entries 3, 4, 7, 8, 11, 12, 15, 16, 19, 20) and 2,4-dimethoxy-1-iodobenzene was obtained quantitatively. Thus, when aryl(2,4-dimethoxyphenyl)iodonium tosylates were treated with phenols in the presence of potassium carbonate the corresponding aryl phenyl ethers were selectively obtained, together with 1-iodo-2,4-dimethoxybenzene, and therefore, the present reaction offers another efficient route for the selective preparation of unsymmetrical diaryl ethers.

Table 1 Optimization of the O-Arylation Conditions



Entry	Solvent	Base	Yield[a] (%)
1	THF	K_2CO_3	63
2	acetone	K_2CO_3	92
3	MeCN	K_2CO_3	96
4	MeCN	Na_2CO_3	58
5	MeCN	Cs_2CO_3	94

[a] Isolated yield.

In conclusion, unsymmetrical diaryl ethers were efficiently obtained in good yields by the reactions of aryl(4-methoxyphenyl)iodonium tosylates, i.e., 4-chlorophenyl(4-methoxyphenyl)iodonium tosylate and 4-methoxyphenyl(4-methylphenyl)iodonium tosylate, with phenols, and aryl(2,4-dimethoxyphenyl)iodonium tosylates, i.e., 4-chlorophenyl(2,4-dimethoxyphenyl)iodonium tosylate and 2,4-dimethoxyphenyl(4-methylphenyl)iodonium tosylate, with phenols in the presence of potassium carbonate in acetonitrile, respectively. The latter iodonium tosylate provided the corresponding unsymmetrical diaryl ethers in good yields with high regioselectivities, together with 1-iodo-2,4-dimethoxybenzene quantitatively.

^{1}H NMR and ^{13}C NMR spectra were obtained with Jeol JNM-ECX400, Jeol JNM-ECS400, and Jeol JNM-ECA500 spectrometers. Mass spectra were recorded on JMS-T100GCV, JMS-HX110, and Thermo LTQ Orbitrap XL spectrometers. IR spectra were measured with a Jasco FT/IR-4100 spectrophotometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel 60 (Kanto Kagaku Co.) was used for column chromatography.

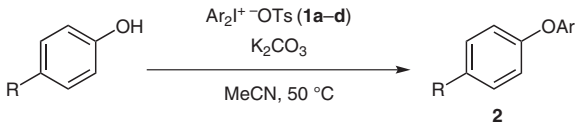
Bis(4-methoxyphenyl)iodonium Tosylate (1a)
Recrystallization (Et_2O–MeOH); white powder; yield: 890 mg (71%); mp 138–140 °C (Lit.[12] 138–139 °C).

IR (Nujol): 824, 1008, 1031, 1170 cm^{-1}.

Bis(4-*tert*-butylphenyl)iodonium Tosylate (1b)
Recrystallization (Et_2O–MeOH); white powder; yield: 981 mg (89%); mp 200–201 °C.

IR (Nujol): 812, 1007, 1030, 1192 cm^{-1}.

Table 2 O-Arylation of Phenols with Symmetrical Diaryliodonium Salts



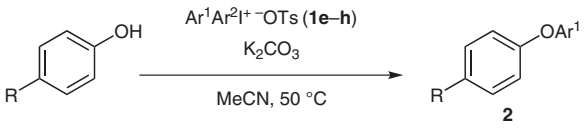
2

1a Ar = 4-$MeOC_6H_4$
1b Ar = 4-*t*-BuC_6H_4
1c Ar = Ph
1d Ar = 4-ClC_6H_4

Entry	$[Ar_2I]^+ {}^-OTs$	R	Time (h)	Product	Yield[a] (%)
1	**1a**	OMe	27	**2a**	68
2	**1b**	OMe	24	**2b**	73
3	**1c**	OMe	24	**2c**	71
4	**1d**	OMe	24	**2d**	67
5	**1a**	Me	24	**2e**	92
6	**1b**	Me	2.5	**2f**	98
7	**1c**	Me	5	**2g**	98
8	**1d**	Me	8	**2h**	96
9	**1a**	H	30	**2c**	90
10	**1b**	H	5	**2i**	92
11	**1c**	H	6	**2j**	93
12	**1d**	H	5	**2k**	97
13	**1a**	Cl	30	**2d**	78
14	**1b**	Cl	2.5	**2l**	95
15	**1c**	Cl	5	**2k**	97
16	**1d**	Cl	6	**2m**	93
17	**1a**	NO_2	30	**2n**	71
18	**1b**	NO_2	24	**2o**	64
19	**1c**	NO_2	24	**2p**	75
20	**1d**	NO_2	24	**2q**	74

[a] Isolated yield.

Table 3 O-Arylation of Phenols with Unsymmetrical Diaryliodonium Salts



2

2d,**h**,**k**,**m**,**q** Ar^1 = 4-ClC_6H_4
2e,**r**,**g**,**h**,**s** Ar^1 = 4-MeC_6H_4
Ar^2 = 4-$MeOC_6H_4$, 2,4-$(MeO)_2C_6H_3$

Entry	$[Ar^1Ar^2I]^+ {}^-OTs$	R	Time (h)	Product	Yield[a] (%)	Ratio
1	**1e**	OMe	24	**2d**/**2a**	67	12:1
2	**1f**	OMe	24	**2e**/**2a**	63	9:1
3	**1g**	OMe	24	**2d**	68	
4	**1h**	OMe	24	**2e**	62	
5	**1e**	Me	6	**2h**/**2e**	96	20:1
6	**1f**	Me	6	**2r**/**2e**	93	8:1
7	**1g**	Me	6	**2h**	98	
8	**1h**	Me	6	**2r**	93	
9	**1e**	H	6	**2k**/**2c**	93	15:1
10	**1f**	H	6	**2g**/**2c**	90	10:1
11	**1g**	H	6	**2k**	95	
12	**1h**	H	6	**2g**	89	
13	**1e**	Cl	6	**2m**/**2d**	91	15:1
14	**1f**	Cl	6	**2h**/**2d**	94	8:1
15	**1g**	Cl	6	**2m**	94	
16	**1h**	Cl	6	**2h**	92	
17	**1e**	NO_2	24	**2q**/**2n**	86	18:1
18	**1f**	NO_2	24	**2s**/**2n**	75	15:1
19	**1g**	NO_2	24	**2q**	75	
20	**1h**	NO_2	24	**2s**	64	

[a] Isolated yield.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.14 (d, *J* = 8.9 Hz, 4 H), 7.53 (d, *J* = 8.9 Hz, 4 H), 7.46 (d, *J* = 8.0 Hz, 2 H), 7.09 (d, *J* = 7.9 Hz, 2 H), 2.27 (s, 3 H), 1.24 (s, 18 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 155.2, 145.8, 137.5, 135.0, 128.9, 128.0, 125.5, 112.9, 34.9, 30.7, 20.8.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{20}H_{26}I$: 393.1074; found: 393.1084.

Diphenyliodonium Tosylate (1c)
Recrystallization (Et_2O–MeOH); white powder; yield: 778 mg (65%); mp 181–182 °C, (Lit.[13] 179–180 °C).

IR (Nujol): 681, 734, 1008, 1030, 1169 cm^{-1}.

Bis(4-chlorophenyl)iodonium Tosylate (1d)
Recrystallization (Et_2O–MeOH); white powder; yield: 457 mg (31%); mp 160–161 °C.

IR (Nujol): 806, 1005, 1029, 1207 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.25 (d, *J* = 8.9 Hz, 4 H), 7.61 (d, *J* = 8.8 Hz, 4 H), 7.45 (d, *J* = 8.0 Hz, 2 H), 7.09 (d, *J* = 7.9 Hz, 2 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 145.7, 137.6, 137.4, 137.0, 131.8, 128.0, 125.5, 114.8, 20.8.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{12}H_8{}^{35}Cl_2I$: 348.9042; found: 348.9041.

4-Chlorophenyl(4-methoxyphenyl)iodonium Tosylate (1e)
Recrystallization (Et_2O–MeOH); white powder; yield: 868 mg (83%); mp 186–187 °C (Lit.[14] 184–185 °C).

IR (Nujol): 847, 1029, 1169, 1302 cm^{-1}.

4-Methoxyphenyl(4-methylphenyl)iodonium Tosylate (1f)
Recrystallization (Et_2O–MeOH); white powder; yield: 693 mg (67%); mp 170–171 °C (Lit.[14] 172–173 °C).

IR (Nujol): 841, 1008, 1030, 1170 cm^{-1}.

4-Chlorophenyl(2,4-dimethoxyphenyl)iodonium Tosylate (1g)
Recrystallization (Et_2O–MeOH); white powder; yield: 726 mg (75%); mp 163–164 °C.

IR (Nujol): 820, 1029, 1050, 1152, 1232 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 8.18 (d, *J* = 8.9 Hz, 1 H), 8.05 (d, *J* = 8.5 Hz, 2 H), 7.55 (d, *J* = 8.9 Hz, 2 H), 7.45 (d, *J* = 8.0 Hz, 2 H), 7.09 (d, *J* = 7.8 Hz, 2 H), 6.79 (d, *J* = 2.6 Hz, 1 H), 6.68 (dd, *J* = 8.9, 2.8 Hz, 1 H), 3.91 (s, 3 H), 3.82 (s, 3 H), 2.27 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 164.7, 158.2, 145.7, 138.4, 137.6, 136.9, 136.5, 131.5, 128.1, 125.5, 114.3, 108.9, 99.7, 96.2, 57.2, 56.0, 20.8.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{14}H_{13}{}^{35}ClIO_2$: 374.9643; found: 374.9634.

2,4-Dimethoxyphenyl(4-methylphenyl)iodonium Tosylate (1h)
Recrystallization (Et_2O–MeOH); white powder; yield: 671 mg (60%); mp 174–175 °C.

IR (Nujol): 818, 1007, 1022, 1155, 1214 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 8.17 (d, *J* = 8.8 Hz, 1 H), 7.93 (d, *J* = 8.3 Hz, 2 H), 7.46 (d, *J* = 8.3 Hz, 2 H), 7.27 (d, *J* = 8.0 Hz, 2 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 6.77 (d, *J* = 2.5 Hz, 1 H), 6.65 (dd, *J* = 8.9, 2.6 Hz, 1 H), 3.91 (s, 3 H), 3.81 (s, 3 H), 2.31 (s, 3 H), 2.27 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 164.6, 158.2, 145.8, 142.1, 138.3, 137.6, 134.7, 132.1, 128.1, 125.5, 112.8, 108.8, 99.7, 96.1, 57.1, 56.0, 20.84, 20.81.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{15}H_{16}IO_2$: 355.0819; found: 355.0179.

Diphenyl Ether (2j)
Diphenyliodonium tosylate (**1c**, 270 mg, 0.6 mmol) was added to a soln of phenol (47 mg, 0.5 mmol) and K_2CO_3 (140 mg, 1.0 mmol) in MeCN (3 mL) at 50 °C and the obtained mixture was stirred for 6 h at 50 °C. The mixture was quenched with H_2O (10 mL) and then extracted with $CHCl_3$ (3 × 25 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by short column chromatography (silica gel, hexane–EtOAc, 5:1) to give **2j**; yield: 79 mg (93%).

Diaryl Ethers 2; General Procedure
The appropriate diaryliodonium tosylate **1** (0.6 mmol) was added to a soln of the phenol (0.5 mmol) and K_2CO_3 (140 mg, 1.0 mmol) in MeCN (3 mL) at 50 °C and the obtained mixture was stirred for 6 h at 50 °C. The mixture was quenched with H_2O (10 mL) and then extracted with $CHCl_3$ (3 × 25 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by short column chromatography (silica gel) to give the diaryl ether.

Bis(4-methoxyphenyl) Ether (2a)
White powder; yield: 78.3 mg (68%); mp 50–51 °C (Lit.[9a] 51–52 °C).

IR (Nujol): 819, 1037, 1246, 1507, 1590 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.92 (d, *J* = 9.1 Hz, 4 H), 6.85 (d, *J* = 9.1 Hz, 4 H), 3.79 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3, 151.6, 119.5, 114.7, 55.7.

4-*tert*-Butylphenyl 4-Methoxyphenyl Ether (2b)
Colorless oil; yield: 93.6 mg (73%).

IR (neat): 828, 1043, 1231, 1501, 1615 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.30 (d, *J* = 8.9 Hz, 2 H), 6.97 (d, *J* = 9.1 Hz, 2 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 6.87 (d, *J* = 9.2 Hz, 2 H), 3.80 (s, 3 H), 1.31 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.0, 155.7, 150.5, 145.3, 126.4, 120.6, 117.1, 114.8, 55.6, 34.2, 31.5.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{17}H_{20}O_2$: 256.1458; found: 256.1459.

4-Methoxyphenyl Phenyl Ether (2c)
Colorless oil; yield: 90.0 mg (90%).

IR (neat): 1037, 1224, 1505, 1589 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.29 (dd, *J* = 8.6, 7.4 Hz, 2 H), 7.03 (t, *J* = 7.5 Hz, 1 H), 6.98 (d, *J* = 8.9 Hz, 2 H), 6.94 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.9 Hz, 2 H), 3.79 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.5, 155.9, 150.1, 129.6, 122.4, 120.8, 117.5, 114.8, 55.6.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{13}H_{12}O_2$ 200.0837; found: 200.0831.

4-Chlorophenyl 4-Methoxyphenyl Ether (2d)
Recrystallization (Et_2O–hexane); white powder; yield: 91.5 mg (78%); mp 52–53 °C (Lit.[15] 54 °C).

IR (Nujol): 824, 1042, 1231, 1506 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 9.1 Hz, 2 H), 6.96 (d, *J* = 8.8 Hz, 2 H), 6.88 (d, *J* = 9.1 Hz, 2 H), 6.86 (d, *J* = 8.8 Hz, 2 H), 3.80 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 156.1, 149.8, 129.5, 127.3, 120.8, 118.7, 114.9, 55.6.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{13}H_{11}{}^{35}ClO_2$: 234.0448; found: 234.0440.

4-Methoxyphenyl 4-Methylphenyl Ether (2e)
White powder; yield: 98.5 mg (92%); mp 49–50 °C (Lit.[16] 49–50 °C).

IR (Nujol): 1043, 1229, 1499 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.09 (d, *J* = 8.5 Hz, 2 H), 6.95 (d, *J* = 9.2 Hz, 2 H), 6.86 (d, *J* = 9.2 Hz, 2 H), 6.85 (d, *J* = 8.5 Hz, 2 H), 3.79 (s, 3 H), 2.31 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.1, 155.6, 150.7, 132.0, 130.1, 120.3, 117.8, 114.8, 55.6, 20.6.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{14}H_{14}O_2$: 234.0448; found: 234.0440.

4-*tert*-Butylphenyl 4-Methylphenyl Ether (2f)
Colorless oil; yield: 117.8 mg (98%).

IR (neat): 826, 1014, 1240, 1502, 1601 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.9 Hz, 2 H), 7.12 (d, *J* = 8.7 Hz, 2 H), 6.91 (d, *J* = 8.9 Hz, 2 H), 6.91 (d, *J* = 8.9 Hz, 2 H), 2.32 (s, 3 H), 1.31 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.3, 155.0, 145.7, 132.6, 130.1, 126.4, 18.9, 117.9, 34.2, 31.5, 20.7.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{17}H_{20}O$: 240.1509; found: 240.1509.

4-Methylphenyl Phenyl Ether (2g)
Colorless oil; yield: 90.3 mg (98%).

IR (neat): 1023, 1238, 1507, 1590 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.28 (dd, *J* = 8.6, 7.4 Hz, 2 H), 7.11 (d, *J* = 8.4 Hz, 2 H), 7.04 (t, *J* = 7.4 Hz, 1 H), 6.96 (d, *J* = 8.6 Hz, 2 H), 6.90 (d, *J* = 8.4 Hz, 2 H), 2.31 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.8, 154.7, 132.8, 130.2, 129.6, 122.8, 119.1, 118.3, 20.7.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{13}H_{12}O$: 184.0883; found: 184.0880.

4-Chlorophenyl 4-Methylphenyl Ether (2h)
White powder; yield: 104.9 mg (96%); mp 54–55 °C (Lit.[17] 56 °C).

IR (Nujol): 821, 1012, 1242, 1507, 1592 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 9.0 Hz, 2 H), 7.14 (d, *J* = 9.0 Hz, 2 H), 6.90 (d, *J* = 9.0 Hz, 2 H), 6.90 (d, *J* = 9.0 Hz, 2 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.5, 154.3, 133.3, 130.3, 129.6, 127.7, 119.5, 119.1, 20.7.

4-*tert*-Butylphenyl Phenyl Ether (2i)
White powder; yield: 104.1 mg (92%); mp 54–55 °C (Lit.[18] 55 °C).

IR (Nujol): 848, 1024, 1242, 1509, 1591 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.6 Hz, 2 H), 7.32 (dd, *J* = 8.4, 7.4 Hz, 2 H), 7.07 (t, *J* = 7.4 Hz, 1 H), 7.00 (d, *J* = 8.3 Hz, 2 H), 6.94 (d, *J* = 8.6 Hz, 2 H), 1.32 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.6, 154.7, 146.1, 129.6, 126.5, 122.9, 118.6, 118.4, 34.3, 31.5.

Diphenyl Ether (2j)
Colorless oil; yield: 79.1 mg (93%).

IR (neat): 1235, 1487, 1584 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33 (dd, *J* = 8.6, 7.4 Hz, 4 H), 7.10 (t, *J* = 7.4 Hz, 2 H), 7.01 (d, *J* = 8.6 Hz, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.2, 129.7, 123.2, 118.9.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{12}H_{10}O$: 170.0726; found: 170.0728.

4-Chlorophenyl Phenyl Ether (2k)
Colorless oil; yield: 99.2 mg (97%).

IR (neat): 1012, 1242, 1506, 1585 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 (dd, *J* = 8.6, 7.5 Hz, 2 H), 7.28 (d, *J* = 8.9 Hz, 2 H), 7.12 (t, *J* = 7.5 Hz, 1 H), 7.00 (d, *J* = 8.6 Hz, 2 H), 6.94 (d, *J* = 8.9 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.9, 155.9, 129.9, 129.7, 128.2, 123.6, 120.0, 118.9.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{12}H_9O^{35}Cl$: 204.0336; found: 204.0335.

4-*tert*-Butylphenyl 4-Chlorophenyl Ether (2l)
Colorless oil; yield: 123.9 mg (95%).

IR (neat): 827, 1011, 1242, 1507, 1588 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 9.1 Hz, 2 H), 7.12 (d, *J* = 9.0 Hz, 2 H), 6.92 (d, *J* = 9.0 Hz, 2 H), 6.92 (d, *J* = 9.0 Hz, 2 H), 1.32 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.3, 154.3, 146.6, 129.6, 127.8, 126.7, 119.7, 118.5, 34.3, 31.5.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{16}H_{17}O^{35}Cl$: 260.0962; found: 260.0963.

Bis(4-chlorophenyl) Ether (2m)
Colorless oil; yield: 111.2 mg (93%).

IR (neat): 1011, 1242, 1507, 1585 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.9 Hz, 4 H), 6.92 (d, *J* = 8.7 Hz, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5, 129.8, 128.7, 120.1.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{12}H_8O^{35}Cl_2$: 237.9952; found: 237.9949.

4-Methoxyphenyl 4-Nitrophenyl Ether (2n)
Pale yellow powder; yield: 81.4 mg (71%); mp 110–111 °C (Lit.[19] 111–112 °C).

IR (Nujol): 1031, 1238, 1342, 1507, 1609 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 9.1 Hz, 2 H), 7.03 (d, *J* = 9.1 Hz, 2 H), 6.96 (d, *J* = 9.3 Hz, 2 H), 6.95 (d, *J* = 9.1 Hz, 2 H), 3.84 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.2, 157.1, 147.8, 142.3, 125.9, 121.9, 116.3, 115.3, 55.7.

4-*tert*-Butylphenyl 4-Nitrophenyl Ether (2o)
Pale yellow powder; yield: 86.8 mg (64%); mp 63–64 °C (Lit.[20] 61.2–61.6 °C).

IR (Nujol): 845, 1015, 1251, 1345, 1490, 1609 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 9.3 Hz, 2 H), 7.44 (d, *J* = 8.9 Hz, 2 H), 7.01 (d, *J* = 8.6 Hz, 2 H), 7.00 (d, *J* = 9.3 Hz, 2 H), 1.35 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 152.1, 148.4, 142.4, 127.1, 125.9, 120.0, 116.8, 34.5, 31.4.

4-Nitrophenyl Phenyl Ether (2p)
Pale yellow powder; yield: 80.7 mg (75%); mp 57–59 °C (Lit.[20] 55.9–56.3 °C).

IR (Nujol): 1111, 1248, 1344, 1507, 1584 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 9.0 Hz, 2 H), 7.44 (dd, *J* = 8.6, 7.5 Hz, 2 H), 7.26 (t, *J* = 7.5 Hz, 1 H), 7.09 (d, *J* = 8.6 Hz, 2 H), 7.01 (d, *J* = 9.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.4, 154.7, 142.5, 130.3, 125.9, 125.4, 120.5, 117.1.

4-Chlorophenyl 4-Nitrophenyl Ether (2q)
Pale yellow powder; yield: 92.4 mg (74%); mp 73–74 °C (Lit.[21] 76.5 °C).

IR (Nujol): 1017, 1248, 1343, 1510, 1599 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 9.2 Hz, 2 H), 7.40 (d, *J* = 9.2 Hz, 2 H), 7.04 (d, *J* = 8.9 Hz, 2 H), 7.02 (d, *J* = 8.9 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.8, 153.3, 142.9, 130.7, 130.4, 126.0, 121.8, 117.2.

Bis(4-methylphenyl) Ether (2r)
White powder; yield: 92.2 mg (93%); mp 48–49 °C (Lit.[22] 50 °C).

IR (Nujol): 812, 1243, 1500, 1606 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10 (d, *J* = 8.6 Hz, 4 H), 6.88 (d, *J* = 8.6 Hz, 4 H), 2.31 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3, 132.4, 130.1, 118.6, 20.6.

4-Methylphenyl 4-Nitrophenyl Ether (2s)
Recrystallization (Et_2O–hexane); pale yellow powder; yield: 73.4 mg (64%); mp 66–67 °C (Lit.[3g] 68–70 °C).

IR (Nujol): 1110, 1250, 1343, 1508, 1591 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 9.5 Hz, 2 H), 7.23 (d, *J* = 8.6 Hz, 2 H), 6.99 (d, *J* = 9.3 Hz, 2 H), 6.98 (d, *J* = 8.6 Hz, 2 H), 2.38 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.7, 152.3, 142.4, 135.2, 130.8, 125.9, 120.4, 116.7, 20.8.

Acknowledgment

Financial support in the form of a Grant-in-Aid for Scientific Research (No. 20550033) from the Ministry of Education, Culture, Sports, Science, and Technology in Japan and Iodine Research Project in Chiba University is gratefully acknowledged.

References

(1) (a) Rao, A. V. R.; Grujar, M. K.; Reddy, K. L.; Rao, A. S. *Chem. Rev.* **1995**, *95*, 2135. (b) Zhu, J. *Synlett* **1997**, 133. (c) Nicolaou, K. C.; Boddy, C. N. C.; Brase, S.; Winssinger, N. *Angew. Chem. Int. Ed.* **1999**, *38*, 2096. (d) Theil, F. *Angew. Chem. Int. Ed.* **1999**, *38*, 2345. (e) Sawyer, J. S. *Tetrahedron* **2000**, *56*, 5045. (f) Evans, D. A.; Katz, J. L.; Peterson, G. S.; Hintermann, T. *J. Am. Chem. Soc.* **2001**, *123*, 12411. (g) Nicolaou, K. C.; Boddy, C. N. C. *J. Am.*

Chem. Soc. **2002**, *124*, 10451. (h) Crowley, B. M.; Mori, Y.; McComas, C. C.; Tang, D.; Boger, D. L. *J. Am. Chem. Soc.* **2004**, *126*, 4310. (i) Frlan, R.; Kikelj, D. *Synthesis* **2006**, 2271. (j) Pitsinos, E. N.; Vidali, V. P.; Couladouros, E. A. *Eur. J. Org. Chem.* **2011**, 1207. (k) Maligres, P. E.; Li, J.; Krska, S. W.; Schreier, J. D.; Raheem, I. T. *Angew. Chem. Int. Ed.* **2012**, *51*, 9091.

(2) (a) Ullmann, F. *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 2174. (b) Ullmann, F. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382. (c) Ullmann, F. *Ber. Dtsch. Chem. Ges.* **1904**, *37*, 853. (d) Lindley, J. *Tetrahedron* **1984**, *40*, 1433; and references cited therein.

(3) (a) Finet, J. P.; Fedorov, A. Y.; Combes, S.; Boyer, G. *Curr. Org. Chem.* **2002**, *6*, 597. (b) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400. (c) Ma, D.; Cai, Q. *Org. Lett.* **2003**, *5*, 3799. (d) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054. (e) Monnier, F.; Taillefer, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 3096. (f) Monnier, M.; Taillefer, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 6954. (g) Khalilzadeh, M. A.; Hosseini, A.; Pilevar, A. *Eur. J. Org. Chem.* **2011**, 1587. (h) Isomura, Y.; Narushima, T.; Kawasaki, H.; Yonezawa, T.; Obora, Y. *Chem. Commun.* **2012**, *48*, 3784. (i) Mulla, S. A. R.; Inamdar, S. M.; Pathan, M. Y.; Chavan, S. S. *Tetrahedron Lett.* **2012**, *53*, 1826. (j) Verma, S.; Kumar, N.; Jain, S. L. *Tetrahedron Lett.* **2012**, *53*, 4665. (k) Kuriyama, M.; Hamaguchi, N.; Onomura, O. *Chem.–Eur. J.* **2012**, *18*, 1591. (l) Chen, J.; Wang, X.; Zheng, X.; Ding, J.; Liu, M.; Wu, H. *Tetrahedron* **2012**, *68*, 8905.

(4) Thomas, A. W. *Diaryl Ethers*, In *Science of Synthesis*, Vol. 31a, Section 31.6.1; Georg Thieme Verlag: Stuttgart, **2007**, 469–543.

(5) (a) Ishiyama, T.; Mori, M.; Suzuki, A.; Miyaura, N. *J. Organomet. Chem.* **1996**, *525*, 225. (b) Still, I. W. J.; Toste, F. D. *J. Org. Chem.* **1996**, *61*, 7677. (c) Hartwig, J. F. *Angew. Chem. Int. Ed.* **1998**, *37*, 2047. (d) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369. (e) Mann, G.; Incarvito, C.; Rheingold, A. L.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 3224. (f) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131. (g) Burgos, C. H.; Barder, T. E.; Huang, X. H.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2006**, *45*, 4321. (h) Hartwig, J. F. *Nature (London, U. K.)* **2008**, *455*, 314. (i) Hu, T. J.; Schulz, T.; Torborg, C.; Chen, X. R.; Wang, J.; Beller, M.; Huang, J. *Chem. Commun.* **2009**, 7330. (j) Kim, H. J.; Kim, M.; Chang, S. *Org. Lett.* **2011**, *13*, 2368. (k) Salvi, L.; Davis, N. R.; Ali, S. Z.; Buchwald, S. L. *Org. Lett.* **2012**, *14*, 170.

(6) (a) Yang, S.; Wu, C.; Ruan, M.; Yang, Y.; Zhao, Y.; Niu, J.; Yang, W.; Xu, J. *Tetrahedron Lett.* **2012**, *53*, 4288.

(7) (a) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: San Diego, **1996**. (b) Chun, J.; Pike, V. W. *J. Org. Chem.* **2012**, *77*, 1891.

(8) Recent reports: (a) Crimmin, M. J.; Brown, A. G. *Tetrahedron Lett.* **1990**, *31*, 2017. (b) Huang, X.; Zhu, Q.; Xu, Y. *Synth. Commun.* **2001**, *31*, 2823. (c) Liu, H.; Bernhardsen, M.; Fiksdahl, A. *Tetrahedron* **2006**, *62*, 3564. (d) Marsh, G.; Stenutz, R.; Bergman, A. *Eur. J. Org. Chem.* **2003**, 2566.

(9) (a) Jalalian, N.; Ishikawa, E. E.; Silva, L. Z. Jr; Olofsson, B. *Org. Lett.* **2011**, *13*, 1552. (b) Jalalian, N.; Petersen, T. B.; Olofsson, B. *Chem.–Eur. J.* **2012**, *18*, 14140.

(10) Hossain, M. D.; Kitamura, T. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 2213.

(11) Dohi, T.; Yamaoka, N.; Kita, Y. *Tetrahedron* **2010**, *66*, 5775.

(12) Zhu, M.; Jalalian, N.; Olofsson, B. *Synlett* **2008**, 592.

(13) Dohi, T.; Ito, M.; Morimoto, K.; Minamitsuji, Y.; Takenaga, N.; Kita, Y. *Chem. Commun.* **2007**, 4152.

(14) Zhang, M.; Kumato, K.; Takei, M.; Fukumura, T.; Suzuki, K. *Appl. Radiat. Isot.* **2007**, *66*, 1341.

(15) Haung, R. L. *J. Chem. Soc.* **1954**, 3088.

(16) Weber, F. C.; Sowa, F. J. *J. Am. Chem. Soc.* **1938**, *60*, 94.

(17) Jammi, S.; Sakthivel, S.; Rout, L.; Mukherjee, T.; Mandal, S.; Mitra, R.; Saha, P.; Punniyamurthy, T. *J. Org. Chem.* **2009**, *74*, 1971.

(18) Haung, R. L. *J. Chem. Soc.* **1954**, 3088.

(19) Abramovitch, R. A.; Alvernhe, G.; Bartnik, R.; Dassanayake, N. L.; Inbasekaran, M. N.; Kato, S. *J. Am. Chem. Soc.* **1981**, *103*, 4558.

(20) Xu, H.; Chen, Y. *Synth. Commun.* **2007**, *37*, 2411.

(21) Raiford, L. C.; Colbert, J. C. *J. Am. Chem. Soc.* **1926**, *48*, 2652.

(22) Reilly, J.; Drumm, P. J.; Boyd Barret, H. S. *J. Chem. Soc.* **1927**, 67.

