Synthesis of Dibenzofurans Directly from Aryl Halides and *ortho*-Bromophenols *via* One-Pot Consecutive *SN*Ar and Intramolecular Palladium-Catalyzed Aryl–Aryl Coupling Reactions

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Received June 27, 2008; accepted July 9, 2008; published online July 9, 2008

A series of dibenzofurans were efficiently and conveniently synthesized *via* one-pot consecutive C(sp^2)–O bond formation reaction (*SN*Ar) in the presence of anhydrous K_2CO_3, followed by C(sp^2)–C(sp^2) bond formation reaction (intramolecular palladium-catalyzed aryl–aryl coupling reaction) between aryl halides and *ortho*-bromophenols. The desired dibenzofurans were obtained in 32—99% isolated yields.

Key words dibenzofuran; one-pot reaction; C(sp^2)–O bond formation reaction; aryl–aryl coupling reaction

Tandem reactions involve a sequence of reactions performed in the same reaction vessel.[1] Nowadays, tandem reactions have emerged as powerful tools to meet the demands of modern organic chemistry due to the synthetic efficiency, molecular diversity, and low production costs, *etc.*[2—5] Recently, we discovered tandem sequences for the efficient synthesis of diaryl ethers from arylmethanesulfonates and aryl halides.[6] Meanwhile, it is well-known that dibenzofurans are good candidates for the study of molecular recognition,[7—9] catalytic reactions[10—12] and the geometry of metal-binding sites.[13] Although Ames *et al.* had reported the synthesis of dibenzofurans, step-wise procedures were needed and the corresponding yields were also not good[14]; lately, Liu *et al.* discovered that the dibenzofurans could be prepared by the reaction of *ortho*-iodophenols with silylaryl triflates in the presence of CsF and palladium, but expensive and excess base and not easily available starting material were used.[15] Thereby, the construction of dibenzofurans with simple, cheap and easily available organic molecules and base in a facile and efficient one-pot reaction is highly desirable. In the continuation of our program aimed at the discovery and development of new tandem reactions,[6] herein we report the synthesis of dibenzofurans directly from aryl halides with *ortho*-bromophenols *via* one-pot C(sp^2)–O bond formation reaction (*SN*Ar) in the presence of anhydrous K_2CO_3, followed by C(sp^2)–C(sp^2) bond formation reaction (intramolecular aryl–aryl coupling reaction) catalyzed by $Pd(OAc)_2$ (Chart 1).

Results and Discussion

Dibenzofurans were efficiently and conveniently prepared *via* one-pot C(sp^2)–O bond formation reaction (*SN*Ar), followed by C(sp^2)–C(sp^2) bond formation reaction (intramolecular palladium-catalyzed aryl–aryl coupling reaction) between aryl halides and *ortho*-bromophenols. As shown in Table 1, the dibenzofurans (**3a**—**j**) were obtained in 32—99% isolated yields. Take entry 1 (Table 1) for example, the mixture of 2-bromophenol (0.5 mmol), 4-fluoronitrobenzene (0.5 mmol), and anhydrous K_2CO_3 (1.0 mmol) in DMF (3 ml) was stirred at 90 °C under an argon atmosphere. When the starting materials were nearly consumed after 0.75 h according to thin-layer chromatography (TLC) analysis, $Pd(OAc)_2$ (0.025 mmol) and PPh_3 (0.05 mmol) were added to the above mixture, which was continued to be stirred at 90 °C for 0.5 h under an argon atmosphere to give 2-nitrodibenzofuran (**3a**) in a 97% yield.

It was found that the steric effects between 4-fluoronitrobenzene and 2-fluoronitrobenzene was obvious. For example, when 4-fluoro- or 2-fluoronitrobenzene was reacted with *ortho*-bromophenols, 2-nitrodibenzofuran (**3a**) and 4-nitrodibenzofuran (**3b**) were obtained in 97% for 1.25 h and 85% for 3.5 h yields, respectively (entries 1 *vs.* 2); 7-fluoro-2-nitrodibenzofuran (**3e**) and 7-fluoro-4-nitrodibenzofuran (**3f**) were obtained in 79% for 1 h and 64% for 6 h yields, respectively (entries 5 *vs.* 6); 8-methoxy-2-nitrodibenzofuran (**3i**) and 8-methoxy-4-nitrodibenzofuran (**3j**) were obtained in 99% for 1 h and 85% for 5.75 h yields, respectively (entries 9 *vs.* 10).

It was noteworthy that when the nitro group of 4-fluoro- or 2-fluoronitrobenzene was substituted by cyano group to be reacted with *ortho*-bromophenols, the yields of the corresponding dibenzofurans decreased; in addition, the *SN*Ar reaction rates of 4-fluoro- or 2-fluorobenzonitrile reacted with *ortho*-bromophenols slowed down sharply as compared with 4-fluoro- or 2-fluoronitrobenzene, such as entries 1 (97%, 0.75 h) *vs.* 3 (48%, 18 h), entries 2 (85%, 1 h) *vs.* 4 (71%, 24 h), entries 5 (79%, 0.5 h) *vs.* 7 (32%, 12 h), and entries 6 (64%, 1 h) *vs.* 8 (39%, 12 h).

Meanwhile, when the *ortho*-bromophenols having the electron-donating group (*e.g.*, methoxy group) were reacted with fluoronitrobenzene, the corresponding yields of dibenzofurans were higher than those having electron-withdrawing

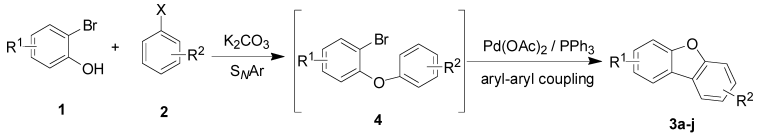

Chart 1. The Synthetic Route of Dibenzofurans **3a**—**j**

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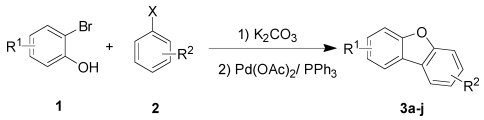
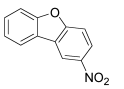
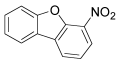
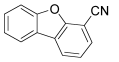
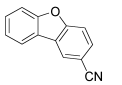
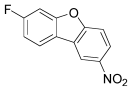
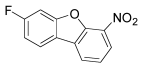
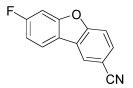
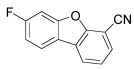
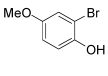
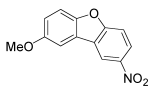
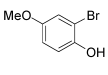
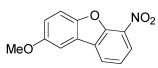
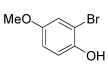
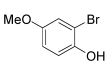
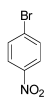
Table 1. An Efficient One-Pot Synthesis of Dibenzofurans (**3a**—**j**) from Aryl Halides and 2-Bromophenols



1 2 3a-j

Entry	2-Bromophenols (**1**)	Aryl halides (**2**)	Dibenzofurans (**3**)	Time (h)[a]	Yield (%)[b]
1			 **3a**	0.75+0.5	97
2			 **3b**	1+2.5	85
3			 **3c**	24+1.5	71
4			 **3d**	18+24	48
5			 **3e**	0.5+0.5	79
6			 **3f**	1+5	64
7			 **3g**	12+6	32
8			 **3h**	12+6	39
9			 **3i**	0.5+0.5	99
10			 **3j**	0.75+5	85
11[c]			**3j**	4+3	83
12[c]			**3i**	7+0.5	68

a) "0.75+0.5" means 0.75 h for the *S*$_N$Ar reaction of compounds **1** and **2** in the presence of K_2CO_3, and 0.5 h for the sequent intramolecular palladium-catalyzed aryl–aryl coupling reaction at 90 °C, respectively; *b*) isolated yields; *c*) under reflux conditions.

group (*e.g.*, fluoro group) (entries 9 *vs.* 5; 10 *vs.* 6).

Finally, other aryl halides, such as 2-chloronitrobenzene and 4-bromonitrobenzene, reacted with 4-methoxy-*ortho*-bromophenol were also investigated. Based upon our previous reports that the leaving ability of halogenes in *S*$_N$Ar reactions decreases in order F>Cl>Br,[6] therefore, 2-chloronitrobenzene or 4-bromonitrobenzene was reacted with 4-methoxy-*ortho*-bromophenol under reflux conditions, and the corresponding yields of **3j** and **3i** were 83% and 68%, respectively (entries 11, 12). These results showed that fluoro derivatives might be replaced by the corresponding bromo or chloro derivatives without causing a significant decrease in the yields.

Conclusion

In conclusion, we have reported an efficient and convenient one-pot synthesis of dibenzofurans *via* *S*$_N$Ar reaction between aryl halides and *ortho*-bromophenols in the presence of anhydrous K_2CO_3, followed by aryl–aryl coupling reaction catalyzed by $Pd(OAc)_2$. Compared to the reported methods,[14,15] the main advantages of this method are as follows: 1) moderate to good yields; 2) use of very inexpensive base and easily available starting materials; 3) simple and practical procedure.

Experimental

All the solvents were of analytical grade and the reagents were used as purchased. TLC was performed with silica gel plates using silica gel 60 GF_{254} (Qingdao Haiyang Chemical Co., Ltd.). Melting points were determined on a digital melting-point apparatus and were uncorrected. ^{1}H-NMR spectra were recorded on a Bruker Avance DMX 400 MHz instrument using TMS as internal standard and $CDCl_3$ as solvent. HR-MS and EI-MS were carried out with APEX II Bruker 4.7T AS and Thermo DSQ GC/MS instruments, respectively.

General Procedure for the Synthesis of Dibenzofurans 3a—j The mixture of 2-bromophenols (**1**, 0.5 mmol), aryl halides (**2**, 0.5 mmol), and anhydrous K_2CO_3 (1.0 mmol) in DMF (3 ml) in 25 ml rockered flask was stirred at 90 °C (for 2-chloronitrobenzene or 4-bromonitrobenzene, under reflux conditions) under an argon atmosphere and the reaction process was checked by TLC. When the starting materials was nearly consumed, $Pd(OAc)_2$ (0.025 mmol) and PPh_3 (0.05 mmol) were added to the above mixture, which was continued to be stirred at 90 °C (for 2-chloronitrobenzene or 4-bromonitrobenzene, under reflux conditions) under an argon atmosphere. When the reaction was complete according to TLC analysis, the reaction mixture was cooled to r.t., poured into ice water (30 ml), and extracted by EtOAc (30 ml×4). Subsequently, the combined organic phase was washed by brine, dried over anhydrous Na_2SO_4, concentrated *in vacuo* and purified by silica gel column chromatography to give the pure dibenzofurans, which were characterized by ^{1}H-NMR (400 MHz), HR-MS, EI-MS and mp.

3a: White solid, mp 153—155 °C (lit.,[14] 153—155 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.43 (1H, t, J=7.6 Hz), 7.55 (1H, m), 7.63 (2H, m), 8.02 (1H, d, J=7.6 Hz), 8.38 (1H, dd, J=9.2, 2.4 Hz), 8.85 (1H, d, J=2.4 Hz); EI-MS m/z: 213 (M^+, 100).

3b: Yellow solid, mp 137—138 °C (lit.,[14] 137—138 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.43 (2H, m), 7.56 (1H, dt, J=8.4, 1.2 Hz), 7.74 (1H, d, J=8.0 Hz), 7.99 (1H, d, J=8.0 Hz), 8.24 (1H, dd, J=7.6, 1.2 Hz), 8.27 (1H, dd, J=8.4, 1.2 Hz); EI-MS m/z: 213 (M^+, 92).

3c: White solid, mp 135—136 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.40 (2H, t, J=7.6 Hz), 7.53 (1H, t, J=8.0 Hz), 7.62 (1H, d, J=8.0 Hz), 7.71 (1H, d, J=7.6 Hz), 7.96 (1H, d, J=7.6 Hz), 8.15 (1H, d, J=7.6 Hz); EI-MS m/z: 192.9 (M^+, 100); HR-MS m/z: 193.0520 $[M]^+$, Calcd 193.0522.

3d: White solid, mp 145—146 °C (lit.,[14] 141—143 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.40 (1H, m), 7.53 (1H, m), 7.61 (2H, m), 7.73 (1H, dd, J=8.4, 1.6 Hz), 7.97 (1H, d, J=8.0 Hz), 8.27 (1H, d, J=0.8 Hz); EI-MS m/z: 192.9 (M^+, 100).

3e: White solid, mp 187—188 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.16 (1H, dt, J=8.8, 2.0 Hz), 7.33 (1H, dt, J=8.8, 2.0 Hz), 7.63 (1H, d, J=9.2 Hz), 7.94 (1H, dd, J=8.8, 2.4 Hz), 8.35 (1H, dd, J=8.8, 2.0 Hz), 8.81 (1H, d, J=2.4 Hz); EI-MS m/z: 231 (M^+, 100); HR-MS m/z: 231.0330 $[M]^+$, Calcd 231.0326.

3f: White solid, mp 166—167 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.17 (1H, dt, J=8.8, 2.0 Hz), 7.45 (2H, m), 7.92 (1H, m), 8.19 (1H, d, J=7.2 Hz), 8.25 (1H, d, J=8.0 Hz); EI-MS m/z: 231 (M^+, 92); HR-MS m/z: 231.0322 $[M]^+$, Calcd 231.0326.

3g: White solid, mp 175—176 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.15 (1H, dt, J=8.8, 2.4 Hz), 7.32 (1H, dd, J=8.8, 2.4 Hz), 7.63 (1H, d, J=8.4 Hz), 7.71 (1H, dd, J=8.4, 1.2 Hz), 7.90 (1H, dd, J=8.4, 1.2 Hz), 8.22 (1H, s); EI-MS m/z: 210.9 (M^+, 100); HR-MS m/z: 211.0432 $[M]^+$, Calcd 211.0428.

3h: White solid, mp 177—177.5 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.15 (1H, dt, J=8.8, 2.0 Hz), 7.38 (2H, m), 7.70 (1H, d, J=8.0 Hz), 7.90 (1H, dd, J=8.4, 5.6 Hz), 8.11 (1H, d, J=8.0 Hz); EI-MS m/z: 210.9 (M^+, 100); HR-MS m/z: 211.0426 $[M]^+$, Calcd 211.0428.

3i: Yellow solid, mp 166—167 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.82 (3H, s), 7.12 (1H, dd, J=9.2, 2.4 Hz), 7.45 (1H, d, J=2.0 Hz), 7.51 (1H, d, J=8.8 Hz), 7.59 (1H, d, J=9.2 Hz), 8.35 (1H, dd, J=9.2, 2.0 Hz), 8.82 (1H, d, J=1.6 Hz); EI-MS m/z: 243 (M^+, 50).

3j: Yellow solid, mp 198—198.5 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.91 (3H, s), 7.13 (1H, dd, J=8.8, 2.4 Hz), 7.40 (2H, m), 7.62 (1H, d, J=9.2 Hz), 8.18 (1H, dd, J=7.6, 1.2 Hz), 8.25 (1H, dd, J=8.4, 1.2 Hz); EI-MS m/z: 243 (M^+, 100); HR-MS m/z: 243.0522 $[M]^+$, Calcd 243.0526.

Acknowledgments This work has been supported by the program for New Century Excellent University Talents, State Education Ministry of China (NCET-06-0868).

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