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Ortho-Phenylenedizinc(II) Compounds. Ultrasound-Promoted Synthesis from o-Diiodobenzene and Zinc Powder and Its Synthetic Application

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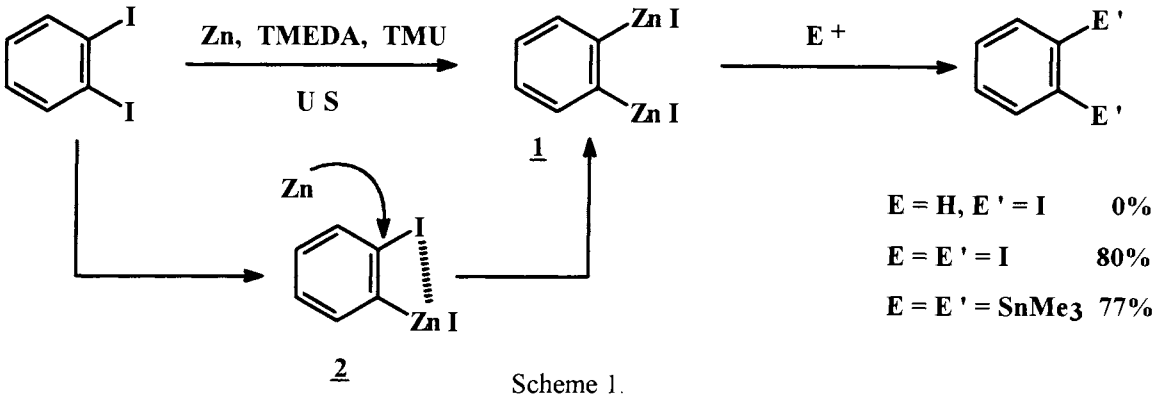
A facile and efficient synthetic procedure of o-phenylenedizinc(II) compound from o-diiodobenzene and zinc powder under the irradiation of ultrasound is reported. The compound was proved to be a unique reagent supplying o-phenylenedianion of high chemoselectivity. Symmetrically 1,2-diaryl or diaroyl substituted benezenes were obtained in good yields by Pd(0)-catalyzed cross-coupling of the compound with aryl halides or acyl halides.

Because of an existence of formal negative charges on adjacent carbon-atoms, o-phenylenedimetals are intriguing not only for synthetic chemists but also for theoretical chemists.[1] The compounds bearing rather negative-metals such as Hg and Sn are obtainable by a direct reaction between o-dihalobenezene and metal (sodium amalgam) or metalate (R_3SnNa), even though the reported yields are moderate (50% and 42%, respectively), whereas ones bearing positive metals such as Li and Mg, which might promise broader scope as synthetic reagents than the formers, are derived from the Hg-derivatives through Hg-Li or Hg-Li followed by Li-Mg exchange.[2] These troublesome access to o-phenylenedimetals have apparently limited their utilization as reagents in organic syntheses.[3] Therefore, new methods for the preparation of o-phenylenedimetals, especially readily available but still reactive species, are desired. In this paper we wish to report a facile and efficient synthesis of o-phenylenedizinc(II) compound (1) and its application to Pd(0)-catalyzed cross-coupling reaction.

In the previous paper, we had reported on the ultrasound (US)-promoted syntheses of arylzinc(II) compound: Irradiations of US brought about a facile cleavage of otherwise inert C-I bonds of aryl iodides with zinc powder, especially those carrying electron withdrawing groups at the o-positions, to produce the corresponding arylzinc(II) compounds in high yields.[4,5] As an extension, we examined the reaction of o-diiodobenzene with zinc powder under US-irradiation conditions and found that the insertion of zinc powder took place, in this case, into the both C-I bonds of o-diiodobenzene. That is, a mixture containing o-diiodobenzene (0.4 mmol), zinc powder (4 equiv.), N,N,N`,N`-tetramethylethylenediamine (TMEDA, 0.2 equiv.)[6] and TMU (0.3 ml) was irradiated by US at 30 °C for 24 hours under nitrogen.[7] The complete disappearance of o-diiodobenzene therefrom was revealed by the treatment of the resulting mixture with aqueous HCl, followed by GLC analysis.[8] Ortho-diiodobenezene was reproduced in a yield of 80% (GLC) by the treatment of the reaction mixture with I_2. Whereas, 1,2-bis(trimethylstannyl)benzene[9] was isolated in a yield of 77% from the reaction mixture after the treatment of the mixture with 2 equivalents of THF-solution of



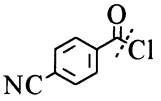
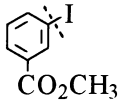
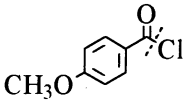
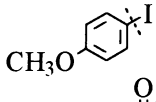
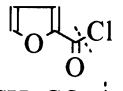
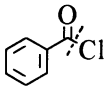
Scheme 1.

$(CH_3)_3SnCl$. These results show the presence of o-phenylenedizinc(II) compound in the reaction mixture (Scheme 1). It is to be noted that previously reported insertion of zinc powder into the C-I bond of aryl iodides was possible only if the bond was activated by the adjecent electron-withdrawing groups.[4] Ortho-diiodobenzene fulfills this requirement for the first insertion of zinc, since an electron-withdrawing iodine places therein.[10] However, for the second insertion, the C-I bond of o-iodophenylzinc(II) intermediate (2), lacks such kind of groups, since the adjecent bond now polarizes reversely.[11] So that, a selective insertion of second zinc into the C-I bond of 2 is of interest in the context of the formation of benzyne from similar intermediates encountered in course of the reaction of o-dihalobenzenes with Li or Mg.[12] Compound (1) in the reaction mixture was stable enough for at least months at ambient temperature to be safely used in further syntheses (vide infra).

To see the utility of 1 in organic syntheses, Pd-catalyzed cross-coupling of the compound with aryl halides or acyl halides was attempted. The results are summarized in Table 1. Various symmetrically 1,2-disubstituted benzenes, including ones carrying such reactive groups as alkoxycarbonyl, cyano, oxo, alkoxy, or furyl were obtained in good yields. Along with the reaction of 1 with electrophiles like I^+ or $(CH_3)_3Sn^+$ (vide supra), successful Pd-catalyzed coupling proves the utility of 1 as a unique reagent of supplying o-phenylenedianion of high chemoselectivity. Two drawbacks of the compound as a synthetic reagent, however, should be noted; 1) 1 did not react well with alkyl-acid halides such as CH_3COBr or CH_3CH_2COCl under the examined conditins (Runs 10 and 11) and 2) 1 did not yield half-substitution products (o-substituted phenylzincs(II)) selectively even if equimolar amounts of 1 and aryl halides or acyl halides were used (Runs 2 and 6): selective stepwise-introduction of two different electrophiles onto 1 is not possible at present.[13] In conclusion, o-phenylenedizinc(II) compound was synthesized, for the first time, in a strikingly facile and simple manner and proved to be a stable and efficient reagent affording an o-phenylenedianion of high chemoselectivity.

Typical procedure is as follows: A solution of 87 mg of 4-cyanobenzoyl chloride (0.53 mmol), 0.27 ml of TMU solution of 1 (0.24 mmol), which was prepared separately by the reaction of 0.416 ml of o-diiodobenzene (3.2 mmol), 834 mg of Zn powder (12.4 mmol), 0.096 ml of TMEDA (0.64 mmol), and 2.4 ml of TMU at 40 °C for 48 h in a ultrasonic cleaner, 5.8 mg of $Pd(PPh_3)_4$ (0.005 mmol), and 0.3 ml of TMU was stirred at 40 °C for 12 h under nitrogen. The resulting solution was chromatographed on a silica-gel column to afford 63 mg (78%) of 1,2-bis(4'-cyanobenzoyl)benzene. Mp 175-177 °C; IR ($CDCl_3$) 1665, 2233 cm^{-1}; ^1H-NMR ($CDCl_3$) δ = 7.6-7.9; ^{13}C-NMR ($CDCl_3$) δ = 194.6, 140.1, 139.0, 132.3, 131.2, 130.0, 129.8, 117.6, 116.5. Found: C, 78.45; H, 3.61; N, 8.21%. Calcd for $C_{22}H_{12}N_2O_2$: C, 78.6; H, 3.6; N, 8.3%.

Table 1. Pd(0)-Catalyzed Syntheses of Symmetrically 1,2-Disubstituted Benzenes[a)]

Run	R–X	Yield / %[b)] 	Run	R–X	Yield / %[b)] 
1		(71)	7		78
2		(24)[c)]			
3		75	8		79
4		59	9		73
5		78	10	CH_3CH_2CO–Cl	0[e)]
6		(33)[d)]	11	CH_3CO–Br	0[f)]

a) Molar ratio of component: 1/RX/Pd(0) = 1/2.2/0.04 (Runs 1,3-5,9,10), 1/2.2/0.02 (Runs 7,8,11), 1/1/0.02 (Runs 2,6). Pd(0) catalyst: $Pd(PPh_3)_4$ (Runs 1,2,5-11), $Pd(dppf)_2$ (Run 3), $Pd(dba)_2$+4(tris(perfluorophenyl)phosphine (Run 4). Reaction Temp.: 40 °C (Runs 1,2,5,7-11), 80 °C (Runs 3,4), room temp. (Run 6). Reaction Time: 12 h.

b) Isolated yield. Yields in parentheses were determined by GLC.

c) Yield of biphenyl was 47% (after HCl-treatment). d) Yield of benzophenone was 26% (after HCl-treatment).

e) Yield of propiophenone was 26% (after HCl-treatment). f) Yield of acetophenone was 8% (after HCl-treatment).

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6) Addition of small amount of TMEDA accelerates the reaction considerably. For example, 4% of o-diiodobenzene was remained in the reaction mixture after the same procedure in the text except for the absence of TMEDA. For a similar effect of TMEDA on the reaction of zinc powder with alkenyl halides: See, B. Jiang and Y. Xu, J. Org. Chem., 56, 7336 (1991).

7) Ultrasonic cleaner (Branson 1200, 30 W) was used for the irradiation of ultrasound. Commercial zinc powder was used without any pre-treatment.

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9) ^{13}C-NMR of the reaction mixture (with CH_3CN-d_3) also showed the complete disappearance of o-diiodobenzene. A signal at 168.5 ppm was assigned to C_1 of 1.

10) The insertion of zinc proceeded in a step-wise manner. That is, if aqueous-HCl was added to the reaction mixture before the completion of the reaction, iodobenzene was detected therein (for example, after the irradiation of US for 16 h, 21% of iodobenezene and 0% of diiodobenezene were detected).

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