

## Coupling reaction of aryl halides promoted by NiCl<sub>2</sub>/PPh<sub>3</sub>/Sm<sup>0</sup>

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An efficient synthesis of biaryls from various aryl halides has been developed and investigated. The coupling reagent is a catalytic mixture of anhydrous NiCl<sub>2</sub> and PPh<sub>3</sub> in the presence of metallic samarium. The reaction occurs rapidly under mild conditions, tolerates a variety of functional groups with high yields.

**Keywords:** coupling, aryl halide, biaryl, NiCl<sub>2</sub>/PPh<sub>3</sub>, samarium

Biaryls are an important class of compounds in organic synthesis which are found in various types of natural products showing unique biological activity. The synthesis of biaryls via coupling reactions has been the subject of numerous past and current investigations.<sup>1</sup> There are many methods to synthesise biaryls, for instance, the classical Ullmann-type reaction;<sup>2,3</sup> the transition metal-catalysed coupling reaction of aryl halides with arylmetals;<sup>4</sup> self-coupling reaction of arylmetallic reagents with oxidants.<sup>5</sup>

Herein, we report that the coupling of aryl halides promoted by NiCl<sub>2</sub>/PPh<sub>3</sub> and metallic samarium. In this system NiCl<sub>2</sub> was used in catalytic amount, PPh<sub>3</sub> was used as ligand, samarium was used as reductive metal. The reaction was shown as follows (Scheme 1).

Metallic samarium, which is similar to magnesium ( $E_{\text{Mg}^{2+}/\text{Mg}^0}^0 = -2.37\text{V}$ ), is of strong reducing power ( $E_{\text{Sm}^{3+}/\text{Sm}^0}^0 = -2.41\text{V}$ ). More recently, there are some reports on the direct use of samarium in organic synthesis.<sup>6</sup> Since metallic samarium in the reaction is of stronger reductivity and higher chemoselectivity than Fe, Zn, Mn, Al, *etc.*, we used samarium as reductant and the result obtained is better than that of Colon.<sup>7</sup> Our experimental results are shown in Table 1.

The experimental results indicated that aryl bromides and aryl iodides can be coupled more quickly than aryl chlorides and biaryls are obtained in high yields using samarium as reductive metal in the same conditions. According to Colon's report, when the other metals are used as reductant, aryl chlorides, aryl bromides and aryl iodides can be coupled effectively. However, for aryl bromides and aryl iodides somewhat more reduction to arenes was found and the overall reaction times were longer than those for aryl chlorides under comparable conditions. Use of samarium as reductive metal makes the reaction milder and faster. The reaction occurs rapidly under mild conditions, tolerates a variety of functional groups and gives high yields. It is worth mentioning that aryl halides

containing nitro or hydroxyl group could not be coupled effectively by this method.

### Experimental

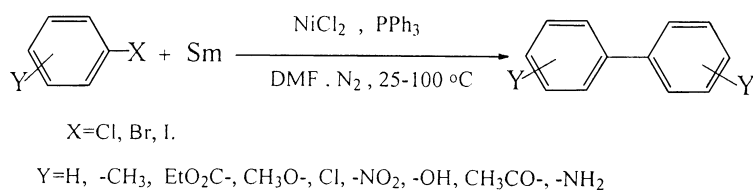
All reactions were conducted under a dinitrogen atmosphere. Melting points are uncorrected. <sup>1</sup>H NMR spectra were recorded on a Bruker 400 MHz instrument as CDCl<sub>3</sub> and DMSO-d<sub>6</sub> solutions using TMS as internal standard. Chemical shifts ( $\delta$ ) are reported in ppm. IR spectra were recorded using KBr disks with a Bruker Vector-22 infrared spectrometer. Metallic samarium was purchased from commercial sources. DMF was redistilled and dried with molecular sieve for 48h before use. NiCl<sub>2</sub> was prepared with NiCl<sub>2</sub>·6H<sub>2</sub>O according to the literature.

*General procedure for the coupling of various aryl halides by NiCl<sub>2</sub>/PPh<sub>3</sub> and samarium:* Samarium powder (0.30 g, 2 mmol), anhydrous NiCl<sub>2</sub> (0.013 g, 0.1 mmol), and triphenylphosphine (0.20 g, 0.76 mmol) were added to a two-necked round-bottomed flask. The flask was evacuated and filled with dinitrogen several times (vacuum line). Anhydrous DMF (15 ml) was added via a syringe through the rubber cap. The reaction flask was then placed in an oil bath at 30°C and stirred magnetically under nitrogen. After the red-brown catalyst had formed, an aryl halide (6 mmol) was added via a syringe to the reaction mixture. The reaction was conducted at 30–100°C until completion (monitored by TLC). Water (20 ml) was added. The reaction mixture was extracted with diethyl ether (3 × 20 ml), the mixed organic layer washed with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (10 ml) and water (10 ml), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the solvent was removed by evaporation under reduced pressure, the crude product was purified by preparative TLC on silica gel (eluent: cyclohexane-ethyl acetate)

*Compound a:* M.p. 69–72°C (lit.<sup>8</sup> 69–72°C)  $\delta_{\text{H}}$  (ppm) 7.13–7.20 (m, 2H), 7.25–7.27 (d, 4H  $J = 7.60$  Hz), 7.52–7.64 (m, 4H).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3033, 1579, 1568, 1479, 1343, 805.

*Compound b:* M.p. 118–120°C (lit.<sup>8</sup> 118–120°C)  $\delta_{\text{H}}$  (ppm) 7.22–7.24 (d, 4H  $J = 8.12$  Hz), 7.46–7.48 (d, 4H  $J = 8.12$  Hz), 2.38 (s, 6H).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3022, 2916, 2849, 1517, 1501, 803.

*Compound c:* M.p. 179–180°C (lit.<sup>8</sup> 179–180°C)  $\delta_{\text{H}}$  (ppm) 6.94–6.96 (d, 4H  $J = 8.0$  Hz), 7.46–7.48 (d, 4H  $J = 8.0$  Hz), 3.84 (s, 6H).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3037, 2957, 2839, 1606, 1500, 1439, 1249.

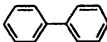
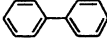
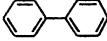
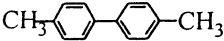
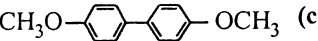
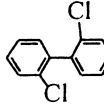
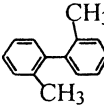
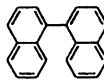
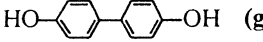
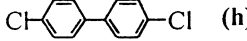
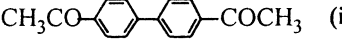
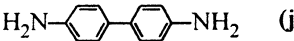
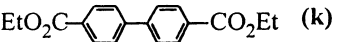


**Scheme 1**

\* To receive any correspondence.

† This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

**Table 1** The results in coupling of various aryl halides

Entry	Substrate	t/h <sup>a</sup>	T/°C <sup>b</sup>	Product	Yield/% <sup>c</sup>
1	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> Cl	24	100		0
2	C <sub>6</sub> H <sub>5</sub> Cl	2	35	 (a)	99
3	C <sub>6</sub> H <sub>5</sub> Br	1.5	25	 (a)	95
4	C <sub>6</sub> H <sub>5</sub> I	1	25	 (a)	88
5	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Cl	1.5	40	 (b)	98
6	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> Cl	1	25	 (c)	84
7	<i>o</i> -ClC <sub>6</sub> H <sub>4</sub> Cl	5	70	 (d)	67
8	<i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Cl	3	40	 (e)	90
9	$\alpha$ -chloronaphane	8	70	 (f)	78
10	<i>p</i> -HOC <sub>6</sub> H <sub>4</sub> Cl	12	70	 (g)	Trace
11	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> Cl	12	25	 (h)	76
12	<i>p</i> -CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> Cl	6	70	 (i)	98
13	<i>p</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> Cl	3	40	 (j)	60
14	<i>p</i> -EtO <sub>2</sub> CC <sub>6</sub> H <sub>4</sub> Cl	8	70	 (k)	74

<sup>a</sup>Reaction time. <sup>b</sup>Reaction temperature. <sup>c</sup>Isolated yield.

**Compound d:** M.p. 59–61°C (lit.<sup>9</sup> 60.5°C)  $\delta_{\text{H}}$  (ppm) 7.32–7.36 (m, 2H), 7.42–7.46 (m, 4H), 7.58–7.60 (m, 2H).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3042, 1590, 1504, 1384, 803.

**Compound e:** Oil. (lit.<sup>9</sup> 18°C)  $\delta_{\text{H}}$  (ppm) 7.22–7.25 (m, 4H), 7.30–7.38 (m, 2H), 7.38–7.39 (d, 2H  $J$  = 6.84 Hz), 2.26 (s, 6H).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3020, 2954, 1457, 1438, 1072, 1009, 804.

**Compound f:** M.p. 155–158°C (lit.<sup>9</sup> 159°C)  $\delta_{\text{H}}$  (ppm) 7.25–7.40 (m, 3H), 7.45–7.50 (m, 6H), 7.57–7.61 (m, 2H), 7.93–7.96 (m, 3H).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3031, 2959, 2925, 2849, 1635, 1462, 1286, 1125.

**Compound h:** M.p. 147–148°C (lit.<sup>9</sup> 149–150°C)  $\delta_{\text{H}}$  (ppm) 7.61–7.59 (d, 4H  $J$  = 8.0 Hz), 7.40–7.38 (d, 4H  $J$  = 8.0 Hz), 2.65 (s, 6H).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3034, 1640, 1590, 1470, 1450, 1390, 1300, 1240, 850.

**Compound i:** M.p. 192–193°C (lit.<sup>8</sup> 193–195°C)  $\delta_{\text{H}}$  (ppm) 7.71–7.73 (d, 4H  $J$  = 8.19), 8.05–8.07 (d, 4H  $J$  = 8.19).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3043, 2920, 1680, 1605, 1553, 1419, 1395, 1274.

**Compound j:** M.p. 127–129°C (lit.<sup>9</sup> 128°C)  $\delta_{\text{H}}$  (ppm) 4.43 (s, 4H), 6.64–6.63 (d, 4H  $J$  = 7.6 Hz), 7.24–7.23 (d, 4H  $J$  = 7.6), (DMSO-*d*<sub>6</sub>).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3400, 3310, 3200, 3030, 1600, 1500, 1320, 820, 700.

**Compound k:** M.p. 113–115°C (lit.<sup>9</sup> 112°C)  $\delta_{\text{H}}$  (ppm) 1.39 (t, 6H), 4.41 (q, 4H), 7.68–7.70 (d, 4H  $J$  = 8.1), 8.13–8.11 (d, 4H  $J$  = 8.1).  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3028, 2988, 2860, 1725, 1635, 1588, 1400, 1211, 867.

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## References

- D.W. Knight, In *Comprehensive Organic Synthesis*; B.M. Trost and O. Fleming, 1., Eds; Pergamon: Oxford, 1991, Vol. 3, 499, Chapter 2, 3.
- (a) P.E. Fanta, *Chem. Rev.*, 1946, **38**, 139; (b) P.E. Fanta, *Chem. Rev.*, 1964, **64**, 613; (c) P.E. Fanta, *Synthesis*, 1974, 9.
- (a) S. Venkatraman and C.J. Li, *Tetrahedron Lett.*, 2000, **41**, 4831; (b) D.D. Hennings; T. Iwama and H. Rawal, *Org. Lett.*, 1999, **1**, 1025.
- F. Diederich and P.J. Stang, Eds. *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH: Weinheim, 1998.
- I. Atsushi, K.G. Kazuya, S.K. Hiroshi and O.M. Koichiro, *Tetrahedron*, 2000, **56**, 9601–9605.
- (a) R. Yanada, N. Negoro, K. Yanada and T. Fujita, *Tetrahedron Lett.*, 1997, **38**, 3271; (b) R. Yanada, N. Negoro, K. Yanada and T. Fujita, *Tetrahedron Lett.*, 1996, **37**, 9313; (c) M. Lautens and P. H. Delanghe, *J. Org. Chem.*, 1995, **60**, 2474; (d) Y. Taniguchi, N. Fujii, K. Takaki and Y. Fujiwara, *J. Organomet. Chem.*, 1995, **491**, 173; (e) T. Yamazaki, J.T. Lin, M. Takeda and T. Kitazume, *Tetrahedron Asymmetry*, 1990, **1**, 351; (f) G.A. Molander and J.B. Etter, *J. Org. Chem.*, 1998, **53**, 6077.
- I. Colon and D.R. Kelsey, *J. Org. Chem.*, 1986, **51**, 2627–2637.
- Catalog Handbook of Fine Chemicals and Laboratory Equipment 2000–2001*, Aldrich Chemical Company Inc., Milwaukee, USA.
- Dictionary of Organic Compounds* 1982, 5th Edition, Chapman and Hall, New York, USA.