

# Communications

## Direct Preparation of Organocadmium Compounds from Highly Reactive Cadmium Metal Powders

**Summary:** Highly reactive cadmium metal powders and a cadmium-lithium alloy were prepared and were used to prepare organocadmium reagents directly from organic halides

**Sir:** The transmetalation reaction of an organomagnesium or organolithium reagent with cadmium halides is a well-known standard preparation method for organocadmium reagents.<sup>1</sup> However, the functional groups on the organocadmium reagent are limited. We would like to report that organocadmium reagents can be prepared by the direct oxidative insertion of highly reactive cadmium with alkyl and aryl halides containing a variety of functional groups.

It has been reported that an organocadmium reagent can be prepared directly from cadmium metal and alkyl halides.<sup>2</sup> However, the reaction was limited to ethyl iodide. Using the general reduction approach which we reported earlier, highly reactive cadmium metal powders as well as a cadmium-lithium alloy can be readily prepared.<sup>3</sup> This metal is highly reactive toward a variety of organic halides. The organocadmium reagents formed undergo the well-known reaction with acid chlorides<sup>4</sup> to form ketones in high yields. In addition, substituted aryl compounds have been produced by cross-coupling reactions of the organocadmium reagents with allyl bromide. Furthermore, this highly reactive metal undergoes Reformatsky-type reactions with  $\alpha$ -bromo esters in ethereal solvents, forming an organocadmium that will react with aldehydes or ketones.

Three general approaches can be used to prepare the metal powders. In method A, lithium naphthalide is first prepared in glyme or THF at room temperature and then transferred via cannula into a second flask containing cadmium chloride.<sup>5</sup> The mixture is stirred for 30 min at room temperature to produce a black slurry. After standing for 6-12 h, the black powders settle, leaving a clear solution above the metal. The solvent can be removed via a cannula at this point and the metal washed with fresh dry solvent to remove naphthalene and lithium salts. A different solvent may be added at this point.

A second approach, method B, allows the preparation of the highly reactive cadmium powders in hydrocarbon rather than ethereal solvents and produces a more highly reactive cadmium than method A.<sup>6</sup> Lithium naphthalide is prepared by sonicating lithium, naphthalene, and

Table I. Optimum Conditions of Preparation of the Organocadmium Reagent



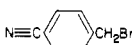
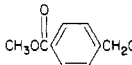


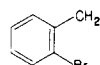
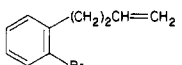
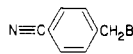
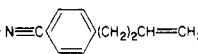

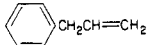

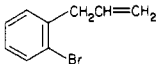
substrate	reduction method	ratio Cd:Rx	temp, °C	time, h
	A or C + iodine	1:1	20	2.5
	A	1:0.85	0	7.0
	A or C + iodine	1:0.9	0	5.0
	C + iodine	1:0.8	20	18.0
	A	1:1	85	36.0
	B	1:1	111	12.0
	C	3:1	66	18.0
	A	1:0.8	85	12
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> Br	C + iodine	1:1	85	9.5

Table II. Cross-Coupling Reactions with Allyl Bromide

cadmium reagent	product	yield, %
		94 <sup>a</sup>
		40 <sup>b</sup>
		52 <sup>a</sup>
		25 <sup>b</sup>

<sup>a</sup> Yields by GLC. <sup>b</sup> Isolated yields.

*N,N,N',N'*-tetramethylethylenediamine in toluene for 8-12 h.<sup>7</sup> The deep purple solution is then transferred via cannula onto cadmium chloride, and the resulting mixture is stirred for 30 min, yielding a black slurry which slowly settles on standing.

A third approach, method C, represents a new convenient method of producing the known cadmium lithium alloy, Cd<sub>3</sub>Li. In this method, lithium (28.94 mmol), cadmium chloride (12.39 mmol), and a catalytic amount of naphthalene are added to glyme or THF (20 mL) and the mixture is refluxed until the lithium disappears, approximately 3-4 h.<sup>8</sup> The resulting black slurry contains the known alloy Cd<sub>3</sub>Li. The alloy Cd<sub>3</sub>Li has been previously prepared by melting lithium and cadmium together in an inert atmosphere.<sup>9</sup> However, there have been no reports of any attempts to use this alloy synthetically. X-ray powder diffraction of the finely divided metal powder displayed spectral lines matching those lines observed for the known alloy, Cd<sub>3</sub>Li, and Cd metal.<sup>10,11</sup> However, el-

(1) Gilman, H.; Nelson, J. F. *Recl. Trav. Chim. Pays-Bas* 1936, 55, 518. Cason, J. *Chem. Rev.* 1947, 40, 15.

(2) Klabunde, K. J.; Murdock, T. O. *J. Org. Chem.* 1976, 41, 1076.

(3) Rieke, R. D.; Li, P. T.; Burns, T. P.; Uhm, S. T. *J. Org. Chem.* 1981, 46, 4323. Rieke, R. D.; Hudnall, P. M. *J. Am. Chem. Soc.* 1972, 94, 7178.

(4) Cason, J. *Chem. Rev.* 1947, 40, 15. Shirley, D. A. *Org. React. (N.Y.)* 1954, 8, 28.

(5) Li (36.84 mmol) and naphthalene (38.58 mmol) in 30 mL of glyme or THF is stirred 4 h under argon. The green lithium naphthalide is transferred via cannula into the CdCl<sub>2</sub> (16.01 mmol) and stirred 30 min. The black cadmium powders settle from the colorless solution in 6-12 h.

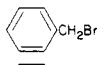
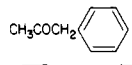
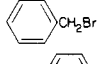
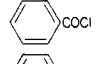
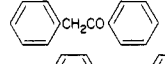
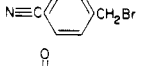
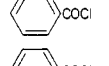
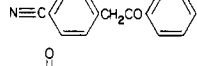
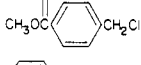
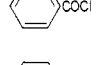
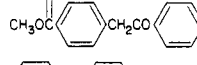

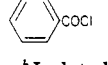
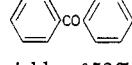
(6) Li (9.993 mmol), naphthalene (11.833 mmol), and TMEDA (11.512 mmol) in 25 mL of toluene is sonicated for 8-12 h under argon.<sup>7</sup> The deep purple lithium naphthalide is transferred via cannula into the CdCl<sub>2</sub> (4.9820 mmol) and stirred 30-60 min. The black cadmium powders settle from the colorless solution in 6-12 h.

(7) Fujita, T.; Watanaba, S.; Suga, K.; Sugahara, K.; Tsuchimoto, K. *Chem. Ind. (London)* 1983, 4, 167.

(8) Li (28.94 mmol), CdCl<sub>2</sub> (12.39 mmol), and naphthalene (2.88 mmol) are stirred in 30 mL of refluxing glyme or THF. The reduction is complete when the lithium piece is consumed.

(9) Van der Merel, C.; Vinke, G. J. B.; Hennepf, J.; van der Lugt, W. *J. Phys. Chem. Solids* 1982, 43, 1013.

Table III. Preparation of Ketones from Acid Chlorides

RX	RCOCl	ketone	yield, %
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> Br	CH <sub>3</sub> COCl	CH <sub>3</sub> CO(CH <sub>2</sub> ) <sub>4</sub> CH <sub>3</sub>	80 <sup>a</sup>
	CH <sub>3</sub> COCl		40 <sup>a</sup>
			90 <sup>a</sup>
			33, <sup>a,c</sup> 19 <sup>b</sup>
			20 <sup>a</sup>
			60 <sup>a</sup>

<sup>a</sup> Yields by GLC. <sup>b</sup> Isolated yields. <sup>c</sup> 53% Coupled product by GLC.

Elemental analysis indicates that the alloy makes up approximately 85% of the mixture.<sup>12</sup> Treatment of the alloy with 1 equiv of I<sub>2</sub> to leach out the majority of the lithium produces a very reactive cadmium metal powder. This metal will react with alkyl and aryl halides, yielding organocadmium reagents.

Table I shows the substrates and reaction conditions for the direct oxidative insertion to a variety of organic halides. The high reactivity of the cadmium metal powders is readily apparent, reacting with benzyl bromides in under 3 h at room temperature and in 18 h in refluxing THF with iodobenzene. This highly reactive metal powder reacts selectively with the benzyl bromide of *o*-bromobenzyl bromide, giving an organocadmium which yields *o*-bromotoluene upon quenching with acid. The organocadmium reagent produced adds to allyl bromide to give the cross-coupled product in high yield. A summary of cross-coupling reactions with allyl bromide is given in Table II.<sup>13</sup>  $\alpha$ -Bromo-*p*-tolunitrile reacts with cadmium metal powder at 0 °C, giving an organocadmium reagent which can react with allyl bromide or an acyl chloride to give products with the cyano group intact.

The organocadmium reagents can be used in the standard ketone synthesis from acid chlorides.<sup>14</sup> However, when highly reactive cadmium is used, a variety of new functional groups can be present in the organocadmium reagent. Table III summarizes some of these results.

The preparation of a Reformatsky-type reagent from cadmium metal and *tert*-butyl  $\alpha$ -bromoacetate has been reported to proceed in Me<sub>2</sub>SO or HMPT.<sup>15</sup> However, the reported yields upon reaction with aldehydes were in the range of 20–60%. The highly reactive cadmium produced by either method A or method C reacts with  $\alpha$ -halo esters to give the corresponding Reformatsky-type reagent which

adds to aldehydes or ketones in high yields.<sup>16</sup> However, the reaction proceeds much faster and in higher yields when using the cadmium–lithium alloy prepared by method C. In the case of benzaldehyde, the  $\beta$ -hydroxy ester, ethyl 3-hydroxy-3-phenylpropionate, dehydrated over the course of the reaction to give 90% ethyl 3-phenyl-2-propenoate after 24 h in refluxing diethyl ether. However, reaction of the Reformatsky reagent with cyclohexanone gave only the  $\beta$ -hydroxyester, ethyl 1-hydroxycyclohexaneacetate in a yield of 92% at 4 h and 100% at 24 h.<sup>17</sup>

In summary, methods have been presented for the preparation of highly reactive cadmium and a cadmium–lithium alloy. These reactive metals have produced a general route to the direct preparation of organocadmium reagents. This approach now allows the preparation of organocadmium reagents with functional groups not tolerated by previous routes.

**Acknowledgment.** We gratefully acknowledge support of the work by the Division of Chemical Sciences, Department of Energy (Contract No. De-AC02-80ER0603).

**Registry No.** Br-*o*-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Br, 3433-80-5; NC-*p*-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Br, 17201-43-3; PhI, 591-50-4; I-*o*-C<sub>6</sub>H<sub>4</sub>Br, 583-55-1; CH<sub>3</sub>(CH<sub>2</sub>)<sub>4</sub>Br, 110-53-2; PhCH<sub>2</sub>Br, 100-39-0; CH<sub>3</sub>OC(O)-*p*-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl, 34040-64-7; CH<sub>3</sub>COCl, 75-36-5; PhCOCl, 98-88-4; BrCH<sub>2</sub>CH=CH<sub>2</sub>, 106-95-6; CH<sub>3</sub>CO(CH<sub>2</sub>)<sub>4</sub>CH<sub>3</sub>, 110-43-0; CH<sub>3</sub>COCH<sub>2</sub>Ph, 103-79-7; PhCH<sub>2</sub>COPh, 451-40-1; NC-*p*-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>COPh, 59824-23-6; CH<sub>3</sub>OC(O)-*p*-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>COPh, 94161-45-2; PhCOPh, 119-61-9; Br-*o*-C<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>)<sub>2</sub>CH=CH<sub>2</sub>, 71813-50-8; NC-*p*-C<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>)<sub>2</sub>CH=CH<sub>2</sub>, 15451-33-9; PhCH<sub>2</sub>CH=CH<sub>2</sub>, 300-57-2; Br-*o*-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CH=CH<sub>2</sub>, 42918-20-7; Cd, 7440-43-9; Cd<sub>3</sub>Li, 85133-98-8; TMEDA, 109-76-2; ethyl bromoacetate, 105-36-2; cyclohexane, 110-82-7; ethyl 1-hydroxycyclohexaneacetate, 5326-50-1; benzaldehyde, 100-52-7; ethyl 3-phenyl-2-propenoate, 103-36-6; lithium naphthalene, 25398-08-7; naphthalene, 91-20-3; cadmium chloride, 10108-64-2.

**Supplementary Material Available:** Full experimental details on the three methods of preparation of highly reactive cadmium and their reactions with alkyl and aryl halides to prepare organocadmium reagents (4 pages). Ordering information is given on any current masthead page.

(16) Reformatsky reaction: Metal powders prepared by method C were reacted with ethyl bromoacetate and cyclohexanone in refluxing diethyl ether for 24 h. GLC analysis on hydrolyzed aliquotes showed 100% 1-hydroxycyclohexaneacetate. GLC conditions: 5% SE 30 on Chromosorb GAW 60/80, temperature program of 120 °C for 2 min then increasing at a rate of 32°/min to 240 °C.

(17) All new compounds reported in this manuscript had correct elemental analyses as well as expected spectroscopic properties.

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(10) Zintl, E.; Schneider, A. *Ztschr. Elektrochem.* 1935, 41, 294.

(11) Powder Diffraction File, 5-0674, Smith, J. V., Ed.; American Society for Testing and Materials, Philadelphia, 1967.

(12) Elemental analysis by Spang Microanalytical Laboratory as mol %: Cd, 85.4; Li, 28.0; Cl, 1.1; C, 5.9; H, 6.9; O, 7.7.

(13) *o*-Bromobenzyl bromide (2.625 g, 10.50 mmol) is added to the cadmium slurry prepared by method A. (13.496 mmol, washed 3 × 30 mL of glyme to remove the naphthalene) over 10 min at 0 °C. After 7 h at 0 °C, allyl bromide (3.1529 g, 26.061 mmol) is added. Four hours later the reaction mixture was quenched with 5 mL of 1 N HCl and worked up by standard procedures to give 76% 4-(2-bromophenyl)-2-butene.

(14) General reaction procedure: Iodine (7.416 mmol) in glyme was added to the cadmium–lithium alloy (14.79 mmol of CdCl<sub>2</sub> reduced). Benzyl bromide (12.6 mmol) was dripped into the black slurry over 30 min. The glyme was stripped off in vacuo and 15 mL of benzene added. Benzoyl chloride (12.1 mmol) was added and stirred 20 h at room temperature. The yield by GLC was 88% benzyl phenyl ketone and 9% bibenzyl. Cadmium powders generated by method A are used without treatment with iodine.

(15) Gaudemar, M. *C.R. Acad. Sci., Ser. C* 1969, 268, 1439.

### Asymmetric Carbon to Nitrogen Bond Formation Using Optically Active Allylic Selenides: A New General Method for the Synthesis of N-Protected Optically Active $\alpha$ -Amino Acids

**Summary:** Optically active allylic selenides undergo oxidative [2,3]-sigmatropic rearrangement to afford optically active, protected allylic amines. The synthetic utility of this process is demonstrated by the synthesis of several N-protected D- $\alpha$ -amino acids in 78–84% enantiomeric excess.

**Sir:** Sigmatropic rearrangements are commonly employed for the intramolecular transfer of stereogenicity<sup>2</sup> in organic