Oxidative Intramolecular Coupling of Amidocuprates as a Novel Route to Amines and Hydrazines

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Amidocuprates, derived from organocopper reagents and lithium amides upon exposure to oxygen at low temperature, provide new amine derivatives in satisfactory yields. Details of this flexible and simple methodology are given. The reaction mechanism is analyzed in terms of an oxidative intramolecular coupling of aminyl radicals with the ligands on Cu in the intermediate amidocuprate. This reaction is a mild and efficient method for N-alkylation, -vinylation, and -arylation by which a number of amines, not easily accessible by normal routes, can be synthesized. Once applied to lithium hydrazides, it also provides a new and straightforward entry to N-substituted hydrazines.

Introduction

The delivery of an amino group to a nucleophilic site constitutes a useful transformation in organic chemistry, and for this purpose a practical electrophilic amination protocol has been developed.[1] Several reagents for electrophilic amination have been reported in which the nitrogen atom is bonded to a leaving group[2] whose leaving ability can be enhanced by interaction with a suitable metal center. Indications are that the formation of the new C−N bond is a S_N2-type reaction.[3]

We reported[4] in an earlier paper that the electrophilic amination of higher order (H.O.)[5] cyanocuprates by bis-(trimethylsilyl)hydroxylamine provides a suitable entry into otherwise inaccessible amine derivatives. The present paper expands upon this investigation by showing that new amine derivatives can be obtained by an even simpler procedure, *i.e.*, by reaction of organocuprates with amines lacking good leaving groups, followed by quenching with molecular oxygen.

Results and Discussion

We found that reaction of lithium amides, obtained by metalation of amines with *n*-BuLi, with an equimolar amount of monoanionic (L.O.)[5] cuprate (procedure A in Scheme 1) affords a clear, fairly stable solution which at low temperature in the presence of oxygen decomposes into a heterogeneous dark mixture. From this mixture a newly formed amine derivative could be recovered (see the Experimental Section).

Scheme 1
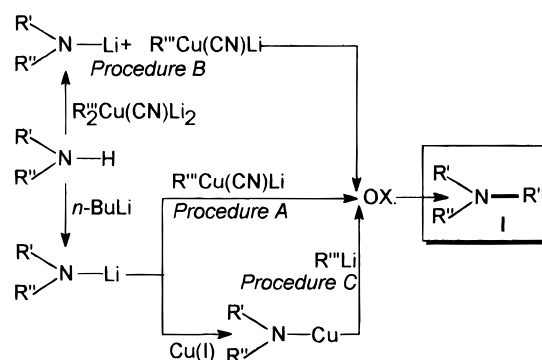
The reaction took place in an analogous manner and with comparable yields whether amines were combined (procedure B) with bis anionic (H.O.) cuprates with deprotonation and *in situ* generation of lithium amides in the first step or by adding (procedure C) cuproamides obtained by transmetalation of lithium amides with CuI, CuBr·Me$_2$S, or CuCN to a suitable organolithium derivative. Since procedure C is the usual method for the generation of amidocuprates,[6] the existence of these species throughout the range of reactions so far reported is inferred.

Even though a Cu-mediated Ullmann condensation leading to C−N bond formation has been the subject of a mechanistic study,[7] to our knowledge only two examples of a synthetically useful N-alkylation of an amine, based on an oxidative coupling of lithium alkyl copper amides, have been previously reported.[8] These procedures utilize 3- or 5-fold excesses of cuprate with respect to the amine used. Furthermore, no description of the mechanism of this reaction has been given. It is noted that the use of organocuprates is crucial for the efficient introduction of nitrogen at donor sites since neither the use of simple organolithium derivatives nor that of Grignard reagents afforded the amine derivatives **I** upon reaction with lithium amides.

The relevant results of the N-alkylation and N-arylation of primary and secondary amines with organocopper

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⊗ Abstract published in *Advance ACS Abstracts,* February 1, 1996.
(1) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988,** *88,* 298. Erdik, E.; Ay, M. *Chem. Rev.* **1989,** *89,* 1947. Mitchell, H.; Leblanc, Y. *J. Org. Chem.* **1994,** *59,* 682 and references cited therein.
(2) Genet, J.-P.; Mallart, S.; Greck, C.; Piveteau, E. *Tetrahedron Lett.* **1991,** *32,* 2359. Greck, C.; Bischoff, L.; Ferreira, F.; Pinel, C.; Piveteau, E.; Genet, J.-P. *Synlett,* **1993,** 475.
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(5) The terms "higher order" (H.O.) and "lower order" (L.O.) refer to the RLi/Cu(I) ratios employed in the cuprate preparation.

(6) Rossiter, B. E.; Eguchi, M. *Tetrahedron Lett.* **1990,** *31,* 965.
(7) Paine, J. A. *J. Am. Chem. Soc.* **1987,** *109,* 1496.
(8) Yamamoto, H.; Maruoka, K. *J. Org. Chem.* **1980,** *45,* 2739. Iwao, M.; Reed, J. N.; Snieckus, V. *J. Am. Chem. Soc.* **1982,** *104,* 5531.

Table 1. Oxygen-Promoted Electrophilic Amination of Cyanocuprates with Lithium Amides

$$\underset{R''}{\overset{R'}{N}}\text{—Li} + R'''Cu(CN)Li \xrightarrow[\text{THF,-78°C}]{O_2} \underset{R''}{\overset{R'}{N}}\text{—R'''} \quad \mathbf{I}$$

Entry	R'	R"	R'''	Product[a]	Yield%[b]	Entry	R'	R"	R'''	Product[a]	Yield%[b]
1	Ph	H	n-Bu	Ia	62	7	Ph	Me	Benzofuryl	Ig	25(45)[c]
2	i-Pr	i-Pr	n-Bu	Ib	50	8	i-Pr	i-Pr	PhCH=CH	Ih	45(55)[c]
3	i-Pr	i-Pr	Ph	Ic	60	9	CH3CH(1-naphthyl)	H	n-Bu	Ii	60
4	Ph-CH2	Ph	Me	Id	50	10	" "	H	Ph	Ij	48
5	Ph-CH2	Me	n-Bu	Ie	45	11	" "	H	(2-OCH3-phenyl)	Ik	55
6	Ph	Me	Thienyl	If	52(60)[c]	12	" "	H	(2-OCH2Ph-phenyl)	Il	46

[a] A darkened bond in the formula indicates the bond created by the carbon-nitrogen bond forming reactions.
[b] Isolated yields; average of three or more runs. [c] GC yields.

reagents are reported in Table 1. Along with the desired amines isolated in satisfactory yields, variable amounts of C–C homocoupling byproducts were also present in the reaction mixtures.

Substitution at the nitrogen played an important role, and secondary amines bearing aliphatic substituents were the most suitable starting materials for the title reaction. Finally, a sizeable reduction of yield was observed upon replacing molecular oxygen with other oxidizing reagents such as $CuCl_2$, copper(II) 2-ethylhexanoate, $VOCl_3$, $Me_3SiOOSiMe_3$, or RuO_2.

In addition to providing a method for monoalkylation at the nitrogen atom (Table 1, entries 1, 2, 4, and 5), this oxidative coupling reaction allows for the N-vinylation (Table 1, entry 8) and -heteroarylation (Table 1, entries 6 and 7) of amines of synthetic interest. These reactions do not have simple or straightforward counterparts in the literature. Regarding N-arylation (Table 1, entry 3), arylamines are structural components in a variety of synthetic and natural biologically active compounds, and many synthetic methods for the construction of an aryl–N bond have been reported,[9] most of which, however, suffer from a need for severe reaction conditions or activated substrates. These difficulties can be overcome by using the oxidative coupling methodology reported herein. For instance, this method was well-suited for use in the convenient synthesis of N-substituted derivatives

(**Ii–l**) of (R)-(+)-1-(1-naphthyl)ethylamine reported in Table 1 (entries 9–12). Apart from the N-alkylation (**Ii**) and N-arylation (**Ij**) products, the chiral N-(2-methoxyphenyl)-(R)-(−)-1-(1-naphthyl)ethylamine (**Ik**) and the N-[2-(benzyloxy)phenyl]-(R)-(−)-1-(1-naphthyl)ethylamine (**Il**), valuable chiral auxiliaries in asymmetric catalytic reactions,[10] although not readily accessible, could be synthesized in fairly good yields. No racemization could be detected during these reactions.[11]

When applied to hydrazines, this reaction proved to be a mild method for the delivery of the hydrazido group to nucleophilic sites, thus opening a new and viable route to functionalized hydrazines (**IIa–c**) from commercially available starting materials. A few representative examples of this latter reaction are reported in Table 2.
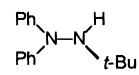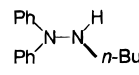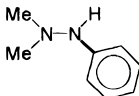
Interestingly, N-alkylation with groups bearing hydrogens at the carbon of the newly formed C–N bond (as in entry 14) led to formation of the corresponding hydrazone as the major product, presumably by hydrogen elimination from the expected hydrazine. The use instead of the usual lithium–hydrazidocuprate of a more stable lithium–zinc–hydrazidocuprate whose stoichiometric composition (see the Experimental Section) can be described as [n-Bu(Ph2N-NR)CuZnCl/LiCl,LiCN], prevented this side reaction.

(9) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992. For recent reports on substitution reactions of N-nucleophiles with aromatic substrates bearing activating groups, see also: Semmelhack, M. F.; Rhee, H. *Tetrahedron Lett.* **1993**, *34*, 1395. Hattori, T.; Sakamoto, J.; Hayashizaka N.; Miyano, S. *Synthesis* **1994**, 199.

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(11) Treatment of (R)-(+)-1-(1-naphthyl)ethylamine in THF at −78 °C with 1 equiv of n-BuLi followed by aqueous quenching gave a compound with spectral data (1H-, 13C-NMR) and [α]D +60 (c = 5, MeOH) identical with those of the starting material.

Table 2. Oxygen-Promoted Electrophilic Amination of Cyanocuprates with Lithium Hydrazides

Entry	R	R'	R"	Product[a]	Yield%[b]
13	Ph	Ph	*t*-Bu	IIa	30(40)[c]
14	Ph	Ph	*n*-Bu	IIb	18(20)[c,d]
15	Me	Me	Ph	IIc	40(60)[c]

[a] A darkened bond in the formula indicates the bond created by the carbon−nitrogen bond-forming reactions. [b] Isolated yields; average of three or more runs. [c] Gc yields. [d] Only trace amounts (2% ca.) of the expected product were isolated according to the standard procedure. A significant increase of yields (18% of isolated product) was achieved by using *n*-BuCu(CN)ZnCl/LiCl instead of *n*-BuCu(CN)Li.
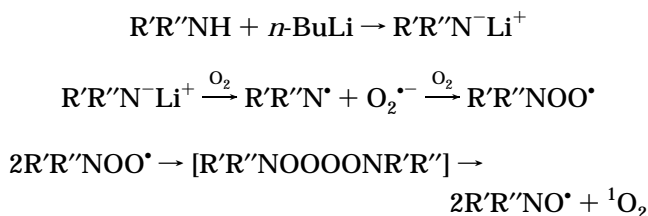
The reaction under study competes with a common side process associated with the inadvertent oxidation by dioxygen of lithioorganocuprates which leads[12] to coupling between the ligands on copper.[13] Rationalization of the new C−N bond formation might suggest, in principle, the intervention of long-lived free radicals as reaction intermediates. Experiments were therefore carried out inside the cavity of an EPR spectrometer under a variety of experimental conditions in order to detect the formation in the present reaction of species such as aminyl radicals, which are known[14,15] to be easily generated by thermolysis of a tetrazene species or by photolysis of di-*tert*-butyl peroxide in the presence of amines.

Not surprisingly, the reaction between diisopropyl, diethyl, or diphenylamine with butyllithium under an inert atmosphere did not lead to the observation of any EPR signals; however, after the reaction mixture was purged with oxygen, intense and broad signals of the corresponding diisopropyl ($a_{2H} = 4.45$ G, $a_N = 14.72$ G, $g = 2.0059_6$), diethyl ($a_{4H} = 10.30$ G, $a_N = 15.20$ G, $g = 2.0059_9$), and diphenyl ($a_{6H} = 1.80$ G, $a_{4H} = 0.80$ G, $a_N = 9.68$ G, $g = 2.0056_8$) nitroxides were observed, whose resolution drastically improved upon removing the excess oxygen with argon. On the other hand, no EPR spectra were observed upon saturating solutions of the amines with oxygen. Although it is known[15] that the reaction of secondary amines with singlet oxygen affords the corresponding nitroxides, the observation of aminoxyl radicals

by treating lithiated amines with molecular oxygen is to our knowledge unprecedented.

On the other hand, the rate constants of the reactions between aminyls and oxygen must be very fast, possibly close to the diffusion-controlled limit. The direct EPR detection of aminyls in oxygenated media is therefore unlikely, especially when taking into consideration the fact that metal-complexed aminyls are much more reactive[16] than neutral aminyls. Even if no direct spectroscopic evidence of the participation of aminyl radicals in these reactions could be obtained, we infer that these species, possibly generated *in situ* via an electron transfer process, may be considered to be the precursors of the observed aminoxyls as outlined in Scheme 2.[17]

Scheme 2

$$R'R''NH + n\text{-BuLi} \rightarrow R'R''N^-Li^+$$

$$R'R''N^-Li^+ \xrightarrow{O_2} R'R''N^\bullet + O_2^{\bullet-} \xrightarrow{O_2} R'R''NOO^\bullet$$

$$2R'R''NOO^\bullet \rightarrow [R'R''NOOOONR'R''] \rightarrow$$
$$2R'R''NO^\bullet + {}^1O_2$$

Similar results were obtained with the amidocuprates from the same amines. When solutions of these amidocuprates were put inside the cavity of the EPR spectrometer prior to oxygen quenching, in no case did they exhibit any EPR signal, even at low temperature ($T \leq -80$ °C). On the other hand, purging the solutions with oxygen resulted again in the observation of intense EPR signals due to diisopropyl, diethyl, or diphenyl nitroxide, thus suggesting that the oxygen-induced decomposition of the amidocuprates might involve the formation of aminyl radicals in a preliminary step.

Finally, an experiment in which interaction of lithium anilide PhHNLi with the cuproamide PhNHCu(CN)Li was followed by quenching with oxygen under the usual conditions led to the isolation of 70% PhN=NPh from dehydrogenation of the corresponding 1,2-diphenylhydrazine. We believe that the formation of a new N−N bond provides further support for the presence of aminyl radicals in the oxidative coupling reaction.

Reliable information is available on the structures of the amidocuprates by ⁷Li and ¹H NMR spectroscopy[18] and by analogy with reported X-ray studies for organocopper compounds.[19] Taking into consideration the Li:Cu and the amide:C-ligand ratios used in this work, the formation of discrete dimers [(R'R''N)₂Cu₂R'''₂]Li₂·2LiCN can be hypothesized. For these species, a roughly planar structure (**III**) with staggered organo and amido ligands, each bound to two metals by a three-center two-electron bond and occupying the corner positions, can be proposed in accordance with the literature reports.[6,18,20] These observations together with previously reported evidence for the formation of radical species upon oxygen-induced

(12) Whitesides, G. M.; San Filippo, J. Jr.; Casey, C. P.; Panek, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 5302.

(13) This synthetically unattractive reaction from which statistical ratios of three products are generated, when performed on products with mixed-ligand reagents, has been very recently reevaluated by Lipshutz through the generation of "kinetic" bis anionic cuprates. Extremely high levels of unsymmetrical ligand coupling have been achieved which allow for a novel straightforward synthesis of biaryls through inter- or intramolecular coupling: Lipshutz, B. H.; Kayser, F.; Maullin, N. *Tetrahedron Lett.* **1994**, *35*, 815. Lipshutz, B. H.; Kayser, F.; Liu, Z.-P. L. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1842 and references therein.

(14) Jones, P. W.; Gesser, H. D. *J. Chem. Soc. B* **1971**, 1873.

(15) Roberts, J. R.; Ingold, K. U. *J. Am. Chem. Soc.* **1973**, *95*, 3228.

(16) Maeda, Y.; Ingold, K. U. *J. Am. Chem. Soc.* **1980**, *102*, 328.

(17) At this stage the formation of the tetraoxide is only speculative and is based on the behavior of peroxy radicals, but no efforts have been made to detect singlet oxygen. As an alternative, it is possible to envisage the coupling of the amino peroxy radicals with aminyl radicals to afford RRNOONRR whose fragmentation would lead to two molecules of the RRNO• nitroxide.

(18) Dieter, R. K.; Hanks, T. W.; Lagu, B. *Organometallics*, **1992**, *11*, 3549.

(19) Olmstead, M. M.; Power, P. P. *J. Am. Chem. Soc.* **1990**, *112*, 8008.

(20) Dieter, R. K.; Tokles, M. *J. Am. Chem. Soc.* **1987**, *109*, 2040.

Scheme 3
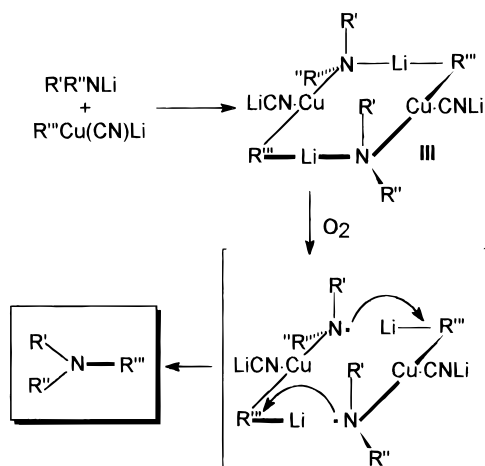
decomposition of amidocuprates allow us to visualize the overall process as depicted in Scheme 3.

No attempts were made to establish the fate of the copper upon decomposition of the organocuprates, but when oxygen-quenched solutions where allowed to warm to room temperature inside the cavity of the EPR spectrometer, a four-line signal attributable to a Cu^{2+} complex [$a(^{63}Cu) = 82$ G, $g = 2.116_8$] was observed.

Nothwithstanding the question it raises concerning the nature of the intermediate(s) and the mechanism, we have demonstrated that, through oxidative intramolecular coupling, a range of amido- and hydrazidocuprates easily generated *in situ* from readily available starting materials can be converted into the corresponding amines and hydrazines, respectively. Overall, the amidocuprate/oxidative decomposition sequence provides a fairly general and attractive entry to C–N bond formation. Generality, flexibility, and the possibility of performing selective functionalization at the nitrogen are important characteristics of this reaction which favorably compares to a very recent, elegant N-arylation procedure based on a transamination reaction coupled with Pd catalysis.[21] Efforts to modify the reaction conditions, broaden the scope, and develop synthetic applications of these and related reactions are currently in progress.

Experimental Section

General Methods. THF was freshly distilled under a nitrogen atmosphere from sodium and benzophenone ketyl. Thiophene, benzofuran, *n*-butyllithium, *tert*-butyllithium, phenyllithium, methyllithium, and CuCN were commercially available and were used without any further purification. The purity of commercially available lithium derivatives was checked according to Gilman.[22] All the air-sensitive reactions were run under a nitrogen atmosphere, and reagents were added through septa using oven-dried syringes. Unless otherwise stated, the LO lithium cyanocuprates were prepared according to the following general procedure: the lithium compound (2.00 mmol) was added to 10 mL of THF at −40 °C. CuCN (2 mmol) was introduced quickly under a nitrogen flow, and the reaction mixture was stirred with dissolution of the salt, which was complete generally after about 20 min. ^{1}H NMR spectra unless otherwise stated were recorded at rt in CDCl$_3$ at an operating frequency of 200 MHz and were referenced to TMS. ^{13}C NMR spectra were recorded at 50.3 MHz. Capillary GC analyses were performed using a 25 m × 0.25 mm, cross-linked 5% methylphenylsilicone capillary

column. High-resolution mass spectra (HRMS, EI/DP) were obtained at 70 eV. Elemental analyses are within ±0.3%.

***N*-Butylaniline (Ia): Typical Procedure.** To a brown clear solution of *n*-BuCuCNLi (2.00 mmol), cooled to −40 °C, was added a THF solution of *N*-lithium anilide (2.00 mmol). The mixture was allowed to react at this temperature for 15 min. In the reaction mixture cooled to −78 °C was introduced a vigorous stream of oxygen for an additional 20 min. A dark precipitate was formed during this time. The reaction mixture was allowed to rise to rt, filtered through a Celite pad, and concentrated, and the crude material was purified by flash chromatography on silica gel with pentane–ether (8:2) to give 0.185 g (62%) of (**Ia**) as a pale yellow liquid: ^{1}H NMR δ 7.3–6.5 (m, 5H), 2.41 (t, 2H), 1.66–1.20 (m, 4H), 0.95 (t, 3H); MS *m/z* (relative intensity) 149 (M$^+$, 64), 106 (100), 77 (40), 51 (21). Spectroscopic data are in agreement with those of a commercial sample.

***N*-Butyldiisopropylamine (Ib).** The typical procedure was followed employing *n*-BuCuCNLi (2.00 mmol) and LDA (2.00 mmol). The crude material was distilled by Kugelrohr (pot temperature, 75 °C/20 mmHg) to give 0.157 g (50%) of a pale yellow liquid: ^{1}H NMR δ 3.8 (m, 2H), 2.39 (t, 2H, *J* = 6.6 Hz), 1.68–1.20 (m, 4H), 1.24 (d, 12H, *J* = 6.3 Hz), 0.95 (t, 3H, *J* = 6.6 Hz); MS *m/z* (relative intensity) 157 (M$^+$, 30), 142 (89), 114 (100), 100 (94), 72 (96), 58 (48). Anal. Calcd for C$_{10}$H$_{23}$N: C, 76.34; H, 14.75; N, 8.91. Found: C, 76.23; H, 14.80; N, 8.95.

***N,N*-Diisopropylaniline (Ic).** The typical procedure was followed, employing PhCuCNLi (2.00 mmol) and LDA (2.00 mmol). After the usual workup, 0.210 g (60%) of a yellow oil was obtained by Kugelrohr distillation (pot temperature 100 °C/20 mmHg): ^{1}H NMR δ 7.69–7.33 (m, 5H), 3.80 (m, 2H), 1.24 (d, 12H, *J* = 6.3 Hz); MS *m/z* (relative intensity) 177 (M$^+$, 58), 162 (60), 120 (100), 77 (59). Anal. Calcd for C$_{12}$H$_{19}$N: C, 81.29; H, 10.81; N, 7.90. Found: C, 82.00; H, 10.40; N, 7.92.

***N*-Methyl-*N*-phenylbenzylamine (Id).** The typical procedure was followed by adding lithium *N*-benzylanilide (2.00 mmol) to MeCuCNLi (2.00 mmol). After the usual workup, 0.197 g (50%) of **Id** was recovered by Kugelrohr distillation (pot temperature, 130 °C/20 mmHg) as a pale yellow viscous oil: ^{1}H NMR δ 7.51–7.10 (m, 10H), 3.51 (s, 2H), 2.91 (s, 3H); MS *m/z* (relative intensity) 197 (M$^+$, 84), 120 (84), 91 (100), 77 (73). Anal. Calcd for C$_{14}$H$_{15}$N: C, 85.23; H, 7.67; N, 7.10. Found: C, 85.71; H, 7.70; N, 7.18.

***N*-Butyl-*N*-methylbenzylamine (Ie).** The typical procedure was followed starting from lithium *N*-benzylmethylamide (2.00 mmol) and *n*-BuCuCNLi (2.00 mmol). After the usual workup, 0.160 g (45%) of a pale yellow viscous oil was recovered by Kugelrohr distillation (pot temperature, 100 °C/20 mmHg): ^{1}H NMR δ 7.31–7.29 (m, 5H), 3.51 (s, 2H), 2.39 (t, 2H, *J* = 6.6 Hz), 2.21 (s, 3H), 1.68–1.6 (m, 4H) 0.95 (t, 3H, *J* = 6.6 Hz); MS *m/z* (relative intensity) 177 (M$^+$, 13), 134 (85), 91 (100), 65 (25). Anal. Calcd for C$_{12}$H$_{19}$N: C, 81.29; H, 10.81; N, 7.90. Found: C, 81.00; H, 10.79; N, 7.95.

Methylphenylthiophene-2-ylamine (If). Lithium *N*-phenylmethylamide (2.00 mmol) was added to the bis-anionic (H.O.) cyanocuprate (C$_4$H$_3$S)$_2$CuCNLi$_2$ made by reacting 4 mmol of 2-thienyllithium with 2 mmol (179 mg) of CuCN. According to the typical procedure, the reaction mixture was allowed to warm to rt, filtered through a Celite pad, and concentrated, and the crude material was purified by flash chromatography on silica gel with pentane–ether (8:2) to give 0.197 g (52%) of **If** as a yellow viscous oil: ^{1}H NMR δ 7.35–7.16 (m, 3H), 7.1–6.8 (m, 4H), 6.68 (m, 1H), 3.34 (s, 3H); ^{13}C NMR (50.3 MHz; CDCl$_3$) δ 128.9, 127.8, 125.8, 124.4, 123.8, 119.9, 119.5, 116.3, 42.0; MS *m/z* (relative intensity) 189 (M$^+$, 100), 174 (31), 173 (36), 130 (10), 104 (4), 77 (19), 51 (16). Anal. Calcd for C$_{11}$H$_{11}$NS: C, 69.80; H, 5.86; N, 7.40; S, 16.94. Found: C, 69.84; H, 5.93; N, 7.39; S, 16.85.

Benzofuran-2-yl-methylphenylamine (Ig). The lithium *N*-phenylmethylamide was added to the L.O. benzofuryl cyanocuprate. After the usual workup, the reaction mixture at rt was filtered through a Celite pad and concentrated, and the crude material was purified by flash chromatography on alumina with pentane–ethyl ether (8:2) to give 0.112 g (25%) of **Ig** as a viscous yellow oil: ^{1}H NMR δ 7.50–7.00 (m, 10H),

(21) Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 7901.

(22) Gilman, H.; Haubein, A. H. *J. Am. Chem. Soc.* **1944**, *66*, 1515.

3.45 (s, 3H); ^{13}C NMR (50.3 MHz; CDCl$_3$) δ 158.0, 150.8, 154.9, 130.2, 129.2, 122.7, 121.3, 120.4, 118.7, 112.5, 110.1, 85.7, 38.6. MS *m/z* (relative intensity) 223 (M$^+$, 100), 208 (25), 180 (22), 91 (10), 77 (26), 51 (19). Anal. Calcd for C$_{15}$H$_{13}$NO: C, 80.68; H, 5.87; N, 6.28. Found: C, 80.50; H, 5.73; N, 6.42.

Diisopropylstyrylamine (Ih). The lithium derivative PhCH=CHLi was obtained *in situ* by transmetalation of PhCH=CHSnBu$_3$ (2 mmol) with *n*-BuLi (2 mmol) at -60 °C in THF (10 mL).[20] Then CuCN (2 mmol) was added at -30 °C, and LDA (2.00 mmol) was injected dropwise following the general procedure previously employed. The crude material was distilled by Kugelrohr (pot temperature, 155 °C/20 mmHg) to give 0.183 g (45%) of **Ih** as a pale yellow liquid: ^{1}H NMR δ 7.30−7.10 (m, 5H), 6.91 (d, 1H, *J* = 14 Hz), 5.24 (d, 1H, *J* = 14 Hz), 3.70 (m, 2H), 1.21 (d, 12H, *J* = 6.6 Hz); ^{13}C NMR (50.3 MHz; CDCl$_3$) δ 140.9, 133.0, 128.5, 123.0, 122.5, 95.2, 46.3, 21.8; MS *m/z* (relative intensity) 203 (M$^+$, 92), 188 (67), 160 (100), 146 (59), 118 (34), 91 (53), 51 (15). Anal. Calcd for C$_{14}$H$_{21}$N: C, 82.70; H, 10.41; N, 6.89. Found: C, 81.90; H, 10.31; N, 6.93.

***N*-Butyl-(*R*)-(+)-1-(1-naphthyl)ethylamine (Ii).** To a brown clear solution of *n*-BuCuCNLi (2.00 mmol), cooled to -40 °C, was added a THF solution of lithium (*R*)-(+)-1-(1-naphthyl)ethylamide (2.00 mmol) prepared by adding *n*-BuLi (1.6 M in hexanes, 1.25 mL, 2 mmol) to a solution of (*R*)-(+)-1-(1-naphthyl)ethylamine (342 mg, 2 mmol) in THF (3 mL) cooled at -40 °C. After the usual treatment according to the typical procedure, the crude material was purified by flash chromatography on silica gel with pentane−ether (3:7) to give 0.272 g (60%) of **Ii** as a pale yellow oil: [α]$_D$ +40 (*c* = 1.7, MeCOMe); ^{1}H NMR δ 8.23−7.47 (m, 7H), 4.66 (q, 1H, *J* = 6.6 Hz), 2.59 (m, 2H), 2.04 (br s, 1H), 1.52 (d, 3H, *J* = 6.6 Hz), 1.37 (m, 4H), 0.88 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (50.3 MHz; CDCl$_3$) δ 141.1, 134.0, 131.3, 129.0, 127.2, 125.8, 125.7, 125.3, 122.9, 122.7, 53.6, 47.7, 32.4, 25.3, 20.5, 14.0; MS *m/z* (relative intensity) 227 (M$^+$, 4), 155 (100), 129 (18), 100 (11), 57 (9). Anal. Calcd for C$_{16}$H$_{21}$N: C, 84.53; H, 9.31; N, 6.16. Found: C, 83.98; H, 9.20; N, 6.12.

***N*-Phenyl-(*R*)-(−)-1-(1-naphthyl)ethylamine (Ij)** was prepared as for **Ii** starting from lithium (*R*)-(+)-1-(1-naphthyl)ethylamide (2.00 mmol) and PhCu(CN)Li (2.00 mmol). The crude material was purified by flash chromatography on silica gel with pentane−ethyl ether (8:2) to give 0.237 g (48%) of **Ij** as a viscous oil: [α]$_D$ −249 (*c* = 1.9, MeOH); ^{1}H NMR δ 8.18 (d, 1H), 7.92 (d, 1H), 7.76 (d, 1H), 7.70−7.34 (m, 4H), 7.08 (t, 2H, *J* = 7.4 Hz), 6.64 (t, 1H, *J* = 7.8 Hz), 6.48 (d, 2H, *J* = 8.6 Hz), 5.28 (q, 1H, *J* = 6.7 Hz), 4.22 (br s, 1H), 1.67 (d, 3H); ^{13}C NMR (50.3 MHz; CDCl$_3$) δ 147.1, 139.9, 134.1, 130.7, 129.5, 129.1, 127.5, 126.1, 125.9, 125.4, 122.8, 122.3, 117.3, 113.2, 49.5, 23.6; MS *m/z* (relative intensity) 247 (M$^+$, 21), 232 (18), 155 (100), 127 (10), 77 (18), 51 (7). Anal. Calcd for C$_{18}$H$_{17}$N: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.90; H, 6.85; N, 5.56.

***N*-(2-Methoxyphenyl)-(*R*)-(−)-1-(1-naphthyl)ethylamine (Ik)** was prepared as for **Ii** starting from lithium (*R*)-(+)-1-(1-naphthyl)ethylamide (2.00 mmol) and *o*-MeO−C$_6$H$_4$-CuCNLi (2.00 mmol) prepared by metalation of 2-bromoanisole with *n*-BuLi in THF at -78 °C followed by addition of CuCN. After the usual workup, the crude material was purified by flash chromatography on silica gel with pentane−ether (8:2) to give 0.305 g (55%) of **Ik** as a white solid: mp 81−82 °C (ether−ethanol); [α]$_D$ −246 (*c* = 0.3, MeOH); ^{1}H NMR δ 8.20 (d, 1H, *J* = 8.6 Hz), 7.92 (d, 1H, *J* = 8.6 Hz), 7.76 (d, 1H, *J* = 8.6 Hz), 7.70-7.32 (m, 4H), 6.82 (m, 1H), 6.60 (m, 2H), 6.25 (m, 1H), 5.28 (q, 1H, *J* = 6.7 Hz), 4.84 (br s, 1H), 3.92 (s, 3H), 1.70 (d, 3H); ^{13}C NMR (50.3 MHz; CDCl$_3$) δ 146.2, 140.1, 136.9, 134.1, 130.7, 129.1, 127.3, 126.0, 125.9, 125.3, 122.6, 122.3, 121.2, 116.4, 111.0, 109.3, 55.5, 49.4, 23.7; MS *m/z* (relative intensity) 277 (M$^+$, 34), 262 (27), 155 (100), 123 (34), 77 (13), 51 (9). Anal. Calcd for C$_{19}$H$_{19}$NO: C, 82.28; H, 6.90; N, 5.05. Found: C, 82.00; H, 6.85; N, 5.00.

***N*-[2-(Benzyloxy)phenyl]-(*R*)-(−)-1-(1-naphthyl)ethylamine (Il).** The experimental procedure starting from lithium (*R*)-(+)-1-(1-naphthyl)ethylamide (2 mmol) and PhOCH$_2$-*o*-C$_6$H$_4$CuCNLi (2 mmol) was the same as that used for the

synthesis of **Ii**. After filtration through a Celite pad, the crude material was purified by flash chromatography (SiO$_2$, pentane−ether (8:2)) to give 0.325 g (46%) of a white solid: mp 70−71°C (cyclohexane); [α]$_D$ −212 (*c* = 0.6, MeOH); ^{1}H NMR δ 8.22 (d, 1H, *J* = 8.6 Hz), 7.95 (d, 1H, *J* = 8.6 Hz), 7.78 (d, 1H, *J* = 8.6 Hz), 7.70−7.30 (m, 9H), 6.92 (d, 1H, *J* = 8.6 Hz), 6.65 (m, 2H), 6.30 (d, 1H), 5.33 (q, 1H, *J* = 6.7Hz), 5.20 (s, 2H), 4.90 (br s, 1H), 1.71 (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (50.3 MHz; CDCl$_3$) δ 145.6, 140.2, 137.5, 137.4, 134.1, 130.8, 129.2, 128.7, 128.3, 128.1, 127.7, 127.4, 126.0, 125.4, 122.6, 122.3, 121.8, 116.3, 111.4, 111.3, 70.8, 49.5, 23.9. Anal. Calcd for C$_{25}$H$_{23}$NO: C, 84.95; H, 6.56; N, 3.96. Found: C, 85.69; H, 6.55; N, 3.94.

1,1-Diphenyl-2-*tert*-butylhydrazine (IIa). 1,1-Diphenylhydrazine (2 mmol) was metalated by *n*-BuLi (2 mmol) at -60 °C in THF (8 mL) and then was added to *t*-BuCuCNLi (2 mmol) at -40 °C. After 30 min, the clear solution was treated with a stream of O$_2$ for 30 min at -78 °C. The reaction mixture was filtered through a Celite pad, the solvent was evaporated, and the crude material was purified by flash chromatography on alumina with pentane−ether (1:1) to give 0.144 g (30%) of **IIa** as a red solid: mp 62−64 °C; ^{1}H NMR (C$_6$D$_6$) δ 7.35−7.10 (m, 10H), 3.50 (br s, 1H), 1.40 (s, 9H); ^{13}C NMR (50.3 MHz; C$_6$D$_6$) δ 152.4, 129.8, 123.2, 122.2, 55.9, 29.6; MS *m/z* (relative intensity) 240 (M$^+$, 36), 184 (100), 168 (47), 77 (57), 65 (4), 51 (19); HRMS (EI) *m/z* calcd for C$_{16}$H$_{20}$N$_2$ 240.1626, found 240.1627. Anal. Calcd for C$_{16}$H$_{20}$N$_2$: C, 79.95; H, 8.39; N, 11.66. Found: C, 80.10; H, 8.37; N, 11.83.

1,1-Diphenyl-2-*n*-butylhydrazine (IIb). Commercial ZnCl$_2$ (300 mg, 2.2 mmol) was melted under reduced pressure (0.02 mmHg) and cooled under argon several times. The anhydrous salt was dissolved in dry THF (5 mL) and added to a solution of *n*-BuLi (1.6 M in hexanes, 1.25 mL, 2 mmol) in THF (2mL) at -78 °C. After 10 min, the temperature of the solution of *n*-BuZnCl/LiCl was raised to -30 °C and CuCN (179 mg, 2 mmol) was added. After dissolution of the copper salt to the resulting clear green-yellow solution, 1,1-diphenyllithium hydrazide (2 mmol) previously obtained from metalation at -60 °C of 1,1-diphenylhydrazine by *n*-BuLi in THF (5 mL) was added. After 30 min, the clear reaction mixture was treated as usual with a stream of oxygen for 45 min at -78 °C. Filtration through a Celite pad, evaporation of the solvent, and Kugelrohr distillation of the crude material (pot temperature 150 °C/0.02 mmHg) gave 0.086 g (18%) of **IIb** as a yellow-red oil: ^{1}H NMR δ 7.40−6.90 (m, 10H), 3.90 (br s, 1H), 2.84 (t, 2H, *J* = 6.0 Hz), 1.6−1.35 (m, 4H), 0.90 (t, 3H, *J* = 7.5 Hz); MS *m/z* (relative intensity) 240 (M$^+$, 48), 183 (100), 168 (87), 115 (7), 77 (67), 51 (23); HRMS (EI) *m/z* calcd for C$_{16}$H$_{20}$N$_2$ 240.1626, found 240.1619. Anal. Calcd for C$_{16}$H$_{20}$N$_2$: C, 79.95; H, 8.39; N, 11.66. Found: C, 79.81; H, 8.28; N, 11.87.

1,1-Dimethyl-2-phenylhydrazine (IIc). 1,1-Dimethylhydrazine (2mmol) was metalated by *n*-BuLi (2 mmol) at -50 °C in THF (8 mL) and then was added to PhCuCNLi (2 mmol) at -40 °C. After 40 min, the clear solution was treated by a stream of O$_2$ for 30 min at -78 °C. The reaction mixture was filtered through a Celite pad, the solvent was evaporated, and the crude material was distilled by Kugelrohr (pot temperature 90 °C/20 mmHg) and then purified by flash chromatography on alumina with pentane−ether (6:4) to give 0.109 g (40%) of **IIc** as a dark oil: ^{1}H NMR (C$_6$D$_6$) δ 6.90−6.20 (m, 5H), 3.40 (br s, 1H), 1.85 (s, 6H); MS *m/z* (relative intensity) 136 (M$^+$, 71), 183 (60), 121 (49), 92 (100), 77 (23), 65 (50), 51 (16), 42 (24); HRMS (EI) *m/z* calcd for C$_8$H$_{12}$N$_2$ 136.1000, found 136.0997. Anal. Calcd for C$_8$H$_{12}$N$_2$: C, 70.55; H, 8.88; N, 20.57. Found: C, 71.00; H, 8.74; N, 20.80.