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Synthesis of Unsymmetrical Biaryls via "Kinetic" Higher Order Cyanocuprates: Scope, Limitations, and Spectroscopic Insights

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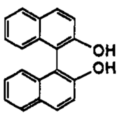
Abstract: Treatment of lower order arylcyanocuprates ArCu(CN)Li with 1 equiv of an aryllithium (Ar′Li) at temperatures around −125 °C leads to higher order reagents $Ar(Ar')Cu(CN)Li_2$. Upon exposure of such reagents at this temperature to ground-state molecular oxygen, good yields of the unsymmetrical biaryl Ar–Ar′ can be realized. Several different types of aryl ligands have been examined, including naphthalenes, to assess the generality of this method. Spectroscopic data (^{13}C NMR) have been obtained on three different cuprates at −130 °C and at higher temperatures to determine if their kinetic nature, as illustrated by their synthetic chemistry, can be substantiated by physical means.

Introduction

The biaryl nucleus is one of the more interesting substructures of many naturally occurring compounds.[1] Its formation as part of a sequence of steps oftentimes represents the key transformation in the series and can ultimately determine the levels of success associated with much synthetic effort. Of course, biaryls also play an important role in many other areas of endeavor, including their uses as nonracemic catalysts (e.g., Noyori's, 2,2′-binaphthols (**1**)[2] and BINAP (**2**)[3]), as bidentate ligands (e.g., bipyridyls **3**),[4] and as precursors to conducting polymers (e.g., polythiophenes **4**)[5] to name a few. It is perhaps, therefore, not surprising that methodology which leads to controlled bond formation in biaryls, in particular regarding *unsymmetrical* cases, is highly valued.[6]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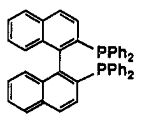
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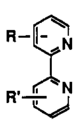
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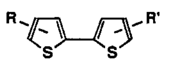
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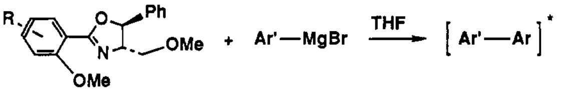
Literature routes commonly in use which effectively address in a general way the more challenging goal of unsymmetrical biaryl C–C bond construction tend to rely on organometallic chemistry.[1,6] Notable among these are (1) Stille couplings,[7] based on reactions between aryl halides and aryl stannanes, which proceed via an arylpalladium intermediate, eq 1; (2) Suzuki couplings,[8] which involve the same aryl halides but utilize arylboronic acids in the presence of catalytic Pd(0), eq 2; and (3) the Meyers oxazoline route,[9] in which the heterocyclic oxazoline directs aromatic nucleophilic substitution by an aryl Grignard, eq 3. The latter is unique in the sense that it allows for control of atropisomerism in cases where sterically congested systems lead to issues of chirality. The feature shared by all of these seminal contributions, as clearly put forth in a recent review by Bringmann,[1] is that in order to arrive at cross-coupled products from intermolecular reactions it is essential that "the two aromatic compounds used are functionally or electronically very different. Thus, both in reductive and oxidative processes electron-rich compounds must be allowed to react with electron-poor partners in order to shift the normally statistical product distribution towards the crossed products." Thus, for the methods illustrated above, the aryl halides (eqs 1 and 2) and aryloxazoline (eq 3) are the electron-deficient partners, while the arylstannanes, boronic acids, and Grignards are the nucleophilic complements in eqs 1–3, respectively. This point is especially germane as it sets the stage for establishing the unique aspect of biaryl synthesis via higher order (H.O.) cyanocuprates: that is, *both* ligands participating in these cuprate-mediated oxidative couplings are introduced as *anions*, and hence, from two aryllithium species (following cuprate formation and oxidation) comes one two-electron C–C bond.

$$\text{Ar—SnR}_3 + \text{Ar'—OTf} \xrightarrow[\text{LiCl, }\Delta]{\text{Pd(0), THF}} \text{Ar'—Ar} \qquad (1)$$

$$\text{Ar—B(OH)}_2 + \underset{\left[\text{X = halide, triflate}\right]}{\text{Ar'—X}} \xrightarrow[\text{Na}_2\text{CO}_3\text{, }\Delta]{\text{Pd(0), THF}} \text{Ar'—Ar} \qquad (2)$$


(3)

Cuprate oxidations have been utilized in the past for various reasons. Whitesides and House[10] found early on that treatment of reaction mixtures containing lower order (L.O.) cuprates R_2CuLi and alkyl halides with $^3O_2$ could give enhanced yields of substitution products. In 1986, Bertz[11] studied oxidations of the

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[1] Bringmann, G.; Walter, R.; Weirich, R. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 977.

[2] Noyori, R.; Tomino, I.; Tamimoto, Y. *J. Am. Chem. Soc.* **1979**, *101*, 3129.

[3] Inove, S.; Takaya, H.P; Tani, K.; Otsuka, S.; Sato, T.; Noyori, R. *J. Am. Chem. Soc.* **1990**, *112*, 4897.

[4] For leading references, see: Ciana, L. D.; Hamachi, I.; Meyer, T. J. *J. Org. Chem.* **1989**, *54*, 1731.

[5] Roncali, J. *Chem. Rev.* **1992**, *92*, 711.

[6] Kaufmann, T. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 291. Altenbach, G.-H. *Organic Synthesis Highlights*; VCH: Weinheim, 1991.

[7] McKean, D. R.; Parrinello, G.; Renaldo, A. F.; Stille, J. K. *J. Org. Chem.* **1987**, *52*, 422. Roth, G. P.; Fuller, C. E. *Ibid.* **1991**, *56*, 3493. Hatanaka, Y.; Hiyama, T.; *Ibid.* **1988**, *53*, 918. Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478.

[8] Suzuki, A. *Pure Appl. Chem.* **1991**, *63*, 419. Ob-e, Y.; Miyaura, N.; Suzuki, A. *Synlett* **1990**, 221. Cox, P. J.; Wang, W.; Snieckus, V. *Tetrahedron Lett.* **1992**, *33*, 2253. Hatanaka, Y.; Fukushima, S.; Hiyama, T. *Chem. Lett.* **1989**, 1711.

[9] Meyers, A. I.; Lutomski, K. A. *J. Am. Chem. Soc.* **1982**, *104*, 879 and references therein. See also: Shindo, M.; Koga, K.; Tomioka, K. *J. Am. Chem. Soc.* **1992**, *114*, 8732.

[10] Whitesides, G. M.; San Filippo, J.; Casey, C. P.; Panek, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 5302. Whitesides, G. M.; Fisher, W. F.; San Filippo, J.; Bashe, R. W.; House, H. O. *Ibid.* **1969**, *91*, 4871.

[11] Bertz, S. H.; Gibson, C. P. *J. Am. Chem. Soc.* **1986**, *108*, 8286.

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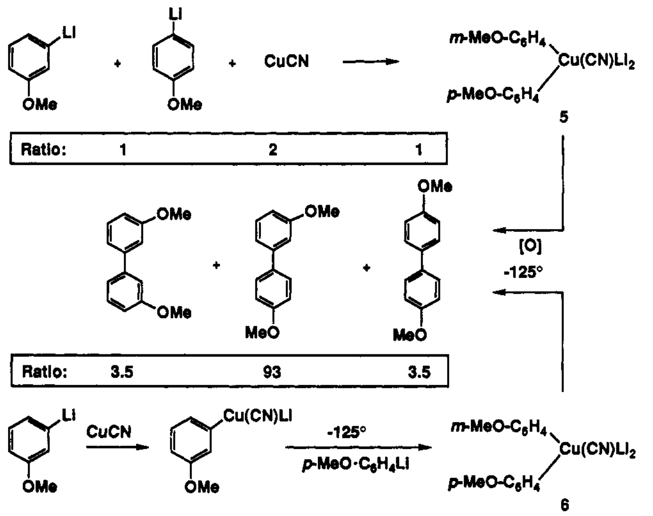
Scheme I

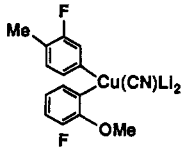
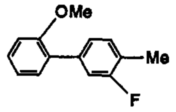
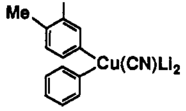
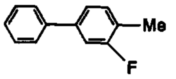
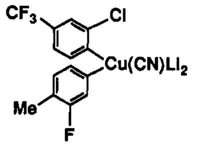
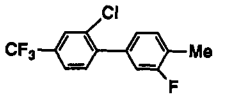
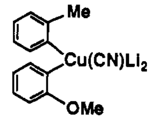
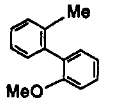
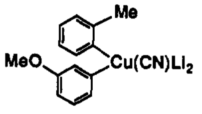
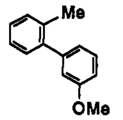
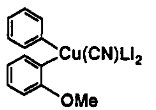
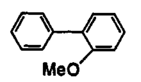
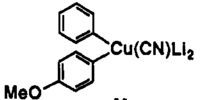
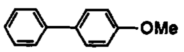
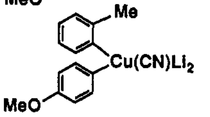
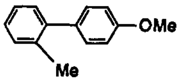


L.O. mixed species (*n*-Bu)(*n*-Pent)CuLi (from CuI) and the corresponding H.O. analog (n-Bu)(n-Pent)Cu(CN)Li$_2$ (from CuCN) at -78 °C. The conclusion, based on the ratios of symmetrical:unsymmetrical products, was "By studying their oxidation, a reaction heretofore not applied to the cyanocuprates, we have been able to obtain definitive evidence that they are, in fact, significantly different from the cuprates prepared from CuI." Some six years later, however, another study from the same laboratory appeared[12] which, on the basis of ^{13}C NMR data, led to the *opposite* conclusion.[13] Other sporadic examples of cuprate oxidations can be found in one of Posner's reviews,[14] and we have updated this list in our account of organocopper chemistry which has recently appeared.[15] The fair statement could thus be made that no procedure for controlled unsymmetrical biaryl cuprate oxidation existed prior to our discovery on the controlled oxidations of "kinetically" prepared H.O. mixed diarylcuprates, as discussed in detail herein.[16]

Results and Discussion

1. Biphenyls. When CuCN was combined with 1 equiv of both *m*- and *p*-anisyllithium in THF between -78 and 0 °C, exposure of the resulting H.O. mixed diarylcuprate (m-MeO-C_6H_4)(p-MeO-C_6H_4)Cu(CN)Li$_2$ to various oxidizing agents (e.g., O_2, *o*-dinitrobenzene, *p*-dinitrobenzene, $CuCl_2$) at -78 °C afforded essentially statistical ratios of the three possible products as determined by capillary GC analysis. Repeating the process by performing the oxidation at -125 °C led to identical results. However, prior formation of either L.O. cyanocuprate [i.e., (m-MeO-C_6H_4)Cu(CN)Li or (p-MeO-C_6H_4)Cu(CN)Li] in 2-methyl THF followed by cooling of the reaction to -125 °C, dropwise addition of the second equivalent of an aryllithium, and oxidation at -125 °C led to a mix of three biaryl products, of which the desired unsymmetrical biaryl constituted >93% (Scheme I). The interpretation that a "kinetic" reagent had been generated at -125 °C was predicated on the additional experiment wherein this species (**6**), upon warming to -78 °C for about 2 min followed by recooling back to -125 °C and oxidation, afforded the 1:2:1 ratio of products previously observed from oxidations of **5**. Conducting the identical experiment (i.e., cuprate formation and oxidation) at temperatures between -78 and -125 °C gave ratios between those noted above (Scheme I).

Table I. Couplings of Kinetically Generated, Mixed Diaryl H.O. Cyanocuprates at -125 °C in 2-Methyl-THF

entry	cuprate	coupling product	yield (%)
1			70
2			90
3			78
4			81
5			84
6			84
7			82
8			83

The generality of the procedure is evident from the variety of representative examples shown in Table I. Neither steric nor stereoelectronic factors appear to play an important role in the couplings. Isolated percent yields of unsymmetrical biaryls tended to hover consistently in the mid-80s, so long as ca. 3 equiv of TMEDA was present in the medium prior to oxidation. Its mode of action in helping to drive what tended to be a 50–60% level of conversion to completion is not obvious, although its likely association with (or, perhaps, pull on) lithium in an otherwise (presumably) defined cuprate cluster could help activate the organometallic toward reductive "decomposition". The major sideproduct(s) of these couplings can be the corresponding phenol(s), an obvious outgrowth of the use of molecular oxygen, although amounts on the order of 5% are usually tolerable. Moreover, separation of the biaryl from this type of byproduct tends to be straightforward, taking advantage of differences in chromatographic polarities and/or acid–base chemistry.

The impact of changes in concentration of the kinetically generated cuprates was briefly studied using the same reagents shown in Scheme I. Whereas oxidation of **5** (0.05 M) at -78 °C gave the expected 1:2:1 ratio of biaryls, decreasing the cuprate concentration by a factor of 6.7 (i.e., to 0.0075 M) led to only a minor improvement in the amount of cross-coupling (1:2.8:1). Likewise, at -86 °C the 1:3.3:1 ratio obtained at 0.034 M, upon dilution by a factor of ca. 3 to 0.010 M, improved to only 1:3.6:1. We conclude, therefore, that temperature is a far more critical

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[12] Bertz, S. H. *J. Am. Chem. Soc.* **1990**, *112*, 4031.

[13] Lipshutz, B. H.; Sharma, S.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 4032.

[14] Posner, G. H. *Org. React.* (*N. Y.*) **1975**, *22*, 253.

[15] Lipshutz, B. H.; Sengupta, S. *Org. React.* (*N. Y.*) **1992**, *41*, 135.

[16] For preliminary work in this area, see: Lipshutz, B. H.; Siegmann, K.; Garcia, E. *J. Am. Chem. Soc.* **1991**, *113*, 8161; *Tetrahedron* **1992**, *48*, 2579. For use of this methodology en route to calphostin C, see: Coleman, R. S.; Grant, E. B. *Tetrahedron Lett.* **1993**, *34*, 2225.

[17] The ratios from experiments run at temperatures between -78 and -125 °C Are as follows: -88 °C, 1:3:1; -105 °C, 1:6:1; -113 °C, 1:10:1.

[18] Lipshutz, B. H.; Koerner, M.; Parker, D. A. *Tetrahedron Lett.* **1987**, *28*, 945.

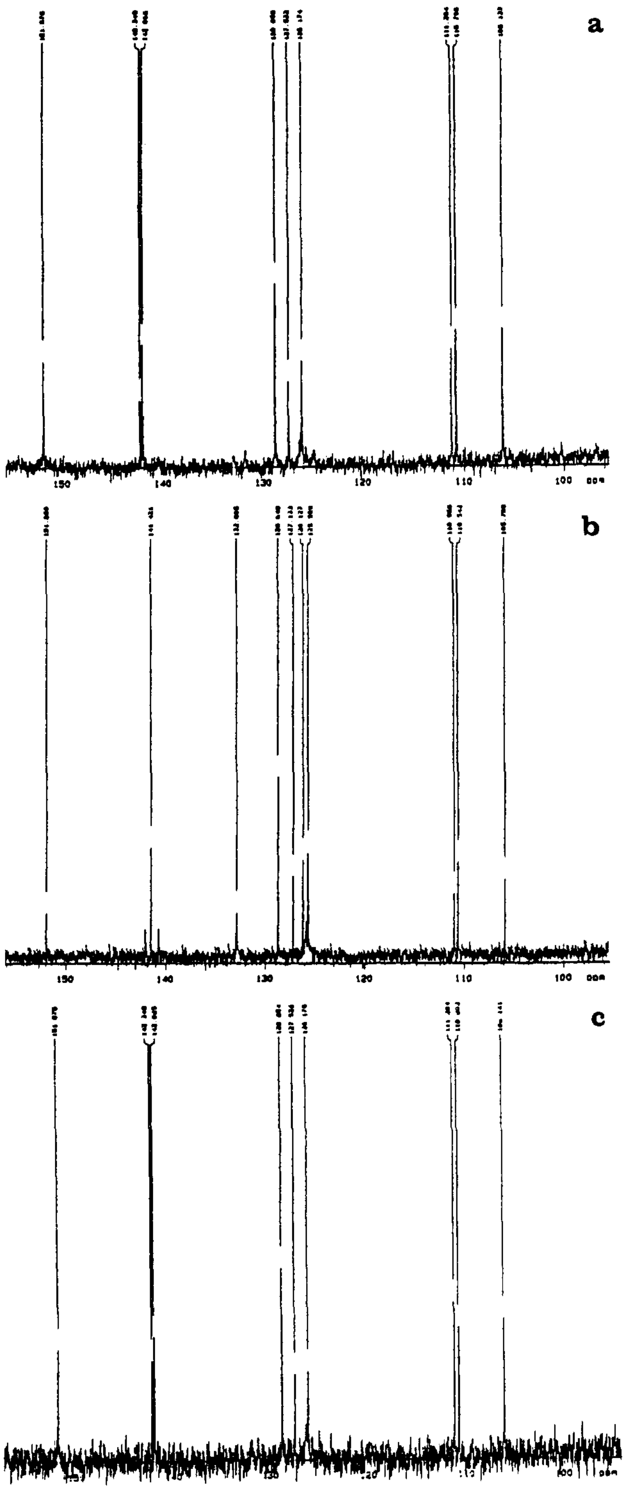
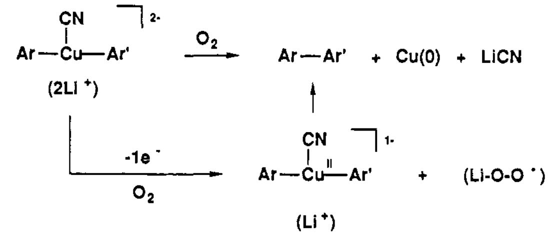


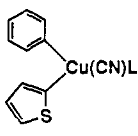
Figure 1. ^{13}C NMR spectra of Ph(2-Th)Cu(CN)Li_2 in 2-MeTHF at (a) −130 °C, (b) −45 °C, and (c) −130 °C (recooled).

parameter than the concentration at which the kinetic cuprate is formed and that decreasing the concentration of the cuprate cannot be used to offset the low temperatures called for by this method.

In an effort to gain physical evidence in support of the concept of a kinetic H.O. cyanocuprate, a ^{13}C NMR spectrum was run on (Ph)(2-Th)Cu(CN)Li_2 (**7**) (2-Th = 2-thienyl), prepared at −130 °C from the addition of PhLi to preformed (2-Th)Cu(CN)Li. A spectrum consisting of nine lines was anticipated, and, indeed, this is precisely what was observed, where each aryl ligand gives rise to four signals, with the CN carbon totaling nine resonances (Figure 1a). Upon warming the sample to −78 °C or above, the spectrum should increase in complexity as the reagent reorganizes to its "thermodynamic" form. This, too, is observed as the sample is warmed to −45 °C (Figure 1b). However, upon recooling the sample to −130 °C, rather than observing no further changes in the spectrum, we find that in fact *it reverts back to the identical spectrum as originally seen at this temperature* (Figure 1c). Similar data were obtained for the H.O. cuprates **8** and **9**, establishing that these observations are not due to any unusual properties associated with the thiophene ligand. The presence or absence of TMEDA had no effect on the spectra. A separate experiment in which **7** was formed at −78 °C and cooled to −130 °C led to an NMR spectrum identical to that observed previously (Figure 1a).

Scheme II





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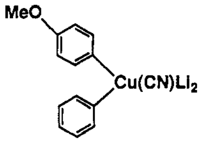

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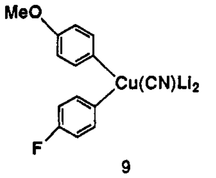

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On the surface, these spectroscopic data do *not* lend credence to the notion that a truly kinetic cuprate is being formed at −125 °C. Indeed, they are clearly at odds with the biaryl-forming experiments which lead to material *in hand*. It also should be recalled that ^{13}C NMR chemical shifts in THF where H.O. cyanocuprates are concerned are not good diagnostic tools for differentiating among species, even at low temperatures.[12,13] The full explanation, therefore, which awaits further study, may well have to do with subtle changes in aggregation-state phenomena as a function of temperature. This follows from the observation that the ^{13}C NMR spectra associated with these mixed H.O. reagents generated under "normal" (i.e., ligand equilibrating) conditions vary with temperature[19] (cf., Figure 1b,c), irrespective of the (coincidental?) overlap with the spectra observed initially at −130 °C (Figure 1a).

Mechanistically, the reaction is likely to proceed via a Cu(II) species following electron transfer to oxygen (Scheme II). Reductive coupling of the ligands would afford the unsymmetrical biaryl, together with LiCN and Cu^0, which is likely to be oxidized as generated to CuO. Other than the observation that during oxidation these reaction mixtures darken considerably (CuO is black), we have no firm evidence to support this mechanistic rationale. A second electron transfer to afford a Cu(III) intermediate is also possible, which would lead to the same biaryl, although the Cu(I) produced would presumably be in the form of CuCN. As pointed out by Pearson,[20] however, Cu(III) species are highly energetically unfavorable, leaving the Cu(II) state as the most likely pathway here. Considering that there is no information currently available on the solid-state structure of H.O. cyanocuprates, it is hard to justify a more lengthy discussion necessarily based on speculation.

In terms of the reagent itself, it is interesting to use this chemistry as another opportunity for distinguishing between "higher order" cyanocuprates (i.e., with the nitrile ligand on copper, as in $R_2Cu(CN)Li_2$) and traditional Gilman cuprates $R_2CuLi{\cdot}LiX$ (X = I, Br). Two different sources of solubilized CuI were studied (CuI·LiBr and CuI·LiI) as precursors to

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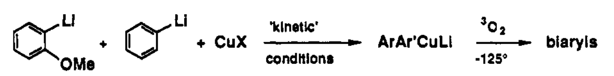
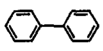
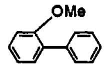
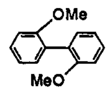
[19] Reversibility in ^{13}C NMR spectra of cuprates has been observed previously, *cf.*: Bertz, S. H.; Dabbagh, G. *J. Am. Chem. Soc.* **1988**, *110*, 3668.

[20] Pearson, R. G.; Gregory, C. D. *J. Am. Chem. Soc.* **1976**, *98*, 4098.

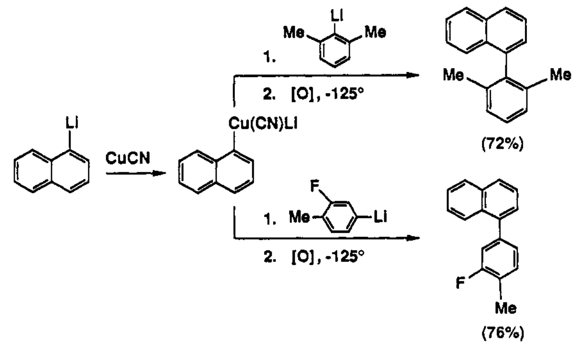
Table II. Oxidations of L.O. vs H.O. Diaryl Cuprates



% Biaryl Products

Cu(I)			
CuI·LiBr:	31	9	7
CuI·LiI:	23	10	8
		versus	
CuCN:	3.5	93	3.5

Scheme III



Scheme IV

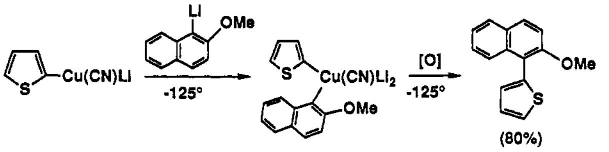
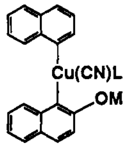
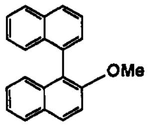
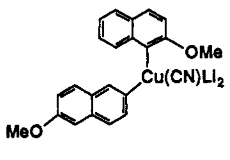
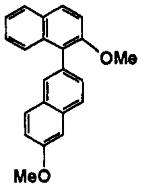
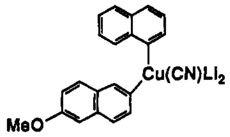
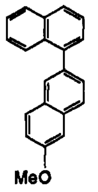
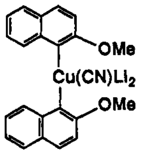
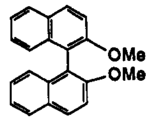
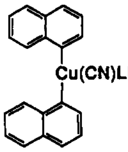
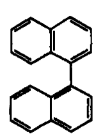


Table III. Couplings of H.O. Dinaphthyl Kinetic Cyanocuprates

entry	cuprate	coupling product	yield (%)
1			80
2			81
3			65
4		 10	82
5			82

Ar(Ar')CuLi. All other reaction parameters, including mode of reagent preparation, solvents, concentrations, length of time for oxidation, oxidant, etc., were identical to those employed with the CuCN-derived reagents. The results are illustrated in Table II. Immediately obvious, by comparison with those from, e.g., Scheme I, is that these are not only poor reactions but also the desired unsymmetrical biaryl is not even the major product. Significant amounts of protio-quenched materials, phenols, etc. make up the mass balance. Thus, the innate characteristics of the H.O. cuprate cluster are very different from those of copper halide origin, an observation fully in line with the general differences in their synthetic chemistry[21] as well as our spectroscopic comparisons.[13]

2. Naphthyl Derivatives. Extension of the method to both aryl-substituted naphthalenes and binaphthyl derivatives was next investigated. Again, the steric component of the process is negligible, exemplified by the attachment of a 2,6-dimethylphenyl moiety to the 1-position of the naphthalene ring (Scheme III). Likewise, an electron-deficient benzene ring (Scheme III) and a heteroaromatic moiety, such as the 2-thienyl group (Scheme IV), could be attached in good yields, the latter example suggesting that heteroaromatic–heteroaromatic couplings may also be realizable via oxidation of bisheteroaromatic H.O. cyanocuprates.

Entry into the binaphthyl series was also readily achieved. Under conditions developed for biphenyl formation, several binaphthyls could be prepared in good yields, as summarized in Table III. For reasons as yet not fully understood, these couplings seem to be somewhat more sensitive to experimental handling than are the biphenyl cases. For example, *t*-BuLi, used for metal–halogen exchange, that is either from a freshly opened bottle or of relatively recent vintage is preferred; aged solutions seemed to occasionally lead to lower yields due to *tert*-butyl-containing coupling products, and, in particular, quenched materials. Both the 1 and 2 positions on the naphthalene ring oxidatively couple without noticeable differences in rate, ratios, or efficiency. The symmetrical case leading to the 2,2'-binaphthol derivative **10** was studied, obviously not as a test of selectivity but rather to establish a competitive edge for this procedure over those which rely on palladium intermediates.[22] That is, product **10** represents the symmetrical equivalent, in essence, of a 2,6-disubstituted phenyl ring coupling with another 2,6-disubstituted phenyl ring, a tough proposition in organopalladium chemistry. Perhaps more importantly, it provides foreshadowing for the particularly exciting *intramolecular* variation as a means of controlling atropisomerism in biaryls of both natural[6,23] and unnatural origin.[2,3,6]

Summary

By combining an aryllithium (ArLi) with a lower order aryl cyanocuprate (Ar'Cu(CN)Li)at −125 °C in 2-methyltetrahydrofuran, a unique reagent is formed which behaves as a kinetic higher order (H.O.) cyanocuprate. Exposure of cuprates of this type to $^3O_2$ at −125 °C leads to very high levels of unsymmetrical biaryls. Polysubstituted phenyl rings and naphthalenes can be coupled in various combinations. The prospects for couplings within the heteroaromatic manifold were briefly discussed. Results on these as well as selected intramolecular variations form the basis of several future reports from these laboratories.

Finally, it is perhaps worth pointing out that over the 40+ year history of organocopper chemistry,[24] virtually every cuprate ever prepared has been done so under ligand equilibrating conditions.

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[21] Bertz, S. H.; Gibson, C. P.; Dabbagh, G. *Tetrahedron Lett.* **1987**, *28*, 4251.

[22] Watanabe, T.; Miyaura, N.; Suzuki, A. *Synlett* **1992**, 207.

[23] For example, see: Ziegler, F. E.; Chliwner, I.; Fowler, K. W.; Kanfer, S. J.; Kuo, S. J.; Sinha, N. O. *J. Am. Chem. Soc.* **1980**, *102*, 790.

[24] Gilman, H.; Jones, R. G.; Woods, L. A. *J. Org. Chem.* **1952**, *17*, 1630.

With the advent of a kinetic alternative, selected cuprate reactions of particular importance may be worth reinvestigation (e.g., 1,4-additions to enones with reagents bearing nonracemic, nontransferrable ligands).[25]

Experimental Section

Materials. All chemicals were purchased from the Aldrich Chemical Co. All solvents for reactions were distilled under a dry nitrogen atmosphere. Diethyl ether and THF were distilled from sodium benzophenone ketyl prior to use. The 2-methyltetrahydrofuran (MeTHF) was distilled from lithium aluminum hydride and then redistilled immediately prior to use from sodium benzophenone ketyl. Hexane was distilled from sodium hydride. Tetramethylethylenediamine (TMEDA) was distilled from potassium hydroxide pellets and then redistilled from metallic sodium and stored over fresh-cut sodium. The aryl iodides were used without further purification. All organolithium reagents were titrated using 1,10-phenanthroline as indicator.[26] CuCN was dried under high vacuum (0.01 Torr) at room temperature for 3 days and then stored in a stoppered flask. Oxygen gas was passed through H_2SO_4, $CaSO_4$, and lastly a dry ice trap to remove traces of water. All reactions were carried out under an inert atmosphere of argon. All glassware and stirring bars were dried overnight at ca. 140 °C prior to use.

Instrumentation. NMR spectra were obtained on a General Electric GN-500 spectrometer at 500 MHz. All spectra were taken in $CDCl_3$ with tetramethylsilane as internal standard. Chemical shifts are given in ppm downfield of the reference. Mass spectra were obtained on an analytical VG 70-250 instrument. Gas chromatographic analyses were performed on a Hewlett-Packard 5890A gas chromatograph equipped with a 60-m fused silica J&W DB-5 capillary column. Flame ionization detection was employed with H_2 as the carrier gas. The standard program to analyze the reaction mixtures was as follows: initial temperature, 50 °C; initial time, 2 min; rate, 20° min; final temperature, 300 °C; final time, 2 min.

Solutions of Aryllithiums. *o*-Tolyllithium, *o*-anisyllithium, *m*-anisyllithium, and *p*-anisyllithium were prepared by the following modified method of Schlosser and Ladenberger.[27] Phenyllithium was also prepared by this procedure, although most experiments using it were conducted with commercial material.

In a 100-mL one-necked flask bearing a fused sintered frit to which another flask can be attached (this flask is similar to the one described by Schlosser[27]) were placed a stirring bar and 10 g of iodobenzene (49 mmol) [or 10 g of 2-iodotoluene (45.9 mmol) or 10 g of 2-iodoanisole, 3-iodoanisole, or 4-iodoanisole (42.7 mmol)]. The liquid aryl iodides were degassed by freezing (−78 °C), evacuating the flask, and then thawing. This procedure was repeated twice. The flask was then evacuated and filled with argon; this procedure was repeated three times. Dry hexane (20 mL, 30 mL in the case of 4-iodoanisole) was added, followed by 1.0 equiv of *n*-butyllithium (2.71 M in hexane), dropwise (over a period of 10 min) via syringe at room temperature. Immediate precipitation of the aryllithiums occurred. In the case of 3-iodo- and 4-iodoanisole, the solution was cooled with a water bath to ensure that the temperature remained below 20 °C and the *n*-butyllithium was added dropwise over a period of 30 min. The mixture was then stirred for 2 h at room temperature. From the precipitated white solid of aryllithiums the hexane was filtered off, and the solid was washed with 20 mL of dry hexane. It was then dried at high vacuum for 3 h. After drying, the flask was filled with argon and cooled to −78 °C. To the cold solid was added 46 mL of dry ether in the case of phenyllithium; 43 mL of dry ether in the case of *o*-tolyllithium; 30 mL of dry ether and then 10 mL of dry THF in the case of *o*-anisyllithium; 40 mL of dry ether in the case of *m*-anisyllithium; 32 mL of dry ether and then 8 mL of dry THF in the case of *p*-anisyllithium. The cooling bath was removed, and the solid aryllithiums dissolved slowly upon warming to room temperature, giving slight yellow, cloudy solutions. These solutions were filtered into a 50-mL flask which was stoppered tightly with triple septa.

To check the purity of the aryllithiums, an aliquot of each solution was quenched with water, extracted with ether, and analysed by GC. In the cases of phenyllithium and *o*-tolyllithium, no signals (except for those of solvent) were detected by GC. The *o*-anisyllithium and *p*-anisyllithium gave only one signal, which was assigned to anisole. The solution of the *m*-anisyllithium always contained ca. 1% of bis-*m*-anisole.

The solutions of the aryllithiums were titrated, the titer usually ranging between 0.9 and 1.1 M. The solutions were stored in the refrigerator at ca. −15 °C, where the titer remained constant for months. *o*-Anisyllithium and *p*-anisyllithium eventually crystallized out at that temperature; however, on warming to room temperature prior to use, the colorless crystals redissolved. It was found that *m*-anisyllithium and *p*-anisyllithium both isomerized slowly in these solutions to apparently the more stable *o*-anisyllithium.

General Method for the Syntheses of Mixed Biaryls. All joints were greased and wrapped with parafilm. A dry three-necked 50-mL or 100-mL flask equipped with a rubber septum (because of pressure changes during cooling, the septum should be secured with copper wire), a hose adapter for argon/vacuum, and a thermometer adapter with septum was used (if problems with foaming during the oxidation with oxygen occur, a 100-mL flask should be used). A gas dispersion tube (Aldrich, porosity 40–60 μm) was put through the septum of the thermometer adapter and could be moved for the oxidation by pushing it into the solution. The open end of the gas dispersion tube was sealed with a small septum. In the flask were placed a stirring bar (2.5 cm long) and 90 mg (1 mmol) of dry CuCN. The flask was then evacuated to ca. 0.01 Torr for at least half an hour and heated twice with a heat gun. The flask was then filled with argon. Evacuation and filling with argon were each repeated twice. With a syringe, 18 mL of dry MeTHF was transferred into the flask, and the suspension was cooled to ca. −78 °C. To the resulting suspension was added exactly 1 mmol (ca. 1 mL of solution) of aryllithium (ArLi). The cooling bath was removed, and the suspension was allowed to warm until all of the CuCN had dissolved. The speed of stirring was adjusted so that the solution was well stirred (this is important in order to get good mixing at these very low temperatures). The resulting water-white to pale yellow (a bright yellow color is an indication of excess CuCN, i.e., hydrolyzed ArLi) solution was then cooled to −125 °C using a pentane/liquid nitrogen cooling bath in a Dewar flask. The whole flask was smothered with pentane (up to the beginning of the necks), and the Dewar was kept covered with a layer of frozen pentane by periodically adding liquid nitrogen during the reaction. A thermocouple was placed in the cooling bath to monitor the temperature. To this solution of the lower order cuprate was added exactly 1 mmol (ca. 1 mL of solution) of Ar′Li via a syringe to the well-stirred solution. Addition should be dropwise and slow, at a speed of ca. 1 drop per second; 5–7 min are required for this addition. The solution was stirred for an additional 8–10 min. Next, 0.5 mL of TMEDA (3.3 mmol) was added dropwise over ca. 3 min, and the solution was stirred for an additional 7 min. The argon was shut off, and the flask was connected to a bubbler via a syringe needle. A strong flow of dry oxygen was passed into the small septum of the gas dispersion tube via a syringe needle, and the gas dispersion tube was pushed into the solution. The color of the solution changes within minutes from light yellow to black. After 1 h, the flask was evacuated under vacuum and purged with argon, and the reaction was then quenched with ca. 2 mL of a 1:1 mixture of methanol/concentrated aqueous $NaHSO_3$ solution. The reaction mixture was then allowed to warm to room temperature and acidified with concentrated hydrochloric acid (ca. 0.5 mL). A sample of this solution was taken, washed with concentrated NaCl solution, and analyzed by GC. The reaction solution (and the GC sample) were poured into a separatory funnel and extracted three to four times from water (ca. 50 mL) with CH_2Cl_2. The combined organic phases were dried with magnesium sulfate and filtered, and the solvent was evaporated in vacuo. The residue was flash chromatographed with CH_2Cl_2/hexane (1:9) on silica gel. The pure fractions were combined, and the solvents were evaporated in vacuo. The resulting pure biaryl was dried on house vacuum for 2 h, after which the weight of the product remained constant.

2-Methoxy-3′-fluoro-4′-methylbiphenyl (Table I, entry 1). (ArLi = *o*-anisyllithium, Ar′Li = *m*-fluoro-*p*-tolyllithium.) The Ar′Li was prepared in situ from Ar′I prior to use as follows. In a dry 25-mL flask filled with argon and equipped with a rubber septum and a stir bar was placed 200 μL (1.5 mmol) of 2-fluoro-4-iodotoluene. Next, 2.8 mL of MeTHF was added and the solution was cooled to −78 °C. To the cooled solution was then added slowly 1.7 mL of *tert*-butyllithium (1.76 M in hexane, 3 mmol), and the solution was kept at −78 °C for an additional 30 min. It was then allowed to warm up to 0 °C. To this pale yellow solution was added 0.7 mL of TMEDA (4.6 mmol), whereupon immediate precipitation (of presumably Li(TMEDA)I) occurs. The suspension was kept at 0 °C for another 30 min, after which 3.5 mL (1 mmol of Ar′Li) of this solution was added via syringe to the cold (−125 °C) solution of

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[25] Alexakis, A.; Mutti, S.; Normant, J. F. *J. Am. Chem. Soc.* **1991**, *113*, 6332. Dieter, R. K.; Tokles, M. *Ibid.* **1987**, *109*, 2040. Corey, E. J.; Naef, R.; Hannon, F. J. *Ibid.* **1986**, *108*, 7114. Bertz, S. H.; Dabbagh, G.; Sundararajan, G. *J. Org. Chem.* **1986**, *51*, 4953. Kretchmer, R. A. *Ibid.* **1972**, *37*, 2744. Alexakis, A.; Sedrani, R.; Mangeney, P.; Normant, J. F. *Tetrahedron Lett.* **1988**, *29*, 4411. Corey, E. J.; Hannon, F. J. *Ibid.* **1987**, *28*, 5233. Tanaka, K.; Ushio, H.; Suzuki, H. *J. Chem. Soc., Chem. Commun.* **1990**, 795.

[26] Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

[27] Schlosser, M.; Ladenberger, V. *J. Organomet. Chem.* **1967**, *8*, 193.

the lower order cuprate, prepared as described above, over a period of ca. 5 min. The solution was stirred for another 10 min and then oxidized and worked up as described above (GC retention time, 9.29 min (Ar–Ar, 9.50 min; Ar′–Ar′, 8.81 min)) to yield a colorless oil, which solidifies after ca. 1 month: 151.4 mg (70%); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.32–6.94 (m, 7 H), 3.84 (s, 3 H), 2.29 (d, $^{4}J(^{19}\mathrm{F}, ^{1}\mathrm{H}) = 2$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 161.8, 159.9, 156.4, 137.9, 137,9, 130.8, 130.6, 129.4, 128.6, 124.8, 123.3, 123.2, 120.8, 116.2, 116.0, 115.1, 111.2, 55.5, 14.3; EIMS *m/z* (relative intensity) 217 (14), 216 (M$^+$, 100), 201 (36), 186 (43); HREIMS calcd for $C_{14}H_{13}FO$, 216.0950, found, 216.0940.

3-Fluoro-4-methylbiphenyl (Table I, entry 2). A dry 50-mL three-necked round-bottom flask equipped with a T-top (for argon/vacuum), a thermometer adapter fitted with a gas dispersion tube (obtained from Aldrich, fritted glass porosity 40–60 μm), and a rubber septum was gently flame-dried under vacuum and then allowed to cool to room temperature under a rapid stream of argon. This procedure was repeated a second time. The round-bottom flask was then charged with copper(I) cyanide (90 mg, 1 mmol) and once again gently flame-dried under vacuum and allowed to cool to room temperature under argon.

Another 10-mL round-bottom flask was flame-dried and allowed to cool to room temperature under a rapid stream of argon. Next, 6 mL of dry MeTHF was added, followed by 0.11 mL (1 mmol, *d* = 1.823) of 1-iodobenzene. The flask was cooled to –78 °C, and then *t*-BuLi (2.1 mmol) was added dropwise. After the addition was complete the reaction mixture was stirred (–78 °C) for 0.5 h.

A separate 10-mL round-bottom flask was flame-dried in the same way and allowed to cool to room temperature under argon. MeTHF (6 mL) was added, followed by 1 mmol of 4-iodo-2-fluorotoluene (0.13 mL). This solution was treated with 2.1 mmol of *t*-BuLi at –78 °C for 0.5 h to generate the second aryllithium.

The flask containing the copper(I) cyanide slurry was cooled to –78 °C. The solution containing the phenyllithium reagent was added via cannula, and the reaction mixture was allowed to warm up to room temperature to form the lower order reagent. After the copper(I) cyanide had completely dissolved, the reaction mixture was recooled to –125 °C (liquid N$_2$/pentane). The reaction was stirred at this temperature for 10 min, after which the solution containing the fluoroaryllithium, maintained at –78 °C, was added dropwise via cannula. After the addition was complete, the reaction mixture was stirred at –125 °C for 10 min. TMEDA (0.7 mL) was then added (dropwise), and the reaction was stirred at –125 °C for another 10 min. The argon flow was then stopped, and dry O$_2$ (passed through a column containing Ca$_2$SO$_4$ and then through a trap immersed in dry ice/acetone) was bubbled through the reaction mixture. The solution turned dark after a few minutes. Oxygen flow was continued for 1 h. The vessel was then briefly evacuated under vacuum and argon flow was reestablished, followed by quenching of the reaction mixture at –125 °C with a MeOH/concentrated aqueous NaHSO$_3$ solution. The reaction mixture was allowed to warm to room temperature and then acidified with concentrated HCl. Extraction with Et$_2$O was followed by washing with brine. The organic phase was then dried (Na$_2$SO$_4$) and filtered, and the solvent was removed under aspirator vacuum. The resulting yellow oil was purified by flash chromatography (silica gel) using hexanes/dichloromethane (9:1) as eluent. The desired compound (0.1676 g, 90%) was obtained as a colorless oil: IR (neat) 3010, 2920, 2850, 1700, 1450, 1160, 650 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54–7.52 (m, 2 H), 7.39 (d, *J* = 7.50 Hz, 2 H), 7.32–7.29 (m, 1 H), 7.25–7.17 (m, 3 H), 2.28 (d, $^{4}J(^{19}\mathrm{F}, ^{1}\mathrm{H}) = 1.00$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 161.58 (d, $J(^{19}\mathrm{F}, ^{13}\mathrm{C}) = 242.87$ Hz), 140.74 (d, $^{2}J(^{19}\mathrm{F}, ^{13}\mathrm{C}) = 10.5$ Hz), 139.94, 131.66, 128.79, 127.47, 126.85, 122.30, 113.59, 113.41, 14.25; EIMS *m/z* (relative intensity), 187.1 (M$^+$ + 1, 12.1), 186.0 (M$^+$, 100.0), 185.0 (47.5), 183.2 (15.0), 109.1 (15.0), 93.1 (12.2); HREIMS calcd for $C_{13}H_{11}F$, 186.0845, found, 186.0833.

3-Fluoro-4-methyl-2′-chloro-5′-(trifluoromethyl)biphenyl (Table I, entry 3)[28] obtained as a colorless oil (0.2247 g, 78%): IR (neat) 3010, 2970, 1450, 1430, 1390, 1250, 1150, 1100, 1050, 850, 820, 750 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.52–7.41 (m, 3 H), 7.15 (t, *J* = 7.50 Hz, 1 H), 7.01–6.99 (m, 2 H), 2.22 (d, $^{4}J(^{19}\mathrm{F}, ^{1}\mathrm{H}) = 1.5$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 160.88 (d, $J(^{19}\mathrm{F}, ^{13}\mathrm{C}) = 244.12$ Hz), 140.11, 137.26, 137.17, 136.31, 131.37, 131.31, 130.06, 130.29, 129.60, 129.33, 128.11, 128.02, 126.72, 126.66, 125.43, 124.77, 124.74, 116.14, 115.94, 14.36; EIMS *m/z* (relative intensity), 290.0 (32.8), 289.0 (M$^+$ + 1, 20.4), 288.0 (M$^+$, 100.0), 286.8 (17.5), 253.0 (10.3), 233.0 (12.3), 184.1 (18.2), 183.1 (40.2), 109.1 (15.0); HREIMS calcd for $C_{14}H_9{}^{37}ClF_4$, 290.0299, found, 290.0299.

2-Methyl-2′-methoxybiphenyl (Table I, entry 4)[29] (ArLi = *o*-anisyllithium, Ar′Li = *o*-tolyllithium) (GC retention time, 8.65 min (Ar–Ar, 9.80 min; Ar′–Ar′, 7.52 min) formed as a colorless oil, which solidifies after ca. 1 month: 160.8 mg (81%); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34–6.94 (m, 8 H), 3.73 (s, 3 H), 2.13 (s, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 156.6, 138.5, 136.7, 131.0, 130.8, 130.0, 129.6, 128.5, 127.3, 125.4, 120.4, 110.6, 55.4, 19.9; EIMS *m/z* (relative intensity) 198 (M$^+$, 100), 183 (29), 168 (24), 167 (28), 165 (34), 155 (15).

2-Methyl-3′-methoxybiphenyl (Table I, entry 5) (ArLi = *m*-anisyllithium, Ar′Li = *o*-tolyllithium) (GC retention time, 9.10 min (Ar–Ar, 10.75 min; Ar′–Ar′, 7.50 min) formed as a colorless oil: 166.7 mg (84%); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.31–6.86 (m, 8 H), 3.82 (s, 3 H), 2.27 (s, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.3, 143.4, 141.8, 135.3, 130.3, 129.7, 129.0, 127.3, 125.7, 121.7, 114.8, 112.3, 55.2, 20.4; EIMS *m/z* (relative intensity) 198 (M$^+$, 100), 197 (26), 183 (16), 167 (58), 165 (27), 155 (19), 153 (17), 152 (16); HREIMS calcd for $C_{14}H_{14}O$, 198.1044, found, 198.1026.

2-Methoxybiphenyl (Table I, entry 6)[30] (ArLi = *o*-anisyllithium, Ar′Li = phenyllithium) (GC retention time, 8.59 min (Ar–Ar, 9.78 min; Ar′–Ar′, 7.36 min) formed as a colorless oil: 154.2 mg (84%); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.53–6.95 (m, 9 H), 3.77 (s, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 156.4, 138.5, 130.7, 129.5, 128.6, 127.9, 126.9, 120.8, 111.2, 55.5; EIMS *m/z* (relative intensity) 184 (M$^+$, 100), 169 (50), 141 (33), 115 (23).

4-Methoxybiphenyl (Table I, entry 7)[31] (ArLi = *p*-anisyllithium, Ar′Li = phenyllithium) (GC retention time, 9.20 min (Ar–Ar, 10.78 min; Ar′–Ar′, 7.24 min) formed as a white solid: 151.8 mg (82%) (contained ca. 3.5% of 2-methoxybiphenyl as seen by GC); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.56–6.96 (m, 9 H), 3.84 (s, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.1, 140.8, 133.8, 128.7, 128.1, 126.7, 126.6, 114.2, 55.3; EIMS *m/z* (relative intensity) 184 (M$^+$, 100), 169 (36), 141 (29), 115 (16).

2-Methyl-4′-methoxybiphenyl (Table I, entry 8)[32] (ArLi = *p*-anisyllithium, Ar′Li = *o*-tolyllithium) (GC retention time, 9.10 min (Ar–Ar, 10.75 min; Ar′–Ar′, 7.50 min) formed as a colorless oil: 165.1 mg (83%); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.25–6.93 (m, 8 H), 3.83 (s, 3 H), 2.27 (s, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 158.5, 141.5, 135.4, 134.3, 130.2, 129.9, 126.9, 125.7, 113.4, 55.2, 20.5; EIMS *m/z* (relative intensity) 198 (M$^+$, 100), 183 (19), 167 (12), 165 (12), 155 (17), 153 (12).

1-(2′,6′-Dimethylphenyl)naphthalene. An oven-dried 100-mL three-necked round-bottom flask equipped with a T-top (for argon/vacuum), a thermometer adapter fitted with a gas dispersion tube, and a rubber septum was dried gently under vacuum with a Bunsen burner and then allowed to cool to room temperature under argon, the process being repeated one additional time. Copper cyanide (90 mg, 1 mmol) was then added, and the flask was once again gently flame-dried under vacuum and allowed to cool to room temperature under argon.

In another oven- and flame-dried 25-mL round-bottom flask was added 20 mL of dry MeTHF followed by 0.146 mL (1 mmol) of 1-iodonaphthalene. The flask was cooled to –78 °C, and 2.1 mmol of *t*-BuLi was added dropwise. After the addition, the reaction was stirred at this temperature for 2 h. Identical treatment of 2-bromo-1,3-dimethylbenzene (0.133 mL, 1 mmol) afforded the second aryllithium reagent.

The flask containing the CuCN slurry was cooled to –78 °C. To the flask was introduced the precooled (–78 °C) naphthyllithium, and the mixture was allowed to warm to –20 °C, forming a homogeneous solution. The resulting L.O. cyanocuprate was then recooled to –130 °C (pentane/liquid N$_2$) and equilibrated at this temperature for ca. 10 min. The dimethylphenyllithium reagent, cooled to –130 °C, was then added dropwise via cannula. After the addition was complete (ca. 30 min), the reaction was stirred at –130 °C for another 20 min. TMEDA (0.7 mL) was then added dropwise, and the reaction was stirred for another 15 min. The argon flow was then stopped, and dry oxygen (passed through a –78 °C trap) was bubbled through the reaction mixture, whereupon the solution turned dark after a few minutes. Oxygen flow was continued for a total of 45 min, after which the reaction vessel was briefly evacuated and the argon flow reestablished. The reaction was then quenched with 2 mL of methanol/concentrated aqueous NaHSO$_3$ solution. The mixture was allowed to warm to room temperature and poured into 100 mL of a solution of 10% NH$_3$ in concentrated NH$_4$Cl. After the mixture stirred for 30 min, the organic layer was separated, the aqueous phase was extracted several times with ether, and the combined extracts were

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(28) The 1-lithio-2-chloro-5-(trifluoromethyl)benzene must be metalated and kept at –78 °C or below so as to prevent benzyne formation.

(29) Widdowson, D. A.; Zhang, Y. Z. *Tetrahedron* **1986**, *42*, 2111. Davies, D. I.; Waring, C. *J. Chem. Soc. C* **1968**, 2332.

(30) Available from the Aldrich Chemical Co.

(31) Available from Lancaster Synthesis, Inc.

(32) Capparelli, M. P.; DeSchepper, R. E.; Swenton, J. S. *J. Org. Chem.* **1987**, *52*, 4953.

subsequently washed with 5% HCl solution, saturated $NaHCO_3$ solution, and brine. The organic phase was dried over $MgSO_4$ and filtered, and the solvent was removed under vacuum. GC analysis of the crude product showed the product ratio bis-*m*-xylene, 1.1; 2-*m*-xylenylnaphtalene, 97; bisnaphthalene, 1.9. Flash chromatography (silica gel) using hexanes/ethyl acetate (95:5) afforded 167 mg (72%) of the desired product as a colorless oil: R_f 0.59 (hexanes/ethyl acetate, 95:5); IR (CH_2Cl_2) 2920, 1940, 1420, 1390, 1240, 1030, 960 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.90 (s, 6 H, CH_3), 7.10–7.65 and 7.80–8.00 (m, 10 H, Ar-H); EIMS *m/z* (relative intensity) 233.2 (19.6), 232.2 (M^+, 100), 231.2 (16.6), 217.1 (44.1), 216.1 (15.6), 215.1 (29), 202.1 (17.6); HREIMS calcd for $C_{18}H_{16}$, 232.1252, found, 232.1252.

1-(3′-Fluoro-4′-methylphenyl)naphthalene was obtained as a colorless oil (0.180 g, 76%): IR (neat) 3100, 3000, 2950, 1510, 1450, 1380, 1280, 1250, 1190, 1100, 1010, 1000, 850, 750, 650 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (t, J = 9.50 Hz, 2 H), 7.82 (d, J = 8.00 Hz, 1 H), 7.49–7.44 (m, 2 H), 7.42–7.36 (m, 2 H), 7.25 (t, J = 8.00 Hz, 1 H), 7.15 (d, J = 8.50 Hz, 2 H), 2.35 (d, $^4J(^{19}F, ^1H)$ = 1.50 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.07 (d, $J(^{19}F, ^{13}C)$ = 243.37 Hz), 140.74 (d, $^2J(^{19}F, ^{13}C)$ = 10.5 Hz), 138.98, 137.77, 131.44, 131.17 (d, $^2J(^{19}F, ^{13}C)$ = 6.75 Hz), 128.29, 127.85, 126.84, 126.14, 125.82, 125.74, 125.48, 125.29, 116.67, 116.49, 14.36; EIMS *m/z* (relative intensity) 237.1 ($M^+ + 1$, 17.9), 236.1 (M^+, 100.0), 235.1 (24.5), 233.1 (14.2), 221.1 (49.8), 220.1 (45.4); HREIMS calcd for $C_{17}H_{13}F$, 236.1001, found, 236.1009.

2-Methoxy-1-(2′-thienyl)naphthalene. The title compound (0.1920 g, 80%) was obtained as a colorless oil: IR (neat) 3100, 3000, 2920, 2800, 1610, 1580, 1400, 1380, 1330, 1200, 1145, 1130, 1080, 1070, 1060, 1000, 910, 880, 840, 675 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 9.00 Hz, 1 H), 7.67 (d, J = 8.00 Hz, 1 H), 7.63 (d, J = 8.00 Hz, 1 H), 7.37 (d, J = 5 Hz, 1 H), 7.29–7.18 (m, 3 H), 7.08 (dd, J = 3.50, 5.00 Hz, 1 H), 6.98–6.97 (m, 1 H), 3.74 (s, 3 H); ^{13}C (125 MHz, $CDCl_3$) δ 155.01, 136.54, 134.42, 130.09, 128.85, 128.48, 127.77, 126.79, 126.69, 126.07, 125.04, 123.65, 118.60, 113.419, 56.733; EIMS *m/z* (relative intensity) 241.1 ($M^+ + 1$, 15.1), 240.1 (M^+, 100.0), 225.1 (50.1), 197.1 (53.1), 165.0 (12.1), 152.1 (13.1), 139.1 (10.1); HREIMS calcd for $C_{15}H_{12}OS$, 240.0608, found, 240.0619.

2-Methoxy-1-naphthylnaphthalene (Table III, entry 1). An oven-dried 100-mL three-necked round-bottom flask equipped with a T-top (for argon/vacuum), a thermometer adapter fitted with a gas dispersion tube, and a rubber septum was dried gently under vacuum with a Bunsen burner and then allowed to cool to room temperature under argon, the process being repeated one additional time. Copper cyanide (90 mg, 1 mmol) was then added, and the flask was once again gently flame-dried under vacuum and allowed to cool to room temperature under argon.

A 10-mL round-bottom flask was flame-dried and allowed to cool to room temperature under a rapid stream of argon. Next, 6 mL of dry MeTHF was added, followed by 0.237 g (1 mmol) of 1-bromo-2-methoxynaphthalene. The flask was cooled to –78 °C, and then *t*-BuLi (2.1 mmol) was added dropwise. After the addition was complete the reaction mixture was stirred at –78 °C for 0.5 h. The solution turned green after a few minutes at –78 °C.

A separate 10-mL round-bottom flask was flame-dried as above and allowed to cool to room temperature under argon. MeTHF (6 mL) was added, followed by 1 mmol of 2-bromo-6-methoxynaphthalene (0.237 g). This solution was treated with 2.1 mmol of *t*-BuLi at –78 °C for 0.5 h to generate the second aryllithium. There was a similar color change observed as with the generation of the first methoxyaryllithium.

The flask containing the copper(I) cyanide slurry was cooled down to –78 °C; the solution containing the naphthyllithium was then added via cannula, and the reaction mixture was allowed to warm to room temperature so as to form the lower order cyanocuprate. After the copper(I) cyanide had completely dissolved (the L.O. cyanocuprate had a slight green coloration), the reaction mixture was recooled to –125 °C (liquid N_2/pentane). The reaction was stirred at this temperature for another 10 min, after which the solution containing the second naphthyllithium, maintained at –78 °C, was added dropwise via cannula. After the addition was complete, the reaction mixture was stirred at –125 °C for 10 min. TMEDA (0.7 mL) was added dropwise, and the reaction was stirred at –125 °C for another 10 min. The argon flow was then stopped, and dry O_2 (passed through a column containing $CaSO_4$ and then through a trap immersed in dry ice/acetone) was bubbled through the reaction mixture. The solution turned dark after a few minutes. Oxygen flow was continued for 1 h, after which the system was briefly evacuated under vacuum. The argon flow was then reestablished, and the reaction mixture was quenched at –125 °C with a MeOH/concentrated aqueous $NaHSO_3$ solution. The mixture was then allowed to warm to room temperature and then acidified with concentrated HCl. After extraction (Et_2O) and washing with brine, the organic phase was dried over Na_2SO_4 and filtered, and the solvent was removed under aspirator vacuum. The resulting yellow oil was purified by flash chromatography (silica gel) using hexanes/dichloromethane (9:1) as eluent. The desired compound (0.2544 g) was obtained as a colorless oil (80%): IR (neat) 3050, 2900, 2850, 1610, 1580, 1500, 1450, 1445, 1350, 1330, 1200, 1140, 1090, 650 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84–7.14 (m, 12 H), 3.88 (s, 3 H), 3.75 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.68, 153.93, 133.76, 133.62, 131.56, 129.82, 129.49, 129.01, 128.87, 127.81, 126.40, 126.24, 125.28, 123.44, 118.69, 113.75, 105.69, 56.64, 55.24; EIMS *m/z* (relative intensity) 315.1 ($M^+ + 1$, 15.1), 314.1 (M^+, 100.0), 299.1 (20.1), 284.1 (19.1), 268.0 (22.1), 255.1 (15.1), 239.1 (12.1), 226.1 (12.1), 157.1 (10.1), 113.1 (13.1); HREIMS calcd for $C_{22}H_{18}O_2$, 314.1307, found, 314.1329.

2-Methoxy-1-(6′-methoxy-2′-naphthyl)naphthalene (Table III, entry 2). The title compound (0.2273 g) was obtained as a colorless oil (81%): IR (neat) 3000, 2920, 2820, 1620, 1590, 1460, 1400, 1380, 1330, 1080, 1060, 1010, 950, 910, 900, 860, 750 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91–7.86 (m, 3 H), 7.80 (d, J = 8.00 Hz, 1 H), 7.56 (t, J = 8.00 Hz, 1 H), 7.41–7.15 (m, 8 H), 3.66 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.54, 134.51, 134.21, 133.65, 132.91, 129.42, 128.94, 128.39, 128.17, 127.76, 127.67, 126.34, 126.12, 125.81, 125.64, 125.52, 125.43, 123.50, 113.71, 56.61; EIMS *m/z* (relative intensity) 285.1 ($M^+ + 1$, 23.1), 284.1 (M^+, 100.0), 269.1 (27.6), 268.1 (19.2), 253.1 (19.5), 252.1 (19.4), 241.1 (18.6), 240.1 (13.4), 239.1 (47.0), 119.6 (18.8); HREIMS calcd for $C_{21}H_{16}O$, 284.1201, found, 284.1222.

1-(6′-Methoxy-2′-naphthyl)naphthalene (Table III, entry 3). The desired compound (0.1847 g) was obtained as a colorless oil (65%): IR (neat) 3050, 2910, 2800, 1605, 1580, 1460, 1400, 1350, 1200, 1140, 1120, 1050, 1040, 1000, 900 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.00 Hz, 1 H), 7.88 (d, J = 8.00 Hz, 1 H), 7.85–7.36 (m, 6 H), 7.18–7.16 (m, 1 H), 3.90 (s, 3 H); ^{13}C (125 MHz, $CDCl_3$) δ 157.80, 140.21, 135.99, 133.82, 133.67, 131.80, 129.54, 128.91, 128.51, 127.52, 127.161, 126.47, 126.08, 125.98, 125.71, 125.37, 123.52, 119.09, 105.623, 55.295; EIMS *m/z* (relative intensity) 285.1 ($M^+ + 1$, 23.1), 284.1 (M^+, 100.0), 239.1 (25.1), 226.1 (11.1), 120.1 (13.1); HREIMS calcd for $C_{21}H_{16}O$, 284.1201, found, 284.1211.

2-Methoxy-1-(2′-methoxy-1′-naphthyl)naphthalene (Table III, entry 4). The desired compound (0.2575 g) was obtained as a colorless oil (82%): IR (neat) 3050, 2920, 2860, 1610, 1590, 1500, 1460, 1450, 1350, 1330, 1200, 1140, 1090, 660 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 9.00 Hz, 1 H), 7.84 (d, J = 8.00 Hz, 1 H), 7.42 (d, J = 9.00 Hz, 1 H), 7.28–7.10 (m, 2 H), 7.08 (d, J = 8.00 Hz, 1 H), 3.72 (s, 3 H); ^{13}C NMR (125 MHz) δ 154.93, 133.97, 129.35, 129.17, 127.88, 126.26, 125.20, 123.46, 119.56, 114.19, 56.83; EIMS *m/z* (relative intensity) 315.3 ($M^+ + 1$, 25.4), 314.2 (M^+, 100.0), 269.2, (11.8), 268.2 (45.4), 239.2 (12.1); HREIMS calcd for $C_{22}H_{18}O_2$, 314.1422, found 314.1297.

1-(1′-Naphthyl)naphthalene (Table III, entry 5).[33] The desired compound (0.1936 g) was obtained as a colorless oil (82%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88–7.86 (m, 2 H), 7.51–7.50 (m, 1 H), 7.42–7.38 (m, 2 H), 7.31 (d, J = 8 Hz, 1 H), 7.22–7.17 (m, 1 H); EIMS *m/z* (relative intensity) 237.2 (17.6), 236.2 (100.0), 235.2 (20.2), 233.2 (11.3), 221.1 (42.7), 220.1 (36.7), 85.0 (18.2), 83.0 (27.7).

NMR Sample Preparation (Cuprates 7–9). The mixed H.O. cyanocuprates **7–9** were prepared in the usual way (1 mmol scale, vide supra).

An oven-dried 5-mm NMR tube was fitted with a rubber septum and cooled to room temperature under a rapid stream of argon. After it reached room temperature, it was cooled to –125 °C (liquid N_2/pentane). After the NMR tube was at this temperature for ca. 5 min, ca. 1 mL of the solution containing the cuprate was transferred via cannula to the NMR tube. The cannula was submerged in a liquid N_2/pentane bath (the cannula had to be bent) so as to keep the cuprate at a constant temperature. After the transfer was completed, the NMR tube was fitted with a second rubber septum which covered the first one to avoid contamination.

Prior to placement of the NMR tube in the probe (equilibrated at –130 °C for 0.5 h), the sample was submerged in liquid N_2 to insure against warming.

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