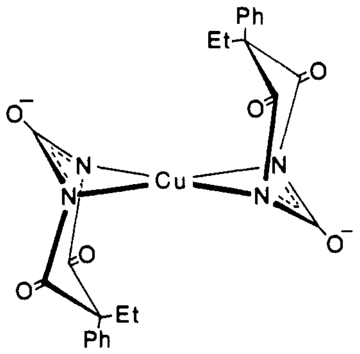

Figure 2. Proposed structure of Cu^{II}(PB)$_2$ complex.

giving rise to symmetric and asymmetric carbonyl vibrations. The band at 1620 cm^{-1} is presumably due to a C=N bond conjugated to one of the carbonyl groups.

The ESR spectra of the complex recorded at liquid nitrogen temperature in methyltetrahydrofuran (MTHF) at three different microwave frequencies are shown in Figure 1. These spectra exhibit a typical copper hyperfine pattern with approximately axial symmetry ($g_{xx} = g_{yy}$). Splittings due to ^{63}Cu and ^{65}Cu were not resolved because of line broadening. In addition, no ESR signals were detected at half-field, $g = 4$, as would be expected from spin-spin interactions between two copper atoms. The X-band spectrum (Figure 1a) resembles that reported for Cu^{II}TPP[9,10] and shows the splitting of the $M_I = -^3/_2$ of the parallel region into nine lines due to spin interactions with four neighboring nuclei, namely, nitrogen (^{14}N, $I = 1$) atoms. Low microwave frequency spectra, where strain broadening is reduced,[11-14] show well-resolved nitrogen hyperfine structures in both the $g_\parallel$ and $g_\perp$ regions. The nine-line pattern of the $M_I = -^3/_2$ and $M_I = -^1/_2$ of the parallel components supports strongly the coordination of four nitrogen atoms with a copper ion as shown in Figure 1b,c. Furthermore, the relative intensities are very close to those predicted for four nitrogens, which suggests that the four nitrogens are equivalent. The room temperature ESR spectrum also shows coupling to four nitrogens. The ESR parameters $g_\parallel$ and $A_\parallel$ were easily obtained from low-temperature spectra. The $g_\perp$ and $A_\perp$ values, on the other hand, were calculated from $g_\parallel$ and $A_\parallel$ and the isotropic values in solution ($g_{iso} = (g_\parallel + 2g_\perp)/3$ and $a_{iso} = (A_\parallel + 2A_\perp)/3$). The nitrogen hyperfine coupling constant in the $g_\perp$ region was approximated by $1/2^{1/2}[A_\parallel{}^N)^2 + (A_\perp{}^N)^2]^{1/2}$, the average in-plane value derived from the perpendicular lines. The ESR spin Hamiltonian parameters are $g_\parallel = 2.209$, $g_\perp = 2.04$, $A_\parallel{}^{Cu} = 0.0192$ cm^{-1}, $A_\perp{}^{Cu} = 0.0029$ cm^{-1}, $A_\parallel{}^N = 0.0016$ cm^{-1}, and $A_\perp{}^N = 0.0012$ cm^{-1}. These ESR parameters are similar to those obtained for Cu^{II}TPP,[9,10] which indicates that, in general, the interactions are comparable. Furthermore, the ESR parameters obtained are characteristic of d^9 ions with an unpaired electron in the d$_{x^2-y^2}$ orbital ($g_\parallel > g_\perp > g_e$).

The ligand field transition energies which are characteristic of the d-d transitions were estimated from visible absorption spectra of Cu^{II}(PB)$_2$. From the spectra obtained in Me$_2$SO, the following values were determined and subsequently used as ligand field transition energies: $\Delta E_{xz} = 23920$ and $\Delta E_{xy} = 15800$ cm^{-1}. These energies and the ESR parameters can be used to determine the nature of the metal-ligand bonds. From the approaches of Roberts and Koski[15] and Kivelson and Neiman,[16] the bonding coefficients α^2, $\beta_1{}^2$, and β^2 were calculated. On the basis of these bonding parameters, the following is proposed: (1) the in-plane σ bonding is moderately covalent with $\alpha^2 = 0.80$, (2) the in-plane π bonding is moderately covalent with $\beta_1{}^2 = 0.71$, and (3) the out-of-plane π bonding is moderately covalent with $\beta^2 = 0.77$.

The structure proposed for this complex based on the spectroscopic evidence presented above is shown in Figure 2. As indicated above, the fact that no ESR signals were detected at $g = 4$, expected for a copper-copper interactions, was used to rule out a dimer. In addition, the ESR data confirmed the fact that the copper atom is bound to four equivalent nitrogens in a square-planar arrangement. There are two reasonable configurations, chair or boat, for the barbiturate ligands in this complex. It is proposed that the barbiturates are in chair forms and the Cu—N bonds are diequatorial with regard to the chelate plane.

Acknowledgment. This research was supported by Grant RR-01008 from the National Institutes of Health for the ESR studies and the Ball State University Research Office. The author thanks Dr. Bruce N. Storhoff for helpful discussions and a review of the manuscript. Thanks are also due to the National Biomedical ESR Center, The Medical College of Wisconsin, Milwaukee, WI, for assistance in obtaining the ESR spectra.

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Oxidation of Organocuprates with Nitroarenes: "Higher Order" Cyanocuprates Are Different[1]

Steven H. Bertz* and Charles P. Gibson

AT&T Bell Laboratories
Murray Hill, New Jersey 07974

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Organocuprates prepared from CuCN have been described as "higher order" *ate* complexes, R$_2$Cu(CN)Li$_2$,[2] thus implying that they are *qualitatively* different from previous organocuprates prepared from CuI or CuBr, traditionally represented[3] as R$_2$CuLi and now termed "lower order". While some of the yields obtained by using CuCN-derived cuprates are somewhat better *quantitatively* than those obtained with reagents made from CuI or CuBr,[4] such observations are not sufficient to establish that these reagents are fundamentally different. 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.

Whitesides et al.[5] reported that organocuprates (prepared from CuI) are oxidized by dioxygen, CuCl$_2$·TMEDA, or nitrobenzene to yield the dimer (R-R) of the organic residue (R). We have studied the oxidation of mixed cuprates, RR′CuLi, where R = Bu (*n*-butyl) and R′ = Pe (*n*-pentyl), were chosen to minimize electronic and steric differences. Of the dozen oxidizing agents screened,[6] the dinitrobenzenes gave the best results in terms of the highest yields, and tetrahydrofuran (THF) proved to be the best solvent.[7] The results for the oxidation of cuprates derived

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[1] New Copper Chemistry. 10. For part 9, see: Bertz, S. H.; Dabbagh, G.; Williams, L. M. *J. Org. Chem.* **1985**, *50*, 4414.

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[3] Although they have generally been represented by empirical formulas, organocuprates are known to be clusters containing more than one Cu atom: (a) Pearson, R. G.; Gregory, C. D. *J. Am. Chem. Soc.* **1976**, *98*, 4098. (b) Hope, H.; Oram, D.; Power, P. P. *J. Am. Chem. Soc.* **1984**, *106*, 1149.

[4] For example, treatment of iodocyclohexane with Bu$_2$Cu(CN)Li$_2$ affords 81% butylcyclohexane, 6% cyclohexane, 1% cyclohexene, and 5% dicyclohexyl. The corresponding yields starting with CuBr are 53%, 7%, 1%, and 5%, respectively. See also ref 2.

[5] Whitesides, G. M.; San Filippo, Jr., J.; Casey, C. P.; Panek, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 5302.

[6] The results for *o*-, *m*-, and *p*-dinitrobenzene and 2,4-dinitrobenzenesulfonyl chloride were the same within experimental error. Nitrobenzene, 2,4-dinitro-1-fluorobenzene, lithium 2,4-dinitrobenzoate, 1,1′-diheptyl-4,4′-bipyridinium dibromide, dioxygen, and iron(III) chloride (2 equiv) were 10–20% less effective. Poor results (<20% nonane) were obtained with 2,4,6-tri-*tert*-butylnitrobenzene, tris(4-bromophenyl)aminium hexachloroantimonate, iodine, and 1 equiv of iron(III) chloride.

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Table I. Oxidation of Cuprates Prepared from CuCN or CuI[a]

entry	preparation[b]	cuprate age	ox time	100 × mmol products[c] octane	 nonane	 decane
1	(CuCN + BuLi) + PeLi	4 s	4 s	11	43	10
2		4 s	1 min	14	48	12
3		36 s	1 min	10	44	9
4		36 s	30 min	17	46	14
5		6 min	1 min	11	45	11
6		30 min	1 min	11	45	10
7	(0.5CuCN + BuLi) + (0.5CuCN + PeLi)	4 s	4 s	32	8	26
8		36 s	1 min	33	10	30
9		30 min	1 min	26	6	25
10	(0.5CuCN + 0.5BuLi) + (0.5CuCN + 0.5PeLi)	4 s	4 s	3	1	3
11		36 s	1 min	3	1	3
12	(CuI + BuLi) + PeLi	4 s	4 s	19	41	24
13		36 s	1 min	27	34	26
14		30 min	1 min	22	37	21
15		36 s	30 min	22	42	21
16	(0.5CuI + BuLi) + (0.5CuI + PeLi)	4 s	4 s	30	28	26
17		36 s	1 min	32	34	24
18		30 min	1 min	23	31	17
19	(0.5CuI + 0.5BuLi) + (0.5CuI + 0.5PeLi)	4 s	4 s	11	13	9
20		36 s	1 min	6	11	15

[a] *o*-Dinitrobenzene (1.0 equiv) was the oxidant. [b] 1.00 mmol each of CuI or CuCN, BuLi, and PeLi was used unless otherwise noted. [c] Yields were measured by GLC using undecane as internal standard and authentic products for calibration. The relative error is estimated to be ≤5%.

from CuCN and CuI with *o*-dinitrobenzene are summarized in Table I. Generally speaking, the yields starting with CuI reflect random coupling as they approach a 1:2:1 product ratio, whereas those from CuCN are strikingly nonrandom.

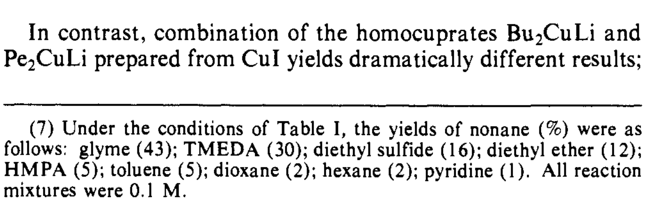
Scheme I

$$\mathrm{CuCN} \xrightarrow{\mathrm{BuLi}} \mathrm{BuCu(CN)Li} \xrightarrow{\mathrm{PeLi}} \mathrm{BuPeCu(CN)Li_2} \xrightarrow[\mathrm{2.HCl}]{\mathrm{1.ox}} \mathrm{Bu{-}Bu + Bu{-}Pe + Pe{-}Pe}$$

In the sequential addition experiments (see Scheme I), CuCN is treated with 1 equiv each of BuLi (−50 °C, 6 min), PeLi (−78 °C, various times referred to as "cuprate age"), *o*-dinitrobenzene (−78 °C, various times referred to as "oxidation time"), and finally methanolic HCl. The ratio of products does not depend upon cuprate age, but it does depend upon oxidation time. In the limit of short times, the ratio of octane/nonane/decane is 1:4:1. When the same experiment is performed starting with CuI, there is more scatter in the data; nevertheless, the highest ratio is ca. 1:2:1. It must be emphasized that, even though it is more dramatic than other examples, this difference in product ratios is, again, a quantitative one. Nevertheless, these ratios have structural significance (vide infra).

The results are qualitatively as well as quantitatively different when the preformed cuprates are combined and the resulting solution is oxidized (Scheme II). A solution prepared from equimolar amounts of $\mathrm{Bu_2Cu(CN)Li_2}$ and $\mathrm{Pe_2Cu(CN)Li_2}$ yields principally octane and decane and only a minor amount of nonane. The amount of nonane does not increase with the age of the cuprate mixture, and it cannot be eliminated by lowering the temperature to −108 °C or by using a deficit of the Li reagents in the preparation of the cuprates. It is lowered to 3% by using nitrobenzene as the oxidizing agent (vide infra).

Scheme II



In contrast, combination of the homocuprates $\mathrm{Bu_2CuLi}$ and $\mathrm{Pe_2CuLi}$ prepared from CuI yields dramatically different results; the amount of nonane is nearly as great as that observed when the two Li reagents are added sequentially to CuI. The amounts of hydrocarbons produced upon oxidation of the admixed organocopper(I) species BuCu and PeCu are much higher than the amounts from the admixed lower order cyanocuprates.

Oxidation of $\mathrm{BuPeCu(CN)Li_2}$ with nitrobenzene (−78 °C, 4 s cuprate age, 4 s oxidation time) yielded a 12:42:10 ratio of octane, nonane, and decane; and nitrobenzene oxidation of the admixed cyanocuprates $\mathrm{Bu_2Cu(CN)Li_2}$ and $\mathrm{Pe_2Cu(CN)Li_2}$ yielded a 28:3:27 ratio of products. These results are very similar to those obtained with *o*-dinitrobenzene, except that the amount of nonane from the admixed cyanocuprates is much lower.

Oxidation of the admixed cuprates with dioxygen gave essentially the same result whether the two preformed cuprates were prepared from CuCN or CuI. The octane:nonane:decane ratio is 24:29:18 for the cuprates prepared from CuCN, and it is 21:28:16 for the CuI-based cuprates. Therefore, cyanocuprate plus nitroarene represents a special combination that may have some synthetic application. For example, we have obtained yields of butylbenzene as high as 65% from the oxidation of the butylphenylcyanocuprate with *o*-dinitrobenzene. For comparison, a 33% yield of butylbenzene was obtained by Whitesides et al.,[5] who used dioxygen to oxidize the mixed cuprate prepared from CuI.

Our results for the oxidation of $\mathrm{BuPeCu(CN)Li_2}$ are consistent with those predicted for some of the structures that have been proposed for organocuprates but not with others (see Table II, supplementary material). Specifically, our 1:4:1 product ratio indicates that this reagent is dimeric in THF, although we cannot distinguish between a square-planar structure[3a] and some of the tetrahedral ones. We can rule out the monomer, several of the tetrahedral cases, and all of the trimers and tetramers. We believe our results for the dialkyl cuprates prepared from CuI are best explained by *intermolecular* exchange of the alkyl groups, which results in a 1:2:1 product ratio regardless of structure. Alternatively, all the structures considered (see Table II, supplementary material) can give rise to a 1:2:1 ratio of products provided that there is no *intramolecular* exchange (or intermolecular exchange) and only vicinal coupling can occur. Both geminal coupling and vicinal coupling by "mononuclear" and "dinuclear" reductive elimination, respectively, are well-precedented, as is the facilitation of reductive elimination by oxidation.[8]

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(7) Under the conditions of Table I, the yields of nonane (%) were as follows: glyme (43); TMEDA (30); diethyl sulfide (16); diethyl ether (12); HMPA (5); toluene (5); dioxane (2); hexane (2); pyridine (1). All reaction mixtures were 0.1 M.

(8) Collman, J. P.; Hegedus, L. S. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1980; pp 232–243.

Our preliminary results for aryl coupling indicate that Ph(p-tolyl)Cu(CN)Li_2 affords a 1:2:1 ratio of PhPh, p-tolylPh, and bis(p-tolyl) when treated with o-dinitrobenzene. If phenyl cuprates are trimeric in solution, as they are in the solid state,[3b] then either there is no *intra*molecular exchange and only vicinal coupling or else there is *inter*molecular exchange.

The necessity for a cluster in the case of BuPeCuLi is confirmed by experiments in which 1 and 2 equiv of 12-crown-4 were included in the reaction mixtures. While 1 equiv had a negligible effect, 2 equiv afforded significantly less coupling. Our interpretation is that the first equivalent complexes Li^+ (either the counterion for a halide or for an anionic cluster[3b]), and the second equivalent disrupts the cuprate cluster by excising Li from it to yield monomeric cuprates, as characterized by Power.[9]

The exact nature of the involvement of CN in the cyanocuprate clusters is still open to debate. We observe only small amounts (~1%) of BuCN or PeCN in the oxidation of "BuPeCu(CN)Li_2" with o-dinitrobenzene. This does not preclude the presence of CN ligands in the clusters, since it might be expected that the CN would be bound more tightly to the metal cluster core than alkyl groups owing to the participation of the CN π (including π^*) orbitals.

In summary, the oxidation of organocuprates with nitroarenes such as nitrobenzene and the dinitrobenzenes can be used as a probe of organocuprate structure and, in favorable cases, can give useful yields of cross-coupled products. Using this new structure probe, it has been determined that dialkyl cyanocuprates such as BuPeCu(CN)Li_2 (and by implication $Bu_2Cu(CN)Li_2$ and $Pe_2Cu(CN)Li_2$) are dimeric in THF solution[10] and that they differ significantly in their structures or ligand exchange rates (or both) from the corresponding cuprates prepared from CuI.

Supplementary Material Available: Table of predicted product distributions from oxidation of various cuprate structures (1 page). Ordering information is given on any current masthead page.

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[9] Hope, H.; Olmstead, M. M.; Power, P. P.; Sandell, J.; Xu, X. *J. Am. Chem. Soc.* **1985**, *107*, 4337.

[10] Vapor pressure depression experiments (cf. ref 3a) have failed in this case (Lipshutz, B. H., personal communication).

Imbricatine, an Unusual Benzyltetrahydroisoquinoline Alkaloid Isolated from the Starfish *Dermasterias imbricata*

Charles Pathirana and Raymond J. Andersen*

Departments of Chemistry and Oceanography
University of British Columbia
Vancouver, B.C., Canada V6T 1W5

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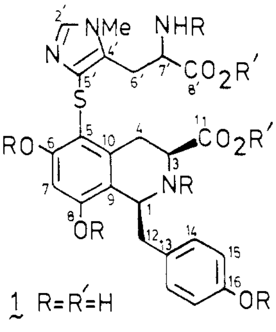
Sea anemones are common sessile marine invertebrates that normally respond to tactile stimulation by contracting and covering their oral disc with a portion of their body column. Biologists long ago discovered that a northeastern Pacific anemone, *Stomphia coccinea*, responds to contact with the starfish *Dermasterias imbricata* in a "striking and extraordinary manner: the anemone releases its basal disc from the substratum, and then propels itself through the water by means of a series of whip like motions".[1] It was subsequently shown that a single chemical substance was responsible for eliciting the "swimming" response.[1,2]

Table I. ^{1}H NMR Assignments

carbon	$\mathbf{1}^a$	$\mathbf{3}^a$	**4**
1	4.67 (dd, 8.4, 4.5)	4.57 (dd, 8, 4)	
3	3.76 (dd, 12.5, 5)	3.20 (dd, 12, 4)	
4	4.03 (dd, 16, 5)	2.90 (dd, 16, 4)	
	2.71 (dd, 12.5, 16)	2.71 (dd, 12, 16)	
5		6.08 (d, 2)	
7	6.42 (s)	6.22 (d, 2)	
12	3.22 (dd, 13.9, 4.5)	3.12 (dd, 14, 4)	
	2.85 (dd, 13.9, 8.4)	2.80 (dd, 14, 8)	
14	7.04 (d, 8)	7.01 (d, 8)	
15	6.71 (d, 8)	6.70 (d, 8)	
2′	7.73 (s): 8.73 (s)^b		8.95 (s)^b
6′	3.30 (dd, 15, 9)		3.44 (d, 7.5, 2 H)^b
	3.02 (dd, 15, 5): 3.34 (d, 8, 2 H)^b		
7′	3.60 (dd, 5, 9): 4.31 (t, 8)^b		4.29 (t, 7.5)^b
9′	3.66 (s): 3.87 (s)^b		3.94 (s)^b

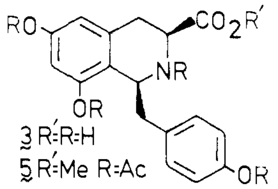
^{a}Spectra run in MeSO-d_6. ^{b}Chemical shifts in D_2O.

We now wish to report the structure of imbricatine (**1**), a novel benzyltetrahydroisoquinoline alkaloid that is capable of inducing *S. coccinea* "swimming" behavior at very low concentrations.[3] Imbricatine also displays significant activity in the L1210 (ED_{50} < 1 μg/mL)[4a] and P388 (T/C 139 at 0.5 mg/kg) antineoplastic assays.[4b]



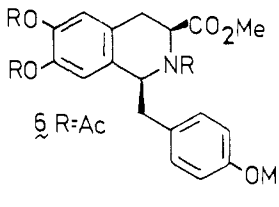
1 R=R′=H

2 R=Ac R′=Me

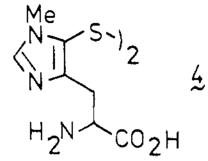


3 R′=R=H

5 R′=Me R=Ac



6 R=Ac



4

A bioassay-guided fractionation of the methanol extract of *D. imbricata*, making use of XAD-4, Biogel P2 (1% HOAc/H_2O), and Sephadex LH 20 (80% MeOH/H_2O) chromatographies, gave pure imbricatine (6–7 mg/animal) as a water-soluble, white amorphous solid.[2b] The molecular formula of imbricatine, $C_{24}H_{26}N_4O_7S$, was determined from the mass spectra of the parent compound (FABMS $M^+ + H$ 515) and the dimethylpentaacetyl derivative **2** (FABMS $M^+ + H$ 753; HREIMS M^+ − OAcbenzyl, obsd 603.1756, required for $C_{27}H_{31}N_4O_{10}S$ 603.1761) prepared from **1** by esterification (MeOH/HCl) and acetylation (Ac_2O/pyridine).

An N-methyl-5-thiohistidine fragment in **1** could be identified by comparing ^{1}H and ^{13}C NMR resonances in the spectrum of imbricatine to the values reported for the symmetrical disulfide **4** (Tables I and II) isolated from echinoderm eggs.[5] Reduction of imbricatine (**1**) with Ra-Ni (MeOH/reflux, 3 h) cleaved the thioether to give the tetrahydroisoquinoline **3** and methylhistidine which was shown to be identical with 3-methylhistidine and

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[1] (a) Ward, J. A. *J. Exp. Zool.* **1965**, *158*, 357. (b) Ross, D. M.; Sutton, L. *J. Exp. Biol.* **1964**, *41*, 751.

[2] (a) Ayer, W. A.; Ross, D. University of Alberta, personal communication, 1982. (b) Singer, P. Ph.D. Thesis. Chemistry Department, University of Alberta, 1975.

[3] The "swimming" behavior is very difficult to quantify; however, application of one to two drops of a 1 mg/mL solution of **1** in seawater to the tentacles of a partially submerged *S. coccinea* consistently elicits the response.

[4] Carried out by (a) Allen, T. Department of Pharmacology, University of Alberta and (b) Bristol Myers Ltd.

[5] Palumbo, A.; Misuraca, G.; D'Ischia, M.; Donaudy, F.; Prota, G. *Comp. Biochem. Physiol. B*: *Comp. Biochem.* **1984**, *78B*, 81.

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