

that they have the arene structures predicted by this model.<sup>39-42</sup>

### Conclusions

The analysis of the structural data presented herein supports our proposal that the structural distortions of the arenes and their substituents in ( $\eta^6$ -arene)Cr(CO)<sub>3</sub> complexes are largely caused by electronic effects and that, except for the bulkiest substituents, these distortions are best explained in terms of the  $\pi$ -donor and  $\pi$ -acceptor interactions between the substituents and the rest of the

(40) For most classes of  $\eta^6$ -arene complexes, only alkyl-substituted derivatives have commonly been prepared. For example, a number of [( $\eta^6$ -arene)<sub>2</sub>Fe]<sup>2+</sup> and [( $\eta^6$ -arene)Fe( $\eta^5$ -cyclohexadienyl)]<sup>+</sup> complexes have been crystallographically characterized, but they are limited to arenes with alkyl substituents: (a) Cameron, T. S.; Clerk, M. D.; Linden, A.; Sturge, K. C.; Zaworotko, M. J. *Organometallics* 1988, 7, 2571-2573. (b) Clerk, M. D.; Sturge, K. C.; White, P. S.; Zaworotko, M. J. *J. Organomet. Chem.* 1989, 368, C33-C37. (c) Atwood, J. L.; Christie, S. D.; Clerk, M. D.; Osmond, D. A.; Sturge, K. C.; Zaworotko, M. J. *Organometallics*, in press. (d) Rogers, R. D.; Sturge, K. C.; Zaworotko, M. J. Unpublished observations.

(41) The complex ( $\eta^6$ -1,4-C<sub>6</sub>H<sub>4</sub>F<sub>2</sub>)<sub>2</sub>V has boat-shaped arene ligands with the fluorine substituents and the ipso-carbon atoms to which they are attached being bent substantially away from the vanadium atom. see: Radonovich, L. J.; Zuerner, E. C.; Efner, H. F.; Klubunde, K. J. *Inorg. Chem.* 1976, 15, 2976-2981.

(42) The X-ray structural results for the electron-rich ( $\eta^6$ -arene)<sub>2</sub>Cr complexes having  $\pi$ -acceptor CF<sub>3</sub> substituents are particularly interesting, since, as expected,<sup>24</sup> these substituents and the ipso-carbon atoms to which they are attached are bent substantially toward chromium, see: (a) Larson, S. B.; Seymour, C. M.; Lagowski, J. J. *Acta Crystallogr., Sect. C* 1985, 41, 1624-1626. (b) Eyring, M. W.; Zuerner, E. C.; Radonovich, L. J. *Inorg. Chem.* 1981, 20, 3405-3410. (c) Larson, S. B.; Seymour, C. M.; Lagowski, J. J. *Acta Crystallogr., Sect. C* 1987, 43, 1626-1628. (d) Faggiani, R.; Hao, N.; Lock, C. J. L.; Sayer, B. G.; McGlinchey, M. J. *Organometallics* 1983, 2, 96-100.

molecule. In addition, this model allows one to predict the distortions of the arenes from planarity and the geometries of the substituents with a remarkably high degree of accuracy. Although our simple valence bond model has a high predictive value and is consistent with the published molecular orbital rationale for the bonding in ( $\eta^6$ -arene) complexes, a series of detailed molecular orbital calculations on ( $\eta^6$ -arene)Cr(CO)<sub>3</sub> complexes (in which the three-dimensional structures of the substituted arene fragments having various substitution geometries and  $\pi$ -donor/ $\pi$ -acceptor substituents are systematically varied) is certainly required for a more fundamental understanding of the origins of the structural distortions in these species.

**Acknowledgment.** We thank the Natural Sciences and Engineering Research Council of Canada, the University of Alberta, and Saint Mary's University for the financial support of this work. We also thank Dr. Bernard D. Santarsiero of the University of Alberta Structure Determination Laboratory for carrying out the Cambridge Crystallographic Data Base search and Nadia Wichrowska and Vivian Mozol for their experimental assistance.

**Registry No.** [ $\eta^6$ -C<sub>6</sub>H<sub>5</sub>(NH<sub>2</sub>)]Cr(CO)<sub>3</sub>, 12108-11-1; [ $\eta^6$ -C<sub>6</sub>H<sub>5</sub>(OMe)]Cr(CO)<sub>3</sub>, 12116-44-8; [ $\eta^6$ -1,4-C<sub>6</sub>H<sub>4</sub>(NMe<sub>2</sub>)<sub>2</sub>]Cr(CO)<sub>3</sub>, 46930-56-7; [ $\eta^6$ -1,4-C<sub>6</sub>H<sub>4</sub>(OMe)<sub>2</sub>]Cr(CO)<sub>3</sub>, 12176-26-0; [ $\eta^6$ -1,4-C<sub>6</sub>H<sub>4</sub>(CO<sub>2</sub>Me)<sub>2</sub>]Cr(CO)<sub>3</sub>, 33039-20-2.

**Supplementary Material Available:** Tables of hydrogen atom coordinates and  $B_{100}$  parameters, anisotropic thermal parameters, bond lengths, and bond angles for the five crystal structures and plots of the data used to generate the least-squares regression analyses described in Table V (25 pages); listings of structure factor amplitudes for the five structures (39 pages). Ordering information is given on any current masthead page.

## Formation and Substitution of Remote Ester-Functionalized Organocopper Reagents

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Remote ester-functionalized aryl and alkyl organocopper compounds have been produced through the use of a highly reactive form of copper. Methyl 5-bromopentanoate and various alkyl halobenzoates undergo oxidative addition with active copper to produce methyl 5-cupriopentanoate and alkyl cupriobenzoates, respectively, in moderate to good yields. These organocopper reagents will cross-couple with acid chlorides to form the corresponding keto esters and with alkyl halides to produce the corresponding alkylated esters in moderate to good yields. The organocopper compounds could also be converted to their respective homocoupled dimers in varying yields by appropriate oxidative or thermal methods. Methyl 5-cupriopentanoate has a slight tendency to undergo an intramolecular cyclization to form, after aqueous workup, cyclopentanone and methanol.

### Introduction

Organocopper compounds<sup>1</sup> are an exceptionally useful class of synthetic reagents primarily due to their ability to undergo substitution reactions<sup>2</sup> with alkyl halides and

1,4-conjugate addition reactions<sup>3</sup> with  $\alpha,\beta$ -unsaturated carbonyl compounds. The  $\alpha$ -cuprio esters have been obtained by forming the enolate of the ester followed by treatment with a suitable copper(I) salt.<sup>4</sup> This approach, obviously, cannot be used for reagents in which the car-

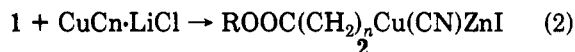
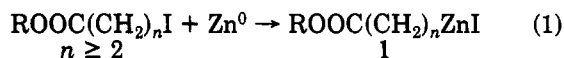
(1) (a) Lipshutz, B. H. *Synthesis* 1987, 325 and references cited therein. (b) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron Lett.* 1984, 40, 5005 and reference cited therein. (c) Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; Wiley: New York, 1980. (d) Bertz, S. H.; Dabbagh, G. J. *Org. Chem.* 1984, 49, 1119. (e) Bertz, S. H.; Dabbagh, G. *J. Am. Chem. Soc.* 1988, 110, 3668. (2) Posner, G. H. *Org. React. (N.Y.)* 1975, 22, 253 and references cited therein.

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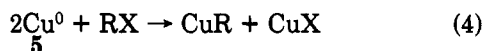
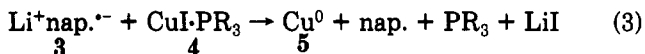
bonyl is remote from the desired copper site due to the incompatibility of most esters with the lithium or Grignard precursors used to form the organocopper reagents. Such reagents can be formed by traditional methods only if steps are taken to first mask the ester, adding time and cost to any synthesis and lowering overall yields. A few isolated examples of remote ester-functionalized organocopper reagents have been reported in the literature, such as  $\text{CH}_3\text{OOC}\equiv\text{CCu}^5$  and  $\text{EtOOC}(\text{CF}_2)_3\text{Cu}$ ,<sup>6</sup> but the synthetic methods employed were not generally applicable to other systems.

In recent years remote ester-functionalized copper-zinc reagents (2) have been produced from  $\omega$ -halo esters and zinc followed by treatment with either catalytic,<sup>7</sup> or more



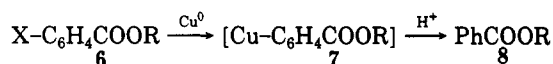
commonly, stoichiometric amounts of a copper(I) salt. The resulting compounds have been used in both substitution and 1,4-addition reactions. These reagents have been the subject of intensive study by Knochel et al.<sup>8</sup> and more recently by Rieke, Wehmeyer, and Zhu.<sup>9</sup> Copper-zinc reagents perform adequately, but from our own studies we have found it unnecessary, in most cases, to employ the intermediate zinc reaction since with active copper it is possible to proceed directly from the  $\omega$ -halo ester to the corresponding organocopper reagent.

Rieke and Ebert<sup>10</sup> have developed a highly reactive form of copper which permits the direct formation of organocopper compounds from organic halides without utilizing the traditional organolithium or Grignard precursors. This active copper is prepared by reducing an ethereal solution of  $\text{CuI}\cdot\text{PR}_3$  with an ethereal solution of lithium naphthalene or biphenylide under argon. The resulting copper is sufficiently reactive to allow direct oxidative addition to alkyl and aryl halides (eqs 3 and 4).



More recently, Rieke and co-workers have produced various activated forms of copper by modifying the original procedure. They have examined the reactions of ethyl 4-cupriobutanoate with acid chlorides, epoxides, and  $\alpha,\beta$ -unsaturated ketones and the reaction of ethyl 3-cupriopropanoate and ethyl 4-cupriobenzoate with benzoyl chloride.<sup>11</sup> In our own laboratory we have also continued to study and develop zerovalent copper and desired to carry out a more complete examination of the substitution reactions of remote ester-functionalized organocopper

Table I. Formation of Alkyl Cupriobenzoates (7) from Alkyl Halobenzoates and Active Copper<sup>a</sup>



compd	orientation	X	R	% yield <sup>b,c</sup> of 8
6a	para	I	Et	70
6b	para	Br	Et	50
6c	meta	I	Et	75
6d	meta	Br	Et	30
6e	ortho	I	Me	80
6f	ortho	Br	Me	77

<sup>a</sup> All reactions were run for 30 min in THF or DME at 0 °C under argon. The  $\text{Cu}^0/\text{RX}$  ratio was 3/1, and the active copper was derived from  $\text{CuI}\cdot\text{P}(\text{Et})_3$ . <sup>b</sup> Quantitation was by GC. <sup>c</sup> The amount of 8 found after quenching the reaction was assumed to be indicative of the amount of organocopper (7) present at the time of the quench.

reagents with a particular emphasis on aryl systems. We wish to report the successful results of these studies.

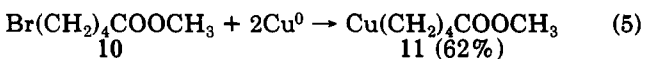
## Results and Discussion

**Alkyl Halobenzoates.** Alkyl bromo- and iodobenzoates react with activated copper to produce alkyl cupriobenzoates in varying yields, as shown in Table I. Good yields were obtained with the alkyl iodobenzoates by utilizing a 3/1 ratio of  $\text{Cu}^0/\text{RX}$  and allowing the reactions to run for 30 min at 0 °C in DME or THF under an atmosphere of argon. It was equally important that  $\text{P}(\text{Et})_3$  be used in the copper(I) phosphine complex reduced to form active copper. Substituting  $\text{P}(n\text{-butyl})_3$  resulted in substantially lower yields. Why  $\text{P}(\text{Et})_3$  significantly enhances the yield in comparison to  $\text{P}(n\text{-butyl})_3$  is not readily apparent. We have, however, found this to be true of nearly all aromatic systems we have examined. Interestingly, Rieke and Wehmeyer have shown that, for primary alkyl bromides, the maximum amount of alkylcopper is obtained when  $\text{P}(n\text{-butyl})_3$  is used.<sup>11a</sup>

The alkyl bromobenzoates are significantly less reactive than their iodo counterparts except for the ortho compounds (6e, 6f) which show almost equal reactivity. This "ortho effect",<sup>12</sup> in which the reactivity of a halogen is substantially improved by the presence of an ortho heteroatom containing an unshared pair of electrons, is well documented for the copper-mediated Ullmann reaction<sup>13</sup> of aryl halides to form biaryls.

Alkyl cupriobenzoates cross-couple in moderate to high yields with acid chlorides to produce keto esters and with alkyl halides to form the corresponding alkylated esters, as demonstrated in Table II. The acylation reaction yields compare favorably with those reported by Rieke et al.<sup>11d</sup> One previous alkylation in which methyl 4-cupriobenzoate, formed from methyl 4-bromobenzoate and activated copper in a 62% yield, was cross-coupled with 1-iodobutane to produce methyl 4-*n*-butylbenzoate in 58% yield was reported by Ebert and Rieke.<sup>10b</sup>

**Methyl 5-Bromopentanoate.** We examined the formation of methyl 5-cupriopentanoate (11) from methyl 5-bromopentanoate (10) and active copper. Although a



variety of reactions conditions were explored, we were unable to improve upon the procedure reported by Rieke and Wehmer.<sup>11a</sup> This method produced a 62% yield of

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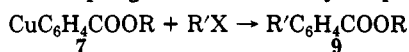
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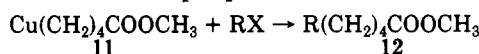
(12) Forrest *J. Chem. Soc.* 1960, 592.

(13) For a review of this reaction see: Fanta. *Chem. Rev.* 1964, 64, 613.

Table II. Cross-Coupling Reactions of Alkyl Cupriobenzoates<sup>a</sup>

compd	orientation	R	R'X	no.	product 9	% yield <sup>b</sup> of 9
7a	para	Et	CH <sub>3</sub> COCl	9a	<i>p</i> -CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> COOR	94 (66)
7a	para	Et	PhCOCl	9b	<i>p</i> -PhCOC <sub>6</sub> H <sub>4</sub> COOR	95 (67)
7a	para	Et	CH <sub>2</sub> =CHCH <sub>2</sub> Br	9c	<i>p</i> -CH <sub>2</sub> =CHCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> COOR	93 (65)
7a	para	Et	CH <sub>3</sub> I	9d	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> COOR	91 (63)
7a	para	Et	CH <sub>3</sub> CH <sub>2</sub> I	9e	<i>p</i> -CH <sub>3</sub> CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> COOR	64 (45)
7a	para	Et	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> I	9f	<i>p</i> -CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C <sub>6</sub> H <sub>4</sub> COOR	56 (39)
7c	meta	Et	CH <sub>3</sub> I	9g	<i>m</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> COOR	75 (56)
7f	ortho	Me	PhCOCl	9h	<i>o</i> -PhCOC <sub>6</sub> H <sub>4</sub> COOR	95 (73)
7f	ortho	Me	CH <sub>3</sub> COCl	9i	<i>o</i> -CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> COOR	53 (41)
7f	ortho	Me	PhCH <sub>2</sub> Br	9j	<i>o</i> -PhCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> COOR	99 (76)
7f	ortho	Me	CH <sub>3</sub> I	9k	<i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> COOR	89 (68)

<sup>a</sup>All reactions were run for 1 h in THF or DME at 25 °C under argon with a 3-fold excess of R'X. <sup>b</sup>Quantitation was by GC. The first value represents the yield based upon the amount of organocopper present just prior to the addition of R'X. The second value (in parentheses) represents the overall yield from starting material.

Table III. Cross-Coupling Reactions of Methyl 5-Cupriopentanoate<sup>a</sup>

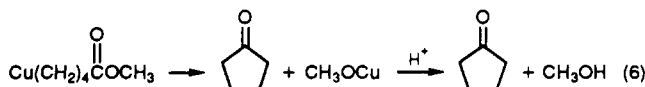
RX	no.	product 12	% yield <sup>b</sup>
PhC(O)Cl	12a	PhC(O)(CH <sub>2</sub> ) <sub>4</sub> COOCH <sub>3</sub>	87 (54)
CH <sub>3</sub> I	12b	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> COOCH <sub>3</sub>	31 (19)
PhCH <sub>2</sub> Br	12c	Ph(CH <sub>2</sub> ) <sub>5</sub> COOCH <sub>3</sub>	64 (40)
CH <sub>2</sub> =CHCH <sub>2</sub> Br	12d	CH <sub>2</sub> =CH(CH <sub>2</sub> ) <sub>3</sub> COOCH <sub>3</sub>	59 (36)

<sup>a</sup>All reactions were run for 30 min in THF or DME at -78 °C under argon with a 3-fold excess of RX. <sup>b</sup>Quantitation was by GC. The first value represents the yield based upon the amount of organocopper present just prior to the addition of RX. The second value (in parentheses) represents the overall yield from starting material.

11. Methyl 5-cupriopentanoate was cross-coupled with a variety of organic halides to produce the corresponding 5-substituted esters in varying yields, as shown in Table III.

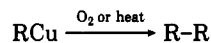
For the cross-coupling with highly reactive substrates such as acid chlorides and allyl and benzyl bromides, the reaction produces moderate to high yields of product. For a simple alkyl halide such as methyl iodide, the yield is poor. These results are not unexpected since it has been well established that primary alkyl iodides cross-couple with simple alkylcopper reagents in low yields,<sup>2</sup> whereas high yields are more readily obtained when organocuprate<sup>2</sup> or higher order organocuprate<sup>1a,b</sup> salts are used. Our yield of 12a is comparable with the cross-coupling yields of various acid chlorides with ethyl 4-cupriobutanoate reported by Rieke and co-workers.<sup>11c,14</sup>

Interestingly, minor side products (typically 10%) consistently found in these reactions after workup are cyclopentanone and methanol. The most likely explanation is an intramolecular cyclization of the methyl 5-cupriopentanoate intermediate with concurrent elimination of methoxide to produce these compounds, as illustrated in eq 6.



**Homocoupling.** Organocopper compounds may be oxidatively homocoupled<sup>2</sup> under a variety of conditions, a common method of which is the bubbling of O<sub>2</sub> through the reaction mixture. Alternatively, these reagents may

Table IV. Homocoupling of Organocopper Reagents



RCu	method	product	
		structure	no. % yield <sup>a</sup>
11	O <sub>2</sub>	MeOOC(CH <sub>2</sub> ) <sub>8</sub> COOMe	13 54 (32)
7f	O <sub>2</sub>	<i>o</i> -MeOOC <sub>6</sub> H <sub>5</sub> -C <sub>6</sub> H <sub>5</sub> COOMe	14 41 (32)
7a	O <sub>2</sub>	<i>p</i> -EtOOC <sub>6</sub> H <sub>5</sub> -C <sub>6</sub> H <sub>5</sub> COOEt	15 58 (41)
7a	heat	<i>p</i> -EtOOC <sub>6</sub> H <sub>5</sub> -C <sub>6</sub> H <sub>5</sub> COOEt	15 74 (52)

<sup>a</sup>Quantitation was by GC. The first value represents the yield based upon the amount of organocopper present just prior to homocoupling. The second value (parentheses) represent the overall yield from starting material.

be thermally dimerized,<sup>2</sup> provided there are no β-protons present which permit a facile β-elimination to occur instead of the desired homocoupling.<sup>15</sup> Thus, as a practical matter, thermal dimerization is generally restricted to aryl- and vinylcopper species.

Table IV shows that moderate yields of dimerization can be achieved by oxidation for both the alkyl and aryl ester-functionalized organocopper compounds. Higher yields, however, are obtained for the arylcopper reagents under thermal homocoupling conditions.

## Conclusions

This work has shown that both aromatic and aliphatic remote ester-functionalized organocopper reagents can be prepared in moderate to good yields and subsequently homocoupled or cross-coupled with suitable substrates to yield substituted esters. This methodology alleviates the need to protect or mask the carbonyl group as in most cases where organocuprates are produced from lithium or Grignard precursors.

## Experimental Section

**General Information.** Melting points were determined on a Laboratory Device Mel-Temp melting point apparatus and were uncorrected. Boiling points were uncorrected. Infrared spectra were recorded on a Beckman Acculab spectrophotometer, neat, between NaCl plates or as KBr disks. <sup>1</sup>H spectra were recorded on a JEOL FXQ 90 (90-MHz) spectrometer using Me<sub>4</sub>Si as an internal shift reference. GC analyses were performed on Perkin-Elmer Model 990 temperature-programmable gas chromatographs equipped with thermal conductivity detectors. All analyses were performed by the internal standard method using authentic samples of the products to determine accurate response factors.

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All manipulations were carried out on an argon/vacuum dual-manifold system. The Airco prepurified argon was further purified by passing it through a catalyst column (Chemical Dynamics Corp. R3-11) and then through a column of anhydrous  $\text{CaSO}_4$  followed by a column of granular KOH. The solvents 1,2-dimethoxyethane (DME) and tetrahydrofuran (THF) were freshly distilled under argon from sodium/potassium alloy. Alkali metals were handled under an argon atmosphere in a Lab ConCo. glovebox equipped with an air circulator and purifying system similar to that described for the argon/vacuum dual manifold.

**Experimental Setup.** All reactions were carried out in 50-mL two-neck round-bottomed flasks each equipped with a reflux condenser, rubber septum, and containing a small Teflon-clad stirring bar. The condenser was connected to the argon/vacuum manifold. All glassware was oven-dried overnight and assembled hot or taken into the glovebox while still hot and assembled and charged.

**Chemicals.** All chemicals purchased were reagent grade or better and used as received unless otherwise stated.

**Formation of  $\text{CuI-PR}_3$  (4).** The copper complexes were prepared by the method of Kauffman and Teter<sup>16</sup> utilizing tributylphosphine or triethylphosphine (Aldrich) and CuI (Lancaster). The complexes were recrystallized once, dried under vacuum overnight, and stored in tightly stoppered bottles under refrigeration until needed. The complexes will keep several months under these conditions.

**Formation of Lithium Naphthalenide and Biphenylide (3).** Typically oven-dried glassware was placed in the glovebox and charged with Li (11 mmol) and either naphthalene or biphenyl (12 mmol). The glassware was assembled as described under the experimental setup and attached to the argon/vacuum manifold. Freshly distilled THF or DME (15–25 mL) was syringed into the flask, and stirring commenced. At 25 °C the reduction took approximately 2 h in THF and 3 h in DME. The reductions were judged complete when no solid Li could be found. The finished reduction was dark green when naphthalene was used and deep blue with biphenyl. The solutions will keep for several hours but should be used as soon as possible. Li and biphenyl were purchased from Aldrich, and naphthalene was from Fisher.

**Formation of Active Copper (5). Method A.** Lithium naphthalenide or biphenylide was prepared as previously described. Another reaction flask was prepared according to the experimental setup and was charged with  $\text{CuI-PEt}_3$  (10 mmol) and THF or DME (5–10 mL), and the solution was then gently swirled to dissolve the salt. The copper salt solution was drawn up into a syringe and quickly injected into the stirring solution of preformed lithium naphthalenide or biphenylide. After 5 min. the brownish red suspension of active copper was ready for subsequent reaction.

**Method B** is similar to method A but with the following change.<sup>11a</sup>  $\text{CuI-P}(n\text{-butyl})_3$  (10 mmol),  $\text{P}(n\text{-butyl})_3$  (16 mmol), and THF or DME (5 mL) are mixed with gentle swirling in the second reaction flask. The active copper can be kept for a few hours with only a slight loss of reactivity, but for best results the preparation should be used as soon as possible.

**Workup and Identification Procedures.** Aliquots (1 mL) were removed from the reaction mixtures via syringe at timed intervals and quenched with HCl (0.01 M, 0.5 mL). The organic layer was analyzed by GC. The remaining contents of the flask (typically 20–45 mL) were poured into HCl (0.01 M, 50 mL),  $\text{CH}_2\text{Cl}_2$  (25 mL) was added, and the layers were separated. The organic layer was washed twice with water and dried over  $\text{MgSO}_4$ . Volatile components were isolated by either fractional distillation or preparative GC. The higher boiling compounds were separated by flash chromatography.<sup>17</sup> The various components were identified by their physical and spectral properties. All compounds synthesized in this work have been previously reported in the literature, and many are commercially available. When possible, authentic samples of the compounds were procured.

**Formation and Reactions of Alkyl Cupriobenzoates (7).** In a typical reaction active copper (15 mmol) was produced by the lithium naphthalenide or biphenylide reduction of  $\text{CuI-P}(\text{Et})_3$  in THF or DME. The alkyl halobenzoate 6 was added (5.0 mmol)

along with the internal standard (typically decane, 2 mmol). The solution was stirred for 20 min to achieve the maximum yield of 7 (typically 70%). To homocouple oxidatively,  $\text{O}_2$  was bubbled through the reaction mixture (1 h). To homocouple thermally, DME was used as the reaction solvent and the solution was heated to reflux (85 °C, 24 h). To cross-couple, 3 equiv (15 mmol) of the organic halide substrate was injected, neat, into the reaction mixture and the solution stirred for 1 h. The cross-coupling reactions utilizing acid chloride substrates were run in DME; the rest were run in THF. The products were quantitated by GC and identified by their spectral and physical properties after workup and isolation as described previously. All of the alkyl halobenzoate starting materials were commercially available (Lancaster) except methyl 2-iodobenzoate which was synthesized by treating 2-iodobenzoyl chloride with methanol.<sup>18</sup> All products have been previously reported in the literature.

**Methyl 2-Iodobenzoate (6e).** This compound was synthesized by treating 2-iodobenzoyl chloride with methanol<sup>18</sup> (14.8 g, 75% yield): bp 158–161 °C (20 Torr) [lit.<sup>18</sup> 103.5 °C (1 Torr)]; IR (neat) 3100–2900, 2800, 1720, 1590, 1430, 1275, 1115, 1010, 742  $\text{cm}^{-1}$  (lit.<sup>19</sup> IR data matched that of sample);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  8.1–7.0 (m, 4 H), 3.9 (s, 3 H).

**Ethyl 4-Acetylbenzoate (9a):** (3.30 mmol, 66% yield); mp 95 °C (lit.<sup>20</sup> mp 95–96 °C); bp 180–183 °C (20 Torr) [lit.<sup>20</sup> bp 140–145 °C (4 Torr)]; saponification and recrystallization from toluene produced the acid, mp 198–199 °C (lit.<sup>20</sup> mp 199–202 °C); IR (KBr) 2925, 2850, 1735, 1705, 1470, 1835, 1280, 1115, 870, 775  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  [ $(\text{CD}_3)_2\text{CO}$ ]  $\delta$  8.1 (m, 4 H), 4.4 (q,  $J = 7.5$  Hz, 2 H), 2.7 (s, 3 H), 1.4 (t,  $J = 7.5$  Hz, 3 H).

**Ethyl 4-Benzoylbenzoate (9b):** (3.35 mmol, 67% yield); bp 240–245 °C (20 Torr) [lit.<sup>21</sup> bp 226–227 °C (13 Torr)]; saponification and recrystallization from toluene produced the acid, mp 195 °C (lit.<sup>22</sup> mp 195 °C); IR (neat) 3061, 2982, 1721, 1662, 1273, 1105, 715  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  8.2–7.4 (m, 9 H), 4.4 (q,  $J = 8$  Hz, 2 H), 1.4 (t,  $J = 8$  Hz, 3 H).

**Ethyl 4-Allylbenzoate (9c):** (3.25 mmol, 65% yield); bp 156–158 °C (20 Torr) [lit.<sup>23</sup> bp 125–126 °C (8 Torr)]; saponification and recrystallization from toluene produced the acid, mp 214–215 °C (lit.<sup>23</sup> mp 215–217 °C); IR (neat) 3100–2950, 2950–2850, 1710, 1640, 1450, 1280, 1105, 710  $\text{cm}^{-1}$ .

**Ethyl 4-Methylbenzoate (9d):** (3.15 mmol, 63% yield); bp 120 °C (20 Torr) (lit.<sup>24</sup> bp 236 °C); IR (neat) 2982, 1716, 1613, 1273, 1177, 1106, 1023  $\text{cm}^{-1}$  [product IR matched that of an authentic commercial sample (Aldrich)];  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.9 (d,  $J = 8.5$  Hz, 2 H), 7.15 (d,  $J = 8.5$  Hz, 2 H), 4.3 (q,  $J = 8.0$  Hz, 2 H), 2.3 (s, 3 H), 1.35 (t,  $J = 8.0$  Hz, 3 H).

**Ethyl 4-Ethylbenzoate (9e):** (2.25 mmol, 45% yield); bp 138–140 °C (20 Torr) [lit.<sup>25</sup> bp 129–130 °C (15 Torr)]; saponification and recrystallization from toluene produced the acid, mp 111–113 °C (lit.<sup>26</sup> mp 113.5 °C); IR (neat) 2970, 2870, 1720, 1615, 1465, 1280, 1185, 1110, 885, 765, 705  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  8.0 (d,  $J = 8.8$  Hz, 2 H), 7.2 (d,  $J = 8.8$  Hz, 2 H), 4.3 (q,  $J = 7.9$  Hz, 2 H), 2.6 (q,  $J = 8.2$  Hz, 2 H), 1.3 (t,  $J = 7.9$  Hz, 3 H), 1.2 ( $J = 8.2$  Hz, 3 H).

**Ethyl 4-*n*-Propylbenzoate (9f):** (3.90 mmol, 39% yield); bp 153–155 °C (20 Torr) [lit.<sup>25</sup> bp 138–139 °C (16 Torr)]; saponification and recrystallization from toluene produced the acid, mp 141–142 °C (lit.<sup>27</sup> mp 141 °C); IR (neat) 2961, 2872, 1718, 1610, 1275, 1178, 1105, 1022, 849, 761, 703  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  7.95 (d,  $J = 8.8$  Hz, 2 H), 7.2 (d,  $J = 8.8$  Hz, 2 H), 4.3 (q,  $J = 7.9$  Hz, 2 H), 2.6 (t,  $J = 8.5$  Hz, 2 H), 1.5 (m,  $J = 8.5$  Hz, 2 H), 1.3

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(t,  $J = 7.9$  Hz, 3 H), 0.9 (t,  $J = 8.5$  Hz 3 H).

**Ethyl 3-Methylbenzoate (9g):** (2.80 mmol, 56% yield); bp 110 °C (20 Torr) [lit.<sup>28</sup> bp 103–105 °C (10 Torr)]; saponification and recrystallization from toluene produced the acid, mp 112–113 °C (lit.<sup>29</sup> mp 111–113 °C); IR (neat) 2981, 2872, 1716, 1609, 1590, 1445, 1367, 1278, 1199, 1105, 1026  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.9–7.2 (m, 4 H), 4.3 (q,  $J = 7.5$  Hz, 2 H), 2.4 (s, 3 H), 1.4 (t,  $J = 7.5$  Hz, 3 H); product IR and NMR data matched that of authentic commercial sample (Aldrich).

**Methyl 2-Benzoylbenzoate (9h):** (3.65 mmol, 73% yield), mp 52 °C (lit.<sup>30</sup> mp 51 °C); IR (KBr) 3000–2850, 1665, 1275, 1080, 930, 775, 712  $\text{cm}^{-1}$  (lit.<sup>30</sup> IR matches that of sample);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.1–7.2 (m, 9 H), 3.6 (s, 3 H); saponification and recrystallization from toluene produced the acid, mp 125–128 °C (lit.<sup>31</sup> mp 126–127 °C).

**Methyl 2-Acetylbenzoate (9i):** (2.05 mmol, 41% yield); bp 117–123 °C (7 Torr) [lit.<sup>32</sup> bp 94–95 °C (2 Torr)];  $^1\text{H}$  NMR ( $\text{CCl}_4$ )  $\delta$  2.50 (s, 3 H), 3.92 (s, 3 H), 7.43–8.15 (m, 4 H) (lit.<sup>32</sup>  $^1\text{H}$  NMR data matched that of sample).

**Methyl 2-Benzylbenzoate (9j):** (3.80 mmol, 76% yield); bp 168 °C (5 Torr); saponification and recrystallization from toluene produced the acid, mp 117–118 °C (lit.<sup>33</sup> mp 118 °C); IR (neat) 3008, 2942, 1717, 1592, 1483, 1258, 1125, 1067, 733, 683  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.0–7.1 (m, 9 H), 4.4 (s, 2 H), 3.8 (s, 3 H).

**Methyl 2-Methylbenzoate (9k):** (3.40 mmol, 68% yield); bp 205–209 °C (lit.<sup>34</sup> bp 215 °C); saponification and recrystallization from toluene produced the acid, mp 107–108 °C (lit.<sup>35</sup> mp 107–108 °C); IR (neat) 2951, 2840, 1723, 1436, 1260, 1080  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.0–7.1 (m, 4 H), 3.85 (s, 3 H), 2.6 (s, 3 H); product IR and NMR data matched that of authentic commercial sample (Aldrich).

**Diphenic Acid, Dimethyl Ester (14):** (2.56 mmol, 32% yield); bp 210–215 °C (20 Torr) [lit.<sup>42</sup> bp 204–206 °C (14 Torr)]; mp 73 °C (lit.<sup>43</sup> mp 74 °C); IR (KBr) 3100–2800, 1720, 1450, 1300, 1140, 1090, 965, 760, 710  $\text{cm}^{-1}$  (lit.<sup>43</sup> IR data matched that of sample);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.1–7.1 (m, 8 H), 3.6 (s, 6 H).

**Diethyl Biphenyl-4,4'-dicarboxylate (15):** (2.08 mmol, 52% yield); mp 110–112 °C; IR (Nujol) 3143, 1704, 1606, 1376, 1270, 1111, 846, 757  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.2–7.5 (m, 8 H), 4.4 (q,  $J = 7.5$  Hz, 4 H), 1.4 (t,  $J = 7.5$  Hz, 6 H); product melting point,

IR, and NMR data matched that of an authentic commercial sample (Lancaster).

**Formation and Reactions of Methyl 5-Cupriopentanoate (11).** Methyl 5-cupriopentanoate was formed by the procedure of Wehmeyer and Rieke.<sup>11a</sup> Typically, active copper (10 mmol) was produced by mixing a solution of lithium naphthalenide or biphenylide (11 mmol) in THF or DME (15 mL) with a solution of  $\text{CuI}\cdot\text{P}(n\text{-butyl})_3$  (10 mmol) and  $\text{P}(n\text{-butyl})_3$  (16 mmol) in THF or DME (5 mL) and allowing the combined mixtures to stir for 20 min. The temperature was lowered to  $-78$  °C, and 10 was added (Aldrich, 4 mmol) along with the internal standard (decane, 2.05 mmol). The solution was stirred for 20 min to maximize the yield of 11 (typically 60%). To homocouple,  $\text{O}_2$  was bubbled through the reaction mixture for 1 h while the temperature remained at  $-78$  °C. To cross-couple, 3 equiv (12 mmol) of the organic halide substrate was injected, neat, into the organocopper solution and the reaction continued with stirring for 1 h. The cross-coupling reaction utilizing benzoyl chloride was run in DME; the rest were run in THF. The reactions were quenched with dilute HCl and quantitated by GC, and the products were identified by their spectral and physical properties after workup and isolation as previously discussed. All products have been previously reported in the literature.

**Methyl 5-Benzoylpentanoate (12a):** (4.32 mmol, 54% yield); mp 35.2 °C; bp 155–157 °C (8 Torr) [lit.<sup>36</sup> bp 132–133 °C (2 Torr)]; IR (neat) 2926, 2843, 1725, 1675, 1442, 1358, 971, 674  $\text{cm}^{-1}$  (lit.<sup>36</sup> IR 1740, 1705  $\text{cm}^{-1}$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.7 (m, 5 H), 3.6 (s, 3 H), 2.9 (t, 2 H), 2.4 (t, 2 H), 1.8 (m, 4 H) (lit.<sup>36</sup>  $^1\text{H}$  NMR data matched that of sample).

**Methyl Hexanoate (12b):** (3.04 mmol, 19% yield); bp 151–153 °C (lit.<sup>37</sup> bp 151 °C); IR (neat) 2956, 2873, 1743, 1436, 1248, 1172  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.7 (s, 3 H), 2.25 (dt, 2 H), 1.6 (m, 2 H), 1.3 (broad s, 4 H), 0.9 (t, 3 H); the product IR and NMR data matched those of an authentic commercial sample (Aldrich).

**Methyl 6-Phenylhexanoate (12c):** (6.4 mmol, 40% yield); bp 165 °C (8 Torr) [lit.<sup>38</sup> bp 135–136 °C (3 Torr)]; IR (neat) 3025, 2925, 2859, 1733, 1483, 1442, 1175  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.2 (m, 5 H), 3.7 (s, 3 H), 2.6 (t,  $J = 8$ , 2 H), 2.3 (t,  $J = 8$  Hz, 2 H), 1.6 (m,  $J = 8$  Hz, 6 H); saponification of a sample of the product followed by an ether extraction and subsequent solvent removal yielded the acid which was purified by distillation, bp 195–200 °C (20 Torr) [lit.<sup>38</sup> bp 201–202 °C (24 Torr)].

**Methyl 7-Octenoate (12d):** (5.76 mmol, 36% yield); bp 105–110 °C (20 Torr) [lit.<sup>39</sup> bp 43–45 °C (0.45 Torr)]; IR (neat) 3075, 2956, 2873, 1741, 1640, 1436, 1249, 1171  $\text{cm}^{-1}$  (lit.<sup>40</sup> IR data matched that of sample);  $^1\text{H}$  NMR  $\delta$  5.7 (1 H,  $-\text{CH}=\text{}$ ), 4.9 (2 H,  $\text{CH}_2=\text{}$ ), 3.6 (3 H,  $-\text{COOCH}_3$ ), 2.2 (2 H,  $-\text{CH}_2\text{COO}-$ ), 1.9–1.2 (8 H,  $-(\text{CH}_2)_4-$ ) (lit.<sup>39</sup>  $^1\text{H}$  NMR data agreed with that of sample).

**Dimethyl Sebacate (13):** (2.56 mmol, 32% yield); bp 173–177 °C (20 Torr) [lit.<sup>41</sup> bp 175 °C (20 Torr)]; mp 31–32 °C (lit.<sup>41</sup> mp 38 °C); IR (neat) 2932, 2856, 1740, 1436, 1362, 1198, 1171  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.7 (s, 6 H), 2.3 (t,  $J = 8$  Hz, 4 H), 1.6 (m,  $J = 8$  Hz, 4 H), 1.3 (broad s, 8 H); product IR and NMR data matched those of an authentic commercial sample (Aldrich).

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