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Reaction of Lithium Dialkyl- and Diarylcuprates with Organic Halides[1,2]

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Abstract: Lithium dialkyl- or diarylcuprates (R_2CuLi) react with aryl iodides in ether solution by competing metal–halogen exchange and coupling reactions. Using appropriate reagents, high yields of the coupled product R–Ar can be obtained by allowing the metal–halogen exchange to proceed to completion in the presence of an excess of R_2CuLi, and oxidizing the resulting mixture of organometallic species present in solution with nitrobenzene or oxygen. This reaction sequence works well with lithium di-*n*-alkyl- and diarylcuprates; it fails with di-*sec*-alkyl- and di-*t*-alkylcuprates. Although most alkyllithium reagents react with aryl iodides only by metal–halogen exchange, methyllithium, uncomplexed with copper, smoothly converts aryl iodides to arylmethanes. Coupling of lithium dialkyl- and diarylcuprates with *alkyl* halides appears to take place without significant metal–halogen exchange. The reaction of lithium diphenylcuprate with (−)-(*R*)-2-bromobutane occurs with the predominant *inversion* of configuration (84–92% stereoselectivity) expected of an S_N2-like displacement. Coupling reactions involving an *n*-alkyl halide as one reaction partner proceed in high yield; those involving *t*-alkyl halides fail. Lithium di-*n*-alkyl-, di-*sec*-alkyl-, and di-*t*-alkylcopper reagents all couple with *n*-alkyl halides. A number of preparations for representative copper(I) ate complexes are described, and the sensitivity of the coupling reactions to the method of preparation of the ate complex, to the nature of the solvent, and to the presence of lithium halides, trialkylphosphines, and dialkyl sulfides in solution are discussed.

A broadly applicable procedure for coupling the organic moiety of an organometallic reagent with that of an organic halide would be a useful member of the class of reactions available for the synthesis of carbon–carbon σ bonds. Unfortunately the com-

$$RM + R'X \longrightarrow R\text{-}R' + MX \qquad (1)$$

monly encountered organometallic derivatives of the main group metals appear to be unsatisfactory as reagents for effecting the formation of carbon–carbon bonds by nucleophilic displacement at a carbon–halogen bond. Although organolithium reagents are strongly basic, they appear to be only weakly nucleophilic toward carbon: reaction of an organolithium compound with an alkyl or aryl halide in hydrocarbon or ether solutions usually leads to mixtures of products derived from competing metal–halogen exchange,[4] α metalation,[5] β elimination, and coupling, with the last reaction apparently proceeding, at least in part, through a complex free-radical mechanism.[6] Organomagnesium reagents are relatively unreactive toward simple alkyl and aryl halides; their reaction with activated halides again leads to mixtures of products.[7,8] Organozinc and organoaluminum compounds exhibit low reactivity toward, *e.g.*, *n*-alkyl halides. At present, the structural factors responsible for low nucleophilicity of these organometallic reagents toward carbon are not entirely evident.

In contrast, organometallic compounds containing carbon–copper(I) bonds provide a class of reagents whose usefulness in coupling reactions with organic halides has been amply demonstrated in certain specialized circumstances. Thus reaction of copper(I) acetylides with acetylenic,[9] aromatic,[10] vinyl,[11a,b] and acyl[11c] ha-

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lides has been used successfully in formation of σ bonds, and a number of thermally stable arylcopper(I) reagents have been observed to couple with aryl, alkyl, and acyl halides.[12,13] Unfortunately, the usefulness of most uncomplexed alkylcopper(I) reagents in coupling reactions is limited, since these compounds decompose thermally more rapidly than they react with organic halides. However, previous work with organocopper(I) compounds has demonstrated that formation of 1:1 "ate" complexes[14] of these reagents with organolithium and organomagnesium reagents simultaneously results in a stabilization of the carbon–copper(I) bond toward thermal decomposition and in an increase in the nucleophilic reactivity toward carbon of the organic moiety bonded to copper.[15,16] Thus, lithium dialkyl- or diarylcuprates appeared to be of interest as reagents for carrying out the displacement of halogen at carbon by organic groups.

This paper reports the results of our examination of the reactivity of lithium diorganocuprates toward organic halides. The results of similar independent investigations have recently been described by Corey and Posner,[17] and several applications of these coupling procedures have been reported since the original descriptions.[18]

Results

Reaction of Methylcopper(I) Derivatives with Aryl Iodides. Pure lithium dimethylcuprate (**1**) can be prepared by dissolving halide-free methylcopper(I) in halide-free methyllithium solution.[15] Reaction of this material with aryl iodides such as iodobenzene or 1-iodonaphthalene in ether solution at room temperature for periods of 8 to 24 hr, followed by hydrolysis, yields the corresponding arylmethane with a maximum conversion of 30–50% based on the aryl iodide. If the organometallic components of the reaction mixtures are oxidized[19] prior to hydrolysis, the yield of arylmethane is increased to 60–70% (Tables I and II). These observations suggest that lithium dimethylcuprate is reactive toward carbon–iodine bonds in a sense that leads to carbon–carbon bond formation. However, the significant increase in the yield of arymethane observed on oxidation of the reaction mixture indicates that at least two reactions are taking place in solution: a reaction leading to coupling (eq 2 or 4), and another reaction involving metal–halogen exchange between the aryl iodide and the cuprate **1** which competes with (or precedes) the coupling reaction (eq 3). The oxidative conversion of a "mixed" lithium phenylmethylcuprate (represented schematically by **2**) to toluene on oxidation

$$\mathrm{PhI} + \underset{\mathbf{1}}{(\mathrm{CH_3})_2\mathrm{CuLi}} \longrightarrow \mathrm{PhCH_3} + (\mathrm{CH_3Cu}) + \mathrm{LiI} \qquad (2)$$

$$\mathrm{PhI} + \underset{\mathbf{1}}{(\mathrm{CH_3})_2\mathrm{CuLi}} \rightleftharpoons \underset{\mathbf{2}}{(\mathrm{Ph})(\mathrm{CH_3})\mathrm{CuLi}} + \mathrm{CH_3I} \qquad (3)$$

$$\mathbf{2} + \mathrm{CH_3I} \longrightarrow \mathrm{PhCH_3} + (\mathrm{CH_3Cu}) \qquad (4)$$

$$\mathbf{2} + \mathrm{O_2} \longrightarrow \mathrm{PhCH_3} \qquad (5)$$

(eq 5) is in accord with the results of previous studies.[19] In an effort to establish the most satisfactory experimental conditions for coupling organocopper reagents with aryl halides, and to define the effect of the terminal oxidation on the yield of coupled product, we have examined the reactions of lithium dimethylcuprate and related substances with iodobenzene and 1-iodonaphthalene in detail.

Three preparations for solutions containing "lithium dimethylcuprate" are available (eq 6–8).[15,20] These

$$2\mathrm{CH_3Li} + \mathrm{CuX} \longrightarrow \underset{\mathbf{1}}{(\mathrm{CH_3})_2\mathrm{CuLi}} + \mathrm{LiX} \qquad (6)$$

$$\mathrm{CH_3Li} + \mathrm{CH_3Cu} \longrightarrow \underset{\mathbf{1}}{(\mathrm{CH_3})_2\mathrm{CuLi}} \qquad (7)$$

$$2\mathrm{CH_3Li} + \mathrm{L{\cdot}CuX} \longrightarrow (\mathrm{CH_3})_2\mathrm{CuLi{\cdot}L} + \mathrm{LiX} \qquad (8)$$

preparations differ in convenience and in the properties of the resulting organometallic reagents. The most amenable to large scale synthetic application is the direct reaction between methyllithium and copper(I) bromide or iodide suspended in ether (eq 6). The composition of these organometallic solutions is not well defined on two counts: for one, they contain variable amounts of lithium halide; for a second, they appear to be significantly more active in certain reactions than solutions containing pure lithium dimethylcuprate (*vide infra*). Preparation of pure lithium dimethylcuprate by reaction of methyllithium with a slight excess of pure methylcopper (eq 7) leads to lithium halide free solutions containing an organocopper reagent of well-defined stoichiometry, but is relatively inconvenient in its requirement that methylcopper(I) be prepared in a separate step. Reaction of methyllithium with an ether-soluble copper(I) halide trialkylphosphine or bis(dialkyl sulfide) complex results in a solution containing the phosphine or sulfide ligand and lithium halide in addition to a lithium dimethylcopper ate complex (eq 8).

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(20) No firm evidence is available concerning the structure(s) or extent(s) of aggregation of the species represented in this paper as R_2CuLi and $R_2CuLi{\cdot}PR_3$. By analogy with the ate complexes formed between methyllithium and either dimethylmagnesium or dimethylzinc,[21] the "lithium dimethylcuprates" probably consist of tetrahedral metal clusters with face-centered bridging alkyl groups. Preliminary low-temperature nmr studies of copper ate complexes are consistent with such a picture and also suggest the existence of higher complexes having composition, *e.g.*, $(RCu){\cdot}(RLi)_3$.[22] Both chemical and spectroscopic evidence indicate qualitatively that trialkylphosphines in solution of copper ate complexes are associated with the metal clusters, but again no structural information concerning the details of this association are at hand.[22]

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Table I. Reaction of Lithium Dialkylcuprates with Iodobenzene[a]

R_2CuLi	Other solution components (concn, M)	Reaction time, hr	Recovered iodobenzene, %	Product	Yield, %[b] Hydrolysis	Yield, %[b] Oxidation[c]
1. $(CH_3)_2CuLi$[d]		1	95	Toluene	3	3
		4	75		6	16
		15	36		24	48
		42	<1		46	70
2. $(CH_3)_2CuLi$[d]	CH_3Li (0.1)	1			4	4
		4			11	35
		15			25	65
		42			48	71
3. $(CH_3)_2CuLi$[d]	LiBr (1.0)	1			~1	~1
		15			29	60
4. $(CH_3)_2CuLi$[d]	LiI (1.0)	1			<1	<1
		34			16	
5. $(CH_3)_2CuLi$[d]	$(n\text{-}C_4H_9)_3P$ (0.5)	1			20	91
		4			18	92
6. $(CH_3)_2CuLi$[e]	LiI (0.5) +	1			<1	<1
	$(n\text{-}C_4H_9)_2S$ (1.0)	4			4	19
		72			37	37
7. $(CH_3)_2CuLi$[f]	LiI (0.5) +	0.25			12	60
	LiBr (1.0)	12			12	60
8. $(CH_3)_2CuLi$[d]	"residue"[g]	1			55	52
		2			99	98
9. $(CH_3)_2CuLi$[d]	CH_3Li (0.1) +	1			3	7
	"residue"[g]	4			80	80
		15			95	95
10. $(n\text{-}C_4H_9)_2CuLiP(n\text{-}Bu)_3$[h]	LiI (0.5)	0.7		$n\text{-}C_4H_9C_6H_5$	<1	50
11. $(sec\text{-}C_4H_9)_2CuLiP(n\text{-}Bu)_3$[h]	LiI (0.5)	0.7[i]		$sec\text{-}C_4H_9C_6H_5$	<1	20
12. "$(n\text{-}C_4H_9)_2CuLi$"[f]	LiI (0.5)	1.0[j]		$n\text{-}C_4H_9C_6H_5$	<1	55
13. "$(sec\text{-}C_4H_9)_2CuLi$"[f]	LiI (0.5)	1.0[j]		$sec\text{-}C_4H_9C_6H_5$	<1	<1

[a] Reactions were carried out in ether solution at 25°, with $[R_2CuLi] = 0.5\ M$, and $[C_6H_5I] = 0.1\ M$, unless otherwise noted. [b] Yields were determined by glpc, and are based on iodobenzene. [c] Oxidations were carried out by diluting the reaction mixture to ~0.1 M in Cu(I) followed by addition of an excess of molecular oxygen at −78°, unless noted otherwise. [d] Prepared by dissolving halide-free methylcopper(I) in halide-free methyllithium solution (eq 7). [e] Prepared by reaction of 2 equiv of methyllithium with 1 equiv of $[(n\text{-}C_4H_9)_2S]_2CuI$ (eq 8) [f] Prepared by reaction of 2 equiv of alkyllithium reagent with a suspension of 1 equiv of CuI (eq 6). [g] "Residue" refers to the materials present in commercial copper(I) iodide which are insoluble in di-n-butyl sulfide. See the text for a discussion of this point. [h] Prepared by reaction of 2 equiv of alkyllithium reagent with 1 equiv of $ICuP(n\text{-}Bu)_3$ (eq 8). [i] Reaction carried out at −10°. [j] THF solution.

The presence of these ligands and their reaction products during the work-up of reactions carried out on a synthetic scale has consistently proved to be a major inconvenience.

Lithium dialkylcuprates containing primary alkyl groups other than methyl can in general be prepared by procedures analogous to those of eq 6, 7, and 8, although the solutions obtained by the procedure of eq 6 may contain alkyllithium reagent in appreciable excess of the stoichiometry required by the formulation R_2CuLi. Grignard reagents cannot in general be substituted for organolithium reagents in the procedure of eq 6. We have *only* been successful in preparing well-characterized *sec*- and *t*-alkylcopper(I) reagents by the procedure of eq 8. The procedures exemplified by eq 6 [with copper(I) bromide], 7, and 8 were also satisfactory for producing ether solutions of lithium diphenylcuprate.

The products of reaction of lithium dimethylcuprate with iodobenzene and with iodonaphthalene were inferred from a comparison of the glpc traces of two aliquots: one aliquot was hydrolyzed directly; the second was first oxidized using an excess of molecular oxygen or nitrobenzene, and then hydrolyzed. Using this analytical procedure, the yield of toluene or 1-methylnaphthalene obtained following the *non*oxidative work-up presumably provides a measure of coupling taking place by some combination of reactions represented by eq 2, 3, and 4. Although a number of precautions were taken to avoid contact between the reaction solution and oxygen (from the air) in the reactions involving a nonoxidative work-up, the possibility that some portion of the toluene or 1-methylnaphthalene formed in these experiments arose from unintentional reaction with an oxidant cannot be rigorously excluded. The *increase* in yield of unsymmetrical dimer on oxidation provides a qualitative measure of the quantity of arylmetallic reagent present in the solution. Additional evidence for the presence of an arylmetallic intermediate is discussed later in this manuscript. Since an excess of lithium dimethylcuprate was used in all studies, and since oxidative coupling of mixed lithium diorganocuprates seems to give approximately statistical yields of symmetrical and unsymmetrical dimers,[19] the probability of symmetrical coupling of the aryl moieties of two arylmetallic reagents under oxidative conditions is much lower than the probability of unsymmetrical coupling.

The data of Table I summarize observations concerning the response of the yield of toluene in coupling of lithium dimethylcuprate with iodobenzene to a number of types of changes in reaction conditions. The reaction of pure lithium dimethylcuprate with iodobenzene in halide-free ether appears to be complete in 24 hr or less at 25°. The yield of toluene in the nonoxidative work-up, and the increase in yield of toluene on oxidation, demonstrate that the products of carbon–carbon bond formation and metal–halogen exchange

Table II. Reaction of Methylcopper Derivatives with 1-Iodonaphthalene

Copper reagent (concn, M)	1-Iodonaphthalene concn, M	Other solution components (concn, M)	Reaction time, hr	Yields, %[a] Naphthalene	1-Methylnaphthalene	1-Iodonaphthalene
$(CH_3)_2CuLi$ (0.38)[b]	0.13		0.5	25	10	67
			2.0	51	29	17
			4.0	58	31	6
			8.0	62	33	
$(CH_3)_2CuLi$ (0.38)[c]	0.13	LiI (0.39)	0.5	72	11	7
			1.0	73	13	3
			2.0	77	14	
			23	69	20	
$(CH_3)_2CuLi$ (0.32)[c]	0.11	LiI (0.32)	2.5	59–70	26–28	3–10
			2.5	(2	62	10)[d]
			2.5	(2	57	16)[e]
			2.5	(4	70	4)[f]
$CH_3CuP(n\text{-}Bu)_3$ (0.38)	0.13		0.5	1	8	91
			2.0	1	31	68
			4.0[g]	5	75	3
$CH_3CuP(n\text{-}Bu)_3$ (0:38)	0.13		2.0	2	33	65
$CH_3CuP(n\text{-}Bu)_3$ (0.38)	0.13	LiI (0.38)	2.0	20	29	51

[a] Based on 1-iodonaphthalene. Reactions were carried out in ether solution at 25° unless otherwise indicated. [b] Prepared by dissolving halide-free methylcopper(I) in halide-free methyllithium solution (eq 7). [c] Prepared by reaction of 2 equiv of methyllithium with a suspension of 1 equiv of CuI (eq 6). [d] Yields obtained on oxidation with O_2 at 0°. If all the oxygen added had dissolved in the reaction solution, its equivalent concentration would have been 1.4 M. [e] Oxidation with O_2 at −78°; equivalent concentration 1.4 M. [f] Oxidation with $PhNO_2$ at 0°; equivalent concentration 0.67 M. [g] The reaction was stirred at 25–27° for 2 hr and then heated to 60–70° for 2 hr.

form at comparable rates. Similar data for reactions with 1-iodonaphthalene are presented in Table II; in this case consumption by the aryl iodide is complete in less than 8 hr. The addition of lithium bromide, lithium iodide, or di-*n*-butyl sulfide to solutions of lithium dimethylcuprate (**1**) prepared from pure methylcopper has relatively little effect on the rate either of the metal–halogen exchange reaction or of the coupling reaction. Addition of 1 equiv of tri-*n*-butylphosphine to a reacting solution of lithium dimethylcuprate and iodobenzene has two effects: it increases the rate of metal–halogen exchange as judged by the yield of toluene obtained on oxidation, and it increases the rate of toluene formation prior to oxidation.

Comparison of entries 1, 3, 4, and 7 of Table I and similar data in Table II establishes that the reaction between aryl iodides and pure lithium dimethylcuprate, prepared from methyllithium and methylcopper(I), is appreciably slower than that with lithium dimethylcuprate prepared by reaction of methyllithium and copper(I) iodide: the latter reaction appears to be complete in 15–30 min, while the former process requires 8–24 hr. Further, although the yield of toluene obtained on oxidation of the latter reaction mixture is comparable to that obtained on oxidation of reaction mixtures incorporating pure lithium dimethylcuprate, the yield of toluene produced in the direct coupling reaction is significantly lower. Thus, it appears that metal–halogen exchange is significantly more rapid using the reagent prepared by reaction of methyllithium and copper(I) iodide than using pure lithium dimethylcuprate.

The reason for the observed differences in reactivity of the organometallic reagents prepared by the procedures represented by eq 6 and 7 is not presently clear. Methyllithium itself reacts readily with iodobenzene to yield toluene.[23] In fact, the *direct* reaction of methyllithium with aryl iodides in the absence of copper salts often gives yields of coupled products comparable or superior to those obtained using lithium dimethylcuprate. However, comparison of entries 1 and 2 of Table I establishes that the presence of methyllithium in excess of the stoichiometry required by the formulation "$(CH_3)_2CuLi$" does not appreciably enhance the reactivity of the copper ate complex in the coupling reaction.

A possible clue to the difference in reactivity of pure lithium dimethylcuprate and material prepared directly from methyllithium and commercial copper iodide appears in comparison of entries 2, 7, 8, and 9 of Table I. The ether-soluble complex of di-*n*-butyl sulfide and copper(I) iodide used in the preparation of pure methylcopper(I) (eq 7) is obtained by dissolving copper(I) iodide in the sulfide. Commercial "copper iodide" ordinarily contains approximately 5% impurities which are insoluble in di-*n*-butyl sulfide. Entries 8 and 9 summarize experiments in which these di-*n*-butyl sulfide insoluble residues were collected and added to copper ate complexes prepared from pure methylcopper. Surprisingly, it appears that addition of these residues to the organocopper solutions significantly enhances their reactivity in the nonoxidative coupling reaction. Work in progress is designed to explore the significance of these observations, and any discussion of the mechanism by which the di-*n*-butyl sulfide insoluble residues might influence the course of the coupling reaction is clearly speculation. Nonetheless, these results raise the intriguing possibility that metals, other than copper, present in the residues may be capable of catalyzing the coupling reaction.[24]

(23) (a) H. Gilman and F. W. Moore, *J. Amer. Chem. Soc.*, **62**, 1843 (1940); (b) W. Langham, R. Q. Brewster, and H. Gilman, *ibid.*, **63**, 545 (1941). In our hands, reaction of 1 equiv of methyllithium with 1 equiv of iodobenzene in ether yielded 91% toluene in 30 min at room temperature. Under similar reaction conditions, 1-iodonaphthalene yielded 86% 1-methylnaphthalene. Consequently, the direct reaction with methyllithium appears to be the method of choice for synthetic methylation reactions involving aryl iodides when other functional groups in the organic iodide are compatible with this organometallic reagent. Comparison of these yields and reaction times with those in Table I provides chemical evidence that solutions of lithium dimethylcuprate do not contain appreciable concentrations of free methyllithium.

(24) Note Added in Proof. Semiquantitative flame spectrophotometric analysis of a representative sample of the di-*n*-butyl sulfide insoluble "residue" in commercial copper(I) iodide has established that

Table III. Reaction of Lithium Diphenyl Cuprate with Aryl and Vinyl Halides

$(C_6H_5)_2CuLi$ (concn, *M*)	Organic halide (concn, *M*)	Additive(s) (concn, *M*)	Reaction time, hr	Product yields, %				
				Iodobenzene	Naphthalene	1-Iodonaphthalene	1 Phenylnaphthalene	1,1′-Binaphthyl
0.16	1-Iodonaphthalene (0.032)	LiBr (*ca.* 0.48)[a]	1	58	60	25	13	
			4	68	75		22	
			19	49	70		28	
0.16		LiBr (*ca.* 0.48)[a] O_2 (excess)[c]	4	*b*			52	5
0.16		LiBr (*ca.* 0.48),[a] O_2 (excess)[d]	4	*b*			53	2
0.16		LiBr (*ca.* 0.48),[a] $PhNO_2$ (0.40)[c]	4	*b*	10		90	
0.16		LiBr (*ca.* 0.48),[a] $MeNO_2$ (0.59)[c]	4	*b*	25		70	
0.16		LiBr (*ca.* 0.48),[a] $CuCl_2$ (0.32)[c]	4	*b*	15		81	
0.18		LiI (*ca.* 0.02)	1	25	24	59	12	
			4	48	56	3	37	
			22	19	44		45	
0.21		LiBr (*ca.* 1.7)	1	*b*	41	34	25	
	(0.042)		3.5	*b*	59	2	39	
				trans-Stilbene			*cis*-Stilbene	
0.24	*trans*-β-Bromostyrene (0.049)	LiBr (*ca.* 0.72)[a]	2.0	75			<2	
			4.0	90			<2	
0.20	*cis*-β-Bromostyrene (0.042)	LiBr (*ca.* 0.60)[a]	2.0	<1			73	
				1,8-Diphenylnaphthalene			1-Phenylnaphthalene	
0.60	1,8-Diiodonaphthalene (0.10)	LiBr (*ca.* 1.8)[a]	24 (reflux)	5			56	
0.60		O_2 (excess)[c]		47			2	

[a] This salt was formed in the reaction solution during the preparation of phenyllithium and during the subsequent formation of lithium diphenylcuprate from phenyllithium and copper(I) bromide. [b] In these runs the yield of iodobenzene was not determined. [c] After the reaction solution had been stirred for the specified time it was cooled to 0° before the oxidant was added. [d] After the reaction solution had been stirred for the specified time it was cooled to −78° before the oxidant was added.

Reaction of lithium di-*n*-butyl- and di-*sec*-butyl-(tri-*n*-butylphosphine)cuprates[20] with iodobenzene yields appreciable quantities of *n*-butyl- and *sec*-butylbenzene, respectively, on oxidative coupling, but no butylbenzenes on nonoxidative hydrolytic work-up (Table I). Apparently metal–halogen exchange can take place with these reagents, but the direct coupling reaction is slow.

Hydrolysis of aliquots of a reaction mixture containing pure lithium dimethylcuprate and iodonaphthalene demonstrates that the decrease in the concentration of iodonaphthalene is accompanied by a corresponding increase in concentration of both 1-methylnaphthalene and naphthalene, the latter compound presumably arising from protonation of a 1-naphthyl organometallic reagent. The data in Table II suggest that nitrobenzene is a slightly more efficient reagent for the oxidative coupling than is molecular oxygen. The last three entries in Table II establish that formation of an ate complex is not a prerequisite for successful coupling. Methyl(tri-*n*-butylphosphine)-copper(I) reacts with 1-iodonaphthalene to give 1-methylnaphthalene. This reaction seems to be accompanied by appreciably less metal–halogen exchange than the corresponding reaction involving methylcopper ate complexes. Unfortunately the presence of tri-*n*-butylphosphine in these reaction mixtures, and the thermal instability of alkylcopper(I) reagents other than methyl, severely limit the practical usefulness of coupling reactions involving the alkyl(tri-*n*-butylphosphine)copper(I) reagents.

For reaction systems in which metal–halogen exchange is faster than direct coupling, there may be practical advantages in certain cases to a coupling scheme involving direct formation of the mixed ate complexes required for oxidative coupling from organolithium reagents. This scheme is most attractive for couplings involving *sec*- or *t*-alkylcopper compounds. The thermal stability of these reagents is sufficiently low that extensive thermal decomposition occurs under the reaction conditions required for coupling and metal–halogen exchange to take place. In contrast, both the formation of mixed ate complexes by reaction of organolithium reagents with copper(I) salts (eq 6 and 8), and their subsequent oxidative coupling, can be carried out at −78°. Thus, for example, *sec*-butylbenzene is formed in higher yield by oxidation of preformed ate complexes than by direct reaction of lithium di-*sec*-butylcuprate with iodobenzene (Table I).

its principal metallic constituents are: Cu (>10%), Fe (>10%), Na (1–10%), Ni (0.1–1.0%), and Cr (0.1–1.0%). A mixture of "pure" lithium dimethylcuprate, prepared using the procedure represented by eq 7, and iron(II) chloride (<20%, based on copper) shows the same reactivity toward iodobenzene as material prepared directly from methyllithium and commercial copper iodide. Nickel(II) bromide significantly enhances both the yield and rate of formation of toluene in the direct coupling reaction of "pure" lithium dimethylcuprate with iodobenzene. Thus, both nickel and iron catalyze the coupling of lithium dimethylcuprate with iodobenzene. Studies of applications and mechanism of this catalysis are continuing.

$$sec\text{-}C_4H_9Li + 4C_6H_5Li \xrightarrow[2.\ O_2,\ -78^\circ]{1.\ 2.5\ CuBr,\ THF,\ -78^\circ} sec\text{-}C_4H_9C_6H_5 \quad (76\%)$$

$$t\text{-}C_4H_9Li + 4C_6H_5Li \xrightarrow[2.\ O_2,\ -78^\circ]{1.\ 2.5\ CuBr,\ THF,\ -78^\circ} t\text{-}C_4H_9C_6H_5 \quad (73\%)$$

Reaction of Lithium Diphenylcuprate with Aryl and Vinyl Halides. The reaction of lithium diphenylcuprate with 1-iodonaphthalene (Table III) appears to follow approximately the same pattern that appeared in reactions of the methyl reagent **1** with 1-iodonaphthalene and iodobenzene. The operation of metal-halogen interchange in this reaction system is unambiguously confirmed by the observation that hydrolysis of a reaction aliquot with D_2O after the metal-halogen exchange has taken place leads to naphthalene having isotopic composition 80% d_1, 20% d_0, and by the simultaneous appearance of iodobenzene and naphthalene in approximately equal yields from hydrolysis of aliquots taken early in the reaction. Metal-halogen exchange is complete in approximately 4 hr at room temperature; the coupling reaction, which may reflect either direct reaction of lithium phenyl(1-naphthyl)cuprate with the iodobenzene formed in the exchange, or thermal decomposition of a 1-naphthylcopper organometallic reagent in the presence of a phenylcopper compound, continues more slowly. Regardless of the mechanism of the thermal coupling reaction, oxidation of the mixture of organometallic reagents obtained after the initial metal-halogen exchange reaction is complete results in efficient conversion of 1-naphthylmetal species present in solution to 1-phenylnaphthylene. Once again, nitrobenzene appears to produce the highest yields of 1-phenylnaphthalene in the oxidative coupling: oxidation with oxygen either at 0° or at −78°, nitromethane, or copper(II) chloride gives appreciably lower yields.

Similarly, reaction of an excess of lithium diphenylcuprate with 1,8-diiodonaphthalene in refluxing diethyl ether solution for extended periods of time appears to result in approximately 50% conversion of the aryl iodide to 1-phenyl-8-copper(I)naphthalene, as judged by the difference in yield of 1-phenyl- and 1,8-diphenylnaphthalene before and after oxidation.

Reaction of lithium diphenylcuprate with *cis*- or *trans*-β-bromostyrene results in high conversions to *cis*- and *trans*-stilbenes, respectively; oxidation is not required in this reaction system to obtain high yields of coupled products. Less than 2% of the stilbene isomer having inverted configuration around the double bond is formed in each case. For reasons discussed previously[25] the observation of retention of stereochemistry in these coupling reactions strongly argues against free β-styryl radicals as reaction intermediates.

Reaction of Lithium Dialkyl- and Diarylcuprates with Alkyl Halides. The reaction of typical lithium diorganocuprates with alkyl halides (Table IV) differs in several important practical aspects from the reactions with aryl halides discussed previously. First, these coupling reactions usually proceed more rapidly and in higher yield than do the corresponding couplings to aryl moieties. Second, there is no evidence for important involvement of metal-halogen exchange in coupling reactions involving alkyl halides in ether solutions: in most of these reactions we have examined, the yields of coupled product obtained after either oxidation or hydrolysis of the reaction mixtures are very similar. Since the oxidation of lithium dialkylcuprates gives good yields of dimeric products,[19] this observation indicates that these reaction solutions did not contain significant concentrations of organometallic compounds corresponding to the starting organic halides, at the point at which the oxidant was added. Although this fact does not by itself exclude the products of metal-halogen exchange as transitory intermediates in the coupling reaction, the observed stereochemistry of the reaction of lithium diphenylcuprate with (−)-(*R*)-2-bromobutane (*vide infra*) renders this reaction course unlikely. Third, couplings involving alkyl halides are significantly improved by using a polar solvent such as tetrahydrofuran as the reaction medium.

Several specific points concerning the data in Table IV deserve brief comment. First, lithium dimethylcuprate (**1**) prepared from methyllithium and copper(I) iodide appears to have the same reactivity toward alkyl halides as does pure **1**. Since the difference between the reactivity of these reagents toward aryl halides seemed to be related to a difference in their activity in metal-halogen exchange, their similarity in a reaction system in which metal-halogen exchange apparently does not take place is not surprising. Second, it appears that it may be possible in certain coupling reactions to use a mixture of organolithium reagent and *catalytic* quantities of copper(I) ion in place of preformed dialkylcuprates to effect the coupling reaction, albeit at appreciable detriment to reaction rate and product yield. The reaction of threefold molar excess of **1** with *n*-octyl iodide to yield *n*-nonane takes place quantitatively in less than 3 hr. Reaction of a similar quantity of methyllithium with *n*-octyl iodide for 12 hr yields only 6% *n*-nonane. However, addition of 5 mol % copper iodide (based on *n*-octyl iodide) to the methyllithium results in a 64% yield of *n*-nonane in 12 hr. Third, lithium di-*n*-butylcuprate reacts with almost equal facility with *n*-pentyl iodide, bromide, chloride, and tosylate to yield *n*-nonane, *provided* that tetrahydrofuran is used as solvent. The use of diethyl ether as solvent results in lower yields of coupled products with *n*-pentyl bromide and chloride; the use of pentane as solvent appears to completely inhibit the direct coupling reaction. These observations are in qualitative accord with the proposition that the response of the coupling reactions to changes in solvent and leaving group are those expected for an S_N2 reaction. Fourth, although 2-bromobutane couples in high yield with lithium di*phenyl*cuprate, the yields of coupled products obtained on reaction of secondary alkyl halides with lithium di*alkyl*cuprates are much lower than those obtained with primary halides. The yields of coupled products obtained using *t*-alkyl halides are so low that the reaction appears to be of no practical utility. In contrast, lithium di-*sec*-alkyl- and di-*t*-alkyl(tri-*n*-butylphosphine)cuprates[20] give good yields of coupled products on reaction with primary alkyl halides. Thus, coupling of a primary with a *sec*-alkyl group is best accomplished either by reaction of a primary alkyl chloride with a "di-*sec*-alkylcuprate," or by reaction of a primarily alkyl bromide with a di-*sec*-alkyl(tri-*n*-butylphosphine)-

(25) G. M. Whitesides and C. P. Casey, *J. Amer. Chem. Soc.*, **88**, 4541 (1966).

Table IV. Reactions of Lithium Dialkyl- and Diarylcuprates with Alkyl Halides[a]

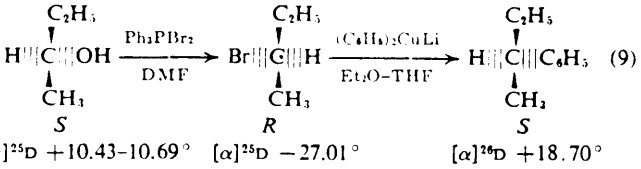
Copper reagent, R_2CuLi (concn, *M*)	Alkyl halide, R′X (concn, *M*)	LiX (concn, *M*)	Time, hr	Solvent	R–R′ yield, %[a] Hydrolysis	Oxidation[b]
$(CH_3)_2CuLi$ (0.5)[c]	n-$C_5H_{11}I$ (0.1)		0.25	Et_2O	18	18
			0.5		30	30
			3.5		98	98
$(CH_3)_2CuLi$ (0.5)[d]	n-$C_5H_{11}I$ (0.1)	LiI (0.5)	0.25		56	56
			0.5		75	75
			3.5		98	98
$(CH_3)_2CuLi$ (0.33)[d]	n-$C_8H_{17}I$ (0.11)	LiI (0.5)	2.7		97	
CH_3Li (0.66) + 5 mol % CuI[e]			12		64	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	n-$C_5H_{11}I$ (0.1)		1		68	72
			2		69	75
			26		70	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	n-$C_5H_{11}I$ (0.1)		1	THF	98	98
			2		98	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	n-$C_5H_{11}Br$ (0.1)		1	n-C_5H_{12}	<2	67
			2		<2	70
			26		<2	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	n-$C_5H_{11}Br$ (0.1)		1	Et_2O	68	72
			2		69	75
			26		70	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	n-$C_5H_{11}Br$ (0.1)		1	THF	98	98
			26		98	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	n-$C_5H_{11}Cl$ (0.1)		1	Et_2O	10	32
			2		9	32
			26		10	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	n-$C_5H_{11}Cl$ (0.1)		1	THF	80	86
			2		80	86
			26		81	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	n-$C_5H_{11}OTs$ (0.1)		1	THF	98	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	$C_3H_7CHBrCH_3$ (0.1)		1	THF	12	12
			2		12	12
			26		12	
$(n$-$C_4H_9)_2CuLi$ (0.4)[c]	$C_2H_5CBr(CH_3)_2$ (0.1)		1	THF	<10	<10
			2		<10	<10
$(n$-$C_4H_9)_2CuLi \cdot PBu_3$ (0.5)[f]	n-$C_5H_{11}I$ (0.1)	LiI (0.5)	1	THF–C_6H_{14}	91	91
$(n$-$C_4H_9)_2CuLi \cdot PBu_3$ (0.5)[f]	n-$C_5H_{11}Br$ (0.1)	(0.5)	1		93	93
$(sec$-$C_4H_9)_2CuLi \cdot PBu_3$ (0.5)[f]	n-$C_5H_{11}Br$ (0.1)	(0.5)	1		94	94
$(t$-$C_4H_9)_2CuLi \cdot PBu_3$ (0.5)[f]	n-$C_5H_{11}Br$ (0.1)	(0.5)	1	THF–C_5H_{12}	92	92
"$(n$-$C_4H_9)_2CuLi$" (0.5)[d]	n-$C_5H_{11}I$ (0.1)	(0.5)	1	Et_2O–C_6H_{14}	53	73
"$(n$-$C_4H_9)_2CuLi$" (0.5)[d]	n-$C_5H_{11}I$ (0.1)	(0.5)	1	THF–C_6H_{14}	39	55
"$(sec$-$C_4H_9)_2CuLi$" (0.5)[d]	n-$C_5H_{11}I$ (0.1)	(0.5)	1		7	7
"$(t$-$C_4H_9)_2CuLi$" (0.5)[d]	n-$C_5H_{11}I$ (0.1)	(0.5)	1	THF–C_5H_{12}	<1	<1
"$(n$-$C_4H_9)_2CuLi$" (0.5)[d]	n-$C_5H_{11}Cl$ (0.1)	(0.5)	1		79	80
"$(sec$-$C_4H_9)_2CuLi$" (0.5)[d]	n-$C_5H_{11}Cl$ (0.1)	(0.5)	1		64	60
			2		60	60
"$(t$-$C_4H_9)_2CuLi$" (0.5)[d]	n-$C_5H_{11}Cl$ (0.1)	(0.5)	1		<1	<1
$(n$-$C_4H_9)_2CuLi \cdot PBu_3$ (0.5)[f]	c-$C_6H_{11}Br$ (0.1)	(0.5)	1	THF–C_6H_{14}[g]	25	25
$(C_6H_5)_2CuLi$ (0.2)[d]	n-$C_8H_{17}I$ (0.1)	LiBr (0.2)	2	Et_2O	99	
$(C_6H_5)_2CuLi$ (0.39)[d]	$C_2H_5CHBrCH_3$ (0.12)	(0.39)	72	THF–Et_2O[g]	87	
$(C_6H_5)_2CuLi$ (0.3)[d]	c-$C_6H_{11}Br$ (0.1)	(0.3)	96	*g*	10	10
$(C_6H_5)_2CuLi$ (0.39)[d]	Adamantyl Br (0.12)	(0.39)	72	*g*	<1	
$(C_6H_5)_2CuLi$ (0.2)[d]	$(CH_3)_3CBr$ (0.1)	(0.2)	4	*g*	<1	
$(CH_2{=}CH)_2CuLi \cdot P(n$-$Bu)_3$ (0.5)[f]	n-$C_8H_{17}I$ (0.1)	LiI (0.5)	0.75		95	91
$(CH_2{=}CHCH_2)_2CuLi$ (0.3)[h]	n-$C_5H_{11}I$ (0.1)	(0.6)	0.75		98[i]	
$(C_6H_5C{\equiv}C)_3CuLi_2$ (0.3)[d]	n-$C_5H_{11}I$ (0.15)	(0.3)	3	Et_2O	<1	

[a] Yields are based on the organic halide. Reactions were carried out in ether at 25°, unless otherwise noted. [b] Oxidation with O_2 at −78°, unless otherwise noted. [c] Prepared by dissolving alkylcopper in alkyllithium solution (eq 7). [d] Prepared by reaction of alkyllithium reagent with copper(I) iodide or bromide (eq 6). The composition of these reagents is uncertain. [e] The amount of CuI added is based on quantity of n-$C_8H_{17}I$ present. [f] Prepared by reaction of alkyllithium reagent with $ICuPBu_3$ (eq 8). [g] Reaction temperature 52°. [h] Prepared by reaction of 2 equiv of allyllithium solution with 1 equiv of $[(n$-$C_4H_9)_2S]_2CuI$ (eq 8). [i] The same yield was obtained from reaction of $CH_2{=}CHCH_2Li$.

cuprate. Coupling of a primary with a *t*-alkyl group can be accomplished by reaction of a primary alkyl halide with a lithium di-*t*-alkyl(tri-*n*-butylphosphine)cuprate; this coupling fails using "di-*t*-alkylcuprate." Finally, although the coupling of lithium diallylcuprate and *n*-pentyl iodide was a rapid and high-yield reaction, comparable yields of 1-octene could be obtained by direct reaction between allyl*lithium* and *n*-pentyl iodide. Thus, in this particular case, formation of the copper ate complex offers no synthetic advantage.

The mild conditions and high yields associated with these coupling reactions afforded an opportunity to examine the stereochemistry of carbon–carbon bond formation during a coupling reaction. Optically active (+)-(*S*)-2-butanol (optical purity 77–79%) was prepared by oxidation of the hydroboration product from *cis*-2-butene and optically active diisopinocampheylborane.[26] This alcohol was converted to 2-bromo-

(26) (a) Prepared from diborane and (−)-α-pinene by the method of H. C. Brown, N. R. Ayyangar, and G. Zweifel, *J. Amer. Chem. Soc.*,

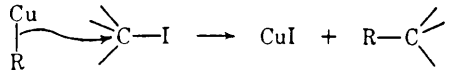


(9)

butane by treatment with triphenylphosphine and bromine in dimethylformamide. This procedure is a modification of a previously published method[27] which minimizes racemization by distilling the bromide from the reaction mixture as it is formed.[28] By analogy with the work of Schaefer[27] and related studies by Snyder[29] we assume this halogenation proceeds with inversion of configuration to produce bromide of the (−)-*R* configuration having $[\alpha]^{25}D$ −27.01° (neat), corresponding to an optical purity of 76 to 81%, depending on the value accepted for the rotation of optically pure 2-bromobutane.[30] Reaction of this bromide with lithium diphenylcuprate in refluxing ether–tetrahydrofuran yielded (+)-(*S*)-2-phenylbutane having $[\alpha]^{26-27}D$ +18.20 to +18.70° (neat),[31] corresponding to 67–68% optically pure material.[34] Thus the coupling of lithium diphenylcuprate with 2-bromobutane proceeds with predominant inversion of configuration. Comparison of the optical purities of the starting bromide and coupled product establishes that the reaction takes place with 84–92% stereoselectivity, depending on the value accepted for the optical rotation of the enantiomerically pure 2-bromobutane.

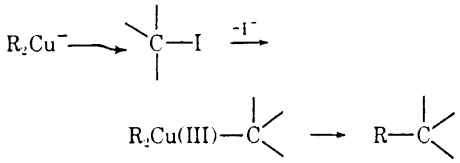
Discussion

The experimental data presented in this paper indicate that the reaction of lithium dialkylcuprates with alkyl halides proceeds without significant metal–halogen exchange, by a mechanism which requires, in at least one instance, predominant inversion of configuration at the carbon atom originally bonded to halogen. Further, the structure of the alkyl group bonded to the metal and to the halogen, the nature of the leaving group, and the polarity of the solvent all exert an influence on the course of the reaction which is consistent with a mechanism for carbon–carbon bond formation which involves an SN2 displacement at carbon. Unfortunately, the available data are not sufficiently detailed to permit a precise description of the bond-forming step. The reaction may involve simply displacement of halide ion at carbon by an alkyl group (eq 10), or some more complex pathway proceeding, for



(10)

example, by nucleophilic displacement with inversion of configuration on the alkyl halide by the *copper* atom (eq 11), followed by collapse of the resulting *formal*



(11)

copper(III)[35] organometallic compound with retention of configuration.[36] Until more information concerning both the state of aggregation and structure of the copper ate complexes and the influence of alkyl halide structure on the rate and stereochemistry of the coupling reaction are available, further speculation on detailed mechanism is pointless.

Reaction of lithium dialkylcuprates with *aryl* halides differs from reaction with alkyl halides, in that metal–halogen exchange is important. The role of this metal–halogen exchange in nonoxidative coupling of copper ate complexes with aryl halides is presently unclear. Initial generation of an arylcopper compound and an alkyl halide by metal–halogen exchange might be followed by nucleophilic displacement of halide ion from the alkyl halide by the arylmetallic reagent (eq 12). Al-

$$R_2CuLi + ArI \rightleftharpoons RI + ArRCuLi \longrightarrow RAr \qquad (12)$$

ternatively, the metal–halogen exchange might simply constitute a side reaction competing with direct coupling of the components (eq 13). Our data do not

$$RI + ArRCuLi \rightleftharpoons R_2CuLi + ArI \longrightarrow RAr \qquad (13)$$

permit an unambiguous distinction between these alternatives at present. However, the observation that di*aryl*cuprates are capable of nonoxidative coupling with aryl iodides establishes that a mechanism for carbon–carbon bond formation does exist which does not involve an SN2 displacement of the type implicated by eq 10 and 11.

From the point of view of potential application of copper "ate" complexes in carbon–carbon bond forming reactions, several practical features of this work are worth emphasizing. First, the most convenient preparation of the prerequisite ate complexes from a synthetic point of view is that involving reaction of 2 equiv of organolithium reagent with 1 equiv of the appropriate copper(I) halide. This preparation is applicable to aryl, vinyl, and primary alkyl reagents, its success with secondary reagents is marginal, and it fails with tertiary reagents. For coupling reactions requiring *t*-alkylcopper(I) reagents, lithium di-*t*-alkyl(tri-*n*-butylphosphine)copper(I) compounds are the

86, 397 (1964). (b) The absolute stereochemistry of 2-butanol has been established by relation to lactic acid. See K. Wiberg, *J. Amer. Chem. Soc.*, **74**, 3891 (1952), and references cited therein.

(27) (a) J. P. Schaefer and D. S. Weinburg, *J. Org. Chem.*, **30**, 2635 (1965); (b) G. A. Wiley, R. L. Hershowitz, B. M. Rein, and B. C. Chung, *J. Amer. Chem. Soc.*, **86**, 964 (1964).

(28) The procedure used here is similar to that developed in the unpublished work of F. R. Jensen and V. Krimsley, University of California at Berkeley.

(29) R. G. Weiss and E. I. Snyder, *Chem. Commun.*, 1358 (1968).

(30) (a) P. S. Skell, R. G. Allen, and G. Helmkamp, *J. Amer. Chem. Soc.*, **82**, 410 (1960), observed $[\alpha]^{25}D$ 32.09° for (+)-2-bromobutane and calculate that the maximum value should be 39.3°; (b) from the data of R. L. Letsinger, L. G. Maury, and R. L. Burwell, *ibid.*, **73**, 2373 (1951), a maximum value for $[\alpha]^{25}D$ of 34.3° may be calculated; (c) F. R. Jensen and D. D. Davis believe the maximum value is within the range 33.1–35.3°. See D. D. Davis, Ph.D. Dissertation, University of California at Berkeley, Aug 1966; (d) P. Salvadori, L. Lardicci, and M. Stagi, *Ricerca Sci.*, **37**, 990 (1967), show that Skell's value[30a] of 39.3° is too high. From their data a maximum value for $[\alpha]^{25}D$ of 35.7° may be calculated; (e) D. G. Goodwin and H. R. Hudson, *J. Chem. Soc., B*, 1333 (1968), observed $[\alpha]^{25}D$ −33.4° for (−)-2-bromobutane and calculated a maximum value of 34.8°. From these results it appears that the actual value lies between 33.4° and 35.7°.

(31) The absolute configuration of (+)-(*S*)-2-phenylbutane has been assigned by relation to 2-butanol,[32] and by relation to α-phenylethanol.[33]

(32) D. J. Cram, *J. Amer. Chem. Soc.*, **74**, 2149 (1952).

(33) D. J. Cram, *ibid.*, **74**, 2137 (1952).

(34) J. Kenyon, P. W. B. Harrison, and J. R. Sheppard, *J. Chem. Soc.*, 658, 661 (1926), reported $[\alpha]^{25}D$ −27.3° for (−)-2-phenylbutane.

(35) *Cf.* A. Levitzki and M. Anbar, *Chem. Commun.*, 403 (1968).

(36) Formally similar oxidative addition reactions have been observed for a wide variety of d^8–d^{10} transition metal complexes. Unfortunately the stereochemistry of these reactions is not presently known. *Cf.* J. P. Collman, *Accounts Chem. Res.*, **1**, 136 (1968); L. Vaska, *ibid.*, **1**, 335 (1968).

only practical choice, despite the problems frequently encountered during work-up procedures. Second, the high reactivity of methyllithium toward aryl iodides indicates that this material, rather than lithium dimethylcuprate, is probably the reagent of choice for methylation of aromatic halides. Third, the relative rates of coupling and metal–halogen exchange in the reaction of lithium dialkylcuprates other than methyl derivatives with aryl halides is such that the yield of unsymmetrical dimer obtainable by direct coupling reaction appears to be less than that obtainable from a combination of metal–halogen exchange followed by oxidative coupling. In certain cases it may prove advantageous to attempt to convert the arylcopper reagents formed during metal–halogen exchange to coupled products by addition of a large excess of alkyl halide to the solution.[37] Alternatively, formation of the lithium reagents of both of the organic groups to be coupled, followed by oxidative coupling of the approximately statistical mixture of "ate" complexes obtained when these reagents are mixed in solution with an appropriate copper salt, may provide a useful route to an unsymmetrical dimer, provided that this material is easily separated from the two symmetrical dimers necessarily formed at the same time.

Experimental Section[38]

Preparation of the Organometallic Reagents. All reactions involving organometallic reagents were carried out under an inert atmosphere of prepurified nitrogen. Ether and tetrahydrofuran were distilled from lithium aluminum hydride immediately before use, and were transferred under nitrogen using hypodermic syringes or stainless steel cannulas.

Solutions of methyllithium (prepared from methyl chloride) in ether, *n*-butyllithium in hexane, *sec*-butyllithium in hexane, and *t*-butyllithium in pentane, obtained from the Foote Mineral Corp., contained less than 0.01 equiv of lithium halide/equiv of alkyllithium reagent. Solutions of methyllithium (prepared from methyl bromide) in ether, obtained from Alfa Inorganics, Inc., were saturated with lithium bromide. Solutions of vinyllithium (THF solution) obtained from Alfa contained 5% lithium chloride by weight. Halide-free solutions of phenyllithium were obtained by the previously described[39] reaction of iodobenzene with *n*-butyllithium in a benzene–hexane mixture. The solid phenyllithium was collected, washed with hexane, and redissolved in ether. After the ether solution was cooled to −78°, the crystalline lithium reagent which separated was collected, redissolved in ether, filtered through a Celite pad, and stored under nitrogen. Ether solutions of phenyllithium containing lithium bromide were prepared from bromobenzene in the usual way. Ethereal solutions of the purified, halide-free phenyllithium were relatively stable when stored in the refrigerator. For example, an ether solution which was initially 3.05 *M* in phenyllithium was found to be 3.00 *M* after 2-months storage at 1–2°.

Analyses of lithium reagents were carried out using the Gilman double-titration procedure,[40] or by titration with a standard solution of 2-butanol in xylene with bipyridyl as an indicator.[41]

The bis(di-*n*-butyl sulfide) and the tri-*n*-butylphosphine complexes of copper(I) iodide were prepared as described previously.[15] Copper(I) iodide was purified using a literature procedure,[42] and an analogous procedure employing saturated aqueous potassium bromide was used to purify commercial copper(I) bromide.

Solutions of pure, halide-free lithium dimethylcuprate were obtained by dissolving a suspension of halide-free methylcopper in an ether solution containing slightly less than 1 equiv of halide-free methyllithium.[15] Halide-containing solutions of lithium dimethylcuprates were obtained either by adding a solution of lithium iodide or lithium bromide in ether to a solution of halide-free lithium dimethylcuprate, or by direct reaction of 2 equiv of methyllithium in ether with a suspension of 1 equiv of copper(I) iodide in diethyl ether at 0°. Solutions of lithium dialkylcuprates containing tri-*n*-butylphosphine (represented in this paper as $R_2CuLi \cdot PBu_3$) were prepared by adding 2 equiv (typically 8.10 mmol, 5.00 ml of 1.62 *N* solution) of methyllithium (as halide-free or halide-containing ether solution), vinyllithium, *n*-butyl-, *sec*-butyl-, or *t*-butyllithium to 1 equiv of tetrakisiodo(tri-*n*-butylphosphine)copper(I) (typically 3.18 g, 8.10 mmol, in 1.5 ml of THF or ether) at −78°. Reaction between the organolithium reagent and the copper(I) halide was essentially instantaneous under these conditions. The resulting solutions ranged in color from colorless to pale pink or yellow, and were stable indefinitely at −78°. The thermal stability of these mixtures varied considerably: lithium di-*t*-butyl(tri-*n*-butylphosphine)cuprate was the least stable, its decomposition being essentially complete after 20 min at 0°; the analogous methyl ate complex showed the greatest stability, displaying little evidence of thermal decomposition after 1.5 hr at the same temperature.

Slightly cloudy solutions of lithium diphenylcuprate ranging in concentration from 0.16 to 0.50 *M* were prepared by adding 2 equiv of ethereal phenyllithium to a cold (0°) suspension of purified copper(I) bromide. These solutions ranged in color from pale yellow to a pale greenish yellow with the least color and turbidity being observed when the solutions were prepared from purified phenyllithium. We were consistently unable to prepare these solution by the addition of ethereal phenyllithium solutions to cold (0 to −78°) suspensions of purified copper(I) iodide. In all cases a black suspension resulted rather than the solutions obtained with copper(I) bromide.[43] Solutions of lithium diphenylcuprate could also be obtained by the addition of 2 equiv of ethereal phenyllithium to an ethereal solution of bis(di-*n*-butyl sulfide)copper(I) iodide. These observations suggest that the decomposition observed during attempts to prepare phenylcopper derivatives from suspensions of copper(I) iodide should be attributed to impurities in the iodide which were not removed by the purification process[42] we employed.

Purified solutions of lithium diphenylcuprate were prepared by the general procedure described previously[15] in which the ether-insoluble phenylcopper was collected and washed with cold (0°) ether under an inert atmosphere. Although the methylcopper reagent prepared by an analogous procedure[15] was essentially free of halide containing impurities, the corresponding phenylcopper reagent contained 10–20 mol % of halide salts. The washed phenylcopper was redissolved in an ethereal solution of halide-free phenyllithium.

Allylcopper(I) and lithium diallylcuprate were prepared from allyllithium. Following a previously described procedure,[44] 1.955 g (6.90 mmol) of tetraallyltin was allowed to react with 27.3 mmol of phenyllithium in 29 ml of ether for 1 hr. After centrifugation to remove the tetraphenyltin, the supernatant ether solution was separated and found to be 0.974 *M* in allyllithium. The addition of 1 equiv of an ethereal solution of allyllithium to a cold (−78°) ethereal solution containing 1 equiv of the bis(di-*n*-butyl sulfide) complex of copper(I) iodide produced a bright red precipitate of allylcopper. Addition of a second equivalent of allyllithium converted the mixture to a pale yellow solution of diallylcuprate.

"Lithium di-*n*-butylcuprate" was prepared by reaction of *n*-butyllithium with copper(I) iodide using the following proce-

(37) The usefulness of this technique has been demonstrated by Corey and coworkers.[17,18]

(38) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer, Model 237, grating spectrophotometer. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The nmr spectra were determined at 60 MHz with a Varian Model A-60 spectrometer. The chemical-shift values are expressed either in hertz or δ (ppm) relative to a tetramethylsilane internal standard. The mass spectra were obtained with a CEC Model 21-130 or a Hitachi (Perkin-Elmer) mass spectrometer. Analytical glpc analyses were performed on F & M Model 810 flame ionization and Model 720 thermal conductivity instruments. Absolute yields of products were calculated from peak areas using internal standard techniques, with response factors obtained with authentic samples.

(39) M. Schlosser and V. Ladenberger, *J. Organometal. Chem.*, **8**, 193 (1967).

(40) H. Gilman, F. K. Cartledge, and S. Y. Sim, *ibid.*, **1**, 8 (1963).

(41) S. C. Watson and J. F. Eastham, *ibid.*, **9**, 165 (1967).

(42) G. B. Kauffman and L. A. Teter, *Inorg. Syn.*, **7**, 9 (1963).

(43) This decomposition may result from the presence of traces of other transition metals in the copper(I) iodide.[23a]

(44) D. Seyferth and M. A. Weiner, *J. Org. Chem.*, **26**, 4797 (1961).

dure. Copper(I) iodide (0.677 g, 3.54 mmol) was placed in a 40-ml centrifuge tube. The tube was capped with a serum stopper, and flamed dry under a stream of nitrogen. Ether (20 ml) was added to the tube, and the resulting suspension was cooled to −50°. At this temperature 4.0 ml (7.08 mmol) of halide-free *n*-butyllithium solution was added. The tube was shaken vigorously for 5 min while holding the temperature between −50 and −20°. Centrifugation at −78° separated the resulting suspension into a small quantity of black solid and a red solution. This solution was transferred to another centrifuge tube and hydrolyzed. Analysis[45] indicated that the hydrolyzed mixture contained butane and copper in the ratio 1.89:1.00. Oxidation of the organometallic solution before hydrolysis using molecular oxygen produced *n*-octane (40%) and *n*-butyl alcohol (25%), calculated on the basis of initial *n*-butyllithium. Similar treatment of *n*-butyllithium produced *n*-butyl alcohol exclusively; pure lithium di-*n*-butylcuprate(I) yields 80% *n*-octane and 5% *n*-butyl alcohol on oxidation.[19]

The exact nature of the mixtures produced by the reaction of *n*-butyllithium with copper(I) iodide in ether remains unclear. However, both the approximate analyses outlined above and the chemical reactivity of the mixtures indicate that they can be considered as mixtures of *n*-butyllithium and lithium di-*n*-butylcuprate.

Preparations of "lithium di-*sec*-butylcuprate" and "lithium di-*t*-butylcuprate" by direct reaction of 2 equiv of alkyllithium reagent with 1 equiv of copper iodide followed an analogous procedure.

Solutions of dilithium tris(phenylethynyl)cuprate were prepared by permitting 18.2 mmol of phenylethynyllithium (obtained by mixing 1.85 g (18.2 mmol) of phenylacetylene and 10.7 ml (18.2 mmol) of methyllithium in 20 ml of ether) to react with 1.15 g (6.06 mmol) of copper(I) iodide at 25° to yield a pale yellow homogeneous solution. If only 2 equiv of phenylethynyllithium was used/equiv of copper iodide, a heterogeneous yellow suspension was formed. Addition of one further equivalent of phenylethynyllithium to this suspension resulted in immediate formation of a pale yellow solution.

Preparation of the Halides and the Hydrocarbon Products. Commercial samples of *trans*-stilbene, 1-phenylnaphthalene, nonane, *n*-hexane, toluene, *n*-butylbenzene, *sec*-butylbenzene, 1-octene, 2,2-dimethylheptane, 3-methyloctane, *t*-butylbenzene, phenylcyclohexane, 1-methylnaphthalene, and *n*-octylbenzene were used for identification and glpc calibration. 1-Iodooctane (Eastman White Label), iodobenzene, and 1-iodopentane were used without further purification. Commercial 1-iodonaphthalene was redistilled before use; bp 151–152° (10 mm), n^{24}D 1.7010 [lit.[46] bp 161–162° (15 mm), n^{14}D 1.7054]. Crude *trans*-β-bromostyrene [*ca.* 10% *cis* (first eluted) and 90% *trans* (eluted second),[47] Eastman Organic Chemicals] was purified by treatment with NaOH in isopropyl alcohol as previously described;[44] bp 59–61.5° (1.5 mm), n^{25}D 1.6060 [lit.[48] bp 45–50° (1.75 mm), n^{25}D 1.6048]; ir (liquid film), 940 cm^{-1} (*trans* CH=CH); nmr (CCl_4) δ 7.19 (5 H aryl CH) and an AB pattern, J = 14 Hz and estimated chemical shifts 6.60 and 7.00 (2 H, vinyl CH). *cis*-β-Bromostyrene was prepared from *trans*-cinnamic acid dibromide as previously described;[49] bp 39–40° (0.5 mm), n^{25}D 1.5984 [lit. bp 55–56° (2 mm),[49] 55–58° (2 mm),[48] n^{25}D 1.5980[48,49]]; nmr (CCl_4) δ 7.1–7.7 (5 H multiplet, aryl CH), 6.87 (1 H doublet, J = 8 Hz, vinyl CH), and 6.23 (1 H doublet, J = 8 Hz, vinyl CH). Previously described procedures were used to prepare *cis*-stilbene,[50a] 1,8-diphenylnaphthalene,[50b] and 1,8-diiodonaphthalene, mp 107–109° (lit.[51] mp 109°).[52]

(−)-α-Pinene, $[\alpha]^{25}$D −47.5° (neat),[53] was converted to the dialkylborane and then allowed to react with *cis*-2-butene in diglyme solution as previously described.[26a] After oxidation of the resulting trialkylborane, the fraction containing 2-butanol, bp 60–120°, was separated, dried by distillation from calcium hydride, and then fractionally distilled in a spinning-band column. The purified (+)-(*S*)-2-butanol was obtained in 55% yield; bp 99–100° (760 mm), n^{25}D 1.3958, d^{25}_4 0.800, $[\alpha]^{25}$D +10.69° (neat) (optical purity, 79%).[54] In a second run where the purification scheme did not include a distillation from calcium hydride, the 2-butanol was obtained in 48% yield; 98–99° (760 mm), n^{25}D 1.3963, d^{25}_4 0.799, $[\alpha]^{25}$D +10.43° (neat) (optical purity, 77%)[54] [lit.[55] bp 99.5°, n^{25}D 1.3950]. In both runs the final product exhibited a single peak on glpc.[47]

The conversion of (+)-(*S*)-2-butanol to (−)-(*R*)-2-bromobutane was effected by an adaptation[28] of a general procedure described previously.[27] To a solution (10–15°) of 15.0 g (0.202 mol) of (+)-(*S*)-2-butanol ($[\alpha]^{25}$D +10.69°, optical purity 79%) and 56.8 g (0.218 mol) of triphenylphosphine in 250 ml of dimethylformamide was added, dropwise and with stirring, sufficient bromine so that the reaction mixture maintained a yellow-orange color. The reaction mixture was slowly warmed to 45° while volatile materials were allowed to distil from the reaction mixture under reduced pressure (0.5 mm) into a cold trap. The crude distillate was partitioned between pentane and water and the organic layer was washed with aqueous $NaHCO_3$, dried, and concentrated. Distillation of the residual liquid in a Teflon spinning-band column afforded 14.1 g (51%) of (−)-(*R*)-2-bromobutane, bp 90° (760 mm), n^{25}D 1.4341, d^{25}_4 1.236, $[\alpha]^{27}$D −26.02° (neat) (optical purity 73 to 78% for maximum rotations of 35.7 and 33.4°, respectively).[30] In a second reaction, (+)-(*S*)-2-butanol ($[\alpha]^{25}$D +10.43°, 77% optically pure) was converted in 63% yield to (−)-(*R*)-2-bromobutane, bp 90–91° (760 mm), n^{24}D 1.4354, d^{25}_4 1.246, $[\alpha]^{25}$D −27.10° (neat) (optical purity 76 to 81% for maximum rotations of 35.7 and 33.4°, respectively)[30] [lit. bp 91.2°,[56a] 90–91.5°,[56b] n^{25}D 1.4350[56b]]. In each case our product exhibited a single peak on glpc analysis.[47] Our experiments suggest that the minimum value for the rotation of (−)-(*R*)-2-bromobutane should be −33.0 to −35.1°.

Reaction of methyllithium with iodobenzene was carried out by adding ~1.62 mmol of methyllithium by syringe to 1.62 mmol of iodobenzene dissolved in 3.5 ml of ether at 25°. The reactions were allowed to stand for 15–30 min, hydrolyzed, and analyzed by glpc.

Reaction of Lithium Dimethylcuprate with Iodobenzene. (Typical Procedure). Iodobenzene (0.204 g, 1 mmol) and a weighed quantity of an internal standard (*n*-octane) were placed in a 15-ml centrifuge tube capped with a serum stopper. The tube was flushed with nitrogen and its contents diluted with ether, then transferred to a 40-ml centrifuge tube containing 5 ml (5.0 mmol) of lithium dimethylcuprate solution at −78°. The tube was allowed to warm to room temperature. Aliquots (~0.5 ml) were removed periodically, and either hydrolyzed by addition of 0.10 ml of water or diluted by *ca.* a factor of 5,[57] oxidized by exposure to oxygen at −78°, and analyzed by glpc. A collected sample of toluene was identified by comparison of ir spectrum and glpc retention times with an authentic sample.

Control experiments indicated that the source of the lithium halides present in these reaction mixtures was not important: reactions containing lithium halide prepared from 1,2-dihaloethane and added to the preformed lithium dimethylcuprate solutions produced the same yields of toluene as did reactions containing lithium halide originally present in the methyllithium solution.

Preparation of "Mixed" Ate Complexes. Unsymmetrical Oxidative Coupling. Copper(I) bromide (1.426 g, 10.0 mmol) was placed in a 40-ml centrifuge tube. The tube was capped with a serum stopper and gently flamed dry under a stream of nitrogen. THF (5 ml) and an ether solution of phenyllithium (9.0 ml, 18 mmol) were added to the tube at 25°. This mixture was shaken vigorously for 5 min. It was then cooled to −78° and 1.25 ml (2.0 mmol) of a

(45) Glpc analyses of *n*-butane were accomplished on a column composed of 3% Apiezon L on alumina. EDTA was employed for copper analysis; *cf.* C. W. Elwell and I. Scholes, "Analysis of Copper and Its Alloys," Pergamon Press, Ltd., London, 1967.

(46) F. Krollpfeiffer, *Ann. Chem.*, **430**, 161 (1923).

(47) A glpc column packed with a nitrile silicone gum, XE-60, suspended on Chromosorb P was employed for this analysis.

(48) L. J. Dolby, C. Wilkins, and T. G. Frey, *J. Org. Chem.*, **31**, 1110 (1966).

(49) S. J. Cristol and W. P. Norris, *J. Amer. Chem. Soc.*, **75**, 2645 (1953).

(50) (a) L. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1955, p 186; (b) H. O. House, R. W. Magin, and H. W. Thompson, *J. Org. Chem.*, **28**, 2403 (1963); (b) H. O. House and R. W. Bashe, II, *ibid.*, **30**, 3942 (1965); **32**, 784 (1967).

(51) R. Scholl, C. Seer, and R. Weitzenbock, *Ber.*, **43**, 2202 (1910).

(52) This experiment was performed in our laboratories by Robert W. Bashe, Ph.D. Dissertation, Aug 1966, Massachusetts Institute of Technology.

(53) The rotation reported for pure (−)-α-pinene is $[\alpha]^{20}$D −51.28° (neat): F. H. Thurber and R. C. Thielke, *J. Amer. Chem. Soc.*, **53**, 1030 (1931). Therefore, the rotation of our sample indicated an optical purity of 93%.

(54) P. J. Leroux and H. J. Lucas [*J. Amer. Chem. Soc.*, **73**, 41 (1951)] report $[\alpha]^{25}$D −13.5° for (−)-2-butanol.

(55) R. F. Brunel, J. L. Crenshaw, and E. Tobin, *ibid.*, **43**, 574 (1921).

(56) (a) J. Timmerman and Y. Delcourt, *J. Chim. Phys.*, **31**, 96 (1934); (b) N. J. Leonard and E. W. Nommensen, *J. Amer. Chem. Soc.*, **71**, 2808 (1949).

(57) The yield of coupled product obtained on oxidation of dialkyl- or arylalkylcuprates decreases on increasing the concentration of the organocopper(I) reagent to values greater than *ca.* 0.1 *M*.

pentane solution of *t*-butyllithium was added. The resulting mixture was shaken thoroughly, for 10 sec, then oxidized by addition of 60 ml of molecular oxygen by syringe at −78°. Hydrolysis and glpc analysis indicated the presence of *t*-butylbenzene (73%, based on *t*-butyllithium).

Coupling Reactions of Lithium Diphenylcuprate with Alkyl and Vinyl Halides. A. *trans*-β-Bromostyrene. To 20.7 ml of a cold (0°) ether solution of lithium diphenylcuprate, prepared from 728 mg (5.0 mmol) of copper(I) bromide and 10.0 mmol of phenyllithium, was added 4 ml of an ether solution containing 1.01 mmol of *trans*-β-bromostyrene and a known weight of hexamethylbenzene (an internal standard). The resulting mixture, from which a yellow-green precipitate slowly separated, was stirred at room temperature under a nitrogen atmosphere. An aliquot removed after 2 hr was quenched in saturated aqueous NH_4Cl (adjusted to pH 9 with added NH_3) and then extracted with benzene. After the benzene solution had been washed with aqueous NaCl, it was dried, concentrated, and analyzed by glpc.[58] The calculated yields were 75% of *trans*-stilbene and 19% of unchanged starting bromide. After a total reaction period of 4 hr, the remaining reaction mixture was quenched, worked up, and analyzed.[58] The components detected (in order of elution)[58] were: starting bromide (4% recovery), biphenyl, hexamethylbenzene (internal standard), and *trans*-stilbene (90% yield). Comparable results (5% bromo olefin and 90% *trans*-stilbene) were obtained in a second reaction. In each case the yield of *cis*-stilbene (eluted before the *trans* isomer) was less than 2%. A collected[58] sample of the *trans*-stilbene was identified with an authentic sample by comparison of infrared spectra and glpc retention times.

B. *cis*-β-Bromostyrene. The corresponding reaction of 5.00 mmol of lithium diphenylcuprate and 1.02 mmol of *cis*-β-bromostyrene in 24.5 ml of ether was run for 2 hr at room temperature. The crude product contained (in order of elution:[58] biphenyl, hexamethylbenzene, and *cis*-stilbene (calculated yields 72 and 73% in two reactions). In each case, the yield of *trans*-stilbene was less than 1%. A collected[58] sample of the *cis*-stilbene was identified with an authentic sample by comparison of infrared spectra and glpc retention times.

C. Iodooctane. The reaction of 5.00 mmol of lithium diphenylcuprate with 1.01 mmol of 1-iodooctane in 24.7 ml of ether containing a weighed amount of 1-methylnaphthalene (an internal standard) was run at room temperature for 2 hr. The crude neutral product contained (listed in order of elution):[58] 1-methylnaphthalene, biphenyl, and *n*-octylbenzene (calculated yields 99 and 100% in two reactions). A collected[58] sample of the *n*-octylbenzene was identified with an authentic sample by comparison of infrared spectra and glpc retention times.

D. (−)-(*R*)-2-Bromobutane. A mixture of 120 mmol of lithium diphenylcuprate and 5.00 g (36.5 mmol) of (−)-(*R*)-2-bromobutane ($[\alpha]^{25}D$ −26.02°, optical purity 73–78%) in a mixture of 129 ml of ether and 180 ml of tetrahydrofuran was refluxed (51–52°) for 72 hr and then quenched in aqueous NH_4Cl and extracted with ether. After the ethereal solution had been washed with aqueous NaCl, dried, and concentrated, distillation of the residual liquid through a Teflon spinning-band column separated 4.33 g (87%) of (+)-(*S*)-2-phenylbutane, bp 170°, $n^{25}D$ 1.4879, d^{25}_4 0.856, $[\alpha]^{27}D$ +18.20° (neat) (optical purity 67%).[59] In a second run employing (−)-(*R*)-2-bromobutane ($[\alpha]^{25}D$ −27.01°, optical purity 76–81%) the (+)-(*S*)-2-phenylbutane was obtained in 67% yield; bp 169–170°, $n^{25}D$ 1.4877, d^{25}_4 0.855, $[\alpha]^{26}D$ +18.70° (neat) (optical purity 68%)[23] (lit.[59] bp 172°, $n^{25}D$ 1.4883). In each case the distilled product exhibited a single peak on glpc.[47] Preliminary experiments studying the reaction of lithium diphenylcuprate with racemic 2-bromobutane were performed with an internal standard (*n*-butylbenzene) present to permit glpc analysis.[47] The following calculated yields of 2-phenylbutane were obtained after a 24-hr reaction period under the specific conditions: 9% in ether at 25°; 54% in ether–1,2-dimethoxyethane (3:4 v/v) at 60–64; 72% in ether–tetrahydrofuran (3:4 v/v) at 52–54°. Under the same conditions reaction of 2-bromobutane with phenyllithium in boiling ether for 24 hr formed 2-phenylbutane in 4% yield. When the time for the reaction with lithium diphenylcuprate in the ether–tetrahydrofuran mixture was extended to 72 hr, the calculated yield of 2-phenylbutane was 84%.

E. 1-Bromoadamantane. To a solution of 4.50 mmol of diphenylcuprate in a mixture of 6.8 ml of tetrahydrofuran and 5.0 ml of ether was added a solution of 322 mg (1.50 mmol) of 1-bromoadamantane in 1.0 ml of tetrahydrofuran. After the resulting solution had been refluxed for 75 hr with no visible evidence of reaction, the solution was hydrolyzed and worked up in the usual way. The crude liquid product contained[58] the starting bromide (retention time 23.4 min) and a number of minor lower boiling components; no peak corresponding to 1-phenyladamantane (retention time 34.4 min) was detected. An authentic sample of 1-phenyladamantane, mp 86–87° (lit.[59a] mp 88–89°), was prepared as previously described.[59a] The spectral properties of the product correspond to those previously described.[59b,c]

Reaction of Lithium Dimethylcuprate with 1-Iodooctane. Ether solutions (6.0 ml) containing 2.00 mmol of iodooctane, a weighed amount of *n*-decane (internal standard), and the various organometallic reagents specified below were stirred at room temperature and aliquots were periodically removed, hydrolyzed, and analyzed.[47,58] In the reaction with 2.00 mmol of lithium dimethylcuprate, after 2.67 hr the calculated yield of *n*-nonane was 97% and only 3% of the *n*-octyl iodide remained. In a similar reaction where 4.00 mmol of methyllithium was treated with only 0.10 mmol (5 mol %) of copper(I) iodide, the calculated yields after a 12-hr reaction period were 19% *n*-octane, 6.5% 1-octene, 64% *n*-nonane, and 2% of the starting iodide. When 4.00 mmol of methyllithium was used with no added copper salt the yields after a 12-hr reaction were 27% *n*-octane, 18% 1-octene, 6% *n*-nonane, and 42% of the unchanged iodooctane. Collected samples of *n*-nonane, *n*-octane, and 1-octene were identified with authentic samples by comparison of infrared spectra and glpc retention times. Two glpc columns were required for analysis. On one column[58] the order of elution was *n*-octane and 1-octene (unresolved), nonane, decane, and 1-iodooctane. A second column[47] was used to resolve *n*-octane (eluted first) from 1-octene (eluted second).

Reaction of Lithium Dimethylcuprate with 1-Iodonaphthalene. Ethereal solutions containing hexamethylbenzene (internal standard) and the molar concentrations of 1-iodonaphthalene and lithium dimethylcuprate indicated in Table II were stirred at room temperature (25–27°) and aliquots were removed at the indicated times and hydrolyzed and analyzed in the usual way. With the glpc column used,[58] the components were eluted in the order naphthalene, 1-methylnaphthalene, hexamethylbenzene, and 1-iodonaphthalene. Collected[58] samples of naphthalene and its 1-methyl derivative were identified with authentic samples by comparison of infrared spectra and glpc retention times. In certain cases halide-free lithium dimethylcuprate was employed; in others the reaction solution contained LiI in a concentration equivalent to the copper reagent. The presence of LiI is indicated in Table II. In certain of the runs an oxidant was added to one aliquot of the reaction mixture at the end of the stated reaction period before the reaction mixture was hydrolyzed and analyzed. Nitrobenzene was added to the reaction solution or a known volume of oxygen was added to the nitrogen atmosphere above the reaction mixture and the mixture was thoroughly mixed by shaking. Addition of oxygen results in immediate formation of a black precipitate; addition of nitrobenzene produces a deep red color in solution.

In reactions of 1-iodonaphthalene with the tri-*n*-butylphosphine complex of methylcopper, the initial reaction mixtures were hydrolyzed with aqueous 2.4 *M* HCl rather than the aqueous NH_4Cl to facilitate separation of the tri-*n*-butylphosphine. In certain of these reactions with the phosphine complex, the initial ether solution was concentrated under reduced pressure and the residue was either dissolved in refluxing tetrahydrofuran or heated to 60–70° without added solvent, for 1–2 hr prior to analysis.[58,60,61] The calculated[60] yields of products were 15–33% naphthalene and 60–85% 1-methylnaphthalene. Although no oxidant was deliberately added to these latter reaction mixtures, the possibility that some oxygen (from the air) may have reached the reaction mixtures can not be excluded, in spite of our efforts to maintain an oxygen-free atmosphere.

As a control experiment, an ether solution of naphthalene (2.96 mmol) and the tri-*n*-butylphosphine complex of methylcopper (10

(58) A glpc column packed with silicone gum, SE-52, suspended on Chromosorb P was employed for this analysis.

(59) (a) H. Stetter, M. Schwartz, and A. Herschhorn, *Chem. Ber.*, **92**, 1629 (1959); (b) R. C. Fort, Jr., and P. von R. Schleyer, *J. Org. Chem.*, **30**, 789 (1965); (c) Z. Dolejšek, S. Hala, V. Hanus, and S. Landa, *Collect. Czech. Chem. Commun.*, **31**, 435 (1966).

(60) A glpc column packed with Carbowax 20M suspended on Chromosorb P was employed for this analysis.

(61) Analyses done with a Carbowax column[60] used biphenyl as an internal standard. On this column the order of elution was: naphthalene, 1-methylnaphthalene, biphenyl, and 1-iodonaphthalene.

mmol) was concentrated and then heated to 50–60° for 2 hr. After hydrolysis, no 1-methylnaphthalene was detected[60] in the crude reaction product. Also an ethereal solution containing hexamethylbenzene, 3.00 mmol of halide-free methyllithium, and 1.00 mmol of 1-iodonaphthalene was stirred for 2 hr at room temperature and then hydrolyzed and analyzed.[58] The calculated yields were 12% naphthalene and 86% 1-methylnaphthalene.

Reaction of Lithium Diphenylcuprate with Aryl Halides. A. 1-Iodonaphthalene. Ether solutions containing 1,2-diphenylethane (an internal standard) and the molar concentrations of lithium diphenylcuprate and 1-iodonaphthalene indicated in Table III were stirred at room temperature (25–27°). At the times indicated (Table III) aliquots were removed, hydrolyzed, and analyzed in the usual way. On the glpc columns used,[58,62] the order of elution of components was: iodobenzene, naphthalene, biphenyl, 1,2-diphenylethane, 1-iodonaphthalene, 1-phenylnaphthalene, and 1,1′-binaphthyl. Collected[58] samples of naphthalene and 1-phenylnaphthalene were identified with authentic samples by comparison of infrared spectra and gas chromatographic retention times. All of the data presented in Table III were obtained with lithium diphenylcuprate which contained some lithium halide. When the cuprate reagent was prepared from washed phenylcopper precipitate and recrystallized phenyllithium so that only 0.1–0.2 equiv of halide salts was present, the initial exchange reaction between the cuprate and 1-iodonaphthalene was slightly slower than the corresponding reaction where excess lithium bromide was present. Certain reaction aliquots were treated with various oxidants prior to hydrolysis and analysis. With the solid and liquid oxidants, the reaction mixtures were stirred for 15 min after addition to ensure complete oxidation. For reaction with oxygen gas, the solutions were stirred while a large excess of gas was passed over the surface of the solution.

As a control experiment, 11.7 ml of an ethereal solution containing 2.50 mmol of phenyllithium and 0.50 mmol of 1-iodonaphthalene was stirred at room temperature, and aliquots were removed, hydrolyzed, and analyzed[58] periodically. Although 96% of the 1-iodonaphthalene had been converted to 1-naphthyllithium (naphthalene after hydrolysis) after 1 hr, no 1-phenylnaphthalene was detected in the reaction mixture even after a 24-hr reaction period.

An ethereal solution prepared from 1.0 mmol of the tri-*n*-butylphosphine complex of copper(I) iodide, 1.0 mmol of phenyllithium, 0.43 mmol of 1-iodonaphthalene, and an internal standard was concentrated under a nitrogen atmosphere and then heated to 90–95° for 2 hr. The resulting mixture was treated with 2.0 ml of deuterium oxide solution containing DCl (20% by weight) and then subjected to the usual isolation and analysis.[58] The calculated yields were: 5% iodobenzene, 24% naphthalene, 52% 1-phenylnaphthalene, and 6% 1,1′-binaphthyl. A collected[58] sample of the naphthalene contained (mass spectrometric analysis) 83% d_1 species and 17% d_0 species. Various attempts to improve the yield of 1-phenylnaphthalene without use of an oxidant such as the use of quinoline as a solvent or the use of no solvent gave crude product mixtures in which the calculated[58] yield of 1-phenylnaphthalene ranged from 0 to 50%.

B. 1,8-Diiodonaphthalene. A solution of 1,2-diphenylethane, 6.0 mmol of lithium diphenylcuprate, and 380 mg (1.00 mmol) of 1,8-diiodonaphthalene in 10 ml of ether was refluxed for 24 hr and then two aliquots were removed. One aliquot was hydrolyzed without addition of an oxidant to give a mixture containing (in order of elution):[58] naphthalene (35% yield), 1,2-diphenylethane, 1-phenylnaphthalene (56% yield), and 1,8-diphenylnaphthalene (5% yield). The second aliquot was cooled to 0°, oxidized with gaseous oxygen, and then hydrolyzed to produce a mixture containing: 1,2-diphenylethane, 1-phenylnaphthalene (2% yield), and 1,8-diphenylnaphthalene (47% yield). Collected[58] samples of naphthalene, 1-phenylnaphthalene, and 1,8-diphenylnaphthalene were identified with authentic samples by comparison of infrared spectra and gas chromatographic retention times. Preliminary experiments had demonstrated that a 24-hr reaction period preceding oxidation was necessary in this case to complete the initial metal–halogen exchange.

Reaction of Lithium Dialkyl- and Diarylcuprates with Alkyl Halides. The data of Table IV were obtained using a common procedure, illustrated here by the coupling of lithium di-*n*-butylcuprate with 1-chloropentane. One milliliter of a THF solution containing 1.0 mmol of 1-chloropentane was added in one portion to a solution of 5.0 mmol of lithium di-*n*-butylcuprate in 5 ml of THF at −78°. This mixture was allowed to stand for 1 hr at 25° with occasional swirling, then cautiously hydrolyzed and analyzed by glpc directly.

Preparative Scale Reaction of Lithium Di-*n*-butyl(tri-*n*-butylphosphine)cuprate with 1-Iodopentane. Tetrakis[iodo(tri-*n*-butylphosphine)copper(I)] (76.6 g, 0.195 mol) was placed in a flame-dried, three-necked, 1-l. flask equipped with a nitrogen inlet and mechanical stirrer. Ether (500 ml) was added after the flask had been evacuated and filled with nitrogen several times. The resulting solution was cooled to −78° and 220 ml (0.39 mol) of *n*-butyllithium in hexane was added with stirring over a 20-min period. 1-Iodopentane (10.0 g, 0.0391 mol) mixed with 10 ml of ether was transferred by cannula into the reaction mixture and stirring continued for 30 min at −78°. The mixture was allowed to warm to room temperature and stirred for 6 hr, then cooled to −20° and cautiously hydrolyzed with 100 ml of 5 *M* hydrochloric acid. The two layers were separated, and the aqueous layer was washed with two 100-ml portions of pentane. The combined organic phase was treated with decolorizing charcoal, filtered through Celite, and dried. Short-path distillation (bp 145–160°) yielded 5.10 g of crude product which glpc analysis indicated to be 80–82% *n*-nonane (theoretical yield 5.00 g). The impurities in this material appeared to be produced by thermal decomposition of tri-*n*-butylphosphine-copper(I) complexes in the distillation pot. A fraction (bp 154–154.5°) taken during redistillation through a gold spinning-band column had $n^{25}D$ 1.4070 and an ir spectrum and glpc retention time identical with those of authentic *n*-nonane.

Reaction of Allyl Organometallic Derivatives with 1-Iodopentane. To a cold (−78°) solution of lithium diallylcuprate prepared from 1.45 g (3.00 mmol) of the bis(*n*-butyl sulfide) complex of copper(I) iodide and 6.00 mmol of allyllithium in 10.2 ml of ether was added 1.0 ml of an ether solution containing 1.00 mmol of 1-iodopentane and a known weight of *n*-nonane (an internal standard). After the mixture had been stirred for 1 hr at −78° it was allowed to warm to 0° (the copper reagent decomposed with separation of metallic copper) and then quenched in an aqueous solution of NH_4Cl and NH_3 and extracted with ether. After the ethereal solution had been washed with water, dried, and concentrated, analysis by glpc[61] indicated the presence of 1-octene (yields in two runs 98 and 100%, first eluted) and *n*-nonane (eluted second). A collected[61] sample of the 1-octene was identified with an authentic sample by comparison of infrared spectra and glpc retention times. A comparable reaction was run with 3.00 mmol of allyllithium and 1.00 mmol of 1-iodopentane in 9.0 ml of ether at 25° for 1 hr. After the mixtures from two identical runs had been hydrolyzed, dried, and concentrated, analysis[61] indicated the presence of 1-octene (yields 98 and 99%).

(62) A glpc column packed with silicone gum, No. SE-30, suspended on Chromosorb P was employed for this analysis.