Regiocontrol in Copper-Catalyzed Cross Coupling of Allylic Chlorides with Aryl Grignard Reagents

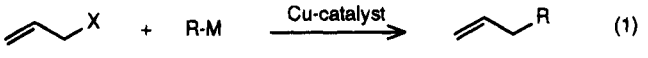
Jan-E. Bäckvall,* Eva S. M. Persson, and Agnes Bombrun

Department of Organic Chemistry, University of Uppsala, Box 531, S-751 21 Uppsala, Sweden

Received February 7, 1994®

The regioselectivity of copper-catalyzed reactions of allylic chlorides with aryl Grignard reagents was studied by variation of addition time of Grignard reagent, temperature, and amount of catalyst. It was found that slow addition of the Grignard reagent, increased temperature, and increased amount of catalyst favors formation of γ-product. Investigation of preformed organocopper species "$Ar_2CuMgBr$" and "ArCu(X)MgBr" showed a striking difference in regioselectivity between the two reagents, the latter giving about 90% γ-selectivity and the former being nonregioselective. It was found that for "ArCu(X)MgBr" the γ-selectivity increased with the electronegativity of the halide X (I < Br < Cl).

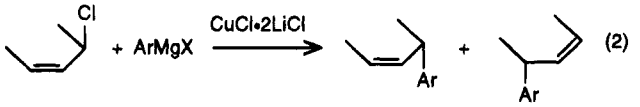
Copper-catalyzed cross-coupling reactions constitute an important class of reactions for the creation of new carbon–carbon bonds.[1] Apart from aryl–aryl, vinyl–vinyl, and aryl–vinyl couplings, copper-catalyzed couplings between an allylic halide or allylic alcohol derivative and an organometallic compound have attracted a lot of attention recently. The principle for these coupling reactions is shown in eq 1 and involves formation of an



X = Cl, Br, OCR, SO_2Ph, OR, $OP(O)(OR)_2$
R = alkyl, aryl, vinyl, allyl
M = -MgX, $-Ti(OR)_3$, ZnX etc.

organocopper intermediate from a transmetalation reaction.[2] The most common type of these reactions in organic synthetic applications is the copper-catalyzed Grignard reaction with allylic substrates,[3–6] but recently a number of copper-catalyzed reactions with other organometallics have been reported.[7,8] An important issue in these reactions is the control of regiochemistry, i.e., whether the leaving group X is displaced α or γ by the organometallic reagent. We recently reported a method for directing the regiochemistry toward either α- or γ-substitution in copper-catalyzed Grignard reactions with primary allylic acetates.[5] Reaction conditions that favored formation of "R_2CuMgX" gave α-substitution, whereas reaction conditions favoring RCu(X)MgX led to γ-substitution. During these studies we observed that the corresponding couplings with aryl Grignard reagents were more complicated leading to no or moderate regioselectivity. Similar observations have been noted by others[4a,8] in the coupling of allylic substrates involving catalytic arylcopper intermediates.

In connection with a project on the total synthesis of *Amaryllidaceae* alkaloids[9] it was required to substitute an allylic chloride by an aryl group with high γ-selectivity. In the present paper we have studied the copper-catalyzed reaction of allylic chlorides with arylmagnesium halides (eq 2) and found procedures which lead to



a certain degree of regiocontrol. The results show that the organocopper intermediates obtained from aryl Grignard reagents (ArMgX) are much more complicated than those obtained from the corresponding alkyl Grignard reagents.

Results

In our previous report[5] on regiocontrol of copper-catalyzed cross-coupling of allylic substrates with alkylmagnesium halides we briefly studied the reactions of allylic chlorides. A high γ-selectivity was observed in these reactions. In the previous study we used Li_2CuCl_4 as the catalyst, which is reduced *in situ* to a copper(I) chloride by the Grignard reagent.[10] Because of the consumption of Grignard reagent when a larger amount of the copper(II) catalyst is used, we have employed CuCl·2LiCl[11] as catalyst in the present study.

Reaction of **1** with *n*-BuMgBr in the presence of a catalytic amount of CuCl·2LiCl (10 mol %) resulted in a

® Abstract published in *Advance ACS Abstracts,* June 15, 1994.

(1) (a) Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978; p 381. (b) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901. (c) Lipshutz, B. H. *Synlett* **1990**, 119. (d) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135.

(2) Wipf, P. *Synthesis* **1993**, 537.

(3) (a) Fouquet, G.; Schlosser, M. *Angew. Chem.* **1974**, *86*, 50. (b) Commercon, A.; Bourgain, M.; Delaumeny, M.; Normant, J. F.; Villieras, J. *Tetrahedron Lett.* **1975**, 3837. (c) Barsantai, P.; Calo, V.; Lopez, L.; Marchese, G.; Naso, F.; Pesce, G. *J. Chem. Soc., Chem. Commun.* **1978**, 1085. (d) Calo, V.; Lopez, L.; Carlucci, W. F. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2953.

(4) (a) Tseng, C. C.; Paisley, S. D.; Goering, H. L. *J. Org. Chem.* **1986**, *51*, 2884. (b) Curran, D. P.; Chen, M. H.; Leszczweski, D.; Elliot, R. L.; Rakiewicz, D. M. *Ibid.* **1986**, *51*, 1612. (c) Underiner, T. L.; Paisley, S. D.; Schmitter, J.; Lesheski, L.; Goering, H. L. *J. Org. Chem.* **1989**, *54*, 2369.

(5) Bäckvall, J. E.; Sellén, M.; Grant, B. *J. Am. Chem. Soc.* **1990**, *112*, 6615.

(6) (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1984**, *25*, 3063. (b) Julia, M.; Righini-Tapie, A.; Verpeaux, J. N. *Tetrahedron* **1983**, *39*, 3283. (c) Yanagisawa, A.; Noritake, Y.; Nomura, N.; Yamamoto, H. *Synlett* **1991**, 251.

(7) (a) Nakamura, E.; Sekyia, K.; Arni, M.; Aoki, S. *J. Am. Chem. Soc.* **1989**, *111*, 3091. (b) Sekiya, K.; Nakamura, E. *Tetrahedron Lett.* **1988**, *29*, 5155.

(8) Arai, M.; Lipshutz, B. H.; Nakamura, E. *Tetrahedron* **1992**, *48*, 5709.

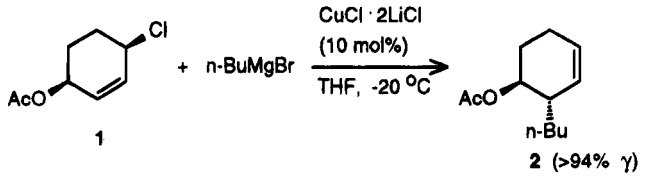
(9) Bäckvall, J. E.; Andersson, P. G.; Stone, G. B.; Gogoll, A. *J. Org. Chem.* **1991**, *56*, 2988.

(10) Tamura, M.; Kochi, J. K. *Synthesis* **1971**, 303.

(11) (a) Schlosser, M.; Bossert, H. *Tetrahedron* **1991**, *47*, 6287. (b) Giner, J. L.; Margot, C.; Djerassi, C. *J. Org. Chem.* **1989**, *54*, 2117.

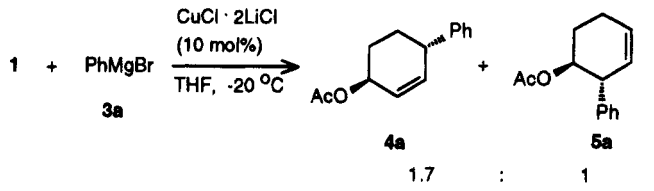
0022-3263/94/1959-4126$04.50/0

highly stereo- and regioselective reaction to give **2**. The

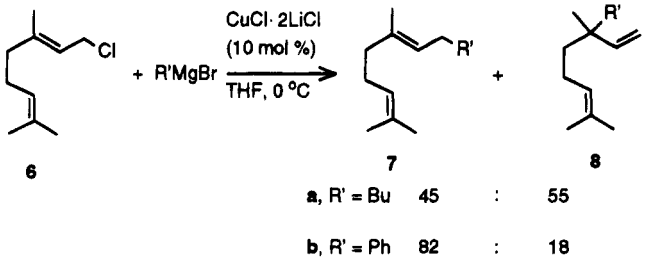


1 2 (>94% γ)

selectivity for the 1,2-isomer (γ-substitution) was >94%, and only the trans isomer (>99% trans) was observed. When the corresponding reaction of **1** was performed with PhMgBr (**3a**) a nonregioselective reaction occurred to give a 1.7:1 mixture between **4a** and **5a**. Analysis of products **4a** and **5a** showed that the reaction was stereospecific in each case with clean anti displacement of the chloride by the phenyl group.



The difference between BuMgBr and PhMgBr was also observed when geranyl chloride was employed as the substrate in the copper-catalyzed Grignard reaction. Thus, the alkyl Grignard afforded a 45:55 ratio between the α- and γ-isomer, whereas the phenyl Grignard showed a preference for α-substitution.



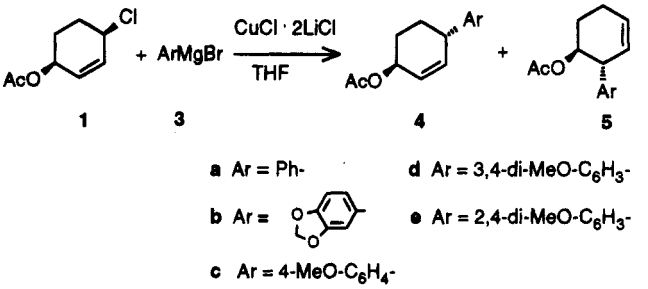
We have previously shown that if a Gilman-type complex, R_2CuMgX, is generated as the major catalytic species α-substitution is favored, whereas if a monoalkylcopper complex, RCu(Cl)MgX, is the major species γ-substitution predominates. A number of parameters were found to govern the formation of either species and, hence, the regioselectivity of the copper-catalyzed cross coupling of alkyl Grignard reagents with allylic substrates. Some of these parameters are (i) addition time of Grignard reagent, (ii) reaction temperature, and (iii) amount of catalyst. Other factors of importance for the regioselectivity were found to be the leaving group and the solvent. Because of the failure to obtain regioselective reactions of allylic substrates involving arylcopper intermediates, it was of interest to study the influence of these factors on copper-catalyzed couplings of aryl Grignard reagents with allylic substrates.

A. Variation of Addition Time. The [3,4-(methylenedioxy)phenyl]magnesium bromide (**3b**) was added at different addition times to a solution containing 0.5 equiv of CuCl·2LiCl and 1 equiv of the allylic chloride **1**. The reaction was performed in THF at room temperature. Addition within 1 min afforded the α-product **4b** and γ-product **5b** in a ratio of 60:40 (Table 1). With an addition time of 15 min the relative yield of α- and γ-product was 38:62. Further prolonging of the addition

Table 1. Variation of the Addition Time of Cu-Catalyzed Cross Coupling between 3b and 1[a]

entry	addition time of Grignard **3b**	product distribn[b,c] (%) **4b:5b**
1	1 min	60:40
2	15 min	38:62
3	1 h	35:65
4	2 h	27:73
5	10 h	27:73

[a] The reaction was performed in THF at 20 °C by adding the Grignard reagent **3b** to a homogeneous solution of 5 mL of CuCl·2LiCl and **1**. [b] The ratio between **4b** and **5b** was determined by ^1H NMR. [c] The yield of **4b** and **5b** was in the range of 65–80%.



time increased the relative yield of γ-product **5b**, which reached the maximum value with an addition time of 2 h (α:γ = 27:73). A further increase of the addition time did not change the ratio between **4b** and **5b**.

B. Variation of Temperature. The reaction between **3b** and **1** in the presence of the copper catalyst was performed at different temperatures with an addition time of the Grignard reagent of 2 h. In the range −23 to 50 °C, the relative yield of γ-product changed from 49 to 74% (Table 2). Reaction at −23 °C gave products **4b** and **5b** in a ratio of 51:49. An increase of temperature increased the relative yield of **5b** and at room temperature the ratio between **4b** and **5b** was 27:73. A further increase of temperature did not significantly increase the relative yield of the γ-product **5b**.

C. Variation of the Amount of Catalyst. The amount of copper catalyst (CuCl·2LiCl) in the cross coupling between **3b** and **1** was investigated with an addition time of the Grignard reagent of 1 h (Table 3). The use of 0.05 equiv of the copper catalyst produced **4b** and **5b** in a ratio of 45:55. An increased amount of catalyst increased the relative yield of the γ-product **5b**. With 0.5 equiv of the copper catalyst the relative yield of the γ-product **5b** was 65% and with 1 equiv it was 74%. With an addition time of the Grignard reagent of 2 h, the same variation was observed with the difference that now the maximum relative yield of **5b** (73–74%) was reached already at 0.5 equiv.

D. Noncatalyzed Reaction. The reaction between **3b** and **1** in the absence of the copper catalyst was investigated. At room temperature reaction occurred at a moderate rate to give **4b** and **5b** in a ratio of 62:38. The conversion of **1** was only 42%, and the yield determined by GC was 19% (**4b** + **5b**). The predominance of the α-product can be explained by a direct nucleophilic displacement of chloride by the Grignard reagent, possibly via a tight ionic intermediate.[1b]

E. The Use of Preformed Organocopper Species. A comparison of the results obtained for the copper-catalyzed aryl Grignard reactions with allylic substrates differ from those obtained with the corresponding alkyl

Table 2. Temperature Effects on the Regioselectivity of Cu-Catalyzed Cross Coupling between 3b and 1[a]

entry	T (°C)	product distribn[b,c] (%) 4b:5b
1	−23	51:49
2	0	36:64
3	20	27:73
4	40[d]	29:71[d]
5	50	26:74

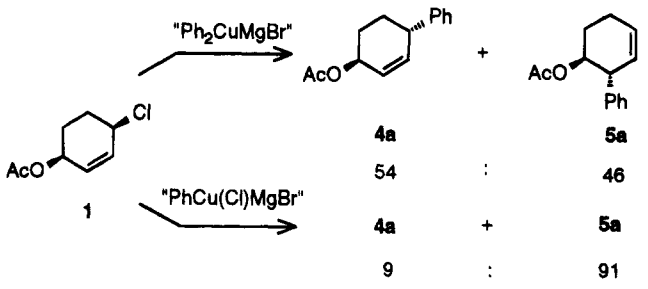
[a] Unless otherwise noted the reaction was performed in THF and the Grignard reagents was added over 2 h employing 50 mol % of CuCl·2LiCl. [b] The ratio between **4b** and **5b** was determined by GC. [c] The yield of **4b** and **5b** was in the range of 60−80%. [d] Addition time 1 h.

Table 3. Variation of the Amount of CuCl·2LiCl in the Cross Coupling between 3b and 1

entry	equiv of CuCl·2LiCl	product distribn[b,c] (%) 4b:5b
1	0.05	45:55
2	0.1	44:56
3	0.2	37:63
4	0.3	36:64
5	0.5	35:65
6	1.0	26:74

[a] The reaction was performed in THF at 20 °C and the Grignard reagent **3b** was added over 1 h. [b] The ratio between **4b** and **5b** was determined by ^{1}H NMR. [c] The yield of **4b** and **5b** was in the range 60−80%.

Scheme 1



Grignard reactions. For example, the maximum γ-selectivity for the aryl Grignard reagent **3b** was in the range of 75%, whereas for *n*-BuMgBr it was in the range of 95% or better.[5] Furthermore, the effect of the variation of the different factors governing the regioselectivity (addition time, temperature, amount of catalyst) was less accentuated for the aryl Grignard reagent compared to the alkyl Grignard reagent. In order to check if there is an inherent lower selectivity for "Ar_2CuMgX" and "ArCu(Cl)MgX" compared to the corresponding alkyl analogues, the arylcopper complexes were prepared and used in stoichiometric amounts in reactions with allyl chlorides. The organocopper complexes "$Ar_2CuMgBr$" and "ArCu(Cl)MgBr" were obtained by reaction of ArMgBr with CuCl·2LiCl in a 2:1 and 1:1 molar ratio, respectively. Reaction of **1** with the "$Ph_2CuMgBr$" afforded a 54:46 mixture between the α- and γ-substitution products **4a** and **5a**, respectively (Scheme 1). If the corresponding reaction was performed with the monoarylcopper complex, "PhCu(Cl)MgBr", a regioselective γ-substitution (91% γ-attack) occurred. The same difference in reactivity between diaryl and monoaryl copper complexes was demonstrated for a few other aryl groups such as 3,4-(methylendioxy)phenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, and 2,4-dimethoxyphenyl (Table 4).

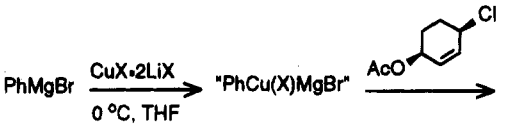
It was of interest to study how the regioselectivity is affected by a variation of the halide on copper in the

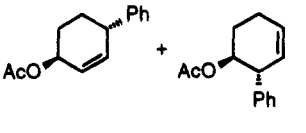
Table 4. Reaction of 1 with Preformed Arylcopper Species[a]

entry	aryl group (Ar)	ratio ArMgBr:Cu[b]	product distribn[c,d] (%) 4:5
1	C_6H_5− (**a**)	1:1	9:91
2		2:1	46:54
3	3,4-(methylenedioxy)-C_6H_3− (**b**)	1:1	10:90
4		2:1	53:47
5	4-$MeOC_6H_4$− (**c**)	1:1	10:90
6	3,4-$(MeO)_2C_6H_3$− (**d**)	1:1	11:89
7	2,4-$(MeO)_2C_6H_3$− (**e**)	1:1	15:85

[a] The reaction was performed in THF at 20 °C by adding **1** to the preformed arylcopper compound. [b] CuCl·2LiCl was used. [c] The ratio between **4** and **5** was determined by ^{1}H NMR. [d] The combined yield of the two isomers was in the range 67−80%.

monoaryl species "ArCu(X)MgBr". We therefore prepared the monoarylcopper species from CuX·2LiX with X = Cl, Br, and I, using copper and Grignard reagent in a 1:1 ratio. Interestingly, the γ-selectivity decreased with decreasing electronegativity of the halide (eq 3).





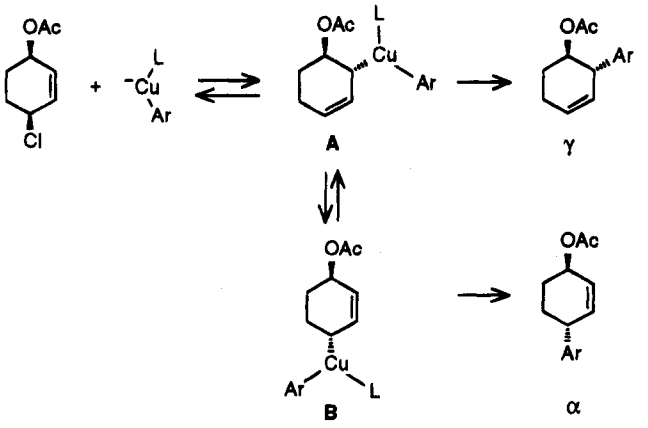
(3)

	4a	5a
X = Cl	9	91
X = Br	25	75
X = I	34	66

Discussion

The mechanism of the copper-catalyzed arylation of allylic chlorides can be discussed in terms of the regio- and stereochemical outcome of the reactions (Scheme 2). The copper-catalyzed substitution of allylic chlorides is stereospecific, and in all reactions the halide has been substituted anti. Attack by copper anti to the leaving group in an S_N2'-fashion[4a,5,6a,12] would produce a σ-allyl-

Scheme 2



(12) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1984**, *49*, 422.

copper(III) intermediate **A**, which may isomerize to intermediate **B**.[4a,5,12] Reductive elimination from **A** or **B** with retention of configuration would give the γ- and α-products, respectively, with the stereochemistry observed.

The regiochemical outcome of the reaction depends on the rate of reductive elimination versus isomerization for **A**, which depends on the ligand L on copper.[5,12] Electron-withdrawing ligands such as a halide will favor reductive elimination,[13] and in this case γ-arylated products are formed predominantly. When L is an aryl group the reductive elimination is presumably slower and isomerization takes place to give a mixture of α- and γ-products. The results in eq 3, where the γ-selectivity decreases when the electronegativity of the ligand (L) decreases (Cl > Br > I), is consistent with this mechanism.

A slow addition of the Grignard reagent, an increased temperature, and an increased amount of catalyst will favor formation of a monoaryl copper species (L = halide) and hence the γ-product.[5]

In the mechanism proposed, isomerization of **A** to **B** seems to occur even with electron-withdrawing ligands, which is in contrast to the analogous *alkylation*[4a,5,12] reactions. This may be explained by the lower reactivity of arylcopper complexes compared with alkylcopper complexes.[14]

Concluding Remarks

We have shown that it is possible to obtain a reasonable regiocontrol in copper-catalyzed aryl couplings with allylic chlorides by the use of CuCl·2LiCl as catalyst. The use of other catalysts in copper-catalyzed aryl couplings with allylic chlorides or allylic carboxylates give poor regioselectivity.[4a,8] It was demonstrated that the chloride as counterion on the organocopper complex plays an important role for the regioselectivity. The lower regioselectivity in the aryl Grignard reactions compared to the alkyl Grignard reactions can be explained by the lower reactivity of arylcopper intermediates.

Experimental Section

NMR spectra were recorded from $CDCl_3$ solutions, ^1H NMR at 400 MHz and ^{13}C at 100.6 MHz. For ^{13}C spectra the chemical shifts are reported with $CDCl_3$ (77.0 ppm) as internal reference while tetramethylsilane (TMS, 0.00 ppm) was used as reference for ^1H NMR spectra. The symbol W_H used in some of the ^1H NMR spectra denotes the width of the signal at half height. Analytical GLC was performed using a 30-m DB5 capillary column. HPLC was performed with a silica column (μ-Porasil, 10-μm packing, 0.4 × 30 cm) using hexane:ethyl acetate as eluent or with a RP8 column (250 × 10 mm) using methanol:water as eluent. A differential refractometer was used as detector. Merck silica gel (230–400 mesh) was used for flash chromatography, and thin-layer chromatography (TLC) was run on Merck precoated silica gel 60-F_{254} plates. To obtain reproducible addition times of the Grignard reagent, a syringe pump was used. Concentrations of the Grignard[15] and lithium reagents[16] were determined by titration. All reactions were carried out in flame-dried glassware under N_2 atmosphere, unless stated otherwise. Tetrahydrofuran (THF) was distilled from potassium benzophenone ketyl solution. Copper(I) chloride was prepared from copper(II) chloride[17] and copper(I) bromide from copper(II) sulfate[18] according to literature procedures. Copper(I) iodide (98%) purchased from Aldrich was purified according to a procedure by Kauffman and Fang.[19] Anhydrous lithium chloride (99%), lithium bromide (99%), geranyl chloride (95%), copper(II) chloride dihydrate (pa), and copper(II) sulfate pentahydrate (98%) were purchased from Aldrich, while anhydrous lithium iodide (99%) was obtained from Merck Schuchhardt. They were used without further purification.

***cis*-1-Acetoxy-4-chloro-2-cyclohexene (1)** was prepared from 1,3-cyclohexadiene according to a literature procedure.[20] The spectral data are consistent with those previously reported.[21]

CuCl·2LiCl:[11] Copper(I) chloride (99 mg, 1.0 mmol) and lithium chloride (85 mg, 2.0 mmol) were dissolved in THF (4 mL).

General Procedure for Copper-Catalyzed Grignard Reactions with Allylic Chlorides. The required amount of CuCl·2LiCl (0.05–1.0 mmol) was transferred from a freshly prepared solution of copper catalyst to the allylic chloride (1.0 mmol) at room temperature. A solution of ArMgBr (3.5 mL, 0.4 M, 1.4 mmol) in THF was added dropwise from a gas-tight syringe connected to a syringe pump during 2 h (or during the time indicated in Table 1) at room temperature (or at the temperature indicated in Table 2). After complete addition, the reaction mixture was stirred for 4 h and then quenched with saturated NH_4Cl(aq) (6 mL) and 2 M NH_4OH(aq) (4 mL). After the mixture was stirred for 30 min the organic layer was collected and the aqueous layer was extracted with ether (4 × 5 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography (silica gel, pentane:ether 95:5) gave a mixture of arylated products as a colorless oil with yields varying from 60 to 80% and α:γ ratios depending on reaction conditions. Spectral data are given below.

General Procedure for Reaction of a Preformed Monoarylcopper Complex with Allylic Chlorides. To a freshly prepared solution of CuCl·2LiCl (6 mL, 0.25 M, 1.5 mmol) was added dropwise a solution of ArMgBr (3.5 mL, 0.4 M, 1.4 mmol) in THF during 1 h at 0 °C from a gas-tight syringe connected to a syringe pump. After complete addition the reaction mixture was stirred another 30 min. The allylic chloride (1.0 mmol) dissolved in THF (2 mL) was added dropwise to the preformed monoarylcopper complex at room temperature from a gas-tight syringe connected to a syringe pump during 1 h. After complete addition, the reaction mixture was stirred for 2 h and then quenched with saturated NH_4Cl(aq) (6 mL) and 2 M NH_4OH(aq) (4 mL). After the mixture was stirred for 30 min the organic phase was collected and the aqueous layer was extracted with ether (4 × 5 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography (silica gel, pentane:ether 95:5) gave a colorless oil with yields varying from 60 to 80% and a γ-selectivity of 90%. Spectral data are given below.

Characterization of Products. Specified spectral data are recorded on pure isomers. In a few cases it was not

(13) It is known that electron-withdrawing ligands accelerate reductive elimination: Yamamoto, T.; Yamamoto, A.; Ikeda, S. *J. Am. Chem. Soc.* **1971**, *93*, 3350, 3360. Kurosawa, H.; Emoto, M.; Ohnishi, H.; Miki, K.; Kasai, N.; Tatsumi, K.; Nakamura, A. *J. Am. Chem. Soc.* **1987**, *109*, 6333. See also: Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987.

(14) Posner, G. H. *Org. React.* **1975**, *22*, 253.

(15) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

(16) Winkle, M. R.; Lansinger, J. M.; Ronald, R. C. *J. Chem. Soc., Chem. Commun.* **1980**, 87.

(17) Keller, R. N.; Wycoff, H. D. *Inorg. Chem.* **1946**, *2*, 1.

(18) Furniss, B. S.; Hannford, A. J.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; John Wiley and Sons: New York, 1989; p 428–429.

(19) Kauffman, G. B.; Fang, L. Y. *Inorg. Synth.* **1983**, *22*, 101.

(20) Bäckvall, J. E.; Granberg, K. L.; Hopkins, R. B. *Acta Chem. Scand.* **1990**, *44*, 492.

(21) Bäckvall, J. E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676.

possible to obtain a single isomers (**4c**, **4d**, **5c**, and **8b**), and in these cases the spectra were recorded from a mixture. Assignment of all ^{1}H NMR are available.

***trans*-1-Acetoxy-2-*n*-butyl-3-cyclohexene (2)**:[5] ^{1}H NMR δ 5.67 (dtd, J = 2, 3.5, 10 Hz, 1H), 5.55 (m, 1H), 4.78 (ddd, J = 3, 6.5, 9 Hz, 1H), 2.19 (m, 1H), 2.15–2.05 (m, 2H), 2.06 (s, 3H), 1.86 (dtd, J = 3, 5.5, 12.5 Hz, 1H), 1.66 (m, 1H), 1.48–1.19 (m, 6H), 0.90 (br t, J = 7 Hz, 3H); ^{13}C NMR δ 170.8, 128.6, 126.2, 73.7, 40.2, 32.6, 28.6, 26.1, 23.2, 22.9, 21.4, 14.0.

***trans*-1-Acetoxy-4-phenyl-2-cyclohexene (4a)**: ^{1}H NMR δ 7.38–7.16 (m, 5H, Ph*H*), 5.95 (ddd, J = 1.5, 2.5, 10 Hz, 1H, =C*H*CHOAc), 5.86 (ddd, J = 2.5, 2.5, 10 Hz, 1H, =C*H*CHAr), 5.42 (m, W_H = 15 Hz, 1H, C*H*OAc), 3.47 (m, W_H = 17 Hz, 1H, C*H*Ph), 2.14 (m, 1H, C*H*HCHPh), 2.10 (m, 1H, C*H*HCHOAc), 2.09 (s, 3H, CH_3), 1.71 (m, 1H, C*H*HCHOAc), 1.63 (m, 1H, C*H*HCHPh); ^{13}C NMR δ 170.8, 144.8, 134.5, 128.5, 127.6, 127.5, 126.4, 69.0, 41.6, 30.0, 27.5, 21.4; IR ($CDCl_3$) 3030, 2944, 1724, 1249. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.54; H, 7.46.

***trans*-1-Acetoxy-2-phenyl-3-cyclohexene (5a)**: ^{1}H NMR δ 7.33–7.20 (m, 5H, Ph*H*), 5.92 (dtd, J = 2.5, 3.5, 10 Hz, 1H, CH_2CH=CH), 5.64 (tdd, J = 2, 3, 10 Hz, 1H, =C*H*CHAr), 4.96 (ddd, J = 3, 6.5, 9 Hz, 1H, C*H*OAc), 3.52 (m, 1H, C*H*Ph), 2.30–2.24 (m, 2H, CH_2CH=), 1.97 (s, 3H, CH_3), 1.94 (dtd, J = 3, 5.5, 13 Hz, 1H, C*H*HCHOAc), 1.74 (tdd, J = 7, 9, 13 Hz, 1H, C*H*HCHOAc); ^{13}C NMR δ 170.5, 142.1, 128.4, 128.3, 127.8, 127.5, 126.7, 75.2, 47.0, 25.5, 23.2, 21.2; IR ($CDCl_3$) 3030, 2931, 1724, 1252. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.54; H, 7.43.

***trans*-1-Acetoxy-4-[3,4-(methylenedioxy)phenyl]-2-cyclohexene (4b)**: ^{1}H NMR δ 6.74 (d, J = 8 Hz, 1H), 6.66 (d, J = 2 Hz, 1H), 6.62 (dd, J = 2, 8 Hz, 1H), 5.93 (s, 2H), 5.89 (m, 1H), 5.83 (m, 1H), 5.38 (m, W_H = 15 Hz, 1H, C*H*OAc), 3.39 (m, W_H = 17 Hz, 1H, C*H*Ar), 2.15 (m, 1H), 2.08 (s, 3H), 2.06 (m, 1H), 1.66 (m, 1H), 1.59 (m, 1H); ^{13}C NMR δ 170.8, 147.6, 146.0, 138.7, 134.6, 127.5, 120.4, 108.2, 108.1, 100.9, 68.9, 41.3, 30.1, 27.4, 21.4; IR ($CDCl_3$) 2932, 1726, 1504, 1486, 1252, 1042. Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 69.08; H, 6.32.

***trans*-1-Acetoxy-2-[3,4-(methylenedioxy)phenyl]-3-cyclohexene (5b)**: ^{1}H NMR δ 6.75 (d, J = 2 Hz, 3H), 6.74 (d, J = 8 Hz, 1H), 6.70 (dd, J = 2, 8 Hz, 1H), 5.93 (s, 2H), 5.89 (dtd, J = 2, 3.5, 10 Hz, 1H), 5.59 (tdd, J = 2, 3, 10 Hz, 1H), 4.89 (ddd, J = 3, 7, 9 Hz, 1H), 3.42 (m, 1H), 2.27–2.20 (m, 2H), 1.99 (s, 3H), 1.91 (dtd, J = 3, 6, 13 Hz, 1H), 1.71 (tdd, J = 7, 9, 13 Hz, 1H); ^{13}C NMR δ 170.5, 147.6, 146.3, 136.0, 127.8, 127.5, 121.5, 108.8, 108.0, 100.9, 75.3, 46.6, 25.5, 23.1, 21.2; IR ($CDCl_3$) 2928, 1725, 1504, 1485, 1252, 1041. Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 69.08; H, 6.32.

***trans*-1-Acetoxy-4-(4-methoxyphenyl)-2-cyclohexene (4c)**: (from a mixture with **5c**) ^{1}H NMR δ 7.09 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 5.92 (m, 1H), 5.83 (m, 1H), 5.39 (m, W_H = 15 Hz, 1H, C*H*OAc), 3.78 (s, 3H), 3.41 (m, W_H = 17 Hz, 1H, C*H*Ar), 2.15–2.02 (m, 2H), 2.08 (s, 3H), 1.76–1.56 (m, 2H); ^{13}C NMR δ 170.3, 158.1, 136.8, 134.9, 128.5, 127.2, 113.8, 69.0, 55.2, 40.7, 30.0, 27.4, 21.3; IR ($CDCl_3$) 2937, 1725, 1510, 1238, 1036, 878. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 72.96, H, 7.36.

***trans*-1-Acetoxy-2-(4-methoxyphenyl)-3-cyclohexene (5c)**: (from a mixture with **4c**) ^{1}H NMR δ 7.16 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 5.89 (m, 1H), 5.61 (m, 1H), 4.91 (ddd, J = 3, 6.5, 9 Hz, 1H), 3.78 (s, 3H), 3.45 (m, 1H), 2.28–2.21 (m, 2H), 1.97 (s, 3H), 1.90 (dtd, J = 3, 6, 13 Hz, 1H), 1.72 (tdd, J = 7, 9, 13 Hz, 1H); ^{13}C NMR δ 170.5, 158.3, 134.1, 129.3, 127.7, 127.5, 113.7, 75.3, 55.2, 46.1, 25.3, 23.1, 21.2; IR ($CDCl_3$) 2937, 1725, 1510, 1238, 1036, 878. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 72.96, H, 7.36.

***trans*-1-Acetoxy-4-(3,4-dimethoxyphenyl)-2-cyclohexene (4d)**: (from a mixture with **5d**) ^{1}H NMR δ 6.81 (d, J = 8 Hz, 1H), 6.71 (dd, J = 2.5, 8 Hz, 1H), 6.69 (d, J = 2.5 Hz, 1H), 5.93 (m, 1H), 5.84 (m, 1H), 5.41 (m, W_H = 15 Hz, 1H, C*H*OAc), 3.87 (s, 3H), 3.86 (s, 3H), 3.41 (m, W_H = 17 Hz, 1H, C*H*Ar), 2.10 (m, 1H), 2.09 (s, 3H), 2.07 (m, 1H), 1.70 (m, 1H), 1.64 (m, 1H); ^{13}C NMR δ 170.8, 149.0, 147.6, 137.4, 134.8, 127.4, 119.5, 111.2, 110.8, 69.0, 55.94, 55.88, 41.3, 30.1, 27.5, 21.4; IR ($CDCl_3$) 2938, 1726, 1516, 1251, 1141, 1028. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.48; H, 7.23.

***trans*-1-Acetoxy-2-(3,4-dimethoxyphenyl)-3-cyclohexene (5d)**: ^{1}H NMR δ 6.79 (m, 5H), 5.93 (dtd, J = 2, 3.5, 10 Hz, 1H), 5.84 (tdd, J = 2, 3, 10 Hz, 1H), 4.94 (ddd, J = 3, 6.5, 9 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.45 (m, 1H), 2.28–2.22 (m, 2H), 1.98 (s, 3H), 1.91 (dtd, J = 3, 6, 13 Hz, 1H), 1.73 (tdd, J = 6.5, 9, 13 Hz, 1H); ^{13}C NMR δ 170.5, 148.8, 147.8, 134.7, 127.7, 127.6, 120.4, 111.6, 111.0, 75.2, 55.82 (two carbons), 46.4, 25.4, 23.0, 21.2; IR ($CDCl_3$) 2937, 1728, 1511, 1236, 1140, 1030. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.48; H, 7.23.

***trans*-1-Acetoxy-4-(2,4-dimethoxyphenyl)-2-cyclohexene (4e)**: ^{1}H NMR δ 6.96 (d, J = 8 Hz, 1H), 6.46 (d, J = 2 Hz, 1H), 6.43 (dd, J = 2, 8 Hz, 1H), 5.89 (m, 1H), 5.84 (m, 1H), 5.38 (m, W_H = 15 Hz, 1H, C*H*OAc), 3.81 (s, 3H), 3.80 (m, W_H = 17 Hz, 1H, C*H*Ar), 3.79 (s, 3H), 2.10 (dddd, J = 2.5, 5.5, 8, 13.5 Hz, 1H), 2.08 (s, 3H), 1.99 (dddd, J = 2.5, 5.5, 8, 13 Hz, 1H), 1.69 (dddd, J = 2.5, 7, 10, 13 Hz, 1H), 1.54 (dddd, J = 2.5, 7.5, 10, 13.5 Hz, 1H); ^{13}C NMR δ 170.8, 159.3, 157.8, 135.3, 128.4, 127.0, 124.9, 103.8, 98.6, 69.1, 55.34, 55.33, 33.9, 27.4, 27.2, 21.4; IR ($CDCl_3$) 3005, 1724, 1505, 1248, 1209, 1031. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.38; H, 7.32.

***trans*-1-Acetoxy-2-(2,4-dimethoxyphenyl)-3-cyclohexene (5e)**: ^{1}H NMR δ 7.05 (d, J = 8 Hz, 1H), 6.44 (d, J = 2 Hz, 1H), 6.43 (dd, J = 2, 8 Hz, 1H), 5.89 (dtd, J = 2, 4, 10 Hz, 1H), 5.55 (tdd, J = 3, 3.5, 10 Hz, 1H), 5.07 (dt, J = 5, 5 Hz, 1H), 3.81 (s, 3H), 3.80 (m, 1H), 3.79 (s, 3H), 2.21–2.15 (m, 2H), 2.00 (s, 3H), 1.78 (dt, J = 5, 6 Hz, 2H); ^{13}C NMR δ 170.5, 159.6, 158.2, 129.6, 127.6, 127.3, 122.3, 103.9, 98.5, 73.3, 55.4, 55.3, 39.5, 24.5, 22.4, 21.4; IR ($CDCl_3$) 3006, 1725, 1505, 1256, 1209, 1037. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.44; H, 7.28.

(6*E*)-2,6-Dimethyl-2,6-dodecadiene (7a):[5,22] ^{1}H NMR δ 5.12 (m, 2H), 2.00 (m, 6H), 1.69 (s, 3H), 1.60 (s, 6H), 1.40–1.20 (m, 6H), 0.90 (t, J = 6.5 Hz, 3H).

3-Butyl-3,7-dimethyl-1,6-octadiene (8a):[5,23] ^{1}H NMR δ 5.64 (dd, J = 10.5, 17.5 Hz, 1H), 5.12 (m, 1H), 4.91 (dd, J = 1.5, 10.5 Hz, 1H), 4.82 (dd, J = 1.5, 17.5 Hz, 1H), 1.96 (m, 2H), 1.63 (s, 3H), 1.54 (s, 3H), 1.32–1.04 (m, 8H), 0.90 (s, 3H), 0.83 (t, J = 6.5 Hz, 3H).

(2*E*)-3,7-Dimethyl-1-phenyl-2,6-octadiene (7b): ^{1}H NMR δ 7.33–7.26 (m, 2H), 7.21–7.19 (m, 3H), 5.36 (qt, J = 1.2, 7.5 Hz, 1H), 5.12 (m, 1H), 3.37 (d, J = 7.5 Hz, 2H), 2.12 (m, 2H), 2.06 (m, 2H), 1.72 (s, 3H), 1.69 (s, 3H), 1.61 (s, 3H); ^{13}C NMR δ 141.8, 136.2, 131.4, 128.30, 128.29, 125.6, 124.3, 123.0, 39.7, 34.2, 26.6, 25.7, 17.7, 16.1; IR ($CDCl_3$) 3028, 2970, 2917, 1452.

3,7-Dimethyl-3-phenyl-1,6-octadiene (8b): ^{1}H NMR δ 7.34–7.28 (m, 4H), 7.20–7.15 (m, 1H), 6.04 (dd, J = 10.5, 17 Hz, 1H), 5.11 (m, 1H), 5.10 (dd, J = 1.5, 10.5 Hz, 1H), 5.05 (dd, J = 1.5, 17.5 Hz, 1H), 1.86–1.69 (m, 4H), 1.66 (s, 3H), 1.51 (s, 3H), 1.38 (s, 3H); ^{13}C NMR δ 147.4, 146.9, 131.3, 128.0, 126.6, 125.7, 124.6, 111.7, 44.3, 41.1, 25.7, 24.9, 23.3, 17.6; IR ($CDCl_3$) 3028, 2970, 2917, 1452.

Acknowledgment. We are grateful to the Swedish Natural Science Research Council for financial support. Adolf Gogoll is gratefully acknowledged for help concerning NMR problems.

Supplementary Material Available: A copy of the ^{1}H NMR spectrum of **8b** and the ^{13}C NMR spectrum of **7b** (2 pages). This material is contained in libraries on microfiche, immediately follows this article on the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(22) Johnson, C. R.; Dhanoa, D. S. *J. Org. Chem.*, **1987**, *52*, 1885.
(23) Calò, V.; Lopez, L.; Giannangelo, P.; Calianno, A. *J. Org. Chem.* **1982**, *47*, 4482.