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Highly Selective Carbon-Carbon Bond Forming Reactions Mediated by Chromium(II) Reagents

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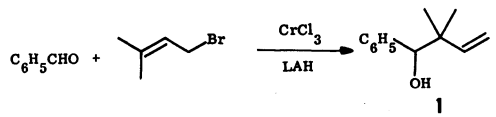
A low valent chromium reagent is generated from chromium(III) chloride and a half mol of lithium aluminum hydride in tetrahydrofuran. The reagent behaves similarly to anhydrous chromium(II) chloride, which is commercially available, and reduces allylic halides to produce unisolable allylchromium species which add efficiently to aldehydes or ketones with high degree of stereo- and chemoselectivity. Particularly, high *threo* selectivity is observed in the reaction of aldehydes and 1-bromo-2-butene and is ascribed to a chair-like six-membered transition state. Simple reduction of allylic and benzylic halides produces biallyls and bibenzyls, while *gem*-dibromocyclopropanes afford the corresponding allenes in excellent yields.

Main group organoelement compounds containing lithium, magnesium, or boron have been basic reagents for carbon-carbon bond formation.[1] These are generally so reactive as to make C–C bonds indiscriminately. In contrast, highly selective reactions are accomplished recently with the aid of transition metal elements such as chromium,[2] samarium,[3] ytterbium,[3] manganese,[4] tin,[5] titanium,[6] and zirconium.[7] This article deals with the Barbier-Grignard type reaction by means of chromium reagents with the emphasis on the chemo- and stereoselectivity.

Preparation of Allylic Chromium Reagent and the Carbonyl Addition. Chromium(II) salts are widely used in organic synthesis as one-electron reducing agents.[8] These are generally prepared and used in aqueous media. Therefore, when organic halides are treated with conventional chromium(II) reagents, the intermediary organochromium species, assumed to be formed at the initial stage of the reaction, are soon attacked by the coexisting water.[9] This has been the largest limitation and the chromium(II) reagents could not be utilized for intermolecular C–C bond forming reactions. We have found that chromium(III) chloride is reduced by lithium aluminum hydride (LAH)[10] in tetrahydrofuran (THF) to form a reagent which behaves quite analogously to chromium(II) chloride. Although the identity has not been established yet, we will call it chromium(II) reagent hereafter. This allows us to work in non-aqueous solutions.

When anhydrous chromium(III) chloride[11] suspended in THF was treated with a half mol of LAH at 0 °C, exothermic reaction took place spontaneously with hydrogen evolution. The initial purple color of the reaction mixture darkened and finally turned dark brown after 10 min. The reagent thus prepared can be stored for more than a month in a refrigerator without appreciable loss of activity. Treatment of a mixture of benzaldehyde and 1-bromo-3-methyl-2-butene with this reagent produced 2,2-dimethyl-1-phenyl-3-buten-1-ol (**1**). The optimum $CrCl_3$/LAH ratio was estimated to be 2 based on the results shown in Table 1. When



1

Table 1. Reaction of benzaldehyde and 1-bromo-3-methyl-2-butene with the chromium reagents generated from various ratio of chromium (III) chloride and lithium aluminum hydride[a]

$CrCl_3$:	$LiAlH_4$	Yield of **1**/%
1	1	25[b]
2	1	90
4	1	48[c]
$CrCl_2$[d]		89

a) Benzaldehyde (1 mmol) and 1-bromo-3-methyl-2-butene (2 mmol) were added to the chromium reagent (4 mmol) in THF (20 cm^3) at room temperature and the reaction was stopped after 3 h. b) Benzyl alcohol was produced as a main product. c) Benzaldehyde remained as evidenced by TLC assay. d) Purchased from Research Organic/Inorganic Chemical Corp.

an equimolar amount of LAH was applied, active hydride remained unchanged and reacted with benzaldehyde competitively to produce benzyl alcohol. In the experiment with a ratio of 4, the yield of the adduct decreased to *ca.* 50%. The same transformation could be achieved by means of the commercially available anhydrous chromium(II) chloride. The results of the reaction between allylic halides (or tosylate) and aldehydes or ketones are listed in Table 2. The general features of the chromium(II) mediated Barbier-Grignard reaction are as follows:

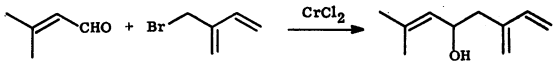
(1) The stoichiometry says that 2 mol of the chromium reagent is required for reduction of each halide.

(2) Although stoichiometric amount of allylic halide was sufficient for aldehyde, the use of excess allylic chromium reagents gives better yields in the reaction with ketones (*vide infra*).

(3) Generally the more substituted γ-carbon of an allyl group is attached to the carbonyl carbon. However, the methylene carbon of 3-bromopropyne preferentially connected with the carbonyl carbon of nonanal to give 1-dodecyn-4-ol (run 20).[12]

(4) *N,N*-Dimethylformamide (DMF) solvent is more effective than THF and, in particular, essential for the reaction with allyl chloride or tosylate.

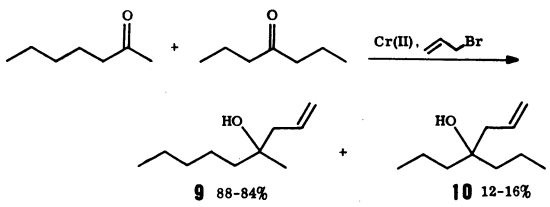
(5) With α,β-unsaturated aldehydes, the reaction proceeds exclusively in 1,2-fashion. Examples are seen in runs 9 and 14 (altemisia alcohol synthesis), and also in the synthesis of Ips dienol (**2**).[13]



Ipsdienol **2**

(6) Ketones are in general less reactive than aldehydes and required 2 mol of halides (*i.e.*, 4 mol of chromium reagent). Thus, chemospecific carbonyl addition is effected (run 17). Furthermore, the reagent discriminated 2-heptanone from 4-heptanone with the selectivity of 88 to 84%. α,β-Unsaturated ketones such as benzylideneacetophenone and 1,4-naphthoquinone do not give the corresponding adduct cleanly.

(7) Nitriles and carboxylates are not affected. Thus, selective carbonyl addition was achieved with respect to aldehydes having cyano or alkoxycarbonyl groups (runs 18 and 19).



9 88-84% **10** 12-16%

(8) Allylation of 4-*t*-butylcyclohexanone resulted in the preferential formation of the axial alcohol (runs 5 and 6). Namely, equatorial attack predominates with the selectivity of 88% (for $CrCl_3$–LAH reagent) and

TABLE 2. CHROMIUM(II) MEDIATED CARBONYL ADDITION OF ALLYL HALIDES[a]

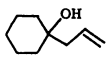
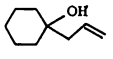
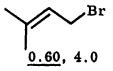
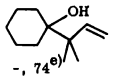
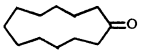
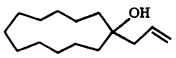
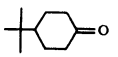
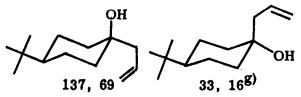
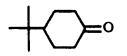
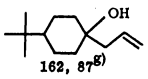
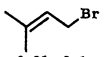
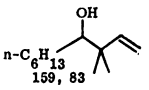
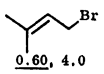
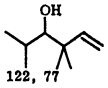
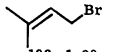
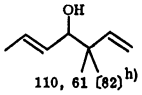
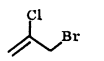
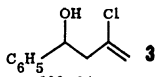
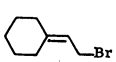
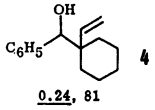
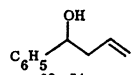
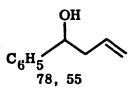
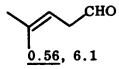
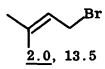
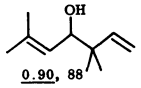
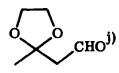
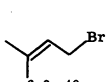
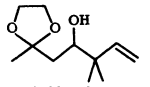
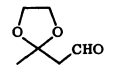
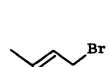
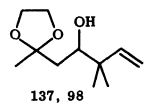
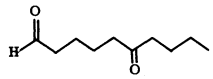
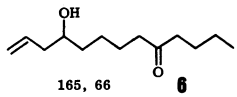
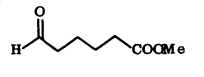
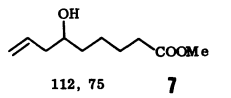
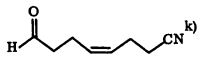
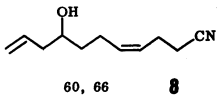
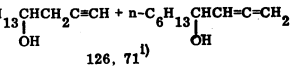
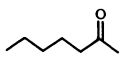
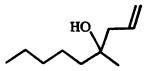
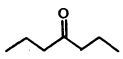
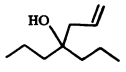
Run	Ketone or aldehyde (mg or g, mmol)	Allyl halide (mg or g, mmol)	Chromium[b] reagent (g, mmol)	Solvent (cm^3)	Reaction time/h	Product[c] (mg, or g, % yield)
1	 104, 1.06	 143, 1.18	A (-, 1.18)	THF (9)	2	 116, 78
2	 129, 1.32	 0.22, 1.32	B (0.32, 2.6)	THF (10)	3	 136, 74
3	 94, 0.96	 0.60, 4.0	A (-, 8.0)	DMF (16)	o.n.[d]	 -, 74[e]
4	 0.21, 1.13	 0.27, 2.3	A (-, 4.5)	THF (8)	3	 0.21, 82[f]
5	 156, 1.01	 0.25, 2.0	B (0.50, 4.1)	THF (12)	2.6	 137, 69 33, 16[g]
6	 146, 0.95	 0.23, 1.89	A (-, 3.8)	THF (12)	3	 162, 87[g]
7	n-C_6H_{13}CHO 119, 1.04	 0.31, 2.1	B (0.51, 4.1)	DMF (10)	3	 159, 83
8	 81, 1.12	 0.60, 4.0	A (-, 8.0)	DMF (13)	o.n.[d]	 122, 77
9	 91, 1.30	 193, 1.30	A (-, 2.6)	THF (10)	2	 110, 61 (82)[h]
10	C_6H_5CHO 65, 0.62	 0.34, 2.2	B (0.53, 4.3)	THF (8)	3	 **3** 106, 94
11	C_6H_5CHO 148, 1.39	 0.49, 2.6	A (-, 5.2)	THF (10)	o.n.[d]	 **4** 0.24, 81
12	C_6H_5CHO 90, 0.85	 134, 1.75	B (0.43, 3.5)	DMF (10)	o.n.[d]	 68, 54

TABLE 2. Continued.

Run	Ketone or aldehyde (mg or g, mmol)	Allyl halide (mg or g, mmol)	Chromium[b] reagent (g, mmol)	Solvent (cm³)	Reaction time/h	Product[c] (mg, or g, % yield)
13	C_6H_5CHO 106, 1.00	 0.44, 2.1	B (0.51, 4.1)	DMF (9)	2,6	 78, 55
14	 0.56, 6.1	 2.0, 13.5	A (-, 27)	THF (30)	3	 0.90, 88
15	 1.29, 9.9	 6.0, 40	A (-, 80)	DMF (110)	o.n.[d]	 1.80, 90 **5**
16	 92, 0.70	 0.22, 1.50	B (0.39, 3.2)	DMF (7)	0.2	 137, 98
17	 0.20, 1.19	 173, 1.43	B (0.35, 2.9)	THF (10)	2.3	 165, 66 **6**
18	 116, 0.80	 117, 0.96	B (0.24, 1.93)	THF (8)	3	 112, 75 **7**
19	 70, 0.51	 0.23, 1.88	B (0.46, 3.8)	THF (8)	3	 60, 66 **8**
20	$n\text{-}C_6H_{13}CHO$ 130, 1.14	 0.26, 2.2	B (0.54, 4.4)	THF (10)	3	 126, 71[i]
21	 66, 0.58	 0.24, 2.0	B (0.56, 4.5)	THF (7)	5.5	 70, 78 **9**
22	 102, 0.89	 0.42, 3.4	B (0.87, 7.1)	THF (11)	4.5	 47, 33 **10**

a) All the reaction was carried out at room temperature under an argon atmosphere. b) A: $CrCl_3$–1/2$LiAlH_4$ reagent. B: $CrCl_2$ reagent. c) Unless otherwise stated products were isolated by preparative TLC or column chromatography. d) Overnight. e) Determined by GLC (PEG 20 M, 5% on Celite 545, 1.5 m, 94 °C) analysis. f) Cyclododecanone (35 mg, 17%) was recovered. g) Stereochemical assignment: *cf.* Ref. 12. The axialalcohol: TLC (SiO_2, hexane–ether 3: 1) R_f 0.27; GLC (PEG 20 M, 10%, on Celite 545, 1.5 m, 140 °C) R_t 37.4 min; ^1H NMR ($CDCl_3$) δ=0.87 (*t*-Bu), and equatorial alcohol: TLC R_f 0.16; GLC, R_t 41.8 min; ^1H NMR δ=0.79. The ratio of the axial alcohol and the equatorial alcohol was estimated by GLC. h) GLC yield. i) The ratio of the acetylene/allene was revealed to be 9.8 : 1 by GLC (Apiezon L 5%, KOH 1%, on Chromosorb WAW, 2 m, 104 °C, R_t 4.0 min and 6.0 min respectively) or 10 : 1 by ^1H NMR. j) Bp 57—60 °C (bath temp)/13 Torr. Found: C, 55.25; H,8.02%. Calcd for $C_6H_{10}O_3$: C, 55.37; ^1H, 7.75%. This material was prepared by ethylene acetalization of ethyl acetoacetate, LAH reduction, followed by oxidation with CrO_3. k) K. Lunkwitz, W. Pritzbow, and G. Schmid, *J. Prakt. Chem.*, **37**, 319 (1968). This was prepared by the Beckmann rearrangement of 8-hydroxy-4-cyclooctenone oxime (mp 104.0—104.7 °C ($CHCl_3$), Found: C, 61.85; H, 8.61; N, 9.05%. Calcd for $C_8H_{12}NO_2$: C, 61.91; H, 8.44; N, 9.08%. *Cf.* M. Ohno, N. Naruse, S. Torimitsu, and I. Terasawa, *J. Am. Chem. Soc.*, **88**, 3168 (1966).

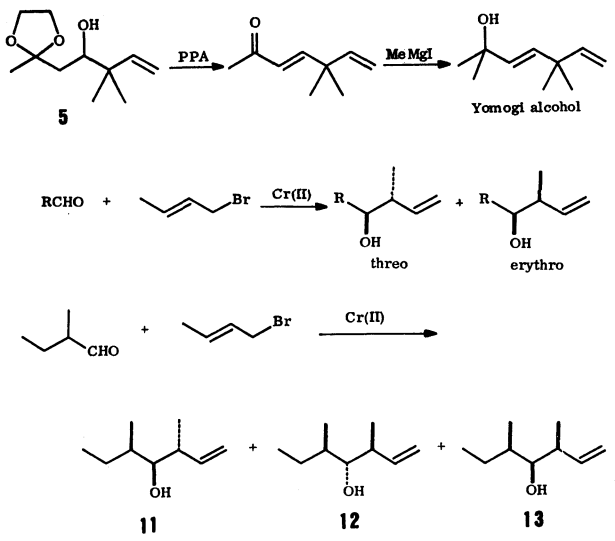
81% (for $CrCl_2$) comparable to that of allylzinc bromide (85%), and better than the Grignard addition (49%) or allyllithium reaction (35%).[14] This is compatible with the empirical rule that the softer the metal atom of allyl metallic compounds becomes, the more important equatorial attack becomes.[14]

(9) Styrene oxide does not undergo allylation and gives instead a mixture of halohydrins. Acetal group

Table 3. Threo-selective synthesis of homoallyl alcohols 1-bromo-2-butene and aldehydes[a]

Run	Aldehyde (mg, mmol)	1-Bromo-2-butene (g, mmol)	Solvent (cm^3)	Chromium[b] reagent (g, mmol)	Reaction time/h	Product (mg, % yield, *threo* : *erythro*[c])
1	PhCHO 140, 1.31	0.34, 2.5	THF (9)	A (—, 5.1)	3.5	206, 96, 100 : 0[d]
2	PhCHO 117, 1.11	0.31, 2.3	THF (7)	B (0.58, 4.7)	4	180, 100, 90 : 10[d]
3	PhCHO 106, 1.00	0.33, 2.4[e]	THF (7)	A (—, 5.0)	3	141, 87, 100 : 0[d]
4	*n*-C_3H_7CHO 74, 1.03	0.23, 1.67	THF (9)	A (—, 3.5)	7.5	78, 59, 93 : 7
5	*i*-C_3H_7CHO 80, 1.11	0.26, 1.91	THF (9)	A (—, 5.5)	3.5	78, 55, 95 : 5
6	*i*-C_3H_7CHO 61, 0.85	0.25, 1.87	THF (6.5)	B (0.40, 3.3)	3.5	88, 81, 97 : 3
7	*n*-$C_5H_{11}CHO$ 98, 0.98	0.25, 1.87	THF (8)	A (—, 4.0)	5	107, 70, 97 : 3
8	*n*-$C_5H_{11}CHO$ 124, 1.24	0.33, 2.5	THF (7)	B (0.61, 5.0)	3	188, 97, 96 : 4
9	*n*-$C_5H_{11}CHO$ 81, 0.81	0.23, 1.68	THF[f] (10)	A (—, 3.8)	1.3	110, 88, 94 : 6
10	*n*-$C_5H_{11}CHO$ 121, 1.21	0.28, 2.1	THF[g] (11)	A (—, 4.5)	4	166, 88, 95 : 5
11	PhCHO 127, 1.20	0.34, 2.5	THF[h] (8.5)	B (0.68, 5.5)	3.5	161, 83, 83 : 17[d]
12	PhCHO 98, 0.92	0.25, 1.81	DMF (7)	A (—, 3.2)	4.3	137, 92, 75 : 25[d]
13	*i*-C_3H_7CHO 78, 1.08	0.25, 1.83	DMF (9)	B (0.45, 3.7)	3	109, 78, 66 : 34
14	*n*-$C_5H_{11}CHO$ 112, 1.12	0.32, 2.4	DMF (9)	A (—, 4.4)	5	115, 77, 68 : 32
15	*t*-C_4H_9CHO 85, 0.98	0.27, 1.97	DMF (8)	A (—, 3.8)	3	88, 63, 37 : 63
16	*t*-C_4H_9CHO 81, 0.94	0.25, 1.83	THF (8)	A (—, 4.3)	3	86, 64, 35 : 65
17	$CH_3CH{=}CHCHO$ 90, 1.29	0.30, 2.2	THF (7)	B (0.56, 4.6)	3	119, 73, 83 : 17[i]

a) Chromium reagent (4 mmol) and 1-bromo-2-butene (2 mmol) were allowed to react with an aldehyde (1 mmol) at room temperature. b) A: $CrCl_3$–1/2$LiAlH_4$ reagent and mmol values are given. B: $CrCl_2$. c) The stereochemistry of the products was determined by comparing the spectral properties and retention times with those of the authentic samples (Ref. 15). d) Determined by ^1H NMR (the absorption of the methine proton H–C–OH): *threo*, δ=4.26 (d, J=6.8 Hz); *erythro*, δ=4.43 (d, J=5.8 Hz). e) *cis*-1-Bromo-2-butene was used. f) At THF refluxing temperature. g) Triphenylphosphine (1.18 g, 4.5 mmol) was added. h) Pyridine (0.86 g, 10.9 mmol, 2 equivalents of chromium) was used. i) Determined by ^{13}C NMR: *threo* (intensity)/*erythro* (intensity) δ=15.83 (94)/15.00(20), 44.32(99)/43.69(20), 115.62(99)/115.03(19).



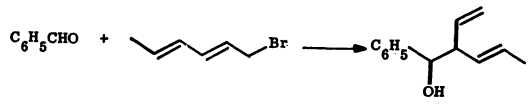
is not affected as evidenced by the reaction of 1-bromo-3-methyl-2-butene with 3,3-ethylenedioxybutanal (runs 15 and 16). The product **5** was subsequently dehydrated and deacetalized with polyphosphoric acid (PPA). Treatment of the resulting enone with methylmagnesium iodide yielded Yomogi alcohol.[15]

threo-*Selective Synthesis of Homoallyl Alcohols.* Benzaldehyde and 1-bromo-2-butene gave only one diastereomer of 2-methyl-1-phenyl-3-buten-1-ol whose stereochemistry was determined later to be *threo* by Heathcock and his coworker.[16] The *threo*-selectivity was found valid for various aldehydes as shown in Table 3 and independent both of the chromium reagents and the stereochemistry of 1-bromo-2-butenes.[17] The selectivity in THF was in general extremely high for relatively unhindered aldehydes (runs 1—11) compared with the reaction of 2-butenylmetals derived from magnesium, zinc, or cadmium.[18] In DMF the *erythro* alcohol (runs 12—14) was produced as much as 25—34%. The

only exception is seen in the reaction of a bulky aldehyde, 2,2-dimethylpropanal, which gave preferentially the *erythro* alcohol irrespective of the solvent (runs 15 and 16). As both *cis*- and *trans*-1-bromo-2-butene gave the *threo* alcohol as the sole product (runs 1, 2, and 3), the stereochemical integrity was lost completely in contrast to the reaction of 2-butenylboron and -silicon derivatives.[17]

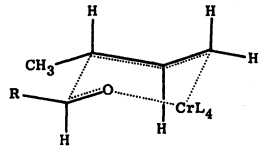
The reaction of 2-methylbutanal with 1-bromo-2-butene under the standard conditions gave three adducts whose stereochemical assignments were based on the ^{13}C NMR spectra of the hydrogenated products. Thus, *threo* selectivity in this case turned out to be 93%, although *α-erythro* induction[16] was 69%.

The C–C bond formation with benzaldehyde and 1-bromo-2,4-hexadiene took place exclusively at the γ-position of the bromide[19] to give **14**. The stereochemistry of the major product was assumed to be the one depicted in analogy to the above results.



14

The *threo* selectivity observed on the relatively unhindered aldehydes is explained reasonably by a chair form transition state I wherein interaction between the methyl and R groups is most reduced.[20] As chromium-



I

(III) ion has an octagonal configuration and consequently accepts six ligands,[21] these ligands will have an effect on the stereoselectivity. The low *threo*-selectivity in DMF may be attributed to the good solvating power of DMF compared with THF and consequently to the increased bulkiness around the chromium metal to disfavor the transition state I. This rationale is applicable to explaining the results of the experiment carried out in the presence of triphenylphosphine (run 10) or pyridine (run 11) which stabilizes the complex of type $RCrCl_2(ligand)_3$.[22]

Reduction of Organic Halides with the Chromium(II) Reagents. In the absence of electrophiles such as aldehydes or ketones allyl halides are dimerized under dehalogenation. For example, 1-bromo-3-methyl-2-butene gave three isomers of the coupling product (see Table 6, runs 1 and 2). Benzylic halides were transformed into the corresponding bibenzyls.[23] However, the assumed intermediate, benzylchromium, did not add across aldehydic carbonyl group. Reductive elimination of vicinal dihalides to olefins proceeded non-stereospecifically as evidenced by the transformation of *trans*-1,2-dibromocyclododecane into a mixture or

Table 4. Reduction of organic halides with the chromium(II) reagents

Run	Halide (mg or g, mmol)	Chromium reagent[a] (mmol)	Solvent (cm^3)	Time h	Product (mg or g, % yield)
1	1-Bromo-3-methyl-2-butene (1.04, 7.0)	A (23)	THF (25)	2	2,7-Dimethyl-2,6-octadiene, 3,3,6-trimethyl-1,5-heptadiene, and 3,3,4,4-tetramethyl-1,5-hexadiene (0.34, 70)[b]
2	1-Bromo-3-methyl-2-butene (0.37, 2.5)	B (6.2)	THF (8)	o.n.[c]	2,7-Dimethyl-2,6-octadiene, 3,3,6-trimethyl-1,5-heptadiene, and 3,3,4,4-tetramethyl-1,5-hexadiene (174, 100)[d]
3	Benzyl bromide (0.23, 1.32)	A (2.6)	THF (9)	40	1,2-Diphenylethane (—, 49[e] [61][f])
4	(Dichloromethyl)benzene (183, 1.14)	A (4.5)	DMF (5)	3	*cis*-1,2-Diphenylethene (16, 16) and *trans*-1,2-diphenylethene (33, 32)
5	(Trichloromethyl)benzene (0.23, 1.2)	A (4.3)	DMF (7.5)	3	Diphenylethyne (45, 43)
6	*trans*-1,2-Dibromocyclododecane (0.62, 1.91)	A (3.8)	DMF (5)	o.n.[c,g]	*cis*-Cyclododecene (86, 29)[h] and *trans*-cyclododecene (121, 41)
7	2-Bromocyclododecanone (0.27, 1.05)	A (5.3)	THF (7)	3.5	Cyclododecanone (187, 96)
8	9,9-Dibromobicyclo[6.1.0]-nonane (0.33, 1.16)	A (5.8)	DMF (10)	2[i]	1,2-Cyclononadiene (—, 100)[j]
9	9,9-Dibromobicyclo[6.1.0]-nonane (0.57, 2.0)	A (10)	THF (24) DMF (2)	2[k]	1,2-Cyclononadiene (152, 63 [71][f])
10	2-Phenyl-1,1-dibromocyclopropane (0.29, 1.04)	A (5.2)	DMF (7)	4	Phenylpropadiene (75, 62)
11	*trans*-2-Methyl-3-phenyl-1,1-dibromocyclopropane (0.29, 1.00)	A (5.0)	DMF (8)	5	1-Phenyl-1,2-butadiene (76, 58)

a) A: $CrCl_3$–1/2$LiAlH_4$ reagent, B: $CrCl_2$. All the reaction was carried out at room temperature unless otherwise specified. b) The mixture of the product was purified by preparative TLC and analyzed. The ratio of these products was determined by GLC (Apiezon L, 5%, KOH 1%, on Chromosorb WAW DMS, 1.5 m, 76 °C) to be 72 : 22 : 6. c) Overnight. d) These products were isolated by distillation (Kugelrohr) and the ratio was found to be 62 : 27 : 11 by the GLC assay. e) Estimated by ^1H NMR. f) Based on the consumed starting material. g) At 90 °C. h) Starting dibromide (30 mg, 5%) was recovered. i) At 60 °C. j) GLC yield. k) At reflux temperature.

cis- and *trans*-cyclododecene. α-Bromocyclododecanone was reduced to the parent ketone quantitatively. Trapping experiment of the intermeidary chromium enolate with methyl iodide or trimethylsilyl chloride failed to give the expected product. Quenching with deuterium oxide resulted in only 38% deuterium incorporation. Therefore, hydrogen abstraction from the solvent has possibly occurred during the reaction.

A salient feature of the chromium(II) reagent is illustrated by the very smooth conversion of *gem*-dibromocyclopropanes to allenes (runs 8—11). The reaction is a key in an effective synthetic route to 1,2-dienes. In this particular transformation, the $CrCl_3$–LAH reagent was essential for clean reaction, as the commercial reagent, anhydrous chromium(II) chloride gave products contaminated with monobromocyclopropanes.

In conclusion, reduction of organic halides with the chromium(II) reagent in anhydrous media gives organochromium intermediates which react with aldehydic carbonyl carbon with high selectivity. This will provide a new tool for selective methodology of C–C bond formation.

Experimental

Distillation was carried out by use of Kugelrohr (Büchi) and boiling points were determined by measuring the bath temperature. All the temperatures are uncorrected. ^1H NMR spectra (tetramethylsilane as an internal standard) were taken in carbon tetrachloride solution on a Varian EM 390 spectrometer or EM 360 spectrometer, chemical shifts being given in ppm units. ^{13}C NMR spectra were recorded on a Varian CMR-20 spectrometer (tetramethylsilane, internal standard). IR spectra were obtained on a Shimadzu IR-27G spectrometer in neat liquid film unless otherwise stated, mass spectra on a Hitachi RMU-6L spectrometer. Chromium(III) chloride hexahydrate was dehydrated by the reported procedure.[11] Anhydrous chromium(II) chloride was purchased from Research Inorganic/Organic Chemical Corp., and all reactions as well as all operations dealing with chromium salts were carried out under an argon or a nitrogen atmosphere. LAH purchased from Metalgesellschaft A.-G., West Germany, was used directly. TLC analyses were carried out with Merck Silica Gel 60 F_{254} plates. Preparative TLC plates (20 cm × 20 cm) were prepared by use of Merck Kiesel-gel PF_{254}. Column chromatography was carried out with silica gel (Wakogel C-100) at atmospheric pressure or under pressure of $4—6 \times 10^5$ N/m^2 (Wakogel C-300). In this text 1 Torr corresponds to 133.322 N/m^2.

Preparation of the Chromium Reagent from Chromium(III) Chloride and Lithium Aluminum Hydride. A Typical Procedure. Lithium aluminum hydride (101 mg, 2.6 mmol) was added portionwise to chromium(III) chloride (0.84 g, 5.3 mmol) suspended in THF (5 cm^3) at 0 °C. Immediate gas evolution occurred with darkening of the initial purple color which finally turned dark brown. After the gas evolution had ceased the reaction mixture was stirred for 5 to 10 min at 0 °C, and the reagent was used for reaction. Replacing THF with DMF was effected by evaporation of THF under reduced pressure, introduction of argon, and addition of DMF.

Reaction of Benzaldehyde with 1-Bromo-3-methyl-2-butene. A Typical Procedure. To the chromium reagent, prepared from chromium(III) chloride (0.37 g, 2.3 mmol) and LAH (44 mg, 1.2 mmol) in THF (5 cm^3), were added benzaldehyde (92 mg, 0.86 mmol) and successively a THF (5 cm^3) solution of 1-bromo-3-methyl-2-butene (173 mg, 1.2 mmol) at room temperature. After 2 h the reaction mixture was treated with water (5 cm^3) and extracted thoroughly with ether. The ethereal solution was washed with brine, dried with sodium sulfate, and concentrated. Distillation of the residue at 105—110 °C (bath temp)/0.12 Torr gave 2,2-dimethyl-1-phenyl-3-buten-1-ol (**1**) (124 mg, 82% yield). In another experiment the yield estimated by GLC was 90%. IR 3425, 3095, 3075, 3035, 1638, 1605, 1490, 1020, 1000, 915, 730, and 702 cm^{-1}; ^1H NMR δ=0.94 (s, 3H), 0.99 (s, 3H), 1.5—1.8 (br s, OH), 4.34 (s, 1H), 4.8—6.2 (m, 3H, vinyl), and 7.26 (s, 5H); MS, *m/e* (rel intensity), 176 (M$^+$, trace), 107 (100), 82 (33), 79 (69), and 70 (64).

The reactions between various aldehydes and allylic bromides are summarized in Table 2. Physical properties of the new compounds follow.

3-Chloro-1-phenyl-3-buten-1-ol (3). Bp 88—93 °C (bath temp)/0.07 Torr; IR 3360, 3050, 3020, 1630, 1605, 1495, 1040, 883, 758, and 700 cm^{-1}; ^1H NMR δ=2.3 (br s, 1H, OH), 2.60 (two d, J=7.5 Hz, 2H), 4.91 (dd, J=7, 5 Hz, 1H), 5.10 (s, 1H), and 7.25 (s, 5H); MS *m/e* (rel intensity), 182 (M$^+$, 0.07), 107 (100), 79 (67), and 77 (33). Found: C, 65.53; H, 6.03%. Calcd for $C_{10}H_{11}ClO$: C, 65.76; H, 6.07%.

Phenyl(1-vinylcyclohexyl)methanol (4). Bp 160—162 °C (bath temp)/0.15 Torr; IR 3450, 3045, 1630, 1605, 1493, 1453, 1040, 1022, 918, 733, and 708 cm^{-1}; ^1H NMR δ=1.1—2.0 (m, 11H), 4.23 (s, 1H), 4.8—5.9 (m, 3H, vinyl), and 7.16 (s, 5H); MS *m/e* (rel intensity), 198 (M$^+-H_2O$, 0.7), 110 (98), 107 (100), 81 (86), and 67 (43). Found: C, 83.33; H, 9.59%. Calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32%.

6,6-Ethylenedioxy-3,3-dimethyl-1-hepten-4-ol (5). Bp 115—120 °C (bath temp)/4 Torr; IR 3510, 3070, 1634, 1368, 1120, 1094, 1036, and 904 cm^{-1}; ^1H NMR δ=1.00 (s, 6H), 1.28 (s, 3H), 1.57 (d, J=9 Hz, 1H), 1.67 (d, J=2 Hz, 1H), 2.95 (br s, 1H, OH), 3.43 (dd, J=9, 2 Hz, 1H), 3.92 (s, 4H), and 4.7—6.1 (m, 3H, vinyl); MS *m/e* (rel intensity), 185 (M$^+-CH_3$, 1.5), 167 (1.5), 97 (100), and 43 (59). Found: C, 65.94; H, 10.29%. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07%.

10-Hydroxy-12-tridecen-5-one (6). Bp 109—112 °C (bath temp)/0.06 Torr; IR 3425, 3080, 1705, 1640, 1128, 1000, and 916 cm^{-1}; ^1H NMR δ=0.8—1.9 (m, 14H), 2.0—2.6 (m, 6H), 3.3—3.8 (m, 1H), and 4.7—6.2 (m, 3H, vinyl); MS, *m/e* (rel intensity), 194 (M$^+-H_2O$, 2), 171 (M$^+-CH_2CH{=}CH_2$, 7), 153 (21), 135 (17), 85 (75), and 57 (100). Found: C, 73.46; H, 11.62%. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39%.

Methyl 6-Hydroxy-8-nonenoate (7). Bp 90—95 °C (bath temp)/0.04 Torr; IR 3450, 3080, 1728, 1632, 1435, 1200, 1092, 998, and 914 cm^{-1}; ^1H NMR δ=1.2—1.9 (m, 6H), 2.0—2.5 (m, 5H), 3.4—3.9 (m+s (δ=3.62), 4H), and 4.9—6.2 (m, 3H, vinyl); MS, *m/e* (rel intensity), 155 (1), 145 (M$^+-CH_2$-$CH{=}CH_2$, 12), 113 (100), 85 (24), and 67 (85). Found: C, 64.20; H, 9.91%. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74%.

*(4Z)-8-Hydroxy-*cis*-4,10-undecadienenitrile (8).* Bp 115—120 °C (bath temp)/0.06 Torr; IR 3430, 3070, 3005, 2265, 1633, 992, and 913 cm^{-1}; ^1H NMR δ=1.1—1.7 (m, 2H), 2.0—2.5 (m, 9H), 3.57 (quintet, J=6 Hz, 1H), 4.7—6.2 (m, 3H, vinyl); MS, *m/e* (rel intensity), 138 (M$^+-CH_2CH{=}CH_2$, 66), 120 (44), 110 (20), 94 (66), and 67 (100). Found: C, 73.53; H, 9.81; N, 7.88%. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81%.

Competitive Reaction of 2-Heptanone and 4-Heptanone. A mixture of 2-heptanone (86 mg, 0.75 mmol) and 4-heptanone (86 mg, 0.75 mmol) dissolved in THF (1.5 cm^3) was added to chromium(II) chloride (0.38 g, 3.1 mmol) suspended in THF (3 cm^3) at 0 °C. Then allyl bromide (186

mg, 1.5 mmol) dissolved in THF (3 ml) was added to the reaction mixture at room temperature in 6 min and the mixture was stirred for 3 h. Work-up and GLC analysis (PEG 20 M, 10%, on Chromosorb W, 1.5 m, 100 °C) revealed that the reaction had proceeded with 54% conversion to give 4-methyl-1-nonen-4-ol (R_t 30.0 min) and 4-propyl-1-hepten-4-ol (R_t 23.7 min) (84 : 16) in 49% yield (91% yield based on the consumed ketones). In a repeated experiment the ratio was 88 : 12.

Conversion of **5** *into Yomogi Alcohol.* A THF (5 cm³) solution of **5** (1.01 g, 5.0 mmol) was added to a THF (5 cm³) solution of PPA (105% H_3PO_4, 1.3 g) under a nitrogen atmosphere and the mixture was stirred for 1 h, then heated to reflux for 3.5 h. Work-up followed by preparative TLC (hexane–ether 3 : 1, R_f 0.74) gave (3*E*)-5,5-dimethyl-*trans*-3,6-heptadien-2-one (0.59 g, 84% yield), bp 123—127 °C (bath temp)/28 Torr. IR 1670, 1616, 1350, 1245, 974, and 908 cm⁻¹; ¹H NMR δ=1.18 (s, 6H), 2.14 (s, 3H), 4.7—6.1 (m (vinyl)+d (δ=5.87, J=16 Hz), totally 4H), and 6.60 (d, J=16 Hz, 1H); MS, *m/e* (rel intensity), 138 (M^+, 4), 123 ($M^+ - CH_3$, 26), 95 (70), 67 (35), and 43 (100). Found: C, 78.06; H, 10.36%. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21%.

To the ether (2 cm³) solution of the dienone (138 mg, 1.00 mmol) excess methylmagnesium iodide (generated from 5 mmol of each of magnesium and methyl iodide in ether (5 cm³)) and the reaction mixture was stirred at room temperature for 30 min. Work-up and distillation gave Yomogi alcohol (124 mg, 81% yield), bp 80 °C (bath temp)/1 Torr, having spectral properties consistent with the reported one.[15]

*Synthesis of Ips-dienol (***2***).* A THF (3 cm³) solution of 2-bromomethyl-1,3-butadiene (0.20 g, 1.35 mmol) was added to a mixture of chromium(II) chloride (0.26 g, 2.1 mmol) and 3-methyl-2-butenal (44 mg, 0.52 mmol) at room temperature and the whole was stirred for 3.6 h. Work-up followed by distillation at 72 °C (bath temp)/0.03 Torr gave the desired product (34 mg, 45% yield) having the correct spectra.[13]

threo-*2-Methyl-1-phenyl-3-buten-1-ol.* A THF (4 cm³) solution of *trans*-1-bromo-2-butene (0.34 g, 2.5 mmol) was added at room temperature over a period of 20 min to a mixture of benzaldehyde (140 mg, 1.31 mmol) and the chromium reagent A prepared by mixing chromium(III) chloride (0.81 g, 5.1 mmol) and LAH (96 mg, 2.5 mmol) in THF (5 cm³). The reaction mixture was stirred for 3.4 h at room temperature. Work-up and distillation at 110 °C (bath temp)/4 Torr gave the title alcohol (0.21 g, 96% yield) which proved uniform on TLC analysis (hexane–ether 3 : 1, R_f 0.35) and GLC (PEG 20 M, 5%, on Celtite 545, 1.5 m, 141 °C; or Apiezon L 5%, KOH 1%, on Chromosorb, 2 m, 140 °C).

Reaction of 2-Methylbutanal with 1-Bromo-2-butene. A THF (6 cm³) solution of 2-methylbutanal (182 mg, 2.1 mmol) and 1-bromo-2-butene (0.62 g, 4.6 mmol) was added to chromium(II) chloride (1.14 g, 9.3 mmol) suspended in THF (9 cm³) over a period of 10 min at room temperature, and the whole was stirred for 3 h. Work-up and column chromatography gave a mixture (0.27 g, 90% yield) of adducts (**11**, **12**, and **13**) with the ratio of 62 : 31 : 7 as revealed by GLC assay (PEG 20 M, 5%, on Celite 545, 1.5 m, 80 °C).

The mixture of the adduct (130 mg) in ethanol (6 cm³) was stirred under a hydrogen atmosphere in the presence of 10% palladium on charcoal for 31 h. Filtration and short column chromatography gave a stereoisomeric mixture of 3,5-dimethyl-4-heptanol. ¹³C NMR ($CDCl_3$, TMS an internal standard) spectra showed clearly two sets of chemical shifts (δ), (intensity): [11.26 (80), 11.86 (100), 12.44 (82), 15.43 (77), 24.99 (77), 27.19 (85), 36.79 (81), 37.74 (87), and 78.41 (80)] for the dihydro derivative of **11**; [11.65 (70), 16.14 (66), 23.52 (71), 37.29 (74), and 80.60 (35)] for the dihydro derivative of **12**. The minor product, the dihydro derivative of **13**, was characterized by the peaks at δ=13.90 (13), 26.46 (11), and 77.98 (7).[17a,25]

*4-Methyl-1-nonen-4-ol (***9***).* Bp 61—65 °C (bath temp)/13 Torr; ¹H NMR δ=0.9—1.6 (m, 12H), 1.13 (s, 3H, Me), 2.20 (d, J=8.1 Hz, 2H), and 5.0—6.1 (m, 3H, vinyl); IR 3390, 1642, 1155, 999, and 913 cm⁻¹. Found: C, 77.07; H, 13.06%. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90%.

*4-Propyl-1-hepten-4-ol (***10***).* Bp 56—59 °C (bath temp)/13 Torr; ¹H NMR δ=0.8—1.5 (m, 15H), 2.11 (d, J=7.2 Hz, 2H), 4.97 (dd, J=2.3, 15.3 Hz, 1H, CH=CH–H), 5.00 (dd, J=2.3, 9.0 Hz, 1H, CH=CH–H), and 5.5—6.0 (m, 1H, CH=CH_2); IR 3400, 1637, 1152, 989, and 919 cm⁻¹. Found: C, 76.68; H, 13.14%. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90%.

threo-*3-Methyl-1-nonen-4-ol.* Bp 88—91 °C (bath temp)/11 Torr; ¹H NMR δ=0.92 (t, J=7.5 Hz, 3H, terminal methyl), 1.04 (d, J=6.6 Hz, 3H, $CHCH_3$), 1.0—1.6 (m, 8H, methylenes), 1.80 (br s, 1H, OH), 2.0—2.4 (m, 1H, $CHCH_3$), 3.2—3.5 (m, 1H, CHOH), 5.01 (dd, J=2.7, 17.1 Hz, 1H, CH=CH–H), 5.18 (dd, J=2.7, 10.8 Hz, 1H, CH=CH–H), and 5.6—5.9 (m, 1H, CH=CH_2); IR 3380, 1638, 1260, 1081, 1001, and 911 cm⁻¹; MS, *m/e* (rel intensity), 141 ($M^+ - CH_3$, 2), 138 ($M^+ - H_2O$, 2), 101 (9), 83 (29), 56 (41), 55 (38), 44 (46), and 40 (100). Found: C, 76.74; H, 13.18%. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90%.

*1-Phenyl-2-vinyl-3-penten-1-ol (***14***).* ¹H NMR δ=1.37 (d, J=6 Hz, 0.78H), 1.62 (d, J=6 Hz, 2.22H), 1.88 (br s, 1H, OH), 2.8—3.5 (two multiplets, 1H), 4.3—4.6 (m, 1H), 4.9—6.0 (m, 5H, olefinic H), and 7.23 (s, 5H, Ph); IR 3450, 3090, 3040, 2980, 2930, 2890, 2865, 1640, 1608, 1500, 1458, 1038, 1024, 997, 968, 914, 760, 718, and 698 cm⁻¹; MS, *m/e* (rel intensity), 170 ($M^+ - H_2O$, 2), 107 (77), 91 (8), 82 (47), 79 (100), 77 (56), 67 (31), and 51 (25). *Cf.* Ref 24.

A Typical Procedure for the Reduction of 1,1-Dibromocyclopropanes. Synthesis of Phenylpropadiene: To the chromium reagent, prepared from chromium(III) chloride (0.82 g, 5.2 mmol) and LAH (99 mg, 2.6 mmol) in THF (5 cm³) and by replacing the solvent with DMF (5 cm³), a DMF (2 cm³) solution of 1,1-dibromo-2-phenylcyclopropane (0.29 g, 1.04 mmol) was added at room temperature and the mixture was stirred for 4 h. Work-up followed by distillation at 80—85 °C (bath temp)/20 Torr gave phenylpropadiene (75 mg, 62% yield): IR 1940, 850, 760, and 692 cm⁻¹; ¹H NMR δ=5.06 (d, J=7 Hz, 2H), 6.05 (t, J=7 Hz, 1H), and 7.15 (s, 5H).

References

1) E. Negishi, "Organometallics in Organic Synthesis," John Wiley and Sons, New York (1980), Vol. 1.

2) Preliminary reports: Y. Okude, S. Hirano, T. Hiyama, and H. Nozaki, *J. Am. Chem. Soc.*, **99**, 3179 (1977); Y. Okude, T. Hiyama, and H. Nozaki, *Tetrahedron Lett.*, **1977**, 3829; T. Hiyama, K. Kimura, and H. Nozaki, *ibid.*, **22**, 1037 (1981).

3) P. Girard, J. L. Namy, and H. B. Kagan, *J. Am. Chem. Soc.*, **102**, 2693 (1980).

4) G. Cahiez and J. F. Normant, *Tetrahedron Lett.*, **1977**, 3383; *Bull. Soc. Chim. Fr.*, **1977**, 570; G. Cahiez, D. Bernard, and J. F. Normant, *Synthesis*, **1977**, 130.

5) Y. Naruta, S. Ushida, and K. Maruyama, *Chem. Lett.*, **1979**, 919; T. Mukaiyama, T. Harada, and S. Shoda, *ibid.*, **1980**, 1507.

6) J. E. McMurry, M. G. Silvestri, M. P. Fleming, T. Hoz, and M. W. Grayston, *J. Org. Chem.*, **43**, 3249 (1978); J. E. McMurry, M. P. Fleming, K. L. Kees, and L. R. Krepsi, *ibid.*, **43**, 3255 (1978).

7) D. A. Evans and L. R. McGee, *Tetrahedron Lett.*, **21**,

3975 (1980); Y. Yamamoto and K. Maruyama, *ibid.*, **21**, 4607, (1980).

8) J. R. Hanson, *Synthesis*, **1974**, 1; Tse-Lok Ho, *ibid.*, **1979**, 1.

9) J. K. Kochi and P. E. Mocadlo, *J. Am. Chem. Soc.*, **88**, 4094 (1966); C. E. Castro and W. C. Kray, Jr., *ibid.*, **88**, 4447 (1966).

10) We have attempted to use *i*-Bu_2AlH, Et_3Al, metallic K, $NaH_2Al(OCH_2CH_2OMe)_2$, $NaBH_4$, BH_3SMe_2, but these reducing agents failed to reduce the chromium(III) ion effectively into the lower valent one.

11) A. R. Pray, *Inorg. Synth.*, **5**, 153 (1954).

12) P. Place, F. Delbecq, and J. Gore, *Tetrahedron Lett.*, **1978**, 3801; C. Verniere, B. Cazes, and J. Gore, *ibid.*, **22**, 103 (1981).

13) R. G. Riley, R. M. Silverstein, J. A. Katzenellenbogen, and R. S. Lenox, *J. Org. Chem.*, **39**, 1957 (1974).

14) M. Gaudemar, *Tetrahedron*, **32**, 1689 (1976).

15) W. Sucrow and W. Richter, *Chem. Ber.*, **103**, 3771 (1970) and references cited therein.

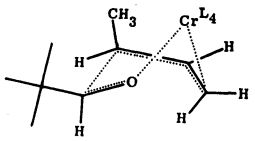
16) C. T. Buse and C. H. Heathcock, *Tetrahedron Lett.*, **1978**, 1685.

17) R. W. Hoffmann and H.-H. Zeiss, *Angew. Chem., Int. Ed. Engl.*, **18**, 306 (1978); *Angew. Chem.*, **92**, 218 (1980); H. Yatagai, Y. Yamamoto, and K. Maruyama, *J. Am. Chem. Soc.*, **102**, 4548 (1980); Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, *ibid.*, **102**, 7107 (1980); M. Yamaguchi and T. Mukaiyama, *Chem. Lett.*, **1980**, 993.

18) G. Courtois and L. Miginiac, *J. Organomet. Chem.*, **69**, 1 (1974).

19) Regioselectivity in the reaction of pentadienylmetals with electrophiles: D. Seyferth and J. Pornet, *J. Org. Chem.*, **45**, 1721 (1980); A. Hosomi, M. Saito, and H. Sakurai, *Tetrahedron Lett.*, **21**, 3783 (1980).

20) The *erythro* selective reaction of 2,2-dimethylpropanal may be understood by the anticipated severe interaction between *t*-butyl and methyl groups and accordingly by a preferred skew boat-like transition state II.



II

21) A. Segnitz, "Methoden zur Herstellung und Umwandlung von Organo-chrom-Verbindungen," in "Methoden der Organischen Chemie," ed by E. Müller (1975), XIII/7, p. 375.

22) K. Nishimura, H. Kuribayashi, A. Yamamoto, and S. Ikeda, *J. Organomet. Chem.*, **37**, 317 (1972); A. Yamamoto, Y. Kato, and T. Yamamoto, *ibid.*, **102**, 57 (1975); K. Maruyama, T. Ito, and Y. Yamamoto, *Chem. Lett.*, **1978**, 479.

23) J. Wellmann and E. Steckhan, *Synthesis*, **1978**, 901.

24) L. Miginiac-Groizeleau, P. Miginiac, and C. Prevost, *Bull. Soc. Chim. Fr.*, **1965**, 3560.

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