An interesting relationship between the rate of the Diels-Alder reaction and the size of the anion is presented. This relationship indicates that effects of salts on the hydrophobic effects may be due to some surface contact between the electrolyte and the organic solute.[17]

Acknowledgment. This work was performed in the laboratories of Professor Ronald Breslow at Columbia University with the support of an NIH postdoctoral fellowship. Professor Breslow is gratefully acknowledged for helpful suggestions and encouraging submission of this manuscript. Dr. David Weidenfeld and Dr. Joseph Dougherty are also acknowledged for helpful suggestions and insights in preparing this manuscript.

Supplementary Material Available: Experimental details (1 page). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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[17] It should be noted that direct surface contact between electrolyte and solute may not fully account for this correlation, and other explanations are certainly possible. The author gratefully acknowledges thoughtful reviewers for pointing this out.

Stereodivergent Additions of Allylic Chromium(III) Reagents to Aldehydes

Carole Jubert, Stefan Nowotny, Dirk Kornemann, Iris Antes, Charles E. Tucker, and Paul Knochel*

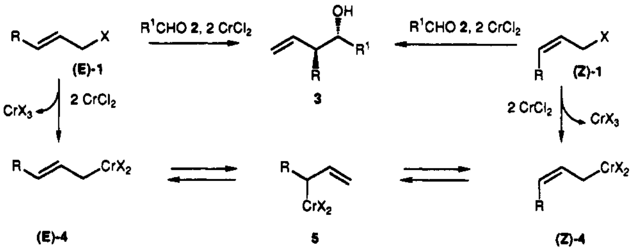
Philipps-Universität Marburg, Fachbereich Chemie, Hans-Meerwein-Stasse, D-3550 Marburg, Germany

Received September 9, 1992

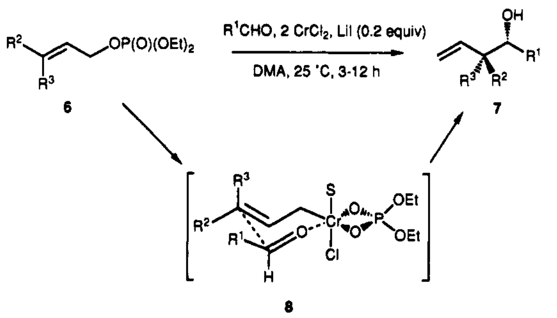
Summary: In contrast to γ-monosubstituted allylic chromium reagents, γ-disubstituted allylic chromium(III) organometallics undergo highly stereoselective stereodivergent additions to aldehydes.

Hiyama[1,2] reported that allylic halides **1** add to aldehydes **2** in the presence of chromium(II) salts. The reaction is highly stereoselective and affords the anti alcohols **3** *regardless* of the stereochemistry of the starting allylic halide.[3] This behavior can be explained by assuming[4] that the intermediate chromium(III) organometallics (*E*)-**4** and (*Z*)-**4** equilibrate rapidly via the chromium(III) species **5** before reacting with an aldehyde **2** (Scheme I).[5] We now report that the reaction of *γ-disubstituted* allylic phosphates **6**[6,7] with aldehydes and $CrCl_2$ in the presence of a catalytic amount of LiI (0.2 equiv)[8] in DMPU[9] is *not* *stereoconvergent* and proceeds with high stereoselectivity (Scheme II and Table I). The presence of the two substituents at the γ-position apparently slows down the equilibration process between the intermediate allylic chromium reagents **4** (Scheme I). The use of a phosphate as a leaving group[7] is not responsible for the high stereoselectivity, as the reaction of (*E*)- and (*Z*)-*mono*substituted allylic phosphates such as (*E*)- and (*Z*)-2-hexenyl phosphate with benzaldehyde in the presence of $CrCl_2$ under various reaction conditions always affords the anti alcohol as major diastereoisomer (stereoconvergent reaction). The observed stereochemistry[10] can be rationalized assuming

Scheme I



Scheme II



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[1] Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* 1977, *99*, 3179.

[2] (a) Hiyama, T.; Okude, Y.; Kimura, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* 1982, *55*, 561. (b) For an excellent review: Saccomano, N. A. In *Comprehensive Organic Synthesis*; Trost, B. M.; Ed.; Pergamon Press: Oxford, 1991, p 173.

[3] (a) Buse, C. T.; Heathcock, C. H. *Tetrahedron Lett.* 1978, 1685. (b) Hiyama, T.; Kimura, K.; Nozaki, H. *Tetrahedron Lett.* 1981, *22*, 1037. (c) Takai, K.; Utimoto, K. *J. Synth. Org. Chem. Jpn.* 1988, *46*, 66.

[4] We thank a reviewer for valuable comments concerning this mechanism.

[5] Since the initial report of Hiyama and Nozaki, the addition of allylic chromium reagents to aldehydes has led to numerous useful synthetic studies: (a) Nagaoka, H.; Kishi, Y. *Tetrahedron Lett.* 1981, *37*, 3873. (b) Lewis, M. D.; Kishi, Y. *Tetrahedron Lett.* 1982, *23*, 2343. (c) Takai, K.; Kimura, K.; Kuroda, T.; Hiyama, T.; Nozaki, H. *Tetrahedron Lett.* 1983, *24*, 5281. (d) Okuda, Y.; Nakatsukasa, S.; Oshima, K.; Nozaki, H. *Chem. Lett.* 1985, 481. (e) Takai, K.; Kuroda, T.; Nakatsukasa, S.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* 1985, *26*, 5585. (f) Okazoe, T.; Takai, K.; Utimoto, K. *J. Am. Chem. Soc.* 1987, *109*, 951. (g) Takai, K.; Kataoka, Y.; Okazoe, T.; Utimoto, K. *Tetrahedron Lett.* 1987, *28*, 1443. (h) Takai, K.; Nitta, K.; Fujimura, O.; Utimoto, K. *J. Org. Chem.* 1989, *54*, 4732. (i) Wender, P. A.; Wisniewski, Grissom, J.; Hoffmann, U.; Mah, R. *Tetrahedron Lett.* 1990, *31*, 6605. (j) Crevisy, C.; Beau, J.-M. *Tetrahedron Lett.* 1991, *32*, 3171. (k) Mulzer, J.; Kattner, L.; Strecker, A. R.; Schröder, C.; Buschmann, J.; Lehmann, C.; Luger, P. *J. Am. Chem. Soc.* 1991, *113*, 4218.

[6] Allylic phosphates are readily prepared from the corresponding alcohols ($(EtO)_2P(O)Cl$ (1.05 equiv), Pyr (2 equiv), 0 °C, 4 h, 95% yield) and are considerably more stable and easier to handle than the corresponding mesylates: (a) Poulter, C. D.; Satterwhite, D. M. *Biochemistry* 1977, *16*, 5470. (b) Poulter, C. D.; King, C.-H. R. *J. Am. Chem. Soc.* 1982, *104*, 1422. For a recent use of allylic phosphates as electrophiles; (c) Yanagisawa, A.; Nomura, N.; Yamamoto, H. *Synlett* 1991, 513.

[7] The insertion of $CrCl_2$ into some allylic phosphates has already been reported: (a) Takai, K.; Nozaki, H. In *Abstracts of the 4th ICOS at Tokyo*, 1982. See also refs 2 and 3c.

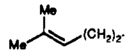
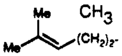
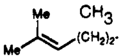
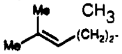
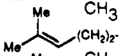
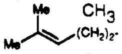
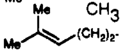
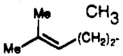
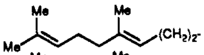
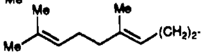
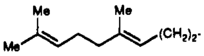
[8] Lithium halides react rapidly with allylic phosphates in DMF at 25 °C to afford the corresponding allylic halide with retention of the stereochemistry of the double bond: Araki, S.; Ohmori, K.; Butsugan, Y. *Synthesis* 1984, 841.

[9] (a) Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* 1982, *65*, 385. (b) Seebach, D.; Beck, A. K.; Mukhopadhyay, T.; Thomas, E. *Helv. Chim. Acta* 1982, *65*, 1101. (c) Bengtsson, M.; Liljefors, T. *Synthesis* 1988, 250.

[10] The relative stereochemistry of compound **7** has been established for **7a** by a detailed stereochemical study performed by: M. Koreeda: Koreeda, M.; Tanaka, Y. *Chem. Lett.* 1982, 1299. Comparison with these spectral data allowed an unambiguous assignment of the relative stereochemistry of **7a** and **7b**.

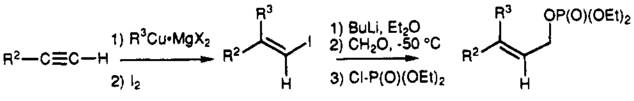
0022-3263/92/1957-6384$03.00/0 © 1992 American Chemical Society

Table I. Homoallylic Alcohols 7a–q Prepared by the Reaction of γ-Disubstituted Allylic Phosphates 6a–f with Aldehydes 2 and $CrCl_2$ and a Catalytic Amount of Lithium Iodide in DMPU

entry	aldehyde 2	allylic phosphate 6			homoallylic alcohol 7	dr[b]	yield[a] (%)
	R^1	R^2	R^3				
1	Ph		CH_3	6a	7a	97:3	94
2	Ph	CH_3		6b	7b	99:1	98
3	Pent		CH_3	6a	7c	94:6	93
4	Pent	CH_3		6b	7d	99:1	94
5	(E)-Pr-CH=CH		CH_3	6a	7e	96:4	77
6	(E)-Pr-CH=CH	CH_3		6b	7f	97:3	84
7	Bu—C≡C-		CH_3	6a	7g	> 99:1	86
8	Bu—C≡C-	CH_3		6b	7h	98:2	89
9	Hex	Pr	Bu	6c	7i	> 99:1	90
10	Hex	Bu	Pr	6d	7j	98:2	64
11	Ph	Pr	Bu	6c	7k	93:7	66
12	Ph	Bu	Pr	6d	7l	> 99:1	75
13	Ph	Me	Bu	6e	7m	97:3	95
14	c-Hex	Me	Bu	6e	7n	90:10	89
15	Ph		Me	6f	7o	95:5	84
16	Hex		Me	6f	7p	93:7	80
17	c-Hex		Me	6f	7q	94:6	86

[a] All yields refer to isolated yields of products being over 98% pure by GC analysis and showing satisfactory ^1H, ^{13}C NMR, IR, and MS spectra. [b] dr = diastereomeric ratio.

a chair transition state[11] such as 8. Especially remarkable is the stereoselectivity observed in the case of the two isomeric phosphates **6c** (R^2 = Pr; R^3 = Bu) and **6d** (R^2 = Bu; R^3 = Pr), since in this case the two substituents R^2 and R^3 have approximately the same size (entries 9 and 10). These two phosphates were prepared by the carbocupration of the corresponding alkyne,[12a] followed by an iodolysis. Conversion of the intermediate pure (*E*)- or (*Z*)-alkenyl iodides (>99:1 stereomeric ratio) to the corresponding lithium derivatives,[12b] followed by the addition of formaldehyde (−50 °C, 1 h) and reaction with ClP(O)(OEt)$_2$ (1.05 equiv, pyridine (2 equiv), CH_2Cl_2 or Et_2O, 0 °C, 4–12 h, 95% yield, eq 1) produces the phosphates

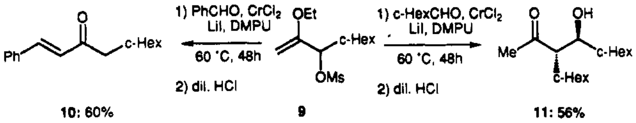


(1)

6c and **6d** in over 99% stereomeric purity. As seen from the Table I, all the reactions are highly stereoselective (>93:7; entries 9–12 of Table I), with either reactive aldehydes such as benzaldehyde or the less reactive aliphatic aldehydes such as heptanal demonstrating clearly the configurational stability of the intermediate allylic chromium reagents.[13,14] All the reactions are complete within a few hours at 25 °C (3–12 h) and proceed well with various types of aldehydes (aromatic, aliphatic, vinylic, and acetylenic, see Table I). However, ketones such as acetophenone do not undergo the addition reaction.

The reactions have to be performed in the presence of LiI, since without this additive low yields result (**7n** is obtained in the absence of LiI in only 28% yield). However, preliminary results show that in certain cases DMPU can be replaced by THF resulting in comparable yields and stereoselectivities.

Finally, the chromium(II)-mediated addition reactions were also performed using *functionalized* allylic mesylates.[2] Especially interesting is the reaction of the readily prepared[15] allylic mesylates **9** with an aldehyde (RCHO (1.0 equiv), $CrCl_2$ (2.0 equiv), LiI (0.2 equiv), DMPU, 60 °C, 48 h; eq 2). After acidic hydrolysis of the reaction mixture, the unsaturated ketone **10** is obtained in 60% yield, the new carbon–carbon bond being formed in this case from the least substituted end of the allylic chromium(III) intermediate (eq 2). However, with cyclohexanecarboxaldehyde the expected anti aldol product **11**[16] is obtained as the only product in 56% isolated yield (eq 2).



10: 60% **9** **11**: 56%

(2)

Further experiments studying the influence of the substitution pattern of the allylic substrates on the stereose-

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(11) (a) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. (b) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357. (c) Yamamoto, Y. *Acc. Chem. Res.* **1987**, *20*, 243. (d) Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970.

(12) (a) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841. (b) Cahiez, G.; Bernard, D.; Normant, J. F. *Synthesis* **1976**, 245.

(13) A few diastereoselective chromium(II)-mediated additions of cyclic γ-disubstituted allylic halides to aldehydes have been reported: (a) Takeshita, H.; Kato, N.; Nakanishi, K.; Tagoshi, H.; Hatsui, T. *Chem. Lett.* **1984**, 1495. (b) Kato, N.; Nakanishi, K.; Takeshita, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1109. (c) Takeshita, H.; Hatsui, T.; Kato, N.; Masuda, T.; Tagoshi, H. *Chem. Lett.* **1982**, 1153.

(14) Typical procedure: reaction of an allylic phosphate with an aldehyde mediated by chromium(II) chloride. Preparation of (1S^*,2R^*)-2,6-dimethyl-2-ethenyl-1-phenyl-5-hepten-1-ol (**7b**) (diastereomeric ratio = 99:1). (*Z*)-Diethyl-3,7-dimethyl-2,6-octadienyl phosphate (**6b**) (1.45 g, 5 mmol), benzaldehyde (0.42 g, 4 mmol), LiI (0.13 g, 1 mmol), and $CrCl_2$ (1.23 g, 10 mmol) in dry DMPU (6 mL) were stirred at 25 °C for 3–12 h. The completion of the reaction was checked by GC analysis of hydrolyzed reaction samples. After the usual workup (extraction with ether, washing with saturated aqueous NH_4Cl), the residual oil was purified by flash chromatography affording the pure alcohol **7b** (0.96 g, 98%) as an oil; the diastereomeric ratio determined by ^1H NMR was 99:1.

(15) Baldwin, J. E.; Höfle, G. A.; Lever, O. W. *J. Am. Chem. Soc.* **1974**, *96*, 7125.

(16) The structure of 11 has been confirmed by X-ray analysis. The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

lectivity in these addition reactions as well as applications to stereoselective ring closure reactions are currently underway in our laboratories.

Acknowledgment. We thank M. Koreeda for helpful discussions and for allowing us to compare our spectral data with unpublished data relative to ref 10. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Supplementary Material Available: Spectral data (^{1}H, ^{13}C NMR, mass spectra and IR) of all new compounds (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Highly Selective Homocoupling Reaction of Allylic Halides Using Barium Metal

Akira Yanagisawa, Hiroaki Hibino, Shigeki Habaue, Yoshiyuki Hisada, and Hisashi Yamamoto*

Department of Applied Chemistry, Nagoya University, Chikusa, Nagoya 464-01, Japan

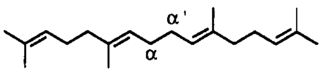
Received August 17, 1992

Summary: The highly α,α' selective and stereocontrolled homocoupling reaction of allylic halides was achieved using barium reagent. The double-bond geometry of the starting allylic chloride was completely retained. α,α' Cross-coupling products were also prepared stereospecifically and regioselectively by this method.

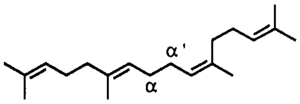
Homo- and cross-coupling of allylic halides are among the most basic carbon–carbon bond forming reaction in organic synthesis.[1] Subsequent to early studies on the use of nickel carbonyl in this coupling process by Corey et al.,[2] many groups have made important contributions to the steady improvement in this methodology.[3-5] Nonetheless, each of the published approaches suffers from some drawbacks and limitations. Described herein is a new method which is believed to be superior to earlier procedures, especially for stereospecificities and regioselectivities. The highly α,α' selective and stereocontrolled homocoupling reaction of allylic halides was first achieved using barium reagent.[6]

We have examined various kinds of metals for homocoupling of geranyl bromide (1, Table I) at low temperature. Alkali metal naphthalenide (1.5 equiv) or reactive alkaline-earth metal (0.7 equiv) in THF was exposed to 1 (1 equiv) at −95 or −78 °C.[7] Among these metals, barium metal was found to be unique for α,α' selective homocoupling reaction ($\alpha,\alpha'/\alpha,\gamma'$ = 97/3, 47% yield, entry 7). Furthermore, the geometric purity of the α,α' product (2/3 = 96/1) indicates that geometric isomerization (trans to cis) of the allylic barium can be kept minimal during the coupling conditions.

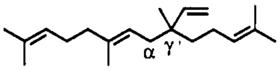
Table I. Effect of Metals on the Regio- and Stereoselectivities of Dimerization Reaction of Geranyl Bromide (1)



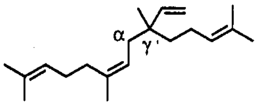
2, α-α'(*EE'*)



3, α-α'(*EZ'*)



4, α-γ'(*E*)



5, α-γ'(*Z*)

entry	M*	T, °C	yield,[a] %	ratio ($\alpha,\alpha'/\alpha,\gamma'$)	ratio of isomers 2–5[b] 2	3	4	5
1	Li–Np[c]	−95	62	69:31	67	2	31	0
2	Na–Np[c]	−95	86	61:39	60	1	39	0
3	K–Np[c]	−95	99	78:22	76	2	22	0
4	Cs–Np[c]	−95	27	65:35	65	0	35	0
5	Mg	−95	61	63:37	60	3	34	3
6	Ca	−78	58	62:38	58	4	38	0
7	Ba	−78	47	97:3	96	1	3	0
8	Cr	−40	85	74:26	68	6	26	0
9	Mn	−40	60	74:26	62	12	26	0

[a] Isolated yield. [b] Determined by GC analysis. [c] Np = naphthalene.

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[1] Reviews: (a) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1. (b) Billington, D. C. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Pattenden, G., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, p 413. (c) Benkeser, R. A. *Synthesis* **1971**, 347. (d) Semmelhack, M. F. *Org. React.* **1972**, *19*, 115. (e) Baker, R. *Chem. Rev.* **1973**, *73*, 487. (f) Black, D. St. C.; Jackson, W. R.; Swan, J. M. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon Press: Oxford, 1979; Vol. 3, p 1127. (g) Billington, D. C. *Chem. Soc. Rev.* **1985**, *14*, 93.

[2] Corey, E. J.; Hamanaka, E. *J. Am. Chem. Soc.* **1964**, *86*, 1641.

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