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THE INFLUENCE OF (ORGANO)METALLICS "METAL-TUNING" ON STEREO- AND REGIO-CHEMICAL CONVERGENCE IN REACTIONS OF ALLYLIC CARBANIONS WITH ALDEHYDES

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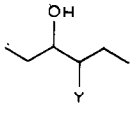
Summary

Although the reaction of heterosubstituted allylic carbanions (**2**) with aldehydes generally produces a mixture of the γ- and α-adducts (**4** and **3**), *syn*-**3** and *anti*-**3** can be prepared either exclusively or predominantly by the proper choice of the organometallic compound added.

The structural unit like **1** is frequently encountered in many important natural products. For the synthesis of such compounds, it is essential to control



(**1a**: Y = C,
1b: Y = O,
1c: Y = S)

the relative stereochemistry between the two adjacent substituents [1]. We intended to control such stereochemistry via the reaction of aldehydes with heterosubstituted allylic carbanions (**2**), eq. 1 [2]. For this approach, it is necessary to control both regio- and stereo-chemical selectivities; i the regioselective reaction at the α-position of **2** and ii the stereoselective formation of either *syn*-**3** or *anti*-**3**. In this paper, we report that such stereo- and regio-chemical [3] convergence can be realized by metal tuning and either the *syn* or *anti* diastereomer can be obtained by the appropriate choice of "M".

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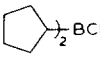
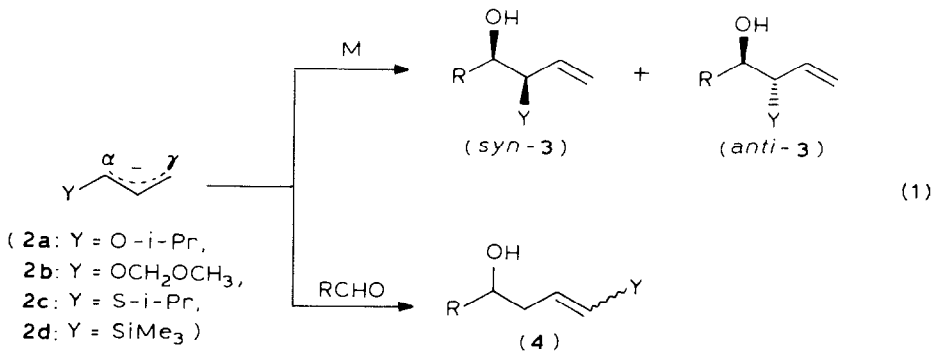
TABLE 1

REACTION OF **2a** AND **2b** WITH BENZALDEHYDE

Entry	2	Additive M	Product ratio			Total yield(%) isolated
			syn-3	*anti*-3	4	
1	**2a**	Bu_3SnCl/BF_3	100	–	–	89
2	**2a**		89	11	–	76
3	**2a**	$EtAlCl_2$	84	16	–	70
4	**2a**	Cp_2ZrCl_2	27	73	–	88
5	**2b**	Et_3Al	92	8	–	80
6	**2b**	Et_2AlCl	41	10	49	31
7	**2b**	Cp_2ZrCl_2	37	63	–	80
8	**2b**	Cp_2ZrCl_2 [a]	48	52	–	73
9	**2b**	Cp_2TiCl_2 [a]	18	82	–	32

[a] 0.5 eq. of M was used.

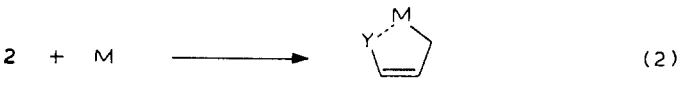


Results and discussion

Stereochemical convergence for Y = O

The reaction of **2a** and **2b** with benzaldehyde in the presence of M was investigated and the results are summarized in Table 1. By using Sn as M, *syn*-**3a** was obtained exclusively in high yield (entry 1). Presumably, Bu_3SnCl reacts at the γ-position of **2** to produce 3-isopropoxy-2-propenyltributylstannane. Although isolation of the intermediate was not tried, previous studies on the alkylation reaction of **2a** suggested regioselectivity [4], in fact this type of an allylic stannane was isolated in the reaction of **2c** and **2d**. Therefore, the *syn(erythro)* selectivity in entry 1 can be explained by an acyclic transition state proposed previously [5].

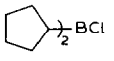
Boron and aluminium exhibit *syn(erythro)* selectivity, though the degree of selectivity is not so high as for tin (entries 2, 3, and 5). In these cases, ClBLn and ClAlLn presumably attack the γ-position of **2** to produce the *Z*-allylmetal **5** owing to the strong coordination ability of the oxygen atom toward B and Al (eq. 2).



Therefore, the *syn* isomer is produced predominantly through the six-membered

TABLE 2

REACTION OF **2c** WITH ALDEHYDES

Entry	RCHO	Additive M	Product ratio			Total yield(%) isolated
			syn-**3**	*anti*-**3**	**4**	
1	PhCHO	Bu_3SnCl/BF_3	90	10	–	78
2	$(CH_3)_2CHCHO$	Bu_3SnCl/BF_3	100	–	–	89
3	PhCHO	Ph_3SnCl/BF_3	85	15	–	80
4	PhCHO	Et_3Al	63	37	–	90
5	$(CH_3)_2CHCHO$	Et_3Al	55	45	–	92
6	PhCHO	Et_2AlCl	75	25	–	94
7	PhCHO	$EtAlCl_2$	55	34	11	78
8	PhCHO	Et_3B	52	48	–	69
9	PhCHO		60	29	11	72
10	PhCHO	n-Bu-9-BBN	65	10	25	69
11	PhCHO	Cp_2ZrCl_2 [a]	10	90	–	83
12	$(CH_3)_2CHCHO$	Cp_2ZrCl_2 [a]	20	80	–	90

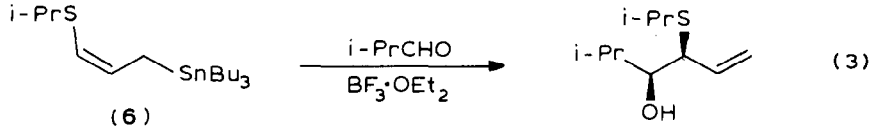
[a] 0.5 eq of M was used.

cyclic transition state [1,6]. The *syn*-selectivity of B and Al is in marked contrast with the *anti*-selectivity of the carbon analogues (crotyl-boron and -aluminum).

On the other hand, Zr and Ti [7] exhibit *anti*-selectivity as reported earlier (entries 4, 7–9). In the simple crotyl system, the direction of the selectivity is always the same with B, Al, Zr, and Ti [1]. It seems that the steric bulk of the two Cp ligands prevents intramolecular coordination as in **5** and hence the double bond is in *E*-geometry. This is confirmed for **2c** and will be discussed later.

Stereochemical convergence for $Y = S$

The reaction of **2c** with aldehydes in the presence of M was examined and the results are summarized in Table 2. Here again, use of Sn produces the *syn* isomer either exclusively or predominantly (entries 1–3). The intermediate **6** was isolated and treatment of **6** with isobutyraldehyde in the presence of $BF_3 \cdot OEt_2$ produced *syn*-**3c** exclusively (eq. 3).

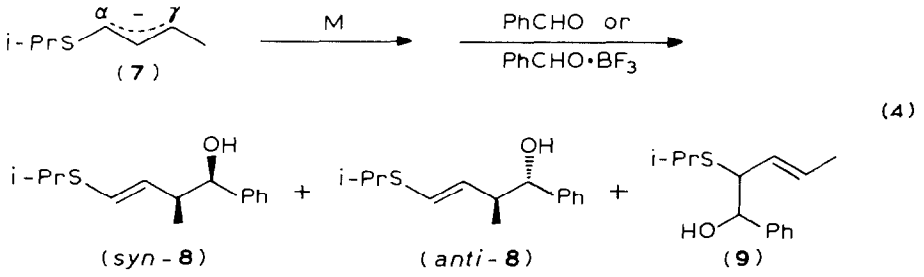


Al and B exhibit low *syn*-selectivity (entries 4–10). The degree of the *syn*-selectivity is lower than that shown in Table 1, cf. entry 7 of Table 2 vs. entry 3 of Table 1 and entry 9 of Table 2 vs. entry 2 of Table 1. The relatively low coordination ability of S toward B and Al, in comparison with the high ability of O, make it difficult to adopt a *Z* geometry as in **5**.

Zr exhibits *anti*-selectivity (entries 11 and 12) [8]. Here again the steric bulk of the two Cp ligands may force the double bond to be in *E* geometry. Irrespective of the

exact mechanism, we are now in a position to prepare both isomers (*syn* (**3a**) and *anti* (**3b**), and **3c**), either exclusively or predominantly by metal tuning.

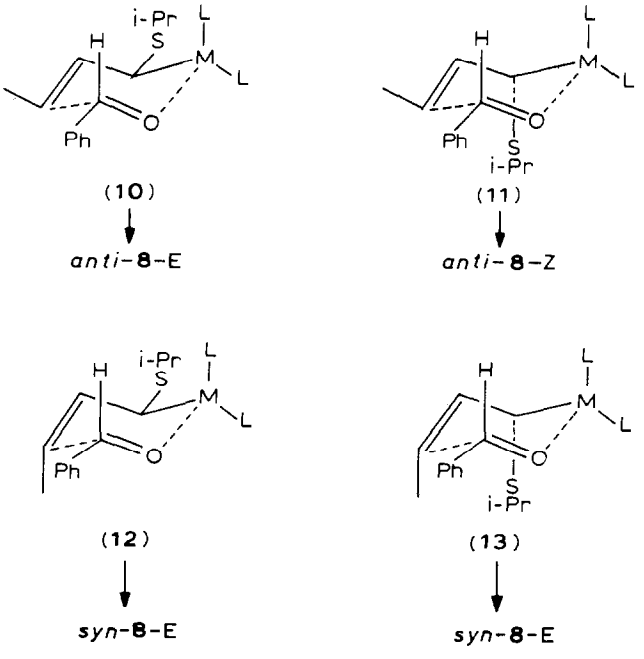
We also investigated the regio- and stereo-selectivity of the one-carbon elongated allylic carbanion **7** (eq. 4).



(4)

Although the Et_3B- and Et_3Al-ate complexes of **7** produced considerable amounts of **9** along with a 1/1 mixture of *syn*-**8** and *anti*-**8** [3], use of Cp_2ZrCl_2 and Cp_2TiCl_2 gave the γ-adduct exclusively (Table 3) [8a]. As expected from the above discussion, the *anti*-**8** was produced predominantly (entries 1 and 2). The exclusive formation of the *E*-isomer in *syn*-**8** is explained as follows. If the six-membered cyclic transition state is involved, the four isomers are derived from the four different transition states (**10**–**13**) (Scheme 1). Apparently, **13** is destabilized due to 1,3-diaxial interaction between the methyl and the i-PrS group. There is not such an interaction in **12**. Therefore, the *E*-isomer is produced in *syn*-**8**.

Quite interestingly, use of $PhCHO \cdot (BF_3)_n$ induced reversal of the diastereoselec-



SCHEME 1. Transition state geometry in the formation of **8**.

TABLE 3

REACTION OF 7 WITH BENZALDEHYDE

Entry	Additive M	RCHO	Product ratio [a]		Total yield(%) isolated
			syn-**8** (*Z*/*E*)	*anti*-**8** (*Z*/*E*)	
1	Cp_2ZrCl_2	PhCHO	18 (–/100)	82 (1/1)	64
2	Cp_2TiCl_2	PhCHO	16 (–/100)	84 (1/4)	50
3	Cp_2ZrCl_2	$PhCHO \cdot BF_3$ [b]	69 (1/3)	31 (1/1)	62
4	Cp_2ZrCl_2	$PhCHO(BF_3)_2$ [b]	78 (2/3)	22 (1/1)	60

[a] Ratio of *Z*- to *E*-olefin. 0.5 eq of M was used. [b] Mixture of PhCHO and $BF_3 \cdot OEt_2$ was added.

tivity from *anti* and *syn* (entries 3 and 4). This inversed stereoselectivity is presumably a reflection of reversal of the transition state from the cyclic six-membered chair to acyclic geometry [9].

Stereochemical convergence for Y = Si

Finally we examined metal tuning in the reaction of **2d** with aldehydes and the results are summarized in Table 4. Here again, use of Sn enables **2d** to react with aldehydes in *syn* manner (entries 1 and 2). Isolation of *syn*-**3** in the pure form was difficult owing to the presence of $BF_3 \cdot OEt_2$ which induced deoxysilylation.

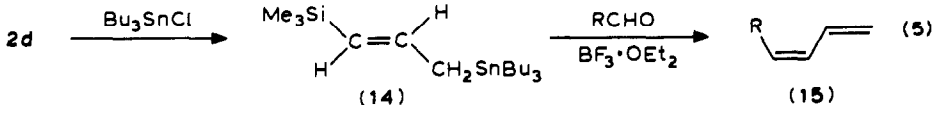
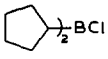
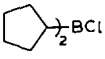
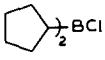
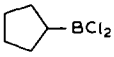


TABLE 4

REACTION OF **2d** WITH ALDEHYDES

Entry	RCHO	Additive M	Product ratio			Total yield(%) isolated
			syn-**3**	*anti*-**3**	**4**	
1	PhCHO	Bu_3SnCl/BF_3	100	–	–	77 [a]
2	n-C_9H_{19}CHO	Bu_3SnCl/BF_3	100	–	–	85 [a]
3	PhCHO	$EtAlCl_2$	4	88	7	66
4	n-PrCHO	$EtAlCl_2$	–	100	–	52
5	CH_3CH=CHCHO	$EtAlCl_2$	14	86	–	46
6	PhCHO	Et_2AlCl	–	58	42	40
7	i-PrCHO		–	100	–	60
8	PhCHO		15	79	6	33
9	PhCHO		–	71	29	62 [b]
10	PhCHO		–	100	–	10
11	PhCHO	n-Bu-9-BBN	2	96	2	6

[a] The total yield isolated refers to the *Z*-diene (**15**). [b] The boron reagent and PhCHO were added at –30°C, though they were normally added at –78°C.

TABLE 5

METAL TUNING IN **2**

Y	M			
	Sn	Al	B	Ti, Zr
C [b]	***S*** [a]	*A*	*A*	*A*
Si	***S***	*A*–*A*	*A*–*A*	*A*
S	***S***	*S*	*S*	*A*
O	***S***	*S*–***S***	*S*–***S***	*A*

S: high *syn*-selectivity. ***A***: high *anti*-selectivity. *S*: *syn*-selectivity. *A*: *anti*-selectivity.
[b] Ref. 1.

The intermediate **14** was isolated and treatment with aldehydes in the presence of $BF_3 \cdot OEt_2$ produced the *Z*-diene **15** (eq. 5) [10].

B and Al generally give the *anti* isomer predominantly and in some cases produce *anti*-**3** exclusively (entries 4 and 7). Although the *anti*-selectivity is very high with cyclopentyldichloroborane and n-Bu-9-BBN, the total yield is disappointing (entries 10 and 11).

In conclusion, the metal tuning in **2** is summarized in Table 5. Irrespective of heteroatoms (Y), Sn–BF_3 always produces *syn*-**3**, while Ti and Zr give *anti*-**3**. Al and B exhibit *anti*-selectivity for Y = C and Si, while they exhibit *syn*-selectivity for Y = S and O. The variation in selectivity is explained through three types of transition state models; the acyclic model, the cyclic six-membered chair with *Z*-geometry, and the cyclic six-membered chair with *E*-geometry.

Experimental

General information concerning instrumental and materials was described previously [11]. Bu_3SnCl, Ph_3SnCl, Cp_2ZrCl_2, Cp_2TiCl_2, $EtAlCl_2$ in hexane, and Et_2AlCl in hexane were purchased from Aldrich Chem. Co. and used as provided. Dicyclopentylboron chloride and cyclopentylboron dichloride were prepared according to the reported procedure through BH_2Cl and $BHCl_2$, respectively [12].

Reaction of ***2a*** *and* ***2b*** *in the presence of M*

The general procedure for the preparation of **2** was described previously [3]. To an ether solution of **2a** (1 mmol) or to a THF solution of **2b** (1 mmol), cooled to −78°C, M (1 mmol) was added and the resulting mixture was stirred at this temperature. Benzaldehyde (1 mmol) was added and the mixture allowed to warm to 0°C, except in the case of entry 1. If Bu_3SnCl was used, $BF_3 \cdot OEt_2$ (1 mmol) was added immediately after the addition of benzaldehyde. The reaction was quenched at 0°C by slow addition of water, except in the case where a borane derivative was used as additive, in which the recovered borane was oxidized with $H_2O/NaOH$. The organic layer was separated and the aqueous layer twice extracted with ether. The combined organic layer was dried over anhydrous $MgSO_4$. The product ratio was determined by GLPC analysis (DC 550, 5%, 3 m) and/or ^1H NMR spectroscopy. Isolation of the products was carried out by a short silica gel column. For the spectroscopic data and structure determination of 1-phenyl-2-isopropoxy-3-butenol and 1-phenyl-2-(methoxymethoxy)-3-butenol, see ref 3. 1-Phenyl-4-(methoxy)meth-

oxy-3-butenol: b.p. 115°C/2 Torr (Kugelrohr); ^{1}H NMR ($CDCl_3$): δ 2.80–3.00 (m, 2), 3.36 (s, 3), 3.40 (br-s, 1), 3.68 (s, 2), 3.84 (t, 1, J 7.0 Hz), 5.80–6.20 (m, 2), 7.20 (s, 5) ppm; IR (CCl_4): 3560, 1600, 1120, 1040 cm^{-1}; MS: m/e (M^+) 208. Anal. Found: C, 69.40; H, 7.82. $C_{12}H_{16}O_3$ calcd.: C, 69.21; H, 7.75%.

Reaction of **2c** *in the presence of M*

To an ether solution of **2c** cooled to −78°C was added an equivalent amount of M. The aldehydes were added and workup was carried out as described above. The structure determination of 1-phenyl-2-(isopropylthio)-3-butenol (**8**) and 3-(isopropylthio)-4-hydroxy-5-methylhexene (**9**) was carried out previously [3]. 1-Phenyl-4-(isopropylthio)-3-butenol: b.p. 125°C/2 Torr (Kugelrohr); ^{1}H NMR ($CDCl_3$): δ 1.25 (d, 6, J 7.0 Hz), 2.01 (br-s, 1), 2.40 (m, 2), 2.91 (septet, 1, J 7.0 Hz), 4.40 (t, 1, J 6.0 Hz), 5.40–5.90 (m, 2), 7.20 (s, 5) ppm; IR (CCl_4): 3480, 1635, 1600, 1450, 1385, 1250 cm^{-1}; MS: m/e (M^+) 222. Anal. Found: C, 70.45; H, 8.02. $C_{13}H_{18}OS$ calcd.: C, 70.23; H, 8.16%. 3-(Isopropylthio)-2-propenyltributylstannane (**6**) was isolated in 92% yield through a short silica gel column; ^{1}H NMR (CCl_4): δ 0.70–2.00 (m, 33), 1.84 (d, 2, J 8.0 Hz), 3.01 (septet, 1, J 7.0 Hz), 5.62 (d, 1, J 10.0 Hz), 5.80 ppm (td, 1, J 8.0 and 10.0 Hz); MS: m/e (M^+) 405.

Reaction of **2d** *in the presence of M*

To a THF solution of **2d** cooled at −78°C was added an equivalent amount of M, and then the aldehydes were added. A similar workup procedure was employed. The structure determination of 1-phenyl-1,3-butadiene, 1-phenyl-2-(trimethylsilyl)-3-buten-1-ol, 1-phenyl-4-(trimethylsilyl)-3-buten-1-ol, 3-(trimethylsilyl)-4-hydroxy-1-heptene, and 3-(trimethylsilyl)-4-hydroxy-5-methyl-1-hexene was carried out as previously described [3]. 3-(Trimethylsilyl)-4-hydroxy-1,5-heptadiene; ^{1}H NMR (CCl_4) *anti* isomer: δ 0.09 (s, 9), 1.22 (dd, 1, J 8.0 and 5.0 Hz), 1.70 (d, 3, J 4.5 Hz), 2.48 (br-s, 1), 4.12 (m, 1), 4.74 (dd, 1, J 16.5 and 2.0 Hz), 4.86 (dd, 1, J 10.0 and 2.0 Hz), 5.36–5.52 (m, 2), 5.80 ppm (ddd, 1, J 10.0, 10.0, and 16.5 Hz); MS: m/e (M^+) 184. Anal. Found: C, 65.04; H, 11.08. $C_{10}H_{20}OSi$ calcd.: C, 65.15; H, 10.94%. The *syn* isomer was not isolated in the pure form, so structure determination was ambiguous but was carried out through extrapolation from the other examples. *Z*-Trideca-1,3-diene; ^{1}H NMR ($CDCl_3$): δ 1.05 (t, 3, J 7.0 Hz), 1.55 (m, 14), 1.95 (m, 2), 4.75 (d, 1, J 9.0 Hz), 4.86 (d, 1, J 18.0 Hz), 5.40 (dt, 1, J 7.0 and 9.0 Hz), 5.81 (dd, 1, J 9.0 and 9.0 Hz), 6.05 ppm (ddd, J 9.0, 9.0, and 18.0 Hz); IR (CCl_4): 990, 910 cm^{-1}; MS: m/e (M^+) 180. Anal. Found: C, 86.77; H, 13.50. $C_{13}H_{24}$ calcd.: C, 86,59; H, 13.41%. 3-Trimethylsilyl-2-propenyltributylstannane (**14**) was isolated in 70% yield from **2d**; ^{1}H NMR (CCl_4): δ 0.10 (s, 9), 0.80–1.70 (m, 27), 1.81 (d, 2, J 8.0 Hz), 5.15 (d, 1, J 18.0 Hz), 5.97 ppm (td, 1, J 8.0 and 18.0 Hz); MS: m/e (M^+) 403.

References

1 For diastereofacial control of **1a**: (a) Y. Yamamoto and K. Maruyama, Heterocycles, 18 (1982) 357 (b) R.W. Hoffmann, Angew. Chem. Int. Ed. Engl., 21 (1982) 555.

2 For preliminary reports on some aspects of the present study: (a) Y. Yamamoto, Y. Saito, and K. Maruyama, Tetrahedron Lett., (1982) 4959 (b) Y. Yamamoto, Y. Saito, and K. Maruyama, J. Chem. Soc. Chem. Commun., (1982) 1326.

3 For the regiochemical convergence via Et_3B- and Et_3Al-ate complexes: Y. Yamamoto, H. Yatagai, S. Saito, and K. Maruyama, J. Org. Chem., 49 (1984) 1096.

4 For example: D.A. Evans, G.C. Andrews, and B. Buckwalter, J. Am. Chem. Soc., 96 (1974) 5560; W.C. Still and T.L. Macdonald., ibid., 96 (1974) 5561.
5 (a) Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, J. Am. Chem. Soc., 102 (1980) 7107 (b) Y. Yamamoto, H. Yatagai, Y. Ishihara, N. Maeda, and K. Maruyama, Tetrahedron Symp., 40 (1984) 2239.
6 For oxygen-substituted allylic boron compounds: (a) R.W. Hoffmann and B. Kemper, Tetrahedron Lett., (1981) 5263; ibid., (1982) 845; (b) P.G.M. Wuts and S.S. Bigelow, J. Org. Chem., 48 (1983) 3489 (c) W.R. Roush, D.J. Harris, and B.M. Lesur, Tetrahedron Lett., (1983) 2227.
7 High *anti*-selectivity is realized through the titanium reagent, H. Hiraoka, K. Furuta, N. Ikeda, and H. Yamamoto, Bull. Chem. Soc. Jpn., 57 (1984) 2777.
8 For *anti*-selective condensation via titanium reagent, see: (a) K. Furuta, Y. Ikeda, N. Meguriya, and H. Yamamoto, Bull. Chem. Soc. Jpn., 57 (1984) 2781 (b) R.W. Hoffmann and B. Kemper, Tetrahedron Symp., 40 (1984) 2219.
9 (a) Presented orally at the post ICOS-IV Kyoto Symp., August 1982; Y. Yamamoto and K. Maruyama, J. Organomet. Chem., 284 (1985) C45; (b) M.T. Reetz and M. Sauerwald, J. Org. Chem., 49 (1984) 2292.
10 P.F. Hudrlik and D. Peterson, J. Am. Chem. Soc., 97 (1975) 1464.
11 Y. Yamamoto, H. Yatagai, and K. Maruyama, J. Am. Chem. Soc., 103 (1981) 1969.
12 H.C. Brown, G.W. Kramer, A.B. Levy, and M.M. Midland, Organic Syntheses via Boranes, 1975, Wiley, New York.