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Synthetic utility of *o*-carborane: novel protective group for aldehydes and ketones☆

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Abstract

o-Carborane acts as a novel protective group of carbonyl compounds. The reaction of lithiocarborane **2**, which was prepared in an essentially quantitative yield from *o*-carborane and *n*-butyllithium, with aldehydes or ketones **1** gave the corresponding addition products, *o*-carboranyl methanol derivatives **3**, in high yields. Cleavage of *o*-carborane from **3** was carried out by treating **3** with catalytic amounts of KOH in THF/H_2O (100/1), giving the corresponding aldehydes or ketones in good to high yields along with recovered *o*-carborane. Accordingly, *o*-carborane may be utilized as a protective group stable under protic and Lewis acid conditions. Selective alkylation of an ester group, selective reduction of an ester, and selective alkylation of a ketone in the presence of an aldehyde are accomplished by using *o*-carborane protective groups. © 1999 Elsevier Science S.A. All rights reserved.

Keywords: *o*-Carborane; Protective group; Carbonyl compounds

1. Introduction

It is widely accepted that acetals and ketals are very useful as protective groups for aldehydes and ketones [1,2]. The protective groups are introduced readily by treating the carbonyl compounds with an alcohol or a diol in the presence of acid, and are stable to aqueous and nonaqueous bases, to nucleophiles including organometallic reagents, and to hydride reduction. However, acetals and ketals are readily cleaved by acid hydrolysis and Lewis acid coordination. The latter property is a drawback of these protective groups in the case of a Lewis acid-mediated reaction, in which a reactive functional group in the substrate is required to react with a Lewis acid without affecting the protective group [3]. Lewis acid-mediated or catalyzed reactions are used frequently in modern organic synthesis. Certain dithio acetals and ketals are stable to Lewis acid but unstable to strong aqueous protic acids. Other protective groups such as cyanohydrins, hydrazones, imines and oximes are less used because their removal is often difficult [1,4]. In this paper we describe *o*-carborane as a novel protective group of aldehydes and ketones, which is stable under aqueous protic acid and Lewis acid conditions and is readily cleaved under basic conditions.

2. Results and discussion

2.1. Cleavage reaction of *o*-carboranyl methanols

Aldehydes and ketones **1** undergo the addition reaction with lithiocarborane **2**, which is prepared by the reaction of *o*-carborane with *n*-BuLi, to afford the corresponding functionalized *o*-carboranyl methanols **3** [5]. As alternative methods, previously we developed the addition reactions of stannyl- [6,7], silyl- [8,9], and

☆ This paper is dedicated to the late Professor Rokuro Ogawara.

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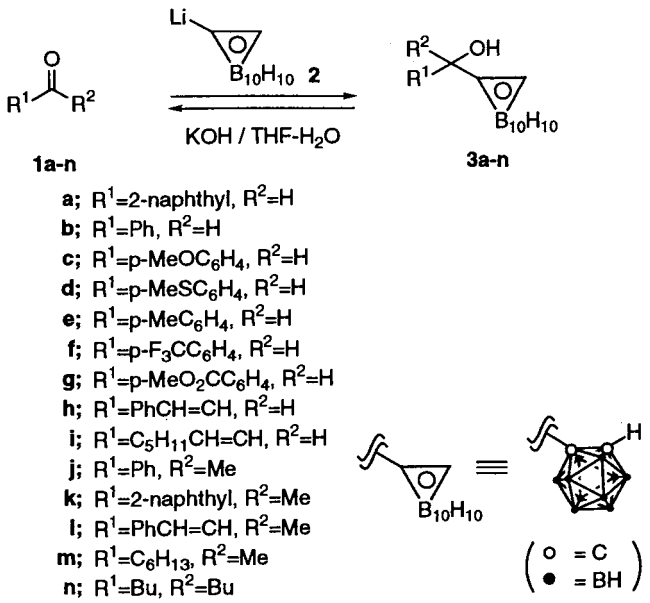
nonmetalated [10] carboranes to various electrophiles including aldehydes and ketones, which proceeded under palladium-catalyzed or tetrabutylammonium fluoride-mediated conditions. Therefore, carboranyl methanols are easily available from aldehydes and ketones under various reaction conditions. If the cleavage of the C–C bond between carbinol and *o*-carborane takes place very readily, the *o*-carborane unit may become a potentially useful protecting group to functionalized carbonyl compounds. We found that *o*-carboranyl methanols **3** were very stable under aqueous protic acid and Lewis acid conditions and were readily cleaved under basic conditions to produce the corresponding carbonyl compounds **1** and *o*-carborane (Eq. (1)).



(1)

Conditions used to cleave *o*-carborane from 1-carboranyl-2-naphthylmethanol **3a** are shown in Table 1. Several bases, such as NaOMe, pyridine, *n*-BuLi, and *t*-BuOK, were examined and KOH was the most suitable for this cleavage. The use of excess (three equivalents) and 1.1 equivalents of KOH in THF gave **1** in fair to good yields (entries 1 and 2). It was found that even a catalytic amount of KOH was enough to induce the cleavage of *o*-carborane (entry 3). Small amounts of 2-naphthylmethanol were obtained as by-product in entries 1–3. However, the presence of small amounts of water in the THF prevented formation of the by-product (entries 4 and 5) and the best result was obtained by using 0.15 equivalents of KOH in THF/H_2O (100/1) as a solvent (entry 4). Under these conditions, *o*-carborane was recovered in high yields (76% isolated yield in entry 4). It is known that *o*-carborane (*closo*) is converted to *nido*-*o*-carborane by treatment with bases. However, under the cleavage conditions, the *closo* framework was stable to KOH. Accordingly, recycling of *o*-carborane is possible. Another attractive point of this protective group is that protected aldehydes and ketones **3** are *readily crystallized* and stable to air, moisture, and acids.

Having established optimum conditions for the decarboranylation of **3a**, we next applied this procedure to various carboranyl methanols **3b**–**n** (Table 2). The carboranyl methanols **3** were prepared in essentially quantitative yield by treating aldehydes and ketones **1** with lithiocarborane **2**. The decarboranylation of **3b** proceeded smoothly to give benzaldehyde **1b** in 84% yield (entry 2). Other aromatic aldehyde derivatives **3c**–**g** bearing either an electron-donating or an electron-withdrawing group gave the corresponding aldehydes in good yields (entries 3–7). Not only aromatic aldehydes but also α,β-unsaturated aldehydes **1h** and **1i** were obtained in good to high yields from the corresponding carboranyl methanols **3h** and **3i** (entries 8 and 9). In the case of disubstituted carboranyl methanols **3j**–**n**, which were prepared readily by the addition of lithiocarborane **2** with the corresponding ketones, the cleavage reaction proceeded smoothly to give the corresponding ketones **1j**–**n** in good to high yields (entries 10–14). The carboranyl methanols **3** were very stable under strong acid or Lewis acid conditions. When benzaldehyde dimethyl acetal was treated with $TiCl_4$ (two equivalents) in dichloromethane, benzaldehyde **1b** was obtained in 82% yield. However, treatment of **3b** with aqueous HCl(1 N) or $TiCl_4$ (two equivalents) for 2 days gave no benzaldehyde, but **3b** was recovered quantitatively.

Table 1
The decarboranylation of 1-carboranyl-2-naphthylmethanol **3a** promoted by KOH at room temperature

Entry	Amount (equivalents) of KOH	Solvent	Yield[a] of **1** (%)
1	3.0	THF	38[b]
2	1.1	THF	58[b]
3	0.15	THF	57[b]
4	0.15	THF/H_2O (100/1)	92
5	0.15	THF/H_2O (10/1)	60

[a] Yields were determined by GC analysis using hexadecane as an internal standard.

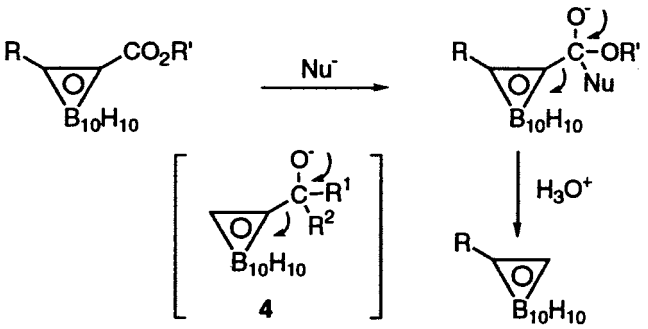
[b] Reduced product (2-naphthylmethanol) was also produced in 8% (entry 1), 17% (entry 2), and 14% (entry 3) yield, respectively.

Table 2
The decarboranylation of various *o*-carboranylmethanols **3** promoted by a catalytic amount of KOH in THF/H_2O (100/1)

Entry	Aldehyde and ketone **1**	Carboranylmethanol **3**	Time (days)	Yield[a] (%) (isolated yield)[b]
1	**1a**	**3a**	2	92[c] (85)
2	**1b**	**3b**	3	84[c]
3	**1c**	**3c**	1	88
4	**1d**	**3d**	1	74
5	**1e**	**3e**	3	70
6	**1f**	**3f**	2	75[c]
7	**1g**	**3g**	2	74
8	**1h**	**3h**	2	86 (74)
9	**1i**	**3I**	2	62
10	**1j**	**3j**	2	78
11	**1k**	**3k**	3	83 (66)
12	**1l**	**3l**	2	93
13	**1m**	**3m**	2	92[d]
14	**1n**	**3n**	2	97

[a] Yields were determined by ^{1}H-NMR using *p*-xylene as an internal standard.
[b] In some cases, the products were isolated by using silica gel column chromatography and the isolated yields are shown in parenthesis.
[c] Yields were determined by GC analysis using hexadecane as an internal standard.
[d] NaOH (0.15 equivalents) was used instead of KOH.

It is known that decarboxylation of *o*-carboranyl carboxylates is accomplished by sodium ethoxide [11], *n*-butyllithium [12], or potassium hydroxide [13], giving the parent *o*-carboranes (Eq. (2)) [14]. In the present reaction, an ionic species **4** generated by treatment of **3** with KOH would undergo a facile cleavage reaction, since *o*-carborane is a reasonably good leaving group (as shown in Eq. (2)).



(2)

2.2. Selective alkylation of ester in the presence of aldehyde

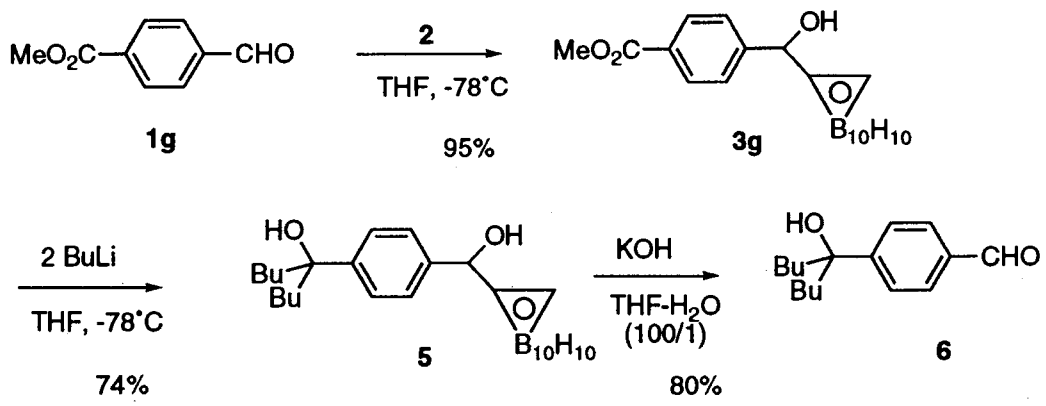
Next we examined representative reactions of bifunctional molecules to demonstrate the synthetic utility of *o*-carborane as a protective group. The addition of lithiocarborane **2** to aldehyde **1a**, which has an ester and aldehyde functional group in the same molecule, at −78°C gave carboranylmethanol **3g** chemoselectively in 95% yield (Scheme 1). The adduct **3g** was treated with *n*-BuLi (three equivalents) at −78°C to give dibutylated compound **5** in 74% yield; only the ester group reacted with *n*-BuLi and the carboranylmethanol group was stable to the reagent. The decarboranylation of **5** proceeded very smoothly by treatment with KOH (0.15 equivalents) in THF–H_2O (100/1), giving the corresponding aldehyde **6** in 80% yield. Here also, *o*-carborane was recovered in an essentially quantitative yield.

2.3. Selective reduction of ester in the presence of aldehyde

The protective group of **3g** was also stable to hydride reduction using lithium aluminum hydride. The reduction of **3g** with lithium aluminum hydride in THF under reflux gave the diol **7** in 95% yield (Scheme 2). Removal of *o*-carborane from **7** proceeded very smoothly under the usual reaction condition, giving the corresponding aldehyde **8**, in which the ester group of **1g** was reduced chemoselectively to the alcohol, in 77% yield.

2.4. Selective alkylation of ketone in the presence of aldehyde

Furthermore, chemoselective allylation of a ketone group in the presence of an aldehyde group was examined by using bifunctional molecule **9** [15] (Scheme 3). The chemoselective addition of *o*-carborane to the alde-



Scheme 1.

hyde group of **9** was accomplished by the palladium catalyzed reaction [6]; the reaction of **9** with *o*-carboranyltributylstannane in the presence of a catalytic amount of $Pd_2dba_3{\cdot}CHCl_3$ (10 mol%)/dppe (20 mol%) in THF under reflux gave the adduct **10** in 69% yield. The reaction of lithiocarborane **2** with **9** gave a mixture of products which arose from the addition to both a ketone and aldehyde group. The reaction of the ketone **10** with *n*-BuLi (two equivalents) gave the alkylated adduct **11**. The decarboranylation of **11**, which was used without purlfication, proceeded very smoothly by treatment with KOH, giving the corresponding aldehyde **12** in 80% yield in two steps from **10**.

2.5. Lewis acid-promoted selective monoallylation of dialdehyde

The *o*-carborane protective group was also stable to Lewis acid-promoted allylation (Scheme 4). The $TiCl_4$-mediated reaction of allyltrimethylsilane with the aldehyde **14**, which was prepared by the selective monoaddition of **2** to **13** (four equivalents), gave homoallylic alcohol **15**. The decarboranylation of crude product **15** proceeded smoothly by the treatment with NaOH (0.15 equivalents) in THF-H_2O (100/1), giving the corresponding monoallylated aldehyde **16** in 67% yield in two steps from **14**. In this case, the use of NaOH was more effective for the cleavage reaction than that of KOH.

These results indicate that *o*-carborane moiety can serve as a useful protective group for aldehydes and that chemoselective protection of an aldehyde functional group in the presence of a ketone and/or ester is achieved using the *o*-carborane protective group.

3. Conclusion

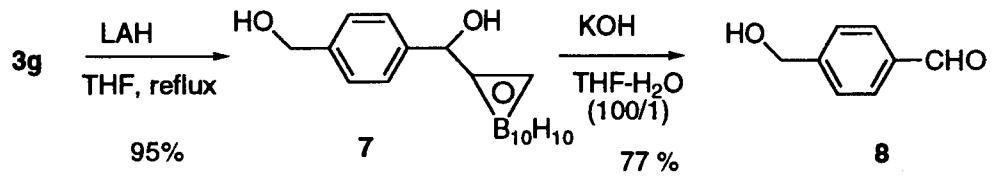
Although acetals and ketals have been very popular and useful protective groups for aldehydes and ketones, those protective groups which are stable to protic and Lewis acid conditions have not been available for organic synthesis. *o*-Carborane can be readily introduced to those carbonyl compounds chemoselectively under the anionic condition or even under the mild conditions, and the corresponding carboranyl carbinols are stable to protic and Lewis acid conditions and cleaved easily under base-catalyzed conditions. We believe that this new protective methodology will be utilized widely in modern organic synthesis.

4. Experimental section

^1H- and ^{13}C-NMR spectra were recorded on a Jeol GSX-270 spectrometer. The chemical shifts are reported in δ units relative to internal tetramethylsilane. IR spectra were recorded on a Shimadzu FTIR-8200A spectrometer. High-resolution mass spectra were recorded on a Jeol JMS-HX11O. Most commercially supplied chemicals were distilled and stored over molecular sieves.

*4.1. A representative procedure of formation (**1a**→**3a**)*

To a solution of *o*-carborane (720 mg, 5 mmol) in dry THF (50 ml) at −78°C was added *n*-BuLi (3.1 ml, 1.6 M in hexane) dropwise with stirring. The mixture was stirred for 30 min at −78°C and **1a** (859 mg, 5.5 mmol) was added. The solution was stirred for 1 h and then warmed to room temperature. After quenching with water, the mixture was extracted with ether and dried over anhydrous magnesium sulfate. Evaporation of the solvents followed by purification using silica gel column chromatography (hexane:ethyl acetate = 5:1) afforded **3a** (1.29 g, 4.3 mmol, 86%). In no case was disubstituted carborane obtained. The use of dilute solutions of lithium carborane (ca. 0.1 M) is essential to obtain selectively the mono-substituted carborane derivatives. Furthermore, in the addition of **2** to alde-



Scheme 2.

hyde **1g**, which contains ester and aldehyde functional groups in the same molecule, carboranylmethanol **3g** was obtained chemoselectively in 95% yield under the same condition (entry 7).

*4.1.1. o-Carboranyl-2-naphthylmethanol (**3a**)*

White solid: m.p. 147°C; IR (KBr) 3585, 3086, 2633, 2603, 2580, 2552, 1356, 1315, 1247, 1184, 1166, 1083 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.87 (m, 3H), 7.78 (s, 1H), 7.54 (m, 2H), 7.45 (dd, $J = 9.0$, 2.0 Hz, 1H), 5.44 (d, $J = 3.5$ Hz, 1H), 3.84 (s, 1H), 2.72 (d, $J = 3.5$ Hz, 1H). HRMS (FAB) Calc. for $C_{13}H_{20}OB_{10}$: m/z 302.2445. Found: m/z 302.2450. Anal. Calc. for $C_{13}H_{20}OB_{10}$: C, 51.98, H, 6.71. Found: C, 51.70, H, 6.41%

*4.1.2. o-Carboranylbenzyl alcohol (**3b**)*

Colorless solid: m.p. 70°C; IR (KBr) 3550, 3100, 2550, 1490, 1460, 1100, 1040, 770, 710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.36 (m, 5H), 5.27 (d, $J = 3.5$ Hz, 1H). 3.81 (bs, 1H), 2.56 (d, $J = 3.5$ Hz, 1H) MS (EI) m/z 250 (M^+), 233 ($M^+ - OH$), 108 ($M^+ -$carborane), 77 (Ar). Anal. Calc. for $C_9H_{18}OB_{10}$; C, 43.18 H, 7.25. Found: C, 42.98, H, 7.09%.

*4.1.3. o-Carboranyl-p-methoxybenzyl alcohol (**3c**)*

White crystal: m.p. 111°C; IR ($CHCl_3$) 3600, 3500 ~ 3150, 3150 ~ 2850, 2840, 2570, 1610, 1500, 1300, 1220, 1170, 1090, 1030 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.25 (d, $J = 9.0$ Hz, 2H), 6.91 (d, $J = 9.0$ Hz, 2H), 5.22 (d, $J = 3.0$ Hz, 1H), 3.83 (s, 3H), 3.78 (bs, 1H), 2.48 (d, $J = 3.0$ Hz, 1H). MS (EI) m/z 280 (M^+), 264 ($M^+ - H$), 121 (MeOPhC), 109 (MeOPh), 94 (OPh), 77 (Ph). HRMS (EI): Calc. for $C_{10}H_{20}O_2B_{10}$ m/z 282.2394. Found m/z 282.2395. Anal. Calc. for $C_{10}H_{20}O_2B_{10}$: C, 42.80, H, 7.19. Found: C, 42.20, H, 6.95%.

*4.1.4. o-Carboranyl-p-methylthiabenzyl alcohol (**3d**)*

White solid: m.p. 117°C; IR (KBr) 3400, 3087, 2572, 1596, 1492, 1434, 1404, 1180, 1091, 1047, 1014 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.24 (s, 4H), 5.23 (d, $J = 3.0$ Hz, 1H), 3.81 (s, 1H), 2.55 (d, $J = 3.0$ Hz, 1H), 2.50 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ 140.76, 134.91, 127.02, 126.13, 78.56, 74.75, 59.26, 15.35. HRMS (FAB) Calc. for $C_{10}H_{20}OB_{10}S$: m/z 298.2166. Found: m/z 298.2170. Anal. Calc. for $C_{10}H_{20}OB_{10}S$: C, 40.52; H, 6.80; S, 10.82. Found: C, 40.52; H, 6.65; S, 11.10%.

*4.1.5. 1-(o-Carboranyl)-p-methylbenzyl alcohol (**3e**)*

Liquid: IR ($CHCl_3$) 3600, 3500 ~ 3150, 3150 ~ 2800, 2570, 1730, 1650, 1610, 1095, 1010, 900 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.20 (s, 4H), 5.23 (d, $J = 3.0$ Hz, 1H), 3.77 (bs, 1H), 2.51 (d, $J = 3.0$ Hz, 1H), 2.37 (s, 3 H). MS (EI) m/z 264 (M^+), 143 (carborane), 121 ($M^+ -$ carborane), 93 (MePh): HRMS (EI) Calc. for $C_{10}H_{20}OB_{10}$ m/z 266.2445. Found m/z 266.2448.

*4.1.6. o-Carboranyl-p-trifluoromethylbenzyl alcohol (**3f**)*

White solid: IR (KBr) 3674, 3553, 3444, 3087, 2970, 2937, 2900, 2582, 1622, 1419, 1384, 1325, 1247, 1168 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.67 (d, $J = 8.0$ Hz, 2H), 7.48 (d, $J = 8.0$ Hz, 2H), 5.34 (d, $J = 3.0$ Hz, 1H), 3.94 (s, 1H), 2.73 (d, $J = 3.0$ Hz, 1H). HRMS (FAB) Calc. for $C_{10}H_{17}OB_{10}F_3$: m/z 320.2162. Found: m/z 320.2152.

*4.1.7. o-Carboranyl-(4-methexycarbonylphenyl)methanol (**3g**)*

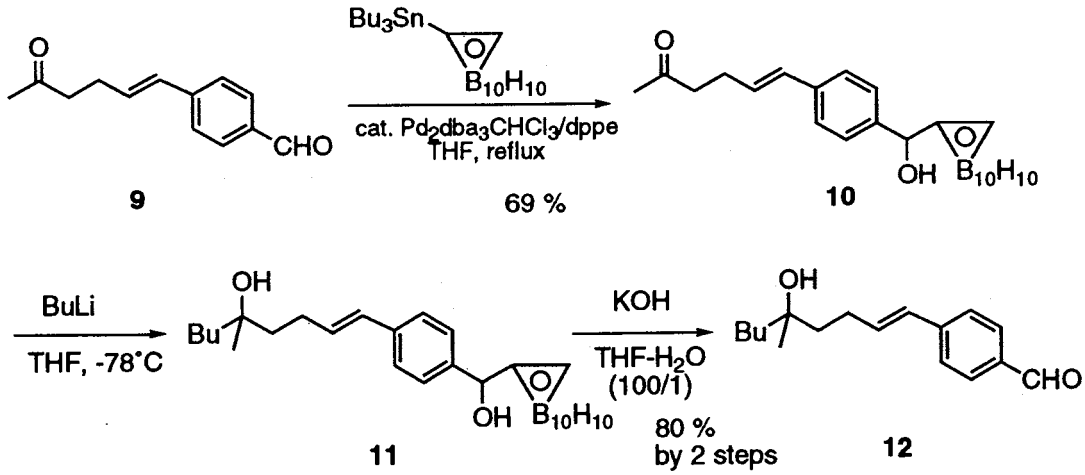
White solid: m.p. 152°C; IR (KBr) 3367, 3088, 2954, 2619, 1685, 1610, 1577, 1434, 1407,1317,1294, 1188,1114, 1085, 1020 cm^{-1}. ^{1}HNMR ($CDCl_3$) δ 8.06 (d, $J = 8.0$ Hz, 2H), 7.42 (d, $J = 8.0$ Hz, 2H), 5.33 (d, $J = 3.5$ Hz, 1H), 3.93 (s, 3H), 3.89 (s, 1H), 2.70 (d, $J = 3.5$ Hz, 1H). HRMS (FAB) Calc. for $C_{11}H_{20}O_3B_{10}$: m/z 310.2343. Found: m/z 310.2355. Anal. Calc. for $C_{11}H_{20}O_3B_{10}$: C, 42.84; H, 6.54. Found: C, 42.76; H, 6.48%.

*4.1.8. trans-1-(o-Carboranyl)-3-phenyl-2-propen-1-ol (**3h**)*

Liquid; IR (CCl_4) 3590, 3500 ~ 3200, 3060, 2560, 1930, 1640, 1480, 1440, 1360, 1180, 1080, 1000, 950 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.43 ~ 7.28 (m, SH), 6.63 (d, $J = 15.0$ Hz, 1H), 6.09 (dd, $J = 15.0$, 7.5 Hz, 1H), 4.77 (dd, $J = 7.5$, 4.0 Hz, 1H), 4.07 (bs, 1H), 2.24 (d, $J = 4.0$ Hz, 1H). MS (EI) 276 (M^+), 143 (carborane), 133 ($M^+ -$carborane). HRMS (EI): Calc. for $C_{11}H_{20}OB_{10}$: m/z 278.2445. Found: m/z 278.2446.

*4.1.9. 1-o-Carboranyl-2-octen-1-ol (**3i**)*

Liquid: IR (CCl_4) 3583, 3435, 3085, 2956, 2927, 2856, 1085, 1018 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 5.77 (dt, $J =$ 15.0, 7.5 Hz, 1H), 5.40 (dd, $J = 15.0$, 8.0 Hz, 1H), 4.52 (dd, $J = 8.0$, 4.0 Hz, 1H) 4.01 (s, 1H), 2.09 (m, 3H), 1.43 ~ 1.26 (m, 6H), 0.90 (t, $J = 6.5$ Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ 137.73, 127.56, 77.92, 73.77, 58.31, 31.93,



Scheme 3.

31.3, 28.28, 22.37, 13.96. HRMS (FAB) Calc. for $C_{10}H_{26}OB_{10}$: m/z 272.2915. Found: m/z 272.2923. Anal. Calc. for $C_{10}H_{26}OB_{10}$: C, 44.42, H, 9.69. Found: C, 44.12, H, 9.42%.

*4.1.10. 1-o-Carboranyl-1-phenylethanol (**3j**)*

White solid: m.p. 118°C; IR (KBr) 3589, 3566, 3367, 3064, 2989, 2586, 1492, 1446, 1379, 1176, 1145, 1072, 914 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.35 ~ 7.48 (m, SH), 3.43 (s, 1H), 2.47 (s, 1H), 1.94 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ 142.63, 128.75, 128.40, 125.70, 74.75, 61.65, 32.19, 28.39. HRMS (FAB) Calc. for $C_{10}H_{20}OB_{10}$: m/z 266.2445. Found: m/z 266.2448. Anal. Calc. for $C_{10}H_{20}OB_{10}$: C, 45.4, H, 7.63. Found: C, 44.8, H, 7.60%.

*4.1.11. 1-o-Carboranyl-1-(2-naphthyl)ethanol (**3k**)*

White solid: m.p. 148°C IR (KBr) 3566, 3078, 3063, 2575, 1598, 1506, 1446, 1380, 1355, 1271, 1215, 1186, 1128, 1076, 1016 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.94 (s, 1H), 7.86 (m, 3H), 7.55 (m, 3H), 3.50 (s, 1H), 2.64 (s, 1H), 2.05 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ 140.0, 132.9, 132.6, 128.6, 128.1, 127.6, 127.0, 126.8, 125.0, 123.4, 84.1, 74.9, 61.74, 32.39. HRMS (FAB) Calc. for $C_{14}H_{22}OB_{10}$: m/z 316.2602. Found: m/z 316.2599. Anal. Calc. for $C_{14}H_{22}OB_{10}$: C, 53.48, H, 7.05. Found: C, 53.31, H, 6.88%.

*4.1.12. 2-o-Carboranyl-4-phenyl-3-buten-2-ol (**31**)*

White solid: m.p. 137°C; IR (KBr) 3589, 3076, 3028, 2997, 2933, 2594, 2563, 1598, 1577, 1494, 1375, 1296, 1274, 1178, 1114, 1018 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.43–7.29 (m, SH), 6.70 (d, $J = 16.0$ Hz, 1H), 6.23 (d, $J = 16.0$ Hz, 1H), 4.07 (s, 1H), 2.23 (s, 1H), 1.67 (s, 3H). HRMS (FAB) Calc. for $C_{12}H_{22}OB_{10}$: m/z 292.2602. Found: m/z 292.2612. Anal. Calc. for $C_{12}H_{22}OB_{10}$: C, 49.6; H, 7.64. Found: C, 49.5; H, 7.50%.

*4.1.13. 2-o-Carboranyloctan-2-ol (**3m**)*

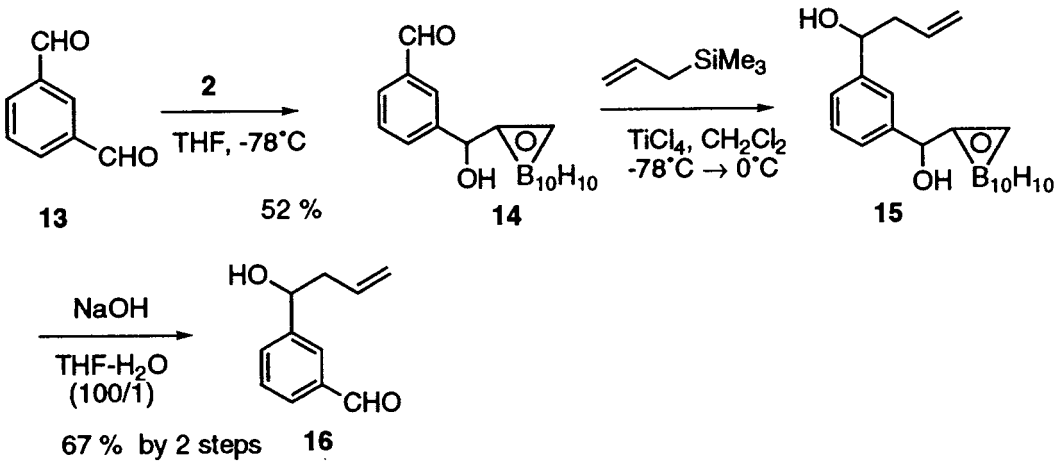
Colorless oil: IR ($CDCl_3$) 3584, 3475, 3091, 2956, 2929, 2858, 2578, 914 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 4.09 (s, 1H), 1.84 (s, 1H), 1.71 (t, $J = 8.0$ Hz, 2H), 1.43 (s, 3H), 1.29 (m, 8H), 0.89 (t, $J = 7.0$ Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ 85.58, 73.46, 60.38, 43.05, 31.67, 29.46, 27.82, 24.42, 22.55, 13.96. Anal. Calc. for $C_{10}H_{28}OB_{10}$: C, 44.09; H, 10.36. Found: C,43.79; H, 10.09%.

*4.1.14. 5-o-Carboranylnonan-5-ol (**3n**)*

Colorless oil: IR (KBr) 3589, 3475, 3089, 2960, 2933, 2873, 2578, 1465, 1380, 1342, 1257, 1124, 1080 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 4.09 (s, 1H), 1.89 (s, 1H), 1.69 (m, 4H), 1.32 (m, 8H), 0.93 (t, $J = 7.0$ Hz, 6H). ^{13}C-NMR ($CDCl_3$) δ 85.58, 75.33, 60.44, 40.14, 26.52, 22.89, 13.88. HRMS (FAB) Calc. for $C_{11}H_{30}OB_{10}$: m/z 288.3228. Found: m/z 288.3232.

*4.2. A representative procedure of cleavage reaction (**3a → 1a**)*

To a THF/H_2O (100/1, 9 ml) solution of **3a** (274 mg, 0.91 mmol) was added KOH (7.7 mg, 0.136 mmol, 0.15 equivalents) at room temperature and the mixture was stirred for 2 days. The reaction was quenched with saturated aqueous ammonium chloride solution. The mixture was extracted with ether, dried over anhydrous magnesium sulfate, and concentrated. Purification by silica gel column chromatography with hexane/ethyl acetate (10:1) gave the corresponding aldehyde **1a** (121 mg, 0.775 mmol, 85%, 92% by GC) first and then *o*-carborane (100 mg, 0.69 mmol, 76%). **1h** and **1k** were also obtained from **3h** and **3k** in the same manner in 74 and 66% isolated yields, respectively (entries 8 and 11). In other cases, yields were determined by ^{1}H-NMR and/or GC analysis as shown in Table 2.



Scheme 4.

4.3. Selective alkylation of ester **1g**

4.3.1. 5-[4-(o-Carboranylhydroxymethyl) phenyl]nonan-5-ol (**5**)

To a solution of compound **3g** (100 mg, 0.32 mmol) in dry THF (3 ml) at −78°C was added *n*-BuLi (0.6 ml, 1.63 M in hexane) dropwise with stirring. The mixture was stirred for 30 min at −78°C and then warmed to room temperature. After quenching with saturated aqueous ammonium chloride solution, the mixture was extracted with ether and dried over anhydrous magnesium sulfate. Evaporation of the solvents followed by purification using silica gel column chromatography (hexane:ethyl acetate = 10:1) afforded **5** (94 mg, 0.24 mmol, 74%) as a colorless liquid: IR (neat) 3361, 3089, 2956, 2933, 2582, 1465, 1411, 1342, 1299, 1288, 1253, 1207 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.40 (d, $J = 8.0$ Hz, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 5.26 (d, $J = 3.0$ Hz, 1H), 3.84 (s, 1H), 2.57 (d, $J = 3.0$ Hz, 1H), 1.82–1.75 (m, 4H), 1.60–1.56 (m, 8H), 0.82 (t, $J = 7.0$ Hz, 6H). HRMS (FAB, $M^+ - H$) Calc. for $C_{18}H_{35}O_2B_{10}$: m/z 393.3568. Found: m/z 393.3567.

4.3.2. 5-(4-Formylphenyl)nonan-5-ol (**6**)

To a THF/H_2O (100/1, 4 ml) solution of **5** (153 mg, 0.39 mmol) was added KOH (3.3 mg, 0.059 mmol, 0.15 equivalents) at room temperature and the mixture was stirred for 1 day. The reaction was quenched with saturated aqueous ammonium chloride solution. The mixture was extracted with ether, dried over anhydrous magnesium sulfate, and concentrated. Purification by silica gel column chromatography with hexane/ethyl acetate (10:1) gave the corresponding aldehyde **6** (77 mg, 0.31 mmol, 80%) as a yellow oil: ^{1}H-NMR ($CDCl_3$) δ 9.98 (s, 1H), 7.85 (d, $J = 8.0$ Hz, 2H), 7.54 (d, $J = 8.0$ Hz, 2H), 1.78 (m, 4H), 1.22 (m, 8H), 0.77 (t, $J = 7.0$ Hz, 6H). HRMS (FAB) Calc. for $C_{16}H_{24}O_2$: m/z 248.1776. Found: m/z 248.1764.

4.4. Selective reduction of ester **1g**

4.4.1. o-Carboranyl-(4-hydroxymethyl phenyl)methanol (**7**)

To a solution of **3g** (163 mg, 0.53 mmol) in dry THF (5 ml) at room temperature was added lithium aluminum hydride (139 ml, 3.70 mmol) with stirring. The mixture was stirred for 4 h under reflux and cooled to 0°C. After quenching with saturated aqueous ammonium chloride solution, the mixture was extracted with ether and dried over anhydrous magnesium sulfate. Evaporation of the solvents followed by purification using silica gel column chromatography (hexane:ethyl acetate = 1:2) afforded **7** (141 mg, 0.50 mmol, 95%) as a white solid: m.p. 132°C; IR (KBr) 3516, 3454, 3205, 3084, 3062, 2916, 2879, 2580, 1419, 1301, 1211, 1091, 1016 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 7.40 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 5.27 (d, $J = 3.0$ Hz, 1H), 4.72 (s, 2H), 3.87 (s, 1H), 2.74 (s, 1H), 1.78 (s, 1H). HRMS (FAB) Calc. for $C_{10}H_{20}O_2B_{10}$: m/z 282.2394. Found: m/z 282.2405. Anal. Calc. for $C_{10}H_{20}O_2B_{10}$: C, 42.8; H, 7.19. Found: C, 42.5; H, 7.08.

4.4.2. 4-Hydroxymethylbenzaldehyde (**8**)

To a THF/H_2O (100/1, 2 ml) solution of **7** (40 mg, 0.143 mmol) was added KOH (1.2 mg, 0.02 mmol, 0.15 equivalents) at room temperature and the mixture was stirred for 2 days. The reaction was quenched with saturated aqueous ammonium chloride solution. The mixture was extracted with ether, dried over anhydrous magnesium sulfate, and concentrated. Purification by silica gel column chromatography with hexane/ethyl acetate (1:1) gave the corresponding aldehyde **8** (15 mg, 0.11 mmol, 77%) as a white needle: IR (KBr) 3427, 2922, 2850, 1678, 1608 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 9.99 (s, 1H), 7.87 (d, $J = 8.0$ Hz, 2H), 7.52 (d, $J = 8.0$ Hz, 2H), 4.80 (s, 2H), 2.08 (bs, 1H). HRMS (FAB) Calc. for $C_8H_8O_2$: m/z 136.0524. Found: m/z 136.0523.

4.5. Selective reduction of ketone **9**

4.5.1. 4-(5-Oxo-l-hexenyl)benzaldehyde (**9**)

This was synthesized via Heck reaction of *p*-bromobenzaldehyde and 5-hexer-2-one, which was prepared by the literature procedure [15]. Colorless oil: IR (KBr) 2922, 2841, 1691, 1600, 1566, 1366, 1164, 914, 742, cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 10.04 (s, 1H), 7.89 (d, $J = 7.2$ Hz, 2H), 7.56 (d, $J = 7.2$ Hz, 2H), 6.52 (d, $J = 15.0$ Hz, 1H), 6.47 (dt, $J = 15.O$, 5.5 Hz, 1H), 2.73 (t, $J = 6.0$ Hz, 2H), 2.62 (dt, $J = 5.5$, 6.0 Hz, 2H), 2.26 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ 207.08, 191.15, 143.12, 134.68, 132.72, 129.64, 129.38, 126.07, 42.16, 29.49, 26.69. HRMS (FAB) Calc. for $C_{13}H_{14}O_2$: m/z 202.0994. Found: m/z 202.0993.

4.5.2. 6-[4-(o-Carboranylhydroxymethyl)phenyl]-5-hexen-2-one (**10**)

A solution of **9** (161 mg, 0.80 mmol), tributylstannylcarborane (442 mg, 0.96 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (167 mg, 0.16 mmol), and bisdiphenylphosphinoethane (dppe) (126 mg, 0.32 mmol) in dry THF (5 ml) was stirred under reflux for 4 h. Evaporation of the solvent followed by purification using silica gel column chromatography (hexane:ethyl acetate = 5:1) afforded **10** (191 mg, 0.55 mmol, 69%) as a yellow oil: IR (KBr) 3583, 3392, 3084, 303O, 2956, 2922, 2576, 1701, 1363, 1087, 1047 cm^{-1}. ^{1}H-NMR ($CDCl_3$) 7.44 (d, $J = 8.0$ Hz, 2H), 7.34 (d, $J = 8.0$ Hz, 2H), 6.50 (d, $J = 16.0$ Hz, 1H), 6.33 (dt, $J = 16.O$, 6.5 Hz, 1H), 5.33 (d, $J = 3.0$ Hz, 1H), 3.91 (s, 1H), 3.31 (d, $J = 3.0$ Hz, 1H), 2.73 (t, $J = 7.0$ Hz, 2H), 2.58 (dt, $J = 7.0$, 6.5 Hz, 2H), 2.27 (s, 3H). ^{13}C-NMR ($CDCl_3$) δ 208.7, 138.5, 137.3, 130.1, 129.9, 126.8, 126.1, 78.76, 74.64, 59.23, 42.93, 29.95, 26.98.

4.5.3. 4-(5-Hydroxy-5-methyl-1-nonenyl)benzaldehyde (**12**)

To a solution of compound **10** (67 mg, 0.19 mmol) in dry THF (2 ml) at -78°C was added *n*-BuLi (0.46 ml, 1.63 M in hexane) dropwise with stirring. The mixture was stirred for 30 min at -78°C and then warmed to room temperature. After quenching with saturated aqueous ammonium chloride solution, the mixture was extracted with ether, dried over anhydrous magnesium sulfate, and concentrated. The residue was dissolved in a THF/H_2O (100/1, 2 ml) solution and KOH (1.6 mg, 0.03 mmol, 0.15 equivalents) was added. The mixture was stirred at room temperature for 2 days. After quenching with saturated aqueous ammonium chloride solution, the mixture was extracted with ether, dried over anhydrous magnesium sulfate, and concentrated. Purification by silica gel column chromatography with hexane/ethyl acetate (4:1) gave the corresponding aldehyde **12** (40 mg, 0.15 mmol, 80%) as a colorless oil: IR (KBr) 3427, 3028, 2956, 2931, 286O, 2594, 1695, 1602, 1566, 1215, 1166 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 10.04, (s, 1H), 7.89 (d, $J = 8.0$ Hz, 2H), 7.56 (d, $J = 8.0$ Hz, 2H), 6.55 (m, 2H), 2.43 (m, 2H), 1.73 (m, 2H), 1.59 (m, 2H), 1.31 (s, 3H), 1.03 (t, $J = 7.0$ Hz, 3H), 1.42 (m, 6H). ^{13}C-NMR ($CDCl_3$) δ 191.7, 143.9, 135.2, 134.9, 130.1, 128.9, 126.3, 72.59, 41.81, 40.83, 27.76, 26.89, 26.12, 23.24, 14.05. HRMS (FAB) Calc. for $C_{17}H_{24}O_2$: m/z 260.1776. Found: m/z 260.1765.

4.6. Selective monoallylation of dialdehyde **13**

4.6.1. 3-(o-Carboranylhydroxymethyl)benzaldehyde (**14**)

To a solution of *o*-carborane (144 mg, 1.0 mmol) in dry THF (100 ml) at -78°C was added *n*-BuLi (0.66 ml, 1.68 M in hexane) dropwise and the mixture was stirred for 30 min at -78°C. This mixture was added to a solution of **13** (522 mg, 3.9 mmol) in THF (10 ml) dropwise at -78°C. The solution was stirred for 1 h and then warmed to room temperature. After quenching with saturated aqueous ammonium chloride solution, the mixture was extracted with ether and dried over anhydrous magnesium sulfate. Evaporation of the solvents followed by purification using silica gel column chromatography (hexane:ethyl acetate = 4:1) afforded **14** (144 g, 0.52 mmol, 52%) as a white solid: m.p. 147.5°C. IR (CCl_4) 3392, 3090, 2579, 1685, 1604, 1230, 1141, 1089, 1047, 1018 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 10.02, (s, 1H), 7.91–7.84 (m, 2H), 7.65–7.55 (m, 2H), 5.37 (d, $J = 3.6$ Hz, 1H), 4.01 (s, 1H), 3.02 (d, $J = 3.6$ Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ 191.6, 139.9, 136.6, 132.7, 130.9, 129.4, 127.3, 74.3, 58.9, 27.7. HRMS (FAB) Calc. for $C_{10}H_{18}O_2B_{10}$: m/z 280.2238. Found: m/z 280.2240.

4.6.2. 3-(1-Hydroxy-3-buteny)benzaldehyde (**16**)

To a solution of **14** (57 mg, 0.21 mmol) and allyltrimethylsilane (36 μl, 0.22 mmol) in dry CH_2Cl_2 (1 ml) at -78°C was added $TiCl_4$ (0.8 ml, 1.0 M in CH_2Cl_2) dropwise and the mixture was stirred for 1 h at -78°C. After quenching with saturated aqueous sodium hydrogen carbonate solution, the mixture was extracted with ether, dried over anhydrous magnesium sulfate, and concentrated. The residue was dissolved in a THF/H_2O (100/1, 2 ml) solution and NaOH (1.2 mg, 0.03 mmol, 0.15 equivalents) was added. The mixture was stirred at room temperature for 1 day. After quenching with saturated aqueous ammonium chloride solution, the mixture was extracted with ether, dried over anhydrous magnesium sulfate, and concentrated. Purification by silica gel column chromatography with hexane/ethyl acetate (10:1) gave the corresponding aldehyde **16** (24 mg, 0.14 mmol, 67%) as a colorless oil: IR (CCl_4) 3408, 3076, 2956, 2927, 2856, 1693, 1641, 1602, 1483, 1466, 1443, 1414, 1389 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 9.99, (s, 1H), 7.87 (t, $J = 1.7$ Hz, 1H), 7.77 (dt, $J = 7.5$, 1.7 Hz, 1H), 7.63 (dt, $J = 7.5$, 1.7 Hz, 1H), 7.50

(t, $J = 7.5$ Hz, 1H), 5.82–5.70 (m, 1H), 5.18 (m, 1H), 5.12 (m, 1H), 4.82 (t, $J = 6.0$ Hz, 1H), 2.61–2.46 (m, 2H), 2.43 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ 192.3, 145.0, 136.5, 133.7, 131.9, 129.0, 128.9, 126.9, 118.9, 72.5, 43.8. HRMS (FAB) Calc. for $C_{11}H_{12}O_2$: m/z 176.0837. Found: m/z 176.0840.

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