Trialkylborane as an Initiator and Terminator of Free Radical Reactions. Facile Routes to Boron Enolates via α-Carbonyl Radicals and Aldol Reaction of Boron Enolates

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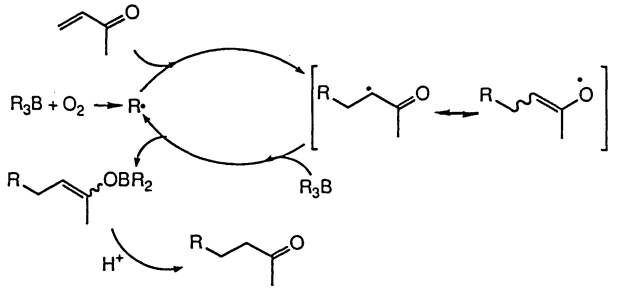
A variety of trialkylborane-induced reactions were examined for the preparation of the α-carbonyl radicals: (1) addition of alkyl radical to methyl vinyl ketone, (2) reduction of α-halo ketone, and (3) intramolecular radical addition to α,β-unsaturated carbonyl moiety. Trialkylborane reacted with α-carbonyl radicals to give boron enolates. The resulting boron enolates were efficiently trapped by carbonyl compounds to give β-hydroxy ketones in good yields.

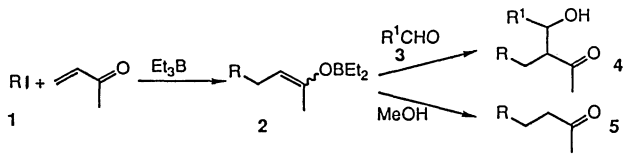
For the past two decades, there have been much effort to develop the utility of organoborane compounds in organic synthesis. Radical reaction is one of the most important synthetic methods in organoborane chemistry.[1] The 1,4-addition of R_3B to α,β-unsaturated carbonyl compounds was reported by Suzuki et al. in 1967.[2] Generally, trialkylboranes react with neither carbonyl compounds nor carbon-carbon unsaturated bonds. The unusual reactivity of α,β-unsaturated carbonyl compounds was originally explained by six-membered ring transition state. Further investigation by Suzuki and Brown[3] proved this reaction to proceed via radical mechanism by the fact that 5 mol% of galvinoxyl free radical (2,6-di-*t*-butyl-α-(3,5-di-*t*-butyl-4-oxo-2,5-cyclohexadien-1-ylidene)-*p*-tolyloxyl free radical) completely interrupted the reaction (Scheme 1).[4]



Scheme 1.

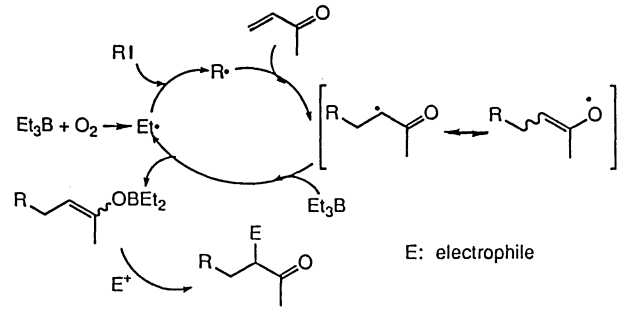
The structure of the intermediate boron enolate was confirmed with ^1H NMR by Köster et al.[5,6] We came to be interested in this radical trapping step where α-carbonyl radical reacted with trialkylborane to give boron enolate. In this paper we would like to report radical reactions in which trialkylborane acts as an initiator of radical reactions and, at the same time, works as a terminator to trap the α-carbonyl radical.[7]

First, addition of other radicals than R group of trialkylborane (R_3B) to α,β-unsaturated carbonyl compounds was investigated as a method to obtain α-carbonyl radicals. It is known that trialkylborane reduces active halides, such as benzyl bromide, via radical mechanism. Alkyl radical generated by the reaction of trialkylborane with oxygen abstracts the bromine atom of benzyl bromide to give benzyl radical.[1] We treated *t*-butyl iodide with triethylborane in the hope that *t*-butyl radical would be formed by the action of ethyl radical and that *t*-butyl radical would react with α,β-unsaturated carbonyl compound prior to ethyl radical. In fact, treatment of *t*-butyl iodide (3.0 mmol) with triethylborane[8] (1.0 mmol) in benzene in the presence of methyl vinyl ketone (1.0 mmol) and benzaldehyde (1.0 mmol) gave the three component coupling product **4a** (63% yield as a 66/34 diastereomeric mixture) along with the compound **4e** (2% yield) derived from the reaction of ethyl radical instead



a: R = *t*-Bu b: R = *i*-Pr c: R = ICH_2 d: R = n-C_6F_{13} e: R = Et

Scheme 2.



Scheme 3.

of *t*-butyl radical (Scheme 2). We are tempted to assume the following radical cycle reaction mechanism (Scheme 3).

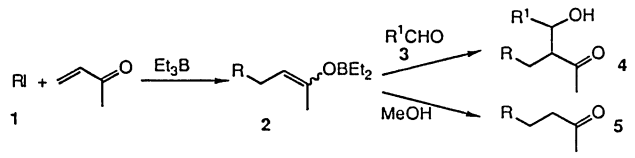
The success of the reaction is ascribed to the characteristics of Et_3B which plays critical two roles: (1) initiation of the radical reaction generating *t*-butyl radical from *t*-butyl iodide and (2) trapping the formed α-carbonyl radical as a boron enolate. Primary iodide such as methyl iodide did not give satisfactory results because ethyl radical from triethylborane competed with primary alkyl radical from alkyl iodide and a mixture of two products were obtained. Not only secondary or tertiary alkyl iodide but also diiodide or perfluoroalkyl iodide such as diiodomethane, perfluorohexyl iodide gave the corresponding adducts in good yield. In the case of Suzuki-Brown's or Köster's work, the nature of the alkyl radicals adding to methyl vinyl ketone are limited because they have to be attached on boron atom directly and therefore hydroboration was mainly used for the preparation of radical sources as trialkylboranes. Meanwhile, in our method, variety of radicals can be used for this purpose taking advantage of the reductive nature of trialkylborane. Methanol worked as an electrophile so efficient as aldehydes affording β-alkylated ketones. The results are summarized in Table 1. In the reaction of diiodomethane, methyl vinyl ketone, and methanol, the use of trioctylborane instead of Et_3B gave octyl iodide indicating the reduction of diiodomethane by octyl radical.

Second, one-electron reduction of α-halo ketones with Ph_3Sn radical was employed to produce α-carbonyl radicals. Recently we have shown that Et_3B is an effective initiator to give triaryltin or triarylgermanium radical from their corresponding hydride in the presence of trace amount of oxygen,[9,10] and that the new system, R_3SnH-Et_3B, enabled us to provide highly selective free radical reactions at lower temperature, e.g. −78 °C.[10,11] Here, this R_3SnH-Et_3B system was utilized for the reductive enolization of α-halo ketones.[12]

The Reformatsky type reaction was carried out as follows. Triethylborane (1.1 mmol) was added to a solution of α-bromo ketone (1.0 mmol) and aldehyde (1.0 mmol) in benzene at 25 °C under an argon atmosphere. To this mixture was slowly added Ph_3SnH (1.0 mmol) to afford β-hydroxy ketone in good yield. In this reaction Et_3B worked as (1) an initiator of the radical reaction generating triphenyltin radical and (2) a terminator trapping the α-carbonyl radical as a boron enolate. The representative results are shown in Table 2. The reaction proceeded chemoselectively so that only formyl group reacted in the presence of ketone (Entries 2 and 14 in Table 2). Whereas the reaction of 7-bromo-6-dodecanone with benzaldehyde gave a mixture of *erythro*- and *threo*-β-hydroxy carbonyl compound (Entry 12 in Table 2), α-bromocyclopentanone or α-bromocyclohexanone provided *threo* adducts with high stereoselectivities.[13] The presence of 5 mol% of galvinoxyl effectively stopped the reaction of α-bromoacetophenone and benzaldehyde. This reaction can be explained by the following radical cycle (Scheme 4).

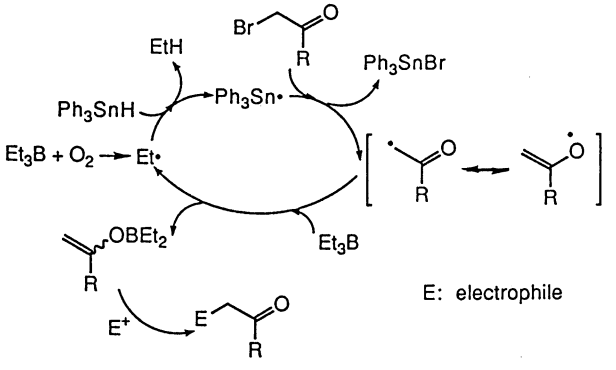
The reaction of α-iodo ketones with carbonyl compounds proceeded without Ph_3SnH. For instance, an addition of Et_3B to a solution of α-iodoacetophenone and benzaldehyde in benzene gave 1,3-diphenyl-3-hydroxy-1-propanone in 86% yield.[14] The results are also shown in Table 2. The *erythro/threo* ratios of the products were exactly the same as those obtained from the reaction of α-bromo ketones. In this reaction Et_3B also worked as (1) an initiator of the radical reaction generating α-carbonyl radical from α-iodo ketone and (2) a terminator trapping this radical as a boron enolate. The presence of 5 mol% of galvinoxyl also interrupted the reaction of α-iodoacetophenone and benzaldehyde effectively.

Table 1. Coupling Reaction of Alkyl Iodide, Methyl Vinyl Ketone, and Electrophiles



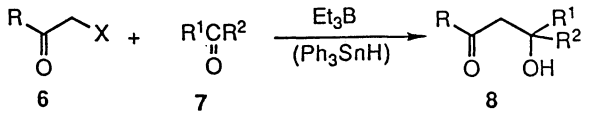
a: R = *t*-Bu b: R = *i*-Pr c: R = ICH_2 d: R = *n*-C_6F_{13} e: R = Et

Entry	RI	R^1CHO or MeOH	Product yield (%) *erythro/threo*
1	*t*-BuI	MeOH	**5a** (79), **5e** (5)
2	*t*-BuI	PhCHO	**4a** (63, 66/34), **4e** (4)
3	*i*-PrI	MeOH	**5b** (79), **5e** (15)
4	*i*-PrI	PhCHO	**4b** (58, 71/29), **4e** (21)
5	*i*-PrI	*n*-$C_6H_{13}CHO$	**4b** (56, 73/27), **4e** (18)
6	CH_2I_2	MeOH	**5c** (69)
7	CH_2I_2	PhCHO	**4c** (74, 61/39)
8	*n*-$C_6F_{13}I$	MeOH	**5d** (62), **5e** (2)
9	*n*-$C_6F_{13}I$	PhCHO	**4d** (31, 77/23), **4e** (2)

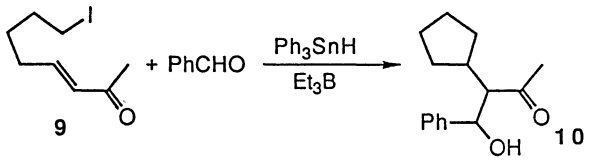


Scheme 4.

Table 2. Reformatsky Type Reaction Mediated by Triethylborane

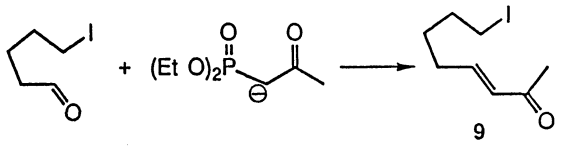


Entry	α-Halo ketone **6**	Carbonyl compound **7**	Product **8**		
				Yield/%	*erythro/threo*
1	α-Bromoacetophenone	PhCHO	**8a**	88	—
2		$CH_3C(O)(CH_2)_8CHO$	**8b**	78	—
3		cyclohexanone	**8c**	81	—
4	2-Bromocyclopentanone	PhCHO	**8d**	92	15/85
5		*n*-$C_6H_{13}CHO$	**8e**	77	8/92
6		*i*-PrCHO	**8f**	73	3/97
7		*t*-BuCHO	**8g**	83	0/100
8	2-Bromocyclohexanone	PhCHO	**8h**	74	22/78
9		*n*-$C_6H_{13}CHO$	**8i**	82	2/98
10		*i*-PrCHO	**8j**	76	9/91
11		*t*-BuCHO	**8k**	82	0/100
12	7-Bromo-6-dodecanone	PhCHO	**8l**	80	65/35
13	α-Iodoacetophenone	PhCHO	**8a**	86	—
14		$CH_3C(O)(CH_2)_8CHO$	**8b**	76	—
15		cyclohexanone	**8c**	77	—
16	2-Iodocyclopentanone	*n*-$C_6H_{13}CHO$	**8e**	64	6/94
17		*i*-PrCHO	**8f**	75	3/97
18		*t*-BuCHO	**8g**	70	0/100
19	2-Iodocyclohexanone	PhCHO	**8h**	83	20/80
20		*i*-PrCHO	**8j**	68	6/94
21		*t*-BuCHO	**8k**	72	0/100



Third, we synthesized 8-iodo-3-octen-2-one (**9**) expecting the intramolecular cyclization under reductive conditions to give an α-carbonyl radical. Treatment of **9** and benzaldehyde with Ph_3SnH-Et_3B gave the cyclized aldol adduct (**10**) in 70% (a mixture of *erythro/threo* or *threo/erythro*=63/37).

To the best of our knowledge, there had been no practical method for this one step cyclization-aldol condensation reaction. 8-Iodo-3-octen-2-one was synthesized from 5-iodopentanal by Horner-Wadsworth-Emmons reaction.[15]



Experimental

Distillation of the products was performed by the use of Kugelrohr (Büchi), and boiling points are indicated by an air bath temperature without correction. All melting points were obtained on a Yanaco MP-50929 melting points apparatus and are uncorrected. The IR spectra were determined on a JASCO IR-810 spectrometer, the mass spectra on a Hitachi M-80 machine, the ^1H and ^{13}C NMR spectra on a Varian XL-200 spectrometer. The chemical shifts of the ^1H NMR are given in δ with Me_4Si as an internal standard, and those of the ^{13}C NMR are given in δ with $CDCl_3$. The analyses were carried out by the staff at the Elemental Analyses Center of Kyoto University. Tetrahydrofuran was freshly distilled from sodium benzophenone ketyls. Purification of products was performed by column chromatography or preparative thin-layer chromatography (TLC) on silica gel.

General Procedure for Three Component Coupling Reaction of Alkyl Iodide, Methyl Vinyl Ketone, and Carbonyl Compound. The reaction of *t*-BuI and methyl vinyl ketone with benzaldehyde is representative. A benzene solution of methyl vinyl ketone (70 mg, 1.0 mmol) was added to a solution of *t*-butyl iodide (0.55 g, 3.0 mmol), Et_3B (1.0 M hexane solution, 1 M=1 mol dm^{-3}, 1.0 ml, 1.0 mmol), and benzaldehyde (0.11 g, 1.0 mmol) in benzene at 25 °C under an argon atmosphere. After stirring for 5 min, concentration of the resulting mixture in vacuo followed by purification by preparative TLC gave 3-(α-hydroxybenzyl)-5,5-dimethyl-2-hexanone (**4a**, 0.15 g) in 63% yield (*erythro/threo*=71/29) along with 3-(α-hydroxybenzyl)-2-hexanone (**4e**, 5 mg, 2%, *erythro/threo*=70/30). Assignment of the stereochemistry of *erythro*- and *threo*- isomers was based on the chemical shift and coupling constant of the carbinol proton (PhCH (OH)R). Heathcock et al. have reported that *threo*-isomers exhibited signals of larger coupling

constant at higher field than those for protons in *erythro*-isomers for the aldol type adduct PhCH(OH)CH(Me)C(=O)R.[16]

erythro-3-(α-Hydroxybenzyl)-5,5-dimethyl-2-hexanone (*erythro*-**4a**): Mp 87.8—88.0 °C (hexane); R_f=0.38 (hexane/ethyl acetate=3/1); IR (neat, before crystallization) 3426, 3024, 2934, 1686, 1466, 1390, 1364, 1055, 743, 699 cm^{-1}; ^{1}H NMR δ=0.74 (s, 9H), 1.60 (dd, *J*=1.4, 14.1 Hz, 1H), 1.87 (dd, *J*=9.7, 14.1 Hz, 1H), 2.02 (s, 3H), 2.42 (d, *J*=2.6 Hz, 1H, -OH), 2.95 (ddd, *J*=1.4, 5.5, 9.7 Hz, 1H, RCHC(=O)Me), 4.75 (dd, *J*=2.6, 5.5 Hz, 1H, PhCH(OH)R), 7.37 (bs, 5H). Found: C, 76.88; H, 9.46%. Calcd for $C_{15}H_{22}O_2$: C, 76.87; H, 9.68%.

threo-3-(α-Hydroxybenzyl)-5,5-dimethyl-2-hexanone (*threo*-**4a**): Bp 150 °C (bath temp, 1.0 Torr, 1 Torr=133.322 Pa); R_f=0.31 (hexane/ethyl acetate=3/1); IR (neat) 3404, 3028, 2954, 2864, 1701, 1474, 1365, 1156, 699 cm^{-1}; ^{1}H NMR δ=0.77 (s, 9H), 1.20 (dd, *J*=2.2, 14.2 Hz, 1H), 1.79 (dd, *J*=9.4, 14.2 Hz, 1H), 2.15 (s, 3H), 2.68 (bs, 1H, -OH), 3.05 (ddd, *J*=2.2, 7.4, 9.4 Hz, 1H, RCHC(=O)Me), 4.62 (bd, *J*=7.4 Hz, 1H, PhCH(OH)R). Found: C, 76.60; H, 9.46%. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46%.

erythro-3-(α-Hydroxybenzyl)-2-hexanone (*erythro*-**4e**): R_f=0.42 (hexane/ethyl acetate=3/1); IR (neat) 3340, 2956, 2928, 2870, 1701, 1458, 1356, 700 cm^{-1}; ^{1}H NMR δ=0.85 (t, *J*=7.2 Hz, 3H), 1.10—1.40 (m, 2H), 1.55—1.80 (m, 2H), 2.00 (s, 3H), 2.74 (d, *J*=2.5 Hz, 1H, -OH), 2.90 (m, 1H), 4.88 (dd, *J*=2.5, 5.8 Hz, 1H, PhCH(OH)R), 7.40 (s, 5H). Found (for a mixture of *erythro*/*threo*=70/30): C, 75.56; H, 8.88%. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79%.

threo-3-(α-Hydroxybenzyl)-2-hexanone(*threo*-**4e**): R_f=0.35 (hexane/ethyl acetate=3/1); IR (neat) 3362, 2956, 2930, 2870, 1702, 1453, 1357, 760, 699 cm^{-1}; ^{1}H NMR δ=0.82 (t, *J*=6.8 Hz, 3H), 1.15—1.40 (m, 3H), 1.45—1.70 (m, 2H), 2.15 (s, 3H), 2.94 (dt, *J*=3.4, 7.8 Hz, 1H), 4.77 (d, *J*=7.8 Hz, 1H, PhCH(OH)R), 7.40 (bs, 5H).

***erythro*-4-Hydroxy-3-(2-methylpropyl)-2-decanone (*erythro*-4b):** Bp 140 °C (bath temp, 1.0 Torr, for a mixture of *erythro*/*threo*=73/27); R_f=0.36 (hexane/ethyl acetate=5/1); IR (neat, for a mixture of *erythro*/*threo*=73/27) 3428, 2952, 2928, 2858, 1701, 1467, 1355 cm^{-1}; ^{1}H NMR δ=0.85—1.03 (m, 9H), 1.20—1.82 (m, 14H), 2.21 (s, 3H), 2.70 (m, 1H, RCHC(=O)Me), 3.81 (m, 1H, R^{1}R^{2}CHOH). Found (for a mixture of *erythro*/*threo*=73/27): C, 73.35; H, 12.48%. Calcd for $C_{14}H_{28}O_2$: C, 73.63; H, 12.36%.

***threo*-4-Hydroxy-3-(2-methylpropyl)-2-decanone (*threo*-4b):** R_f=0.36 (hexane/ethyl acetate=5/1); ^{1}H NMR δ=0.85—1.03 (m, 9H), 1.20—1.82 (m, 14H), 2.22 (s, 3H), 2.65 (m, 1H, RCHC(=O)Me), 3.70 (m, 1H, R^{1}R^{2}CHOH).

***erythro*-3-(α-Hydroxybenzyl)-5-iodo-2-pentanone (*erythro*-4c):** The title compound quickly decomposed at room temperature under air. R_f=0.27 (hexane/ethyl acetate=3/1); IR (neat, for a mixtire of *erythro*/*threo*=61/39) 3382, 2920, 1702, 1492, 1453, 1356, 1175, 1051, 1025, 762, 700 cm^{-1}; ^{1}H NMR δ=2.08 (s, 3H), 2.15 (m, 1H), 2.45 (m, 1H, -OH), 3.00 (m, 2H), 4.98 (d, *J*=5.6 Hz, 1H, PhRCHOH), 7.35 (bs, 5H).

***threo*-3-(α-Hydroxybenzyl)-5-iodo-2-pentanone (*threo*-4c):** The title compound also quickly decomposed at room-temperature under air. R_f=0.27 (hexane/ethyl acetate=3/1); ^{1}H NMR δ=2.20 (s, 3H), 2.15 (m, 1H), 2.45 (m, 1H, -OH), 3.00 (m, 2H), 4.79 (d, *J*=7.3 Hz, 1H, PhRCHOH), 7.35 (bs, 5H).

The structures of *erythro*- and *threo*-3-(α-hydroxybenzyl)-5-iodo-2-pentanones were confirmed by the reduction of the compounds with *n*-Bu$_3$SnH-Et$_3$B to give the corresponding aldol adduct. Tributyltin hydride (0.26 g, 0.90 mmol) and Et$_3$B (1.0 M in hexane, 0.10 ml, 0.10 mmol) were added to a mixture of *erythro*-**4c**/*threo*-**4c** (161 mg, 0.51 mmol/104 mg, 0.32 mmol) in benzene at 25 °C under an argon atmosphere. After stirring for 1 day to this mixture were added KF (100 mg) and water (1.0 ml). The resulting heterogeneous mixture was stirred vigorously. Filtration, concentration of the organic layer, and purification by silica-gel column chromatography gave 76 mg (0.48 mmol) of *erythro*-3-(α-hydroxybenzyl)-2-pentanone (78% yield) and 48 mg of its *threo*-isomer (78% yield).

erythro-3-(α-Hydroxybenzyl)-2-pentanone: Bp 100 °C (1.0 Torr, bath temp); R_f=0.40 (hexane/ethyl acetate=3/1); IR (neat) 3402, 2964, 2876, 1702, 1456, 1359, 1026, 764, 701 cm^{-1}; ^{1}H NMR δ=0.86 (t, *J*=7.5 Hz, 3H), 1.60—1.85 (m, 2H), 2.02 (s, 3H), 2.75 (bs, 1H, -OH), 2.84 (m, 1H), 4.90 (d, *J*=6.0 Hz, 1H, RPhCHOH), 7.35 (bs, 5H). Found: C, 74.97; H, 8.46%. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39%.

threo-3-(α-Hydroxybenzyl)-2-pentanone: Bp 100 °C (1.0 Torr, bath temp); R_f=0.40 (hexane/ethyl acetate=3/1); IR (neat) 3412, 2964, 2932, 2876, 1703, 1455, 1358, 1213, 1169, 767, 701 cm^{-1}; ^{1}H NMR δ=0.83 (t, *J*=7.5 Hz, 3H), 1.30—1.75 (m, 2H), 2.16 (s, 3H), 2.78 (bs, 1H, -OH), 2.87 (m, 1H), 4.80 (d, *J*=7.9 Hz, RPhCHOH), 7.35 (bs, 5H). Found: C, 74.75; H, 8.56%. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39%.

***erythro*-5,5,6,6,7,7,8,8,9,9,10,10,10-Tridecafluoro-3-(α-hydroxybenzyl)-2-decanone (*erythro*-4d):** R_f=0.47 (hexane/ethyl acetate=3/1); white solid; IR (neat before crystallization, for a mixture of *erythro*/*threo*=77/23) 3406, 1714, 1364, 1240, 1194, 1145, 1107, 1044, 766, 731, 701 cm^{-1}; ^{1}H NMR δ=2.17 (s, 3H), 2.64 (d, *J*=5.5 Hz, 1H, -OH), 2.75 (m, 2H), 2.70 (m, 1H, R^{1}R^{2}CHC(=O)Me), 4.76 (dd, *J*=5.5, 7.2 Hz, 1H, PhCH(OH)R), 7.33 (m, 5H). Found (for a mixture of *erythro*/*threo*=77/23): C, 41.11; H, 2.61%. Calcd for $C_{17}H_{13}O_2F_{13}$: C, 41.14; H, 2.64%.

***threo*-5,5,6,6,7,7,8,8,9,9,10,10,10-Tridecafluoro-3-(α-hydroxybenzyl)-2-decanone (*threo*-4d):** R_f=0.47 (hexane/ethyl acetate=3/1); ^{1}H NMR δ=1.89 (s, 3H), 2.40 (d, *J*=2.5 Hz, 1H, -OH), 2.70 (m, 2H), 3.29 (m, 1H, R^{1}R^{2}CHC(=O)Me), 4.75 (dd, *J*=2.5, 7.0 Hz, 1H, PhCH(OH)R), 7.36 (m, 5H).

Methanol Quenching of the Boron Enolates Generated by the Radical Addition of Alkyl Iodide to Methyl Vinyl Ketone in the Presence of Triethylborane. The reaction of *t*-BuI and methyl vinyl ketone is representative. A benzene solution of methyl vinyl ketone (70 mg, 1.0 mmol) was added to a solution of *t*-butyl iodide (0,55 g, 3.0 mmol), Et$_3$B (1.0 M hexane solution, 1.0 ml, 1.0 mmol), and methanol (0.08 ml, 2.0 mmol) in benzene at 25 °C under an argon atmosphere. After stirring for 5 min, concentration of the resulting mixture and purification by preparative TLC gave 5,5-dimethyl-2-hexanone[17] (**5a**, 0.10 g, 79% yield) along with 2-hexanone (**5e**, 5 mg, 5%).

5-Methyl-2-hexanone (5b): The compound was identical with the sample purchased from Aldrich Chemical Co.[18]

5-Iodo-2-pentanone (5e): The compound slowly decomposed under air at room temperature. R_f=0.47 (hexane/ethyl acetate=5/1); IR (neat) 2956, 1711, 1453, 1420, 1364, 1221, 1176, 701 cm^{-1}; ^{1}H NMR δ=2.07 (tt, *J*=6.7, 7.0 Hz, 2H), 2.17 (s, 3H), 2.60 (t, *J*=7.0 Hz, 2H), 3.23 (t, *J*=6.7 Hz, 2H).

Found: C, 28.49; H, 4.45%. Calcd for C_5H_9OI: C, 28.32; H, 4.28%.

5,5,6,6,7,7,8,8,9,9,10,10,10-Tridecafluoro-2-decanone (5d): Bp 83 °C (bath temp, 20 Torr), R_f=0.53 (hexane/ethyl acetate=5/1); IR (neat) 2922, 2852, 1723, 1364, 1238, 1194, 1144, 1020 cm^{-1}; ^1H NMR δ=2.23 (s, 3H), 2.42 (m, 2H), 2.78 (t, J=7.5 Hz, 2H). Found: C, 30.55; H, 1.81%. Calcd for $C_{10}H_7OF_{13}$: C, 30.79; H, 1.81%.

Methanol Quenching of the Boron Enolates Generated by the Radical Addition of Diiodomethane to Methyl Vinyl Ketone in the Presence of Trioctylborane. A benzene solution of methyl vinyl ketone (70 mg, 1.0 mmol) was added to a solution of diiodomethane (0.80 g, 3.0 mmol), Oct_3B (1.0 M THF solution, 1.0 ml, 1.0 mmol), and methanol (0.08 ml, 2.0 mmol) in benzene at 25 ° under an argon atmosphere. After stirring for 5 min, concentration of the resulting mixture and purification by preparative TLC gave 5-iodo-2-pentanone (**5a**, 0.11 g, 54% yield) and 0.11 g (48%) of octyl iodide.

Triethylborane Mediated Reformatsky Type Reaction of α-Bromo Ketones[19] (or α-Iodo Ketones[20]) and Carbonyl Compounds. The reaction of α-bromoacetophenone and benzaldehyde is representative. A hexane solution of Et_3B (1.0 M, 1.1 ml, 1.1 mmol) was added to a solution of α-bromoacetophenone (0.20 g, 1.0 mmol) and benzaldehyde (0.11 g, 1.0 mmol) in benzene (3.0 ml) at 25 °C under an argon atmosphere. To the mixture was added slowly a benzene solution of Ph_3SnH (0.2 M, 5.0 ml, 1.0 mmol) and the resulting mixture was stirred for 5 min at 25 °C. Then 100 mg of KF and 1.0 ml of water were added and the mixture was stirred vigorously. Filtration and purification by preparative TLC on silica gel gave 1,3-diphenyl-3-hydroxy-1-propanone (**8a**, 0.20 g, 88% yield).[21] In the case of α-iodoacetophenone, the reaction proceeded without an addition of Ph_3SnH.

3-Hydroxy-1-phenyl-1,12-tridecanedione (8b): Mp 50.2—50.5 °C (hexane); R_f=0.29 (hexane/ethyl acetate 5/1); IR (neat, before crystallization) 3400, 2910, 2846, 1706, 1681, 1449, 1379, 1270, 1166, 1079, 752, 688 cm^{-1}; ^1H NMR δ=1.25—1.70 (m, 16H), 2.14 (s, 3H), 3.03 (dd, J= 8.6, 17.7 Hz, 1H), 3.20 (dd, J=3.1, 17.7 Hz, 1H), 3.24 (bs, 1H, -OH), 4.20—4.35 (m, 1H, R^1R^2CHOH), 7.50—7.70 (m, 3H), 8.00—8.03 (m, 2H). Found: C, 74.78, H, 9.27%. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27%.

1-(2-Oxo-2-phenylethyl)cyclohexanol (8c): Mp 77.0—77.2 °C (hexane); R_f=0.70 (hexane/ethyl acetate=3/1); IR (neat, before crystallization) 3510, 3050, 2934, 2854, 1675, 1448, 1380, 749, 687 cm^{-1}; ^1H NMR δ=1.25—1.90 (m, 10H), 3.12 (s, 2H), 4.00 (s, 1H, -OH), 7.45—7.75 (m, 3H), 7.96—8.07 (m, 2H). Found: C, 77.02; H, 8.32%. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31%.

***erythro*-2-(α-Hydroxybenzyl)cyclopentanone (*erythro* 8d),[22]**

***threo*-2-(α-Hydroxybenzyl)cyclopentanone (*threo* 8d),[21]**

***erythro*-2-(1-Hydroxy-2-methylpropyl)cyclopentanone (*erythro* 8f),[23]**

***threo*-2-(1-Hydroxy-2-methylpropyl)cyclopentanone (*threo* 8f),[22]**

***erythro*-2-(1-Hydroxy-2,2-dimethylpropyl)cyclopentanone (*erythro* 8g),[22]**

***erythro*-2-(α-Hydroxybenzyl)cyclohexanone (*erythro* 8f),[21]**

***threo*-2-(α-Hydroxybenzyl)cyclohexanone (*threo* 8h),[21]**

***erythro*-2-(1-Hydroxy-2-methylpropyl)cyclohexanone (*erythro* 8j),[21]**

***threo*-2-(1-Hydroxy-2-methylpropyl)cyclopentanone (*threo* 8j),[21]**

***erythro*-2-(1-Hydroxy-2,2-dimethylpropyl)cyclohexanone (*erythro* 8k).[21]**

The spectral data of these compounds were identical with those described in the literature.

***erythro*-2-(1-Hydroxyheptyl)cyclopentanone (*erythro* 8e):** R_f=0.54 (hexane/ethyl acetate=5/1); IR (neat) 3400, 2922, 2854, 1735, 1458, 1376, 1272, 1156 cm^{-1}; ^1H NMR δ=0.84 (t, J=6.9 Hz, 3H), 1.15—2.45 (m, 18H), 4.25 (m, 1H); Found: C, 72.80; H, 11.28%. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18%.

***threo*-2-(1-Hydroxyheptyl)cyclopentanone (*threo* 8e):** R_f=0.63 (hexane/ethyl acetate=5/1); IR (neat) 3400, 2922, 2854, 1735, 1458, 1376, 1272, 1156 cm^{-1}; ^1H NMR δ=0.84 (t, J=6.9 Hz, 3H), 1.15—2.45 (m, 18H), 3.73 (m, 1H). Found: C, 72.80; H, 11.28%. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18%.

***erythro*-2-(1-Hydroxyheptyl)cyclohexanone (*erythro* 8i):** R_f=0.48 (hexane/ethyl acetate=5/1); IR (neat, for a mixture of *erythro*/*threo*=2/98) 3446, 2930, 2856, 1701, 1451, 1312, 1131 cm^{-1}; ^1H NMR δ=0.84 (t, J=6.9 Hz, 3H), 1.15—2.45 (m, 19H), 3.90 (m, 1H), 4.12 (m, 1H); Found (for a mixture of *erythro*/*threo*=2/98): C, 73.32; H, 11.56%. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39%.

***threo*-2-(1-Hydroxyheptyl)cyclohexanone (*threo* 8i):** R_f=0.48 (hexane/ethyl acetate=5/1); ^1H NMR δ=0.84 (t, J=6.9 Hz, 3H), 1.15—2.45 (m, 20H), 3.73 (m, 1H).

***erythro*-7-(Hydroxyphenylmethyl)-6-dodecanone (*erythro*-8l):** R_f=0.55 (hexane/ethyl acetate=5/1); IR (for a mixture of *erythro*/*threo*=65/35) 3340, 2922, 2852, 1702, 1458, 1376, 699 cm^{-1}; ^1H NMR δ=0.75—0.95 (m, 6H), 1.05—1.80 (m, 14H), 2.08—2.48 (m, 2H), 2.78—3.06 (m, 2H), 4.88 (dd, J=2.5, 6.0 Hz, 1H), 7.35 (bs, 5H). Found (for a mixture of *erythro*/*threo*=65/35): C, 78.35; H, 10.67%. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41%.

***threo*-7-(α-Hydroxybenzyl)-6-dodecanone (*threo*-8l):** ^1H NMR δ=0.75—0.95 (m, 6H), 1.05—1.80 (m, 14H), 2.08—2.48 (m, 2H), 2.78—3.06 (m, 2H), 4.80 (d, J=6.9 Hz, 1H), 7.45—7.60 (m, 3H), 7.68—7.77 (m, 2H).

Triethylborane-Mediated Reformatsky Type Reaction of α-Bromoacetophenones and Benzaldehyde in the Presence of Garvinoxyl. A hexane solution of Et_3B (1.0 M, 1.1 ml, 1.1 mmol) was added to a solution of α-bromoacetophenone (0.20 g, 1.0 mmol), benzaldehyde (0.11 g, 1.0 mmol), and Garvinoxyl (42 mg, 0.10 mmol) in benzene (3.0 ml) at 25 °C under an argon atmosphere. To the mixture was added slowly a benzene solution of Ph_3SnH (0.2 M, 5.0 ml, 1.0 mmol) and the resulting mixture was stirred for 5 min at 25 °C. Then 100 mg of KF and 1.0 ml of water were added and the mixture was stirred vigorously. Filtration and purification by preparative TLC on silica gel gave 1,3-diphenyl-3-hydroxy-1-propanone (**8a**, 80 mg, 36% yield) and complex mixture.

Preparation of 8-Iodo-3-octen-2-one. 5-Iodo-1-pentanol (0.80 g, 3.7 mmol) was added dropwise to a dispersion of PDC (pyridinium dichromate, 2.0 g, 5.3 mmol) in CH_2Cl_2 (40 ml) at room temperature under air. After stirring for 1 h, the liquid phase of the resulting mixture was filtered through silica gel. The precipitate was washed with ether (10 ml, twice) and poured on the silica gel. The combined organic layers were concentrated and purified by silica-gel column chromatography to give 0.38 g (1.8 mmol) of 5-iodopentanal in 48% yield. This aldehyde was quite unsta-

ble under air at room tempareture and it was required to carry out the next step immediately. (Diethyloxyphosphinyl)acetone (0.37 g, 1.9 mmol) was added to a generally prepared THF solution of LDA (lithium diisopropylamide, 0.5 M, 3.8 ml, 1.9 mmol) at 0 °C under an argon atmosphere. After stirring for 1 h at 0 °C this yellow brown mixture was transferred into a THF solution of 5-iodopentanal (0.5 M, 3.6 ml, 1.8 mmol) by syringe. The resulting mixture was stirred for 15 min at 0 °C, 15 min at room temperature, and 30 min at THF reflux. After cooling, the reaction mixture was poured into water and extracted by ethyl acetate (10 ml, twice). The combined organic layers were washed with brine. Concentration and purification by silica-gel column chromatography gave 0.20 g (0.77 mmol, 43%) of 8-iodo-3-octen-2-one (**9**): R_f=0.29 (hexane/ethyl acetate=5/1); IR (neat) 2930, 2854, 1697, 1672, 1626, 1426, 1361, 1254, 1206, 1180, 976 cm^{-1}; ^1H NMR δ=1.52—1.75 (m, 2H), 1.78—1.97 (m, 2H), 2.22—2.36 (m, 2H), 2.25 (s, 3H), 3.20 (t, J=6.7 Hz, 2H), 6.10 (d, J=15.9 Hz, 1H), 6.79 (dt, J=15.9, 6.8 Hz, 1H). Found: C, 38.25; H, 5.23%. Calcd for $C_8H_{13}OI$: C, 38.12; H, 5.20%.

Cyclization-Aldol Condensation of 8-Iodo-3-octen-2-one and Benzaldehyde. A benzene solution of Ph_3SnH (0.18 M, 3 ml, 0.55 mmol) was added dropwise to a mixture of 8-iodo-3-octen-2-one (0.13 g, 0.50 mmol), benzaldehyde (58 mg, 0.55 mmol), and Et_3B (1.0 M in hexane, 0.55 ml, 0.55 mmol) in benzene (7 ml) at room temperature under an argon atmosphere. After stirring for 30 min at room temperature, 50 mg of KF and 2 ml of water were added and stirred vigorously. The resulting mixture was filtered through Celite 545 and washed with brine. The aqueous layer was extracted by ethyl acetate (10 ml, twice). Combined organic layers were concentrated and purified by preparative TLC. 81 mg of 3-cyclopentyl-4-hydroxy-4-phenyl-2-butanone (**10**, 0.35 mmol, 70% yield, *erythro/threo* or *threo/erythro*=55/45) was obtained. **10**: R_f=0.37 (hexane/ethyl acetate=5/1); IR (neat, for a mixture of *erythro/threo* or *threo/erythro*=63/37) 3424, 2950, 2868, 1701, 1453, 1353, 760, 731, 700 cm^{-1}; ^1H NMR (for major) δ=1.07—1.40 (m, 2H), 1.40—2.07 (m, 6H), 1.94 (s, 3H), 2.08—2.40 (m, 1H), 2.68 (bs, 1H, -OH), 2.98 (dd, J=6.5, 8.3 Hz, 1H, R^1R^2CHC(=O)Me), 4.97 (m, 1H, PhRCHOH), 7.35 (m, 5H); ^1H NMR (for minor) δ=1.07—1.40 (m, 2H), 1.40—2.07 (m, 6H), 1.86 (s, 3H), 2.08—2.40 (m, 1H), 2.81 (dd, J=4.4, 9.9 Hz, 1H, R^1R^2CHC(=O)Me), 3.92 (bs, 1H, -OH), 4,97 (m, 1H, PhRCHOH), 7.35 (m, 5H). Found (for a mixture of *erythro/threo* or *threo/erythro*=63/37): C, 77.26; N, 8.68%. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68%.

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