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Highly Controlled Chemoselectivity of Tin Enolate by Its Hybridization State. Anionic Complex of Tin Enolate Coordinated by Tetrabutylammonium Bromide as Halo Selective Reagent

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Abstract: The control of reactivity and/or selectivity of organotin(IV) enolates has been studied by means of a high coordination method in which the hybridization state of tin was effectively changed. An anionic tin complex, five-coordinated tin enolate **1**(*h*), was formed by the coordination of bromide anion from tetrabutylammonium bromide (Bu_4NBr) to neutral four-coordinated tin(IV) enolates **1**(*e*). The highly coordinated enolates which attained a marked change in chemoselectivity have higher nucleophilicity to organic halides. In addition, they showed low nucleophilicity toward carbonyl moieties by the coordination of the bromide anion, whereas carbonyl addition readily proceeds using the usual four-coordinated tin enolate. NMR studies revealed the generation of HMPA- or bromide-anion-coordinated tin enolates in equilibrium between four-coordinated enolate **1c**(*e*) and five-coordinated enolate **1c**(*h*), showing a considerable upfield shift $\delta(^{119}Sn)$ and increasing values of the coupling constants $^1J(^{119}Sn-^{13}C)$. In detailed NMR analyses of highly coordinated tin enolate, it was shown that the contribution of highly coordinated species **1**(*h*) to the equilibrium between **1**(*e*) and **1**(*h*) became more significant as the added amount of ligands such as Bu_4NBr or HMPA was increased. Considering these results, it was assumed that the bromide-anion-coordinated tin enolate was generated, which showed a unique reactivity and selectivity. The effective control of chemoselectivity in the intermolecularly competitive reaction between organic halides and carbonyl compounds was demonstrated using two types of tin enolates, four-coordinated enolate and highly coordinated anionic enolate; halide displacement reaction exclusively took place using the bromide-anion-coordinated enolate, and the usual four-coordinated enolates reacted with only carbonyl compounds.

Introduction

The hybridization of the metal center of organometallic reagents is very important in organic syntheses because of its close relationship with reactivity of the reagents. The appropriate coordination by solvents or ligands to the metal often leads to improved results for organic reactions using organometallic compounds. The reactivity and/or selectivity of organometallic reagents would be freely changed if the hybridization could be exactly controlled.

Organotin(IV) compounds commonly exist as a tetrahedral structure around the tin center.[1,2] Variation in the ligands added can change the hybridization to give trigonal bipyramidal and octahedral structures including five- and six-coordinate tin centers, which are highly coordinated, respectively.[2,3] We could then expect changes in the reactivity or selectivity of tin compounds by high coordination.

Among the extensive studies of organotin(IV) reagents in the context of carbon−carbon bond formation,[4] of particular interest are organotin enolates,[5] which have both relative stability and reactivity. In general, tin(IV) enolates hardly couple with halide moieties[6] despite high reactivity toward carbonyl moieties such as aldehydes and reactive ketones (Scheme 1).[7−9] We have previously reported the generation of HMPA (hexamethylphosphoric triamide)-coordinated tin enolates in which a change of reactivity and selective coupling at halide moieties in α-halo ketones by structural rehybridization of the tin compound have been demonstrated.[10−13] However, α-halo ketones are special substrates because two functional groups (carbonyl and halide) are linked and interactive. Their reactivities are far different from the simple carbonyl compounds or simple organic halides which are monofunctional. To discuss the intrinsic selectivity

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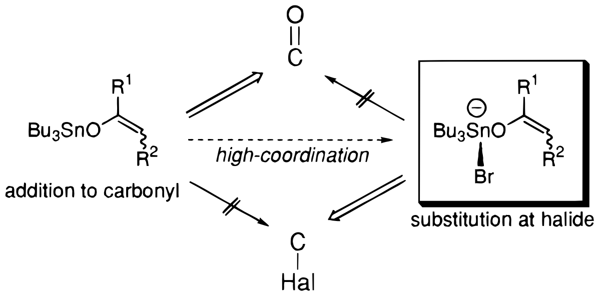
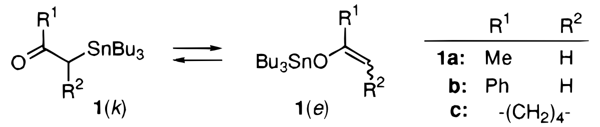
S0002-7863(97)02190-2 CCC: $15.00

Scheme 1



Scheme 2



of tin enolates, the reaction with the monofunctional substrates should be investigated. Enholm et al. have recently utilized our HMPA-methodology for the coupling with simple organic halides.[14,15] However, the HMPA-coordinated tin enolates are not practical for organic synthesis because excess amounts of halides and HMPA are required owing to the low reactivity of the tin enolates coordinated by HMPA.[14−18]

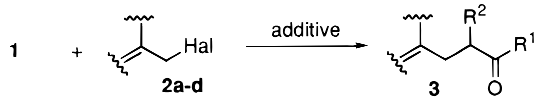
In this paper, we propose an anion type of five-coordinated tin enolates which are formed by the coordination of the bromide anion from tetrabutylammonium bromide (Bu_4NBr) to neutral tin(IV) enolates (Scheme 1). The anion-coordinated enolates which attained a marked change of chemoselectivity have highly selective nucleophilicity to organic halides greater than HMPA-coordinated enolates. In addition, they proved to lose the inherent nucleophilicity toward carbonyl moieties by the coordination of the bromide anion, whereas the coordination of HMPA did not show such distinct loss. The detailed behavior of the coordination is discussed in terms of the NMR data. Moreover, the effective control of chemoselectivity in the intermolecularly competitive reaction between halides and carbonyls was demonstrated.

Results and Discussion

Organotin enolates exist as equilibrium mixtures of keto and enol forms [**1**(*k*) and **1**(*e*)], and their ratio largely depends on their substituents and conditions (Scheme 2).[19] Higher reactivity toward carbonyls is generally shown by enol-types than by keto-types.[20] Three representative types of tin enolates are shown in Scheme 2; **1a** and **1c** exclusively exist in keto and enol forms, respectively, and **1b** is a mixture of both forms.[10,19]

Reaction of Tin Enolates with Halides. First, the reactions with allylic halides **2** were investigated, and their results are summarized in Table 1. Without any additives, no reaction with cinnamyl bromide **2a** took place at room temperature for 7 h (entry 1).[6] A moderate yield was obtained in the presence of HMPA (entry 2) which was previously reported to promote the haloselective coupling in the case of α-halo ketones.[10−12] A higher yield (77%) was obtained by the addition of Bu_4NBr at room temperature (entry 3), whereas Bu_4NCl gave a low yield (entriy 4). The striking effect of Bu_4NBr was also observed even in the reaction with lower reactive cinnamyl chloride **2b** in comparison to the bromide **2a**, whereas HMPA did not promote the coupling at all (entries 5−7). The high yield obtained with addition of Bu_4NI was due to halogen exchange between Bu_4NI and benzyl bromide in which Bu_4NBr acted as a promoter toward benzyl iodide (entry 9). An enol-type of enolate (**1c**) which is fairly coordinated and more reactive than a keto-type (**1a**) gave higher yields of the coupling product in the presence of Bu_4NBr with either cinnamyl bromide **2a** or chloride **2b** at room temperature (entries 13 and 15). Only S_N2-type products were exclusively formed without any S_N2'-type ones.

Table 1. Reaction of Tin Enolate **1** with Allylic Halide **2**[a]

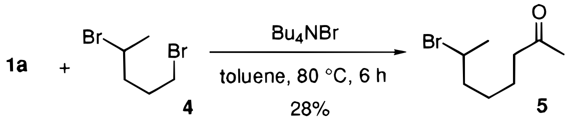


entry	enolate **1**	allylic halide **2**	additive	*t* (h)	product **3**	yield (%)
1	**1a**	**2a** cinnamyl bromide	none	7	**3a**	0
2	**1a**	**2a** cinnamyl bromide	HMPA	4	**3a**	46
3	**1a**	**2a** cinnamyl bromide	Bu_4NBr	4	**3a**	77
4	**1a**	**2a** cinnamyl bromide	Bu_4NCl	4	**3a**	23
5	**1a**	**2b** cinnamyl chloride	none	42	**3a**	0[b]
6	**1a**	**2b** cinnamyl chloride	HMPA	4	**3a**	0
7	**1a**	**2b** cinnamyl chloride	Bu_4NBr	2	**3a**	66
8	**1a**	**2c** benzyl bromide	Bu_4NBr	4	**3b**	67
9	**1a**	**2c** benzyl bromide	Bu_4NI	7	**3b**	74
10	**1a**	**2c** benzyl bromide	HMPA	21	**3b**	28
11	**1a**	**2d** benzyl chloride	Bu_4NBr	4	**3b**	37
12	**1c**	**2a** cinnamyl bromide	HMPA	5	**3c**	81
13	**1c**	**2a** cinnamyl bromide	Bu_4NBr	5	**3c**	93[c]
14	**1c**	**2b** cinnamyl chloride	HMPA	3	**3c**	0[c]
15	**1c**	**2b** cinnamyl chloride	Bu_4NBr	3	**3c**	93

[a] Unless otherwise noted, reactions were carried out in THF (1 mL) using tin enolate **1** (1.2 mmol), halide **2** (1.0 mmol), and additive (1.8 mmol) at room temperature. [b] 60 °C. [c] Toluene was used as solvent.

Next, we investigated the reaction with simple alkyl halides **2** (Table 2). In this case, too, Bu_4NBr acted as an effective additive more than Bu_4NCl or HMPA, although high reaction temperature was required. A free radical reaction mechanism could be excluded by the fact that a radical inhibitor did not depress the coupling at all (entries 9 and 10).

While the substitution reaction of primary bromide or iodide proceeded in the presence of Bu_4NBr, vinylic and secondary alkyl halides were inert under the conditions using Bu_4NBr.[21] This chemoselectivity was applied to the selective coupling at the primary bromide site in 1,4-dibromopentane **4** to give 7-bromo-2-octanone (**5**), exclusively (eq 1).



(1)

NMR Studies of Highly Coordinated Tin Enolates. We can assume that a five-coordinated tin enolate (**1**(*h*)) is generated

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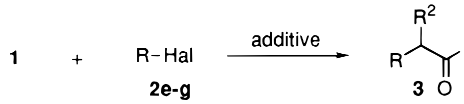
(21) No reactions were confirmed in the reactions between **1c** and bromobenzene at 110 °C for 30 h and **1a** and 2-bromobutane at 80 °C for 8 h in the presence of Bu_4NBr in toluene.

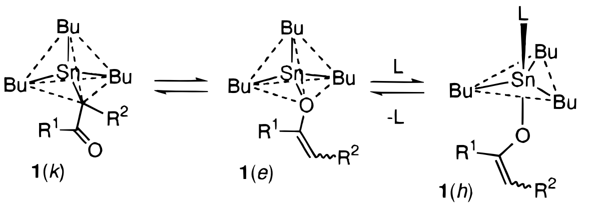
Table 2. Reaction of Tin Enolate **1** with Alkyl Halide **2**[a]



entry	enolate **1**	alkyl halide **2**	additive	*t* (h)	product **3**	yield (%)
1	**1a**	**2e** PrBr	Bu_4NBr	4	**3e**	33
2	**1a**	**2e** PrBr	Bu_4NCl	19	**3e**	11
3	**1a**	**2e** PrBr	Et_4NCl	19	**3e**	0
4	**1a**	**2e** PrBr	HMPA	72	**3e**	0[b]
5	**1a**	**2f** PrI	Bu_4NBr	4	**3e**	42
6	**1a**	**2g** $Ph(CH_2)_3Br$	Bu_4NBr	8	**3f**	43
7	**1b**	**2e** PrBr	Bu_4NBr	4	**3e**	35
8	**1b**	**2f** PrI	Bu_4NBr	4	**3e**	33
9	**1c**	**2e** PrBr	Bu_4NBr	6	**3e**	62
10	**1c**	**2e** PrBr	Bu_4NBr	6	**3e**	58[c]
11	**1c**	**2f** PrI	Bu_4NBr	6	**3e**	58

[a] Unless otherwise noted, reactions were carried out in toluene (1 mL) using tin enolate **1** (1.2 mmol), halide **2** (1.0 mmol) and additive (1.8 mmol) at 80 °C. [b] THF was used as a solvent at 60 °C. [c] Radical inhibitor (TEMPO, 0.1 mmol) was added.

Scheme 3



by addition of Bu_4NBr in which the bromide anion acts as a ligand (L) to the tin center (Scheme 3). In our previous report, the coordination of HMPA to tin enolate contributes to upfield shifts of Sn peaks in the ^{119}Sn NMR spectrum and to increasing the coupling constants $J(^{119}Sn-^{13}C)$, compared with the four-coordinated tin enolate **1**(*e*).[10] The tautomerism between keto isomer **1**(*k*) and enol isomer **1**(*e* or *h*) has been dealt with using keto-type enolate **1a**. It is noteworthy that the enol isomer of **1a** was exclusively coordinated and that no coordination toward the keto isomer was observed. This selective coordination led to increase of the ratio of the enol form.[10]

We now employed an enol-type of tin enolate (**1c**) to avoid the confusion of the keto−enol tautomerization, focusing on only the equilibrium between four- and five-coordinated tin enolates [**1**(*e*) and **1**(*h*)]. The interaction between the tin enolate and some additives was examined by ^{119}Sn NMR (Figure 1). The signal of **1c**(*e*) showed the peak at ca. 90 ppm without any additives in C_6D_6 (Figure 1i). Adding of HMPA or Bu_4NBr (equimolar) to tin enolates **1c** contributed to upfield shifts of ^{119}Sn (Figure 1ii, iv). These signals showed the generation of highly coordinated tin enolate. No shift indicated little interaction between the tin enolate and Bu_4NI (Figure 1v); therefore, Bu_4NI was suggested to act not as a ligand to tin but as an iodide source of the halogen exchange in the reaction of tin enolate **1a** with benzyl bromide **2c** (Table 1, entry 9). There was no observable signal, perhaps because of the broadening in the presence of Bu_4NCl which had an excessively strong effect on the tin enolate (Figure 1iii). The signal of Bu_3SnCl which could be formed if a naked enolate anion species was generated was not observed. Surprisingly, low yields of the coupling products were obtained (Table 1, 2) despite using Bu_4NCl which is considered to be a stronger base as a ligand to tin than Bu_4NBr or Bu_4NI.

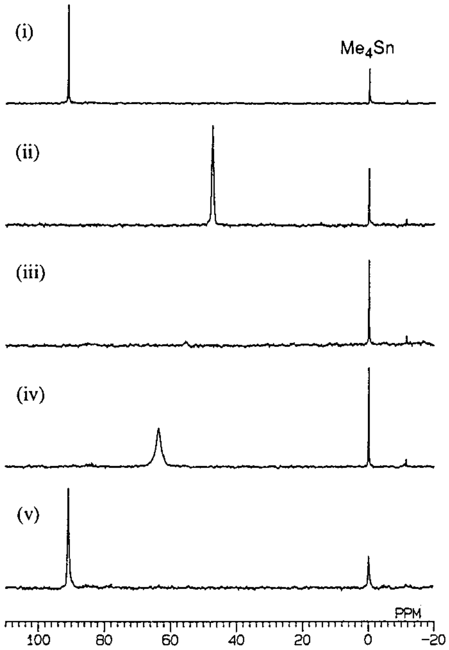


Figure 1. Effect of the additives (equimolar amount to **1c**) on ^{119}Sn NMR spectra of tin enolate **1c** in benzene-d_6 using Me_4Sn as an internal standard: (i) none, (ii) HMPA, (iii) Bu_4NCl, (iv) Bu_4NBr, (v) Bu_4NI.

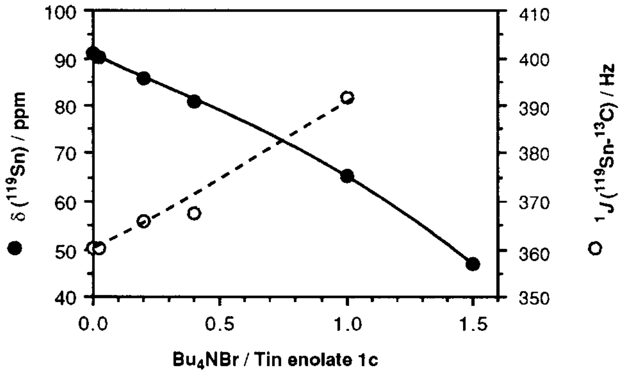


Figure 2. Correlation of chemical shift $\delta(^{119}Sn)$ and coupling constant ^1J $(^{119}Sn-^{13}C)$ with equivalents of Bu_4NBr to tin enolate **1c**.

The increase of the amount of Bu_4NBr caused a considerable upfield shift $\delta(^{119}Sn)$ and increasing values of the coupling constants $^1J(^{119}Sn-^{13}C)$ as shown in Figure 2.[22-24] These results clearly revealed the equilibrium between **1c**(*e*) and **1c**(*h*), and these data reflect the statistical average of the equilibrium. The contribution of **1**(*h*) to the equilibrium was more significant as the added amount of Bu_4NBr was increased. Unfortunately, the samples to which more Bu_4NBr was added could not be measured owing to the low solubility.

Next, HMPA was alternatively employed for detailed NMR examination of the equilibrium between **1c**(*e*) and **1c**(*h*) due to its free solubility in organic solvents. Figure 3 shows high coordination of tin enolate **1c**, indicating upfield shifts $\delta(^{119}Sn)$ and increasing coupling constants $J(^{119}Sn-^{13}C)$.

A coupling constant $^1J(^{119}Sn-^{13}C)$ increases linearly with s character of the tin atom.[25] In five-coordinated tributyltin complexes, three butyl groups are bonded to the central tin atom by sp^2 hybrid orbitals of tin while bonded by sp^3 hybrid orbitals

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(22) In general, an increase of coordination number of tin compounds from four to five causes upfield shifts of $\delta(^{119}Sn)$ and high values of coupling constants $^nJ(^{119}Sn-^{13}C)$.

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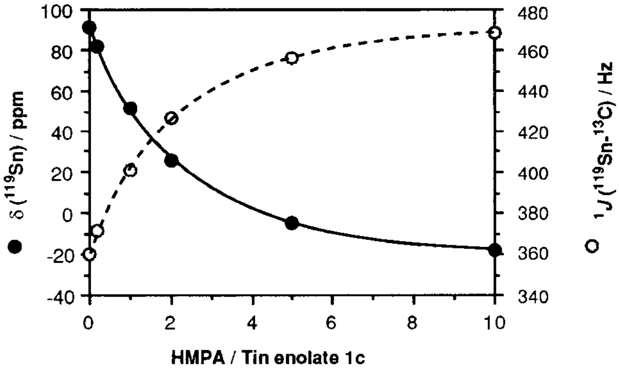


Figure 3. Correlation of chemical shift $\delta(^{119}Sn)$ and coupling constant ^1J ($^{119}Sn-^{13}C$) with equivalents of HMPA to tin enolate **1c**.

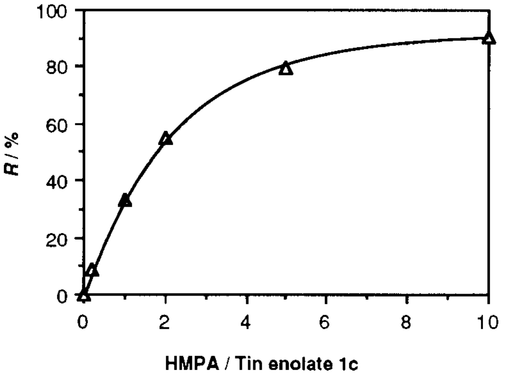


Figure 4. Correlation of the contribution of five-coordinated species with equivalents of HMPA to tin enolate **1c**.

in four-coordinated tin compounds.[24] Using these hypotheses, the theoretical calculation gave an estimate of the contribution ratio **1c**(*h*)/**1c** in equilibration of **1c**(*e*) and **1c**(*h*) (expressed by *R*). The relation of coupling constant *J* with *R* is given by

$$J = k\{(1 - R)/4 + R/3\} \qquad (2)$$

R can be expressed as

$$R = 3(J/J_0 - 1) \qquad (3)$$

where R = contribution ratio of five-coordinated tin enolate **1c**(*h*) toward total tin enolate **1c** species, k = slope of the linear relationship, J = coupling constant, J_0 = coupling constant of four-coordinated enolate. Figure 4 shows the relationship between the amount of HMPA and *R*.

About 50% contribution of **1c**(*h*) was found in addition of 1.5 equiv of HMPA, which is the condition of the investigated reaction depicted in Table 1 or 2. The equilibrium between **1c**(*e*) and **1c**(*h*) lies at a degree of ca. 90% toward **1c**(*h*), when 10 equiv of HMPA was added. These results obtained from the HMPA system indicate the effective high coordination in the case of using the bromide anion from Bu_4NBr, although the direct measurement could not be performed. We suppose that the resulting highly coordinated enol-type of the trigonal bipyramidal anionic complex effected the halo selective coupling (Scheme 4).

Competitive Reaction between Halides and Carbonyls. Use of the bromide-anion-coordinated tin enolate was also applied to the intermolecularly competitive reaction between halides and carbonyls. As shown in Table 3, in the competitive reaction between cinnamyl bromide **2a** and cyclohexanone **6a** with tin enolate **1b**, highly chemoselective control was observed.

Scheme 4

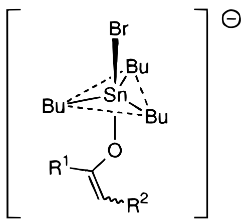
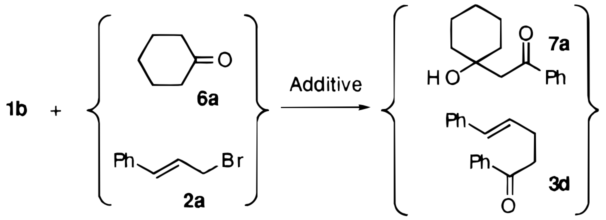


Table 3. Competitive Reaction of Tin Enolate **1b** between Cyclohexanone **6a** and Cinnamyl Bromide **2a**[a]



entry	additive	solvent	total yield (%)	**7a**:**3d**
1[b]	none	THF	40	>99:<1
2	HMPA	THF	80	11:89
3	Bu_4NCl	THF	21	<1:>99
4	Bu_4NBr	THF	72	<1:>99
5	Bu_4NBr	$CHCl_3$	28	<1:>99
6	Bu_4NBr	DMSO	62	<1:>99
7	Bu_4NBr	toluene	84	<1:>99
8	Bu_4NBr	CH_2Cl_2	90	<1:>99
9	Bu_4NBr	MeCN	99	<1:>99

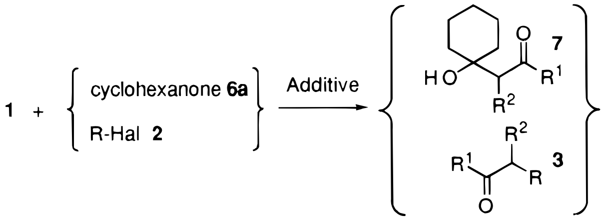
[a] Tin enolate **1b** (1.2 mmol), cyclohexanone **6a** (1.0 mmol), cinnamyl bromide **2a** (1.0 mmol), additive (1.8 mmol), solvent (1 mL), 60 °C, 3 h. [b] 6 h.

Only the carbonyl attack to form **7a** took place without an additive (entry 1). Addition of HMPA considerably changed the chemoselectivity from carbonyl to halide (entry 2), furnishing **3d** in 89% selectivity. Exclusive halide substitution reaction proceeded in the presence of Bu_4NBr, giving **3d** in over 99% selectivity (entry 4). The addition of Bu_4NCl, however, gave only a low chemical yield (21%) despite the exclusive halo selective coupling, perhaps because the too-strong interaction of Cl anion depressed the reactivity (entry 3). Bu_4NBr contributed to both chemoselectivity and chemical yield. High chemoselectivities were obtained with Bu_4NBr in various solvents (entries 4−9). Among the solvents investigated, acetonitrile effected the highest yield and selectivity (entry 9).

The competitive reactions of tin enolate **1** between cyclohexanone **6a** and various halides **2** are summarized in Table 4. In all cases, a pronounced change of chemoselectivity was attained by Bu_4NBr, to give **3** selectively, while no addition of Bu_4NBr afforded only carbonyl adduct **7**. In particular, all organic bromides underwent effective couplings, although moderate halo selectivity was observed in the reaction with benzyl chloride **2d** because of its low reactivity (entry 12).

Furthermore, the competitive reaction between benzaldehyde **6b** and ethyl 2-bromoacetate **2i** was investigated as shown in Table 5. Using bromo ester **2i** as a halide attained the halo selective control under mild conditions (Table 5). The high yield and selectivity were caused by Bu_4NBr (entry 4), whereas the predominant aldehyde addition took place without an additive, with HMPA or Bu_4NI (entries 1−3). The reaction in the presence of Bu_4NCl resulted in low yields. Only the bromide coordination, generating a five-coordinated anionic tin complex, showed excellent enhancement of the halide coupling even in the presence of aldehyde.

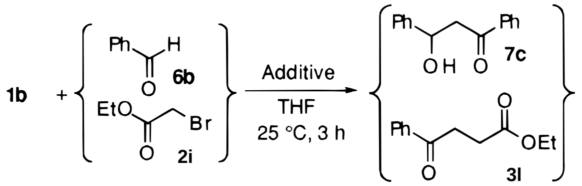
Table 4. Competitive Reaction of Tin Enolates **1** between Cyclohexanone **6a** and Halides **2**



entry	enolate **1**	halide **2**	additive	solvent	total yield (%)	products	**7:3**
1[a]	**1b**	**2c** benzyl bromide	none	THF	30	**7a:3i**	>99:<1
2[b]			Bu_4NBr	MeCN	56		<1:>99
3[a]	**1b**	**2a** cinnamyl bromide	none	THF	40	**7a:3d**	>99:<1
4[b]			Bu_4NBr	MeCN	99		<1:>99
5[a]	**1b**	**2h** allyl bromide	none	THF	30	**7a:3j**	>99:<1
6[b]			Bu_4NBr	THF	38		<1:>99
7[a]	**1c**	**2c** benzyl bromide	none	THF	39	**7b:3k**	>99:<1
8[b]			Bu_4NBr	THF	81		<1:>99
9[a]	**1c**	**2a** cinnamyl bromide	none	THF	51	**7b:3c**	67:33
10[b]			Bu_4NBr	toluene	62		<1:>99
11[a]	**1c**	**2d** benzyl chloride	none	THF	13	**7b:3k**	>99:<1
12[b]			Bu_4NBr	CH_2Cl_2	60		17:83

[a] Tin enolate **1** (1.2 mmol), **6a** (1.0 mmol), **2** (1.0 mmol), solvent (1 mL), 60 °C, 6 h. [b] Tin enolate **1** (1.2 mmol), **6a** (1.0 mmol), **2** (1.0 mmol), additive (1.8 mmol), solvent (1 mL), 60 °C, 3 h.

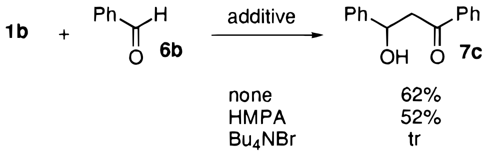
Table 5. Competitive Reaction of **1b** between Benzaldehyde **6b** and Ethyl 2-Bromoacetate **2i**[a]



entry	additive	yield (%)	**7c:3l**
1	none	69	91:9
2	HMPA	>99	73:27
3	Bu_4NI	86	72:27
4	Bu_4NBr	>99	<1:>99
5	Bu_4NCl	<5	<1:>99

[a] Tin enolate **1b** (1.2 mmol), **6b** (1.0 mmol), **2i** (1.0 mmol), additive (1.8 mmol), THF (1 mL), 25 °C, 3 h.

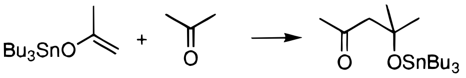
Scheme 5[a]



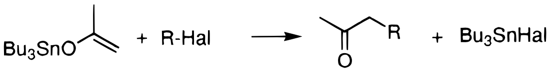
[a] Reagents and conditions: Tin enolate **1b** (1.2 mmol), **6b** (1.0 mmol), additive (1.8 mmol), THF (1 mL), 25 °C, 3 h.

Reactivity of Bromide-Anion-Coordinated Tin Enolate toward Aldehydes. Scheme 5 shows the intrinsic reactivity of four-coordinated and highly coordinated enolates toward an aldehyde. In the reaction of **1b** with benzaldehyde **6b**, HMPA scarcely changed the reactivity, showing little depression of the yield as compared with no additive reaction. However, high coordination by Bu_4NBr retarded the carbonyl addition, giving only a trace amount of the product, and the starting aldehyde was recovered. The results in Scheme 5 demonstrate the useful and unique role of Bu_4NBr as a selective promoter. The anionic highly coordinated tin enolates then proved to be powerful reagents for halo selective reaction because they have a low carbonyl addition character in addition to the strengthened reactivity toward halides.

Mechanistic Discussion for Chemoselective Control. The chemoselectivities toward halides or carbonyls summarized in Scheme 1 can be explained by the thermodynamics and kinetics of these reactions. The carbonyl addition and the halide substitution of tin enolates give tin alkoxide and tin halide, respectively, as shown in eqs 4 and 5.



(4)



(5)

We can compare the degree of thermodynamic stabilization of these types of tin compounds by the addition of ligands. The extremely high-field shift $\delta(^{119}Sn)$ of Bu_3SnBr in C_6D_6 was observed in the presence of equimolar amount of Bu_4NBr (133.7 → −18.9 ppm). On the contrary, little shift of Bu_3SnOMe was observed (101.2 → 95.1 ppm) in the same conditions. Comparing the result of Figure 2 (in the case of tin enolate **1c**, 91.0 → 65.3 ppm), the order of the degree of stabilization by the addition of a ligand is tin halide > tin enolate > tin alkoxide. For the high coordination system, a carbonyl addition (eq 4) is thermodynamically unfavored and a halide substitution (eq 5) is favored as compared with the system without ligands. Next, we should consider the polarization at the reaction site of tin enolates, which reflects the nucleophilicity of them. The addition of HMPA increased the difference of $\delta(^{13}C)$ between vinylic carbons of **1c** as shown in Figure 5. Therefore, the activation energy of the reaction with halides (eq 5) is lowered by the high coordination of tin enolates.

However, another factor should be considered in the carbonyl addition (eq 4) in which the coordination of carbonyl oxygen to the tin center is very significant in the transition state.[26] In the system with ligands, this coordination is unlikely to occur as compared with the system without ligands, and the activation energy in eq 4 increases. This factor is probably more important than that of the polarization in the carbonyl addition. The

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[26] Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 1920−1923.

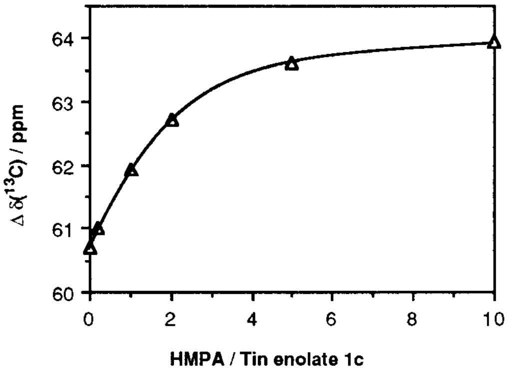

Figure 5. Correlation of the difference of δ(^{13}C) between vinylic carbons of **1c** with equivalents of HMPA to tin enolate **1c**.

different effect in the reaction with aldehyde between Bu_4NBr and HMPA (Scheme 5) can be explained by the distributing charge on the tin complex which is either neutral or anionic. The coordination of the anionic ligand to the tin center might considerably weaken the interaction between the tin enolate and carbonyl group.

Conclusion

In our search for high coordination of tin enolates, we have studied their selective control for C−C bond formation. A five-coordinated tin enolate can be readily formed by addition of appropriate ligands such as the bromide anion from Bu_4NBr or HMPA where the hybridization of tin can be changed from the four-coordinated one. In particular, bromide-anion-coordinated tin enolates effectively couple with various halides, and they completely lose the carbonyl addition character. The tin enolates without a ligand intrinsically are reactive toward carbonyl but not to halide. Therefore, the pronounced change of chemoselectivity observed in the anionic high coordination method is very useful for organic syntheses.

Experimental Section

General. Melting points were taken on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were recorded as thin films or as solids in KBr pellets on a Hitachi 260−30 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained with a Hitachi R-90H (90 and 22.6 MHz), a JEOL JNM-GSX-270 (270 and 67.9 MHz), or a JEOL JNM-GSX-400 (400 and 100 MHz) spectrometers, respectively, with TMS as internal standard. Mass spectra were recorded on a JEOL JMS-DS303 or a Shimadzu GCMS-QP2000A spectrometer. GLC analyses were performed on a Shimadzu GC-8A with FID using a 2 m × 3 mm column packed with SE-52. Flash chromatography was performed on silica gel (Wakogel C-300). Bulb-to-bulb distillation (Kügelrohr) was accomplished in a Sibata GTO-250RS at the oven temperature and pressure indicated. Yields were determined by GLC or ^{1}H NMR using internal standards.

Materials. THF and benzene were distilled from sodium and benzophenone. HMPA was distilled from CaH_2. Tetrabutylammonium halides were dried in vacuo before use. Tin enolates **1a**−**c** were prepared by known methods.[8] Halides **2a**−**i** and **4** and carbonyls **6a**−**b** were commercial products.

General Procedure for Substitution of Halides with Tin Enolate. A mixture of a tin enolate **1** (1.2 mmol) and an additive (1.8 mmol) in dry THF (1 mL) was stirred for 10 min under nitrogen. To this solution was added a halide **2** (1.0 mmol), and the resulting solution was stirred under the reaction conditions noted in Tables 1 and 2. Volatiles were removed under reduced pressure, diethyl ether (30 mL) and aqueous NH_4F (15%, 15 mL) were added, and the resulting Bu_3SnF was filtered off. The filtrate was washed with water (30 mL × 2), dried ($MgSO_4$), and evaporated. Flash chromatography of the resultant residue on silica gel gave pure products.

Chemoselective Reaction of Tin Enolate between Halides and Carbonyls. A mixture of a tin enolate **1** (1.2 mmol) and an additive (1.8 mmol) in a dry solvent (1 mL) was stirred for 10 min under nitrogen. To this solution was added a mixture of halide **2** (1.0 mmol) and carbonyls (1.0 mmol), and the resulting solution was stirred under the reaction conditions noted in Tables 3−5. After workup of the reaction mixture as above, ratios of **3** to **7** were determined by ^{1}H NMR or GLC.

Preparation and Measurement of NMR Samples. The samples were prepared from tin enolate **1c** (0.4 mmol) and an additive in dry C_6D_6 (0.4 mL). ^{119}Sn NMR spectra were recorded at room temperature on a JEOL JNM-GSX-400 (149 MHz) with Me_4Sn as internal standard.

Spectral Data. The spectral data of compounds **3b, e,** and **g** were in excellent agreement with commercial available samples, and the compounds **3l**[12] and **7c**[27] were identified by the spectral data described in the literature.

6-Phenyl-5-hexen-2-one (3a): IR (neat) 1700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.14 (m, 5H), 6.37 (d, 1H, J = 15.62 Hz), 6.16 (dt, 1H, J = 15.62, 6.83 Hz), 2.54 (t, 2H, J = 6.83 Hz), 2.43 (q, 2H, J = 6.83 Hz), 2.10 (s, 3H); ^{13}C NMR (22.6 MHz, $CDCl_3$) δ 207.1, 137.0, 130.2, 128.4, 128.1, 126.6, 125.6, 42.6, 29.5, 26.7; MS *m/z* 174 (M^+); HRMS calcd for $C_{12}H_{14}O$ 174.1045, found *m/z* 174.1046 (M^+). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.75; H, 8.10.

2-(3-Phenyl-2-propyl)cyclohexanone (3c): IR (neat) 1700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.17 (m, 5H), 6.39 (d, 1H, J = 16.11 Hz), 6.23−6.16 (m, 1H), 2.71−2.64 (m, 2H), 2.53−1.33 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.5, 137.6, 131.6, 128.5, 128.4, 127.0, 126.0, 50.7, 42.1, 33.6; MS *m/z* 215 (M^+ + 1), 214 (M^+); HRMS calcd for $C_{15}H_{18}O$ 214.1358, found *m/z* 214.1355 (M^+). Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.23; H, 8.27.

1,5-Diphenyl-4-penten-1-one (3d): mp 59−60 °C; IR (neat) 1680 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.98 (m, 2H), 7.59−7.16 (m, 8H), 6.47 (d, 1H, J = 15.62 Hz), 6.29 (dt, 1H, J = 15.62, 6.84 Hz), 3.15 (t, 2H, J = 7.33 Hz), 2.66 (td, 2H, J = 7.33, 6.84 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 199.3, 137.4, 136.9, 132.0, 130.8, 129.1, 128.6, 128.5, 128.0, 127.0, 126.0, 38.2, 27.5; MS *m/z* 236 (M^+); HRMS calcd for $C_{17}H_{16}O$ 236.1202, found *m/z* 236.1184 (M^+). Anal. Calcd for $C_{17}H_{16}O$: C, 86.41; H, 6.82. Found: C, 86.21; H, 6.79.

6-Phenyl-2-hexanone (3f): IR (neat) 1700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.15 (m, 5H), 2.63−2.59 (m, 2H), 2.45−2.41 (m, 2H), 2.10 (s, 3H), 1.63−1.59 (m, 4H); ^{13}C NMR (22.6 MHz, $CDCl_3$) δ 208.5, 142.0, 128.2, 128.1, 125.6, 43.5, 35.7, 30.9, 29.8, 23.4; MS *m/z* 177 (M^+ + 1), 176 (M^+); HRMS calcd for $C_{12}H_{16}O$ 176.1201, found *m/z* 176.1189 (M^+). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.52; H, 9.17.

2-Propylcyclohexanone (3h): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41−1.15 (m, 13H), 0.90 (t, 3H, J = 6.83 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.6, 50.5, 41.9, 33.8, 31.6, 28.0, 24.8, 20.3, 14.2; MS *m/z* 140 (M^+); HRMS calcd for $C_9H_{16}O$ 140.1201, found *m/z* 140.1210.

1,3-Diphenylpropan-1-one (3i): mp 68−69 °C; IR (KBr) 1660 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.0−7.9 (m, 2H), 7.6−7.4 (m, 3H), 7.35−7.15 (m, 5H), 3.31 (t, 2H, J = 7.57 Hz), 3.07 (t, 2H, J = 7.57 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 199.2, 141.3, 136.9, 133.0, 128.6, 128.5, 128.4, 128.0, 126.1, 40.4, 30.1; MS *m/z* 210 (M^+, 23); HRMS calcd for $C_{15}H_{14}O$ 210.1045, found *m/z* 210.1042 (M^+). Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.48; H, 6.75.

1-Phenyl-4-penten-1-one (3j): bp 70 °C/1 mmHg; IR (neat) 1680 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.95 (m, 2H), 7.58−7.54 (m, 1H), 7.48−7.44 (m, 2H), 5.96−5.86 (m, 1H), 5.09 (dd, 1H, J = 17.09, 1.46 Hz), 5.01 (dd, 1H, J = 10.25, 1.46 Hz), 3.07 (t, 2H, J = 7.32 Hz), 2.53−2.47 (m, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 199.3, 137.2, 136.9, 132.9, 128.5, 127.9, 115.2, 37.7, 28.1; MS *m/z* 160 (M^+, 3.9); HRMS calcd for $C_{11}H_{12}O$ 160.0889, found *m/z* 160.0884 (M^+).

2-Benzylcyclohexanone (3k): bp 110 °C/1 mmHg; IR (neat) 1700 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4−7.1 (m, 5H), 3.24 (dd, 1H, J = 13.67, 4.39 Hz), 2.65−1.25 (m, 10H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 212.5, 140.4, 129.1, 128.3, 125.9, 52.4, 42.1, 35.4, 33.4, 28.0,

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[27] Hasegawa, E.; Ishiyama, K.; Horaguchi, T.; Shimizu, T. *J. Org. Chem.* **1991**, *56*, 1631−1635.

25.0; MS m/z 188 (M^+, 100); HRMS calcd for $C_{13}H_{16}O$ 188.1202, found m/z 188.1198 (M^+). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.90; H, 8.62.

7-Bromo-2-octanone (5): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.13 (qd, 1H, $J = 1.46, 6.34$ Hz), 2.45 (t, 2H, $J = 7.32$ Hz), 2.14 (s, 3H), 1.70 (d, 3H, $J = 6.34$ Hz), 1.88−1.35 (m, 6H); ^{13}C NMR (22.6 MHz, $CDCl_3$) δ 208.2, 51.2, 43.2, 40.7, 29.8, 27.1, 26.3, 22.9; MS m/z 208 ($M^+ + 2$), 206 (M^+); HRMS calcd for $C_8H_{15}OBr$ 206.0306, found m/z 206.0310 (M^+).

1-(2-Oxo-2-phenylethyl)cyclohexanol (7a): mp 78 °C; IR (KBr) 3500, 1668 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.0−7.9 (m, 2H), 7.6−7.4 (m, 3H), 3.98 (s, 1H), 3.12 (s, 2H), 1.78−1.2 (m, 10H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 201.9, 137.5, 133.5, 128.6, 128.1, 70.9, 47.7, 37.8, 25.7, 21.9; MS m/z 218 (M^+, 8.7); HRMS calcd for $C_{14}H_{18}O_2$ 218.1307, found m/z 218.1303 (M^+). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.18; H, 8.33.

2-(1-Hydroxycyclohexyl)cyclohexanone (7b): IR (neat) 3500, 1690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 1H), 2.43−1.12 (m, 19H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 216.3, 71.9, 58.9, 43.8, 36.1, 33.2, 29.0, 28.2, 25.9, 25.5, 21.6, 21.3; MS m/z 196 (M^+); HRMS calcd for $C_{12}H_{20}O_2$ 196.1464, found m/z 196.1459 (M^+). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.31; H, 10.29.

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