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Unique Reactivities of New Highly Coordinated Ate Complexes of Organozinc Derivatives

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Organozinc reagents have been extensively used in organic synthesis.[1] The most important classes of organozinc derivatives have been organozinc halides and diorganozincs, and these have been prepared either by oxidative addition reaction of zinc metal to organic halides or by transmetalation reaction of organolithio or organomagnesio compounds with zinc chloride. As a new type of synthetic reagent, triorganozincates were reported to be convenient and synthetically useful for transferring various organic moieties to α,β-unsaturated ketones in a 1,4-fashion.[2] Lithium trialkylzincates were also reported to be useful as metalating reagents of aromatic halides or vinyl halides.[3] The outer shell of the zinc atom in a lithium trialkylzincate is filled with 16 electrons, and there is a room for an additional ligand to coordinate to form a favorable 18-electron state. There are some reports on tetraalkylzincates[4] and X-ray studies of the complexes which have disclosed that in the crystal structure of tetraalkylzincates there is a tetrahedral arrangement about the zinc atom.[5] However the reactivities of tetraalkylzincates have not been well studied. The unique tetrahedral form of these complexes made us study the reactivity of these tetraalkylorganozincates and related modified organozincates. The ^{1}H-NMR study of organozincates indicated the difference between these highly coordinated zincates and lithium trimethylzincate. Studies to compared the reactivity of these reagents disclosed a different regioselectivity for epoxide opening and a different reactivity toward halogen−metal exchange. These results support that these highly coordinated zincates should be distinguished from ordinary lithium trialkylzincates in structure and reactivity.
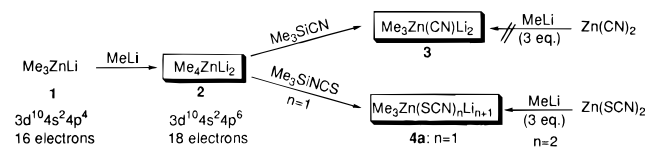
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Table 1. ^{1}H-NMR of Zincates in THF (−20 °C)

entry	metal reagent	δ_{Me} (ppm)[a]
1	MeLi	−1.96
2	Me_2Zn	−0.84
3	Me_3ZnLi	−1.08
4	Me_4ZnLi_2	−1.44
5	$Me_3Zn(SCN)Li_2$	−1.23
6	$Zn(SCN)_2 + 3MeLi$	−1.31
7	$Me_3Zn(CN)Li_2$	−1.20
8	$Zn(CN)_2 + 3MeLi$	−1.95

[a] The δ values are relative to β methylene proton (1.85 ppm) to THF.

First, preparation of highly coordinated zincates were investigated, and ^{1}H-NMR spectra of the zincates were measured for the preliminary estimation of the component of the zincate solution. Dilithium tetramethylzincate was prepared by the reaction of zinc chloride with 4 equiv of methyllithium in THF using the modified reported procedure.[4a] The methyl signal of Me_4-$ZnLi_2$ in THF (−1.44 ppm) was observed midway as a sharp singlet between the signals of Me_3ZnLi (−1.08 ppm) and MeLi (−1.96 ppm). High-field shift from the value of Me_3ZnLi is considered to indicate the more anionic character of the zincates. Measurement at −78 °C gave very similar results with a slight high-field shift of each signal. Addition of one more equivalent of MeLi to the Me_4ZnLi_2 solution resulted in a broad singlet signal at −1.49 ppm at −20 °C which separated at −78 °C into two signals corresponding to the signals of MeLi and those of Me_4ZnLi_2. Addition of 1 equiv of Me_3SiCN or Me_3SiNCS to the Me_4ZnLi_2 solution should give the zincates with methyl group replacement by the CN or SCN ligand. As we expected, the reaction of the tetramethylzincate with Me_3SiCN and Me_3-SiNCS gave the new zincates, $Me_3Zn(CN)Li_2$ (**3**) and Me_3Zn-$(SCN)Li_2$ (**4a**), of which methyl signals were observed as sharp singlets (−1.20 ppm for **3** and −1.23 ppm for **4a**).[6a] As an alternative way to prepare CN- or SCN-ligated zincates, the reaction of $Zn(CN)_2$ or $Zn(SCN)_2$ with 3 equiv of methyllithium was examined. From the preliminarly ^{1}H-NMR study, the reaction of $Zn(CN)_2$ with MeLi is sluggish and no formation of a zincate was observed,[6b] while the reaction of $Zn(SCN)_2$ with MeLi gave a zincate (−1.31 ppm) similar to **4a** (Table 1). These results indicate that the different species of zincates are formed except for the reaction of $Zn(CN)_2$ with MeLi, and the more anionic character of these highly coordinated zincates than that of Me_3ZnLi encouraged us to investigate the following reactions.

Regioselectivity of intermolecular ring-opening reaction of epoxides has been investigated focusing on the nature of the organometallic reagent, such as the Lewis acidity or the basicity.[7] Styrene oxide was reacted with various organometallic derivatives, and the ratio of two isomeric compounds, 1-phenyl-1-propanol (**6**) and 2-phenyl-1-propanol (**7**) was estimated. The results are as listed in Table 2. Reaction with Me_3ZnLi gave almost equal amounts of **6** and **7**. Me_4ZnLi_2 also showed similar selectivity, while the reaction with Me_3-$Zn(CN)Li_2$ and $Me_3Zn(SCN)Li_2$ gave **7** as a major product, and the reaction with MeLi and $Me_2Cu(CN)Li_2$ gave **6** as a major product. Although the reasons for the divergent selectivity are not clear at present, the inverse selectivity between $Me_3Zn(CN)$-Li_2 and $Me_2Cu(CN)Li_2$ is attractive from a synthetic viewpoint.

Our next interest was focused on the intramolecular ring-opening reaction of epoxide **8** using the zincates as metalating

(6) (a) The signal of tetramethylsilane newly generated in the mixture was observed at 0.00 ppm together with disappearance of the signal of Me_3-SiCN (0.38 ppm) or Me_3SiNCS (0.40 ppm). (b) For recent discussion on the structure of $Zn(CN)_2$, see: Hoskins, B. F.; Robson, R. *J. Am. Chem. Soc.* **1990**, *112*, 1546−1554.

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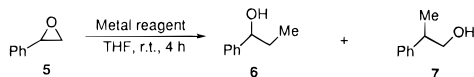
Table 2. Intermolecular Epoxide-Opening Reactions

entry	metal reagent	yield (%) **6 + 7**	**6:7**
1	Me$_3$ZnLi	70	56:44
2	Me$_4$ZnLi$_2$	93	51:49
3	Me$_3$Zn(CN)Li$_2$	41	29:71
4	Me$_3$Zn(SCN)Li$_2$	trace	37:63
5	Zn(SCN)$_2$ + 3MeLi	trace	32:68
6	MeLi	trace	71:29
7	Me$_2$Cu(CN)Li$_2$	93	68:32
8	Me$_2$Cu(SCN)Li$_2$	100	61:39

agents.[8] Interestingly, Me$_3$ZnLi showed almost completely opposite regioselectivity from those of the other modified zincates for the ring-opening reaction (Table 3). Especially, the reaction with Me$_3$ZnLi and the reaction with Me$_3$Zn(SCN)-Li$_2$ showed almost perfect reverse regioselectivity. The reaction with Me$_3$ZnLi gave *endo*-cyclized 1,2,3,4-tetrahydroquinoline derivative (**10**) as a major product, while the reaction with Me$_3$-Zn(SCN)Li$_2$ gave *exo*-cyclized indoline derivative (**9**). Interestingly, the cyano-modified reagents, Me$_3$Zn(CN)Li$_2$ and Me$_2$Cu-(CN)Li$_2$, showed completely opposite regioselectivity in this system. R$_2$Cu(CN)Li$_2$ compounds have been called "higher order cuprates",[9] and the structure of these cuprates has been a controversial issue.[10] However recent studies on the structure revealed that the CN ligand is not on the Cu atom but on the Li atom.[11] The structures of highly coordinated zincates with the CN or SCN ligand have never been studied. Taking the tendency of zinc derivatives to form complexes with tetrahedral configuration (sp^3-hybridized structure) into account, we cannot omit the possibility of the ligation of CN or SCN to the Zn atom.
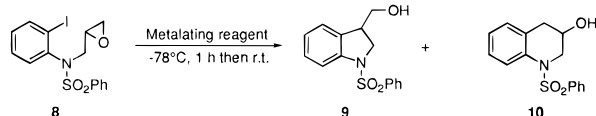
Intramolecular carbometalation was then examined using iodine−zinc exchange reaction of allyl 2-iodophenyl ether (**13**). When **13** was treated with Me$_3$ZnLi, halogen−metal exchange reaction proceeded smoothly, but no intramolecular carbometa-

(8) We recently reported a regioselective ring-opening reaction of epoxyorganometallic compounds which derived from halogen−metal exchange reaction using ate complexes. Kondo, Y.; Matsudaira, T.; Sato, J.; Murata, N.; Sakamoto, T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 736−738.
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Table 3. Intramolecular Epoxide-Opening Reaction

entry	metalating reagent	yield (%) **9 + 10**	**9:10**
1	Me$_3$ZnLi	86	4:96
2	Me$_4$ZnLi$_2$	67	87:13
3	Me$_3$Zn(CN)Li$_2$	57	80:20
4	Me$_3$Zn(SCN)Li$_2$	92	97:3
5	Zn(SCN)$_2$ + 3MeLi	80	81:19
6	Me$_2$Cu(CN)Li$_2$	50	12:88

lation was observed. On the other hand, the reaction of **13** with Me$_4$ZnLi$_2$ followed by hydrolysis gave 3-methyldihydrobenzo-[*b*]furan (**15**) in 42% yield, which probably results from intramolecular carbozincation.
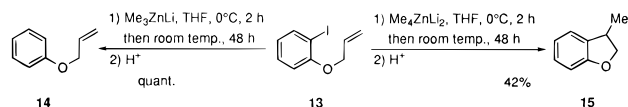
We have reported that Me$_3$ZnLi is useful for iodine−zinc exchange reaction of functionalized aromatic iodides; however, aromatic bromides were unreactive to this metalation process.[3a] Since Me$_4$ZnLi$_2$ is considered to have more anionic character, the bromine−zinc exchange reaction of bromobenzene was then investigated. The reaction was carried out at −20 °C, and the resulting metal species was trapped with benzaldehyde to give benzhydrol in 47% yield (Table 4). Under the same reaction conditions, the reaction with Me$_3$ZnLi did not proceed at all, and MeLi was also found inactive under the same conditions. The modified zincates, Me$_3$Zn(CN)Li$_2$ and Me$_3$-Zn(SCN)Li$_2$, showed moderate reactivity toward the bromine−zinc exchange reaction, and benzhydrol was obtained in 22% and 23% yields, respectively. These results also support the structural difference between the highly coordinated zincates and Me$_3$ZnLi.
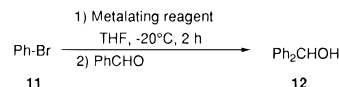
Table 4. Bromine−Zinc Exchange Reaction

entry	metalating reagent	yield (%)
1	MeLi	0
2	Me$_3$ZnLi	0
3	Me$_4$ZnLi$_2$	47
4	Me$_3$Zn(CN)Li$_2$	22
5	Me$_3$Zn(SCN)Li$_2$	23

Further studies on the structural analyses of the new highly coordinated organozincates are underway together with their applications for organic syntheses.

Supporting Information Available: Representative experimental procedures and ^{1}H-NMR spectra for the zincates (6 pages). See any current masthead page for ordering and Internet access instructions.

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