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^{7}Li- and ^{31}P NMR spectra of cyclopentanone lithium enolate in ethereal solvents: identification of the HMPA-coordinated aggregate structures

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This paper is dedicated to Professor K. C. Nicolau (Scripps Research Institute) and Professor D. Seebach (ETH) on their honor of the Tetrahedron Prize.

Abstract—The structures of cyclopentanone lithium enolate under HMPA titration in 0.04–0.8 M diethyl ether and dimethyl ether solvents have been investigated using the low-temperature ^{7}Li, ^{31}P, and ^{13}C NMR. The progressive solvation by HMPA occurs for the tetra- and dimeric enolates, and upon addition of >2 equiv. of HMPA, the lithium enolate has been converged on a mixture of tetra-HMPA coordinated tetramer and bis-HMPA coordinated dimer with the ratio of 5:95 and <1:99 in diethyl ether and dimethyl ether, respectively. Neither monomeric nor trimeric enolate is detectable under such HMPA titration.

1. Introduction

Organolithium compounds generally exist as aggregates in both solid state[1–3] and solution.[4–8] The aggregation states play crucial roles to determine the reactivity and selectivity in organic reactions.[9–12] NMR is a particularly powerful tool for elucidating the aggregation structure in solution. Actually, the $^{6/7}$Li–^{15}N or $^{6/7}$Li–^{13}C coupling patterns provide direct evidence of monomeric, dimeric, tetrameric, and higher oligomeric structures of lithium amide[4] and alkyllithium species.[5] On the other hand, there have been few NMR studies of lithium enolates because of the lack of the $^{6/7}$Li–^{17}O vicinal coupling.[9] Therefore, Jackman conducted to determine the tetrameric aggregation state of isobutyrophenone lithium enolate in ethereal solvents by combination of vapor pressure osmometry, $^{6/7}$Li and ^{13}C chemical shifts, and ^{7}Li quadrupole splitting constants.[6]

HMPA addend modulates the reactivity of the lithium enolate in a way to realize the high selectivity in alkylation.[11,12] This effect has well been utilized in the three-component coupling prostaglandin (PG) synthesis.[13] In this regard, we have analyzed the structure of cyclopentanone lithium enolate in the presence of HMPA in THF using ^{7}Li and ^{31}P NMR.[14] Further, kinetic studies, coupled with the structural analyses, elucidated the origin of the HMPA effects on the enhancement of the reactivity and selectivity.[14] There, the ^{31}P chemical shift and ^{31}P–^{7}Li long-range coupling obtained at low-temperature served to determine HMPA-coordinated dimeric structures in solution. We here describe the study on the enolate structure in diethyl ether and dimethyl ether solvents.[15] In such open-chain ethereal solvents, both the ^{7}Li and ^{31}P signals were sharper than in THF at low temperature (−100 to −110 °C) and well discriminated enough to complement particularly the assignment of the ^{7}Li signals for the HMPA-coordinated structures in THF. Thus, a mixture of the HMPA-involved tetrameric and dimeric enolates observed in such ethereal solvents eventually converged on the corresponding tetra-HMPA coordinated tetramer and bis-HMPA coordinated dimer in the presence of HMPA more than 2 equiv.

2. Results and discussion

2.1. NMR analysis of the enolate in the presence of HMPA

The structures of cyclopentanone lithium enolate (**1**) in diethyl ether or dimethyl ether were studied using low-temperature ^{7}Li, ^{31}P, and ^{13}C NMR with their chemical shifts and coupling constants, $^{2}J(^{7}\text{Li}–^{31}\text{P})$, observed in HMPA–Li solvates.[16] The solution of lithium enolate **1** was prepared by reaction of 1-(trimethylsiloxy)cyclopentene

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Keywords: Lithium enolate; HMPA titration; ^{7}Li NMR; ^{31}P NMR; Tetrameric structure; Dimeric structure.

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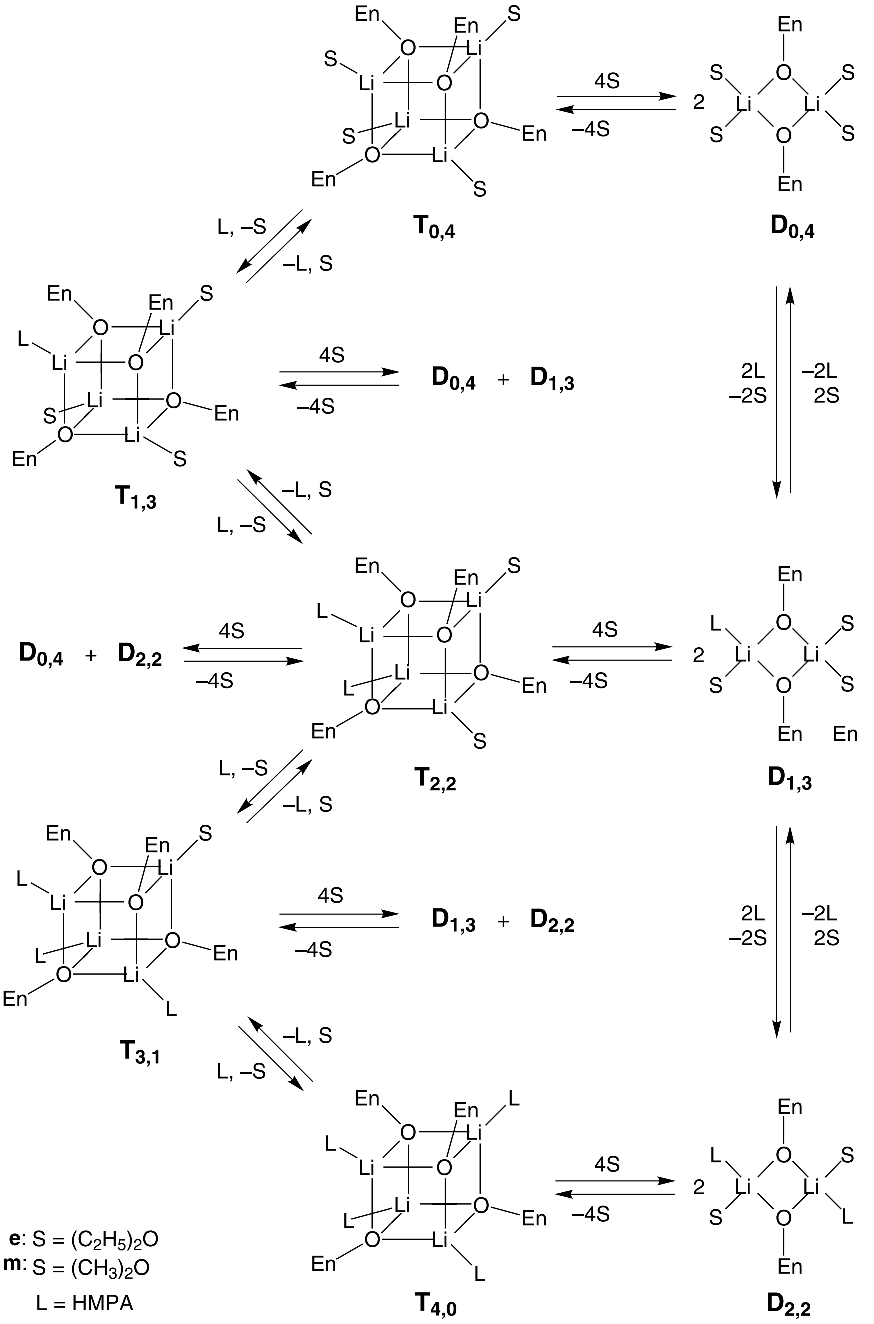
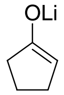


Scheme 1. Equilibrium of cyclopentanone lithium enolate in the presence of HMPA.

and *n*-butyllithium in an ethereal solvent. In the presence of HMPA, the enolate **1** was found to establish the dynamic equilibrium illustrated in Scheme 1 in such a solvent. In this Scheme, for both the tetramer **T** and the dimer **D**, the first subfix represents the number of attached HMPAs and the second subfix denotes the number of coordinated ethereal ligands.[17] The latter is associated with **e** or **m**, representing diethyl ether and dimethyl ether, respectively. The equilibrium point is thermodynamically determined by the enolate concentration, the quantity of HMPA, and the properties of the ethereal solvent S.[18,19] In the presence of excess HMPA the enolate largely exists as an bis-HMPA coordinated dimer $\mathbf{D}_{2,2}$ which equilibrates with some tetra-HMPA coordinated tetramer $\mathbf{T}_{4,0}$. This $\mathbf{T}_{4,0}/\mathbf{D}_{2,2}$ ratio depends on the basicity of S.[18,19] Monomers[16] and trimers,[20] however, were not observed.



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2.1.1. ^{7}Li and ^{31}P NMR in diethyl ether.

Figure 1, A and B shows the ^{7}Li- and ^{31}P NMR spectra of 0.16 M diethyl ether solutions of **1** at −100 °C.[21] The signals in such an ethereal solvent were much more sharper than in THF presumably due to the slower S/L ligand exchange on the NMR time scale at this temperature.[14] Although lithium enolate **1** was

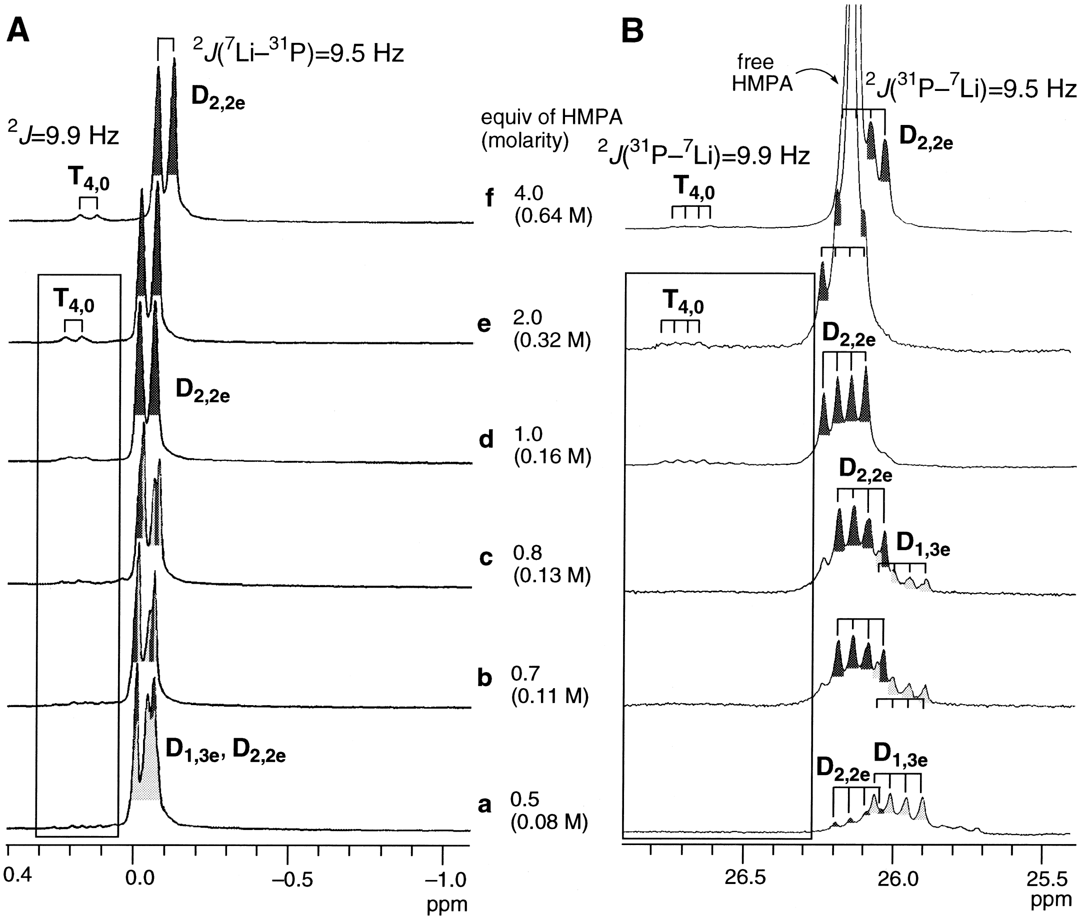

Figure 1. HMPA titration of a 0.16 M diethyl ether solution of cyclopentanone lithium enolate **1** at −100 °C. A: ^{7}Li NMR spectra. B: ^{31}P NMR spectra. The enclosed spectra are enlarged and shown in Figure 2.

insoluble in this solvent in the absence of HMPA, it dissolved upon the addition of >0.5 equiv. of HMPA in 0.16 M solution. The addition of 2 equiv. of HMPA yielded two doublets, at 0.21 and −0.03 ppm, with $^2J(^7\mathrm{Li}-^{31}\mathrm{P})$=9.9 and 9.5 Hz (Fig. 1, Ae). Further increase in HMPA (4 equiv.) had no effect on the signal pattern with the same ratio of two doublets (Fig. 1, Af), although there was a significant upfield shift;[22] these doublets were assignable to $\mathbf{T_{4,0}}$ (minor) and $\mathbf{D_{2,2e}}$ (major), respectively, in a 5:95 ratio. In the presence of <1 equiv. of HMPA, three additional peaks were observed in a 0.1 to −0.1 ppm region in ^{7}Li NMR (Fig. 1, Aa–c). The inside singlet peak at −0.03 ppm (Fig. 1, Aa) disappeared at higher HMPA concentrations, resulting in a doublet due to $\mathbf{D_{2,2e}}$, as judged by the $^2J(^7\mathrm{Li}-^{31}\mathrm{P})$ value of 9.5 Hz (Fig. 1, Ad).[14,16] The transient singlet was therefore assigned to the HMPA-free ^{7}Li atom in $\mathbf{D_{1,3e}}$, and the outside doublet to the HMPA-coordinated ^{7}Li atoms in $\mathbf{D_{1,3e}}$ and $\mathbf{D_{2,2e}}$. In a similar manner, the profile of the successive conversion to $\mathbf{D_{1,3e}}$ and then to $\mathbf{D_{2,2e}}$ during HMPA titration was also clearly monitored by ^{31}P NMR signals (Fig. 1, B). A signal due to $\mathbf{D_{1,3e}}$ appeared at 26.0 ppm with the $^2J(^{31}\mathrm{P}-^7\mathrm{Li})$ value of 10.3 Hz upon the addition of 0.5 equiv. of HMPA (Fig. 1, Ba); with the increase in HMPA, this signal decreased, and a signal due to $\mathbf{D_{2,2e}}$ appeared at 26.1 ppm with ^2J=9.5 Hz, predominating at 1 equiv. of HMPA (Fig. 1, Bd). After the addition of 2 equiv. of HMPA, the coordinated and free HMPAs were partially overlapped, but the side signals around a huge free HMPA signal can be assigned to $\mathbf{D_{2,2e}}$. Minor tetramer $\mathbf{T_{4,0}}$ was observed at 26.7 ppm as a quartet in the presence of 2 equiv. of HMPA (Fig. 1, Be) with the same $\mathbf{T_{4,0}}/\mathbf{D_{2,2e}}$ integral ratio (ca. 5:95) as in the ^{7}Li NMR.

Enlarging the 0.1–0.3 ppm region in the ^{7}Li spectra (Fig. 1, A) showed four types of 1:1 doublets at 0.13, 0.16–0.17, 0.20–0.21, 0.22 ppm (Fig. 2, A). The intensities of these doublets changed with the increase in HMPA and the precedent three kinds of doublets disappeared at the addition of 2 equiv. of HMPA to give sole doublet at 0.21 ppm (Fig. 2, Ae). These precedent three doublets could, therefore, be assigned to the ^{7}Li atoms in the HMPA-coordinated complexes, $\mathbf{T_{1,3e}}$, $\mathbf{T_{2,2e}}$, and $\mathbf{T_{3,1e}}$ formed by the progressive HMPA solvation of the tetramer with the increase in added HMPA.[23] Here, the HMPA-free ^{7}Li signals in the tetramers are superimposed on the most intense low-field peak at 0.01 ppm (Fig. 1, Aa–d). In a similar manner, as shown in the enlarged ^{31}P spectra in the 26.3–27.0 ppm region (Fig. 2, B), the four tetramers, $\mathbf{T_{1,3e}}$, $\mathbf{T_{2,2e}}$, $\mathbf{T_{3,1e}}$, and $\mathbf{T_{4,0}}$, yielded four kinds of a 1:1:1:1 quartet with ^2J values of 9.9–11.2 Hz at 26.7, 26.5, 26.6, and 26.7 ppm, respectively, well correlating with the structural assignment in the ^{7}Li NMR. Thus, the profile of four kinds of ^{7}Li doublets and ^{31}P quartets and the change in their relative intensities during HMPA titration indicated that the successive coordination of four HMPA to Li cations in the tetrameric structure to converge on $\mathbf{T_{4,0}}$ with HMPA addend more than 2 equiv.

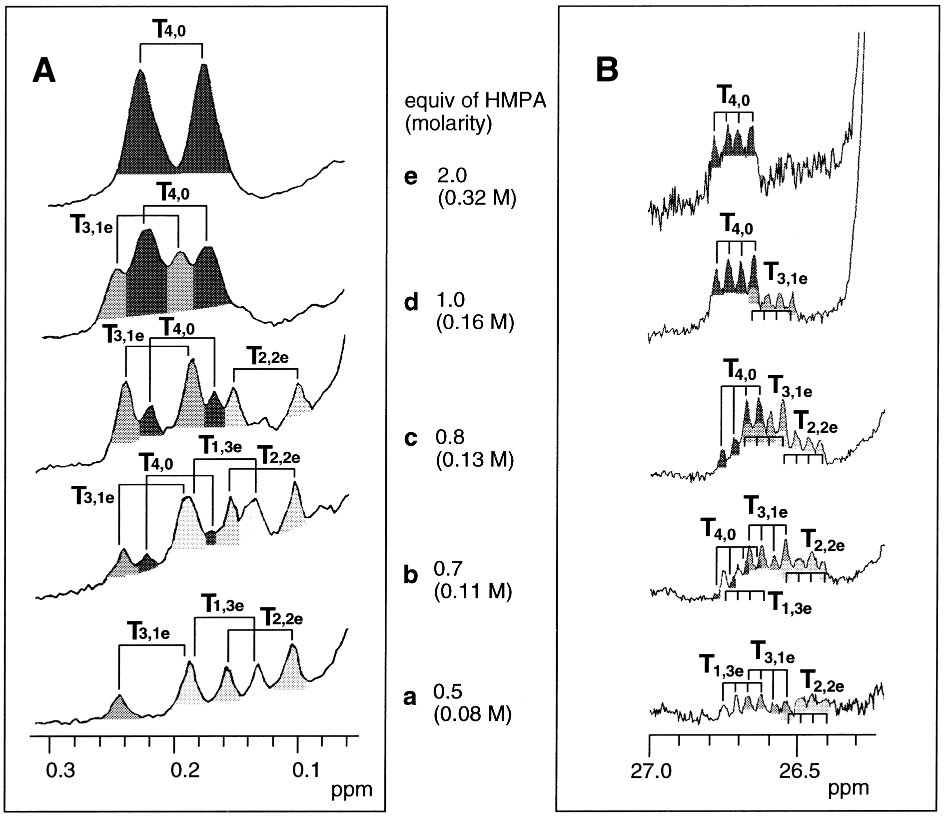

Figure 2. Enclosed spectra in Figure 1. A: ^{7}Li NMR spectra. B: ^{31}P NMR spectra.

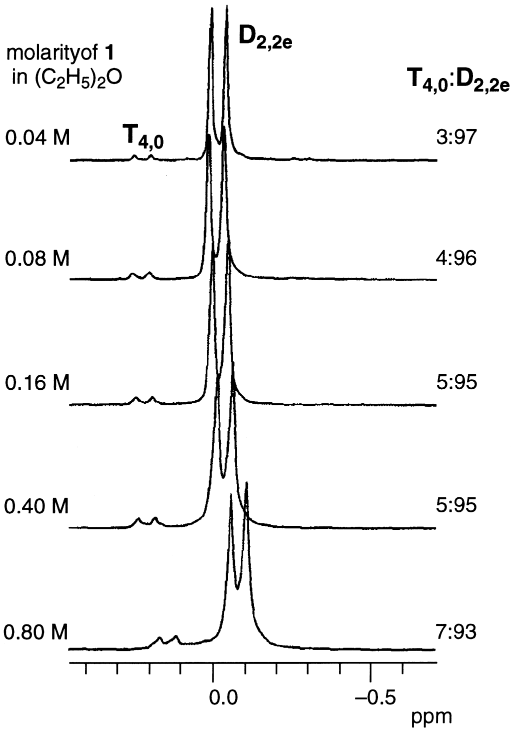

Figure 3. Concentration dependence of ^{7}Li NMR spectra of cyclopentanone lithium enolate **1** (−100 °C) in diethyl ether in the presence of 2 equiv. of HMPA.

In addition, the $\mathbf{T_{4,0}}/\mathbf{D_{2,2e}}$ ratio was independent of the quantity of added HMPA in a range of more than 2 equiv. (Fig. 1, Ae and f), but was influenced by the enolate concentration (Fig. 3). Thus, the relative ratio varied from 7:93 to 3:97 upon the dilution of **1** from 0.80 to 0.04 M, confirming the above structural assignment and the presence of a dynamic equilibrium between $\mathbf{T_{4,0}}$ and $\mathbf{D_{2,2e}}$ shown in Scheme 1.

2.1.2. ^{7}Li and ^{31}P NMR in dimethyl ether.

The lithium enolate **1** is soluble in this solvent even without HMPA. Figure 4A and B, shows the ^{7}Li- and ^{31}P NMR spectra of 0.32 M dimethyl ether solutions of **1** at −110 °C. Without HMPA, the lithium enolate gave a ^{7}Li broad singlet at 0.16 ppm (Fig. 4, Aa).[24] Upon the addition of 2 equiv. of HMPA, **1** mostly exists as a bis-HMPA coordinated dimer, giving a 1:1 doublet at 0.21 ppm in the ^{7}Li spectrum and 1:1:1:1 quartet at 26.3 ppm in the ^{31}P spectrum, with the same coupling constants, $^{2}J(^{7}\mathrm{Li}-^{31}\mathrm{P})={}^{2}J(^{31}\mathrm{P}-^{7}\mathrm{Li})=9.5$ Hz (Fig. 4, Ai and Bi, respectively). The formation of dimers was monitored by the characteristic signal patterns of ^{7}Li NMR and the change in their signal intensities due to three different Li atoms in $\mathbf{D_{1,3m}}$ and $\mathbf{D_{2,2m}}$ during the HMPA titration. Thus, the addition of 0.2 equiv. of HMPA (Fig. 4, Ac) yielded a doublet with a coupling constant of 10.1 Hz at 0.28 ppm and a singlet at 0.22 ppm. Both signals are assignable to the ^{7}Li atoms in $\mathbf{D_{1,3m}}$. When 0.5 equiv. of HMPA was added (Fig. 4, Ad), the latter doublet appeared at 0.24 ppm, assignable to $\mathbf{D_{2,2m}}$. This doublet signal was intensified at the expense of the initially observed doublet

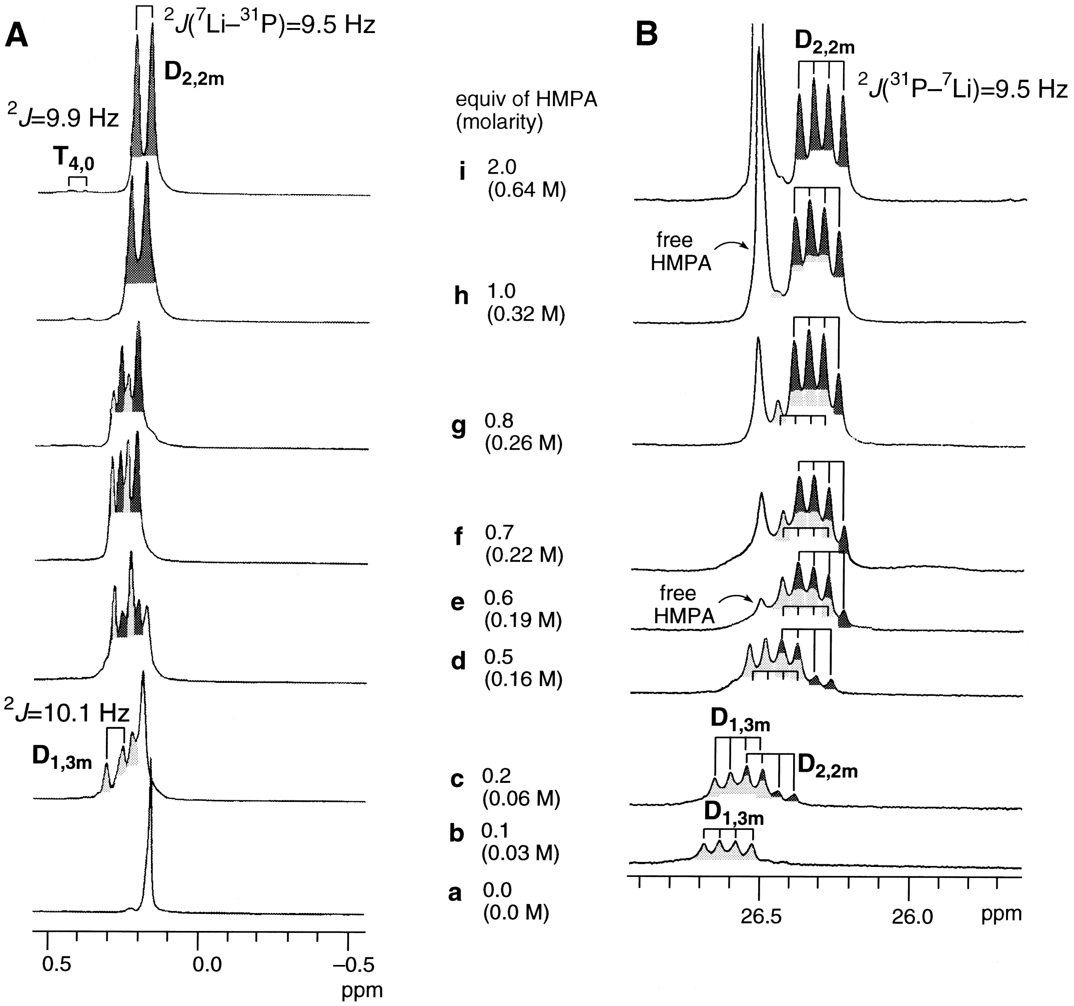

Figure 4. HMPA titration of a 0.32 M dimethyl ether solution of cyclopentanone lithium enolate **1** at −110 °C. A: ^{7}Li NMR spectra. B: ^{31}P NMR spectra.

Table 1. ^{7}Li and ^{31}P chemical shifts and coupling constants of the HMPA-solvated dimers and tetramers formed from cyclopentanone lithium enolate (**1**) in diethyl ether[a]

HMPA (equiv.)	^{7}Li (s^b) δ^c	^{7}Li (d^b) δ^c ($^2J(^7$Li–^{31}P)^d)		^{7}Li (d^b) δ^c ($^2J(^7$Li–^{31}P)^d)			
	$\mathbf{D_{1,3e}}$	$\mathbf{D_{1,3e}}$	$\mathbf{D_{2,2e}}$	$\mathbf{T_{1,3e}}$	$\mathbf{T_{2,2e}}$	$\mathbf{T_{1,3e}}$	$\mathbf{T_{4,0}}$
0.5	−0.03	−0.02 (10.1)		0.16 (11.2)	0.13 (10.7)	0.22 (11.2)	
0.7	−0.03	−0.01^e (10.1)	−0.01^e (9.5)	0.17 (11.1)	0.13 (10.7)	0.22 (11.2)	0.20 (9.9)
0.8	−0.03	−0.01^e (10.1)	−0.01^e (9.5)		0.13 (10.7)	0.22 (11.2)	0.20 (9.9)
1.0			−0.02 (9.5)			0.22 (11.2)	0.20 (9.9)
2.0			−0.03 (9.5)				0.21 (9.9)
4.0			−0.06 (9.5)				0.18 (9.9)
HMPA (equiv.)		^{31}P (q^b) δ^c ($^2J(^{31}$P–^{7}Li)^d)		^{31}P (q^b) δ^c ($^2J(^{31}$P–^{7}Li)^d)			
		$\mathbf{D_{1,3e}}$	$\mathbf{D_{2,2e}}$	$\mathbf{T_{1,3e}}$	$\mathbf{T_{2,2e}}$	$\mathbf{T_{1,3e}}$	$\mathbf{T_{4,0}}$
0.5		26.0 (10.3)	26.1 (9.5)	26.7 (11.1)	26.5 (10.2)	26.6 (11.1)	
0.7		26.0 (10.3)	26.1 (9.5)	26.7 (11.1)	26.5 (10.2)	26.6 (11.1)	26.7 (10.0)
0.8		26.0 (10.3)	26.1 (9.5)		26.5 (10.2)	26.6 (11.1)	26.7 (9.9)
1.0			26.1 (9.5)			26.6 (11.1)	26.7 (10.0)
2.0			26.1 (9.5)				26.7 (9.9)
4.0			26.1 (9.5)				26.7 (9.9)

[a] Spectra were recorded at −100 °C.

[b] s, singlet; d, doublet, and q, quartet.

[c] The chemical shifts are reported relative to external standard as described in Section 4.

[d] All coupling constants *J* are reported in Hertz.

[e] Two doublets due to $\mathbf{D_{1,3e}}$ and $\mathbf{D_{2,2e}}$ are overlapped.

Table 2. ^{7}Li and ^{31}P chemical shifts and coupling constants of the HMPA-solvated dimers and tetramers formed from cyclopentanone lithium enolate (**1**) in dimethyl ether[a]

HMPA (equiv.)	^{7}Li (s[b]) δ[c]	^{7}Li (d[b]) δ[c] ($^2J(^7Li-^{31}P)$[d])	^{7}Li (d[b]) δ[c] ($^2J(^7Li-^{31}P)$[d])		^{31}P (d[b]) δ[c] ($^2J(^{31}P-^7Li)$[d])	
	$\mathbf{D_{1,3m}}$	$\mathbf{D_{1,3m}}$	$\mathbf{D_{2,2m}}$	$\mathbf{T_{4,0}}$	$\mathbf{D_{1,3m}}$	$\mathbf{D_{2,2m}}$
0.1					26.6 (10.3)	
0.2	0.22	0.28 (10.1)			26.6 (10.3)	26.5 (9.5)
0.5		0.27 (10.1)	0.24 (10.1)		26.4 (10.3)	26.3 (9.5)
0.6					26.3 (10.3)	26.3 (9.5)
0.7		0.27 (10.1)	0.24 (9.5)		26.3 (10.3)	26.3 (9.5)
0.8		0.29 (10.1)	0.25 (9.5)		26.3 (10.3)	26.3 (9.5)
1.0			0.23 (9.5)	0.42 (9.9)		26.3 (9.5)
2.0			0.21 (9.5)	0.43 (9.9)		26.3 (9.5)

[a] Spectra were recorded at −110 °C.
[b] s, singlet; d, doublet, and q, quartet.
[c] The chemical shifts are reported relative to external standard as described in Section 4.
[d] All coupling constants *J* are reported in Hertz.

(Fig. 4, Af–h), and became the sole signal upon the addition of 2 equiv. of HMPA (Fig. 4, Ai).[25] In addition, a very small doublet of 9.9 Hz was detected at 0.43 ppm (at low field), indicating the formation of the tetramer $\mathbf{T_{4,0}}$ (<1%) (Fig. 4, Ai) (see also the structural convergence in diethyl ether shown in Fig. 2). The same structural conclusion was provided by ^{31}P NMR analysis (Fig. 4B). Thus, the two quartets due to $\mathbf{D_{1,3m}}$ and $\mathbf{D_{2,2m}}$ appeared at 26.3–26.6 ppm with $^2J(^{31}P-^7Li)=10.3$ Hz and 26.3–26.5 ppm with $^2J=9.5$ Hz, respectively. The intensity of the quartet belonging to $\mathbf{D_{1,3m}}$ became maximal at the addition of 0.6 equiv. of HMPA (Fig. 4, Be). The second quartet due to $\mathbf{D_{2,2m}}$ overwhelmed $\mathbf{D_{1,3m}}$ at the addition of 0.8 equiv. of HMPA (Fig. 4, Bg) and became exclusive after the addition of 2 equiv. of HMPA. In addition, a tiny broad singlet due to free HMPA appeared at 26.5 ppm at the addition of 0.6 equiv. of HMPA and grew up with the increase in HMPA addend (Fig. 4, Be–i), revealing the existence of the dynamic equilibria among the enolate aggregates $\mathbf{D_{0,4m}}$, $\mathbf{D_{1,3m}}$, $\mathbf{D_{2,2m}}$, and free HMPA as shown in Scheme 1. Unfortunately, a quartet for $\mathbf{T_{4,0}}$ was not observed in the ^{31}P NMR spectra because of the low resolution due to the miniscule amount of tetramer, and the ^{31}P–^{7}Li multi-coupling.

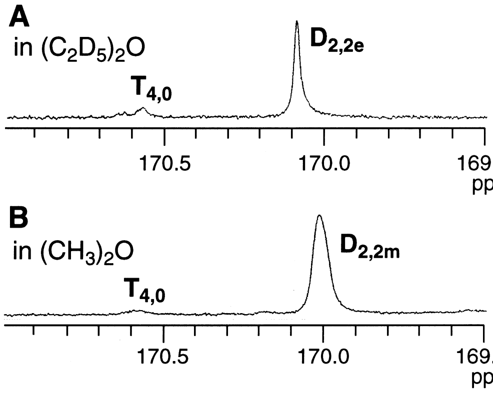

Figure 5. ^{13}C signals of the oxygen-bearing carbon atoms. A: Tetramer $\mathbf{T_{4,0}}$ (170.6 ppm) and dimer $\mathbf{D_{2,2e}}$ (170.1 ppm) formed from **1** (0.16 M) in diethyl-d_{10} ether with 0.32 M HMPA. B: Tetramer $\mathbf{T_{4,0}}$ (170.6 ppm) and dimer $\mathbf{D_{2,2m}}$ (170.0 ppm) for med from **1** (0.32 M) in dimethyl ether with 0.64 M HMPA.

Full spectral data for the HMPA-coordinated aggregates of cyclopentanone lithium enolate are summarized in Tables 1 and 2.

2.2. ^{13}C NMR

The predominance of the dimeric structures in the presence of HMPA was also reflected in the ^{13}C NMR signals of their oxygen-bearing carbons of the lithium enolate (Fig. 5). In diethyl-d_{10} ether, a 0.16 M solution of **1** in the presence of 2 equiv. of HMPA resulted in broad signals appearing at 170.6 and 170.1 ppm, which were assigned to $\mathbf{T_{4,0}}$ and $\mathbf{D_{2,2e}}$, respectively, with a $\mathbf{T_{4,0}/D_{2,2e}}$ ratio of 5:95 (Fig. 5A). The corresponding signals in dimethyl ether containing 2 equiv. of HMPA were seen at 170.6 (<1%) and 170.0 ppm, (Fig. 5B). These signal ratios were the same as those observed in the ^{7}Li NMR (Figs. 1, A and 4A).

2.3. Quadrupole splitting constant (QSC)

The QSC values are considered to correlate with the degree of aggregation and the solvation of lithium.[14] In this context, the QSC values[26,27] were calculated from the observed dipole–dipole relaxation times for the hydrogen-bearing vinylic carbon and ^{7}Li spin–lattice relaxation times, (i.e., for $T_1(^{13}C)$ and $T_1(^7Li)$), in 0.32 M diethyl- and dimethyl ether solutions of **1** in the presence of 4 equiv. of HMPA[28] at 30 °C, $T_1(^{13}C)$: 2.50 and 3.27 s, respectively; $T_1(^7Li)$: 1.11 and 1.35 s, respectively; to give values of 113 and 117 kHz, respectively, whose values are similar as that obtained in

Table 3. Spin–lattice relaxation times (T_1) and quadrupole splitting constants (QSC) for lithium enolate **1** at 30 °C

Solvent	Viscosity (mPa s)[a]	Concentration (M)	HMPA (equiv.)	Compound	$T_1(^{13}C)$ (s)	$T_1(^7Li)$ (s)	QSC (kHz)
$(C_2H_5)_2O$	0.23	0.32	4	$\mathbf{D_{2,2e}}$	2.50	1.11	113
$(CH_3)_2O$	1.3×10^{-4}	0.32	4	$\mathbf{D_{2,2m}}$	3.27	1.35	117
THF-d_8	0.49	0.2	5		1.56	0.66	116[b]

[a] Viscosities at 25 °C for $(C_2H_5)_2O$ and THF are taken from Ref. 30 and for $(CH_3)_2O$ from Ref. 29.
[b] Ref. 14.

THF (116 kHz) (Table 3).[14] Thus, when the lithium enolate almost exists as the $\mathbf{D}_{2,2}$ type complex, the coordinated ethereal ligands do not influence the QSC values significantly. On the other hand, longer relaxation times were observed in diethyl- and dimethyl ether than in THF as shown in Table 3, reflecting on their solvent viscosities in the order of dimethyl ether (1.3×10^{-4} mPa s at 25 °C[29])< diethyl ether (0.23 mPa s at 25 °C[30])<THF (0.49 mPa s at 25 °C[30]).[6,26a]

3. Conclusion

The lithium enolate **1**, which presumably exists as a mixture of tetramer $\mathbf{T}_{0,4}$ and dimer $\mathbf{D}_{0,4}$ in diethyl ether and dimethyl ether, undergoes the successive S/L ligand exchange by the increase in added HMPA to converge on tetra-HMPA coordinated tetramer, $\mathbf{T}_{4,0}$ (minor product) and bis-HMPA coordinated dimers, $\mathbf{D}_{2,2e}$ and $\mathbf{D}_{2,2m}$ (major products), respectively, with 2 equiv. of HMPA per Li. Here, the ratio of the tetra-HMPA coordinated tetramer and bis-HMPA coordinated dimer was independent of the quantity of added HMPA, but was influenced by the enolate concentration. Thus, the ratio of such tetramer and dimer changes in order of 5:95, <1:99, and 0:100 in diethyl ether, dimethyl ether, and THF,[14] respectively, depending on the basicity of S. The clear-cut signal assignment and the profile of the convergence to $\mathbf{T}_{4,0}$ and $\mathbf{D}_{2,2}$ under HMPA titration gave no indication of any monomers[16] and trimers.[20] In addition, no monomers were detected even at an enolate concentration as low as 0.04 M or at the concentration of >2 equiv. of HMPA.

These substantial structural studies in combination with those and kinetic studies in THF,[14] will provide basic information for considering the roles of triorganotin(IV) halides, dialkylzinc compounds, and other additives in the HMPA-involved enolate systems[31] to modulate the reactivity and selectivity for the enolate alkylation reaction particularly useful for the three component coupling PG synthesis.[13]

4. Experimental

4.1. General

All apparatus used in the reactions were dried in an oven (100 °C) overnight and baked out with a heat gun under reduced pressure to remove air and moisture, and then filled with argon (Ar) after they had cooled to room temperature. The air and moisture sensitive materials were manipulated under Ar using a glove box, vacuum line, and syringe techniques.

4.1.1. Solvent and materials. Diethyl ether was distilled over sodium benzophenone ketyl. Diethyl-d_{10} ether were distilled over sodium benzophenone ketyl under vacuum, and then transferred into a receiver containing a sodium–potassium alloy and distilled under vacuum. These solvents were degassed prior to use. Hexamethylphosphoric triamide (HMPA) was obtained from Tokyo Kasei and distilled over CaH_2 under reduced pressure. 1-(Trimethylsiloxy)cyclopentene was purchased as commercial grade (97%). NMR studies were done using the enol silyl ether of 99.8% purity after distillation (bp 156 °C, 101 kPa) equipped with a Hempel-type distilling column. HMPA and the enol silyl ether were stored in ampoules under Ar. *n*-Butyllithium in hexane was purchased from Nacalai Tesque, Inc., and stored in a Schlenk tube equipped with a Young's tap under Ar at 4 °C. Diphenylacetic acid used as an indicator was recrystallized from methanol and dried at 60 °C under high vacuum.

4.1.2. NMR spectroscopy. All the NMR experiments were recorded on a JEOL JNM Λ-500 spectrometer operated at 194.25 MHz (^{7}Li), 202.35 MHz (^{31}P), or 125.65 MHz (^{13}C). The ^{7}Li and ^{31}P chemical shifts were referenced to external standards, 0.41 M LiCl/THF-d_8 (δ 0.0) and 1.0 M $P(C_6H_5)_3$/THF-d_8 (δ −6.0), respectively, at −100 °C. Shiming was performed on the external reference at −100 °C, and ^{7}Li and ^{31}P NMR spectra were then taken without locking. The ^{13}C chemical shifts were referenced to tetramethylsilane/THF-d_8 (δ 0.0) as an external standard at −100 °C. Digital resolutions were 0.59, 0.79 and 0.46 Hz for ^{7}Li, ^{31}P and ^{13}C, respectively. The ^{7}Li and ^{13}C relaxation times were measured with the inversion-recovery method, and data were processed by nonlinear least-squares programs.

4.2. Preparation of cyclopentanone lithium enolate for ^{7}Li- and ^{31}P NMR spectroscopic analysis

4.2.1. Enolate samples in diethyl ether (Figs. 1 and 2). 1-(Trimethylsiloxy)cyclopentene (78.2 mg, 0.500 mmol) was placed into a 10-mL test tube capped by a septum with positive Ar pressure. Diethyl ether (1.5 mL) was added, and then the solution was transferred through a stainless cannula into a 20-mL Schlenk tube. To the solution was added *n*-butyllithium (1.43 M hexane solution, 0.344 mL, 0.500 mmol) at 0 °C via a syringe under Ar purge. The mixture was vigorously stirred at room temperature for 2.0 h. Resulted solution was cooled to 0 °C with an ice bath, and 0.5 equiv. of HMPA (44.8 mg, 0.25 mmol) was added, followed by an additional diethyl ether to give a total volume of 3.1 mL. The suspension including precipitate caused by undissolved lithium enolate was treated with HMPA, and the mixture was stirred for 10 min at 10 °C to become a clear solution. A 5-mm NMR tube was charged with this solution (750 μL), and was cooled to 77 K, and then sealed with a flame under vacuum. Samples added by 0.7, 0.8, 1, 2 and 4 equiv. of HMPA were prepared according to this procedure. Spectral confidence was confirmed by repeating the same preparation procedure. NMR samples in diethyl ether were stable at −80 °C for at least 1 year.

4.2.2. 0.80 M Solution of 1 in diethyl ether (Fig. 3). A diethyl ether solution of the lithium enolate (59.4 mg, 0.600 mmol) prepared as described above was transferred through a stainless cannula in a 5-mm NMR tube, and solvents were removed under reduced pressure. After the tube was filled with Ar, HMPA (104 μL, 0.600 mmol) and diethyl ether were added at 0 °C to the residue to give a total volume of 750 μL.

4.2.3. 0.04–0.40 M Solutions of 1 in diethyl ether (Fig. 3). A diethyl ether solution of the lithium enolate was prepared as described above. Here, the use of diethyl ether distilled from sodium benzophenone ketyl was not suitable in the preparation of highly diluted solution of the lithium enolate (<0.08 M) because of the contamination of undesirable peaks in the upfield. Therefore, the solvent must be distilled further over sodium–potassium alloy under vacuum using apparatus with Young's taps.

4.2.4. Enolate samples in dimethyl ether (Fig. 4). 1-(Trimethylsiloxy)cyclopentene (42.7 μL, 0.240 mmol) was placed into a 5-mm NMR tube via a micro-syringe. To this tube cooled to −78 °C was filled with dimethyl ether (0.600 μL), followed by the addition of *n*-butyllithium (1.43 M hexane solution, 0.168 mL, 0.240 mmol) at the same temperature under Ar atmosphere. The mixture was left to stand at −40 °C for 2.0 h. To the resulting solution was added HMPA (4.00 μL, 0.024 mmol). A 5-mm NMR tube was charged with this solution (750 μL), cooled to 77 K, then sealed with a flame under vacuum. Samples added by 0.1, 0.2, 0.5, 0.6, 0.7, 0.8, 1 and 2 equiv. of HMPA were prepared according to this procedure.

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