Structures of β-Amino Ester Enolates: New Strategies Using the Method of Continuous Variation

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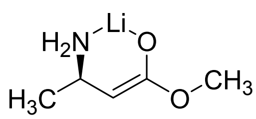
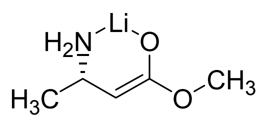
Supporting Information



(*R*)-**5**



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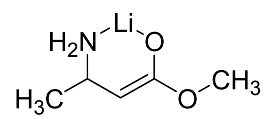
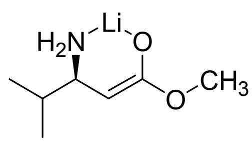


rac-**5**



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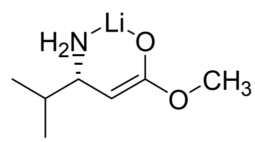

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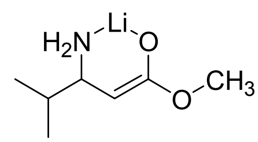

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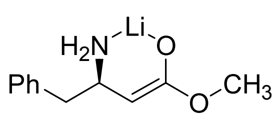

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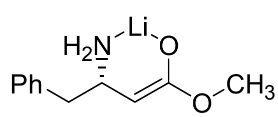

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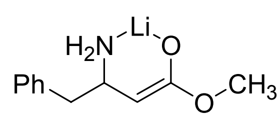
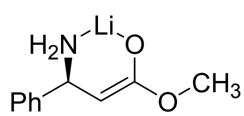
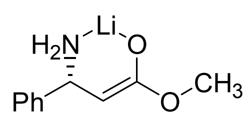


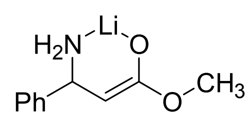
rac-**7**



(*S*)-**8**



(*R*)-**8**



rac-**8**

I. Experimental Procedures

A. Method for preparation of NMR spectroscopy samples

Separate stock solutions of [^{6}Li]LiHMDS and the appropriate β-amino ester were prepared in small vials. An NMR tube was fit with a septum and connected to a Schlenk line using a vacuum hose and needle. After the NMR tube was flame dried, the tube was placed under argon and in a -78 °C bath. The appropriate amount of base solution was added followed by the substrate and/or solvent solutions using gas-tight syringes. After all the components were added, the sample was placed under partial vacuum, and the sample tube was sealed with an oxygen torch. Prior to recording the spectra, the samples were warmed in a 0 °C bath for 10-15 minutes followed by a few seconds of gentle shaking to ensure complete mixing and enolization.

B. Method of integration

NMR resonances were integrated using Varian's software, VNMR. After weighted Fourier transform with drift correction and 64,000 points and phasing, a baseline correction was applied when possible. Deconvolution was performed in the absolute intensity mode, with the default parameters for contributions from Lorentzian and Gaussian line shapes, and using the line list for well resolved spectra. For poorly resolved spectra, the resonances were indicated using the "mark" and "use mark" commands.

C. Preparation of compounds

The precursors to **5-7** were prepared from the Boc-protected, optically pure amino acids by Arndt-Eistert homologation.[1] The Boc protection was removed by refluxing 0.25 M Boc-β-amino ester and 1.0 mole equivalent of *p*-toluenesulfonic acid monohydrate in methanol for about 3.5 hours or until deprotection was complete by TLC. The methanol was removed by rotary evaporation followed by full vacuum. The tosylate salt was recrystallized in THF/MeOH overnight in a -20 °C freezer. The free base was obtained by condensing ammonia at -78 °C into a slurry of the tosylate salt and ether. After the reaction was allowed to warm to RT and the excess ammonia had dissipated, the ammonium tosylate was removed by filtration. Ether was removed by rotary evaporation, and the β-amino ester was further purified by a pot-to-pot transfer under reduced pressure.

The precursor to **8** was prepared according to a literature protocol.[2] Enantiomeric excess of the *N*-trifluoromethylacetyl-β-phenylglycine derivative was measured by gas chromatography on an Alltech Chirasil-Val capillary column.

The β-amino esters were stored at -20 °C and were checked for degradation by ^{1}H NMR spectroscopy prior to use.

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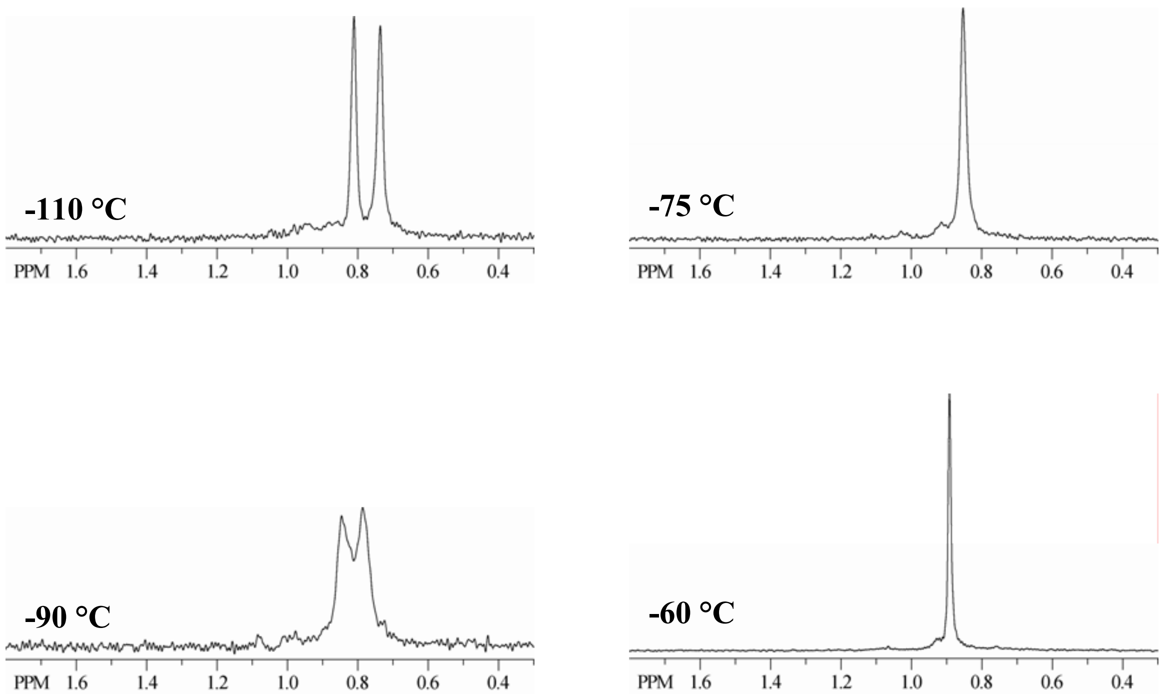
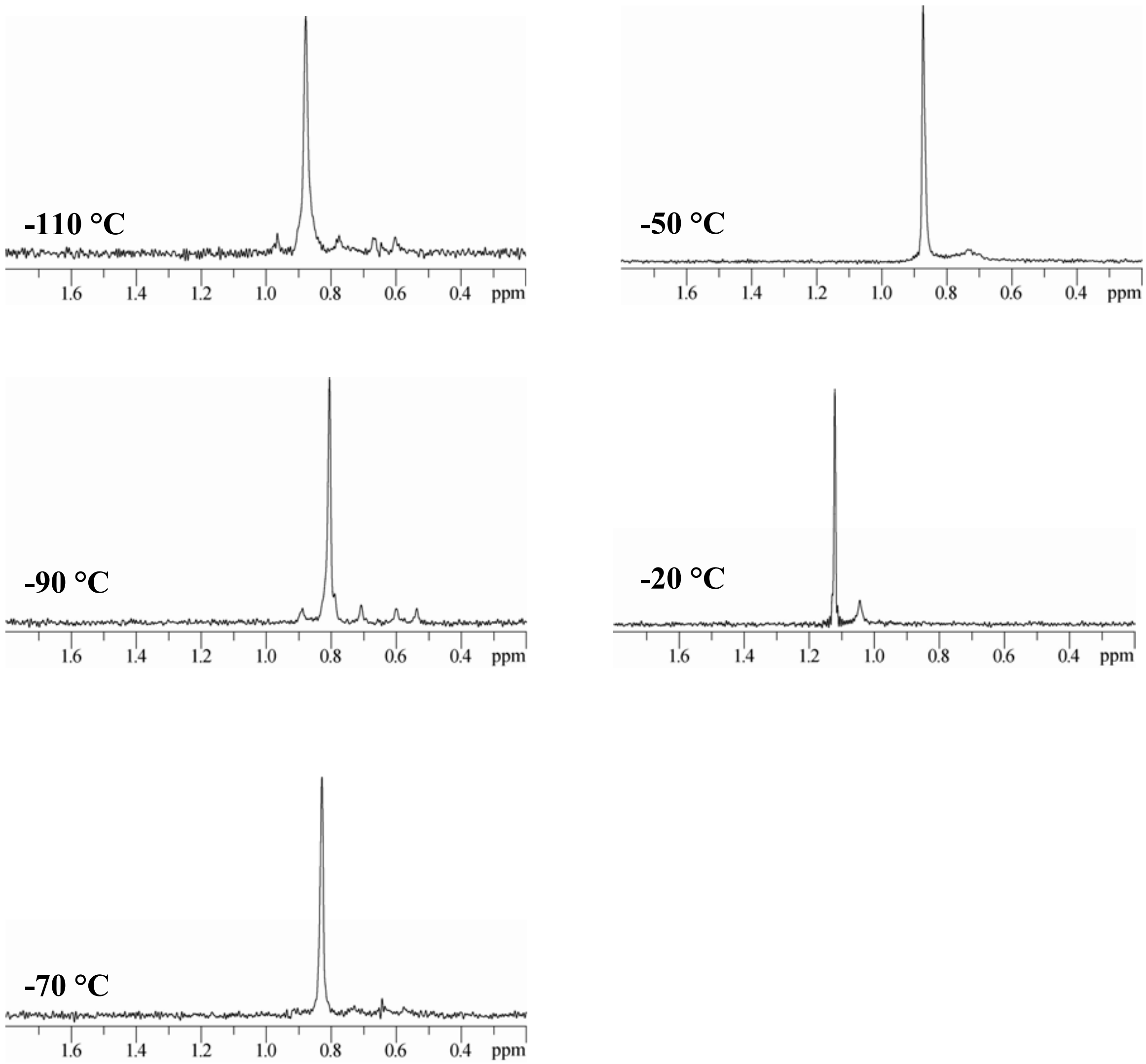
[1] Podlech, J.; Seebach, D. *Liebigs Ann*. **1995**, 1217-1228.

[2] Davis, F. A.; Reddy, R. E.; Szewczyk, J. M. *J. Org. Chem*. **1995**, *60*, 7037; Davis, F. A.; Reddy, R. E.; Szewczyk, J. M.; Reddy, G. V.; Portonovo, P. S.; Zhang, H.; Fanelli, D.; Reddy, R. T.; Zhou, P.; Carroll, P. J. *J. Org. Chem*. **1997**, *62*, 2555-2563.

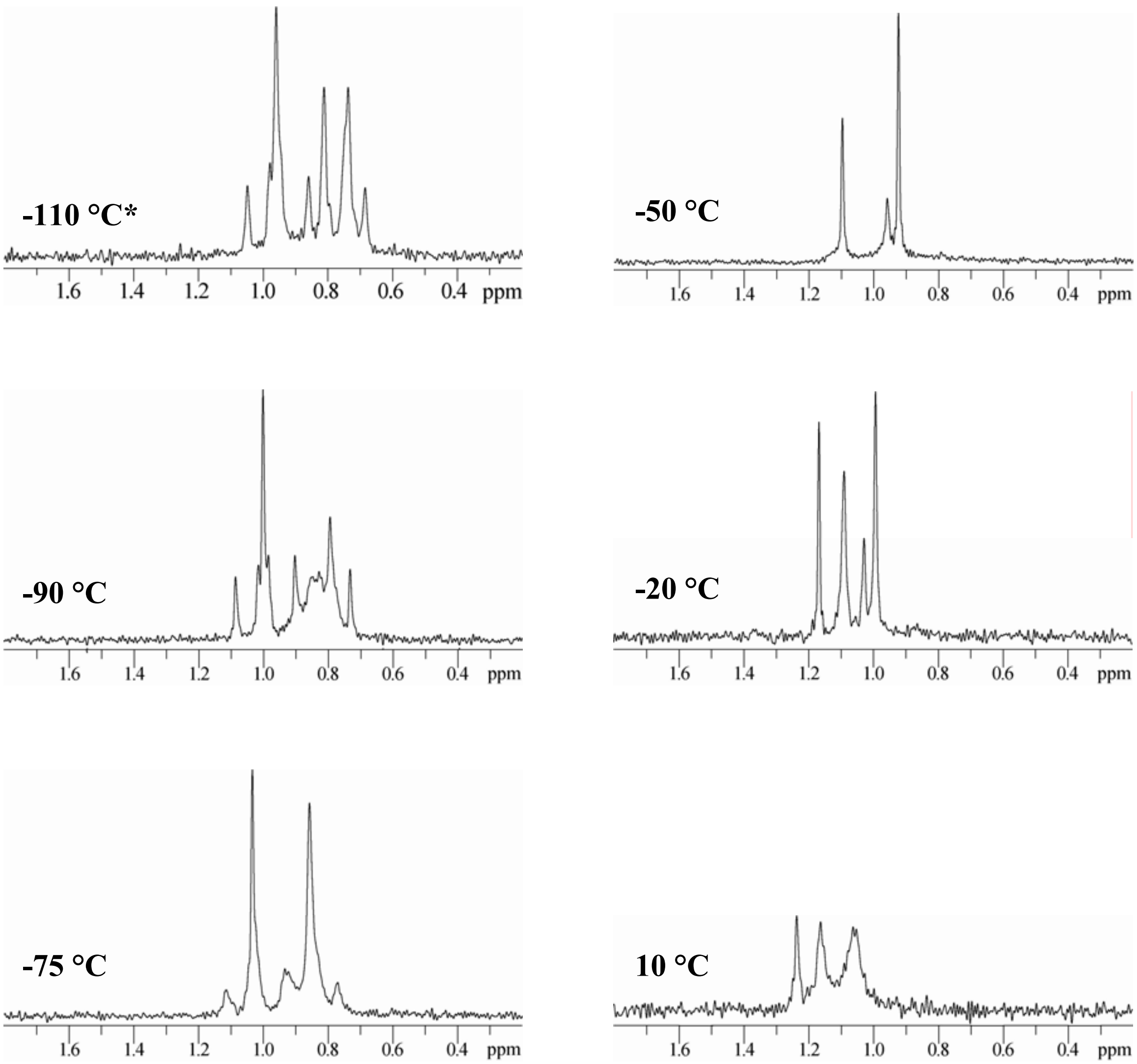
II. (*S*)-β-Valine and (*R*)-β-Valine



II.A. ^{6}Li NMR spectra (58.8 MHz) of [^{6}Li](*S*)-**6** at various temperatures. All samples are 0.10 M total enolate concentration and 9.0 M THF/toluene.

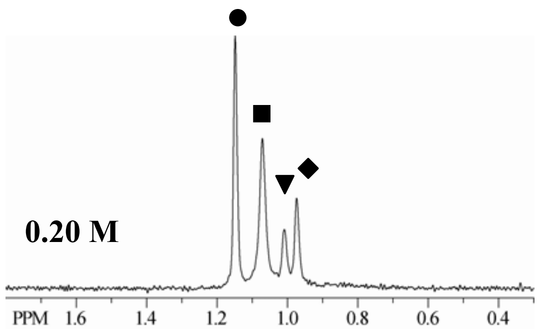


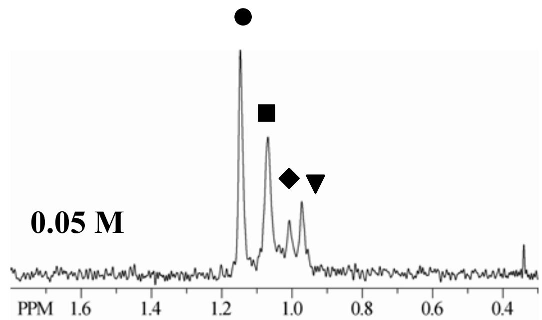
II.B. ^{6}Li NMR spectra (58.8 MHz) of [^{6}Li]*rac*-**6** at various temperatures. All samples are 0.10 M total enolate concentration and 9.0 M THF/toluene.

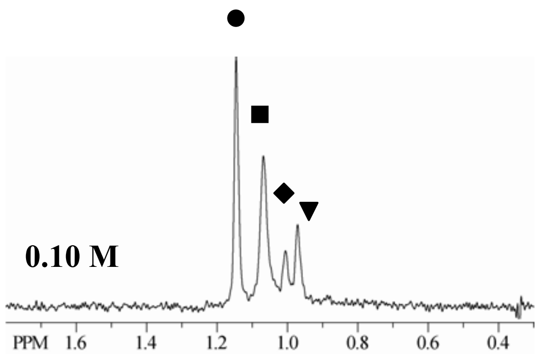


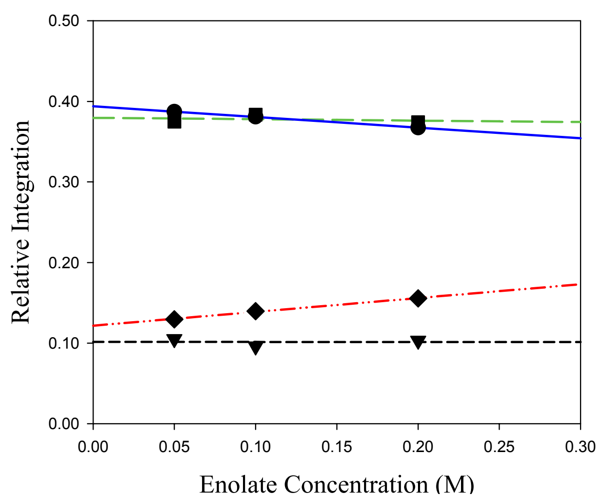
II.C. ^{6}Li NMR spectra (58.8 MHz) of a mixture of [^{6}Li](*R*)-**6** and [^{6}Li](*S*)-**6** (mole fraction of **R**=0.80) at various temperatures. All samples are 0.10 M total enolate concentration and 9.0 M THF/toluene.

* Spectrum recorded at 73.6 MHz.



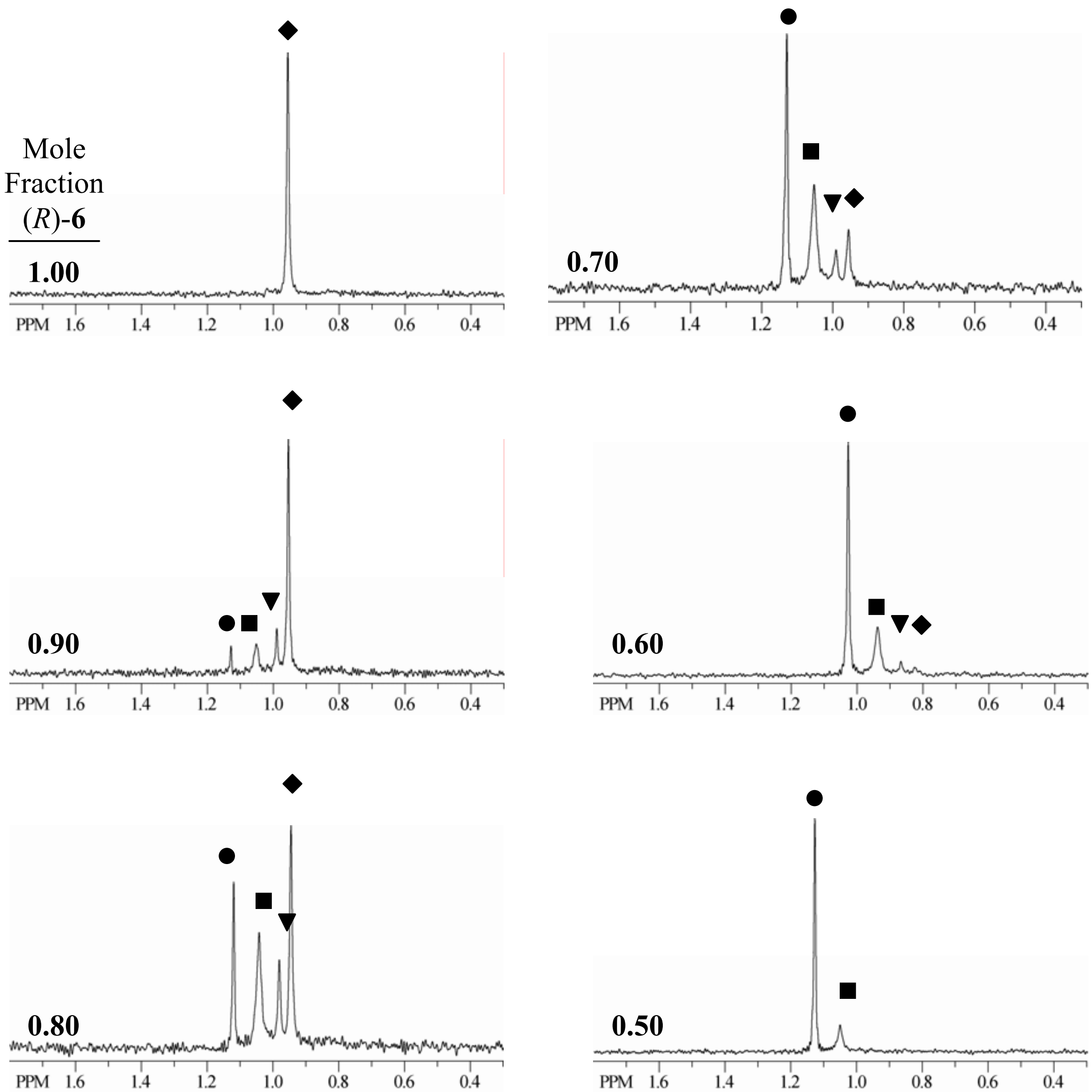




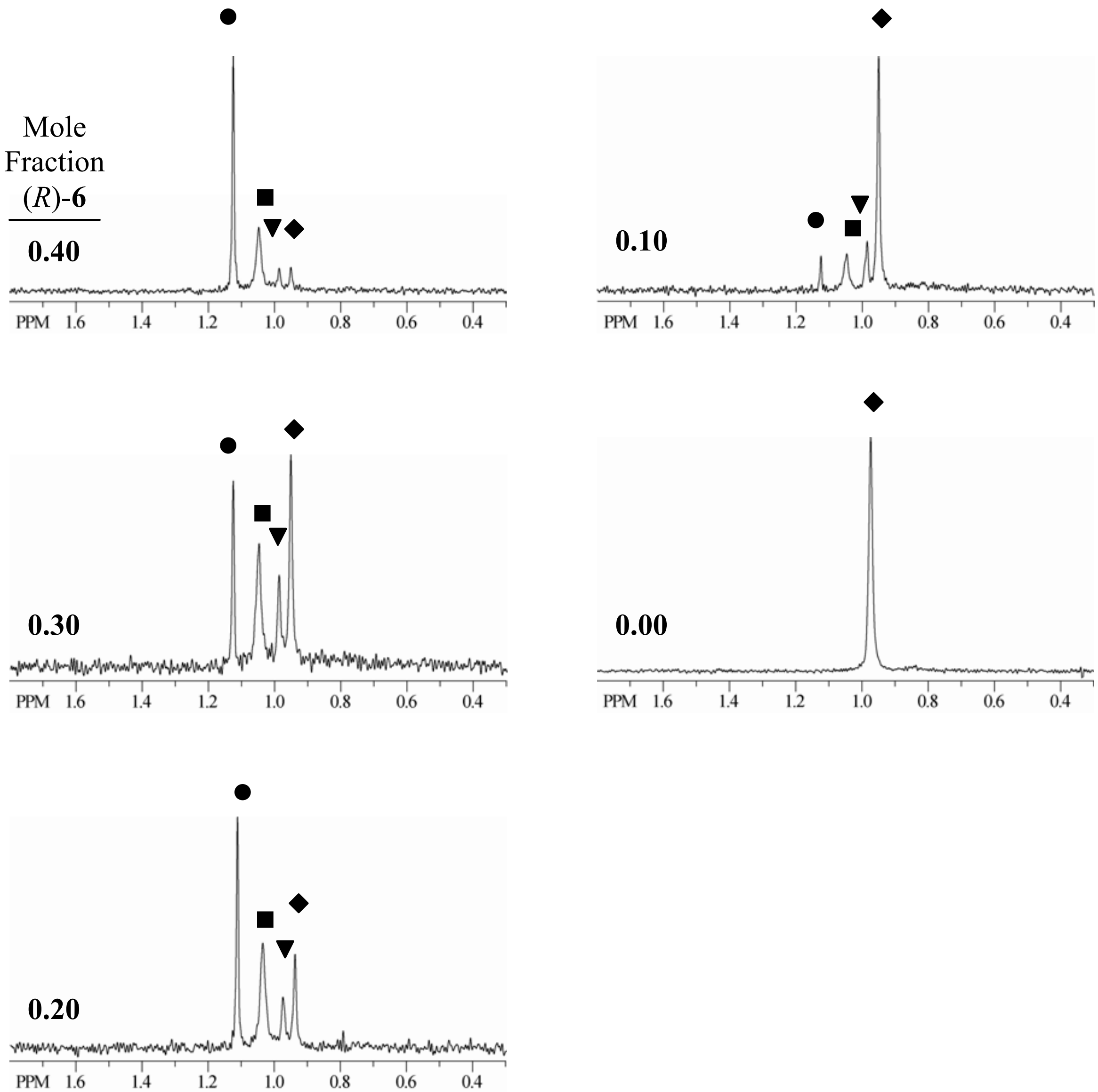


[enolate] (M)	Relative Integrations (●)	(■)	(▼)	(◆)
0.05	0.39	0.37	0.11	0.13
0.10	0.38	0.38	0.10	0.14
0.20	0.37	0.37	0.10	0.16

II.D. Variation of enolate concentration for a mixture of [^{6}Li](*S*)-**6** and [^{6}Li](*R*)-**6** (mole fraction of **S**=0.30). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*R*)-**6** and [^{6}Li](*S*)-**6** (mole fraction of **S**=0.30) at various enolate concentrations. All samples are 9.0 M THF/toluene and were recorded at -20 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration The lines represent a linear least squares fit. (◆) $\mathbf{R}_6$+S_6 (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2S_4$+$\mathbf{R}_4S_2$ (●) $\mathbf{R}_3S_3$ such that **R** = [^{6}Li](*R*)-**6** and **S** = [^{6}Li](*S*)-**6.**



II.E. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**6** and [^{6}Li](*S*)-**6** at various mole fractions in 9.0 M THF/toluene at -20 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (●) $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [^{6}Li](*R*)-**6** and **S** = [^{6}Li](*S*)-**6.**

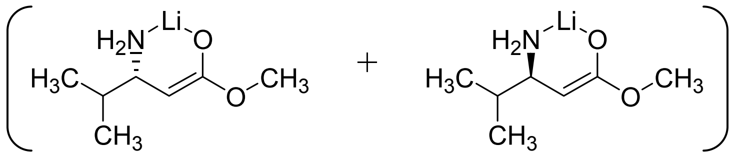


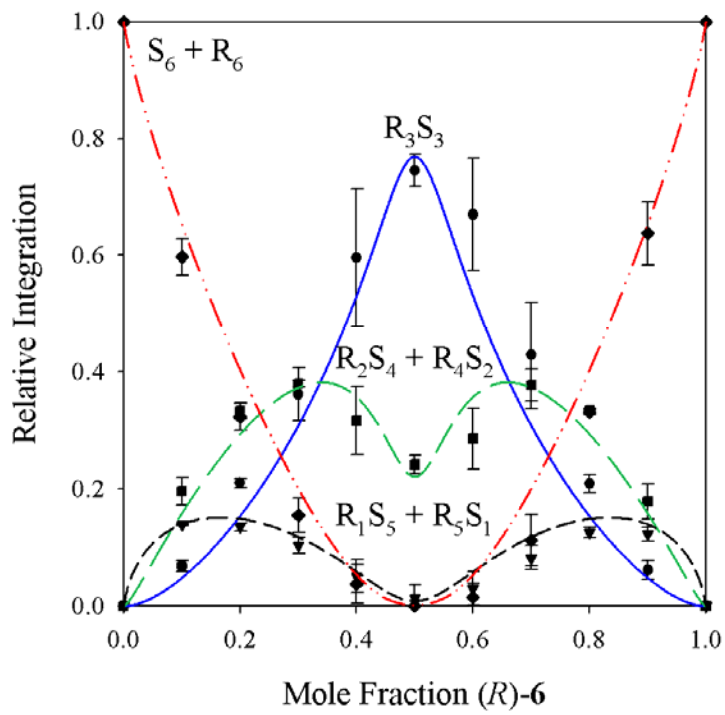
II.E. (cont.) ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**6** and [^{6}Li](*S*)-**6** at various mole fractions in 9.0 M THF/toluene at -20 ºC. Samples are 0.10 M in total enolate concentration. **(◆)** $\mathbf{R}_6$+$\mathbf{S}_6$ **(▼)** $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ **(■)** $\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ **(●)** $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [^{6}Li](*R*)-**6** and **S** = [^{6}Li](*S*)-**6.**

II.F. Table of the relative integrations for the spectra in **II.E.**[a]

Mole Frac. (*R*)-**6**	Relative Integrations $\mathbf{R_3S_3}$ (●)	$\mathbf{R_4S_2}$+$\mathbf{R_2S_4}$ (■)	$\mathbf{R_5S_1}$+$\mathbf{R_1S_5}$ (▼)	$\mathbf{R_6}$+$\mathbf{S_6}$ (◆)
1.00	0.00±0.00	0.00±0.00	0.00±0.00	1.00±0.00
0.90	0.06±0.02	0.18±0.03	0.123±0.012	0.64±0.05
0.80	0.21±0.02	0.334±0.004	0.126±0.009	0.331±0.004
0.70	0.43±0.09	0.38±0.03	0.08±0.02	0.11±0.04
0.60	0.670±0.096	0.29±0.05	0.03±0.03	0.01±0.03
0.50	0.75±0.03	0.242±0.016	0.01±0.02	0.00±0.00
0.40	0.60±0.12	0.32±0.06	0.05±0.03	0.04±0.03
0.30	0.36±0.05	0.380±0.006	0.103±0.014	0.16±0.03
0.20	0.210±0.008	0.333±0.014	0.134±0.007	0.32±0.02
0.10	0.068±0.010	0.20±0.02	0.138±0.002	0.60±0.03
0.00	0.00±0.00	0.00±0.00	0.00±0.00	1.00±0.00

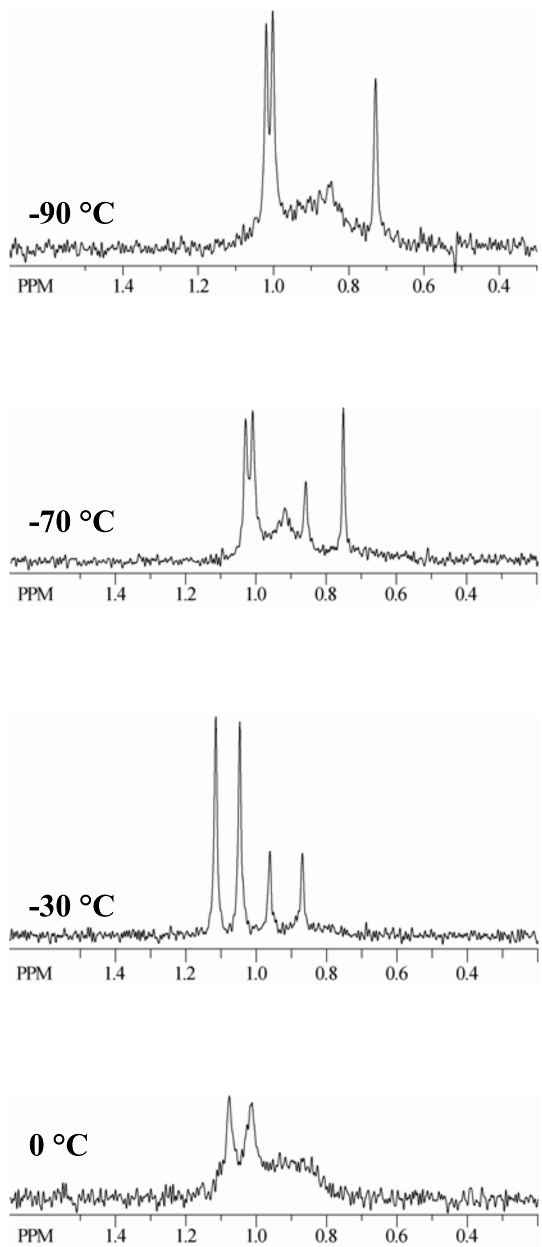
[a] (◆) $\mathbf{R_6}$+$\mathbf{S_6}$ (▼) $\mathbf{R_5S_1}$+$\mathbf{R_1S_5}$ (■) $\mathbf{R_2S_4}$+$\mathbf{R_4S_2}$ (●) $\mathbf{R_3S_3}$ such that **R** = [^{6}Li](*R*)-**6** and **S** = [^{6}Li](*S*)-**6.**



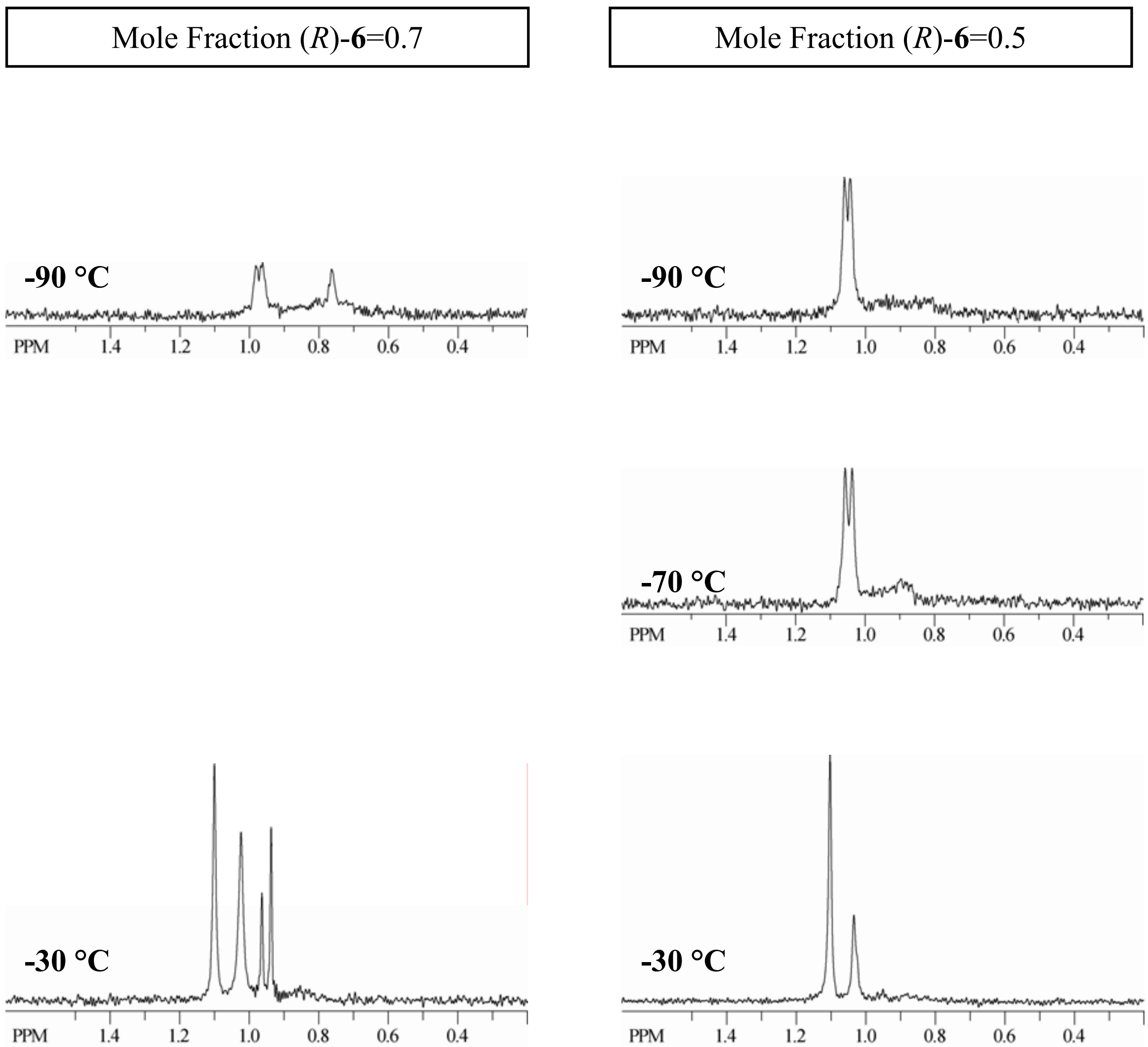


II.G. Job Plot of [^{6}Li](*R*)-**6**/[^{6}Li](*S*)-**6** (9.0 M THF/toluene; -20 ºC) hexamers. The relative integrations are plotted as a function of the mole fraction of [^{6}Li](*R*)-**6**. (◆) $\mathbf{R_6}$+$\mathbf{S_6}$ (▼) $\mathbf{R_5S_1}$+$\mathbf{R_1S_5}$ (■) $\mathbf{R_4S_2}$+$\mathbf{R_2S_4}$ (●) $\mathbf{R_3S_3}$ such that **R** = [^{6}Li](*R*)-**6** and **S** = [^{6}Li](*S*)-**6**. The curves result from a parametric fit, affording ϕ_0=0.01134; ϕ_1=0.0924; ϕ_2=0.9574; ϕ_3=5.

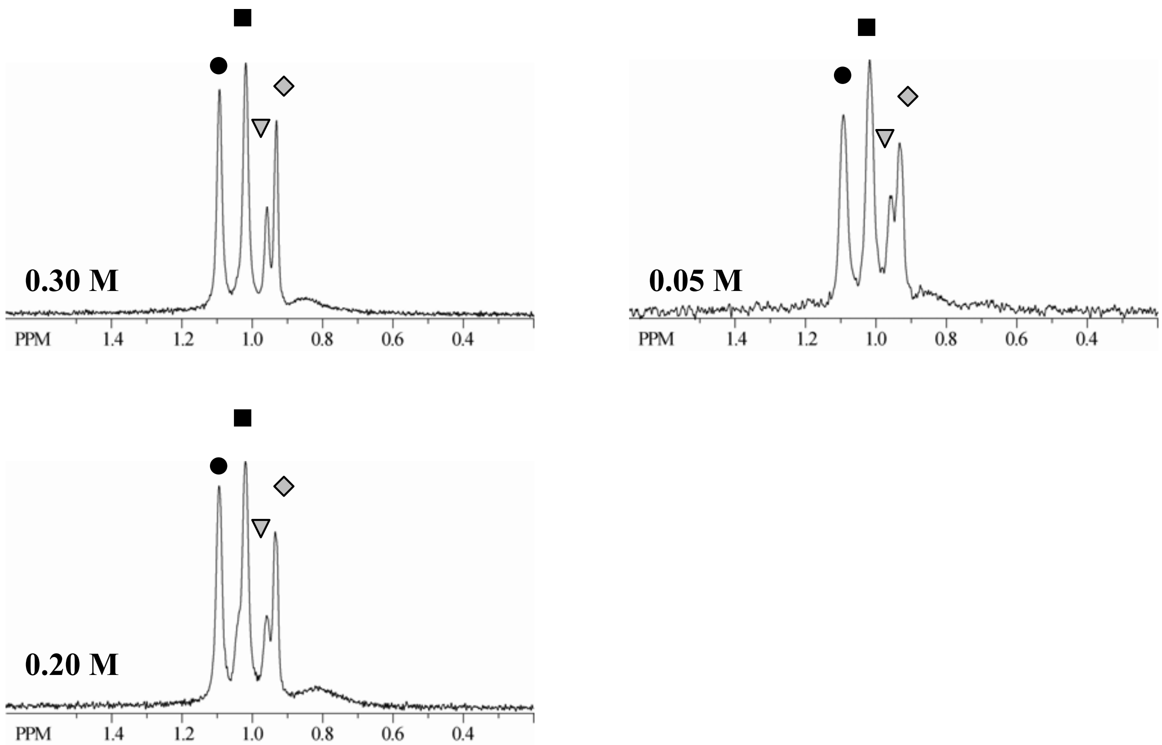
III. (*S*)-β-Valine and (*R*)-β-Alanine

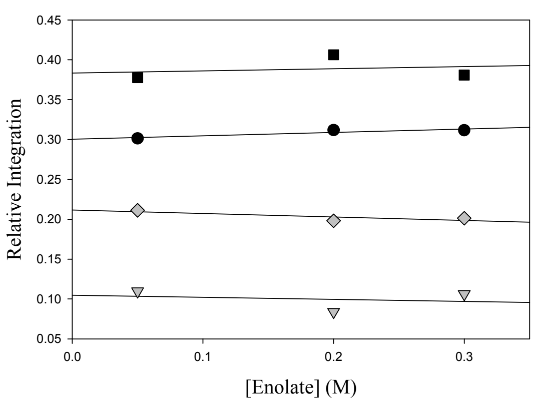


III.A. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**6** and [^{6}Li](*S*)-**5** (mole fraction of **6**=0.3) at various temperatures. Samples are 0.10 M total enolate concentration and 3.0 M THF/toluene.



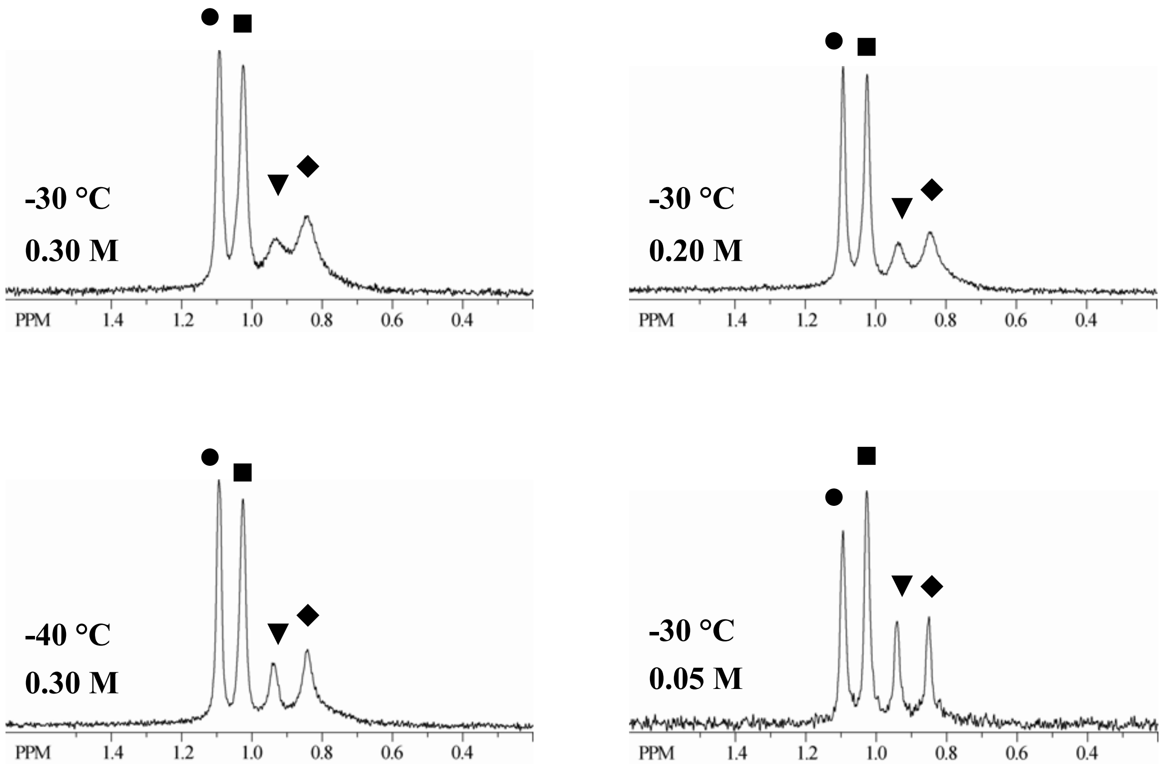
III.B. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**6** and [^{6}Li](*S*)-**5** at various temperatures. Samples are 0.10 M total enolate concentration and 3.0 M THF/toluene.

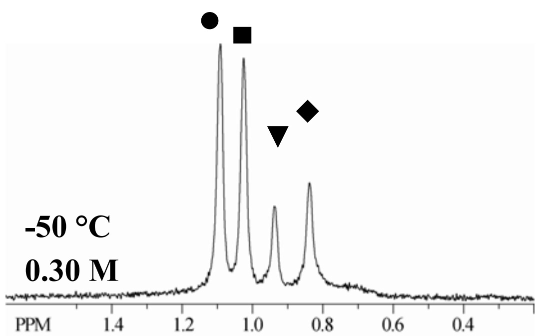




[enolate] (M)	Relative Integrations (●)	(■)	(▽)	(◇)
0.05	0.30	0.38	0.11	0.21
0.20	0.31	0.41	0.08	0.19
0.30	0.31	0.38	0.11	0.20

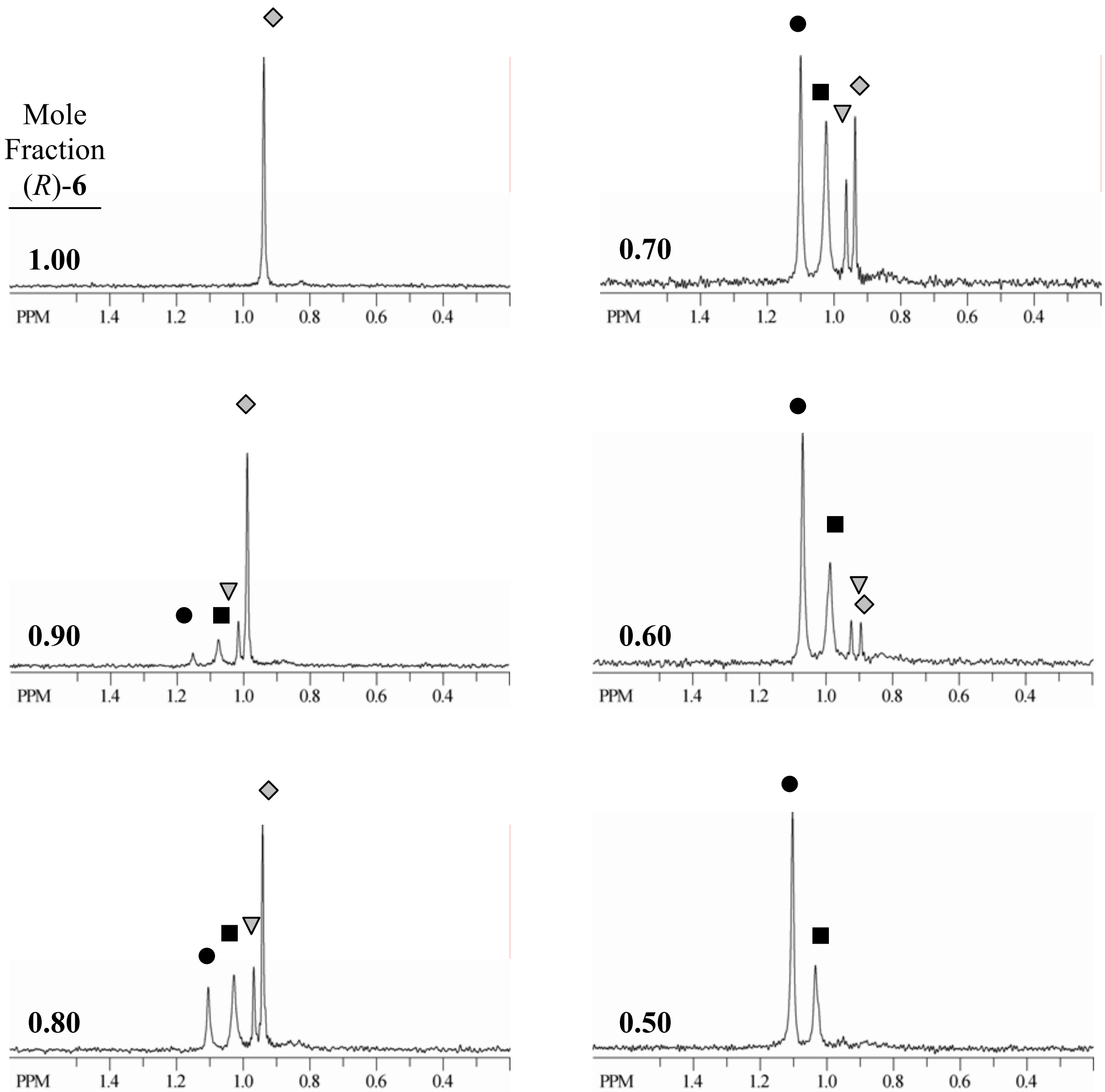
III.C. Variation of enolate concentration for a mixture of [^{6}Li](*S*)-**6** and [^{6}Li](*R*)-**5** (mole fraction of **S'**=0.70). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*S*)-**6** and [^{6}Li](*R*)-**5** (mole fraction of **S'**=0.70) at various enolate concentrations. All samples are 3.0 M THF/toluene and were recorded at -30 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R}_6$ (▼) $\mathbf{R}_5\mathbf{S'}_1$ (■) $\mathbf{R}_4\mathbf{S'}_2$+$\mathbf{R}_2\mathbf{S'}_4$ (●) $\mathbf{R}_3\mathbf{S'}_3$ (▽) $\mathbf{R}_1\mathbf{S'}_5$ (◇) $\mathbf{S'}_6$ such that **S'** = [^{6}Li](*S*)-**6** and **R** = [^{6}Li](*R*)-**5**.



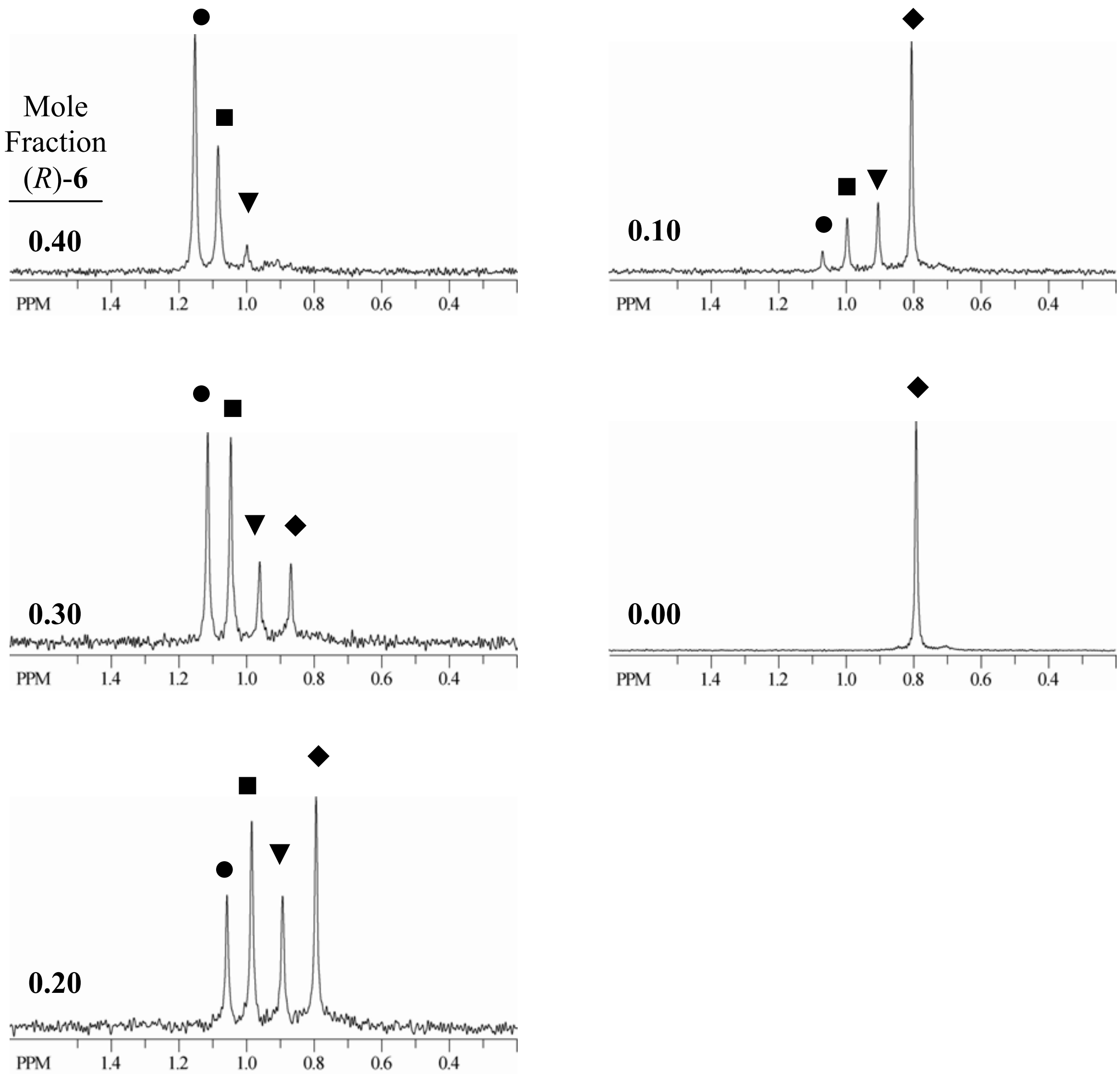


[enolate] (M)	Relative Integrations (●)	(■)	(▼)	(◆)
0.05	0.30	0.36	0.16	0.17
0.20	0.28	0.32	0.12	0.28
0.30	0.27	0.31	0.12	0.30

III.D. Variation of enolate concentration for a mixture of [^{6}Li](*S*)-**6** and [^{6}Li](*R*)-**5** (mole fraction of **S'**=0.30). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*S*)-**6** and [^{6}Li](*R*)-**5** (mole fraction of **S'**=0.30) at various enolate concentrations. All samples are 3.0 M THF/toluene. The sample with total enolate concentration of 0.30 M is shown at various temperatures. The data in the table is from the spectra taken at -30 °C. (◆) $\mathbf{R}_6$ (▼) $\mathbf{R}_5\mathbf{S'}_1$ (■) $\mathbf{R}_4\mathbf{S'}_2$+$\mathbf{R}_2\mathbf{S'}_4$ (●) $\mathbf{R}_3\mathbf{S'}_3$ (▽) $\mathbf{R}_1\mathbf{S'}_5$ (◇) $\mathbf{S'}_6$ such that **S'** = [^{6}Li](*S*)-**6** and **R** = [^{6}Li](*R*)-**5**.



III.E. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**6** and [^{6}Li](*S*)-**5** at various mole fractions in 3.0 M THF/toluene at -30 ºC. Samples are 0.10 M total enolate concentration. (◆) **R**$_6$ (▼) **R**$_5$**S'**$_1$ (■) **R**$_4$**S'**$_2$+**R**$_2$**S'**$_4$ (●) **R**$_3$**S'**$_3$ (▽) **R**$_1$**S'**$_5$ (◇) **S'**$_6$ such that **S'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*S*)-**5**.



III.E. (cont.) ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**6** and [^{6}Li](*S*)-**5** at various mole fractions in 3.0 M THF/toluene at -30 ºC. Samples are 0.10 M total enolate concentration. (◆) $\mathbf{R}_6$ (▼) $\mathbf{R}_5\mathbf{S'}_1$ (■) $\mathbf{R}_4\mathbf{S'}_2$+$\mathbf{R}_2\mathbf{S'}_4$ (●) $\mathbf{R}_3\mathbf{S'}_3$ (▽) $\mathbf{R}_1\mathbf{S'}_5$ (◇) $\mathbf{S'}_6$ such that **S'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*S*)-**5**.

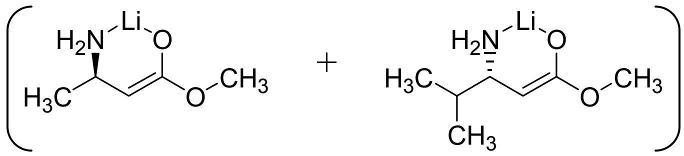
III.F. Table of the relative integrations for the spectra in **III.E.**[a]

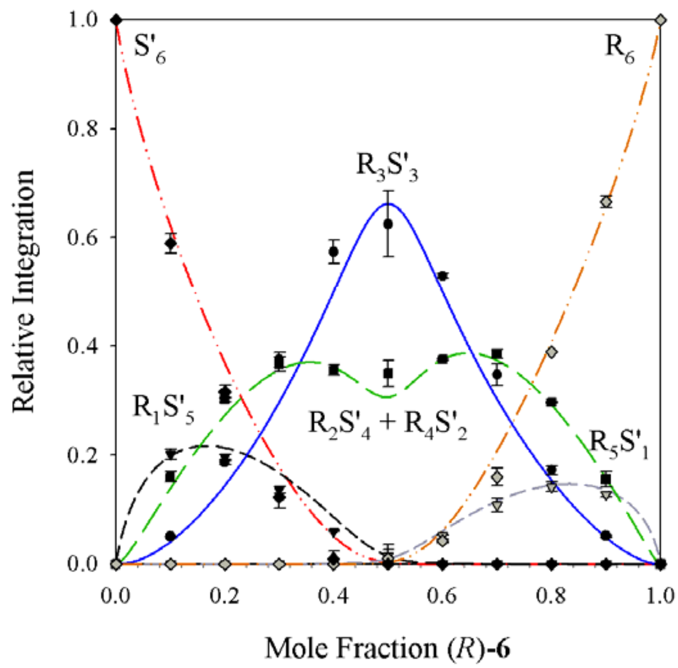
Mole Frac. (*R*)-**6**	Relative Integrations **$R_3S'_3$** (●)	**$R_4S'_2$+$R_2S'_4$**[b] (■)	**$R_1S'_5$** (▽)	**$R_5S'_1$** (▼)
1.00	0.000±0.00	0.00±0.00	0.00±0.00	0.00±0.00
0.90	0.051±0.003	0.16±0.01	0.127±0.005	0.00±0.00
0.80	0.172±0.008	0.30±0.01	0.14±0.01	0.00±0.00
0.70	0.35±0.02	0.39±0.01	0.11±0.01	0.00±0.00
0.60	0.529±0.005	0.376±0.002	0.053±0.001	0.00±0.00
0.50	0.63±0.06	0.35±0.02	0.02±0.02	0.00±0.00
0.40	0.57±0.02	0.36±0.01	0.00±0.000	0.061±0.001
0.30	0.38±0.01	0.37±0.01	0.000±0.000	0.136±0.007
0.20	0.186±0.003	0.302±0.004	0.00±0.00	0.196±0.005
0.10	0.050±0.00005	0.159±0.009	0.000±0.000	0.201±0.009
0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00

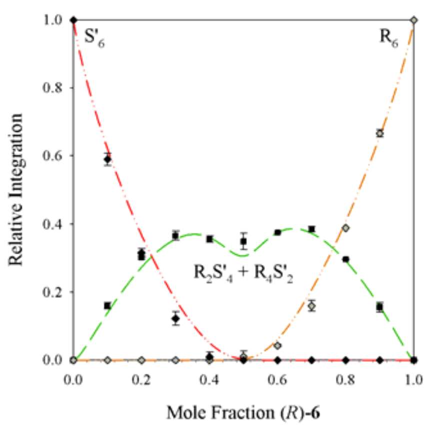
Mole Frac. (*R*)-**6**	Relative Integrations **S'_6** (◇)	**R_6** (◆)
1.00	1.00±0.00	0.00±0.00
0.90	0.67±0.01	0.00±0.00
0.80	0.389±0.0005	0.00±0.00
0.70	0.16±0.02	0.00±0.00
0.60	0.042±0.004	0.00±0.00
0.50	0.01±0.02	0.00±0.00
0.40	0.00±0.00	0.01±0.01
0.30	0.00±0.00	0.12±0.02
0.20	0.00±0.00	0.32±0.01
0.10	0.00±0.00	0.59±0.02
0.00	0.00±0.00	1.00±0.00

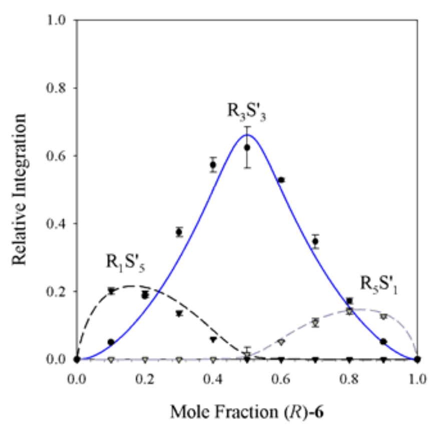
[a] (◆) **R_6** (▼) **$R_5S'_1$** (■) **$R_4S'_2$+$R_2S'_4$** (●) **$R_3S'_3$** (▽) **$R_1S'_5$** (◇) **S'_6** such that **S'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*S*)-**5**.

[b] The relative integrations of the **$R_2S'_4$** and **$R_4S'_2$** aggregates are summed due poor resolution of their resonances.



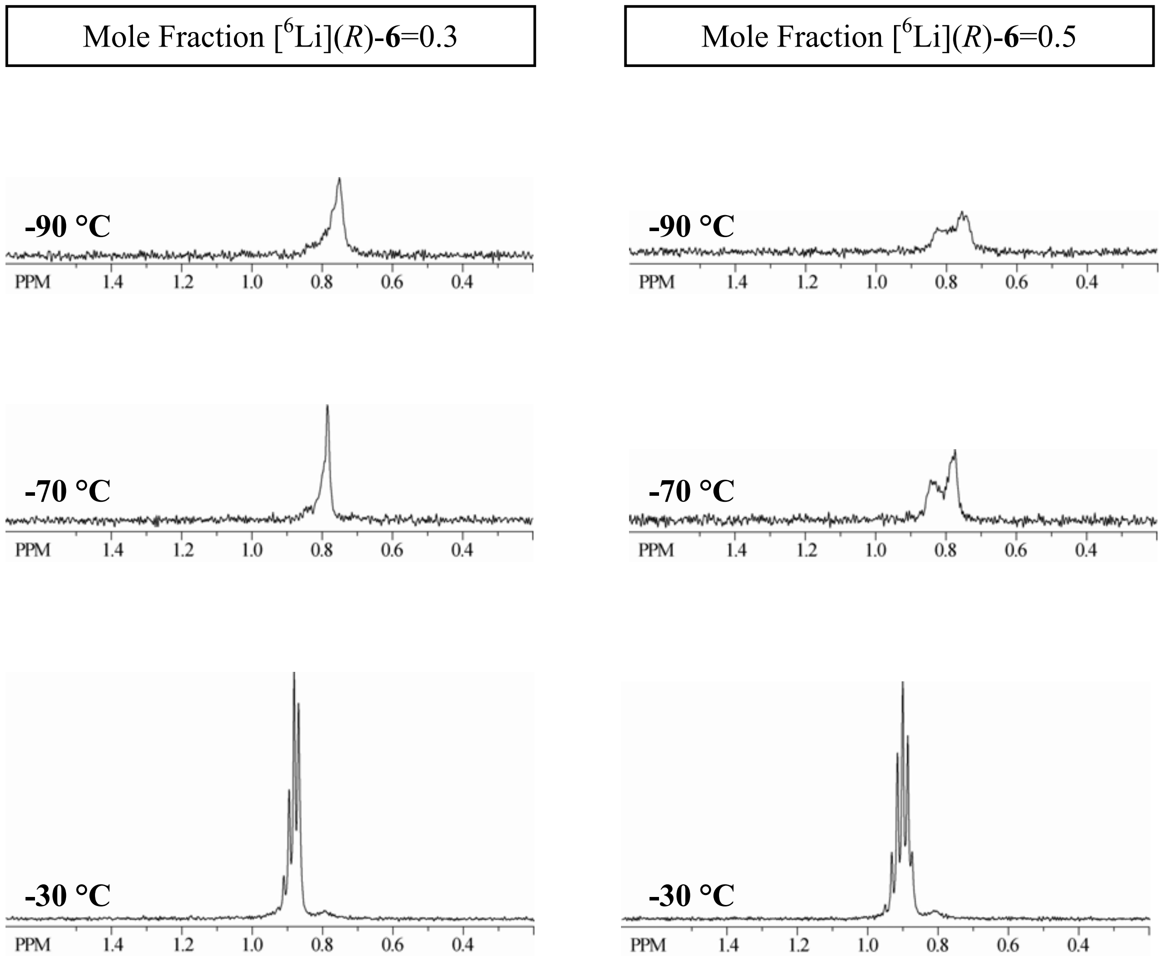




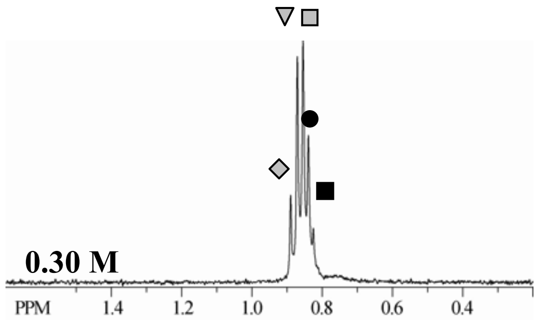


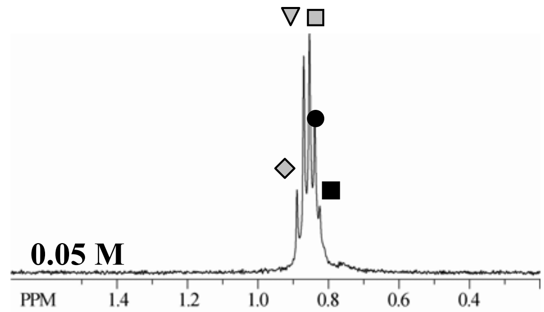
III.G. Job Plot of [^{6}Li](*R*)-**6**/[^{6}Li](*S*)-**5** (3.0 M THF/toluene; -30 ºC) hexamers. The relative integrations are plotted as a function of the mole fraction of [^{6}Li](*R*)-**6**. (◆) **R_6** (▼) **$R_5S'_1$** (■) **$R_4S'_2$+$R_2S'_4$** (●) **$R_3S'_3$** (▽) **$R_1S'_5$** (◇) **S'_6** such that **S'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*S*)-**5**. The relative integrations of the **$R_2S'_4$** and **$R_4S'_2$** aggregates are summed due to poor resolution of their resonances. The curves result from a parametric fit, affording ϕ_0=1.00; ϕ_1=0.86; ϕ_2=3.91; ϕ_3=14.08; ϕ_4=4.84; ϕ_5=0.84; ϕ_6=1.96.

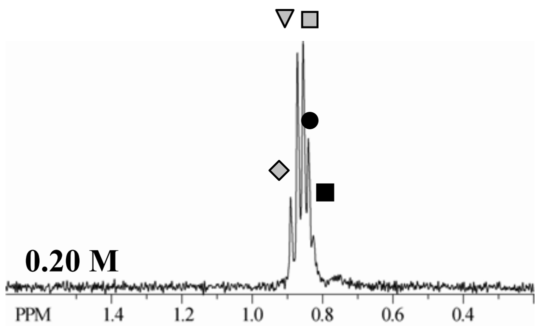
IV. (*R*)-β-Valine and (*R*)-β-Alanine

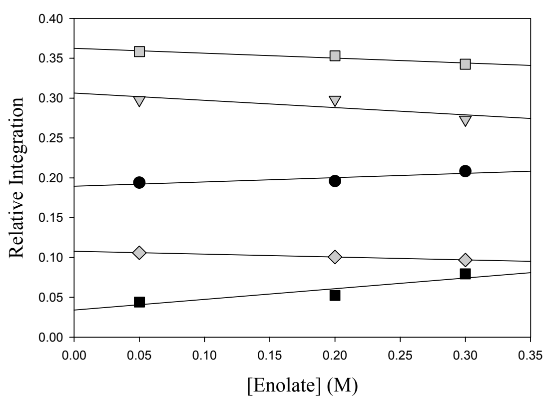


IV.A. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)- **6** and [^{6}Li](*R*)-**5** at various temperatures. All samples are 0.10 M total enolate concentration and 3.0 M THF/toluene.



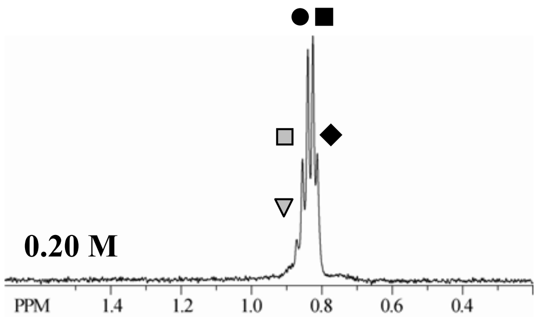


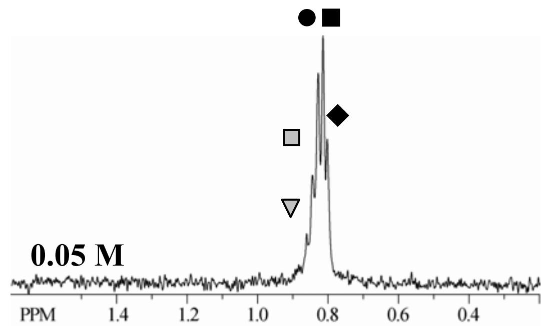


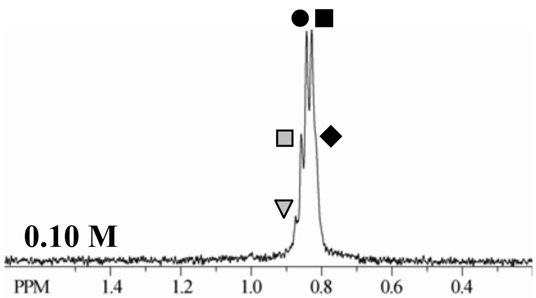


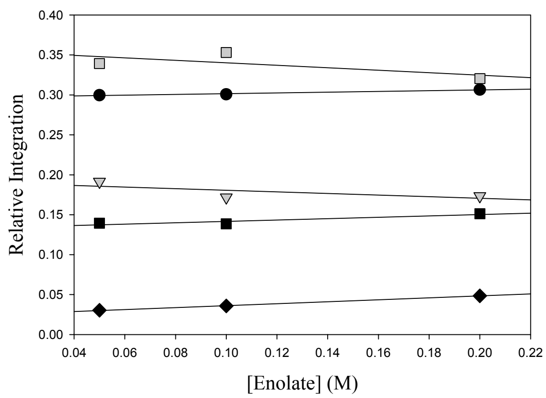
[enolate] (M)	Relative Integrations (◇)	(▽)	(▢)	(●)	(■)
0.05	0.11	0.30	0.36	0.19	0.04
0.20	0.10	0.30	0.35	0.20	0.05
0.30	0.10	0.27	0.34	0.21	0.08

IV.B. Variation of enolate concentration for a mixture of [^{6}Li](*R*)-**6** and [^{6}Li](*R*)-**5** (mole fraction of **R'**=0.70). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*R*)-**6** and [^{6}Li](*R*)-**5** (mole fraction of **R'**=0.70) at various enolate concentrations. All samples are 3.0 M THF/toluene and were recorded at -30 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R}_6$+$\mathbf{R}_5\mathbf{R'}_1$ (■) $\mathbf{R}_4\mathbf{R'}_2$ (●) $\mathbf{R}_3\mathbf{R'}_3$ (▢) $\mathbf{R}_2\mathbf{R'}_4$ (▽) $\mathbf{R}_1\mathbf{R'}_5$ (◇) $\mathbf{R'}_6$ such that **R'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*R*)-**5**.



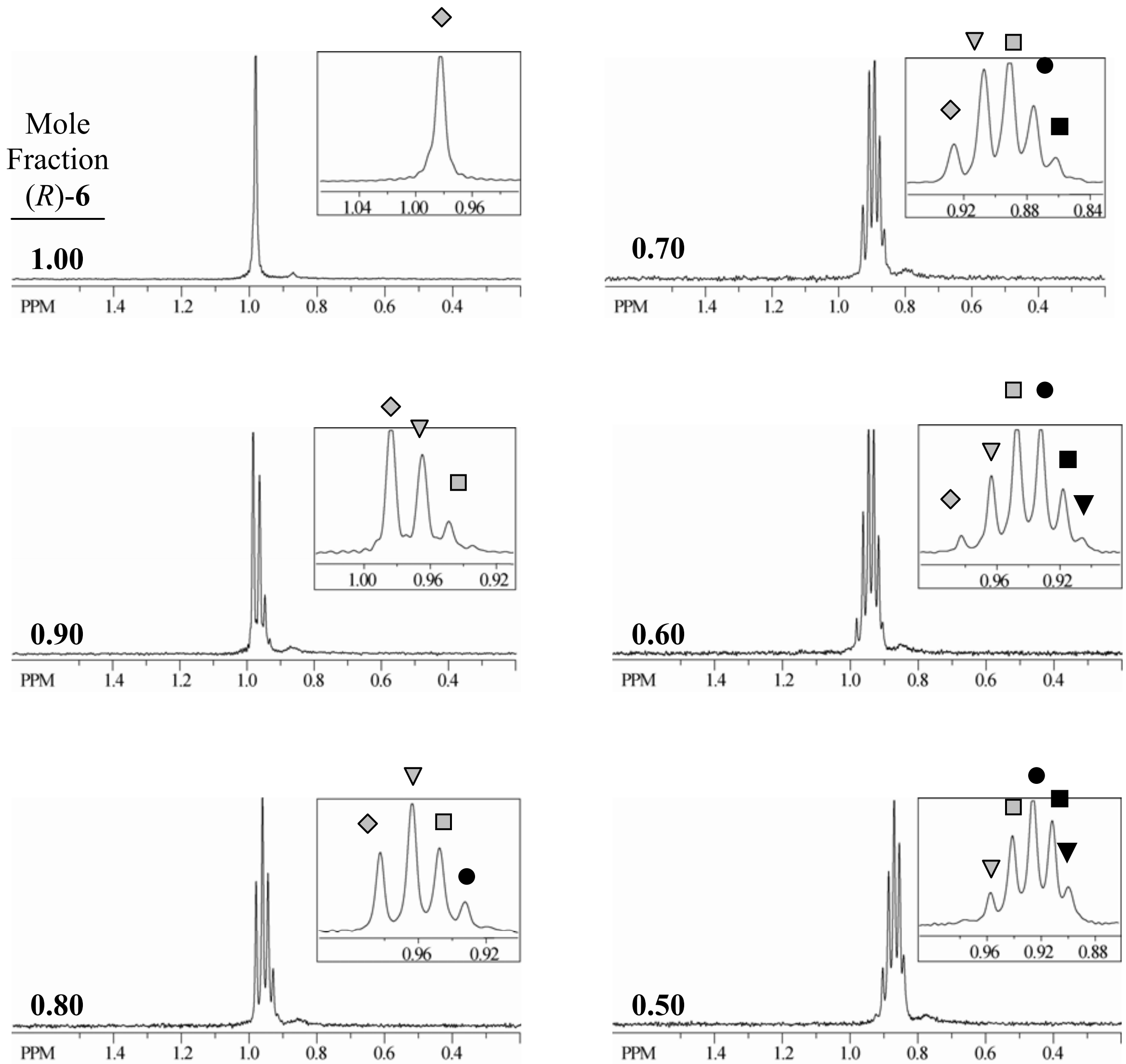




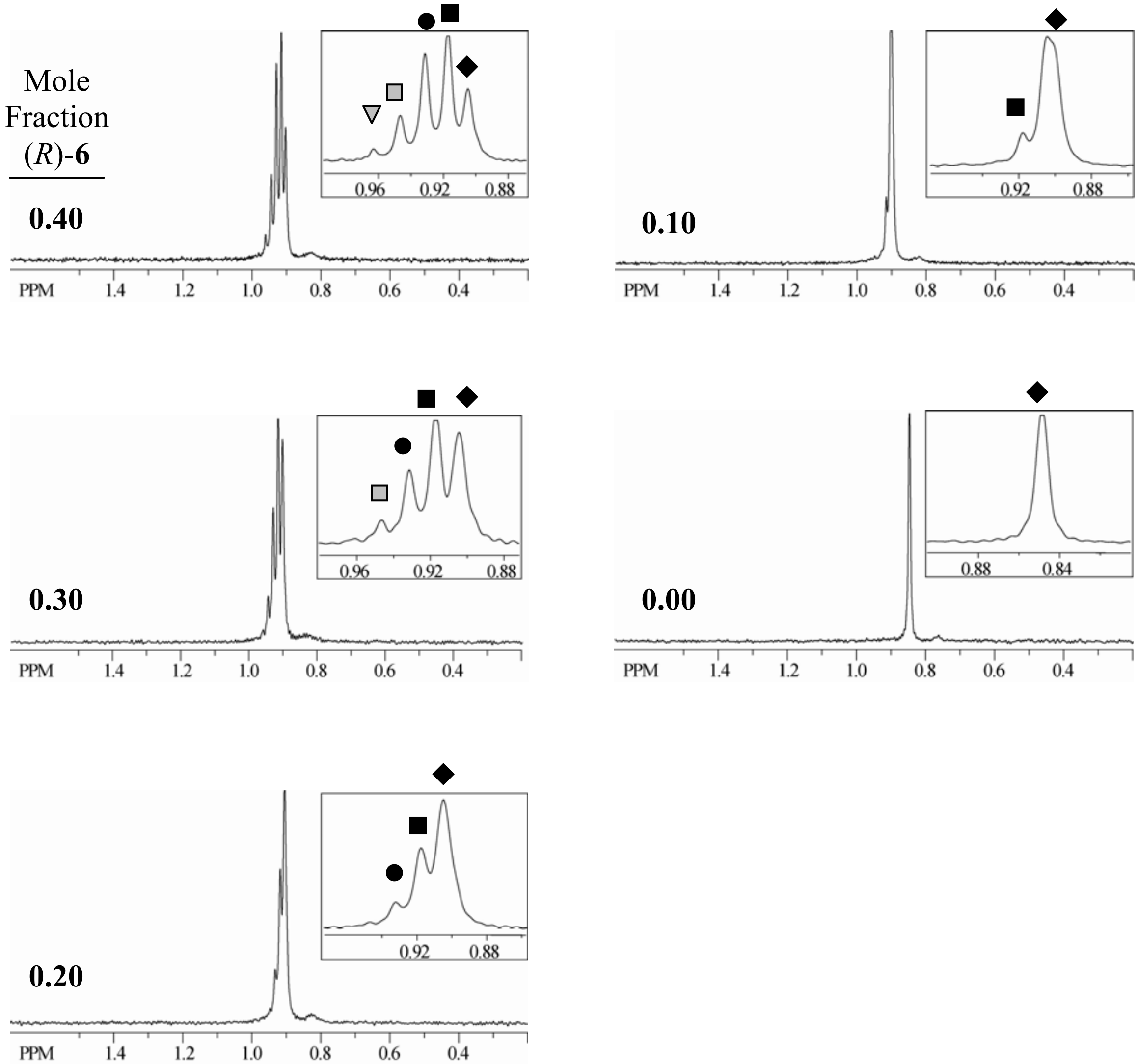


[enolate] (M)	Relative Integrations (▽)	(□)	(●)	(■)	(◆)
0.05	0.19	0.34	0.30	0.14	0.03
0.10	0.17	0.35	0.30	0.14	0.04
0.20	0.17	0.32	0.31	0.15	0.05

IV.C. Variation of enolate concentration for a mixture of [^{6}Li](*S*)-**6** and [^{6}Li](*R*)-**5** (mole fraction of **R'**=0.30). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*R*)-**6** and [^{6}Li](*R*)-**5** (mole fraction of **R'**=0.30) at various enolate concentrations. All samples are 3.0 M THF/toluene and were recorded at -30 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R}_6$+$\mathbf{R}_5\mathbf{R'}_1$ (■) $\mathbf{R}_4\mathbf{R'}_2$ (●) $\mathbf{R}_3\mathbf{R'}_3$ (□) $\mathbf{R}_2\mathbf{R'}_4$ (▽) $\mathbf{R}_1\mathbf{R'}_5$ (◇) $\mathbf{R'}_6$ such that **R'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*R*)-**5**.



IV.D. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**6** and [^{6}Li](*R*)-**5** at various mole fractions in 3.0 M THF/toluene at -30 ºC. Samples are 0.10 M total enolate concentration. (◆) $\mathbf{R}_6$+$\mathbf{R}_5\mathbf{R'}_1$ (■) $\mathbf{R}_4\mathbf{R'}_2$ (●) $\mathbf{R}_3\mathbf{R'}_3$ (▣) $\mathbf{R}_2\mathbf{R'}_4$ (▽) $\mathbf{R}_1\mathbf{R'}_5$ (◈) $\mathbf{R'}_6$ such that **R'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*R*)-**5**.



IV.D. (cont.) ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**6** and [^{6}Li](*R*)-**5** at various mole fractions in 3.0 M THF/toluene at -30 ºC. Samples are 0.10 M total enolate concentration. (◆) $\mathbf{R}_6$+$\mathbf{R}_5\mathbf{R'}_1$ (■) $\mathbf{R}_4\mathbf{R'}_2$ (●) $\mathbf{R}_3\mathbf{R'}_3$ (▣) $\mathbf{R}_2\mathbf{R'}_4$ (▽) $\mathbf{R}_1\mathbf{R'}_5$ (◇) $\mathbf{R'}_6$ such that **R'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*R*)-**5**.

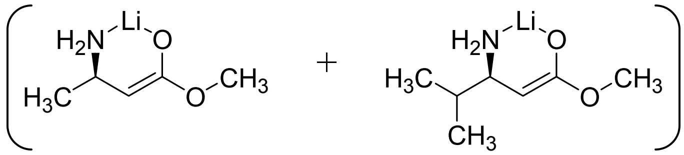
IV.E. Table of the relative integrations for the spectra in **IV.D.**[a]

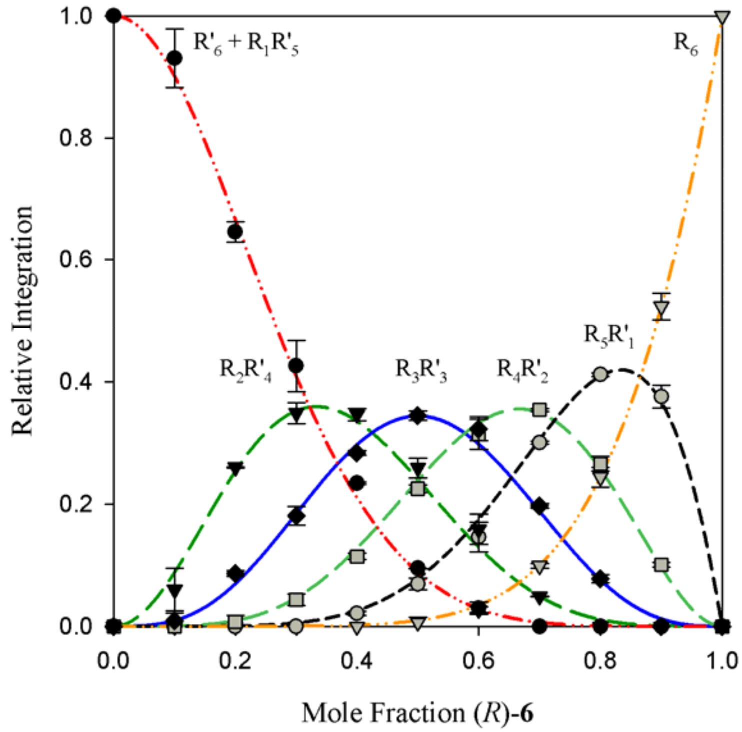
Mole Frac. (*R*)-**6**	Relative Integrations **R'**$_6$ (◇)	**R**$_1$**R'**$_5$ (▽)	**R**$_2$**R'**$_4$ (▣)	**R**$_3$**R'**$_3$ (●)
1.00	1.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
0.90	0.52±0.02	0.38±0.02	0.101±0.004	0.00±0.00
0.80	0.24±0.02	0.412±0.003	0.27±0.01	0.078±0.007
0.70	0.099±0.004	0.300±0.002	0.354±0.002	0.197±0.004
0.60	0.028±0.005	0.15±0.02	0.31±0.03	0.32±0.02
0.50	0.006±0.009	0.07±0.01	0.225±0.006	0.345±0.007
0.40	0.00±0.00	0.021±0.003	0.114±0.005	0.284±0.004
0.30	0.00±0.00	0.00±0.00	0.04±0.01	0.18±0.02
0.20	0.00±0.00	0.00±0.00	0.008±0.011	0.087±0.005
0.10	0.00±0.00	0.00±0.00	0.00±0.00	0.01±0.01
0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00

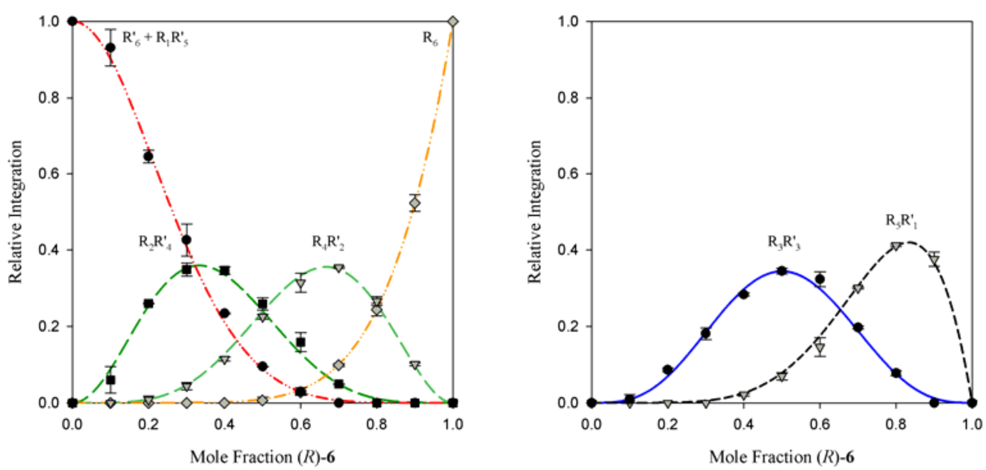
Mole Frac. (*R*)-**6**	Relative Integrations **R**$_4$**R'**$_2$ (■)	**R**$_5$**R'**$_1$ + **R'**$_6$[b] (◆)
1.00	0.00±0.00	0.00±0.00
0.90	0.00±0.00	0.00±0.00
0.80	0.00±0.00	0.00±0.00
0.70	0.049±0.0004	0.00±0.00
0.60	0.16±0.03	0.03±0.01
0.50	0.26±0.02	0.095±0.001
0.40	0.35±0.01	0.234±0.002
0.30	0.35±0.02	0.43±0.04
0.20	0.260±0.001	0.65±0.02
0.10	0.06±0.04	0.93±0.05
0.00	0.00±0.00	1.00±0.00

[a] (◆) **R**$_6$+**R**$_5$**R'**$_1$ (■) **R**$_4$**R'**$_2$ (●) **R**$_3$**R'**$_3$ (▣) **R**$_2$**R'**$_4$ (▽) **R**$_1$**R'**$_5$ (◇) **R'**$_6$ such that **R'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*R*)-**5**.

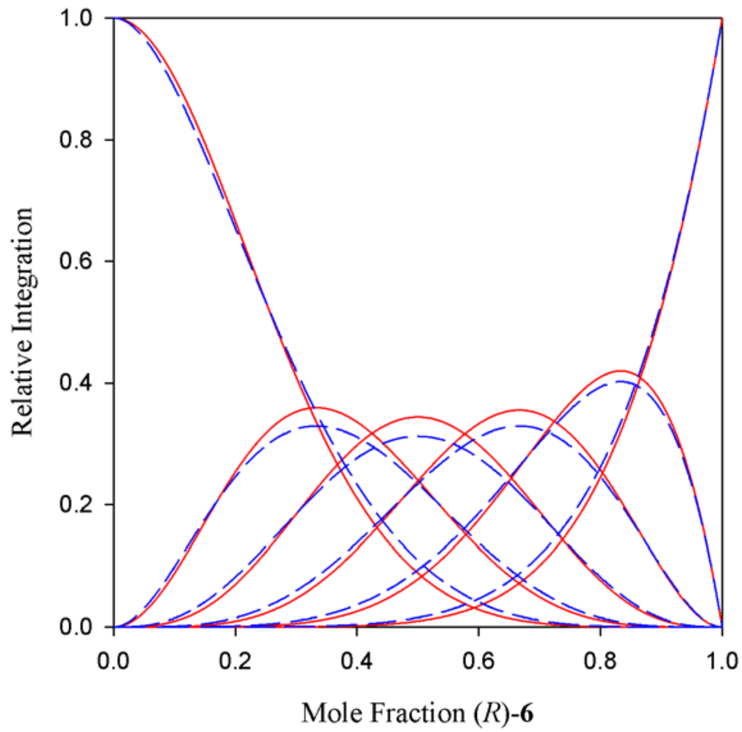
[b] The relative integrations of the **R**$_6$ and **R**$_5$**S'**$_1$ aggregates are summed due to poor resolution of their resonances.







IV.F. A Plot of [^{6}Li](*R*)-**6**/[^{6}Li](*R*)-**5** (3.0 M THF/toluene; -50 ºC) hexamers. The relative integrations are plotted as a function of the mole fraction of [^{6}Li](*R*)-**6**. (◆) **R**$_6$+**R**$_5$**R'**$_1$ (■) **R**$_4$**R'**$_2$ (●) **R**$_3$**R'**$_3$ (▣) **R**$_2$**R'**$_4$ (▽) **R**$_1$**R'**$_5$ (◇) **R'**$_6$ such that **R'** = [^{6}Li](*R*)-**6** and **R** = [^{6}Li](*R*)-**5**. The relative integrations of the **R**$_6$ and **R**$_5$**S'**$_1$ aggregates are summed due to poor resolution of their resonances. The curves result from a parametric fit, affording ϕ_0=1.00; ϕ_1=2.04; ϕ_2=2.88; ϕ_3=3.66; ϕ_4=4.03; ϕ_5=3.99; ϕ_6=3.45.

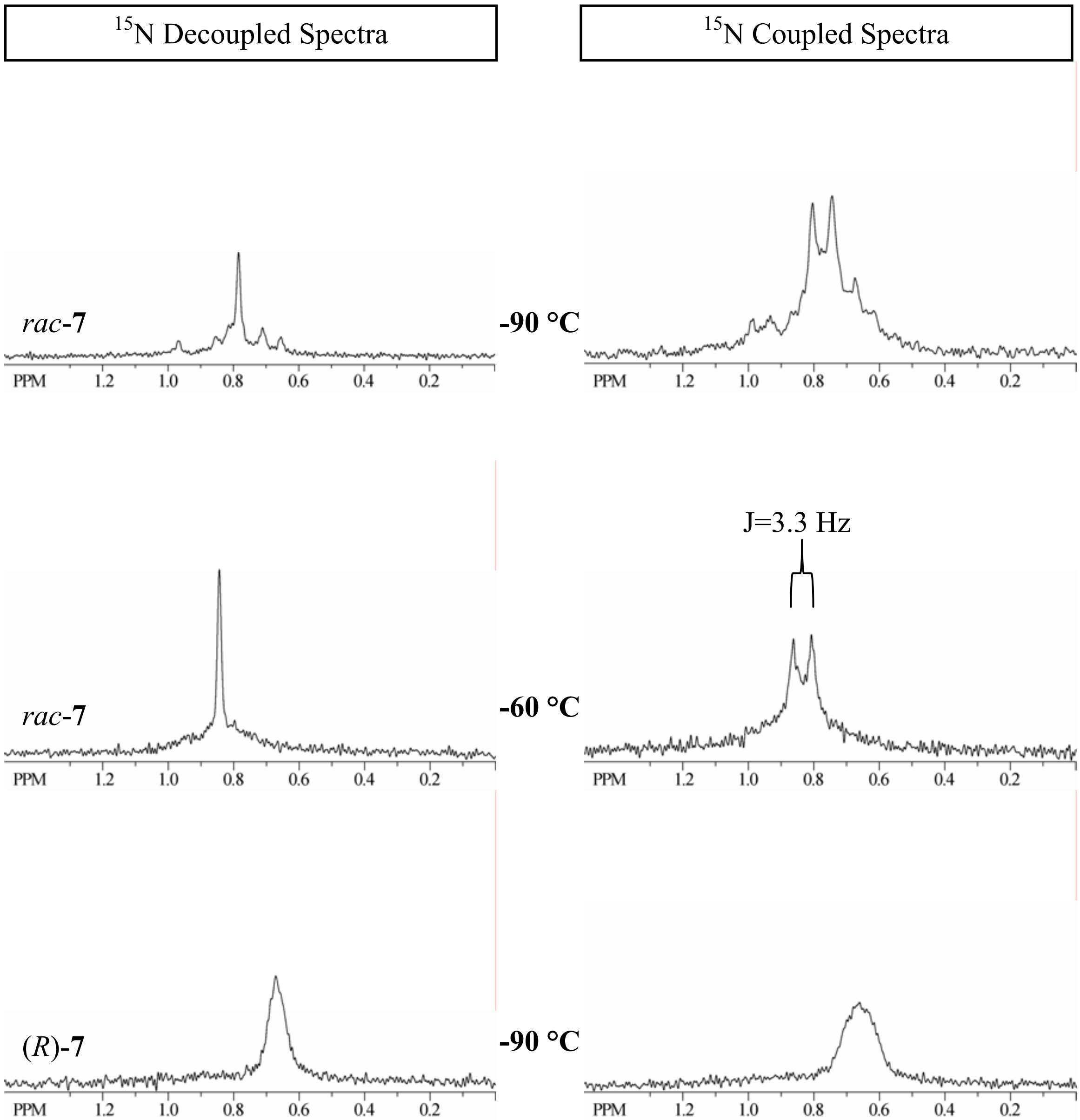


IV.G. The fit in **IV.F.** is overlaid with the expected statistical distribution of an ensemble of hexamers.

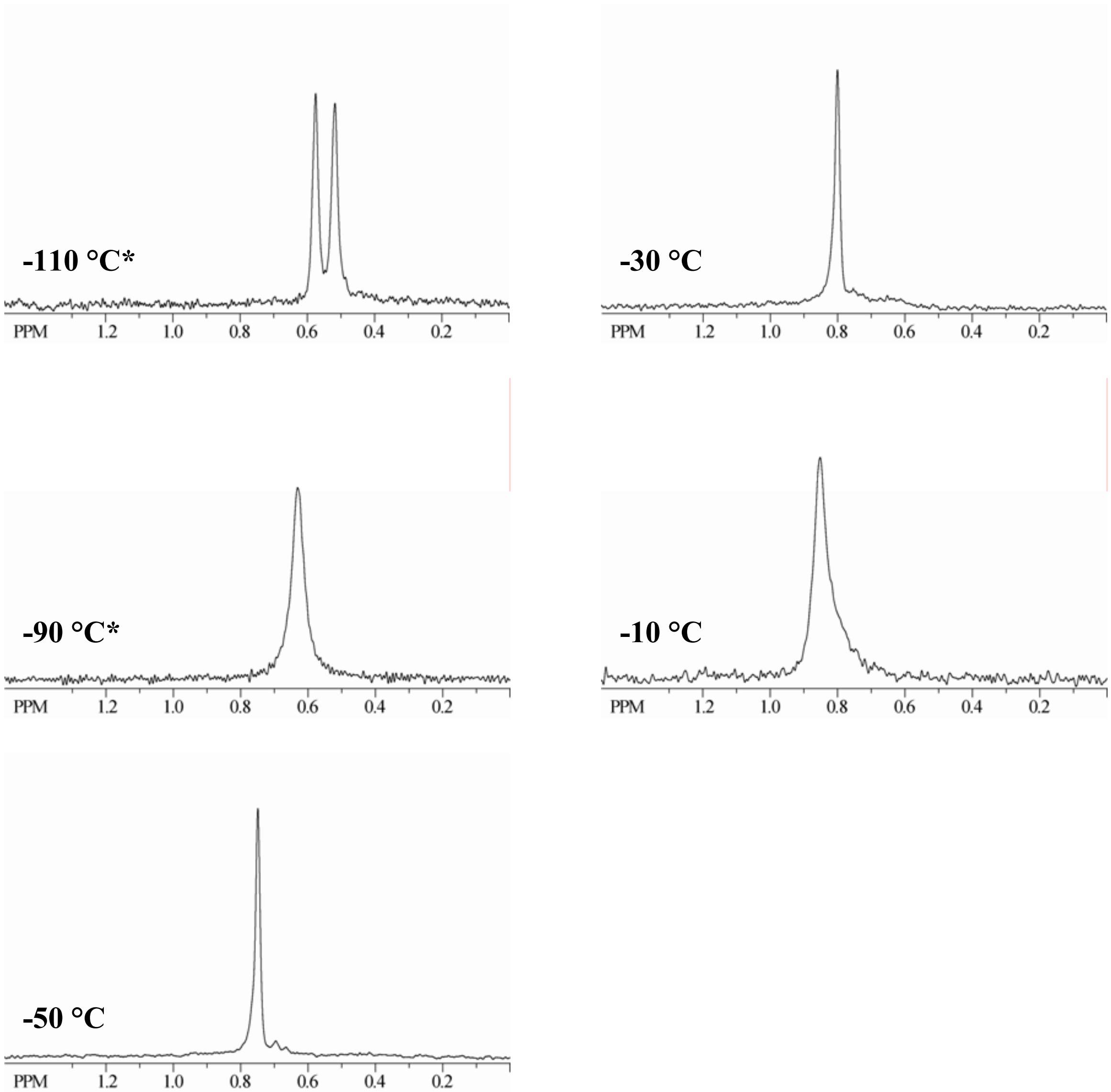
(———) Fit to data (ϕ_0=1.00; ϕ_1=2.04; ϕ_2=2.88; ϕ_3=3.66; ϕ_4=4.03; ϕ_5=3.99; ϕ_6=3.45)

(– – – –) Statistical distribution (ϕ_0=1.; ϕ_1=6; ϕ_2=15; ϕ_3=20; ϕ_4=15; ϕ_5=6; ϕ_6=1)

V. (*S*)-β-Phenylalanine/(*R*)-β-Phenylalanine

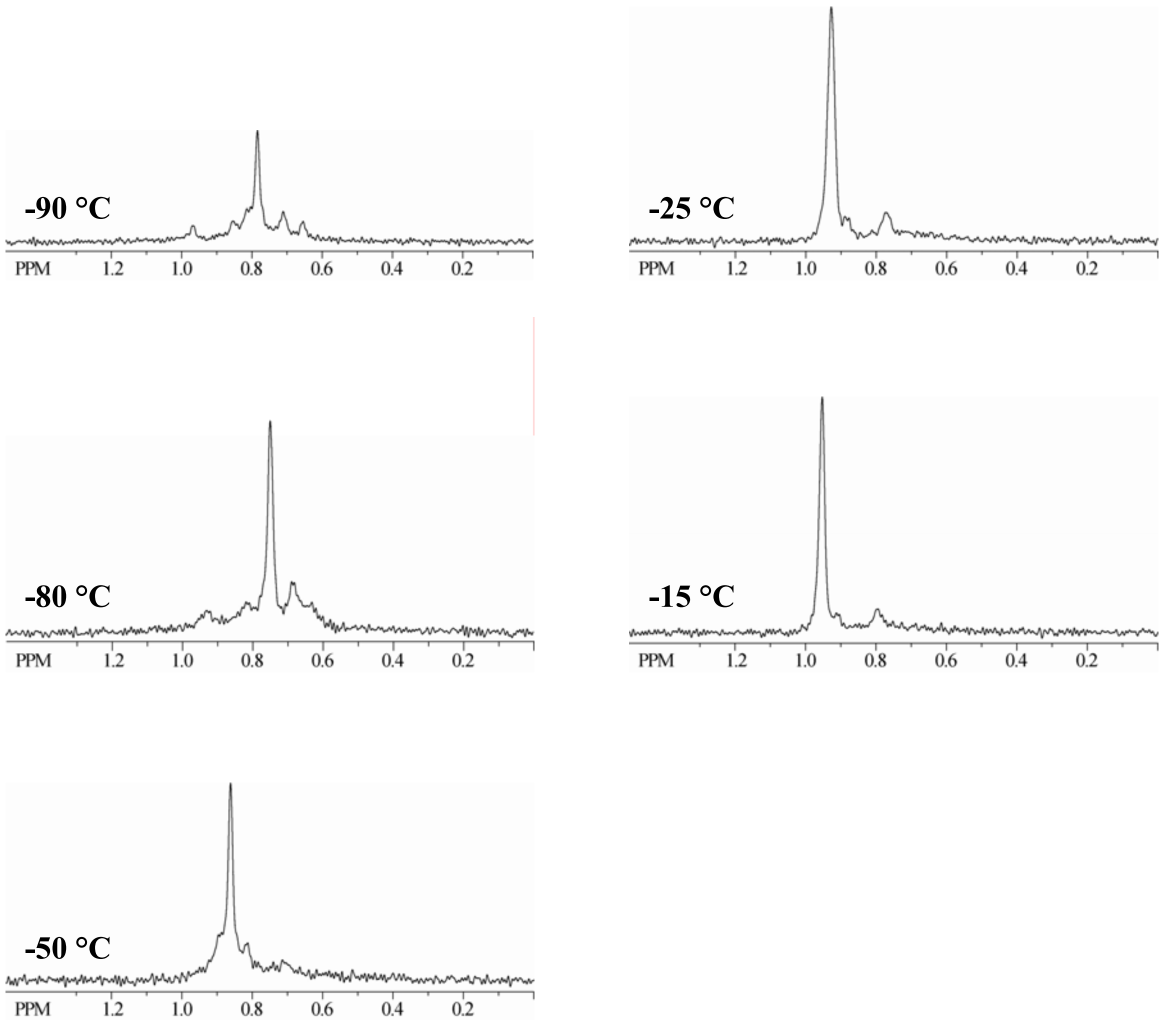


V.A. ^{6}Li NMR spectra (58.8 MHz) of [^{15}N,^{6}Li]*rac*-**7** and [^{15}N,^{6}Li](*R*)-**7** at various temperatures. All samples are 0.10 M in total enolate concentration and 9.0 M THF/toluene.

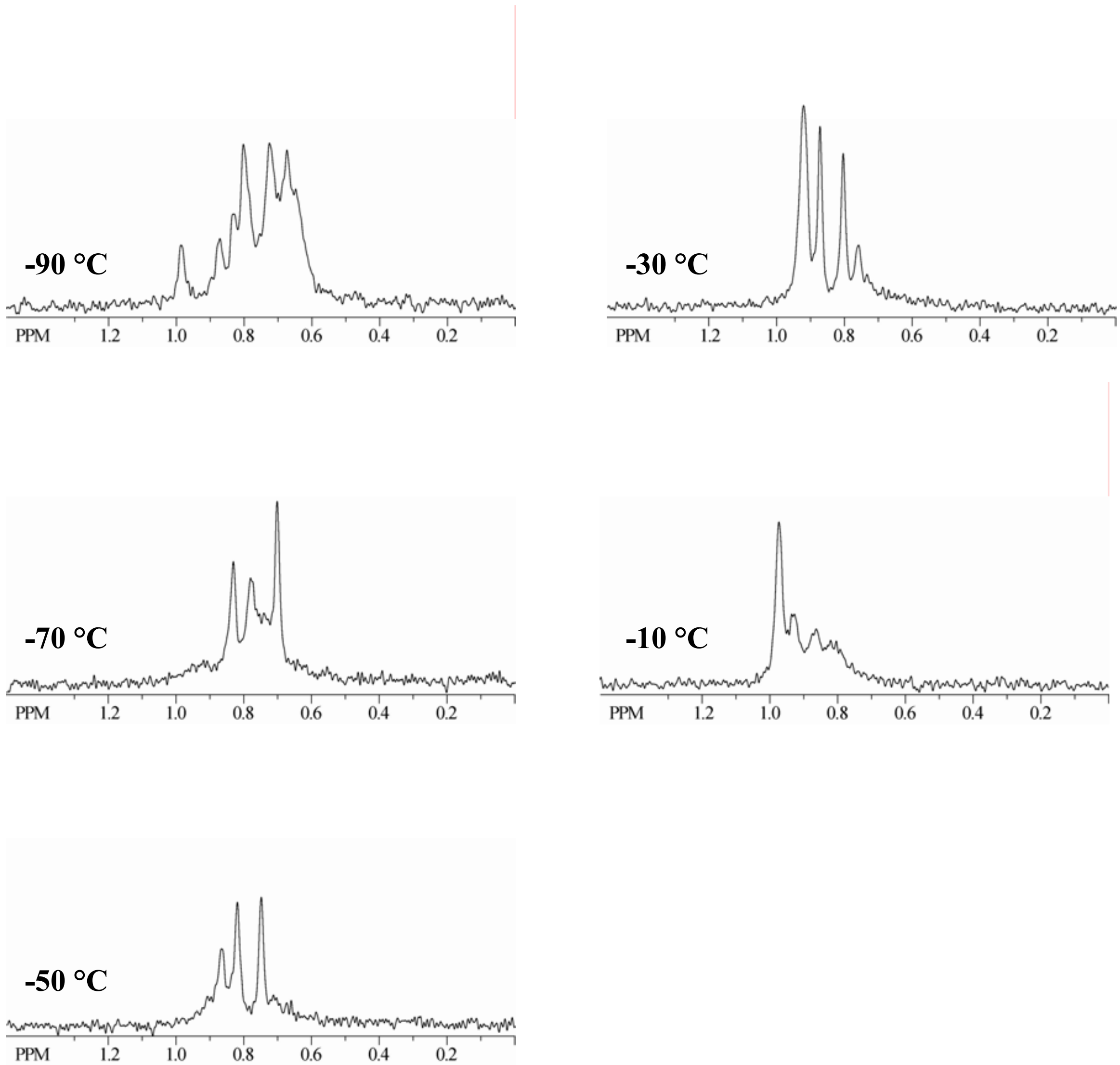


V.B. ^{6}Li NMR spectra (58.8 MHz) of [^{6}Li](*R*)-**7** at various temperatures. All samples are 0.10 M total enolate concentration and 9.0 M THF/toluene.

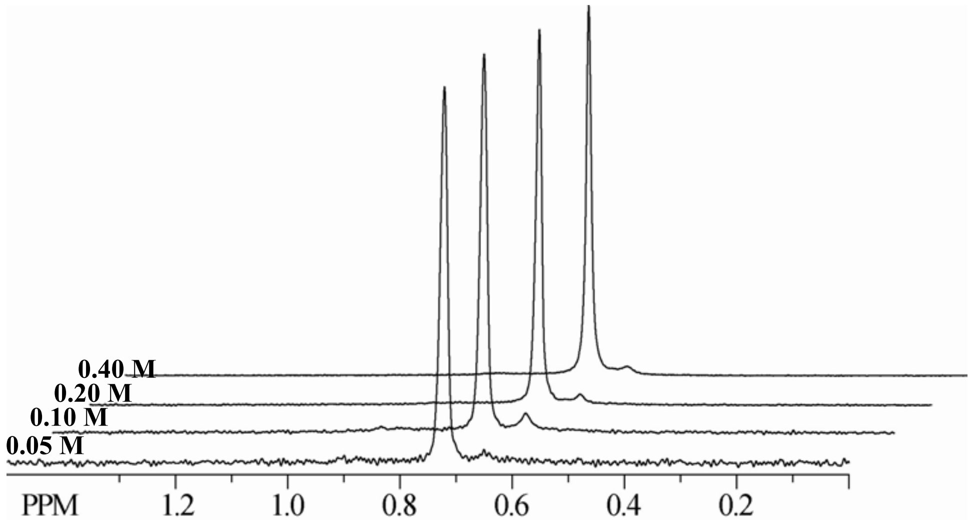
* Spectra were recorded at 73.6 MHz.



V.C. ^{6}Li NMR spectra (58.8 MHz) of [^{6}Li]*rac*-**7** at various temperatures. All samples are 0.10 M total enolate concentration and 9.0 M THF/toluene.

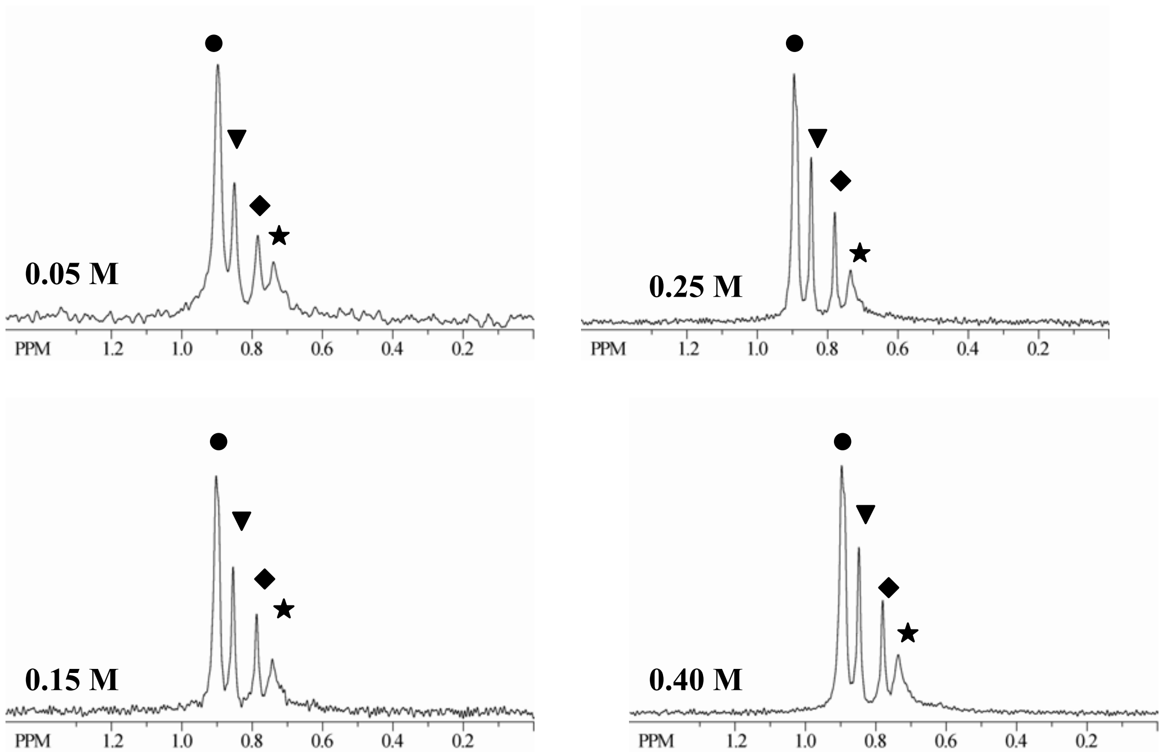


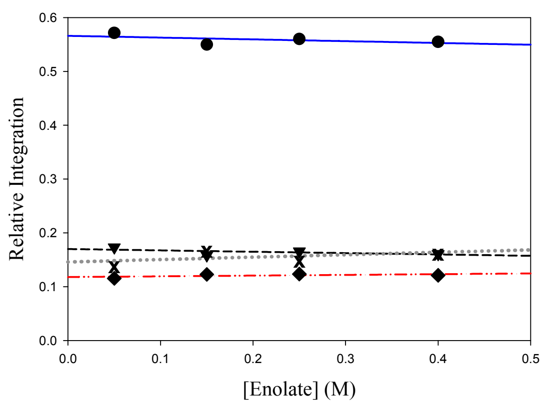
V.D. ^{6}Li NMR spectra (58.8 MHz) of a mixture of [^{6}Li](*R*)-**7** and [^{6}Li](*S*)-**7** (mole fraction of **R**=0.80) at various temperatures. All samples are 0.10 M total enolate concentration and 9.0 M THF/toluene.



[enolate] (M)	Relative Integrations 0.73 ppm	0.65 ppm
0.05	1	0.05
0.10	1	0.08
0.20	1	0.07
0.40	1	0.04

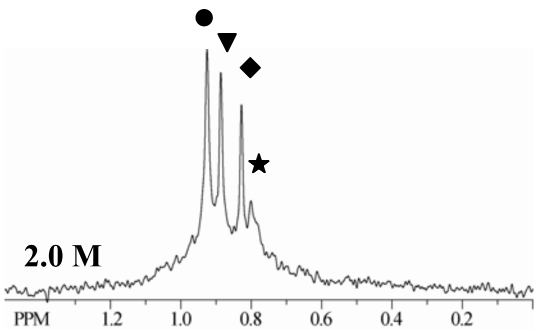
V.E. Variation of enolate concentration for [^{6}Li](*S*)-**7**. ^{6}Li NMR spectra (73.6 MHz) of [^{6}Li](*S*)-**7** at various enolate concentrations at -25 ºC. All samples are 9.0 M THF/toluene. To determine if the peak at 0.65 ppm was a different aggregate (tetramer, dimmer, etc.), the absolute enolate concentration was varied. Integration of the peaks shows no significant variation in the peak ratios as a function of absolute enolate concentration.

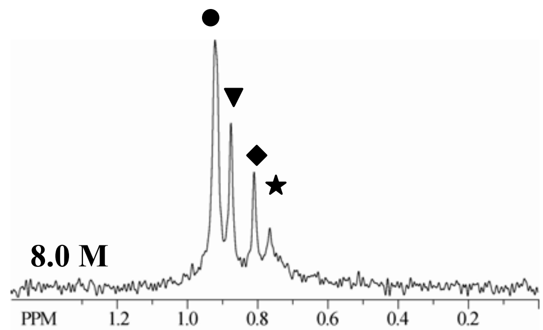


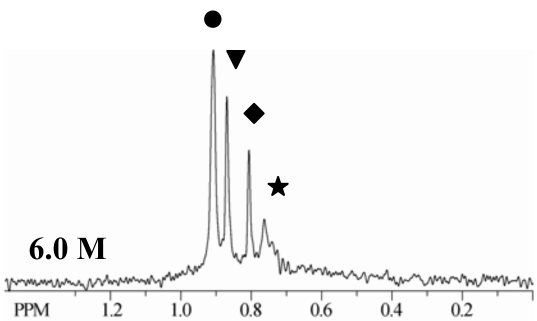


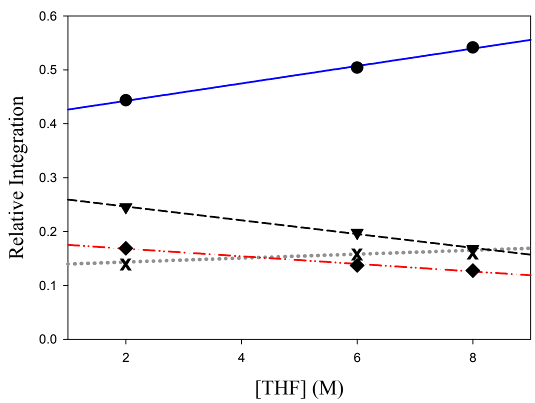
[enolate] (M)	Relative Integrations (●)	(▼)	(◆)	(★)
0.05	0.57	0.17	0.12	0.14
0.15	0.55	0.16	0.12	0.17
0.25	0.56	0.17	0.12	0.15
0.40	0.55	0.16	0.12	0.16

V.F. Variation of enolate concentration for a mixture of [^{6}Li](*R*)-**7** and [^{6}Li](*S*)-**7** (mole fraction of **R**=0.30). ^{6}Li NMR spectra (58.8 MHz) of a mixture of [^{6}Li](*R*)-**7** and [^{6}Li](*S*)-**7** (mole fraction of **R**=0.3) at various enolate concentrations. All samples are 9.0 M THF/toluene and were recorded at -25 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (●) $\mathbf{R}_3\mathbf{S}_3$+$\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (★) impurity such that **R** = [^{6}Li](*R*)-**7** and **S** = [^{6}Li](*S*)-**7**.



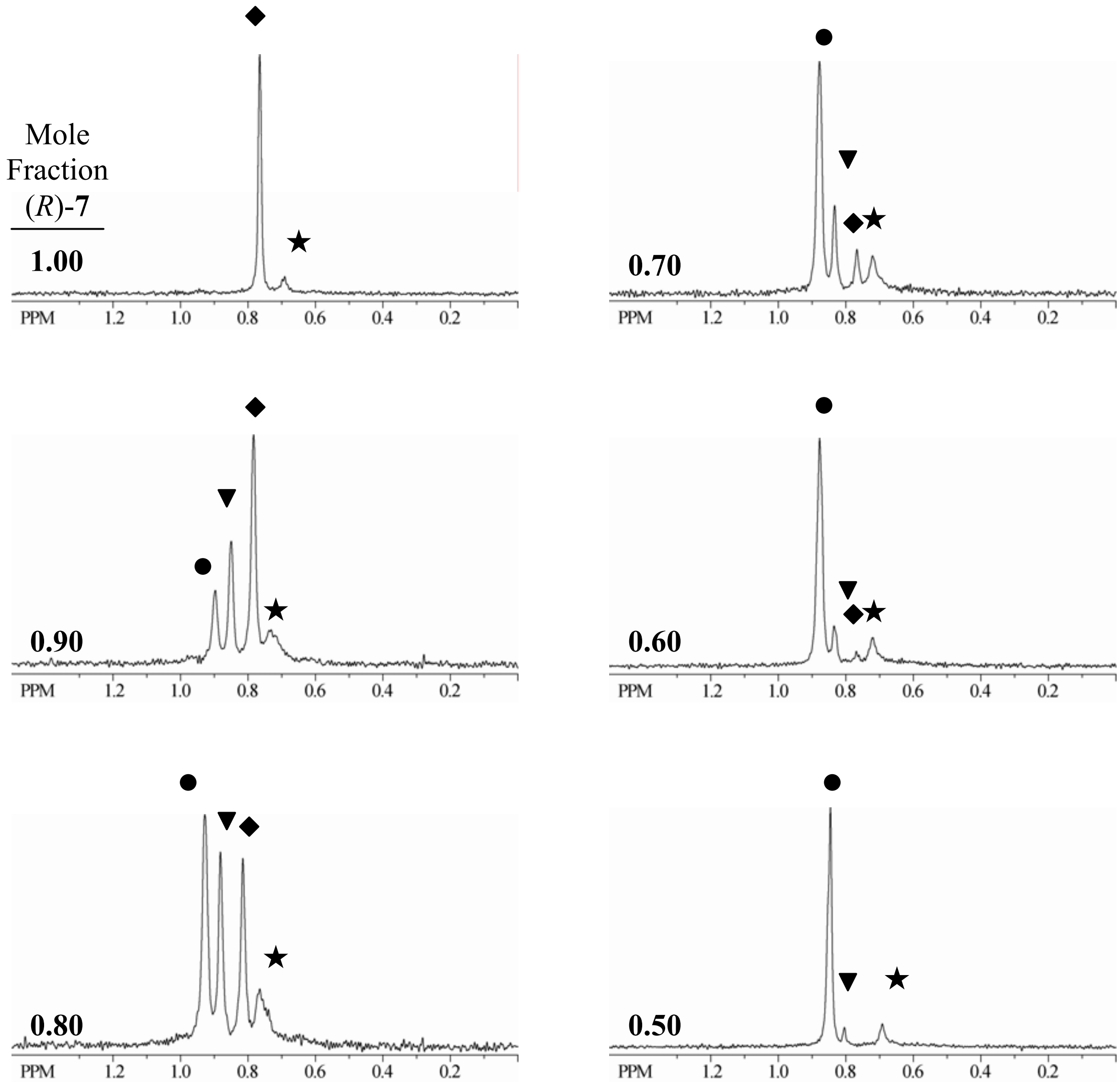




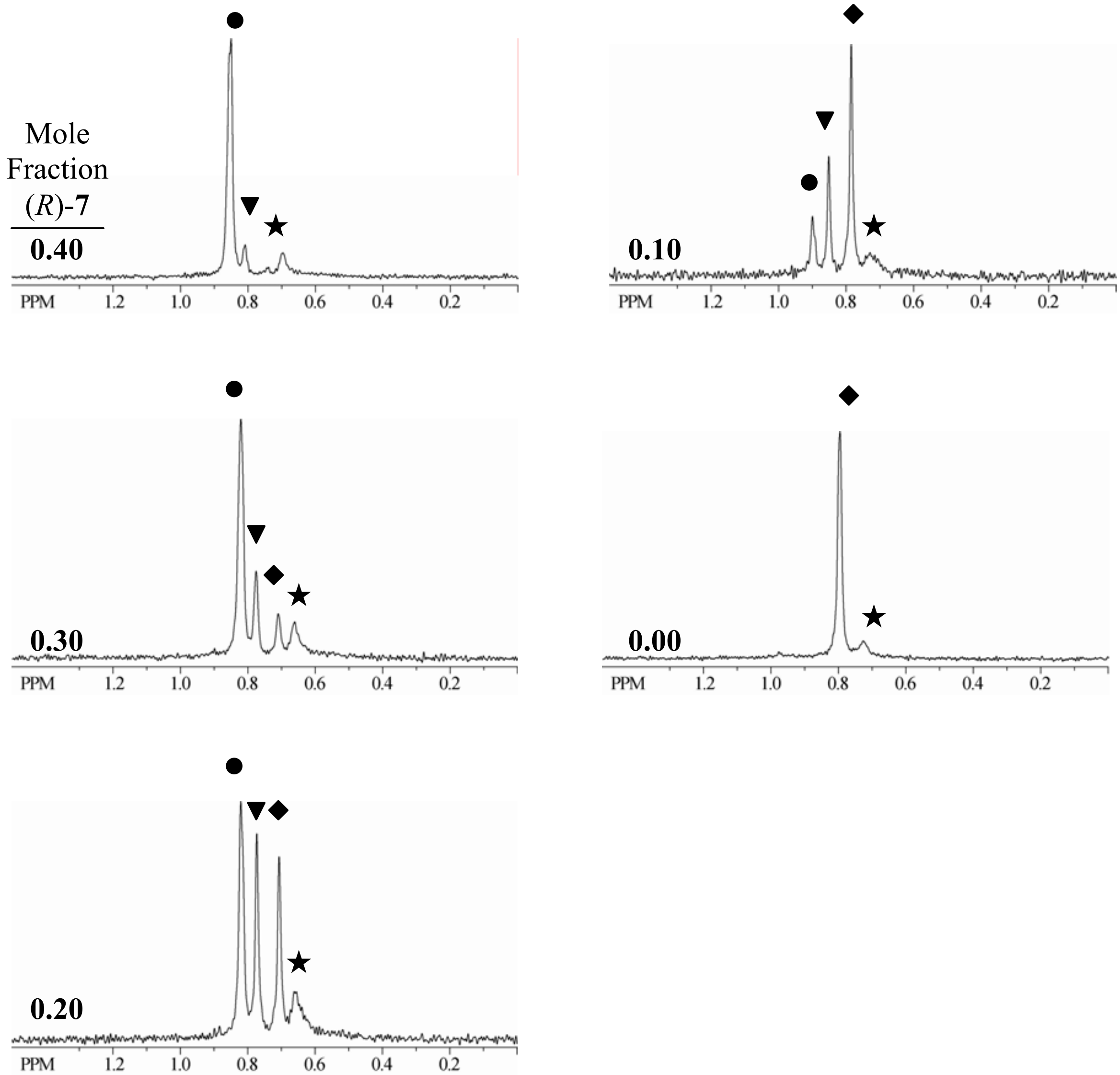


[THF] (M)	Relative Integrations (●)	(▼)	(◆)	(★)
2.0	0.44	0.25	0.17	0.14
6.0	0.50	0.20	0.14	0.16
8.0	0.54	0.17	0.13	0.16

V.G. Variation of THF concentration for a mixture of [^{6}Li](*R*)-**7** and [^{6}Li](*S*)-**7** (mole fraction of **S**=0.30). ^{6}Li NMR spectra (58.8 MHz) of a mixture of [^{6}Li](*R*)-**7** and [^{6}Li](*S*)-**7** (mole fraction of **S**=0.30) at various THF/toluene concentrations. All samples are 0.10 M total enolate and were recorded at -25 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (●) $\mathbf{R}_3\mathbf{S}_3$+$\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (★) impurity such that **R** = [^{6}Li](*R*)-**7** and **S** = [^{6}Li](*S*)-**7**.



V.H. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**7** and [^{6}Li](*S*)-**7** at various mole fractions in 9.0 M THF/toluene at -25 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (●) $\mathbf{R}_3\mathbf{S}_3$+$\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (★) impurity such that **R** = [^{6}Li](*R*)-**7** and **S** = [^{6}Li](*S*)-**7**.



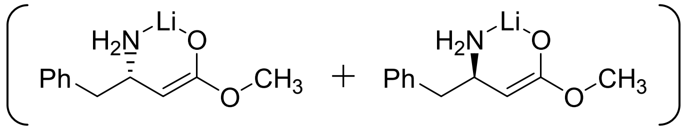
V.H. (cont.) ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**7** and [^{6}Li](*S*)-**7** at various mole fractions in 9.0 M THF/toluene at -25 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (●) $\mathbf{R}_3\mathbf{S}_3$+$\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (★) impurity such that **R** = [^{6}Li](*R*)-**7** and **S** = [^{6}Li](*S*)-**7**.

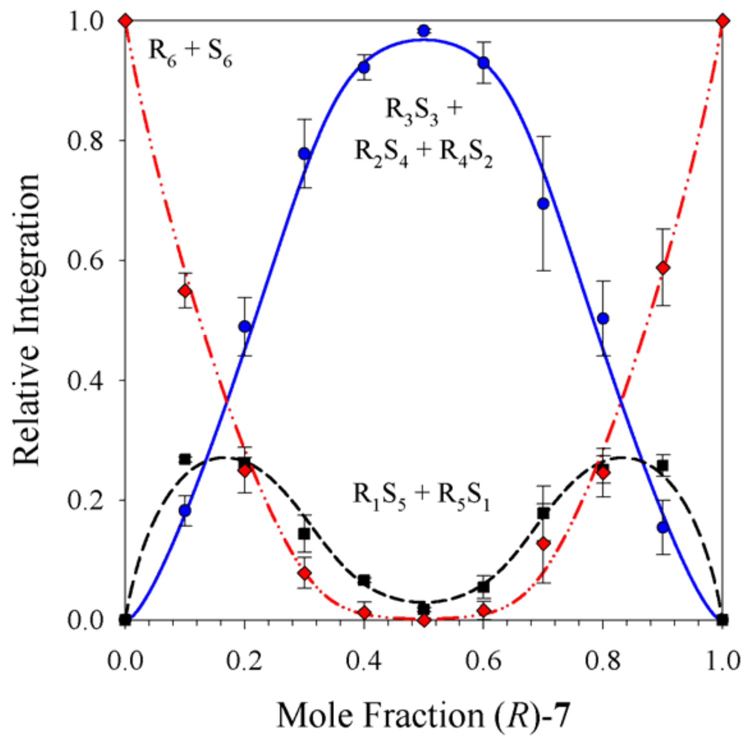
V.I. Table of the relative integrations for the spectra in **V.H**.[a]

Mole Frac. (R)-**7**	Relative Integrations $\mathbf{R}_6$+$\mathbf{S}_6$ (◆)	$\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (▼)	$\mathbf{R}_4\mathbf{S}_2$+$\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_3\mathbf{S}_3$[b] (●)
1.00	1.00±0.00	0.00±0.00	0.00±0.00
0.90	0.59±0.06	0.26±0.02	0.15±0.05
0.80	0.25±0.04	0.25±0.02	0.50±0.06
0.70	0.13±0.07	0.18±0.05	0.69±0.11
0.60	0.02±0.02	0.05±0.02	0.93±0.03
0.50	0.00±0.00	0.02±0.003	0.98±0.003
0.40	0.01±0.02	0.07±0.003	0.92±0.02
0.30	0.08±0.03	0.14±0.03	0.78±0.06
0.20	0.25±0.04	0.26±0.010	0.49±0.05
0.10	0.55±0.03	0.27±0.004	0.18±0.03
0.00	1.00±0.00	0.00±0.00	0.00±0.00

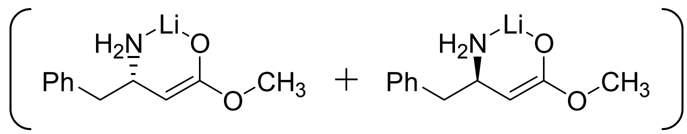
[a] (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (●) $\mathbf{R}_3\mathbf{S}_3$+$\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (★) impurity such that **R** = [^{6}Li](*R*)-**7** and **S** = [^{6}Li](*S*)-**7**.

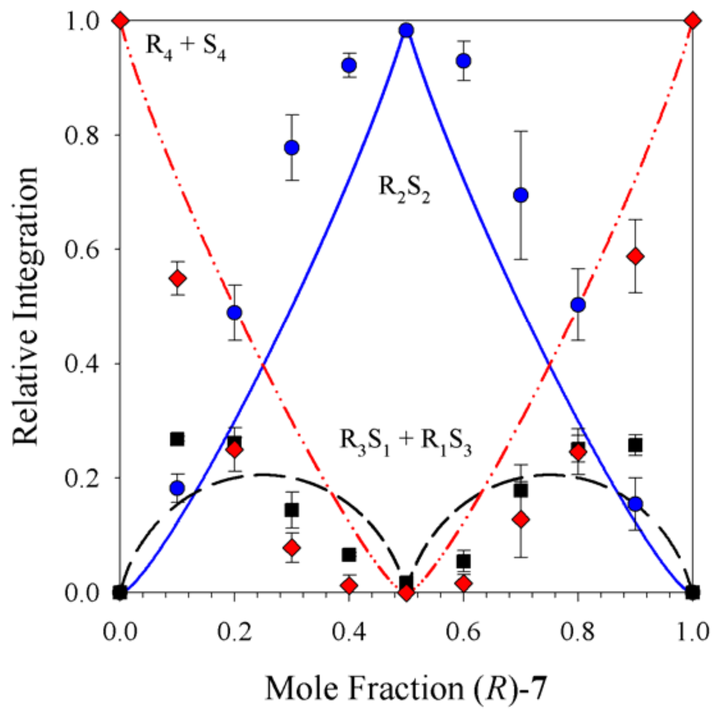
[b] The $\mathbf{R}_3\mathbf{S}_3$ and $\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ peaks were integrated as a single peak due to poor resolution.





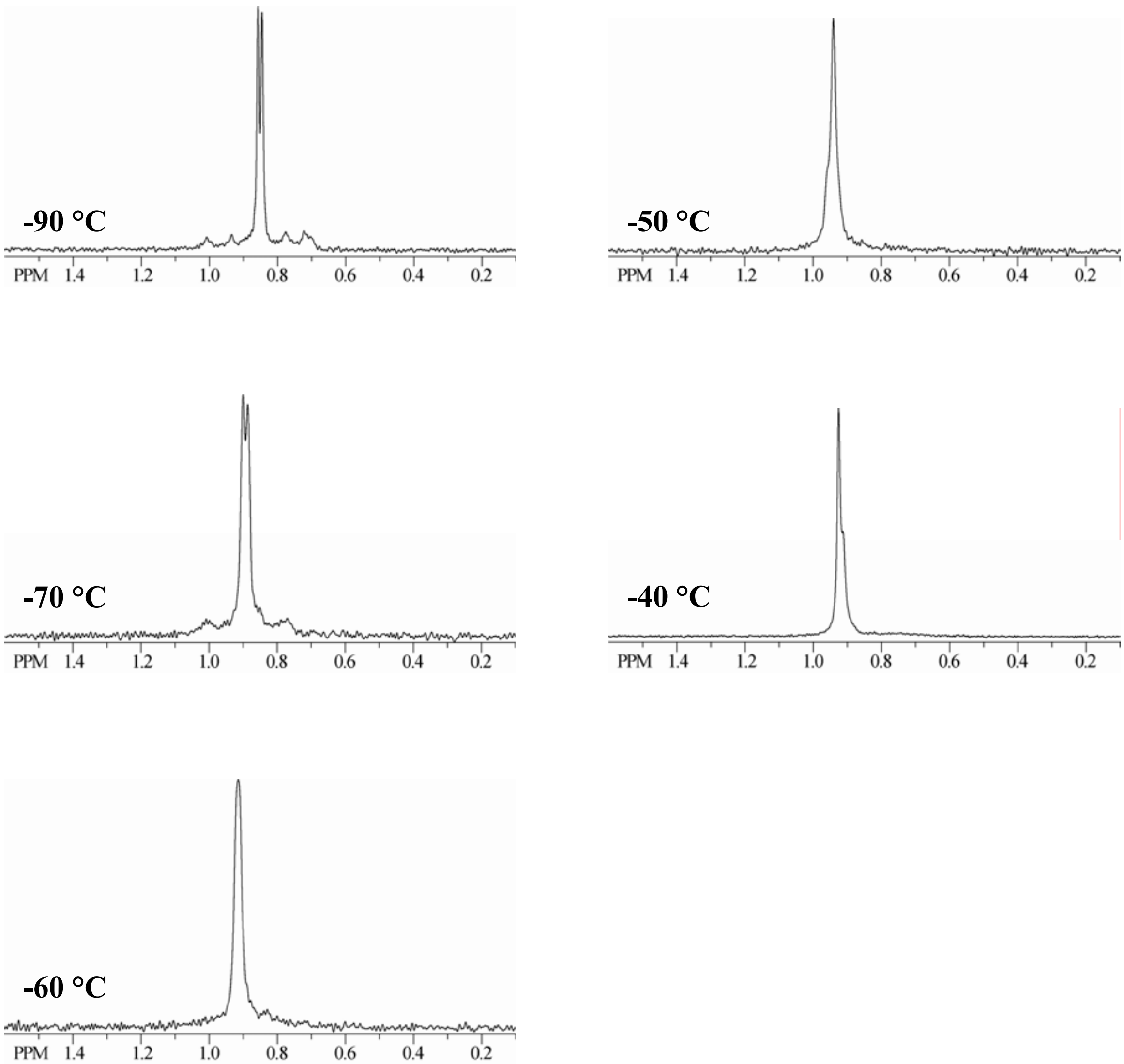
V.J. Job Plot of [^{6}Li](*R*)-**7**/[^{6}Li](*S*)-**7** (9.0 M THF/toluene; -25 ºC) hexamers. The relative integrations are plotted as a function of the mole fraction of [^{6}Li](*R*)-**7**. (◆) $\mathbf{R_6}$+$\mathbf{S_6}$ (▼) $\mathbf{R_5S_1}$+$\mathbf{R_1S_5}$ (●) $\mathbf{R_3S_3}$+$\mathbf{R_2S_4}$+$\mathbf{R_4S_2}$ such that **R** = [^{6}Li](*R*)-**7** and **S** = [^{6}Li](*S*)-**7**. The $\mathbf{R_3S_3}$, $\mathbf{R_2S_4}$, and $\mathbf{R_4S_2}$ aggregates are assigned as spectroscopically indistinguishable. The curves result from a parametric fit, affording ϕ_0=1; ϕ_1=2.17; ϕ_2=19.3; ϕ_3=13.6.



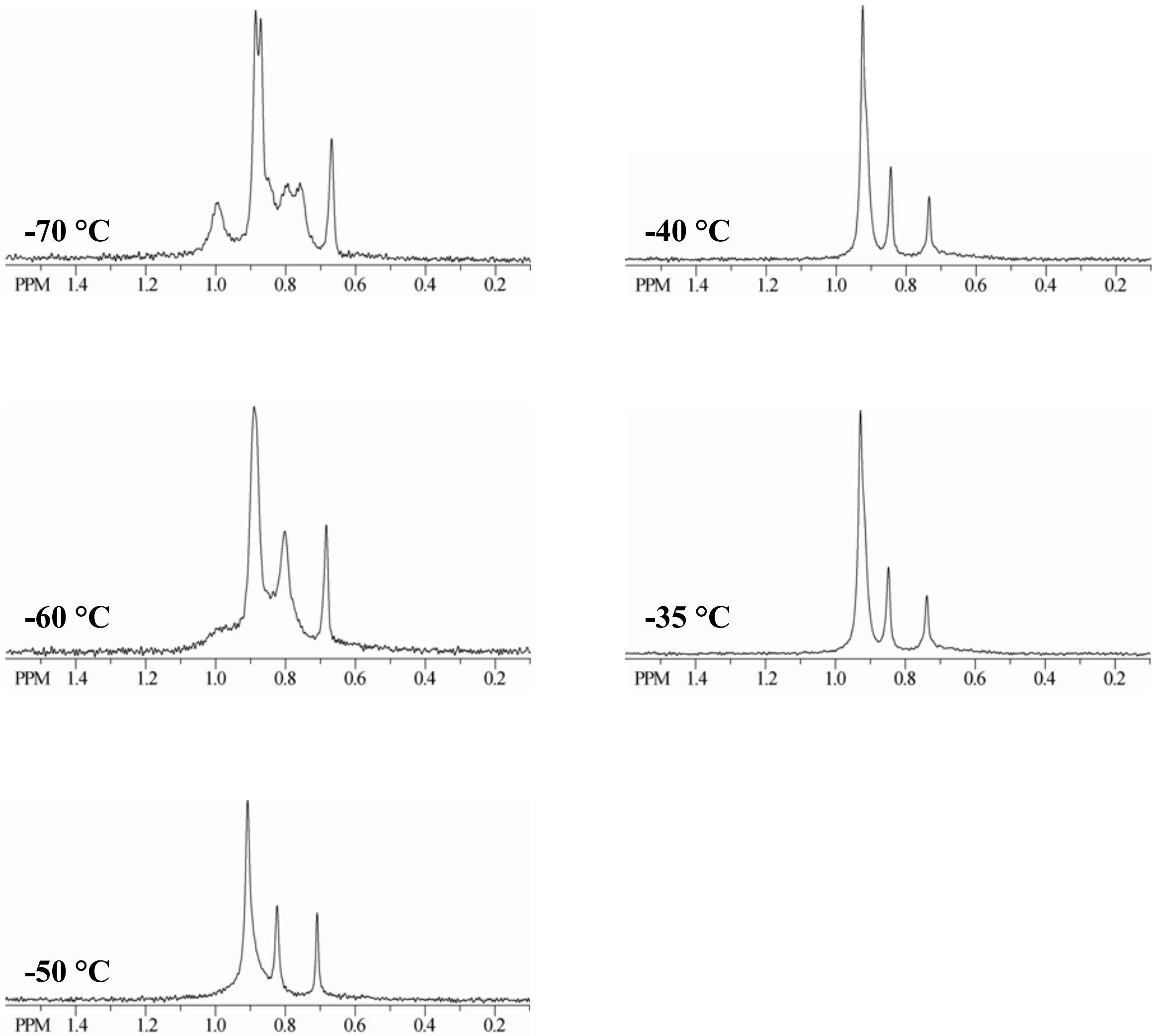


V.K. Job Plot of [^{6}Li](*R*)-**7**/[^{6}Li](*S*)-**7** (9.0 M THF/toluene; -25 ºC) fit to tetramer model. (◆) $\mathbf{R_4}$+$\mathbf{S_4}$ (▼) $\mathbf{R_3S_1}$+$\mathbf{R_1S_3}$ (●) $\mathbf{R_2S_2}$ such that **R** = [^{6}Li](*R*)-**7** and **S** = [^{6}Li](*S*)-**7.** The relative integrations are plotted as a function of the mole fraction of [^{6}Li](*R*)-**7**. The curves result from a parametric fit, affording ϕ_0=1; ϕ_1=10.1; ϕ_2=1041.

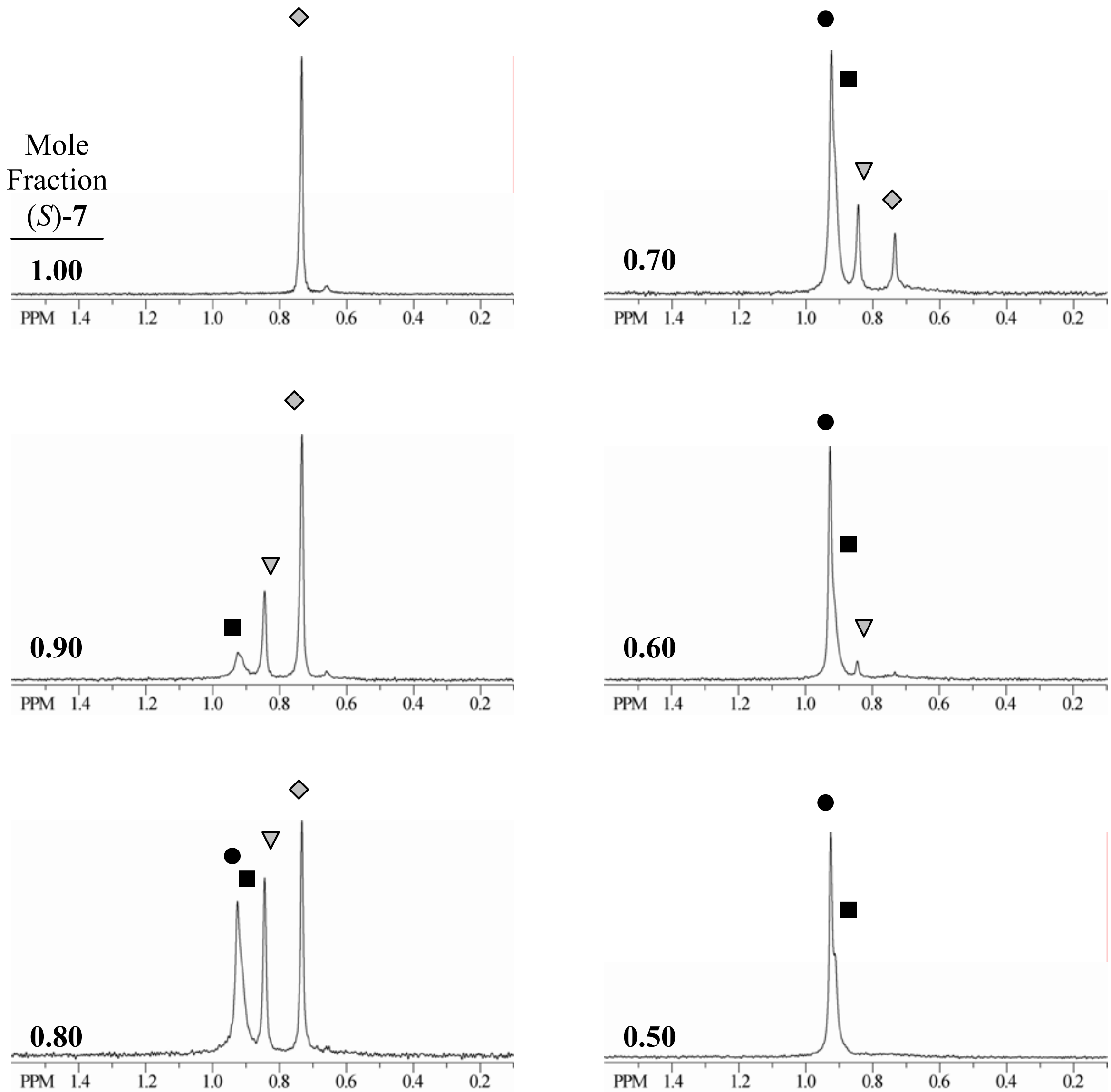
VI. (*S*)-β-Phenylalanine and (*R*)-β-Alanine



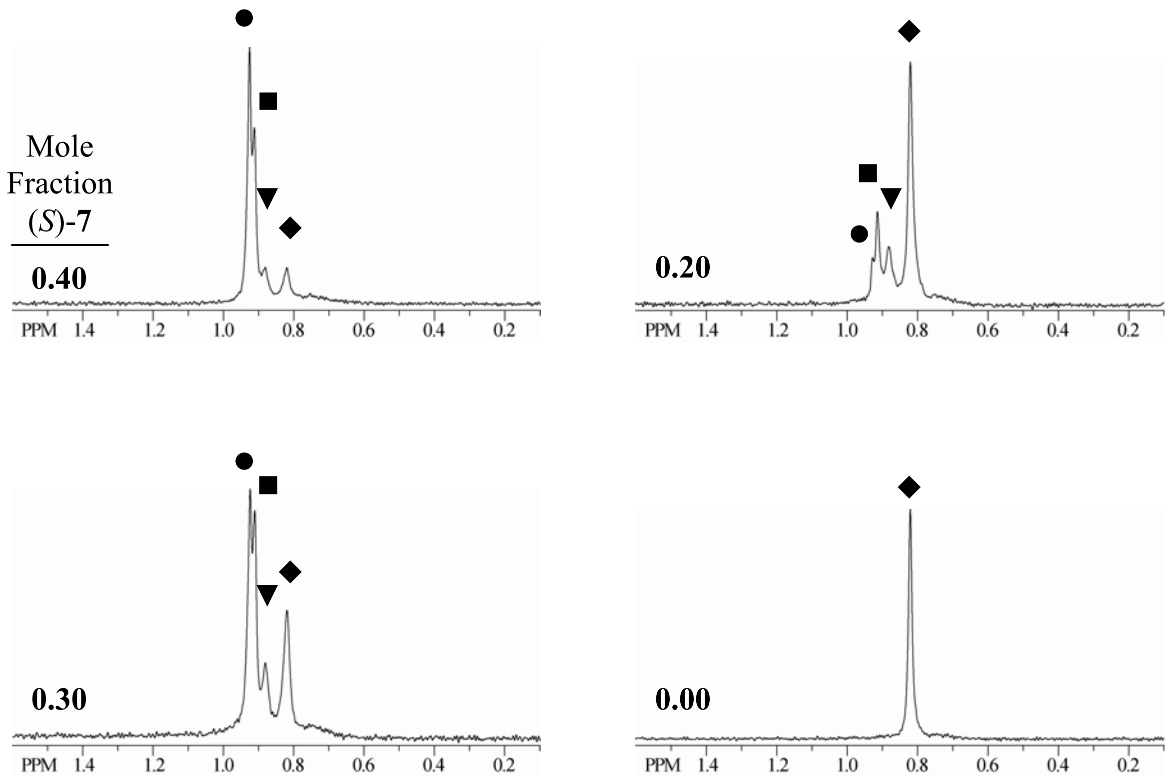
VI.A. ^{6}Li NMR spectra (58.8 MHz) of a mixture of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** (mole fraction of **7**=0.5) at various temperatures. All samples are 0.10 M total enolate concentration and 9.0 M THF/toluene.



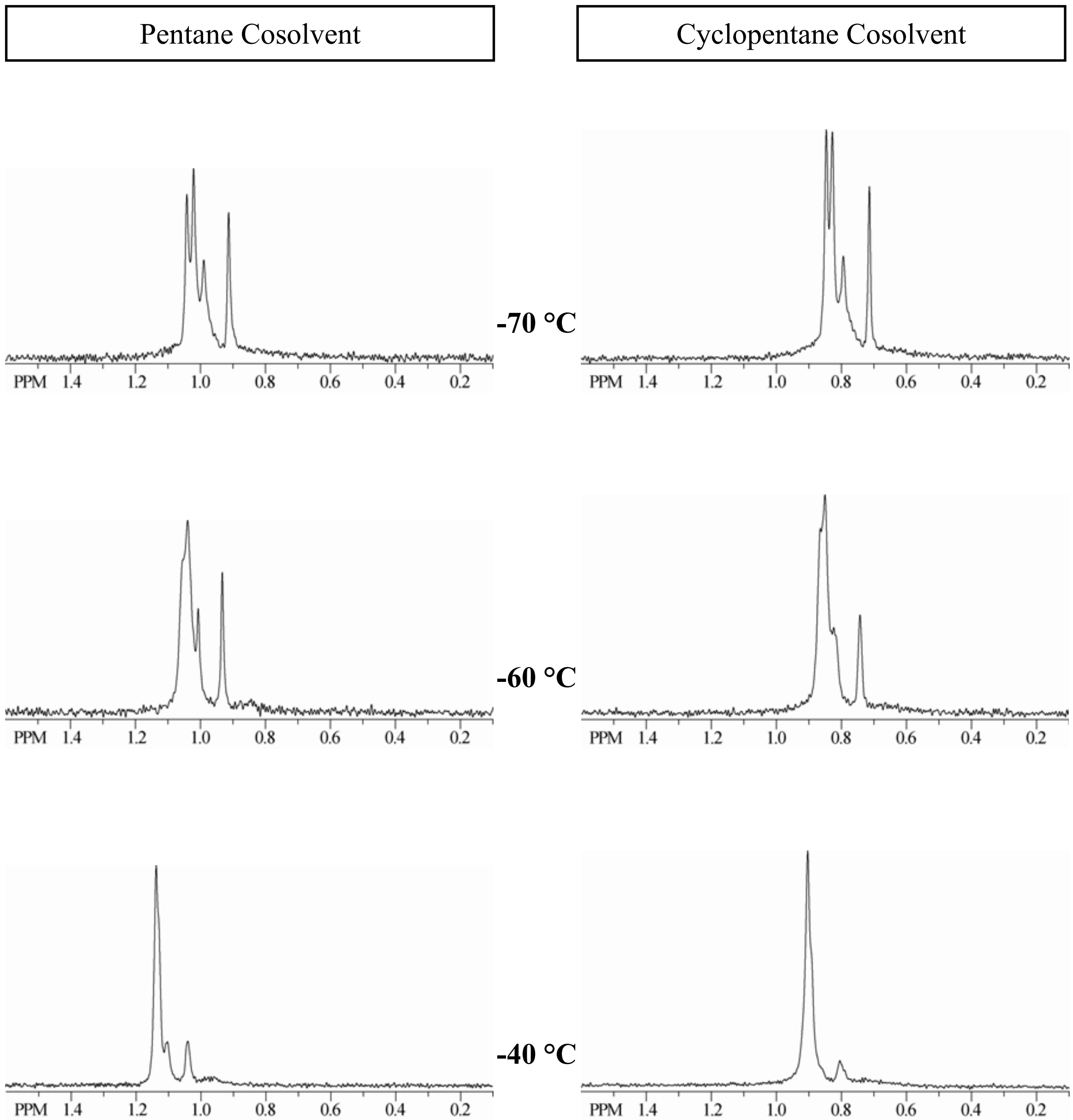
VI.B. ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** (mole fraction of **7**=0.7) at various temperatures. All samples are 0.10 M total enolate concentration and 9.0 M THF/toluene.



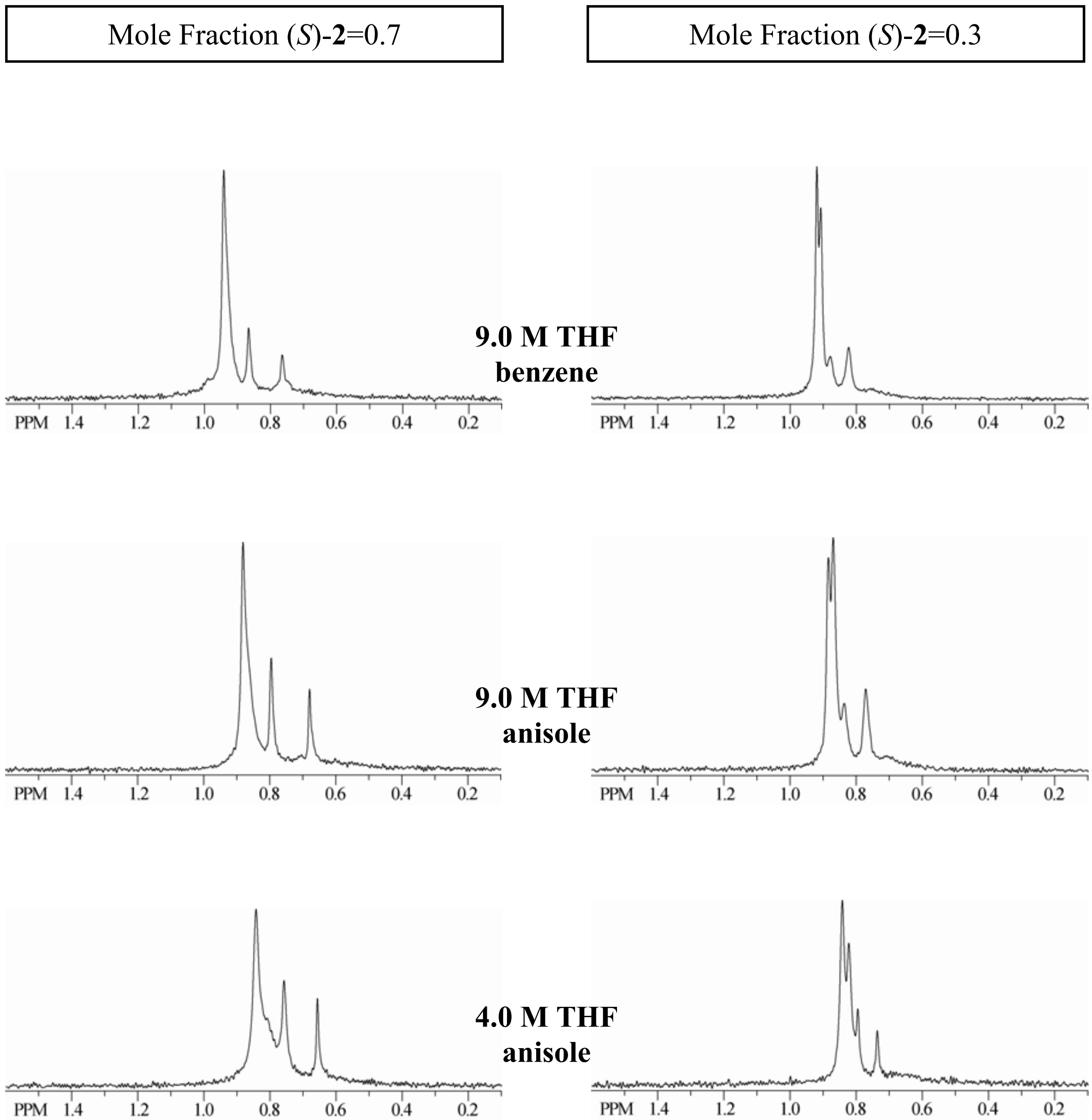
VI.C. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** at various mole fractions in 9.0 M THF/toluene at -40 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$ (▼) $\mathbf{R}_5\mathbf{S'}_1$ (■) $\mathbf{R}_4\mathbf{S'}_2$+$\mathbf{R}_2\mathbf{S'}_4$ (●) $\mathbf{R}_3\mathbf{S'}_3$ (▽) $\mathbf{R}_1\mathbf{S'}_5$ (◇) $\mathbf{S'}_6$ such that **S'** = [^{6}Li](*S*)-**7** and **R** = [^{6}Li](*R*)-**5**.



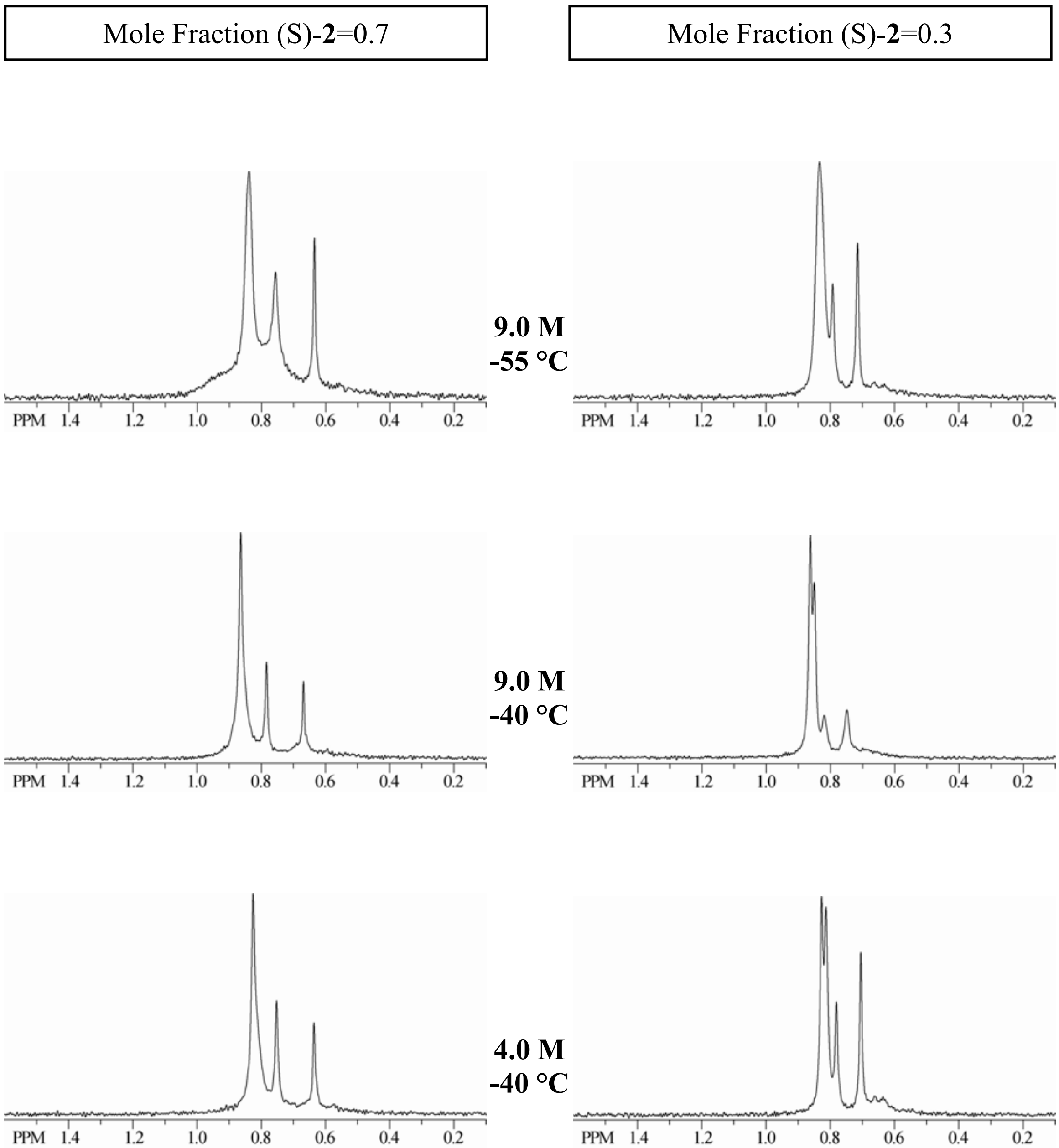
VI.C. (cont.) ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** at various mole fractions in 9.0 M THF/toluene at -40 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$ (▼) $\mathbf{R}_5\mathbf{S'}_1$ (■) $\mathbf{R}_4\mathbf{S'}_2$+$\mathbf{R}_2\mathbf{S'}_4$ (●) $\mathbf{R}_3\mathbf{S'}_3$ (▽) $\mathbf{R}_1\mathbf{S'}_5$ (◇) $\mathbf{S'}_6$ such that **S'** = [^{6}Li](*S*)-**7** and **R** = [^{6}Li](*R*)-**5**.



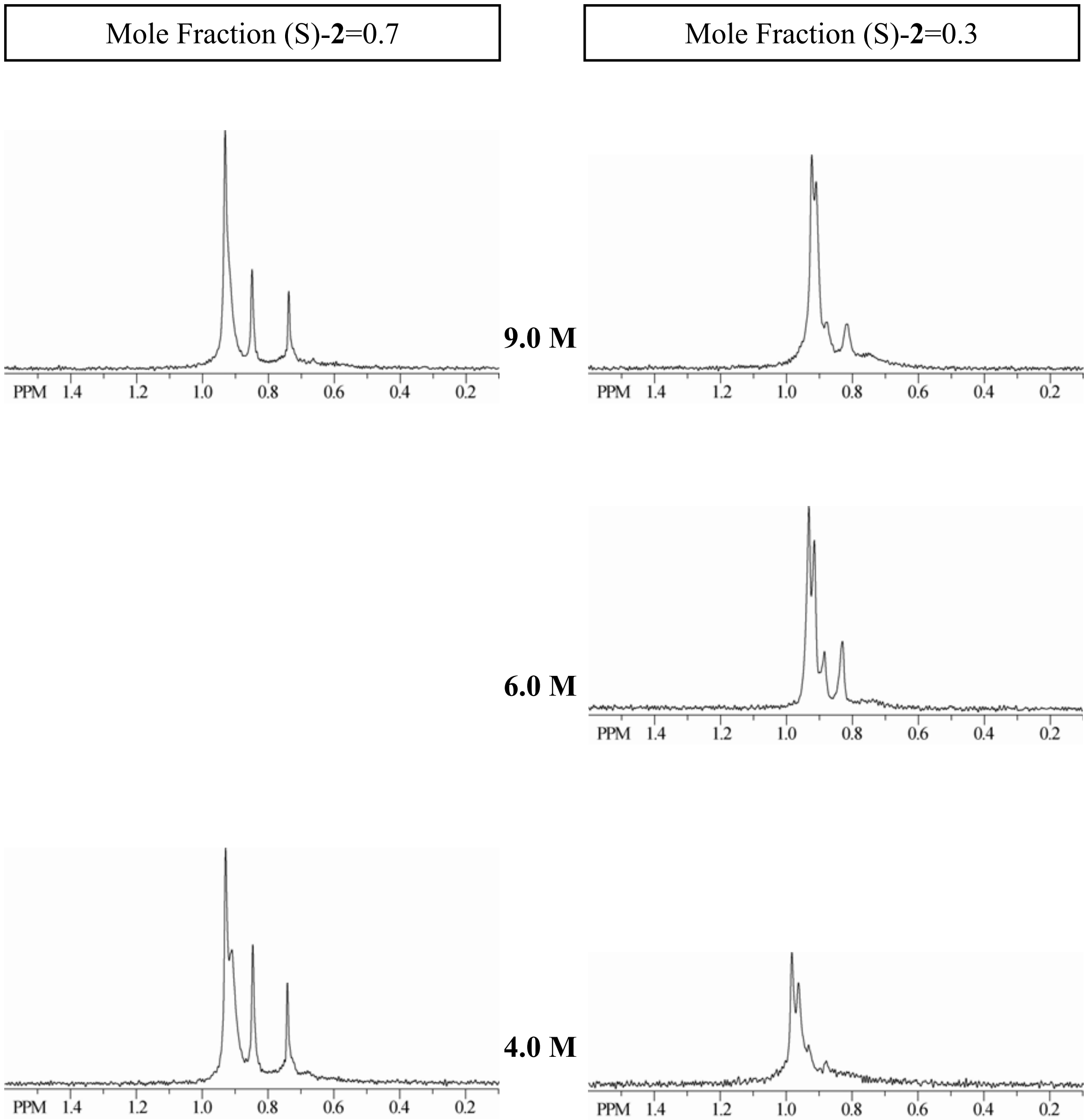
VI.D. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** (mole fraction of **7**=0.3) in non-aromatic cosolvents at various temperatures. All samples are 0.10 M total enolate concentration and 6.0 M THF.



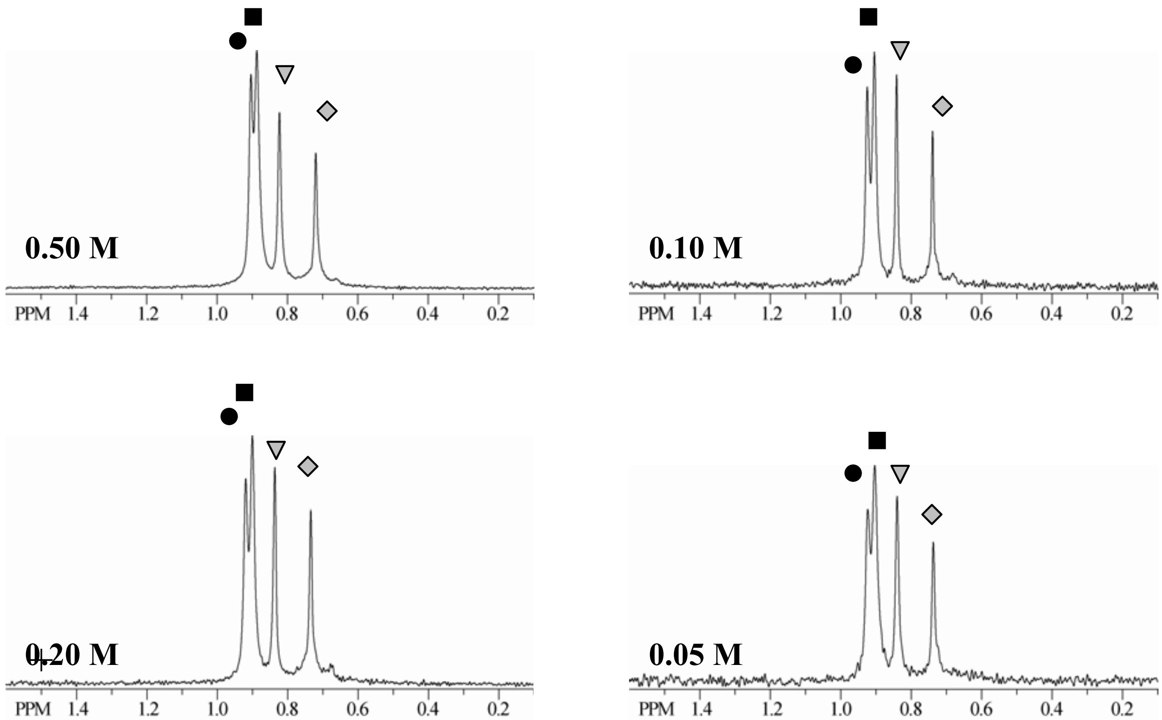
VI.E. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** with benzene or anisole as a co-solvent in various THF concentrations. All samples are 0.10 M in total enolate concentration and were recorded at -40 ºC.

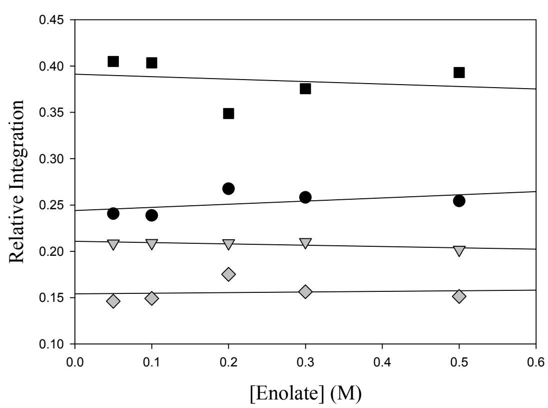


VI.F. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** with *tert*-butylbenzene as a co-solvent at various THF concentrations. All samples are 0.10 M total enolate concentration.



VI.G. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** with toluene as a co-solvent at various THF concentrations. All samples are 0.10 M total enolate concentration and were recorded at -40 ºC.

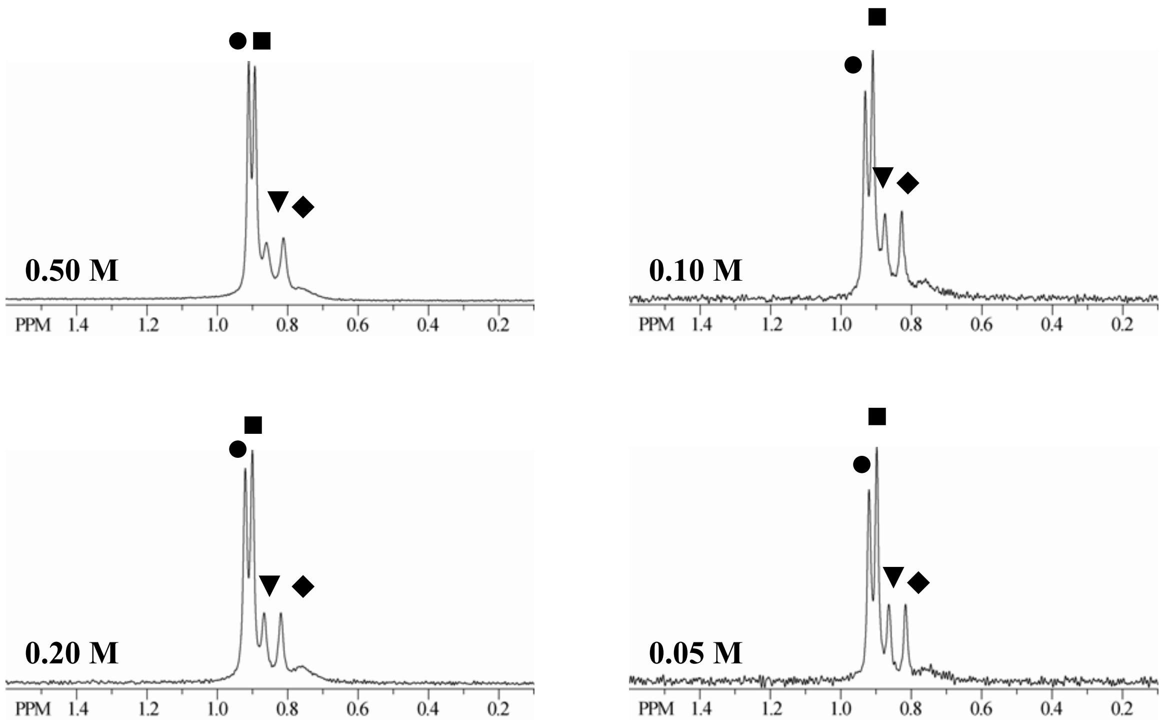


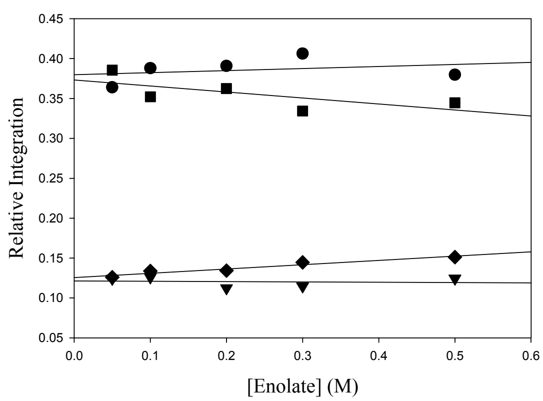


[enolate] (M)	(●)	(■)	(▽)	(◇)
0.05	0.24	0.40	0.21	0.15
0.10	0.24	0.40	0.21	0.15
0.20	0.27	0.35	0.21	0.18
0.30	0.26	0.38	0.21	0.16
0.50	0.25	0.39	0.20	0.15

Relative Integrations

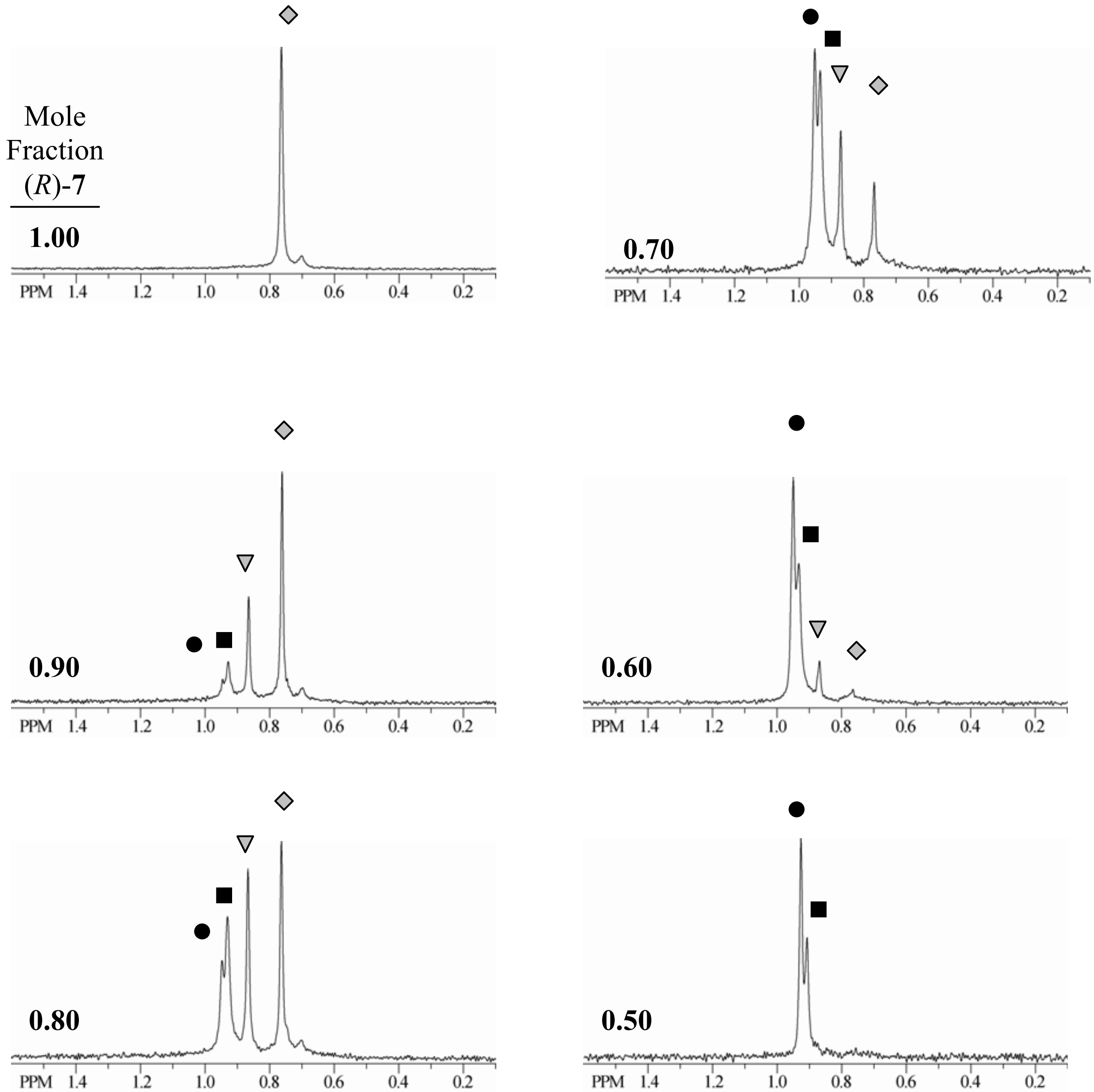
VI.H. Variation of enolate concentration for a mixture of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** (mole fraction of **7**=0.70). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** (mole fraction of **7**=0.70) at various enolate concentrations. All samples are 4.0 M THF/toluene and were recorded at -30 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R_6}$ (▼) $\mathbf{R_5S'_1}$ (■) $\mathbf{R_4S'_2}$+$\mathbf{R_2S'_4}$ (●) $\mathbf{R_3S'_3}$ (▽) $\mathbf{R_1S'_5}$ (◇) $\mathbf{S'_6}$ such that **S'** = [^{6}Li](*S*)-**7** and **R** = [^{6}Li](*R*)-**5**.



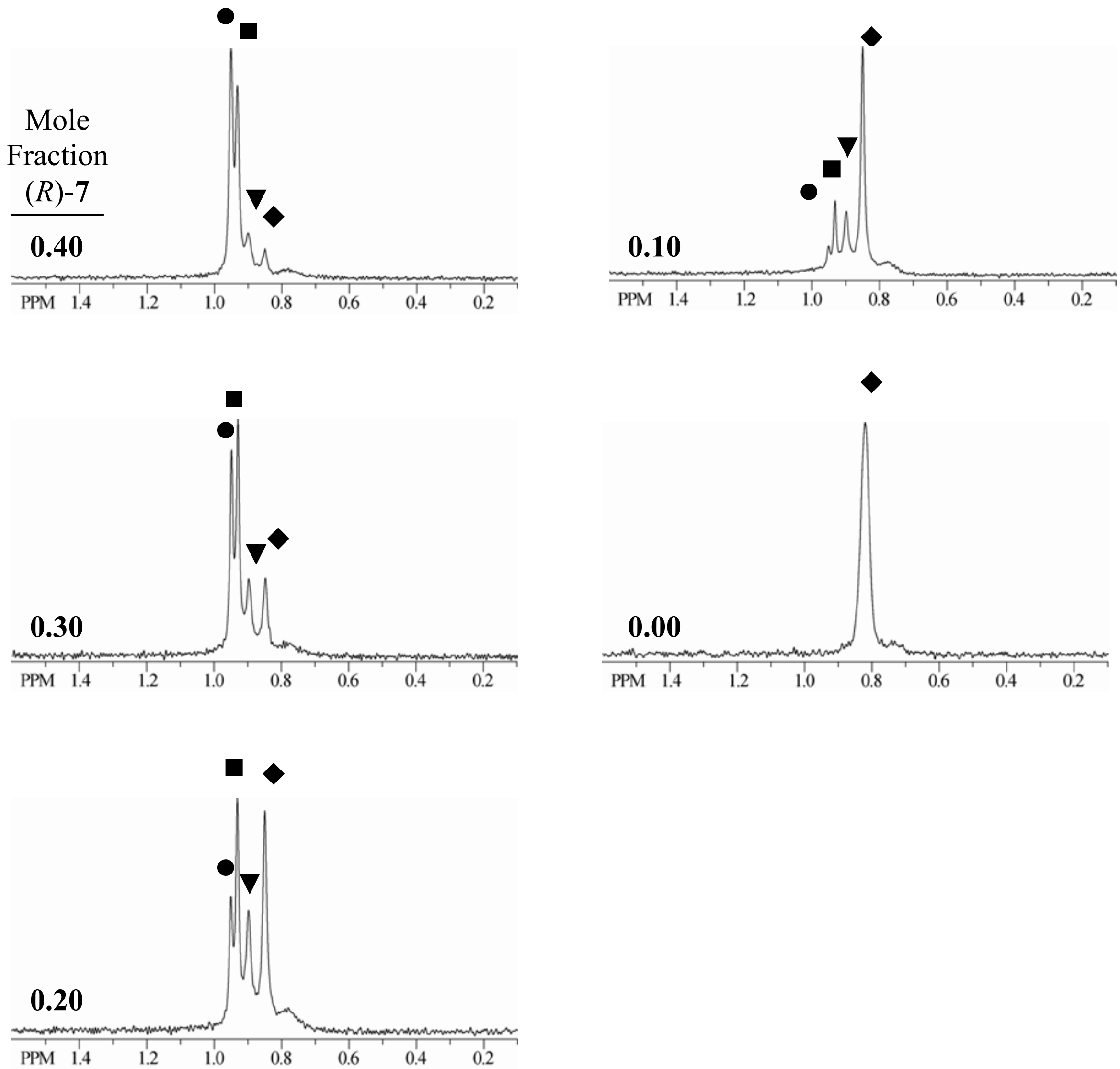


[enolate] (M)	Relative Integrations (●)	(■)	(▼)	(◆)
0.05	0.24	0.40	0.21	0.15
0.10	0.24	0.40	0.21	0.15
0.20	0.27	0.35	0.21	0.18
0.30	0.26	0.38	0.21	0.16
0.50	0.25	0.39	0.20	0.15

VI.I. Variation of enolate concentration for a mixture of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** (mole fraction of **7**=0.30). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** (mole fraction of **7**=0.30) at various enolate concentrations. All samples are 4.0 M THF/toluene and were recorded at -30 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R_6}$ (▼) $\mathbf{R_5S'_1}$ (■) $\mathbf{R_4S'_2{+}R_2S'_4}$ (●) $\mathbf{R_3S'_3}$ (▽) $\mathbf{R_1S'_5}$ (◇) $\mathbf{S'_6}$ such that **S'** = [^{6}Li](*S*)-**7** and **R** = [^{6}Li](*R*)-**5**.



VI.J. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** at various mole fractions in 4.0 M THF/toluene at -30 ºC. *S*amples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$ (▼) $\mathbf{R}_5\mathbf{S'}_1$ (■) $\mathbf{R}_4\mathbf{S'}_2$+$\mathbf{R}_2\mathbf{S'}_4$ (●) $\mathbf{R}_3\mathbf{S'}_3$ (▽) $\mathbf{R}_1\mathbf{S'}_5$ (◇) $\mathbf{S'}_6$ such that **S'** = [^{6}Li](*R*)-**7** and **R** = [^{6}Li](*S*)-**5**.



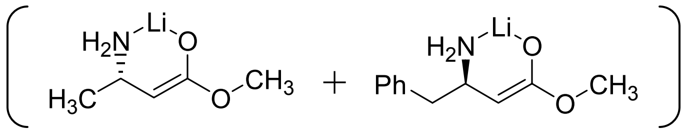
VI.J. (cont.) ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*S*)-**7** and [^{6}Li](*R*)-**5** at various mole fractions in 4.0 M THF/toluene at -30 ºC. Samples are 0.10 M in total enolate concentration. **(◆) R**$_6$ **(▼) R**$_5$**S'**$_1$ **(■) R**$_4$**S'**$_2$+**R**$_2$**S'**$_4$ **(●) R**$_3$**S'**$_3$ **(▽) R**$_1$**S'**$_5$ **(◇) S'**$_6$ such that **S'** = [^{6}Li](*R*)-**7** and **R** = [^{6}Li](*S*)-**5**.

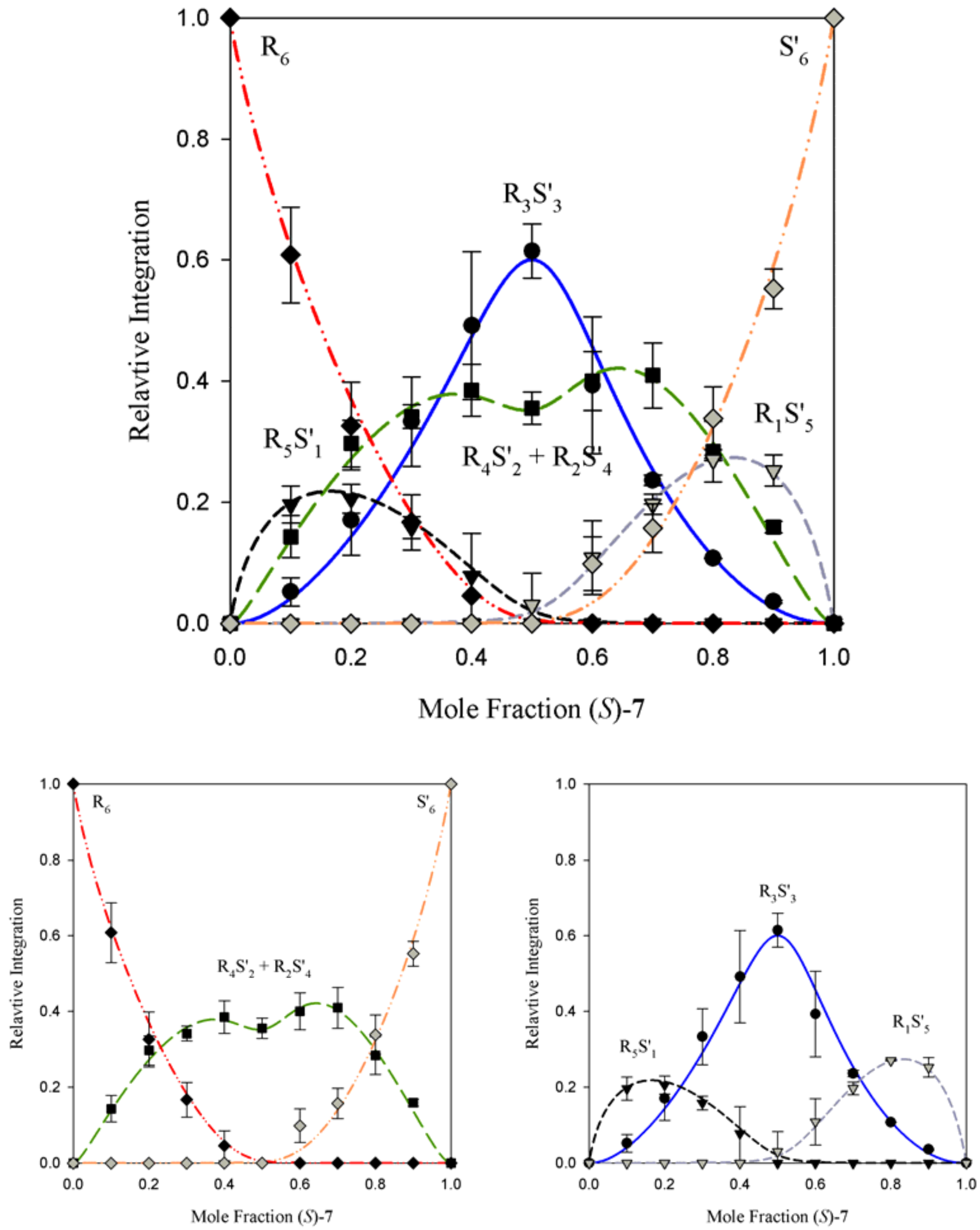
VI.K. Table of the relative integrations for the spectra in **VI.J**[a]

Mole Frac. (*S*)-**7**	**S'**$_6$ (◇)	**R**$_1$**S'**$_5$ (▽)	**R**$_2$**S'**$_4$ (▣)	**R**$_3$**S'**$_3$ (●)
	Relative Integrations			
1.00	1.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
0.90	0.55±0.03	0.25±0.03	0.159±0.010	0.036±0.002
0.80	0.34±0.05	0.270±0.002	0.28±0.05	0.1075±0.0004
0.70	0.16±0.04	0.20±0.02	0.41±0.05	0.236±0.008
0.60	0.10±0.04	0.11±0.06	0.40±0.05	0.39±0.11
0.50	0.00±0.00	0.03±0.05	0.36±0.03	0.61±0.04
0.40	0.00±0.00	0.00±0.00	0.39±0.04	0.49±0.12
0.30	0.00±0.00	0.00±0.00	0.34±0.02	0.33±0.07
0.20	0.00±0.00	0.00±0.00	0.30±0.04	0.17±0.06
0.10	0.00±0.00	0.00±0.00	0.14±0.04	0.05±0.02
0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00

Mole Frac. (*S*)-**7**	**R**$_4$**S'**$_2$ (■)	**R**$_5$**S'**$_1$ (▼)	**R**$_6$ (◆)
	Relative Integrations		
1.00	0.00±0.00	0.00±0.00	0.00±0.00
0.90	0.036±0.002	0.00±0.00	0.00±0.00
0.80	0.1075±0.0005	0.00±0.00	0.00±0.00
0.70	0.236±0.009	0.00±0.00	0.00±0.00
0.60	0.39±0.11	0.00±0.00	0.00±0.00
0.50	0.61±0.04	0.00±0.00	0.00±0.00
0.40	0.49±0.12	0.08±0.07	0.05±0.04
0.30	0.33±0.07	0.16±0.02	0.17±0.05
0.20	0.17±0.06	0.21±0.02	0.33±0.07
0.10	0.05±0.02	0.20±0.03	0.61±0.08
0.00	0.00±0.00	0.00±0.00	1.00±0.00

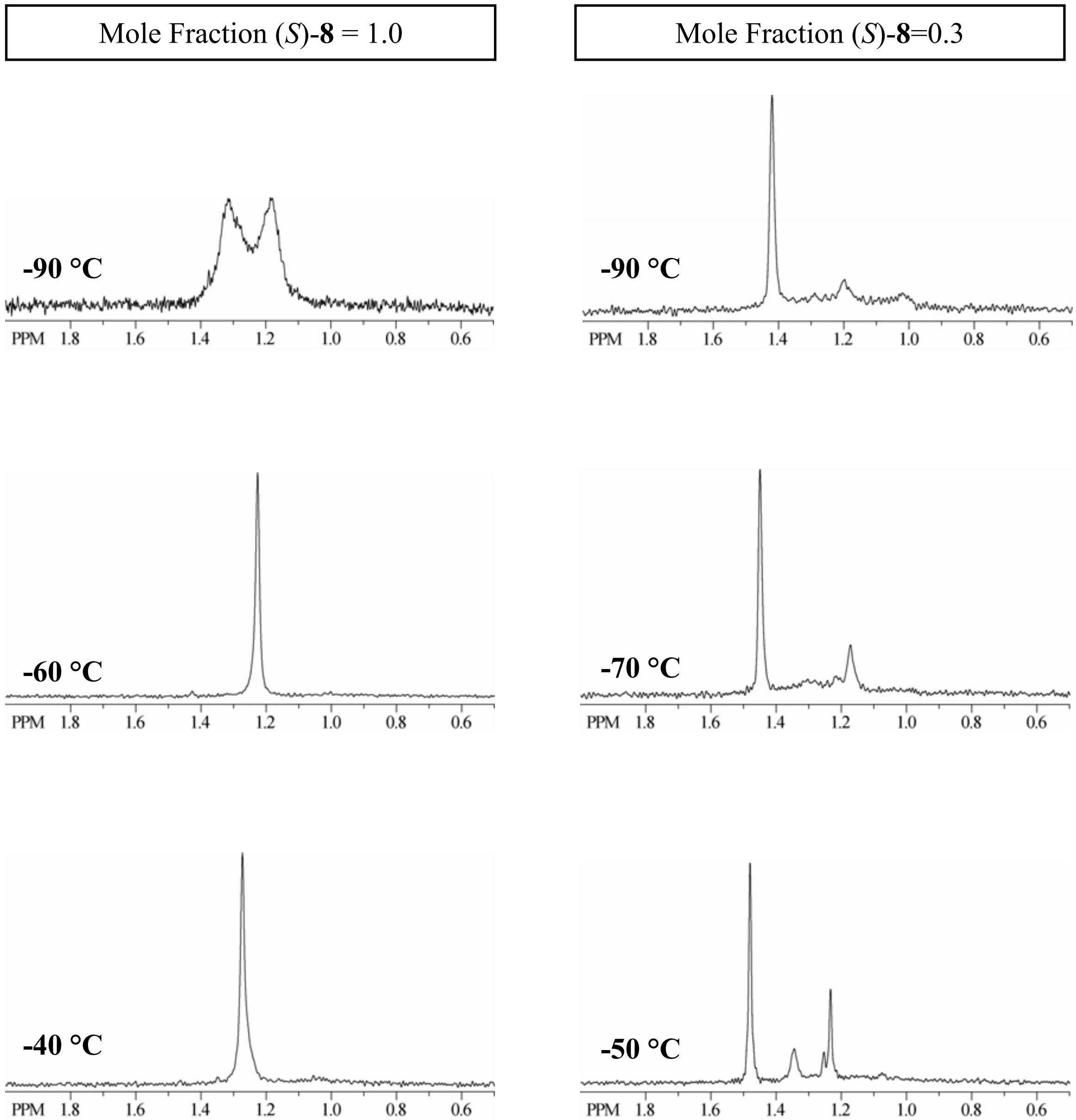
[a] **(◆) R**$_6$ **(▼) R**$_5$**S'**$_1$ **(■) R**$_4$**S'**$_2$+**R**$_2$**S'**$_4$ **(●) R**$_3$**S'**$_3$ (▽) **R**$_1$**S'**$_5$ (◇) **S'**$_6$ such that **S'** = [^{6}Li](*S*)-**7** and **R** = [^{6}Li](*R*)-**5**.



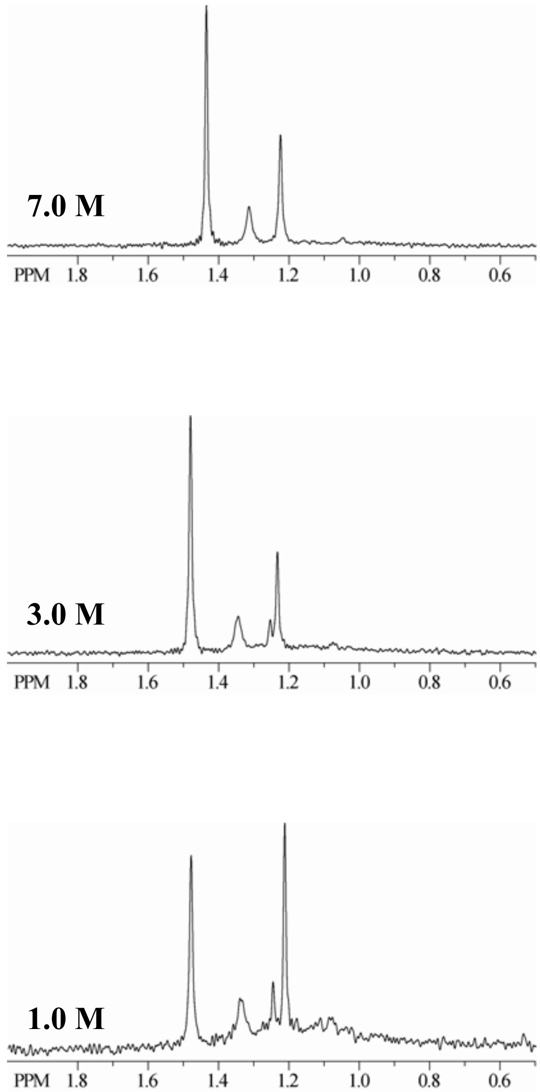


VI.L. Job Plot of [6Li](*S*)-**7**/[6Li](*R*)-**5** (4.0 M THF/toluene; -30 ºC) hexamers. The relative integrations are plotted as a function of the mole fraction of [6Li](*S*)-**7**. The relative integrations of the $\mathbf{R_2S'_4}$ and $\mathbf{R_4S'_2}$ aggregates are summed due to poor resolution of their resoncances. (◆) $\mathbf{R_6}$ (▼) $\mathbf{R_5S'_1}$ (■) $\mathbf{R_4S'_2{+}R_2S'_4}$ (●) $\mathbf{R_3S'_3}$ (∇) $\mathbf{R_1S'_5}$ (◇) $\mathbf{S'_6}$ such that **S'** = [6Li](*S*)-**7** and **R** = [6Li](*R*)-**5**. The curves result from a parametric fit, affording ϕ_0=1.2; ϕ_1=0.85; ϕ_2=3.0; ϕ_3=8.8; ϕ_4=3.9; ϕ_5=1.11; ϕ_6=1.0.

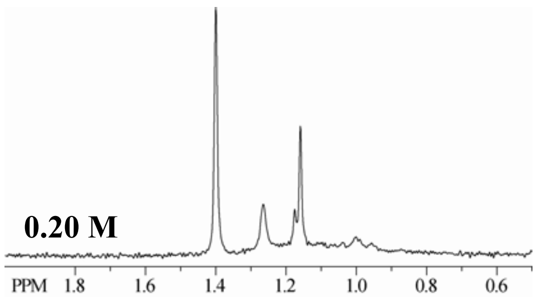
VII. (*S*)-β-Phenylglycine/(*R*)-β-Phenylglycine

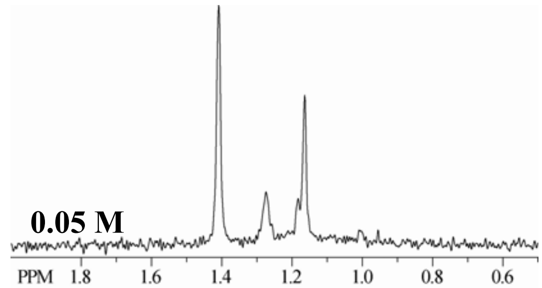


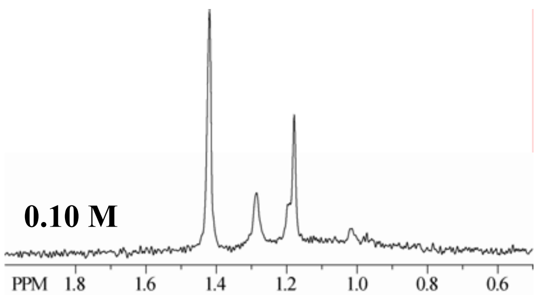
VII.A. ^{6}Li NMR spectra of [^{6}Li](*R*)-**8** (58.8 MHz) and a mixture of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**8** (mole fraction of **R**=0.70) (73.6 MHz) at various temperatures. The [^{6}Li](*R*)-**8** sample is 9.0 M THF/toluene. The mixture of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**8** sample is 3.0 M THF/toluene. Both samples are 0.10 M total enolate concentration.

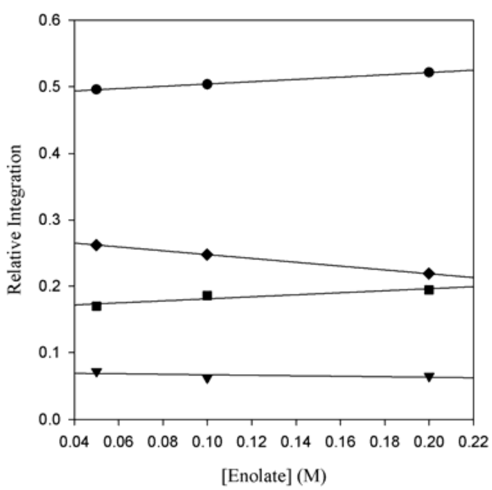


VII.B. ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**8** (mole fraction **S**=0.30) at various THF/toluene concentrations. All samples are 0.10 M total enolate and were recorded at -50 ºC.



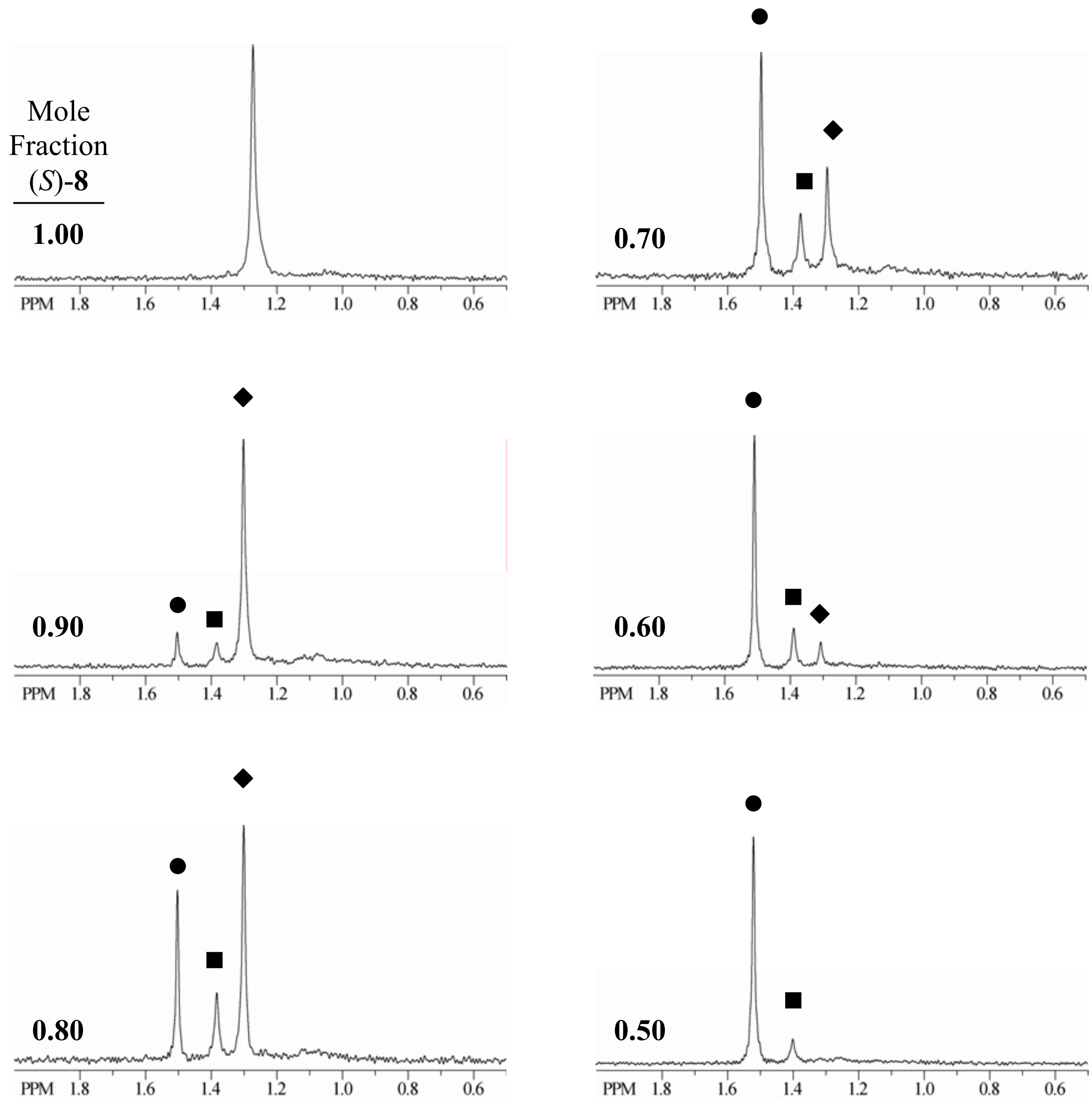




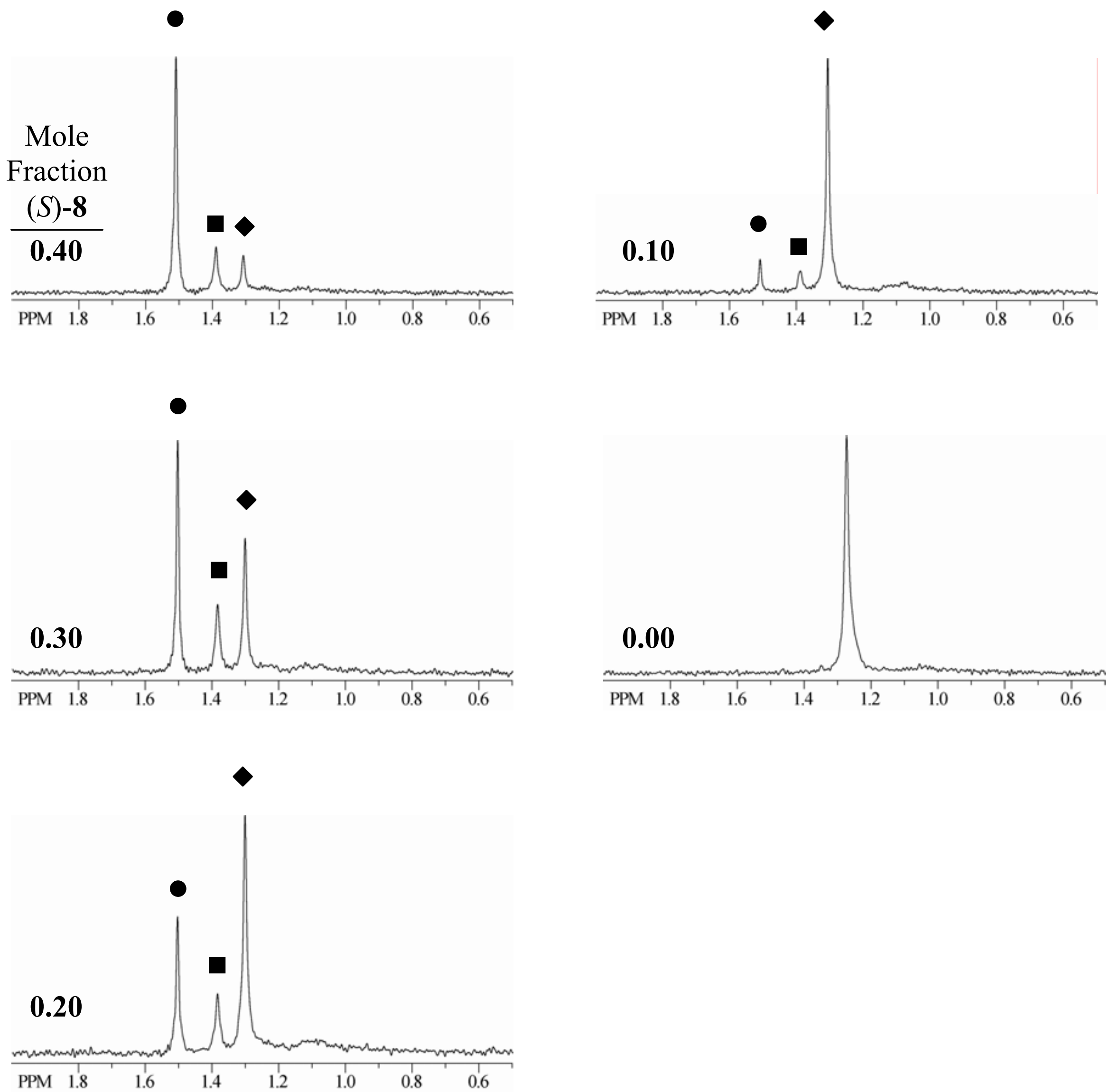


[enolate] (M)	Relative Integrations (●)	(■)	(▼)	(◆)
0.05	0.50	0.17	0.07	0.26
0.10	0.50	0.19	0.06	0.25
0.20	0.52	0.19	0.07	0.22

VII.C. Variation of enolate concentration for a mixture of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**8** (mole fraction of **R**=0.70). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**8** (mole fraction of **R**=0.70) at various enolate concentrations. All samples are 3.0 M THF/toluene and were recorded at -50 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (●) $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [^{6}Li](*R*)-**8** and **S** = [^{6}Li](*S*)-**8.**



VII.D. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**8** at various mole fractions in 9.0 M THF/toluene at -40 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$+$\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (●) $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [^{6}Li](*R*)-**8** and **S** = [^{6}Li](*S*)-**8**.



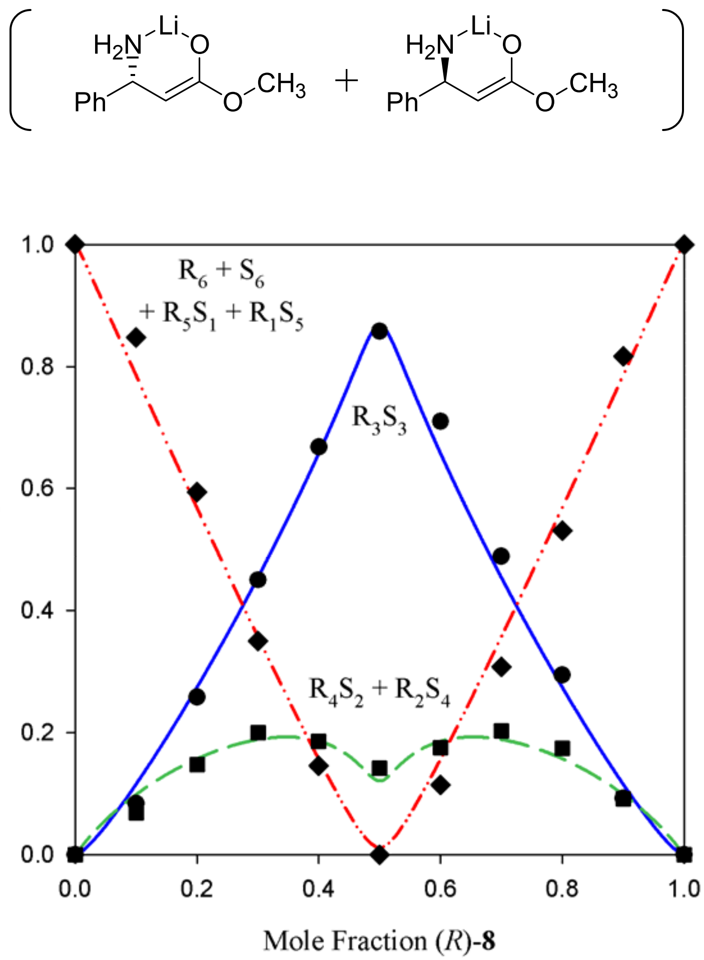
VII.D. (cont.) ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**8** at various mole fractions in 9.0 M THF/toluene at -40 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$+$\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (●) $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [^{6}Li](*R*)-**8** and **S** = [^{6}Li](*S*)-**8**.

VII.E. Table of the relative integrations for the spectra in **VII.D**.[a]

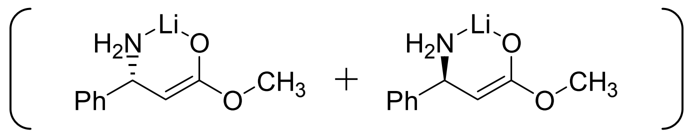
Mole Frac. (*S*)-**8**	Relative Integrations: $\mathbf{R}_3\mathbf{S}_3$ (●)	$\mathbf{R}_4\mathbf{S}_2+\mathbf{R}_2\mathbf{S}_4$ (■)	$\mathbf{R}_6+\mathbf{S}_6+\mathbf{R}_5\mathbf{S}_1+\mathbf{R}_1\mathbf{S}_5$[b] (◆)
1.00	0.00	0.00	1.00
0.90	0.09	0.09	0.82
0.80	0.29	0.17	0.53
0.70	0.49	0.20	0.31
0.60	0.71	0.18	0.11
0.50	0.86	0.14	0.00
0.40	0.67	0.19	0.15
0.30	0.45	0.20	0.35
0.20	0.26	0.15	0.59
0.10	0.08	0.07	0.85
0.00	0.00	0.00	1.00

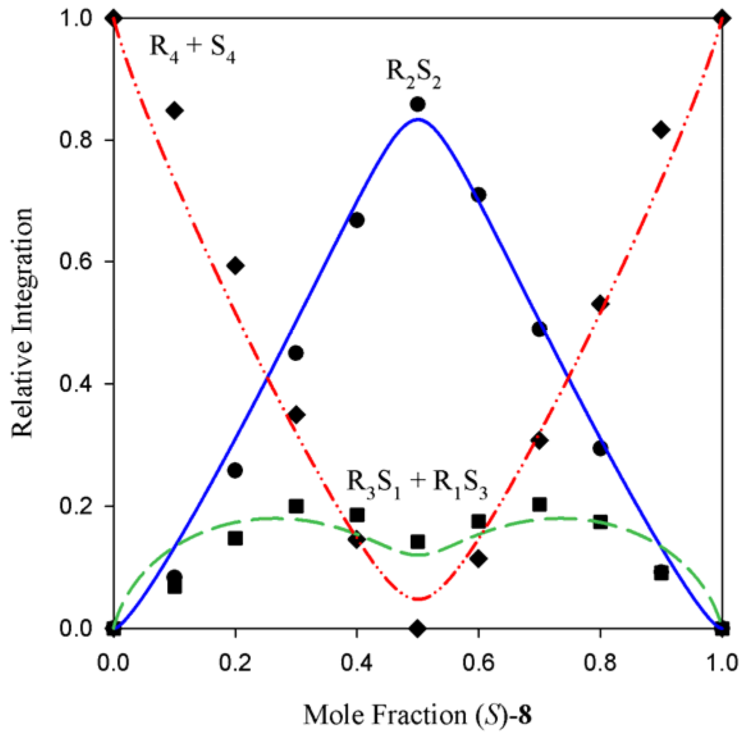
[a] (◆) $\mathbf{R}_6+\mathbf{S}_6+\mathbf{R}_5\mathbf{S}_1+\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2\mathbf{S}_4+\mathbf{R}_4\mathbf{S}_2$ (●) $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [^{6}Li](*R*)-**8** and **S** = [^{6}Li](*S*)-**8**.

[b] The $\mathbf{R}_6$, $\mathbf{S}_6$, $\mathbf{R}_5\mathbf{S}_1$, and $\mathbf{R}_1\mathbf{S}_5$ aggregates are spectroscopically indistinguishable.

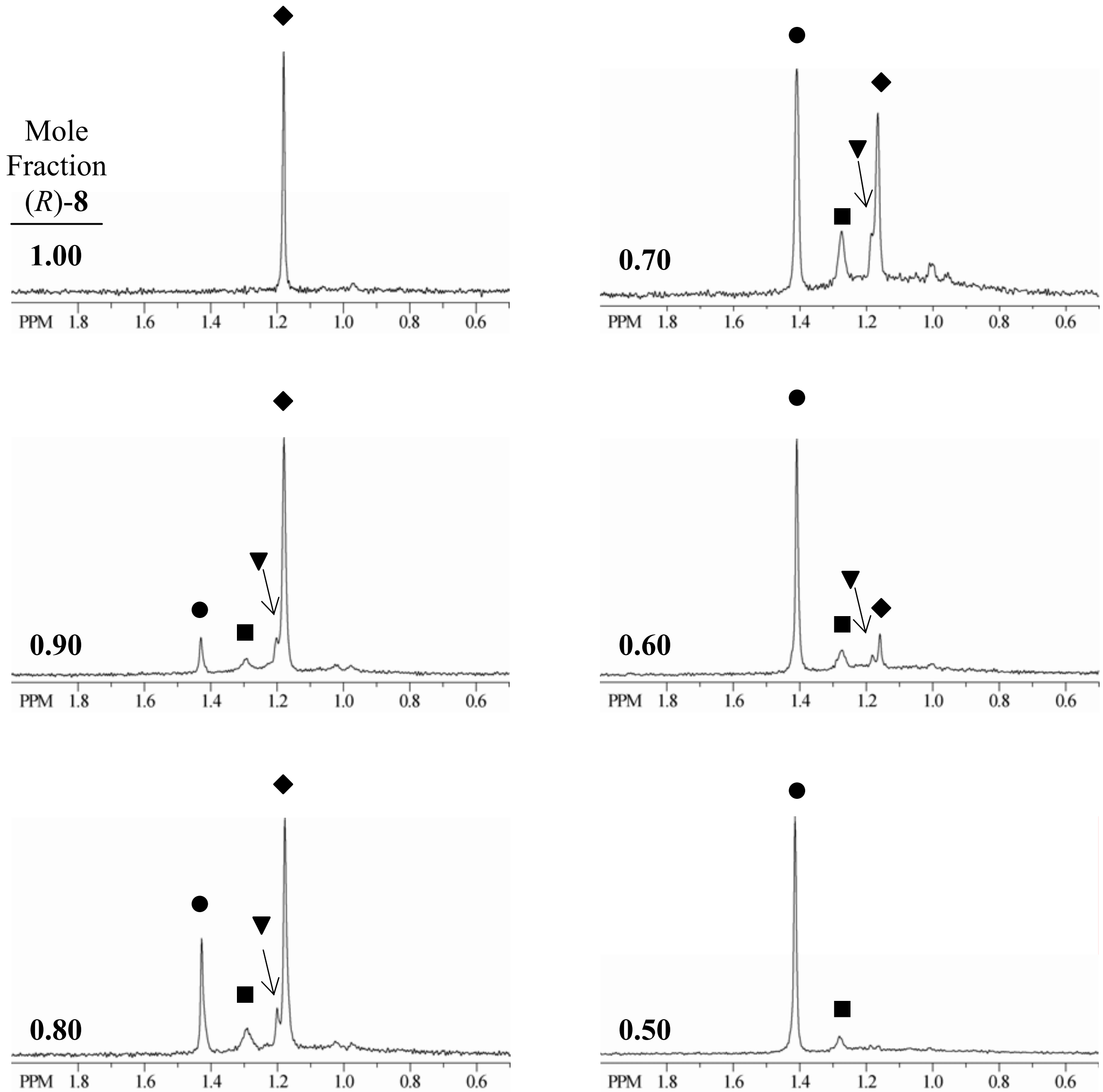


VII.F. Job Plot of [6Li](*R*)-**8**/[6Li](*S*)-**8** (9.0 M THF/toluene; -40 ºC) hexamers. The relative integrations are plotted as a function of the mole fraction of [6Li](*R*)-**8**. The $\mathbf{R}_6$, $\mathbf{S}_6$, $\mathbf{R}_5\mathbf{S}_1$, and $\mathbf{R}_1\mathbf{S}_5$ aggregates are assigned as spectroscopically indistinguishable. (◆) $\mathbf{R}_6+\mathbf{S}_6+\mathbf{R}_5\mathbf{S}_1+\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2\mathbf{S}_4+\mathbf{R}_4\mathbf{S}_2$ (●) $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [6Li](*R*)-**8** and **S** = [6Li](*S*)-**8**. The curves result from a parametric fit (p. Sxx), affording ϕ_0=0.70; ϕ_1=0.11; ϕ_2=0.93; ϕ_2=10

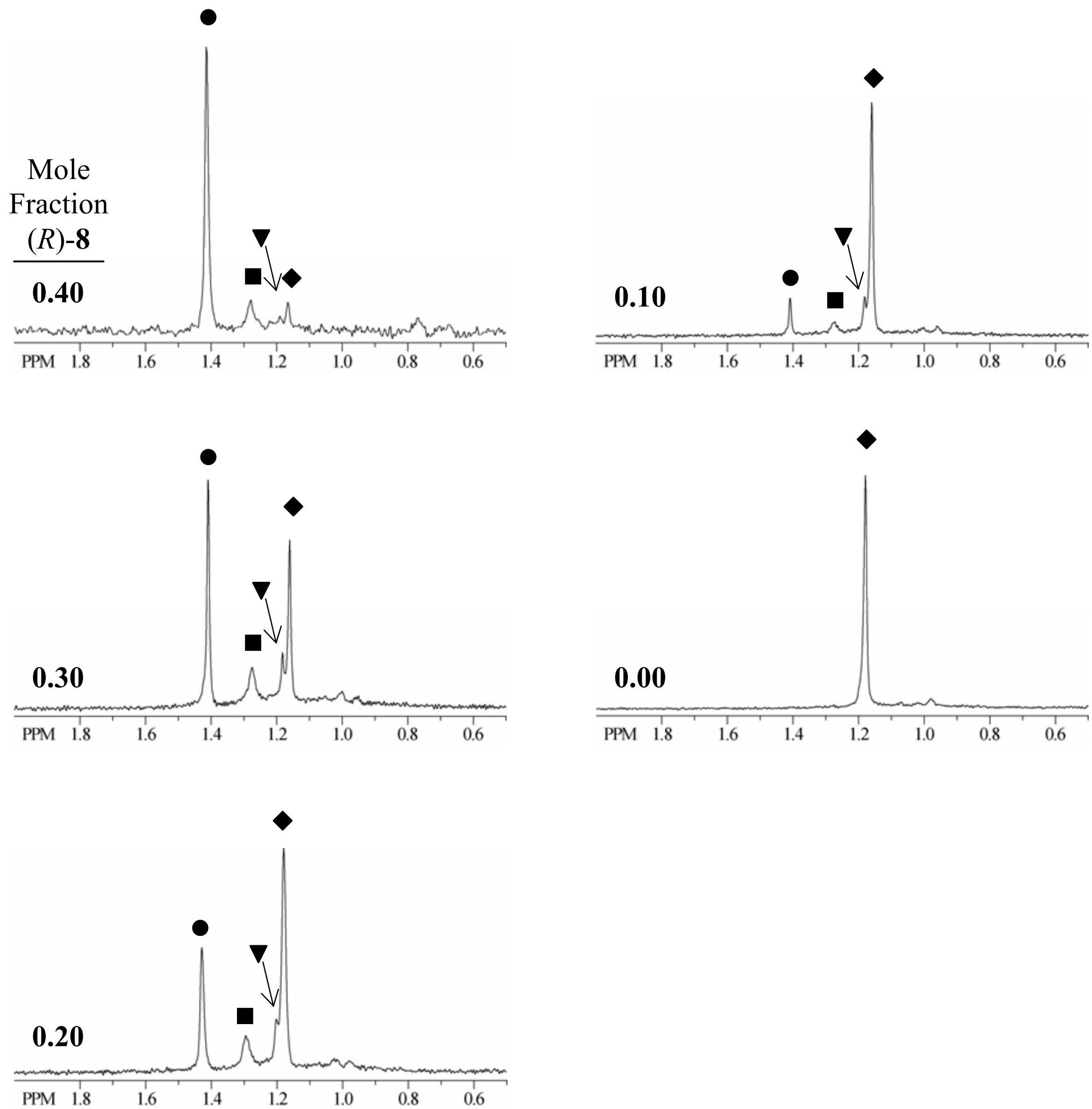




VII.G. Job Plot of [^{6}Li](*R*)-**8**/[^{6}Li](*S*)-**8** (9.0 M THF/toluene; -40 ºC) fit to tetramer model. The relative integrations are plotted as a function of the mole fraction of (*R*)-**8**. (◆) $\mathbf{R_4}$+$\mathbf{S_4}$ (■) $\mathbf{R_3S_1}$+$\mathbf{R_1S_3}$ (●) $\mathbf{R_2S_2}$ such that **R** = [^{6}Li](*R*)-**8** and **S** = [^{6}Li](*S*)-**8**. The curves result from a parametric fit, affording ϕ_0=1; ϕ_1=0.63; ϕ_2=5.86.



VII.H. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**8** and [^{6}Li](*R*)-**8** at various mole fractions in 3.0 M THF/toluene at -50 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (●) $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [^{6}Li](*R*)-**8** and **S** = [^{6}Li](*S*)-**8.**

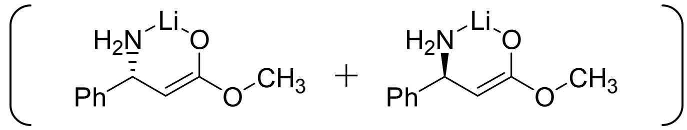


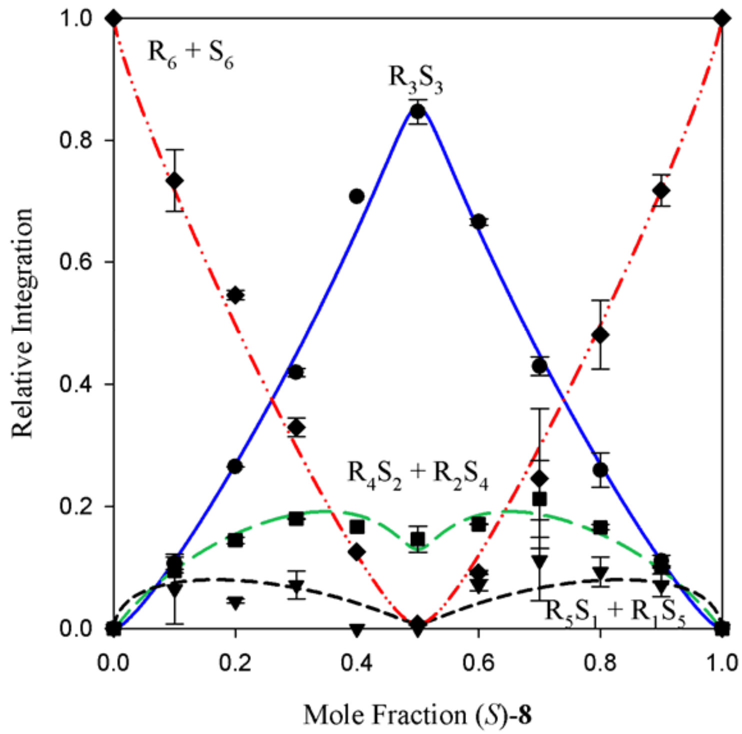
VII.H. (cont.) ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**8** and [^{6}Li](*R*)-**8** at various mole fractions in 3.0 M THF/toluene at -50 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (●) $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [^{6}Li](*R*)-**8** and **S** = [^{6}Li](*S*)-**8.**

VII.I. Table of the relative integrations for the spectra in **VII.H.**[a]

Mole Frac. (*S*)-**8**	Relative Integrations: $\mathbf{R}_3\mathbf{S}_3$ (●)	$\mathbf{R}_4\mathbf{S}_2$+$\mathbf{R}_2\mathbf{S}_4$ (■)	$\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (▼)	$\mathbf{R}_6$+$\mathbf{S}_6$ (◆)
1.00	0.00±0.00	0.00±0.00	0.00±0.00	1.00±0.00
0.90	0.11±0.01	0.100±0.001	0.07±0.02	0.72±0.03
0.80	0.26±0.03	0.166±0.004	0.09±0.02	0.48±0.06
0.70	0.43±0.01	0.21±0.06	0.11±0.07	0.25±0.11
0.60	0.67±0.01	0.171±0.001	0.07±0.01	0.092±0.003
0.50	0.85±0.02	0.15±0.02	0.00±0.00	0.007±0.002
0.40	0.71±0.00	0.17±0.00	0.00±0.00	0.13±0.00
0.30	0.42±0.01	0.180±0.001	0.07±0.02	0.33±0.02
0.20	0.265±0.001	0.144±0.005	0.045±0.003	0.55±0.01
0.10	0.11±0.01	0.095±0.003	0.06±0.06	0.73±0.05
0.00	0.00±0.00	0.00±0.00	0.00±0.00	1.00±0.00

[a] (◆) $\mathbf{R}_6$+$\mathbf{S}_6$ (▼) $\mathbf{R}_5\mathbf{S}_1$+$\mathbf{R}_1\mathbf{S}_5$ (■) $\mathbf{R}_2\mathbf{S}_4$+$\mathbf{R}_4\mathbf{S}_2$ (●) $\mathbf{R}_3\mathbf{S}_3$ such that **R** = [^{6}Li](*R*)-**8** and **S** = [^{6}Li](*S*)-**8.**

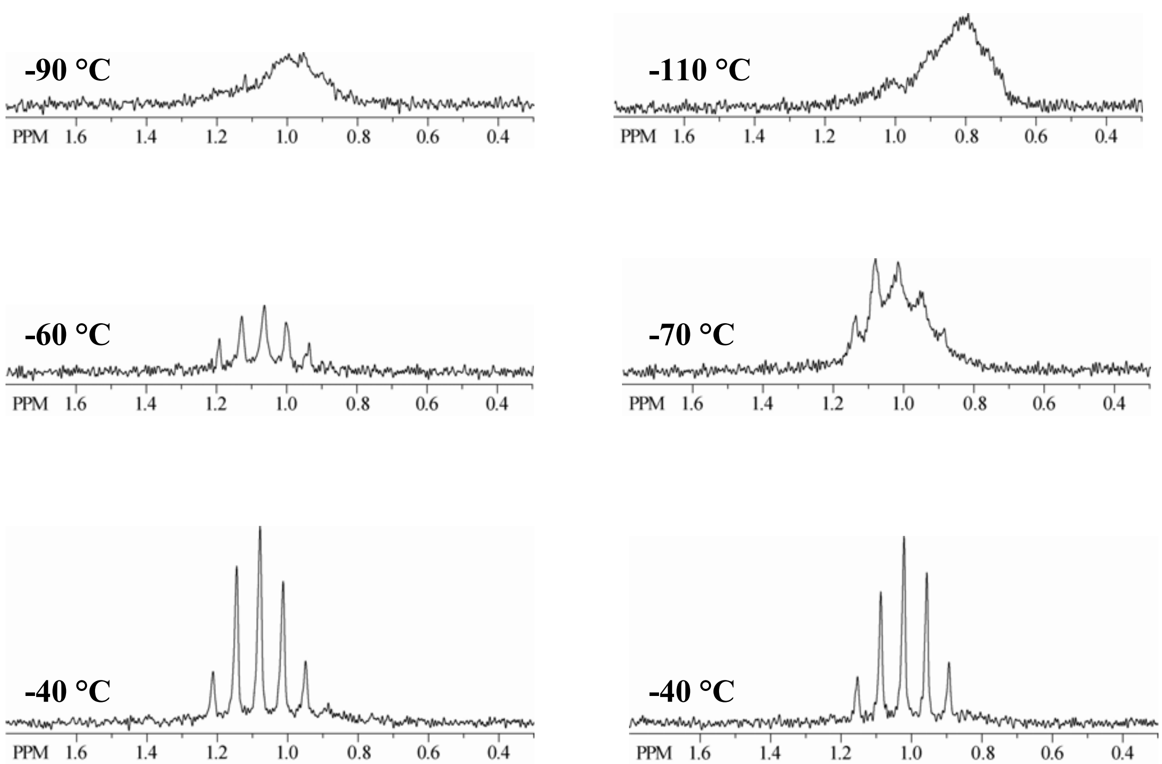




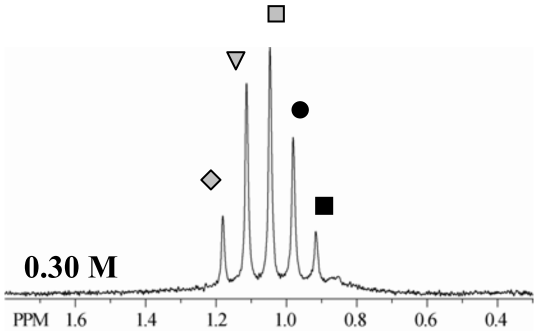
VII.J. Job Plot of [^{6}Li](*R*)-**8**/[^{6}Li](*S*)-**8** (3.0 M THF/toluene; -50 ºC) hexamers. The relative integrations are plotted as a function of the mole fraction of [^{6}Li](*R*)-**8**. (◆) $\mathbf{R_6}$+$\mathbf{S_6}$ (▼) $\mathbf{R_5S_1}$+$\mathbf{R_1S_5}$ (■) $\mathbf{R_4S_2}$+$\mathbf{R_2S_4}$ (●) $\mathbf{R_3S_3}$ such that **R** = [^{6}Li](*R*)-**8** and **S** = [^{6}Li](*S*)-**8**. The curves result from a parametric fit, affording ϕ_0=0.090; ϕ_1=0.018; ϕ_2=0.101; ϕ_3=1.

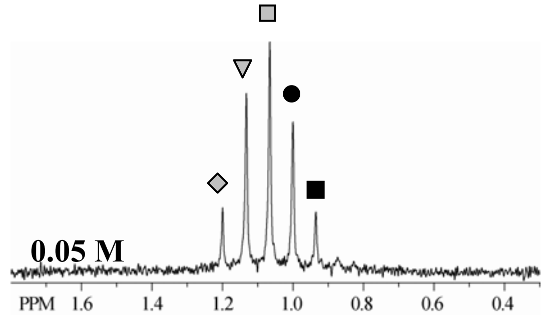
VIII. (*S*)-β-Phenylglycine and (*R*)-β-Alanine *Note this is R/R' mix

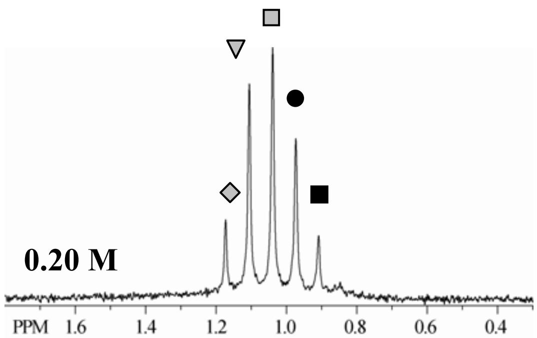
Mole Fraction (*R*)-**8**=0.7	Mole Fraction (*R*)-**8**=0.5

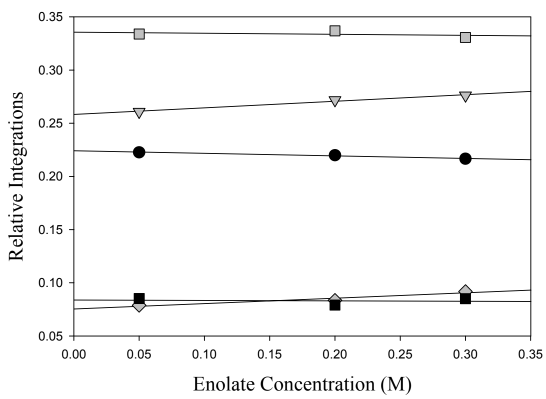


VIII.A. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**5** at various temperatures. All samples are 0.10 M total enolate concentration and 3.0 M THF/toluene.



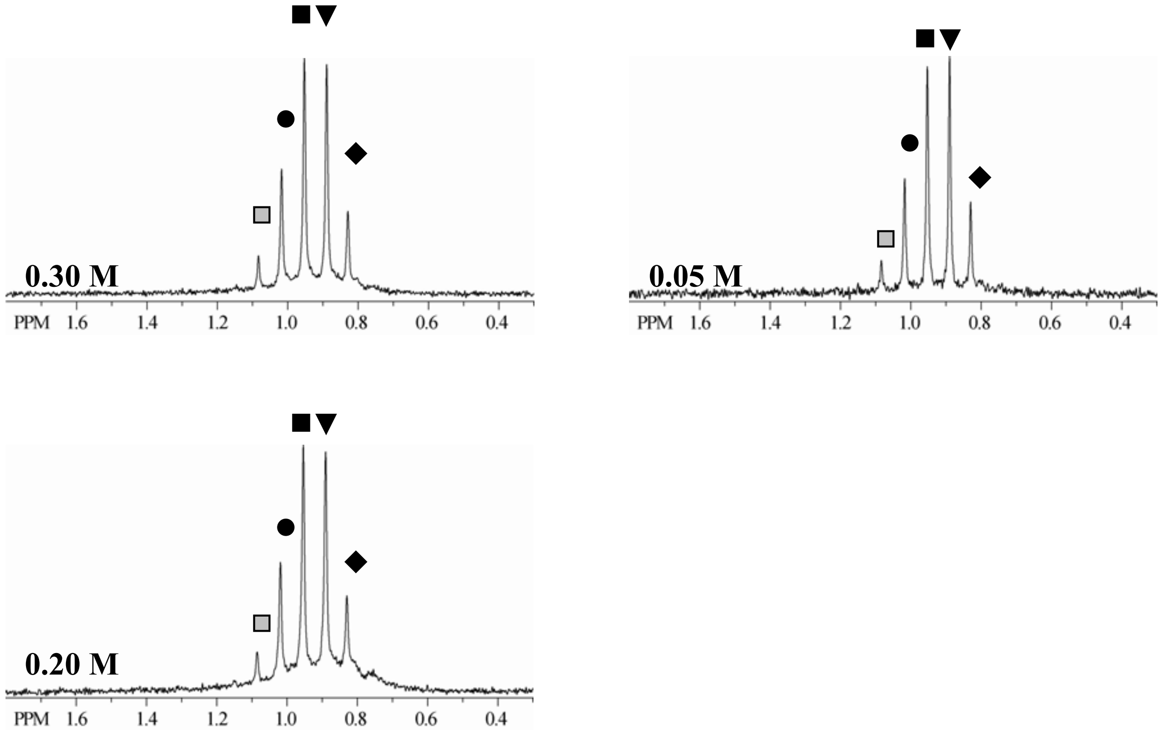


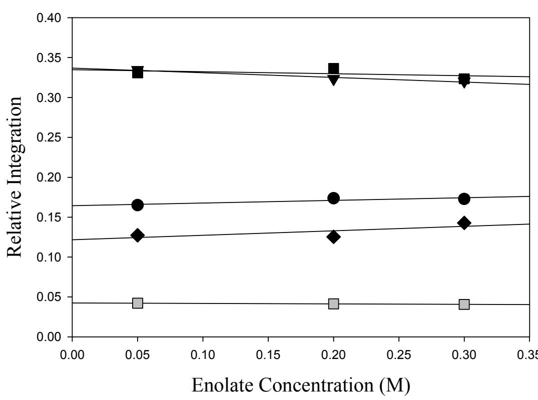




[enolate] (M)	Relative Integrations (◇)	(▽)	(□)	(●)	(■)
0.050	0.079	0.261	0.334	0.223	0.085
0.200	0.083	0.272	0.337	0.220	0.079
0.300	0.092	0.276	0.331	0.216	0.085

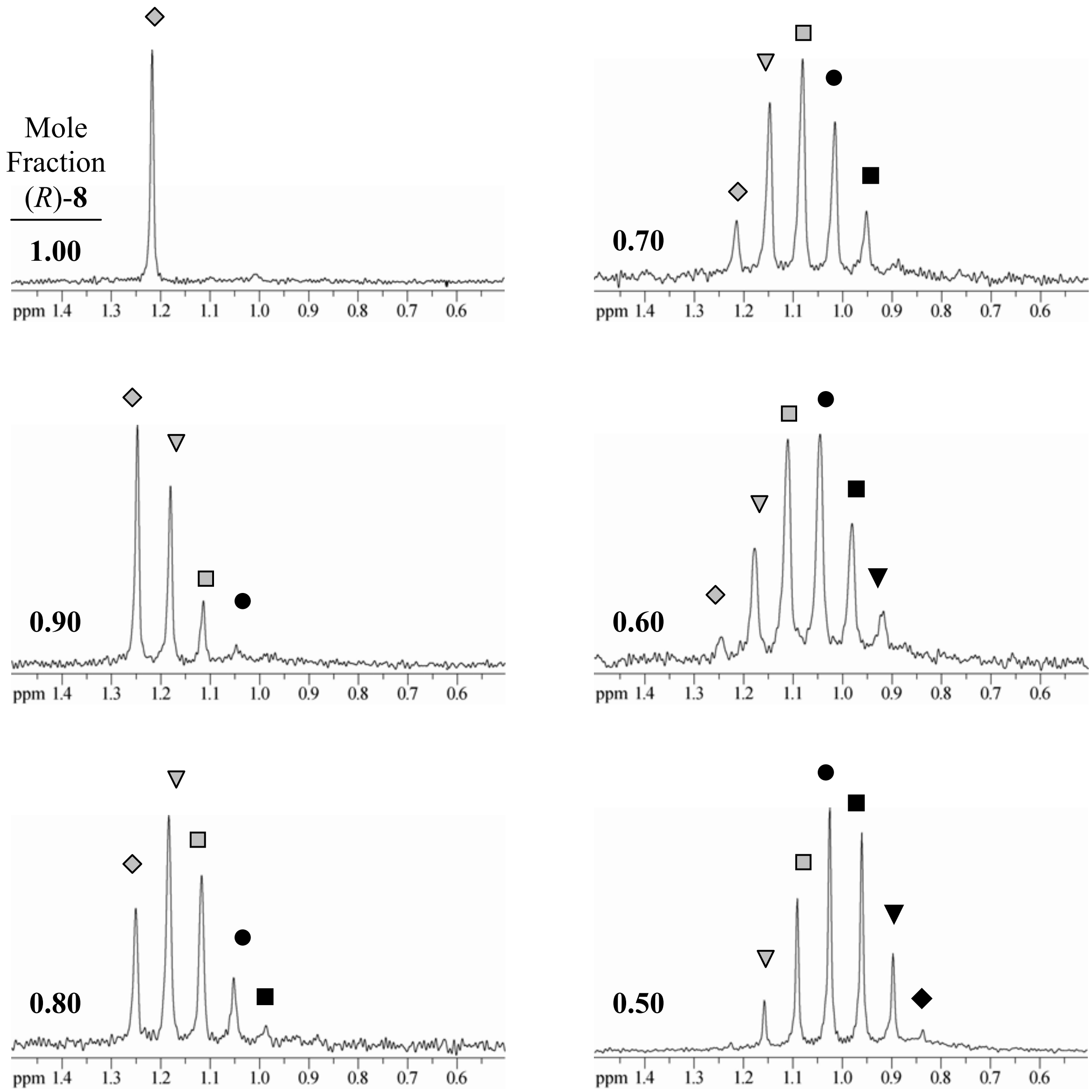
VIII.B. Variation of enolate concentration for a mixture of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**5** (mole fraction of **R'**=0.70). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**5** (mole fraction of **R'**=0.70) at various enolate concentrations. All samples are 3.0 M THF/toluene and were recorded at -40 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R}_6$ (▼) $\mathbf{R}_5\mathbf{R'}_1$ (■) $\mathbf{R}_4\mathbf{R'}_2$ (●) $\mathbf{R}_3\mathbf{R'}_3$ (□) $\mathbf{R}_2\mathbf{R'}_4$ (▽) $\mathbf{R}_1\mathbf{R'}_5$ (◇) $\mathbf{R'}_6$ such that **R'** = [^{6}Li](*R*)-**8** and **R** = [^{6}Li](*S*)-**5**.



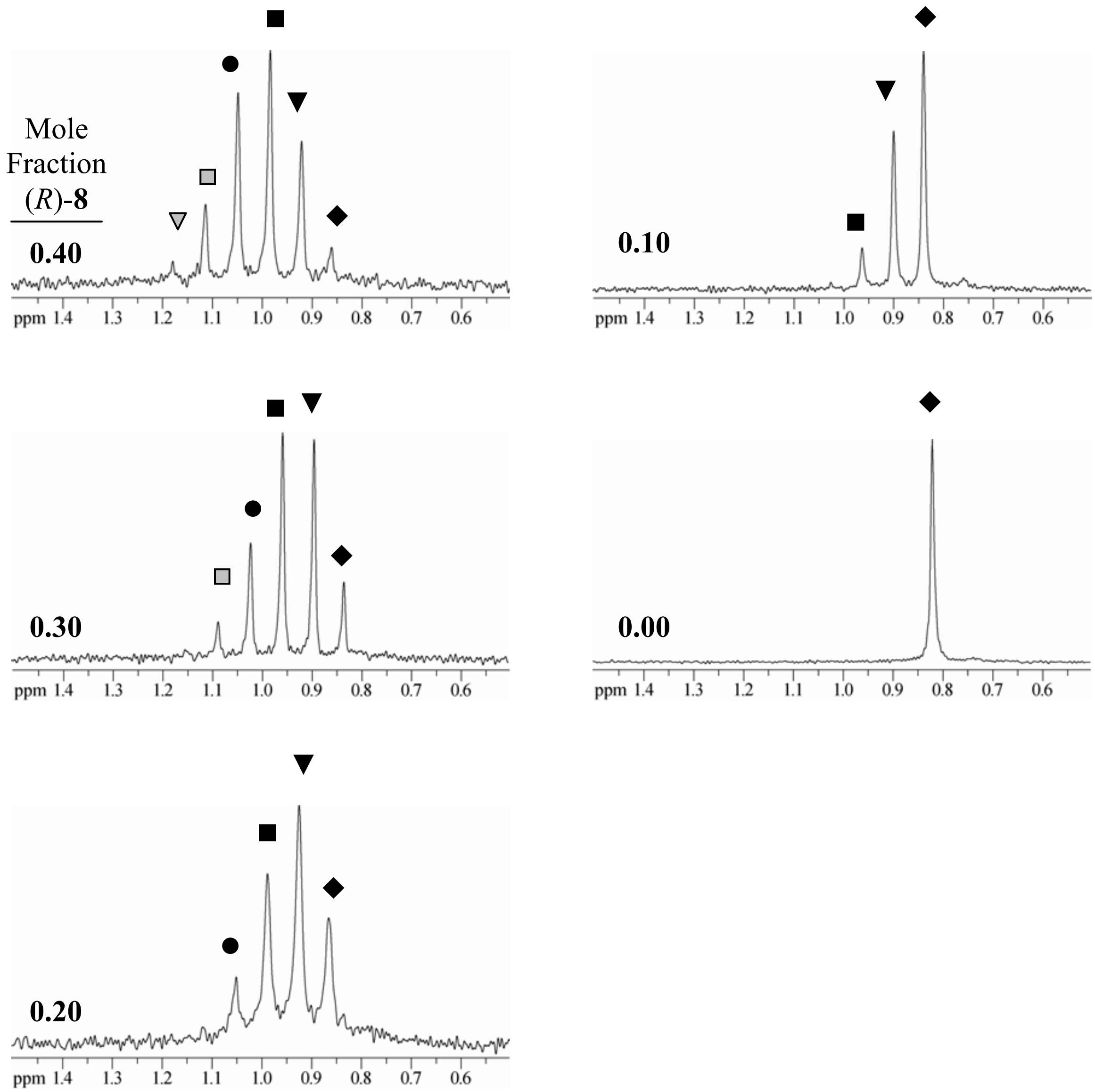


[enolate] (M)	Relative Integrations (■ grey)	(●)	(■)	(▼)	(◆)
0.05	0.04	0.17	0.33	0.34	0.13
0.20	0.04	0.17	0.34	0.32	0.13
0.30	0.04	0.17	0.32	0.32	0.14

VIII.C. Variation of enolate concentration for a mixture of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**5** (mole fraction of **R'**=0.30). ^{6}Li NMR spectra (73.6 MHz) of a mixture of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**5** (mole fraction of **R'**=0.30) at various enolate concentrations. All samples are 3.0 M THF/toluene and were recorded at -40 ºC. The relative integrations of the peaks are plotted versus the total enolate concentration. The lines represent a linear least squares fit. (◆) $\mathbf{R}_6$ (▼) $\mathbf{R}_5\mathbf{R'}_1$ (■) $\mathbf{R}_4\mathbf{R'}_2$ (●) $\mathbf{R}_3\mathbf{R'}_3$ (grey ■) $\mathbf{R}_2\mathbf{R'}_4$ (▽) $\mathbf{R}_1\mathbf{R'}_5$ (◇) $\mathbf{R'}_6$ such that **R'** = [^{6}Li](*R*)-**8** and **R** = [^{6}Li](*S*)-**5**.



VIII.D. ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**5** at various mole fractions in 3.0 M THF/toluene at -40 ºC. Samples are 0.10 M in total enolate concentration. (◆) **R**$_6$ (▼) **R**$_5$**R'**$_1$ (■) **R**$_4$**R'**$_2$ (●) **R**$_3$**R'**$_3$ (□) **R**$_2$**R'**$_4$ (▽) **R**$_1$**R'**$_5$ (◇) **R'**$_6$ such that **R'** = [^{6}Li](*R*)-**8** and **R** = [^{6}Li](*S*)-**5**.



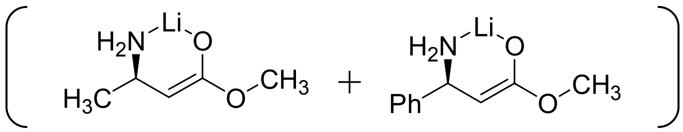
VIII.D. (cont.) ^{6}Li NMR spectra (73.6 MHz) of mixtures of [^{6}Li](*R*)-**8** and [^{6}Li](*S*)-**5** at various mole fractions in 3.0 M THF/toluene at -40 ºC. Samples are 0.10 M in total enolate concentration. (◆) $\mathbf{R}_6$ (▼) $\mathbf{R}_5\mathbf{R'}_1$ (■) $\mathbf{R}_4\mathbf{R'}_2$ (●) $\mathbf{R}_3\mathbf{R'}_3$ (▣) $\mathbf{R}_2\mathbf{R'}_4$ (▽) $\mathbf{R}_1\mathbf{R'}_5$ (◇) $\mathbf{R'}_6$ such that **R'** = [^{6}Li](*R*)-**8** and **R** = [^{6}Li](*S*)-**5**.

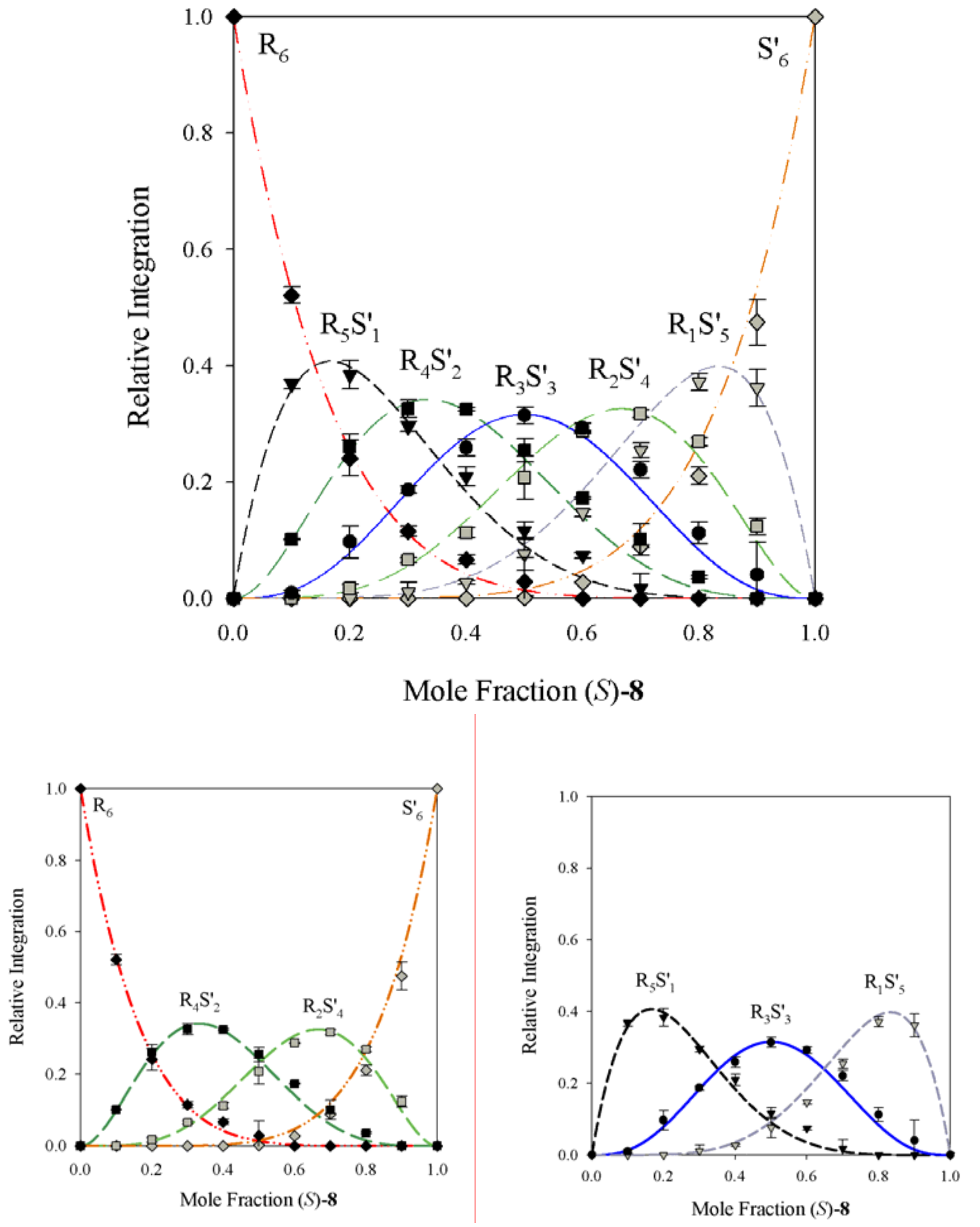
VIII.E. Table of the relative integrations for the spectra in **VIII.D**.[a]

Mole Frac. (*S*)-**8**	Relative Integrations **R'$_6$** (◇)	**R'$_5$R$_1$** (▽)	**R'$_4$R$_2$** (▣)	**R'$_3$R$_3$** (●)
1.00	1.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
0.90	0.47±0.04	0.36±0.03	0.12±0.01	0.04±0.06
0.80	0.21±0.01	0.37±0.01	0.27±0.01	0.11±0.02
0.70	0.09±0.002	0.25±0.01	0.32±0.01	0.22±0.01
0.60	0.03±0.001	0.15±0.01	0.29±0.001	0.29±0.01
0.50	0.002±0.003	0.08±0.03	0.21±0.04	0.31±0.01
0.40	0.00±0.00	0.03±0.003	0.11±0.01	0.26±0.01
0.30	0.00±0.00	0.01±0.02	0.07±0.004	0.19±0.01
0.20	0.00±0.00	0.00±0.00	0.02±0.01	0.10±0.03
0.10	0.00±0.00	0.00±0.00	0.00±0.00	0.01±0.01
0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00

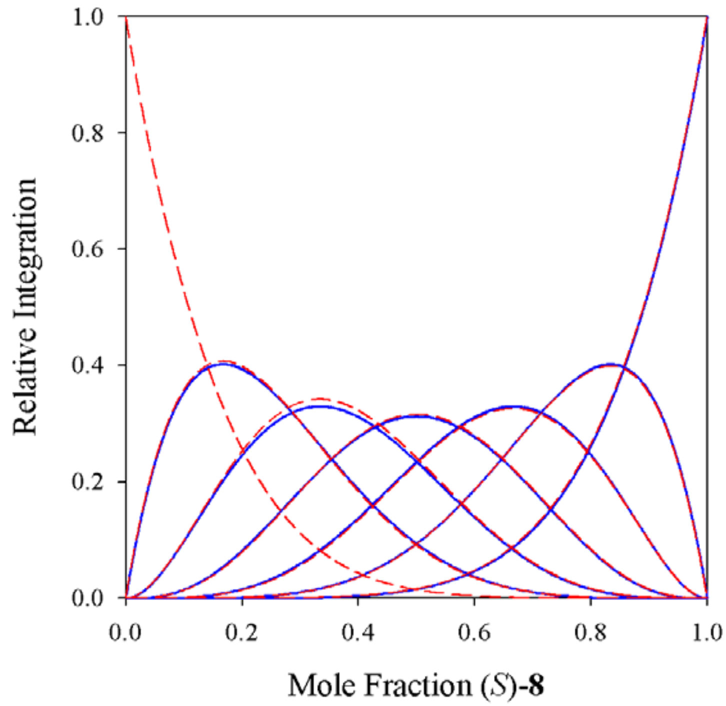
Mole Frac. (*S*)-**8**	Relative Integrations **R'$_2$R$_4$** (■)	**R'$_1$R$_5$** (▼)	**R$_6$** (◆)
1.00	0.00±0.00	0.00±0.00	0.00±0.00
0.90	0.00±0.00	0.00±0.00	0.00±0.00
0.80	0.04±0.003	0.00±0.00	0.00±0.00
0.70	0.10±0.03	0.02±0.02	0.00±0.00
0.60	0.17±0.002	0.07±0.005	0.00±0.00
0.50	0.25±0.02	0.12±0.02	0.03±0.04
0.40	0.32±0.003	0.21±0.02	0.07±0.01
0.30	0.33±0.02	0.29±0.01	0.12±0.01
0.20	0.26±0.02	0.38±0.02	0.24±0.03
0.10	0.10±0.008	0.37±0.01	0.52±0.01
0.00	0.00±0.00	0.00±0.00	1.00±0.00

[a] **(◆) R$_6$ (▼) R$_5$R'$_1$ (■) R$_4$R'$_2$ (●) R$_3$R'$_3$ (▣) R$_2$R'$_4$ (▽) R$_1$R'$_5$ (◇) R'$_6$** such that **R'** = [^{6}Li](*S*)-**8** and **R** = [^{6}Li](*R*)-**5**.





VIII.F. A Plot of [^{6}Li](*S*)-**8**/[^{6}Li](*R*)-**5** (3.0 M THF/toluene; -40 ºC) hexamers. The relative integrations are plotted as a function of the mole fraction of [^{6}Li](*S*)-**8**. (◆) **R**$_6$ (▼) **R**$_5$**R'**$_1$ (■) **R**$_4$**R'**$_2$ (●) **R**$_3$**R'**$_3$ (▣) **R**$_2$**R'**$_4$ (▽) **R**$_1$**R'**$_5$ (◇) **R'**$_6$ such that **R'** = [^{6}Li](*S*)-**8** and **R** = [^{6}Li](*R*)-**5**. The curves result from a parametric fit, affording ϕ_0=1.00; ϕ_1=1.53; ϕ_2=2.28; ϕ_3=3.15; ϕ_4=4.32; ϕ_5=6.09; ϕ_6=8.76.



VIII.G. The fit in **VIII.F.** is overlaid with the expected statistical distribution of an ensemble of hexamers.

(———) Fit to data (ϕ_0=1.00; ϕ_1=1.53; ϕ_2=2.28; ϕ_3=3.15; ϕ_4=4.32; ϕ_5=6.09; ϕ_6=8.76)

(– – – –) Statistical distribution (ϕ_0=1; ϕ_1=6; ϕ_2=15; ϕ_3=20; ϕ_4=15; ϕ_5=6; ϕ_6=1)

IX. Multi-author References

13. (a) Guertin, K. R.; Gardner, C. J.; Klein, S. I.; Zulli, A. L.; Czekaj, M.; Gong, Y.; Spada, A. P.; Cheney, D. L.; Maignan, S.; Guilloteau, J.-P.; Brown, K. D.; Colussi, D. J.; Chu, V.; Heran, C. L.; Morgan, S. R.; Bentley, R. G.; Dunwiddie, C. T.; Leadley, R. J.; Pauls, H. W. *Bioorg*. *Med*. *Chem*. *Lett*. **2002**, *12*, 1671. (b) Czekaj, M.; Klein, S. I.; Guertin, K. R.; Gardner, C. J.; Zulli, A. L.; Pauls, H. W.; Spada, A. P.; Cheney, D. L.; Brown, K. D.; Colussi, D. J.; Chu, V.; Leadley, R. J.; Dunwiddie, C. T. *Bioorg*. *Med*. *Chem*. *Lett*. **2002**, *12*, 1667.