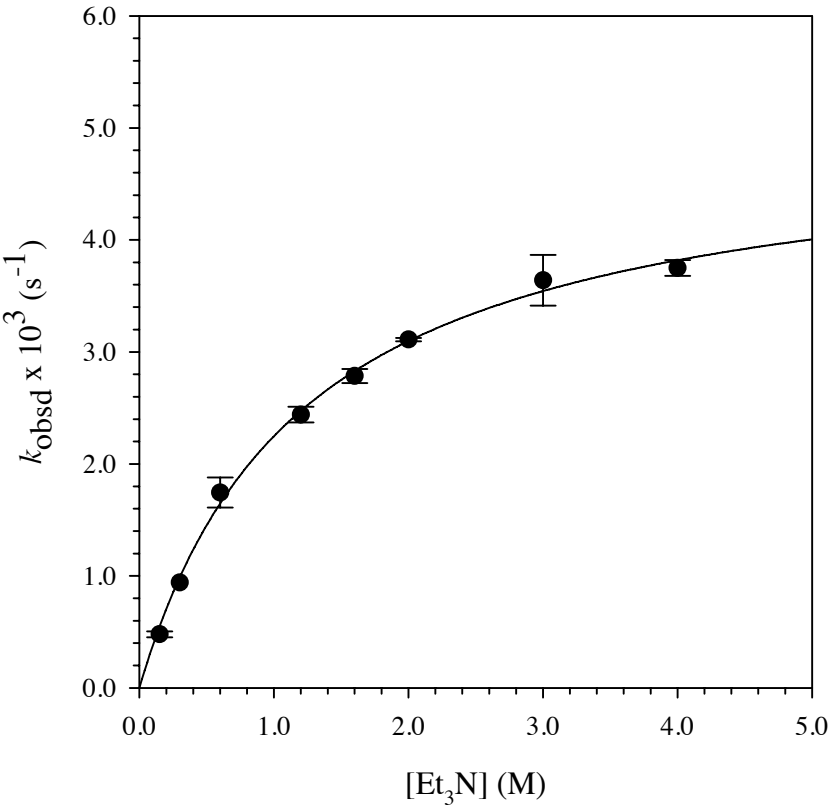
Lithium Hexamethyldisilazide-Mediated Enolizations: Influence of Triethylamine on *E*/*Z* Selectivities and Enolate Reactivities

Peter F. Godenschwager and David B. Collum*
Department of Chemistry and Chemical Biology
Baker Laboratory, Cornell University,
Ithaca, New York 14853-1301

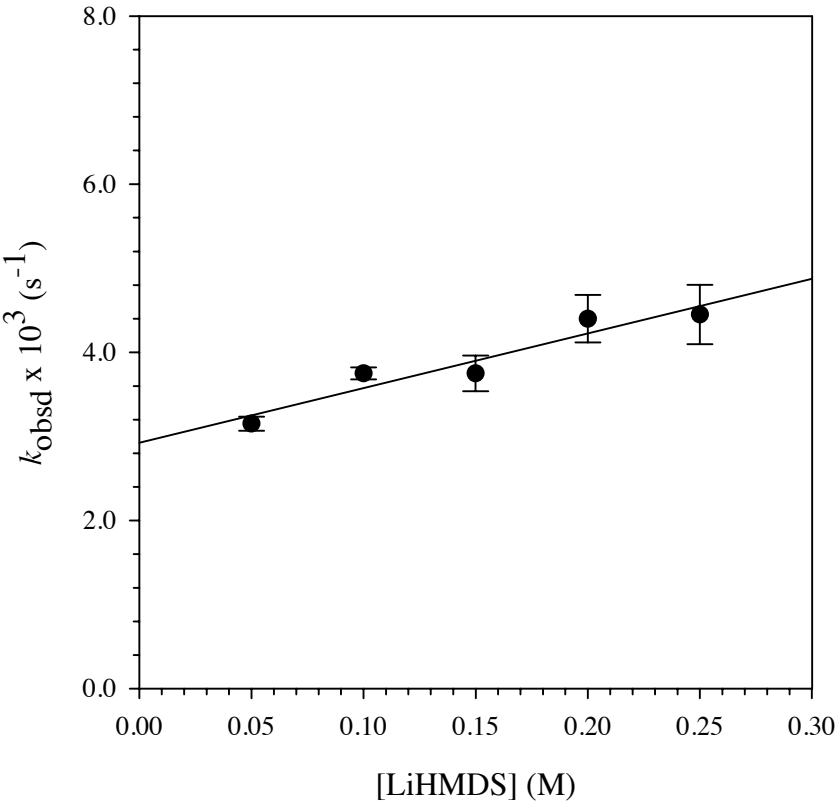
Supporting Information



I. Plot of k_{obsd} vs [Et_3N] in toluene for the enolization of **5-**d_3 (0.005 M) by LiHMDS (0.10 M) at -78 °C. The line depicts the unweighted least-squares fit to $k_{obsd} = a[Et_3N]/(1 + b[Et_3N])$ ($a = 4.0 \pm 0.1$, $b = 8.2 \pm 0.6 \times 10^{-1}$).

II. Table of data for plot in section **I**.

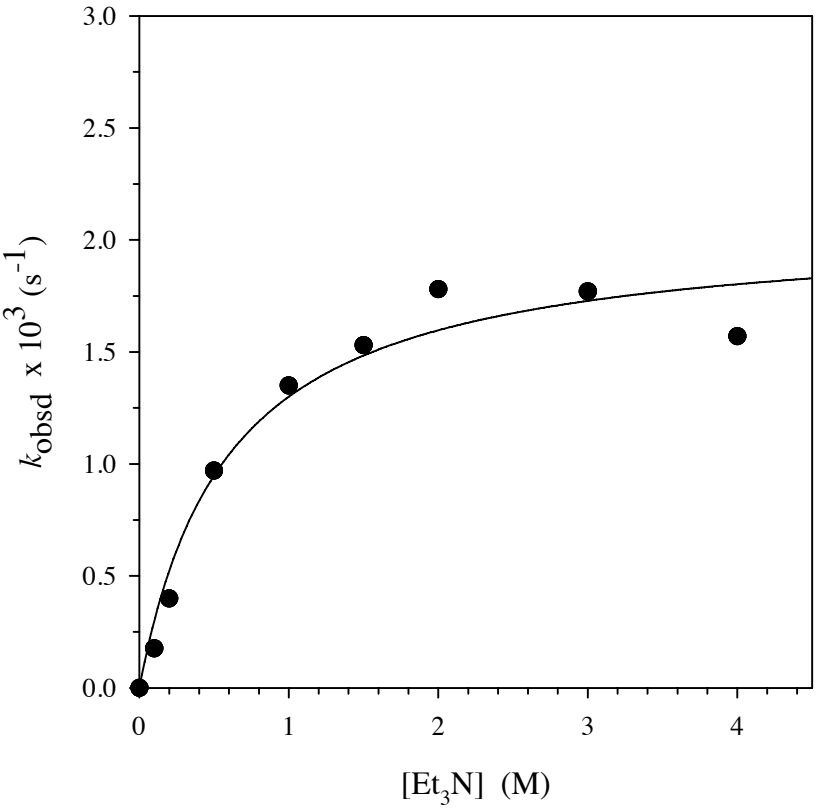
[Et_3N] (M)	$k_{obsd}1$ (s^{-1})	$k_{obsd}2$ (s^{-1})	k_{obsd}(avg) (s^{-1})
0.15	4.97 ± 0.05E-4	4.60 ± 0.06E-4	4.7 ± 0.2E-4
0.30	9.4 ± 0.1E-4	9.4 ± 0.1E-4	9.4 ± 0.0E-4
0.60	1.84 ± 0.03E-3	1.65 ± 0.03E-3	1.7 ± 0.1E-3
1.2	2.49 ± 0.08E-3	2.39 ± 0.04E-3	2.44 ± 0.07E-3
1.6	2.83 ± 0.06E-3	2.74 ± 0.07E-3	2.78 ± 0.06E-3
2.0	3.10 ± 0.05E-3	3.12 ± 0.09E-3	3.11 ± 0.01E-3
3.0	3.48 ± 0.05E-3	3.8 ± 0.1E-3	3.6 ± 0.2E-3
4.0	3.8 ± 0.1E-3	3.7 ± 0.1E-3	3.75 ± 0.07E-3



III. Plot of k_{obsd} vs [LiHMDS] for the enolization of **5-**d_3 in 4.0 M Et_3N/toluene at -78 °C. The curve depicts the unweighted least-squares fit to $k_{obsd} = a$[LiHMDS] + b ($a = 5 \pm 1 \times 10^{-3}$, $b = 3.0 \pm 0.1 \times 10^{-3}$).

IV. Table of data for plot in section **III**.

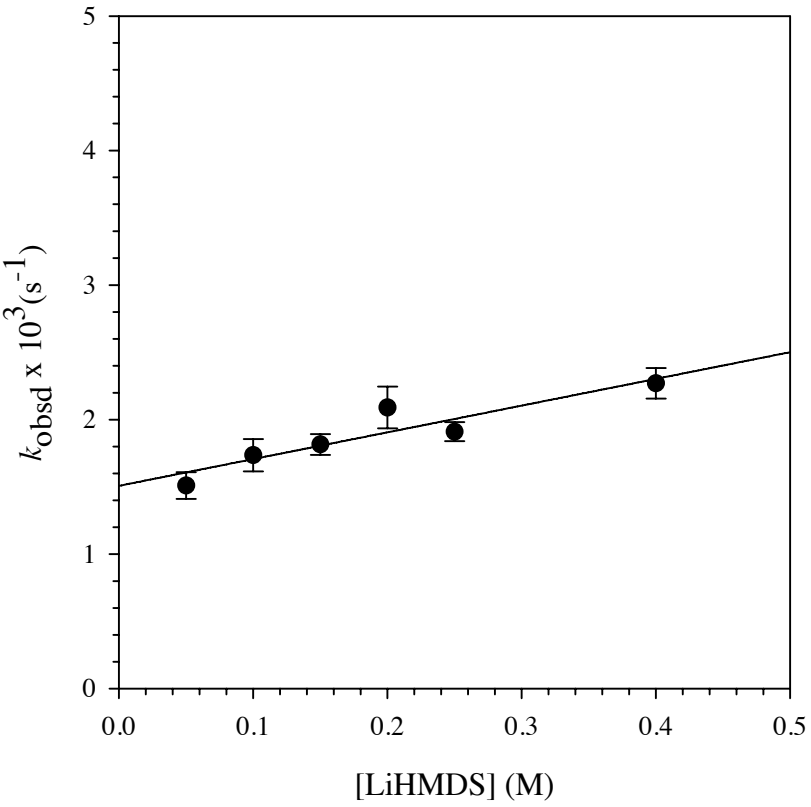
[LiHMDS] (M)	$k_{obsd}1$ (s^{-1})	$k_{obsd}2$ (s^{-1})	k_{obsd}(avg) (s^{-1})
0.05	3.21 ± 0.06E-3	3.09 ± 0.07E-3	3.15 ± 0.08E-3
0.10	3.8 ± 0.1E-3	3.7 ± 0.1E-3	3.75 ± 0.07E-3
0.15	3.6 ± 0.1E-3	3.9 ± 0.1E-3	3.7 ± 0.2E-3
0.20	4.2 ± 0.1E-3	4.6 ± 0.1E-3	4.4 ± 0.2E-3
0.25	4.2 ± 0.1E-3	4.7 ± 0.1E-3	4.4 ± 0.3E-3



V. Plot of k_{obsd} vs [Et_3N] for the enolization of isopropyl propionate by LiHMDS (0.10 M) in toluene at -78 ºC. The curve depicts the unweighted least-squares fit to $k_{obsd} = a[Et_3N]/(1 + b[Et_3N])$ ($a = 3.5 \pm 0.6 \times 10^{-3}$, $b = 1.6 \pm 0.4$).

VI. Table of data for plot in section **V**.

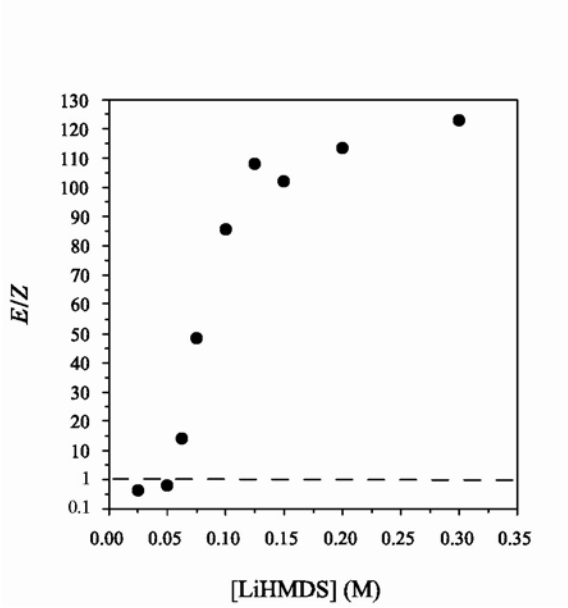
[Et_3N] (M)	k_{obsd} (s^{-1})
0.10	1.76 ± 0.01E-4
0.20	3.99 ± 0.02E-4
0.50	9.71 ± 0.09E-4
1.0	1.35 ± 0.01E-3
1.5	1.55 ± 0.02E-3
2.0	1.78 ± 0.01E-3
3.0	1.77 ± 0.03E-3
4.0	1.57 ± 0.01E-3



VII. Plot of k_{obsd} vs [LiHMDS] for the enolization of isopropyl propionate in 2.5 M Et_3N/toluene at -78 ºC. The curve depicts the unweighted least-squares fit to $k_{obsd} = a$[LiHMDS] + b ($a = 1.9 \pm 0.4 \times 10^{-3}$, $b = 1.50 \pm 0.09 \times 10^{-3}$).

VIII. Table of data for the plot in section **VII**.

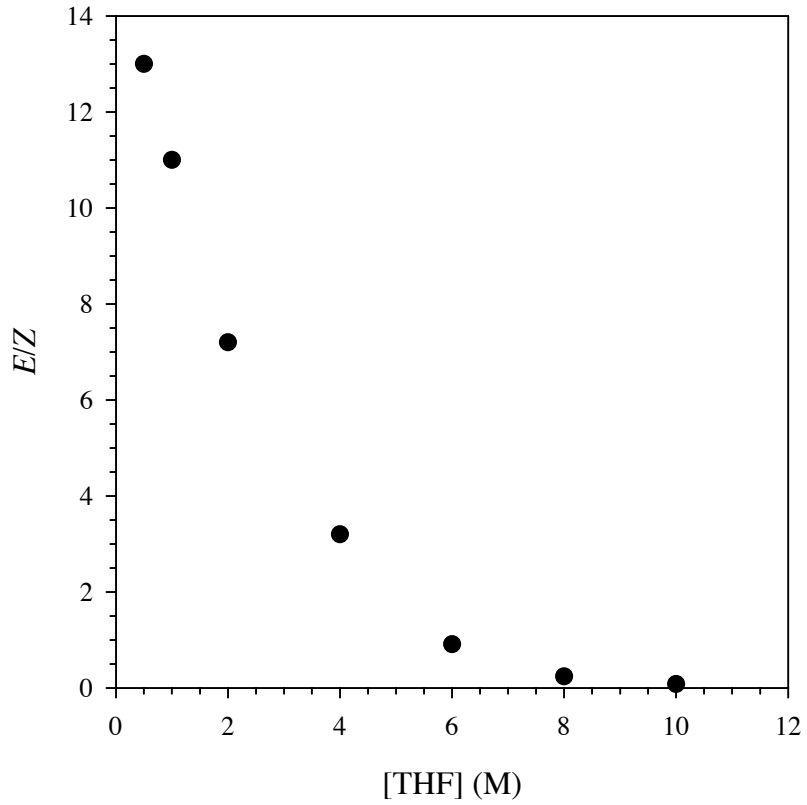
[LiHMDS] (M)	$k_{obsd}1$ (s^{-1})	$k_{obsd}2$ (s^{-1})	k_{obsd}(avg) (s^{-1})
0.05	1.44 ± 0.01E-3	1.58 ± 0.02E-3	1.51 ± 0.09E-3
0.10	1.82 ± 0.02E-3	1.65 ± 0.01E-3	1.7 ± 0.1E-3
0.15	1.76 ± 0.02E-3	1.87 ± 0.01E-3	1.82 ± 0.07E-3
0.20	2.20 ± 0.02E-3	1.98 ± 0.02E-3	2.0 ± 0.1E-3
0.25	1.86 ± 0.03E-3	1.96 ± 0.02E-3	1.91 ± 0.07E-3
0.40	2.19 ± 0.03E-3	2.35 ± 0.03E-3	2.2 ± 0.1E-3



IX. Plot of *E*/*Z* selectivity for the enolization of **5** (0.05 M) by LiHMDS in 1.5 M Et_3N/toluene at -78 ºC.

X. Table of data for the plot in section **IX**.

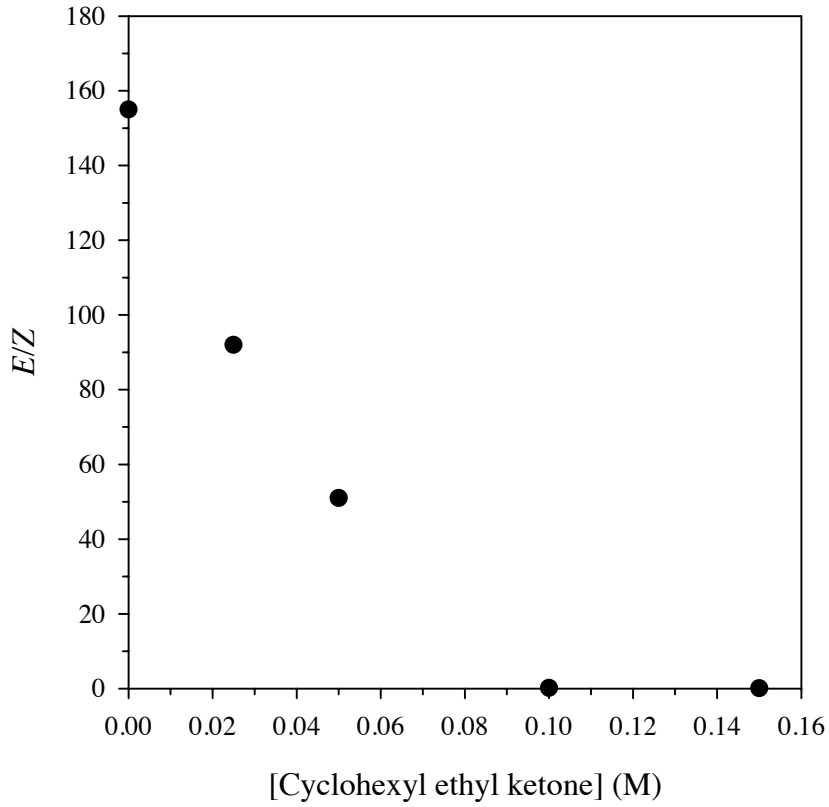
[LiHMDS] (M)	*E*/*Z* **1**	*E*/*Z* **2**	*E*/*Z* (avg)
0.025	1 : 4.4	1 : 3.2	1 : 3.8
0.05	1 : 2.3	1 : 1.8	1 : 2.1
0.0625	11.4 : 1	16.7 : 1	14 : 1
0.075	49 :1	48 : 1	49 : 1
0.1	88 : 1	83 : 1	86 : 1
0.125	110 : 1	106 : 1	108 : 1
0.15	106 : 1	98 : 1	102 : 1
0.2	107 : 1	120 : 1	114 : 1
0.3	138 : 1	108 : 1	123 : 1



XI. Plot of *E*/*Z* selectivity vs. [THF] for the enolization of **5** (0.05 M) by LiHMDS (0.15 M) in toluene at -78 ºC.

XII. Table of data for the plot in section **XI**.

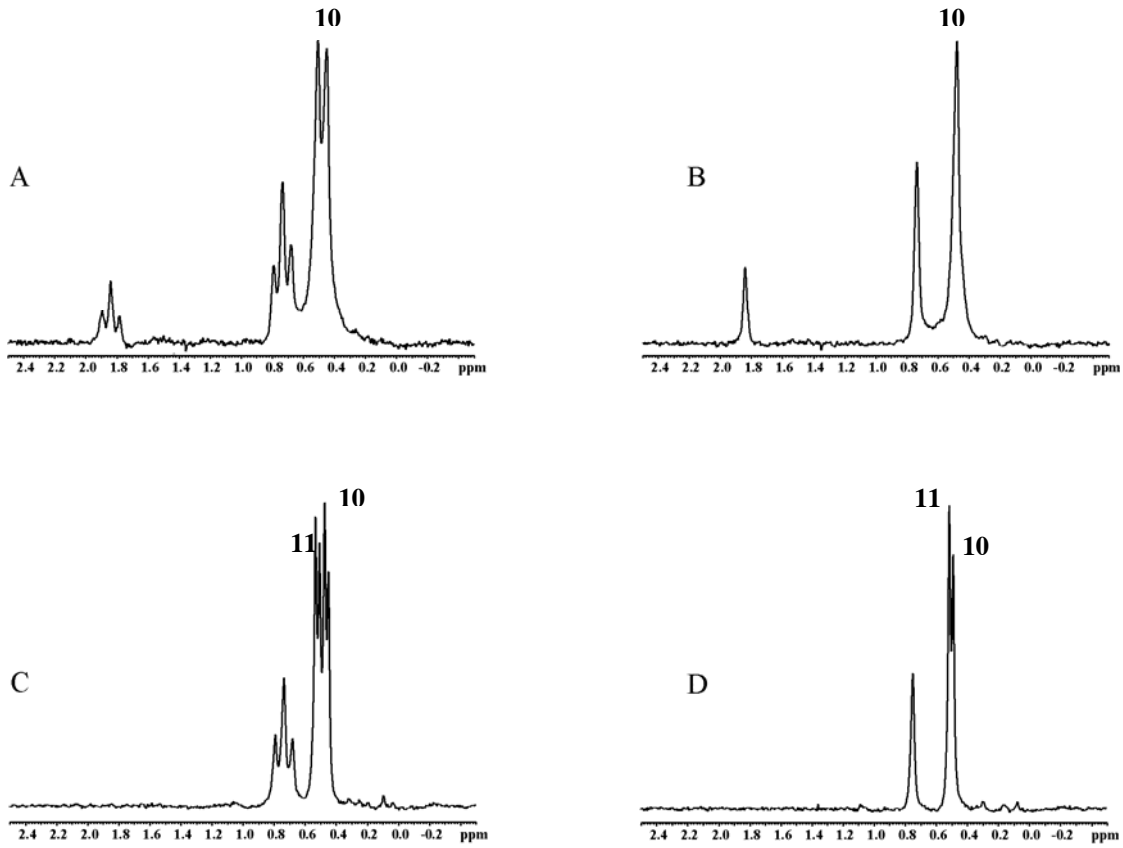
[THF]	*E*/*Z*
0.5	13 : 1
1.0	11 : 1
2.0	7.2 : 1
4.0	3.2 : 1
6.0	1 : 1.1
8.0	1 : 4.2
10.0	1 : 13



XIII. Plot of *E*/*Z* selectivity vs. [cyclohexyl ethyl ketone] for the enolization of **5** (0.05 M) by LiHMDS (0.15 M) in 1.5 M Et_3N/toluene at -78 ºC.

XIV. Data for the plot in section **XIII**.

[Cyclohexyl ethyl ketone] (M)	*E*/*Z* of 2-methyl-3-pentanone
0	155 : 1
0.025	92 : 1
0.05	51 : 1
0.10	1 : 5
0.15	1 : 10



XV. ^{6}Li spectra recorded on [^{6}Li,^{15}N]LiHMDS (0.15 M), Et_3N (1.5 M), and **5** (0.05 M) in toluene at -100 ºC. (A) Enolization takes place at -100 ºC showing *E* enolate mixed dimer **10**; (B) Spectrum (A) decoupled; (C) Enolization takes place at 0 ºC showing *E* enolate mixed dimer **10** and *Z* enolate mixed dimer **11**; (D) Spectrum (C) decoupled.

XVI. *E*/*Z* selectivities for the enolization of **5** (0.05 M) by LiHMDS (0.15 M) in the presence of trialkyl amines at -78 ºC in toluene.

Amine	*E*/*Z*
Et_3N[a]	102 : 1
DMEA[b]	90 : 1
$(i\text{-Pr})_2EtN$[b]	40 : 1
$(i\text{-Bu})_3N$[b]	60 : 1

[a] 1.5M ligand. [b]1.0M ligand

XVII. *E*/*Z* selectivities for the enolization of **5** (0.05 M) by LiHMDS (0.15 M) in the presence of ethereal ligands at -78 ºC in toluene.

Ligand	*E*/*Z*
THF (0.5 M)	13 : 1
THF (10 M)	1 : 13
2,2,5,5-tetramethyl THF (1.5 M)	42 : 1
cineole (1 M)	38 : 1

XVIII. *E*/*Z* selectivities for the enolization of **5** (0.05 M) by LiHMDS (0.15 M) in the presence of polydentate ligands at -78 ºC in toluene.

Ligand	*E*/*Z*
TMEDA	33 : 1
TMCDA	26 : 1
$Me_2NCH_2CH_2OMe$ (1.5 M)	3 : 1
$Me_2NCH_2CH_2OMe$ (0.10 M)	52 : 1

XIX. *E*/*Z* selectivity of methyl propionate at -78 ºC.

lithium amide	ligand	*E*/*Z*
LDA	THF	9 : 1
LDA	THF / HMPA	1 : 5
LiHMDS	THF	1 : 8
LiHMDS	Et_3N	22 : 1

XX. *E*/*Z* selectivities for the enolization of various ketones (0.05 M) by LiHMDS (0.15 M) in Et_3N (1.5 M)/toluene at -78 ºC. [a]60 ºC

ketone	*E*/*Z*
3-pentanone	142 : 1
2-methyl-3-pentanone	102 : 1
cyclohexyl ethyl ketone	79 : 1
ethyl phenyl ketone	3.4 : 1

XXI. Stereoselectivities of aldol reaction of ketone enolates (0.05 M) generated by LiHMDS (0.15 M) in Et_3N (1.5 M)/toluene at -78 °C with 0.15 M isobutyraldehyde.

ketone	anti / syn
3-pentanone	8 : 1
2-methyl-3-pentanone	25 : 1
cyclohexyl ethyl ketone	>30 : 1

XXII. Stereoselectivities of aldol reaction of 2-methyl-3-pentanone enolate (0.05 M) generated by LiHMDS (0.15 M) in various enolization and aldol solvent systems at -78 °C with 0.15 M isobutyraldehyde.

enolization solvent	aldol solvent	anti / syn
1.5 M Et_3N / toluene	1.5 M Et_3N / toluene	25 : 1
1.5 M Et_3N / toluene	1.5 M Et_3N / 1.5 M THF / toluene	18 : 1
THF	THF	1 : 4

XXIII. Stereoselectivities of aldol reaction of 3-pentanone enolate (0.05 M) generated by LiHMDS (0.15 M) in 1.5 M Et_3N/toluene and various aldol solvent systems at -78 °C with 0.15M isobutyraldehyde.

aldol solvent (1.5 M)	anti / syn
HMPA	1 : 1.5
2,2,5,5-tetramethyl THF	7 : 1
$MeOCH_2CH_2NMe_2$	2.5 : 1
sparteine	2.5 : 1
TMEDA	4 : 1