Lithium Diisopropylamide-Mediated Reactions of Imines, Unsaturated Esters, Epoxides, and Aryl Carbamates: Influence of Hexamethylphosphoramide and Ethereal Cosolvents on Reaction Mechanisms.

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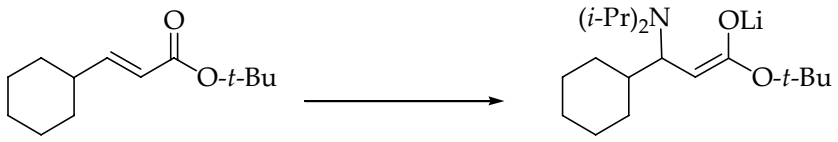

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XIV Synthesis of *t*-butyl triethylphosphonoacetate

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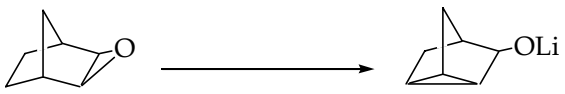
XXV Plot of k_{obsd} vs [THF] for the Michael addition of LDA to ester **3** in 2.0 equiv HMPA/2,5-Me_2THF



5 **6**

XXVI Synthesis of alcohol **34**

XXVII ^{1}H and ^{13}C NMR Spectra of **34**

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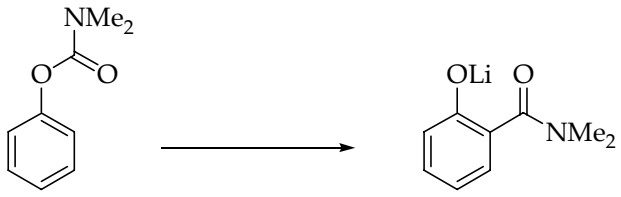
XXXVI Plot of k_{obsd} vs [THF] for the deprotonation of *exo*-2,3-epoxynorbornane **5** by LDA in hexane



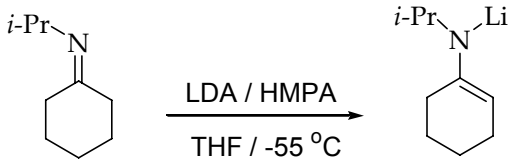
7 **8**

XXXVII ^{6}Li and ^{15}N NMR spectra of [^{6}Li,^{15}N]LDA with carbamate **7** in 4.0 equiv HMPA/THF/pentane

XXXVIII Plot of k_{obsd} vs [HMPA] for the ortholithiation of **7** by LDA in THF/hexane

XXXVIX Plot of k_{obsd} vs [LDA] for the ortholithiation of **7** in 4.0 equiv HMPA/THF/hexane

XXXX Plot of k_{obsd} vs [THF] for the ortholithiation of **7** by LDA in 4.0 equiv HMPA/hexane



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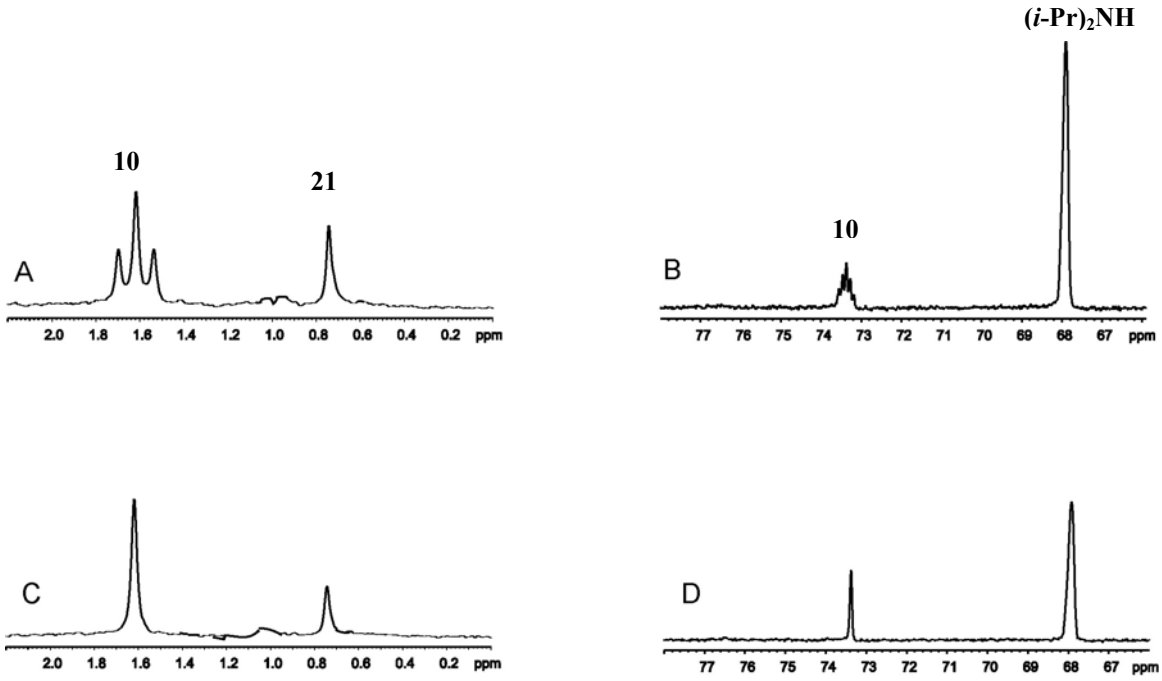
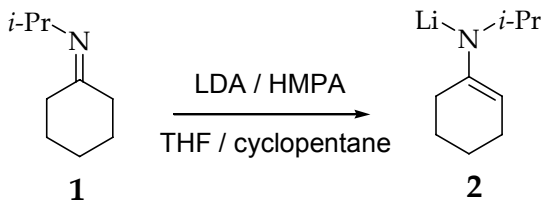


I. ^{6}Li and ^{15}N NMR spectra of 0.10 M [^{6}Li,^{15}N]LDA with 0.25 equiv imine **1** in 0.40 M HMPA /10.0 M THF/pentane at -90 ˚C after aging at -55 ˚C for 60 min: (A) ^{6}Li spectrum; (B) ^{15}N spectrum; (C) ^{6}Li{^{15}N} spectrum; (D) ^{15}N{^{6}Li} spectrum.



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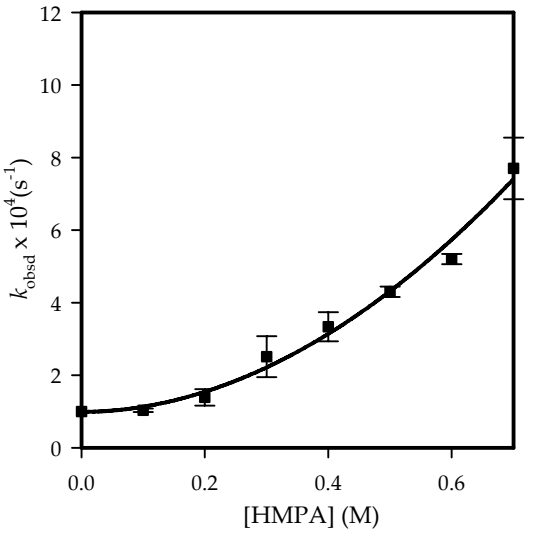
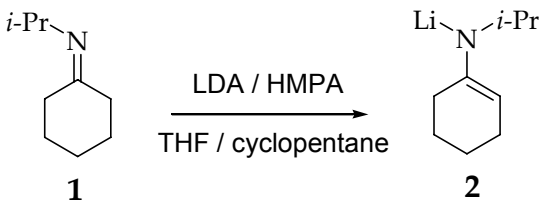


II. Plot of k_{obsd} vs [HMPA] for the lithiation of imine **1** (0.005 M) by 0.10 M LDA in 8.0 M THF/cyclopentane at -55 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{HMPA}]^n + k'$ ($k = (1.3 \pm 0.1) \times 10^{-3}$, $k' = (1.0 \pm 0.2) \times 10^{-4}$, $n = 2.0 \pm 0.3$).

[HMPA] (M)[a]	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.00	0.999 ± 0.003	0.992 ± 0.006	0.996 ± 0.005
0.10	1.07 ± 0.01	1.00 ±0.02	1.04 ± 0.05
0.20	1.23 ± 0.01	1.55 ± 0.01	1.40 ± 0.2
0.30	2.91 ± 0.03	2.11 ± 0.03	2.51 ± 0.6
0.40	3.62 ± 0.05	3.05 ± 0.05	3.3 ± 0.4
0.50	4.40 ± 0.01	4.20± 0.02	4.3 ± 0.1
0.60	5.30 ± 0.02	5.10 ± 0.01	5.2 ± 0.1
0.70	8.30 ± 0.02	7.10 ± 0.02	7.7 ± 0.8

[a][HMPA] refers to the concentration of free (uncoordinated) HMPA.



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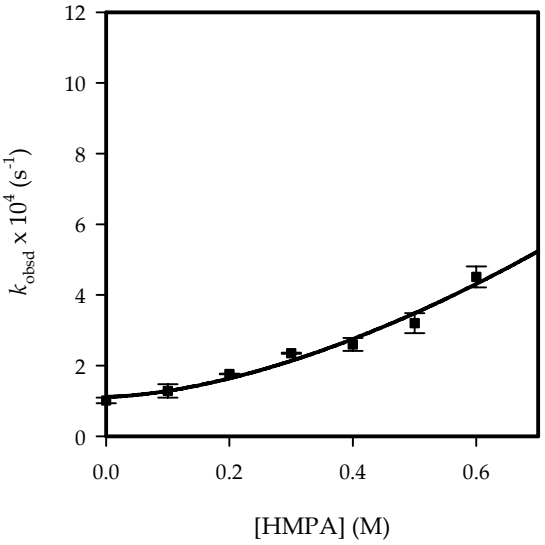
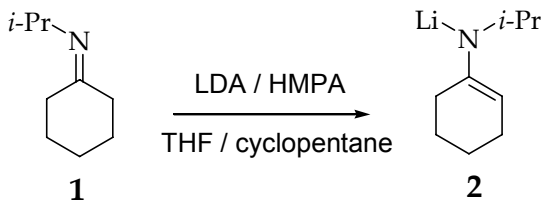


III. Plot of k_{obsd} vs [HMPA] for the lithiation of imine **1** (0.005 M) by 0.10 M LDA in 4.0 M THF/cyclopentane at -55 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{HMPA}]^n + k'$ ($k = (6.4 \pm 0.8) \times 10^{-4}$, $k' = (1.1 \pm 0.2) \times 10^{-4}$, $n = 1.5 \pm 0.2$)

[HMPA] (M)[a]	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.00	0.96 ± 0.02	1.07 ± 0.02	1.1 ± 0.2
0.10	1.42 ± 0.02	1.15 ± 0.02	1.46 ± 0.06
0.20	1.76 ± 0.02	1.77 ± 0.02	1.76 ± 0.01
0.30	2.36 ± 0.05	2.34 ± 0.03	2.35 ± 0.01
0.40	2.73 ± 0.05	2.47 ± 0.02	2.6 ± 0.2
0.50	3.00 ± 0.04	3.40 ± 0.03	3.2 ± 0.3
0.60	4.30 ± 0.03	4.27 ± 0.03	4.29 ± 0.02

[a][HMPA] refers to the concentration of free (uncoordinated) HMPA.



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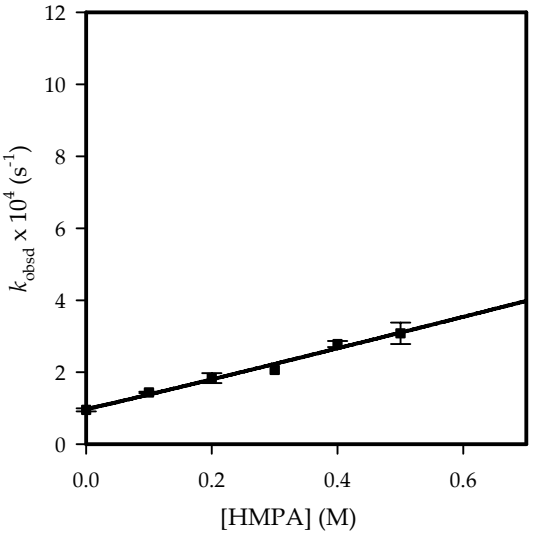
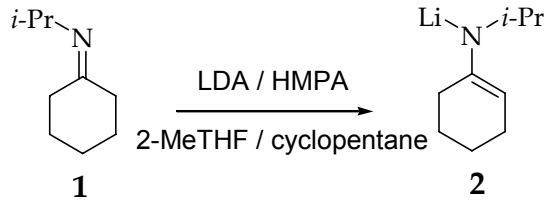


IV. Plot of k_{obsd} vs [HMPA] for the lithiation of imine **1** (0.005 M) by 0.10 M LDA in 2.0 M THF/cyclopentane at -55 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{HMPA}]^n + k'$ (k = (4.3 ± 0.6) x 10^{-4}, k' = (9.7 ± 1.2) x 10^{-5}, n = 1.02 ± 0.02).

[HMPA] (M)[a]	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.00	0.92 ± 0.01	0.98 ± 0.02	0.95 ± 0.04
0.10	1.45 ± 0.02	1.42 ± 0.02	1.44 ± 0.02
0.20	1.93 ± 0.03	1.74 ± 0.02	1.84 ± 0.02
0.30	2.06 ± 0.03	2.06 ± 0.02	2.06 ± 0.01
0.40	2.80 ± 0.06	2.72 ± 0.02	2.78 ± 0.08
0.50	3.29 ± 0.04	2.87 ± 0.03	3.1 ± 0.3

[a][HMPA] refers to the concentration of free (uncoordinated) HMPA.



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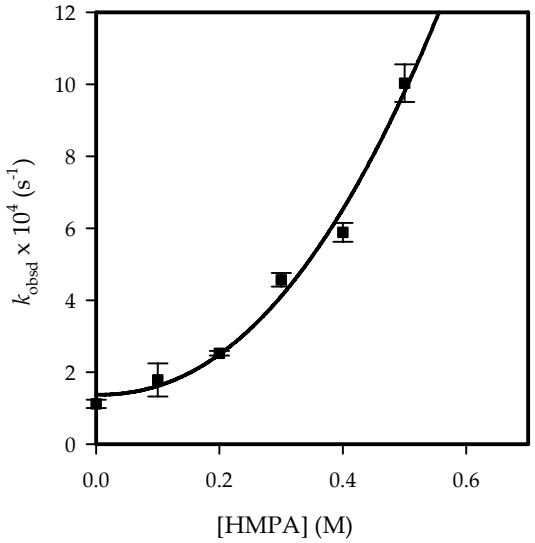
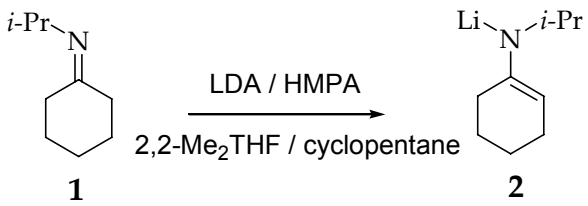


V. Plot of k_{obsd} vs [HMPA] for the lithiation of imine **1** (0.005 M) by 0.10 M LDA in 8.0 M 2-MeTHF/cyclopentane at -55 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{HMPA}]^n + k'$ ($k = (3.4 \pm 0.8) \times 10^{-3}$, $k' = (1.1 \pm 0.4) \times 10^{-4}$, $n = 2.0 \pm 0.3$).

[HMPA] (M)[a]	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.00	1.20 ± 0.02	1.04± 0.05	1.1 ± 0.1
0.10	1.51 ± 0.05	1.46 ± 0.02	1.49 ± 0.05
0.20	2.48 ± 0.02	2.57 ± 0.03	2.53 ± 0.06
0.30	4.70 ± 0.03	4.43 ± 0.09	4.6 ± 0.2
0.40	6.07 ± 0.06	5.7 ± 0.1	5.9 ± 0.3
0.50	10.4 ± 0.1	9.66 ± 0.09	10.0 ± 0.5

[a][HMPA] refers to the concentration of free (uncoordinated) HMPA.



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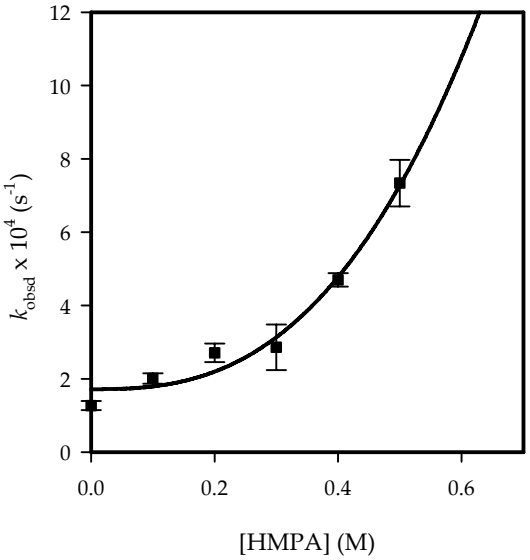
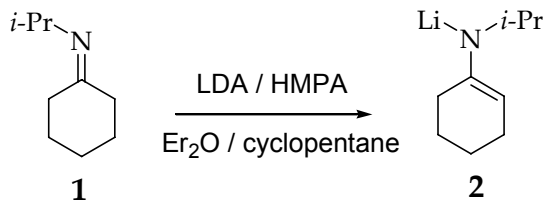
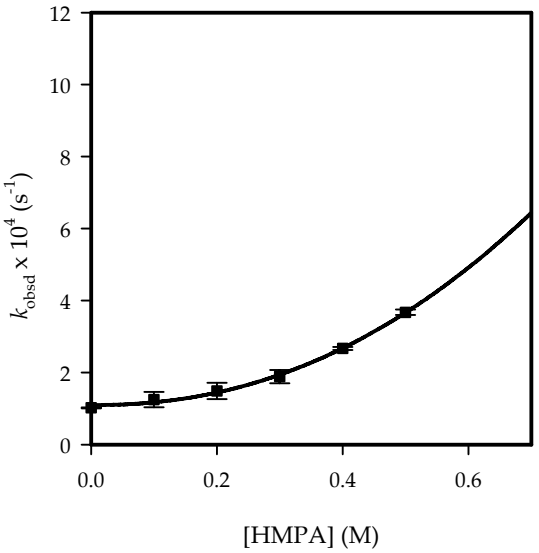


VI. Plot of k_{obsd} vs [HMPA] for the lithiation of imine **1** (0.005 M) by 0.10 M LDA in 8.0 M 2,5-Me_2THF/cyclopentane at -55 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[HMPA]^n + k'$ (k = (2.2 ± 0.8) x 10^{-3}, k' = (1.4 ± 0.4) x 10^{-4}, n = 2.2 ± 0.5).

[HMPA] (M)[a]	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.00	1.18 ± 0.02	1.36 ± 0.02	1.3± 0.1
0.10	2.11 ± 0.03	1.91 ± 0.03	2.0 ± 0.1
0.20	2.89 ± 0.04	2.53 ± 0.02	2.7 ± 0.3
0.30	3.30 ± 0.03	2.42 ± 0.03	2.9 ± 0.6
0.40	4.57 ± 0.04	4.83 ± 0.02	4.7 ± 0.2
0.50	6.89± 0.07	7.79 ± 0.06	7.3 ± 0.6

[a][HMPA] refers to the concentration of free (uncoordinated) HMPA.

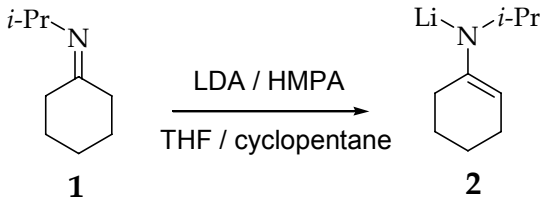




VII. Plot of k_{obsd} vs [HMPA] for the lithiation of imine **1** (0.005 M) by 0.10 M LDA in 8.0 M Et_2O/cyclopentane at -55 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[HMPA]^n + k'$ ($k = (1.0 \pm 0.1) \times 10^{-3}$, $k' = (1.10 \pm 0.07) \times 10^{-4}$, $n = 2.2 \pm 0.2$).

[HMPA] (M)[a]	$k_{obsd\ 1} \times 10^4$ (s^{-1})	$k_{obsd\ 2} \times 10^4$ (s^{-1})	k_{obsd} (avg) $\times 10^4$ (s^{-1})
0.00	1.03 ± 0.03	1.01± 0.03	1.02 ± 0.01
0.10	1.10 ± 0.03	1.40 ± 0.03	1.3 ± 0.2
0.20	1.33 ± 0.04	1.65 ± 0.06	1.49 ± 0.01
0.30	1.76 ± 0.04	2.02 ± 0.02	1.89 ± 0.01
0.40	2.64 ± 0.03	2.70 ± 0.04	2.7 ± 0.2
0.50	3.62 ± 0.04	3.73 ± 0.03	3.7 ± 0.3

[a][HMPA] refers to the concentration of free (uncoordinated) HMPA.



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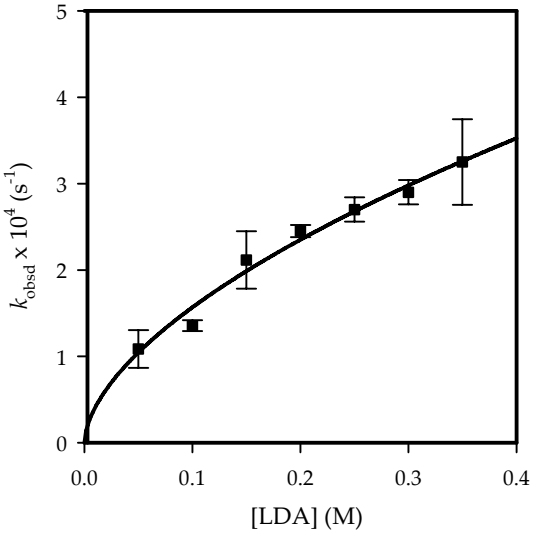
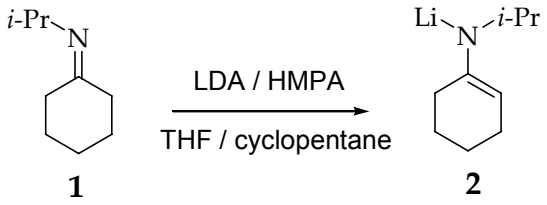


VIII. Plot of k_{obsd} vs [LDA] for the lithiation of imine **1-d_4** (0.005 M) in 0.70 M free HMPA /THF (8.0 M)/cyclopentane at -40 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{LDA}]^n$ ($k = (6.0 \pm 0.4) \times 10^{-4}$, $n = 0.58 \pm 0.04$).

[LDA] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.05	0.93 ± 0.05	1.24 ± 0.06	1.1 ± 0.2
0.10	1.40 ± 0.08	1.31 ± 0.04	1.36 ± 0.06
0.15	2.35 ± 0.07	1.88 ± 0.06	2.1 ± 0.3
0.20	2.5± 0.2	2.40 ± 0.07	2.45 ± 0.07
0.25	2.80 ± 0.01	2.6 ± 0.1	2.7 ± 0.1
0.30	3.0 ± 0.1	2.8 ± 0.2	2.9 ± 0.1
0.35	2.9 ± 0.1	3.63 ± 0.07	3.3 ± 0.5



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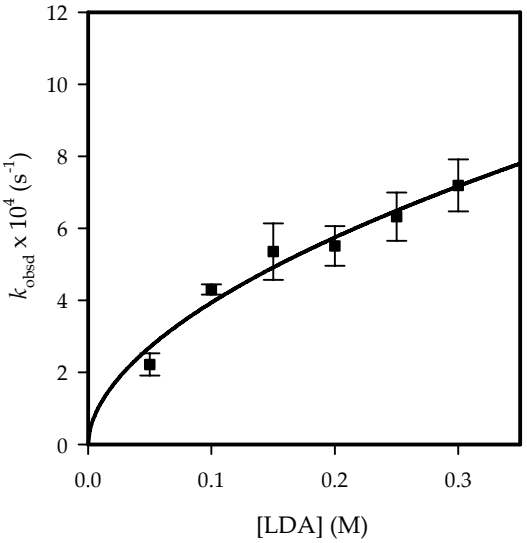
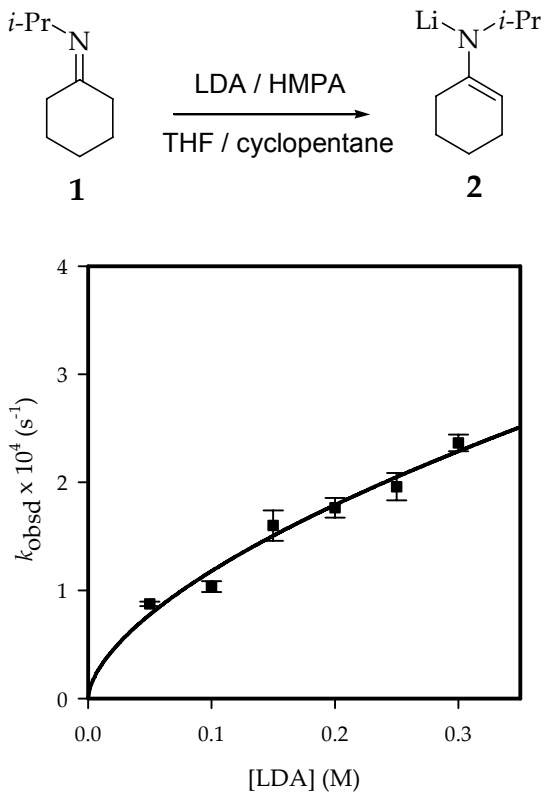


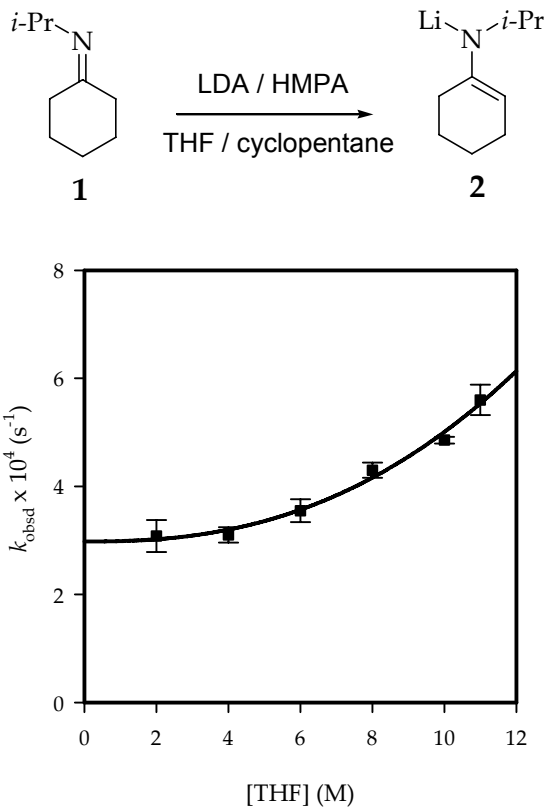
IX. Plot of k_{obsd} vs [LDA] for the lithiation of imine **1** (0.005 M) in 0.40 M free HMPA /THF (8.0 M)/cyclopentane at -55 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{LDA}]^n$ ($k = (1.4 \pm 0.2) \times 10^{-3}$, $n = 0.54 \pm 0.07$).

[LDA] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.050	2.00 ± 0.05	2.44 ± 0.02	2.2 ± 0.3
0.100	4.4 ± 0.1	4.20 ± 0.02	4.3 ± 0.1
0.150	4.8 ± 0.1	5.91 ± 0.08	5.4 ± 0.8
0.200	5.12 ± 0.08	5.90 ± 0.08	5.5 ± 0.6
0.250	6.80 ± 0.01	5.85 ± 0.01	6.4 ± 0.7
0.300	6.68 ± 0.01	7.70 ± 0.02	7.2 ± 0.7



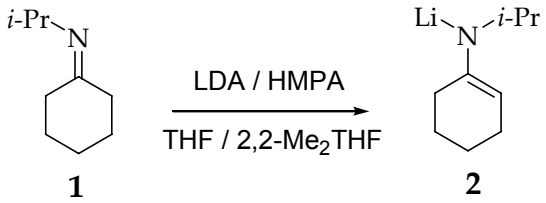
X. Plot of k_{obsd} vs [LDA] for the lithiation of imine **1** (0.005 M) in 0.10 M free HMPA/THF (8.0 M)/cyclopentane at -55 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{LDA}]^n$ ($k = (4.7 \pm 0.5) \times 10^{-4}$, $n = 0.60 \pm 0.07$).

[LDA] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.050	0.86 ± 0.01	0.89 ± 0.01	0.88 ± 0.02
0.100	1.00 ± 0.02	1.07 ± 0.01	1.04 ± 0.05
0.150	1.70 ± 0.01	1.50 ± 0.03	1.6 ± 0.1
0.200	1.83 ± 0.01	1.70 ± 0.03	1.77 ± 0.09
0.250	1.87 ± 0.02	2.05 ± 0.03	2.0 ± 0.1
0.300	2.31 ± 0.03	2.42 ± 0.05	2.37 ± 0.08

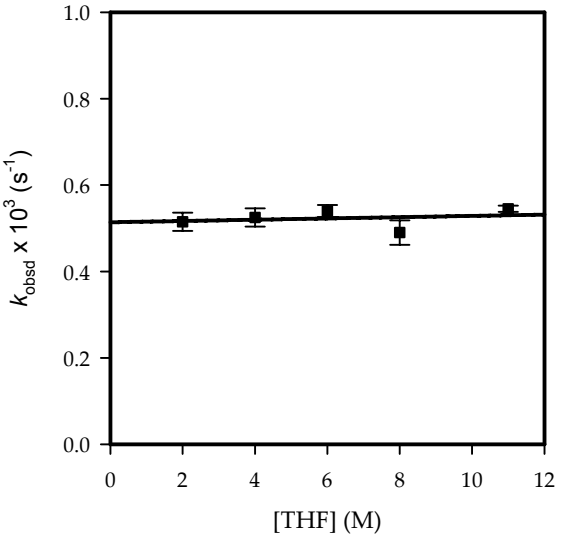


XI. Plot of k_{obsd} vs [THF] for the lithiation of imine **1** (0.005 M) by 0.10 M LDA in 0.50 M free HMPA/cyclopentane at -55 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[THF]^n + k'$ (k = (7.6 ± 0.8) x 10^{-7}, k' = (3.0 ± 0.1) x 10^{-4}, n = 2.4 ± 0.4).

[THF] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
2.00	3.29 ± 0.02	2.87 ± 0.02	3.1 ± 0.3
4.00	3.00 ± 0.02	3.20 ± 0.05	3.1 ± 0.1
6.00	3.70 ± 0.04	3.40 ± 0.03	3.6 ± 0.2
8.00	4.40 ± 0.01	4.20± 0.02	4.3 ± 0.1
10.0	4.90 ± 0.04	4.81 ± 0.03	4.86 ± 0.07
11.0	5.40 ± 0.01	5.80± 0.04	5.6 ± 0.3

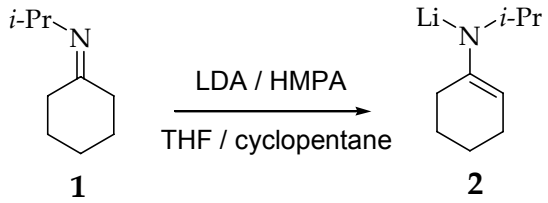


1 **2**

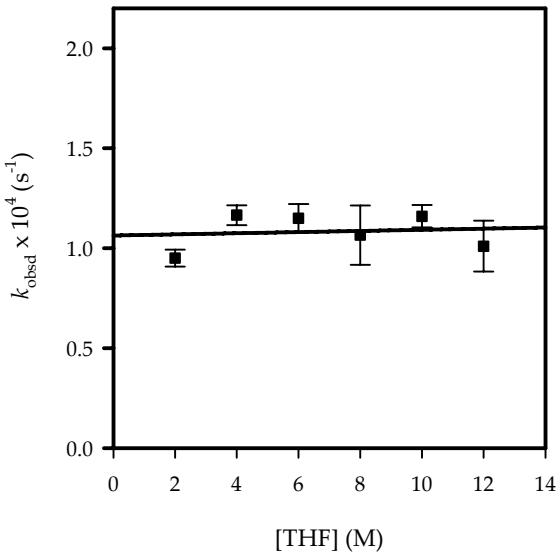


XII. Plot of k_{obsd} vs [THF] for the lithiation of imine **1** (0.005 M) by 0.10 M LDA in in 0.50 M free HMPA/2,5-Me_2THF at -55 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[THF] + k'$ ($k = (1.5 \pm 0.3) \times 10^{-6}$, $k' = (5.1 \pm 0.2) \times 10^{-4}$).

[THF] (M)	$k_{obsd\ 1} \times 10^3$ (s^{-1})	$k_{obsd\ 2} \times 10^3$ (s^{-1})	k_{obsd} (avg) $\times 10^3$ (s^{-1})
2.00	0.53 ± 0.01	0.50 ± 0.02	0.52 ± 0.02
4.00	0.51 ± 0.02	0.54 ± 0.02	0.53 ± 0.02
6.00	0.53 ± 0.01	0.55 ± 0.02	0.54 ± 0.01
10.0	0.47 ± 0.02	0.51 ± 0.01	0.49 ± 0.03
11.0	0.55 ± 0.02	0.54 ± 0.02	0.55 ± 0.01

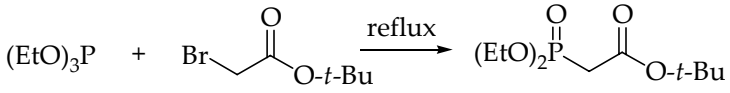


1 **2**



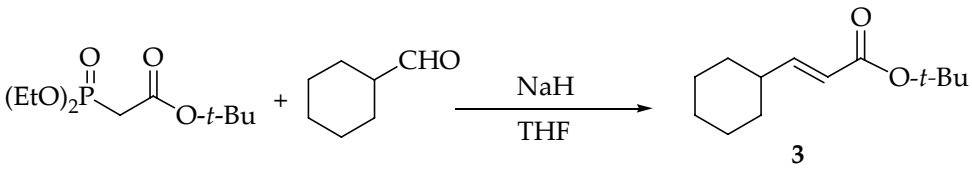
XIII. Plot of k_{obsd} vs [THF] for the lithiation of imine **1** (0.005 M) by 0.10 M LDA in 0.10 M free HMPA/cyclopentane at -55 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[THF] + k'$ ($k = (2.9 \pm 0.1) \times 10^{-6}$, $k' = (1.1 \pm 0.1) \times 10^{-4}$).

[THF] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
2.00	0.92 ± 0.01	0.98 ± 0.02	0.95 ± 0.04
4.00	1.20 ± 0.02	1.13 ± 0.02	1.17 ± 0.05
6.00	1.20 ± 0.02	1.10 ± 0.02	1.15 ± 0.07
8.00	1.00 ± 0.02	1.07 ± 0.01	1.04 ± 0.05
10.0	1.20 ± 0.02	1.12 ± 0.01	1.16 ± 0.06
12.0	0.92 ± 0.02	1.10 ± 0.02	1.0 ± 0.1



XIV. Synthesis of *t*-butyl triethylphosphonoacetate

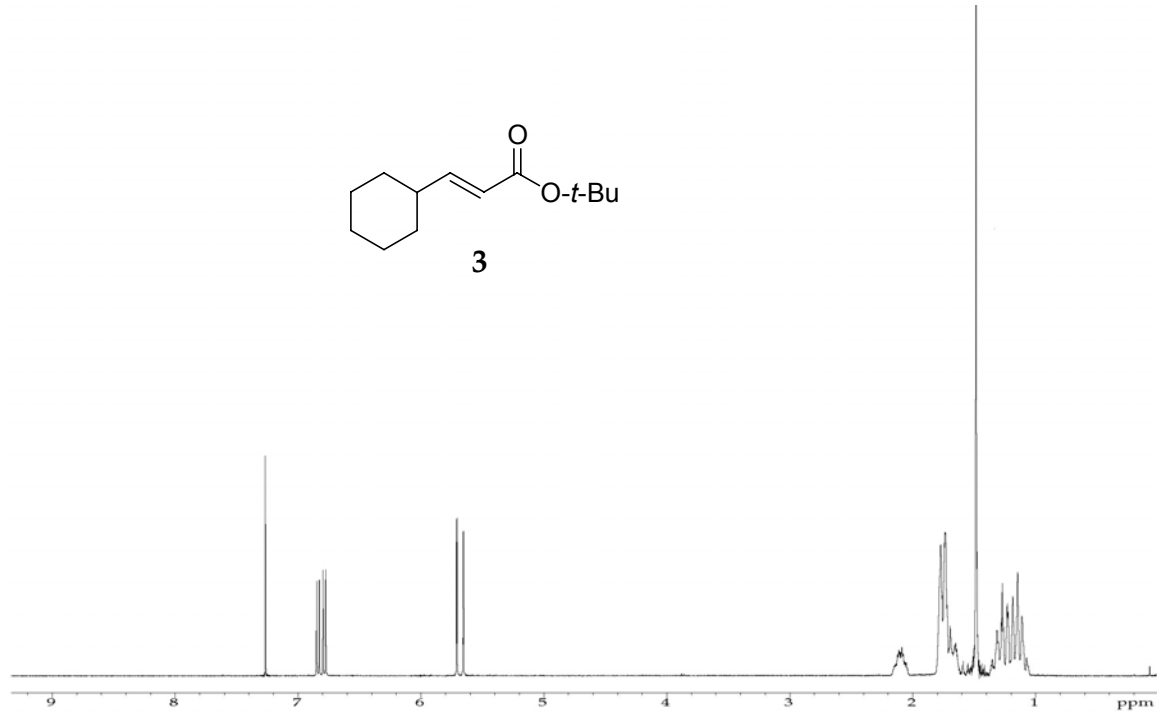
Triethylphosphite (10.6 g, 64.0 mmol) was added to *t*-butyl bromoacetate (12.5 g, 64.0 mmol) and heated to 100 ˚C for 1 h and heated to reflux for 3 h. After reaction was completed, fractional distillation under full vacuum gave *t*-butyl triethylphosphonoacetate (14.5 g, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (3H, d, *J* = 9.0 Hz), 2.28 (2H, d, *J* = 21.0 Hz), 1.35 (6H, t, *J* = 9.0 Hz), 1.45 (9H, s).

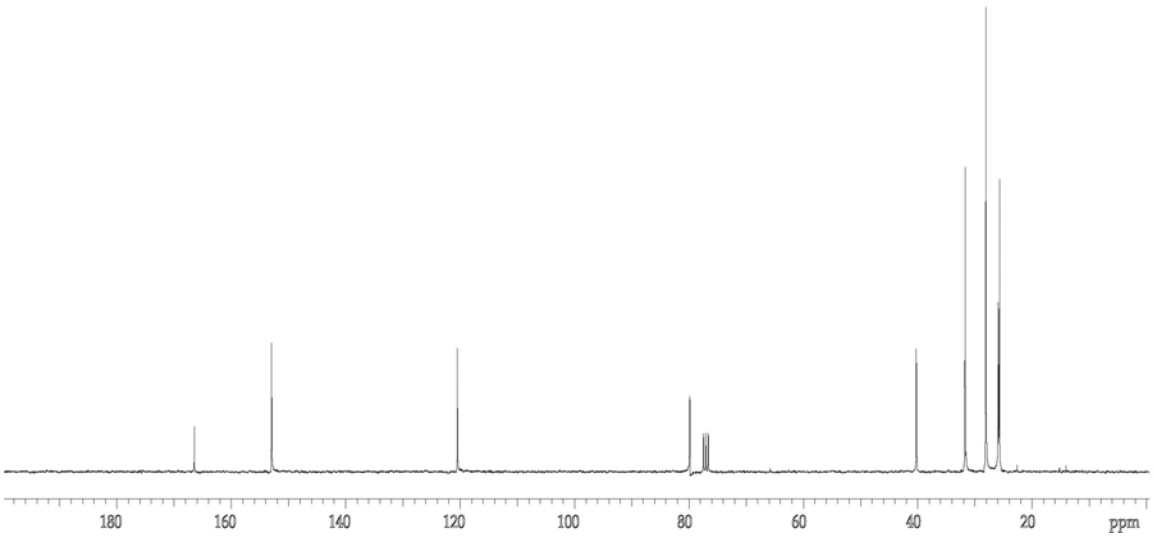


3

XV. Synthesis of *t*-butyl 3-cyclohexylpropionate **3**

t-Butyl triethylphosphonoacetate (6.3 g, 25.0 mmol) in 30 mL of THF was added dropwise to a slurry of 50% sodium hydride (1.2 g, 25.0 mmol) in 50 mL of dry THF at 0 ˚C. The solution was stirred for 1 h at room temperature until hydrogen gas evolution ceased. Cyclohexane carboxaldehyde (2.8 g, 25.0 mmol) was added dropwise using a cold water-bath to keep the internal reaction temperature below 30 ˚C. After stirring for 3 h, 50 mL of water was added to the mixture. The aqueous layer was extracted with diethyl ether (3 x 10 mL). The combined organic layers were dried with $MgSO_4$. After the solvent was removed, the remaining residue was fractionally distilled to give the crude product. Flash chromatography (3% EtOAc/hexane) afforded *t*-butyl-3-cyclohexylpropionate (4.4 g, 84% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (1H, dd, *J* = 16.0, 5.8 Hz), 5.64 (1H, dd, *J* = 16.0, 5.8 Hz), 2.01 (1H, m), 1.66 (4H, s), 1.40 (9H, s), 1.16-1.26 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 152.9, 120.5, 79.8, 40.2, 31.7, 28.1, 25.9, 25.6; MS *m*/*z* 210 (M^+), 154, 137, 73, 57(100), 41.



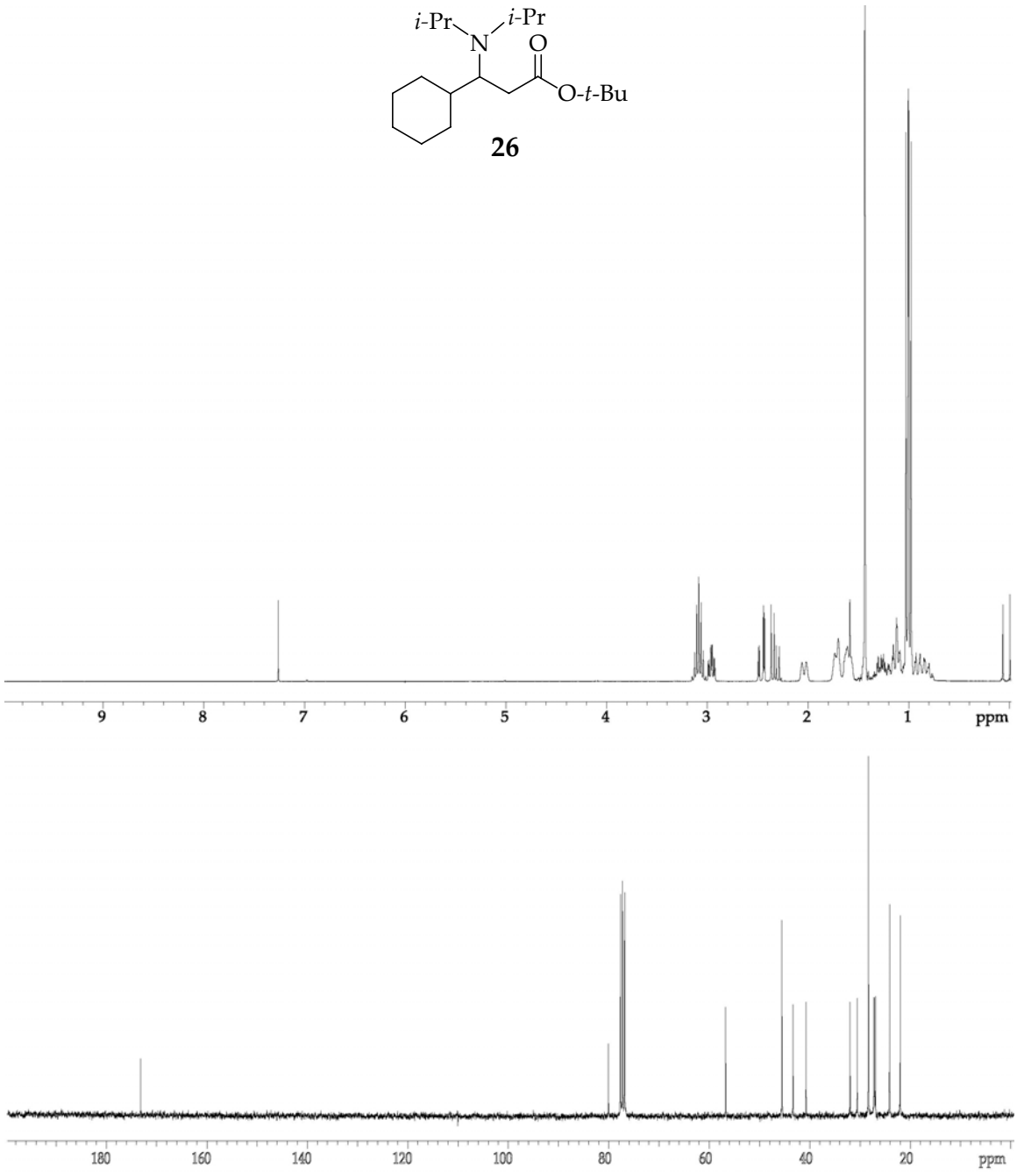


XVI. ^{1}H and ^{13}C NMR Spectra of **3**

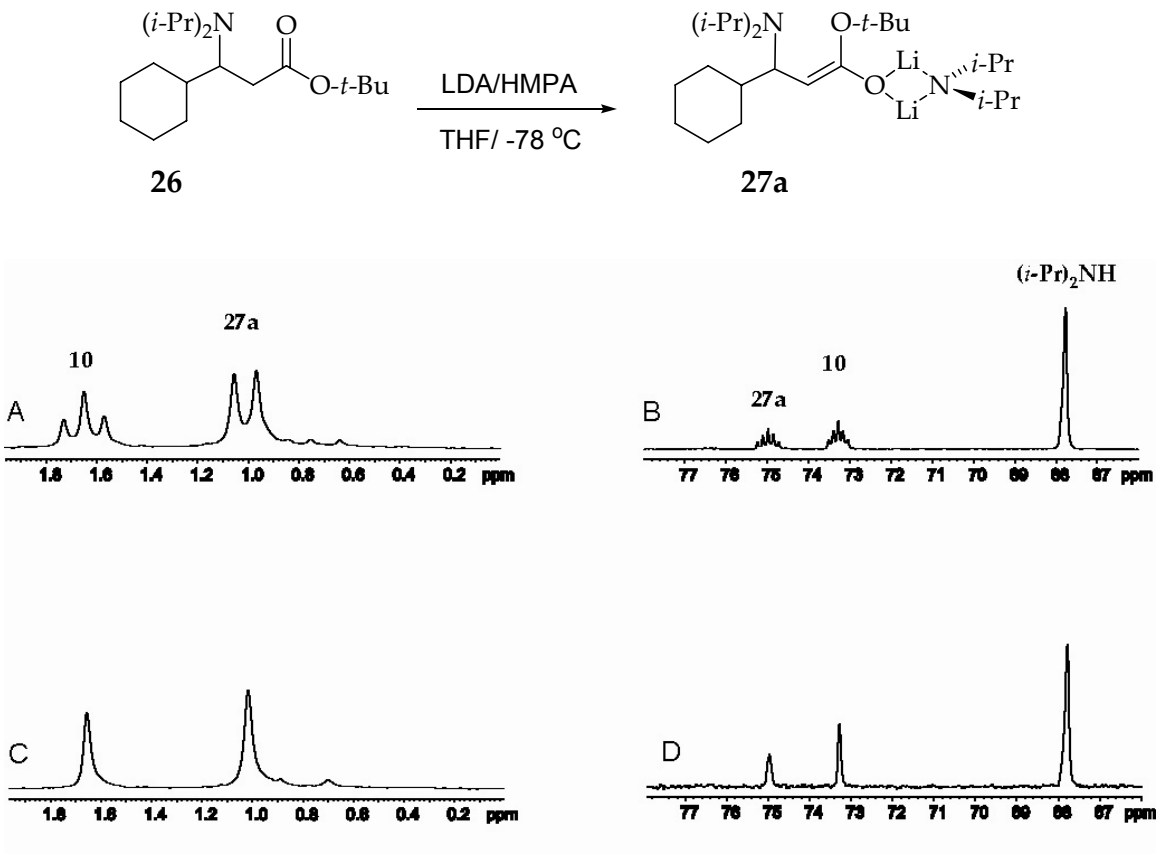
3 **26**

XVII. Synthesis of *t*-butyl 3-cyclohexyl-3-*N*,*N*-diisopropylaminopropionate **26**

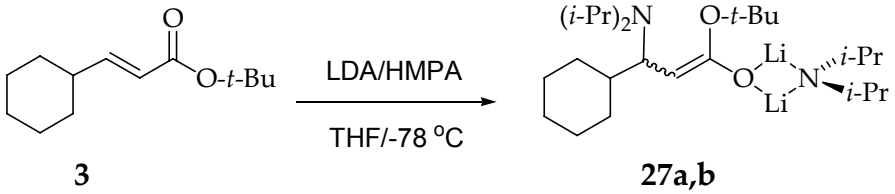
t-Butyl-β-cyclohexylpropiolate (0.63 g, 3.0 mmol) in 3 mL of THF was added to LDA (0.64 g, 6.0 mmol) in 15 mL of THF at -78 °C. The solution was stirred for 30 min and then warmed to room temperature with stirring for 1 h. 10 mL of water was added to the mixture. The aqueous layer was extracted with diethyl ether (3 x 10 mL). After the solvent was removed in vacuo, the remaining residue was dissolved in CH_2Cl_2 (5 mL). The solution was washed with 4.0 M HCl (3 x 3 mL). The aqueous layer was neutralized with 10% NaOH, and extracted with diethyl ether (3 x 3 mL). The combined organic layers were dried with $MgSO_4$. The solvent was removed. Flash chromatography (30% EtOAc/hexane) afforded *t*-butyl 3-cyclohexyl-3-*N*,*N*-diisopropylaminopropionate **26** (0.68 g, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.08 (2H, m), 2.95 (1H, t, d, *J* = 9.0, 3.0 Hz), 2.36 (2H, m), 2.15 (1H, m), 1.54 (9H, s), 1.25 (5H, m), 1.03 (6H, d, *J* = 6.6 Hz), 0.98 (6H, d, *J* = 6.6 Hz), 0.88 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 80.1, 56.7, 45.5, 43.3, 40.7, 31.9, 30.5, 28.3, 27.2, 27.1, 26.9, 24.1, 22.0; MS *m*/*z* 311 (M^+), 228, 172(100), 130, 70, 57.



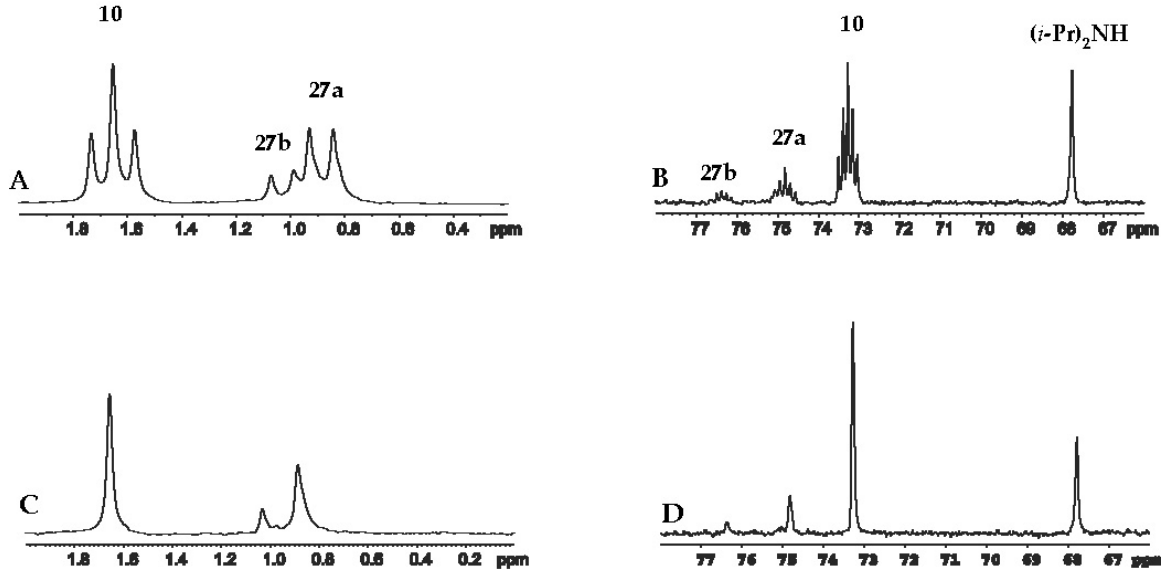
XVIII. ^{1}H and ^{13}C NMR Spectra of **26**



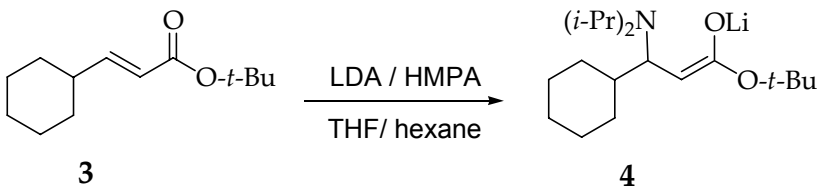
XIX. ^{6}Li and ^{15}N NMR spectra of 0.10 M [^{6}Li,^{15}N]LDA with 0.25 equiv amine **26** in 0.40 M HMPA /10.0 M THF/ pentane at -90 ˚C after aging at -78 ˚C for 60 min: (A) ^{6}Li spectrum; (B) ^{15}N spectrum; (C) ^{6}Li{^{15}N} spectrum; (D) ^{15}N{^{6}Li} spectrum.



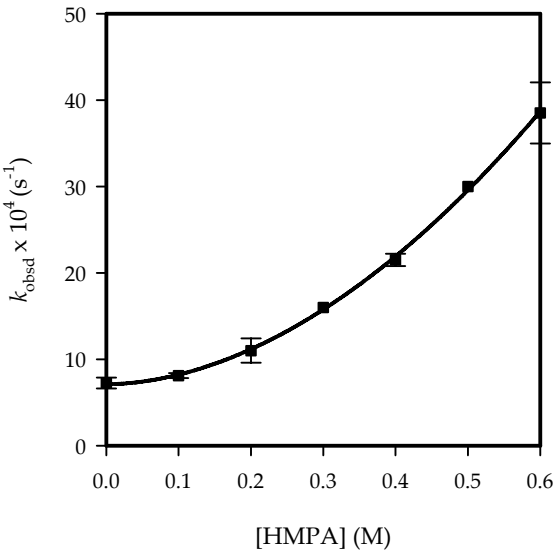
3 **27a,b**



XX. ^{6}Li and ^{15}N NMR spectra of 0.10 M [^{6}Li,^{15}N]LDA with 0.25 equiv ester **3** in 0.40 M HMPA /10.0 M THF/ pentane at -90 ˚C after aging at -78 ˚C for 60 min: (A) ^{6}Li spectrum; (B) ^{15}N spectrum; (C) ^{6}Li{^{15}N} spectrum; (D) ^{15}N{^{6}Li} spectrum.



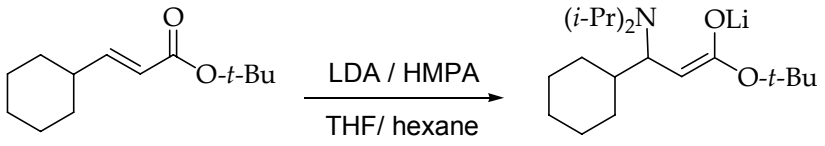
3 **4**



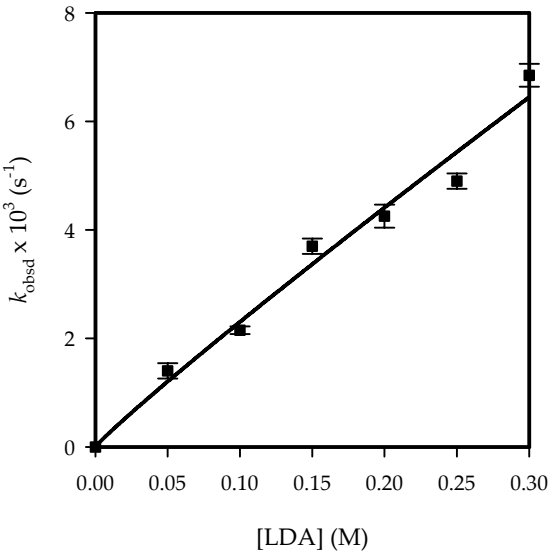
XXI. Plot of k_{obsd} vs [HMPA] for the Michael addition of 0.10 M LDA to ester **3** (0.004 M) in THF (10.0 M)/hexane at -78 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{HMPA}]^n + k'$ ($k = (7.1 \pm 0.3) \times 10^{-3}$, $k' = (8.2 \pm 0.2) \times 10^{-2}$, $n = 1.87 \pm 0.06$).

[HMPA] (M)[a]	$k_{obsd\,1}$ x 10^4 (s^{-1})	$k_{obsd\,2}$ x 10^4 (s^{-1})	k_{obsd} (avg) (s^{-1})
0.00	6.8 ± 0.1	7.7 ± 0.1	7.3 ± 0.6
0.10	6.9 ± 0.2	8.3 ±0.2	8.1 ± 0.3
0.20	12.0 ± 0.5	10.0 ± 1	11 ± 1
0.30	16 ± 1	16 ± 2	16 ± 0.7
0.40	22 ± 1	21 ± 1	21.5 ± 1
0.50	28 ± 2	28 ± 2	28 ± 1
0.60	41 ± 1	36 ± 2	40 ± 1

[a][HMPA] refers to the concentration of free (uncoordinated) HMPA.

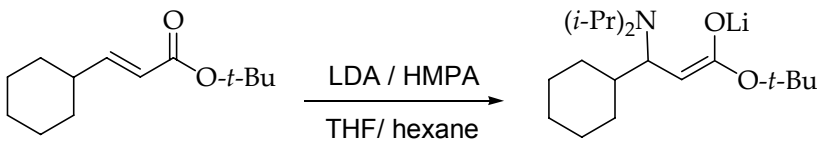


3 **4**

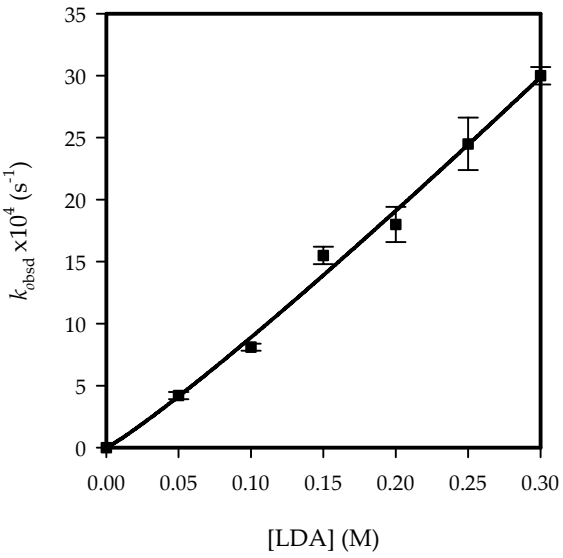


XXII. Plot of k_{obsd} vs [LDA] for the Michael addition of LDA to ester **3** (0.004 M) in 0.40 M free HMPA/THF (10.0 M)/hexane at -78 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{LDA}]^n$ ($k = (2.0 \pm 0.3) \times 10^{-1}$, $n = 1.0 \pm 0.1$).

[LDA] (M)	$k_{obsd\ 1} \times 10^3$ (s^{-1})	$k_{obsd\ 2} \times 10^3$ (s^{-1})	k_{obsd} (avg) $\times 10^3$ (s^{-1})
0.05	1.5 ± 0.2	1.3 ± 0.1	1.4 ± 0.1
0.10	2.1 ± 0.1	2.2 ± 0.2	2.15 ± 0.07
0.15	3.8 ± 0.1	3.6 ± 0.1	3.7 ± 0.1
0.20	4.4 ± 0.2	4.1 ± 0.1	4.3 ± 0.2
0.25	5.0 ± 0.1	4.8 ± 0.2	4.9 ± 0.1
0.30	7.0 ± 0.1	6.7 ± 0.1	6.9 ± 0.2

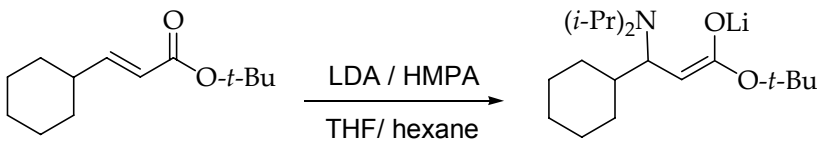


3 **4**

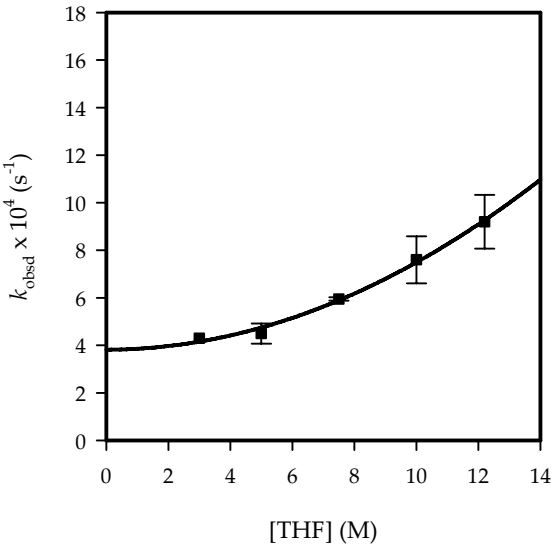


XXIII. Plot of k_{obsd} vs [LDA] for the Michael addition of 0.10 M LDA to ester **3** (0.004 M) in 0.10 M free HMPA/THF (10.0 M)/hexane at -78 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{LDA}]^n$ ($k = (1.1 \pm 0.1) \times 10^{-2}$, $n = 1.10 \pm 0.06$).

[LDA] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.05	4.0 ± 0.1	4.4 ± 0.1	4.2 ± 0.3
0.10	7.9 ± 0.2	8.3 ± 0.1	8.1 ± 0.3
0.15	16 ± 1	15 ± 1	15.5 ± 0.7
0.20	19 ± 2	17 ± 2	18 ± 1
0.25	26 ± 1	23 ± 1	24.5 ± 2.0
0.30	30 ± 2	29 ± 2	30.0 ± 0.7

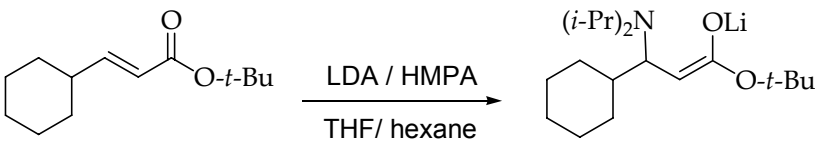


3 **4**

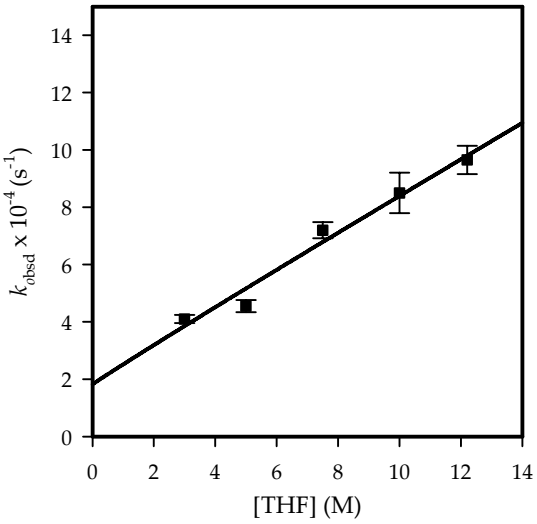


XXIV. Plot of k_{obsd} vs [THF] for the Michael addition to ester **3** (0.004M) by 0.10 M LDA in 0.10 M free HMPA/hexane at -78 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[THF]^n + k'$ ($k = (3.8 \pm 0.5) \times 10^{-6}$, $k' = (3.8 \pm 0.3) \times 10^{-4}$, $n = 2.0 \pm 0.4$).

[THF] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
3.0	4.3 ± 0.1	4.3 ± 0.1	4.3 ± 0.1
5.0	4.8 ± 0.2	4.2 ± 0.2	4.5 ± 0.4
7.5	6.0 ± 0.1	5.9 ± 0.1	5.95 ± 0.07
10.0	8.3 ± 0.2	6.9 ± 0.1	7.6 ± 0.9
12.2	1.0 ± 0.2	8.4 ± 0.1	9.2 ± 1.0

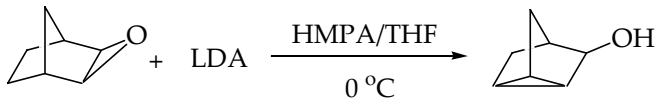


3 **4**



XXV. Plot of k_{obsd} vs [THF] for the Michael addition of 0.10 M LDA to ester **3** (0.004M) in 0.10 M free HMPA/2,5-Me_2THF at -78 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[THF] + k'$ ($k = (1.5 \pm 0.3) \times 10^{-7}$, $k' = (5.1 \pm 0.2) \times 10^{-5}$).

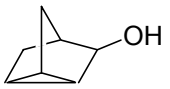
[THF] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
3.0	4.2 ± 0.1	4.0 ± 0.1	4.3 ± 0.1
5.0	4.4 ± 0.2	4.7 ± 0.2	4.6 ± 0.2
7.5	7.0 ± 0.1	7.5 ± 0.1	7.2 ± 0.3
10.0	8.0 ± 0.1	9.0 ± 0.1	8.5 ± 0.7
12.2	10.0 ± 0.2	9.3 ± 0.3	9.7 ± 0.5



5 **6**

XXVI. Synthesis of alcohol **6**

Exo-2,3-Epoxynorbornane (1.10 g, 10.0 mmol) in 10 mL of THF was added to LDA (1.27 g, 12.0 mmol) in 50 mL of THF and HMPA (48.0 mmol) at 0 ˚C. The solution was stirred for 1 hr and then. 10 mL of water was added to the mixture. The aqueous layer was extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with water (3 x 15 mL), dried with $MgSO_4$. The solvent was removed. Flash chromatography (40% EtOAc/hexane) afforded alcohol **6** (0. 88g, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.82 (1H, s), 1.80 (1H, s), 1.76 (1H, m), 1.22 (7H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 77.8, 35.8, 30.8, 29.5, 16.4, 13.8 10.8; MS *m*/*z* 110 (M^+), 91, 79, 66(100), 55.



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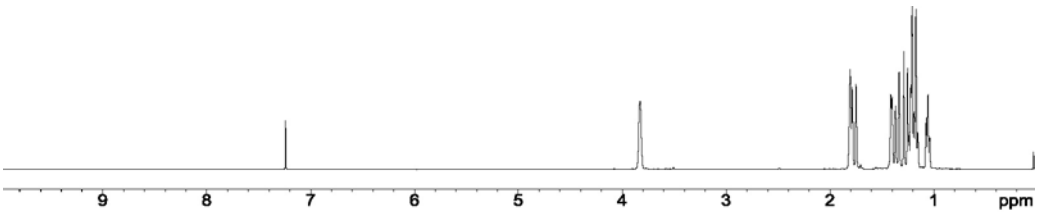
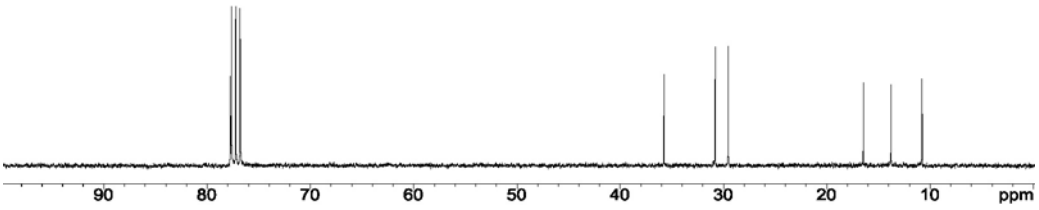
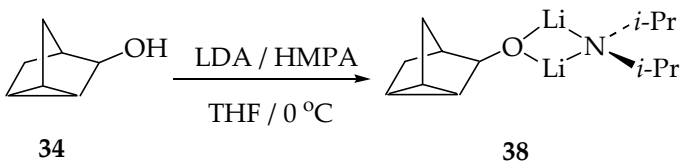
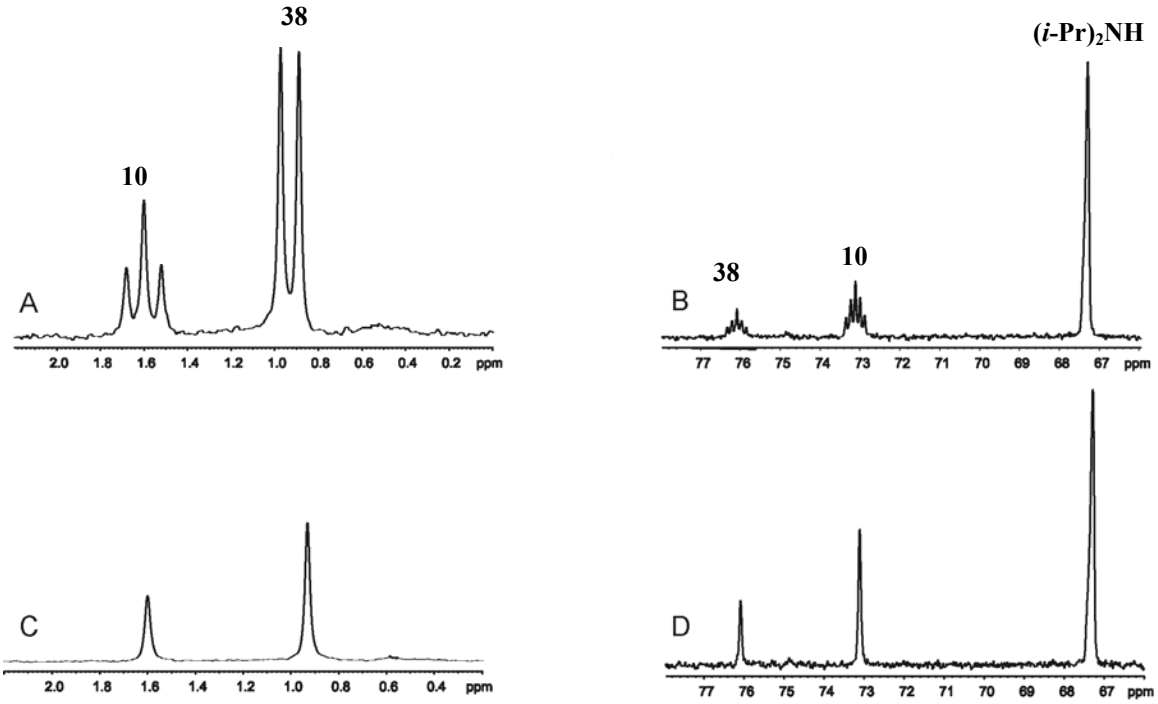




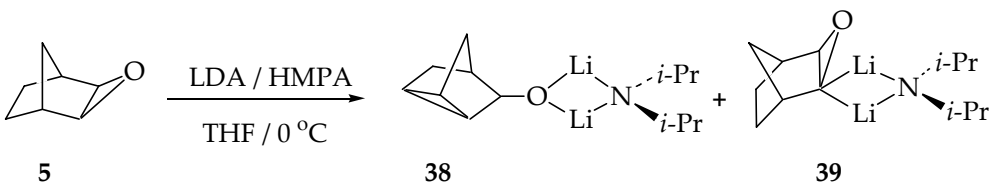
XXVII ^{1}H and ^{13}C NMR Spectra of **34**



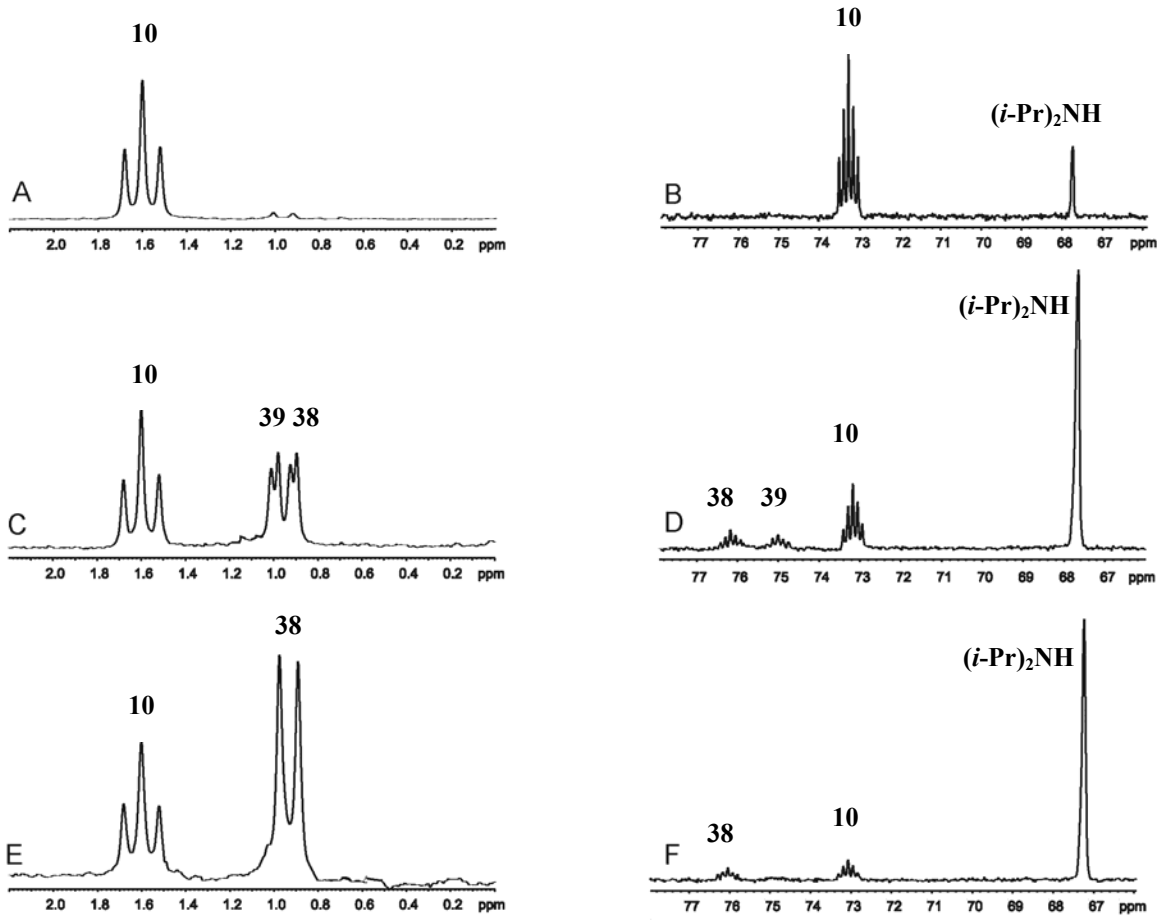
34 **38**



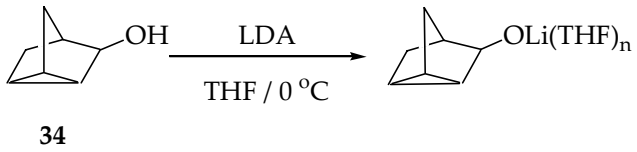
XXVIII. ^{6}Li and ^{15}N NMR spectra of 0.10 M [^{6}Li,^{15}N]LDA with 0.25 equiv alcohol **34** in 0.40 M free HMPA /10.0 M THF/pentane at -90 ˚C after aging at 0 ˚C for 50 min: A) ^{6}Li spectrum; (B) ^{15}N spectrum; (C) ^{6}Li{^{15}N} spectrum; (D) ^{15}N{^{6}Li} spectrum.



5 **38** **39**



XXIX ^{6}Li and ^{15}N NMR spectra of 0.10 M [^{6}Li,^{15}N]LDA with 0.25 equiv *exo*-2,3-epoxynorbornane **5** in 0.40 M HMPA /10.0 M THF/pentane at -90 ˚C before aging at 0 ˚C: (A) ^{6}Li spectrum; (B) ^{15}N spectrum; after aging at 0 ˚C for 45 min: (C) ^{6}Li spectrum; (D) ^{15}N spectrum; after aging at 0 ˚C for 90 min: (E) ^{6}Li spectrum; (F) ^{15}N spectrum.



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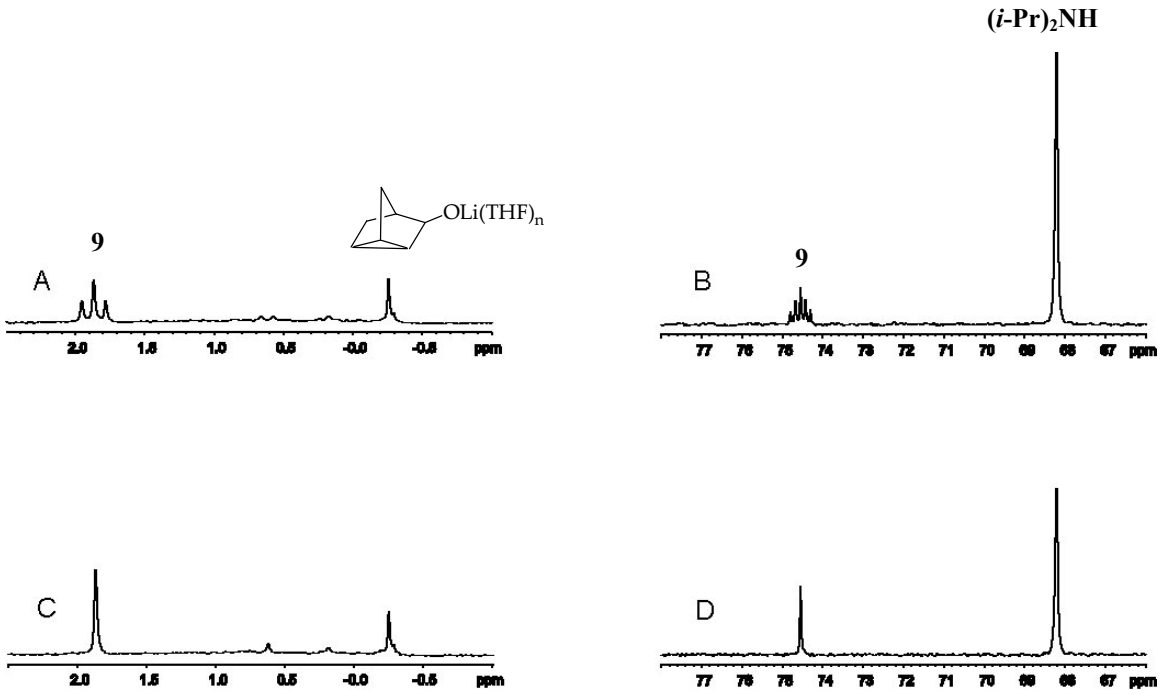
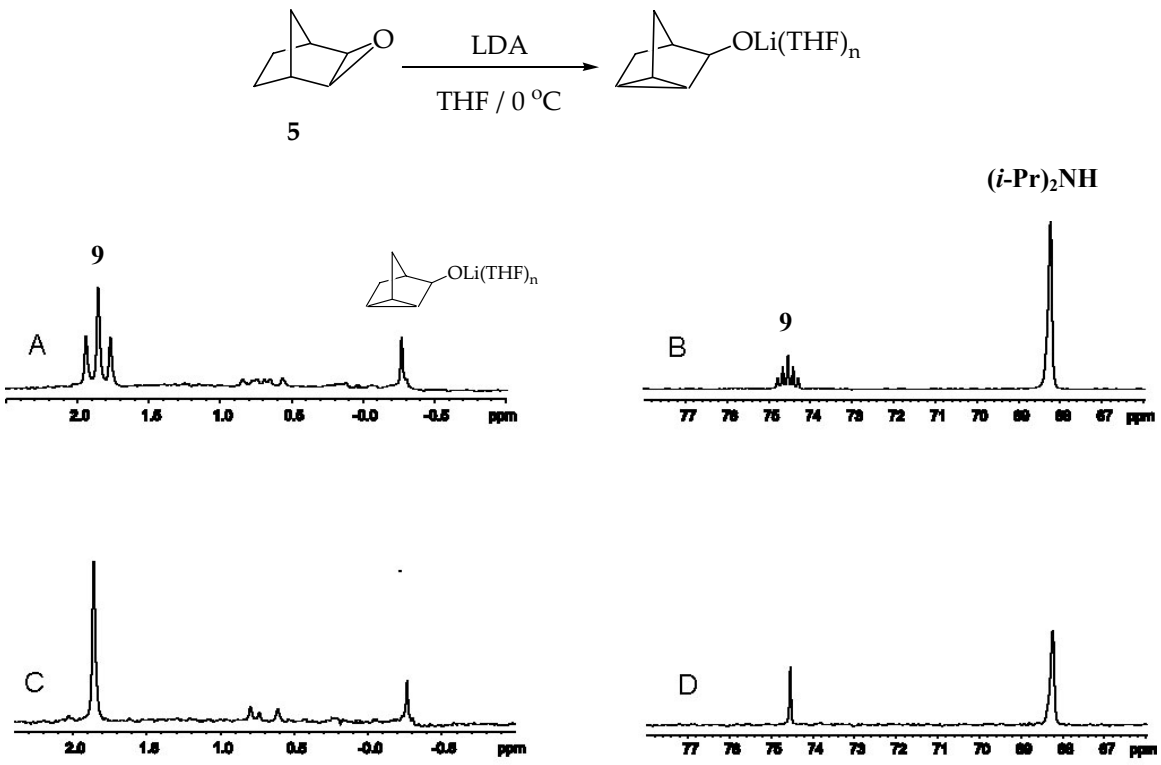
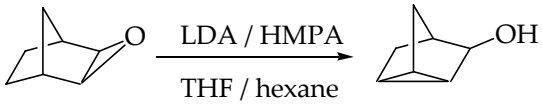


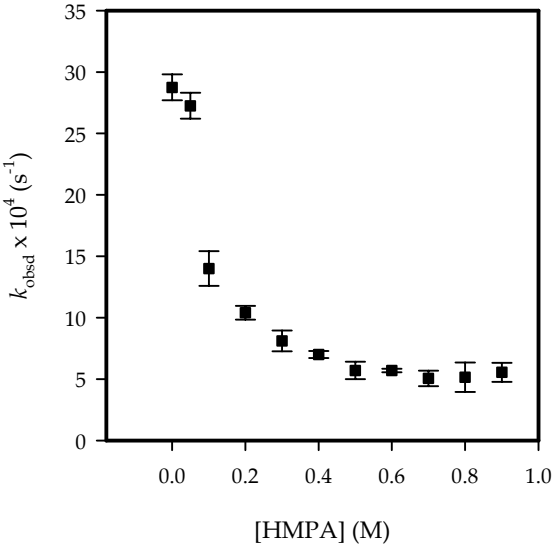
XXX. ^{6}Li and ^{15}N NMR spectra of 0.10 M [^{6}Li,^{15}N]LDA with 0.25 equiv alcohol **34** in 10.0 M THF/pentane at -90 ˚C after aging at 0 ˚C for 60 min:
(A) ^{6}Li spectrum; (B) ^{15}N spectrum; (C) ^{6}Li{^{15}N} spectrum; (D) ^{15}N{^{6}Li} spectrum.



XXXI. ^{6}Li and ^{15}N NMR spectra of 0.10 M [^{6}Li,^{15}N]LDA with 0.25 equiv *exo*-2,3-epoxynorbornane **5** in 10.0 M THF/pentane at -90 ˚C after aging at 0 ˚C for 60 min: (A) ^{6}Li spectrum; (B) ^{15}N spectrum; (C) ^{6}Li{^{15}N} spectrum; (D) ^{15}N{^{6}Li} spectrum.



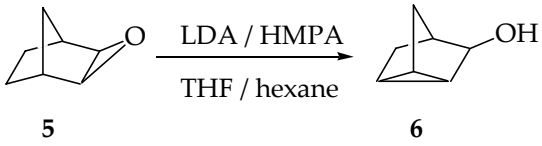
5 **6**



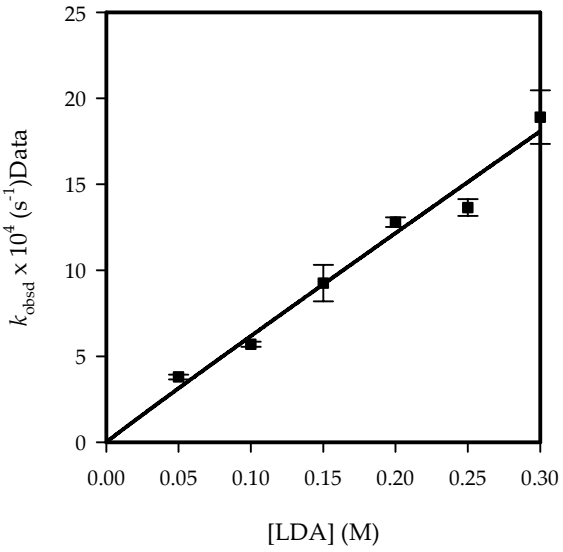
XXXII. Plot of k_{obsd} vs [HMPA] for the deprotonation of *exo*-2,3-epoxynorbornane **5** (0.004 M) by 0.10 M LDA in THF (10.0 M)/hexane at 0 ˚C.

[HMPA] (M)[a]	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.00	28.0 ± 0.1	29.5 ± 0.2	29 ± 1
0.05	26.5 ± 0.2	28.0 ± 0.2	27.3 ± 1.3
0.10	13.0 ± 0.2	15.0 ± 0.1	14 ± 1
0.20	10.0 ± 0.1	10.8 ± 0.2	10.4 ± 0.6
0.30	7.5 ± 0.2	8.7 ± 0.2	8.1 ± 0.8
0.40	6.8 ± 0.2	7.2 ± 0.1	7.0 ± 0.3
0.50	6.2 ± 0.2	5.2 ± 0.3	5.7 ± 0.7
0.60	5.6 ± 0.1	5.8 ± 0.2	5.7 ± 0.1
0.70	4.6 ± 0.2	5.5 ± 0.1	5.1 ± 0.6
0.80	6.0 ± 0.2	4.3 ± 0.1	5.2 ± 1.1
0.90	6.1 ± 0.1	5.0 ± 0.1	5.6 ± 0.8

[a][HMPA] refers to the concentration of total HMPA.

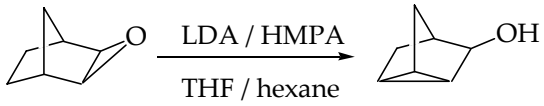


5 **6**



XXXIII. Plot of k_{obsd} vs [LDA] for the deprotonation of *exo-2,3*-epoxynorbornane **5** (0.004 M) in 0.50 M free HMPA/THF (10.0 M)/hexane at 0 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{LDA}]^n$ ($k = (5.8 \pm 0.9) \times 10^{-3}$, $n = 1.0 \pm 0.1$).

[LDA] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.05	3.7 ± 0.1	3.9 ± 0.2	3.8 ± 0.1
0.10	5.6 ± 0.2	5.8 ± 0.2	5.7 ± 0.1
0.15	8.5 ± 0.1	10.0 ± 0.1	9 ± 1
0.20	12.6 ± 0.4	13.0 ± 0.1	12.8 ± 0.3
0.25	13.3 ± 0.3	14 ± 1	13.7 ± 0.5
0.30	17.8 ± 0.2	20.2 ± 0.2	19 ± 2



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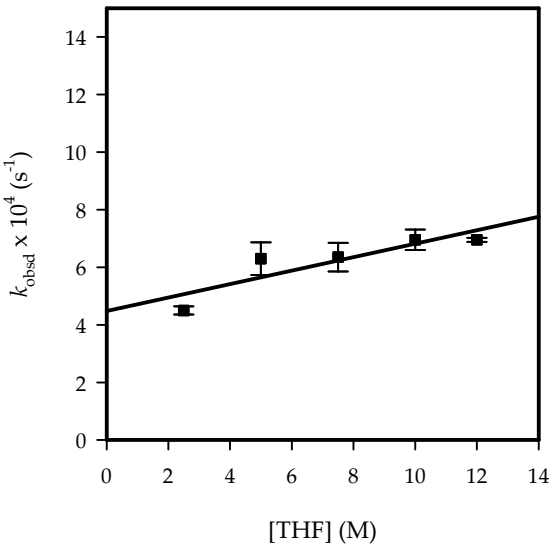
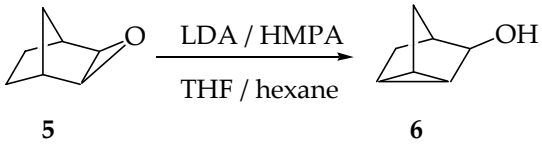


XXXIV. Plot of k_{obsd} vs [THF] for the deprotonation of *exo*-2,3-epoxynorbornane **5** (0.004 M) by 0.10 M LDA in 0.30 M free HMPA/hexane at 0 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[THF] + k'$ ($k = (2.3 \pm 0.1) \times 10^{-5}$, $k' = (4.5 \pm 0.6) \times 10^{-4}$).

[THF] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
2.5	4.4 ± 0.1	4.6 ± 0.1	4.5 ± 0.1
5.0	6.7 ± 0.2	5.9 ± 0.2	6.3 ± 0.6
7.5	6.0 ± 0.1	6.7 ± 0.1	6.4 ± 0.5
10.0	6.7 ± 0.2	7.2 ± 0.3	7.0 ± 0.4
12.2	7.0 ± 0.2	6.9 ± 0.2	6.95 ± 0.07



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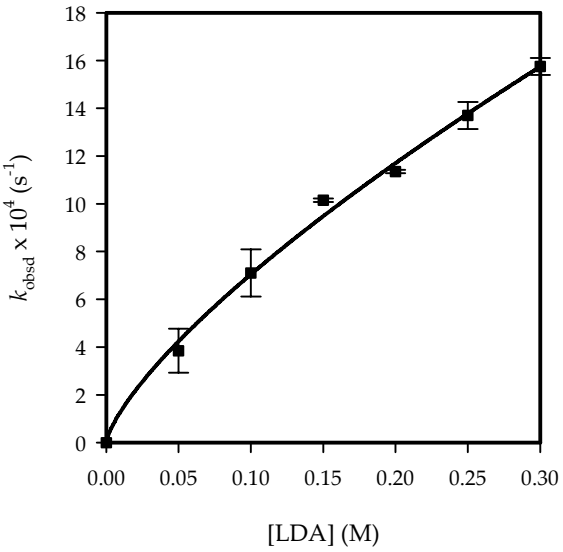
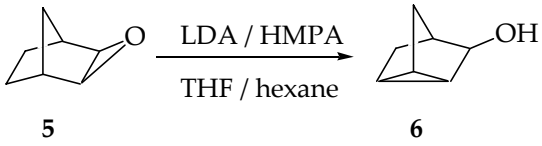
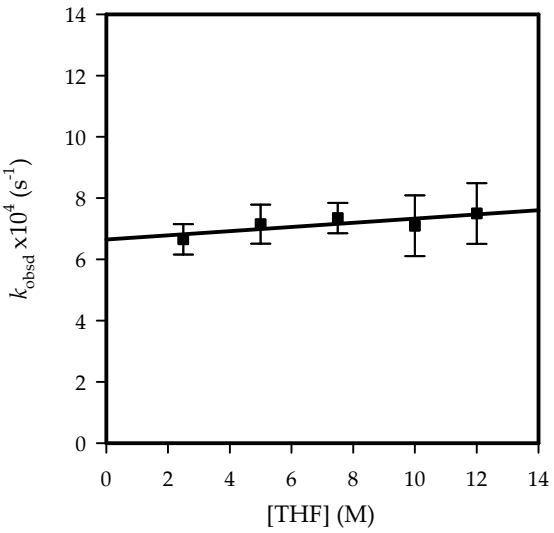


XXXV. Plot of k_{obsd} vs [LDA] for the deprotonation of *exo*-2,3-epoxynorbornane **5** (0.004 M) in THF (10.0 M)/hexane at -15 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[LDA]^n$ ($k = (3.8 \pm 0.2) \times 10^{-3}$, $n = 0.73 \pm 0.04$).

[LDA] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.05	3.2 ± 0.1	4.5 ± 0.2	3.9 ± 0.9
0.10	6.4 ± 0.4	7.8 ± 0.2	7.1 ± 0.9
0.15	10.1 ± 0.1	10.2 ± 0.1	10.15 ± 0.07
0.20	11.3 ± 0.4	11.4 ± 0.2	11.35 ± 0.07
0.25	13.3 ± 0.1	14.1 ± 0.1	13.7 ± 0.6
0.30	15.5 ± 0.2	16.0 ± 0.2	15.8 ± 0.4

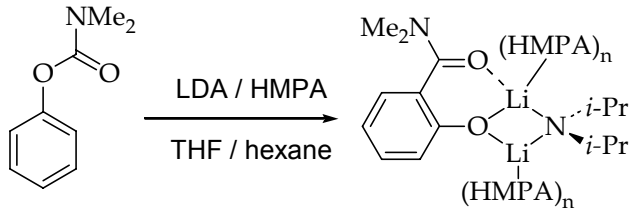


5 **6**

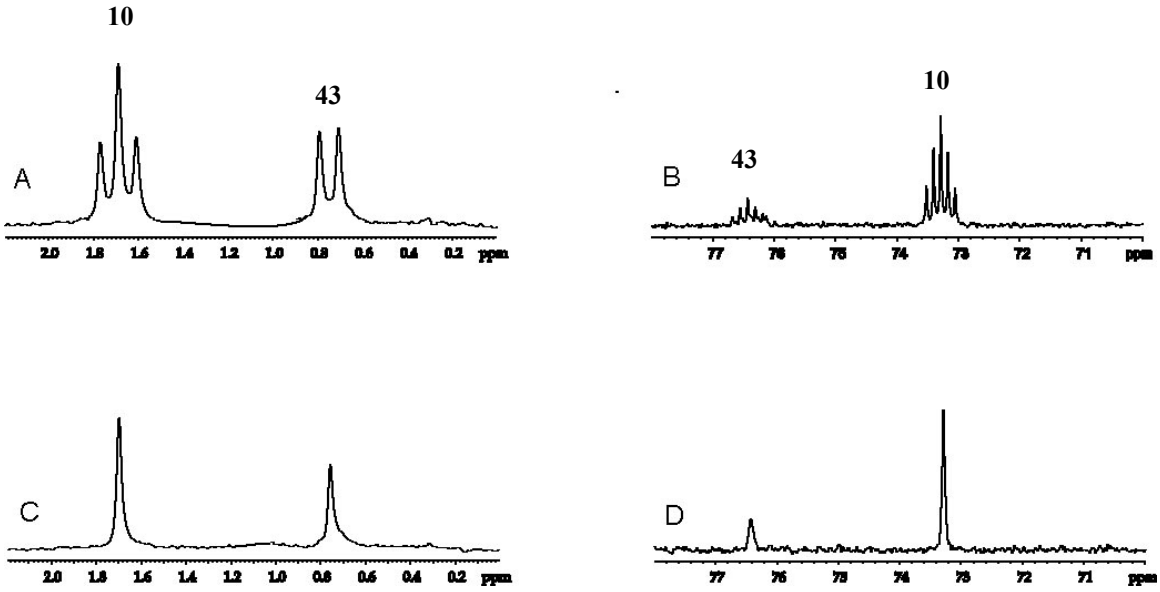


XXXVI. Plot of k_{obsd} vs [THF] for the deprotonation of *exo*-2,3-epoxynorbornane **5** (0.004M) by 0.10 M LDA in hexane at -15 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[THF]^n + k'$ (k = (6.6 ± 0.2) x 10^{-4}, k' = (6.8 ± 0.35) x 10^{-6}).

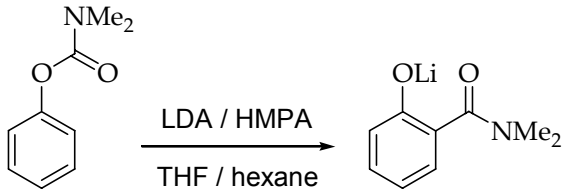
[THF] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
2.5	7.0 ± 0.2	6.3 ± 0.2	6.7 ± 0.5
5.0	6.7 ± 0.2	7.6 ± 0.2	7.2 ± 0.6
7.5	7.0 ± 0.1	7.7 ± 0.1	7.4 ± 0.5
10.0	6.4 ± 0.4	7.8 ± 0.3	7.1 ± 0.9
12.2	8.4 ± 0.2	6.8 ± 0.2	7.5 ± 0.9



7 **43**



XXXVII. ^{6}Li and ^{15}N NMR spectra of 0.10 M [^{6}Li,^{15}N]LDA with 0.25 equiv carbamate **7** in 0.40 M HMPA /10.0 M THF/pentane at ˚C after aging at -40 ˚C for 60 min: (A) ^{6}Li spectrum; (B) ^{15}N spectrum; (C) $^{6}Li\{^{15}N\}$ spectrum; (D) $^{15}N\{^{6}Li\}$ spectrum.



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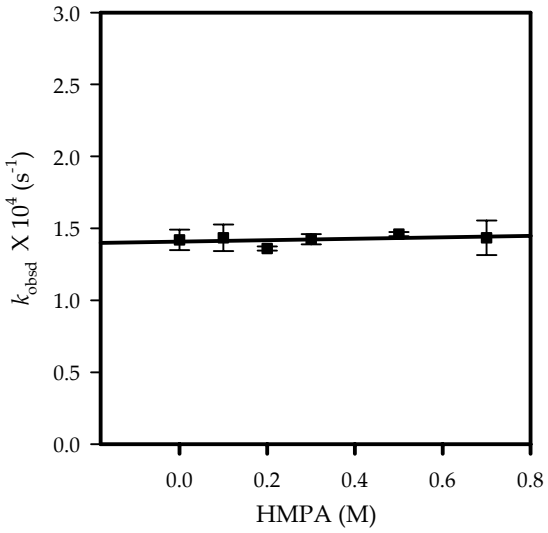
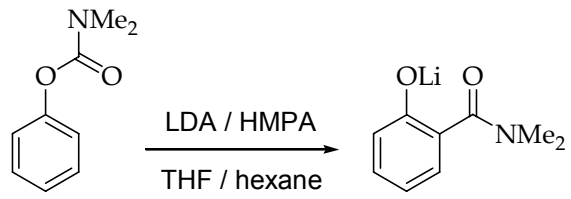


XXXVIII. Plot of k_{obsd} vs [HMPA] for the ortholithiation of carbamate **7** (0.004 M) by 0.10 M LDA in THF (10.0 M)/hexane at -40 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k$[HMPA] + k' (k = (2.45 ± 0.06) x 10^{-3}, k' = (1.11 ± 0.01) x 10^{-4}).

[HMPA] (M)[a]	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.00	1.37 ± 0.01	1.47 ± 0.02	1.42 ± 0.07
0.10	1.37 ± 0.02	1.50 ± 0.01	1.44 ± 0.09
0.20	1.45 ± 0.01	1.37 ± 0.02	1.36 ± 0.01
0.30	1.45± 0.02	1.40 ± 0.02	1.43 ± 0.04
0.50	1.45 ± 0.02	1.47 ± 0.01	1.46 ± 0.01
0.70	1.35 ± 0.01	1.35 ± 0.01	1.4 ± 0.1

[a][HMPA] refers to the concentration of free (uncoordinated) HMPA.



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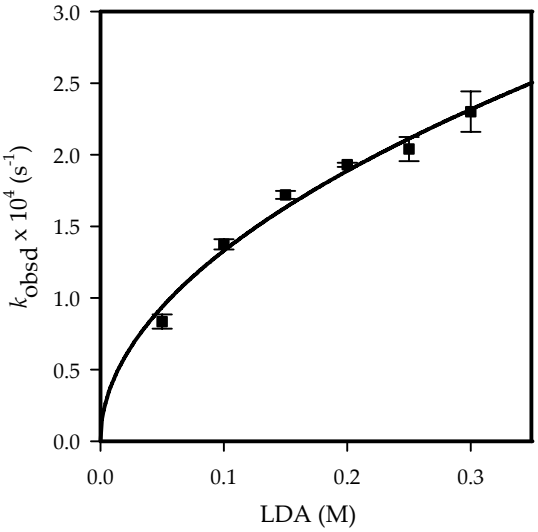
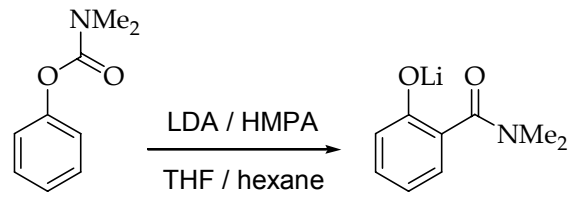


XXXIX. Plot of k_{obsd} vs [LDA] for ortholithiation of carbamate **7** (0.004 M) in 0.20 M free HMPA/THF (10.0 M)/hexane at -40 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{LDA}]^n$ ($k = (4.3 \pm 0.3) \times 10^{-3}$, $n = 0.51 \pm 0.04$).

[LDA] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
0.05	0.87 ± 0.01	0.80 ± 0.02	0.84 ± 0.05
0.10	1.35 ± 0.02	1.40 ± 0.02	1.37 ± 0.04
0.15	1.74 ± 0.01	1.70 ± 0.01	1.72 ± 0.03
0.20	1.92 ± 0.01	1.94 ± 0.01	1.93 ± 0.01
0.25	1.98 ± 0.01	2.10 ± 0.01	2.04 ± 0.08
0.30	2.20 ± 0.02	2.40 ± 0.01	2.30 ± 0.14



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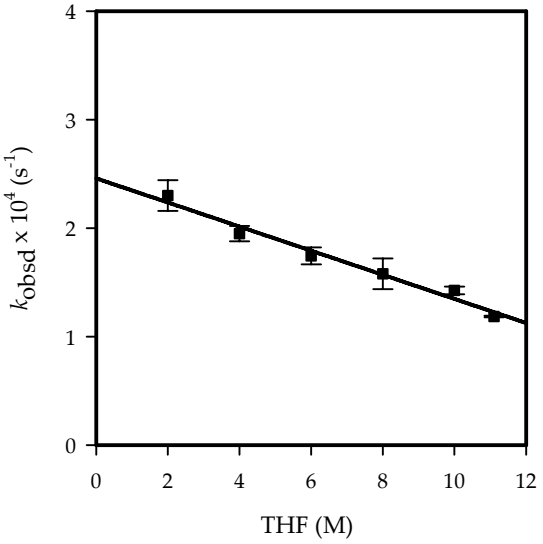

XXXX. Plot of k_{obsd} vs [THF] for ortholithiation of carbamate **7** (0.004 M) by 0.10 M LDA in 0.30 M free HMPA/hexane at -40 ˚C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[THF] + k'$ ($k = (1.1 \pm 0.1) \times 10^{-4}$, $k' = (2.45 \pm 0.06) \times 10^{-3}$).

[THF] (M)	$k_{obsd\ 1}$ x 10^4 (s^{-1})	$k_{obsd\ 2}$ x 10^4 (s^{-1})	k_{obsd} (avg) x 10^4 (s^{-1})
2.0	2.20 ± 0.01	2.40 ± 0.01	2.3 ± 0.1
4.0	2.00 ± 0.02	1.90 ± 0.02	1.95 ± 0.07
6.0	1.68 ± 0.01	1.48 ± 0.01	1.58 ± 0.1
8.0	1.69 ± 0.01	1.80 ± 0.01	1.43 ± 0.04
10.0	1.45 ± 0.02	1.40 ± 0.01	1.19 ± 0.01
11.1	1.19 ± 0.02	1.18 ± 0.02	1.75 ± 0.08