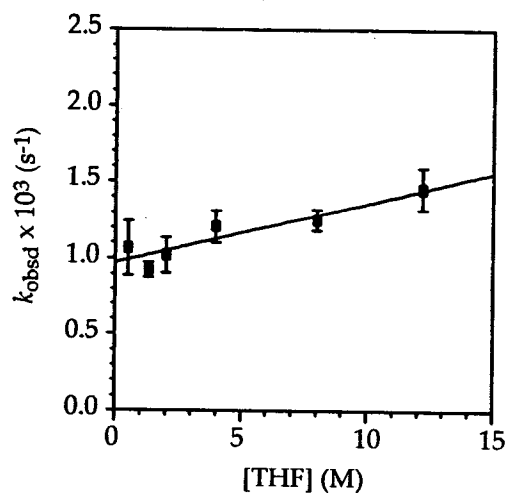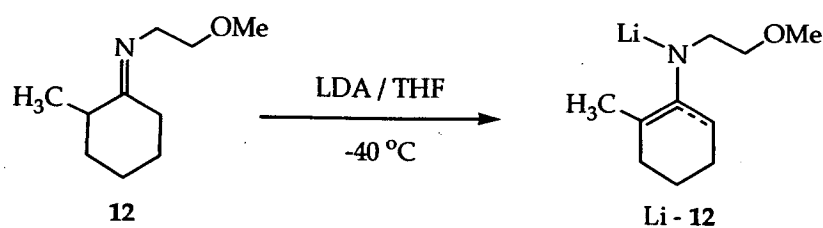XXXIV. Plot of k_{obsd} vs [LDA] in neat THF (12.3 M) for the lithiation of **11** $(0.005\ M)^a$ at -65 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[LDA]^n$ ($k = 4.0 \pm 0.2 \times 10^{-3}$, $n = 0.57 \pm 0.05$).
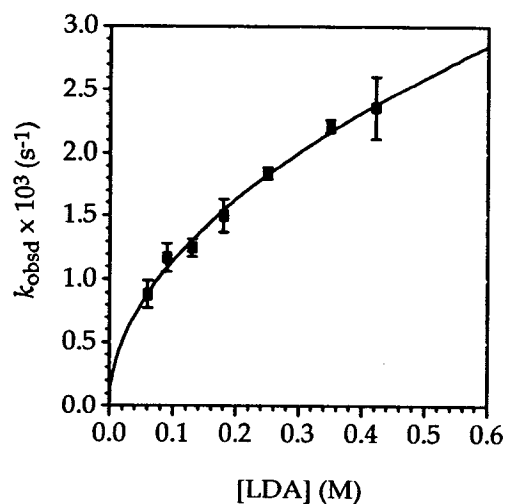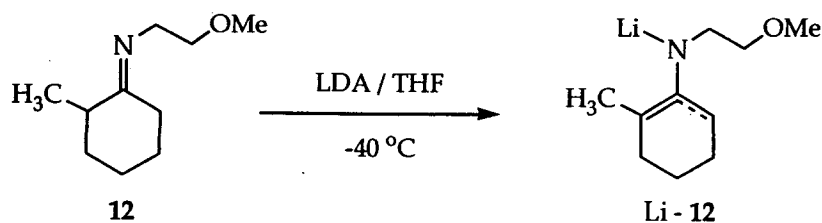
[LDA] (M)	k_{obsd} x 10^3 (s^{-1})		Average k_{obsd} x 10^3 (s^{-1})
0.044	0.52(2)	0.60(3)	0.56
0.074	0.93(4)	0.83(4)	0.88
0.124	1.12(2)	1.27(2)	1.20
0.194	1.8(3)	1.5(2)	1.7
0.294	2.2(2)		2.2
0.394	2.3(2)		2.3
0.494	2.6(3)		2.6

^{a}Imine **11** is generated in situ by alkylating lithiated **3** (Li-**3** 0.006 M) with CH$_3$I (0.005 M) at -65 °C.

XXXV. Plot of k_{obsd} vs free [THF] in hexane cosolvent for the lithiation of **12** (0.005 M) by LDA (0.13 M) at -40 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k$[THF] $+ k'$ ($k = 3.9 \pm 0.7 \times 10^{-5}$, $k' = 0.97 \pm 0.05 \times 10^{-3}$).

[THF] (M)	$k_{obsd} \times 10^3$ (s^{-1})		Average $k_{obsd} \times 10^3$ (s^{-1})
0.50	1.19(3)	0.94(1)	1.07
1.31	0.89(2)	0.96(1)	0.93
2.00	1.10(3)	0.94(1)	1.02
4.00	1.28(6)	1.13(1)	1.21
8.00	1.30(3)	1.20(3)	1.25
12.2	1.55(4)	1.36(4)	1.46

XXXVI. Plot of k_{obsd} vs [LDA] in THF (8.0 M) and hexane cosolvent for the lithiation of **12** (0.005 M) at -40 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[LDA]^n$ ($k = 3.7 \pm 0.1 \times 10^{-3}$, $n = 0.51 \pm 0.02$).
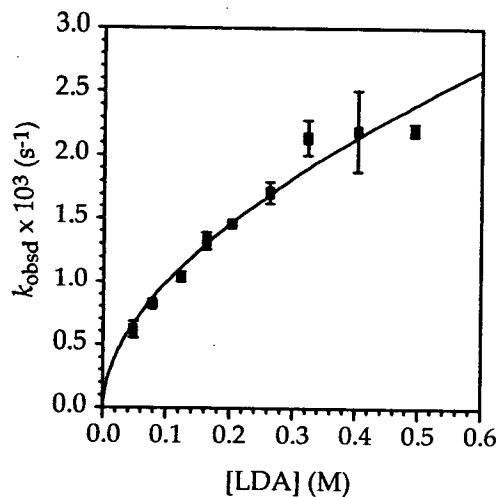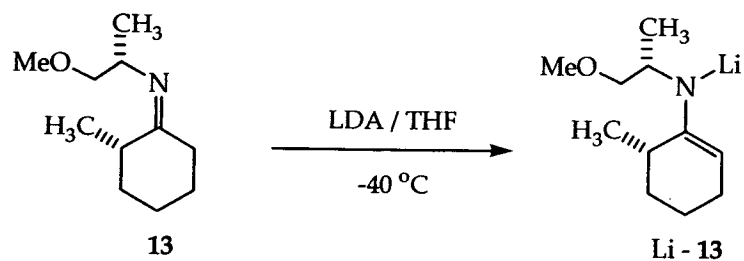
[LDA] (M)	$k_{obsd} \times 10^3$ (s^{-1})		Average $k_{obsd} \times 10^3$ (s^{-1})
0.060	0.95(2)	0.80(2)	0.88
0.090	1.09(2)	1.25(3)	1.17
0.130	1.20(3)	1.30(3)	1.25
0.180	1.59(4)	1.41(4)	1.50
0.250	1.82(6)	1.87(6)	1.84
0.350	2.24(8)	2.17(7)	2.21
0.422	2.18(4)	2.5 (1)	2.4
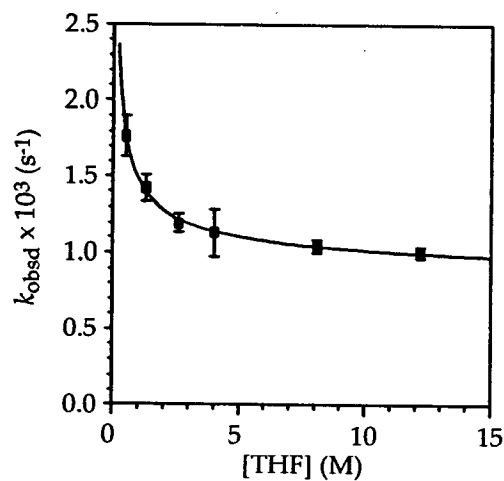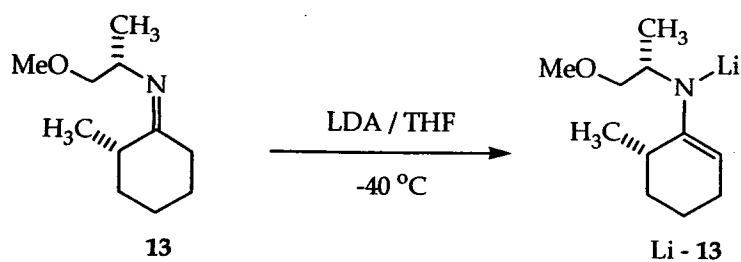
XXXVII. Plot of k_{obsd} vs free [THF] in hexane cosolvent for the lithiation of **13** (0.005 M)^a by LDA (0.123M) at -40 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{THF}]^n + k'$ ($k = 6.6 \pm 0.8 \times 10^{-4}$, $k' = 8.2 \pm 0.7 \times 10^{-4}$, $n = -0.53 \pm 0.08$).

[THF] (M)	$k_{obsd} \times 10^3$ (s^{-1})		Average $k_{obsd} \times 10^3$ (s^{-1})
0.50	1.86(7)	1.67(20)	1.77
1.31	1.36(3)	1.48(3)	1.42
2.55	1.15(2)	1.24(2)	1.20
3.98	1.02(5)	1.24(3)	1.13
8.09	1.07(2)	1.01(3)	1.04
12.2	1.03(2)	0.98(2)	1.01

^{a}Imine **13** (**13**:**15** = 6:1) is generated in situ by alkylating lithiated **4** (Li-**4** 0.007 M) with CH$_3$I (0.005 M) at -40 °C.

XXXVIII. Plot of k_{obsd} vs [LDA] in THF (8.0 M) and hexane cosolvent for the lithiation of **13** (0.005 M)[a] at -40 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[LDA]^n$ ($k = 3.5 \pm 0.2 \times 10^{-3}$, $n = 0.55 \pm 0.05$).

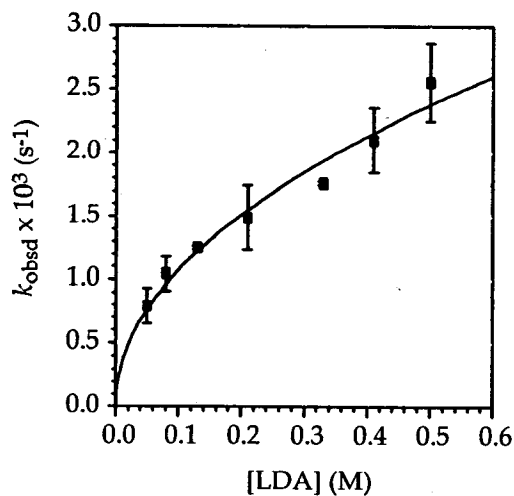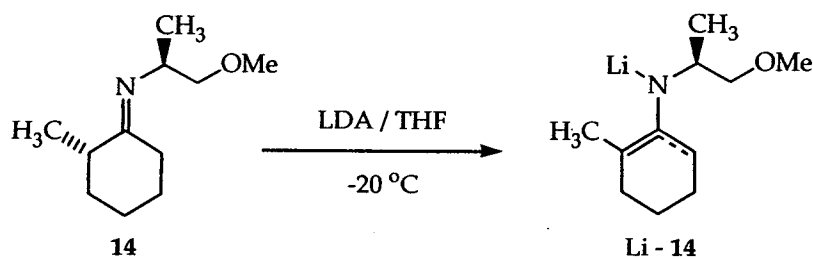| [LDA] (M)	$k_{obsd} \times 10^3$ (s^{-1})		Average $k_{obsd} \times 10^3$ (s^{-1})
0.048	0.57(2)	0.66(1)	0.62
0.078	0.83(3)	0.82(2)	0.83
0.123	1.07(2)	1.01(3)	1.04
0.163	1.37(5)	1.28(3)	1.33
0.203	1.45(4)	1.47(5)	1.46
0.263	1.8(2)	1.65(8)	1.7
0.323	2.2(2)	2.0(1)	2.1
0.403	2.4(1)	1.95(8)	2.2
0.493	2.2(2)	2.16(9)	2.2

[a]Imine **13** (6:1 dr) is generated in situ by alkylating lithiated **4** (Li-**4** 0.007 M) with CH_3I (0.005 M) at -40 °C.
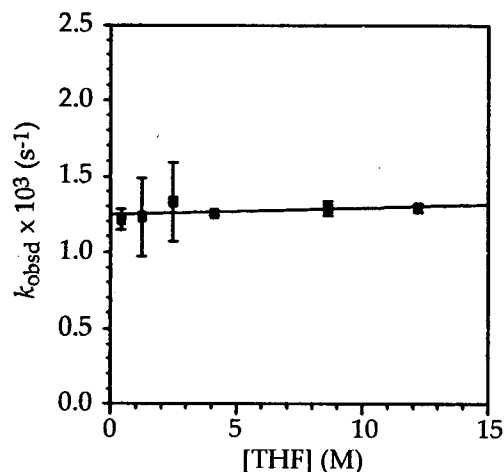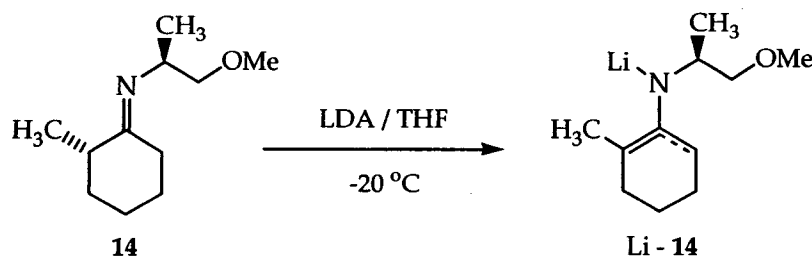
XXXIX. Plot of k_{obsd} vs free [THF] in hexane cosolvent for the lithiation of **14** (0.005 M)^a by LDA (0.13 M) at -20 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[\text{THF}] + k'$ ($k = 4 \pm 4 \times 10^{-6}$, $k' = 1.24 \pm 0.03 \times 10^{-3}$).

[THF] (M)	$k_{obsd} \times 10^3$ (s^{-1})			Average $k_{obsd} \times 10^3$ (s^{-1})
0.28	1.26(5)	1.16(4)		1.21
1.10	1.52(6)	1.02(5)	1.15(3)	1.23
2.34	1.18(2)	1.63(6)	1.18(3)	1.33
3.98	1.26(4)	1.24(4)		1.25
8.50	1.32(6)	1.25(5)		1.29
12.2	1.31(5)	1.27(3)		1.29

^{a}The lithiation of a 1:10:1:10 mixture of **13:14:15:16** (total concentration 0.005 M) at -20 °C stops at 50~60% conversion, which represents the lithiations of **13**, **14** and **15**. The calculated k_{obsd} is used as that of **14** since both **13** and **15** react at similar rates as **14** and constitute < 20% of the reacting species. (See Figure 2A in the text.)

XL. Plot of k_{obsd} vs [LDA] in THF (4.0 M) and hexane cosolvent for the lithiation of **14** (0.005 M)[a] at -20 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[LDA]^n$ ($k = 3.4 \pm 0.2 \times 10^{-3}$, $n = 0.50 \pm 0.05$).

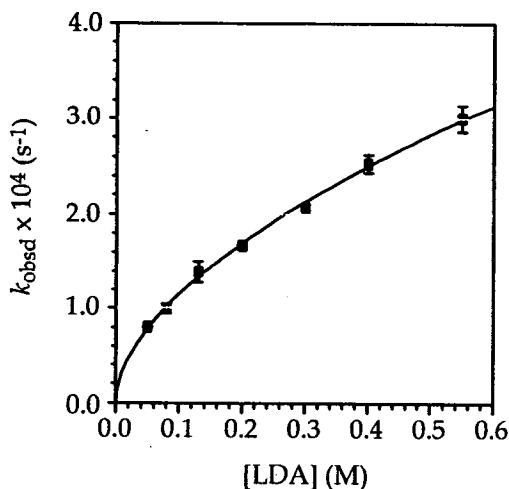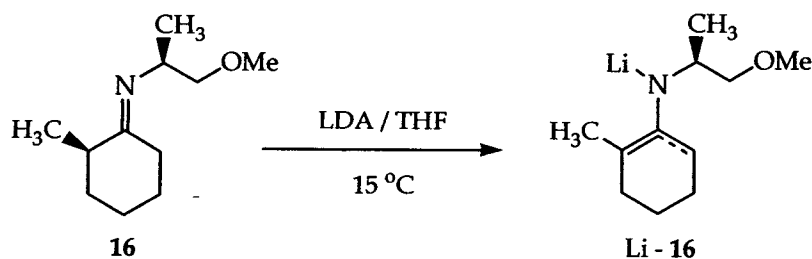| [LDA] (M)	$k_{obsd} \times 10^3$ (s^{-1})		Average $k_{obsd} \times 10^3$ (s^{-1})
0.050	0.89(3)	0.69(2)	0.79
0.080	1.14(4)	0.95(3)	1.05
0.130	1.26(4)	1.24(4)	1.25
0.210	1.31(4)	1.67(5)	1.49
0.330	1.75(7)	1.77(9)	1.76
0.410	1.92(8)	2.28(6)	2.10
0.500	2.8(2)	2.3 (1)	2.6

[a]The lithiation of a 1:10:1:10 mixture of **13:14:15:16** (total concentration 0.005 M) at -20 °C stops at 50~60% conversion, which represents the lithiations of **13**, **14** and **15**. The calculated k_{obsd} is used as that of **14** since both **13** and **15** react at similar rates as **14** and constitute < 20% of the reacting species. (See Figure 2A in the text.)
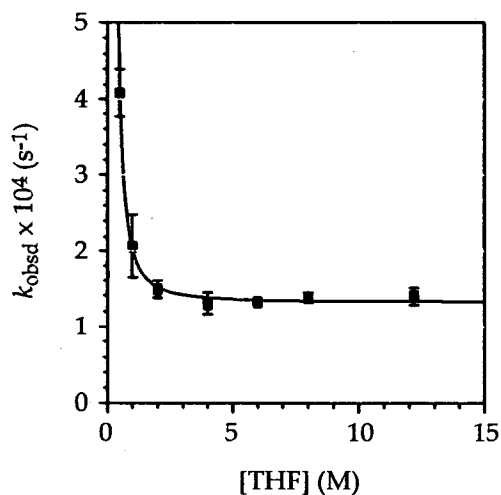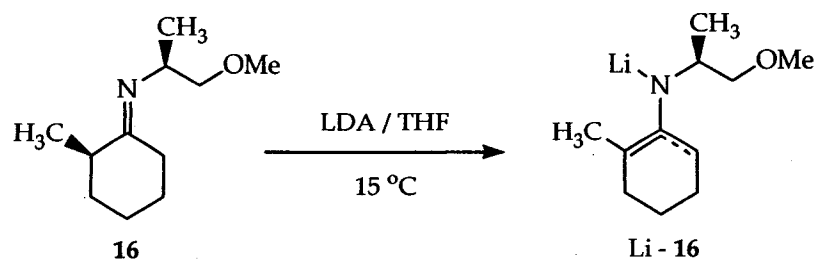
XLI. Plot of k_{obsd} vs free [THF] in hexane cosolvent for the lithiation of **16** (0.005 M)^a by LDA (0.13M) at 15 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[THF]^n + k'$ ($k = 7.1 \pm 0.7$ x 10^{-5}, $k' = 1.32 \pm 0.03$ x 10^{-4}, $n = -2.0 \pm 0.1$).

| [THF] (M)	k_{obsd} x 10^4 (s^{-1})		Average k_{obsd} x 10^4 (s^{-1})
0.50	4.31(7)	3.86(7)	4.09
1.00	2.31(3)	1.76(3)	2.06
2.00	1.56(3)	1.40(2)	1.48
4.00	1.40(1)	1.20(2)	1.30
6.00	1.33(3)	1.30(2)	1.32
8.00	1.33(2)	1.42(3)	1.38
12.2	1.31(2)	1.47(3)	1.39

^{a}The lithiation of a 1:10:1:10 mixture of **13:14:15:16** (total concentration 0.005 M) at 15 °C reaches 50~60% conversion instantaneously followed by a much slower reaction to completion. The latter decay represents the lithiation of **16**. The calculation of the k_{obsd}'s of **16** did not include the points of the first 600 seconds. (See Figure 2B in the text.)

XLII. Plot of k_{obsd} vs [LDA] in neat THF (12.3 M) for the lithiation of **16** (0.005 M)[a] at 15 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[LDA]^n$ ($k = 4.17 \pm 0.07 \times 10^{-4}$, $n = 0.56 \pm 0.01$).

[LDA] (M)	$k_{obsd} \times 10^4$ (s^{-1})		Average $k_{obsd} \times 10^4$ (s^{-1})
0.050	0.80(2)	0.81(2)	0.81
0.080	0.96(2)	1.03(2)	1.00
0.130	1.31(2)	1.47(3)	1.39
0.200	1.67(3)	1.68(4)	1.68
0.300	2.05(4)	2.09(3)	2.07
0.400	2.59(4)	2.46(4)	2.53
0.550	2.9(1)	3.1(1)	3.0

[a]The lithiation of a 1:10:1:10 mixture of **13:14:15:16** (total concentration 0.005 M) at 15 °C reaches 50~60% conversion instantaneously followed by a much slower reaction to completion. The latter decay represents the lithiation of **16**. The calculation of the k_{obsd}'s of **16** did not include the points of the first 600 seconds. (See Figure 2B in the text.)
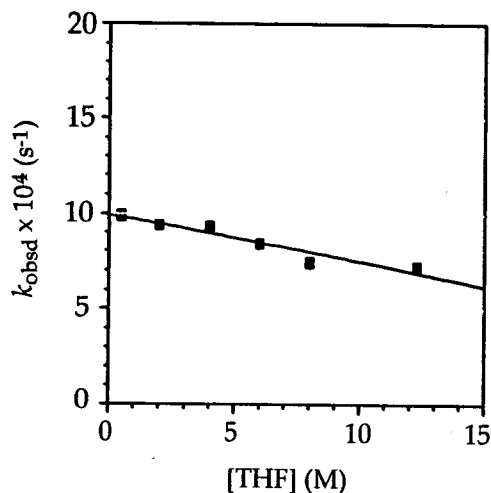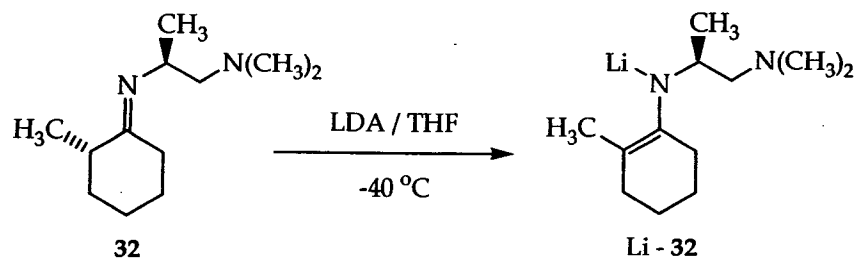
XLIII. Plot of k_{obsd} vs free [THF] in hexane cosolvent for the lithiation of **32**[a] (0.005 M) by LDA (0.13 M) at -40 °C. The curve depicts an unweighted least-squares fit to k_{obsd} = k[THF] + k' (k = -2.5 ± 0.4 x 10^{-5}, k' = 1.0 ± 0.3 x 10^{-3}).

| [THF] (M)	k_{obsd} x 10^4 (s^{-1})
0.50	9.9(5)
2.00	9.4(3)
4.00	9.3(4)
6.00	8.4(4)
8.00	7.4(3)
12.2	7.2(3)

[a]The substrate was made from racemic 2-methylcyclohexanone and racemic amine. Only one of the enantiomers is shown in the equation. k_{obsd}'s were obtained from biphasic lithiation as described in sections **XXXIX** and **XL**.
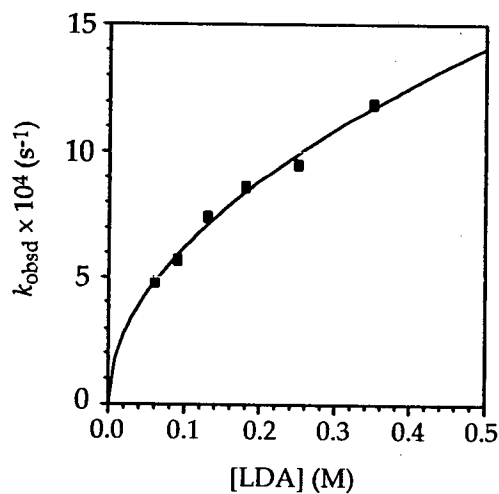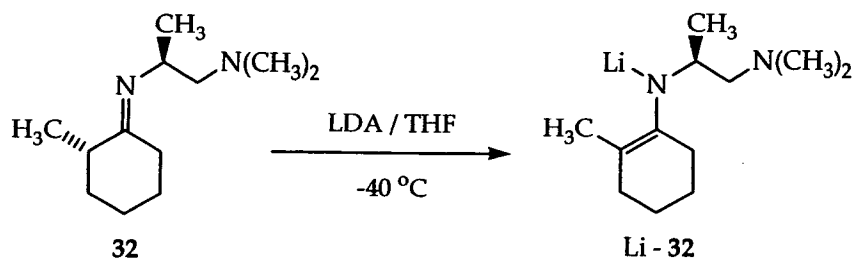
XLIV. Plot of k_{obsd} vs [LDA] in THF (8.0 M) for the lithiation of **32**[a] (0.005 M) at -40 °C. The curve depicts an unweighted least-squares fit to $k_{obsd} = k[LDA]^n$ ($k = 2.0 \pm 0.1 \times 10^{-3}$, $n = 0.51 \pm 0.03$).

[LDA] (M)	$k_{obsd} \times 10^4$ (s^{-1})
0.060	4.8(2)
0.090	5.7(5)
0.130	7.4(3)
0.180	8.6(4)
0.250	9.5(5)
0.350	11.9(5)

[a]The substrate was made from racemic 2-methylcyclohexanone and racemic amine. Only one of the enantiomers is shown in the equation. k_{obsd}'s were obtained from biphasic lithiation as described in sections **XXXIX** and **XL**.

XLV. Determination of Relative Rate Constants (k_{rel}'s) of imine (1-16) lithiations by LDA in THF at -40 °C.[a]

Compd	k_{obsd} [s⁻¹] (-78 °C)			k_{obsd} [s⁻¹] (-65 °C)			k [s⁻¹] (-40 °C)[b]	k_{rel} (compared to 10)
	k_1	k_2	$k_{average}$	k_1	k_2	$k_{average}$		
3	0.0049(2)	0.0052(1)	0.0051	0.0148(8)	0.0162(9)	0.0155	0.095	60,000
4	0.000596(5)	0.000642(3)	0.000619	0.0031(1)	0.00283(7)	0.0030	0.038	24,000
6	0.0049(1)	0.0043(2)	0.0046	0.0118(9)	0.0148(5)	0.0133	0.073	46,000
7	0.00033(2)	0.00034(2)	0.00034	0.0015(4)	0.0012(4)	0.0014	0.013	8,100
8	0.0015(1)	0.00153(8)	0.0015	0.007(1)	0.006(1)	0.0065	0.071	44,000
11	0.000235(4)	0.000288(7)	0.000262	0.00112(2)	0.00127(2)	0.00120	0.014	8,800

Compd	k_{obsd} [s⁻¹] (0 °C)			k_{obsd} [s⁻¹] (15 °C)			k [s⁻¹] (-40 °C)[b]	k_{rel} (compared to 10)
	k_1	k_2	$k_{average}$	k_1	k_2	$k_{average}$		
9	0.00056(2)	0.00077(3)	0.00067	0.00212(6)	0.0025(2)	0.0023	0.000011	7.0
10	0.0000304(5)	0.0000350(3)	0.0000327	0.000094(1)	0.000067(1)	0.000081	0.0000016	1.0
16	0.0000571(5)	0.0000578(2)	0.0000574	0.000131(2)	0.000147(3)	0.000139	0.0000031	2.0

Compd	k_{obsd} [s⁻¹] (-40 °C)			k [s⁻¹] (-40 °C)	k_{rel} (compared to 10)
	k_1	k_2	$k_{average}$		
1	0.00211(3)	0.00210(4)	0.00211	0.00211	1,300
2	0.000196(6)	0.000174(3)	0.000185	0.000185	120
5	0.000297(4)	0.000297(5)	0.000297	0.000297	190
12	0.00155(4)	0.00136(4)	0.00146	0.00146	910
13	0.0010392	0.00098(2)	0.00101	0.00101	630
14	0.000211(4)	0.000264(4)	0.000239	0.000239	150

[a] Rate constants (k_{obsd}) of lithiations are measured by in situ IR under pseudo-first-order conditions: 0.005M imine, neat THF (free [THF] = 12.2M), 0.13M LDA. [b] Rate constants at -40 °C are calculated by the extrapolation from k_{obsd}'s at two other temperatures (-78 °C and -65 °C or 15 °C and 0 °C) using the eq: $\ln k/T = -\Delta H/(RT) + C$.

XLVI. Optimized geometry and calculated free energy of $(Me_2NLi \cdot OMe_2)_2$ (analogue of disolvated LDA dimer in THF) and table of selected bond lengths.
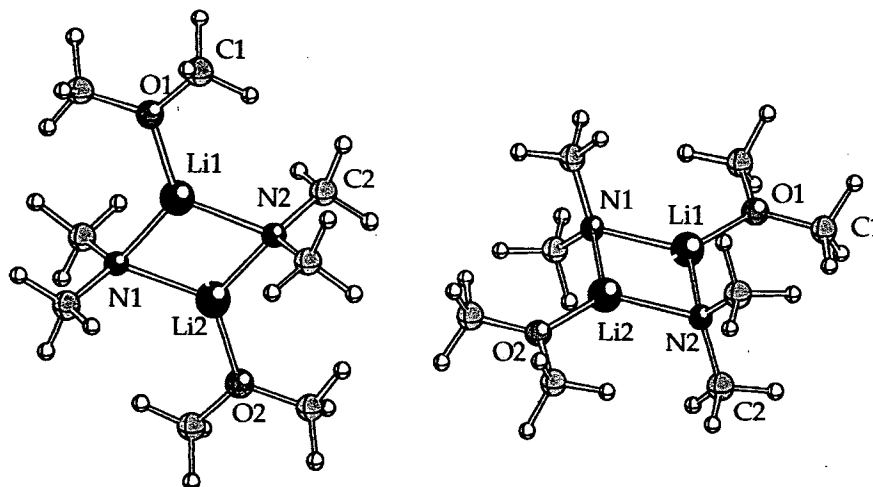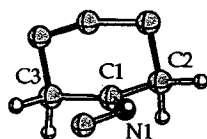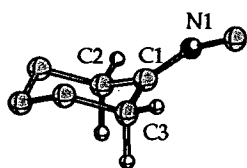

$(Me_2NLi \cdot OMe_2)_2$, Hartrees: -594.09706

$\frac{1}{2}(Me_2NLi \cdot OMe_2)_2$, Hartrees: -297.04853
(used to calculate ground states in sections **XLVII– LXXI**)

Table of selected bond lengths (Å) of the structure shown above.

Li1-Li2	2.366
Li1-O1	1.932
Li2-O2	1.932
Li1-N1	1.978
Li1-N2	1.981
Li2-N1	1.981
Li2-N2	1.979
O1-C1 (all 4)	1.423
N1-C2 (all 4)	1.449

XLVII. Optimized geometries[a] and calculated free energies for the lithiation of *N*-methyl analogue of imines **1** and **2**.

A: Substrate Structure
Hartrees: -329.15858
Ground State: **A** +
½(Me₂NLi•OMe₂)₂
Hartrees: -626.20711
$\Delta G = 0$
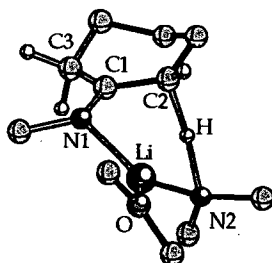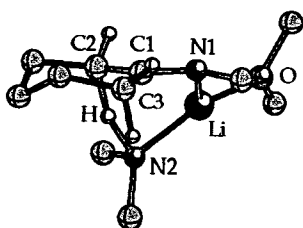
B: Transition Structure
for deprotonation of
anti axial H
Hartrees: -626.17397
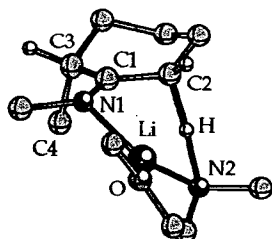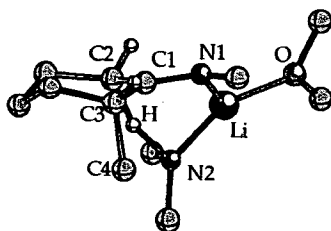$\Delta G^{\ddagger} = 20.8$ kcal/mol
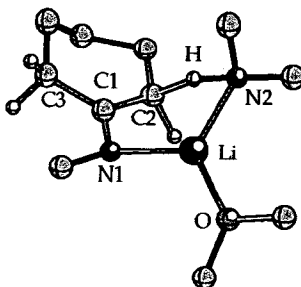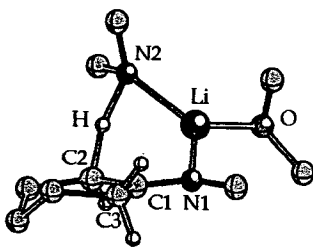
C: Transition Structure
for deprotonation of
anti equatorial H
Hartrees: -626.17228
$\Delta G^{\ddagger} = 21.8$ kcal/mol
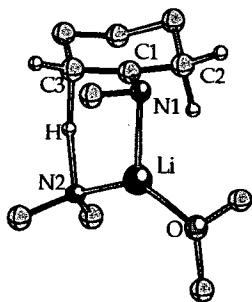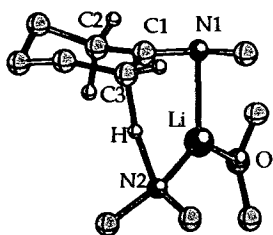
D: Transition Structure
for deprotonation of
syn axial H
Hartrees: -626.16535
$\Delta G^{\ddagger} = 26.2$ kcal/mol
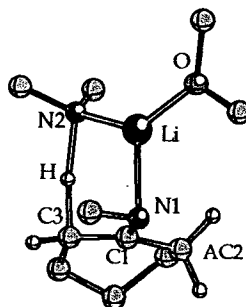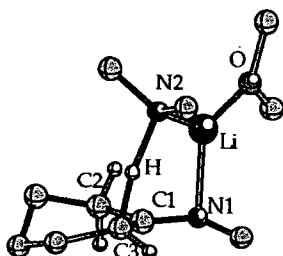
E: Transition Structure
for deprotonation of
syn equatorial H
Hartrees: -626.16224
$\Delta G^{\ddagger} = 28.1$ kcal/mol

[a]Most protons are omitted for clarity.

XLVIII Table of selected bond lengths (Å) of structures in section **XLVII**.

	A	B	C	D	E
C1-C2	1.519	1.452	1.454	1.526	1.526
C1-C3	1.524	1.525	1.524	1.446	1.448
C1-N1	1.276	1.320	1.319	1.319	1.319
C2-H	--	1.349	1.349	--	--
C3-H	--	--	--	1.339	1.314
N2-H	--	1.424	1.417	1.470	1.505
N1-Li	--	2.001	1.992	2.088	2.076
N2-Li	--	1.955	1.956	1.959	1.953
O-Li	--	1.932	1.934	1.912	1.914

XLIX. Optimized geometries[a] and calculated free energies for the lithiation of *N*-methyl analogue of imine **9**.
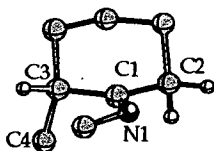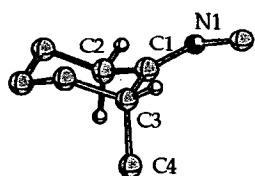
A: Substrate Structure –
syn **axial 2-methyl**
Hartrees: -368.44327
Ground State: **A** +
½(Me₂NLi•OMe₂)₂
Hartrees: -665.49180
$\Delta G = 0$
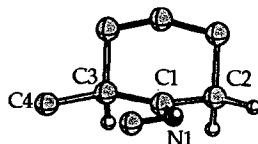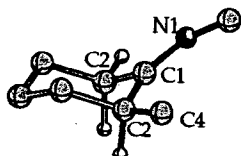
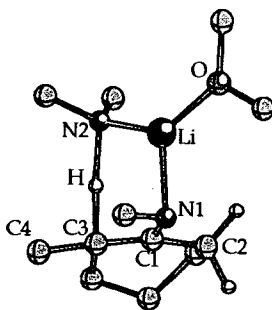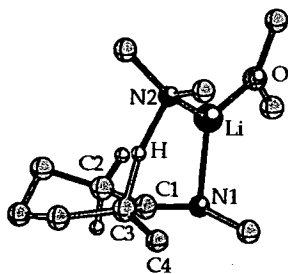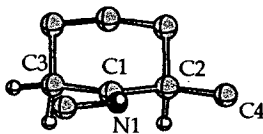**B:** Substrate Structure –
syn **equatorial 2-methyl**
Hartrees: -368.43665
(+4.2 kcal/mol compared
with **A**, not used to calculate
$\Delta G^{\ddagger}$)

C: Transition Structure
for deprotonation of
anti **axial** H
Hartrees: -665.45694
$\Delta G^{\ddagger} = 21.9$ kcal/mol
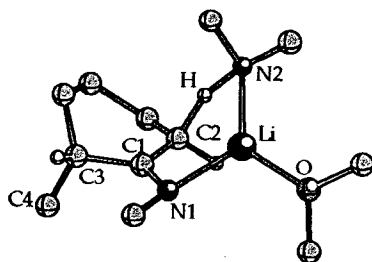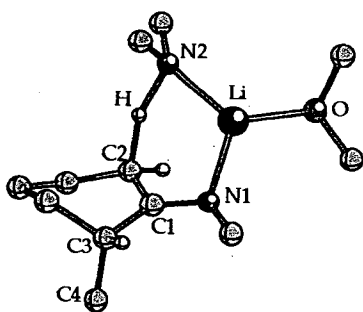
D: Transition Structure
for deprotonation of
anti **equatorial** H
Hartrees: -665.45352
$\Delta G^{\ddagger} = 24.0$ kcal/mol

E: Transition Structure
for deprotonation of
syn **equatorial** H
Hartrees: -665.43645
$\Delta G^{\ddagger} = 34.7$ kcal/mol

[a]Most protons are omitted for clarity.

**L.** Table of selected bond lengths (Å) of structures in section **XLIX**.

	A	B	C	D	E
C1-C2	1.521	1.525	1.453	1.451	1.537
C1-C3	1.532	1.540	1.533	1.529	1.457
C3-C4	1.544	1.535	1.547	1.544	1.536
C1-N1	1.277	1.275	1.320	1.318	1.321
C2-H	--	--	1.349	1.360	--
C3-H	--	--	--	--	1.331
N2-H	--	--	1.427	1.414	1.498
N1-Li	--	--	2.006	2.006	2.062
N2-Li	--	--	1.963	1.959	1.955
O-Li	--	--	1.932	1.933	1.918

LI. Optimized geometries[a] and calculated free energies for the lithiation of *N*-methyl analogue of imine **10**.
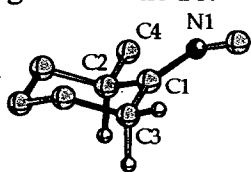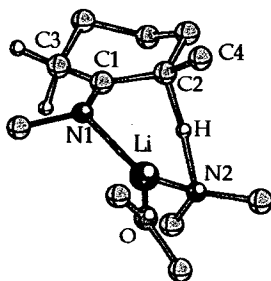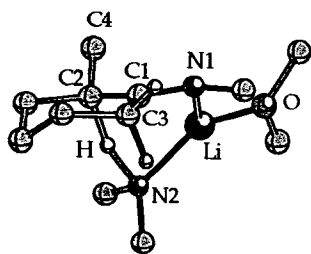

A: Substrate Structure –
***anti* equatorial 2-methyl**
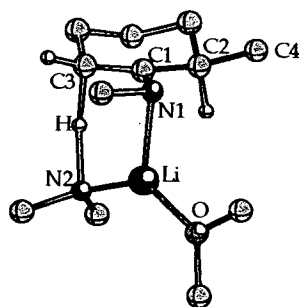Hartrees: -368.44533
(-1.3 kcal compared with
XLIX-A)
Ground State: **A** +
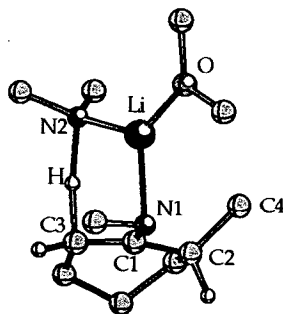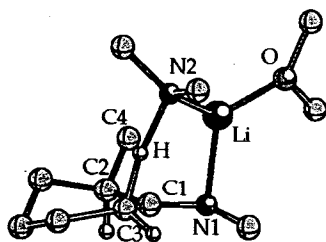½(Me$_2$NLi•OMe$_2$)$_2$
Hartrees: -665.49386
$\Delta G = 0$
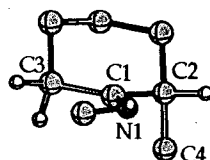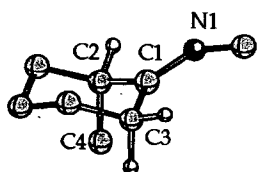
B: Substrate Structure –
***anti* axial 2-methyl**
Hartrees: -368.44383
(+0.9 kcal/mol compared with
A, not used to calculate $\Delta G^{\ddagger}$)

C: Transition Structure
for deprotonation of
***anti* axial** H
Hartrees: -665.45774
$\Delta G^{\ddagger} = 22.6$ kcal/mol
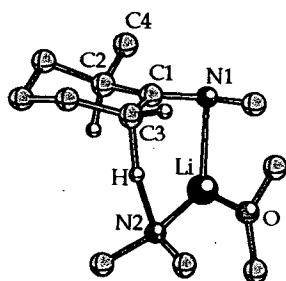
D: Transition Structure
for deprotonation of
***syn* axial** H
Hartrees: -665.45142
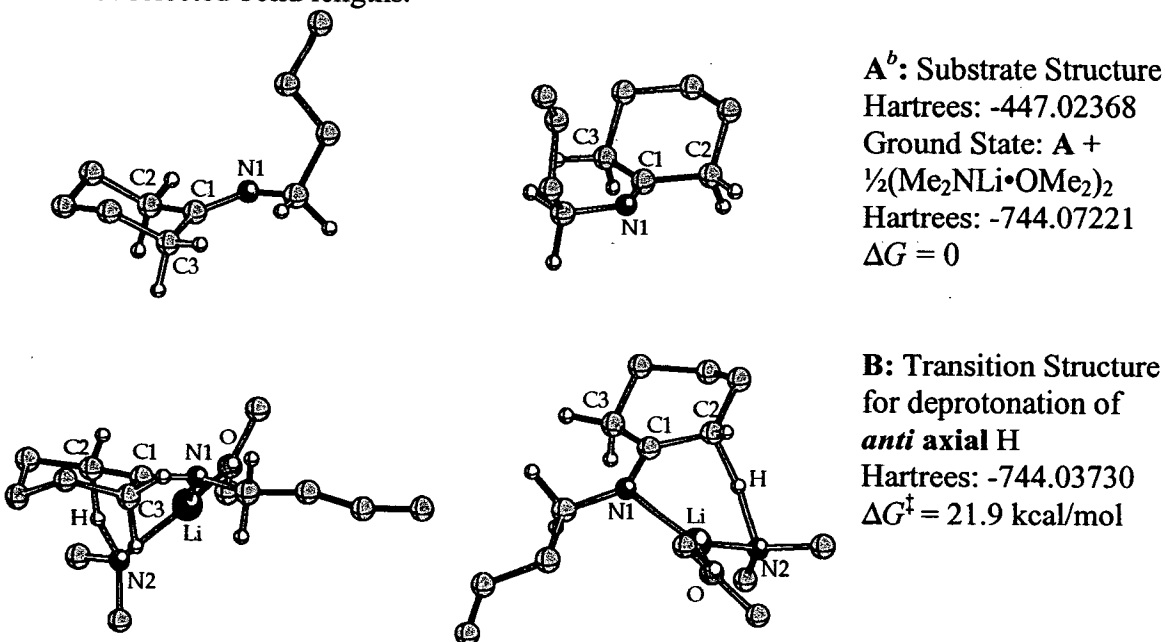$\Delta G^{\ddagger} = 26.6$ kcal/mol

E: Transition Structure
for deprotonation of
***syn* equatorial** H
Hartrees: -665.44766
$\Delta G^{\ddagger} = 29.0$ kcal/mol

[a]Most protons are omitted for clarity.

LII. Table of selected bond lengths (Å) of structures in section **LI.**

	A	B	C	D	E
C1-C2	1.527	1.528	1.457	1.540	1.538
C1-C3	1.523	1.524	1.528	1.448	1.449
C2-C4	1.529	1.543	1.535	1.535	1.537
C1-N1	1.276	1.277	1.322	1.320	1.320
C2-H	--	--	1.365	--	--
C3-H	--	--	--	1.342	1.317
N2-H	--	--	1.412	1.465	1.497
N1-Li	--	--	1.999	2.084	2.085
N2-Li	--	--	1.955	1.956	1.955
O-Li	--	--	1.927	1.914	1.918

LIII. Optimized structures[a] and calculated free energies for the lithiation of imine **1** and table of selected bond lengths.
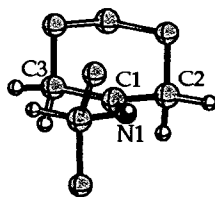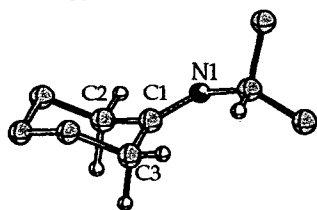

A[b]**: Substrate Structure**
Hartrees: -447.02368
Ground State: **A** +
½(Me₂NLi•OMe₂)₂
Hartrees: -744.07221
$\Delta G = 0$

B: Transition Structure
for deprotonation of
anti axial H
Hartrees: -744.03730
$\Delta G^{\ddagger} = 21.9$ kcal/mol

[a]Most protons are omitted for clarity. [b]The most stable rotamer.

Table of selected bond lengths (Å) of the structures shown above.

|	A	B
C1-C2	1.519	1.453
C1-C3	1.524	1.526
C1-N1	1.277	1.319
C2-H	--	1.351
N2-H	--	1.424
N1-Li	--	2.012
N2-Li	--	1.960
O-Li	--	1.940

LIV. Optimized geometries[a] and calculated free energies for the lithiation of imines **2**, **9** and **10**.
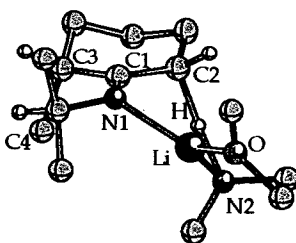

A: Imine of cyclohexanone (**2**)
Hartrees: -407.73919
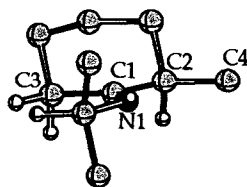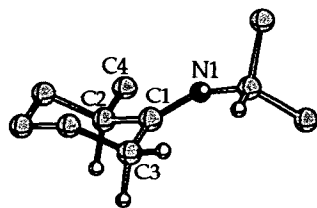Ground State: **A** + ½(Me₂NLi•OMe₂)₂
Hartrees: -704.78712
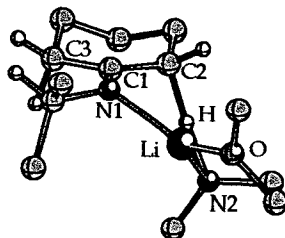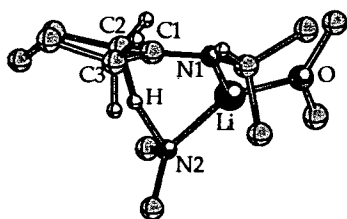
B: Transition Structure for deprotonation of *anti* axial H of A
Hartrees: -704.75034
$\Delta G^{\ddagger} = 23.1$ kcal/mol
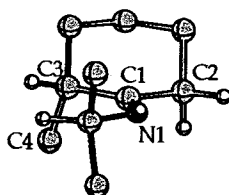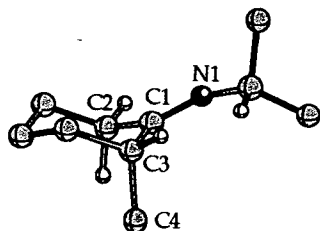
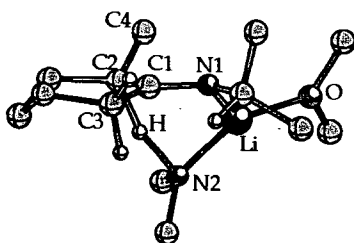**C:** *Syn* imine of 2-methylcyclohexanone (**9**)
Hartrees: -447.02368
Ground State: **C** + ½(Me₂NLi•OMe₂)₂
Hartrees: -744.07221
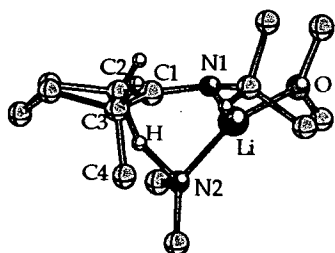
D: Transition Structure for deprotonation of *anti* axial H of C
Hartrees: -744.03514
$\Delta G^{\ddagger} = 23.2$ kcal/mol

E: *Anti* imine of 2-methylcyclohexanone (**10**)
Hartrees: -447.02730
(-2.3 kcal/mol compared with **C**)
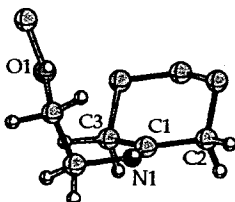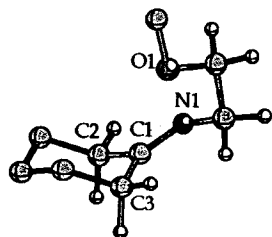Ground State: **E** + ½(Me₂NLi•OMe₂)₂
Hartrees: -744.07583
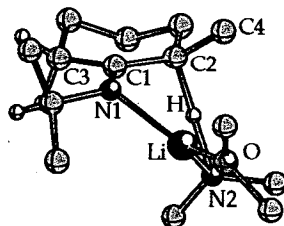
F: Transition Structure for deprotonation of *anti* axial H of E
Hartrees: -744.03399
$\Delta G^{\ddagger} = 26.2$ kcal/mol

[a]Most protons are omitted for clarity.

LV. Table of selected bond lengths (Å) of structures in section **LIV**.

|	A	B	C	D	E	F
C1-C2	1.519	1.454	1.530	1.459	1.521	1.455
C1-C3	1.524	1.530	1.525	1.534	1.533	1.537
C2-C4	--	--	1.529	1.535	--	--
C3-C4	--	--	--	--	1.544	1.546
C1-N1	1.277	1.319	1.276	1.321	1.277	1.319
C2-H	--	1.354	--	1.307	--	1.355
N2-H	--	1.417	--	1.468	--	1.419
N1-Li	--	2.018	--	2.015	--	2.018
N2-Li	--	1.967	--	1.958	--	1.966
O-Li	--	1.944	--	1.947	--	1.942

LVI. Optimized geometries[a] and calculated free energies for the lithiation of imine **3**
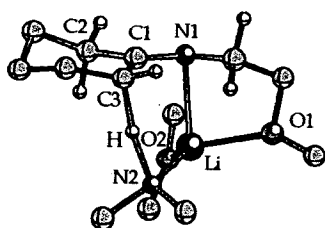

A[b]: Substrate Structure
Hartrees: -482.93357
Ground State: **A** +
½(Me$_2$NLi•OMe$_2$)$_2$
Hartrees: -779.98210
$\Delta G = 0$
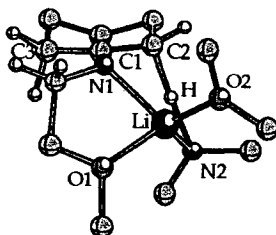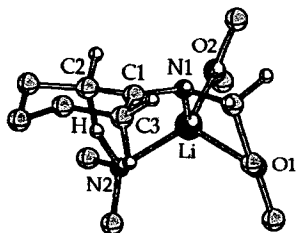
B: Transition Structure
for deprotonation of
***anti* axial** H
Hartrees: -779.95501
$\Delta G^{\ddagger} = 17.0$ kcal/mol
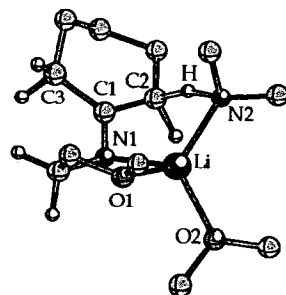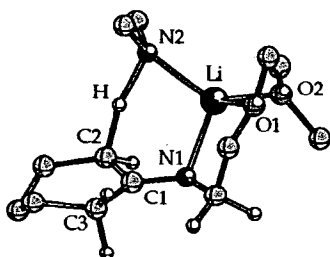
C: Transition Structure
for deprotonation of
***anti* equatorial** H
Hartrees: -780.95158
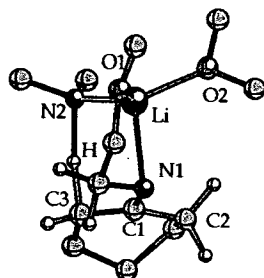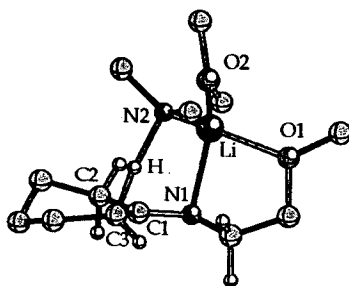$\Delta G^{\ddagger} = 19.1$ kcal/mol
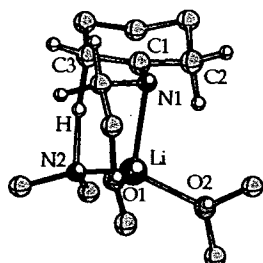
D: Transition Structure
for deprotonation of
***syn* axial** H
Hartrees: -779.95014
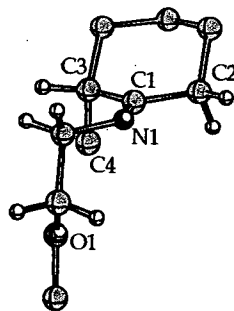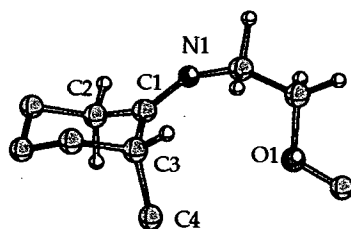$\Delta G^{\ddagger} = 20.0$ kcal/mol

E: Transition Structure
for deprotonation of
***syn* equatorial** H
Hartrees: -779.94664
$\Delta G^{\ddagger} = 22.2$ kcal/mol

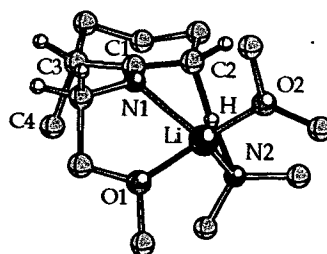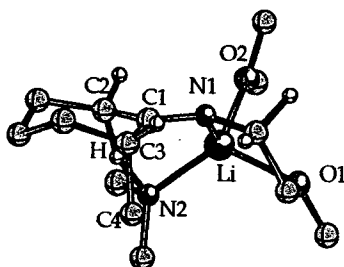[a]Most protons are omitted for clarity. [b]The most stable rotamer.

LVII. Table of selected bond lengths (Å) of structures in section **LVI.**

|	A	B	C	D	E
C1-C2	1.518	1.451	1.453	1.527	1.526
C1-C3	1.522	1.529	1.530	1.450	1.451
C1-N1	1.277	1.318	1.315	1.316	1.316
C2-H	--	1.331	1.322	--	--
C3-H	--	--	--	1.333	1.309
N2-H	--	1.448	1.450	1.474	1.507
N1-Li	--	2.067	2.061	2.234	2.212
N2-Li	--	1.984	1.995	1.983	1.981
O1-Li	--	2.077	2.087	2.024	2.032
O2-Li	--	1.989	2.017	1.978	1.980

LVIII. Optimized geometries[a] and calculated free energies for the lithiation of imine **11**.

A[b]: Substrate Structure –
syn **axial 2-methyl**
Hartrees: -522.21855
Ground State: **A** +
½(Me₂NLi•OMe₂)₂
Hartrees: -819.26708
$\Delta G = 0$

B: Transition Structure
for deprotonation of
anti **axial** H
Hartrees: -819.23637
$\Delta G^{\ddagger} = 19.3$ kcal/mol
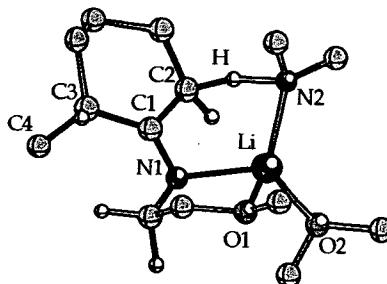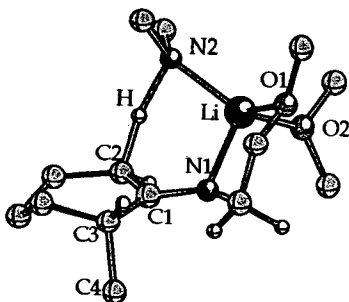
C: Transition Structure
for deprotonation of
anti **equatorial** H
Hartrees: -819.23609
$\Delta G^{\ddagger} = 19.4$ kcal/mol
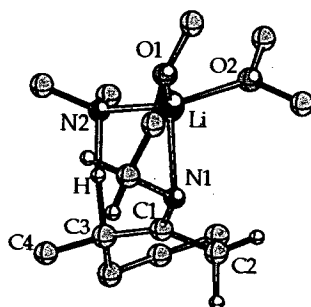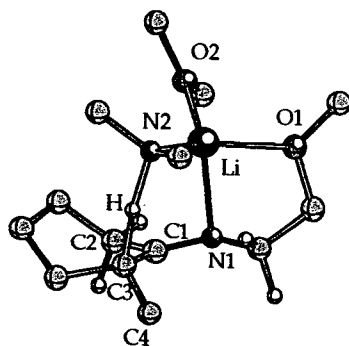
D: Transition Structure
for deprotonation of
syn **equatorial** H
Hartrees: -819.22174
$\Delta G^{\ddagger} = 28.4$ kcal/mol

[a]Most protons are omitted for clarity. [b]The most stable conformer.

LIX. Table of selected bond lengths (Å) of structures in section **LVIII**.

	A	B	C	D
C1-C2	1.521	1.453	1.455	1.524
C1-C3	1.531	1.537	1.534	1.461
C3-C4	1.544	1.545	1.547	1.536
C1-N1	1.276	1.317	1.317	1.318
C2-H	--	1.335	1.323	--
C3-H	--	--	--	1.382
N2-H	--	1.446	1.450	1.422
N1-Li	--	2.048	2.044	2.253
N2-Li	--	1.993	1.976	1.999
O1-Li	--	2.083	2.084	2.015
O2-Li	--	1.992	1.993	1.983

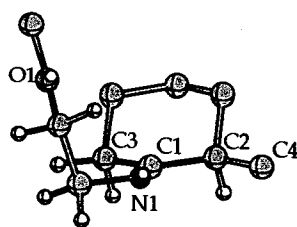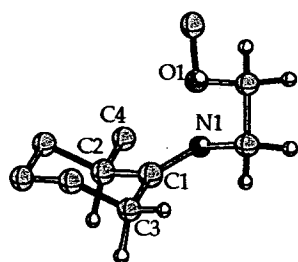**LX.** Optimized geometries[a] and calculated free energies for the lithiation of imine **12**.

A[b]: Substrate Structure –
***anti* equatorial 2-methyl**
Hartrees: -522.2157
(-1.9 kcal/mol compared
with **LVIII-A**)
Ground State: **A** +
½(Me₂NLi•OMe₂)₂
Hartrees: -819.27010
$\Delta G = 0$

B: Transition Structure
for deprotonation of
***anti* axial H**
Hartrees: -819.23831
$\Delta G^{\ddagger} = 19.9$ kcal/mol

C: Transition Structure
for deprotonation of
***syn* axial H**
Hartrees: -819.23685
$\Delta G^{\ddagger} = 20.8$ kcal/mol
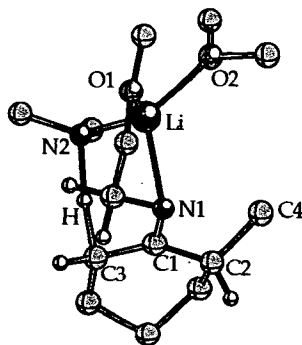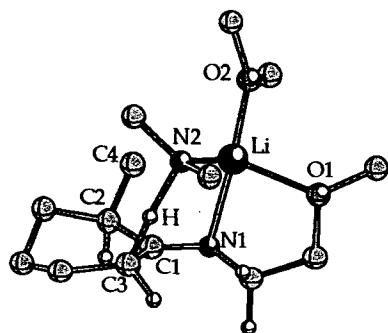
D: Transition Structure
for deprotonation of
***syn* equatorial H**
Hartrees: -819.23067
$\Delta G^{\ddagger} = 24.7$ kcal/mol

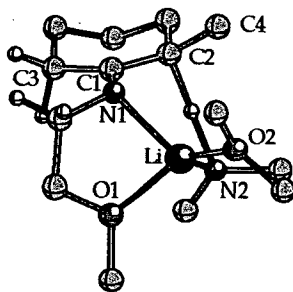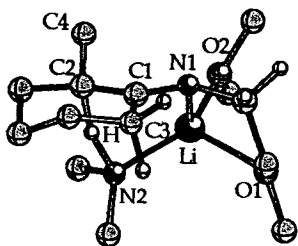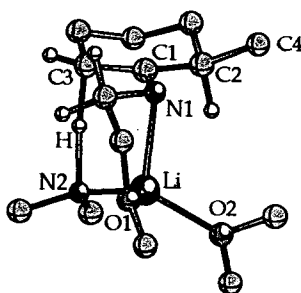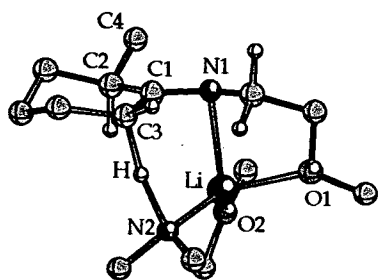[a]Most protons are omitted for clarity. [b]The most stable conformer.

LXI. Table of selected bond lengths (Å) of structures in section **LX.**

	A	B	C	D
C1-C2	1.528	1.456	1.541	1.537
C1-C3	1.522	1.532	1.451	1.452
C2-C4	1.529	1.534	1.535	1.534
C1-N1	1.276	1.321	1.316	1.316
C2-H	--	1.343	--	--
C3-H	--	--	1.336	1.321
N2-H	--	1.439	1.467	1.485
N1-Li	--	2.072	2.240	2.264
N2-Li	--	1.982	1.988	1.985
O1-Li	--	2.066	2.027	2.037
O2-Li	--	1.933	1.983	2.005

**LXII.** Optimized geometries[a] and calculated free energies for the lithiation of imine **4** (analogues of **7** and **8**).
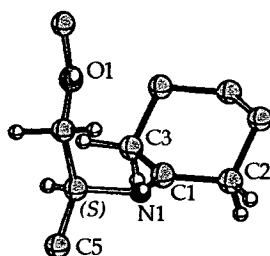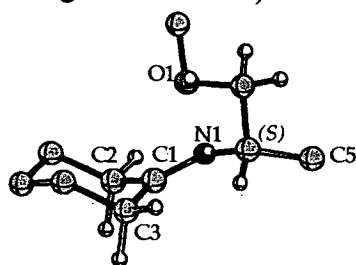
A1[b]**: Substrate Structure**
(analogue of **8**)
Hartrees: -522.22367
Ground State: **A1** +
½(Me₂NLi•OMe₂)₂
Hartrees: -819.27220
$\Delta G = 0$
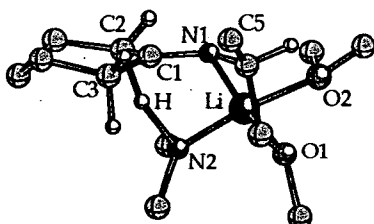
B1: Transition Structure
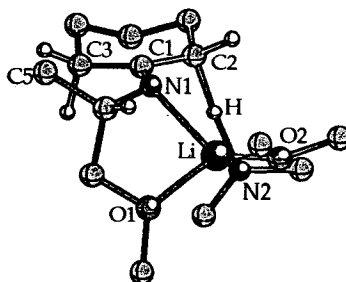for deprotonation of
***anti* axial** H
Hartrees: -819.23360
$\Delta G^{\ddagger} = 24.2$ kcal/mol
(A^{1,3} strain caused by C5)

C1: Transition Structure
for deprotonation of
***anti* equatorial** H
Hartrees: -819.23959
$\Delta G^{\ddagger} = 20.4$ kcal/mol
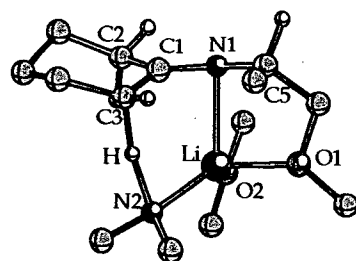
D1: Transition Structure
for deprotonation of
***syn* axial** H
Hartrees: -29.9 kcal/mol
(A^{1,3} strain caused by C5)
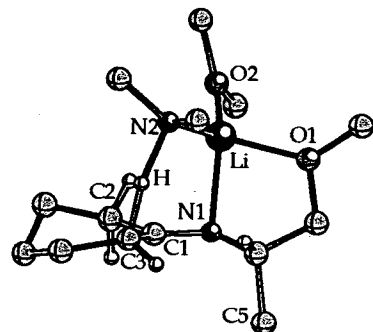
E1: Transition Structure
for deprotonation of
***syn* equatorial** H
Hartrees: -819.23679
$\Delta G^{\ddagger} = 22.2$ kcal/mol

LXII. (Continued)

A2: Substrate Structure (analogue of **7**)
Hartrees: -522.22335
(+0.2 kcal/mol compared with **A1**, not used to calculate $\Delta G^{\ddagger}$)
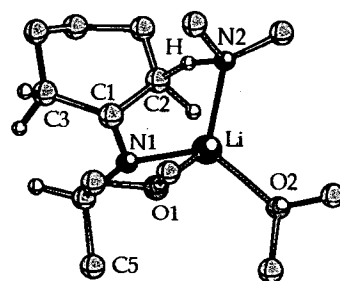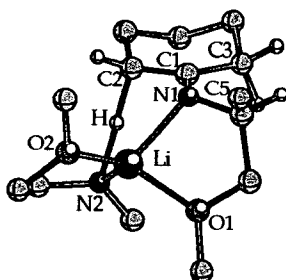
B2: Transition Structure for deprotonation of *anti* **axial** H
Hartrees: -819.24346
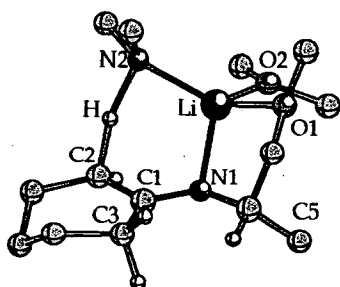$\Delta G^{\ddagger} = 18.0$ kcal/mol
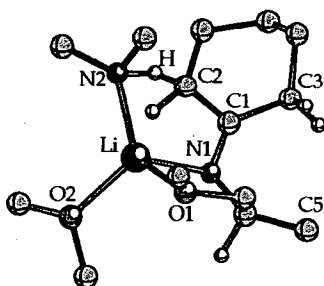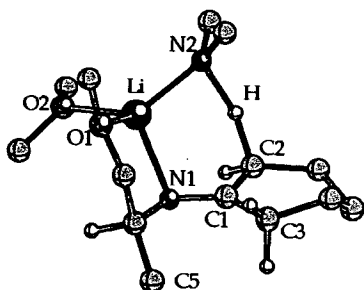
C2: Transition Structure for deprotonation of *anti* **equatorial** H
Hartrees: -819.23286
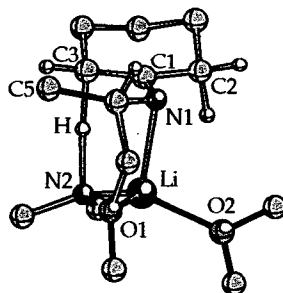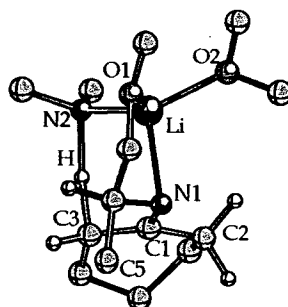$\Delta G^{\ddagger} = 24.7$ kcal/mol
($A^{1,3}$ strain caused by C5)
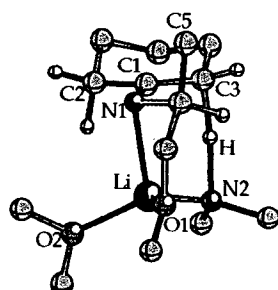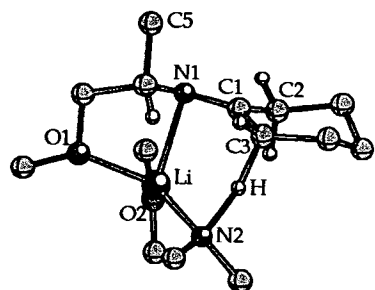
D2: Transition Structure for deprotonation of *syn* **axial** H
Hartrees: -819.24056
$\Delta G^{\ddagger} = 19.8$ kcal/mol
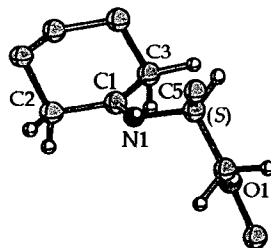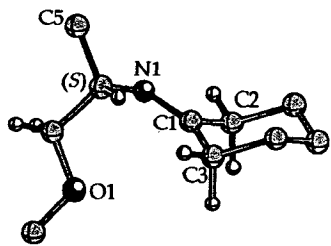
E2: Transition Structure for deprotonation of *syn* **equatorial** H
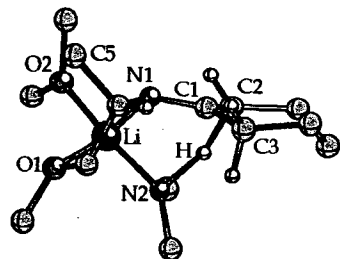Hartrees: -819.22166
$\Delta G^{\ddagger} = 31.7$ kcal/mol
($A^{1,3}$ strain caused by C5)

[a]Most protons are omitted for clarity. [b]The most stable isomer.

LXIII. Table of selected bond lengths (Å) of structures in section **LXII**.

	A1	B1	C1	D1	E1	A2	B2	C2	D2	E2
C1-C2	1.518	1.453	1.453	1.536	1.527	1.522	1.452	1.455	1.527	1.536
C1-C3	1.522	1.533	1.530	1.451	1.452	1.519	1.530	1.532	1.450	1.451
C1-N1	1.277	1.318	1.315	1.317	1.316	1.277	1.317	1.316	1.316	1.317
C2-H	--	1.329	1.319	--	--	--	1.322	1.309	--	--
C3-H	--	--	--	1.347	1.304	--	--	--	1.331	1.312
N2-H	--	1.437	1.450	1.444	1.511	--	1.444	1.461	1.472	1.492
N1-Li	--	2.109	2.070	2.273	2.223	--	2.071	2.099	2.246	2.244
N2-Li	--	1.994	2.003	1.974	1.978	--	1.989	1.992	1.981	1.968
O1-Li	--	2.060	2.086	2.000	2.011	--	2.058	2.070	2.007	2.005
O2-Li	--	2.031	2.038	1.981	1.981	--	1.998	2.030	1.977	1.989

A1 and **A2** are only a (six-membered) ring-flip away, therefore, the more stable **A1** is used to calculate the ground state. The following four transition structures are preferred for different types of deprotonations: **B2** for *anti* axial, **C1** for *anti* equatorial, **D2** for *syn* axial and **E1** for *syn* equatorial. **A2**, **B1**, **C2** and **D1** are disfavored due to $A^{1,3}$ strain. Possible non-chelating involved transition structures are not shown since they are guaranteed to be of higher energy. One can imagine that if 4-*tert*-butyl is introduced to **A1** and **A2**, both will be conformationally anchored and become diastereomers. Then 4-*tert*-butyl-**A1** (imine **8**) will only accommodate two equatorial deprotonations: **C1** and **E1**; while 4-*tert*-Butyl-**A2** (imine **7**) will only accommodate two axial deprotonations: **B2** and **D2**.

LXIV. Optimized geometries[a] and calculated free energies for the lithiation of imine **13**.

A[b]: Substrate Structure –
Hartrees: -561.50850
Ground State: **A** +
$\frac{1}{2}(Me_2NLi \cdot OMe_2)_2$
Hartrees: -858.55703
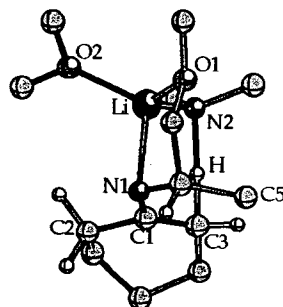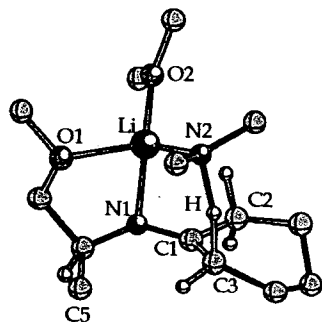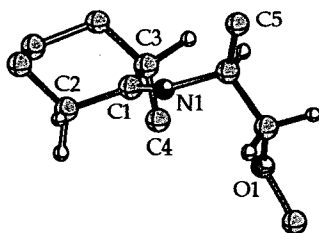$\Delta G = 0$
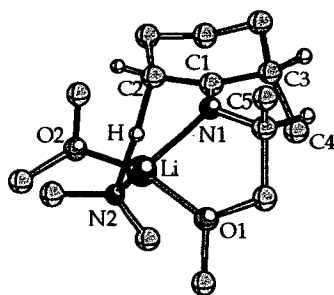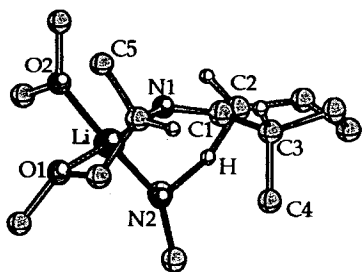
B[c]: Transition Structure
for deprotonation of
anti **axial** H
Hartrees: -858.52547
$\Delta G^{\ddagger} = 19.8$ kcal/mol
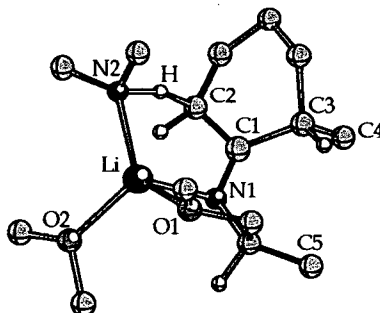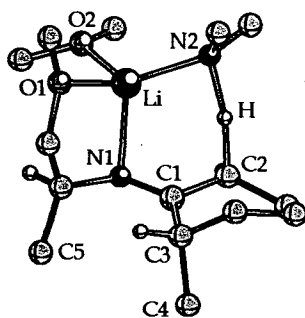
C: Transition Structure
for deprotonation of
anti **equatorial** H
Hartrees: -858.51223
$\Delta G^{\ddagger} = 28.1$ kcal/mol
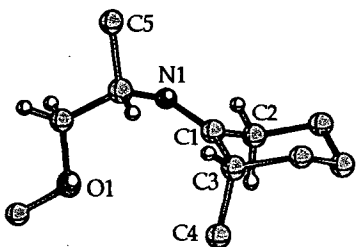(A[1,3] strain caused by C5)

[a]Most protons are omitted for clarity. [b]The most stable rotamer. [c]Only *anti* **axial** and *anti* **equatorial** deprotonations are calculated; *syn* **equatorial** deprotonation should be disfavored by A[1,3] strain caused by both C4 and C5. (See sections **LVIII-D** and **LXII-E2**.)

LXV. Table of selected bond lengths (Å) of structures in section **LXIV**.

|	A	B	C
C1-C2	1.521	1.453	1.451
C1-C3	1.532	1.537	1.536
C3-C4	1.544	1.546	1.544
C1-N1	1.277	1.317	1.318
C2-H	--	1.337	1.340
N2-H	--	1.443	1.424
N1-Li	--	2.054	2.092
N2-Li	--	1.996	1.995
O1-Li	--	2.070	2.080
O2-Li	--	2.004	2.037

LXVI. Optimized geometries[a] and calculated free energies for the lithiation of imine **14**.

A[b]: Substrate Structure –
Hartrees: -561.51093
(-1.5 kcal/mol compared
with **LXIV-A**)
Ground State: **A** +
½(Me$_2$NLi•OMe$_2$)$_2$
Hartrees: -858.55946
$\Delta G = 0$
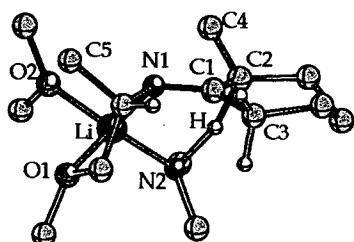
B[c]: Transition Structure
for deprotonation of
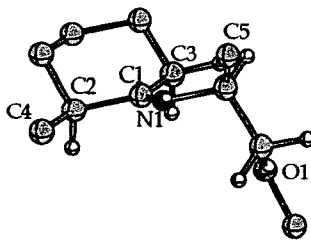***anti*** **axial** H
Hartrees: -858.52567
$\Delta G^{\ddagger} = 21.1$ kcal/mol
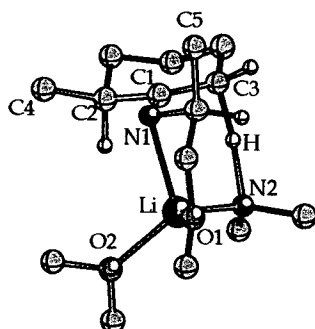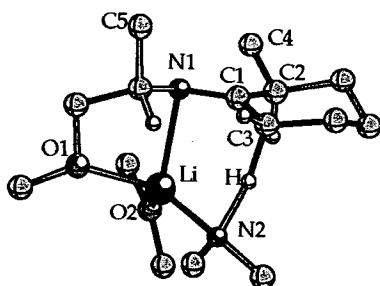
C: Transition Structure
for deprotonation of
syn **axial** H
Hartrees: -858.52566
$\Delta G^{\ddagger} = 21.2$ kcal/mol

[a]Most protons are omitted for clarity. [b]The most stable rotamer. [c]Only ***anti*** **axial** and ***syn***
axial deprotonations are calculated; ***syn*** **equatorial** deprotonation should be disfavored
by A^{1,3} strain caused by C5. (See section **LXII-E2**).

LXVII. Table of selected bond lengths (Å) of structures in section **LXVI.**

	A	B	C
C1-C2	1.529	1.457	1.542
C1-C3	1.523	1.533	1.452
C2-C4	1.529	1.533	1.535
C1-N1	1.276	1.321	1.317
C2-H	--	1.347	--
C3-H	--	--	1.334
N2-H	--	1.430	1.464
N1-Li	--	2.078	2.249
N2-Li	--	1.993	1.985
O1-Li	--	2.052	2.008
O2-Li	--	2.004	1.983

LXVIII. Optimized geometries[a] and calculated free energies for the lithiation of imine **15**.

A[b]: Substrate Structure –
Hartrees: -561.50835
Ground State: **A** +
½(Me$_2$NLi•OMe$_2$)$_2$
Hartrees: -858.55688
$\Delta G = 0$

B[c]: Transition Structure
for deprotonation of
anti axial H
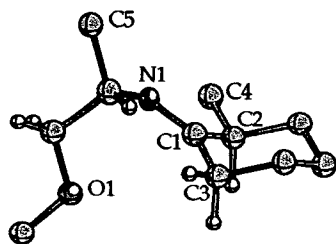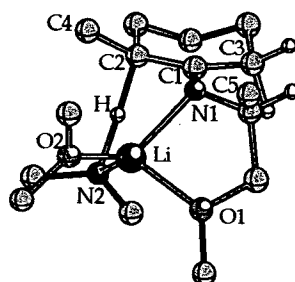Hartrees: -858.51607
$\Delta G^{\ddagger} = 25.6$ kcal/mol
(chelation, A^{1,3} strain
caused by C5)

C: Transition Structure
for deprotonation of
anti axial H
Hartrees: -858.51821
$\Delta G^{\ddagger} = 24.2$ kcal/mol
(no chelation)

D: Transition Structure
for deprotonation of
anti equatorial H
Hartrees: -858.52297
$\Delta G^{\ddagger} = 21.3$ kcal/mol

[a]Most protons are omitted for clarity. [b]The most stable rotamer. [c]Only **anti axial** and **anti equatorial** deprotonations are calculated, **syn equatorial** deprotonation should be disfavored by A^{1,3} strain caused by C4. (See section **LVIII-D**).
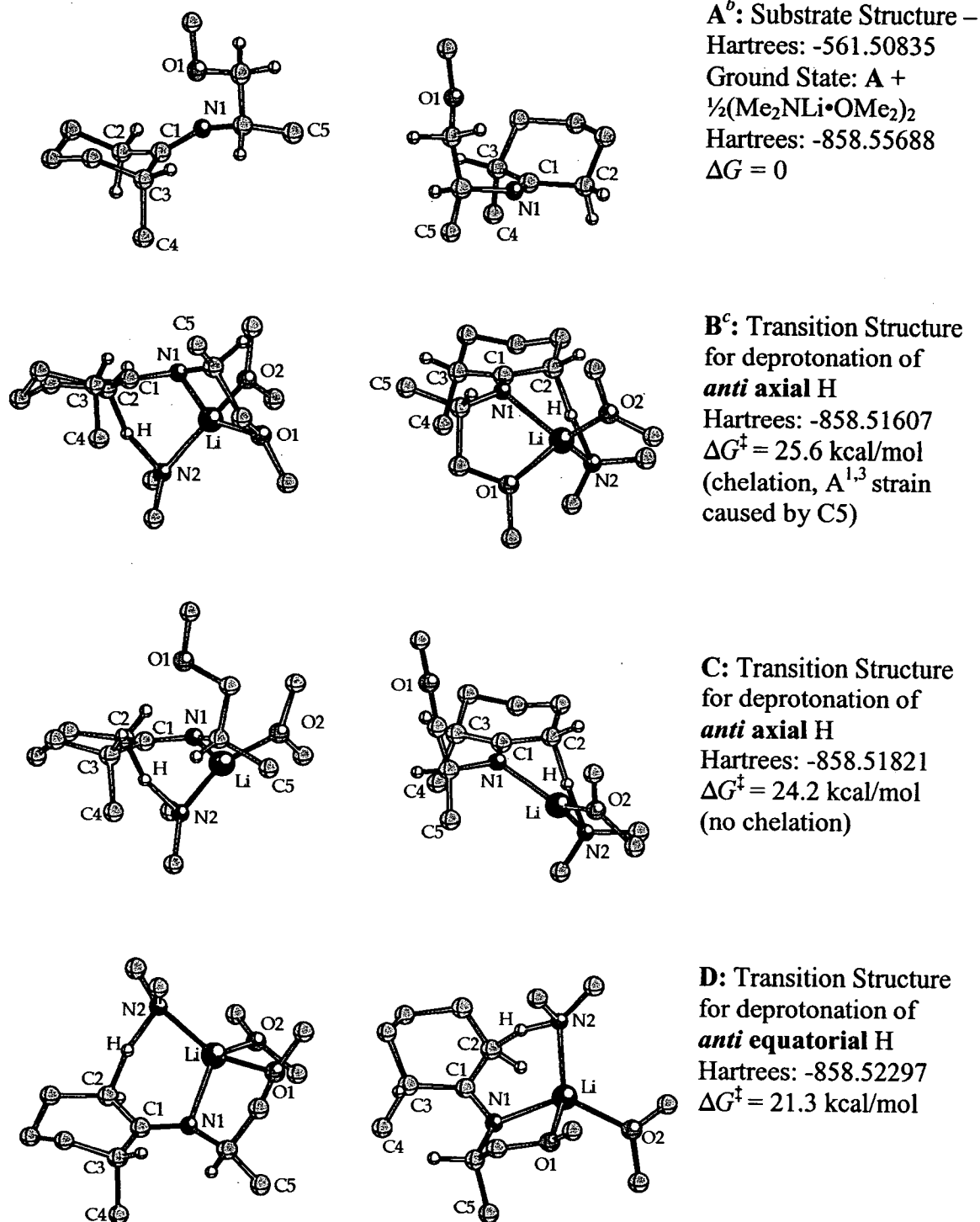
LXIX. Table of selected bond lengths (Å) of structures in section **LXVIII.**

	A	B	C	D
C1-C2	1.520	1.456	1.454	1.456
C1-C3	1.530	1.541	1.536	1.536
C3-C4	1.543	1.545	1.546	1.546
C1-N1	1.278	1.318	1.321	1.316
C2-H	--	1.341	1.356	1.325
N2-H	--	1.436	1.420	1.438
N1-Li	--	2.068	2.012	2.065
N2-Li	--	1.989	1.965	2.003
O1-Li	--	2.047	4.806	2.075
O2-Li	--	1.998	1.944	2.040

LXX. Optimized geometries[a] and calculated free energies for the lithiation of imine **16**.
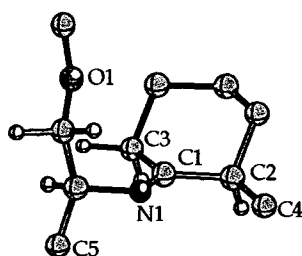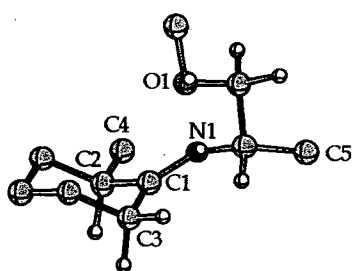
A[b]**:** Substrate Structure –
Hartrees: -561.51155
(-2.0 kcal/mol compared
with **LXVIII-A**)
Ground State: **A** +
½(Me$_2$NLi•OMe$_2$)$_2$
Hartrees: -858.56008
$\Delta G = 0$
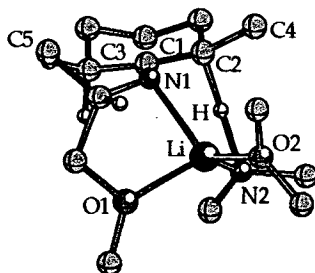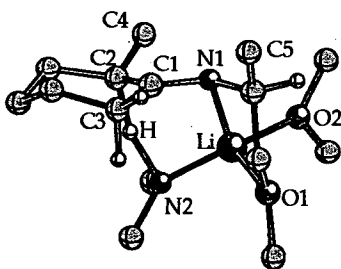
B: Transition Structure
for deprotonation of
***anti* axial** H
Hartrees: -858.51840
$\Delta G^{\ddagger} = 26.1$ kcal/mol
(chelation, A^{1,3} strain
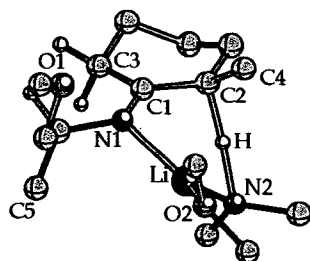caused by C5)
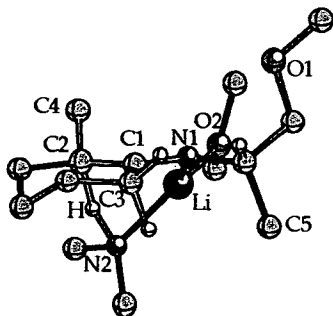
C: Transition Structure
for deprotonation of
***anti* axial** H
Hartrees: -858.51579
$\Delta G^{\ddagger} = 27.8$ kcal/mol
(no chelation)
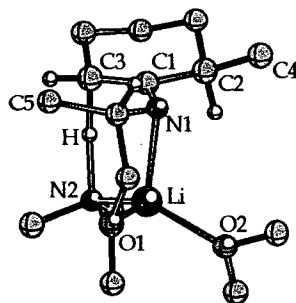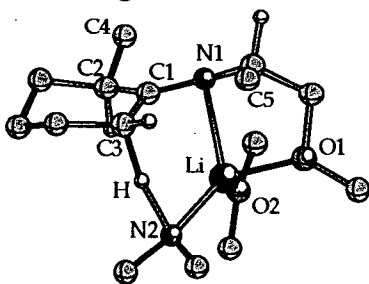
D: Transition Structure
for deprotonation of
***syn* axial** H
Hartrees: -858.50947
$\Delta G^{\ddagger} = 31.7$ kcal/mol
(chelation, A^{1,3} strain
caused by C5)

E: Transition Structure
for deprotonation of
***syn* axial** H
Hartrees: -858.51020
$\Delta G^{\ddagger} = 31.3$ kcal/mol
(no chelation)

LXX. (Continued)

F: Transition Structure for deprotonation of *syn* equatorial H
Hartrees: -858.52053
$\Delta G^{\ddagger} = 24.8$ kcal/mol

[a]Most protons are omitted for clarity. [b]The most stable rotamer.

LXXI. Table of selected bond lengths (Å) of structures in section **LXX.**
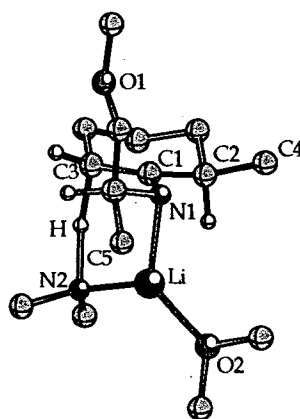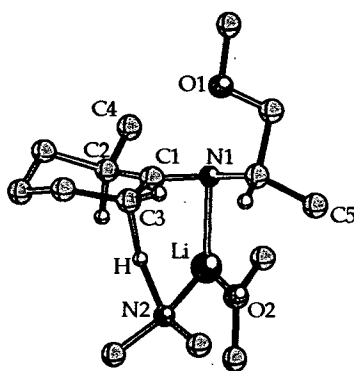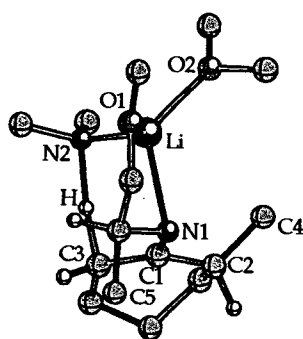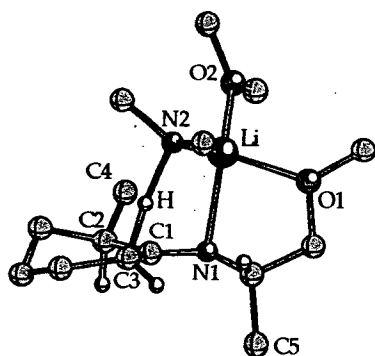
	A	B	C	D	E	F
C1-C2	1.528	1.457	1.460	1.553	1.545	1.539
C1-C3	1.523	1.534	1.532	1.452	1.444	1.454
C2-C4	1.529	1.533	1.536	1.535	1.535	1.534
C1-N1	1.276	1.321	1.322	1.317	1.324	1.317
C2-H	--	1.342	1.373	--	--	--
C3-H	--	--	--	1.344	1.361	1.312
N2-H	--	1.443	1.402	1.442	1.437	1.487
N1-Li	--	2.113	2.004	2.277	2.085	2.293
N2-Li	--	1.980	1.955	1.973	1.963	1.987
O1-Li	--	2.071	4.012	1.998	2.941	2.003
O2-Li	--	1.988	1.943	1.989	1.922	2.006

LXXII. General Experimental Procedures:

A. General Procedures to Make Cyclohexanone Imines, 2-Methylcyclohexanone Imines (*syn/anti* mixtures) and 4-*t*-Butylcyclohexanone Imines.[ref 1]

Method (1). In a system containing a Dean-Stark trap arranged for azeotropic removal of water, the ketone (20 mmol) and the amine (20 to 40 mmol) were dissolved in 15 mL benzene and heated to reflux until the theoretical amount of water was collected in the trap. Removal of benzene and fractional distillation of the light yellow residue with a Vigreux column under vacuum (0.15 torr) gave the imine product as clear viscous oil, showing both moisture and light sensitivity. Imines **4, 7/8** and **13/14/15/16** were made with Method (1).

Method (2). In a 25 mL round bottom flask equipped with a magnetic stir bar and 4Å molecular sieves (5 g), the ketone (20 mmol) and the amine (20 to 40 mmol) were dissolved with 10 mL anhydrous ether and stirred at room temperature until GC analysis showed more than 90% conversion of the reaction. Filtration of the molecular sieves and removal of ether gave light yellow residue. Distillation of the residue as described in method (1) gave the imine product. Imines **1, 2, 3, 5, 6, 9/10** and **11/12** were made with method (2).

Both methods gave 70% - 90% yields based on the starting ketone.

B. IR Spectroscopic Analyses of Standard Lithiation.

Spectra were recorded with an in situ IR spectrometer fitted with a 30-bounce, silicon-tipped probe optimized for sensitivity. The spectra were acquired in 32 scans (30 sec intervals) at a gain of one and a resolution of eight. A representative reaction was carried out as follows: the IR probe was inserted through a Teflon adapter and O-ring seal in an oven-dried, cylindrical flask fitted with a magnetic stir bar and T-joint. The T-joint was capped by a septum for injections and a nitrogen line. Following evacuation under full vacuum and flushing with nitrogen, the flask was charged with a solution of LDA (140 mg, 1.30 mmol, 0.130 M) in THF (10 mL) and cooled to an internal reaction temperature of −40.0 ± 0.5 °C as determined with a thermocouple. After recording a background spectrum, imine **12** (0.050 mmol, 0.005M) was added neat or as a stock solution (20 v % in THF, for reactions at < 40 °C) with stirring. IR spectra were recorded