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Lithium Diisopropylamide-mediated Enolizations: Solvent-Independent Rates -- Solvent-Dependent Mechanisms

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Supporting Information

I. Plots of k_{obsd} versus [THF] in toluene cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, 0.004 M) by LDA (0.10 M)

II. Plot of k_{obsd} versus [LDA] for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, 0.004 M) in neat THF

III. Plot of k_{obsd} versus [HMPA] for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester-d_1 (**1**-d_1, 0.004 M) by LDA (0.10 M) in various THF concentrations

IV. Plots of k_{obsd} versus [LDA] in THF (9.4 M) and hexane cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester-d_1 (**1**-d_1, ≤0.004 M) with HMPA

V. Plot of k_{obsd} versus [DMPU] in THF (8.2 M) and hexane cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, 0.004 M) by LDA (0.10 M)

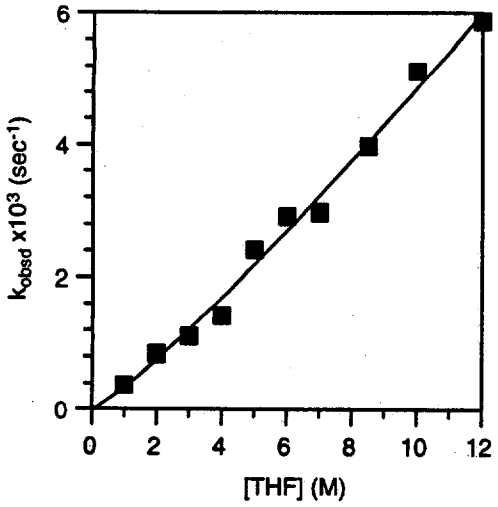
VI. Plots of k_{obsd} versus [LDA] in THF (8.2 M) and hexane cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, ≤0.004 M) with DMPU

VII. Plots of k_{obsd} versus [THF] in hexane cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, 0.004 M) with DMPU

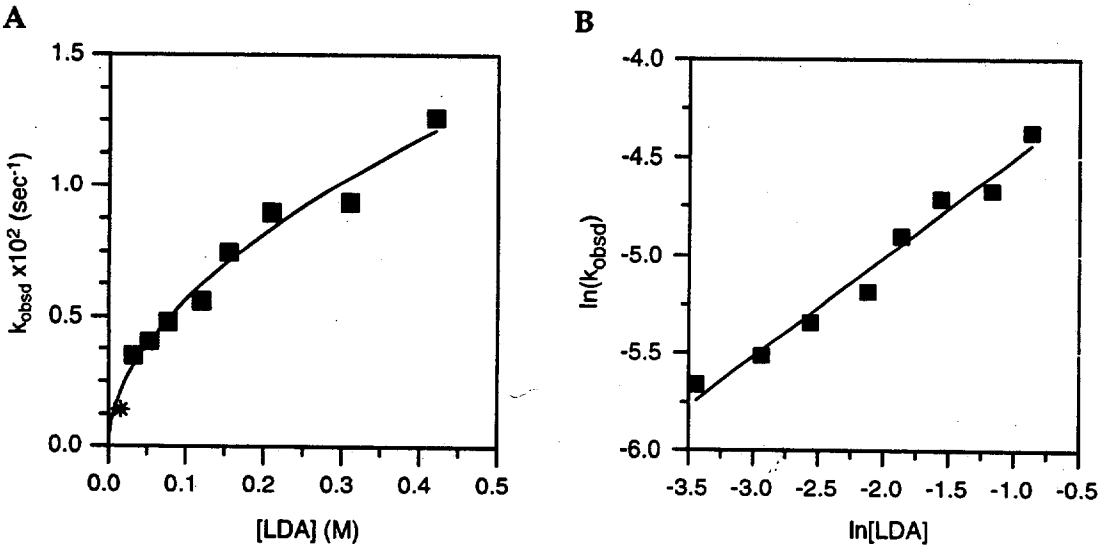
VIII. Plot of k_{obsd} versus [*t*-BuOMe] in hexane cosolvent for the enolization of cyclohexylpyrrolidin-1-yl-methanone (**6**, 0.0025 M) by LDA (0.050 M)

IX. Plot of k_{obsd} versus [LDA] for the enolization of cyclohexyl-pyrrolidin-1-yl-methanone (**6**, 0.003 M) in neat *t*-BuOMe

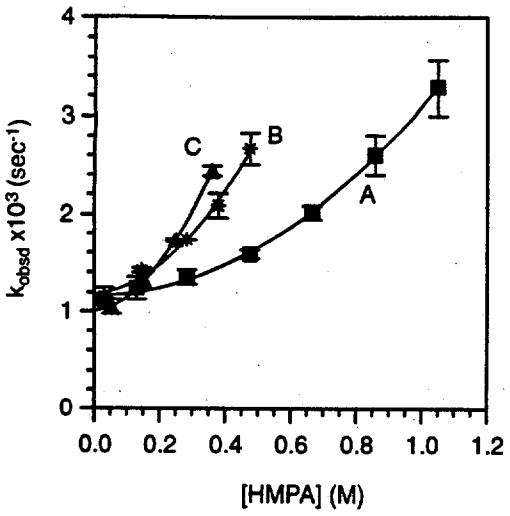
X. Tables of data for plots in Sections I-IX



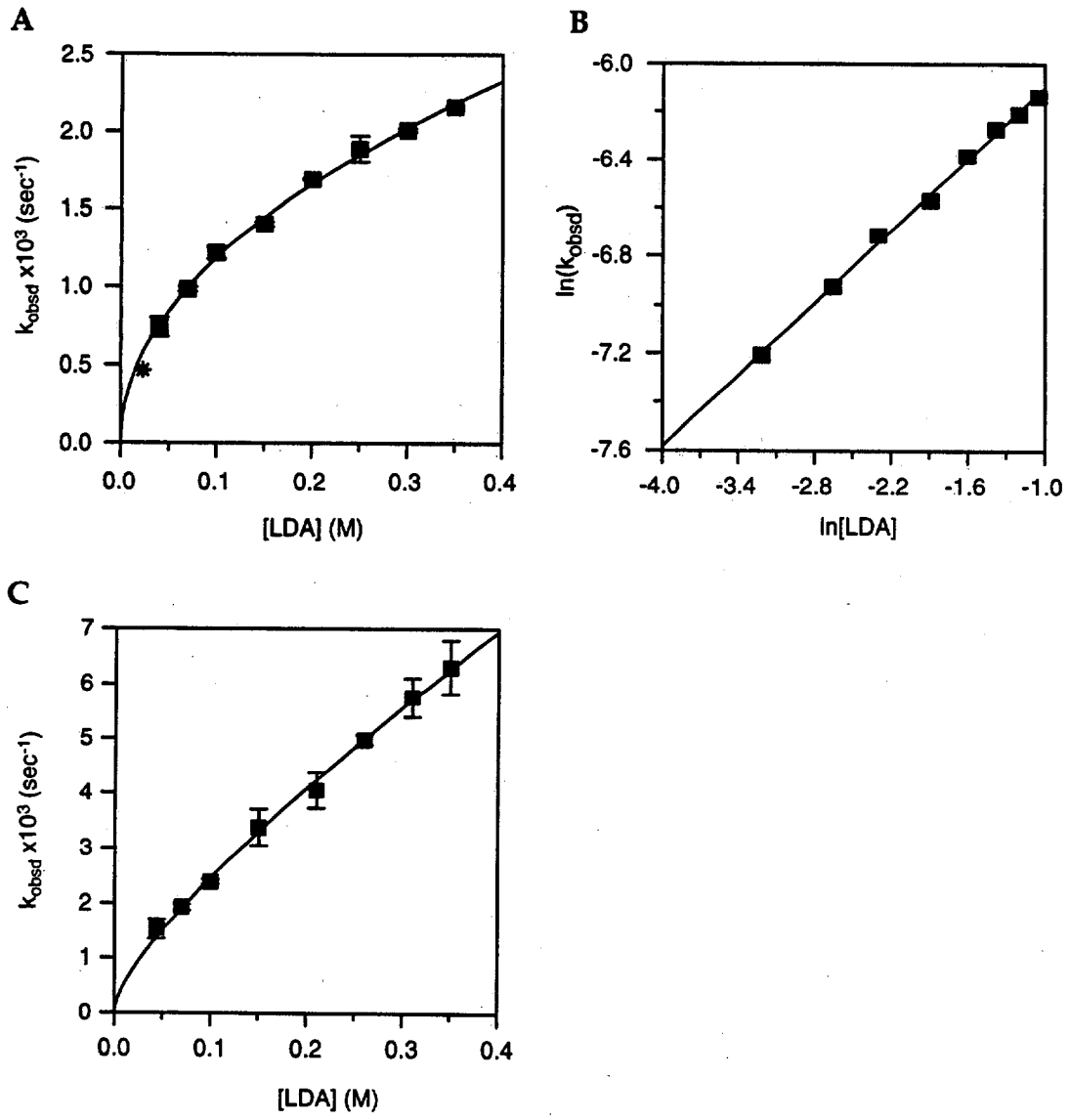
I. Plot of k_{obsd} versus [THF] in toluene cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, 0.004 M) by LDA (0.10 M) at -53 ± 0.5 °C. The curve depicts the result of an unweighted least-squares fit to $k_{obsd} = k[THF]^n + k'$ (Table 1).



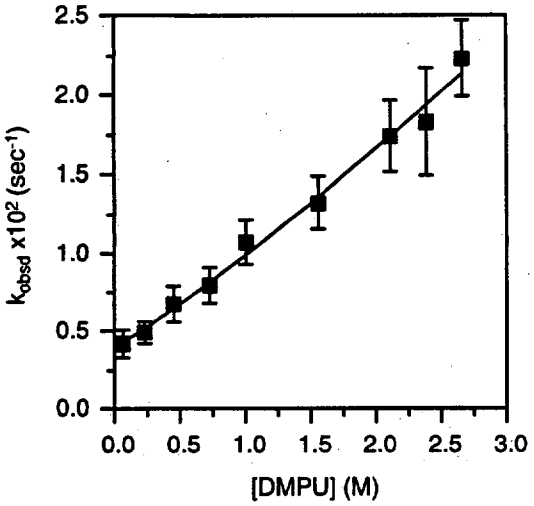
II. (A) Plot of k_{obsd} versus [LDA] for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, 0.004 M) by LDA in neat THF at -53 ± 0.5 °C. The curve depicts the result of an unweighted least-squares fit to $k_{obsd} = k[LDA]^n$ (Table 1). The asterisk (*) was not included in the fit. **(B)** log-log variant of plot in (A).



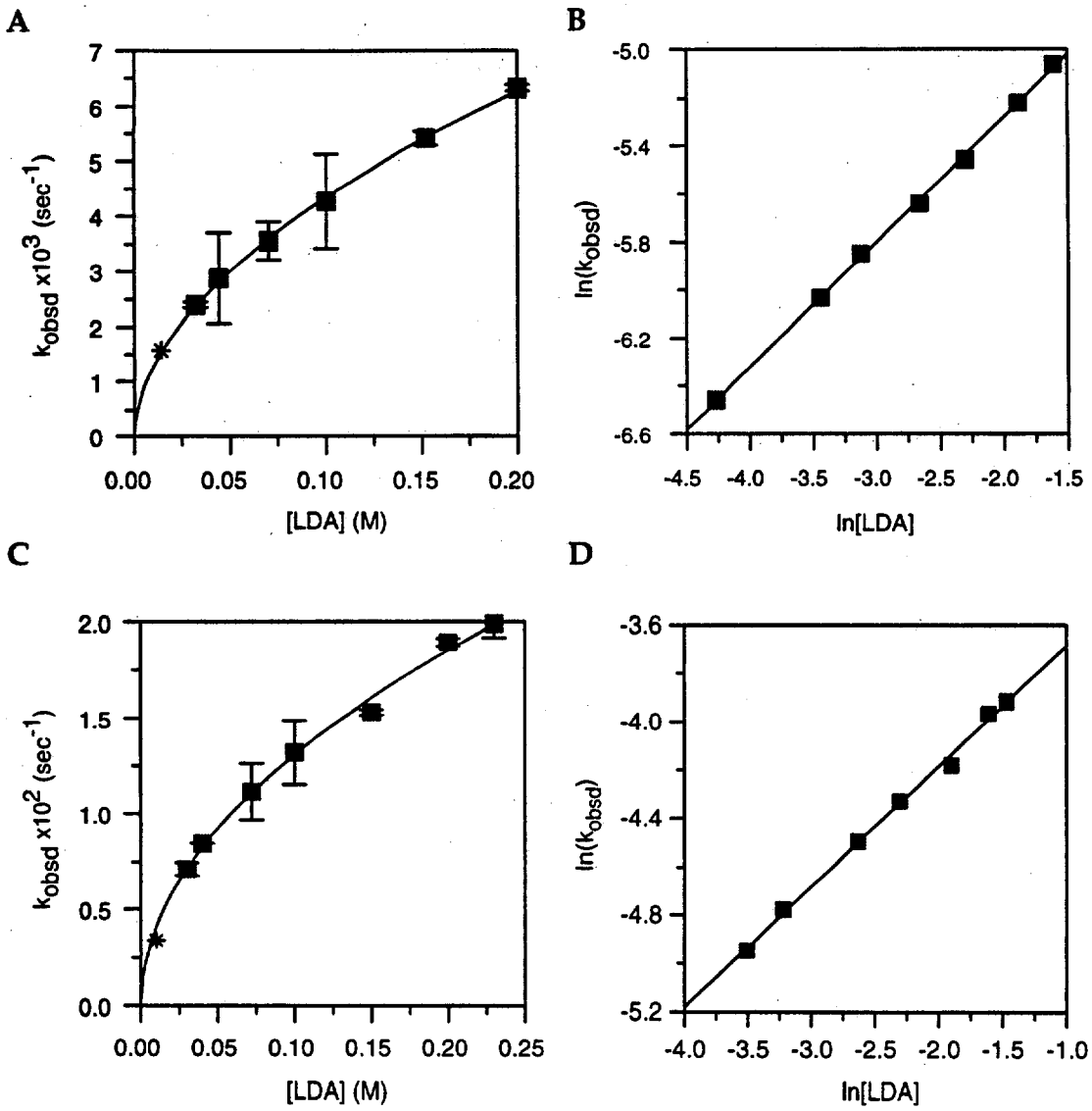
III. Plots of k_{obsd} versus [HMPA] in hexane cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester-d_1 (**1-d_1**, 0.004 M) by LDA (0.10 M) at -35 ± 0.5 °C with: **A** THF (9.4 M) in hexane cosolvent; **B** THF(2.0 M) in hexane cosolvent; **C** THF (0.20 M) in cyclopentane cosolvent. The curves depict the results of unweighted least-squares fits to $k_{obsd} = k[HMPA]^n + k'$. The values of n are 1.97 ± 0.09, 1.88 ± 0.30 , and 1.82 ± 0.08 for curves A, B, and C (respectively, Table 1).



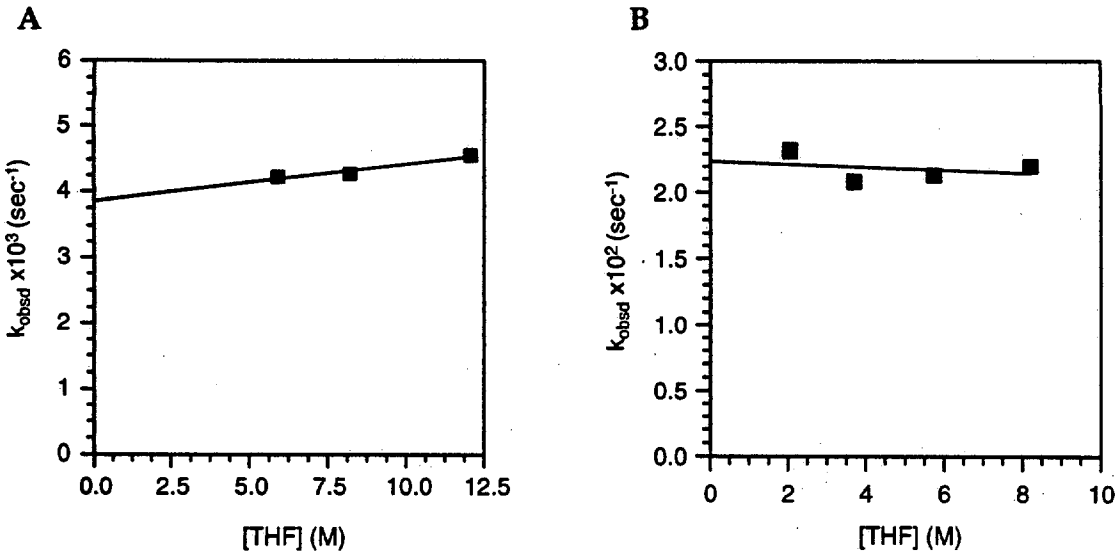
IV. Plots of k_{obsd} versus [LDA] in THF (9.4 M) and hexane cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester-d_1 (**1**-d_1, ≤0.004 M) by LDA at -35 ± 0.5 °C with: **(A)** HMPA (0.10 M). The curve depicts the result of an unweighted least-squares fit to $k_{obsd} = k[LDA]^n$; **(B)** Log-log variant of plot in (A); **(C)** HMPA (0.80 M). The curve depicts the result of an unweighted least-squares fit to $k_{obsd} = k[LDA]^{0.5} + k'[LDA]^n$ (Table 1). The asterisk (*) was not included in the fit.



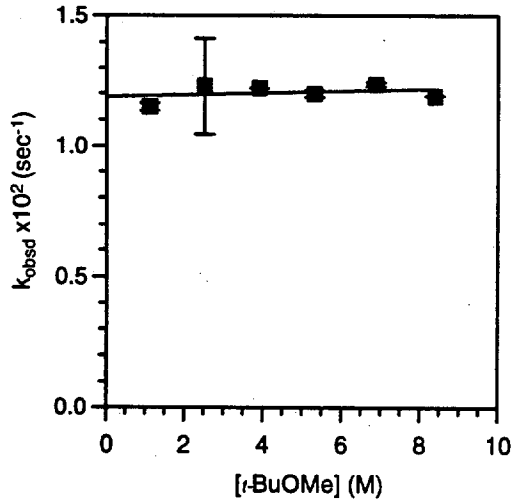
V. Plot of k_{obsd} versus [DMPU] in THF (8.2 M) and hexane cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, 0.004 M) by LDA (0.10 M) at -53 ± 0.5 °C. The curve depicts the result of an unweighted least-squares fit to $k_{obsd} = k[DMPU]^n + k'$ (Table 1).



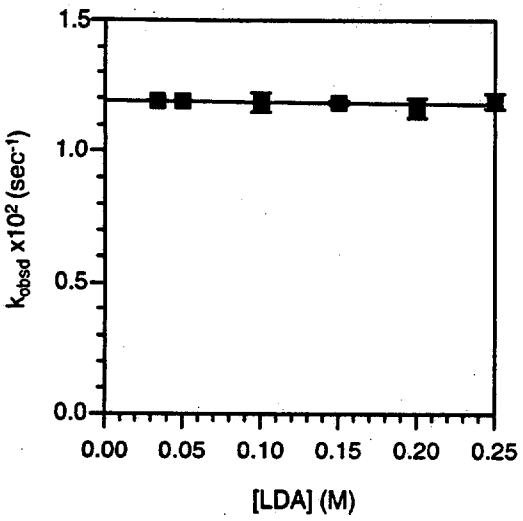
VI. Plots of k_{obsd} versus [LDA] in THF (8.2 M) and hexane cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, ≤0.004 M) at -53 ± 0.5 °C with: **(A)** DMPU (0.066 M); **(B)** Log-log variant of (A); **(C)** DMPU (1.56 M). The curves depict the results of unweighted least-squares fits to $k_{obsd} = k[LDA]^n$ (Table 1); **(D)** Log-log variant of (B). The asterisks (*) were not included in the fits.



VII. Plots of k_{obsd} versus [THF] in hexane cosolvent for the enolization of cyclohexanecarboxylic acid *tert*-butyl ester (**1**, 0.004 M) by LDA (0.10 M) at -53 ± 0.5 °C with: **(A)** DMPU (0.066 M); **(B)** DMPU (1.56 M). The curves depict the results of unweighted least-squares fits to $k_{obsd} = k[THF] + k'$. Poor solubility of a putative LDA/DMPU complex precluded measurements below 5.0 M THF in plot **(A)**.



VIII. Plot of k_{obsd} versus [*t*-BuOMe] in hexane cosolvent for the enolization of cyclohexylpyrrolidin-1-yl-methanone (**5**, 0.0025 M) by LDA (0.050 M) at 0 °C. The curve depicts the result of an unweighted least-squares fit to $k_{obsd} = k[t\text{-BuOMe}] + k'$ (Table 1).



IX. Plot of k_{obsd} versus [LDA] for the enolization of cyclohexyl-pyrrolidin-1-yl-methanone (**6**, 0.003 M) by LDA in neat *t*-BuOMe at 0 °C. The curve depicts the result of an unweighted least-squares fit to $k_{obsd} = k[LDA] + k'$ (Table 1).

X. Tables of data for plots in Sections I.

Data for Figure I

[THF] (M)	$k_{obsd}1$ (sec^{-1})
1.00	0.000370 ± 1E-5
2.00	0.000845 ± 1E-5
3.00	0.00111 ± 3E-5
4.00	0.00142 ± 2E-5
5.00	0.00241 ± 5E-5
6.00	0.00292 ± 8E-5
7.00	0.00298 ± 1E-4
8.50	0.00397 ± 8E-5
10.0	0.00512 ± 1E-4
12.0	0.00587 ± 2E-4

Data for figure II

[LDA] (M)	$k_{obsd}1$ (sec^{-1})
0.016	0.00143 ± 8E-5
0.032	0.00348 ± 3E-4
0.053	0.00403 ± 1E-4
0.077	0.00480 ± 1E-4
0.120	0.00560 ± 3E-4
0.155	0.00746 ± 3E-4
0.210	0.00897 ± 5E-4
0.310	0.00936 ± 4E-4
0.420	0.0126 ± 9E-4

Data for figure IIIA

[HMPA] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	k_{obsd}(avg) (sec^{-1})
0.030	0.00113 ± 5E-5	0.00110 ± 4E-5	0.00112 ± 2E-5
0.130	0.00132 ± 2E-5	0.00116 ± 4E-5	0.00124 ± 1E-4
0.283	0.00141 ± 2E-5	0.00130 ± 1E-4	0.00136 ± 7E-5
0.475	0.00162 ± 5E-5	0.00156 ± 1E-5	0.00159 ± 4E-5
0.666	0.00207 ± 8E-5	0.00197 ± 1E-4	0.00202 ± 7E-5
0.858	0.00246 ± 5E-5	0.00275 ± 1E-4	0.00261 ± 2E-4
1.05	0.00349 ± 9E-5	0.00309 ± 1E-4	0.00329 ± 3E-4

Data for Figure IIIB

[HMPA] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	$k_{obsd}(avg)$ (sec^{-1})
0.030	0.00122 ± 3E-5	0.00109 ± 5E-5	0.00116 ± 9E-5
0.145	0.00144 ± 4E-5	0.00140 ± 3E-5	0.00142 ± 2E-5
0.283	0.00174 ± 7E-5	0.00173 ± 4E-5	0.00174 ± 0E-5
0.379	0.00217 ± 5E-5	0.00201 ± 6E-5	0.00209 ± 1E-4
0.475	0.00256 ± 8E-5	0.00279 ± 1E-4	0.00268 ± 2E-4

Data for Figure IIIC

[HMPA] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	$k_{obsd}(avg)$ (sec^{-1})
0.053	0.000992 ± 3E-5	0.00110 ± 1E-5	0.00105 ± 8E-5
0.153	0.00126 ± 4E-5	0.00138 ± 2E-5	0.00132 ± 9E-5
0.249	0.00173 ± 5E-5	0.00172 ± 3E-5	0.00173 ± 1E-5
0.360	0.00247 ± 1E-5	0.00240 ± 5E-5	0.00244 ± 5E-5

Data for Figure IVA

[LDA] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	$k_{obsd}(avg)$ (sec^{-1})
0.023	0.000468 ± 2E-5		
0.040	0.000786 ± 2E-5	0.000697 ± 2E-5	0.000741 ± 6E-5
0.070	0.000972 ± 3E-5	0.000993 ± 3E-5	0.000983 ± 1E-5
0.100	0.00119 ± 3E-5	0.00124 ± 3E-5	0.00122 ± 4E-5
0.150	0.00139 ± 5E-5	0.00141 ± 4E-5	0.00140 ± 2E-5
0.200	0.00169 ± 6E-5	0.00169 ± 8E-5	0.00169 ± 1E-1
0.250	0.00183 ± 4E-5	0.00195 ± 9E-5	0.00189 ± 8E-5
0.300	0.00202 ± 7E-5	0.00200 ± 9E-5	0.00200 ± 1E-5
0.350	0.00215 ± 6E-5	0.00216 ± 7E-5	0.00216 ± 1E-5

Data for Figure IVB

[LDA] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	$k_{obsd}(avg)$ (sec^{-1})
0.040	0.00165 ± 2E-5	0.00140 ± 4E-5	0.00152 ± 1E-4
0.070	0.00190 ± 3E-5	0.00198 ± 5E-5	0.00194 ± 5E-5
0.100	0.00241 ± 4E-5	0.00235 ± 5E-5	0.00238 ± 4E-5
0.150	0.00315 ± 8E-5	0.00361 ± 1E-4	0.00333 ± 3E-4
0.210	0.00429 ± 8E-5	0.00382 ± 7E-5	0.00405 ± 3E-4
0.260	0.00504 ± 1E-4	0.00491 ± 1E-4	0.00498 ± 9E-5
0.310	0.00601 ± 1E-4	0.00550 ± 2E-4	0.00576 ± 3E-4
0.350	0.00665 ± 2E-4	0.00596 ± 1E-4	0.00630 ± 5E-4

Data for Figure V

[DMPU] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	$k_{obsd}3$ (sec^{-1})	k_{obsd}(avg) (sec^{-1})
0.0657	0.00480 ± 5E-5	0.00360 ± 1E-4		0.00420 ± 8E-4
0.231	0.00539 ± 8E-5	0.00443 ± 7E-5		0.00491 ± 7E-4
0.452	0.00757 ± 9E-5	0.00591 ± 1E-4		0.00674 ± 1E-3
0.729	0.00712 ± 1E-4	0.00875 ± 2E-4		0.00794 ± 1E-3
1.00	0.0117 ± 3E-4	0.00969 ± 2E-4		0.0107 ± 1E-3
1.56	0.0114 ± 3E-4	0.0134 ± 3E-4	0.0147 ± 4E-5	0.0132 ± 2E-3
2.11	0.0183 ± 7E-4	0.0148 ± 6E-4	0.0190 ± 4E-5	0.0174 ± 2E-3
2.39	0.0159 ± 1E-3	0.0207 ± 6E-4		0.0183 ± 3E-3
2.66	0.0240 ± 1E-3	0.0206 ± 1E-3		0.0223 ± 2E-3

Data for Figure VIA

[LDA] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	k_{obsd}(avg) (sec^{-1})
0.014	0.00157 ± 3E-5		
0.032	0.00236 ± 7E-5	0.00243 ± 7E-5	0.00240 ± 5E-5
0.044	0.00230 ± 2E-5	0.00346 ± 9E-5	0.00288 ± 8E-4
0.070	0.00379 ± 4E-5	0.00329 ± 4E-5	0.00354 ± 3E-4
0.100	0.00480 ± 5E-5	0.00360 ± 2E-4	0.00420 ± 8E-4
0.152	0.00532 ± 8E-5	0.00550 ± 7E-5	0.00541 ± 1E-4
0.200	0.00629 ± 7E-5	0.00637 ± 1E-4	0.00633 ± 6E-5

Data for Figure VIB

[LDA] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	$k_{obsd}3$ (sec^{-1})	k_{obsd}(avg) (sec^{-1})
0.010	0.00342 ± 8E-5			
0.030	0.00687 ± 1E-4	0.00736 ± 1E-4		0.00712 ± 4E-4
0.040	0.00852 ± 4E-4	0.00830 ± 1E-4		0.00841 ± 2E-4
0.072	0.0101 ± 2E-4	0.0122 ± 2E-4		0.0112 ± 1E-4
0.100	0.0114 ± 3E-4	0.0134 ± 3E-4	0.00147 ± 4E-4	0.0132 ± 2E-3
0.150	0.0154 ± 5E-4	0.0152 ± 3E-4		0.0153 ± 1E-4
0.200	0.0188 ± 5E-4	0.0191 ± 6E-4		0.0190 ± 2E-4
0.230	0.0194 ± 5E-4	0.0204 ± 5E-4		0.0199 ± 7E-4

Data for Figure VIIA

[THF] (M)	k_{obsd} (sec^{-1})
5.90	0.00422 ± 4E-5
8.21	0.00420 ± 5E-4
12.1	0.00456 ± 6E-5

Data for Figure VIIB

[THF] (M)	k_{obsd} (sec^{-1})
2.05	0.0232 ± 1E-3
3.69	0.0208 ± 9E-4
5.75	0.0213 ± 1E-3
8.21	0.0220 ± 2E-3

Data for Figure VIII

[*t*-BuOMe] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	k_{obsd}(avg) (sec^{-1})
1.12	0.0116 ± 3E-4	0.0114 ± 4E-4	0.0115 ± 1E-4
2.52	0.0110 ± 4E-4	0.0136 ± 4E-4	0.0123 ± 2E-3
3.92	0.0122 ± 5E-4	0.0122 ± 4E-4	0.0122 ± 0E-4
5.32	0.0121 ± 2E-4	0.0119 ± 2E-4	0.0120 ± 1E-4
6.88	0.0124 ± 3E-4	0.0123 ± 4E-4	0.0124 ± 1E-4
8.40	0.0119 ± 3E-4	0.0119 ± 3E-4	0.0119 ± 0E-4

Data for Figure IX

[LDA] (M)	$k_{obsd}1$ (sec^{-1})	$k_{obsd}2$ (sec^{-1})	k_{obsd}(avg) (sec^{-1})
0.034	0.0199 ± 2E-4	0.0119 ± 9E-4	0.0119 ± 0E-4
0.050	0.0119 ± 3E-4	0.0119 ± 3E-4	0.0119 ± 0E-4
0.100	0.0121 ± 5E-4	0.0116 ± 4E-4	0.0119 ± 3E-4
0.150	0.0118 ± 3E-4	0.0119 ± 2E-4	0.0119 ± 1E-4
0.200	0.0119 ± 1E-4	0.0114 ± 3E-4	0.0117 ± 4E-4
0.250	0.0117 ± 1E-4	0.0121 ± 3E-4	0.0119 ± 3E-4