# $^{1}$H Pure Shift DOSY: a Handy Tool to Evaluate the Aggregation and Solvation of Organolithium Derivatives

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## Supporting Information

### Experimental Section

# Experimental Section

### Preparation of the sample

All syntheses and sample preparations of air-sensitive compounds were performed in an argon atmosphere. All solvents were dried over sodium, and degassed in a vacuum system before being used.

### Preparation of *n*-Butyllithium Solution in Tetrahydrofuran-$d_8$

A solution of commercial *n*-butyllithium in pentane (1 mL) was syringed in a tube fitted with a septum and flushed under dry argon. The tube was then placed under vacuum (20 mmHg) for 2 h to remove the main part of the pentane. Freshly distilled tetrahydrofuran-$d_8$ was then added (1 mL) at −78 °C to the resulting concentrated solution, and the resulting solution was titrated[1].

### Preparation of LDA/*n*-BuLi/*n*-BuOLi with internal references:

Freshly distilled di*iso*propylamine (0.14 mL) dissolved in THF (0.3 mL) was introduced into an NMR tube placed under argon. The solution (0.34M) was treated first with an equimolar amount of *n*-BuLi (*c* = 1M) in THF at 185K. The quantitative formation of the amide was controlled by 1D $^{1}$H and $^{6}$Li NMR experiments. Then, two equivalents of *n*-BuLi were added into the solution. A second step consisted of the progressive addition of *n*-BuOH into the LDA/*n*-BuLi mixture until a (1: 2: 0.9) ratio was reached. Then 0.15 mL from a mixture containing SQA (0.1 mL), CDDE (0.1 mL) and TPB (30 mg) preliminarily diluted in THF-$d_8$ (5 mL) was added to the above sample as internal references for the DOSY experiments.

### Preparation of *n*-BuLi/*n*-BuOLi with internal references:

Controlled aliquots of *n*-BuOH were added to the solution of pure *n*-BuLi (*c* = 1 M) until a (1:0.66) ratio was reached. Then 0.15 mL from a mixture containing SQA (0.1 mL), CDDE (0.1 mL) and TPB (30 mg) preliminarily diluted in THF-$d_8$ (5 mL) was added to the above sample as internal references for the DOSY experiments.

### NMR parameters and conditions

NMR spectra were recorded at 185K on a Bruker AVIII 500 spectrometer operating at 500.13 MHz for $^{1}$H, 194.40 MHz for $^{7}$Li, 125.13 MHz for $^{13}$C and 73.60 MHz for $^{6}$Li. Experiments were run under TopSpin (version 2.1, Bruker Biospin, Karlsruhe) with a BBFO {$^{1}$H,X} probe and a z gradient coil giving a maximum gradient of 50 G.cm$^{-1}$.

**$^{1}$H DOSY** experiments was acquired with the standard Bruker ledbpgp2s program[2] using 16 $t_1$ increments of 32 transients. The acquisition time was 1 s and the relaxation delay was 2.5 s (D1). Diffusion time was between 0,5 and 0.6 s (D20) and rectangular gradient pulse duration was between 1.5 and 2 ms (P30). Gradient recovery delays of 150 µs followed the application of each gradient pulse. Data was accumulated by linearly varying the diffusion encoding gradients over a range from 2 to 95 % for 16 gradient increment values.

**$^{7}$Li DOSY** experiment was acquired with the standard Bruker dstebpgp3s program[3] using double stimulated echo, LED, with bipolar gradient pulses and 3 spoil gradients for 16 $t_1$ increments of 32 transients. The acquisition time was 2.5 s, and the relaxation delay (D1) was 5 s. Diffusion time was 0.9 s (D20) and rectangular gradient pulse duration was 4 ms (P30). Gradient recovery delays of 150 µs followed the application of each gradient pulse. Data was accumulated by linearly varying the diffusion encoding gradients over a range from 2 to 95 % for 16 gradient increment values.

**$^{1}$H PS-DOSY**[4] experiments were acquired with the sequence of Figure 1 with one stimulated echo using a 20 ms Rsnob selective pulse with 100 Hz bandwidth, with Gz2=1.8 G.cm$^{-1}$; 16 $t_1$ increments of 32 transients were acquired with 1/SW = 20 ms in a total time of 5 h. Coherence transfer selection gradient pulses were rectangular with a width of 1 ms and the amplitudes $Gz1_a$, G $z1_b$, and G $z1_c$ of 25, -25, and -50 G.cm$^{-1}$. The delays $\tau_a$ and $\tau_b$ were 0.0038 s and 0.0029 ms, respectively. Individual rows of the pseudo-2-D diffusion databases for PS-DOSY were phased and baseline corrected. Diffusion time was between 0.25 - 0.4 s and rectangular gradient pulse duration was between 2 - 2.5 ms. Gradient recovery delays were 150 µs followed the application of each gradient pulse. Data was accumulated by linearly varying the diffusion encoding gradients over a range from 2 to 95 % for 16 gradient increment values.

**DOSY processing**

$^{1}$H DOSY experiments were processed using DOSYm® software which is based on Gifa MaxEnt algorithm proposed by Marc-Andre Delsuc[5].

$^{1}$H PS-DOSY experiments were processed using dynamic center software (Bruker software). This program allows the use of the pure exponential equation for relevant processing methods:

$$S(g) = I_0 * e^{\left(-\gamma^2 * g^2 * \delta^2 * \left(\Delta - \delta/3\right) * D\right.}$$

The diffusion coefficient was determined by fitting the peak areas to the Stejskal-Tanner equation from $T_1/T_2$ analysis.

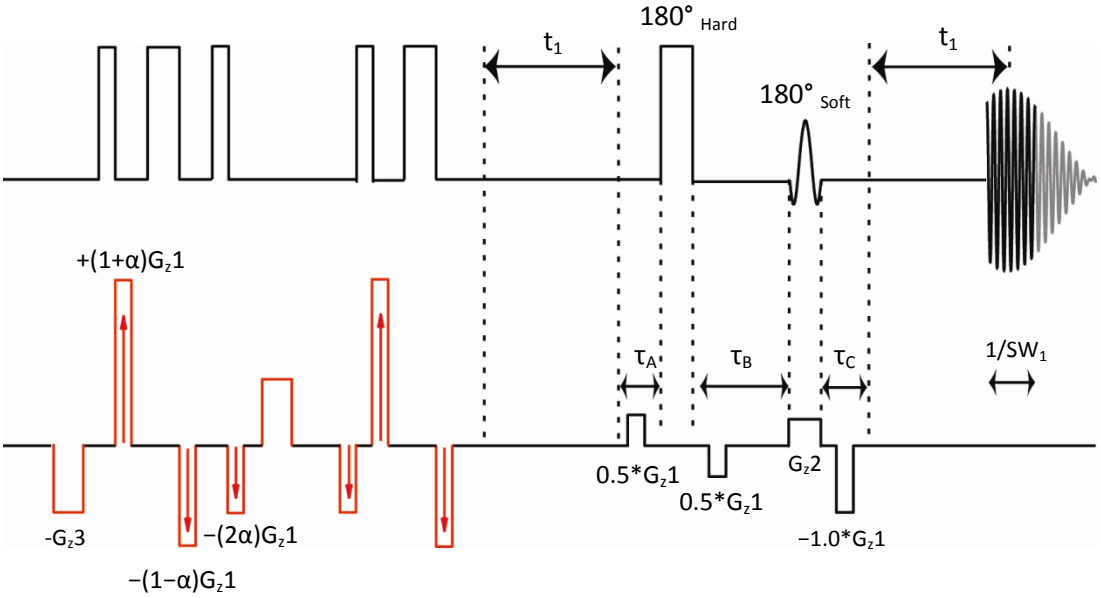


**Figure S1. $^{1}$H Pure Shift DOSY sequence**

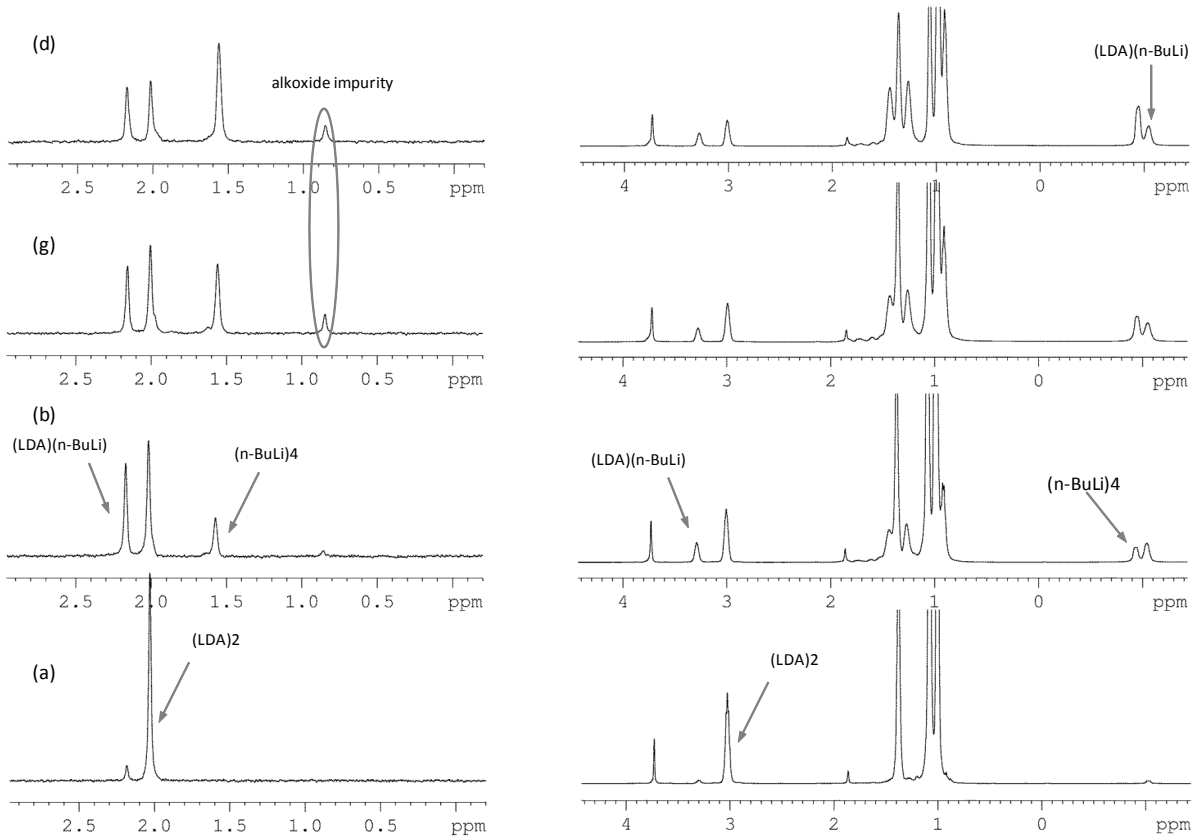


**Figure S2. $^{6}$Li (left) and 'H (right) spectra of LDA/*n*-BuLi mixtures in THF-$d_8$ at 185K: (a) pure LDA (0.34M), b) LDA/*n*-BuLi (1 : 0.66) ; (c) LDA/*n*-BuLi/ (1 : 1.33) d) LDA/*n*-BuLi/ (1 : 2)**

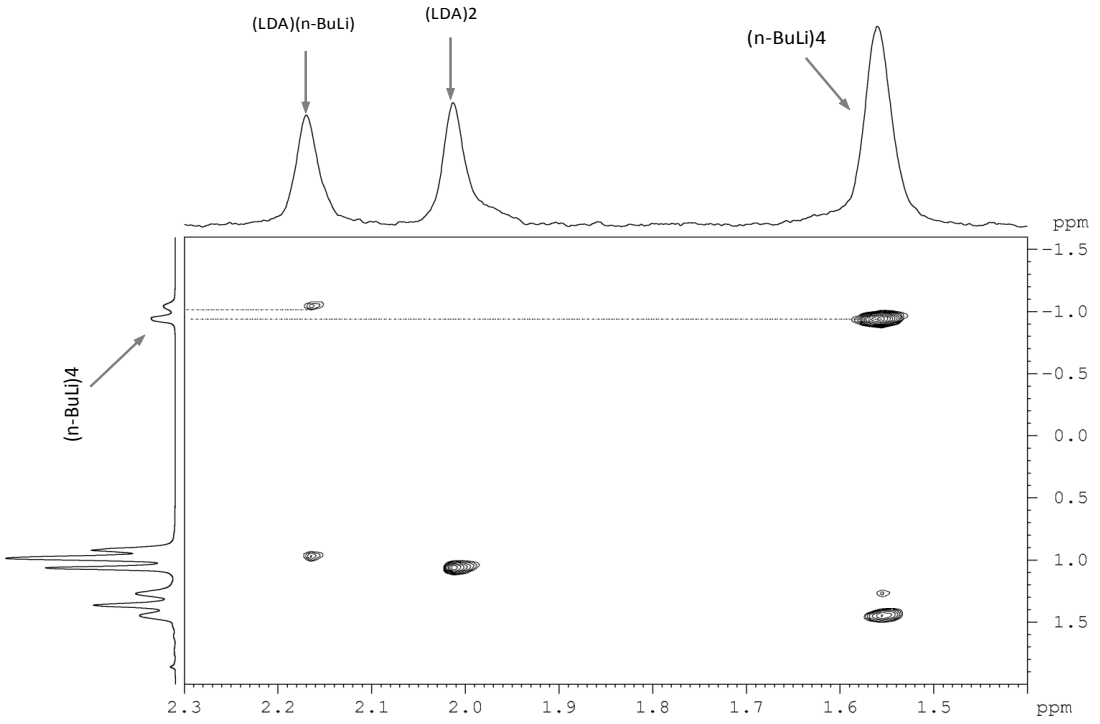


**Figure S3. 2D $^{6}$Li-$^{1}$H HOESY spectrum (mixing times $\tau_m$=860 ms) for LDA/*n*-BuLi (1 : 2) in THF-$d_8$ at 185K**

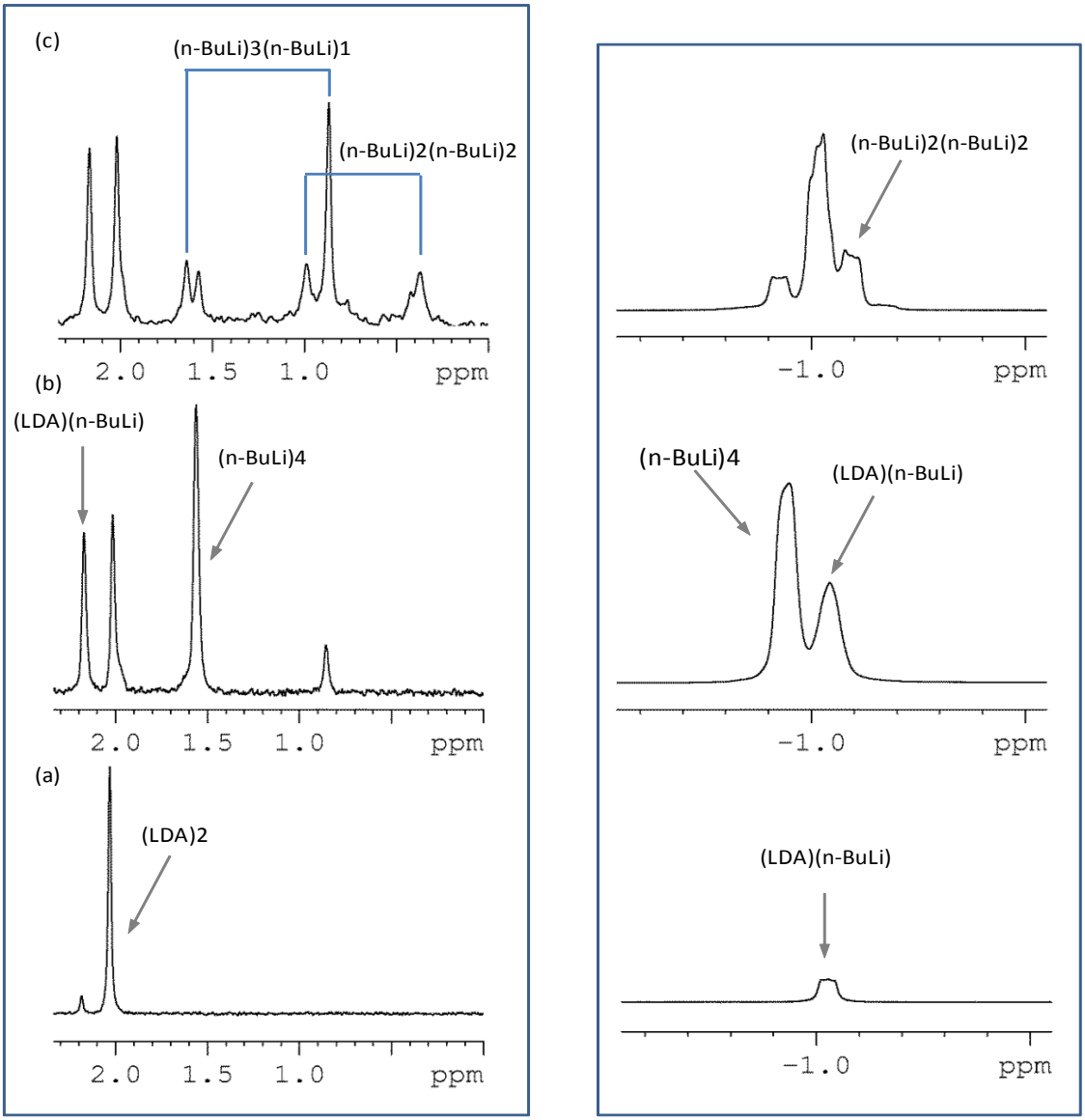


**Figure S4. $^{6}$Li (left) and 'H (right) spectra of LDA/*n*-BuLi/*n*-BuOH mixtures in THF-$d_8$ at 185K: (a) pure LDA (0.34M), b) LDA/*n*-BuLi (1 : 2) ; (c) LDA/*n*-BuLi/*n*-BuOH (1 : 2 : 0.9)**

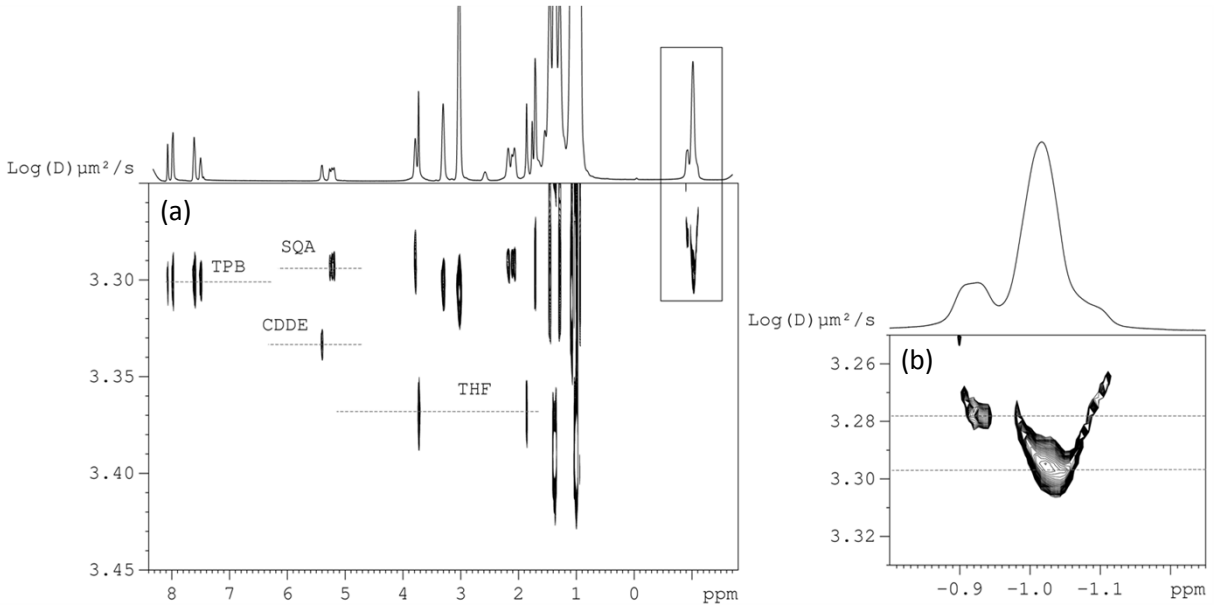


**Figure S5. (a) $^{1}$H DOSY spectrum for LDA/*n*-BuLi/*n*-BuOH (1 : 2 : 0.9) in THF-$d_8$ at 185K with internal references (Butane, Cyclododecene (CDDE), Squalene (SQA), 1,3,5-Triphenylbenzene (TPB). (b) Zoom of alpha methylene region**

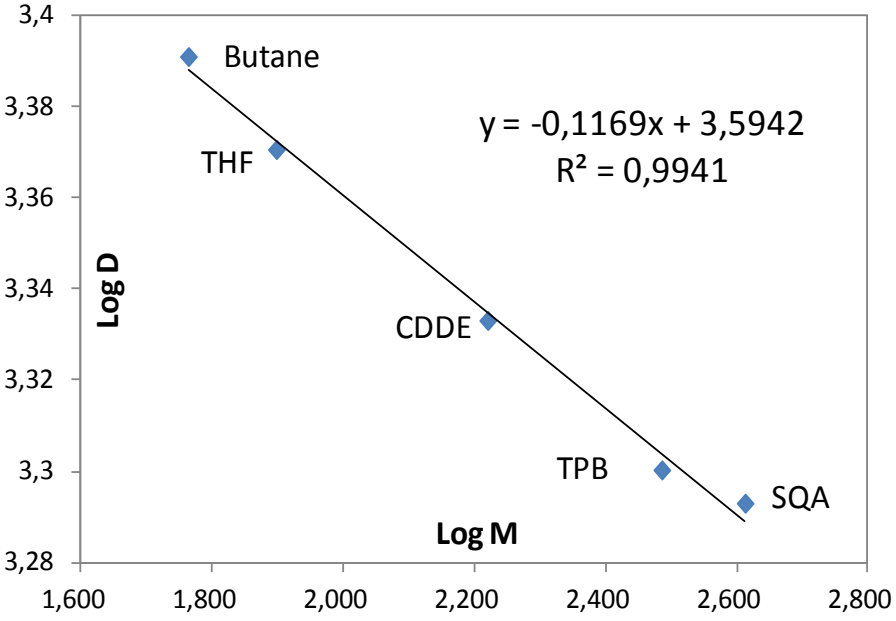


**Figure S6. Log(D)-Log(FW) analysis of $^{1}$H DOSY spectrum for LDA/*n*-BuLi/*n*-BuOH (1 : 2 : 0.9)**

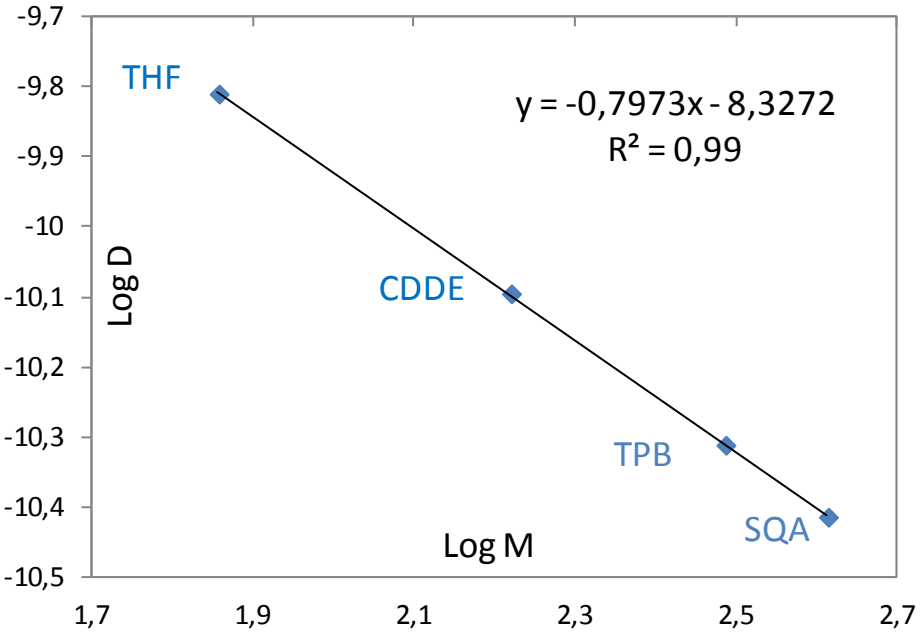


**Figure S7. Log(D)-Log(FW) analysis of $^{1}$H PS-DOSY spectrum for LDA/*n*-BuLi/*n*-BuOH (1 : 2 : 0.9)**

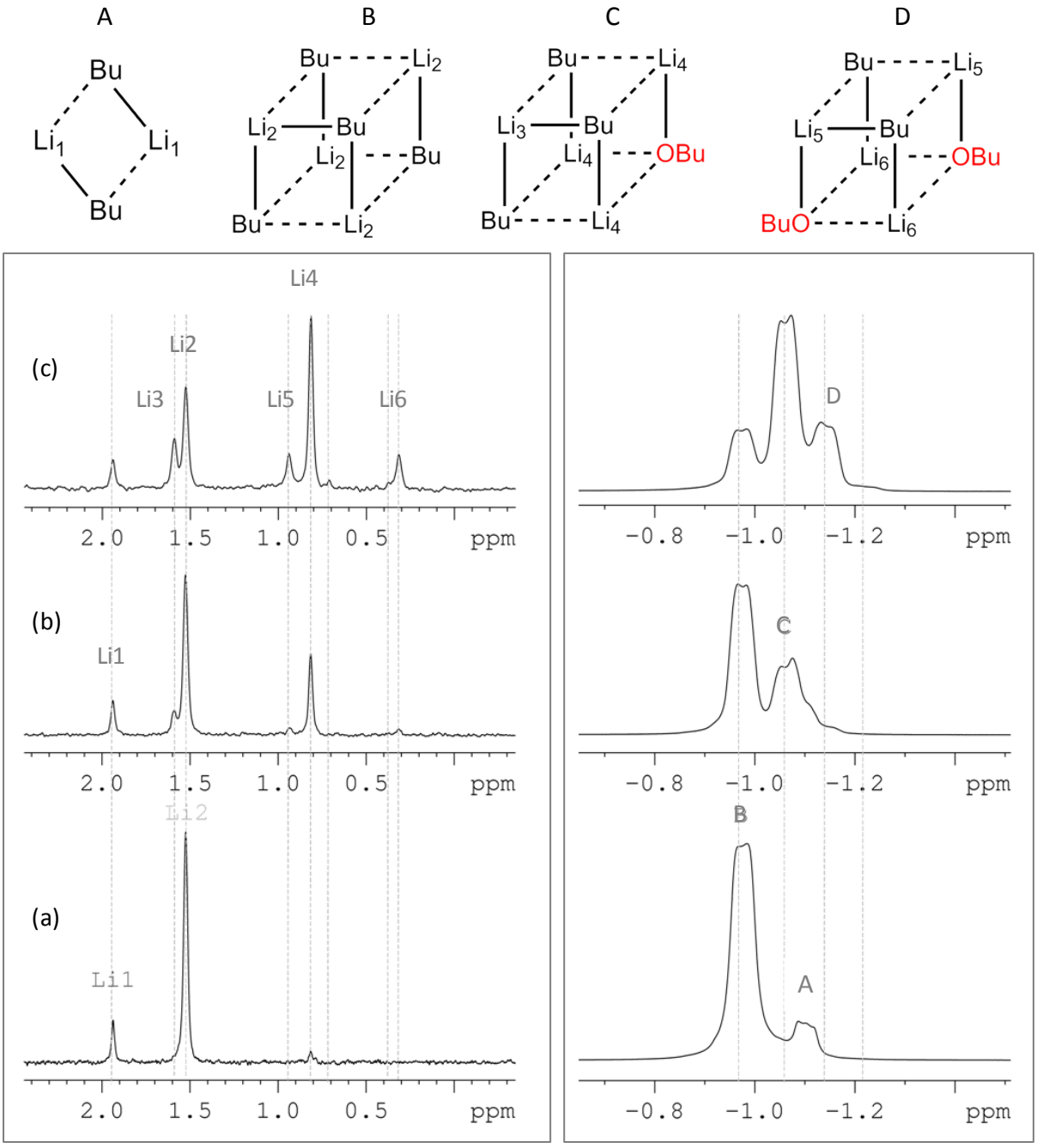


**Figure S8. $^{6}$Li (left) and $^{1}$H (right) spectra of *n*-BuLi/*n*-BuOLi mixtures in THF-$d_8$ at 185K: (a) pure *n*-BuLi; (b) *n*-BuLi/*n*-BuOLi (1 : 0.25) ; (c) *n*-BuLi /*n*-BuOLi (1 : 0.66)**

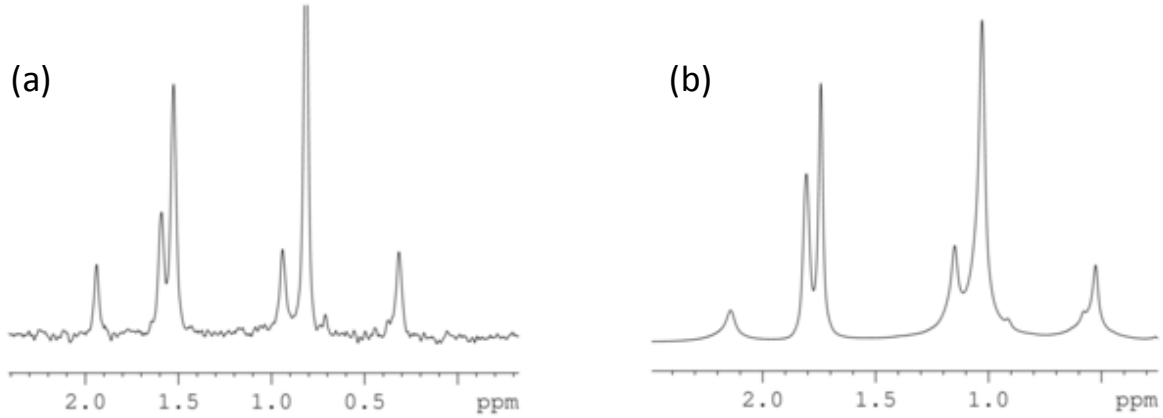


**Figure S9. $^{6}$Li (a) and $^{7}$Li (b) spectra of *n*-BuLi/*n*-BuOLi mixture (1 : 0.66) in THF-$d_8$ at 185K**

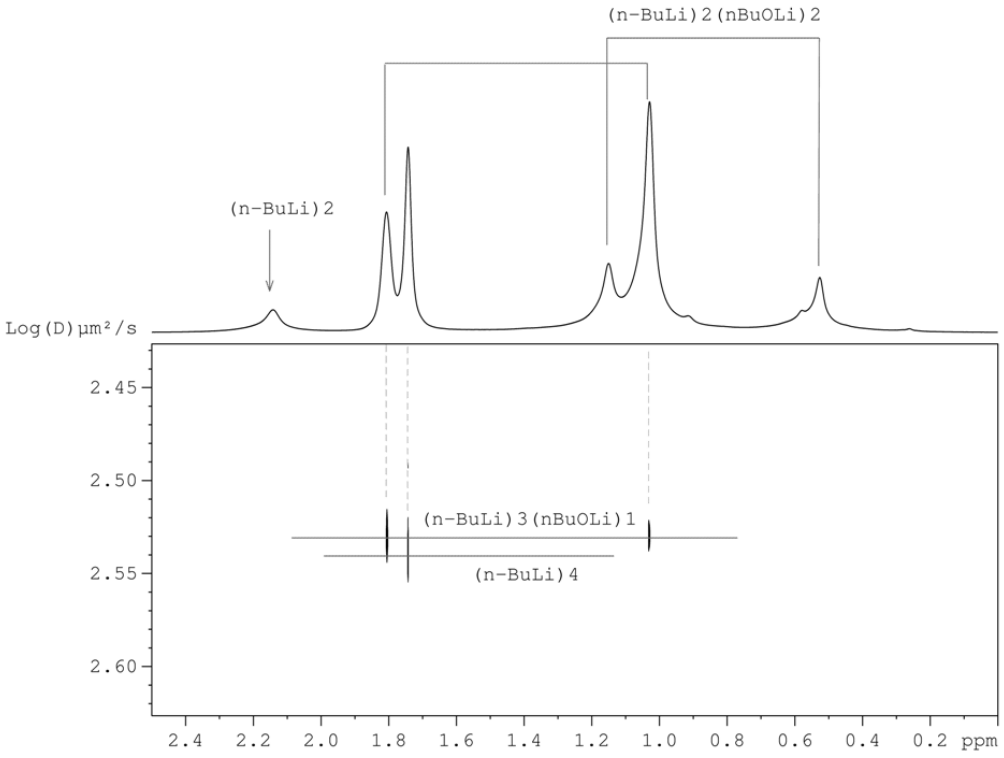


**Figure S10. $^{7}$Li DOSY spectrum for *n*-BuLi/*n*-BuOLi (1 : 0.66) in THF-$d_8$ at 185K**

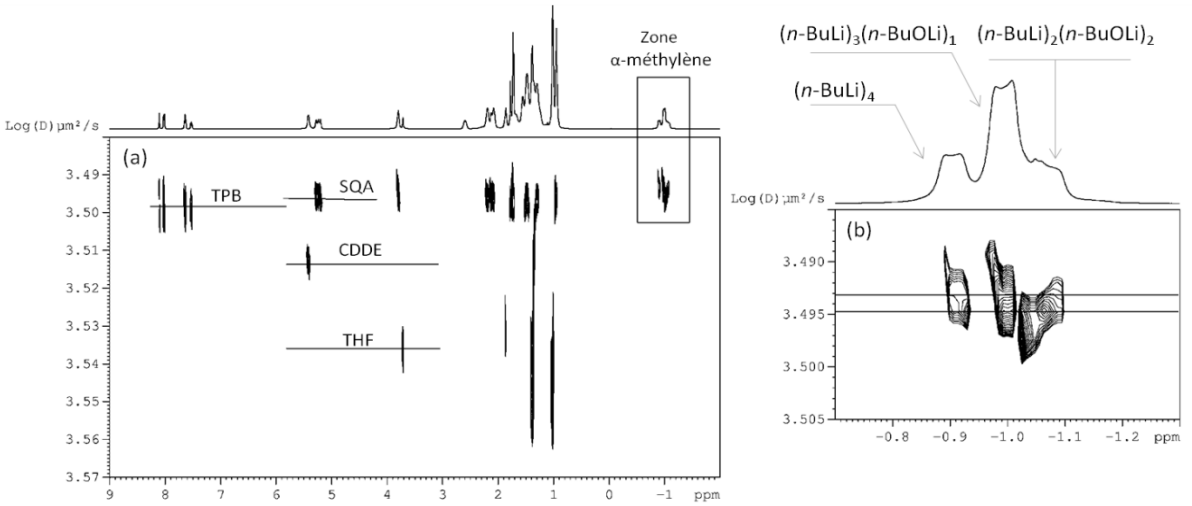


**Figure S11. $^{1}$H DOSY spectrum for *n*-BuLi/*n*-BuOLi (1 : 0.66) in THF-$d_8$ at 185K with internal references (Butane, Cyclododecene (CDDE), Squalene (SQA), 1,3,5-Triphenylbenzene (TPB)). (b) Zoom for alpha methylene region**

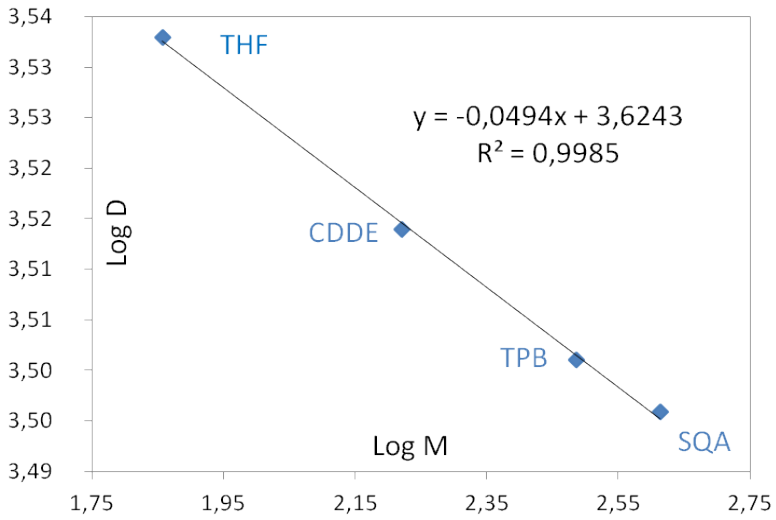


**Figure S12. Log(D)-Log(FW) analysis of $^{1}$H DOSY spectrum for *n*-BuLi/*n*-BuOLi (1 : 0.66)**

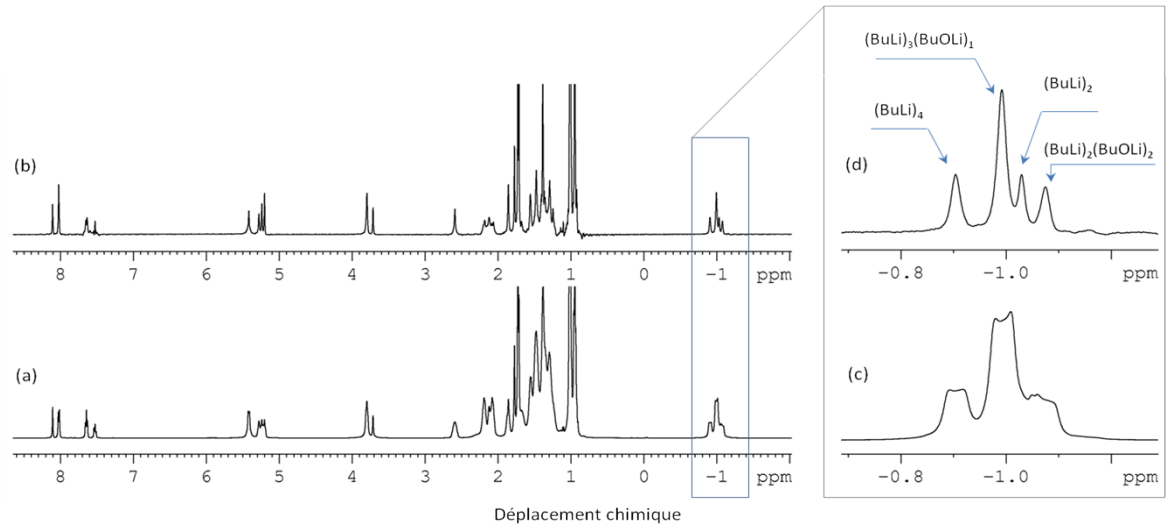


**Figure S13. $^{1}$H (a) and $^{1}$H PS (b) spectra of *n*-BuLi/*n*-BuOLi mixture (1 : 0.66) in THF-$d_8$ at 185K**

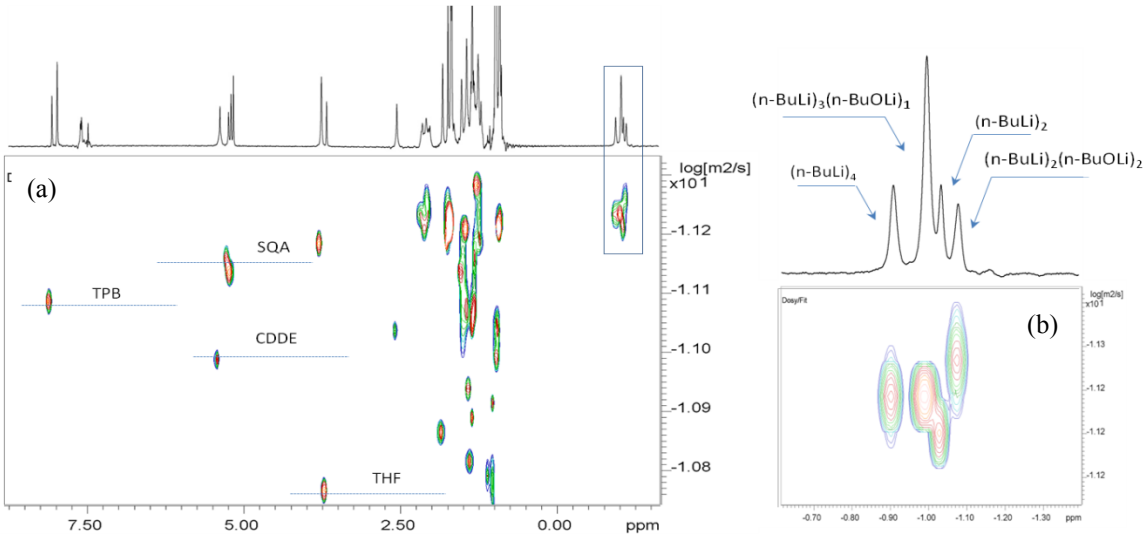


**Figure S14. (a) $^{1}$H PS-DOSY spectrum for *n*-BuLi /*n*-BuOLi (1 : 0.66) in THF-$d_8$ with internal references (CDDE, SQA, TPB). (b) Zoom for alpha methylene region**

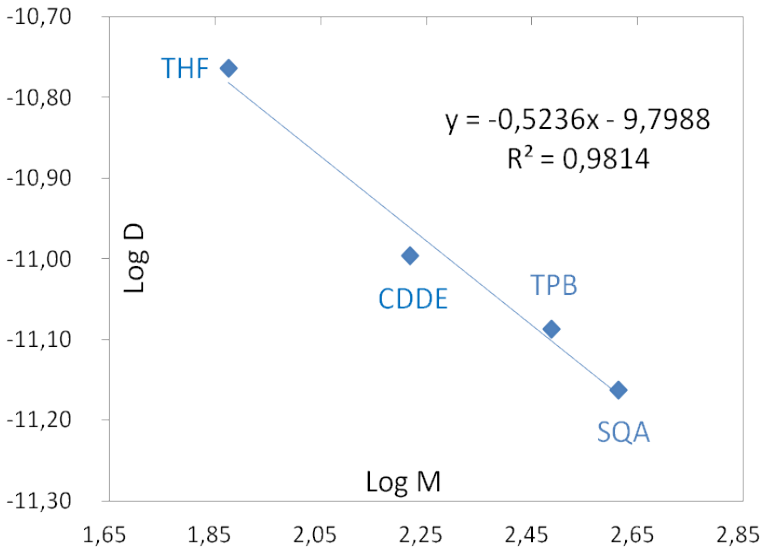


**Figure 15. Log(D)-Log(FW) analysis of $^{1}$H PS-DOSY spectrum for *n*-BuLi/*n*-BuOLi (1 : 0.66)**

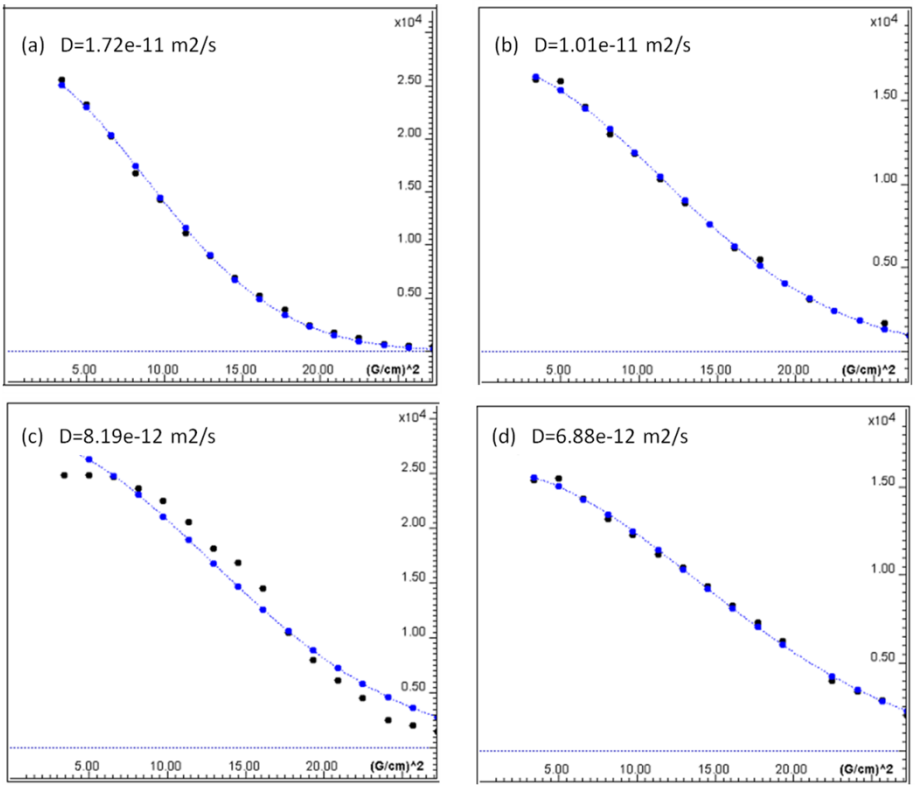


**Figure S16. Signal attenuation curves from $^1$H PS-DOSY of (a) THF, (b) CDDE, (c) TPB (d) SQA**

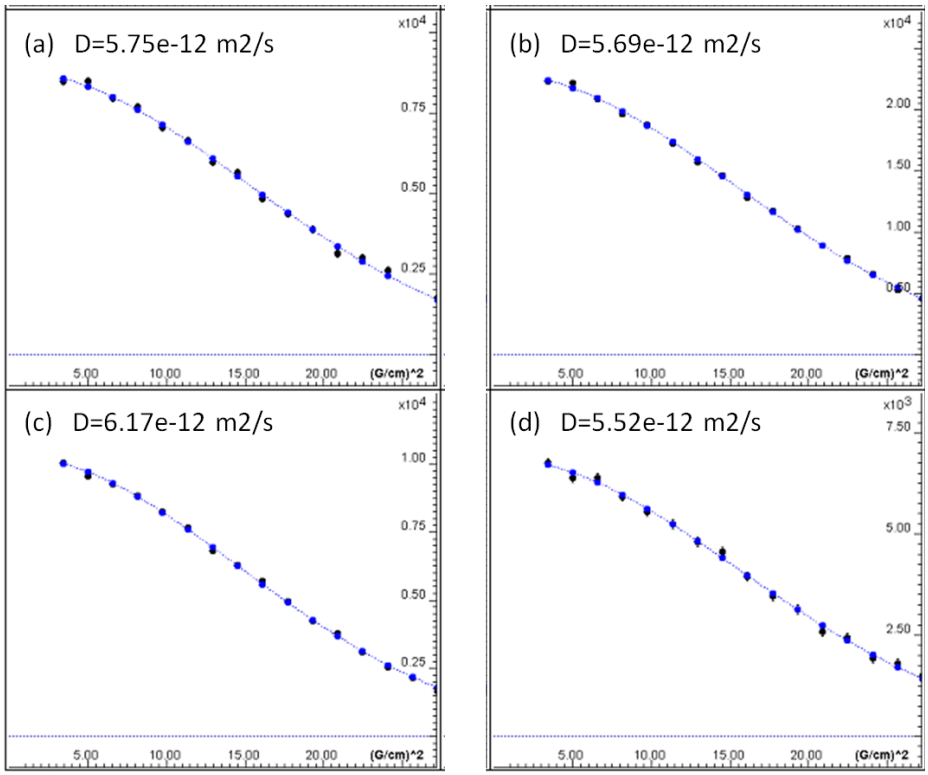


**Figure S17. Signal attenuation curves from $^1$H PS-DOSY of (a) (*n*-BuLi)$_4$, (b) (*n*-BuLi)$_3$(*n*-BuOLi)$_1$, (c) (*n*-BuLi)$_2$, (d) (*n*-BuLi)$_2$(*n*-BuOLi)$_2$**

| Compounds | $^1$H DOSY | | | | |
|---|---|---|---|---|---|
| | FW (gmol$^{-1}$) | Log(D) m$^2$s$^{-1}$ | **N*THF** | **FW*** (gmol$^{-1}$) | Error % |
| THF | 64 | 3.5330 | | 72 | |
| Squalene (SQA) | 411 | 3.4959 | | 411 | |
| Triphenylbenzene (TPB) | 306 | 3.5011 | | 306 | |
| Cyclododecene (CDDE) | 166 | 3.5140 | | 166 | |
| **(*n*-BuLi)$_4$ ●(THF)$_4$** | **477.4** | **3.4925** | **~ 4** | **544** | **6,5%** |
| **(*n*-BuLi)$_3$/(*n*-BuOLi)$_1$ ●(THF)$_4$** | **440.1** | **3.4941** | **~ 3** | **560** | **12%** |
| **(*n*-BuLi)$_2$/(*n*-BuOLi)2 ●(THF)$_4$** | **425.9** | **3.4948** | **~ 2** | **576** | **15%** |

**Table S1. Analysis of $^1$H DOSY results for *n*-BuLi /*n*-BuOLi (1 : 0.66) in THF-*d*$_8$ (FW* Theoretical mass of solvated specie)**

| Compounds | $^1$H DOSY | | | | |
|---|---|---|---|---|---|
| | FW (g.mol$^{-1}$) | Log(D) m$^2$.s$^{-1}$ | **N*THF** | **FW*** (g.mol$^{-1}$) | Error % |
| Butane | | 3.3910 | | | |
| THF | 72 | 3.3706 | | 72 | |
| Cyclododecene (CDDE) | 166 | 3.3331 | | 411 | |
| Triphenylbenzene (TPB) | 306 | 3.3003 | | 306 | |
| Squalene (SQA) | 411 | 3.2930 | | 166 | |
| **(LDA)$_2$●(THF)$_2$** | **304** | **3.3040** | **2** | **358** | **4.5%** |
| **(LDA)(*n*-BuLi)●(THF)$_2$** | **309** | **3.3031** | **2** | **315** | **1%** |
| **(*n*-BuLi)$_4$●(THF)$_4$** | **507** | **3.2780** | **4** | **544** | **3.5%** |

**Table S2. Analysis of $^1$H DOSY results for LDA/*n*-BuLi/*n*-BuOH (1 : 2 : 0.9) (FW*: Theoretical mass of solvated specie**

| Compounds | $^1$H PS-DOSY | | | | |
|---|---|---|---|---|---|
| | FW (gmol$^{-1}$) | Log(D) m$^2$s$^{-1}$ | **N*THF** | **FW*** (gmol$^{-1}$) | Error % |
| Squalene (SQA) | 411 | -11.16 | | 411 | |
| Triphenylbenzene (TPB) | 306 | -11.09 | | 306 | |
| Cyclododecene (CDDE) | 166 | -11.00 | | 166 | |
| THF | 72 | -10.76 | | | |
| **(*n*-BuLi)$_4$ ●(THF)$_4$** | **566** | **-11.24** | **~4** | **544** | **2%** |
| **(*n*-BuLi)$_3$/(*n*-BuOLi)$_1$ ●(THF)$_4$** | **579** | **-11.25** | **~4** | **560** | **1.7%** |
| **(*n*-BuLi)$_2$ ●(THF)$_4$** | **490** | **-11.21** | **~4** | **416** | **8.2%** |
| **(*n*-BuLi)$_2$/(*n*-BuOLi)$_2$ ●(THF)$_4$** | **612** | **-11.26** | **~□** | **576** | **3%** |

**Table S3. Analysis of $^1$H PS-DOSY results for *n*-BuLi /*n*-BuOLi (1 : 0.66) in THF-*d*$_8$ (FW* Theoretical mass of solvated specie)**

**References**


**1**. L. Duhamel, J.-C. Plaquevent, *J. Organomet. Chem*. 1993, **448**, 1.

**2**. D. Wu, A. Chen and C.S. Johnson Jr., *J. Magn. Reson. A* 1995, **115**, 260.

**3**. (a) A. Jerschow and N. Mueller, *J. Magn. Reson. A* 1996,**123**, 222; (b) A. Jerschow and N. Mueller, *J. Magn. Reson*. *A* 1997, **125**, 372.

**4**. J. A. Aguilar, S. Faulkner, M. Nilsson, and G. A. Morris, *Angew. Chem. Int. Ed.* 2010, **49**, 3901.

**5**. J. L. Pons, T. E. Malliavin and M. A. Delsuc, *J. Biomol. NMR* 1996, **8**, 445.