NMR Spectroscopy of Organolithium Compounds, XV[1]

Two-Dimensional 6Li,1H-NMR Shift Correlation by Multiple Quantum Spectroscopy and Polarization Transfer: New Tools for Structural Research in the Field of Organolithium Compounds[2]

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Sizable scalar 6Li,1H spin-spin coupling constants have been observed for the new dilithio compound (Z)-2-lithio-1-(o-lithiophenyl)ethene (3) which allow an assignment of the two nonequivalent 6Li resonance signals measured for the dimer of 3.

Two-dimensional 6Li,1H shift correlation experiments based on multiple quantum spectroscopy as well as on polarization transfer are introduced as new tools for structural research in the field of organolithium compounds.

Among the two-dimensional NMR methods, shift correlations[3] are by far the most important experiments for the determination of chemical structures. In the field of alkyl- and aryllithium compounds, which are characterized by the strong tendency to form oligomeric aggregates in solution[4], homonuclear 6Li,6Li correlations (6Li,6Li COSY)[5] and heteronuclear 6Li,13C correlations by polarization transfer (6Li,13C HETCOR)[6] as well as by heteronuclear multiple quantum coherences (6Li,13C HMQC)[7] have been reported and applied to solve structural problems. Similarly, for lithiated amides and phosphorus compounds 6Li,15N and 6Li,31P shift correlations, respectively, have been described[8].

With respect to the scalar spin-spin couplings involved, 6Li,13C interactions are of sizable magnitude (3–16 Hz), and the characteristic multiplets observed in 13C-NMR spectra of organolithium clusters due to 13C,6Li coupling provide valuable information about the cluster size[9]. Because of the higher gyromagnetic ratio of 7Li, 13C,7Li coupling constants are even larger, but the stronger quadrupolar moment of 7Li as compared to 6Li renders their detection often difficult due to severe line-broadening effects.

In contrast, homonuclear Li,Li coupling constants are small (< 1 Hz), and the first indirect proof of their existence was provided by a 6Li,6Li COSY experiment[5a]. This finding was verified only recently by direct observation[10] and by application of the 6Li,6Li INADEQUATE experiment[11].

The situation is similar for 6,7Li,1H coupling constants. Their existence has been deduced generally from line-broadening effects in the 6,7Li-NMR spectra[12]. With two exceptions, the lithium iridium hydride complex 1[13] and the lithium aluminum hydride amine complex 2[14], where large line splittings due to direct 7Li,1H spinspin interactions over one bond have been reported (8.4 and 10.5 Hz, respectively), 6,7Li,1H couplings are thus also rather small and difficult to measure.

In the present communication, we describe the first observation of larger 6Li line splittings due to 6Li,1H spin-spin coupling transmitted over two or three bonds and the first application of two-dimensional 6Li,1H-NMR shift correlations to the determination of the structure of a new organolithium compound.

1

R = Si(CH3)3

2
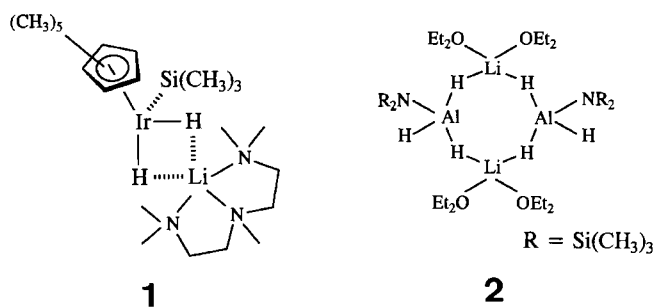
Results

(Z)-2-Lithio-1-(o-lithiophenyl)ethene (3) has recently been synthesized by Maercker et al.[15] and shown by NMR spectroscopy[16] to exist as a dimer 4, a structure found already for two derivatives of 3, (E)-1-lithio-2-(o-lithiophenyl)-1-phenyl-1-hexene (5)[5b,17] and (E)-2-lithio-1-(o-lithiophenyl)-1-phenyl-1-pentene (6)[10].

The remarkable feature of 3 is its stability as a static dimer 4 in diethyl ether even at room temperature. In tetrahydrofuran and dimethoxyethane exchange processes are indicated by line broadening and coalescence of the two 6Li-NMR signals (see below) at room temperature and −6°C, respectively. The thermal stability of 4 in diethyl ether has the advantage that all NMR investigations can be performed at room temperature where line-broadening effects due to solvent viscosity – a typical result of low-temperature measurements in ethereal solvents, which often prevents the observation of small line splittings – are negligible.

NMR measurements were carried out in [D10]diethyl ether with 6Li-labeled material. Extensive 6Li,1H spin-spin coupling in 4 is already indicated by splittings and broadening effects in the 1H-NMR spectrum which are most pronounced for the olefinic protons H(1) and H(2) as well as for the aromatic protons H(4′) and H(6′). These splittings

3

4

5   **6**   **7**
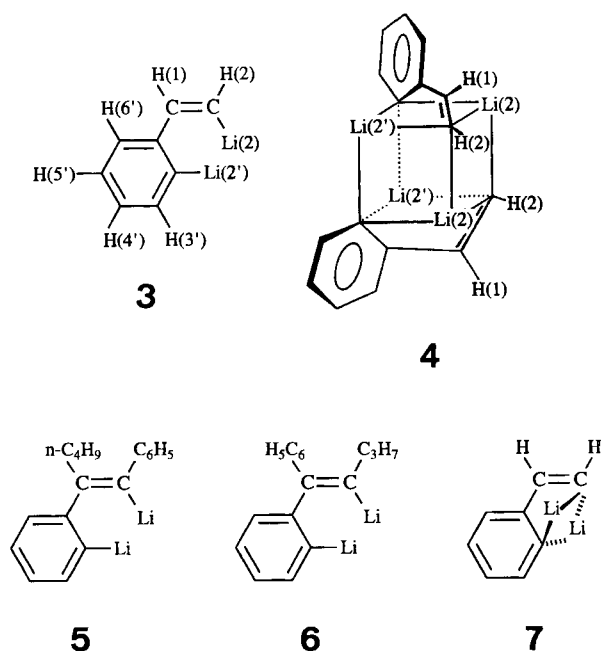
and broadening effects disappear upon ^{6}Li decoupling (Figure 1). The coupling is more clearly documented in the ^{6}Li-NMR spectrum (Figure 2a), which shows two signals due to the two chemically non-equivalent Li sites in structure **4**. This is one of the strongest arguments in favor of the dimeric structure, since for a Li-bridged monomer **7** only one ^{6}Li resonance is expected.
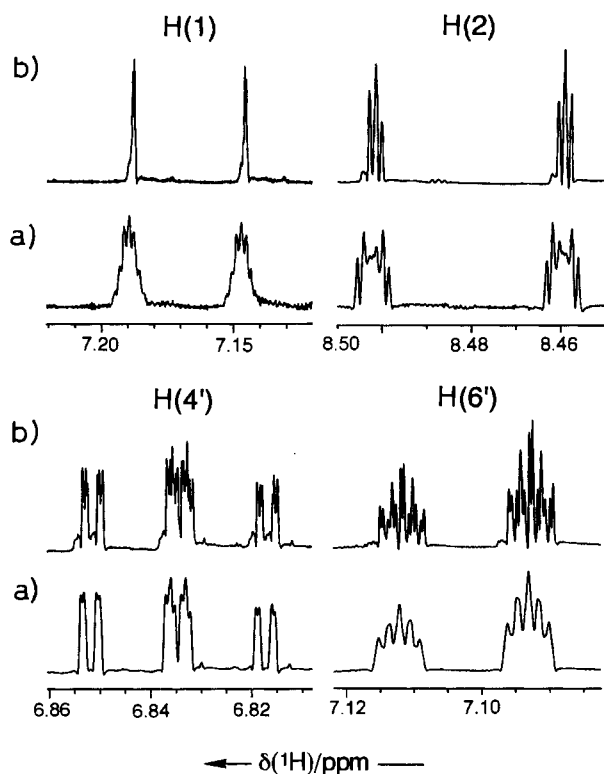

Figure 1. Selected multiplets from the 400-MHz ^{1}H-NMR spectrum of **4** which show the effect of ^{6}Li,^{1}H spin-spin coupling; a) ^{6}Li-coupled; b) ^{6}Li-decoupled

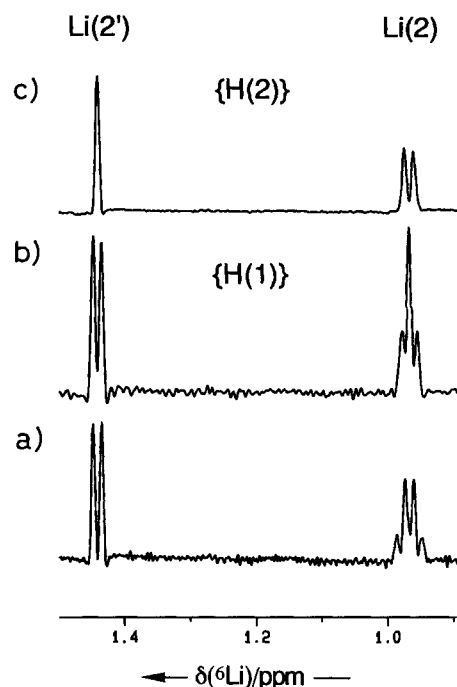Figure 2. a) 58.9-MHz ^{6}Li-NMR spectrum of **4**; b), c) the effect of selective decoupling of ^{1}H(1) and ^{1}H(2), respectively

Another interesting and important aspect of the ^{6}Li-NMR spectrum is the multiplet structure of the two ^{6}Li resonances. The quadruplet of the high-field signal is revealed as a doublet of triplets by classical selective ^{1}H-decoupling experiments (Figure 2b, c). From the geometry of the dimer as shown in **4** and the general assumption of Karplus-like behavior also of vicinal ^{6}Li,^{1}H coupling constants, one can expect that only Li(2) couples with both H(1) *and* H(2). Furthermore, each Li(2) nucleus should couple with the H(2) protons of both styryl moieties by a geminal ^{6}Li,^{1}H interaction, while coupling with the H(1) protons involves only that styryl moiety where H(1) is in a vicinal *trans* position relative to Li(2). When we disregard the considerably smaller coupling constants with the protons of the aromatic rings, these interactions explain the observed doublet-of-triplets structure of the Li(2) resonance. Thus, the spectrum shown in Figure 2a is the first example where the assignment of chemically non-equivalent Li atoms in an organolithium cluster can be based solely on ^{6}Li,^{1}H coupling constants. From the line splittings we find $^2J[H(2),Li(2)] = 0.75$ Hz, $^2J[H(2),Li(2')] = 0.69$ Hz, and $^3J[H(1),Li(2)] = 0.80$ Hz.

After we had established sizable ^{6}Li,^{1}H coupling constants for **4**, the realization of ^{6}Li,^{1}H shift correlation experiments was possible by straightforward application of standard pulse sequences. So far, heteronuclear shift correlation experiments between spin-1 and spin-$^1/_2$ nuclei have been published for the pair ^{2}H,^{1}H[18].

The ^{6}Li,^{1}H HMQC Experiment

For this experiment we used pulse sequence (1)[19] and phase-sensitive detection. A delay Δ_1 of 222 ms, corresponding to $1/6J$, and an average coupling of 0.75 Hz, served for

the preparation of antiphase ^{1}H magnetization. This value is a compromise between the optimal delays of $1/2J$ and $1/4J$ expected for AX and AX$_2$ systems of spin-$^1/_2$ nuclei[20] which change to $1/4J$ and $1/8J$, respectively, if the evolution of the A magnetization is caused by a spin-1 nucleus. Using phase-sensitive detection and high resolution in F_1, which is possible because of the small ^{6}Li chemical shift difference of only 30 Hz, we have been able to resolve the ^{6}Li,^{1}H coupling in F_2 and a splitting due to the homonuclear ^{6}Li,^{6}Li coupling in F_1. ^{1}H,^{1}H coupling operates during both t_1 and t_2 and thus appears in both frequency dimensions, F_1 and F_2 (Figure 3b). A detailed density matrix analysis of the cross peak structure is presently carried out. The experiment clearly
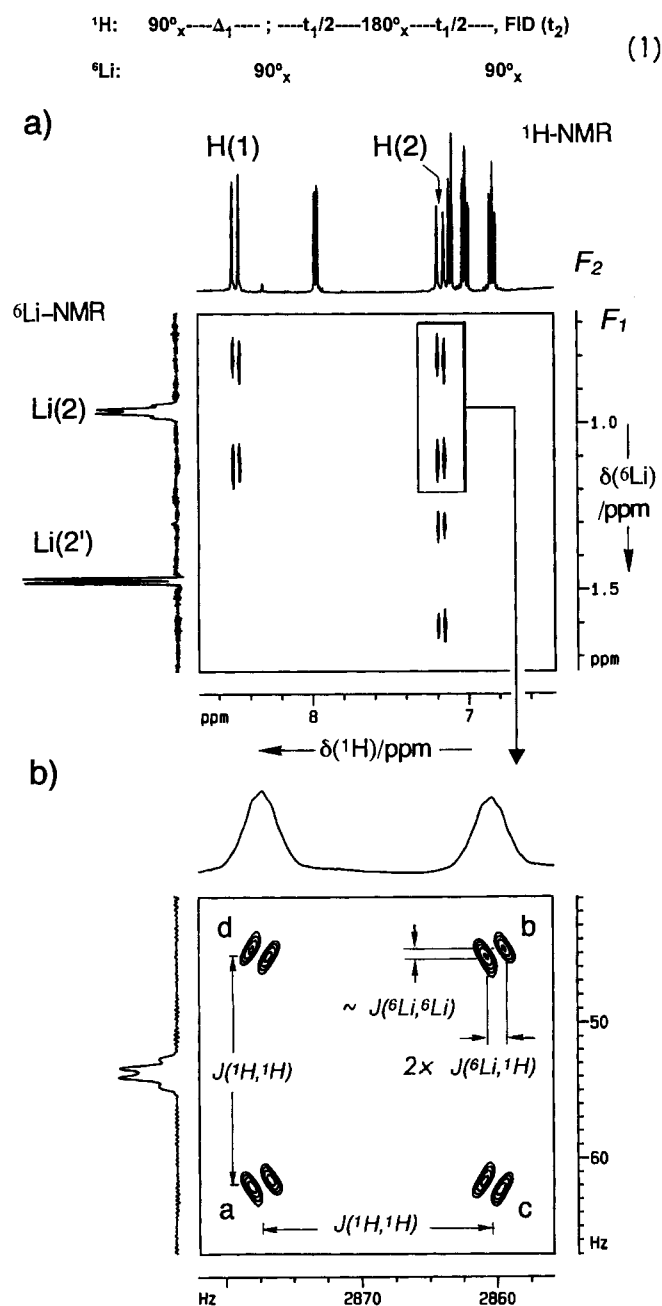
$$^1\text{H:} \quad 90°_x\text{---}\Delta_1\text{----} ; \text{----}t_1/2\text{----}180°_x\text{----}t_1/2\text{----}, \text{ FID (}t_2\text{)}$$
$$^6\text{Li:} \qquad\qquad 90°_x \qquad\qquad 90°_x \tag{1}$$

Figure 3. a) 400-MHz two-dimensional ^{1}H,^{6}Li-HMQC experiment [Eq. (1)] for 4; b) enlarged cross peaks for the H(2),Li(2) correlation

supports the results of the selective ^{6}Li decoupling experiment shown in Figure 2.

The ^{6}Li,^{1}H-HETCOR Experiment

Because application of the INEPT sequence[21] to the detection of X nuclei, which are coupled to second-order ^{1}H spin systems[22], often fails, we investigated the ^{6}Li,^{1}H spin system of 4 with the DEPT sequence[23]. In a one-dimensional experiment with ^{6}Li detection and different pulse angles for the read pulse [pulse sequence (2)] the spectra shown in Figure 4 were obtained. A satisfactory editing of the two lithium resonance signals was not achieved, which shows that the actual situation is more complicated. Nevertheless, the relative intensity of the Li(2) signal decreases if the pulse angle θ is varied from 45° through 90° to 135°. This can be rationalized if the Li(2) signal is regarded as part of an LiX$_2$Y system, where negative contributions to the signal intensity arise from the LiX$_2$ coupling. According to the unperturbed DEPT experiment, for a true LiH$_2$ system the signal should be eliminated for $\theta = 90°$ and inverted for $\theta = 135°$, while an LiH system yields equal intensities in both cases.

$$^1\text{H:} \quad 90°_x\text{----}\Delta_1\text{----}180°_x\text{----}\Delta_1\text{----}\theta\text{----------------}^1\text{H-BB}$$
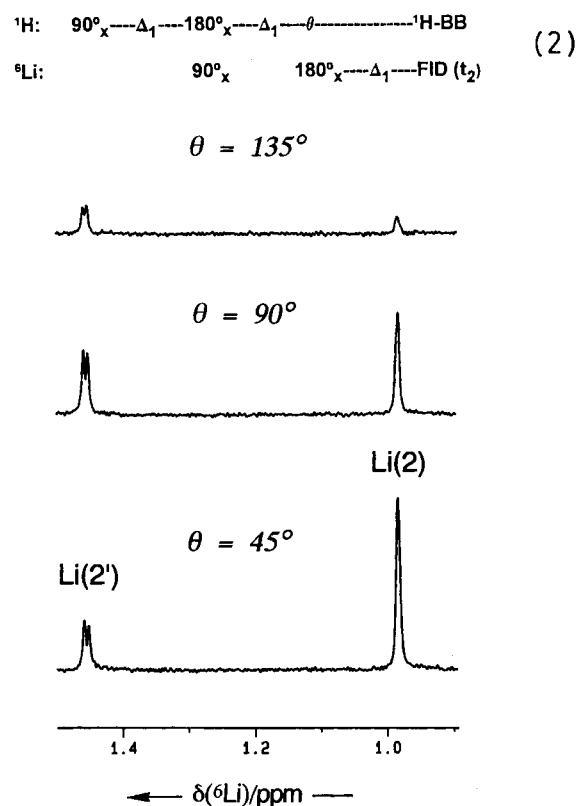$$^6\text{Li:} \qquad\qquad 90°_x \qquad\quad 180°_x\text{----}\Delta_1\text{----FID (}t_2\text{)} \tag{2}$$

Figure 4. 58.9-MHz ^{6}Li-NMR spectra of 4 observed with the DEPT sequence [Eq. (2)] with different pulse angles for the read pulse

A remarkable feature of these spectra is, however, the doublet observed for Li(2'), despite ^{1}H broad-band decoupling. This shows that two chemically non-equivalent Li(2') nuclei exist and that 4 thus displays reduced symmetry. Low-temperature experiments at high resolution (0.08 Hz/ pt) then proved that indeed both ^{6}Li resonances split into

two separate signals if homonuclear ^{6}Li,^{6}Li decoupling is applied (Figure 5). At present it is not clear if this signal separation is due to a dynamic process or a consequence of the intrinsic temperature dependence of the ^{6}Li chemical shift.

a)

b)
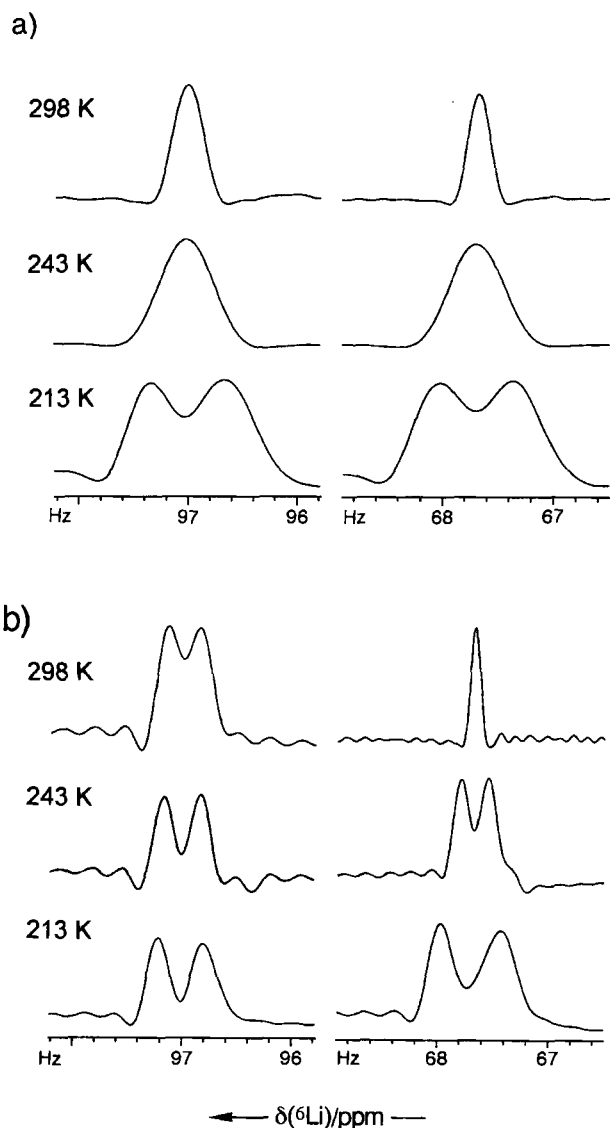

——— δ(^{6}Li)/ppm ———

Figure 5. 58.9-MHz {^{1}H}^{6}Li-NMR spectra of **4** at different temperatures; a) without and b) with homonuclear ^{6}Li decoupling; line narrowing by GAUSSIAN multiplication

The non-equivalence observed for Li(2′) also remains in the two-dimensional spectrum which was recorded on the basis of a DEPT polarization transfer by using pulse sequence (3). The 2D spectrum observed is shown in Figure 6 and demonstrates that the ^{1}H,^{6}Li polarization transfer is effective enough to generate cross peaks of sufficient intensity.
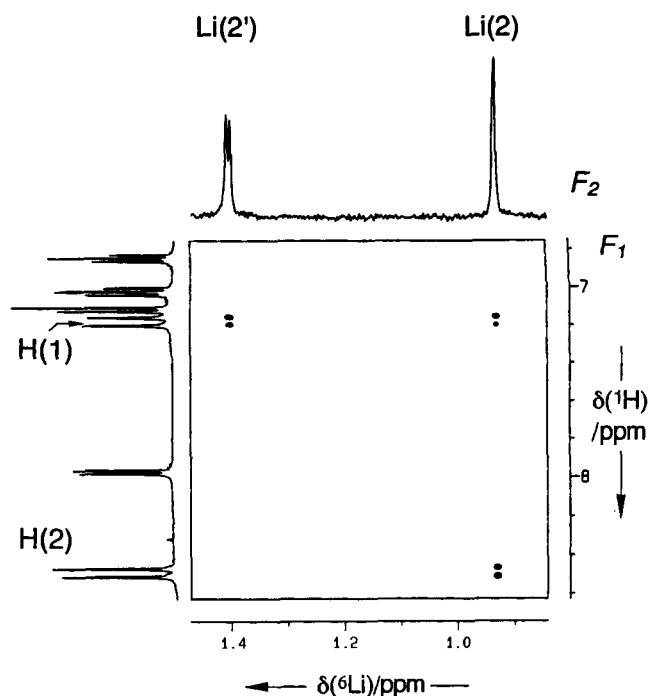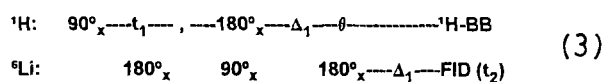
^{1}H: 90°$_x$---t$_1$--- , ----180°$_x$---Δ$_1$---θ------------^{1}H-BB

^{6}Li: 180°$_x$ 90°$_x$ 180°$_x$----Δ$_1$----FID (t$_2$)   (3)

Figure 6. Two-dimensional ^{1}H,^{6}Li shift correlation for **4** based on the DEPT sequence [Eq. (3)]

Conclusion

In summary, ^{6}Li,^{1}H shift correlations based on multiple quantum spectroscopy as well as on polarization transfer are valuable additions to the list of NMR experiments already known for structural research in the field of organolithium compounds. In this context it is interesting that for vinyllithium, where the ^{6}Li,^{1}H coupling constants are in the order of 0.4 Hz, even the simple fully coupled polarization transfer sequence[18,24] has been employed successfully to determine the magnitude and even the relative signs of ^{6}Li,^{1}H coupling constants[25].

Experimental

^{6}Li-labeled **3** was synthesized under argon as described in ref.[15] by reaction of benzol[*b*]tellurophene[26] in pentane with a hexane solution of [^{6}Li]butyllithium. After washing with pentane, the precipitate of **3** was dissolved in [D$_{10}$]diethyl ether to yield a 0.3 M solution.

NMR spectra were measured with a Bruker AMX 400 spectrometer operating at 400.13 MHz for ^{1}H and 58.88 MHz for ^{6}Li. All experiments were performed with a 5-mm inverse multinuclear probe head and, with the exception of those shown in Figure 5, at room temperature. {^{6}Li}^{1}H spectra were obtained by applying the MLEV-16 sequence[27] at the ^{6}Li frequency on the X channel. Homonuclear ^{6}Li decoupling was achieved by applying a CW irradiation during the acquisition time using the following sequence:

1   open ADC
2   delay to block the receiver (1μs)
3   CW irradiation for 0.3 × dwell time (s)
4   delay to reactivate receiver (1μs)
5   signal detection
6   go to 2, repeat
7   close ADC

For the phase-sensitive ^{6}Li,^{1}H HMQC spectrum (Figure 3), the TPPI method[28] and the following experimental parameters were used: sweep widths 60 Hz (F_1), 1 kHz (F_2); data points 128 (t_1), 512 (F_1), 4K (t_2, F_2); 64 transients; t_1 increment 4.16 ms; preparation delay $\Delta_1 = 222$ ms, relaxation delay 1 s, acquisition time 2.06 s; sine^2 window functions in both dimensions; total exp. time 7.5 h.

For the DEPT spectra (Figure 4) 128 transients were accumulated with a preparation delay of 333 ms and a relaxation delay of 3 s. The phase-sensitive 2D version used sweep widths of 1 kHz (F_1) and 60 Hz (F_2), 128 and 512 (1K) data points, respectively, 16 transients per t_1 experiment and a t_1 increment of 317 μs. The total exp. time was 6.5 h.

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