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Organolithium Chemistry: NMR-Based Distinction of Cyclic Dimers from Cyclic Trimers by ^{6}Li{^{13}C}-HMQC-TOCSY

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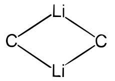
Abstract: Isotopically ^{6}Li-labeled lithioorganic cyclic dimers may not be distinguished from cyclic trimers or higher oligomers by conventional ^{13}C-NMR spectroscopy: both a cyclic dimer and a trimer will exhibit a quintet due to coupling of ^{13}C with two neighboring ^{6}Li nuclei. However, a clear distinction can be made by means of a 2D ^{6}Li{^{13}C}-HMQC-TOCSY experiment without ^{13}C decoupling during the acquisition period: in a ^{13}C isotopomer, the existence of two chemically equivalent (dimer) or nonequivalent (trimer) Li nucleus sites gives rise to specific cross peak patterns. The distinction is based on ^{13}C,^{6}Li magnetization transfer and subsequent homonuclear magnetization transfer between appropriate ^{6}Li spins. Thus, a dimer reveals a pair of cross peaks located at the chemical shift of the ^{13}C satellites in the f$_2$ (^{6}Li) domain, whereas a trimer leads to an extra cross peak at the chemical shift of the ^{6}Li main signal. The usage of the novel method is exemplified for a lithioorganic trimer and a dimer model compound.

Introduction

The aggregate size of an organolithium compound in solution may often be deduced from NMR line multiplicities due to ^{13}C,^{6,7}Li coupling.[1] The pioneering work of Fraenkel,[2] introducing ^{6}Li isotopic labeling, was followed by a variety of applications.[3] Due to the favorable properties of the ^{6}Li isotope (spin $I = 1$; very small quadrupole moment), the ^{6}Li-labeling technique is now common routine.[4] Provided that intermolecular chemical exchange is slow with respect to the involved coupling constants, ^{13}C,^{6}Li coupling patterns observed in ^{13}C-NMR spectra usually allow the identification of aggregate sizes: a 1:1:1 triplet for a monomer, a 1:2:3:2:1 quintet for a dimer, and a 1:2:3:4:3:2:1 septet for a tetramer. However, ambiguous situations may be found. Consider the cores of a cyclic dimer, **1**, and a cyclic trimer, **2**.



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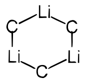

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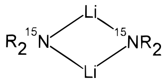
In the ^{13}C-NMR spectrum, both **1** and **2** would reveal a quintet due to coupling of ^{13}C with two neighboring ^{6}Li nuclei. Hence, simple 1D ^{13}C-NMR spectra may not be employed in order to distinguish between **1** and **2**. For a related case, Gilchrist and Collum[5] developed a very clever NMR method which allows discrimination between a ^{15}N-labeled cyclic lithioamide dimer, **3**, and a higher oligomer, presumably cyclic trimer **4**.



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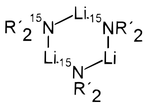

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Whereas zero quantum coherence between ^{15}N and ^{6}Li may evolve in the case of trimer **4**, this is not possible for dimer **3**. Consequently, in appropriate 2D NMR spectra **3** and **4** reveal different typical cross peak patterns. However, the application of this method to "true" organolithium compounds (i.e., C-metalated species) is largely prohibited due to preparative difficulties in ^{13}C-labeling at specific molecular sites. With natural abundance ^{13}C (1.1%) the latter method would not work.

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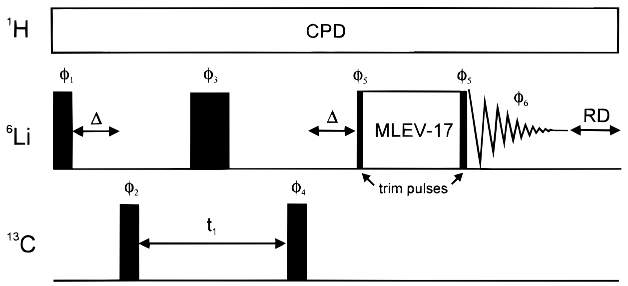


Figure 1. Pulse sequence of ^{6}Li{^{13}C}-HMQC-TOCSY without ^{13}C decoupling during acquisition. Phase cycle: $\phi_1 = x$; $\phi_2 = x, -x$; $\phi_3 = x$; $\phi_4 = x, x, -x, -x$; $\phi_5 = (y)_4, (-y)_4$; $\phi_6 = x, -x, -x, x$.

For completeness, it should be noted that classical physicochemical methods for aggregate size determination of organolithium compounds which are based on colligative measurements are known as well. These include, e.g., cryoscopy,[6] vapor phase osmometry,[7] differential pressure barometry,[8] or ebullioscopy.[9] However, the drawbacks of these methods are the following: (i) The result is just one single number for the degree of aggregation. Hence, noninteger numbers must be interpreted to reflect binary equilibria, which may not necessarily be true. Likewise, artifacts from byproducts or from decomposition may lead to erroneous conclusions. (ii) Colligative methods are limited to the physical properties of the solvent (boiling/freezing point).

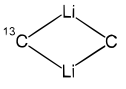
In this paper, a novel NMR application is described which makes use of ^{6}Li{^{13}C}-HMQC-TOCSY to get a quick, easy, and reliable distinction between dimer **1** and trimer **2**. No ^{13}C-labeling is required; thus, elaborate synthetic work can be avoided.

Methods

Due to sensitivity reasons, "inverse" (^{1}H-detected) 2D NMR techniques have become popular in recent years.[10,11] Though predominantly applied to ^{1}H and ^{13}C, these methods may include other heteronuclei with spin quantum numbers $I > 1/2$ as well. Consider a ^{6}Li-detected ^{6}Li{^{13}C} heteronuclear multiple quantum coherence[12] (^{6}Li{^{13}C}-HMQC) experiment. Provided that ^{13}C decoupling was applied during the acquisition period, a single cross peak would be obtained in a 2D correlation plot. When ^{13}C decoupling during t_2 is omitted, heteronuclear ^{6}Li,^{13}C coupling will be effective during FID sampling, leading to cross peak splitting in f_2.

The pulse sequence of ^{6}Li{^{13}C}-HMQC-TOCSY[14] (TOCSY = total correlation spectroscopy) is depicted in Figure 1. Here, subsequent to the ^{6}Li,^{13}C magnetization transfer, a suitable mixing sequence (MLEV-17[15] or equivalent) leads to homonuclear magnetization transfer from ^{6}Li spins coupled to ^{13}C to other, ^{12}C-bound ^{6}Li nuclei. Additional constant low-power ^{1}H decoupling ensures intensity gain due to the NOE.

The basic idea of the dimer/trimer distinction is as follows. Consider the core of a ^{13}C-isotopomeric dimer, **5**: a ^{6}Li{^{13}C}-HMQC experiment *without* ^{13}C decoupling during t_2 will result in a pair of cross peaks located at the ^{13}C chemical shift in f_1 and at the chemical shift of the ^{13}C satellites of the main ^{6}Li resonance line in f_2. Adding an additional mixing sequence (TOCSY, ROESY, NOESY) will not lead to a change of the spectrum. Provided that **5** remains intact with respect to the length of the mixing period (no intermolecular exchange), the two isochronous Li nuclei bonded to the ^{13}C isotope still reveal *J* coupling. A different situation is found in the core **6** of a ^{13}C-isotopomeric trimer (or, by analogy, a higher aggregate). Here, chemically nonequivalent lithium sites are present. First, a ^{6}Li{^{13}C}-HMQC experiment will reveal a pair of cross peaks in the same way as for **5**. However, an additional ^{6}Li,^{6}Li mixing sequence will lead to magnetization transfer including the ^{6}Li nucleus *remote* from ^{13}C (drawn bold in **6**), the resonance line of which is *not* split due to *J* coupling. Hence, a third cross peak additional to the HMQC-generated pair will appear at the ^{6}Li chemical shift of an all-^{12}C isotopomer.[16] Thus, the simple overall rule is as follows: if an organolithium compound shows a quintet for the signal of the metalated ^{13}C, then perform a ^{6}Li-detected ^{6}Li{^{13}C}-HMQC-TOCSY spectrum without ^{13}C decoupling during t_2. If only two cross peaks are present, the compound is a cyclic dimer. If three cross peaks appear, it must be a trimer or some other higher aggregated species with an adequate bonding situation.



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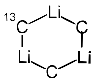

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The experiments described in the following text were performed on a special triple resonance probehead: the inner coil is tunable between the frequencies of ^{15}N and ^{31}P whereas the outer coil is triply tuned to ^{1}H, ^{2}H, and ^{13}C. After optimizing the shim by using the ^{2}H lock signal, experiments which involve ^{6}Li spin lock were performed without ^{2}H lock to avoid disturbance of the ^{2}H lock signal. The field stability of modern superconducting magnets usually is sufficient in order to perform the described experiments over a duration of several hours or even several days. Likewise, the employed spectrometer matrix shim stability is excellent, thus making autoshim corrections unnecessary.

Since the ^{2}H channel is not used in the ^{6}Li{^{13}C}-HMQC-TOCSY experiment, "normal" probeheads for ^{1}H,^{13}C measurements may be employed as well. The Larmor frequencies of ^{2}H and ^{6}Li are so close that the lock channel may be used for ^{6}Li detection even without detuning the probe channel. Of course, considerably longer ^{6}Li pulse widths (up to several hundredths of a microsecond) must be expected in these cases. Moreover, the ^{2}H channel must be capable of withstanding hard ^{6}Li pulses and several watts of ^{6}Li spin lock for a several seconds interval.

Results

Materials. In order to demonstrate the applicability of the method outlined above to organolithium compounds, we chose **7**[17] as a model of a dimer and **8**[18] as an example of a trimer. Both **7** and **8** were enriched 96% by the ^{6}Li isotope. In toluene-d_8 solution, both **7** and **8** adopt the structures represented by the formulas.

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(16) By rigorous inspection, due to the ^{13}C isotope effect the chemical shift of the remote ^{6}Li atom drawn bold in **6** is not identical to the ^{6}Li chemical shift of an all-^{12}C isotopomer. However, this ^3J effect is negligible. By contrast, the ^1J ^{13}C isotope effect may be observed for the two ^{6}Li atoms directly bound to ^{13}C; see the text and Figure 4.

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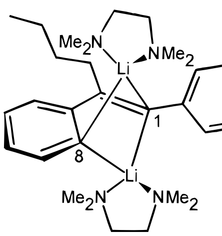

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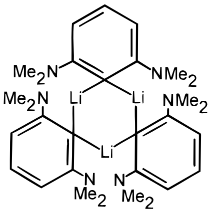

8

Compound **7** is the addition−second metalation product of nBuLi and diphenylacetylene and has been extensively studied by NMR, X-ray analysis, and MNDO calculations.[17] Actually, **7** is *not* a dimer but a monomeric entity instead. However, the bonding situation of the doubly bridging lithium atoms is completely identical to the situation found in a genuine dimer (e.g., phenyllithium−TMEDA[19]). Thus, in benzene-d_6 or toluene-d_8, the lithiated carbon atoms C1 and C8 in **7** exhibit the typical ^{13}C quintets due to coupling with two ^{6}Li isotopes, $J(^{13}C,^{6}Li) = 5.7$ and 7.5 Hz, respectively. The reason why compound **7** had been chosen as a model dimer is its low reactivity toward the solvent (toluene-d_8) over a long period of orientational NMR experiments. Any other genuine dimeric organolithium compound would principally perform in the very same way.

Compound **8** (monomeric entity: [1,3-bis(dimethylamino)-phen-2-yl]lithium) is a genuine trimeric entity in toluene-d_8 which has been studied by X-ray analysis and NMR in Brandsma's and our group.[18] Similar to **7**, **8** is relatively unreactive toward toluene-d_8.

Dimer Case. Figure 2shows a ^{6}Li{^{13}C}-HMQC-TOCSY spectrum obtained on model dimer **7** at −40 °C. No ^{13}C decoupling was applied during t_2. The transmitter in f_1 was placed close to the resonance line of C1 ($\delta = 202.0$ ppm). As expected, a pair of cross peaks appears at the ^{13}C satellites' chemical shift positions of the ^{6}Li main signal in f_2 and at the chemical shift of C1 in f_1. As expected from the principles outlined in the Methods, no extra cross peak is observed. The resonance line of the second metalated carbon atom, C8 in **7**, appears at $\delta = 189.0$ ppm in the 1D ^{13}C-NMR spectrum. Obviously due to the relatively long ^{13}C 90° pulse width, off resonance effects suppress a folded-in second pair of cross peaks originating from the ^{13}C8 satellites. In practice, such folding-in would not cause serious spectral problems. Rather, it might be exploited for additional gain of information.

The length of the mixing period (2 s) has been adjusted with respect to the ^{6}Li spin−lattice relaxation time, T_1, of the all-^{12}C isotopomer (ca. 22 s; see below). Increasing the mixing period to 5 s leads to the same result, however, with a lower signal-to-noise ratio. This manifests in increased t_1 noise artifacts at the ^{6}Li main signal chemical shift.

In a control experiment, the spectrum of Figure 2 was re-recorded with the temperature raised to −10 °C. Under these conditions, the *inter*molecular lithium exchange rate is considerably higher compared to the conditions of Figure 2. Thus, during the TOCSY mixing period an appreciable amount of ^{6}Li spins formerly bound to ^{13}C and involved in heteronuclear ^{6}Li{^{13}C} double quantum coherence transfer exchange their chemical position to an all-^{12}C isotopomer. Hence, it should be expected that this population of exchanged ^{6}Li spins now gives rise to an additional cross peak at the chemical shift of the ^{6}Li main peak. This is experimentally confirmed in Figure 3. As a consequence, when the ^{6}Li{^{13}C}-HMQC-TOCSY experiment is performed, care must be taken not to introduce artifacts due to chemical exchange phenomena.

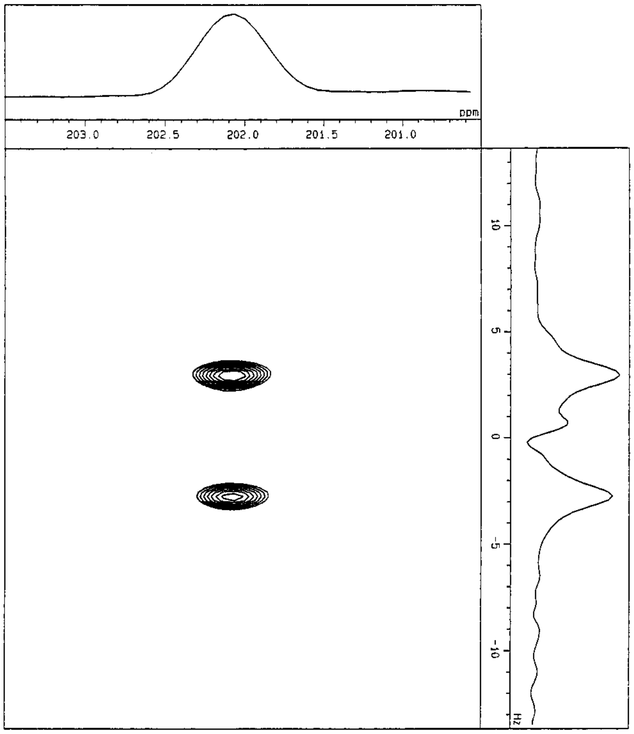

Figure 2. ^{6}Li{^{13}C}-HMQC-TOCSY spectrum of **7** in toluene-d_8, 0.25 M, −40 °C, experimental time 6.0 h, pulse sequence of Figure 1, mixing time 2 s: horizontal, f_1 (^{13}C); vertical, f_2 (^{6}Li). The region of metalated carbon C1 was selected in f_1. No ^{13}C decoupling was applied during t_2. One-dimensional slices have been taken at the top of the f_2-upfield cross peak. The scale in f_2 does not represent the true chemical shift.

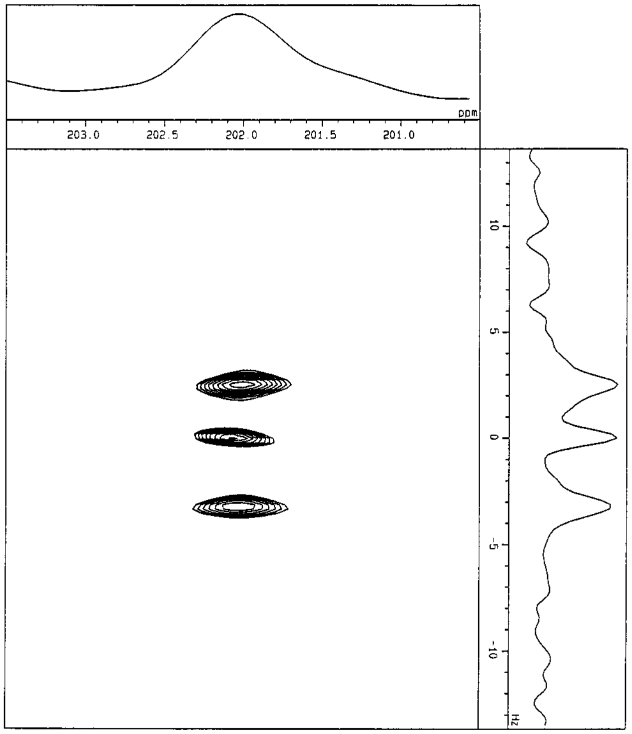

Figure 3. ^{6}Li{^{13}C}-HMQC-TOCSY spectrum of **7** in toluene-d_8, 0.25 M, −10 °C, experimental time 7.7 h, pulse sequence of Figure 1, mixing time 5 s. The center cross peak arises from artifacts due to intermolecular exchange. For further explanations, see Figure 2.

Trimer Case. Figure 4 shows a ^{6}Li{^{13}C}-HMQC-TOCSY spectrum analogous to that in Figure 2, now obtained on trimer **8**. Similar to the results of Figure 2, heteronuclear double quantum coherence manifests in the appearence of a pair of cross peaks at the ^{6}Li chemical shifts of the ^{13}C satellites.

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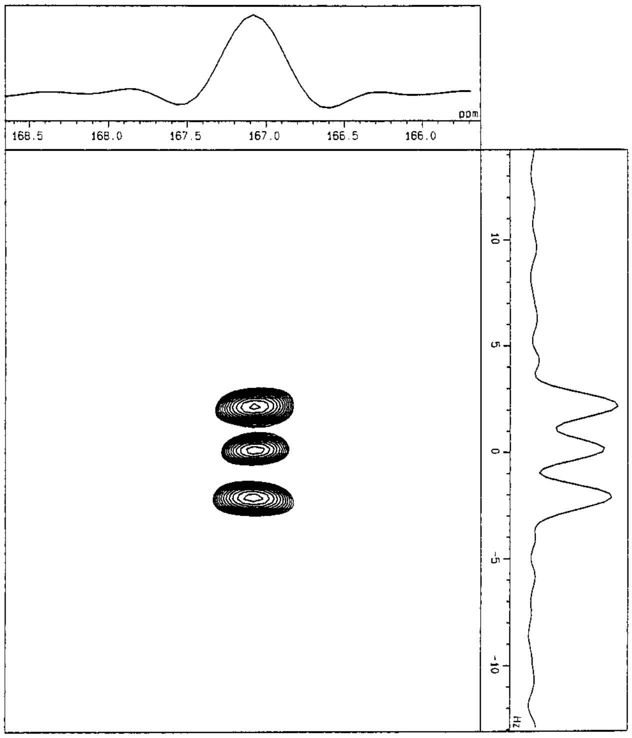

Figure 4. ^{6}Li{^{13}C}-HMQC-TOCSY spectrum of **8** in toluene-d_8, 0.25 M, 24 °C, experimental time 10.2 h, pulse sequence of Figure 1, mixing time 10 s. The center cross peak identifies the trimeric nature of **8**. For further explanations, see Figure 2.

During the mixing period magnetization is transferred from the ^{6}Li spins involved in heteronuclear ^{6}Li{^{13}C} double quantum coherence (the Li positions adjacent to ^{13}C in **6**) to the remote Li position (bold in **6**). This leads to a third cross peak at the chemical shift of the main ^{6}Li resonance line of an all-^{12}C isotopomer. Note that this additional cross peak is not located exactly midway between the two outer ones: due to the ^{13}C isotope effect exerted on ^{6}Li, the ^{13}C satellites appear shifted slightly upfield. The additional cross peak reveals the trimeric nature of **8**.

As was the case for the HMQC-TOCSY spectrum of **7** in Figure 2, the length of the mixing period is estimated from the ^{6}Li spin−lattice relaxation time of the all-^{12}C isotopomer of **8** (34 s at 23 °C). Shorter mixing periods lead (as expected) to a decrease of the intensity of the center cross peak relative to the outer ones. Longer mixing periods lead to an increase in intensity of the center cross peak at the expense of an overall decreased signal-to-noise ratio. Note that concerning the length of the appropriate mixing times $T_{1\rho}$ is the relevant parameter instead of T_1.

To check the results of Figure 4 against artifacts due to intermolecular exchange (cf. Figure 3), the experiment was repeated at −40 °C instead of +24 °C, with the mixing time reduced to 5 s, according to a shorter T_1 of ^{6}Li. The result was identical to that of Figure 4.

Pulse Sequence Variations. Some variants of the pulse sequence shown in Figure 1 have been tested. These were as follows:

(i) *^{1}H decoupling:* Omitting the constant ^{1}H decoupling leads to a significant loss of sensitivity. Hence, it is trivial to make use of the NOE gain.

(ii) *Mixing sequence:* We have found MLEV-17 to give the best performance when employed as a mixing sequence. A HMQC-NOESY[20] experiment on **8** yields somewhat poorer results. HMQC-ROESY[21] with (pulse − delay)$_n$ spin lock is comparable to HMQC-NOESY with respect to sensitivity.

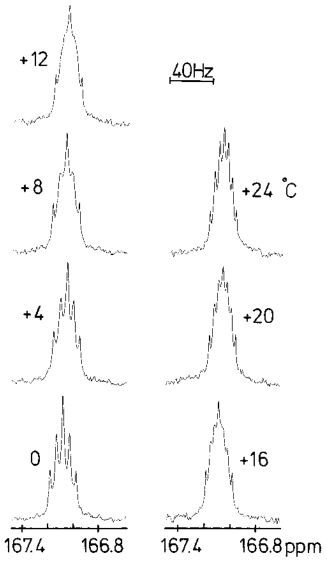

Figure 5. Series of temperature dependent ^{13}C-NMR spectra of the lithiated carbon atom of **8** in toluene-d_8, 0.25 M.

(iii) *Coherence transfer:* A HSQC[22] experiment has been carried out instead of HMQC on **8**. The result is somewhat poorer, presumably due to the higher number of pulses and delays employed in HSQC.

(iv) *BIRD:* The suppression of the main signal of the detected nucleus by use of the BIRD[23] sandwich in advance of the HMQC sequence is routine in ^{1}H,^{13}C experiments. However, in the present ^{6}Li,^{13}C case no significant improvement was observed. The ^{6}Li main peak suppression is sufficient even without BIRD. This may be a consequence of the relatively short relaxation delays employed which lead to a higher degree of saturation of the ^{6}Li main peak over its ^{13}C satellites (different T_1; see below). Moreover, due to the long ^{6}Li relaxation times, usage of BIRD unnecessarily increases the duration of the experiment.

(v) *Pulsed Field Gradients:* The ^{6}Li main signal suppresion should significantly improve when the pulsed field gradient (PFG) variant of HMQC-TOCSY is employed. This has been confirmed in our laboratory and will be reported in future papers.

Alternative Trimer Identification. In the special case of **8**, the trimeric structure found by X-ray analysis in toluene-d_8 solution may be nicely demonstrated independently by a series of single-pulse 1D temperature dependent ^{13}C-NMR spectra. As is shown in Figure 5, the ^{13}C signal of the metalated carbon atom in **8** shows a 1:2:3:2:1 quintet at 0 °C, $J(^{13}\text{C},^6\text{Li}) = 6.4$ Hz. Under these conditions, **8** is “static” in terms of the NMR time scale and coupling is observed between ^{13}C and its two directly neighboring ^{6}Li atoms ($J = 6.4$ Hz). Upon increasing temperature, coalescence will eventually be observed at +12 °C. At even higher temperatures, an *intra*molecular exchange process leads to coupling of ^{13}C with all present ^{6}Li sites, leading to a 1:2:3:4:3:2:1 septet ($J = 4.3$ Hz). Note that under the high-temperature conditions of Figure 5 no detectable amounts of *inter*molecular exchange are present: this would lead to scrambling of the ^{13}C signal splitting into one single line. The dynamic phenomenon found for **8** is similar to the behavior

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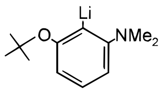
observed for a chemically related compound, [1-methoxy-3-(dimethylamino)phen-2-yl]lithium (**9**),[24] and for *t*-BuLi (**10**)[25] under comparable conditions (i.e., in apolar solvents).



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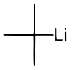

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Discussion

In the field of organolithium chemistry, dimers are much more common than trimers. However, both dimers and trimers yield the same ^{13}C-NMR multiplicity pattern (quintet in ^{6}Li-enriched material). Hence, a simple distinction by ^{13}C-NMR is not possible. The ^{6}Li{^{13}C}-HMQC-TOCSY method now allows an unambiguous discrimination of a cyclic organolithium dimer from a cyclic trimer or an equivalent higher aggregated species. One of the merits of the method is the possibility of employing natural ^{13}C abundance. Though not yet tested so far, in cases of favorable ^{7}Li spin−lattice relaxation times, natural abundance lithium material (92.6% ^{7}Li) might principally be employed as well in analogous ^{7}Li{^{13}C}-HMQC-TOCSY experiments.

The intermolecular exchange rate of lithium must be well below the inverse length of the TOCSY mixing period. This is a crucial requirement to preclude artificial results. Thus, sufficiently low temperatures must be kept. A further prerequisite is the existence of resolved scalar ^{13}C,^{6}Li coupling to create multiple quantum coherence.

From a sensitivity point of view, ^{6}Li detection in a ^{6}Li{^{13}C}-HMQC experiment is not meaningful since the magnetic moment of ^{6}Li is smaller than that of ^{13}C. However, the identification of a trimeric organolithium compound is based on the appearance of an additional cross peak midway between the cross peaks at the ^{6}Li chemical shifts of the ^{13}C satellites. Hence, it would be worthless to employ an analogous ^{13}C-detected experiment. Here, the crucial additional central cross peak would coincide with the center peak of the ^{13}C-observed quintet due to ^{13}C,^{6}Li coupling in a trimer. Furthermore, the dimer/trimer distinction in the described way is based on relatively good spectral resolution in the f$_2$ domain (better than ca. 1 Hz). Hence, it is reasonable to detect the ^{6}Li nucleus with its small chemical shift range instead of ^{13}C which has large spectral dispersion.

Of the mixing sequences, MLEV-17 has turned out to be most efficient. At first glance, this seems surprising since MLEV-17 is an isotropic mixing sequence designed to exploit scalar coupling instead of cross relaxation in the rotating frame. A tentative explanation is as follows: scalar intramolecular ^{6}Li,^{6}Li couplings in organolithium compounds, though being very small, have been observed by using ^{6}Li{^{6}Li}-COSY.[17,26] Due to the very long mixing time employed in Figure 4, MLEV-17 might well lead to homonuclear coherence transfer between ^{6}Li nuclei via scalar coupling, in addition to the incoherent NOE transfer. Thus, isotropic mixing and cross relaxation effects may act cumulatively when using MLEV-17.

The chosen lengths of the mixing periods in the ^{6}Li{^{13}C}-HMQC-TOCSY experiments have been estimated from the ^{6}Li spin−lattice relaxation times, T_1, of the main signals which were found to be 22 s for **7** and 34 s for **8** at 24 °C. However, T_1 of ^{13}C-bound ^{6}Li is shorter than T_1 of ^{12}C-bound ^{6}Li due to efficient dipolar relaxation from ^{13}C. Thus, at the same temperature, T_1 of the ^{13}C satellite ^{6}Li signals in **8** is 26% shorter than T_1 of the main signal. Moreover, during the spin lock period, $T_{1\rho}$ is efficient rather than T_1.

Principally, the ^{6}Li{^{13}C}-HMQC-TOCSY experiments of Figures 2 and 4 provide the unambiguous dimer/trimer discrimination. However, we recommend to additionally record the analogous ^{6}Li{^{13}C}-HMQC experiments. This yields information about the maximum obtainable signal-to-noise ratio and may give an estimation of the magnitude of t_1 noise artifacts.

In principle, a selective 1D ^{6}Li{^{13}C}-HMQC-TOCSY experiment[27] could lead to the desired answer in a much shorter time. This experiment would consist of the pulse sequence shown in Figure 1 with fixed delays instead of the variable t_1 period and the second 90° ^{13}C pulse being selective (reminiscent of the SELINCOR[27c] experiment). The results obtained on **7** and **8** would be identical to the f$_2$ slices of Figures 2 and 4, respectively. However, we strongly recommend against the 1D version since it must be guaranteed that the main ^{6}Li resonance line of the all-^{12}C isotopomer must be effectively suppressed. This is usually ensured by careful pulse calibration and by phase cycling. Insufficient main signal suppression in a 1D experiment, however, would erroneously identify a genuine dimer as being a trimer. The risk of such erroneous interpretations is tremendously reduced in a 2D experiment: here, the extra cross peak which identifies a trimer (Figure 4) *must* appear at the f$_1$ chemical shift of the ^{13}C resonance line under consideration. Hence, the cross peak spreading in the f$_1$ domain of the 2D experiment provides an additional insurance against misinterpretations.

In the special case of **8** the ^{6}Li{^{13}C}-HMQC-TOCSY identification of **8** as a trimer is redundant since here the temperature dependent ^{13}C-NMR spectra (Figure 5) provide clear evidence for the trimer due to the line multiplicities. Also note that this series of ^{13}C-NMR spectra contains only a single set of signals for all carbon atoms of **8** over the whole temperature range. Only the multiplicity of the metalated carbon signal changes. This rules out a dimer/trimer equilibrium. Moreover, cryoscopic measurements in benzene previously identified **8** as a trimer.[18] However, we have deliberately chosen **8** with its known structural features as a test compound for the ^{6}Li{^{13}C}-HMQC-TOCSY method to demonstrate the performance of the new NMR technique.

It should be emphasized that the application of HMQC-TOCSY for the identification of aggregate sizes is inherently not restricted to the system ^{6}Li,^{13}C in organolithium compounds. Analogous ^{1}H,^{13}C applications to C_s- or C_2-symmetric molecules with identical subunits and degenerate protons should work as well. A ^{13}C nucleus at a suitable position lifts the degeneracy. Once the ^{13}C satellites of an adequate ^{1}H nucleus are selected by ^{1}H{^{13}C}-HMQC, an additional ^{1}H,^{1}H coherent (TOCSY) or incoherent (ROESY, NOESY) magnetization transfer to the proton site at the ^{12}C subunit would provide useful information. Related structural identifications have been reported.[21b,28]

Conclusions

Cyclic dimers of organolithium compounds may be distinguished from trimers or higher aggregates by using the ^{6}Li{^{13}C}-HMQC-TOCSY experiment. No specific ^{13}C-labeling is required for its successful application. The idea behind the

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method is to lift the degeneracy of lithium sites. In a ^{13}C isotopomer of a dimer the two lithium nuclei are equivalent whereas this is not the case for the three lithium nuclei in a trimer: the lithium site remote from ^{13}C shows no scalar $^{6}Li,^{13}C$ coupling. Hence, its resonance line appears approximately midway between the two lines of the ^{13}C-bound ^{6}Li nucleus. This feature is exploited for the trimer identification. Provided that ^{13}C decoupling is omitted during the acquisition period, dimers reveal a single pair of cross peaks at the ^{6}Li chemical shifts of the ^{13}C satellites. By contrast, in a trimer the mixing period leads to magnetization transfer from ^{13}C-bound ^{6}Li nuclei to the remote, ^{12}C-bound site. This manifests in a third cross peak at the chemical shift of the ^{6}Li main signal. Potential artifacts (false identification of a genuine dimer as being a trimer) from appreciably high rates of intermolecular lithium exchange are prevented by performing the $^{6}Li\{^{13}C\}$-HMQC-TOCSY experiment at temperatures well below that of ^{13}C quintet scrambling.

Experimental Section

Compounds **7**[17] and **8**[18] were synthesized as described earlier. *n*-Butyllithium isotopically enriched 96% by ^{6}Li[3c] was employed for the metalation of the precursor material. All experiments involving organolithium compounds were conducted under an atmosphere of purified argon.

NMR spectra were recorded on a JEOL Alpha 500 spectrometer (11.7 T; ^{1}H, 500 MHz). Sample concentrations were 0.25 M for **7** and 0.25 M for **8** (based on the X-ray trimer, i.e., 0.75 M based on the monomeric unit). For the spectra of Figures 2−4, a 5 mm triple resonance probehead was employed: the inner coil is tunable from ^{15}N to ^{31}P, whereas the outer coil is triply tuned to ^{1}H, ^{2}H, and ^{13}C. The $^{6}Li\{^{13}C\}$-HMQC-TOCSY experiments were performed in an unlocked mode. The 90° pulse widths were as follows: ^{6}Li, 19.8 μs (hard pulse), 78.0 μs (attenuated during MLEV-17 spin lock); ^{13}C, 45.0 μs. The trim pulse length was 2 ms. Spectral parameters of Figures 2−4 were 512 complex data points in t_2, zero filled to 2048 points, 16 increments in t_1, zero filled to 128 points, 64 scans per t_1 increment, spectral widths 400 Hz (f_2, ^{6}Li) and 1000 Hz (f_1, ^{13}C), acquisition time 1.28 s, relaxation delay 7−10 s, ^{6}Li spin lock field 3.2 kHz, and spin lock power ca. 2 W. Constant low-power ^{1}H decoupling was applied throughout in order to obtain NOE gain. Referencing of the ^{13}C-NMR spectra is based on the solvent (toluene-d_8) signal: δ(C-para) = 125.2 ppm. The scale of the ^{6}Li spectra given in hertz does not reflect the chemical shift. Instead, the ^{6}Li main signal has been set to $\delta = 0$. All 2D spectra were recorded in the phase sensitive mode by using the Ruben, States, Haberkorn method[29] for quadrature detection in f_1. For the imaginary part of the FID set, phase Φ_2 of the first ^{13}C pulse in Figure 1 was decremented by 90° as compared to the real part. Exponential weighting in t_2 (BF 0.2−0.5) and a Gaussian window in t_1 (GF 30.0, BF −1.0) were applied. Spectral resolutions after zero filling were 0.2 Hz in f_2 and 8.0 Hz in f_1. No sample spinning was carried out. The delays, Δ, in the pulse sequence of Figure 1 were set to $1/(2J)$, with J being the $^{13}C,^{6}Li$ coupling constant (5.7 Hz for **7** and 4.3 Hz for **8**).

The series of temperature dependent ^{13}C-NMR spectra (Figure 5) was recorded on a 5 mm multinuclear probehead with 32k complex data points, zero filled to 64k, spectral width 25 000 Hz, relaxation delay 10 s, 800 scans per individual temperature, 60° pulse angle (=6.0 μs), and exponential line broadening (BF 1.0).

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