Chiral Organometallic Reagents, XIII[◇]

Structural Aspects of Differentially Solvated Benzyllithium Contact Ion Pairs

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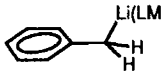
The solvation and ion pair nature of α-(phenylthio)benzyllithium (**2d**) in THF solution were investigated by NMR-spectroscopic methods. The effect of additives such as diethyleneglycol dimethyl ether or of 12-crown-4 was studied. The results were compared to those of benzyllithium compounds **4** and **6**, containing a pentaoxapentadecane ansa chain. These compounds exist as contact ion pairs in which lithium is held at the anionic carbon. This is reflected in the ^{6}Li,^{13}C coupling and ^{1}H,^{6}Li-HOESY contacts in the NMR spectra.

In THF, benzyllithium (**1**) is a monomeric solute[2]. The absence of any ^{6}Li,^{13}C coupling in the ^{13}C-NMR spectra of benzyllithium compounds[3] *in solution* suggests that they exist as solvent-separated ion pairs or, if "normal" contact ion pairs were the prevailing species, they should undergo rapid dynamic processes, which render a ^{6}Li,^{13}C coupling undetectable at least to date. Rapid dynamics of α-substituted benzyllithium compounds **2** is revealed by their low configurational stability[4]. The racemization barrier was determined[1] for the sulfur- (**2a**), selenium- (**2b**), and nitrogen substituted (**2c**) benzyllithium compounds in THF with $\Delta G^{\neq}$ ranging around 9–10 kcal mol^{-1}. More detailed investigations[1,5] showed that $\Delta H^{\neq}$ is typically around 7 kcal mol^{-1} and $\Delta S^{\neq}$ around -13 cal mol^{-1} K^{-1} for the racemization process, the rate-determining step of which has been discussed to be the transformation of the contact ion pair to the solvent-separated ion pair[1].



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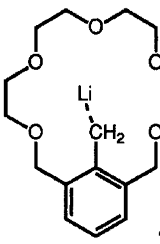
2 **3**

a: X = SCH_2Ph
b: $SeCH_2Ph$
c: N(Me)iPr
d: SPh

A wealth of information exists on contact ion pairs of benzyllithium compounds **1** or **2** *in the solid state*[6–8]. If the lithium ion in the solid state is ligated to three heteroatoms of the solvent the benzyl unit is monohapto-bound. This situation should also prevail in THF solutions at low temperatures. At room temperature the trihapto-bound benzyllithium species may become a major constituent in solution, as was found for **2c**[9]. We wanted to learn more about the ion pairs of benzyllithium compounds in solution mainly by having recourse to ^{1}H,^{6}Li-HOESY experiments[10]. A limiting case for the contact ion pair situation would be given by the crown ether compound **4**.



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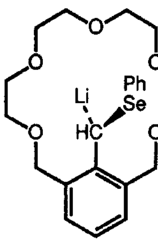

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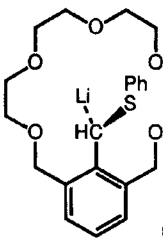

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Efforts were initially directed[11] at the synthesis of the seleno-substituted benzyllithium compound **5**. These met with only limited success but opened access to the crowned benzyllithium compounds **4** and **6** as described in the following.

Our synthesis startet with the crown ether derivative **7**[12]. An attempt to form the bis(phenylselenoacetal) by reaction of the aldehyde **7** with benzeneselenol and $ZnCl_2$[13] resulted instead in the formation of **8** in modest yield (34%). Apparently, the intermediate (phenylseleno)benzyl cation did not add benzeneselenol but rather was reduced by the latter to give **8**.

Deprotonation of **8** by bases to the benzyllithium compound **5** was ineffective[11]. However, treatment of **8** with *tert*-butyllithium cleanly afforded the benzyllithium compound **4** and *tert*-butyl phenyl selenide[14]. The former is stable in THF solution up to about −30 °C. For NMR investigations a solution of **8** in [D$_8$]THF was treated with 1.1 equivalents of freshly sublimed *tert*-butyllithium (2.5 M in C_6D_{12}). The 500-MHz ^{1}H-NMR spectrum recorded at −70 °C reveals the symmetric nature of the lithium compound **4** (cf. **4a**). Thus, a 2H doublet (J = 7.0 Hz) appearing at δ = 6.40 is assigned to the *meta* protons H_m and a 2H singlet at δ = 1.91 to the protons at the benzylic carbanionic center. For comparison, the signals of the benzylic

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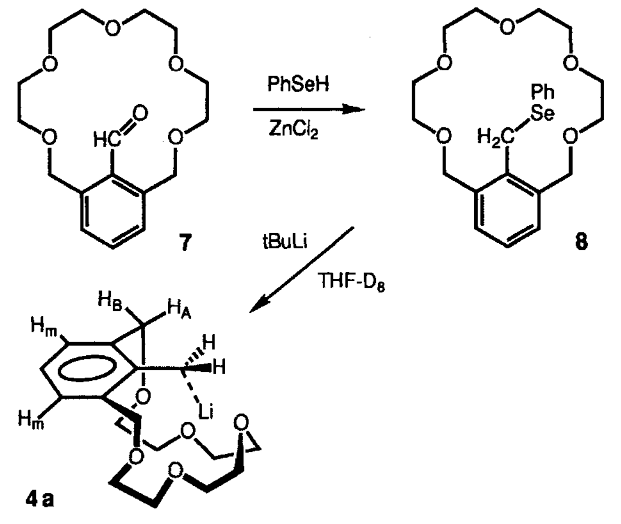
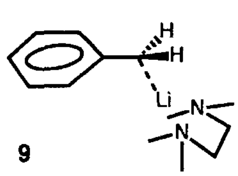


hydrogen atoms in benzyllithium (**1**) coordinated to 1.0 equivalent of TMEDA, i.e. in **9** (25 °C, [D$_8$]THF), appear at δ = 1.59. The signals of the hydrogen atoms of the benzylic ether moiety H$_A$ and H$_B$ of **4** appear as an AB system (J_{AB} = 9.1 Hz) at δ = 4.12 and 4.21. The fact that H$_A$ and H$_B$ are diastereotopic shows that the CH$_2$Li group does not flip rapidly through the crown ring. For comparison, the spectrum of the formyl compound **7** shows the corresponding benzylic protons as a singlet at δ = 4.78[12], the vinyl compound (not shown) undergoes a ring flip with a barrier of 11 kcal mol^{-1}[11].



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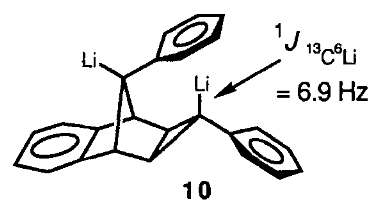

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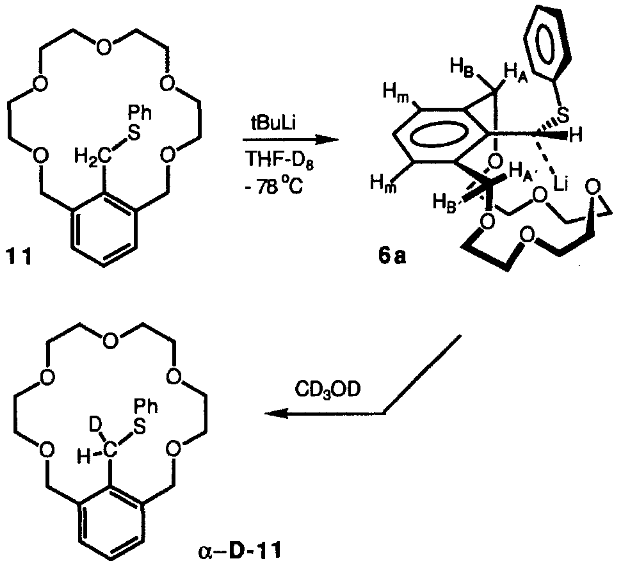
The 125-MHz ^{13}C-NMR spectrum of **4** shows no peculiarities with the exception of the signal of the anionic carbon which appears as a quartet at δ = 39.9 due to a 7.0-Hz coupling to ^{7}Li. From a gated-decoupling experiment the C,H coupling constant of the anionic carbon was determined to be 136 Hz showing that this carbon atom is pyramidalized to a considerable extent. On the other hand, no carbon-lithium coupling is observed even at low temperatures for solutions of the simple benzyllithium compound **9**. The benzylic carbon atom of **9** gives rise to a singlet at δ = 37.1 at 25 °C in [D$_8$]THF with a C,H coupling constant of 131 Hz[7]. Therefore, the solution structures of **4** and **9** are similar, even with regard to the pyramidalization of the benzylic anionic carbon atom. While the spectrum of **9** shows no carbon-lithium coupling, even at low temperatures (−150 °C[3]), the existence of a lithium-carbon coupling in **4** reveals that the lithium ion is firmly bound in the latter to the anionic carbon atom caused by the presence of the crown. The only other case, in which a carbon-lithium coupling is observed in the spectrum of a benzyllithium compound is **10**[15], in which lithium is held close to the benzyl group among other factors by the proximal aryl ring. The $^1J(^{13}C,^6Li)$ coupling constant reported for **10** (6.9 Hz) is larger than the one in **4**, as the above-mentioned $^1J(^{13}C^7Li)$ coupling constant corresponds to a $^1J(^{13}C^6Li)$ of 2.6 Hz. A coupling constant around 3 Hz is remarkably small[16] for a $^{13}C^6Li$ coupling. We tried to measure this value directly in a second experiment, in which ^{6}Li-**4** was generated from **8** and *n*Bu-^{6}Li in [D$_8$]THF. While the ^{13}C-NMR signal of the anionic carbon is broadened, the $^6Li^{13}C$ coupling cannot be resolved.

This sample, however, was used for a ^{1}H,^{6}Li-HOESY experiment at −80 °C in [D$_8$]THF: Cross peaks between proton signals and the ^{6}Li signal at δ = 1.26 from external LiCl in D$_2$O are due to the hydrogen atoms at the anionic carbon atom and the hydrogen atoms at the remote end of the crown ether ring. The benzylic ether protons as well as the aromatic protons gave no cross peaks. Thus, the structure **4a** should give a quite concise representation of the ion pair arrangement in **4**.

For comparison, the ^{1}H,^{6}Li-HOESY spectrum of the TMEDA complex **9** in [D$_8$]THF at 25 °C shows also cross peaks to the benzylic protons and to the TMEDA methyl protons. Again, no cross peak to the aromatic ring protons is observed. Compound **9** therefore exists in the [D$_8$]THF solution as a contact ion pair in which the lithium atom is coordinated to TMEDA. Probably the coordination geometry of the ion pair **9** is similar to the one present in the case of **4a**.

At last, the identity of the lithium compound **4** was secured by the addition of diphenyl diselenide to the NMR sample regenerating the "starting material" **8** in quantitative yield. The lithium compound **4** could also be trapped by diphenyl disulfide resulting in the formation of **11**, which was prepared by this route (50% yield after recrystallization).



The thioether **11** can be deprotonated by *tert*-butyllithium to the lithium compound **6**, which is thermally stable up to about 0 °C. The deprotonation of **11** by *tert*-butyllithium is slow at −78 °C. When carried out in an NMR tube, the latter was kept for about 60 seconds in an ice bath and recooled to −78 °C. This resulted in about 60% conversion of **11** to **6**. In a second experiment a quantitative deprotonation of **11** to **6** was effected by *n*-butyl-^{6}Li in [D$_8$]THF for 14 d at −78 °C.

The 125-MHz ^{13}C-NMR spectrum of the latter solution reveals the C_1 symmetry of the compound, as all carbon atoms give rise to separate signals. The anionic carbon atom leads to a triplet at $\delta = 32.0$ (−55 °C) due to coupling to ^{6}Li with a coupling constant of 3.1 Hz (in the solution of ^{7}Li-**6** the $^1J(^{13}C^7Li)$ value was 9.0 Hz). The anionic carbon gives rise to a $^1J_{CH}$ coupling of 155 Hz. The ^{6}Li NMR signal occurs at $\delta = 0.48$ based on external LiCl in D_2O. A ^{1}H,^{6}Li-HOESY experiment at −70 °C shows again intensive cross peaks to the proton at the anionic carbon and to the protons at the remote part of the crown ether chain, as was found before for the benzyllithium compound **4**.

The lack of cross peaks to the benzylic ether hydrogen atoms in **6** indicates that there is no contact between Li and the oxygen atoms bound to the benzylic carbon atoms. The lithium ion is probably coordinated only to the three oxygen atoms in the remote part of the crown ether chain as well as to the anionic carbon. Thus, in **6a** the coordination of the lithium ion is reminiscent of a three-dentate, acyclic ether ligand such as diglyme rather than a coordination to a crown ether such as 12-crown-4.

The 500-MHz ^{1}H-NMR spectrum of **6** shows two signals for the *meta* protons H_m at $\delta = 6.62$ and 6.82. The signal of the proton of the anionic carbon could be located by a ^{1}H,^{13}C-COSY experiment at $\delta = 3.48$ superimposed by multiplets of the protons of the poly(ethyleneglycol) chain. In **6** all benzylic protons of the crown ether moiety are diastereotopic. Assignments are based on the data of ^{1}H,^{1}H-COSY experiments and reveal for the benzyl ether protons two AB systems: AB system I at $\delta = 4.07$ and 5.56, $J_{AB} = 8.5$ Hz, and AB system II at $\delta = 4.31$ and 4.65, $J_{AB} = 9.1$ Hz. One hydrogen signal is shifted significantly downfield by approximately 1 ppm. This indicates proximity of this proton to the edge of the *S*-aryl group, which should hold for H_A in **6a**. The shape and position of the two AB systems did not change on varying the temperature from −55 to +25 °C. This shows that the enantiomerization of **6** must have a barrier of at least 15 kcal mol^{-1}, i.e. at least 2 kcal mol^{-1} higher than the racemization barrier of **2a**! A ring flip of the carbanion through the crown ether chain is not a viable route for the racemization of **6** in view of the conformational stability of **4**. Racemization of **6** could therefore only occur by transformation of the contact ion pair to a solvent-separated ion pair, in which the carbanion is lifted off the lithium, followed by rotation around the $C_{ipso}-C_\alpha$ bond, and reattachment of the anion to lithium. Such a rotation should equilibrate H_A with $H_{A'}$ and H_B with $H_{B'}$, the onset of which cannot be observed in the ^{1}H-NMR spectrum at room temperature. Thus, once the formation of a solvent-separated ion pair is impeded, racemization stops.

At the end of these experiments [D$_4$]methanol was added to the NMR tube resulting in the formation of the monodeuterated α-D-**11**. The latter shows a 500-MHz ^{1}H-NMR spectrum identical with that of a sample prepared independently from α-deuterated **7**. The NMR data of α-deuterated **11** are characteristic as the two benzyloxy moieties are diastereotopic due to the presence of deuterium at C_α, giving rise to two AB multiplets at $\delta = 4.26$ and 4.86 as well as 4.26 and 4.87, respectively.

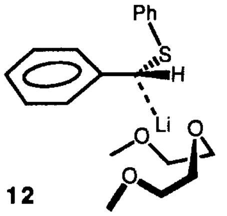
Since the ether complexes **4a** and **6a** are best described as benzyllithium being coordinated *intramolecularly* to three oxygen atoms as in diglyme rather than to all five oxygens of the crown ether, an investigation of related *intermolecular* diglyme complexes of a benzyllithium compound seemed appropriate. We chose for our studies the phenylthio-substituted benzyllithium compound **2d**, structurally related to **6**. First, we examined the NMR spectra of **2d** in THF without any additives. More precisely, all measurements were carried out in THF/[D$_8$]THF (1 : 1) in order to detect possible ^{1}H,^{6}Li-HOESY contacts to the solvent.

^{6}Li-**2d** was generated from the parent hydrocarbon benzyl phenyl sulfide by deprotonation with *n*-butyl-^{6}Li in this solvent mixture at −15 °C.

At 25 °C the benzylic proton of **2d** appears at $\delta = 3.03$, and the benzylic carbon atom gives rise to a signal at $\delta = 35.8$ with $^1J_{CH} = 149$ Hz. On cooling to −80 °C, the proton signal is only slightly shifted to higher field (2.99 ppm), and the carbon signal ($^1J_{CH} = 152$ Hz) is also shifted to higher field ($\delta = 35.1$). Due to hindered rotation around the $C_\alpha-C_{ipso}$ bond, separate resonances for all carbon atoms and protons of the carbon bound phenyl ring are observed in the low-temperature (−80 °C) spectrum. The ^{1}H,^{6}Li-HOESY spectrum at 25 °C shows an intensive cross peak to the benzylic proton and a weaker one to the *ortho* protons of the carbon-bound phenyl ring. Cross peaks to the THF resonances indicate coordination of lithium to the solvent molecules. Compound **2d** therefore exists in THF solution as a contact ion pair in which lithium is coordinated to the anionic α-carbon atom and to several solvent molecules. Such a solution structure corresponds to that found for **2d** · (THF)$_3$ in the solid state[8].

The diglyme complex **2d** · diglyme was generated by the addition of 1.1 equiv. of diglyme to a solution of **2d** in THF/[D$_8$]THF (1 : 1) at −15 °C. The ^{1}H-NMR spectrum of this complex exhibits a signal of the benzylic proton at $\delta = 3.03$ (25 °C) and 3.00 at −80 °C, i.e. almost the same proton chemical shifts as for the benzylic proton of **2d** in neat THF. The ^{13}C-NMR spectrum at 25 °C ($\delta_{C_\alpha} = 36.0$, $^1J_{CH} = 150$ Hz) is also very similar to that of **2d** in THF. At −80 °C, however, the signal of the α-carbon atom ($\delta = 37.4$) is significantly shifted to lower field and showed a larger C,H coupling constant of 159 Hz, indicating that the carbon-lithium contact is weakened to some extent. The $^1J_{CH}$ coupling constant is thus very similar to that (155 Hz) measured for **6**, revealing that hybridization and pyramidalization of anionic carbon atoms in **2d** · diglyme (cf. **12**) and in **6** are very similar.

The $^1H,^6Li$-HOESY spectrum of **2d** · diglyme at 25 °C exhibits again an intensive cross peak to the α-proton and a weaker one to the *ortho* protons of the carbon-bound phenyl ring. An additional cross peak is observed to the diglyme resonances. The cross peaks to the solvent THF are still observable but significantly weakened compared to those of the $^1H,^6Li$-HOESY spectrum of **2d** at 25 °C in the absence of diglyme. These data suggest that diglyme, at the applied concentration, cannot completely displace the THF from the coordination sphere of lithium and that diglyme and THF compete for free coordination sites at lithium in a dynamic equilibrium. Moreover, the similarity between the spectra of **6a** and **2d** · diglyme suggests that the complex **2d** · diglyme also exists as a contact ion pair (cf. **12**) in solution and that intermolecular coordination of lithium to diglyme closely resembles the situation observed in the case of **6a**.



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Finally, the adduct of **2d** and 12-crown-4 in THF/[D$_8$]THF (1 : 1) was generated by the addition of 1.1 equiv. of the crown ether to a solution of **2d** at 0 °C. At 25 °C the ^1H-NMR spectrum exhibits the benzylic proton signal at $\delta = 3.18$ and the ^{13}C-NMR spectrum the α-carbon signal at $\delta = 42.0$ with a carbon-proton coupling constant of 168 Hz, a value characteristic of planar sp^2-hybridized carbon atoms. This indicates the loss of the carbon-lithium contact originally present in **2d**. The existence of a solvent-separated ion pair was supported by the $^6Li,^1H$-HOESY spectrum: no contact was observed between lithium and the benzylic proton at the anionic carbon atom. Instead, an intensive cross-peak to the crown ether hydrogen atoms demonstrates the strong solvation of lithium by 12-crown-4.

In conclusion, the benzyllithium compounds **4** and **6** are suitable models for contact ion pairs with reduced ion dynamics in solution. This allowed Li-C coupling constants to be measured for **4** and **6**. $^1H,^6Li$-HOESY experiments showed that the lithium ion is attached to the anionic center and is held in place mainly by the remote oxygen atoms of the crown ether ring.

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Experimental

All organolithium compounds were prepared in flame-dried glassware under argon. The sample tubes containing organolithium compounds were thoroughly purged with argon or nitrogen and sealed with serum caps and parafilm. – ^1H, ^{13}C, and ^6Li NMR: Bruker AC 300, Bruker AM 400, and Bruker AMX 500. – $^1H,^1H$-COSY, $^1H,^{13}C$-COSY, and $^1H,^6Li$-HOESY: Bruker AM 400 and Bruker AMX 500. – ^6Li-NMR spectra were referenced to an external 1.0 M solution of ^6LiCl in deuterium oxide. – Phase-sensitive $^1H,^6Li$-HOESY spectra: number of experiments: 64 or 128; number of scans: 16 to 64; data matrix (after zero-filling in *F*1): 128 (*F*1) × 512 (*F*2) points or 256 (*F*1) × 512 (*F*2) points; window function: exponential in *F*2, squared sine bell in *F*1.

1. *17-[(Phenylseleno)methyl]-2,5,8,11,14-pentaoxa[15](1,3)-benzenophane* (**8**): To a suspension of 0.54 g (4.0 mmol) of anhydrous $ZnCl_2$ in 25 ml of anhydrous CH_2Cl_2 were added at room temp. 1.26 g (8.0 mmol) of benzeneselenol and over a period of 4 h by a motor-driven syringe a solution of ca. 4 mmol of 17-formyl-2,5,8,11,14-pentaoxa[15](1,3)benzenophane (obtained according to ref.[12]) in 3 ml of CH_2Cl_2. After stirring for 12 h the dark yellow solution was diluted with 50 ml of ether and washed successively twice with 10 ml each of 5% aqueous hydrochloric acid, 20 ml of water, 20 ml of a saturated aqueous $NaHCO_3$ solution, 20 ml of water, and 20 ml of brine. The organic phase was dried with $MgSO_4$ and concentrated. The oily residue was triturated twice with 20 ml each of petroleum ether to remove diphenyl diselenide. On addition of 5 ml of ether to the oily residue the product **8** crystallized as colorless needles. It was twice recrystallized from ether to give 0.64 g (34%) of colorless needles, m.p. 105–106 °C. – ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 3.46-3.67$ (several m, 16H, OCH_2CH_2O), 4.23 (d, $J = 10.8$ Hz, 2H, $ArCH_2O$), 4.80 (s, 2H, $ArCH_2SePh$), 4.84 (d, $J = 10.8$ Hz, 2H, $ArCH_2O$), 7.09–7.23 [several m, 6H, H_o (SePh), H_m (SePh), H_p (Ar)], 7.50–7.52 [m, 2H, H_m (Ar)]. – ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 24.3$ ($ArCH_2SePh$), 69.6, 70.2, 70.6, 70.7, 72.2 (OCH_2CH_2O, $ArCH_2O$), 126.4, 126.8, 128.7, 130.9, 131.1, 133.4 [C_o (SePh), C_m (SePh), C_p (SePh), C_o (Ar), C_m (Ar), C_p (Ar)], 137.3, 138.9 [C_i (SePh), C_i (Ar)]. – $C_{23}H_{30}O_5Se$ (465.4): calcd. C 59.35, H 6.50; found C 59.37, H 6.63.

2. *17-(Lithiomethyl)-2,5,8,11,15-pentaoxa[15](1,3)benzenophane* (**4**): 37.2 mg (80 μmol) of **8** was dissolved in 0.8 ml of [D$_8$]THF in a dry NMR tube under nitrogen. To this solution was added at −78 °C by means of a syringe a solution of 88 μmol of tBu^7Li in [D$_{12}$]cyclohexane (2.5 M solution). The butyllithium solution solidifying on the wall of the tube was brought into solution by briefly shaking the tube outside the cooling bath. – ^1H NMR (500 MHz, [D$_8$]THF, −70 °C): $\delta = 1.91$ (s, 2H, H_α), 3.44–3.62 (several m, 12H, OCH_2CH_2O), 3.74 (m, 2H, OCH_2CH_2O), 3.87 (m, 2H, OCH_2CH_2O), 4.12 (d, $J = 9.1$ Hz, 2H, $ArCH_2O$), 4.21 (d, $J = 9.1$ Hz, 2H, $ArCH_2O$), 5.25 (t, $J = 7.0$ Hz, 1H, H_p), 6.40 (d, $J = 7.0$ Hz, 2H, H_m). In addition, the signals of *tert*-butyl phenyl selenide appeared at $\delta = 7.36$ (t, $J = 7.6$ Hz, 2 H_m), 7.43 (t, $J = 7.4$ Hz, 1 H_p), 7.66 (dd, $J = 7.9$ and 1 Hz, 2 H_o). – ^{13}C NMR (125 MHz, [D$_8$]THF, −70 °C): $\delta = 39.9$ [q, $J(^{13}C^7Li) = 7.0$, $J(^{13}C,^1H) = 136$ Hz C_α], 69.8, 69.9, 70.1, 71.0, (OCH_2CH_2O), 77.0 ($ArCH_2O$), 100.0 (C_p), 118.6 (C_o), 131.3 (C_m), 153.9 (C_i). – The ^{6}lithium derivative of **4** was prepared as before from 50.0 mg (107 μmol) of **8** in 1.0 ml of [D$_8$]THF and 118 μmol of nBu-^6Li (1.36 M in hexane). – ^6Li NMR (73 MHz, [D$_8$]THF, −80 °C): $\delta = 1.26$.

3. *[^{6}Li]Benzyllithium · TMEDA*[7] (^{6}Li-**9**): To a solution of 200 mg (1.70 mmol) of TMEDA in 1.0 ml of toluene, 1.0 ml of diethyl ether, and 0.5 ml of THF was added 1.69 mmol of a nBu^6Li solution in *n*-hexane[3] at 0 °C. After 1 d at −30 °C, a precipitate had formed which was separated from the remaining solution, washed three times with *n*-hexane and dried in vacuo. The colorless solid was dissolved in 1.0 ml of [D$_8$]THF and the solution transferred to an NMR tube. – ^1H NMR (300 MHz, [D$_8$]THF, 25 °C): $\delta = 1.59$ (s, 2H, H_α), 2.20 (s, 12H, TMEDA CH_3), 2.34 (s, 4H, TMEDA CH_2), 5.45 (t, $J = 6.9$ and 8.2 Hz, 1H, H_p), 6.12 (d, $J = 8.2$ Hz, 2H, H_o), 6.35 (dd, $J = 6.9$ and 8.2 Hz, 2H, H_m). – ^{13}C NMR (75 MHz, [D$_8$]THF, 25 °C): $\delta = 37.0$ (C_α), 46.5 (TMEDA CH_3), 58.7

(TMEDA CH_2), 105.0 (C_p), 117.2 (C_o), 128.5 (C_m), 161.4 (C_i). – ^{6}Li NMR (73 MHz, $[D_8]$THF, 25 °C): $\delta = 0.77$. – ^{1}H,^{6}Li-HOESY [400 MHz (^{1}H), 59 MHz (^{6}Li), $[D_8]$THF, 25 °C]: relaxation delay 4.0 s, mixing time 1.5 s.

4. *17-[(Phenylthio)methyl]-2,5,8,11,14-pentaoxa[15](1,3)-benzenophane* (**11**): To a solution of 960 mg (2.1 mmol) of **8** in 20 ml of THF was slowly added at −78 °C 2.5 mmol (1.1 equiv.) of a 1.5 M solution of *n*-butyllithium in hexane. The solution turned yellow, and a precipitate formed. After stirring for 1 h a solution of 655 mg (3.0 mmol) of diphenyl disulfide in 2 ml of THF was slowly added. Stirring was continued for 3 h at −78 °C, and the mixture was allowed to reach room temp. After 12 h 50 ml of ether was added, and the solution was washed twice with 10 ml each of 10% aqueous KOH, twice with 10 ml of water, twice with 10 ml of brine, and dried with $MgSO_4$. The solution was concentrated, and residual solvent was removed at 60 °C/10^{-3} Torr. The solid residue was recrystallized twice from ether/petroleum ether/CH_2Cl_2 (5:4:2) to give 440 mg (50%) of **11** as colorless needles, m.p. 131 °C. – ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.5–3.7 (several m, 16 H, OCH_2CH_2O), 4.30 (d, J = 10.8 Hz, 2 H, $ArCH_2O$), 4.79 (s, 2 H, $ArCH_2SPh$), 4.93 (d, J = 10.8 Hz, 2 H, $ArCH_2O$), 7.2–7.3 [several m, 6 H; H_o (SPh), H_m (SPh), H_p (SPh), H_p (Ar)], 7.46 [d, J = ca. 8 Hz, 2 H, H_m (Ar)]. – ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 30.3 ($ArCH_2SPh$), 69.7, 70.2, 70.6, 70.7, 72.2 (OCH_2CH_2O, $ArCH_2O$), 125.8, 126.8, 128.6, 129.6, 130.9 [C_o (SPh), C_m (SPh), C_p (SPh), C_o (Ar), C_m (Ar), C_p (Ar)], 137.7 [C_i (SPh), C_i (Ar)]. – $C_{23}H_{30}O_5S$ (418.5): calcd. C 66.00, H 7.22; found C 65.90, H 7.11.

5. *17-[Lithio(phenylthio)methyl]-2,5,8,11,14-pentaoxa[15]-(1,3)benzenophane* (**6**): A solution of 30.0 mg (72 µmol) of **11** in 0.8 ml of $[D_8]$THF was allowed to react with 32 µl (79 µmol) of a 2.5 M solution of *tert*-butyllithium in $[D_{12}]$cyclohexane as described under 2. The tube was taken out of the cooling bath and placed into ice/water for about 60 s in order to dissolve the *tert*-butyllithium and to generate **6** from **11**. This resulted in ca. 60% conversion. – ^{1}H NMR (500 MHz, $[D_8]$THF, −55 °C): δ = 3.5–3.8 (several m, 17 H, H_α, OCH_2CH_2O), 4.06 (d, J = 8.5 Hz, 1 H, $ArCH_2O$), 4.31 (d, J = 9.2 Hz, 1 H, $ArCH_2O$), 4.65 (d, J = 9.2 Hz, 1 H, $ArCH_2O$), 5.57 (d, J = 8.5 Hz, 1 H, $ArCH_2O$), 5.99 [t, J = 7.2 Hz, 1 H, H_p (Ar)], 6.62 [d, J = 6.2 Hz, 1 H, H_m (Ar)], 6.70 [t, J = 7.1 Hz, 1 H, H_p (SPh)], 6.82 [dd, J = 7 and 1 Hz, 1 H, H_m (Ar)], 6.92 [t, J = 7.7 Hz, 2 H, H_m (SPh)], 6.98 [d, J = 7.3 Hz, 2 H, H_o (SPh)]. On warming to 25 °C the chemical shifts and the coupling patterns did not change. – ^{13}C NMR (125 MHz, $[D_8]$THF, −55 °C): δ = 32.2 [q, $J(^{13}C,^{7}Li)$ = 9.0 Hz, C_α], 68.0, 69.4, 69.5, 69.8, 69.9, 70.3, 71.1, 72.3 (OCH_2CH_2O), 76.2, 76.9 ($ArCH_2O$), 110.1 [C_p (Ar)], 121.9 [C_p (SPh)], 124.2 [C_o (SPh)], 128.1 [C_m (SPh)], 131.9 [C_m (Ar)], 132.8 [$C_{m'}$ (Ar)]. The signals of the four quaternary C atoms [C_o (Ar), C_i (Ar), C_i (SPh)] could not be detected. – ^{6}Li-**6** was generated from 29.0 mg (69 µmol) of **11** in 0.8 ml of $[D_8]$THF and 51 µl (76 µmol) of a 1.5 M solution of *n*Bu-^{6}Li in hexane over a period of 14 d at −78 °C. – ^{1}H NMR (500 MHz, $[D_8]$THF, −70 °C): δ = 3.48 (s, 1 H, H_α), 3.51–3.81 (several m, 14 H, OCH_2CH_2O), 4.02–4.05 (m, 2 H, OCH_2CH_2O), 4.07 (d, J = 8.5 Hz, 1 H, $ArCH_2O$), 4.31 (d, J = 9.1 Hz, 1 H, $ArCH_2O$), 4.65 (d, J = 9.1 Hz, 1 H, $ArCH_2O$), 5.56 (d, J = 8.5 Hz, 1 H, $ArCH_2O$), 5.99 [t, J = 7.2 Hz, 1 H, H_p (Ar)], 6.63 [dd, J = 7.4 and 1.5 Hz, 1 H, H_m (Ar)], 6.71 [tt, J = 7.1 and 1.3 Hz, 1 H, H_p (SPh)], 6.83 [dd, J = 7.3 Hz, 1.6 Hz, 1 H, $H_{m'}$ (Ar)], 6.93 [t, J = 7.7 Hz, 2 H, H_m (SPh)], 6.98 [dd, J = 8.4 Hz, 1.2 Hz, 2 H, H_o (SPh)]. – ^{13}C NMR (125 MHz, $[D_8]$THF, −70 °C): δ = 32.0 [t, $J(^{13}C,^{6}Li$, −55 °C) = 3.3, $J(^{13}C,^{1}H$, −55 °C) = 155 Hz), C_α], 68.0, 69.3, 69.4, 69.8, 69.9, 70.2, 71.0, 72.4 (OCH_2CH_2O), 76.1, 76.9 ($ArCH_2O$), 110.2 [C_p (Ar)], 121.9 [C_p (SPh)], 124.2 [C_o (SPh)], 128.1 [C_m (SPh)], 131.9 [C_m (Ar)], 132.8 [$C_{m'}$ (Ar)], 152.5, 154.4 [C_i (Ar), C_i (SPh)]. The signals of the two quaternary C atoms [C_o (Ar), $C_{o'}$ (Ar)] could not be detected. – ^{6}Li NMR (59 MHz, $[D_8]$THF, −70 °C): δ = 0.48.

The reaction was quenched by the addition of $[D_4]$methanol to give α-D-**11**. – ^{1}H NMR (500 MHz, $[D_8]$THF, 25 °C): δ = 3.44–3.64 (several m, 16 H, OCH_2CH_2O), 4.26 (d, J = 12.8 Hz, 1 H, $ArCH_2O$), 4.26 (d, J = 12.8 Hz, 1 H, $ArCH_2O$), 4.81 (broad s, 1 H, ArCHDSPh), 4.85 (d, J = 12.8 Hz, 1 H, $ArCH_2O$), 4.86 (d, J = 12.8 Hz, 1 H, $ArCH_2O$), 7.10–7.25 [several m, 6 H, H_o (SPh), H_m (SPh), H_p (SPh), H_p (Ar)], 7.44–7.46 [m, 2 H, H_m (Ar)].

6. *17-[Deuterio(phenylthio)methyl]-2,5,8,11,14-pentaoxa[15]-(1,3)benzenophane* (α-D-**11**): α-D-**7** was prepared as described in ref.[12] by using α-deuterio-*N*,*N*-dimethylformamide instead of undeuterated material. α-D-**7** was converted into α-D-**8** as described under 1. (27%). – ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.45–3.60 (several m, 16 H, OCH_2CH_2O), 4.23 (d, J = 10.8 Hz, 1 H, $ArCH_2O$), 4.23 (d, J = 10.8 Hz, 1 H, $ArCH_2O$), 4.79 (broad s, 1 H, ArCHDSePh), 4.83 (d, J = 10.8 Hz, 1 H, $ArCH_2O$), 4.84 (d, J = 10.8 Hz, 1 H, $ArCH_2O$), 7.09–7.23 [several m, 6 H, H_o (SePh), H_m (SePh), H_p (SePh), H_p (Ar)], 7.50–7.52 [m, 2 H, H_m (Ar)]. – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.1 [t, $J(^{13}C,^{2}H)$ = 21.8 Hz, ArCHDSePh], 69.6, 70.1, 70.6, 70.7, 72.1 (OCH_2CH_2O, $ArCH_2O$), 126.4, 126.8, 128.7, 130.8, 131.1, 133.4, 137.3, 138.9 [C_o (SePh), C_m (SePh), C_p (SePh), C_o (Ar), C_m (Ar), C_p (Ar), C_i (SePh), C_i (Ar)]. – $C_{23}H_{29}DO_5Se$ (466.5): calcd. C 59.22, H 6.70; found C 59.29, H 6.78.

300 mg (0.6 mmol) of α-D-**8** was converted into α-D-**11** as described under 4. to give 170 mg (68%) of α-D-**11**. – ^{1}H NMR (500 MHz, $[D_8]$THF, 25 °C): δ = 3.44–3.62 (several m, 16 H, OCH_2CH_2O), 4.26 (d, J = 10.4 Hz, 1 H, $ArCH_2O$), 4.26 (d, J = 10.4 Hz, 1 H, $ArCH_2O$), 4.81 (broad s, 1 H, ArCHDSPh), 4.86 (d, J = 10.4 Hz, 1 H, $ArCH_2O$), 4.87 (d, J = 10.4 Hz, 1 H, $ArCH_2O$), 7.09–7.25 [several m, 6 H, H_o (SPh), H_m (SPh), H_p (SPh), H_p (Ar)], 7.44–7.46 [m, 2 H, H_m (Ar)]. – ^{13}C NMR (75 MHz, $[D_8]$THF, 25 °C): δ = 30.3 [t, $J(^{13}C,^{2}H)$ = 22.0 Hz, ArCHDSPh), 71.1, 71.2, 71.6, 71.9, 73.0 (OCH_2CH_2O, $ArCH_2O$), 125.9, 127.4, 129.4, 129.6, 131.3, 138.9, 139.3, 139.6 [C_o (SPh), C_m (SPh), C_p (SPh), C_o (Ar), C_m (Ar), C_p (Ar), C_i (SPh), C_i (Ar)]. – $C_{23}H_{29}DO_5S$ (419.6): calcd. C 65.84, H 7.44; found C 65.82, H 7.04.

7. *[^{6}Li]-α-(Phenylthio)benzyllithium* (^{6}Li-**2d**): A solution of 0.55 mmol of *n*Bu^{6}Li in *n*-hexane was evaporated to dryness in vacuo. The remaining *n*Bu^{6}Li was dissolved in 1.0 ml of THF/$[D_8]$THF (1:1) at −15 °C. To this solution was added 100 mg (0.50 mmol) of benzyl phenyl sulfide[17]. After 15 min at −15 °C, the resulting yellow solution was transferred into an NMR tube. – ^{1}H NMR (500 MHz, THF/$[D_8]$THF, 1:1, 25 °C): δ = 3.03 (s, 1 H, H_α), 5.94 [t, J = 7.0 Hz, 1 H, H_p (Ph)], 6.59 [dd, J = 7.0 and 7.2 Hz, 2 H, H_m (Ph)], 6.67 [t, J = 7.2 Hz, 1 H, H_p (SPh)], 6.70 [bd, J = 7.2 Hz, 2 H, H_o (Ph)], 6.89 [dd, J = 7.2 and 8.0 Hz, 2 H, H_m (SPh)], 7.10 [d, J = 8.0 Hz, 2 H, H_o (SPh)]. – ^{13}C NMR (75 MHz, THF/$[D_8]$THF, 1:1, 25 °C): δ = 35.8 (d, J = 149 Hz, C_α), 111.8 [d, J = 157 Hz, C_p (Ph)], 118.8 [bd, J = 154 Hz, C_o (Ph)], 122.0 [d, J = 160 Hz, C_p (SPh)], 125.3 [d, J = 159 Hz, C_o (SPh)], 128.0 [d, J = 158 Hz, C_m (SPh)], 128.3 [d, J = 152 Hz, C_m (Ph)], 151.8 [s, C_i (SPh)], 157.0 [s, C_i (Ph)]. – ^{6}Li NMR (73 MHz, THF/$[D_8]$THF, 1:1, 25 °C): δ = 2.75. – ^{1}H,^{6}Li-HOESY [500 MHz (^{1}H), 73 MHz (^{6}Li), THF/$[D_8]$THF, 1:1, 25 °C]: relaxation delay 6.0 s, mixing time 1.6 s. – ^{1}H NMR (500 MHz, THF/$[D_8]$THF, 1:1, −80 °C): δ = 2.99 (s, 1 H, H_α), 5.87 [t, J = 6.8 Hz, 1 H, H_p (Ph)], 6.51–6.60 [m, 3 H, H_o (Ph), H_m (Ph), $H_{m'}$ (Ph)], 6.68 [d, J = 8.0 Hz, 1 H, $H_{o'}$ (Ph)], 6.73 [t, J = 7.2 Hz, 1 H, H_p (SPh)], 6.95 [dd, J = 7.2 and 7.8

Hz, 2H, H_m (SPh)], 7.06 [d, J = 7.8 Hz, 2H, H_o (SPh)]. – ^{13}C NMR (125 MHz, THF/[D_8]THF, 1:1, −80°C): δ = 35.1 (d, J = 152 Hz, C_α), 110.7 [d, J = 157 Hz, C_p (Ph)], 115.9 [d, J = 155 Hz, C_o (Ph)], 119.7 [d, J = 154 Hz, $C_{o'}$ (Ph)], 122.1 [d, J = 158 Hz, C_p (SPh)], 124.8 [d, J = 159 Hz, C_o (SPh)], 127.8 [d, J = 151 Hz, C_m (Ph)], 128.2 (d, J = 157 Hz, C_m (SPh)], 128.8 [d, J = 153 Hz, $C_{m'}$ (Ph)], 151.2 [s, C_i (SPh)], 156.1 [s, C_i (Ph)].

8. *[^{6}Li]-α-(Phenylthio)benzyllithium-Diglyme* (^{6}Li-**2d** · diglyme): To a solution of 0.50 mmol of ^{6}Li-**2d** in THF/[D_8]THF (1:1) at −15°C (see above) was added 74 mg (0.08 ml, 0.55 mmol) of diglyme. The red solution was kept at −15°C for 15 min and then transferred to an NMR tube. – ^{1}H NMR (500 MHz, THF/[D_8]THF, 1:1, 25°C): δ = 3.03 (s, 1H, H_α), 3.23 (s, 6H, diglyme OCH_3), 3.38–3.40 (m, 4H, diglyme OCH_2), 3.47–3.49 (m, 4H, diglyme-OCH_2), 5.90 [t, J = 7.0 Hz, 1H, H_p (Ph)], 6.57 [dd, J = 7.0 and 7.2 Hz, 2H, H_m (Ph)], 6.66–6.69 [m, 3H, H_o (Ph), H_p (SPh)], 6.89 [dd, J = 7.2 and 8.1 Hz, 2H, H_m (SPh)], 7.09 [d, J = 8.1 Hz, 2H, H_o (SPh)]. – ^{13}C NMR (75 MHz, THF/[D_8]THF, 1:1, 25°C): δ = 36.0 (d, J = 150 Hz, C_α), 59.1 (q, J = 140 Hz, diglyme OCH_3), 71.3 (t, J = 141 Hz, diglyme OCH_2), 72.8 (t, J = 141 Hz, diglyme OCH_2), 111.4 [d, J = 157 Hz, C_p (Ph)], 118.6 [bd, J = 152 Hz, C_o (Ph)], 122.0 [d, J = 160 Hz, C_p (SPh)], 125.3 [d, J = 159 Hz, C_o (SPh)], 128.0 [d, J = 158 Hz, C_m (SPh)], 128.3 [d, J = 151 Hz, C_m (Ph)], 151.9 [s, C_i (SPh)], 156.9 [s, C_i (Ph)]. – ^{6}Li NMR (73 MHz, THF/[D_8]THF, 1:1, 25°C): δ = 1.78. – ^{1}H,^{6}Li-HOESY [500 MHz (^{1}H), 73 MHz (^{6}Li), THF/[D_8]THF, 1:1, 25°C]: relaxation delay 6.0 s, mixing time 1.6 s. – ^{1}H NMR (400 MHz, THF/[D_8]THF, 1:1, −80°C): δ = 3.00 (s, 1H, H_α), 3.22 (s, 6H, diglyme OCH_3), 3.38 (br. s, 4H, diglyme OCH_2), 3.45 (br. s, 4H, diglyme OCH_2), 5.67 [t, J = 6.4 Hz, 1H, H_p (Ph)], 6.37 [d, J = 7.6 Hz, 1H, H_o (Ph)], 6.42–6.48 [m, 3H, $H_{o'}$ (Ph), H_m (Ph), $H_{m'}$ (Ph)], 6.71 [t, J = 7.0 Hz, 1H, H_p (SPh)], 6.94 [dd, J = 7.0 and 7.9 Hz, 2H, H_m (SPh)], 7.06 [d, J = 7.9 Hz, 2H, H_o (SPh)]. – ^{13}C NMR (100 MHz, THF/[D_8]THF, 1:1, −80°C): δ = 37.4 (d, J = 159 Hz, C_α), 59.2 (q, J = 141 Hz, diglyme OCH_3), 70.5 (t, J = 142 Hz, diglyme OCH_2), 72.0 (t, J = 143 Hz, diglyme OCH_2), 108.2 [d, J = 156 Hz, C_p (Ph)], 114.5 [d, J = 155 Hz, C_o (Ph)], 118.6 [d, J = 151 Hz, $C_{o'}$ (Ph)], 121.9 [d, J = 155 Hz, C_p (SPh)], 124.7 [d, J = 159 Hz, C_o (SPh)], 127.7 [d, J = 151 Hz, C_m (Ph)], 128.1 [d, J = 156 Hz, C_m (SPh)], 128.7 [d, J = 150 Hz, $C_{m'}$ (Ph)], 151.8 [s, C_i (SPh)], 155.7 [s, C_i (Ph)].

9. *[^{6}Li]-α-(Phenylthio)benzyllithium · (12-Crown-4)* [^{6}Li-**2d** · (12-crown-4)]: A solution of 0.50 mmol of ^{6}Li-**2d** in THF/[D_8]THF (1:1) prepared at −15°C (see above) was warmed to 0°C. To this solution was added 97 mg (0.09 ml, 0.55 mmol) of 12-crown-4. After 15 min at 0°C, the resulting orange-red solution was transferred into an NMR tube. – Note: lowering the temperature below 0°C led to precipitation of the complex. – ^{1}H NMR (500 MHz, THF/[D_8]THF, 1:1, 25°C): δ = 3.18 (s, 1H, H_α), 3.56 (s, 16H, 12-crown-4 OCH_2), 5.46 [t, J = 6.8 Hz, 1H, H_p (Ph)], 6.26 [bd, J = 7.4 Hz, 2H, H_o (Ph)], 6.37 [dd, J = 6.8 and 7.4 Hz, 2H, H_m (Ph)], 6.69 [t, J = 7.2 Hz, 1H, H_p (SPh)], 6.93 [dd, J = 7.2 and 7.9 Hz, 2H, H_m (SPh)], 7.14 [d, J = 7.9 Hz, 2H, H_o (SPh)]. – ^{13}C NMR (100 MHz, THF/[D_8]THF, 1:1, 25°C): δ = 42.0 (d, J = 168 Hz, C_α), 69.4 (t, J = 142 Hz, 12-crown-4 OCH_2), 105.0 [d, J = 157 Hz, C_p (Ph)], 113 [bs, C_o (Ph)], 118 [bs, $C_{o'}$ (Ph)], 121.8 [d, J = 157 Hz, C_p (SPh)], 125.0 [d, J = 160 Hz, C_o (SPh)], 128.0 [d, J = 156 Hz, C_m (SPh)], 128.5 [bs, C_m (Ph), $C_{m'}$ (Ph)], 153.1 [s, C_i (SPh)], 155.6 [s, C_i (Ph)]. – ^{6}Li NMR (73 MHz, THF/[D_8]THF, 1:1, 25°C): δ = 2.08. – ^{1}H,^{6}Li-HOESY [500 MHz (^{1}H), 73 MHz (^{6}Li), THF/[D_8]THF, 1:1, 25°C]: relaxation delay 6.0 s, mixing time 1.6 s.

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