

Organic Cume
 University of Missouri-Columbia
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 Dr. Rainer Glaser

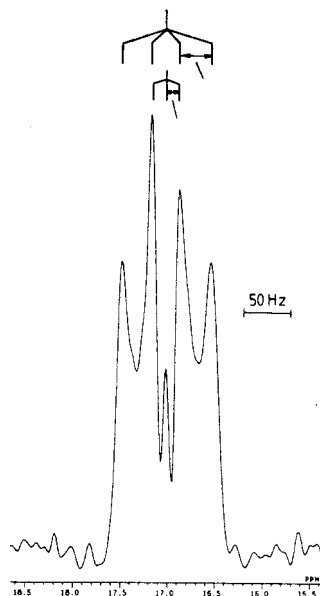
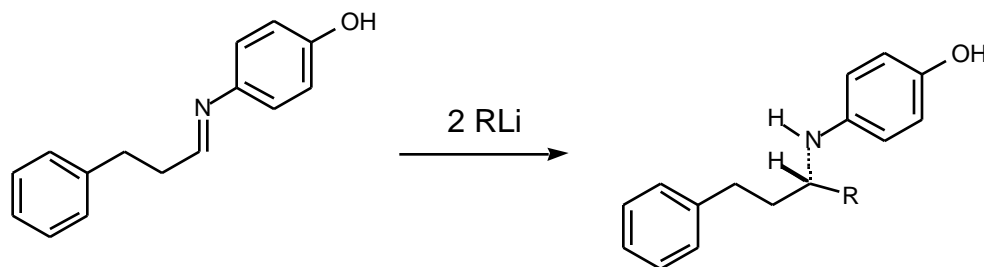


Figure 1. ^{13}C NMR spectrum of *tert*-butyllithium in THF-d_6 , natural isotope abundance. C1 signal with slight resolution enhancement (1.4 M, -90°C).

	Max.	Yours
Question 1	32	
Question 2	54	
Question 3	14	
Total	100	

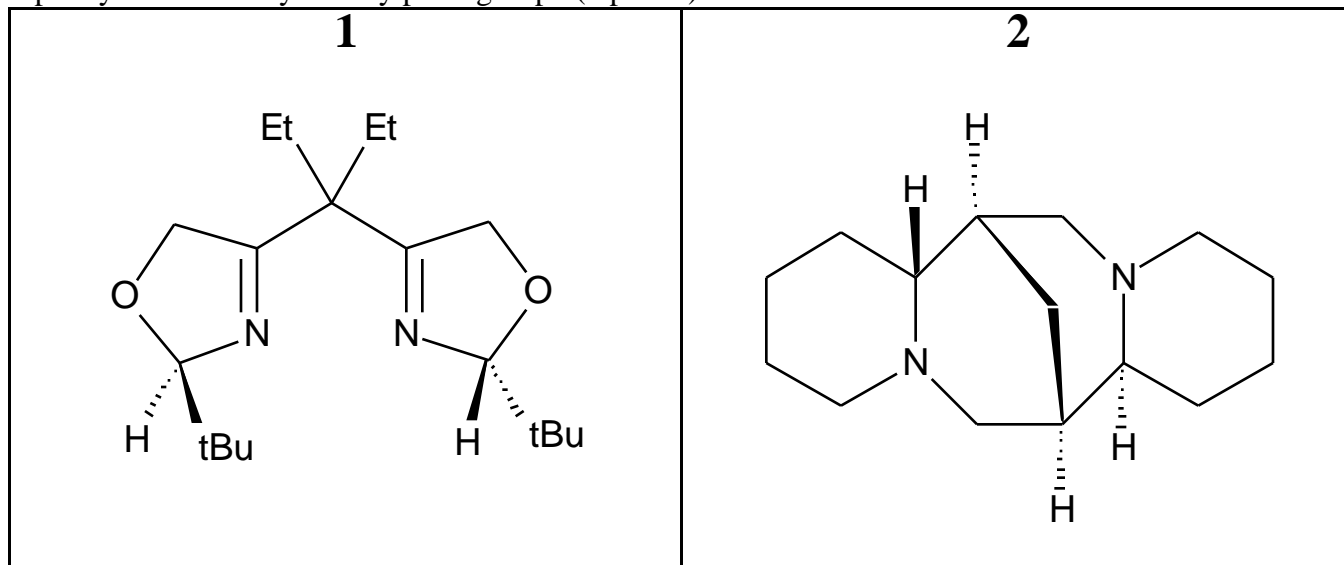
Question 1. Enantioselective Nucleophilic Addition to Imines.Denmark, S. E.; Nakajima, N.; Nicaise, O. J.-C. *J. Am. Chem. Soc.* **1994**, *116*, 8797.

In the “classical” nucleophilic addition of organolithium compounds to imines, the nucleophile can attack from either face of the imine, which prefers the *E*-configuration for steric reasons, and a racemate is formed. In the presence of a chiral ligand such as **1** or **2**, however, significant enantiomeric excess can be observed in several cases as shown in the Table.



R	T [°C]	Ligand	Yield (%)	ee (%)
Me	-63	1 (1.0)	96	91
Me	-63	1 (0.2)	81	82
CH=CH ₂	-78	1 (1.0)	95	89
CH=CH ₂	-78	1 (0.2)	82	82
<i>n</i> Bu	-94	2 (1.0)	90	91
<i>n</i> Bu	-78	2 (0.2)	91	79

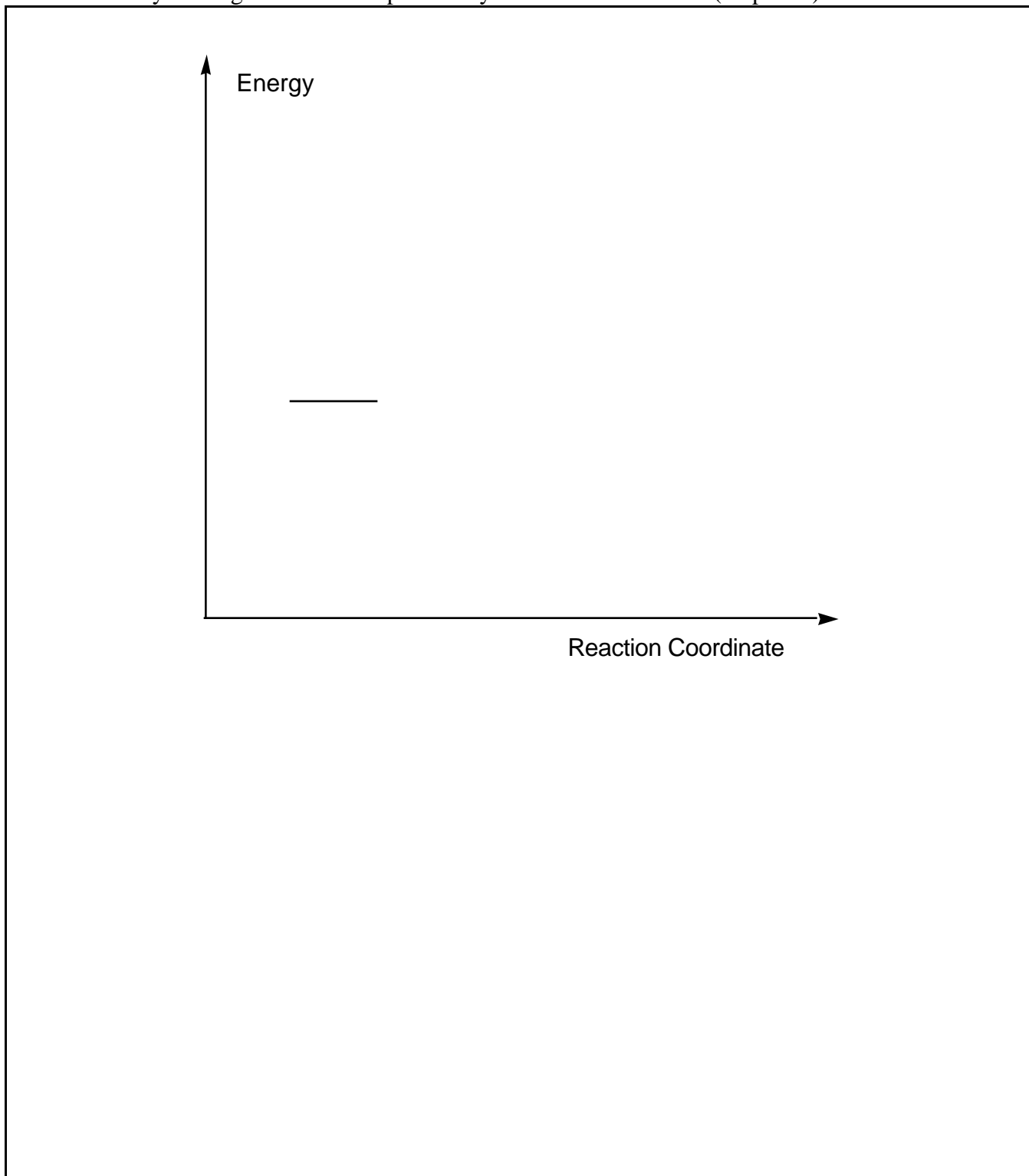
(a) Two bi-dentate ligands **1** and **2** are shown. For each of these ligands, mark each chiral carbon atom with a star, name the configuration at each of these chiral center using the R/S nomenclature, and specify the overall symmetry point group. (8 points)



(b) The nitrogen atoms of the bis(oxazoline) shown above are not chiral, of course, because these N atoms are sp^2 hybridized. However, the N-atoms in the other ligand, (-)-sparteine, become asymmetric N atoms once they are complexed to the lithium cation. Specify the configurations of both N atoms in the (-)-sparteine *when complexed to Li^+* using the R/S nomenclature. Briefly explain how you determined the R/S labels. (6 points, ***a model will definitely help to get this right!!***)

(c) It is highly significant that these reactions remain enantioselective when the chiral auxiliary is used in less-than-stoichiometric amounts. As can be seen from the table, in some cases a high enantiomeric excess is retained when only 20 mol% of **1** or **2** are used. For **2** only, discuss what feature of the reaction determines whether you need stoichiometric amounts of the additive or whether catalytic amounts suffice. (The authors most likely tried the reaction also “fully catalytic”, e.g. [additive] < 1%, but that apparently did not work.) (8 points)

(d) Explain the underlying principle of such enantioselective syntheses using qualitative transition state theory. The plot should contain (i) the potential energy diagram for the reaction *in the absence* of the chiral auxiliary and (ii) the potential energy diagrams for the reaction of the imine *in the presence* of the chiral auxiliary leading to both of the potentially formed enantiomers. (10 points)



Question 2. Aggregation of Organolithium Compounds (points)

(See: Schleyer, et al. *Organometallics* **1987**, 6, 2371.)

(a) In this problem, we will be dealing with ^1H , ^{13}C , ^6Li , and ^7Li NMR spectroscopy. Let's start with a mini-review of the NMR properties of these nuclei. Provide numbers for the shaded cells.

(8 points total; 1 point each for the cells to the left and 1.5 each for the cells to the right.)

Nuclide	Spin, I	Nat. Abun.	Rel. Sens.	Gyro. ratio	NMR freq.
^1H	1/2		1.00	26.7519	100.00
$^2\text{H} = \text{D}$			$9.95 \cdot 10^{-3}$	4.1066	15.351
^6Li	1	7.42	$8.5 \cdot 10^{-3}$	3.9371	14.716
^7Li	3/2	92.58			38.86
^{13}C			$1.59 \cdot 10^{-2}$	6.7283	

(b) Remember that the multiplicity M is given by $M = 2nI + 1$ (n = number of equivalent neighbors). Considering the I values of carbon and lithium, we realize that the coupling of one ^{13}C to one ^6Li nucleus would result in a _____ (specify multiplicity) with line intensities _____ whereas the coupling of a ^{13}C to one ^7Li nucleus would result in a _____ (specify the multiplicity) with line intensities _____. In Figure 1, the natural abundance ^{13}C NMR spectrum is shown of *tert.*-butyllithium in **deuterated THF** in the region of the quaternary C1 atom (centered at about 17 ppm). Considering the indicated splitting patterns, explain whether *tert.* butyllithium is monomeric, dimeric or tetrameric in THF. (12 p.; 2 points each blank, 4 points for expl.)

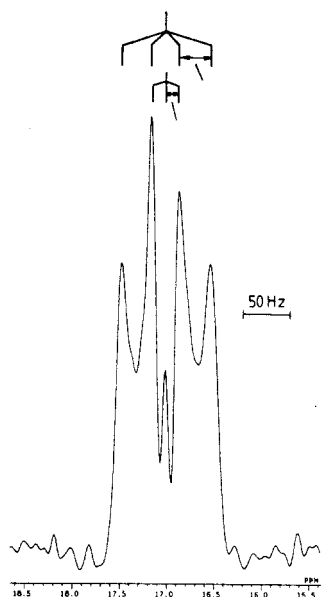


Figure 1. ^{13}C NMR spectrum of *tert.*-butyllithium in THF-d_6 , natural isotope abundance. C1 signal with slight resolution enhancement (1.4 M, -90°C).

(c) We have seen already that the ^{13}C - ^6Li coupling constants are less compared to the ^{13}C - ^7Li coupling constants. In the ^{13}C NMR spectrum of the quarternary carbon of *tert.* butyllithium in deuterated diethyl ether, we find a signal that is split into seven lines due to ^{13}C - ^7Li coupling. (Ignore the weak lines caused by the isotopomers.) Considering the indicated splitting patterns, explain whether *tert.* butyllithium is monomeric, dimeric or tetrameric in diethyl ether. Explain the splitting pattern. (5 points for each explanation)

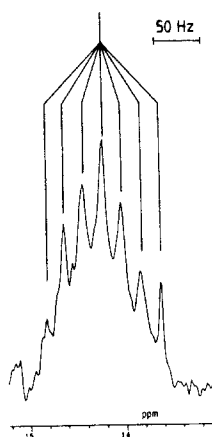


Figure 2. ^{13}C NMR spectrum of *tert.*-butyllithium in diethyl ether, natural isotope abundance. C1 signal with slight resolution enhancement (1.4 M, $-64\text{ }^\circ\text{C}$).

(d) Thus, *tert.*-butyllithium is a nice example of a metal organic compound being _____ in nonpolar solvents (aliphatic and aromatic hydrocarbons), _____ in more bulky donating solvents (diethyl ether), and _____ in a less crowded donating solvent (THF). Of course, we all know from extensive gas phase studies and theoretical work that *tert.* butyllithium is tetrameric in the gas phase. (2 points each blank).

(e) In Figures 5 and 6, the ^{13}C NMR spectra are shown of ^6Li enriched **mesityllithium** in the presence of PMDTA (a tridentate ligand: N,N,N',N'',N'''-pentamethyldiethylenetriamine) in deuterated THF.

- * Give the structure of mesityllithium. (2 easy points)
- * Give the structure of PMDTA. (2 more very easy points)
- * Considering the NMR spectrum shown in Figure 6, explain whether mesityllithium is monomeric, dimeric, or tetrameric in THF. (4 easy points; **Note:** HOESY = heteronuclear NOESY)
- * Considering Figure 6, assign the ^1H NMR resonances occurring at 1.95, 2.23, and 2.38 ppm and explain your assignments. (6 points)
- * Suggest a structure for the organometallic species under these conditions. (4 points)

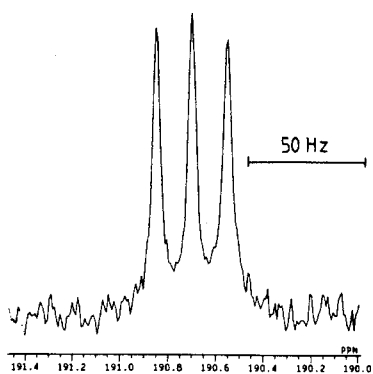


Figure 5. ^{13}C NMR spectrum of **3**, 96% enriched with ^6Li , ^{13}C labeled carbon, 0.5 M, $\text{THF-}d_8$, -100°C , with 1 equiv of PMDTA.

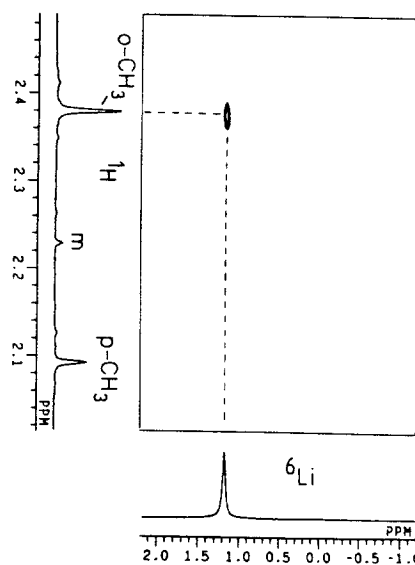


Figure 6. ^6Li - ^1H HOESY of **3**, contour plot, $\text{THF-}d_8$, -15°C , without amine ligands, 96% enriched with ^6Li (mixing time $\tau = 2.0$ s; m = mesitylene).

Structure and Preparation of Mesityllithium:

PMDTA Structure:

Explain aggregation state:

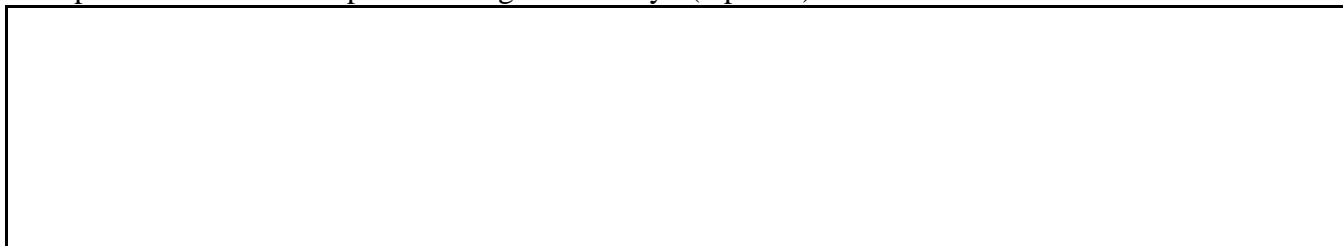
Make and explain the ^1H NMR assignments:

Suggest a structure for the organometallic species:

Question 3. Mixed Organolithium Aggregates. (14 points)

(See: van Koten, et al. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 219.)

(a) Consider the reaction of toluene with *n*-butyllithium. Draw the structure of the major organolithium compound formed and explain this regiochemistry. (4 points)



(b) Consider the reaction of C1-¹⁴C-labeled 2,4,6-trimethylbenzene with *n*-butyllithium. Draw the structures of the reagent and of all products obtained after quenching of the lithiated intermediate with deuteriumoxide. (4 points)



(c) The reaction of the closely related compound 1,3-bis(dimethylaminoethyl)-2,4,6-trimethylbenzene with *n*-butyllithium (48 h, hexane, RT) followed by addition of Me₃SiCl results in one major product. Draw the structure of the starting material and of the major product. Suggest an explanation for the regiochemistry. (6 points)

