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Articles

X-ray Crystal Structure Analysis of an Octameric Lithium *N*-Isopropylbenzamide Aza Enolate Complex

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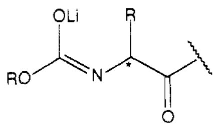
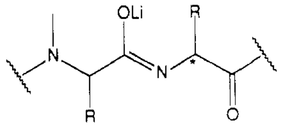
Lithiated *N*-isopropylbenzamide crystallized from a THF solution containing equimolar amounts of TMEDA. The X-ray crystal structure shows the unique solvent-free octameric aggregate $[C_{10}H_{12}NOLi]_8$ (1) of *E* aza enolate units (Figure 2). Crystal data: monoclinic, space group $P2_1/c$, a = 16.242 (7) Å, b = 22.02 (2) Å, c = 23.61 (2) Å, β = 103.98 (4)°, Z = 4. Four of these aza enolate units form four-membered Li, O, C, N, chelate rings along top and bottom edges of $(LiO)_4$ cubes; the other four act as Li, N, C, O bridges between two such cubes, with the Li and O atoms being part of the cubes and the N atom an "external" ligand (Figure 3). NMR measurements (NOE, temperature dependence) and cryoscopy in THF indicate that there are different species in solution. The structure is compared with that of a previously published hexameric aggregate containing three THF molecules. The results are discussed in view of peptide alkylations through polylithiated and LiX-solvated derivatives. A comparison is made between dimeric subunits in these crystal structures and hydrogen-bonded dimers formed from simple amides and occurring in proteins and in DNA. The four-ring chelates present in these complex structures of a lithiated amide, which can also be viewed as an imino carboxylate, are quite different from the polymeric structures of Li carboxylates.

Introduction

In our work on lithiation and C-alkylation of small peptides we found that amide groups and N-terminal carbamate protecting groups can be converted to aza enolates (A, B), thus avoiding epimerization of the neighboring stereogenic centers.[2] In the absence of information about the structure of these moieties, we have pictured them as being O-lithiated and having a *Z* configuration around the C=N double bond. In an attempt to provide structural data, we tried to grow single crystals of simple lithiated carboxylic acid amides for X-ray diffraction and, at the same time, studied the solution structure of such species by cryoscopy and NMR spectroscopy.[1,3] Similar investigations turned out to be of great value for a better understanding of the chemistry of lithium enolates.[2,4]



A



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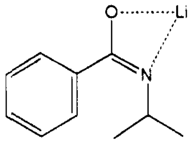

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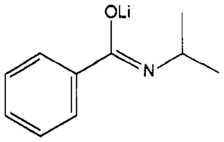

D

We were first successful with the lithiated *N*-isopropylbenzamide, which was generated from the parent amide with *n*-butyllithium in THF/hexane: in the presence of 1 equiv of TMEDA—known to cause deaggregation of Li compounds—suitable single crystals separated that contained a hexameric aggregate of the Li amide and three THF molecules, but no TMEDA. The crystal structure analysis revealed[5] that four of the components have *E* configurations with the Li being coordinated to both the oxygen and the nitrogen, forming an unusual four-membered chelate (C). The remaining two amide components have a *Z* configuration (D), with the corresponding lithium atoms bearing THF molecules as fourth ligands. The third THF molecule per hexamer is incorporated in a disordered fashion (see Figure 1), presumably causing the structure to be less accurate.[5] So far, hexameric aggregates containing a hexagonal prism built of six lithium and six oxygen or nitrogen atoms have only been found to crystallize from nondonor solvents (pentane, hexane, toluene, or mixtures thereof).[6-8] We now report the structure of another modification of the lithiated benzamide (crystallized under the same conditions as specified above for

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(1) Part of the Ph.D. thesis of T.M., Dissertation No. 9206, ETH Zürich, 1990.

(2) Review article: Seebach, D. *Angew. Chem.* **1988**, *100*, 1685; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624. Seebach, D.; Bossler, H.; Gründler, H.; Shoda, S.; Wenger, R. *Helv. Chim. Acta*, in press.

(3) Part of C. P. Hidber's Diplomarbeit, ETH Zürich, 1989.

(4) Arnett, E. M.; Fisher, F. J.; Nichols, M. A.; Ribeiro, A. A. *J. Am. Chem. Soc.* **1990**, *112*, 801 and references cited therein.

(5) Maetzke, T.; Hidber, C. P.; Seebach, D. *J. Am. Chem. Soc.*, in press.

(6) Hexameric Li enolates: Williard, P. G.; Carpenter, G. B. *J. Am. Chem. Soc.* **1985**, *107*, 3345; **1986**, *108*, 462.

(7) Hexameric Li enolate of ethyl 2-(diethylamino)acetate: Jastrzebski, J. T. B. H.; van Koten, G.; van de Mieroop, W. F. *Inorg. Chim. Acta* **1988**, *142*, 169. The structure described herein contains five-membered chelate rings (Li, O, C, C, N); we found this structure only recently, so it is not cited in our paper on the hexameric Li aza enolate.[5]

(8) Hexameric Li hexamethylene imide: Barr, D.; Clegg, W.; Hodgson, S. M.; Lamming, G. R.; Mulvey, R. E.; Scott, A. J.; Snaith, R.; Wright, D. S. *Angew. Chem.* **1989**, *101*, 1279; *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1241.

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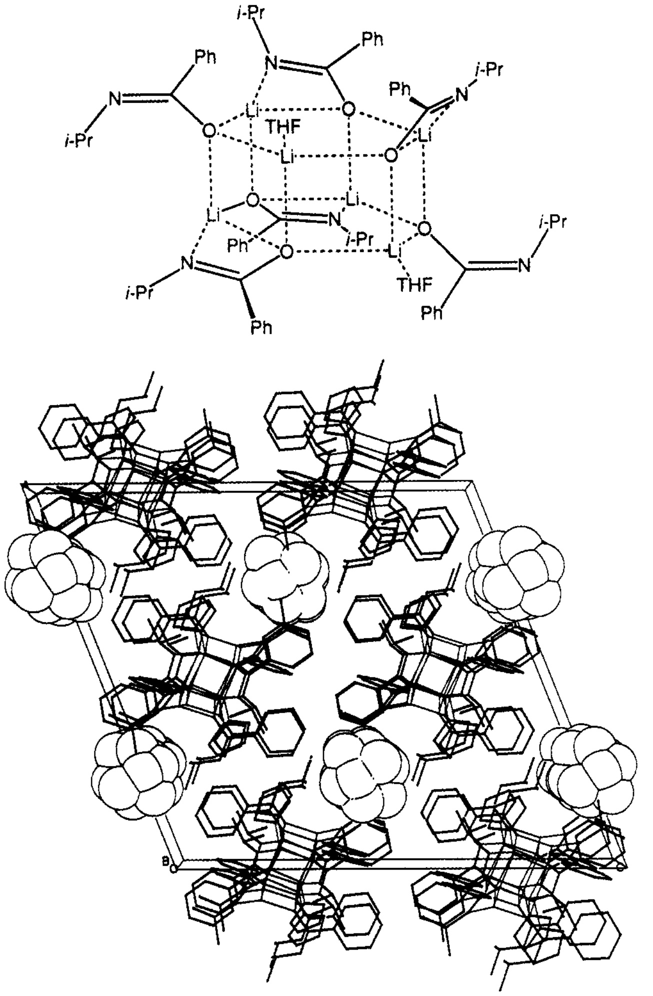


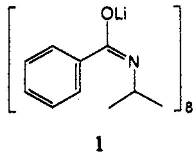
Figure 1. Hexameric unit and packing diagram of $\{[C_6H_5C(NCH(CH_3)_2)OLi]_6\cdot 2THF\}\cdot THF$.[5] The atoms of the disordered THF molecule are drawn with van der Waals radii.

the hexamer) containing a solvent-free octameric aggregate, with much more accurate atomic coordinates.

Crystal Structure of the Octameric Aggregate 1: An Aza Enolate Bridged Dimer of Two Li, O Cubes

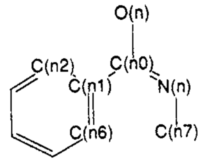
N-Isopropylbenzamide was deprotonated with 1 equiv of *n*-butyllithium in THF. The lithium derivative crystallized as colorless cubes at ambient temperature from THF/hexane (diffusion technique) in the presence of 1 equiv of TMEDA.

The X-ray crystal structure analysis reveals that the lithiated *N*-isopropylbenzamide crystallized as the octameric complex 1 containing two tetrameric subunits with a central Li, O cube bridged by four amide molecules (see Figures 2 and 3). The eight oxygen as well as the eight lithium atoms are located at the vertices of the two cubes, the eight nitrogen atoms of each aza enolate being the "outer" ligands for the metal atoms. Those benzamide units that are not involved in bridging the two tetrameric subunits form four-membered chelate rings, the Li–O bond being a Li–O edge of a Li, O cube. The "bridgehead" lithium atoms Li3, Li4, Li5, and Li6 have a tetragonal-pyramidal ligand sphere. The ligand atoms of Li1, Li2, Li7, and Li8 are located on *one* half-space, so that these lithium atoms have a sort of "naked" outside that, however, is shielded by the phenyl rings of the bridging amide units. This shielding may be the reason for the fact that no donor solvent molecule is incorporated at this ligand site to replace the aza enolate nitrogen.



1

Table I. Bond Lengths (Å) in the Crystal Structure of the Octameric Lithium *N*-Isopropylbenzamide Complex 1



n (amide no.)	C(*n*0)–O(*n*)	C(*n*0)–N(*n*)	C(*n*0)–C(*n*1)	C(*n*7)–N(*n*)
1	1.306 (6)	1.293 (7)	1.497 (9)	1.468 (8)
2	1.305 (7)	1.298 (8)	1.490 (7)	1.477 (8)
3	1.330 (6)	1.280 (7)	1.487 (8)	1.474 (7)
4	1.328 (7)	1.277 (7)	1.504 (7)	1.483 (8)
5	1.312 (6)	1.273 (7)	1.513 (8)	1.470 (7)
6	1.306 (7)	1.281 (8)	1.507 (9)	1.48 (1)
7	1.307 (7)	1.288 (8)	1.522 (9)	1.459 (8)
8	1.299 (6)	1.288 (8)	1.522 (9)	1.460 (7)
mean value	1.31	1.28	1.51	1.47

The chelating amide subunits as well as the bridging ones have *E* configurations about the aza enolate double bonds. As corresponding bond lengths and angles of the eight amide subunits are equal within the standard deviation (see Table I), there are only small differences in the torsion angles. The C–O bond lengths are in the range 1.299 (6)–1.330 (6) Å (mean 1.31 Å). The mean value corresponds to the C–O distances in ester[9] and amide[10] lithium enolates. The C–N bond lengths are in the range 1.273 (7)–1.298 (8) Å (mean 1.28 Å) and are slightly longer than in an aluminum aza enolate[11] (1.26 Å) and in imino esters[12] (1.26 Å), but shorter than in carboxylic acid amides[13] (1.35 Å). The Li–O distances within the four-membered chelate rings are in the range 2.19 (1)–2.21 (1) Å and are much longer than the other "coordinative" Li–O distances in the complex, which are between 1.89 (1) and 2.02 (1) Å (mean 1.96 Å). This effect of elongation of the Li–O distance in a four-membered chelate ring is also present in the hexameric modification. The Li–N distances are in the range 1.99 (1)–2.01 (1) Å (mean 2.00 Å; in most TMEDA chelates of lithium the Li–N distances are in the range 2.15–2.20 Å).

The bond angles C(*n*1)–C(*n*0)–N(*n*) are in the range 123.0 (6)–125.9 (5)° and thus are somewhat larger than 120°. The angles C(*n*1)–C(*n*0)–O(*n*), which are in the range 112.6 (4)–115.9 (5)°, however, are significantly smaller than 120°. With values of 119.4 (4)–122.7 (5)° for the angles O(*n*)–C(*n*0)–N(*n*) there is no significant distortion.

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(9) Seebach, D.; Amstutz, R.; Laube, T.; Schweizer, W. B.; Dunitz, J D. *J. Am. Chem. Soc.* **1985**, *107*, 5403.

(10) Laube, T.; Dunitz, J. D.; Seebach, D. *Helv. Chim. Acta* **1985**, *6* 1373. Bauer, W.; Laube, T.; Seebach, D. *Chem. Ber.* **1985**, *118*, 76

(11) Kai, Y.; Yasuoka, N.; Kasai, N.; Kakudo, M. *Bull. Chem. So Jpn.* **1972**, *45*, 3388. See also: Kai, Y.; Yasuoka, N.; Kasai, N.; Kakud M. *J. Organomet. Chem.* **1971**, *32*, 165.

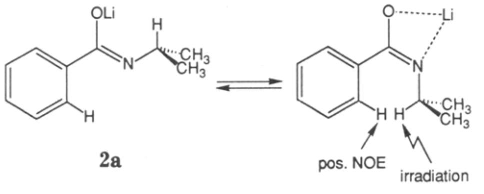
(12) Mean value of 18 structures from the Cambridge Structural D tabase, Cambridge Crystallographic Data Centre, University Chemi Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

(13) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orp A. G.; Taylor, R. *J. Chem. Soc. Perkin Trans. 2* **1987**, S1.

In the eight subunits the atoms of each aza enolate moiety and the lithium that is coordinated to the nitrogen have almost a coplanar arrangement: the torsion angles O(n)–C(n0)–N(n)–Li are in the range 1.8–4.8°, and the torsion angles C(n1)–C(n0)–N(n)–C(n7) between the phenyl and isopropyl substituents on the C—N double bonds are 6.3–8.5° in the bridging aza enolates and 2.9–4.6° in the chelating ones. In the bridging subunits the phenyl rings are turned out of the plane of the aza enolate moiety by a larger amount (C(n2)–C(n1)–C(n0)–N(n) = 60.8–72.2°) than in the chelating subunits (C(n2)–C(n1)–C(n0)–N(n) = 46.3–53.9°).

NMR Measurements and Cryoscopy. When the crystals of 1 are dissolved in THF-d_8, two species can be detected in a 1:1 ratio by ^{1}H NMR spectroscopy. Two heptuplet signals of the tertiary H atom of the isopropyl group appear at 3.52 and 4.27 ppm with the signal of THF at 1.85 ppm serving as internal standard. Also, two doublets appear for the methyl groups.

A NOE experiment was expected to show one species to be the *Z* isomer **2a** and the other one to be the *E*-configurated aza enolate **2b**. The latter is present in the crystal structure and should have a close contact of the tertiary proton of the isopropyl group and the proton in the ortho position of the phenyl ring. It turns out that spin transfer occurs between the two types of isopropyl CH protons (see Figure 4), indicating interconversion of the two species within the NMR time scale. Thus, there is a positive nuclear Overhauser effect in the region of the phenyl protons in both irradiation experiments (saturation of the signal at 3.52 ppm has a stronger effect than at 4.27 ppm).



2a **2b**

When the sample tube is warmed, the ^{1}H NMR spectrum shows coalescence of the split signals from the isopropyl group (see Figure 5); at 124 °C there is a uniform spectrum.

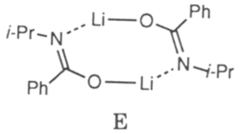
There is another remarkable effect in the region of the aromatic protons of the NMR spectrum. At 27 °C there is a signal, the integral of which corresponds to one proton, that is shifted to lower field by about 0.9 ppm from the signal of the other aromatic protons. At 124 °C two signals closer to each other are seen having an integrated ratio of 2:3.

Although it is likely that the two species seen by ^{1}H NMR spectroscopy are the *Z*/*E* isomers **2a**,**b**, the NMR measurements must be considered nonconclusive at this point (see the Discussion).

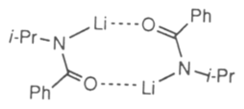
Finally, a cryoscopic molecular weight determination[14] in THF (at −108 °C) revealed a degree of aggregation of 2.65. Thus, there is a much lower degree of aggregation in the THF solution at low temperature than in the crystal grown at room temperature (frequently, aggregation of lithium derivatives decreases when the temperature of a solution is lowered).[15,16]

Discussion

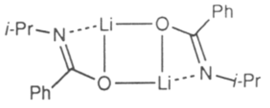
The structure described here is the first octameric aggregate of a Li derivative. It can be viewed not only as consisting of two $(LiO)_4$ cubes but also as being built from four dimeric units E (see Figure 3). Two of these units form the connecting building blocks between the cubes and contain no four-ring chelation. The other two are the "caps" of the octameric arrangement (see Figure 3) and form an array of three four-membered rings, formally a 1,5-dilithio-4,8-diaza-2,6-dioxatricyclo[4.2.0.0^{2,5}]octane skeleton. The bond lengths in these subunits are such that the three formulas E, E′, and E″ can be used to describe them. The imino/amido tautomers E and E′ are the Li analogues of hydrogen-bonded dimeric amides F and F′ (formed *inter*-[17] or *intra*molecularly[18] and present in peptides, proteins, and nucleic acids).



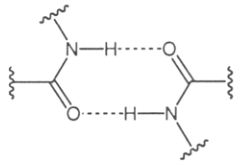
E



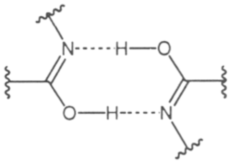
E′



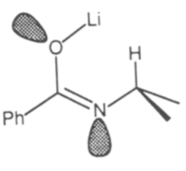
E″



F



F′



G

In the hexameric aggregate of lithiated isopropyl benzamide (Figure 1) there is also one such eight-membered-ring subunit (E); on the other hand, it contains two *Z* aza enolates (G), the nitrogen atoms of which form neither *intra*- nor *inter*aggregate bonds with lithium atoms. The NMR measurements indicate that such *Z* forms of Li aza enolates might be more likely to occur in solution.[19]

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[14] This measurement was carried out by Dr. W. Bauer of the Universität Erlangen-Nürnberg with the apparatus described in: Bauer, W.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 1972.

[15] Heinzer, J.; Oth, J. F. M.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 1848.

[16] The aggregation number 2.65 measured would, for instance, correspond to a 2:1 mixture of a tetramer and a dimer. More extensive NMR measurements would be necessary in order to determine which species are actually present in these solutions. For leading references to papers describing elaborate NMR measurements see ref 2 and: W.; Bauer, Schleyer, P. v. R. Recent Results in NMR Spectroscopy of Organolithium Compounds: In *Advances in Carbanion Chemistry*; Sniekus, V., Ed.; JAI Press: Greenwich, CT, 1990, in press; Vol. 1.

[17] Beak, P.; Covington, J. B.; Zeigler, J. M. *J. Org. Chem.* **1978**, *43*, 177. Ducharme, Y.; Wuest, J. D. *Ibid.* **1988**, *53*, 5787. Winkler, F. K.; Dunitz, J. D. *Acta Crystallogr., Sect. B* **1973**, *29*, 268.

[18] Perrin, C. L.; Dwyer, T. J.; Rebek, J., Jr.; Duff, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 3122. Jeong, K.-S.; Tjivikua, T.; Rebek, J., Jr. *Ibid.* **1990**, *112*, 3215. Review: Rebek, J., Jr. *Angew. Chem.* **1990**, *102*, 261; *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 245.

[19] As pointed out in the section on the NMR measurements, no definite conclusions can be drawn about the solution structure: the two species detected could be *E*/*Z* isomeric, or they could have the same geometry and occupy different positions within the same aggregate, thus allowing spin transfer to occur.

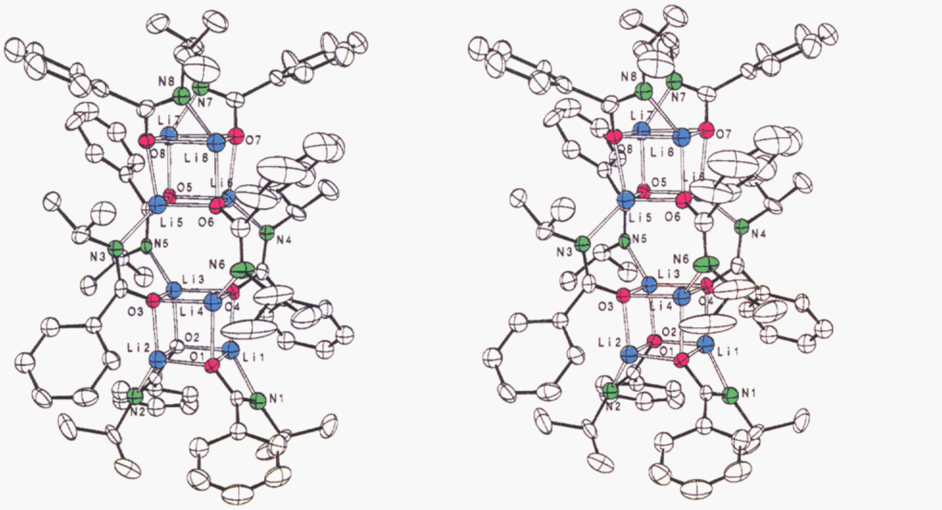


Figure 2. Stereo drawing (ORTEP) of the crystal structure of the octameric complex 1 of lithium *N*-isopropylbenzamide. The ellipsoids are drawn at the 50% level.

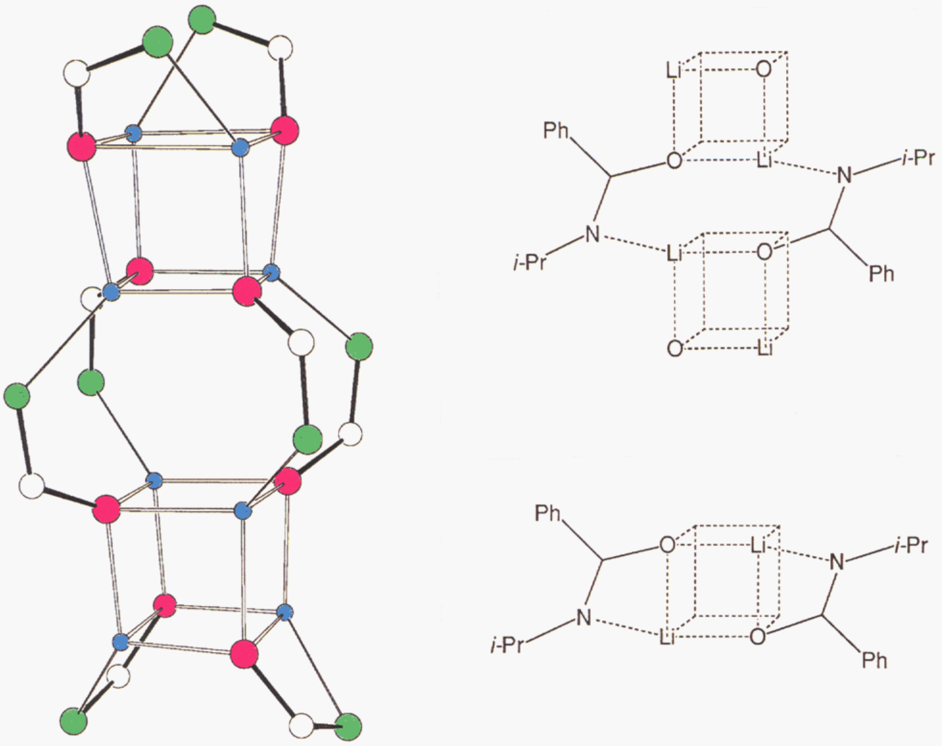
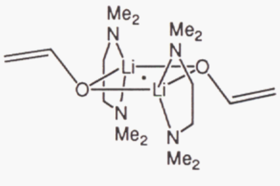
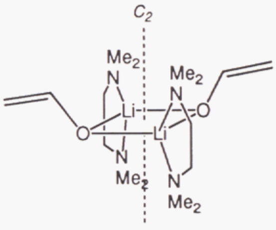


Figure 3. Subunits of the structure of 1 shown in Figure 2: (left) arrangement of Li, N, C, and O atoms (eight each) of the octameric aggregate, with the phenyl and isopropyl substituents left out (a C_2 axis runs through the centers of the two cubes); (right) two types of dimeric subunits occurring in the octamer 1.

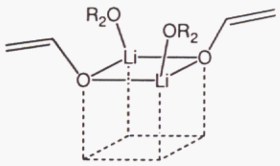
It is intriguing that surprising features of the hexameric and octameric structures of lithiated amides as described in this and in our previous paper[5] may be discussed in terms of smaller subunits or building blocks, just as for those of Li enolates (usually not C_i but C_2 symmetry, see H–J)[2,9] and of $(LiNR_2)_x$ aggregates.[8]



H (C_i)



I (C_2)



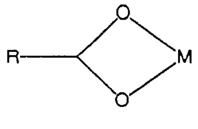
J

The lithiated amide, which can also be considered as an imino carboxylate, has preferentially the *E* configuration in the crystalline state, and there appears to be a tendency for the formation of planar four-membered chelate rings. This structural feature differs from the one observed with Li carboxylates; they do not form rings K but, rather,

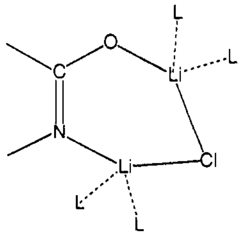
Table II. Fractional Atomic Coordinates for $[C_{10}H_{12}NOLi]_8$ (1)

atom	x/a	y/b	z/b
Li1	1.0945 (6)	0.2061 (5)	0.1474 (4)
O1	1.0597 (2)	0.2053 (2)	0.0518 (1)
N1	1.1696 (3)	0.1559 (2)	0.1093 (2)
C10	1.1277 (3)	0.1720 (2)	0.0577 (2)
C11	1.1503 (3)	0.1546 (3)	0.0020 (2)
C12	1.1549 (3)	0.2001 (3)	−0.0385 (2)
C13	1.1750 (4)	0.1850 (3)	−0.0902 (3)
C14	1.1863 (4)	0.1261 (4)	−0.1053 (3)
C15	1.1801 (4)	0.0804 (4)	−0.0661 (3)
C16	1.1617 (4)	0.0942 (3)	−0.0133 (3)
C17	1.2506 (4)	0.1230 (3)	0.1198 (3)
C18	1.2367 (5)	0.0580 (3)	0.1388 (3)
C19	1.3161 (4)	0.1561 (4)	0.1674 (3)
Li2	1.0580 (6)	0.2909 (5)	0.0599 (4)
O2	1.0966 (2)	0.2928 (2)	0.1555 (1)
N2	1.1597 (3)	0.3417 (2)	0.0938 (2)
C20	1.1579 (3)	0.3271 (2)	0.1468 (3)
C21	1.2208 (3)	0.3477 (3)	0.2002 (2)
C22	1.2600 (3)	0.3042 (3)	0.2408 (2)
C23	1.3198 (4)	0.3228 (3)	0.2906 (3)
C24	1.3370 (4)	0.3840 (3)	0.3022 (3)
C25	1.2960 (4)	0.4279 (3)	0.2639 (3)
C26	1.2372 (4)	0.4091 (3)	0.2131 (3)
C27	1.2324 (4)	0.3743 (3)	0.0807 (3)
C28	1.2651 (4)	0.3371 (4)	0.0358 (3)
C29	1.2004 (4)	0.4368 (3)	0.0545 (3)
Li3	0.9722 (6)	0.2903 (4)	0.1441 (4)
O3	0.9388 (2)	0.2934 (2)	0.0587 (1)
N3	0.8090 (3)	0.3285 (2)	0.0108 (2)
C30	0.8892 (3)	0.3255 (2)	0.0162 (2)
C31	0.9368 (3)	0.3541 (3)	−0.0234 (2)
C32	0.9817 (3)	0.3183 (3)	−0.0541 (2)
C33	1.0281 (4)	0.3451 (3)	−0.0903 (3)
C34	1.0288 (4)	0.4074 (3)	−0.0970 (3)
C35	0.9840 (4)	0.4432 (3)	−0.0668 (2)
C36	0.9377 (3)	0.4170 (3)	−0.0310 (2)
C37	0.7535 (4)	0.3586 (3)	−0.0401 (3)
C38	0.7043 (4)	0.4083 (3)	−0.0186 (3)
C39	0.6933 (4)	0.3105 (3)	−0.0746 (3)
Li4	0.9436 (6)	0.2050 (5)	0.0661 (4)
O4	0.9769 (2)	0.2004 (2)	0.1521 (1)
N4	0.8894 (3)	0.1614 (2)	0.2048 (2)
C40	0.9639 (3)	0.1684 (2)	0.1968 (2)
C41	1.0447 (3)	0.1445 (3)	0.2358 (2)
C42	1.1029 (3)	0.1847 (3)	0.2693 (2)
C43	1.1796 (4)	0.1634 (3)	0.3047 (2)
C44	1.1972 (4)	0.1019 (3)	0.3054 (2)
C45	1.1409 (4)	0.0617 (3)	0.2712 (2)
C46	1.0645 (3)	0.0831 (3)	0.2370 (2)
C47	0.8786 (4)	0.1300 (3)	0.2581 (3)
C48	0.8386 (4)	0.1748 (4)	0.2925 (3)
C49	0.8222 (4)	0.0753 (3)	0.2406 (3)
Li5	0.7552 (6)	0.2821 (5)	0.0648 (4)
O5	0.7881 (2)	0.2926 (2)	0.1505 (1)
N5	0.9094 (3)	0.3456 (2)	0.1861 (2)
C50	0.8301 (3)	0.3380 (3)	0.1802 (2)
C51	0.7736 (3)	0.3802 (2)	0.2045 (2)
C52	0.7112 (4)	0.4140 (3)	0.1666 (3)
C53	0.6583 (4)	0.4515 (3)	0.1906 (3)
C54	0.6680 (4)	0.4563 (3)	0.2490 (3)
C55	0.7291 (4)	0.4225 (3)	0.2864 (3)
C56	0.7819 (4)	0.3848 (3)	0.2642 (3)
C57	0.9525 (4)	0.3996 (3)	0.2159 (2)
C58	0.9851 (4)	0.4372 (3)	0.1707 (3)
C59	1.0246 (4)	0.3815 (3)	0.2660 (2)
Li6	0.7913 (6)	0.2032 (4)	0.1518 (4)
O6	0.7553 (2)	0.1930 (2)	0.0642 (1)
N6	0.8540 (3)	0.1478 (2)	0.0250 (2)
C60	0.7786 (4)	0.1507 (3)	0.0326 (3)
C61	0.7108 (4)	0.1047 (3)	0.0075 (3)
C62	0.6852 (5)	0.0632 (4)	0.0439 (4)
C63	0.6243 (5)	0.0189 (4)	0.0195 (6)
C64	0.5914 (7)	0.0186 (5)	−0.0393 (6)
C65	0.6124 (6)	0.0607 (5)	−0.0764 (5)
C66	0.6739 (5)	0.1033 (4)	−0.0515 (4)
C67	0.8805 (5)	0.0957 (4)	−0.0057 (5)
C68	0.9124 (6)	0.1170 (5)	−0.0559 (4)
C69	0.9507 (6)	0.0622 (4)	0.0392 (5)
Li7	0.6662 (6)	0.2886 (5)	0.1470 (4)
O7	0.6710 (2)	0.1893 (2)	0.1551 (1)
N7	0.5948 (3)	0.2530 (2)	0.1968 (2)
C70	0.6168 (3)	0.1985 (3)	0.1872 (2)
C71	0.5860 (3)	0.1409 (3)	0.2113 (3)
C72	0.5593 (4)	0.0919 (3)	0.1728 (3)
C73	0.5362 (4)	0.0379 (3)	0.1966 (3)
C74	0.5398 (4)	0.0313 (4)	0.2547 (4)
C75	0.5663 (5)	0.0794 (4)	0.2916 (4)
C76	0.5883 (5)	0.1338 (3)	0.2692 (3)
C77	0.5281 (4)	0.2681 (3)	0.2262 (3)
C78	0.5674 (4)	0.2979 (3)	0.2857 (3)
C79	0.4671 (4)	0.3120 (3)	0.1873 (3)
Li8	0.6413 (6)	0.1939 (5)	0.0726 (4)
O8	0.6333 (2)	0.2939 (2)	0.0645 (2)
N8	0.5316 (3)	0.2264 (2)	0.0260 (2)
C80	0.5579 (4)	0.2817 (3)	0.0329 (2)
C81	0.5067 (4)	0.3369 (3)	0.0061 (3)
C82	0.4958 (4)	0.3849 (3)	0.0435 (3)
C83	0.4478 (5)	0.4368 (4)	0.0204 (6)
C84	0.4148 (6)	0.4393 (5)	−0.0393 (6)
C85	0.4274 (5)	0.3942 (4)	−0.0774 (4)
C86	0.4731 (4)	0.3423 (4)	−0.0539 (4)
C87	0.4447 (4)	0.2101 (3)	−0.0036 (3)
C88	0.4045 (4)	0.1784 (3)	0.0393 (3)
C89	0.4471 (5)	0.1703 (4)	−0.0553 (3)

polymeric arrangements in which the metal is coordinated to only one oxygen of each carboxylate group.[20,21]



K



L

Originally, we were interested in obtaining structural information about lithiated amides in connection with our work on peptide alkylations. The results presented here indicate that structures of lithiated peptides are most

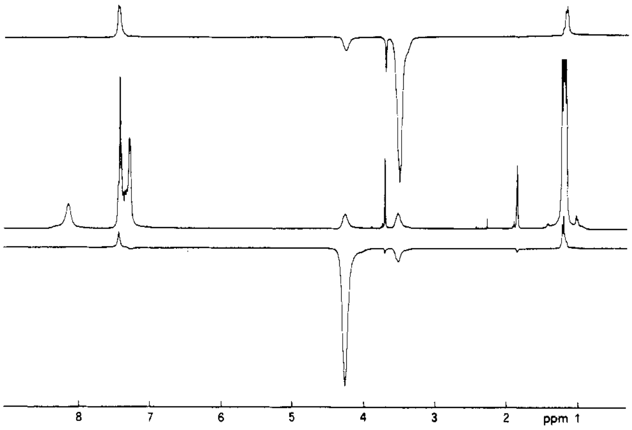


Figure 4. ^1H NMR spectrum (300 MHz) of a solution obtained by dissolving the crystals of 1 in THF-d_8 (NOE experiments).

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(20) See the conclusion section of our previous paper.[5]

(21) In Ca^{2+} carboxylates of proteins O, C, O, Ca four-membered rings are seen. Of ca. 50 structures of Ca carboxylates that we found in the Cambridge file,[12] only one contains such a four-membered ring (calcium malonate)! Karipides, A.; Ault, J.; Reed, A. T. *Inorg. Chem.* **1977**, *16*, 3299. Marsh, R. E.; Schomaker, V. *Inorg. Chem.* **1979**, *18*, 2331.

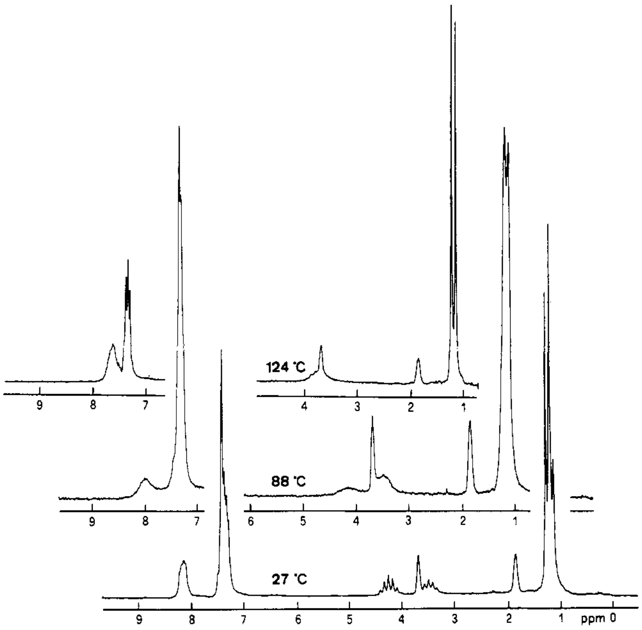

Figure 5. ^{1}H NMR spectra (80 MHz) at different temperatures of a solution obtained by dissolving 1 in THF-d_8.

certainly very complex and that a number of different, rapidly interconverting species may be present in solution. To our surprise, nitrogen successfully competes with oxygen for ligand sites in these species. Thus, presentations of polylithiated peptides such as A and B above must be considered naive, pragmatic, or should we say just practical. The situation is even more complicated in the "real world"; it turns out that polylithiated peptides must often be solubilized by added Li salts (LiCl, $LiNR_2$) and that these additives may drastically change reactivity and selectivity. This LiX effect[2] is probably both a common salt effect on the solvent properties and, specifically, a deaggregation effect. We assume that aggregates between polylithiated amides are broken up to give mixed aggregates with the added salt (see L). Our structural investigations are now aimed at crystallizing such mixed aggregates.[2]

Experimental Section

To a solution of *N*-isopropylbenzamide (1.006 g, 6.16 mmol) and TMEDA (0.96 mL, 6.4 mmol) in 2.5 mL of THF was added under argon at −10 °C *n*-butyllithium (4.0 mL, 6.4 mmol). The slightly yellow solution was transferred immediately into a beaker in a desiccator. The atmosphere of the desiccator was saturated with hexane by putting 15 mL of this solvent outside the beaker. After 2 days at room temperature beautiful colorless cubes had separated.

X-ray Crystal Structure Analysis of $C_{80}H_{96}N_8O_8Li_8$. A crystal (0.4 × 0.4 × 0.4 mm) was fixed under nitrogen (glovebag) in a capillary (i.d. 0.5 mm) with hexadecane and mounted on an Enraf-Nonius CAD4 four-circle diffractometer with graphite monochromator. Crystal data: monoclinic, space group $P2_1/c$, $a = 16.242$ (7) Å, $b = 22.02$ (2) Å, $c = 23.61$ (2) Å, $\beta = 103.98$ (4)°, $V = 8193$ Å^3, $M_r = 1353.21$, $Z = 4$, $D_{calcd} = 1.10$ g cm^{-3}, $\mu = 0.38$ cm^{-1}, $F(000) = 2880$. Data were collected at −100 °C with use of Mo Kα radiation ($\lambda = 0.71069$ Å) in the 2θ range 3–44°. Intensities of 9413 independent reflections were measured, and 5634 with $I > 3\sigma(I)$ were used for the refinement. Absorption corrections were not applied. The structure was solved by direct methods (SHELXS-86[22]). In the final refinement (BIG SHELX[23]) some atom positions for C, N, O, and Li were refined isotropically; the other ones were refined anisotropically. A riding model with idealized geometry was employed for H atom refinement; 844 parameters were refined, and a weighting scheme ($w^{-1} = \sigma^2 F_o$) was used. The final values for R and R_W were 0.066 and 0.057, respectively, with the final Fourier difference map showing a maximum of 0.32 e Å^{-3} and a minimum of −0.29 e Å^{-3}. The crystallographic figures were prepared with ORTEP.[24] The atomic coordinates are given in Table II.

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Registry No. 1 (cc entry), 130011-55-1; 1 (salt entry), 129985-86-0.

Supplementary Material Available: Tables of crystallographic data, atom coordinates and thermal parameters, bond distances, bond angles, and torsion angles and a drawing of compound 1 (11 pages); a table of observed vs calculated structure factors (33 pages). Ordering information is given on any current masthead page.

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(22) Sheldrick, G. M. SHELXS-86, Program for the Solution of Crystal Structures; University of Göttingen, Göttingen, FRG, 1986.

(23) BIG SHELX-76, UCLA version, 1985.

(24) Johnson, C. K. ORTEP-II; Report ORNL-5138, Oak Ridge National Laboratory: Oak Ridge, TN, 1976.