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ORIGINAL PAPER

Crystal Structures of Hexameric and Dimeric Complexes of Lithioisobutyrophenone

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Abstract The crystal structures of two unsolvated hexameric complexes and one *N,N,N′,N′*-tetramethyl-1,2-ethanediamine (TMEDA)-solvated dimeric complex of the lithium enolate of 2-methyl-1-phenyl-1-propanone (lithioisobutyrophenone, LiIBP) are reported. The unsolvated LiIBP complexes crystallize from benzene-d_6 to yield two different types of crystals that have similar structures: one in the triclinic space group P-1 with a = 10.7944(7), b = 11.9350(8), c = 12.0956(8) Å; α = 117.5560(10), β = 100.8090(10), γ = 92.3030(10)° and Z = 1 and a second in the monoclinic space group C2/c with a = 17.6011(11), b = 14.7389(9), c = 21.0943(13) Å; β = 105.2510(10)° and Z = 4. The two LiIBP hexamers differ slightly in the conformations of the enolate moieties around the Li_6O_6 core. The hexamer in both the triclinic as well as the monoclinic polymorph is located on a crystallographic inversion center that each generates the other half of the cluster. The TMEDA-solvated LiIBP dimer crystallizes from hexanes in the monoclinic space group C2/c with a = 11.8472(6), b = 14.8268(7), c = 19.2719(9) Å; β = 98.8480(10)° and Z = 4. The center of the dimer is located on a crystallographic C2 axis. These complexes represent only the second reported crystal structures of either an unsolvated hexamer or a solvated dimer of a lithium enolate of a simple monocarbonyl ketone.

Keywords Crystal structure · Lithioisobutyrophenone · Lithium enolate · LiIBP complexes

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Introduction

Lithium enolates, usually formed by the deprotonation of a ketone with a lithium amide base, are important synthetic organic reagents and are used to form new carbon–carbon bonds in alkylation and aldol condensation reactions [1]. They have been shown to exist as ion pairs and aggregates in the solid-state and non-hydroxylic solvents [2]; aggregates have often been proposed to be the reactive species in a reaction [3, 4]. Since 1981, when the first solid-state lithium enolate structures were reported by Seebach et al. [5] only 24 crystal structures containing a lithium enolate derived from a ketone have been reported [6]. Remarkably, only five of those contain lithium enolates of simple monocarbonyl ketones, including: the lithium enolate of 3,3-dimethyl-2-butanone (pinacolone) as an unsolvated hexamer, [7] tetramers that are solvated by tetrahydrofuran (THF) [5] and pyridine, [8] and a dimer solvated by *N,N,N′*-trimethyl-1,2-ethanediamine (TriMEDA) [9]. In this paper, we report three X-ray crystal structures of complexes of the lithium enolate of 2-methyl-1-phenyl-1-propanone (lithioisobutyrophenone, LiIBP). Two are unsolvated hexamers that yield polymorphic crystals and one dimer that is solvated by *N,N,N′,N′*-tetramethyl-1,2-ethanediamine (TMEDA). The solution structures of LiIBP have been previously studied in ethereal solvents such as THF, dioxane, dioxolane and 1,2-dimethoxyethane (DME) using NMR [10]. LiIBP is tetrameric at room temperature in monodentate ethers and mostly dimeric in bidentate DME [10].

Experimental Section

Materials

2-Methyl-1-phenyl-1-propanone (isobutyrophenone, Aldrich) was purified by vacuum distillation and stored under nitrogen. Lithium bis(trimethylsilyl)amide (LiHMDS, Aldrich, 1.0 M solution in hexanes) was used without further purification. TMEDA (Aldrich) was distilled from calcium hydride and stored under nitrogen. Hexane (Fisher) was degassed with nitrogen and stored over 4 Å molecular sieves. Benzene-d_6 (Cambridge Isotope Laboratories) was distilled from sodium metal and benzophenone and was stored under nitrogen.

Preparation of the Lithioisobutyrophenone Crystals

The triclinic LiIBP crystals (CCDC-653236) were serendipitously prepared during an NMR kinetics experiment where 1 mL of a 1.0 M LiHMDS/hexanes solution (0.41 mmol) was placed in an NMR tube and the solvent removed under vacuum. Benzene-d_6 (0.82 mL) was added to the tube and over 50 min, isobutyrophenone (47.4 mg, 0.32 mmol) was added in five portions as the solution was kept at 5 °C. The solution was allowed to remain in the NMR for 24 h at room temperature at which point crystals were observed to have grown. The monoclinic LiIBP hexamer complex (CCDC-653235) was prepared by placing 1 mL of a 1.0 M LiHMDS/hexanes solution in a 1.5 mL gas chromatography vial and the solvent was removed under vacuum; this resulted in 68.2 mg (0.41 mmol) of solid LiHMDS. About 1 mL of benzene-d_6 was added to dissolve LiHMDS. Isobutyrophenone (108.6 μL, 0.74 mmol) was added to the vial and it was sealed under nitrogen. The solution was stirred and a solid formed after several minutes. The solution was reheated to dissolve the solid and was then allowed to slowly cool to room temperature over the course of several hours, forming crystals suitable for X-ray analysis.

The dimeric LiIBP–TMEDA complex (CCDC-653234) was prepared by placing LiHMDS (132.1 mg, 0.79 mmol), 1.5 mL of hexanes, isobutyrophenone (92.7 μL, 0.63 mmol) and TMEDA (93.3 μL, 1.0 mmol) in a sealed vial under nitrogen. A solid appeared after several minutes. The vial was heated until the solid had dissolved and allowed to slowly cool back to room temperature over the course of several hours, yielding crystals suitable for X-ray analysis.

In all cases, the isolated crystals were quickly suspended in mineral oil at ambient temperature, a suitable crystal was selected, cut to an appropriate size and mounted with the help of mineral oil on a 50 μm MicroMesh MiTeGen Micromount.

Crystallographic Study

Diffraction data were collected using a Bruker AXS SMART APEX CCD diffractometer at 100(2) K using monochromatic Mo Kα radiation with the omega scan technique. The unit cells were determined using SMART, [11] and SAINT+ [12], and the data were corrected for absorption using SADABS [13] The structure was solved by direct methods and refined by full matrix least squares against F^2 with all reflections using Shelxtl [14]. Refinement of an extinction coefficient was found to be insignificant. All non-hydrogen atoms were refined anisotropically. The TMEDA ligand in the dimer is disordered over two positions with an occupancy ratio of 0.839(3) to 0.161(3). All disordered atoms were restrained with a rigid bond restraint, i.e. the components of the anisotropic displacement parameters for 1,2 and 1,3 distances in the direction of the bonds were restrained to be equal within a standard deviation of 0.01. The anisotropic displacement parameters of the minor component were further restrained to be isotropic within a standard deviation of 0.01. Methyl carbon atom C10c in the monoclinic hexamer is located in very close proximity to Li atom Li1 and, to take potentially unusual C–H bond lengths due to Li···H interactions into account, its hydrogen atoms were located in the difference density Fourier map and their positions were fully refined. All other hydrogen atoms were placed in calculated positions, and all hydrogen atoms (including those on C10c) were isotropically refined with a displacement parameter 1.5 (methyl) or 1.2 times (aromatic) that of the adjacent carbon atom. Crystal data and experimental details for the three complexes are listed in Table 1.

Results and Discussion

Unsolvated LiIBP Hexamers

Thermal ellipsoid plots of the two LiIBP hexamers are shown in Figs. 1 and 2. While these two complexes are crystallographically distinct and exhibit a different packing, their overall molecular structures are similar. Fig. 3 presents the two hexamer structures (without hydrogen atoms) with their Li_6O_6 cores overlaid. The structures of the two hexamers differ in the conformations of their enolate moieties. Both exhibit typical organolithium hexamer

Table 1 Crystallographic data and structure refinement summary for the polymorphic hexameric LiIBP and dimeric LiIBP–TMEDA complexes

CCDC deposit no.	653236	653235	653234
Empirical formula	$C_{60}H_{66}Li_6O_6$	$C_{60}H_{66}Li_6O_6$	$C_{32}H_{54}Li_2N_4O_2$
Formula weight	924.77	924.77	540.67
Temperature (K)	100(2) K	100(2) K	100(2) K
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	P-1	C2/c	C2/c
Unit cell dimensions	a(Å) = 10.7944(7)	a(Å) = 17.6011(11)	a(Å) = 11.8472(6)
	b(Å) = 11.9350(8)	b(Å) = 14.7389(9)	B(Å) = 14.8268(7)
	c(Å) = 12.0956(8)	c(Å) = 21.0943(13)	c(Å) = 19.2719(9)
	a(°) = 117.5560(10)	a(°) = γ(°) = 90	a(°) = γ(°) = 90
	β(°) = 100.8090(10)	β(°) = 105.2510(10)	β(°) = 98.8480(10)
	γ(°) = 92.3030(10)		
Volume (Å^3)	1,342.51(15)	5,279.6(6)	3,344.9(3)
Z	1	4	4
Calculated density (mg/m^3)	1.144	1.163	1.074
Absorption coefficient (mm^{-1})	0.070	0.071	0.066
F(000)	492	1,968	1,184
Crystal size (mm^3)	0.39 × 0.35 × 0.30	0.42 × 0.36 × 0.31	0.45 × 0.395 × 0.20
Reflections collected/unique	13,963/6,644	26,413/6,562	17,149/4,163
Maxi. and Min. transmission	0.979 and 0.912	0.978 and 0.850	0.987 and 0.947
Data/restraints/parameters	6644/0/331	6562/0/339	4163/94/264
R(int)	0.0208	0.0299	0.0198
Goodness-of-fit on F^2	1.114	1.018	1.053
Final *R* indices [$I > 2\sigma(I)$]	R1 = 0.0531, wR2 = 0.1284	R1 = 0.0443, wR2 = 0.1127	R1 = 0.0396, wR2 = 0.1122
R indices (all data)	R1 = 0.0565, wR2 = 0.1310	R1 = 0.0569, wR2 = 0.1225	R1 = 0.0433, wR2 = 0.1165
Largest diffraction peak and hole (e/Å^3)	0.431 and –0.247	0.469 and –0.191	0.342 and –0.175

Li_6O_6 “barrel” cores, [15] where the two six-membered non-planar Li_3O_3 rings resemble cyclohexane chair conformations. The hexamers in both the polymorphs are located on a crystallographic inversion center that each generates the other half of the molecules. To date, only one other unsolvated hexamer crystal structure of a lithium enolate of a simple monocarbonyl ketone, lithiopinacolonate, has been reported [7]. The Li_6O_6 core and the Li–O (1.884(2)–1.945(2) Å), C–O (1.3543(14)–1.3587(14) Å), and C=C (1.3410(17)–1.3489(16) Å) bond distances in both LiIBP hexamers are similar to those found in lithiopinacolonate. There is one significant difference between the LiIBP and the lithiopinacolonate hexamer structures: the distances between the lithium cations and the vinyl carbons of the pinacolonate enolate were quite short, averaging 2.46(8) (terminal $=CH_2$) and 2.49(6) (C(–O)=) Å, suggestive of stabilizing Li-π interactions [7]. No Li-π interactions are evident in either LiIBP hexamer as the corresponding Li–(C=C) average bond distances range from 2.68(29) to 2.78(6) (C(–O)=) Å and 3.16(13) to 3.28(13) ($=C(CH_3)_2$) Å, most likely due to the increased size of LiIBP.

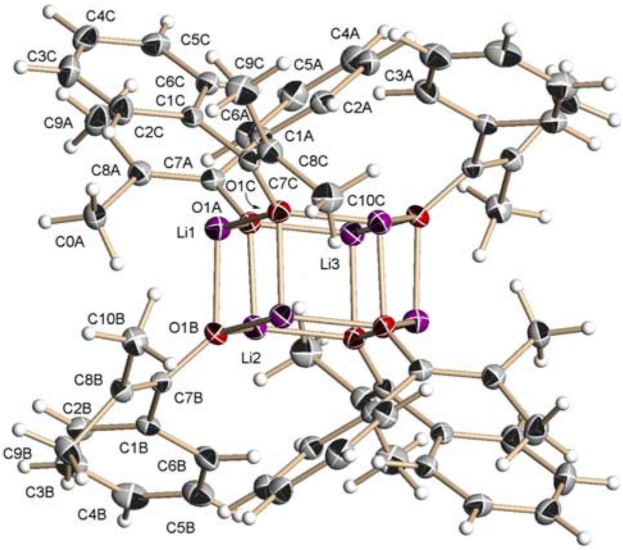

Fig. 1 A thermal ellipsoid plot of the triclinic LiIBP hexamer complex (CCDC-653236) including the atomic numbering scheme for non-hydrogen atoms at the 50% probability level. Non-labeled atoms are created by the inversion center

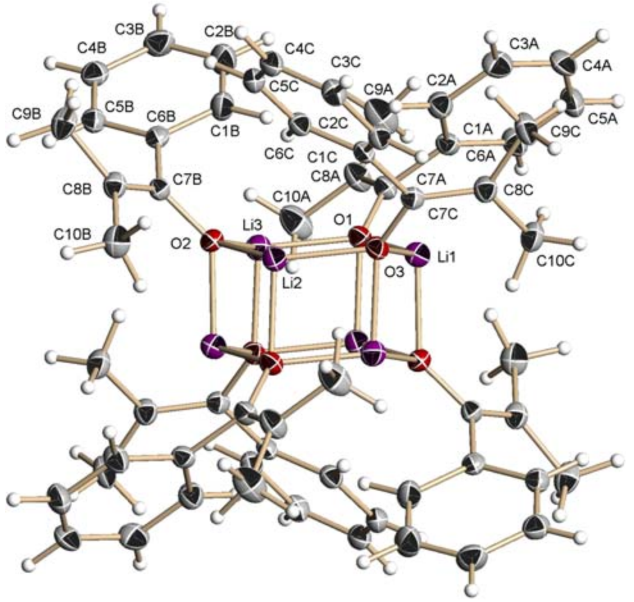

Fig. 2 A thermal ellipsoid plot of the monoclinic LiIBP hexamer complex (CCDC-653235) including the atomic numbering scheme for non-hydrogen atoms at the 50% probability level. Non-labeled atoms are created by the inversion center

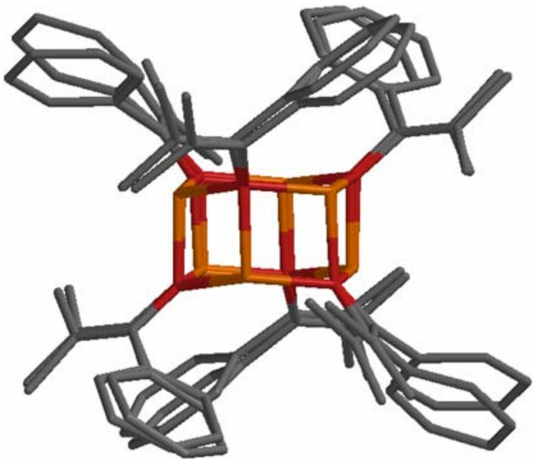

Fig. 3 Structural differences between the two LiIBP hexameric complexes as illustrated by overlaying their Li_6O_6 hexameric cores. Cylinders are used and hydrogen atoms have been omitted for clarity

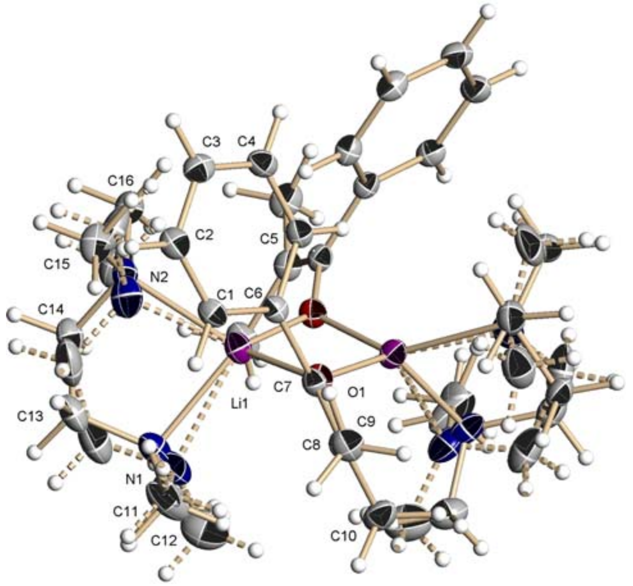

Fig. 4 A thermal ellipsoid plot of the LiIBP–TMEDA dimer, including the atomic numbering scheme for non-hydrogen atoms at the 50% probability level. Non-labeled atoms are created by the inversion center. Bonds to and within the minor TMEDA moiety are indicated by dashed lines

LiIBP–TMEDA Dimer

A thermal ellipsoid plot of this complex is shown in Fig. 4. Significant structural features of this complex include: crystallographic disorder in one TMEDA ligand; chelation of the lithium cations by the two nitrogen atoms of TMEDA; a slightly non-planar (5.2°) Li_2O_2 ring; and that both phenyl groups of the enolate lie on the same side of the Li_2O_2 dimer ring. The Li–O (1.8723(15)–1.9008(16) Å), Li–N (2.035(15)–2.259(13) Å), C–O (1.3288(9) Å) and C = C (1.3565(11) Å) bond lengths in this LiIBP–TMEDA complex are similar to those found in the previously-reported lithiopinacolate-TriMEDA dimmer [9]. The crystallographic disorder in one TMEDA ligand is likely due to the similar size and energy of the two conformations of the overall dimer complexes. The non-planarity of the Li_2O_2 dimer core and the relative positions of the enolate phenyl groups are a result of the crystallographic symmetry. LiIBP–TMEDA dimers with approximate C2 and C*i* symmetries had similar energies (within 0.47 kcal/mol) when modeled using semi-empirical (PM3) calculations [16]. No Li-π interactions to the enolate C=C bond were observed as those Li–C bond distances are 3.011 and 3.827 Å respectively.

Supplementary Data

CCDC Deposits #653234, 653235, and 653236. These data may be obtained free of charge by emailing: http://www.ccdc.cam.ac.uk/data_request/cif.

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