X-ray Crystal Structure of the Hexameric Lithium Enolate of Ethyl N,N-Diethylglycinate

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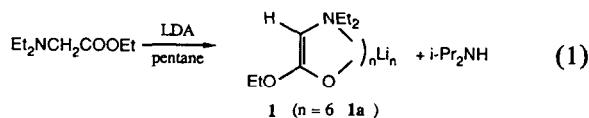1018 WV Amsterdam, The Netherlands*

Considering the central importance of (metal) ester enolates as reactive intermediates in synthetic organic chemistry (e.g. see ref. 1) it is surprising that so little is known about the actual structures of the metallated species involved. The isolation of pure solid lithium derivatives of esters were described more than 10 years ago [2–4], yet it was only very recently that Seebach *et al.* reported the first X-ray crystal structures of the lithium enolates of three esters, namely; tert-butyl propionate, tert-butyl 2-methylpropionate and methyl 3,3-dimethylbutanoate [5]. The first two of these lithium ester enolates were characterized as dimeric TMEDA (tetramethylethylenediamine) adducts, in which the anionic enolate oxygen atoms bridge between the two lithium atoms and the two TMEDA molecules each coordinate as a bidentate chelate to a lithium atom. The third enolate was isolated as a tetrameric THF solvate in which the four lithium atoms and the four anionic enolate oxygen atoms form a cube. This structural type has also been found for some ketone enolates [6–8].

Although reactions of some lithium derivatives of simple amino-acid esters, e.g. tert-butyl N,N-dimethylglycinate [9], trimethylsilyl N,N-bis(trimethylsilyl)-glycinate [10] and ethyl N,N-bis(trimethylsilyl)-glycinate [11] with aldehydes have been reported, to our knowledge nothing is known about their structures either in the solid state or in solution. We now report the synthesis, NMR characterization, and X-ray crystal structure of the lithium enolate of ethyl N,N-diethylglycinate.

Addition of ethyl N,N-diethylglycinate to a solution of lithium diisopropylamine (LDA) in pentane in a 1:1 molar ratio at room temperature affords, after evaporation of all volatile material *in vacuo*, the lithium enolate (1) in quantitative yield as a

yellow oil, see eqn. (1). The purity of this product was determined by ^1H NMR after hydrolysis in benzene with H_2O. These spectra showed only ethyl N,N-diethylglycinate and no diisopropylamine.

$$Et_2NCH_2COOEt \xrightarrow[\text{pentane}]{\text{LDA}} \left[\begin{array}{c} H \\ EtO \end{array} \diagdown \begin{array}{c} NEt_2 \\ \diagup \\ O \end{array} \right)_n Li_n + i\text{-}Pr_2NH \quad (1)$$

1 (n = 6 **1a**)

Colourless crystals could be grown from pentane solutions of **1** at −20 °C and one of suitable size was chosen for an X-ray single crystal diffraction study. The results of the structure determination and refinement showed these crystals to be Li_6-$[OC(OEt)=C(H)NEt_2]_6$ (**1a**), the hexameric lithium enolate of ethyl N,N-diethylglycinate. Crystals of **1a** are orthorhombic, space group *Pbca* with four molecules in a unit cell of dimensions $a = 20.716(2)$, $b = 22.439(3)$ and $c = 13.377(1)$ Å. 8172 independent intensities were measured on a Nonius CAD-4 diffractometer using graphite monochromated Mo $K\alpha$ radiation; 5698 of these were below the $3\sigma(I)$ level and were treated as unobserved. The structure was solved by Multan 11/82 using RANTAN [12], generating 2^9 phase sets. Of the 36 non-hydrogen atoms 33 were found from the E map. After block-diagonal least-squares refinement the Li and H atoms were located from a ΔF synthesis. Continued refinement, anisotropic for C, N, O and Li, and isotropic for H converged to $R = 0.059$. An extinction correction was applied, but no absorption correction was applied (crystal dimensions $0.33 \times 0.38 \times 0.43$ mm; $\mu = 0.68$ cm^{-1}). See also 'Supplementary Material'.

The molecule in the asymmetric unit gives rise to a hexameric aggregate as depicted in Fig. 1. The molecular structure is based on a central Li_6O_6 hexagonal prism with the hexagonal face defined by alternate Li and O atoms and the edges by Li–O bonds. The bottom half of the hexamer is related to the top half by a crystallographic inversion center located at the center of the hexagonal prism. The three crystallographically independent enolate moieties associated with one hexameric face bear a close resemblance to one another. Each of the anionic enolate oxygen atoms is bonded to three lithium atoms and consequently each Li is thus bonded to three O atoms. Through intramolecular coordination of the neutral N-donor of each organic moiety to one lithium centre, Li–N bond distance of 2.12 Å (mean), all the lithium atoms require a tetrahedral coordination geometry. As a result of this intramolecular Li–N coordination all enolate moieties have an E geometry.

This is the first example of an ester enolate structure which is stabilized by intramolecular Li–N

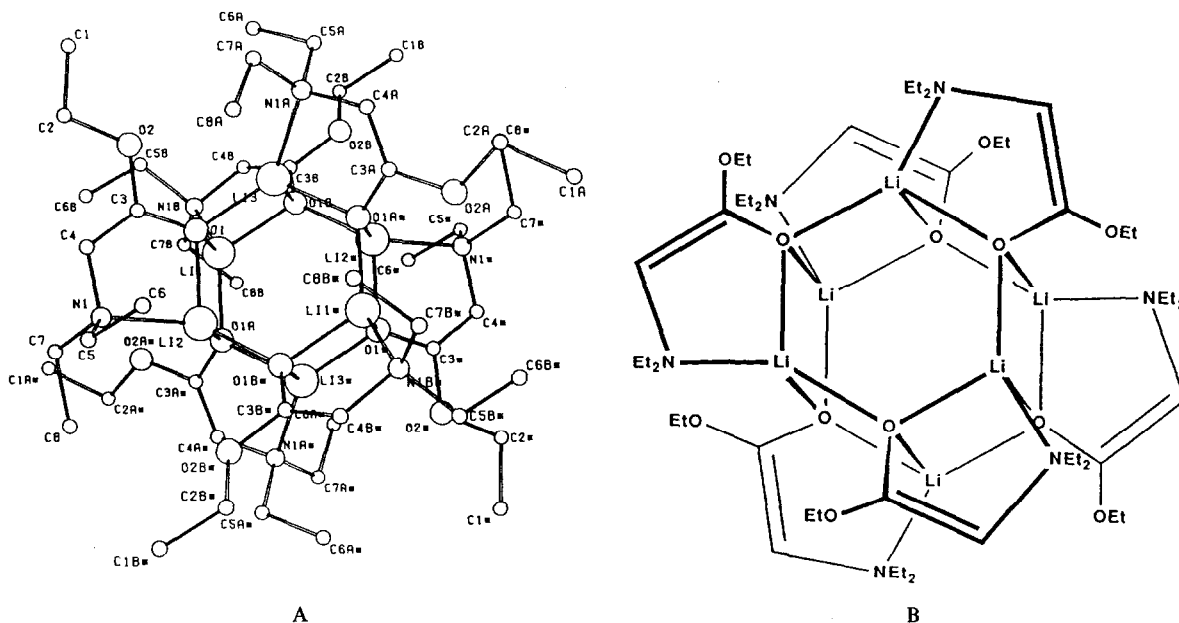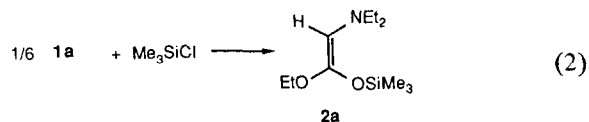*Author to whom correspondence should be addressed.

Fig. 1. (A) PLUTO drawing of Li₆[OC(OEt)=C(H)NEt₂]₆ (1a) with the adopted numbering scheme: Li(1)–O(1) 2.009(7), Li(1)–O(1A) 1.928(7), Li(1)–O(1B) 1.976(7), Li(2)–O(1) 1.972(6), Li(2)–O(1A) 2.015(7), Li(2)–O(1B*) 1.909(7), Li(3)–O(1) 1.922(7), Li(3)–O(1B) 2.026(7), Li(3)–O(1A*) 1.980(7), Li(1)–N(1B) 2.119(7), Li(2)–N(1) 2.124(7), Li(3)–N(1A) 2.122(7). (B) Schematic drawing of 1a.

coordination. Recently we reported the structure of the lithium enolate of 2-[*N,N*-(dimethylamino)-methyl]acetophenone in which each anionic oxygen enolate atom is bonded to a Li₃ face of a nearly regular Li₄ tetrahedron and each NMe₂ group is coordinated apically to a lithium atom [8]. The overall hexameric geometry observed for 1a is similar to that observed in the unsolvated lithium enolate of pinacolone and the THF solvate of the potassium enolate of pinacolone. For the former structure, because of the relatively short interatomic distances between Li and the sp²-hybridized carbons, it has been proposed that electron donation occurs from the C=C π bonds to a fourth unoccupied coordination site on the lithium atoms [13]. In the latter structure each potassium attains a tetrahedral geometry through coordination of THF at this fourth site [14].

At 30 °C the ¹H NMR spectrum of crystalline 1a, which has a dissymmetric structure, dissolved in toluene-d₈, shows four sharp multiplet resonances for the anisochronous N(C*H₂*CH₃)₂ protons at 1.95, 2.51, 3.05 and 3.20 ppm, respectively. Above 30 °C these signals begin to broaden and at 80 °C finally coalesce to a single broad resonance at 2.70 ppm. (At 110 °C quartet fine structure becomes visible.) These data suggest that the hexameric aggregate is retained in solution and that at ambient temperatures the Li–N coordination is inert on the NMR

time scale. However, at higher temperatures fluctional processes probably involving Li–N dissociation/association take place.

Reaction of a benzene solution of pure 1a with Me₃SiCl in a 1:1 molar ratio affords in quantitative yield only one isomer (2a) of the trimethylsilyl ketene acetal Et₂N(H)C=C(OEt)OSiMe₃ (see eqn. (2)) as a colourless oil. Since in the starting material 1a the enolate moieties have E geometry, it is most likely that 2a has Z geometry.

$$1/6 \; \mathbf{1a} \quad + \; Me_3SiCl \; \longrightarrow \quad \underset{\mathbf{2a}}{\overset{\displaystyle H \diagdown \quad \diagup NEt_2}{\underset{\displaystyle EtO \diagup \quad \diagdown OSiMe_3}{\Big|\Big|}}} \qquad (2)$$

Preliminary NMR studies of solutions of the non-crystalline lithium enolate (1) have shown that together with the hexamer (1a) other species are present. Reaction of this mixture with Me₃SiCl also affords only pure 2a. However, when this reaction is carried out with 1 from which diisopropyl-amine has not been removed, two isomeric trimethyl-silyl ketene acetals are formed, i.e. 2a and the E isomer. This observation indicates that for 1 in the presence of diisopropylamine an equilibrium probably exists between unsolvated lithium enolate species in which the enolate moieties have E geometry and diisopropylamine solvated lithium enolate species in which the enolate units have Z geometry.

Model studies by other workers have shown that in species of the latter type a Z geometry for the enolate moiety would seem to be more favourable on steric grounds [15].

The lithium enolate studied here is an important precursor to novel metal enolates (e.g., with zinc) that are interesting starting materials for a range of new organic molecules. How the different geometrical structures of **1a** and **1** influence those of metal enolates derived therefrom and in particular allow stereospecific synthesis of, for example, *trans*-β-lactams are now under investigation. Results of these studies will be reported in forthcoming papers.

Supplementary Material

Lists of atomic coordinates, bond distances and angles, thermal parameters and structure factors can be obtained from the Director of the Cambridge Crystallographic Data Centre, University Chemical laboratory, Lensfield Road, Cambridge CB2 1EW, U.K. Any request should be accompanied by a full literature citation for this communication.

Acknowledgements

References

1 D. A. Evans, J. V. Nelson and T. R. Taber, in N. L. Eliel and S. H. Wilen (eds.), 'Topics in Stereochemistry, Vol. 13, Stereoselective Aldol Condensations', Wiley, New York, 1982, pp. 1–115.
2 L. Lochman and D. Lim, *J. Organomet. Chem.*, *50*, 9 (1973).
3 V. Halaska and L. Lochman, *Collect Czech. Chem. Commun.*, *38*, 1780 (1973).
4 M. W. Rathke and D. F. Sullivan, *J. Am. Chem. Soc.*, *95*, 3050 (1973).
5 D. Seebach, R. Amstutz, T. Laube, W. B. Schweizer and J. D. Dunitz, *J. Am. Chem. Soc.*, *107*, 5403 (1985).
6 R. Amstutz, W. B. Schweizer, D. Seebach and J. D. Dunitz, *Helv. Chim. Acta*, *64*, 2617 (1981).
7 D. Seebach, R. Amstutz and J. D. Dunitz, *Helv. Chim. Acta*, *64*, 262 (1981).
8 J. T. B. H. Jastrzebski, G. van Koten, M. J. N. Christophersen and C. H. Stam, *J. Organomet. Chem.*, *292*, 319 (1985).
9 A. M. Touzin, *Tetrahedron Lett.*, 1477 (1975).
10 A. Shanzer, L. Somekh and D. Butina, *J. Org. Chem.*, *44*, 3967 (1979).
11 K. Rueleman, K. D. Kaufmann and K. Ickert, *Z. Chem.*, *10*, 393 (1970).
12 S-H. Zhang and M. M. Woolfson, *Acta Crystallogr., Sect. A*, *38*, 683 (1982).
13 P. G. Williard and G. B. Carpenter, *J. Am. Chem. Soc.*, *107*, 3345 (1985).
14 P. G. Williard and G. B. Carpenter, *J. Am. Chem. Soc.*, *108*, 462 (1986).
15 T. Laube, J. D. Dunitz and D. Seebach, *Helv. Chim. Acta*, *68*, 1373 (1985).