Synthesis and Structure of a Monomeric Chiral Lithium Dialkylaluminium Amide Derived from Schöllkopf's Bis-lactim Ether and α-(Methylbenzyl)benzylamine

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Dedicated to the memory of Ron Snaith in recognition of his great contribution to lithium chemistry

Keywords: Lithium / Aluminium / Chirality / Amides / Structure elucidation

Crystals of a monomeric lithium dialkylaluminium amide containing two different chiral amide moieties have been isolated from the reaction of lithiated Schöllkopf's bis-lactim ether complexed by pmdta with the diethylaluminium amide of (*S*)-α-(methylbenzyl)benzylamine, with single crystal X-ray diffraction revealing a migration of the Li cation in the aluminate from its initial position on the pyrazine ring of the lactim ether precursor.

Introduction

Lithium aluminates can show significantly different reactivity and selectivity when compared to that of their constituent parts — the nucleophilic alkyllithium or lithium hydride and the organoaluminium species — the reactivity of the latter being dominated primarily by its Lewis acidic properties.[1a−1c] By analogy, lithium dialkylaluminium amides have the potential to play a similar role, although synthetic activity has largely focused on the amidohydroaluminates.[2a,2b] However, some interest in their solid-state structures has developed since they fall within an important broader group of main-group heterobimetallic complexes containing group 1 metals, a family of complexes whose reactivity and selectivity is only gradually coming to be understood and exploited.[3a−3e] The lithium dialkylaluminium amide complexes that have been structurally characterised to date are comprised primarily of (N_2MM') rings,[4a−4d] the two metals not surprisingly being bridged by the N_{amido} atoms, for example $[Me_2Al(Bn_2N)_2]Li\cdot(THF)$],[5] although further association into a ladder-type structure[6] and bridging through Me groups has also been observed.[7]

Recently, we have been interested in two related areas dealing with the structural chemistry of chiral lithium amide bases which are important in the synthesis of biologically active compounds. The first area is the alkali-metal complexes of α-(methylbenzyl)benzylamine,[8a−8c] which have become prominent in β-amino acid and β-lactam syntheses,[9a−9d] and we have been extending our studies to the reactions of this and similar chiral amines with group 13 organometallic compounds. The second area concerns the lithium complexes of Schöllkopf's bis-lactim ether, 1-lithio-3,6-diethoxy-2-isopropyl-1,2-dihydropyrazine,[10a−10c] and we recently reported the structure of the complex coordinated by the tridentate donor pmdta, (*R*)-**1**, represented in Figure 1.[11]

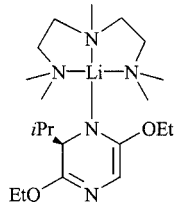

Figure 1. Lithiated Schöllkopf's bis-lactim ether, (*R*)-**1**, coordinated by pmdta

In bringing these two "precursor" areas together we have now synthesised and structurally characterised, by single-crystal X-ray diffraction, the first lithium dialkylaluminium amide, **2**, which is both monomeric in the solid state and comprised of two completely different chiral amide bases.

Results and discussion

Prompted by extensive studies on the formation of aluminium amides from dibenzylamine[12] we found that the thermal elimination of EtH from the reaction of Et_3Al and

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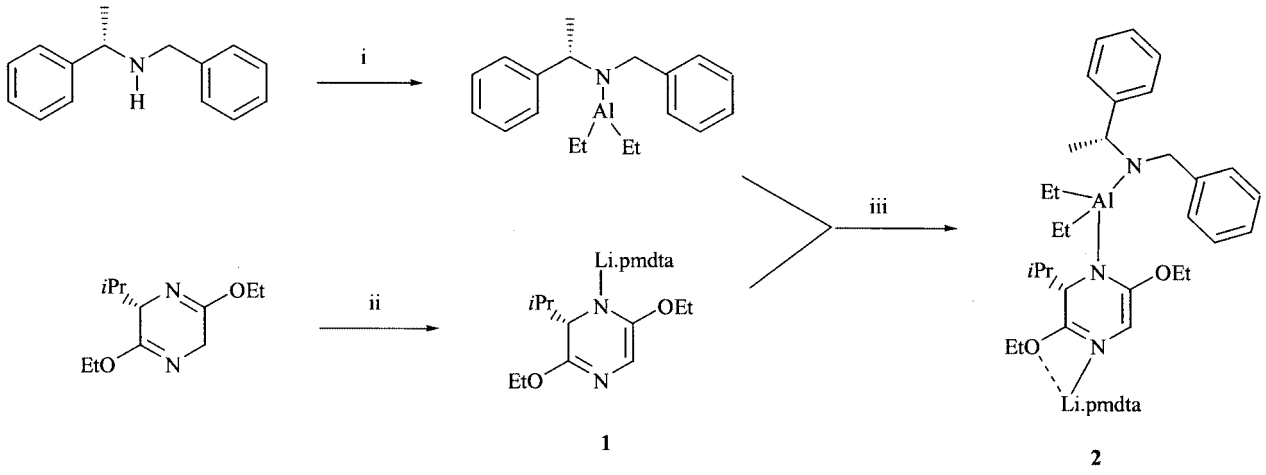

Scheme 1. Reaction conditions; i. Et_3Al, toluene, 120 °C, 4−6 h; ii. *n*BuLi, pmdta, toluene, −30 °C to room temp.; iii toluene, −30 °C to room temp.

(*S*)-α-(methylbenzyl)benzylamine occurs on heating to 120 °C (Scheme 1), although no crystalline product has yet been obtained from this reaction. This may be influenced by the fact that EtH elimination does not appear to occur quantitatively.

Following an analogous procedure to that described for the synthesis of $[Me_2Al(Bn_2N)_2]Li\cdot(py)]$,[13] a toluene solution of the lithiated Schöllkopf's bis-lactim ether, (*S*)-**1**, was added to a toluene solution of the aluminium amide generated in situ. A deep orange coloured solution was formed from which a low yield of orange crystals were isolated after approximately one week at −25 °C. By this time the solution had become dark red.

A second crop of crystals was then extracted after refrigeration at 4 °C over several days. However, the collective yield was still not high (32%) and no further solid product was obtained even at lower temperatures, with a dark red oil being observed to have formed. The crystals melt to a deep red between 142−144 °C and, as would be expected, are highly sensitive to atmospheric moisture and oxygen. Elemental analysis, multi-dimensional NMR studies, and single crystal X-ray diffraction identified the crystals as the chiral heterobimetallic species **2** (Figure 2).

Complex **2** crystallises in the orthorhombic space group $P2_12_12_1$ with four molecules in the unit cell. Although the crystal quality was not exceptionally high, leading to a large amount of weak intensities and high R_{int} value, the structural solution was of sufficient quality to allow us to assign definitive atom connectivities. The first striking feature of the structure comes directly from a comparison with the parent lithiated bis-lactim ether **1**. As can be seen, the Li cation, with its accompanying pmdta molecule, migrates from one N in the pyrazine ring in **1** to the opposite one in **2** as the lithium aluminate is formed. The Li(1)−O(2) bond at 2.543(11) Å would be considered long, however, an analysis of the bond angles at the sp^2 pyrazine nitrogen attached to Li reveals a high degree of asymmetry [Li(1)−N(3)−C(22) 108.7(5)°, Li(1)−N(3)−C(21)

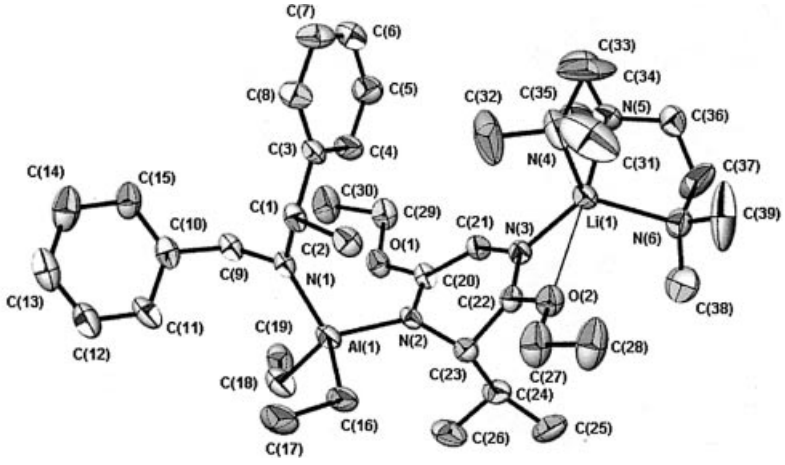

Figure 2. Molecular structure of (*S,S*)-**2**; thermal ellipsoids shown at 50% probability; all H atoms omitted for clarity; selected bond length (Å) and angles (°); Li(1)−N(3) 2.014(12), Li(1)−N(4) 2.117(14), Li(1)−N(5) 2.127(13), Li(1)−O(2) 2.543(11), Al(1)−N(1) 1.860(5), Al(1)−N(2) 1.939(5), C(21)−N(3) 1.423(8), C(22)−N(3) 1.265(7), N(2)−C(23) 1.449(7) N(2)−C(20) 1.352(7); Al(1)−N(2)−C(23) 122.0(4), Al(1)−N(2)−C(20) 126.4(4), Li(1)−N(3)−C(22) 108.7(5), Li(1)−N(3)−C(21) 136.2(5), C(21)−N(3)−C(22) 114.1(5), C(20)−N(2)−C(23) 111.5(5), N(2)−C(23)−C(22) 105.2(5)

136.4(5)°] with the Li cation clearly associating itself preferentially with the C=N bond [C(21)−N(3) 1.423(8) Å, C(22)−N(3) 1.265(7) Å] and the ethoxy O atom. The Li−N_{amido} distance in **2** of 2.014(12) Å is only marginally longer than that in **1** [1.965(3) Å] and is typical of four-coordinate Li complexed by pmdta. Not unexpectedly there are two significantly different Al−N bond lengths. They are 1.860(5) Å and 1.939(5) Å for Al(1)−N(1, 2) respectively indicating that the tetravalent Al center is bound more tightly to the α-(methylbenzyl)benzylamido group than to the pyrazine ring. Though there are no direct structural comparisons available for **2** since all analogous compounds contain bridging N rather than terminal, the Al(1)−N(1) distance is nevertheless similar to those commonly found in complexes with a dialkylaluminium dibenzylamido moiety in which Al is four coordinate (e.g. 1.982 Å in $[Bn_2NAlMe_2]_2$),[14] while the bond from Al(1)−N(2) is longer than that commonly found {e.g. 1.934(2) Å in $[Me_2Al(Bn_2N)_2]Li\cdot(py)$]}.[13] This is undoubtedly to relieve steric interactions between the Al centre and the pyrazine ring and is compensated for by the shorter Al(1)−N(1) bond.

It is hard to reason the migration of the Li^+ solely on steric grounds, i.e. avoidance of the *i*Pr group, since the presence of the two Et and the α-(methylbenzyl)benzylamido groups on the Al centre amounts to a substantial degree of steric bulk, most likely equivalent to that offered by pmdta on the Li cation. However, it is notable that in both **1** and **2** the metals locate themselves on the side of the pyrazine ring opposite the *i*Pr group, and, indeed, in **2** both Li and Al are located on the same side of the slightly buckled ring. If we assume the precursor to the aluminate is an intermediate containing a mixed-metal aggregate structured around the formation of a (Li-*N*-Al-N) four-membered ring then the steric strain could easily influence the cleavage of the Li^+-N^- bond and separation of the pmdta-bound Li cation. We had speculated when reporting the solution studies on (*R*)-**1** that, even without any additional chemical factors, a relocation of the Li cation was possible though our evidence was circumstantial.[11] As such, several co-incident factors may effect the migration of the lithium ion and aluminate formation: the possibility of solvent-separated ion pairs in **1** facilitated by the ethoxy groups, the sterically assisted weakening and ultimate cleavage of the Li^+-N^- bond, and the greater electrophilicity of Al^{3+} over that of Li^+. The Li cation then satisfies its coordinative demands by bonding with the available electron density associated with the N=C bond and the OEt group.

It is important to note that it would not be possible to form complex **2** by the alternate route which would involve swapping the metals on the constituent components, principally because the pmdta complex of α-(methylbenzyl)-benzylamidolithium undergoes facile transformation to an aza-allyl complex at low temperature.[8c] However, this could indicate one possibility for the gradual presence of the red oil in the reaction mixture if an electronic rearrangement in solution occurs which allows for the formation of (*S*)-[{Ph(Me)CH}($PhCH_2$)NLi·(pmdeta)] and its subsequent decomposition.

From this structural study there is no doubt that **1**, **2** and any Lewis base (L) complexes of α-(methylbenzyl)benzylamidolithium, $[\{PhC(Me)H\}(PhCH_2)NLi\cdot(L)_k]_n$, would behave very differently to each other in synthetic procedures, an aspect which needs to be further explored.

Experimental Section

Crystallographic Data for (*S,S*)-2: $C_{35}H_{68}AlLiN_6O_2$, M = 686.91, T = 123 K, orthorhombic $P2_12_12_1$, a = 14.300(3), b = 16.848(3), c = 17.659(4) Å, V = 4254.5(15) Å^3, D_c = 1.072 g·cm^{-3}, Z = 4; $F(000)$ = 1504, $\mu_{Mo\text{-}K\alpha}$ = 0.85 cm^{-1}, $2\theta_{max}$ = 56.6°, N_{tot} = 43347, N = 10455 [R(int) = 0.2173], N_o = 5801, final R, R_w = 0.076, 0.17 [$I > 2\sigma(I)$], GooF 0.938. Crystals were coated in oil, mounted on a fibre,[15] and data collected on an Enraf−Nonius KappaCCD at 123 K with Mo-K_α radiation (λ = 0.71073Å). The structure was solved by direct methods (SHELXS-97)[16] and refined by full-matrix least-squares on F^2 using the X-Seed interface.[17] All H atoms were placed in calculated positions (C−H 0.95 Å) and included in the final least-squares refinement. All other atoms were located and refined anisotropically. The absolute stereochemistry could not be accurately determined since the Flack parameter was indeterminate and the final assignment was based on a knowledge of the starting materials.

CCDC-197094 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Synthesis of (*S,S*)-2: Et_3Al (5 mmol, 5 mL of a 1 M solution in hexanes) was added to a toluene solution of (*S*)- α-(methylbenzyl)-benzylamine (5 mmol, 1.05 mL) and heated to 120 °C for 6 h. On cooling to room temperature this was then added to a chilled (−30 °C) equimolar toluene solution of (*S*)-**1**, prepared by the method previously described for (*R*)-**1**.[11] The reaction mixture was allowed to warm slowly to room temperature and stirred overnight before being placed in the freezer at −25 °C. After approximately one week a moderate crop of yellow crystals were obtained. These were isolated and washed with cold toluene. A further crop of crystals were obtained after a further duration at 4 °C. These were analytically identical to the first crop. Yield 32% (1.1 g), m.p. 142−144 °C (decomp. to dark red melt). ^{1}H NMR (300 MHz, 25 °C, [D_6]benzene): δ = 7.79 (d, 2 H, *o*), 7.73 (d, 2 H, *o*), 7.34 (m, 4 H, *m*), 7.15 (m, 2 H, *p*), 4.84 (s, 1 H, C=C*H*), 4.68 (d, 1 H, PhCH_2), 4.47 [q, 3 H, Ph(Me)C*H*), 4.40 (d, 1 H, *i*Pr-C*H*), 4.06 (d, 1 H, PhCH_2), 3.95 (q, 2 H, CH_2O···Li), 3.66 (q, 2 H, CH_2O), 2.45 (m, 1 H, Me_2CH), 1.87 (m, 6 H, $AlCH_2CH_3$), 1.80 (br., 3 H, PhC(*Me*)H], 1.79, 1.71, 1.65, 1.58 (br., 4 × s, 23 H, pmdta), 1.39 (d, 3 H, Me_2CH), 1.00 (d, 3 H, Me_2CH), 0.68 (m, 4 H, $AlCH_2CH_3$) ppm. ^{13}C NMR (75.5 MHz, 25 °C, [D_6]benzene): δ = 158.1 (*q*C), 148.1 (*q*C), 147.5 (*q*C), 128.0 (*o*CH), 127.5 (*m*CH), 123.9 (*p*CH), 123.8 (*p*CH), 81.5 (N-*C*=C), 61.7 (C=*C*-O), 61.0 (CH_2O), 58.0 [Ph*C*(Me)], 56.4 (CH_2O), 54.6 (CH_2N), 52.7 ($PhCH_2$), 51.9 (MeN), 43.8 (Me_2N), 25.4 (Me_2C), 24.5 (Me_2C), 18.4 (CH_3), 14.0 (CH_3), 11.1 (CH_2Al) ppm. $C_{35}H_{68}AlLiN_6O_2$ (638.9): calcd. C 68.20, H 9.98, N 12.23; found C 67.89, H 9.79, N 12.07.

Acknowledgments

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