Lithium aluminum hydride LiAlH₄ is a versatile reducing and hydrogenating reagent in both inorganic and organic synthesis. Although more than 60 functional groups are known to react with LiAlH₄, very little is known of the reactive intermediates involved in these syntheses. We report here the isolation of the intermediates 1 and 2.

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\text{HN(SiMe}_3)\text{Al + LiAlH}_4 \rightarrow \frac{1}{2} \text{[(Me}_3\text{Si)}_2\text{NAIHLi} \cdot 2\text{Et}_2\text{O}]_2 + \text{LiH}\text{H}_2\text{O} + \text{HN(SiMe}_3)\text{LI}\text{H}_4\text{.}
\]

The overall reaction to form the trisubstituted aluminum compound proceeds stepwise, whereby the reactive mono-substituted intermediate 1 and the disubstituted intermediate 2 can be isolated. Although the isolation of 1 and 2 does not necessarily prove that these compounds are intermediates in the reaction pathway suggested above, this is, however, chemically plausible. LiAlH₄ was allowed to react with hexamethyldisilylamine in diethyl ether. The reaction mixture was stirred for 24 h at room temperature and filtered, whereupon crystals of 1 were obtained after 3 d at −35 °C. The crystals, were directly mounted onto the diffractometer from mother-liquor at ca. −50 °C, thus permitting an X-ray structure analysis. At approximately −30 °C the colorless crystals start to “effervesce” and turn into a white insoluble powder. We assume that they lose hydrogen.

The bond lengths of benzoquinone itself and hydrogenating reagent in both inorganic and organic synthesis are in good agreement with the values quoted in the literature. To our knowledge, a shorter Li–H contact has only been found (168 and 192 pm, determined by X-ray structure analysis) in [tBu,AlHLi]. The shortest Li–H contact (159.6 pm) is found by spectroscopic techniques in molecular LiH₄. The average Al–H distance of 161.0 pm is in good agreement with the values quoted in the literature. Addition of HN(SiMe₃)₂ to LiAlH₄ in diethyl ether and subsequent refluxing for 3 h by stirring for 12 h at room temperature leads to formation of the disubstituted intermediate 2. Crystals were grown in good yield at −18 °C. Under these conditions the reaction is stopped after substitution of two equivalents of bis(trimethylsilyl)amine rather than allowing the trisubstituted product 3 to be formed. Crystals of 2 were mounted on the diffractometer at ca. −10 °C and started to effervesce above +5 °C. Presumably they also lose hydrogen. Figure 2 shows the monomeric structure of 2 in the solid state. The most striking feature is the central Al₃Li four-membered kite-shaped ring, in which the lithium atom bridges the two aluminum-bound hydrogen atoms. The bond angles show that 2 has a relatively strained structure. The average H–Al–H bond distance in 1 is 177.7 pm and therefore significantly shorter than in solid LiH (204.0 pm) or even LiAlH₄ (188–216 pm). To our knowledge, a shorter Li–H contact has only been found (168 and 192 pm, determined by X-ray structure analysis) in [tBu,AlHLi]. The shortest Li–H contact (159.6 pm) is found by spectroscopic techniques in molecular LiH₄. The average Al–H distance of 161.0 pm is in good agreement with the values quoted in the literature. Addition of HN(SiMe₃)₂ to LiAlH₄ in diethyl ether and subsequent refluxing for 3 h by stirring for 12 h at room temperature leads to formation of the disubstituted intermediate 2. Crystals were grown in good yield at −18 °C. Under these conditions the reaction is stopped after substitution of two equivalents of bis(trimethylsilyl)amine rather than allowing the trisubstituted product 3 to be formed. Crystals of 2 were mounted on the diffractometer at ca. −10 °C and started to effervesce above +5 °C. Presumably they also lose hydrogen. Figure 2 shows the monomeric structure of 2 in the solid state. The most striking feature is the central Al₃Li four-membered kite-shaped ring, in which the lithium atom bridges the two aluminum-bound hydrogen atoms. The bond angles show that 2 has a relatively strained structure. The average H–Al–H bond distance in 1 is 177.7 pm and therefore significantly shorter than in solid LiH (204.0 pm) or even LiAlH₄ (188–216 pm). To our knowledge, a shorter Li–H contact has only been found (168 and 192 pm, determined by X-ray structure analysis) in [tBu,AlHLi]. The shortest Li–H contact (159.6 pm) is found by spectroscopic techniques in molecular LiH₄. The average Al–H distance of 161.0 pm is in good agreement with the values quoted in the literature. Addition of HN(SiMe₃)₂ to LiAlH₄ in diethyl ether and subsequent refluxing for 3 h by stirring for 12 h at room temperature leads to formation of the disubstituted intermediate 2. Crystals were grown in good yield at −18 °C. Under these conditions the reaction is stopped after substitution of two equivalents of bis(trimethylsilyl)amine rather than allowing the trisubstituted product 3 to be formed. Crystals of 2 were mounted on the diffractometer at ca. −10 °C and started to effervesce above +5 °C. Presumably they also lose hydrogen. Figure 2 shows the monomeric structure of 2 in the solid state. The most striking feature is the central Al₃Li four-membered kite-shaped ring, in which the lithium atom bridges the two aluminum-bound hydrogen atoms. The bond angles show that 2 has a relatively strained structure.
gle in 2 (94.3°) is 12.9° smaller than that in 1 (107.2°). The average H–Li–H angle (73.6°), however, is even 33.8° smaller than that in 1 (107.4°). The intramolecular bridging of the lithium atom leads to a longer Li–H distance (average 193.3 pm; but 177.7 pm in 1), which is comparable to the distance in LiAlH₄.[7] The hydrogen atoms are forced close together to the transannular distance of 233.1 pm. Despite this steric strain the molecule does not dissociate in solution. The ¹⁷Li-NMR spectrum of 2 shows a ¹⁷J(Li,H) coupling constant of 10.5 Hz (Fig. 3). This is in good agreement with the only other known ¹⁷J(Li,H) coupling (8.4 Hz) detected in the ¹³H/¹⁷Li-NMR spectra of [CpIrH₂Li₁Li₂(pmdeta)] (pmdeta = (Me₅C₅CH₂)₂NMe)₁[13] This supports our suggestion[14] that there is more covalent character in bonds to lithium than was previously considered likely. In 2 the ¹³Li–¹³H coupling is only resolvable in the temperature window –30 °C to –70 °C. Outside this window the triplet structure of the signal is lost (Fig. 3), at higher temperatures as a result of exchange and at lower temperatures probably as a result of Li quadrupole effects. The coupling could not be verified in the ¹³H-NMR experiment because the hydride signals are too broad. Furthermore, the ¹⁷J(Li,H) coupling could not be observed in 1 at any temperature between room temperature and –120 °C in [D₆]toluene. 1 is fluctuative in solution. This fluctuationality could indicate a monomer/dimer equilibrium superposed on a μ₁ and/or μ₂ and/or μ₃ hydride bridging exchange.

 Experimental

1: HN(SiMe₅)₂ (7 mL, 33.3 mmol) was added over 8 h to a suspension of LiAlH₄ (26 g, 33.3 mmol) in diethyl ether (30 mL). The mixture was stirred for 24 h at room temperature. Subsequent filtration furnished a clear solution, storage of which at –35 °C afforded colorless crystals after about one week. ¹³H NMR ([D₆]toluene, ca. 25 °C): δ = 0.35 (s, 36H of SiMe₅), 1.08 (t, 24H of CH₃CH₂), 3.35 (q, 16H of CH₂CH₂); ¹⁷Li NMR ([D₆]toluene, ca. 25 °C): δ = 0.37.

2: A solution of HN(SiMe₅)₂ (8 mL, 38.1 mmol) in diethyl ether (20 mL) was added to a suspension of LiAlH₄ (0.71 g, 18.7 mmol) in diethyl ether (20 mL). The mixture was stirred for 12 h at room temperature. After the precipitate was filtered off, colorless crystals separated from the clear solution after several days at –18 °C. ¹³H NMR ([D₆]toluene, ca. 25 °C): δ = 0.47 (36H of SiMe₅), 0.94 (t, 12H of CH₂CH₂), 3.19 (q, 8H of CH₂CH₂); ¹⁷Li NMR ([D₆]toluene, ca. 25 °C): δ = 0.31, (–50 °C): 0.4, ¹⁷J(Li,H) = 10.5 Hz, IR: ν (AlH) = 1754 cm⁻¹ (s).

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[5] Crystal data: 1: CaH₅Li₃N₃O₃Si₄Al₃, M = 691.2, monoclinic, space group P2₁/c, a = 21.157(4), b = 9.387(2), c = 24.983(5) Å, β = 95.71(3)°, V = 4937 Å³, Z = 4, eₚo = 0.930 Mgm⁻², F(000) = 1536, δ = 0.71073 Å, T = 153 K, μ(MoKα) = 0.328 mm⁻¹. Data were collected on a Siemens-Stoe AED using an oil-coated rapidly-cooled crystal of dimensions 0.5 × 0.4 × 0.2 mm by the 2θ/ω method (8° ≤ 2θ ≤ 50°). Of a total of 8921 collected reflections, 8643 were unique and 5201 were employed in structure refinement [R(F) > 3σ(F), data-to-parameter ratio 12.8:1]. The structure was solved by direct methods and refined by full-matrix least squares to R and Rs values of 0.070 and 0.069, respectively. 2: CaH₅Li₃N₃O₃Si₄Al₃, M = 505.0, triclinic, space group P1, a = 11.225(4), b = 11.4165(5), c = 14.460(3) Å, α = 90.13(3), β = 100.64(5), γ = 112.07(2), V = 1682.3 Å³, Z = 2, eₚo = 0.997 Mgm⁻², F(000) = 560, δ = 0.71073 Å, T = 153 K, μ(MoKα) = 0.219 mm⁻¹. Data were collected on a Siemens-Stoe AED using an oil-coated rapidly-cooled crystal of dimensions 0.5 × 0.4 × 0.2 mm by the 2θ/ω scan method (8° ≤ 2θ ≤ 50°). Of 11310 collected reflections, 8893 were unique and 5793 were employed in the structure refinement (R > 0σ) data-to-parameter ratio 19.8:1. The structure was solved by direct methods and refined by full-matrix least squares to R and Rs values of 0.055 and 0.058, respectively. In both cases the program used was the SHELX87, PC version. All hydrogen atoms were located in a difference Fourier map and were refined using a riding model with common refined U values for chemically equivalent atoms. The terminal hydrogen atoms were refined freely in both structures. Further details of the crystal structure investigations are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, GB-Cambridge CB2 1EW (UK), on quoting the full journal citation.

Total Synthesis of the Carbohydrate Fragments of Esperamicin A₁

By K. C. Nicolaou* and David Clark

Esperamicin A₁[1][1] (1) is one of the most prominent members of the naturally occurring enediyne anticancer antibiotics.[2] In this communication, we report the total synthesis of both its carbohydrate chains 2 and 3[2] (Scheme 1) in their

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