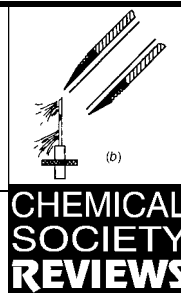


Cryo crystal structure determination and application to intermediates



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Ever since Wilhelm Conrad Röntgen discovered X-rays a century ago and von Laue, Friedrich, Knipping, Braggs and Braggs developed an analytical method almost nine decades ago, single crystal structure analysis has become the most powerful analytical tool used to elucidate unequivocally the three dimensional structure of solid matter. New X-ray detectors like image plates or CCD-detectors permit the collection of two datasets a day. However, this recent development should not only result in a higher 'turn-over' of crystal structure determinations, but should also be utilized in new research approaches. One can think of monitoring chemical reactions in terms of Echtzeit crystallography. The challenge is to synthesize, crystallize and analyze reaction intermediates by cryo crystal structure determination. Alkali organometallic compounds are omnipresent in any chemical laboratory where they are used as highly reactive starting materials in a vast number of reactions. It would be of great use to be able to freeze out intermediates along a reaction pathway in order to deduce new synthetic routes and concepts from the structural knowledge obtained by single crystal structure determinations.

1 Introduction

Reading the leading journals in chemical science, the perception might arise that about seventy percent of the published articles present, or at least refer to, new compounds characterized by single crystal structure analysis. In fact single crystal structure analysis is more and more regarded as the ultimate proof of the synthesis of a new compound. Furthermore, authors currently discuss the reactivity of molecules largely in terms of their

structural features. For instance the basic understanding needed to comprehend the physiological effects of proteins is their structural determination. Although limited in the variety of chemical elements present, their enormous conformational freedom makes the structural information a *condition sine qua non*. Current developments in organometallic chemistry increasingly lead to unstable compounds. Synthetically oriented chemists tend to work in more and more shallow depressions of the energy hyperface, because thermodynamically unstable compounds promise a wider variety of reaction pathways. This opens up new synthetic routes to target materials.

This is one of the reasons why alkali organometallics are an outstanding class of compounds. Unfortunately their high reactivity in most cases prevents their isolation and characterization by classical single crystal structure analysis, hence they are almost exclusively used *in situ*. Knowledge about the reaction intermediates is mostly deduced afterwards from knowledge about the stable starting material and/or the products. However, we aimed to get first hand structural information from thermodynamically unstable intermediates to facilitate the planning of organometallic syntheses.

Classical single crystal structure analysis at room temperature is widely used to study compounds in deep depressions of the energy hyperface. Nevertheless, up to now the derived experimental knowledge about the structural parameters of the solid state is unattained by any other analytical method. However, results from NMR spectroscopic experiments in solution may be used more unambiguously, because in many cases the synthesis is performed in solution as well. This brings up a well known dilemma: on the one hand compounds sometimes have to be crystallized to obtain a single crystal structure analysis to be able to interpret unequivocally the NMR solution spectra. On the other hand it is not guaranteed that the results from the solid state structure can directly be transferred to solution. This experimental gap is closed by solid state NMR spectroscopy. Hence single crystal structure analysis in combination with NMR spectroscopy in solution and in the solid state are the three experiments which describe most chemical compounds completely. Certainly, single crystal structure analysis still plays the leading rôle among the three methods.

The fundamental principles of cryogenic single crystal structure analysis have had to be extended to reactive intermediates and thermally unstable precursors. A 'snap-shot' structure analysis at different positions along a reaction pathway necessarily requires that one maintains a cold chain all the way from the synthesis to the end of the data collection. Special attention was turned to the requirements of the synthetic chemist as well as those of the crystallographer. To achieve a high degree of acceptance, the method has had to be as simple and reliable as possible. Complicated and time consuming devices and techniques, commonly not used in a synthetic and/or X-ray laboratory, would not have promoted the aim of determining structures of intermediates. The present article tries to encourage both synthetic chemists and crystallographers to have a closer look at reaction intermediates.

Section 2 presents the devices and methods for manipulating reactive and/or low melting single crystals. Section 3 describes a home-made low-cost low temperature device to maintain the

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techniques. He spent some time in the group of Professor P. v. R. Schleyer at Erlangen (1989) and a year in Cambridge, UK, with Dr R. Snaith and Dr P. R. Raithby (1991). In 1995 he became an associate professor at the University of Würzburg. His main areas of research are the syntheses of alkaline earth organometallic compounds and sulfur-nitrogen chemistry, both with their main emphasis on materials science.



crystal at cryogenic temperatures during data collection at the diffractometer. Finally, in section 4 some chemical examples from our work are presented, in which all three of the above mentioned analytical tools have successfully been used to study phase transitions and reorganizations of reaction intermediates in the solid state.

2 Crystal handling at low temperature

The advantages of crystal structure determination at low temperature compared to conventional room temperature measurements are well known.¹ Crystals unstable under ambient conditions as well as compounds which are liquids or gases under these conditions can be studied in the solid state. Many compounds cocrystallize with solvent. The vapor pressure of crystal solvent is still high and allows diffusion out of the lattice. Normally this destroys the crystal, or at least the intensities of the reflections change during data collection. Cooling of the crystal prevents the solvent from escaping the lattice. Cooling of proteins protects them from radiation damage even with high power synchrotron radiation.² Therefore, in most cases only one crystal is needed to collect the complete dataset. Moreover, the problem of intensity decay with increasing $\sin \theta/\lambda$ is less severe when cooling the crystal, and hence the quality of the data set is improved resulting in a more accurate structure determination. At low temperature the atoms vibrate more isotropically and the residual electron density map is less contaminated by the diffuse electron density arising from anharmonic behavior. Thus the location of hydrogen atoms and electron deformation density work is facilitated.

There are several home-made devices for maintaining a cold environment for the crystal while data are collected.³ Other devices are commercially available. However, to get the most out of low temperature data collection, it is essential to handle the compounds at low temperature continuously, *i.e.* from crystallization until and during data collection.

2.1 Method

The overall aim of crystal handling techniques should be to keep operations as simple as possible, so that they can readily be taught to beginners. This is the only way of guaranteeing that the know-how will stay in the X-ray laboratory even though specialists may leave.

Many methods have been employed by crystallographers to select a crystal and to transfer it to the diffractometer at temperatures below room temperature. Bärnighausen and Veith published a paper, where they described a nitrogen cooled half pipe, in which crystals can be handled below ambient temperatures.⁴ Laube and Dunitz constructed a closed glass apparatus to grow and transfer single crystals into capillaries at low temperatures.⁵ Boese and Bläser developed special techniques to manipulate single crystals and to transfer capillaries to the diffractometer at dry ice temperatures.⁶

Another technique is the *in situ* crystallization of samples in capillaries on the diffractometer. Simon initiated the method of zone melting by moving the capillary through heated apertures in a cold gas stream.⁷ Mootz and Boese developed a technique to grow single crystals by scanning the shock cooled sample in a capillary with an IR light focus.⁸ More recently, Boese utilized an IR laser instead.⁹ Blake and others use a heated wire loop to melt partially a shock cooled sample in a capillary.¹⁰ No doubt there are many other laboratory-specific, unpublished strategies to grow or to handle crystals below ambient temperatures.

Unfortunately, *in situ* crystallization is limited. For organometallic compounds for instance it is impossible to predict how much donating solvent is required to coordinate a metal. In general, the synthetic work has to be done in a chemical laboratory in a Schlenk flask with reasonable amounts of starting material. Furthermore, in our opinion sealing of crystals in capillaries at low temperature is not facile. Manipulating capillaries at low temperature requires sophisticated glassware,

commonly not available to the working synthetic chemist. Moreover such manipulations normally need months or years of practice.

Because of this we have not used any capillaries over the last ten years. Instead we have constructed a low temperature device from easily available parts, which is a symbiosis of the nitrogen cooled half pipe published by Veith and Bärnighausen⁴ and the oil-drop mounting technique, pioneered by Hope.¹¹ It enables the crystallographer to investigate the crystal quality using a polarizing microscope, as well as to mount the crystal at a fixed temperature ranging from room temperature down to $-100\text{ }^{\circ}\text{C}$.¹² Fig. 1 shows the device. Boil-off from liquid nitrogen is directed through glass tubing towards the microscope slide on which the sample resides.



Fig. 1 Low temperature device for crystal handling

At the beginning of crystal manipulation, the sample is located in an ordinary Schlenk flask, as generally used in a chemical laboratory. The whole batch of crystals in their mother liquor and the Schlenk gas is cooled down. The Schlenk flask with the sample is almost entirely immersed in the cooling agent (normally ethanol–dry ice), preventing the vessel from icing on the outside. Through the neck of the flask a small spoon is allowed to cool down in the mother liquor. Afterwards a portion of crystals is scooped up and covered with cold inert oil from a syringe. (If the crystals dry out very quickly, this can even be done within the mother liquor, preventing the crystals from being dried by the cold Schlenk gas).

In Fig. 2 the nozzle of the mounting device can be seen in more detail. The microscope slide is provided with a small depression. This indentation is filled with oil and cooled by the nitrogen gas stream. The crystals on the small spoon are now rapidly transferred to the microscope and immersed in the oil.



Fig. 2 The nozzle at the microscope slide

The cold, inert gas atmosphere and the surrounding oil prevent the crystals from being attacked by moisture and/or oxygen. Fig. 3 shows the mounting device in a laboratory environment.



Fig. 3 The mounting device at the bench

The oil allows washing, splitting and selecting of crystals of suitable quality. When a suitable crystal has been selected, an electrical pistol drill is used to drill a hole into a dry ice block. With a fiber which is already fixed on a goniometer pin the crystal is picked out of the oil, captured on the tip of the fiber and transferred into the hole in the dry ice block.

Under these conditions most of the crystals survive the short transportation to the low temperature nozzle at the diffractometer. There the crystal mount can easily be detached from the dry ice block and screwed onto the goniometer head. If lower temperatures are required a copper block with a hole cooled with liquid nitrogen can be used instead. When subjected to the lower temperature of the diffractometer cooling device, the oil freezes and the crystal orientation is fixed. This technique provides several striking advantages compared to the use of capillaries: free access to the sample (no limitations of glass joints, rubber stoppers, *etc.*), no mechanical stress to the crystal by pushing down into a (possibly too narrow) capillary, no fixing problems (since we started using the technique we have never observed a wobbling crystal) the crystal cannot dry up, because there is no capillary volume which can be filled with crystal solvent.

Two kinds of oil which differ in viscosity are used in our laboratory. Both are perfluorinated polyethers. They can be regarded as 'liquid Teflon' (PTFE); neither have reacted with a compound nor shown miscibility with a solvent. These two oils are miscible with each other in any ratio, therefore a mixture suitable for crystal manipulation in the temperature range between room temperature and $-80\text{ }^{\circ}\text{C}$ can be obtained. The high transparency of both oils even allows the employment of a polarizing microscope to investigate the crystal quality over the whole temperature range.

2.2 Device used

A schematic overview of the device used is given in Fig. 4. Cold nitrogen gas is generated from liquid nitrogen stored in a 7 l glass dewar. The main heater immersed in the liquid nitrogen causes nitrogen to evaporate. The gas flows through double-walled glass tubes with a silvered vacuum jacket and is directed towards the microscope slide by a Teflon nozzle.

The nitrogen gas is generated in a metal cylinder without a base and recoiled in a copper tube, projecting into the liquid nitrogen. This copper tube is attached to the vertical glass tube *via* a Teflon tube. The glass tubes are connected *via* a silicon o-ring and held together by a screw cap to prevent glass breakage.

The nozzle is fixed to the horizontal glass tube. The shape of the nozzle causes the gas stream to flatten and to spread at the

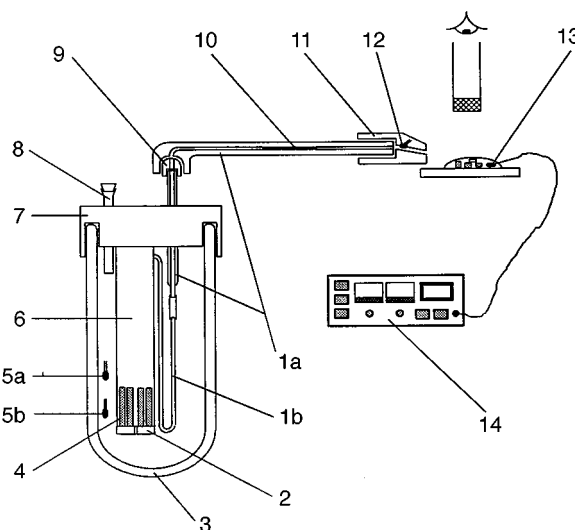


Fig. 4 Scheme of the low temperature device for crystal handling: gas-stream pipe (1a,b), bottom element (2) taking the main heaters (4), thermo-insulation container (3), level sensors (5a,b), evaporation tube (6), thermo-insulated lid (7), refill tube (8), teflon adapter (9), gas-stream heater (10), gas-stream Teflon nozzle (11), internal thermocouple (12), external thermocouple (13), controller (14)

outlet. Hence the whole slide is surrounded by cold gas. The shape of the nozzle, the aerodynamic favourable shape of the sample immersed in a 'puddle' of oil and the relatively high flow rate of the cold gas stream prevent the sample from icing. The nozzle is equipped with an integrated heater preventing the outlet from icing.

The whole device is supplied with direct current from an electronic controller. Any constant temperature between room temperature and $-100\text{ }^{\circ}\text{C}$ can be reached by either tuning the power of the main heater causing more or less liquid nitrogen to be evaporated or tuning the power of the stream heater (10 in Fig. 4). The electric parts are protected against overheating by a level sensor integrated in a safety circuit arrangement. The safety circuit guarantees the power supply being switched off if the nitrogen level becomes too low. The nitrogen flow rate and the temperature of the stream heater are adjusted by two potentiometers.

In our experience the mounting device is easy to make and even easier to maintain. However, the device is now commercially available. With a single filling it can operate for up to 5 hours, usually long enough to find a suitable crystal. It is refilled by simply adding liquid nitrogen without interrupting the investigation.

2.3 Conclusion

The combination of cooling the sample and using the oil drop mounting technique facilitates the handling of very sensitive crystals. With some practice, the transfer of the crystal from the mother liquor to the diffractometer can be realized within 30 seconds. It is very easy for beginners to learn the technique (much easier than mounting crystals in capillaries) and therefore it is accepted in the laboratory. Now there are crystallographers in our laboratory who have never had the experience of mounting a crystal in a capillary. With the suitable cryoprotectants and mounting techniques even the structure determination of very fragile proteins is facilitated.²

3 Low temperature set-up at the diffractometer

Once a single crystal of a sensitive and low melting material has been transferred to the diffractometer a very reliable cooling device is required to keep the crystal at cryogenic conditions during data collection. Again, the aim of simplicity determines the device to be robust and easy to maintain at low running

costs. We have constructed a low temperature device which can readily be modified to suit any diffractometer type. It can be used at any constant temperature in the range of +50 to -190°C and ours has run for five years without being switched off.

3.1 Cold gas stream generation

The cold gas stream generation is based on the same principles already discussed in section 2.2: boil-off from liquid nitrogen is directed through double-walled silvered glass tubing with a vacuum jacket towards the crystal. The whole device consists of three main parts: the storage dewar, the transfer line and the nozzle (Fig. 5).¹³

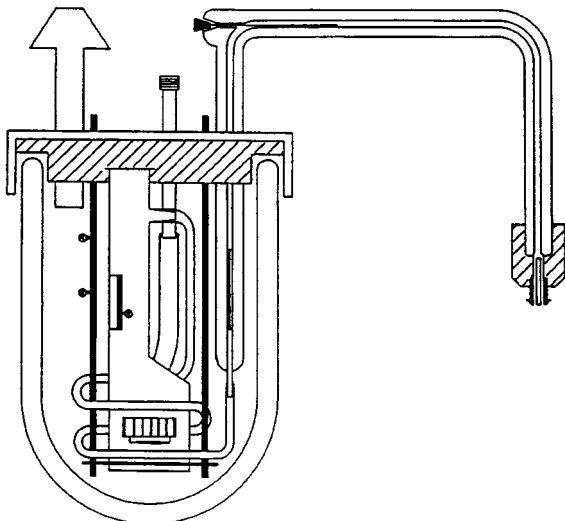


Fig. 5 Scheme of the low temperature device at the diffractometer

The storage dewar of the evaporator is a commercially available 30 l glass dewar. Cold nitrogen gas is generated in a brass cylinder immersed in liquid nitrogen. The bottom of the cylinder is fitted with a heating element made up from ceramic power resistors (main heater). The gas is directed through a helix of copper tubing which is immersed in the liquid phase for recooling. The gas leaves this tubing at a temperature only marginally higher than the boiling point of liquid nitrogen. The copper tubing is connected with the glass transfer line. It is formed like an upside down 'u' with an outer diameter of 40 mm and an inner diameter of 8 mm. Hence the inner cold gas stream is thermoinsulated by a concentric vacuum jacket of about 15 mm thickness. A heating element is centered inside the inner tube to warm the gas stream temperature to the required value. In a feed-back system it is connected to the main heater. Best results are obtained with transfer lines where the length of the horizontal part is minimized (150 to 200 mm) and the length of the leaving leg, connected to the nozzle, is 1300 to 1500 mm long. These dimensions have two basic advantages: the whole device can be positioned above the diffractometer to prevent glass breakage and the leaving gas stream is extremely laminar because of the long outlet. The gas falls down the nozzle rather than being pumped. This saves liquid nitrogen and a homogeneous and constant gas stream is one of the best precautions to prevent icing of the crystal during data collection. The device uses 0.6 l liquid nitrogen per hour almost independent of the required temperature.

We decided to have a stationary jet¹³ rather than to move the nozzle along with the crystal. In most diffractometer types (especially with an area detector system, but also with a Huber off-set chi circle, Nonius CAD4 or axs platform) there is plenty of space 'above' the crystal and even at a full four circle machine the stationary jet can be directed in at a 45° angle above the collimator without causing severe angle limitations. A transfer line made of a single piece guarantees the best achievable thermoinsulation. The 'thermal leakage' at connections in flexible arrangements causes drastically higher

liquid nitrogen consumption and the minimum temperature is much higher. In addition, due to the crystal mounting technique discussed in section 2.1 moving the nozzle along with the goniometer main axis is unnecessary.

The oil drop mounting technique ensures the crystal is always fixed at the tip of the glass fiber [Fig. 6(a)]. Nothing reaches up in the warm gas coating stream to cause turbulence. The stream is only disturbed by the lower part of the fiber but the thermal gradient is always directed away from the crystal and does not cause any changes in the crystal's orientation. Mounting a crystal in a capillary leaves the upper part towering in the warm gas coating stream and causes a thermal gradient directed towards the crystal [Fig. 6(b)]. The temperature at the crystal (*i.e.* its orientation) is dependent on the orientation of the capillary in the cold gas stream. Icing and the loss of the orientation of the crystal relative to the diffractometer geometry are the consequences. Since we do not mount crystals in capillaries we do not move our low temperature nozzle. The aerodynamically favourable shape of a drop and the thin glass fiber cause a minimum of turbulence.

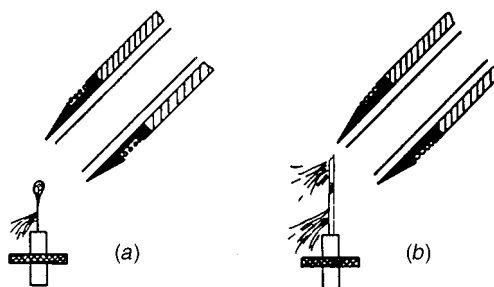


Fig. 6 Crystal mounting with a stationary 45° dual stream low temperature nozzle; oil drop mounting on the tip of a fiber (a) causing less turbulence than a crystal in a capillary (b)

3.2 Nozzle

We found the design of the low temperature nozzle crucial for good results. It should provide a laminar warm gas coating stream to preclude condensation of humidity on the cold gas stream. Likewise, the cold gas area should be as large as possible to tolerate a slight misalignment of the nozzle without any effect on the crystal orientation.

The two commercially available nozzle types—the one chamber and the two chamber nozzle—do not match these two basic requirements. In the one chamber nozzle the metal tip is electrically heated to generate the warm gas coating stream. In fact, however, our experience shows that the cold gas stream is compressed by the heating to such an extent that nearly no cold gas area remains. We mounted a thermocouple of the size of a single crystal on the goniometer head and the measurements revealed that the temperature at the crystal position is up to 50°C higher than the reading on the instrumentation display (depending on the nozzle heater power setting). We suspect that the nozzle design prevents icing of the crystal by raising the temperature of the complete gas stream, although the nozzle tip is conical to prevent this effect.

The tip of the two chamber nozzle is not heated but needs a separate dry gas supply. The coating stream is generated by a second gas flow. Even to provide dry compressed air requires considerable effort. Furthermore the flow adjustment of both gas streams relative to each other is quite complicated and turns out to be irreproducible. Therefore we constructed our own nozzle to combine the advantages of both known designs. Simple electrical heating and a single gas source lead to the dual stream nozzle.

The dual stream nozzle¹³ consists of three parts: the stainless steel nozzle tip, an outer Teflon tube and a thin walled inner tube (Fig. 7). The steel nozzle tip is fitted with a circular groove in which the heating coil resides. Two holes take the sensors for the thermostat, which provides temperature constancy better

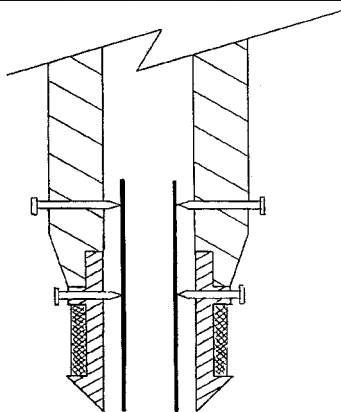


Fig. 7 The dual stream nozzle at the diffractometer

than ± 1 °C to guarantee a constant flow rate of the coating stream relative to the inner cold gas stream. The steel nozzle tip is screwed flush into the outer Teflon tube which is connected to the vertical leg of the transfer line. A thin walled inner tube is placed concentrically in the steel-Teflon outlet, dividing the whole gas stream into an inner (6 mm diameter) and an outer (1 mm concentric thickness) region. Because it is not trivial to machine very thin walled Teflon tubing we looked for a substitute. An ordinary plastic straw is now operating as the inner tube. It is held by three sharpened nylon screws placed in two ring sections. This arrangement physically separates the coating stream from the cold gas stream. Only the concentric stream between the inner and the outer tube is electrically heated to +30 °C. The inner tube precludes the inner stream from being compressed. The heating (*i.e.* expansion) accelerates the flow rate of the coating stream relative to the inner and more dense cold gas stream. This causes the stretching of the cold gas lip further out from the nozzle tip. This effect, as used by a Bunsen burner, permits small gas flow rates and relative long distances between the nozzle tip and the crystal. The adjustment of both streams is simply achieved by electronic regulation of the heating power. No additional gas supply is needed. The whole set-up required for sample cooling at the diffractometer is commercially available as well.

4 Applications to metastable compounds and reaction intermediates

4.1 Butyllithium

Alkyl lithium compounds are particularly important in synthetic chemistry as deprotonating and substituting reagents and as catalysts in polymerization.¹⁴ As long ago as 1917, Schlenk and

Holtz reported the first synthesis of alkyl lithium compounds;¹⁵ but until very recently no information about the crystal structures of BuⁿLi and of donor-free BuⁿLi has been available. This is probably due to the fact that these compounds (especially BuⁿLi) are pyrophoric and that BuⁿLi is an oil at room temperature. Without doubt the single crystal structure analysis of these frequently used organolithium reagents requires cryogenic techniques for crystal handling under protective conditions as discussed in the previous two sections. They facilitate the crystallization and the single crystal structure determination of donor-free BuⁿLi, BuⁿLi and also of the metastable adduct of BuⁿLi with one equivalent of diethyl ether.¹⁶

For the crystallization, a temperature was chosen at which the nearly saturated solution could be prepared; this should be as low as possible to avoid phase transitions during low temperature data collection (here: -90 °C). The limiting values taken into account were the melting point of BuⁿLi [-76 °C according to literature, the melting point of the crystals investigated here, however, was -34(2) °C] and the temperature at which decomposition of BuⁿLi·Et₂O might occur (-40 °C for BuⁿLi·Et₂O). To achieve a gradual and controlled crystallization, all solutions were prepared at -80 °C. The crystallization period was extended to one week by re-dissolving crystals initially formed, thus leaving a small number of nucleation sites in the solution.¹⁷ During the preparation of crystals for data collection (selecting and mounting a crystal and transporting it to the diffractometer) the temperature of a sample never exceeded -45 °C. The use of inert gas Schlenk techniques and sealing with inert oil were necessary to prevent the extremely oxygen- and moisture-sensitive crystals from reacting with air.

All three compounds are discrete aggregates and no interactions between oligomers were found such as have been observed, for example, in the solid-state structure of MeLi (the shortest Li-C distance between two oligomeric units is 382 pm found in BuⁿLi; in MeLi it is 252 pm¹⁸). The framework of BuⁿLi consists of six Li atoms in a trigonal antiprismatic (distorted octahedral) conformation (approximately D_{3d} symmetry) with six short (av. 242.9 pm), and six long (av. 293.9 pm) Li-Li distances (Fig. 8, top left). Analogous to various lithium organics¹⁸ six faces of the octahedron are each capped by a single Buⁿ unit; two almost equilateral (and opposite) triangular faces with the longest edges remain unoccupied. Each α -carbon atom is coordinated to two Li atoms positioned at the corners of one of these (non-capped) triangles through short bonds (av. 215.9 pm), whereas the bond to the Li atom at the corner of the opposite triangle is significantly longer (av. 227.0 pm). Hence, the Buⁿ moieties do not lie centrally over the isosceles Li triangles but are shifted to one edge (Fig. 8, right). As a result of this, short distances occur between the β -C atoms and the Li atoms, which may be interpreted as electrostatic interactions (Li-C _{β} distance: av. 228.7 pm; notice that they are in the range of the longer Li-C _{α} bonds). At the same time this conformation has short Li-H _{α} and Li-H _{β} distances [204(2) and 203(2) pm]. The hydrogen atoms at the α -C and β -C atoms are arranged staggered with respect to the nearest Li atom. In conclusion, BuⁿLi shows similar structural characteristics to the cyclic alkyl lithium compounds mentioned above. Apparently a four-fold coordination of the Li atoms by including β -C atoms is preferred in spite of the elongation of a Li-C _{α} bond. It is this disposition of the lithium to the C _{β} carbon that causes short Li...H contacts. They are due to steric strain rather than to agostic Li...H interactions. The arrangement of the short metal hydrogen distances in kite shaped Li(μ -H)₂C four-membered rings indicates that the hydrogen atoms have to avoid the lithium rather than have to be coordinated to the metal. Otherwise an almost linear Li...H-C arrangement with even shorter Li...H contacts would have been preferred.

BuⁿLi consists of tetrameric units of almost T_d symmetry (Fig. 8, top right) in the crystal. Each face of the Li₄ tetrahedron

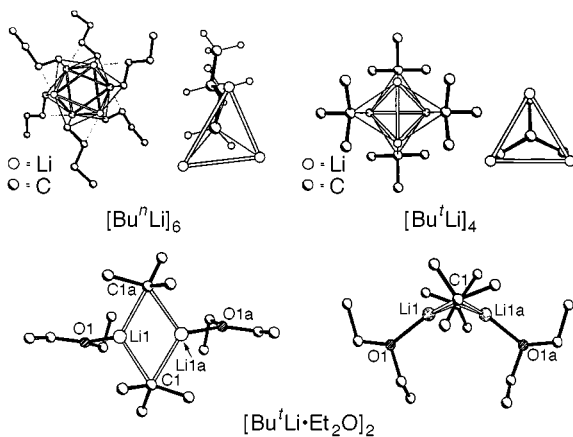


Fig. 8 The structures of $[\text{Bu}^t\text{Li}]_6$, $[\text{Bu}^t\text{Li}]_4$ and $[\text{Bu}^t\text{Li}\cdot\text{Et}_2\text{O}]_2$

is capped by a Bu^t group so that the (terminal) Me groups are eclipsed with respect to the corresponding Li atoms of the (within the standard deviation) equilateral triangles. This conformation again involves comparatively short Li– C_β distances (av. 237.4 pm). Thus, the structure of Bu^tLi is essentially different from that of MeLi in which the hydrogen atoms of the Me groups (in contrast to the conformation of C_β atoms in Bu^tLi) are staggered relative to the Li atoms.¹⁶ As in Bu^tLi Li– C_β interactions may participate in determining the conformation of Bu^tLi , especially since the β -C atoms would preferentially be staggered for steric reasons. Moreover these contacts provide solubility of the tetrahedral monomers in hydrocarbons different to the polymeric structure of $[(\text{MeLi})_4]_\infty$. The Li– C_α bond lengths (av. 224.6 pm) are in the range of the values observed in similar compounds, while the Li–Li distances in Bu^tLi (av. 241.2 pm) are significantly shorter [Li–Li and Li–C (pm) in MeLi :¹⁸ 256 and 227, respectively]. Compared to methyl and ethyl groups the more electron releasing Bu^t group supplies more electron density to the Li_4 core of the complex. As a consequence the repulsion of the four Li cations is less pronounced than in MeLi or EtLi .

Although Bu^tLi is known to cleave diethyl ether in a vigorous reaction to give EtOLi , C_2H_4 and various other products, we crystallized Bu^tLi from diethyl ether. The colorless crystals melt at -38°C . It should be noted that solutions of Bu^tLi in diethyl ether are stable even with a large excess of ether ($\text{Et}_2\text{O}:\text{Bu}^t\text{Li} \approx 6:1$). Over a wider temperature range (up to about -40°C), as observed in NMR studies, $\text{Bu}^t\text{Li}\cdot\text{Et}_2\text{O}$ is a dimer which is generated crystallographically from the monomeric unit through a two-fold axis (Fig. 8, bottom left). The central four-membered ring consisting of two Li and two bridging α -C atoms of the Bu^t groups is folded along the C...C diagonal by about 30° . A staggered arrangement of the eight substituents along the C...C vector (six methyl groups and two lithium atoms) can only be achieved by this fold (Fig. 8, bottom right). This steric crowding provides as well a possible explanation for the absence of a second donating Et_2O molecule per Li atom in the solid state as postulated for Bu^tLi in diethyl ether solution.

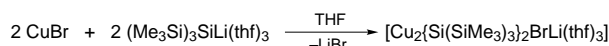
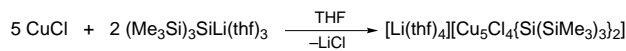
4.2 Lithium silylcuprates

The last example in section 4.1 clearly demonstrates that in the structural investigation of intermediates and metastable compounds not only cryogenic techniques are required but also substituents with sufficient steric demand to stabilize kinetically the products. It is vital to freeze out a molecule 'at the right time' (i.e. for instance before the ether cleavage reaction in the $[\text{Bu}^t\text{Li}\cdot\text{Et}_2\text{O}]_2$ complex¹⁶) but it is also necessary to stabilize the system with bulky groups to get the chance to isolate intermediates. The Me_3C -group is probably a good choice but the $(\text{Me}_3\text{Si})_3\text{Si}$ -group provides considerably more steric demand. Since the development of the tris(trimethylsilyl)silyl

ligand by Gilman and Smith¹⁹ it is widely used both in transition metal chemistry and main group metal chemistry.²⁰ The good solubility of the products in hydrocarbons makes it a versatile ligand. Taking the electron releasing properties of $-\text{Si}(\text{SiMe}_3)_3$ into account, we thought of this ligand as a good candidate to capture unstable products.

On the one hand the importance of silyl groups in organic synthesis is undoubted and on the other hand very few structural details are known of the species involved in the lithium cuprate reactions. More commonly these species have been employed as *in situ* reagents predominantly in organic syntheses.²¹ The growing interest in organocopper compounds, in particular the consideration of the theoretical aspects,²² encouraged us to react the tris(trimethylsilyl)silyl ligand with copper(I) halides.²³ $(\text{Me}_3\text{Si})_3\text{SiLi}(\text{thf})_3$ ²⁴ was reacted with Cu^ICl and Cu^IBr at -78°C . The different reactivity of Cu^ICl compared with that of Cu^IBr (it shows for example a lower tendency than Cu^ICl to disproportionate) should give rise to different unprecedented lithium silylcuprates.

$(\text{Me}_3\text{Si})_3\text{SiLi}(\text{thf})_3$ was reacted with Cu^ICl in the ratio of 1 : 2 and with Cu^IBr in a 1 : 1 ratio in THF.^{23a} Pure $(\text{Me}_3\text{Si})_3\text{SiLi}(\text{thf})_3$ is extremely pyrophoric and should be handled with care. All manipulations should be performed under an inert atmosphere of dry argon. Both reaction mixtures were immediately transferred to a deep freeze at -30°C .



Scheme 1

Under these conditions the first two lithium silylcuprates were isolated and structurally characterized. The complexes were found to be extremely air- and moisture-sensitive. During crystal selection and mounting the flask and the flushing argon was cooled down to ca. -50°C . At temperatures slightly above -30°C both compounds decompose instantaneously.

The structure analysis of the first complex reveals the formula $[\text{Li}(\text{thf})_4][\text{Cu}_5\text{Cl}_4\{\text{Si}(\text{SiMe}_3)_3\}_2]$,^{23a} (Fig. 9, left). This non-predictable formula can be rationalized with hindsight as a $[\text{Li}(\text{thf})_4][\text{Cu}\{\text{Si}(\text{SiMe}_3)_3\}_2]$ containing an excess of 4 CuLi units.

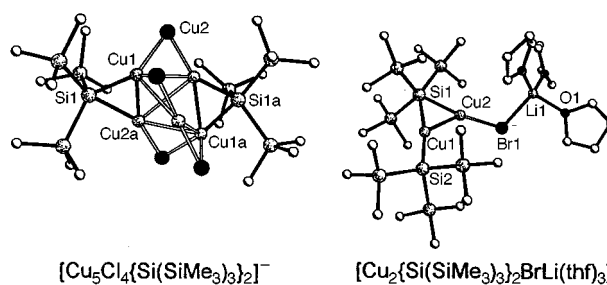


Fig. 9 The structures of the lithiumsilylcuprates $[\text{Cu}_5\text{Cl}_4\{\text{Si}(\text{SiMe}_3)_3\}_2]^-$ and $[\text{Cu}_2\{\text{Si}(\text{SiMe}_3)_3\}_2\text{BrLi}(\text{thf})_3]$

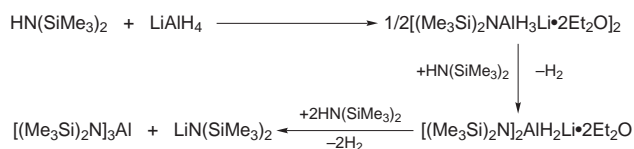
Fig. 9 shows the cuprate anion. The $\text{Li}(\text{thf})_4$ cation has been omitted for clarity. To the best of our knowledge it is the first structurally characterized lithium silylcuprate. The silicon atom is in quite an unusual bonding situation. The central Si(1) is bonded to the three trimethylsilyl groups and to two copper atoms, leading to five-coordinated silicon: μ_2 -bridging for silyl groups is very rare,²⁵ although it is well documented for alkyl and aryl bridging carbons. The two Si–Cu bonds are equally long (234.8 and 233.4 pm). The bridged Cu(1)–Cu(2a) bond is, with 240.3 pm, by far the shortest of the Cu–Cu distances and 25 pm shorter than the others in the complex. So the almost equilateral triangle SiCu_2 can be described in terms of a three-center two-electron bond.

In contrast to $[\text{Li}(\text{thf})_4][\text{Cu}_5\text{Cl}_4\{\text{Si}(\text{SiMe}_3)_3\}_2]$, $[\text{Cu}_2\{\text{Si}(\text{SiMe}_3)_3\}_2\text{BrLi}(\text{thf})_3]^{23b}$ is a contact ion pair. It contains two differently bound $(\text{Me}_3\text{Si})_3\text{Si}$ groups and an additional LiBr equivalent. The tris(trimethylsilyl)silyl group around $\text{Si}(1)$ is coordinated *side on* to a very short $\text{Cu}(1)\text{--Cu}(2)$ bond, again leading to a five-coordinated central $\text{Si}(1)$ atom. The $\text{Cu}(1)\text{--Cu}(2)$ distance is 236.9 pm and more than 3 pm shorter than in the last complex. In this example the three-center two-electron bond does not form an equilateral triangle. While the $\text{Si}(1)\text{--Cu}(2)$ bond is 228.3 pm long, the $\text{Si}(1)\text{--Cu}(1)$ bond is more than 12 pm longer (240.6 pm). The shortest $\text{Si}\text{--Cu}$ bond is that of the terminally-bound tris(trimethylsilyl)silyl group around $\text{Si}(2)$ and $\text{Cu}(1)$ (226.6 pm). $\text{Cu}(2)$ is coordinated by a $(\text{thf})_3\text{LiBr}$ group.

In view of the $\text{Li}\text{--Br}$ and $\text{Cu}\text{--Br}$ bond length the $(\text{thf})_3\text{LiBr}$ group could be considered as the leaving group in this complex. When reacted further $\text{Cu}_2\{\text{Si}(\text{SiMe}_3)_3\}_2$ might be the product. However, in the light of the growing importance of lithium cuprates as *in situ* synthetic tools in organic reactions certainly more structural information of this reactive species is required to elucidate reaction mechanistic and to design new synthetic concepts. Apparently the μ_2 -bridging of a short $\text{Cu}\text{--Cu}$ distance is not limited to carbon. Further experiments to isolate other intermediates in the reactions of copper(I) halides, as well as to elucidate the final products, are underway.

4.3 Lithium aluminum hydrides

While butyllithium discussed in section 4.1 is a frequently used deprotonating reagent, lithium aluminum hydride, LiAlH_4 , is a versatile reducing and hydrogenating reagent in both inorganic and organic synthesis. Although more than 60 functional groups are known to react with LiAlH_4 , very little is known of the reactive species involved in these syntheses. Nöth and coworkers investigated the reaction of aliphatic secondary amines with LiAlH_4 by ^7Li and ^{27}Al NMR spectroscopy from solution and determined the structure of $[(\text{Pr}^i)_2\text{N}_4\text{AlLi}\cdot 2\text{thf}]^{26}$ and $[(\text{Pr}^i)_2\text{N}_3\text{AlHLi}]_\infty^{26}$. We reported the isolation of two intermediates in the following reaction (Scheme 2).²⁷



Scheme 2

The isolation of products along this reaction pathway shows that the overall reaction to form the trisubstituted aluminum compound $\text{Al}[\text{N}(\text{SiMe}_3)_2]_3^{28}$ proceeds stepwise. The reactive mono-substituted complex $[(\text{Me}_3\text{Si})_2\text{NAIH}_3\text{Li}\cdot(\text{OEt}_2)_2]_2$ and the disubstituted $[(\text{Me}_3\text{Si})_2\text{N}]_2\text{AlH}_2\text{Li}\cdot(\text{OEt}_2)_2$, can be isolated. Lithium aluminum hydride was reacted in diethyl ether with di(trimethylsilyl)amine. The reaction mixture was stirred at room temperature for 24 hours. After filtering, crystals of $[(\text{Me}_3\text{Si})_2\text{NAIH}_3\text{Li}\cdot 2\text{Et}_2\text{O}]_2$ are obtained after 3 days at -35°C . These crystals, directly mounted from mother-liquor at *ca.* -50°C , have been investigated by single crystal structure analysis. At approximately -30°C the colorless crystals start to effervesce like champagne and turn into a white insoluble powder. We assume they lose hydrogen. $[(\text{Me}_3\text{Si})_2\text{NAIH}_3\text{Li}\cdot 2\text{Et}_2\text{O}]_2$ (Fig. 10, left) is a dimer in the solid state.

The aluminum in the central eight-membered $\text{Al}_2\text{H}_4\text{Li}_2$ -ring is coordinated by three hydride atoms and one $\text{N}(\text{SiMe}_3)$ ligand. The lithium atoms form two bridges between the two $(\text{Me}_3\text{Si})_2\text{NAIH}_3$ units *via* $\text{Li}\text{--H}$ contacts. Each of them is also coordinated by two diethyl ether molecules. The average $\text{Li}\text{--H}$ distance in $[(\text{Me}_3\text{Si})_2\text{NAIH}_3\text{Li}\cdot 2\text{Et}_2\text{O}]_2$ is 177.7 pm and therefore significantly shorter than in solid LiH (204.0 pm)²⁹ or even in AlH_4Li (188–216 pm).³⁰ The very similar dimeric structures of $[(\text{Me}_2\text{PhSi})_3\text{CAIH}_3\text{Li}\cdot 2\text{thf}]_2$,³¹ $[\text{Mes}^*\text{AlH}_3\text{Li}\cdot 2\text{thf}]_2^{32}$ and

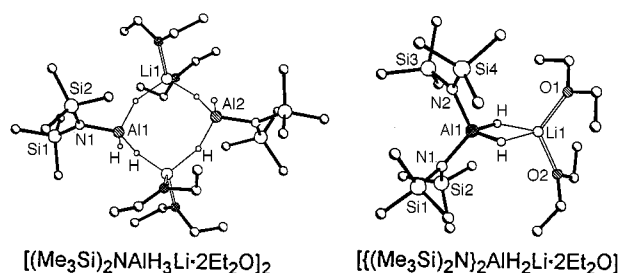


Fig. 10 The structures of the lithium aluminum hydrides

$[\text{Ph}_3\text{C}_6\text{H}_2\text{AlH}_3\text{Li}\cdot 2\text{Et}_2\text{O}]_2^{32}$ prove that this structural type is not limited to amido aluminum complexes.

Addition of $\text{HN}(\text{SiMe}_3)_2$ to LiAlH_4 in diethyl ether and subsequent refluxing for 3 hours and stirring for 12 hours at room temperature leads to the formation of the disubstituted complex $[(\text{Me}_3\text{Si})_2\text{N}]_2\text{AlH}_2\text{Li}\cdot 2\text{Et}_2\text{O}$. Crystals were grown in good yield at -18°C . Under these conditions the reaction is stopped after the substitution of the second equivalent of di(trimethylsilyl)amine rather than going on to the trisubstituted product $\text{Al}[\text{N}(\text{SiMe}_3)_2]_3$. Crystals of $[(\text{Me}_3\text{Si})_2\text{N}]_2\text{AlH}_2\text{Li}\cdot 2\text{Et}_2\text{O}$ were mounted on the diffractometer at *ca.* -10°C and started to effervesce above $+5^\circ\text{C}$. They lose hydrogen as well. Fig. 10, right, shows that the structure of $[(\text{Me}_3\text{Si})_2\text{N}]_2\text{AlH}_2\text{Li}\cdot 2\text{Et}_2\text{O}$ in the solid state is monomeric. The most striking feature is the central AlH_2Li four-membered kite-shaped ring, where the lithium atom bridges the two aluminum-bonded hydride atoms. The structure of $[\text{Li}\{\text{N}(\text{Bu}^t)\text{CH}(\text{Bu}^t)\text{CH}_2\text{N}(\text{Bu}^t)\}\text{AlH}_2]_4^{33}$ resembles this structural feature within an $\text{Al}_2\text{H}_6\text{Li}_4$ twelve-membered ring. In contrast to the $\text{C}(\mu\text{--H})_2\text{Li}$ bonding situation discussed earlier, this interaction seems to be chemical bonding. The hydride atoms in the $\text{Al}(\mu\text{--H})_2\text{Li}$ four-membered ring differ from the hydrogen atoms in the $\text{C}(\mu\text{--H})_2\text{Li}$ ring being negatively charged and thus attractive to the positively charged lithium atom. This coordination is even present in solution and can be verified by a NMR experiment. The bond angles show that $[(\text{Me}_3\text{Si})_2\text{N}]_2\text{AlH}_2\text{Li}\cdot 2\text{Et}_2\text{O}$ forms a rather strained structure. The average $\text{H}\text{--Al}\text{--H}$ bond angle in the monomer (94.3°) is 12.9° smaller than in the dimer (107.2°). The average $\text{H}\text{--Li}\text{--H}$ angle in $[(\text{Me}_3\text{Si})_2\text{N}]_2\text{AlH}_2\text{Li}\cdot 2\text{Et}_2\text{O}$ (73.6°) is as much as 33.8° smaller than in $[(\text{Me}_3\text{Si})_2\text{NAIH}_3\text{Li}\cdot 2\text{Et}_2\text{O}]_2$ (107.4°). The intramolecular bridging of the lithium atom leads to a longer LiH distance (av. 193.3 pm; *cf.* 177.7 pm in $[(\text{Me}_3\text{Si})_2\text{NAIH}_3\text{Li}\cdot 2\text{Et}_2\text{O}]_2$), which is comparable to the distance in AlH_4Li . The hydride atoms are forced close together in the transannular distance of 233.1 pm.

Despite this steric strain the molecule does not dissociate in solution. The ^7Li NMR spectrum of $[(\text{Me}_3\text{Si})_2\text{N}]_2\text{AlH}_2\text{Li}\cdot 2\text{Et}_2\text{O}$ shows a $^1J(\text{Li},\text{H})$ coupling constant of 10.5 Hz (Fig. 11). This is in good agreement with J_{LiH} coupling constants in lithium organics.³⁴

In $[(\text{Me}_3\text{Si})_2\text{N}]_2\text{AlH}_2\text{Li}\cdot 2\text{Et}_2\text{O}$ the $^7\text{Li}\text{--H}$ coupling is only resolvable in the temperature window of -30°C to -70°C . Outside this window the triplet structure of the signal is lost, at higher temperatures as a result of exchange and at lower temperatures probably by ^7Li quadrupole effects and rising viscosity of the solution. The coupling could not be verified in the ^1H NMR experiment because the hydride signals are too broad. Furthermore, the $^1J_{\text{LiH}}$ coupling could not be observed in $[(\text{Me}_3\text{Si})_2\text{NAIH}_3\text{Li}\cdot 2\text{Et}_2\text{O}]_2$ at any temperature between room temperature and -120°C in $[\text{D}_8]\text{toluene}$. It is fluctuating in solution. This fluctuality could consist in a monomer–dimer equilibrium superposed in a μ_1 and/or μ_2 and/or μ_3 hydride bridging exchange.

A recent report of Roesky and coworkers on reactions of primary and secondary amines with LiAlH_4 and $\text{Na}(\text{AlHET}_3)$ and the isolation and structural determination of related intermediates proves,³⁵ that our knowledge for describing and

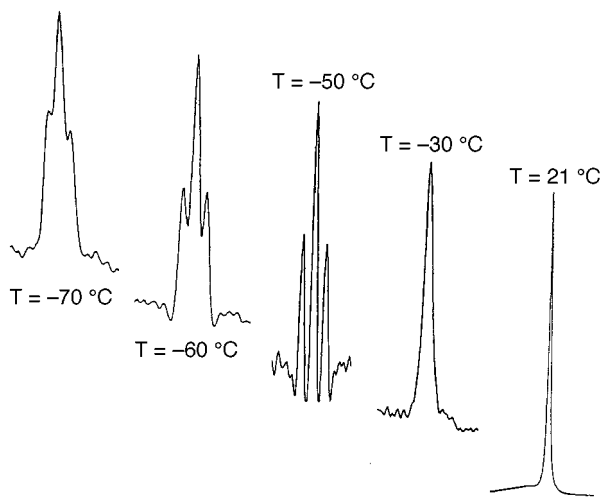


Fig. 11 Experimental ${}^7\text{Li}$ NMR spectra of $[(\text{Me}_3\text{Si})_2\text{N}]_2\text{AlH}_2\text{Li}\cdot 2\text{Et}_2\text{O}$ at various temperatures. The chemical shift at $-50\text{ }^\circ\text{C}$ is 0.4, the coupling constant ${}^1J_{(\text{Li},\text{H})}$ 10.5 Hz.

predicting reaction pathways in this area of chemistry is not by any means satisfactory. To extend our understanding, a great deal of structural work on intermediates is still required. With the latest progress in cryo crystal structure analysis and in the area detector technology this seems feasible.

5 Conclusion

The last pages have demonstrated that the cryogenic single crystal structure analysis has been successfully developed and used to gain structural information on reaction intermediates and reactive metal organic systems. The classical structure analysis, very well established for thermodynamically stable compounds, can readily be extended by cryogenic techniques to work on metastable compounds as well. Some examples may have shown that, although the structure analysis plays the leading rôle, complementary analytical information is required to elucidate phenomena in solution or in the solid state. Spectroscopic data are still needed for the comprehensive description of a chemical system. Once the structure has been determined it should not only be noted for deposition at a data base, but it should also promote new original ideas and synthetic concepts towards making target molecules. Mutual learning by chemists and crystallographers will give a tremendous impetus to all fields of chemistry and alkali metal chemistry and this will be a particularly flourishing area of research.

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