EPSRC Research Grant Report Upgrade of low-temperature equipment for X-ray crystallography GR/M79233/01

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Background and context

The grant was used for the acquisition, installation and operation of a Cryostream low-temperature device from Oxford Cryosystems, replacing the original and unsatisfactory device supplied by Siemens (now Bruker-Nonius) with our SMART CCD diffractometer in 1994. The Cryostream has been used for almost every data set collected since its installation in 1999 (a few samples have required room-temperature study for various reasons). It has thus supported a wide range of chemical research, in collaborative projects with many groups in Newcastle, at other UK Universities, in other countries, and in industry, and it has contributed to results reported so far in about 80 publications, several Ph.D. theses, and numerous conference lectures and posters. Results have featured in top-ranking journals and at large international meetings. Commercial pharmaceutical research has been strongly supported. Through this work, we have maintained our position as a leading crystallographic research laboratory with a strong international reputation.

Key advances and supporting methodology

The Cryostream is a well-known and highly regarded low-temperature device for crystallography; we still have one of the very first models (number 3, delivered in 1986) running on another diffractometer. Thus we were confident of its reliability, and in this we have not been disappointed. The device has been in operation without serious problems ever since it was delivered and installed; only routine maintenance has been needed, together with some minor amendments (with excellent and rapid response from the manufacturer) to deal with the effects of an unidentified source of electrical noise interference.

The apparatus has been routinely operated to give sample temperatures between 100 K and room temperature, depending on the nature of each experiment and the sample. The most common operating temperature is 150 K (reduced from a previous norm of 160 K, with no increase in the consumption of liquid nitrogen); lower temperatures have been used mainly for measurement of high-precision, high-angle data sets for experimental charge density studies, and higher temperatures when samples have undergone destructive phase transitions on further cooling. Reliable operation, largely without user intervention except for a weekly refill of the main pressurised nitrogen supply, has recently been improved even more by the addition of an electronic auto-fill control system.

Approximately 800 data sets have been measured since the Cryostream was installed. This figure could have been significantly higher, but we moved the entire crystallography research facility during 2002, and suffered a protracted period without operation as a result of a succession of equipment problems, probably arising from the relocation of the equipment (mainly faults in the water chiller system, X-ray generator, and an electrical supply problem that was obscure and took a long time to track down and correct).

About 80 papers have been published from these results so far; a complete list of 65 with the Principal Investigator as an author is attached. Visitors and former colleagues who are no longer in Newcastle have published the others, and a current list is not available. Several other papers are in

press and in preparation. A perceptive reviewer may notice that a few of the listed publications were submitted before the formal start date of the grant. This is because the equipment was actually ordered, installed and in operation before the grant officially began, payment being made from another account until it could be repaid from the grant. This shows how great was the need to replace the previous apparatus.

The equipment has been personally used by many researchers, though none of them was directly supported financially by this grant. In addition to the PI, there have been 6 staff and visitors of post-doctoral status, and 7 Ph.D. research students.

Research groups receiving significant support from this facility are 10 in Newcastle, and a similar number elsewhere in the UK and abroad. Most of these are EPSRC-supported (as well as other Research Councils, charities and industry), and the availability of reliable low-temperature crystallographic data collection has been an important ingredient in their success. Some selected results are given below. In addition, we have had a collaboration with scientists at DERA (now QinetiQ), in the study of triboluminescent complexes with potential application as damage sensors in composite materials, and have carried out research for a number of pharmaceutical firms, including a major continuing contract with GlaxoSmithKlyne, who are now outsourcing a large proportion of their crystallographic characterisation work.

A selection of results from the wide range of supported projects is provided here.

1. Metal alkoxides and polyoxometalates (with R. J. Errington; Figure 1)

During the period of this grant, some very large molecular systems have been studied. These are usually anionic polynuclear clusters with a multiple charge, and there are several tetraalkylammonium cations, frequently also with disordered solvent molecules present in the structure. Although a number of samples have required the greater intensity of synchrotron radiation (with beam-time allocated on an EPSRC grant), we have been able to collect most data sets in Newcastle. Low-temperature facilities are essential with such flexible counterions. Major concentration has been on polyoxotungstates and polyoxomolybdates partially substituted with other metals, mainly Ti, Zr or Hf, carrying organic ligands providing further chemical functionality. Three substantial papers, each containing several crystal structures, are in preparation for *J. Am. Chem. Soc.*



Fig. 1 (left): the hydroxy-bridged anion $[(W_5O_{18}ZrOH)_2]^{6-}$ in a monster structure that also contains $[W_6O_{19}]^{2-}$, $[W_{10}O_{32}]^{4-}$ and $(N^nBu_4)^+$ ions.

Fig. 2 (right): a new diphosphine providing high catalytic activity and selectivity in a palladium complex.

2. Complexes of novel diphosphine ligands with catalytic applications (with S. Doherty and J. G. Knight; Figure 2)

A range of new ligands and their complexes (mainly with Pd) have been investigated, to relate the observed structures to the very high catalytic activity and selectivity in polymerisation reactions. Several papers have been published, with others to be written.

3. Complexes of ligands incorporating nucleobases (with A. Houlton and B. R. Horrocks; Figure 3)

Nucleobases have been coordinated to metals directly and through alkyl tethers with substituents containing N and S atoms; the metals include Pd, Pt, Zn, Cd, Hg and alkali metals. A variety of degrees of aggregation has been found, with intermolecular hydrogen bonding also playing an important role in the structures. Structural results have featured on two journal covers.



Fig. 3 (left): A Pd complex of a ligand incorporating two nucleobases, which are self-complementary for hydrogen bonding.

Fig. 4 (right): The DNA-dependent protein kinase inhibitor OK-1035 ($C_{12}H_9N_5O$).

4. Bioorganic and medicinal chemistry (with B. T. Golding, R. J. Griffin and I. R. Hardcastle; Figure 4)

Our facilities have supported the research of the Newcastle Anti-Cancer Drug Design Initiative and other aspects of bioorganic chemistry, including toxicology studies. A number of results are awaiting publication.

5. Compounds of s-block elements (with R. E. Mulvey and K. W. Henderson; Figure 5)

A series of mixed-metal alkali metal compounds (containing both Li and each of the heavier metals), and some mixed M/Zn complexes have been studied, with novel structures. The "inverse crown ether" concept has been extended to incorporate multiply deprotonated ferrocene, leading to a major new research project.



Fig. 5 (left): fourfold-deprotonated ferrocene encapsulated by an "inverse crown" of amido-bridged Na and Mg. **Fig. 6** (right): two views of the complex polymeric structure of the compound with simple formula K(chp), where chp is deprotonated 6-chloro-2-pyridone.

6. Complexes of s-block elements with pyridones and related ligands (personal research group; Figure 6)

One research student has completed his Ph.D. thesis on work with alkali metal complexes of pyridones and aminopyridines, and another is currently investigating further pyridone complexes. With auxiliary crown-ether ligands, largely monomeric complexes are formed, but without these, a variety of polymeric structures are found, including coordinated alcohol solvents, for these compounds, which are used as synthetic intermediates. Some papers have been published, and several others are planned, following completion of some homologous series of complexes using all the alkali metals Na to Cs.

7. Organolanthanide complexes with applications in organic synthesis and catalysis (with K. J. Izod; Figure 7)

This project has, in fact, taken in also some related Group 2 complexes and explored structural similarities. Ligands have been sterically demanding, leading to complexes with unusually low coordination numbers, and to some clusters. The work has also included some alkali metal complexes, and structural characterisation of the ligands themselves. This project has been further boosted by the recent appointment of my former research student (S. T. Liddle) to a University Fellowship and his involvement in related research, results of which are yet to be published.



Fig. 7 (left): a tetranuclear Yb complex with a cuboidal Yb_4O_4 core. Fig. 8 (right): Laplacian of the electron density around the P atom of an uncoordinated ligand used in Pd-centred catalysts.

8. Structure-activity relationships for catalyst precursor complexes and their ligands (Industrial CASE funded by Ineos Acrylics; Figure 8)

In an attempt to understand the factors affecting the catalytic activity and selectivity of some palladium diphosphine complexes in acrylics production (closely related to project 2 above), we have carried out standard crystallographic studies on a range of complexes, and also some high-resolution charge density experiments with selected complexes and their uncoordinated ligands. Some of this work has been performed at Daresbury SRS with short-wavelength radiation, but several data sets have been collected in Newcastle. These experiments have employed the lowest temperatures, usually 100 K, in order to minimise atomic vibrations and enhance high-angle diffraction intensities. The work constitutes the main part of a recently submitted Ph.D. thesis (P. A. Champkin) and is expected to generate several publications, though some additional work is needed first to complete the study; one is already in preparation. We have concluded that the main contribution is steric rather than electronic, though the effects are subtle and simple cone-angle models are inadequate for an explanation.

9. Supramolecular coordination chemistry of polycarboxylic acids (personal research group; Figure 9)

Complexes of benzene polycarboxylic acids [particularly pyromellitic acid (1,2,4,5-substituted), trimesic acid (1,3,5), trimellitic acid (1,2,4), and mellitic acid (1,2,3,4,5,6)] have been prepared with a range of transition metals, by hydrothermal and slow-diffusion methods. Most of them are polymeric, with bridging ligands derived from the parent acids by complete or partial deprotonation of the carboxylic groups and with additional ligands such as water, alcohols, and organic nitrogen bases. Novel results include some microporous structures and some complex hydrogen bonding patterns. Several papers will be submitted for publication in early 2003. This work is being carried out by Ph.D. students.



Fig. 9 (left): the microporous channel structure of a copper complex of pyromellitic acid. Fig. 10 (right): a highly triboluminescent Tb complex.

10. Other projects (with various research groups in the UK, abroad, and in industry; one example in Figure 10)

Several smaller-scale projects have been pursued. These include a long-standing collaboration with a research group in Barcelona (funded from time to time by the British Council) on thiolate and other sulfur-based ligands; studies of metal cluster complexes with groups in Iran and Saudi Arabia, and occasional studies of inorganic and organic compounds from other UK university chemistry departments. We have also been working with a number of pharmaceutical companies, and have a well established contract with Glaxo-Wellcome, more recently superseded by a new contract with the successor firm GlaxoSmithKlyne; work in these areas is protected by non-disclosure agreements and details can not be included in this report. We have also been involved in a project with QinetiQ (formerly DERA), studying intensely triboluminescent materials, which have potential application as damage sensors in composite materials. This has involved, among other aspects, confirming at low temperature the centrosymmetric structures of some triboluminescent compounds (about which there had been some doubt in the literature), and reinvestigating cases of reported structural disorder, to which cause the triboluminescence has been unconvincingly attributed. One intriguing result, for which the superb temperature control of the Cryostream was a vital tool, shows that a highly triboluminescent material undergoes an order-disorder phase change on very slow cooling to 100 K (giving an excellent structure with a high degree of pseudo-symmetry), but that the roomtemperature structure is effectively quenched in a metastable form on flash-cooling (leading to a poorly determined version of the known disordered structure). A report of this work is almost ready for submission to J. Mater. Chem.

Project plan review

The installation and operation of the equipment has been according to plan. Although we suffered major down-time during 2002, following relocation of crystallography research, none of this loss was caused by the Cryostream. The new location of the equipment is much better, and future

operation will benefit significantly from the move. The Cryostream is expected to remain in use for many years to come.

Research impact and benefits to society

As noted above, the equipment has been used to support the research of about 20 groups. This includes

- research in catalysts and their precursors, which has industrial support (mainly from Ineos Acrylics and ICI);
- research in anti-cancer drug design, which is well supported by medical charities and is part of a major expansion of research facilities in Newcastle with SRIF funding;
- research in polyoxometalates as soluble molecular models and precursors for metal oxides and other important materials and surfaces, with industrial funding;
- research in complexes of ligands derived from nucleobases, with a range of Research Council support and featured twice on journal covers;
- reactive intermediates in organometallic lanthanide and *s*-block element chemistry, supported by EPSRC and the Royal Society;
- chiral organic synthesis, with Research Council and industrial support;
- applications of "inverse crowns" incorporating main-group metals, which provided the front cover of *Angewandte Chemie* and have led to new EPSRC funding recently;
- supramolecular coordination chemistry, in an area enjoying much international attention, for which a funding proposal is being prepared.

In addition, our ongoing research contract with GlaxoSmithKlyne contributes significantly to the development of new pharmaceutical materials, with impact on medical health. We have also been able to provide results for some other pharmaceutical firms, and are actively seeking further industrial partners, especially smaller firms in the local area.

Expenditure

The grant has been used as proposed originally, for the purchase of the Cryostream system and the running costs of its operation (mainly liquid nitrogen) during the grant period. In accordance with the application and award, there has been no expenditure on personnel or travel. The total amount of the grant was only £26,274, and the benefit obtained from it is huge, permeating into many research activities.

Further research or dissemination activities

The Cryostream is expected to continue its reliable operation for many years, almost certainly beyond the lifetime of the SMART diffractometer (8 years old and now officially obsolete, but still in constant use) and into that of its successor in due course. Results will thus continue to be produced for the foreseeable future, in research areas described above and in new areas as yet unidentified. These results (and many that have already been obtained but not yet published) will be disseminated in the normal way, through journal publications and conference presentations. We have recently moved into research areas that involve combined synthetic and structural work within my own research group (carried out by Ph.D. students), and expect these to grow, in addition to the collaborative work carried out with other groups. Our main current interests are in complexes of *s*-block metals (concentrating up to now on alkali metals, but extending to Group 2 from this year) with polyfunctional compounds of synthetic interest, such as pyridones and aminophenols; and in supramolecular coordination chemistry of polyfunctional ligands, especially carboxylic acids. We are also seeking further industrial research partners.