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Celebration of inorganic lives: Interview with Alan M. Sargeson☆

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Details of the life and career of Professor A.M. Sargeson FRS, a leading Australian coordination chemist, are revealed in an interview with Professor Lindoy conducted in Canberra in May, 2004.

Q. Let us start at the beginning: Where were you born and what was your early childhood like?

I was born in Armidale, northern New South Wales, in 1930 and I had two older brothers. My father was an officer of the court, clerk of Petty Sessions, and my mother came from a grazier's family at Wentworth in the far west of NSW near Mildura. We left Armidale after I was about 6 months old and went to Cessnock, a poor coal-mining town and lived there for about 4 years. I am told as a child I was very busy and inquisitive which brought me a lot of strife but I was not unhappy. We then moved to Taree, near the coast, and this was an especially nice place to live for the next 4 years. This total period covered the depression but it did not seem to bother my parents unduly. We were not wealthy and we always had food but not many material possessions. My parents were interested in many things. My father was a keen fisherman and a scratch golfer as well as being trained as a lawyer and my mother was also an excellent golfer. In Taree, there were two notable events ca. 1936. Zane Grey landed a sea-plane on the Manning River on one of his big-game fishing expeditions and Babe Didricksen, the USA professional womens' golf champion, played an exhibition match with my father and the local professional because the local women's competition was not strong enough. He beat her 7 up and 6 to play and she was not pleased. So, we were raised with a lot of healthy outdoor life and activity. My father was also a very knowledgeable person in a general sense and he introduced us to a lot of nature and was unusually perceptive about health issues. However, despite these entertaining diversions, both parents were diligent and made sure that we did our homework and other duties. So, we had a good life in hard times.

Q. When you went to school did you enjoy that experience?

Not greatly. I think I liked living out of doors too much for school to be attractive. I should also say that the period after the outbreak of war in 1939 was pretty hectic and I went to five schools in the next 5 years, as my father was moved to different Court Houses. Some of the intervals were rather short so that did not really promote learning. However, in a 2-year period we had in Cootamundra when I was 14–15, I had a very able science teacher. Her maiden name was Daphne Morton and she really activated my interest in science to the point where I tormented my father and a local pharmacist for samples of chemicals so that I could do little experiments by myself. In time, the pharmacist would hide when he saw me coming. I also had a gifted maths teacher, Head Master Corrigan, who managed to raise my interest and understanding significantly, in that subject.

Q. Then you went on and finished high school?

Well I then went back to Sydney and, almost immediately, on to Maitland Boys High School in the Hunter Valley north of Sydney where I finished the 2 years to qualify for the university. I had rather good teachers in Maitland I must say, especially in maths (Doyle), physics (Calhoun) and

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english (Hickey) and by the time I finished school I pretty much wanted to be a science teacher. As a consequence, I applied for and got a scholarship from the NSW Education Department to the Teachers College and the University of Sydney to do science. This was a path not uncommon in those days when university scholarships and bursaries were scarce. Later, I learned that both Ron Nyholm and Frank Dwyer went by the same path to the U of S albeit somewhat earlier.

Q. What did your parents think about you studying science?

They were quite keen about me doing so, that was not a special problem. They wanted me to have a degree and a secure teaching job because they were so influenced by the depression. They were less keen later on in my continuing in science. It was an unusual event for them to see someone going for a higher degree and they were not convinced that it was in my best interest. However, they did not protest too much and by then I was rather determined to extend my education into the research area. I simply needed to know more as I became more involved.

Q. Turning back now to your undergraduate days — did you have any special experiences or interactions during that period?

I think that was an interesting time at the University of Sydney as it was the beginning of the PhD programme and because Le Fevre and others brought distinguished overseas visitors to the university and they included people like Alexander Todd, C.K. Ingold, H.J. Emeleus, E.A. Guggenheim and Henry Eyring to name some. They were all stimulating lecturers and of course renowned chemists, so we were unusually well-served at the time I have to say. Le Fevre was not responsible for all of those visitors but he certainly invited a valuable English contingent. Henry Eyring came out primarily as a Mormon Bishop if I remember rightly. Every so often the Mormons had to spend a year proselytising the laity and he spent his stint in Australia doing that, leavened by visits to chemistry centres. I was also well-served by my lecturers. Those that influenced me most were Frank Dwyer, Frank Lions, Stephen Angyal, Ern Richie, G.K. Hughes, J. Cymerman-Craig and Tom Iredale. David Mellor was not so involved then because he was producing the chemical history of the Australian war effort and we had few lectures from him.

So in first year, I did chemistry, physics, maths and geography. Geography was a bad choice—McDonald Holmes was a poor lecturer and I got out of that very quickly. I did chemistry, physics and maths in second year and then the chemistry course became so much more interesting with specialization in inorganic, organic and physical that I knew I was committed to continuing in chemistry. So I chose the physics and mathematics courses to more suit my interest in chemistry. By the third year, I was doing only chemistry and in those days you had a regular third year chemistry year and then there was a special chemistry course which was heavily dominated by the organic chemists, especially in the natural products area. Not surprisingly, I finished up doing an honours degree in chemistry with Ern Richie and I have to say that that was a bit of a disaster. We were both disenchanted by the end. Fortunately for me, I had done a small research project with Dwyer earlier and he was doing interesting work and was willing to take me on as a graduate student. That proved an important development for me.

Q. What happened next?

Well I did the doctorate degree with Dwyer and I learned an enormous amount from him. After that, I also completed the Diploma in Education as part of my teacher's scholarship commitment and did some research on the side as well. By then, I was much more interested in the prospect of being a chemistry lecturer than teaching in a High School. Fortunately, I managed to persuade the NSW Education Department to let me go that path and they were enlightened enough to see it as a teaching brief fulfilling the scholarship purposes albeit at a different level. I have to say that was an unusually broad and charitable view for such an authoritarian organization and I have very good reason to be grateful to them for that opportunity. Then I taught chemistry, part-time, for a year in the newly created University of Technology in Sydney at night classes for the students that came after work. That was a tough job, tough for me and tough for them; some of them fell asleep and there was not much you could do about that as they were obviously tired and I was not a brilliant lecturer. Anyway, we got through the year and they took me out for a beer at the end so it could not have been too bad. Then, I applied for a lectureship in Adelaide. Such lectureships were few and far between in 1955. I was short-listed for the position and made a trip to Melbourne to be interviewed by D O Jordan at Ormond College. He was Head of Department at the University of Adelaide and I think he was attending an ANZAAS conference in Melbourne on this occasion. We talked at length and Adelaide finally gave me the job. So I then joined Bruce West as the other inorganic lecturer at the U of A. It was a very happy time for me and started me essentially on a permanent academic career.

Q. What happened at Adelaide?

Well I did some research there, largely developing things that I had started in Dwyer's lab and especially the stereospecificity effects of chiral ligands on co-ordination com-

plexes. I also made and resolved some thio-oxalato complexes, developed a neat way to make and crystallize EDTA metal complexes and collaborated with Wolfgang Sasse for an interval. Wolfgang was a graduate student of Geoffry Badger's and had carried out some important work on the dimerization of pyridine with Raney nickel to make dipyridyls. That process was very interesting to a co-ordination chemist since it produced 2,2′-dipyridyl in 30 g lots very cheaply. To buy it from chemical companies at the time was expensive (∼$2 per gram in the days when our research budget was ∼$100 per year). Badger consulted for ICI (Aust) then and what grew out of Sasse's research were Diquat and Paraquat, two important ICI herbicides, which were used for a long time. However, I do not think that Australia finished up with all that much of a return from those endeavours since the products were returned to England to boost an ailing ICI (UK). In any event, my point of contact with Sasse was that and one of the side-products he got from the dimerization process was a yellow nickel complex which turned out to have two pyridyl–pyrrole ligands bound to nickel and an additional dipyridyl attached, i.e. an octahedral tris(didentate) complex of a very unusual kind which we characterised. Two of the ligands were anionic and the other was neutral and this non-electrolyte precipitated from the reaction mixture. The extrusion of a C atom from pyridine to give the pyrrole residue and its link to another pyridine were also unusual features and Sasse and I together unravelled this story and published the work in Proc. Chem. Soc. The complex remains unusual to this day.

So it was not an uninteresting time to begin in Adelaide and I persisted with the general co-ordination chemistry there and especially with the stereospecificity issues. Towards the end of my second year Dwyer was appointed to a professorship at Pennsylvania State University and many in Australia were alarmed at the prospect of losing him. So ANU in Canberra and CSIRO in Melbourne got together and generated a proposal to provide the resources and opportunity to keep him in Australia. Dwyer did not really want to go to America but things had become so tough in Sydney for him that he felt he had to move. He had been very successful in America during his first visit 1952–3 and he could have flourished there but from a social point of view he wanted his children to be educated in Australia. The upshot was that ANU and CSIRO together made him an offer to establish a research group in the John Curtin School of Medical Research at ANU which would be called the Unit of Biological Inorganic Chemistry. By this time of course Dwyer was actively engaged in biological aspects of inorganic chemistry so that it was not an inappropriate name for that Unit. I have to say that Adrian Albert, the Professor of Medical Chemistry in the Curtin School, was not very happy about this arrangement. He wanted Dwyer to be part of his department but Dwyer insisted on this independence and I think that that was an important decision. This arrangement then allowed him to remain in Australia and at the beginning of 1958 he moved to Canberra and he asked me to join him to help set up the biological inorganic chemistry operation along with a technician, Ian Reid, J.W. Hogarth (a retiree who had done many of the analyses on Mawson's samples from Antarctica) and John Broomhead and Brother Garvin as graduate students also coming from Sydney. U of A gave me leave and in January 1958 we all moved off to the John Curtin School.

Initially, we just had one big laboratory, in Experimental Pathology, and that was a tight squeeze but before long they finished the laboratories on the top floor of Adrian Albert's wing (four floors) and we were installed in part of that space as an independent research group. It was an important development, not only for me but also for others that came later. They included Brice Bosnich, Tom McDermot (former Sydney students) and Dave Buckingham who came from New Zealand. All of those were subsequently successful chemists elsewhere or in Australia. Brother Garvin was committed to his teaching Order and ultimately served as its head for an interval. You have to recognise that this development preceded by years the biological inorganic fashion that became so popular later especially in the USA.

Although, I was linked to Dwyer, it was in a temporary position and I was still formally on leave from the University of Adelaide. About half way through the year when I went back to Adelaide for a visit, Jordan asked me if I intended to stay at ANU and we had a rather frank discussion. I said I would like to stay there if the opportunity arose. Finally, it turned out that my temporary research fellowship was rearranged to make it a regular Research Fellowship and I gave up the tenured lectureship in Adelaide to take up this impermanent job in Canberra. Looking back, it was not a very rational decision but it turned out well finally.

Q. So you were really in at the beginning of biological inorganic chemistry?

To my knowledge that was the first time that those words had been linked in a formal sense and, of course, it arose from Dwyer's interests and the growth of molecular medicine and biochemistry. Dwyer had talked some about bio-inorganic chemistry in the USA in the early 50's and he was editing a book with D.P. Mellor in 1961 in which there was a chapter on biologically active complexes that stemmed from earlier times in Sydney. I remember the day when we were sitting around the table in the Sydney lab and Dwyer said to us "look these phenanthroline complexes are rather like protonated strychnine. They are big cations and they ought to be bitter and may be toxic. Why don't you taste a little" and we all said "why don't you"? Then we all did something very stupid and tasted $[Ni(phen)_3]^{2+}$ together. He turned out to be absolutely right. It was bitter but nowhere near as bitter as strychnine or brucine. Following that Buddy Rogers at the CSIRO animal health laboratories in the University of Sydney (later Zoology Professor, U of A) agreed to check

some of the properties of these complexes with animals and as a result, their very active inhibition of cholinesterase was discovered. When the complex was injected into rats, for example, they were paralysed progressively from the feet up—rather like curare. This aspect did not develop much more until we went to Canberra where Albert Shulman and Panzy Wright from the University of Melbourne's Physiology Department became involved. It transpired that the Fe(II) and Ni(II) tris(tetra-methyl-phenanthroline) complexes showed very substantial bacteriostatic properties and stopped the bugs growing at micromolar levels. In those days especially, there was a major problem in the hospitals with *Staphylococcus aureous* (golden staph) infections and Hildred Butler, a medico at the Royal Melbourne Children's Hospital offered to test the intense red Fe(II) complex on new born babies because it was easy to see that they were properly covered. They looked pretty gruesome to the horrified mothers but it worked like a charm in terms of stopping the golden staph from developing and of course that was important information. Then others in the Curtin School and notably Harry Rosenberg became interested in what way the complexes functioned but they could not find an answer. None of the major metabolic pathways seemed to be affected. Quite accidentally, we never conducted the tests for long enough to show that no new generations arose. If we had done so then we would have realised that the DNA replication had been stopped. That is what Jacqueline Barton discovered almost 20 years later. It would have been a very likely prospect for us, because at that time in the Curtin School, John Cairns was doing unravelling experiments of DNA and evaluating its rate and mode of replication. So there was an understanding of the technology nearby. The other important aspect of this work was that Monsanto and ANU patented the molecules and their use as antibacterial agents and Bert Halpern at Monsanto developed and patented cheap syntheses for the bases. The major competitor at the time was hexachlorophene and the drug companies backed it simply because they were suspicious of the metal in the complexes. In retrospect, it was a very unfortunate choice since major problems arose from that drug which are now well-documented whereas the mutation rate for the complexes is very low and to our knowledge they are still problem free for topical applications. I have used the Fe and Ni complexes for more than 40 years for skin infections and they may well be valuable in that role in the future for organisms which become resistant to antibiotics.

Q. What else was happening?

Well, the inorganic synthesis side of things was maintained and the inorganic reactivity aspects were developing. We learned about the racemisation of cobalt(III) amine complexes triggered by charcoal and electron transfer with traces of labile Co(II). John Broomhead did some work on the racemisation of nickel-mixed phenanthroline and dipyridyl complexes and continued that later. Bosnich did quite a lot of ruthenium dipyridyl chemistry for his doctorate and that helped trigger his ruthenium chemistry later and McDermott also did some chiral discrimination chemistry which he persisted with in the USA and when he came back to Australia. Buckingham did a lot of synthetic and redox work while he was there, especially with osmium complexes and that was an important study for him and others later, notably T.J. Meyer. All this time, Dwyer was becoming more and more interested in the biological aspects and Bert Halpern resigned from the Research Manager's post with Monsanto in Melbourne to join the group as a Senior Research Fellow. By then, Dwyer was involved in amino acid chemistry. He had recognised that the natural isomer was relatively cheap and easily obtained but that the enantiomer which you had to get by resolution was very much more expensive. The reason for that was simply that the resolving agents were usually cationic alkaloids like strychnine and brucine and there was only the natural form with which to do the resolution. This usually gave one optically pure isomer from the least soluble diastereoisomer but not necessarily full resolution of the most soluble form. Then Dwyer had this smart idea that you could use a chiral cationic co-ordination complex where both pure chiral forms were equally accessible and use them to isolate the two chiral forms of the amino acid anion equally pure. Halpern devised and executed a very simple way of doing this and the amino acid chemistry eventually turned out to be interesting for all of us in one way or another. However, after about a year of these activities Dwyer died unfortunately from a massive coronary occlusion and just before I was committed to go to Henry Taube on some study leave. The Dean of the day thought that the viability of the group was impaired by Dwyer's death and Halpern was not tenured unfortunately (Fig. 1). Taube agreed to postpone my visit and I remained in Canberra to write up all the papers that were extant. Halpern went off to Syntex in Mexico to join the group that had been started by Djerassi, Birch, Stork, Smith, Sondheimer and others which led to cheap contraceptive pills from Mexican yams. So you can see how accidents can influence pathways. Much later, Bert Halpern moved from Syntex to Stanford and joined up with Kornberg and Lederberg to develop skills and strategies which were to become important to him later. I allude to coupled chromatography and mass spectrometric analyses in endeavours to detect life in outer space and especially via amino acid derivatives. When Halpern returned to Australia at Wollongong as the first Professor of Chemistry there, he installed that technology to detect metabolic disorders in children, e.g. phenyl ketonurea, where either a pathway has diminished or is hyperactive and over produces. That was an important development for this country and globally because nowadays the mass spectrometers are used clinically to detect these metabolic problems. In the process, Halpern in collaboration with David Danks discovered several new diseases and that work has been continued by Alan Duffield and others to this day.

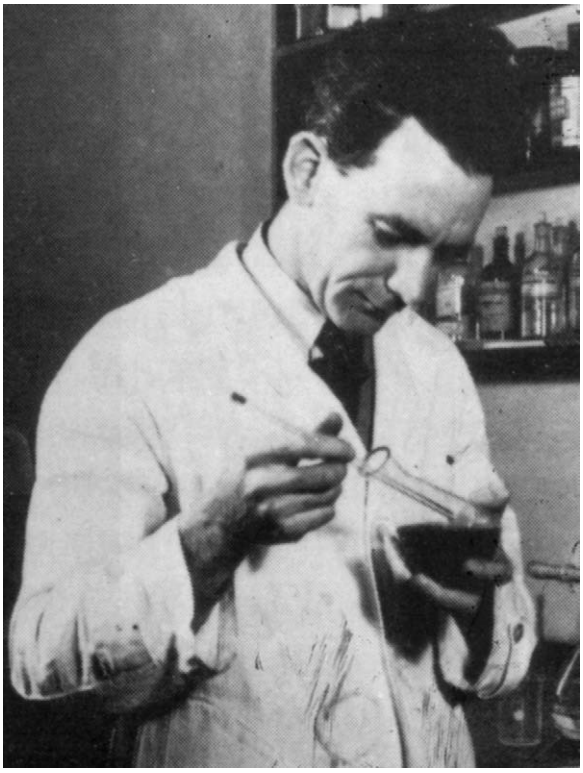

Fig. 1. F.P. Dwyer.

Q. What followed this?

Well, I finished publishing the remainder of the papers before going off to spend a study leave with Henry Taube. Fortunately, he had moved to Stanford from Chicago in the interval and that had such a good climate relative to Chicago that I was quite delighted. So Marietta and our new baby, Kirsten, and I set off around October 1963 to Stanford and we arrived, I think, about 2 weeks before Kennedy was assassinated. That was a catastrophic event I have to say and the USA, Palo Alto, Stanford and the whole research group were profoundly distressed. Conspiracy theories abounded and it was seen as an attack on their society rather than an act of a deranged individual. The response was so bad that we even contemplated coming home but we stuck it out and it turned out to be a memorable year for us. Taube was not only an extremely interesting chemist but also a fine and generous person and we had a tremendous time there. He allowed me remarkable freedom given that I was essentially a salaried post-doc. I not only got a lot of research done and published several papers with him but I also travelled extensively and met many American colleagues with whom I had corresponded or knew from the literature. NMR was also burgeoning in Stanford as a result of the Varian brothers and Djerassi had triggered an interest in ORD devices. So I had access to technology that was either not yet available in Canberra or was much more primitive there. I learned a lot and also, on a journey in April 1964 when we drove from coast to coast and back again something like 8000 miles in 5 weeks. That was a mammoth trip talking at different universities on route and meeting many people. It was a most stimulating experience in addition to the time with Taube so we had very good reason to be pleased with our visit to the USA and the results from it. On this journey and also on two side trips, I met some fine chemists and also very entertaining personalities, including, Bob Connick, Fred Basolo, Ralph Pearson, Jim Collman, Bodie Douglas, Daryle Busch, John Bailar, Ted Brown, Stan Piper, Joe Bunnett, Harry Gray, Ed King, Wayne Wilmarth, Arthur Adamson and Saul Winstein to name some. Meeting all of these people who had influenced the subject, and talking with them was really an important influence for my own chemistry apart from the social pleasures entailed and a lifelong friendship with Taube.

Q. When did you leave for home?

We left for home in late September by continuing around the world and particularly I wanted to go to England and Denmark. I have to say we did not do much chemistry in England. We enjoyed London, went to Norwich to meet Stephen Mason with whom I had corresponded on chirality issues and I also met Martin Tobe at UCL. At the time, he was not too interested in the paper with Bobby Jordan supporting the conjugate base hydrolysis pathway but he was converted finally. It was very interesting to visit Denmark and meet Jannik Bjerrum and Clauss E. Schäffer, one having been such a major contributor to the understanding of equilibria in co-ordination chemistry and the other an important contributor to the theory of inorganic spectroscopy. In the process, of course, I met Carl Ballhausen as well so it was a very interesting stay. I also gave a disastrous talk at the Orsted Institute which I would prefer to forget but the Danes are forgiving and I mended my bridges later. My contact with Clauss E. Schäffer was unusually strong even after such a short time and despite our rather different interests that friendship and professional association has continued all of our lives along with other strong associations in Denmark. So, I have very good reasons to be grateful for that detour also (Fig. 2).

On our return to Canberra after a year's absence, the group of course was almost non-existent, just myself and a PhD scholar, Keith Turnbull. However, the Curtin School agreed for me to persist with the Biological Inorganic Chemistry Unit albeit at a somewhat reduced level. Initially, I recruited two graduate students, a technician and then David Buckingham as a Research Fellow. Things began to hum again. We got our synthetic work going well and did some very nice co-ordination chemistry especially with chiral amine complexes which were novel. To that point, there was a belief that such amines could not be resolved into their chiral forms and we brought resolution and understanding to that issue. We also did quite a lot of interesting work on the base hydrolysis mechanisms and spontaneous aquation

Fig. 2. A.M. Sargeson and Clauss E. Schäffer at the Hamburg ICCC meeting. 1976.

mechanisms of Co(III) amine complexes and that aspect flourished especially with all of us working as a team. In these endeavours we were lucky to recruit some very able scholars, one from Denmark, Inge Olsen (later Creaser) and Pat and Lui Marzilli who had known Buckingham at Brown University. We did not have a lot of space but we had a lot of energy. So the group flourished and we enjoyed it (Fig. 3).

Q. David Buckingham stayed on with you for a long time and you published much together. Do you want to comment on that?

It turned out to be very good for both of us. Buckingham was very able and skilled and we complemented each other in some ways and I think we both have good reason to be grateful for that period. Later on, he clearly wanted to develop his own activity and so we simply agreed to bifurcate but that was after we had moved to the Research School of Chemistry. That move was done with mixed feelings. It was clear that it was going to be attractive in a number of ways but it was also true that there were aspects of our life in the Medical School, especially the interaction with the biologists, which we rather enjoyed. Well, we really did not have any choice since the biologists were saying—we see biology going in a different direction so it is more appropriate to have you in the Chemistry School because you are not really biologists. We could not resist that sensibly and we also had a very substantial advantage in going to the Chemistry School since its resources were

Fig. 3. A.M. Sargeson, L. Marzilli, P. Marzilli, I. Olsen (Creaser).

significantly greater than those in the Curtin School per academic. It was also interesting that the Research School of Chemistry was essentially non-departmental and individual faculty members did not have empires and allocated funding as they had in the Curtin School departments. Also, the money was moved to where it was needed by consensus. That strategy actually turned out to be a valuable asset to ANU and, in time, the development across ANU proceeded more along those lines than by the departmental route. It meant that the resources went to the most needed area to do research that was required and well-rated. It meant that those who did it well-flourished better than those that did not and so a natural balance was established in that way and in many respects the School was happier as a result. The conflicts that had gone on with the entrenched positions in the medical school and in the physics school for example were minimised and it was an important lesson for ANU to learn. Birch and Craig really deserve credit for setting the establishment up in that manner. It served ANU and many of us well.

Q. LFL: about this time you were doing many mechanistic studies involving cobalt(III) complexes?

Well, it was mechanistic and synthetic studies both together. The two things always went side by side with the synthesis side being really important. It was also a major endeavour in stereochemistry because there were issues relating to absolute configuration and there was the chiral nitrogen amine chemistry that was a rather novel and virtually unknown in organic chemistry. So we had to unravel its major aspects and what governed it as well as the way that it governed the behaviour of compounds. Also, it was important to establish the parameters for the associative versus the dissociative chemistry in a similar manner to what had been done for organic chemistry. In that sense inorganic chemistry at the co-ordination chemistry level was becoming of age and we were able to understand such things better than in the past.

Q. LFL: where did this lead?

It led to improved methods of synthesis for a start, so that aspect at that time was fairly important. In addition, it became clear even before Dwyer that the metal ions could influence the reactivity of organic molecules in a fairly profound way. That really triggered some imine chemistry and also amino acid and peptide synthesis chemistry and as we talked and made molecules of various kinds so the metal ion–amino acid ester and peptide chemistry developed. The vista of reactivity in organic chemistry involving bound metal centres became not only attractive but also consuming in the sense of trying to control it and understand how profoundly the metal ion influenced such behaviour. There was little hard evidence about mechanism at the beginning although interesting reactivity enhancements had been known for some time but the important features of it were not really understood. There were guesses in the literature but we really did not know the precise way the metal functioned.

At the time, we made the move from the John Curtin School to the RSC. We began to think about experiments that would tell us what governed those things and we continued that activity for a considerable period in the Research School. It also coincided with some very gifted people joining the group. Jack Harrowfield and Greg Jackson had returned from post-doctoral appointments with Brice Bosnich in Toronto. They were both very skilled co-ordination chemists and Geoffrey Lawrence and Peter Lay came from Melbourne to join the group and they were also gifted chemists. Lawrie Gahan from La Trobe and Inge Creaser who had been in Sweden and Denmark came back from overseas also joined the group. We had good students and resources which were adequate and the group really began to hum. Many cobalt(III) complexes were made where reactive ligands were tied irreversibly to the metal and where the reactivity issues could be investigated using both inter- and intra-molecular nucleophiles and tracer experiments. Those experiments pinpointed important features of how the co-ordinated metal ion influenced the organic reactivity. It became obvious that you could manipulate iminoacids to give a variety of amino acids by, addition reactions, reductions and oxidations. The metal in a way functioned both as a protecting and as an activating group and sometimes as a reaction inhibitor. The inhibition aspect was not unimportant since we saw intermediates and controlled reactions, for example in organic oxidations, simply because the metal slowed them down and even allowed the identification and isolation of some of the intermediates. Sulfenates for example were stabilised for the first time and that is a good example of a way of reducing the reactivity of a very active species so that you can then control it better and even divert it. This was a quite novel aspect of the development, not only to speed things up but to control the situation using the metal ion to steer the chemistry and in that respect we did some unusual experiments. It was surprising at the time and revealing to show the degree to which metal ions can influence reactions.

This kind of chemistry was not unique. It was also happening elsewhere both in co-ordination chemistry and in organometallic chemistry but overall it was an important development for the time. Also for us, it finally led to the prospect of synthesizing organic cages for metal ions. By starting with three elements of the cage bound to the metal centre and then by reacting those with two reagents to build the caps on the top and on the bottom of the three tied elements, the cages were made incredibly simply in one reaction. In a matter of 2 or 3 h, with quite remarkable efficiency, we could do the chemistry in this template manner and very much better than by standard organic methods. Those molecules kept us busy for a long time, not only synthetically but because their properties were so interesting and they complemented the cryptate chemistry since they

were biased towards transition metal chemistry rather than main group chemistry.

Q. How did the name sepulchrate arise?

That was quite interesting. We were elated when we made the first of these cage complexes and it was really entertaining. Jack Harrowfield, Tony Herlt and I had a discussion about how we might do it. It arose from some work with co-ordinated exo-immines where a bridge between one chelate and another had been built. That was some research and a structural study that Michael Snow did while he was in the group on leave. It became evident that if you made an exo-immine complex from formaldehyde then you could react it at the carbon center with a nucleophile. In the course of the discussion what emerged was that if you had three such immines on a trigonal face and you reacted it with ammonia then you should be able to cap the bridgehead. Essentially, it was like synthesizing the corners of hexamethlyenetetraamine. So, Tony Herlt, my research assistant did the experiment while I went off to Western Australia to give some lectures (Sept–Oct). When I came back, I had forgotten about this experiment but later towards the end of the year, I asked Tony what had happened to the experiment to cap $[Co(en)_3]^{3+}$ and he said "well I got this forest of proton signals and it looks a real mess" and I said well show me the NMR. Immediately, I recognised the overlapping AB systems of the methylene groups and I said "That's it, I am sure of it, you have got it and it has 3-fold symmetry". So it was a very exciting moment and of course we did get the ^{13}C spectrum as soon as possible and then saw only two carbon signals, one for the caps and one for the ethylenediamine fragments, due to the 3-fold and three 2-fold symmetry axes which made it certain. Then we had to think about a name for it because the IUPAC name was half a mile long and impractical for daily use. The cryptate-like names came to mind immediately. They were all a bit necrotic and Jack Harrowfield said 'why don't we call it sepulchrate?' and that name stuck; sarcophagene followed in the same vein but sepulchrate was very catchy. In retrospect, it is a pity that we did not call it diazasepulchrate then they could all have been sepulchrates but we were not thinking far enough ahead at that point (Fig. 4).

Q. Anything else about the cages?

Well, the thing that was really astonishing was that the Co(III) cage was very similar in properties to the tris-ethylenediamine template except that the rate constant for the electron transfer between the (II) and (III) oxidation states was about 100,000-fold faster. This was a staggering change when the molecules were so similar. So it took quite a while to unravel the reasons and to recognise that the essential issue was the strain that was built into the cage

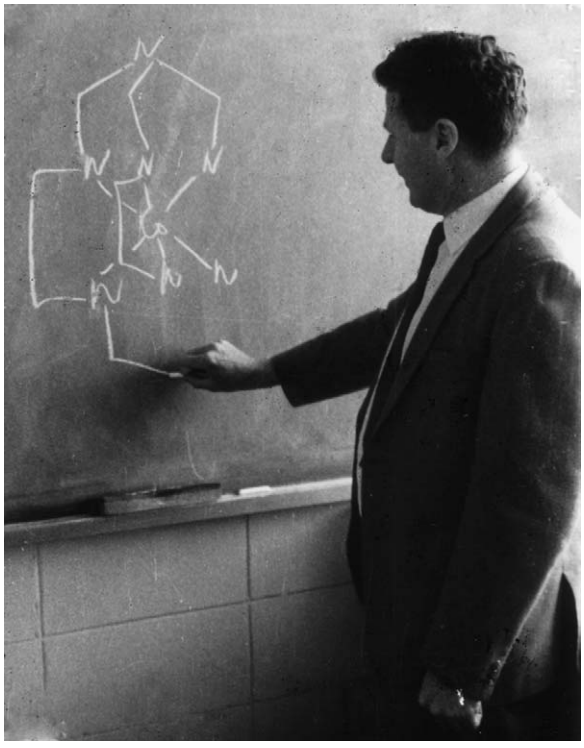

Fig. 4. A.M. Sargeson, just after the initial synthesis of cobalt(III) sepulchrate.

relative to the non-cage complexes. In addition, once we got the cobalt out of the cage and put other metals ions in then we were astonished at how stable some of these complexes were. The zinc complex for example was essentially a kinetically inert species and so we knew that we had changed the inherent reactivity of the zinc ion quite dramatically. It implied that you could make surprisingly stable complexes with such ligands even to the point where they could be resolved into stable chiral forms. Remarkably, the high spin manganese(II) complex was found to be optically stable despite the "normal" rapid exchange of simple ligands with this metal ion. It took about 10 years to unravel all of these issues and to build bigger cages and explore their properties, to put paraffin tails on the cages to make a new type of detergent and to look at the biological activity of those molecules. We also made cage polymers of them so that metal ions could be trapped and reduced to an extremely low level in solution. Then there were other aspects of using them for medicinal reagents especially for keeping radioactive metals in the cage so that they could be used to irradiate specific cancer sites and then be excreted unchanged. Clearly, facets of that kind were worth exploring and continue to be so.

Q. You might like to give us some perspective on where inorganic chemistry is heading?

Well that is a fairly tall order I have to say and I am wary about responding but there are some things that are

fairly obvious and not least of those is the nano-technology development already in train. Construction and exploration of big systems and their properties is clearly fruitful. There are many opportunities for using inorganic systems in medicinal systems and that is also fairly obvious but what is not so obvious and what is necessary is that a lot of basic chemistry is still needed. That basic chemistry is really the way in which you can understand and control metal compounds. The message comes from the cages, other multidentates and other large assemblies. What was not foreseen was the magnitude of the effects of multibonding in these assemblies. Stabilities, both thermodynamic and kinetic are much larger than expected in relation to simple complexes. This derives from the multiple binding points in these assemblies. Simply, if one bond is broken and the structure remains substantially intact then the return rate for recombination is greatly enhanced by the intramolecularity of the process. This gives the whole structure a kinetic stability overall even though each individual bond rupture remains rapid. The stability is evident in multidentates, metalloproteins and multidentate multinuclear structures and of course in the design of multinuclear assemblies to maintain such stability the design of the ligand is important, e.g. the less flexible the better.

The hexamine zinc cages in relation to simple zinc amine complexes is a good example. In the latter, the exchange of Zn^{2+} with the ligands is very fast (microseconds), with the cage nothing happens in days or months. Simply, in the cage after the Zn–N bond breaks the N atom never gets far from the metal ion and the return is rapid. Porphyrins are another good example where the metal in the centre is stabilised but they rely more on the rigidity of the structural framework and the energy required to distort it in order to break the M–N bond. Another area which might be fruitful is to wrap a polymer or peptide or polysaccharide around a metal or several metals and tie the end to the assembly to keep it intact. Such assemblies could have many uses in chemistry and biology. Simply, making them and learning about their properties will be a fascinating experience and I would have enjoyed that but who knows where the next major breakthrough will come from.