

Organic Microanalysis at University of Otago in its 75th Year

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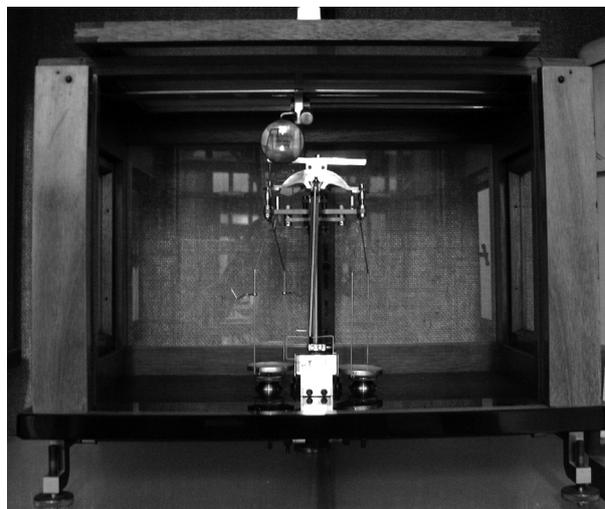
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Organic Microanalysis, the analysis of organic compounds on a milligram scale had its beginnings in Austria around 1910. When Fritz Pregl, who had graduated in medicine at University of Graz in 1894, returned to Graz after further study in Europe to take up his position at the Medico-Chemical Institute he found his studies on the identification of bile acids hindered by lack of sufficient material for accurate analysis. It was while at Innsbruck University, during the 1910-13 period, that he devoted much of his time to the development of new analytical procedures and he continued this work on his recall to University of Graz in 1913 (Pregl was Vice-Chancellor of University of Graz, 1920-21 and received many awards for his work including a Nobel Prize in 1923).

Fritz Pregl asked William Kuhlmann, who worked in the balance works of Paul Bunge to refine their precious metals assay balance. By very careful design and precision grinding and alignment of the agate knife edges, he was able to produce a balance sensitive to 0.001 mg with a weighing capacity of 20 g. Pregl and his group then modified and refined the methods of organic analysis to exploit the advantage of being able to accurately weigh milligrams of sample. His very detailed procedures, which are required when working on this scale, and methods for the preparation of reagents of suitable purity were published in his 1917 monograph *Die Quantitative Microanalyse* (J. Springer, Berlin) by which time he was satisfied that the methods were suitably robust to be followed by others. This monograph was soon translated into English and later editions incorporated modifications and improvements taken from publications of other research groups. Following the award of the Nobel Prize, chemists from many countries came to the Medico-Chemical Institute at Graz to study organic microanalysis under his guidance.

When Frederick Soper arrived at Otago in 1936 to take up the position of Professor of Chemistry, he realized that the local interest in natural products chemistry at that time would be greatly facilitated if analysis on a micro scale was readily available. He obtained the necessary finance and asked Charles Carter, the Senior Lecturer in the Chemistry Department, to purchase the equipment as specified by Pregl and set up a laboratory. The Kuhlmann balance (now in a display case in the Undergraduate Building) was purchased in 1937 and the laboratory, with the appropriate equipment, was soon set up and providing a service not only for the local research group but also for some other New Zealand natural products chemists. With only the book for guidance, Charles Carter had meticulously followed the detailed procedures as set out by Pregl. Looking back, this achievement is all the more remarkable when we consider that the gas furnaces in that small basement laboratory, with its low ceiling, must have been far from ideal conditions to give reproducible moisture adsorption on glass surfaces, which was so critical in the method for

carbon and hydrogen. Charlie did a lot of analyses for my MSc thesis, so many that Dr Stanley Slater (my supervisor, later Professor of Chemistry at VUC) included his name on the resulting publication.



The Kuhlmann balance purchased by the Department of Chemistry, University of Otago, in 1937 and used for organic microanalyses until 1958 - for a description of it: see text. Moving the 5 mg rider over the notched beam gives milligrams and tenths of a milligram. The next two significant figures were obtained by calculating the algebraic sum of the extreme positions of successive Left and Right oscillations of the swinging pointer over the scale. The position of the pointer had to be noted to one tenth of a division.

In 1949, the opportunity arose for the Department to develop the laboratory further when Dr. Tsu Sheng Ma was appointed to the staff. He was very well versed with the methods. After graduating from Tsinghau University in China, he studied organic microanalysis at University of Chicago where the head of the research group was one who had earlier worked with Pregl. Our laboratory was moved into larger space but still in the basement with its low ceiling. More equipment was purchased and a wider range of analyses were developed and on standby, so that the laboratory could provide a range of analytical procedures to research workers throughout New Zealand with little delay. But it was realized that Ma would return to US as soon as the opportunity arose and I was asked to understudy him whenever possible. This was to be a thorough training in the disciplined methods of a wide range of analytical procedures. T S Ma left to take up a position at Washington Square College (New York) in 1951 and I was appointed formerly to look after the laboratory in 1952.

Gradually, over the years, developments in analytical procedures and equipment have been introduced as time and funding have allowed. The University Grants Committee was very supportive of the laboratory, knowing that it was better to have one well equipped laboratory than several small units. The greatest demand is, and was for the deter-

mination of carbon, hydrogen and nitrogen, and it is not surprising that it is in this field that there has been much research and development. Initially, gas furnaces were replaced with electrical heating. Then analyzers were produced, which automated the combustion procedure, and well tested automated analyzers are available now, where the products of combustion are measured electronically rather than by weighing (carbon dioxide and water) or volume (nitrogen). However, being a service laboratory, no new procedure can be introduced until it is thoroughly tested. During my 1954 study leave at Glasgow University, my interest was concerned mainly with polycyclic aromatic hydrocarbons, but I took the opportunity to visit the research groups in the microchemical laboratories at Birmingham (Ronald Belcher) and Belfast Universities (Cecil Wilson). Then, in 1957, I spent a very profitable two weeks in the CSIRO microanalytical laboratory in Melbourne, working with W. Zimmermann and his team, and this led to several modifications to our equipment. Zimmermann had worked in the laboratory at I.G. Farbenindustrie in Ludwigshafen before coming to Australia and, besides having a successful method for the direct determination of oxygen, he used air damped Bunge balances, electric furnaces and some new reagents that improved reliability.

For my study leave in 1961, I returned to the Belcher laboratories at Birmingham University, where I was assigned to work on various problems in organic analysis, particularly the analysis of perfluorinated organic compounds and sub-micro methods, which they were developing. Belcher was well known internationally and through his introductions I was able to visit the analytical laboratories of the pharmaceutical companies of Geigy (H. Wagner) and Sandoz Ltd. (W. Schoniger) in Basel (Switzerland), and the Royal Dutch Shell (Pete Gouverneur) in Amsterdam, as well as several in UK. Schoniger was responsible for much of the early work on the development of the oxygen-filled flask method for the analysis of halogens, *etc.* I recall Wagner saying that he did not mind spending time with me, it was not every day they had a visitor from New Zealand. The 60th anniversary of Pregl's original work was marked with a special conference in Graz, Austria, in 1970. Although few new developments in analytical procedures were disclosed in lectures, the trade display was magnificent and, besides the various analyzers and balances that were available commercially, there was also on show the beginnings of the change to today's analyzers with electronic measurement. The contact the laboratory has had with laboratories overseas has always been valuable because of the very wide range of compound types that are received and especially since many samples cannot be regarded as routine.

At Birmingham, I was present in the laboratory when about 10 cm of a quartz combustion tube disappeared in an explosion during analysis for carbon and hydrogen. Some years later, we had a similar incident in our own laboratory when analyzing organometallic perchlorates. It was not a new problem and it was soon overcome with some modifications to the procedure. At one time, we were receiving large quantities of very hygroscopic samples and the accepted Pregl method for dealing with these was te-

dious and not entirely satisfactory. It was while discussing this problem with a Dutch analyst at a conference in Amsterdam that I obtained sufficient information to allow us to develop a very straightforward procedure using home made aluminium foil capsules to contain the samples.

The Otago laboratory has been particularly fortunate with its staff. In the early days in particular, with gas heating and before the introduction of automated analyzers, the whole procedure for an analysis required scrupulous attention to detail and very careful observation to note anything unusual. When the number of samples for analysis was relatively small, it was usual for the staff who worked in the laboratory to have other duties in the teaching laboratories as well. Verdon Chettleburgh had a fourteen year association with the laboratory from 1951 and he maintained the service while I was on study leave in 1954 and then again in 1961. For all microanalytical work, a reference or standard substance is always analyzed with each series of samples and for the sequential determination of carbon and hydrogen and for nitrogen (the Dumas method), the first sample analyzed each day after the equipment has equilibrated is a reference sample. By operating continuously throughout the day, and eating lunch as opportunity permitted during an analytical cycle (no OSH in those days), it was possible to get through a good run of samples with just the one reference sample. It is always useful to have easy contact with those submitting samples for analysis, so that any problems can be discussed (but travel within NZ was never that easy - even attending a one day meeting in Wellington took three days!). The annual NZIC conference was particularly useful in bringing chemists together, and Verdon was able also to visit other university departments while travelling on other business. Wendy Grimmett joined the laboratory in 1957 to help with an increasing number of samples. When she left in 1963, she was replaced by Doreen Petrie and who was involved in the 1970-71 move into the new laboratory. When the new science buildings were being planned, a convenient site was found for the laboratory on the first floor of the Chemistry Undergraduate Building. The laboratory was designed not only as a service laboratory but also with space for several research students and it housed the Varian CH7 mass spectrometer as well. When apparatus (particularly balances) arrive from overseas they are in specially designed boxes to eliminate damage during transit, but shifting equipment that is already assembled and in use over a relatively long distance presents a problem. I am reminded by Doreen that the balances were partially dismantled to avoid damaging knife edges, *etc.*, and then transported, one at a time, to the new laboratory. This was done by resting each balance on her lap in the front seat of my car while I drove very carefully across to the new laboratory. Later, Bob Monk joined us in the laboratory and, when he left in 1978, Bob McAllister shifted in from the undergraduate laboratories. Marianne Dick became full-time in the laboratory in 1983 when Doreen left and she took over responsibility for running the laboratory when I retired in 1988. Since then the laboratory has continued to develop. In particular, it was equipped with the new Carlo Erba analyzers with electronic measurement of the combustion products for the determination of carbon, hydrogen and nitrogen which by

then had been shown to be reliable. Also, with the retirement of some of the microanalysts in Australia and the cut-backs on laboratories, the local laboratory now receives samples from some Australian research groups. In 2005, the laboratory was on the move again, this time a consolidation within the Department because the large research space was no longer required. The same analytical service was provided by Marianne and Bob with occasional help from Dianne Clark during busy periods. Bob McAllister took over responsibility for running the laboratory in 2010 when Marianne retired and he has been joined by Pauline Bandeen.

There have been many incidents of note during my association with the laboratory, but one stands out. Don Hannah was involved in a project involving the fusion of samples with metallic potassium. While we were discussing this at his bench, some potassium set fire to the alcohol in the

beaker he used to clean the potassium. I picked up the nearest book and put it on the beaker - (fortunately the fire went out) and carried on with the discussion. It was some time later that I was told that the book I had used to snuff out the fire contained all the results of Don's research for the year.

Some years back, when high resolution mass spectrometry became fashionable, I was told that the days of the laboratory were numbered, that mass spectrometral measurement would replace microanalysis. But the opposite has happened and sample numbers have increased. Modern instrumentation quickly provides a lot of useful information, research proceeds faster with the result that more samples are sent for analysis not fewer. And I am confident that the laboratory will continue to provide an accurate analytical service for many years to come.