BASIL LYTHGOE
18 August 1913—18 April 2009
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Elected FRS 1958

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Basil Lythgoe was distinguished as an organic chemist. He began his career at the University of Manchester, where he had studied for his undergraduate and PhD degrees, before moving to University of Cambridge. During this period he collaborated with Alexander Todd on the structural elucidation and total synthesis of the natural nucleosides, and was also noted for his investigation of the structure of the natural substance macrozamin. In 1953 he moved to the chair of organic chemistry at the University of Leeds, running a research group from which several graduate students went on to academic careers of the highest distinction. At Leeds he worked on the structure of the alkaloid taxine 1 and calciferol, among other natural substances. Lythgoe’s work was characterized by a combination of insight and high experimental skill.

LEIGH, MANCHESTER, HUDDERSFIELD, MANCHESTER

Basil Lythgoe was born in Leigh, Lancashire, the second of three children of Peter Whittaker Lythgoe and Agnes Lythgoe. His father, Peter, distinguished himself at Leigh Grammar School by winning numerous prizes and then worked in the office of a local textile firm while also attending night classes; in 1923 he became company secretary. His mother, Agnes, had had little formal education but was a voracious reader. They made a home where their children could study, and equipped it with encyclopaedias and other suitable reading material. Lythgoe followed his father to Leigh Grammar School. A couple of years before Lythgoe arrived at the school, Meredith G. Evans (FRS 1947), who was to become professor of physical chemistry at Leeds from 1929 to 1939, left the school.

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A county grant enabled Lythgoe to proceed to the University of Manchester in 1930. The grant covered only the university fees and so he continued to live at the family home, from which he commuted daily to Manchester. Towards the end of the academic year 1932–1933 Lythgoe developed a severe throat infection and had to defer his final degree examinations. He completed his degree in 1934, obtaining first class honours. His postgraduate work in fact began in his final undergraduate year 1933–1934, the University of Manchester being co-operative in making the necessary arrangements. A recreational interest that developed at this time was rock climbing, and this continued until advanced years precluded it.

Lythgoe obtained his PhD degree in 1936 under the supervision of I. W. Heilbron (FRS 1931), holder of the Sir Samuel Hall Chair of Chemistry, and four publications resulted from it. Two of them concerned pyrones, oxygen-containing heterocycles, an interest of Heilbron’s that predated his supervision of Lythgoe (1, 3). The other two are concerned with natural pigments (2, 4). Heilbron was not the easiest of colleagues or research supervisors, sometimes expressing criticism when encouragement was needed. Some of Heilbron’s other research students experienced that to a much greater degree than Lythgoe. Heilbron’s academic roots were to a large extent in Continental Europe as he had studied for his PhD at Leipzig with A. R. Hantzch (Cook 1960). At this time, Lythgoe became aware that Heilbron had introduced into England laboratory techniques and procedures from Germany and Switzerland, including ultraviolet/visible spectroscopy and chromatographic separation.

On completing his PhD, Lythgoe joined ICI in Huddersfield. He probably saw this as filling in time until a university post became available, but there was more to it than that. He spent several rewarding months researching a synthetic dye and quite possibly he linked that in his mind to his work at Manchester on natural pigments. His tenure at ICI was short, and he soon returned to the University of Manchester as an assistant lecturer. During this time he worked with Alexander Todd (FRS 1942, PRS 1975–1980), who had taken up the Sir Samuel Hall Chair after Heilbron’s departure for Imperial College. During this period at Manchester Lythgoe resided at Donner House, the university staff house, where he met Kate Hallum. Originally from St Andrews, she had graduated in mathematics at Cambridge before going to Manchester. They were married in 1946, by which time Lythgoe had moved from Manchester for Cambridge with Todd. There were two sons from their marriage, John (born 1948) and Andrew (born 1950).

**Cambridge**

Lythgoe’s initial position at Cambridge was as an ‘assistant in research’, which he presumably considered an advance over his assistant lecturer post at Manchester. Todd had been appointed to the 1702 Chair of Chemistry, one of the senior professorships at the University of Cambridge that might reasonably be compared with the Lucasian Chair of Mathematics, the incumbents of which have included Isaac Newton (FRS 1672, PRS 1703–1727) and Stephen Hawking (FRS 1974). Todd and Lythgoe were separated in age only by six years, so the academic seniority gap was disproportionate to the age gap. Lythgoe was later promoted to a lectureship at Cambridge and obtained a fellowship at King’s College. Once he had moved to Cambridge, Lythgoe obtained the MA degree by incorporation. From then on in documents such as university calendars he gave his degrees as MA (Cambridge) PhD (Manchester) without reference to his BSc (Hons I) from Manchester. Professor Peter Gray
Figure 1. Structure of macrozamin.

(FRS 1977), a pupil of Lythgoe’s at Cambridge, says: ‘He [Lythgoe] always made me feel rather uncomfortable. I realise now that he was just as nervous as I was.’

Nucleosides were the dominant theme in the Todd–Lythgoe collaboration, both at Manchester (5–9) and at Cambridge (10–14). Francis Crick (FRS 1959) readily acknowledged that determination of the correct structure of DNA would not have been possible without the information on nucleosides and nucleotides provided by ‘Lord Todd and his colleagues’ (Brock 2004). The work concerned with adenine (6) is an obvious example of the usefulness of the work by Todd, Lythgoe and their colleagues to the determination of the DNA structure. The adenine–thymine base pair is one of the two ‘Watson–Crick pairs’ in the DNA structure (Watson & Crick 1953). Adenine is also a precursor to the nucleoside adenosine, synthesis of which is the subject of work by Davoll, Lythgoe and Todd (12). In another work authored by Davoll, Lythgoe and Todd (10), a means of breaking down an organic structure by oxidation with sodium metaperiodate is described. This method was subsequently widely used by others; for example, Weiss et al. (1959) apply it to amino sugars with an acknowledgement of what their work owed to that of Davoll, Lythgoe and Todd.

Once he became a lecturer, Lythgoe built up his own research programme, and there can be little doubt that he had Todd’s encouragement in doing so. His paper of 1949 is the first not to have either Heilbron or Todd among the authors (14). Nucleosides remained Lythgoe’s primary research activity up to the time of his departure from Cambridge for Leeds in 1953. That Lythgoe and Todd had a productive professional relationship is obvious, but that had run its course. There were no joint publications after 1948, and Lythgoe gets only the briefest mention in Todd’s autobiography, A Time to Remember (Todd 1983).

In a later work at Cambridge, Lythgoe investigated the structure of macrozamin, a very toxic natural substance (15–18). Macrozamin occurs in plants of the genus Macrozamia, which grow only in Australia. Plants of this genus have caused major loss of livestock in Australia, and by about a decade before Lythgoe’s work the toxic agent macrozamin had been isolated from a particular species of the genus, M. spiralis (Cooper 1940). Lythgoe was supplied with a sample of macrozamin taken from another species, M. Riedlei, and there began his work on the structure on macrozamin (16). Its full structure is now known to be as shown in figure 1.

Lythgoe drew particular attention to the azoxy group, and pointed out that it had not previously been encountered in a natural product. Later (15), he was to synthesize azoxymethane (see figure 2), a simple structure containing the azoxy group with obvious potential application to the laboratory synthesis of structures containing this group.
In later work independent of Lythgoe’s, though certainly invoking it in the interpretation, it was shown that the natural substance cycasin (figure 3) also has this nitrogen linkage (Nishida et al. 1955).

In 1958, five years after leaving Cambridge, Lythgoe was made a Fellow of the Royal Society, and his work on macrozamin and that on nucleosides both featured in the citation, which also praises Lythgoe for his ‘high experimental skill’. The experimental section of a research paper in organic chemistry often has to be quite lengthy because of the multiplicity of the operations. Obvious examples among very many of such operations are Soxhlet extraction, atmospheric and vacuum distillation, melting point determinations and running IR and UV spectra. Such operations in themselves are fairly pedestrian, and an undergraduate will obtain experience of some of them. When in a research project a large number of such operations have to be carried out in sequence to obtain a desired end, thoroughness and attention to detail are needed. Lythgoe’s ‘high experimental skill’ was manifest in his superb mastery of the laboratory procedures and his ability to apply and co-ordinate them in a complex research programme. The training of research students went hand in hand with that. During Lythgoe’s earlier research, aids that help simplify operations in the organic chemistry laboratory and make them more reliable, such as QuickFit glassware, were not available.

**Leeds**

*Research into alkaloids and vitamin D*

Lythgoe took up the professorship of organic chemistry at the University of Leeds in 1953, and was to remain there until his retirement in 1978. He succeeded Professor Frederick Challenger, who, like Lythgoe, was to live to be in his nineties. Lythgoe’s work on taxine alkaloids began in 1952 and continued well into the 1960s. Taxine alkaloids (note the plural) occur in yew trees and are poisonous. Isolation of a ‘nitrogen-free derivative’ of taxine 1 is described in his paper of 1958 (20). A structure for this was determined (25) and, in follow-up work using
nuclear magnetic resonance (NMR), this was found to be in error only in the position of the one exocyclic methylene group (25). The correct structure of taxine 1 is shown in figure 4. (In the ‘nitrogen-free derivative’ used in Lythgoe’s programme of work, the structure linked to the oxygen attached to the carbon at position 5 had been replaced by the O-cinnamoyl structure.) The methylene group at position 14 was investigated by placing a double bond at positions 13–14 and converting the oxygen attached to the carbon at position 13 to a methoxy group. When the resulting compound was studied by NMR the single ‘olefinic proton’ (25) at position 14 was identified, and that there had been a methylene group at that position in the original structure could be concluded.

At the time of this work on taxines, NMR had only fairly recently been introduced into organic chemistry and it enabled Lythgoe to finalize his determination of the structure of the alkaloid. He used to make clear to undergraduate students his view that methods such as NMR complement rather than replace classical organic chemistry approaches.

Calciferol (vitamin D2, see figure 5) features frequently in Lythgoe’s publications over a very long period. As he himself acknowledged (19), the structure of calciferol had long been known by the time Lythgoe began work on the substance as it had been one of the earliest natural products to be studied by X-ray crystallography (Bernal 1932). Cholecalciferol (vitamin D3) has a structure differing from calciferol only in the absence of one methyl group in the side chain attached to the five-membered ring. The triene structure is a feature of cholecalciferol and its ‘relatives’. In his paper from 1958 (21), Lythgoe described synthesis of this triene starting from a bicyclic $\alpha\beta$-unsaturated lactone. One of its rings was opened up and the structure made into a phosphorous (Wittig) derivative. Two such structures could then be made to combine to give the triene required. The procedure was equally successful when a different $\alpha\beta$-unsaturated lactone was used as the starting material. It might be noted that that was early days for Wittig reagents, and possibly Lythgoe saw that as one of the strengths of the work in the 1958 paper (21). Wittig himself received a Nobel Prize in 1979 for the contribution his reagents had made to preparative organic chemistry.

The cholestane structure, illustrated in figure 6, features in the biosynthesis of calciferol from cholesterol.
Some of Lythgoe’s work in this area consisted of laboratory conversion of cholesterol derivatives to cholestane derivatives (23, 24, 26, 27). One of his last research papers, published a year after his retirement, continues the theme of conversion of cholesterol derivatives to cholestane ones (28). Obviously this work was leading to a total synthesis of vitamin D3, and in an endowed lecture given a couple of years after his retirement (29) Lythgoe makes two points apropos of that. One is that total synthesis of vitamin D3 is very lengthy, making it ‘ineffective as a preparative method’ in comparison with partial synthesis from cholesterol. The other is that in biochemical investigations, vitamin D3 with isotopic labelling (carbon 13)
at selected sites is often required, and total synthesis is likely to be more suitable for that. Dudley H. Williams (FRS 1983) was one of Lythgoe’s PhD students who worked with him on calciferol. Williams’ career was to mirror Lythgoe’s in that he went from Leeds to Cambridge to work with Todd.

There is an intriguing aspect to Lythgoe’s research career. His work on nucleosides was relevant to the determination of the structure of DNA. The respective roles of model building and of X-ray crystallography in the determination of the DNA structure have been the subject of a great deal of discussion and comment (e.g. Maddox 2002). Calciferol was one of the early natural substances to be investigated by X-ray crystallography, as noted previously, and largely through the work of Dorothy Hodgkin (FRS 1947) other structures, including vitamin B12 and insulin, were later to be determined by this method. When Lythgoe was a student at Manchester, W. L. Bragg (FRS 1921), by then a Nobel laureate, held the Langworthy chair of physics at the university. All of this would have raised Lythgoe’s awareness of the advances in X-ray crystallography. In expressing his admiration for Hodgkin’s work on vitamin B12, Todd prophesied that X-ray crystallographers might ‘put organic chemists out of business’ (Ferry 1998). Would Lythgoe have expressed that view, even in a tongue-in-cheek manner as Todd probably had? In his calciferol work, Lythgoe’s concentration on intermediates in its biosynthesis and their production in the laboratory represents the effective complementarity of the crystallographer’s art and the organic chemist’s.

Chemistry at Leeds and headship of the chemistry department

Lythgoe moved to the chair of organic chemistry at Leeds in 1953, as noted. The professor of inorganic chemistry at Leeds at that time was E. G. Cox (FRS 1954), and the professor of physical chemistry was F. S. Dainton (FRS 1957). The three professors were therefore all elected FRS at about the same time. Lythgoe was the only one to remain in his chair at Leeds until retirement age. Cox, like W. H. Bragg, was the father of another FRS; his son was the geologist Keith Cox (1933–1998, FRS 1988).

The organic chemistry department at the time of Lythgoe’s arrival had a number of staff in his approximate age bracket, including A. T. Austin, who, having graduated at the University of Melbourne, came to England to do a PhD at University College London under C. K. Ingold (FRS 1924). There was also P. A. Briscoe, who had graduated at Bristol and, after war service, studied for a PhD at Leeds under Challenger. The older staff included J. W. Baker, E. A. Rothstein and W. A. Wightman.

At that time the UK universities were expanding, and Lythgoe was able to make many new appointments. They included J. E. Saxton, who, prior to coming to Leeds in 1956, had worked successively with Sir Robert Robinson (FRS 1920, PRS 1945–1950) and R. B. Woodward (ForMemRS 1956). B. E. Cross, another Lythgoe appointee, came to Leeds aged about 40, having previously been at the ICI Akers Research Laboratory where he had conducted distinguished research into plant hormones. F. G. Holliman, who was appointed to a personal chair in the department of organic chemistry in 1966, had previously held a chair at the University of Cape Town. As well as conducting his own research programme and teaching the whole of the first year organic course, he did about 50% of the administration of the department, an arrangement which worked well enough.

Lythgoe was a little dated in his policies as a head of department. Each member of the staff could expect to be assigned one or two research students and a suitable budget; they were not
Figure 7. Basil and Kate Lythgoe with two of their grandchildren at Newby Hall in North Yorkshire, 1985. (Online version in colour.)

encouraged to apply for external funding for further research students and postdocs. He was also rather isolationist. The school of chemistry coffee bar was a venue for social intercourse between lecturers and students, but Lythgoe’s staff were discouraged from using it. Instead he arranged for coffee to be served to the organic chemists at a fixed time each morning and afternoon in one of the tutorial rooms. He lectured only to final-year undergraduates, which meant that those who did inorganic and physical chemistry in their final year instead of organic and inorganic, or (like the writer of this memoir) organic and physical, were not taught by him at all. However, his former research students speak of him in positive terms and acknowledge his willingness to give them strong references for ‘life after Leeds’. Colleagues and former students all acknowledge Lythgoe’s profound knowledge of organic chemistry.

At the initiative of Vice-Chancellor Edward Boyle, Lythgoe’s retirement from Leeds was marked by a symposium on natural product chemistry. Lythgoe’s formal correspondence with Boyle includes a statement of deep concern that the education cuts of the 1970s would lead to there being too few new university teachers to sustain academic excellence. He was referring to organic chemistry, which he thought might become a ‘dark continent’, but that was an issue across all academic disciplines in all universities in the UK.
FAMILY MATTERS AND FINAL YEARS

Before he retired from Leeds, Lythgoe had the satisfaction of seeing his sons graduate: John in electrical and electronic engineering at the University of Birmingham and Andrew in materials science at the University of Liverpool. Both followed industrial careers and were to marry and have families. Two of John’s three children feature in the photograph at figure 7.

Kate Lythgoe died in 2003. Shortly afterwards Lythgoe moved from Leeds to Worcestershire where his younger son, Andrew, and his family were living. Towards the end he suffered from dementia.

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The portrait photograph was provided to the Royal Society by the subject. It was taken by Bassano Portrait Studios (copyright unknown).

AUTHOR PROFILE

Clifford Jones

Clifford Jones is a graduate of the University of Leeds (BSc 1974, PhD 1977, DSc 2005). He has held academic posts at Macquarie University, the University of New South Wales and the University of Aberdeen. His research activity in fuels and combustion has led to a large number of publications from the early 1980s to the present time. He has written 30 books, the most recent of which is about nuclear powered generation of electricity. Topics of his other books include coal science, hydrocarbon process safety, temperature measurement, fire protection engineering and offshore oil and gas decommissioning. In 2019 he was awarded a Distinguished Fellowship of the Royal Australian Chemical Institute. His current affiliations are the University of Chester where he is a Visiting Professor and the University of Aberdeen where he is Reader Emeritus. He is deeply interested in scientific biography and has written a number of entries for the Oxford Dictionary of National Biography.

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