

ARTHUR JOHN BIRCH
3 August 1915 — 8 December 1995



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Elected FRS 1958

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Arthur John Birch AC CMG FAA FRS was one of the great masters of organic chemistry of the twentieth century. His extraordinary creativity left its imprint across the breadth of the subject in its broadest sense, from synthesis to biochemistry to organometallic chemistry. He remains best known for the reaction that bears his name, the Birch reduction of aromatic compounds by solutions of sodium and ethanol in liquid ammonia. This process has wide application, most notably in the commercial synthesis of oral contraceptives, giving rise to his being called ‘the father of the pill’, although he himself preferred the more remote ‘grandfather’ relationship. His polyketide theory, which accounts for the biosynthetic origins of a wide range of natural products, is less widely acknowledged today simply because it has become absorbed into the accepted knowledge base of the subject. His final researches on the use of diene iron tricarbonyl derivatives in synthesis are equally distinguished and have prompted others to extend their application. During his career he was involved in the design of three new university chemistry buildings, one of which now bears his name, and contributed influential advice to governments on national science policies.

The authors of this memoir knew Arthur Birch from complementary perspectives. Rod Rickards was as an undergraduate at Sydney University when he first met him in 1954, on a crowded evening tram going home down George Street. Banter with a fellow student suggested that the unknown Professor of Organic Chemistry was quite a lad, who worked on things like sex hormones. A quiet voice alongside them said, ‘You want to be careful what you say on these trams, you never know whom you are sitting next to.’ It was immediately apparent who sat alongside them. The Professor was undoubtedly more amused than the petrified students, and at a post-retirement symposium in his honour in Canberra in 1981 Birch recounted the incident with glee. In between these events Rod attended Birch’s undergraduate

lectures, became one of his research students, initially in Sydney and then in Manchester, and one of his staff in Manchester and Canberra. Finally he had the sad honour of speaking at his funeral.

John Cornforth was a year behind Birch at Sydney University and followed him to Robinson's laboratory at Oxford. He married Rita Harradence, Birch's contemporary at Sydney, who also went to Oxford one year after Birch. The three were lifelong friends.

EARLY YEARS

Arthur Birch was born in Sydney on 3 August 1915, the only child of Arthur Spencer Birch and Lily Bailey. His father was born in Northamptonshire, England, left school at the age of 12 years and home at 14, and then lived in Canada, Fiji and New Zealand, where he met Lily. Lily was born in central Tasmania but had emigrated to New Zealand at 27 years of age, and was 37 when they married. Arthur was born a year later, after the couple moved to Sydney. His father became pastry chef at a major Sydney hotel, and later was manager of Woolworth's cafeterias. Arthur 'sauntered carelessly through primary school' in the suburb of Woollahra but became interested in science. His father encouraged this with some apparatus and books bought with a legacy from an aunt, and Arthur 'taught himself organic chemistry' from about the age of 12 years. With his father now ailing, he was selected to go to the renowned Sydney Technical High School, where he did well academically while pursuing his own initiatives.

Chemistry initially fascinated him aesthetically rather than intellectually, although in later years he was clearly moved by the intellectual 'highs' that came from being the first to see and understand fundamental truths of chemical and biological behaviour. The beautiful natural product chemistry of the Australian bush intrigued him, with its range of odours from eucalypt trees, brilliant flower colours, and strange coloured resins exuding from the trunks of eucalypts and grass trees. He was to return to all these themes in due course as a scientist.

CAREER PATH

Sydney, 1933–38

Sydney University, the oldest in Australia, was then the only university in the state of New South Wales, with about 3000 students. Its first Professor of Organic Chemistry was Robert (later Sir Robert) Robinson (FRS 1920), from 1913 to 1915. In his final school examination in 1932 Arthur Birch was ranked third in chemistry in the state, winning a Public Exhibition exempting him from university fees. His rivals included Rita Harradence, later to become Lady Cornforth, who topped the state. These were the years of the Depression. His father was declining and died in 1937, so his family could offer him little more than accommodation. To pursue his desire to learn he washed bricks, coached other students, and won the only scholarship available at the end of his first year. The Sydney Chemistry Department in the 1930s lacked resources and ready access to the international chemical world, but its undergraduates were rich in talent and made their own fortunes. Birch's competition with Rita Harradence continued, and on graduation at the end of their honours year in 1936 they were to share the University Medal in Chemistry. Ern Ritchie (later professor at Sydney University) was in the same year, Allan Maccoll (professor at University College London) was a year ahead, and a

year behind were John Cornforth (Nobel laureate) and Ron (later Sir Ronald) Nyholm (FRS 1958) (also professor at University College London).

Birch's formal entry into research began in his fourth year, the honours year in the Sydney system. His honours degree and MSc supervisor, Professor J. C. Earl, gave him a bottle of *Eucalyptus dives* leaf oil, a by-product of piperitone production, and then went on sabbatical leave. The result was five publications, four with Birch as sole author, on monoterpene natural products. The schoolboy's interests were bearing fruit. In 1938 he was awarded a scholarship of the Royal Commission for the Exhibition of 1851 to study for a doctoral degree in England. No PhD degrees were awarded in Australia then, and there were few opportunities for those with such degrees, so he chose to work with Robert Robinson in Oxford and sailed from Sydney as World War II developed in Europe.

Oxford, 1938–48

Birch's 10 years at Oxford, 1938–48, were not normal years for anyone alive at that time. A letter from him, written shortly after he started work at the Dyson Perrins Laboratory (DP), expressed pleasure at the ready availability of chemicals and disgust at the quality of the apparatus and equipment. Robinson had given him a problem of synthesis based on a speculation, later found to be baseless, that the peculiar lipids of mycobacteria contained fatty acids doubly branched at the positions next to the carboxyl group. Methods for the preparation, separation and handling of such compounds were largely undeveloped at the time. Birch did a creditable job with the preparation and gained his DPhil from the work in 1940. He never worked with fatty acids again. His predoctoral years were darkened by the approach and outbreak of the war in Europe.

Oxford was never bombed, and workers in the DP shared the life of most civilians in Britain: the blacked-out nights, the multifarious shortages and the resulting queues (even for films), the nutritionally adequate but uninteresting food (someone mistranslated the motto *Alchymista spem alit aeternam* above the DP entrance as 'Eternal Spam nourishes the chemist') and, for the first two years and more, the increasingly ominous news. In practice, people adapted: finding, for example, the Zionist restaurant that could make boiled red cabbage palatable by cooking it with vinegar and a little spice, or the pub that sporadically dispensed draught cider. Birch joined the Home Guard ('Dad's Army'); his autobiography (18)* comments on it with characteristic wry humour.

Robinson was soon involved with numerous committees directing the contribution of science to the country's war effort. He could not devote much time to his students and he had no deputy. This meant that students were unusually free to follow their own ideas: this was excellent for those who could think for themselves and learn from their work and from interaction with able peers, but less so for those who expected to be taught.

A certain amount of support was available for postdoctoral workers, and after his DPhil Birch became, mysteriously, an ICI employee to whom a government grant was funnelled. His brief was to synthesize analogues of steroid hormones. His autobiography (18) gives a fascinating account of the complications caused by his success (ICI was bound by cartel agreements, and Robinson was bound by a promise to send all samples for testing to Sir Charles Dodds (FRS 1942)). That work, by that recalcitrant junior, laid the foundation for what is today an immense industry.

* Numbers in this form refer to the bibliography at the end of the text.

In 1941 Cornforth assembled some indications from the literature and showed that 2-methoxynaphthalene could be reduced by sodium in boiling ethanol to an enol ether readily hydrolysed by acids to 2-tetralone. A paper recording this procedure and some developments was published (with Rita Cornforth and Robinson) (Cornforth *et al.* 1942). Birch saw how much more useful this discovery might be if it could be applied to benzenes, which are less easily reducible than naphthalenes. He searched the literature and found an initially fortuitous discovery by C. B. Wooster in 1937 (Wooster & Godfrey 1937; Wooster 1939) that benzene, toluene and methoxybenzene could be reduced to dihydro derivatives by sodium and ethanol in liquid ammonia. Early in 1943, Birch tried this procedure with methoxybenzene. Physical techniques were primitive in those days, and chemistry was often needed to find out what was happening. He added a little of his reaction product to a solution of dinitrophenylhydrazine in hydrochloric acid. A slowly developing crystalline yellow precipitate dissolved when the mixture was heated and was redeposited as beautiful orange-red crystals. That test-tube experiment said it all: the addition of hydrogen was necessarily to the 2- and 5-positions of methoxybenzene. The enol ether group was hydrolysed by the acid to cyclohex-3-enone and thence by slower isomerization to cyclohex-2-enone, each of which formed its characteristic coloured derivative with the hydrazine. The Birch reduction was born (1). Birch spent much time, despite Robinson's disapproval, exploring and developing the reaction.

The most direct application of the new method to the preparation of steroid hormone analogues was the conversion of oestradiol glyceryl ether into 19-nortestosterone by way of an unconjugated isomer. Robinson provided only 0.5 g of oestrone and refused a further supply when the first experiments showed practical difficulties. The situation was saved by Gilbert Stork, who generously gave Birch 5 g of oestrone. 19-Nortestosterone proved to be a potent anabolic androgen, and the unconjugated isomer was an oestrogen. Part of the enormous importance of these artificial hormone mimics is that variations in structure can lead to specific biological effects, whereas with natural hormones effects are sometimes multiple and influenced by transformations *in vivo*.

Although the Birch reduction was certainly his principal achievement at Oxford, Birch made several contributions to some of Robinson's schemes for steroid synthesis, including a widely applicable method for the introduction of angular methyl groups.

Almost the last event of Birch's Oxford days was his marriage to Jessie Williams, an event seen by all his friends as the best thing that could have happened to him.

Cambridge, 1949–52

In January 1949 Birch moved to Cambridge University as Smithson Fellow of the Royal Society. This appointment carried prestige, reasonable remuneration, and an independence that unfortunately precluded him from receiving university research support other than through the generosity of Sir Alexander (later Lord) Todd FRS, who was a good friend to Birch on several occasions and whose opinion Birch respected greatly, especially on administrative matters. Todd allocated him Herchel Smith as a PhD student, a fortunate event that would later have major ramifications. In contrast to Oxford, the Cambridge laboratory facilities were excellent, and they made good progress with steroid synthesis directed towards androgenic and progestational hormones.

By Birch's own admission, however, he was at that time becoming rather bored with synthesis, and the surrounding research projects of Todd and others reawakened his interest in natural products. Initially this found expression in deducing the correct structures of published

natural products, and in collaborating with others to define the structures of new compounds. Much more significant for the subsequent development of organic chemistry, however, was his increasing interest in biosynthesis, the detailed process whereby natural products are formed by enzymes in living systems. This would become Birch's second major contribution to science.

Alone after her husband's death, Birch's mother, Lily, had followed him to Oxford in 1939. During the progressive development of Parkinson's disease, Birch had cared for her largely on his own, until the advent of Jessie Williams as her nurse in 1947. Lily Birch accompanied the newly married couple to Cambridge, and died there in 1951. In the same year Birch was invited to accept the Chair of Organic Chemistry at his alma mater, Sydney University, and with his wife's concurrence he decided to accept this challenge. After 14 years' absence he was homesick for Australia, and it would be a better place in which to bring up their three young children than postwar Britain.

Sydney, 1952–55

In 1952 Birch returned to Sydney to take up his first tenured academic appointment, as Professor of Organic Chemistry and Head of Department in a chemistry school of nearly 1000 students, with little teaching and less administrative experience. The chair had been vacant for several years, even its continued existence the subject of university controversy. The Depression and war years had passed, but the department still lacked resources and international contacts. The laboratories in sandstone buildings around the Vice-Chancellor's quadrangle ('the vice quad') were ancient and poorly equipped. Spectroscopy was limited to a manually driven ultraviolet spectrometer, and the small bottle of the novel solvent tetrahydrofuran could be used only if 90% could be recovered. The state government provided finance for a new building by mistake, confusing chemistry with pharmacy, but honoured its public commitment. This was the first of three such building designs with which Birch was to be involved, although the building itself was not erected until after his departure from Sydney in 1955.

The research projects chosen had to make the most of these facilities, in the hands of research students who mostly did only honours or master's degrees. Those who wanted to pursue a doctorate still usually went to England, although it was now possible in Sydney. Birch's classic publication on the biosynthesis of phenolic natural products, 'Studies in relation to biosynthesis. Part 1', embodying ideas developed largely in Cambridge, was published by the *Australian Journal of Chemistry* in 1953 (3), having been rejected by the *Journal of the Chemical Society* on the grounds that it lacked experimental support. Proof of the hypothesis required the radiolabelled compounds that were now becoming available as a result of developments in isotope technology during the war. With financial assistance from the Nuffield and Rockefeller Foundations to buy ^{14}C -labelled acetate and to train students in its use, the first experimental support for the acetate hypothesis was presented in 1955. These students were shortly to follow their supervisor to England.

Birch also accomplished some structural work on natural products and some synthetic chemistry in Sydney, but the research environment was too restrictive. In 1954 he was elected a Fellow of the newly formed Australian Academy of Science. In 1955 he declined an offer of a foundation chemistry chair in the Research School of Physical Sciences at the new Australian National University (ANU) in Canberra. It would be 12 years before he joined the ANU, taking instead the renowned organic chemistry chair at the University of Manchester

vacated by Professor E. R. H. (later Sir Ewart) Jones FRS on his way to Oxford. His dissatisfaction on leaving Sydney in late 1955 prompted newspaper headlines like 'Beggars in mortarboards. Why the professor resigned.' The departure for England of Birch and other senior chemists was a factor leading to the subsequent reorganization of Australian universities under Commonwealth rather than State auspices and funding. Birch later dryly suggested, 'I probably made my best contribution to the Australian university system by then publicly quitting it'.

Manchester, 1956–67

Manchester was different. The Australian students who joined Birch in the industrial, commercial and cultural centre of northern England were used to the brilliant clear light and the sand and surf of their own country. They now frequently found themselves in thick, damp smog, at times barely able to see street lights glinting through the gloom at midday. They drank warm beer with the locals, learned to understand the North Country accent, watched Manchester United play football, and cheered the Australian cricketers at Old Trafford. Birch, too, liked the people, and the city because 'it was easier to get out of than, say, London'. But the 'red brick' university dating back to 1851 was also different from Sydney, and its faculty lists, which included Nobel laureates, reflected the illustrious scientific tradition that Birch felt honoured to join.

Birch's research flourished. In Cambridge he had realized that microorganisms rather than higher plants were the preferred vehicles for experimental biochemistry. They were prolific producers of the phenolic compounds in which he was interested, and could be grown readily in the laboratory. The Manchester Chemistry Department already had such a facility, established by Birch's predecessor, E. R. H. Jones. He now appointed Herchel Smith, his PhD student from Cambridge, to the lecturing staff, and they collaborated on biosynthetic research. Herchel learned and introduced radiotracer techniques, which greatly accelerated the biosynthetic studies. Direct quantitative ^{14}C assay of compounds was performed on open planchettes under an end-window Geiger counter, avoiding the cumbersome combustions to carbon dioxide gas and thus leaving the compounds available for further purification or degradative chemistry. The low counting efficiency was offset by the competence and convenience of the producing microorganisms.

Herchel Smith and Birch also resumed their Cambridge collaboration on sex-hormone synthesis, until Herchel wanted independence in this area and Birch withdrew. Herchel was highly successful, ultimately achieving an effective total synthesis of norgestrel and its analogues, which were to become widely used constituents of modern oral contraceptives. The basic chemistry was conducted in Manchester, but no patents were then filed. In 1961 Herchel moved to Wyeth Pharmaceutical Industries in Pennsylvania as Research Director, taking with him two Mancunian PhD students who happened to be in the right place at the right time. Subsequent royalties enabled Herchel Smith to retire in 1973; at his death in 2001 his estate value was estimated in excess of £100 million. He generously bequeathed some £90 million to be shared between his alma mater Cambridge University and Harvard University, supplementing the £15 million given to Cambridge during his lifetime. Birch's work on the reduction of aromatic rings was crucial to this success, a fact that gave him intellectual satisfaction.

During this period Birch used intermediates prepared by his metal-ammonia reduction chemistry in several areas apart from the steroid work. On the one hand they were elaborated by various means to natural products; on the other they were reacted with metal carbonyls to provide the organometallic species that were to interest Birch until his retirement.

The old Manchester laboratories had been periodically extended since their opening in 1872, when they were considered the best in the country (Burkhardt 1954), and now had character and history but were outdated and inflexible. They were reasonably equipped with ultraviolet and infrared spectrometry, and the physical chemists might allow their mass spectrometer to be used for organic work if the sample was volatile. But organic chemistry was changing rapidly, with increasing dependence on sophisticated instrumentation. Fortunately, Associated Electrical Industries (AEI) was making the world's best mass spectrometers only a few miles away, and AEI's development engineers were happy to test the capabilities of instruments on their production line. In due course a new chemistry building was designed and built, and in its turn it became the best equipped in the UK. Organic mass spectrometry became routine with the acquisition of the classic AEI MS 9 spectrometer. Proton nuclear magnetic resonance (NMR) spectrometry was emerging from the realm of physics to revolutionize organic chemistry, so the government commissioned AEI to design and build NMR spectrometers to save England from having to import state-of-the-art American Varian instruments. After much delay the department acquired one, which detected passing buses better than precessing protons and was superseded in the new building by a Varian A60.

The advent of such instrumentation changed the face of natural product chemistry worldwide. Birch's structural work in Sydney and initially in Manchester was primarily of the classical type, dependent on microanalyses to indicate molecular formulae, reaction chemistry to establish functionality and to break structures apart, the occasional use of ultraviolet or infrared spectroscopy, and analytical reasoning. To this he had added his own requirement of biosynthetic rationality, at times convincing in itself. Mass spectrometry now defined precise molecular formulae and suggested structural fragments, whereas ^1H NMR spectroscopy looked directly at the intact molecule, mapping hydrogen atoms and their environments. Birch recognized the importance of these advances and ensured they were available, but he was not one to tie himself to technology. Instead, once his biosynthetic hypotheses were firmly established by experiment on known compounds, he reversed the logic and used radiotracer incorporations *in vivo* to assist the structure determination of unknown natural products. This innovative although somewhat cumbersome approach was valuable in difficult cases but was soon surpassed by the increasing power of NMR analysis alone. Much later, with the availability of ^{13}C -labelled compounds, the two techniques would successfully merge, until direct spectrometry again prevailed.

Birch was elected to the Fellowship of the Royal Society in 1958 and became established as one of the world's leading organic chemists. Scientific conferences, connections with industry (notably Syntex in Palo Alto and Mexico City, and Roche in Basle), periods in Nigeria to establish research, and even the occasional family holiday drew him away from the department, where research students jokingly appointed him to the BOAC Chair of Chemistry (after the national airline, the British Overseas Airways Corporation). A less sympathetic undergraduate referred to 'the occasional smell of stale cigar smoke in a lift'. Although not inclined towards overall university administration, he nevertheless promoted departmental interests, setting up and chairing the first Department of Biological Chemistry in Manchester.

One conference Birch attended was the 1st IUPAC (International Union of Pure and Applied Chemistry) Symposium on Natural Products, held in Sydney, Canberra and Melbourne in 1960. In Canberra the establishment of a Research School of Chemistry at the ANU was discussed, with Birch and Professor David Craig (FRS 1968) and Professor Ronald (later Sir Ronald) Nyholm (FRS 1958), now both at University College London, as the three

Foundation Professors. Craig had been a professorial colleague of Birch's in Sydney, whereas Nyholm had been at the New South Wales University of Technology. This unique but onerous opportunity was ultimately accepted only by Birch and Craig; Nyholm decided to stay in England. Imaginatively code-named 'Project C' by the ANU to prevent premature exposure (Foster & Varghese 1996, pp. 229–234), the basic building was designed in a flat in Half Moon Street, London, by Melbourne architects in close consultation with all three covert 'Advisers'. The ANU supported PhD scholars and postdoctoral fellows in Manchester and London from 1965, who transferred with the professors to Canberra in 1967.

Canberra, 1967–80, and retirement

Canberra was different, too. The remarkable ANU was and still is unique, not only in Australia. Conceived to provide research and postgraduate training to rebuild the nation after World War II, it inherited undergraduate faculties from the Canberra University College in 1960. Prominent expatriates were recruited to lead the generously funded research schools in its Institute of Advanced Studies, and chemistry was the fifth to be established. 'Project C' emerged from a hockey field as a structurally elegant and technically efficient building, with the internal flexibility needed for a rapidly advancing science, and laboratories designed for sophisticated instrumentation. For the organic chemists there was then a mass spectrometer and a 100 MHz ^1H NMR spectrometer; by 2004 the school would run six mass spectrometers, and six NMR spectrometers operating from 200 to 800 MHz. The Research School of Chemistry was officially opened by Birch's Cambridge mentor, by this time Lord Todd of Trumington, in 1968.

Counter to ANU practice and causing opposition from those who believed that 'nothing should be done for the first time', the 'Advisers' had prescribed a school comprising research groups without the traditional departmental divisions, overseen by a Dean rather than a Director, and sited adjacent to the existing Chemistry Department to promote interaction. Birch was the Dean Elect from 1965, and Foundation Dean from 1967 to 1970. He served again as Dean from 1973 to 1976, and retired as Foundation Professor of Organic Chemistry in 1980. The school's prime purpose was to conduct fundamental research at the highest international level, some aspects of which had potential application to Australian industry and national interests. In so doing it would provide opportunities and training for young Australians, both at home and overseas. The school's research record into the twenty-first century has vindicated the judgement of its founders. The main building of the Research School was named in honour of Arthur Birch at a ceremony, which, despite failing health, he attended with great satisfaction in August 1995.

Birch's personal research in Canberra developed his Manchester themes further, but with increasing emphasis on the organometallic chemistry of tricarbonyliron complexes with organic ligands. Metal–ammonia reduction provided the cyclohexadiene ligands, the reactivity of which was substantially altered and stereospecifically controlled by the transition metal attached laterally in a reversible fashion. Efficient syntheses of highly functionalized natural products emerged, but the concepts and methods were general and lent themselves to exploitation. With his major biosynthetic hypotheses now confirmed and the results of isotope incorporation studies becoming routine, this area was gradually phased out. Natural product studies were initiated using the new automated countercurrent distribution apparatus to resolve complex mixtures, such as the phenolic resins from Australian grass trees that he had observed as a youth, but also gave way to the new developments in organometallic research.

In 1980 Birch reached the then mandatory retirement age of 65 years. In February 1981 the Research School of Chemistry honoured his achievements and contributions with a major symposium, involving participants from across Australia and overseas. Professor Albert Eschenmoser (ForMemRS 1986) of the Eidgenössische Technische Hochschule, Zürich, gave the inaugural Birch Lecture, since then an annual event on the school's calendar. At the symposium dinner Birch was presented with the Leighton Memorial Medal of the Royal Australian Chemical Institute (RACI) (its most prestigious medal, awarded 'in recognition of eminent services to chemistry in Australia in the broadest sense') by the Governor-General of the Commonwealth of Australia, His Excellency the Right Honourable Sir Zelman Cowen, and delivered the Leighton Address on 'Creative and accountable research' (15). Shortly afterwards, he took up the inaugural Newton–Abraham Visiting Professorship at Oxford, returning to the ANU in 1982 as a University Fellow in the Department of Chemistry. In 1987 he was awarded the Tetrahedron Prize for Creativity in Organic Chemistry. In 1994 the RACI made him one of their few Honorary Fellows, and in 1996 the Organic Chemistry Division of the Institute named their premier award in his honour.

The establishment of the Research School at the ANU demanded more of Birch's time in onerous school organization and broader university administration than at Manchester, particularly during the periods of his deanship. This drawback was partly offset by the absence of undergraduate teaching responsibilities, but far greater compensation came from observing the success of his endeavours. Demands on his time from outside the university also increased, which as a professional scientist he felt a moral obligation to meet both before and after his retirement. He was appointed Treasurer of the Australian Academy of Science from 1969 to 1973, Vice-President and then President of the Royal Australian Chemical Institute in 1977–78, and was elected President of the Australian Academy of Science from 1982 to 1986. During his Presidency of the Academy he was instrumental both in reorganizing and in securing much needed headquarters for its administration. The offices now occupy an elegantly refurbished 1927 government hostel, which retains its distinctive original exterior and is listed on the Register of Significant Twentieth Century Architecture, adjacent to the 'Dome', a Canberra architectural landmark housing the conference hall of the Academy.

As an international scientist of standing, Birch's advice was also extensively sought beyond academia by governments in Australia and overseas. One of his major undertakings was to chair the 1976–77 Independent Inquiry into the Commonwealth Scientific and Industrial Research Organisation (CSIRO), the large and widespread Australian government research body (12). The inquiry reaffirmed the role of the CSIRO as strategic, mission-oriented research in the national context. It proposed radical changes to its long-standing structure, however, including notably the grouping of the many operating units of the organization, the Divisions, into six Institutes under an Advisory Council and Executive. Most of the recommendations were accepted and implemented by the government, not entirely to the joy of the scientists involved; subsequent changes built on these recommendations. He was appointed Foundation Chair of the Australian Marine Sciences and Technologies Advisory Committee from 1978 to 1981. In 1987 he was made a Companion of the Order of Australia (AC) for his contributions to science in Australia.

At the international level, he was an examiner for the Organization for Economic Cooperation and Development (OECD) on Science and Technology Policy in Denmark. For an extended period from 1979 to 1987 he was Consultant to the UNESCO Development Programme project 'Strengthening research and teaching in universities' in the People's

Republic of China, and made six visits to that country, advising on technical and laboratory management and instrument centres. International honours included appointments as Academician of the USSR Academy of Science in 1976 and Foreign Fellow of the Indian National Academy of Science in 1989.

Birch's scientific autobiography, incisively entitled *To see the obvious*, was written over the last 10 years of his life for the American Chemical Society series 'Profiles, pathways and dreams. Autobiographies of eminent chemists' (18). With Arthur now seriously ill, the editor and publishers responded to an urgent request from Jessie Birch, and it was published just before his 80th birthday in August 1995.

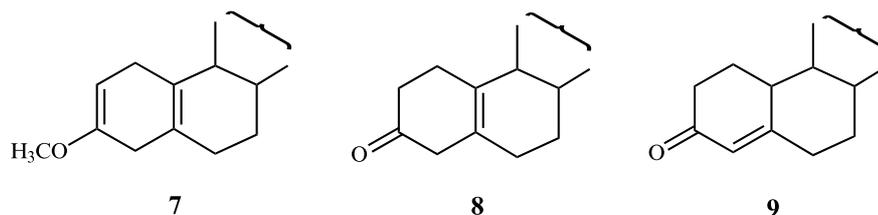
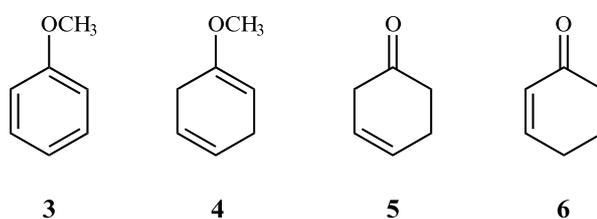
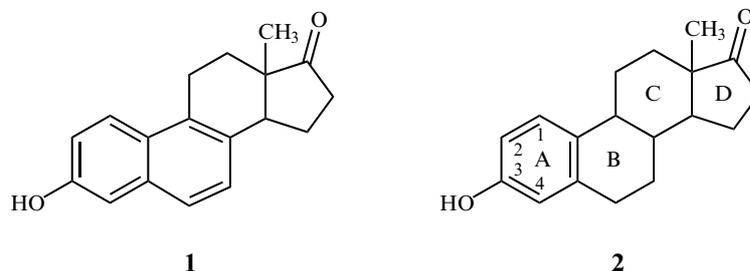
SCIENTIFIC RESEARCH

Birch's scientific research is described in more than 400 publications, which range in subject matter from organic synthesis to biochemical processes and organometallic chemistry. In this memoir we can do no more than attempt to outline the origins, essence and significance of his three major research themes: the Birch reduction, his polyketide theory of biosynthesis, and his studies of the organic chemistry of transition metal complexes.

The Birch reduction

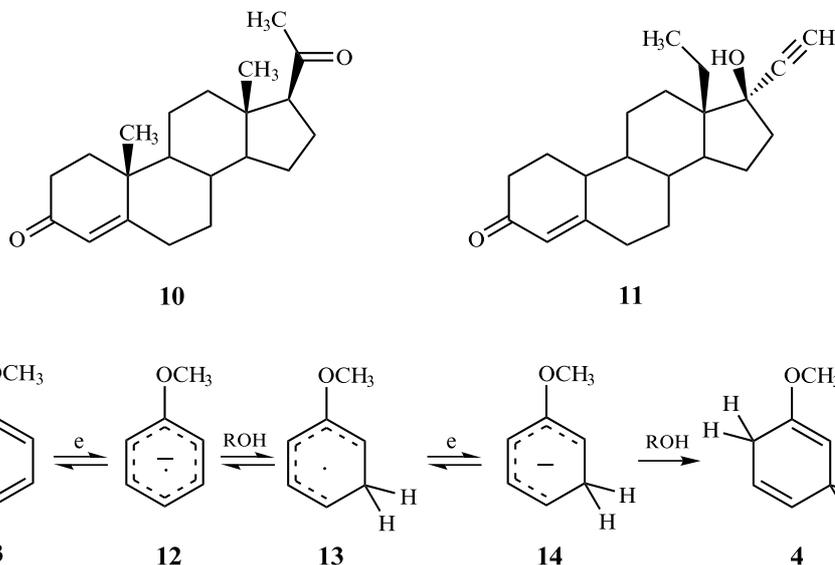
Solution of the structures of many steroids during the 1930s led immediately to efforts to bring these biologically important compounds into the domain of synthetic organic chemistry, which at that time was heavily biased towards derivatives of benzene and other aromatics readily supplied by the distillation of coal. Thus, sterols tended to be seen as 'hydroaromatic' compounds. It is no coincidence that the first steroid to be synthesized was the naphthalenoid equilenin (**1**) and that the second was oestrone (**2**). Alicyclic chemistry had been stimulated by work on the essential oils, but synthetic methods and control of stereoisomerism were still rudimentary. Methods for reduction were especially backward. Metallic sodium in association with alcohols was one of the more powerful reagents: it could, for example, reduce esters to alcohols and could add two hydrogen atoms to many naphthalenes but it was largely ineffective for reducing solitary benzene rings. For that, hydrogenation over large amounts of platinum black or at high pressures and temperatures over nickel or copper–chromium catalysts was the most general method; however, it was stereochemically indiscriminate and it could alter or remove functional groups. Full appreciation of aromatics in steroid synthesis was also delayed by a curious failure to recognize that vinyl ethers are easily hydrolysed by mild acids to carbonyl compounds. Methoxyl groups on aromatic or saturated carbon atoms need vigorous methods for cleavage—the classical reagent is boiling hydriodic acid—and it seemed to be taken for granted that vinyl ethers would be similarly resistant.

Birch's crucial experiment in 1943, already outlined in the section on his Oxford days, combined two recent discoveries: that solitary aromatic rings could add two hydrogen atoms when treated in liquid ammonia with a combination of sodium metal and an alcohol, and that vinyl ethers were excellent sources of carbonyl compounds. Thus his methoxybenzene (**3**) gave, on reduction, the 2,5-dihydro derivative (**4**), which was hydrolysed by mild acid to cyclohex-3-en-1-one (**5**) and thence by acid-catalysed isomerization to cyclohex-2-en-1-one (**6**) (1). Several important steroid hormones are formally derivatives of cyclohexenone; in addition, cyclohexenones are useful intermediates for further synthesis. In Birch's hands



phenolic ethers became packaged cyclohexenones, stable to many manipulations of functional groups elsewhere in the molecule and unpacked by a procedure that left many of these groups untouched. In a series of mostly single-author papers published between 1944 and 1950, Birch laid the foundations of this uniquely useful and, as it turned out, timely method (2). Dialkylaminobenzenes were shown to be reduced in the same manner as alkoxybenzenes (a procedure that has perhaps received less attention than it deserves). Allylic and benzylic alcohols were deoxygenated. The technical difficulty—that many substrates were insoluble in liquid ammonia—was palliated by substituting 2-hydroxyethyl or glyceryl ethers for the usual methyl ethers. Other workers, later, found that lithium was preferable to sodium in some special cases. Birch's original assignment to synthesize analogues of steroid hormones was to succeed beyond measure—but largely in other hands.

Herchel Smith, his graduate student at Cambridge and his colleague at Manchester, devised along with others some commercially practical methods for synthesizing oestrone (2) and many analogues, and the last intermediate in these syntheses was almost always a methoxybenzene. When the Birch reduction was applied to these intermediates, hydrogen was added at the 1- and 4-positions (steroid numbering), and the products (7) by acid-catalysed hydrolysis and rearrangement gave enones (8) and (9). The structural element (9) occurs, of course, in many natural androgens and progestogens as well as in the adrenal hormones, but these also feature an angular methyl group between rings A and B, as in progesterone (10).

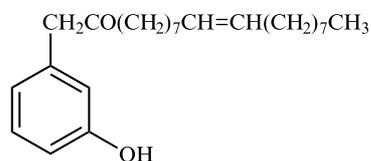


The synthetic enones lacked this angular methyl group between rings (A) and (B). It was possible, although inefficient, to introduce it via halocarbene addition to suitably protected intermediates (**8**). However, the principle of the contraceptive pill (daily oral intake of a combination of progestogen and oestrogen) had meanwhile been discovered and, unpredictably, many synthetic compounds devoid of this angular methyl group were found to be equal or superior (for this purpose) to the natural hormones. The progestogen norgestrel (**11**) made Herchel Smith a multimillionaire.

Although the Birch reduction is a practical method *par excellence* (**10**), Birch felt bound to understand its mechanism: why were the protons added where they were, and what was the role of the alcohol? His final paper on this subject was a collaboration with Leo Radom, who used *ab initio* calculations to substantiate a mechanism already adumbrated by the early experimental work (**13**). From methoxybenzene (**3**), acceptance of a solvated electron from the sodium–ammonia solution leads, reversibly, to a radical-anion (**12**) that in turn accepts, reversibly, a proton from the alcohol. The resulting neutral radical (**13**) accepts, reversibly, a second electron to form a stabilized anion (**14**). The final addition of a second proton to this anion is virtually irreversible in the usual conditions for Birch reduction and it leads to the terminal product 2,5-dihydro-1-methoxybenzene (**4**). This and similar products were not only sources of cyclohexenones but after complexation with metal carbonyls were also the basis for what Birch called lateral control of synthesis (see later).

Studies in relation to biosynthesis

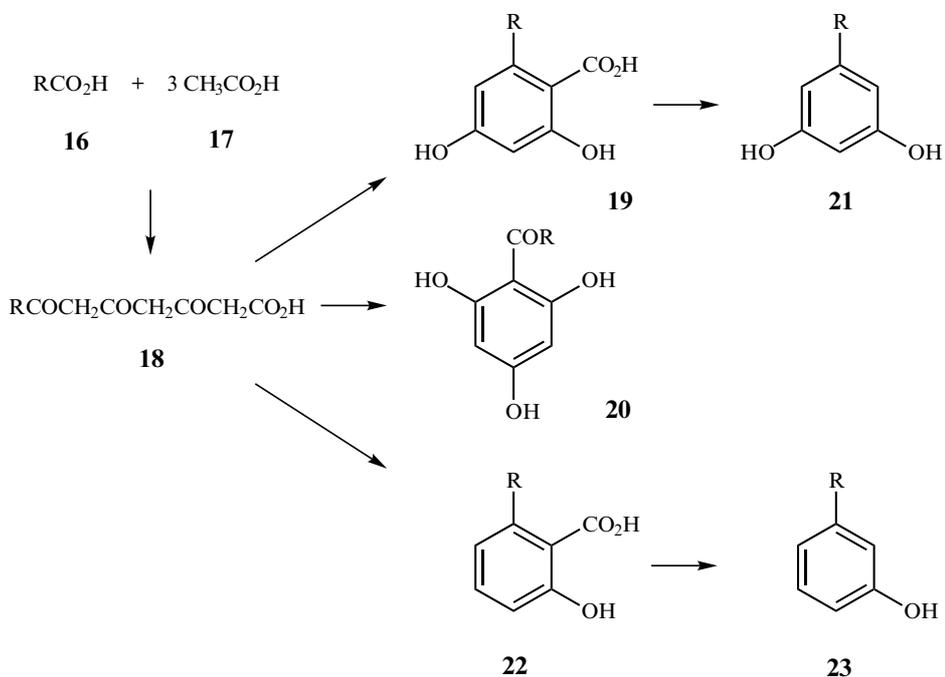
By the early 1950s the fundamental role of amino acids in the biosynthesis of alkaloids and some aromatic compounds had been recognized, as had the role of acetic acid in fatty acid and steroid biosynthesis. In contrast, the origin of the increasing numbers of phenolic compounds isolated from various plant and microbial sources was not yet understood. It was such a compound from a New Guinean tree that provided Birch with the inspiration for his second major contribution to science, his polyketide theory of aromatic biosynthesis. The original authors



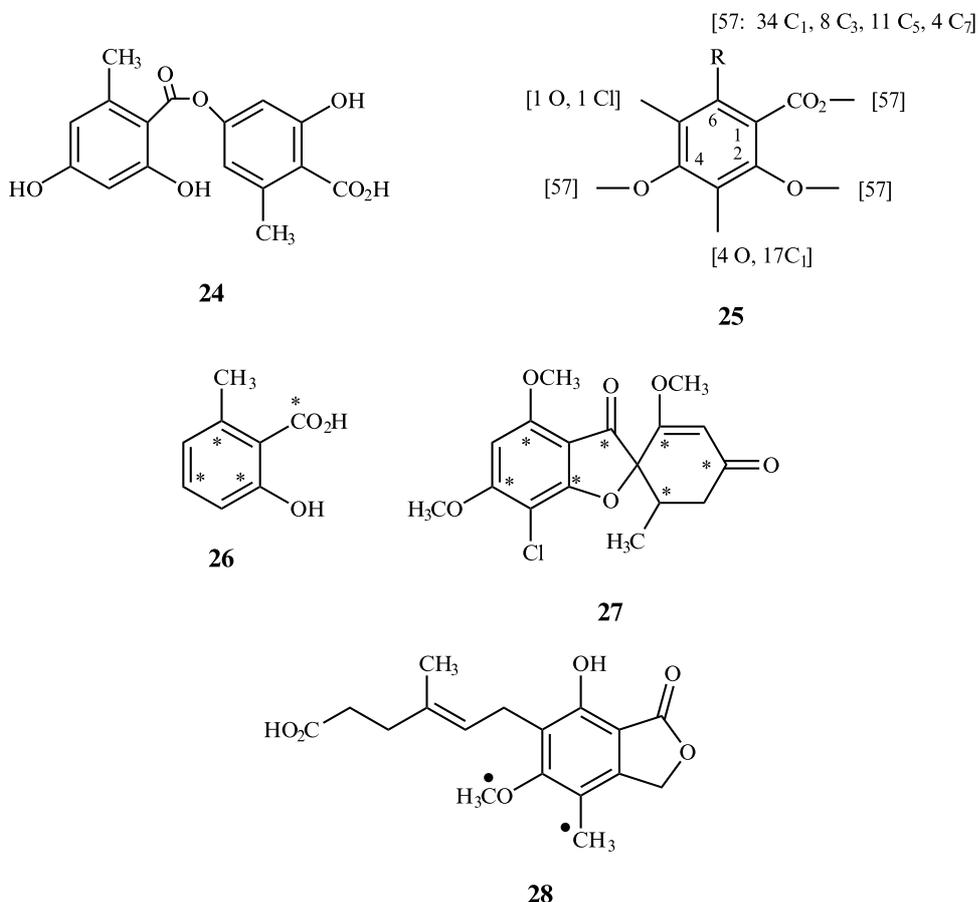
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had recognized that the carbonyl group in the side chain of campospermonol (**15**) defined a C_{18} 'oleyl radical with ... possible generic connection with the fatty oils' (Jones & Smith 1928). Birch realized that if the presumed acetate-derivation of this segment was extended further and coupled with decarboxylation and loss of oxygen, it could account for the origin of the phenolic ring, and in particular the position of the phenolic hydroxyl *meta* to the side chain.

From this emerged his 'acetate hypothesis', published from Sydney in 1953, whereby 'the head-to-tail linkage of acetate units (**17**) could lead to phenolic substances in several ways' (3). Ring closure of polyketonic intermediates of the type (**18**) through aldol condensation or C-acylation could yield orcinol (**19**) or phloroglucinol (**20**) derivatives, respectively (scheme 1). Superimposition of other biochemically acceptable reactions, such as decarboxylation, reduction, dehydration, oxidation and halogenation, on these basic processes would extend the range of possible products (for example **21–23**). The chain-initiating acid RCO_2H (**16**) could be acetic or other natural aliphatic acids, or aromatic acids such as hydroxycinnamic acids in the case of



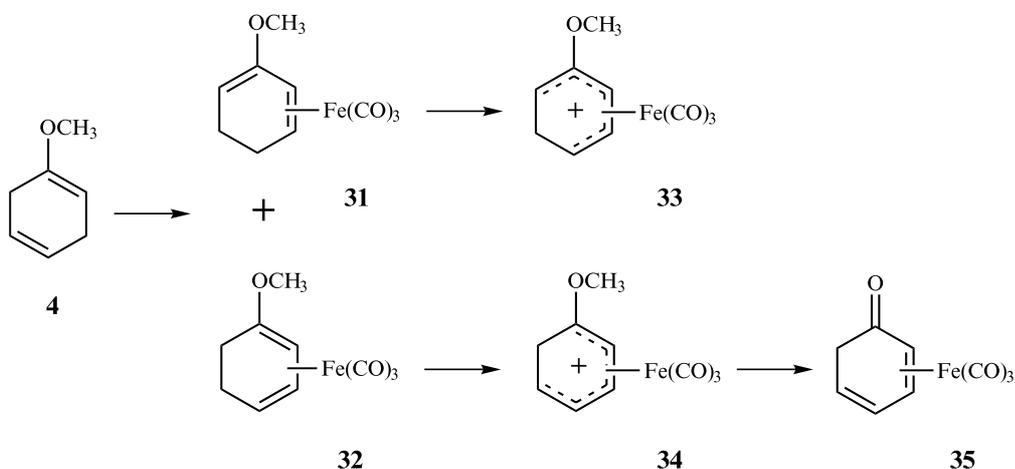
Scheme 1.



plant stilbenes and flavonoids. The carbon skeleton and residual oxygen functionality of the resulting metabolite defined the folded polyketonic intermediate. Birch later termed such metabolites 'polyketides', in deference to the early ideas of J. N. Collie (Collie 1907).

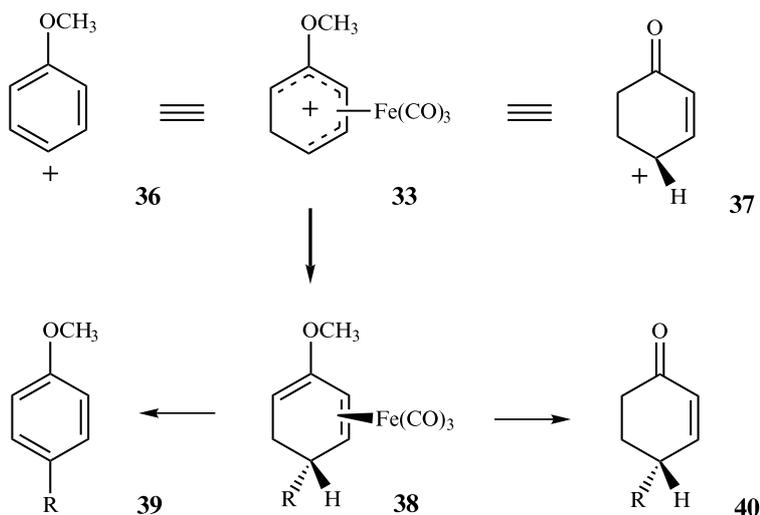
Initial support for the acetate hypothesis came from structural analysis of a range of phenolic metabolites. Lecanoric acid (**24**) is the simplest of the lichen depsides, containing two orsellinic acid (**19**; R = CH₃) units in ester linkage. Partial structure **25** summarizes the structures of the acid units present in all the depsides then known (4). Particularly convincing was the presence of carboxyl at position 1, oxygen at positions 2 and 4, and an odd-numbered alkyl chain at position 6 of all these units, in full agreement with Birch's hypothesis. In contrast, positions 3 and 5 carried occasional oxygen, chlorine and methyl substituents, arising by secondary modifications.

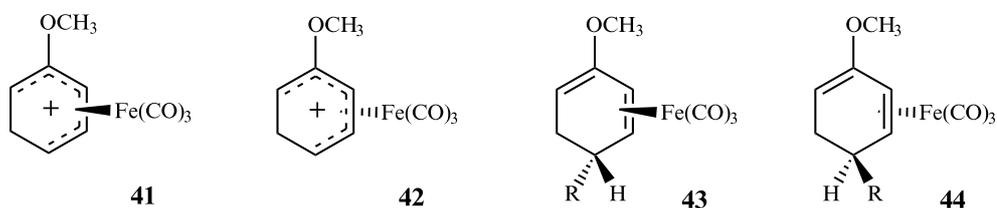
Biochemical proof of the hypothesis was provided by examination of the distribution of radioactive carbon (indicated by asterisks) in 6-methylsalicylic acid (**26**) produced by growing the fungus *Penicillium griseofulvum* in the presence of [*carboxyl*-¹⁴C]-labelled acetic acid (4). Like campospermonol (**15**), this metabolite has also lost an oxygen from its polyketonic precursor by reduction and dehydration, but in contrast retains the carboxyl group. This was the Sydney forerunner of an extended series of radioisotope studies of the biosynthetic origins of diverse fungal and bacterial metabolites, performed in Manchester and using detailed



An extensive series of iron tricarbonyl complexes of substituted cyclohexadienes was prepared, and their novel reactivity with a range of reagents studied (11). The presence of the attached but readily removable transition metal resulted in 'superimposed lateral control of reactivity, stereochemistry and structure' of the organic ligand (14). For example, the salt (33) could behave as the synthetic equivalent either of an aryl cation (36) or of a cyclohex-2-enone cation (37), depending on the reaction sequence chosen. Thus reaction with a nucleophile (R) afforded the neutral complex (38). Subsequent iron tricarbonyl removal coupled with dehydrogenation then gave the *p*-substituted anisole (39), whereas coupling with acid hydrolysis gave the 4-substituted cyclohex-2-enone (40).

The iron carbonyl group blocks one face of the ring system (33), and controls the reaction stereochemistry by forcing the nucleophile to attack specifically from the other face (electrophiles attack from the same face), affording the relative stereochemistry (38) shown. This is not always significant, but the salt (33) and the neutral complex (38) are both chiral and

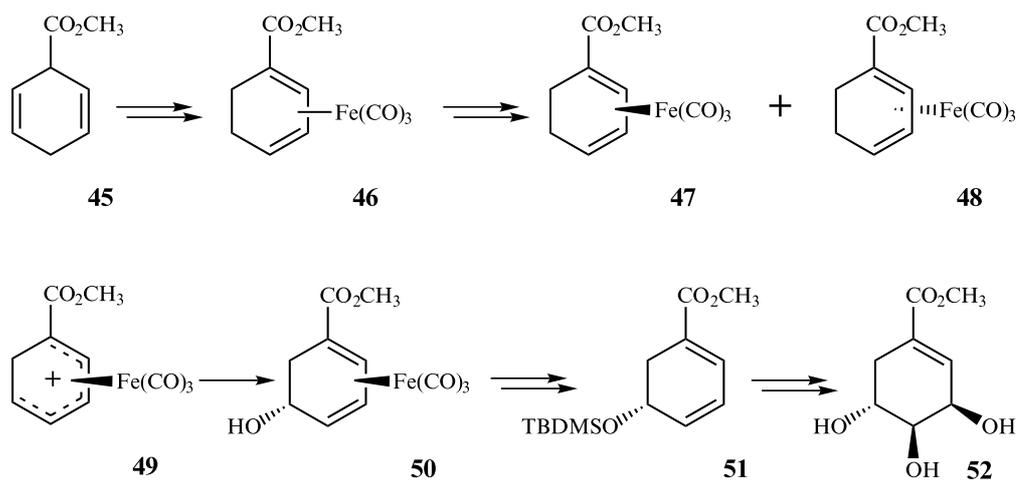




potentially resolvable into their mirror image pairs, the enantiomers (**41** and **42**) and (**43** and **44**), respectively. The products from such stereochemically pure materials, if they themselves are chiral as is the ketone (**40**), will be stereochemically pure.

The potential of the chemistry is illustrated in one of his last publications, a synthesis of the important biochemical pathway intermediate shikimic acid (scheme 2) (17). The starting dihydrobenzene in this case is methyl 1,4-dihydrobenzoate (**45**), prepared from benzoic acid by Birch reduction and methylation. Complexation with iron tricarbonyl gave a mixture of dienes isomerized by acid into the single isomer (**46**). This complex could be separated into its mirror image components (**47** and **48**) by hydrolysis to the acid, salt formation with (+)- or (-)-phenylethylamine, and re-esterification (16). Hydride removal from the enantiomer (**47**) with triphenylmethyl tetrafluoroborate now yielded the cation (**49**), which gave the neutral alcohol complex (**50**) on stereospecific reaction with hydroxide ion. Protection of the hydroxyl group as its *tert*-butyldimethylsilyl ether and removal of the iron by oxidation with trimethylamine *N*-oxide provided the free diene (**51**). *Cis*-diol formation with osmium tetroxide and removal of the protecting silyl group with fluoride ion gave stereochemically pure (-)-methyl shikimate (**52**). Alternative chemistry, again laterally controlled by the iron tricarbonyl group, enabled conversion of the mirror image complex (**48**) to the same product (**52**).

Birch explored many facets of this chemistry over some 20 years, even beyond his retirement. The powerful methodology has not been used to the extent that he expected, however,



Scheme 2. (TBDMS = *tert*-butyldimethylsilyl.)

probably for several reasons. The range of substituted cyclohexadienes readily available from Birch reductions has limitations, and metal complexation frequently yields a mixture of the conjugated diene complexes, only one of which is required. Furthermore, the transition metal has to be employed stoichiometrically, and, although iron pentacarbonyl is relatively cheap, applications of organometallic chemistry in organic synthesis were turning increasingly towards catalytic processes.

ARTHUR BIRCH THE PERSON

This memoir has sought to outline Birch's life and career, and his major contributions to chemistry and science at large. His achievements stand on their own merits. His extraordinary talent and his love for his chosen science are obvious, as are his preparedness to accept challenges and his commitment and determination to succeed. Readers will have inferred his ability to lead, glimpsed his dry humour, and seen his concern for the wellbeing of his family. His scientific persona emerges clearly in his scientific autobiography (18). His Oxford mentor, Sir Robert Robinson, regarded Birch as the student who most resembled him, a compliment accepted by Birch with mixed feelings. Comments by renowned chemists of his era are definitive (18). Sir Derek Barton FRS regarded him as 'ten years ahead of his time in three areas: reduction chemistry, biosynthesis, and organometallics'. Few chemists achieve this in a single area, let alone in three, and with the pace and maturity of chemistry in the twenty-first century it may no longer even be possible. Birch achieved it with relatively few collaborators and limited resources, even by the standards of the time. Carl Djerassi described him as 'a maverick, a lone wolf'.

For the present memoir, Djerassi commented further:

My enormous regard for Arthur Birch as the quintessence of an original chemical mind can be most succinctly shown by two facts. In the early 1950s I persuaded Syntex—at that time a small pharmaceutical research company in Mexico City—to hire Arthur as one of its chemical consultants. This was the beginning of Arthur's longest professional relation with a pharmaceutical company. Much more significant is my personal conviction that I was the first chemist to publish the word 'Birch Reduction' in the literature. But while naming an important chemical reaction after its discoverer is a standard form of homage among chemists, I converted mine into the ultimate compliment: transforming it also into a verb. At Syntex in Mexico City in the mid 1950s, it was standard phraseology 'to birch an aromatic methyl ether.' Que viva Don Arturo Birch!

Birch's close academic colleague David Craig recalled their interaction over many years in these terms:

Although Arthur and I came from the same undergraduate stable in the University of Sydney he was older and we did not meet at that time. We came to know each other well when in 1951 we were appointed to chairs in Sydney, he in Organic Chemistry at 36 and I in Physical Chemistry at 31. The Head of School was Raymond Le Fèvre [FRS 1959]. I doubt that Le Fèvre felt comfortable with these two brash youngsters. He was probably relieved when in 1955–56 we went back to the UK, Arthur to Manchester and I to London.

Starting in 1963 and with the strong support of our colleagues and the University, Arthur and I shared the task of establishing the Research School of Chemistry within the ANU. It was a great moment when the School opened its doors in 1967 with Arthur as the first Dean. We were confident that chemistry in Australia had moved forward. The School prospered. We had the same ideas—a firm commitment to a non-departmental structure and a determination that research should have priority over management and administration. In the alternation of the Deanship between Arthur and me we had an unspoken agreement never to interfere or to look back over what the other had done.

Arthur stood out, a man of purpose, academic values, good judgment and principles. I was fortunate to have been able to work closely with him over a long period.

His advice to governments was rational and influential. Malcolm Fraser, Prime Minister of Australia from 1975 to 1983 and Minister for Education and Science at the official opening of the ANU Research School of Chemistry in 1968, wrote:

I remember Professor Arthur Birch well. His contribution to the highest scientific research in Australia and overseas won a most distinguished, world-wide reputation. He played a significant, indeed indispensable role in establishing the Research School of Chemistry at the Australian National University. As a university established to foster fundamental research and post-graduate training in Australia, Professor Birch's contribution was outstanding. Its research schools were regarded of real significance to building this country.

The government then believed in the integrity of academic freedom and the need for fundamental research if science was to advance in Australia and if scientists of the highest international standing were to be attracted to Australia. Professor Birch became a valued advisor to government. He chaired the 1976–77 Independent Inquiry into the Commonwealth Scientific and Industrial Research Organisation and laid the foundations for that organization's continued relevance and importance. Its task was to accomplish strategic mission-orientated research. His service to Australia continued as Foundation Chair of the Australian Marine Sciences and Technologies Advisory Committee in 1978.

When asked by government, he felt an obligation to provide service beyond the particular confines of his own discipline. As a consequence he made a most distinguished and broad-ranging contribution to the advancement of science in Australia.

Those who worked for Birch were also fortunate. Research students at their bench soon learnt to recognize the smell of cigar smoke nearby, and to expect the ensuing laconic 'Anything new?' Of necessity they also learnt to select from the many ideas he would suggest to them, and to design and perform the experiments themselves. The sole exceptions were his signature reductions in which he liked to participate, preferably using a conical flask stoppered with cotton wool, frosted at the base by the evaporating liquid ammonia, and swirled by hand as he added pieces of sodium and watched them dissolve in transient blue patches. With longer acquaintance, particularly during his Canberra years, they saw not only the scientist but also a man of warmth and sympathy, good company and an engaging raconteur, fluent in French, which he enjoyed speaking, and with a liking for Mozart.

With regard to his science Birch was certainly self-centred, a trait that may be necessary for outstanding achievement. Was he content with the recognition that he achieved? There were clear reservations as he looked back in an interview at the age of 79 years (Wright 1995). In the Australian system he could not obtain significant research support beyond his retirement; other countries would have welcomed his continuing involvement. His assistance or even his advice had not been sought for 10 years—'I haven't been made use of properly in this country'. He was critical of both government and industry in Australia. Although he was clearly proud of the Research School of Chemistry and its achievements, his answer when asked if it was worth the sacrifice on his part was 'probably no'. He was certainly nominated several times for the Nobel Prize, although he did not believe in such major awards.

Behind the frank professional scientist, however, Arthur Birch was a private person. Those who knew Birch before his marriage noticed with pleasure the effect that it had on him. Before, he was a lone wolf who had always had to make his own way; now, he had constant support and love and he could give it too. John and Rita Cornforth were touched when, very late in his life, he told them that they were like a brother and sister to him. He was a welcome visitor to their Sussex home.

In his biography he acknowledges his debt to Jessie, as a nurse for his ailing mother in Oxford and Cambridge, as his wife and mother of their five children, and as the support for his career: ‘she shared my scientific achievements’. She accompanied him twice from England to the other side of the world, where she now lives in the second of their Canberra homes. The first, which she helped to design in the style of a Roman villa around a pool, won the architectural award for a Canberra residence in 1968. An artist in her own right, she has been employed by the National Gallery of Australia and has made other contributions to arts organization, the theatre, and family planning. Her enthusiasm for golf was not shared by her husband; even as her caddy he was ‘useless’. Jessie, their children Sue, Michael, Frank, Rosemary and Chris, and their 10 ‘bright and beautiful grandchildren who made him a rich man’ were a source of great pride, pleasure, and ultimately strength during the terminal stages of his illness.

Birch’s family, and his fighting spirit and humour, sustained him through long illness and successive operations. He died in Canberra on 8 December 1995. He disliked pomp and ceremony, and had said that there should be neither service nor eulogy at his funeral; the occasion was to be more in the spirit of an Irish wake. His wishes were essentially met at his cremation and the subsequent gathering at the Australian Academy of Science on 11 December 1995.

HONOURS AND DISTINCTIONS

Honours and honorary degrees

1962	MSc (<i>ad.e.grad.</i>) University of Manchester
1977	DSc (<i>honoris causa</i>) University of Sydney
1979	Companion of the Most Distinguished Order of St Michael and St George (CMG)
1981	MA (<i>ad.e.grad.</i>) Oxon.
1982	DSc (<i>honoris causa</i>) Monash University
	DSc (<i>honoris causa</i>) University of Manchester
1987	Companion of the Order of Australia (AC)

Elected fellowships and memberships

1954	Fellow, Australian Academy of Science
1958	Fellow, Royal Society
1960	Fellow, Royal Institute of Chemistry (Chartered Chemist)
1968	Fellow, Royal Australian Chemical Institute
1976	Full Foreign Academician, USSR Academy of Science (first election in Australia)
1978	President, Royal Australian Chemical Institute
1980	Honorary Fellow, Royal Society of Chemistry
1982–85	University Fellow, Australian National University
1982–86	President, Australian Academy of Science
1986	Honorary Fellow, Royal Society of New South Wales
1989	Foreign Fellow, Indian National Academy of Science
1994	Honorary Fellow, Royal Australian Chemical Institute

Distinctions and named lectureships

1937	University Medal in Chemistry, University of Sydney
1945	UK Defence Medal (1940–45)
1954	H. G. Smith Memorial Medal, Royal Australian Chemical Institute

- 1960 Simonsen Lectureship, Chemical Society
University Medal, Université Libre de Bruxelles
Fritsche (Gunther) Award for Terpene Chemistry, American Chemical Society
- 1961 Canadian Institute of Chemistry Visiting Professor
- 1963 E. C. Franklin Award for Outstanding Contribution to Chemistry, Phi Lambda
Upsilon, Stanford University
Smith Lectures, University of Oklahoma
- 1966 Royal Society Delegate, Romania
Wilson Baker Lecturer, Bristol University
- 1972 Flintoff Medal, Chemical Society
Purkyne Award for Contributions to Biochemistry, Czechoslovak Medical Society
Matthew Flinders Medal and Lecture, Australian Academy of Science
Davy Medal, Royal Society (first award in Australia)
- 1974 Liversidge Lecturer, Royal Society of New South Wales
- 1976 Ritchie Lecture, University of Sydney
- 1980 A. E. Leighton Memorial Medal, Royal Australian Chemical Institute
Masson Memorial Lecturer, University of Melbourne
- 1980–81 Newton–Abraham Professor, University of Oxford
- 1981 Robert Robinson Lectureship, Royal Society of Chemistry
Richard Martin Lecture, Université Libre de Bruxelles
- 1982 Natural Products Award, Royal Society of Chemistry
- 1985 Présenté à l'Académie des Sciences de l'Institut de France
- 1986 Plaque, Jurusan Kimia, Institut Teknologi Bandung
- 1987 Tetrahedron Prize for Creativity in Organic Chemistry
- 1990 ANZAAS Medal, Australia and New Zealand Association for the Advancement of
Science
- 1991 Médaille Homage, Centre National de la Recherche Scientifique, Produits Naturelles
- 1992 Dedicated issue, *Australian Journal of Chemistry*
- 1995 Main building of Research School of Chemistry, Australian National University,
named the Arthur Birch Building

ACKNOWLEDGEMENTS

Details of Arthur Birch's early life and some factual information on his subsequent career are drawn from his scientific autobiography, *To see the obvious*, published by the American Chemical Society in 1995. We are grateful to the Birch family, including Jessie, Sue, Michael, Frank, Rosemary, and particularly Chris, for helpful comments and for providing a curriculum vitae and publication list. His colleagues Professor Carl Djerassi and Professor David Craig FRS, and former Australian Prime Minister Malcolm Fraser, kindly responded to invitations for personal recollections. We ourselves accept responsibility for other narrative and scientific aspects of this memoir.

The frontispiece photograph was taken by Bob van der Tooren A.R.M.I.T., Member A.I.P.P., Melbourne, and is reproduced with permission.

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