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**A Biography to Mark the Centenary of the Birth
of Robert Burns Woodward**

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Series Editor: Dr Anna Simmons

Robert Burns Woodward
in his Own Words

Dr Peter J.T. Morris

April 2017

What happened on Tuesday 10 April 1917? The Second Battle of Arras started on the Western Front and the British Army made major gains on the

Woodward then went to the nearby Massachusetts Institute of Technology at the age of sixteen and took his B.S. in 1936. He failed to achieve passing grades at the end of his first year and resumed his studies a year later following a programme laid down by the chemistry department. Woodward

Siiri Anne (born 1939) and Jean Kirsten (born 1944). Irja Woodward died in Newton, Massachusetts, in 1996. They were divorced in 1946 and

and changed the way it was planned. The physical instrumentation allowed the reactions to be monitored and the products to be traced. The new theories of organic chemistry (organic reaction mechanisms and theories of stereochemistry) now allowed the organic chemist to predict the course of hitherto unknown reactions or how a small change in a reactant, the use of a catalyst or a change of solvent would alter the course of the reaction. Synthetic chemists now had great new powers in their hands and Woodward made full use of them.

Woodward's early synthetic work, up until the early 1950s, was the then fashionable field of steroids. Between the 1930s and 1950s, steroids were seen as wonder drugs capable of changing the face of medicine, a hope which, as

and the closed ring could be reopened by a photochemical process. As the group was very concerned with stereochemistry, they could easily see that the photochemical opening of the ring produced the opposite isomer to the one which on heating formed the ring compound being photolysed. Clearly there was a fundamental process at work here and Woodward was determined to get to the bottom of it. However Woodward, although well versed in organic reaction mechanisms, was not a theoretical chemist and he soon realised he needed help. By good fortune a young theoretical chemist called Roald Hoffmann was a member of the Society of Fellows. Woodward's initial insights sharpened by Hoffmann's deep understanding of molecular orbital theory quickly produced a set of rules (the Woodward-Hoffmann rules) about how certain concerted intramolecular cyclic chemical

depart for the great chemistry laboratory in the sky when he was still at the peak of his powers rather than endure a prolonged dotage troubled by health

ii) Now stored as part of the Woodward papers at the Harvard archives, <http://oasis.lib.harvard.edu/oasis/deliver/~hua06001> (accessed 17 March 2017), call mark HUGFP 68.32f.

iii) Information about von Tippleskirch's internment and death was taken from correspondence of the period sold on eBay in 2013.

iv) R.B. Woodward, "The Arthur C. Cope Award Lecture", in *Robert Burns Woodward: Architect and Artist in the World of Molecules*, eds. Otto Theodor Benfey and Peter J.T. Morris (Philadelphia: Chemical Heritage Foundation, 2001), pp. 418-452, on p. 426.

v) The Austin Research Fellowship is mentioned in the acknowledgements of his 1937 thesis which can be downloaded from the MIT website: <http://hdl.handle.net/1721.1/12465> (accessed 17 March 2017).

vi) See http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1965/woodward-nomination.html (accessed 17 March 2017).

vii) Two examples are given by Frank Westheimer in his recollections of Woodward, see *Sources for the Biography* above.

viii) Although it was a Sunday, it was unusual that he was at home as he rarely took time off, so one wonders if he had been feeling unwell beforehand.

ix) Fukui, a Japanese chemist of similar age to Woodward, had independently been working on the relationship between the symmetry of molecular orbitals and chemical reactions.

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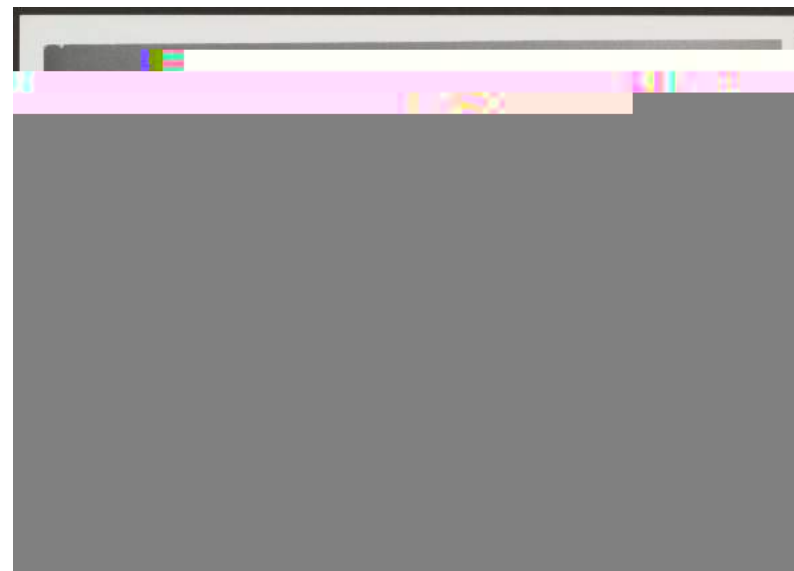
Series Editor: Dr Anna Simmons

Robert Burns Woodward in his Own Words

Dr Peter J.T. Morris
Science Museum, London

The Sixth Wheeler Lecture

Royal Society of Chemistry, 17 May 2013



Robert Burns Woodward holding model of Vitamin B12, photograph, c. 1973.!

HUGFP 68.38.1p (Box 2), olvwork294150. Harvard University Archives

I must begin by thanking the Historical Group for its kindness in giving me its Wheeler Award.

But every privilege carries with it some kind of responsibility, and I have, at this moment, a responsibility which I cannot but regard as a heavy one—that of presenting to all of you a lecture, appropriate to the occasion, and it may be hoped, of some general interest to an audience among whose members there must certainly be a wide diversity in background.

...

Well, then, here I stand with the problem still before me WHAT TO SAY? And now, the solution. I present it with considerable diffidence, since what I am about to describe is highly personal, idiosyncratic and very far removed from the kind of lecture with which I am familiar!![1]

By now you may have guessed that these words are not my own, but those of Robert Burns Woodward taken from the opening of his famous Cope Lecture. Originally, I intended to explain why Woodward became a great chemist - that he was a great chemist is beyond dispute and easily explained - and I found this completely impossible. He seems to have been a prodigy from the age of twelve without the need for any external assistance apart from the fabled Baron von Tippleskirch [2]. Kurt von Tippleskirch was the German Consul in Boston in the 1920s who obtained copies of German chemistry journals for the twelve-year old Woodward, one of which was the 1928 issue of *Annalen der Chemie* containing the first paper by Otto Diels and Kurt Alder [3]. My next idea was to discuss various aspects of Woodward's thinking and personality, but any comments seemed very thin without quoting the great man himself. This in turn gave me the idea of giving the stage over to Woodward so that his words would more or less speak for himself - and for me! I downloaded or otherwise collected all of the known papers of Woodward (he did not publish any books) and searched them for suitable material. As they are chemical papers, they do not give much insight into the personal asp

OF WHAT RELEVANCE is this history to the story of my personal scientific saga? I will admit freely that in some measure, I have just arbitrarily seized the occasion to right what I consider a grievous historical injustice. BUT there are connections. We can dismiss the obvious ones briefly and in a jocular vein. It is true that like Couper I bear Scottish blood. But I left my mother's home early, never to return. Let there be no unduly adverse implications here. Glad as I was to escape the maternal wing, I know that my mother was a powerful and very helpful positive force in my development. To conclude this category, I did not go mad -

The determination of a complicated structure can be—at least it was,
in general in the past—a very complicated and difficult task. ...
However, with ad

[the synthesis of new substances] is an area which is entirely creative in spirit, and in which there is unlimited opportunity for art and imagination. [21]

Speakin

And the organic chemist had the thrilling ability to create new forms of matter:

Crystallization is one of the most beautiful processes known and no true chemist fails to experience a thrill when he brings a new form of

throughout the process, it and its concealed nitrogen atom have withstood chemical operations, variegated in nature and in some instances of no little severity. It had mobilised its special directive and reactive capacities dutifully, and had not once obtruded a willful and diverting reactivity of its own. Now it must discharge but one more responsibility—to permit itself gracefully to be dismantled, not be used again until someone might see another opportunity to adopt so useful a companion on another synthetic adventure. And perform this final act of grace it did. [38]

Before returning to the notion of surprise that has already been mentioned, I first wish to consider the restraints on the sensuous and fun elements of chemistry.

Constraints

While he greatly enjoyed the creative aspects of synthesis, Woodward also believed it was important that this almost frivolous creativity was constrained by the need to obey the laws of Nature; hence organic chemistry was both art and science. In the Cope Lecture, he said:

While in mathematics, presumably one's imagination may run riot without limit, in chemistry one's ideas, however beautiful, logical, elegant, imaginative they may be in their own right, are simply without value unless they are actually applicable to the one physical environment we have—in short, they are only good if they work! I personally very much enjoy the very special challenge which this physical restraint on fantasy presents. [39]

And earlier in the “Art and Science” paper:

... at each of the many stages of such syntheses the chemist is ordinarily creating entirely new forms of matter which have never existed before. This circumstance will make it clear that the chemist can in fact create at will an uncounted variety of entirely new substances, limited only by the known laws governing the interrelationships of atoms within molecules. [40]

The ability to create new molecules while being able to predict and obey the rules laid down by nature showed the power of chemistry. He claimed in “Synthesis” that:

It can scarcely be gainsaid that the successful outcome of a synthesis of more than thirty stages provides a test of unparalleled rigor of the predictive capacity of the science, and of the degree of its understanding of its portion of the environment. Since organic

chemistry has produced syntheses of this magnitude, we can, by this yardstick, pronounce its condition good... [41]

An Enlightenment Chemist?

The milli-Woodwards march remorselessly onward, but there is one last aspect of Woodward that I would like to discuss. This paper has emphasised the importance of sensuousness and creativity for Woodward. These aspects of his chemistry make him very much a Romantic chemist and are illustrated by his prose style, as is shown, for example, in the opening of his key paper on the strychnine synthesis:

Strychnine! The fearsome poisonous properties of this notorious substance attracted the attention of XVIIIth century Europe to the *Strychnos* species which grows in the rain forests of the Southeast Asian Archipelagos and the Coromandel Coast of India, and gained for the seeds and bark of those plants a widespread use for the extermination of rodents, and other undesirables, as well as a certain vogue in medical practice—now known to be largely unjustified by any utility. [42]

But he was of Scottish blood, as he put it himself, and there is more than a trace of the Scottish Enlightenment in his thinking:

For almost 50 years now, I have been involved in an affair with chemistry. It has been throughout—and still is—a richly rewarding involvement, with numerous episodes of high drama and intense engagement, with the joys of enlightenment and achievement, with the special pleasures which come from the perception of order and beauty in Nature—and with much humour. [43]

An important element of this enlightenment through engagement with Nature was the aspect of surprise: surprise at the failure of a reaction to take place, which often happened, or surprise at a seemingly inexplicable reaction, of which he listed “four mysterious reactions” that surprised him around 1960 [44]. It was another mysterious reaction three years later that led to the development of the Woodward-Hoffmann Rules. He had already commented in his “Art and Synthesis” paper that “the unexpected is always important and its study should be welcomed, since it is likely to lead to further understanding...” [45], but in the same paper, he noted that surprise could occur in other ways:

It is possible to introduce delightful elements of surprise into synthetic work. An apparently rather dull grouping of atoms suddenly, under the impact of especially chosen reagents, undergoes unusual transformations which are of great utility in progress towards the

objective. The impact on an observer may be compared with that of the traveller down an uninteresting street, who turns through a hidden doorway into a delightful and charming garden. [46]

- 2008, **47**, 1736-1740. Also see Jeffrey I. Seeman, "The Woodward-Doering/Rabe-Kindler Total Synthesis of Quinine: Setting the Record Straight", *Angewandte Chemie International Edition*, 2007, **46**, 1378-1413.
7. Robert Burns Woodward and William von Eggers Doering, "The Total Synthesis of Quinine", *Journal of the American Chemical Society*, 1945, **67**, 860-874, on p. 860 (footnote 2). This paper is reproduced in Benfey and Morris, *Robert Burns Woodward*, pp. 63-77.
 8. Benfey and Morris, *Robert Burns Woodward*, p. 867 (footnote 48).
 9. "Synthesis", p. 156.
 10. "Cope Lecture", pp. 421-422.
 11. "Art and Science", p. 25.
 12. "Synthesis", p. 156.
 13. "Synthesis", p. 157.
 14. "Art and Science", p. 25.
 15. "Synthesis", p. 165.
 16. "Synthesis", p. 165.
 17. "Synthesis", p. 165.
 18. "Art and Science", p. 41.
 19. "Synthesis", p. 180.
 20. "Synthesis", p. 155.
 21. "Art and Science", p. 28 and p. 40.
 22. "Art and Science", p. 41.
 23. Reproduced in Benfey and Morris, *Robert Burns Woodward*, p. 125.
 24. Robert Burns Woodward, "The Total Synthesis of Chlorophyll", *Pure and Applied Chemistry*, 1961, **2**, 383-404, on p. 383. This paper is reproduced in Benfey and Morris, *Robert Burns Woodward*, pp. 256-277.
 25. Robert Burns Woodward, *et al.*, "The Total Synthesis of Strychnine", *Tetrahedron*, 1958, **19**, 247-288, on p. 253. This paper is reproduced in Benfey and Morris, *Robert Burns Woodward*, pp. 136-177. For the similarities between mountaineering and organic synthesis, see Peter J.T. Morris, "Reaching the Summit", *Chemistry and Industry*, 10 July 2000, 433-435.
 26. Robert Burns Woodward, "Recent Advances in the Chemistry of Natural Products", *Pure and Applied Chemistry*, 1968, **17**, 519-547, on p. 535. The synthesis of the corrin nucleus of Vitamin B₁₂ had been divided between Woodward's group at Harvard and Albert Eschenmoser's group at ETH, Zurich. The Harvard group had referred to the left and right halves of the nucleus, whereas the Zurich group had used west and east (probably with the geographical position of the two groups in mind as well as the spatial arrangement of the molecule). Woodward abandoned left/right when he realised the negative connotations of "sinstraline" for an intermediate rather than "hesperimine" (see pp. 538-539). This paper is reproduced in Benfey and Morris, *Robert Burns Woodward*, pp. 314-342.
 27. "Art and Science", p. 28.
 28. "Art and Science", p. 31.
 29. "Total Synthesis", p. 46.
 30. Robert Burns Woodward, "Experiments on the Synthesis of Oestrone. I. The 2-(p-Phenylethyl)-furans as Components in the Diene Synthesis", *Journal of the American Chemical Society*, 1940, **62**, 1.24 0t6 322.1(f)3(f0.

42. Robert Burns Woodward *et al*