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CHLOROPHYLL *a* SYNTHESIS: A PREFATORY NOTE

Although the preliminary communication on his chlorophyll synthesis had appeared in 1960, Woodward had only written part of the experimental section for a full paper when he died in 1979. In 1980 Professor Bill Doering asked me if I would undertake the writing-up of Woodward's synthesis of chlorophyll *a*. My high regard for Bob Woodward led me to agree to do this and in due course five boxes of record books and spectra arrived by air. One of the seventeen record books was missing. Willy Leimgruber had died in 1981, and it emerged that his record book had been removed for use in a memorial symposium organised by Hoffman–LaRoche and the North Jersey Section of the American Chemical Society. Professor Kishi kindly furnished me with a photocopy of it in 1983.

An examination of the mass of material soon convinced me that I should need assistance in the task of composition. Preliminary attempts to secure support for this were unsuccessful. This was not altogether surprising since this was an unusual, even unique, venture, and did not fit well in to grant application forms. In the event the whole project was put on hold when shortly afterwards I took on the job of Head of the Chemistry Department at Queen Mary College.

Having completed my stint in 1987 I returned to the chlorophyll project, and was pleased when the Maxwell Foundation generously agreed to provide support for two assistants during the summer of 1989. I took on two of our top graduates from the 1989 class (Miss Diana Garside and Mr Aslam Galia, both of whom are going on to do organic research) to help with the composition and checking. Dr Asun Valles joined us for one month from Barcelona to help particularly with new spectroscopic measurements on samples which had been in Dr Alfred Bader's care, and which he kindly made available. Although the samples were nearly thirty years old, most of them were still chromatographically pure, and gave excellent IR, NMR and mass spectra.

The write-up took seven man-months of effort. We occupied the seminar room in the Chemistry building at Queen Mary College for the months of August and September. I would especially like to thank my colleagues for their forebearance during this period.

It is a sign of the professionalism of Woodward's research effort that we could go back after 30 years to the original record books and the original spectra without difficulty. In the event, in one or two cases we could not find the spectrum mentioned in the preliminary publication, but since each experiment was usually carried out several times, it was always possible to find an original record. In all cases the experimental method has been derived from the original record book, and the spectroscopic results quoted have been checked with the original trace. In a few cases we have been able to make further spectroscopic measurements on the original samples to make confirmatory points. Such experimental data are given in square brackets and are dated August 1989. (RBW died 8 July 1979). The first part of the experimental (which RBW wrote in the mid 60s) has been freely used, but for the sake of uniformity it has been completely rewritten, with no attempt to emulate his characteristic style. The manuscript is now finished, although it remains to be sent to my co-authors for their comments.

The past two months of hectic activity have highlighted for me some of the ways in which organic chemistry has changed—usually, but not always, for the better—in the past 30 years. For a start, there have, of course, been considerable advances in organic synthesis during this period. To take an apposite example, Barton's discovery of the conjugate addition of isocyanoacetate esters to nitroalkenes[1] provides a very attractive entry into the pyrrole series; and other examples are

1. Barton, D. H. R.; Zard, S. Z. *J. Chem. Soc. Chem. Commun.* **1985,** 1098.

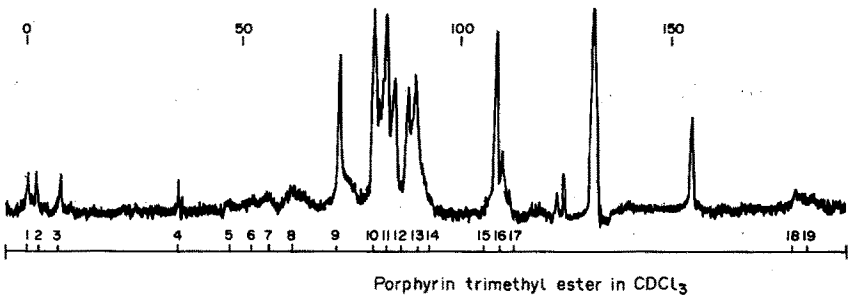

Fig. i. NMR spectrum of porphyrin (**35**), 0.15 M in $CDCl_3$, 60 MHz *ca.* 1960. The original measures 19.5 × 6 cm.

mentioned in the text. In spite of these advances the general route adopted will, I believe, be found in most respects to have stood the test of time in terms of concept, cost and convenience.

Another change, which might at first sight seem quite trivial, concerns thin-layer chromatography. No TLC plates are affixed in any of the record books, and there is no reference at all to TLC. It seems incredible now that 30 years ago we were working without this major technique. On the debit side one finds the tendency in recent times to attempt to play down the importance of elementary analysis as an indicator of composition and purity. As the sequel shows, Woodward very properly insisted on elemental analysis for all new compounds which were stable and available in appropriate amount.

The biggest single change, however, must be due to the impact of NMR spectroscopy. In 1960 it was just beginning to be applied routinely to organic chemistry. Fig. i. shows the NMR spectrum

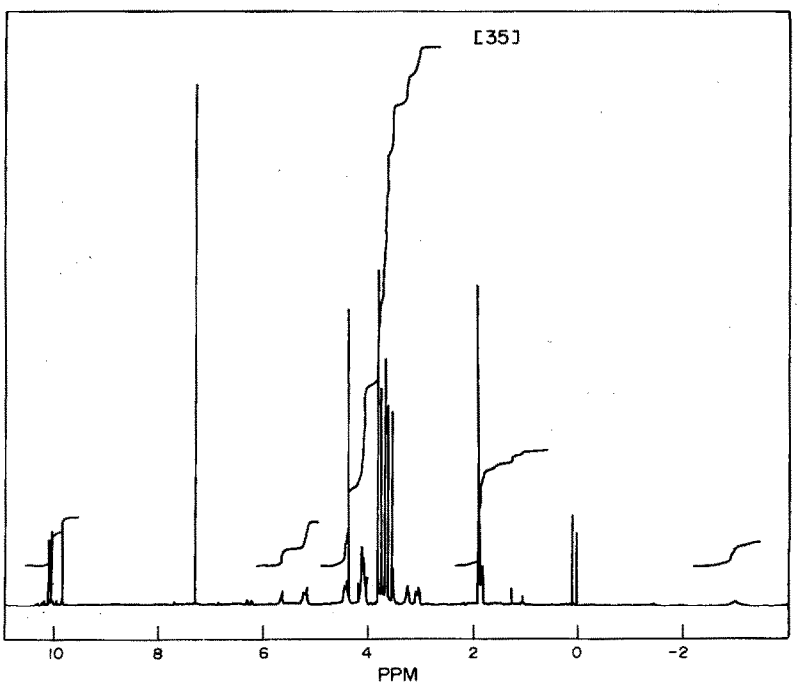

Fig. ii. NMR spectrum of the same porphyrin, 1.8×10^{-2} M in $CDCl_3$, 250 MHz, September 1989.

of the first porphyrin (**35**) recorded at 60 MHz in 1961. I am told that the spectrum was drawn on waxed paper with a hot wire! Fifty four milligrams of the porphyrin were dissolved in 0.5 ml of deuteriated chloroform. (The spectrum has been marked up by RBW).

Fig. ii. shows the spectrum taken in 1989 on a sample 30 years old. In this case 5.0 mg of the sample was dissolved in 0.4 ml of $CDCl_3$, and the spectrum was observed at 250 MHz (a similar spectrum was observed with 0.35 mg/0.4 ml). The improvement speaks for itself, and the technique is, of course, attended by a range of auxiliaries of very considerable power. As will become apparent, we have been able to apply certain of these techniques at various points in the following synthetic sequence, and in all cases the original structural conclusions have been confirmed.

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