



OBITUARY

Franz Sondheimer 1926–1981

Franz Sondheimer who died tragically on 11 February 1981 whilst on sabbatical leave at Stanford University, had the rare satisfaction of achieving text book fame in his lifetime. His annulene syntheses brought about a clarification of our understanding of that long-established, but somewhat vague concept of organic chemistry, aromaticity. He came to England from his birthplace, Stuttgart, as an eleven-year old and adapted to the completely new environment so thoroughly that, by the age of only nineteen, he graduated top of the chemistry class at Imperial College, just ahead of M. C. Whiting. His first research experience (with Sir Ian Heilbron and the author) established an interest and an expertise in acetylene chemistry which he never lost. He studied the novel formation of pentenynol (1) from epichlorohydrin and

sodium acetylide and explored some of its reactions, including the Glaser coupling to the diacetylenic glycol (2), a reaction later to become the basis of his annulene work. Postdoctoral collaboration with R. A. Raphael resulted in the syntheses of linoleic and linolenic acids and established a pattern for the use of the acetylenic unit in synthesis. Already at this stage he had figured as an author in eighteen definitive publications.

Inspired by R. B. Woodward's first lecture in London, he went to Harvard where he was a key member of the exceptionally able quartet, which in just two years, completed the historic steroid synthesis, an event which heralded a new era in the approach to synthetic problems. By now Sondheimer had acquired a considerable reputation as a highly competent and productive research worker and, on the initiative of Gilbert Stork, he was invited to succeed Carl Djerassi in charge of research and development at Syntex in Mexico City under the wise and successful leadership of George Rosenkranz.

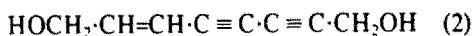
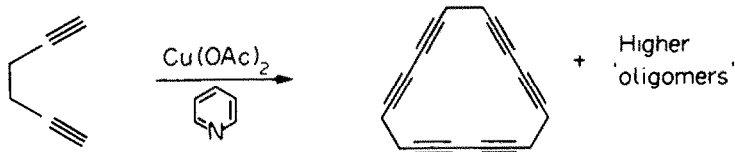
Here outstanding progress had been made in the derivation of cortisone from the readily available diosgenin and in the preparation of norethisterone and the revelation of its hormonal properties. It was into this ebullient and exciting environment that Sondheimer was introduced in January 1952, to lead a team of some twenty five chemists in ventures which resulted in the establishment of short direct routes from diosgenin and several related sapogenins to cortisone and also to all of the major sex hormones. Inevitably he was concerned with much developmental work involving not only these routes but the synthesis of analogues such as stereochemical isomers, higher and lower homologues, dehydro-compounds (Δ^1 , Δ^6) and oxygenated variants, i.e. at the 2-, 6-, 11- and 16-positions. The chemistry of the steroid group was by no means exhausted and many publications ensued.

In 1956, whilst barely thirty, he responded to an invitation to head the Department of Organic Chemistry at the Weizmann Institute in Israel. This provided him with an ideal environment at this stage of his career, he had administrative but no teaching duties and could devote himself largely to a research programme over which he now had complete control; these next eight years were to be his most productive. He was soon joined by a group of highly talented postdoctorals and his Syntex and Harvard experience stood him in good stead for studies on the methylsteroids, of interest in relation to biogenesis, and for synthetic work on the steroid sapogenins, the cardiac aglycones and the polyterpenes.

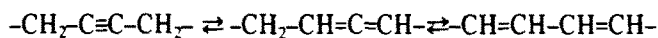
In the natural product area Sondheimer's outstanding accomplishment in the Israel period was the synthesis of the sapogenin, tigogenin, in remarkably high yield. Considerable clarification of the stereochemistry at C_{16} , C_{17} and C_{18} was achieved and interconversions, some already known, others newly effected, resulted in the virtually complete structural inter-relationship of all the steroid sapogenins as well as of some of the steroid alkaloids.

Around 1960 synthesis in the triterpene series was a challenging objective, with its considerable stereochemical complication, little or no interconversion background, and no commercially available materials to act as comfortable relays. Sondheimer made some notable forays into this field but he wisely decided not to continue when he realised that his other main line was far more likely to produce novel and significant results.

Much of his work at the Weizmann Institute was based on his Harvard and Syntex experience, but it was a reversion to his earliest love, that of acetylene chemistry, that led to his most original and memorable contribution to organic chemistry, the creation of the annulenes. The inclusion of the linear acetylenic bond into cyclic systems had long aroused much interest and, with macrocyclic polyacetylenes as the target, he embarked upon an investigation of the oxidative coupling of $\alpha\omega$ -diacetylenes. Cyclohexadeca-1,3,9,11-tetrayne was the first "dimer" to be obtained and, following the development of an improved oxidation method (cupric acetate in pyridine) devised by Eglinton, tri-

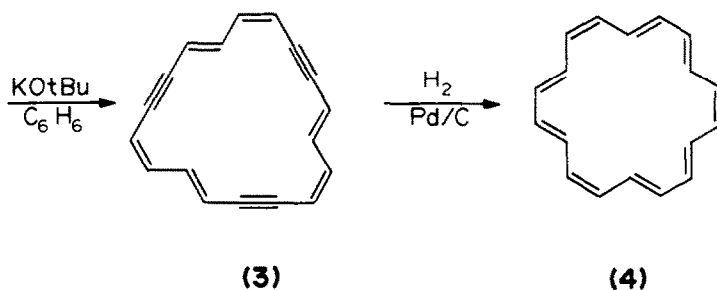


tetra- and higher coupled systems were isolated. Base-catalysed isomerisation, long known (Favorski) in the open chain series,



applied to these compounds resulted in highly coloured reaction mixtures and it was evident that fully conjugated cyclic systems were being formed and that higher analogues of benzene and cyclo-octatetraene might be obtainable by partial hydrogenation. The 18-membered reddish-brown hexaene triyne (3) was the first of this type (the dehydroannulenes) and the successful completion of its partial hydrogenation was most appropriately announced at a Harvard seminar late in 1959.

Hückel had predicted in 1931 that aromatic character should be exhibited by compounds with $[4n + 2]$ π -electrons and [18] annulene (4) at last provided the opportunity to test its generality. Its thermal



stability was immediately obvious, in due course classical substitution (nitration, bromination, acylation) was effected and X-ray crystallographic analysis revealed its essentially planar structure (6 "cisoid" and 12 "transoid" C-C bonds and no alternation). NMR spectra, when later it became possible for these to be recorded at low temperatures, revealed the unique ability of [18] annulene and subsequently other "diatropic" molecules, with aromatic character, to sustain a diamagnetic ring current in an applied magnetic field; inner proton bands (deshielded) at high field and outer proton bands (shielded) at low field, the converse being observed with the $[4n]$ "paratropic" systems.

Sondheimer was one of the first appointees to the newly established Research Professorships of the Royal Society; initially he went to Cambridge (1964) and from 1967 he was at University College, London. Here in England again after fourteen years absence the annulenes were vigorously pursued and ultimately members of the series from [14] to [24] were obtained in pure crystalline form, along with the much more accessible dehydroannulenes (e.g. 3) ranging from [12] to [30], in which diatropic character was also evident in the $[4n + 2]$ π -electron members. An extensive series of deuterated and other substituted annulenes were prepared for conformational mobility and related studies and the aromatic character of the dianions derived (*K* in thf) from both annulenes and dehydroannulenes was explored. Variants such as annulenones and annulenediones (which proved to be quinones of an aromatic system) and benzannulenes were synthesised, *via* the dehydro-types, and much effort was devoted to making analogues of pyrrole and furan in this series; aza [17] and [21] annulene derivatives were found to be diatropic and a series of thia-annulenes also showed alternating properties.

Lasting impressions of his enthusiasm for his researches, and his perfectionist attitude towards them, remain in the minds of those with whom he was associated in the many places where he worked or visited. His enthusiasm for, and expertise in, such diverse activities as piloting his own plane and collecting early books on science (the Sondheimer Boyle Collection is now at Cornell) were remarkable. Many of us will cherish memories of a kind and warm-hearted colleague. Unhappily, periods of depression from which he suffered for a number of years grew deeper and longer, and at last he determined to shed the burden under which he had struggled for so long and which he felt had become intolerable for him and those close to him to bear.

Sondheimer was associated with more than 300 publications; many of them are quoted in the following reviews:

Syntheses in the Cardiac-active Steroid Field. *Chem. Brit.* 1965, 1, 454. Recent Advances in the Chemistry of Large-ring Conjugated Systems. *Pure Appl. Chem.* 1963, 7, 363.

The Annulenes. *Accts. Chem. Res.* 1972, **5**, 81.

Planar Dehydro [8] annulenes (with N. Z. Huang). *Accts. Chem. Res.* 1982, **15**, 96.

This contribution is abbreviated from a Biographical Memoir written for the Royal Society by the author and Dr. Peter Garratt. Acknowledgement is made there to the many colleagues who provided reminiscences.

E. R. H. JONES