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OBITUARY

In memory of Harold M. Flowers

We are deeply saddened to report the death of Harold M. Flowers, on February 22, 1996, just 2 weeks past his 69th birthday. Harold was born in Leeds, England, where he spent his early years. He was active in the British Zionist Youth movement of Habonim, while he received his doctorate in chemistry from the University of Leeds in 1950. As a dedicated Zionist he emigrated to Israel in February, 1953 together with his wife Sylvia, where they joined Kibbutz Amiad.

In 1956, Harold was drawn back to science, and came to the Department of Organic Chemistry at the Weizmann Institute of Science. He joined the laboratory of David Shapiro, a pioneer in the synthesis of gangliosides and among the first generation of scientists of the Sieff Institute, which became the Weizmann Institute in 1949. Together with Shapiro, Harold achieved in the late 50s the first complete synthesis of sphingosine and its phosphoryl choline ester, sphingomyelin. Subsequently, he successfully synthesized the more simple glycosphingolipids, gluco- and galactocerebrosides, and developed a novel method for the stepwise synthesis of more complex glycosphingolipids. By 1968, he was able to apply this method to obtain for the first time a dihydroceramide derivative of a trisaccharide. He also synthesized cerebroside sulphates for the first time. This work provided model compounds and substrates for biological studies. In particular, it was a decisive factor leading to a better understanding of some of the hereditary diseases of glycolipid metabolism, especially Gaucher's disease, and to the development of enzyme replacement therapy for its treatment.

While still at the Department of Organic Chemistry, Harold started a program for the synthesis of disaccharides of biological interest, such as those that form building blocks of the blood group substances or the proteoglycans. He also became interested in the mechanism of chemical glycosylation and in developing methods for controlling the anomericity of the products. He continued and expanded this program after his move to the Department of Biophysics, which was chaired by Ephraim Kazir and subsequently by Nathan Sharon. He was associated here until his retirement in 1992. Some of the many disaccharides synthesized by him for the first time provided essential proof of structure of glycoconjugates and served as a source of much needed compounds for immunological testing. These compounds included Fucα(1,2)Gal, a constituent of the ABO blood group determinants and GlcUβ(1,3)Gal, of the linkage region of the proteoglycans. In 1961–63, while on leave of absence at the laboratory of Roger Jeanloz at Harvard Medical School and Massachusetts General Hospital, he synthesized Galβ(1,3)GlcNAc (lacto-*N*-biose I), one of the human milk oligosaccharides. In addition, he synthesized GlcNAcβ(1,6)MurNAc, assumed at the time to be the repeating unit of the bacterial cell wall peptidoglycan, and showed that it differed from the disaccharide isolated from the peptidoglycan, thus pointing out the correct structure of the repeating unit as GlcNAcβ(1,4)MurNAc. He was also the first to synthesize the repeating unit of a glycosaminoglycan, namely hyalobiuronic acid.

In Boston, Harold made friends with a number of American, British and Japanese scientists who worked together with him. One of these was M.C. Glick, with whom Harold established close collaboration and spent several sabbaticals in the 70s, 80s and early 90s. In 1990 his stay in the Glick laboratory was supported by The Children's Hospital/Weizmann Institute Program, a program which sponsors exchange of scientists from both Institutions. The program is funded by The Children's Hospital of Philadelphia. At this time, he developed an immunoaffinity column to detect polysialic acid in α-2,8-linkage which made it possible to detect the product synthesized by α-2,8-polysialyltransferase. He was the first to describe the activity of this enzyme in human neuroblastoma although the presence of polymers of

sialic acid in α-2,8-linkage had been detected several years previously.

During a sabbatical year in 1967 with Zeev Hassid at the University of California, Berkeley, he participated in studies of the biosynthesis of plant polysaccharides. Additional academic leaves included studies in laboratories at MIT, Boston, Denver Jewish Hospital, Rand Afrikaans University, Johannesburg, and Lattobe University, Melbourne.

In the laboratory, Harold impressed everyone with his speed and technical prowess. His sense of experimentation was impeccable. Although his expertise was in carbohydrate synthesis, he was fascinated by the biology of the cell. Indeed, during 1976 his pleasure obtained examining under a microscope the surface membranes he had prepared will never be forgotten by his colleagues. Harold always did experiments himself, even when he had PhD students or post-doctoral fellows. The synthesis of sugars is both a labor and an art, and machines cannot replace delicate fingers here, as is the case with the synthesis of peptides. Harold was both an artist and an artisan in this field, and he loved his work.

Harold wrote a number of comprehensive reviews which included several on oligosaccharide synthesis in *Methods of Enzymology*, volumes 50 and 138 and a definitive review on the "Chemistry and Biochemistry of D and L fucose" in *Advances in Carbohydrate Chemistry and Biochemistry*, volume 39. With M.C. Glick he wrote a review on surface membranes for *The Glycoconjugates*, volume 2.

As a person, Harold was unassuming and his love and commitment to Israel was always foremost in his life. As part of this commitment he served in the Israel Defense Forces. He maintained strict standards of life for himself and his family. His indulgence was literature and classical music, particularly opera. The breadth of his knowledge can only be classed as Renaissance. Indeed he could challenge and was successful in most verbal duels. He was an ardent walker and visited most of the world's famous mountains and treks. The stories of his numerous travels in recent years with Sylvia both amused and amazed us. Even before retirement, he traveled widely, and we remember at one of the scientific conferences we attended together in Japan, Harold found time to climb to the top of Mount Fuji. There is hardly a place in the world that Harold and Sylvia have not visited. Not only by car or bus, but also on foot, with backpacks.

Harold died of a heart attack immediately after leaving the swimming pool of the Weizmann Institute. He had a full life with family, friends and colleagues and he died pursuing one of his daily pleasures. He is survived by his charming wife of 44 years, Sylvia, two daughters in Israel and one son in South Africa, in addition to eight grandchildren. May his memory be blessed.

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