Göran Magnusson

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Göran Magnusson was involved in research on several topics in organic chemistry. His achievements in studies of biologically active carbohydrates, in particular, led to international recognition. His unusual talent for creative, interdisciplinary research and his ability to motivate and stimulate his co-workers were cornerstones in his short but successful career. Göran's research was presented in more than 150 papers which not only deal with structural and synthetic studies of carbohydrates and natural products, but also include mechanistic studies of the rearrangement of epoxy alcohols and related compounds. In addition to being a scientist, Göran's imagination and ambition also led to his involvement in the start-up of several companies with activities in the Biotechnology field. The author had the privilege and pleasure to carry out his PhD studies under Göran's supervision and to start his own career in the stimulating and generous environment created by Göran after his appointment to the Chair of Organic Chemistry at Lund Institute of Technology.

Göran was born in 1942 in Simrishamn on the southeastern tip of Sweden. After the war his family moved to Lund where he grew up and later began his studies in senior high school by reading classics. He soon came to the conclusion that a classical education was not the right choice for him and left school to work in a laboratory at AB Åkerlund & Rausing, a packaging industry in Lund. During this period he read *Silent Spring* by Rachel Carson and this made such an impression on him that he decided to make the natural sciences, and chemistry in particular, his career in life. He therefore took evening classes in subjects on the natural sciences so that he could enter the senior technical high school in Helsingborg. There he specialized in chemistry and after graduating in 1965 he again worked at AB Åkerlund & Rausing for a year before setting out on his academic career. This began with studies in chemistry and chemical engineering at Lund Institute of Technology, which had recently been founded at Lund University. At Lund Institute of Technology, he soon stood out among his fellow students due to the purposefulness with which he carried out his studies. Early on he showed a special interest in synthetic organic chemistry and this turned out to be the field to which he would devote the rest of his career.

Göran Magnusson (1942–2000)

After receiving his Masters degree, it was natural for Göran to embark on a PhD program. This began in 1970 under the supervision of Professor Börje Wickberg who was working with natural product chemistry at Lund Institute of Technology. Together with Wickberg, Göran first directed his interests toward isolation and structural determination of sesquiterpene secondary metabolites from mushrooms of the species *Lactarius*. These metabolites have a pungent taste and were later shown by Olov Sterner, one of the PhD students succeeding Göran, to be formed from the common precursor stearoyl velutinal as part of a chemical defense system. However, on Göran's own initiative, the focus of his research was soon shifted to studies of the total synthesis of some of the isolated sesquiterpenes, which represented formidable synthetic challenges at that time. His efforts, while working together with Jan Froborg, another student in Wickberg's group, resulted in the construction of the vellerane skeleton and a total synthesis of racemic velleral, vellerolactone and pyrovellerolactone. In fact, these synthetic studies were so well received that Göran obtained the title of non-tenured associate professor simultaneously with receiving his PhD in 1975. Göran's ability to be engaged in different research projects, as well as his engineering skills, became evident at this time. Thus, he completed some syntheses of pheromones from the pine sawfly, in parallel with bringing his PhD project to a successful conclusion. He also developed a trap for collecting compounds purified by gas-liquid chromatography and a disposable, slow-addition funnel for use in small-scale preparative reactions.

Before going abroad to take up a post-doctoral position, Göran was employed for a year as research associate at the Department of Clinical Chemistry at the University Hospital in Lund, where research was focused on glycobiology. It was here that for the first time he came to appreciate the fundamental role of carbohydrates in cell–cell signaling and in adhesion between cells and pathogens such as bacteria and viruses. While recovering from surgery he read *Monosaccharide Chemistry* by Robin Ferrier and Peter Collins, which was the second book that became a turning point in his career. At this time his interest was mainly focused on synthetic aspects of carbohydrate chemistry, primarily synthesis and transformations of carbohydrate thioortho esters. However, within a couple of years he would return to the carbohydrate field and initiate a vigorous research program focused on the roles of carbo-

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hydrates as points of attachment for pathogens and as tumor-associated antigens. As a post-doctoral fellow Göran continued to develop his knowledge in natural product synthesis by studying synthesis of alkaloids with Professor Ernest Wenkert at Rice University in Houston, Texas. This resulted in synthesis of eburnamonine, quebrachamine, vincadine and epivincadine.

Göran returned from his post-doctoral period in 1979 to become head of the Organic Chemistry Section at Sockerbolaget R&D, located in Arlöv between Lund and Malmö. There he built up the section, which initially was meant to produce compounds of pharmaceutical interest from plant material. Early on this task proved less realistic and Göran, together with his colleague and friend Torbjörn Frejd, instead directed the research activities in the section towards the rapidly developing field of "biologically active carbohydrates". During four very productive years their team at Sockerbolaget quickly moved towards a position as one of the leading groups in synthetic carbohydrate chemistry. The group developed a simple procedure for the synthesis of 2-bromoethyl glycosides from different carbohydrates. These derivatives could then be used as inhibitors in studies of protein–carbohydrate interactions, or converted *via* robust reactions into neoglycolipids and neoglycoproteins for use as diagnostics or in production of monoclonal antibodies. With the different carbohydrate derivatives in hand the group entered into collaborative studies of the role of adhesion of pathogens, such as *Escherichia coli* and *Streptococcus pneumoniae*, to glycoconjugate receptors on epithelial cells.

In 1983 Göran left Sockerbolaget to take up a position as research scientist, funded by the Swedish Natural Science Research Council, at the Department of Organic Chemistry at Lund Institute of Technology. This allowed Göran to continue and expand his research in the carbohydrate field, but also to work on natural product synthesis, again in collaboration with Torbjörn Frejd who had moved to Lund Institute of Technology at the same time. Some years later Göran applied for the chair in organic chemistry to succeed Professor Börje Wickberg at Lund Institute of Technology after his retirement. He accepted the position in 1990 and stayed there to the end of his career.

In Lund Göran turned his attention towards obtaining a detailed understanding of the binding of protein adhesins from different pathogens to carbohydrates belonging to the globo-series of glycolipids. *E. coli*, which is the causative agent in 80–90% of all urinary tract infections, was studied first in collaboration with Professor Staffan Normark at Umeå University, and later together with Professor Scott Hultgren at Washington University School of Medicine in St. Louis. Göran's group used synthetic fragments of the pentasaccharide recognized by *E. coli,* which infect the upper urinary tracts including the kidneys, to determine the exact saccharide epitope recognized by different subclasses of bacterial protein adhesins. A detailed picture of the hydrogen bonding pattern between saccharide and adhesin was obtained in investigations based on a set of monodeoxy- and deoxyfluoro-derivatives of the disaccharide galabiose, which constitutes the minimal epitope recognized by the bacterium. Shortly after Göran's death the results of these studies were found to be in excellent agreement with the interactions in the crystalline complex between the tetrasaccharide globotetraose and one of the *E. coli* adhesins, as determined in Scott Hultgren's group. *Streptococcus suis*, a pathogen which causes meningitis, septicemia and pneumonia in pigs as well as meningitis in humans, also expresses adhesins which bind to the galabiose moiety of glycolipids. Göran's group therefore mapped the interactions between the adhesin of *S. suis* and galabiose in the same manner as used for *E. coli*. Whereas attempts to capitalize on these studies and develop carbohydrate based inhibitors of bacterial attachment have so far not been very rewarding for *E. coli* the opposite is true for *S. suis*. Here, oligovalent dendritic galabiosides have been discovered which inhibit bacterial attachment at the nanomolar concentration.

As revealed by his studies of bacterial adhesion, Göran fully recognized the importance of membrane-anchored glycolipids in different biological interactions. Since ceramide, the lipid moiety in glycolipids found in animals, was cumbersome to synthesize he developed short and efficient routes to neoglycolipids based on substitution of either 2-bromoethyl or dibromoisobutyl glycosides by alkyl thiols. These neoglycolipids were then used to investigate the binding between globotriose and verotoxin, which is produced by *E. coli* and causes diarrhea. Again, use of a comprehensive set of deoxy analogues, in combination with molecular modeling, allowed construction of a detailed picture of the carbohydrate–protein interaction. Glycolipids are also of major importance as tumor associated antigens displayed on the surface of cancer cells. Such antigens commonly contain *N*-acetylneuraminic acid, a sialic acid known to be one of the more challenging monosaccharides to incorporate in oligosaccharides by chemical means. As a step towards solving this problem Göran's group developed a new *N*-acetylneuraminic acid donor which allowed sialylations to be performed with high stereoselectivity and also provided access to bis-sialic acids known to be extremely difficult to prepare. The carboxy group of *N*-acetylneuraminic acid is known to form lactones with hydroxy groups on adjacent carbohydrates and such lactones are believed to be unique to tumor cells. They thus constitute ideal candidates in attempts to direct the immune system towards cancers, but their chemical lability had so far hampered such attempts. Göran found an elegant, yet simple, solution to this problem when he realized that antibodies raised against the corresponding lactams should be able to cross-react with the lactones expressed on cancer cells but not with the non-lactonised sialic acid derivatives found on normal cells. Initial immunological studies confirmed that this approach worked and Göran had carried out a comprehensive synthetic program, which was to be continued into immunology at the time when his career ended prematurely.

Development of methodology is an important aspect of carbohydrate chemistry, as in all other fields of chemistry. As mentioned above Göran made contributions that advanced our ability to incorporate sialic acids in glycoconjugates. However, his discovery of the 2-trimethylsilylethyl group as an ideal anomeric protective group in oligosaccharide synthesis will most likely be remembered as his most important contribution to development of methodology. The 2-trimethylsilylethyl group was found to be stable under almost all conditions used in oligosaccharide synthesis, yet it could be removed, or converted into anomeric leaving groups, under mild conditions. Later, this protective group was also developed into an anomeric linker for solid phase carbohydrate synthesis. Other developments of methodology in Göran's group concerned manipulations of the 4,6-*O*-methoxybenzylidene, the *N*-trichloroethoxycarbonyl and the *p*-methoxyphenyl protective groups.

In spite of the large efforts made by Göran in the carbohydrate field he did not leave behind the interest in total synthesis that he developed during his PhD studies and post-doctoral period. At Lund Institute of Technology he was involved in efforts to synthesize Taxol together with Professor Torbjörn Frejd. He also accomplished total synthesis of lignans, such as burseran, cubebin and hinokinin, as well as the antimicrobial and antileukemic fungal natural product botryodiplodin, and its stereoisomer epibotryodiplodin. Synthesis of the latter natural products was stimulated by, and based on, mechanistic and synthetic studies of the rearrangement of epoxy alcohols and related compounds that were ongoing in his group. The unsaturated aldehydes, which were obtained from rearrangement of epoxyalcohols, were also used to assemble conformationally restricted compounds. In an ingenious way,

typical of Göran's unusual ability to connect one part of his research to a seemingly unrelated part, such restricted compounds were employed to prove the existence of an anomeric effect in furanosides. Later, these studies were extended in a completely different direction, *i.e.* towards preparation of polycyclic oxanorbornanes, which are rigid compounds that may interact favorably with proteins that constitute targets for drugs.

Göran always believed that being a scientist at an institute of technology carried a commitment to consider and develop applied perspectives of his research. In agreement with this conviction he was involved in starting and directing several companies. The most prominent of these was Symbicom AB, a biotechnology company which he participated in funding together with leading scientists in microbiology and medicine. His talent for leadership, and his broad interdisciplinary knowledge, were of uppermost importance when he served as chairman of the board of Symbicom AB for eight years. After Symbicom AB was purchased by AB Astra in 1994, he participated in initiating several companies with activities ranging from development of molecular modeling, to carbohydrate based diagnostics and drugs for treatment of cancer. In all of these companies his wife, Pia, was instrumental in building up organizational routines and managing the daily activities without which no company can function and survive.

Göran was equipped with an unusual portion of common sense and inventiveness, which he shared generously with those around him. As a scientist he was quiet and controlled but still outspoken and resolute in committee work. These qualities came to serve the scientific society well when he became a member of the Swedish Natural Science Research Council and the MISTRA program board. On these boards his broad knowledge, natural authority and persistence made him an efficient spokesman for chemical research in Sweden and abroad.

Göran had a warm personality and cared much for his coworkers. At Lund Institute of Technology he guided twelve PhD students to their doctoral degree and among these he was most popular in his role as supervisor. Students in his group were given an unusual freedom to develop their projects according to their own ideas and interests. While listening to the views of his students Göran displayed an exceptional talent in combining visions with tangible ideas. Furthermore, intuition and an excellent knowledge of human nature meant that he often succeeded in stimulating his co-workers to achievements close to the limits of their ability. It is not surprising that this led to many valuable results that aroused international attention.

Göran's roots were deeply embedded in the countryside of Skåne in southern Sweden. He spent his free time together with his wife Pia in their summer home in Skillinge, which often became a meeting place for discussions concerning everything from intricate chemical questions to the cultivation of crayfish in the pond by his house. Those of us who had the privilege of enjoying Göran's and Pia's hospitality, and of developing our careers close to Göran, are deeply indebted for the knowledge and wisdom he shared with us on all occasions.