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William Summer Johnson: An Appreciation

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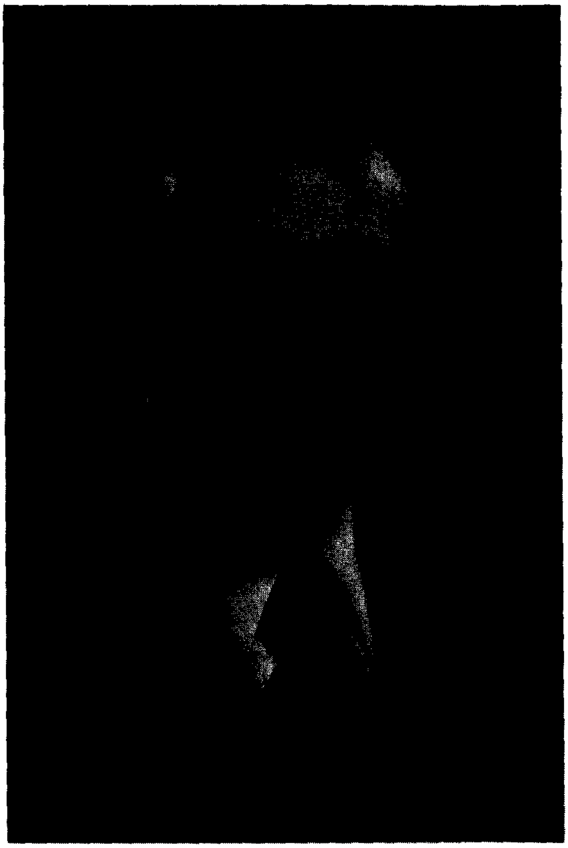

A penetrating mind and a powerful imagination are not always associated with a warm heart and a sympathetic understanding of other people and their problems. When they are and when you can add to them a sense of humor, you will find that you have someone very like William S. Johnson. His entry to research in the late thirties came at a time when the challenge presented to synthetic organic chemists by the steroids had been taken up by many workers, and it offered an exciting vista for any newcomer to the chemical scene. It is therefore not surprising that Bill Johnson got caught up in this field and that the manifold problems of steroid synthesis should have dominated his early researches. But there was more to his early attraction to steroid synthesis than merely following a fashion, or it would not in one form or another have remained the central feature of his work over some 40 years of active research.

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The 1930s saw the birth of what we nowadays call bioorganic chemistry, although it could be argued that it was merely the return of organic chemistry to its original objective, viz., the chemistry of living matter. As one who grew up chemically during this period I would attribute this birth or rebirth to three main things. First, the isolation of several vitamins which made them open to attack by organic chemists and the discovery that some of them at least are involved in enzyme action as components of coenzymes; second, the isolation of the secondary sex hormones and later the cortical hormones and the recognition of their relationship to the sterols and bile acids; third, the discovery or, better put, the rediscovery of adsorption chromatography. In these now distant days the hold of the classical organic chemist devoted to structural studies by degradation and synthesis but with little or no feeling for biological function or significance was very strong. As a result the number of us attracted into these new fields which involved problems of structure in relation to function was at first rather small. However, as new discoveries began to come along thick and fast, and especially after the elucidation of the general structure of the steroid nucleus, the number moving into this new area increased rapidly. There were undoubtedly some who leapt upon the bandwagon because of the opportunity it gave them to exercise the traditional skills of the organic chemist without being seriously interested in the deeper problems of function or of biosynthesis. I do not belittle them or the achievements made by them over the years, but I do not think Bill Johnson was one of them. What I do not know, for I have never asked him, is whether his interest in stereochemical control of chemical synthesis, so wonderfully displayed and so vital in the world of nature, was sparked off initially by his encounter with the steroids in his early graduate work. I suspect that it was, for chance frequently plays a large part in determining our fields of interest; but whether it was or not, there can be no doubt that it has been the dominant theme of his life's work.

Although I had a preliminary flutter with the steroids in the pre-Rosenheim/King era, it was the vitamin–coenzyme field that attracted me in the early thirties; and I was deeply involved in it by 1938. Partly for this reason, and partly ere long because of other preoccupations associated with the war, I paid only passing attention to work in the steroid field and so noticed little of the early work of W. S. Johnson in Wisconsin. I was brought up with a jolt, however, and because fully aware of him in 1951/52 when he and his students published two elegant synthesis of estrone. This is not the place to discuss them in detail, but quite apart from their elegance from a classical standpoint they revealed an unusual feeling in their author for the dynamic aspects of stereochemistry. Further evidence of Johnson's feeling for stereochemistry and his ability to take maximum advantage of its dynamic aspects to control and direct the synthesis of complex molecules was soon forthcoming. In 1953 he published a fantastic synthesis of epiandrosterone in the course of which he carried out a two-stage reduction of a tetracyclic ketone which involved the setting up of six centers of asymmetry and obtained directly a product with the desired *trans–anti–trans–anti–trans* configuration. That was to me at the time a veritable *tour de force*!

I first met him in person in the autumn of 1954 when we were both discharging the not over-arduous duties of visiting professors, he at Harvard and I at M.I.T. We saw quite a lot of one another during that period, and I can recall not infrequent triangular and somewhat convivial sessions with our mutual friend Bob Woodward. Since that time I have been privileged to remain in touch with him as a valued friend. Those were the days immediately following the establishment of squalence as a precursor of cholesterol in rat liver. Although the full story of the cholesterol biosynthesis was not to be revealed for some years yet, that discovery gave validity to the old hypothesis of Robinson and led to a fresh outburst of experimental work and theoretical speculation. From his previous synthetic studies it is, I think easy to see how the stereochemical control shown in the squalene–cholesterol conversion would fascinate Johnson; and indeed it did, for he soon began to develop his now classical work on biomimetic syntheses of polycylic systems based on polyene cyclizations. I confess that in the early stages of his studies on this topic I thought he might have bitten off more than he could chew; but how wrong I was! I grossly underestimated the combination of experimental skill, insight, and ingenuity he brought to bear on it, not to mention the tenacity he has displayed over the years despite the chairmanship of a large and developing chemical school and the temptation to beachcomb in the balmy climate in California.

In a recent review published in this Journal (1976, 5, 51) Bill Johnson sets out a remarkable story culminating in the syntheses by biomimetic procedures of a variety of steroid derivatives with the natural all-*trans* configuration. These were achieved by the stereospecific cationic polyene cyclization methods he has so successfully developed. The conversion of an open-chain tetraenic acetal having no chiral centers into a tetracyclic compound having seven such centers and producing only two out of a possible 64 racemates is a striking tribute to the power of his methods.

At this, the time of his formal retirement, however, he can look back on a splendid record of achievement. Not only has his research contributed notably to bioorganic chemistry, but it has also enriched our theoretical and practical knowledge of addition reactions among unsaturated compounds. What in the longer term may be equally important is the inspiration and especially the friendship and help he has given to the young men and women who have worked with him. I, an old friend and admirer, salute him and wish him many happy years in his retirement.