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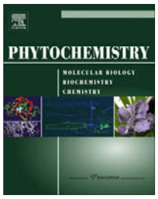

Announcement

Helen A. Stafford – 2008 Recipient of the PSNA Phytochemistry Pioneer Award

(Photographs provided by Anne Scarff, niece of Helen Stafford)

The Early Beginnings

Our President, Norman Lewis, has prevailed on myself (Frank Loewus) to act as a surrogate for Helen Stafford who was unable to attend this meeting and her formal acceptance of the Phytochemistry Pioneer Award of the Phytochemical Society of North America (PSNA) due to health reasons. I share this obligation with Daneel Ferreira whose expertise in plant phenolics will address Helen's contributions in this regard.

It was 1952 when I joined Birgit Vennesland's group in the Department of Biochemistry at the University of Chicago. There I met Helen, an instructor in botany as well as postdoctoral student involved in Birgit's studies on organic acid metabolism and I became aware of Helen's growing knowledge of organic acid metabolism in plants as well as her patient manner of sharing this talent. Prior to her departure to begin her tenure at Reed College, an outstanding institution of undergraduate study, Helen presented a seminar on ascorbic acid biosynthesis in plants and animals drawn from three back-to-back papers by Isherwood and Mapson that had just appeared in the Biochemical Journal. Her 45 minute presentation rested in my mind like a perfect song. Even now, 56 years later, her message remains, clear and exciting, the mark of an accomplished teacher.

When I moved to USDA labs in Berkeley, CA in 1955 to begin work on loss of fresh flavor and appearance in frozen strawberries during storage, it was memory of Helen's seminar on ascorbic acid that motivated me to study the biosynthesis of Vitamin C in plants. The following year I invited Helen to spend her three month academic summer break in my lab while we explored the curious fact that theoretical cleavage of the six-carbon chain of ascorbic acid between either C2/C3 or C4/C5 ultimately produced the four-carbon dicarboxylic acid, L-tartaric acid, a major organic acid constituent of the grape. Our experimental results failed to provide fresh clues in this regard but Helen returned to Reed College determined to survey the occurrence and distribution of tartaric acid in plants. By enlisting her eager undergraduate students in this project, she found L-tartaric acid to be a major organic acid in species other than the grape, notably the common geranium.

Another ten years passed before Kazumi Saito at Kyoto University reported that L-tartaric acid in the grape was a metabolic product of C4/C5 cleavage of the six-carbon chain of L-ascorbic acid. In 1973, George Wagner, a graduate student in my lab at Buffalo discovered that L-tartaric acid from geranium arose due to cleavage of L-ascorbic acid at C2/C3, the C1-C2 fragment forming oxalic acid. Then, in 1998, Glen Wheeler and Nicholas Smirnoff at Exeter University established an eight-step biosynthetic pathway of ascorbic acid in plants that set the stage in 2002 for Seth DeBolt at the University of Adelaide to complete the story of L-tartaric acid biosynthesis in the grape by both C4/C5 and C2/C3 cleavage depending upon subcellular and developmental processes. (Incidentally, each advance of our understanding regarding L-tartaric acid biosynthesis involved a graduate student as principal investigator.)

It was Helen Stafford's determined efforts to wrest from nature the information needed by these students to further explore the complexities of tartaric acid formation in plants that set in motion this train of discoveries. Not unlike Thomas Jefferson's decision to send Lewis and Clark on their perilous journey up the Missouri and down the Columbia Rivers so he could establish the wisdom of the Louisiana Purchase or the history of Pasteur's efforts to resolve underlying conflicts over fermentation versus putrefaction that mark these heroic individuals as Pioneers. So too, Helen Stafford has earned the distinction of being a Phytochemistry Pioneer for opening up the pathway from D-glucose to L-tartaric acid and incidentally, playing an important part in establishing the role of

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ascorbic acid as a major metabolic source of oxalic acid in all plants.

The Proanthocyanidins (Condensed Tannins)

Helen's even more extensive contributions were on the so-called condensed tannin biosynthetic pathway. I (Daneel Ferreira) met Helen on my first visit to the United States from far-away South Africa while participating in the First North American Tannin Conference held in Port Angeles, Washington, August 1988 over twenty years ago. At that meeting I was privileged to renew my relationship with Dick Hemingway and Eddie Haslam, and to meet Norman Lewis, Herbert Hergert, and above all, Helen Stafford, for the first time. The conveners of the meeting, Dick Hemingway and Joe Karchesy, placed the papers on biosynthesis, read by Lewis, Stafford and Hergert, at the very beginning of the program, hence emphasizing the crucial importance of understanding both the chemistry and enzymology of the biosynthesis of the proanthocyanidins and other phenolics.

Very appropriately, Helen's contribution was titled, "The Enzymology of Proanthocyanidin Biosynthesis." She comprehensively reviewed the enzymology of the biosynthesis of the building blocks of 2,3-trans configuration up to the C_6-C_3-C_6 level. At the time, the origin of building blocks of 2,3-cis configuration, and the elusive "condensing enzyme" were not yet known. In her presentation and the derived chapter that was published in "Chemistry and Significance of Condensed Tannins", eds. R.W. Hemingway, J.J. Karchesy, Plenum Press, New York, 1989, 47-70, Helen presented various Figures that depicted all the major steps of the proanthocyanidin pathway, except the aforementioned two. To this day, several of these Schemes, represented by the Figure are still shown in biosynthesis sequences, taking into consideration the considerable amount of new information that has been added over the past 20 years. Is that not true testimony to the pioneering contributions that Helen Stafford has made to this complicated area of study? Incidentally, in a collaborative work with Rick Dixon of the Noble Foundation we delineated one of the routes towards the formation of constituent units with 2,3-cis configuration (Science, 2003, 299, 396–399). However, the much hypothesized "condensing enzyme" has yet to be identified (Fig. 1).

At the aforementioned Tannin Conference, one of my talks dealt with "Base-Catalyzed Pyran Rearrangements of Profisetinidins".

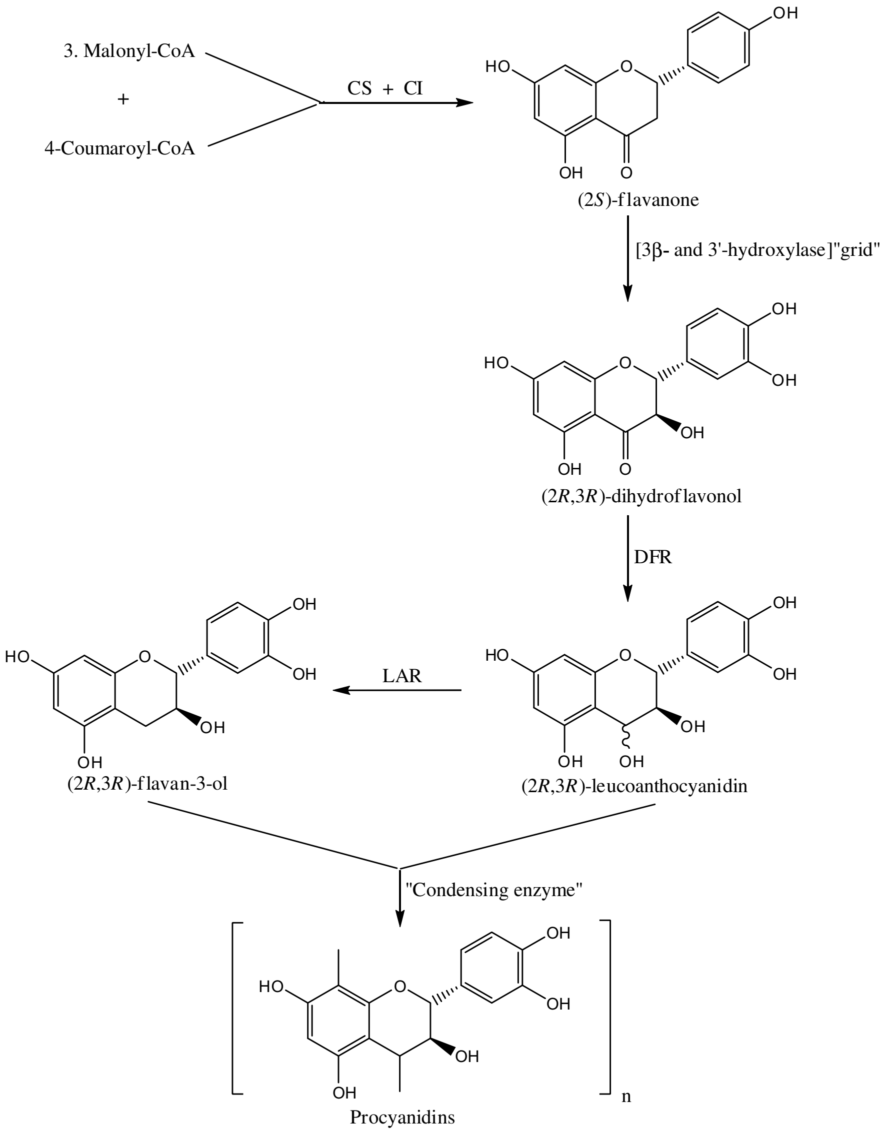

Fig. 1. Helen Stafford's proposal for the biosynthesis of procyanidins via (2R,3R)-flavan-3-ols and (2R,3R)-flavan-3,4-diols [CS = chalcone synthase; CI = chalcone isomerase; DFR = dihydroflavonol reductase; LAR = leucoanthocyanidin reductase].

First, I described the facile formation of the four fisetinidol-catechin regioisomeric starting materials via mild acid-catalyzed coupling of fisetinidol-4á-ol and catechin. In this context, the 0.1 M HCl solution that we used to activate the flavan-3,4-diol played, in principle, the same role as Helen's "condensing enzyme." Needless to say what an energetic discussion ensued when I, solely to provoke Helen, told the audience that chemically we did not really need Helen's mysterious "condensing enzyme" to efficiently form the interflavanyl bond!

Helen published her first paper on the proanthocyanidins very fittingly in Phytochemistry back in 1980, 19, 131-135. She followed that with more than 20 manuscripts, underpinned by meticulous experimentation, published in a variety of journals. If one considers what she has achieved in this complex area of research with the support of mostly undergraduate students, it serves as testament of her strong mind, dedication, diligence, and above all, her pioneering spirit to wander where so few had the audacity to go.

Besides Helen's dedication to research and teaching, she also has a life-long history of service to the plant sciences, hence fully complying with the tripartite mission of university/college professors. She served as an editorial board member of Plant Physiology from 1964 to 1992, on the Commission for Undergraduate Education in Biological Sciences from 1968 to 1971, and as an NSF panel member for metabolic biology from 1973 to 1975. Helen has also played a leading role in the Phytochemical Society of North America (PSNA), serving as president (1977-1978), and as Editor-in-Chief (1989-1993) of its popular publication, Recent Advances in Phytochemistry, a series that has chronicled the proceedings of the annual meetings of the PSNA for more than 30 years. Her outstanding contributions in the field of plant secondary metabolites, was recognized in 1996 when she received the Charles Reid Barnes Life Membership Award of the American Society of Plant Physiology.

Helen has always been a staunch opponent of unequal treatment for women in science. Her dedicated efforts in this regard culminated in a science school (Biology, Chemistry, Mathematics, and Physics) at Reed College where there is due recognition for the principle of gender equality among the teaching faculty and staff.

Helen, we as colleagues and all the students that you influenced in so many positive ways, salute and honor you for the integrity and honesty of your scientific endeavors, for expanding our horizons, for being a loyal colleague and friend, and for the indelible impressions that you have left on research towards opening up the pathway from D-glucose to L-tartaric acid, for playing an important part in establishing the role of ascorbic acid as a major metabolic source of oxalic acid in plants, and for providing fundamental insight into the biosynthesis of the proanthocyanidins. (Reprinted, in part, with permission from the 2008 PSNA Newsletter.)

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