## This Week's Citation Classic\_

Cahn R S, Ingold C K & Prelog V. The specification of asymmetric configuration in organic chemistry. *Experientia* 12:81-94, 1956. [Chemical Society, London, England; University College, London, England; and

[Chemical Society, London, England; University College, London, England; and Eidgenössische Technische Hochschule, Zürich, Switzerland]

This paper presented a new system for specification of configuration of organic stereoisomers by descriptors R, S, r, and s. [The  $SC^{(0)}$  indicates that this paper has been cited explicitly in over 660 publications since 1961.]

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October 4, 1982

"The reason why my paper with Robert Sidney Cahn (June 9, 1899-September 15, 1981) and Sir Christopher Kelk Ingold (October 28, 1893-December 8, 1970) became a *Citation Classic* is because it satisfied the need for an unambiguous, general system for specification of the innumerable stereoisomers of an organic compound of known constitution.

"Descriptors D and L were formerly used for that purpose but they became so ambiguous that in 1951, C. Buchanan wrote in a note to Nature: 'Surely it would be better to abandon the prefixes D and L, except for those parts of the carbohydrate and *a*-amino acid fields in which they do serve a useful purpose." The same year, a paper appeared in the Journal of the Chemical Society by Cahn and Ingold<sup>2</sup> in which they redefined the descriptors D and L to preclude their ambiguity.

"In 1954, the anniversary meeting of the Chemical Society was held in Manchester. At the end of it a dance was organized by ICI in its Hexagon House in Blakeley. Only a few participants did not dance but drank beer and discussed chemistry instead; among them, the president of the society, Ingold; the editor of its journal, Cahn; and myself. I remember that I vigorously criticized some parts of their paper and that at the end of the evening they invited me to join them in writing an article on the subject. I gratefully accepted the offer without thinking about the consequences.

"During numerous meetings held in England and in Switzerland, we laid down the principles of a new system and eventually, in 1956, we published the resulting paper in the Swiss journal Experientia.

"It was very important that the editors of Beilsteins Handbuch,<sup>3</sup> the late F. Richter and O. Weissbach, accepted our proposals and used them for specification of many thousands of stereoisomers. (Richter, the chief editor of *Beilsteins Handbuch*, died in 1961, before the fourth supplement appeared. He was succeeded by Hans-Günther Boit.) They called our attention to several imperfections, and their remarks as well as the benevolent criticism of other colleagues incited us to improve and extend the system and to write a second paper on it, which appeared in 1965.<sup>4,5</sup>

"Since then, the system, which is often called the CIP-system, has been used extensively not only in scientific periodicals, monographs, and handbooks, but it also penetrated into most of the textbooks of organic chemistry and biochemistry. The International Union of Pure & Applied Chemistry (IUPAC) Commission on Nomenclature of Organic Chemistry has included it in its rules, and Chemical Abstracts uses it for specification of stereoisomers. Its principles have also become the basis for the specification of cis-trans-isomers and of heterotopicity as well as for specification of the steric course of asymmetric syntheses and enzymatic reactions. Indeed, the system has become so ingrained that the papers on which it is based are almost never cited anymore by its habitual users.

"Experience accumulated during the last 16 years has shown that there is a need for a more precise formulation or even for a revision of some parts of the system. To cover this need, a paper by myself and G. Helmchen about the basic principles (treated so far only pragmatically!) and a revision of the CIP-system appeared this summer in Angewandte Chemie and its international edition."<sup>6,7</sup>

2. Cahn R S & Ingold C K. Specification of configuration about quadricovalent asymmetric atoms.

 Bolt H G, ed. Beilsteins Handbuch der Organischen Chemie. Viertes Ergänzungswerk. Berlin: Springer-Verlag, 1972. Vol. 1, p. X.

6. Prelog V & Helmchen G. Grundlagen des CIP-Systems und Vorschläge für eine Revision.

<sup>1.</sup> Buchanan C. Configurational notation of the tartaric acids. Nature 167:689-90, 1951.

J. Chem. Soc. 1951:612-22.

<sup>4.</sup> Cahn R S. Ingold C K & Prelog V. Spezifikation der molekularen Chiralität. Angew. Chem. 78:413-47, 1965.

<sup>5. -----</sup> Specification of molecular chirality. Angew. Chem. Int. Ed. 5:385-415, 1965.

Angew. Chem. 94:614-31, 1982.