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Impossible things in stereochemistry

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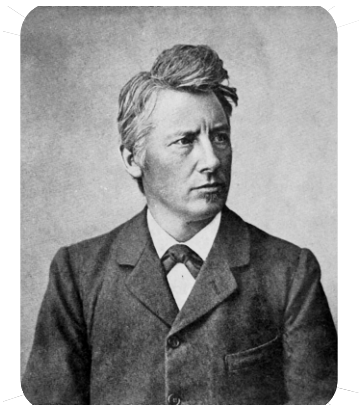
Alice ... said: 'one can't believe impossible things'.
'I dare say you haven't had much practice', said the Queen.
'When I was your age, I always did it for half an hour a day.
Why, sometimes I've believed as many as six impossible things
before breakfast...'

Lewis Carrol
Through the Looking-Glass And What Alice Found There
1871

Stereochemistry, like any other science, consists fully of previously 'impossible' things, the creation of which is carefully prepared by predecessors. What remains is only to see them, to realize them and to make them possible. Sometimes the whole life needed to do that, but more often it is even not enough.



J. H. vant't Hoff
(30.08.1852–01.03.1911)

J. A. Le Bel
(21.01.1847–06.08.1930)

Jacobus Henricus van't Hoff had seen an 'impossible' thing in stereochemistry, and having had recognised it, by irrepressible flight of fancy† had created a clear and unambiguous possibility for the identification of chirality of known organic compounds and a programme for the synthesis of a new. On 14 pages, he described his idea of asymmetrical tetrahedral carbon with four different substituents (a proposal for the development of three-dimensional chemical structural formulae). This occurred early in September 1874, van't Hoff being a student of Utrecht University, after he just had reached 22. Immediately had he nobly admitted that such an idea had concurrently been suggested by his French colleague Joseph Achille Le Bel, who had given all his life to prove this idea.

The concept of van't Hoff[1,2(*a*),(*b*)] had become the Ariadne's thread in the labyrinths of stereochemistry for a long time.‡

From the multitude of van't Hoff's predictions,[1] we will turn our attention to the key ones. He proposed to obtain the simplest methane derivatives with monoatomic substituents HCBrClF by decarboxylation of the corresponding acid and probably he himself planned to synthesise them, having had already obtained $ClCH_2Br$ from CCl_3CO_2H.[4] After many unsuccessful attempts it became possible to obtain (*S*)-(+)-HCBrClF only in 1997.[5(*a*)]

The prediction of the chirality of allenes, which do not have asymmetric atom, still possessing molecular dissymmetry as a whole was fundamentally important. This opened a way to

† 'Fancy in science' – this was the title of a public lecture delivered by van't Hoff on the inauguration as a professor of Amsterdam University in 1878. Van't Hoff's fancy included only one assumption and lies literally in the following: 'Starting from the supposition of the motionless state of radicals across the C atom, we would not be able to explain these phenomena (of optical isomery) unless by tetrahedral grouping of these radicals around the C atom… one can clear that on the models of tetrahedra agglutinated from cardboard'.[1]

‡ The discovery of van't Hoff had been carefully prepared by his great predecessors. L. Pasteur already resolved the enantiomers of his salt in 1848 (see ref. 3) and, in 1860, said: 'Are the atoms of the right acid grouped on the spirals of a dextrogirated helix, or placed at the summits of an irregular tetrahedron, or disposed accordingly to some particular asymmetric grouping or other? We cannot answer these questions. But it cannot be a subject of doubt that there exists an arrangement of the atoms in an asymmetric order, having a non-superimposable image. It is not less certain that the atoms of the left acid realize precisely the asymmetric grouping which is the inverse of this' [see ref. 2(*a*)].

The great Russian chemist A. M. Butlerov had already created his theory of chemical structure (1860): the existence of compounds of the same composition, having different properties, means that they are isomers, which have strictly defined chemical structure. The search for isomers in different classes of compounds and for transformations with the change of chemical structure (rearrangements) became a programme for the development of organic chemistry for many years. Butlerov proposed a reasoned idea of a tetrahedral structure of the carbon atom (1862).

In 1869, V. V. Markovnikov has already described his universally known rule,[2(*d*)] according to which many asymmetric carbon compounds are formed (the doctoral thesis 'Materials on the question of the mutual influence of atoms in organic compounds'; Kazan, 27.04.1869, opponents A. M. Zaitsev and A. M. Butlerov)..

Finally, J. Wislicenus, who studied the isomery of (±)- and (-)-lactic acids, wrote in 1873 wrote 'that it could not be interpreted differently unless having assumed that the reason of such difference lied only in different spatial arrangement of atoms'.[2(*e*)]

This statement was probably the main stimulus for the van't Hoff's flight of fancy.

numerous molecularly chiral systems.[5(b)] In 1956, optically active hexahelicene was obtained, representing the left- or right-handed helices of Pasteur's dreams. The next principal prediction of van't Hoff involved asymmetric heteroatoms: even in 1877, he pondered on the arrangement of bonds at the nitrogen atom. In the same year, J. Wislicenus put the question of the possibility of asymmetric nitrogen in ammonium salts, while W. J. Pope resolved a chiral ammonium salt by the second method of L. Pasteur in 1899 [for a brief story, see ref. 6(*a*)]. The exhaustive answer to the question why W. J. Pope could not resolve these compounds by the first method of Pasteur was recently found.[6(b)]

The asymmetric three-coordinated nitrogen atom seemed impossible for a long time, as far as, for example, the inversion frequency of the N pyramide in NH_3 is 10^{10} Hz. However, in 1980, an optically active compound with the asymmetric nitrogen atom in the open chain was synthesised.[7]

Imagination of many chemists was captivated by the possibility of mechanical linkage of molecules as interwoven rings (catenanes), rotaxanes or knots. This impossible thing was implemented in 1960. This fundamental achievement means that the molecules are bodies, which can be interlaced, like chain links (the corresponding results had already been discussed in *Tetrahedron*).[2(a),§]

A crucially important step in the development of stereochemistry is hypervalence. In 1952, V. L. Tal'rose discovered the methonium ion. The stereochemistry of other atoms has been developed,[10(a)–(c)], for example, the Voronkov's draconoids of hypervalent silicon.[10(d)]

Van't Hoff placed high emphasis to coordination and inorganic chemistry. In the American edition of his book, the supplement of A. Werner was published. In these fields, there are absolutely impossible things. For example, this is the structure of keplerate with more than 500 atoms and the highest Euclidean symmetry.[11(a)]

Contemporary stereochemistry is characterised by continuous growth in the complexity of its objects,[11(b)] but has still a lot of unseen simple 'impossible' things. Evidence for this is the recently found astonishing stability of a previously unknown *ortho-ortho*-isomer of Tröger's base[11(c)] to racemization.

It is noteworthy that the simplest inorganic compounds, NH_3 and N_2 crystallise in chiral space groups $P2_13$ and, therefore, can be the objects of global spontaneous symmetry breaking. Moreover, the polymerization of N_2 in a chiral structure (space group $I2_13$) was achieved recently.[12]

A decade after the above van't Hoff's discovery, he created the basis of a new science – physical chemistry (for which he obtained the first Nobel prize in chemistry in 1901), in order to find the exact conditions for interconversion of conglomerates, racemates and double salts, to predict the kinetic resolution of racemates, asymmetric synthesis and the multitude of previously impossible things.¶

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§ The directed synthesis of catenanes by A. Lüttringhaus and G. Schill was described in ref. 8, where I managed to predict the mass spectrum of catenanes, which, it seemed to me, should have been the unambiguous proof of their topological structure. This prediction had been confirmed two years later and found widespread use.[9] In 1994, D. Amabilino *et al*. used this method to confirm the structure of olimpiadane – [5]catenane.[9(b)] Finally, we managed to obtain a supramolecular (H-bonded) [3]catenane chiral structure, which crystallises in a chiral space group and undergoes spontaneous resolution.[9(c)] A molecule tied in the knot has also been obtained.[9(d)] In the building of many catenanes, the methods of coordination chemistry have been used.[9(f)] My prediction[8] that '...catenanes were to be looked in Nature' (cited by G. Schill[9(a)]) was soon confirmed, and at the present time we see intensive development in the field of structural DNA nanotechnology.[9(h)]

¶ The Russian translation of the book[13] by J.-H. van't Hoff was edited by the Nobel prize winner N. N. Semenov in 1936. He wrote about van't Hoff's book: 'This book is one of such books, that as milestones mark the main way for the development of knowledge of the mankind". N. N. Semenov supported the development of stereochemistry in the Institute of Chemical Physics created by him in 1931. Recently theoretical analysis for the mechanism of the high sensitivity of helix formation of poly(phenylacetylene) with crown ether pendants to small enantiomeric excess of amino acids [studied by E. Yashima (see references in a paper of this issue, p. 231)] has been conducted in this Institute.[14]