Parity Rule. Algorithmic Method for the Assignment of Chiral Centers

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Synopsis. A simple new algorithm is presented for the assignment of *R/S* configuration of chiral centers described in any projection form.

The configuration *R* and *S* of a chiral center (such as carbon with four ligands) is generally determined by the sequence rule procedure:[1,2] This procedure involves, in the last step, a mental transfer of the molecule described in a two dimensional surface. Such a mental transfer can become more and more difficult with increasing molecular complexity and even experienced chemists may make mistakes in this step.

Here we wish to present a simple algorithm for the assignment of chiral center configuration. This method requires no transformation of the first projection described and is, furthermore, applicable to complex molecules.

The method is outlined as follows:

(1) Assign the priority numbers for each group surrounding the chiral center.

(2) Take the number of the group which is clearly directed forward, and then the three others in a clockwise manner. Thus a sequence of four numbers is obtained.[3]

(3) Then take each of the first three numbers in the sequence, and count *how many* smaller numbers follow each one from left to right. Take the sum of these counts.

(4) In the case of an *R*-configuration, the resulting sum will be even. For an *S*-configuration, the operation will yield an odd sum.[4]

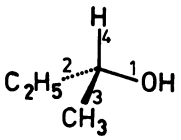

Fig. 1.

For example, consider the configuration of 2-butanol (Fig. 1). The number of the methyl group (No. 3) directed forward is taken first. Then the three other groups (No. 4, No. 1, No. 2) are taken in a clockwise manner. Thus the sequence 3-4-1-2 is obtained. After No. 3, TWO smaller numbers (No. 1 and No. 2) follow. After No. 4, TWO smaller numbers (No. 1 and No. 2) follow. After No. 1, NO smaller number follows. TWO+TWO+ZERO=FOUR, an even sum is obtained. This indicates that the configuration is *R*.

The Figs. 2—5 show the flexibility of this method for many different projection forms.

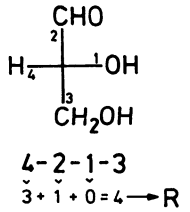

Fig. 2.

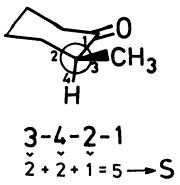

Fig. 3.

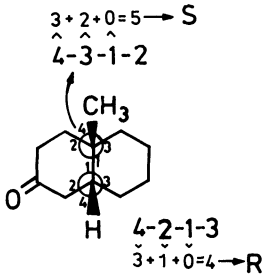

Fig. 4.

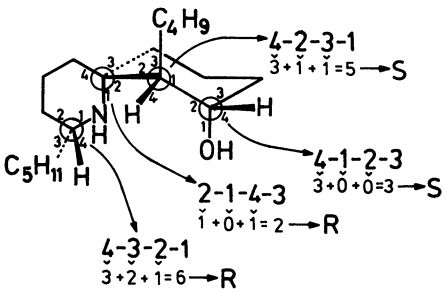

Fig. 5.

The rule will always give the correct answer provided the diagram is clearly drawn.[5] This method has advantages over the others,[6-10] in which many numbers or tables must be memorized. Here, the sequence to be remembered is simply "forward directed group first," "the three others in a clockwise manner," "how many smaller numbers follow" and "even=*R*." The rule will be particularly useful when there are many chiral centers to be assigned and verified.

The author thanks Dr. G. P. Moss for his helpful suggestion about the examples 7—10.

References

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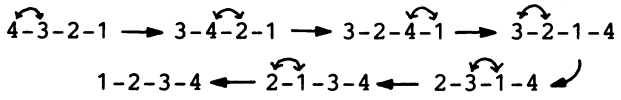
3) Regardless of which number is taken in second place, the result is the same as long as the clockwise manner is respected.

4) This algorithm is based on the following facts.

1° The sequence 1-2-3-4 corresponds to the *R*-configuration.

2° When two numbers of a sequence are interchanged, the related configuration is inversed.

3° The sums of the number of smaller numbers following in the sequence correspond to the number of changes necessary to afford the series 1-2-3-4. For example, from the sequence 4-3-2-1, one can arrive at the sequence 1-2-3-4 with the six following exchanges:



5) It must be noted that in some representations, it becomes difficult (Figs. 6—8) or even impossible (Figs. 9—10) to choose a forward directed group. In Fig. 6, only the backward directed group is indicated. In such cases, one must choose, as the forward directed group, one of the two neighbouring groups on either side of the backward directed group. In the case of Figs. 7—10, the problems are due to the representations themselves. The configuration of a chiral center represented as in Fig. 11 (a planar carbon) cannot be known without some further information. The true configuration of Fig. 11 must be either 12 or 14, and in each case, it is different. This ambiguous representation can be found in Figs. 7—10. In Figs. 7—8, we know what are intended here. But in the case of Fig. 9, we are not sure of the configuration of the carbon in question. The starred carbon in Fig. 10 which appeared in IUPAC E rule[11] is almost planar and it will be impossible to determine its configuration.

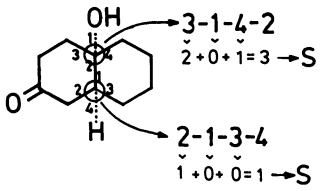


Fig. 6.

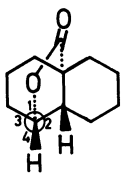


Fig. 7.

Fig. 8.

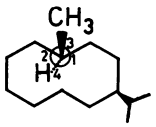


Fig. 9.

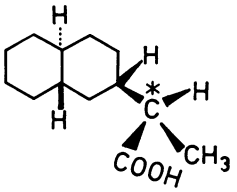


Fig. 10.

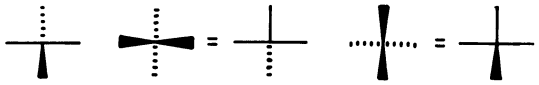


Fig. 11. Fig. 12. Fig. 13. Fig. 14. Fig. 15.

We wish to insist that the figures must be clearly drawn.

1° Generally, it is sufficient to indicate only one well chosen group directed forward or backward for each chiral center as in Fig. 13 and Fig. 15, and its configuration will be clear. (It is assumed that the Fisher type representation Fig. 12 or Fig. 14 is implicated in them)

2° If there are two groups directed respectively forward and backward on the opposite sides of one chiral center as in Fig. 11, its configuration is locally ambiguous.

Thus the configuration of encircled carbons in Fig. 7 and Fig. 8 will be clearer in Fig. 16 and Fig. 17. Figure 9 may be drawn as in Fig. 18, and Fig. 10 as in Fig. 19 or Fig. 20.

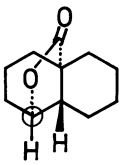


Fig. 16.

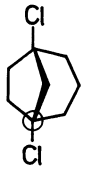


Fig 17.

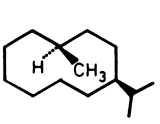


Fig. 18.

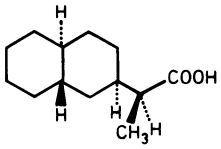


Fig. 19.

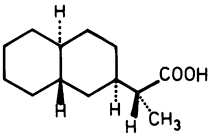


Fig. 20.

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