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QUANTITATIVE ASPECTS OF CHIRALITY. II. ANALYSIS OF DISSYMMETRY FUNCTION BEHAVIOUR WITH DIFFERENT CHANGES IN THE STRUCTURE OF THE MODEL SYSTEMS

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The efficiency of the developed method of dissymmetry functions was studied using various model systems. The alteration of the dissymmetry function was analysed with systematic variations of the bond lengths, valence angles and masses of atoms in model tetrahedra. The behaviour of the dissymmetry function was studied for conformationally labile systems and chiral polyhedra. In general, it was found that in all cases the alteration of the dissymmetry function is in agreement with the speculative representations of the changes in degree of chirality.

INTRODUCTION

To evaluate the efficiency of the dissymetry function (*DF*) method elaborated in Part I,[1] it is necessary to study the properties of *DF* in different model systems and to study its behaviour with systematic structural changes.

To evaluate the 'sensitivity' of DF to modifications of molecular structure we have tried to determine whether such a change in the weight of any point m_i and corresponding change in the radius, vector $\mathbf{R}_i$ (coordinate of the point i), for which the value of *DF* does not change is possible.

Let us consider the point with mass m and radius vector $\mathbf{R}$ (x_1, x_2, x_3), which is substituted for the point m' and $\mathbf{R}'$. Since the value of *DF* is determined by the position of the object in the reduced system of coordinates, it is necessary to preserve the components of the inertia tensor. The tensor of inertia can be written as

$$\mathbf{T}_{ik} = \sum_s m_s[\mathbf{R}_s^2\delta_{ik} - x_i(s)x_k(s)] \qquad \delta_{ik} = \begin{cases} 1, & i = k \\ 0, & i \neq k \end{cases}$$

To preserve the inertia centre position it is necessary to satisfy the equality

$$\mathbf{R}' = (m/m')\mathbf{R}$$

and therefore the equality

$$\mathbf{T} = \mathbf{T}' = \sum_s m_s'[\mathbf{R}'^2_s\delta_{ik} - x_i'(s)x_k'(s)]$$

is true if

$$m(\mathbf{R}^2\delta_{ik} - x_ix_k) = m'[(m/m')\mathbf{R}^2\delta_{ik} - (m/m')^2x_ix_k]$$

or

$$(\mathbf{R}^2\delta_{ik} - x_ix_k) = -(m/m')^2(\mathbf{R}^2\delta_{ik} - x_ix_k)$$

and thus

$$m/m' = 1$$

The following conclusion is evident: it is impossible to change the weight of one point and simultaneously to change the radius vector and preserve without change the tensor of inertia and consequently *DF*.

ANALYSIS OF MODEL SYSTEMS

We have calculated the values of *DF* for molecules of different groups of symmetry (Table 1). As expected, *DF* proved to be different from zero only for systems with the C_n, D_n symmetry.

In order to study the behaviour of the dissymmetry function with regular structure changes, the values of *DF*† of model tetrahedra were calculated (see also Ref. 2) in which initially all the valence angles were 109·5°

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† In this work dissymmetry functions corresponding the atom masses DF^M, DF_P^M, DF_R^M, DF_{PR}^M are used.[1]

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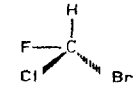
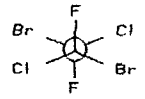
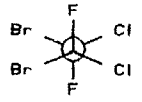
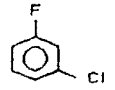
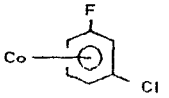
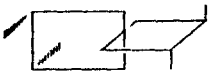
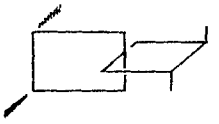
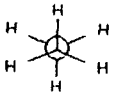
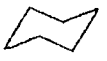
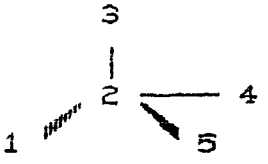
Table 1. Dissymmetry of model structures

Structure	Symmetry group	LD^S_1	LD^S_2	LD^S_4	LD^S_6	*DF*
	C_1	111	674	439	307	316
	C_i	270	0	787	640	0
	C_2	206	640	926	700	541
	C_s	0	2080	1393	965	0
	C_1	807	2749	1833	1353	1532
	S_4	758	1285	0	1734	0
	D_2	388	388	2532	2035	938
 $\varphi = 30^\circ$	D_3	1.7	1.7	22	9	4.9
	D_3	238	531	1098	1038	616
	D_{3d}	0	0	121	0	0

the bonds lengths (intervals between points) 1·54 Å and atomic masses (point masses) $m_i = i$ (a.m.u.). The following parameters were varied: (a) values of m_5 from 5 to 90 (a.m.u.), (b) all the bond lengths l_{2-i} from 1·54 to 10 Å and (c) bond length l_{2-1} from 1·54 to 10 Å.



As can be seen from Figure 1, the value of DF^M increases monotonically and for higher m_5 reaches a plateau, and the value of DF_P^M decreases and tends to zero at higher m_5. Probably, with a background of high m_5 mass, the differences between the other substituents level out.

It is also interesting to analyse how the components of DF change when m_5 changes. The corresponding correlations clearly show that in all cases there is a monotonic increase of all LD.[1]

The increase in DF^M with alteration of the length of one or all bonds of the model tetrahedron (Figure 2) is

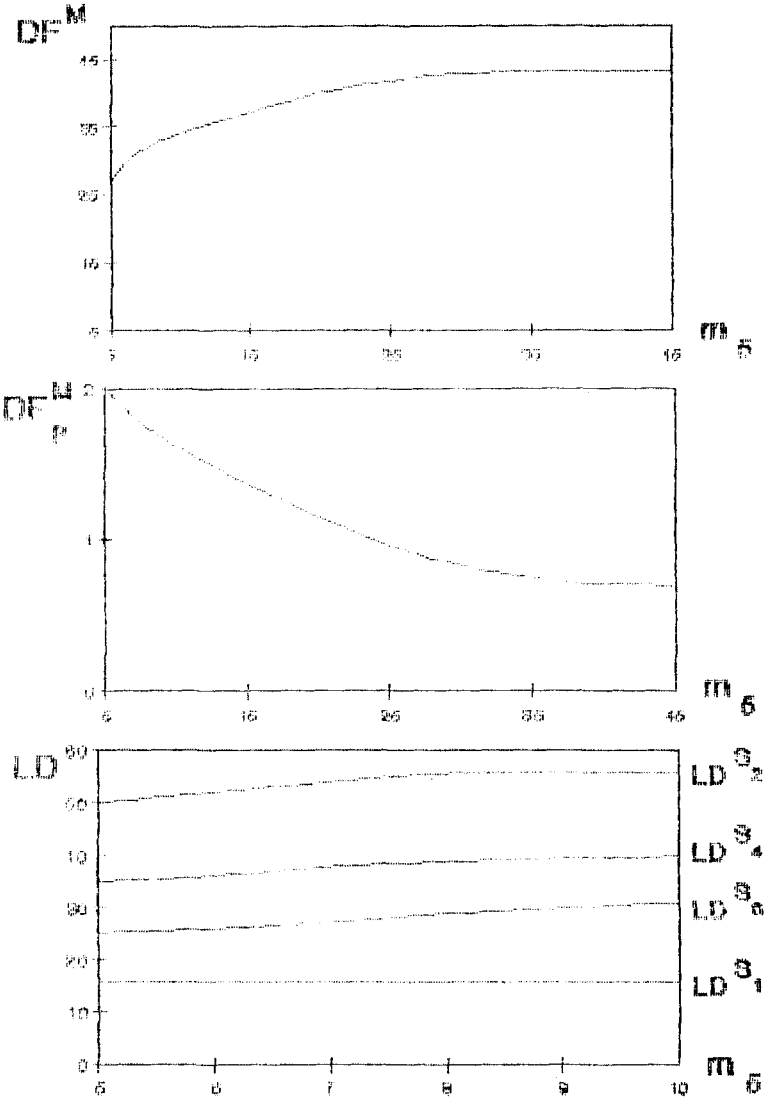


Figure 1. Changes in DF and its components for the model tetrahedron with variations in mass m_5

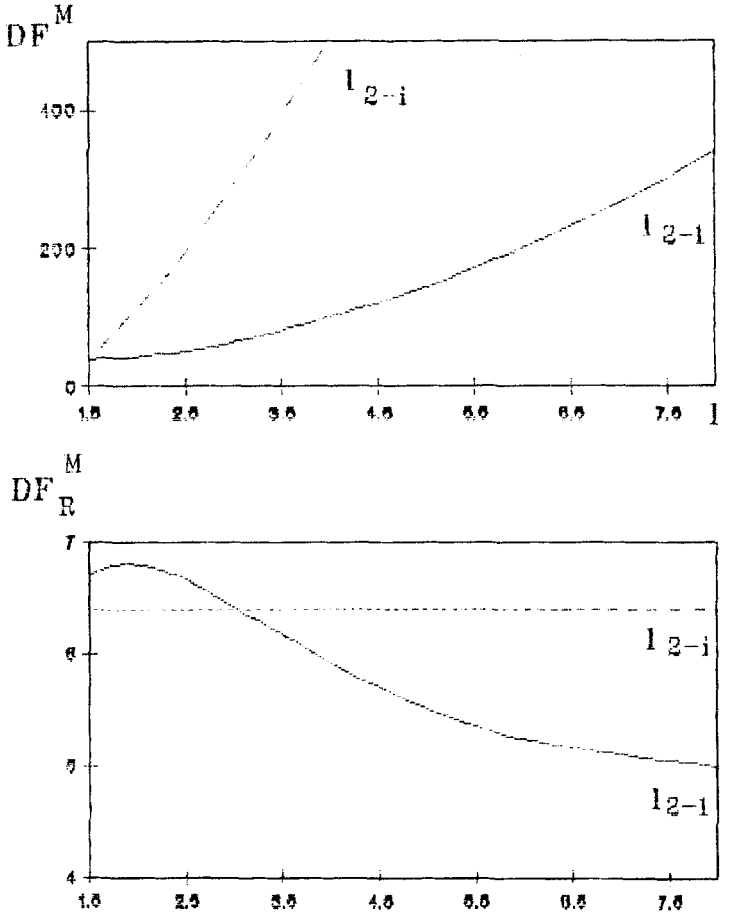


Figure 2. *Dependence of DF* on linear sides of the model tetrahedron

caused by the increase in l, which determines the *LD*. The results are different for the corresponding dependence for DF_R^M. In this case with increase in all the linear sizes of the tetrahedron, as could be expected, its 'level of chirality' remains constant and with increase in one of the bond lengths it decreases, since the system tends to be of the 'pivot' kind.

We then analysed the changes in *DF* with angular deformations of a model tetrahedron (Figure 3): (a) diagonal twist;[3] (b) tetrahedral compression;[3] and (c) transfer without achiral intermediate.[3]

As an argument we used the average valence angle θ, which is defined as the arithmetic mean of five independent angles of the tetrahedron: 123, 124, 423, 521, 523. In order to represent the *DF* suitably a conventional sign (+ or −) is introduced, depending on the region of configuration spaces in which the initial or final tetrahedron is situated. As is shown in Figure 3, in the cases of diagonal twist (a) and tetrahedral compression (b), the *DF* continuously changes on passing from one enantiomer to another, becoming zero with a flat form (achiral intermediate). In enantiomerization without an achiral intermediate (c), the function has a gap in the place of the link between the homochiral subclasses.[4] Hence it can be concluded that the offered *DF* is a piecewise-continuous function. A change in the molecular structure usually brings about a change in the *DF*, and the latter proves our intuitive imagining of the change in the 'degree of chirality' of the molecules.

When studying the properties of the *DF*, we thought it necessary to analyse the change in the dissymmetry function in the case of a decrease in the difference in the substituents at the chiral centre. We calculated the *DF* for the following set of model structures:[5]

$$D—(CH_2)_n—CH(OH)—(CH_2)_n—H, \qquad n = 1–4$$

It is clear that with an increase in n the 'level of chirality' should decrease. Whereas with such changes in

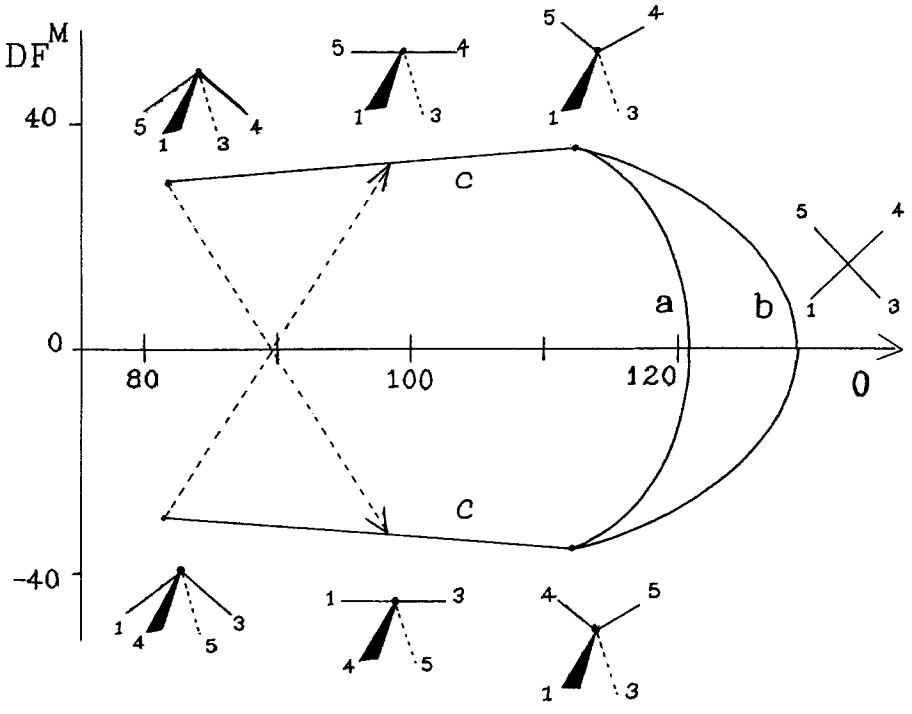


Figure 3. Modes of enantiomerization of a chiral tetrahedron. The + or − signs are conventionally ascribed to the function *DF* for differentiating the enantiomers

structure *DF* increases (Figure 4), which is probably due to the increase in the number of atoms and size of the molecules, the normalized DF_R^M decreases. We also analysed the change for the described case of the value of DF^M(OH), characterizing the dissymmetry of the functional OH group surroundings.[1] As can be seen in Figure 4, the DF_R^M and DF^M(OH) change in parallel.

A necessary aspect of the study of the behaviour of *DF* with structural changes in the molecules is the analysis of the *DF* of conformationally mobile systems. From Figure 5, it is clear that with changes in the torsion angle in the ethane molecule all the eclipsed and hindered conformations are achiral. These conformations are maximally dissymmetric when the torsion angle $\phi = (2n + 1) \cdot 30^\circ$, $n = \overline{0 \cdot 5}$.

From above, it is clear that the dissymmetry function is sensitive to different changes in the structure of molecules and its behaviour is usually in agreement with the traditional knowledge of stereochemistry.

We thought it worth carrying out an analysis of the dissymmetry of chiral polyhedra (polytopes) to study the effectiveness of the method for such systems and also to study the regularities of the influence of structure on the 'degree of chirality' of the coordination compounds.

The models of chiral polyhedra with coordination numbers 4 (tetrahedron, trigonal pyramid), 5 (tetragonal pyramid, trigonal bipyramid) and 6 (octahedron) were built with bond lengths of 1 Å and atom masses $a = 20$, $b = 30$, $c = 40$, $d = 50$, $e = 60$, $f = 70$ a.e.m.

The mass 10 a.e.m. was placed in the centre of the polyhedron. All the possible chiral polyhedra of the mentioned types were counted according to data from Ref. 6. The results of the calculations of the dissymmetry characteristics of these systems are given in Table 2.

It is easy to see that in all cases an increase in the number of the same substituent in a chiral centre results in a decrease in the dissymmetry of the molecule. This agrees with the fact that the development of this process should result in an achiral system. The use of the value DF_{PR}^M allows one to define the so-called 'inner chirality' of the molecule, depending only on the position of the ligands and the type of polyhedron. The dissymmetry of the polyhedron decreases with increase in their coordination number, which is understandable as in this instance the system tends to a spherical symmetry. For pentacoordinated compounds the trigonal bipyramids are more dissymmetric than the tetragonal pyramids,

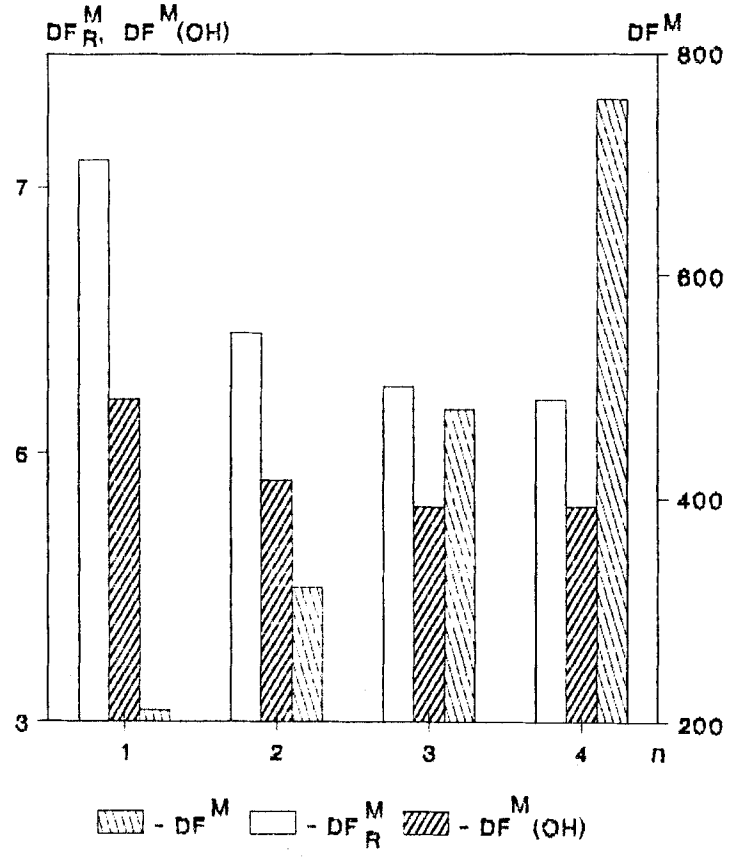


Figure 4. Changes in DF^M, DF_R^M and DF^M(OH) with a decrease in the difference in the substitutents at the chiral centre for D—$(CH_2)_n$—CH(OH)—$(CH_2)_n$—H

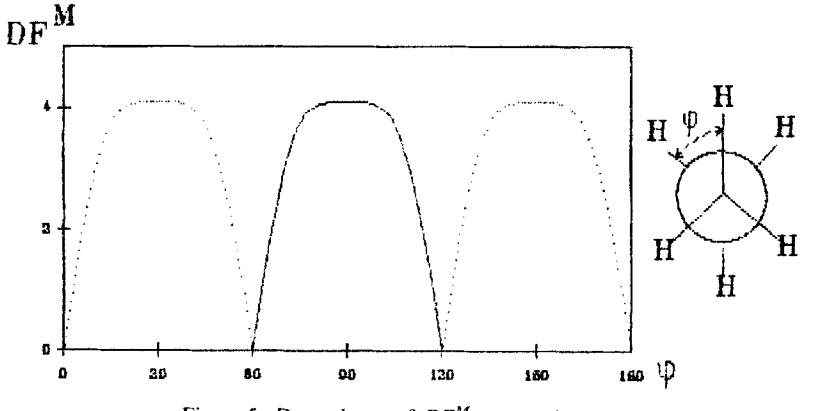
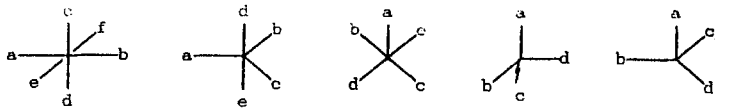


Figure 5. Dependence of DF^M on rotation angle

Table 2. Polyhedron dissymmetry for different types of polyhedra as illustrated

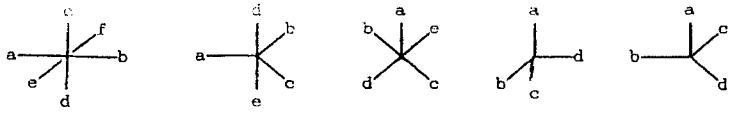


A	B	C	D	E
[(*ab*)(*cd*)(*ef*)]	[(*de*)(*abc*)]	[(*a*)(*bc*)(*de*)]	[(*abcd*)]	[(*a*)(*bcd*)]

No.	Type of polyhedron	Number of same ligands	Positions of substituents	DF^{M}_{PR}
1	A	0	(*ab*)(*cd*)(*ef*)	0·3594
2	A	0	(*ab*)(*ce*)(*df*)	0·3546
3	A	0	(*ab*)(*cf*)(*de*)	0·3530
4	A	0	(*ac*)(*bd*)(*ef*)	0·3554
5	A	0	(*ac*)(*be*)(*df*)	0·3491
6	A	0	(*ac*)(*bf*)(*de*)	0·3461
7	A	0	(*ad*)(*bc*)(*ef*)	0·3541
8	A	0	(*ad*)(*be*)(*cf*)	0·3419
9	A	0	(*ad*)(*bf*)(*ce*)	0·3404
10	A	0	(*ae*)(*bc*)(*df*)	0·3465
11	A	0	(*ae*)(*bd*)(*cf*)	0·3405
12	A	0	(*ae*)(*bf*)(*cd*)	0·3367
13	A	0	(*af*)(*bc*)(*de*)	0·3420
14	A	0	(*af*)(*bd*)(*ce*)	0·3376
15	A	0	(*af*)(*be*)(*cd*)	0·3362
16	A	2	(*ac*)(*ad*)(*ef*)	0·3397
17	A	2	(*ac*)(*ae*)(*df*)	0·3320
18	A	2	(*ac*)(*af*)(*de*)	0·3297
19	A	2	(*ad*)(*ae*)(*cf*)	0·3195
20	A	2	(*ad*)(*af*)(*ce*)	0·3167
21	A	2	(*ae*)(*af*)(*cd*)	0·3075
22	A	2,2	(*ac*)(*ae*)(*cf*)	0·3058
23	A	2,2	(*ac*)(*af*)(*ce*)	0·2999
24	A	2,2,2	(*ac*)(*ae*)(*ce*)	0·2966
25	A	3	(*ad*)(*ae*)(*af*)	0·2768
26	B	0	(*ab*)(*cde*)	0·4279
27	B	0	(*ac*)(*bde*)	0·4143
28	B	0	(*ad*)(*bce*)	0·4036
29	B	0	(*ae*)(*bcd*)	0·3977
30	B	0	(*bc*)(*ade*)	0·4043
31	B	0	(*bd*)(*ace*)	0·3997
32	B	0	(*be*)(*acd*)	0·3988
33	B	0	(*cd*)(*abe*)	0·4009
34	B	0	(*ce*)(*abd*)	0·4050
35	B	0	(*de*)(*abc*)	0·4157
36	B	2	(*ae*)(*acd*)	0·3671
37	B	2	(*ad*)(*ace*)	0·3703
38	B	2	(*ac*)(*ade*)	0·3811
39	C	0	(*e*)(*ab*)(*cd*)	0·3972
40	C	0	(*d*)(*ab*)(*ce*)	0·4026
41	C	0	(*c*)(*ab*)(*de*)	0·4146
42	C	0	(*e*)(*ac*)(*bd*)	0·3869
43	C	0	(*d*)(*ac*)(*be*)	0·3888
44	C	0	(*b*)(*ac*)(*de*)	0·4112
45	C	0	(*e*)(*ad*)(*bc*)	0·3850
46	C	0	(*c*)(*ad*)(*be*)	0·3868
47	C	0	(*b*)(*ad*)(*ce*)	0·3972
48	C	0	(*d*)(*ae*)(*bc*)	0·3821
49	C	0	(*c*)(*ae*)(*bd*)	0·3835

continued

Table 2. (*Continued*)



A [(*ab*)(*cd*)(*ef*)] B [(*de*)(*abc*)] C [(*a*)(*bc*)(*de*)] D [(*abcd*)] E [(*a*)(*bcd*)]

No.	Type of polyhedron	Number of same ligands	Positions of substituents	DF^{M}_{PR}
50	C	0	(*b*)(*ae*)(*cd*)	0·3904
51	C	0	(*a*)(*bc*)(*de*)	0·4116
52	C	0	(*a*)(*bd*)(*ce*)	0·4011
53	C	0	(*a*)(*be*)(*cd*)	0·3976
54	C	0	(*e*)(*ab*)(*cd*)	0·4116
55	C	2	(*e*)(*ac*)(*ad*)	0·2634
56	C	2	(*d*)(*ac*)(*ae*)	0·2704
57	C	2	(*a*)(*ac*)(*de*)	0·2241
58	C	2	(*c*)(*ad*)(*ae*)	0·2705
59	C	2	(*a*)(*ad*)(*ce*)	0·2169
60	C	2	(*a*)(*ae*)(*cd*)	0·2148
61	C	2	(*c*)(*ac*)(*ae*)	0·2383
62	C	2,2	(*a*)(*ac*)(*ce*)	0·2857
63	C	3	(*a*)(*ad*)(*ae*)	0·2463
64	D	0	(*abcd*)	0·4966
65	E	0	(*a*)(*bcd*)	0·5114
66	E	0	(*b*)(*acd*)	0·4877
67	E	0	(*c*)(*abd*)	0·4734
68	E	0	(*d*)(*abc*)	0·4677
69	E	2	(*a*)(*abc*)	0·4367
70	E	2	(*b*)(*abc*)	0·4367
71	E	2	(*c*)(*abc*)	0·4213

and in tetracoordinated compounds a trigonal pyramid is more dissymmetric than a tetrahedron.

Analysis of the correlation of chiral octahedral structures with their dissymmetry indicates an interesting and important regularity: if in the fixed set of ligands on the opposite sides of the line, passing through the centre, there are ligands that are very similar in their properties (e.g. in their masses), then the dissymmetry of such a system is maximum, and vice versa. For pyramidal structures a ligand with small mass at the peak of the pyramid stimulates an increase in the dissymmetry.

POSSIBILITIES OF APPLICATION OF DISSYMMETRY FUNCTION METHOD

We presume that for the analysis of the properties of molecules (P) due to chirality, the method of dissymmetry functions can be applied with the hypothesis that the higher the dissymmetry of a molecule is the more differences there are in the properties of enantiomers caused by chirality, i.e. the greater is the difference in enantiomers under the influence of different chiral phenomena on the one hand and the stronger is the dissymmetrizing influence of a molecule on its surrounding on the other. Here, it should be borne in mind that in a number of cases it is not the dissymmetry of the whole molecule which is important but the dissymmetry of the surroundings of the same fragment (e.g. the reaction centre).

Hence the whole problem can be expressed in terms of making and analysing a correlation $P = f(DF)$. On the analogy of the Taft–Hammett equations, the sphere of application of the given model is bounded by the reaction series,[7] i.e. the whole set of molecules under study must take part in a one-type physico-chemical process, when only the structure of a molecule (its fragment) changes, while all the remaining factors (temperature, solubility, reaction conditions, etc.) remain constant. It should be emphasized that in the given approach it is possible not to take into account different intramolecular interactions as they are similar for each of the enantiomers and their relative reaction ability for a fixed chiral influence (e.g. the same chiral reagent) will probably be determined by the structural differences of the enantiomers, which are taken into account by the

dissymmetry function. Unlike the Taft–Hammett models, in our case the parameter *DF* is not taken empirically but is calculated from the geometry of the molecules and fundamental properties of the atoms. Hence we do not have to confine ourselves only to a linear correlation dependence. It should also be noted that the flexibility of the proposed model is based on the rational choice of the properties of atoms in the calculation of the *DF*, depending on the problem to be solved.

The application of the proposed method to the solution of definite stereochemical problems we will be illustrating in forthcoming publications.

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