ical methods that the cyclohexane ring in the hexachlorocyclohexanes can best be represented as a modified chair form.

There is an alternating axis of symmetry in the structure, and the bond between any carbon atom and its constituent may be parallel to this axis or in an equatorial position somewhat above or below the perpendicular to the axis. The configurations assigned to the different isomers on this basis are shown in Fig. 2. Various designations, such as polar, equatorial, epsilon, and gamma, have been given to these bonds. It is suggested that the positions be named according to a recent proposal by Barton *et al.* (*6*). The term *axial* is used for substituents parallel to the axis of symmetry and is symbolized *a*; equatorial substituents are symbolized *e*.

References

1. J. A. Kolka, H. D. Orloff, and M. E. Griffing, *J. Am. Chem. Soc.* **76**, 3940 (1954).
2. S. J. Cristol, *ibid.* **71**, 1894 (1949).
3. L. Maquenne, *Les Sucres et leurs principaux derives* (Carre et Naud, Paris, 1900), p. 190.
4. H. G. Fletcher, Jr., L. Anderson, and H. A. Lardy, *Org. Chem.* **16**, 1238 (1951).
5. O. Bastiansen, Ellefsen, and O. Hassel, *Acta Chem. Scand.* **3**, 918 (1949).
6. D. H. R. Barton *et al.*, *Science* **119**, 49 (1954).

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Partial Charges on Atoms in Organic Compounds

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The recent development of a simplified theory and method of estimating quantitatively the contribution to charge distribution made by atomic electronegativities (*1–3*) should be of especial interest in organic chemistry. This paper outlines the fundamental ideas and methods of calculation, presents numerical data for facilitating application, and discusses the interpretation of chemical phenomena.

The chief quantitative indication of molecular charge distribution hitherto available has been the experimentally determinable electric dipole moment. This value indicates only the over-all charge distribution, with no evidence of the relative importance, or even of the existence, of the several factors involved (*4*). In addition to the atomic charges and bond polarity introduced by the initial differences in atomic electronegativity, there are also possible effects arising from differences in atomic radius, from hybridization unsymmetric with respect to the nucleus, from polarization of nonbonding electron pairs, from the interaction of separate bonds to the same atoms, from electrostatic interaction between atoms not directly joined, and from the mobility of electrons of multiple bonds.

The reason for listing these factors now is to emphasize at once the complexity of charge distribution and the folly of expecting too much from the evaluation of the dipole moment or of any of its contributing factors, such as bond polarities and atomic charges. Nevertheless, such data are useful where they are helpful in interpreting chemical phenomena.

The method of estimating the charge distribution that would result from the effect of initial electronegativity differences on bond polarity is speculative. However, it introduces some ideas whose demonstrated utility in inorganic applications (*3*) justifies careful consideration in organic chemistry.

One of the most important of these ideas is the principle of electronegativity equalization: *When two or more atoms initially different in electronegativity combine chemically, their electronegativities become equalized in the molecule.* The intermediate electronegativity of the molecule is taken as the geometric mean of the electronegativities of all the atoms before combination. The equalization of electronegativities occurs through the adjustment of the polarity of the bonds, which is pictured as resulting in a partial charge on each atom. That is, electron loss causes increase and electron gain causes decrease in electronegativity. If it is assumed (*2*) that the electronegativity of an atom changes linearly with charge, and that, as an arbitrary standard, the bond in an isolated molecule of NaF is 75-percent ionic, it is possible to determine that change in the electronegativity of an atom that would correspond to the complete gain or loss of one electron. The partial charge on an atom in a molecule is then estimated as the ratio of the change in electronegativity that is undergone when the free atom joined the molecule to the change that the atom would have undergone in acquiring unit electronic charge.

Data for calculating approximate partial charges on atoms in organic molecules are given in Tables 1 and 2. Table 1 lists the electronegativities [expressed as stability ratio (SR) values (*1*)] of some elements commonly occurring in organic compounds, together with logarithms of the electronegativities (for use in calculating geometric mean values for molecules), and the changes in electronegativity corresponding to the acquisition of unit charge. Table 2 simplifies the calculation of molecular values by listing the log SR sums for a number of common organic radicals and functional groups.

Table 1. Electronegativities of some elements and data for estimating the charge on combined atoms; $\delta_E = (SR_{compound} - SR_E)/\Delta SR_{E \rightarrow E^+}$.

Element (E)	SR_E	Log SR_E	$\Delta SR_{E \rightarrow E^+}$
C	3.790	0.5786	4.050
H	3.550	.5502	3.919
O	5.210	.7168	4.749
N	4.490	.6522	4.408
F	5.750	.7597	4.988
Cl	4.930	.6928	4.618
Br	4.530	.6561	4.426
I	3.840	.5843	4.077
P	3.340	.5237	3.802
S	4.110	.6138	4.216
Si	2.620	.4183	3.418

Table 2. Log *SR* sums for organic radicals and functional groups.

Group	No. of atoms	Σlog SR	Group	No. of atoms	Σlog SR
CH	2	1.1288	CHO	3	1.8456
CH_2	3	1.6790	COOH	4	2.5624
CH_3	4	2.2292	COO	3	2.0122
C_2H_5	7	3.9082	CO	2	1.2954
C_3H_7	10	5.5872	$CONH_2$	5	3.0480
C_4H_9	13	7.2662	COCl	3	1.9882
C_5H_{11}	16	8.9452	NH_2	3	1.7526
C_6H_{13}	19	10.6242	NH	2	1.2024
C_6H_5	11	6.2226	NO	2	1.3690
C_6H_4	10	5.6724	NO_2	3	2.0858
C_6H_3	9	5.1222	CF_3	4	2.8577
$CH_3C_6H_4$ / $C_6H_5CH_2$	14	7.9016	CF_2	3	2.0980
			CF	2	1.3383
OH	2	1.2670	SH	2	1.1640
CN	2	1.2308	SO_3H	5	3.3144

Some suggestions are offered here as an aid to the successful application of atomic-charge data.

1) The existence of partial charges on the atoms of a molecule implies not only polarity of the bonds but also special susceptibility of the charged atoms to the electrostatic interactions with other and separate charged atoms of the same molecule, if geometry permits. The molecular geometry may therefore be an important cofactor in the behavior of the molecule.

2) Steric influences apart from the electrostatic influences just referred to may also affect the molecule's behavior.

3) Much of organic chemistry involves multiple bonds in which certain electrons are more than ordinarily mobile. Such electrons may be especially susceptible to electrostatic influences introduced by bond polarity and may tend to oppose its expected effect. Mobility of outer unshared electron pairs may also be significant.

4) The availability on an atom of electrons for chemical reaction will, in general, be expected to diminish with increasing positive charge and to increase with increasing negative charge.

5) In evaluating the electron-releasing or electron-withdrawing power of an atom or group, it is necessary to take into account not only the charges on the atoms most directly involved but also the charge capacity of these atoms as influenced by the attached atoms or groups of atoms. The latter may be regarded as reservoirs that may permit an atom to release considerable charge without becoming excessively positive or to withdraw considerable charge without becoming excessively negative.

References

1. R. T. Sanderson, *J. Chem. Educ.* **29**, 539 (1952).
2. ———, *ibid.* **31**, 2 (1954).
3. ———, *ibid.* **31**, 238 (1954).
4. J. A. A. Ketelaar, *Chemical Constitution* (Elsevier, Houston, 1953), p. 285.

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New Blocking Agent against the Development of LSD-25 Psychosis

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Our clinical observations on Meratran (*1*), alpha-(2-piperidyl) benzhydrol hydrochloride, followed the experimental work of Brown and Werner (*2*). It differs significantly from other central nervous system stimulants such as the amphetamines. No cardiovascular pressor reactions, no appetite loss, and little disturbance in nocturnal sleep have been observed with this compound, which may be used therapeutically in mild depressive states (*3*) as well as in narcolepsy and certain selected motor tic syndromes (*4*). Himwich and his associates (*5*) state that Meratran is not a sympathomimetic drug. They have demonstrated that the central reticular substance of the rabbit brain is stimulated by the compound, followed by cortical stimulation, and Heath (*6*) found that Meratran has a unique ability to cause rapid high-voltage activity in the septal area of the monkey electrographically.

These clinical and experimental results impressed us with the fact that other compounds of similar chemical configuration might also be of value as therapeutic agents in disorders of the central nervous system. Brown and Werner (*7*) have found that the gamma-isomer of Meratran, alpha-(4-piperidyl) benzhydrol hydrochloride, prevents or diminishes central stimulation induced in the mouse by various agents, including amphetamine, morphine, cocaine, and Meratran.

In June 1954, we began to study this gamma-isomer of Meratran clinically; thus far we find that it appears to have therapeutic value in certain dissociation syndromes, although inconsistently in the dosage range used. Some cases of acute schizophrenia, alcoholic hallucinosis, senile and arteriosclerotic hallucinosis, and, to a lesser extent, some of the more chronic schizophrenic syndromes respond to the oral administration of this drug to a degree that has encouraged us to continue our observations, which will be reported later. Because of the dramatic way in which it has cleared up hallucinated, deluded, and dissociated patients on occasion, and despite the fact that its action has not been consistent, we decided to study the possible effect of this gamma-isomer of Meratran as a blocking agent against model psychoses produced by lysergic acid diethylamide (LSD-25) ingestion (*8*). Preliminary results are reported here (*9*).

In the first experiment (*10*) two healthy male graduate students in psychology swallowed 100 μg of LSD-25 in 100 ml of distilled water on the morning of 6 Nov. 1954. Typical psychotic responses occurred. In the first student, age 25, weight 88 kg, a 5½-hr psychosis resulted. He wrote:

> The pervading feeling was that there was a gulf between me and the rest of the environment. It seemed that it would be impossible for me to communicate