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Tables of proposed values for the Orientational Parameter of the Substituent. II.

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ABSTRACT

In this report we present the second group of Tables of Standard Values for the orientational parameter of several substituents.

Keywords: Orientational effect, substituent effect, QSAR, SAR, rotational partition function, drug-receptor interaction.

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INTRODUCTION

Time ago, and from the analysis of the molecular rotational partition function led to the following definition of the Orientational Parameter (OP) of substituent "t", ϕ_t [1]:

$$\varphi_t = \sum_{p=1}^{n} m_{p,t} R_{p,t}^2 \qquad (1)$$

where the summation over p includes the n atoms composing substituent p, $m_{p,t}$ is the mass of the p-th atom belonging to substituent t and $R_{p,t}$ being the distance from the p-th atom to the atom to which the substituent is attached. In part I of this series we described the physical meaning of this parameter, the method to calculate it and several values for monoatomic, diatomic, triatomic, n-C_nH2_{n+1}, O-n-C_nH2_{n+1}, NRR', and cycloalkanes (with a single ring) substituents [2]. In this second part we present the OP values for several substituents usually found in Medicinal Chemistry journals.

RESULTS

Table 1-4 show the proposed values of the Orientational Parameters for several substituents. We ordered the substituents in alphabetical order.

Table 1.

Substituent	ϕ (amu·Å^2)		Substituent	ϕ (amu·Å^2)
1-Chloroethyl	389.76		2-Dimethylaminoethoxy	1663.13
1-Fluoroethyl	250.62		3-Cyanophenyl	1614.64
2-Fluoroethoxy	762.82		3-Chlorophenyl	1782.94
2-Methylphenyl	963.01		3-Nitrophenyl	2146.71
2-Hydroxyethoxy	714.98		3-Hydroxyphenyl	1201.52
2-Bromoethylamino	1873.75		3-Aminophenyl	1201.25
2-Chloroethylamino	993.47		3-Methoxyphenyl	1582.28
2-Phenylethyl	2378.56		3-Fluorophenyl	1289.59
2-Methylpropyl	547.80		3-Isopropoxyphenyl	2680.68
2-Phenoxyethyl	3210.36		3-Hydroxypropoxy	1300.16
2-(Pyrrol-1-yl)ethyl	1815.74		3-Fluoropropoxy	1386.40
2-(Morpholin-4-yl)ethyl	2713.24		3-Phenylpropyl	3734.90
2-(Pyrrolidin-1-yl)ethyl	2002.77		3-Methylphenyl	1210.25
2,2,2-Trifluoroethyl	746.87		(3-Chlorophenyl)methyl	3089.48
1,3-Benzodioxol-5-yl	2198.74		3-Trifluoromethoxyphenyl	4218.70
2-Bromo-3,4,5-trimethylphenyl	5670.10		3-Trifluoromethylphenyl	2914.72
2-Fluorophenyl	1019.55		3-Phenylprop-2-enyl	3438.03
2-(4-Methylphenyl)ethyl	3434.31			

Table 2.

Substituent	ϕ (amu·Å^2)		Substituent	ϕ (amu·Å^2)
4-Triflylphenyl	6857.81		4-Chlorophenyl	2103.65
4-Nitrophenyl	2618.89		4-Trifluoromethoxyphenyl	4647.58
4-Cyanophenyl	1855.33		(4-Fluorophenyl)methyl	2402.04
4-Fluorophenyl	1410.36		(4-Nitrophenyl)methyl	4046.98
4-Mesylphenyl	4151.14		4-Chlorobenzyl	2831.25
4-Methoxyphenyl	1991.22		4-Methoxybenzyl	3232.77
4-Hydroxyphenyl	2184.30		4-Trifluoromethylphenyl	3497.37
4-Methylphenyl	1336.63			

Table 3.

Substituent	ϕ (amu·Å^2)		Substituent	ϕ (amu·Å^2)
Allyl	339.18		Dimethylaminosulfonamido	1511.69
Acetyl	222.84		Difluoromethoxy	598.29
Acetamido	222.26		Dimethylaminomethyl	470.72
Acetoxy	423.30		Diethoxymethyl	1187.74
Aminosulfonyl	471.16		Ethylthio	558.26
Benzodioxan-6-yl	2748.20		Ethylamino	349.39
Benzyl	1294.28		Ethoxycarbonyl	768.49
But-1-en-1-yl	522.51		Furan-2-yl	571.19
Butoxycarbonyl	2106.07		Fluoromethyl	170.96
Benzofuran-2-yl	2149.27		Formamido	320.35
Carboxyl	218.06		Hydroxymethyl	125.22
Chloromethyl	291.97		Isopropoxy	475.03
Cyanomethyl	352.10		Isopropanesulfonamido	1534.96
Cyclopropanesulfonamido	1453.74		Isopropanesulfinamido	1240.11

Table 4.

Substituent	ϕ (amu·Å^2)		Substituent	ϕ (amu·Å^2)
Isoquinolin-6-yl	2591.07		Pyrid-4-yl	820.96
iso-Propyl	249.56		Phenyl	839.49
Imidazol-1-yl	551.53		Propanoyl	371.63
Methoxycarbonyl	433.82		Phenylthio	1929.79
Methylamino	134.43		Propylthio	1023.17
Methylenedioxy	186.53		Phenoxy	1287.65
Mesylamido	904.95		Quinolin-2-yl	2498.72
Mesyl	437.39		*tert*-Butyl	338.69
Methylthio	265.78		Thien-3-yl	902.33
Methanesulfenyl	316.91		Thien-2-yl	802.66
Naphthalen-1-yl	2019.75		Trifluoromethoxy	700.38
Naphthalen-2-yl	2624.20		Triflyl	1083.18
Pyrid-3-yl	815.62		Trifluoromethanesulfenyl	912.48

If you are interested in obtaining specific OP values for any substituents not listed in these Tables, you may contact the author. Prof. Dr. Bruce K. Cassels (Faculty of Sciences, U. of Chile) is gratefully acknowledged for very helpful comments.

REFERENCES

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