Superlipophilicity (Xenophilicity) and Microlipophilicity of Perfluorinated Saturated Groups. Part 1. Qualitative Selection Criteria for Biologically Active Substances Containing Perfluorinated Fragments

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The most effective modern drugs and pesticides are inhibitors of specific enzymes. New screening technologies are aimed mainly at searching for such compounds. One way to make biologically active substances is analogs synthesis. However, "the hits" found in initial screening may be rejected even before optimizing the enzyme-substrate interaction. The problems may be as follows:

1). Production of such compound is unprofitable.

2). Compound or its decomposition products are highly toxic to useful plants (organisms).

3). Persistence is unsatisfactory.

4). Compound shows poor permeability in living tissue.

Because of this, functional groups, which makes possible high but predictable variation of screening "hits" properties are actually demanded. Perfluorinated saturated groups are the most promising from this point of view. Steadily growing large-scale production of perfluorinated precursors and low application rates and dosage of modern active substances, low toxicity and bioavailability of perfluorinated carboxylic acids, the main intermediates of biodegradation, enhanced oxidative and thermal stability - all these advantages in biologically active molecules design are associated with the perfluorinated groups.

Being strong electron acceptors the perfluorinated groups usually increase hydrophilicity of neighbours groups. Considering small polarizability of C-F and S-F bonds, one can describe the properties of perfluorinated groups as **xenophilicity**, because they are pushed out all media of living issue. Macroscopically, this phenomenon appears in increased lipophilicity. It should be noted that we can use perfluoroalkyl radicals 2-3 times shorter than hydrocarbon groups to achieve the same effect, and the resulting maximal values are inaccessible using natural lipophils. Since this property is factually outside the semantic meaning of term "lipophilicity", I name it **"superlipophilicity"**. Combination of superlipophilicity and enhanced hydrophilicity leads to amphiphilicity and consequently to enhanced permeability. On the level of enzyme-substrate interaction macroscopic concepts are unsuitable, therefore perfluorinated groups-enzyme interaction may be described in term "microlipophilicity".

The report deals with literature on some examples of biologically active substances containing perfluorinated groups; approaches and methods are suggested to control molecular properties by introduction of perfluorinated groups; the estimation of different perfluorinated group sources is given.