Crystal Structures of Potential Sweeteners. The Kier Glucophore Geometry

Justyna Kalinowska-Tluscik, Marta Janas, Ewa Miekina, Barbara J. Oleksyn, *Faculty of Chemistry, Jagiellonian University, Krakow, Poland.* E-mail: kalinows@chemia.uj.edu.pl

We compare molecular geometry and interactions of new potential sweeteners which were designed using chemical modification of a known sweet compound [1] and bioisosteric replacement. We determined crystal structures of three arylsulfonylalcanoic acids and one bioisoster containing a tetrazole instead of the carboxylic group. Unfortunately, last of them occured to be bitter. However, it is not very surprising since the sweet and bitter tastes are strongly related.

According to the geometrical model of glucophore given by Kier, there are three fundamental fragments of a sweet compound which interact with a sweet taste receptor [2]. A sweetener should contain a donor and an acceptor of hydrogen bond and a fragment which can be involved in hydrophobic interactions [3]. Distances between those fragments define a glucophore. However, the geometry of our sweet compounds in the crystalline state do not agree with the Kier model.

We observed a pair of very strong hydrogen bonds in sweet compounds building a dimer *via* inversion centre whereas in tetrazole the dimeric structure does not occur. That can explain why the bioisoster is bitter.

[1] Polanski J., Ratajczak A., *J. Mol. Str.,* 1997, **407**,71. [2] Kier L.M., *J. Pharm. Sci.,* 1972, **61**, 1394. [3] Shallenberger R.S., *Food Chem.,* 1996, **56**, 209.

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