CHEMISTRY LETTERS, pp. 611-612, 1983. © The Chemical Society of Japan 1983

SWEET TASTING PSEUDO-SUGARS

Tetsuo SUAMI,* Seiichiro OGAWA, and Tatsushi TOYOKUNI
Department of Applied Chemistry, Faculty of Science and
Technology, Keio University, Hiyoshi, Yokohama 223

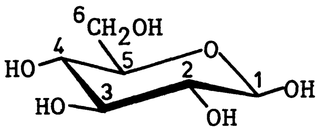
Pseudo-DL-glucose and pseudo-DL-galactose, in which the ring-oxygens of pyranoid sugars have been replaced by a methylene group, are equally sweet as their respective true sugars. It has thus been demonstrated that the displacement of the ring-oxygen in a pyranoid sugar by the methylene group affords no prejudicial effect on the sweetness.

The common molecular feature of various sweet tasting compounds has been established by Shallenberger1) as a bifunctional entity of an AH and a B component, together with a third hydrophobic bonding site (X). The AH, B system seems to be a prerequisite for the primary sensory quality of sweetness, and the third hydrophobic component may be associated with the intensity of sweetness.2–4) The AH is a proton donor and the B is a proton acceptor, and the required distance between these two components (AH–B) is 30 nm.1) The third bonding site (X) is located 35 nm apart from the A of AH and 55 nm from the B.5)

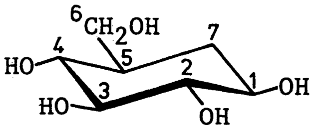
In a pyranoid sugar series, only one pair of vicinal hydroxyl groups (in a staggered conformation) is responsible to the primary AH, B unit for the sweet taste.6–8) In a case of D-glucopyranose, the hydroxyl group on C-4 has been assigned as the AH and the oxygen atom of the hydroxyl group on C-3 has been ascribed to the B in the $^{4}C_{1}$ conformation. The X function has been assigned to C-6, establishing the triangular saporous unit.

During a course of synthetic study on the pseudo-sugar chemistry, an important question arose: Is a pseudo-sugar a sweet tasting compound or not ? A pseudo-sugar is the name of a class of compounds in which ring-oxygens of pyranoid (or furanoid) sugar molecules have been displaced by methylene groups. The term "pseudo-sugar" was first proposed by McCasland,9) who synthesized pseudo-α-DL-talose as a first pseudo-sugar in 1966. In 1973, a first naturally occurring pseudo-sugar: pseudo-α-D-galactose was discovered as a fermentation product of *Streptomyces sp.* MA-4145 and had antibiotic activity against *Klebsiella pneumoniae* MB-1264.10)

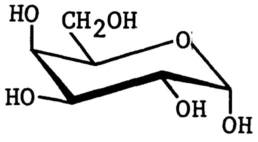
Pseudo-sugars closely resemble true sugars structurally and conformationally, since the geometry of the pyranose ring is practically the same as that of cyclohexane ring and the ring oxygen can be replaced by the methylene group with minimal deviation from the regular pyranose structure.11) Therefore, the essential glucophore (AH, B), implicating the third hydrophobic unit (X), for the sweet taste may exist in pseudo-glucose and pseudo-galactose molecules.



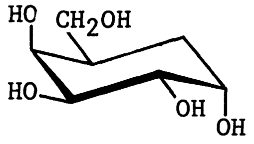
β-D-Glucose



Pseudo-β-DL-glucose**



α-D-Galactose



Pseudo-α-DL-galactose**

** Only one enantiomer of the DL-form is depicted. The tentative numbering is used for the pseudo-sugars in accordance with the numbering of a true sugar for the sake of convenience.

In fact, it has been demonstrated that pseudo-β-DL-glucose[12,13] and pseudo-α-DL-galactose[13,14] taste sweet. A relative sweetness has been determined by comparison of sweetness of pseudo-sugars with 10% (w/v) aqueous solution of sucrose. The relative sweetness of pseudo-β-DL-glucose is 0.5 that of sucrose (= 1) and this pseudo-sugar tasted just about as sweet as D-glucose (0.5–0.6).[15] The relative sweetness of pseudo-α-DL-galactose is 0.4–0.5 that of sucrose.

Since the relative sweetness of L-glucose is about as same as that of the D-enantiomer,[16] each pseudo-β-D-glucose and pseudo-β-L-glucose may taste equally as sweet as D-glucose.

These results make it clear that the ring-oxygen of a pyranoid sugar is not essential for sweetness and the ring-oxygen can be displaced by a methylene group without any detrimental effect on the sweetness of glucose and galactose. This might be true in other sweet tasting pyranoid sugars.

This work was supported in part by a Grant-in-Aid for Scientific Research No. 355376 from the Japanese Ministry of Education, Science and Culture.

References

1) R. S. Shallenberger and T. E. Acree, *Nature (London)*, 216, 480 (1967).
2) E. W. Deutsch and C. Hansch, *Nature (London)*, 211, 75 (1966).
3) R. S. Shallenberger, *Pure Appli. Chem.*, 50, 1409 (1978).
4) L. Hough and R. Khan, *TIBM* March, 1978, 61.
5) L. B. Kier, *J. Pharm. Sci.*, 61, 1394 (1972).
6) G. G. Birch, C. K. Lee, and E. Rolf, *J. Sci. Food Agric.*, 21, 650 (1970).
7) G. G. Birch and C. K. Lee, *J. Food Sci.*, 39, 947 (1975).
8) M. G. Lindley and G. G. Birch, *J. Sci. Food Agric.*, 26, 117 (1975).
9) G. E. McCasland, S. Furuta, and L. J. Durham, *J. Org. Chem.*, 31, 1516 (1966).
10) T. W. Miller, B. H. Arison, and G. Albert-Schonberg, *Biotechnol. Bioeng.*, 15, 1075 (1973).
11) E. L. Eliel, N. J. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York (1965), p. 366.
12) T. Suami, S. Ogawa, K. Nakamoto, and I. Kasahara, *Carbohydr. Res.*, 58, 240 (1977).
13) S. Ogawa, M. Ara, T. Kondoh, M. Saitoh, R. Masuda, T. Toyokuni, and T. Suami, *Bull. Chem. Soc. Jpn.*, 53, 1121 (1980).
14) G. E. McCasland, S. Furuta, and L. J. Durham, *J. Org. Chem.*, 33, 2841 (1968).
15) R. Schaffer, "The Carbohydrate IA," ed by W. Pigman and D. Horton, Academic Press, New York (1972), p. 93.
16) R. S. Shallenberger, T. E. Acree, and C. Y. Lee, *Nature (London)*, 221, 555 (1969).

(Received February 18, 1983)