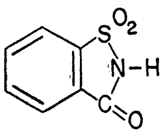
Correlation of Chemical Structure and Taste in the Saccharin Series

Abstract. Results of experiments with approximately 80 saccharin derivatives show that substitution in the number 2 or 3 position gives tasteless compounds. Substitution in the benzene ring of saccharin with the electron-withdrawing nitro group gives a bitter tasting substance. Substitution with an electron-donating group results in a sweet taste. Perhaps a "lock and key" fit at a receptor site is necessary for taste.

Many attempts have been made to explain the tastes of substances in terms of their chemical structures. Although limited correlations have been found, no unifying generalizations have been possible (*1*).

Unlike the salt and sour tastes, the sweet and bitter are not confined to single chemical groups, but are found in practically every class of compounds. Finzi and Colonna (*2*), after a critical survey of the correlation of chemical structure and taste, concluded that it was impossible to derive any law for aromatic compounds and that sweet taste depends not on any single factor, such as a certain taste-producing group, but on the entire chemical complex of the particular compound studied.

One of the better-known sweetening agents is saccharin (I), discovered in 1879 by Remsen and Fahlberg (*3*). Many compounds related to saccharin have been prepared in the intervening years. Cohn (*4*) summarized some of this information by concluding that the sweet taste is lost if the sulfimide ring is opened, or if the imide hydrogen is replaced; and that substitution in the benzene nucleus reduces the sweet, and introduces a bitter taste.

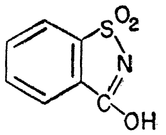


I

This study reports the taste, and any possible correlations with chemical structure, of approximately 80 saccharin derivatives. The saccharin derivatives were tasted, and the particular taste recorded, usually simply as being present or absent. The results (for about 60 compounds) are shown in Table 1. Some generalizations that may be drawn from these results are given below.

Replacement of the imide hydrogen with another chemical group gave, in almost every case, a tasteless compound. Both sweet and bitter substances were converted to tasteless substances by this substitution in the 2-position. The only apparent exceptions were three compounds in Table 1 (Nos. 34 to 36). Here, the bitter taste may be the result of the contribution of the basicity of the relatively high molecular-weight tertiary amino group. These results seem to lend evidence to the belief that the sweet taste is attributable to the anion (*5*). Or, perhaps the sense of taste resembles other types of physiological responses, and is subject to the "lock and key" concept of biological activity (*6*). Substitution on the imide nitrogen, then may affect the specific molecular shape which must fit the receptor site. Thus, these 2-substituted compounds then are not complementary to the taste receptors, and display no taste. However, some workers have reported 2-substituted saccharins which do not ionize or hydrolyze, yet have a sweet taste (*7*).

Another possible explanation for the lack of taste of the 2-substituted saccharins may be that isomerization of the lactam form to the lactim form (II) is necessary for sweet (and bitter) taste. Substitution in the 2-position destroys the possibility of formation of this lactim form. The group $=C=N$, which is present in the lactim form, imparts a bitter or burning taste (*8*).



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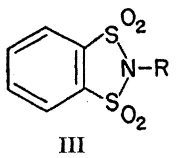
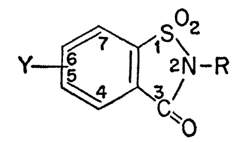
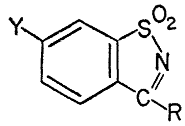
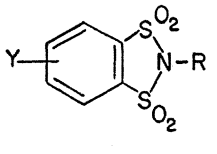


III

In *o*-benzenedisulfonimide, the replacement of the imide hydrogen by an alkyl group (III) changes the taste from sweet with a bitter after-component, to practically tasteless. This effect is analogous to the results of 2-substitution in saccharin.

Table 1. Taste of saccharin derivatives. Abbreviations: S., Sweet; B., bitter; none, tasteless; Slt., slightly; Mod., moderately.

Compound No.	Y	R	Taste
			
1	4-NO_2	H	Slt. S. (not B.)
2	5-NO_2	H	Mod. B. (not S.)
3	6-NO_2	H	Slt. S., then very B.
4	7-NO_2	H	Mod. B. (not S.)
5	4-NH_2	H	S.
6	5-NH_2	H	None
7	4-$NHCOCH_3$	H	None
8	5-$NHCOCH_3$	H	None
9	6-SO_2NH_2	H	Slt. sweet-astringent
10	4-NO_2	C_2H_5	None
11	4-NO_2	*n*-C_3H_7	None
12	4-NO_2	$SCCl_3$	None
13	5-NO_2	CH_3	None
14	5-NO_2	C_2H_5	None
15	6-NO_2	C_2H_5	None
16	6-NO_2	*n*-C_3H_7	None
17	6-NO_2	*i*-C_3H_7	Mod. B.
18	6-NO_2	*n*-C_4H_9	Mod. B.
19	6-NO_2	$CH_2CH=CH_2$	Slt. B.
20	6-NO_2	*n*-C_5H_{11}	Slt. B.
21	6-NO_2	$SCCl_3$	Slt. B.
22	6-NH_2	C_2H_5	None
23	6-NH_2	*n*-C_5H_{11}	None
24	6-SO_2NH_2	CH_3	Slt. B.
25	6-SO_2NH_2	*n*-C_3H_7	None
26	H	CH_3	None
27	H	C_2H_5	None
28	H	*n*-C_3H_7	None
29	H	*i*-C_3H_7	None
30	H	$CH_2CH=CH_2$	None
31	H	*n*-C_5H_{11}	None
32	H	cyclo-C_5H_9	None
33	H	$CH_2CH_2N(CH_3)_2$	Slt. numbing
34	H	$CH_2CH_2N(C_2H_5)_2$	Mod. B.
35	H	$CH_2CH_2N(n\text{-}C_4H_9)_2$	Mod. B.
36	H	$CH_2CH_2CH_2N(C_2H_5)_2$	Mod. B.
37	H	$COOC_2H_5$	None
38	H	$CON(C_2H_5)_2$	None
39	H	$CSN(C_2H_5)_2$	None
40	H	CH_2-2-saccharin	None
41	H	$(CH_2)_2$-2-saccharin	None
42	H	$(CH_2)_3$-2-saccharin	None
43	H	$(CH_2)_4$-2-saccharin	None
44	H	$(CH_2)_5$-2-saccharin	None
45	H	$(CH_2)_{10}$-2-saccharin	None
46	H	$CH(C_2H_5)CH_2$-2-saccharin	None
47	H	$(CH_2)_2NCH_3(CH_2)_2$-2-saccharin	None
			
48	H	$N(C_2H_5)_2$	None
49	NO_2	$N(C_2H_5)_2$	Slt. B.
50	H	$OCH(CH_3)_2$	None
			
51	H	H	S., B. aftertaste
52	H	CH_3	None
53	H	C_2H_5	None
54	H	*n*-C_3H_7	None
55	H	*n*-C_4H_9	None
56	H	$(CH_2)_2N(C_2H_5)_2$	Slt. B.
57	H	$(CH_2)_3N(C_2H_5)_2$	Slt. B.
58	H	$(CH_2)_2N(n\text{-}C_4H_9)_2$	Slt. B.

Inspection of compounds 1 through 9 in Table 1 in general shows that substitution in the benzene ring has a tendency to emphasize the bitter component in the taste. This is especially true with an electron-withdrawing group such as the nitro group. For example, 6-nitrosaccharin has a slightly sweet first taste and then an extremely bitter after-taste. Noyes (*9*) has shown that reduction of the nitro to the electron-donating amino group in 6-aminosaccharin results in a sweet-tasting compound. According to Finzi and Colonna (*2*), conversion to the 6-acetamidosaccharin gives a tasteless compound. My results with the 4-, 5-, and 7-nitrosaccharins, which are somewhat comparable, show them to be either slightly sweet or moderately bitter in taste. The 4- and 5-aminosaccharins are quite sweet and tasteless, respectively. The 4- and 5-acetamidosaccharins are tasteless.

In addition to the inductive effect of a group attached to the ring on taste, resonance may play a part in taste. The 4- and 6-nitrosaccharins, which are ortho and para, respectively, to the carbonyl group, have slightly sweet components to the taste. The 5- and 7-nitrosaccharins, which are meta to the carbonyl group, have no sweet components and show only the bitter taste. The ortho and para substituted 4- and 6-aminosaccharins are quite sweet, while the meta substituted 5-aminosaccharin is tasteless. Perhaps the resonance contributions of these groups to the relative acidity of the molecule, or to the relative ease of formation of the lactim form, is responsible for the differences in taste of the above saccharin derivatives.

Substitution in the 3-position has the same effect as substitution in the 2-position; tasteless compounds are produced (Nos. 48 to 50 in Table 1).

As previously reported (*5*), opening of the heterocyclic ring destroys the sweet (and bitter) taste (compounds not included in Table 1).

It is interesting to note that doubling the saccharin molecule results in lack of taste (Table 1, Nos. 40 to 47).

It will be noticed that many of these saccharin derivatives have a bitter taste. Indeed saccharin itself has a bitter after-taste (*10*). It then appears that the bitter taste is widespread in saccharin-like compounds. Thus, the saccharin moiety may basically possess a bitter taste component.

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Recent Change in the Pattern of Tree Growth in Northern Arizona

Abstract. A significant change in growth pattern among the ponderosa pines (*Pinus ponderosa* Laws.) of the Flagstaff region, northern Arizona, occurred in 1947–1948. This is the first such change since 1904–1905. Evidence appears to verify the existence of a tension zone which fluctuates in altitude as a result of changes in the distribution and quantity of the rainfall as recorded through soil moisture.

Recent reports (*1*) of glacier advances during 1948–1949 in Washington and during 1950–1954 in British Columbia suggest the importance of a change in the pattern of tree growth at the same time in northern Arizona.

Field work in the American Southwest has revealed (*2*) three definite growth patterns associated with three rainfall or soil moisture types. A predominantly winter rainy season characterizes the Central California, or Sierra, type, and the pattern consists of growth layers which are rather uniform in thickness, single within the annual increment, and entire around the circuit of the trunk.

Under the West Texas type, rainfall occurs chiefly during the long summer season, and the West Texas pattern consists of growth layers of great variability in thickness, of much lenticularity, and of multiplicity within the annual increment.

The Northern Arizona type has a double rainy season, one in winter and one in summer, which promotes, in general, two intervals of major soil-moisture replenishment and two of depletion. The Northern Arizona pattern consists of a combination of the other two patterns: a sequence of growth layers characterized by the uniformity and simplicity of the Central California pattern alternates with a sequence characterized by the variability and complexity of the West Texas pattern.

Studies of soil moisture and rainfall, temperature, length of growing season, growth-layer anatomy (*3*), and daily growth have given strong support to two earlier concepts concerning the causes of the Northern Arizona pattern. First, the West Texas rainfall type and growth pattern apparently extend westward at low elevations, whereas the Central California type and pattern extend eastward at high elevations. At the contact in northern Arizona a tension zone is set up, and it is in this zone

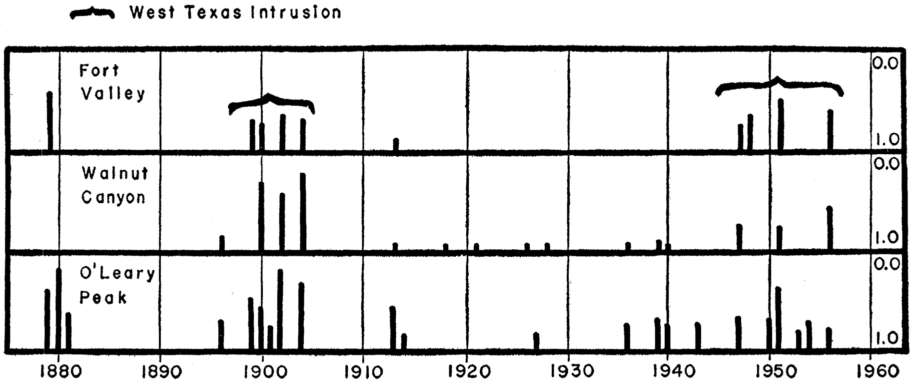

Fig. 1. Migration of the tension zone in the ponderosa pine forest of northern Arizona. Height of lines indicates degree of variability and lenticularity based on a qualitative ratio scale. The plot for Fort Valley includes 32 trees from Fort Valley high in the tension zone, 7300 to 7500 ft elevation, 6 to 7 miles southwest of the San Francisco Peaks; the plot for Walnut Canyon includes 14 trees from Walnut Canyon National Monument, low in the tension zone, 6800 to 6900 ft elevation, some 17 miles southeast of the San Francisco Peaks; and the plot for O'Leary Peak includes 41 trees near O'Leary Peak at the lowest edge of the tension zone, 7150 to 7300 ft elevation, some 6 to 7 miles northeast of the San Francisco Peaks.