order to obtain sufficient product for repeated crystallizations, some caution must be observed in interpreting the specific activity figures shown in Table II. It is obvious, however, that only a relatively small proportion of the radioactivity in the crude acidic triterpene fractions was contributed by the triterpenes themselves. The generally higher specific activity of β-sitosterol and ursolic acid I in the flower-stem section is probably a contribution largely from the flower parts themselves, this being a general phenomenon observed in our studies thus far. On this account and perhaps others, it seems best to delay any further interpretation of the interesting high specific activity shown by ursolic acid I in the flower-stem section. The chromatographic procedure for separating oleanolic acid and the ursolic acids does not separate ursolic acids I and II, the latter both remaining at the starting line. Since both of the ursolic acids are present in *S. officinalis* L. (3) this represents somewhat of a problem for tracer work. For the work herein described it seems highly probable that ursolic acid II, possessing a much greater solubility than ursolic acid I, was removed in the crystallizations described and that the specific activity indicated for ursolic acid I is indeed due to this compound.

In a number of as yet unpublished experiments it has been found that 2-C^{14}-acetate or -mevalonate presented to several Labiates in the manner described gave rise to C^{14}-labeled sterol and triterpenes in all parts of the plants examined. Barring actual transport of sterol or triterpene during the experiments (which seems highly unlikely at this time), this information together with the present report gives strong evidence in favor of sterol and triterpene synthesis *in situ* for either leaf, stems, or flowers. It should be added that because of the diverse pathway taken by acetate in its metabolism, the present data are not informative regarding the mode of biosynthesis of either sterol or triterpene.

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Notes

Saccharin Derivatives V. Synthesis of 5-Aminosaccharin and Related Compounds

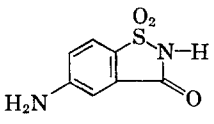
By ALTON WARREN and GLENN H. HAMOR

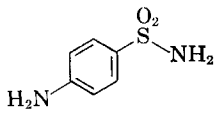
The synthesis of the following compounds is reported: 5-nitrosaccharin, 5-aminosaccharin, 5-acetamidosaccharin, 2-methyl-5-nitrosaccharin, and 2-ethyl-5-nitrosaccharin. These substances lacked a sweet taste, being either bitter or tasteless.

AS PART of a continuing study of saccharin derivatives, the preparation of 5-aminosaccharin and related compounds was desired. Various saccharins have been reported to have local anesthetic (1) or analgesic and antihistaminic (2) activity. The compounds were also synthesized to be included in a forthcoming paper on the relationship of chemical structure to taste in the saccharin series.

The 5-nitrosaccharin was needed to further substantiate previous work in which attempts to prepare 5-nitrosaccharin, using procedures described in the literature, gave instead a mixture of two nitrosaccharins which was shown to consist of 6-nitrosaccharin and 4-nitrosaccharin (3).

Our final reason for synthesis of 5-aminosaccharin will have primarily historical meaning. Backeberg and Marais in the early 1940's were interested in the preparation of 5-aminosaccharin because of its structural similarity to sulfanilamide, as shown below (4). They obtained 5-acetamidosaccharin but could not get the desired compound on deacetylation attempts. With the knowledge that sulfanilamide exerts its bacteriostatic action by competing with *p*-aminobenzoic acid (5), there should be no logical reason for expecting 5-aminosaccharin to have similar activity. However, 5-aminosaccharin was synthesized to fill this void in the history of sulfanilamide-like compounds.





The parent compound, 5-nitrosaccharin, from which all the others were prepared, was synthesized according to the following series of reactions:

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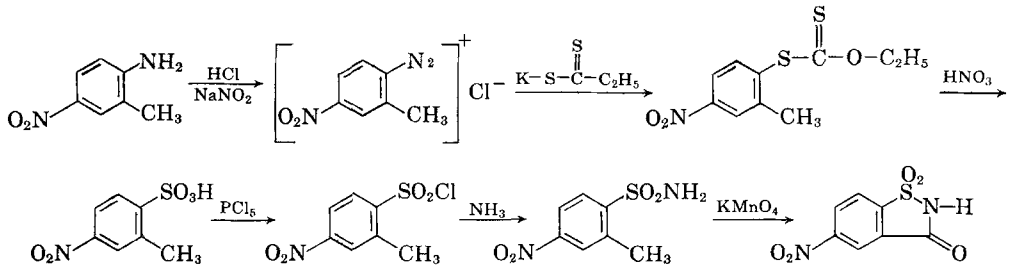
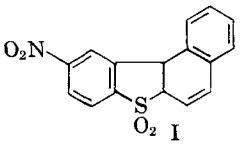


Reduction of 5-nitrosaccharin by hydrogen with palladium-on-carbon catalyst, followed by acetylation, gave 5-aminosaccharin and 5-acetamidosaccharin. N-Alkylation of 5-nitrosaccharin gave 2-methyl-5-nitrosaccharin and 2-ethyl-5-nitrosaccharin. As the above reactions are well-known, only general procedures and physical properties of the saccharin derivatives will be listed in the experimental section.

After completion of our synthesis of 5-nitrosaccharin, the report of Davies and Porter of the University of Melbourne describing the synthesis of 5-nitrosaccharin appeared in the literature (6). The compound was prepared for use as supporting evidence for the structure of 10,11-dihydro-6-nitro-9-thia-3,4-benzofluorene-9,9-dioxide (I). Oxidation



I

of this substance with potassium permanganate gave 5-nitro-2-sulfobenzoic acid which was converted to 5-nitrosaccharin and compared with the 5-nitrosaccharin prepared from an authentic sample of 5-nitro-2-sulfobenzoic acid.

This paper then reports the preparation of three new compounds: 5-aminosaccharin, 2-methyl-5-nitrosaccharin, and 2-ethyl-5-nitrosaccharin, along with the known 5-nitrosaccharin and 5-acetamidosaccharin. These substances lacked a sweet taste, being either bitter or tasteless.

EXPERIMENTAL[1]

5-Nitrosaccharin.[2]—This compound was prepared by alkaline potassium permanganate oxidation of 4-nitro-*o*-toluene sulfonamide by the method used by Noyes (7) to synthesize 6-nitrosaccharin. The 4-nitro-*o*-toluenesulfonamide, m. p. 157° (reported m. p. 157°) (8), was synthesized according to the series of reactions shown above. Recrystallization of the 5-nitrosaccharin from ethyl acetate gave yields of approximately 30% of fine, yellowish-white crystals, m. p. 212–214° (reported m. p. 228°)[3] (6).

Anal.[4]—Calcd. for $C_7H_4N_2O_5S$: C, 36.84; H, 1.77. Found: C, 36.83; H, 1.85.

5-Aminosaccharin.—Reduction of 5-nitrosaccharin using hydrogen with palladium-on-charcoal catalyst, according to standard procedures (3), followed by recrystallization of the product from water gave crystalline 5-aminosaccharin (77%) m. p. 291–293°. Dilute solutions of the compound in ethanol displayed a bluish fluorescence.

Anal.—Calcd. for $C_7H_6N_2O_3S$: C, 42.42; H, 3.05. Found: C, 42.36; H, 3.10.

5-Acetamidosaccharin.—5-Aminosaccharin was acetylated using acetic anhydride, with the aid of pyridine, using published procedures (3, 9). Almost quantitative yields of cream-colored crystalline product, m. p. 304–305° (capillary tube) (reported m. p. 299°) (4), was obtained. This 5-acetamidosaccharin was identical to that of Backeberg and Marais as shown by no depression of a mixed melt.[5]

Anal.—Calcd. for $C_9H_8N_2O_4S$: C, 44.99; H, 3.37. Found: C, 44.89; H, 3.47.

2-Methyl-5-nitrosaccharin.—The method of Merritt, Levey, and Cutter (10) was employed for the preparation of this compound (1). Yellow to white needle crystals of 2-methyl-5-nitrosaccharin, m. p. 169–170° (23%) were obtained.

Anal.—Calcd. for $C_8H_6N_2O_5S$: C, 39.67; H, 2.50. Found: C, 40.04; H, 2.51.

2-Ethyl-5-nitrosaccharin.—This compound was prepared by the same procedure used for the 2-methyl derivative. Yellowish-white, crystalline 2-ethyl-5-nitrosaccharin, m. p. 114–115° (28%) was obtained.

Anal.—Calcd. for $C_9H_8N_2O_5S$: C, 42.18; H, 3.15. Found: C, 42.41; H, 3.06.

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[1] Melting points were taken with a Fisher-Johns melting point apparatus and are uncorrected.
[2] *Chem. Abstr.* nomenclature: 5-nitro-1,2-benzisothiazolin-3-one-1,1-dioxide.
[3] When a sample of the material melting at 228° becomes available, a mixed melt with our sample will be run.
[4] Analyses were performed by Elek Micro Analytical Laboratories, Los Angeles, Calif.
[5] The authors are indebted to J. L. C. Marais, University of Witwatersrand, Johannesburg, South Africa, for supplying the sample of 5-acetamidosaccharin.