in the other eight butanol, shaken with water, was placed. An equal portion of buffer (0.5 molal trisodium phosphate, commercial hydrate) was added to the first funnel. After shaking and equilibration, the buffer was transferred to the next funnel. This was followed by successive extractions and transfers until all funnels contained the two layers.[5] The fractions were isolated by acidification, separation and drying of the butanol, and concentration. The presence of the monomers in the expected places was established by the experiments which follow.

Paper Chromatography and Isolation of Monomer I.—Single drops of unconcentrated butanol solutions zero through eight from the countercurrent extraction were placed on individual strips of Whatman filter paper no. 1 (3.5 cm. by 40 cm.) together with drops of solution of the known monomers I, II and III and developed 4 to 6 hours with moist benzene:ligroin (2:1 by volume). Blue to green spots appeared upon spraying the dried, developed chromatograms with a 2% aqueous solution of phosphomolybdic acid and then exposing the moist strips to ammonia vapor.[10] With moist benzene:ligroin as developer monomers I and II were found in funnels five to eight, and with moist ligroin as developer monomer III was found exclusively in funnel zero.

Monomer I was also isolated in crystalline form from the vacuum distillation of combined butanol solutions five through seven.

Molecular Weight of Combined Fractions Zero and One.—The number average molecular weight of the thick grease from combined fractions zero and one was determined by an ebullioscopic method using a modified Menzies–Wright apparatus.[11] Five determinations with methyl ethyl ketone as solvent gave values from 460–484, a result close to, but perhaps slightly higher than, that expected of dimeric material. These two fractions therefore constitute a dimer-rich portion of hydrol lignin suitable for ultimate separation.

Source of Monomers for Physical Data. Monomer I. 3-(4-Hydroxy-3,5-dimethoxyphenyl)-1-propanol was obtained from hydrol lignin according to Hibbert's method.[3]

Monomer II. 3-(4-Hydroxy-3-methoxyphenyl)-1-propanol.—The ethyl ester of 4-acetylferulic acid (13.2 g.)[12] was reduced with low pressure hydrogen in 150 ml. of acetic acid with 0.1 g. of platinum oxide as catalyst. The catalyst was filtered off and the solution poured into ice. White crystals appeared which after distillation and crystallization from ether had a m.p. 45–46.5°. The saturated ester (6 g.) was dissolved in 200 ml. of anhydrous ether and reduced with 5 g. of lithium aluminum hydride.[13] The reduction yielded 3 g. of a colorless, slightly cloudy oil of $n^{25}D$ 1.5543 in agreement with previous workers.[3]

Monomer III. 1-(4-Hydroxy-3,5-dimethoxyphenyl)-propane.—Pyrogallol 1,3-dimethyl ether gave with propionyl chloride the propionate,[14] which through a Fries reaction[15] and Clemmensen reduction[16] yielded monomer III.

(10) R. F. Riley, THIS JOURNAL, **72**, 5782 (1950).

(11) H. Morawetz, *J. Polymer Sci.*, **6**, 117 (1951).

(12) L. S. Fosdick and A. C. Starke, THIS JOURNAL, **62**, 3352 (1940).

(13) C. F. H. Allen and J. R. Byers, *ibid.*, **71**, 2683 (1949).

(14) M. F. Hunter, A. B. Cramer and H. Hibbert, *ibid.*, **61**, 516 (1939).

(15) C. E. Coulthard, J. Marshall and F. L. Pyman, *J. Chem. Soc.*, 280 (1930).

(16) The Clemmensen Reduction in "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1942, Method III, p. 167.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

Constitution of Planteose[1]

BY DEXTER FRENCH, GENE M. WILD, BURBANK YOUNG AND WILLIAM J. JAMES

RECEIVED JULY 16, 1952

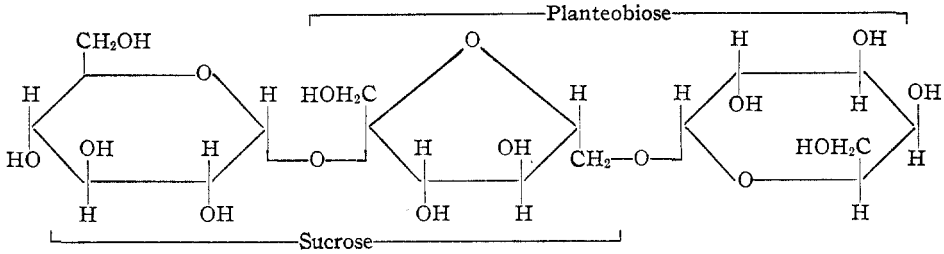
Planteose is shown to be 6-(α-D-galactopyranosyl)-β-D-fructofuranosyl-α-D-glucopyranoside. Hydrolysis by almond emulsin gives galactose and sucrose. Mild acid hyrolysis gives glucose and a ketose disaccharide, planteobiose, 6-(α-D-galactopyranosyl)-D-fructose (syn., melibiulose) which on reduction gives melibiitol (6-α-D-galactopyranosyl D-glucitol) and epimelibiitol (1-α-D-galactopyranosyl D-mannitol).

In 1943, Wattiez and Hans reported[2] the isolation from seeds of *Plantago major* and *P. ovata* of a new crystalline non-reducing trisaccharide, planteose. This compound of glucose, fructose and galactose was easily distinguishable from raffinose by its crystal habit, optical rotation, $[\alpha]D + 125.5°$, its melting point, 124°, its water of crystallization, 6.73% (corresponding to 2 H_2O), and by its optical rotation change during acid hydrolysis (ratio of final to initial rotation, 0.775). But of most importance was the fact that planteose was not attacked by yeast invertase, whereas raffinose is easily cleaved. Hydrolysis by emulsin was reported to be slow, but eventually led to complete breakdown to the component monosaccharides. A search of the literature has not revealed any work on planteose subsequent to the original publication of Wattiez and Hans.

A preliminary examination of planteose indicated that the sugar was indeed distinct from raffinose and that it had the characteristics described by Wattiez and Hans. Planteose was found to have very nearly the same papergram mobility as its isomer, raffinose. Partial acid hydrolysis produced glucose and a reducing disaccharide, planteobiose, which responded to the phloroglucinol-HCl papergram spray for fructose, and which was not oxidized by bromine water or alkaline iodine solution. The ease of the first step in acid hydrolysis pointed to the presence in planteose of a sucrose-type linkage. The attachment of the galactose unit to the fructose unit seemed probable both from the failure of invertase to act on planteose as well as from the chemical and chromatographic evidence that planteobiose was a galactosyl fructose. Observation that planteobiose had the same papergram mobility as the ketose disaccharide component of the melibiose pyridine isomerization mixture suggested that planteobiose was probably identical with melibiulose, with carbon 6 of the fructose unit as the point of attachment of the galactosyl unit. From the high optical rotation of planteose, one would expect the galactose to be present in the α-galactopyranosyl form. These considerations led to the formula for planteose given below.

(1) Journal Paper No. J-2122 of the Iowa Agricultural Experiment Station, Ames, Iowa. Project 1116. Presented before the Sugar Division of the American Chemical Society, Atlantic City, N. J., Sept., 1952.

(2) N. Wattiez and M. Hans, *Bull. acad. roy. med. Belg.*, **8**, 386 (1943); *C. A.*, **39**, 4849 (1945).



Planteose: 6-(α-D-galactopyranosyl)-β-D-fructofuranosyl-α-D-glucopyranoside

This formula was tested by identification of the fragments which would be obtained if either of the glycosidic bridges is broken. Action of an α-galactosidase should give galactose and sucrose. For this purpose, the α-galactosidase of almond emulsin was chosen, since it is known to be relatively free from invertase action[3] and since Wattiez and Hans had reported the cleavage of planteose by such an enzyme preparation. Pilot experiments using chromatographic techniques indicated that the initial cleavage products were indeed galactose and sucrose, though as the enzymolysis continued, partial hydrolysis of the sucrose also occurred. By allowing the digestion to proceed for only a limited time it was easily possible to separate substantial quantities of galactose and sucrose from the unchanged planteose using the Whistler–Durso method.[4] The sucrose was crystallized and identified by comparison with standards on paper chromatograms, and also by comparison of the X-ray diffraction pattern with that of an authentic specimen.

Acid hydrolysis of planteose was followed polarimetrically and gave a reaction rate comparable to that obtained with sucrose (Fig. 1). At the conclusion of the first stage of hydrolysis, the only products revealed by paper chromatography were glucose and planteobiose, which were easily separated on a charcoal column.[4] The glucose was crystallized as the monohydrate and identified by its X-ray pattern and specific rotation.

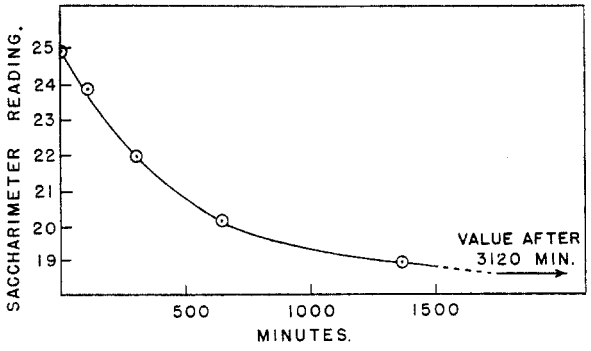


Fig. 1.—Hydrolysis of planteose by dilute acid: 3.15% planteose in 0.154 *M* H_2SO_4; *t*, 35–37°; rotation measured in a 2-dm. tube.

In order to prove the structure of planteobiose, it was reduced by the sodium borohydride method[5] to give a mixture of disaccharide sugar alcohols from which melibiitol readily crystallized after treatment with methanol, and was compared with an authentic specimen similarly prepared from melibiose, using X-ray diffraction patterns of the free alcohol, and melting points and mixed melting points of both the free alcohol and its acetate. Isolation of the epimeric disaccharide alcohol from the mother liquors was achieved by acetylation and crystallization of the acetate from methanol. Through the kindness of Dr. Whistler we had available a small amount of authentic epimelibiose (6-(α-D-galactopyranosyl)-D-mannose)[6] from which we were able to prepare the crystalline epimelibiitol and its crystalline acetate, the latter agreeing in properties with the corresponding substance obtained from planteobiose.

Although Wattiez and Hans regarded planteose as a sugar characteristic of the genus *Plantago*, we feel that it may occur considerably more widespread in nature, in particular, in association with raffinose, stachyose and allied compounds. The detection of planteose (as planteobiose after mild acid hydrolysis) in plants known to contain raffinose and stachyose, for example in rhizomes of *Teucrium canadense* and in ash manna (*Fraxinus ornus*), together with the known[7] presence of sucrose, raffinose and stachyose in various parts of *Plantago* plants, makes it seem rather likely that in all these plants there is an enzyme system capable of carrying on transgalactosidation reactions, with primary groups of terminal galactose, glucose or fructose units serving as possible acceptors for the galactose unit being transferred.

Experimental

Planteose.—Seeds[8] of *Plantago ovata* were ground in a Wiley mill and extracted with diethyl ether to remove the bulk of the fat. The air-dried material was then extracted in a soxhlet apparatus with methanol for 3 days. The methanol extract was evaporated by a warm air stream to dryness, dissolved in 10–20 parts of water and treated with ordinary baker's yeast to remove fermentable sugars, chiefly sucrose. After the fermentation was complete the yeast cells were removed by filtration and the filtrate was placed upon a charcoal column.[4] The dilute ethanol eluate was collected in fractions and each fraction was tested with Seliwanoff reagent (resorcinol-HCl). Fractions giving a positive test were evaporated to dryness and tested for the presence of planteose by paper chromatography. Planteose was generally obtained in the 10–15% ethanol eluates. The dry sirup was taken up with a small amount of water, 1.5 volumes of ethanol was added, the mixture was filtered with carbon and the clear filtrate was treated with additional alcohol so that the final concentration was about 85% ethanol. After seeding with crystals obtained by the spontaneous crystallization of the purest fractions, the solution was allowed to crystallize at room temperature for 2–3 days. The crystals were filtered off and washed, and after two recrystallizations from 85% ethanol showed $[\alpha]_D$ +129.0°, (*c* 4, H_2O); another preparation showed +130.4° (*c* 5, H_2O). Moisture content by drying in a vacuum oven to constant weight required 67 hr. at 80–85°. *Anal.* Calcd. for $C_{18}H_{32}O_{16}\cdot 2H_2O$: 6.67. Found: H_2O, 6.64.

(3) C. Neuberg, *Biochem. Z.*, **3**, 528 (1907).
(4) R. L. Whistler and D. F. Durso, THIS JOURNAL, **72**, 677 (1950).
(5) M. Abdel-Akher, J. K. Hamilton and F. Smith, *ibid.*, **73**, 4691 (1951).
(6) R. L. Whistler and D. F. Durso, *ibid.*, **73**, 4189 (1951).
(7) H. Herissey and M. Gravot, *J. pharm. chim.*, **22**, 537 (1935).
(8) Purchased from S. B. Penick and Co., 50 Church St., New York, N. Y.; *Plantago psyllium* seeds also have been used.

Solubility of Planteose.—Crystalline planteose, 2 g., was equilibrated with 0.5 g. of water for 6 days at 25°. The crystals were removed by suction filtration and a weighed portion of the filtrate was evaporated to dryness *in vacuo* in a tared beaker: solids content of saturated sirup, 66.6% by weight. Similarly, 1 g. of crystalline planteose was agitated at 25° for 7 days with 5 ml. of 85% (by volume) ethanol, the crystals were removed by gravity filtration and the filtrate was caught in a tared beaker, weighed and evaporated to dryness; solids content of the alcoholics olution, 2.8% by weight.

Planteose Hendecaacetate.—One-half gram of planteose was acetylated at 130° with sodium acetate–acetic anhydride. After 30 min. the acetic anhydride was removed in a warm air stream and finally the solid residue was warmed *in vacuo* to 80–85°. The mixture was then extracted with warm benzene, filtered and the filtrate evaporated to dryness. The glassy residue was taken up in 95% ethanol and an equal volume of *n*-butyl alcohol was added. On standing 2–3 days 0.4 g. of the acetate crystallized as brilliant prisms m.p. 135° (cor.), $[\alpha]^{26}D$ +97 (*c* 1, $CHCl_3$).

X-Ray Data on Planteose.—The crystals used were large perfect individuals obtained by slow growth in 85% ethanol. The density, determined by flotation in a mixture of carbon tetrachloride and chloroform, was 1.566 (average value of three determinations). Copper Kα Weissenberg patterns gave a_0 + 8.61 ± 0.05 Å., b_0 = 32.37 ± 0.07 Å. and c_0 = 8.17 ± 0.02 Å. Reflections of all forms except odd orders of (*h*00), (0*k*0) and (00*l*) were present, which together with the orthorhombic symmetry and optical activity of the material indicate the space group D_2^4–$P2_12_12_1$. This space group requires 4 molecules per unit cell. *Anal.* Calcd. for $C_{18}H_{32}O_{16}\cdot 2H_2O$: mol. wt., 540.5. Found: mol. wt., (1.566)(8.17)(32.37)(8.61)(6.06)(10^{-1})/(4) = 536.9.

Periodate Oxidation.—Planteose dihydrate, 10^{-4} mole, was treated with 9×10^{-4} mole of sodium periodate in 25 ml. at room temperature. From time to time aliquots were withdrawn and titrated for acid produced and periodate remaining. After 68 hr., when the reaction had essentially stopped, the acid produced (presumably formic acid) corresponded to 1.8 moles per mole of planteose (theor., 2), and the periodate consumed was 4.6 moles per mole of planteose (theor., 5). After treating the oxidized product with an excess of sodium borohydride, the Seliwanoff test for fructose was negative, though a similarly oxidized and reduced sample of melezitose gave a positive fructose test.

Diazouracil Reaction.—Planteose, raffinose, melezitose and sucrose were tested[9,10] using 50 mg. of each sugar in 1 ml. of water. To each was added about 7 mg. of diazouracil, the mixture was rubbed with a stirring rod to break up the particles of diazouracil and chilled to 5° in an ice–water-bath. One-tenth ml. of 2 *N* sodium hydroxide was then added to each tube and the mixtures were allowed to stand in the cold. After 10 min., 1 drop of 0.1 *M* magnesium chloride was added to each. Sucrose and raffinose gave a definite bluish precipitate, but planteose and melezitose gave only a reddish-brown precipitate.

Hydrolysis of Planteose by Emulsin.—Emulsin was prepared by grinding sweet almonds in a mortar, extracting the fat with ether, and extracting the enzyme with water. Addition of a few drops of acetic acid precipitated inactive protein. After filtering, the crude enzyme solution was precipitated with ethanol to remove sugars, filtered off, redissolved in water and used without further purification. After checking the enzyme for freedom from sugars and for activity on planteose, a 1.02-g. sample of planteose was treated with 40 ml. of the enzyme solution and the reaction was followed by observing the change in optical rotation. During 13 days the observed saccharimeter reading (2-dm. tube) dropped from 18.0 to 13.8° (calcd. final value for complete hydrolysis to galactose and sucrose, 9.9). At this point, paper chromatograms showed the presence of unchanged planteose, sucrose, galactose and traces of glucose and fructose. In order to avoid further destruction of the sucrose, the enzyme hydrolysis mixture was heated to boiling and the sugars present were separated on a charcoal column.[4] The monosaccharide fraction contained galactose and traces of glucose and fructose. The disaccharide fraction readily gave crystals by treating the sirup with glacial acetic acid. The crystals were identified as sucrose by comparison with sucrose on a paper chromatogram and by comparison of the X-ray diffraction powder pattern with that of an authentic specimen.

Acid Hydrolysis of Planteose.—Anhydrous planteose, 1.048 g., was dissolved in 25 ml. of H_2O; 15 ml. of this solution was mixed with 5 ml. of 0.618 *M* sulfuric acid and the rotation was followed in a 2-dm. all-glass tube. After 3120 min. at 35–37° the rotation had fallen to a constant value (see Fig. 1) and the resulting solution was neutralized with dilute sodium hydroxide. Paper chromatography of the hydrolysate at this point showed glucose and planteobiose to be the only sugars present. After separation on a charcoal column,[4] the fractions containing glucose were deionized and evaporated to a sirup showing $[\alpha]^{23}D$ +50.7° (*c* 1, H_2O). The sirup was treated with glacial acetic acid which induced crystal formation. After washing the crystals by decantation, the acetic acid was evaporated, the residue was taken up with a small amount of water, seeded with a trace of glucose hydrate and allowed to crystallize by evaporation at room temperature. The dry residue was identified as glucose hydrate by comparing its X-ray powder pattern with that of an authentic specimen. The planteobiose fractions from the charcoal separation were saved for the following experiments.

Effect of Temperature on Optical Rotation of Planteobiose.—Planteobiose sirup, 1.5 g. wet weight, was diluted with 15 ml. of water and the optical rotation was measured at 2° and 25° in a 2-dm. tube: saccharimeter reading at 2°, 55.5; at 25°, 55.2.

Melibiitol from Planteobiose.—A 0.15-g. fraction of planteobiose, containing a small amount of glucose, was reduced[5] with sodium borohydride. After deionizing and evaporating the colorless solution to dryness, 0.085 g. of a sirup was obtained. This sirup was dissolved in methyl alcohol and seeded very lightly with melibiitol. After 2 days at room temperature, the crystals of melibiitol were filtered off and washed with ethanol. The melibiitol was found to be identical with the material obtained by the corresponding reduction of melibiose and showed[11] $[\alpha]^{28}D$ +113° (*c* 2, H_2O) and m.p. 176–177° (cor.). The X-ray powder patterns of both melibiitol samples were identical and gave: 11.36,[12] 20[13]; 8.63, 15; 6.74, 15; 5.60, 25; 5.10, 40; 5.37, 75; 4.14, 100; 3.96, 15; 3.81, 15; 3.67, 20; 3.54, 15; 3.44, 25; 3.28, 15; 3.13, 20; 3.03, 5.

Melibiitol Acetate from Planteobiose.—The melibiitol from planteobiose was acetylated using the hot acetic anhydride–sodium acetate method, and the acetate was extracted from the dried acetylation mixture with warm benzene, filtered, and crystallized from aqueous ethanol. After recrystallization the substance agreed in properties with an acetate prepared from authentic melibiitol; m.p. 96–98° (cor.), and $[\alpha]^{26}D$ +66° (*c* 1, $CHCl_3$).

Epimelibiitol.—A 0.15-g. sample of epimelibiose[6] was reduced with sodium borohydride, deionized, evaporated and crystallized from methanol. After recrystallization the material showed a m.p. of 157–158° (cor.) and an X-ray powder pattern as follows: 6.65,[12] 90[13]; 5.78, 90; 5.32, 40; 4.86, 100; 4.60, 100; 4.37, 40; 4.11, 35; 3.89, 100; 3.48, 30; 3.31, 50; 3.02, 20; 2.81, 10; 2.73, 40; 2.65, 25.

Epimelibiitol Acetate from Planteobiose.—The mother liquors from the crystallization of melibiitol from planteobiose were evaporated to dryness, dried *in vacuo* at 80–85° and acetylated by the hot sodium acetate–acetic anhydride method. After evaporating the acetic acid and anhydride from the acetylation mixture, the residue was extracted with benzene, filtered and evaporated. The dry residue crystallized readily from methanol when seeded with a trace of authentic epimelibiitol acetate, prepared in a similar fashion from pure epimelibiitol. After recrystallization from butanol both samples showed a m.p. of 122° (cor.) and an X-ray powder pattern as follows: 6.97,[12] 100[13]; 6.48, 75; 6.08, 50; 5.42, 30; 4.90, 100; 4.72, 10; 4.41, 25; 4.26, 40; 4.02, 50.

Planteobiose from *Teucrium canadense* and *Fraxinus ornus*.—Extracts of *Teucrium canadense* (germander) were obtained by disintegrating fresh rhizomes with water in the Waring blendor, filtering to remove fiber and precipitating high molecular weight substances with three volumes of

(9) H. W. Raybin, THIS JOURNAL, **59**, 1402 (1937).

(10) H. W. Raybin, *ibid.*, **55**, 2603 (1933).

(11) M. L. Wolfrom and T. S. Gardner, *ibid.*, **62**, 2533 (1940) give $[\alpha]^{24}D$ +116° (*c* 1.4, H_2O) and m.p. 173°.

(12) *d* value in Å.

(13) Relative intensity on basis of 100 for strongest line.

methanol. Papergrams of the resulting mixture showed a series of non-reducing oligosaccharides including sucrose, raffinose, stachyose and higher compounds. Sucrose and raffinose were obtained in crystalline form from the mixture using the charcoal separation method.[4] After brief acid hydrolysis, the mixture was separated on a papergram and examined for reducing sugars (alkaline copper method, using phosphomolybdic acid to locate areas in which reduction has taken place) and ketoses (phloroglucinol–hydrochloric acid). Reducing sugars included fructose, glucose, planteobiose, melibiose and less mobile oligosaccharides. Ketoses included fructose and planteobiose only. Similar results were obtained with Ash manna (*Fraxinus ornus*, obtained from S. B. Penick and Co.), except that the original manna also contains reducing sugars including planteobiose.

Chromatographic Data.—Paper chromatograms were prepared using the multiple ascent technique[14] with Eaton and Dikeman paper No. 613 and the butanol–pyridine–water mixture 3:2:1.5.[14] Reducing sugars were located[15] by the copper spray followed by phosphomolybdic acid. Ketose-containing sugars were located by spraying with a saturated solution of phloroglucinol in 0.4 *N* hydrochloric acid followed by heating in an oven at 100° to bring out the ketose color test. The $R_f/(1 - R_f)$ values found were as follows: planteose, 0.20; raffinose, 0.22; planteobiose, 0.45; sucrose, 0.69; galactose, 0.69; glucose, 0.89; fructose, 1.1.

(14) A. Jeanes, C. S. Wise and R. J. Dimler, *Anal. Chem.*, **23**, 415 (1951).

(15) D. French, D. W. Knapp and J. H. Pazur, THIS JOURNAL, **72**, 5150 (1950).

AMES, IOWA

[CONTRIBUTION FROM THE SCHENLEY LABORATORIES, INC.]

Antituberculous Compounds. III. Benzothiazole and Benzoxazole Derivatives

BY LEON KATZ

RECEIVED SEPTEMBER 2, 1952

Derivatives of 2-hydrazinobenzothiazole and 2-hydrazinobenzoxazole have been synthesized for testing as antituberculous agents. In addition, four compounds containing the benzothiazole nucleus and capable of complexing cupric ions have been synthesized. Although none of the compounds possessed outstanding antituberculous properties the derivatives of 2-hydrazinobenzoxazole had significant antifungal activity.

In a previous communication[1] three series of compounds prepared from 2-hydrazinobenzothiazoles were described. The present paper reports other derivatives of 2-hydrazinobenzothiazole as well as derivatives of the isosteric 2-hydrazinobenzoxazole.

TABLE I

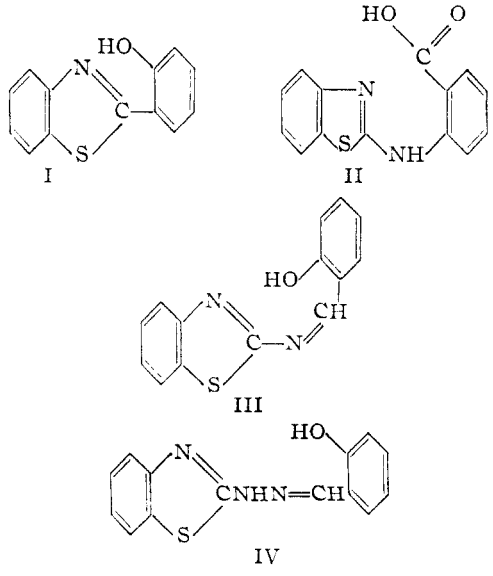
HYDRAZONES OF 2-HYDRAZINOBENZOTHIAZOLE

Carbonyl component	Yield, %	M.p., °C.	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
Benzalacetone	98	180–182[a]	$C_{17}H_{15}N_3S$	69.62	69.34	5.12	5.01	14.33	14.03
Anisalacetone	94	144–146[e]	$C_{18}H_{17}ON_3S$	66.87	66.90	5.26	5.00	13.00	12.67
Salicylideneacetone	99	177–179[b]	$C_{17}H_{15}ON_3S$	66.02	66.18	4.85	4.91	13.59	13.77
p-Dimethylaminobenzalacetone[f]	86	189–192[c]	$C_{19}H_{20}N_4S$	67.86	68.06	5.95	5.93	16.67	16.76
Salicylaldehyde	89	257[d]	$C_{14}H_{11}ON_3S$	62.45	62.74	4.08	4.15	15.61	15.60

Recrystallized from: [a] aqueous ethanol; [b] isopropyl alcohol; [c] isopropyl alcohol–ethylene chloride mixture; [d] glacial acetic acid; [e] aqueous acetic acid; [f] this compound was prepared by Dr. Horwitz following the procedure of H. Rupe, A. Collin and L. Schmiderer, *Helv. Chim. Acta*, **14**, 1340 (1931).

The recent disclosure that the thiosemicarbazone of benzalacetone[2] possessed outstanding antitubercular activity prompted us to condense 2-hydrazinobenzothiazole with α,β-unsaturated ketones. These hydrazones are included in Table I.

Several recent reports[3] have hypothesized that the antitubercular action of such drugs as 8-hydroxyquinoline, *p*-aminosalicyclic acid, Tibione[4] and the halogenated diphenyl ethers is due to their ability to complex cupric ions. Sorkin[5] and co-workers demonstrated that the antitubercular activity of 8-hydroxyquinoline was increased significantly (25–40 fold) in the presence of cupric ions. As a consequence, four compounds (I–IV), containing the benzothiazole moiety were synthesized



(1) L. Katz, THIS JOURNAL, **73**, 4007 (1951).

(2) H. Frahm and A. Lembke, *Zent. Bakt., I Abt.*, **154**, (8) 315 (1949).

(3) E. Carl and P. Marquardt, *Z. Naturforschg.*, **46**, 280 (1949); K. Liebermeister, *ibid.*, **56**, 79, 254 (1950).

(4) "Tibione" is the Schenley registered trade-mark for *p*-acetylaminobenzaldehyde thiosemicarbazone known generically as Amithiozone.

(5) E. Sorkin, W. Roth and H. Erlenmeyer, *Experientia*, **7**, 64 (1951); E. Sorkin and W. Roth, *Helv. Chim. Acta*, **34**, 427 (1951). The latter reference contains an excellent group of references pertaining to the action of metal ions on the bacteriological properties of various compounds.