washed well with U. S. P. chloroform. The filtrate was concentrated under reduced pressure and the white crystalline residue taken up in two liters of hot absolute ethanol. Upon cooling, the β-gentiobiose octaacetate separated as very pure white crystalline needles: m. p. 195–196° (corr.); yield 50.5 g., 74.1%.

α-*d*-Glucose-1,2,3,4-tetraacetate.—α-*d*-Glucose-1,2,3,4-tetraacetate was prepared in a manner similar to that of β-*d*-glucose-1,2,3,4-tetraacetate with the following exceptions. The chloroform extract of the tetraacetate was shaken with an ice-cold, saturated solution of sodium bicarbonate in order to remove all acetic acid. It was then washed with ice water, dried over anhydrous sodium sulfate, filtered and concentrated to a thick sirup. The concentrate was taken up in a small amount of methanol and the triphenylcarbinol allowed to separate out. After filtering, the methanol was removed under reduced pressure and the resulting sirup repeatedly taken up in chloroform, and reconcentrated. The sirup thus obtained was dissolved in dry ether and shaken with calcium chloride in order to remove any water or methanol still present. The sirup remaining after the removal of the ether under reduced pressure was used for the preparation of α-gentiobiose octaacetate.

α-Gentiobiose Octaacetate.—Thirty-eight grams of the α-*d*-glucose-1,2,3,4-tetraacetate sirup, silver oxide (15 g.), preheated "Drierite" (75 g.), iodine (5 g.), acetobromoglucose (20 g.) and dry, alcohol-free chloroform (300 cc.) were used in this preparation. The reaction was carried out according to the method described for β-gentiobiose octaacetate. The sirup obtained by concentrating the chloroform solution of the reaction products was taken up in absolute ethanol (250 cc.) and rubbed with a glass rod. Crystallization began after a few minutes. A yield of 50.9% (16.8 g.) of α-gentiobiose octaacetate was obtained. After two recrystallizations the product melted at 191–192° (corr.) and $[\alpha]^{29.5}\text{D}$ +51.6° (*c*, 4.29; *l*, 2; $CHCl_3$) C. S. Hudson and J. M. Johnson[12] reported a m. p. 188–189° (corr.) and $[\alpha]^{30}\text{D}$ +52.4° for the product obtained by the action of acetic anhydride and zinc chloride on β-gentiobiose octaacetate.

Acknowledgment.—The authors wish to acknowledge the assistance given by William G. Dauben and Harold D. McDowell during the progress of this work.

Summary

1. An improved Königs–Knorr synthesis has increased the yield of β-gentiobiose octaacetate from 23.4 to 75–80% of the theoretical.

2. A 50% yield of α-gentiobiose octaacetate has been obtained by condensing acetobromoglucose with α-*d*-glucose-1,2,3,4-tetraacetate. So far as the authors are aware, this is the first time that a 6-linked α-octaacetate has been prepared by this method.

3. The complete synthesis of α- and β-gentiobiose octaacetates by this method may be completed in approximately one week.

4. Trityl bromide, a side product, has been introduced as a tritylating agent, thus decreasing both the time and cost of preparing the gentiobiose octaacetates.

[12] C. S. Hudson and J. M. Johnson, This Journal, 39, 1272 (1917).

Columbus, Ohio Received September 3, 1938

NOTES

The Activity Coefficient of Perchloric Acid, and a Correction to the Value of the Argentous-Argentic Oxidation Potential in Perchloric Acid

By Don DeVault

The calculation of activity coefficients by Pearce and Nelson[1] from their measurements of the vapor pressure of perchloric acid solutions is apparently incorrect. Rosenfeld[2] has completely recalculated their data, obtaining results varying from 7.0% higher at 0.6 molal to 85.4% lower at 12 molal. Professor Redlich[3] has checked his values. Professor William C. Bray and I have also recalculated the data. The method which Pearce and Nelson report using gave us activity coefficients about 5% lower than those of Redlich and Rosenfeld. Although we examined a number of possibilities, we could not find the source of disagreement with Pearce and Nelson.

Our values of the activity coefficients agree with those of Redlich and Rosenfeld if we substitute, as did they, activity coefficients of hydrochloric acid for those of perchloric acid at 0.6 molal and lower concentration. This procedure receives justification from the electromotive force measurements of Popoff, Riddich, Wirth and Ough,[4]

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[1] Pearce and Nelson, This Journal, 55, 3075 (1933).

[2] Landolt–Börnstein, "Physikalisch-chemische Tabellen," Erg. B. III, 2144 (1936).

[3] Private communication to Professor Bray. See also Redlich. Rosenfeld and Stricks, This Journal, 58, 375 (1936).

[4] Popoff, Riddich, Wirth and Ough, *ibid.*, 53, 1195 (1931).

which show that $\gamma_{HClO_4} = \gamma_{HCl}$ up to 0.4 molal. The difference between the activity coefficients in dilute solution calculated from vapor pressure data directly and calculated from the more extensive hydrochloric acid data indirectly are probably due in the main to experimental error in the former measurements, for the assumption of errors of 0.001–0.006 mm. in the vapor pressure of water above the perchloric acid solutions in the points discarded would bring the calculations into agreement. We choose, therefore, the Landolt–Börnstein values as the most probable ones until more experimental work is done.

The Pearce and Nelson activity coefficient values were used to calculate the potentials of the hydrogen half-cells in perchloric acid and also of the perchloric–nitric acid liquid junctions in a series of researches by Professor A. A. Noyes and collaborators[5–9] on the oxidation potentials of strong oxidizing agents. The corrected activity coefficients lead to values of the argentous-argentic potential in 4 *m* perchloric acid[8] of **1.970** v. at 0.2° and **1.987** v. at 25.0°, changes of −12 and −13 mv., respectively. The corrections to the values in mixed nitric–perchloric acid solutions[8] have the small effect of changing the slope of the line in Fig. 2 (representing an average number of nitrates per silver atom in the argentic nitrate complex) from 1.6 to 1.5.

The hydrogen half-cell and the liquid junction potential corrections are of opposite sign and nearly cancel each other in the measurements of the argentous–argentic potential in nitric acid,[5,8] the cerous–ceric,[6] the thallous–thallic,[7] and the cobaltous–cobaltic[9] potentials in nitric acid. Dr. C. S. Garner[10] has corrected these potentials taking into account the newer Landolt–Börnstein values for the activity coefficient of nitric acid also. The over-all corrections range from −1.3 to +0.6 mv. and are probably negligible in view of the uncertainties in the liquid junction potentials. No other arguments or conclusions in these papers are affected by these changes.

I wish to acknowledge with gratitude the help and advice of Professor Bray, Dr. C. D. Coryell and Dr. C. S. Garner in preparing this note.

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(5) Noyes and Kossiakoff, THIS JOURNAL, **57**, 1238 (1935).

(6) Noyes and Garner, *ibid.*, **58**, 1265 (1936).

(7) Noyes and Garner, *ibid.*, **58**, 1268 (1936).

(8) Noyes, DeVault, Coryell and Deahl, *ibid.*, **59**, 1326 (1937).

(9) Noyes and Deahl, *ibid.*, **59**, 1337 (1937).

(10) Garner, Thesis, Calif. Inst. of Tech., 1938.

The Physical Constants of *cis*-Pentene-2

BY MARY L. SHERRILL AND ELIZABETH H. LAUNSPACH

In a recent article[1] the synthesis of *cis*-pentene-2 by the semi-reduction of pentyne-2 was reported. The designation of this pentene-2 as the *cis* form was based on the method of preparation and the assignment of structure was confirmed by its ultraviolet absorption in the Schumann region.[2] Because the quantity of the pentene-2 was insufficient for column fractionation, it was thought that there might be traces of pentyne present which would have the most marked effect on the boiling point and the density. The work has been repeated and the pentene-2 fractionated twice through a Fenske column (Column A). This column was 35 × 1.5 cm., with 1-turn 4-mm. glass helices. The reflux ratio for the two fractionations of the pentyne-2 was 1:20. The index of refraction was identical with that of the earlier preparation but the boiling point and the density were appreciably lower. The physical constants remained unchanged by the second fractionation and it is believed that the values so obtained constitute the most reliable data for the pure *cis*-pentene-2. Absorption spectrum measurements on this product gave no evidence of the presence of any of the *trans* isomer. These results therefore confirm the assignment of the *cis* structure to the higher boiling pentene-2, as is the case for the higher boiling isomer of butene-2.

The pentyne-2 was prepared in satisfactory yield from 2,3-dibromopentane by the action of alcoholic potassium hydroxide. This reaction takes place in two stages: the first being the formation of the pentyne-2 together with a mixture of 2-bromopentene-2 and 3-bromopentene-2. In the second stage of the reaction with more concentrated potassium hydroxide and prolonged heating at a higher temperature, these bromopentenes are converted into pentyne-2. In some cases appreciable amounts of pentyne-1 were also obtained; by further treatment with alcoholic potash this was transformed into pentyne-2. It is of interest to note that the 2,3-dibromopentane was prepared from pentene-2 which was a mixture of 25% of the *cis* and 75% of the *trans* isomer. In the course of fourteen different preparations of pentyne-2 there was always a 25% yield of pentyne-2 in the first stage of the reaction.

Half mole portions of a constant boiling frac-

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(1) Sherrill and Matlack, THIS JOURNAL, **59**, 2134 (1937).

(2) Carr and Stücklen, *ibid.*, **59**, 2138 (1937).

tion of pentyne-2 (b. p. 55.9 ± 0.05° at 760 mm., n^{20}_D 1.4040, d^{20}_4 0.7115) were hydrogenated in an alcohol–water solution in the presence of colloidal palladium. Slightly less than the theoretical quantity of hydrogen was used. The pentene with alcohol distilled from the mixture through a Vigreux column at 34–36°. The hydrocarbon (78.5% yield) freed from alcohol had a refractive index n^{20}_D 1.3824. One fractionation through Fenske column A gave (1) 5% boiling at 36.8–37.0° and (2) 90% boiling at 37.0 ± 0.05°; the refractive indices of these fractions were, respectively, n^{20}_D 1.3824 and 1.3822, that of the residue was n^{20}_D 1.3840. In a second fractionation of (2) the entire distillate (98%) boiled constantly at 37.0 ± 0.05°, had a refractive index n^{20}_D 1.3822 and a density d^{20}_4 0.6562. The refractive index of the residue was n^{20}_D 1.3826.

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RECEIVED AUGUST 1, 1938

The Specific Heat of "Lucite" (Methyl Methacrylate Polymer)

BY FRANK T. GUCKER, JR., AND WILLIAM L. FORD

We have found the polymerized methyl methacrylate plastic now made by the du Pont Company under the trade name of "Lucite" a useful insulating material in our calorimetric work. Many of its physical properties have been tabulated.[1] For our purposes, the specific heat was important and, since we could not find it listed, we determined it as follows.

Fifteen disks each 3 mm. thick were cut from a Lucite rod, $^3/_8$ inch (9 mm.) in diameter. A small hole was drilled in the center of each. The disks were then threaded on pieces of fine copper wire and suspended from the thermel tubes in one calorimeter of the apparatus developed in this Laboratory[2] for measuring heat capacities of aqueous solutions. The disks were spaced apart to allow free circulation of water, with which the calorimeter was filled to the standard height. The resistance ratio required to balance this calorimeter against the tare was then measured in the usual way, with an accuracy of about 0.01%. The heat capacity of the Lucite was calculated from this ratio and the known heat capacities of the water, the calorimeter and the copper wire. Since the heat capacity of the 3 g. of Lucite was only about 0.3% of that of the whole system, the uncertainty in its value is about 3%. The results of two independent experiments actually agreed somewhat better than that, yielding 0.342 and 0.344, and we may take as the probable value of the specific heat 0.343 (±0.005) cal. deg.$^{-1}$ g.$^{-1}$.

Although its specific heat is larger than that of Pyrex glass, its density is only half as great, and the heat capacity *per unit volume* is only 82% of that of glass. This factor, in combination with a thermal conductance less than half that of glass, equal transparency, great mechanical strength and easy machining, makes Lucite a useful substitute for glass as an insulating material in calorimetric work.

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RECEIVED JULY 5, 1938

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[1] "Methacrylate Resins," *Ind. Eng. Chem.*, **28**, 1160 (1936).

[2] Gucker, Ayres and Rubin, THIS JOURNAL, **58**, 2118 (1936).

The Methylation of Sugars

BY B. CLIFFORD HENDRICKS AND ROBERT E. RUNDLE

The importance of fully methylated sugars as reference compounds in carbohydrate chemistry has led to many attempts to find more satisfactory methods for their synthesis. Irvine and Purdie[1,2] used methyl iodide and silver oxide in their preparation. A more generally used method[3] is that of Haworth in which dimethyl sulfate and sodium hydroxide are the reagents used. More recently West and Holden[4] have modified the method of Haworth by using carbon tetrachloride as a solvent, a more concentrated alkali and a different method of hexoside hydrolysis to obtain the free methylated sugar.

The authors found that the concentrated alkali, used by West and Holden for the last step in the methylation, produced sugar decomposition. Their first steps, however, were satisfactory for partial methylation.

Muskat[5] has shown that methylation may be accomplished by using free alkali metal and methyl iodide on a hexoside in liquid ammonia. He used potassium which is expensive and prepared only small amounts of the sugars. If sodium metal is substituted for the potassium the cost is reduced but for larger quantities of reactants the insolubility of the tetrasodium salts

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[1] Irvine and Purdie, *J. Chem. Soc.*, **83**, 1021 (1903).

[2] Irvine and Purdie, *ibid.*, **85**, 1052 (1904).

[3] Haworth, *ibid.*, **107**, 11 (1915).

[4] West and Holden, THIS JOURNAL, **56**, 930 (1934).

[5] Muskat, *ibid.*, **56**, 695 (1934).

of the hexosides makes it difficult to methylate more than one or two carbons of the sugar. For that reason the procedure here reported uses liquid ammonia only for completing methylation started by the West and Holden process.

Experimental

Forty grams of hexoside with 25 ml. of water was put into a flask equipped with a heavy stirrer, separatory or dropping funnel and attached to a condenser. This mixture was then warmed to 50° by a water-bath. A mixture of 108 ml. of dimethyl sulfate in 150 ml. of carbon tetrachloride was then added and the resulting mixture vigorously stirred. A solution of 92 g. of sodium hydroxide in 130 ml. of water was introduced into the flask by means of the separatory funnel at the rate of one drop in two seconds. This rate was increased in such manner that heat resulting barely raised the reaction mixture to the boiling point of the carbon tetrachloride. After the first half of the alkali solution was used the remainder was added more rapidly and the stirring continued for thirty minutes after the last addition.

The contents of the flask were then treated as directed by West and Holden[4] except the partially methylated sirup was dried thoroughly in preparation for the ammonia methylation. To accomplish this it was dissolved in ethyl ether, this solution dried by calcium chloride and after filtering the ether evaporated under reduced pressure.

The liquid ammonia methylation was done in two unsilvered Dewar flasks of about 750 ml. capacity. Flask number one equipped with separatory funnel, an outlet tube and protected from moisture by some desiccant such as calcium oxide was to contain the sirup. The other flask was connected to the first by a glass tube which extended to the bottom of the second. This second flask also had an outlet tube closed by a clamp by means of which liquid ammonia could be forced into flask one by closing the clamp.

Into the first flask 500 ml. of liquid ammonia was passed direct from the tank. A piece of metallic sodium was added to dry the ammonia, after which the sirup was added. The 150 ml. of liquid in the second Dewar received the shavings of metallic sodium (3–4 g.). The sodium salt of the methylated hexoside was then prepared by forcing small portions of the sodium–ammonia solution into the first flask, containing the sirup, as described above. As the hexoside reacts with the sodium the blue color of the solution clears. Successive additions of the sodium were continued until the blue color persisted for an hour after the last addition. At that point 12 ml. of methyl iodide was added dropwise through the separatory funnel. Less of the iodide was used if less than the prepared amount of sodium–ammonia solution had been previously consumed. The liquid ammonia was then permitted to vaporize off and the residue neutralized by 2 *N* hydrochloric acid. After neutralization 400 ml. more of 2 *N* hydrochloric acid was added and the mixture steam hydrolyzed.[4] The product of this hydrolysis was isolated and crystallized as described by West and Holden.

The authors successfully prepared the following tetramethylhexoses by this combination method.

Tetramethyl- M. p., °C.			α-*d*-Glucose 92.5–93.5	α-*d*-Mannose 49–50	α-*d*-Galactose 70.5–71.5
Specific rotation	Init.	$[\alpha]^{0}\text{D}$	+104.0	+11.5	+146.0
		$[\alpha]^{25}\text{D}$	+104.0	+ 6.3	+150.5
	Final	$[\alpha]^{0}\text{D}$	+ 80.4	+ 2.5	+112.1
		$[\alpha]^{25}\text{D}$	+ 84.8	− 0.2	+119.9

The yield for the tetramethyl α-*d*-glucose was 20–25 g.: for the other two somewhat less. Those two sugars were rather difficult to crystallize[6] though the quantity of sirup in each case was as great as for the glucose.

In this combination method of methylation the amounts of methylating agents used were but slightly more than the theoretical, making the cost comparatively small. The time required was more than for the procedure of West and Holden but much less than that by Haworth's method. The quantities of sugars processed were larger than those used by Muskat.

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(6) Accomplished by aid of seed crystals generously furnished by Dr. M. L. Wolfrom of The Ohio State University.

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RECEIVED JULY 29, 1938

The Ineffectiveness of β-Aminopyridine in Blacktongue

BY F. M. STRONG, R. J. MADDEN AND C. A. ELVEHJEM

Subbarow, Dann, and Meilman[1] recently reported that β-aminopyridine was highly active in the treatment of blacktongue in dogs. Our attempts to demonstrate the activity of this compound have given uniformly negative results.

The compound was prepared by a Hoffman degradation of nicotinamide according to Pollak,[2] and after being purified by distillation (b. p. 132–134° at 20 mm.) and crystallization from Skelly solve "B," formed glittering, colorless plates, m. p. 61–63°. *Anal.* Calcd. for $C_5H_6N_2$: C, 63.82; H, 6.43. Found: C, 63.80; H, 6.35.

The picrate was prepared in dilute alcohol solution, and after being crystallized from alcohol melted at 200–201°. The chloroaurate precipitated instantly on mixing aqueous solutions of the reactants and was crystallized from 1–1 hydrochloric acid as red-brown needles, m. p. 237–239° (dec.). *Anal.* Calcd. for $C_5H_6N_2 \cdot HAuCl_4$: Au, 45.4. Found: Au, 44.8, 44.8.

The dihydrochloride which was obtained from the free base and concentrated hydrochloric acid was recrystallized twice from concentrated hydrochloric acid and then from absolute alcohol. Colorless, granular crystals of m. p. 170–173°

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(1) Subbarow, Dann and Meilman, THIS JOURNAL, **60**, 1510 (1938).

(2) Pollak, *Monatsh.*, **16**, 54 (1895).

were obtained. *Anal.* Calcd. for $C_5H_8N_2Cl_2$: Cl, 42.47. Found: Cl, 42.34, 42.54. Mixed with a sample of β-aminopyridine dihydrochloride kindly sent to us by Dr. Y. Subbarow, the melting point was 173–175°. There thus seems to be no question but that the compound assayed in each laboratory was actually β-aminopyridine.

The following results were obtained when the compound was administered to dogs suffering from blacktongue. The method of producing blacktongue has been described.[3]

1. On 6/13 a 6800-g. dog showing slight symptoms of blacktongue was given 23 mg. of β-aminopyridine orally, and on the next day a further oral dose of 23 mg. was given. During the next two days the symptoms became progressively worse, and the weight dropped 100 g. On 6/15 two 30-mg. doses of nicotinic acid were fed. Two days later the symptoms were much improved and the dog weighed 7200 g. On 6/22 the weight was 8000 g. and the dog was completely cured.

2. On 6/21, 100 mg. of β-aminopyridine was given orally to a 5400-g. dog suffering from severe blacktongue. Two days later the symptoms were slightly worse, and the weight had dropped to 4900 g. One hundred mg. of nicotinic acid was then fed. Four days later the dog weighed 5500 g. and was completely cured.

3. An aqueous solution of β-aminopyridine dihydrochloride containing 6.67 mg. per cc. was adjusted to *p*H 4.4 with sodium hydroxide. A dog which had been kept on the blacktongue-producing diet until its weight had dropped from 5600 g. to 4800 g., but in which symptoms of blacktongue had not yet appeared, was given daily doses of 20, 20, 20, 20, 15 and 15 mg., respectively, of the dihydrochloride by subcutaneous injection of the above solution. During this six-day period (7/7–13) the weight remained at 5000 g., and no symptoms of blacktongue appeared. On each of the four succeeding days (7/13–16) 15 mg. of nicotinic acid were administered by subcutaneous injection. After four days of this treatment the animal's weight had increased to 5600 g., and three days later (7/19) to 6200 g.

4. A 4250-g. dog suffering from rather severe blacktongue was given three 20-mg. doses of β-aminopyridine dihydrochloride on three successive days. Administration was by subcutaneous injection of the above described solution, which had been readjusted to *p*H 1.8 (approximately the *p*H of a solution of 6.67 mg. of the pure dihydrochloride in 1 cc. distilled water). Since the dog weighed only 3800 g. and was much worse on the third day, the dose for the fourth day was increased to 40 mg. On the fifth day of the assay the dog weighed 3400 g., and was in such bad condition that death ensued, despite the injection of 30 mg. of nicotinic acid.

5. A 10-kg. dog was given 100 mg. of β-aminopyridine dihydrochloride daily for three days (7/29–31). The substance was injected subcutaneously in the form of a solution containing 12.3 mg. per cc., *p*H 1.25. The β-aminopyridine used in this case was obtained from Dr. T. Spies, University of Cincinnati. The symptoms of blacktongue which were slight at first had become worse at the end of the third day, and the weight had dropped to 9600 g. The dog was allowed to remain untreated for two more days and the weight dropped to 9100 g., while the symptoms became very severe. One hundred mg. nicotinic acid was then injected (8/2) and after two days the dog weighed 9600 g. and showed definite improvement. On 8/5 50 mg. of nicotinic acid was injected and on 8/8 the weight was 10,100, and the animal was completely cured.

6. A 9200-g. dog was given 100 mg. of β-aminopyridine dihydrochloride daily for three days (8/19–21). The substance was injected subcutaneously in the form of a solution containing 12.3 mg. per cc., *p*H 1.25. The β-aminopyridine dihydrochloride used in this case was obtained from Dr. Y. Subbarow, Harvard University. The symptoms of blacktongue which were slight at first remained unchanged but the weight dropped to 8900 g. The dog was allowed to remain untreated for one more day and the weight dropped to 8400, while the symptoms remained the same. One hundred mg. of nicotinic acid was then injected (8/23) and after two days the dog weighed 9200 g. and the symptoms of blacktongue were markedly improved. On 8/25 100 mg. of nicotinic acid was injected and on 8/29 the animal weighed 10,400 g. and was completely cured.

In this connection it has been found in this Laboratory (unpublished data) that β-aminopyridine cannot replace nicotinic acid as a growth essential for *Staph. aureus.*

It is evident from these results that β-aminopyridine as tested in our laboratory has no activity as compared to nicotinic acid in the treatment of blacktongue.

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(3) Woolley, Strong, Madden and Elvehjem, *J. Biol. Chem.*, **124**, 715 (1938).

The Inactivity of β-Aminopyridine in Blacktongue

BY Y. SUBBAROW AND W. J. DANN

Dr. Elvehjem has informed us privately of his findings as reported in the preceding communication and as a result we have re-examined the question of the activity of β-aminopyridine in blacktongue. We have been unable to repeat our earlier observation that small doses of this substance will cure blacktongue, or to account for the cures then obtained. It is, however, clear that our earlier conclusion is incorrect and that β-aminopyridine is not a blacktongue preventive factor.

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