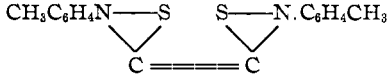
tolyl thiourea. This was purified by crystallization from alcohol and melted at 140–141°.[1]

**The Formation of *p*-Tolylisothiocyanate from Cyclic Dichloromethylene-*p*-tolylimidosulfide,** $CH_3C_6H_4N(-S-)CCl_2 \longrightarrow CH_3C_6H_4NCS$.—The cyclic sulfide is so explosive when heated to its melting point 145° that it is unsafe to decompose more than very small quantities at a time. Volumes of irritable gases containing chlorine are given off and a brown colored residue is left behind. Five grams of the sulfide were decomposed by heating in an oil bath at 140–145°. After the violent reaction had subsided and the mixture was cool, the residue was pulverized finely and thoroughly washed with ether and water. The ether solution was saved. The brown product was insoluble in all common organic solvents and did not melt at 270°. It was apparently identical with the product obtained by heating trichloromethylsulf-*p*-toluide. It was dried at 90°. Nitrogen determinations agreed with the calculated value for a polymer of *p*-tolylisothiocyanate. The compound contained sulfur but did not give a test for chlorine.



Calc. for $(C_8H_7NS)$: N, 9.4. Found: N, 9.51, 9.50.

The ether solution obtained above was evaporated, when a small amount of oil was obtained which was *p*-tolylisothiocyanate. We did not obtain enough of this oil for distillation. When mixed with a few drops of aniline and the mixture warmed, there was an evolution of heat and a crystalline product formed which melted at 140–142°. It was identified as phenyl-*p*-tolylthiourea.

NEW HAVEN, CONN.

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[CONTRIBUTION FROM THE CARBOHYDRATE LABORATORY, BUREAU OF CHEMISTRY, UNITED STATES DEPARTMENT OF AGRICULTURE.]

## THE OPTICAL ROTATORY POWERS OF SOME ACETYLATED DERIVATIVES OF MALTOSE, CELLOSE AND LACTOSE.

BY C. S. HUDSON AND RALPH SAYRE.

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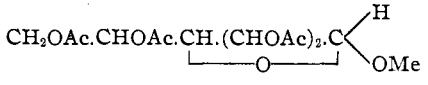
**The Rotatory Powers of the β-Heptacetates of Methyl Maltoside and Methyl Celloside.**—If the molecular rotations of the alpha and beta forms of tetracetyl methyl glucoside,



are denoted by (A + B) and (—A + B),[2] respectively, the molecular

[1] Hugershoff, *Ber.*, **36**, 1141 (1903).

[2] Hudson and Dale, THIS JOURNAL, **37**, 1264 (1915).

rotations of the alpha and beta forms of heptacetyl methyl maltoside may be expressed as (A + B′) and (—A + B′), respectively, where A represents the rotation that is due to the terminal asymmetric carbon atom and B or B′ that due to the remainder of the corresponding structures. The difference of the rotations of the alpha and beta forms of the acetylated glucosides is 2A, and it has been shown in the article cited that this value is +53900, hence A = +26950. If the value of B′ were known it should be possible, knowing A, to calculate the rotations of the two forms of heptacetyl methyl maltoside. A value for B′ can be obtained from the observed molecular rotations of the alpha and beta forms of maltose octacetate, since this substance differs in structure from acetylated methyl maltoside only in respect to the terminal asymmetric carbon atom, which has the acetyl group in place of the methyl. The rotations of the two forms of the octacetate may accordingly be expressed as (A′ + B′) and (—A′ + B′) and their sum is 2B′, which has been found to be +125400,[1] or B′ = +62700. Hence the specific rotation of alpha heptacetyl methyl maltoside (M. W. 650) is calculated to be (+26950 + 62700)/650 = +138°, and that of the beta modification (—26950 + 62700)/650 = +55°. Fischer and Armstrong[2] have prepared from the action of silver carbonate upon acetochloromaltose in methyl alcoholic solution a crystalline heptacetyl methyl maltoside, of m. p. 121--122°, but they have not recorded its rotation. By the same method Foerg[3] prepared the same substance, found it to melt at 125–127°, but did not record its rotation. Koenigs and Knorr[4] prepared from acetonitromaltose in methyl alcoholic solution by the action of barium carbonate and a trace of pyridine, a heptacetyl methyl maltoside of m. p. 128–129° and specific rotation in benzene +61°. Judging from the values of the melting points, the substances are identical and probably consist of the beta form, because the acetohalogen sugar derivatives yield in general the glucosides of that series. The nearness of the recorded rotation in benzene (+61°) to that calculated for the beta modification in chloroform (+55°) also supports this conclusion, but we have considered it necessary to prepare the substance anew in order that its rotation in chloroform might be measured. The value which we find in this solvent is +54°, which agrees almost exactly with the calculated rotation and proves clearly that the substance is the beta form of heptacetyl methyl maltoside. While no method is known for preparing the alpha modification, the agreement between calculation and experiment in the case of the beta form makes it very probable that the calculated value for the alpha form is not far from correct.

[1] Hudson and Johnson, THIS JOURNAL, 37, 1277 (1915).

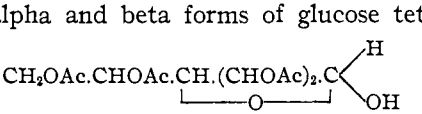
[2] *Ber.*, 34, 2895 (1901).

[3] *Monatsh.*, 23, 48 (1902).

[4] *Ber.*, 34, 4344 (1901).

By precisely similar calculation the rotations of the alpha and beta forms of heptacetyl methyl celloside may be calculated, the rotation of the acetylated cellose chain B″ being obtained from the rotations of the alpha and beta forms of cellose octacetate. It has been found that B″ = +8800,[1] hence the specific rotation of alpha heptacetyl methyl celloside (M. W. 650) is written (+26950 + 8800)/650 = +56° and that of the beta form (—26950 + 8800)/650 = —28°. Skraup and Koenigs[2] have prepared from acetochlorocellose in methyl alcoholic solution by the action of silver carbonate a heptacetyl methyl celloside which melted at 173°, but its rotation is not recorded. We have prepared this substance in pure condition and find it to melt at 187° (uncorr.) and to show the specific rotation in chloroform of —25.4°, which is in good agreement with the calculated value for β-heptacetyl methyl celloside.

**The Rotatory Powers of the β-Heptacetates of Maltose, Cellose and Lactose.**—If the alpha and beta forms of glucose tetracetate,



were known, it should be possible to obtain from the difference of their molecular rotations the value of the rotatory power of the end asymmetric carbon atom, and by combining this value with those for the acetylated maltose, cellose or lactose chains, to obtain the rotations of the respective heptacetates of these biose sugars. These calculations would be entirely similar in method to those just indicated. Since the alpha form of glucose tetracetate has not been described, it is necessary to base the calculations upon some other similar pair of derivatives, and we have selected the alpha[3] and beta[4] tetracetates of galactose, which have recently been carefully purified in this laboratory, and their rotations in chloroform found to be +141° and +22°.[5] If the rotation of their end asymmetric carbon atom be written A″ and that of the acetylated galactose residue B″′, the molecular rotation (M. W. 348) for the alpha form is (A″ + B″′), for the beta (—A″ + B″′), and the difference is 2A″, (141 — 22)348 = +41400, hence A″ = +20700. Using this value, the specific rotation of alpha maltose heptacetate (M. W. 636) is calculated to be (+20700 + 62700)/636 = +131°, while that of the beta modification becomes (—20700 + 62700)/636 = +66°. E. and H. Fischer[6] prepared the beta form from acetochloromaltose and record its melting point as 179–180°

[1] Hudson and Johnson, THIS JOURNAL, **37**, 1278 (1915).

[2] *Monatsh.*, **22**, 1034 (1901).

[3] Skraup and Kremann, *Ibid.*, **22**, 1045 (1901).

[4] Unna, Inaugural Diss., Berlin, 1911, p. 2.

[5] Hudson and Yanovsky, forthcoming publication. See THIS JOURNAL, **38**, 1226–1227 (1916).

[6] *Ber.*, **43**, 2523 (1910).

(corr.) and its initial specific rotation in acetylene tetrachloride $+72.6°$, rising slowly to $76.7°$. The rise is probably due to the slow establishment in solution of equilibrium between the alpha and beta forms by the mutarotation reaction. We have prepared and purified this beta form in order to measure its rotation in chloroform. The initial product showed $[\alpha]_D = +78°$ in this solvent, but on successive recrystallizations of the material from chloroform and ether, the value slowly fell; and only after sixteen recrystallizations did it become constant, indicating that the material was the pure beta form. The specific rotation of the pure substance was $+67.8°$ in chloroform, which agrees well with the calculated value for $\beta$-maltose heptacetate.

The specific rotations of the alpha and beta heptacetates of cellose may be calculated in the same manner from the data already mentioned to be $(+20700 + 8800)/636 = +46°$ for the alpha and $(-20700 + 8800)/636 = -19°$ for the beta modification. The cellose heptacetate which Fischer and Zemplen[1] prepared from iodo-acetyl cellose melted at 195–197° and showed $[\alpha]_D = 20°$ in chloroform. We have prepared this substance from acetobromocellose, and obtained $+18°$ for the rotation of the crude substance; but on crystallization the value gradually became lower without, however, becoming constant before the supply of material was exhausted. After eighteen recrystallizations the value was $-2°$, which is $17°$ from the calculated value, but it seems reasonable to suppose that further purification would bring the values nearer.

The specific rotations of the alpha and beta forms of lactose heptacetate may be calculated from $A'' = +20700$ and $B''' = +16600$, which is the value for one-half the sum of the molecular rotations of the alpha and beta octacetates of lactose,[2] to be $(+20700 + 16600)/636 = +59°$ for the alpha, and $(-20700 + 16600)/636 = -6°$ for the beta form. We have prepared lactose heptacetate, which does not appear to have been crystallized previously, by the action of silver carbonate on acetobromolactose in acetone solution. As in the case of cellose heptacetate, the amount of material available was not sufficient for completely purifying the beta form. The crude product, rotating $+12°$ in chloroform, was recrystallized twenty times, yielding a substance of rotation $-0.3°$ in chloroform, which is about 6° higher than that calculated for $\beta$-lactose heptacetate. Since the rotation has not yet reached a constant value, it is to be supposed that further purification would have made the agreement closer.

## Experimental.

**Purification of Heptacetyl Methyl Maltoside.**—The acetobromomaltose used was prepared by the method of Dale,[3] which consists in treat-

[1] *Ber.*, 43, 2539 (1910).

[2] Hudson and Johnson, THIS JOURNAL, 37, 1270 (1915).

[3] THIS JOURNAL, 37, 2745 (1915).

ing the sugar with a saturated solution of hydrobromic acid in acetic anhydride. The compound could not be made to crystallize, but the amorphous sirup obtained by adding petroleum ether to its chloroform solution was sufficiently pure for our purpose. The replacement of bromine by the methoxy group was carried out in the usual manner by boiling the methyl alcoholic solution of the bromo compound under a reflux condenser with an excess of freshly prepared silver carbonate. The heptacetyl methyl maltoside was purified by recrystallization from 95% alcohol until its rotation became constant. The pure substance melted at 125° (uncorr.). A chloroform[1] solution containing 1.5781 g. in 50 cc. solution rotated 6.75° to the right in a 4 decimeter tube, hence $[\alpha]_D^{20} = +53.5°$. A duplicate measurement, using 3.0005 grams in 50 cc., gave $[\alpha]_D^{20} = 53.8°$.

**Purification of Heptacetyl Methyl Celloside.**—Part of the acetobromocellose employed was made from cellose by the action of acetic anhydride saturated with hydrobromic acid; the remainder was prepared by dissolving the octacetate of cellose in glacial acetic acid saturated with hydrobromic acid, in accordance with the directions given by Fischer and Zemplen.[2] The bromo compound is easily obtained crystalline and in good yield by either method. The preparation and purification of the acetylated methyl celloside was carried out in precisely the same way as that followed in making the heptacetyl methyl maltoside. The pure substance melted at 187° (uncorr.). A chloroform[1] solution containing 1.4962 grams in 50 cc. solution rotated 3.00° to the left in a 4 decimeter tube, hence $[\alpha]_D^{20} = -25.1°$. A second measurement, using 3.0588 g. in 50 cc., gave $[\alpha]_D^{20} = -25.7°$.

**Purification of Maltose Heptacetate.**—The sirupy acetyl bromomaltose was dissolved in acetone and shaken for several hours with freshly prepared silver carbonate. As soon as the bromine had been completely replaced, the silver salts were filtered off, and the acetone solution was evaporated under low pressure until crystallization occurred spontaneously. The mother liquor from this crystallization yielded a further quantity of crystals on the addition of ether. The material was recrystallized by adding ether to its chloroform solution. The specific rotation was lowered by sixteen recrystallizations from +78° to the constant value $[\alpha]_D^{20} = +67.8°$ in chloroform.[2] The pure substance melted at 181° (uncorr.). Mutarotation occurs in chloroform, the rotation rising in about five weeks to the value +110°; a drop of dilute ammonia added to the solution brings the mixture to the same equilibrium in a few hours. The initial rotation of the pure substance in acetylene tetrachloride was found to be +65.0°, rising slowly to +95.4°. As acetyl determinations

[1] Chloroformum Purificatum, U. S. P.

[2] *Ber.*, 43, 2537 (1910).

do not appear to have been made on any of the heptacetates of the disaccharides, we hydrolyzed two half-gram portions of the pure compound with N/4 $H_2SO_4$ and found 46.82 and 47.23% $CH_3CO$ in comparison with 47.36%, the theoretical value.

**Purification of Cellose Heptacetate.**—The method used for preparing cellose heptacetate was in every way similar to that for the corresponding maltose derivative, except that the former did not crystallize spontaneously from acetone solution. Crystallization took place almost immediately, however, on adding ether after distilling off most of the acetone. The substance was recrystallized eighteen times by adding ether to its solution in chloroform, whereby the melting point was raised from 195° to 204° (uncorr.), and the specific rotation in chloroform[1] was lowered from +18° to —2.4°, without, however, reaching a constant value. The compound mutarotates in chloroform, the rotation of the equilibrium mixture being +22.6°. Two half-gram portions of the substance rotating +5° showed, on analysis, 47.56 and 47.67% $CH_3CO$; theoretical, 47.36%.

**Preparation of Lactose Heptacetate.**—Acetobromolactose was prepared in crystalline form by treating lactose with a saturated solution of hydrobromic acid in acetic anhydride. The acetone solution of the bromo compound was shaken with freshly prepared silver carbonate until a few drops filtered from the mixture and diluted with water gave no precipitate with silver nitrate solution. The silver salts were then filtered off and the filtrate evaporated to a thick sirup under diminished pressure. At first considerable difficulty was encountered in crystallizing the heptacetate, but we have found that if the acetone solution is evaporated to a sufficiently high concentration, the addition of several times its volume of ether invariably causes crystallization in a few minutes. The yield of crude product is about 60–70% of the weight of sugar taken. The substance can be recrystallized without difficulty by adding ether to its chloroform solution, and if the amount of ether added is relatively small, the compound comes out very slowly in beautiful transparent prisms, often half a centimeter in length. Twenty such recrystallizations lowered the specific rotation in chloroform[1] from +12 to —0.3°, although even then a constant value was not reached. The purest material obtained melted at 83° (corr.). In its general properties, lactose heptacetate closely resembles the corresponding compounds of maltose and cellose, although it is considerably more soluble than either in alcohol, acetone and chloroform. Like them, it mutarotates in solution, the rotation in chloroform rising to +52.8°.

The substance was identified as a lactose derivative by saponification with alcoholic potash, the resulting sugar being recognized as lactose by its rotatory power in water.

[1] Chloroformum Purificatum, U. S. P.

On combustion 0.1628 and 0.2025 g. subs. yielded 0.2913 and 0.3659 g. $CO_2$ and 0.0863 and 0.1059 g. $H_2O$, corresponding to 48.8 and 49.2% C and 5.93 and 5.85% H. Calc. for lactose heptacetate ($C_{26}H_{36}O_{18}$): 49.3% C and 5.70% H.

An acetyl estimation was made by boiling two half-gram portions for four hours with 100 cc. $N/4$ $H_2SO_4$ in a quartz flask with a quartz reflux condenser, yielding 47.05 and 47.45% $CH_3CO$ in comparison with the theoretical value, 47.36%.

WASHINGTON, D. C.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE ILLINOIS WESLEYAN UNIVERSITY.]

# THE QUANTITATIVE DETERMINATION OF MORPHINE IN THE VARIOUS ORGANS WHEN INJECTED INTO CATS AND RABBITS.

BY A. W. HOMBERGER AND J. C. MUNCH.

Received May 6, 1916.

During the past few years one of the authors has had submitted to him, at different times, organs from cadavers for the analysis of poisons—especially morphine and opium. In two cases, the suspects had been embalmed. In one case after seven days, and in the other after fifteen days, of interment, the liver, kidneys, stomach and spleen were brought for examination. The quantitative relations as well as the general chemical conduct of the alkaloids found in the different organs, raised the question as to whether this was due to the embalming fluid, or whether the length of time after burial were the cause of the fluctuating assimilation and distribution.

The following paper deals with a series of experiments carried out on cats and rabbits in order to find, if possible, what the effect of the embalming would be on the amount of alkaloid in the different organs in case death had resulted from alkaloid poisoning, to ascertain how much of the original product could be recovered under those conditions, and to find what organs might be the strongest assimilators of such alkaloids. The alkaloid used in this case was morphine.

The morphine used in these investigations was Merck & Company's "Morphinae Sulphas," U. S. P. VIII. Qualitative examination showed it to be free from foreign materials such as starch or other opium alkaloids. Quantitative determinations of the morphine present, by Mayer's Reagent, and determinations of the sulfuric acid present, as barium sulfate, showed that the morphine sulfate used agreed with the formula

$$(C_{17}H_{19}NO_3)_2.H_2SO_4.5H_2O.$$

The desired amount of morphine sulfate was weighed out on an analytical balance, dissolved in distilled water and hypodermically injected into the mesenteric circulation. After a lapse of three hours, to allow for fixation in the organs of the body, the animals were chloroformed