

CRYSTALLINE 1-iodo-1-desoxy-2,3; 4,6-diisopropylidene-L-sorbose

THOMAS S. GARDNER AND JOHN LEE

Received June 4, 1947

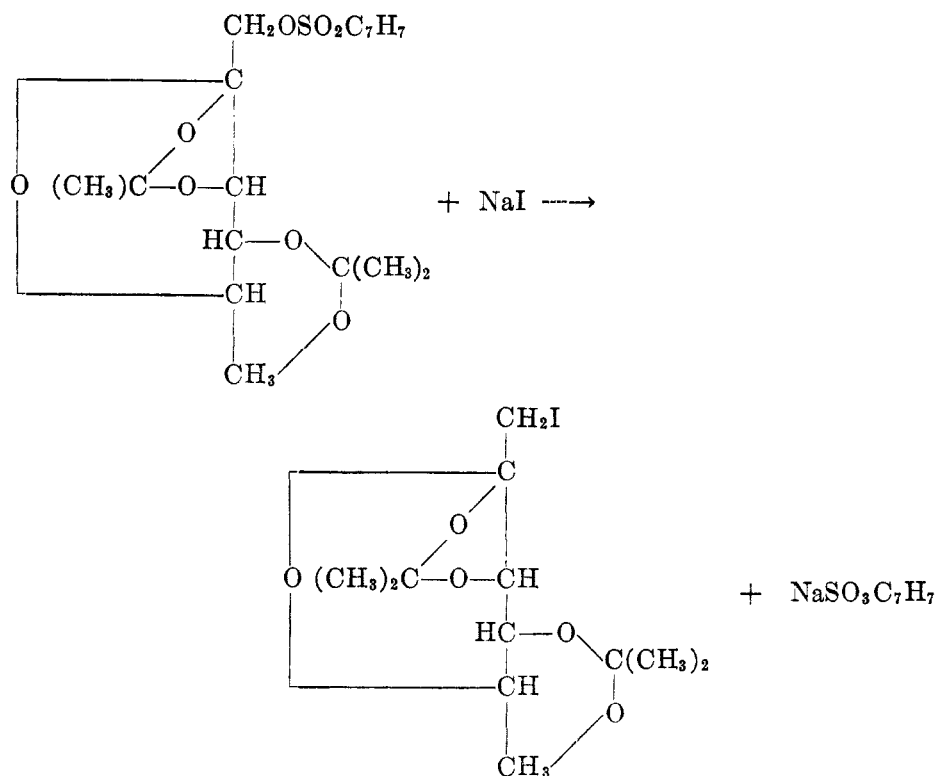
The substitution of tosyloxyl by iodine using sodium iodide in acetone (1) or acetylacetone (2) has been used as a characterization test for primary alcoholic groups. This procedure has been based on the observation that tosyl esters on secondary alcoholic groups are not replaced under similar conditions (1).

An apparent anomaly occurs in the case of tosyl esters adjacent to a keto group. The general opinion was expressed in a recent review on this reaction (3) as follows: "A tosyloxyl group on the primary alcoholic carbon 1 of certain keto sugar derivatives is unreactive." Other investigators state that the reaction is either very slow or does not take place at all (4).

However, in a few cases the reaction has been shown to take place. A sirupy 1,6-diiodo-1,6-didesoxy-2,3-acetone-L-sorbose was prepared by the action of sodium iodide in acetone on the 1,6-ditosyl compound at 130° for five days (5). A crystalline 1-iodo-1-desoxy-2,3-monoacetone-D-fructomethyllose was prepared at 125° for 48 hours from the 1-tosyl derivative with sodium iodide in acetone (6). A crystalline 1-iodo-1-desoxy-2,3-monoacetone-L-sorbomethyllose was prepared at 125° for 36 hours with sodium iodide in acetone (5). An impure 1-iodo-1-desoxy-4-tosyl-monoacetone-D-xylulose was prepared as a sirup contaminated with the unchanged 1,4-ditosyl derivative at 100° for 8 hours (7). However, 1-tosyl-2,3; 4,5-diacetonefructose was found to undergo no change during 8 hours at 100° with sodium iodide in acetone (5, 7) and 3 days at 130° also failed to yield an iodo derivative (5).

From this it appears that in the methyllose forms of fructose and sorbose the C₁ tosyloxy ester adjacent to a keto group may be replaced by the iodine group but the reaction is much slower than with a tosyloxy ester group removed from the keto group by at least one carbon. The difference in reaction between the two types of primary alcoholic groups is clearly demonstrated by work on the rate of tosylation (8) and tritylation (9) of 1,2;3,4-diacetone-D-galactose and 2,3;4,6-diacetone-L-sorbose. In each case the rate of reaction of the C₆ primary hydroxyl of the galactose derivative was several times faster than the C₁ primary alcoholic group of the sorbose derivative.

In this investigation we wish to report a study made on the preparation of crystalline 1-iodo-1-desoxy-2,3; 4,6-diisopropylidene-L-sorbose (1-iodo-1-desoxy diacetonesorbose) from the corresponding 1-tosyloxy compound by the general reaction as follows:



This is the first report of this type of crystalline derivative from a carbohydrate of the general formula, *i.e.* $(\text{CH}_2\text{O})_x$, in contrast to the methylose sugar derivatives cited above (5, 6). The 1-iodo-1-desoxy compound was prepared using sodium iodide in acetone at 100° for long periods of time in a step-wise iodination. It was found that on iodination in one step only 50–80% conversion was obtained at 100° for 100 hours. Iodination at 120° for 4 hours, using acetylacetone as a solvent, gave the starting material apparently unchanged, while at 150° for 4 hours complete decomposition of the compound took place, with the liberation of free iodine.

Crystalline 1-iodo-1-desoxy-diacetonesorbose was found to be an unstable compound. It decomposed in a few weeks at room temperature to a black tarry mass but it could be stored for several weeks at 4° . Solutions in organic solvents at 25° darkened in a few days if exposed to light. Good qualitative tests for iodine were obtained using hot concentrated nitric acid to decompose the compound. However, hot 10% potassium hydroxide solutions only partially decomposed the iodo derivative in five minutes.

1-Iodo-1-desoxy-L-sorbose was prepared by hydrolysis of 1-iodo-1-desoxy-diacetonesorbose with glacial acetic acid and water by the method used by Raymond (10) on 6-iodo-6-desoxy-diacetonegalactose. This method was found to be more satisfactory than the hydrochloric acid hydrolysis method (12). 1-Iodo-1-desoxysorbose was found to be so unstable that aqueous solutions de-

composed and liberated free iodine while being purified and even at 4° free iodine was liberated.

The starting material 1-tosyl-diacetone-L-sorbose was further characterized by conversion to its parent substance, 1-tosyl-L-sorbose, a known compound. It is probable that step-wise iodination of other C₁ tosyloxyl esters adjacent to a keto group may be accomplished under the conditions described.

The lability of this type of iodo sugar suggests its use with active alcoholic groups and a suitable catalyst. New types of glycosides and esters might be prepared. Also, if di-sugar ethers similar to the type previously postulated (11) could be prepared they would be of interest for structure characterization.

Acknowledgment. We are indebted to Dr. Al Steyermark of the Microchemical Division of these laboratories and his co-workers for the microchemical analyses.

EXPERIMENTAL

1-Tosyl-2,3,4,6-diisopropylidene-L-sorbose. Distilled 2,3; 4,6-diisopropylidene-L-sorbose was treated with *p*-toluenesulfonyl chloride in dry pyridine. It was recrystallized from alcohol-water solutions, m.p. 101-102° [α]_D²⁰ +2.8° (c, 5) in chloroform, for which m.p. 102-103°; and [α]_D²⁵ +4.2° was previously reported (12).

Anal. Calc'd for C₁₉H₂₈O₈S: C, 55.03; H, 6.33; S, 7.74.

Found: C, 54.91; H, 6.06; S, 7.54.

1-Tosyl-L-sorbose. Eight grams of 1-tosyl-2,3,4,6-diisopropylidene-L-sorbose was dissolved in 100 ml. of glacial acetic acid immersed in a boiling water-bath. One hundred ml. of water was added gradually over 30 min. and heating was continued for 2.5 hours. Charcoal was added, the material filtered, concentrated *in vacuo* to 50 ml., and dehydrated twice by the addition of 50 ml. of ethanol and concentration. The syrup crystallized from a mixture of alcohol, ether, and petroleum ether; yield 4 g., m.p. 119-120°, [α]_D²⁰ -13.8° in pyridine (c, 5) for which m.p. 116° and [α]_D²⁰ -13.2° had been reported (12).

Anal. Calc'd for C₁₃H₁₈O₈S: C, 46.70; H, 5.43; S, 9.59.

Found: C, 46.76; H, 5.43; S, 9.66.

1-Iodo-1-desoxy-2,3,4,6-diisopropylidene-L-sorbose. Eight grams of 1-tosyl-2,3,4,6-diisopropylidene-L-sorbose, 100 ml. of acetone and 20 g. of sodium iodide were heated for 100 hours at 100° under 1000 lbs. nitrogen pressure. On cooling, the regenerated sodium *p*-toluenesulfonate was removed by filtration, the acetone removed *in vacuo* under 35°, and the residue extracted three times with ether.

The ether extracts were combined and washed with dilute sodium thiosulfate solution and water. On drying and concentration under 35°, the sirupy residue crystallized from alcohol diluted with water to the haze point. Analysis indicated approximately 50% conversion to the iodo derivative.

The procedure was repeated at 100° for 100 hours on the dried crystalline material, using a weight of sodium iodide equivalent to the compound. Five recrystallizations from aqueous alcohol served to purify the readily crystalline product for analysis. The pure compound proved to be unstable at room temperature; after a few days in the air it decomposed to a black tarry mass; m.p. 82-83° [α]_D²⁰ -22.5° in chloroform (c, 4). For analysis the substance was dried for 4 hours at 25° over P₂O₅ *in vacuo* and was subsequently stored at 0°.

Anal. Calc'd for C₁₂H₁₈IO₅: C, 38.93; H, 5.17; I, 34.28.

Found: C, 39.64; H, 5.32; I, 34.68.

All attempts to improve the purity of the sample by other methods resulted in decomposition characterized by appearance of black specks in the sample, which spread to engulf the substance.

SUMMARY

The replacement of a C₁ tosyloxyl ester adjacent to a keto group by iodine has been accomplished by step-wise iodination using sodium iodide in acetone to produce 1-iodo-2,3; 4,6-diisopropylidene-L-sorbose as a crystalline compound.

NUTLEY, N. J.

REFERENCES

- (1) OLDHAM AND RUTHERFORD, *J. Am. Chem. Soc.*, **54**, 366 (1932).
- (2) MURRAY AND PURVES, *J. Am. Chem. Soc.*, **62**, 3194 (1940).
- (3) TIPSON, CLAPP, AND CRETCHER, *J. Org. Chem.*, **12**, 133 (1947).
- (4) REBER AND REICHSTEIN, *Helv. Chim. Acta*, **29**, 343 (1946).
- (5) MÜLLER AND REICHSTEIN, *Helv. Chim. Acta*, **21**, 263 (1938).
- (6) MORGAN AND REICHSTEIN, *Helv. Chim. Acta*, **21**, 1023 (1938).
- (7) LEVENE AND TIPSON, *J. Biol. Chem.*, **120**, 607 (1937).
- (8) HOCKETT AND DOWNING, *J. Am. Chem. Soc.*, **64**, 2463 (1942).
- (9) HOCKETT, FLETCHER, AND AMES, *J. Am. Chem. Soc.*, **63**, 2516 (1941).
- (10) RAYMOND, U. S. Patent 2,365,777, Dec. 26, 1944.
- (11) GARDNER AND PURVES, *J. Am. Chem. Soc.*, **65**, 444 (1943).
- (12) SULLIVAN, *J. Am. Chem. Soc.*, **67**, 837 (1945).