## Summary

Some *o*-phenylbiphenyls have been examined for optical activity; they have not been resolved. A discussion of their suitability for an examination of the postulate of "synchronized rotation" is given.

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[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

# The Mechanism of Walden Inversion in Sugars: The Inversion of *p*-Toluenesulfonyl Esters of Rhamnose

BY IRVING E. MUSKAT[1]

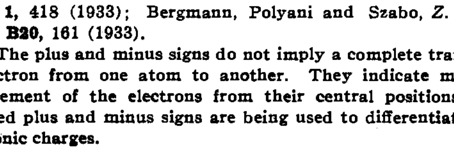
It has been observed that an inversion of the hydroxyl groups in the sugars may occur in the course of reactions in which there is the possibility of the formation of anhydro compounds as intermediates. Thus, Ohle and Vargha[2] obtained 5,6-anhydromonoacetone glucose on treating 6-*p*-toluenesulfonyl-monoacetone-glucose with sodium methylate. On hydrolyzing the anhydro compound they recovered about 50% of the expected monoacetone-glucose together with a mixture of products from which they isolated some monoacetone-*l*-idose—the inverted compound. From this they concluded that the ethylene oxide linkage could absorb not only in the cis position but also in the trans position, thus giving rise to a Walden inversion.

Fischer, Bergmann and Schotte[3] showed that on treating 2-chloromethylmannoside (or glucoside?) with ammonia, an amino-sugar derivative was formed which they designated as "methyl-epiglucosamine." It was later shown[4] that this "methyl-epiglucosamine" had the structure of 3-aminomethylaltroside and was formed through an intermediate anhydro compound. Bodycote, Haworth and Hirst[5] adduced evidence to show also that 2-*p*-toluenesulfonyl-β-methylglucoside is converted by means of ammonia to the same "methyl-epiglucosamine"—the inverted product. Here again it was shown that an anhydro compound probably was formed as an intermediate, and the ethylene oxide linkage underwent scission in such a way as to give rise to an inverted product.

Mathers and Robertson[6] studied the alkaline-hydrolysis of 2,3-di-*p*-toluenesulfonyl-4,6-dimethyl-α-methylglucopyranoside. They found that an inversion had occurred during the hydrolysis but did not prove definitely the structures of their products.

In these investigations the sugar derivatives chosen permitted the formation of anhydro compounds and it was necessary to determine experimentally which carbon atom was involved in the inversion. On the other hand, in the research now reported it was possible to cause an inversion of the hydroxyl groups without the possibility of the intermediate formation of anhydro compounds. This greatly simplifies the problem and it should be possible to cause the inversion of any hydroxyl group the *p*-toluenesulfonyl ester of which can be prepared. Since the *p*-toluenesulfonyl esters of sugars are readily prepared, this procedure may lead to a simple method for the preparation of the rarer sugars, and their derivatives, from the more commonly occurring sugars.

It is logical to assume[7] that a Walden inversion is most likely to occur in those reactions in which one of the groups attached to the asymmetric carbon atom is removable together with the bonding electron pair (II).[8]



It is not suggested that a Walden inversion will necessarily occur in all reactions of type (II), but

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[1] National Research Fellow in Chemistry.

[2] Ohle and Vargha, *Ber.*, **62**, 2435 (1929).

[3] Fischer, Bergmann and Schotte, *ibid.*, **53**, 509 (1920).

[4] Levene and Meyer, *J. Biol. Chem.*, **55**, 221 (1923); Freudenberg, Burkhart and Braun, *Ber.*, **59**, 714 (1926).

[5] Bodycote, Haworth and Hirst, *J. Chem. Soc.*, 151 (1934).

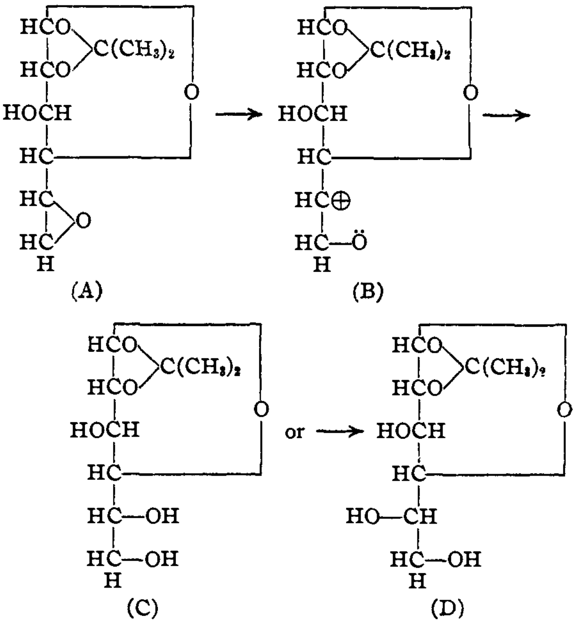
[6] Mathers and Robertson, *ibid.*, 1077 (1933).

[7] F. C. Whitmore, THIS JOURNAL, **54**, 3436 (1932); Wallis, *ibid.* **55**, 2598 (1933); *ibid.*, **56**, 491 (1934); see also A. R. Olson, *J. Chem Phys.*, **1**, 418 (1933); Bergmann, Polyani and Szabo, *Z. physik Chem.*, **B20**, 161 (1933).

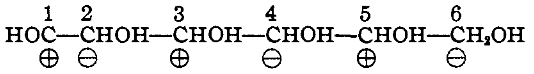
[8] The plus and minus signs do not imply a complete transfer of an electron from one atom to another. They indicate merely a displacement of the electrons from their central positions. The encircled plus and minus signs are being used to differentiate them from ionic charges.

that only in reactions as represented in (II) may a Walden inversion of this kind be expected.

It is now possible to deduce why Walden inversions have been found to occur during the hydrolysis of anhydro compounds of sugars. Thus, in the hydrolysis of 5,6-anhydro-monoacetoneglucose (A), the ethylene oxide linkage most probably breaks between the fifth carbon atom and the oxygen atom with the bonding electron pair attached to the oxygen, leaving the fifth carbon atom with a positive charge (as shown in (B)). The intermediate (B) then absorbs water to give the normal sugar (C), or an inversion occurs at the fifth carbon atom to give the inverted sugar (D). Whether an inversion will or will not occur, and if it will, to what extent, will depend on the steric effects in the sugar molecule and the experimental conditions.



The cleavage of the ethylene oxide linkage between the oxygen and carbon atom (5) follows directly from the following suggested electronic structure of the aldohexose sugars.



$$\overset{1}{\underset{\oplus}{\mathrm{HOC}}}\text{—}\overset{2}{\underset{\ominus}{\mathrm{CHOH}}}\text{—}\overset{3}{\underset{\oplus}{\mathrm{CHOH}}}\text{—}\overset{4}{\underset{\ominus}{\mathrm{CHOH}}}\text{—}\overset{5}{\underset{\oplus}{\mathrm{CHOH}}}\text{—}\overset{6}{\underset{\ominus}{\mathrm{CH_2OH}}}$$

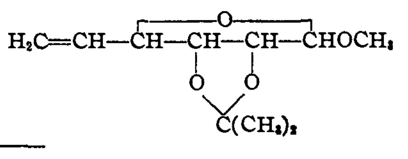
This *electronic structure* and *its significance in* the interpretation of sugar reactions will be discussed in a later paper.

Carbon atom (5) is electropositive relative to carbon atom (6); consequently the oxide linkage is more easily broken at carbon atom (5). It is significant that a Walden inversion has never been observed during the hydrolysis of sugar lactones or the interconversion of furanose and pyranose sugars. This finds a ready explanation in the fact that the oxide linkages are between electropositive carbon atoms of carboxyl, aldehyde, or ketone groups on one hand, and a relatively electronegative alcoholic carbon atom on the other. The linkage between the oxygen atom and the most electropositive carbon atom breaks; thus no inversion of the asymmetric alcoholic carbon atoms can occur.

In order to cause an inversion of any particular hydroxyl group in a given sugar it is therefore necessary, according to this theory, to split off the oxygen atom together with its octet of electrons, thus leaving the carbon atom with a positive charge. Since it is known that the *p*-toluenesulfonyl ester of a primary alcohol group will react readily (in the course of two hours) with sodium iodide in acetone solutions to give an iodo derivative, it appeared probable that hydrolysis of the appropriate *p*-toluenesulfonyl ester of sugar derivatives might lead to Walden inversion at the carbon atom to which it was attached. Furthermore, Phillips[9] has shown that alkaline hydrolysis of the *p*-toluenesulfonyl esters of simple carbinols may be accompanied by almost complete Walden inversion. Consequently, the *p*-toluenesulfonyl esters of acetone methylrhamnofuranoside and of acetone methylrhamnopyranoside were prepared and their hydrolysis in alkaline media studied.

The results obtained, shown in Table I, prove conclusively that an inversion occurred during the hydrolysis of the two *p*-toluenesulfonyl esters to give in the first case 2,3-acetone-methyl-6-desoxy-*d*-gulofuranoside, and in the second case 2,3-acetone-methyl-6-desoxy-*l*-talopyranoside.

Under different conditions of hydrolysis of the *p*-toluenesulfonyl ester of the furanose sugar, an unsaturated sugar derivative which distilled at 80° under 3 mm. pressure and had a specific rotation of +14° (in methyl alcohol) was formed. It probably is the methylglycoside of 2,3-acetone-*l*-mannofuranal (5,6) having the structure



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[9] Phillips, *J. Chem. Soc.*, **123**, 44 (1923); *ibid.*, **127**, 399 (1925).

TABLE I

| Compound | Properties observed | Acetone methyl-glycoside | *p*-Toluene sulfonyl ester | Unsubstituted sugar | *p*-Bromo-phenylhydrazone |
|---|---|---|---|---|---|
| *l*-Rhamnose (6-desoxy-*l*-mannose)<br>Furanose derivative | B. or m. p., °C. | B 100–105 (0.7 mm.) | M 80 | M 86 (105°) | M 160 |
| | $[\alpha]^{25}_{D}$ | −66.7 | −12.2 | −7.7 → +8.9 | 0 |
| | Solvent | $CH_3OH$ | $CH_3OH$ | $H_2O$ | $C_2H_5OH$ |
| | $n^{25}_{D}$ | 1.4487 | | | |
| Inverted product (6-desoxy-*d*-gulose) | B. or m. p., °C. | B 100 (1 mm.) | M 60 | M 65 (app.) | M 162 |
| | $[\alpha]^{25}_{D}$ | −16.9 | +22.3 | +14 → −14 | −6.1 → +13 |
| | Solvent | $CH_3OH$ | $CH_3OH$ | $H_2O$ | $C_2H_5OH$ |
| | $n^{25}_{D}$ | 1.4560 | | | |
| | Formula | $C_{10}H_{18}O_5$ | $C_{17}H_{24}O_7S$ | $C_6H_{12}O_5$ | $C_{12}H_{17}O_4N_2Br$ |
| | Calcd. | C, 55.02 | C, 54.80 | C, 43.87 | C, 43.23 |
| | | H, 8.3 | H, 6.5 | H, 7.3 | H, 5.2 |
| | | $OCH_3$, 14.22 | S, 8.60 | | Br, 24.0 |
| | Found | C, 55.16 | C, 54.77 | C, 43.38 | C, 43.66 |
| | | H, 8.4 | H, 6.6 | H, 7.4 | H, 5.5 |
| | | $OCH_3$, 14.78 | S, 8.52 | | Br, 23.9 |
| *l*-Rhamnose (6-desoxy-*l*-mannose)<br>Pyranose derivative | B. or m. p., °C. | B 99 (0.3 mm.) | M 57 | | |
| | $[\alpha]^{25}_{D}$ | −14.2 | +14 | | |
| | Solvent | $CH_3OH$ | $CH_3OH$ | | |
| | $n^{25}_{D}$ | 1.4533 | | | |
| Inverted product (6-desoxy-*l*-talose) | B. or m. p., °C. | B 90 (0.8 mm.) | M 76.5 | | |
| | $[\alpha]^{25}_{D}$ | −15.5 | +3.1 | | |
| | Solvent | $CH_3OH$ | $CH_3OH$ | | |
| | $n^{25}_{D}$ | 1.4520 | | | |
| | Formula | $C_{10}H_{18}O_5$ | $C_{17}H_{24}O_7S$ | | |
| | Calcd. | C, 55.02 | C, 54.80 | | |
| | | H, 8.3 | H, 6.5 | | |
| | | $OCH_3$, 14.22 | S, 8.60 | | |
| | Found | C, 55.98 | C, 54.82 | | |
| | | H, 8.2 | H, 6.7 | | |
| | | $OCH_3$, 15.39 | S, 8.62 | | |

## Experimental Part

**Hydrolysis of 5-*p*-Toluenesulfonyl-2,3-acetone-methylrhamnofuranoside.**—To 4 g. of the ester prepared according to the method of Levene and Muskat[10] in 100 cc. of methyl alcohol was added an equal volume of 2 *N* potassium hydroxide in methyl alcohol. Forty cc. of water was then added for clarification and polarimetric readings taken. No hydrolysis could be detected on standing at room temperature for twenty-four hours or after refluxing for thirty minutes. However, after forty hours at 74° hydrolysis was complete. Water was then added and the mixture extracted with chloroform, washed free of alkali and dried. The chloroform was removed by vaporization under reduced pressure. A yellow sirup (2.3 g.) remained which contained no sulfur. It was distilled under reduced pressure. A few drops distilled over at about 65° under 2 mm. pressure (probably the unsaturated derivative described later), and the major portion (about 2 g.) distilled at about 100° under 1 mm. pressure.

**Preparation of *p*-Toluenesulfonyl Ester of Acetone-methyl-desoxyhexoside (II).**—*p*-Toluenesulfonyl chloride (1.6 g.) was added to a solution of acetone-methyldesoxyhexoside (1 g.) in dry pyridine (1.5 cc.). The mixture was allowed to stand overnight at room temperature and then dissolved in chloroform with addition of water. The aqueous portion was extracted twice with small quantities of chloroform. The combined chloroform extracts were then washed successively with dilute hydrochloric acid, dilute sodium hydroxide and water. The chloroform solution was now dried over anhydrous sodium sulfate, filtered and the solvent removed by vaporization under diminished pressure. The product was a pale yellow sirup which crystallized from ligroin (30–40°) in white needles, m. p. 60°. The compound was very soluble in the usual organic solvents with the exception of ligroin. The yield of the ester is nearly quantitative.

**Hydrolysis of Acetone Methyldesoxyhexoside in Acid Medium.**—The acetone-methyldesoxyhexoside (1.2 g.) was hydrolyzed with 1% sulfuric acid (50 cc.) by slowly boiling the reaction mixture for ninety minutes. All the acetone-methyldesoxyhexoside had dissolved within this time. The solution was rendered neutral with barium carbonate, filtered and the water removed under diminished pressure, at a temperature not exceeding 40°. The residual sirup was dissolved in acetone and filtered from barium salts. The acetone was removed by vaporization under diminished pressure but the resulting amorphous powder could not be crystallized. The powder melted at about 65°, and a mixture with known *l*-rhamnose melted at 52–58°. It reduced Fehling's solution even in the cold.

The *p*-bromophenylhydrazone of the inverted desoxyhexose obtained above was prepared in the usual manner.

**Methylglycoside of 2,3-Acetone-*l*-mannofuranol-(5,6).**—5-*p*-Toluenesulfonyl-2,3-acetone-methylrhamnofurano-

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(10) Levene and Muskat, *J. Biol. Chem.*, **106**, 761 (1934).

side (4 g.) was dissolved in 100 cc. of methyl alcohol and 100 cc. of 2 *N* potassium hydroxide in methyl alcohol solution was added. About 10 cc. of water was added and the solution was heated on the water-bath for forty hours. The sirupy residue was extracted several times with chloroform. The combined chloroform extracts were washed with water until free from alkali and then dried over anhydrous sodium sulfate. The chloroform was removed by vaporization under reduced pressure. A yellow sirup (2.0 g.) remained, which distilled at 80° under 3 mm. pressure. It absorbed bromine readily, $n_D^{25}$ 1.4485, $[\alpha]_D^{25}$ +14° (in methyl alcohol, about 1% solution).

*Anal.* Calcd. for $C_{10}H_{16}O_4$: C, 59.97; H, 8.0; $OCH_3$, 15.49. Found: C, 59.56; H, 8.2; $OCH_3$, 15.98.

The author wishes to express his appreciation to Drs. P. A. Levene and R. S. Tipson for their many helpful suggestions during the progress of this work.

## Summary

A theory is presented to explain Walden inversions in sugars. The theory has been tested by a study of the hydrolysis of the *p*-toluenesulfonyl esters of rhamnose. These esters yielded inverted products on alkaline hydrolysis. It should be possible, in this manner, to cause the inversion of any hydroxyl group the *p*-toluenesulfonyl ester of which can be prepared, and thus lead to a simple method for the preparation of the rarer sugars and their derivatives, from the more commonly occurring sugars.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF IOWA STATE COLLEGE]

# Alkaline Oxidation of Lignin

BY A. W. WALDE AND R. M. HIXON

The use of ammonia as a pulping agent for the grasses and the recovery of lignin from the black liquor has been described previously.[1] Where the preparation of lignin is the main objective, it has been found more convenient to remove the hemicelluloses from the tissue by dilute acid hydrolysis before extraction of the lignin with ammonia. This modification avoids the filtration difficulties associated with the colloidal properties of the hemicelluloses.

Freshly prepared ammonia lignin, like other alkali lignins, softens and coalesces when heated in water to about 60°. On cooling, it solidifies to a brittle, friable mass. This characteristic property is gradually lost within four to six weeks after preparation. In an effort to correlate this physical change with chemical properties, a study has been made of the alkaline oxidation reactions of lignin.

While the ease of oxidation[2] of lignin has been recognized for many years, it was surprising to find that the reaction with alkaline iodine solutions could be made quantitative. Iodoform was identified as one of the oxidation products as previously reported by Harris, Sherrard and Mitchell.[3] The oxidized lignin residue contains iodine and carboxy groups. This oxidized lignin derivative is tentatively designated as "iodo-carboxy-lignin," the term being used with the indefinite connotations still necessary with the term lignin.

## Experimental

**Preparation of Ammonia Lignin from Oat Hulls.**—Three kilograms of oat hulls were hydrolyzed for four hours at 90° with 0.6 *N* hydrochloric acid, rendering approximately 50% of the tissue soluble. These conditions of time, temperature and acid concentration give maximum yields of reducing sugars with minimum decomposition.[4] The washed, hydrolyzed hulls were transferred to a steel digester, covered with aqueous ammonia (one volume of sp. gr. 0.90 with an equal volume of water) and digested for eight hours under 100 pounds pressure. After cooking, most of the ammonia was recovered by blowing the hot ammonia vapors into cold water. The ammoniacal liquor was drained through cloth directly into a stone filter; the oat hull residues were washed twice with water and the wash water combined with the filtrate. A second filtration of the liquor removed any suspended cellulosic material. The lignin in the ammoniacal liquor was recovered in one of two ways: by evaporation and aeration to reduce the basicity of the solution, or by precipitation with dilute hydrochloric acid at about 50°. After allowing time to settle and decanting the supernatant liquor, the lignin was filtered on a large Büchner funnel and washed free from chlorides. It was dried at 40° until it lost its plastic character, and then at 105° for two hours; yield, 135–150 g.

*Anal.* (Calcd. to ash-free basis): $OCH_3$, 13.1; C, 63.78; H, 6.02; N, 3.04; ash, 3.7.

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[1] Peterson and Hixon, *Iowa State Coll. J. Sci.*, **7**, 25 (1932).

[2] A discussion of the studies on oxidation reactions of lignin will be found in the literature summary by Phillips, *Chem. Rev.*, **14**, 103–170 (1934).

[3] Harris, Sherrard and Mitchell, THIS JOURNAL, **56**, 889 (1934).

[4] Bryner, Thesis, Iowa State Coll., June, 1934.