

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

Detosylation of 4- and 5-Tosyl¹ Monoacetone *l*-Methylrhamnosides

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Since Ferns and Lapworth² have pointed out the fact that the group R-SO₃-O- functions as a halide atom, it is evident that the replacement of a tosyl group on an asymmetric carbon atom may be accompanied by a Walden inversion. Indeed in the sugar series such occurrences were reported first by Mathers and Robertson³ and later by Oldham and Rutherford⁴ and by Ohle and Just.⁵ In all the described cases, however, opportunity existed for an ethylene oxidic ring formation as an intermediate step in the rearrangement. The question naturally arose as to whether a Walden inversion occurs in cases not permitting the oxidic ring formation. Work in this direction was initiated in this Laboratory several years ago and some of the negative results have been reported in a preliminary note.⁶

On the other hand, Muskat⁷ thought he had obtained evidence in favor of the occurrence of Walden inversion on alkaline hydrolysis of 5-tosyl monoacetone *l*-methylrhamnoside. Depending upon conditions of hydrolysis, Muskat obtained either an unsaturated derivative distilling at 80° (3 mm.) or a saturated substance distilling at 100° (1 mm.). The latter product on hydrolysis was supposed to form the simple sugar, *d*-gulomethylose. The properties of the substance, its strong reducing power in the cold, mutarotation of the amorphous product and the sign of the equilibrium rotation did not agree with the found properties of *d*-gulomethylose.⁸

However, the possibility was not excluded that the higher boiling material obtained by Muskat was a mixture of several substances containing gulomethylose among the other products. The problem, therefore, required a rigorous reinvestigation.

The Nature of the Higher Boiling Material.—As a result of such an investigation, the conclusion was reached that the higher boiling material ob-

(1) Term introduced by Hess and Pfeleger to designate *p*-toluene sulfonyl radical [K. Hess and R. Pfeleger, *Ann.*, **507**, 48 (1933)].

(2) J. Ferns and A. Lapworth, *J. Chem. Soc.*, **101**, 273 (1912).

(3) D. S. Mathers and G. J. Robertson, *ibid.*, 696, 1076 (1933).

(4) J. W. H. Oldham and J. K. Rutherford, *THIS JOURNAL*, **54**, 366 (1932).

(5) H. Ohle and F. Just, *Ber.*, **68**, 601 (1935).

(6) P. A. Levene and J. Compton, *THIS JOURNAL*, **57**, 777 (1935).

(7) I. E. Muskat, *ibid.*, **56**, 2653 (1934).

(8) P. A. Levene and J. Compton, *J. Biol. Chem.*, **111**, 335 (1935).

tained by Muskat was slightly impure monoacetone *l*-methylrhamnopyranoside.

1. The tosyl derivative of this material obtained by Muskat with a melting point of 60°, $[\alpha]_D +22^\circ$ (methanol), and the same material obtained by us, on recrystallization gave a product melting at 61–62°, $[\alpha]^{24}_D +22^\circ$ (methanol), and the mixed melting point with 4-tosyl monoacetone *l*-methylrhamnopyranoside showed no depression.

2. The same tosyl derivative on reductive detosylation by the method of Freudenberg and Brauns⁹ gave a substance with the properties of monoacetone *l*-methylrhamnopyranoside.

3. On hydrolysis with dilute acid the higher boiling fraction gave a sugar whose *p*-bromophenylhydrazone had the properties of the corresponding hydrazone of rhamnose.

The Origin of the Higher Boiling Material.—The higher boiling material was not a product of a ring shift in course of the reaction but had its origin in the contamination of the monoacetone *l*-methylrhamnopyranoside with the corresponding derivative of the pyranoside. The evidence in favor of this conclusion is as follows.

1. The tosyl derivative obtained from the monoacetone *l*-methylrhamnoside prepared in the conventional way and having a melting point of 79–80° could be separated into several fractions as shown in Table I.

2. It was shown by analysis of the various hydrolytic fractions that only the substance melting at 82–83° was the pure furanoside, and that the remaining fractions were mixtures of the furanoside with pyranoside. More precisely, the results were as follows.

(a) The fraction melting at 82–83° on alkaline hydrolysis yielded practically exclusively the unsaturated product (most probably of a mannal nature) together with a minimal residue of the unchanged monoacetone *l*-methylrhamnopyranoside.

The same product on reductive hydrolysis yielded exclusively monoacetone *l*-methylrhamnopyranoside.

(b) The other fractions gave smaller yields of low boiling material and increasing quantities of

(9) K. Freudenberg and P. Brauns, *Ber.*, **55**, 3238 (1922).

the higher boiling fractions. From the latter fraction a tosyl derivative could be obtained melting at 61°, showing no depression of melting point when mixed with 4-tosyl monoacetone *l*-methylrhamnopyranoside. On reductive hydrolysis this tosyl derivative yielded a product identical with monoacetone *l*-methylrhamnopyranoside.

(c) Pure 4-tosyl monoacetone *l*-methylrhamnopyranoside, m. p. 61–62°, on alkaline hydrolysis, did not yield the unsaturated derivative, but gave exclusively the higher-boiling material which, on retosylation, yielded a tosyl derivative with the properties of the original material.

Thus, it is evident that monotosyl derivatives of rhamnose, in which the opportunity for oxide formation is excluded, behave similarly to the tosyl derivatives of other sugars, namely, they undergo alkaline detosylation without Walden inversion.¹⁰

It may be added that the two tosyl derivatives with melting point of 82–83° and of 61–62° were shown definitely to have the furanoside and the pyranoside ring structures, respectively.

From the experience gained during this work it is found that absolutely pure monoacetone *l*-methylrhamnopyranoside is obtained most advantageously by reductive detosylation of the tosyl derivative melting at 82–83°

Experimental

A. Preparations

Monoacetone Methylrhamnopyranoside.—Two methods were employed in the preparation of this material, each resulting in the simultaneous formation of monoacetone methylrhamnopyranoside as an impurity.

(a) Fifty grams of anhydrous rhamnose¹¹ was suspended in 1000 cc. of acetone containing 5% of absolute methyl alcohol. Anhydrous copper sulfate (100 g.) was then added and sufficient concentrated sulfuric acid to make the solution 0.2%. The mixture was shaken at room temperature for twenty hours, after which it was worked up as previously described; total yield of monoacetone methylrhamnopyranosides, 45.1 g., having the same specific rotations and refractive indices as previously recorded.¹¹

(b) Fifty grams of monoacetone rhamnose¹² was dissolved in 1000 cc. of absolute methyl alcohol containing 1% of anhydrous hydrogen chloride. The mixture was allowed to stand at room temperature overnight, after which it was allowed to reflux on the steam-bath for thirty minutes. The solution was made neutral with excess silver carbonate, filtered and concentrated under dimi-

inished pressure to a thin sirup which distilled completely under diminished pressure; yield, 40 g.; b. p. 99–100° (0.8 mm.); n_D^{25} 1.4485; $[\alpha]_D^{25}$ –63.0° (c, 3.379, methyl alcohol); $[\alpha]_D^{25}$ –45.5° (c, 2.504, water).

Anal. Calcd. for C₁₀H₁₈O₆: OCH₃, 14.22. Found: OCH₃, 14.22.

There remained after distillation of the monoacetone methylrhamnopyranosides 8 g. of unchanged monoacetone rhamnose, b. p. 130–136° (0.8 mm.), and a small amount (0.5 g.) of methylrhamnopyranoside, b. p. 148–154° (0.5 mm.).

5-Tosyl¹ Monoacetone Methylrhamnopyranoside.—This compound was prepared according to the procedure of Levene and Muskat,¹¹ with slight modifications.

Monoacetone methylrhamnopyranoside (20 g.) prepared as described in method (a) or (b) above, was dissolved in 30 cc. of dry pyridine and 32 g. of tosyl chloride added. Shaking was maintained until solution was complete, after which the mixture was allowed to stand overnight at room temperature. The mixture was then thoroughly cooled and 2 cc. of water added. After standing for thirty minutes the partially crystallized mass was poured with vigorous stirring into 250 cc. of ice-cold saturated sodium bicarbonate solution. The sirupy product first separating soon solidified and was removed by filtration, washed thoroughly with water and dried; yield 22 g. The product recrystallized from methyl alcohol had a melting point of 80–81°. After a second and third recrystallization, a constant melting point of 82–83° was obtained; $[\alpha]_D^{25}$ –13.6° (c, 3.168, methyl alcohol). Continued recrystallization of the mixed crystals obtained from the mother liquors gave fractions having the properties shown in Table I.

TABLE I

FRACTIONATION OF TOSYL DERIVATIVES OF MONOACETONE METHYLRHAMNOPYRANOSIDE

| Fraction | M. p., °C. | $[\alpha]_D^{25}$ in methanol |
|----------|--------------|-------------------------------|
| I | 82–83 (max.) | –13.6° (c, 3.168) |
| II | 74–75 | –5.6° (c, 3.046) |
| III | 68–69 | –1.7° (c, 2.964) |
| IV | 64–65 | +5.6° (c, 3.030) |
| V | 57–58 | +12.1° (c, 2.708) |

Monoacetone Methylrhamnopyranoside.—Acetonation of methylrhamnopyranoside according to the procedure of Levene and Muskat¹³ led to the formation of pure monoacetone methylrhamnopyranoside, b. p. 104–105° (0.8 mm.); n_D^{25} 1.4545; $[\alpha]_D^{25}$ –11.9° (c, 3.366, methanol).

4-Tosyl Monoacetone Methylrhamnopyranoside.—Twenty grams of monoacetone methylrhamnopyranoside was tosylated and the product isolated in the manner described for 5-tosyl monoacetone methylrhamnopyranoside; yield 25.5 g.; melting point after one recrystallization from methyl alcohol, 61–62°. Further recrystallizations from this solvent changed neither the melting point nor specific rotation; $[\alpha]_D^{25}$ +21.94° (c, 3.030 methanol).

Anal. Calcd. for C₁₇H₂₄O₇S: C, 54.80; H, 6.45; S, 8.60. Found: C, 54.98; H, 6.46; S, 8.69.

B. Alkaline Hydrolysis

1. Pure 5-Tosyl Monoacetone Methylrhamnopyranoside.—(Fraction I, Table I.) Forty grams of pure 5-tosyl

(13) P. A. Levene and I. E. Muskat, *J. Biol. Chem.*, **105**, 431 (1934).

(10) J. W. H. Oldham and G. J. Robertson, *J. Chem. Soc.*, 685 (1935).

(11) P. A. Levene and I. E. Muskat, *J. Biol. Chem.*, **105**, 761 (1934).

(12) K. Freudenberg, *Ber.*, **59**, 838 (1926).

monoacetone methylrhamnifuranoside (m. p. 82–83°; $[\alpha]^{25}_D -13.5^\circ$) was dissolved in 1500 cc. of methyl alcohol and 120 g. (20 moles) of potassium hydroxide dissolved in 1300 cc. of water was added to the boiling solution. The reaction was 95% complete after refluxing on the steam-bath for sixty hours at 78° after which the solution was cooled and the excess of alkali exactly neutralized by means of 25% hydrochloric acid. Sufficient calcium chloride was then added to saturate the solution, after which it was exhaustively extracted with chloroform. The chloroform extract was allowed to stand over calcium chloride for twenty-four hours, filtered, and concentrated under diminished pressure. The resulting sirup distilled in two fractions: *first*, b. p. 56–60° (0.3 mm.), yield 16.0 g. n^{25}_D 1.4491; *second*, b. p. 82–85° (0.3 mm.), yield 0.8 g., n^{25}_D 1.4501.

Anal. First fraction. Calcd. for $C_{19}H_{16}O_4$: C, 59.97; H, 8.0; OCH_3 , 15.49. Found: C, 59.64; H, 8.21; OCH_3 , 15.21. *Second fraction.* Calcd. for $C_{19}H_{18}O_5$: C, 55.02; H, 8.30; OCH_3 , 14.22. Found: C, 54.85; H, 8.38; OCH_3 , 14.42.

A portion of the second fraction (0.6 g.) (b. p. 82–85° at 0.3 mm.), was dissolved in 1 cc. of dry pyridine and 0.8 g. of tosyl chloride added. After standing overnight at room temperature the solution was worked up as described for the tosylation of monoacetone methylrhamnifuranoside (yield 0.65 g.; m. p. 77–78°). After one recrystallization from methyl alcohol a constant melting point of 82–83° was obtained which was unchanged on admixture with an authentic specimen of 5-tosyl monoacetone methylrhamnifuranoside; specific rotation of this material $[\alpha]^{25}_D -13.05^\circ$ (c 3.064, methanol).

The various conditions employed in attempts to obtain from pure 5-tosyl monoacetone methylrhamnifuranoside the product described by Muskat⁷ are summarized in Table II.

2. **Mixed 4- and 5-Tosyl Monoacetone Methylrhamnosides**, m. p. 68°.—(Fraction III, Table I.) Four grams of mixed crystals of 4- and 5-tosyl monoacetone methylrhamnosides (m. p. 68°) was dissolved in 200 cc. of methyl alcohol and 12 g. of potassium hydroxide dissolved in 140 cc. of water added on the steam-bath. Refluxing was maintained for seventy-five hours, when the reaction was complete. After cooling, the hydrolysis products were isolated in the manner described above (1). Two fractions were obtained: *first*, b. p. 58–60° (0.3 mm.), yield 0.6 g.; *second*, b. p. 82–85° (0.3 mm.), yield 1.1 g.

Retosylation of the high boiling sirup (0.7 g.) with tosyl

chloride (1.2 g.) in the presence of pyridine (1.0 cc.) gave a tosyl compound (0.8 g.) melting at 59–60°. After one recrystallization from methyl alcohol a constant melting point of 60–61° was obtained; $[\alpha]^{25}_D +20.2^\circ$ (c, 2.868, methanol). A mixed melting point of this material with pure 4-tosyl monoacetone methylrhamnifuranoside (m. p. 61–62°) showed no depression.

3. **Impure 5-Tosyl Monoacetone Methylrhamnifuranoside**, m. p. 79–80°.—Inasmuch as the 5-tosyl monoacetone methylrhamnifuranoside (m. p. 80°) previously reported¹⁰ had a lower melting point than that employed in experiment 1, a sample of this compound (unfractionated) with m. p. 79–80° was used: 40 g. of 5-tosyl monoacetone methylrhamnoside (m. p. 79–80°) was dissolved in 1500 cc. of methyl alcohol and 120 g. of potassium hydroxide dissolved in 1300 cc. of water added on the steam-bath. The temperature (80°) was maintained for fifty hours when the reaction was about 95% complete. After cooling, the solution was worked up as described above; yield in three fractions: *first*, 17.1 g., *second*, 1.5 g., and *third*, 3.0 g. with b. p. 58–60° (0.3 mm.), 80–82° (0.3 mm.), and 83–85° (0.3 mm.), respectively.

The first fraction consisted of the unsaturated compound, whereas the second consisted of a mixture of monoacetone methylfuranoside and monoacetone methylpyranoside and the third was pure pyranoside, as shown on retosylation.

The second fraction (b. p. 80–82° at 0.3 mm.) was dissolved in 2.5 cc. of dry pyridine and 2.2 g. of tosyl chloride added. The mixture was allowed to stand overnight, after which it was worked up as described above; yield 1.4 g. Recrystallization from methyl alcohol gave a product (m. p. 58°) which after the fourth crystallization had risen to 67–68° $[\alpha]^{25}_D$ 0.00° (c, 2.976 methanol). From the mother liquors there was obtained a small amount of mixed 4- and 5-tosyl compounds, m. p. 55–58°.

The third fraction (b. p. 83–85° at 0.3 mm.) was divided into two parts. (a) A portion of this material (0.5 g.) was retosylated with tosyl chloride (0.8 g.) in the presence of dry pyridine (1.2 cc.) by allowing to stand overnight at room temperature; yield 0.6 g. After one recrystallization a substance of constant melting point of 60–61° was obtained which when mixed with pure 4-tosyl monoacetone methylrhamnifuranoside showed no depression; specific rotation of this material, $[\alpha]^{25}_D +22.1^\circ$ (c, 3.032 methanol).

Anal. Calcd. for $C_{17}H_{24}O_7S$: C, 54.80; H, 6.45; S, 8.60. Found: C, 54.60; H, 6.30; S, 8.72.

TABLE II

EFFECT OF ALKALINE HYDROLYSIS MIXTURES ON PURE 5-TOSYL MONOACETONE METHYL RHAMNIFURANOSIDE (M. P. 82–83°)

| Expt. | Wt., g. | KOH, moles | Methanol, cc. | Water, cc. | Temp., °C. | Time, hours | % Yield of unsatd. compd. of b. p. 60° (0.3 mm.) |
|-------|---------|--------------------------|---------------|------------|------------|-------------|--|
| I | 4 | 20 | 200 | 40 | 74 | 50 | 95 |
| II | 2 | 20 | 100 | 0 | 100 | 30 | 90 |
| III | 4 | 20 | 160 | 180 | 80 | 48 | 95 |
| IV | 2 | 2 | 200 | 20 | 125 | 18 | 90 |
| V | 2 | 2 | 80 | 60 | 100 | 18 | 90 |
| VI | 2 | 20 | 100 | 40 | 37 | 2 mo. | No reaction |
| VII | 2 | 20 (NaOCH ₃) | 100 | 30 | 70 | 50 | 98 |

(b) A second portion of this material (third fraction) (1.0 g.) was dissolved in 40 cc. of 1% sulfuric acid solution and allowed to reflux slowly for ninety minutes. The solution was rendered exactly neutral with barium hydroxide, treated with charcoal, and filtered. Upon concentrating under diminished pressure at 40° there was obtained 0.8 g. of sirupy material which on heating reduced Fehling's solution.

Four-tenths gram of this sirup was converted to the *p*-bromophenylhydrazone using one mole of *p*-bromophenylhydrazine in 5 cc. of absolute ethyl alcohol. There was thus obtained 0.35 g. of material, m. p. 168°, unchanged by further recrystallization from ethyl alcohol. A mixed melting point of this material with an authentic specimen of rhamnose *p*-bromophenylhydrazone (m. p. 167–168°) showed no depression. The mutarotation of the above *p*-bromophenylhydrazone in ethyl alcohol was in the same direction as that of rhamnose *p*-bromophenylhydrazone.

$[\alpha]^{25}_D - 11.29^\circ \xrightarrow{24 \text{ hrs.}} +5.8^\circ \xrightarrow{2 \text{ weeks}} -21.29^\circ \text{ the latter,}$
 $[\alpha]^{25}_D - 12.5^\circ \xrightarrow{30 \text{ hrs.}} +10.2^\circ \xrightarrow{2 \text{ weeks}} -23.1^\circ$

No other *p*-bromophenylhydrazone was found in the reaction product, thus showing that rhamnose was the only sugar present in the third fraction.

Anal. Calcd. for $C_{12}H_{17}O_4N_2Br$: C, 43.24; H, 5.14; N, 8.40. Found: C, 43.35; H, 5.02; N, 8.61.

4. Pure 4-Tosyl Monoacetone Methylrhamnopyranoside.—Four grams of 4-tosyl monoacetone methylrhamnopyranoside (m. p. 61–62°) was dissolved in 150 cc. of methyl alcohol and 130 cc. of water containing 12 g. (20 moles) of potassium hydroxide added to the solution on the steam-bath. After refluxing for sixty hours, hydrolysis was complete and the excess alkali was neutralized with carbon dioxide. The solution was evaporated to dryness at 40° under diminished pressure and the resulting solid thoroughly extracted with ether. The ether extract was dried over calcium chloride, filtered, and concentrated under diminished pressure to a thick sirup which distilled completely, b. p. 84–85° (0.3 mm.); yield 2.0 g.; $[\alpha]^{25}_D - 20.5^\circ$ (c, 3.230, methanol); $n^{25}_D 1.4544$.

Anal. Calcd. for $C_{10}H_{15}O_5$: C, 55.02; H, 8.30; OCH_3 , 14.22. Found: C, 55.12; H, 8.40; OCH_3 , 14.35.

Retosylation of monoacetone methylrhamnopyranoside thus obtained (0.86 g.) with tosyl chloride (1.5 g.) in the presence of dry pyridine (1.2 cc.) followed by isolation and crystallization as previously described yielded 0.90 g. of material, m. p. 61–62°. A mixed melting point of this material with 5-tosyl monoacetone methylrhamnopyranoside showed no depression. Specific rotation $[\alpha]^{25}_D + 21.8^\circ$ (c, 3.028, methanol).

C. Reductive Alkaline Hydrolysis

1. Pure 5-Tosyl Monoacetone Methylrhamnopyranoside.—(Fraction I, Table I.) Two grams of 5-tosyl monoacetone methylrhamnopyranoside (m. p. 82–83°) was dissolved in 100 cc. of 80% methyl alcohol and 25 g. of 4% sodium amalgam added under good stirring. After fourteen hours at room temperature the reaction was complete. The excess alkali was neutralized with a stream of carbon dioxide and the solution evaporated to dryness at 40° under diminished pressure. The resulting solid was thor-

oughly extracted with hot ether and the extract dried over calcium chloride, filtered and concentrated under diminished pressure; yield, 1.1 g. with b. p. 78–80° (0.2 mm.); $[\alpha]^{25}_D - 75.45^\circ$ (c, 2.770, methanol); $n^{25}_D 1.4466$.

Anal. Calcd. for $C_{10}H_{15}O_5$: C, 55.02; H, 8.30; OCH_3 , 14.22. Found: C, 54.99; H, 8.35; OCH_3 , 14.21.

Retosylation of 0.5 g. of this pure material with 0.8 g. of tosyl chloride dissolved in 1 cc. of dry pyridine in the usual manner, gave a yield of 0.6 g. of 5-tosyl monoacetone methylrhamnopyranoside (m. p. 82–83°). The melting point was unchanged when mixed with an authentic specimen of 5-tosyl monoacetone methylrhamnopyranoside.

2. Mixed 4- and 5-Tosyl Monoacetone Methylrhamnopyranosides, m. p. 57–58°.—Fraction V, Table I. The mixed crystals of 4- and 5-tosyl monoacetone methylrhamnopyranosides (2.5 g.) dissolved in 250 cc. of 80% methyl alcohol were detosylated by use of 36 g. of 4% Na-Hg amalgam during fourteen hours. The product isolated as described above had a boiling point of 82–85° (0.3 mm.); yield 1.1 g.; $[\alpha]^{25}_D - 38.18^\circ$ (c, 3.156, methanol); $n^{25}_D 1.4520$.

3. Pure 4-Tosyl Monoacetone Methylrhamnopyranoside.—(a) Ten grams of 4-tosyl monoacetone methylrhamnopyranoside was dissolved in 500 cc. of 80% methyl alcohol and 125 g. of 4% Na-Hg amalgam added. Good stirring was maintained for fourteen hours, after which the reaction was complete. The solution was worked up and the product isolated as previously described; yield 5.4 g.; b. p. 84–85° (0.3 mm.); $[\alpha]^{25}_D - 17.76^\circ$ (c, 3.294, methanol); $n^{25}_D 1.4541$.

Anal. Calcd. for $C_{10}H_{15}O_5$: C, 55.02; H, 8.30; OCH_3 , 14.22. Found: C, 54.94; H, 8.41; OCH_3 , 14.00.

Retosylation of 0.5 g. of this material with tosyl chloride (0.8 g.) in presence of dry pyridine (1 cc.) yielded in the usual manner, 0.6 g. of material of m. p. 61–62°; $[\alpha]^{25}_D + 21.88^\circ$ (c, 3.014, methanol). A mixed melting point with original 4-tosyl monoacetone methylrhamnopyranoside showed no depression.

(b) The alkaline hydrolysis of mixed crystals of 4- and 5-tosyl methylrhamnopyranosides (m. p. 68 or 80°) leads to the production of an unsaturated low boiling material and monoacetone methylrhamnopyranoside which in turn, upon tosylation, yields 4-tosyl monoacetone methylrhamnopyranoside (m. p. 60–61°). To prove further that this material was identical with 4-tosyl monoacetone methylrhamnopyranoside, a sample thus obtained was detosylated and the properties of the monoacetone methylrhamnopyranoside obtained were compared with those of the known derivative of this structure.

4-Tosyl monoacetone methylrhamnopyranoside (0.8 g.) with m. p. 60–61° was dissolved in 80 cc. of 80% methyl alcohol and 12 g. of 4% Na-Hg amalgam added. The time of reaction and method of isolation was carried out exactly as described previously; yield 0.4 g.; b. p. 82–85° (0.3 mm.); $[\alpha]^{25}_D - 21.30^\circ$ (c, 3.380, methanol); $n^{25}_D 1.4539$.

Anal. Calcd. for $C_{10}H_{15}O_5$: C, 55.02; H, 8.30; OCH_3 , 14.22. Found: C, 55.03; H, 8.19; OCH_3 , 14.26.

D. Proof of Structure of 4- and 5-Tosyl Monoacetone Methylrhamnopyranosides

Inasmuch as the methylglycofuranosides are hydrolyzed

TABLE III
HYDROLYSIS OF MONOACETONE METHYL RHAMNOSIDES WITH 0.1 *N* HCl AT 100°

| Monoacetone methylrhamnoside obtained by | % Solution | Initial $[\alpha]_D^{20}$ | After 30 min. |
|---|------------|---------------------------|---------------|
| (1) Reductive hydrolysis of tosyl derivative of m. p. 82-83 ^{oa} | 3.346 | -58.0° | + 5.0° |
| (2) Reductive hydrolysis of tosyl derivative of m. p. 61-62 ^{ob} | 4.280 | - 6.0° | -35.8° |
| (3) Simultaneous methylation and acetonation of rhamnose, or "methylation" of monoacetone rhamnose ^b | 2.830 | -45.5° | - 8.4° |
| (4) Acetonation of methylrhamnopyranoside ^b | 3.236 | - 4.8° | -35.1° |

^a Final value of specific rotation calculated as free rhamnose.

^b Final values of specific rotations calculated as methylrhamnosides.

at a much greater rate than the glycopyranosides,¹⁴ the ring structure of such compounds may be determined easily. Accordingly the hydrolysis rates of the monoacetone methylrhamnosides (purified and crude) were determined in the following manner. Known weights of the monoacetone methylrhamnosides were dissolved in hydrochloric acid (0.1 or 0.03 *N*) and diluted to exactly 5 cc.

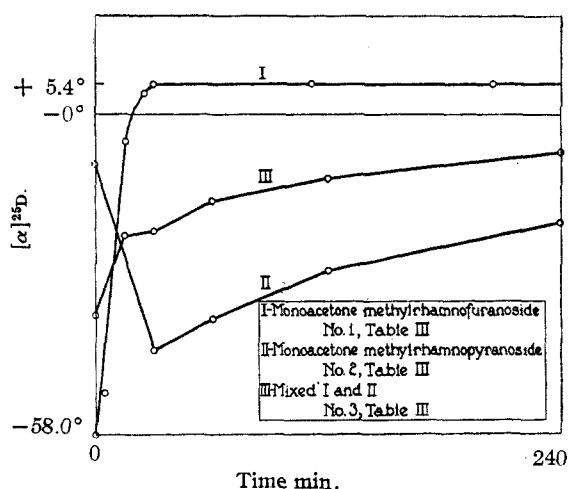


Fig. 1.—Rate of hydrolysis of monoacetone methylrhamnosides with 0.03 *N* HCl at 100°.

with hydrochloric acid (0.1 or 0.03 *N*). The specific rotation was observed immediately and the solution then heated in a sealed tube at 100° for the time specified. The tubes were now cooled and the rotation of the solution

(14) P. A. Levene and G. M. Meyer, *J. Biol. Chem.*, **78**, 363 (1928); H. G. Bott, E. L. Hirst and J. A. B. Smith, *J. Chem. Soc.*, 658 (1930).

again noted. The results obtained in this manner are given in Table III and in Fig. 1.

We wish to express our thanks and gratitude to Messrs. Geigy and Company for their generous gift of the *l*-rhamnose used in these experiments.

Summary

1. The usual methods of preparing monoacetone *l*-methylrhamnopyranoside are attended by the simultaneous formation of monoacetone *l*-methylrhamnopyranoside, at times to the extent of 30-40%.

2. Alkaline hydrolysis of pure 5-tosyl monoacetone *l*-methylrhamnopyranoside leads to the production of an unsaturated compound in 90-95% yield together with monoacetone *l*-methylrhamnopyranoside.

3. Alkaline hydrolysis of 4-tosyl monoacetone *l*-methylrhamnopyranoside yields quantitatively monoacetone methylrhamnopyranoside.

4. Tosyl monoacetone *l*-methylrhamnoside with m. p. 80° is a mixture containing, in addition to the furanoside, a small proportion of the pyranoside. Alkaline hydrolysis of this product leads to formation of the unsaturated derivative together with a small proportion of monoacetone *l*-methylrhamnopyranoside.

5. Alkaline hydrolysis of the 4- and 5-tosyl monoacetone *l*-methylrhamnosides is accomplished without Walden inversion.

NEW YORK, N. Y.

RECEIVED JULY 2, 1935