THE HYDROFORMYLATION OF 3,4-DI-O-ACETYL-D-XYLAL

by

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ABSTRACT

3,4-Di-O-acetyl-D-xylal was treated in the presence of dicobalt octacarbonyl with carbon monoxide and hydrogen at elevated temperatures and pressures. From deacetylation of the reaction products, 1-α(orβ)-hydroxymethyl-2-hydro-D-xylal and 1-α(orβ)-formyl-2-hydro-D-xylal were obtained; that is, a hydroxymethyl group and a formyl group were added respectively at carbon one of the original unsaturated sugar.

Sodium borohydride reduction in aqueous solution of 1-α(orβ)-formyl-2-hydro-D-xylal produced 1-α(orβ)-hydroxymethyl-2-hydro-D-xylal. 1-α(orβ)-Formyl-2-hydro-D-xylal gave an acetate which is described.

Periodate oxidation of the sugar alcohol gave the dialdehyde which on treatment with p-nitrophenylhydrazine hydrochloride yielded glyoxal-bis-p-nitrophenylhydrazone and 2-deoxy-D,L-tetrose p-nitrophenylhydrazone as major degradation products.

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INTRODUCTION

The hydroformylation reaction has been applied to several types of olefinic unsaturated compounds to yield homologous aldehydes or alcohols.

It has been found (1, 2) that the carbon chain of carbohydrates can be lengthened by the addition of carbon monoxide and hydrogen to unsaturated sugars (3) to yield sugar alcohols.

Branched or straight-chain aldehydes and alcohols have been produced by the addition of carbon monoxide and hydrogen to olefins (4). It is then possible that the hydroformylation of an unsaturated sugar would yield one or a mixture of new branched or straight-chain sugars or sugar alcohols. Hydrogenation of the double bond to yield a 1,2-dihydro carbohydrate is also possible.

In addition to the above method sugars having more carbon atoms than the starting compounds have been prepared by several methods (5) involving the addition of hydrocyanic acid, nitromethane, and the Grignard reagent to the appropriate sugar.

The present work describes the hydroformylation of 3,4-di-O-acetyl-D-xylal and the characterization of the reaction products.

HISTORICAL INTRODUCTION

1. Unsaturated Sugars (glycals)

(a) Synthesis

Glycals were first reported by Fischer (6) in 1914. 3,4,6-Tri-O-acetyl-D-glucal was obtained by treating 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide with zinc dust in fifty percent acetic acid.

The method of glycal synthesis has been changed little. However in 1954, Helferich and co-workers (7) shortened the procedure. They acetylated D-glucose, brominated the acetate, and converted the resulting bromo compound to the corresponding unsaturated sugar without isolating the above intermediates. The method of reduction of the crude bromo sugar was similar to that employed by Fischer. However, sodium acetate was added to neutralize the excess hydrobromic acid formed in the bromination procedure. Also, copper sulphate was added to catalyze the reaction. These modifications gave increased yields of the final product.

(b) Reactions

The reactions of the glycals have been summarized by Helferich (3). Because of their special properties, these compounds have found frequent use as intermediates in further syntheses.

Although glycals have been found to exhibit unique properties, they also have been shown to undergo many reactions characteristic of olefinic compounds.

Fischer, in 1914 (6), treated a solution of 3,4,6-tri-O-acetyl-D-glucal in glacial acetic acid with hydrogen in the

presence of a platinum catalyst. 1,2-Dihydro-3,4,6-tri-O-acetyl-D-glucal was obtained.

The action of oxidizing agents on unsaturated sugars has been studied extensively. Levene and Tipson (8) treated D-galactal with perbenzoic acid and obtained D-galactose and another compound that was probably D-talose. The two sugars were not obtained in equal amounts.

The addition of hydroxyl groups to the double bond of a glycal has been found to yield only one sugar under certain conditions. Hockett and Millman (9) treated D-galactal with hydrogen peroxide in t-butanol in the presence of a small amount of osmium tetroxide. Although they obtained D-galactose, no D-talose was found. Some cleavage of the double bond occurred, with the production of what was thought to be D-lyxonic acid.

The double bond of a glycal has been shown to migrate under fairly mild conditions. Lohaus and Widmaier (10) treated 3,4,6-tri-O-acetyl-D-galactal with boiling water. From the reaction mixture they isolated 4,6-di-O-acetyl-D-pseudogalactal (the double bond had shifted to the 2,3 position). This compound gave typical aldehyde reactions. It reduced Fehling's solution and when it was treated with ethyl orthoformate, the corresponding ethyl acetal was obtained.

Water has been found to add across the double bond of an unsaturated sugar. Isbell and Pigman (11) obtained 2-deoxy-D-galactose by treating D-galactal with water.

2. Hydroformylation (Oxo Reaction)

The reactivity of carbon monoxide was not studied until the twentieth century. Fischer and Tropsch formed small quantities of formic esters from carbon monoxide and methyl alcohol and ethyl alcohol in 1921 (12). In 1926 Fischer and Tropsch (13) announced that higher homologues of methane were formed when mixtures of hydrogen and carbon monoxide were passed at atmospheric pressure over a catalyst of iron or cobalt at elevated temperatures.

Smith, Hawk and Golden (14), in 1930, treated ethylene with carbon monoxide and hydrogen in the presence of a catalyst. They obtained hydrocarbons plus a water soluble oxygen containing oil. It was their opinion that the oxygen containing compounds were formed first in the reaction and that they were next dehydrated with subsequent polymerization.

In 1943, Roelen (15) disclosed the following reaction:

$$RCH{=}CH_2 + CO + H_2 \xrightarrow[125\text{-}200 \text{ atm.}]{90\text{-}200^\circ} RCH_2CH_2CHO$$

The catalysts contained cobalt, thorium oxide, kieselguhr, and sometimes copper. Ethylene treated according to this reaction yielded forty percent propionaldehyde, twenty percent diethyl ketone and forty percent higher boiling aldehydes and ketones.

An important series of syntheses with carbon monoxide was developed in Germany during the last war and not disclosed until after 1946. Carbon monoxide was shown to react under pressure (200 atmospheres) at elevated temperatures (200-300°) and in the presence of carbonyl catalysts (especially nickel or cobalt

carbonyls) with a variety of types of organic molecules. For example: (16)

$$CH_2=CH_2 + CO + H_2O \longrightarrow CH_3CH_2COOH$$

With a revival of carbonylation after the war several new potential fields have appeared. For example Tyson and Shaw (17) synthesised 3-indole carboxaldehyde by treating potassium indole with carbon monoxide at elevated pressures in the presence of N,N-dimethyl formamide.

Initially carbonylation and hydrofromylation reactions were catalyzed by a variety of heterogeneous catalysts, but in 1948 Adkins and Krsek (18) concluded that the best results were obtained using a homogeneous catalyst, specifically dicobalt octacarbonyl. For the reaction with an alkene they postulated the following mechanism:

$$2Co + 8CO \underset{150^\circ}{\rightleftharpoons} \left[Co(CO)_4\right]_2$$

$$\left[Co(CO)_4\right]_2 \xrightleftharpoons[125^\circ]{H_2} 2Co(CO)_3COH$$

$$4Co(C)_3COH + 4CH_2=CH_2 \xrightleftharpoons[125^\circ]{H_2} 4CH_3CH_2CHO + \left[Co(CO)_3\right]_4$$

$$\left[Co(CO)_3\right]_4 + 4CO \underset{125^\circ}{\rightleftharpoons} 2\left[Co(CO)_4\right]_2$$

In 1949, Adkins and Krsek (19) modified the hydroformylation

technique by using benzene instead of ether as the solvent. This allowed the reactions to proceed at lower temperatures and pressures. These workers subjected a number of unsaturated compounds to the hydroformylation reactions. Hexene-1 was converted to a mixture of n-heptaldehyde and 2-methyl hexaldehyde. Compounds of the type $RCH=CH_2$ (where R was $-CO_2C_2H_5$, $-CH_2O_2CCH_3$ and $-CH(O_2CCH_3)_2$) added the formyl group exclusively in the terminal position.

A further modification of the hydroformylation reaction was introduced by Pino (20) in 1951. By adding ethyl orthoformate to the reaction mixture, the aldehydes produced were subsequently converted to the corresponding ethyl acetals. In this way, secondary reactions of the carbonyl groups were inhibited.

In 1950, Wender, Levine and Orchin (21) found that crotonaldehyde, which Adkins and Krsek (19) found was converted to n-butyraldehyde at 120-125°, was converted to n-butanol at 180-185°. These workers postulated the following mechanism for the reaction:

$$2Co + 8CO \rightleftharpoons \left[Co(CO)_4\right]_2$$

$$\left[Co(CO)_4\right]_2 \rightleftharpoons 2\cdot Co(CO)_4$$

$$\cdot Co(CO)_4 + H_2 \rightleftharpoons H\cdot + Co(CO)_3COH$$

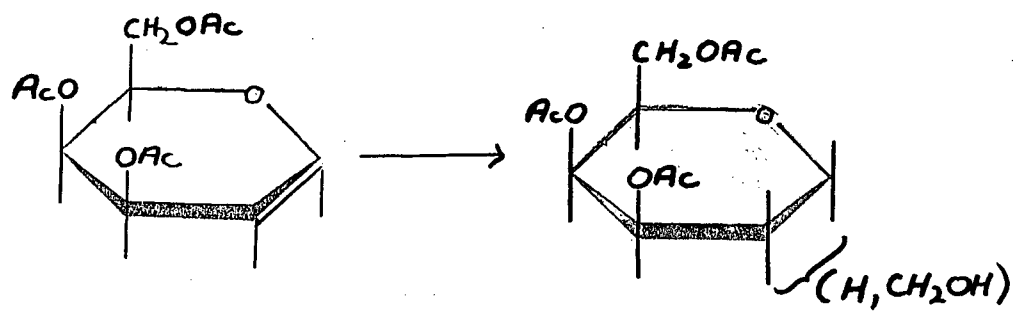
$$H\cdot + RCHO \rightleftharpoons \cdot RCHOH$$

$$RCHOH + Co(CO)_3COH \rightleftharpoons RCH_2OH + \cdot Co(CO)_4$$

This mechanism involves cobalt hydrocarbonyl, and various workers have sought evidence for the presence of this compound in the oxo reaction. Wender, Mettin, and Orchin (22) treated pinacol under hydroformylation conditions. Among the reaction products obtained was pinacolone. As the pinacol-pinacolone rearrangement is a known example of an acid catalyzed reaction, the presence of cobalt hydrocarbonyl was indicated. This compound was the only strong acid that could have been present in the reaction mixture.

Homologation of alcohols via the oxo reaction has also been found to take place. This too was thought to be catalyzed by the acid cobalt hydrocarbonyl. Wender, Levine and Orchin (23) subjected t-butyl alcohol to hydroformylation conditions at 160-180° and obtained a good yield of isoamyl alcohol. By treating methanol similarly, Wender, Friedel and Orchin (24) obtained ethanol as the major product.

In 1956 Rosenthal and Read (1) synthesized a new crystalline seven-carbon branched-chain carbohydrate by application of the oxo reaction to 3,4,6-tri-O-acetyl-D-galactal. A hydroxymethyl group was added to the unsaturated carbohydrate.



In summary, many olefinic unsaturated compounds have been found to react with carbon monoxide and hydrogen in the presence of a cobalt catalyst at elevated pressures and temperatures.

Aldehydes containing one more carbon atom than the original compound were usually produced. However in some instances they were not isolated due to hydrogenation of the carbonyl group, polymerization, and other side reactions.

Pino and Ercoli (25) were the first to do a reaction of this nature with a carbon-nitrogen double bond. In 1953 they hydroformylated pyridine with carbon monoxide and hydrogen in the presence of cobalt catalysts to give several products of which N-formyl piperidine and N-methyl piperidine were the major portions. More recently, in 1958, the synthesis of 3-phenyl, 3-methyl, and 3-benzyl-phthalimidine was achieved by application of the oxo reaction to aromatic ketoximes by Rosenthal, Astbury, and Hubscher (26).

The most recent new applications of the oxo reaction in the field of natural products involve terpenes and steroids. In 1952 LoCicero and Johnson (27) hydroformylated camphene to give an aldehyde which was structurally related to isocamphenilanaldehyde. In 1957 Bordena (28) applied the oxo reaction to α-pinene, and β-pinene and obtained a product which was seventy per cent aldehyde. In 1959 Nussbaum et al (29) hydroformylated 3β,20β-dihydroxy-Δ^5-pregnene at 195° to obtain a 6α-hydroxymethyl steroid. They concluded that the hydroformylation of complex molecules was stereospecific. Beal, Rebenstorf, and Pike (30) obtained a steroid having an added 6α-hydroxymethyl group by hydroformylation at 180°.

3. Deacetylation

For the deacetylation of sugar acetates the methods devel-

oped by Zemplén and co-workers are still widely employed although other deacetylation procedures (31) have been found.

Zemplén and Kunz (32), in 1923, first effected deacetylation of a sugar acetate with sodium alkoxide. By treating D-glucose penta-acetate with an excess of sodium ethoxide dissolved in absolute ethanol, they obtained a D-glucose-sodium ethoxide addition product. It was thought that the reaction involved transesterification, since ethyl acetate was also isolated.

Three years later, Zemplén (33) modified the reaction by using sodium methoxide in methanol. Cellobiose octa-acetate was dissolved in chloroform and a methanolic solution of excess sodium methoxide was added. The precipitated cellobiose-alkoxide addition product was decomposed with water, the alkali neutralized with acetic acid, and the product was crystallized from ethanol.

The method was improved when Zemplén and Pascu (34) found it was sufficient for sodium methoxide to be present in trace amounts to effect deacetylation. D-Mannitol hexa-acetate was dissolved in absolute methanol containing a catalytic amount of sodium methoxide. D-Mannitol was obtained in good yield.

4. p-Nitrophenylhydrazones of Sugars

In 1922 Bergmann, Schotte and Lechinsky (35) obtained 2-deoxy-D-glucose-p-nitrophenylhydrazone from 2-deoxy-D-glucose using p-nitrophenylhydrazine as reagent. Canary yellow crystals were obtained from alcohol.

In 1930 Brigl and Schinle (36) reacting 2-methyl-D-glucose with phenylhydrazine and a catalytic amount of acetic acid ob-

tained a phenylhydrazone in good yield. Heating the mixture for a further hour with more reagent produced a methoxyl free glucosazone. This observation was confirmed in 1931 by Haworth, Hirst and Teece (37). The loss of methoxyl during the transformation was confirmed by analysis.

EXPERIMENTAL

Preparation of 3,4-Di-O-acetyl-D-xylal

3,4-Di-O-acetyl-D-xylal was synthesized by a modification of the method of Helferich and co-workers (7). To a stirred solution of acetic anhydride (210 ml.), freshly distilled, and perchloric acid (80%, 2 ml.), D-xylose (50 gm.), dried, was added slowly in a thirty minute interval. During this time the temperature was kept between 50 and 60° by cooling in a water bath. The mixture was stirred an additional fifteen minutes after the addition and then left to stand overnight at room temperature in a dark place.

Red phosphorus (16 gm.) was added slowly in a ten minute interval to the stirred reaction mixture, the mixture cooled to 25-30° and then bromine (96 gm.) was added dropwise for twenty minutes while the stirred reaction was kept between 25 and 30°. After the addition of the bromine the mixture was stirred for ten minutes and then water (19 ml.) added dropwise during twenty-five minutes. After the addition of water stirring was continued for forty minutes. The phosphorus was removed by filtration and the residue washed with glacial acetic acid (25 ml.). The resulting solution of α-bromo 2,3,4-tri-O-acetyl-D-xylose was clear and dark red.

Hydrated sodium acetate (200 gm.) was dissolved in water (150 ml.) and glacial acetic acid (250 ml., 95%) added. After cooling the solution to -15° with a ice-salt mixture, zinc dust (110 gm.) and a solution of hydrated copper sulphate (11 gm. in 25 ml. of water) were added. When the blue color disappeared

from the mixture the solution of α-bromo 2,3,4-tri-O-acetyl-D-xylose was added dropwise over an interval of thirty-five minutes to the stirred solution. The mixture was maintained at -10° by adding small pieces of solid carbon dioxide to the reaction mixture, which was then stirred for a further three hours at -10°. On completion of the reaction the mixture was suction-filtered into ice-water, the funnels being kept cool with small pieces of solid carbon dioxide. The filtrate was extracted with chloroform (3 x 300 ml.). The chloroform solution was washed with six portions (600 ml. each) of ice-water, followed by washing with cold bicarbonate solution, and finally washing with ice-cold water until neutral to litmus. After drying at 0° overnight over anhydrous calcium chloride the solution was filtered and the chloroform removed under reduced pressure (water aspirator). Benzene was added and removed under reduced pressure as before. The product was a light yellow syrup; yield 22 gm.

The crude mixture was subjected to vacuum distillation. The first fraction, which distilled at 82-84° (0.25 m.m. pressure) was 3,4-di-O-acetyl-D-xylal. Yield 9.8 gm. (15%). The product was colorless oil. $[\alpha]_D^{22} = -310°$ (c,1 in chloroform). Lit. value: $[\alpha]_D^{19} = -314°$ (c,2 in chloroform). (38).

Synthesis of Dicobalt Octacarbonyl

Dicobalt octacarbonyl was prepared by the method of Wender and co-workers (39).

Cobalt (II) carbonate (30 gm.) suspended in anhydrous thiophene-free benzene (80 ml.), was placed in a glass liner con-

tained in a stainless steel bomb having a void of 278 ml. (the Super-Pressure apparatus was made by the American Instrument Co.) Hydrogen and carbon monoxide were admitted to a total pressure of 3200 p.s.i. (1:1). The mixture was heated to 160° and left at this temperature for one hour with rocking. It was then cooled to room temperature; the final pressure was 2640 p.s.i. The dark mixture was filtered and the residue washed with benzene. A red-black solution was obtained.

Hydroformylation No. 1

The procedure was based on that of Adkins (18) and Rosenthal (1).

3,4-Di-O-acetyl-D-xylal (9.8 gm.) was added to an anhydrous thiophene-free benzene solution (50 ml.) together with preformed dicobalt octacarbonyl (a solution containing 13 gm.). The combined solution was placed in the glass liner of a high pressure hydrogenator having a void of 280 ml. The bomb was flushed three times with carbon monoxide to remove traces of oxygen and then charged with carbon monoxide (1540 p.s.i.) and hydrogen (1540 p.s.i.). After the hydrogenator was rocked for three minutes the combined gas pressure was 2960 p.s.i. at 21°. The bomb was heated with rocking to 125-135° for forty-five minutes. On cooling to room temperature (21°). The observed pressure drop was 250 p.s.i. The contents of the liner were removed and the liner washed with absolute ethanol (50 ml.). The solution was heated at 75° for thirty minutes and run through a mixed absorbent column (20 cm. x 5 cm.) of sieved acid-washed alumina and celite 535 (2:1 by weight). After elution with benzene-

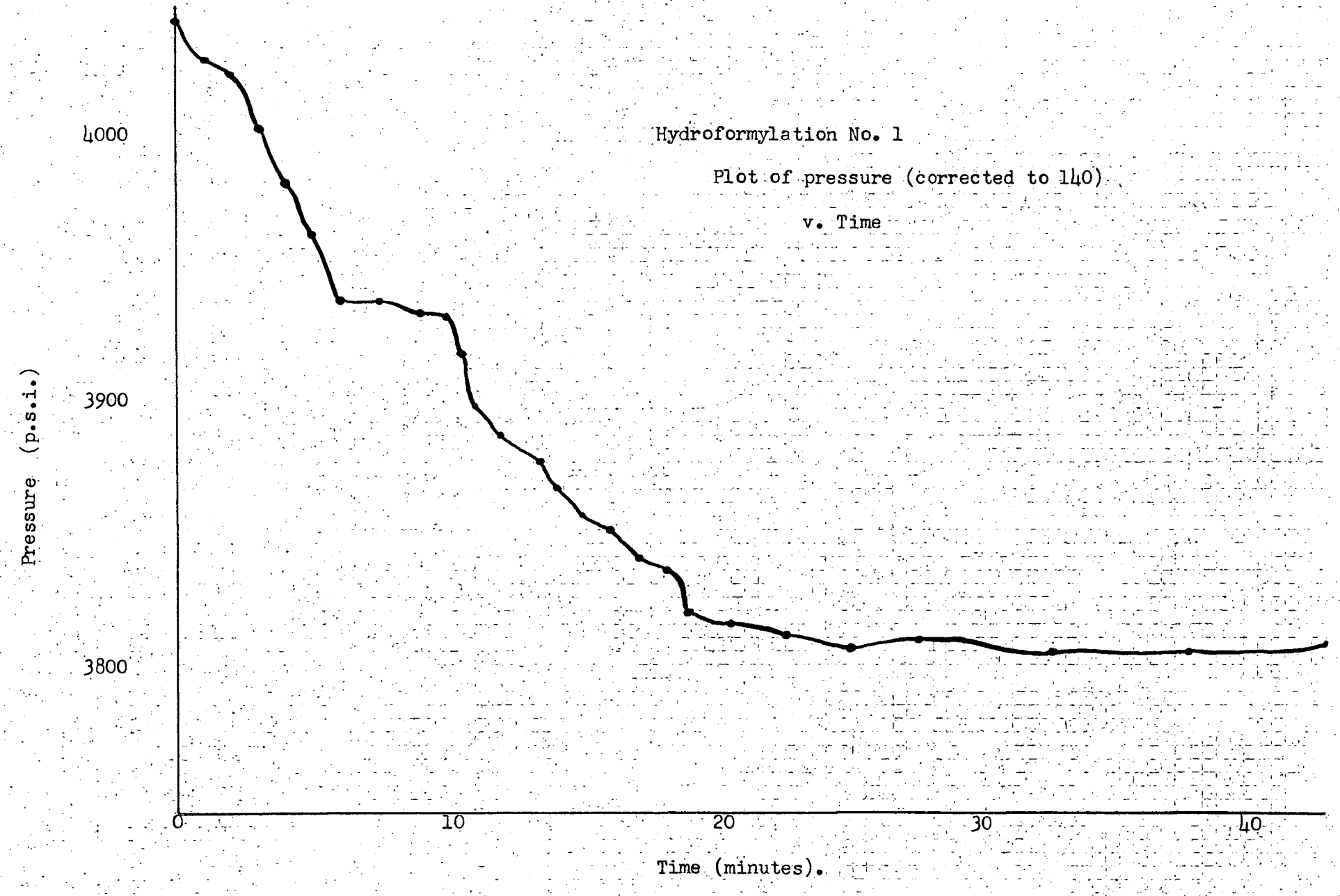
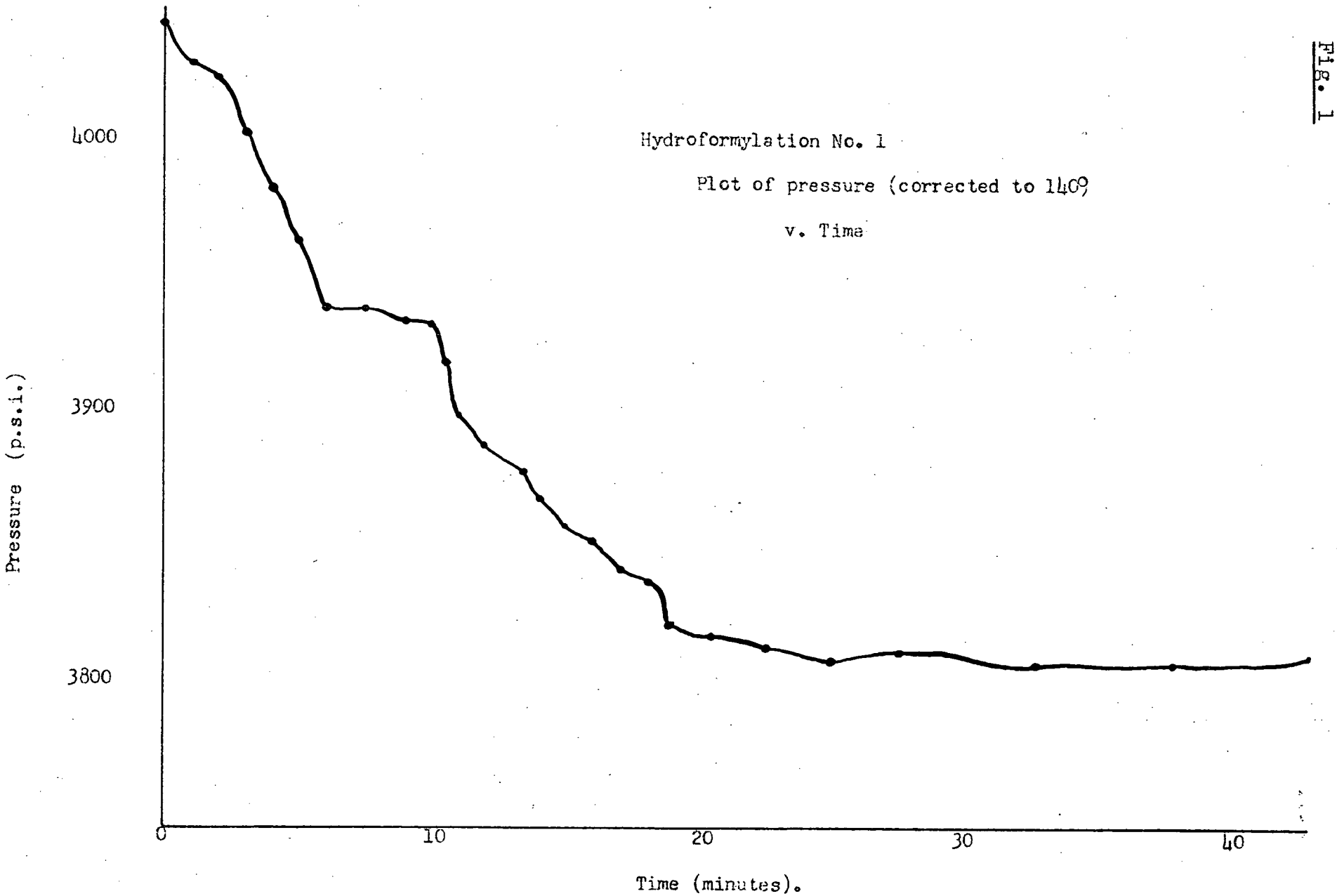

Hydroformylation No. 1
Plot of pressure (corrected to 140)
v. Time
4000
3900
3800
Pressure (p.s.i.)
0
10
20
30
40
Time (minutes).

Fig. 1

Hydroformylation No. 1

Plot of pressure (corrected to 140°) v. Time



ethanol (4:1 v/v, 600 ml.) and removal of the solvent at 35° under reduced pressure (water aspirator) a light yellow syrup remained. The syrup was dried several times by azeotroping it with small portions of anhydrous benzene. The product reduced Fehling's solution at room temperature; yield 9.4 gm. (87%).

Hydroformylation No. 2

This was similar to hydroformylation No. 1. Identical amounts of 3,4-di-O-acetyl-D-xylal and preformed dicobalt octacarbonyl were used. The initial pressure of hydrogen was 1550 p.s.i. and that of carbon monoxide 1550 p.s.i. After heating for one hour at 125° the pressure drop on cooling was 260 p.s.i. After working the product as previously, the product was a light brown sweet smelling oil; yield 8.6 gm. (82%). The product gave a positive Fehling's test on warming.

Deacetylation of Product of Hydroformylation No. 1

The method used was a modification of that developed by Zemplén and Pacsu (34).

The product (9.4 gm.), dried by repeated azeotroping with benzene, was dissolved in a 0.05N sodium methylate solution (200 ml.). The solution was stoppered to exclude moisture and left at room temperature for three hours. After addition of water to dissolve solid material the solution was passed successively through columns (22 cm. x 2 cm.) containing a cation exchange resin (Amberlite IR-120, Rohm and Haas Co., Philadelphia, Penn.) (40) and an anion exchange resin (Duolite A-4, Chemical Process Co., Redwood City, Calif.) (40). The

columns were washed with distilled water (1000 ml.) to remove the remaining material. The eluant was evaporated to a syrup under reduced pressure and the residual water removed by repeated distillation with 100% ethanol under reduced pressure; yield 2.8 gm. (60%). This brown syrup (product A) reduced Fehling's solution on warming.

Paper Chromatography of Product A

Paper chromatography, using a modification of the method described by Wolfrom and Schumacher (41) was employed to examine product A. A descending chromatogram (50 x 10 cm.) was prepared from Whatman No. 1 filter paper. The paper was spotted (0.5 mg. / spot) with a solution of product A in water and then placed in chromatographic chamber maintained at room temperature. The chromatogram was developed with n-butanol-water (saturated) (42) for fifteen hours. After drying the paper was sprayed with sodium metaperiodate-alkaline permanganate reagent developed by Lemieux and Bauer (43) and a similar paper sprayed with p-anisidine trichloroacetate solution developed by Jones et al (42). Spraying with the periodate-permanganate reagent produced three spots (R_f 0.07; R_f 0.23; R_f 0.45). Spraying with the p-anisidine reagent produced two spots (R_f 0.07; R_f 0.45).

Continuous Flow Chromatography of Product A

The method used was based on that of Flood, Hirst and Jones (44).

Whatman No. 1 cellulose (150 gm.) was used to prepare an absorbent column (400 x 30 mm.). The column was prewet with

butanol-water (600 ml., saturated) and product A (0.84 gm. dissolved in 3 ml. solvent) was added. Development was effected with butanol-water (600 ml. saturated). Fractions (4 ml. each) were collected in an automatic fractional collector. Aliquots (0.5 ml.) from each fraction were placed on filter paper and sprayed with periodate-permanganate reagent to ascertain whether or not carbohydrate was present. Fractions containing carbohydrate occurred in three distinct zones and these were combined and the solvent evaporated yielding three yellow oils.

	R_f	Yield	%Yield
Product B	0.07	0.056 gm.	8
Product C	0.23	0.387	55
Product D	0.45	0.260	37
		0.705	

% recovery from the column: 81

Optical rotaion measurements were performed on each of the products:

Product B $[\alpha]_D^{22} = +23^\circ$ (c, 3.8 in water)

Product C $[\alpha]_D^{22} = +22^\circ$ (c, 1.0 in water)

Product D $[\alpha]_D^{22} = +12^\circ$ (c, 3.7 in water)

Deacetylation of Product of Hydroformylation No. 2

The product of Hydroformylation No. 2 was immediately placed on a Florisil column (20 x 7 cm.). No solid cobalt was present in the reaction mixture. The column was developed with petroleum ether (500 ml., 30-60°) to take off a purple band which was discarded. The column was then developed with benzene-ethyl acetate (98:2, 500 ml.). The eluate was collected (P).

The column was then developed with benzene-ethanol (95:5, 500 ml.). The eluate was collected (Q). Fraction P was evaporated down to give an oil which gave a positive Fehling's test. This oil (2.5 gm.) was deacetylated using identical conditions as previously. The product (0.88 gm.) was a colourless oil (Product E). A portion (110 mg.) was run down Whatman No. 3 paper and the lower zone (located with p-anisidine spray) cut out and extracted with water to yield a white solid (J). J is discussed later.

Fraction Q was evaporated down to an oil (2.04 gm.) which did not reduce Fehling's solution. Deacetylation followed by deionization produced an oil (0.94). This was combined with product G.

Paper Chromatography of Product E

Paper chromatography using the modification of the method of Wolfrom and Schumaker (41) already described in the examination of product A was used to examine product E. The conditions were the same using a developer and butanol-water-ethanol-ammonium hydroxide (41) running for sixteen hours. After drying the paper was sprayed with sodium metaperiodate-alkaline permanganate reagent and a similar chromatogram was sprayed with p-anisidine trichloroacetate reagent.

Spraying with p-anisidine produced three spots (R_f 0.07; R_f 0.32; R_f 0.52). Spraying with periodate-permanganate reagent revealed five spots (R_f 0.07; R_f 0.28; R_f 0.32; R_f 0.38; R_f 0.52).

A chromatographic separation of product E into its components was then attempted using Whatman No. 3 filter paper as adsorbent. Four sheets of Whatman No. 3 filter paper (58 x 46 cm.) were spotted (2 mg./spot) with product E (610 mg.) and the paper run as descending chromatograms in a chromatocab using a butanol-water-ethanol-ammonium hydroxide (40:19:11:1) solvent (41). The sheets were run for twenty-three hours and then strips were cut from the sheets and sprayed with periodate-permanganate reagent. Five zones were visible (R_f 0.07; R_f 0.28; R_f 0.32; R_f 0.38; R_f 0.52). The papers were then cut up and parts bearing similar zones combined. The paper was then eluted with water. The solvent was removed and the products weighed.

	R_f	Yield	%Yield	Nature
Product X	0.07	0.036	2.9	Reducing
Product Y	0.28	0.037	2.9	Non Reducing
Product Z	0.32	0.044	3.5	Reducing
Product (G + Q)	0.38	0.923	72.	Non Reducing
Product H	0.52	0.200	18.	Reducing
		1.240		

% recovery from paper: 82%

No further work was performed on products X, Y, and Z because of lack of time.

Product G $[\alpha]_D^{22} = +22.4^\circ$ (c, 0.96 in water)

Product H $[\alpha]_D^{22} = +12.8^\circ$ (c, 1.10 in water)

Products G and C were combined and designated as I.

Products H and D were combined and designated as J.

Fraction I crystallized on standing and was recrystallized from methanol-isopropyl ether. It was a white solid; m.p. 86-87° $[\alpha]_D^{22} = +25.3^\circ$ (c, 1.2 in water). I did not reduce Fehling's solution. Anal. (45). Calc. for $C_6H_{12}O_4$; C, 48.60; H, 8.10%. Found: C, 48.16; H, 7.86%.

I.R. spectrum (~~KBr~~) of I (cm^{-1}):

3660(w), 3580(w), 3020(s), 2400(m), 1520(w), 1475(w), 1425(w), 1220 (s), 1075(w), 1045(w), 930(w), 900 (w), 850(w), 805(w), 760(m), 725(sh), 670(w).

Fraction J was a sweet-smelling syrup. This was re-chromatographed using Whatman No. 3 filter paper and identical

procedure as for the chromatography of product E. Upon extracting the paper with water and evaporating the solution to dryness a white solid was obtained. It was recrystallized from methanol-isopropyl ether; m.p. 145-147°, $[\alpha]_D^{25}$=+19.3° (c, 1.2 in water). J reduced Fehling's solution and gave a positive Schiff's test. Anal. (45). Calc. for $C_6H_{10}O_4$: C, 49.36; H, 6.85%. Found: C, 49.19; H, 6.93%.

I.R. spectrum (KBr) of J (cm^{-1}):

3440 (sh), 3320 (sh), 3220 (s), 2960 (sh), 1725 (sh), 1665 (s), 1620 (w), 1580 (s), 1495 (s), 1360 (w), 1345 (sh), 1315 (w), 1285 (s), 1250 (m), 1175 (m), 1155 (m), 1150 (sh), 1125 (sh), 1100 (m), 1075 (m), 1035 (w), 1015 (w), 975 (w), 950 (w), 900 (w), 875 (m), 820 (w), 800 (sh), 785 (s), 710 (w), 680 (m), 660 (m).

Qualitative Tests on Hydroformylation Products

Infra-red Analyses - A Perkin-Elmer Model 21 double-beam recording spectrophotometer with a sodium chloride prism was used. The solid samples were ground into a disc with potassium bromide.

Fehling's Test - Carbonyl groups were detected with Fehling's solution using the method reported by Shriner and Fuson (46).

Somogyi Analysis of Fraction J (1-α(or β)-Formyl-2-Hydro-D-Xylal).

Fraction J was subjected to a Somogyi analysis (47,48).

Fraction J (5.1 mg.) was dissolved in water (5 ml.) and added to the Somogyi reagent (5 ml.) in a large test tube. The tube was covered and left in a boiling water bath for fifteen minutes. The solution was then cooled and sulphuric acid added (5N, 1 ml.). The solution was then titrated with sodium thiosulphate (0.00538N).

Volume thiosulphate solution used = 11.75 ml.

A blank titration on the Somogyi reagent (5 ml.) was performed after heating with an equal volume of water.

Volume of thiosulphate solution used = 25.62 ml.

A standard determination using a known compound was performed. 2-Deoxy-D-glucose (1.1 mg.) was treated in the same manner as Fraction J.

Volume of thiosulphate required for titration = 22.80 ml.

Volume of thiosulphate corresponding to 1 mg of standard

$$= \frac{25.62 - 22.80}{1.1} = 2.55 \text{ ml.}$$

Wt. of Fraction J present

$$= \frac{25.62 - 11.75}{2.55} = 5.44 \text{ mg.}$$

Molecular weight of 2-deoxy-D-glucose = 164 gm.

Molecular weight of Fraction J (assuming $C_6H_{10}O_4$) = 146 gm.

$$\%\text{sugar in Fraction J} = \frac{5.44}{5.1} \times \frac{146}{164} \times 100\% = 95\%$$

Sodium Borohydride Reduction of Fraction J (Sugar)

The method was that of Wright and Hayward (49).

Fraction J had been shown previously to be reducing towards Fehling's solution. A portion of the compound (53 mg.) together with sodium borohydride (40 mg.) were dissolved in water (0.5 ml.) and allowed to stand at room temperature for twenty-four hours. To the solution 6N acetic acid (0.1 ml.) was added. The mixture was diluted with water to 10 ml. and then shaken with anion and cation exchange resins (Duolite A-4. Chem. Process Co., Redwood City, Calif. and Amberlite IR-120. Rohn and Haas Co., Philadelphia, Penn. respectively). The resins

were washed and the washings added to the deionized solution which was evaporated to a colorless oily product under reduced pressure. The oil (46 mg.) failed to solidify after treatment with ethyl acetate or isopropyl ether. The oil was non-reducing towards Fehling's solution indicating that reduction was complete. The oil was purified by allowing it to run the length of a paper chromatogram using Whatman No. 1 paper and the solvent n-butanol-water-ethanol-ammonium hydroxide (42). The product was eluted off the paper with water and the solvent evaporated. The product was a white solid. It was recrystallized from methanol-isopropyl ether; m.p. 86-87°. Using Whatman No. 1 paper and solvent n-butanol-water-ethanol-ammonium hydroxide, portions of the product and fraction I were run side by side on the same sheet of paper for forty-two hours. On spraying with sodium metaperiodate solution in water and potassium permanganate (43) spots were obtained for each at similar distances (33 cm.) from the origin.

I.R. Spectrum ($CHCl_3$) of reduction product (cm^{-1}):

3660 (w), 3580 (w), 3020 (s), 2400 (m), 1520 (w), 1475 (w), 1425 (w), 1220 (s), 1075 (w), 1045 (w), 930 (w), 900 (w), 850 (w), 805 (w), 760 (m), 725 (sh), 670 (w).

Preparation of 2-Deoxy-D-Glucose p-Nitrophenylhydrazone

2-Deoxy-D-glucose p-nitrophenylhydrazone was prepared as a model. A portion of 2-deoxy-D-glucose (46 mg.), p-nitrophenylhydrazine hydrochloride (47 mg.) and sodium acetate (105 mg.) were dissolved in water (1 ml.) and methanol (1 ml.). The solution was shaken for two minutes and left standing overnight.

A canary yellow solid was collected by filtration. Recrystallization from methanol yielded 50 mg.; m.p. 188-190°. Literature value 190-191°. (35)

I.R. Spectrum (KBr) (cm^{-1}):

3440 (m), 3340 (m), 3240 (m), 2920 (w), 1600 (s), 1550 (w), 1495 (m), 1475 (m), 1325 (s), 1280 (m), 1260 (m), 1185 (w), 1170 (w), 1110 (m), 1090 (m), 1075 (m), 1065 (m), 1045 (m), 1020 (m), 1030 (m), 995 (m), 945 (w), 880 (w), 835 (m), 815 (w), 750 (m), 695 (w).

Periodate Oxidation of Fraction I

Sodium metaperiodate solution was made roughly 1N and standardised by adding excess of a known solution (0.0101N) of arsenious oxide and back-titrating with standard iodine solution (0.0107N). The method used was that described by Vogel (50). The periodate was calculated to be 1.05N.

Fraction I (518 mg.) was dissolved in sodium periodate solution (3.68 ml., 10% excess). This solution was kept in the dark at room temperature for twenty hours. A portion of the solution (0.9 ml.) stood in a closed polarimeter tube and readings of the optical rotaion were performed periodically:

Time in Hours	$[\alpha]_D^{23}$
0	22°
0.25	16°
0.5	12°
1.0	9°
2.0	7°

3.0	7°
24.0	7°

The reaction was assumed to be complete after twenty hours and an aliquot from the final solution was withdrawn and titrated with iodine solution after first adding an excess of arsenious oxide solution. For the last operation 2 ml. of the solution were withdrawn and diluted with water (2 ml.). Of the resulting solution a portion (1 ml.) was pipetted into an excess (40 ml.) of arsenious oxide solution (0.0101N). Sodium bicarbonate (4 gm.) was added and the mixture left to stand for fifteen minutes. On back-titrating with iodine solution (0.0107N) using starch indicator 32.74 ml. of iodine were required.

m. equivs. periodate solution present

$$= \left[(40 \times 0.0101) - (32.74 \times 0.0107)\right] \times 8$$

$$= 0.055 \times 8 = 0.440$$

m. equivs. periodate present originally

$$= 3.68 \times 1.05 = 3.86$$

m. equivs. periodate consumed

$$= 3.86 - 0.440 = 3.42$$

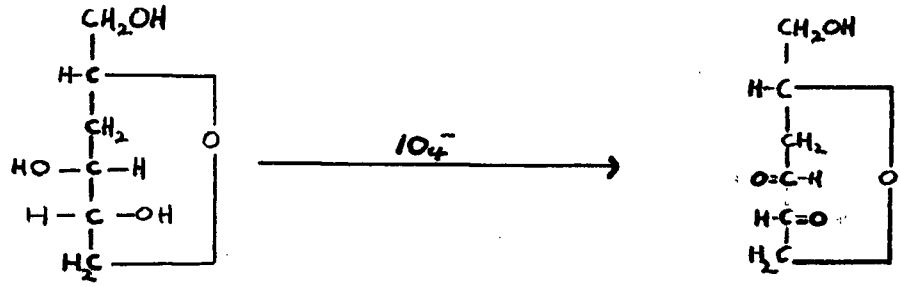
m. equivs. of fraction I used = 3.5

Number of moles of periodate consumed per mole of compound

$$= \frac{3.42}{3.5} = 0.98$$

The product was neutralized with barium chloride (1 gm.) in water (5 ml.). A white precipitate was produced which was filtered off and washed. Saturated sodium bicarbonate solution (20 ml.) was added to the filtrate. A white precipitate formed

which was filtered off and washed and the filtrate evaporated to dryness. The residue was extracted with three portions (40 ml. each) of methanol to remove organic materials. The extracts were evaporated to a solid, white, water soluble residue (0.508 gm.) which gave a rapidly positive Fehling's test. This residue was assumed to be the dialdehyde (II).



p-Nitrophenylhydrazone Derivative of Oxidation Product (II)

The oxidation product (0.508 gm.), sodium acetate (1.2 gm.) and p-nitrophenylhydrazine hydrochloride (1.1 gm.) were dissolved in methanol (10 ml.) and water (3 ml.) and heated to 60° on a water bath for fifteen minutes, shaken for thirty minutes and then left to stand overnight at room temperature. The product consisted of a yellow-red solid (III) (0.73 gm.) and a red solution (IV). The solution was evaporated to dryness yielding a red-brown solid (1.1 gm.). This solid was hardly soluble in benzene but an appreciable amount dissolved in chloroform to yield a yellow solution (V). The residual, chloroform insoluble, solid was partially soluble in ethanol yielding a red-brown solution which on evaporation gave a brown oil (VIII) (0.074 gm.). The ethanol and chloroform insoluble portion (VII) (0.322 gm.) was a colorless crystalline solid

which showed characteristic inorganic properties in refusing to melt or burn with an organic flame or give a Molisch test. In addition an aqueous solution of VII produced a white precipitate with silver nitrate solution. VII was thought to be sodium chloride.

Chromatography of Fraction V on Florisil

Fraction V (0.67 gm.) was dissolved in N,N-dimethylformamide (0.6 ml.) and added to the top of a florisil column (2 x 15 cm.). Development with benzene: alcohol (99:1, 100 ml.) produced two orange-coloured zones. Further solvent (30 ml.) removed the lower band XI. The column was then allowed to dry and then extruded and the top part (IX) of the extended visible upper zone and the rest of the upper zone (X) cut out and extracted with ethanol. Upon evaporation of the solution containing the three zones to dryness three solids remained.

	m.p.	yield
IX (top zone)	128-133°	0.054 gm.
X (middle zone)	110-140°	0.585
XI (lower zone)	143-150°	0.024

Zone IX was recrystallized from ethanol-water; m.p. 133-135°.

I.R. Spectrum (KBr) of IX (cm^{-1}):

3450 (sh), 3260 (w), 2900 (w), 1645 (m), 1595 (s), 1525 (sh), 1510 (sh), 1500 (m), 1490 (sh), 1325 (s), 1305 (sh), 1265 (m), 1175 (w), 1110 (m), 1000 (w), 845 (w), 840 (m), 750 (w), 692 (w).

This was identical with that of an authentic sample of 2-deoxy-D-tetrose p-nitrophenylhydrazone.

Zone X (0.58 gm.) was dissolved in N,N-dimethylformamide (0.5 ml.) and applied to the top of a florisil column (2 x 14 cm.). Development with benzene-ethanol (98:2, 100 ml.) separated two zones (0 cm. and 5 cm. from the top of the column). The column was allowed to dry and then extruded. The two zones were cut out and extracted with ethanol. On evaporation of the solvents two solids (XV and XVI) remained.

	m.p.	yield
XV (top zone)	128-133°	0.530 gm.
XVI (bottom zone)	141-149°	0.038

XV was recrystallized from ethanol-water; m.p. 133-135°. I.R. spectrum (KBr) of XV was identical with that of IX and with that of an authentic sample of 2-deoxy-D-tetrose p-nitrophenylhydrazone.

For XV and IX $[\alpha]_D^{26} = 0°$ (C,1.08 in ethanol).

Chromatography of Fraction III on Florisil

Fraction III (o.73 gm.) was dissolved in N,N-dimethylformamide (o.8 ml.) and applied to the top of a florisil column (2 x 16 cm.). Development with benzene (80 ml.) eluted rapidly a red-black band (XIV) which was collected and treated with petroleum ether (30-60°, 20 ml.) to precipitate a scarlet red solid; m.p. 333-335°, yield 0.195 gm.

I.R. spectrum (KBr) of XIV (cm^{-1}):

3760 (w), 3460 (w), 3270 (m), 3100 (sh), 1655 (sh), 1600 (db,s),

1565 (s), 1532 (m), 1505 (sh), 1500 (s), 1480 (s), 1315 (db,s), 1290 (db,s), 1275 (db,s), 1175 (m), 1140 (m), 1105 (s), 1000 (sh), 998 (w), 920 (w), 885 (w), 840 (w), 835 (s), 752 (s), 700 (sh), 692 (w).

This was identical with that of an authentic sample of glyoxal bis-p-nitrophenylhydrazone. Mixed m.p. of XIV with an authentic sample of glyoxal bis-p-nitrophenylhydrazone was undepressed.

After elution of XIV a band remained at the top of the column (XII) and an orange coloured zone (XIII) persisted throughout the length of the column. The column was allowed to dry and then extruded. Zone XII was cut off and eluted with N,N-dimethylformamide and ethanol. Evaporation of the solvent yielded a yellow solid; m.p. $>350^{\circ}$, yield 0.084 gm. Zone XIII was extracted with N,N-dimethylformamide and ethanol, the solvent evaporated to yield a red-orange solid (0.49 gm.) which was dissolved in N,N-dimethylformamide (0.4 ml.) and added to the top of a florisil column (2 x 17 cm.). Benzene (100 ml.) eluted a red-black band (XVIII) which was collected and treated with petroleum ether ($30-60^{\circ}$, 20 ml.) to precipitate a scarlet solid; m.p. $333-335^{\circ}$, yield 0.418 gm. Mixed m.p. with an authentic sample of glyoxal bis-p-nitrophenyl hydrazone was undepressed. The I.R. spectrum (KBr) of XVIII was identical with that of an authentic sample of glyoxal bis-p-nitrophenyl-hydrazone.

After elution of band XVIII a band XVII remained at the top of the column. Extrusion of the column, elution with ethanol, and evaporation of the solvent yielded a yellow solid: m.p. $>350^{\circ}$, yield 0.029 gm.

Preparation of Glyoxal Bis-p-Nitrophenylhydrazone

Glyoxal (100 mg.), sodium acetate (450 mg.), and p-nitrophenylhydrazine hydrochloride (510 mg.) were dissolved in methanol (5 ml.) and water (2 ml.). A red precipitate formed immediately and was filtered off and washed with water. The solid was recrystallized from N,N-dimethylformamide-petroleum ether (30-60°); m.p. 333-335°, yield 0.42 gm. (68%).

I.R. Spectrum (KBr) (cm^{-1}):

3760 (w), 3460 (w), 3270 (m), 3100 (sh), 1655 (sh), 1600 (db,s), 1565 (s), 1532 (m), 1505 (sh), 1500 (s), 1480 (s), 1315 (db,s), 1290 (db,s), 1275 (db,s), 1175 (m), 1140 (m), 1105 (s), 1000 (sh), 998 (w), 920 (w), 885 (w), 840 (m), 835 (s), 752 (s), 700 (sh), 692 (w).

Summary of Treatment of Oxidation Product

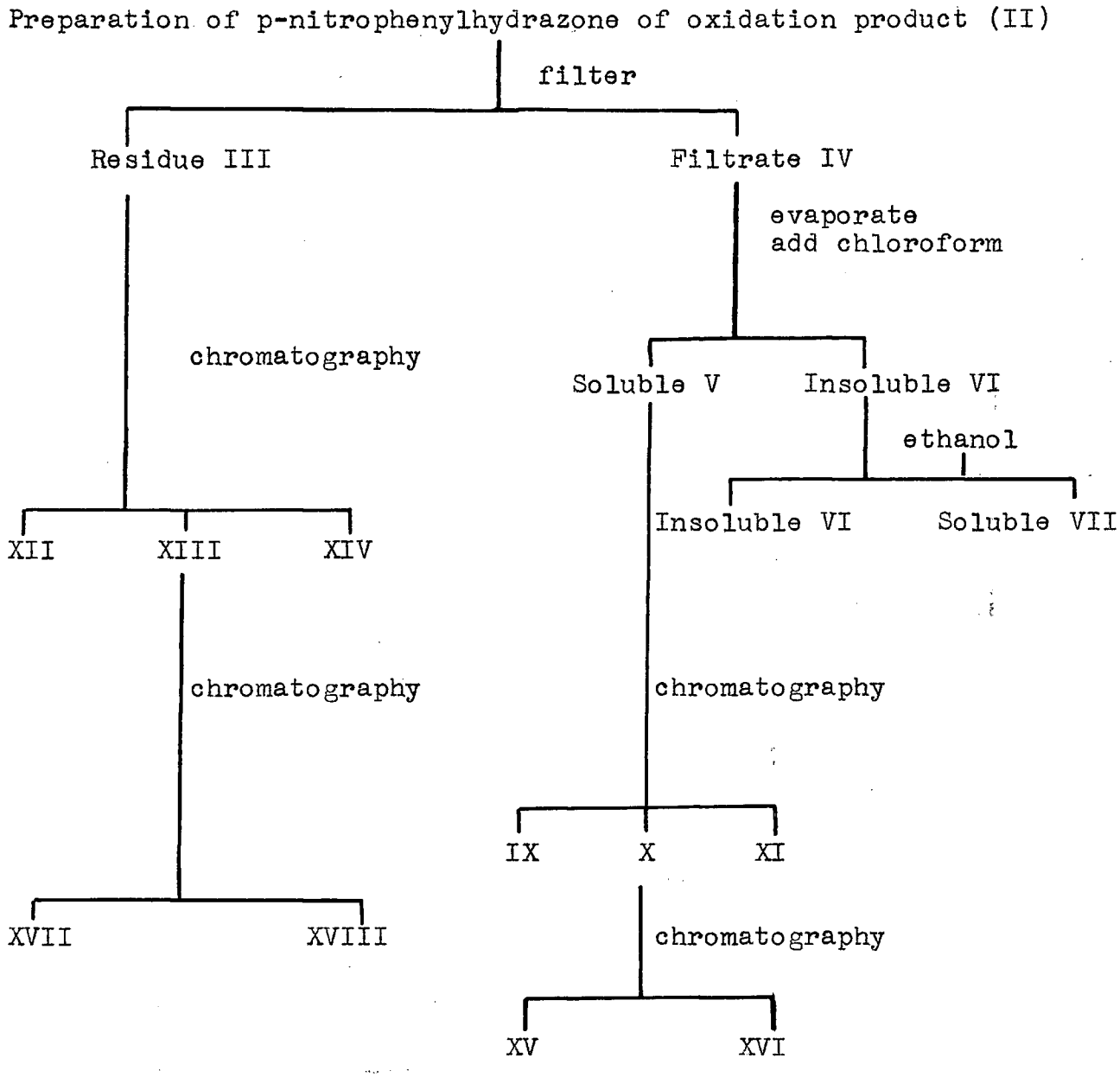


Table II

Summary of Products Obtained From Chromatography of Oxidation Products

Product	Colour	m.p.	Weight (gm)	Identity
VII	yellow-white	>350°	0.322	Inorganic
VIII	yellow	-	0.074	-
IX	red	133-135°	0.054	2-Deoxy-D,L-tetrose p-nitrophenylhydrazone
XI	yellow	143-150°	0.024	-
XV	red	133-135°	0.530	2-Deoxy-D,L-tetrose p-nitrophenylhydrazone
XVI	yellow	141-149°	0.038	-
XII	brown	>350°	0.084	-
XIV	scarlet	333-335°	0.195	Glyoxal bis-p-nitrophenylhydrazone
XVII	yellow	>350°	0.029	-
XVIII	scarlet	333-335°	0.418	Glyoxal bis-p-nitrophenylhydrazone
			1.734	

Theoretical total recovery = 1.93 gm.

Weight of 2-deoxy-D,L-tetrose p-nitrophenylhydrazone = 0.58 gm.

Theoretical yield = 0.83 gm.

% Yield = 70%

Weight of glyoxal bis-p-nitrophenylhydrazone = 0.61 gm.

Theoretical yield = 1.10 gm.

% Yield = 54%

Preparation of Derivatives

1. Acetylation of Fraction J (1-α(or β)-Formyl-2-Hydro-D-Xylal)

The method employed was essentially that described by Vogel (51).

Fraction J (48 mg.) was slowly added to a warm (50°) solution of acetic anhydride (0.3 ml.) and anhydrous zinc chloride (0.1 gm.). The mixture was warmed (50°) for a further one hour on a water bath. On pouring into ice-water (25 ml.) an oil separated. The oil was separated from the rest of the solution using a separatory funnel. The oil was dried by repeated azeotroping with small quantities of benzene. The oil (40 mg.) was dissolved in benzene-petroleum ether (1 ml., 1:2) and placed on the top of a florisil column (12 x 3 cm.) and the column developed with benzene-petroleum ether (45 ml., 1:2). Small fractions (5 ml.) were collected. A small amount (8 mg.) of oil was present after evaporation of the eluant. No further product was eluted with benzene-petroleum ether (60 ml., 1:1). Using benzene-ethanol (70 ml., 99:1) as developer, a solid white product (28 mg.) was obtained on evaporation of the eluant. This was recrystallized from methanol-isopropyl ether; m.p. 55-57°, $[\alpha]_D^{26}$ +13.2° (c,1.3 in water).

Anal. Calc. for $C_{10}H_{14}O_6$; C, 52.19; H, 6.08%.

Found: C, 51.63; H, 5.79%.

2. Benzoylation of Fraction I (1- α(or β)-Hydroxymethyl-2-Hydro-D-Xylal

The compound was benzoylated by a modification of the method of Smith and Van Cleve (52).

A portion of the compound (46 mg.) was dissolved in anhy-

dous pyridine (2 ml.) in a ground glass flask, and benzoyl chloride (0.4 ml.) added to the solution with a micro-pipette. The flask was fitted with a ground glass inverted drying tube, left in a water bath (90-100°) for forty minutes, and then cooled to room temperature. Cooling brought about the formation of crystals (probably a benzoyl choride-pyridine complex). When the mixture was poured into a saturated sodium bicarbonate solution (15 ml.) oily droplets formed. After it was shaken for several minutes, the mixture was extracted twice with portions (20 ml. each) of chloroform. The combined chloroform extracts were washed with water (50 ml.) and with three separate portions of ice-cold hydrochloric acid (3N, 30 ml. each), followed by four separate washes with water (40 ml. each). The solution was then neutral to litmus and was dried overnight over calcium chloride. After filtration, the solution was concentrated (water aspirator) at room temperature to a syrup. Removal of the last traces of pyridine was affected by drying the product over phosphorous pentoxide at reduced pressure at the boiling point of acetone for one day. The oily product (37 mg.) was dissolved in benzene-petroleum ether (0.5 ml., 1:1) and added to the top of a florisil column (10 x 1 cm.). Development with benzene-petroleum ether (40 ml., 1:1) failed to remove any solid. After unsuccessful development with benzene-petroleum ether (50 ml., 2:1), benzene (50 ml.) and benzene-ethanol (30 ml., 0.5%) the column was developed with benzene-ethanol (80 ml., 1%). After evaporating the solvent a white solid (26 mg.) was left. This was recrystallized from ethanol-water; m.p. 159-161°, $[\alpha]_D^{20}$ +21° c, 1.8 in chloroform). Anal. Calc. for $C_{27}H_{24}O_7$(three benzoyl

groups): C, 70.41; H, 5.25%.

Calc. for $C_{20}H_{20}O_6$(two benzoyl groups): C, 67.51; H, 5.62%.

Found: C, 68.55; H, 5.50%.

3. Attempted Preparation of 2,5-Dichlorophenylhydrazone of Fraction J (1-α(orβ)-Formyl-2-Hydro-D-Xylal)

Fraction J (72 mg.) was dissolved in water (1 ml.) and added to a solution of 2,5-dichlorophenylhydrazine (291 mg.) in ethanol (2 ml.). Acetic acid (8N, 2 ml.) was added together with sodium acetate (sufficient to give pH of about 4). The solution was heated at 100° for an hour and then left for two days. A solid residue appeared. This was filtered off; yield 64 mg. This was recrystallized from ethanol/water; m.p. 156-159°. Anal. Calc. for $C_{12}H_{14}Cl_2N_2O_3$: C, 47.20; H, 4.6; N, 9.2%

Found: C, 43.91; H, 3.68; N, 10.96%

The filtrate was evaporated down to a solid residue (61 mg.) which was dissolved in benzene (1 ml.) and applied to the top of a florisil column (10 x 1 cm.). Elution with benzene-alcohol (99:1, 60 ml.) and evaporation of the solvent produced a light yellow solid (36 mg.). This was treated with Norite and recrystallized from ethanol-water; m.p. 158-160°.

Anal. Calc. for $C_{12}H_{14}Cl_2N_2O_3$: C, 47.20; H, 4.6; N, 9.2%

Found: C, 43.86; H, 3.85%

Calc. for N. acetyl derivative of 2,5-Dichlorophenylhydrazine

($C_8H_9Cl_2N_2O$): C, 43.30; H, 3.50

DISCUSSION

3,4-Di-O-acetyl-D-xylal, synthesized by a modification of the method of Helferich (7) was obtained in 15% yield. The compound was found to be stable over a period of a few days after distilling if kept at -10°. Prolonged standing even at this temperature caused deterioration and standing for short periods in daylight at room temperature was found to be disasterous. It is recommended that the xylal be used soon after preparation.

The catalyst for the reaction, dicobalt octacarbonyl, was preformed by the action of carbon monoxide and hydrogen on cobalt (II) carbonate at elevated temperatures and pressures. Dicobalt octacarbonyl was found to be stable if kept in a stoppered flask at -10°. It is extremely toxic and unpleasant to work with and precautions were taken to use a well ventillated fume hood when working with it.

It has been shown that glycals react with water under certain conditions to form 2-deoxy sugars (11) or pseudoglycals (10). It was noted (54) that the amount of moisture present in the carbon monoxide used was very small so that only negligible amounts of these compounds could have been produced in the reaction.

The hydroformylations were carried out under the same conditions using a benzene solvent and equal concentrations of carbon monoxide and hydrogen. It was found that on an average between two and three moles of synthesis gas was consumed per mole of gas. Theoretically when an aldehyde is formed from the

glycal two moles of gas are absorbed per mole of glycal. When an alcohol is formed then the theoretical consumption is three moles of gas. That between two and three moles of gases are consumed is an indication that a mixture of aldehyde and alcohol is present in the product. One explanation is that an aldehyde is the primary product which becomes hydrogenated to the corresponding alcohol. Hydrogenation under the reaction conditions is apparently only partial as a sizeable fraction of the product was aldehyde. Assuming the truth of the postulate that the primary aldehyde product is reduced subsequently to the alcohol is left with the conclusion that the aldehyde is the precursor of the alcohol. This was proved and is discussed later.

It is notable that the products obtained by Nussbaum et al (29) and Beal (30) were sugar alcohols and the product obtained by Rosenthal (2) was mainly sugar alcohol. However the Nussbaum and Beal workers hydroformylated at 180-190° - a temperature at least 40° above that of the present work. Rosenthal in obtaining a quantity of aldehyde worked at about the same temperature (120°) as the present work but allowed the reaction to go for a considerable length of time (five hours) as opposed to the present one hour. Since the aldehyde has been obtained in about the same yield as the sugar alcohol it is reasonable to suppose that moderating the conditions still further would allow mainly aldehyde to be isolated.

The hydroformylation products after deacetylation were fractionated into three components (fractions B, C, D) using a butanol-water (saturated) developer. Fractions B and D were

sugars and C was a sugar alcohol. Using a butanol-water-ethanol-ammonium hydroxide developer five components (X, Y, Z, G and H) were isolated. Fractions X, Z and H were sugars while fractions Y and G were sugar alcohols. All the fractions were water-soluble. Fractions C, D, G and H were the major products. Fractions C and G were identical as were fractions D and H. Fractions X, Y and Z were not characterized as they were minor components and also because of lack of time.

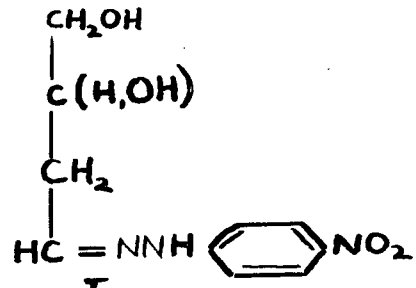
Fraction C was eventually crystallized. Carbon and hydrogen analyses corresponded to those of a compound having an empirical formula $C_6H_{12}O_4$.

Fraction D when crystalline gave carbon and hydrogen analyses corresponding to a compound having an empirical formula $C_6H_{10}O_4$.

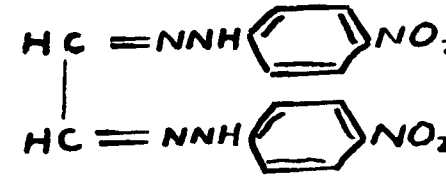
A reduction of fraction C with sodium borohydride gave a compound having identical R_f value, melting point, and infrared spectrum to that of fraction D. It has been shown (49, 55) that sodium borohydride in aqueous solution will reduce an aldehydo group to a hydroxy methyl group. Fractions C and D are thus related. Fraction D is the precursor of fraction C and by hydrogenation is converted into fraction C during the course of the hydroformylation.

Periodate oxidation of fraction C was carried out. Periodate oxidation is known to cleave adjacent hydroxyl groups (56). It was shown by titration data that approximately one mole of periodate was consumed per mole of carbohydrate (based on a formula $C_6H_{12}O_4$). Therefore fraction C contained one pair of adjacent hydroxyl groups. That cleavage had in fact taken

place was shown by the fact that the product gave a positive Fehling's test, indicating the presence of the dialdehyde. Reaction of the oxidation product to form the p-nitrophenylhydrazone derivative produced as the major components 2-deoxy-D,L-tetrose p-nitrophenylhydrazone (I) and glyoxal bis-p-nitrophenylhydrazone (II)

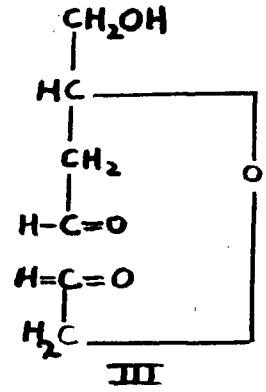


I



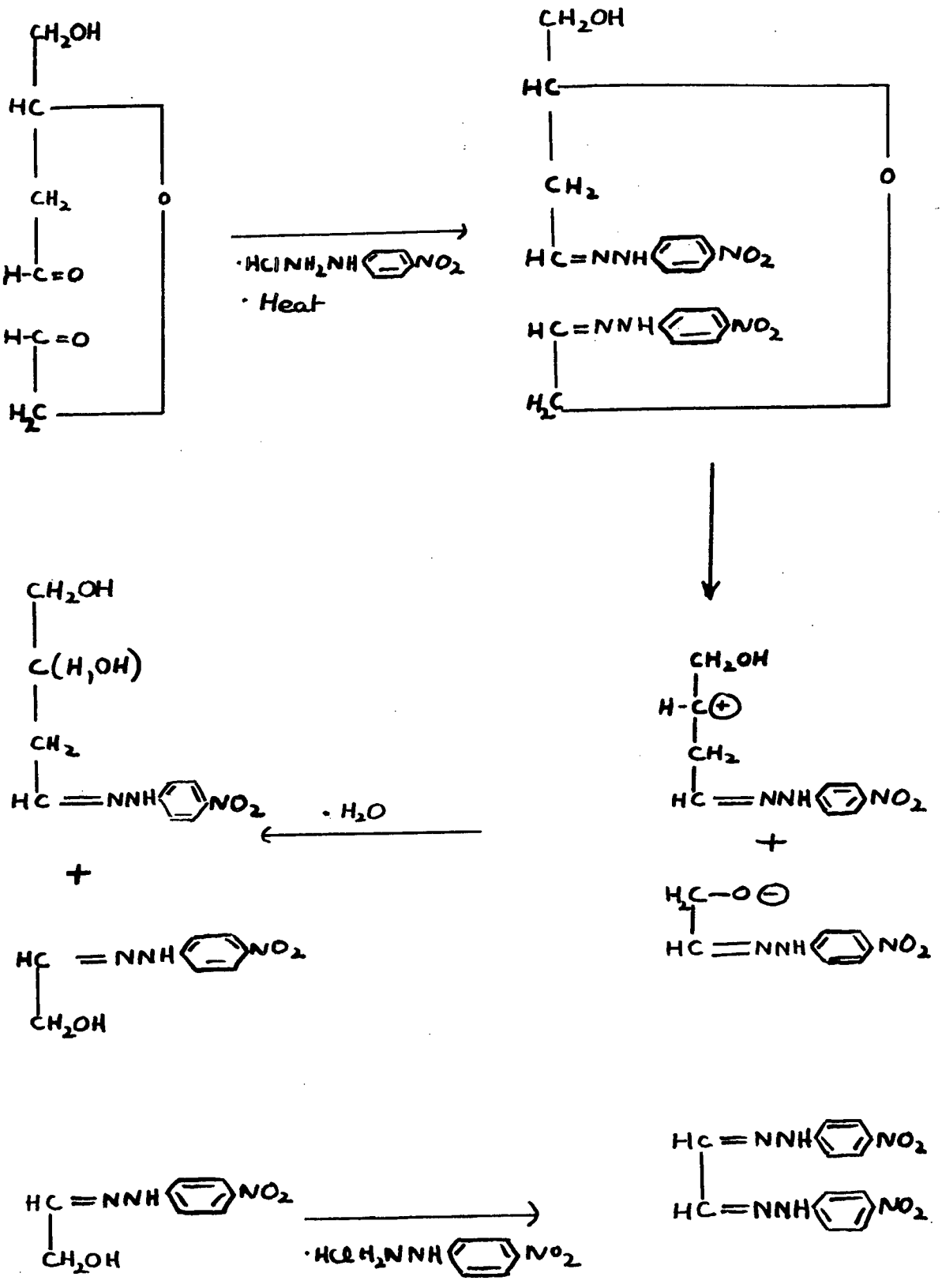
II

These products could be produced from the dialdehyde (III) by cleavage of the ether linkage between C_1 and C_5.



III

The fact that the 2-deoxy-D-tetrose p-nitrophenylhydrazone formed in the reaction was found to be optically inactive to sodium D light is significant. This would indicate that the C_1 is racemized in the course of the cleavage so that the ether link was severed between C_1 and the ether oxygen atom rather than between C_5 and the ether oxygen. A plausible mechanism would be:

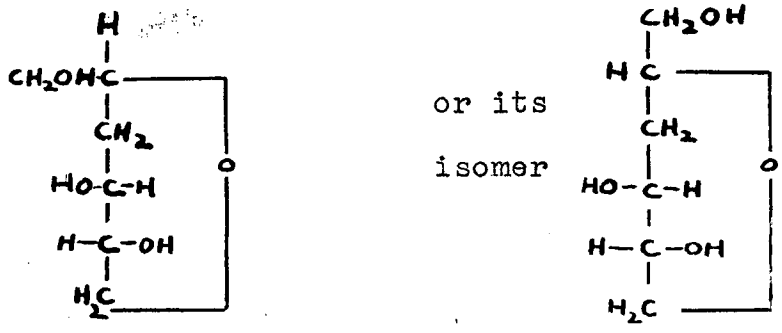

CH2OH
HC
CH2
O
H-C=O
H-C=O
H2C
·HClNH2NH
NO2
· Heat
CH2OH
HC
CH2
O
HC=NNH
NO2
HC=NNH
NO2
H2C
CH2OH
C(H,OH)
CH2
HC=NNH
NO2
· H2O
+
HC=NNH
NO2
CH2OH
CH2OH
H-C⊕
CH2
HC=NNH
NO2
+
H2C-O⊖
HC=NNH
NO2
HC=NNH
NO2
CH2OH
·HClH2NNH
NO2
HC=NNH
NO2
HC=NNH
NO2

A planar form of the carbonium ion intermediate would allow racemization.

The structure of compound C must fit the conclusions previously drawn. That is:

1. No carbonyl group is present.
2. The compound had one pair of adjacent hydroxyl groups.
3. It had an empirical formula $C_6H_{12}O_4$.
4. It was formed by sodium borohydride reduction of a carbonyl compound having an empirical formula $C_6H_{10}O_4$.
5. Periodate oxidation of the compound followed by treatment with p-nitrophenylhydrazine reagent produced as major components 2-deoxy-D,L-tetrose p-nitrophenylhydrazone and glyoxal bis-p-nitrophenylhydrazone.

A compound fitting all these facts is



This indicates that in the course of the hydroformylation of 3,4-di-O-acetyl-D-xylal a hydroxy methyl group was added at C_1.

On the evidence of the sodium borohydride reduction it is evident that the other major component of the hydroformylation was the compound (VI) having a formyl group added at C_1.

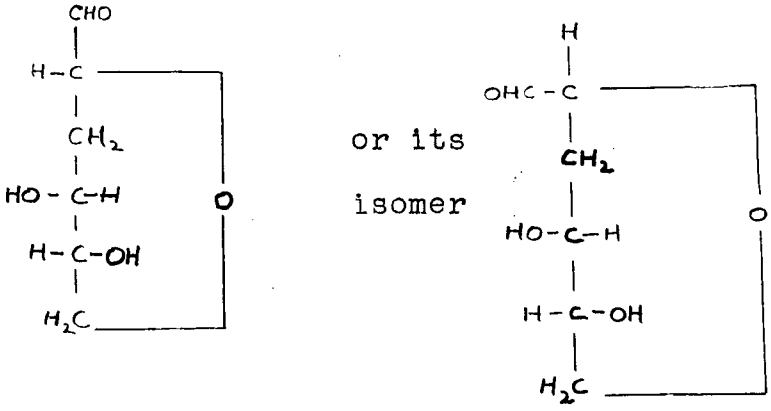
Any formulation of compound D (VI) must fit the following conclusions:

1. A carbonyl group is present.
2. The compound has an empirical formula $C_6H_{10}O_4$.

3. It is reduced by sodium borohydride in aqueous solution to compound C.

4. On acetylation a compound having empirical formula $C_{10}H_{14}O_6$ is produced.

A compound fitting all these facts is



In conclusion, a new six carbon polyol, 1-α (or β)-hydroxymethyl-2-hydro-D-xylal, has been prepared by the hydroformylation of 3,4-di-O-acetyl-D-xylal. A new six carbon sugar, 1-α (or β)-formyl-2-hydro-D-xylal, was also formed and must have been hydrogenated to the corresponding alcohol in the reaction mixture.

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