"PENTAERYTHRITOL DERIVATIVES -

REDUCTION WITH LITHIUM ALUMINUM HYDRIDE"

BY

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ACKNOWLEDGMENT

ABSTRACT

7-phenyl-2:6:8-trioxaspiro $(3:5)$ nonane (presumably a new compound) was prepared in 65 - 75% yield by the action of potassium hydroxide on monobenzal pentaerythrityl monobromide.

Attempts to prepare dipentaerythritol from the above compound and the alkoxide of monobenzal pentaerythritol, or monobenzal pentaerythritol in the presence of an acid catalyst proved to be unsuccessful.

The trimethylene oxide ring of 7-phenyl-2:6:8-trioxaspiro $(3:5)$ nonane was readily attacked by lithium aluminum hydride to give 5-methyl-5-hydroxymethyl-2-phenyl-1,3-dioxan in almost quantitative yield.

An independent synthesis of 5-methyl-5-hydroxymethyl-2-phenyl-1,3-dioxan has been carried out from benzaldehyde and trimethylol ethane in the presence of an acid catalyst.
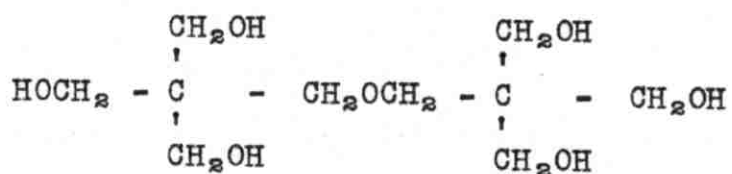
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INTRODUCTION

Dipentaerythritol is a compound used excessively in the manufacture of alkyd resins and rosin esters. The compound has been described in the literature as a white, odorless, crystalline solid which is non-hygros-copic, stable in air and practically non-volatile[1].

No direct preparation of this compound has been reported, and its only source of production is a by-product formed in the preparation of pentaerythritol from the reaction of formaldehyde and acetaldehyde under alkaline conditions.

The object of this research was to study the feasibility of a direct synthesis of dipentaerythritol from monobenzalpentaerythritol and 7-phenyl-2:6:8-trioxaspiro (3:5) nonane.

Dipentaerythritol, an ether having the formula

$$HOCH_2 - \underset{\underset{CH_2OH}{|}}{\overset{\overset{CH_2OH}{|}}{C}} - CH_2OCH_2 - \underset{\underset{CH_2OH}{|}}{\overset{\overset{CH_2OH}{|}}{C}} - CH_2OH$$

is derived from 2 molecules of pentaerythritol by elimination of 1 molecule of water.
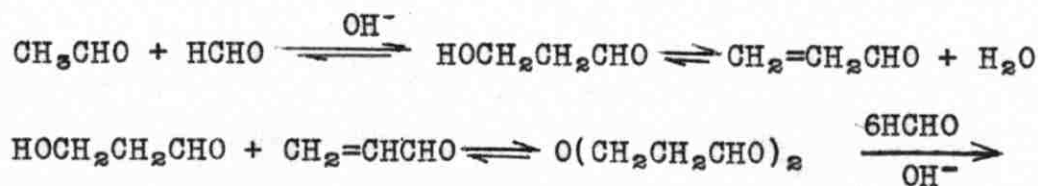
There is no record of its synthesis from pentaerythritol and it is generally obtained as a by-product of the preparation of pentaerythritol from formaldehyde and acetaldehyde in an alkaline medium. It is present in varying amounts in technical pentaerythritol, usually of the order of 5 to 15 percent, and the total commercial product available is about 1 - 2 percent of the total pentaerythritol production.

The separation of dipentaerythritol from large quantities of pentaerythritol by crystallization from water is difficult due to the formation of a double compound $(CH_2OH)_3CCH_2OCH_2C(CH_2OH)_3 \cdot 4C(CH_2OH)_4$, m.p. 185-190°C. This double compound can be recovered unchanged by recrystallizing from hot water[2]. Friederich and Brün, were the first to separate dipentaerythritol by nitrating technical pentaerythritol and using the differing solubilities in acetone to separate dipentaerythritol hexanitrate from pentaerythritol
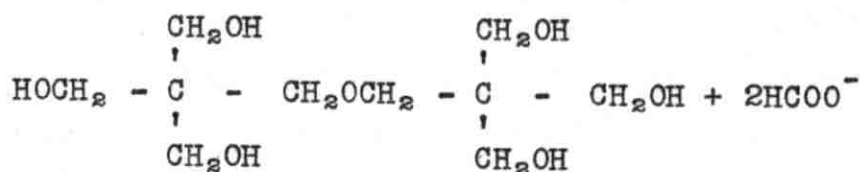
tetranitrate. Hydrolysis of the hexanitrate under reducing conditions, followed by recrystallization from water, gave pure dipentaerythritol in poor yield[3].

The yield of dipentaerythritol was substantially increased when pentaerythritol was used as a reactant in the Tollen's condensation. Twenty six to thirty three percent of polypentaerythritols, (mainly dipentaerythritol), were obtained by carrying the condensation in 45 percent formaldehyde and enough potassium hydroxide to give the solution 3.0 to 5.8 percent alkalinity. Bried reported that the higher the concentration of formaldehyde and acetaldehyde used in the preparation of pentaerythritol, the higher is the percentage of dipentaerythritol formed. Both Bried, and Friederich and Brün reported that a 3:1 molar ratio of formaldehyde and acetaldehyde gives the best yield of dipentaerythritol in a pentaerythritol process[4].

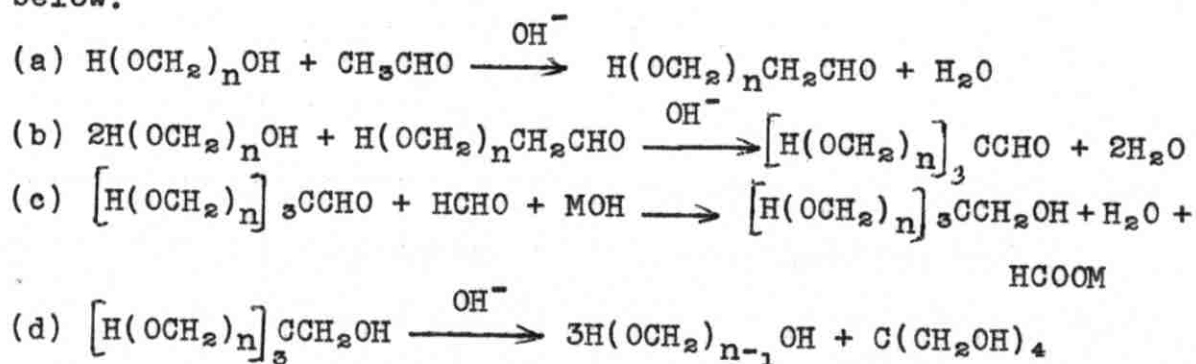A general mechanism for the formation of dipentaerythritol by the condensation of formaldehyde and acetaldehyde under alkaline conditions was proposed by Wawzonek and Rees[5]. The mechanism proposed was postulated as follows:

$$CH_3CHO + HCHO \overset{OH^-}{\rightleftharpoons} HOCH_2CH_2CHO \rightleftharpoons CH_2=CH_2CHO + H_2O$$

$$HOCH_2CH_2CHO + CH_2=CHCHO \rightleftharpoons O(CH_2CH_2CHO)_2 \xrightarrow[OH^-]{6HCHO}$$

$$\underset{\substack{\uparrow \\ CH_2OH}}{\overset{\substack{CH_2OH \\ \uparrow}}{HOCH_2 - C}} - CH_2OCH_2 - \underset{\substack{\uparrow \\ CH_2OH}}{\overset{\substack{CH_2OH \\ \uparrow}}{C}} - CH_2OH + 2HCOO^-$$
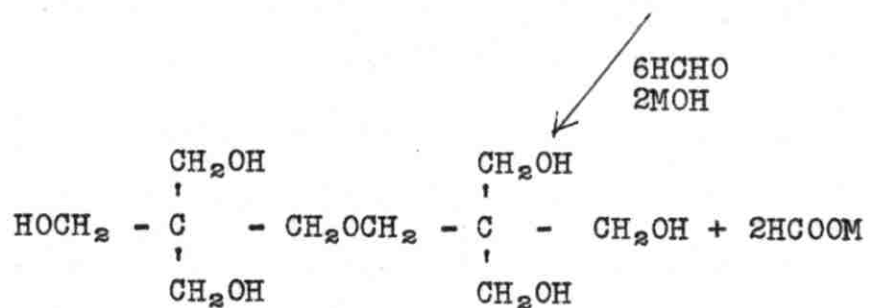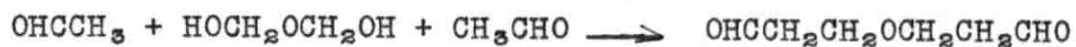
Another mechanism presented by Barth, Snow and Wood[6] is based on the assumption that formaldehyde exists in aqueous solution as polyoxymethylene chains and reacts with an active methylene group as the hemiacetal group, $-OCH_2OH$. This mechanism accounts for the formation of all the polypentaerythritols formed as by-products in the pentaerythritol reaction and follows the general pattern shown below:

(a) $H(OCH_2)_nOH + CH_3CHO \xrightarrow{OH^-} H(OCH_2)_nCH_2CHO + H_2O$

(b) $2H(OCH_2)_nOH + H(OCH_2)_nCH_2CHO \xrightarrow{OH^-} \left[H(OCH_2)_n\right]_3 CCHO + 2H_2O$

(c) $\left[H(OCH_2)_n\right]_3CCHO + HCHO + MOH \longrightarrow \left[H(OCH_2)_n\right]_3CCH_2OH + H_2O + HCOOM$

(d) $\left[H(OCH_2)_n\right]_3CCH_2OH \xrightarrow{OH^-} 3H(OCH_2)_{n-1}OH + C(CH_2OH)_4$

In the above reactions, three polymeric hydrated chains react with a molecule of acetaldehyde and the resulting molecule undergoes a Cannizzaro reaction with alkali and formaldehyde to give the complex molecule shown in equation (c). This molecule dissociates again to form polyoxymethylene chains and pentaerythritol. According to this mechanism, dipentaerythritol is postulated to be formed from dimeric formaldehyde and acetaldehyde by the following

sequence of reactions:

$$OHCCH_3 + HOCH_2OCH_2OH + CH_3CHO \longrightarrow OHCCH_2CH_2OCH_2CH_2CHO$$

$$\downarrow \text{6HCHO} \atop \text{2MOH}$$

$$HOCH_2 - \underset{\underset{CH_2OH}{|}}{\overset{\overset{CH_2OH}{|}}{C}} - CH_2OCH_2 - \underset{\underset{CH_2OH}{|}}{\overset{\overset{CH_2OH}{|}}{C}} - CH_2OH + 2HCOOM$$

The starting material, 7-phenyl-2:6:8-trioxaspiro (3:5) nonane (IV) was prepared from pentaerythritol by the following series of reactions:

$$C(CH_2OH)_4 \xrightarrow{\quad HBr \quad} (HOCH_2)_3CCH_2Br$$
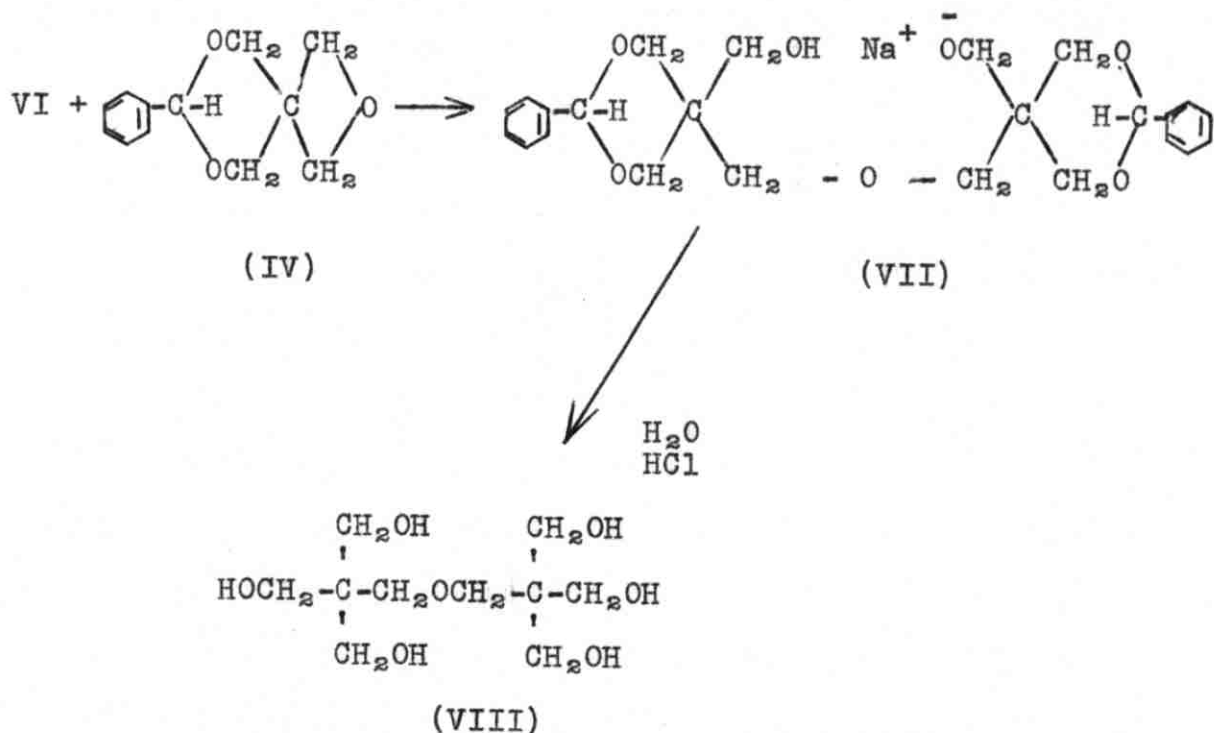
$$(I) \qquad\qquad\qquad (II)$$
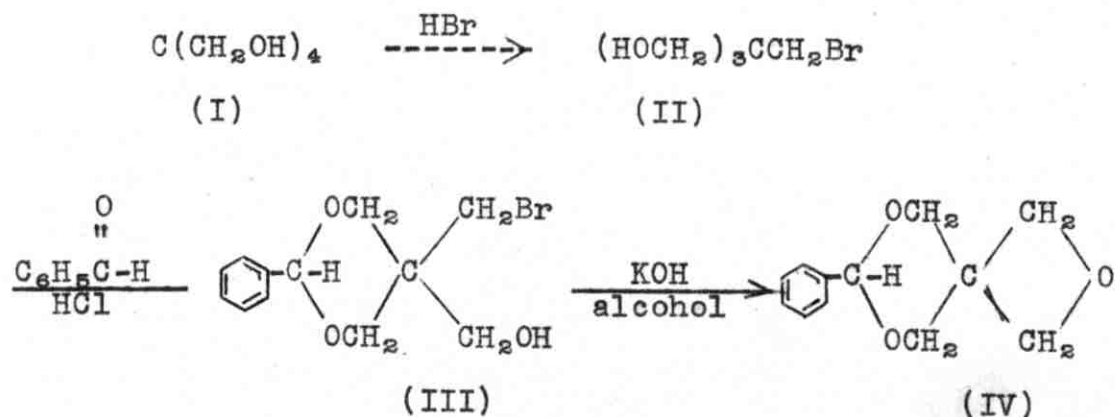
Pentaerythritol monobromide (II) was prepared by the action of 48% hydrobromic acid on pentaerythritol in glacial acetic acid, followed by transesterification of the bromo-acetate and exhaustive extraction of the dry product with ether. The melting point of the recrystallized monobromide was 75 - 76°C. This method of preparation is the one developed by Matar[7].

The monobromide dissolved in water was heated to 80°C and then treated with benzaldehyde and catalytic amounts of hydrochloric acid. The mixture was then shaken for four hours at room temperature and the precipitated benzal derivative was recrystallized from n-hexane-benzene to give pure monobenzal pentaerythritol monobromide (III), melting

at 73 - 74°C. This method of preparation is a modification of the procedure used by Gulen[8].

Treatment of the monobenzal pentaerythrityl monobromide (III) with alcoholic potassium hydroxide, followed by removal of the precipitated potassium bromide and evaporation of the solvent, gave a yellowish solid melting over a wide range. Distillation of the crude solid gave two distinct fractions. The first fraction was collected at 134-138/1 mm. and recrystallized from petroleum ether to give needles melting at 78 - 79°C. Upon sodium fusion and treatment with silver nitrate, this compound gave no precipitate of silver bromide. It was shown to be 7-phenyl-2:6:8-trioxaspiro (3:5) nonane (IV) (presumably new compound) by reduction with lithium aluminum hydride to 5-methyl-5-hydroxy methyl-2-phenyl-1,3-dioxan (IX). The second fraction, b.p. 160 - 176°C/1 mm., was identified as monobenzal pentaerythrityl monobromide (III) by mixed melting point with an authentic sample. This method of isolation and purification of the product proved to be impractical due to the extensive decomposition which occurred during the distillation. Seeking a new method of purification, the crude solid obtained from the dehydrobromination step was chromatographed on a column of alumina. It was found that the trimethylene oxide (IV) could be eluted from the column smoothly with petroleum ether and benzene, while the bromohydrin contaminant required benzene-ether mixture for

elution.   The combined petroleum ether-benzene fractions
were evaporated and the residue was recrystallized from
petroleum ether to give pure IV in 65 - 75% yield, M.P.
78 - 79°C.

Further investigation showed that compound (IV)
could be obtained in pure form by concentrating the alco-
holic solution, after filtering the potassium bromide,
and cooling the mixture to induce precipitation.   The
precipitate formed was recrystallized from petroleum ether
to give pure IV, melting point 78 - 79°C, in 60% yield.
This method gives slightly lower yield than the one
employing chromatographic separation, but is much more
convenient to run on a large scale.

The plan for the prepaation of dipentaerythritol
(VIII) from compounds (IV) and (V) is outlined in the
following sequence of reactions.

(I)   (V)

(VI)

$$VI + \underset{(IV)}{\overset{\displaystyle OCH_2 \quad CH_2}{\underset{\displaystyle OCH_2 \quad CH_2}{C_6H_5-C-H \quad C \quad O}}} \longrightarrow$$

(IV)

(VII)

$$\underset{HCl}{\overset{\displaystyle H_2O}{\downarrow}}$$

$$\underset{(VIII)}{\overset{\displaystyle CH_2OH \qquad CH_2OH}{HOCH_2-C-CH_2OCH_2-C-CH_2OH}}$$
$$CH_2OH \qquad CH_2OH$$

(VIII)

Monobenzal pentaerythritol (V) was prepared by the action of benzaldehyde on pentaerythritol (I) in the presence of catalytic amounts of hydrochloric acid[8].

Treatment of V in xylene with sodium gave the corresponding alkoxide to which a solution of IV in xylene was added and the mixture refluxed for twenty four hours. The suspension formed was treated with dilute hydrochloric acid and steam distilled to remove the benzaldehyde. The residue remaining after steam distillation consisted of an aqueous layer and some residual polymer. The aqueous layer was filtered and evaporated to give an oily residue which, upon acetylation (acetic anhydride and pyridine), gave a brown gummy product. Distillation of this product under diminished

pressure gave a fraction collected at 150 - 170°C/1 mm., identified as pentaerythrityl tetraacetate by trans-esterification (sodium and ethyl alcohol) to pentaerythritol (I), melting at 259 - 261°C. A mixed melting point with an authentic sample showed no depression. No further fraction could be isolated from this distillation due to the extensive decomposition that occurred at higher temperatures.

Attempts to isolate dipentaerythritol from the oily residue left after the evaporation of the aqueous solution, by recrystallization from water and by extraction with acetone, were unsuccessful. Substitution of xylene by collidine, toluene and dioxane gave the same results and no detectable amounts of VIII could be isolated.

Another approach to the preparation of dipentaery-thritol from IV and V involved use of tetrahydrofuran as the solvent and p-toluene sulfonic acid as the catalyst. The reaction mixture was kept at 40°C for twelve hours, hydrolyzed and steam distilled. The residual solution was evaporated to give a crude solid, melting over a wide range. Recrystallization of the product from water gave pentaerythritol (I); no dipentaerythritol could be isolated.

The structure of 7-phenyl-2:6:8-trioxaspiro (3:5) Nonane (IV) was proved by reduction with lithium aluminum hydride to the corresponding 5-methyl-5-hydroxymethyl-2-

phenyl-1,3-dioxan (IX).
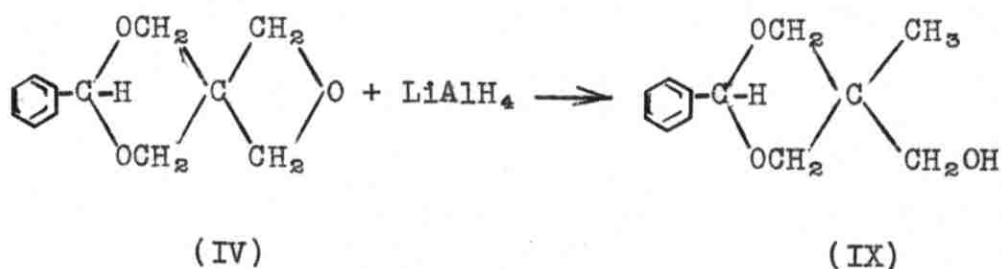
The reduction was carried out smoothly in dry tetrahydro-
furan at reflux temperature and the excess lithium
aluminum hydride was destroyed with water. After the
aluminum hydroxide precipitate was dissolved in alkali,
the mixture was extracted with ether and the ether layer
dried and evaporated to give a crude product which upon
recrystallization from hexane-benzene mixture gave a
solid, melting at 100 - 101°C. The solid was identified
as 5-methyl-5-hydroxymethyl-2-phenyl-1,3-dioxan (IX) by
mixed melting point with an authentic sample prepared from
analytical trimethylol ethane and benzaldehyde in an
acidic medium by a procedure similar to the one used for
the preparation of III. Hydrolysis of IX in hydrochloric
acid solution gave trimethylol ethane (X), M.P. 198 - 199°C,
undepressed upon admixture with an authentic sample.
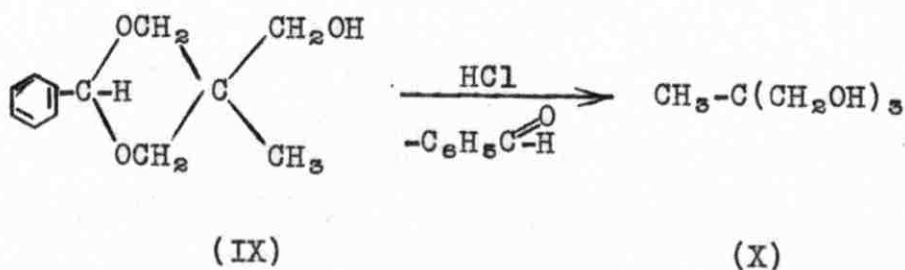
Many compounds of pentaerythritol containing intra-
molecular ether linkages have been described /the litera-
ture[9,10,11,12]. The general method of formation of these
1,3 epoxide derivatives is by the action of potassium
hydroxide on pentaerythritol halides.

The action of potassium hydroxide on monobenzal-
pentaerythrityl monobromide (III) to form 7-phenyl-2:6:8-
trioxaspiro (3:5) nonane (IV) probably proceeds in a manner
similar to the corresponding reaction of 1,2 bromohydrins[13].

$$\text{(III)} \quad \xrightarrow{OH^-} \quad \text{(IIIb)}$$

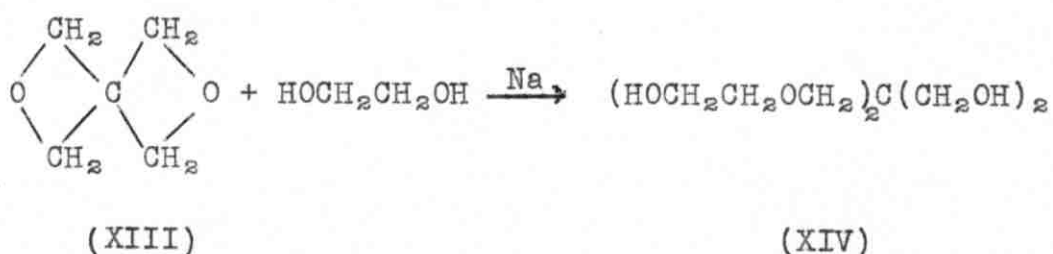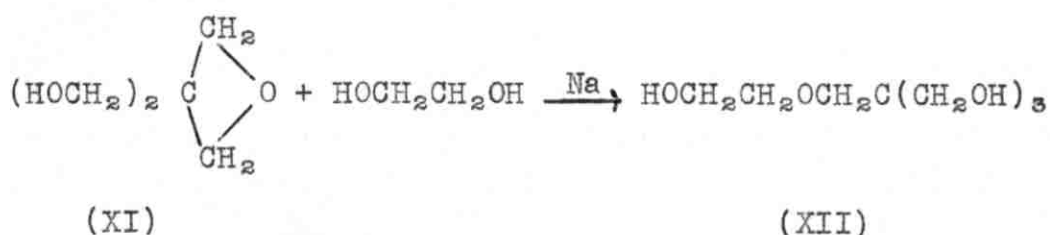$$\xrightarrow{-Br} \quad \text{(IV)}$$
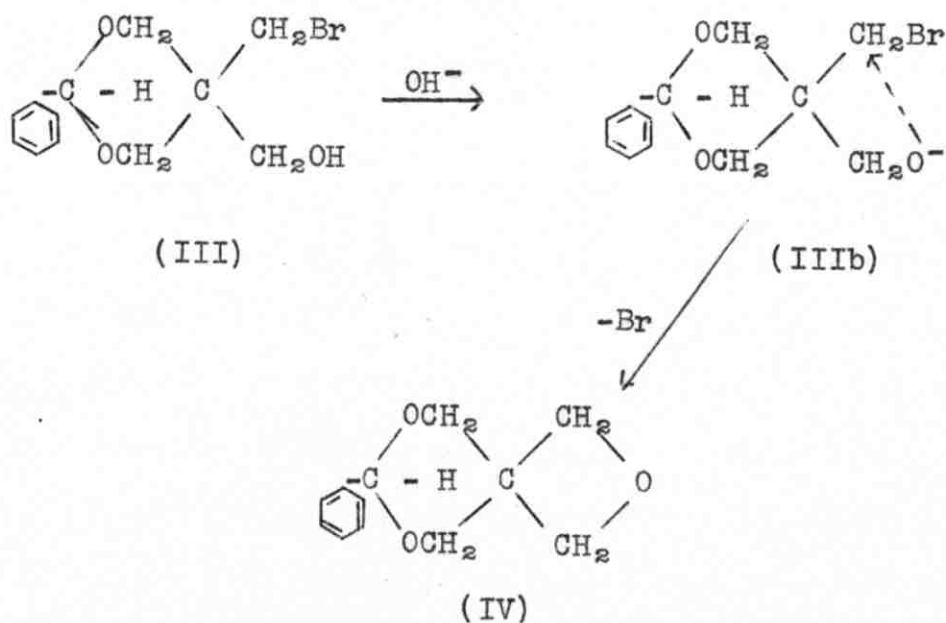
In the conversion of the bromohydrin (III) into the oxide
(IV) by the action of potassium hydroxide, the first step
is the formation of an alcoholate ion (IIIb). In the
second step, the negatively charged oxygen atom in (IIIb)

- 12 -

attacks the carbon atom from the face of the tetrahedron opposite the apex where the bromine atom is attached to give an intramolecular ether. The separation of the oxide (IV) from III by fractional distillation under reduced pressure proved to be impracticable. Further investigation showed that the mixture could be separated effectively on a column of alumina. The clear cut separation was due to the wide difference in absorbability of the two components. The slightly polar ether (IV) is much less adsorbed by the column than the polar bromohydrin (III) and so it can be eluted down with a solvent of lower eluant power than that needed to elute the latter.

Since no direct synthesis of dipentaerythritol (VIII) is recorded in the literature, the preparation of this compound was attempted by treating an oxetane derivative of pentaerythritol with a suitable derivative of pentaerythritol. To this effect, two different routes were follwed:
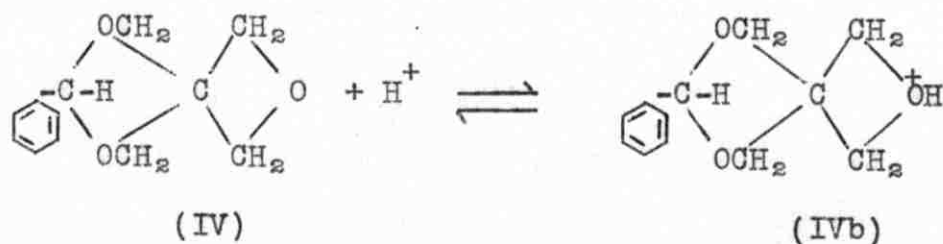
Route I: 7-phenyl-2:6:8-trioxaspiro (3:5) nonane (IV) was treated with the alkoxide of monobenzal pentaerythritol (VI) as shown on pages 8 - 9. It will be noticed that in IV the two potential hydroxyl groups have been blocked by an acetal linkage in order to prevent their participation in the reaction. Compound V, from which the alkoxide was made, was prepared from pentaerythritol (I) by blocking two of the four hydroxyl groups by an acetal linkage in order to make the derivative more soluble in an
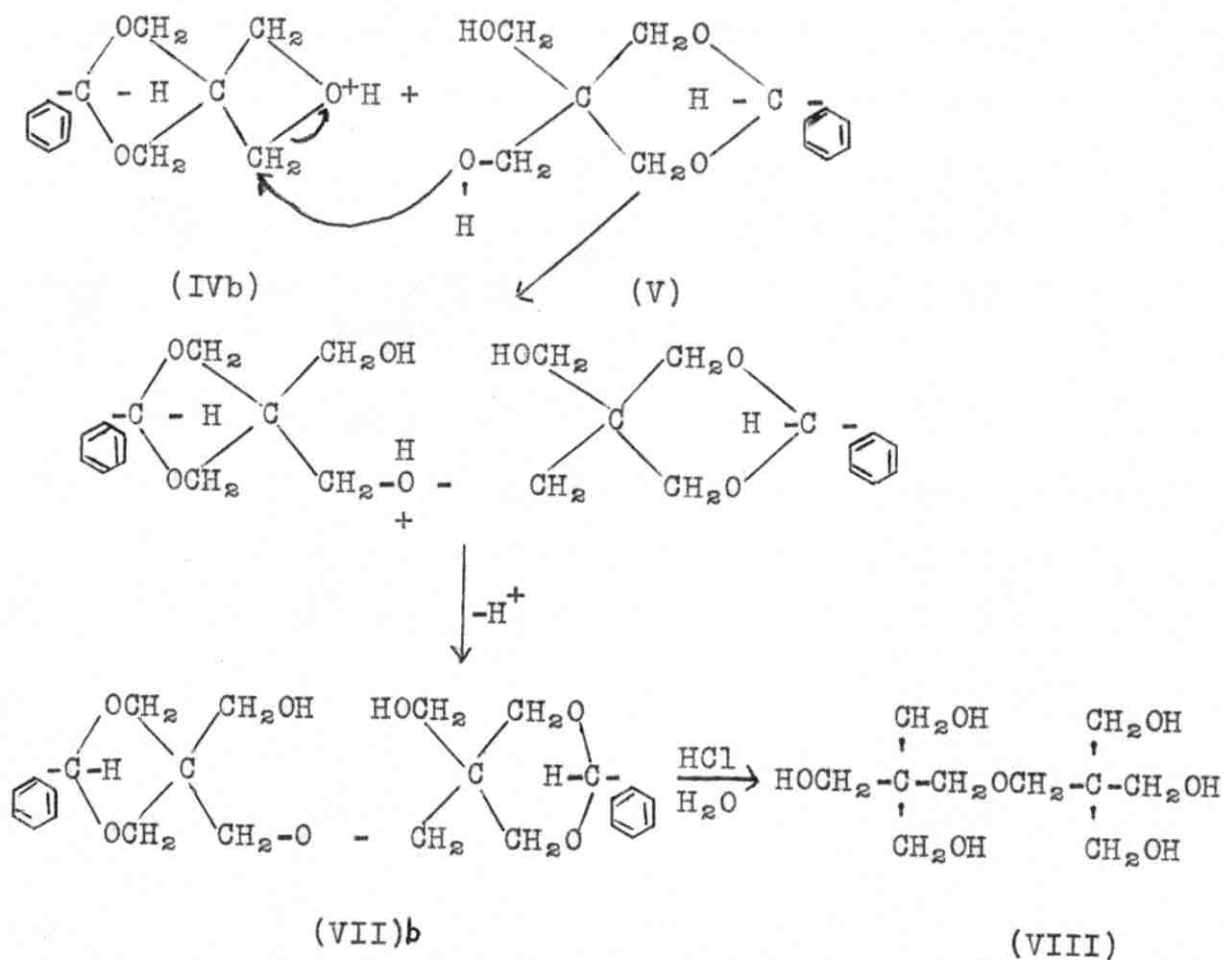
organic medium. The reaction was expected to take place
in a manner analogous to the formation of the mono - or
diethylene glycol ethers of pentaerythritol (XII and XIV)
from ethylene glycol and 3,3-bis-(hydroxymethyl)-oxacyclo-
butane (XI) or 2,6-dioxaspiro (3:3) heptane (XIII) respec-
tively[14].

$$(HOCH_2)_2 \; C \overset{CH_2}{\underset{CH_2}{<}} O \; + \; HOCH_2CH_2OH \; \xrightarrow{Na} \; HOCH_2CH_2OCH_2C(CH_2OH)_3$$

(XI)   (XII)

$$O \overset{CH_2}{\underset{CH_2}{<}} C \overset{CH_2}{\underset{CH_2}{>}} O \; + \; HOCH_2CH_2OH \; \xrightarrow{Na} \; (HOCH_2CH_2OCH_2)_2C(CH_2OH)_2$$

(XIII)   (XIV)

Even though the reaction was carried out at 100 to 170°C.
in different solvents, no dipentaerythritol could be isolated.

Route II: Dipentaerythritol was expected to be
formed via an acid - catalyzed opening of the oxide ring of
7-phenyl-2:6:8-trioxaspiro (3:5) nonane (IV) by monobenzal
pentaerythritol (V) according to the following mechanism:

(IV)   (IVb)

OCH₂ CH₂ ... (IVb) ... (V)

(VII)b

$$\xrightarrow[\text{H}_2\text{O}]{\text{HCl}} \text{HOCH}_2-\overset{\text{CH}_2\text{OH}}{\underset{\text{CH}_2\text{OH}}{\text{C}}}-\text{CH}_2\text{OCH}_2-\overset{\text{CH}_2\text{OH}}{\underset{\text{CH}_2\text{OH}}{\text{C}}}-\text{CH}_2\text{OH}$$

(VIII)

The proton is postulated to add to the oxide (IV) to give the conjugated acid (IVb), in which the carbon-oxygen linkage is greatly weakened. The second step of the reaction would then be a nucleophilic displacement on carbon, in which the oxygen of the oxide ring is displaced by the oxygen of a hydroxyl group in V. The reaction was expected to take place in a manner similar to the acid - catalyzed opening of the oxide ring of 3,3-bis-(hydroxy methyl)-oxacyclobutane (XI) by methyl and ethyl alcohol[7]. However, no dipentaery-thritol was isolated from this process and instead a gummy product was obtained. The failure of this reaction may

perhaps be attributed to some kind of steric hindrance
which prevents the approach of the alcohol group to the
alpha carbon of the oxetane. The same behavior has been
observed by Matar[7] in an attempt to open the oxide ring
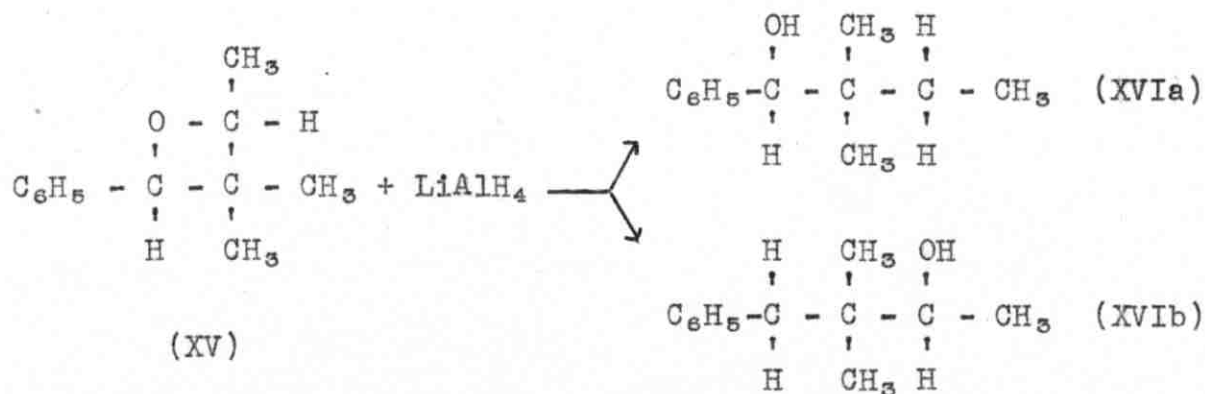of XI by n-propyl alcohol instead of methyl and ethyl
alcohol.

In view of the fact that the reductive cleavage of
new oxetanes (trimethylene oxides) can be employed in the
elucidation of their structures[15], the reductive cleavage
of 7-phenyl-2:6:8-trioxaspiro(3:5) nonane with lithium
aluminum hydride was carried out in tetrahydrofuran. The
reaction proceeded smoothly to give 5-methyl-5-hydroxy-
methyl-2-phenyl-1,3-dioxan (IX) in excellent yield.

(IV)

(IX)
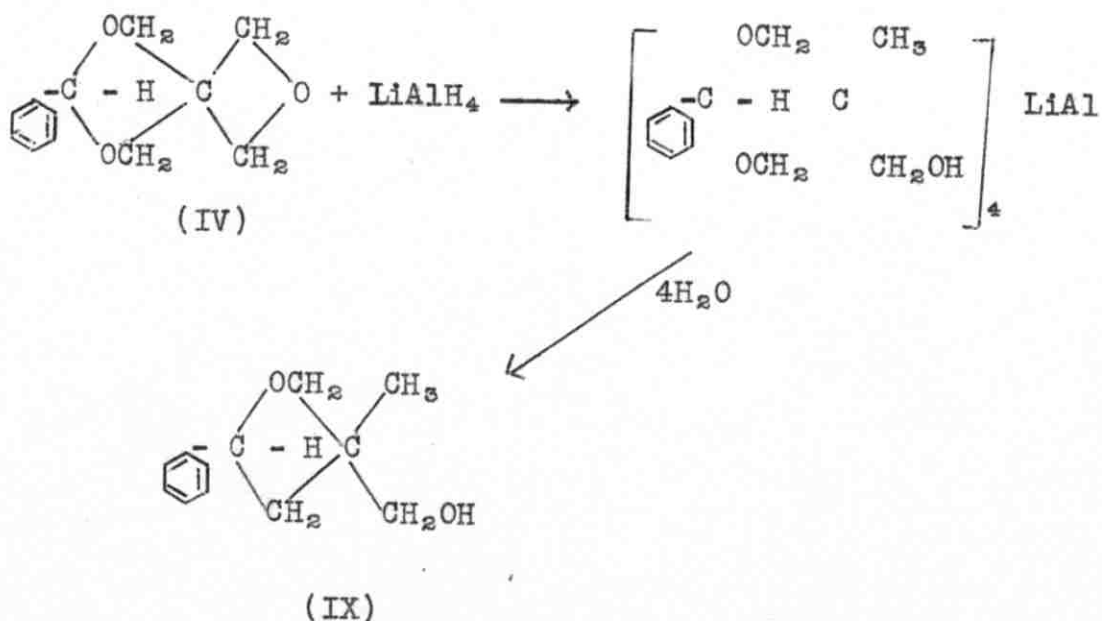
The mechanism of this reduction, probably involves an
attack by the hydride ion on the alpha carbon atom of the

oxide ring to cause a cleavage of the C-O bond. The
alkoxide ion formed coordinates immediately with a neutral
hydride molecule to form the $Al(OR)_4^-$ complex which upon
treatment with water gives compound (IX)[16].

Recently, some interesting work has been done on the
reductive cleavage of 1,3 epoxides by lithium aluminum
hydride. The first attempt was in 1954, when Büchi, during
the course of a study on the reaction of carbonyl compounds
with 2-methyl-2-butene in the presence of ultraviolet light,
prepared 2-phenyl-3:3:4- trimethyl oxetane (XV) and attempted
to reduce it with lithium aluminum hydride. It was expected
that the hydride ion would attack the alpha-carbon to give
compound (XVIa or b) but no detectable reaction took place
even at 140°C.[17].

$$CH_3$$
$$O - C - H$$
$$C_6H_5 - C - C - CH_3 + LiAlH_4 \longrightarrow$$
$$H \quad CH_3$$
$$(XV)$$

$$OH \quad CH_3 \quad H$$
$$C_6H_5 - C - C - C - CH_3 \quad (XVIa)$$
$$H \quad CH_3 \quad H$$

$$H \quad CH_3 \quad OH$$
$$C_6H_5 - C - C - C - CH_3 \quad (XVIb)$$
$$H \quad CH_3 \quad H$$

The stability of a highly substituted 1,3-epoxide to lithium
aluminum hydride has also been observed by Allen[18], who
reported that Δ^5-pregnene-11β-ol-3,20-dione-17α, 21-oxide-
3,20-Bis-ethylene ketal (XVII) was recovered unchanged after

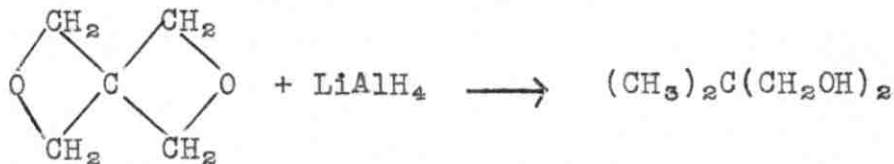treatment with lithium aluminum hydride in ether.
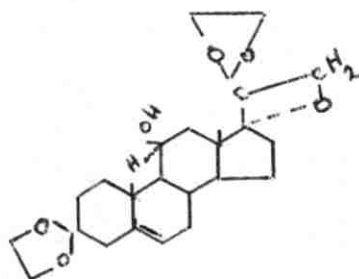
(XVII)

LiAlH₄ → no reaction.

In 1956, Aprahamian[19] studied the effect of lithium aluminum hydride on 2,6-dioxaspiro (3:3) heptane (XVII) and found that reduction proceeded smoothly to give 2,2-dimethyl-1,3-propanediol (XIX).

(XVIII)   (XIX)

At about the same time, Searles[15], reported the reduction of trimethylene oxide and ten other oxetanes carrying one or two alkyl or aryl substituents at different positions.   In each case the reaction gave a single alcohol product. These reductions were carried either in ether or in tetra-hydrofuran. The yields in the latter solvent were in general higher than in the former.

The data of Searles clearly indicate that alkyl

substituents at 3,3-positions decrease somewhat the reactivity of the ring. This can be shown by comparing the result obtained from the reduction of trimethylene oxide with that of 3,3-dimethyloxetane in tetrahydrofuran. While the former gave 1-propanol in 65% yield when the reaction was carried for 7 hours, the latter gave 2,2-dimethyl-1-propanol in 32% yield only, even when the reaction period was extended to 20 hours. According to Searles[15], the deactivation associated with 3,3-dialkyl substituents could be attributed to two factors: (I) the "Thorpe-I$_{ng}$old effect", according to which the mutual repulsion of groups at position 3 will decrease the distortion of the internal bond angle and make the ring more stable. (II) the effect of 3,3 substituents in diminishing the basicity of the oxetane, thus decreasing the ability of the ring oxygen to coordinate with lithium ion during the reaction. This coordination is necessary in that it results in a stronger "pull" on the oxygen, thus aiding the displacement process.

W$_e$ have checked the reduction of trimethylene oxide with lithium aluminum hydride in this laboratory under exactly the same conditions as those used for the reduction of 7-phenyl-2:6:8-trioxaspiro(3:5) nonane (IV). Our result has confirmed that reported by Searles.

From the work of Büchi and Allen and from the extensive studies of S$_e$arles and his cowerkers, it is apparent that the reduction of oxetanes by lithium aluminum

hydride is sensitive to steric effects. Two substituents
at position three may cause marked deactivation, while the
presence of four substituents at positions 2,3,3,4 may
render the oxetane completely indifferent to the reducing
agent. In view of these facts, it is remarkable that our
compound, 7-phenyl-2:6:8-trioxaspiro (3:5) nonane (IV), can
be reduced to the corresponding alcohol by lithium alumin-
um hydride in almost quantitative yield. The reason why
IV is so vulnerable to this reagent is not quite clear.
One possible explanation is that in this compound the two
substituents at position three are "held back" by the six
membered dioxane ring and are thus unable to have any
effect on/normal strain associated with the internal bond
angle of the oxetane ring.

the

Preparation of Pentaerythritol Monobromide (II)

The procedure for the preparation of this compound is the one used by Matar[7].

To a 3 liters two-necked flask (ground glass joints) fitted with a dropping funnel and a reflux condenser were added 200 g (1.47 mole) of pentaerythritol (I), 1.5 liters of glacial acetic acid and 17 ml of 48% hydrobromic acid. The mixture was refluxed for 1.5 hours, then 170 ml of 48% hydrobromic acid was added and the mixture was refluxed for 3 hours. At the end of this period, another 96 ml of 48% hydrobromic acid was added and the refluxing was continued for 3 more hours. The solution was heated under water suction to remove as much of the acetic acid and water as possible. The remaining solution was transferred to a vacuum distillation apparatus and heated for 15 minutes at 140 - 150°C./10 mm. The light brown viscous residue was treated with 750 ml of absolute ethyl alcohol and 50 ml of 48% hydrobromic acid. The flask was provided with a fractionating column and the solution was fractionated slowly until about 500 ml of the azotropic mixture of ethyl alcohol and ethyl acetate was collected at a temperature of 71 - 72°C. Another 750 ml portion of ethyl alcohol was added and the fractionation was continued slowly until 750 ml more distillate was collected with a temperature ranging from 71 to

78°C. The flask was transferred to the vacuum distillation
set-up and the remaining alcohol was removed as completely
as possible at 10 mm. (the temperature should not rise
above 140°C.). Benzene (500 ml) was added to the brown
viscous residue, distilled off at atmospheric pressure and
finally heated to 140°C./10 mm. The same procedure was
repeated to remove all the water present in the residue. The
viscous residue was refluxed with 500 ml of dry ether with
frequent shaking until it became white and granular. After
cooling thoroughly in a refrigerator, the ether layer was
decanted and the solid washed twice with 200 ml portions of
cold dry ether. The product was dried in a vacuum desicca-
tor over calcium chloride and paraffin wax, ground and extra-
cted exhaustively with 600 ml of dry ether in a soxhlet
extractor (10 hours of extraction were required). The ether
extract was cooled overnight in the refrigerator and the
precipitated monobromopentaerythritol (II) was collected by
filtration under suction and washed with 200 ml of cold dry
ether. The crude product, melting at 70 - 72°C., weighed
150 - 160 g (51 - 54%). One recrystallization from a
mixture of 120 ml chloroform and 80 ml of ethyl acetate
raised the melting point to 75 - 76°C., recovery (85 -
90%).

Preparation of Monobenzal Pentaerythrityl Monobromide (III)

The procedure adopted for this preparation was a
modification of the method used by Gulen[8].

To a solution of 20 g (0.1 mole) of monobromo-
pentaerythritol (II) in 50 ml of distilled water was added
0.6 ml of conc. hydrochloric acid and the mixture was heated
to 70 - 80°C on a water bath. To the hot solution 10.6 g
(0.1 mole) of benzaldehyde was added and the mixture was
shaken mechanically at room temperature for 4 hours. The
precipitate was collected on a Buchner funnel, washed with a
dilute solution of sodium carbonate and finally with
distilled water. The dry product was recrystallized from
a 1:1 mixture of benzene and hexane to give 20 g of mono-
benzal pentaerythrityl monobromide (III) in 69% yield,
melting point 73 - 74°C.

Preparation of 7-phenyl-2:6:8-trioxaspiro (3:5) Nonane (IV)

Twenty grams (0.07 mole) of monobenzal pentaerythri-
tyl monobromide (III) dissolved in 50 ml of absolute ethyl
alcohol was introduced into 250 ml. 3-necked flask fitted
with a condenser and a mechanical stirrer. To this solution
5.6 g (0.1 mole) of potassium hydroxide in 50 ml of absolute
ethyl alcohol was added and the mixture was refluxed with
efficient stirring for 3 hours. After cooling, the solution
was filtered to remove the potassium bromide. The alcoholic
solution was evaporated under reduced pressure almost to
dryness and cold water was added to dissolve the excess
potassium hydroxide. The mixture was extracted with ether
and the ether layer dried and evaporated to a crude yel-
lowish solid melting over a wide range. The solid was

dissolved in a minimum amount of benzene and chromatographed
on a column of alumina. The trimethylene oxide (IV) was
eluted from the column smoothly with petroleum ether and
benzene (4:2, 2:2, 2:4, 3:7), while the monobenzal penta-
erythrityl monobromide contaminant required benzene-ether
mixture. The combined petroleum ether-benzene fractions
were evaporated to give a residue of 9.4 - 11.0 g, melting
point 74 - 77°C., yield 65 - 75%. After one recrystalliza-
tion from petroleum ether, the melting point was raised to
78 - 79°C. The analytical sample melted at the same
temperature.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84.

found: C, 70.05; H, 6.85.

In further investigation on the purification of (IV),
the solution left after the filtration of the potassium
bromide was concentrated under diminished pressure to one
third its original volume. The remaining solution was
cooled in the refrigerator to induce precipitation and the
precipitate formed was filtered under suction and washed
with water to remove any potassium hydroxide present. The
solid was dried and recrystallized from petroleum ether to
give a pure product, melting at 78 - 79°C., yield 60%.

Preparation of Monobenzalpentaerythritol (V)

The procedure used for the preparation of this comp-
ound is the same as that used by Gulen[8].

In a 3 liters, three-necked, round-bottomed flask,

fitted with a dropping funnel and a mechanical stirrer were placed 180 g (1.32 mole) of pentaerythritol (I) and 1.3 liters of water. The mixture was heated until all the solid dissolved and then it was allowed to cool slowly. At 25°C. the stirring was started and 6.6 ml of concentrated hydrochloric acid was added through the open neck of the flask, followed by 30 ml of benzaldehyde added dropwise from the dropping funnel. After the addition of benzaldehyde was completed the mixture was stirred for 3 more hours. The precipitate was collected on a Buchner funnel and washed with cold dilute sodium carbonate solution. The solid was transferred to a 3 liters round-bottomed flask, one liter of dilute solution of sodium carbonate was added and the mixture was refluxed for 10 minutes. The hot mixture was filtered through a fluted filter paper using a hot water funnel and the solid remaining was washed with 50 ml of hot water. The combined aqueous filtrates were cooled in the refrigerator for several hours and the crystals collected on a Buchner funnel and dried. The dry product was refluxed for 15 minutes with 200 ml of toluene and the hot mixture was allowed to cool to room temperature with stirring to prevent the formation of large lumps. Finally the mixture was cooled in the refrigerator for 5 hours and the solid was collected and washed with 100 ml of cold toluene. The dry product of monobenzalpentaerythritol (V), melting at 134 - 135°C. was 215 - 227 g (73 - 77%) of the theoretical yield).

Attempted Preparation of Dipentaerythritol (VIII)

In a 500 ml, three necked flask, provided with a
condenser, a dropping funnel and an efficient mechanical
stirrer, were placed 22.4 g (0.1 mole) of monobenzal-
pentaerythritol (V) and 200 ml of dry xylene. The mixture
was heated up to boiling and then 2.3 g (0.1 mole) of
metallic sodium was added in small portions. After all the
sodium had reacted, 20.6 g (0.1 mole) of 7-phenyl-2:6;8-
trioxaspiro (3:5) nonane (IV) in 80 ml of xylene was added
dropwise through the dropping funnel and the mixture was
refluxed for 24 more hours. The orange suspension was
treated with 60 ml of 2N hydrochloric acid and the mixture
was refluxed for 3 hours. The solution was transferred to
a steam distillation flask and steam distilled until the
solvent and the benzaldehyde were completely removed. The
aqueous solution was cooled to room temperature and then
filtered through a fluted filter paper to get rid of the
gummy by-product formed in the reaction. The clear solution
was evaporated to dryness under reduced pressure to give a
brown viscous residue. Benzene (200 ml) was added to this
residue and distilled off at atmospheric pressure, then at
reduced pressure. The same procedure was repeated with a
second 200 ml portion of benzene in order to ensure complete
removal of water from the residue.

The acetylation was carried by treating the solid
residue, about 7 g, with 50 ml (54.15 g, 0.53 mole) acetic

anhydride in 100 ml of pyridine. The mixture was shaken
until all the solid dissolved and then was left overnight
at room temperature. The solution was evaporated under
reduced pressure, to remove most of the acetic anhydride
and pyridine, and the residual mixture was poured over
ice. The ice mixture was stirred for one hour and the
acetic acid formed was neutralized with solid sodium car-
bonate. The mixture was extracted exhaustively with ether
and the ether layer washed with dilute solution of sodium
carbonate and distilled water, dried and evaporated to give
a brown oily residue. The residue was distilled at reduced
pressure in a modified claisen flask, to give a first frac-
tion collected at 150 - 170°C./1 mm. Further distillation
gave no second fraction due to the extensive decomposition
that occurred at higher temperature.

The 150 - 170°C./1 mm fraction was treated with
0.4 g of metallic sodium and 100 ml of absolute ethyl alco-
hol and the mixture was refluxed for one hour. The solution
was fractionated slowly through a Vigreux column until about
80 ml of distillate were collected. The remaining solution
was cooled in the refrigerator and the precipitate formed
was collected on a Buchner funnel and recrystallized from
water to give pure pentaerythritol (I) melting at 259 - 61°C.
A mixture with an authentic sample showed no depression in
the melting point.

In another attempt, the residue, left after the

evaporation of the aqueous layer obtained from the steam
distillation, was recrystallized from water to give a small
amount of solid, melting over a wide range.

Another portion of the above oily residue was treated
with acetone to induce crystallization, and the solid was
collected on a Buchner funnel. The dry solid (3 g) was
extracted in a soxhlet apparatus with 200 ml of dry acetone
(15 hours were needed) and the acetone extract was cooled to
room temperature. The precipitate formed was collected under
suction to give 0.9 g of product, melting at 63 - 72°C.
Recrystallization from 3:1 chloroform-benzene mixture did not
show any change in the melting point. The dry residue rem-
aining in the thimble showed decomposition at 280°C.

Substitution of xylene by collidine, toluene and
dioxane in the above reaction gave no detectable amount of
dipentaerythritol (VIII).

Another attempt to prepare dipentaerythritol (VIII)
was carried in the presence of an acid catalyst. In a 250 ml
round-bottomed flask fitted with a condenser, protected by
a calcium chloride tube, was placed 5.2 g (0.023 mole) of
V dissolved in 60 ml of dry tetrahydrofuran, a solution of
4.7 g (0.023 mole) of IV in 20 ml of tetrahydrofuran and
0.2 g of toluene-sulfonic acid. The solution was kept in
a thermostat, at 40°C., for 12 hours, then 30 ml of 0.5 N
hydrochloric acid was added and the mixture was refluxed
for 2 hours. The hydrolyzed solution was steam distilled,
to remove the benzaldehyde and the residual aqueous layer

was evaporated under reduced pressure to give a solid,
melting at 157 - 163°C. The solid residue was recrystal-
lized from water to give 2.2 g of pure pentaerythritol,
melting at 259 - 61°C. Admixture with an authentic sample
showed no depression in melting point. Not a small
amount of dipentaerythritol could be isolated.

R_eduction of 7-phenyl-2:6:8-trioxaspiro (3:5) Nonane (IV)
With Lithium Aluminum Hydride

In a 250 ml three-necked flask, fitted with a
mechanical stirrer, a dropping funnel and a reflux condenser
protected with a calcium chloride tube, were placed 3 g
(0.079 mole) of lithium aluminum hydride and 40 ml of tetra-
hydrofuran[*]. To the well stirred mixture was added 4.1 g
(0.02 mole) of 7-phenyl-2:6:8-trioxaspiro (3:5) nonane (IV)
in 40 ml of tetrahydrofuran in the course of one hour. The
mixture was refluxed for 4 more hours and the excess lithium
aluminum hydride was discharged cautiously with water. A
20 per cent solution of sodium hydroxide was added to dissolve
the aluminum hydroxide and the alkaline suspension was
extracted with ether. The ether layer was dried and evapora-
ted to give 3.9 g of crude product, melting at 95 - 98°C.,

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* Tetrahydrofuran was dried by lithium aluminum hydride added
  in small portions with continuous stirring until the rea-
ction was subsided. The tetrahydrofuran was distilled and
received in a container protected by a calcium chloride
tube.

(94.5% of the theoretical). The crude product was recrystallized from a mixture of one part benzene to two parts hexane to give 3.6 g of 5-methyl-5-hydroxymethyl-2-phenyl-1,3-dioxan (IX), melting point 100 - 101°C. Yield 87%. A mixture with an authentic sample (prepared by the method described below) showed no depression in the melting point.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 69.21; H, 7.74

Found: C, 69.28; H, 7.79

Preparation of 5-methyl-5-hydroxymethyl-2-phenyl-1,3-dioxan (IX)

To a solution of 12 g (0.1 mole) of trimethylol ethane (X) in 40 ml of distilled water was added 0.6 ml of concentrated hydrochloric acid and the mixture was heated to 70—80°C. on a water bath. To the hot solution 10.6 g (0.1 mole) of benzaldehyde was added and the mixture was shaken mechanically at room temperature for 3 hours. The precipitate was collected on a Buchner funnel, washed with a dilute solution of sodium carbonate and finally with distilled water. The dry product (16 g) was recrystallized from a mixture of one part benzene to two parts hexane to give 12.5 g of 5-methyl-5-hydroxymethyl-2-phenyl-1,3-dioxan (IX) in 60% yield, melting point 99-100°C. A mixture with the c ompound produced by the reduction of 7-phenyl-2:6:8-trioxaspiro (3:5) nonane (IV) melted at the same temperature.

Hydrolysis of 5-methyl-5-hydroxymethyl-2-phenyl-1,3-dioxan(IX)

In a 200 ml round bottom flask, fitted with a reflux

condenser were added 4 g (0.019 mole) of 5-methyl-5-hydroxy-
methyl-2-phenyl-1,3-dioxan (IX), 40 ml of 0.5N hydrochloric
acid and 30 ml of dioxane. The mixture was refluxed for 4
hours and the hot solution was transferred to a steam distil-
lation flask and steam distilled until all the benzaldehyde
was removed. The aqueous solution was evaporated to dryness
under reduced pressure and the solid residue was recrystal-
lized twice from ethyl acetate to give 0.3 g of trimethylol
ethane (X) (13%), melting point 198 - 199°C. The same
melting point was observed when the product was mixed with
an authentic sample.

Preparation of Trimethylene Oxide[20]

A 1 liter four necked flask was fitted with an effi-
cient mechanical stirrer, a thermometer, a dropping funnel
and a Vigreux column to carry the trimethylene oxide vapors
through a spiral condenser. In this flask were placed
337 g (6 moles) of potassium hydroxide and 30 ml of water and
the contents were heated to 140°C. with stirring (higher
temperature would have decreased the yield since it favors
the formation of unsaturated product). The flask was kept
hot to prevent the solidification of the potassium hydro-
xide at its upper part. Ice water was circulated through
the spiral condenser to condense the low boiling trimethy-
lene oxide, and 417 g (3 moles) of 3-bromo-1-propanol were
added slowly through the dropping funnel. The time required
for the addition was about one hour. After all the bromo-

hydrin was added, the mixture was stirred, with continued heating at 140 - 150°C., until about 75 ml of distillate were collected. Potassium hydroxide (30 g) were then added and the mixture was refractionated with 30 cm Vigreux column to give 26 g of trimethylene oxide boiling point 47 - 50°C., yield 15%.

Reduction of Trimethylene Oxide with Lithium Aluminum Hydride

In a 250 ml three necked round bottomed flask fitted with a mechanical stirrer, a dropping funnel and a reflux condenser protected by a calcium chloride tube was placed 7.5 g (0.188 mole) of lithium aluminum hydride and 70 ml of tetrahydrofuran. To the stirred mixture was added 5 g (0.085 mole) of trimethylene oxide through the dropping funnel. The addition took one hour and the mixture was refluxed for 4 more hours. Cold water was added cautiously to discharge the excess lithium aluminum hydride and the aluminum hydroxide formed was dissolved in hydrochloric acid. The solution was extracted exhaustively with ether and the ether layer was dried and fractionated in a 30 cm Vigreux column until the tetrahydrofuran started distilling off. To the remaining solution was added 2 g (0.09 mole) of metallic sodium in small portions and the mixture was ref-luxed for 3 hours. The suspension mixture was evaporated to dryness under reduced pressure at a temperature 30-40°C. and water was added to react with the excess sodium. The

solution was extracted with ether and the ether layer was dried over sodium sulfate. To the dry ether layer were added 20 ml of bromobenzene and the mixture was fractionated through 30 cm Vigreux column to give 2.8 g of product collected between 80 - 97°C. (54%). Treatment of the distillate with 3,5-dinitrobenzoyl chloride gave n-propyl-3,5-dinitrobenzoate, melting at 73 - 74°C.

Preparation of 3,5-dinitrobenzoyl Chloride[21]

A mixture of 3 g (0.014 mole) of 3,5-dinitrobenzoic acid and 6 g (0.024 mole) of phosphorus pentachloride in a test tube were warmed gently to start the reaction. After the rapid reaction had subsided, the mixture was boiled for about five minutes. The hot liquid was poured on a watch glass and the mass was allowed to solidify. The solid was transferred to a clean clay plate and rubbed with a spatula in order to remove the phosphorus oxychloride formed in the reaction. The residual acid chloride was used immediately for the preparation of the derivative as described below.

Preparation of n-propyl-3,5-dinitrobenzoate[21]

One gram of the crude n-propyl alcohol from the above distillate was mixed with 5 g of the newly prepared 3,5-dinitrobenzoyl chloride in a test tube and the mixture was boiled for 5 minutes. Ten ml of distilled water were added and the solution was cooled in the refrigerator until the product solidified. The precipitate was collected on a Buchner funnel, washed with 20 ml of 2% solution of

sodium carbonate and recrystallized from a mixture of ethyl alcohol and water. The pure n-propyl-3,5-dinitrobenzoate (66%), melted at 73-74°C. Admixture of the product to an authentic sample, prepared from n-propyl alcohol and 3,5-dinitrobenzoyl chloride, caused no depression in the melting point.

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