PREPARATION OF DIETHERS

OF

PENTAERYTHRITOL

BY

Abdur-Rahman Abdun-Nur

submitted in partial fulfillment for the requirements

of the degree Master of Science

in the Chemistry Department of the

American University of Beirut

Beirut, Lebanon

June 1961

PREPARATION OF DIETHERS

OF

PENTAERYTHRITOL

A-R. Abdun-Nur

ACKNOWLEDGMENT

The author wishes to express his gratitude to the Research Corporation and the Arts & Sciences Research Committee for financial support.

The author also wishes to thank Professor C.H. Issidorides who suggested this problem and encouraged it with steady interest and counsel.

ABSTRACT

Diethers of pentaerythritol were prepared in high yield from the corresponding diacetals and diketals by reduction with lithium aluminum hydride - boron fluoride etherate (or aluminum chloride).

Pentaerythritol dimethyl ether was prepared in good yield from methyl alcohol and 2,6 dioxaspiro (3,3) heptane.

A method is described for the preparation of 2,6-dioxaspiro (3,3) heptane in a yield (50 - 60%) which is considerably better than the one reported in the chemical and patent literature (17 - 32%)[11, 13, 14, 15, 16, 17, 18].

TABLE OF CONTENTS

TABLE OF CONTENTS

LIST OF FIGURES

Page

INTRODUCTION

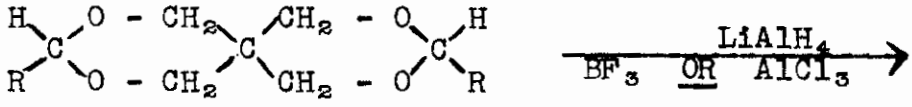
Pentaerythritol (I) is a colorless solid melting at 263°C.

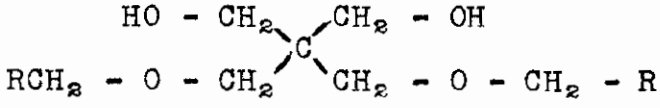
$$C(CH_2OH)_4$$

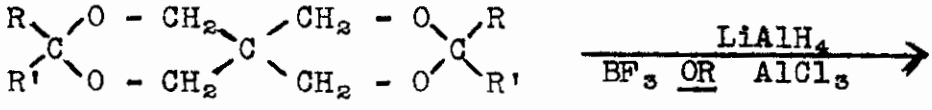
(I)

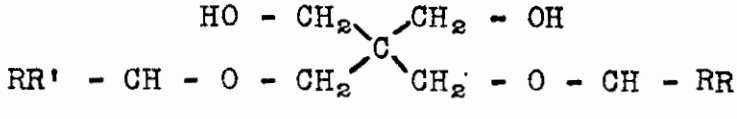
Being a tetrahydric alcohol, it can form mono, di, tri or tetra ethers. Some of these ethers find industrial application as intermediates in the preparation of pharmaceutical products, plasticizers and emulsifiers[1,2]. They are also used as ingredients of alkyds and other resins, and as floatation agents[3].

The purpose of this research was to prepare diethers of pentaerythritol via reduction of the corresponding diacetals or diketals, by a mixture of lithium aluminum hydride and boron fluoride etherate (or aluminum chloride).









HISTORICAL

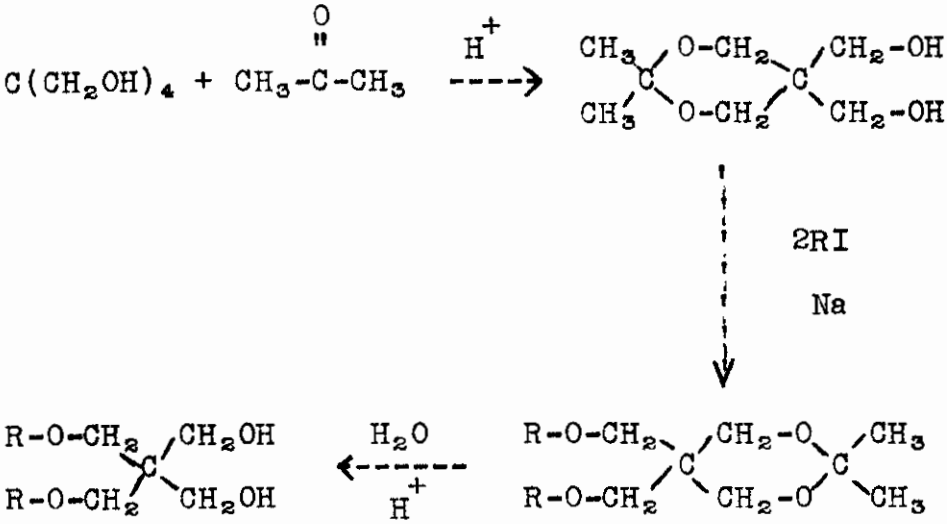
One of the methods generally used for the preparation of tetraethers of pentaerythritol is the reaction of pentaerythritol tetrabromide with metal alkoxides[4]. The low yields of this reaction have been attributed to the neopentyl structure of pentaerythritol tetrabromide, which sterically hinders bimolecular substitution reactions[5]. The same method may be used for the preparation of diethers of pentaerythritol. For example, Glattfeld and Schneider prepared pentaerythritol diethyl ether in 25% yield by the reaction of pentaerythritol dibromide with sodium ethoxide in liquid ammonia[6].

$$(CH_2OH)_2C\begin{matrix}CH_2Br\\CH_2Br\end{matrix} + 2C_2H_5ONa \xrightarrow{\text{liq.}NH_3} (CH_2OH)_2C\begin{matrix}CH_2-O-C_2H_5\\CH_2-O-C_2H_5\end{matrix} + 2NaBr$$

Certain bromides may react directly with pentaerythritol in a basic medium to give the corresponding ethers. Pentaerythritol di-tert butyl ether has been prepared by the action of tert-butyl chloride on pentaerythritol in pyridine[4]. Nichols and Yanovsky have reported the preparation of pentaerythritol mono, di, tri or tetra allyl ethers by the reaction of pentaerythritol and allyl bromide in 50 % aqueous sodium hydroxide[7]. By a modified procedure[8], Evans and

Gallaghan have prepared pentaerythritol diallyl ether in 35% yield.

To prepare diethers of pentaerythritol, Orthner and Freyes blocked two of the hydroxyl groups by ketal formation, treated the corresponding monoketal with an alkyl halide in the presence of sodium, and finally removed the protecting group by acid hydrolysis[9]. The yields were low.

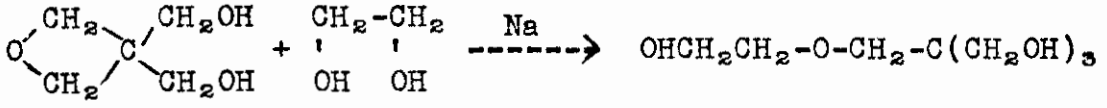


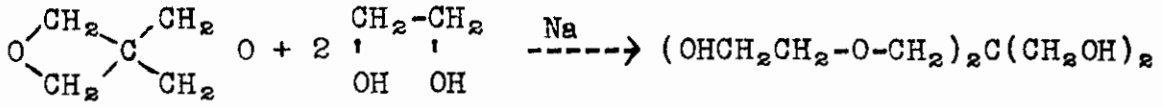
A novel method for the preparation of mono and diethers of pentaerythritol was developed by Wawzonek and Rees. By running the Tollen's condensation of acetaldehyde and formaldehyde in 50% methanol, they were able to isolate pentaerythritol mono and dimethyl ethers[10]. When the condensation of acetaldehyde and formaldehyde was carried in 50% ethylene glycol, the monoethylene glycol ether (II) and bis(ethylene glycol) ether (III) were obtained[11]. The method involved tedious fractionation and the yields were low.

$OH\text{-}CH_2CH_2\text{-}O\text{-}CH_2\text{-}C(CH_2OH)_3$ (II)

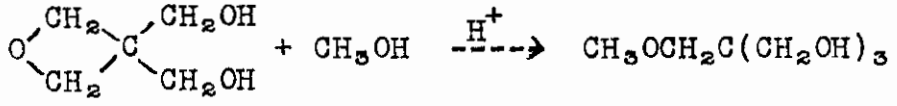
$(OH\text{-}CH_2CH_2\text{-}O\text{-}CH_2)_2C(CH_2OH)_2$ (III)

The key step in a recent method for the preparation of ethers of pentaerythritol involves ring opening of a trimethylene oxide with alcohols. The method was first introduced by Wawzonek and Issidorides to prepare (II) and (III)[11].

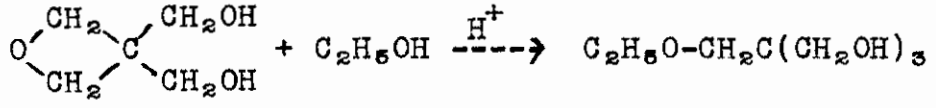




Extending the above reaction Issidorides and Matar obtained the monomethyl and monoethyl ethers of pentaerythritol starting with 3,3(bis-hydroxy methyl) oxacyclo butane (IV)[12].



(IV)



RESULTS

A. Preparation of Diacetals and Diketals of Pentaerythritol:

The diacetals and diketals used in this investigation were conveniently prepared from pentaerythritol and the corresponding aldehyde or ketone (acid catalysis).

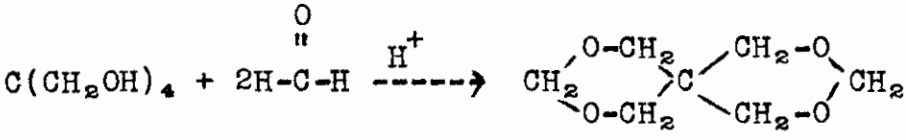
For the preparation of pentaerythritol diformal (V) the alcohol was condensed with formaldehyde (40% solution) in the presence of concentrated hydrochloric acid at 100°C. The product, after extraction with ether and recrystallization from petroleum ether, melted at 49 - 50°C. (Reported[19] m.p. 50°C.)

Pentaerythritol dibenzal (VI) was prepared by azeotropic distillation of a mixture consisting of pentaerythritol, benzene, benzaldehyde and catalytic amounts of p-toluenesulfonic acid. Recrystallization from butanol gave the pure product melting at 160 - 160.5°C. (Reported[20] m.p. 160°C.)

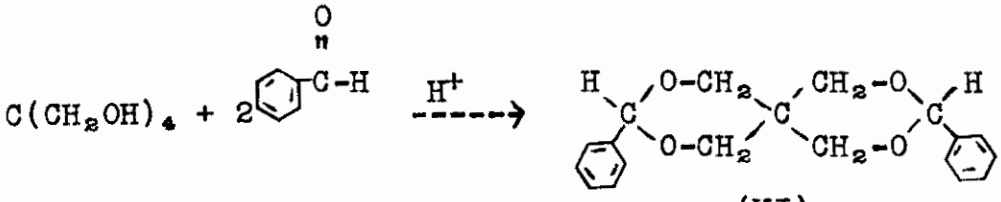
Pentaerythritol dicyclohexanone (VII) was obtained by the condensation of pentaerythritol w ith cyclohexanone in the presence of sulfuric acid. Ethanol was a suitable solvent for recrystallization of this compound, which melted at 134 - 135°C. (Reported[21] m.p. 135°C.)

Pentaerythritol dicyclopentanone (VIII), melting at 152 - 152.5°C. (ethanol), was prepared by essentially the same method, using cyclopentanone instead of cyclohexanone. (Reported[21] m.p. 152°C.)

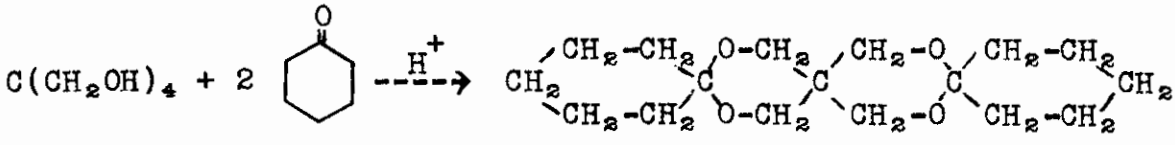
The condensation of pentaerythritol with acetaldehyde gave a liquid diacetal which was isolated by vacuum distillation. The product (IX) boiled at 94-96°C./8 mm. (Reported[22] b.p. 93 - 95°C./8 mm.)



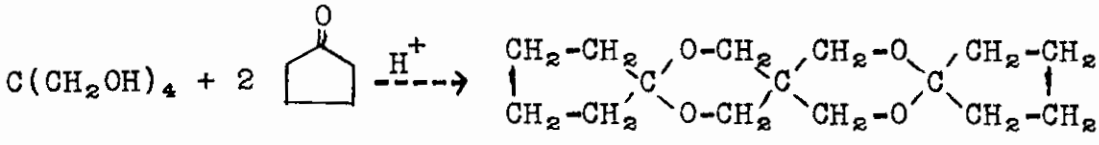
(V)



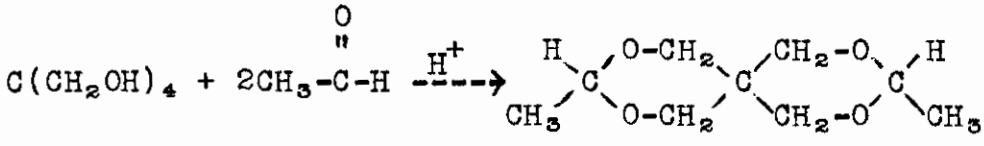
(VI)



(VII)



(VIII)

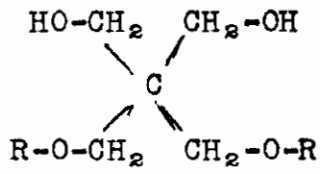


(IX)

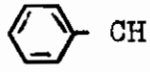
B. Preparation of Diethers of Pentaerythritol:

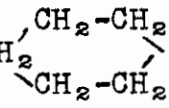
Reduction of four of the diacetals and diketals described above (VI, VII, VIII, IX) by a mixture of lithium aluminum hydride and boron fluoride etherate (or aluminum

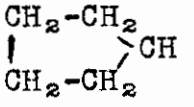
chloride), gave the corresponding diethers of pentaerythritol in high yields (X_a, X_b, X_c and X_d respectively).



(X)

a : R = 

b : R =  (cyclohexyl)

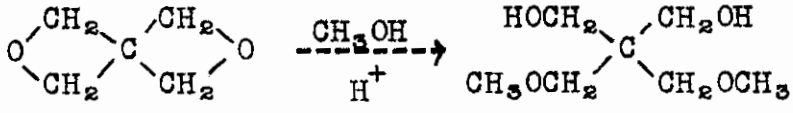
c : R =  (cyclopentyl)

d : R = CH_3CH_2 -

The general procedure for the reduction was as follows: A mixture of lithium aluminum hydride and boron fluoride etherate (or aluminum chloride) was prepared in sodium-dried ether, at 0° to -5°C., under anhydrous conditions. The diacetal or diketal was then added either in the solid form or in solution (sodium-dried ether). After stirring for one hour at 0° to -5°C. and for two hours at reflux temperature, the reaction mixture was decomposed by 10% sulfuric acid and extracted repeatedly with ether. The combined ether extracts were washed, dried and evaporated to dryness. The crude product was then purified either by recrystallization from a suitable solvent or by distillation under reduced pressure.

Pentaerythritol diethyl ether is a known compound and was characterized by preparation and determination of the saponification equivalent of its diacetate. Microanalytical data are included for the new compounds X_a, X_b, X_c. The results are summarized in table 1.

Surprisingly enough, the diformal of pentaerythritol (V) did not respond to the conditions of the reductive cleavage described above. No dimethyl ether could be isolated, even after chromatography of the reaction mixture; instead, the starting material was recovered. However, the dimethyl ether could be prepared in good yield by acid catalyzed opening of the oxetane rings of 2,6-dioxaspiro (3,3) heptane (XI) with methanol.



(XI) (XII)

The product, after recrystallization from petroleum ether (30 - 50°), melted at 33 - 35°C. (Reported[23] m.p. 34 -35°C.)

C. Preparation of 2,6-Dioxaspiro (3,3) Heptane:

The starting material for the preparation of this spirocyclic oxetane was pentaerythritol dibromide, obtained by the action of 48% hydrobromic acid on a refluxing solution of pentaerythritol in acetic acid, according to the method of Beyaert and Hansens[24] as modified by Aprahamian[25].

Several unsuccessful attempts were made to improve the yield of the spirocyclic oxetane by modifying the isolation

Table 1

Compound	% yield $AlCl_3$ Method	% yield BF_3 Method	m.p.	b.p.	Anal. Calcd.	Found	Sap.Eq. Calcd.	Found
Pentaerythritol Dibenzyl ether (X_a)	80%	85%	72-74°C	-	C, 72.12% H, 7.65%	72.20% 7.66%	-	-
Pentaerythritol Dicyclo hexyl ether (X_b)	85%	91%	57.5-58.5°C	-	C, 67.96% H, 10.74%	68.14% 10.71%	-	-
Pentaerythritol Dicyclo pentyl ether (X_c)	75%	80%	63-64°C	-	C, 66.14% H, 10.36%	66.29% 10.28%	-	-
Pentaerythritol Diethyl ether (X_d)	72%	82.5%	-	$\frac{114\text{-}6^\circ}{6\text{ mm.}}$ (Rep.[6] $\frac{115^\circ}{5\text{ mm.}}$)	-	-	138	136.5

techniques described in the literature. The yield of 2,6-dioxaspiro (3,3) heptane never exceeded 17% (yields reported in the literature including several patents 25%[13,18], 17%[11], 20%[14,16], 32%[17]).

The compound was finally obtained by the simple expedient of slow addition of an ethanolic solution of the dibromide to a distilling solution of potassium hydroxide (excess) in ethanol. The yield of the pure product, isolated after chromatography and recrystallization from petroleum ether (m.p. 89 - 90°C.; Reported[26] 89 - 90°C.), was 52 - 61%.

EXPERIMENTAL

Part I

Preparation of Pentaerythritol Diacetals and Diketals

Preparation of Pentaerythritol Diformal:

The procedure adopted for the preparation of this compound is a modification of the method described by Read[19].

A mixture of pentaerythritol (50 gm), 40% formaldehyde (50 gm) and concentrated hydrochloric acid (1 ml) was heated on a water bath for 1.5 hours. The aqueous solution was then extracted with twenty 50-ml portions of ether. The combined ether extracts were washed with 30 ml of 5% sodium bicarbonate and 30 ml of distilled water, dried over anhydrous sodium sulfate and filtered. The ether was evaporated and the residual oil distilled under reduced pressure. The yield of the product boiling at 81 - 85°C./1 mm was 35.5 gm. (61% of the theoretical).

Crystallization from petroleum ether (40 - 70°) gave the diformal melting at 49 - 50°C. (Reported[19] 50°C.).

Preparation of Pentaerythritol Dibenzal[20]:

In a 250 ml round-bottomed flask provided with a constant water separator (connected to a reflux condenser), were placed 6.8 gm (0.05 mole) of pentaerythritol, 21 gm (0.2 mole) of benzaldehyde, 0.5 gm of p-toluenesulfonic acid and 100 ml of dry benzene. The flask was heated gently and the water was collected in a measuring cylinder. The theo-

retical amount of water (0.1 mole, 1.8 ml) was collected within two hours. Half of the solvent was then distilled, the reaction mixture cooled and the precipitated product removed by filtration and washed with water. Recrystallization from butanol or carbon tetrachloride gave pentaerythritol dibenzal melting at 160°C. (Reported[20] 160°C.), yield 90%.

Preparation of Pentaerythritol Dicyclopentanone[21]:

Three grams of pentaerythritol (0.02 mole), 11.6 gm of cyclopentanone (0.12 mole) and five drops of concentrated sulfuric acid were stirred for three days at room temperature. Potassium hydroxide was then added until the reaction mixture was alkaline. The product that separated was collected and washed thoroughly with water. Recrystallization from ethanol gave 2.3 gm (24% yield) of pentaerythritol dicyclopentanone melting at 151 - 152.5°C. (Reported[21] 152°C.)

Preparation of Pentaerythritol Dicyclohexanone[21]:

A mixture of 6 gm (0.04 mole) of pentaerythritol, 25 gm (0.26 mole) cyclohexanone and five drops of concentrated sulfuric acid was stirred for one day at room temperature. The mixture was neutralized and poured into a large volume of cold water. The solid that separated was removed by filtration, washed with cold water and dried. Recrystallization from ethanol gave 10 gm of the product (87% yield) melting at 135 - 135.5°C. (Reported[21] 135°C.)

Preparation of Pentaerythritol Diacetal:

In a 500 ml, three necked round-bottomed flask fitted with a mechanical stirrer, a dropping funnel and a reflux condenser were placed 40 gm of pentaerythritol and 250 ml of water. The mixture was heated gently until the solid dissolved, then allowed to coal slowly - without stirring - to room temperature. Stirring was started and 1 ml of concentrated hydrochloric acid was added followed by 70 ml of acetaldehyde from the dropping funnel during the course of 1.5 hours. The mixture was then stirred for four hours at room temperature, neutralized with solid sodium bicarbonate and extracted with twenty 50-ml portions ofether. The combined ether extracts were washed with 50 ml of distilled water, dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue was distilled under reduced pressure. The yield of pentaerythritol diacetal boiling at 94 - 96°C./8 mm. was 46 gm (84% of the theoretical amount). (Reported[22] 93 - 95°C./8 mm.)

Part II

Preparation of Pentaerythritol Diethers

1. Preparation of Pentaerythritol Dibenzyl Ether:

A. Aluminum Chloride Method:

A 500 ml, three necked, round-bottomed flask was equipped with an air tight stirrer and a two-way addition tube provided with a condenser (protected by a calcium chloride

tube) and a dropping funnel. An Erlenmeyer flask containing 2.2 gm (0.007 mole) of pentaerythritol dibenzal was fitted to the third neck of the flask by a section of rubber tubing (Fig. 1). Aluminum chloride (3.8 gm, 0.028 mole) was placed in the flask which was then cooled for 0.5 hours in an ice-salt bath. Sodium-dried ether (25 ml) was added to dissolve the aluminum chloride. A suspension of 0.3 gm (0.007 mole) of lithium aluminum hydride in 20 ml of sodium-dried ether was then added dropwise to the well stirred solution during a period of 0.5 hours.

To the efficiently stirred, cold mixture, pentaerythritol dibenzal was added in portions (during ten minutes) by raising the containing flask. When the addition was complete, the mixture was stirred at -5° to 0°C. for one hour. At the end of this period, the ice-salt bath was removed and the mixture was stirred at reflux temperature for two hours.

The reaction mixture was then decomposed by the slow addition of 100 ml of ice-cold 10% sulfuric acid. During this addition, the temperature was kept as low as possible by means of an ice-salt bath. The ether layer was separated and the aqueous solution extracted with ten 25-ml portions of ether. The combined ether extracts were washed with two 30-ml portions of 5% sodium bicarbonate and finally with 30 ml of water. The ether was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The crude product, was recrystallized from alcohol-water mixture to give 1.8 gm (80% of the theoretical) of pentaerythritol

dibenzyl ether melting at 72 - 74°C.

Anal. Calcd. for $C_{18}O_4H_{24}$: C, 72.12%; H, 7.65%

Found: C, 72.20%; H, 7.66%

B. Boron Fluoride Method:

A 250 ml, three necked, round-bottomed flask was equipped with an air tight stirrer and a two-way addition tube provided with a condenser (protected by a calcium chloride tube) and a dropping funnel. An Erlenmeyer flask containing 3.1 gm (0.01 mole) of pentaerythritol dibenzal was fitted to the third neck of the flask by a section of rubber tubing (Fig. 1). Boron fluoride etherate (5.6 gm, 0.04 mole) was placed in the flask and cooled for 0.5 hours in an ice-salt bath. A suspension of 0.4 gm (0.01 mole) of lithium aluminum hydride in 30 ml of sodium-dried ether was then added dropwise through the dropping funnel to the well stirred solution during a period of 0.5 hours.

To the efficiently stirred, cold mixture, pentaerythritol dibenzal was added, in portions (during ten minutes) by raising the containing flask. When the addition was complete, the mixture was stirred at -5 to 0°C. for one hour. At the end of this period the ice-salt bath was removed and the mixture was stirred at reflux temperature for two hours.

A total of 100 ml of ice-cold 10% sulfuric acid was then added to the cold reaction mixture, very slowly at first. During this addition, the temperature was kept as low as possible by means of an ice-salt bath. The ether layer was

separated, and the aqueous layer was extracted with ten 25-ml portions of ether. The combined ether extracts were washed with two 30-ml portions of 5% sodium bicarbonate and finally with 30 ml of water. The ether was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The crude product was recrystallized from alcohol-water mixture giving 2.6 gm (85% of the theoretical) of pentaerythritol dibenzyl ether melting at 72 - 74°C., undepressed upon admixture with the sample prepared by the lithium aluminum hydride - aluminum chloride method.

2. Preparation of Pentaerythritol Dicyclohexyl Ether:

A. Aluminum Chloride Method:

The procedure was similar to the one described for the preparation of pentaerythritol dibenzyl ether. (1-A).

Pentaerythritol dicyclohexanone (8 gm, 0.025 mole) was treated with a mixture of 13.4 gm (0.1 mole) of aluminum chloride (in 100 ml of sodium-dried ether) and 1 gm (0.025 mole) of lithium aluminum hydride in 40 ml of sodium-dried ether. The addition of the lithium aluminum hydride suspension took 40 minutes.

The aqueous layer was extracted with ten 50-ml portions of ether. The crude product obtained after evaporation of the ether was recrystallized from water - ethanol mixture giving 6.8 gm (85% of the theoretical) of the product melting at 57.5 - 58.5°C.

Anal. Calcd. for $C_{17}O_4H_{32}$: C, 67.96%; H, 10.74%

Found: C, 68.14%; H, 10.71%

B. Boron Fluoride Method:

The procedure was similar to the one described for the preparation of pentaerythritol dibenzyl ether. (1-B).

Pentaerythritol dicyclohexanone (5.9 gm, 0.02 mole) was treated with 11.5 gm (0.08 mole) of boron fluoride etherate and 0.8 gm (0.02 mole) of lithium aluminum hydride in 60 ml of sodium-dried ether. The crude product, obtained after evaporation of the ether, was recrystallized from ethanol-water mixture giving 5.4 gm (91% of the theoretical) of pentaerythritol dicyclohexyl ether melting at 57.5 - 58.5°C., undepressed upon admixture with the sample prepared by the lithium aluminum hydride - aluminum chloride method.

3. Preparation of Pentaerythritol Dicyclopentyl Ether:

A. Aluminum Chloride Method:

The procedure was similar to the one described for the preparation of pentaerythritol dibenzyl ether. (1-A).

Pentaerythritol dicyclopentanone (5.4 gm, 0.02 mole) was treated with 10.7 gm (0.08 mole) of aluminum chloride (in 80 ml of sodium-dried ether) and 0.8 gm (0.02 mole) of lithium aluminum hydride suspended in 40 ml of sodium-dried ether. The addition of lithium aluminum hydride suspension took 40 minutes.

The crude product, obtained after evaporation of the ether, was recrystallized from petroleum ether (40 - 70°)

giving 4 gm (75% of the theoretical) of the product melting at 63 - 64°C.

Anal. Calcd. for $C_{15}O_4H_{28}$: C, 66.14%; H, 10.36%

Found: C, 66.29%; H, 10.28%

B. Boron Fluoride Method:

The procedure was similar to the one described for the preparation of pentaerythritol dibenzyl ether. (1-B).

Pentaerythritol dicyclopentanone (5.4 gm, 0.02 mole) was treated with 11.8 gm (0.08 mole) of boron fluoride etherate and 0.8 gm (0.02 mole) of lithium aluminum hydride in 60 ml of sodium-dried ether.

The crude product, obtained after evaporation of the ether, was recrystallized from petroleum ether (40 - 70°) giving 4.3 gm (80% of the theoretical) melting at 63 - 64°C., undepressed upon admixture with the sample prepared by the lithium aluminum hydride - aluminum chloride method.

4. Preparation of Pentaerythritol Diethyl Ether:

A. Aluminum Chloride Method:

A 500 ml, three necked, round-bottomed flask was equipped with an air tight stirrer, a condenser (protected by a calcium chloride tube) and a dropping funnel. Aluminum chloride (26.8 gm, 0.2 mole) was placed in the flask and cooled in an ice-salt bath for 0.5 hours. Sodium-dried ether (150 ml) was added to dissolve the aluminum chloride. A suspension of 2 gm (0.05 mole) of lithium aluminum hydride in 50 ml of sodium-dried ether was next added dropwise to the well

stirred solution during a period of one hour.

To the efficiently stirred cold mixture a solution of 9.5 gm (0.05 mole) of pentaerythritol diacetal in 30 ml of sodium-dried ether was next introduced through the dropping funnel during 15 minutes. When the addition was complete the mixture was stirred at -5 to 0°C. for one hour. At the end of this period, the ice-salt bath was removed and the mixture was stirred at reflux temperature for two hours.

The reaction mixture was then decomposed by the slow addition of 150 ml of ice-cold 10% sulfuric acid. During this addition, the temperature was kept as low as possible by means of an ice-salt bath. After separation of the ehter layer, the aqueous layer was extracted with twenty 50-ml portions of ether. The combined ether extracts were washed with 50 ml of 5% sodium bicarbonate, dried over anhydrous sodium sulfate and filtered. The crude oil, obtained after evaporation of the ether, was distilled under reduced pressure giving 6.9 gm (72% of the theoretical) of pentaerythritol diethyl ether boiling at 114 - 116°C./5 mm. (Reported[6] 115°C./5 mm.)

B. Boron Fluoride Method:

Forty gm (0.28 mole) of boron fluoride etherate were placed in a 500-ml three necked, round-bottomed flask equipped with an air tight stirrer, a condenser (protected by a calcium chloride tube) and a dropping funnel. The flask was cooled in an ice-salt bath for 0.5 hours. A suspension of

2.6 gm (0.07 mole) of lithium aluminum hydride in 100 ml of sodium-dried ether was next added dropwise to the well stirred solution during a period of one hour.

To the efficiently stirred mixture, a solution of 13 gm (0.07 mole) of pentaerythritol diacetal in 40 ml of sodium-dried ether, was added dropwise during 15 minutes. When the addition was complete, the mixture was stirred at -5 to 0°C. for one hour. At the end of this period the ice-salt bath was removed and the mixture stirred at reflux temperature for two hours.

The reaction mixture was then decomposed by the slow addition of 150 ml of ice cold 10% sulfuric acid. During this addition, the temperature was kept as low as possible by means of an ice-salt bath. After separation of the ether layer, the aqueous layer was extracted with twenty 50-ml portions of ether. The combined ether extracts were washed with 50 ml of 5% sodium bicarbonate, dried over anhydrous sodium sulfate and filtered. The crude oil, obtained after evaporation of the ether, was distilled under reduced pressure giving 10.7 gm (82.5% of the theoretical) of the product boiling at 114 - 116°C./ 5 mm. (Reported[6] 115°C./5 mm.)

C. Preparation of Pentaerythritol Diethyl Ether Diacetate[12]:

In a 250 ml, round-bottomed flask fitted with a condenser, protected by a calcium chloride tube, were placed 10 gm (0.05 mole) of pentaerythritol diethyl ether, 60 gm of acetic anhydride and one ml of dry pyridine. The mixture was

heated on a steam bath for 12 hours. The excess acetic anhydride was then removed under reduced pressure. The residue was cooled, poured with stirring into 100 gm of ice, neutralized with solid sodium bicarbonate and extracted with ten 50-ml portions of ether. The combined ether extracts were washed with 50 ml of water, dried over anhydrous sodium sulfate and filtered. The ether was next removed and the residual oil distilled under reduced pressure giving 10.2 gm (78% of the theoretical) of the diacetate boiling at 142 - 143°C./ 8 mm.

Sap. Eq. Calcd. for; $C_{13}O_6H_{24}$: 138

Found: 136.5

5. Attempted Reduction of Pentaerythritol Diformal:

The procedure was similar to the one described for the preparation of pentaerythritol diacetal (4-A) and (4-B).

Pentaerythritol diformal (8 gm, 0.05 mole) was titrated with a mixture of 26.3 gm (0.2 mole) of aluminum chloride (or 28.3 gm of boron fluoride etherate) in 125 ml of sodium-dried ether and 1.9 gm of lithium aluminum hydride in 60 ml of sodium-dried ether. The addition of the lithium aluminum hydride suspension took 40 minutes.

The aqueous layer was extracted with twenty 50-ml portions of ether. The crude product, obtained after evaporation of the ether was recrystallized from petroleum ether (40 - 70°) giving 6.4 gm (80% recovery) of pentaerythritol diformal, identical with an authentic sample (m.p., mixed m.p.,

infrared spectrum).

Part III

Preparation of Pentaerythritol Dimethyl Ether

Preparation of Pentaerythritol Dibromide:

The procedure described below is that of Bayaert and Hansens[24] as modified by Aprahamian[25].

A mixture of 360 gm (2.64 mole) of pentaerythritol, 2160 ml of glacial acetic acid and 28.8 ml of 48% hydrobromic acid was placed in a 5-liter, two necked, round-bottomed flask equipped with a dropping funnel and a reflux condenser. The mixture was refluxed for one hour, then 1225 ml of 48% hydrobromic acid was introduced dropwise through the dropping funnel during one hour. Refluxing was then continued for 20 more hours. At the end of this period the solution was heated under reduced pressure to remove as much of the acetic acid and water as possible; and was finally heated for 0.5 hours at 140 - 150°C./10 mm.

The residue was transferred to a 2-liter, two necked, round-bottomed flask (equipped with an efficient fractionating column) and treated with 90 ml of 48% hydrobromic acid and 900 ml of absolute ethyl alcohol. The mixture was fractionated slowly until 950 ml of the distillate was collected. A second 900 ml portion of absolute ethyl alcohol was added, and the fractionation was continued slowly until 900 ml more distillate was collected. (The boiling point during the first distillation remained constant at 71°C. corresponding

to the ethanol - ethyl acetate azeotrope; it rose slowly to 78° during collection of the second portion of the distillate).

The remaining alcohol was removed as completely as possible under reduced pressure (110°C./5 mm.). The viscous residue was then refluxed with 1000 ml of dry benzene for twenty minutes. The solution was cooled in the refrigerator for 2 hours and the precipitated pentaerythritol dibromide was collected by filtration and dried in a vacuum desiccator over paraffin wax for one day. Recrystallization from 750 ml of hot water gave 440 gm (63.5% of the theoretical) of the product melting at 110 - 111°C. (Reported[24] 110 - 111°C.)

Preparation of 2,6 Dioxaspiro (3,3) Heptane:

A 500 ml, round-bottomed flask was connected by a Claisen head to a dropping funnel (protected by a calcium chloride tube) and a condenser (set for downward distillation and provided with an adapter leading into a 50 cc. graduated cylinder. (Fig. 2)).

Forty grams of potassium hydroxide (Merck: Darmstadt - 5012) were placed into the flask, followed immediately by 70 ml of absolute ethyl alcohol. The mixture was heated gently (heating mantle) and when the alcohol just began to distill (about 5 minutes), a solution of 30 gm (0.12 mole) of pentaerythritol dibromide in 60 ml of absolute alcohol was added dropwise while the flask was heated. The addition took ten minutes. During this period the rate of

heating was regulated so that 30 ml of alcohol were distilled off. When the addition was complete, the mixture in the flask was cooled immediately to room temperature and extracted with ten 50-ml portions of ether (removed by decantation). The combined ether extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure (30 - 35°C./20 mm.) to a volume of 25 ml. The oily residue obtained was chromatographed on a column of alumina (Woelm: 200 gm containing 3% water). The column was eluted with petroleum ether (30 - 50° , nine 80-ml fractions). The combined petroleum ether fractions were recrystallized from petroleum ether (40 - 70°) giving 5.7 - 7 gm (50 - 60% of the theoretical) of the product melting at 89 - 90°C. (Reported[26] 89 - 90°C.). Infrared spectrum: $\lambda(CHCl_3)$ 935, 980, 1210, 2820, 1130 and 1450 cm^{-1}. (Fig. 3). (Reported[39] λ (CCl_4) 933, 981, 1222, 2820 cm^{-1}).

Reaction of 2,6 dioxaspiro (3,3) Heptane with Hydrobromic Acid. Preparation of Pentaerythritol Dibromide[28]:

A solution of 4 gm (0.04 mole) of 2,6 dioxaspiro (3,3) heptane and 60 ml of 48% hydrobromic acid was refluxed for half an hour, diluted with water to 100 ml, neutrallized with solid sodium bicarbonate and extracted with ten 25-ml portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate, filtered and evaporated to dryness. Recrystallization of the residue from water gave 7.7 gm (73% of the theoretical) of pentaerythritol dibromide melting at 110° -

111°C., undepressed upon admixture with an authentic sample.

Preparation of Pentaerythritol Dimethyl Ether:

The procedure adopted for the preparation of this compound is a modification of the method described by Issidorides and Matar for the preparation of pentaerythritol monomethyl ether[12].

A mixture of 6 gm (0.06 mole) of 2,6 dioxaspiro (3,3) heptane, 50 ml of methyl alcohol and 0.5 ml of concentrated sulfuric acid was stirred for two days in a flask protected with a calcium chloride tube. The solution was diluted with 50 ml of water, neutralized with solid sodium carbonate and extracted with eight 25-ml portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate and filtered. Evaporation of the ether, under reduced pressure, left an oily residue which solidified on cooling. Recrystallization from petroleum ether (40 - 70°) gave 5.9 gm (60% of the theoretical) of the product melting at 33 - 35°C. (Reported[10] 34 - 35°C.).

Preparation of Pentaerythritol Dimethyl Ether Diacetate[12]:

Pentaerythritol dimethyl ether (10 gm, 0.05 mole) was esterified with acetic anhydride according to the method described for the preparation of pentaerythritol diethyl ether diacetate (II-4-C.).

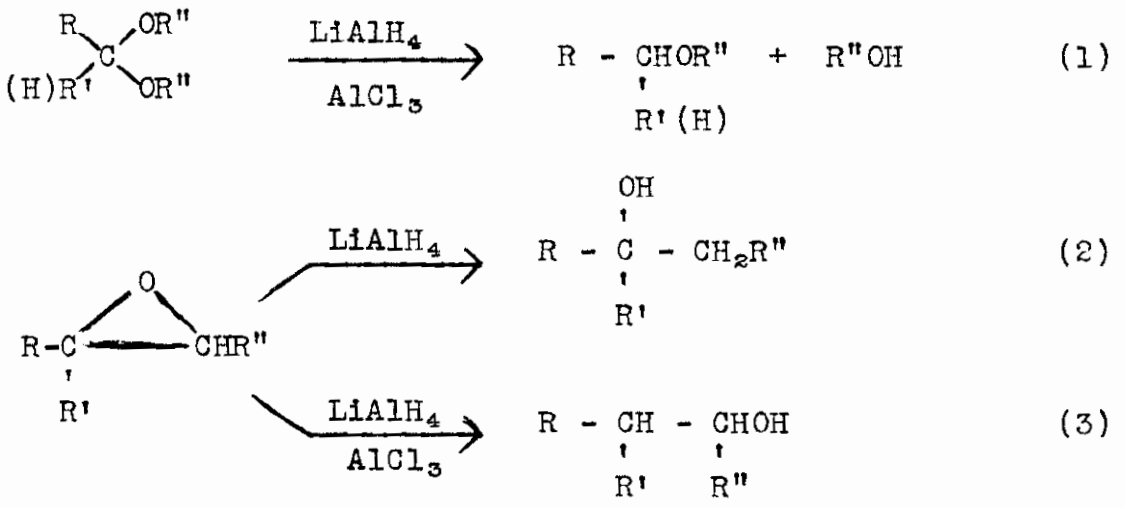
The yield of the ester boiling at 147 - 148°C./15 mm. was 11.2 gm (72% of the theoretical).

Sap. Eq. Calcd. for $C_{11}O_6H_{20}$: 124

Found: 125

DISCUSSION

Lithium aluminum hydride - aluminum chloride (LAH - $AlCl_3$) was introduced by Eliel and his coworkers[29,30] as a reagent for the reduction of acetals, ketals and their thio analogs to the corresponding ethers. (Reaction 1). In the course of their extensive studies of the "mixed hydride", the Notre Dame group also made the further discovery that the reagent is capable of effecting cleavage of epoxides in a direction opposite to the one observed when lithium aluminum hydride alone is used[31,32]. (Reactions 2 and 3).

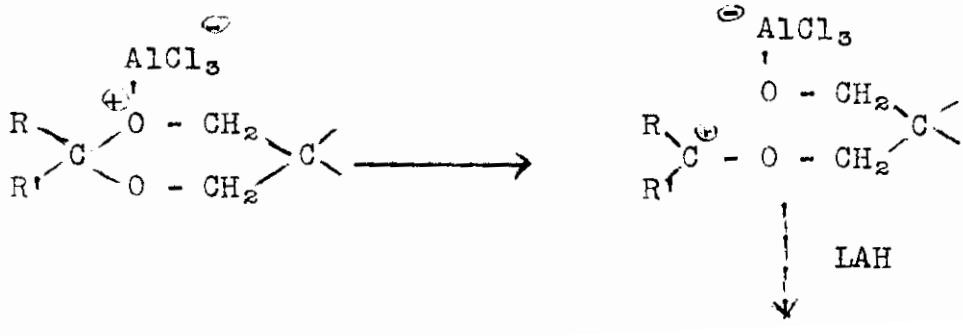


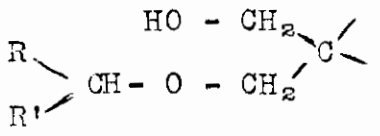
In view of the ease with which pentaerythritol forms diacetals and diketals, reduction by the "mixed hydride" appeared to offer an especially convenient route to pentaerythritol diethers.

In the course of this investigation, we have had the opportunity of using LAH - $AlCl_3$ as well as lithium aluminum

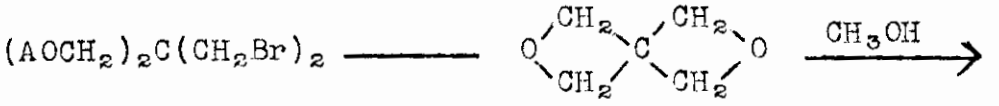
hydride - boron fluoride etherate (LAH - BF_3) as reducing agents, and found the latter to be superior. Diacetals and diketals of pentaerythritol could be reduced to the corresponding diethers in high yield by either reagent, but the yield obtained with LAH - BF_3 was consistently higher (80% - 90%). Furthermore, boron fluoride etherate was more convenient in handling and less troublesome during the final step of decomposition. The results are summarized in Table 1, page 9. While this investigation was in progress, Pettit and Kasturi[33] reported the use of LAH - BF_3 for the direct reduction of esters to ethers.

It is noteworthy and somewhat surprising that the diformal of pentaerythritol did not respond to the conditions used for the preparation of the dibenzyl, dicyclohexyl, dicyclopentyl and diethyl ethers of pentaerythritol from the corresponding diacetals and diketals (LAH - $AlCl_3$ or LAH - BF_3 in ether at reflux). Instead of the expected dimethyl ether, we recovered the starting material. Assuming the reaction to proceed by the mechanism indicated below, one possible explanation for the failure of the diformal to react is perhaps to be found in the higher energy barrier associated with the first step when the carbonium ion intermediate has R = R' = H.





The dimethyl ether of pentaerythritol (XII) was prepared from 2,6 dioxaspiro (3,3) heptane (XI) and methyl alcohol, by an extension of the method previously described[12] for the preparation of pentaerythritol monomethyl ether.



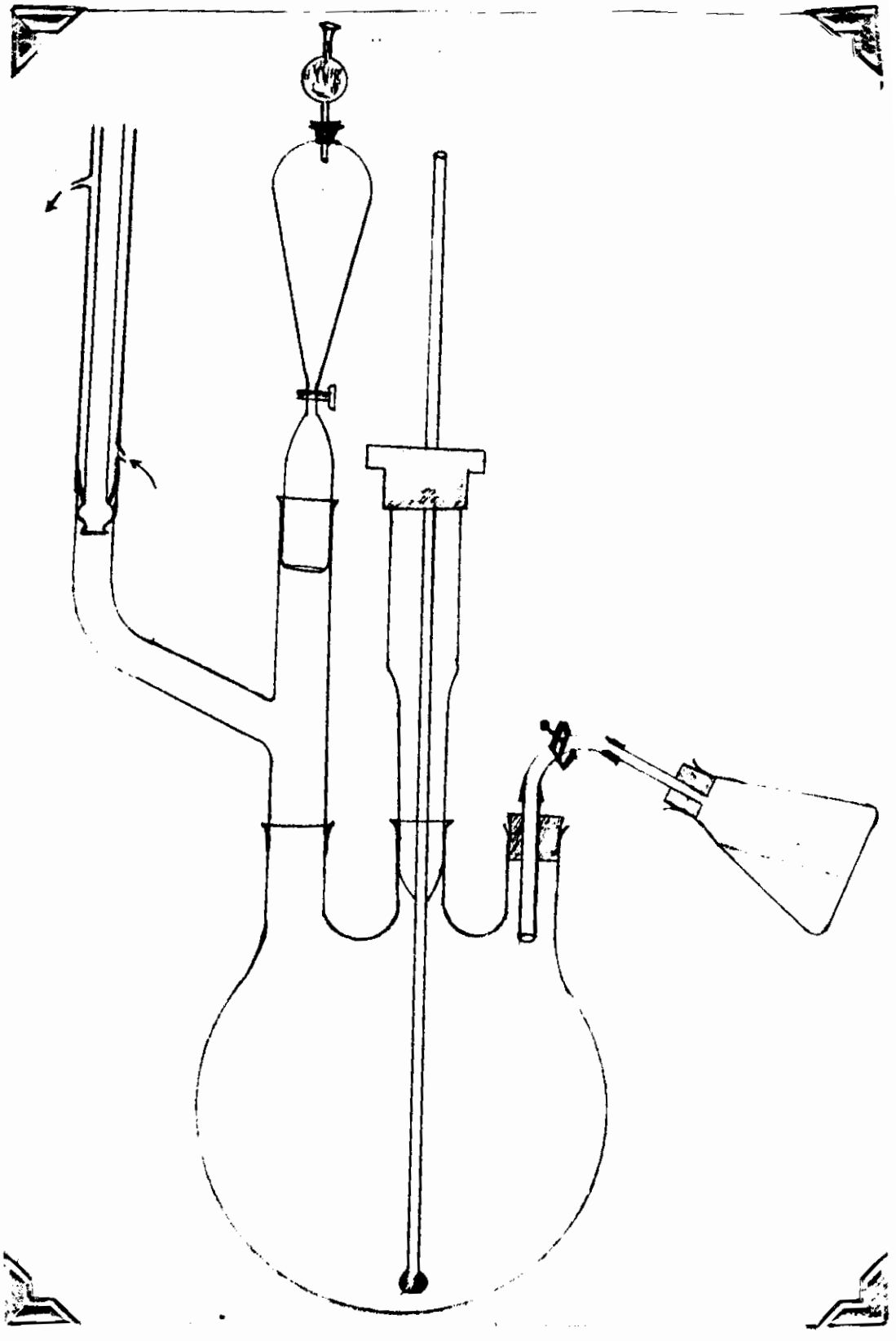
XI

$(OHCH_2)_2C(CH_2OCH_3)_2$

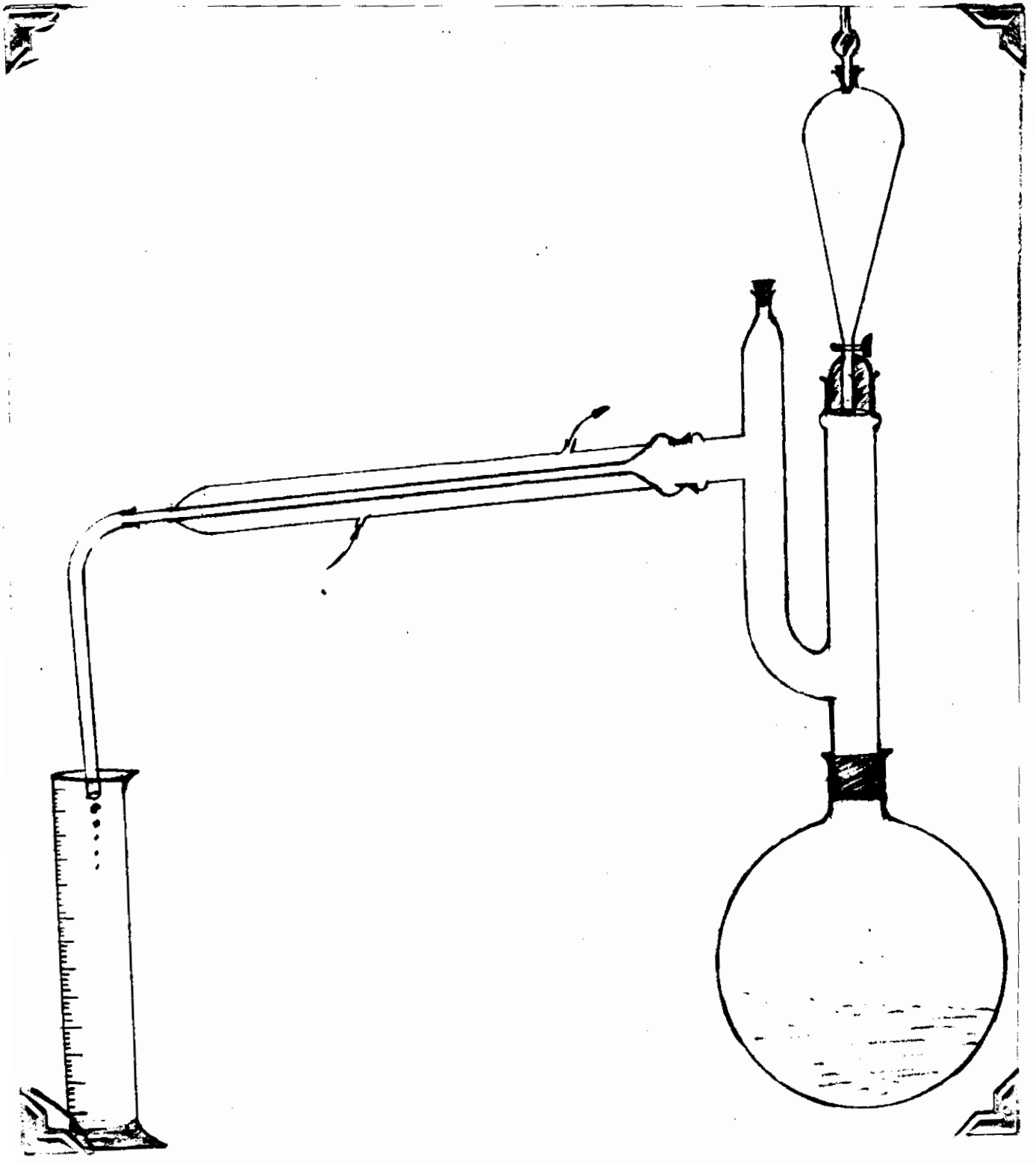
XII

This alternative route to diethers of pentaerythritol is seriously handicapped by the low yield reported in the chemical and patent literature for the preparation of 2,6 dioxaspiro (3,3) heptane (25%[13,18], 17%[11], 20%[14,16], 32%[17]). The spirocyclic oxetane (XI) and other related intramolecular ethers of pentaerythritol have been prepared by dehydrohalogenation of pentaerythritol halides, but the reaction is extremely sensitive to experimental conditions, as evidenced by the number of side products that have been reported for the dehydrohalogenation of pentaerythrityl dihalides[18,28,34]. During the present investigation we made several unsuccessful attempts to improve the yield of the spirocyclic oxetane by modifying the isolation techniques

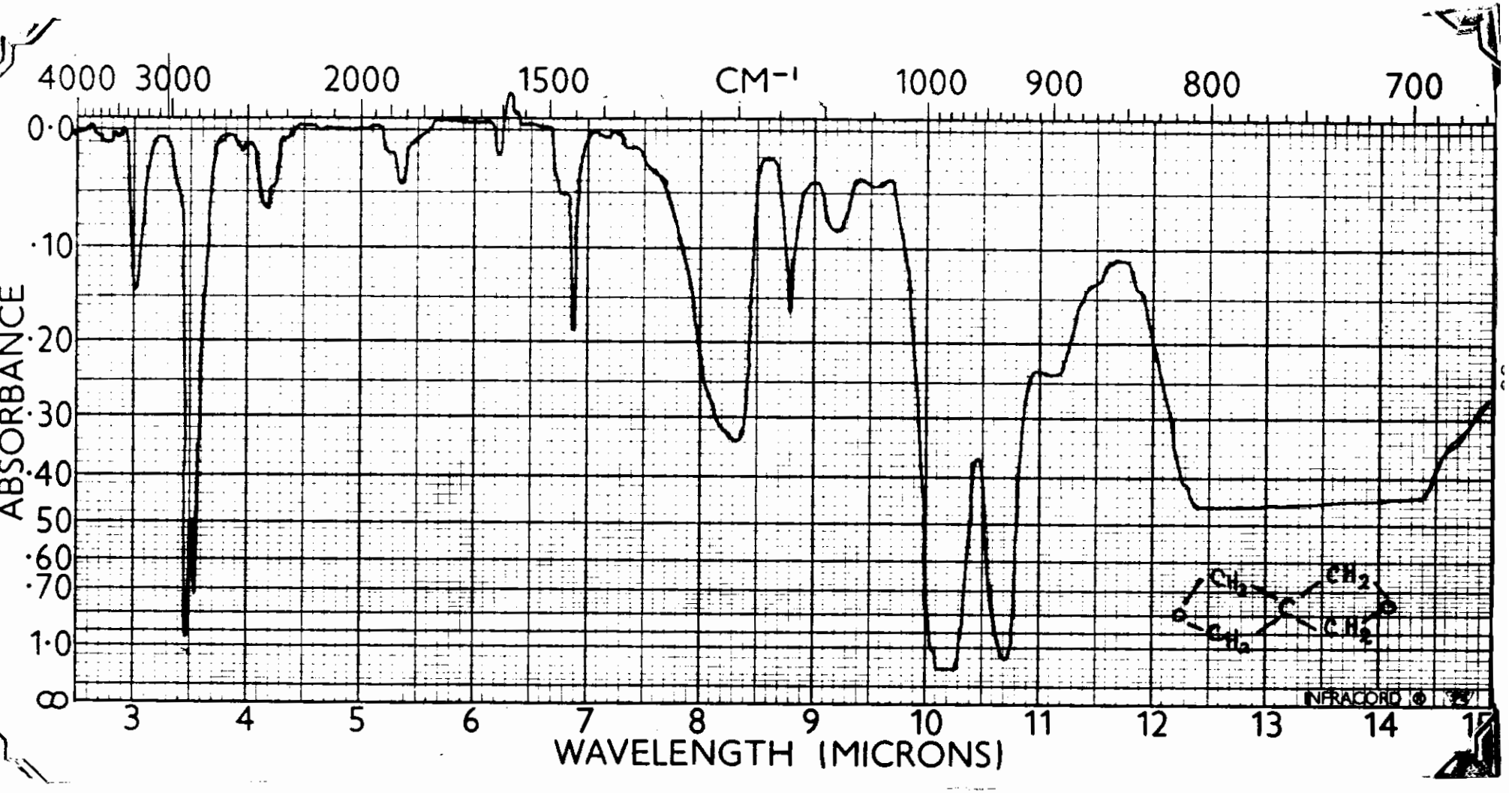
described in the literature, but the yield of (XI) never exceeded 1%. The compound was finally obtained by the simple expedient of slow addition of an ethanolic solution of pentaerythritol dibromide to a distilling solution of excess potassium hydroxide in ethanol. This procedure practically eliminates formation of oily by-products and gives (XI), after chromatography and recrystallization, in 52 - 61% yield. The compound sublimes readily and shows infrared bands at $\lambda(CHCl_3)$ 935, 980, 1210, 2820, 1130 and 1450 cm^{-1}. (Reported[35] $\lambda(CCl_4)$ 933, 981, 1222, 2820 cm^{-1}).



(Fig. 1) Preparation of Pentaerythritol Diethers



(Fig. 2) Preparation of 2,6 Dioxaspiro (3,3) Heptane.


4000 3000 2000 1500 CM⁻¹ 1000 900 800 700
0·0
·10
·20
·30
·40
·50
·60
·70
1·0
ABSORBANCE
3 4 5 6 7 8 9 10 11 12 13 14
WAVELENGTH (MICRONS)
INFRACORD

(Fig. 3)

BIBLIOGRAPH

1.- Bowman, P.I., Barth, R.J., and Burrell H. (to Heyden Chemical Corp.): U.S. Patent, v. 2, p. 401, 743 (1946).

2.- Sokol, H.,(to Heyden Chemical Corp.): U.S. Patent, v. 2 p. 527, 970 (1950).

3.- Berlon, E., Barth, R.H., and Snow, J.E., The Pentaerythritol, New York, Reinhold Publishing Corporation 1958, p. 118.

4.- Backer, H.J., and Dijken, G.: Rec. Trav. Chim, 55, 22 (1936).

5.- Dostrovsky, I., Hughes, E.D., and Ingold, G.K.,: J. Chem. Soc., 187 (1946).

6.- Glattfeld, J.W.E., and Schneider, J.M.: J. Am. Chem. Soc., 60, 415 (1938).

7.- Nichols, P.L., and Yanovsky, E.,: J. Am. Chem. Soc., 67, 46 (1945).

8.- Evans, R., and Gallaghan, J.A.,: J. Am. Chem.Soc., 75, 1248 (1953).

9.- Orthner, L., and Freyess, G., Ann., 484, 131 (1930).

10.- Wawzonek, S., and Rees, D., J. Am. Chem. Soc., 70, 2433 (1948).

11.- Wawzonek, S., and Issidorides, C.H., J. Am. Chem. Soc., 75, 2373 (1953).

12.- Issidorides, C.H., and Matar, A.I., J. Am. Chem. Soc., 77, 6382 (1955).

13.- Backer, H.J., and Keuning, K.J., Rec. Trav. Chim., 53, 812 (1934).

14.- Henriquez, P.C., Rec. Trav. Chim., 53, 1139 (1934).

15.- Köhler, R., and Pietsch, H., (to Henkel and Company, G.m.b.H.) U.S. Patent, v. 2, 764, 575 (1956).

16.- Kiyohisa, F., Yasuo W., and Ryohei O., (Kyoto Univ.) Bull. Inst. Chem. Research, Kyoto Univ., 31, 222 (1953).

17.- Henkel and Co., G.m.b.H. (Helmut Pietsch and Horstmar Nagel, inventors) Ger., 875, 804 (1953).

18.- Govaert, F., and Beyaert, M., Proc. Kon. Ned. Akad. Wet., v. XLII, No. 7, 1939.

19.- Read, J., J. Chem. Soc. 2090 (1912).

20.- Bograchov, E., J. Am. Chem. Soc., 72, 2268 (1950).

21.- Micović, V.M., and Stojiljković, (Miss) A., Tet., 4, 186 (1958).

22.- Berlow, E., Barth, R.H., and Snow, J.E., The Pentaerythritols, New York, Reinhold Publishing Corporation, p. 147.

23.- ibid., p. 122.

24.- Beyaert, M., and Hansens, M., Natuurw. Tijdschr. (Belg), 22, 249 (1940).

25.- Aprahamian, N., M.S. Thesis, Am. Univ. Beirut., 1957, p. 12.

26.- Issidorides, C.H., and Aprahamian, N., J. Org.Chem., 21, 1534 (1956).

28.- Issidorides, C.H., Gulen, R.C., Aprahamian, N.S., J. Org. Chem., 21, 997 (1956).

29.- Eliel, E.L., and Rerick, M., J. Org. Chem., 23, 1088 (1958) .

30.- Eliel, E.L., and Badding, V.G., J. Am. Chem. Soc., 81, 6087 (1959).

31.- Eliel, E.L., and Delmonte, D.W., J. Am. Chem. Soc., 78, 3226 (1956).

32.- Eliel, E.L., and Delmonte, D.W., J. Am. Chem. Soc., 80, 1744 (1958).

33.- Pettit, G.R., and Kasturi, T.R., J. Org. Chem., 875, 25, 1960).

34.- Berlow, E., Barth, R.H., and Snow, J.E., "The Pentaerythritols", New York, Reinhold Publishing Corporation, p. 126.

35.- Sirkar, S.C., and Voelz, F.L., J. Chem. Phy., 23, 1684 (1955).