THE PYRIDINE DENITRATION OF CIS- AND

TRANS-1,2-CYCLOHEXANEDIOL DINITRATES

By

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ABSTRACT

Refluxing cis- and trans-1,2-cyclohexanediol
dinitrates in excess anhydrous pyridine at 118°-120°C
lead to a slow decomposition of the dinitrates and the
formation of a gaseous product. It was found that the
trans-dinitrate decomposed 1.8 times faster than the
cis-isomer, and that no 2-nitroxycyclohexanols or
1,2- cyclohexanediols were formed. Nine components
were detected in the reaction mixture by paper
chromatography. Pyridinium nitrate, succinic and
adipic acids, and a polymer were shown to be produced
in the trans-denitration mixture. The use of
3-methylheptane in place of pyridine as solvent gave
the decomposition products: oxalic, succinic and
adipic acids, water, carbonized material, a reddish-
brown gas and unsaturated compounds. The reaction
of quinoline with the trans-dinitrate at 165°C yielded
mainly water and a pyridine soluble polymer.

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GENERAL INTRODUCTION

In recent years Hayward and coworkers have shown
that the action of dry pyridine on the hexanitrates of
mannitol and dulcitol selectively removed the 3- (or chem-
ically equivalent 4-) nitrate group. A similar partial
denitration of the pentitol pentanitrates was also observed.
The relative rates of these reactions appeared to be a function
of the configuration of the acylic molecules.

In an attempt to determine the required stereo-
chemical relationship between nitrate groups for selective
denitration, cis- and trans- 1,2-cyclohexanediol dinitrates
of known configuration were selected for study. As these
isomers may have different conformations, it was expected
that they would show some selectivity and difference in
reactivity toward pyridine.

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HISTORICAL INTRODUCTION

A. Selective Denitration of Polynitrate Esters

Wigner in 1903 (71) observed that alcoholic pyridine reacted with mannitol hexanitrate to give a pentanitrate, but that the reagent had no effect on dulcitol hexanitrate even at the boiling point. On the other hand, he found that warm, dry pyridine caused a reaction accompanied by evolution of a gas and the formation of dulcitol pentanitrate. This work was confirmed by McKeown and Hayward in 1955 (44) who showed that the denitrating action of the pyridine is specific to the 3- (or equivalent 4-) position of the dulcitol hexanitrate.

Hayward (31) had earlier shown that D- mannitol -1,2,3,5,6- pentanitrate was obtained by pyridine reaction on D- mannitol hexanitrate at room temperature. No inversion of configuration occured in these selective reactions.

The gas produced from the D- mannitol hexanitrate was analyzed by Brown and Hayward (14). From a 0.368M solution of the hexanitrate in pyridine at $30 \pm 5^{o}C$, a gas consisting of nitric oxide, nitrous oxide, and nitrogen was evolved. The amount and composition of the gas mixture were sensitive to traces of moisture in the pyridine. Establishment of a material balance for the reaction indicated that approximately two moles of pyridine suffered ring cleavage while 0.25 moles of hexanitrate was completely denitrated and 0.75 moles of pentanitrate was found.

Elrick and collaborators (23) have recently shown that

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treatment of D-mannitol hexanitrate with an aqueous acetone
solution of ammonium carbonate also gave a good yield of the
same D-mannitol pentanitrate.

Tichanowitsch (59) in 1864 had obtained a pentanitrate
of mannitol by passing dry ammonia gas into an etheral solution
of mannitol hexanitrate.

Bowering in 1956 (12) found that the newly synthesized
allitol hexanitrate reacted more slowly with dry pyridine at
room temperature than the corresponding D-mannitol derivative,
and produced pyridinium nitrate but no gaseous products. A 76%
yield of an oily product which was thought to be the pentanitrate
was obtained.

Wright (70) in 1957 synthesized and identified the
new explosive compounds xylitol, ribitol and L-arabitol penta-
nitrates. These crystalline compounds reacted with dry pyridine
in much the same manner as the hexitol hexanitrates. The xylitol
derivative evolved more gas and gave a reaction mixture darker
in color than those obtained with the arabitol and ribitol com-
pounds. Partially denitrated syrups were recovered from each
of the three pyridine solutions on dilution with water.

Jackson (35) in 1957 prepared the dinitrates of the
three known 1,4 : 3,6- dianhydrohexitols (isomannide, iso-
sorbide and isoiodide) and tested their reaction with pyridine.
Isomannide dinitrate was found to react more rapidly than iso-
sorbide dinitrate, and the latter faster than isoiodide dinitrate.
The investigation of the reaction products is still going on.

The action of pyridine on nitrocellulose has also been

studied. Angelis(2) found that pyridine-moistened nitro-
cellulose gave an 80% yield of the original weight of nitro-
cellulose with a nitrogen content reduced from an original 12%
to 9-10% nitrogen indicating decomposition. Giannini (26)
extended this work in 1924, and showed that a gas containing
carbon dioxide, nitric oxide, nitrous oxide, and nitrogen was
given off.

In 1944 Gladding and Purves (28) found that pure, dry
pyridine caused a vigorous decomposition of dissolved, stabil-
ized gun-cotton at 100°C.

Pyridine-induced elimination reactions were shown to
occur by Lawe (39) in 1953. Secondary and tertiary nitrates
refluxed with pyridine formed olefins. Thus cyclohexyl nitrate
and tertiary butyl nitrate gave cyclohexene and butylene
respectively. Primary nitrate esters formed quaternary ammonium
salts (26,39)

Ryan and Casey (54) in 1928 studied the effect of
primary, secondary and tertiary amines on various carbohydrate
nitrate esters. Dimethylaniline reacted with mannitol hexanitrate
at an elevated temperature to evolve a gas consisting of 70%
nitrous oxide and 30% nitrogen. Tertiary aliphatic amines
reacted at reflux temperatures with primary nitrate esters to
form quarternary salts (26,39)

In 1946 Segall (55) showed that excess hydroxylamine
in pyridine at room temperature acted on cellulose trinitrate to
give a cellulose dinitrate with the evolution of one mole of
nitrogen per mole of an-hydroglucose. The nitrate groups

attacked proved to be secondary in nature. The product was stable to pyridine. Methoxylamine reacted similarly except that no nitrogen was evolved. With excess hydroxylamine hydrochloride the product appeared to be a cellulose ketoxime dinitrate and the gas evolved consisted of 85% nitrous oxide and 15% nitrogen.

Falconer and Purves (25) recently showed that the hydroxylamine-pyridine solution at room temperature reacted with cellulose trinitrate to give cellulose - 3,6- dinitrate, a base stable compound.

Hayward (32) investigated the action of free hydroxylamine in pyridine on methyl-α- and β-D-glucopyranoside tetranitrates. He found that an alcoholic solution of hydroxylamine had little or no effect on these compounds, but that a vigorous exothermic reaction ensued on addition of hydroxylamine in anhydrous pyridine to methyl-β-D-glucoside tetranitrate. Nitrogen gas was evolved in the ratio of 1.3 moles per mole of tetranitrate, and the product contained methyl-β-D-glucoside-2,3,6-trinitrate (53%), methyl-β-D-glucoside-3,6-dinitrate (33%), and an unidentified methyl-β-D-glucoside trinitrate.

Rooney (53) showed that methyl-β-D-glucopyranoside tetranitrate reacted slowly with hydroxylamine hydrochloride in pyridine at room temperature and evolved a gas composed of 70% nitrous oxide and 30% nitrogen. The syrupy products obtained consisted of a mixture of partially nitrated methyl-glucosides and completely denitrated polyoxime products.

Methyl-β-D-glucopyranoside-2,3,6-trinitrate and a substance
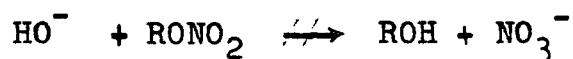believed to be methyl-β-D-glucopyranoside-2,6-dinitrate were
isolated.

When simple alkyl nitrate esters were heated with
ammonia, or primary or secondary aliphatic amines, N-alkylation
occurred. Piperidine (27) and diethylamine have been alkylated
by heating with primary, secondary, and tertiary alkyl nitrates.

The action of quinoline on methyl-β-D-glucoside
tetranitrate was also investigated by Swan (58). Some de-
nitration occurred accompanied by evolution of a gas.

B.   Mechanism of Denitration

Recent studies (5,6,41) have established the simul-
taneous occurrence of three distinct reactions in the alkaline
cleavage of nitrate esters. These reactions, illustrated with
hydroxide ion, are as follows:

(a) Nucleophilic substitution

$$HO^- + RONO_2 \longrightarrow ROH + NO_3^-$$

(b) Elimination of β-hydrogen

$$HO^- + R\text{-}CH_2CH_2ONO_2 \longrightarrow RCH = CH_2 + H_2O + NO_3^-$$

(c) Elimination of α - hydrogen

$$HO^- + RCH_2ONO_2 \longrightarrow RCH = O + H_2O + NO_2^-$$
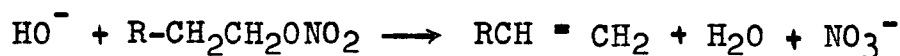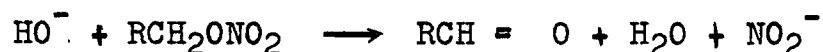
Neutral hydrolysis occurs too, where water acts as a nucleo-
philic agent.

$$HO^- + -\overset{|}{\underset{|}{C}}- X \longrightarrow HO-\overset{|}{\underset{|}{C}}- + X^-$$

where X = ONO_2 or a halogen.

However, in alkaline hydrolysis there is some retention of configuration in going from nitrate to alcohol. The most reasonable mechanism appears to be that involving cleavage of the O-N bond, analogous to the usual acyl-oxygen cleavage in carboxylate esters (22).

A base independent carbonium ion process (SN1) is also available. This was shown to take place in alcohol-producing hydrolyses of tertiary butyl nitrate and partially in the neutral hydrolysis of isopropyl nitrate (5).

Olefin-formation occurs must extensively in the hydrolysis (either neutral or alkaline) of tertiary butyl nitrate (5,41) but small amounts of olefin are found in the alkaline hydrolyses of ethyl (2%) and isopropyl (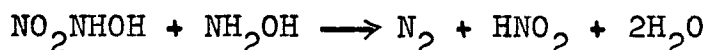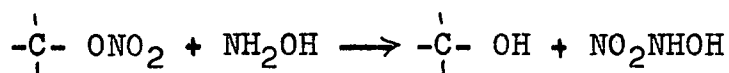10%) nitrates (5). It has been definitely established that NO_2^- is formed directly from the nitrate ester, and is not the result of a secondary reaction in which alcohol is oxidized to aldehyde (5).

It appears that pyridine, and mixtures of pyridine and hydroxylamine, and other amines, cause nitroxy-bond cleavage of nitrate esters. Segall in 1946 (55) postulated the following reaction on the basis of the labile hydrogen atom in hydroxylamine:

$$-\overset{|}{\underset{|}{C}}- ONO_2 + NH_2OH \longrightarrow -\overset{|}{\underset{|}{C}}- OH + NO_2NHOH$$

$$NO_2NHOH + NH_2OH \longrightarrow N_2 + HNO_2 + 2H_2O$$

Hayward and coworkers (31,32,44) and Rooney (53) showed that no inversions occurred in the denitration reactions with pyridine, and pyridine and hydroxylamine mixtures.

In the thermal decomposition of nitrate esters, most investigators agree that the initial step is the scission of the nitroxy bond to give NO_2 and an alkoxyl radical (RO·) (3,50, 40,68). Thermal decomposition of cellulosenitrate produced carbon monoxide, carbon dioxide, nitric oxide, nitrous oxide, nitrogen dioxide, nitrogen, methane, hydrogen, water and formaldehyde (68). Working at 30 mm pressure Wolfrom (68) reported water, formic acid, formaldehyde, glyoxal and carbonyl compounds as the main thermal decomposition products. He suggested that the initial product at any pressure was a fragmented oxycellulose nitrate. The highter the ambient pressure, the greater was the proportion of this initial product undergoing additional degradation. As the pressure increased above 60 mm., all the fragmented oxycellulose nitrate disappeared and the rate of change in the yields of the organic products with pressure decreased, producing a range of pressure (200-500 mm.) in which the yields were almost pressure independent. The value for the total carbonyl, however, decreased steadily with pressure which could, he explained, be due to the further oxidation of formaldehyde, glyoxal and formic acid, and that the three latter compounds were produced by the further degradation of the more complex entities (trioses, etc.). The possible mechanisms are shown below:
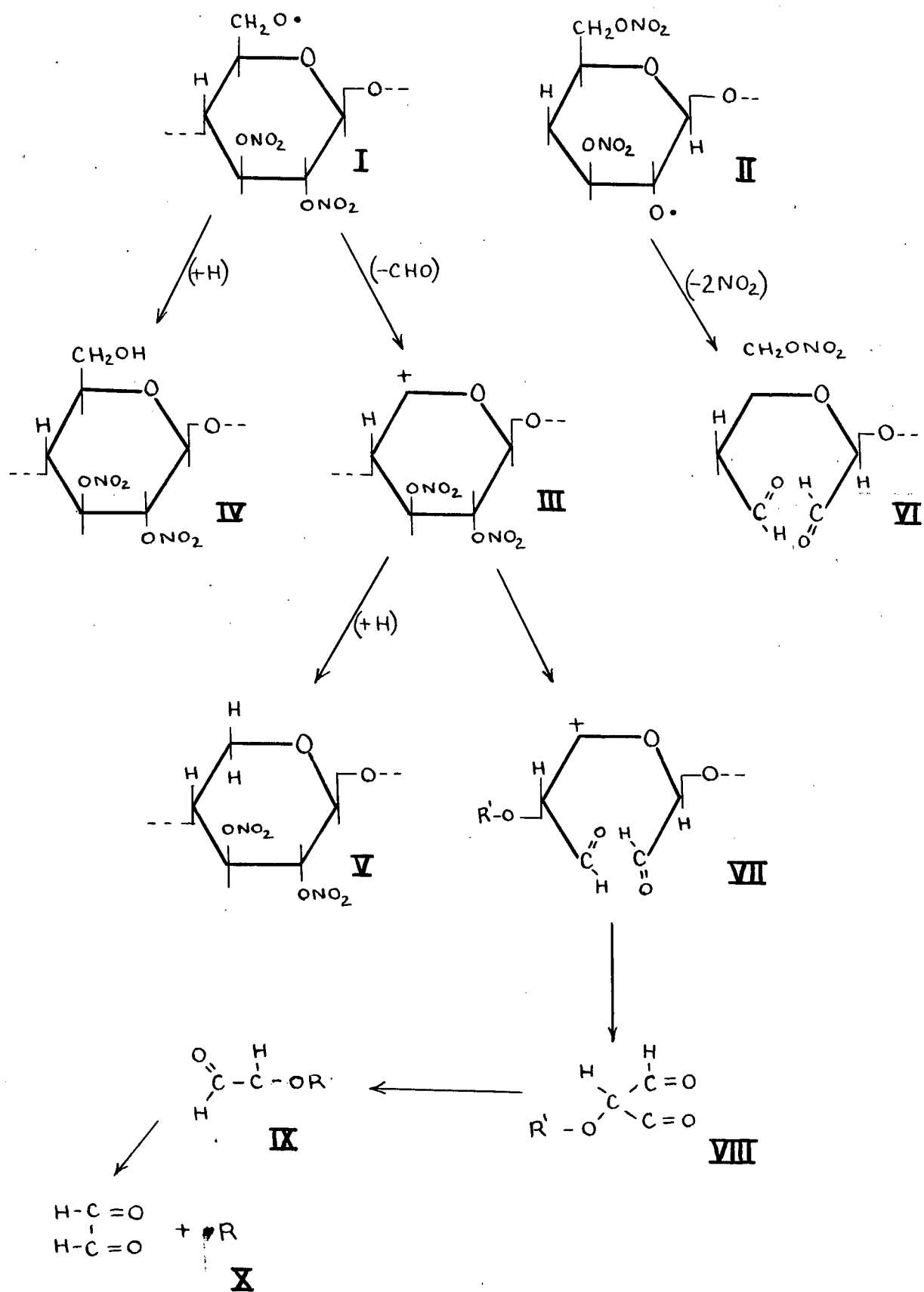
With vicinal dinitrates, Kuhn and Angelie (38) showed that cis- and trans-1,2- cyclohexanediol dinitrates in vapour form were degraded at 260° - 280°C to higher than 70% yields of adipaldehyde and nitric oxide. They proposed the following mechanism:

$$RCH(ONO)-CH(ONO)R \longrightarrow RCH(O\cdot)-CH(ONO)R + NO$$

$$2\ RCHO + NO.$$
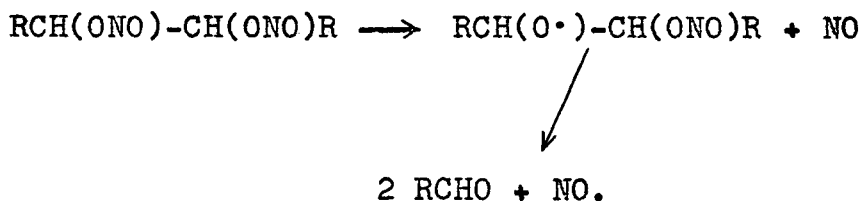
In the liquid state and in a nitrogen atmosphere, 70% of the decomposed trans-1,2-dinitrites could be identified as aldehyde, dialdehyde, diol and α-hydroxy-ketone.

C.   Conformational Studies of 1,2-Cyclohexane Derivatives

It is well known that a relationship exists between the conformation of cyclohexane derivatives and their physical properties. (Auwers-Skita Rule). Pitzer and Beckett (49) and later workers (1,8) have shown that for cis - trans-pairs of disubstituted cyclohexanes, the isomer which has the higher index of refraction and the higher density is the isomer with the lowest conformational stability.

It was shown by Ottar in 1947 that both axial and equatorial oxygen atoms exist in both the cis- and trans-cyclohexane-1,2-diols. The diaxial conformation is understood to predominate in the case of the trans-diol (Pitzer, Review 1956).

In 1950, Smith and Byrne (56) showed that the relative

rates of esterification of cyclohexane-1,2- dicarboxylic acids depend on the geometrical and positional arrangement of the carboxyl groups, particularly on the number of equatorial groups available for reaction. From the rate constants obtained for acid-catalyzed esterification, the cis- isomer was found to be esterified twice as fast as the trans- isomer. It was concluded that the trans- isomer had an axial-axial conformation, whereas the cis-acid was axial-equatorial.

Kilpatrick and Morse (36) in 1953 showed that the dissociation constant of an acid depended upon the structure of the molecule and was a function of the orientation and spatial interaction of dipolar groups and the distance of the dipolar centers from the ionizable proton. The trans-1,2- cyclohexane-dicarboxylic acid and the trans- -1- hydroxy-cyclohexane -2-carboxylic acid were stronger in water than the corresponding cis-isomers, but weaker in solvents of lower dielectric constants (methanol, ethanol, and ethylene glycol). It was concluded that the more stable configuration was the one in which the distance between the groups was largest, thus favoring the axial-axial conformation over the equatorial-equatorial for the trans- isomer. Hence, the trans- isomer was diequatorial in water, but diaxial in non-aqueous solvents.

Pascual (48) in 1949 showed that the differing reactivity of the hydroxyl and carboxyl groups in 1- hydroxycyclohexane -2-carboxylic acid must be related to the conformation. The trans-isomers were found to be less reactive than the cis - isomers. These differences were ascribed to the relatively greater ease of

esterification and hydrolysis of an equatorial as compared with an axial substituent.

The trans-isomers of 1,2- dihalocyclohexane were shown to exist as equilibrium mixtures of the diaxial and the diequatorial conformations (10). Tulinskie and collaborators (62) found that the dipole moment of trans-1,2- dichlorocyclohexane at $40^{\circ}C$ in benzene solution almost equalled that in vapour state at $239^{\circ}C$, showing an absence of any appreciable shift to another form of different moment with change of temperature and molecular environment. The trans- 1,2- dichlorocyclohexane was estimated to have 56% equatorial-equatorial form in the gaseous state ($239^{\circ}C$) and 72% in benzene at $40^{\circ}C$.

D. Elimination Reactions of 1,2- Cyclohexane Derivatives

The elimination of tosyl (p- toluenesulfonyl) groups from the cyclohexane ring has been studied in some detail.

The most common reactions of esters of sulfonic acids are nucleophilic displacements, by the SN1 and SN2 mechanisms, at the alkyl carbon atom. Nucleophilic attack on sulfur is not observed unless the reactivity at the alkyl carbon atom is markedly decreased. Bunton and Frei (16) in 1951 showed that the alkaline hydrolysis of phenyl-p-toluenesulfonate in H_2O^{18} solution introduced the O^{18} atom into the p- toluene sulfonate but not the phenolate.

$$C_7H_7-SO_2-OC_6H_5 + H_2O^{18} \longrightarrow C_7H_7SO_2O^{18}H + C_6H_5O^-$$
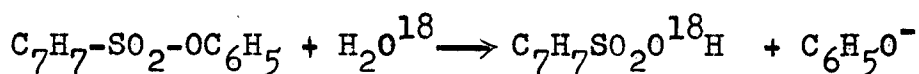
Detosylation in carbohydrates with sodium iodide in acetone solution was found by Oldham and Rutherford in 1932 (47) to be restricted to the primary tosylate groups. Some exceptions (11,61,46) to this generalization have been reported, and it now appears that a secondary tosylate group may be reactive towards sodium iodide if it is contiguous to one in a primary position. There are also a few cases (34) of an isolated secondary tosylate reacting with sodium iodide. Quite recently Tipson, Clapp and Cretcher (60) have shown that the tosylate group of some secondary aliphatic alcohols, and of cyclohexanol, borneol, and menthol, reacted with sodium iodide to form sodium tosylate. Evidently the secondary tosylate groups in these compounds are considerably more reactive than are similar groups in a carbohydrate molecule. The other products of the reaction were not identified.

Clark and Owen (17) in 1949 found that the trans -2-hydroxycyclohexyl-p-tolvene sulfonate reacted readily with sodium iodide in acetone solution at 85°C to give after five hours a high yield of sodium tosylate and trans-2-iodocyclohexanol.

Winstein and Buckles (64,65) in 1942 showed that trans-1-bromo-2-acetoxycyclohexane and trans -1,2- dibromocyclohexane with silver acetate in dry glacial acetic acid produced trans-diacetates, whereas with the presence of small amounts of water inversion took place. They also observed that cis-2-chlorocyclo-hexylacetate was unaffected by silver acetate under conditions in which the trans-isomer readily gave trans-diacetate. These workers attributed the low reactivity of the cis- derivatives to its inability to form an intermediate ring compound.

In 1948, Winstein and coworkers (67) studied the rates of acetolysis of tosyl-oxycyclohexane, I, trans-2-acetoxytosyloxy-cyclohexane, II, and cis-2-acetoxytosyloxycyclohexane, III, in glacial acetic acid. They showed that the relative reactivities were: I, $1 \cdot 00 > $ II, $0 \cdot 30 \gg$ III, 4.5×10^{-4}. Also, the trans-2-acetoxy-p-bromo-benzenesulfonoxycyclohexane was found to be 630 times more reactive than the corresponding cis-isomer. Both acetolyses yielded the trans- diacetate. In order to correlate the observed reactivities, Winstein and coworkers suggested that the reaction of the trans-2-acetoxycyclohexyltosylate, I, proceeded by way of a one-stage ring closure mechanism to yield the acetoxonium ion, II, and that this process involved a much more favourable free-energy of activation than does the formation of the ion, III, by dissociation of the cis- ester, IV, for which participation of the neighbouring acetoxy group would involve prohibitive strain.

III

IV

OTs O-C(=O)CH$_3$

O-C(=O)CH$_3$ OH
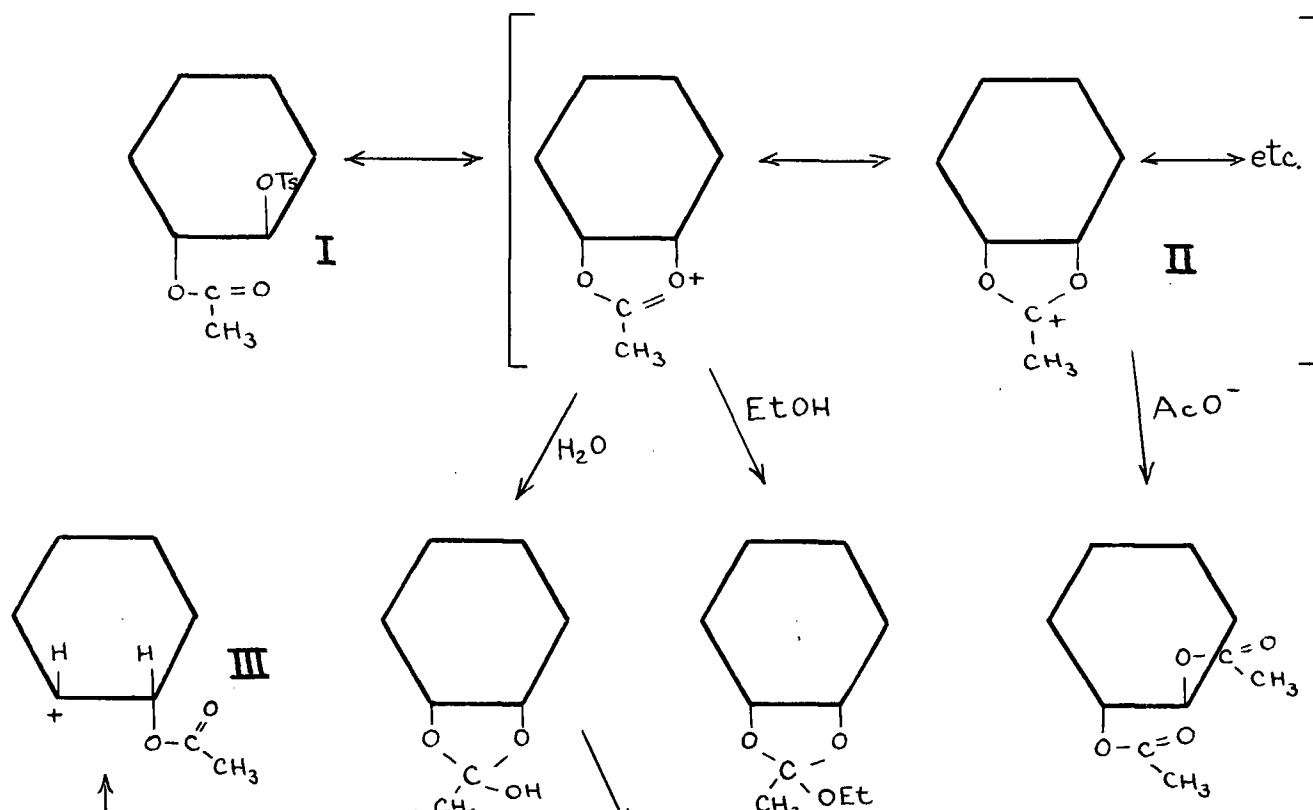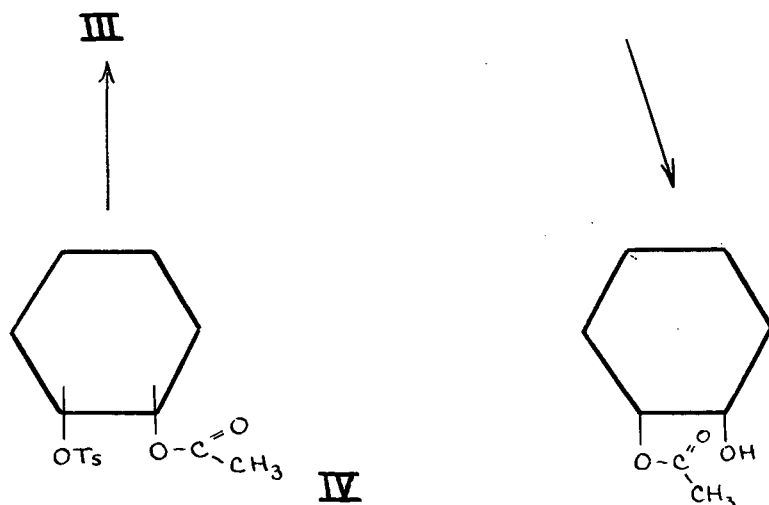
Furthermore, the participation of neighbouring groups in the replacement reactions were calculated to be in the order of decreasing activity as follows: $I > OAc. > Br > OCH_3$. Neighbouring chlorine atom or hydroxy group showed little tendency for participation and in these cases the rate – determining ionization was predominantly the formation of the open carbonium ion.

H AS+

H

H+ AS

H

where AS = I, OAc, Br, OCH_3, Cl, OH. In cis- and trans-1,2- dibromobenzenesulfonoxycyclohexane, the rate constants for acetolysis was found to be equal. Therefore, Winstein concluded, the arenesulfonoxy groups were inaffective in this participation.

Clarke and Owen (17) in 1949 supported the views of Winstein and coworkers (67) in intermediate ring formation in

their observations of the much greater reactivity of the trans-2-hydroxycyclohexyl-p-tolvene sulfonate and trans-2-hydroxycyclohexyl-methane sulfonate toward alkali, sodium iodide and lithium chloride as compared to the cis- derivatives. The trans- compounds with alkali, sodium iodide or lithium chloride gave cyclohexene oxide, trans-2-iodocyclohexanol or trans-2-chlorocyclohexanol respectively. The cis- compounds, with alkali, gave cyclohexanone, and with the aqueous reagent, cis-cyclohexane -1,2-diol, and reacted only slowly with sodium iodide or lithium chloride. Replacement of the sulfonyloxy group in the trans- series resulted in overall retention of configuration, probably as a result of two successive inversions, whilst in the cis- series, where formation of an intermediate cyclic compound was less likely, a single inversion occurred.

Cristol and Franzus (19) in 1957 studied the rate constants for acetolysis of cis- and trans -2-nitroxy-p-tolvene-sulfonoxycyclohexane, and cis- and trans-2-nitroxybromobenzene-sulfonoxycyclohexane in acetic acid at 88°C. They found that the trans-isomers were less than twice as reactive as the corresponding cis-isomers, and very much less than the corresponding acetoxy compounds studied earlier by Winstein (67). The affect of the nitroxy groups seemed to be limited to their inductive effect (similar to the cis-acetoxy and the arenesulfonoxy groups of Winstein (67)) which thus slowed down the rate significantly. An intermediate, such as the one shown below may have been formed.
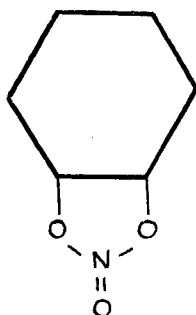
The elimination process may be stereospecific, but, in certain cases at least, is not the rate determining step of the overall reaction. Cristol and coworkers (20) in 1956 found that the elimination with sodium iodide in n-propyl alcohol at $70^{o}C$ of trans-1,2-dibromocyclohexane, trans-2-bromocyclohexyl-p-toluene sulfonate, and trans-2-bromocyclohexyl-p-bromobenzene-sulfonate followed the reactivity ratios of 1:23:90 respectively. This appeared to be consistent with the concerted elimination process of equation I, where the carbon-X bond is broken.
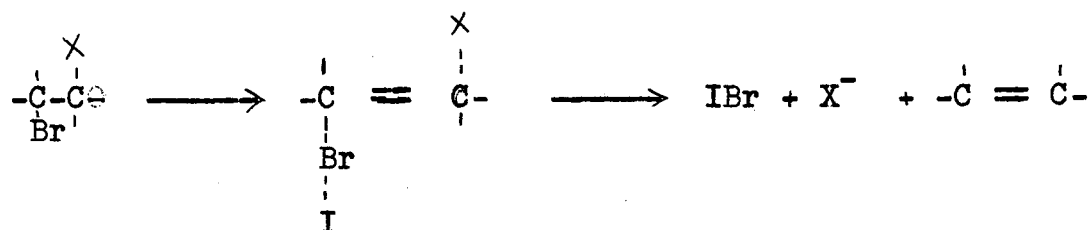
where X = OTs, Br, OBs.

A reasonable path for the overall slow cis- elimination was postulated as follows:
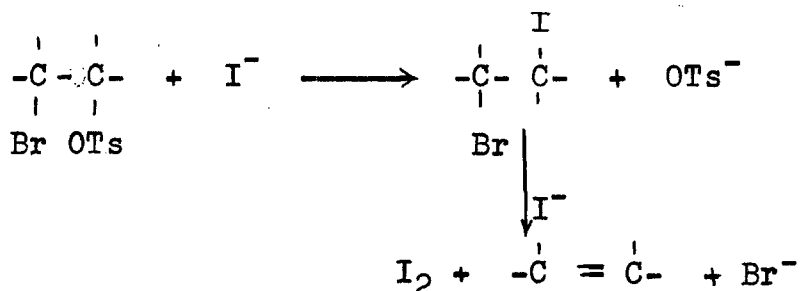
Cis- and trans-2-bromocyclohexyl nitrates were found to have the same rates of elimination and were also much slower as compared to the cis- arenesulfonate derivatives. Assuming that the rate-determining step in either case involved displacement of either bromide or nitrate (more likely bromide) by iodide, then, according to Cristol and coworkers, the following mechanism was possible.

$$\begin{array}{ccc}
-\!\overset{|}{\underset{Br}{C}}\!-\!\overset{|}{\underset{ONO_2}{C}}\!- & \xrightarrow[\text{slow}]{I^-} & -\!\overset{|}{\underset{I}{C}}\!-\!\overset{ONO_2}{\underset{|}{C}}\!- \;+\; Br^-
\end{array}$$

(trans-iodo)

I^- rapid

$$I_2 \;+\; -\!\overset{|}{C}\; =\; \overset{|}{C}\; -\; +\; Br^-$$

$I^- \uparrow$ fast

and $\quad -\!\overset{ONO_2}{\underset{Br}{C}}\!-\!\overset{|}{C}\!- \quad \xrightarrow[\text{slow}]{I^-} \quad -\!\overset{|}{\underset{I}{C}}\!-\!\overset{|}{\underset{ONO_2}{C}}\!-$
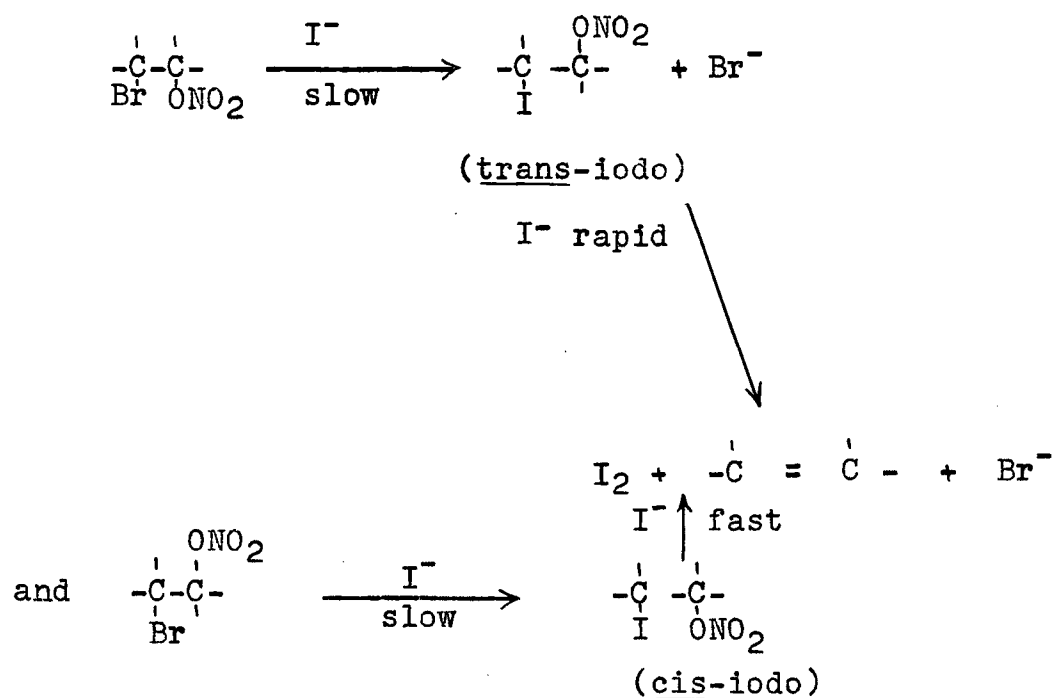
(cis-iodo)

The cis-iodo compound resulting from displacement on the trans-isomer might be expected to epimerise with iodide ion in a relatively fast process and thus render unimportant the question of whether a cis- or a trans- iodo compound was formed. The lower rate constants of the nitrate esters were thought to be due to the relative ineffectiveness of nitrate as a displaceable group compared with bromide or arenesulfonates (in trans-

elimination), or that of bromide or nitrate compared with arene-sulfonate (in the first step of the process with the cis- isomers). The concept of displacement preceding certain eliminations in these cyclic systems finds considerable support in recent work of Hine and Brader (33) .

Ring contraction where a cyclohexane ring contracts to a cyclopentane ring was studied by Barton (7) in 1950. A 1,2-shift occurs in which the ring bond plays the part of the migrating group. Only an equatorial substituent can form part of the trans- system necessary for such a 1,2-shift to occur.

The rearrangements of 2-amino-cyclohexands have been studied by Pollack and Curtin (51) and McCasland (43). The possible conformations of the cis- and trans- compounds are shown in (I) and (II).

I

II
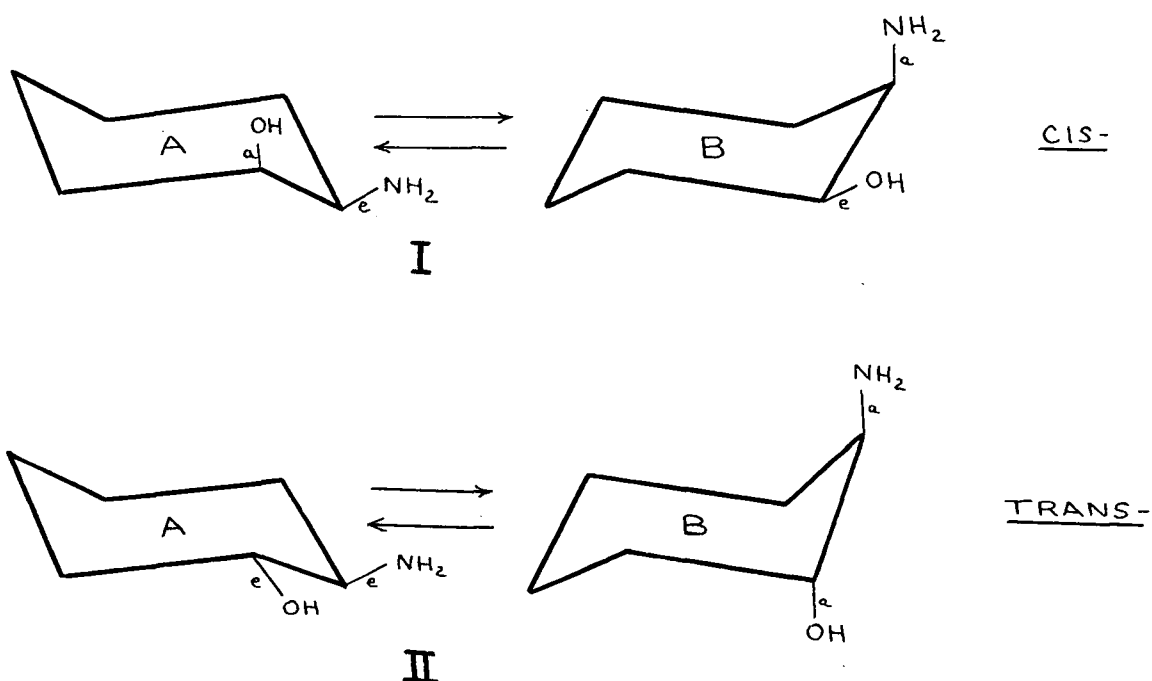
McCasland (43) in 1951 found that the trans-2-amino-cyclohexanol on treatment with nitrous acid gave a high yield of cyclopentylmethanol, which indicated that (II) reacted as (IIA) (equatorial-equatorial), and not as (IIB) (axial-axial). The cis-2-aminocyclohexanol (I), however, yielded a mixture of the cyclo-entylmethanol and cyclohexanone indicating that it reacted partly as (IA) and partly as (IB). An axial-axial conformation would give an epoxide. This work and the work of Barton in 1950, explained the formation of an epoxide and a Ketone in Clarke and Owen's (17) work of 1949.

Although most of the trans-1,2-di-substituted cyclohexane compounds illustrated here were found to be much more reactive than the corresponding cis-isomers, a few exceptions did occur. The rates of acetolysis of cis- and trans-2-nitroxybromobenzenesulfonoxycyclohexane were very much less than the corresponding acetoxy compounds, and it seemed that the inductive effect of the nitroxy groups were responsible. The rates of elimination with sodium iodide of cis- and trans-2-bromocyclohexylnitrates were found to be the same, and were also much slower as compared to the cis-arenesulfonate derivatives. The nitrate seemed to be ineffective here as a displaceable group.

DISCUSSION OF RESULTS

A. cis- and trans- Cyclohexanediol Dinitrates

These compounds were prepared so that their behavior with pyridine could be investigated and compared with the results of previous investigations of the pyridine-denitration reactions. (31,39,44)

trans-1,2-Cyclohexanediol dinitrate was first synthesized in 1951 by Christian and Purves (18) by the nitration of the trans-1,2-cyclohexanediol. Their compound had m.p.18.5° - 19°C. Soffer and coworkers (57) and Brook and Wright (13) reported b.p.92° - 93°C at 1 mm. and n_D^{27} 1·4732, and b.p. 118°C at 5.5 mm. and n_D^{20} 1·4756 respectively. The trans- dinitrate prepared for this work was a colorless oil with b.p.66° - 67°C at o.03 mm. and $n_D^{27·5}$ 1·4732.

cis- 1,2- Cyclohexanediol dinitrate was also originally made by Christian and Purves (18) by the nitration of the cis-1,2-cyclohexanediol in a nitric-sulfuric acid mixture at o°C (m.p. 24.5° - 25°C). Soffer and coworkers (57), using a nitric-acetic acid-acetic anhydride mixture, obtained an oil after vacuum distillation of the crude product, b.p. 106° - 108°C at 1 mm. and n_D^{27} 1·4758. The cis- dinitrate was prepared for this work according to Soffer's method and had b.p. 106° - 108°C at 1 mm. and n_D^{27} = 1·4757.

B. cis- and trans- 2-Nitroxycyclohexanols

Since cis- and trans- 2-nitroxycyclohexanols were likely

products in the pyridine reaction on the corresponding dinitrates, samples of these compounds were synthesized by established methods.

trans- 2-Nitroxycyclohexanol was first prepared by Brook and Wright (13) in 1951 by a 100% nitric acid nitration of 1,2-epoxycyclohexane. Their product was obtained as a colorless oil (55% yield) with b.p. 100° - $105^{\circ}C$ at 3.5 mm. and n_D^{20} 1.4789. The trans- 2-nitroxycyclohexanol prepared for this work was made by treating trans- 2-bromocyclohexanol (64) with silver nitrate in dry acetonitrile at $0^{\circ}C$. After distillation (b.p. $78^{\circ}C$ at 0.75 mm.), the oil readily crystallized out in the cold to a colorless solid (m.p. 29° - $31^{\circ}C$)

cis- 2-Nitroxycyclohexanol was prepared for this work before the synthesis of Cristol and Franzus (19) appeared in the journals in 1957. cis- 1,2- Cyclohexanediol was partially acetylated by the method of Winstein (65) to give a colorless oily product after vacuum distillation. (b.p. $103^{\circ}C$ at 4.5 mm. and $n_D^{24.5}$ 1.4572). This oil is believed to be a mixture of the monoacetate and the diacetate (19,65). Nitration of this product at $-10^{\circ}C$ in a nitric acid-phosphorus pentoxide mixture yielded a colorless oil (b.p. $93^{\circ}C$ at 1.3 mm. and $n_D^{24.5}$ 1.4537). Cristol and Franzus (19), using a nitric-sulfuric acid mixture at $-70^{\circ}C$ obtained a colorless oil after distillation with b.p. 68°-$73^{\circ}C$ at 0.5 mm. These products probably contained some diacetate. Deacetylation of the cis- 1-acetoxy-2-nitroxycyclohexane was carried out in dilute barium methylate-methanol solution. Cristol and Franzus (19) using a 1.4M-sodium hydroxide

solution in 75% ethanol, and obtained a 54% yield of a colorless oil with b.p. 63°C at 0.3 mm. and n_D^{20} 1·4797. The barium methylate-methanol method gave a 36% yield of the mononitrate.

C.   Decomposition of cis- and trans- 1,2- Cyclohexanediol Dinitrates.

Refluxing the respective dinitrates in excess dry pyridine at 118° - 120°C caused a decrease in dinitrate content with time. (Figure 1.). The decomposition of the dinitrates was a "First Order Reaction" in that the plot of the logarithm of the concentration of unreacted dinitrate against reaction time gave a straight line for both the cis- and the trans- isomers. The trans- dinitrate decomposed 1.8 times faster than the cis- dinitrate as shown by the calculated half-life times (23.9 and 43.9 hours respectively).

Referring to the work of Christian and Purves (18), the trans- dinitrate was shown to be about twice as unstable thermally as the cis-dinitrate at 106°C, but the cis- isomer reacted more rapidly with 0·1M sodium hydroxide at 100°C in 50% aqueous ethanol solution than the trans- isomer.

Suspecting thermal decomposition we heated the dinitrate with a hydrocarbon solvent, 3-methylheptane, which had almost the same refluxing temperature as the pyridine-dinitrate mixture. After a forty-eight-hour refluxing period, it was observed that about 30% of the dinitrate remained unchanged as against 25% for the pyridine run. In the 3-methylheptane case, insoluble black

FIG. I
DECOMPOSITION OF DINITRATES
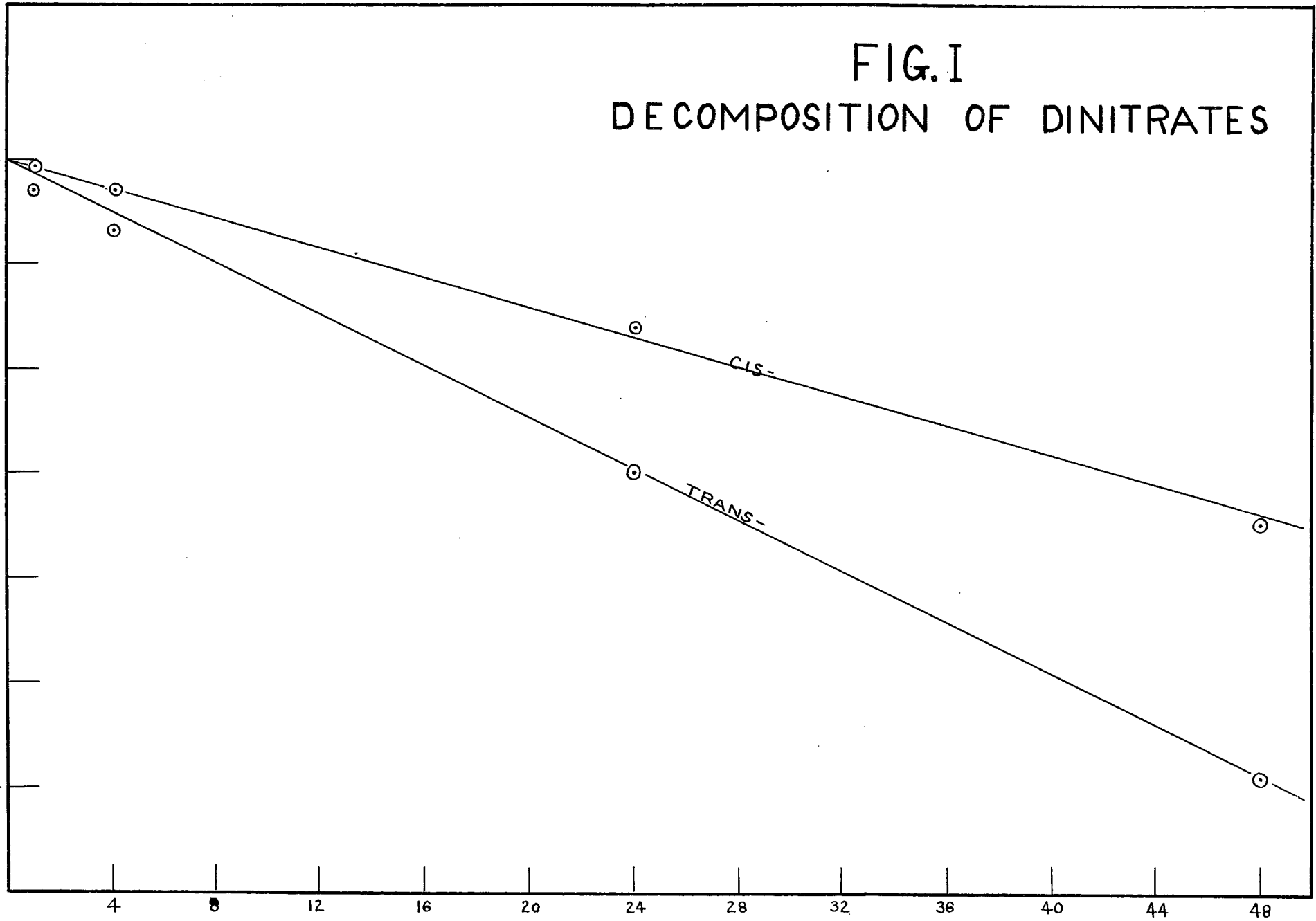
product (11% by weight of dinitrate used) and a colorless liquid
were formed in the reaction mixture. The black product burned
and did not dissolve in sulfuric acid and N,N-dimethylformarnide,
and was thought to be largely free carbon. The colorless liquid
was non-flammable and insoluble in benzene but soluble in water
and believed to be water. In the pyridine run, 9.3% of a black
powder was also formed, but it was found to be soluble in con-
centrated sulfuric acid. It is most probable that thermal decom-
position does occur to a large extent, and that in the case of
the pyridine run, the basic media aided in the polymerization
of the dinitrate and pyridine decomposition products.

The presence of small amounts of water (1% - 3% by
volume of pyridine used) seemed to inhibit the decomposition of
the dinitrates. Table I shows the results at one hour reaction
time for the cis-dinitrate with pyridine containing 1-3% by volume
of water. With increase in water content there was a decrease in
dinitrate decomposition. Less intensely colored reaction mixtures
were obtained with an increase in water content from 1% to 10%.
This was observed in runs carried out at 81°C and at reflux
temperatures.

The quenching of the pyridine reaction mixture in excess
cold water followed by removal of the unreacted dinitrate with
ether extractions gave the so-called "aqueous-pyridine solution".
On evaporating it to dryness, an aqueous-pyridine residue was left
behind. The yield of this dark material was over twice greater
for the trans- than for the cis- isomer, and increased exponent-
ially with reaction time (Table II).

TABLE I.

DECOMPOSITION OF THE DINITRATES

Run[*]	Reflux time (hr.)	Moles Water added	Dinitrate Recovered			
			% Recovered	$n_D^{24.5}$	%N[**]	% diol
(CIS-) 1	1	nil	96.9	1.4763	13.15 13.45	--
2	4	nil	93.6	1.4763	13.35 13.56	--
3	24	nil	70.0	1.4763	--	--
4[***]	48	nil	44.4	1.4763	--	--
5	1	0.0083	96.6	1.4763	--	--
6	1	0.0170	97.3	1.4764	13.22 13.27	--
7	1	0.0340	98.0	1.4763	--	--
(TRANS-) 1[***]	1	nil	93.9	1.4747	--	--
2[***]	4	nil	85.4	1.4745	13.84 13.84	--
3	24	nil	50.8	1.4743	--	96
4[***]	48	nil	25.5	1.4745	--	99

[*] Moles of dinitrate/moles of pyridine used = 0.04

[**] Nitrogen analyses done by the method of Brown and Purves (15) and Ma and Zuazaga (42). Freshly prepared cis- and trans-dinitrates had $n_D^{24.5}$ 1.4763 and $n_D^{24.5}$ 1.4745 respectively, and 13.62, 13.59% N (Theoretically 13.59%N.)

[***] Reaction mixture quenched in excess water.

TABLE II.

AQUEOUS PYRIDINE RESIDUE

	Run	Weight Dinitrate (gm.)	Reflux time (hr.)	Aqueous Pyridine Residue (gm.)
(CIS-)	8	4.0	4	0.10
	3	2.1	48	0.16
(TRANS-)	5	4.0	50 min.	0.09
	6	4.0	70 min.	0.11
	7	4.0	4	0.37
	2	4.0	4	0.34
	8	4.0	10	0.43
	4	3.0	48	0.61

Examination of this material showed the presence of
pyridinium nitrate, adipic and succinic acids, and the absence
of the diols and the mononitrates.

Pyridinium nitrate was shown to be produced only in
the presence of moisture (14). During the present investigation,
when the reflux condenser and drying tube were detached from the
reaction flash, pyridinium nitrate crystallized out immediately
on the "wet" upper half of the reaction flask.

The formation of adipic acid could be explained on
the basis of previous works on thermal decomposition of nitrate
and nitrite esters (38,68,69). The decomposition of our nitrate
would have undergone the following steps:
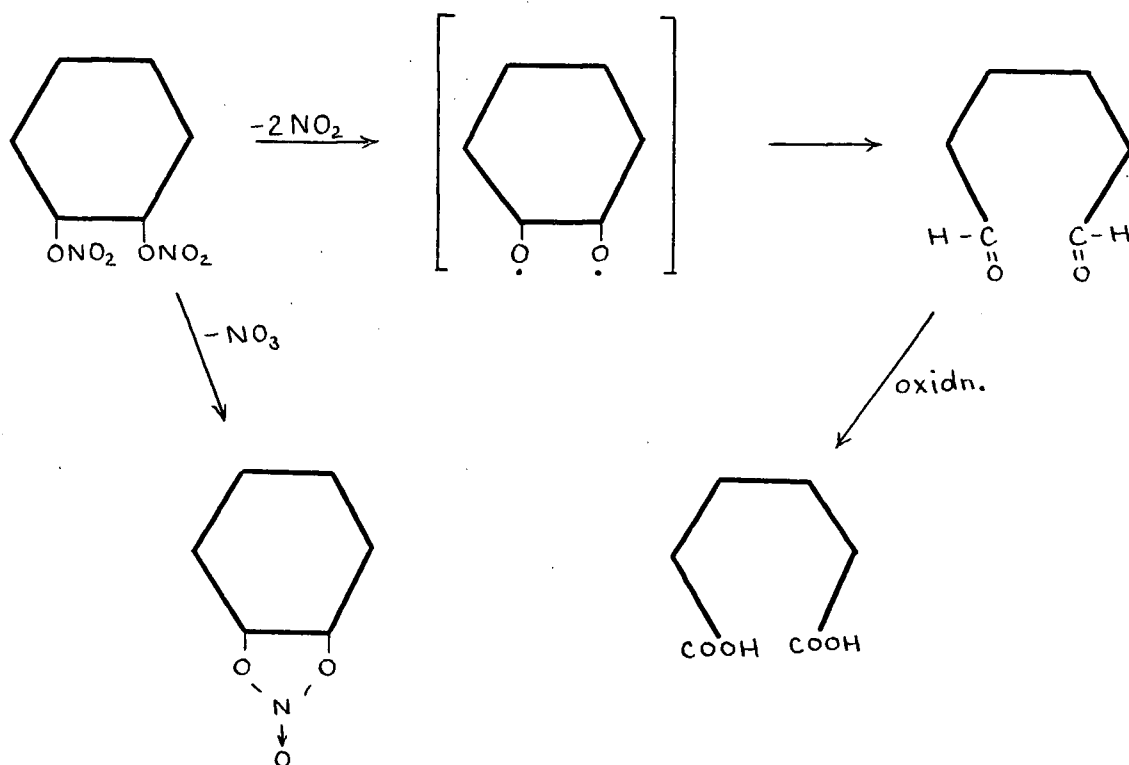
The adipaldehyde is easily oxidized by air to adipic acid, and would be probably immediately oxidized in the hot reaction mixture containing different oxides of nitrogen (14).

The formation of succinic acid should be accompanied with the production of oxalic acid if an elimination reaction or thermal decomposition occurred. The interference of pyridinium nitrate prevented the detection of the oxalic acid. According to Hughes and Ingold (37), elimination reactions take place in disubstituted compounds with axial-axial (<u>trans-</u>) and axial-equatorial (<u>cis-</u>) conformations — more readily in the former case. Thermal decomposition of esters give olefins only in the cases where the conformation of the 1,2-substituents are axial-equatorial (<u>cis-</u>) and axial-axial (<u>trans-</u>), and where a planar transition state is possible. In either case, the reactions probably are:


oxalic and succinic acids
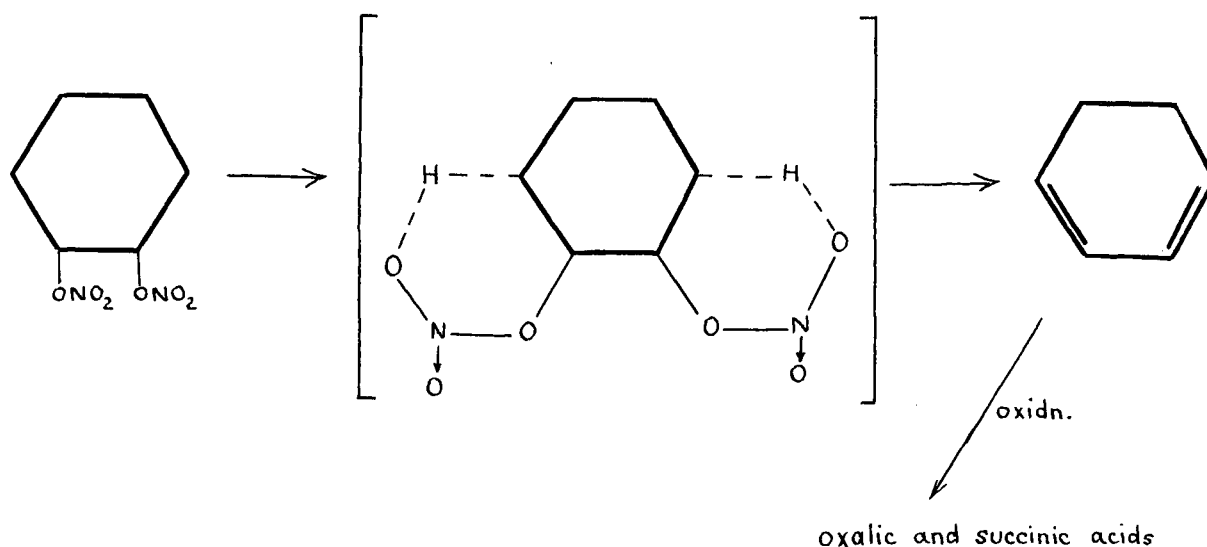
1,3-cyclohexadiene readily polymerizes when exposed to light.
Under the oxidative conditions in the reaction mixture, the
diene was probably oxidized to oxalic and succinic acids.

In 3-methylheptane with trans-1,2-cyclohexanediol
dinitrate at about the same reflux temperature as that of the
pyridine-dinitrate mixture, it was shown that oxalic, succinic
and adipic acids were formed as decomposition products. Again,
thermal decomposition, elimination and oxidation reactions would
account for these products.

The reaction products also included some lead-tetra-
acetate-oxidizable material which did not correspond to the cis-
and trans- diols. If any diol was formed by thermal decom-
position of the dinitrate, it may have undergone oxidation to
the adipaldehyde and then to the adipic acid stage.

The presence of carbonyl compounds in the pyridine
reaction products was demonstrated by the formation of several
colored spots with p-anisidine reagent. Glutaconaldehyde is
known to be produced from pyridine by the oxidative opening of
the ring (71). In acid solution it has the yellow-brown di-
aldehyde structure and in the basic media it is in the form of
the dark red enolate ion.

$$OHC- CH_2- CH = CH - CHO \rightleftharpoons {}^{-}OCH = CH - CH = CH-CHO$$
$$(acid) \qquad\qquad + H^+ (base)$$
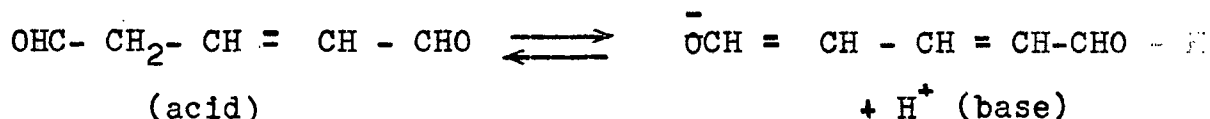
In the present case, glutaconaldehyde, if formed probably
polymerized or condensed with the decomposition products from the
dinitrate.

When the pyridine-reaction mixture was vacuum dis-
tilled at room temperature after one hour of refluxing, a
colorless distillate was collected. This solution, when acidified
with hydrochloric acid, reacted with aniline to produce a red
solution. Paper chromatography showed the presence of a new red
derivative which did not correspond to glutaconaldehyde
dianilide (71). Phenylhydrasine gave no crystalline derivative
with the distillate but heating produced a red color indicating
again that some carbonyl compounds may have been present.

The presence of unsaturated compounds and (or) easily
oxidizable low molecular weight aldehydes and alcohols was demon-
strated by permanganate-carbonate reduction of the distillate.
Acidification of the reduced solution produced some non-acidic
material melting at 130° - 140^oC.

The distillate of the 3-methylheptane-dinitrate
reaction mixture also showed unsaturation with both bromine and
permanganate solutions. Presence of some easily oxidizable
material was also noticed when a small amount of an acidic sub-
stance precipitated out of the distillate after standing for a
few days at room temperature.

The reaction with quinoline of the trans- dinitrate at
165^oC produced water and some dark pyridine-soluble polymer.

CONCLUSIONS

The decomposition of cis- and trans- 1,2-cyclohex-
anediol dinitrates by pyridine, 3-methylheptane and quinoline
produced oxalic, succinic and adipic acids, pyridinium nitrate,
water, aldehydes, alcohols, unsaturated compounds, polymeric
materials and a gaseous product. The absence of the 2-nitroxy-
cyclohexanols and 1,2-cyclohexanediols among the products was
noted in all cases.

Although water was produced in the 3-methylheptane
and quinoline reactions, it was not shown to be present in the
pyridine reactions. Its presence indicated vigorous oxidation
conditions in the reaction mixtures, and also the possibility
of the formation of other fragmentary products such as formal-
dehyde, formic acid, glyoxylic acid and carbon dioxide which
were not detected.

Oxalic acid was not detected in the pyridine reaction
products because of the interference of the pyridinium nitrate;
it was believed to be produced however, together with succinic
acid through thermal decomposition and (or) elimination reactions.
Adipic acid originated from the ring opening of the dinitrates
by thermal denitration followed by oxidation.

The various polymers formed appeared to be secondary
decomposition products from the dinitrate and the pyridine.
When a basic media was not present, as in the 3-methylheptane
reactions, carbonization was observed rather than polymerization.

The absence of 2-nitroxycyclohexanols and 1,2-cyclo-
hexanediols could not be attributed to a lack of free proton
because of the profound decomposition suffered by both the

pyridine and the dinitrate.

The conformation of the trans-1,2-cyclohexanediol dinitrate must be at least partially axial-axial in order to explain the production of oxalic and succinic acids. The hydrolysis work of Christian and Purves (18) supported this view.

The rates of decomposition depended upon the conformation of the isomers; the trans- dinitrate decomposed 1.8 times faster than the cis- isomer in pyridine solution.

EXPERIMENTAL

A. Materials

Nitric Acid: Red fuming nitric acid, supplied by Baker and Adams, was dried by distilling in vacuo from twice its weight of concentrated sulfuric acid.

Pyridine: Reagent-grade pyridine was dried by refluxing with technical grade barium oxide and distilled. The fraction boiling between 114° and $115^{\circ}C$ was collected and stored over calcium hydride. It was distilled from calcium hydride under anhydrous conditions just before use.

Quinoline: Reagent grade quinoline was distilled in vacuo and the middle fraction collected to give a pale yellow liquid, b.p. $115^{\circ} - 116^{\circ}C$ at 18 mm.

3-Methylheptane: Technical grade Bios Laboratory product was washed with concentrated sulfuric acid (until the washings were colorless) and then with water. It was dried over anhydrous magnesium sulfate and then over calcium hydride before being distilled. The fraction boiling between 116° and $117^{\circ}C$ was used.

Hexane-Methanol Chromatography Solvent: Technical-grade hexane was washed several times with concentrated sulfuric acid, then with water, and dried over anhydrous magnesium sulfate. The fraction distilling between 67° and $69^{\circ}C$ was saturated with reagent-grade methanol and used in partition paper chromatography.

cis- and trans- 1,2- Cyclohexanediols: cis- 1,2-
Cyclohexanediol was prepared from cyclohexene by the method
of Clark and Owen (17). It was recrystallized from ethyl
acetate and melted correctly at 97° - 98°C.

trans- 1,2- Cyclohexanediol was also prepared from
cyclohexene by a modification of method of Roebuch and Adkins
(52). Recrystallization from ethylacetate yielded a colorless
product, m.p. 102° - 103°C.

Barium Methylate: Barium methylate for deacetylation
reaction was prepared by refluxing 25 gm. barium oxide with
50 ml. absolute methanol for two hours. The insoluble barium
hydroxide was filtered off, and the filtrate diluted to 100 ml.
with absolute methanol. Titration with IN- sulfuric acid
established the normality of the solution.

Palladized Charcoal Catalyst: The palladium on
charcoal catalyst for hydrogenobysis of nitrate groups was
prepared by the method of Hartung (30).

Alumina: Merck's acid-washed alumina was used for
column-chromatographic separation of nitrate esters.

Diphenylamine Reagent: Diphenylamine reagent for
testing for the presence of nitrate was prepared after the
method of Mulliken (45).

Lead Tetracetate Spray Reagent: A solution of lead
tetraacetate 1.0 gm. in benzene (100 ml.) was shaken with
charcoal and filtered. The dry paper chromatograms were
moistened with a little xylene, sprayed with the reagent and
dried at room temperature. Wherever glycols were present, the

lead reverted to the bivalent state whereas the brown lead dioxide precipitated on the rest of the paper. White patches on a brown background were considered to be a positive test.

p- Anisidine Spray Reagent:

p-Anisidine reagent was prepared by dissolving 5 gm. pure p-anisidine in 166 ml. n- butanol, and then adding 3.8 ml. of concentrated hydrochloric acid. The chromatogram was dried, then sprayed with this reagent and developed at 130° - 150°C in an oven for a few minutes. This reagent is frequently used for detecting aldohexoses, ketohexoses, aldopentoses and uronic acids. Different shades of colors are produced.

Bromocresol Green Spray Reagent: Bromocresol green (0.04 gm.) was dissolved in 95% ethanol to give a green solution. Thoroughly-dried chromatograms were sprayed with this reagent. Yellow patches on a green background were considered to be positive tests for the presence of acids.

Paper-Partition Chromatography:

(1) Organic Acids: The chromatography solvents Butanol-Formic Acid - Water (4:1:5) and (2:1:1), Butanol- Acetic Acid-Water (4:1:5), and Phenol-Formic Acid-Water (75:1:25) were used for the separation and identification of organic acids present in the reaction products.

(2) Nitrate Esters: Hexane-Methanol Chromatography solvent was used to separate the nitrate esters. This method was developed in this laboratory by Michael Jackson.

B. Syntheses of 1,2-Cyclohexanediol Dinitrates

(a) Trans-1,2-Cyclohexanediol Dinitrate

trans-1,2- Cyclohexanediol Dinitrate was prepared
by the method of Soffer and coworkers (57). trans-1,2- Cyclo-
hexanediol was nitrated by an anhydrous nitric acid, acetic acid
and acetic anhydride mixture. The yellow nitrate product was
purified by vacuum distillatiion to give a colorless, musty-
smelling oil, b.p. 66° - 67°C at 0.03 mm.

$n_D^{27.5}$ 1.4732   Yield = 67%.

(b) cis- 1,2- Cyclohexanediol Dinitrate

The same method of nitration was carried out on the
cis- 1,2- cyclohexanediol. The yellowish oily product was
purified by fractional distillation to give a colorless, musty-
smelling oil, b.p. 74° - 76°C at 0.03 mm. or 106° - 108°C at
1 mm. $n_D^{27.0}$ 1.4757.

Hydrogenation of about 1 gm. samples of the trans-
and cis- 1,2- cyclohexanediol dinitrates at 40 p.s.i. hydrogen
and room temperature using 40 ml. alcohol as solvent and 1 gm.
of palladized charcoal as catalyst, yielded 95% to 98% of the
theoretical amount of the respective diols.

C. Syntheses of 2-Nitroxycyclohexanols

(a) trans- 2- Nitroxycyclohexanol

Twenty-five grams (0.15 m.) of silver nitrate was
dissolved in 31 ml. of dry reagent-grade acetonitrile. The

temperature of the mixture was lowered to 0°C, and <u>trans</u>-2-bromocyclohexanol (25 gm., o.14 m.) (66) was added dropwise with gentle swirling. The mixture was then kept at 0°C for 48 hours and then at room temperature for another 21 hours. The whitish precipitate was then filtered off, and the clear solution warmed up to 85°C for 5 minutes. The precipitate that formed was filtered off and the filtrate was extracted with dry ether. The ether extract (100 ml.) was washed with 50 ml. water and evaporated. The product remaining was a yellowish oil. (19.2 gm.) On distillation, a colorless oil was obtained, b.p. 78°C at 0.75 mm. Yield was 11.7 gm. or 52% of theoretical yield. This oil crystallized out into a white solid with m.p. 29°.o - 31°.0C. Hydrogenation of a sample of this product using palladized charcoal as a catalyst gave a colorless crystalline product that melted from 100° to 102°C. Recrystallization from ethyl acetate gave a new melting point of 105°C and a mixed melting point with an authentic sample of <u>trans</u>-1,2-cyclohexanediol was not depressed.

(b)   <u>cis</u>-2- Nitroxycyclohexanol

<u>cis</u>-2- Nitroxycyclohexanol was prepared by the following scheme.
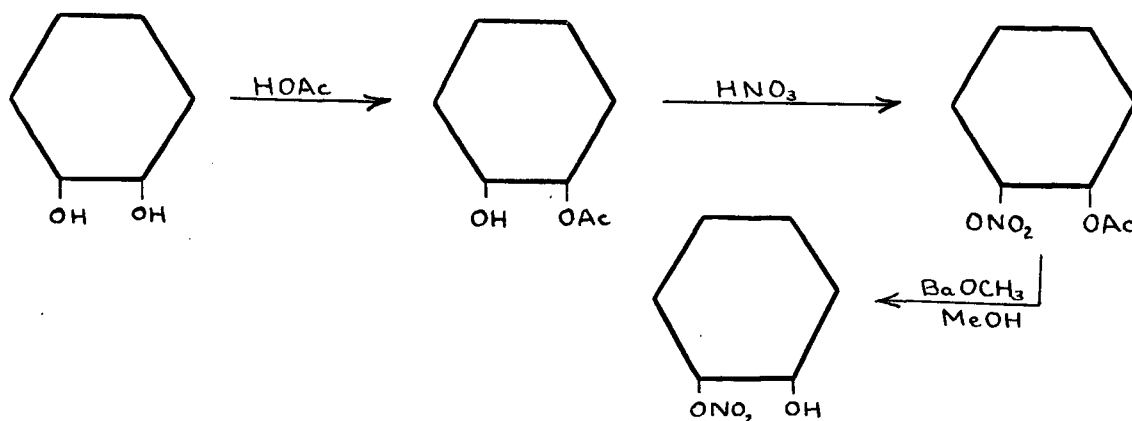
(i) Acetylation of cis-1,2- Cyclohexanediol

The monoacetate of cis-1,2-cyclohexanediol was prepared by the method of Winstein (65). A colorless oil was obtained with b.p. 103°C at 4.5 mm. and $n_D^{24.5}$ 1.4572. This oil is understood to be made up mostly of the monoacetate and to have a cis- orientation.

(ii) Nitration of cis-2- Acetoxycyclohexanol

To 16.8 gm. (o.27 m.) of ice-cold fuming anhydrous nitric acid was added 12 ml. of dry chloroform. This mixture was cooled to about -10°C before 0.6 gm. of phosphorus pentoxide was added with stirring. To this nitration mixture was then added slowly (dropwise) and with stirring the monoacetate (21.0 gm.). Addition took 30 minutes, and the reaction mixture was then let to stand for 75 minutes at 0.° C. It was then poured into 300 ml. of ice-cold water, where an oily product separated out on the bottom. Two ether extractions of 150 ml. each was followed by washing with 20 ml. of 5% sodium carbonate solution, and twice with 35 ml. of water. Drying for half an hour over anhydrous sodium sulfate and then distilling off the ether produced a light yellow-colored oil. Vacuum distillation yielded a colorless oil with b.p. 93°C at 1.3 mm. and $n_D^{24.5}$ 1.4537. Yield: 14.9 gm.

(iii) Deacetylation of the cis-1- Acetoxy-2-nitroxycyclohexane.

About 5.8 gm. of the nitrated acetate was dissolved in 120 ml. of absolute methanol and the solution cooled to 0°C.

Then 4.3 ml. of 0.275N barium methylate was added and the
solution swirled and left to stand for 24 hours at 0°C. IN-
sulfuric acid was added till the solution was acidic to phenol-
phthalein followed by reagent grade barium carbonate to
neutralize any excess acid present. The solution was filtered
and then evaporated down to give a yellowish oil that partly
crystallized out. Hexane extraction removed the oily product
from the crystalline material that was found to melt at 97° -
98°C. The hexane extract showed two nitrate spots in hexane-
methanol paper chromatography — the unreacted nitrated acetate
at R_f 0.20, and, what is considered to be the mononitrate at
R_f 0.51. By pouring this oil on a dry alumina column and
eluting it with, first, a benzene-ethanol (500:1) mixture, then,
benzene-ethanol (20:1), the unreacted cis-1-acetoxy-2-nitroxy-
cyclohexane was eluted off before the cis-2-nitroxycyclohexanol.
Any cis-1,2- cyclohexanediol present would have stayed on the
column. On evaporation of the solvent, a yellowish oil was
collected (1.64 gm.) or 36%.

Hydrogenation (40 p.s.i. hydrogen) of a sample of
this oil at room temperature using palladized charcoal as
catalyst, yielded a colorless crystalline product with m.p.
93°- 96°C. Mixed melting-point with genuine cis-1,2- cyclo-
hexanediol did not lower the melting point of the latter.

D. Decomposition of cis- and trans- 1,2-Cyclohexanediol
    Dinitrates in Pyridine Solution

(a) Preliminary Experiments:

1,2- cyclohexanediol dinitrate (3 gm.) was dissolved
in 30 ml. of dry pyridine, and the colorless solution was
refluxed at 118° - 120°C in anhydrous conditions. At about
100°C the solution started to turn yellow, and after forty
minutes of refluxing it was dark amber, and crystalline pyri-
dinium nitrate and a brownish-red gas appeared in the reflux
condenser. Lengthy refluxing produced insoluble black residue
and more colored gas. When a dry-ice-acetone trap (-85°C) was
attached to the straight water-cooled reflux condenser, only a
blue solid (N_2O_3) was collected. After a given refluxing period,
the reaction mixture was allowed to cool to room temperature,
filtered, and then poured into about 250-300 ml. of ice-cold
water where a heavy oil separated out in an amber-colored
solution. Several ether extractions of this aqueous-pyridine
solution removed the colored oil. In several runs, this water-
quenching step was omitted. Instead, the pyridine-reaction
mixture was distilled at room temperature under vacuo to give
a colorless pyridine-like distillate and a dark-colored oily
residue. This oily residue was first checked for the presence
of any mononitrate by paper-chromatography using Hexane-Methanol
solvent, and then either taken up with some ether and washed
with an equal amount of cold water, or immediately chromatographed
on an alumina column.

Several runs were made with pyridine containing from
0.5% to 3.0% by volume of water, and the reaction rates were
found to be inhibited. With increase in refluxing time, the
amount of insoluble jet-black material that formed in the
refluxing reaction mixture increased. A 3 gm. (0.0.45 m.)
sample of the trans- 1,2-cyclohexanediol dinitrate in 30 ml.
dry pyridine after two days of refluxing gave 0.28 gm. of a
black powder that was found to be insoluble in pyridine, ether,
acetone, formamide, dimethylformamide, 30% NaOH, and concen-
trated hydrochloric acid, but was soluble in cold concentrated
sulfuric acid to give a dark solution. 74.5% of the trans-
dinitrate reacted and only 0.610 gm. of a hard-plastic-like
material was found in the aqueous-pyridine solution after
vacuum distillation of the solvent.

A 2.1 gm. (0.0.02 m.) sample of the cis-1,2-cyclo-
hexanediol dinitrate in 21 cc (0.26m.) dry pyridine after two
days of refluxing gave 0.24 gm. of the black precipitate that
was also found to be soluble only in concentrated sulfuric
acid. 55.6% of the cis-dinitrate reacted, and only 0.164 gm.
of the aqueous-pyridine residue was obtained.

(b) Isolation of the Unreacted Dinitrate:

About one gram of the oily residue, previously
obtained by vacuum distillation of the reaction mixture at
room temperature, was poured on top of a dry alumina column
(1.8 x 50 cms.) and eluted with ether. The dinitrate ran
with the front, leaving dark yellow, bluish green, and red

the pyridinium nitrate (R_f 0.26), and the p-anisidine-HCl
reagent exposed two spots for Run 5 (50 min. refluxing) ——
a reddish-brown spot at R_f 0.26, and a yellowish-brown spot
at R_f 0.46. The reagent was found to have no effect on the
pyridinium nitrate. An aqueous-pyridine residue obtained
after four hours of refluxing did not give any spottings with
the p-anisidine reagent, but showed eight to nine spots of
various colors under ultra-violet light. Bromocresol green
also picked up a strong acid spot just below the starting front.

Run 3 (cis-dinitrate), after 48 hour refluxing period,
gave with bromocresol green strong acid spots at R_f 0.10 and
0.20 (the latter was also positive to diphenylamine reagent
and corresponded to pyridinium nitrate), a weak acid spot at
R_f 0.33 and a strong basic spot (blue patch) at R_f 0.42. A
corresponding acetone extract of Run 1 (trans-dinitrate), after
an hour of refluxing, showed a weak acid spot at R_f 0.12, and
a strong one at R_f 0.22 (also positive to diphenylamine test and
corresponding to pyridinium nitrate) and a weak acid spot at
R_f 0.44. Nothing was picked up with lead tetraacetate spray.

(ii) Butanol-Acetic-Acid-Water Solvent (2:1:1)

p-Anisidine reagent brought out two spots for Run 5
(50 min. refluxing) and four spots for Run 6 (70 min. refluxing).
The R_f values were 0.26 (dark red); 0.62 (yellowish-brown),
0.77 (yellowish-brown) and 0.91 (dark red). The R_f values 0.62
and 0.77 were both found in the two runs. Ultraviolet light
showed between four to five spots, and the diphenylamine reagent
picked up the pyridinium nitrate @ R_f 0.20. Bromocresol green,

however, showed a strong acid spot at R_f 0.84 corresponding
to adipic acid (Run 8, 10 hr. refluxing)

(iii) <u>Butanol-Acetic Acid Water Solvent (4:1:5)</u>

Acetone extract of Run 8 (10 hr. refluxing) and the
aqueous extract of Run 4 (48 hr. refluxing) both gave strong
acid spots with bromo-cresol green at R_f 0.83 corresponding
to adipic acid. A weak acid spot appeared at R_f 0.73 corres-
ponding to succinic acid. The presence of any oxalic acid was
camoflaged by acidic pyridinium nitrate.

(iv) <u>Phenol-Formic Acid-Water Solvent (75:1:25)</u>

<u>(Upward Flow)</u>

For acetone extract of Run 8 and aqueous extract of
Run 4, strong acid spots were detected with bromo-cresol green
at R_f 0.74, corresponding to adipic acid, and weak acid spots
at R_f 0.63, corresponding to succinic acid. Oxalic acid, if
present, should show up at R_f 0.32, but again acidic pyridinium
nitrate interferred.

(v) <u>Xylene-Methyl-ethyl-ketone-Water Solvent (1:1:1)</u>

In the aqueous extract of Run 4 (48 hours refluxing),
lead-tetraacetate reagent picked up only a narrow white streak
extending from the spotting line. Standard <u>trans</u>- and <u>cis</u>-
cyclohexane, 1,2- diols spottings did not correspond with that
streak.

Bromo-cresol green, however, showed a heavy yellow
streak extending almost half-way down the paper. A standard
pyridinium nitrate spot did not move from its original spotting
position and was detected by the diphenylamine reagent.

(vi) <u>Butanol-Formic acid-Water Solvent (4:1:5)</u>

Aqueous extract of Run 4 (trans-) showed a strong acid spot
at R_f 0.87, and a weak one at R_f 0.76 corresponding to adipic
and succinic acids respectively. Acidic pyridinium nitrate
again interfered in the detection of any oxalic acid.

(d) <u>Isolation of the Mononitrate</u>

One gram sample of the colorless <u>cis</u>- 1,2-cyclo-
hexanediol dinitrate was dissolved in 10 ml. of dry pyridine,
and the solution was well stoppered and left to stand for
33 days at room temperature. Samples were taken out after
the first, second, and third hour, and then at twenty-four
periods, and chromatographed against standard dinitrate and
mononitrate in hexane-methanol solvent. No mononitrate or
diol was detected at any time by diphenylamine reagent and
lead tetraacetate. After 33 days, the solution became orange-
yellow in color and contained some pyridinium nitrate.

About 0.3 gm. samples of freshly distilled <u>trans</u>-
1,2-cyclohexanediol dinitrate were dissolved in 3 ml. of
freshly distilled pyridine containing from 0% to 10% of water
by volume. These were heated at $81^{o}C$ for 4 days, and samples
taken out at various time intervals and chromatographed in
hexane-methanol solvent. No mononitrate was ever detected.
The sample containing dry pyridine became yellowish in 45
minutes, reddish-brown in 48 hours, and dark-amber after 96
hours. Samples containing water were all lighter in color
after 96 hours.

About 3 gm. of freshly prepared trans- 1,2-cyclo-hexanediol dinitrate was refluxed with 30 ml. pyridine containing 25% by volume of water. After a 60 minute period, the solution turned only yellow in color, and paper chromatography showed no mononitrate.

When 30 ml. of BaO-dried pyridine was decanted off dry potassium hydroxide pellets and refluxed with 3 gm. of trans-1,2-cyclohexanediol dinitrate for an hour, no mononitrate was detected in the residual oil, after the reaction mixture was vacuum distilled at room temperature. But, with the addition of a small amount of water (1 - 3% by volume) followed by refluxing for an hour, some mononitrate was detected in the residual oil. This was shown by chromatographing the residual oil against standard trans- 1,2-cyclohexanediol dinitrate (R_f 0.80) and trans- 2 nitroxycyclohexanol (Rf 0.33) in hexane-methanol. Alumina column chromatography using dry ether as eluant could give a good separation of the mononitrate from the dinitrate in the residual oil. About 1 gm. sample of the residual oil was poured on top of a dry alumina column (1.8 x 50 cm.) and dry ether added. The dinitrate flowed with the front, and was washed off in about 30 minutes, while the mono-nitrate only appeared after an interval of 30 to 40 minutes. Diphenylamine reagent was used to check for the appearance and disappearance of the nitrates.

(e) Examination of the Distillate from the Reaction Mixture:

About 4.1 gm. of trans- 1,2-cyclohexanediol dinitrate

was refluxed for 50 minutes with 40 ml. of Analar Reagent
pyridine that was not previously dried over barium oxide.
Then the reaction mixture was distilled at $30^{\circ}C$ and reduced
pressure to give a colorless distillate that smelled strongly
of pyridine.

To 3 ml. of this distillate was added some concen-
trated hydrochloric acid to make the solution acidic. Then
about 0.2 ml. of freshly distilled, colorless aniline was added.
The solution turned pink immediately. This mixture was chroma-
tographed in Butanol-Water solvent against genuine glutaconal-
dehyde dianihide-hydrochloride (71). The latter ran at R_f 0.75
as an reddish-orange spot, while the former as a red spot at
R_f 0.45.

To 2 ml. of the distillate, about 4 ml. of glacial
acetic acid was added till the solution was acidic and then
about 1 ml. of phenylhydrazine solution. The solution turned
yellow, and heating just below the boiling temperature turned
it red. No crystallization occurred in the frigidaire overnight.

The distillate was found to reduce 1%- potassium
permanganate in 2% sodium carbonate slowly at room temperature.
To 20 ml. of the distillate at 40° - $50^{\circ}C$ was added slowly about
20 ml. of this 1% permanganate-carbonate solution. When the
decolorization seemed to have stopped, the manganese dioxide was
filtered off. Concentrated hydrochloric acid was then added till
the solution was acidic; Some crystalline material appeared as
a suspension in the yellowish solution. Ether extraction removed
the crystalline suspension and most of the yellowish color. The

evaporation of the ether extract yielded a mixture of white crystals and orange-colored powder. (0.125 gm.) This material melted and burned when heated leaving a charred mass. Chromatography in Butanol-Water gave a yellowish spot at R_f 0.84 and an acid spot at R_f 0.04 (standard succinic, glutanic and adipic acids had higher R_f values). When some of the ether extract of this crystalline material was added to an aqueous-pyridine solution, some light, flake-like, golden crystals appeared, which after filtration melted at 130° to 140^oC, and were found not to be acidic.

E.   Decomposition of <u>trans-</u> 1,2-Cyclohexanediol Dinitrate
in 3-Methylheptane Solution

(a)   Preliminary Experiments:

trans- 1,2-Cyclohexanediol dinitrate (1.99 gm.) was
dissolved in 25 ml. 3-methylheptane at room temperature, and
the colorless mixture was refluxed at 119° - 120°C gently for
40 hours in anhydrous conditions. Immediately a brownish-red
gas that smelled of nitrogen dioxide was evolved. After eight
hours, the solution became only slightly yellow and some color-
less droplets were noticed to condense out with the 3-methyl-
heptane in the cooler part of the reflux condenser. Next
morning, a coating of black, insoluble material appeared adhering
to the bottom and sides of the reaction flask, together with
some colorless crystalline material in the condenser. This
crystalline product was acidic to bromocresol green. With pro-
longed refluxing more insoluble black residue formed. After
48 hours, the reaction mixture was swirled up, and decanted
from the insoluble black residue. This was then washed twice
with small amounts of 3-methylheptane, vacuum-dried at room
temperature, and then extracted with 30 ml. pyridine, and again
with an additional 20 ml. in order to remove the last trace of
color. The black residue was air-dried overnite and weighed.
(0.22 gm.) It was found to be insoluble in acetone, alcohol,
ether, N,N-dimethylformamide, 30% - NaOH and concentrated
sulfuric acid.

The red-colored pyridine extract was evaporated down

at 45° - 50°C to give a dark gummy material. (0.090 gm.)
This substance was extracted with a total of 50 ml. of hot
water, and the extracts evaporated down at 45° - 50°C to give
a yellow oily material, which, after standing overnite in vacuo
and over phosphorous pentoxide, partially crystallized out
(0.050) gm.) Paper chromatography of this material in Butanol-
Acetic Acid-Water (4:1:5) showed the presence of three acids
that corresponded to oxalic (R_f 0.26), succinic (R_f 0.76), and
adipic (R_f 0.84). If an ether instead of a pyridine extraction
was carried out on the black residue, followed by an aqueous
extraction of the ether extract, then the aqueous extract would
be almost colorless. On evaporation to dryness at 45° - 50°C,
almost colorless crystalline material was obtained. Chromato-
graphy in Phenol-Formic Acid-Water (75:1:25)(upward flow)
yielded three acid spots corresponding again to oxalic (R_f 0.32),
succinic (R_f 0.61), and adipic acid (R_f 0.75). Chromatography
in Xylene-Methylethylketone-Water (1:1:1), and development of
the paper chromatogram with lead tetraacetate spray reagent
revealed a white streak at R_f 0.13, whereas genuine cis- and
trans- diols ran at R_f 0.30 and R_f 0.20 respectively.

(b) Isolation of the Unreacted Dinitrate:

The decanted yellow reaction solution from the black
residue was distilled at 65°- 70°C at 80 mm. to give a colorless
distillate and a yellowish oily residue. The latter weighed
1.435 gm., and when chromatographed in Hexane-Methanol solvent,
showed, besides the unreacted dinitrate, trace amounts of the

trans- 2-nitroxycyclohexanol. This oily residue (1.184 gm.)
was put on an alumina column (1.8 x 50) cms. and eluted with
dry ether. The dinitrate travelled with the front leaving the
yellow-colored material behind. On evaporation of the ether
solution, 0.572 gm. of a colorless oil was left behind.
Chromatography showed the presence of the dinitrate only.
$n_D^{24.5}$ = 1.4675 (should be about 1.4745 if pure dinitrate).
This oil was then subjected to high vacuum of 3 mm. at 60°C
for half an hour, and then for an hour at 2 mm. at room
temperature. Weighing gave (0.497 gms.) and $n_D^{24.5}$ = 1.4719.
A 0.468 gm. sample of the oil was then hydrogenated with
50 ml. ethanol and 1 gm. palladized charcoal at 48 p.s.i. of
hydrogen at room temperature. After 5 hours the colorless
solution showed no nitrate test with diphenylamine reagent.
It was filtered, washed, and evaporated down to dryness at
45° - 50°C. Light-brown crystals formed. After drying in
vacuum over phosphorus pentoxide, the yield was 0.278 gm. and
m.p. 96° - 100°C. After dissolving these crystals in ethyl-
acetate followed by filtration, washing and evaporation, a
new yield of 0.263 gm. of colorless crystals was obtained m.p.
98° - 101°. (100% diol yield). Mixed melting points with
genuine trans- diol gave m.p. 103°-4° . Purification with
charcoal, followed by three consecutive fractional crystal-
lizations only yielded material of m.p. 103° - 104°C. On the
basis of hydrogenolysis, then, 30.2% of the trans- 1,2-cyclo-
hexandiol dinitrate remained unreacted.

(c) <u>Examination of the Distillate from the Reaction
   Mixture</u>:

   <u>trans</u>- 1,2-Cyclohexanediol dinitrate (2.62 gm.)
dissolved in 30 ml. 3-methylheptane was refluxed at 120°C for
88½ hours. The reaction solution was then decanted off the
black residue, and distilled at 65° - 70°C and 80 mm. To
this distillate was added bromine till the color stopped
being discharged. About 0.1 ml. of liquid bromine was used.
The colorless solution was then evaporated off at 65° - 70°C
and 60 mm. to leave a light yellow, medicine-smelling oil
(0.072 gm.). 3-Methylheptane did not discharge the bromine
color.

   In an earlier run, the distillate was found to
deposit a small amount (1 mg.) of white crystalline material
after standing stoppered for a few days at room temperature.
These crystals were acidic to bromocresol green.

   Baeyer's test for unsaturation was then carried
out. To 1 ml. of the distillate was added a drop of 2%
potassium permanganate solution and shaken up. The colour of
the permanganate was discharged immediately. Several more
drops were also decolorised. 3-methylheptane did not show
any decolorizing effects.

F. Decomposition of trans- 1,2-Cyclohexanediol Dinitrate
    in Quinoline Solution:

trans- 1,2-Cyclohexanediol dinitrate (0.6 gm.) was
mixed with 6 cc of quinoline, and the temperature of the
mixture was raised to 165°C within the first hour, and main-
tained at 160° - 165°C till the end of the second hour. During
that time some crystalline material crystallized out in the
condenser, and a colorless insoluble liquid was seen to reflux
in the condenser. No mononitrate nor dinitrate was detected
in the mixture by paper chromatography. Distillation at 160°C
yielded a few droplets of a colorless liquid which was found
to be insoluble in quinoline and benzene, but soluble in water.

Heating of 2.62 gm. of trans- 1,2-cyclohexanediol
dinitrate in 25 ml. of quinoline for $7\frac{1}{2}$ hours between 145° -
165°C yielded some blue solid (N_2O_3) in a dry-ice trap (-85°C).
No diol nor mononitrate was detected in the black reaction
mixture — only the unreacted dinitrate. About 120 cc of
sodium-dried benzene was added to the reaction mixture, and
the heavy precipitation occurred. Azeotroping of this mixture
for 6 hours yielded 0.6 ml. of a colorless liquid which showed
all the properties of water. On filtering the benzene-quino-
line solution, 1.07 gm. of a dark-brown material was collected.
This substance was insoluble in water, slightly soluble in
acetone, and very soluble in pyridine.

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