THE CHEMISTRY OF NITRATE ESTERS

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I. INTRODUCTION

Esters of nitric acid have been known for over a century, but although certain ones, especially cellulose nitrate and glycerol trinitrate, more popularly known by the misnomers nitrocellulose and nitroglycerin, have seen wide use in explosives and propellants, very little was known concerning their chemical properties. In more recent years interest in these compounds has grown, and considerable

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TABLE 1

Synthesis of nitrate esters

Ester	Method	Yield	References
		per cent	
Methyl	ROH + HNO_3		(39, 125)
	ROH + HNO_3 + H_2SO_4	66–90	(22, 46)
	CH_3NHNO_2 + HNO_3	Nearly quantitative	(60)
Ethyl	ROH + HNO_3 + H_2SO_4		(32, 34, 106)
	ROH + HNO_3		(39, 113)
	ROH + $C_6H_5COONO_2$		(61)
	RI + $AgNO_3$	72	(12, 21)
	RI + $AgNO_3$ in CH_3NO_2 or $C_6H_5NO_2$		(62)
	ROOH + HNO_3	50	(10)
n-Propyl	ROH + HNO_3		(39, 126, 168)
Isopropyl	RBr + $AgNO_3$		(12)
	RI + $AgNO_3$		(148)
Allyl	RBr + $AgNO_3$		(73)
	ROH + HNO_3 in $(CH_3CO)_2O$	95	(45)
n-Butyl	ROH + HNO_3		(39)
	ROH + HNO_3 + H_2SO_4	80–90	(19, 92, 106, 143)
Isobutyl	ROH + HNO_3 + H_2SO_4		(33, 35)
sec-Butyl	RBr + $AgNO_3$	49	(89)
	ROH + HNO_3 + H_2SO_4		(19)
	ROH + HNO_3 in $(CH_3CO)_2O$	78	(103)
tert-Butyl	ROH + HNO_3 in CH_2Cl_2	56–60	(102, 111)
	$(CH_3)_2C{=}CH_2$ + HNO_3 in CH_2Cl_2	47–76	(111)
	RCl + $AgNO_3$ in ether		(12)
Methallyl	RCl + $AgNO_3$ in CH_3CN	45	(54)
n-Amyl	ROH + HNO_3 in organic solvent		(93)
	ROH + HNO_3 + H_2SO_4		(106)
Isoamyl	ROH + HNO_3	"Theoretical"	(25)
	ROH + HNO_3 + H_2SO_4	95	(31, 34)
2-Amyl	ROH + HNO_3 in $(CH_3CO)_2O$	93–94	(103)
3-Amyl	ROH + HNO_3 in $(CH_3CO)_2O$	82	(103)
tert-Amyl	ROH + HNO_3 in $CHCl_3$	65–77	(111)
	$(CH_3)_2C{=}CHCH_3$ + HNO_3 in CCl_4 or CH_2Cl_2	47–67	(111)
Cyclopentyl	ROH + HNO_3 + H_2SO_4	69	(91)
	RBr + $AgNO_3$	38	(91)
n-Hexyl	RBr + $AgNO_3$ in CH_3CN	77	(54)
	ROH + HNO_3 in CH_3COOH-$(CH_3CO)_2O$		(153)
	ROH + HNO_3 + H_2SO_4		(106)
Methylisobutylcarbinyl	ROH + HNO_3 in $(CH_3CO)_2O$	95	(103)
Cyclohexyl	ROH + HNO_3 in CH_3COOH-$(CH_3CO)_2O$		(153)
	ROH + HNO_3 in $(CH_3CO)_2O$		(81)
	RI + $AgNO_3$	16.8	(56)
	ROH + HNO_3 + H_2SO_4	69	(91)
n-Heptyl	ROH + HNO_3 + H_2SO_4		(106)
n-Octyl	ROH + HNO_3	90	(25)
	RI + $AgNO_3$ in CH_3CN	61	(54)
2-Octyl	ROH + HNO_3 + H_2SO_4	65–69	(88, 146)
	RI + $AgNO_3$ in CH_3CN	46	(54)
	RBr + $AgNO_3$ in C_6H_6	59	(88)
	ROH + HNO_3 in CH_3COOH-$(CH_3CO)_2O$		(153)
n-Nonyl	ROH + HNO_3 + H_2SO_4		(107)
n-Decyl	ROH + HNO_3 at 0–5°C.		(25)
	ROH + HNO_3 + H_2SO_4		(107)
n-Dodecyl	ROH + HNO_3 + H_2SO_4		(107)
	From "Lorol"		(96)
Myristyl (*n*-$C_{14}H_{29}$)	ROH + HNO_3		(25)
Cetyl (*n*-$C_{16}H_{33}$)	ROH + fuming HNO_3 in $(CH_3CO)_2O$		(96)
Benzyl	RCl + $AgNO_3$		(15, 102)
	RCl + $AgNO_3$ in CH_3CN	64	(54)
	$C_6H_5CH_2HgCl$ or $(C_6H_5CH_2)_2Hg$ + HNO_3		(164)

TABLE 1—*Concluded*

Ester	Method	Yield	References
		per cent	
p-Methylbenzyl	RBr + $AgNO_3$		(16)
	RCl + $AgNO_3$		(15)
o-Nitrobenzyl	RCl + $AgNO_3$		(15)
m-Nitrobenzyl	RCl + $AgNO_3$		(15)
p-Nitrobenzyl	RCl + $AgNO_3$		(15)
	RCl + $AgNO_3$ in C_2H_5OH		(154)
p-Bromobenzyl	RCl + $AgNO_3$		(15)
2,4,6-Trinitrobenzyl	RBr + $AgNO_3$	52	(59)
	ROH + HNO_3	70	(59)
α-Phenethyl	RCl + $AgNO_3$		(15)
β-Phenethyl	RCl + $AgNO_3$		(15)
Benzhydryl (diphenylmethyl)	RCl + $AgNO_3$ in ether	75	(108)
	RCl + $AgNO_3$		(37)
	RCl + $AgNO_3$		(15)
Trityl (triphenylmethyl)	RCl + $AgNO_3$ in ether	Quantitative	(108)
	RCl + $AgNO_3$ in CCl_4		(40)
	RCl + $AgNO_3$		(37)

effort has been expended in the study of the physical and chemical properties of nitrate esters. A point has been reached where the chemistry of nitrate esters is becoming an important part of the rapidly growing field of organic chemistry.

This review is concerned principally with the simple aliphatic mononitrates and a few of the dinitrates and polynitrates, the latter being included only when a reaction is involved which is of significance in nitrate ester chemistry. The vast fund of technological information in the literature concerned with nitroglycerin, nitrocellulose, and ethylene glycol dinitrate is quite important and informative, but has little application to the general subject of this review. Accordingly, this material has not been covered appreciably here.

The literature is reviewed through volume 47 (1953) of *Chemical Abstracts*; also included are selected papers that have appeared in the literature in 1954.

II. SYNTHESIS

The preparation of nitrate esters is generally accomplished by one of two methods: esterification of the appropriate alcohol or reaction of a suitable alkyl halide with silver nitrate. Other methods have been used in a few instances. A comprehensive summary of methods used for synthesis of the simpler mononitrates is given in table 1.

A. ESTERIFICATION OF ALCOHOLS

1. With mixed acids

The most common method of converting alcohols to nitrate esters is that involving the use of a mixture of nitric and sulfuric acids. The nitrating mixture generally consists of nearly equal volumes of concentrated nitric (specific gravity 1.42) and sulfuric (specific gravity 1.84) acids, with a small amount of urea or urea nitrate to destroy any nitrous acid present. Sufficient mixed acid is used to provide an excess of nitric acid with respect to the alcohol. The esterification is normally carried out in the cold, by slow addition of the alcohol (either pure or in sulfuric acid) to the mixed acid. Adequate stirring and careful control of temperature and rate of addition reduce or eliminate the undesirable side reaction, which is oxidation of the alcohol (146). The ester, which forms rapidly, is separated from the excess acid either by pouring the reaction mixture into cold water or by careful distillation. Good yields of primary and secondary nitrates have been obtained in this manner.

Similar esterifications have been carried out using mixtures of nitric acid and acetic anhydride, with acetic acid also present in some instances. Techniques similar to those used with the nitric–sulfuric acid mixture may be applied, or the esterifications may be carried out by the simultaneous slow addition of 100 per cent nitric acid and the alcohol to acetic anhydride at room temperature (81, 103).

2. With nitric acid alone

Nitrate esters may be prepared by the action of nitric acid alone on alcohols. Absolute nitric acid is used for this purpose, and the reactions are carried out in the same way as those with nitric–sulfuric acid mixtures. Urea is generally added to destroy nitrous acid.

Inert organic solvents have occasionally been used in esterifications of alcohols with nitric acid. Tertiary butyl nitrate has been made in 60 per cent yield by the addition of 98.6 per cent nitric acid to a cold (−30°C.) solution of the alcohol in methylene chloride (102, 111). Yields up to 77 per cent of *tert*-amyl nitrate have been obtained in similar preparations with chloroform as the solvent (111).

B. REACTION OF SILVER NITRATE WITH ALKYL HALIDES

1. Heterogeneous reactions

The metathetical reaction between silver nitrate and an alkyl halide to produce the corresponding nitrate ester is an extremely useful method of preparation of a number of nitrate esters. The majority of nitrate ester syntheses of this type are carried out in a heterogeneous fashion. Ordinarily the esters are synthesized by stirring powdered silver nitrate with a solution of the alkyl halide in an inert solvent at room temperature, benzene (87), ether (12), nitromethane (63), and nitrobenzene (63) being most commonly used as solvents.[2]

In several cases, the conversion of alkyl halides to nitrates can be achieved in the absence of a solvent (12).

Ethanol can be used as a solvent (11, 26), but solvolysis of the nitrate ester is an undesirable side reaction in this case.

2. Homogeneous reactions

The relatively high solubility of silver nitrate in acetonitrile affords a method of nitrate ester synthesis from silver nitrate and alkyl halides in which the reaction mixture is homogeneous. Thus, this method is used to prepare 2,4,6-trinitrobenzyl nitrate from the corresponding bromide (59).

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[2] The examples given here are merely illustrative of the cases cited. For a comprehensive list of syntheses of simple nitrate esters, see table 1.

The versatility of the acetonitrile method is demonstrated by the preparation of a number of nitrate esters from the halides and silver nitrate, using acetonitrile as solvent (54).

Iodides or bromides are commonly used in the preparation of the simple primary or secondary nitrates. Chlorides of the tertiary, allylic, or benzyl type are, however, sufficiently reactive to be metathesized by silver nitrate, and thus can be used in the preparation of the corresponding nitrate esters.

C. MISCELLANEOUS PREPARATIONS

Although the majority of nitrate esters are prepared by either nitric acid esterification or silver nitrate metathesis, a number of methods have been used in the synthesis of special types of nitrate esters. While the methods described in preceding sections are generally applicable, the syntheses described in this section are, for the most part, fairly limited in scope.

Methyl nitrate is obtained from the nitrolysis of methylnitramine (60):

$$CH_3NHNO_2 \xrightarrow{HNO_3} \underset{\text{Methyl nitrate}}{CH_3ONO_2} + N_2O$$

Ethyl hydroperoxide reacts readily with nitrous acid to give a fair yield of ethyl nitrate (10).

Another preparation of ethyl nitrate involves the ethanolysis of benzoyl nitrate (61):

$$C_2H_5OH + C_6H_5COONO_2 \longrightarrow C_6H_5COOH + \underset{\text{Ethyl nitrate}}{C_2H_5ONO_2}$$

Benzyl nitrate is isolated as one of the products of the reaction of benzyl mercuric chloride or dibenzylmercury with nitric acid in the presence of oxides of nitrogen (164).

Nitration of cyclohexane, *n*-heptane, or *n*-octane with nitrogen pentoxide gives rise to cyclohexyl, 2-heptyl, or 2-octyl nitrate, respectively. Cyclohexyl nitrite is oxidized by nitrogen pentoxide to cyclohexyl nitrate (165).

A number of products are obtained from the electrochemical nitration of ethylene, including ethyl and butyl nitrates (122), but yields are extremely low.

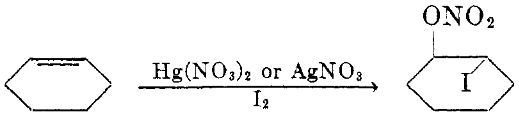
Electrolysis of mixtures of sodium nitrate and sodium salts of carboxylic acids yields mixtures of products, among which are mono- and dinitrate esters (55, 57, 58, 138). The method is not of preparative value however, because of the low yields and the complexity of the product mixtures.

β-Hydroxynitrates are obtained from the addition of nitric acid to epoxides (120). Unsymmetrical 1,2-epoxides yield predominantly primary nitrate esters (78). Kinetically, the addition shows a first-order dependence on the concentration of nitrate ion, hydronium ion, and epoxide (127).

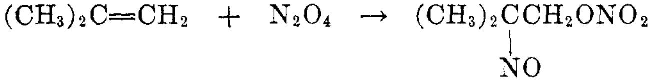
The reaction of dinitrogen tetroxide with propylene oxide is reported to yield a nitrite-nitrate (133), from which a hydroxy nitrate can be made by hydrolysis.

Nitrate esters of iodohydrins can be prepared by treating the appropriate olefin with a mixture of mercuric nitrate or silver nitrate and iodine. Typical examples are the preparation of ethylene and cyclohexene iodohydrin nitrates (20):

$$CH_2{=}CH_2 \xrightarrow[I_2]{Hg(NO_3)_2} ICH_2CH_2ONO_2$$



The addition of dinitrogen tetroxide to an olefin yields, in addition to a number of other products, a nitroso nitrate. For example, addition of dinitrogen tetroxide to isobutylene yields, as one of the products, 2-methyl-2-nitrosopropyl nitrate (112):



$$(CH_3)_2C{=}CH_2 + N_2O_4 \rightarrow (CH_3)_2\underset{NO}{\underset{|}{C}}CH_2ONO_2$$

A number of other examples of this addition appear in the literature (42, 145).

Nitrate esters are obtained in a number of instances as by-products in the reaction between an alkyl bromide or iodide and silver nitrite (29, 87, 89, 91).

Formation of nitrate esters in these reactions of halides with silver nitrite can be prevented by using a low temperature (0°C.) for the reaction (90).

Certain highly methylated benzene derivatives, on treatment with fuming nitric acid, give substituted benzyl nitrates, usually mixtures of isomers (149, 150, 151).

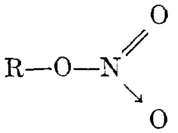
A mixture of 98 per cent nitric acid and phosphorus pentoxide is used successfully to prepare di- and trinitroxycyclohexanes (38).

Polynitrates are prepared by esterification of the corresponding polyalcohols with mixed acid, using the same techniques as those applied in the preparation of mononitrates[3] (116).

III. Physical Properties

The lower nitrate esters are colorless mobile liquids boiling slightly higher than the corresponding alcohols. They possess pleasant, sweetish odors, some quite similar to those of the parent alcohols. The nitrates are somewhat more dense than the alcohols and have slightly higher refractive indices. The esters are quite insoluble in water, but are very soluble in alcohols and ethers.

The nitrate esters show characteristic absorption bands in the infrared near 6.1, 7.8, and 11.8 microns (97), and the latter band has been used for quantitative estimation of ethyl nitrate in complex gaseous mixtures (99). Both the infrared (98) and ultraviolet (105) spectra provide evidence for the structure



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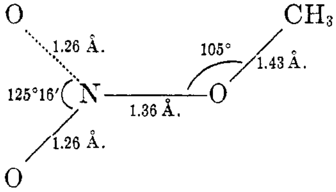
[3] References given in this section are illustrative only, and are not intended to be comprehensive.

and against a previously proposed peroxidic structure R—O—O—N=O. The lower primary nitrates, from methyl to *n*-butyl, all have dipole moments of approximately 2.9 D (39).

The molecular structure of methyl nitrate has been derived from Raman spectra and electron diffraction experiments. The Raman evidence (36) shows that the ONO_2 group is coplanar and that the carbon atom is in a plane perpendicular to the ONO_2 group.

Electron diffraction studies lead to the following structure for methyl nitrate (124):



This is in agreement with the findings of the Raman spectra experiments in that the ONO_2 group is coplanar and that a plane of symmetry exists, defined by the C—O—N bonds.

IV. CHEMICAL PROPERTIES

A. SOLVOLYTIC DECOMPOSITION

1. Hydrolysis

It has long been recognized that hydrolytic decomposition of nitrate esters involves the occurrence of other reactions besides the normal ester hydrolysis to alcohol and nitrate ion or nitric acid. Considerable confusion has existed, especially in the older literature, regarding these side reactions, with some investigators believing that they arise from a subsequent oxidation–reduction between the alcohol and nitric acid (52), and others regarding the side reactions as proceeding simultaneously with, and independently of, the normal hydrolysis (18, 83, 85). More recent studies (12, 14, 102) have established the simultaneous occurrence of three distinct reactions in the hydrolysis of nitrate esters. These reactions, illustrated with hydroxyl ion, are as follows:

(*a*) Nucleophilic substitution:

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

(*b*) Elimination of β-hydrogen:

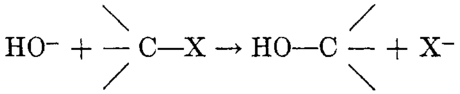
$$HO^- + RCH_2CH_2ONO_2 \rightarrow RCH{=}CH_2 + H_2O + NO_3^-$$

(*c*) Elimination of α-hydrogen:

$$HO^- + RCH_2ONO_2 \rightarrow RCH{=}O + H_2O + NO_2^-$$

Similar reactions can occur in neutral hydrolysis, with water acting as the nucleophilic agent. While these reactions are written as bimolecular, any of these processes, under suitable conditions, can also proceed by a unimolecular mechanism.

The substitution reaction, giving alcohol and nitrate ion, predominates in both alkaline and neutral hydrolysis of primary and secondary nitrate esters (12), although some products of both elimination processes are obtained from alkaline hydrolysis. Two possible bimolecular mechanisms for the substitution reaction have been considered. On the basis of similarities in the kinetics of nitrate ester hydrolysis and displacement reactions of alkyl halides, it has been proposed that both classes of compounds react by nucleophilic displacements on carbon (13),



$$\mathrm{HO^- + {>}C{-}X \rightarrow HO{-}C{<} + X^-}$$

where X may be halogen or $—ONO_2$. That this mechanism does, indeed, obtain in neutral hydrolysis has been shown by the fact that an optically active nitrate is converted to the alcohol having the inverted configuration (41). However, in alkaline hydrolysis there is some retention of configuration in going from nitrate to alcohol, a result which suggests that a different mechanism is operative. The most reasonable mechanism appears to be that involving cleavage of the oxygen–nitrogen bond, analogous to the usual acyl–oxygen cleavage in carboxylate esters (43).

In addition to the bimolecular processes for substitution, a base-independent carbonium-ion process (S_N1) is also available. The alcohol-producing reaction has been shown to proceed by this mechanism exclusively in the hydrolysis of *tert*-butyl nitrate (12, 102), and partially in the neutral hydrolysis of isopropyl nitrate (12).

Olefin formation occurs most extensively (up to 45 per cent) in the hydrolysis (either neutral or alkaline) of *tert*-butyl nitrate (12, 102), but small amounts of olefin are formed in the alkaline hydrolysis of ethyl (2 per cent) and isopropyl (10 per cent) nitrates (12). This elimination reaction apparently proceeds by a second-order (E2) process for the ethyl and isopropyl esters, and by a first-order (E1) process for *tert*-butyl nitrate.

It has been definitely established that nitrite ion is formed directly from the nitrate ester and is not the result of a secondary reaction in which alcohol is oxidized to aldehyde (12, 27, 28).

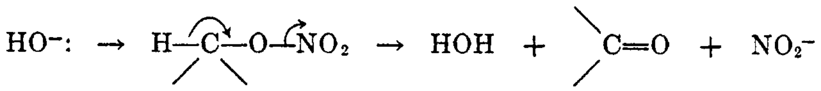
The formation of nitrite ion and a carbonyl compound from a nitrate ester was formerly believed to arise through the intermediate production of an alkyl hydroperoxide, which then might lose water to form the carbonyl compound

$$\mathrm{RCH_2ONO_2 + H_2O \rightarrow RCH_2OOH + HNO_2}$$

$$\mathrm{RCH_2OOH \rightarrow RCHO + H_2O}$$

(84, 105). This theory had its foundation in the fact that ethyl nitrate can be prepared from ethyl hydroperoxide and nitrous acid (10). Evidence cited to support the hydroperoxide theory includes the oxidation of mercaptans to disulfides by nitrate esters in alkaline solution (83) and the formation of diethyl peroxide when butyl nitrate is hydrolyzed in the presence of diethyl sulfate (105).

The fact that nitrite ion and carbonyl compound are formed in equivalent amounts and that no nitrite ion is formed from nitrate esters having no α-hydrogen atoms is the basis for the now generally accepted mechanism for nitrite formation, i.e., an elimination reaction:



This is entirely analogous to other β-elimination reactions, except that the resulting double bond is between carbon and oxygen instead of between two carbon atoms. The kinetics are second order (first order in nitrate and first order in hydroxide ion), and the mechanism is almost certainly bimolecular (12).

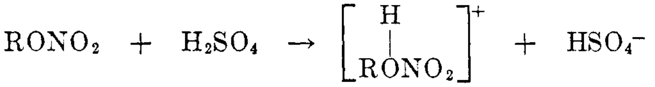
The amount of nitrite ion formed varies from traces in the case of methyl nitrate (12, 83) to 35 per cent in the case of isobutyl nitrate (83), and yields of benzaldehyde up to 90 per cent have been reported from the alkaline hydrolysis of benzyl nitrate (28, 102).

The hydrolysis of nitrate esters is accelerated only slightly by acids (123), and no detailed study of products has been made under acid conditions.

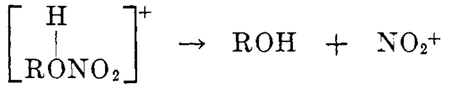
The rate of hydrolysis of primary and secondary nitrates, even in the presence of alkali, is extremely slow compared with the hydrolysis of alkyl halides (12). The effects on the rate (in base) of varying such factors as solvent, structure of the alkyl group, and nucleophilic character of the reagent are the same for nitrates as for halides (13) and are in accordance with the predictions of the Hughes–Ingold theory (77) for reactions between an ion and a neutral molecule.

2. *In concentrated sulfuric acid*

Cryoscopic and spectroscopic evidence indicates that, in concentrated sulfuric acid, nitrate esters undergo complex ionization, yielding nitronium ion NO_2^+; this is similar to the ionization shown by certain sterically hindered benzoic acids. A van't Hoff *i* factor approaching 5 has been found for ethyl nitrate (71, 94, 121) and a value greater than 4 for isoamyl nitrate (121). This has been interpreted (94) as being due to ionization in the following manner:



$$RONO_2 + H_2SO_4 \rightarrow \left[\begin{array}{c} H \\ | \\ RONO_2 \end{array}\right]^+ + HSO_4^- \qquad (1)$$



$$\left[\begin{array}{c} H \\ | \\ RONO_2 \end{array}\right]^+ \rightarrow ROH + NO_2^+ \qquad (2)$$

$$ROH + 2H_2SO_4 \rightarrow ROSO_3H + H_3O^+ + HSO_4^- \qquad (3)$$

The ultraviolet absorption spectrum of a sulfuric acid solution of ethyl nitrate is almost identical with that of a solution of nitric acid in sulfuric acid, but is different from that of a chloroform solution of the ester (94).

That the ionization is more complex than that given by equation 1 alone is also indicated by the fact that the ester is not regenerated when the sulfuric acid solution is poured into cold water.

The formation of nitronium ion probably explains the potency of sulfuric acid solutions of nitrate esters as nitrating agents.

Certain highly alkylated benzyl nitrates, on treatment with sulfuric acid, are converted to aromatic nitro compounds, with the nitro group replacing the nitroxymethyl group (149, 150). For example, 5-bromo-2,3,4,6-tetramethylbenzyl nitrate is converted into 5-bromo-2,3,4,6-tetramethylnitrobenzene (bromonitroisodurene).

3. Alcoholysis

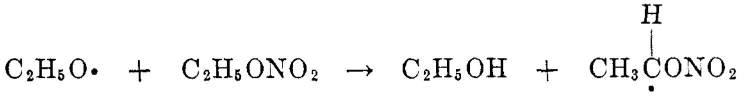
In the absence of water, the reaction of alkyl nitrates with alcoholic potassium hydroxide produces the mixed ethers rather than the alcohols (30, 33, 34, 35). Ethers are also obtained from the action of sodium alkoxides on nitrate esters.

B. THERMAL DECOMPOSITION

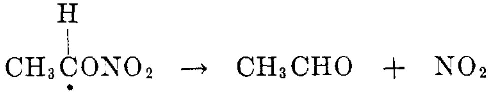
The thermal decomposition of nitrate esters has been studied by a number of investigators (1, 99, 100, 128, 129, 132, 159). With a few exceptions mentioned at the end of this section, the compound chosen in this study has been ethyl nitrate.

The principal product obtained from this decomposition is ethyl nitrite, with nitromethane and methyl nitrite being minor products. On the basis of the earlier kinetic studies which relied completely on manometric data (1, 129), the following incorrect mechanism was proposed:

$$C_2H_5ONO_2 \rightleftarrows C_2H_5O\cdot + NO_2 \qquad (4)$$



$$C_2H_5O\cdot + C_2H_5ONO_2 \rightarrow C_2H_5OH + CH_3\overset{\displaystyle H}{\underset{\bullet}{C}}ONO_2 \qquad (5)$$



$$CH_3\overset{\displaystyle H}{\underset{\bullet}{C}}ONO_2 \rightarrow CH_3CHO + NO_2 \qquad (6)$$

$$2NO_2 + C_2H_5OH \rightarrow C_2H_5ONO + HONO_2 \qquad (7)$$

Such a mechanism has been adequately refuted by the latest work on this subject, in which the course of the reaction was followed by infrared spectrometry (99, 100). Here it was found that ethyl nitrite is the principal product formed in the early stages of reaction, with nitromethane and methyl nitrite occurring in minor quantities. The original mechanism would set an upper limit of 50 per cent on the yield of ethyl nitrite, based on the ethyl nitrate decomposed, whereas yields as high as 75 per cent were found. Reactions 5 and 6 can likewise be rejected on the basis of this study, since acetaldehyde, which should be a major product if the proposed mechanism were operative, is present in the products in only very small amounts, as shown by the relatively low absorption in the carbonyl absorption region at ca. 5.7 μ.

The following mechanism appears to fit all the experimental facts:

$$C_2H_5ONO_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_2H_5O\cdot + NO_2 \tag{8}$$

$$C_2H_5O\cdot \longrightarrow CH_3\cdot + CH_2O$$

$$2CH_2O + 3NO_2 \longrightarrow 3NO + 2H_2O + CO + CO_2 \tag{9}$$

$$2CH_3\cdot + 7NO_2 \longrightarrow 7NO + 3H_2O + 2CO_2 \tag{10}$$

$$CH_3\cdot + NO_2 \longrightarrow CH_3NO_2$$

$$CH_3\cdot + NO_2 \longrightarrow CH_3O\cdot + NO$$

$$CH_3O\cdot + NO \longrightarrow CH_3ONO$$

$$C_2H_5O\cdot + NO \xrightarrow{k_2} C_2H_5ONO \tag{11}$$

The observed lowering of the rate by addition of nitrogen dioxide (100, 128, 129) is explained by the fact that the nitrogen dioxide accelerates the reverse of step 8. Similarly, the inhibiting effect of oxygen on the rate (100) involves oxidation of the nitric oxide formed in steps 9 and 10 to nitrogen dioxide.

The effect of nitric oxide on the rate of decomposition of ethyl nitrate is quite informative. At low concentrations of nitric oxide there is a sharp increase in the rate as nitric oxide is added, but as the concentration of nitric oxide increases, the rate appears to approach a limiting value. This appears to refute a previously (131) proposed exchange reaction between nitric oxide and ethyl nitrate:

$$NO + C_2H_5ONO_2 \rightarrow NO_2 + C_2H_5ONO \tag{12}$$

If reaction 12 were to occur, there should be a continual increase in the rate with addition of nitric oxide, contrary to what is observed. In the presence of excess nitric oxide the reaction apparently reduces essentially to steps 8 and 11. A kinetic treatment based on this latter assumption leads to the expression:

$$\frac{-\mathrm{d}\ln(C_2H_5ONO_2)}{\mathrm{d}t} = \frac{k_1}{1 + \dfrac{k_{-1}(NO_2)}{k_2(NO)}}$$

This rate expression predicts that addition of nitric oxide should cause the rate to approach a limiting value corresponding to k_1.

Addition of acetaldehyde enhances the rate by virtue of the fact that it reacts rapidly with nitrogen dioxide (100, 104).

Excellent first-order kinetics are observed when the ethyl nitrate decomposition is carried out in the presence of both nitric oxide and acetaldehyde. The nitric oxide reacts with the ethoxyl radical, and the acetaldehyde destroys the nitrogen dioxide as it is formed. The following general rate expression is thus obtained (100):

$$k = 10^{16.85}e^{-41,230/RT}\text{sec.}^{-1}$$

The decomposition of *n*-propyl nitrate has been investigated in the temperature range 165–187°C., using manometric techniques (130). The reaction is first order and essentially homogeneous. The rate constant over the temperature interval studied was found to be given by the expression:

$$k = 10^{14.7}e^{-36,860/RT}\text{sec.}^{-1}$$

A kinetic study of the decomposition of *n*-propyl nitrate at 181°C. (101) reveals that this decomposition is similar in many respects to the decomposition of ethyl nitrate. The principal products, as revealed by infrared and visible region spectra, are *n*-propyl nitrite, nitroethane, nitrogen dioxide, and nitric oxide. The effect of additives upon the reaction appears to parallel the results observed in the ethyl nitrate decomposition (99, 100). Nitrogen dioxide and oxygen inhibit the decomposition and nitric oxide has an accelerating effect.

The following reaction sequence appears to fit all the observed facts:

$$C_3H_7ONO_2 \rightleftarrows C_3H_7O\cdot + NO_2$$

$$C_3H_7O\cdot \rightarrow C_2H_5\cdot + CH_2O$$

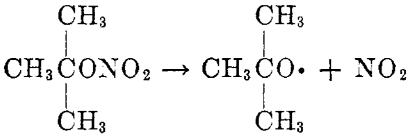
$$CH_2O + NO_2 \rightarrow NO + H_2O + CO$$

$$C_3H_7O\cdot + NO \rightarrow C_3H_7ONO$$

$$C_2H_5\cdot + NO_2 \rightarrow C_2H_5NO_2$$

$$C_2H_5\cdot + C_3H_7ONO_2 \rightarrow C_2H_5NO_2 + C_3H_7O\cdot$$

Preliminary studies on the decomposition of *tert*-butyl nitrate (101) at 181°C. indicate that the products of the decomposition are *tert*-butyl nitrite, acetone, nitromethane, methyl nitrite, nitrogen dioxide, and nitric oxide. These are readily accounted for by the following sequence of reactions:



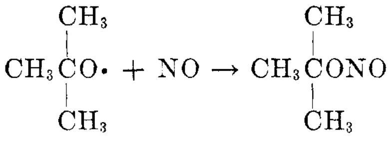
$$CH_3\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}ONO_2 \rightarrow CH_3\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}O\cdot + NO_2$$

$$(CH_3)_3CO\cdot \rightarrow CH_3\cdot + CH_3COCH_3$$

$$CH_3\cdot + NO_2 \rightarrow CH_3NO_2$$

$$CH_3\cdot + NO_2 \rightarrow CH_3ONO$$

$$NO_2 + CH_3COCH_3 \rightarrow NO + \text{products}$$



$$CH_3\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}O\cdot + NO \rightarrow CH_3\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}ONO$$

Acetone is a major product of this decomposition. This is in accord with previous findings on the decomposition of *tert*-butoxyl radicals derived from the homolytic cleavage of di-*tert*-butyl peroxide.

Studies on the inflammation of alkyl nitrate vapors (3, 4, 66, 67, 68, 69, 70) have demonstrated the existence of three modes of thermal decomposition: chemiluminescence, explosion, and decomposition without glow. The luminescent mode, as obtained at low pressures in the case of methyl nitrate, is attributed to the methoxyl radical and, as such, is substantiation of the primary reaction being the fission of the alkoxyl–nitrogen bond (67). Explosion limits of methyl and ethyl nitrates are increased by potassium chloride and potassium iodide surfaces (68).

More recently the flame velocities of methyl and ethyl nitrate vapors have been determined at low pressures and found to be independent of pressure (3, 4). Product analyses show the presence of carbon monoxide, water, nitric oxide, hydrogen, nitrogen, nitrous oxide, carbon dioxide, and formaldehyde in the case of methyl nitrate. Ethyl nitrate yields a more complex mixture, containing, as well, methane, acetylene, and acetaldehyde.

The combustion of liquid nitrate esters can be studied over a wide range of pressures by igniting the liquid contained in a glass capillary tube and measuring the rate of regression of the surface (2, 75, 155).

After combustion at atmospheric pressure 70–90 per cent of the nitrogen from ethyl nitrate is found as nitric oxide, the remainder being nitrogen and nitrous oxide. As the pressure is increased a second flame, which is thought to correspond to the complete reduction of nitric oxide, appears. The depression of the burning rate by the addition of small quantities of lead tetramethyl supports the assumption of a radical mechanism. At higher concentrations, however, lead tetramethyl causes an acceleration of burning rate, requiring a different mechanism, as yet not elucidated, to be operative (2). Deuterated ethyl nitrate is found to burn more slowly than the ordinary material by a factor of 1.4, which requires an isotopic effect in bond breaking as well as the change of diffusional coefficients of the hydrogen atoms (155).

The explosive decomposition of nitrate esters appears to follow a path different from that of the thermal decomposition (44). The general reaction for the explosive decomposition can be expressed as:

$$2RCHR'ONO_2 \rightarrow 2RCOR' + NO_2 + NO + H_2O$$

The ketone or aldehyde corresponding to oxidation of the parent alcohol of the nitrate ester is obtained. Methyl, ethyl, *n*-propyl, *n*-butyl, isobutyl, and benzyl nitrates all yield the corresponding aldehydes upon explosive decomposition, and α-phenylethyl nitrate yields acetophenone.

Photolysis of ethyl nitrate yields a variety of products (65). If ethyl nitrate is photolyzed at 95°C. with 2537 Å. ultraviolet light, the following compounds can be found among the products: nitrogen dioxide, nitric oxide, nitrous oxide, nitrogen, nitromethane, hydrogen, carbon monoxide, carbon dioxide, formaldehyde, and acetaldehyde.

C. NITRATION BY NITRATE ESTERS

1. Aromatic systems

There are several instances in which nitrate esters are used in aromatic nitration. Toluene is readily nitrated at 40°C. by ethyl nitrate in 98 per cent sulfuric acid to yield 44.5 per cent of *p*-nitrotoluene (188). In the nitration of toluene, β-chloroethyl nitrate and *n*-butyl nitrate are also quite effective.

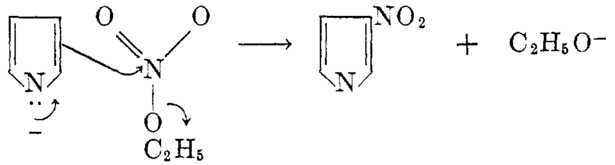
This nitration can be formulated according to the generally accepted concepts concerning the nitration of aromatic systems (79). Evidence is presented earlier in support of the fact that ethyl nitrate dissociates in concentrated sulfuric acid to nitronium ion, NO_2^+, which apparently serves as the nitrating agent.

A number of Lewis acids can be used as effective nitration catalysts with nitrate esters. Thus, benzene and toluene are nitrated by ethyl nitrate in the presence of aluminum chloride (24).

The nitration of benzene with ethyl nitrate, in somewhat lower yields, can be achieved by the use of other catalysts. Typical examples of these nitration catalysts are stannic chloride, antimony pentachloride, and ferric chloride (166).

Ethyl nitrate can be used in the nitration of a number of other aromatic systems including biphenyl (136), carbazole (136), 2,2′-dimethoxybiphenyl (136), phenol (24), anisole (24), and indole (6).

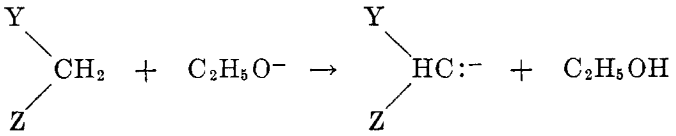
The sodium salt of pyrrole reacts with ethyl nitrate to yield β-nitropyrrole. This nitration is different from that of the other aromatic systems discussed here, in that the nitration is performed under essentially basic conditions. Probably the reaction proceeds by way of a nucleophilic attack by the pyrrole anion on the nitrate ester, displacing ethoxide ion (5):



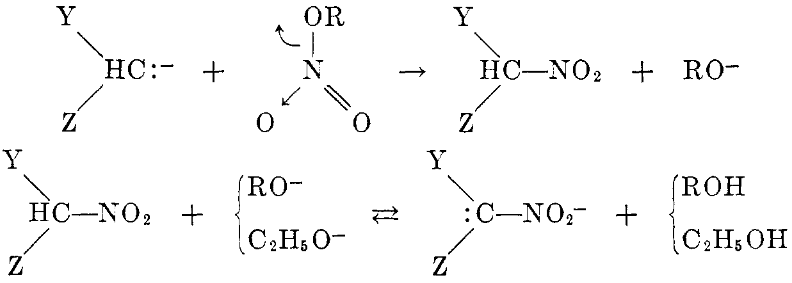
2. Active methylene compounds

Certain compounds containing active methylene groups are readily nitrated by means of primary or secondary alkyl nitrates in the presence of ethoxide ion. While the reaction proceeds in good yield with such compounds as phenylacetonitrile and related compounds, and with certain cyclic ketones, no examples of nitration of open-chain aliphatic compounds have been found; e.g., it has been reported (176) that ethyl acetate cannot be nitrated in this manner.

The reaction apparently involves a nucleophilic displacement by the anion of the active methylene compound on the nitrogen atom of the ester, thus:



$$\mathrm{YZ}CH_2 + C_2H_5O^- \rightarrow \mathrm{YZ}HC{:}^- + C_2H_5OH$$



Y represents an electron-attracting group, such as phenyl or carbonyl, and Z may be another such group or an alkyl group.

The initial product is the salt of a nitro compound, from which either the *aci*- or the normal form of the free nitro compound may be obtained. Where two equivalent active methylene groups are available, as in cyclohexanone, either the mononitro (172) or the dinitro (173) derivative may be prepared by controlling the relative amounts of reactants, although with cyclopentanone only the dinitro compound has been isolated (174).

In the nitration of derivatives of arylacetic acids, the products can be readily hydrolyzed and decarboxylated to give the corresponding arylnitromethanes. Indeed, the nitration of phenyl- and *p*-bromophenylacetic esters leads directly to the salts of the arylnitromethanes by spontaneous decarboxylation of the intermediate nitro esters (179, 180). By further treatment of either the aryl nitromethanes or of aryl nitroacetonitriles with alkali, good yields of the corresponding stilbenes may be obtained (182).

In several instances (146, 162), but not all (76, 163), where optically active nitrate esters were used, transient optical activity has been reported for the salts, but in no case has optical activity been found in the free nitro compounds.

A summary of nitrations of this type is given in table 2.

3. N-Nitration

N-Nitration by nitrate esters is achieved in a few instances. Phenylnitramine can be prepared from ethyl nitrate and aniline in the presence of either sodium in ether (8) or potassium ethoxide (17).

Nitration of ethylurea or ethyl urethan by ethyl nitrate in sulfuric acid yields the corresponding nitro derivative (161):

$$C_2H_5NHCONH_2 \xrightarrow[H_2SO_4]{C_2H_5ONO_2} C_2H_5NHCONHNO_2$$

$$NH_2COOC_2H_5 \xrightarrow[H_2SO_4]{C_2H_5ONO_2} O_2NNHCOOC_2H_5$$

N-Nitration is presumed to occur in the reaction of hydrazine with nitrate esters (see Section IV,E) and is written as the primary step in the decomposition of hydroxylamine with ethyl nitrate in the presence of sodium ethoxide (7):

$$C_2H_5ONO_2 + H_2NOH \xrightarrow{NaOC_2H_5} O_2NNHOH + C_2H_5OH$$

$$O_2NNHOH + H_2NOH \longrightarrow N_2 + HNO_2 + 2H_2O$$

TABLE 2

Reactions of nitrate esters with active methylene compounds

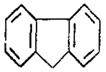
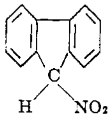
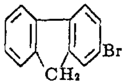
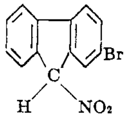
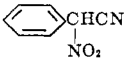
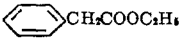
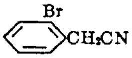
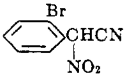
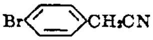
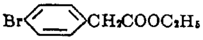
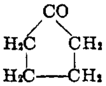
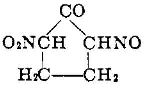
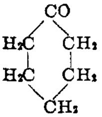
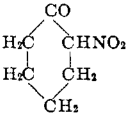
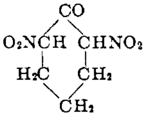
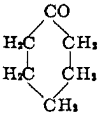
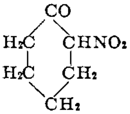
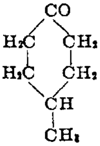
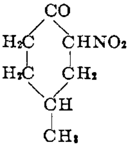
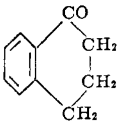
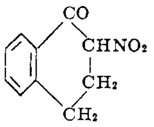
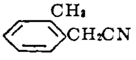
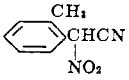
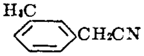
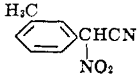
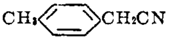
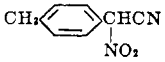
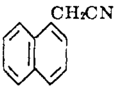
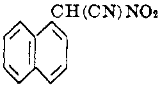
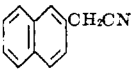
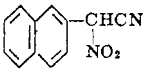
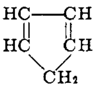
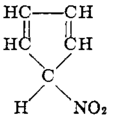
Compound Nitrated	Nitrate Ester	Product: Salt of	Yield	References
			per cent	
	Ethyl		>70	(181)
	*d*- and *l*-2-Octyl		62.5	(162)
	Methyl		75-82	(23)
	Ethyl		70-80	(177)
	d-, *l*-, and *dl*-2-Octyl		80	(163)
	Ethyl		>30, 80	(176, 179)
	Ethyl		ca. 30	(178)
	Ethyl		85-90	(175)
	Ethyl			(180)
	Ethyl		ca. 100	(174)
	Ethyl		66-83	(172)
	Ethyl		ca. 100	(173)
	*l*-2-Octyl			(146)
	*d*-, *l*-, and *dl*-2-Octyl		30-34	(146)

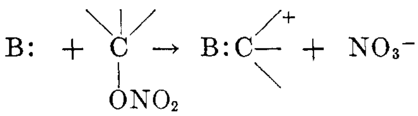
TABLE 2—*Concluded*

Compound Nitrated	Nitrate Ester	Product: Salt of	Yield	References
			per cent	
	Ethyl		ca. 100	(157)
	d-, *l*-, and *dl*-2-Octyl			(76)
	Ethyl		"Good"	(183)
	Ethyl		ca. 75	(184)
	Ethyl			(185)
	Ethyl			(186)
	Ethyl			(187)
	Ethyl			(160)

Nitrosation is possible in the reaction of an amine with a nitrate ester. Nitrosodiphenylamine is one of the products obtained in the reaction of diphenylamine with ethyl nitrate (139).

D. ALKYLATION WITH NITRATE ESTERS

A number of reactions are known in which nitrate esters act as alkylating agents. These reactions apparently proceed via a displacement at the α-carbon atom of the ester, as distinguished from the attack on the nitrogen atom, which leads to nitration products. The alkylation reaction may be written as



$$B\colon + \underset{ONO_2}{\overset{\diagdown | \diagup}{C}} \rightarrow B\colon C\overset{\diagup +}{\underset{\diagdown}{-}} + NO_3^-$$

where B: represents a generalized nucleophilic reagent, either a neutral molecule such as ammonia or a negative ion like the malonic ester anion.

When nitrate esters are heated with ammonia or primary or secondary aliphatic amines, N-alkylation occurs. Methyl (80), ethyl (80), and n-propyl (169) amines have been prepared from the corresponding nitrates and ammonia in sealed tubes at 100°C. Piperidine (64) and diethylamine (64) have been alkylated by heating with primary, secondary, and tertiary alkyl nitrates.

Primary aromatic amines, such as aniline (140), the toluidines (141), and *m*-xylidine (141), react with alkyl nitrates to give the amine nitrate and the *N*-alkylated amine. Secondary and tertiary aromatic amines, however, give oxidation–reduction and condensation products, usually highly colored and difficult to characterize (142). Diphenylnitrosoamine, for example, has been obtained from diphenylamine and ethyl nitrate.

Hydrazine is readily alkylated at room temperature by nitrate esters of the benzyl type (108, 110) and, apparently, to a lesser extent by aliphatic nitrates.

Pyridine and tertiary aliphatic amines react at reflux temperatures with primary nitrate esters to form quaternary ammonium salts (16, 96). Secondary and tertiary nitrates, however, undergo elimination reactions under the same conditions to form olefins (96). Dimethylaniline and benzyl nitrate form a quaternary salt (119), although, as noted above, aliphatic nitrates are reduced by such amines.

S-Alkylation with nitrate esters has also been reported. Methyl and ethyl isothiuronium nitrates are formed by heating thiourea with the appropriate nitrate esters (158). Trimethyl- and triethylsulfonium nitrates have been obtained from the reaction at room temperature (and over a long period of time) of the dialkyl sulfides with the corresponding alkyl nitrates (137).

Benzylmalonic ester (118) and benzylacetoacetic ester (117) have been prepared by the reaction of benzyl nitrate with the sodio derivatives of malonic and acetoacetic esters. Other nitrate esters, however, react with similar carbanions to form nitro rather than alkyl derivatives (see table 2).

E. REDUCTION OF NITRATE ESTERS

Reductions of nitrate esters by a number of different reducing agents are reported in the literature. Research in this field is not, in general, detailed or extensive, but for the most part consists of isolated examples of the action of various reducing agents upon the simple aliphatic nitrate esters. As yet, nitrate ester reduction is not particularly useful as a synthetic or analytical tool, probably because the product is nearly always the parent alcohol from which the ester is made.

1. *Electrolytic*

Electrolytic reduction of simple nitrate esters proceeds smoothly at *ca.* 1 v. *vs.* the standard calomel electrode. The reaction involves a two-electron change, yielding the parent alcohol and nitrite ion (81, 134) as products. Ethyl nitrate, cyclohexyl nitrate, and the dinitrates of *cis*- and *trans*-cyclohexanediol are all reduced in good yield to the corresponding alcohols. As would be expected, the number of electrons involved in a nitrate ester reduction is proportional to the number of nitrate ester groups. Thus, reduction of butyl nitrate is a two-electron reduction, reduction of ethylene glycol or cyclohexanediol dinitrate a four-electron reduction, of nitroglycerin a six, and of pentaerythritol tetranitrate an eight (171).

2. By Grignard reagents

A few instances are reported of reactions of nitrate esters with Grignard reagents. Dimethylhydroxylamine is obtained from methyl nitrate and methylmagnesium iodide (114).

Similarly, the action of methylmagnesium iodide on ethyl nitrate leads to the formation of dimethylhydroxylamine, and diethylhydroxylamine is formed in the general reaction between ethylmagnesium iodide and a nitrate ester (74).

3. By hydrazines

Hydrazine and substituted hydrazines are effective as reducing agents for nitrate esters. In the presence of a platinum or palladium catalyst, *n*-hexyl nitrate reacts with hydrazine to yield hexyl alcohol, nitrous oxide, nitrogen, and water. When methylhydrazine is used, two additional products are formed: namely, methane and ethane (95).

In the absence of the platinum or palladium catalyst, the reaction between a nitrate ester and hydrazine is considerably slower and somewhat more complicated. The simple aliphatic nitrates, such as the ethyl and *n*-butyl esters, are converted to the parent alcohols in addition to several gaseous products which include nitrogen, nitrous oxide, hydrazoic acid, and ammonia (110). A possible course for the reaction is as follows:

$$RONO_2 + NH_2NH_2 \rightarrow ROH + NH_2NHNO_2$$

The unstable nitrohydrazine can conceivably decompose in two ways. An E2 elimination of nitrous acid gives rise to diimide:

$$NH_2NHNO_2 \xrightarrow{N_2H_4} NH{=}NH + HNO_2$$

Nucleophilic displacement of nitrite ion by hydrazine yields tetrazane:

$$NH_2NH_2 + NH_2NHNO_2 \rightarrow NH_2NHNHNH_2 + HNO_2$$

The gaseous products can arise by decomposition of these labile intermediates. Nitrous oxide is probably formed by the reaction of hydrazine with nitrous acid (50).

The reaction of phenylhydrazine with ethyl nitrate at elevated temperatures to give nitrogen, aniline, and ammonium nitrate has been reported (169a). From the same reactants at ordinary temperatures in the presence of sodium ethoxide, a number of products are obtained, including nitrite ion, nitrogen, benzene, biphenyl, phenyl azide, azobenzene, aniline, and nitrobenzene (17a).

4. Hydrogenolysis

A limited number of cases of hydrogenolysis of a nitrate ester have been reported (93). If *n*-amyl nitrate is reduced with palladium on charcoal, Raney nickel, or platinum, the products are amyl alcohol and ammonia. However, if palladium on calcium carbonate is used in the reduction, the products are the alcohol and nitrogen. The palladium–calcium carbonate reduction is useful in the denitration of nitrated carbohydrate derivatives where the presence of ammonia will cause undesirable side reactions.

5. *By lithium aluminum hydride*

Lithium aluminum hydride is another useful reagent in reductive denitration. Cyclohexyl, *n*-hexyl, and 2-octyl nitrates, and the dinitrates of *cis*- and *trans*-cyclohexanediol, are all reduced in essentially quantitative yield to the alcohols by lithium aluminum hydride (153).

6. *By metal–acid mixtures*

As would be expected, metal–acid mixtures are effective in the reduction of nitrate esters. The action of tin and hydrochloric acid yields the corresponding alcohol (147). Similarly, iron and acetic acid react with *n*-butyl nitrate to yield the parent alcohol (144). This reduction finds application in the sugar series in the denitrations with zinc or iron in acetic acid (47).

7. *By sulfides*

Hydrogen sulfide and ammonium sulfide are also used to reduce nitrate esters. Hydrogen sulfide reacts with ethyl nitrate to form ethyl alcohol, ammonia, and sulfur (86); *n*-butyl nitrate is acted upon by ethanolic ammonium sulfide to yield *n*-butyl alcohol and sulfur (144). The latter reaction appears to be quite dependent upon the pH and the molecular species of sulfide present (109). The reaction of *n*-butyl nitrate with sodium hydrosulfide yields *n*-butyl alcohol and sodium nitrite as the main products. If ammonium hydrosulfide is used, the principal nitrogen-containing product is ammonia, and 4 gram-atoms of sulfur are produced per mole of nitrate. Above pH 13, either sodium or ammonium hydrosulfide reduces butyl nitrate to nitrite ion and *n*-butyl alcohol, with the formation of 1 gram-atom of sulfur. The reaction is apparently second order kinetically and is catalyzed by hydroxyl ion and by polysulfide.

A mechanism has been proposed (115) for the sulfide denitration of nitrocellulose: namely, hydrolysis of the ester followed by reduction of nitrate ion. However, it has been shown that this mechanism does not obtain in the reaction of *n*-butyl nitrate with sulfides (109). It has further been shown that another conceivable mechanism—reduction of the nitrate ester to the corresponding nitrite ester, followed by subsequent reaction of the nitrite with sulfide—is not operative. The most reasonable mechanism for the sulfide denitration, therefore, appears to involve nucleophilic attack by sulfide or polysulfide upon the nitrogen atom of the nitrate ester, with displacement of alkoxide ion, similar to the primary reaction proposed in the hydrazine denitration (110).

8. *Miscellaneous reductions*

Nitrate esters are also acted upon by metallic sodium. The products of the reaction between sodium and methyl, ethyl, or amyl nitrate are sodium nitrite and the parent alcohol (as its sodium salt) (32, 34).

Nearly all of the cases of nitrate ester reduction reported above appear to proceed without cleavage of the carbon–oxygen bond in the ester. This cleavage occurs, however, in the reduction of butyl nitrate with strong hydriodic acid, from which butyl iodide, nitrogen dioxide, and iodine are produced (33).

Fission of the carbon–oxygen bond also occurs in the conversion of the primary nitrate group in a sugar nitrated in the 6-position to the corresponding iodide by means of sodium iodide in acetone. This latter reaction apparently involves a concerted displacement of nitrate by iodide (47).

V. Typical Industrial Applications

Nitrate esters have a variety of industrial applications, examples of which will be mentioned in this section.

Probably the most widely recognized application of nitrate esters is their use as high explosives or as ingredients of smokeless powder and rocket propellants. Among the simple aliphatic nitrates, nitroglycerin and ethylene glycol dinitrate are, by far, the compounds most widely used for this purpose (156). The pure compounds have the disadvantage of being quite sensitive to shock. Despite this, nitroglycerin has seen widespread use in "shooting" oil wells. However, nitroglycerin and ethylene glycol dinitrate can be stored, shipped, and handled conveniently if adsorbed on some suitable material, such as kieselguhr, or when formulated into propellants.

Methyl and ethyl nitrates have been used as explosives and have been found to be about equivalent to trinitrotoluene in explosive power (156), but, because these compounds are rather volatile liquids, they are difficult to handle as explosives and their use is limited.

Methyl nitrate has been considered for use as a propellant, both alone and mixed with methanol (170), but because of its explosive nature, it does not appear to be entirely satisfactory for this purpose. Propyl nitrate, on the other hand, is useful as a monopropellant in liquid-propellant motors (48).

Several nitrate esters, including methyl, ethyl, and β-chloroethyl, have been used as additives in both gasoline and diesel fuels as combustion accelerators and as antiknock agents (9, 51, 53, 72).

Ethyl, propyl, and *sec*-butyl nitrates are rather effective in stabilizing trichloroethylene, which is used in cleaning iron or aluminum (82).

Ethyl and butyl nitrates are useful as catalysts with phosphoric esters in the manufacture of ketene from acetic acid (152).

VI. Physiological Properties and Hazards Involved (167)

In addition to the hazards presented by nitrate esters because of their flammability and explosive nature, the toxicity of these compounds deserves consideration also. Only glycerol trinitrate has been studied extensively with regard to physiological properties, but other nitrate esters appear to have similar but milder effects.

The toxicity of these compounds is due mainly to their effects on the blood and the circulatory system. Nitrate esters oxidize hemoglobin to methemoglobin and, by depression of the muscles in the vascular walls, cause a peripheral vasodilation, resulting in lowered systolic blood pressure and increased pulse and respiratory rates. On the basis of this vasodilator action, several of the nitrate esters, including amyl nitrate and glycerol trinitrate, are widely used therapeutically for the relief of high blood pressure.

The most characteristic symptom of poisoning by nitrate esters (particularly that due to glycerol trinitrate) is severe headache and a feeling of pressure on the front and back of the head. The dilation of the peripheral blood vessels results in a shift of blood to the splanchnic area and may cause a decreased supply of blood to the brain (in spite of cerebral vasodilation), resulting in vertigo or fainting. Apparent immunity to glycerol trinitrate may be built up by continued exposure.

Nitrate esters may be absorbed by inhalation, through the skin, or through the digestive tract, and precautions should be taken to avoid prolonged exposure or contact. It is believed that persons addicted to alcohol may be especially susceptible to these compounds.

VII. REFERENCES

(1) ADAMS, G. K., AND BAWN, C. E. H.: Trans. Faraday Soc. **45**, 494 (1949).
(2) ADAMS, G. K., PARKER, W. G., AND WOLFHARD, H. G.: Discussions Faraday Soc. **No. 14**, 101 (1953).
(3) ADAMS, G. K., AND SCRIVENER, J.: Fifth Symposium (International) on Combustion, Pittsburgh, August, 1954, p. 162 of Abstracts.
(4) ADAMS, G. K., AND WISEMAN, L. A.: "*Selected Combustion Problems*", AGARD Combustion Colloquium, Cambridge University, England, 7-11 December 1953, pp. 282-6. Butterworths Publications, Ltd., London (1954).
(5) ANGELI, A., AND ALLESANDRI, P. E.: Atti accad. Lincei [5] **20**, 311.
(6) ANGELI, A., AND ANGELICO, F.: Gazz. chim. ital. **30**, **II**, 270 (1900).
(7) ANGELI, A., AND ANGELICO, F.: Gazz. chim. ital. **34**, 50 (1904).
(8) ANGELI, A., AND MARAGLIANO, M. V.: Atti accad. Lincei [5] **14**, II, 127 (1905). Cited in *The Nitramines* by H. J. Backer. Translation by H. Stone of article by H. J. Backer in Sammlung Chem. und Chem. Tech. Vorträge **18**, 359-474 (1912).
(9) AUBERT, M., CLERGET, P., AND DUCHENE, R.: Compt. rend. **201**, 879 (1935).
(10) BAEYER, A., AND VILLIGER, V.: Ber. **34**, 755 (1901).
(11) BAKER, J. W.: J. Chem. Soc. **1934**, 987.
(12) BAKER, J. W., AND EASTY, D. M.: J. Chem. Soc. **1952**, 1193.
(13) BAKER, J. W., AND EASTY, D. M.: J. Chem. Soc. **1952**, 1208.
(14) BAKER, J. W., AND EASTY, D. M.: Nature **166**, 156 (1950).
(15) BAKER, J. W., AND HEGGS, T. G.: Chemistry & Industry **1954**, 464.
(16) BAKER, J. W., AND NATHAN, W. S.: J. Chem. Soc. **1936**, 236.
(17) BAMBERGER, E.: Ber. **53B**, 2321 (1920).
(17a) BAMBERGER, E., AND BILLETER, O.: Helv. Chim. Acta **14**, 219 (1931).
(18) BERTHELOT, M.: Compt. rend. **131**, 519 (1900).
(19) BERTONI, G.: Gazz. chim. ital. **20**, 372 (1890).
(20) BIRCKENBACH, L., AND GOUBEAU, J.: Ber. **67B**, 1425 (1934).
(21) BIRON, E.: Chem. Zentr. **1901**, **I**, 366.
(22) BLACK, A. P., AND BABERS, F. H.: In *Organic Syntheses*, edited by A. H. Blatt, Coll. Vol. II, p. 412. John Wiley and Sons, Inc. New York (1943).
(23) Reference 22, p. 512.
(24) BODKER, E.: Bull. soc. chim. France [4] **3**, 726 (1908).
(25) BOUVEAULT, L., AND WAHL, A.: Bull. soc. chim. France [3] **29**, 956 (1903).
(26) BURKE, K. A., AND DONNAN, F. G.: J. Chem. Soc. **85**, 565 (1904).

(27) Carlson, T.: Arkiv Kemi Min. Geol. **3**, art. 8, 1–5; Chem. Abstracts **2**, 3344 (1908).
(28) Carlson, T.: Ber. **40**, 4191 (1907).
(29) Cenker, M.: Ph.D. Thesis, Purdue University, February, 1949.
(30) Chapman, E. T., and Smith, M. H.: J. Chem. Soc. **20**, 576–86 (1867).
(31) Chapman, E. T., and Smith, M. H.: J. Chem. Soc. **20**, 581 (1867).
(32) Chapman, E. T., and Smith, M. H.: J. Chem. Soc. **20**, 584 (1867).
(33) Chapman, E. T., and Smith, M. H.: J. Chem. Soc. **22**, 158 (1869).
(34) Chapman, E. T., and Smith, M. H.: Z. Chem. **1868**, 172.
(35) Chapman, E. T., and Smith, M. H.: Z. Chem. **1869**, 432.
(36) Chedin, J.: J. phys. radium **10**, 445–54 (1939); Chem. Abstracts **34**, 1250 (1940).
(37) Cheeseman, G. W. H.: Chemistry & Industry **1954**, 281.
(38) Christian, W. R., and Purves, C. B.: Can. J. Chem. **29**, 926 (1951).
(39) Cowley, E. G., and Partington, J. R.: J. Chem. Soc. **1933**, 1252.
(40) Cristol, S. J., and Leffler, J. E.: J. Am. Chem. Soc. **76**, 4468 (1954).
(41) Cristol, S. J., Shadan, A., and Franzus, B.: Abstracts of Papers Presented at the 125th National Meeting of the American Chemical Society, 1954, p. 20 N.
(42) Crowder, J. A. (to Solvay Process Co.): U. S. patent 2,402,315; Chem. Abstracts **40**, 6092 (1946).
(43) Day, J. N. E., and Ingold, C. K.: Trans. Faraday Soc. **37**, 689 (1941).
(44) Deniges, G.: Compt. rend. **202**, 1998 (1936).
(45) Desseigne, G.: Bull. soc. chim. France **1946**, 98.
(46) Desseigne, G.: Mém. poudres **30**, 59 (1948); Chem. Abstracts **44**, 7221 (1950).
(47) Dewar, J., and Fort, G.: J. Chem. Soc. **1944**, 492.
(48) Diplock, B. R., Lofts, D. L., and Grimston, R. A.: J. Roy. Aeronaut. Soc. **57**, No. 505, 19–28 (1953); Chem. Abstracts **47**, 5686 (1953).
(49) Ellis, R. W., Smythe, B. M., and Treharne, E. D.: Fifth Symposium (International) on Combustion, Pittsburgh, August, 1954, p. 135 of Abstracts.
(50) Ephraim, F.: *Inorganic Chemistry*, 5th edition, revised by P. C. L. Thorne and E. R. Roberts, p. 673. Interscience Publishers, Inc., New York (1949).
(51) Établissements Delattre et Fronard rèunis: French patent 972,288 (January 29, 1951); Chem. Abstracts **46**, 8845 (1952).
(52) Farmer, R. C.: J. Chem. Soc. **117**, 806 (1920).
(53) Ferretti, P.: Ricerca sci. **14**, 217 (1943); Chem. Abstracts **43**, 6805 (1949).
(54) Ferris, A. F., McLean, K. W., Marks, I. G., and Emmons, W. D.: J. Am. Chem. Soc. **75**, 4078 (1953).
(55) Fichter, F., and Metz, F.: Helv. Chim. Acta **19**, 597 (1936).
(56) Fichter, F., and Petrovich, A.: Helv. Chim. Acta **24**, 253 (1941).
(57) Fichter, F., Segrist, W., and Buess, H.: Helv. Chim. Acta **18**, 18 (1935).
(58) Fichter, F., and Sutter, P.: Helv. Chim. Acta **21**, 891 (1938).
(59) Fieser, L. F., and Doering, W. von E.: J. Am. Chem. Soc. **68**, 2252 (1946).
(60) Franchimont, A. P. N.: Rec. trav. chim. **29**, 311 (1910).
(61) Francis, F. E.: J. Chem. Soc. **89**, 1 (1906).
(62) Gand, E.: Bull. soc. chim. France **1950**, 118.
(63) Gand, E.: Bull. soc. chim. France **1950**, 120.
(64) Gibson, D. T., and Macbeth, A. K.: J. Chem. Soc. **119**, 438 (1921).
(65) Gray, J. A., and Style, D. W. G.: Trans. Faraday Soc. **49**, 52 (1953).
(66) Gray, P.: Discussions Faraday Soc. **14**, 135 (1953).
(67) Gray, P.: Proc. Roy. Soc. (London) **221**, 462 (1954).
(68) Gray, P., and Yoffe, A. D.: J. Chem. Soc. **1950**, 3180.
(69) Gray, P., and Yoffe, A. D.: Nature **164**, 830 (1949).
(70) Gray, P., and Yoffe, A. D.: Proc. Roy. Soc. (London) **A200**, 114 (1949).
(71) Hantzsch, M.: Z. physik. Chem. **61**, 292 (1907).
(72) Heinze, R., Marde, M., and Veidt, M.: Oel u. Kohle **37**, 422 (1941); Chem. Abstracts **36**, 4993 (1942).

(73) HENRY, L.: Ber. **5**, 452 (1872).
(74) HEPWORTH, H.: J. Chem. Soc. **119**, 251 (1921).
(75) HILDENBRAND, D. L., AND WHITTAKER, A. G.: Fifth Symposium (International) on Combustion, Pittsburgh, August, 1954, p. 65 of Abstracts.
(76) HORNE, W. H., AND SHRINER, R. L.: J. Am. Chem. Soc. **55**, 4652 (1933).
(77) HUGHES, E. D., AND INGOLD, C. K.: J. Chem. Soc. **1935**, 252.
(78) INGHAM, J. D., AND NICHOLS, P. L., JR.: J. Am. Chem. Soc. **76**, 4477 (1954).
(79) INGOLD, C. K.: *Structure and Mechanism in Organic Chemistry*, pp. 269–83. Cornell University Press, Ithaca, New York (1953).
(80) JUNCADELLA, E.: Ann. **110**, 254 (1859).
(81) KAUFMAN, F., COOK, H. J., AND DAVIS, S. M.: J. Am. Chem. Soc. **74**, 4997 (1952).
(82) KLABUNDE, W.: U. S. patent 2,435,312 (February 3, 1948); Chem. Abstracts **42**, 2916 (1948).
(83) KLASON, P., AND CARLSON, T.: Arkiv Kemi Min. Geol. **3**, art. 7, 1–11; Chem. Abstracts **2**, 3344 (1908).
(84) KLASON, P., AND CARLSON, T.: Ber. **39**, 2752 (1906).
(85) KLASON, P., AND CARLSON, T.: Ber. **40**, 4183 (1907).
(86) KOPP, E.: Ann. **64**, 320 (1847).
(87) KORNBLUM, N., LICHTIN, N. N., PATTON, J. T., AND IFFLAND, D. C.: J. Am. Chem. Soc. **69**, 307 (1947).
(88) KORNBLUM, N., LICHTIN, N. N., PATTON, J. T., AND IFFLAND, D. C.: J. Am. Chem. Soc. **69**, 313 (1947).
(89) KORNBLUM, N., PATTON, J. T., AND NORDMANN, J. B.: J. Am. Chem. Soc. **70**, 746 (1948).
(90) KORNBLUM, N., TAUB, B., AND UNGNADE, H. E.: J. Am. Chem. Soc. **76**, 3209 (1954).
(91) KORNBLUM, N., AND TEITLEBAUM, C.: J. Am. Chem. Soc. **74**, 3076 (1952).
(92) KREUK, L. J. DE: Rec. trav. chim. **61**, 819 (1942).
(93) KUHN, L. P.: J. Am. Chem. Soc. **68**, 1761 (1946).
(94) KUHN, L. P.: J. Am. Chem. Soc. **69**, 1974 (1947).
(95) KUHN, L. P.: J. Am. Chem. Soc. **73**, 1510 (1951).
(96) LANE, E. S.: J. Chem. Soc. **1953**, 1172.
(97) LECOMTE, J., AND MATHIEU, J. P.: J. chim. phys. **39**, 57 (1942).
(98) LENORMANT, H., AND CLEMENT, P. L.: Bull. soc. chim. France **1946**, 559.
(99) LEVY, J. B.: J. Am. Chem. Soc. **76**, 3254 (1954).
(100) LEVY, J. B.: J. Am. Chem. Soc. **76**, 3790 (1954).
(101) LEVY, J. B., AND ADRIAN, F. J.: NavOrd Report 2608, 22 December 1952.
(102) LUCAS, G. R., AND HAMMETT, L. P.: J. Am. Chem. Soc. **64**, 1928 (1942).
(103) LUFKIN, J. E.: U. S. patent 2,396,330; Chem. Abstracts **40**, 3462 (1946).
(104) MACDOWELL, C. A., AND THOMAS, J. H.: Trans. Faraday Soc. **46**, 1030 (1950).
(105) MATSUSHIMA, Y.: Collected Papers Faculty Sci. Osaka Univ., Ser. C, Chem. **11**, No. 3, 1 (1949); Chem. Abstracts **46**, 1434 (1952).
(106) MEDARD, L.: J. chim. phys. **31**, 283 (1934).
(107) MEDARD, L., AND ALQUIER, R.: J. chim. phys. **32**, 63 (1935).
(108) MERROW, R. T., AND BOSCHAN, R. H.: J. Am. Chem. Soc. **76**, 4622 (1954).
(109) MERROW, R. T., CRISTOL, S. J., AND VAN DOLAH, R. W.: J. Am. Chem. Soc. **75**, 4259 (1953).
(110) MERROW, R. T., AND VAN DOLAH, R. W.: J. Am. Chem. Soc. **76**, 4522 (1954).
(111) MICHAEL, A., AND CARLSON, G. H.: J. Am. Chem. Soc. **57**, 1268 (1935).
(112) MICHAEL, A., AND CARLSON, G. H.: J. Org. Chem. **5**, 1 (1940).
(113) MILLON: Ann. **47**, 373 (1843).
(114) MOREAU, C.: Compt. rend. **132**, 838 (1901).
(115) NADAI, A.: Z. physik. Chem. **136**, 289 (1928).
(116) NAOUM, P. P.: *Nitroglycerine and Nitroglycerine Explosives*, p. 25. Williams & Wilkins Company, Baltimore, Md. (1928).

(117) Nef, J. U.: Ann. **309,** 172 (1899).
(118) Nef, J. U. Ann. **309,** 173 (1899).
(119) Nef, J. U.: Ann. **309,** 174 (1899).
(120) Nichols, P. L., Magnusson, A. B., and Ingham, J. D.: J. Am. Chem. Soc. **75,** 4255 (1953).
(121) Oddo, G., and Scandola, E.: Gazz. chim. ital. **40, II,** 179 (1910).
(122) Öhman, V.: *The Svedberg* (Mem. Vol.) **1944,** 413.
(123) Olivier, S. C. J., and Berger, G.: Rec. trav. chim. **41,** 641 (1922).
(124) Pauling, L., and Brockway, L. O.: J. Am. Chem. Soc. **59,** 13 (1937).
(125) Perkin, W. H.: J. Chem. Soc. **55,** 682 (1889).
(126) Perkin, W. H.: J. Chem. Soc. **55,** 683 (1889).
(127) Petty, W. L., and Nichols, P. L., Jr.: J. Am. Chem. Soc. **76,** 4385 (1954).
(128) Phillips, L.: Nature **160,** 753 (1947).
(129) Phillips, L.: Nature **165,** 564 (1950).
(130) Phillips, L.: Thesis, University of London, 1949; *cf.* reference 89.
(131) Pollard, F. H., Marshall, H. S. B., and Pedler, A. E.: Nature **171,** 1154 (1953).
(132) Pollard, F. H., Wyatt, R. M. H., and Marshall, H. S. B.: Nature **165,** 564 (1950).
(133) Pujo, A. M., and Boileau, J.: Compt. rend. **237,** 1422 (1953).
(134) Radin, N., and De Vries, T.: Anal. Chem. **24,** 971 (1952).
(135) Raley, J. H., Rust, F. F., and Vaughan, W. E.: J. Am. Chem. Soc. **70,** 88 (1948).
(136) Raudnitz, H.: Ber. **60,** 738 (1927).
(137) Ray, F. E., and Szasz, G. J.: J. Org. Chem. **8,** 121 (1943).
(138) Rudin, M.: Helv. Chim. Acta **25,** 636 (1942).
(139) Ryan, H., and Casey, M. T.: Sci. Proc. Roy. Dublin Soc. **19,** 101–11 (1928).
(140) Ryan, H., and Casey, M. T.: Sci. Proc. Roy. Dublin Soc. **19,** 102–3 (1928).
(141) Ryan, H., and Casey, M. T.: Sci. Proc. Roy. Dublin Soc. **19,** 104–5 (1928).
(142) Ryan, H., and Casey, M. T.: Sci. Proc. Roy. Dublin Soc. **19,** 106–8 (1928).
(143) Ryan, H., and Coyle, V. J. R.: Proc. Roy. Irish Acad. **37,** 361 (1927).
(144) Ryan, H., and Coyle, V. J. R.: Proc. Roy. Irish Acad. **37,** 366 (1927).
(145) Scaife, C. W., Baldock, H., and Smith, A. E. W.: British patents 586,344, 586,022, 575,604, 575,618; U. S. patent 2,424,510; Chem. Abstracts **41,** 6893 (1947).
(146) Shriner, R. L., and Parker, E. A.; J. Am. Chem. Soc. **55,** 766 (1933).
(147) Sidgwick, N. V.: *The Organic Chemistry of Nitrogen*, new edition, revised by T. W. J. Taylor and W. Baker, p. 8. Oxford University Press, Oxford (1942).
(148) Silva, R. D.: Ann. **154,** 254 (1870).
(149) Smith, L. I., and Horner, J. W.: J. Am. Chem. Soc. **62,** 1349 (1940).
(150) Smith, L. I., Taylor, F. L., and Webster, I. M.: J. Am. Chem. Soc. **59,** 1082 (1937).
(151) Smith, L. I., and Tenenbaum, D.: J. Am. Chem. Soc. **57,** 1293 (1935).
(152) Societa Rhodiaceta: French patent 930,682 (February 2, 1948); Chem. Abstracts **43,** 5413 (1949).
(153) Soffer, L. M., Parrotta, E. W., and Di Domenico, J.: J. Am. Chem. Soc. **74,** 5301 (1952).
(154) Staedel, W.: Ann. **217,** 214 (1883).
(155) Steinberger, R.: Fifth Symposium (International) on Combustion, Pittsburgh, August, 1954, p. 63 of Abstracts.
(156) Stettbacker: *Die Schiess und Sprengstoffe*, Leipzig, 1919. Review by P. P. Naoum: Z. ges. Schiess u. Sprengstoffw. **15,** 3 (1920).
(157) Straus, F., and Ekhard, W.: Ann. **444,** 163 (1925).
(158) Taylor, J.: J. Chem. Soc. **111,** 657 (1917).
(159) Thiele, H.: Angew. Chem. **A60,** 65 (1948).
(160) Thiele, J.: Ber. **33,** 666 (1900).
(161) Thiele, J., and Lackman, A.: Ann. **288,** 285 (1895).
(162) Thurston, J. T., and Shriner, R. L.: J. Am. Chem. Soc. **57,** 2163 (1935).
(163) Thurston, J. T., and Shriner, R. L.: J. Org. Chem. **2,** 190 (1937).

(164) Titov, A. I., and Rusanov, D. E.: Doklady Akad. Nauk (S.S.S.R.) **82,** 65–8 (1952); Chem. Abstracts **47,** 2688 (1953).

(165) Titov, A. I., and Schitov, N. V.: Doklady Akad. Nauk (S.S.S.R.) **81,** 1085 (1951); Chem. Abstracts **46,** 7992 (1952).

(166) Tronov, B. V., and Sibgatullin, N.: J. Russ. Phys. Chem. Soc. **62,** 2267 (1930).

(167) Von Oettingen, W. F.: National Institute of Health Bulletin **No. 186** (1946).

(168) Wallach, O., and Schulze, E.: Ber. **14,** 421 (1881).

(169) Wallach, O., and Schulze, E.: Ber. **14,** 422 (1881).

(169a) Walther, R.: J. prakt. Chem. **53,** 433 (1896).

(170) Wheeler, W. H., Whittaker, H., and Pike, H. H. M.: J. Inst. Fuel **20,** 137–156, 159 (1947); Chem. Abstracts **41,** 5307 (1947).

(171) Whitnack, G. C., Nielsen, J. M., and Gantz, E. S. C.: J. Am. Chem. Soc. **76,** 4711 (1954).

(172) Wieland, H., Garbsch, P., and Chavan, J. J.: Ann. **461,** 298 (1928).

(173) Wieland, H., Garbsch, P., and Chavan, J. J.: Ann. **461,** 301 (1928).

(174) Wieland, H., Garbsch, P., and Chavan, J. J.: Ann. **461,** 303 (1928).

(175) Wislicenus, W., and Elvert, H.: Ber. **41,** 4122 (1908).

(176) Wislicenus, W., and Endres, A.: Ber. **35,** 1755 (1902).

(177) Wislicenus, W., and Endres, A.: Ber. **35,** 1757 (1902).

(178) Wislicenus, W., and Fischer, M.: Ber. **43,** 2235 (1910).

(179) Wislicenus, W., and Grützner, R.: Ber. **42,** 1932 (1909).

(180) Wislicenus, W., and Grützner, R.: Ber. **42,** 1933 (1909).

(181) Wislicenus, W., and Waldmüller, M.: Ber. **41,** 3336 (1908).

(182) Wislicenus, W., and Wren, H.: Ber. **38,** 502–10 (1905).

(183) Wislicenus, W., and Wren, H.: Ber. **38,** 503 (1905).

(184) Wislicenus, W., and Wren, H.: Ber. **38,** 504 (1905).

(185) Wislicenus, W., and Wren, H.: Ber. **38,** 506 (1905).

(186) Wislicenus, W., and Wren, H.: Ber. **38,** 507 (1905).

(187) Wislicenus, W., and Wren, H.: Ber. **38,** 509 (1905).

(188) Wright, H. R., and Donaldson, W. J.: U. S. patent 2,416,974 (March 4, 1947); Chem. Abstracts **41,** 3485 (1947).