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DUAL REACTIVITY OF NITRO-COMPOUNDS IN ALKYLATION AND ACYLATION REACTIONS

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I. INTRODUCTION

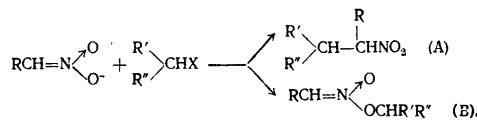
In recent years the scale of the studies on the chemistry of aliphatic nitro-compounds has been steadily increasing. Among the wide variety of the reactions which have attracted the attention of numerous investigators the alkylation and acylation of nitro-compounds merit attention. In the first place these reactions are of considerable theoretical interest since it is here that the dual reactivity of nitro-compounds is shown in a particularly pronounced form. Furthermore, they have attracted the attention of investigators for a long time as a method for preparing various nitro-derivatives and a wide variety of carbonyl compounds. However, despite the large number of studies on this problem, the available data have not been reviewed so far. The aim of the present review is to collect and compare the literature data on the alkylation and acylation of nitro-compounds with nitro-groups at saturated carbon atoms.

In the first section of the review the work done on the alkylation and acylation of mononitro-compounds, i.e. compounds with not more than one nitro-group at a single carbon atom, is considered. The second part deals with polynitro--compounds with several nitro-groups at a single carbon atom.

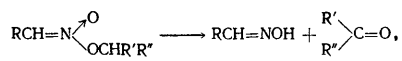
II. ALKYLATION AND ACYLATION OF MONONITRO--COMPOUNDS

1. Alkylation of *C*-Halogeno-Derivatives

In the alkylation of nitro-compounds their salts are employed as a rule. Consequently anions are actually involved in the reaction. Since the anions of nitro-compounds have two reaction centres (the oxygen of the nitro-group and the carbon bound to the latter), two modes of alkylation of nitro-compounds may be expected:

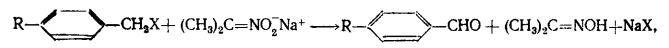


In the first case (*C*-alkylation) nitro-compounds are formed (A) while in the second case (*O*-alkylation) the products should be nitronic esters (B). As will be shown later, nitronic esters are as a rule unstable to heat and break down into a carbonyl compound and an oxime:



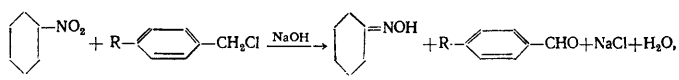
i.e. the breakdown of the ester involves intramolecular oxidation–reduction and ultimately the nitro-compound is reduced to the oxime and the halogeno-derivative is oxidised to the corresponding carbonyl compound.

The alkylation of mononitro-compounds has been studied in greatest detail in reactions with various halides of the benzyl type. In almost all cases such reactions results in alkylation of the oxygen only. Thus in the reactions with various *p*-substituted benzyl halides the sodium salt of 2-nitropropane yields only the corresponding benzaldehydes (in yields of 68–77%) and acetone oxime, i.e. the breakdown products of nitronic esters [1] †



where R = CH_3, Br, CH_3CO, CH_3OCO, CN, CF_3, $\overset{+}{N}(CH_3)_3I^-$.

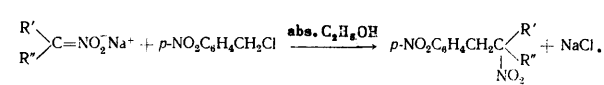
Similar results were obtained in the reactions of benzyl chloride with the potassium salt of 2-nitropropane [3], with the sodium salts of phenylnitromethane [4] and phenylnitroacetonitrile [4], and also with nitrocyclohexane [5]. The authors proposed the last reaction as a method for the preparation of alicyclic oximes and carbonyl compounds:



where R = H and CH_3.

The reaction of the silver salt of phenylnitroacetonitrile with benzyl chloride also gives an *O*-alkylation product [6].

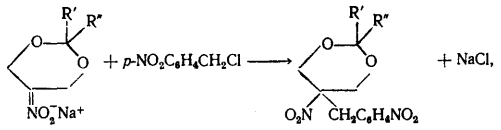
Among benzyl halides, *p*-nitrobenzyl chloride occupies an exceptional position, since, in contrast to all other benzyl halides, it alkylates alkali metal salts of nitroalkanes (nitroethane, 1- and 2-nitropropane, 1- and 2-nitrobutane, nitrocyclohexane, and nitrocyclopentane) almost exclusively at a carbon atom with formation of *p*-nitrophenyl-substituted nitroalkanes in yields between 30 and 60%: [7]



It is necessary to use a considerable excess of the nitroalkane, since otherwise polyalkylation products are formed [for example 1,1-bis-(*p*-nitrobenzyl)nitroethane may form from nitroethane [8]].

† The authors recommended this reaction as a general method for the synthesis of substituted benzaldehydes (see also Ref. 2).

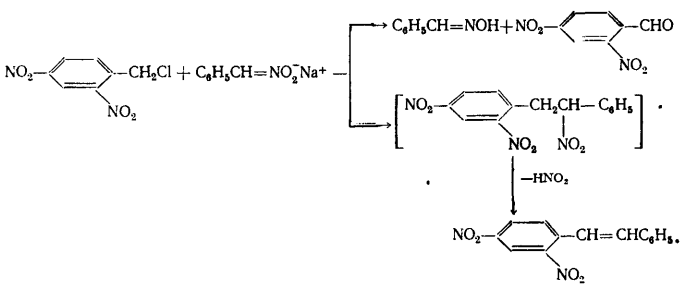
p-Nitrobenzyl chloride can also be successfully used for the *C*-alkylation of derivatives of 5-nitro-1,3-dioxan[9]:



where R′ = H and R″ = C_6H_5 (a) or R′ = R″ = CH_3 (b). In the reaction of this halide with the sodium salt of phenylnitromethane both *C*- and *O*-alkylation take place[4]. The mercury salt of phenylnitromethane does not enter into a similar reaction[4].

When *p*-nitrobenzyl halides are allowed to react with salts (sodium and silver) of phenylnitroacetonitrile, only the oxygen is alkylated[4]. It has been stated that *o*-nitrobenzyl chloride gives bis-(*o*-nitrobenzyl)nitromethane on reacting with the sodium salt of nitromethane[10], but the yield has not been given.

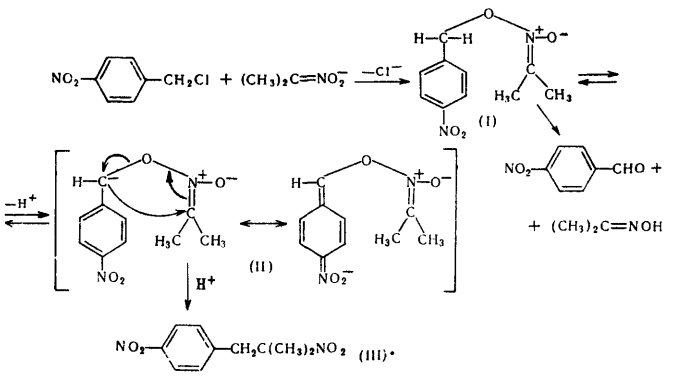
2,4-Dinitrobenzyl chloride and the sodium salt of phenylnitromethane yield both *O*- and *C*-derivatives. However, in the latter case, the product is unstable and breaks down to give 2,4-dinitrostilbene[4]:



C-Alkylation takes place in the reaction of 2,4-dinitrobenzyl chloride with the sodium salt of 2-nitropropane (yield 33%)[11].

The above data show that in the alkylation of the salts of nitroalkanes with benzyl halides it is virtually only *p*-nitrobenzyl chloride that gives products of alkylation exclusively at the carbon atom; in all the remaining cases *O*-alkylated derivatives are almost the only products. This is seen particularly clearly in the following example: in the reaction of the sodium salt of 2-nitropropane with nitro-substituted benzyl chlorides the *para*-isomer gives only *C*-alkylated products (yield 83%), the *ortho*-isomer gives products corresponding to 46% *C*-alkylation and 30% *O*-alkylation, while the *meta*-isomer and the unsubstituted benzyl chloride give rise to *O*-alkylation alone (in 73% yield)[11].

The study of the kinetics of the reaction of the lithium salt of 2-nitropropane with *o*-, *m*-, and *p*-nitrobenzyl chlorides (in ethanol at 30°) showed that the reaction is of the second order and its rate is approximately the same as that of the reaction of potassium iodide (in acetone) with the same halides[11]. Hass and Bender[11] put forward the following mechanism for the reaction of the salts of nitroalkanes with benzyl halides: both in *O*- and in *C*-alkylation the initial stage is alkylation of the oxygen with formation of the nitronic ester (I) which then either breaks down into an aldehyde and an oxime or ionises to give a resonance-stabilised carbanion (II). As a result of intramolecular rearrangement the latter then yields the *C*-alkylation product (III):



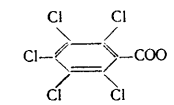
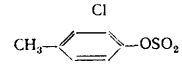
The presence of a nitro-group in the *para*-position of the benzyl ring greatly facilitates the removal of a proton from compound (I) and thereby leads to complete conversion of (I) into (II), i.e. ultimately to *C*-alkylation.

However, this mechanism does not explain why the mode of alkylation depends on the nature of the group being substituted in the *p*-nitrobenzyl system. Thus Kornblum and coworkers[12,13] showed that in the reaction of the lithium salt of 2-nitropropane with various *p*-nitrobenzyl derivatives the ratio of the products of *C*- and *O*-alkylation varies sharply with the group being substituted (see Table).

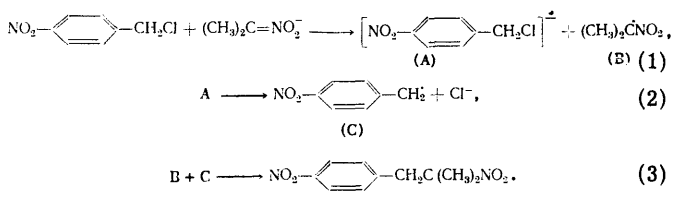
Another argument against the mechanism of Hass and Bender[11] was adduced by Boyd and Kelly[14], who showed that in the *C*-alkylation of nitro-compounds with allyl halides there is no allyl rearrangement which would have to take place if Hass and Bender's hypothesis of the initial formation of *O*-alkylation products and their subsequent rearrangement to *C*-alkylation products were correct.

Recently Kornblum and coworkers[15] suggested a new alkylation mechanism to account for the specificity of the reactions of nitroalkane salts with *p*-nitrobenzyl derivatives. They believe that, whereas *O*-alkylation involves the usual nucleophilic substitution at the oxygen atom of the

TABLE. Mode of reaction of *p*-$NO_2C_6H_4CH_2X$ with the lithium salt of 2-nitropropane (in dimethylformamide at -16°) depending on the nature of X.[12,13]

X	C-Alkylation, %	O-Alkylation, %
$\overset{+}{N}(CH_3)_3$ (25°)	93	0
	93	0
Cl	95	1
	40	32
Br	17	65
I	7—9	81

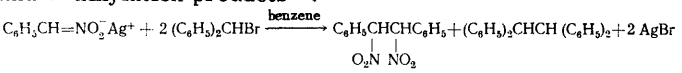
nitro-group, *C*-alkylation is a more complex anionic-radical process:



In this mechanism the first stage of the reaction consists in the transfer of an electron from the nitroalkane anion to the aromatic system [Eqn. (1)], this being followed by the loss of a chloride ion by the radical-anion (A) [Eqn. (2)] and the recombination of the two radicals (B) and (C) [Eqn. (3)].

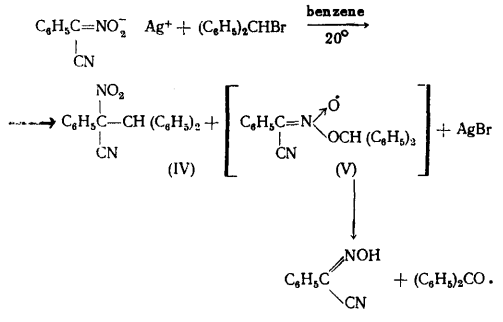
This hypothesis is based on the study of alkylation kinetics [15] (the slight increase of the rate of *C*-alkylation on going from *p*-nitrobenzyl chloride to the bromide and then the iodide, which is untypical for an S_N2-process) and was confirmed by the detection of radical-anions in the reaction mixture (by the ESR method).

The reactions of mononitro-compounds with α-phenyl substituted benzyl halides and with di- and tri-phenyl halogenomethanes are more complex. Thus in the reaction of the silver salt of phenylnitromethane with diphenylbromomethane, 1,2-diphenyl-1,2-dinitroethane and the symmetrical tetraphenylethane are obtained instead of the expected *C*- and *O*-alkylation products [16]:

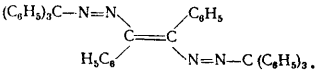


The authors believe that the unstable silver salt of phenylnitromethane breaks down with formation of diphenyldinitroethane and silver, the latter reacting with the initial bromide to give tetraphenylethane.

The reaction of the silver salt of phenylnitroacetonitrile gives, although in low yield, the *C*-alkylation product — triphenylnitropropionitrile (IV). [17] However, it was shown subsequently [18] that the principal mode of this reaction is *O*-alkylation with formation of the nitronic ester (V) which decomposes into α-isonitrosobenzyl cyanide and benzophenone:

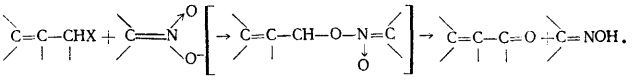


The reaction of triphenylchloromethane with the mercury salt of phenylnitromethane gives the *C*-alkylation product, 1,1,1,2-tetraphenyl-2-nitroethane, in 33–40% yield [4,17]. The reaction of triphenylchloromethane with the silver salt of phenylnitroacetonitrile is much more complex [17,19]. Initially it was believed that the *C*-alkylation product is formed [17], but later it was shown that the reaction gives rise to αα′-bis-(triphenylmethaneazo)stilbene [19]:



In addition, it proved possible to isolate triphenylmethyl isocyanate and a compound of unknown structure [19] with the empirical formula $C_{14}H_{11}N_{13}O$.

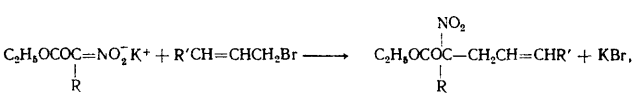
Halides of the allyl type, whose reactivity is similar to that of benzyl halides, alkylate mononitro-compounds at the oxygen atom as a rule. Thus the reaction of alkali metal salts of nitroalkanes with a series of allyl halides of different structures containing one or two allylic halogen atoms, gives rise to αβ-unsaturated mono- and di-aldehydes or ketones as a result of the breakdown of the intermediate nitronic esters [20]:



Both primary and secondary nitroalkanes and primary and secondary allyl bromides and chlorides may be used in the reaction (best results were obtained with the salts of 2-nitropropane [20] and nitrocyclohexane [21]). This reaction serves as a basis for the preparative synthesis of unsaturated aldehydes, for example citral and its homologues [21,22], which are used in the manufacture of perfumes.

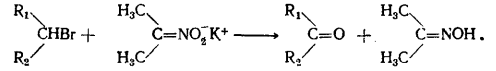
O-Alkylation is also achieved with the aid of a cyclic halide of the allyl type, 3-bromocyclohexene, which reacts with the sodium salt of 2-nitropropane with formation of an unsaturated ketone (cyclohexenone) and acetone oxime [23]. Another product is cyclohexadiene (formed by the dehydrohalogenation of the initial bromide).

Mononitro-compounds have been alkylated at the carbon atom by allyl halide in only a few cases. Thus the reaction of the salts of nitroacetic and nitromalonic esters with allyl halides gives small yields (10–30%) of the corresponding *C*-derivatives [14] ‡:



where R = H and C_2H_5OCO and R′ = H and CH_3.

Many investigators have studied the alkylation of various mononitro-compounds with alkyl halides. In almost all cases the oxygen atom was alkylated with formation of nitronic esters (sometimes isolated in a pure form) or their decomposition products. The potassium salt of 2-nitropropane reacts with various alkyl halides (undecyl and dodecyl bromide, 1-piperonyl-2-bromoethane, and others) with formation of aldehydes and acetone oxime [3]:

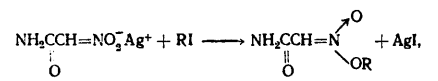


The corresponding oxime is also formed in the reaction of the sodium salt of 1,1,2-triphenyl-2-nitroethane with methyl iodide [25]. When the potassium salt of 9-nitrofluorene reacts with alkyl halides, fluorenone oxime is formed and also the corresponding aldehyde, ketone, or olefin, depending on the nature of the halide (primary, secondary, or tertiary) [26]. Similar results were obtained with the silver salt of 2-bromo-9-nitrofluorene [27].

The reaction of the sodium salt of phenyl- and *p*-bromophenylnitromethane with methyl iodide is unusual, the products being stilbene (or 4,4′-dibromostilbene) and

‡ In a paper published in 1873 [24] an attempt to synthesise 4-nitropent-1-ene from the potassium salt of nitroethane and allyl iodide is described; however, the reaction product was not identified.

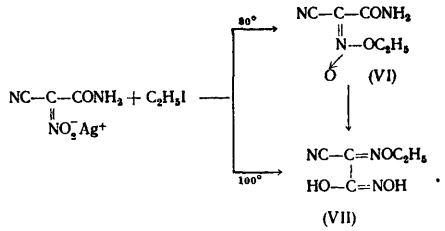
benzaldehyde[26]. The reaction of the sodium salt of phenylnitromethane with t-butyl bromide gives only the free phenylnitromethane[26]. In many cases stable nitronic esters, resulting from *O*-alkylation, can be isolated when alkyl halides react with salts of mononitro-compounds. Such esters were obtained, for example, in the reaction of the silver salt of nitroacetamide with various alkyl iodides[28,29]:



where R = CH_3, C_2H_5, n-C_3H_7, and iso-C_5H_{11}. The silver salt of the diamide of nitromalonic acid does not enter into a similar reaction[30].

When the silver salt of phenylnitroacetonitrile reacts with methyl iodide, it is possible to isolate a relatively stable nitronic ester[6,31]; in another study only the decomposition product of this ester, an oxime, was obtained[32]. The results of the reaction of *p*-bromophenylnitroacetonitrile were similar[33].

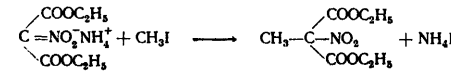
The reaction of the silver salt of fulminic acid (cyanonitroacetamide) with ethyl iodide also gives a nitronic ester (VI),[34] or, at a higher temperature, its rearrangement product (VII):[35,36]



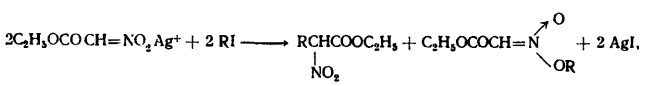
(VII)

A stable nitronic ester was obtained from the silver salt of 3-methyl-4-nitro-5-iso-oxazolone and ethyl iodide[37].

Only a few examples of *C*-alkylation of mononitro-compounds with alkyl halides are known. Thus α-methyl-α-nitromalonic ester is formed in the reaction between methyl iodide and ammonium nitromalonate[38]:

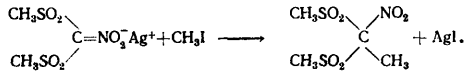


However, when ethyl iodide is used, let alone other alkyl halides, the reaction proceeds with considerable difficulty[39]. The reaction of the sodium salt of 2-chloro-2-nitroethanol with methyl iodide also yields a *C*-alkylation product[40] — 2-chloro-2-nitro-1-propanol (yield not stated)[40]. The silver salt of nitroacetic ester reacts with alkyl iodides with formation of both *O*- and *C*-alkylation products (the yield of the latter is 20–25%)[41]:



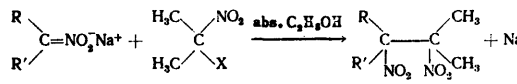
where R = CH_3 and C_2H_5. Alkyl bromides do not enter into this reaction[41].

There exist also patent data on the preparation of *C*-derivatives by the alkylation of nitromalonic ester with alkyl halides and also other alkylating agents (sulphites, sulphonates, and others), but the details of the experimental procedure are not indicated[42]. Backer[43] mentions the *C*-alkylation of the silver salt of bis(methylsulphonyl)nitromethane with methyl iodide but the yield of the product was very low:



It is also interesting that the reaction of 1-(*p*-nitrophenyl)-2-bromoethane with the sodium salt of 2-nitropropane results in alkylation at the carbon atom with formation of 3-methyl-3-nitro-1-(*p*-nitrophenyl)butane (yield 54%)[11].

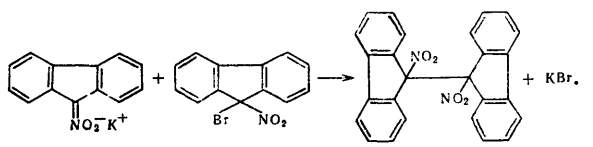
Seigle and Hass[44,45] showed that the reaction of alkali metal salts of secondary nitroalkanes with halogenonitro-compounds in which the halogen and the nitro-group are attached to the same carbon atom yields vicinal dinitroalkanes:



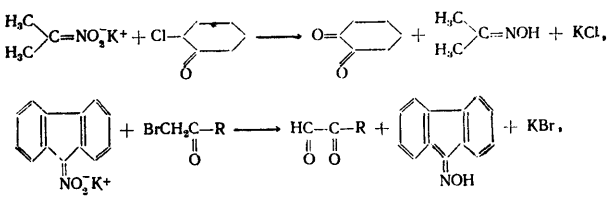
where R and R′ = CH_3, C_2H_5, and $-(CH_2)_5-$, and X = Cl, Br, and I. The yields of the *C*-alkylation products are 10% for the chloride, 20–30% for the bromide, and 43% for the iodide§.

Primary nitro-compounds do not enter into this reaction as a rule[44]; however, Nenitzescu and Isacescu[26] succeeded in obtaining 1,2-diphenyl-1,2-dinitroethane by allowing the sodium salt of phenylnitromethane to react with phenyliodonitromethane. The salts of *p*-bromo- and *p*-methyl-phenylnitromethanes do not react with this iodide[26].

The potassium salt of 9-nitrofluorene reacts with 9-bromo-9-nitrofluorene to give 1,2-di(biphenylene)-1,2-dinitroethane[26]:



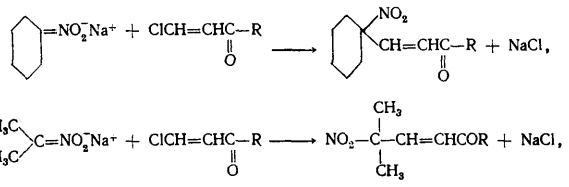
Of the other halogeno-derivatives which react with mononitro-compounds, halogeno-ketones should be mentioned. Thus the reaction of the potassium salt of 2-nitropropane with 2-chlorocyclohexanone[3] gave 1,2-cyclohexadione, while the reaction of the potassium salt of 9-nitrofluorene with bromoacetone and ω-bromoacetophenone resulted in the formation of methyl- and phenyl-glyoxal respectively (in yields of 85–95%) and fluorenone oxime[47]:



where R = CH_3 and C_6H_5.

§ Later it was shown that the yield of nitroalkanes depends significantly on the purity of the initial nitro-compounds: thus when pure 2-nitropropane is used, it is possible to increase the yield of 2,3-dimethyl-2,3-dinitrobutane to 50% for the chloride and to 80% for the bromide[46].

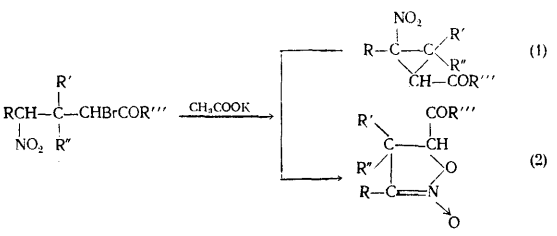
Only rather unusual halogeno-ketones, such as β-chlorovinyl ketones, alkylate nitro-compounds at the carbon atom, and even then as a rule with low yields [48-50]:



where R = CH_3, C_2H_5, n-C_3H_7, C_6H_5, p-$CH_3C_6H_4$, p-ClC_6H_4, and p-BrC_6H_4.

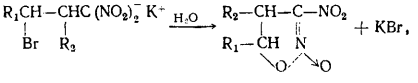
An attempt to condense the potassium salt of nitroethane with iodoacetic ester was unsuccessful[51]. Chloroacetic ester reacted with the potassium salt of 9-nitrofluorene to give fluorenone oxime and ethyl glyoxylate[26].

An unusual type of alkylation of nitro-compounds has been described in a number of papers of Kohler, Smith, and others. They showed that, when compounds of the type $RCH(NO_2)CR'R''CHBrCOR'''$, containing a halogen in the γ-position with respect to the nitro-group and in the α-position with respect to the carbonyl, are heated with potassium acetate, intramolecular alkylation takes place with formation of either cyclopropane derivatives (*C*-alkylation)[52-58] or isoxazoline oxides (*O*-alkylation)[59-64]:



The formation of nitrocyclopropanes [reaction (1)] occurs only when primary nitro-compounds are used (R = H); secondary nitro-compounds give only the *O*-alkylation products [reaction (2)].[62]

Tartakovskii et al. showed recently[65] that, when two nitro-groups are present in the γ-position with respect to halogen, only *O*-alkylation takes place, *N*-oxides of nitroisoxazolines being formed¶:



where R_1 = H and CH_3OCO, R_2 = H, CH_3, and C_6H_5, and R_1–R_2 = $-(CH_2)_3-$ and $-(CH_2)_4-$.

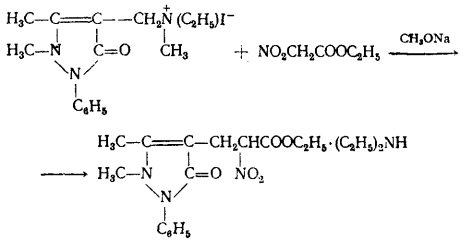
2. Alkylation with Mannich Bases and Quaternary Ammonium Bases

Alkylation with Mannich bases is known to take place according to one of two mechanisms (see, for example, Hellman and Opitz[67]): the so-called "elimination–addition" mechanism or the nucleophilic substitution mechanism.

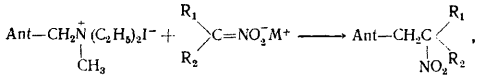
All tertiary Mannich bases with even only one labile hydrogen atom in the β-position with respect to the nitrogen (or the vinylogues of such bases) alkylate according to the first of the above mechanisms, which comprises two stages: (a) elimination of the amine from the Mannich base with formation of an unsaturated compound and (b) the Michael addition of the component to be alkylated to the unsaturated compound.

In the present review we shall consider the alkylation of mononitro-compounds only by Mannich bases which are incapable of alkylation by the above mechanism, i.e. those that react according to the nucleophilic substitution mechanism. This reaction is successful only in those cases where quaternary ammonium salts of Mannich bases incapable of undergoing deamination are used, since after removal of the tertiary amine, the bases form a carbonium ion stabilised by electron delocalisation and capable of reacting with the anion of the nitro-compound to be alkylated[67].

For example, 2-nitropropane is not alkylated by dimethyl-(β-nitroisobutyl)amine[68]. Also there is no alkylation when nitroacetic ester reacts with the tertiary Mannich base derived from antipyrine[69]†. On the other hand, when a quaternary salt, the methiodide of diethylaminomethylantipyrine, is used, nitroacetic ester can be alkylated with a 48% yield[71]:

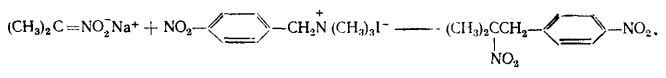


The alkylation of the potassium salt of the anilide of nitroacetic ester[71] and the sodium salt of nitromalonic ester takes place similarly[69]:



where R_1 = H and R_2 = $CONHC_6H_5$ or R_1 = R_2 = $COOC_2H_5$; M = Na and K, and Ant = antipyrine residue. The methiodide of 1-dimethylamino-2-methyl-2-nitropropane (Mannich base derived from nitropropane) proved to be unsuitable for *C*-alkylation of nitro-compounds[68].

Several examples of related reactions, the alkylation of the salts of mononitro-compounds with quaternary ammonium bases, have been described. Thus Schechter and Kaplan[72] obtained a 63% yield of the corresponding *C*-alkylation products by allowing the sodium salt of 2-nitropropane to react with trimethyl-(p-nitrobenzyl)ammonium iodide:

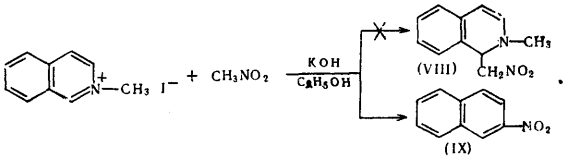


In the absence of the p-nitro-group in the phenyl ring, only benzaldehyde is formed[72], i.e. only *O*-alkylation takes place.

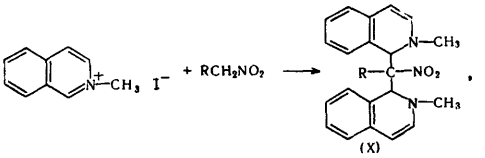
¶ A recent communication[66] described the conversion of the potassium salt of β-bromoethyl dinitroacetate, on boiling in acetone, into αα-dinitro-γ-butyrolacetone, i.e. intramolecular *C*-alkylation with formation of a five-membered ring takes place.

† The assertion by Dornow and Thies[70] that alkylation does occur in this case proved to be incorrect; in fact only the salt of one of the initial reaction components is formed[69].

The reaction of nitroalkanes with quaternary quinolinium and isoquinolinium salts is unusual. When nitromethane reacts with the methiodide of isoquinoline, 2-nitronaphthalene (IX) is obtained instead of the expected product (VIII):[73]

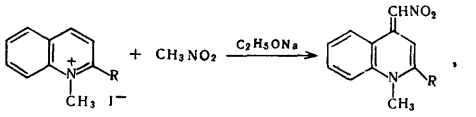


Under similar conditions nitroethane and 1-nitropropane give only bis-[1-(2'-methyl-1',2'-dihydroisoquinolyl)]-nitroalkanes (X):[73]



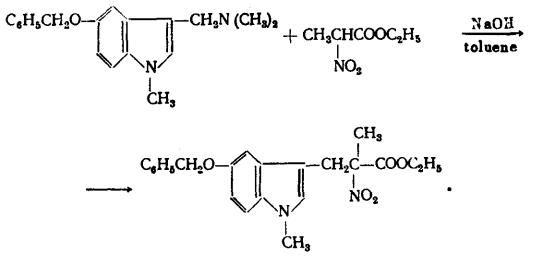
where R = CH_3 and C_2H_5. In addition to compound (IX), nitromethane also gives a small compount of compound (X) (R = H).[73]

The reaction of nitromethane with quinolinium or 2-methylquinolinium methiodide takes place in a different manner — with formation of 1-methyl-4-nitromethylene-quinolanes:

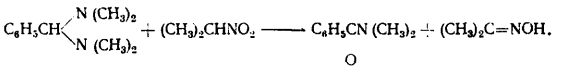


where R = H and CH_3. The reaction does not occur when a substituent is present in position 4 of the quinoline ring[74].

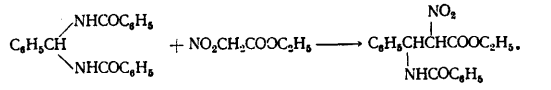
Only one example of the alkylation of nitro-compounds with a tertiary Mannich base (incapable of being deaminated), of the *N*-methylgramine series, is known. When 5-benzyloxy-1-methylgramine reacts with nitropropionic ester in the presence of sodium hydroxide, the desired alkylation product is formed in 14% yield[75]:



In this section it is also appropriate to mention the alkylation of mononitro-compounds with *N*-substituted benzylidenebisamines. Thus *NN'*-benzylidenebisdimethylamine reacts with 2-nitropropane to give a mixture of benzoic acid dimethylamide and acetone oxime[3]:

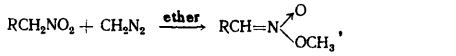


The author explains this reaction by the decomposition of the nitronic ester formed as an intermediate as a result of *O*-alkylation. Similar results were also obtained with benzylidenebispiperidine[3]. On the other hand, the reaction of nitroacetic ester with *NN'*-benzylidenebisbenzamide results only in *C*-alkylation with formation of ethyl β-phenyl-β-benzamido-α-nitropropionate[76]:



3. Alkylation with Other Alkylating Agents

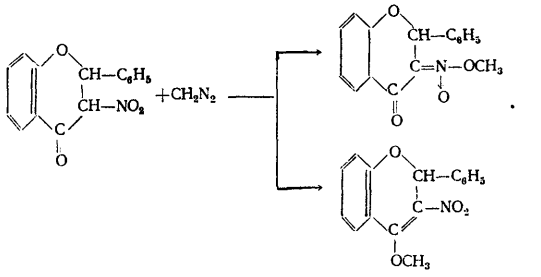
Apart from the alkylating agents enumerated above, a number of others are used in reactions with mononitro-compounds (diazomethane, dimethyl sulphate, olefin oxides, and others). With a few exceptions, the alkylation always involves the formation of nitronic esters or products of their further reaction. Thus a number of workers have shown[77,78,80,81] that diazomethane can be successfully used for the *O*-alkylation of nitro-compounds. Arndt and Rose[77], who studied the behaviour of nitro-compounds of different types in the reaction with diazomethane, concluded that the more acidic is the nitro-compound the more readily it is alkylated by diazomethane:



where R = C_6H_5, *p*-BrC_6H_4, C_6H_5CO, C_2H_5OCO, *p*-$CH_3C_6H_4SO_2$, etc.

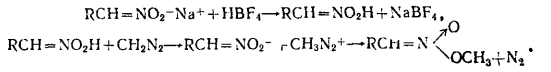
While phenylnitromethane reacts with diazomethane over a period of three days, the reaction with nitroacetic ester is completed in 2 h and that with nitromalonic ester is practically instantaneous. The reaction of diazomethane with *aci*-nitro-compounds is even faster than with true nitro-compounds[77].

It has recently been shown that the cyclic α-nitro-ketone 3-nitroflavanone is readily alkylated by diazomethane[78], yielding a mixture of two products — a nitronic ester and the ester of the enol form of the initial ketone:

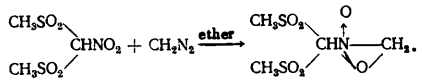


It is noteworthy that the nitro-compounds which are relatively weak acids (for example, nitromethane[79] and 1-phenyl-3-nitropropane[80]) do not enter into this reaction‡.

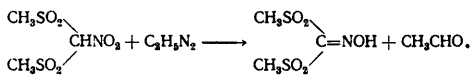
‡ The difficulty of alkylating compounds of this kind, which is probably due to the low rate of proton transfer from the nitro-compound to diazomethane, can be overcome by treating a salt of the nitro-compound with diazomethane, with subsequent addition of tetrafluoroboric acid, the mechanicsm being as follows[80].



The reaction of diazomethane with bis(methylsulphonyl)-nitromethane also results in *O*-alkylation with formation (in quantitative yield) of a nitronic ester which, according to the author, is the *N*-oxide of *N*-[bis(methylsulphonyl)-methyl]epoxymethyleneimine [81]:

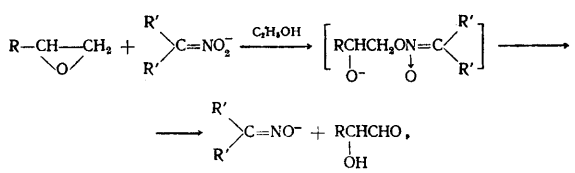


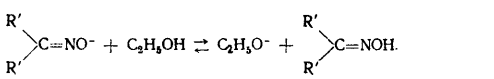
After the reaction of bis(methylsulphonyl)nitromethane with diazoethane, the same investigator [81] was able to isolate only the decomposition products of the *O*-nitronic ester — bis(methylsulphonyl)isonitrosomethane and acetaldehyde:

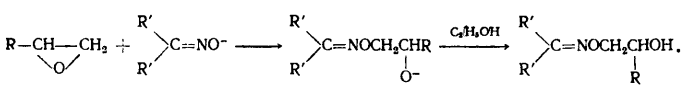


A nitronic ester is also formed when phenylnitromethane (in the form of the sodium salt) is alkylated with dimethyl sulphate [77,82]. The reaction of dimethyl sulphate with the potassium salt of 9-nitrofluorene is similar [83]: it yields a nitronic ester which decomposes to fluorenone oxime and formaldehyde on raising the temperature.

Bachman and Hokama [84] introduced into the reaction with nitroalkanes various olefin oxides (ethylene, propene, and styrene oxides) in an alkaline medium (in the presence of lithium alkoxide) and obtained only the oximes and the oxime ethers whose formation they regard as due to *O*-alkylation followed by decomposition of the reaction products into the carbonyl compounds and the oxime:

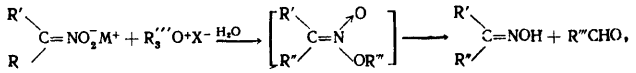




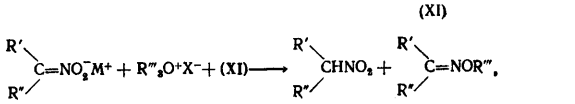


In another study on the alkylation of nitro-compounds by olefin oxides [85] the latter were introduced into the reaction with various mononitroalkanes in pyridine solution. The reactions are very complex, the corresponding γ-nitro--alcohols (*C*-alkylation products) either not forming at all or their yield not exceeding several per cent. The main products are 1-(2′-hydroxyalkyl)pyridinium nitrites and 3,4,5-trimethoxyisoxazole from primary nitroalkanes, while secondary nitroalkanes give in addition vicinal dinitroalkanes, ketones, and ketone oximes.

The reaction of the salts of mononitro-compounds with rather unusual alkylating agents such as trialkyloxonium salts has been investigated in fair detail. Thus Donaruma [86] allowed salts of nitrocyclohexane, nitrocyclopentane, and 2-nitropropane to react with trialkyloxonium fluoroborates, chloroferrates, and chloroaluminates, and in all cases observed the formation of *O*-alkylation products — oximes (XI) and the *O*-alkylated oximes (XII) (ethers):



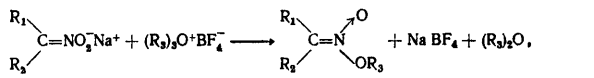
(XI)



(XII)

where R′ and R″ = $-(CH_2)_4-$, $-(CH_2)_5-$, and CH_3, R‴ = = CH_3 and C_2H_5, X = BF_4, $FeCl_4$, and $AlCl_4$, and M = Na and K. The best yields of oximes (50–80%) and their ethers (20–35%) are obtained when trialkyloxonium fluoroborates are used, particularly when R‴ = C_2H_5; triethyloxonium chloroferrate and chloroaluminate react to a much smaller extent, due to side-processes (in particular due to the formation of sparingly soluble iron and aluminium salts of the nitroalkanes by double decomposition with ferric chloride and aluminium chloride, the salts being precipitated during the alkylation).

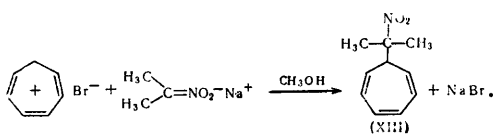
Quite recently Kornblum and Brown [80,87] used the reaction with trimethyl- and triethyl-oxonium fluoroborates to prepare nitronic esters from many aliphatic and aliphatic–aromatic mononitro-compounds:



where R_1 = CH_3, n-C_3H_7, *p*-BrC_6H_4, and *p*-$NO_2C_6H_4$, R_2 = = H and CH_3, and R_3 = CH_3 and C_2H_5. The reaction was carried out in methylene chloride at 0°, the yield of the esters being very high (80–95%). It is noteworthy that the nitronic esters from purely aliphatic nitro-compounds had not been isolated before this study.

There are patent data on the alkylation of salts of primary or secondary aliphatic and alicyclic nitro-compounds with alcohols and phenols in neutral or acid media [88], the reaction resulting in *O*-alkylation with formation of oximes. The reaction can also be carried out in the presence of ammonia, amines, or ammonium salts.

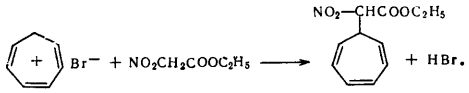
Interesting results were obtained in the alkylation of nitro-compounds with tropylium bromide. Thus by allowing tropylium bromide to react with the sodium salt of 2-nitropropane, Bersohn [23] obtained a high yield (68%) of the *C*-alkylation product — 1-(dimethylnitromethyl)cyclohepta--2,4,6-triene (XIII):



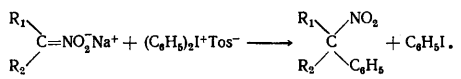
(XIII)

He believes [23] that initially the *O*-alkylation product forms and then readily dissociates into the initial ions with subsequent formation of the thermodynamically stable *C*-alkylation product. This process is much faster than the usual breakdown of nitronic esters into the oxime and the carbonyl compound and therefore the *C*-alkylation derivative gradually accumulates: *O*-alkylation products were not detected in this reaction.

The alkylation of nitroacetic ester with tropylium bromide takes place in exactly the same way, the only product being ethyl cycloheptatrienylnitroacetate[89]:

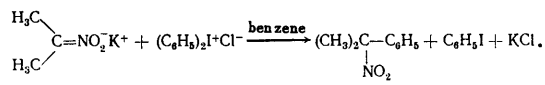


Yet another case of *C*-alkylation (more precisely arylation) of nitro-compounds was described recently by Kornblum and Taylor[90]: by allowing salts of primary and secondary nitroalkanes to react with diphenyliodonium toluenesulphonate in dimethylformamide, they obtained a good yield (55–70%) of the corresponding phenylnitroalkanes:



where $R_1 = CH_3$, n-C_3H_7, and n-C_7H_{15}, R_2 = H and CH_3, and R_1–R_2 = –$(CH_2)_5$–.

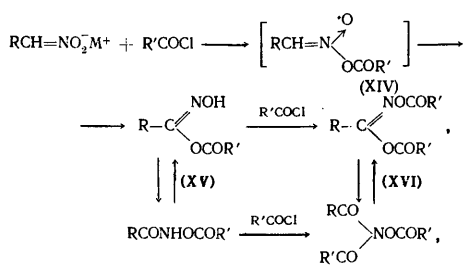
It proved impossible to make the potassium salt of phenylnitromethane undergo a similar reaction[91]. Diphenyliodonium chloride can be used successfully instead of the toluenesulphonate; the potassium salt of 2-nitropropane is then converted into 2-phenyl-2-nitropropane in 63% yield[92]:



4. Acylation of Mononitro-Compounds

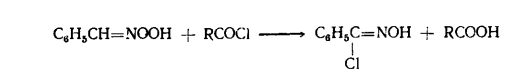
Much less attention has been given in the literature to the acylation of mononitro-compounds than to their alkylation. However, here too various acylating agents have been investigated — acyl halides, acid anhydrides, ketene, acyl cyanides, and others. In almost all cases *O*-acylation takes place exclusively with formation of nitronic acid anhydrides which then as a rule undergo further reactions.

The acylation of mononitro-compounds by acyl halides has been studied in greatest detail. Thus the reactions of salts of primary nitroalkanes with acetyl chloride and benzoyl chloride yield various acylhydroxamic acids, (XV) and (XVI), the products of the rearrangement of the anhydrides (XIV) and subsequent repeated acylation[93–95]:



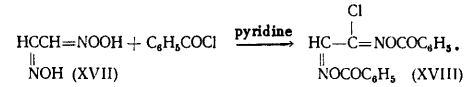
where R = H and CH_3 and R′ = CH_3 and C_6H_5.

Similar results were obtained in the acylation of the sodium salts of arylnitromethanes[83,96,97]. The acylation of *aci*-phenylnitromethane yields the chloride of benzohydroxamic acid[83]:

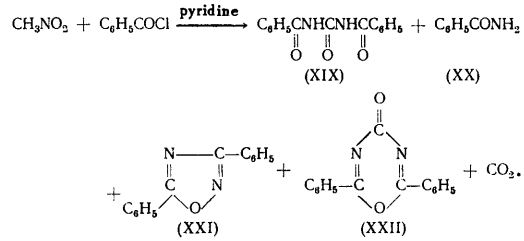


where R = CH_3 and C_6H_5. In many cases no products could be identified after the reaction of primary nitroalkanes with acyl halides[98–100].

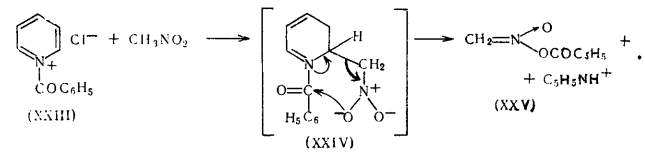
The acylation of primary mononitro-compounds by acid chlorides in pyridine solution is unusual. Thus in the reaction of phenylnitromethane and ω-nitroacetophenone with benzoyl chloride in pyridine the main product is in both cases dibenzohydroxamic acid ($C_6H_5CONHOCOC_6H_5$).[101] On the other hand, when *aci*-phenylnitromethane is used in a similar reaction, the product is the chloride of benzoylbenzohydroxamic acid ($C_6H_5CCl{=}NOCOC_6H_5$).[102] Under the same conditions methazonic acid (XVII) gives dibenzoylchloroglyoxime (XVIII):[102]



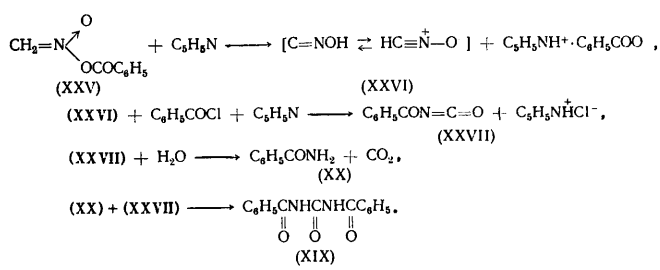
The reaction of benzoyl chloride with nitromethane in pyridine solution is much more complex[101]. It proceeds with evolution of carbon dioxide and the formation of *NN′*-dibenzoylurea (XIX) as the main product; in addition benzamide (XX), benzonitrile, 3,5-diphenyl-1,2,4-oxadiazole (XXI), and a substance with the empirical formula $C_{15}H_{10}N_2O_2$, possibly 2,6-diphenyl-4-oxo-1,3,5-oxadiazine (XXII), were isolated from the reaction mixture:



The authors of this investigation believe that in this case the acylating agent is benzoylpyridinium chloride (XXIII) which initially combines with nitromethane to give an intermediate (XXIV), and the latter then decomposes into the mixed anhydride (XXV):



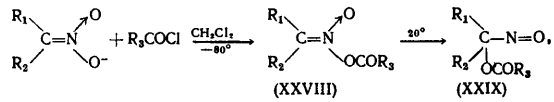
To account for the formation of *NN′*-dibenzoylurea (XIX), the authors proposed further the following mechanism:



The reasons for the formation of the other products are obscure. It is interesting that, on replacing pyridine by quinoline or dimethylaniline, not even traces of compound (XIX) are formed[101].

The acylation of secondary mononitro-compounds by acyl halides has been investigated in greatest detail by White and

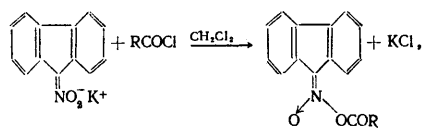
Considine [103,104]. They found that the initial products of the reactions of salts of secondary nitroalkanes with acid chlorides are the anhydrides (XXVIII), as in the case of other mononitro-compounds. On raising the temperature of the reaction mixture, a pale blue colour gradually appears, due to the extremely ready isomerisation of the nitronic anhydrides to nitrosoacyloxy-compounds (XXIX) [104] §:



(XXVIII) (XXIX)

where R_1 and R_2 = CH_3, C_6H_5, and $-(CH_2)_5-$ and R_3 = CH_3, C_6H_5, and p-$NO_2C_6H_4$. The authors were unable to obtain C-acylation products; judging from the infrared spectra, the latter are formed in amounts smaller than 1%.

In some cases on acylating secondary nitro-compounds with acyl halides it proved possible to isolate stable nitronic esters. Thus Nenitzescu and Isacescu [83] obtained O-acetyl and O-benzoyl-9-*aci*-nitrofluorenes (XXX) by allowing the potassium salt of 9-nitrofluorene to react with acetyl and benzoyl chlorides respectively:



(XXX)

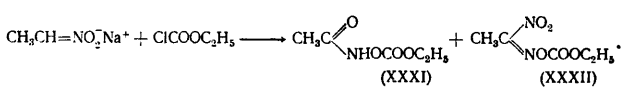
where R = CH_3 and C_6H_5. Subsequently White and Considine [103] confirmed the structure of compound (XXX) (R = = C_6H_5).

Another interesting case of the formation of a stable nitronic anhydride has been described by Thurston and Shriner [6]: when the sodium or silver salt of phenylnitroacetonitrile was treated with benzoyl chloride, O-benzoyl-*aci*-nitrophenylacetonitrile was obtained:



where M = Na and Ag. The authors demonstrated the structure of the product and thereby disproved the assertion of Wieland and Höchtlen [17] that they isolated the C-benzoyl derivative in a similar reaction with benzoyl bromide¶. According to Foster's data [107], the reaction of 1-nitrobornane with benzoyl chloride also yields a stable nitronic anhydride, but the product was not characterised.

The use of the ethyl ester chlorocarbonic acid as the acylating agent has been as a rule unsuccessful — no products have been identified [98,100]. In only one case, in the acylation of the sodium salt of nitroethane, Nef [94] and then Jones [95] succeeded in isolating ethoxycarbonylacetohydroxamic (XXXI) and ethoxycarbonylethylnitrolic (XXXII) acids:

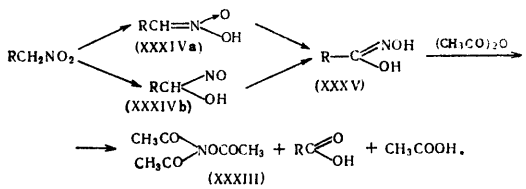


(XXXI) (XXXII)

§ In another study it was shown that, in the reaction between the sodium salt of 2-nitropropane and benzoyl chloride in ether (in the form of suspension), only benzoic acid is formed even under anhydrous conditions [105].

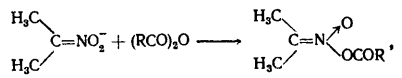
¶ White and Considine [104] showed that, contrary to the data of Wislicenus and Pfeilsticker [106], the formation of the C-acylation product, 1-benzoyl-3-nitroindene, in the reaction of the potassium salt of 3-nitroindene with benzoyl chloride is also unlikely.

Several papers describe the acylation of mononitro-compounds by acid anhydrides. On heating mononitroalkanes (nitromethane, nitroethane, 1-nitropropane, and phenylnitromethane) with acetic anhydride in the presence of sodium acetate or pyridine, Urbański [108] obtained in all cases only triacetylhydroxylamine (XXXIII). He believes that initially the nitro-compounds isomerise to the *aci*-form (XXXIVa) or nitrosohydroxy-compounds (XXXIVb) and then to hydroxamic acids (XXXV); the latter then undergo cleavage and acetolysis with formation of compound (XXXIII) and carboxylic acids:



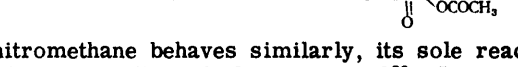
(XXXIVa) (XXXIVb) (XXXV) (XXXIII)

Quite different results were obtained in the reaction of acid anhydrides with secondary nitroalkanes. Thus acetic and propionic anhydrides react with 2-nitropropane (in toluene in the presence of potassium acetate) or its sodium salt (in ethereal suspension) to give relatively stable nitronic anhydrides [105] †:

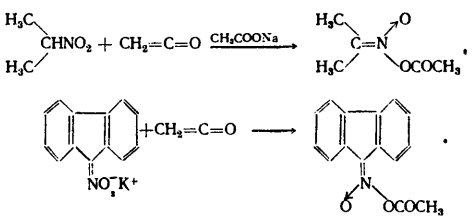


where R = CH_3 and C_2H_5. Unlike acetic or propionic anhydride, benzoic anhydride is completely inert under analogous conditions [105].

When keten is used as the acylating agent, the nature of the reaction products also depends on whether the initial nitro-compound is primary or secondary. Thus 1-nitropropane reacts with keten to form *NN*-diacetylpropiohydroxamic acid [109]:



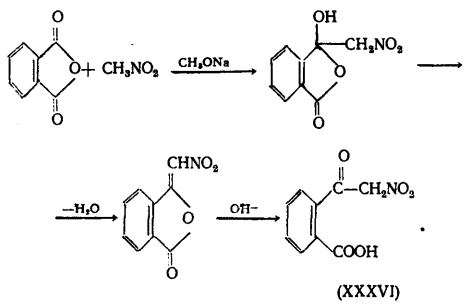
Phenylnitromethane behaves similarly, its sole reaction product being acetylbenzohydroxamic acid [83]. In contrast to the primary nitro-compounds, the secondary compounds yield nitronic anhydrides on reacting with keten [83,109]:



Thus in all the cases enumerated above O-acylation occurred. Only a few examples of acylation at the carbon atom with formation of α-nitroketones are described in the literature. In the study of the reaction of nitromethane with phthalic anhydride in the presence of sodium methoxide, Gabriel [110] obtained a very low yield of 2-nitroacetylbenzoic acid (XXXVI). He believes that the first stage of the process involves the addition of nitromethane

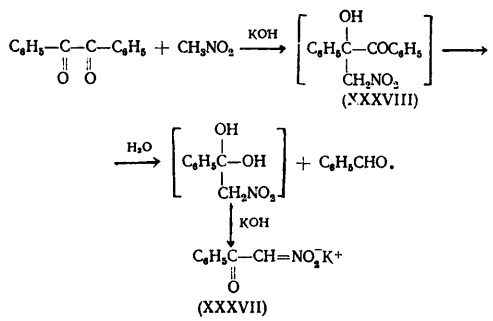
† This was subsequently confirmed by Urbański and Gurzyńska [109].

to the carbonyl double bond of the anhydride with subsequent elimination of a water molecule and hydrolysis:



(XXXVI)

In another study Yakubovich [111] treated nitromethane with benzil in the presence of twice the required amount of potassium hydroxide and obtained the potassium salt of ω-nitroacetophenone (XXXVII) and a whole series of other products. In his view, initially nitromethane adds to one of the carbonyls and then the addition product (XXXVIII) is cleaved to (XXXVII):



(XXXVII)

Nevertheless, it proved impossible to isolate compound (XXXVIII) as an intermediate; on the other hand, in the reaction between nitromethane and diacetyl an addition product of this type is formed smoothly.

In 1959 Bachman and Hokama [112,113] developed a general method for the synthesis of α-nitroketones by the *C*-acylation of primary nitroalkanes. They showed that *C*-acylation products will form only when rather unusual acylating agents, such as acyl cyanides, are employed:

$$RCH{=}NO_2^-M^+ + R'COCN \longrightarrow R'COCHR + MCN,$$
$$\qquad\qquad\qquad\qquad\qquad\quad NO_2$$

where R = H, CH_3, and n-C_3H_7, R′ = CH_3 and C_6H_5, and M = Na and Li. The yields are 30–70%. When secondary nitroalkanes and used, α-nitroketones do not form. The lithium salts of nitroalkanes give better results than the sodium salts. t-Butyl alcohol, pyridine, and tetrahydrofuran are used as solvents. *O*-acylation products were never observed.

The authors offer the following explanation for this sharp difference in the behaviour (with respect to the salts of nitro-compounds) of acyl halides and acid anhydrides, on the one hand, and acyl cyanides, on the other. In the first case the reactions are so fast that thermodynamic equilibrium is not attained and *O*-acylation takes place, since the transition state then has a lower energy of formation than in *C*-acylation (by virtue of the higher electronegativity of oxygen compared with carbon). The reaction with acyl cyanides is much slower, equilibrium is attained, and the thermodynamic stability of the final products begins to play a decisive role; the latter is known to be always higher in the case of *C*-acyl derivatives [114].

III. ALKYLATION AND ACYLATION OF POLYNITRO--COMPOUNDS

In contrast to mononitro-compounds, whose alkylation has been the subject of a fairly large number of studies, the number of known examples of the alkylation of polynitro--compounds is much smaller. Thus in 1899 Hantzsch and Rinckenberger [115] obtained 1,1,1-trinitroethane by allowing the silver salt of nitroform to react with methyl iodide in ether:

$$C(NO_2)_3^-Ag^+ + CH_3I \longrightarrow CH_3C(NO_2)_3 + AgI.$$

The authors note that the potassium salt of nitroform does not enter into a similar reaction‡. They also state [115] that the reaction of the silver salt of nitroform with iodine cyanide gives trinitroacetonitrile:

$$C(NO_2)_3^-Ag^+ + ICN \longrightarrow (NO_2)_3C{-}CN + AgI.$$

Somewhat later Hantzsch and Caldwell [117] established that, when the silver salt of nitroform is allowed to react with methyl iodide at -75°, the initial step is the formation of the addition product $C(NO_2)_3Ag.2CH_3I$, which on raising the temperature is converted into trinitroethane in non--polar solvents. In the presence of hydroxyl-containing solvents (for example alcohols) this complex yields only the free nitroform. On the other hand, the reaction of the silver salt of nitroform with methyl iodide in aqueous, alcoholic, or ethereal solution gives only trinitroethane and traces of nitroform. The authors explain these results by postulating that in solution the silver salt reacts in the ionic form yielding the more stable *C*-alkylation product (trinitroethane); on the other hand, its addition product with methyl iodide reacts intramolecularly, forming the methyl ester $(NO_2)_2C{=}NO{-}OCH_3$. The latter, being unstable in a non-polar medium, isomerises to trinitroethane and in the presence of water hydrolyses to nitroform [117,118].

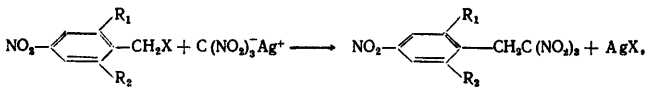
The same workers showed that the silver salt of nitroform reacts with ethyl iodide [117], benzyl iodide [115,117], allyl iodide [117], and bromoacetic ester [115], but no products were identified§. An attempt to make monochloromethyl ether [120] and triphenylchloromethane [17,120] react with the silver salt of nitroform was also unsuccessful, the reason being (according to the authors) that the water of crystallisation, which is always present in the molecule of the silver salt, hydrolyses the above halogeno-derivatives faster than they can react.

Meisenheimer and Schwarz [120] and Hantzsch [121] showed that bromonitroform and iodonitroform do not react with the silver salt of nitroform. In 1947 a paper was published, describing the alkylation of the silver salt of nitroform with various substituted benzyl halides [122] [*p*-nitrobenzyl bromide, 2,4,6-trinitrobenzyl iodide, *p*-di(iodomethyl)benzene, 1,3-di(iodomethyl)-5-nitrobenzene, and

‡ According to a recent communication [116], on carrying out the reaction in acetone, it proved possible to obtain 1,1,1-trinitroethane from the potassium salt of nitroform and methyl iodide (yield not indicated).

§ According to patent data [119], 4,4,4-trinitrobut-1-ene forms on reaction between the silver salt of nitroform and allyl bromide (in ether).

1,3,5-tri(iodomethyl)benzene], the products being the corresponding trinitroethyl derivatives of benzene, for example



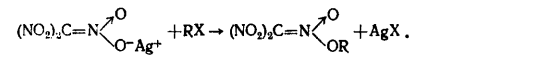
where R_1 and R_2 = H and NO_2 and X = Br and I. The reactions were carried out in ether. The authors noted that in all cases they also observed the formation of unstable coloured oils (probably *O*-alkylation products), which decomposed with evolution of nitrogen oxides.

In 1952 an American patent [123] described the preparation of 1,1,1,2- and 1,1,1,3-tetranitropropane by the reaction of the silver salt of nitroform (in boiling ether) with the corresponding halogenonitro-compounds — 1-bromo-1-nitro- and 1-bromo-2-nitro-ethane. However, the patent gives no experimental details and the yields of the products are not stated.

In 1963 Hammond et al. [124] described the alkylation of the silver salt of nitroform with various halogeno-derivatives. The reaction in acetonitrile solution was studied in greatest detail. The authors showed that primary straight-chain alkyl iodides and also allyl bromide and iodide give the corresponding *C*-alkylation products in yields of 30–60%:

$$C(NO_2)_3^-Ag^+ + RX \xrightarrow{CH_3CN} RC(NO_2)_3 + AgX,$$

where R = n-alkyl and $CH_2{=}CHCH_2$ and X = I and Br. Secondary and cyclic alkyl halides and propargyl bromide, 1,3-di-iodopropane, and 1,4-dibromobutyne yield a complex mixture of products which could not be identified¶; allyl chloride, 1-bromo-2,4-dinitrobenzene, and 1-iodo-2-nitrobenzene do not react at all. When α-halogeno-acids are used, the corresponding nitrates are formed instead of the expected products, as a result of the substitution of the halogen by the nitrate group. The authors explain the failure of the above syntheses by the *O*-alkylation of the silver salt of nitroform under these conditions with formation of unstable nitronic esters:



The latter decompose with liberation of nitrate ions. The authors believe that another possible pathway involving the formation of nitrates, the gradual decomposition of the silver salt of nitroform to yield nitrate ions, is unlikely.

They also showed [124] that in the reaction of the silver salt of nitroform with chloromethyl ether and bromomethyl acetate the only product is trinitroethanol whose formation can be explained by the condensation of nitroform with formaldehyde, produced by the decomposition of the initial α-halogeno-ethers. The reaction of t-butyl bromide gave only *N*-t-butylacetamide — the product of the reaction of the halide with the solvent (acetonitrile). Hammond et al. [124] showed that the use of other solvents in the alkylation of the silver salt of nitroform (methyl and ethyl acetate, methyl and ethyl formate, acetone, ethanol, benzene) does not increase the yield compared with that obtained in acetonitrile, but the reactions are much faster. In contrast to the system in acetonitrile, in methyl acetate they were able to achieve the reaction of the silver salt with epi-iodohydrin and β-methylallyl bromide, the products, 4,4,4-trinitro-1,2-epoxybutane and 2-methyl-4,4,4-trinitrobut-1-ene, being obtained in yields of 19 and 27% respectively [124].

The study of the kinetics of the reaction of the silver salt of nitroform with methyl iodide in acetonitrile at 25.5° showed that the reaction is of third order overall, i.e. the silver cation participates as an electrophilic catalyst forming an ion pair in the transition state [124]:

$$C(NO_2)_3^- + R{-}I + Ag^+ \rightarrow (NO_2)_3C^-R^+IAg.$$

Thus the reaction is simultaneously of both S_N1- and S_N2-type.

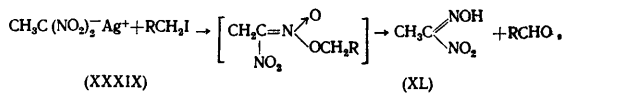
Recently Tartakovskii et al. [126] showed that, when nitroform is treated with diazomethane, *O*-alkylation occurs with the formation of an unstable, very reactive nitronic ester.

Only a few papers have been published on the alkylation of salts of 1,1-dinitroalkanes (mainly silver salts). Duden [127] showed in 1893 that the silver salt of dinitromethane reacts with methyl iodide and ethyl iodide (in the absence of solvent) with the formation of the expected 1,1-dinitroalkanes:

$$HC(NO_2)_2^-Ag^+ + RI \rightarrow RCH(NO_2)_2 + AgI,$$

where R = CH_3 and C_2H_5. The author notes that the reactions are far from smooth, the products containing a considerable amount of unstable oils, which decompose even on slight heating.

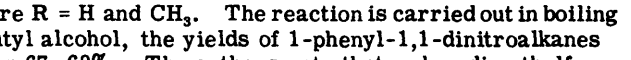
In 1894 Nef [100] found that, when the silver salt of 1,1-dinitroethane reacts with methyl and ethyl iodide, the expected 2,2-dinitropropane formed only in the first case and even then in a low yield. The main products of the reaction were ethylnitrolic acid and the corresponding aldehyde (formaldehyde or acetaldehyde) and also free 1,1-dinitroethane. The author explains the formation of these products by the preferential *O*-alkylation of the silver salt of dinitroethane, resulting in the nitronic ester (XXXIX) which is unstable to heat and decomposes to ethylnitrolic acid (XL) and an aldehyde:



(XXXIX) (XL)

where R = H and CH_3.

A quite recent publication described the phenylation, at the carbon atom, of the potassium salts of 1,1-dinitroethane and 1,1-dinitropropane with diphenyliodonium toluenesulphonate [91]:

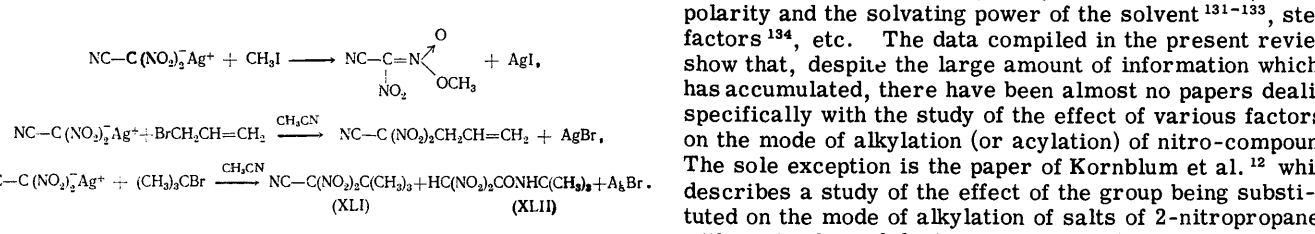


where R = H and CH_3. The reaction is carried out in boiling t-butyl alcohol, the yields of 1-phenyl-1,1-dinitroalkanes being 67–68%. The authors note that, when dimethylformamide is used as the reaction medium, the desired products are formed in yields less than 5%, the principal product being nitrobenzene. The attempt to use the potassium salt of phenyldinitromethane in a similar reaction was unsuccessful.

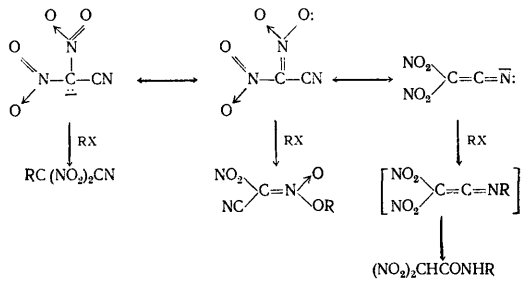
Unusual results were obtained in the alkylation of the silver salt of dinitroacetonitrile [124,128]. As a rule no identifiable products can be obtained in reactions of this kind. Only with methyl iodide, t-butyl bromide, and allyl bromide is the reaction relatively successful; with methyl iodide, only *O*-alkylation takes place (a stable methyl ether forms in 58% yield), the reaction with allyl bromide gives the *C*-alkylation product (yield 35%), while in the reaction

¶ According to patent data [125], 1,1,1,6,6,6-hexanitrohex-3-yne can be obtained by the reaction of the silver salt of nitroform with 1,4-dibromobut-2-yne in methyl acetate.

with t-butyl bromide a mixture of *C*- and *N*-alkylation products is formed [compounds (XLI) and (XLII) respectively, in yields of 17 and 18%]:



The authors' explanation of the results is that, being "polydentate" (i.e. having several reaction centres), the anion of dinitroacetonitrile can be alkylated in one of three ways, yielding *C*-, *O*-, or *N*-alkyl derivatives:



These results clearly contradict the generally accepted theory of Kornblum et al.[129] according to which the closer is the transition state in nucleophilic substitution reactions to a carbonium ion, the greater the probability of the formation of a bond with the most electronegative atom of the polydentate anion (in the anion of dinitroacetonitrile such atoms are the oxygen of the nitro-group and the nitrogen of the cyano-group). Allyl bromide and t-butyl bromide are known to form carbonium ions much more readily than methyl iodide (the fact that t-butyl bromide reacts with the silver salt of dinitroacetonitrile as a carbonium ion is demonstrated by the formation of the same products in the analogous reaction of t-butyl alcohol[128]). Nevertheless, *C*-alkylation takes place with allyl and t-butyl bromides. The authors explain this as follows: the transition state in these reactions, involving the participation of large planar ions, is sterically facilitated and therefore when two ions approach one another there is a greater probability of the formation of a bond with the geometric centre of the charge density of the dinitroacetonitrile anion (i.e. with the carbon atom) than with an individual electronegative atom (oxygen or nitrogen)[124,128].

There are no publications dealing with the acylation of polynitro-compounds, only isolated, negative data being available. Thus Hantzsch and Rinckenberger[115] noted that it is impossible to achieve the reaction of the silver salt of nitroform with chlorocarbonic ester. The use of acyl halides as acylating agents in reactions with the silver salt of nitroform (in acetonitrile) only results in the formation of the corresponding carboxylic acids[124].

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The data presented in this review show that alkylation and acylation reactions are typical and perhaps the most distinctive examples of the dual reactivity of nitro-compounds. The mode of alkylation (or acylation) of ambidentate anions (i.e. anions with two reaction centres), to which the anions of nitro-compounds belong, is known to be influenced by a number of factors: the nature of the cation[129], the heterogeneity or homogeneity of the medium[130], the polarity and the solvating power of the solvent[131-133], steric factors[134], etc. The data compiled in the present review show that, despite the large amount of information which has accumulated, there have been almost no papers dealing specifically with the study of the effect of various factors on the mode of alkylation (or acylation) of nitro-compounds. The sole exception is the paper of Kornblum et al.[12] which describes a study of the effect of the group being substituted on the mode of alkylation of salts of 2-nitropropane with *p*-nitrobenzyl derivatives. For this reason, systematic studies in this field are necessary to elucidate the influence of the structure and reaction conditions on the mode of alkylation of nitro-compounds.

On the basis of the available data, it is so far possible to arrive at only one conclusion, namely that, despite the wide variety of reaction conditions used, the main mode of reaction is alkylation (or acylation) of the oxygen of the nitro-group. *C*-Alkylation occurs only with a few alkylating agents (for example, in alkylation with *p*-nitrobenzyl chloride, see p. 719). It appears that the mode of reaction is not influenced significantly either by the nature of the cation or the nature of the reaction medium, i.e. factors which have a very important role in reactions of other ambidentate anions. Probably the mode of alkylation is greatly influenced by the structure of the nitro-compound itself. Thus salts of phenylnitroacetonitrile are always acylated at the oxygen only, even with *p*-nitrobenzyl chloride[4], which as a rule alkylates mononitro-compounds at the carbon atom.

After the manuscript had been sent to the editors, a number of papers with a direct bearing on the present topic have been published and we decided it was necessary to consider them if only briefly.

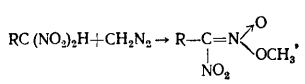
1. Mononitro-compounds. The work of Teuber and Glosauer[135], who succeeded in obtaining the corresponding *C*-alkylation products by treating the sodium salts of 2-nitropropane and nitrocyclohexane with *o*-nitrobenzyl chloride, is noteworthy. There has also been an interesting communication[136] according to which the reaction of triphenylchloromethane with the sodium salt of nitrocamphor gives a stable nitronic ester (in 44% yield) — an *O*-alkylation product. In another study[137] the intermediate stages of the reaction of triphenylchloromethane with the silver salt of phenylnitroacetonitrile were investigated (c.f. Ref. 19).

Polyanskaya et al.[138] state that in the reaction of nitroacetic ester with alkyl halides in the presence of amines (for example triethylamine), esters of α-nitroalkanecarboxylic acids are formed, i.e. alkylation at the carbon atom takes place. A few more examples of *C*-alkylation of 2-nitropropane (in the form of the sodium salt) with β-chlorovinyl ketones have been described by Belyaev and Shamanovskaya[139].

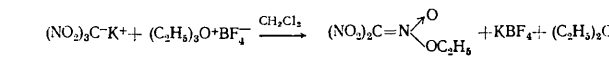
Two papers describe interesting cases of intramolecular *C*-alkylation of mononitro-compounds. Thus on treatment of 1-iodo-3-nitropropane with lithium amide in liquid ammonia, nitrocyclopropane forms in high yield (87%).[140] Etheredge[141] found that a bridge nitro-compound, 1-nitrobicyclo[3,2,1]octane, forms in 19% yield in the reaction of 2-(3-nitrocyclohexyl)ethyl toluenesulphonate with sodium hydride in dimethylformamide.

2. Polynitro-compounds. Here mention must be made in the first place of the work of Tartakovskii and

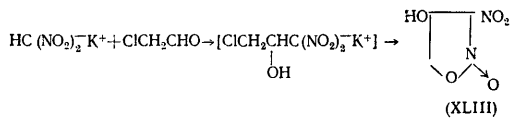
coworkers on the preparation of *O*-methyl derivatives of dinitromethane [142] and nitroform [143] (see also Ref. 126) by the action of diazomethane in benzene on dinitromethane and nitroform respectively:



where R = H and NO_2. The same workers obtained [143] the *O*-ethyl derivative of nitroform by alkylating the potassium salt of nitroform with triethyloxonium fluoroborate:

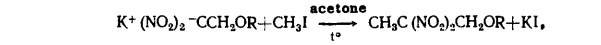


In another paper [144] they describe the synthesis of a cyclic nitronic ester (XLIII) by the intramolecular *O*-alkylation of the potassium salt of 1-chloro-3,3-dinitro-2-propanol — an intermediate in the reaction between the potassium salt of dinitromethane and chloroacetaldehyde:



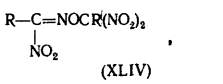
(XLIII)

Recently Ungnade and Kissinger [145] described two examples of *C*-alkylation (in yields of 80–90%) of salts of 2,2-dinitroethyl alkyl ethers with methyl iodide:



where R = CH_3 and $ClCH_2CH$.

Ustynyuk et al.[146] studied the action of various acylating agents (acid chlorides and anhydrides and acetyl nitrate) on salts of 1,1-dinitroethane and 1,1-dinitropropane and established that in all cases the reactions result in the formation of self-condensation products of the initial dinitroalkanes (XLIV) (in yields of 30–50%):



(XLIV)

where R = CH_3 and C_2H_5. The structure of compound (XLIV) was confirmed by spectroscopic methods [147].

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